STUDY GUIDE & SOLUTIONS MANUAL

Organic Chemistry

FOURTH EDITION



Paula Yurkanis Bruice

to my students

TABLE OF CONTENTS

CHAPTER 1	Electronic Structure and Bonding • Acids and Bases	
	Important Terms	1
	Solutions to Problems	5
	Practice Test	32
SPECIAL TOPIC I	pH, pK_a, and Buffers	34
	Problems	47
	Solution to Problems	49
CHAPTER 2	An Introduction to Organic Compounds: Nomenclature, Physical Properties, and Representation of Structure	
	Important Terms	58
	Solutions to Problems	62
	Practice Test	82
CHAPTER 3	Alkenes: Structure, Nomenclature, and an Introduction to Reactivity • Thermodynamics and Kinetics	
	Important Terms	84
	Solutions to Problems	87
	Practice Test	99
SPECIAL TOPIC II	Exercise in Drawing Curved Arrows	104
	Problems	106
	Answers	115
SPECIAL TOPIC III	Kinetics	122
	Problems	122
	Solutions to Problems	123
CHAPTER 4	Reactions of Alkenes	
	Important Terms	124
	Solutions to Problems	127
	Practice Test	149
SPECIAL TOPIC IV	Exercise in Model Building	151
CHAPTER 5	Stereochemistry: The Arrangement of Atoms in Space. The Stereochemistry of Addition Reactions	
	Important Terms	152
	Solutions to Problems	158
	Practice Test	192

TO THE STUDENT

As you study organic chemistry, make certain you fully understand each new fact that you encounter. While studying the material, you should be continuously asking yourself "why?": Why does that reaction occur? Why is that product formed? Why is that compound more stable? If you truly understand each new piece of information, you will be creating a foundation upon which to lay subsequent information. A strong foundation will allow you to master a great deal of material with much less effort than you would have to put out if you were memorizing your way through the material.

Often it is the new vocabulary that you encounter when you are first exposed to a discipline that can be the biggest hurdle to mastering the material. For that reason I have included a list of the important terms and their definitions at the beginning of each chapter in the Study Guide. Reading these is a good way to review some of the important aspects of the chapter.

There are two kinds of problems in the textbook. The problems at the end of each section within a chapter are designed to let you see if you have understood the material presented in that section, and to reinforce the material. You should do these problems as you encounter them. The problems at the end of each chapter integrate the concepts in the chapter and sometimes include concepts that were mastered in previous chapters. Try to do as many of these as possible. The more problems you do, the more comfortable you will become with organic chemistry, and the more you will enjoy it.

Organic chemists use curved arrows to show the bonds that break and the bonds that form in an organic reaction. When you start studying organic reactions in Chapter 3, take time to do the exercise on drawing curved arrows that you will find on page 101. There is also an exercise in model building (page 151) that will help you with the material in Chapter 5.

Good luck in your study. If you have any comments or suggestions about how the Study Guide could be improved for those students who will follow you, I would be very happy to hear from you.

Paula Yurkanis Bruice
Department of Chemistry and Biochemistry
University of California, Santa Barbara
Santa Barbara, CA 93106
pybruice@chem.ucsb.edu

CHAPTER 6	Reactions of Alkynes • Introduction to Multistep Synthesis	
	Important Terms	194
	Solutions to Problems	196
	Practice Test	211
CHAPTER 7	Electron Delocalization, Resonance, and Aromaticity • More About Molecular Orbital Theory	
	Important Terms	213
	Solutions to Problems	215
	Practice Test	234
CHAPTER 8	Reactions of Dienes • Ultraviolet/Visible Spectroscopy	
	Important Terms	237
	Solutions to Problems	240
	Practice Test	262
CHAPTER 9	Reactions of Alkanes • Radicals	
	Important Terms	265
	Solutions to Problems	266
	Practice Test	278
CHAPTER 10	Substitution Reactions of Alkyl Halides	
	Important Terms	280
	Solutions to Problems	282
	Practice Test	300
CHAPTER 11	Elimination Reactions of Alkyl Halides • Competition Between Substitution and Elimination	
	Important Terms	302
	Solutions to Problems	303
	Practice Test	330
CHAPTER 12	Reactions of Alcohols, Ethers, Epoxides, and Sulfur-Containing Compounds • Organometallic Compounds	
	Important Terms	332
	Solutions to Problems	334
	Practice Test	367
CHAPTER 13	Mass Spectrometry and Infrared Spectroscopy	
	Important Terms	369
	Solutions to Problems	371
	Practice Test	392
CHAPTER 14	NMR Spectroscopy	
	Important Terms	394
	Solutions to Problems	397
	Practice Test	420

CHAPTER 15 Aromaticity • Reactions of Benzene
Important Terms 422
Solutions to Problems 424
Practice Test 437

CHAPTER 16 Reactions of Substituted Benzenes
Important Terms 439
Solutions to Problems 441
Practice Test 477

CHAPTER 17 Carbonyl Compounds I: Nucleophilic Acyl Substitution
Important Terms 479
Solutions to Problems 482
Practice Test 514

CHAPTER 18 Carbonyl Compounds II: Nucleophilic Acyl Addition, Nucleophilic Acyl Substitution, and Nucleophilic Addition-Elimination • Reactions of α,β-Unsaturated Compounds
Important Terms 516
Solutions to Problems 519
Practice Test 552

CHAPTER 19 Carbonyl Compounds III: Reactions at the α-Carbon
Important Terms 554
Solutions to Problems 556
Practice Test 596

CHAPTER 20 More About Oxidation-Reduction Reactions
Important Terms 598
Solutions to Problems 600
Practice Test 626

CHAPTER 21 More About Amines • Heterocyclic Compounds
Important Terms 628
Solutions to Problems 630
Practice Test 657

CHAPTER 22 Carbohydrates
Important Terms 659
Solutions to Problems 662
Practice Test 678

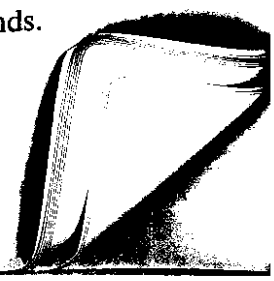
CHAPTER 23 Amino Acids, Peptides, and Proteins
Important Terms 680
Solutions to Problems 683
Practice Test 703

CHAPTER 24	Catalysis	
	Important Terms	705
	Solutions to Problems	707
CHAPTER 25	The Organic Mechanisms of the Coenzymes	
	Important Terms	726
	Solutions to Problems	728
CHAPTER 26	Lipids	
	Important Terms	744
	Solutions to Problems	747
CHAPTER 27	Nucleosides, Nucleotides, and Nucleic Acids	
	Important Terms	764
	Solutions to Problems	767
CHAPTER 28	Synthetic Polymers	
	Important Terms	782
	Solutions to Problems	785
CHAPTER 29	Pericyclic Reactions	
	Important Terms	804
	Solutions to Problems	806
CHAPTER 30	The Organic Chemistry of Drugs: Discovery and Design	
	Important Terms	824
	Solutions to Problems	826
Answers to Practice Tests		832

CHAPTER 1
Electronic Structure and Bonding • Acids and Bases

Important Terms

acid	a substance that donates a proton.
acid-base reaction	a reaction in which an acid donates a proton to a base.
acid dissociation constant	a measure of the degree to which an acid dissociates.
acidity	a measure of how easily a compound gives up a proton.
antibonding molecular orbital	a molecular orbital that results when two atomic orbitals with opposite signs interact. Electrons in an antibonding orbital decrease bond strength.
atomic number	tells how many protons (or electrons) the neutral atom has.
atomic orbital	an orbital associated with an atom.
atomic weight	the average mass of the atoms in the naturally occurring element.
aufbau principle	states that an electron will always go into the available orbital with the lowest energy.
base	a substance that accepts a proton.
basicity	describes the tendency of a compound to share its electrons with a proton.
bond dissociation energy	the amount of energy required to break a bond homolytically (each of the atoms retains one of the bonding electrons) or the amount of energy released when a bond is formed.
bonding molecular orbital	a molecular orbital that results when two atomic orbitals with the same sign interact. Electrons in a bonding orbital increase bond strength.
bond length	the internuclear distance between two atoms at minimum energy (maximum stability).
Brønsted acid	a substance that donates a proton.
Brønsted base	a substance that accepts a proton.
buffer solution	solution of a weak acid and its conjugate base.
carbanion	a compound containing a negatively charged carbon.
carbocation	a compound containing a positively charged carbon.
condensed structure	a structure that does not show some (or all) of the covalent bonds.
conjugate acid	the compound formed when a base accepts a proton.
conjugate base	the compound formed when an acid loses a proton.



core electrons	electrons in filled shells.
covalent bond	a bond created as a result of sharing electrons.
degenerate orbitals	orbitals that have the same energy.
delocalized electrons	electrons that do not belong to a single atom nor are they shared in a bond between two atoms.
dipole	a positive end and a negative end.
dipole moment (μ)	a measure of the separation of charge in a bond or in a molecule.
double bond	composed of a sigma bond and a pi bond.
electron affinity	the energy given off when an atom acquires an electron.
electronegative	describes an element that readily acquires an electron.
electronegativity	the tendency of an atom to pull electrons toward itself.
electropositive	describes an element that readily loses an electron.
electrostatic attraction	an attractive force between opposite charges.
electrostatic potential map	a map that allows you to see how electrons are distributed in a molecule.
equilibrium constant	the ratio of products to reactants at equilibrium (or the ratio of the rate constants for the forward and reverse reactions).
excited-state electronic configuration	the electronic configuration that results when an electron in the ground state has been moved to a higher energy orbital.
formal charge	the number of valence electrons − (the number of nonbonding electrons + 1/2 the number of bonding electrons).
free radical (radical)	a species with an unpaired electron.
ground-state electronic configuration	a description of which orbitals the electrons of an atom occupy when they are all in their lowest energy orbitals.
Heisenberg uncertainty principle	states that both the precise location and the momentum of an atomic particle cannot be simultaneously determined.
Henderson-Hasselbalch equation	$pK_a = pH + \log[HA]/[A^-]$
Hund's rule	states that when there are degenerate orbitals, an electron will occupy an empty orbital before it will pair up with another electron.
hybrid orbital	an orbital formed by hybridizing (mixing) atomic orbitals.
hydride ion	a negatively charged hydrogen.

hydrogen ion (proton)	a positively charged hydrogen.
inductive electron withdrawal	the pull of electrons through sigma bonds by an atom or a group of atoms.
ionic bond	a bond formed through the attraction of two ions of opposite charges.
ionic compound	a compound composed of a positive ion and negative ion.
ionization energy	the energy required to remove an electron from an atom.
isotopes	atoms with the same number of protons but a different number of neutrons.
Kekulé structure	a model that represents the bonds between atoms as lines.
Lewis acid	a substance that accepts an electron pair.
Lewis base	a substance that donates an electron pair.
Lewis structure	a model that represents the bonds between atoms as lines or dots and the nonbonding electrons as dots.
lone-pair electrons	valence electrons not used in bonding.
mass number	the number of protons plus the number of neutrons in an atom.
molecular orbital	an orbital associated with a molecule.
molecular orbital (MO) theory	describes a model in which the electrons occupy orbitals as they do in atoms but the orbitals extend over the entire molecule.
node	a region within an orbital where there is zero probability of finding an electron.
nonbonding electrons	valence electrons not used in bonding.
nonpolar covalent bond	a bond formed between two atoms that share the bonding electrons equally.
octet rule	states that an atom will give up, accept, or share electrons in order to achieve a filled shell. Because a filled second shell contains eight electrons, this is known as the octet rule.
orbital	the volume of space around the nucleus where an electron is most likely to be found.
orbital hybridization	mixing of atomic orbitals.
organic compound	a compound that contains carbon.
Pauli exclusion principle	states that no more than two electrons can occupy an orbital and that the two electrons must have opposite spin.
pH	the pH scale is used to describe the acidity of a solution ($pH = -\log[H^+]$).
pi (π) bond	a bond formed as a result of side-to-side overlap of *p* orbitals.

pK_a	describes the tendency of a compound to lose a proton (pK_a = -log K_a, where K_a is the acid dissociation constant).
polar covalent bond	a bond formed between two atoms that do not share the bonding electrons equally.
potential map (electrostatic potential map)	a map that allows you to see how electrons are distributed in a molecule.
proton	a positively charged hydrogen; a positively charged atomic particle.
proton transfer reaction	a reaction in which a proton is transferred from an acid to a base.
quantum mechanics	the use of mathematical equations to describe the behavior of electrons in atoms or molecules.
radical (free radical)	a species with an unpaired electron.
resonance	having delocalized electrons.
resonance contributors	structures with localized electrons that approximate the true structure of a compound with delocalized electrons.
resonance hybrid	the actual structure of a compound with delocalized electrons.
sigma (σ) bond	a bond with a symmetrical distribution of electrons about the internuclear axis.
single bond	a single pair of electrons shared between two atoms.
tetrahedral bond angle	the bond angle (109.5°) formed by an sp^3 hybridized central atom.
tetrahedral carbon	an sp^3 hybridized carbon; a carbon that forms covalent bonds using four sp^3 hybrid orbitals.
trigonal planar carbon	an sp^2 hybridized carbon.
triple bond	composed of a sigma bond and two pi bonds.
valence electrons	an electron in an outermost shell.
valence shell electron pair repulsion (VSEPR) model	a model that combines the concepts of atomic orbitals and shared electron pairs with minimization of electron repulsions.
wave equation	an equation that describes the behavior of each electron in an atom or a molecule.
wave functions	a series of solutions of a wave equation.



Solutions to Problems

1. The mass number = the number of protons + the number of neutrons

The atomic number = the number of protons. All isotopes have the same atomic number; in the case of oxygen it is 8.

Therefore:

The isomer of oxygen with a mass number of 16 has 8 protons and 8 neutrons.
The isomer of oxygen with a mass number of 17 has 8 protons and 9 neutrons.
The isomer of oxygen with a mass number of 18 has 8 protons and 10 neutrons.

2. Using the aufbau principle (electrons go into available orbitals with the lowest energy) and the Pauli exclusion principle (no more than 2 electrons in each atomic orbital), and remembering that the relative energies of the atomic orbitals are:

$$1s < 2s < 2p < 3s < 3p < 4s < 3d < 4p < 5s < 4d < 5p$$

The question can be answered if you remember that there is one *s* atomic orbital and 3 degenerate *p* atomic orbitals.

potassium's 19th electron is in a 4*s* orbital.

$1s\ (2e^-),\ 2s\ (2e^-),\ 2p\ (6e^-),\ 3s\ (2e^-),\ 3p\ (6e^-),\ 4s\ (1e^-)$

3. Cl $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^5$

Br $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 4s^2\ 3d^{10}\ 4p^5$

I $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 4s^2\ 3d^{10}\ 4p^6\ 5s^2\ 4d^{10}\ 5p^5$

To write the electronic configurations for Br and I, you need to remember that there are 5 degenerate *d* atomic orbitals.

Notice that because the three atoms are in the same column of the periodic table, they all have the same number of valence electrons (7), and the valence electrons are in similar orbitals (2 are in an *s* orbital and 5 are in *p* orbitals).

4. The atomic numbers can be found in the periodic table on the last page of the text. Notice that elements in the same column of the periodic table have their valence electrons in similar orbitals.

a. carbon (atomic number = 6): $1s^2\ 2s^2\ 2p^2$
silicon (atomic number = 14): $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^2$

b. oxygen (atomic number = 8): $1s^2\ 2s^2\ 2p^4$
sulfur (atomic number = 16): $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^4$

c. fluorine (atomic number = 9): $1s^2\ 2s^2\ 2p^5$
bromine (atomic number = 35): $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 4s^2\ 3d^{10}\ 4p^5$

d. magnesium (atomic number = 12): $1s^2\ 2s^2\ 2p^6\ 3s^2$
calcium (atomic number = 20): $1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6\ 4s^2$

5. The polarity of a bond can be determined by the difference in the electronegativities (given in Table 1.3) of the atoms sharing the bonding electrons

a. KCl has the most polar bond (3.0 - 0.8 = 2.2), whereas it is 1.8 for LiBr, 1.6 for NaI, and 0 for Cl_2.

b. Cl_2 has the least polar bond because the two chlorine atoms share the bonding electrons equally.

6. **a.** LiH and HF are polar (they have a red end and a blue end).

b. A potential map marks the edges of the molecule's electron cloud. The electron cloud is largest around the H in LiH because that H has more electrons around it than the H's in the other molecules.

c. Because the hydrogen of HF is blue, we know that that compound has the most positively charged hydrogen.

7. Solved in the text.

8. To answer this question, compare the electronegativities of the two atoms sharing the bonding electrons using Table 1.3 on page 10 of the text. (Note that if the atoms being compared are in the same row of the periodic chart, the atom on the right is the more electronegative; if the atoms being compared are in the same column, the one closer to the top of the column is the more electronegative.)

a. $\overset{\delta- \ \delta+}{HO—H}$ **c.** $\overset{\delta+ \ \delta-}{H_3C—NH_2}$ **e.** $\overset{\delta- \ \delta+}{HO—Br}$ **g.** $\overset{\delta+ \ \delta-}{I—Cl}$

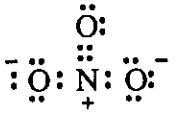
b. $\overset{\delta- \ \delta+}{F—Br}$ **d.** $\overset{\delta+ \ \delta-}{H_3C—Cl}$ **f.** $\overset{\delta- \ \delta+}{H_3C—MgBr}$ **h.** $\overset{\delta+ \ \delta-}{H_2N—OH}$

9. By answering this question you will see that a formal charge is a bookkeeping device. It does *not necessarily* tell you which atom has the greatest electron density or is the most electron deficient.

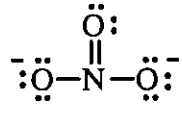
a. oxygen
b. oxygen (it is the more red)
c. oxygen
d. hydrogen (it is the most blue)

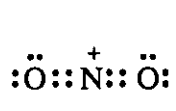
Notice that in hydroxide ion, the atom with the formal negative charge **is** the atom with the greater electron density. In the hydronium ion, however, the atom with the formal positive charge **is not** the most electron deficient atom.

10.

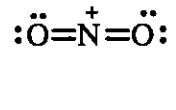
a. 

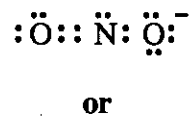
or



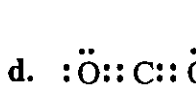
b. 

or

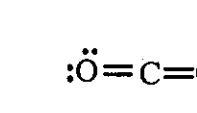


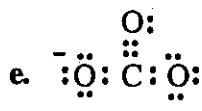
c. 

or

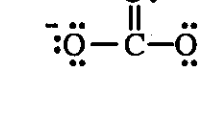
d. 

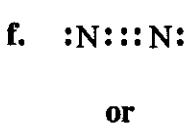
or



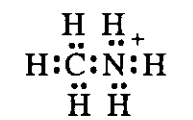
e. 

or

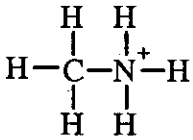


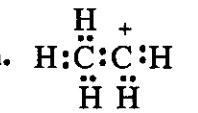
f. 

or

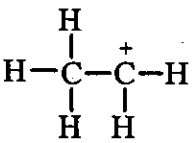
g. 

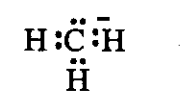
or



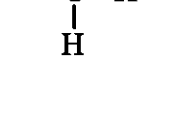
h. 

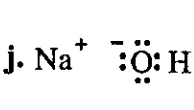
or



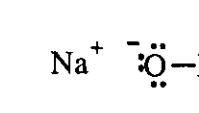
i. 

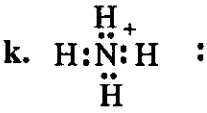
or



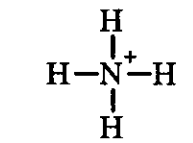
j. 

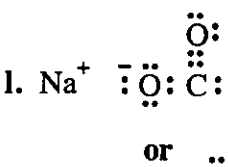
or



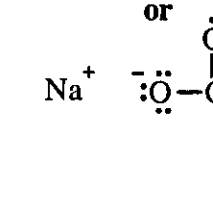
k. 

or

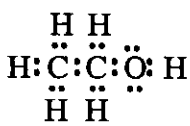
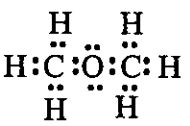


l. 

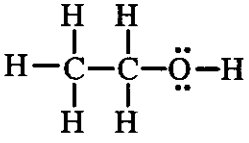
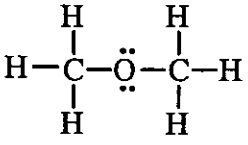
or



11.

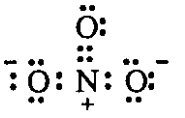
a.  and 

or

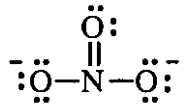
 and 

10.

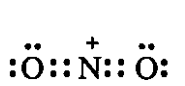
a.



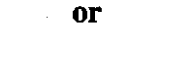
or



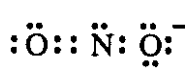
b.



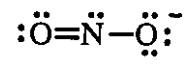
or



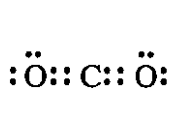
c.



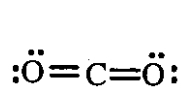
or



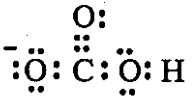
d.



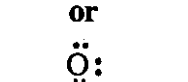
or



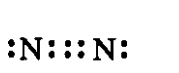
e.



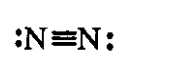
or



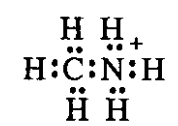
f.



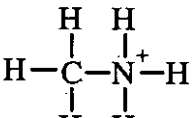
or



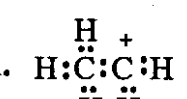
g.



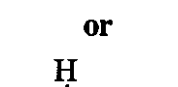
or



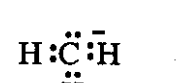
h.



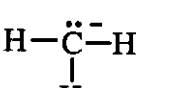
or



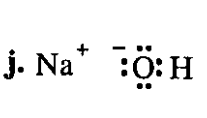
i.



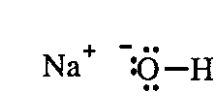
or



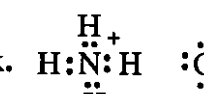
j.



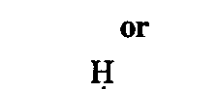
or



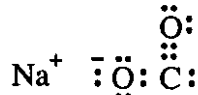
k.



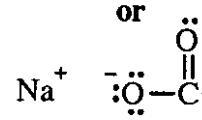
or



l.

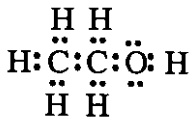


or

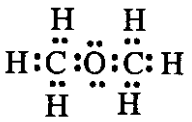


11.

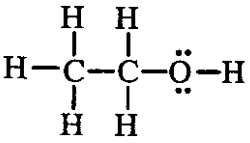
a.



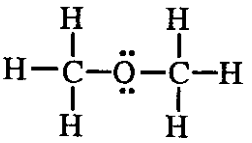
and

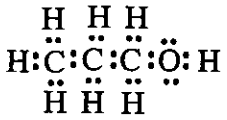
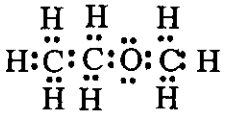
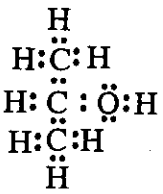


or

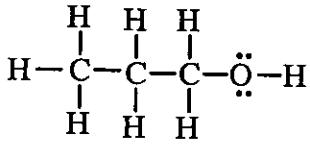
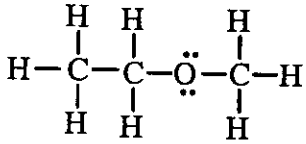
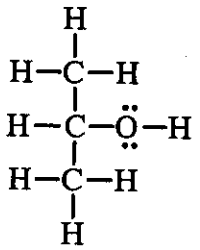


and

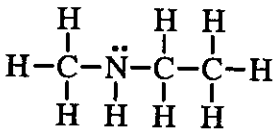


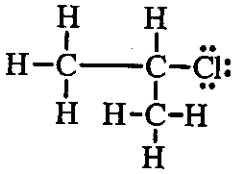
b.  and  and 

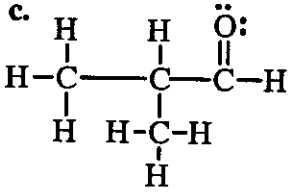
or

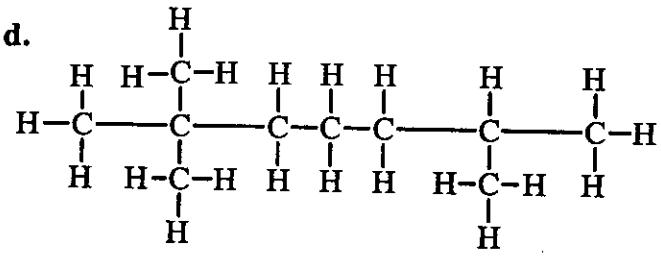
 and  and 

12.

a. 

b. 

c. 

d. 

13. He_2^+ has three electrons. Two are in a bonding orbital and one is in an antibonding orbital. Because there are more electrons in the bonding orbital than in the antibonding orbital, He_2^+ exists.

14.

a. π^* side-to-side overlap forms a π bond;
the overlap of opposite phase (colors) orbitals forms an antibonding (*) orbital.

b. σ^* end-on overlap forms a σ bond;
the overlap of opposite phase (colors) orbitals forms an antibonding (*) orbital.

c. σ^* end-on overlap forms a σ bond;
the overlap of opposite phase (colors) orbitals forms an antibonding (*) orbital.

d. σ end-on overlap forms a σ bond;
the overlap of same phase (colors) orbitals forms an antibonding (*) orbital.

15. The carbon-carbon bonds form as a result of sp^3—sp^3 overlap.
The carbon-hydrogen bonds form as a result of sp^3—s overlap.

16. CH_4 with 0 lone pairs has bond angles of 109.5°
H_2O with 2 lone pairs has bond angles of 104.5°

The bond angle decreases as the number of lone pairs increases because a lone pair is more diffuse than a bonding pair.
Therefore, H_3O^+ with 1 lone pair has bond angles in between those two;
its bond angles will be less than 109.5° and greater than 104.5°.

17. The hydrogens of the ammonium ion are the bluest atoms. Therefore, they have the least electron density. In other words, they have the most positive (least negative) electrostatic potential.

18. Water is the most polar—it has a deep red area and the most intense blue area.
Methane is the least polar—it is all the same color with no red or blue areas.

19. Bonding electrons in shells farther from the nucleus form **longer** and **weaker** bonds due to poorer overlap of the bonding orbitals. Therefore:

a. relative lengths of the bonds in the halogens are: $\mathbf{Br_2 > Cl_2}$.
relative strengths of the bonds are: $\mathbf{Cl_2 > Br_2}$.

b. relative lengths: HBr > HCl > HF
relative strengths: HF > HCl > HBr

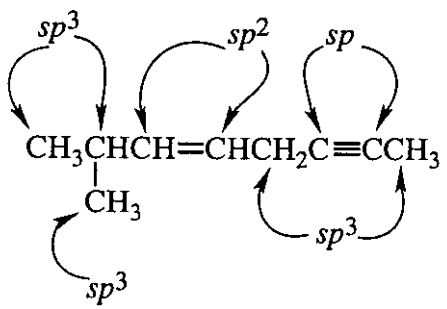
20. We know the σ bond is stronger than a π bond because the σ bond in ethane has a bond dissociation energy of 88 kcal/mol, whereas the bond dissociation energy of the double bond (σ + π) in ethene is 152 kcal/mole, which is less than twice as strong.

Because the σ bond is stronger, we know that it has more effective orbital-orbital overlap.

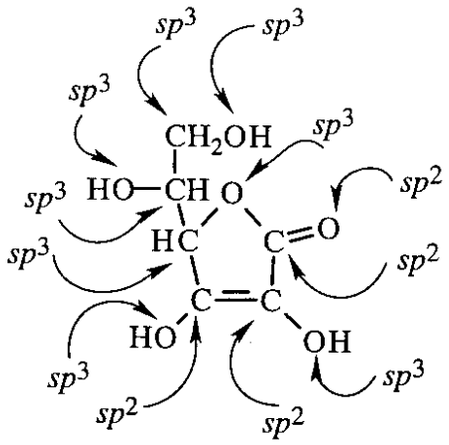
21. The carbon-carbon sigma bond formed by sp^2—sp^2 overlap is stronger because an sp^2 orbital has 33.3% *s* character, whereas an sp^3 orbital has 25% *s* character.
Because electrons in an *s* orbital are closer on average to the nucleus than those in a *p* orbital, the greater the *s* character in the interacting orbitals, the stronger (and shorter) bond.

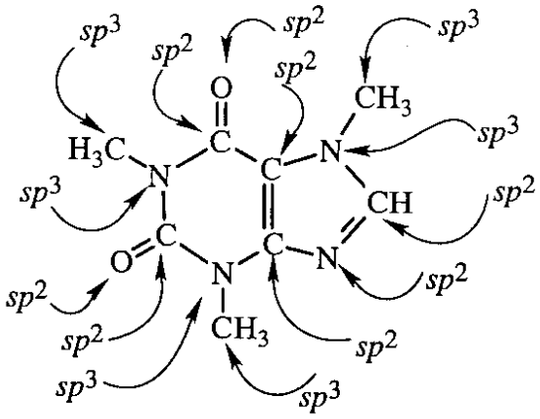
22.

a.



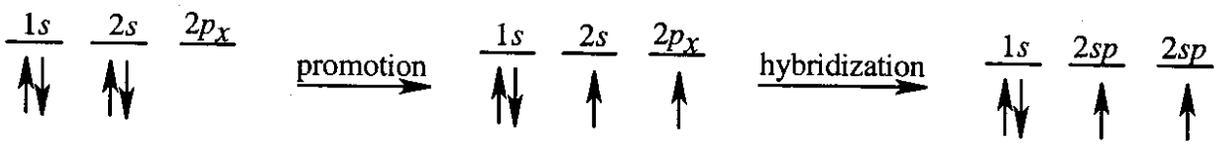
b.



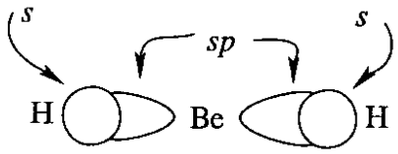


23. a. BeH_2

Because beryllium does not have any unpaired electrons in its ground state, it cannot form any bonds unless it promotes an electron. After promotion, hybridization of the two orbitals (an *s* orbital and a *p* orbital) that contain unpaired electrons results in two *sp* hybrid orbitals.



Each *sp* orbital of beryllium overlaps with the *s* orbital of a hydrogen. The two *sp* orbitals orient themselves to get as far away from each other as possible, resulting in a bond angle of **180°**.

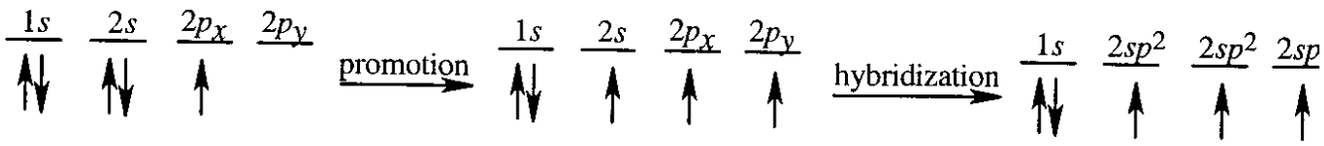


bond angle = 180°

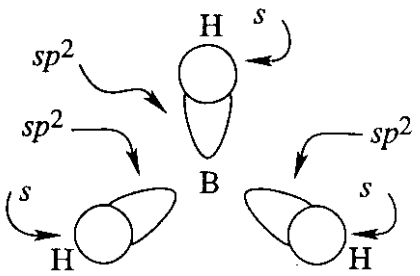
Notice that because beryllium does not have an electron in a *p* orbital, it cannot form a π bond.

b. BH_3

Without promotion, boron could form only one bond because it has only one unpaired electron. Promotion gives it three unpaired electrons. When the three orbitals (one *s* orbital and two *p* orbitals) containing the unpaired electrons are hybridized, three sp^2 orbitals result.



Each sp^2 hybrid orbital overlaps with the *s* orbital of hydrogen. The three sp^2 orbitals orient themselves to get as far away from each other as possible, resulting in bond angles in of **120°**.

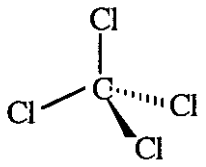


bond angles = 120°

c. CCl_4

The carbon in CCl_4 is bonded to four atoms, so it uses four sp^3 hybrid orbitals.

Each carbon-chlorine bond is formed by the overlap of an sp^3 orbital of carbon with a *p* orbital of chlorine. Because the four sp^3 orbitals orient themselves to get as far away from each other as possible, the bond angles are all **109.5°**.



bond angles = 109.5°

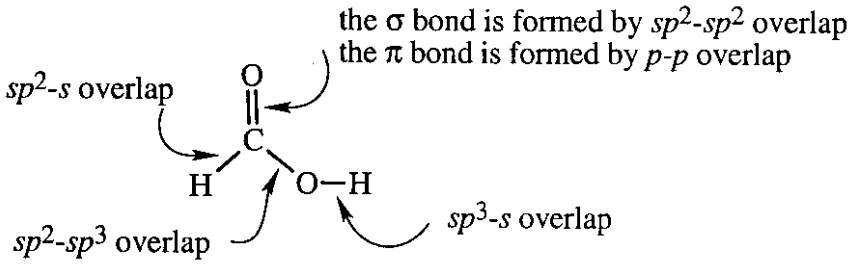
d. CO_2

The carbon in CO_2 is bonded to two atoms, so it uses two *sp* hybrid orbitals. Each carbon-oxygen bond is a double bond. One of the bonds of each double bond is formed by the overlap of an *sp* orbital of carbon with an sp^2 orbital of oxygen. The second bond of the double bond is formed as a result of side-to-side overlap of a *p* orbital of carbon with a *p* orbital of oxygen. Because the two *sp* orbitals orient themselves to get as far away from each other as possible, the bond angle in CO_2 is **180°**.

O═C═O

bond angle = 180°

e. The double-bonded carbon and the double-bonded oxygen in HCOOH use sp^2 hybrid orbitals. The single-bonded oxygen uses sp^3 hybrid orbitals and each hydrogen uses an *s* orbital.



f. The triple bond consists of one σ bond and two π bonds. Each nitrogen uses an *sp* hybrid orbital to form the σ bond and a *p* orbital to form each of the two π bonds.

$N \equiv N$ the σ bond is formed by *sp*-*sp* overlap
each π bond is formed by *p*-*p* overlap

24. The electrostatic potential map of ammonia is not symmetrical in shape because it is not symmetrical in the distribution of the charge—the nitrogen end is more electron rich than the three hydrogens.
The electrostatic potential map of the ammonium ion is symmetrical in shape because it is symmetrical in the distribution of the charge. Its symmetry results from the fact that the nitrogen atom forms a bond with each of the four hydrogens and the four bond angles are all the same.

25. **a, e, g, h**



Because Be is *sp* hyridized, the bond angle in $BeCl_2$ is 180° and the compound does not have a dipole mome
Because C is sp^3 hyridized, the bond angles in CH_2Cl_2 are 109.5° and the compound has a dipole moment.

26. **a.** **(1)** $^+NH_4$ **(2)** HCl **(3)** H_2O **(4)** H_3O^+

b. **(1)** $^-NH_2$ **(2)** Br^- **(3)** NO_3^- **(4)** HO^-

27.

if the lone pairs are not shown:

a. CH_3OH as an acid $\quad CH_3OH + NH_3 \rightleftharpoons CH_3O^- + \overset{+}{N}H_4$

CH_3OH as a base $\quad CH_3OH + HCl \rightleftharpoons CH_3\overset{+}{O}H_2 + Cl^-$

b. NH_3 as an acid $\quad NH_3 + HO^- \rightleftharpoons \overset{-}{N}H_2 + H_2O$

NH_3 as a base $\quad NH_3 + HBr \rightleftharpoons \overset{+}{N}H_4 + Br^-$

if the lone pairs are shown:

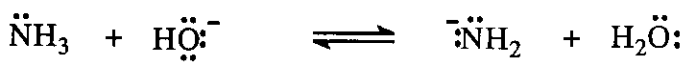
a. CH_3OH as an acid



CH_3OH as a base



b. NH_3 as an acid



NH_3 as a base



28. **a.** The lower the pK_a, the stronger the acid, so the compound with pK_a = 5.2 is the stronger acid.

b. The greater the dissociation constant, the stronger the acid, so the compound with dissociation constant = 3.4×10^{-3} is the stronger acid.

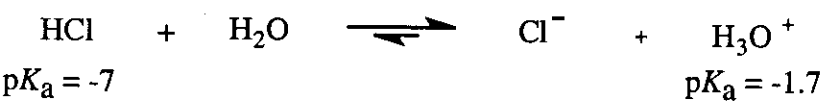
29.

$$K_a = K_{eq}[H_2O]$$

$$K_{eq} = \frac{K_a}{[H_2O]} = \frac{4.53 \times 10^{-6}}{55.5} = 8.16 \times 10^{-8}$$

30. Notice that in each case, the equilibrium goes away from the strong acid and toward the weak acid.

a.



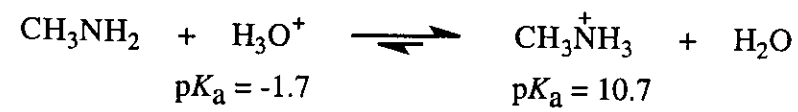
pK_a = -7 pK_a = -1.7



pK_a = 4.8 pK_a = -1.7

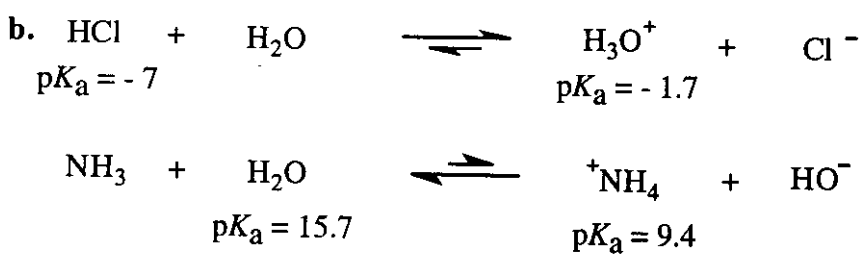


pK_a = 40 pK_a = 15.7



pK_a = -1.7 pK_a = 10.7

b.

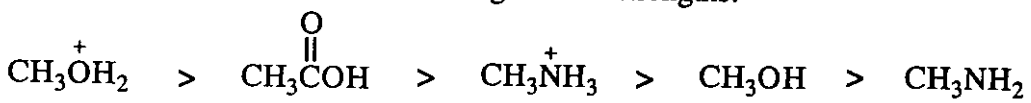


31. **a.** CH_3COO^- is the stronger base.
Because HCOOH is the stronger acid, it has the weaker conjugate base.

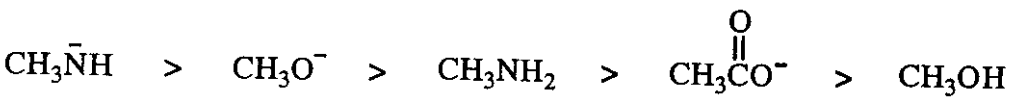
b. $^-NH_2$ is the stronger base.
Because H_2O is the stronger acid, it has the weaker conjugate base.

c. H_2O is the stronger base.
Because $CH_3OH_2^+$ is the stronger acid, it has the weaker conjugate base.

32. The conjugate acids have the following relative strengths:



The bases, therefore, have the following relative strengths:



33.

$$K_{eq} = \frac{K_a \text{ of the reactant acid}}{K_a \text{ of the product acid}}$$

For **a** the reactant acid is HCl and the product acid is H_3O^+.

For **b** the reactant acid is CH_3COOH and the product acid is H_3O^+.

For **c** the reactant acid is H_2O and the product acid is $CH_3NH_3^+$.

For **d** the reactant acid is $CH_3NH_3^+$ and the product acid is H_3O^+.

a. $K_{eq} = \dfrac{10^{7}}{10^{1.7}} = 10^{7 - 1.7} = 10^{5.3} = 2.0 \times 10^{5}$

b. $K_{eq} = \dfrac{10^{-4.8}}{10^{1.7}} = 10^{-4.8 - 1.7} = 10^{-6.5} = 3.2 \times 10^{-7}$

c. $K_{eq} = \dfrac{10^{-15.7}}{10^{-10.7}} = 10^{-15.7 + 10.7} = 10^{-5} = 1.0 \times 10^{-5}$

d. $K_{eq} = \dfrac{10^{-10.7}}{10^{1.7}} = 10^{-10.7 - 1.7} = 10^{-12.4} = 4.0 \times 10^{-13}$

34.

a. $CH_3OCH_2CH_2OH$ because of the CH_3O group that withdraws electrons inductively

b. $CH_3CH_2CH_2\overset{+}{O}H_2$ because oxygen is more electronegative than nitrogen and, therefore, is better at withdrawing electrons inductively

c. $CH_3CH_2OCH_2CH_2OH$ because the electron-withdrawing oxygen is closer to the OH group

d. $CH_3CH_2\overset{O}{\overset{\|}{C}}OH$ because the electron-withdrawing C=O is closer to the OH group

35.

$$CH_3\underset{F}{\underset{|}{C}}HCH_2OH > CH_3\underset{Cl}{\underset{|}{C}}HCH_2OH > \underset{Cl}{\underset{|}{C}}H_2CH_2CH_2OH > CH_3CH_2CH_2OH$$

The first two compounds are the most acidic because they have the electron-withdrawing substituent closest to the O—H bond. The first compound is more acidic than the second because fluorine is more electronegative than chlorine.
The second listed compound is a stronger acid than the third listed compound because the chlorine in the third compound is farther away from the O—H bond.
The last-listed compound does not have a substituent that withdraws electrons inductively, so it is the least acidic of the compounds.

36. The weaker acid has the stronger conjugate base.

a. $CH_3\underset{Br}{\underset{|}{C}}H\overset{O}{\overset{\|}{C}}O^-$ **b.** $CH_3\underset{Cl}{\underset{|}{C}}HCH_2\overset{O}{\overset{\|}{C}}O^-$ **c.** $CH_3CH_2\overset{O}{\overset{\|}{C}}O^-$ **d.** $CH_3\overset{O}{\overset{\|}{C}}CH_2CH_2O^-$

37. Solved in the text.

38. **a.** Because HF is the weakest acid, F^- is the strongest base.

b. Because HI is the strongest acid, I^- is the weakest base.

39. **a.** oxygen **b.** H_2S **c.** CH_3SH

As you saw in Problem 37, the size of an atom is more important than its electronegativity in determining stability. So even though oxygen is more electronegative than sulfur, H_2S is a stronger acid than H_2O and CH_3SH is a stronger acid than CH_3OH because the sulfur atom is larger—therefore, the electrons in the its conjugate base are spread out over a greater volume of causing it to be a more stable base. The more stable the base, the stronger its conjugate acid.

40.

a. $CH_3C{\equiv}\overset{+}{N}H$

b. CH_3CH_3 or CH_4

c. $F_3C\overset{O}{\overset{\|}{C}}OH$

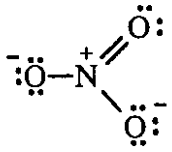
d. an sp^2 hybridized oxygen

e. $sp > sp^2 > sp^3$

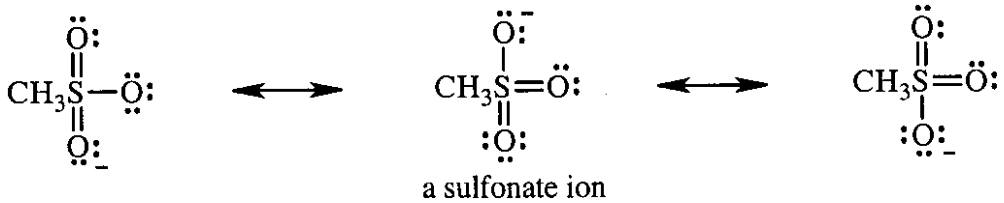
f. $sp > sp^2 > sp^3$

g. HNO_3 is more acidic than HNO_2.

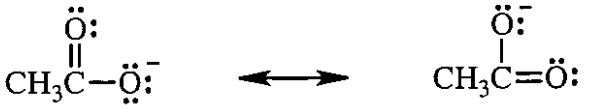
When the structure of the conjugate base of each acid is drawn out, you can see that NO_3^- has a positively charged nitrogen and NO_2^- does not. The positive charge decreases the electron density on the oxygen by inductive electron withdrawal, thereby stabilizing it.
A stable base is a weak base. Therefore, it has the stronger conjugte acid.



41. When a sulfonic acid loses a proton, the electrons left behind are shared by three oxygen atoms. In contrast, when a carboxylic acid loses a proton, the electrons left behind are shared by only two oxygen atoms. The sulfonate ion, therefore, is more stable than the carboxylate ion. The more stable the base, the stronger is its conjugate acid. Thus the sulfonic acid is a stronger acid than the carboxylic acid.



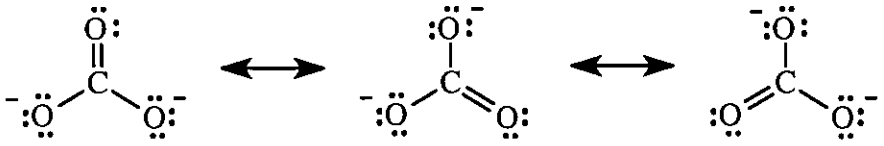
a sulfonate ion



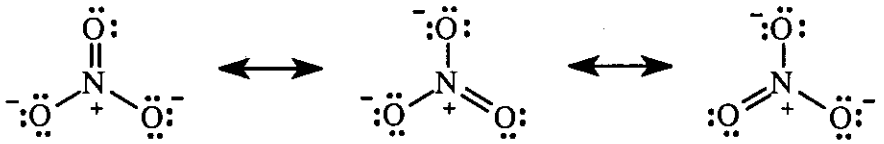
a carboxylate ion

42.

a.



b.



43. greater than pH 10.4

As long as the pH is greater than the pK_a of the compound, the majority of the compound will be in its basic form.

44. **a.** 10.4 (two log units more basic than the pK_a)

b. 2.7 (one log unit more acidic than the pK_a)

c. 4.9 (If 10% is in its basic form, 90% will be in its acidic form, so the pH needs to be one log unit more acidic than the pK_a.)

d. 7.3 ($pH = pK_a$)

e. 9.3 (If 1% is in its acidic form, 99% will be in its basic form, so the pH needs to be two log units more basic than the pK_a.)

45.

a.	**b.**	**c.**
1. neutral	**1.** charged	**1.** neutral
2. neutral	**2.** charged	**2.** neutral
3. equal amounts of both	**3.** charged	**3.** neutral
4. charged	**4.** charged	**4.** neutral
5. charged	**5.** equal amounts of both	**5.** neutral
6. charged	**6.** neutral	**6.** neutral
7. charged	**7.** neutral	**7.** neutral

46. **a. 1.** pH = 4.9

2. pH = 10.7

b. 1. pH > 6.9 Because the basic form is the form in which the compound is charged, the pH needs to be more than two units more basic than the pK_a.

2. pH < 8.7 Because the acidic form is the form in which the compound is charged, the pH needs to be more than two units more acidic than the pK_a.

47.

a. CH_3COO^- **c.** H_2O **e.** CH_3CH_2OH **g.** $HC{\equiv}N$ **i.** NO_3^-

b. $CH_3CH_2\overset{+}{N}H_3$ **d.** CH_3CH_2OH **f.** $\overset{+}{N}H_4$ **h.** NO_2^- **j.** Br^-

48.

a. $ZnCl_2 + CH_3OH \rightleftharpoons CH_3\overset{+}{O}H\ \overset{-}{Z}nCl_2$

b. $FeBr_3 + Br^- \rightleftharpoons Br{-}\bar{F}eBr_3$

c. $AlCl_3 + Cl^- \rightleftharpoons Cl{-}\bar{A}lCl_3$

d. $BF_3 + \underset{\underset{HCH}{\|}}{O} \rightleftharpoons \overset{+}{O}{-}\bar{B}F_3\ \underset{\underset{HCH}{\|}}{}$

49. **a, b, c,** and **h** are Brønsted acids (protonating-donating acids). Therefore, they react with HO^- by donating a proton to it.

d, e, f, and **g** are Lewis acids. They react with HO^- by accepting a pair of electrons from it.

a. $CH_3OH + HO^- \rightleftharpoons CH_3O^- + H_2O$

b. $\overset{+}{N}H_4 + HO^- \rightleftharpoons NH_3 + H_2O$

c. $CH_3\overset{+}{N}H_3 + HO^- \rightleftharpoons CH_3NH_2 + H_2O$

d. $BF_3 + HO^- \rightleftharpoons HO{-}\bar{B}F_3$

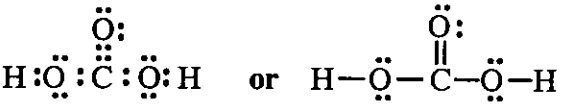
e. $\overset{+}{C}H_3 + HO^- \rightleftharpoons CH_3OH$

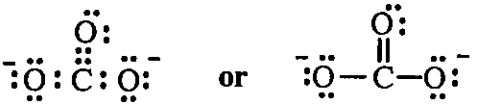
f. $FeBr_3 + HO^- \rightleftharpoons HO-\bar{F}eBr_3$

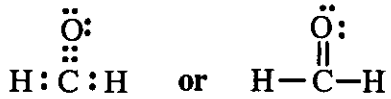
g. $AlCl_3 + HO^- \rightleftharpoons HO-\bar{A}lCl_3$

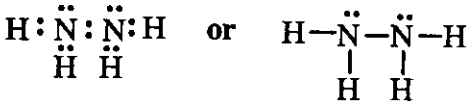
h. $CH_3COOH + HO^- \rightleftharpoons CH_3COO^- + H_2O$

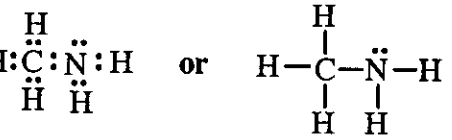
50.

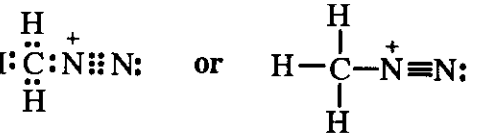
a.  or

b.  or

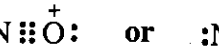
c. 

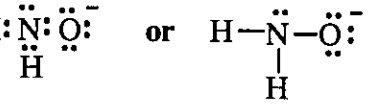
d. 

e. 

f. 

g.

h. 

i. 

51.

a. sp^3, tetrahedral
b. sp^2, trigonal
c. sp^3, tetrahedral
d. sp^2, trigonal
e. sp^3, tetrahedral
f. sp^2, trigonal
g. sp, linear
h. sp^3, tetrahedral
i. sp^3, tetrahedral

52.

a. $CH_3CH_2CH_3$ **b.** $CH_3CH{=}CH_2$ **c.** $CH_3C{\equiv}CCH_3$ or $CH_3CH_2C{\equiv}CH$

53. **a.** 107.3 ° **c.** 109.5° **e.** 104.5° **g.** 109.5° **i.** 109.5°

b. 107.3° **d.** 104.5°* **f.** 120° **h.** 180°

*104.5° is the correct prediction based on the bond angle in water.
However, the bond angle is actually somewhat larger (111.7°) because the bond opens up to minimize the interaction between the electron clouds of the relatively bulky CH_3 groups.

54. formal charge = the number of valence electrons – (the number of lone-pair electrons + 1/2 the number of bonding electrons)

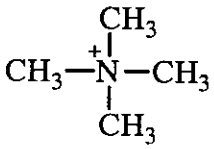
a. formal charge = 6 – (6 + 1) = 6 – 7 = – 1



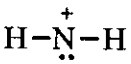
b. formal charge = 6 – (5 + 1) = 6 – 6 = 0



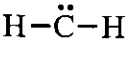
c. formal charge = 5 – (4) = + 1



d. formal charge = 5 – (2 + 2) = 5 – 4 = + 1

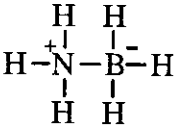


e. formal charge = 4 – (2 + 2) = 4 – 4 = 0

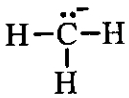


f. N has a formal charge = 5 – (4) = + 1

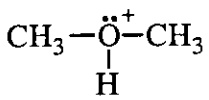
B has a formal charge = 3 – (4) = - 1



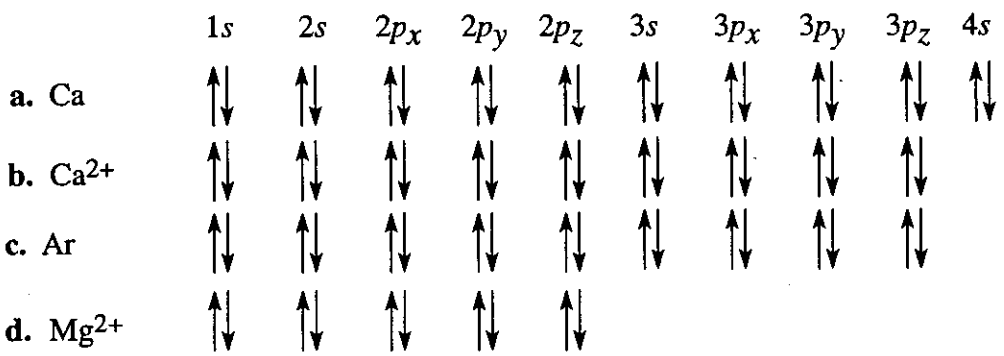
g. formal charge = 4 − (2 + 3) = 4 − 5 = − 1



h. formal charge = 6 − (2 + 3) = 6 − 5 = + 1

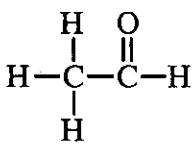


55.

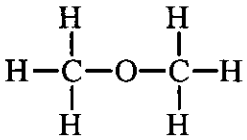


56.

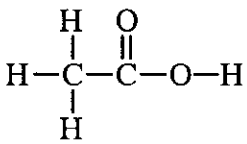
a.



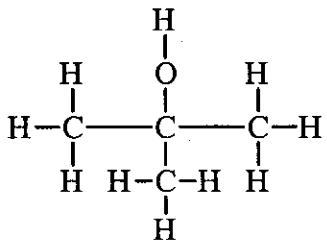
b.



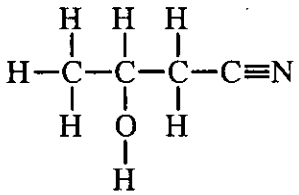
c.



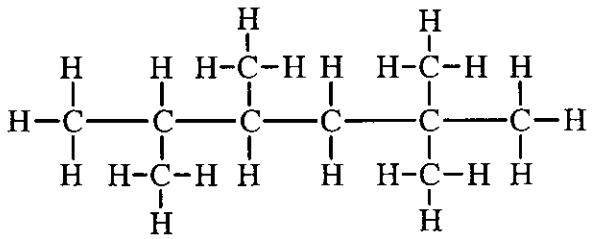
d.



e.



f.



57.

a. $CH_3 \rightarrow Br$ **c.** $HO \leftarrow NH_2$ **e.** $CH_3 \rightarrow OH$

b. $CH_3 \leftarrow Li$ **d.** $I \rightarrow Br$ **f.** $(CH_3)_2N \leftarrow H$

58.

a. $CH_3\overset{sp^2}{\underset{\Downarrow}{C}}H=CH_2$ **c.** $CH_3CH_2\overset{sp^3}{\underset{\Downarrow}{O}}H$ **e.** $CH_3\overset{sp^2}{\underset{\Downarrow}{C}}H=NCH_3$

b. $CH_3\overset{O}{\overset{\Vert}{C}}CH_3$ ($O \Leftarrow sp^2$) **d.** $CH_3\overset{sp}{\underset{\Downarrow}{C}}\equiv N$ **f.** $CH_3O\overset{sp^3}{\underset{\Downarrow}{C}}H_2CH_3$

59. The open arrow points to the shorter of the two indicated bonds in each compound.

For **1**, **2**, and **3**: a triple bond is shorter than a double bond which is shorter than a single bond.

For **4** and **5**: Because an *s* orbital is closer to the nucleus than a *p* orbital, the greater the *s* character in the hybridized orbital, the shorter is the bond. Therefore, the bond formed by a hydrogen and an *sp* hybridized carbon is shorter than the bond formed by a hydrogen and an sp^2 hybridized carbon, which is shorter than the bond formed by a hydrogen and an sp^3 hybridized carbon. (See Table 1.7 on page 37 of the text.)

1. $CH_3\overset{sp^3}{C}H=\overset{sp^2}{C}H\overset{sp^2}{\underset{\Downarrow}{C}}\equiv\overset{sp}{C}H$

2. $\Rightarrow \overset{O}{\overset{\Vert}{C}}\overset{sp^2}{}$ $CH_3\overset{sp^3}{C}H_2\overset{sp^3}{O}H$ (sp^3, sp^2, sp^3)

3. $CH_3\overset{sp^3}{N}H\overset{sp^3}{C}H_2\overset{sp^3}{C}H_2\overset{sp^2}{N}=\overset{sp^2}{C}H\overset{sp^3}{C}H_3$

4. $H_2C=\overset{sp^2}{C}H\overset{sp}{\underset{\Downarrow}{C}}\equiv\overset{sp}{C}-H$

5. $H_2C=\overset{sp^2}{C}H\overset{sp}{C}\equiv\overset{sp}{C}-\overset{sp^3}{C}(CH_3)_2-H$ (sp^3 from CH_3)

60. If the solution is more acidic than the pK_a of the compound, the compound will be in its acidic form (with the proton). If the solution is more basic than the pK_a of the compound, the compound will be in its basic form (without the proton).

a. at pH = 3 $CH_3\overset{\overset{O}{\|}}{C}OH$

at pH = 6 $CH_3\overset{\overset{O}{\|}}{C}O^-$

at pH = 10 $CH_3\overset{\overset{O}{\|}}{C}O^-$

at pH = 14 $CH_3\overset{\overset{O}{\|}}{C}O^-$

b. at pH = 3 $CH_3CH_2\overset{+}{N}H_3$

at pH = 6 $CH_3CH_2\overset{+}{N}H_3$

at pH = 10 $CH_3CH_2\overset{+}{N}H_3$

at pH = 14 $CH_3CH_2NH_2$

c. at pH = 3 CF_3CH_2OH

at pH = 6 CF_3CH_2OH

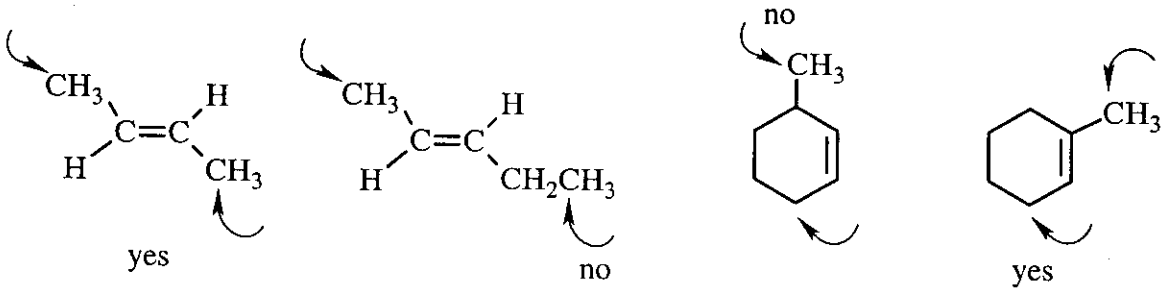
at pH = 10 CF_3CH_2OH

at pH = 14 $CF_3CH_2O^-$

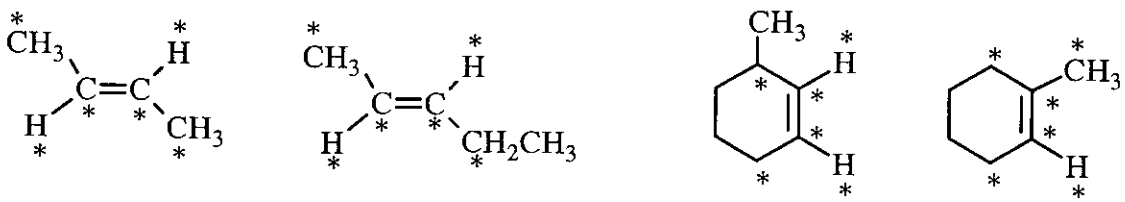
61. If the central atom is sp^3 hybridized, the molecule will have tetrahedral bond angles. Therefore, the following have tetrahedral bond angles.

$$H_2O,\ H_3O^+,\ NH_3,\ {}^+NH_4,\ {}^-CH_3$$

62. In an alkene, six atoms are in the same plane: the two sp^2 hybridized carbons and the two atoms that are bonded to each of the two sp^2 hybridized carbons. The other atoms in the molecule will not be in the same plane with these six atoms.



If you put stars next to the six atoms that lie in a plane in each molecule, you might be able to see more clearly whether the indicated atoms lie in the same plane.



63.

a. $CH_3COOH + CH_3O^- \rightleftharpoons CH_3COO^- + CH_3OH$

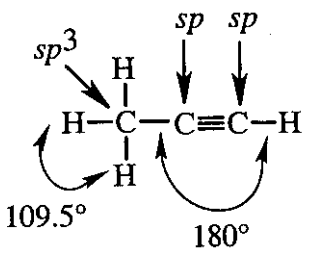
b. $CH_3CH_2OH + {}^-NH_2 \rightleftharpoons CH_3CH_2O^- + NH_3$

c. $CH_3COOH + CH_3NH_2 \rightleftharpoons CH_3COO^- + CH_3\overset{+}{N}H_3$

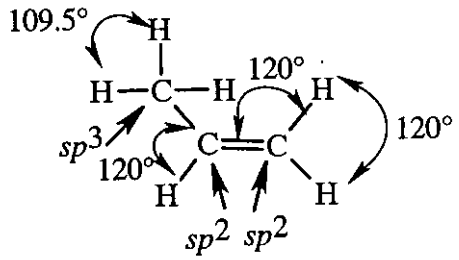
d. $CH_3CH_2OH + HCl \rightleftharpoons CH_3CH_2\overset{+}{O}H_2 + Cl^-$

64.

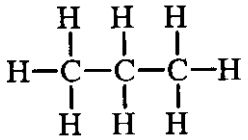
a.



b.



c.



The 3 carbons are all sp^3 hybridized.
All the bond angles are 109.5°.

65. The log of $10^{-4} = -4$, the log of $10^{-5} = -5$, the log of $10^{-6} = -6$, etc.
Because the $pK_a = -\log K_a$, the pK_a of an acid with a K_a of 10^{-4} = is $-(-4) = 4$.
An acid with a K_a of 4.0×10^{-4} is a stronger acid than one with a K_a of 1.0×10^{-4}.
Therefore, the pK_a can be estimated as being between 3 and 4.

a. **1.** between 3 and 4
2. between -2 and -1
3. between 10 and 11
4. between 9 and 10
5. between 3 and 4

b. **1.** $pK_a = 3.4$
2. $pK_a = -1.3$
3. $pK_a = 10.2$
4. $pK_a = 9.1$
5. $pK_a = 3.7$

c. Because the lower the pK_a the stronger the acid, nitric acid is the strongest acid.

66.

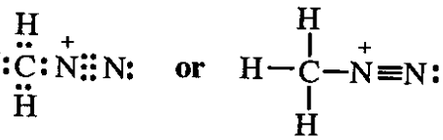
a.

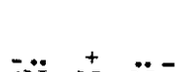
$$CH_3CH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCOOH > CH_3\underset{\displaystyle Cl}{\underset{|}{C}}HCH_2COOH > ClCH_2CH_2CH_2COOH > CH_3CH_2CH_2COOH$$

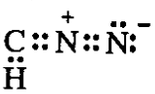
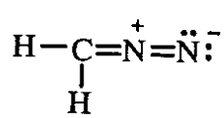
b. The electron-withdrawing substituent makes the carboxylic acid more acidic, because it stabilizes its conjugate base by decreasing the electron density around the oxygen atom.

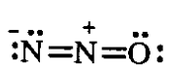
c. The closer the electron-withdrawing Cl is to the acidic proton, the more it can decrease the electron density around the oxygen atom, so the more it stabilizes the conjugate base.

67.

a.  **or**

c.  **or** 

b.  **or** 

d.  **or** 

68. The reaction with the most favorable equilibrium constant is the one with the greatest difference between the strengths of the reactant acid and the product acid. (i.e., the one that has the strongest reactant acid and the weakest product acid.

a. 1. CH_3OH is a stronger reactant acid ($pK_a = 15.5$) than CH_3CH_2OH ($pK_a = 15.9$), and both reactions form the same product acid ($^+NH_4$). Therefore, the reaction of CH_3OH with NH_3 has the more favorable equilibrium constant.

2. Both reactions have the same reactant acid (CH_3CH_2OH). The product acids are different: $^+NH_4$ is a stronger product acid ($pK_a = 9.4$) than $CH_3NH_3^+$ ($pK_a = 10.7$). Therefore, the reaction of CH_3CH_2OH with CH_3NH_2 has the more favorable equilibrium constant.

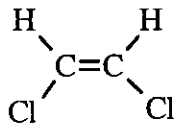
b. Now we have to compare "apples" and "oranges" because the reaction with the most favorable equilibrium constant in **1** and the reaction with the most favorable equilibrium constant in **2** do not have any species in common: **1** has the stronger reactant acid, whereas **2** has the weaker product acid. Therefore, the equilibrium constants have to be calculated.

The reaction of CH_3OH with NH_3 has an equilibrium constant = 7.9×10^{-7}
($K_{eq} = K^{-15.5}/K^{-9.4} = K^{-6.1} = 7.9 \times 10^{-7}$).

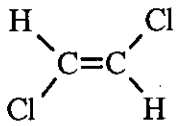
The reaction of CH_3CH_2OH with CH_3NH_2 has an equilibrium constant = 6.3×10^{-6}
($K_{eq} = K^{-15.9}/K^{-10.7} = K^{-5.2} = 6.3 \times 10^{-6}$).

Therefore, the reaction of CH_3CH_2OH with CH_3NH_2 has the greatest equilibrium constant of the four reactions.

69.



The dipole moment is 2.95 because the two Cl's are withdrawing electrons in the same direction.



The dipole moment is 0 because the two Cl's are withdrawing electrons in opposite directions.

70.

$$K_a = \frac{[H^+]\,[HO^-]}{[H_2O]}$$

$$K_a = \frac{(1 \times 10^{-7})(1 \times 10^{-7})}{55.5}$$

$$K_a = 1.80 \times 10^{-16}$$

$$pK_a = -\log 1.80 \times 10^{-16}$$

$$pK_a = 15.7$$

The answer can also be obtained in the following way:

$$K_a = \frac{[H^+]\,[HO^-]}{[H_2O]}$$

$$K_a\,[H_2O] = [H^+]\,[HO^-]$$

take the log of both sides

$$\log K_a + \log [H_2O] = \log [H^+] + \log [HO^-]$$

multiply both sides by -1

$$-\log K_a - \log [H_2O] = -\log [H^+] - \log [HO^-]$$

$$pK_a - \log [H_2O] = pH + pOH$$

$$pK_a - \log [H_2O] = 14$$

$$pK_a = 14 + \log [H_2O]$$

$$pK_a = 14 + \log 55.5$$

$$pK_a = 14 + 1.7$$

$$pK_a = 15.7$$

71. From the following equilibria you can see that a carboxylic acid is neutral when it is in its acidic form and charged when it is in its basic form. An amine is charged when it is in its acidic form and neutral when it is in its basic form.

$$RCOOH \rightleftharpoons RCOO^- + H^+$$

$$R\overset{+}{N}H_3 \rightleftharpoons RNH_2 + H^+$$

Charged species will dissolve in water and neutral species will dissolve in ether. In separating compounds you want essentially all (100:1) of each compound in either its acidic form or its basic form.

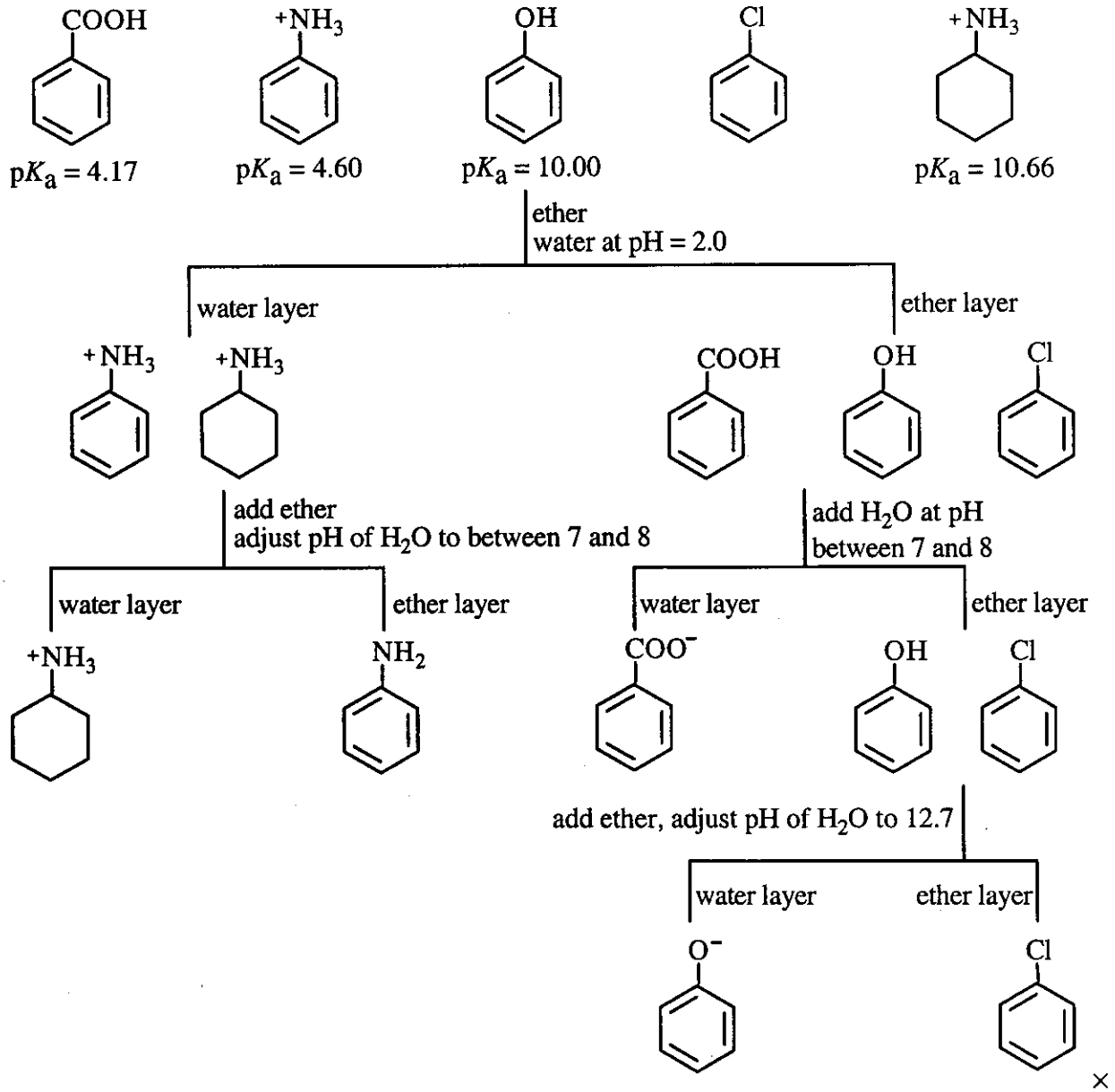
From the Henderson-Hasselbalch equation it can be calculated that in order to obtain a 100:1 ratio of acidic form:basic form, the pH must be two pH units lower than the pK_a of the compound; and in order to obtain a 100:1 ratio of basic form:acidic form, the pH must be two pH units greater than the pK_a of the compound.

a. If both compounds are to dissolve in water, they both must be charged. Therefore, the carboxylic acid must be in its basic form, and the amine must be in its acidic form. To accomplish this, the pH will have to be at least two pH units greater than the pK_a of the carboxylic acid and at least two pH units less than the pK_a of the ammonium ion. In other words, it must be between pH 6.8 and pH 8.7.

b. For the carboxylic acid to dissolve in water, it must be charged (in its basic form), so the pH will have to be greater than 6.8. For the amine to dissolve in ether, it will have to be neutral (in its basic form), so the pH will have to be greater than 12.7 to have essentially all of it in the neutral form. Therefore, the pH of the water layer must be greater than 12.7.

c. To dissolve in ether, the carboxylic acid will have to be neutral, so the pH will have to be less than 2.8 to have essentially all the carboxylic acid in the acidic (neutral) form. To dissolve in water, the amine will have to be charged, so the pH will have to be less than 8.7 to have essentially all the amine in the acidic form. Therefore, the pH of the water layer must be less than 2.8.

72. Charged compounds will dissolve in water and uncharged compounds will dissolve in ether. The acidic forms of carboxylic acids and alcohols are neutral and the basic forms are charged. The acidic forms of amines are charged and the basic forms are neutral.



73. If light is shone on a molecule of H_2 or Br_2, one of the two electrons in a bonding MO can be promoted to an empty antibonding MO. The electron in the antibonding MO will cancel out the electron that is left in the bonding MO, so overall there will be no bonding. In other words, H_2 or Br_2 will have been broken up into hydrogen atoms or bromine atoms. The energy difference between the bonding and antibonding MO's is greater in the case of H_2 than in the case of Br_2. Therefore, less energy is required to break Br_2 into bromine radicals.

74. Using the following reaction as an example:

$$CH_3OH + NH_3 \rightleftharpoons CH_3O^- + \overset{+}{N}H_4$$

$$K_{eq} = \frac{[\text{products}]}{[\text{reactants}]}$$

$$K_{eq} = \frac{[CH_3O^-][\overset{+}{N}H_4]}{[CH_3OH][NH_3]}$$

$$K_a \text{ reactant acid} = \frac{[H^+][CH_3O^-]}{[CH_3OH]}$$

$$K_a \text{ product acid} = \frac{[H^+][NH_3]}{[\overset{+}{N}H_4]}$$

$$K_{eq} = \frac{K_a \text{ reactant acid}}{K_a \text{ product acid}} = \frac{\dfrac{[H^+][CH_3O^-]}{[CH_3OH]}}{\dfrac{[H^+][NH_3]}{[\overset{+}{N}H_4]}}$$

$$= \frac{\dfrac{[CH_3O^-]}{[CH_3OH]}}{\dfrac{[NH_3]}{[\overset{+}{N}H_4]}}$$

$$= \frac{[CH_3O^-][\overset{+}{N}H_4]}{[NH_3][CH_3OH]}$$

75. For a discussion of how to do problems such as Problems 75-77, see **Special Topic I** (pH, pK_a, and Buffers) on p. 34.

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

1. When the value of the pH is equal to the value of the pK_a, the concentration of buffer in the acidic form equals the concentration of buffer in the basic form.
2. When the solution is more acidic than the pK_a, more buffer species is in the acidic form than in the basic form
3. When the solution is more basic than the pK_a, more buffer species is in the basic form than in the acidic form.

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

Because the pH of the blood (~7.4) is greater than the pK_a of the buffer (6.1), more buffer species is in the basic form than in the acidic form. Therefore, the buffer is better at neutralizing excess acid.

76. a.

$$\text{fraction present in the acidic form} = \frac{\text{amount in the acidic form}}{\text{amount in the acidic form} + \text{amount in the basic form}}$$

$$= \frac{[HA]}{[HA] + [A^-]}$$

Because there are two unknowns, we must define one in terms of the other.

By using the definition of the acid dissociation constant, we can determine $[A^-]$ in terms of [HA].

$$K_a = \frac{[H^+]\,[A^-]}{[HA]}$$

$$[A^-] = \frac{K_a\,[HA]}{[H^+]}$$

Substituting the value of $[A^-]$ into the equation gives the fraction that is present in the acidic form

$$\frac{[HA]}{[HA] + [A^-]} = \frac{[HA]}{[HA] + \frac{K_a\,[HA]}{[H^+]}} = \frac{1}{1 + \frac{K_a}{[H^+]}} = \frac{[H^+]}{[H^+] + K_a}$$

Therefore, the percent that is present in the acidic form is given by:

$$\frac{[H^+]}{[H^+] + K_a} \times 100$$

Because the pK_a of the acid is given as 5.3, we know that K_a is 5.0×10^{-6} ($pK_a = -\log K_a$).

Because the pH of the solution is given as 5.7, we know that $[H^+]$ is 2.0×10^{-6} ($pH = -\log[H^+]$).

Substituting into the equation that gives the percent that is present in the acidic form:

$$\frac{2.0 \times 10^{-6}}{2.0 \times 10^{-6} + 5.0 \times 10^{-6}} \times 100$$

$$\frac{2.0 \times 10^{-6}}{7.0 \times 10^{-6}} \times 100 = 29\%$$

b. percent present in the acidic form $= \dfrac{[H^+]}{[H^+] + K_a} = .80$

$$[H^+] = .80\,([H^+] + K_a)$$

$$[H^+] = .80\,[H^+] + .80\,K_a$$

$$.20\,[H^+] = .80\,K_a$$

$$[H^+] = 4\,K_a$$

$$[H^+] = 4 \times 5.0 \times 10^{-6}$$

$$[H^+] = 20 \times 10^{-6}$$

$$pH = 4.7$$

77.

a. $K_a = \dfrac{[H^+]\,[A^-]}{[HA]}$

$$1.74 \times 10^{-5} = \frac{x^2}{1.0 - x}$$

$$1.74 \times 10^{-5} = x^2$$

$$x = 4.16 \times 10^{-3}$$

$$pH = 2.38$$

b. $K_a = \dfrac{[H^+]\,[A^-]}{[HA]}$

$$2.00 \times 10^{-11} = \frac{x^2}{0.1 - x}$$

$$2.00 \times 10^{-12} = x^2$$

$$x = 1.41 \times 10^{-6}$$

$$pH = 5.85$$

c. This question can be answered by plugging the numbers into the Henderson-Hasselbalch equation.

$$pK_a = pH + \log \frac{[acid]}{[base]}$$

$$3.76 = pH + \frac{0.3}{0.1}$$

$$3.76 = pH + \log 3$$

$$3.76 = pH + 0.48$$

$$pH = 3.76 - 0.48 = 3.28$$

Chapter 1 Practice Test

1. Answer the following:

a. Which is a stronger acid, HCl or HBr?

b. Which is a stronger base, NH_3 or H_2O?

c. Which bond has a greater dipole moment, a carbon-oxygen bond or a carbon-fluorine bond?

d. Which has a dipole moment of zero, $CHCl_3$ or CCl_4?

2. What is the hybridization of the carbon atom in each of the following compounds?

$\overset{+}{C}H_3$ $\qquad$ $\overset{-}{C}H_3$ $\qquad$ $\overset{\bullet}{C}H_3$

3. Draw the Lewis structure for HCO_3^-.

4. The following compounds are drawn in their acidic forms, and their pK_a's are given. Draw the form in which each compound would predominantly exist at pH = 8.

CH_3COOH	CH_3CH_2OH	$CH_3\overset{H}{\overset{+}{O}}H$	$CH_3CH_2\overset{+}{N}H_3$
pK_a = 4.8	pK_a = 15.9	pK_a = −2.5	pK_a = 11.2

5. Which compound has greater bond angles, H_3O^+ or $^+NH_4$?

6. What is the conjugate base of NH_3?

7. Give the structure of a compound that contains five carbons, two of which are sp^2 hybridized and three of which are sp^3 hybridized.

8. **a.** What products would be formed from the following reaction?

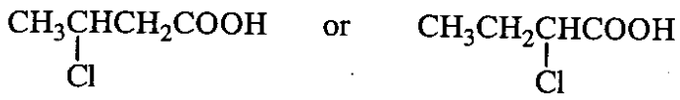
$CH_3OH + \overset{+}{N}H_4 \rightleftharpoons$

b. Does the reaction favor reactants or products?

9. **a.** What orbitals do carbon's electrons occupy before promotion?

b. What orbitals do carbon's electrons occupy after promotion?

10. Which of the following compounds is a stronger acid?



11. For each of the following compounds indicate the hybridization of the atom to which the arrow is pointing:



12. Indicate whether each of the following statements is true or false:

a. A pi bond is stronger than a sigma bond.	T	F
b. A triple bond is shorter than a double bond.	T	F
c. The oxygen-hydrogen bonds in water are formed by the overlap of an sp^2 orbital of oxygen with an *s* orbital of hydrogen.	T	F
d. HO^- is a stronger base than $^-NH_2$.	T	F
e. A double bond is stronger than a single bond.	T	F
f. A tetrahedral carbon has bond angles of 107.5°.	T	F
g. A Lewis acid is a compound that accepts a share in a pair of electrons.	T	F

ANSWERS TO ALL THE PRACTICE TESTS CAN BE FOUND AT THE END OF THE SOLUTIONS MANUAL

SPECIAL TOPIC I

pH, pK_a , and Buffers

This is a continuation of the discussion on acids and bases found in Section 1.16 - 1.21 on pages 39 - 55 of the text. Now we will see how the pH of solutions of acids and bases can be calculated. We will look at three different kinds of solutions.

1. A solution made by dissolving a strong acid or a strong base in water.
2. A solution made by dissolving a weak acid or a weak base in water.
3. A solution made by dissolving a weak acid and its conjugate base in water. Such a solution is known as a **buffer solution**.

Before we start, we need to review a few terms.

An acid is a compound that donates a proton, and a base is a compound that accepts a proton.

The degree to which an acid (HA) dissociates is described by its acid dissociation constant (K_a).

$$HA \rightleftharpoons H^+ + A^-$$

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

The strength of an acid can be indicated by its acid dissociation constant or by its pK_a value.

$$\mathbf{pK_a = -\log K_a}$$

The stronger the acid, the **larger** its dissociation constant and the **smaller** its pK_a value.

For example, an acid with a dissociation constant of 1×10^{-2} ($pK_a = 2$) is stronger than an acid with a dissociation constant of 1×10^{-4} ($pK_a = 4$).

While the pK_a scale is used to describe the strength of an acid, the pH scale is used to describe the acidity of a solution. In other words, the pH scale describes the concentration of hydrogen ions in a solution.

$$\mathbf{pH = -\log [H^+]}$$

The smaller the pH, the more acidic the solution. Acidic solutions have pH values < 7; a neutral solution has a pH = 7; basic solutions have pH values > 7.

A solution with a pH = 2 is more acidic than a solution with a pH = 4.
A solution with a pH = 12 is more basic than a solution with a pH = 8.

Determining the pH of a Solution

To determine the pH of a solution, the concentration of hydrogen ion $[H^+]$ in the solution must be determined.

Strong Acids

A strong acid is one that dissociates completely in solution. Strong acids have pK_a values < 1.

Because a strong acid dissociates completely, the concentration of hydrogen ions is the same as the concentration of the acid: a 1.0 M HCl solution contains 1.0 M $[H^+]$; a 1.5 M HCl solution contains 1.5 M $[H^+]$. Therefore, to determine the pH of a strong acid, the $[H^+]$ value does not have to be calculated; it is the same as the molarity of the strong acid.

solution	$[H^+]$	pH
1.0 M HCl	1.0 M	0
1.0×10^{-2} M HCl	1.0×10^{-2} M	2.0
6.4×10^{-4} M HCl	6.4×10^{-4} M	3.2

Strong Bases

Strong bases are compounds such as NaOH or KOH that dissociate completely in water.

Because they dissociate completely, the $[HO^-]$ is the same as the molarity of the strong base.

The pOH scale describes the basicity of a solution. The larger the pOH, the more basic the solution.

$$\mathbf{pOH = -\log [HO^-]}$$

$[HO^-]$ and $[H^+]$ are related by the water ionization constant (K_w).

$$\mathbf{K_w = [H^+]\,[HO^-] = 10^{-14}}$$
$$\mathbf{pH + pOH = 14}$$

solution	$[HO^-]$	pOH	pH
1.0 M NaOH	1.0 M	0	$14.0 - 0 = 14.0$
1.0×10^{-4} M NaOH	1.0×10^{-4} M	4.0	$14.0 - 4.0 = 10.0$
7.8×10^{-2} M NaOH	7.8×10^{-2} M	1.1	$14.0 - 1.1 = 12.9$

Weak Acids

A weak acid does not dissociate completely in solution. This means that $[H^+]$ must be calculated before the pH can be determined.

Acetic acid (CH_3COOH) is an example of a weak acid. It has an acid dissociation constant of 1.74×10^{-5} ($pK_a = 4.76$). The pH of a 1.00 M solution of acetic acid can be calculated as follows:

$$CH_3COOH \rightleftharpoons H^+ + CH_3COO^-$$

$$K_a = \frac{[H^+][CH_3COO^-]}{[CH_3COOH]}$$

Each molecule of acetic acid that dissociates forms one proton and one molecule of acetate ion. Thus the concentration of protons in solution equals the concentration of acetate ions. Each has a concentration that can be represented by x. The concentration of acetic acid therefore is whatever we started with minus x.

$$1.74 \times 10^{-5} = \frac{(x)(x)}{1.00 - x}$$

The denominator $(1.00 - x)$ can be simplified to 1.00 because 1.00 is much greater than x.

(When we actually calculate the value of x, we see that it is 0.004. And $1.00 - 0.004 = 1.00$.)

$$1.74 \times 10^{-5} = \frac{x^2}{1.00}$$

$$x = 4.17 \times 10^{-3}$$

$$pH = -\log 4.17 \times 10^{-3}$$

$$pH = 2.38$$

Formic acid (HCOOH) has a pK_a value of 3.75. The pH of a 1.50 M solution of formic acid can be calculated as follows:

A compound with a $pK_a = 3.75$ has an acid dissociation constant of 1.78×10^{-4}.

$$HCOOH \rightleftharpoons H^+ + HCOO^-$$

$$K_a = \frac{[H^+][HCOO^-]}{[HCOOH]}$$

$$1.78 \times 10^{-4} = \frac{(x)(x)}{1.50 - x} = \frac{x^2}{1.50}$$

$$x^2 = 2.67 \times 10^{-4}$$

$$x = 1.63 \times 10^{-2}$$

$$\text{pH} = -\log 1.63 \times 10^{-2}$$

$$\text{pH} = 1.79$$

Weak Bases

When a weak base is dissolved in water, it accepts a proton from water, creating hydroxide ion.

Determining the concentration of hydroxide allows the pOH to be determined, and this in turn allows the pH to be determined.

The pH of a 1.20 M solution of sodium acetate can be calculated as follows:

$$CH_3COO^- + H_2O \rightleftharpoons CH_3COOH + HO^-$$

$$\frac{K_W}{K_a} = \frac{[HO^-][CH_3COOH]}{[CH_3COO^-]}$$

$$\frac{1.00 \times 10^{-14}}{1.74 \times 10^{-5}} = \frac{(x)(x)}{1.20 - x}$$

$$5.75 \times 10^{-10} = \frac{x^2}{1.20}$$

$$x^2 = 6.86 \times 10^{-10}$$

$$x = 2.62 \times 10^{-5}$$

$$\text{pOH} = -\log 2.62 \times 10^{-5}$$

$$\text{pOH} = 4.58$$

$$\text{pH} = 14.00 - 4.58$$

$$\text{pH} = 9.42$$

Notice that by setting up the equation equal to K_W/K_a, we can avoid the introduction of a new term (K_b).

Buffer Solutions

A buffer solution is a solution that maintains nearly constant pH in spite of the addition of small amounts of H^+ or HO^-. That is because a buffer solution contains both a weak acid and its conjugate base. The weak acid can donate a proton to any HO^- added to the solution, and the conjugate base can accept any H^+ that is added to the solution, so the addition of HO^- or H^+ does not significantly change the pH of the solution.

(In order to maintain approximately constant pH, the amount of H^+ or HO^- added to the solution cannot exceed the concentration of the conjugate acid or base in the solution.)

A buffer can maintain nearly constant pH in a range of one pH unit on either side of the pK_a of the conjugate acid. For example, an acetic acid/sodium acetate mixture can be used as a buffer in the pH range 3.76 – 5.76 because acetic acid has a $pK_a = 4.76$; methylammonium ion/methylamine can be used as a buffer in the pH range 9.7 – 11.7 because the methylammonium ion has a $pK_a = 10.7$.

The pH of a buffer solution can be determined from the Henderson-Hasselbalch equation. This equation comes directly from the expression defining the acid dissociation constant. Its derivation is found on page 52 of the text.

Henderson-Hasselbalch equation

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

The pH of an acetic acid/sodium acetate buffer solution (pK_a of acetic acid = 4.76) that is 1.00 M in acetic acid and 0.50 M in sodium acetate is calculated as follows:

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

$$4.76 = pH + \log \frac{1.00}{0.50}$$

$$4.76 = pH + \log 2$$

$$4.76 = pH + 0.30$$

$$pH = 4.46$$

Remember from Section 1.20 that compounds exist primarily in their acidic forms in solutions that are more acidic than their pK_a's and primarily in their basic forms in solutions that are more basic than their pK_a's. Therefore, it could have been predicted that the above solution will have a pH less than the pK_a of acetic acid because there is more conjugate acid than conjugate base present in the solution.

There are three ways a buffer solution can be prepared:

1. Weak Acid and Weak Base

A buffer solution can be prepared by mixing a solution of a weak acid with a solution of its conjugate base.

The pH of a formic acid/sodium formate buffer (pK_a of formic acid = 3.75) solution prepared by mixing 25 mL of 0.10 M formic acid and 15 mL of 0.20 M sodium formate is calculated as follows:

$$\text{molarity} = \frac{\text{moles}}{\text{liters}} = \frac{\text{millimoles}}{\text{milliliters}}$$

The number of millimoles (mmol) of each of the buffer components can be determined by multiplying the number of milliliters (mL) by the molarity (M) .

$$25 \text{ mL} \times 0.10 \text{ M} = 2.5 \text{ mmol formic acid}$$

$$15 \text{ mL} \times 0.20 \text{ M} = 3.0 \text{ mmol sodium formate}$$

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

$$3.75 = pH + \log \frac{2.5}{3.0}$$

$$3.75 = pH + \log 0.83$$

$$3.75 = pH - 0.08$$

$$pH = 3.83$$

It could have been predicted that the above solution would have a pH greater than the pK_a of formic acid because there is more conjugate base than conjugate acid present in the solution.

2. Weak Acid and Strong Base

A buffer solution can be prepared by mixing a solution of a weak acid with a strong base such as NaOH. The NaOH reacts completely with the weak acid, thereby creating the conjugate base. For example, if 20 mmol of a weak acid and 5 mmol of a strong base are added to a solution, the 5 mmol of strong base will react with 5 mmol of weak acid, creating 5 mmol weak base and leaving behind 15 mmol of weak acid.

The pH of a solution prepared by mixing 10 mL of a 2.0 M solution of a weak acid with a pK_a of 5.86 with 5.0 mL of a 1.0 M solution of sodium hydroxide can be calculated as follows:

The formulas describing the fraction present in the acidic or basic form are obtained from the definition of the acid dissociation constant.

$$\text{fraction present in the acidic form} = \frac{[HA]}{[HA]+[A^-]}$$

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

$$[A^-] = \frac{K_a[HA]}{[H^+]}$$

$$\text{fraction present in the acidic form} = \frac{[HA]}{[HA]+[A^-]} = \frac{[HA]}{[HA]+\dfrac{K_a[HA]}{[H^+]}} = \frac{1}{1+\dfrac{K_a}{[H^+]}}$$

$$= \frac{[H^+]}{K_a+[H^+]}$$

$$\text{fraction present in the basic form} = \frac{[A^-]}{[HA]+[A^-]}$$

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

$$[HA] = \frac{[H^+][A^-]}{K_a}$$

$$\text{fraction present in the basic form} = \frac{[A^-]}{[HA]+[A^-]} = \frac{[A^-]}{[A^-]+\dfrac{[H^+][A^-]}{K_a}}$$

$$= \frac{1}{1+\dfrac{[H^+]}{K_a}}$$

$$= \frac{K_a}{K_a+[H^+]}$$

Preparing Buffer Solutions

The type of calculations discussed on pages 39-42 can be used to determine how to make a buffer solution.

For example, how can 100 mL of a 1.00 M buffer solution of pH = 4.24 be prepared if you have available to you 1.50 M solutions of acetic acid, sodium acetate, HCl, and NaOH?

acetic acid has a $pK_a = 4.76$

$$\text{fraction present in the acidic form at pH} = 4.24 = \frac{[H^+]}{K_a + [H^+]}$$

$$\frac{[H^+]}{K_a + [H^+]} = \frac{5.75 \times 10^{-5}}{1.74 \times 10^{-5} + 5.75 \times 10^{-5}}$$

$$= \frac{5.75 \times 10^{-5}}{7.49 \times 10^{-5}}$$

$$= 0.77$$

$$= \frac{5.75 \times 10^{-5}}{7.49 \times 10^{-5}}$$

$$= 0.77$$

If a 1.00 M buffer solution is desired, the buffer must be 0.77 M in acetic acid and 0.23 M in sodium acetate.

Recalling that

$$M = \frac{\text{moles}}{\text{liter}}$$

$$M = \frac{\text{millimoles}}{\text{milliliters}} = \frac{\text{mmol}}{\text{mL}}$$

The formulas describing the fraction present in the acidic or basic form are obtained from the definition of the acid dissociation constant.

$$\text{fraction present in the acidic form} = \frac{[HA]}{[HA]+[A^-]}$$

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

$$[A^-] = \frac{K_a[HA]}{[H^+]}$$

$$\text{fraction present in the acidic form} = \frac{[HA]}{[HA]+[A^-]} = \frac{[HA]}{[HA]+\dfrac{K_a[HA]}{[H^+]}} = \frac{1}{1+\dfrac{K_a}{[H^+]}}$$

$$= \frac{[H^+]}{K_a+[H^+]}$$

$$\text{fraction present in the basic form} = \frac{[A^-]}{[HA]+[A^-]}$$

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

$$[HA] = \frac{[H^+][A^-]}{K_a}$$

$$\text{fraction present in the basic form} = \frac{[A^-]}{[HA]+[A^-]} = \frac{[A^-]}{[A^-]+\dfrac{[H^+][A^-]}{K_a}}$$

$$= \frac{1}{1+\dfrac{[H^+]}{K_a}}$$

$$= \frac{K_a}{K_a+[H^+]}$$

There are three ways such a buffer solution can be prepared:

1. **By mixing the appropriate amounts of acetic acid and sodium acetate in water, and adding water to obtain a final volume of 100 mL.**

   The amount of acetic acid needed:

$$[CH_3COOH] = 0.77\ M$$

$$\frac{x\ \text{mmol}}{100\ \text{mL}} = 0.77\ M$$

$$x = 77\ \text{mmol}$$

Therefore, we need to have 77 mmol of acetic acid in the final solution.

To obtain 77 mmol of acetic acid from a 1.50 M solution of acetic acid:

$$\frac{77\ \text{mmol}}{y\ \text{mL}} = 1.50\ M$$

$$y = 51.3\ \text{mL}$$

Notice that the formula M = mmol/mL was used twice. The first time it was used to determine the number of mmol of acetic acid that was needed in the final solution. The second time it was used to determine how that number of mmol could be obtained from an acetic acid solution of a known concentration.

The amount of sodium acetate needed:

$$[CH_3COO^-] = 0.23\ M$$

$$\frac{x\ \text{mmol}}{100\ \text{mL}} = 0.23$$

$$x = 23\ \text{mmol}$$

To obtain 23 mmol of sodium acetate from a 1.50 M solution of sodium acetate:

$$\frac{23\ \text{mmol}}{y\ \text{mL}} = 1.50\ M$$

$$y = 15.3\ \text{mL}$$

The desired buffer solution can be prepared using:

51.3 mL 1.50 M acetic acid
15.3 mL 1.50 M sodium acetate
33.4 mL H_20

2. By mixing the appropriate amounts of acetic acid and sodium hydroxide, and adding water to obtain a final volume of 100 mL.

Sodium hydroxide is used to convert some of the acetic acid into sodium acetate. This means that acetic acid will be the source of both acetic acid and sodium acetate.

The concentrations needed are: $[CH_3COOH] = 1.00\ M$

$[NaOH] = 0.23\ M$

The amount of acetic acid needed:

$$[CH_3COOH] = 1.00\ M$$

$$\frac{x\ \text{mmol}}{100\ \text{mL}} = 1.00\ M$$

$$x = 100\ \text{mmol}$$

To obtain 100 mmol of acetic acid from a 1.50 M solution of acetic acid:

$$\frac{100\ \text{mmol}}{y\ \text{mL}} = 1.50\ M$$

$$y = 66.7\ \text{mL}$$

The amount of sodium hydroxide needed:

$$[NaOH] = 0.23\ M$$

$$\frac{x\ \text{mmol}}{100\ \text{mL}} = 0.23\ M$$

$$x = 23\ \text{mmol}$$

To obtain 23 mmol of sodium hydroxide from a 1.50 M solution of NaOH:

$$\frac{23\ \text{mmol}}{y\ \text{mL}} = 1.50\ M$$

$$y = 15.3\ \text{mL}$$

The desired buffer solution can be prepared using: 66.7 mL 1.50 M acetic acid
15.3 mL 1.50 M NaOH
18.0 mL H_2O

3. By mixing the appropriate amounts of sodium acetate and hydrochloric acid, and adding water to obtain a final volume of 100 mL.

Hydrochloric acid is used to convert some of the sodium acetate into acetic acid.

This means that sodium acetate will be the source of both acetic acid and sodium acetate.

The concentrations needed are: $[CH_3COONa] = 1.00\ M$

$[HCl] = 0.77\ M$

The amount of sodium acetate needed:

$$[CH_3COONa] = 1.00\ M$$

$$\frac{x\ \text{mmol}}{100\ \text{mL}} = 1.00\ M$$

$$x = 100\ \text{mmol}$$

To obtain 100 mmol of sodium acetate from a 1.50 M solution of sodium acetate:

$$\frac{100\ \text{mmol}}{y\ \text{mL}} = 1.5\ M$$

$$y = 66.7\ \text{mL}$$

The amount of hydrochloric acid needed:

$$[HCl] = 0.77\ M$$

$$\frac{x\ \text{mmol}}{100\ \text{mL}} = 0.77\ M$$

$$x = 77\ \text{mmol}$$

To obtain 77 mmol of hydrochloric acid from a 1.50 M solution of HCl:

$$\frac{77\ \text{mmol}}{y\ \text{mL}} = 1.50\ M$$

$$y = 51.3\ \text{mL}$$

100 mL of a 1.00 M acetic acid/acetate buffer cannot be made from these reagents, because the volumes needed (66.7 mL + 51.3 mL) add up to more than 100 mL. To make this buffer using sodium acetate and hydrochloric acid, you would need to use a more concentrated solution of sodium acetate or a more concentrated solution of HCl.

Problems on pH, pK_a, and Buffers

1. Calculate the pH of each of the following solutions.

a. 1×10^{-3} M HCl

b. 0.60 M HCl

c. 1.40×10^{-2} M HCl

d. 1×10^{-3} M KOH

e. 3.70×10^{-4} M NaOH

f. 1.20 M solution of an acid with a pK_a = 4.23

g. 1.60×10^{-2} M sodium acetate (pK_a of acetic acid = 4.76)

2. Calculate the pH of each of the following buffer solutions:

a. A buffer prepared by mixing 20 mL of 0.10 M formic acid and 15 mL of 0.50 M sodium formate (pK_a of formic acid = 3.75).

b. A buffer prepared by mixing 10 mL of 0.50 M aniline and 15 mL of 0.10 M HCl (pK_a of the anilinium ion = 4.60).

c. A buffer prepared by mixing 15 mL of 1.00 M acetic acid and 10 mL of 0.50 M NaOH (pK_a of acetic acid = 4.76).

3. What fraction of a carboxylic acid with pK_a = 5.23 would be ionized at pH = 4.98?

4. What would be the concentration of formic acid and sodium formate in a 1.00 M buffer solution with a pH = 3.12?

5. You have found a bottle labeled 1.00 M RCOOH. You want to determine what carboxylic acid it is, so you decide to determine its pK_a. How would you do this?

6. **a.** How would you prepare 100 mL of a buffer solution that is 0.30 M in acetic acid and 0.20 M in sodium acetate using a 1.00 M acetic acid solution and a 2.00 M sodium acetate solution?

b. The pK_a of acetic acid is 4.76. Would the pH of the above solution be greater or less than 4.76?

7. You have 100 mL of a 1.50 M acetic acid/sodium acetate buffer solution that has a pH = 4.90. How could you change the pH of the solution to 4.50?

8. You have 100 mL of a 1.00 M solution of an acid with a $pK_a = 5.62$ to which you add 10 mL of 1.00 M sodium hydroxide. What fraction of the acid will be in the acidic form? How much more sodium hydroxide will you need to add in order to have 40% of the acid in the acidic form?

9. Describe three ways to make a 1.00 M acetic acid/sodium acetate buffer solution with a pH = 4.00.

10. You have available to you 1.50 M solutions of acetic acid, sodium acetate, sodium hydroxide, and hydrochloric acid. How would you make 50 mL of each of the buffers described in the preceding problem?

11. How would you make a 1.0 M buffer solution with a pH = 3.30?

12. You are planning to carry out a reaction that will produce protons. In order for the reaction to take place at constant pH, it will be carried in a solution buffered at pH = 4.2. Would it be better to use a formic acid/formate buffer or an acetic acid/acetate buffer?

Answers to Problems on pH, pK_a, and Buffers

1.

a. $pH = -\log 1 \times 10^{-3}$

$pH = 3$

b. $pH = -\log 0.60$

$pH = 0.22$

c. $pH = -\log 1.40 \times 10^{-2}$

$pH = 1.85$

d. $pOH = -\log 1 \times 10^{-3}$

$pOH = 3$

$pH = 14 - 3 = 11$

e. $pOH = -\log 3.70 \times 10^{-4}$

$pOH = 3.43$

$pH = 10.57$

f. $pK_a = 4.23$, $K_a = 5.89 \times 10^{-5}$

$$K_a = \frac{[H^+][A^-]}{[HA]}$$

$$5.89 \times 10^{-5} = \frac{x^2}{1.20}$$

$$x^2 = 7.07 \times 10^{-5}$$

$$x = 8.41 \times 10^{-3}$$

$$pH = 2.08$$

g.

$$\frac{K_w}{K_a} = \frac{[HO^-][HA]}{[A^-]}$$

$$\frac{1.0 \times 10^{-14}}{1.74 \times 10^{-5}} = \frac{x^2}{1.60 \times 10^{-2}} \qquad (K_a = 10^{-4.76} = 1.74 \times 10^{-5}$$

$$5.75 \times 10^{-10} = \frac{x^2}{1.60 \times 10^{-2}}$$

$$x^2 = 9.20 \times 10^{-12}$$

$$x = 3.03 \times 10^{-6}$$

$$pOH = 5.52$$

$$pH = 14.00 - 5.52 = 8.48$$

2. **a.** formic acid: 20 mL x 0.10 M = 2.0 mmol
sodium formate: 15 mL x 0.50 M = 7.5 mmol

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

$$3.75 = pH + \log \frac{2.0}{7.5}$$

$$3.75 = pH + \log 0.27$$

$$3.75 = pH + (-0.57)$$

$$pH = 4.32$$

b. aniline: 10 mL x 0.50 = 5.0 mmol ⟶ 3.5 mmol aniline (RNH_2)

HCl: 15 mL x 0.10 = 1.5 mmol ⟶ 1.5 mmol anilinium hydrochloride ($R\overset{+}{N}H_3$)

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

$$4.60 = pH + \log \frac{1.5}{3.5}$$

$$4.60 = pH + \log 0.43$$

$$4.60 = pH + (-0.37)$$

$$pH = 4.97$$

c. acetic acid: 15 mL x 1.00 = 15 mmol ⟶ 10 mmol acetic acid

NaOH: 10 mL x 0.50 = 5.0 mmol ⟶ 5.0 mmol sodium acetate

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

$$4.76 = pH + \log \frac{10}{5.0}$$

$$4.76 = pH + \log 2$$

$$4.76 = pH + 0.30$$

$$pH = 4.46$$

3. The ionized form is the basic form.

$$\frac{K_a}{K_a + [H^+]} = \frac{5.89 \times 10^{-6}}{5.89 \times 10^{-6} + 10.47 \times 10^{-6}} = \frac{5.89 \times 10^{-6}}{16.36 \times 10^{-6}}$$

$$= 0.36$$

4.

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

$$3.75 = 3.12 + \log \frac{[HA]}{[A^-]}$$

$$0.63 = \log \frac{[HA]}{[A^-]}$$

$$4.27 = \frac{[HA]}{[A^-]}$$

$$[HA] = 4.27[A^-]$$

$$[HA] + [A^-] = 1.0\ M$$

$$4.27[A^-] + [A^-] = 1.0\ M$$

$$5.27[A^-] = 1.0\ M$$

$$[A^-] = 0.19\ M$$

$$[\text{sodium formate}] = 0.19\ M$$

$$[\text{formic acid}] = 0.81\ M$$

5.

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

when $[HA] = [A^-]$,

$$pK_a = pH$$

Preparing a solution of x mmol of RCOOH and 1/2 x mmol NaOH will give a solution in which $[RCOOH] = [RCOO^-]$.

For example: 20 mL of 1.00 M RCOOH = 20 mmol
10 mL of 1.00 M NaOH = 10 mmol

This will give a solution that has 10 mmol RCOOH and 10 mmol $RCOO^-$.

The pH of this solution is the pK_a of RCOOH.

6. **a.**

$$\frac{x \text{ mmol}}{100 \text{ mL}} = 0.30 \text{ M} \qquad \frac{x \text{ mmol}}{100 \text{ mL}} = 0.20 \text{ M}$$

x = 30 mmol of acetic acid $\qquad$ x = 20 mmol of sodium acetate

$$\frac{30 \text{ mmol}}{y \text{ mL}} = 1.00 \text{ M} \qquad \frac{20 \text{ mmol}}{y \text{ mL}} = 2.00 \text{ M}$$

y = 30 mL of 1.00 M acetic acid $\qquad$ y = 10 mL of 2.00 M acetic acid

The buffer solution could be prepared by mixing: 30 mL of 1.00 M acetic acid
10 mL of 2.00 M sodium acetate
60 mL of water

b. Because the concentration of buffer in the acidic form (0.30 M) is greater than the concentration of buffer in the basic form (0.20 M), the pH of the solution will be less than 4.76.

7.

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

original solution

$$4.76 = 4.90 + \log \frac{[HA]}{[A^-]}$$

$$-0.14 = \log \frac{[HA]}{[A^-]}$$

$$0.72 = \frac{[HA]}{[A^-]}$$

$$[HA] = 0.72[A^-]$$

$$[HA] + [A^-] = 1.50 \text{ M}$$

$$0.72[A^-] + [A^-] = 1.50 \text{ M}$$

$$1.72[A^-] = 1.50 \text{ M}$$

$$[A^-] = 0.87 \text{ M}$$

$$[HA] = 0.63 \text{ M}$$

desired solution

$$4.76 = 4.50 + \log \frac{[HA]}{[A^-]}$$

$$0.26 = \log \frac{[HA]}{[A^-]}$$

$$1.82 = \frac{[HA]}{[A^-]}$$

$$[HA] = 1.82[A^-]$$

$$[HA] + [A^-] = 1.50\ M$$

$$1.82[A^-] + [A^-] = 1.50\ M$$

$$2.82[A^-] = 1.50\ M$$

$$[A^-] = 0.53\ M$$

$$[HA] = 0.97\ M$$

The original solution contains 87 mmol of A^- (100 mL x 0.87 M).
The desired solution with a pH = 4.50 must contain 53 mmol of A^-.
Therefore, 34 mmol of A^- (87 – 53 = 34) must be converted to HA.
This can be done by adding 34 mmol of HCl to the original solution.

If you have a 1.00 M HCl solution, you will need to add 34 mL to the original solution in order to change its pH from 4.90 to 4.50.

$$\frac{34\ mmol}{x\ mL} = 1.00\ M$$

$$x = 34\ mL$$

Note that after adding HCl to the original solution, it will no longer be a 1.50 M buffer; it will be more dilute (150 mm/134 mL = 1.12 M).

The change in the concentration of the buffer solution will be less if a more concentrated solution of HCl is used to change the pH. If you have a 2.00 M HCl solution:

$$\frac{34\ mmol}{x\ mL} = 2.00\ M$$

$$x = 17\ mL$$

You will need to add 17 mL to the original solution, and the concentration of buffer species will be 1.28 M (150 mm/117 mL = 1.28 M).

8.

acid: 100 mL x 1.00 = 100 mmol ⟶ 90 mmol HA

NaOH: 10 mL x 1.00 = 10 mmol ⟶ 10 mmol A^-

Therefore, 90% is in the acidic form.

For 40% to be in the acidic form you need:

40 mmol HA

60 mmol A^-

You need to have 60 mmol rather than 10 mmol in the basic form. To get the additional 50 mmol in the basic form, you would need to add 50 mL of 1.0 M NaOH.

9.

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

$$4.76 = 4.00 + \log \frac{[HA]}{[A^-]}$$

$$0.76 = \log \frac{[HA]}{[A^-]}$$

$$5.75 = \frac{[HA]}{[A^-]}$$ now take the antilog of both sides

$$[HA] = 5.75[A^-]$$

$$[HA] + [A^-] = 1.0\ M$$

$$5.75[A^-] + [A^-] = 1.0\ M$$

$$6.75[A^-] = 1.0\ M$$

$$[A^-] = 0.15\ M$$

$$[HA] = 0.85\ M$$

a.

[acetic acid] = 0.85 M

[sodium acetate] = 0.15 M

b.

[acetic acid] = 1.00 M

[NaOH] = 0.15 M

c.

[sodium acetate] = 1.00 M

[HCl] = 0.85 M

10. a.

$$\frac{x \text{ mmol}}{50 \text{ mL}} = 0.85 \text{ M}$$

$$x = 42.5 \text{ mmol of acetic acid}$$

$$\frac{42.4 \text{ mmol}}{y \text{ mL}} = 1.50 \text{ M}$$

$$y = 28.3 \text{ mL of 1.50 M acetic acid}$$

$$\frac{x \text{ mmol}}{50 \text{ mL}} = 0.15 \text{ M}$$

$$x = 7.5 \text{ mmol of sodium acetate}$$

$$\frac{7.5 \text{ mmol}}{y \text{ mL}} = 1.50 \text{ M}$$

$$y = 5.0 \text{ mL of 1.50 M sodium acetate}$$

28.3 mL of 1.50 M acetic acid
5.0 mL of 1.50 M sodium acetate
16.7 mL of H_2O

b.

$$\frac{x \text{ mmol}}{50 \text{ mL}} = 1.00 \text{ M}$$

$$x = 50 \text{ mmol of acetic acid}$$

$$\frac{50 \text{ mmol}}{y \text{ mL}} = 1.50 \text{ M}$$

$$y = 33.3 \text{ mL of 1.50 M acetic acid}$$

$$\frac{x \text{ mmol}}{50 \text{ mL}} = 0.15 \text{ M}$$

$$x = 7.5 \text{ mmol of NaOH}$$

$$\frac{7.5 \text{ mmol}}{y \text{ mL}} = 1.50 \text{ M}$$

$$y = 5.0 \text{ mL of 1.50 M NaOH}$$

33.3 mL of 1.50 M acetic acid
5.0 mL of 1.50 M NaOH
11.7 mL of H_2O

c.

$$\frac{x \text{ mmol}}{50 \text{ mL}} = 1.00 \text{ M}$$

$$x = 50 \text{ mmol of sodium acetate}$$

$$\frac{50 \text{ mmol}}{y \text{ mL}} = 1.50 \text{ M}$$

$$y = 33.3 \text{ mL of } 1.50 \text{ M sodium acetate}$$

$$\frac{x \text{ mmol}}{50 \text{ mL}} = 0.85 \text{ M}$$

$$x = 42.5 \text{ mm}$$

$$\frac{42.5 \text{ mmol}}{y \text{ mL}} = 1.5 \text{ M}$$

$$y = 28.3 \text{ mL of } 1.5 \text{ M HCl}$$

We cannot make the required buffer with these solutions, because 33.3 mL + 28.3 mL > 50 mL.

11. Because formic acid has a $pK_a = 3.75$, a formic acid/formate buffer can be a buffer at pH = 3.30.

$$pK_a = pH + \log \frac{[HA]}{[A^-]}$$

$$3.75 = 3.30 + \log \frac{[HA]}{[A^-]}$$

$$0.45 = \log \frac{[HA]}{[A^-]}$$

$$2.82 = \frac{[HA]}{[A^-]}$$

$$[HA] = 2.82[A^-]$$

$$[HA] + [A^-] = 1.0 \text{ M}$$

$$2.82[A^-] + [A^-] = 1.0 \text{ M}$$

$$3.82[A^-] = 1.0 \text{ M}$$

$$[A^-] = 0.26\ M$$
$$[HA] = 0.74\ M$$

The solution must have [formic acid] = 0.74 M and [sodium formate] = 0.26 M.

12. At pH = 4.20, 74% of the formate buffer will be in the basic form.

pH = 4.20, $[H^+] = 6.31 \times 10^{-5}$ Formic acid has a $pK_a = 3.75$, $K_a = 1.78 \times 10^{-4}$.

$$\frac{K_a}{K_a + [H^+]} = \frac{1.78 \times 10^{-4}}{1.78 \times 10^{-4} + 6.31 \times 10^{-5}} = \frac{1.78 \times 10^{-4}}{1.78 \times 10^{-4} + 0.63 \times 10^{-4}}$$

$$= \frac{1.78 \times 10^{-4}}{2.41 \times 10^{-4}}$$

$$= 0.74$$

At pH = 4.20, 22% of the acetate buffer will be in the basic form.

pH = 4.20, $[H^+] = 6.31 \times 10^{-5}$ Acetic acid has a $pK_a = 4.76$, $K_a = 1.74 \times 10^{-5}$.

$$\frac{K_a}{K_a + [H^+]} = \frac{1.74 \times 10^{-5}}{1.74 \times 10^{-5} + 6.31 \times 10^{-5}}$$

$$= \frac{1.78 \times 10^{-5}}{8.05 \times 10^{-5}}$$

$$= 0.22$$

The reaction to be carried out will generate protons that will react with the basic form of the buffer in order to keep the pH constant. Therefore, the formate buffer is preferred because it has a greater percentage of the buffer in the basic form.

CHAPTER 2
An Introduction to Organic Compounds: Nomenclature, Physical Properties, and Representation of Structure

Important Terms

alcohol — a compound with an OH group in place of one of the hydrogens of an alkane (ROH).

alkane — a hydrocarbon that contains only single bonds.

alkyl halide — a compound with a halogen in place of one of the hydrogens of an alkane.

alkyl substituent — a substituent formed by removing a hydrogen from an alkane.

amine — a compound in which one or more of the hydrogens of NH_3 is replaced by an alkyl substituent (RNH_2, R_2NH, R_3N).

angle strain — the strain introduced into a molecule as a result of its bond angles being distorted from their ideal values.

anti conformer — the staggered conformer in which the largest substituents bonded to the tw carbons are opposite each other. It is the most stable of the staggered conformers.

axial bond — a bond of the chair form of cyclohexane that is perpendicular to the plane in which the chair is drawn (an up-down bond).

banana bonds — the bonds in small rings that are slightly bent as a result of orbitals overlapping at an angle rather than overlapping head-on.

boat conformation — the conformation of cyclohexane that roughly resembles a boat.

boiling point — the temperature at which the vapor pressure of a liquid equals the atmospheric pressure.

chair conformation — the conformation of cyclohexane that roughly resembles a chair. It is the most stable conformation of cyclohexane.

cis fused — two rings fused together in such a way that if the second ring were considered to be two substituents of the first ring, the two substituents would be on the same side of the first ring.

cis isomer — the isomer with both hydrogens on the same side of the double bond.

cis-trans stereoisomers (geometric isomers) — geometric (or *E*, *Z*) isomers.

common name — nonsystematic nomenclature.

conformation — the three-dimensional shape of a molecule at a given instant.

conformational analysis — the investigation of various conformations of a compound and their relative stabilities.

conformers different conformations of a molecule.

constitutional isomers (structural isomers) molecules that have the same molecular formula but differ in the way the atoms are connected.

cycloalkane an alkane with its carbon chain arranged in a closed ring.

1,3-diaxial interaction the interaction between an axial substituent and the other two axial substituents on the same side of the cyclohexane ring.

dipole-dipole interaction an interaction between the dipole of one molecule and the dipole of another.

eclipsed conformation a conformation in which the bonds on adjacent carbons are parallel to each other as viewed looking down the carbon-carbon bond.

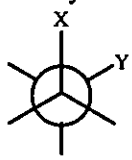
equatorial bond a bond of the chair form of cyclohexane that juts out from the ring in approximately the same plane that contains the chair.

ether a compound in which an oxygen is bonded to two alkyl groups (ROR).

flagpole hydrogens the two hydrogens in the boat conformation of cyclohexane that are closest to each other.

functional group the center of reactivity of a molecule.

gauche conformer a staggered conformer in which the largest substituents bonded to the two carbons are gauche to each other; i.e., they have a dihedral angle of approximately 60°.



The substituents are gauche to each other.

gauche interaction the interaction between two atoms or groups that are gauche to each other.

geometric isomers (cis-trans stereoisomers) cis-trans (or *E*, *Z*) isomers.

half-chair conformer the least stable conformation of cyclohexane.

homolog a member of a homologous series.

homologous series a family of compounds in which each member differs from the next by one methylene group.

hydrocarbon a compound that contains only carbon and hydrogen.

hydrogen bond an unusually strong dipole-dipole attraction (5 kcal/mol) between a hydrogen bonded to O, N, or F and the lone pair of a different O, N, or F.

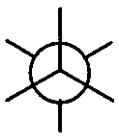
induced dipole-induced dipole interaction an interaction between a temporary dipole in one molecule and the dipole that the temporary dipole induces in another molecule.

IUPAC nomenclature	systematic nomenclature.
melting point	the temperature at which a solid becomes a liquid.
methylene group	a CH_2 group.
Newman projection	a way to represent the three-dimensional spatial relationships of atoms by looking down the length of a particular carbon-carbon bond.
packing	the property that determines how well individual molecules fit into a crystal lattice.
parent hydrocarbon	the longest continuous carbon chain in a molecule.
perspective formula	a way to represent the three-dimensional spatial relationships of atoms using two adjacent solid lines, one solid wedge and one hatched wedge.
polarizability	the ease with which an electron cloud of an atom can be distorted.
primary alcohol	an alcohol in which the OH group is bonded to a primary carbon.
primary alkyl halide	an alkyl halide in which the halogen is bonded to a primary carbon.
primary amine	an amine with one alkyl group bonded to the nitrogen.
primary carbon	a carbon bonded to only one other carbon.
primary hydrogen	a hydrogen bonded to a primary carbon.
quaternary ammonium salt	a nitrogen compound with four alkyl groups bonded to the nitrogen.
ring-flip (chair-chair interconversion)	the conversion of a chair conformer of cyclohexane into the other chair conformer. Bonds that are axial in one chair conformer are equatorial in th other chair conformer.
sawhorse projection	a way to represent the three-dimensional spatial relationships of atoms by looking at the carbon-carbon bond from an oblique angle.
secondary alcohol	an alcohol in which the OH group is bonded to a secondary carbon.
secondary alkyl halide	an alkyl halide in which the halogen is bonded to a secondary carbon.
secondary amine	an amine with two alkyl groups bonded to the nitrogen.
secondary carbon	a carbon bonded to two other carbons.
secondary hydrogen	a hydrogen bonded to a secondary carbon.
skeletal structure	a structure that shows the carbon-carbon bonds as lines and does not show the carbon-hydrogen bonds.
skew-boat conformer	one of the conformations of a cyclohexane ring.

solubility the extent to which a compound dissolves in a solvent.

solvation the interaction between a solvent and another molecule (or ion).

staggered conformation a conformation in which the bonds on one carbon bisect the bond angle on the adjacent carbon when viewed looking down the carbon-carbon bond.



steric hindrance hindrance due to groups occupying a volume of space.

steric strain the repulsion between the electron cloud of an atom or group of atoms and the electron cloud of another atom or group of atoms.

straight-chain alkane an alkane in which the carbons form a continuous chain with no branches.

structural isomers (constitutional isomers) molecules that have the same molecular formula but differ in the way the atoms are connected.

symmetrical ether an ether with two identical substituents bonded to the oxygen.

systematic nomenclature IUPAC nomenclature.

tertiary alcohol an alcohol in which the OH group is bonded to a tertiary carbon.

tertiary alkyl halide an alkyl halide in which the halogen is bonded to a tertiary carbon.

tertiary amine an amine with three alkyl groups bonded to the nitrogen.

tertiary carbon a carbon bonded to three other carbons.

tertiary hydrogen a hydrogen bonded to a tertiary carbon.

torsional strain the repulsion felt by the bonding electrons of one substituent as they pass close to the bonding electrons of another substituent.

trans-fused two rings fused together in such a way that if the second ring were considered to be two substituents of the first ring, the two substituents would be on opposite sides of the first ring.

trans isomer the isomer that has the hydrogens on opposite sides of the double bond.

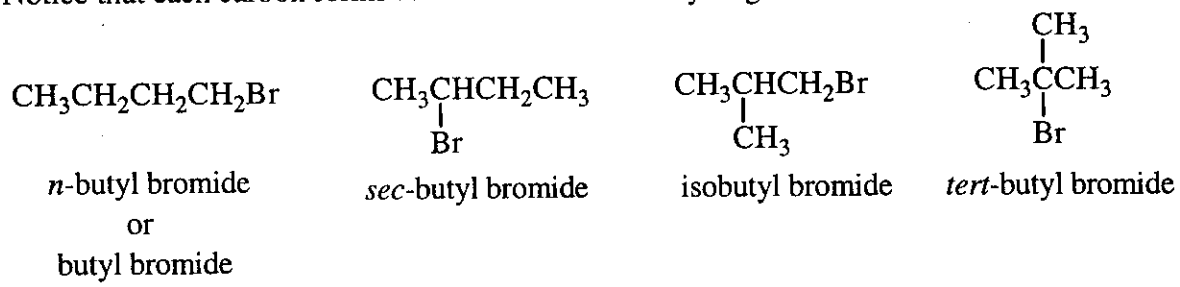
twist-boat conformer one of the conformations of a cyclohexane ring.

unsymmetrical ether an ether with two different substituents bonded to the oxygen.

van der Waals forces induced dipole-induced dipole interactions.

Solutions to Problems

1. Notice that each carbon forms fours bonds and each hydrogen and bromine forms one bond.



n-butyl bromide or butyl bromide

sec-butyl bromide

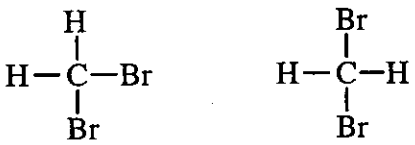
isobutyl bromide

tert-butyl bromide

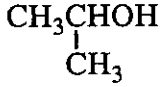
2. Dibromomethane does not have constitutional isomers.

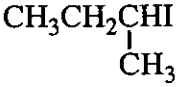
If carbon were flat, the two structures shown below would be different, because the Br's would be 90° apart in one compound and 180° apart in the other compound.

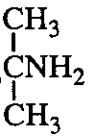
Because carbon is tetrahedral, the two structures are identical.

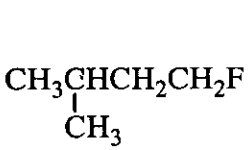


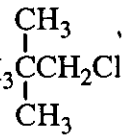
3.

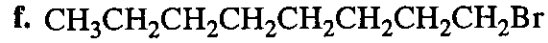
a. 

c. 

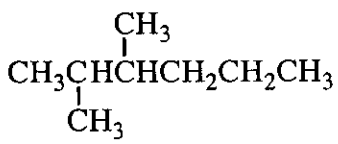
e. 

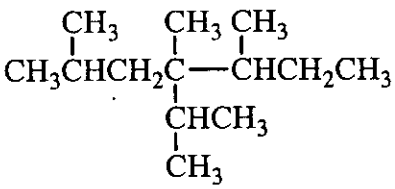
b. 

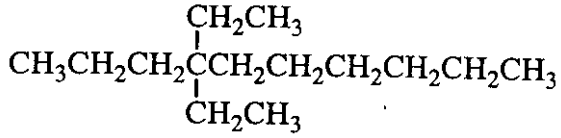
d. 

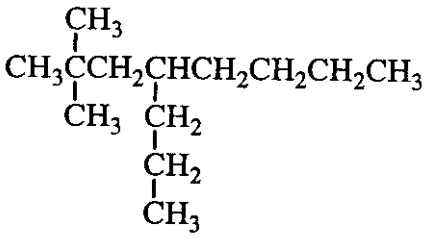
f. 

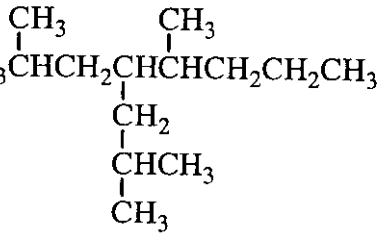
4.

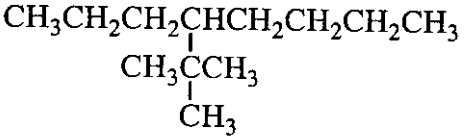
a. 

b. 

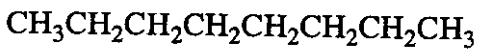
c. 

d. 

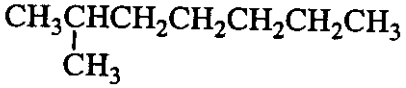
e. 

f. 

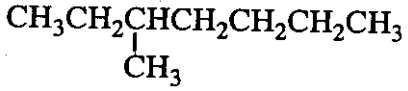
5. a.

#1 

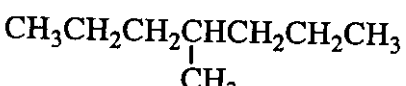
octane

#2 

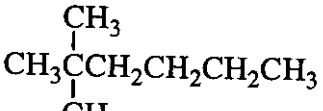
2-methylheptane

#3 

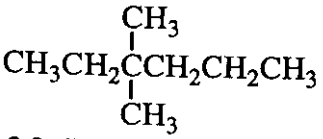
3-methylheptane

#4 

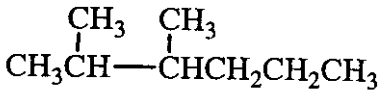
4-methylheptane

#5 

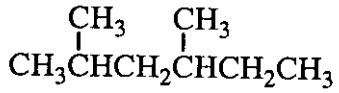
2,2-dimethylhexane

#6 

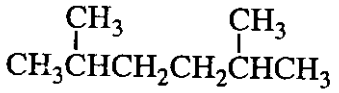
3,3-dimethylhexane

#7 

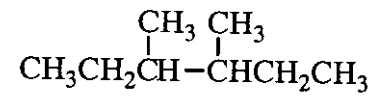
2,3-dimethylhexane

#8 

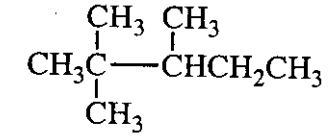
2, 4-dimethylhexane

#9 

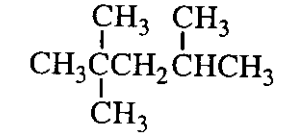
2,5-dimethylhexane

#10 

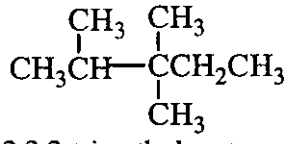
3,4-dimethylhexane

#11 

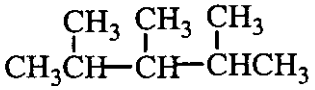
2,2,3-trimethylpentane

#12 

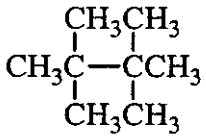
2,2,4-trimethylpentane

#13 

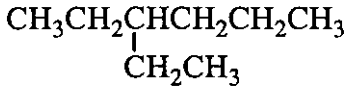
2,3,3-trimethylpentane

#14 

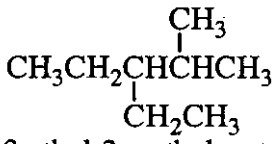
2,3,4-trimethylpentane

#15 

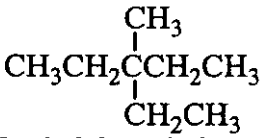
2,2,3,3-tetramethylbutane

#16 

3-ethylhexane

#17 

3-ethyl-2-methylpentane

#18 

3-ethyl-3-methylpentane

b. The systematic names are under the compound.

c. Only #1 (*n*-octane) and #2 (isooctane) have common names.

d. #2, #7, #8, #9, #12, #13, #14, #17

e. #3, #8, #10, #11

f. #5, #11, #12, #15

6.

a. 2,2,4-trimethylhexane

b. 2,2-dimethylbutane

c. 3,3-diethylhexane

d. 2,5-dimethylheptane

e. 3,3-diethyl-4-methyl-5-propyloctane

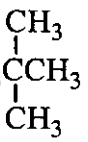
f. 3-methyl-4-propylheptane

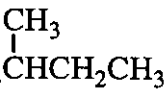
g. 5-ethyl-4,4-dimethyloctane

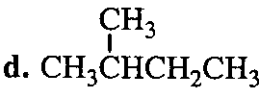
h. 4-isopropyloctane

7.

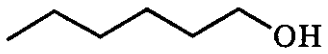
a. $CH_3CH_2CH_2CH_2CH_3$ pentane

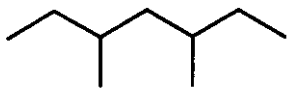
b.  2,2-dimethylpropane

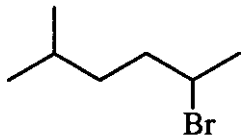
c.  2-methylbutane

d.  2-methylbutane

8.

a. 

b. 

c. 

d. 

9.

a. 1-ethyl-2-methylcyclopentane

b. ethylcyclobutane

c. 4-ethyl-1,2-dimethylcyclohexane

d. 3,6-dimethyldecane

e. 2-cyclopropylpentane

f. 1-ethyl-3-isobutylcyclohexane

g. 5-isopropylnonane

h. 1-*sec*-butyl-4-isopropylcyclohexane

10.

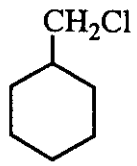
a. *sec*-butyl chloride
2-chlorobutane
secondary

b. isohexyl chloride
1-chloro-4-methylpentane
primary

c. cyclohexyl bromide
bromocyclohexane
secondary

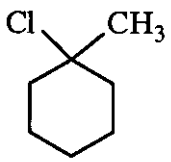
d. isopropyl fluoride
2-fluoropropane
secondary

11.

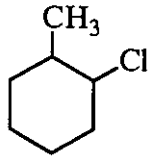
a. 

chloromethylcyclohexane

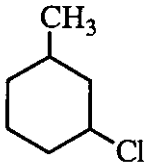
Note that the name of a $-CH_2Cl$ substituent is "chloromethyl", because a Cl is in place of one of the H's of a methyl substituent.

b. 

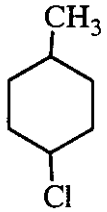
1-chloro-1-methylcyclohexane

c. 

1-chloro-2-methylcyclohexane



1-chloro-3-methylcyclohexane



1-chloro-4-methylcyclohexane

12. **a.**

1. methoxyethane
2. ethoxyethane
3. 4-methoxyoctane
4. 1-propoxybutane
5. 2-isopropoxypentane
6. 1-isopropoxy-3-methylbutane

b. No.

c.

1. ethyl methyl ether
2. diethyl ether
3. no common name
4. butyl propyl ether
5. no common name
6. isopentyl isopropyl ether

13.

CH_3OH
common = methyl alcohol
systematic = methanol

CH_3CH_2OH
common = ethyl alcohol
systematic = ethanol

$CH_3CH_2CH_2OH$
common = propyl alcohol or *n*-propyl alcohol
systematic = 1-propanol

$CH_3CH_2CH_2CH_2OH$
common = butyl alcohol or *n*-butyl alcohol
systematic = 1-butanol

$CH_3CH_2CH_2CH_2CH_2OH$
common = pentyl alcohol or *n*-pentyl alcohol
systematic = 1-pentanol

$CH_3CH_2CH_2CH_2CH_2CH_2OH$
common = hexyl alcohol or *n*-hexyl alcohol
systematic = 1-hexanol

14.

a. 1-pentanol
primary

b. 4-methylcyclohexanol
secondary

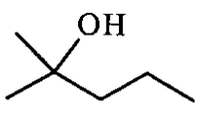
c. 5-chloro-2-methyl-2-pentanol
tertiary

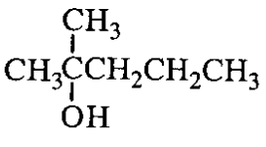
d. 5-methyl-3-hexanol
secondary

e. 2,6-dimethyl-4-octanol
secondary

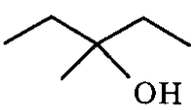
f. 4-chloro-3-ethylcyclohexanol
secondary

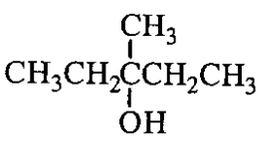
15.



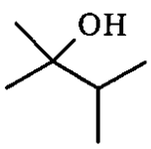


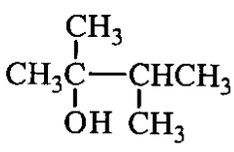
2-methyl-2-pentanol





3-methyl-3-pentanol





2,3-dimethyl-2-butanol

16. **a.** hexylamine
1-hexanamine

b. butylpropylamine
N-propyl-1-butanamine

c. *sec*-butylisobutylamine
N-isobutyl-2-butanamine (notice that the longest continuous chain has 4 carbons)

d. diethylpropylamine
N,N-diethyl-1-propanamine

e. cyclohexylamine
cyclohexanamine

17.

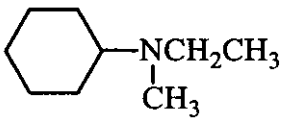
a. $CH_3CH_2CH_2NHCH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_3$

b. $CH_3CH_2NHCH_2CH_3$

c. $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH_2CH_2CH_2NH_2$

d. $CH_3CH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{N}}CH_2CH_2CH_3$

e. $CH_3CH_2\underset{\displaystyle H_3C\diagdown\ \diagup CH_3}{\underset{|}{\overset{\displaystyle N}{}}}CHCH_2CH_3$

f. 

18. **a.** 6-methyl-1-heptanamine
isooctylamine
primary

b. 3-methyl-*N*-propyl-1-butanamine
isopentylpropylamine
secondary

c. *N*-ethyl-*N*-methylethanamine
diethylmethylamine
tertiary

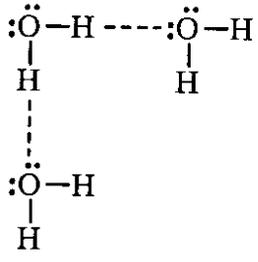
d. 2,5-dimethylcyclohexanamine
no common name
primary

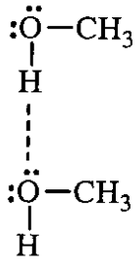
19. **a.** The bond angle is predicted to be similar to the bond angle in water (104.5°)
b. The bond angle is predicted to be similar to the bond angle in ammonia (107.3°)
c. The bond angle is predicted to be similar to the bond angle in water (104.5°)
d. The bond angle is predicted to be similar to the bond angle in the ammonium ion (109.5°)

20. **a.** 1, 4, and 5

b. 1, 2, 4, 5, and 6

21. **a.** Each water molecule has two hydrogens that can form hydrogen bonds, whereas each alcohol molecule has only one hydrogen that can form a hydrogen bond. Therefore, there are more hydrogen bonds between water molecules than between alcohol molecules.

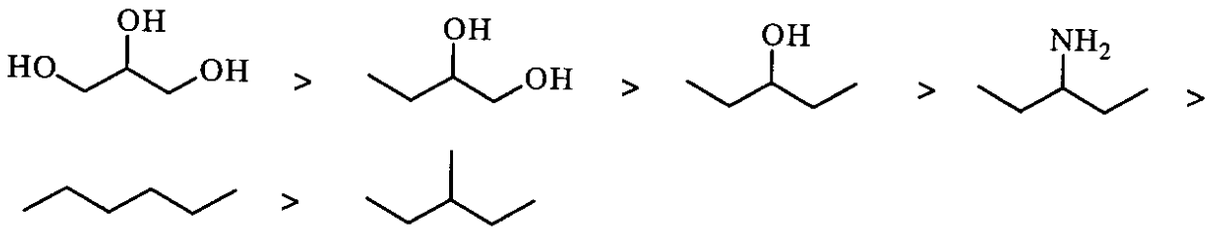




b. Each water molecule has two hydrogens that can form hydrogen bonds, whereas each ammonia has three hydrogens that can form hydrogen bonds. However, oxygen is more electronegative than nitrogen, so the hydrogen bonds between water molecules are stronger than the hydrogen bonds between ammonia molecules. Because the number of hydrogen bonds supports ammonia as having the higher boiling point but the strength of the hydrogen bonds supports water, we could not have predicted which would have the higher boiling point. However, being told that water has the higher boiling point we can conclude that the greater electronegativity of oxygen compared to nitrogen is more important than the number of hydrogens that can form hydrogen bonds.

c. Each water molecule has two hydrogens that can form hydrogen bonds, whereas each molecule of hydrogen fluoride has only one hydrogen that can form a hydrogen bond. However, fluorine is more electronegative than oxygen. Again we cannot predict which will have the higher boiling point, but we can conclude from the fact that water has the higher boiling point that *in this case* the greater number of hydrogens that can form hydrogen bonds is more important than the greater electronegativity of fluorine compared to oxygen.

22.



23.

a. $CH_3CH_2CH_2CH_2CH_2CH_2Br$ > $CH_3CH_2CH_2CH_2CH_2Br$ > $CH_3CH_2CH_2CH_2Br$

b. $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ > $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ >

$CH_3CHCH_2CH_2CH_2CH_2CH_3$ > $CH_3C(CH_3)_2C(CH_3)_3$

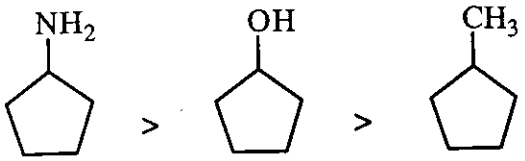
c. $CH_3CH_2CH_2CH_2CH_2OH$ > $CH_3CH_2CH_2CH_2OH$ > $CH_3CH_2CH_2CH_2Cl$ >

$CH_3CH_2CH_2CH_2CH_3$

24.

a. $HOCH_2CH_2CH_2OH > CH_3CH_2CH_2OH > CH_3CH_2CH_2CH_2OH > CH_3CH_2CH_2CH_2Cl$

b.



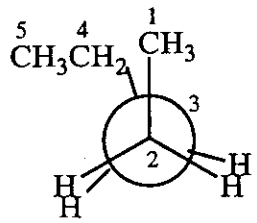
The amine is more soluble in water than the alcohol, because the amine has two hydrogens that can form hydrogen bonds with water.

25. Because cyclohexane is a nonpolar compound it will have the lowest solubility in the most polar solvent, which, of the solvents given, is ethanol.

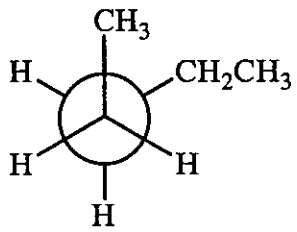
$CH_3CH_2CH_2CH_2CH_2OH$	$CH_3CH_2OCH_2CH_3$	CH_3CH_2OH	$CH_3CH_2CH_2CH_2CH_2CH_3$
1-pentanol	diethyl ether	ethanol	hexane

26.

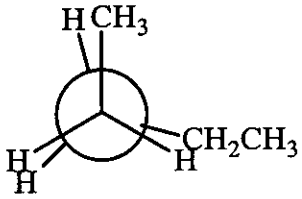
a.



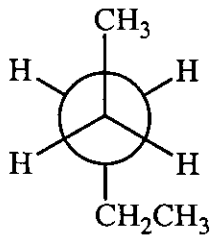
A



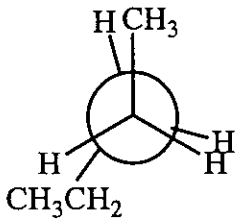
B



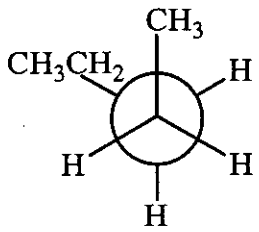
C



D

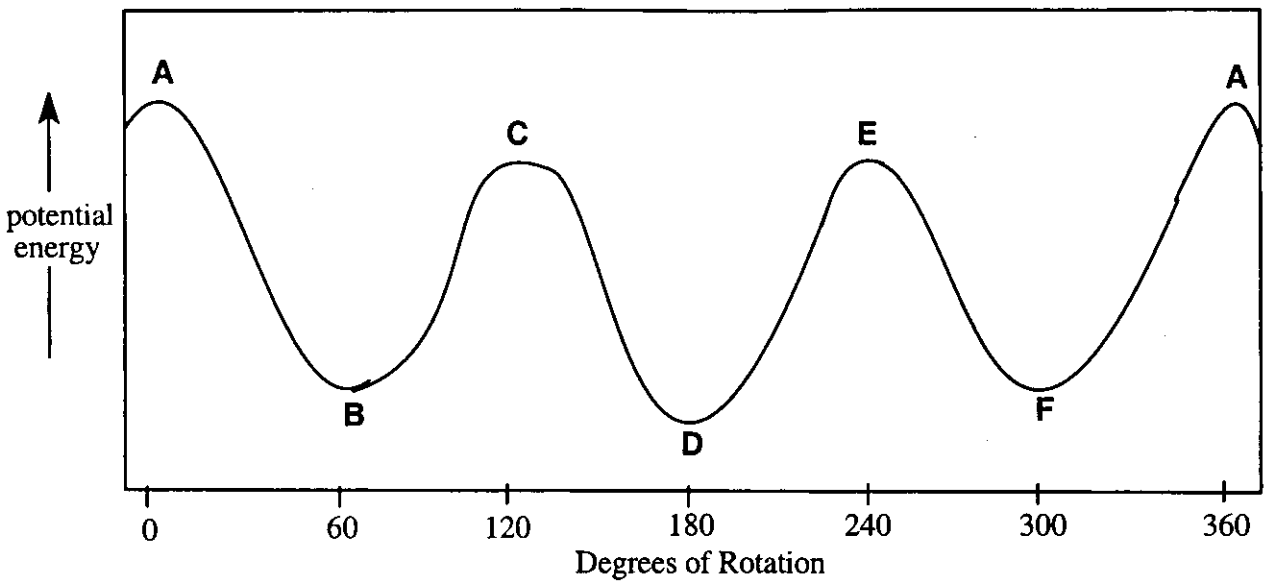


E



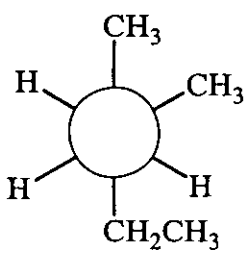
F

b.

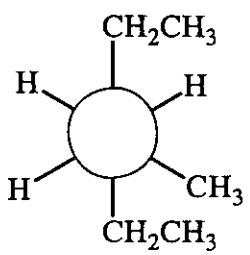


27.

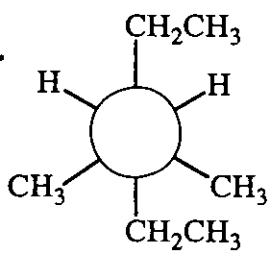
a.



b.



c.



28.

a. $180^\circ - \frac{360^\circ}{8}$

$180^\circ - 45^\circ = 135^\circ$

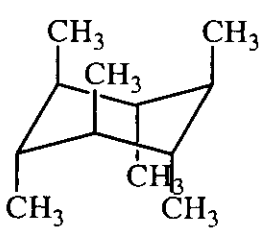
b. $180^\circ - \frac{360^\circ}{9}$

$180^\circ - 40^\circ = 140^\circ$

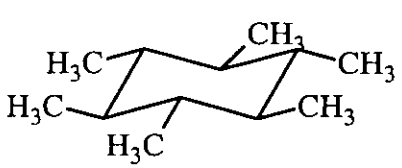
29. Hexethal would be expected to be the more effective sedative because it is more nonpolar than barbital since hexethal has a hexyl group in place of the ethyl group of barbital. Being more nonpolar, hexethal will be better able to penetrate the nonpolar membrane of the cell.

30.

a.



b.



31. The "strainless" heat of formation of cycloheptane is 7 (- 4.92) = - 34.4 kcal/mol
The actual heat of formation of cycloheptane is - 28.2 kcal/mol (from Table 2.9 on p. 96 of the text.)

You can get the total strain energy of cycloheptane by subtracting the strainless heat of formation from the actual heat of formation: - 28.2 - (- 34.4) = 6.2 kcal/mol

32. Two 1,3-diaxial (gauche) interactions cause the chair conformer of fluorocyclohexane to be 0.25 kcal/mol less stable when the fluoro substituent is in the axial position than when it is in the equatorial position.
The gauche conformer of 1-fluoropropane has one gauche interaction (See Figure 2.14 on p. 99 the text). Therefore, the gauche conformer is (0.25/2) = 0.13 kcal/mol more stable than the anti conformer that has no gauche interactions.

33.

$$K_{eq} = \frac{\text{[equatorial conformer]}}{\text{[axial conformer]}} = \frac{5.4}{1}$$

$$\%\text{ of equatorial conformer} = \frac{\text{[equatorial conformer]}}{\text{[equatorial conformer]} + \text{[axial conformer]}} \times 100$$

$$= \frac{5.4}{5.4 + 1} \times 100 = \frac{5.4}{6.4} \times 100 = 84\%$$

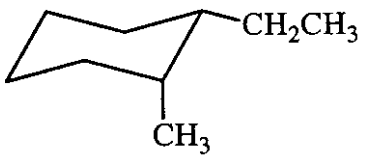
34. Because bromine has a larger diameter than chlorine, one would expect bromine to have a larger ΔG°. However, the C—Br bond is longer than the C—Cl bond, which causes bromine to be farther away than chlorine from the other axial substituents. Apparently, the longer bond more than offsets the larger diameter.

35. Both *trans*-1,4-dimethylcyclohexane and *cis*-1-*tert*-butyl-3-methylcyclohexane have a conformer with two substituents in the equatorial position and a conformer with two substituents in the axial position. *cis*-1-*tert*-Butyl-3-methylcyclohexane will have a higher percentage of the diequatorial-substituted conformer because the bulky *tert*-butyl substituent will have a greater preference for the equatorial position.

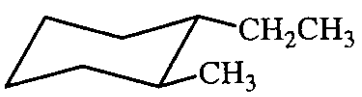
36. **a.** cis **b.** cis **c.** cis **d.** trans **e.** trans **f.** trans

37.

a.



b.

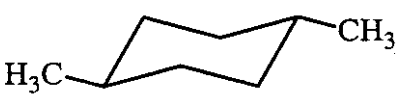


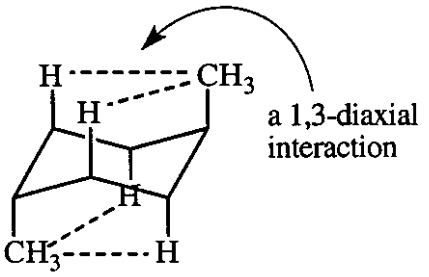
c. *trans*-1-Ethyl-2-methylcyclohexane is more stable because both substituents are in equatorial positions.

38.

a. one equatorial and one axial
b. both equatorial and both axial
c. both equatorial and both axial
d. one equatorial and one axial
e. one equatorial and one axial
f. both equatorial and both axial

39. **a.** One chair conformer of *trans*-1,4-dimethylcyclohexane has both substituents in equatorial positions, so it does not have any 1,3-diaxial interactions. The other chair conformer has both substituents in axial positions. When a substituent is in an axial position, it experiences two 1,3-diaxial interactions, so this chair has a total of four 1,3-diaxial interactions. Since the 1,3-diaxial interaction between a methyl group and a hydrogen causes a strain energy of 0.9 kcal/mol, the chair conformer with both substituents in axial positions is 4 x 0.9 = 3.6 kcal/mol less stable than the chair conformer with both substituents in equatorial positions.

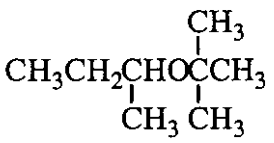


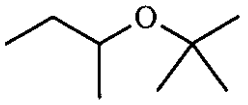


b. Each of the chair conformers of *cis*-1,4-dimethylcyclohexane has one substituent in an equatorial position and one in an axial position. Therefore, the two conformers have the same energy. The difference in energy between them is 0 kcal/mol.

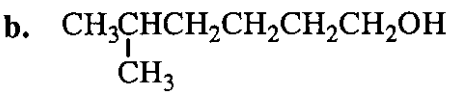
40. Both Kekulé and skeletal structures are shown.

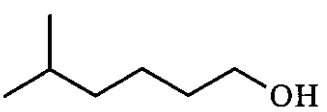
a.



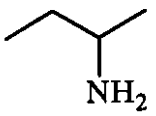


b.

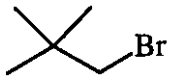




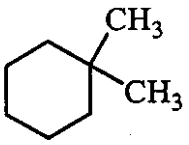
c. $CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HNH_2$

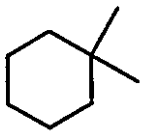


d. $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}CH_2Br$

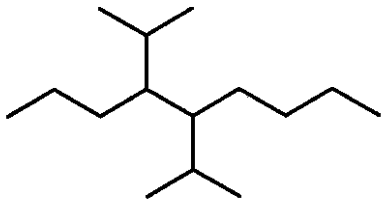


e.

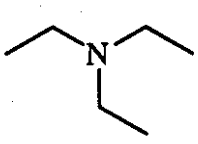




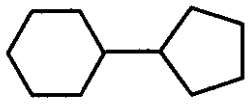
f. $CH_3CH_2CH_2\underset{\displaystyle CHCH_3}{\underset{|}{C}}HCH_2CH_2CH_2CH_3$ (CH₃ above, CHCH₃ below)



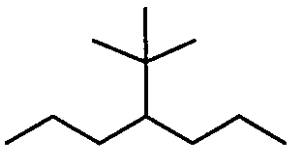
g. $CH_3CH_2\underset{\displaystyle CH_2CH_3}{\underset{|}{N}}CH_2CH_3$



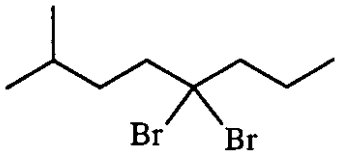
h.



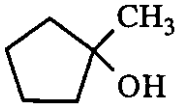
i. $CH_3CH_2CH_2\underset{\displaystyle CH_3CCH_3}{\underset{|}{C}}HCH_2CH_2CH_3$ (CH_3 above, CH_3 below)

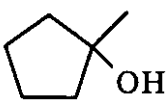


j. $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH_2\underset{\displaystyle Br}{\underset{|}{C}}CH_2CH_2CH_3$ (Br above)

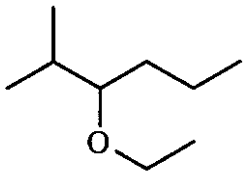


k.

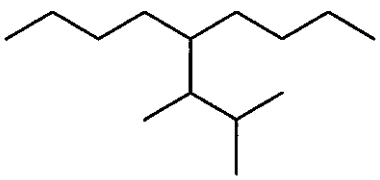




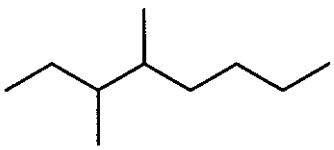
l. $CH_3\underset{\displaystyle OCH_2CH_3}{\underset{|}{C}}HCHCH_2CH_2CH_3$ (CH_3 above, OCH_2CH_3 below)



m. $CH_3CH_2CH_2CH_2\underset{\displaystyle CHCH_3}{\underset{|}{CH}}\underset{\displaystyle CHCH_3}{\underset{|}{CH}}CH_3$



n. $CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{CH}}CHCH_2CH_2CH_2CH_3$



41. **a.** 5-bromo-2-methyloctane

b. 2,2,6-trimethylheptane

c. 2,3,5-trimethylhexane

d. 3,3-diethylpentane

e. 5-bromo-*N*-ethyl-1-pentanamine

f. 5-methyl-3-hexanol

g. 3-ethoxyheptane

h. 1-bromo-4-methylcyclohexane

i. *N,N*-dimethylcyclohexanamine

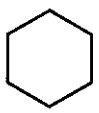
j. 3-ethylcyclohexanol

k. 1,3-dimethoxypropane

42. **a.** 3 **b.** 6 **c.** 3

43. The first conformer is the most stable because the three substituents are more spread out, so its gauche interactions will not be as large—the Cl in the first conformer is between a CH_3 and an H, whereas the Cl in the other two conformers is between two CH_3 groups.

44.

a. 

b. $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}\underset{\displaystyle CH_3}{\underset{|}{C}}CH_3$ (with CH_3 groups above and below each C)

c. $CH_3\underset{\displaystyle CH_3}{\underset{|}{CH}}CH_2\underset{\displaystyle CH_3}{\underset{|}{CH}}CH_3$

45.

a. 1-ethoxypropane
ethyl propyl ether

b. 4-methyl-1-pentanol
isohexyl alcohol

c. 2-butanamine
sec-butylamine

d. 2-chlorobutane
sec-butyl chloride

e. 2-methylpentane
isohexane

f. 2-bromo-2-methylbutane
tert-pentyl bromide

g. cyclohexanol
cyclohexyl alcohol

h. bromocyclopentane
cyclopentyl bromide

i. 2-propanamine
isopropylamine

j. *N*-ethyl-2-butanamine
sec-butylethylamine

46.

a. 1-bromohexane
b. pentyl chloride
c. 1-butanol
d. 1-hexanol
e. hexane
f. 1-pentanol
g. 1-bromopentane
h. butyl alcohol
i. octane
j. isopentyl alcohol
(The alcohol has the higher boiling point because it forms stronger hydrogen bonds. If you were asked to compare their solubilities in water, the amine is more soluble because it forms more hydrogen bonds)
k. hexylamine (it can form more hydrogen bonds)

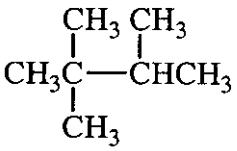
47. Ansaid is more soluble in water. It has a fluoro substituent that can hydrogen bond to water. Motrin has a nonpolar isobutyl substituent in place of Ansaid's fluoro substituent.

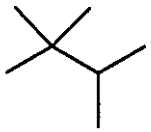
48.

a. correct
b. 4-ethyl-2,2-dimethylheptane
c. 3-methylcyclohexanol
d. 2,2-dimethylcyclohexanol
e. 5-(2-methylpropyl)nonane
f. 1-bromo-3-methylbutane
g. correct
h. 2,5-dimethylheptane
i. 5-bromo-2-pentanol
j. 3-ethyl-2-methyloctane
k. 2,3,3-trimethyloctane
l. 5-methyl-*N*,*N*-dimethyl-3-hexanamine

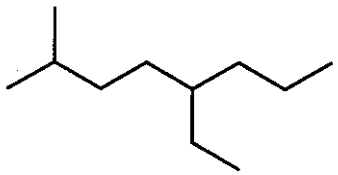
49. B has the highest energy. They are all diaxial-substituted cyclohexanes, so each one has four 1,3-diaxial interactions. Only B has a 1,3-diaxial interaction between CH_3 and Cl, which will be greater than a 1,3-diaxial interaction between CH_3 and H or a1,3-diaxial interaction between Cl and H.

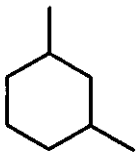
50. The only one is 2,2,3-trimethylbutane.

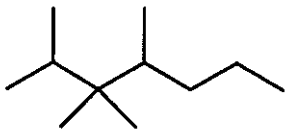


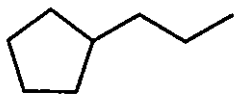


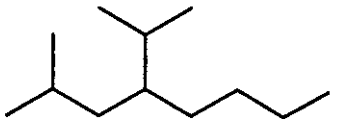
51.

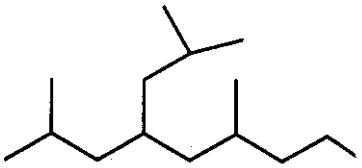
a. 

b. 

c. 

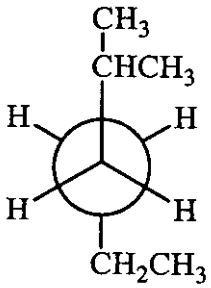
d. 

e. 

f. 

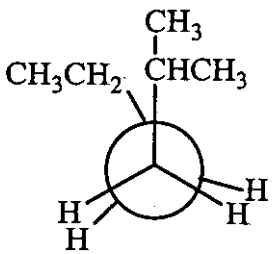
52.

a.



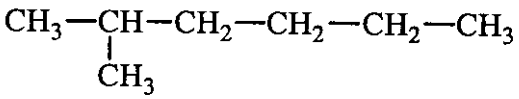
most stable

b.

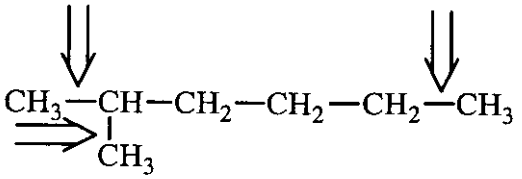


least stable

c. Rotation can occur about all the C—C bonds. There are six carbon-carbon bonds in the compound, so there are five other carbon-carbon bonds, in addition to the C_3-C_4 bond, about which rotation can occur.



d. Three of the carbon-carbon bonds have staggered conformers that are equally stable because each is bonded to a carbon with three identical substituents.



53. **C** and **D** are cis isomers. (In **C** both substituents are downward pointing; in **D** both substituents are upward pointing.)

54.

$CH_3CH_2CH_2CH_2CH_2Br$	**a.** 1-bromopentane **b.** pentyl bromide	primary alkyl halide
$CH_3CH_2CH_2\underset{\displaystyle Br}{\underset{\vert}{C}}HCH_3$	**a.** 2-bromopentane **b.** none	secondary alkyl halide
$CH_3CH_2\underset{\displaystyle Br}{\underset{\vert}{C}}HCH_2CH_3$	**a.** 3-bromopentane **b.** none	secondary alkyl halide
$CH_3\underset{\displaystyle CH_3}{\underset{\vert}{C}}HCH_2CH_2Br$	**a.** 1-bromo-3-methylbutane **b.** isopentyl bromide	primary alkyl halide
$CH_3CH_2\underset{\displaystyle CH_3}{\underset{\vert}{C}}HCH_2Br$	**a.** 1-bromo-2-methylbutane **b.** none	primary alkyl halide
$CH_3CH_2\underset{\displaystyle CH_3}{\overset{\displaystyle Br}{\overset{\vert}{\underset{\vert}{C}}}}CH_3$	**a.** 2-bromo-2-methylbutane **b.** *tert*-pentyl bromide	tertiary alkyl halide
$CH_3\underset{\displaystyle CH_3}{\overset{\displaystyle Br}{\overset{\vert}{\underset{\vert}{C}}}}HCH_3$	**a.** 2-bromo-3-methylbutane **b.** none	secondary alkyl halide
$CH_3\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\overset{\vert}{\underset{\vert}{C}}}}CH_2Br$	**a.** 1-bromo-2,2-dimethylpropane **b.** neopentyl bromide	primary alkyl halide

c. Four isomers do not have common names.

d. Four isomers are primary alkyl halides.

e. Three isomers are secondary alkyl halides.

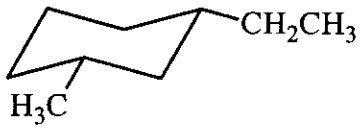
f. One isomer is a tertiary alkyl halide.

55.

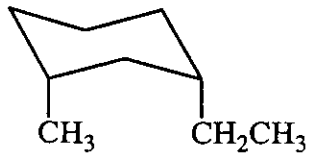
a. butane
b. 1-propanol
c. 4-propyl-1-nonanol
d. 5-isopropyl-2-methyloctane or 2-methyl-5-(1-methylethyl)octane
e. 6-chloro-4-ethyl-3-methyloctane
f. 1-methoxy-5-methyl-3-propylhexane
g. 6-isobutyl-2,3-dimethyldecane
h. 8-methyl-4-decanamine

56.

a.



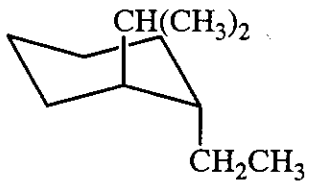
more stable



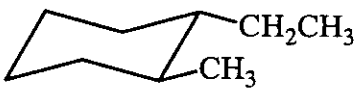
b.



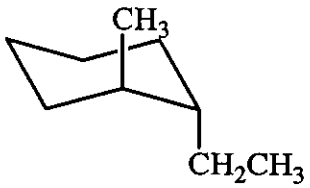
more stable



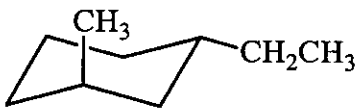
c.



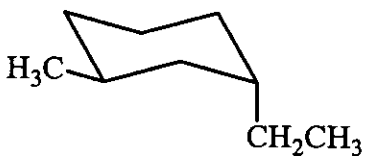
more stable



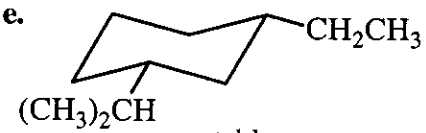
d.



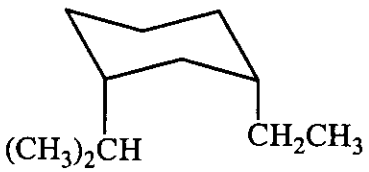
more stable



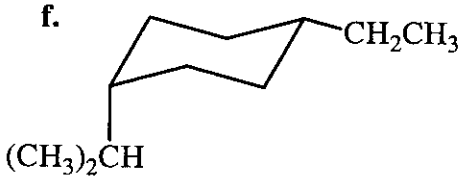
e.

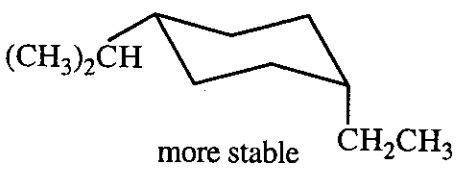


more stable



f.



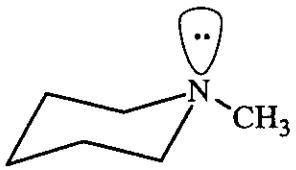


more stable

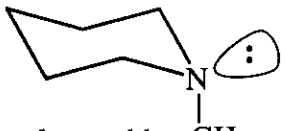
57. Alcohols with low molecular weights are more water soluble than alcohols with high molecular weights because, as a result of having fewer carbons, they have a smaller nonpolar component that has to be dragged into water.

58.

a.



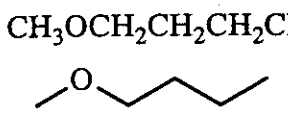
more stable



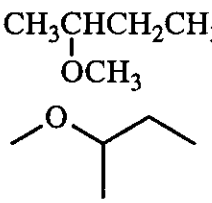
less stable

b. We know that there is more room for a substituent in the equatorial position. Because we have been told that the more stable conformer has the methyl group in the equatorial position, we can conclude that the methyl group takes up more room than the lone pair.

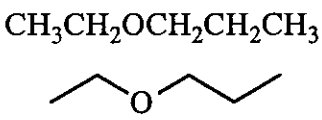
59. Six ethers have molecular formula = $C_5H_{12}O$.



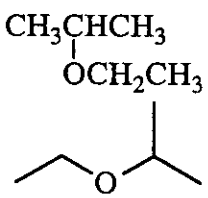
1-methoxybutane
butyl methyl ether



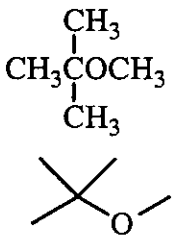
2-methoxybutane
sec-butyl methyl ether



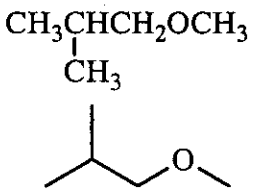
1-ethoxypropane
ethyl propyl ether



2-ethoxypropane
ethyl isopropyl ether

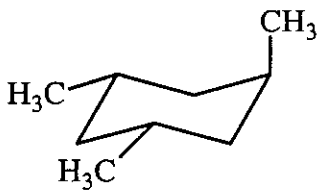


2-methoxy-2-methylpropane
tert-butyl methyl ether



1-methoxy-2-methylpropane
isobutyl methyl ether

60. The most stable conformer has two CH_3 groups in equatorial positions and one in an axial position. (The other conformer would have two CH_3 groups in axial positions and one in an equatorial position.)



61. **a.** 6-methyl-*N*-methyl-3-heptanamine

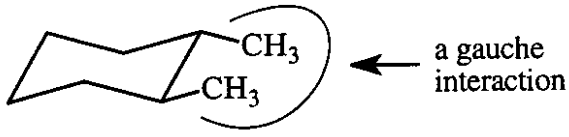
b. 3-ethyl-2,5-dimethylheptane

c. 1,4-dichloro-5-methylheptane

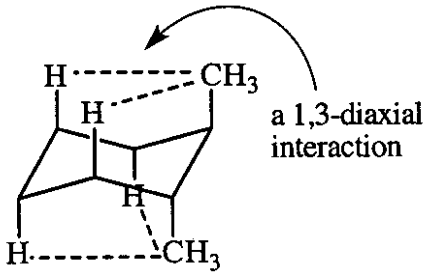
d. 5-(1,1-dimethylpropyl)nonane or 5-neopentylnonane

e. 5-(2-ethylbutyl)-3,3-dimethyldecane

62. One chair conformer of *trans*-1,2-dimethylcyclohexane has both substituents in equatorial positions, so it does not have any 1,3-diaxial interactions. However, Figure 2.12 on p. 98 of the textbook shows that the two methyl substituents are gauche to one another (as they would be in gauche butane), giving it a strain energy of 0.9 kcal/mol.

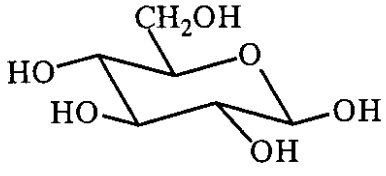


The other chair conformer of *trans*-1,2-dimethylcyclohexane has both substituents in axial positions. When a substituent is in an axial position, it experiences two 1,3-diaxial interactions. This chair conformer, therefore, has a total of four 1,3-diaxial interactions. Each diaxial interaction is between a CH_3 and an H, so each results in a strain energy of 0.9 kcal/mol. Therefore this chair conformer has a strain energy of 3.6 kcal/mol.



Thus, one conformer is 2.7 kcal/mole more stable than the other.

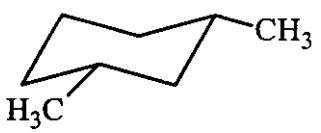
63.

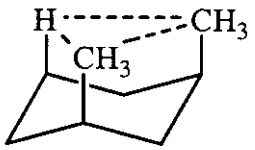


64. **a.** 1-Hexanol has a higher boiling point than 3-hexanol because the alkyl group in 1-hexanaol can better engage in van der Waals interactions. The OH group of 3-hexanol makes it more difficult for is 6 carbons to lie close to the 6 carbons of another molecule of 3-hexanol.

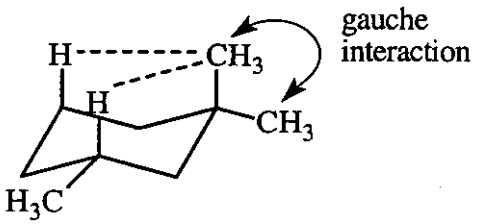
b. The floppy ethyl groups in diethyl ether interfere with the ability of the oxygen atom to engage in hydrogen bonding with water.

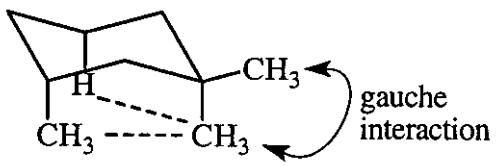
65. One of the chair conformers of *cis*-1,3-dimethylcyclohexane has both substituents in equatorial positions, so there are no unfavorable 1,3-diaxial interactions. The other chair conformer has three 1,3-diaxial interactions, two between a CH_3 and an H and one between two CH_3 groups. We know that a 1,3-diaxial interaction between a CH_3 and an H is 0.9 kcal/mol. Subtracting 1.8 from 5.4 results in a value of 3.6 kcal/mol for the 1,3-diaxial interaction between the two CH_3 groups.





66. The conformer on the left has a gauche interaction between the two CH_3 groups (0.9 kcal/mol) and two 1,3-diaxial interactions between a CH_3 and an H (2 x 0.9 kcal/mole) for a total strain energy of 2.7 kcal/mol.



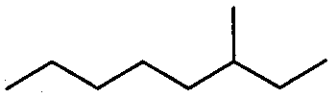


The conformer on the right has a gauche interaction between the two CH_3 groups (0.9 kcal/mol) and three 1,3-diaxial interactions, two between a CH_3 and an H (1.8 kcal/mole) and one between two CH_3 groups (3.6 kcal/mole; see Problem 65) for a total strain energy of 6.3 kcal/mol.

The conformer on the left will predominate at equilibrium.

Chapter 2 Practice Test

1. Name the following compound:



2. Draw the following conformers of hexane considering rotation about the C_3—C_4 bond:

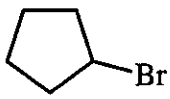
a. the most stable of all the conformers

b. the least stable of all the conformers

c. a gauche conformer

3. Give two names for each of the following compounds:

a. $CH_3CH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCH_3$ **b.** $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH_2CH_2OH$ **c.**



4. Label the three compounds in each set in order of decreasing boiling point. (Label the highest boiling compound #1, the next #2, and the lowest boiling #3.)

a. $CH_3CH_2CH_2CH_2CH_2Br$ $CH_3CH_2CH_2Br$ $CH_3CH_2CH_2CH_2Br$

b. $CH_3CH_2CH_2CH_2CH_3$ $CH_3CH_2CH_2CH_2OH$ $CH_3CH_2CH_2CH_2Cl$

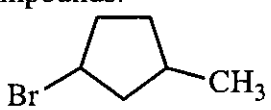
c. $CH_3\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle CH_3}{\overset{|}{C}}}}-\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle CH_3}{\overset{|}{C}}}}CH_3$ $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH_2CH_2CH_2CH_3$

5. Give the systematic name for each of the following compounds:

a. $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH_2\underset{\displaystyle OH}{\underset{|}{C}}HCH_2CH_3$

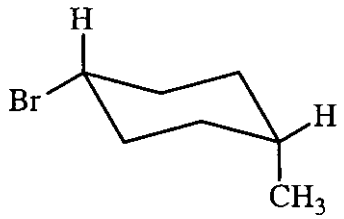
b. $CH_3CH_2\underset{\displaystyle CH_2CH_2CH_2CH_3}{\underset{|}{C}}HOCH_2CH_3$

c.



d. $CH_3\underset{\displaystyle CH_2CH_3}{\underset{|}{C}}H\overset{\displaystyle Cl}{\overset{|}{C}}HCH_2CH_2CH_2Cl$

6. Draw the other chair conformer.



7. Draw the most stable conformer of *trans*-1-isopropyl-3-methylcyclohexane.

8. Which of the following has:

a. the higher boiling point: diethyl ether or butyl alcohol?

b. the greater solubility in water: 1-butanol or 1-pentanol?

c. the higher boiling point: hexane or isohexane?

d. the higher boiling point: pentylamine or ethylmethylamine?

e. the greater solubility in water: ethyl alcohol or ethyl chloride?

9. Give two names for each of the following compounds:

a. $CH_3CHCH_2CH_2Br$ (with CH_3 branch)

b. $CH_3CHCH_2CH_2OH$ (with CH_3 branch)

c. $CH_3CHCH_2CH_2NH_2$ (with CH_3 branch)

10. Which is more stable:

a. A staggered conformer or an eclipsed conformer?

b. The chair conformer of methylcyclohexane with the methyl group in the axial position or the chair conformer of methylcyclohexane with the methyl group in the equatorial position?

c. Cyclohexane or cyclobutane?

11. Give the structure of the following:

a. a secondary alkyl bromide that has three carbons

b. a secondary amine that has three carbons

c. an alkane with no secondary hydrogens

d. a constitutional isomer of butane

e. three compounds with molecular formula C_3H_8O

CHAPTER 3
Alkenes: Structure, Nomenclature, and an Introduction to Reactivity
Thermodynamics and Kinetics

Important Terms

acyclic	noncyclic.
addition reaction	a reaction in which atoms or groups are added to the reactant.
alkene	a hydrocarbon that contains a double bond.
allyl group	$CH_2{=}CHCH_2{-}$
allylic carbon	an sp^3 carbon adjacent to a vinyl carbon.
Arrhenius equation	relates the rate constant of a reaction to the energy of activation and to the temperature at which the reaction is carried out ($k = Ae^{-E_a/RT}$).
cis isomer	the isomer with the hydrogens on the same side of the double bond.
degree of unsaturation	the number of π bonds and/or rings in a hydrocarbon.
***E* isomer**	the isomer with the high-priority groups on opposite sides of the double bond.
electrophile	an electron deficient atom or molecule.
electrophilic addition reaction	an addition reaction in which the first species that adds to the reactant is an electrophile.
endergonic reaction	a reaction with a positive $\Delta G°$.
endothermic reaction	a reaction with a positive $\Delta H°$.
enthalpy	the heat given off ($-\Delta H°$) or the heat absorbed ($+\Delta H°$) during the course of a reaction.
entropy	a measure of the freedom of motion in a system.
exergonic reaction	a reaction with a negative $\Delta G°$.
exothermic reaction	a reaction with a negative $\Delta H°$.
experimental energy of activation ($E_a = \Delta H^{\dagger} - RT$)	a measure of the approximate energy barrier to a reaction. (It is approximate because it does not contain an entropy component.)
first-order rate constant	the rate constant of a first-order reaction.
first-order reaction (unimolecular reaction)	a reaction whose rate is dependent on the concentration of one reactant.

free energy of activation ($\Delta G^{\dagger}$)	the true energy barrier to a reaction.
functional group	the center of reactivity of a molecule.
geometric isomers (cis-trans stereoisomers)	cis-trans (or *E*, *Z*) isomers.
Gibbs standard energy change	the difference between the free energy content of the products and the free energy content of the reactants at equilibrium under standard conditions (1M, 25 °C, 1 atm).
intermediate	a species formed during a reaction that is not the final product of the reaction.
kinetics	the field of chemistry that deals with the rates of chemical reactions.
kinetic stability	is indicated by $\Delta G^{\dagger}$. If $\Delta G^{\dagger}$ is large, the compound is kinetically stable (not very reactive). If $\Delta G^{\dagger}$ is small, the compound is kinetically unstable (is very reactive).
mechanism of the reaction	a description of the step-by-step process by which reactants are changed into products.
nucleophile	an electron-rich atom or molecule.
rate constant	a measure of how easy it is to reach the transition state of a reaction (to get over the energy barrier of the reaction).
rate-determining step or rate-limiting step	the step in a reaction that has the transition state with the highest energy.
reaction coordinate diagram	describes the energy changes that take place during the course of a reaction.
saturated hydrocarbon	a hydrocarbon that is completely saturated with hydrogen (contains no double or triple bonds).
second-order rate constant	the rate constant of a second-order reaction.
second-order reaction (bimolecular reaction)	a reaction whose rate is dependent on the concentration of two reactants, or on the square of the concentration of a single reactant.
solvation	the interaction between a solvent and another molecule (or ion).
thermodynamics	the field of chemistry that describes the properties of a system at equilibrium.

thermodynamic stability is indicated by $\Delta G°$. If $\Delta G°$ is negative, the products are more stable than the reactants. If $\Delta G°$ is positive, the reactants are more stable than the products.

trans isomer the isomer with the hydrogens on opposite sides of the double bond.

transition state the highest point on a hill in a reaction coordinate diagram. In the transition state, bonds in the reactant that will break are partially broken and bonds in the product that will form are partially formed.

unsaturated hydrocarbon a hydrocarbon that contains one or more double or triple bonds.

vinyl group

$CH_2{=}CH{-}$

vinylic carbon a carbon that is doubly bonded to another carbon.

***Z* isomer** the isomer with the high-priority groups on the same side of the double bond.

Solutions to Problems

1. **a.** C_5H_8 **b.** C_4H_6 **c.** $C_{10}H_{16}$ **d.** C_8H_{10}

2. **a.** 3 **b.** 4 **c.** 1 **d.** 3 **e.** 13

3.

a. $CH_3CH{=}CH_2$



b. $CH_3C{\equiv}CH$

$CH_2{=}C{=}CH_2$

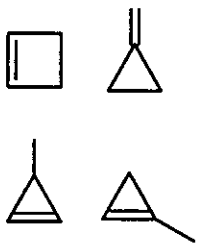


c. $HC{\equiv}CCH_2CH_3$

$CH_3C{\equiv}CCH_3$

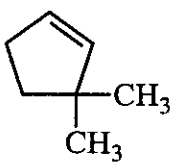
$CH_2{=}CHCH{=}CH_2$

$CH_2{=}C{=}CHCH_3$



4.

a.



b. $CH_3C(CH_3)_2{=}CCH_2CH_2CH_2Br$

c. $CH_3CH_2OCH{=}CH_2$

d. $CH_2{=}CHCH_2OH$

5.

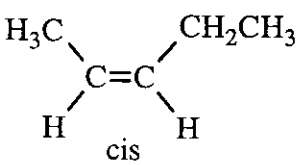
a. 4-methyl-2-pentene
b. 2-chloro-3,4-dimethyl-3-hexene
c. 1-bromocyclopentene
d. 1-bromo-4-methyl-3-hexene
e. 1,5-dimethylcyclohexene
f. 1-butoxy-1-propene

6. **a.** 5 **b.** 4 **c.** 4 **d.** 6

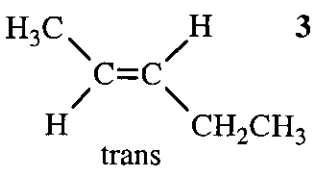
7. **a.** 1 and 3

b.

1.

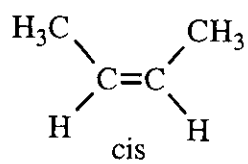


cis

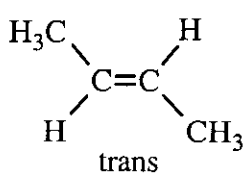


trans

3.

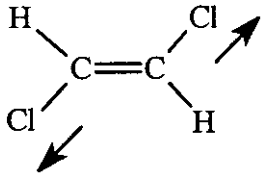


cis



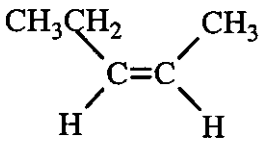
trans

8. Only **C** has a dipole moment of zero because the bond dipoles cancel since they are in opposit directions.

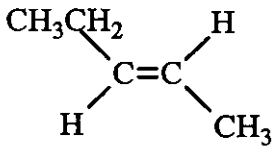


9.

1.

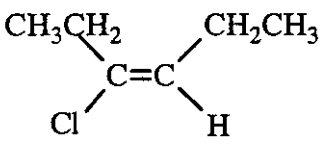


Z

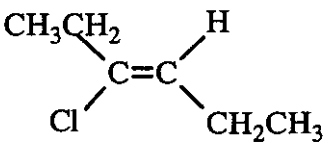


E

2.

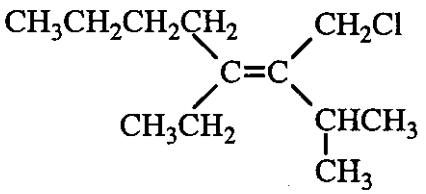


E

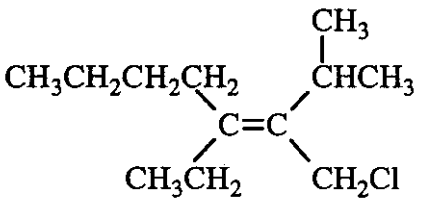


Z

3.

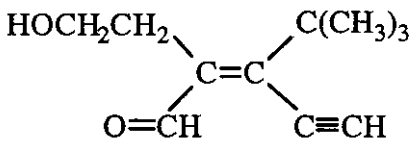


Z

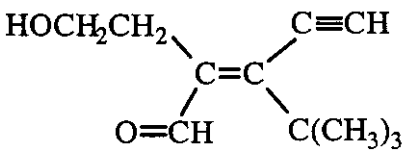


E

4.

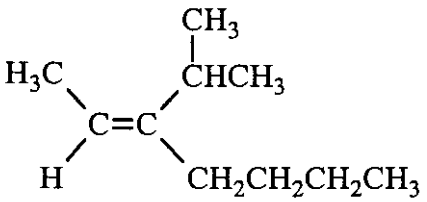


Z



E

10.



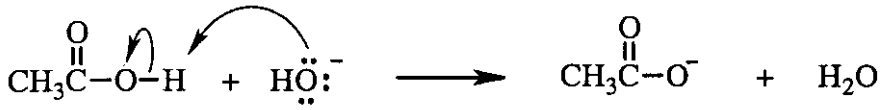
11.

nucleophiles: H^- CH_3O^- $CH_3C{\equiv}CH$ NH_3

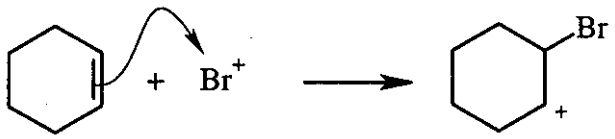
electrophiles: $AlCl_3$ $CH_3\overset{+}{C}HCH_3$

12.

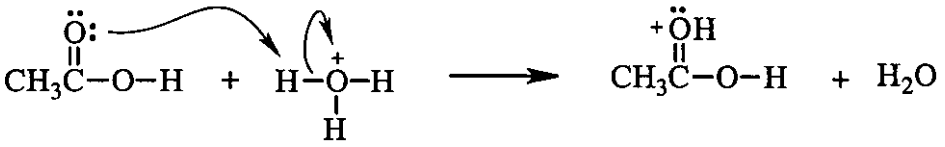
a.



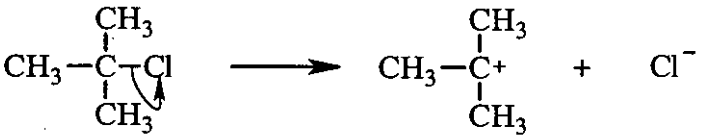
b.



c.



d.



13. **a.** Because the equilibrium constants for all the monosubstituted cyclohexanes in Table 2.10 on page 99 of the text are positive, they all have negative $\Delta G°$ values. (recall that $\Delta G° = -RT \ln K_{eq}$)

b. the *tert*-butyl substituent

c. the *tert*-butyl substituent

d. $\Delta G° = -RT \times \ln K_{eq}$

$\Delta G° = -1.986 \times 10^{-3} \times 298 \times \ln 18$

$\Delta G° = -0.59 \times \ln 18$

$\Delta G° = -0.59 \times 2.89$

$\Delta G° = -1.7$ kcal/mol (or -7.1 kJ/mol)

14. **a.** Solved in the text.

b. $\Delta G^\circ = -RT \ln K_{eq}$

$-2.1 = -1.986 \times 10^{-3} \times 298 \times \ln K_{eq}$

$\ln K_{eq} = 3.56$

$K_{eq} = 35$

$$K_{eq} = \frac{[\text{isopropylcyclohexane}]_{\text{equatorial}}}{[\text{isopropylcyclohexane}]_{\text{axial}}} = \frac{35}{1}$$

$$\frac{[\text{isopropylcyclohexane}]_{\text{equatorial}}}{[\text{isopropylcyclohexane}]_{\text{equatorial}} + [\text{isopropylcyclohexane}]_{\text{axial}}} = \frac{35}{35+1}$$

$$= \frac{35}{36}$$

$$= 0.97 = 97\%$$

c. Isopropylcyclohexane has a greater percentage of the conformer with the substituent in the equatorial position because the isopropyl substituent is a larger substituent than the fluoro substituent. The larger the substituent, the less stable is the conformer in which the substituent is in the axial position because of the 1,3-diaxial interactions.

15. ΔS° is more significant in reactions in which the number of reactant molecules and the number of product molecules are not the same.

a. **1.** A + B $\rightleftharpoons$ C

2. A + B $\rightleftharpoons$ C

b. None of the four reactions has a positive ΔS°.
In order to have a positive ΔS°, the products must have greater freedom of motion than the reactants.

16. **a.** (1) $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$

(recall that $T = {}^\circ C + 273$)

$\Delta G^\circ = -12 - (273 + 30)(.01)$

$\Delta G^\circ = -12 - 3 = -15$ kcal/mol

$\Delta G^\circ = -R\,T \ln K_{eq}$

$\Delta G^\circ = -(1.986 \times 10^{-3})(303) \ln K_{eq}$

$-15 = -0.60 \ln K_{eq}$

$\ln K_{eq} = 25$

$K_{eq} = 7.2 \times 10^{10}$

a. (2) $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$

$\Delta G^\circ = -12 - (273 + 150)(.01)$

$\Delta G^\circ = -12 - 4 = -16$ kcal/mol

$\Delta G^\circ = -(1.986 \times 10^{-3})\,(423) \ln K_{eq}$

$-16 = -0.84 \ln K_{eq}$

$\ln K_{eq} = 19$

$K_{eq} = 1.8 \times 10^8$

b. For this reaction: the calculations show that increasing the temperature causes ΔG° to be more negative.

c. For this reaction: the calculations show that increasing the temperature causes K_{eq}, to be smaller. (Remember that $\ln K_{eq} = \Delta G^\circ/RT$).

17. **a.**

bonds broken		bonds formed	
π bond of ethene	63	C—H	101
H—Cl	103	C—Cl	85
	166		186

$\Delta H^\circ = 166 - 186 = -20$ kcal/mol

b.

bonds broken		bonds formed	
π bond of ethene	63	C—H	101
H—H	104	C—H	101
	167		202

$\Delta H^\circ = 167 - 202 = -35$ kcal/mol

c. Both are exothermic.

d. Both reactions have sufficiently negative ΔH° values to expect that they would be exergonic as well.

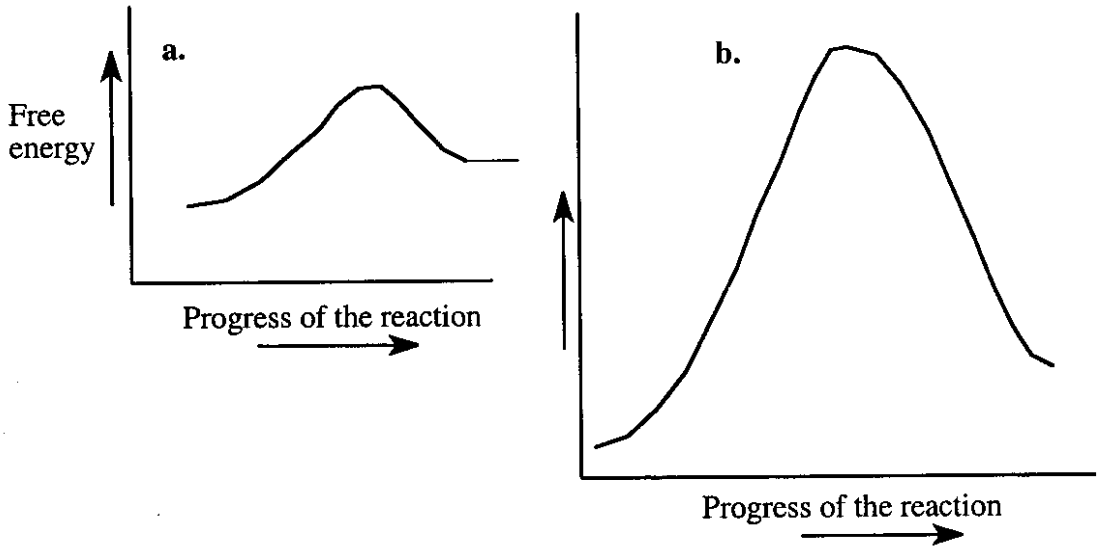
18. **a.** **a** and **b** because the product is more stable than the reactant

b. **b** because it has the smallest rate constant (highest hill) leading from the product to the transition state

c. **c** because it has the largest rate constant (smallest hill) leading from the product to the transition state

19. A thermodynamically **unstable** product is one that is less stable than the reactant.

A kinetically **unstable** product is one that has a large rate constant (reforms reactant rapidly), whereas a kinetically **stable** product is one that has a small rate constant (reforms reactant slowly).



20. **a.** Solved in the text.

b. Decreasing the concentration of methyl chloride will decrease the rate of the reaction to 1×10^{-8} Ms^{-1}.

c. Changing the concentration will not affect the rate constant (k) of the reaction, because rate constants do not depend on the concentration or the reactants.

21. The rate constant for a reaction can be increased by **decreasing** the stability of the reactant or by **increasing** the stability of the transition state.

22. Taking the logarithm of both sides of the Arrhenius equation gives the following equation, which we can use to answer the questions:

$$\ln K = \ln A - \frac{E_a}{RT}$$

a. Increasing the experimental activation energy will decrease the rate constant of a reaction (will cause the reaction to be slower).

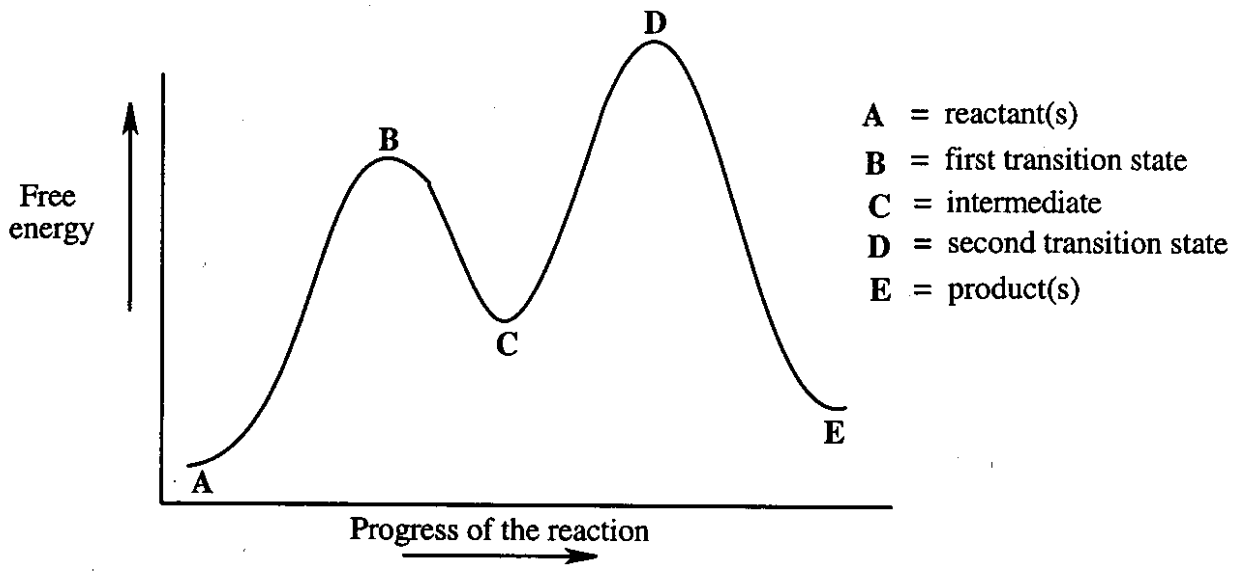
b. Increasing the temperature will increase the rate constant of a reaction (will cause the reaction to go faster).

23. **a.** The first reaction has the greater equilibrium constant.

$$K_{eq} = \frac{1 \times 10^{-3}}{1 \times 10^{-5}} = 1 \times 10^{2} \qquad K_{eq} = \frac{1 \times 10^{-2}}{1 \times 10^{-3}} = 1 \times 10$$

b. Because both reactions start with the same concentration, the first reaction will form the most product because it has the greater equilibrium constant.

24.



25.

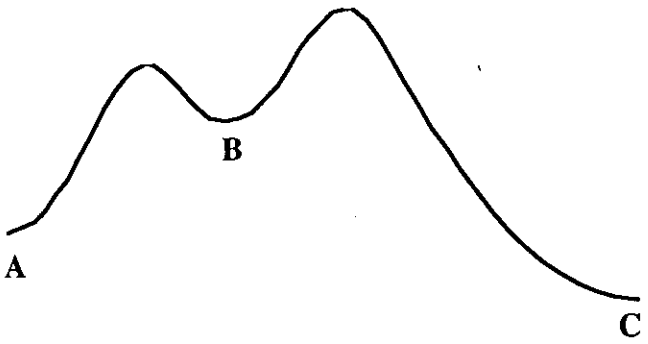
a. The first step (in the forward direction) has the greatest free energy of activation.

b. The first-formed intermediate is more apt to revert to reactants.

c. The second step is the rate-determining step because it has the transition state with the highest energy.

Notice that the second step is rate-determining even though the first step has the greatest energy of activation (steepest hill to climb). That is because it is easier for the intermediate that is formed in the first step to go back to starting material than to undergo the second step of the reaction. So, the second step is the rate-limiting step.

26.



a. one

b. two

c. the second step (k_2) (In this particular diagram, $k_2 > k_1$: if you had made the transition stat for the second step a lot higher, you could have had a diagram in which $k_1 > k_2$.)

d. the second step (k_{-1})

e. the second step in the reverse direction (k_{-1})

f. B to C

g. C to B

27.

a. 3,8-dibromo-4-nonene

b. (*Z*)-4-ethyl-3,7-dimethyl-3-octene

c. 1,5-dimethylcyclopentene

d. 3-ethyl-2-methyl-2-heptene

28.

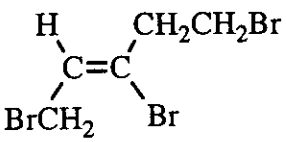
a. $CH_2{=}CHCH_2CH_2CH_2CH_3$

b. $CH_2{=}CHCH(CH_3)CH_2CH_3$

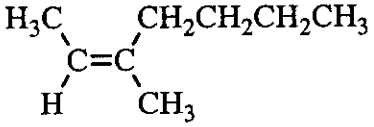
c. $CH_2{=}CHC(CH_3)_2CH_3$

29.

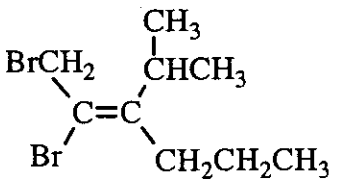
a.



b.

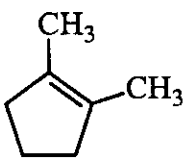


c.



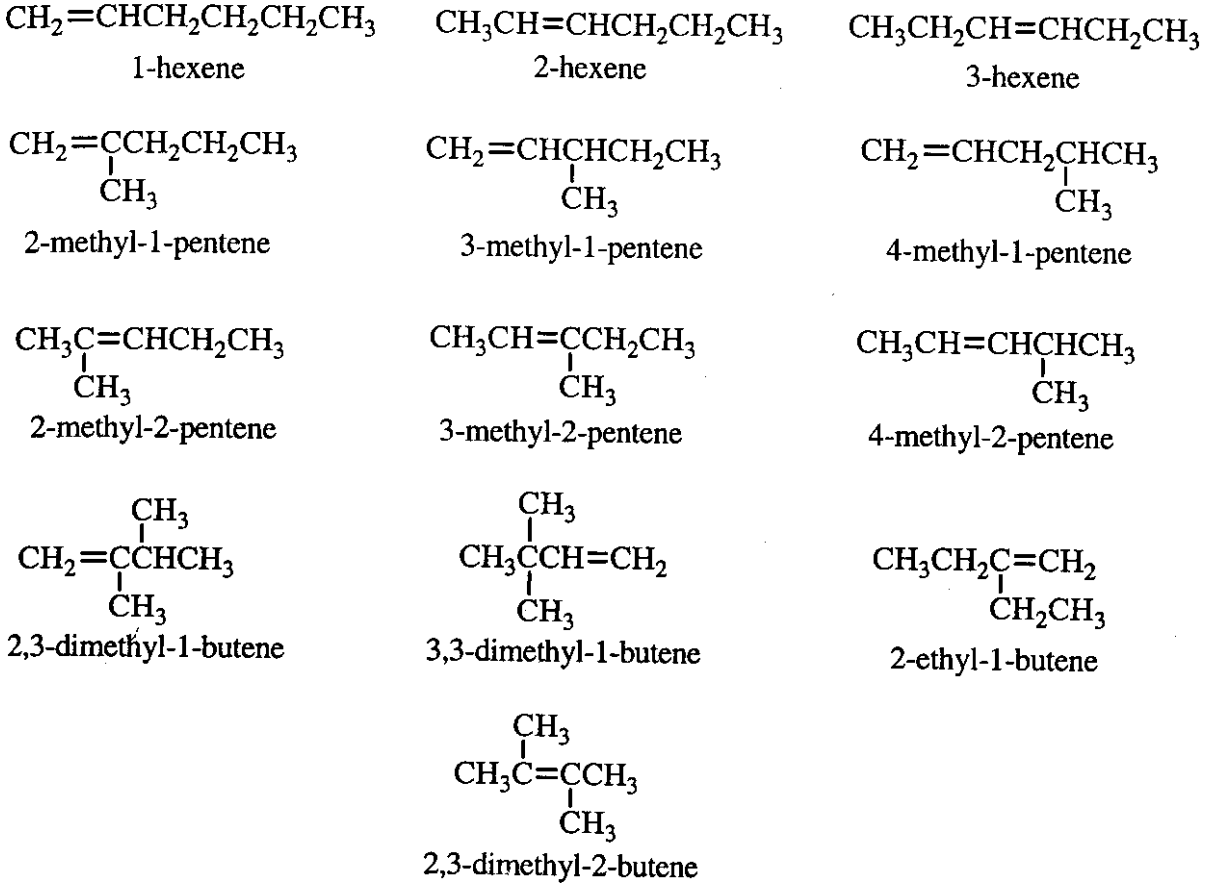
d. $CH_2{=}CHBr$

e.



f. $CH_2{=}CHCH_2NHCH_2CH{=}CH$

30.



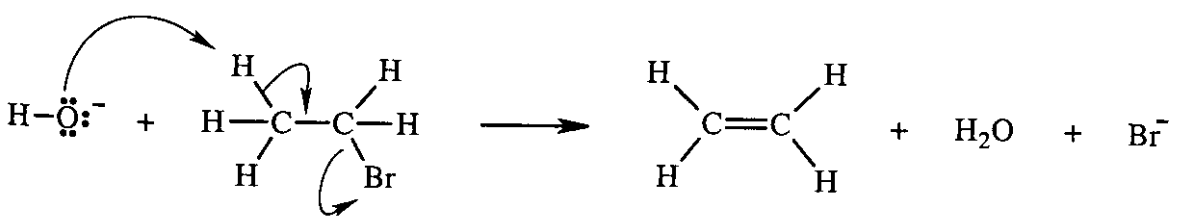
Of the compounds shown above, the following have *E* and *Z* isomers:

2-hexene, 3-hexene, 3-methyl-2-pentene, 4-methyl-2-pentene

31.

a. (*E*)-3-methyl-3-hexene
b. *trans*-8-methyl-4-nonene or (*E*)-8-methyl-4-nonene
c. *trans*-9-bromo-2-nonene or (*E*)-9-bromo-2-nonene
d. 2,4-dimethyl-1-pentene
e. 2-ethyl-1-pentene
f. *cis*-2-pentene or (*Z*)-2-pentene

32.



33. $\Delta G^\circ = -RT \ln K_{eq}$

$\ln K_{eq} = -\Delta G^\circ/RT$

$\ln K_{eq} = -\Delta G^\circ/0.59$ kcal/mol

a. $\ln K_{eq} = -2.72/0.59$ kcal/mol
$\ln K_{eq} = -4.6$
$K_{eq} = [B]/[A] = 0.01$

b. $\ln K_{eq} = -0.65/0.59$ kcal/mol
$\ln K_{eq} = -1.10$
$K_{eq} = [B]/[A] = 0.33$

c. $\ln K_{eq} = 2.72/0.59$ kcal/mol
$\ln K_{eq} = 4.6$
$K_{eq} = [B]/[A] = 100$

d. $\ln K_{eq} = 0.65/0.59$ kcal/mol
$\ln K_{eq} = 1.10$
$K_{eq} = [B]/[A] = 3.0$

34. If the number of carbons is 40, $C_nH_{2n+2} = C_{40}H_{82}$. Therefore, a compound with molecular formula $C_{40}H_{56}$ is missing 26 hydrogens. This means that it has a total of 13 rings and π bonds, since each ring and π bond causes the compound to have two fewer hydrogens. Knowing that it has two rings and no triple bonds, one can conclude that it has 11 double bonds.

35. **a.** *Z* **b.** *E* **c.** *E* **d.** *Z*

36. If the number of carbons is 30, $C_nH_{2n+2} = C_{30}H_{62}$. A compound with molecular formula $C_{30}H_{50}$ is missing 12 hydrogens. Because it has no rings, squalene has 6 π bonds (12/2 = 6).

37.

a. $-I > -Br > -OH > -CH_3$

b. $-OH > -CH_2Cl > -CH{=}CH_2 > -CH_2CH_2OH$

c. $-CH{=}CH_2 > -CH(CH_3)_2 > -CH_2CH_2CH_3 > -CH_3$

d. $-OH > -NH_2 > -CH_2OH > -CH_2NH_2$

e. $-Cl > -COCH_3 > -CN > -CH{=}CH_2$

38.

a. 2-pentene
b. correct
c. 3-methyl-1-hexene
d. 3-heptene
e. 4-ethylcyclohexene
f. 2-chloro-3-hexene
g. correct
h. 2-methyl-1-hexene
i. 1-methylcyclopentene or methylcyclopentene
j. 3-methyl-2-pentene

39.

a. 2
b. 3
c. C to D
d. D
e. B
f. endergonic
g. exergonic

40. $\Delta G^\circ = \Delta H^\circ - T\Delta S^\circ$

a. $\Delta G^\circ = 20 - (298)(25 \times 10^{-3}) = 20 - 7.5$
$\Delta G^\circ = 12.5$ kcal/mol

$\Delta G^\circ = -RT \ln K_{eq}$
$12.5 = -1.986 \times 10^{-3} \times 298 \ln K_{eq}$
$12.5 = -0.59 \ln K_{eq}$
$-21.2 = \ln K_{eq}$
$6.3 \times 10^{-10} = K_{eq}$

b. $\Delta G^\circ = 20 - (398)(25 \times 10^{-3}) = 20 - 10$
$\Delta G^\circ = 10.0$ kcal/mol

$10.0 = -1.986 \times 10^{-3} \times 398 \ln K_{eq}$
$10.0 = -0.79 \ln K_{eq}$
$12.7 = \ln K_{eq}$
$3.1 \times 10^{5} = K_{eq}$

41.

a. $\Delta G^\circ = -RT \ln K_{eq}$
$\Delta G^\circ = -RT \ln 10$
$\Delta G^\circ = -1.986 \times 10^{-3} \times 298 \times 2.3$
$\Delta G^\circ = -1.36$ kcal/mol

b. $\Delta G^\circ = \Delta H^\circ - 0$
$-1.36 = \Delta H^\circ - 0$
$\Delta H^\circ = -1.36$ kcal/mol

c. $\Delta G^\circ = 0 - T\Delta S^\circ$
$-1.36 = 0 - 298\Delta S^\circ$
$\Delta S^\circ = 1.36/298 = 4.56 \times 10^{-3}$ kcal/(mol deg) = 4.56 cal/(mol deg)

42. $\Delta G^\circ = -RT \ln K_{eq}$
$\ln K_{eq} = -\Delta G^\circ/RT$
$\ln K_{eq} = -\Delta G^\circ/0.59$ kcal/mol
$\ln K_{eq} = -3.8/0.59$ kcal/mol
$\ln K_{eq} = -6.4$
$K_{eq} = [B]/[A] = 0.0017$
$[B]/[A] = 0.0017/1 = 1.7/1000$

The previous calculation shows that for every 1000 molecules in the chair conformation. there are 1.7 molecules in a twist-boat conformation.
This agrees with the statement in Section 2.12 that for every thousand molecules of cyclohexane in a chair conformation, there are no more than two molecules in a twist-boat conformation.

43. A step-by-step description of how to solve this problem is given in the box entitled "Calculating Kinetic Parameters".

E_a can be determined from the Arrhenius equation ($\ln k = - E_a/RT$), because a plot of $\ln k$ versus $1/T$ gives a slope = $- E_a/R$

$\ln 2.11 \times 10^{-5} = -10.77$	$T = 304$	$1/T = 3.29 \times 10^{-3}$
$\ln 4.44 \times 10^{-5} = -10.02$	$T = 313$	$1/T = 3.19 \times 10^{-3}$
$\ln 1.16 \times 10^{-4} = -9.06$	$T = 324.5$	$1/T = 3.08 \times 10^{-3}$
$\ln 2.10 \times 10^{-4} = -8.47$	$T = 332.8$	$1/T = 3.00 \times 10^{-3}$
$\ln 4.34 \times 10^{-4} = -7.74$	$T = 342.2$	$1/T = 2.92 \times 10^{-3}$

$$\text{slope} = -8290$$
$$E_a = -(\text{slope})\, R$$
$$E_a = -(-8290) \times 1.98 \times 10^{-3} \text{ kcal/mol}$$
$$E_a = 16.4 \text{ kcal/mol}$$

To find $\Delta G°$:

$-\Delta G° = RT \ln kh/Tk_b$

From the graph used to determine E_a, one can find the rate constant (k) at 30°. (It is 1.84×10^{-5} s^{-1}.)

$$-\Delta G° = 1.98 \times 10^{-3} \times 303 \ln (1.84 \times 10^{-5} \times 6.625 \times 10^{-27})/(303 \times 1.3805 \times 10^{-10})$$
$$-\Delta G° = 1.98 \times 10^{-3} \times 303 \ln (1.22 \times 10^{-31})/(4.18 \times 10^{-8})$$
$$-\Delta G° = 1.98 \times 10^{-3} \times 303 \ln 2.92 \times 10^{-24}$$
$$-\Delta G° = 1.98 \times 10^{-3} \times 303 \times (-54.2)$$
$$\Delta G° = 32.5 \text{ kcal/mol}$$

To find $\Delta H°$:

$$\Delta H° = E_a - RT$$
$$\Delta H° = 16.4 - 1.98 \times 10^{-3} \times 303$$
$$\Delta H° = 16.4 - 0.6$$
$$\Delta H° = 15.8 \text{ kcal/mol}$$

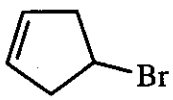
To find $\Delta S°$:

$$\Delta S° = (\Delta H° - \Delta G°)/T$$
$$\Delta S° = (15.8 - 32.5)/303$$
$$\Delta S° = (-16.7)/303$$
$$\Delta S° = 0.055 \text{ kcal/(mol deg)} = 55 \text{ cal/(mol deg)}$$

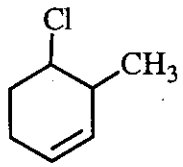
Chapter 3 Practice Test

1. Name the following compounds:

a. $CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH{=}CH_2$

b. 

c. $CH_3CH_2CH{=}CHCH_2CH_2\underset{\displaystyle CH_2CH_3}{\underset{|}{C}}HCH_3$

d. 

2. Label the following substituents in order of decreasing priority in the *E, Z* system of nomenclature. Label the highest priority #1.

$-\overset{\displaystyle O}{\overset{\|}{C}}CH_3$ $\qquad -CH{=}CH_2$ $\qquad -Cl$ $\qquad -C{\equiv}N$

3. Correct the incorrect names.

a. 3-pentene

b. 2-vinylpentane

c. 2-ethyl-2-butene

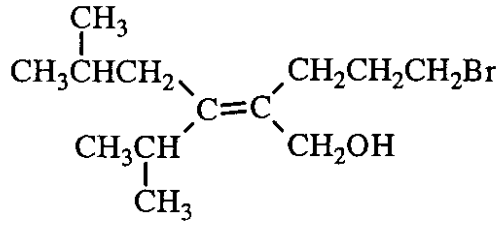
d. 2-methylcyclohexene

4. Indicate whether each of the following statements is true or false:

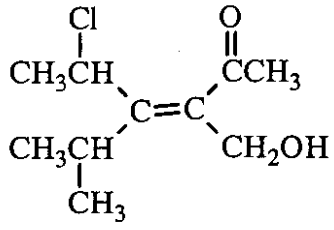
a. Increasing the energy of activation, increases the rate of the reaction.	T	F
b. Decreasing the entropy of the products compared to the entropy of the reactants makes the equilibrium constant more favorable.	T	F
c. An exergonic reaction is one with a $-\Delta G°$.	T	F
d. An alkene is an electrophile.	T	F
e. The higher the energy of activation, the more slowly the reaction will take place.	T	F
f. Another name for *trans*-2-butene is *Z*-2-butene.	T	F
g. *trans*-2-Butene has a dipole moment of zero.	T	F
h. A reaction with a negative $\Delta G°$ has an equilibrium constant greater than one.	T	F

5. Do the following compounds have the *E* or the *Z* configuration?

a.



b.



6. Draw structures for the following:

a . allyl alcohol

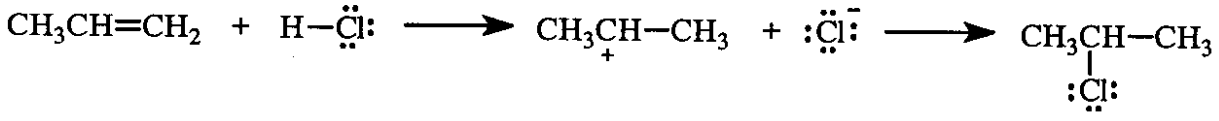
b. 3-methylcyclohexene

c. *cis*-3-heptene

d. vinyl bromide

7. How many π bonds and/or rings does a hydrocarbon have if it has a molecular formula of C_8H_8?

8. Using curved arrows show the movement of electrons in the following reaction:



9. Which of the following have cis-trans isomers?

a. 1-pentene

b. 4-methyl-2-hexene

c. 2-bromo-3-hexene

d. 2-methyl-2-hexene

10. Which of the following has a more favorable equilibrium constant (i.e., favors products over reactants)?

a. A reaction with a $\Delta H°$ of 4 kcal/mol or a reaction with a $\Delta H°$ of 7 kcal/mol?

b. A reaction that takes place at 25 °C or the same reaction that takes place at 35 °C?

c. A reaction in which two reactants form one product or a reaction in which one reactant forms two products?

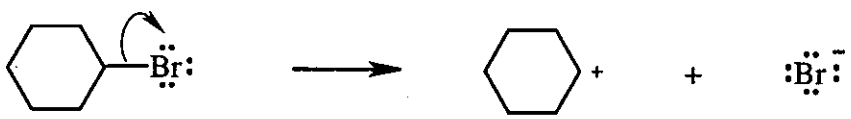
SPECIAL TOPIC II

An Exercise in Drawing Curved Arrows
"Pushing Electrons"

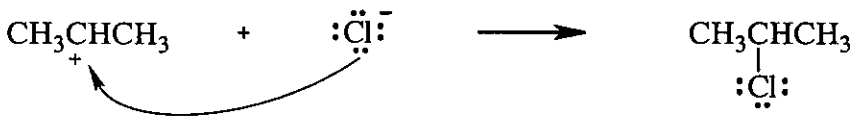
This is an extension of what you learned about drawing curved arrows in Section 3.6 on pages 123-124 of the text. Working through these problems will take just a little of your time. It will, however, be time well spent, because curved arrows will be used throughout the course and it is important that you are comfortable with this notation. (You will not encounter some of the reaction steps shown in this exercise for weeks or even months, so don't worry about why the chemical changes take place.)

Chemists use curved arrows to show how electrons move as covalent bonds break and/or new covalent bonds form. The tail of the arrow is positioned at the point where the electrons are in the reactant, and the head of the arrow points to where these same electrons end up in the product.

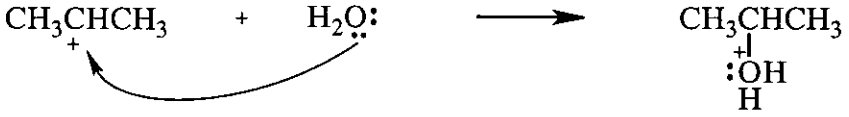
In the following reaction step, the bond between bromine and a carbon of the cyclohexane ring breaks and both electrons in the bond end up with bromine in the product. Thus, **the arrow starts at the electrons that carbon and bromine share in the reactant,** and **the head of the arrow points at bromine** because this is where the two electrons end up in the product. The carbon of the cyclohexane ring is positively charged in the product because it has lost the two electrons it was sharing with bromine. The bromine is negatively charged in the product because it has gained the electrons that it shared with carbon in the reactant. The fact that two electrons move in this example is indicated by the two barbs on the arrowhead.



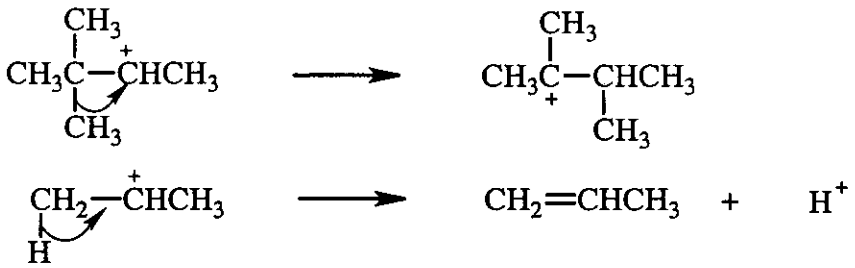
Notice that the arrow always starts at a bond or at a lone pair. It does not start at a negative charge.



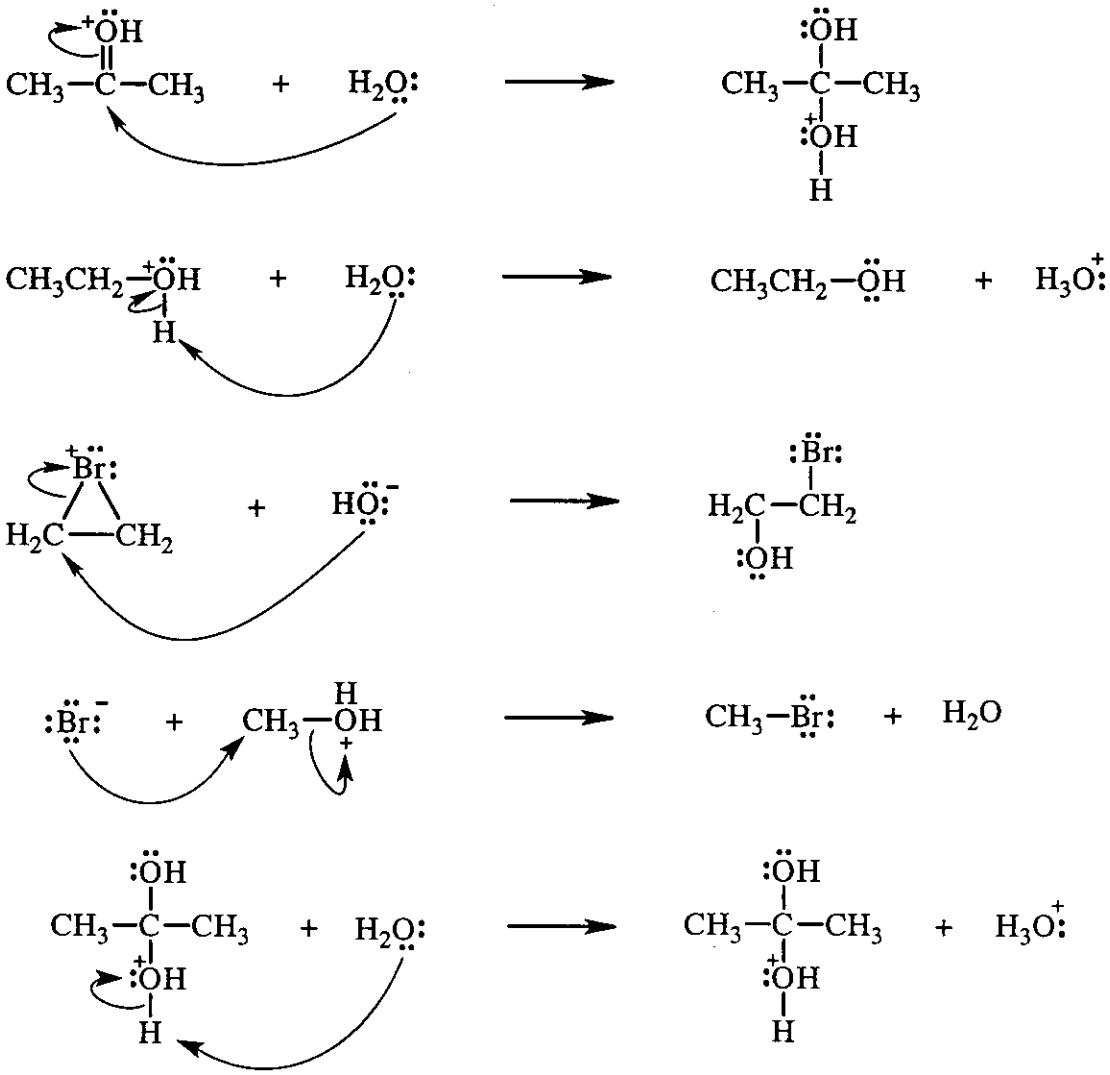
In the following reaction step a bond is being formed between the oxygen of water and a carbon of the other reactant. The arrow starts at one of the lone pairs of the oxygen and points at the atom (the carbon) that will share the electrons in the product. The oxygen in the product is positively charged because the electrons that oxygen had to itself in the reactant are now being shared with carbon. The carbon that was positively charged in the reactant is not charged in the product, because it has gained a share in a pair of electrons.



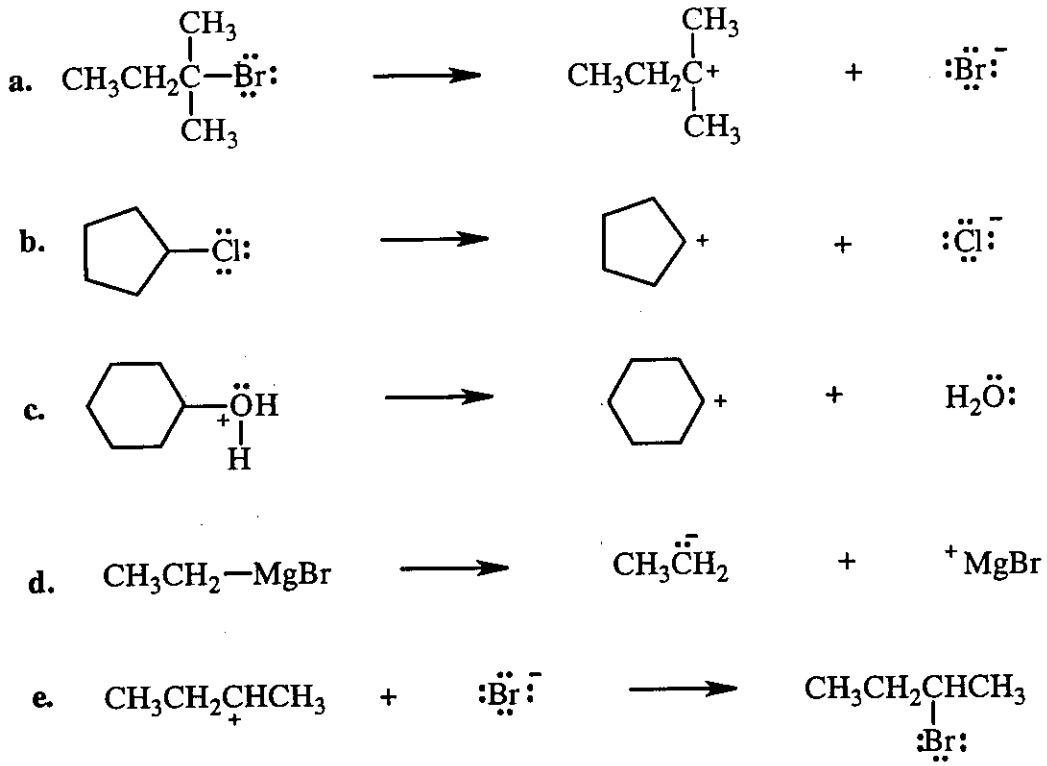
In the next examples, a bond breaks and a bond forms in the same step. As in the previous examples, the arrow starts at the point where the electrons are in the reactant, and the head of the arrow points to where these same electrons end up in the product (at the carbon atom in the first example, and between the carbons in the next example). Notice that the atom that loses a share in a pair of electrons (C in the first example, H in the second) ends up with a positive charge.



In the examples that follow, a nucleophile attacks an atom, causing a bond to break, with the result that the bonding electrons move to a positively charged atom.

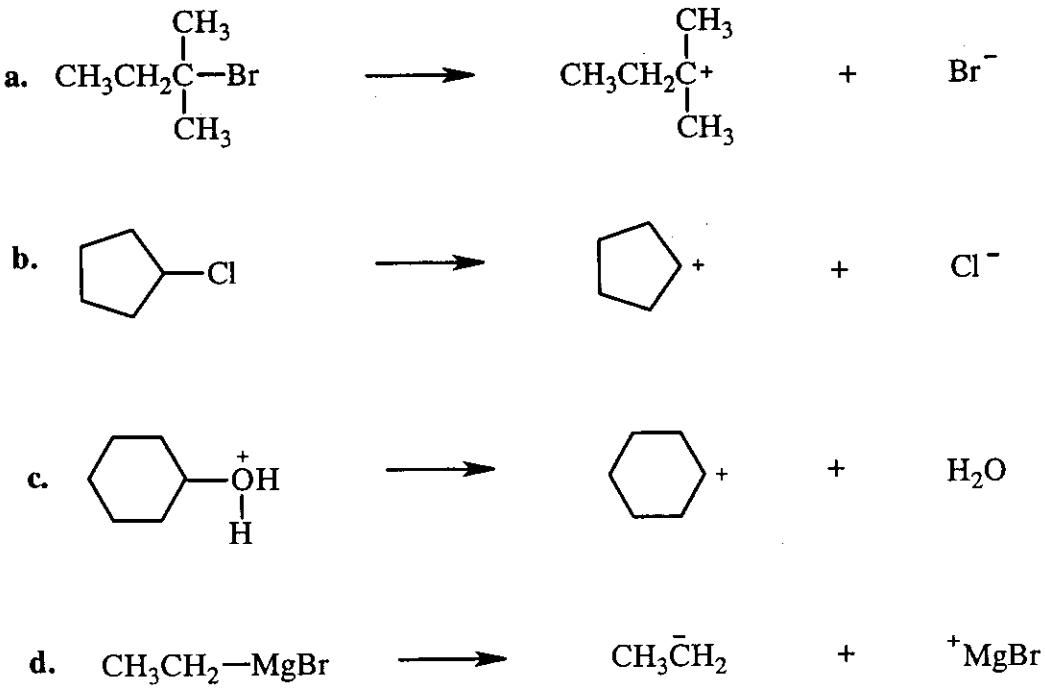


Problem 1. Draw curved arrows to show the movement of the electrons in the following reaction steps. (You will find the answers immediately after this exercise.)



Frequently chemists do not show the lone-pair electrons when they write reactions. The following are the same reaction steps you just saw except that the lone pairs are not shown.

Problem 2. Draw curved arrows to show the movement of the electrons.



The lone pairs of Br^- in example **e** have to be shown in the reactant because an arrow can start only at a bond or at a lone pair. Bromine's lone pairs do not have to be shown in the product.

e. $CH_3CH_2\overset{+}{C}HCH_3 + :\ddot{B}r:^- \longrightarrow CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$

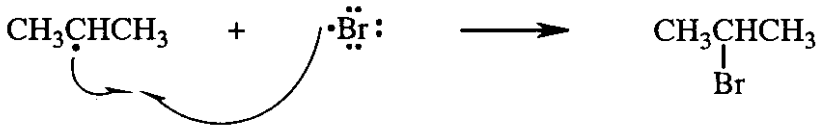
In the examples in Problems 1 and 2 that show a reaction step in which a bond breaks, both of the bonding electrons end up on one of the atoms that shared the electrons in the bond. Because two electrons move, an arrowhead with two barbs is used to show their movement.

In the examples in Problems 1 and 2 that show a reaction step in which a bond is formed, the two electrons that form the bond come from the same atom. Because two electrons move, an arrowhead with two barbs is used to show their movement.

Sometimes a bond breaks in such a way that each of the bonded atoms gets one of the bonding electrons. An arrowhead with one barb represents the movement of one electron.



Sometimes a bond is formed using one electron from one atom and one electron from the other atom that forms the bond. Because one electron comes from each atom, an arrowhead with one barb is used to show the movement of each electron.



Problem 3. Draw curved arrows to show the movement of the electrons.

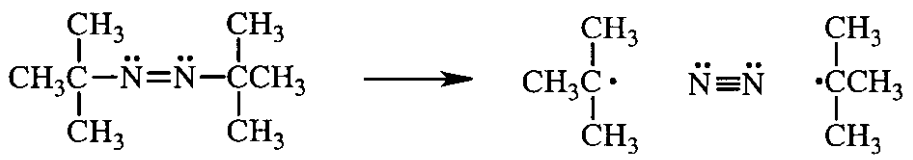
a. $CH_3CH_2-\ddot{C}l: \longrightarrow CH_3\dot{C}H_2 + \cdot\ddot{C}l:$

b.



c. $CH_3\ddot{O}-\ddot{O}CH_3 \longrightarrow CH_3\ddot{O}\cdot + \cdot\ddot{O}CH_3$

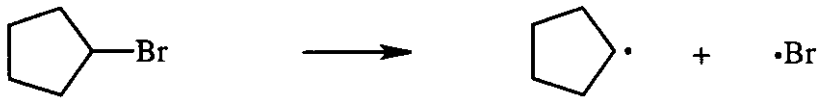
d.



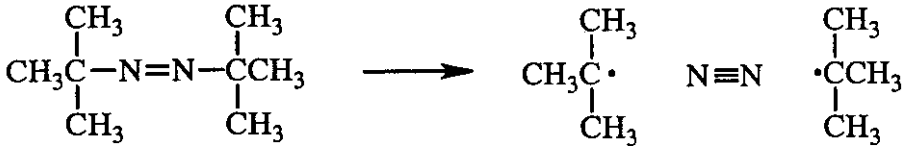
The following are the same reaction steps you just saw except that the lone pairs are not shown.

Problem 4. Draw curved arrows to show the movement of the electrons.

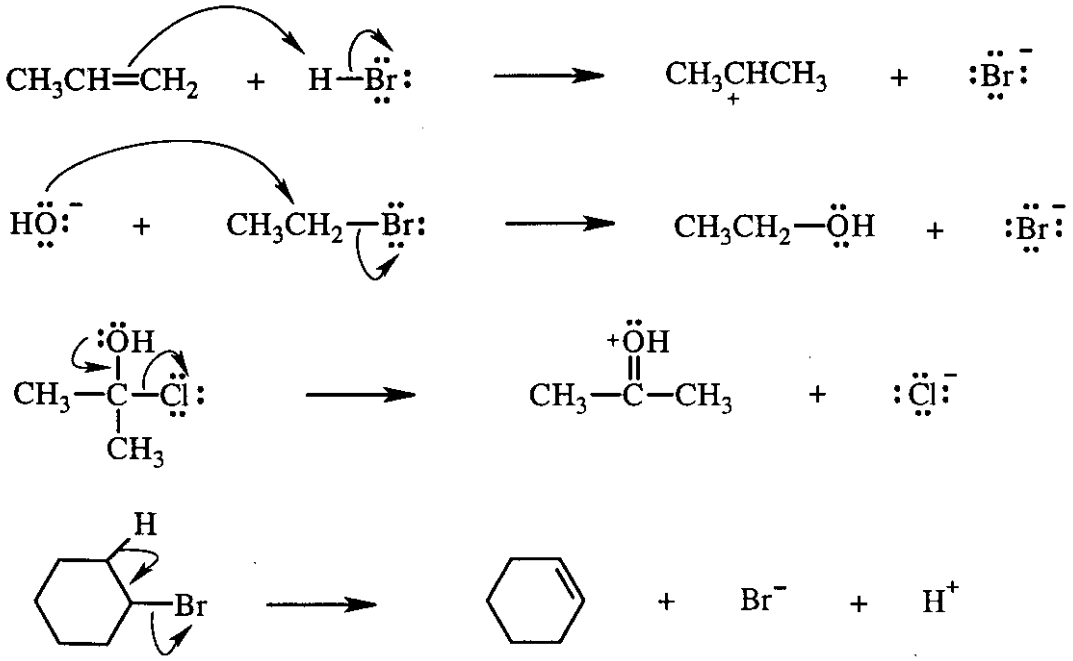
a. $CH_3CH_2—Cl \longrightarrow CH_3\dot{C}H_2 + \cdot Cl$

b. 

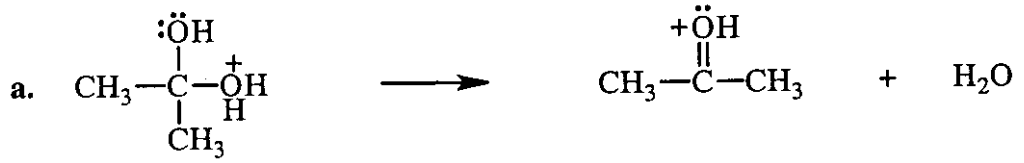
c. $CH_3O—OCH_3 \longrightarrow CH_3O\cdot + \cdot OCH_3$

d. 

In many reaction steps, two pairs of electrons move simultaneously. In each of the examples, follow the arrows to see how the electrons move. Notice how the movement of the electrons allows you to determine the structure of the products and the charges on the products.



Problem 5. Draw curved arrows to show the movement of the electrons that result in the formation of the given product.

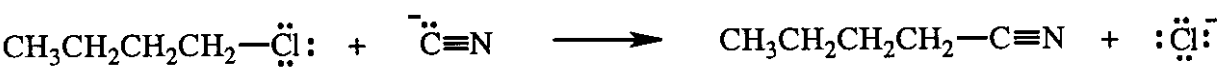


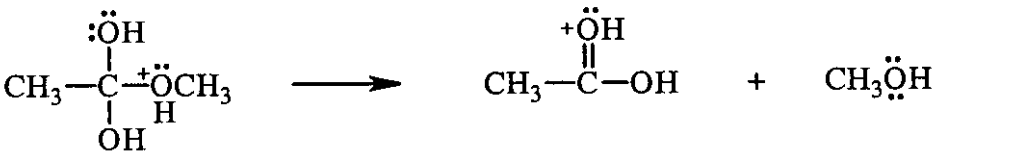
b. $CH_3CH_2CH{=}CH_2 + H{-}Cl \longrightarrow CH_3CH_2\overset{+}{C}H{-}CH_3 + Cl^-$

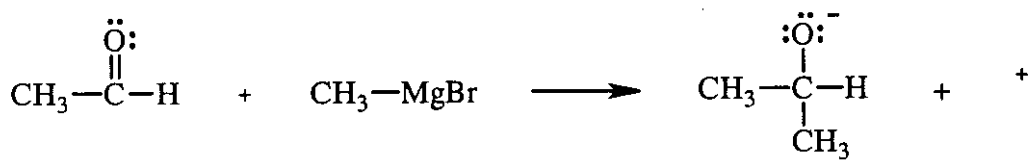


Problem 6. Draw curved arrows to show the movement of the electrons.

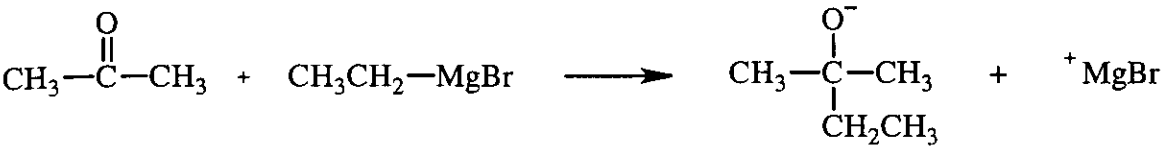
a. $CH_3CH{=}CHCH_3 + H{-}\ddot{O}{-}H \longrightarrow CH_3\overset{+}{C}H{-}CH_2CH_3 + H_2\ddot{O}:$

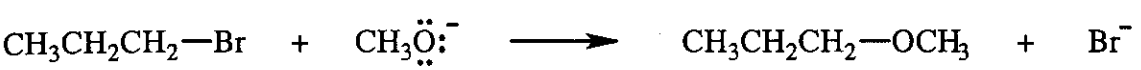


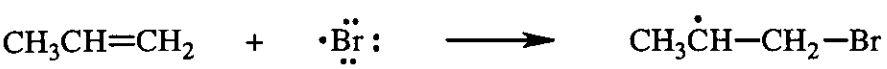


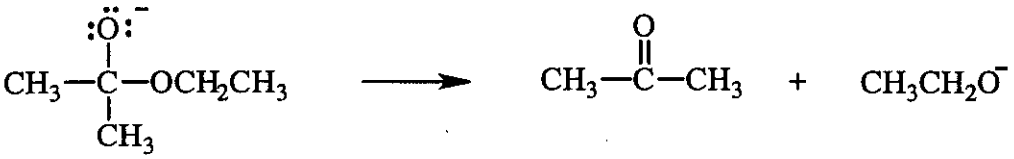


Problem 7. Draw curved arrows to show the movement of the electrons.

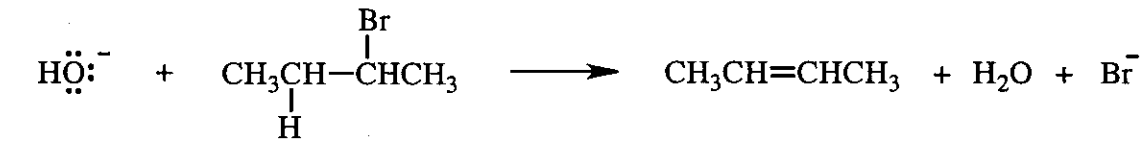
a. 

b. 

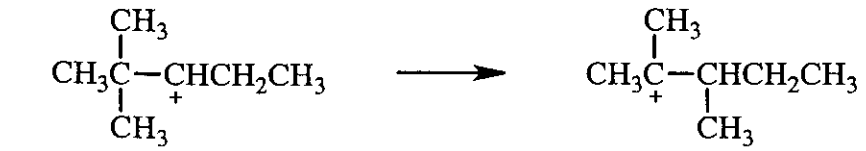
c. 

d. 

Problem 8. Draw curved arrows to show the movement of the electrons.

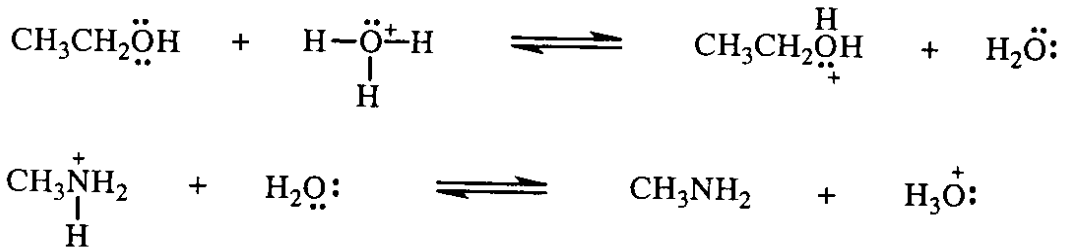
a. 

b. 

c. 

d. 

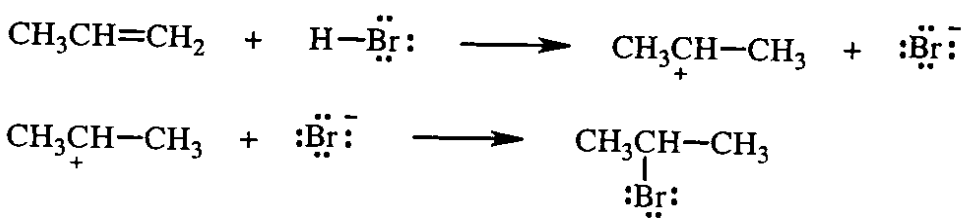
Problem 9. Draw curved arrows to show the movement of the electrons.



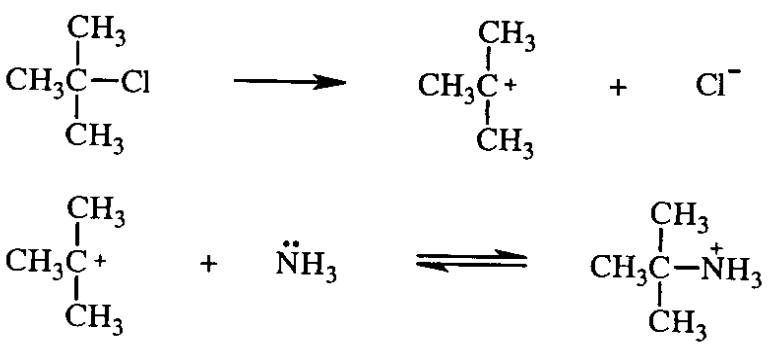
Curved arrows are used to show the movement of electrons in each step of a reaction.

Problem 10. Draw curved arrows to show the movement of the electrons in each step of the following reaction sequences.

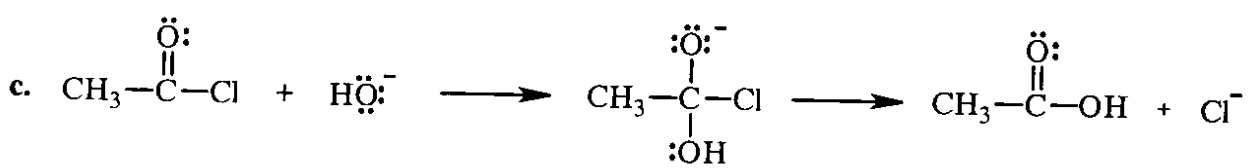
a.



b.

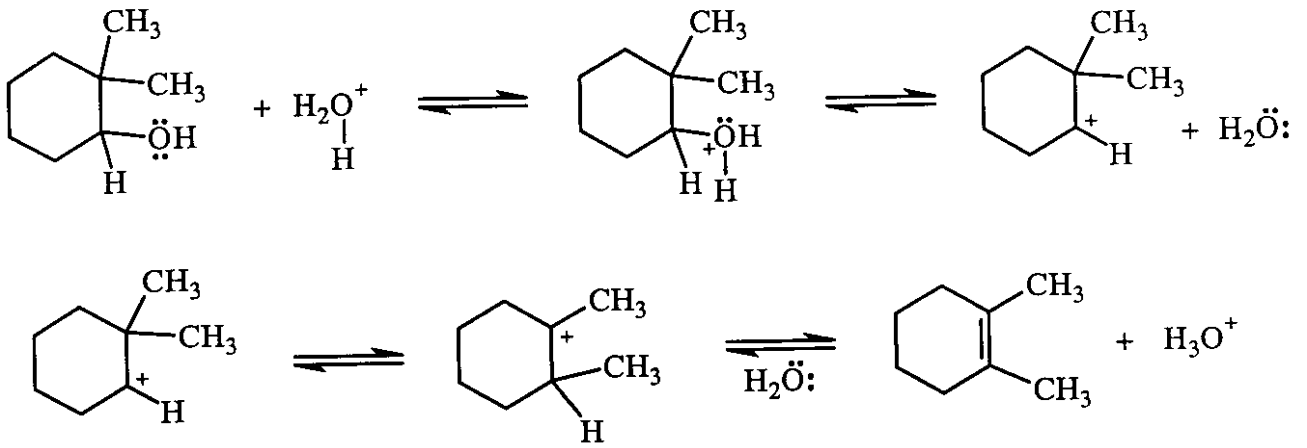


c.

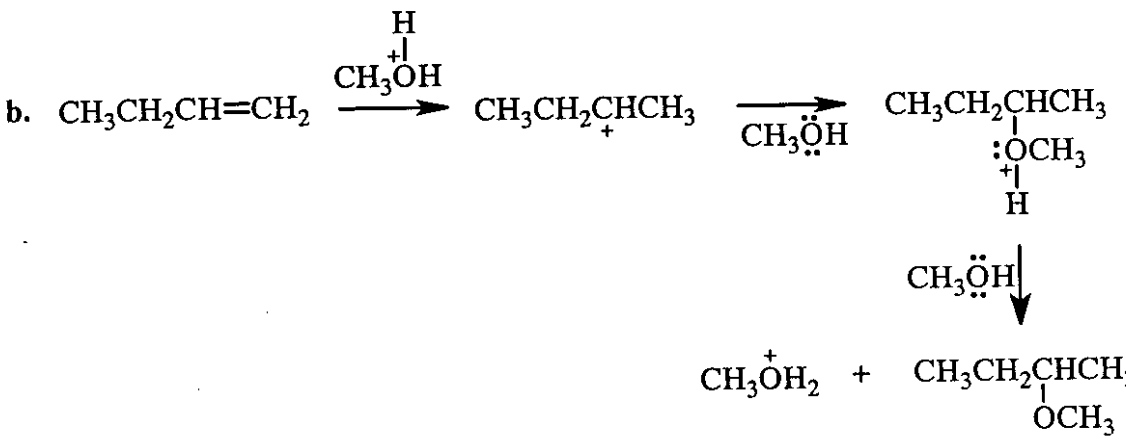


Problem 11. Draw curved arrows to show the movement of the electrons in each step of the following reactions.

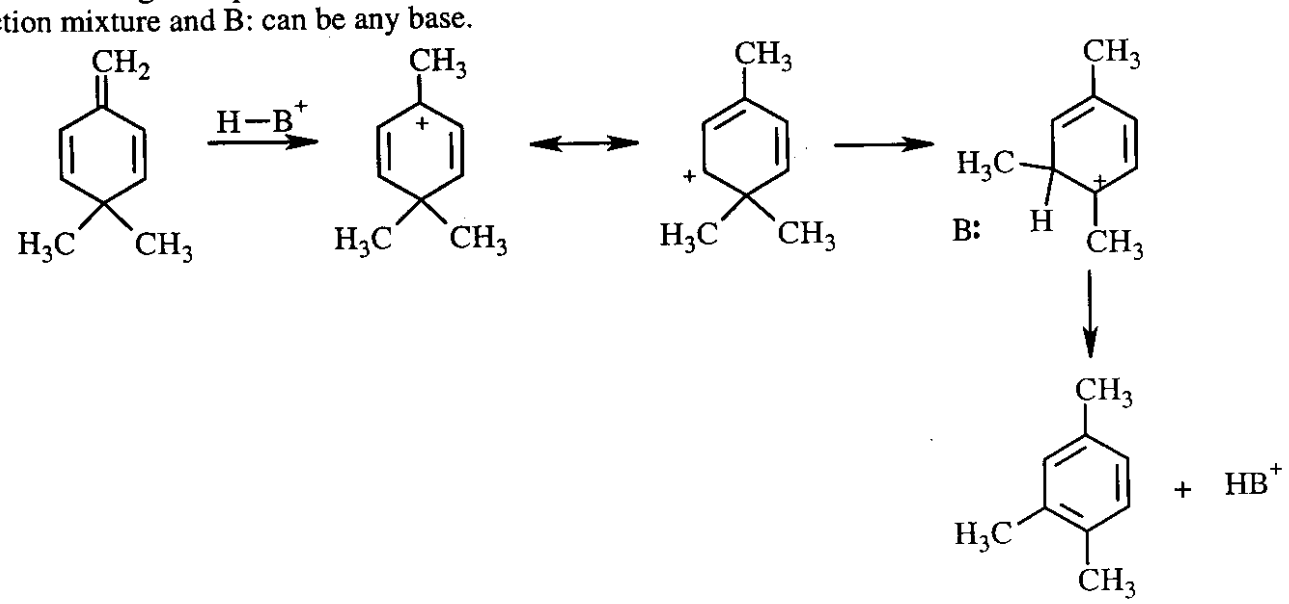
a.



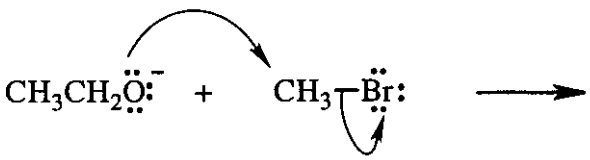
b.

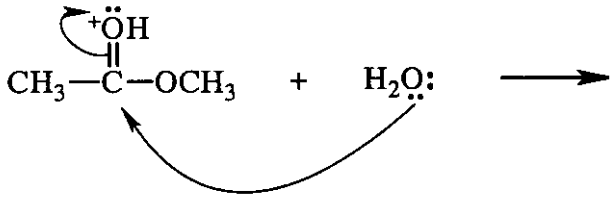


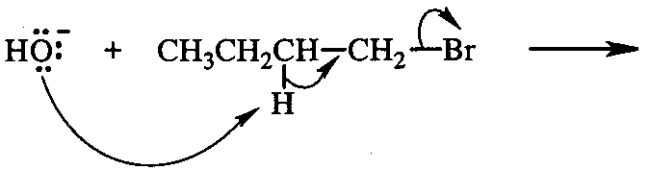
c. In the following example, the acid and base are not specified: HB^+ represents any acid present in the reaction mixture and B: can be any base.

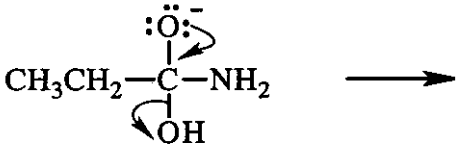


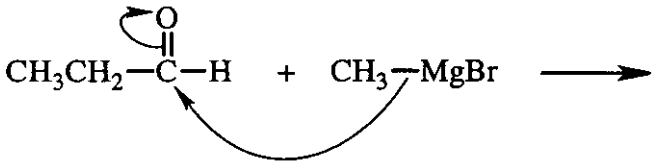
Problem 12. Use what the curved arrows tell you about electron movement to determine the product of each reaction step.

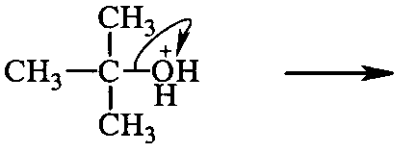
a. 

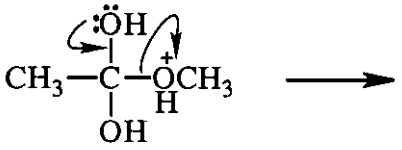
b. 

c. 

d. 

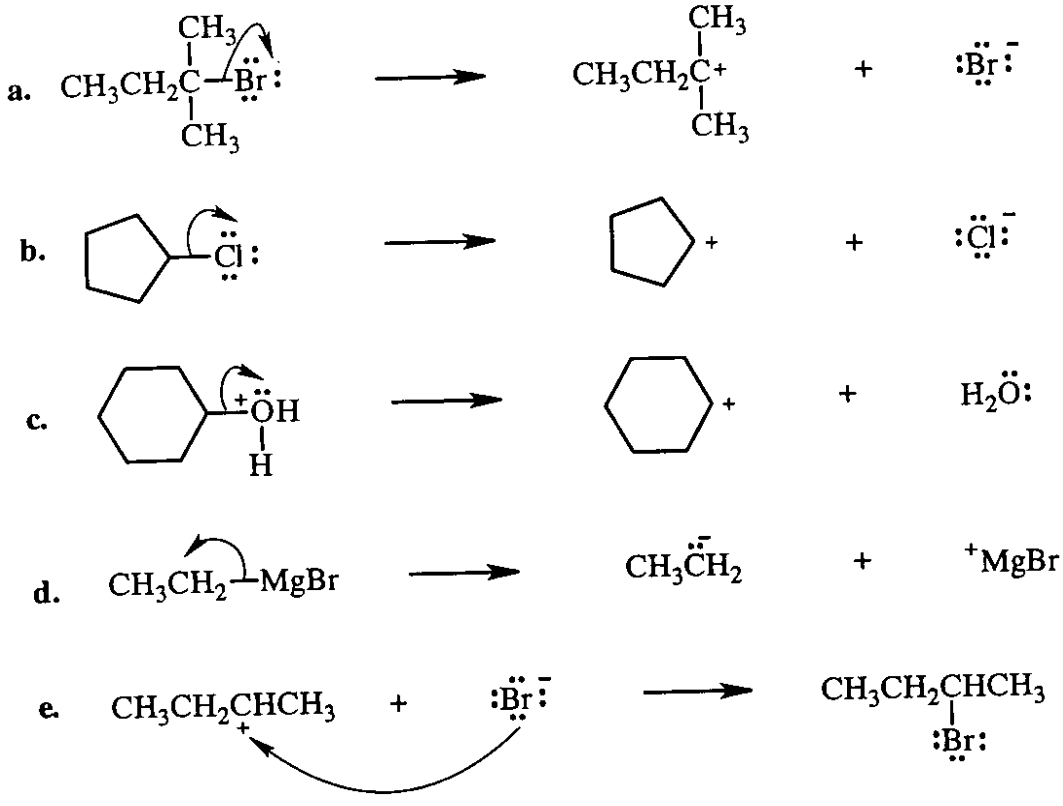
e. 

f. 

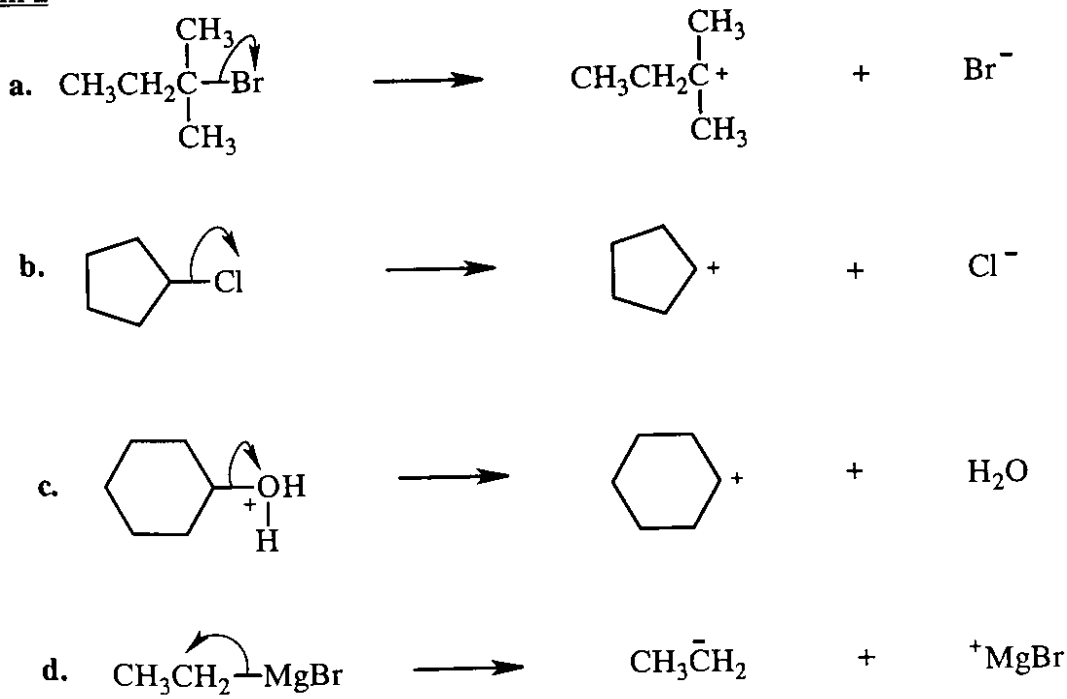
g. 

Answers to Electron Pushing Problems

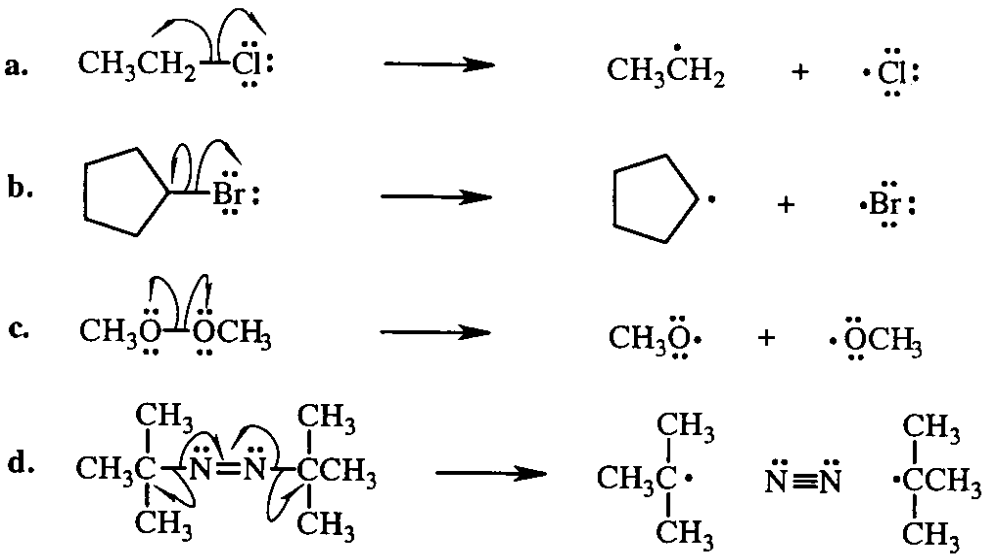
Problem 1



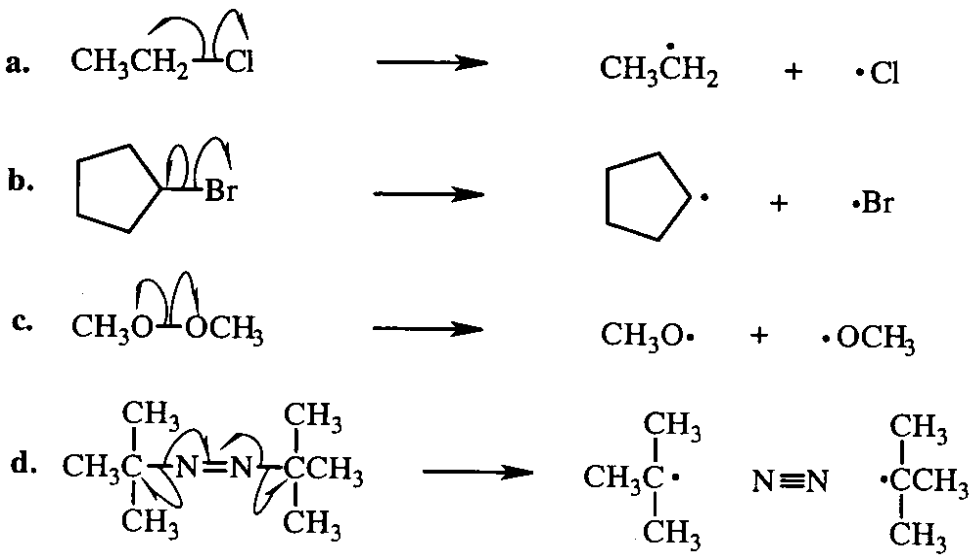
Problem 2



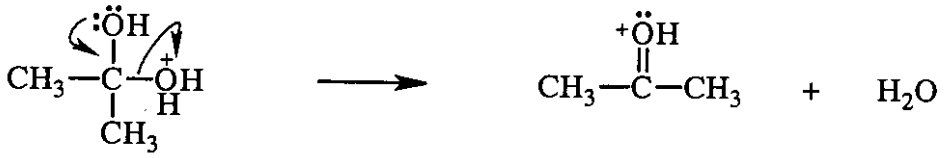
Problem 3



Problem 4



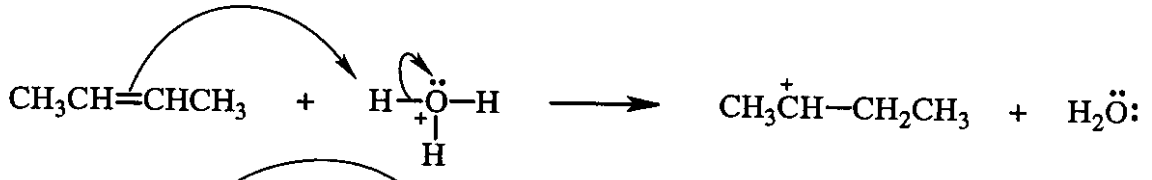
Problem 5

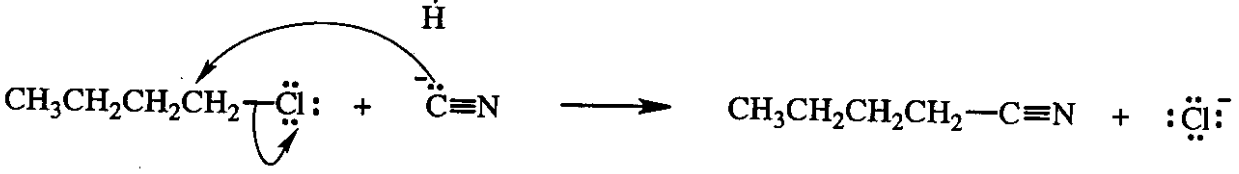
a. 

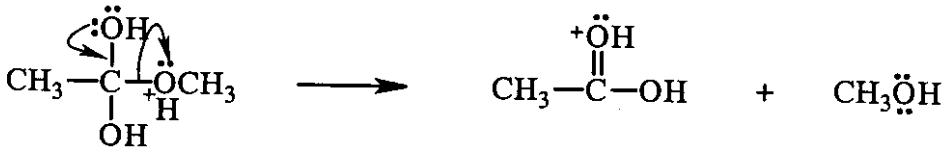
b. 

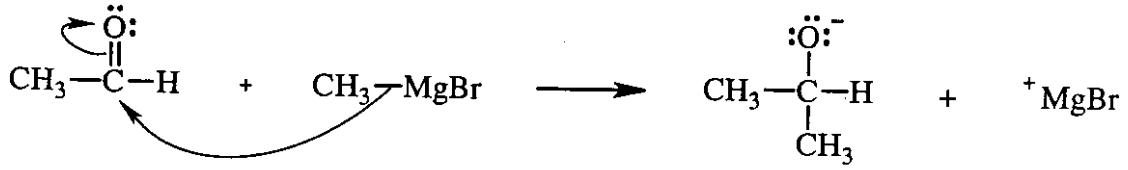
c. 

Problem 6

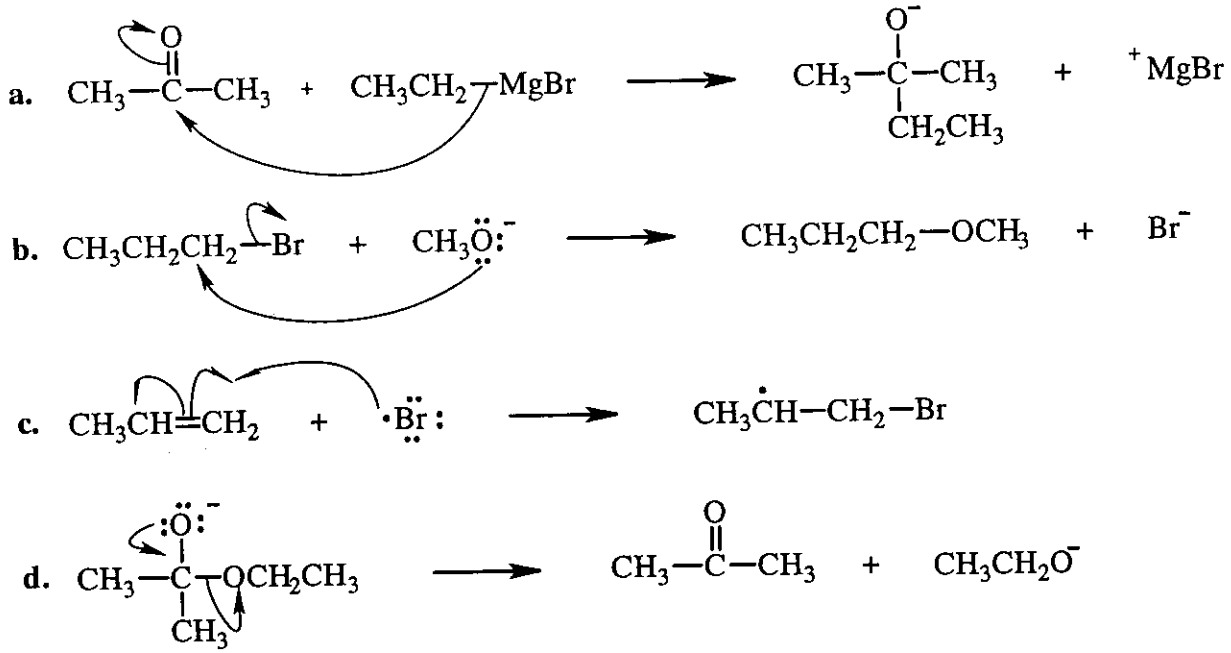
a. 

b. 

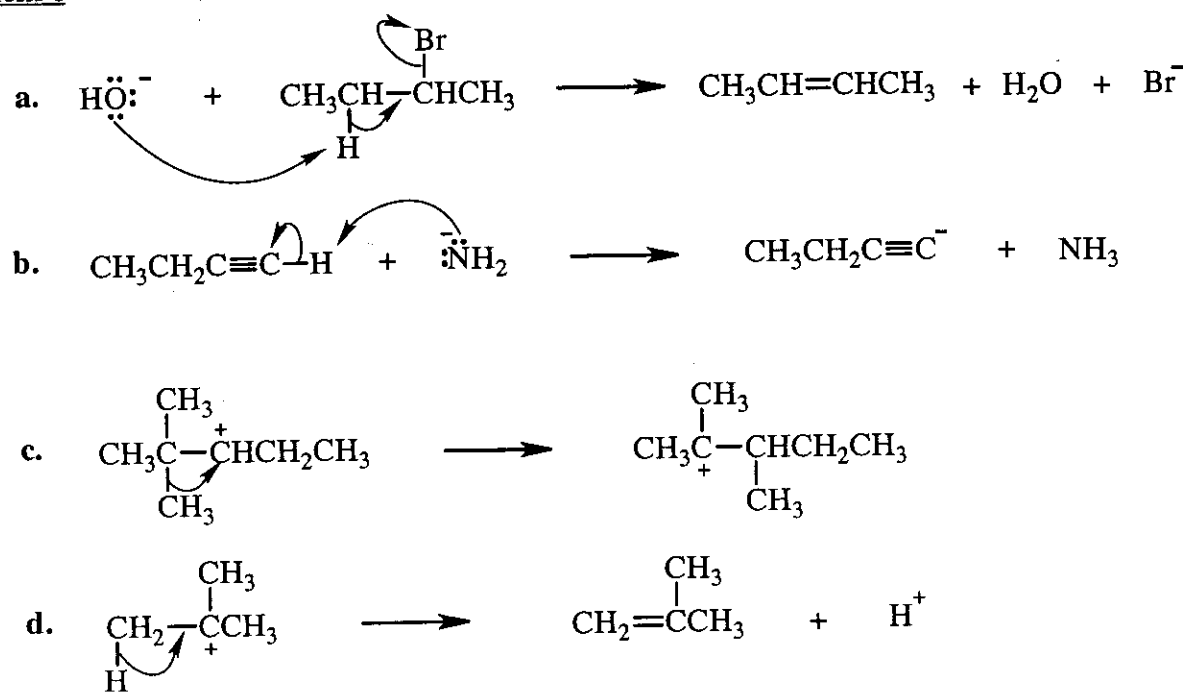
c. 

d. 

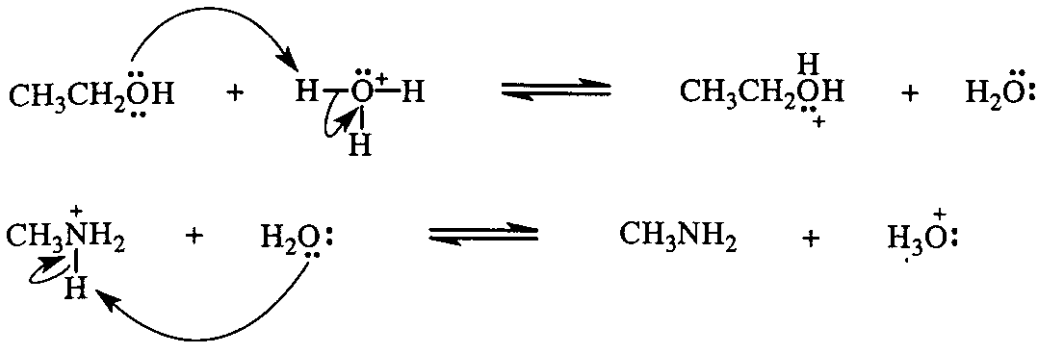
Problem 7



Problem 8

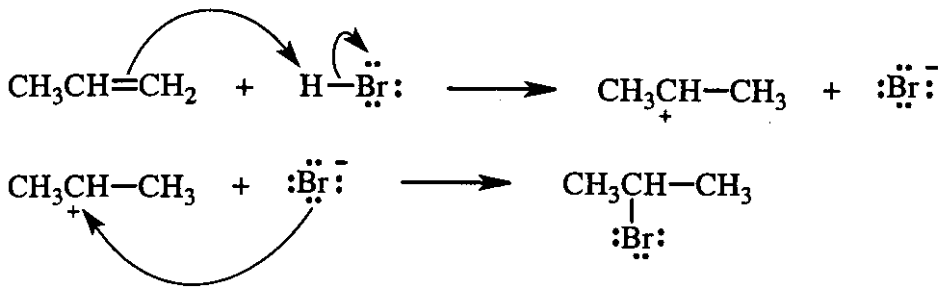


Problem 9

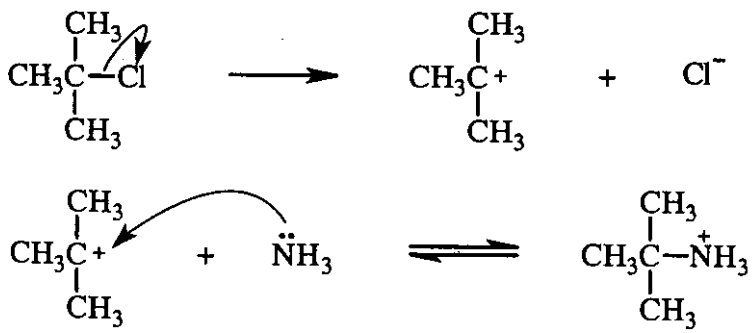


Problem 10

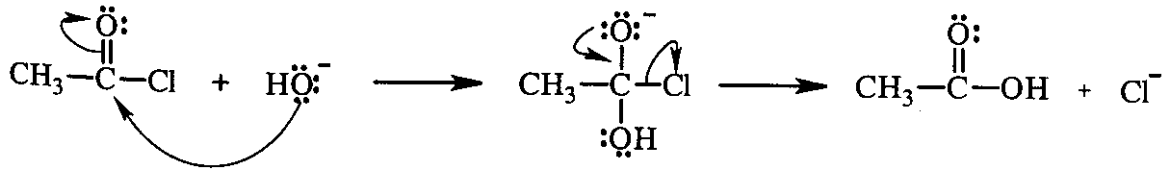
a.



b.

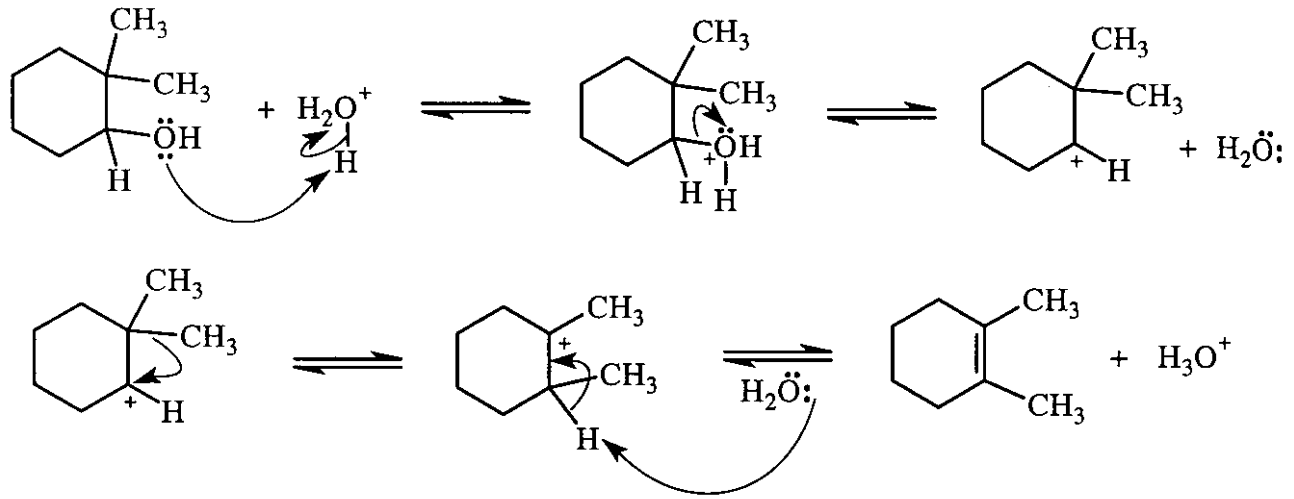


c.

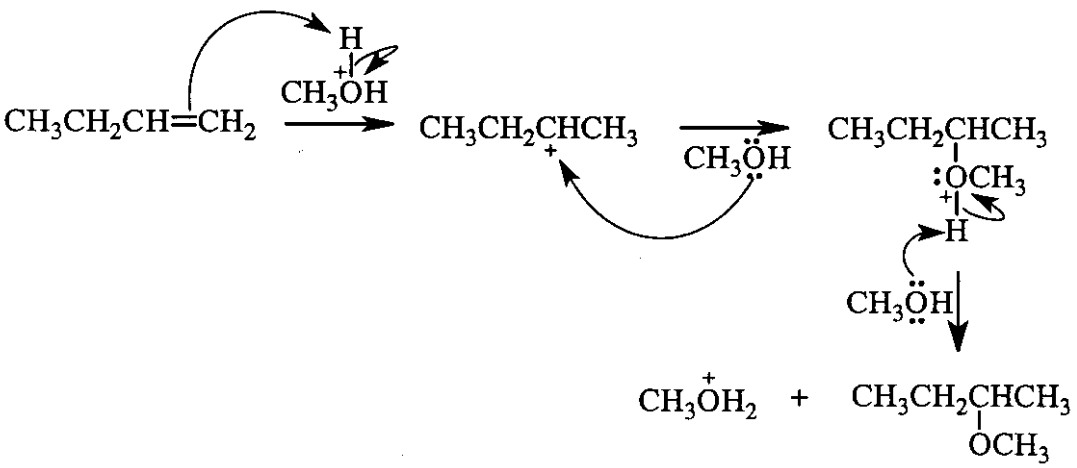


Problem 11

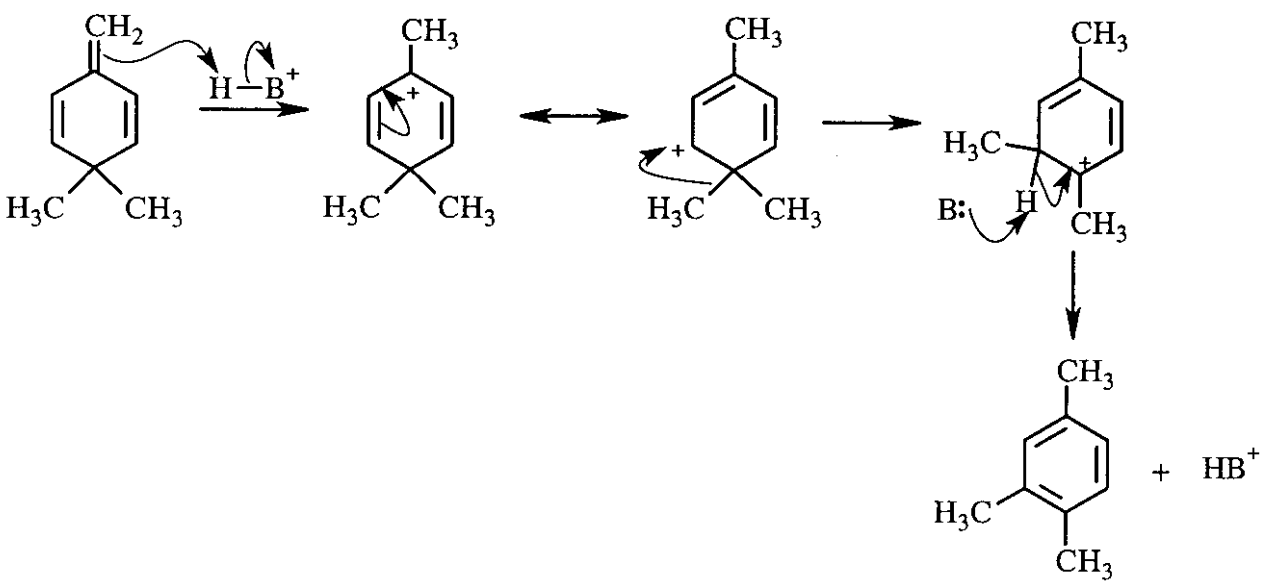
a.



b.

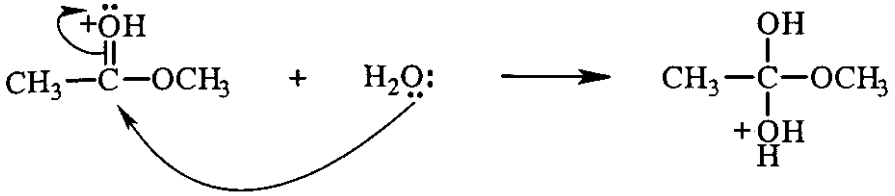


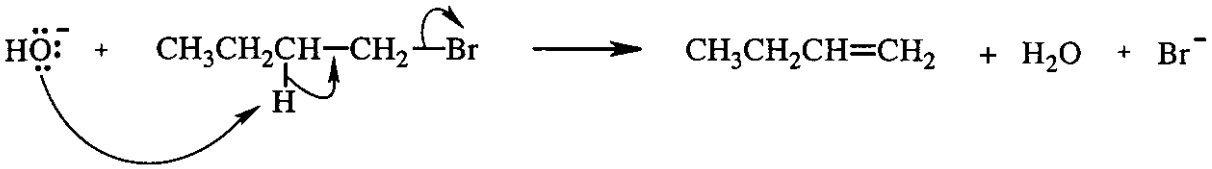
c.

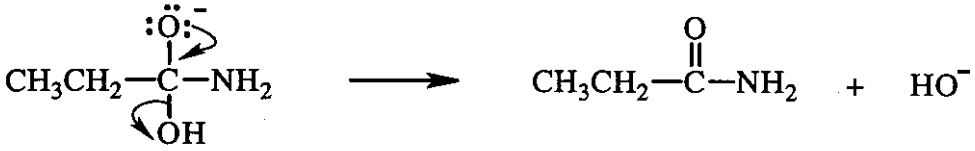


Problem 12

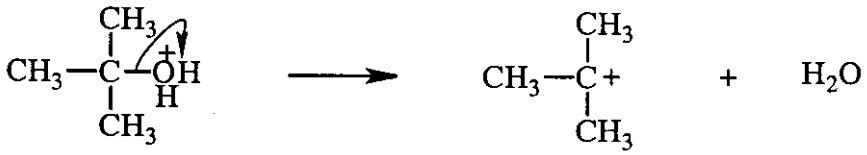
a. $CH_3CH_2\ddot{O}:^- + CH_3-\ddot{Br}: \longrightarrow CH_3CH_2OCH_3 + Br^-$

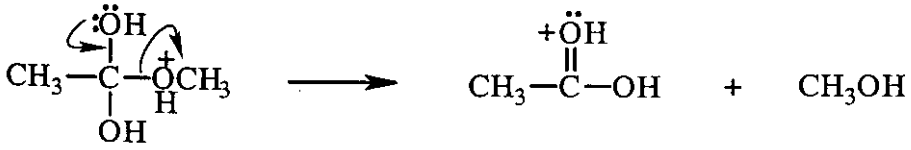
b. 

c. 

d. 

e. 

f. 

g. 

SPECIAL TOPIC III

Kinetics

This is a continuation of the discussion on kinetics found in Section 3.7 of the text. Note that the rate laws are derived in Appendix III.

1. How long would it take for the reactant of a first-order reaction to decrease to one-half its initial concentration if the rate constant is $4.5 \times 10^{-3}\ s^{-1}$ and the initial concentration of the reactant is:
a. 1.0 M? **b.** 0.50 M?

2. How long would it take for the reactants of a second-order reaction to decrease to one-half their initial concentration if the rate constant is $2.3 \times 10^{-2}\ M^{-1}s^{-1}$ and the initial concentration of both reactants is: **a.** 1.0 M? **b.** 0.50 M?

3. How many half-lives are required for a first-order reaction to reach > 99% completion?

4. The initial concentration of a reactant undergoing a first-order reaction is 0.40 M. After 5 minutes, the concentration of the reactant is 0.27 M; after an additional 5 minutes, the concentration of the reactant is 0.18 M; and after an additional 5 minutes, the concentration of the reactant is 0.12 M.

a. What is the average rate of the reaction during each five-minute interval?
b. What is the rate constant of the reaction?

5. What percentage of a compound, undergoing a first-order reaction with a rate constant of $2.7 \times 10^{-5}\ s^{-1}$, would have reacted at the end of two hours?

6. How long would it take for a first-order reaction with a rate constant of $5.3 \times 10^{-4}\ s^{-1}$ to reach 70% completion?

7. The following data were obtained in a study of the rate of inversion of sucrose at 25°C. The initial concentration of sucrose was 1.00 M.

Time (minutes)	0	30	60	90	130	180
Sucrose inverted (M)	0	0.100	0.195	0.277	0.373	0.468

a. What is the order of the reaction?
b. What is the rate constant of the reaction?

8. Calculate the activation energy of a first-order reaction that is 20% complete in 15 minutes at 40 °C or 20% complete in 3 minutes at 60 °C.

9. Analysis of an aqueous solution of sucrose shows that 80 grams of the original 100 grams of sucrose remain after 10 hours. At this rate, how much sucrose would be left after 24 hours?

Solutions to Problems in Special Topic III

1. a.

$$\text{half-life of a first-order reaction} = t_{1/2} = \frac{\ln 2}{k_1}$$

$$= \frac{0.693}{k_1}$$

$$= \frac{0.693}{4.5 \times 10^{-3}\ s^{-1}}$$

$$= 154 \text{ seconds}$$

$$= 2 \text{ minutes, } 34 \text{ seconds}$$

b. The half-life of a first-order reaction is independent of concentration, so the answer is the same as for **a** (15.4 seconds).

2.

a. $\text{half-life of a second-order reaction} = t_{1/2} = \frac{1}{k_2 a}$

$$= \frac{1}{2.3 \times 10^{-2}\ M^{-1}s^{-1}\ (1.00\ M)}$$

$$= 43 \text{ seconds}$$

b. $$t_{1/2} = \frac{1}{2.3 \times 10^{-2}\ M^{-1}s^{-1}\ (0.50\ M)}$$

$$= \frac{1}{1.15 \times 10^{-2}\ s^{-1}}$$

$$= 87 \text{ seconds}$$

3. One-half of the compound reacts during the first half-life. One half of what is left after the first half-life reacts during the second half-life. One half of what is left after the second half-life reacts during the third half-life, etc.

number of half-lives	percentage completion	
1	0.50 (100) = 50	50
2	0.50 (50) = 25	75
3	0.50 (25) = 12.5	87.5
4	0.50 (12.5) = 6.25	93.8
5	0.50 (6.25) = 3.125	96.9
6	0.50 (3.125) = 1.5625	98.4
7	0.50 (1.5625) = 0.78125	99.2

Seven half-lives are required.

4. **a.**

$$\text{rate} = \frac{\text{change in concentration}}{\text{change in time}}$$

1st interval: $$\text{rate} = \frac{0.40\text{ M} - 0.27\text{ M}}{5\text{ min}} = \frac{0.13\text{ M}}{5\text{ min}} = 2.60 \times 10^{-2}\text{ M min}^{-1}$$

2nd interval: $$\text{rate} = \frac{0.27\text{ M} - 0.18\text{ M}}{5\text{ min}} = \frac{0.09\text{ M}}{5\text{ min}} = 1.80 \times 10^{-2}\text{ M min}^{-1}$$

3rd interval: $$\text{rate} = \frac{0.18\text{ M} - 0.12\text{ M}}{5\text{ min}} = \frac{0.06\text{ M}}{5\text{ min}} = 1.20 \times 10^{-2}\text{ M min}^{-1}$$

Thus, the **rate** of the reaction decreases with decreasing concentration.

b. rate = k [reactant], using the average concentration of the reactant during the 5 minute interval.

1st interval: $2.60 \times 10^{-2}\text{ M min}^{-1} = k\,(0.335\text{ M})$

$$k = 7.8 \times 10^{-2}\text{ min}^{-1}$$

2nd interval: $1.80 \times 10^{-2}\text{ M min}^{-1} = k\,(0.225\text{ M})$

$$k = 8.0 \times 10^{-2}\text{ min}^{-1}$$

3rd interval: $1.20 \times 10^{-2}\text{ M min}^{-1} = k\,(0.15\text{ M})$

$$k = 8.0 \times 10^{-2}\text{ min}^{-1}$$

The **rate constant**, as its name indicates, is constant during the course of the reaction.

5. a = the initial concentration
x = the concentration that has reacted at time = t

$$\ln \frac{a}{a-x} = k_1 t$$

$$\ln \frac{100}{100-x} = 2.70 \times s^{-1}\ \text{(2 hours)}$$

$$\ln \frac{100}{100-x} = 2.70 \times s^{-1}\ \text{(7200 seconds)}$$

$$\ln \frac{100}{100-x} = 0.0844$$

$$\frac{100}{100-x} = 1.21$$

$$100 = 121 - 1.21x$$

$$1.21x = 21$$

$$x = 17.4\ \%$$

6.

$$\ln \frac{a}{a-x} = k_1 t$$

$$\ln \frac{100}{100-70} = 5.30 \times s^{-1}\, t$$

$$t = \frac{\ln 3.33}{5.30 \times 10^{-4}\ s^{-1}}$$

$$t = \frac{1.20}{5.30 \times s^{-1}}$$

$$t = 2260 \text{ seconds}$$

$$t = 37.6 \text{ minutes}$$

7.

1st order

$$k_1 = \frac{-\ln \frac{a-x}{a}}{t}$$

$$k_1 = \frac{-\ln \frac{1.000-0.100}{1.000}}{30} = \mathbf{3.51 \times 10^{-3}}$$

$$k_1 = \frac{-\ln \frac{1.000-0.195}{1.000}}{60} = \mathbf{3.62 \times 10^{-3}}$$

$$k_1 = \frac{-\ln \frac{1.000-0.277}{1.000}}{90} = \mathbf{3.60 \times 10^{-3}}$$

$$k_1 = \frac{-\ln \frac{1.000-0.373}{1.000}}{130} = \mathbf{3.59 \times 10^{-3}}$$

2nd order

$$k_2 = \frac{\frac{1}{a-x} - \frac{1}{a}}{t}$$

$$k_2 = \frac{\frac{1}{1.000-0.100} - \frac{1}{1.000}}{30} = \frac{1.111-1.000}{30} = \mathbf{3.70 \times 10^{-3}}$$

$$k_2 = \frac{\frac{1}{1.000-0.195} - 1.000}{60} = \mathbf{4.03 \times 10^{-3}}$$

$$k_2 = \frac{\frac{1}{1.000-0.277} - 1.000}{90} = \mathbf{4.26 \times 10^{-3}}$$

$$k_2 = \frac{\frac{1}{1.000-0.373} - 1.000}{130} = \mathbf{4.57 \times 10^{-3}}$$

$$k_1 = \frac{-\ln \frac{1.000 - 0.468}{1.000}}{180} = \mathbf{3.51 \times 10^{-3}} \qquad k_2 = \frac{\frac{1}{1.000 - 0.468} - 1.000}{180} = \mathbf{4.89 \times 10^{-3}}$$

a. Because the calculated rate constants are relatively constant when the data are plugged into a first-order equation and vary considerably when the data are plugged into a second-order equation, one can conclude that the reaction is first-order.

b. $3.59 \times 10^{-3}\ \text{min}^{-1}$

8.

$$k \text{ at } 40\ ^\circ\text{C} = \frac{\ln \frac{1.00}{1.00 - 0.20}}{15\ \text{min}} = 1.49 \times 10^{-2}\ \text{min}^{-1}$$

$$k \text{ at } 60\ ^\circ\text{C} = \frac{\ln \frac{1.00}{1.00 - 0.20}}{3\ \text{min}} = 7.44 \times 10^{-2}\ \text{min}^{-1}$$

$$\ln k_2 - \ln k_1 = \frac{-E_a}{R}\left(\frac{1}{T_2} - \frac{1}{T_1}\right)$$

$$\ln 7.44 \times 10^{-2} - \ln 1.49 \times 10^{-2} = \frac{-E_a}{1.986 \times 10^{-3}\ \text{kcal}}\left(\frac{1}{333} - \frac{1}{313}\right)$$

$$-2.60 - (-4.21) = \frac{-E_a}{1.986 \times 10^{-3}}(0.00300 - 0.00319)$$

$$1.61 = \frac{-E_a}{1.986 \times 10^{-3}}(-0.00019)$$

$$E_a = \frac{1.61 \times 1.986 \times 10^{-3}}{0.00019}$$

$$E_a = 16.8\ \text{kcal/mol}$$

9. Sucrose is hydrolyzed to form a mixture of glucose and fructose. Because there is an excess water (it is the solvent), the reaction is a pseudo first-order reaction.

First, the rate constant of the reaction must be determined:

$$\ln \frac{a}{a - x} = k_1 t$$

$$\ln \frac{100}{80} = k_1 \text{ x } 10 \text{ hours}$$

$$k_1 = 2.23 \text{ x } 10^{-2} \text{ hr}^{-1}$$

$$\ln \frac{a}{a - x} = k_1 t$$

$$\ln \frac{100}{100 - x} = 2.23 \text{ x } 10^{-2} \text{ (24 hr)}$$

$$\ln \frac{100}{100 - x} = 0.535$$

$$\frac{100}{100 - x} = 1.71$$

$$100 = 171 - 1.71x$$

$$1.71x = 71$$

$$x = 41.5 \text{ g have reacted}$$

Therefore, 58.5 g would be left.

CHAPTER 4
Reactions of Alkenes

Important Terms

acid-catalyzed reaction	a reaction catalyzed by an acid.
alkoxymercuration-demercuration	addition of an alcohol to an alkene using mercuric acetate followed by sodium borohydride and sodium hydroxide.
carbene	a neutral carbon with a lone-pair of electrons and an empty orbital.
carbocation rearrangement	the rearrangement of a carbocation to a more stable carbocation.
catalyst	a compound that increases the rate at which a reaction occurs without being consumed in the reaction. Because it does not change the equilibrium constant of the reaction, it does not change the amount of product that is formed.
catalytic hydrogenation	the addition of hydrogen to a double or a triple bond with the aid of a metal catalyst.
concerted reaction	a reaction in which all the bond-making and bond-breaking processes take place in a single step.
constitutional isomers (structural isomers)	molecules that have the same molecular formula but differ in the way the atoms are connected.
dimer	a molecule formed by joining together two identical molecules.
electrophilic addition reaction	an addition reaction in which the first species that adds to the reactant is an electrophile.
free radical	an atom or molecule with an unpaired electron.
halohydrin	an organic molecule that contains a halogen atom and an OH group.
Hammond postulate	states that the transition state will be more similar in structure to the species (reactants or products) that it is closer to energetically.
heat of hydrogenation	the heat ($\Delta H°$) released in a hydrogenation reaction.
heterogeneous catalyst	a catalyst that is insoluble in the reaction mixture.
heterolytic bond cleavage (heterolysis)	breaking a bond with the result that both bonding electrons stay with one of the atoms.
homogeneous catalyst	a catalyst that is soluble in the reaction mixture.
homolytic bond cleavage (homolysis)	breaking a bond with the result that each of the atoms gets one of the bonding electrons.
hormone	a compound that controls growth and other changes in tissues.

hydration	addition of water to a compound.
1,2-hydride shift	the movement of a hydride ion from one carbon to an adjacent carbon.
hydroboration-oxidation	the addition of borane to an alkene (or to an alkyne) followed by reaction with hydrogen peroxide and hydroxide ion.
hydrogenation	addition of hydrogen.
hyperconjugation	delocalization of electrons by overlap of carbon-hydrogen or carbon-carbon σ bonds with an empty p orbital.
initiation step	the step in which radicals are created, or the step in which the radical needed for the first propagation step is created.
Markovnikov's rule	the actual rule is: "When a hydrogen halide adds to an asymmetrical alkene, the addition occurs such that the halogen attaches itself to the carbon atom of the alkene bearing the least number of hydrogen atoms." Chemists use the rule as follows: The hydrogen adds to the sp^2 carbon that is bonded to the greater number of hydrogens. A more general rule is: The electrophile adds to the sp^2 carbon that is bonded to the greater number of hydrogens.
mechanism of the reaction	a description of the step-by-step process by which reactants are changed into products.
1,2-methyl shift	the movement of a methyl group with its bonding electrons from one carbon to an adjacent carbon.
oxymercuration-demercuration	addition of water using a mercuric salt of a carboxylic acid as a catalyst, followed by reaction with sodium borohydride.
pericyclic reaction	a concerted reaction that involves a cyclic rearrangement of electrons.
peroxide effect	causes the electrophile in an addition reaction of HBr to be a bromine radical instead of a proton.
pheromone	a chemical substance used for the purpose of communication.
primary alkyl radical	an alkyl radical with the unpaired electron on a primary carbon.
primary carbocation	a carbocation with the positive charge on a primary carbon.
propagation step	in the first of a pair of propagation steps, a radical (or an electrophile or a nucleophile) reacts to produce another radical (or an electrophile or a nucleophile) that reacts in the second propagation step to produce the radical (or the electrophile or the nucleophile) that was the reactant in the first propagation step.
radical (often called a free radical)	an atom or molecule with an unpaired electron.

Impor[illegible]

aci[illegible]

	an addition reaction in which the first species that adds is a radical.
	a reaction in which radicals are formed and react in repeating propagatin steps.
	a compound that traps radicals.
	a compound that creates radicals.
[illegible]ective reaction	a reaction that leads to the preferential formation of one constitutional isomer over another.
secondary alkyl radical	an alkyl radical with the unpaired electron on a secondary carbon.
secondary carbocation	a carbocation with the positive charge on a secondary carbon.
steric effect	an effect due to the space occupied by a substituent.
steric hindrance	refers to bulky groups at the site of a reaction that make it difficult for t reactants to approach one another.
termination step	two radicals combine to produce a molecule in which all the electrons a paired.
tertiary alkyl radical	an alkyl radical with the unpaired electron on a tertiary carbon.
tertiary carbocation	a carbocation with the positive charge on a tertiary carbon.

Solutions to Problems

1.

a. $CH_3CH_2\overset{+}{C}(CH_3)_2$ > $CH_3CH_2\overset{+}{C}HCH_3$ > $CH_3CH_2CH_2\overset{+}{C}H_2$

b. The halogen atoms decrease the stability of the carbocation because, since they are more electronegative than a hydrogen, they are more effective than a hydrogen at withdrawing electrons away from the positively charged carbon. This increases the concentration of positive charge on the carbocation which makes it less stable.

Because fluorine is more electronegative than chlorine, the fluorine-substituted carbocation is less stable than the chlorine-substituted carbocation.

$CH_3\overset{+}{C}H(CH_3)CH_2CH_2$ > $CH_3\overset{+}{C}H(Cl)CH_2CH_2$ > $CH_3\overset{+}{C}H(F)CH_2CH_2$

2. **a.** The bond orbitals of the carbon that is adjacent to the positively charged carbon are the bond orbitals that are available for overlap with the vacant *p* orbital. Because the methyl cation does not have a carbon adjacent to the positively charged carbon, there are no bond orbitals available for overlap with the vacant *p* orbital.

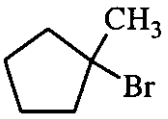
b. An ethyl cation is more stable because it has three carbon-hydrogen bond orbitals available for overlap with the vacant *p* orbital, while a methyl cation does not have any carbon-hydrogen bond orbitals available for overlap with the vacant *p* orbital.

3. **a.** products **b.** reactants **c.** reactants **d.** products

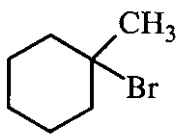
4.

a. $CH_3CH_2CH(Br)CH_3$

b. $CH_3CH_2C(CH_3)(Br)CH_3$

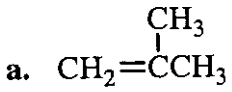
c. 

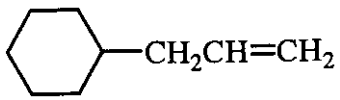
d. $CH_3C(CH_3)(Br)CH_2CH_2CH_2CH_3$

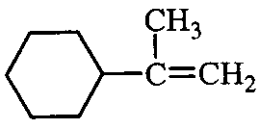
e. 

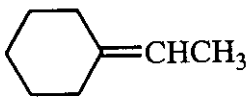
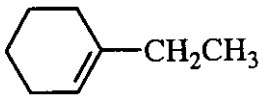
f. $CH_3CH_2CH(Br)CH_3$

5.

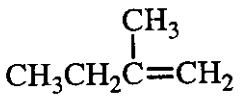
a. 

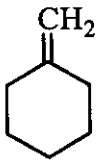
b. 

c. 

d.  or 

6.

a. 

b. 

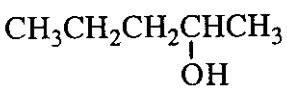
In both **a** and **b**, the compound that is more highly regioselective is the o where the choice is between forming a tertiary carbocation or a primary carbocation.
In the less regioselective compound, the choice is between forming a terti carbocation or a secondary carbocation, so the difference in the stability the two possible carbocations is not as great.

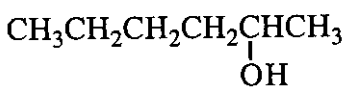
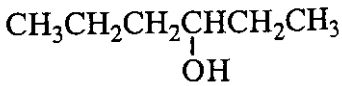
7. As long as the pH is greater than –2.5 and less than about 15, more than 50% of 2-propanol would be in its neutral, nonprotonated form.
Because when the pH = pK_a, half the compound is in its acid form and half is in its basic form, a a pH less than – 2.5, more than half of the compound will be in its positively charge protonated form. At a pH greater than about 15, more than half of the compound will exist as the negatively charged anion.

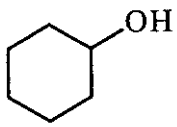
8.

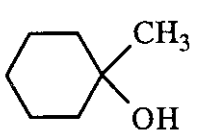
a. 3 transition states
b. 2 intermediates
c. the neutral alcohol
d. the second and third steps in the forward direction

9.

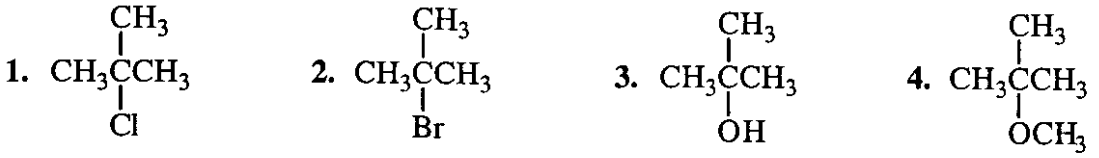
a. 

c.  and 

b. 

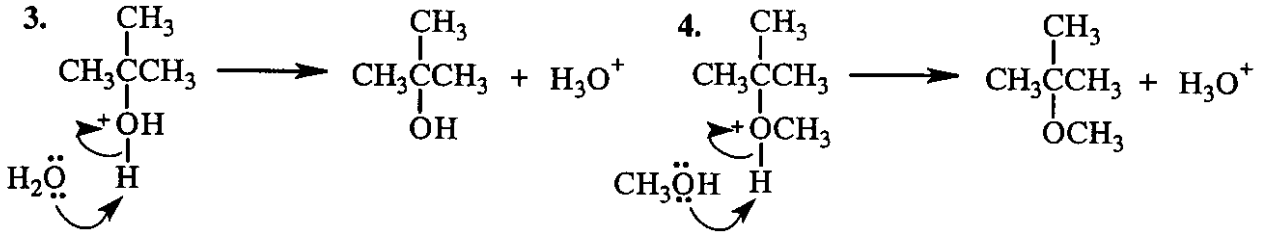
d. 

10. **a.**



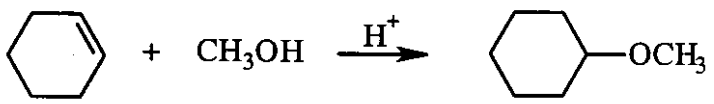
b. The first step in all the reactions is addition of an electrophilic proton (H^+) to the carbon of the CH_2 group.
The *tert*-butyl carbocation is formed as an intermediate in each of the reactions.

c. The nucleophile that adds to the *tert*-butyl carbocation is different in each reaction.
In reactions #3 and #4, there is a third step—a proton is lost from the group that was the nucleophile in the second step of the reaction.

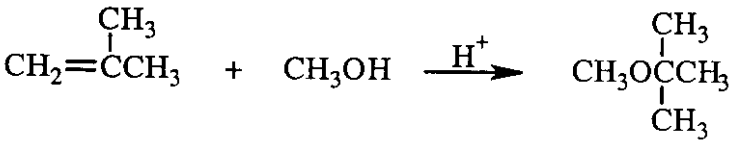


11.

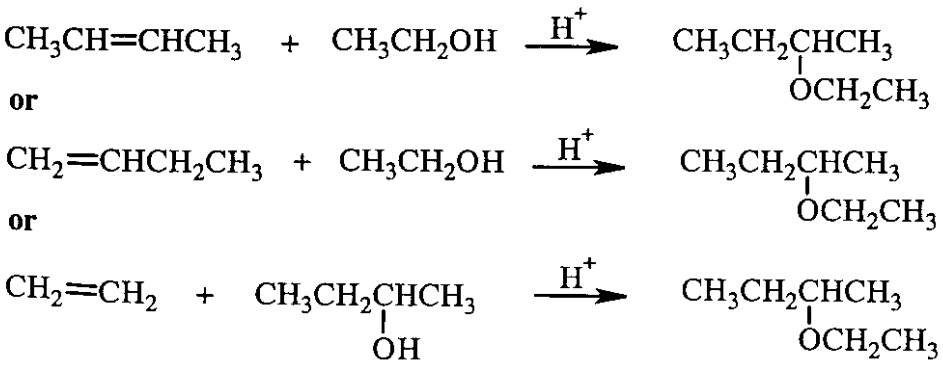
a.



b.



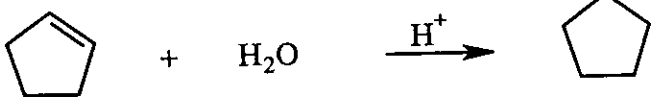
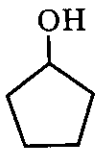
c.



d. $CH_3CH{=}CHCH_3 + H_2O \xrightarrow{H^+} CH_3\underset{\displaystyle OH}{\underset{|}{C}}HCH_2CH_3$

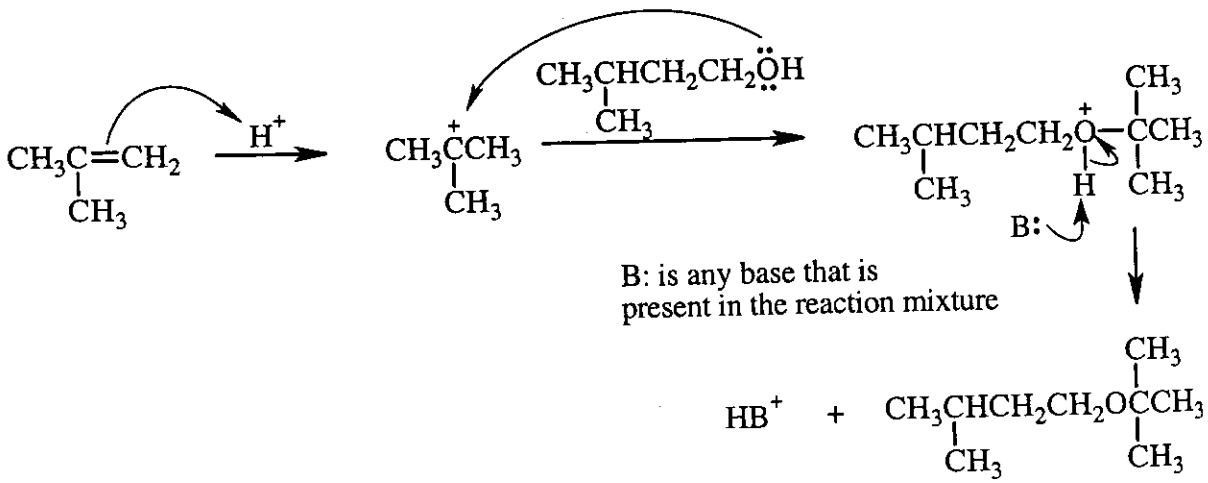
or

$CH_2{=}CHCH_2CH_3 + H_2O \xrightarrow{H^+} CH_3\underset{\displaystyle OH}{\underset{|}{C}}HCH_2CH_3$

e.  $+ H_2O \xrightarrow{H^+}$ 

f. $CH_3CH_2CH{=}CHCH_2CH_3 + H_2O \xrightarrow{H^+} CH_3CH_2\underset{\displaystyle OH}{\underset{|}{C}}HCH_2CH_2CH_3$

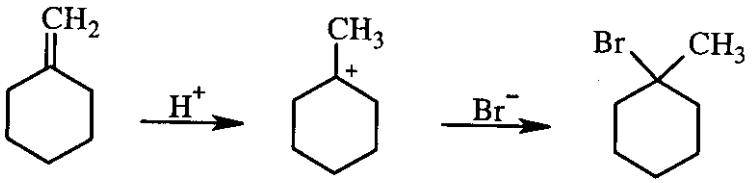
12.



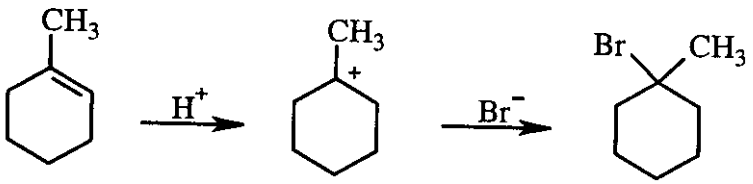
13. Solved in the text.

14.

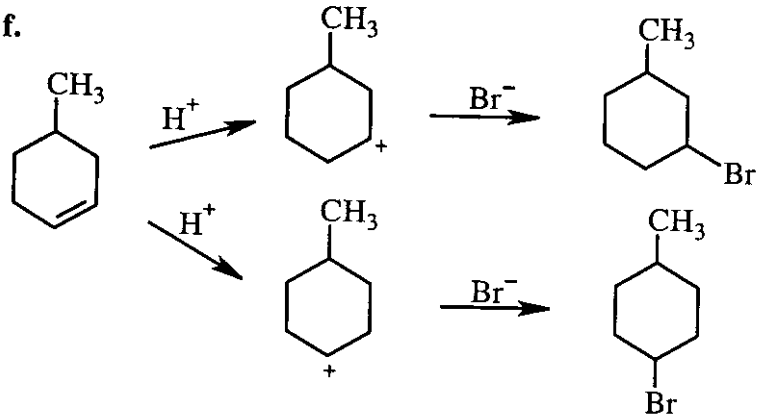
a. $CH_3CHCH{=}CH_2$ (CH$_3$ on C2) $\xrightarrow{H^+}$ $CH_3\overset{+}{C}HCH_3$ (CH$_3$ on C2) **secondary** $\xrightarrow[\text{shift}]{\text{1,2-hydride}}$ $CH_3\overset{+}{C}CH_2CH_3$ (CH$_3$ on C2) **tertiary** $\xrightarrow{Br^-}$ $CH_3CBrCH_2CH_3$ (CH$_3$ on C2)

b. 

c. $CH_3CHCH_2CH{=}CH_2$ (CH$_3$ on C2) $\xrightarrow{H^+}$ $CH_3CHCH_2\overset{+}{C}HCH_3$ (CH$_3$ on C2) $\xrightarrow{Br^-}$ $CH_3CHCH_2CHCH_3$ (CH$_3$ on C2, Br on C4)

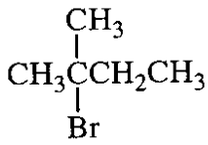
d. 

e. $CH_2{=}CHC(CH_3)_2CH_3$ $\xrightarrow{H^+}$ $CH_3\overset{+}{C}HC(CH_3)_2CH_3$ **secondary** $\xrightarrow[\text{shift}]{\text{1,2-methyl}}$ $CH_3CH\overset{+}{C}(CH_3)_2CH_3$ **tertiary** $\xrightarrow{Br^-}$ $CH_3CH(Br)C(CH_3)_2CH_3$

f. 

1-Bromo-3-methylcyclohexane and 1-bromo-4-methylcyclohexane will be obtained in approximately equal amounts because in each case the initially formed carbocation is secondary.

15.

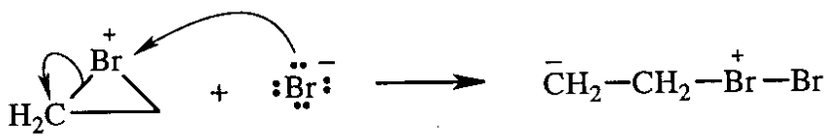


Addition of H^+ would form a carbocation that could rearrange.

Addition of Br^+ forms a cyclic bromonium ion rather than a carbocation so there is no rearrangement.

16. **a.** The first step in the reaction of ethene with Br_2 forms a cyclic bromonium ion, whereas the first step in the reaction of ethene with HBr forms a carbocation.

b. If the bromide ion were to attack the positively charged bromine atom, a highly unstable compound (with a negative charge on carbon and a positive charge on bromine) would be formed.



Notice that the electrostatic potential maps of the cyclic bromonium ions on p. 158 of the text show that the ring carbons are the least electron dense (most blue) atoms in the intermediate.

17. The nucleophile that is present in greater concentration is more apt to collide with the carbocation intermediate. Therefore, if the solvent is a nucleophile, the major product will come from reaction of the solvent with the carbocation or cyclic bromonium (or chloronium) ion intermediate, because the concentration of the solvent is much greater than the concentration of the other nucleophile. (For example, in "a" the concentration of CH_3OH is much greater than the concentration of Cl^-.)

a. $ClCH_2C(CH_3)_2OCH_3$ and $ClCH_2C(CH_3)_2Cl$

major

b. $CH_3CH(I)CH_3$ and $CH_3CH(Br)CH_3$

major

c. $CH_3CH_2CH(OH)CH_3$ and $CH_3CH_2CH(Cl)CH_3$

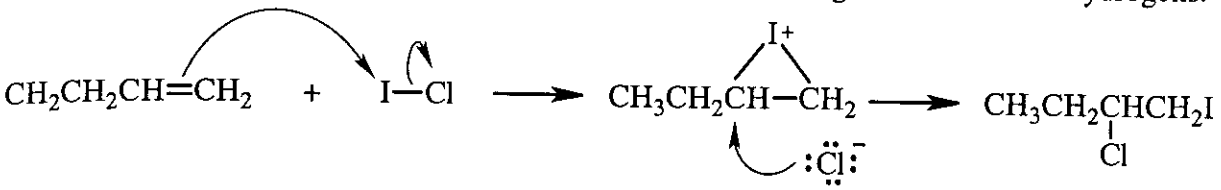
major

d. $CH_3CH_2CH(OCH_3)CH_3$ and $CH_3CH_2CH(Br)CH_3$

major

18. As elements, sodium and potassium achieve an outer shell of eight electrons by losing the single electron they have in the 3*s* (in the case of Na) or 4*s* (in the case of K) orbital, thereby becoming Na^+ and K^+. In order to form a covalent bond, they would have to regain electrons in these orbitals, thus losing the stability associated with having an outer shell of eight electrons and no extra electrons.

19. Because chlorine is more electronegative than iodine, iodine will be the electrophile. Therefore, it will become attached to the sp^2 carbon that is bonded to the greater number of hydrogens.

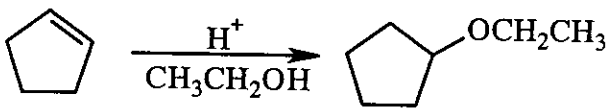


20.

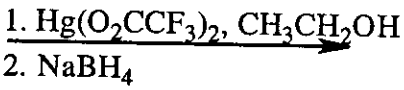
a. $CH_2CHCH_2CH_3$ (Br, Br) **b.** $CH_2CHCH_2CH_3$ (Br, OH) **c.** $CH_2CHCH_2CH_3$ (Br, OCH_2CH_3) **d.** $CH_2CHCH_2CH_3$ (Br, OCH_3)

21. Notice that the addition of water or the addition of an alcohol to an alkene can be carried out using an acid catalyst (Section 4.5) or by mercuration/demercuration (Section 4.8).

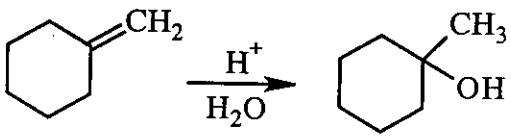
a.



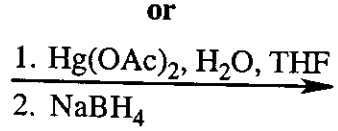
or



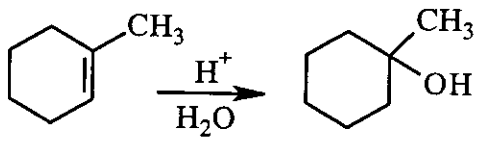
b.



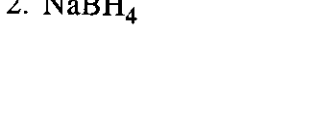
or



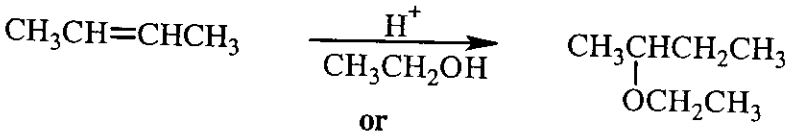
or



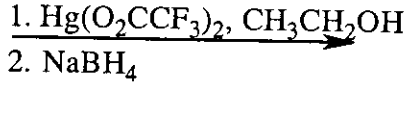
or



c.



or



d. $CH_2{=}C(CH_3)CH_2CH_3 \xrightarrow[CH_3OH]{H^+} CH_3C(CH_3)(OCH_3)CH_2CH_3$

or

$\xrightarrow[2.\ NaBH_4]{1.\ Hg(O_2CCF_3)_2,\ CH_3OH}$

22.

a. $CH_2{=}C(CH_3)CHCH_3 \xrightarrow{H^+} CH_3\overset{+}{C}(CH_3)CHCH_3 \xrightarrow{\text{1,2-hydride shift}} CH_3CH_2\overset{+}{C}CH_3 \xrightarrow{H_2O} CH_3CH_2C(Cl)$

b. $CH_2{=}C(CH_3)CHCH_3 \xrightarrow[2.\ NaBH_4]{1.\ Hg(OAc)_2,\ H_2O,\ THF} CH_3C(CH_3)(OH)CHCH_3$

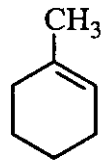
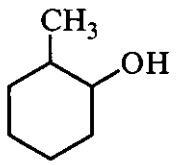
In **a**, a carbocation rearrangement is required to get the desired product from the given starting m

In **b**, the desired product must be obtained from a reaction that will not form a carbocation intern

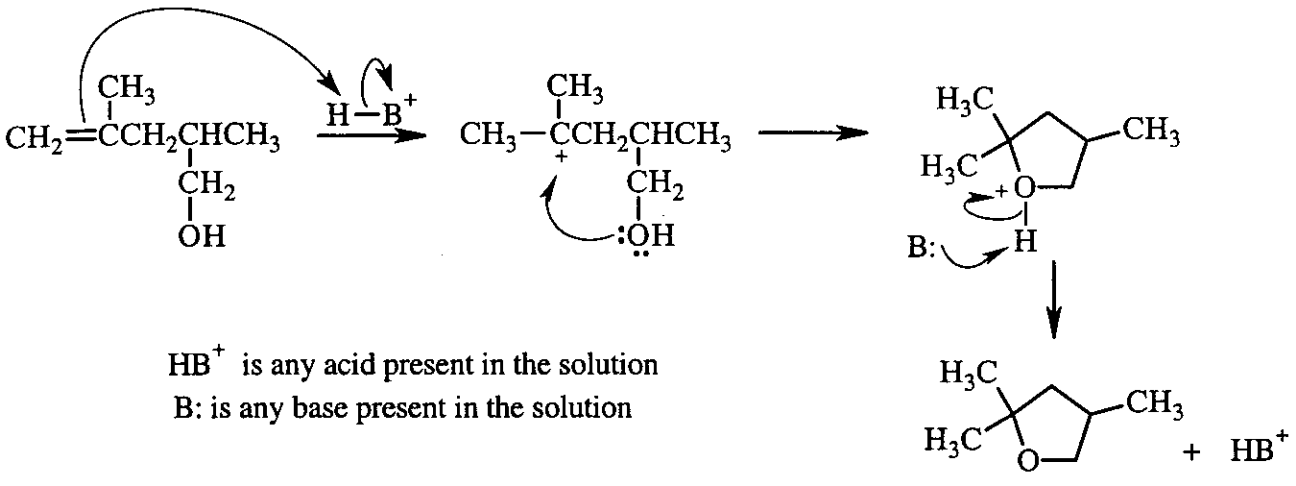
23. Because one mole of BH_3 reacts with three moles of an alkene, one third of a mole of BH_3 is needed to react with each mole of alkene. Therefore, two thirds of a mole of BH_3 is needed to react with two moles of an alkene (in this case, 1-pentene).

24.

a. $CH_3C(CH_3){=}CHCH_3 \xrightarrow[2.\ HO^-,\ H_2O_2,\ H_2O]{1.\ BH_3} CH_3C(CH_3)(OH)CHCH_3$

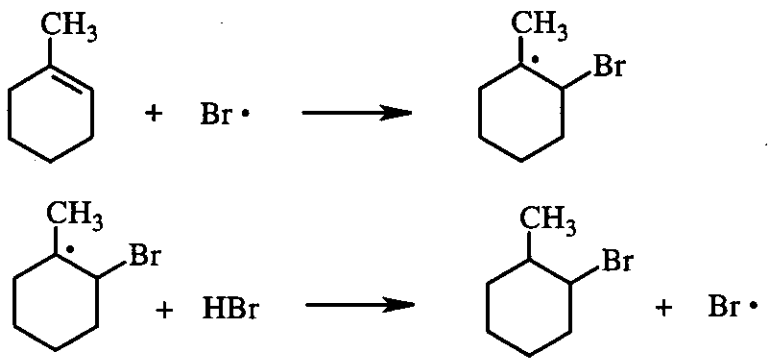
b.  $\xrightarrow[2.\ HO^-,\ H_2O_2,\ H_2O]{1.\ BH_3}$ 

25. Addition of a proton to the carbon that is bonded to the greater number of hydrogens forms a carbocation intermediate. The alcohol group in the same molecule is the nucleophile that reacts with the carbocation.



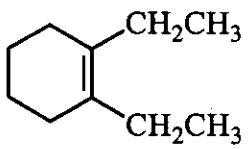
HB^+ is any acid present in the solution
B: is any base present in the solution

26.

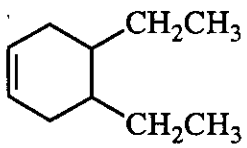


27. Because alkene A has the smaller heat of hydrogenation, it is more stable.

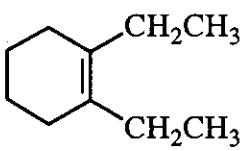
28.

a. 

This alkene is the most stable bcacause it has the greatest number of alkyl substituents bonded to the sp^2 carbons.

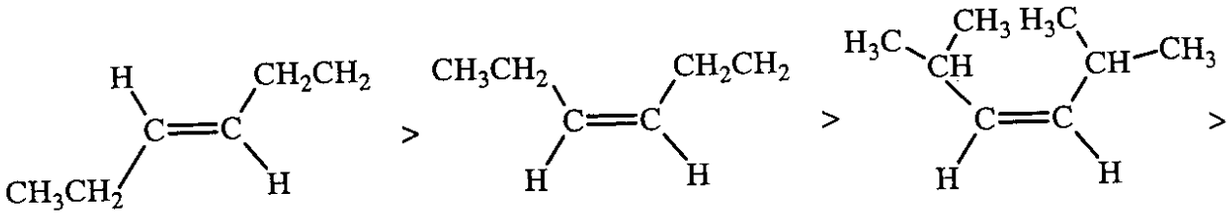
b. 

This alkene is the least stable bcacause it has the fewest number of alkyl substituents bonded to the sp^2 carbons.

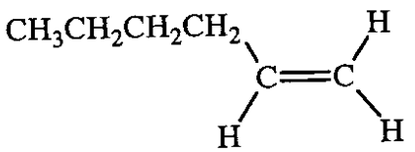
c. 

This alkene has the smallest heat of hydrogenation because it is the most stable of the three alkenes.

29.



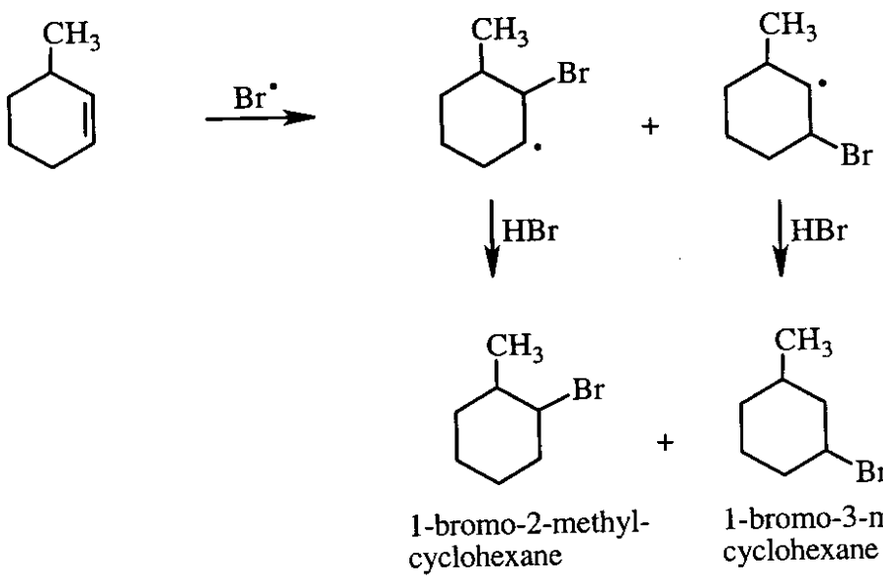
2 trans substituents > 2 cis substituents > 2 cis substituents that cause greater steric strain >



one substituent

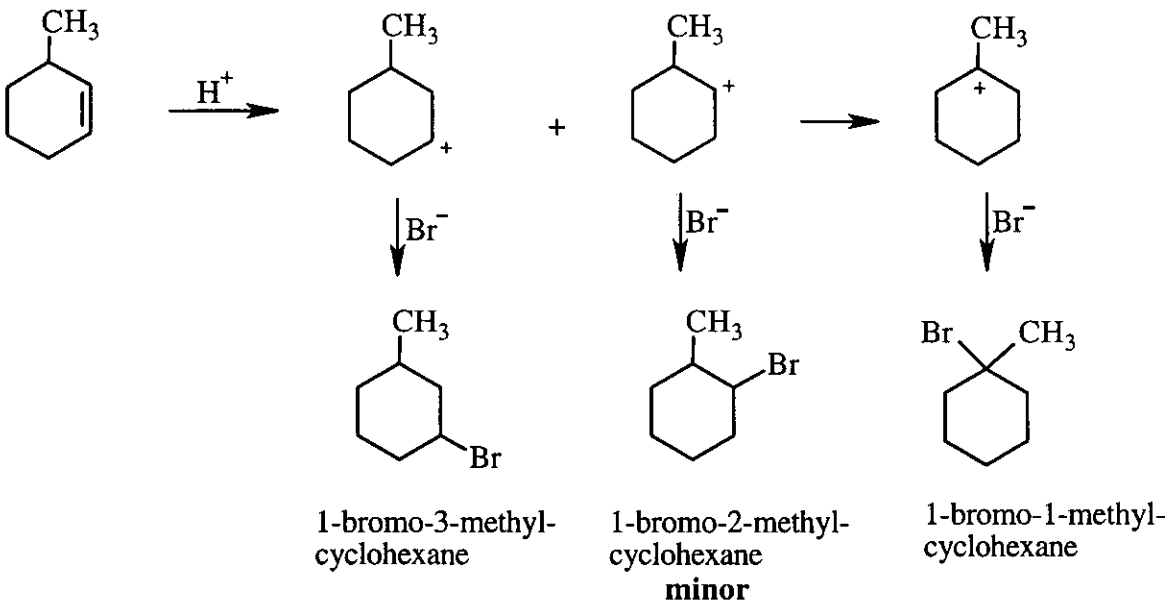
30. Solved in the text.

31. The reaction of 3-methylcyclohexene with HBr and peroxide would form approximately equal amounts of 1-bromo-2-methylcyclohexane (the desired product) and 1-bromo-3-methylcyclohexane because the bromine radical could add to either the 1-position or the 2-position of the alkene since in both cases a secondary radical would be formed. Thus, only half as much of the desired product would be formed from 3-methylcyclohexene than from 1-methylcyclohexene.



1-bromo-2-methylcyclohexane + 1-bromo-3-methylcyclohexane

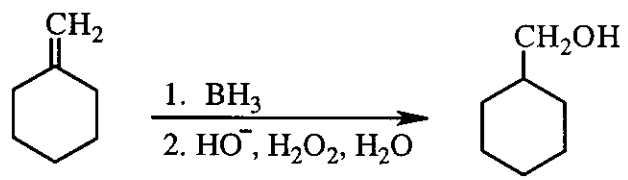
If 3-methylcyclohexene were treated with HBr in the absence of peroxide, little 1-bromo- 2-methylcyclohexane (the desired product) would be formed because the secondary carbocation with a positive charge at the 2-position would rearrange to a more stable tertiary carbocation.

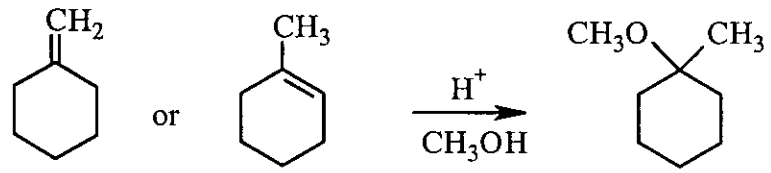


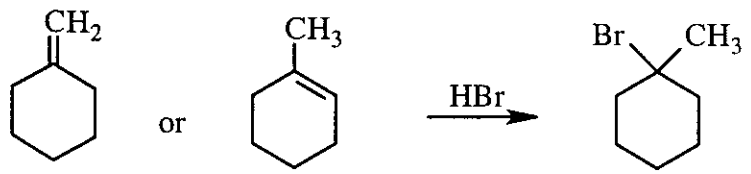
32.

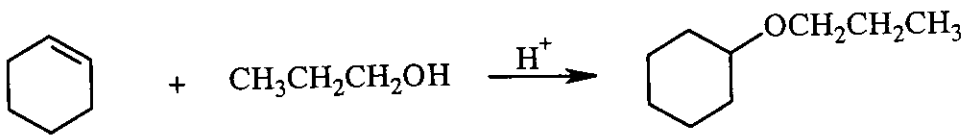
a. $CH_3CH{=}CH_2 \xrightarrow[CH_3OH]{H^+} CH_3\underset{\displaystyle OCH_3}{\underset{|}{C}}HCH_3$

b. $CH_3CH_2CH{=}CHCH_3 + Br_2 \longrightarrow CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}H\overset{\displaystyle Br}{\overset{|}{C}}HCH_3$

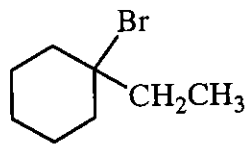
c. 

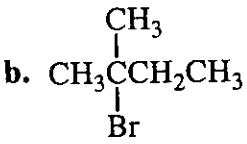
d. 

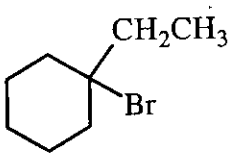
e. 

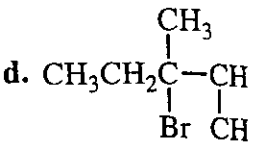
f. 

33.

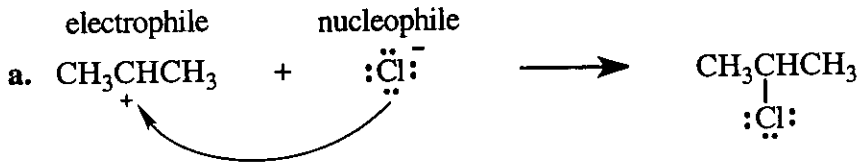
a. 

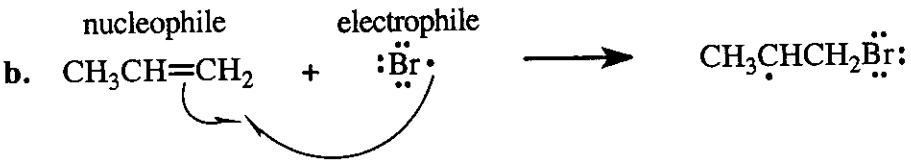
b. 

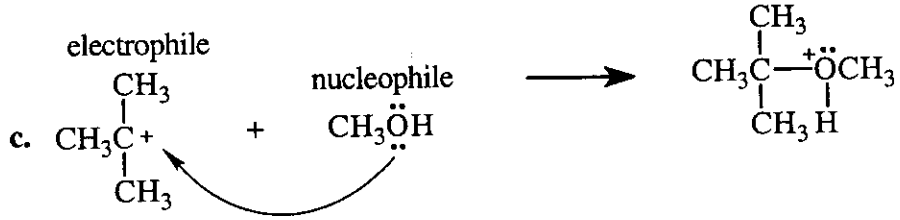
c. 

d. 

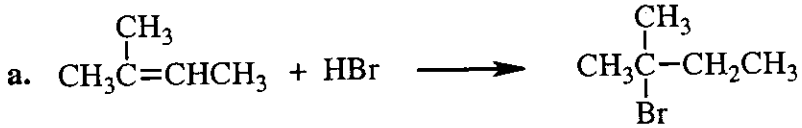
34.

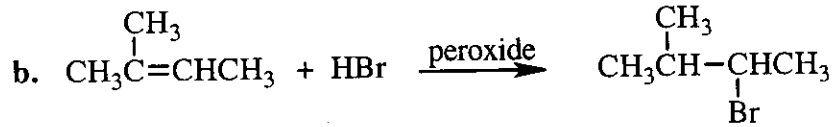
a. 

b. 

c. 

35.

a. 

b. 

c. $CH_3C(CH_3)=CHCH_3 + HI \longrightarrow CH_3C(CH_3)(I)CH_2CH_3$

d. $CH_3C(CH_3)=CHCH_3 + HI \xrightarrow{\text{peroxide}} CH_3C(CH_3)(I)CH_2CH_3$

e. $CH_3C(CH_3)=CHCH_3 + ICl \longrightarrow CH_3C(CH_3)(Cl)CH(I)CH_3$

f. $CH_3C(CH_3)=CHCH_3 \xrightarrow[Pd]{H_2} CH_3CH(CH_3)CH_2CH_3$

g. $CH_3C(CH_3)=CHCH_3 + Br_2 + \text{excess NaCl} \longrightarrow CH_3C(CH_3)(Cl)CH(Br)CH_3$

h. $CH_3C(CH_3)=CHCH_3 \xrightarrow[2.\ NaBH_4]{1.\ Hg(OAc)_2,\ H_2O} CH_3C(CH_3)(OH)CH_2CH_3$

i. $CH_3C(CH_3)=CHCH_3 + H_2O \xrightarrow{\text{trace HCl}} CH_3C(CH_3)(OH)CH_2CH_3$

j. $CH_3C(CH_3)=CHCH_3 + Br_2 \xrightarrow[CH_2Cl_2]{} CH_3C(CH_3)(Br)CH(Br)CH_3$

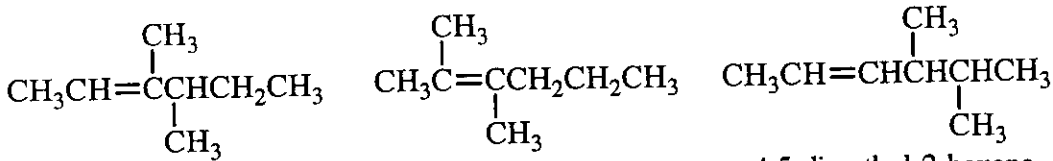
k. $CH_3C(CH_3)=CHCH_3 + Br_2 \xrightarrow{H_2O} CH_3C(CH_3)(HO)CH(Br)CH_3$

l. $CH_3C(CH_3)=CHCH_3 + Br_2 \xrightarrow{CH_3OH} CH_3C(CH_3)(CH_3O)CH(Br)CH_3$

m. $CH_3C(CH_3)=CHCH_3 \xrightarrow[2.\ H_2O_2,\ HO^-]{1.\ BH_3} CH_3CH(CH_3)CH(OH)CH_3$

n. $CH_3C(CH_3)=CHCH_3$ —(1. $Hg(O_2CCF_3)_2$, CH_3OH; 2. $NaBH_4$)→ $CH_3C(CH_3)(OCH_3)CH_2CH_3$

36.

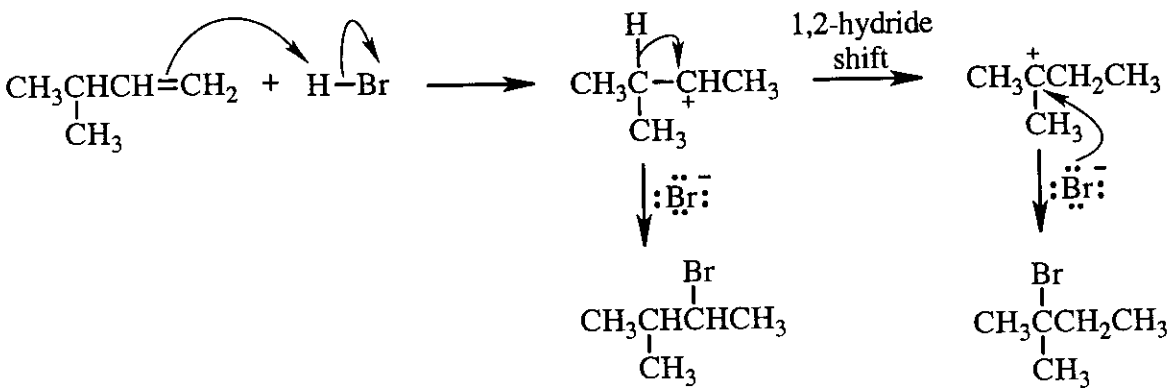


3,4-dimethyl-2-hexene | 2,3-dimethyl-2-hexene | 4,5-dimethyl-2-hexene

2,3-Dimethyl-2-hexene is the most stable because it has the greatest number alkyl substituents bonded to the sp^2 carbons. Because it is the most stable, it has the smallest heat of hydrogenation.

4,5-Dimethyl-2-hexene has the fewest alkyl substituents bonded to the sp^2 carbons. making it the least stable of the three alkenes. It, therefore, has the greatest heat of hydrogenation.

37.



38.

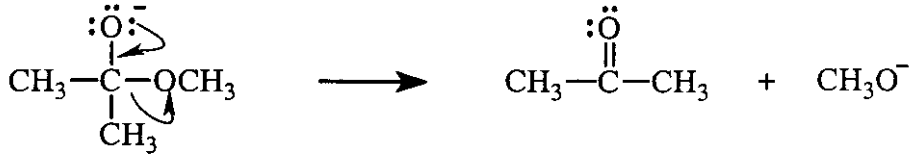
a. $CH_3C(CH_3)=CCH_3(CH_3)$

This compound is most stable. It has 4 alkyl substituents bonded to the sp^2 carbons.

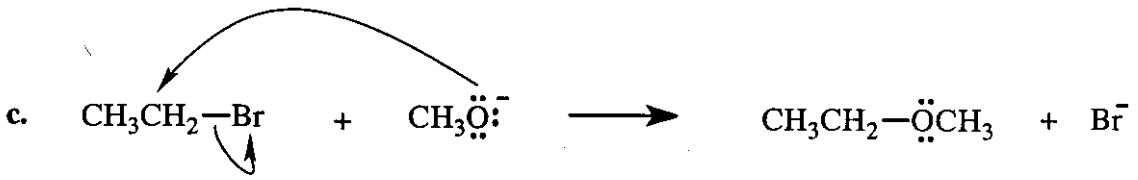
b. $CH_2=CHCH_2CH_2CH_2CH_3$ $CH_2=CHCH_2CH(CH_3)_2$ $CH_2=CHCH(CH_3)CH_2CH_3$ $CH_2=CHC(CH_3)_2CH_3$

These compounds are the least stable. Each has only one alkyl substituent bonded to the sp^2 carbons.

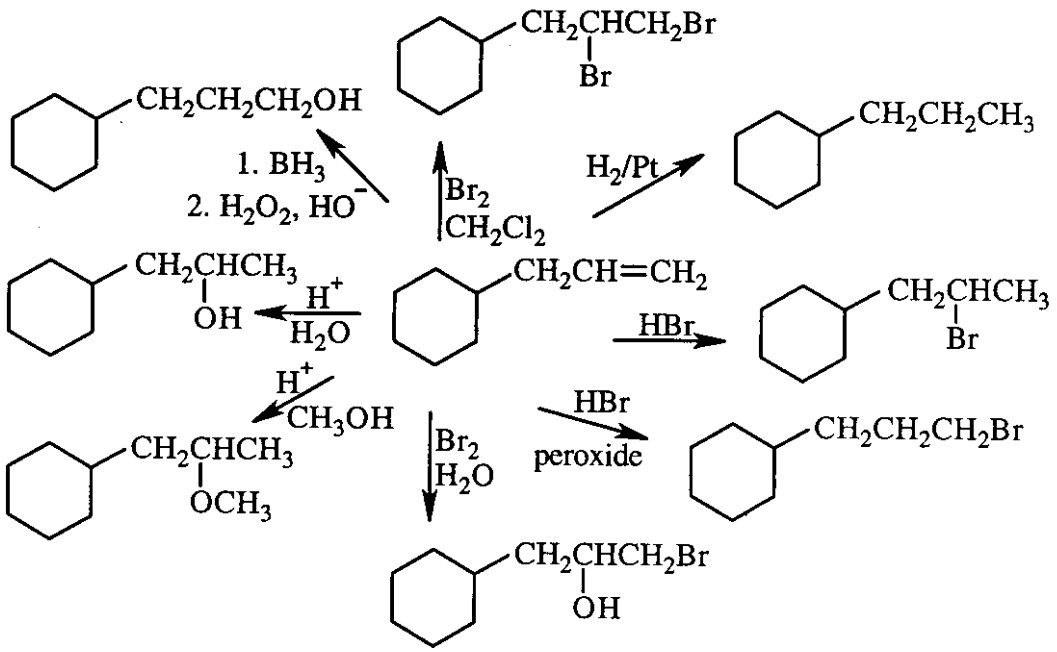
39.

a. 

b. 

c. 

40.


CH2CHCH2Br
Br
CH2CH2CH2OH
1. BH3
2. H2O2, HO−
Br2
CH2Cl2
H2/Pt
CH2CH2CH3
CH2CHCH3
OH
H+
H2O
CH2CH=CH2
HBr
CH2CHCH3
Br
H+
CH3OH
CH2CHCH3
OCH3
Br2
H2O
HBr
peroxide
CH2CH2CH2Br
CH2CHCH2Br
OH

41.

a. CH_3-Cl

Cl uses a 3 sp^3 orbital in bond formation, while Br uses a 4 sp^3 orbital. Cl, therefore, forms a shorter and stronger bond with carbon.

b. $CH_3CH_2\underset{\displaystyle H}{\underset{|}{C}}H_2$

A primary radical is less stable than a secondary radical, so it is harder to break a bond that results in the formation of a primary radical than it is to break a bond that results in the formation of a secondary radical.

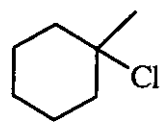
c. CH_3-CH_3

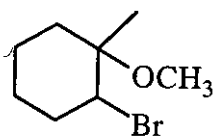
A methyl radical is less stable than a primary radical, so it is harder to break a bond that results in the formation of two methyl radicals than it is to break a bond that results in the formation of a methyl radical and a primary radical.

d. $Br-Br$

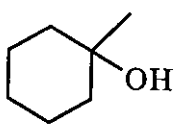
I forms a weaker bond than Br because I uses a 5 sp^3 orbital in bond formation, while Br uses a 4 sp^3 orbital.

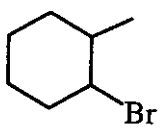
42.

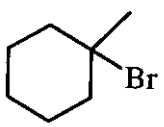
a. 

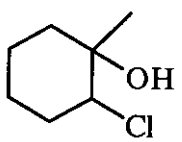
b. 

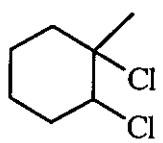
c. no reaction without an acid catalyst

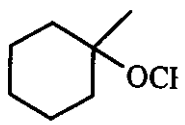
d. 

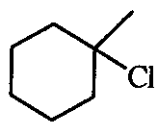
e. 

f. 

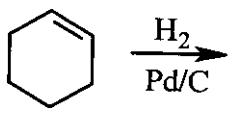
g. 

h. 

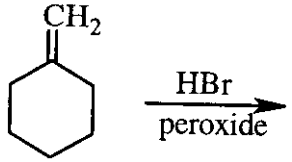
i. 

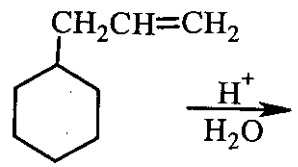
j. 

43.

a. 

b. $CH_3CH_2CH_2CH{=}CH_2 \xrightarrow{HCl}$

c. 

d. 

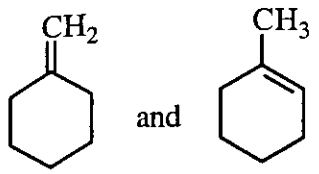
e. $CH_3CH_2CH{=}CHCH_2CH_3 \xrightarrow[H_2O]{Br_2}$

f. $CH_3CH_2CH{=}CHCH_2CH_3 \xrightarrow[NaBr\ excess]{Cl_2}$

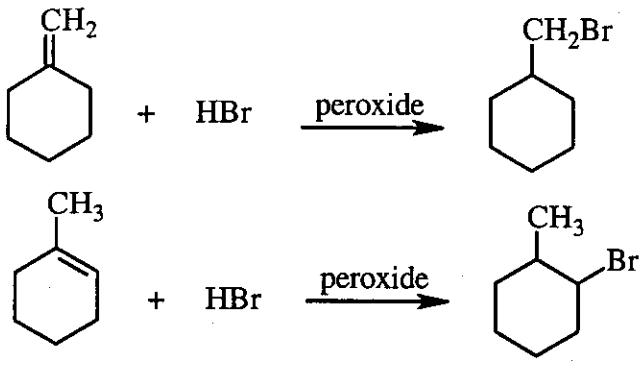
or

$CH_3CH_2CH{=}CHCH_2CH_3 \xrightarrow[NaCl\ excess]{Br_2}$

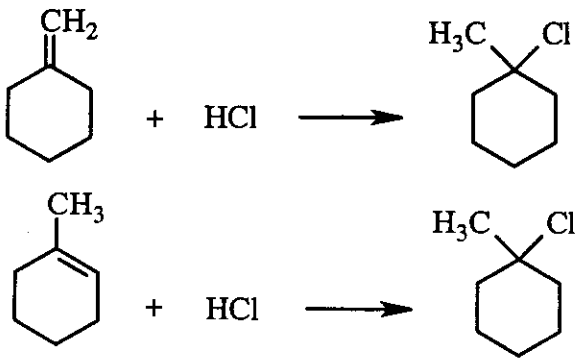
44.

a. 

b. No.



c. Yes.



d. Peroxide has no effect on the addition of HCl, so both compounds will give the same product (the product shown in **c**).

45.

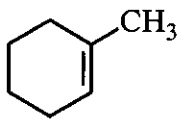
a. CH_3CCH_3 (with CH_3 above and $^+$ below the central C)

b. $CH_3\dot{C}HCH_2CH_3$

c. $CH_3\underset{+}{C}HCH_3$

d. $CH_3CH_2CH_2\dot{C}HCH_3$

e. $CH_3C(CH_3)=CHCH_2CH_3$

f. 

g. $CH_3\underset{+}{C}HCH_2CH_2Cl$

46. **a.** To determine their relative rates of hydration, the rate constant of each alkene is divided by the smallest rate constant of the series (3.51×10^{-8}).

propene $= 4.95 \times 10^{-8}/3.51 \times 10^{-8} = 1.41$

cis-2-butene $= 8.32 \times 10^{-8}/3.51 \times 10^{-8} = 2.37$

trans-2-butene $= 3.51 \times 10^{-8}/3.51 \times 10^{-8} = 1$

2-methyl-2-butene $= 2.15 \times 10^{-4}/3.51 \times 10^{-8} = 6.12 \times 10^{3}$

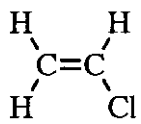
2,3-dimethyl-2-butene $= 3.42 \times 10^{-4}/3.51 \times 10^{-8} = 9.74 \times 10^{3}$

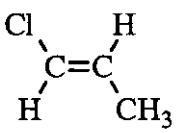
b. Both compounds form the same carbocation, but since (*Z*)-2-butene is less stable than (*E*)-2-butene, (*Z*)-2-butene has a smaller free energy of activation.

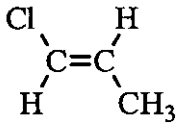
c. 2-Methyl-2-butene reacts faster because it forms a tertiary carbocation in the rate-limiting step, while *cis*-2-butene forms a less stable secondary carbocation.

d. Both compounds form tertiary carbocation intermediates. However, 2,3-dimethyl-2-butene has two sp^2 carbons that can react with a proton to form the tertiary carbocation whereas 2-methyl-2-butene has only one sp^2 carbon that can react with a proton to form the tertiary carbocation. Therefore there will be more collisions with the proper orientation that lead to a productive reaction in the case of 2,3-dimethyl-2-butene.

47.

a. 

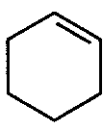
b. 

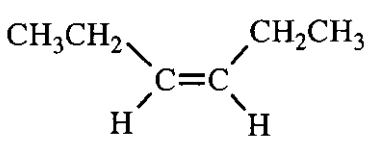
c. 

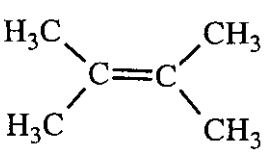
48. Only a symmetrical alkene will form the same alkyl halide when it reacts with HBr in the presence of peroxides that it forms when it reacts with HBr in the absence of peroxides.

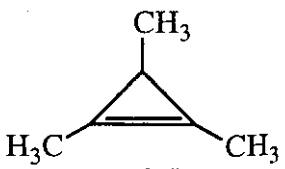
a. 

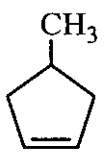
b. There are many more symmetrical alkenes in the case of an alkene with an even number of carbon atoms.

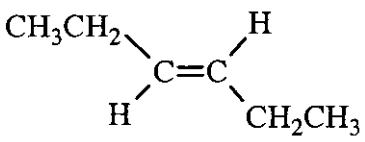


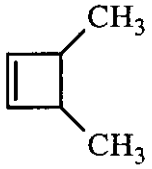


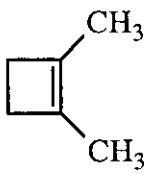








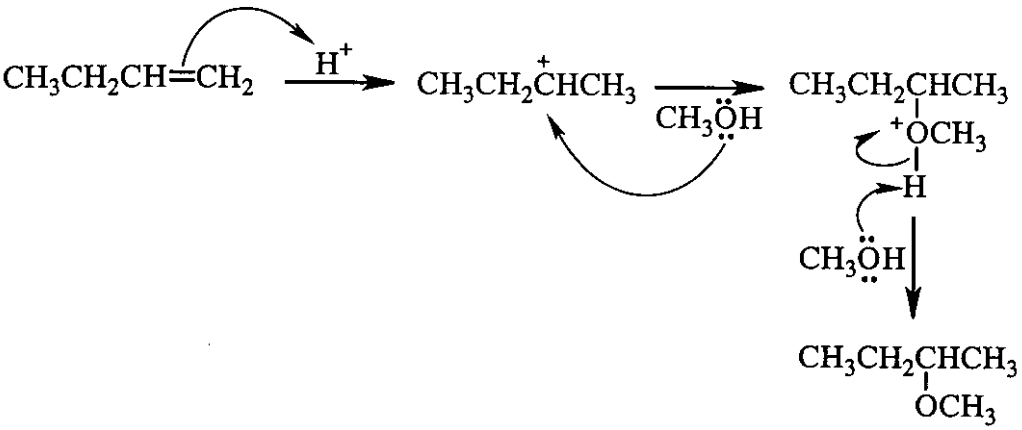




49. No, he should not follow the student's advice. Markovnikov's rule would indicate that the secondary carbocation is more stable than the primary carbocation. However because of the electron-withdrawing fluoro substituents in this compound, the primary carbocation is more stable than the secondary carbocation, since in the latter the positive charge is closer to the fluoro substituents. So the major product will be 1,1,1-trifluoro-3-iodopropane, not 1,1,1-trifluoro-2-iodopropane, the compound that would be predicted to be the major product by Markovnikov's rule.

50.

a.



b. the first step

c. H^+

d. 1-butene

e. the *sec*-butyl cation

f. methanol

51. **a.** Both 1-butene and 2-butene react with HCl to form 2-chlorobutane.

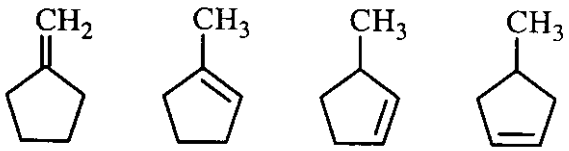
b. Both alkenes form the same carbocation, but because 2-butene is more stable than 1-butene, 2-butene has the greater free energy of activation.

c. Because 1-butene has the smaller free energy of activation, it will react more rapidly with HCl.

d. Both compounds form the same carbocation, but since (Z)-2-butene is less stable, it will react more rapidly with HCl.

52.

a. 4 alkenes

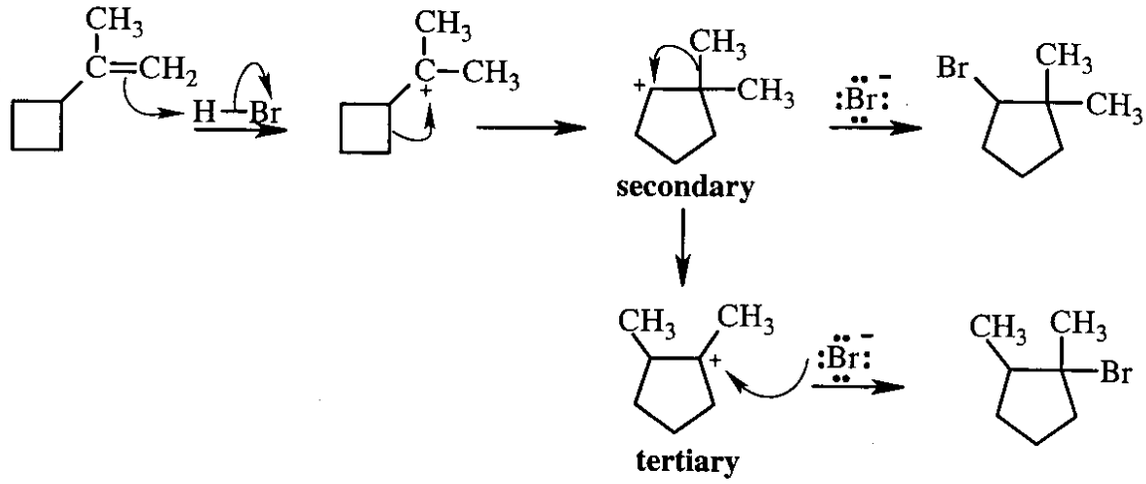


b. 1-Methylcyclopentene is the most stable.

c. Because 1-methylcyclopentene is the most stable, it would have the smallest heat of hydrogenation.

53.

a.

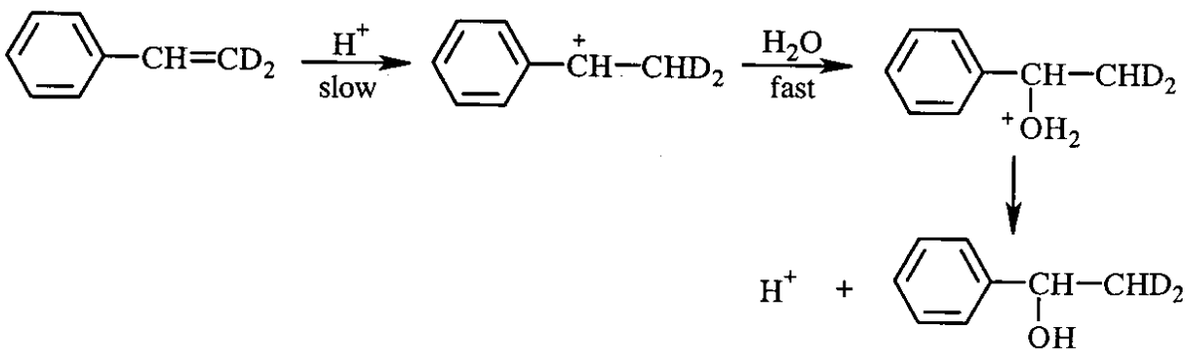


b. The initially formed carbocation is tertiary.

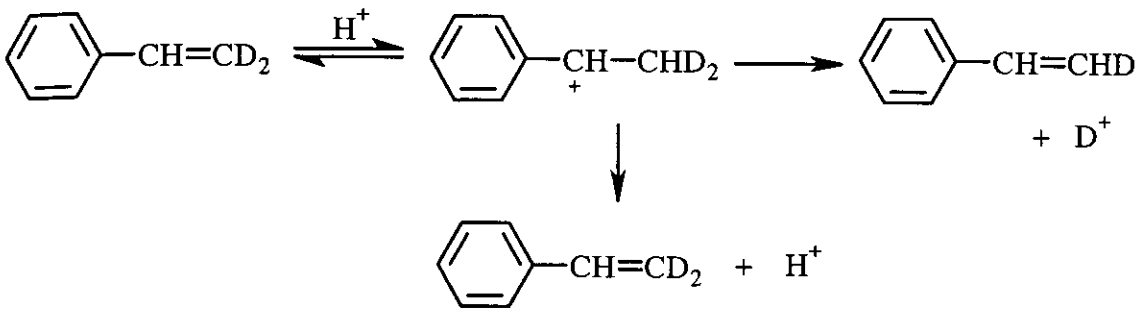
c. The rearranged carbocation is secondary, which then undergoes another rearrangement to a more stable tertiary carbocation.

d. The initially formed carbocation rearranges in order to release the strain in the four-membered ring. (A tertiary carbocation with a strained four-membered ring is less stable than a secondary carbocation with an unstrained five-membered ring.)

54. It tells us that the first step of the mechanism is the slow step. If the first step is slow, the carbocation will react with water in a subsequent fast step, which means that the carbocation wi not have time to lose a proton to reform the alkene.

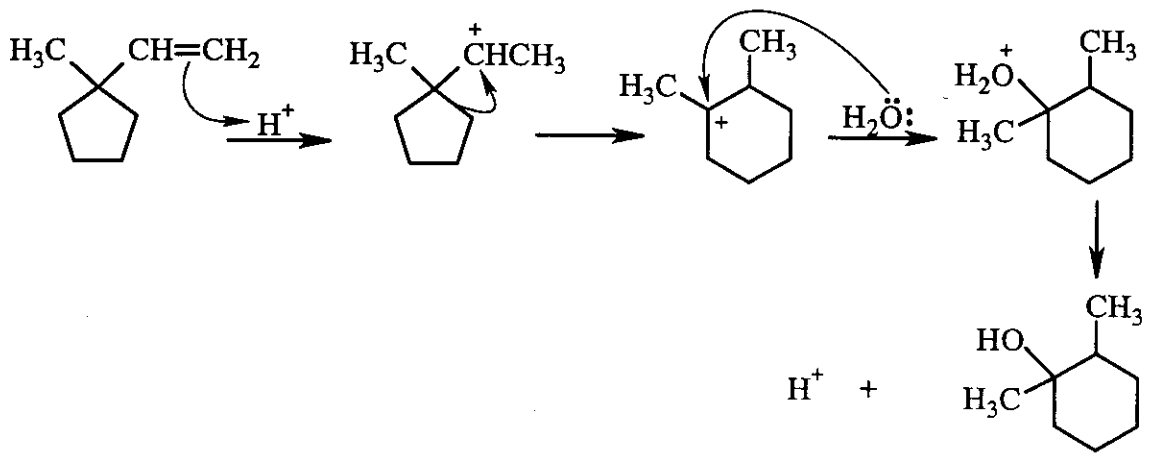


If the first step were not the slow step, an equilibrium would be set up between the alkene and the carbocation, and because the carbocation could lose either H^+ or D^+ when it reformed the alkene, all the deuterium (D) would not be retained in the alkene.

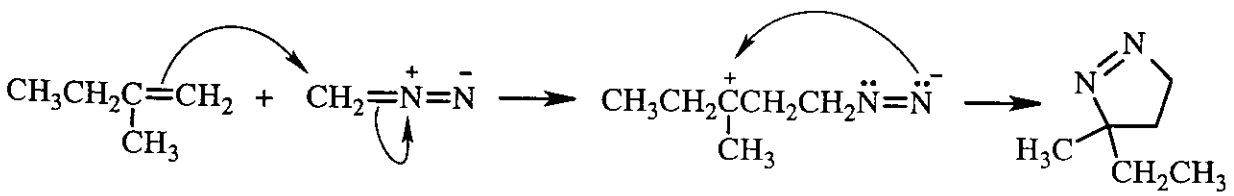


55.

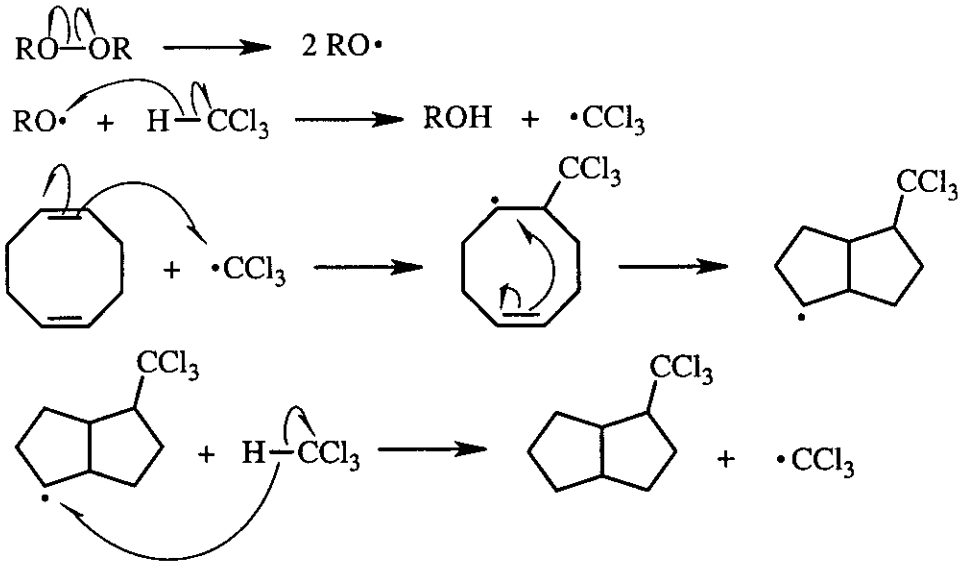
a. A proton adds to the alkene, forming a secondary carbocation, which undergoes a ring-expansion rearrangement to form a more stable tertiary carbocation.



b. At first glance this appears to be a difficult mechanism, but examination of the reaction shows that the only electrophile available to the alkene adds to the sp^2 carbon bonded to the most hydrogens (the one that results in the formation of the most stable carbocation). This is followed by the addition of the nucleophilic nitrogen to the other sp^2 carbon.

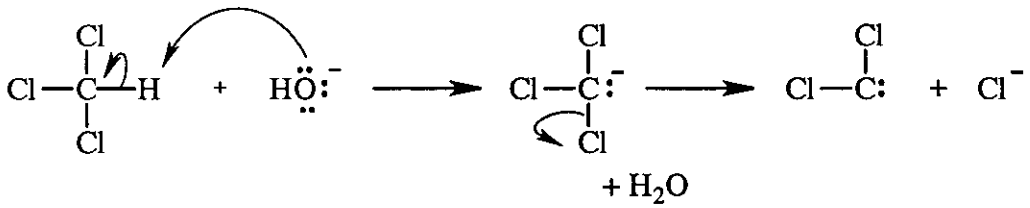


c. The weak oxygen-oxygen bond breaks homolytically, forming a radical that abstracts a hydrogen atom from $HCCl_3$. The radical that is formed adds to the double bond. A π electron of the other double bond pairs with the unpaired electron, forming a bond that divides the ring. The new radical abstracts a hydrogen atom from $HCCl_3$, and the propagation steps are repeated.

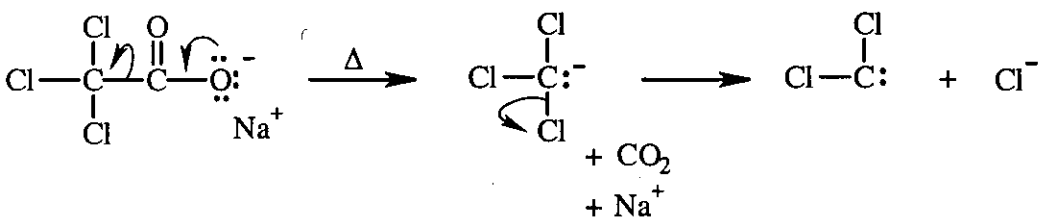


56.

a.



b.



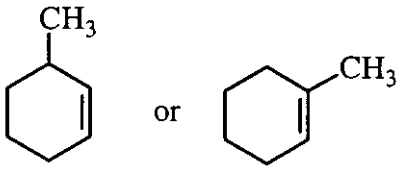
Chapter 4 Practice Test

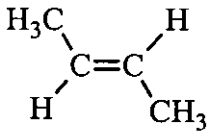
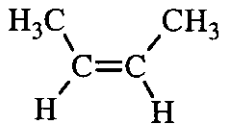
1. Which member of each pair is more stable?

a. $CH_3\overset{+}{C}HCH_2CH_3$ or $CH_3\overset{CH_3}{\overset{|}{\overset{+}{C}}}CH_3$

b. $CH_3CH_2CH_2\dot{C}H_2$ or $CH_3CH_2\dot{C}HCH_3$

c. $CH_3CH_2\overset{+}{C}H_2$ or $ClCH_2CH_2\overset{+}{C}H_2$

d.  or

e.  or 

2. Which would be a better compound to use as a starting material for the synthesis of 2-bromopentane?

$CH_3CH_2CH_2CH{=}CH_2$ or $CH_3CH_2CH{=}CHCH_3$

3. The addition of H_2 in the presence of Pd/C to alkenes **A** and **B** results in the formation of the same alkane. The addition of H_2 to alkene **A** has a heat of hydrogenation ($-\Delta H°$) of 29.7 kcal/mol, while the addition of H_2 to alkene **B** has a heat of hydrogenation of 27.3 kcal/mol. Which is the more stable alkene, **A** or **B**?

4. What is the major product of each of the following reactions?

a. $CH_2{=}\overset{CH_3}{\overset{|}{C}}CH_2CH_3 + HBr \longrightarrow$

b. $CH_3\overset{CH_3}{\overset{|}{C}}HCH{=}CH_2 + HCl \longrightarrow$

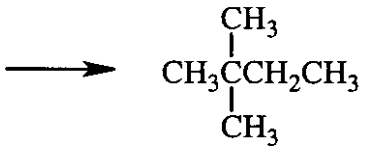
c. $CH_3CH_2CH{=}CH_2 + Cl_2 \xrightarrow{H_2O}$

d. $CH_3\overset{CH_3}{\overset{|}{\underset{CH_3}{\underset{|}{C}}}}CH{=}CH_2 + HBr \longrightarrow$

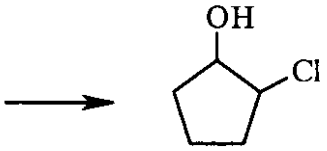
5. Write out the propagation steps that occur in the addition of HBr to 1-methylcyclohexene in the presence of peroxides.

6. Indicate how each of the following compounds could be synthesized using an alkene as one of the starting materials:

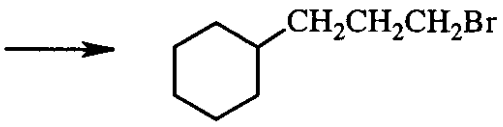
a.



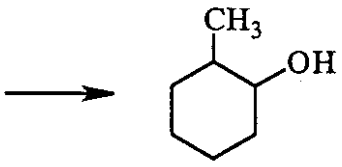
b.



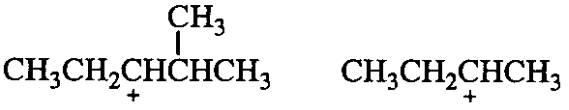
c.

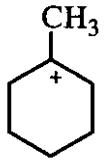


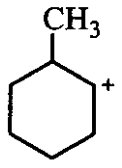
d.



7. Indicate the carbocations that you would expect to rearrange to give a more stable carbocation.







8. What product would be obtained from the hydroboration-oxidation of the following alkenes?

a. 2-methyl-2-butene **b.** 1-ethylcyclopentene

9. Indicate whether each of the following statements is true or false:

a. The addition of Br_2 to 1-butene to form 1,2-dibromobutane is a concerted reaction. T F

b. The reaction of 1-butene with HCl will form 1-chlorobutane as the major product if hydrogen peroxide is added to the reaction mixture. T F

c. 2,3-Dimethyl-2-pentene is more stable than 3,4-dimethyl-2-pentene. T F

d. The reaction of HBr with 3-methylcyclohexene is more highly regioselective than the reaction of HBr with 1-methylcyclohexe. T F

Special Topic IV

Exercise in Model Building

Do the following exercises using molecular models.

1. Build the enantiomers of 2-bromobutane.
   - **a.** Try to superimpose them.
   - **b.** Show that they are mirror images.
   - **c.** Which one is (*R*)-2-bromobutane?

2. Build the erythro enantiomers of 3-bromo-2-butanol.
   - **a.** Where are the Br and OH substituents (relative to each other) in the Fischer projection? (Recall that in a Fischer projection, the horizontal lines represent bonds that point out of the plane of the paper toward the viewer, and the dashed lines represent bonds that point back from the plane of the paper away from the viewer.)
   - **b.** Where are the Br and OH substituents (relative to each other) in the most stable conformer considering rotation about the C-2—C-3 bond?

3. **a.** Build the compounds labeled "1" and "2" shown on the top of page 201 of the text.
   b. Build their mirror images.
   c. Show that "1" is superimposable on its mirror image but '2" is not.

4. Build the three stereoisomers of 2,3-dibromobutane.

5. Build the four stereoisomers of 2,3-dibromopentane.
   Why does 2,3-dibromopentane have four stereoisomers, while 2,3-dibromobutane has only three stereoisomers?

6. Build (*S*)-2-pentanol.

7. Build (2*S*,3*R*)-3-bromo-2-butanol. Rotate your model so it is in a Fischer projection. Compare its structure with the structure of (2*S*,3*R*)-3-bromo-2-butanol shown on page 205 of the text.

8. Build the compounds shown in Problem 33 on page 208 of the text. Name the compounds.

9. Build (*S*)-1-bromo-2-methylbutane. Substitute the Br^- with an HO^- to form 2-methyl-1-butanol. What is the configuration of your model of 2-methyl-1-butanol?

10. Build ethanol. Which of the hydrogens is the pro-*R*-hydrogen?

11. Build two models of *trans*-2-pentene. Add Br_2 to opposite sides of the double bond, forming the two enantiomers shown on page 226 of the text. Rotate them so they are Fischer projections. Are they erythro or threo enantiomers? Compare your answer with that given in the text.

12. Build models of the molecules shown in Problem 86 on page 237 of the text. What is the configuration of the chirality center in each of the molecules?

CHAPTER 5
Stereochemistry: The Arrangement of Atoms in Space; The Stereochemistry of Addition Reactions

Important Terms

absolute configuration	the three-dimensional structure of a chiral compound. The configuratio designated by *R* or *S*. The configuration is called absolute to distinguis from a relative configuration.
achiral (optically inactive)	a molecule or object that contains an element (a plane or a point) of symmetry.
amine inversion	results when a compound containing an sp^3 hybridized nitrogen with a nonbonding pair of electrons rapidly turns inside out.
anti addition	an addition reaction in which the two added substituents add to opposit sides of the molecule.
asymmetric carbon	a carbon atom that is bonded to four different substituents.
biochemistry	the chemistry associated with living organisms.
chiral (optically active)	a chiral molecule has a nonsuperimposable mirror image.
chirality center	an atom that is bonded to four different substituents.
cis isomer	the isomer with substituents on the same side of a cyclic structure, or the isomer with the hydrogens on the same side of a double bond.
cis-trans isomers	geometric (or *E*, *Z*) isomers.
chromatography	a separation technique in which the mixture to be separated is dissolved a solvent and the solution is passed through a column packed with an adsorbent stationary phase.
configuration	the three-dimensional structure of a chiral compound. The configuratior designated by *R* or *S*.
configurational isomers	stereoisomers that cannot interconvert unless a covalent bond is broken. Cis-trans isomers and optical isomers are configurational isomers.
constitutional isomers (structural isomers)	molecules that have the same molecular formula but differ in the way th atoms are connected.
dextrorotatory	the enantiomer that rotates polarized light in a clockwise direction.
diastereomer	a configurational isomer that is not an enantiomer.
diastereotopic hydrogens	two hydrogens bonded to the same carbon that will result in a pair of diastereomers when each of them is replaced in turn with deuterium.
enantiomers	nonsuperimposable mirror-image molecules.

enantiomerically pure	only one enantiomer is present in an enantiomerically pure sample.
enantiomeric excess	how much excess of one enantiomer is present in a mixture of a pair of enantiomers.
enantiotopic hydrogens	two hydrogens bonded to a carbon that is bonded to two other groups that are nonidentical.
enzyme	a protein that catalyzes a biological reaction.
erythro enantiomers	the pair of enantiomers with similar groups on the same side (in the case of stereoisomers with adjacent asymmetric carbons) when drawn in a Fischer projection.
Fischer projection	a method of representing the spatial arrangement of groups bonded to an asymmetric carbon. The asymmetric carbon is the point of intersection of two perpendicular lines; the horizontal lines represent bonds that project out of the plane of the paper toward the viewer, and the vertical lines represent bonds that project back from the plane of the paper away from the viewer.
isomers	nonidentical compounds with the same molecular formula.
isomers that contain asymmetric carbons	these can be enantiomers, diastereomers, and meso compounds.
levorotatory	the enantiomer that rotates polarized light in a counterclockwise direction.
meso compound	a compound that possesses asymmetric carbons and a plane of symmetry.
observed rotation	the amount of rotation observed in a polarimeter.
optical purity	how much excess of one enantiomer is present in a mixture of a pair of enantiomers.
optically active (chiral)	rotates the plane of polarized light.
optically inactive (achiral)	does not rotate the plane of polarized light.
pair of enantiomers	a pair of nonsuperimposable mirror image molecules.
perspective formula	a method of representing the spatial arrangement of groups bonded to a chirality center. Two bonds are drawn in the plane of the paper; a solid wedge is used to depict a bond that projects out of the plane of the paper toward the viewer, and a hatched wedge is used to represent a bond that projects back from the paper away from the viewer.
plane of symmetry	an imaginary plane that bisects a molecule into a pair of mirror images.
plane-polarized light	light that oscillates in a single plane passing through the direction the light travels.

polarimeter	an instrument that measures the rotation of polarized light.
polarized light	light that oscillates in only one plane.
prochirality center	a carbon (bonded to two hydrogens) that will become an asymmetric carbon (a chirality center) if one of the hydrogens is replaced by deuterium.
pro-*R*-hydrogen	replacing this hydrogen with deuterium creates an asymmetric carbon with the *R* configuration.
pro-*S*-hydrogen	replacing this hydrogen with deuterium creates an asymmetric carbon with the *S* configuration.
racemic mixture (racemic modification, racemate)	a mixture of equal amounts of a pair of enantiomers.
***R* configuration**	after assigning relative priorities to the four groups bonded to a chirality center, if the lowest-priority group is on a vertical axis in a Fischer projection (or pointing away from the viewer in a perspective formula), an arrow drawn from the highest-priority group to the next highest-priority group goes in a clockwise direction.
regioselective	describes a reaction that leads to the preferential formation of one constitutional isomer over another.
relative configuration	the configuration of a compound relative to the configuration of another compound.
resolution of a racemic mixture	separation of a racemic mixture into the individual enantiomers.
***S* configuration**	after assigning relative priorities to the four groups bonded to a chirality center, if the lowest-priority group is on a vertical axis in a Fischer projection (or pointing away from the viewer in a perspective formula), an arrow drawn from the highest-priority group to the next highest-priority group goes in a counterclockwise direction.
specific rotation	the amount of rotation that will be caused by a compound with a concentration of 1.0 g/mL in a sample tube 1.0 decimeter long.
stereocenter (stereogenic center)	an atom at which the interchange of two groups produces a stereoisomer.
stereochemistry	the field of chemistry that deals with the structure of molecules in three dimensions.
stereoisomers	isomers that differ in the way the atoms are arranged in space.
stereoselective	describes a reaction that leads to the preferential formation of one stereoisomer over another.
stereospecific	describes a reaction in which the reactant can exist as stereoisomers and each stereoisomeric reactant leads to a different stereoisomeric product.

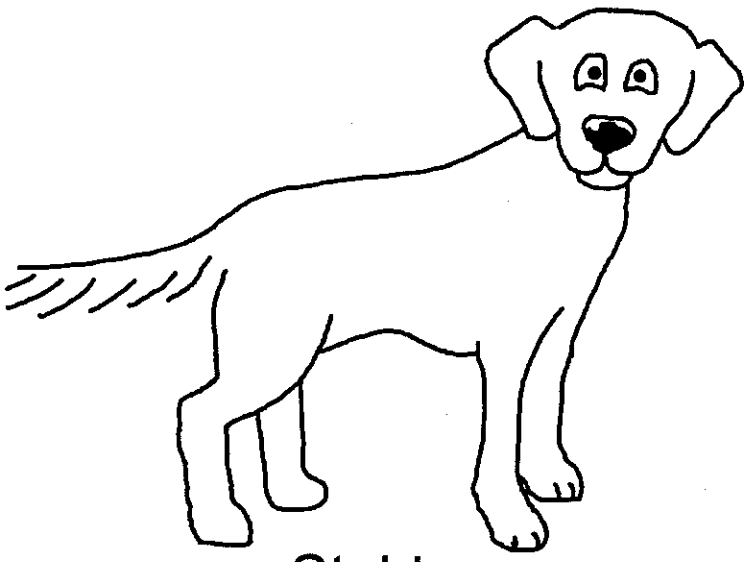
structural isomers (constitutional isomers)	molecules that have the same molecular formula but differ in the way the atoms are connected.
syn addition	an addition reaction in which the two added substituents add to the same side of the molecule.
threo enantiomers	the pair of enantiomers with similar groups on opposite sides (in the case of stereoisomers with adjacent asymmetric carbons) when drawn in a Fischer projection.
trans isomer	the isomer with substituents on the opposite sides of a cyclic structure, or the isomer with the hydrogens on the opposite sides of a double bond.

Do not confuse the terms **conformation** and **configuration**.

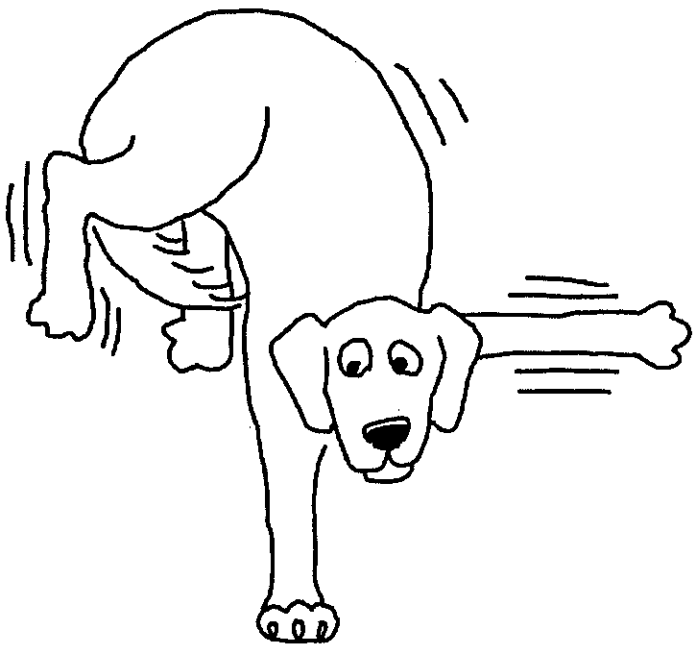
Conformations are different spatial arrangments of the same compound (see page 88 of the text). They result from rotation about single bonds. They cannot be separated. Some conformations are more stable than others.

Configurational isomers are different compounds. They do not readily interconvert; bonds have to be broken to convert one configurational isomer to another.

Different Conformations

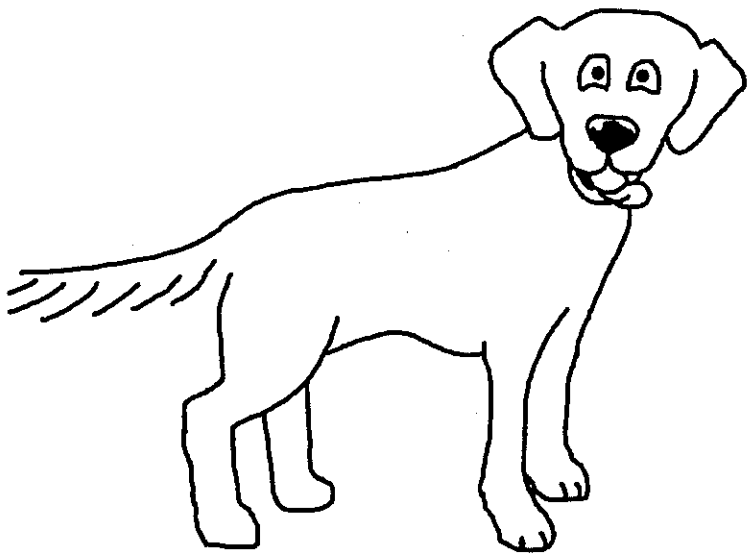


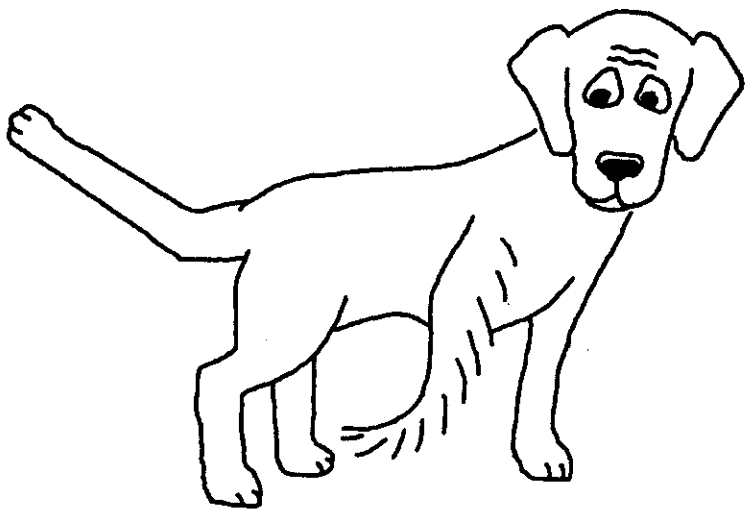
Stable



Unstable

Different Configurations



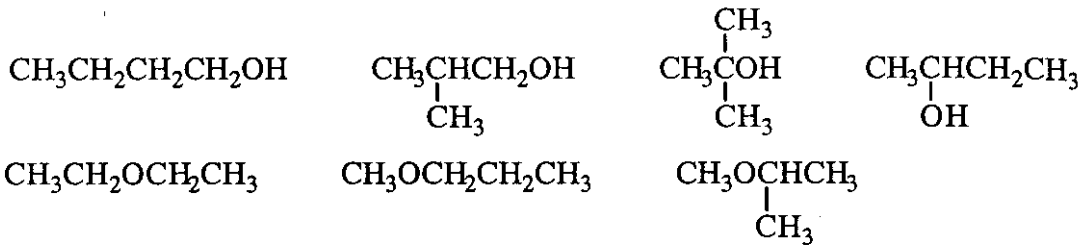


Solutions to Problems

1.

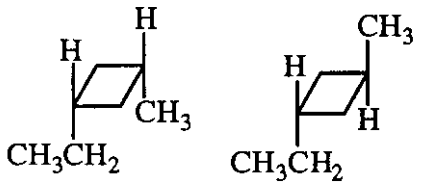
a. $CH_3CH_2CH_2OH$ CH_3CHOH (with CH_3 branch) $CH_3CH_2OCH_3$

b. There are seven constitutional isomers with molecular formula $C_4H_{10}O$.

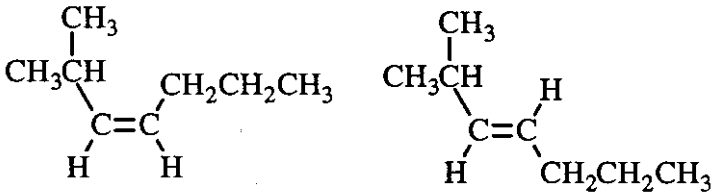


2.

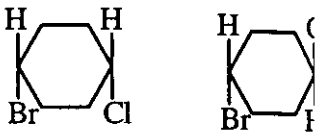
a.



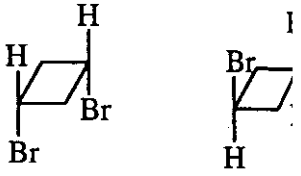
b.



c.



d.



cis-1,3-dibromocyclobutane

trans-1,3-dibromocyclobut

3. **a.** F, G, J, L, N, P, Q, R, S, Z

b. A, C, D, H, I, M, O, T, U, V, W, X, Y

Whether B, E, and K are chiral or achiral depends on how they are drawn. For example, if B is drawn with two equal loops, it is achiral; if the loops differ in size, it is chiral.

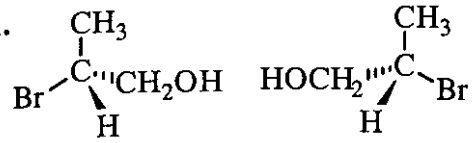
4. **a**, **c**, and **f** have asymmetric carbons.

5. Solved in the text.

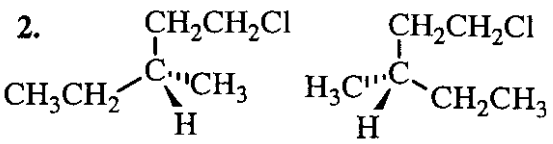
6. **a**, **c**, and **f**, because in order to be able to exist as a pair of enantiomers, the compound must have an asymmetric carbon (except in the case of certain compounds with unusual structures. See Problem 88.)

7. Draw the first enantiomer with the groups in any order you want. Then draw the second enantiomer by drawing the mirror image of the first enantiomer.

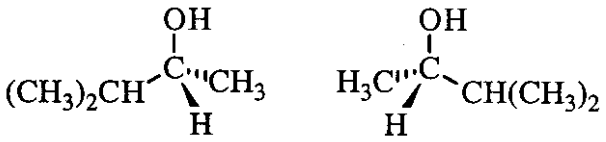
a. **1.**



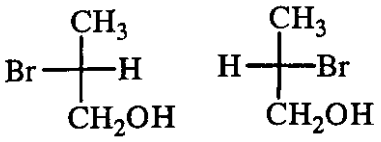
2.



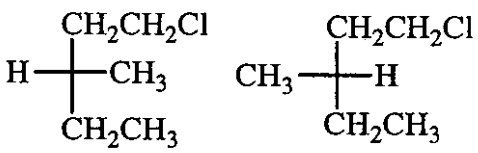
3.



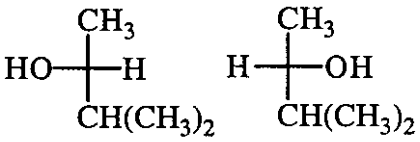
b. **1.**



2.



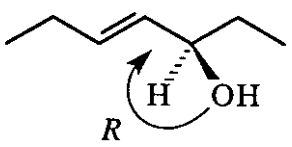
3.



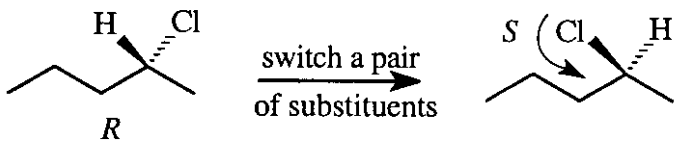
8. **a.** *R*

b. *R*

c. To determine the configuration, draw the structure with the fourth bond. Remember that it cannot be drawn between the two solid bonds.



d. Draw the structure with the fourth bond. Switch a pair so that the H is on a dotted bond. The configuration of the compound with the switched pair is *S*. Therefore, the configuration of the compound given in the question is *R*.



9. The easiest way to determine whether two compounds are identical or enantiomers is to determine their configurations: If both are *R* (or both are *S*), they are identical.
If one is *R* and the other is *S*, they are enantiomers.

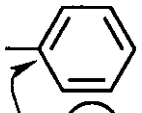
a. enantiomers **b.** enantiomers **c.** enantiomers **d.** enantiomers

10.

a. $-CH_2OH$ (1) $-CH_3$ (3) $-CH_2CH_2OH$ (2) $-H$ (4)

b. $-CH{=}O$ (2) $-OH$ (1) $-CH_3$ (4) $-CH_2OH$ (3)

c. $-CH(CH_3)_2$ (2) $-CH_2CH_2Br$ (3) $-Cl$ (1) $-CH_2CH_2CH_2Br$ (4)

d. $-CH{=}CH_2$ (2) — C attached to 2 C's; $-CH_2CH_3$ (3);  (1) — C attached to 3 C's; $-CH_3$ (4)

11. **a.** *S* **b.** *R* **c.** *S* **d.** *S*

12.

$$\text{observed specific rotation} = \frac{\text{observed rotation}}{\text{concentration x length}}$$

$$[\alpha] = \frac{\alpha}{\text{concentration x length}} = \frac{+13.4°}{\frac{2}{50} \text{ x } 5 \text{ dm}} = \frac{+13.4°}{0.2} =$$

13. **a.** levorotatory **b.** dextrorotatory

14. **a.** $-24°$ **b.** $0°$

15.

a. 50% of the mixture is excess (+)-mandelic acid.

$$\text{optical purity} = 0.50 = \frac{\text{observed specific rotation}}{\text{specific rotation of the pure enantiomer}}$$

$$0.50 = \frac{\text{observed specific rotation}}{+158^\circ}$$

$$\text{observed specific rotation} = +79^\circ$$

b. 0° (It is a racemic mixture.)

c. 50% of the mixture is excess (−)-mandelic acid.

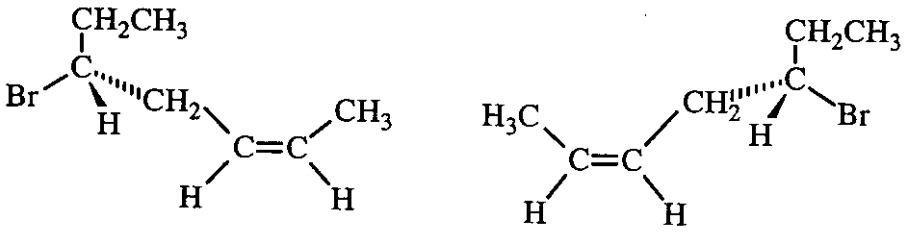
observed specific rotation = −79°

16. **a.** From the data given, you cannot determine what the configuration of naproxen is.

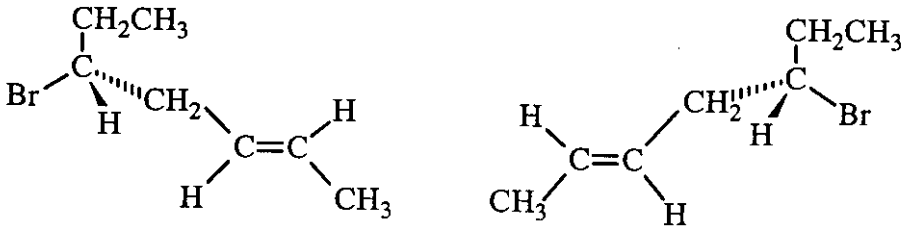
b. 97% of the commercial preparation is (+)-naproxen; 3% is a racemic mixture
Therefore, the commercial preparation forms 98.5% (+)-naproxen and 1.5% (–)-naproxen.

17. Solved in the text.

18. As a result of the double bond, the compound has a cis isomer and a trans isomer. Because the compound also has an asymmetric carbon, the cis isomer can exist as a pair of enantiomers and the trans isomer can exist as a pair of enantiomers.



cis enantiomers



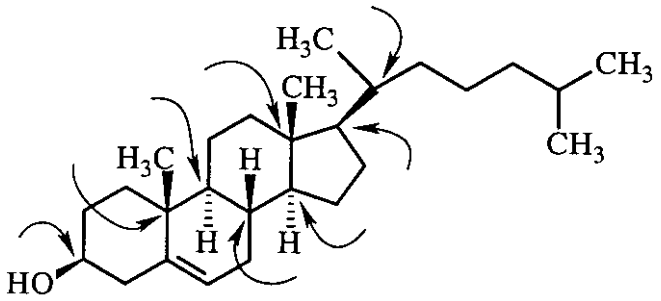
trans enantiomers

19. **a.** enantiomers

b. identical compounds (Therefore, they are not isomers.)

c. diastereomers

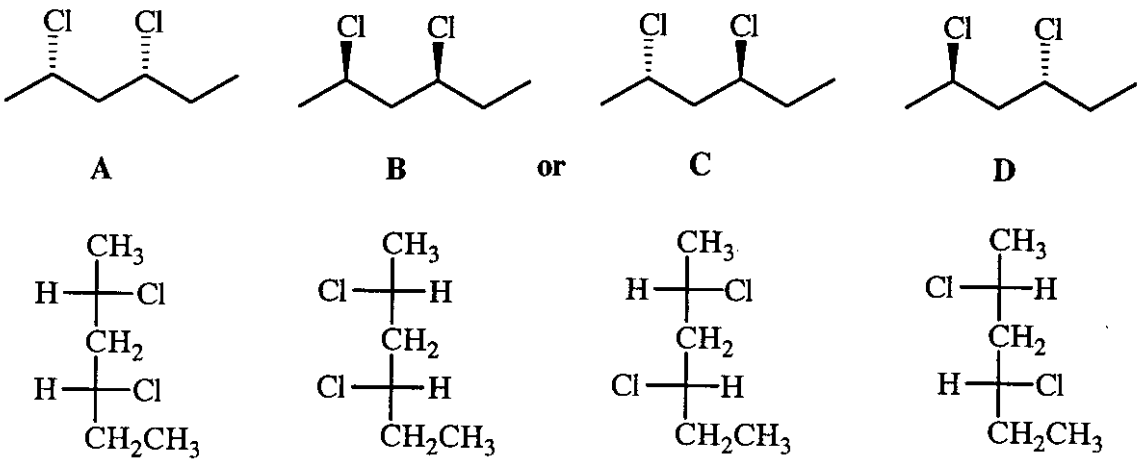
20. **a.** First find the sp^3 carbons that are bonded to four different substituents; these are the asymmetric carbons. Cholesterol has eight asymmetric carbons. They are indicated by arrows.



b. $2^8 = 256$

c. Only one of the stereoisomers is found in nature.

21.

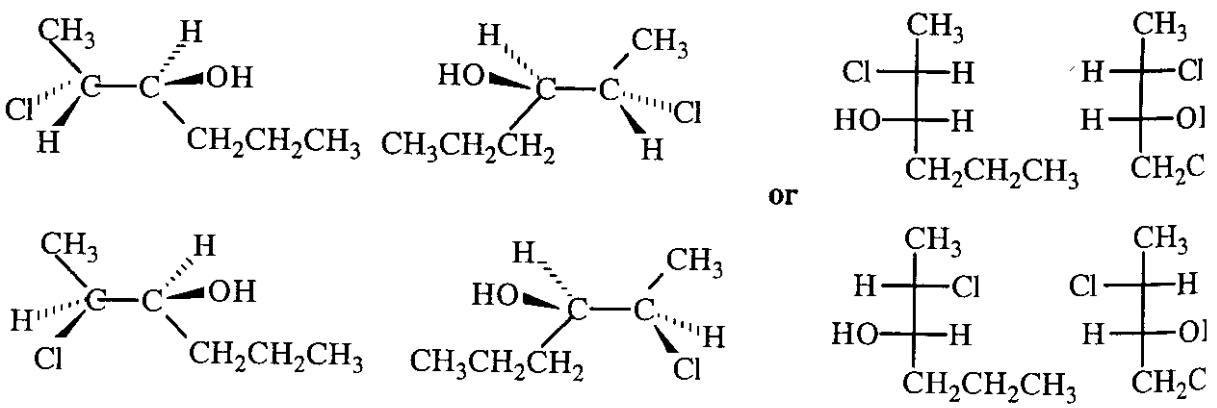


enantiomers: **A** and **B**
C and **D**

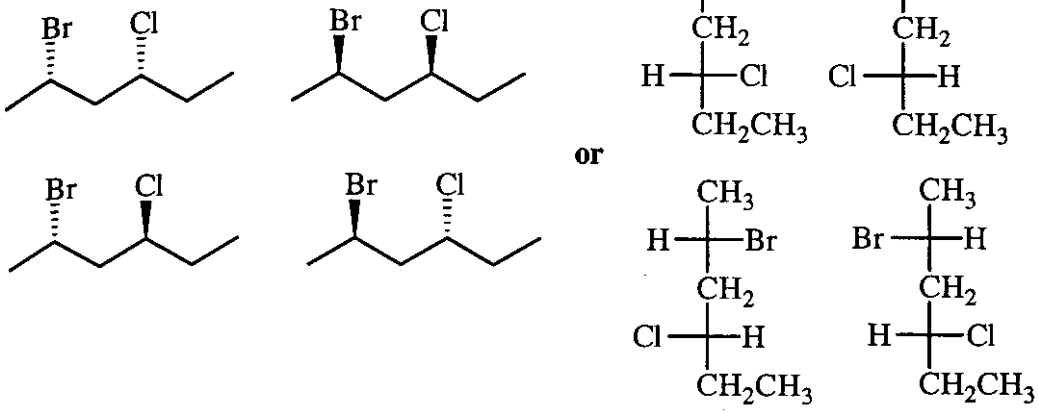
diastereomers: **A** and **C** **B** and **C**
A and **D** **B** and **D**

22.

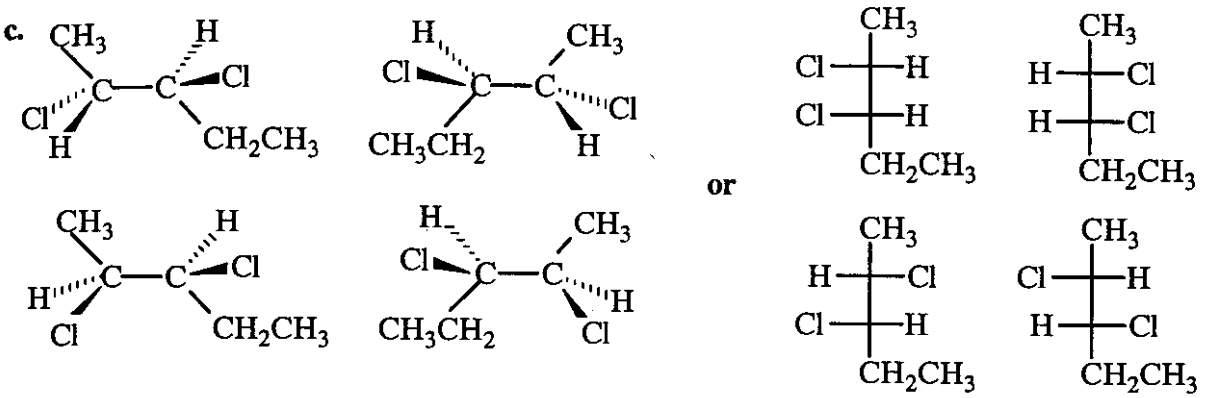
a.



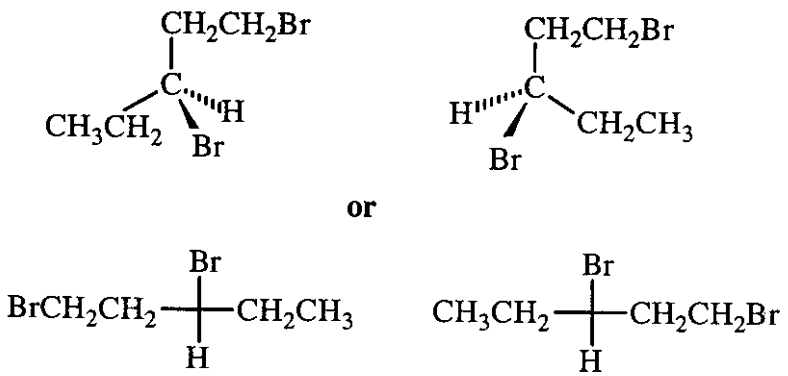
b.


Br Cl
Br Cl
Br Cl
Br Cl
or
CH3 H Br CH2 H Cl CH2CH3
CH3 Br H CH2 Cl H CH2CH3
CH3 H Br CH2 Cl H CH2CH3
CH3 Br H CH2 H Cl CH2CH3

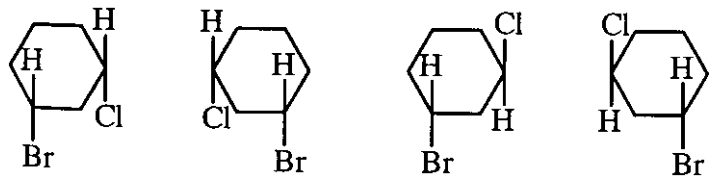
c.


CH3 H Cl C C Cl H CH2CH3
H Cl CH3 C C Cl CH3CH2 H
CH3 H H Cl C C Cl Cl CH2CH3
H Cl CH3 C C H CH3CH2 Cl
or
CH3 Cl H Cl H CH2CH3
CH3 H Cl H Cl CH2CH3
CH3 H Cl Cl H CH2CH3
CH3 Cl H H Cl CH2CH3

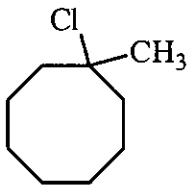
d.


CH2CH2Br C H CH3CH2 Br
CH2CH2Br C H CH2CH3 Br
or
Br BrCH2CH2 CH2CH3 H
Br CH3CH2 CH2CH2Br H

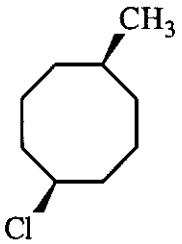
23.


H H Cl Br
H H Cl Br
Cl H H Br
Cl H H Br

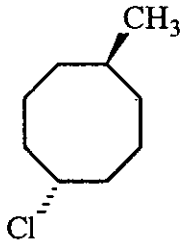
24.



1-chloro-1-methyl-cyclooctane



cis-1-chloro-5-methyl-cyclooctane

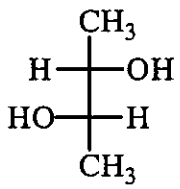


trans-1-chloro-5-methyl-cyclooctane

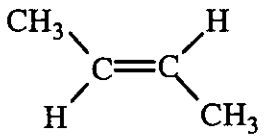
25. There is more than one diastereomer for **a, b,** and **d**.
c has only one diastereomer.

To draw a diastereomer of **a, b,** or **d**, switch any one pair of substituents bonded to one of the asymmetric carbons. Because any one pair can be switched, your diastereomer won't be the same as the one drawn here unless you happened to switch the same pair.

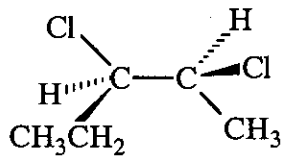
a.



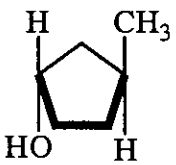
c.



b.



d.



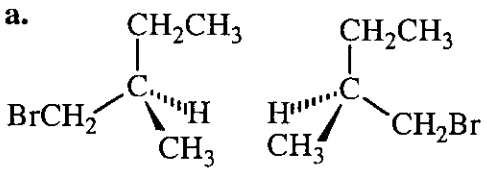
26. **b**, **d**, and **f**

c and **e** do not have a stereoisomer that is a meso compound, because they do not have asymmetric carbons

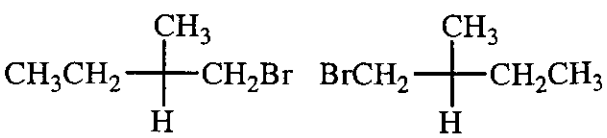
27. Solved in the text.

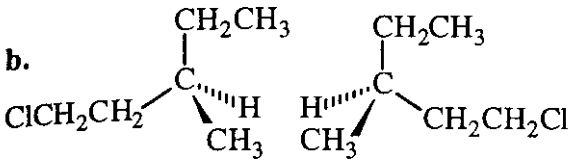
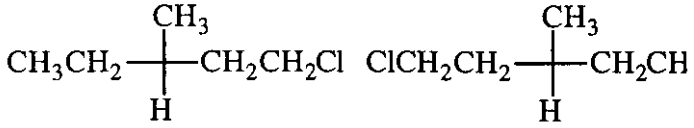
28.

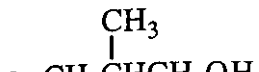
a.

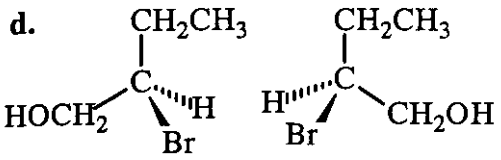
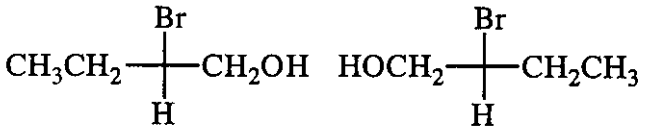


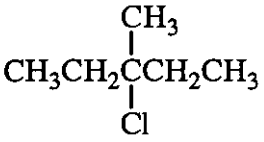
or

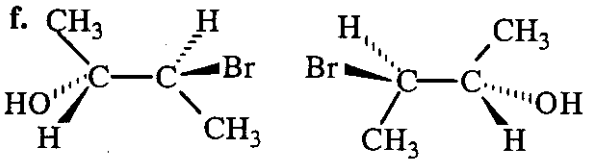


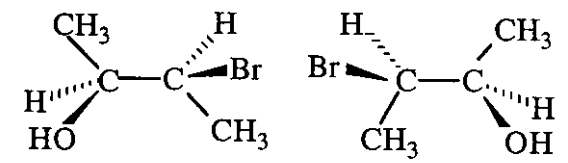
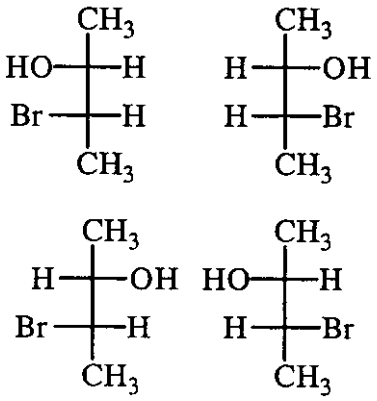
b.  **or** 

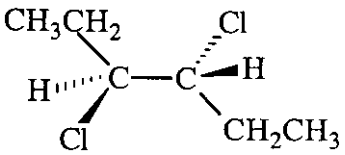
c.  no stereoisomers because the compound does not have an asymmetric carbon

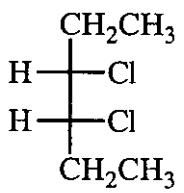
d.  **or** 

e.  no stereoisomers because the compound does not have an asymmetric carbon

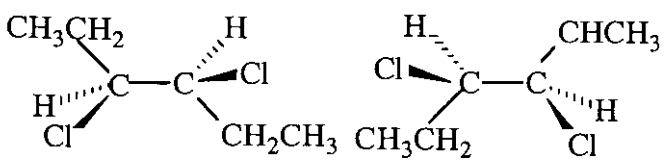
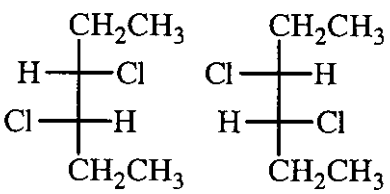
f. 

 **or** 

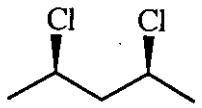
g. 

a meso compound **or** 

a meso compound

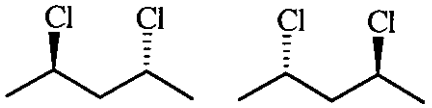
 

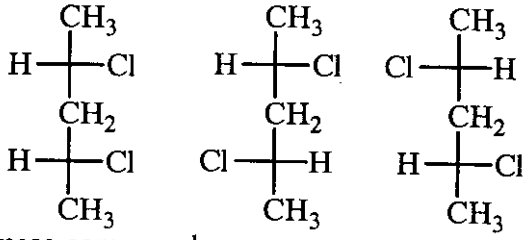
h.



a meso compound

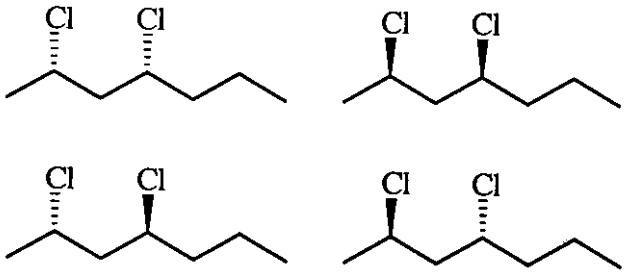
or



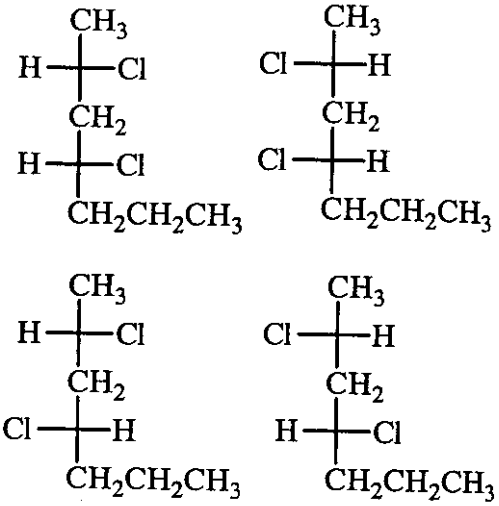


a meso compound

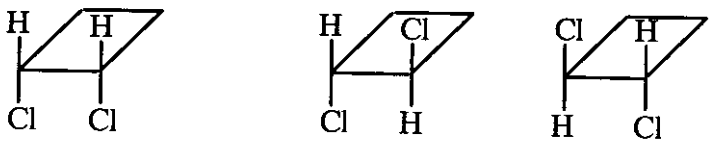
i.



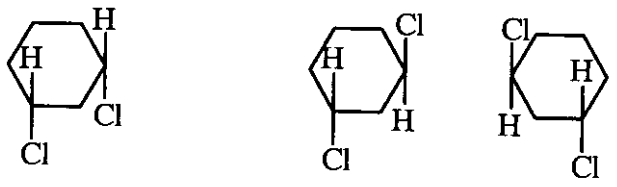
or



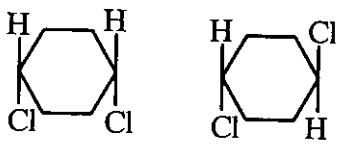
j.



k.



l.

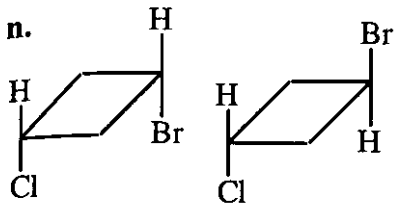


This compound does not have any asymmetric carbons, so it has only cis-trans isomers.

m.



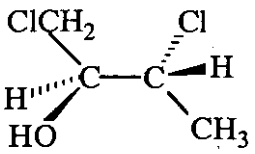
n.



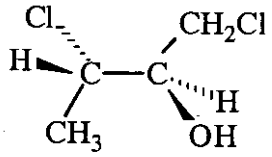
This compound does not have any asymmetric carbons, so it has only cis-trans isomers.

29.

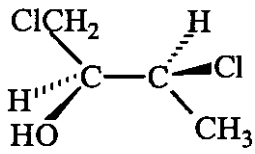
a.



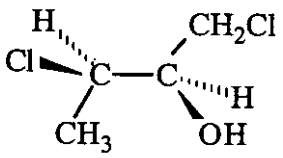
(2*S*,3*R*)-1,3-dichloro-2-butanol



(2*R*,3*S*)-1,3-dichloro-2-butanol

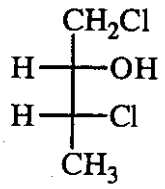


(2*S*,3*S*)-1,3-dichloro-2-butanol

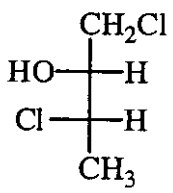


(2*R*,3*R*)-1,3-dichloro-2-butanol

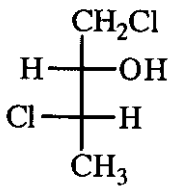
b.



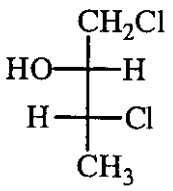
(2*S*,3 *R*)-1,3-dichloro-2-butanol



(2*R*,3 *S*)-1,3-dichloro-2-butanol

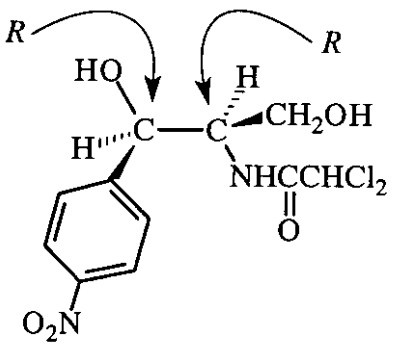


(2*S*,3 *S*)-1,3-dichloro-2-butanol



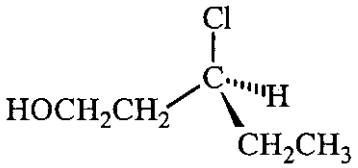
(2*R*,3 *R*)-1,3-dichloro-2-butanol

30.

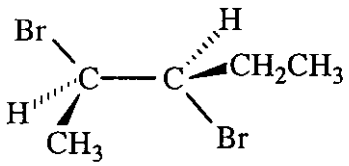


31. Your answer might be correct yet not look like the answers shown here. If you can get the answer shown here by interchanging **two** pairs of groups bonded to an asymmetric carbon, then your answer is correct. If you get the answer shown here by interchanging **one** pair of groups bonded to an asymmetric carbon, then your answer is not correct.

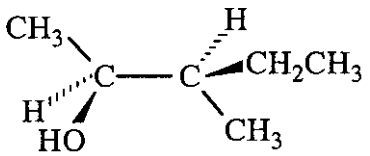
a.



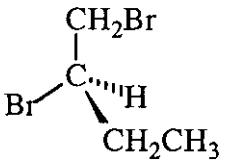
b.



c.

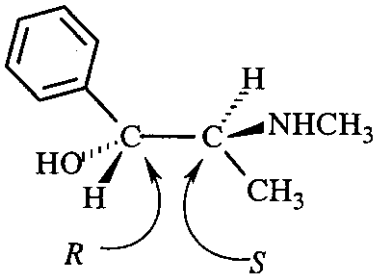


d.



32. **a.** Because there are two asymmetric carbons, there are four possible stereoisomers.

b.



33. **a.** (2*R*,3*R*)-2,3-dichloropentane

b. (2*R*,3*R*)-2-bromo-3-chloropentane

c. (1*R*,3*S*)-1,3-cyclopentanediol (naming the compound clockwise) or (1*S*,3*R*)-1,3-cyclopentanediol (naming the compound counterclockwise)

d. (3*R*,4*S*)-3-chloro-4-methylhexane

34. Solved in the text.

35. We see that the *S*-alkyl halide reacts with HO^- to form the *S*-alcohol. We were told that the product (the *S*-alcohol) is (+). We can, therefore, conclude that the (–) alcohol has the *R* configuration.

36. From the structures given on page 210 of the text, you can determine the configuration of the asymmetric carbon in each compound.

a. *R** **b.** *R** **c.** *S** **d.** *S*

37. Only **b** is true.

38. Greater than 98% is excess of the *S* enantiomer. The remainder is a racemic mixture, so greater than 99% is the *S* enantiomer

39. **a.** enantiotopic **c.** neither

b. diastereotopic **d.** diastereotopic (remember that cis-trans isomers are diastereomers)

40. Compound A has two stereoisomers because it has a chirality center.

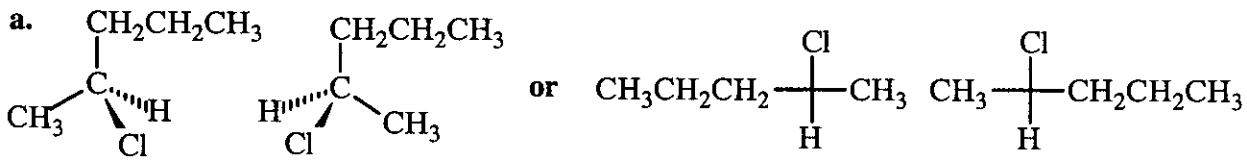
Compound B has only one stereoisomer because it does not have a chirality center.

Compound C has a chirality center but, because of the lone pair, the two enantiomers rapidly interconvert, so it exists as a single compound.

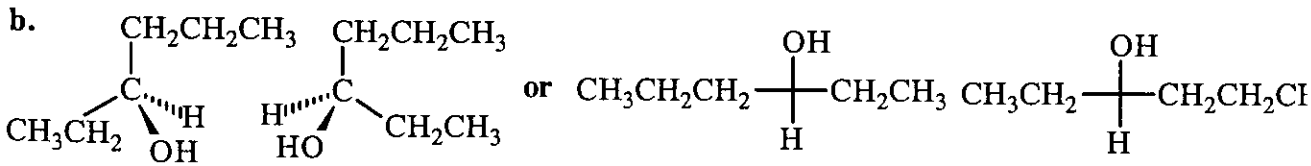
41. **a.** no **b.** no **c.** no **d.** yes **e.** no **f.** no

42. Only the stereoisomers of the major product of each reaction are shown.

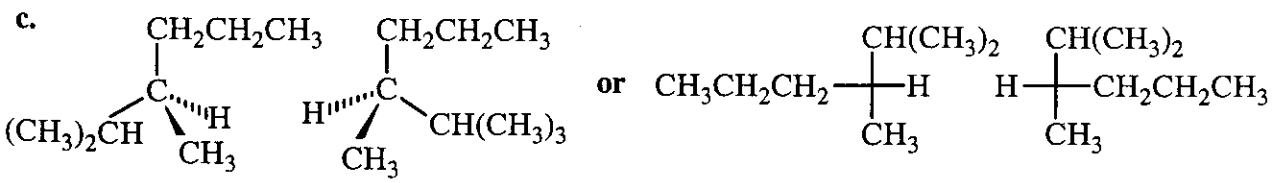
a.



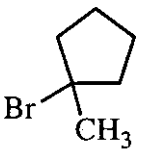
b.



c.

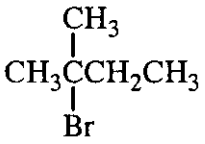


d.



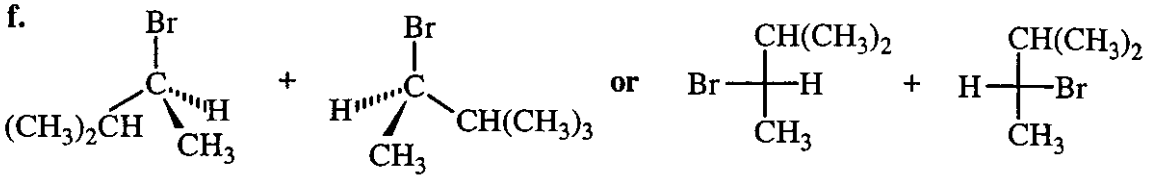
This compound does not have any stereoisomers because it does not have an asymmetric carbon.

e.



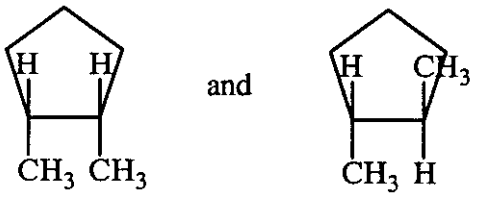
This compound does not have any stereoisomers because it does not have an asymmetric carbon.

f.

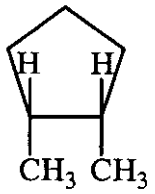


43.

a.



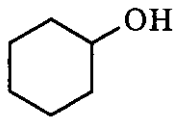
b.



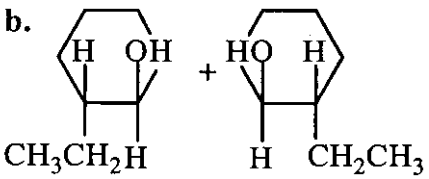
Hydrogen will be more likely to add to the side of the ring where the hydrogen substituent is than to side of the ring where the methyl substituent is because hydrogen provides less steric hindrance than a methyl group.

44.

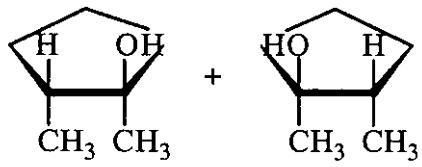
a.



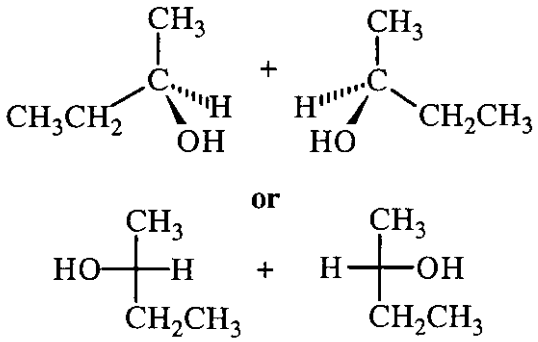
b.



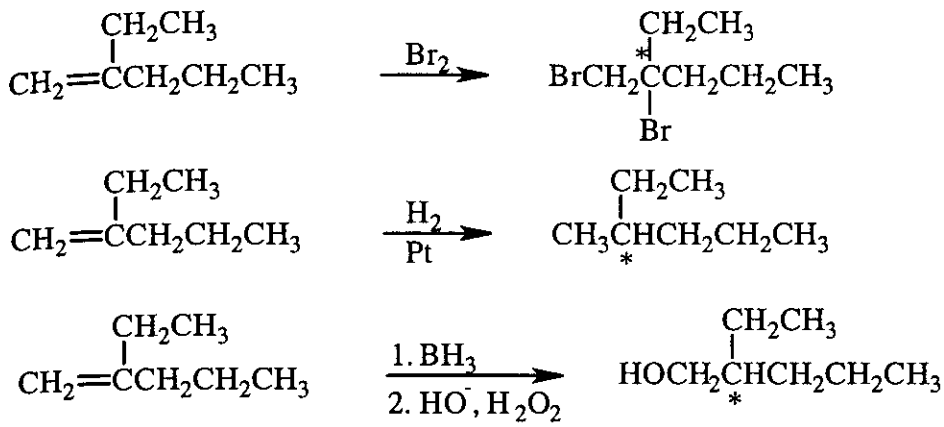
c.



d.



45.



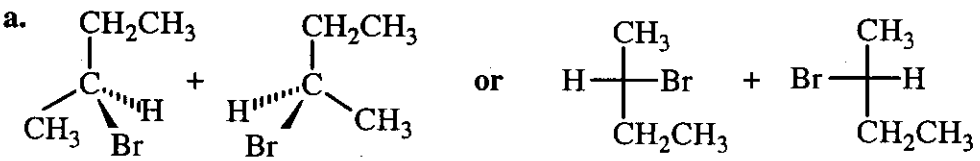
(* indicates an asymmetric carbon)

Each of the reactions forms a compound with one asymmetric carbon from a compound with no asymmetric carbons. Therefore, each of the products is a racemic mixture.

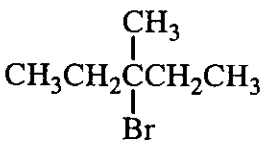
46. Because *trans*-2-butene forms a cyclic bromonium ion intermediate, it forms only the erythro enantiomers. If the reaction formed a carbocation intermediate, both the erythro pair of enantiomers and the threo pair of enantiomers would be formed because both syn and anti addition could occur.

47.

a.

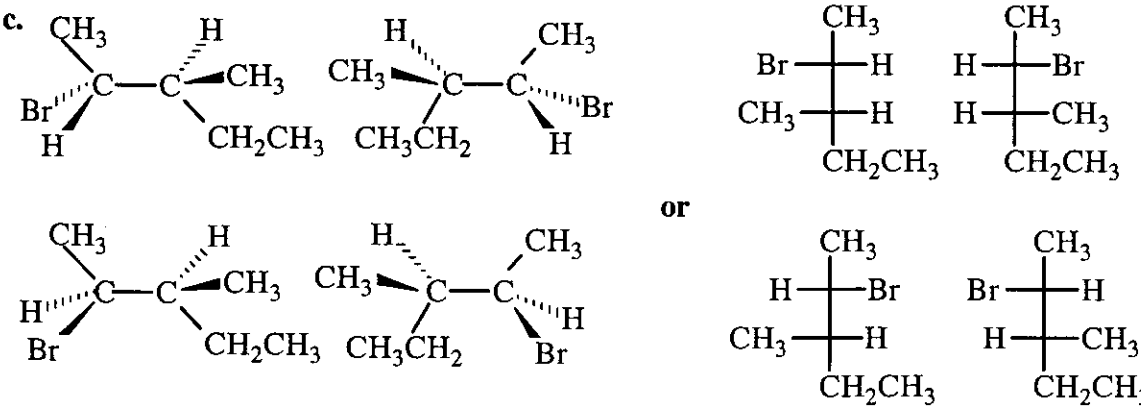


b.

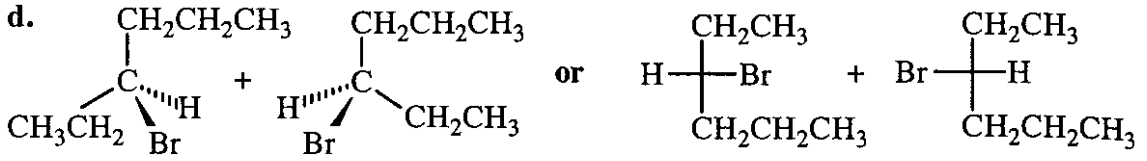


This compound does not have an asymmetric carbon.

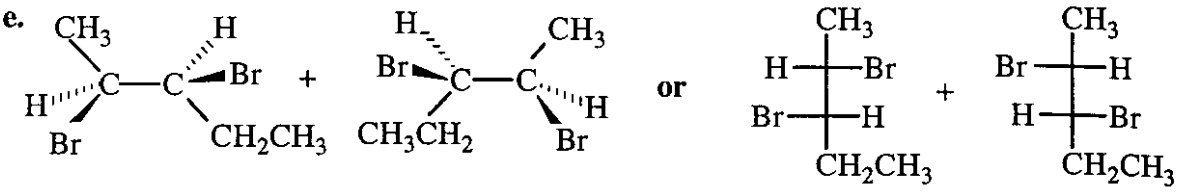
c.



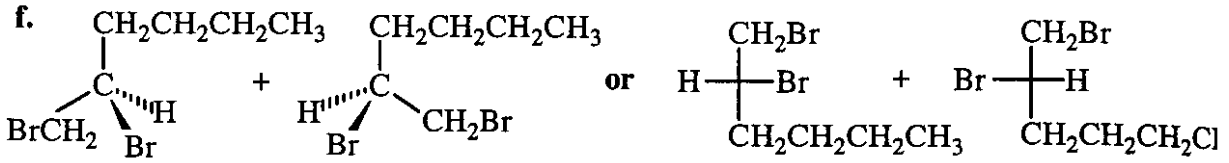
d.



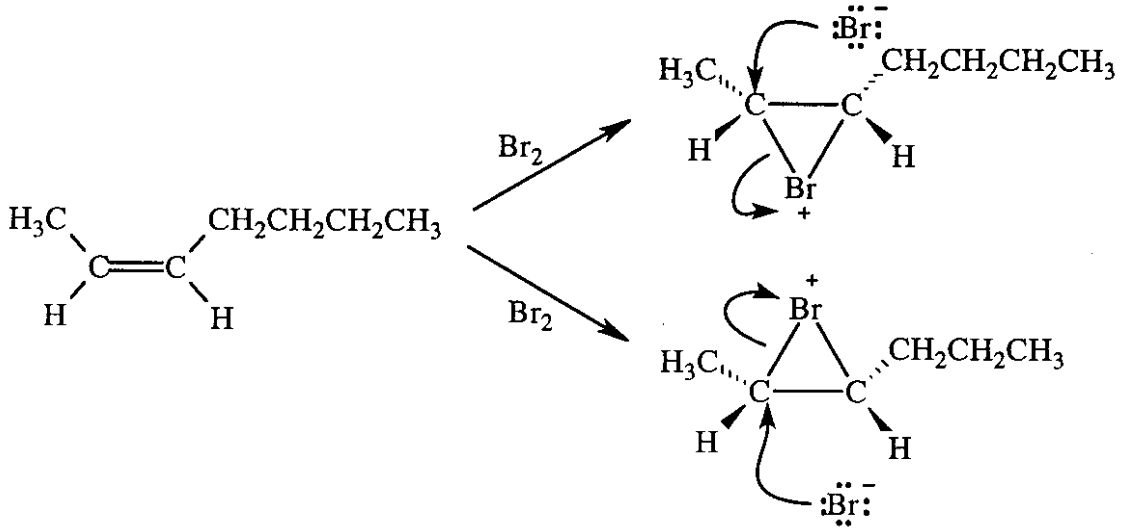
e.



f.

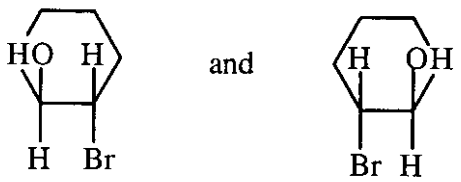


48. Two different bromonium ions are formed because Br^+ can add to the double bond either from the top of the plane or from the bottom of the plane defined by the alkene, and the two bromonium ions are formed in equal amounts. Attacking the less hindered carbon of one bromonium ion forms one stereoisomer, while attacking the less hindered carbon of the other bromonium ion forms the other stereoisomer.

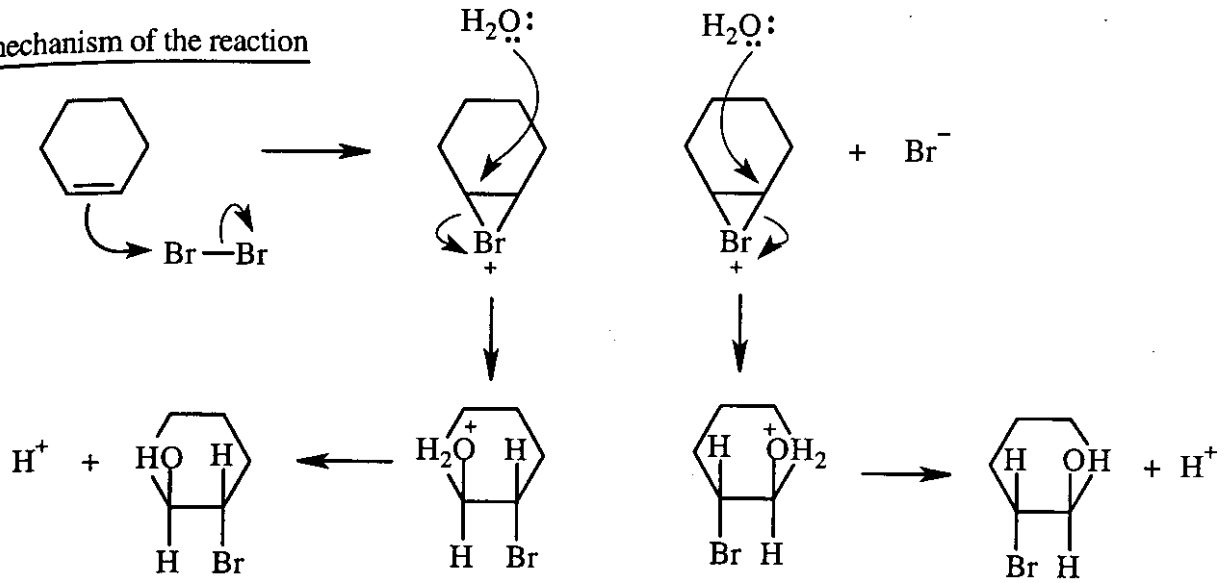


49.

a.

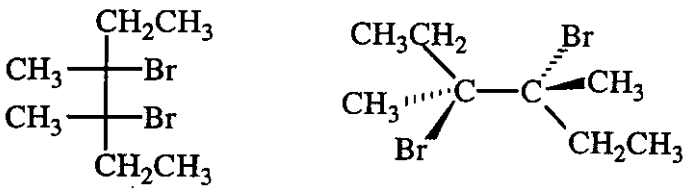


b. mechanism of the reaction

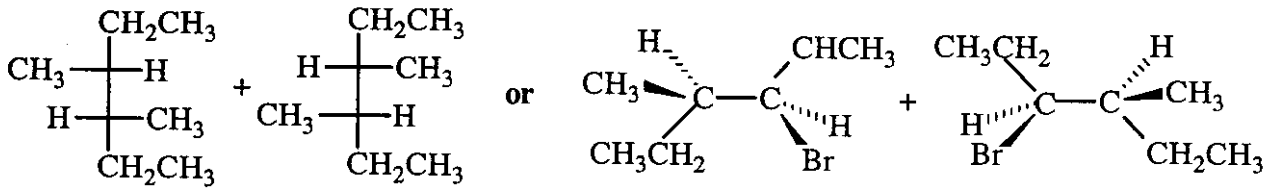


50.

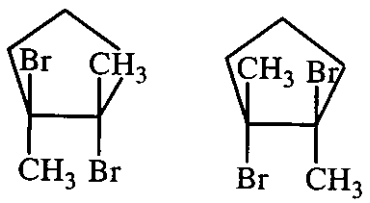
a.



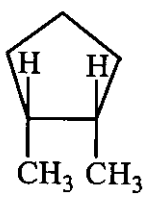
b.



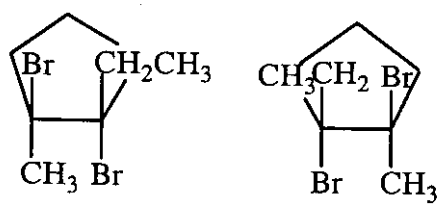
c.



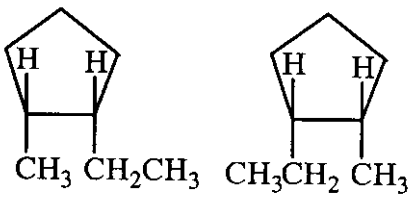
e.



d.



f.

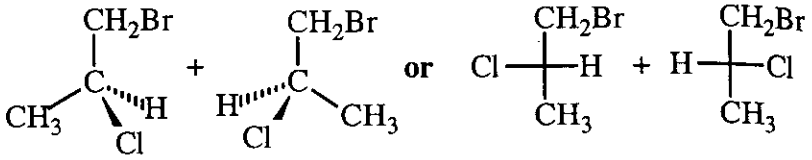


51.

a. CH_3CHCH_2Br (Cl)

1-bromo-2-chloropropane

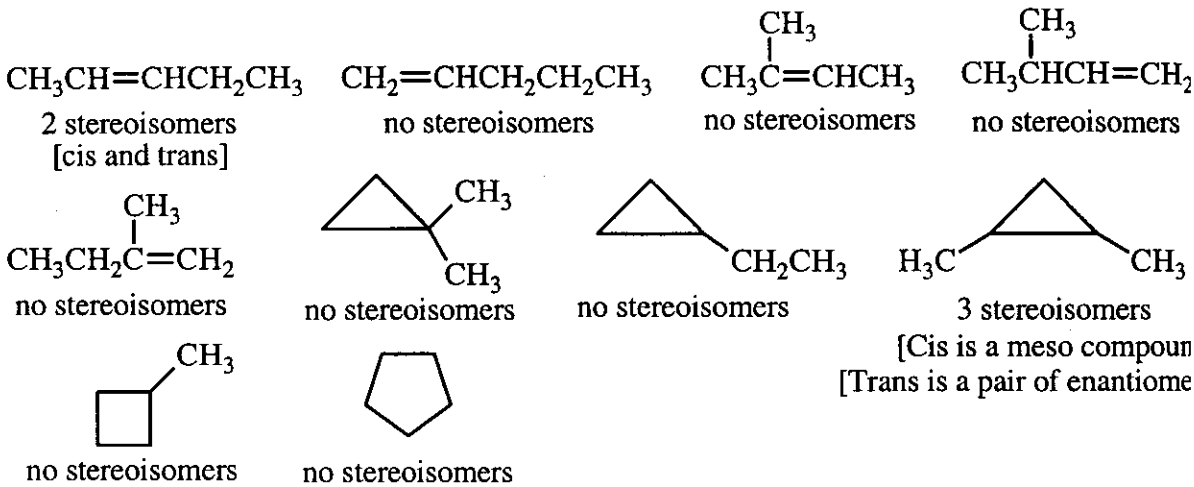
b. The *R* and *S* enantiomers will be formed in equal amounts.



52. **a.** (*R*)-malate and (*S*)-malate (A product with one asymmetric carbon would be formed from reactant with no asymmetric carbons. Thus, the product would be a racemic mixture.)

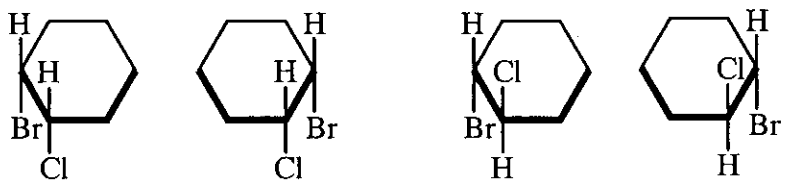
b. (*R*)-malate and (*S*)-malate (A product with one asymmetric carbon would be formed from reactant with no asymmetric carbons. Thus, the product would be a racemic mixture.)

53.

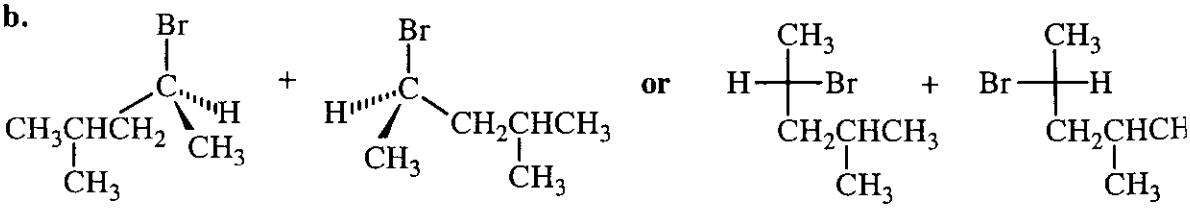


54.

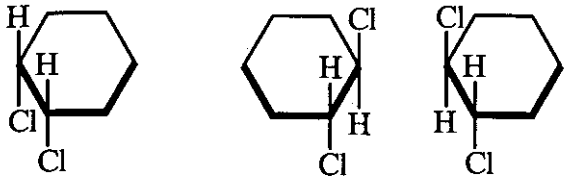
a.



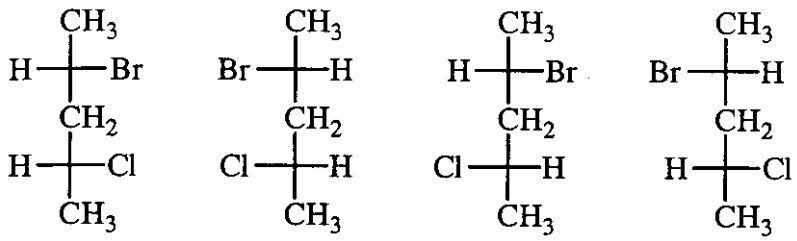
b.



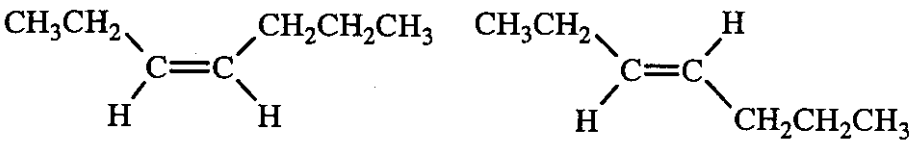
c.



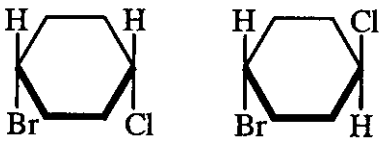
d.



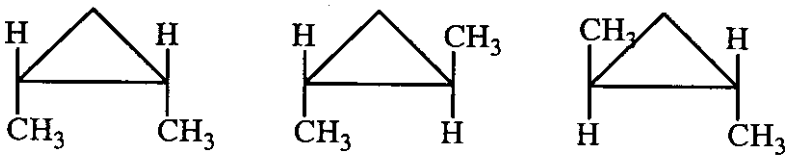
e.



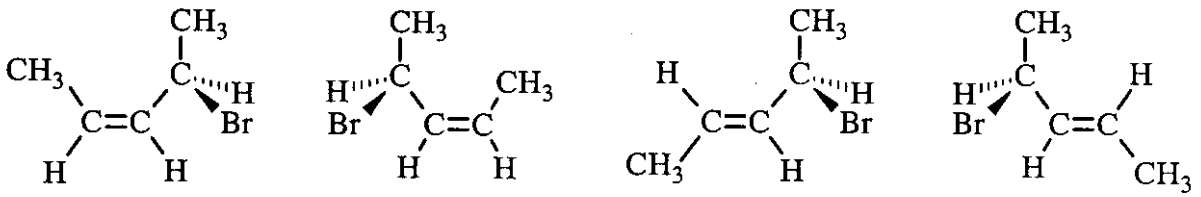
f.



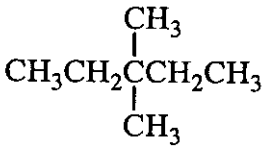
g.



h.

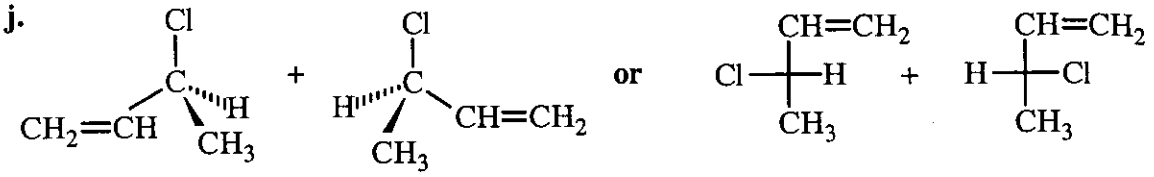


i.

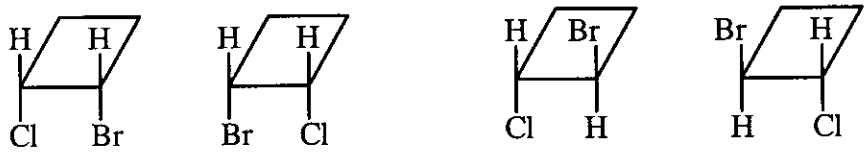


No isomers are possible for this compound because it does not have an asymmetric carbon.

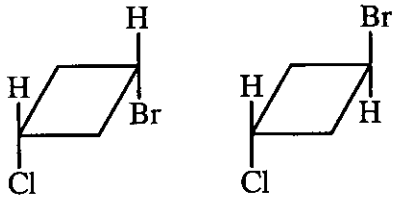
j.



k.



l.



55. **a.** (*R*)-2-ethyl-4-methyl-1-hexene

b. (*E*)-1-bromo-2-chloro-2-fluoro-1-iodoethene

c. (*Z*)-2-bromo-1-chloro-1-fluoroethene

d. (*E*)-4-(2-chloroethyl)-2,3-dimethyl-3-octene

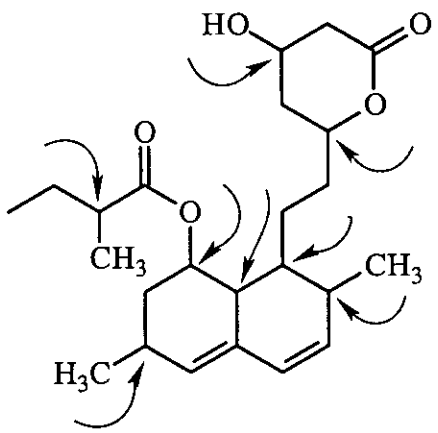
e. 8-bromo-2-ethyl-1-octene

f. (*E*)-1,3-dibromo-4,7-dimethyl-3-octene

g. (*S*)-2-methyl-1,2,5-pentanetriol

h. (2*R*,3*R*)-3-chloro-2-pentanol

56. Mevacor has eight asymmetric carbons.



57. **a.** constitutional isomers

b. enantiomers

c. diastereomers

d. constitutional isomers (One is 3-chloro-2-pentanol and the other is 2-chloro-3-pentanol.)

e. diastereomers

f. constitutional isomers

g. identical (By naming them, you see that they both have the *R* configuration.)

h. identical

i. diastereomers

j. enantiomers

k. constitutional isomers

l. enantiomers

m. identical

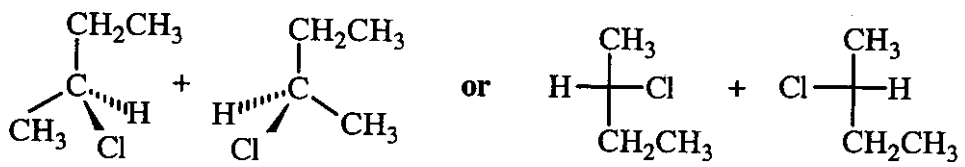
n. diastereomers

o. identical

p. identical

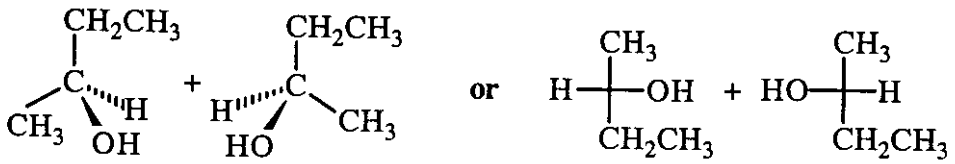
58.

1.



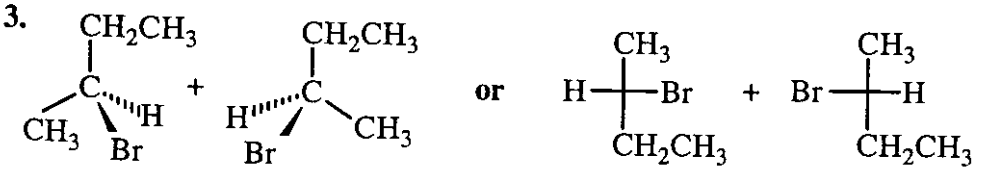
Both cis and trans give these products.

2.



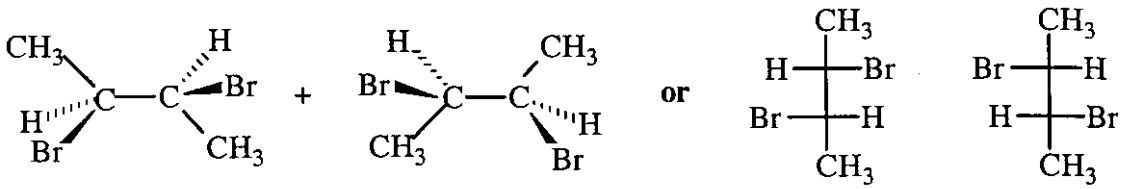
Both cis and trans give these products.

3.

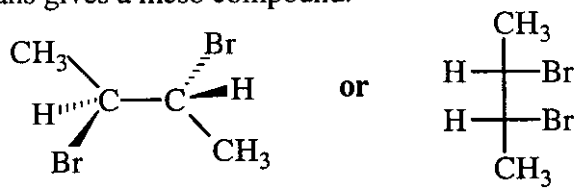


Both cis and trans give these products.

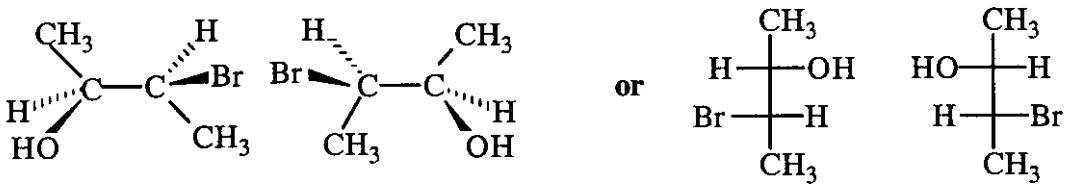
4. Cis gives the threo pair.



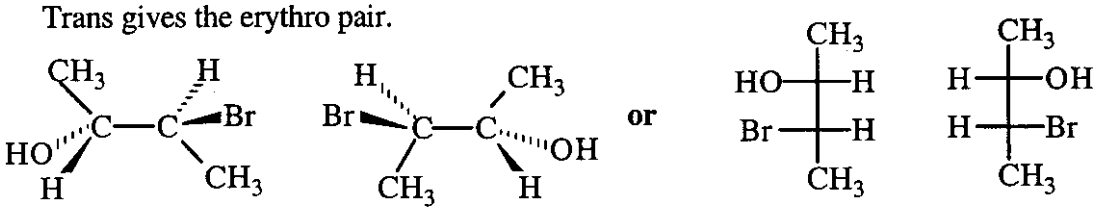
Trans gives a meso compound.



5. Cis gives the threo pair.



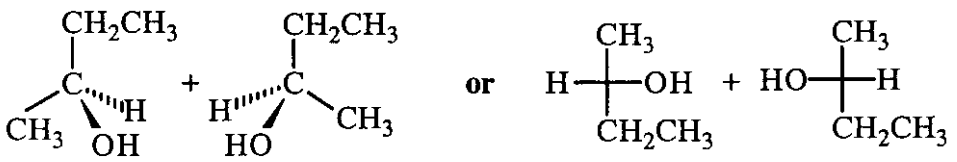
Trans gives the erythro pair.



6. $CH_3CH_2CH_2CH_3$

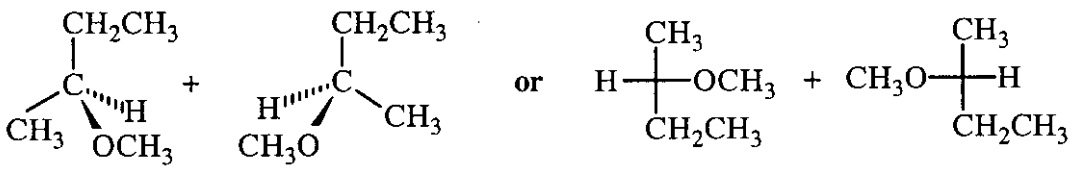
Both cis and trans give this product.

7.



Both cis and trans give these products.

8.



Both cis and trans give these products.

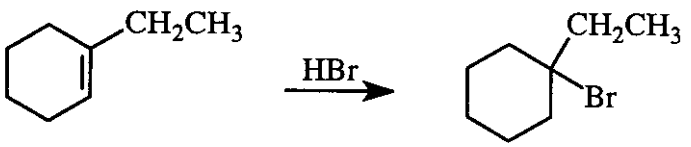
b. For the cis and trans isomers to form different products, the reaction must form two new asymmetric carbons in the product.
Therefore, the cis and trans alkenes form different products when they react with Br_2 in CH_2Cl_2 and when they react with Br_2 in H_2O.

59.

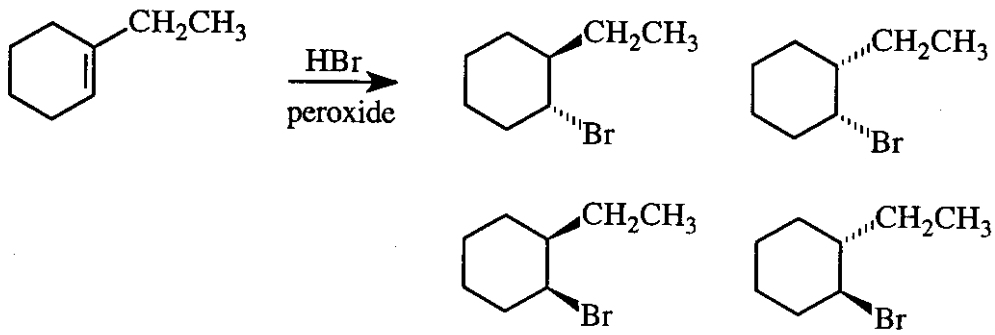
c	does not have stereoisomers; it is, therefore, achiral.
e and **h**	have 2 stereoisomers (cis and trans); both are achiral.
a, d, f, i, and **j**	have 3 stereoisomers; 2 are chiral and 1 is achiral.
b and **g**	have 4 stereoisomers, all of which are chiral.

60.

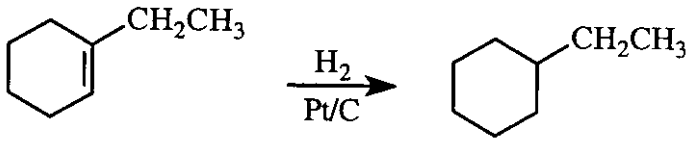
a.



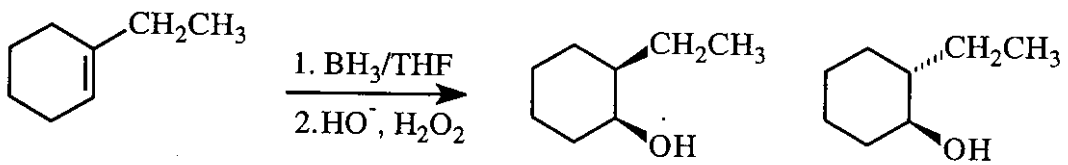
b.



c.

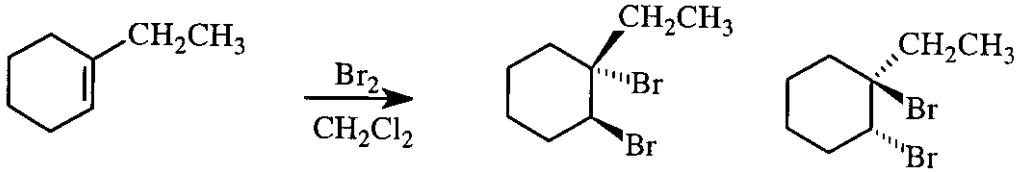


d.



(the H and OH are added to the same side)

e.



(the two Br's are added to opposite sides)

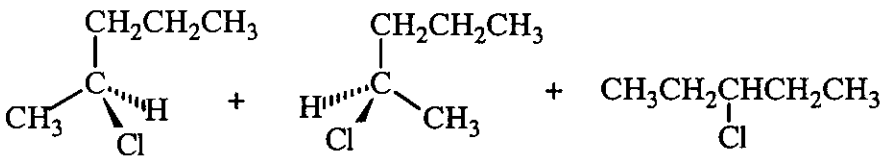
61. **a.** (*R*)-citric acid (^{14}C has a higher priority than ^{12}C)

b. The reaction is catalyzed by an enzyme. Only one stereoisomer is formed in an enzyme-catalyzed reaction because an enzyme has a chiral binding site which allows reagents to be delivered to only one side of the functional group of the compound.

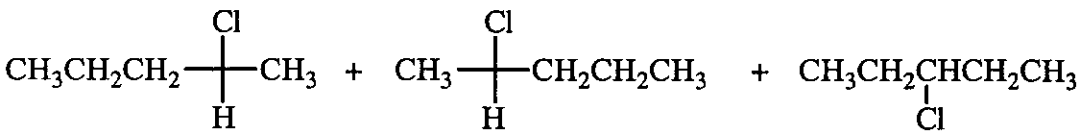
c. The product of the reaction will be achiral because if it doesn't have a ^{14}C, the two CH_2COOH groups will be identical so it will not have an asymmetric carbon.

62.

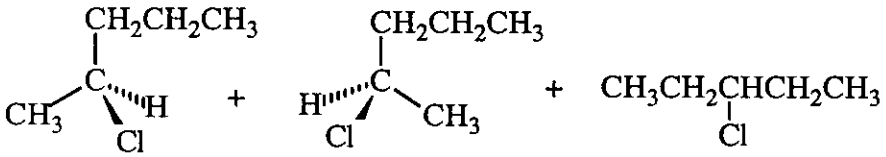
a.



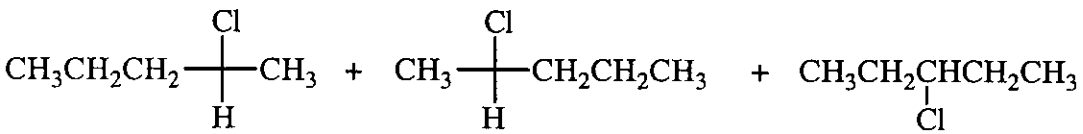
or



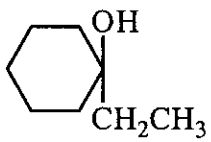
b.



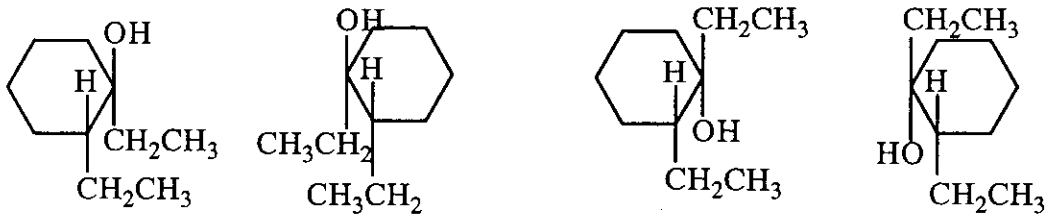
or



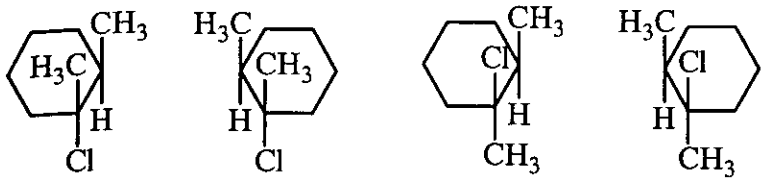
c.



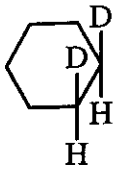
d.



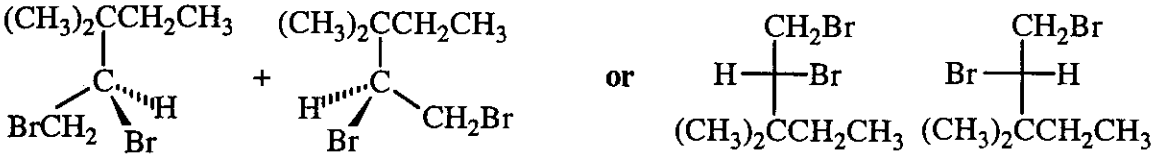
e.



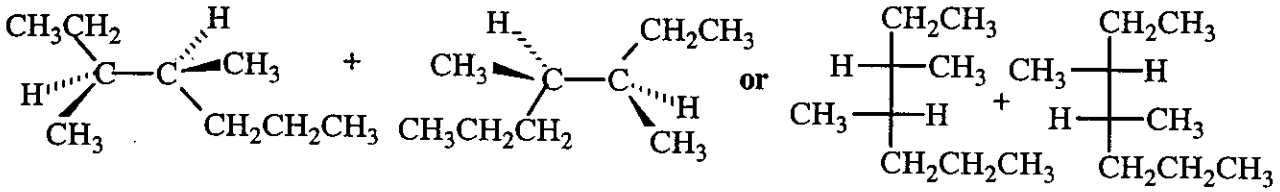
f.



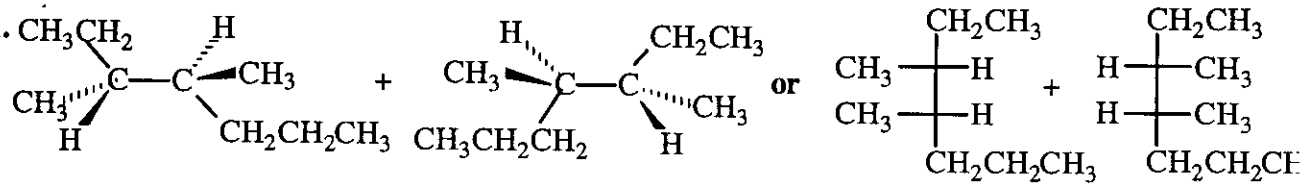
g.



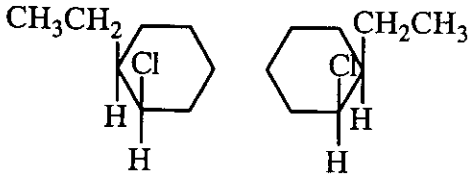
h.



i.



j.



63.

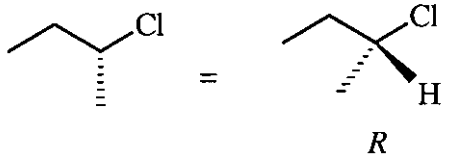
optical purity = $\frac{+1.4°}{+8.7°}$ = .16 = 16% excess *R* enantiomer

100% - 16% = 84% is a racemic mixture

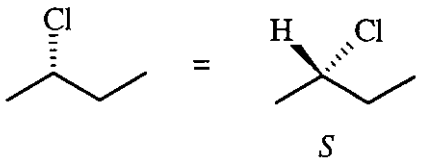
R enantiomer = 1/2 (84%) + 16% = 42% + 16% = 58%

64. Use molecular models to answer this question.

a. *R* **b.** *S* **c.** *S* **d.** *R*

e. 

R

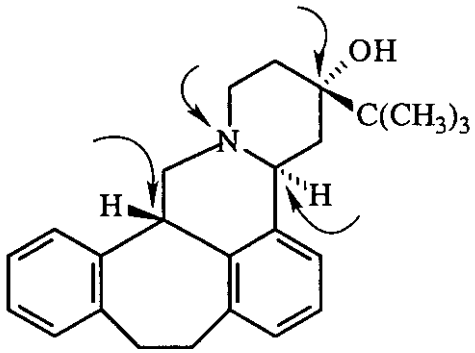
f. 

S

65.

$$[\alpha] = \frac{\alpha}{l \times c} = \frac{-1.8°}{[2.0\ \text{dm}]\ [0.15\text{g/mL}]} = -6.0°$$

66. Butaclamol has three asymmetric carbons. It also has an asymmetric nitrogen. Thus, it has a t of four chirality centers.



67. **a**, **b**, **c**, **e** (think of a British car and an American car), and **h** are chiral.

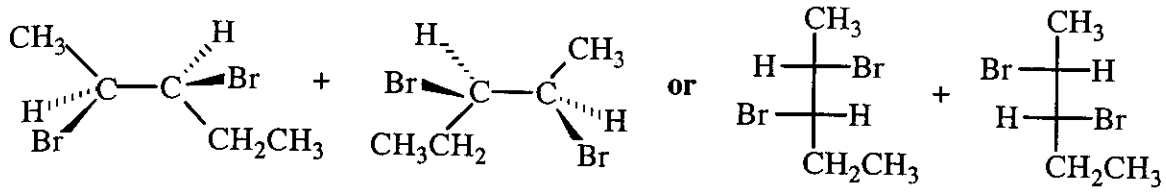
d, **f**, and **g** are each superimposable on its mirror image. These, therefore, are achiral.

68. *R* and *S* are related to (+) and (–) in that if one configuration (say, *R*) is (+), the other one is (-

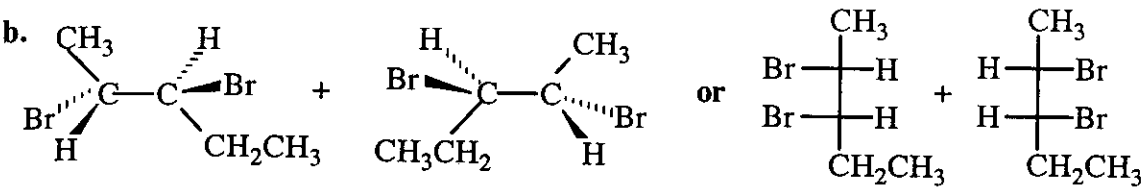
Because some compounds with the *R* configuration are (+) and some are (–), there is no way determine whether a particular *R* enantiomer is (+) or (–) without putting the compound in a polarimeter or going to the library to see if someone else has previously determined how it rotates light.

69.

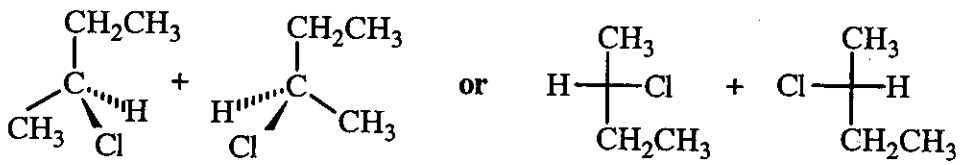
a.



b.

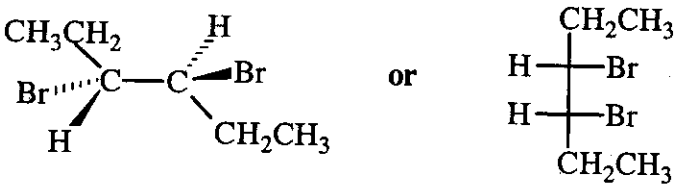


c.

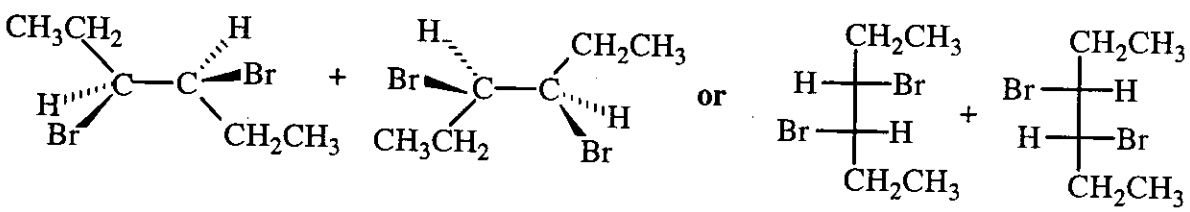


d. $BrCH_2CH_2CH_2CH_3$ This compound does not have isomers because it deos not have an asymmetric carbon.

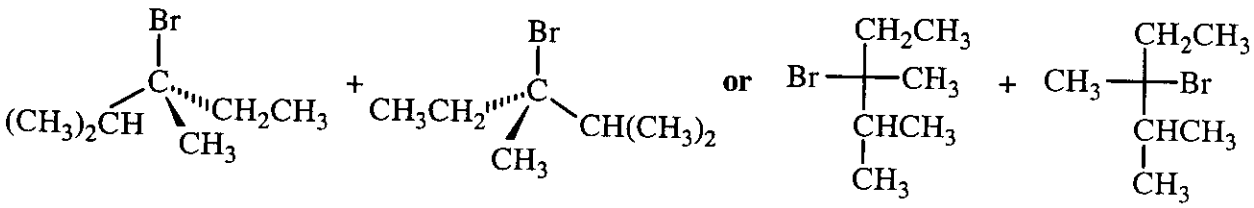
e.



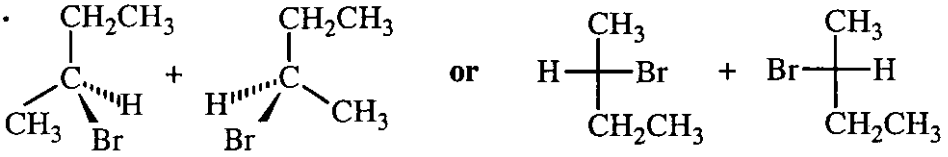
f.



g. The initially formed carbocation is secondary. It undergoes a 1,2-methyl shift to form a tertiary carbocation that gives the products shown below.

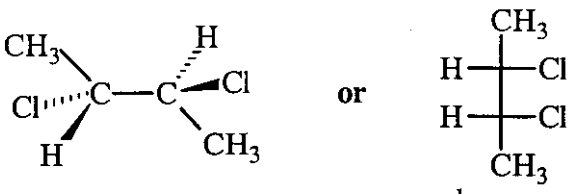


h.



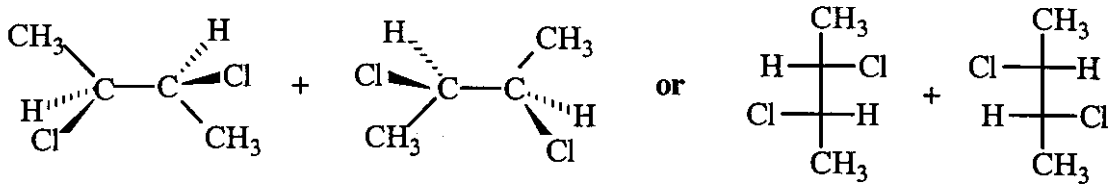
Both cis and trans give these products.

i.

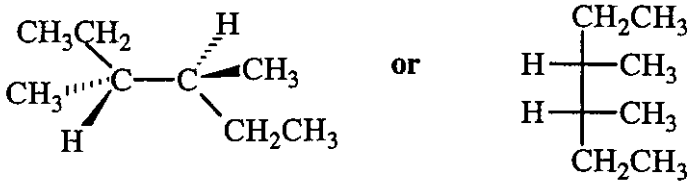


a meso compound

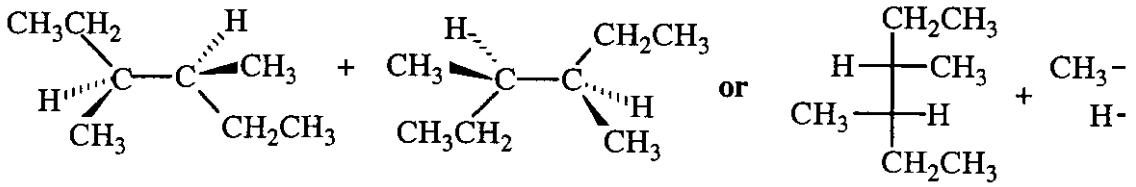
j.



k.

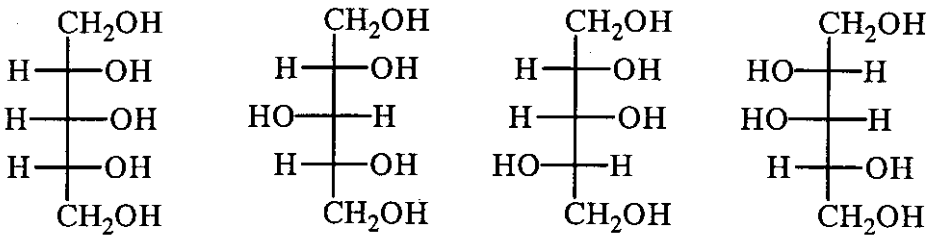


l.



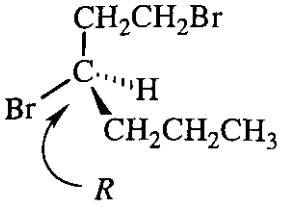
70.

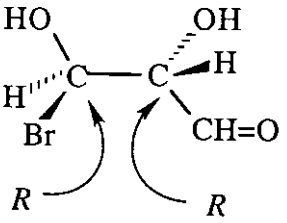
a. The compound has four stereoisomers.

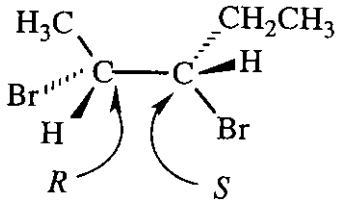


b. The first two stereoisomers are optically inactive because they are meso compounds.

71.

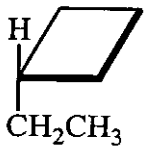
a. 

b. 

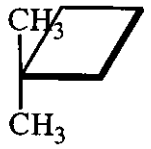
c. 

72.

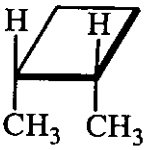
a. and **b.**



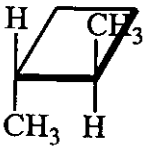
ethylcyclobutane

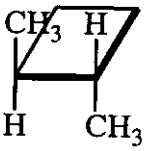


1,1-dimethylcyclobutane

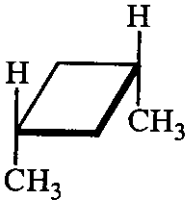


cis-1,2-dimethylcyclobutane

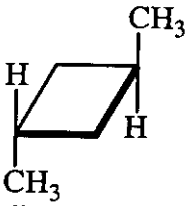




trans-1,2-dimethylcyclobutane



cis-1,3-dimethylcyclobutane



trans-1,3-dimethylcyclobutane

c. **1.** ethylcyclobutane
1,1-dimethylcyclobutane
1,2-dimethylcyclobutane
1,3-dimethylcyclobutane

2. **a.** the three isomers of 1,2-dimethylcyclobutane
b. the two isomers of 1,3-dimethylcyclobutane

3. **a.** 1,2-dimethylcyclobutane
b. 1,3-dimethylcyclobutane

4. the two trans stereoisomers of 1,2-dimethylcyclobutane

5. all the isomers except the two trans stereoisomers of 1,2-dimethylcyclobutane

6. *cis*-1,2-dimethylcyclobutane
(Note: *cis*-1,3-dimethylcyclobutane is not a meso compound, because it does not have asymmetric carbons.)

7. the two trans stereoisomers of 1,2-dimethylcyclobutane

8. **a.** *cis*-1,3-dimethylcyclobutane and *trans*-1,3-dimethylcyclobutane
b. *cis*-1,2-dimethylcyclobutane and either of the enantiomers of *trans*-1,2-dimethylcyclobutane

73.

$$\text{observed specific rotation} = \frac{\text{observed rotation}}{\text{concentration x length}}$$

$$[\alpha] = \frac{\alpha}{\text{concentration x length}} = \frac{-6.52°}{0.187 \text{ x } 1 \text{ dm}} = -34.9°$$

$$\text{\% optical purity} = \frac{\text{observed specific rotation}}{\text{specific rotation of the pure enantiomer}} \text{ x } 100$$

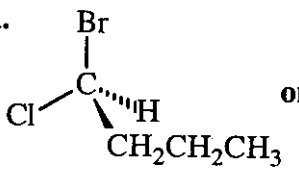
$$\text{\% optical purity} = \frac{-34.9°}{-39.0°} \text{ x } 100$$

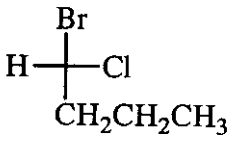
$$\text{\% optical purity} = 89.5\%$$

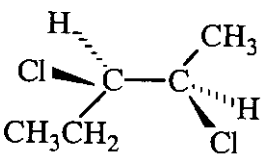
$$\text{\% of the (+)-isomer} = \frac{100 - 89.5}{2} = 5.25\ \%$$

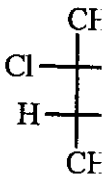
$$\text{\% of the (−)-isomer} = 89.5 + 5.25 = 94.75\ \%$$

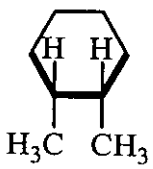
74.

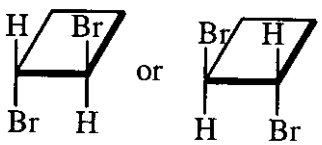
a. 

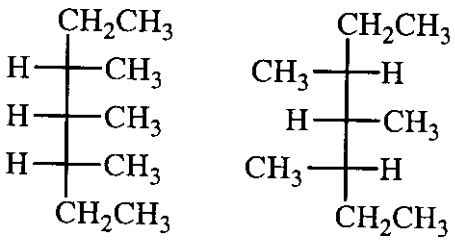
or 

b. 

or 

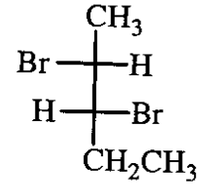
c. 

d. 

e. 

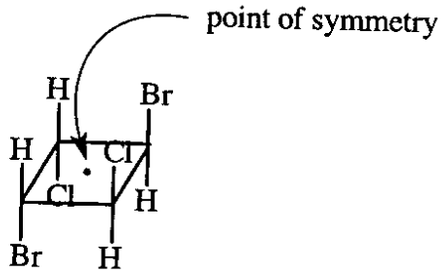
75. In the transition state for amine inversion, the nitrogen atom is sp^2 hybridized, which means it has bond angles of 120°. A nitrogen atom in a three-membered ring cannot achieve a 120° bon angle, so the amine inversion that would interconvert the enantiomers cannot occur. Therefore the enantiomers can be separated.

76. The compound shown below would not be obtained, because none of the bonds attached to C-2 were broken during the reaction. Therefore, the configuration at C-2 cannot change.

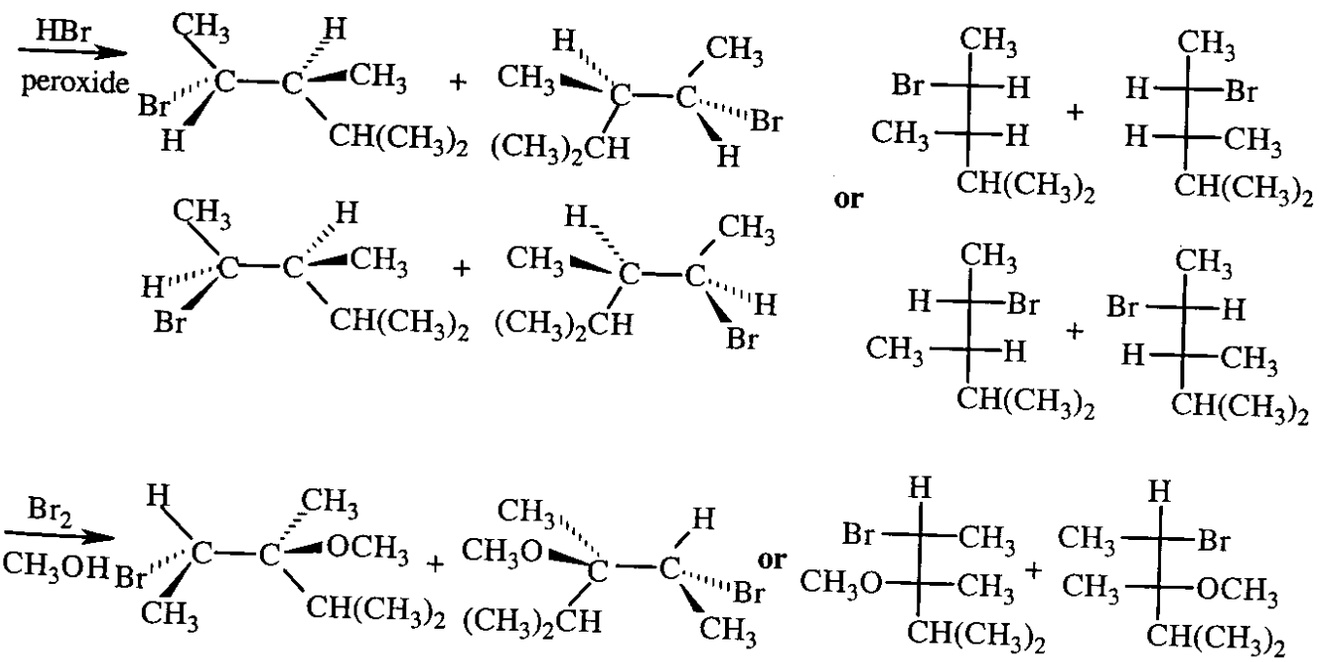


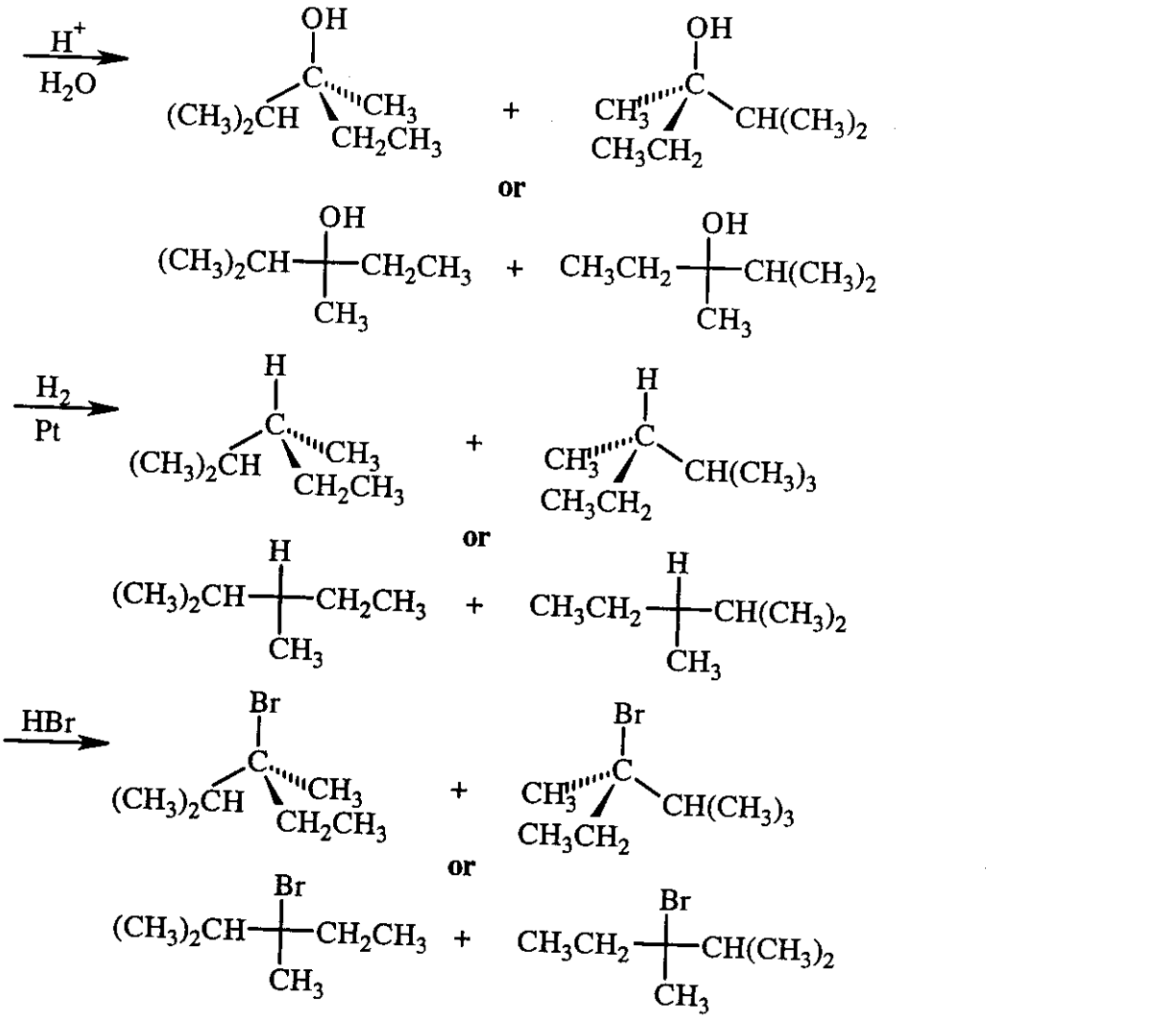
77. The fact that the optical purity is 72% means that there is 72% enantiomeric excess of the *S* isomer and 28% racemic mixture. Therefore, the actual amount of the *S* isomer in the sample is 72% + 1/2(28%) = 86%. So the amount of the *R* isomer in the sample is 100% - 86% = 14%.

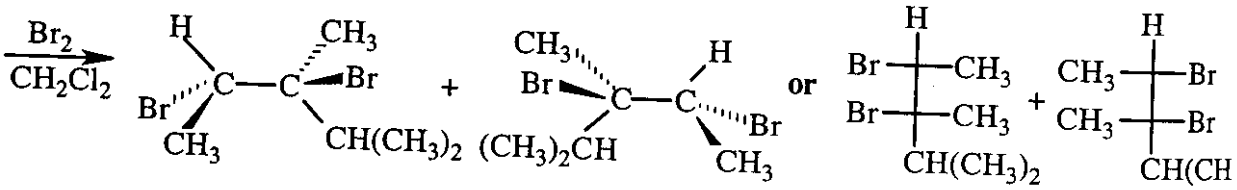
78. The compound is not optically active because it has a center of symmetry. A center of symmetry is a point, and if a line is drawn to this point from an atom or group and the line then extended an equal distance beyond the point, the line would touch an identical atom or group.

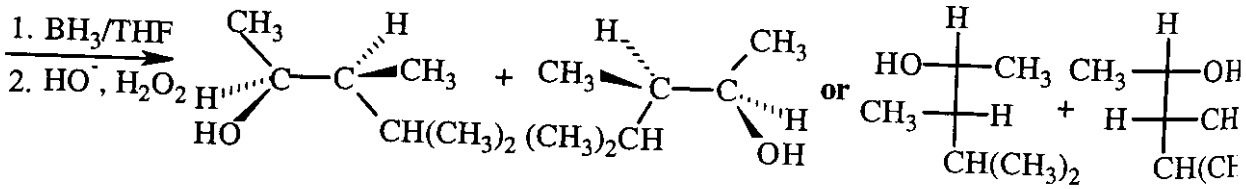


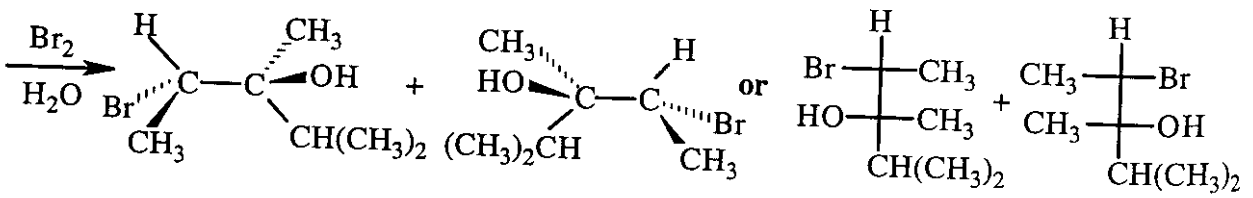
79.




H+
H2O
OH
(CH3)2CH
CH3
CH2CH3
+
CH3CH2
CH(CH3)2
or
(CH3)2CH
CH2CH3
CH3
CH3CH2
CH(CH3)2
H2
Pt
H
(CH3)2CH
CH2CH3
CH3
CH3CH2
CH(CH3)3
or
(CH3)2CH
CH2CH3
CH3
CH3CH2
CH(CH3)2
HBr
Br
(CH3)2CH
CH2CH3
CH3
CH3CH2
CH(CH3)3
or
(CH3)2CH
CH2CH3
CH3
CH3CH2
CH(CH3)2

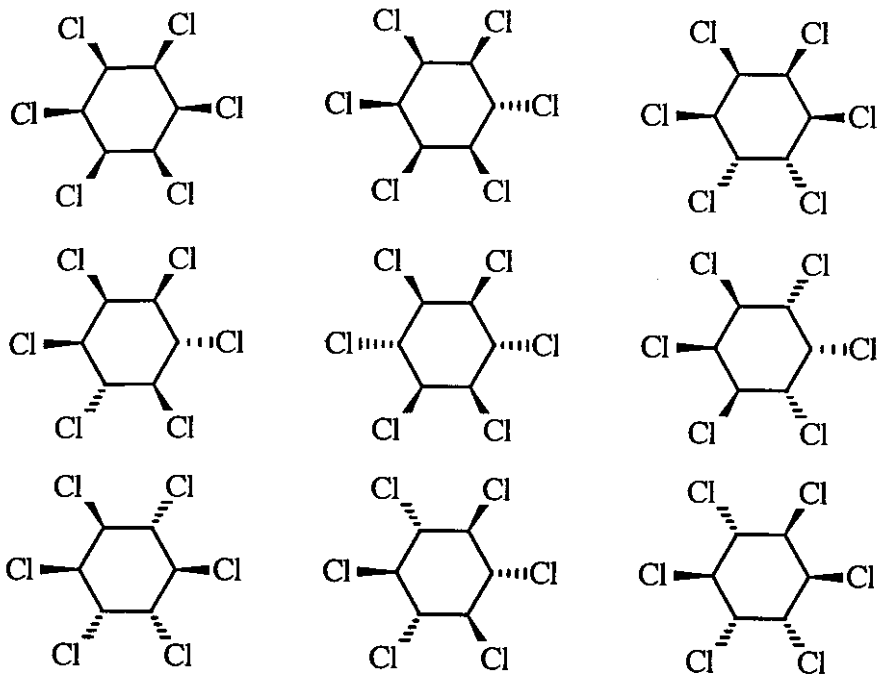

Br2
CH2Cl2
H
Br
CH3
CH(CH3)2
(CH3)2CH
or
Br
CH3
CH(CH3)2
CH(CH


1. BH3/THF
2. HO-, H2O2
CH3
H
HO
CH(CH3)2
(CH3)2CH
OH
or
HO
CH3
CH(CH3)2
CH(CH

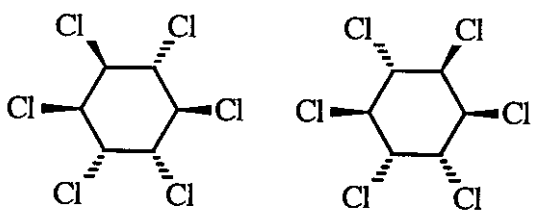

Br2
H2O
H
CH3
Br
OH
CH(CH3)2
HO
(CH3)2CH
Br
or
Br
HO
CH(CH3)2
CH3
OH
CH(CH3)2

80.

a.

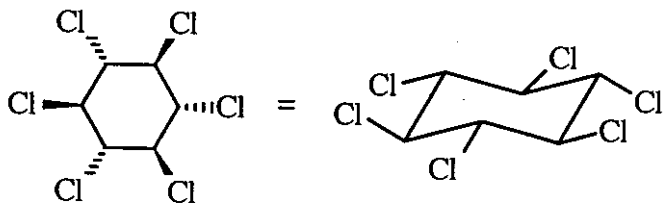


b.



This is a pair of enantiomers because they are nonsuperimposable mirror images.

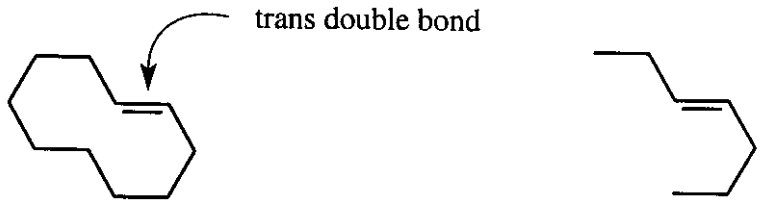
c.



This is the most stable isomer because, since the chloro substituents are all trans to each other, they can all be in the more stable equatorial position. (There is less steric strain when a substituent is in the equatorial position.)

81. Yes.

82. A six-membered ring is too small to accommodate a trans double bond, but a ten-membered ring is large enough to accommodate a trans double bond.

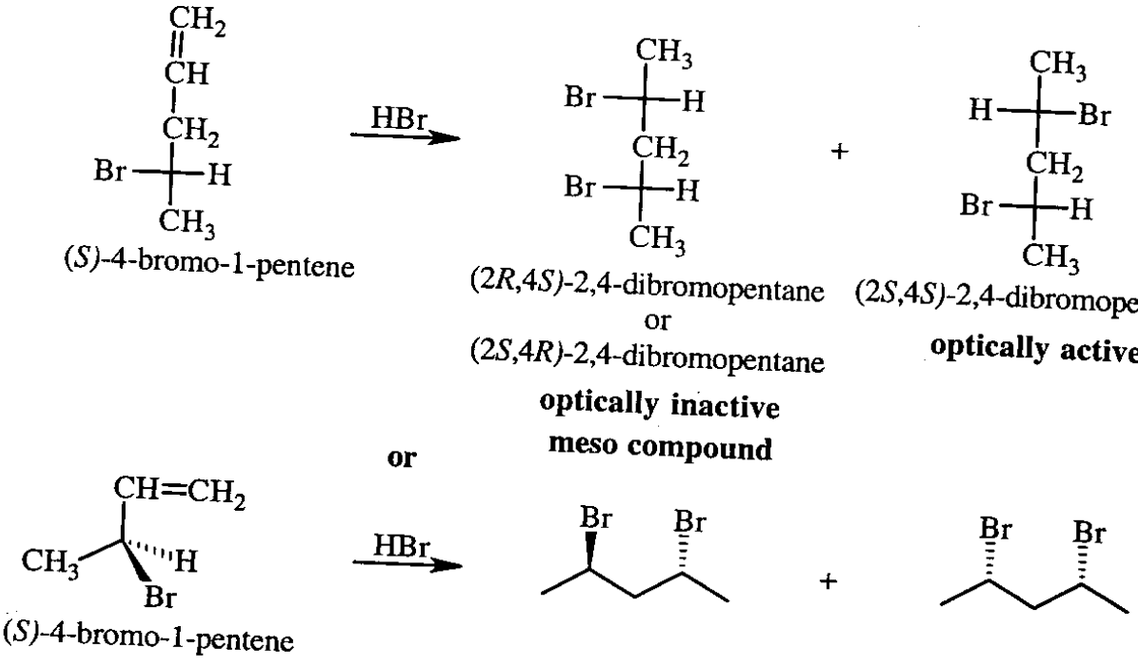


a ten-membered ring

a six-sided structure with a trans double bond

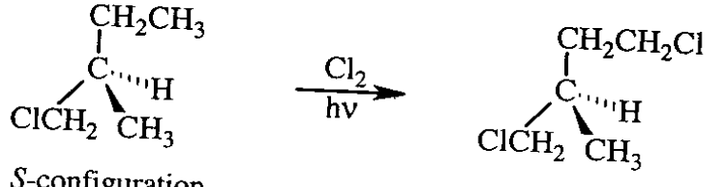
83. Because fumarate is the trans isomer and it forms an erythro product, the enzyme must cata an anti addition of D_2O.

84.

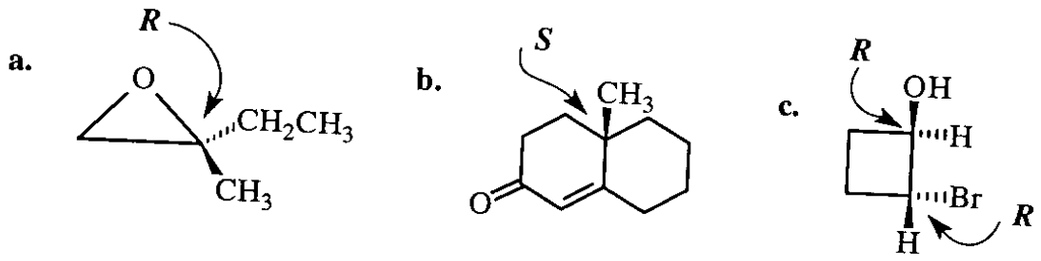


The configuration at C-4 does not change, because no bonds to this carbon are broken.
The new asymmetric carbon at C-2 can have either the *R* or the *S* configuration.
The product with C-2 in the *R* configuration has a plane of symmetry; therefore, it is achiral (optically inactive).
The product with C-2 in the *S* configuration does not have a plane of symmetry; therefore, it i chiral (optically active).

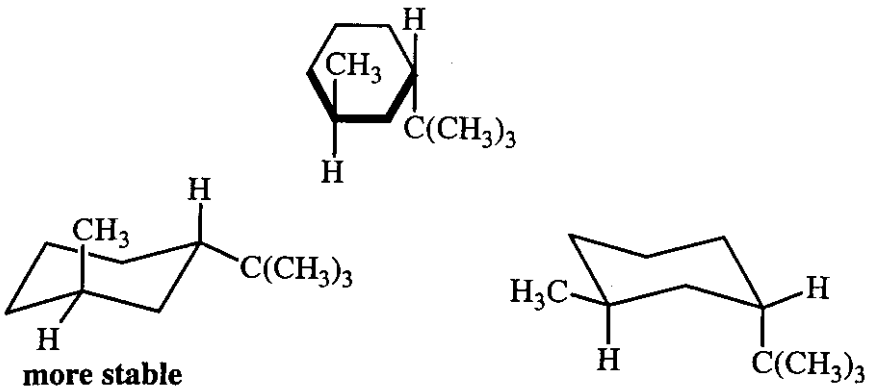
85. We can determine that (–)-1,4-dichloro-2-methylbutane has the *S* configuration because in the process of forming it from (*S*)-(+)-1-chloro-2-methylbutane, no bonds to the asymmetric carbo are broken. Therefore, the configuration of the asymmetric carbon is known.

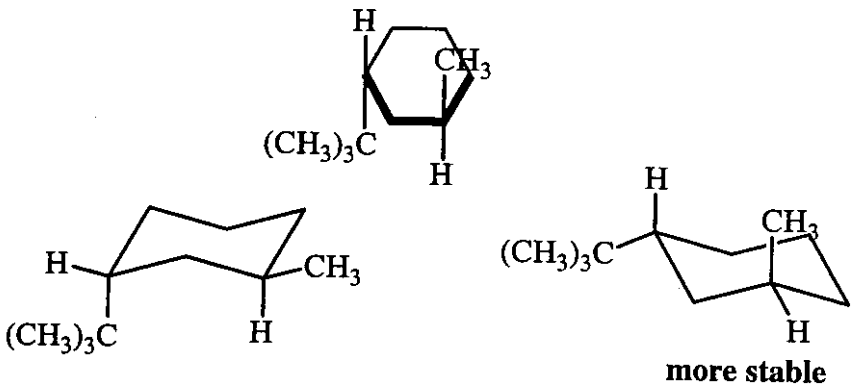


86.



87. The trans compound exits as a pair of enantiomers.



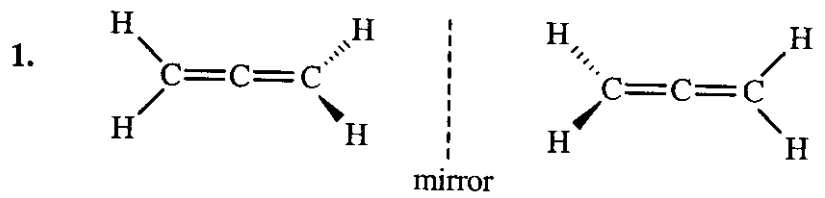


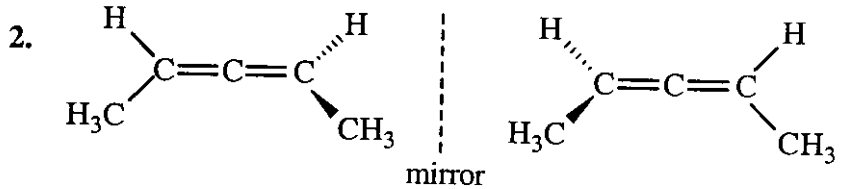
As a result of ring-flip, each enantiomer has two chair conformations. In each case, the more stable conformation is the one with the larger group (the *tert*-butyl group) in the equatorial position.

88. **a.** The compounds do not have any asymmetric carbons.

b. **1.** is not chiral.

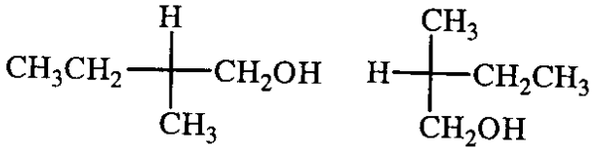
2. is chiral. Because of its unusual geometry, it is a chiral molecule, even though it does not have any asymmetric carbons, because it cannot be superimposed on its mirror image. This will be easier to understand if you build models.



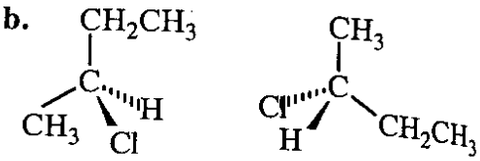


Chapter 5 Practice Test

llowing compounds identical or a pair of enantiomers?

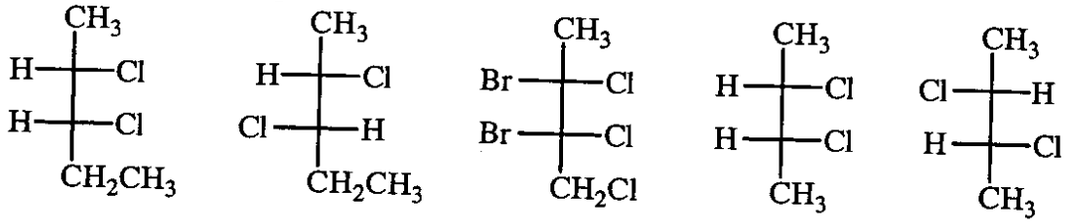


b.



2. 30 mL of a solution containing 2.4 g of a compound rotates the plane of polarized light −0.48° in a polarimeter with a 2 decimeter sample tube. What is the specific rotation of the compound?

3. Which are meso compounds?



4. Draw the constitutional isomers with molecular formula C_4H_9Cl.

5. Draw the stereoisomers of:

a. 2,3-dibromobutane

b. 2,3-dibromopentane

6. Give the stereochemistry of the products that would be obtained from each of the following reactions:

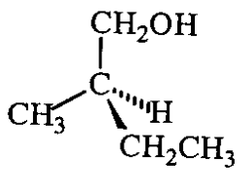
a. 1-butene + HCl

b. 2-pentene + HBr

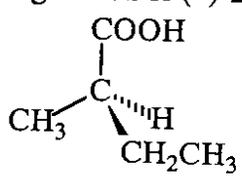
c. *trans*-3-hexene + Br_2

d. *trans*-3-heptene + Br_2

7. *R*-(−)-2-methyl-1-butanol can be oxidized to (+)-2-methylbutanoic acid without breaking any of the bonds to the asymmetric carbon. What is the configuration of (−)-2-methylbutanoic acid?



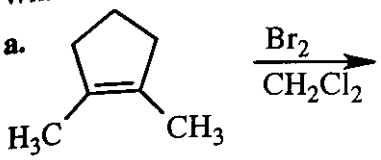
(*R*)-(−)-2-methyl-1-butanol



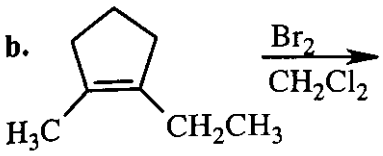
(+)-2-methylbutanoic acid

8. What stereoisomers would be obtained from each of the following reactions?

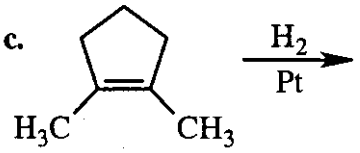
a.



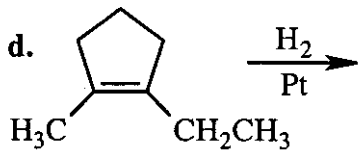
b.



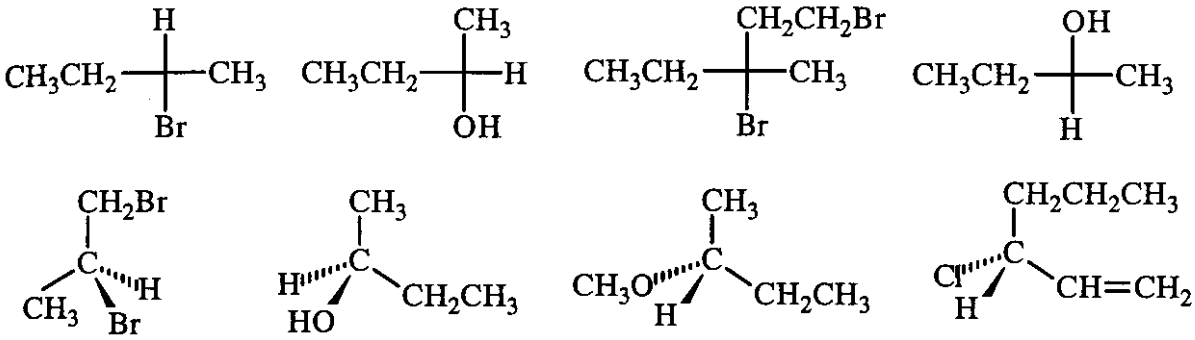
c.



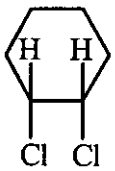
d.



9. Which of the following have the *R* configuration?



10. Draw a diastereomer of the following compound:



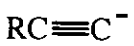
11. Indicate whether each of the following statements is true or false:

a. Diastereomers have the same melting points.	T	F
b. The addition of HBr to 3-methyl-2-pentene is a stereospecific reaction.	T	F
c. The addition of HBr to 3-methyl-2-pentene is a stereoselective reaction.	T	F
d. The addition of HBr to 3-methyl-2-pentene is a regioselective reaction.	T	F
e. Meso compounds do not rotate polarized light.	T	F
f. 2,3-Dichloropentane has a stereoisomer that is a meso compound.	T	F
g. All chiral compounds with the *R* configuration are dextrorotatory.	T	F
h. A compound with three asymmetric carbons can have a maximum of nine stereoisomers.	T	F

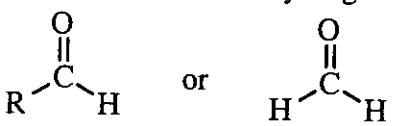
CHAPTER 6
Reactions of Alkynes • Introduction to Multistep Synthesis

Important Terms

acetylide ion — the conjugate base of a terminal alkyne



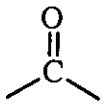
aldehyde — a compound with a carbonyl group that is bonded to an alkyl group and t hydrogen (or bonded to two hydrogens).



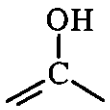
alkylation reaction — a reaction that adds an alkyl group to a reactant.

alkyne — a hydrocarbon that contains a triple bond.

carbonyl group — a carbon doubly bonded to an oxygen.



enol — an α,β-unsaturated alcohol.



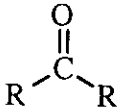
geminal dihalide — a compound with two halogen atoms bonded to the same carbon.

internal alkyne — an alkyne with its triple bond not at the end of the carbon chain.

keto-enol tautomers — a ketone and its isomeric α,β-unsaturated alcohol.



ketone — a compound with a carbonyl group that is bonded to two alkyl groups.



pi-complex — a complex formed between an electrophile and a triple bond.

polymer — a large molecule made by linking up many small molecules called monomers.

radical anion — a species with a negative charge and an unpaired electron.

retrosynthetic analysis or retrosynthesis	working backward (on paper) from a target molecule to available starting materials.
tautomerization	interconversion of tautomers.
tautomers	isomers that are in radpid equilibrium. The keto and enol tautomers differ in the location of a double bond and a hydrogen.
terminal alkyne	an alkyne with its triple bond at the end of the carbon chain.
vinylic cation	a compound with a positive charge on a vinylic carbon.
vinylic radical	a compound with an unpaired electron on a vinylic carbon.

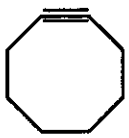
Solutions to Problems

1. The molecular formula of a noncyclic hydrocarbon with 14 carbons and no π bonds is $C_{14}H_{30}$ (C_nH_{2n+2}).
Because a compound has two fewer hydrogens for every ring and π bond, a compound with or ring and 4 π bonds (2 triple bonds) would have 10 fewer hydrogens than the C_nH_{2n+2} formul
Thus, the molecular formula of is **$C_{14}H_{20}$**.

2.

a. $ClCH_2CH_2C{\equiv}CCH_2CH_3$

b.



c. $CH_3CHC{\equiv}CH$ (CH₃ branch)

d. $HC{\equiv}CCH_2Cl$

e. $HC{\equiv}CCH_2C(CH_3)_2CH_3$

f. $CH_3C{\equiv}CCH_3$

3.

$HC{\equiv}CCH_2CH_2CH_2CH_3$
1-hexyne
butylacetylene

$CH_3C{\equiv}CCH_2CH_2CH_3$
2-hexyne
methylpropylacetylene

$CH_3CH_2C{\equiv}CCH_2CH_3$
3-hexyne
diethylacetylene

$CH_3CH_2CHC{\equiv}CH$ (CH₃ branch)
3-methyl-1-pentyne
sec-butylacetylene

$CH_3CHCH_2C{\equiv}CH$ (CH₃ branch)
4-methyl-1-pentyne
isobutylacetylene

$CH_3CHC{\equiv}CCH_3$ (CH₃ branch)
4-methyl-2-pentyne
isopropylmethylacetylene

$CH_3C(CH_3)_2C{\equiv}CH$
3,3-dimethyl-1-butyne
tert-butylacetylene

4.

a. 5-bromo-2-pentyne
b. 6-bromo-2-chloro-4-octyne
c. 1-methoxy-2-pentyne
d. 3-ethyl-1-hexyne

5. Alkyl substituents that are bonded to *sp* carbons stabilize the compound by hyperconjugation—just as alkyl substituents that are bonded to sp^2 carbons stabilize alkenes (Section 4.11).
Therefore, an internal alkyne is more stable than a terminal alkyne because an internal alkyne has two alkyl substituents bonded to the *sp* carbons, whereas a terminal alkyne has only one alkyl substituent bonded to an *sp* carbon.

6.

a. sp^2–sp^2	**d.** sp–sp^3	**g.** sp^2–sp^3
b. sp^2–sp^3	**e.** sp–sp	**h.** sp–sp^3
c. sp–sp^2	**f.** sp^2–sp^2	**i.** sp^2–sp

7. The less stable reactant will be the more reactive reactant, if the less stable reactant has the more stable transition state **and** the difference in the stabilities of the reactants is less than the difference in the stabilities of the transition states, **or** if the less stable reactant has the less stable transition state **and** the difference in the stabilities of the reactants is greater than the difference in the stabilities of the transition states.

8.

a. $BrCH{=}CHCH_3$

b. $CH_2{=}C(Br)CH_3$

c. $CH_3C(Br)(Br)CH_3$

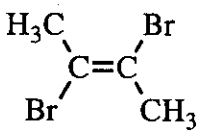
d. $CH_3C(Br){=}CCH_3$ (Br)

e. $CH_3CH_2C(Br)(Br)CH_3$

f. $CH_3C(Br)(Br)CH_2CH_2CH_3$ + $CH_3CH_2C(Br)(Br)CH_2CH_3$

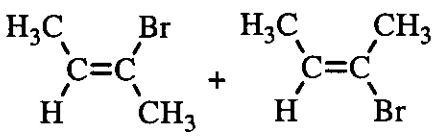
9.

a.



Only anti addition occurs, because the intermediate is a cyclic bromonium ion.

b.



Both anti and syn addition can occur, because the intermediate is a radical.

10. Because the alkyne is not symmetrical, two ketones will be obtained.

$CH_3CH_2C(=O)CH_2CH_2CH_2CH_3$ and $CH_3CH_2CH_2C(=O)CH_2CH_2CH_3$

11.

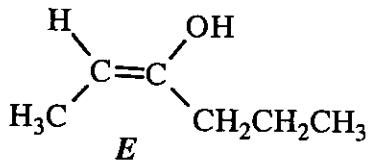
a. $CH_3C{\equiv}CH$ **b.** $CH_3CH_2C{\equiv}CCH_2CH_3$ **c.** $HC{\equiv}C$– 

The best answer for **"b"** is 3-hexyne, because it would form only the desired ketone. 2-Hexyne would form two different ketones, so only half of the product would be the desired ketone.

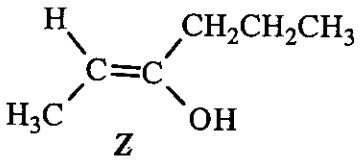
12.

a. $CH_2{=}C(OH)CH_3$ Because the ketone has identical substituents bonded to the carbonyl carbon, it has only one enol tautomer.

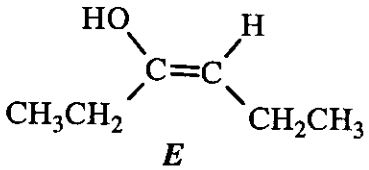
b. $CH_3CH{=}C(OH)CH_2CH_2CH_3$ and $CH_3CH_2C(OH){=}CHCH_2CH_3$ *E* and *Z* isomers are possible for each of these enols.



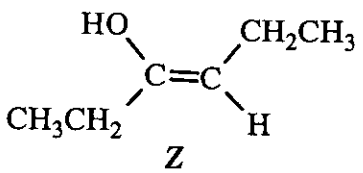
E



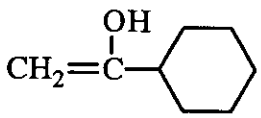
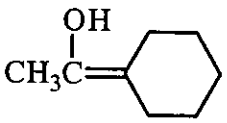
Z



E



Z

c.  and 

Because each enol has indentical groups on one of its sp^2 carbons, *E* and *Z* isomers are not possible for either one.

13.

a. (1) $CH_3CH_2C(=O)CH_3$

(2) $CH_3CH_2CH_2C(=O)H$

b. (1) $CH_3CH_2C(=O)CH_3$

(2) $CH_3CH_2C(=O)CH_3$

c. (1) $CH_3CH_2CH_2C(=O)CH_3$ and $CH_3CH_2C(=O)CH_2CH_3$

(2) $CH_3CH_2CH_2C(=O)CH_3$ and $CH_3CH_2C(=O)CH_2CH_3$

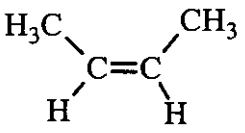
major product because there is less steric hindrance to addition of BH_3 at the 2-position

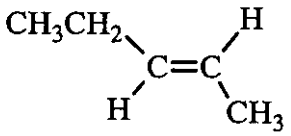
14. Ethyne (acetylene)

An alkyne can form an aldehyde only if the OH group adds to a terminal *sp* carbon. When water adds to a terminal alkyne, the proton adds to the terminal *sp* carbon. Therefore, the only way the OH group can add to a terminal *sp* carbon is if there are two terminal *sp* carbons in the alkyne. In other words, the alkyne must be ethyne.

15.

a. $CH_3CH_2CH_2C{\equiv}CH$ (1-pentyne) or $CH_3CH_2C{\equiv}CCH_3$ (2-pentyne) $\xrightarrow[Pt]{H_2}$ $CH_3CH_2CH_2CH_2CH_3$

b. $CH_3C{\equiv}CCH_3$ (2-butyne) $\xrightarrow[\text{Lindlar catalyst}]{H_2}$ 

c. $CH_3CH_2C{\equiv}CCH_3$ (2-pentyne) $\xrightarrow[NH_3\ liq]{Na}$ 

d. $CH_3CH_2CH_2CH_2C{\equiv}CH$ (1-hexyne) $\xrightarrow[\text{Lindlar catalyst}]{H_2}$ or $\xrightarrow[NH_3]{Na}$ $CH_3CH_2CH_2CH_2CH{=}CH_2$

16. The base used to remove a proton must be stronger than the base that is formed as a result of proton removal. A terminal alkyne has a pK_a ~ 25. Therefore, the base used to remove a proton from a terminal alkyne must be a stronger base than the terminal alkyne. In other words, any base whose conjugate acid has a pK_a greater than 25 can be used.

17. The electronegativities of carbon atoms decrease in the order: $sp > sp^2 > sp^3$.
The more electronegative the carbon atom, the less stable it will be with a positive charge.

a. $CH_3\overset{+}{C}H_2$ **b.** $H_2C{=}\overset{+}{C}H$

18. The reaction will not favor products because the carbanion that would be formed is a stronger base than the amide ion. (Recall that the equilibrium favors reaction of the strong and formation of the weak; Section 1.17)

$$\underset{\substack{pK_a = 50\\ \text{weaker acid}}}{CH_3CH_3} + \underset{\text{weaker base}}{\bar{N}H_2} \rightleftharpoons \underset{\text{stronger base}}{CH_3\bar{C}H_2} + \underset{\substack{pK_a = 36\\ \text{stronger acid}}}{NH_3}$$

19.

a. $CH_3CH_2CH_2\bar{C}H_2 > CH_3CH_2CH{=}\bar{C}H > CH_3CH_2C{\equiv}\bar{C}$

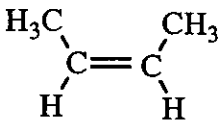
b. $\bar{N}H_2 > CH_3C{\equiv}\bar{C} > CH_3CH_2O^- > F^-$

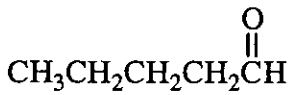
20. Solved in the text.

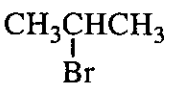
21.

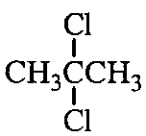
a. $HC{\equiv}CH \xrightarrow[2.\ CH_3CH_2CH_2Br]{1.\ \bar{N}H_2} CH_3CH_2CH_2C{\equiv}CH$

b. $HC{\equiv}CH \xrightarrow[2.\ CH_3Br]{1.\ \bar{N}H_2} CH_3C{\equiv}CH \xrightarrow[Na/NH_3\ liq]{H_2\ /Lindlar\ catalyst\ or} CH_3CH{=}CH_2$

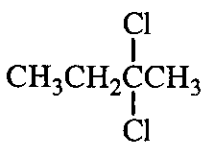
c. $HC{\equiv}CH \xrightarrow[2.\ CH_3Br]{1.\ \bar{N}H_2} CH_3C{\equiv}CH \xrightarrow[2.\ CH_3Br]{1.\ \bar{N}H_2} CH_3C{\equiv}CCH_3 \xrightarrow[Lindlar\ catalyst]{H_2}$ 

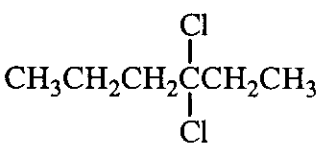
d. product of **a** $\xrightarrow[2.\ HO^-,\ H_2O_2,\ H_2O]{1.\ disiamylborane}$ 

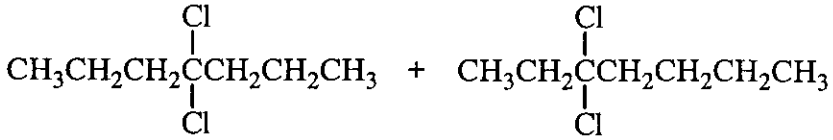
e. product of **b** $\xrightarrow{HBr}$ 

f. $HC{\equiv}CH \xrightarrow[2.\ CH_3Br]{1.\ \bar{N}H_2} CH_3C{\equiv}CH \xrightarrow{excess\ HCl}$ 

22.

a. 

b. 

c. 

23.

a. $CH_3C{\equiv}CCH_2CH_2CH_3$

b. $CH_3CH_2C{\equiv}CCHCH_2CH_2CH_3$ (with CH_2CH_3 branch)

c. $CH_3C{\equiv}CH$

d. $CH_2{=}CHC{\equiv}CH$

e. $CH_3OC{\equiv}CH$

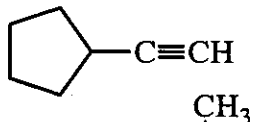
f. $CH_3CC(CH_3){\equiv}CCH(CH_3)CH_2CH_3$

g. $BrC{\equiv}CCH_2CH_2CH_3$

h. $HC{\equiv}CCH_2Br$

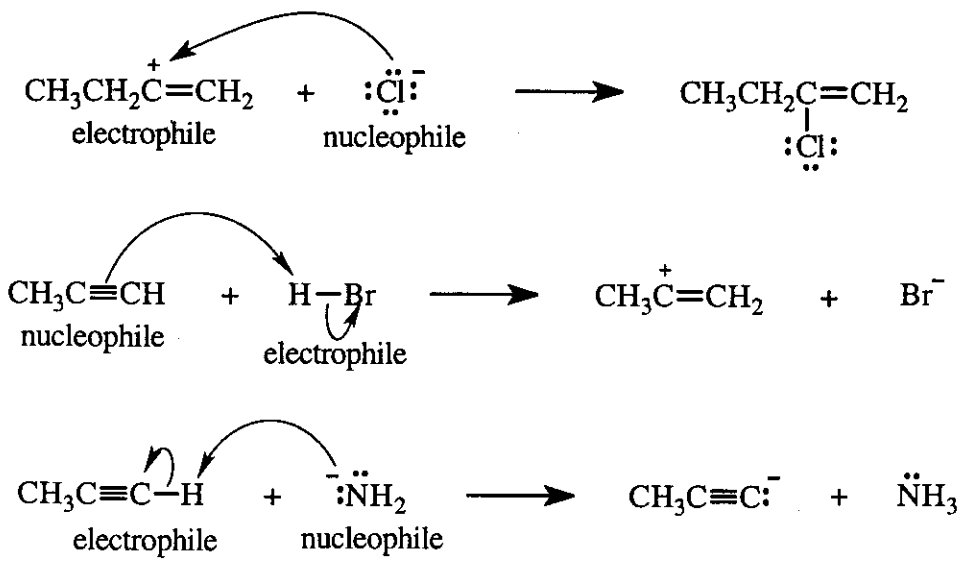
i. $CH_3CH_2C{\equiv}CCH_2CH_3$

j. $CH_3CC(CH_3)_2{\equiv}CC(CH_3)_2CH_3$

k. 

l. $CH_3C{\equiv}CCH_2CH(CH_3)CH(CH_3)CH_3$

24.



25.

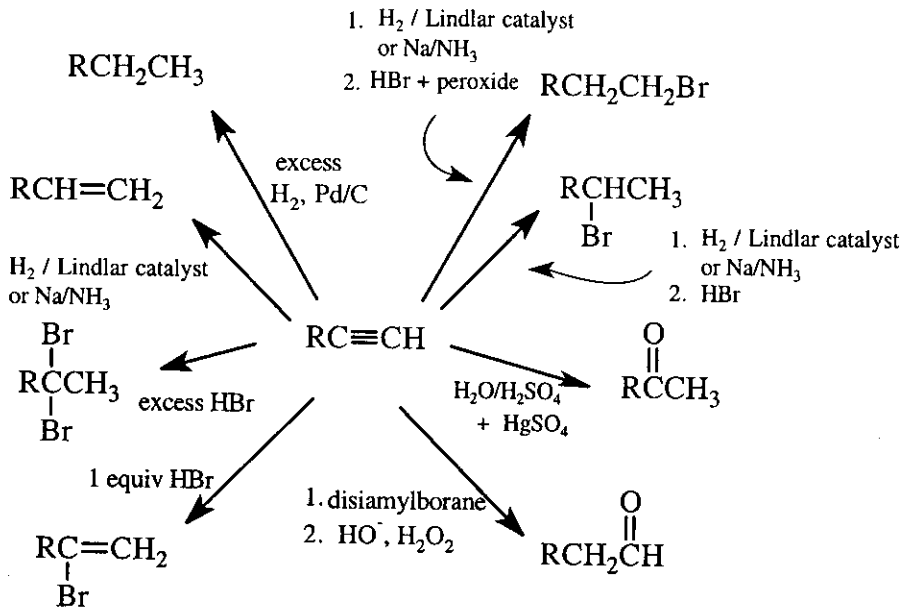
a. 5-bromo-2-hexyne

b. 5-methyl-2-octyne

c. 5,5-dimethyl-2-hexyne

d. 6-chloro-2-methyl-3-heptyne

26.



27. **a.** 4-methyl-2-hexyne

b. 7-bromo-3-heptyne

c. correct

d. 2-pentyne

28.

$HC{\equiv}CCH_2CH_2CH_2CH_2CH_3$
1-heptyne
pentylacetylene

$CH_3C{\equiv}CCH_2CH_2CH_2CH_3$
2-heptyne
butylmethylacetylene

$CH_3CH_2C{\equiv}CCH_2CH_2CH_3$
3-heptyne
ethylpropylacetylene

$CH_3CH_2CH_2CHC{\equiv}CH$ (CH_3)
3-methyl-1-hexyne

$CH_3CH_2CHCH_2C{\equiv}CH$ (CH_3)
4-methyl-1-hexyne

$CH_3CHCH_2CH_2C{\equiv}CH$ (CH_3)
5-methyl-1-hexyne
isopentylacetylene

$CH_3CH_2CHC{\equiv}CCH_3$ (CH_3)
4-methyl-2-hexyne
sec-butylmethylacetylene

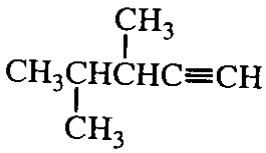
$CH_3CHCH_2C{\equiv}CCH_3$ (CH_3)
5-methyl-2-hexyne
isobutylmethylacetylene

$CH_3CHC{\equiv}CCH_2CH_3$ (CH_3)
2-methyl-3-hexyne
ethylisopropylacetylene

$CH_3CC{\equiv}CCH_3$ (CH_3, CH_3)
4,4-dimethyl-2-pentyne
tert-butylmethylacetylene

$CH_3CCH_2C{\equiv}CH$ (CH_3, CH_3)
4,4-dimethyl-1-pentyne
neopentylacetylene

$CH_3CH_2CC{\equiv}CH$ (CH_3, CH_3)
3,4-dimethyl-1-pentyne
neohexylacetylene



3,4-dimethyl-1-pentyne

29.

a. $CH_3CH_2CH_2C{\equiv}CH \xrightarrow[2.\ HO^-,\ H_2O_2]{1.\ \text{disiamylborane}} CH_3CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}H$

b. $CH_3CH_2CH{=}CH_2 \xrightarrow[2.\ HO^-,\ H_2O_2]{1.\ BH_3} CH_3CH_2CH_2CH_2OH$

c. $CH_3CH_2CH_2C{\equiv}CCH_2CH_2CH_3 + H_2O \xrightarrow{H_2SO_4} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2CH_3$

This symmetrical alkyne will give the greatest yield of the desired ketone. Because the reactant is not a terminal alkyne, the reaction can take place without the mercuric ion catalyst.

d. $CH_3CH_2CH_2CH{=}CH_2 + HBr \xrightarrow{\text{peroxide}} CH_3CH_2CH_2CH_2CH_2Br$

30. **a.** H_2/Lindlar catalyst **b.** Na, NH_3 **c.** excess H_2/Pt

31. The molecular formula of the hydrocarbon is $C_{32}H_{56}$.

$C_nH_{2n+2} = C_{32}H_{66}$

With one triple bond, two double bonds, and one ring, the degree of unsaturation is 5. Therefore, the compound is missing 10 hydrogens from C_nH_{2n+2}.

32.

a. $CH_2{=}C(Br)CH_3$

b. $CH_3C(Br)_2CH_3$

c. $BrCH{=}C(Br)CH_3$

d. $BrCH(Br)C(Br)CH_3$

e. $CH_3C(=O)CH_3$

f. $CH_3CH_2C(=O)H$

g. $BrCH{=}CHCH_3$

h. $CH_3CH_2CH_3$

i. $CH_3CH{=}CH_2$

j. $CH_3CH{=}CH_2$

k. $CH_3C{\equiv}C^-$

l. $CH_3C{\equiv}CCH_2CH_2CH_2CH_2CH_3$

33.

a. $CH_3CH{=}C(Br)CH_3$

b. $CH_3CH_2C(Br)_2CH_3$

c. $CH_3C(Br){=}CCH_3$ (Br)

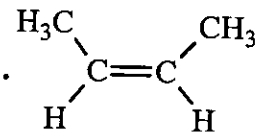
d. $CH_3C(Br)(Br)-C(Br)CH_3$ (Br)

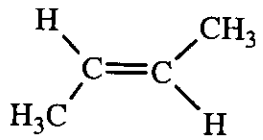
e. $CH_3C(=O)CH_2CH_3$

f. $CH_3C(=O)CH_2CH_3$

g. $CH_3C(Br){=}CHCH_3$

h. $CH_3CH_2CH_2CH_3$

i. 

j. 

k. no reaction

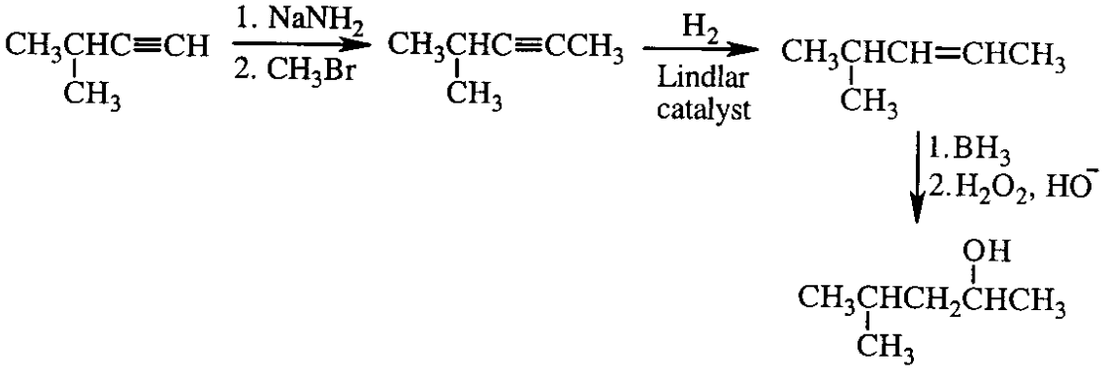
l. no reaction

34.

a. **1.** $CH_3CH(CH_3)C{\equiv}CH \xrightarrow[2.\ CH_3Br]{1.\ NaNH_2} CH_3CH(CH_3)C{\equiv}CCH_3 \xrightarrow[\text{Lindlar catalyst}]{H_2} CH_3CH(CH_3)CH{=}CHCH_3$

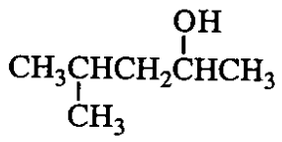
$CH_3CH(CH_3)CH{=}CHCH_3 \xrightarrow[H_2SO_4]{H_2O} CH_3C^{+}(CH_3)CHCH_2CH_3 \xrightarrow{H_2O} CH_3C(OH)(CH_3)CH_2CH_2CH_3$

2. 4-methyl-2-pentanol can be prepared by the same synthesis used to prepare 2-methyl-2-pentanol (see below), or it can be prepared using hydroboration-oxidation instead of hydration.

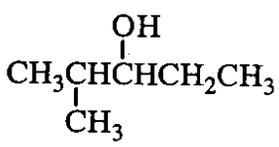


b. 4-Methyl-2-pentanol also will be obtained from "**1**" because in the third step of the synthesis, the proton can add to either of the sp^2 hybridized carbons.

(Some 2-methyl-3-pentanol may be obtained if the nucleophile reacts with the secondary carbocation before rearrangement to the more stable tertiary carbocation takes place.)

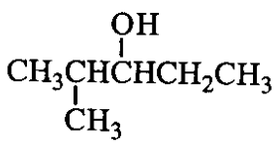


4-methyl-2-pentanol



2-methyl-3-pentanol

2-Methyl-3-pentanol also will be obtained from "**2**" because in the third step of the synthesis, boron can add to either of the sp^2 hybridized carbons. Because a carbocation is not formed as an intermediate, a carbocation rearrangement cannot occur.



2-methyl-3-pentanol

35. **a.** 3-heptyne

b. 5-methyl-3-heptyne

c. correct

d. 6,7-dimethyl-3-octyne

e. correct

f. correct

36. only **c** and **e** are keto-enol tautomers.

37.

a. $HC{\equiv}CH \xrightarrow[HgSO_4]{H_2O,\ H_2SO_4} CH_2{=}CHOH \rightleftharpoons CH_3CH$ (O double bonded)

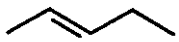
enol

b. $HC{\equiv}CH \xrightarrow[2.\ CH_3CH_2Br]{1.\ NaNH_2} CH_3CH_2C{\equiv}CH \xrightarrow[\text{Lindlar catalyst}]{H_2} CH_3CH_2CH{=}CH_2$

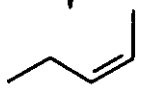
$CH_3CH_2CH{=}CH_2 \xrightarrow[CH_2Cl_2]{Br_2} CH_3CH_2\underset{Br}{CH}CH_2Br$

c. $HC{\equiv}CH \xrightarrow[2.\ CH_3Br]{1.\ NaNH_2} HC{\equiv}CCH_3 \xrightarrow[HgSO_4]{H_2O,\ H_2SO_4} CH_3\overset{O}{\overset{\|}{C}}CH_3$

d. $HC{\equiv}CH \xrightarrow[2.\ CH_3Br]{1.\ NaNH_2} HC{\equiv}CCH_3 \xrightarrow[2.\ CH_3CH_2Br]{1.\ NaNH_2} CH_3C{\equiv}CCH_2CH_3$

$CH_3C{\equiv}CCH_2CH_3 \xrightarrow[NH_3]{Na}$ 

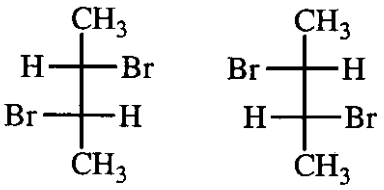
e. $HC{\equiv}CH \xrightarrow[2.\ CH_3Br]{1.\ NaNH_2} HC{\equiv}CCH_3 \xrightarrow[2.\ CH_3CH_2Br]{1.\ NaNH_2} CH_3C{\equiv}CCH_2CH_3$

$CH_3C{\equiv}CCH_2CH_3 \xrightarrow[\text{Lindlar catalyst}]{H_2}$ 

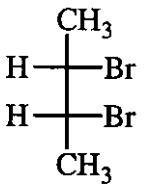
f. $HC{\equiv}CH \xrightarrow[2.\ CH_3Br]{1.\ NaNH_2} HC{\equiv}CCH_3 \xrightarrow[2.\ CH_3CH_2Br]{1.\ NaNH_2} CH_3C{\equiv}CCH_2CH_3$

$CH_3C{\equiv}CCH_2CH_3 \xrightarrow[Pd/C]{H_2}$ 

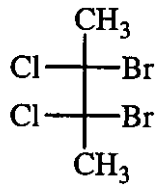
38. **a.** Syn addition of H_2 forms *cis*-2-butene. And when Br_2 adds to *cis*-2-butene, the threo pair of enantiomers is formed.



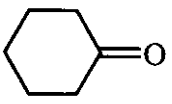
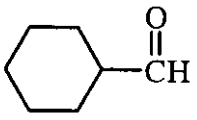
b. Reaction with sodium and liquid ammonia forms *trans*-2-butene. And when Br_2 adds to *trans*-2-butene, a meso compound is formed.



c. Anti addition of Cl_2 forms *trans*-2,3-dichloro-2-butene. And when Br_2 adds to *trans*-2,3-dichloro-2-butene, a meso compound is formed.



39.

a. $CH_3CH_2\overset{O}{\overset{\|}{C}}CH_3$ **b.** $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}CH_3$ **c.**  **d.** 

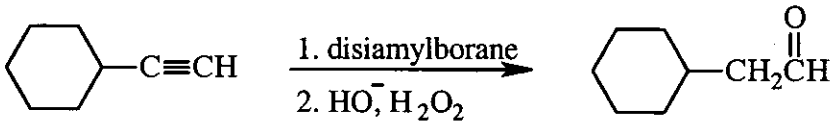
40.

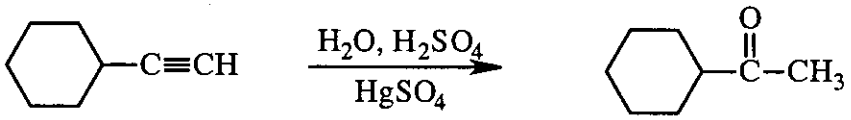
a. $HC{\equiv}CH \xrightarrow[2.\ CH_3CH_2CH_2CH_2Br]{1.\ NaNH_2} CH_3CH_2CH_2CH_2C{\equiv}CH$

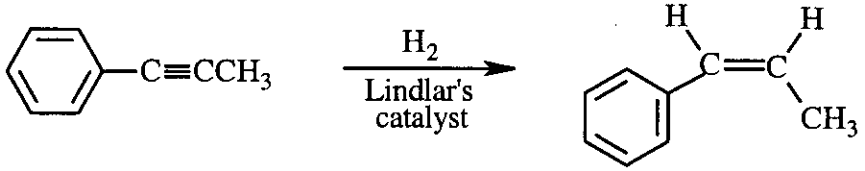
$$\xrightarrow[H_2SO_4]{H_2O,\ HgSO_4} CH_3CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}CH_3$$

b. $HC{\equiv}CH \xrightarrow[2.\ CH_3CH_2Br]{1.\ NaNH_2} CH_3CH_2C{\equiv}CH \xrightarrow[\text{or } Na/NH_3\ liq]{H_2,\ Lindlar\ catalyst} CH_3CH_2CH{=}CH_2 \xrightarrow{HBr} CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$

c. $HC{\equiv}CH \xrightarrow[2.\ CH_3CH_2CH_2Br]{1.\ NaNH_2} CH_3CH_2CH_2C{\equiv}CH \xrightarrow[\text{or } Na/NH_3\ liq]{H_2,\ Lindlar\ catalyst} CH_3CH_2CH_2CH{=}CH_2 \xrightarrow[H_2SO_4]{H_2O} CH_3CH_2CH_2\underset{\displaystyle OH}{\underset{|}{C}}HCH_3$

d. 

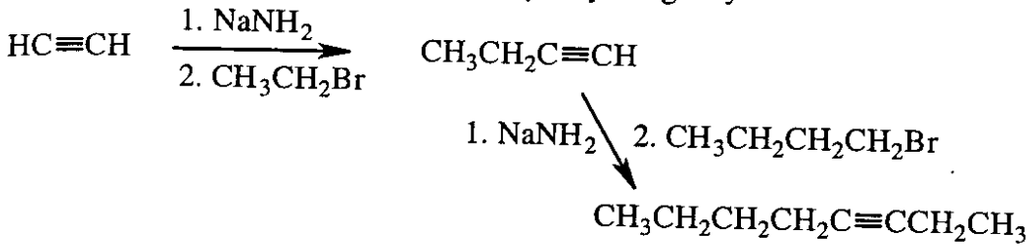
e. 

f. 

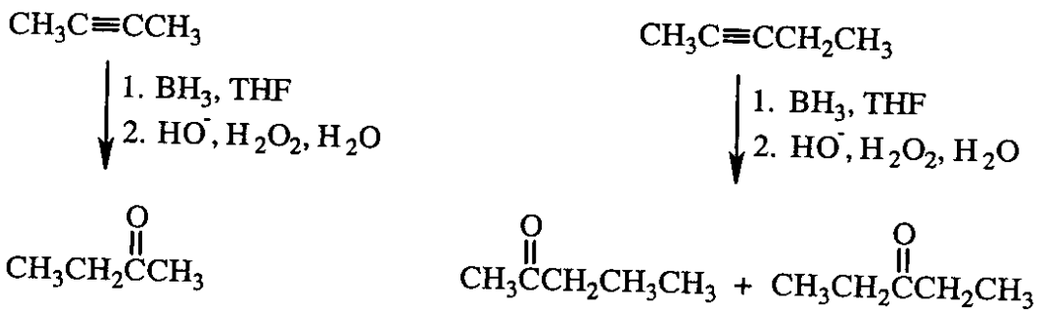
41. She can make 3-octyne by using 1-hexyne instead of 1-butyne. She would then need to use ethy bromide (instead of butyl bromide) for the alkylation step:

$$CH_3CH_2CH_2CH_2C{\equiv}CH \xrightarrow[2.\ CH_3CH_2Br]{1.\ NaNH_2} CH_3CH_2CH_2CH_2C{\equiv}CCH_2CH_3$$

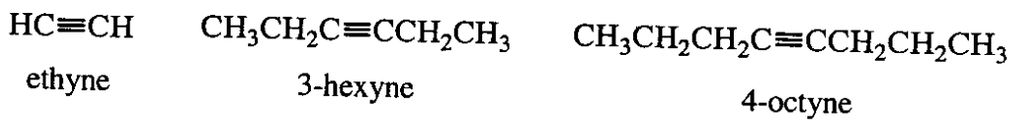
Or she could make the 1-butyne she needed by alkylating ethyne:



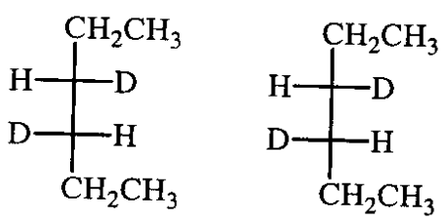
42. **a.** Only one product is obtained from the hydroboration-oxidation of 2-butyne because the alkyne is symmetrical. Two different products can be obtained from hydroboration-oxidation of asymmetrical 2-pentyne.



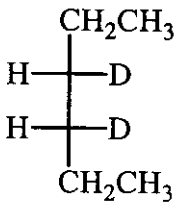
b. Only one product will be obtained from hydroboration-oxidation of any symmetrical alkyne, such as ethyne, 3-hexyne, and 4-octyne.



43. **a.** The first step forms a trans alkene. Syn addition to a trans alkene forms the threo pair of enantiomers.



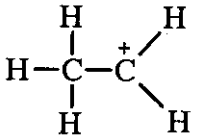
b. The first step forms a cis alkene. Syn addition to a cis alkene forms the erythro pair of enantiomers, but since each asymmetric carbon is bonded to the same four groups, the product is a meso compound.



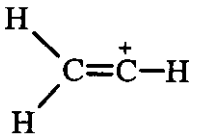
44. There are two reasons why hyperconjugation is less effective in stabilizing a positive charge on vinylic cation than a positive charge on an alkyl cation.

First, an sp^2-s bond is stronger than an sp^3-s bond, so the sp^2 orbitals are less able to donate electron density to the adjacent positively charge carbon.

Second, an sp^2 carbon has 120° bond angles compared to the 109.5° bond angles of an sp^3 carbon, so the orbitals of an sp^2 carbon are farther away, which makes them less able to interac with the positively charged carbon.



an alkyl cation

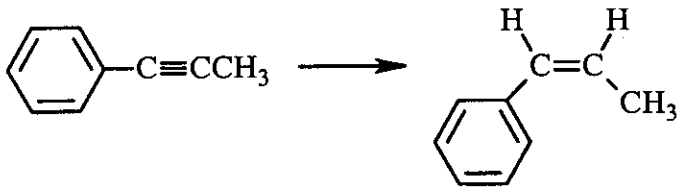


a vinylic cation

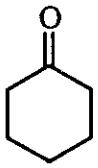
Chapter 6 Practice Test

1. What reagents could be used to convert the given starting material into the desired product?

a. 

b. 

2. Draw the enol tautomer of the following compound:

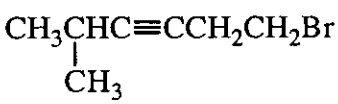


3. Give the structure of *sec*-butyl isobutyl acetylene.

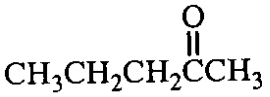
4. Indicate whether each of the following statements is true or false:

a. A terminal alkyne is more stable than an internal alkyne.	T	F
b. Propyne is more reactive than propene toward reaction with HBr.	T	F
c. 1-Butyne is more acidic than 1-butene.	T	F
d. An sp^2 hybridized carbon is more electronegative than an sp^3 hybridized carbon.	T	F

5. Give the systematic name for the following compound:



6. What alkyne would be the best reagent to use for the synthesis of the following ketone?



7. Rank the following compounds in order of decreasing acidity:
(Label the most acidic compound #1.)

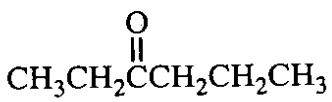
NH_3 $CH_3C{\equiv}CH$ CH_3CH_3 H_2O $CH_3CH{=}CH_2$

8. Give an example of a ketone that has two enol tautomers.

9. Show how the target molecules could be prepared from the given starting materials.

a. $CH_3CH_2C{\equiv}CH \longrightarrow CH_3CH_2CH_2CH_2CH_2CH_3$

b. $CH_3CH_2C{\equiv}CH \longrightarrow CH_3CH_2CH_2CH_2Br$

c. $CH_3CH_2C{\equiv}CH \longrightarrow$ 

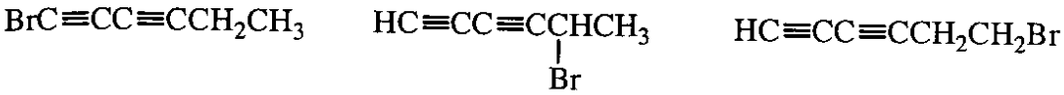
Important Terms

allylic carbon	a carbon adjacent to an sp^2 carbon of a carbon-carbon double bond.
allylic cation	a compound with a positive charge on an allylic carbon.
antibonding π* molecular orbital	the molecular orbital formed by side-to-side overlapping of out-of-phase *p* orbitals.
antibonding σ* molecular orbital	the molecular orbital formed by the overlap of out-of-phase orbitals with some *s* character.
aromatic compound	compounds that are unusually stable because of large delocalization energies (see Section 15.1).
asymmetric molecular orbital	a fully asymmetric molecular orbital is one that does not have a plane of symmetry but would have if one half of the MO were turned upside down.
benzylic carbon	a carbon, joined to other atoms by single bonds, that is bonded to a benzene ring.
benzylic cation	a compound with a positive charge on a benzylic carbon.
bonding π molecular orbital	the molecular orbital formed by side-to-side overlapping of in-phase *p* orbitals.
bonding σ molecular orbital	the molecular orbital formed by the overlap of in-phase orbitals with some *s* character.
contributing resonance structure	a structure with localized electrons that approximates the true structure of a compound with delocalized electrons.
delocalization energy (resonance energy)	the extra stability associated with a compound as a result of having delocalized electrons.
delocalized electrons	electrons that are not localized on a single atom or between two atoms.
electron delocalization	the sharing of electrons by more than two atoms.
highest occupied molecular orbital (HOMO)	the highest energy molecular orbital that contains electrons.
linear combination of molecular orbitals (LCAO)	the combination of atomic orbitals to produce molecular orbitals.
localized electrons	electrons that are restricted to a particular locality.
lowest unoccupied molecular orbital (LUMO)	the lowest energy molecular orbital that does not contain an electron.

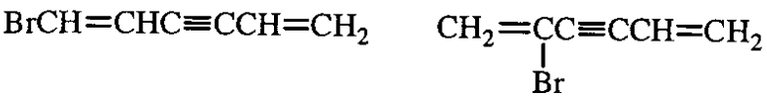
nonbonding molecular orbital	because the *p* orbitals are too far apart to overlap significantly, the molecular orbital that results neither favors nor disfavors bonding.
resonance	electron delocalization.
resonance contributor (resonance structure)	a structure with localized electrons that approximates the true structure c a compound with delocalized electrons.
resonance electron donation	donation of electrons by electron delocalization.
resonance energy (delocalization energy)	the extra stability associated with a compound as a result of having delocalized electrons.
resonance hybrid	the actual structure of a compound with delocalized electrons; it is represented by two or more structures with localized electrons.
separated charges	a positive and a negative charge that can be neutralized by the movemer of electrons.
resonance structure (resonance contributor)	a structure with localized electrons that approximates the true structure a compound with delocalized electrons.
symmetric molecular orbital	an orbital with a plane of symmetry so that one half is the mirror image the other half.

Solutions to Problems

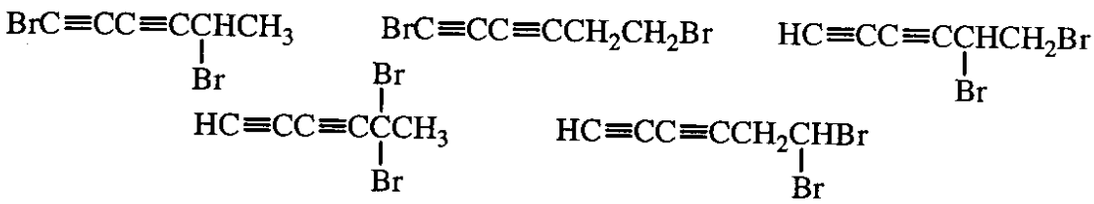
1. a. 1. If stereoisomers are not included, 3 different monosubstituted compounds can be formed. If stereoisomers are included, four different monosubstituted compounds can be formed because the second listed compound has an asymmetric carbon.



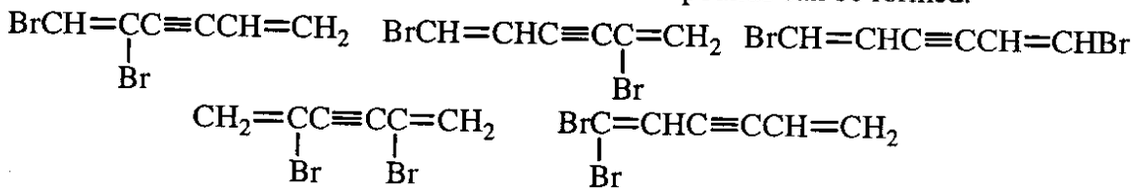
2. If stereoisomers are not included, 2 different monosubstituted compounds can be formed. If stereoisomers are included, three different monosubstituted compounds can be formed because the first compound has a double bond that can have cis-trans isomers.



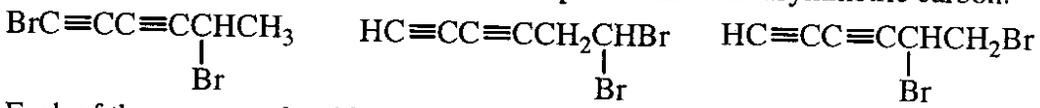
b. 1. Ignoring stereoisomers, **5** different disubstituted compounds can be formed.



2. Ignoring stereoisomers, **5** different disubstituted compounds can be formed.

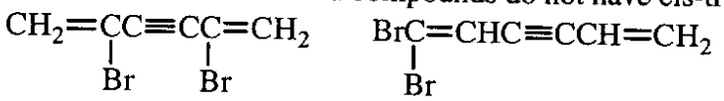


c. 1. Three of the five different disubstituted compounds have an asymmetric carbon.

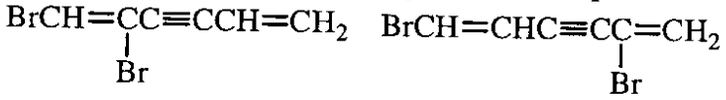


Each of the compounds with an asymmetric carbon can have the *R* or the S configuration. Therefore, **8** disubstituted products are possible: (2 x 3) + 2 compounds without an asymmetric carbon.

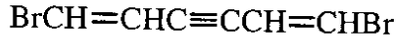
2. Two of the five disubstituted compounds do not have cis-trans isomers.



Two of the five disubstituted compounds have a pair of cis-trans isomers.

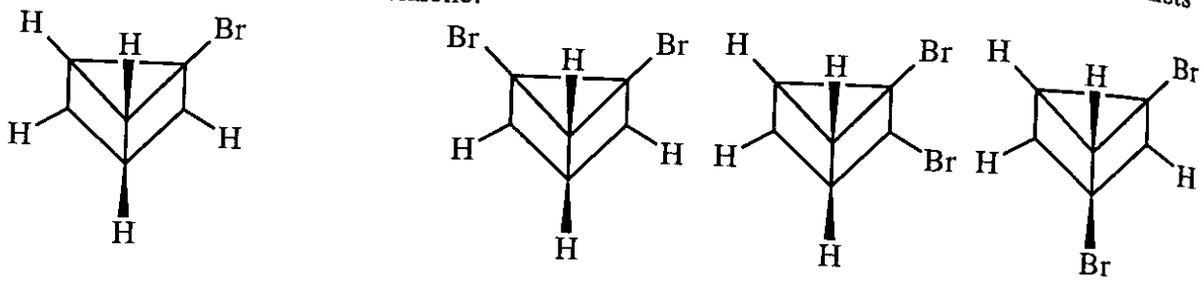


One of the five disubstituted compounds has two pairs of cis-trans isomers.

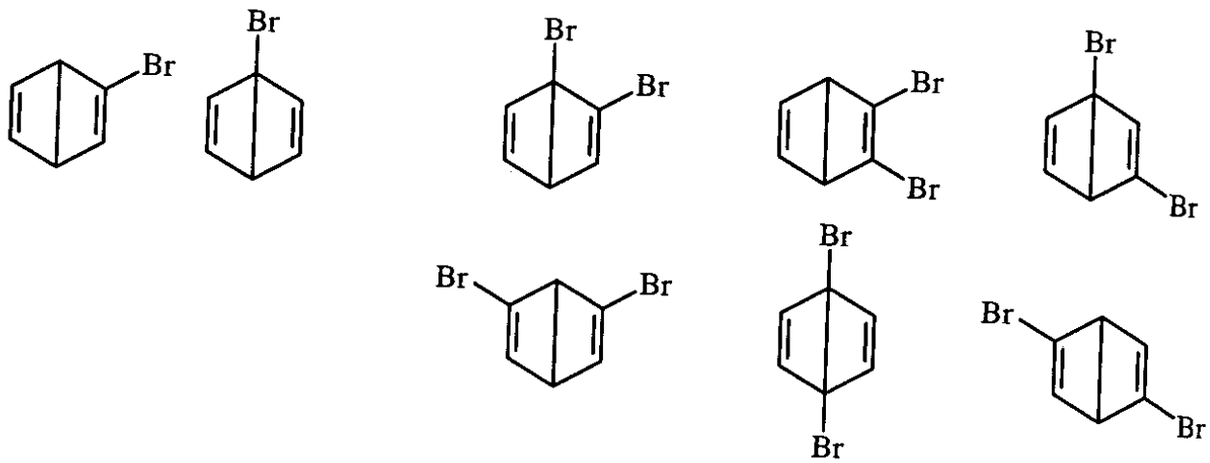


Therefore, **10** disubstituted compounds are possible.

2. Ladenburg benzene is a better proposal. It would form 1 monosubstituted compound, three disubstituted compounds, and would not add Br_2, all in accordance with what early chemists knew about the structure of benzene.



Dewar benzene is not in accordance with what early chemists knew about the structure of benzene, because it would form two monosubstituted compounds, 6 disubstituted compounds, and it would add Br_2.

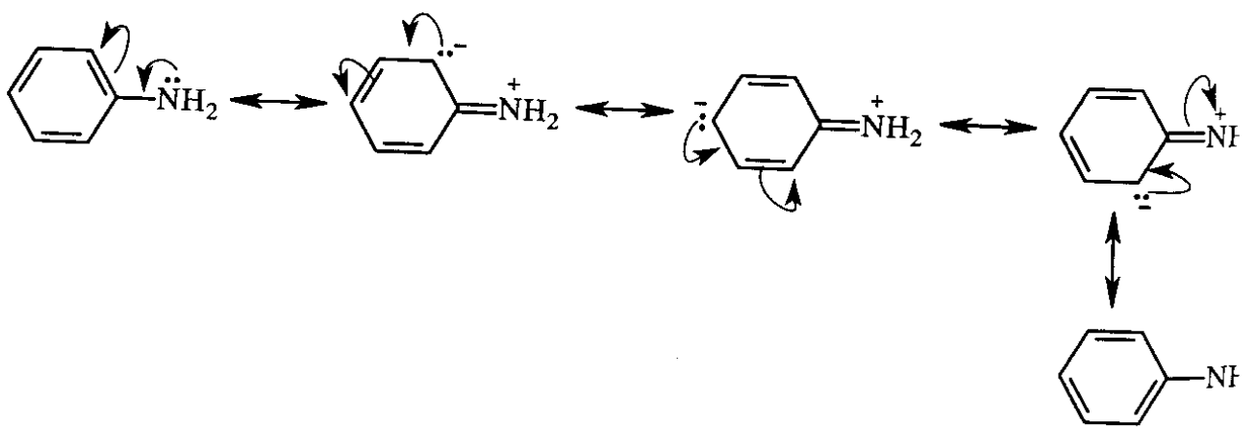


3. **a.** From examination of the contributing resonance structures in Figure 7.4 on page 271 of the text, one can conclude that all the carbon-oxygen bonds in the carbonate ion should be the same length.

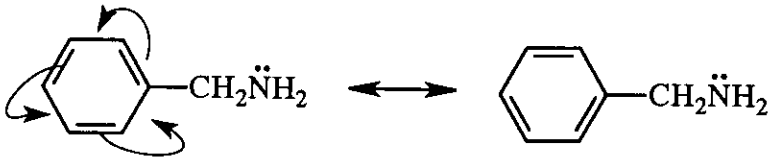
b. Because the two negative charges are shared equally by three oxygens, each oxygen should have two thirds of a negative charge.

4. **a.** **1**, **2**, **3**, **5**, and **6**

1.



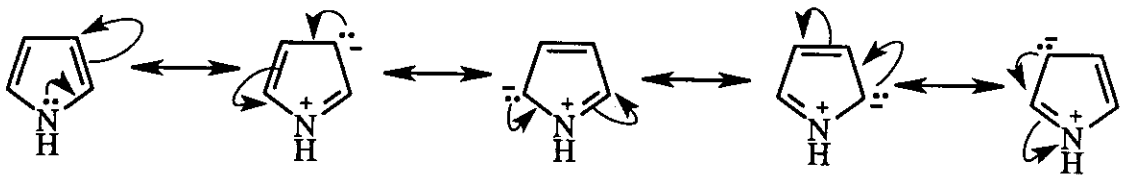
2. Because the substituent is not able to participate in resonance, the only resonance structures are the two resonance structures of the benzene ring.



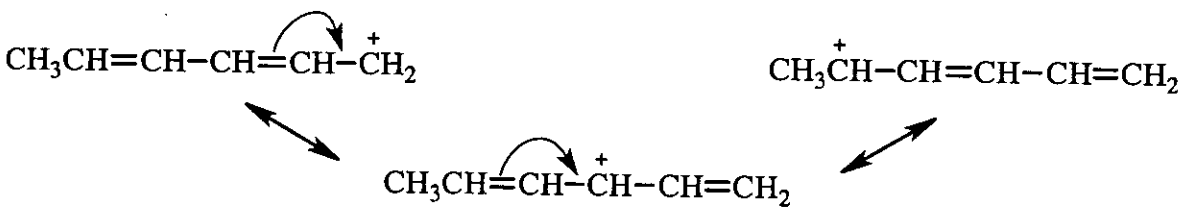
3.



5.



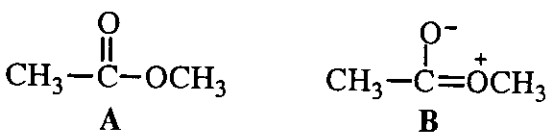
6.



5. The resonance contributor that makes the greatest contribution to the hybrid is labeled "**A**". "**B**" contributes less to the hybrid than "**A**", and "**C**" contributes less to the hybrid than "**B**".

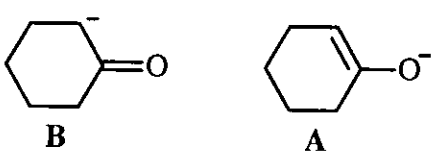
a. Solved in the text.

b.



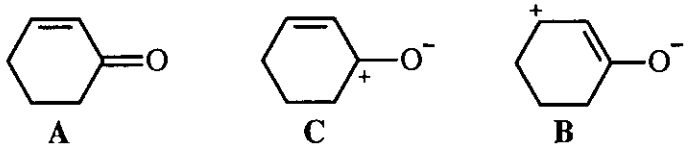
A **B**

c.



B **A**

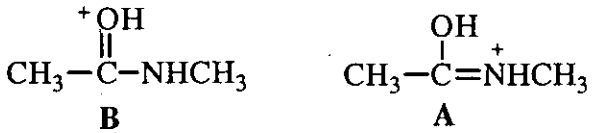
d.



A **C** **B**

B is more stable than C because the electronegative oxygen atom is closer to the positive charge in C

e.



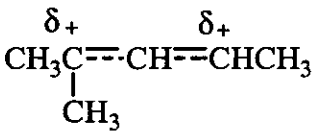
B **A**

f. $CH_3-\overset{+}{C}H-CH=CH-CH_3$ $CH_3CH=CH-\overset{+}{C}H-CH_3$

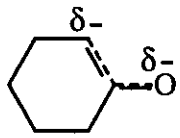
equally stable

6.

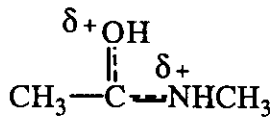
a.



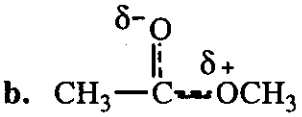
c.



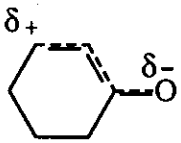
e.



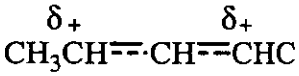
b.



d.



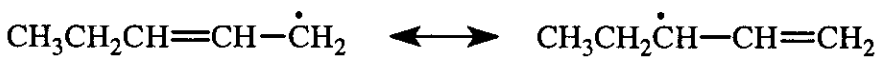
f.



7.

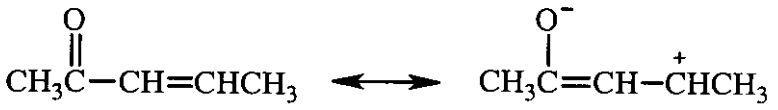
a.



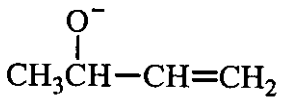


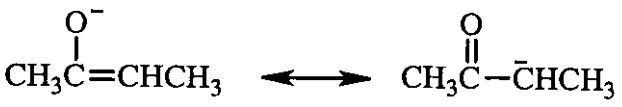
more stable because the unpaired electron is shared by a primary and a secondary carbon

b. 



more stable because the positive change in on a secondary carbon

c. 



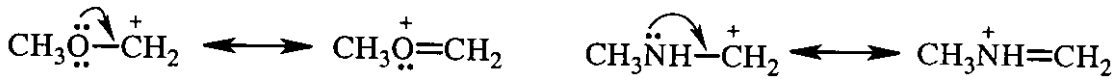
more stable because only in this compound is the negative charge delocalized

d. 

more stable because the positive charge is on a N rather than on an O

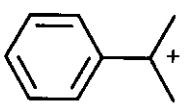


8. **a.** Because nitrogen is less electronegative than oxygen, it is better able to stabilize the positive charge by resonance.

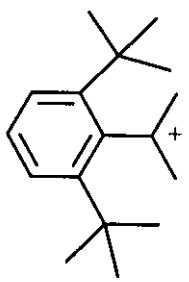


more stable

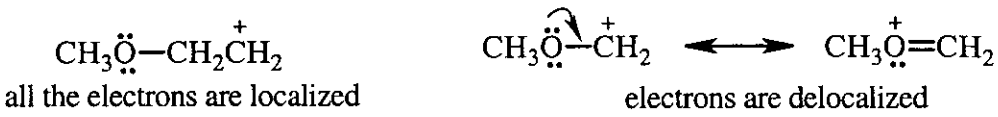
b. In order for electron delocalization to occur, the atoms that share the electrons must be in the same plane. The two *tert*-butyl groups prevent the positively charged carbon and the benzene ring from being in the same plane. Therefore, the carbocation cannot be stabilized by electron delocalization.



more stable

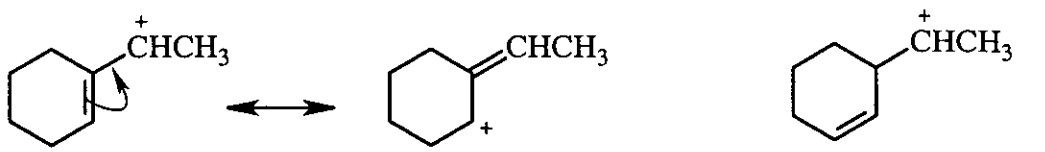


c. The compound with delocalized electrons is more stable than the compound in which all the electrons are localized.



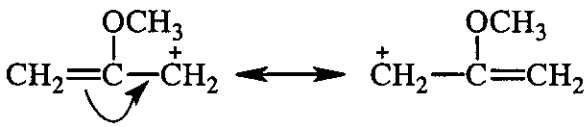
all the electrons are localized — electrons are delocalized

d. The compound with delocalized electrons is more stable than the compound in which all the electrons are localized.

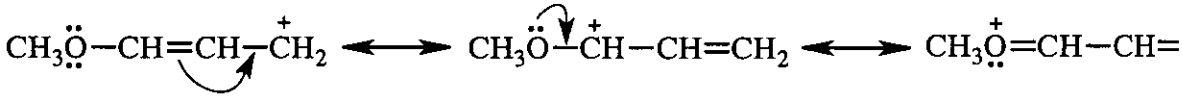


electrons are delocalized — all the electrons are localized

e. The OCH_3 group destabilizes the carbocation in the first species and destabilizes it in the second species.



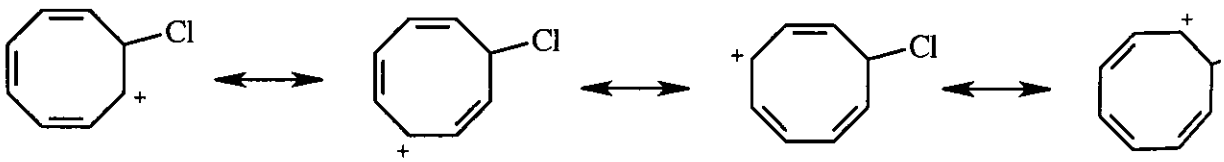
The OCH_3 group destabilizes the carbocation by inductive electron withdrawal.



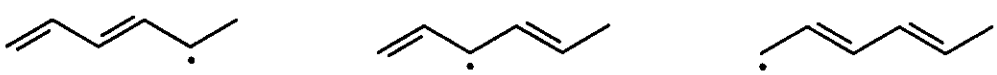
The OCH_3 group stabilizes the carbocation by resonance electron donation.

9. **a.** Solved in the text.

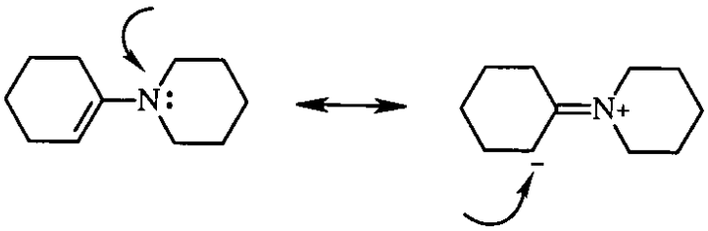
b. The contributing resonance structures show that there are four sites that could react with HO^-



c. The contributing resonance structures show that there are three sites that could react with a bromine radical.



d. The contributing resonance structures show that there are two sites that could be protonated.



10. Solved in the text.

11. In each case, the compound shown is the stronger acid because the negative charge that results when it loses a proton can be delocalized. Electron delocalization is not possible for the other compound in each pair.

a. $CH_3CH{=}CHOH \longrightarrow H^+ + CH_3CH{=}CHO^- \longleftrightarrow CH_3\bar{C}HCH{=}O$

b. $CH_3\overset{O}{\overset{\|}{C}}{-}OH \longrightarrow H^+ + CH_3\overset{O}{\overset{\|}{C}}{-}O^- \longleftrightarrow CH_3C{=}O^-$

c. $CH_3CH{=}CHOH \longrightarrow H^+ + CH_3CH{=}CHO^- \longleftrightarrow CH_3\bar{C}HCH{=}O$

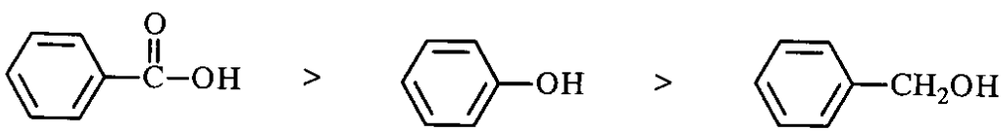
d. $CH_3CH{=}\overset{+}{C}HNH_3 \longrightarrow H^+ + CH_3CH{=}CHNH_2 \longleftrightarrow CH_3\bar{C}HCH{=}\overset{+}{N}H_2$

12. **a.** Ethylamine is a stronger base because when the lone pair on the nitrogen in aniline is protonated, it can no longer be delocalized into the benzene ring.

b. Ethoxide ion is a stronger base because a negatively charged oxygen is a stronger base than a neutral nitrogen.

c. Ethoxide ion is a stronger base because when the phenolate ion is protonated, the pair of electrons that is protonated can no longer be delocalized into the benzene ring.

13. The carboxylic acid is the most acidic because its conjugate base has greater resonance stabilization than does the conjugate base of phenol. The alcohol is the least stable because, unlike the negative change on the conjugate base of phenol, the negative change on its oxygen atom cannot be delocalized.



14. The ψ_3 molecular orbital of 1,3-butadiene has 3 nodes (two vertical and one horizontal).
The ψ_4 molecular orbital of 1,3-butadiene has 4 nodes (three vertical and one horizontal).

15. **a.** ψ_1 and ψ_2 are bonding molecular orbitals, and ψ_3 and ψ_4 are antibonding molecular orbitals.
b. ψ_1 and ψ_3 are symmetric molecular orbitals, and ψ_2 and ψ_4 are asymmetric molecular orbital
c. ψ_2 is the HOMO and ψ_3 is the LUMO in the ground state.
d. ψ_3 is the HOMO and ψ_4 is the LUMO in the excited state.
e. If the HOMO is symmetric, the LUMO is asymmetric and vice versa.

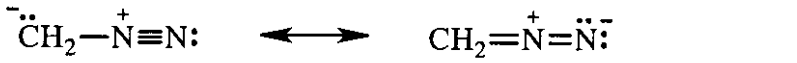
16. **a.** ψ_1, ψ_2, and ψ_3 are bonding molecular orbitals, and ψ_4, ψ_5, and ψ_6 are antibonding molecular orbitals.
b. ψ_1, ψ_3, and ψ_5 are symmetric molecular orbitals, and ψ_2, ψ_4, and ψ_6 are asymmetric molecular orbitals.
c. ψ_3 is the HOMO and ψ_4 is the LUMO in the ground state.
d. ψ_4 is the HOMO and ψ_5 is the LUMO in the ground state.
e. If the HOMO is symmetric, the LUMO is asymmetric and vice versa.

17. **a.** The ψ_1 molecular orbital of 1,3-butadiene has 3 bonding interactions and the ψ_2 molecular orbital has 2 bonding interactions.
b. The ψ_1 molecular orbital of 1,3,5,7-octatetraene has 7 bonding interactions and the ψ_2 molecular orbital has 6 bonding interactions.

Notice that the ψ_1 molecular orbital has one bonding orbital between each of the overlapping p orbitals. Notice also that as the energy of the molecular orbital increases, the number of bondin interactions decreases.

18. **a, d, f, g, i, j, l, m**

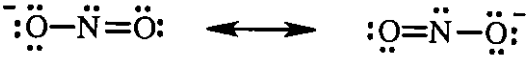
19. **a.** and **b.**

1. 

More stable, because the negative charge is on nitrogen rather than on carbon.

2. 

More stable, because the negative charge is on oxygen rather than on nitrogen.

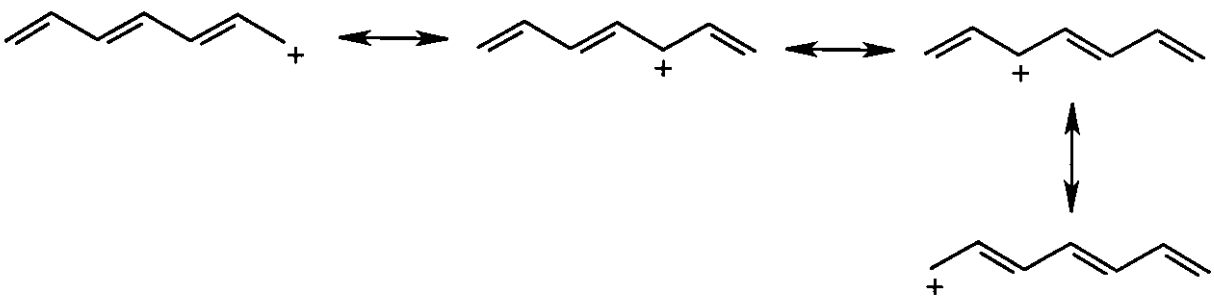
3. 

Both are equally stable.

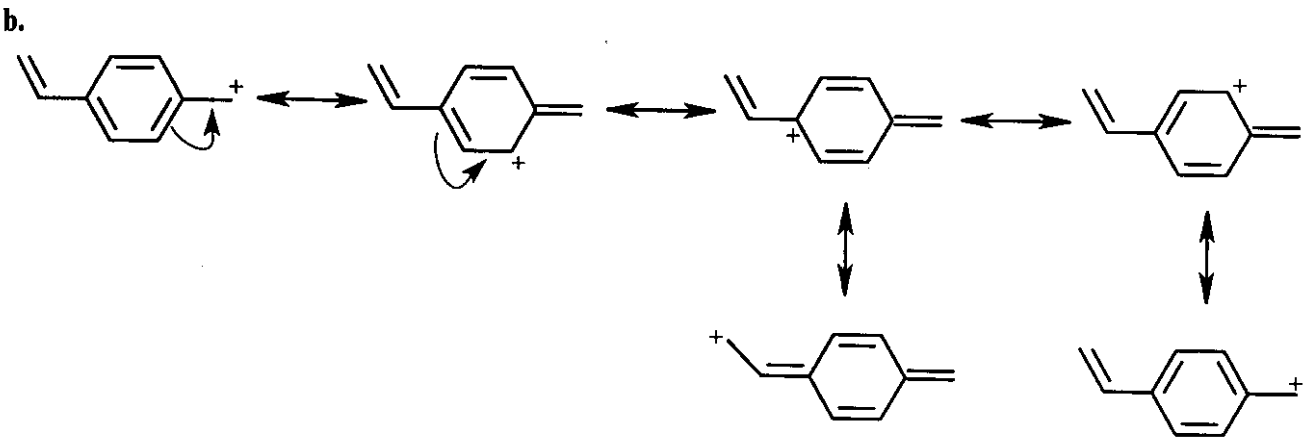
Additional resonance structures could be drawn for each of these three species, but they are relatively unstable because they have an incomplete octet.

20.

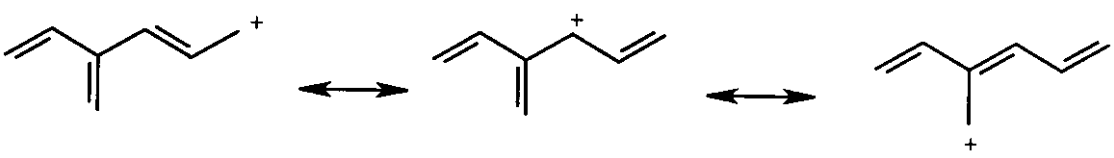
a.



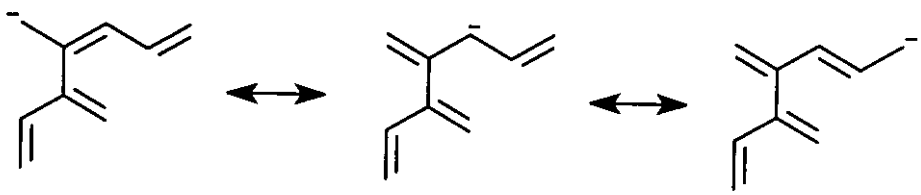
b.



c.



d.



21. **a.** different compounds
b. resonance contributors
c. different compounds
d. resonance contributors
e. different compounds

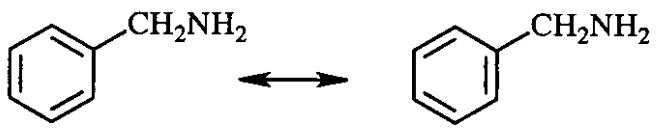
Notice that in the structures that are different compounds, both atoms and electrons have changed their locations.
In contrast, in structures that are resonance contributors, only the electrons have moved.

22. **a.**

1. $CH_3CH{=}CHOCH_3 \longleftrightarrow CH_3\bar{C}HCH{=}\overset{+}{O}CH_3$

major minor

2.



the two resonance contributors have the same stability

3. $CH_3\bar{C}HC{\equiv}N \longleftrightarrow CH_3CH{=}C{=}\bar{N}$

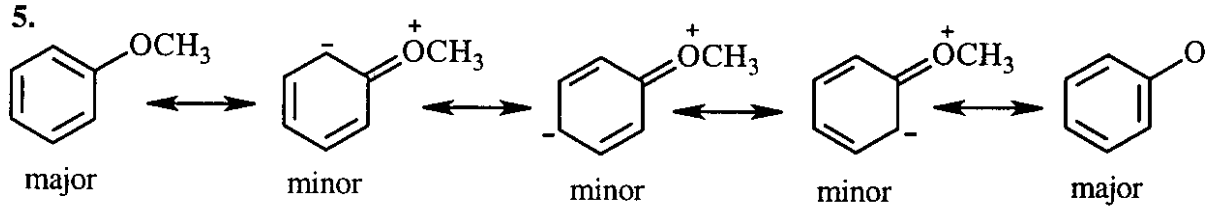
minor major

4.



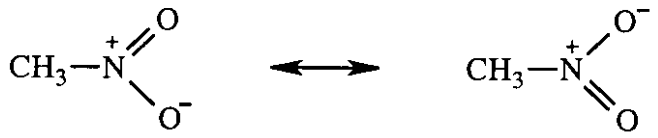
the two resonance contributors have the same stability

5.



major minor minor minor major

6.



the two resonance contributors have the same stability

7. $CH_3CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3 \longleftrightarrow CH_3CH_2\overset{O^-}{\overset{|}{C}}=\overset{+}{O}CH_2CH_3$

major minor

8. $CH_3CH=CHCH=C\dot{H}CH_2 \longleftrightarrow CH_3\dot{C}HCH=CHCH=CH_2$

minor major

$CH_3CH=CH\dot{C}HCH=CH_2$

major

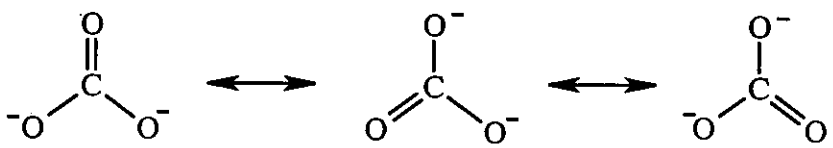
9. $H\overset{O}{\overset{\|}{C}}NHCH_3 \longleftrightarrow H\overset{O^-}{\overset{|}{C}}=\overset{+}{N}HCH_3$

major minor

10. $CH_3CH=CH\overset{+}{C}H_2 \longleftrightarrow CH_3\overset{+}{C}HCH=CH_2$

minor major

11.

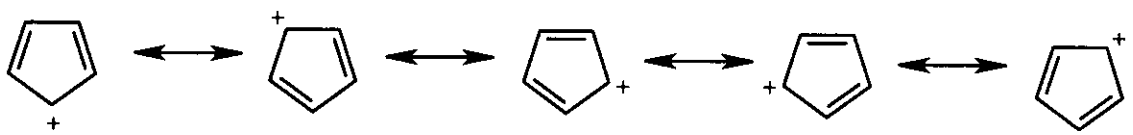


each of the three resonance contributors has the same stability

12. $H\overset{O}{\overset{\|}{C}}CH=CH\bar{C}H_2 \longleftrightarrow H\bar{C}\overset{O}{\overset{\|}{C}}HCH=CH_2 \longleftrightarrow H\overset{O^-}{\overset{|}{C}}=CHCH=CH_2$

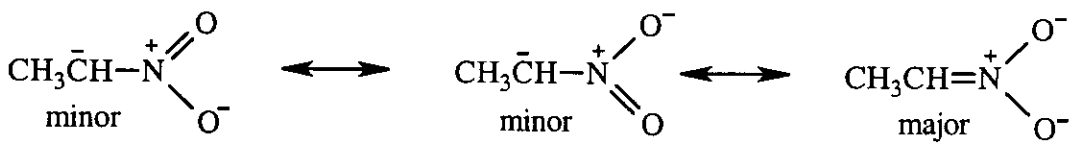
minor minor major

13.

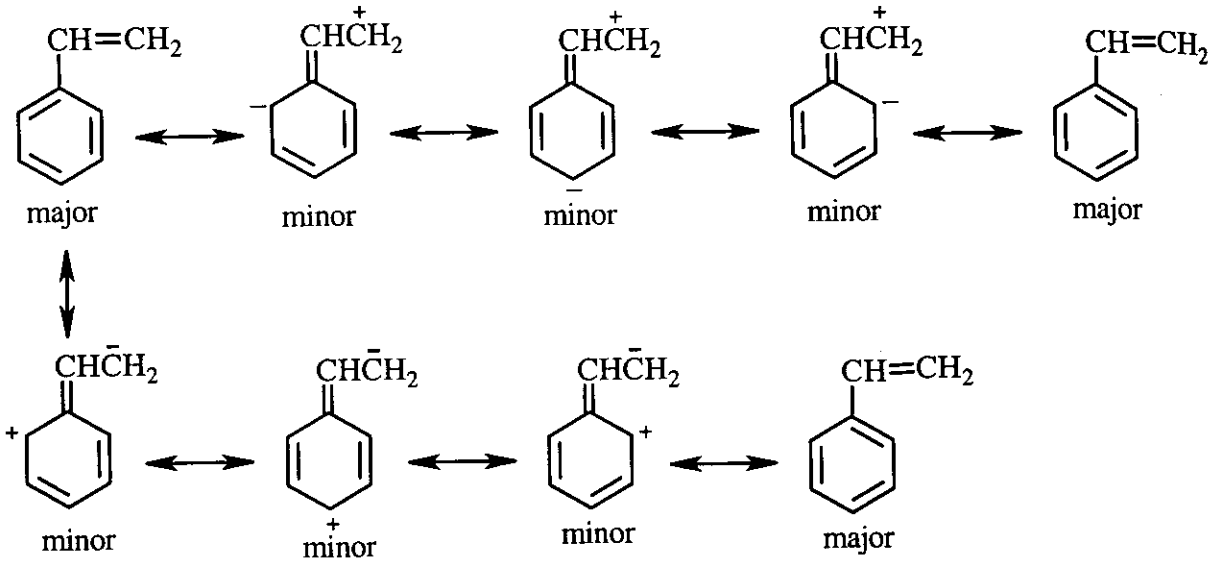


The five contributors are equally stable.

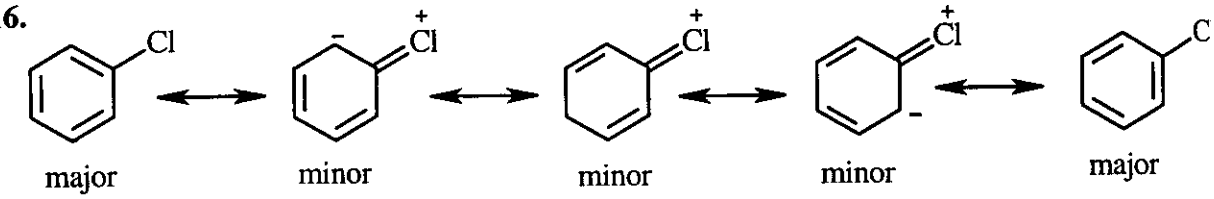
14.



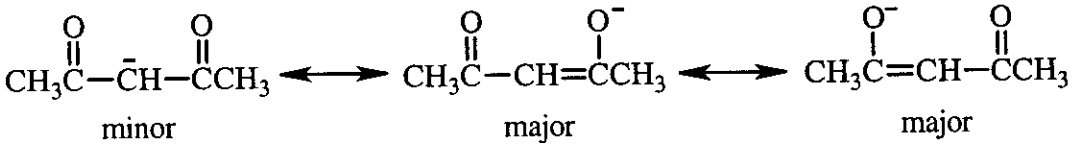
15. The electrons can move in two different direction. They can move out of the benzene ring toward the alkene group; they can move into the benzene ring away from the alkyl group.



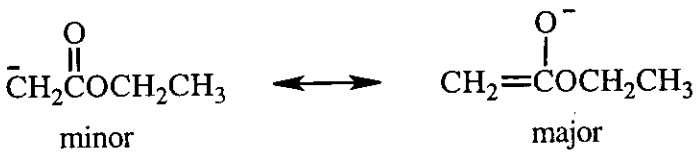
16.



17.



18.



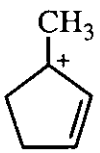
b. **2, 4, 6, 11,** and **13**

23.

a. $CH_3\overset{+}{C}HCH{=}CH_2$

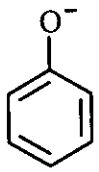
This makes the greater contribution because the positive charge is on a secondary carbon.

b.



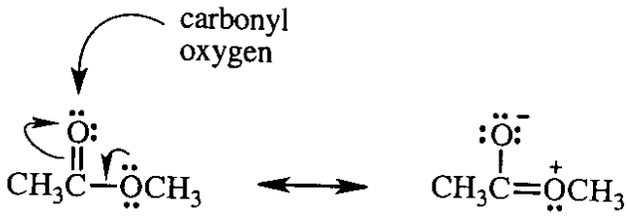
This makes the greater contribution because the positive charge is on a tertiary carbon.

c.

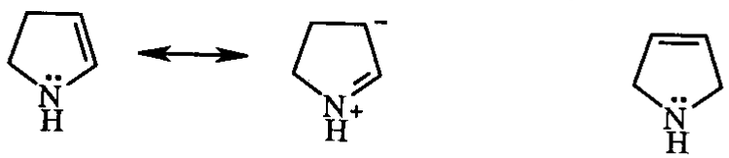


This makes the g
contribution bec
negative charge i
an oxygen atom.

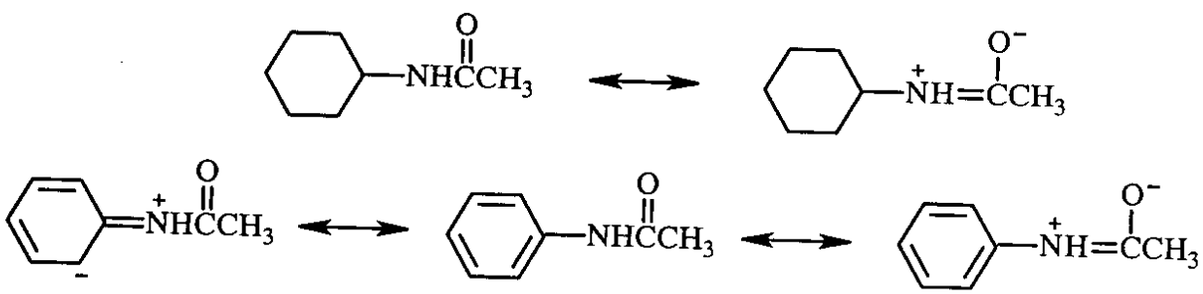
a. The resonance contributors show that the carbonyl oxygen has the greater electron density.



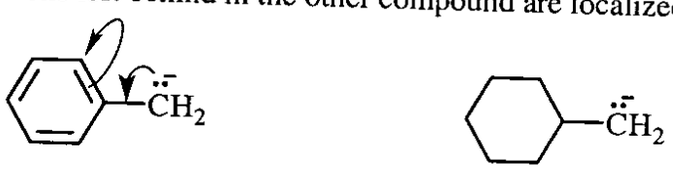
b. The compound on the right has the greater electron density on its nitrogen because the compound on the left has a resonance contributor with a positive charge on the nitrogen.



c. The compound with the cyclohexane ring has the greater electron density on its oxygen because the lone pair on the nitrogen can be delocalized onto the oxygen.
There is less delocalization onto oxygen by the lone pair in the compound with the benzene ring because the lone pair can also be delocalized away from the oxygen into the benzene ring.

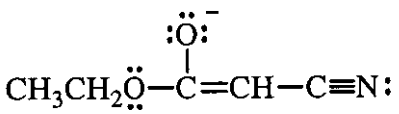


25. The methyl group on benzene can lose a proton easier than the methyl group on cyclohexane because the electrons left behind on the carbon in the former can be delocalized into the benzene ring.
In contrast, the electrons left behind in the other compound are localized on the carbon.

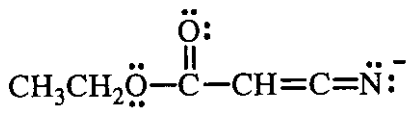


26. The carbocation is stable because the positive charge is shared by 10 carbon atoms (the central carbon and 3 carbons of each of the 3 benzene rings).

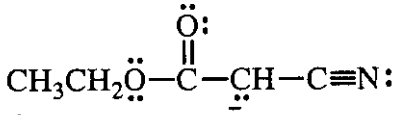
27.



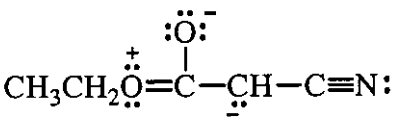
#1 most stable because the negative charge is on oxygen



#2 because the negative charge is on nitrogen



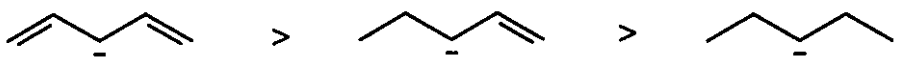
#3 because the negative charge is on carbon



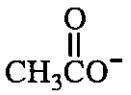
#4 the least stable because the negative charge is on carbon and it has separated charges

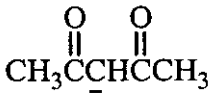
28. The more the electrons that are left behind when the proton is removed can be delocalized, the greater the stability of the base. The more stable the base, the more acidic its conjugate acid.

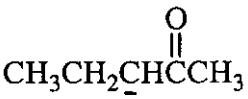
The negative charge on the base in the first compound can be delocalized onto two other carbons; the negative charge on the base in the second compound can be delocalized onto one other carbon; the negative charge on the base in the last compound cannot be delocalized.

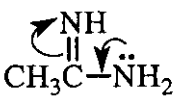


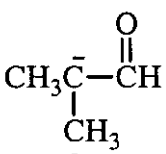
29.

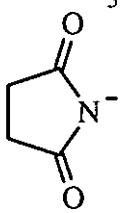
a.  the negative charge is shared by 2 oxygens

b.  the negative charge is shared by a carbon and 2 oxygens

c.  the negative charge is shared by a carbon and an oxygen

d.  this compound has delocalized electrons

e.  the negative charge is shared by a carbon and an oxygen

f.  the negative charge is shared by a nitrogen and 2 oxygens

30. The stronger base is the less stable base of each pair in Problem 29.

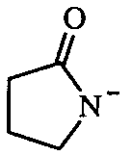
a. $CH_3CH_2O^-$ Less stable because the negative charge cannot be delocalized.

b. $CH_3\overset{\overset{O}{\|}}{C}\overset{-}{C}HCH_2\overset{\overset{O}{\|}}{C}CH_3$ Less stable because the negative charge can be delocalized onto only one carbonyl oxygen.

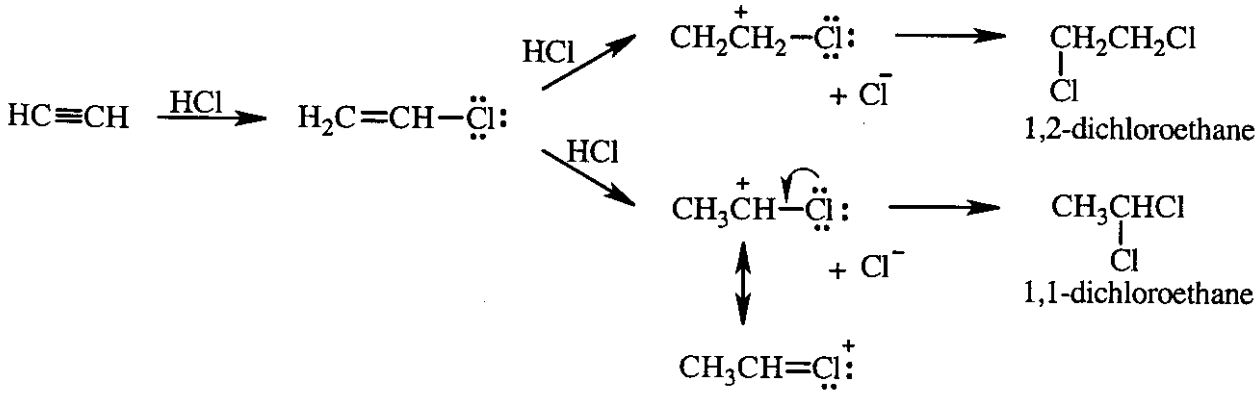
c. $CH_3\overset{-}{C}HCH_2\overset{\overset{O}{\|}}{C}CH_3$ Less stable because the negative charge cannot be delocalized.

d. $CH_3\overset{\overset{NH_2}{|}}{C}HNH_2$ Less stable because neither of the nitrogen lone pairs can be delocalized.

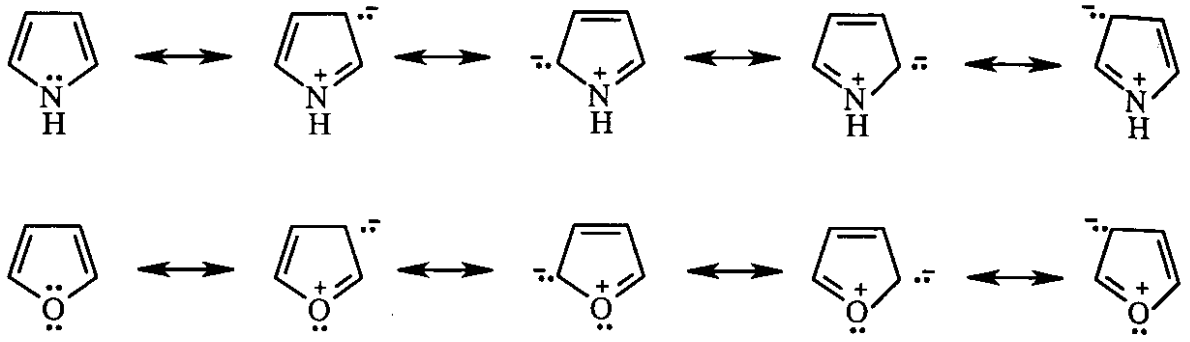
e. $CH_3\overset{-}{C}(\overset{\overset{CH_2}{\|}}{CH})\overset{|}{CH_3}$ Less stable because the negative charge is delocalized onto a carbon.

f.  Less stable because the negative charge can be delocalized onto only one carbonyl oxygen.

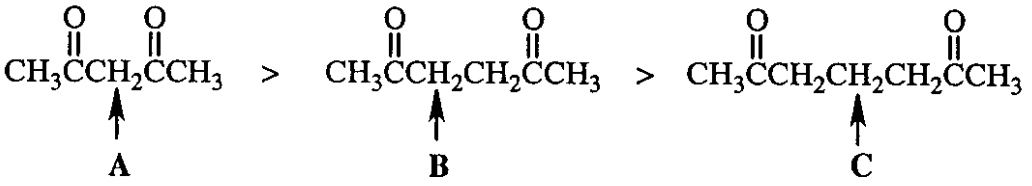
31. The carbocation leading to 1,1-dichloroethane is more stable than the carbocation leading to 1,2-dichloroethane because the positive charge on the intermediate leading to 1,1-dichloroethane is shared by carbon and chlorine. Since the more stable carbocation is the one that is easier to form, the final product of the reaction is 1,1-dichloroethane.



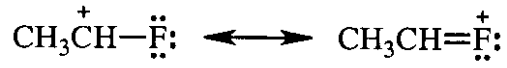
32. The resonance contributors of pyrrole are more stable because the positive charge is on nitrogen. In furan, the positive charge is on oxygen which, being more electronegative, is less stable with a positive charge.



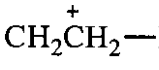
33. **A** is the most acidic because the electrons left behind when the proton is removed can be delocalized onto two oxygen atoms. **B** is the next most acidic because the electrons left behind when the proton is removed can be delocalized onto one oxygen atom. **C** is the least acidic because the electrons left behind when the proton is removed cannot be delocalized.



34. Of the two possible carbocations that can be formed in reaction **a**, the more stable carbocation is the one formed by adding the electrophile to the sp^2 carbon bonded to the greater number of hydrogens. It is more stable because the positive charge is shared by carbon and fluorine.



the carbocation formed by adding the electrophile to the sp^2 carbon bonded to the greater number of hydrogens



the carbocation formed by not adding the electrophile to the sp^2 carbon bonded to the greater number of hydrogens

Of the two possible carbocations that can be formed in reaction **b**, the more stable carbocation is the one formed by not adding the electrophile to the sp^2 carbon bonded to the greater number of hydrogens. The fluoro substituent is not in a position to help to stabilize the positive charge in either carbocation. In the carbocation formed by not adding the electrophile to the sp^2 carbon bonded to the greater number of hydrogens, the electron-withdrawing fluoro substituent is farther away from the positive charge.

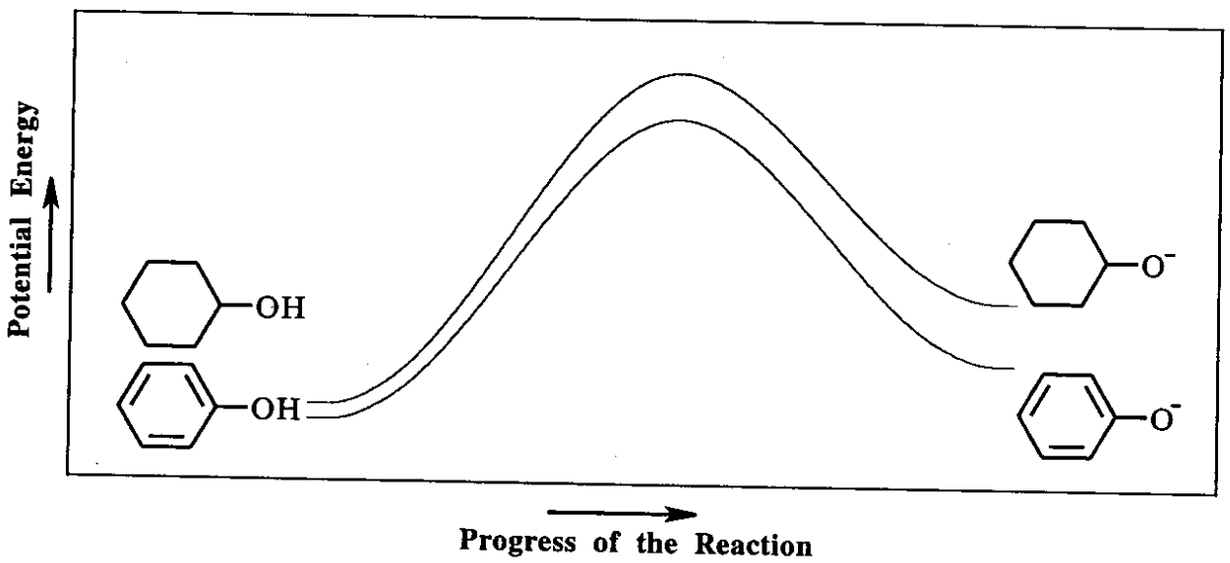
$CH_3\overset{+}{C}HCF_3$

the carbocation formed by adding the electrophile to the sp^2 carbon bonded to the greater number of hydrogens

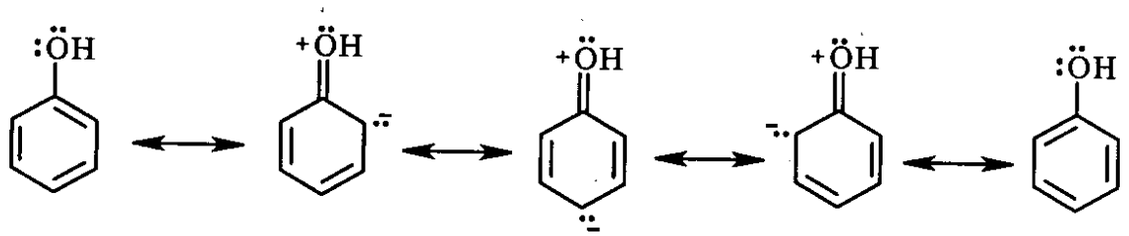
$\overset{+}{C}H_2CH_2CF_3$

the carbocation formed by not adding the electrophile to the sp^2 carbon bonded to the greater number of hydrogens

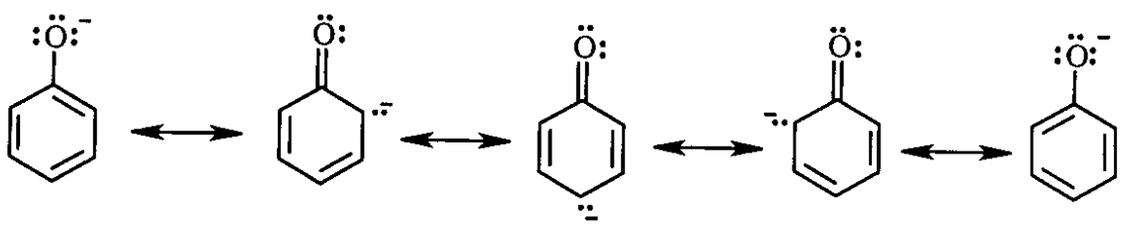
35. **a.** and **d.**



b.



c.

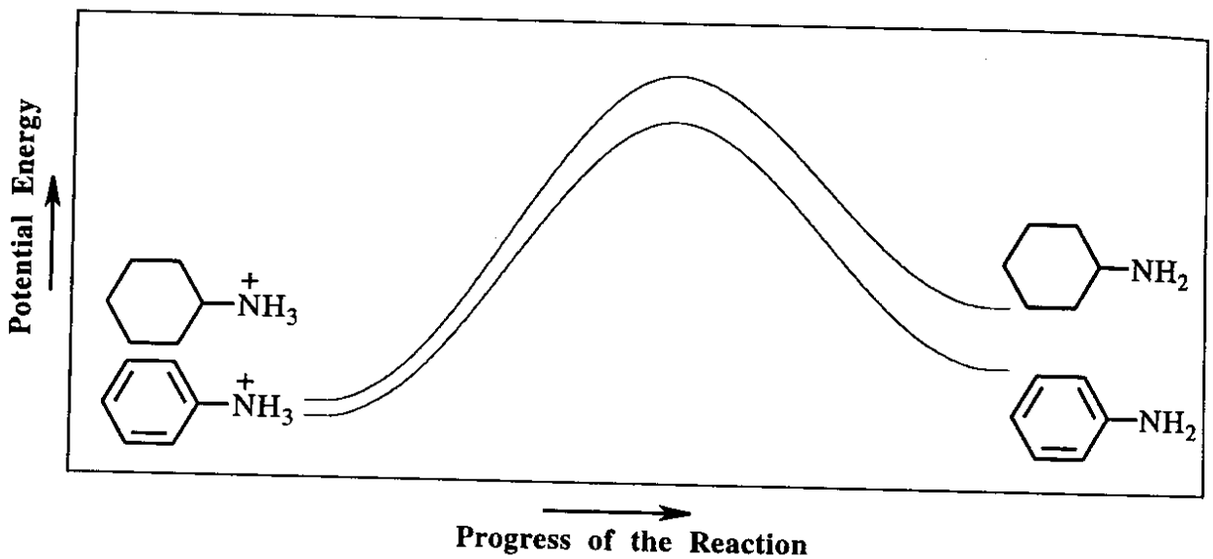


d. The resonance contributors in "**c**" are more stable than the resonance contributors in "**b**" because in "**b**" a positive charge is on the most electronegatice atom (the oxygen). Therefore, the phenolate ion has greater resonance stabilization than phenol. Thus, as shown in the energy diagram, the difference in energy between the phenolate ion and the cyclohexoxide ion is greater than the difference in energy between phenol and cyclohexanol.

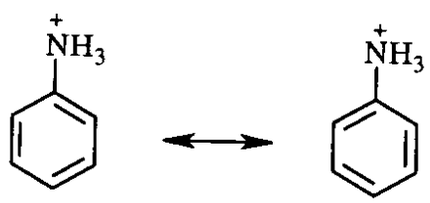
e. Because of the greater resonance stabilization of the phenolate ion compared to phenol, phenol has a larger K_a than cyclohexanol.

f. Because it has a larger K_a (a lower pK_a), phenol is a stronger acid.

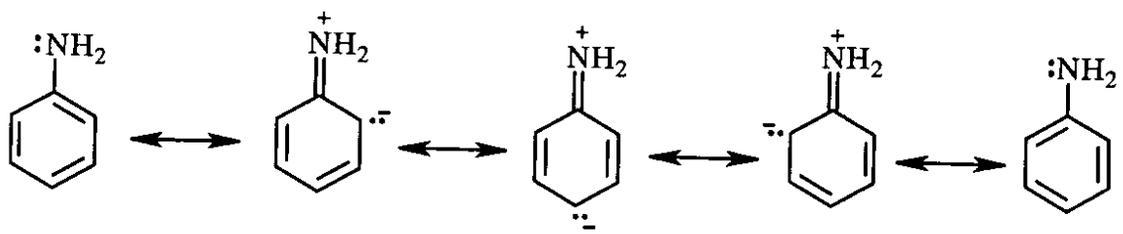
36.



b.



c.



d. Aniline has greater resonance stabilization than the anilinium ion. Thus in the energy diagram, the difference in energy between aniline and cyclohexylamine is greater than the difference in energy between the anilinium ion and the cyclohexylammonium ion.

e. Because of the greater resonance stabilization of aniline compared to the anilinium ion, the anilinium ion has a larger K_a than the cyclohexylammonium ion.

f. Because it has a larger K_a (a lower pK_a), the anilinium ion is a stronger acid than the cyclohexylammonium ion. Therefore, cyclohexylamine is a stronger base than aniline. (The stronger the acid, the weaker its conjugate base.)

37. **a.** It has 8 molecular orbitals.

b. ψ_1, ψ_2, ψ_3, and ψ_4 are bonding molecular orbitals; ψ_5, ψ_6, ψ_7, and ψ_8 are antibonding molecular orbitals.

c. ψ_1, ψ_3, ψ_5 and ψ_7 are symmetric molecular orbitals; ψ_2, ψ_4, ψ_6, and ψ_8 are asymmetric molecular orbitals.

d. ψ_4 is the HOMO and ψ_5 is the LUMO in the ground state.

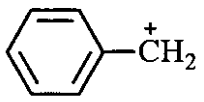
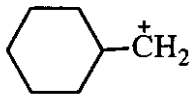
e. ψ_5 is the HOMO and ψ_6 is the LUMO in the ground state.

f. The HOMO is symmetric, the LUMO is asymmetric and vice versa.

g. It has 7 nodes between the nuclei.

Chapter 7 Practice Test

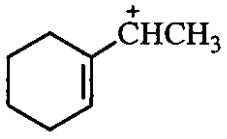
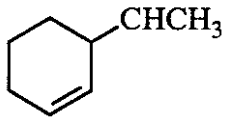
1. For each of the following pairs of compounds indicate the one that is the more stable:

a.  or 

b. $CH_3\bar{C}HCH_3$ or $CH_3\bar{C}HC{\equiv}CH$

c. $CH_3\bar{C}HCH_2\overset{O}{\overset{\|}{C}}CH_3$ or $CH_3\bar{C}H\overset{O}{\overset{\|}{C}}CH_3$

d. $CH_2{=}CH\overset{+}{C}H_2$ or $CH_2{=}CHCH_2\overset{+}{C}H_2$

e.  or 

2. Draw resonance contributors for the following:

a. $CH_3CH{=}CH{-}\ddot{\underset{\cdot\cdot}{O}}CH_3$

b. $CH_3CH{=}CH{-}CH{=}CH{-}\overset{+}{C}H_2$

c. $\bar{C}H_2{-}CH{=}CH{-}\overset{O}{\overset{\|}{C}}H$

3. Which compounds do not have delocalized electrons?

$CH_3CH_2NHCH{=}CHCH_3$ $\quad CH_3\overset{CH_3}{\overset{|}{\underset{+}{C}}}CH_2CH{=}CH_2$ $\quad CH_2{=}CHCH_2CH{=}CH_2$

$CH_2{=}CH\overset{O}{\overset{\|}{C}}CH_3$ $\quad CH_3CH_2NHCH_2CH{=}CHCH_3$ 

4. Which of the following pairs are resonance contributors?

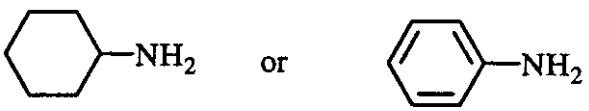
a. CH_3CH_2OH and CH_3OCH_3

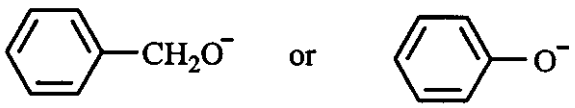
b. $CH_3\overset{\overset{O}{\|}}{C}OH$ and $CH_3\overset{\overset{O}{\|}}{C}O^-$

c. $CH_3\overset{\overset{O}{\|}}{C}OH$ and $CH_3\overset{\overset{O^-}{|}}{C}=\overset{+}{O}H$

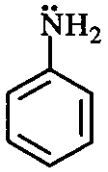
d. $CH_3CH_2\overset{\overset{O}{\|}}{C}H$ and $CH_3CH=\overset{\overset{OH}{|}}{C}H$

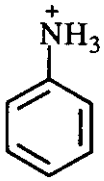
5. Which is a stronger base?

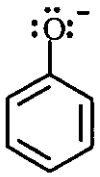




6. Draw resonance contributors for the following:

a. 

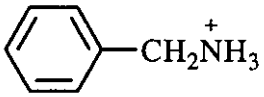
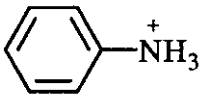
b. 

c. 

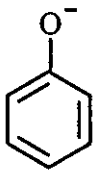
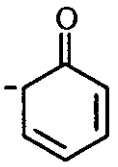
7. For each of the following pairs of compounds indicate the one that is the more acidic:

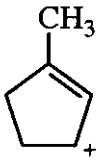
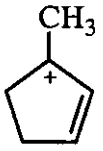
a.  or 

b. $CH_3CH_2CH_3$ or $CH_3CH{=}CH_2$

c.  or 

8. Which resonance contributor makes a greater contribution to the resonance hybrid?

a.  or 

b.  or 

9. Indicate whether the following statements is true or false:

a. A compound with four conjugated double bonds will have four molecular orbitals. T F

b. ψ_1 and ψ_2 are symmetric molecular orbitals. T F

c. If ψ_3 is the HOMO in the ground state, ψ_4 will be the HOMO in the excited state. T F

d. If ψ_3 is the LUMO, ψ_4 will be the HOMO. T F

e. If the ground-state HOMO is symmetric, the ground-state LUMO will be asymmetric. T F

10. Rank the following carbocations in order of decreasing stability:

$CH_3CH{=}CH\overset{+}{C}H_2$ $CH_3CH{=}CH\overset{+}{C}HCH_3$ $CH_3CH{=}CHCH\overset{+}{C}H_2$ $CH_3CH{=}CH\overset{+}{C}\underset{\displaystyle CH}{\overset{|}{C}}$

CHAPTER 8
Reactions of Dienes • Ultraviolet and Visible Spectroscopy

Important Terms

1,2-addition (direct addition)	addition to the 1- and 2-positions of a conjugated system.
1,4-addition (conjugate addition)	addition to the 1- and 4-positions of a conjugated system.
allene	a compound with two adjacent double bonds.
bicyclic compound	a compound that contains two rings that share at least one carbon.
bridged bicyclic compound	a bicyclic compound in which the rings share two nonadjacent carbons.
common intermediate	an intermediate that two compounds have in common.
conjugate addition (1,4-addition)	addition to the 1- and 4-positions of a conjugated system.
conjugated double bonds	double bonds separated by one single bond.
cumulated double bonds	double bonds that are adjacent to one another.
cycloaddition reaction	a reaction in which two π-electron-containing reactants combine to form a cyclic product.
[4 + 2] cycloaddition reaction	a cycloaddition reaction in which four π electrons come from one reactant and two π electrons come from the other reactant.
Diels-Alder reaction	a [4 + 2] cycloaddition reaction.
diene	a hydrocarbon with two double bonds.
dienophile	an alkene that reacts with a diene in a Diels-Alder reaction.
direct addition (1,2-addition)	addition to the 1- and 2-positions of a conjugated system.
electromagnetic radiation	radiant energy that displays wave properties.
electronic transition	promotion of an electron from its HOMO to its LUMO.
endo	a substituent is endo if it and the bridge are on opposite sides of the bicyclic compound.
equilibrium control	thermodynamic control.
excited state	the electronic configuration of an atom or a molecule that results when an electron in the ground-state electronic configuration has been moved to a higher-energy orbital.

exo	a substituent is exo if it and the bridge are on the same side of the bicyclic compound.
ground state	the electronic configuration of an atom or a molecule when all the electrons are in their lowest-energy orbitals.
highest occupied molecular orbital (HOMO)	the highest energy molecular orbital that contains electrons.
isolated double bonds	double bonds separated by more than one single bond.
kinetic control	when a reaction is under kinetic control, the relative amounts of the products depend on the rates at which they are formed.
kinetic product	the product that is formed the fastest.
λ_{max}	the wavelength at which there is maximum UV/Vis absorbance.
lowest unoccupied molecular orbital (LUMO)	the lowest energy molecular orbital that does not contain electrons.
molar absorptivity	the absorbance obtained from a 1.00 M solution in a cell with a 1.00 cm light path.
pericyclic reaction	a reaction that takes place in one step as a result of a cyclic reorganization of electrons.
polyene	a compound that has several double bonds.
proximity effect	an effect caused by one species being close to another.
red shift	a shift to a longer wavelength.
***s*-cis-conformation**	the conformation in which two double bonds of a conjugated diene are on the same side of a connecting single bond.
***s*-trans-conformation**	the conformation in which two double bonds of a conjugated diene are on opposite sides of a connecting single bond.
spectroscopy	study of the interaction of matter and electromagnetic radiation.
tetraene	a compound with four double bonds.
thermodynamic control	when a reaction is under thermodynamic control, the relative amounts of the products depend on their stabilities.
thermodynamic product	the most stable product.
triene	a compound with three double bonds

ultraviolet light	electromagnetic radiation with wavelengths ranging from 180 to 400 nm.
UV/Vis spectroscopy	the absorption of electromagnetic radiation to determine information about conjugated systems.
visible light	electromagnetic radiation with wavelengths ranging from 400 to 780 nm.
wavelength	distance from any point on one wave to the corresponding point on the next wave.

Solutions to Problems

1.

a. 1,5-cyclooctadiene

b. 1-hepten-4-yne

c. 4-methyl-1,4-hexadiene

d. 5-vinyl-5-octen-1-yne

e. 1,6-dimethyl-1,3-cyclohexadiene

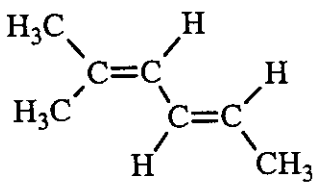
f. 3-butyn-1-ol

g. 1,3,5-heptatriene

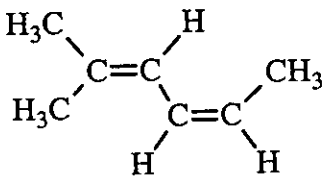
h. 2,4-dimethyl-4-hexen-1-ol

2. **a** and **c** have only two stereoisomers because in each case there are two identical substituent bonded to one of the sp^2 carbons.

a.

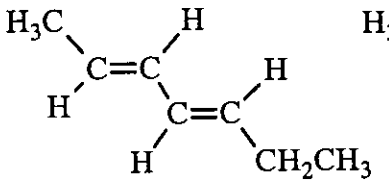


(*E*)-2-methyl-2,4-hexadiene

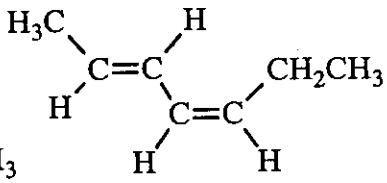


(*Z*)-2-methyl-2,4-hexadiene

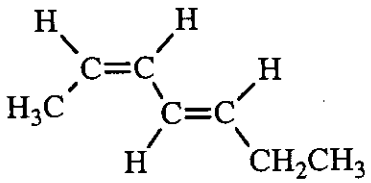
b.



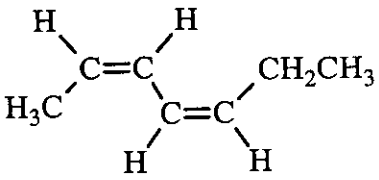
(2*E*,4*E*)-2,4-heptadiene



(2*E*,4*Z*)-2,4-heptadiene

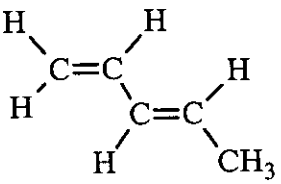


(2*Z*,4*E*)-2,4-heptadiene

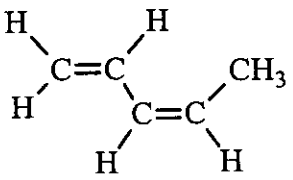


(2*Z*,4*Z*)-2,4-heptadiene

c.



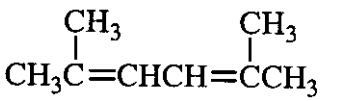
(*E*)-1,3-pentadiene



(*Z*)-1,3-pentadiene

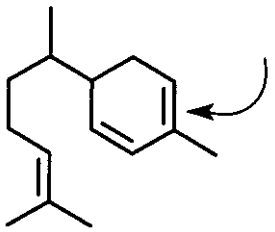
$CH_2{=}CHCH_2CH{=}CH_2$ < $CH_3CH{=}CHCH{=}CH_2$ < $CH_3CH{=}CHCH{=}CHCH_3$ <

1,4-pentadiene 1,3-pentadiene 2,4-hexadiene

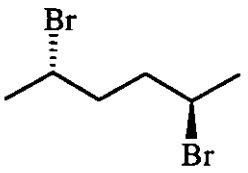


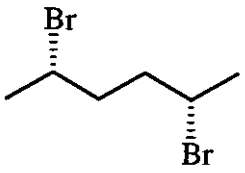
2,5-dimethyl-2,4-hexadiene

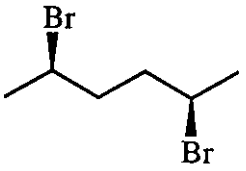
4. The indicated double bond is the most reactive in an electrophilic substitution reaction because addition of an electrophile to this double bond forms the most stable carbocation (a tertiary allylic carbocation).



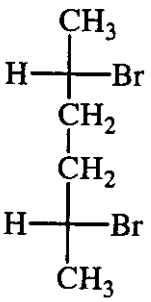
5.

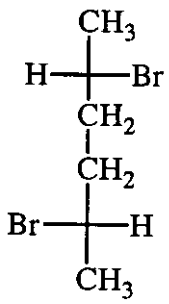


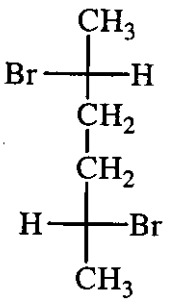


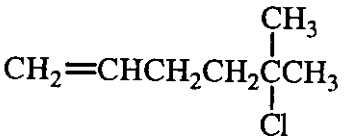


or





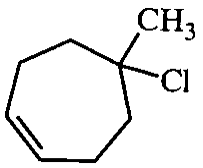




No stereoisomers are possible for this compound.

6.

a.

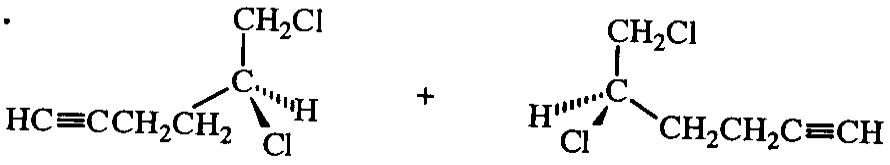


The intermediate is a tertiary carbocation.

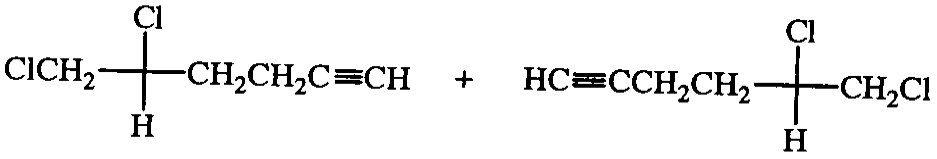
c. $CH_2{=}CHCH_2CH_2CH_2\overset{\displaystyle CH_3}{\overset{|}{\underset{\displaystyle Br}{\underset{|}{C}}}}CH_3$

The intermediate is a tertiary carbocation.

b.

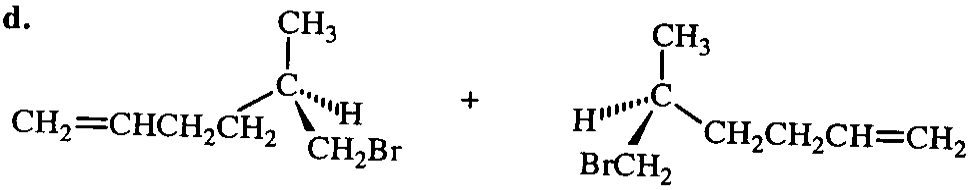


or

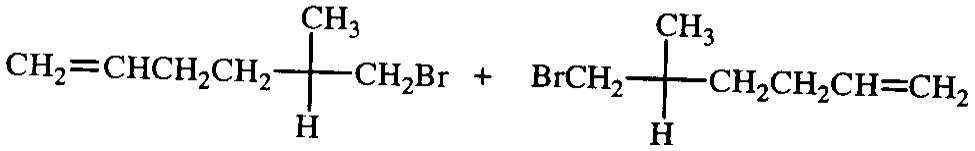


The double bond is more reactive than the triple bond.

d.



or



The intermediate is a tertiary radical.

$$CH_2{=}CH{-}CH{=}CH{-}CH{=}CH_2 \xrightarrow{HBr}$$

$CH_3{-}\underset{\displaystyle Br}{\underset{|}{CH}}{-}CH{=}CH{-}CH{=}CH_2$

$CH_3{-}CH{=}CH{-}\underset{\displaystyle Br}{\underset{|}{CH}}{-}CH{=}CH_2$

$CH_3{-}CH{=}CH{-}CH{=}CH{-}\underset{\displaystyle Br}{\underset{|}{CH_2}}$

8.

a. $CH_3CH{=}CH{-}CH{=}CHCH_3$

$\downarrow Cl_2$

$CH_3\overset{+}{C}lH{-}CH{-}CH{=}CHCH_3 \longleftrightarrow CH_3\underset{\displaystyle Cl}{\underset{|}{CH}}{-}CH{=}CH{-}\overset{+}{C}HCH_3$

$\downarrow Cl^-$ $\qquad$ $\downarrow Cl^-$

$CH_3\underset{\displaystyle Cl}{\underset{|}{CH}}\underset{\displaystyle Cl}{\underset{|}{CH}}CH{=}CHCH_3$ + $CH_3\underset{\displaystyle Cl}{\underset{|}{CH}}CH{=}CH\underset{\displaystyle Cl}{\underset{|}{CH}}CH_3$

1,2-addition product $\qquad$ **1,4-addition product**

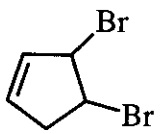
b. $CH_3CH{=}CH\overset{\displaystyle Br}{\overset{|}{C}}CH_2CH_3$ + $CH_3\underset{\displaystyle Br}{\underset{|}{CH}}CH{=}\overset{\displaystyle CH_3}{\overset{|}{C}}CH_2CH_3$

1,2-addition product $\qquad$ **1,4-addition product**

c. $CH_3CH_2\overset{\displaystyle Br}{\overset{|}{C}}-\overset{\displaystyle CH_3}{\overset{|}{C}}{=}CHCH_3$ + $CH_3CH_2C{=}\overset{\displaystyle Br}{\overset{|}{C}}CHCH_3$

1,2-addition product $\qquad$ **1,4-addition product**

d.



+



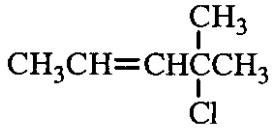
1,2-addition product $\qquad$ **1,4-addition product**

9. **a.** Addition at C-1 forms the more stable carbocation, because the positive charge is shared by two secondary allylic carbons.
b. DCl was used to cause the 1,2- and 1,4-products to be different. If HCl had been used the 1,2- and 1,4-products would have been the same.

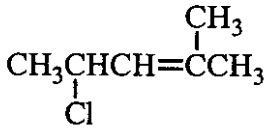
10. **a.** The rate-determining step is formation of the carbocation
b. The product-determining step is reaction of the carbocation with the nucleophile.

11. **a.** Solved in the text.

b.

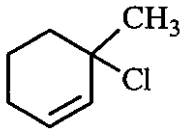


kinetic product

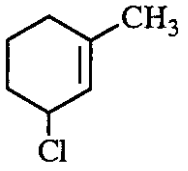


thermodynamic product

c.

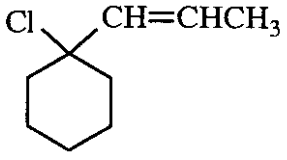


kinetic product

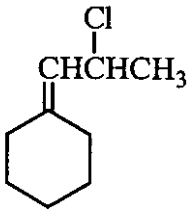


thermodynamic product

d.



kinetic product



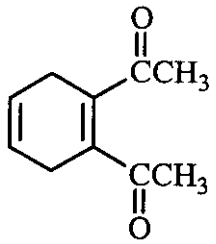
thermodynamic product

12. In order for a Diels-Alder reaction to occur, the overlapping orbitals of the reactants must have the same color (the same symmetry). In a [2+2] cycloaddition reaction at room temperature (in the ground state electronic configuration), the HOMO of one of the reactants will be symmetric and the LUMO of the other will be asymmetric (see Figure 7.8 on p. 287 of the text). Thus, they will not have the same symmetry and the reaction will not occur.

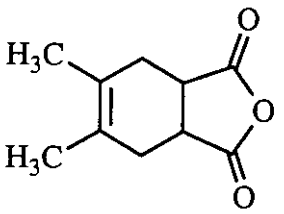
In contrast, a [2+2] cycloaddition reaction does occur under photochemical conditions. Under photochemical conditions one of the alkenes will be in an excited state. Therefore, its HOMO will be asymmetric and will be able to overlap with the asymmetric LUMO of the other alkene.

13.

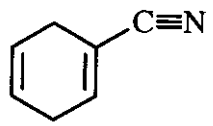
a.



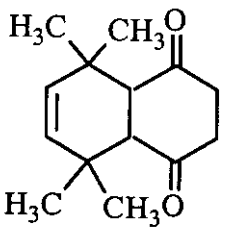
c.



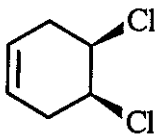
b.



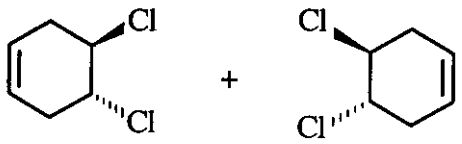
d.



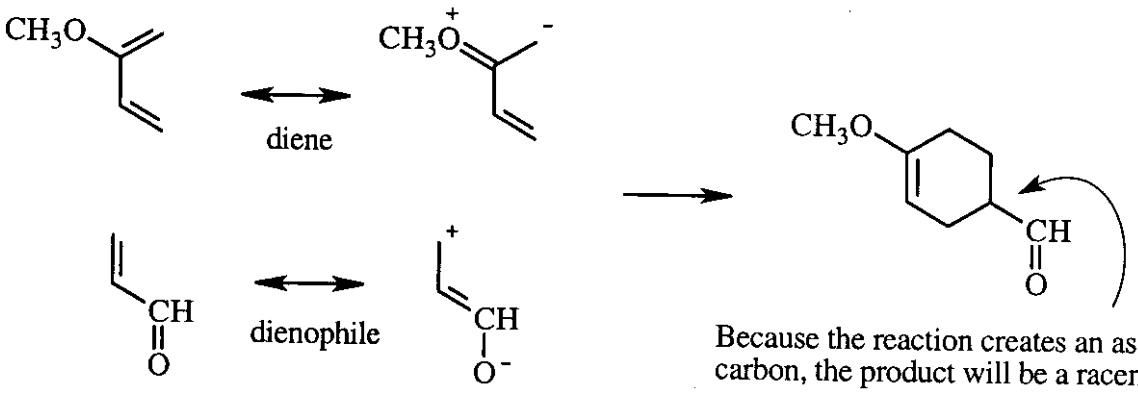
14. **a.** It is not optically active because it is a meso compound. (It has 2 asymmetric carbons and a plane of symmetry.)



b. It is not optically active because it is a racemic mixture. (Identical amounts of the enantiomers will be obtained.)



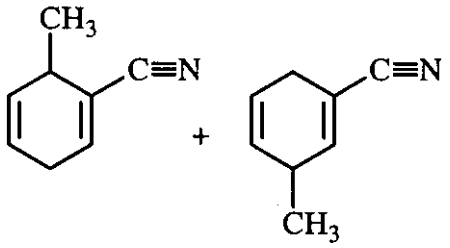
15. First draw the resonance contributors to determine where the charges are on the reactants. The major product is obtained by joining the negatively charged carbon of the diene with the positively charged carbon of the dienophile.



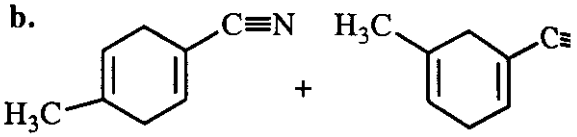
Because the reaction creates an asymmetric carbon, the product will be a racemic mixture.

16.

a.



b.



17. **a** and **d** will not react, because they are both locked in an *s*-trans conformation.

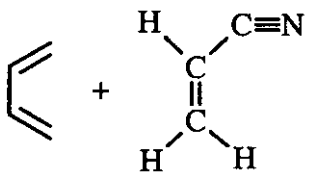
c and **e** will react, because they are both locked in an *s*-cis conformation.

b and **f** will react, because they can rotate into an *s*-cis conformation.

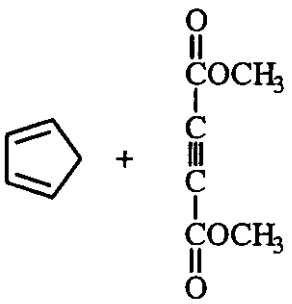
18. Solved in the text.

19.

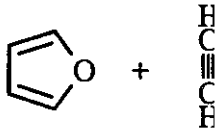
a.



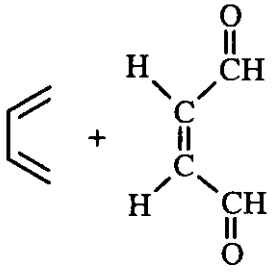
c.



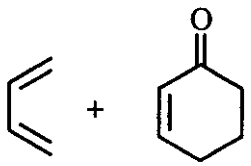
e.



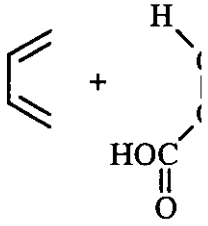
b.



d.



f.



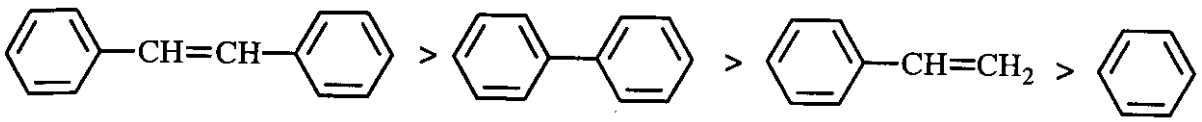
20. Diethyl ether does not have any π bonds. Therefore it does not have a π* molecular orbital. Without a π* molecular orbital neither an $n \rightarrow \pi^*$ nor a $\pi \rightarrow \pi^*$ electronic transition can oc

$$A = c\, l\, \varepsilon$$

$$c = \frac{A}{l\,\varepsilon}$$

$$c = \frac{0.52}{12{,}600} = 4.1 \times 10^{-5}\ \text{M}$$

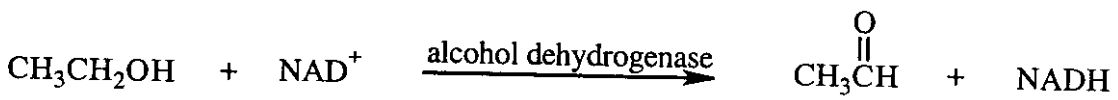
22.



23. **a.** Blue is the result of absorption of light of a longer wavelength than light that produces purple. The compound on the right has an auxochrome ($N(CH_3)_2$) that will cause it to absorb at a longer wavelength. Therefore, it is the blue compound.

b. They will be the same color at pH = 3 because the $N(CH_3)_2$ group will be protonated and, therefore, will not possess the lone pair that causes the compound to absorb light of a longer wavelength.

24. NADH is formed as a product; it absorbs light at 340 nm. Therefore, the rate of the oxidation reaction can be determined by monitoring the increase in absorbance at 340 nm as a function of time.



25. **a.** 1-octen-6-yne

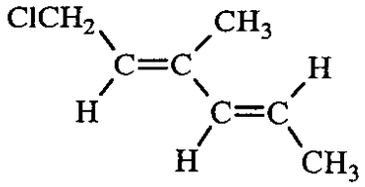
b. (Z)-3-hexen-1-ol

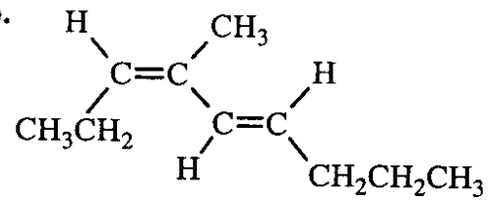
c. 1,5-octadiyne

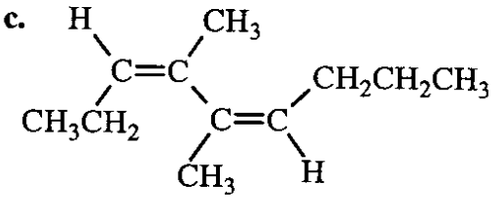
d. 5-chloro-1,3-cyclohexadiene

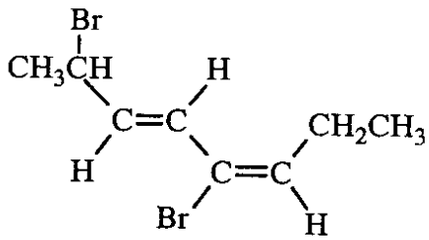
e. 1-methyl-1,3,5-cycloheptatriene

26.

a. 

b. 

c. 

d. 

27. **a.** There are six linear dienes with molecular formula C_6H_{10}.

b. Two are conjugated dienes. $CH_2{=}CHCH{=}CHCH_2CH_3$

$CH_3CH{=}CHCH{=}CHCH_3$

c. Two are isolated dienes. $CH_2{=}CHCH_2CH{=}CHCH_3$

$CH_2{=}CHCH_2CH_2CH{=}CH_2$

There are also two cumulated dienes. $CH_2{=}C{=}CHCH_2CH_2CH_3$

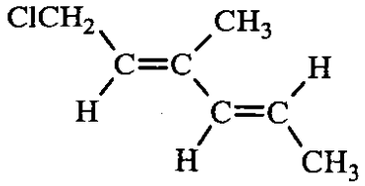
$CH_3CH{=}C{=}CHCH_2CH_3$

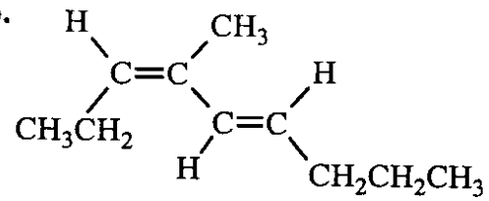
28. Both compounds form the same product when they are hydrogenated, so the difference in heats of hydrogenation will depend only on the difference in the stabilities of the reactants. Because 1,2-pentadiene has cumulated double bonds and 1,4-pentadiene has isolated double bonds, 1,2-pentadiene is less stable and, therefore, will have a greater heat of hydrogenation (a more negative $\Delta H°$).

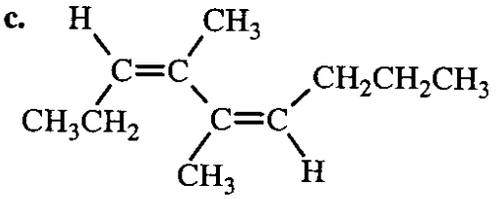
$$\underset{\text{1,2-pentadiene}}{CH_2{=}C{=}CHCH_2CH_3} \xrightarrow[Pd/C]{H_2} CH_3CH_2CH_2CH_2CH_3$$

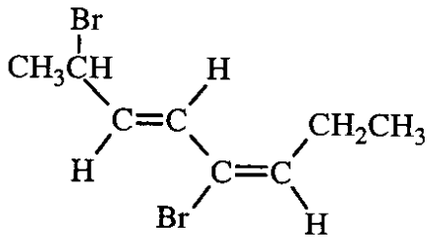
$$\underset{\text{1,4-pentadiene}}{CH_2{=}CHCH_2CH{=}CH_2} \xrightarrow[Pd/C]{H_2} CH_3CH_2CH_2CH_2CH_3$$

26.

a. 

b. 

c. 

d. 

27. **a.** There are six linear dienes with molecular formula C_6H_{10}.

b. Two are conjugated dienes. $CH_2{=}CHCH{=}CHCH_2CH_3$

$CH_3CH{=}CHCH{=}CHCH_3$

c. Two are isolated dienes. $CH_2{=}CHCH_2CH{=}CHCH_3$

$CH_2{=}CHCH_2CH_2CH{=}CH_2$

There are also two cumulated dienes. $CH_2{=}C{=}CHCH_2CH_2CH_3$

$CH_3CH{=}C{=}CHCH_2CH_3$

28. Both compounds form the same product when they are hydrogenated, so the difference in heats of hydrogenation will depend only on the difference in the stabilities of the reactants. Because 1,2-pentadiene has cumulated double bonds and 1,4-pentadiene has isolated double bonds, 1,2-pentadiene is less stable and, therefore, will have a greater heat of hydrogenation (a more negative $\Delta H°$).

$$CH_2{=}C{=}CHCH_2CH_3 \xrightarrow[Pd/C]{H_2} CH_3CH_2CH_2CH_2CH_3$$

1,2-pentadiene

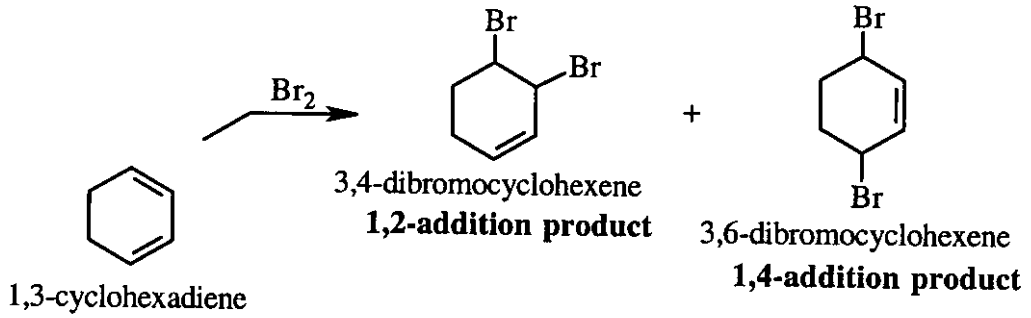
$$CH_2{=}CHCH_2CH{=}CH_2 \xrightarrow[Pd/C]{H_2} CH_3CH_2CH_2CH_2CH_3$$

1,4-pentadiene

29. (3*E*,6*E*)-3,7,11-trimethyl-1,3,6,10-dodecatetraene

The configuration of the double bond at the 1-position and at the 10-position is not specified because isomers are not possible at those positions since there are 2 hydrogens on C-1 and two methyl groups on C-11.

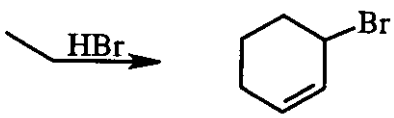
30. The reaction of 1,3-cyclohexadiene with Br_2 forms 3,4-dibromocyclohexene as the 1,2-addition product and 3,6-dibromocyclohexene as the 1,4-addition product. (Recall that in naming the compounds, the double bond is at the 1,2-position.) The reaction of 1,3-cyclohexadiene with HBr forms 3-bromocyclohexene as both the 1,2-addition product and the 1,4-addition product.



3,4-dibromocyclohexene
1,2-addition product

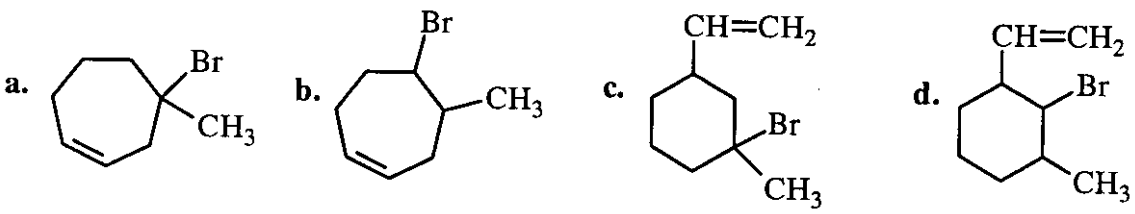
3,6-dibromocyclohexene
1,4-addition product

1,3-cyclohexadiene



3-bromocyclohexene
1,2-addition product
1,4-addition product

31.



32.

a. $CH_2{=}CHCH{=}CHCH{=}CH_2$ (1,3,5-hexatriene) $\xrightarrow{HBr}$ $CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH{=}CHCH{=}CH_2$ (**A**) +

$CH_3CH{=}\underset{\displaystyle Br}{\underset{|}{C}}HCH{=}CH_2$ (**B**) + $CH_3CH{=}CHCH{=}CHCH$ (**C**)

b. **A** will predominate if the reaction is under kinetic control because it is the 1,2-product an therefore will be the product formed most rapdily as a result of the proximity effect. In addition, **A** will be the 1,2-product regardless of which end of the conjugate system rea with the electrophile.

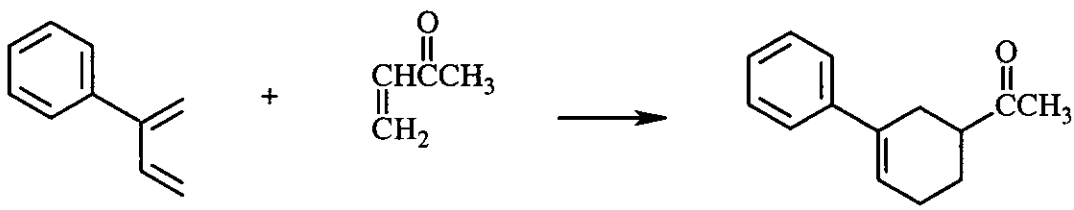
c. **C** will predominate if the reaction is under thermodynamic control because it is the most stable diene. (It is the most substituted conjugated diene.)

33. **a.** The absorption at 236 nm is due to a $\pi \rightarrow \pi^*$ transition, and the absorption at 314 nm is d to an $n \rightarrow \pi^*$ transition.

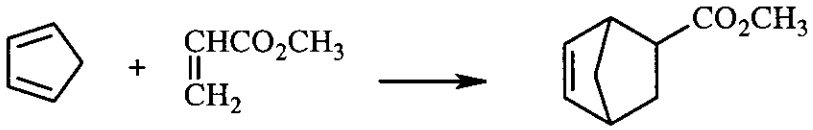
b. The one at 236 nm (the $\pi \rightarrow \pi^*$ transition) shows the greater absorbance.

34.

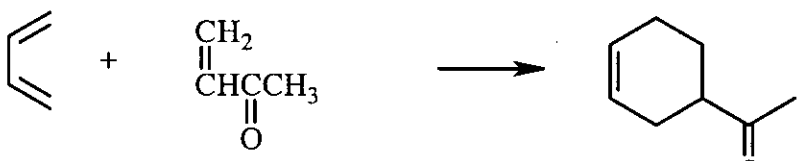
a.



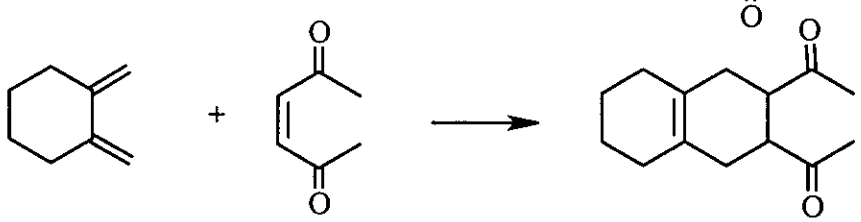
b.



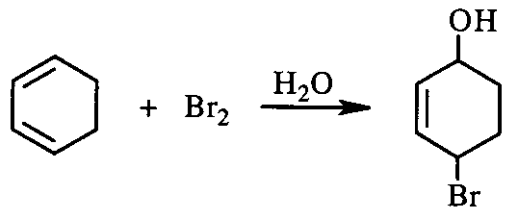
c.



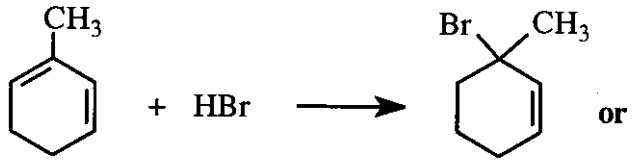
d.

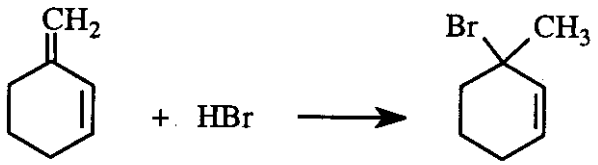


a. **1.**

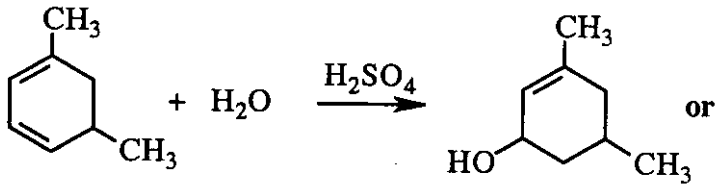


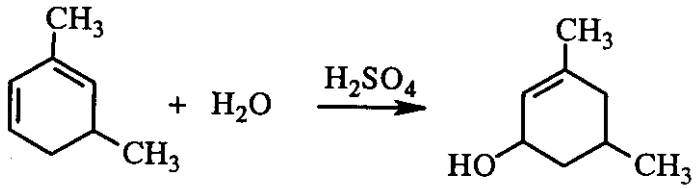
2.





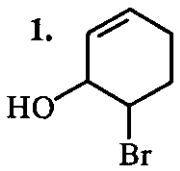
3.



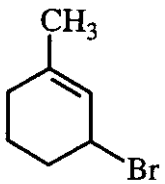


b.

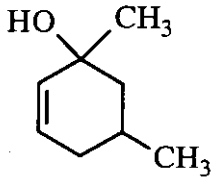
1.



2.



3.



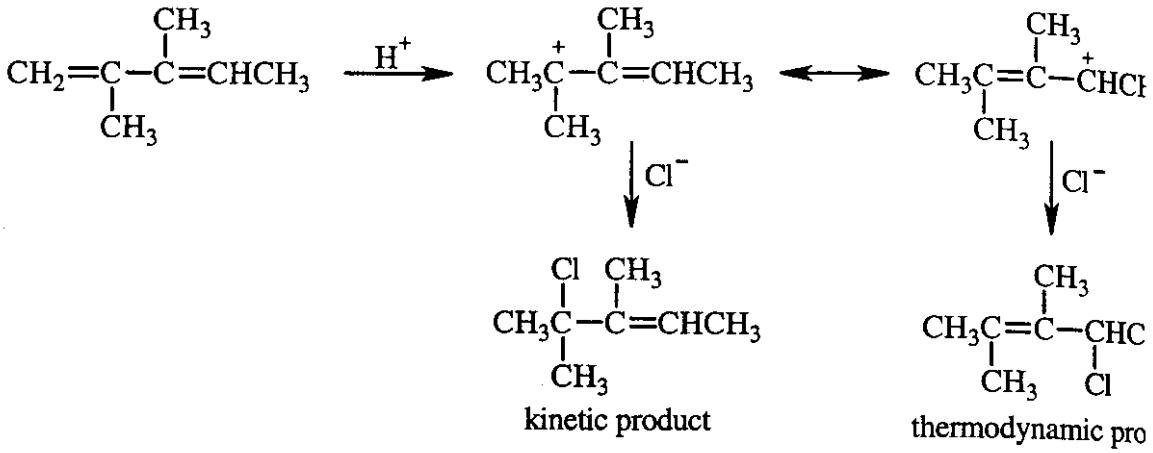
36. The diene is the nucleophile, and the dienophile is the electrophile in a Diels-Alder reaction.

a. An electron-donating substituent in the diene would increase the rate of the reaction, because electron donation would increase its nucleophilicity.

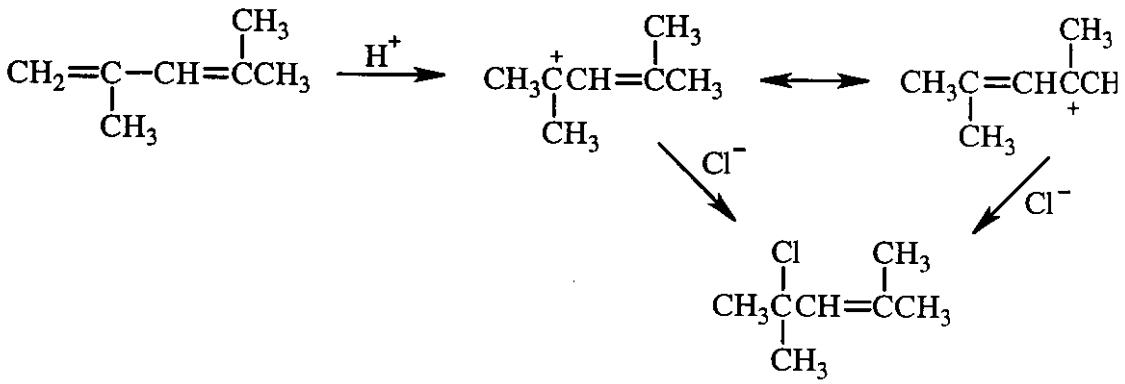
b. An electron-donating substituent in the dienophile would decrease the rate of the reaction, because electron donation would decrease its electrophilicity.

c. An electron-withdrawing substituent in the diene would decrease the rate of the reaction, because electron withdrawal would decrease its nucleophilicity.

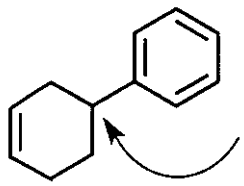
37. **a.** Addition of an electrophile to C-1 forms a carbocation with two resonance contributors, a tertiary allylic carbocation and a secondary allylic carbocation. Addition of an electrophil C-4 forms a carbocation with two resonance contributors, a tertiary allylic carbocation an primary allylic carbocation. Therefore, addition to C-1 results in formation of the more s carbocation intermediate, and the more stable intermediate leads to the major products.



b. Addition of an electrophile to C-1 forms a carbocation with two resonance contributors; are *tertiary allylic* carbocations.
Addition of an electrophile to C-4 forms a carbocation with two resonance contributors, *secondary allylic* carbocation and a *primary allylic* carbocation.
Therefore, addition to C-1 results in formation of the more stable carbocation.
Only one product is formed, because the two resonance contributors are identical since tl carbocation is symmetrical.)

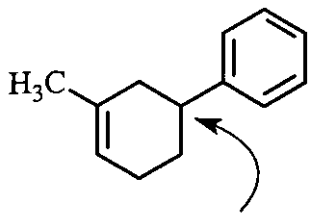


a.

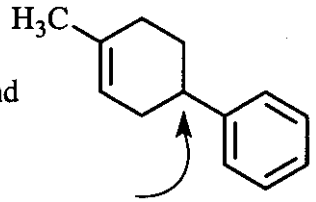


Because the reaction creates an aymmetric carbon in the product, the product will be a racemic mixture.

b.

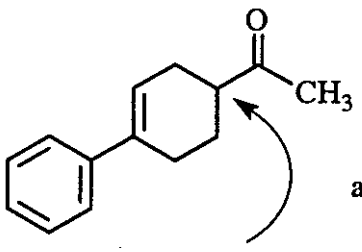


and

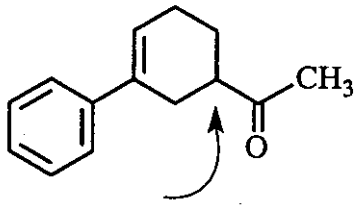


Because the reaction creates an aymmetric carbon in each of the products, each product will be a racemic mixture.

c.

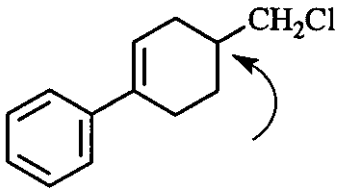


and

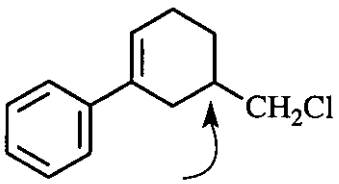


Because the reaction creates an aymmetric carbon in each of the products, each product will be a racemic mixture.

d.



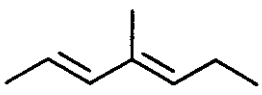
and



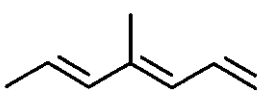
Because the reaction creates an aymmetric carbon in each of the products, each product will be a racemic mixture.

39.

a.



and



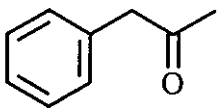
The λ_{max} will be at a longer wavelength.

b. $CH_2{=}CHCH{=}CHCH{=}CH_2$ and $CH_2{=}CHCH{=}CHC(=O)CH_3$

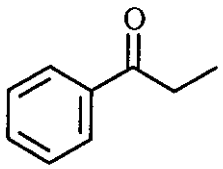
It will show 1 absorption band.
a $\pi \longrightarrow \pi^*$ transition

It will show 2 absorption bands.
a $\pi \longrightarrow \pi^*$ transition
and
an $n \longrightarrow \pi^*$ transition

c.

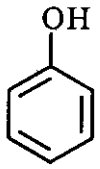


and

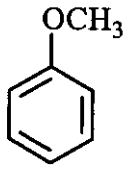


The λ_{max} will be at a longer wavelength because the carbonyl group is conjugated with the benzene ring.

d.



and

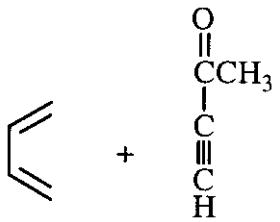


The λ_{max} of the phenolate ion will be at a longer wavelength than the λ_{max} of phenol.

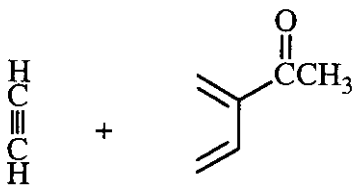
Since the pK_a of phenol is ~10, the λ_{max} will be at a longer wavelength at pH =11 than at pH = 7.

The λ_{max} is pH independent.

40. The first pair is the preferred set of reagents because it has the more nucleophilic diene and th more electrophilic dienophile.

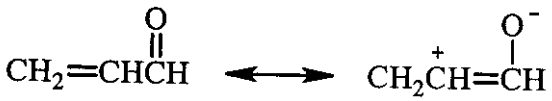


or

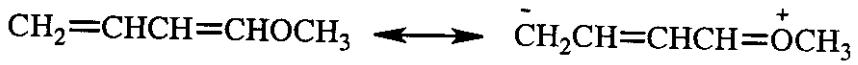


A Diels-Alder reaction is a reaction between a nucleophilic diene and an electrophilic dienophile.

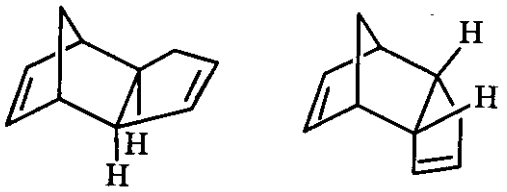
a. The compound shown below is more reactive in both **1** and **2**, because electron delocalization increases the electrophilicity of the dienophile.



b. The compound shown below is more reactive, because electron delocalization increases the nucleophilicity of the diene.



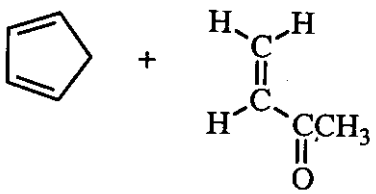
42.



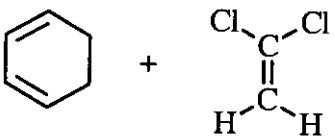
exo endo

43.

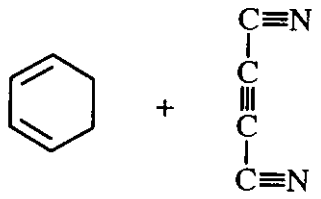
a.



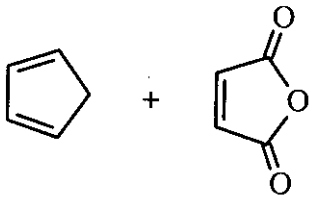
b.



c.

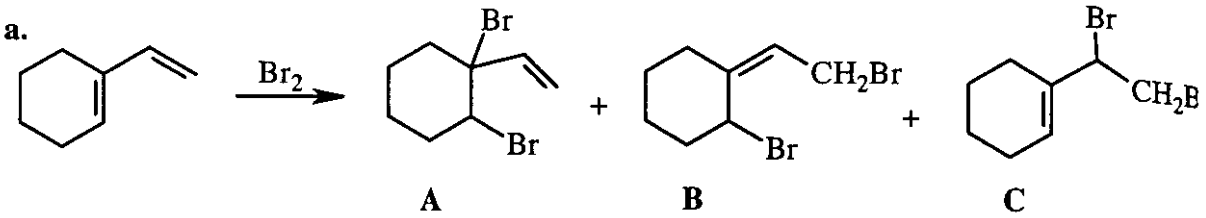


d.



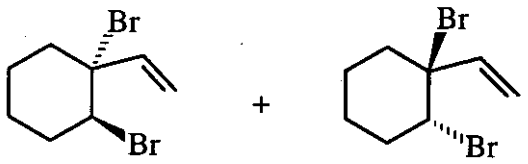
44.

a.

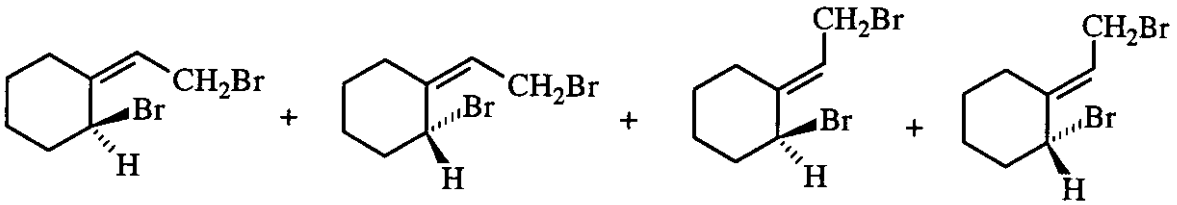


A **B** **C**

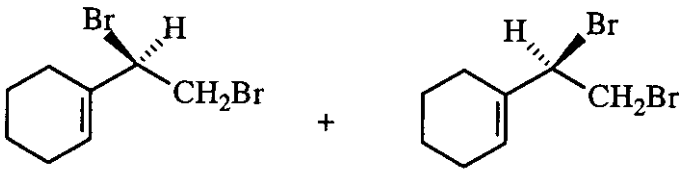
b. **A** has two asymmetric carbons but only two stereoisomers are obtained because addition of can occur only in an anti fashion.



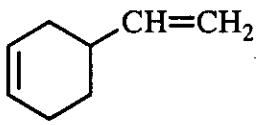
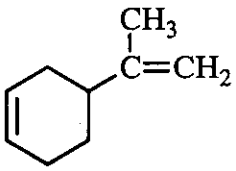
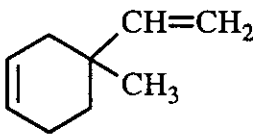
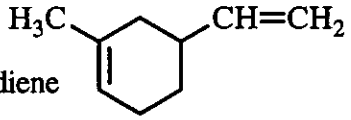
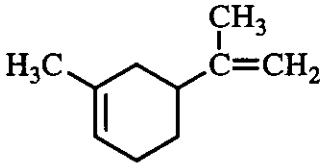
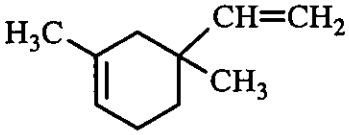
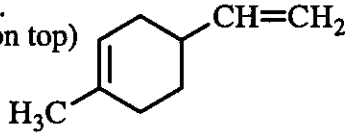
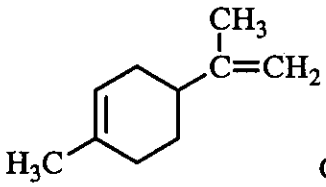
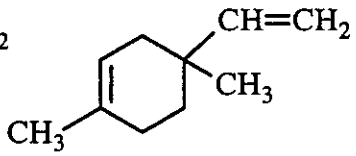
B has four stereoisomers because it has an asymmetric carbon and a double bond that can be in either the *E* or *Z* configuration.



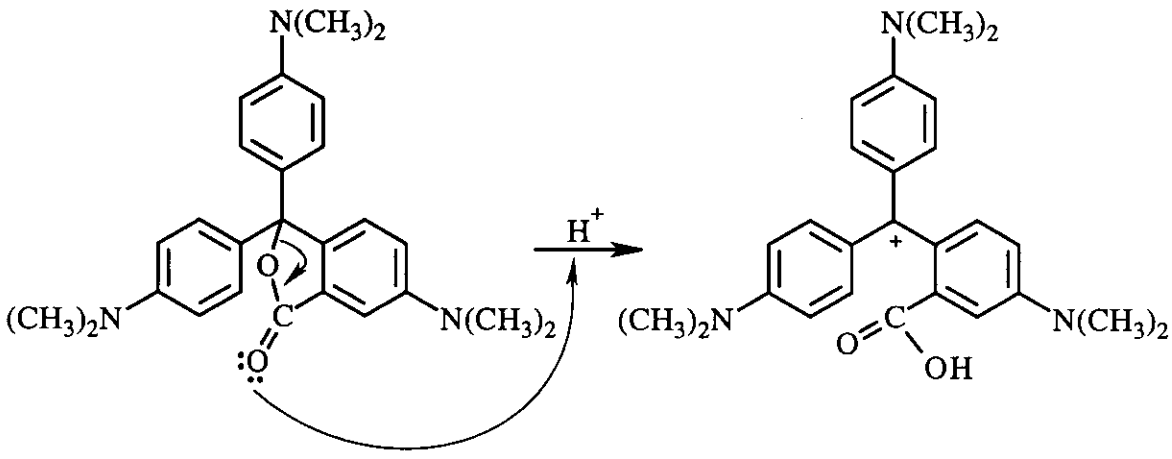
C has two stereoisomers because it has one asymmetric carbon.



Nine of the compounds are shown below. Since each has one asymmetric carbon, each can have either the *R* or the *S* configuration. Therefore, 18 different products can be obtained.

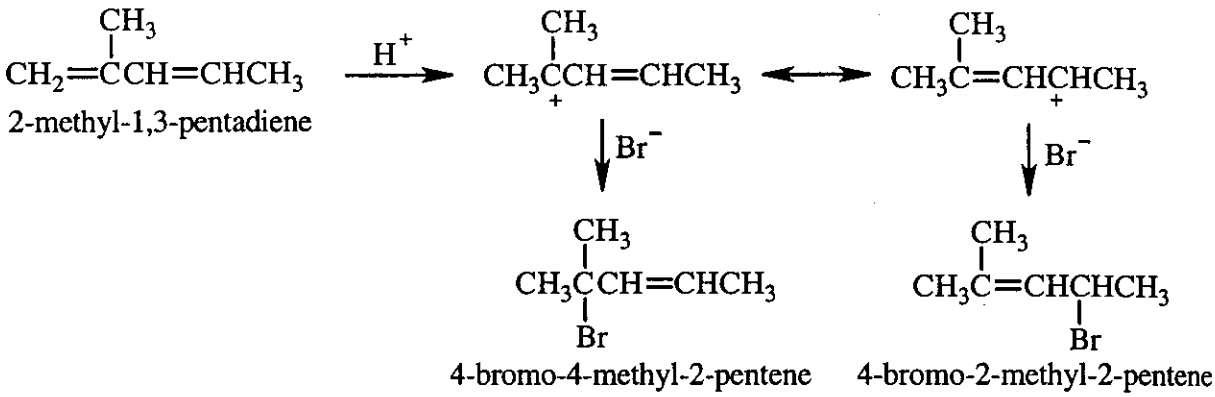
	1,3-Butadiene is the electrophile.	The 3,4-bond of 2-methyl-1,3-butadiene is the electrophile.	The 1,2-bond of 2-methyl-1,3-butadiene is the electrophile.
1,3-Butadiene is the nucleophile.			
2-Methyl-1,3-butadiene is the nucleophile. (the 1-position is on top)			
2-Methyl-1,3-butadiene is the nucleophile. (the 4-position is on top)			

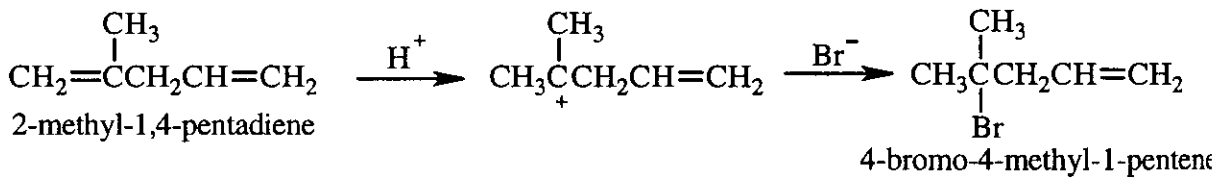
46. Before the addition of acid, the compound is colorless because the benzene rings are not conjugated with each other, since they are separated from each other by two single bonds. In the presence of acid, a carbocation is formed in which the three benzene rings are conjugated with each other. The conjugated carbocation is highly colored.

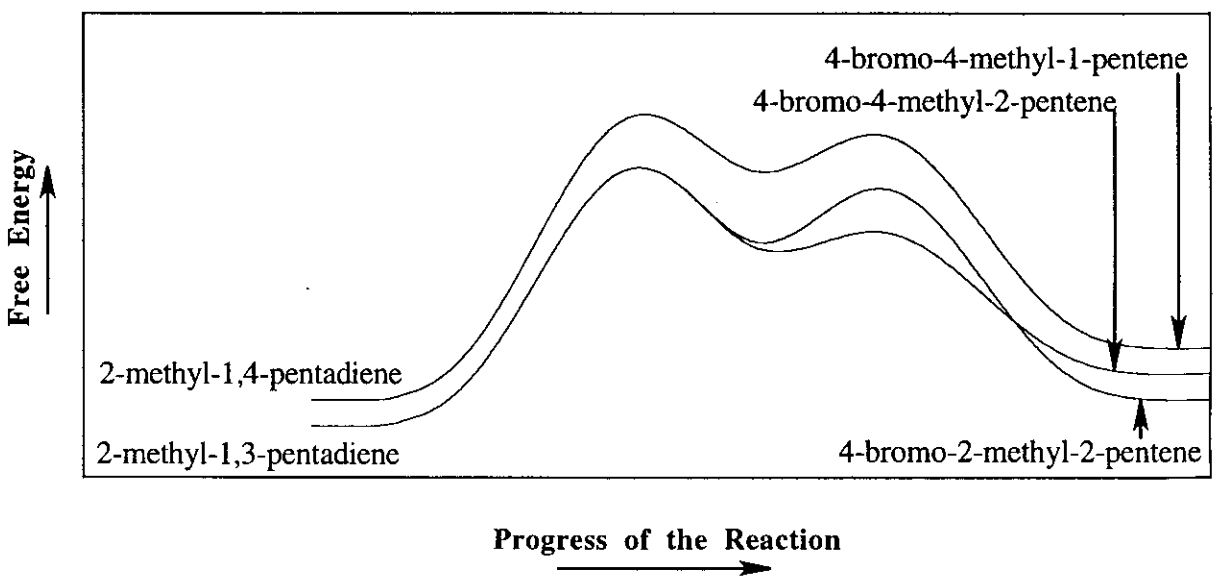


47. The rate-limiting step of the reaction is the formation of the carbocation intermediate. 2-Methyl-1,3-pentadiene (with conjugated double bonds) is more stable than 2-methyl-1,4-pentadiene (with isolated double bonds). 2-Methyl-1,3-pentadiene forms a more stable carbocation than does 2-methyl-1,4-pentadiene.

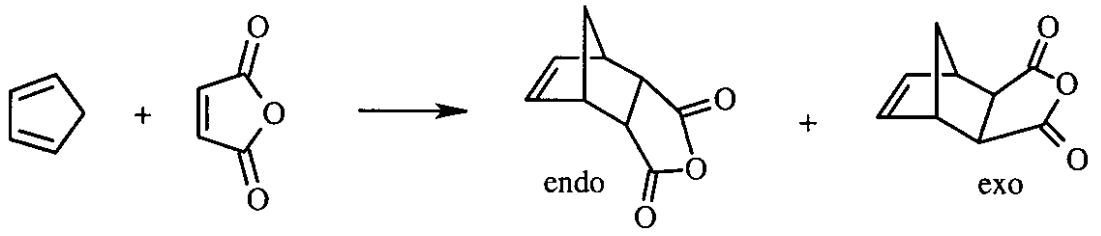
Since the more stable reactant forms the more stable carbocation, the relative free energies of activation of the rate-limiting steps of the two reactions depend on whether the difference in the stabilities of the reactants is greater or less than the difference in the stabilities of the transition states (which depend on the difference in stabilities of the carbocations). Because the difference in the stabilities of the reactants is less than the difference in the stabilities of the transition states, the rate of reaction of HBr with 2-methyl-1,3-pentadiene is the faster reaction. (If the difference in the stabilities of the reactants had been greater than the difference in the stabilities of the transition states, the rate of reaction of HBr with 2-methyl-1,4-pentadiene would have been the faster reaction.)







48. His recrystallization was not successful. Because maleic anhydride is a dienophile, it reacts with cyclopentadiene in a Diels-Alder reaction.



49. Since only benzene absorbs light of 260 nm, the concentration of benzene can be determined by measuring the amount of absorbance at 260 nm, using the Beer-Lambert law, since the length of the light path of the cell is known and the molar absorptivity of benzene at 260 nm can be looked up (or can be determined from the absorbance at 260 nm given by a solution of benzene with a known concentration).

the Beer-Lambert law: $A = c\,l\,\varepsilon$

50. High temperatures are required in order to break the bonds formed by the overlapping in-phase orbitals. The Diels-Alder product will not reform at high temperatures, because a [4+2] cycloaddition will not occur unless both of the reactants are in their ground states.

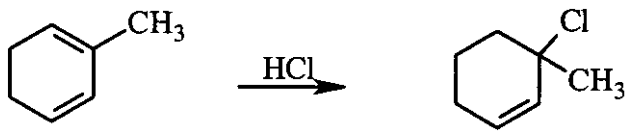
51. Maleic anhydride reacts with cyclopentadiene as in the above problem. The function of maleic acid in this reaction is to remove the cyclopentadiene, since removal of a product drives the equilibrium toward products. (See Le Châtelier's principle on page 373 of the text.)

52. The bridgehead carbon cannot have the 120° bond angle required for the sp^2 hybridized carbon of a double bond. With a 120° bond angle, the compound would be too strained to exist.

53. **a.** Unless the reaction is being carried out under kinetic control, the amount of product obtained is not dependent on the rate at which the product is formed, so the relative amounts of products obtained will not tell you which product was formed faster.

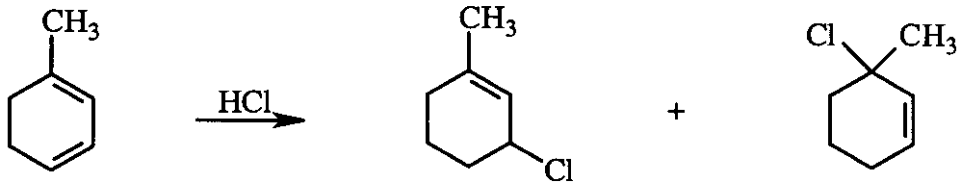
b. In a thermodynamically controlled reaction, the product distribution depends on the realative stabilites of the products since the products come to equilibrium. Thus if the distribution of products that is obtained does not reflect the relative stabilities of the products, the reaction must have been kinetically controlled.

54. He should follow his friend's advice. If he uses 2-methyl-1-3,cyclohexadiene, the product that is formed faster will be 3-chloro-3-methylcyclohexene both if the proximity effect controls which product is formed faster and if the more stable transition state controls which product is formed faster. Thus the experiment will not be able to differentiate between the two.



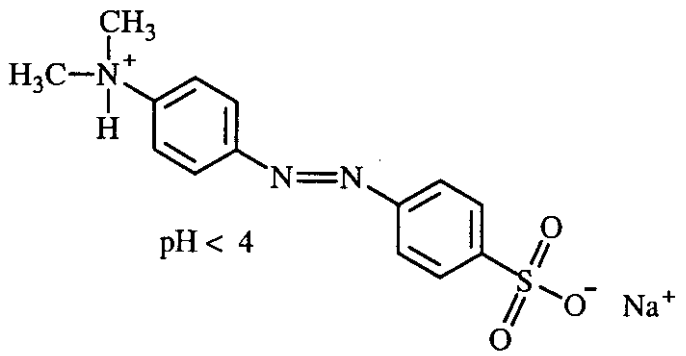
3-chloro-3-methylcyclohexene

If he follows his friend's advice and uses 1-methyl-1-3,cyclohexadiene, the product that is formed faster will be 3-chloro-1-methylcyclohexene only if the proximity effect controls which product is formed faster. The product will be 3-chloro-3-methylcyclohexene if the more stable transition state controls which product is formed faster.



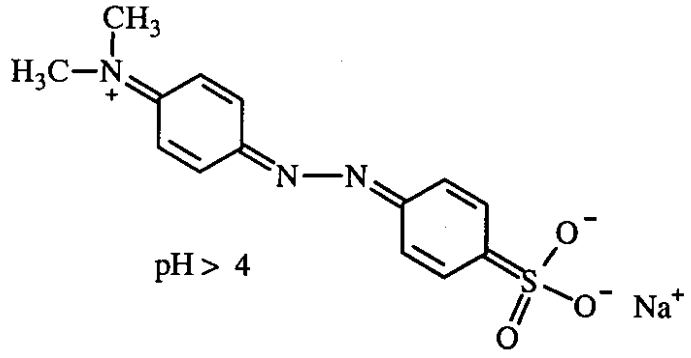
3-chloro-1-methylcyclohexene 3-chloro-3-methylcyclohexene

55. **a.** At pH < 4, the lone pair of the nitrogen of the $N(CH_3)_2$ group is protonated, so it cannot interfere with the fully conjugated system.



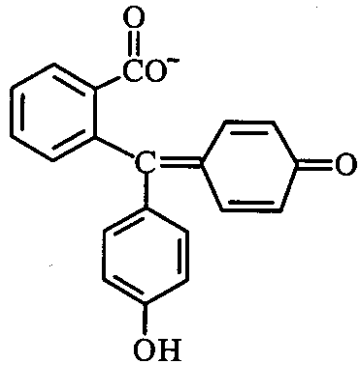
pH < 4

At pH > 4, the nitrogen of the $N(CH_3)_2$ group is not protonated and the lone pair can be delocalized into the benzene ring. This decreases the conjugation and, therefore, light of shorter wavelengths will be absorbed; hence, the change in color from red to yellow.



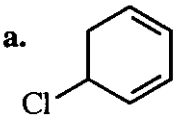
b. In acidic solutions, the three benzene rings are isolated from one another.

In basic solutions, as a result of loss of the proton from one of the OH groups, there is a greater degree of conjugation.

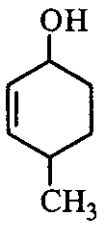


Chapter 8 Practice Test

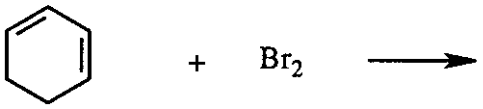
1. Give the systematic name for the following compounds:

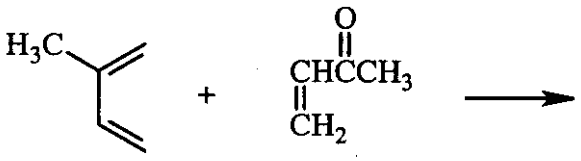
a. 

b. $CH_3C{\equiv}CCH_2CH_2CH_2CH{=}CH_2$

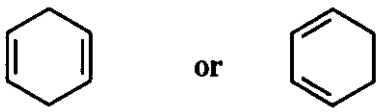
c. 

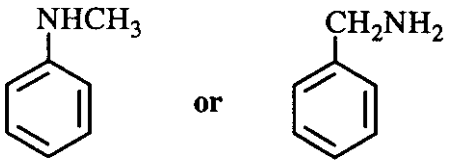
2. Give the products of the following reactions:

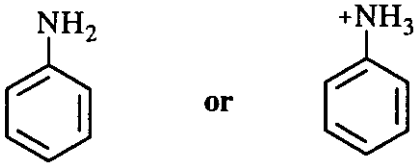
a. 

b. 

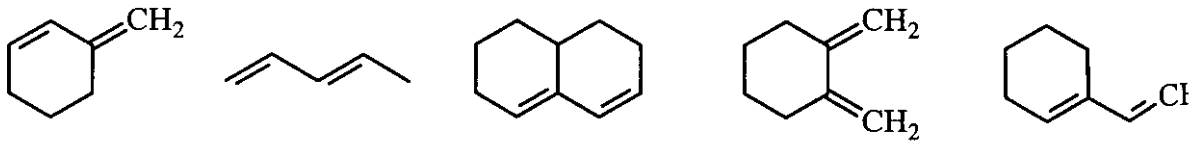
3. Which compound has the greater λ_{max}? (300 nm is a greater λ_{max} than 250 nm.)

a. 

b. 

c. 

4. Which of the following dienes can be used in a Diels-Alder reaction?



5. A 0.038 M solution of cyclohexanone shows an absorbance of 0.75 at 280 nm in a 1.00 cm cell. What is the molar absorptivity of cyclohexanone at 280 nm?

6. Indicate whether each of the following statements is true or false.

a. A conjugated diene is more stable than an isomeric isolated diene. T F

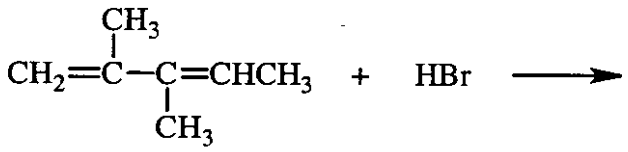
b. A single bond formed by an sp^2—sp^2 overlap is longer than a single bond formed by an sp^2—sp^3 overlap. T F

c. The thermodynamically controlled product is the major product obtained when the reaction is carried out under mild conditions. T F

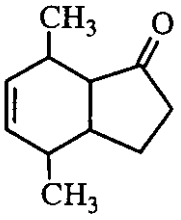
d. 1,3-Hexadiene is more stable than 1,4-hexadiene. T F

e. A chromophore that exhibits both $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions will have the $n \rightarrow \pi^*$ transition at a longer wavelength. T F

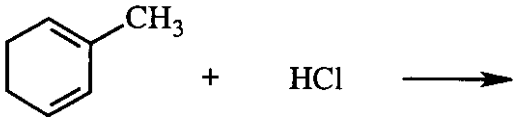
7. Give the four products that would be obtained from the following reaction. Ignore stereoisomers.



8. What reactants are necessary for the synthesis of the following compound via a Diels-Alder reaction?



9. Two 1,2-products and two 1,4-products can be obtained from the following reaction:



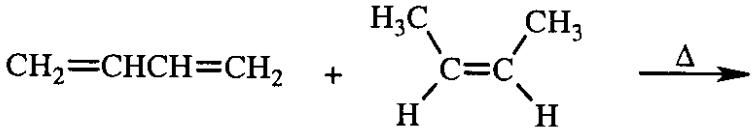
a. Which are the predominant 1,2- and 1,4-products?

b. Which of the above two products is the product of thermodynamic control?

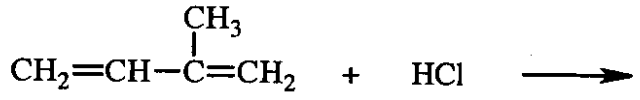
10. What reagents could be used to convert the given starting material into the given product?

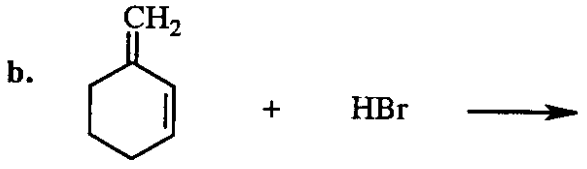


11. Give the product of the following reaction, showing its configuration:



12. For each of the following reactions give the major 1,2- and 1,4-products. Label the product of kinetic control and the product of thermodynamic control.

a. 

b. 

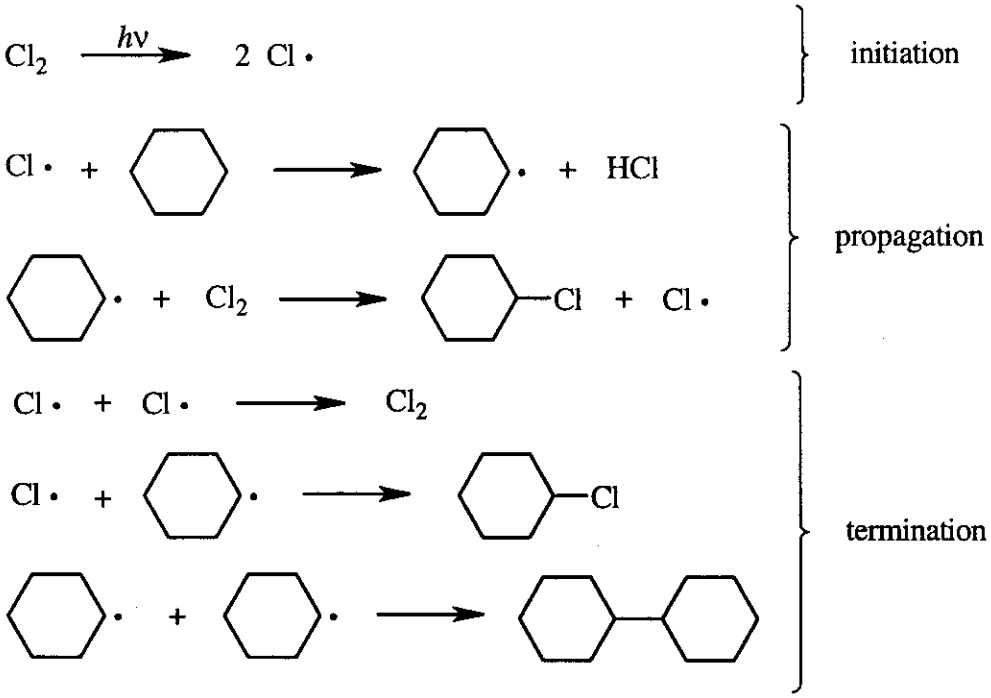
13. A solution of a compound with a molar absorbtivity of 1,200 at 297 nm gives an absorbance of 0.76 at that wavelength in a 1 cm quartz cell. What is the concentration of the solution?

Important Terms

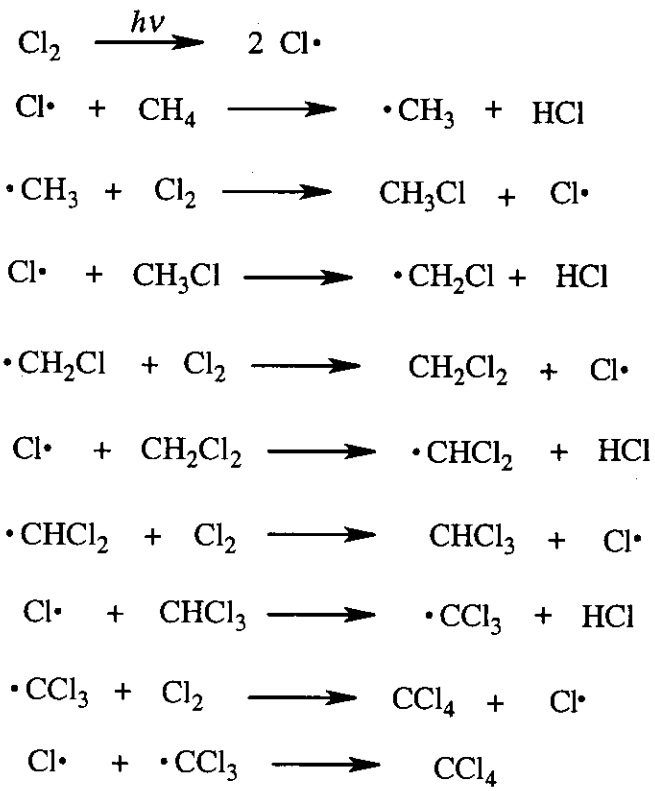
alkane	a hydrocarbon that contains only single bonds.
combustion	a reaction with oxygen that takes place at high temperatures and converts alkanes to carbon dioxide and water.
free radical	an atom or a molecule with an unpaired electron.
halogenation	the reaction of an alkane with a halogen.
homolytic bond cleavage	breaking a bond with the result that each of the atoms of the bond gets one of the bonding electrons.
initiation step	the step in which radicals are created, or the step in which the radical needed for the first propagating step is created.
paraffin	an older word for alkanes, which means "little affinity."
propagation step	in the first of a pair of propagation steps, a radical (or an electrophile or a nucleophile) reacts to produce another radical (or an electrophile or a nucleophile) that reacts in the second propagation step to produce the radical (or the electrophile or the nucleophile) that was the reactant in the first propagation step.
radical (often called a free radical)	an atom or a molecule with an unpaired electron.
radical chain reaction	a reaction in which radicals are formed and react in repeating propagating steps.
radical inhibitor	a compound that traps radicals.
radical substitution reaction	a substitution reaction that has a radical intermediate.
reactivity-selectivity principle	the greater the reactivity of a species, the less selective it will be.
saturated hydrocarbon	a hydrocarbon that contains only single bonds (is saturated with hydrogen).
termination step	two radicals combine to produce a molecule in which all the electrons are paired.

Solutions to Problems

1.

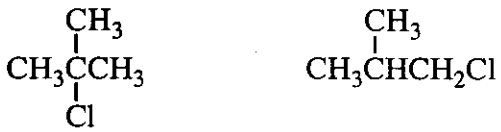


2.



3. Solved in the text.

4.



$1 \times x = x$ $\qquad$ $9 \times 1 = 9$

$$\% \text{ 1-chloro-2-methylpropane} = \frac{9}{9+x} = 0.64$$

$$9 = 0.64\,(9 + x)$$
$$9 = 5.76 + 0.64x$$
$$3.24 = 0.64x$$
$$x = 5$$

It is 5 times easier for a chloride radical to remove a hydrogen atom from a tertiary carbon than from a primary carbon.

5.

a. 3	**c.** 5	**e.** 5	**g.** 2	**i.** 4
b. 3	**d.** 1	**f.** 5	**h.** 1	

6. Note: the denominator used in each of these problems is obtained by adding the numerators.

a. $CH_3CH_2CH_2CH_2CH_2Cl$ $\qquad$ $CH_3CH_2CH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCH_3$ $\qquad$ $CH_3CH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCH_2CH_3$

$6 \times 1 = 6$ $\qquad$ $4 \times 3.8 = 15.2$ $\qquad$ $2 \times 3.8 = 7.6$

$\frac{6}{28.8} = 21\%$ $\qquad$ $\frac{15.2}{28.8} = 53\%$ $\qquad$ $\frac{7.6}{28.8} = 26\%$

b. $ClCH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_3$ $\qquad$ $CH_3\underset{\displaystyle Cl}{\underset{|}{C}}H\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH_2CHCH_3$ $\qquad$ $CH_3\underset{\displaystyle Cl}{\underset{|}{C}}HCHCH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_3$

$12 \times 1 = 12$ $\qquad$ $2 \times 5 = 10$ $\qquad$ $4 \times 3.8 = 15.2$

$\frac{12}{37.2} = 32\%$ $\qquad$ $\frac{10}{37.2} = 27\%$ $\qquad$ $\frac{15.2}{37.2} = 41\%$

c. $ClCH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2CH_2CH_3$ $CH_3\underset{\displaystyle Cl}{\underset{|}{C}}HCH_2CH_2CH_3$ $CH_3\underset{\displaystyle Cl}{\underset{|}{C}}HCHCH_2CH_3$

$6 \times 1 = 6$ $1 \times 5 = 5$ $2 \times 3.8 = 7.6$

$\frac{6}{29.2} = 21\%$ $\frac{5}{29.2} = 17\%$ $\frac{7.6}{29.2} = 26\%$

$CH_3CHCH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCH_3$ $CH_3CHCH_2CH_2CH_2Cl$

$2 \times 3.8 = 7.6$ $3 \times 1 = 3$

$\frac{7.6}{29.2} = 26\%$ $\frac{3}{29.2} = 10\%$

7.

a. $CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$ $CH_3CH_2CH_2CH_2Br$

$4 \times 82 = 328$ $6 \times 1 = 6$

$\frac{328}{328 + 6} = \frac{328}{334} = 98\%$

b. $CH_3\underset{\displaystyle Br}{\underset{|}{C}}CH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}CH_3$ CH_3

$1 \times 1600 = 1600$

$\frac{1600}{1943} = 82\%$

other products

	1600
9×1	$= 9$
2×82	$= 164$
2×82	$= 164$
6×1	$= 6$
	1943

8.

$CH_3\underset{\displaystyle Br}{\underset{|}{C}}CH_3$ CH_3CHCH_2Br

$1 \times 1600 = 1600$ $9 \times 1 = 9$

$\frac{1600}{1609} = 99.4\%$ for bromination compared with 36% for chlorination

a. $CH_3CH_2CH_2CH_2CH_2Br$ $\quad$ $CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_2CH_3$ $\quad$ $CH_3CH_2CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$

$\frac{6}{498} = 1\%$ $\quad$ $\frac{164}{498} = 33\%$ $\quad$ $\frac{328}{498} = 66\%$

b. $BrCH_2\overset{\displaystyle CH_3}{\overset{|}{C}}HCH_2CH_2\overset{\displaystyle CH_3}{\overset{|}{C}}HCH_3$ $\quad$ $CH_3\overset{\displaystyle CH_3}{\overset{|}{C}}CH_2CH_2\overset{\displaystyle CH_3}{\overset{|}{C}}HCH_3$ $\quad$ $CH_3\overset{\displaystyle CH_3}{\overset{|}{C}}HCHCH_2\overset{\displaystyle CH_3}{\overset{|}{C}}HCH_3$

$\frac{12}{3540} = 0.3\%$ $\quad$ $\frac{3200}{3540} = 90.4\%$ $\quad$ $\frac{328}{3540} = 9.3\%$

g. $BrCH_2\overset{\displaystyle CH_3}{\overset{|}{C}}HCH_2CH_2CH_3$ $\quad$ $CH_3\overset{\displaystyle CH_3}{\overset{|}{C}}CH_2CH_2CH_3$ $\quad$ $CH_3\overset{\displaystyle CH_3}{\overset{|}{C}}HCHCH_2CH_3$

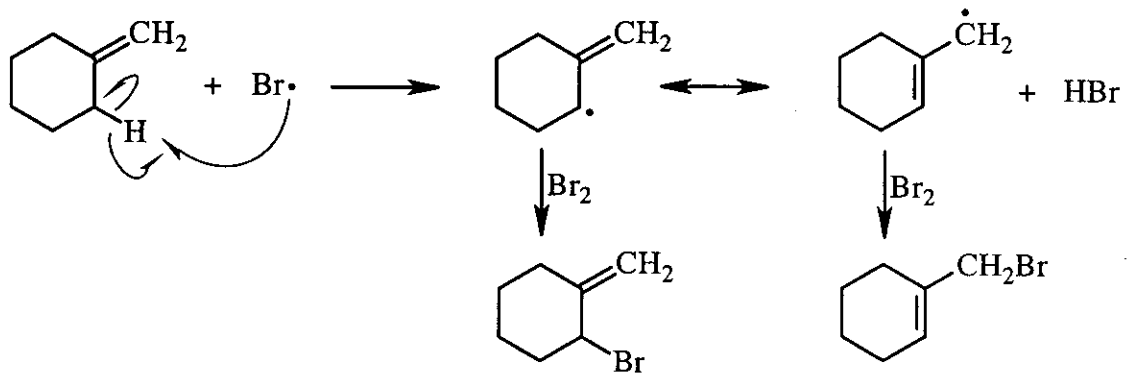
$\frac{6}{1937} = 0.3\%$ $\quad$ $\frac{1600}{1937} = 82.6\%$ $\quad$ $\frac{164}{1937} = 8.5\%$

$CH_3\overset{\displaystyle CH_3}{\overset{|}{C}}HCH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$ $\quad$ $\frac{164}{1937} = 8.5\%$

$CH_3\overset{\displaystyle CH_3}{\overset{|}{C}}HCH_2CH_2CH_2Br$ $\quad$ $\frac{3}{1937} = 0.2\%$

10. **a.** Chlorination, because the halogen is substituting for a primary hydrogen
b. Bromination, because the halogen is substituting for a tertiary hydrogen.
c. Because the molecule has only one kind of hydrogen, only one monohalogenated product will be obtained by both bromination and chlorination.

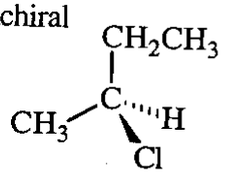
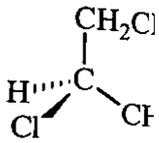
11.



12. Solved in the text.

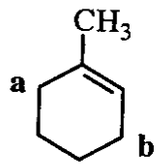
13.

a. $CH_3CH(CH_3)CH_3 \xrightarrow[h\nu]{Cl_2} CH_3CH(CH_2Cl)CH_3$ (achiral) + $CH_3C(Cl)(CH_3)CH_3$ (achiral)

b. $CH_3CH_2CH_2CH_3 \xrightarrow[h\nu]{Cl_2} CH_3CH_2CH_2CH_2Cl$ (achiral) +  (chiral) +  (chiral)

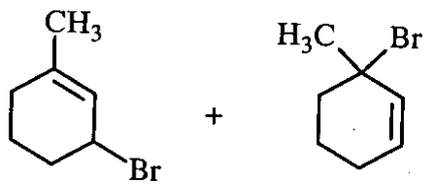
(chiral and chiral: enantiomers)

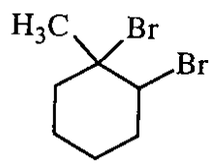
14.

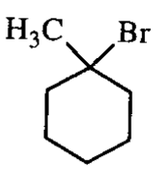


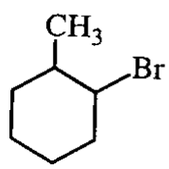
1-methylcyclohexene

a. **1.** There are two sets of allylic hydrogens, **a** and **b**. Removal of one of the **a** allylic hydrogen atoms forms an intermediate in which the unpaired electron is shared by two secondary carb Removal of one of the **b** allylic hydrogen atoms forms an intermediate in which the unpaired electron is shared by a tertiary carbon and a secondary carbon.
Therefore the major products are obtained by removing a **b** allylic hydrogen.

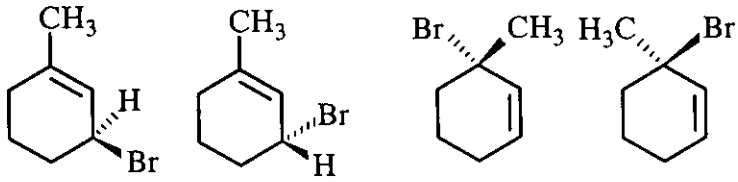


2. 

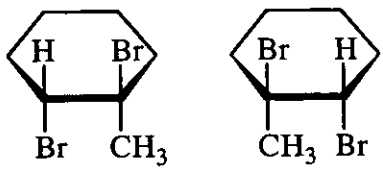
3. 

4. 

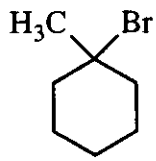
b. 1. Each of the products has one asymmetric carbon.
The *R* and the *S* isomer will be obtained for each product.



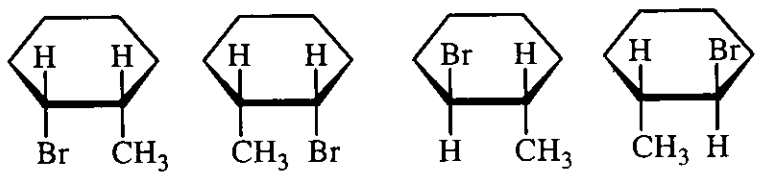
2. The product has two asymmetric carbons.
Because addition of Br_2 is anti, only the products with the bromine atoms on opposite sides of the ring are obtained.



3. The products does not have an asymmetric carbon, so it does not have stereoisomers.



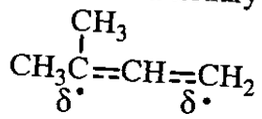
4. The product has two asymmetric carbons.
Because radical addition of HBr can be either syn or anti, four products are obtained.

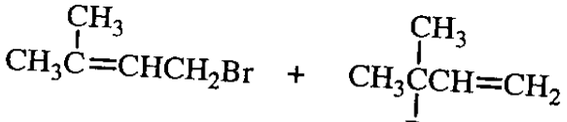


15.

a. $CH_2{=}CHCHCH_2CH_3$ (Br) + $BrCH_2CH{=}CHCH_2CH_3$

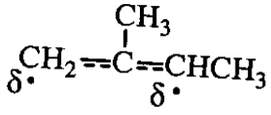
b. In the radical intermediate that leads to the major products, the unpaired electron is shared by a primary carbon and a tertiary carbocation.

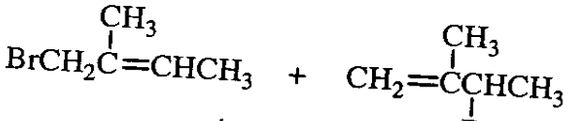




major products

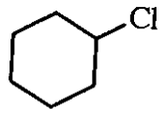
In the radical intermediate that leads to the minor products, the unpaired electron is shared by a primary and a secondary carbocation. It, therefore, is not as stable as the intemediate that leads to the major products.
In bromination, selectivity is much more important than probability, so even though twice as many hydrogens are available for removal by a bromine radical that leads to the minor products, they will be minor products because the easier to remove hydrogens lead to the major products.



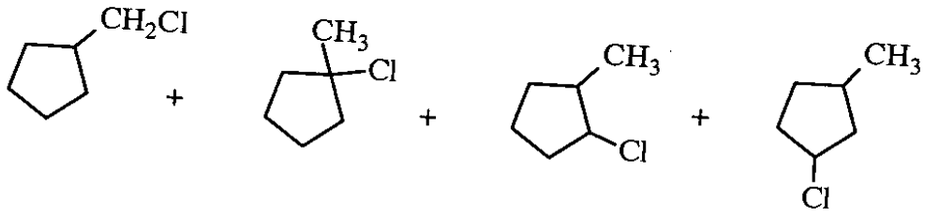


minor products

c. $CH_3CH_2C(CH_3)(Br)CH_2CH_2CH_3$ major product

d. 

e. no reaction

f. 

16.

a. $(CH_3)_3CCH_3$

dimethylpropane

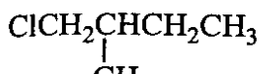
b. $CH_3CH_2CH(CH_3)CH_2CH_2CH_3$

3-methylhexane

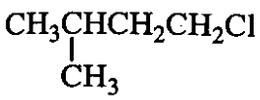


2-methylbutane

a primary alkyl halide

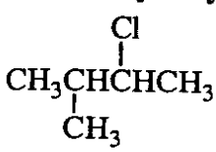


Substitution of any one of 6 hydrogens leads to this product.
percentage of this product that is formed = 36
percentage formed per hydrogen available = 36/6 = 6



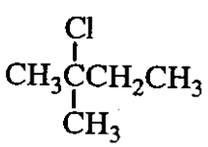
Substitution of any one of 3 hydrogens leads to this product.
percentage of this product that is formed = 18
percentage formed per hydrogen available = 18/3 = 6

a secondary alkyl halide



Substitution of any one of 2 hydrogens leads to this product.
percentage of this product that is formed = 28
percentage formed per hydrogen available = 28/2 = 14

a tertiary alkyl halide



Substitution of any one of 1 hydrogen leads to this product.
percentage of this product that is formed = 18
percentage formed per hydrogen available = 18/1 = 18

At 300 °C, the relative rates of removal of a hydrogen atom from a tertiary, secondary, and primary carbocation are:

$$18 : 14 : 6 = 3 : 2.3 : 1$$

In Section 9.3, we saw that at room temperature the relative rates are:

$$5 : 3.8 : 1$$

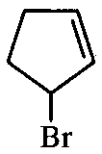
Thus we can conclude that at higher temperatures, there is less discrimination by the radical between a tertiary, seconday, and primary hydrogen atom.

18. The chlorine radical is more reactive at the higher temperature (600°C), so it is less selective.

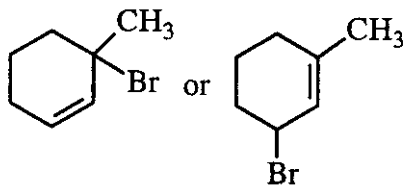
19. Abstraction of a hydrogen atom from ethane by an iodine radical is a highly endothermic reaction (ΔH° = 101 - 71 = 30 kcal/mol; see Table 3.1 on p. 129 of the text), so the iodine radicals will reform I_2 rather than abstract a hydrogen atom.

$$\underset{\text{101 kcal/mol}}{CH_3CH_3} + I\cdot \longrightarrow CH_3\dot{C}H_2 + \underset{\text{71 kcal/mol}}{HI}$$

20.

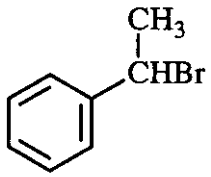
a. 

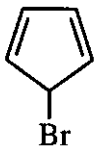
b. $CH_2{=}CHCHCH_2CH_3$ (Br on the CHCH) or $BrCH_2CH{=}CHCH_2CH_3$

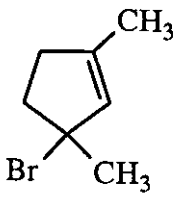
c. 

d. CH_3CHCH_2Cl (CH_3 on the CH)

e. CH_3CCH_3 (Br on the C)

f. 

g. 

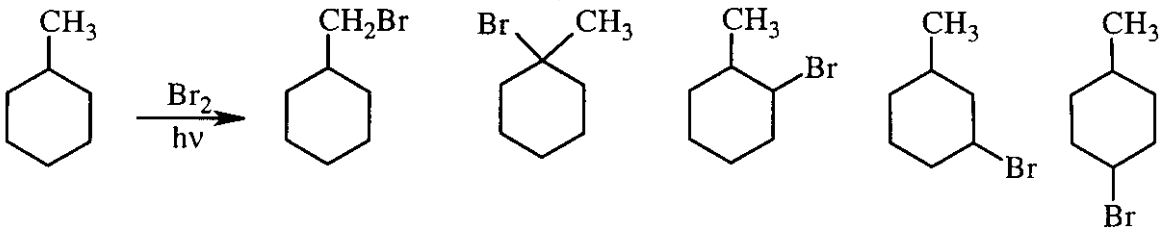
h. 

In **b** and **c**, because one product is under kinetic control and the other is under thermodynamic the major product will depend on the conditions under which the reaction is carried out.

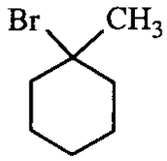
21. It is easier to break a C-H bond than a C-D bond.
(Deuterium is an isotope of hydrogen; it has an additional neutron.)
Because a bromine radical is less reactive than a chlorine radical, a bromine radical has a gr preference for the more easily broken C-H bond. Bromination, therefore, would have a gre deuterium kinetic isotope effect than chlorination.
This is reminiscent of the relative rates of 1600 : 1 for bromination and 5 : 1 for chlorination removal of a hydrogen from a tertiary carbon versus from a primary carbon.

22.

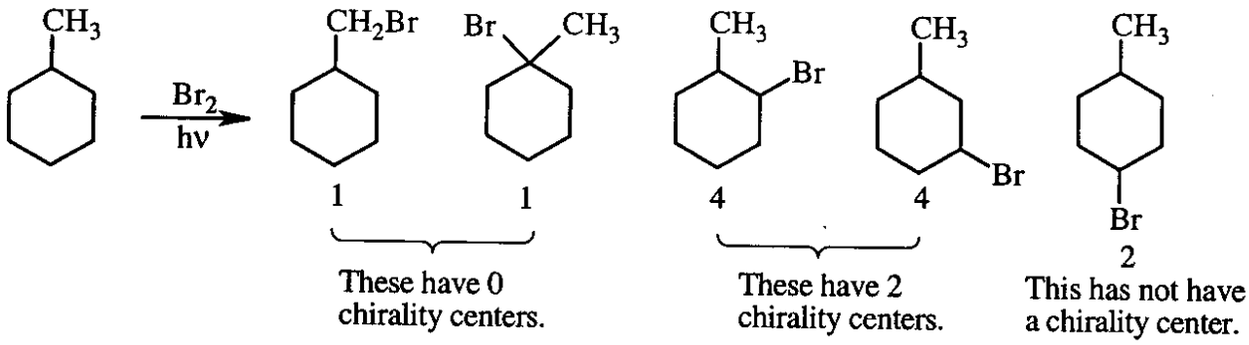
a. Theoretically five monobromination products are possible, but some will be obtained in very small amounts.



b. A bromine radical is very selective, much preferring to remove a hydrogen atom from a tertiary carbon than from a secondary or primary carbon. 1-Bromo-1-methylcyclohexane would be obtained in greatest yield because it is the only one formed by removing a hydrogen atom from a tertiary carbon.

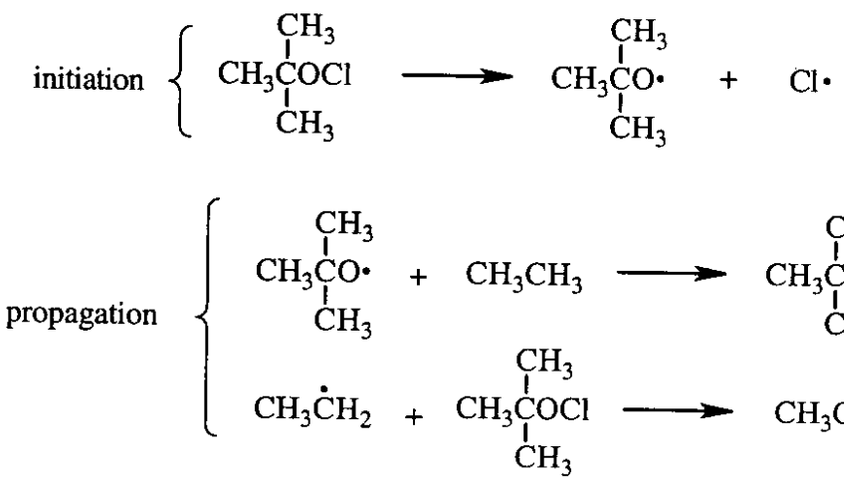


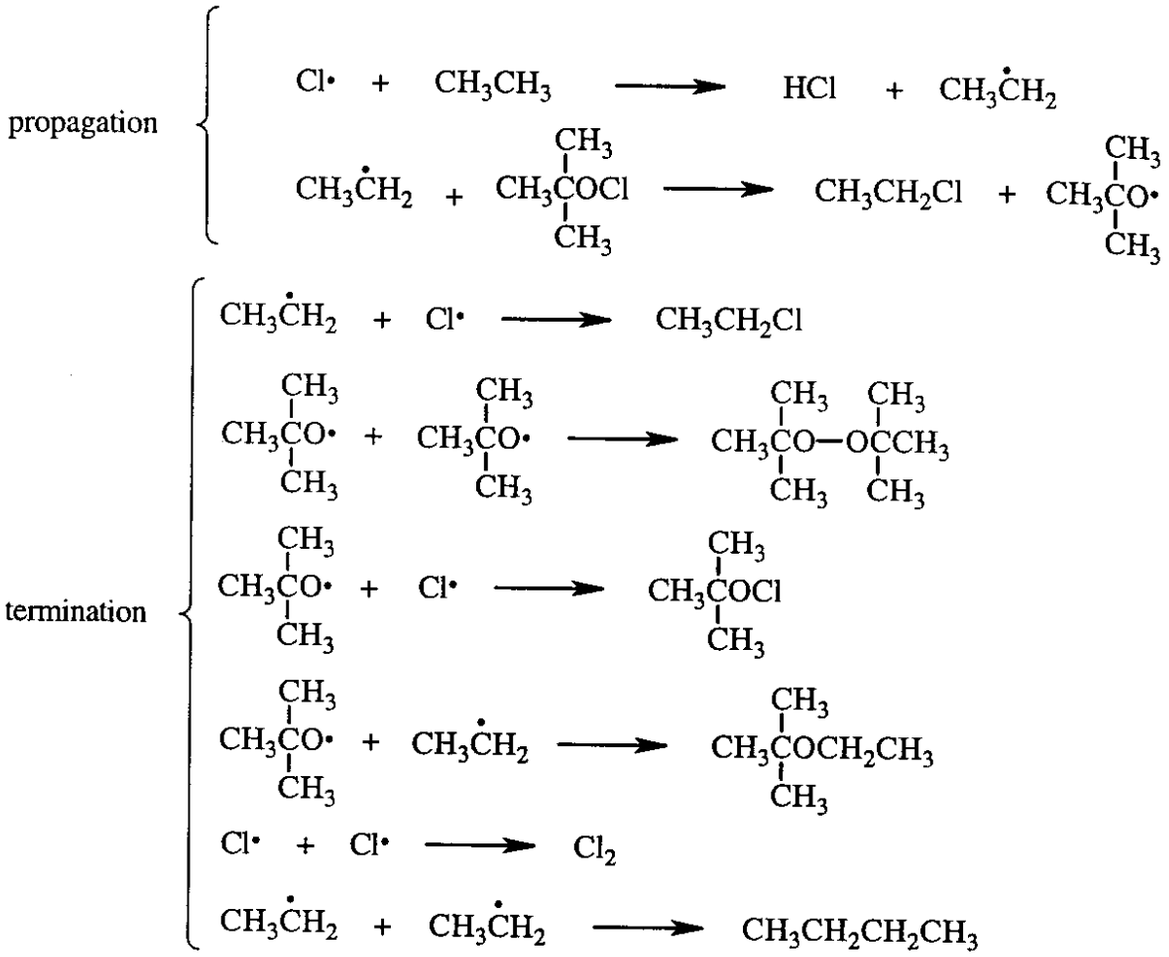
c. The number of possible isomers for each compound is indicated below each structure.



A total of 12 stereoisomers can be obtained.

23. **a.** One difference between this reaction and the monochlorination of ethane is the source of the chlorine radical. This reaction has two sets of propagation steps because two different radicals are generated in the initiation step. This reaction also has several more termination steps because of the two different radicals generated in the initiation step.





24.

a. ΔH° = bonds broken − bonds formed

CH_3-H	$Cl-Cl$	CH_3-Cl	$H-Cl$
105	58	84	103

ΔH° = [105 kcal/mol + 58 kcal/mol] − [84 kcal/mol + 103 kcal/mol]

ΔH° = 163 − 187 = −24 kcal/mol

b.

	ΔH°
$CH_3-H + {}^\bullet Cl \longrightarrow {}^\bullet CH_3 + H-Cl$	105 − 103 = 2 kcal/mol
${}^\bullet CH_3 + Cl-Cl \longrightarrow CH_3-Cl + {}^\bullet Cl$	58 − 84 = −26 kcal/mol
	−24 kcal/mol

c. If you cancel the things that are the same on opposite sides of the equations and then add the two equations, you are left with the equation in "**a**".

$$CH_3{-}H + \cancel{{}^{\bullet}Cl} \longrightarrow \cancel{{}^{\bullet}CH_3} + H{-}Cl$$

$$\cancel{{}^{\bullet}CH_3} + Cl{-}Cl \longrightarrow CH_3{-}Cl + \cancel{{}^{\bullet}Cl}$$

$$CH_4 + Cl_2 \longrightarrow CH_3Cl + HCl$$

25. The first propagation step is very endothermic, so it would not be able to compete with the first propagation step shown in Problem 24b.

		$\Delta H°$
$CH_3{-}H + {}^{\bullet}Cl \longrightarrow CH_3{-}Cl + {}^{\bullet}H$	$105 - 84 =$	21 kcal/mol
${}^{\bullet}H + Cl{-}Cl \longrightarrow H{-}Cl + {}^{\bullet}Cl$	$58 - 103 =$	−45 kcal/mol
		−24 kcal/mol

26. The methyl radical that is created in the first propagation step reacts with Br_2, forming bromomethane.

$$Br{\bullet} + CH_4 \longrightarrow {\bullet}CH_3 + HBr$$

$${\bullet}CH_3 + Br_2 \longrightarrow CH_3Br + {\bullet}Br$$

If HBr is added to the reaction mixture, the methyl radical that is created in the first propagation step can react with Br_2 or with the added HBr. Because reaction with HBr reforms methane, the overall rate of formation of bromomethane is decreased.

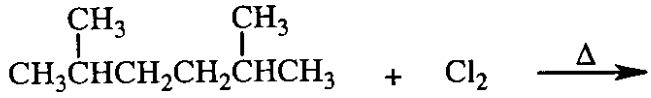
$$Br{\bullet} + CH_4 \longrightarrow {\bullet}CH_3 + HBr$$

$${\bullet}CH_3 + Br_2 \longrightarrow CH_3Br + {\bullet}Br$$

$${\bullet}CH_3 + HBr \longrightarrow CH_4 + {\bullet}Br$$

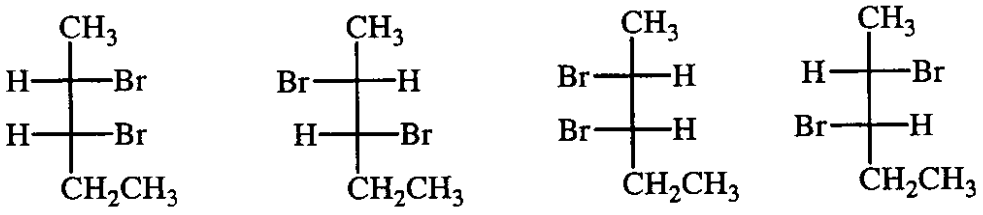
Chapter 9 Practice Test

1. How many monochlorinated products would be obtained from the following reaction? (Ignore stereoisomers.)



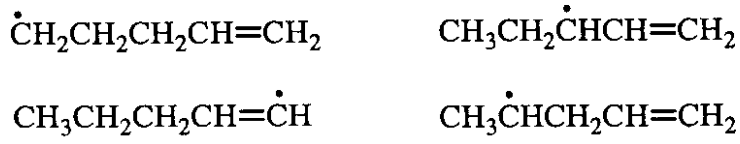
2. Give the first propagation step in the monochlorination of ethane.

3. When (*S*-)-2-bromopentane is brominated, 2,3-dibromopentanes are formed. Which of the following compounds are **not** formed?



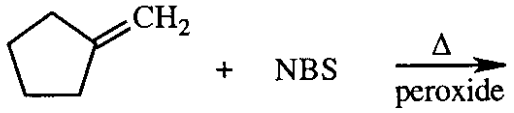
4. Determine the $\Delta H°$ of the two propagation steps in the monochlorination of ethane, using Table 3.1 on page 129 of the text.

5. Label the radicals in order of decreasing stability. (Label the most stable #1.)

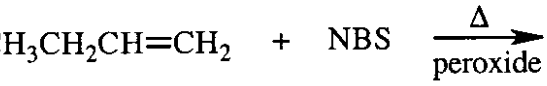


6. Give the product(s) of the following reactions, ignoring stereoisomers:

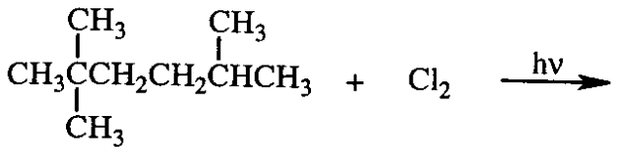
a.



b.



7. **a.** Give the products that will be obtained from monochlorination of the following alkane at room temperature: (Ignore stereoisomers.)



b. What product will be obtained in greatest yield?

c. What product would be obtained in greatest yield if the alkane were brominated instead of chlorinated?

8. Calculate the yield of 2-chloro-2-methylbutane formed when 2-methylbutane is chlorinated in the presence of light at room temperature.

CHAPTER 10
Substitution Reactions of Alkyl Halides

Important Terms

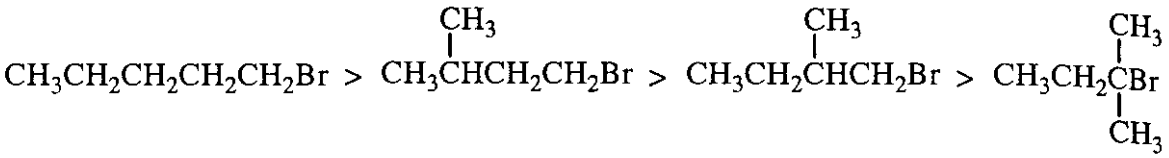
aprotic solvent	a solvent that does not have a hydrogen bonded to an oxygen or to a nitrogen.
backside attack	nucleophilic attack on the side of the carbon opposite to the side bonded to the leaving group.
base	a substance that accepts a proton.
basicity	describes the tendency of a compound to share its electrons with a proton.
bimolecular	involving two molecules.
complete racemization	formation of a pair of enantiomers in equal amounts.
dielectric constant	a measure of how well a solvent can insulate opposite charges from one another.
elimination reaction	a reaction that removes atoms or groups from the reactant to form a π bonc
first-order reaction	a reaction whose rate is dependent on the concentration of one reactant.
intimate ion pair	results when the covalent bond that joined the cation and anion has broken but the cation and anion are still next to each other.
inversion of configuration	turning the carbon inside out like an umbrella so that the resulting product has a configuration opposite to that of the reactant.
ion-dipole interaction	the interaction between an ion and the dipole of a molecule.
kinetics	the field of chemistry that deals with the rates of chemical reactions.
leaving group	the group that is displaced in a nucleophilic substitution reaction.
Le Châtelier's principle	states that if an equilibrium is disturbed, the components of the equilibriun will adjust in a way that will offset the disturbance.
nucleophile	an electron-rich atom or molecule.
nucleophilicity	a measure of how readily an atom or molecule with a lone pair attacks an atom.
nucleophilic substitution reaction	a reaction in which a nucleophile substitutes for an atom or group.
partial racemization	formation of a pair of enantiomers in unequal amounts.
protic solvent	a solvent that has a hydrogen bonded to an oxygen or to a nitrogen.
rate constant	describes how difficult it is to overcome the energy barrier of a reaction.

rate law	the equation that shows the relationship between the rate of a reaction and the concentration of the reactants.
second-order reaction	a reaction whose rate is dependent on the concentration of two reactants.
S_N1 reaction	a first-order nucleophilic substitution reaction.
S_N2 reaction	a second-order nucleophilic substitution reaction.
solvent-separated ion pair	results when the cation and anion are separated by one or more solvent molecules.
solvolysis	reaction with the solvent.
steric effects	effects due to the fact that groups occupy a certain volume of space.
steric hindrance	refers to bulky groups at the site of a reaction that make it difficult for the reactants to approach each other.
substitution reaction	a reaction that changes one substituent of a reactant for another.
unimolecular	involving one molecule.

Solutions to Problems

1. It decreases the magnitude of the rate constant, which causes the reaction to be slower.

2.



3. **a.** Solved in the text.

b. The S_N2 reaction of (*R*)-2-bromobutane with hydroxide ion will form (*S*)-2-butanol.

c. The S_N2 reaction of (*S*)-3-chlorohexane and with hydroxide ion will form (*R*)-3-hexanol.

d. The S_N2 reaction of 3-iodopentane (it does not have an asymmetric carbon) with hydroxid ion will form 3-pentanol (it does not have an asymmetric carbon).

4.

a. RO^- because ROH is a weaker acid than RSH.

b. RS^- because it is less well solvated by water.

5. **a.** aprotic **b.** aprotic **c.** protic **d.** aprotic

6. Solved in the text.

7.

a. $CH_3CH_2Br + HO^-$ HO^- is a stronger nucelophile than H_2O.

b. $CH_3CHCH_2Br + HO^-$ (with CH_3 on the CH) The alkyl halide has less steric hindrance.

c. $CH_3CH_2Cl + CH_3S^-$ CH_3S^- is a stronger nucleophile than CH_3O^- in a solvent that can form hydrogen bonds.

d. $CH_3CH_2Br + I^-$ Br^- is a weaker base than Cl^- so Br^- is a better leaving group.

8. Solved in the text.

9. **a.** Reaction of an alkyl halide with ammonia gives a low yield of primary amine because as soon as the primary amine is formed, it can react with another molecule of alkyl halide to form a secondary amine.

b. The alkyl azide is not treated with hydrogen until after all the alkyl halide has reacted with azide ion. Therefore, when the primary amine is formed, there is no alkyl halide for it to react with to form a secondary amine.

10. In each reaction, the conjugate acid of the leaving group is stronger than the conjugate acid of the nucleophile. That means the leaving group is the weaker base (better leaving group).

H_2O	HCl	$RC{\equiv}CH$	HBr
$pK_a = 15.7$	$pK_a = -7.0$	$pK_a = 25$	$pK_a = -9.0$
H_2S	HBr	$HC{\equiv}N$	HI
$pK_a = 7.0$	$pK_a = -9.0$	$pK_a = 9.1$	$pK_a = -10.0$
ROH	HI	$\overset{+}{N}H_4$	HBr
$pK_a = 15.5$	$pK_a = -10.0$	$pK_a = 9.4$	$pK_a = -9.0$
RSH	HBr	$CH_3CH_2\overset{+}{N}H_2CH_3$	HI
$pK_a = 10.5$	$pK_a = -9.0$	$pK_a = 10.8$	$pK_a = -10.0$
NH_3	HCl		
$pK_a = 36$	$pK_a = -7.0$		

11.

a. $CH_3CH_2OCH_3$ **c.** $CH_3CH_2\overset{+}{N}(CH_3)_3\ Br^-$

b. $CH_3CH_2N_3$ **d.** $CH_3CH_2SCH_2CH_3$

12.

$$CH_3CH_2Cl + K^+I^- \underset{}{\overset{\text{acetone}}{\rightleftharpoons}} CH_3CH_2I + K^+Cl^-$$

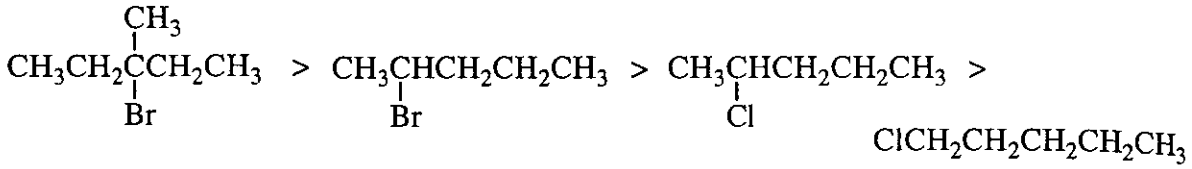
K^+Cl^- precipitates out in acetone, which drives the reaction to the right.

13.

$$\begin{matrix} CH_3 \\ | \\ CH_3CBr \\ | \\ CH_3 \end{matrix} > \begin{matrix} \\ \\ CH_3CHBr \\ | \\ CH_3 \end{matrix} > CH_3CH_2CH_2Br > CH_3Br$$

14. Because ethyl bromide and methyl bromide cannot dissociate to form a carbocation (the carbocation is too unstable to be formed), the alkyl halides have to react by an S_N2 pathway. The nucleophile (H_2O) is very weak, so the S_N2 reactions are very slow.

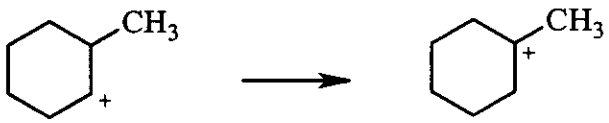
15.



16. **a.** The secondary carbocation that is formed initially will undergo a 1,2-hydride shift to form a tertiary carbocation.



b. The secondary carbocation that is formed initially will undergo a 1,2-hydride shift to form a tertiary carbocation.



c. The secondary carbocation that is formed initially will undergo a 1,2-methyl shift to form a tertiary carbocation.

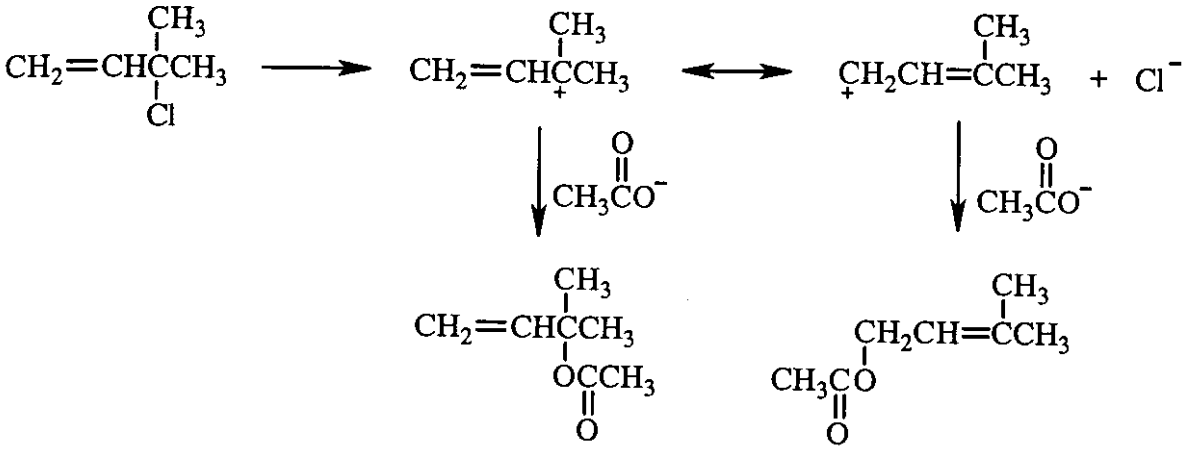


d. The same substitution product will be obtained from S_N1 and S_N2 reactions. Notice that because the configuration of the asymmetric carbon is not specified, the configuration of th product cannot be specified. If the configuration at C-4 were specified, one stereoisomer would be obtained from an S_N2 reaction (the product with the inverted configuration compared to the configuration of the reactant), and two products would be obtained (one w the inverted configuration and one with the retained configuration) from an S_N1 reaction.

e. This alkyl halide cannot undergo an S_N1 reaction because an S_N1 reaction would require t formation of an primary carbocation. It can only undergo an S_N2 reaction. So no product would form in an S_N1 reaction.

f. The same substitution product will be obtained from S_N1 and S_N2 reactions. However, the S_N2 reaction would be quite slow because of steric hindrance.

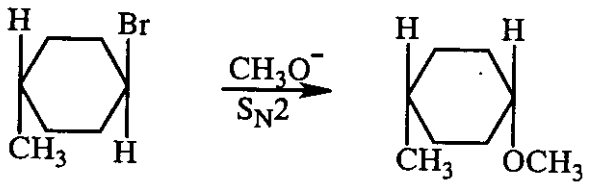
17.



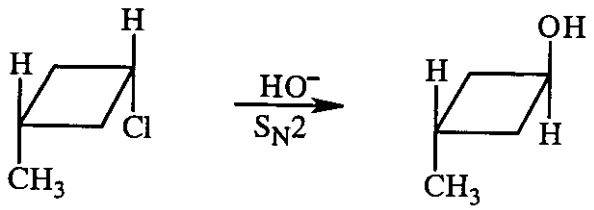
18. The trans isomer will be formed in greater yield because the departing bromide ion can block the approach of the incoming nucleophile to the side of the carbocation vacated by the bromide ion.

19. **a.**

1. The reactant does not have any asymmetric carbons.
The S_N2 reaction proceeds with back-side attack.

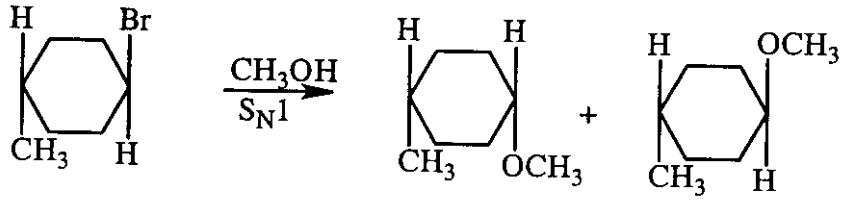


2. The reactant does not have any asymmetric carbons.
The S_N2 reaction proceeds with back-side attack.

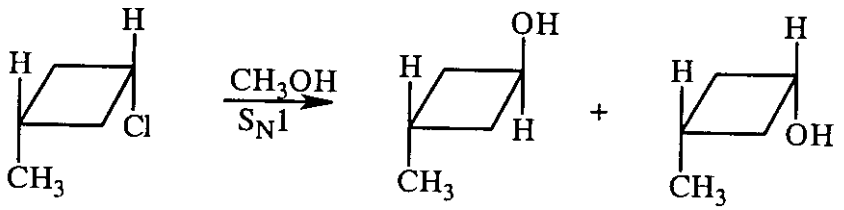


b.

1.



2.



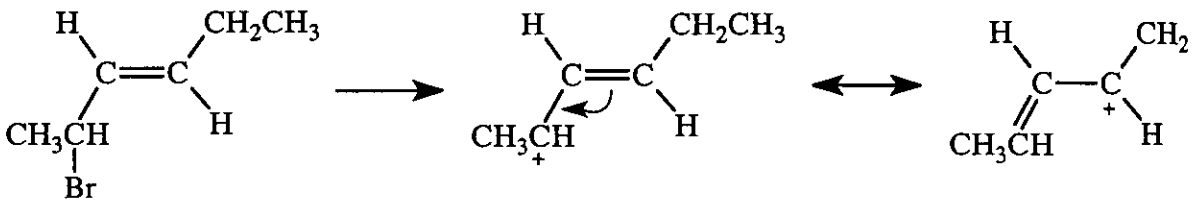
20. Because the rate of an S_N1 reaction is not affected by increasing the concentration of the nucleophile, while the rate of an S_N2 reaction is increased when the concentration of the nucleophile is increased, you first have to determine whether the reactions are S_N1 or S_N2 reactions.

a is an S_N2 reaction because the configuration of the product is inverted compared with the reactant.
b is an S_N2 reaction because the reactant is a primary alkyl halide.
c is an S_N1 reaction because the reactant is a tertiary alkyl halide.

Because they are S_N2 reactions, **a** and **b** will go faster if the concentration of the nucleophile is increased.

Because it is an S_N1 reaction, the rate of **c** will not change if the concentration of the nucleophile is increased.

21. *trans*-4-Bromo-2-hexene is more reactive in an S_N1 solvolysis reaction, because the carbocation that is formed is stabilized by electron delocalization. (It is a secondary allylic carbocation.) The carbocation formed by the other alkyl halide is less stable because the secondary carbocation cannot be stabilized by resonance.



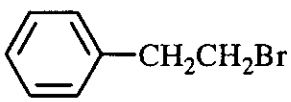
22.

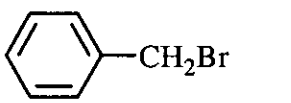
a. $CH_3CH_2CH_2I$ — I^- is a weaker base than Br^-, so I^- is a better leaving group.

b. CH_3OCH_2Cl — The electron-withdrawing methoxy group increases the electrophilicity of the carbon bonded to the leaving group.

c. $CH_3CH_2\underset{\displaystyle CH_3}{\overset{|}{C}}HBr$ — This compound has less steric hindrance.

d. $CH_3CH_2\underset{\displaystyle CH_3}{\overset{|}{C}}HCH_2Br$ — A primary carbon is less sterically hindered than a secondary carbon.

e.  — A primary carbon is less sterically hindered than a secondary carbon.

f.  — Nucleophilic attack cannot occur on an sp^2 hybridized carbon.

g. $CH_3CH{=}CH\underset{\displaystyle Br}{\overset{|}{C}}HCH_3$ — Nucleophilic attack cannot occur on an sp^2 hybridized carbon.

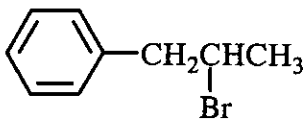
23.

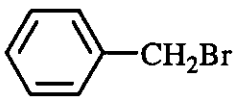
a. $CH_3CH_2CH_2I$ — I^- is a weaker base than Br^-, so I^- is a better leaving group.

b. CH_3OCH_2Cl — The methoxy group stabilizes the carbocation by resonance electron donation.

c. The two compounds are equally reactive.

d. $CH_3CH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HBr$ — A secondary carbocation is more stable than a primary carbocation.

e.  — A secondary carbocation is more stable than a primary carbocation.

f.  — A benzyl cation is more stable than an aryl cation.

g. $CH_3CH{=}CH\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$ — An allyl cation is more stable than a vinyl cation.

24.

a. $CH_3CH{=}CHCH_2Br \xrightarrow{CH_3O^-} CH_3CH{=}CHCH_2OCH_3$

b.

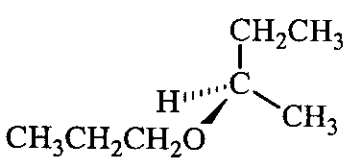
$$CH_3CH{=}CHCH_2Br \longrightarrow CH_3CH{=}\overset{+}{C}HCH_2 \longleftrightarrow CH_3\overset{+}{C}HCH{=}CH_2$$

$$\downarrow CH_3O^- \qquad\qquad \downarrow CH_3O^-$$

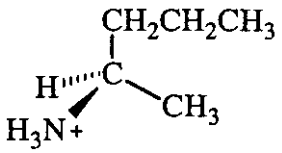
$$CH_3CH{=}CHCH_2OCH_3 \quad + \quad CH_3\underset{\displaystyle OCH_3}{\underset{|}{C}}HCH{=}CH_2$$

25.

a. An S_N2 reaction, because of the high concentration of a good nucleophile.

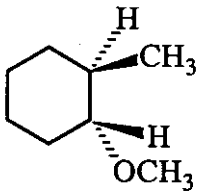


b. An S_N2 reaction, because a good nucleophile is used.

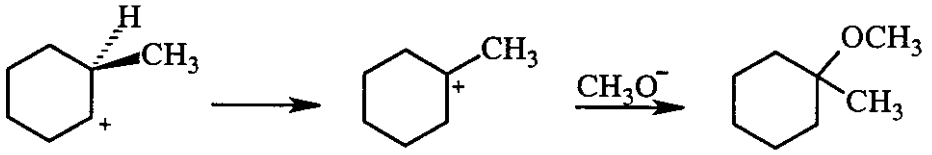


Even though ammonia is not negatively charged, it is a good nucleophile. Recall that an amine is a much stronger base than an alcohol. (The pK_a of a protonated alcohol is ~ −2.5. The pK_a of the ammonium ion is 9.4; see Appendix II in the text.)

c. An S_N2 reaction, because of the high concentration of a good nucleophile.

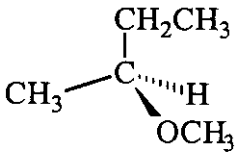


d. An S_N1 reaction, because a poor nucleophile is used. Notice that the initially formed secondary carbocation rearranges to a more stable tertiary carbocation.

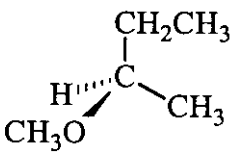


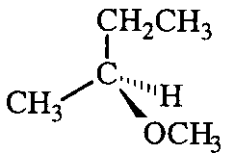
The product does not have a chirality center.

e. An S_N2 reaction, because of the high concentration of a good nucleophile.

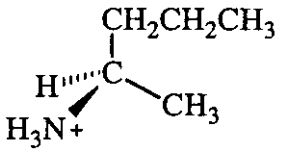


f. An S_N1 reaction, because a poor nucleophile is used.



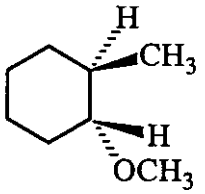


b. An S_N2 reaction, because a good nucleophile is used.

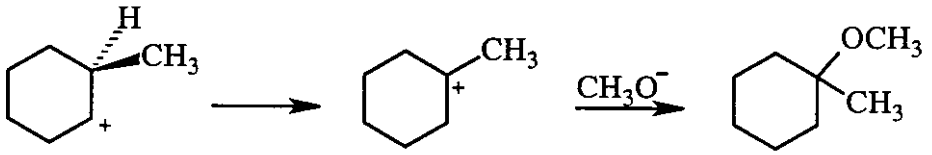


Even though ammonia is not negatively charged, it is a good nucleophile. Recall that an amine is a much stronger base than an alcohol. (The pK_a of a protonated alcohol is ~ −2.5. The pK_a of the ammonium ion is 9.4; see Appendix II in the text.)

c. An S_N2 reaction, because of the high concentration of a good nucleophile.

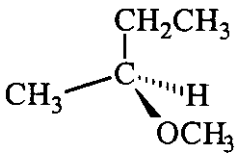


d. An S_N1 reaction, because a poor nucleophile is used. Notice that the initially formed secondary carbocation rearranges to a more stable tertiary carbocation.



The product does not have a chirality center.

e. An S_N2 reaction, because of the high concentration of a good nucleophile.



f. An S_N1 reaction, because a poor nucleophile is used.



26. **a.** Solved in the text.

b. $$\frac{S_N2}{S_N2 + S_N1} = \frac{k_2[\text{2-bromobutane}]\,[HO^-]}{k_2[\text{2-bromobutane}]\,[HO^-] + k_1[\text{2-bromobutane}]}$$

$$\frac{S_N2}{S_N2 + S_N1} = \frac{3.20 \times 10^{-5} \times 1 \times 10^{-3}}{3.20 \times 10^{-8} + 1.50 \times 10^{-6}} = \frac{3.20 \times 10^{-8}}{3.20 \times 10^{-8} + 150 \times 10^{-8}} = \frac{3.20}{153} = .02$$

$$= 2\,\%$$

27. **a.** Increasing the polarity will decrease the rate of the reaction because the concentration of charge on the reactants is greater (the reactants are charged) than the concentration of charge on the transition state.

b. Increasing the polarity will decrease the rate of the reaction because the concentration of charge on the reactants is greater (the reactants are charged) than the concentration of charge on the transition state.

c. Increasing the polarity will increase the rate of the reaction because the concentration of charge on the reactants is less (the reactants are not charged) than the concentration of charge on the transition state.

28.

a. $CH_3Br + HO^- \longrightarrow CH_3OH + Br^-$

HO^- is a better nucleophile than H_2O.

b. $CH_3I + HO^- \longrightarrow CH_3OH + I^-$

I^- is a better leaving group than Cl^-.

c. $CH_3Br + NH_3 \longrightarrow CH_3\overset{+}{N}H_3 + Br^-$

NH_3 is a better nucleophile than H_2O.

d. $CH_3Br + HO^- \xrightarrow{DMSO} CH_3OH + Br^-$

DMSO will not stabilize the nucleophile by hydrogen bonding.

e. $CH_3Br + NH_3 \xrightarrow{EtOH} CH_3\overset{+}{N}H_3 + Br^-$

The more polar solvent will be more able to stabilize the transition state.

29. Solved in the text.

30. Acetate ion will be a more reactive nucleophile in dimethyl sulfoxide because dimethyl sulfox will not stabilize the nucleophile by hydrogen bonding, while methanol will stabilize it by hydrogen bonding.

31. Only an S_N1 reaction will give the product with retention of configuration. Since the S_N1 reaction is favored by a polar solvent, a greater percentage of the reaction will take place by an S_N1 pathway in 50% water/50% ethanol, the more polar of the two solvents.

32.

a. CH_3OH **b.** CH_3NH_2 **c.** CH_3SH **d.** CH_3SH **e.** CH_3OCH_3 **f.** $CH_3\overset{+}{N}H_2CH_3$

(Notice that the product in "c" is not protonated because its pK_a is ~ -7; the product in "f" is protonated because its pK_a is ~ 11).

33. **a.**

1. $3° > 2° > 1°$
2. An S_N1 reaction is not affected by the strength of the nucleophile, but a weak nucleophile favors an S_N1 by disfavoring an S_N2 reaction.
3. An S_N1 reaction is not affected by the concentration of the nucleophile, but a low concentration of a nucleophile favors an S_N1 by disfavoring an S_N2 reaction.
4. If the reactant is charged, an S_N1 reaction will be favored by the least polar solvent that will dissolve the reactant.
   If the reactant is not charged, an S_N1 reaction will be favored by a protic polar solvent.

b.

1. $1° > 2° > 3°$
2. A strong nucleophile favors an S_N2 reaction.
3. A high concentration of a nucleophile favors an S_N2 reaction.
4. If the reactant is charged, an S_N2 reaction will be favored by the least polar solvent that will dissolve the reactant (generally an aprotic polar solvent).
   If the reactant is not charged, an S_N2 reaction will be favored by a protic polar solvent.

34. If the atoms are in the same row, the stronger base is the stronger nucleophile. If the atoms are in the same column, the larger atom is the stronger nucleophile because the solvent will form stronger hydrogen bonds with the smaller atom.

a. HO^- **c.** H_2S **e.** I^-

b. $^-NH_2$ **d.** HS^- **f.** Br^-

35. The weaker base is the better leaving group.

a. H_2O **c.** H_2S **e.** I^-

b. NH_3 **d.** HS^- **f.** Br^-

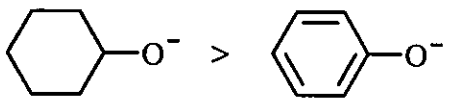
36.

a. HO^- **c.** HS^- **e.** CH_3NH_2 **g.** $CH_3\overset{\overset{O}{\|}}{C}O^-$

b. CH_3O^- **d.** $CH_3CH_2S^-$ **f.** $^-C{\equiv}N$ **h.** $CH_3C{\equiv}C^-$

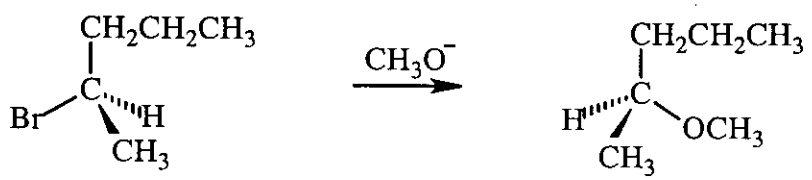
37.

a. $CH_3CH_2S^- > CH_3CH_2O^- > CH_3\overset{\overset{O}{\|}}{C}O^-$ **c.** $NH_3 > H_2O$

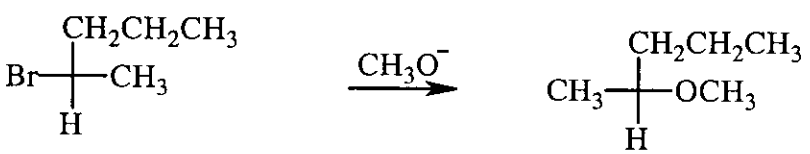
b.  **d.** $I^- > Br^- > Cl^-$

38. The pK_a would increase (it would be a weaker acid) because of a decreased tendency to form a charged species in a less polar solvent.

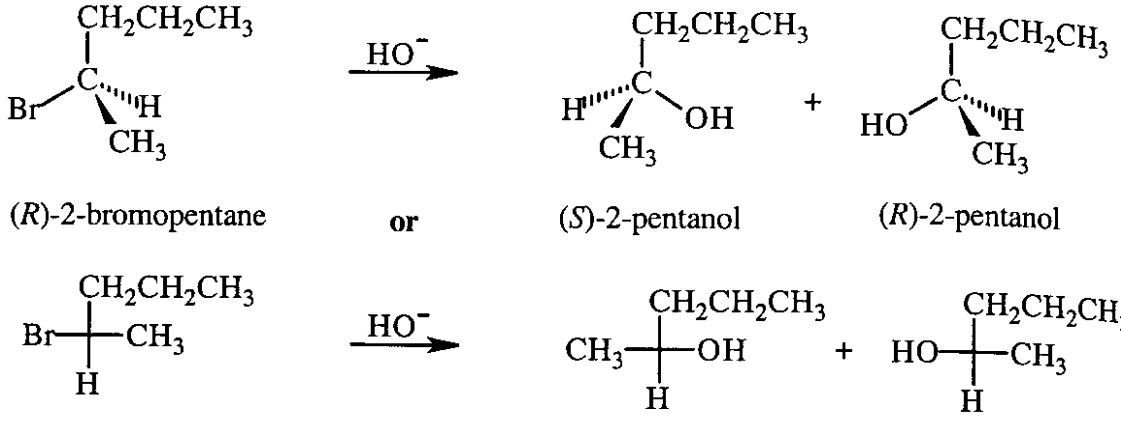
39. **a.** The S_N2 reaction proceeds with inversion of configuration.



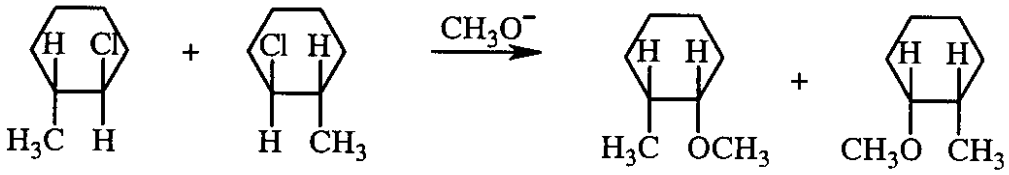
(*R*)-2-bromopentane **or** (*S*)-2-pentanol



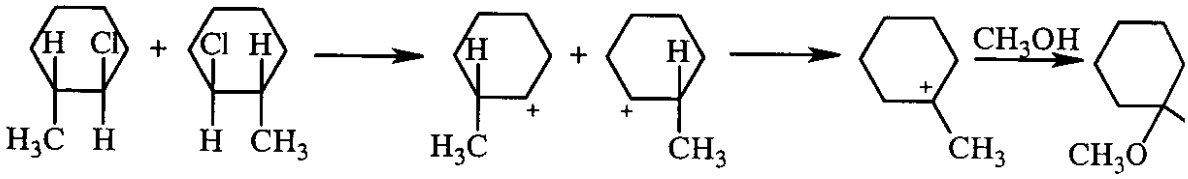
b. The S_N1 reaction proceeds with racemization (either complete or partial).



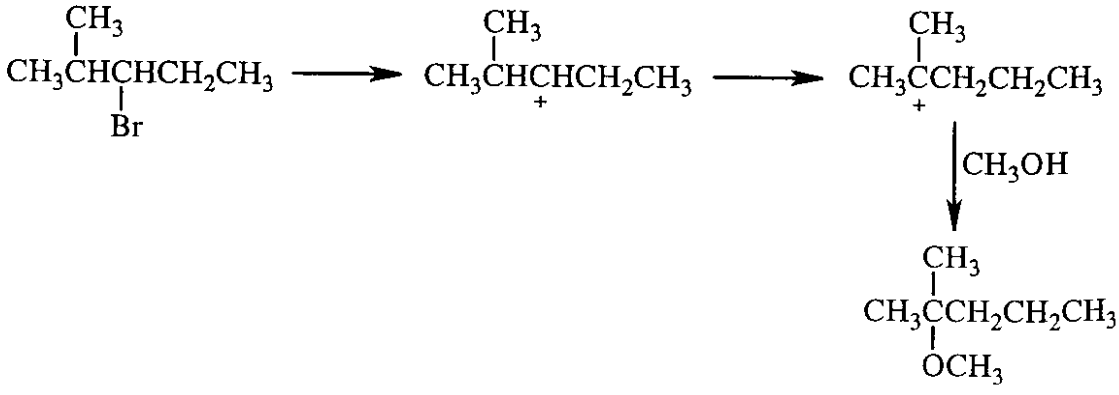
c. *trans*-1-Chloro-2-methylcyclohexane exists as a pair of enantiomers. The S_N2 reaction proceeds with back-side attack.



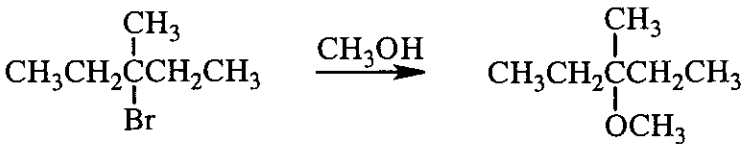
d. *trans*-1-Chloro-2-methylcyclohexane exists as a pair of enantiomers. The asymmetric carbon is lost when the carbocation that is formed in the S_N1 reaction undergoes a 1,2-hydride shift.



e. 3-Bromo-2-methylpentane exists as a pair of enantiomers. The asymmetric carbon is lost when the carbocation that is formed in the S_N1 reaction undergoes a 1,2-hydride shift.

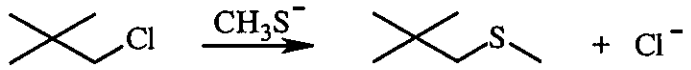


f. 3-Bromo-3-methylpentane does not have an asymmetric carbon.

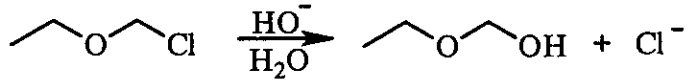


40. Methoxide ion will be a stronger nucleophile in DMSO because DMSO cannot stabilize the anion by hydrogen bonding.

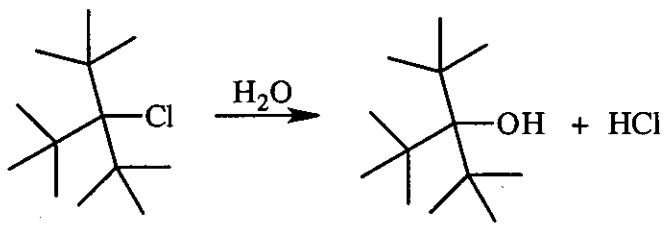
41.

a. 

The nucleophile is less sterically hindered.

b. 

The electron-withdrawing oxygen increases the electrophilicity of the carbon that the nucleophile attacks.

c. 

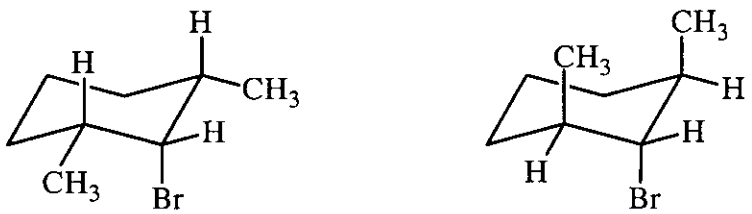
Steric strain is decreased when Cl^- dissociates to form the carbocation in the rate-limiting step since the hybridization of the carbon atom changes from sp^3 to sp^2, allowing the bond angle between the bulky groups to increase from 109.5° to 120°.

d. $(CH_3)_3CBr \xrightarrow{H_2O} (CH_3)_3COH + HBr$

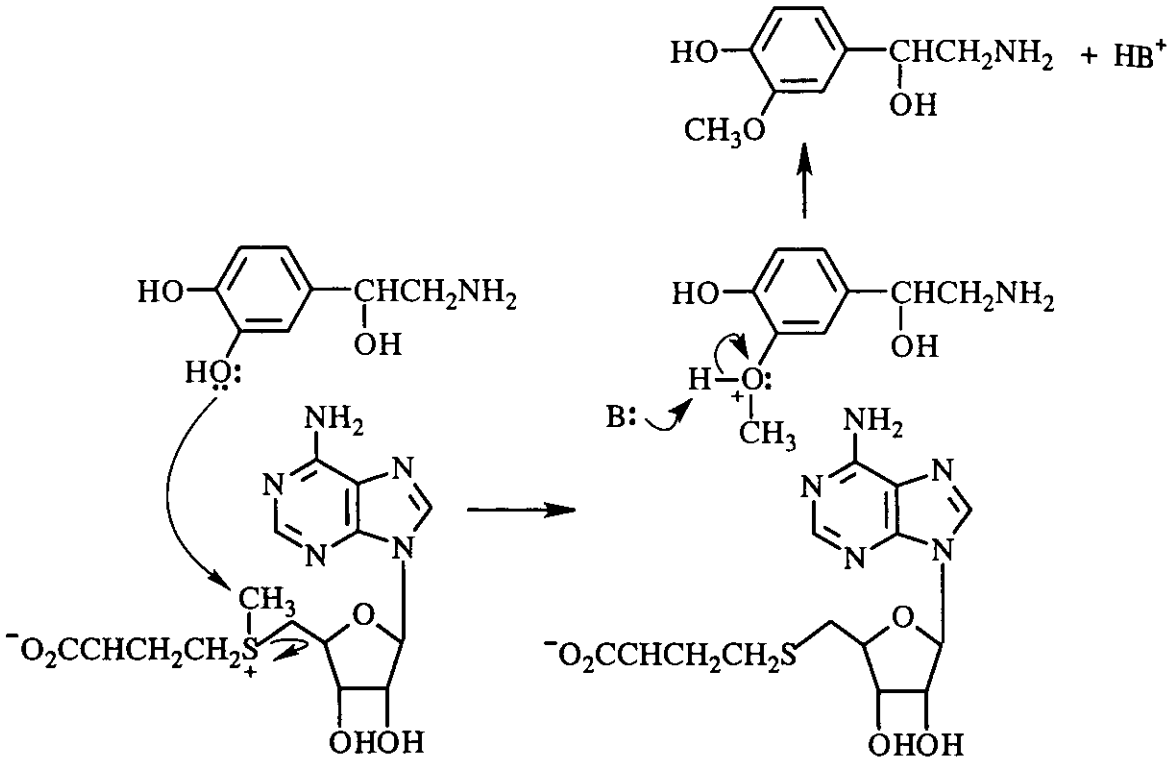
Because the reactants are neutral, the reaction will be faster in the more polar solvent.

42. The all-cis isomer is more reactive in an S_N2 reaction.

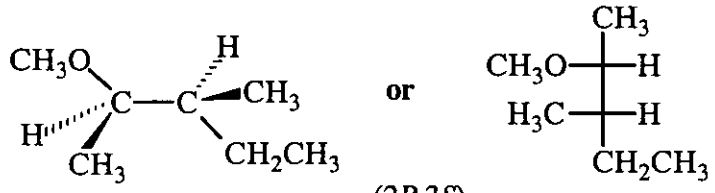
In an S_N2 reaction, the leaving group must be in an axial position in order to allow backside attack to occur without steric hindrance from the cyclohexane ring. When the bromine is in the axial position in the all-cis isomer, both methyl substituents are in equatorial positions, so the reaction takes place via the most stable conformer. In the other isomer, the conformer with bromine in the axial position (the reactive conformer) has both methyl substituents in less stable axial positions.



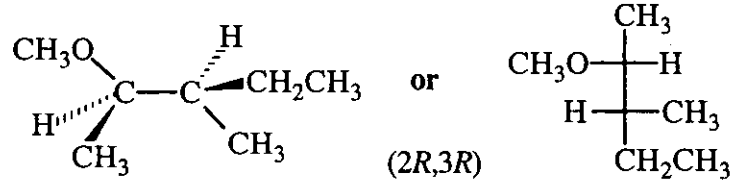
43.



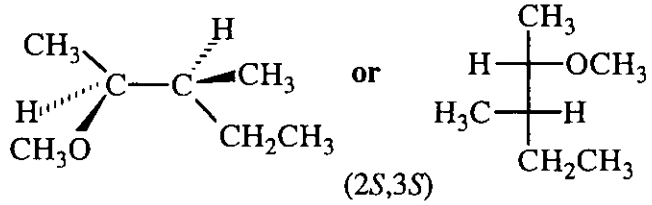
44.

a. 

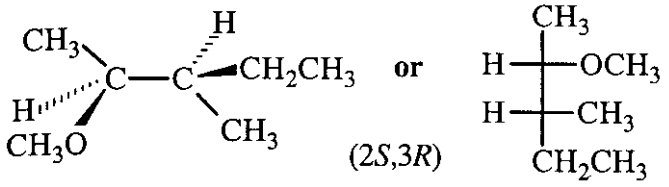
(2*R*,3*S*)

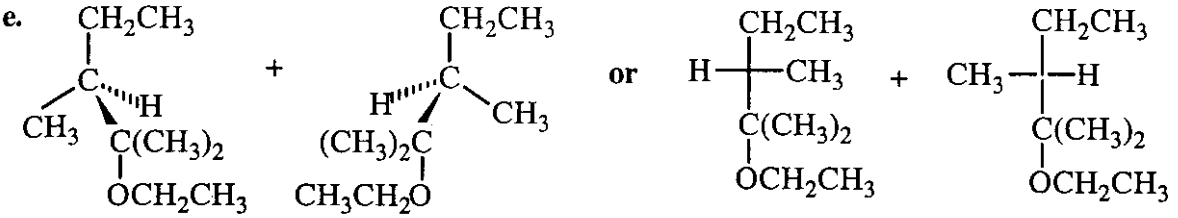
b. 

(2*R*,3*R*)

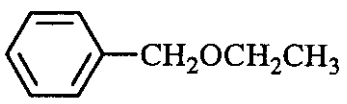
c. 

(2*S*,3*S*)

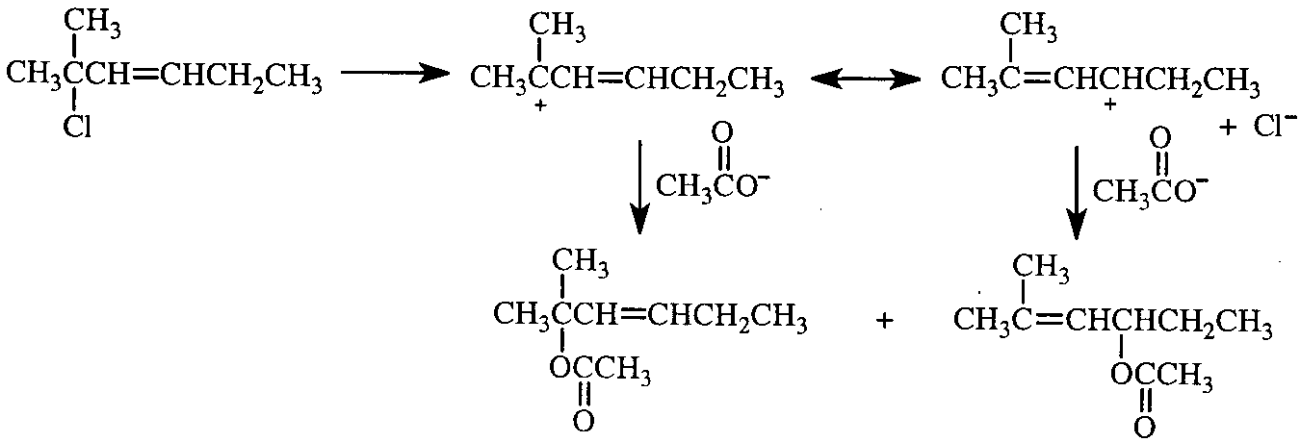
d. 

e. 

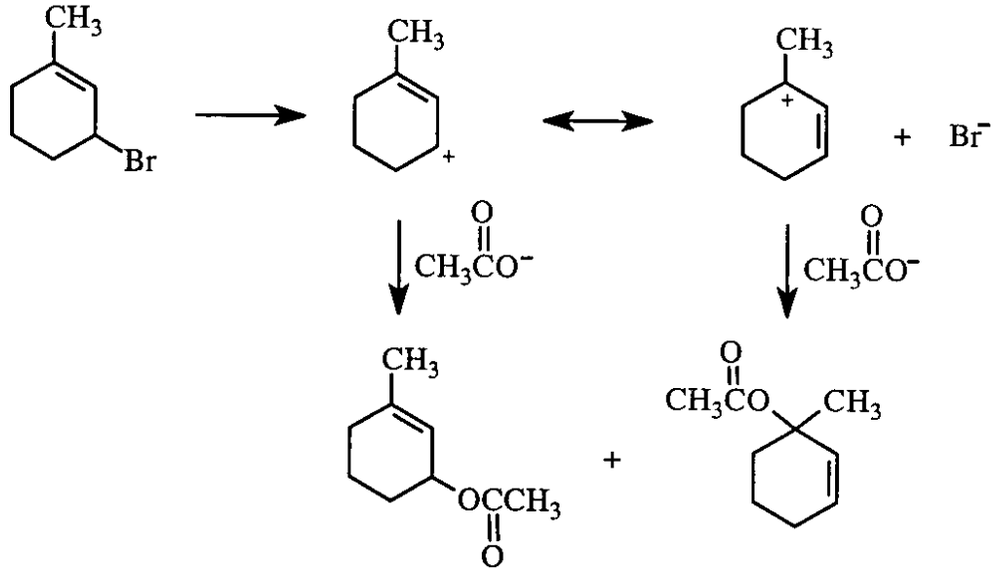
The alkyl halide dissociates to form a carbocation that undergoes a 1,2-methyl shift. Because the carbocation is planar, the methly groups with its pair of electrons can add either to the top or the bottom of the carbocation.
Therefore, the asymmetric carbon in the product can have either the *R* or the *S* configuration.

f. 

45. **a.** We can predict that this is an S_N1 reaction, because acetate ion is a relatively weak nucleophile and the alkyl halide are sterically hindered.



b. We can predict that this is an S_N1 reaction, because acetate ion is a relatively weak nucleophile.

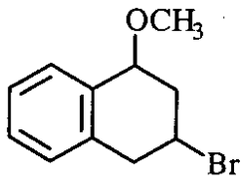


46. **a.** The reaction with quinuclidine had the larger rate constant because quinuclidine is less sterically hindered as a result of the substituents on the nitrogen being pulled back into a ring structure.

b. The reaction with quinuclidine had the larger rate constant for the same reason given in **a.**

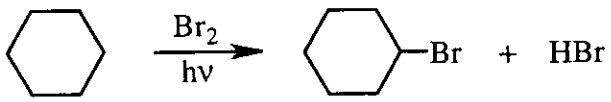
c. Isopropyl iodide had the larger ratio because, since it is more sterically hindered than methyl iodide, it is more affected by differences in the amount of steric hindrance in the nucleophile.

47. Because methanol is a poor nucleophile, the reaction will take place predominately via an S_N1 pathway. A secondary benzylic carbocation is more stable and, therefore, is easier to form than a secondary carbocation, so the product will be the one shown.

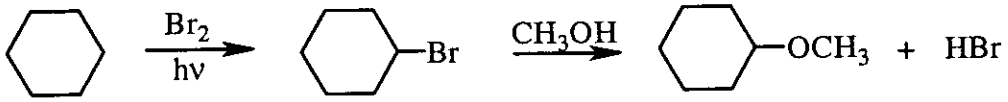


48.

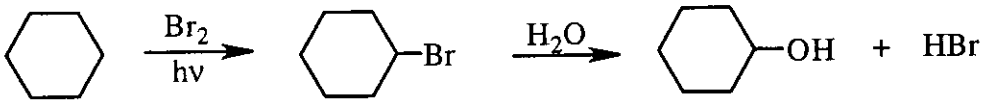
a.



b.

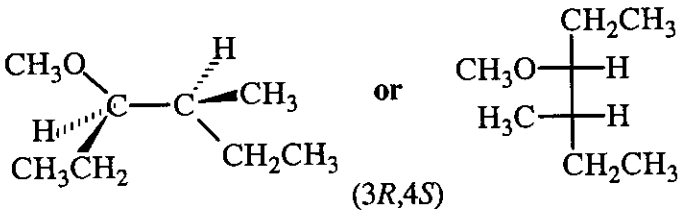


c.



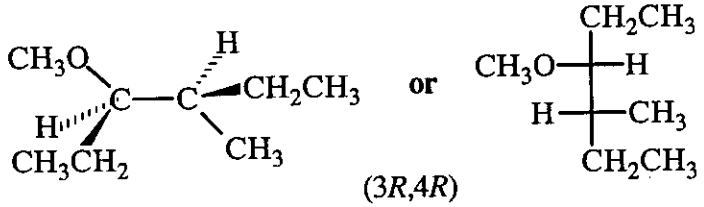
49.

a.



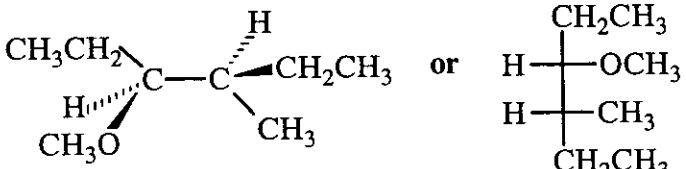
(3*R*,4*S*)

b.



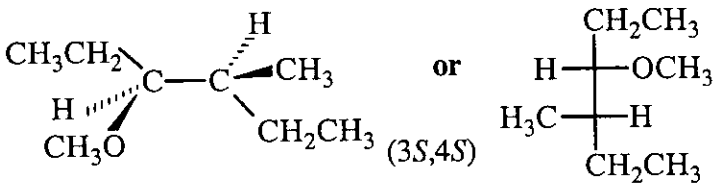
(3*R*,4*R*)

c.



(3*S*,4*R*)

d.

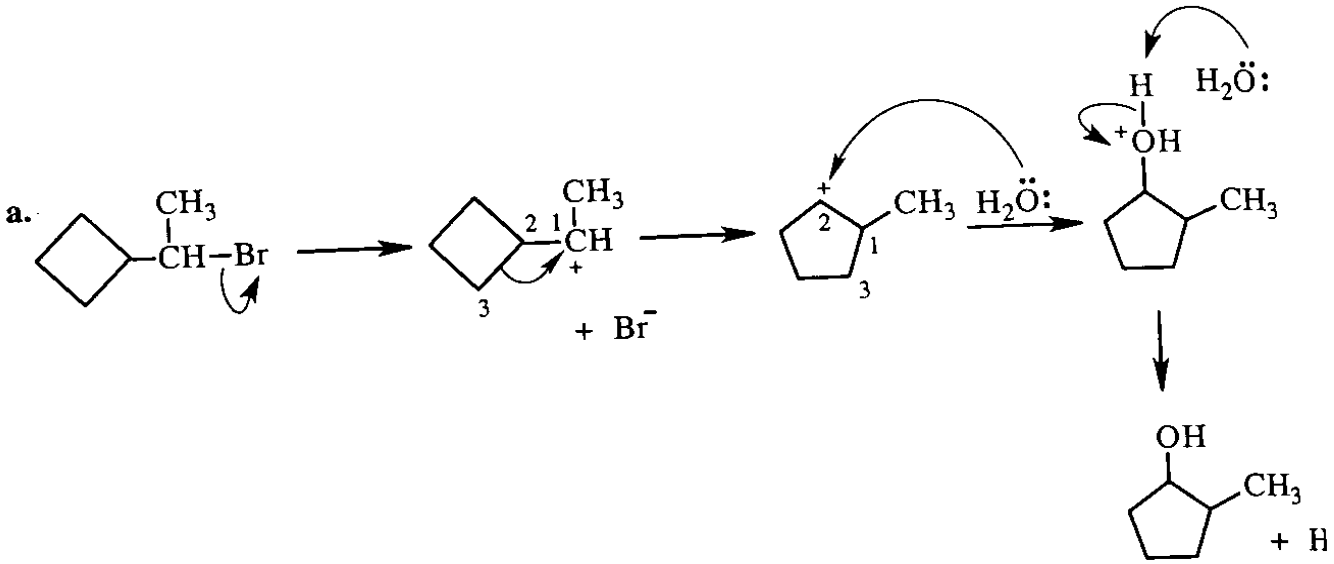


(3*S*,4*S*)

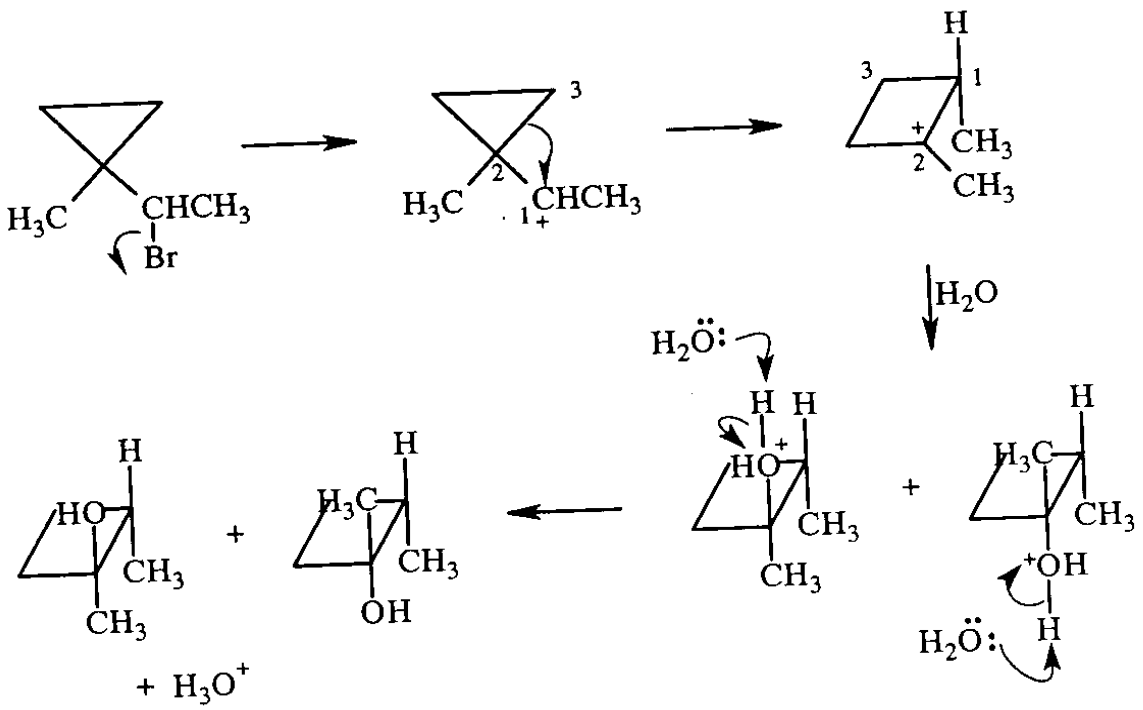
50. Tetrahydrofuran can solvate a charge better because the floppy ethyl substituents of diethyl ether provide steric hindrance, making it difficult for the nonbonding electrons of the oxygen to approach the compound to be solvated.

51.

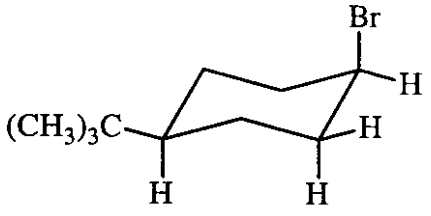
a.


CH3
CH–Br
CH3
CH
+ Br−
CH3
H2Ö:
H
+OH
CH3
OH
CH3
+ H

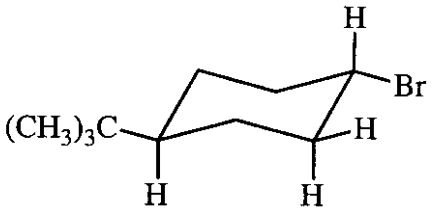
b.


H3C
CHCH3
Br
H3C
CHCH3
H
CH3
CH3
H2O
H2Ö:
HO
CH3
CH3
H3C
CH3
+OH
H2Ö:
H
HO
CH3
CH3
H3C
CH3
OH
+ H3O+

52. The cis isomer would be expected to react faster in an S_N1 reaction.
The rate-limiting step in an S_N1 reaction is formation of the carbocation intermediate.
Both isomers form the same carbocation. The cis isomer (with one substituent in the equatorial position and one in the axial position) is less stable than the trans isomer (with both substituents in the equatorial position). Since the cis isomer is less stable, it has the smaller energy of activation and, therefore, the faster reaction rate.

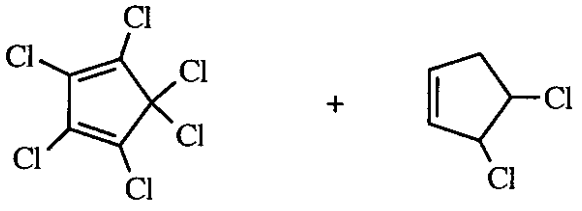


cis-1-bromo-4-*tert*-butylcyclohexane



trans-1-bromo-4-*tert*-butylcyclohexane

53. A Diels-Alder reaction between hexachlorocyclopentadiene and 3,4-dichlorocyclopentene forms Chlordane.



54. It will not undergo an S_N2 reaction, because of steric hindrance to backside attack.

It will not undergo an S_N1 reaction, because the carbocation that would be formed is unstable, since the ring structure prevents it from achieving the 120° bond angles required for an sp^2 hybridized carbon.

Chapter 10 Practice Test

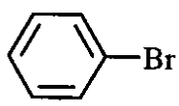
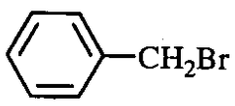
1. Which of the following is more reactive in an S_N1 reaction?

a. $CH_3CH_2CH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HBr$ or $CH_3CH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2Br$

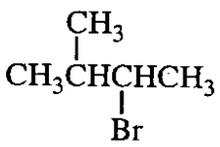
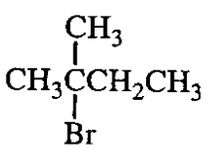
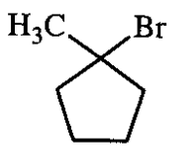
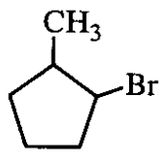
b. $CH_3CH{=}\underset{\displaystyle Br}{\underset{|}{C}}CH_3$ or $CH_3CH{=}CH\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$

2. Which of the following is more reactive in an S_N2 reaction?

a. $CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HBr$ or $CH_3CH_2\underset{\displaystyle CH_2CH_3}{\underset{|}{C}}HBr$

b.  or 

3. Which of the following alkyl halides forms a constitutional isomer as a result of an S_N1 reaction that is different from the isomer formed as a result of an S_N2 reaction?

4. Indicate whether each of the following statements is true or false:

a. Increasing the concentration of the nucleophile favors an S_N1 reaction over an S_N2 reaction. T F

b. Ethyl iodide is more reactive than ethyl chloride in an S_N2 reaction. T F

c. In an S_N1 reaction, the product with the retained configuration is obtained in greater yield. T F

d. The rate of a substitution reaction in which none of the reactants is charged will increase if the polarity of the solvent is increased. T F

e. An S_N2 reaction is a two-step reaction. T F

f. The pK_a of a carboxylic acid is greater in water than it is in a mixture of dioxane and water. T F

5. Answer the following:

a. Which is a stronger base, CH_3O^- or CH_3S^-?

b. Which is a better nucleophile in an aqueous solution, CH_3O^- or CH_3S^-?

6. For each of the following pairs of S_N2 reactions, indicate the one that occurs with the greater rate constant:

a. $CH_3CH_2CH_2Cl + HO^-$ or $CH_3\underset{\displaystyle Cl}{\underset{|}{C}}HCH_3 + HO^-$

b. $CH_3CH_2CH_2Cl + HO^-$ or $CH_3CH_2CH_2I + HO^-$

c. $CH_3CH_2CH_2Br + HO^-$ or $CH_3CH_2CH_2Br + H_2O$

d. $CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH_3 \xrightarrow[H_2O/CH_3OH]{CH_3O^-}$ or $CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH_3 \xrightarrow[CH_3OH]{CH_3O^-}$

e. $BrCH_2CH_2CH_2CH_2NHCH_3$ or $BrCH_2CH_2CH_2NHCH_3$

7. Circle the aprotic solvents:

a. dimethyl sulfoxide **b.** diethyl ether **c.** ethanol **d.** hexane

8. How would increasing the polarity of the solvent affect the following?

a. the rate of the S_N2 reaction of methyl amine with 2-bromobutane

b. the rate of the S_N1 reaction of methyl amine with 2-bromobutane

c. the rate of the S_N2 reaction of methoxide ion with 2-bromobutane

d. the pK_a of acetic acid

e. the pK_a of phenol

CHAPTER 11
Elimination Reactions of Alkyl Halides • Competition Between Substitution and Elimination

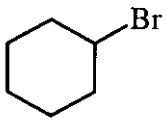
Important Terms

anti elimination	an elimination reaction in which the substituents being eliminated are removed from opposite sides of the molecule.
anti-periplanar	parallel substituents on opposite sides of a molecule.
bifunctional molecule	a molecule with two functional groups.
dehydrohalogenation	elimination of a proton and a halide ion.
deuterium kinetic isotope effect	ratio of the rate constant obtained for a compound containing hydrogen and the rate constant obtained for an identical compound in which one or more of the hydrogens have been replaced by deuterium.
elimination reaction	a reaction that removes atoms or groups from the reactant to form a π bond.
β-elimination reaction or 1,2-elimination reaction	an elimination reaction where the groups being eliminated are bonded to adjacent carbons.
E1 reaction	a first-order elimination reaction.
E2 reaction	a second-order elimination reaction.
intermolecular reaction	a reaction that takes place between two molecules.
intramolecular reaction	a reaction that takes place within a molecule.
kinetic isotope effect	a comparison of the rate of reaction of a compound with the rate of reaction of a compound in which one of the atoms has been replaced by an isotope.
regioselectivity	the preferential formation of a constitutional isomer.
syn elimination	an elimination reaction in which substituents being eliminated are removed from the same side of the molecule.
syn-periplanar	parallel substituents on the same side of a molecule.
target molecule	the desired end product of a synthesis.
Williamson ether synthesis	formation of an ether from the reaction of an alkoxide ion with an alkyl halide.
Zaitsev's rule	the more stable alkene product is obtained by removing a proton from the β-carbon that is bonded to the fewest hydrogens.

Solutions to Problems

1.

a. $CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$ The alkene that is formed is more stable than the alkene that is formed from the other alkyl halide.

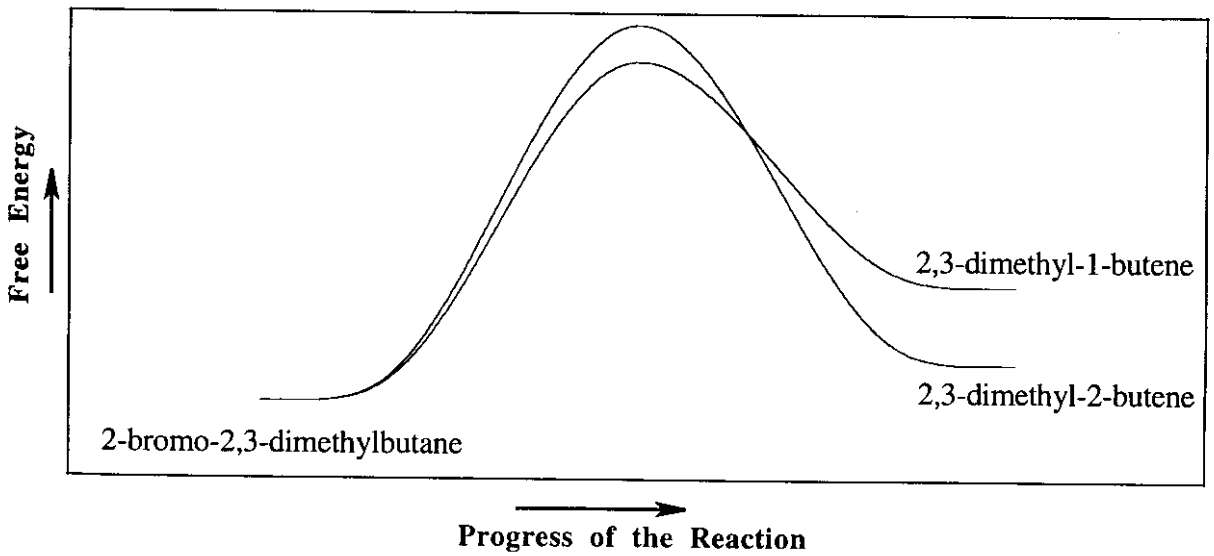
b.  Br is a better leaving group (weaker base) than Cl.

c. $CH_3CH_2CH_2\underset{\displaystyle Br}{\underset{|}{\overset{\displaystyle CH_3}{\overset{|}{C}}}}CH_3$ The alkene that is formed is more stable than the alkene that is formed from the other alkyl halide.

d. $CH_3\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle CH_3}{\overset{|}{C}}}}CH_2CH_2Cl$ The other alkyl halide cannot undergo an E2 reaction because it doesn't have any β-hydrogens.

2. The reaction of 2-bromo-2,3-dimethylbutane with sodium *tert*-butoxide forms two alkene elimination products. Because of steric hindrance, the least stable alkene (2,3-dimethyl-1-butene) is the one that is easier to make.

$$\underset{\text{2-bromo-2,3-dimethylbutane}}{CH_3C(CH_3)(Br)CH(CH_3)CH_3} \xrightarrow{(CH_3)_3CO^-} \underset{\text{2,3-dimethyl-1-butene}}{CH_2{=}C(CH_3)CH(CH_3)CH_3} + \underset{\text{2,3-dimethyl-2-butene}}{CH_3C(CH_3){=}CHCH_3}$$



3.

a. $CH_3CH{=}CHCH_3$ Removal of a β-hydrogen from the most substituted carbon forms the most stable "alkene-like" transition state.

b. $CH_2{=}CHCH_2CH_3$ Removal of a β-hydrogen from the least substituted carbon forms the most stable "carbanion-like" transition state.

c. $CH_3C(CH_3){=}CHCH_2CH_3$ Removal of a β-hydrogen from the most substituted carbon forms the most stable "alkene-like" transition state.

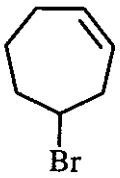
d. $CH_3CH{=}CHCH{=}CH_2$ The β-hydrogen is removed that will lead to a conjugated alkene.

e.  The β-hydrogen is removed that will lead to a conjugated alkene.

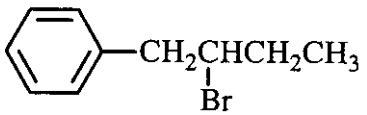
f. $CH_3CH(CH_3)CH{=}CHCH_3$ Removal of a β-hydrogen from the least substituted carbon forms the most stable "carbanion-like" transition state.

4.

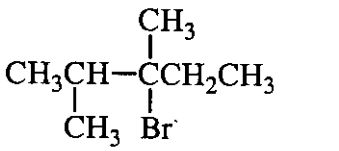
a. $CH_3CH(CH_3)CH(Br)CH_2CH_3$ It forms the more stable alkene; the alkene has a greater number of substituents bonded to the sp^2 carbons.

b.  It forms is more stable alkene; the new double bond is conjugated with the double bond that is already there.

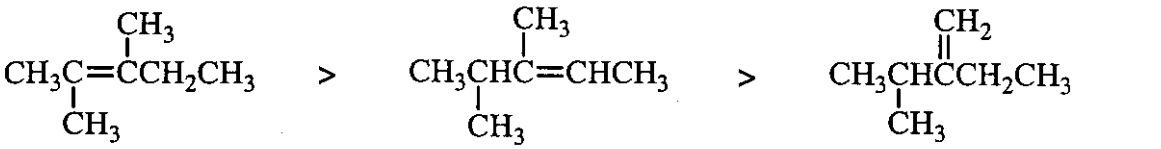
c. $CH_3CH_2CH(Br)CH_2CH_3$ It has four hydrogens that can be removed to form an alkene with two substituents on the sp^2 carbons so it has a greater probability of an effective collision with the nucleophile than the other alkyl halide that has only two such hydrogens.

d.  It forms the more stable alkene; the new double bond is conjugated with the phenyl substituent.

5.



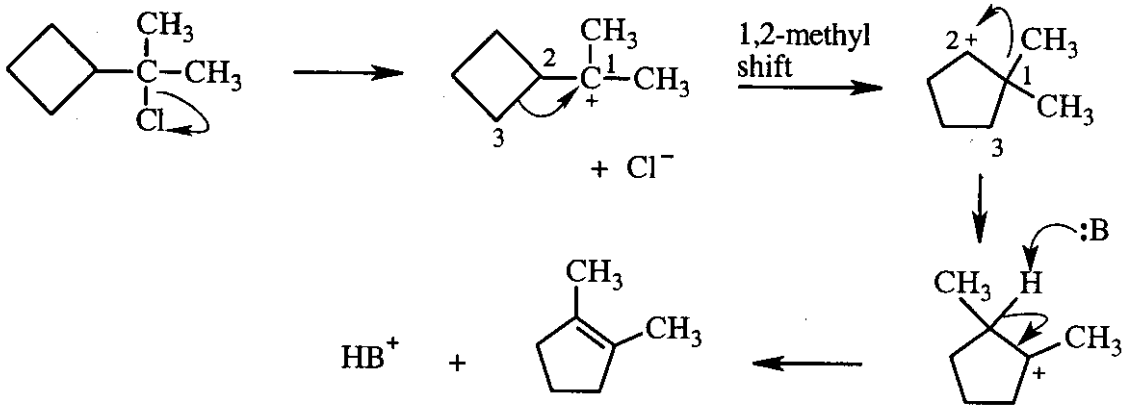
3-bromo-2,3-dimethylpentane



Four alkyl substituents are bonded to the sp^2 carbons. > Three alkyl substituents are bonded to the sp^2 carbons. > Two alkyl substituents are bonded to the sp^2 carbons.

6. The major product is the one predicted by Zaitsev's rule, because the fluoride ion dissociates in the first step, forming a carbocation. Loss of a proton from the carbocation will follow Zaitsev's rule, as it does in all E1 reactions.

7.



8.

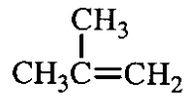
a. E2 beause a strong base is used.

$CH_3CH{=}CHCH_3$

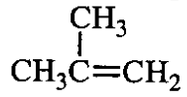
b. E1 because a weak base is used.

$CH_3CH{=}CHCH_3$

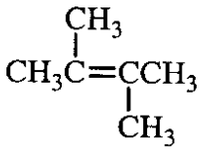
c. E1 because a weak base is used.



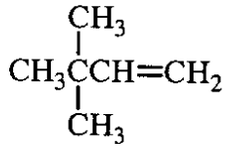
d. E2 because a strong base is used.



e. E1 because a weak base is used.



f. E2 because a strong base is used.



Notice that even though the same alkyl halide is used in "e" and "f", different products are obtained because the carbocation that forms under S_N1 conditions rearranges.

9.

a.

$$\frac{\text{E2}}{\text{E2}+\text{E1}} = \frac{k_2[\textit{tert}\text{-butyl bromide}]\,[HO^-]}{k_2[\textit{tert}\text{-butyl bromide}]\,[HO^-] + k_1[\textit{tert}\text{-butyl bromide}]}$$

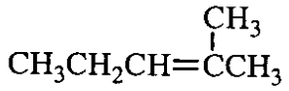
$$\frac{\text{E2}}{\text{E2}+\text{E1}} = \frac{7.1\times10^{-5}\ \times 5.0}{7.1\times10^{-5}\ \times\ 5.0\ +\ 1.5\times10^{-5}} = \frac{35.5\times10^{-5}}{35.5\times10^{-5}+\ 1.5\times10^{-5}} = \frac{35.5}{37} = .96$$

$$= 96\%$$

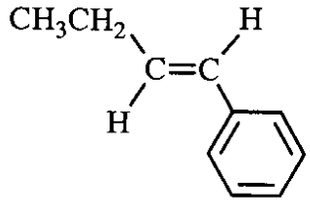
b.

$$\frac{\text{E2}}{\text{E2}+\text{E1}} = \frac{7.1\times10^{-5}\ \times 2.5\times10^{-3}}{7.1\times10^{-5}\ \times 2.5\times10^{-3}+150\times10^{-7}} = \frac{1.78\times10^{-7}}{1.78\times10^{-7}\ +150\times10^{-7}} = \frac{1.78}{152} = 1.2\%$$

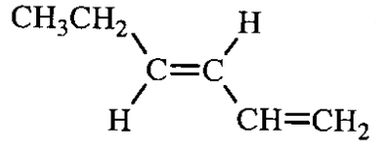
10.

a. **1.** 

No stereoisomers are possible.

2. 

The major product has the bulkier group bonded to one sp^2 carbon on the opposite side of the double bond from the bulkier group bonded the other sp^2 carbon.

3. 

The major product is the conjugated diene with the bulkier groups on opposite sides of the double bond.

b. In none of the reactions is the major product dependent on whether you started with the *R* or *S* enantiomer.

11.

a. Solved in the text.

b. $CH_3CH_2CH{=}C(CH_3)CH_3$

c. CH_3CH_2, H, H_3C, $CH_2CH_2CH_3$ around C=C

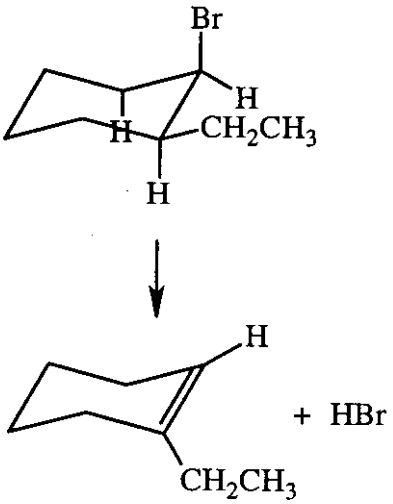
d. CH_3 on cyclohexene

12. Elimination occurs when the H and Br to be eliminated are in axial positions.

When Br is in an axial position in the cis isomer, it has an axial hydrogen on each of the adjacent carbons. The one bonded to the same carbon as the ethyl group will be more apt to be the one eliminated with Br because the product formed is more stable and, therefore, more easily formed than the product formed when the other H is eliminated with Br.

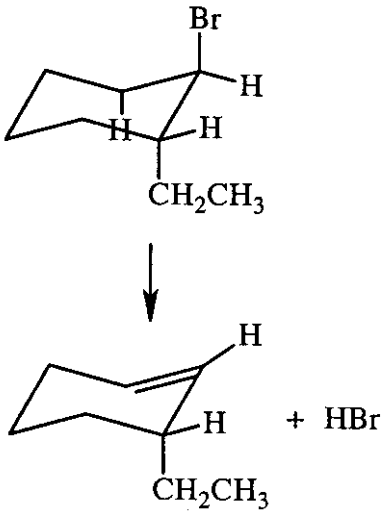
When Br is in an axial position in the trans isomer, it has an axial hydrogen on only one adjacent carbon, and it is not the carbon that is bonded to the ethyl group. Therefore, a different product is formed.

cis-1-bromo-2-ethylcyclohexane



1-ethylcyclohexene

trans-1-bromo-2-ethylcyclohexane

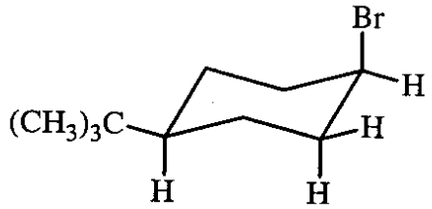


3-ethylcyclohexene

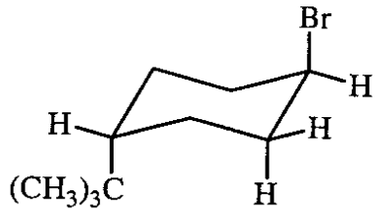
13. In order to undergo an E2 reaction, the substituents that are to be eliminated must both be in axial positions.

When bromine and an adjacent hydrogen are in axial positions, the large *tert*-butyl substituent is in an equatorial position in the cis isomer and in an axial position in the trans isomer.

Because a large substituent is more stable in an equatorial position than in an axial position, elimination of the cis isomer occurs through its more stable chair conformer, while elimination of the trans isomer has to occur through its less stable chair conformer. The cis isomer, therefore, reacts more rapidly in an E2 reaction.



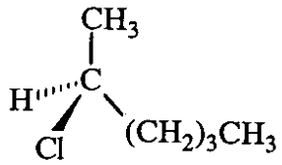
cis-1-bromo-4-*tert*-butylcyclohexane



trans-1-bromo-4-*tert*-butylcyclohexane

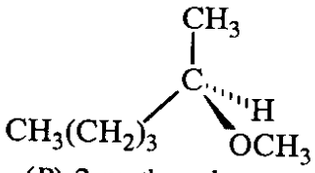
14.

a.



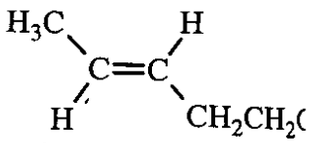
(*S*)-2-chlorohexane

$\xrightarrow[S_N2/E2]{CH_3O^-}$



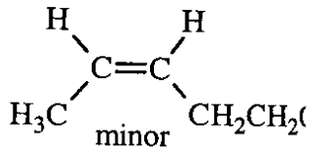
(*R*)-2-methoxyhexane

+



major elimination produc

+

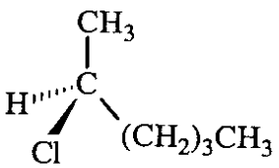


minor

+ $CH_2{=}CHCH_2CH_2CH_2$

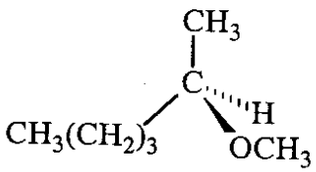
minor

b.



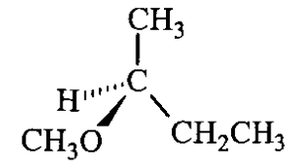
(*S*)-2-chlorohexane

$\xrightarrow[S_N1/E1]{CH_3OH}$



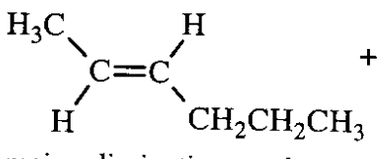
(*R*)-2-methoxyhexane

+



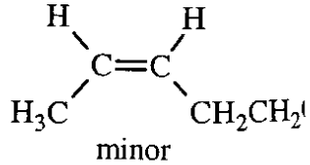
(*S*)-2-methoxyhexane

+



major elimination product

+

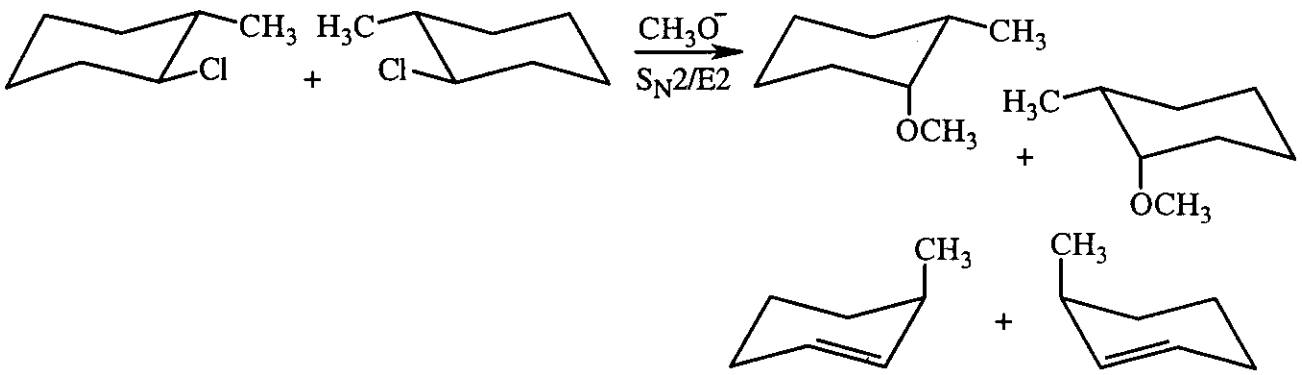


minor

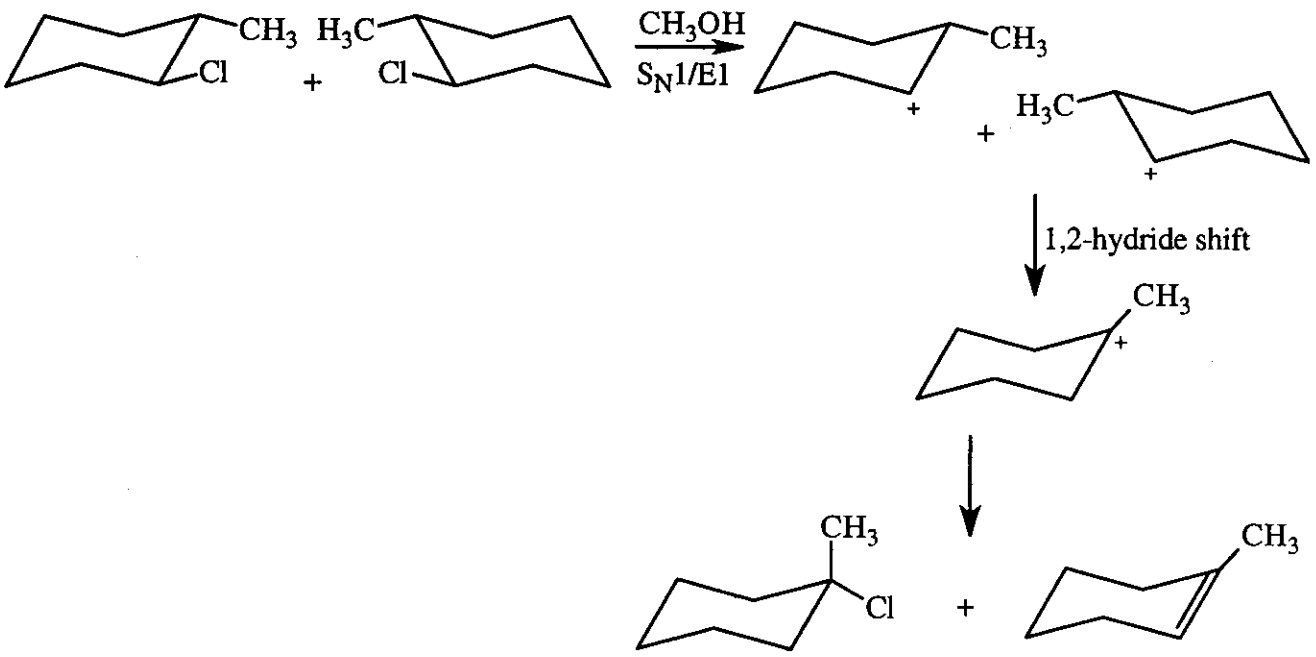
+ $CH_2{=}CHCH_2CH_2CH_2CH_3$

very minor

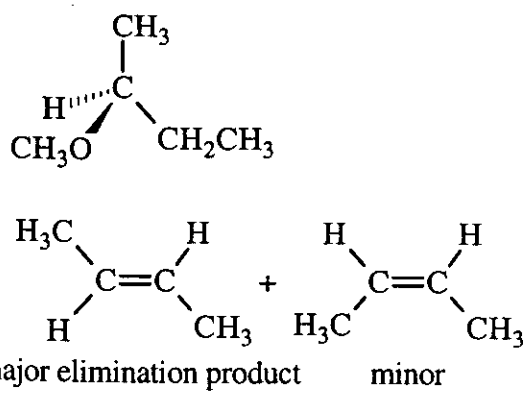
c.



d.

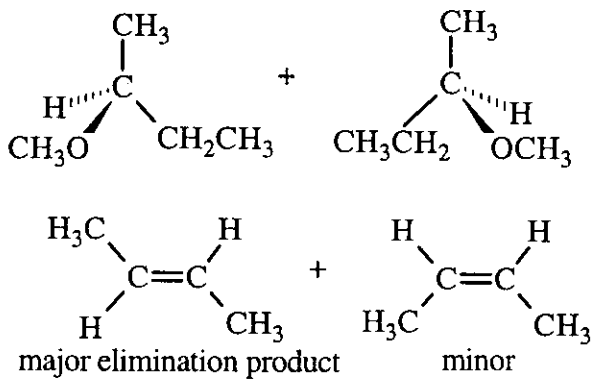


e.



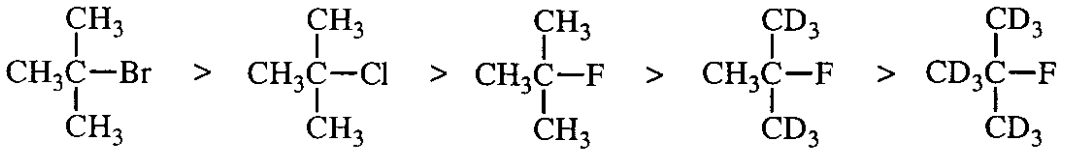
major elimination product minor

f.



major elimination product minor

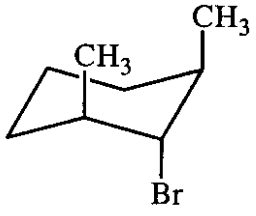
15. Br is the weakest base so it is the best leaving group, and F is the worst leaving group. It is easier to break a C—H bond than a C—D bond, so the more β-hydrogens that are replaced by a deuterium, the slower the rate of the E2 reaction will be.



16. The rate-limiting step in an E1 reaction is carbocation formation. Because the proton is removed in a subsequent fast step, the difference in the rate of removal of an H^+ versus a D^+ would not be reflected in the rate constant. Therefore, the deuterium kinetic isotope effect would be close to 1.

17. Because CH_3S^- is a stronger nucleophile and weaker base than CH_3O^-, the ratio of substitution (where CH_3S^- reacts as a nucleophile) to elimination (where CH_3S^- reacts as a base) will increase when the nucleophile is changed from CH_3O^- to CH_3S^-.

18. In order to undergo an elimination reaction under E2 conditions, the substituents that are to be eliminated (H and Br) must both be in axial positions. Drawing the compound in the chair conformation shows that when Br is in an axial position, the adjacent hydrogens are in equatorial positions, so an elimination reaction can't take place.



19. **a. 1.** no reaction

2. no reaction

3. substitution and elimination

4. substitution and elimination

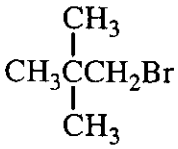
b. 1. primarily substitution

2. substitution and elimination

3. substitution and elimination

4. elimination

20.



1-bromo-2,2-dimethylpropane

a. The bulky *tert*-butyl substituent blocks the backside of the carbon bonded to the bromine to nucleophilic attack, making an S_N2 reaction difficult. An S_N1 reaction is difficult because the carbocation formed when the bromide ion departs is an unstable primary carbocation.

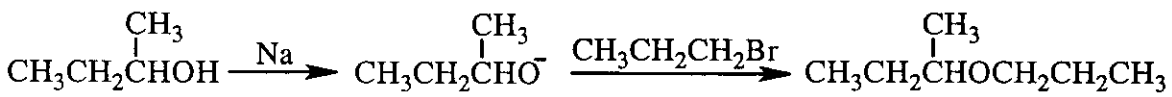
b. It cannot undergo an E2 reaction, because the β-carbon is not bonded to a hydrogen.
It cannot undergo an E1 reaction, because that would require formation of a primary carbocation.

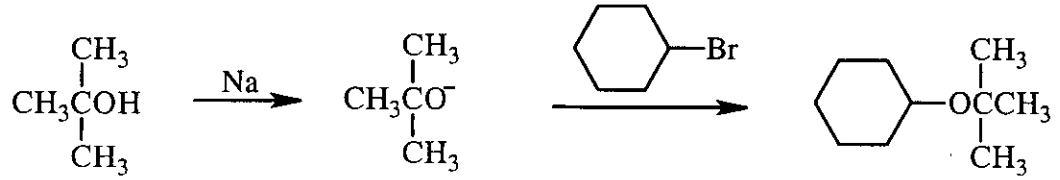
21. Because a strong base is used in the Williamson ether synthesis, the reaction is an S_N2 reaction, so a competing E2 reaction can also occur.

a. $CH_3CH_2CH_2Br + CH_3CH_2CH_2CH_2O^- \longrightarrow CH_3CH_2CH_2CH_2OCH_2CH_2CH_3$
butyl propyl ether
$+ \; CH_3CH{=}CH_2$
propene

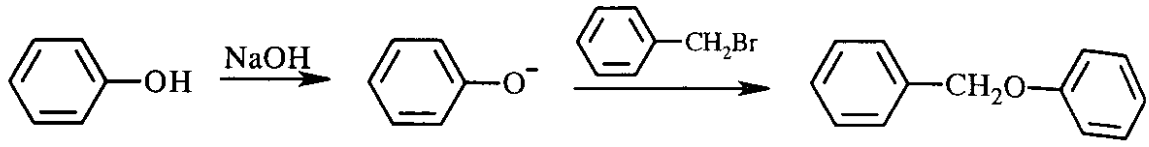
b. $CH_3CH_2CH_2CH_2Br + CH_3CH_2CH_2O^- \longrightarrow CH_3CH_2CH_2CH_2OCH_2CH_2CH_3$
butyl propyl ether
$+ \; CH_3CH_2CH{=}CH_2$
1-butene

22.

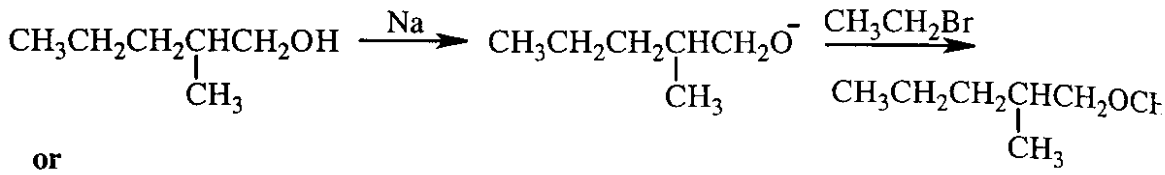
a. 

b. 

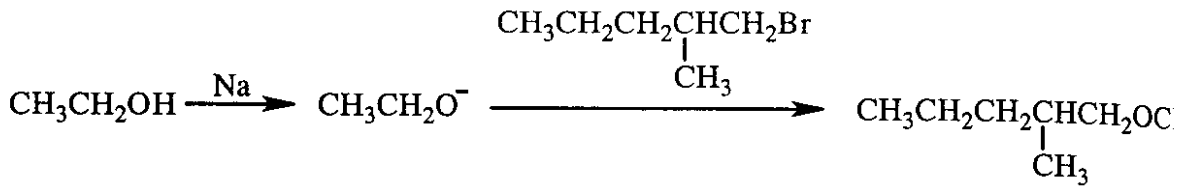
c.



d.

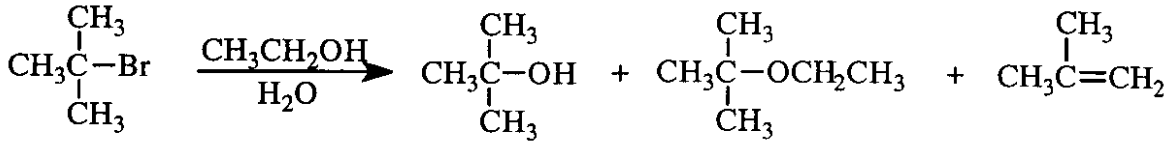


or



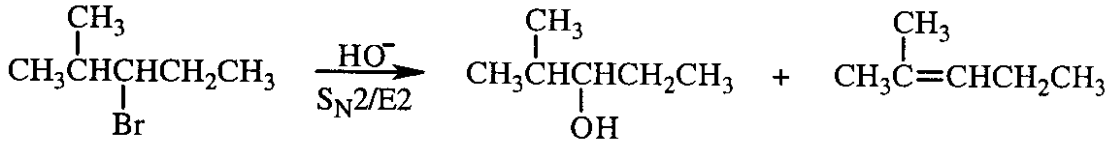
Both methods can be used to synthesize the target molecule. The first method is preferred because ethyl bromide has less steric hindrance than does 1-bromo-2-methylpentane.

23.

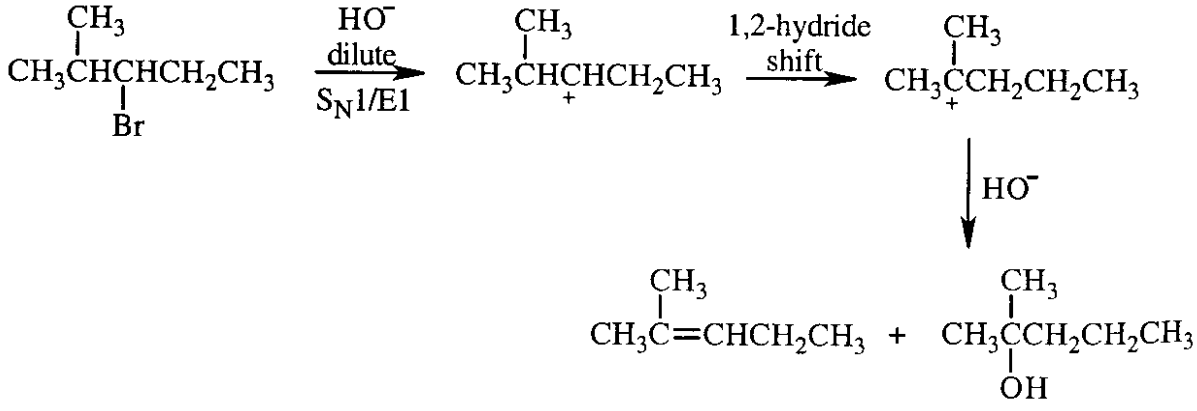


24.

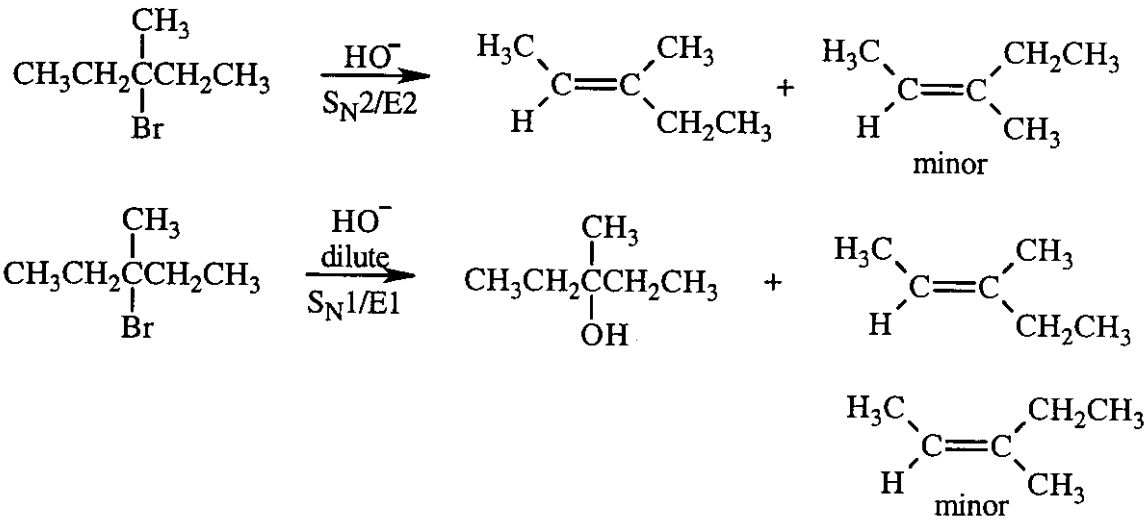
a.



The S_N2 reaction will form the substitution product with the inverted configuration compared to the configuration of the starting material. But, because the configuration of the starting material is not specified (we do not know if it is the *R* isomer, the *S* isomer, or a mixture of *R* and *S*), we cannot specify the configuration of the S_N2 product.



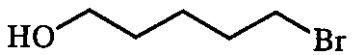
b.



25. Because an allene is less stable than an alkyne, it is harder to make.

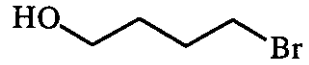
26.

a.



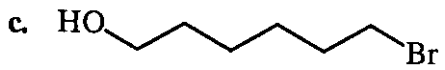
because it forms a six-membered ring, while the other compound would form a seven-membered ring. A seven-membered ring is more strained than a six-membered ring so the six-membered ring is formed more easily (see Table 2.9 on p. 96 of the text).

b.



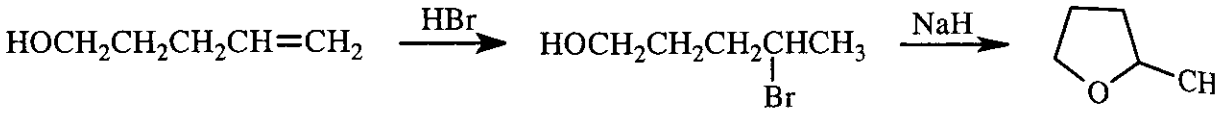
because it forms a five-membered ring, while the other compound would form a four-membered ring. A four-membered ring is more strained than a five-membered ring so the five-membered ring is formed more easily.

c.



because it forms a seven-membered ring, while the other compound would form an eight-membered ring. An eight-membered ring is more strained than a seven-membered ring so the seven-membered ring is formed more easily; also, the Br and OH are less likely to be in the proper position relative to one another for reaction because there are more bonds around which rotation to an unfavorable conformation can occur in the compound that leads to the eight-membered ring (Section 24.6).

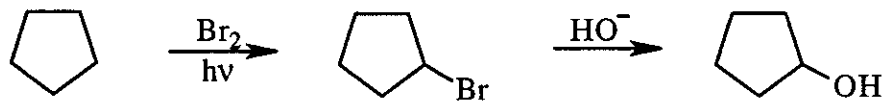
27.



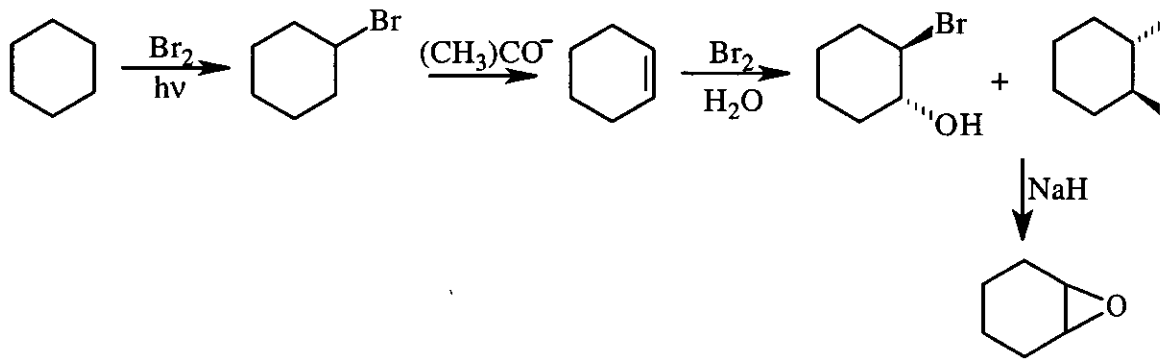
The synthesis shown in the text will give a higher yield of the target molecule because the alkoxide ion attacks the back-side of a primary alkyl halide.
In the synthesis shown above, the alkoxide ion attacks the back-side of a secondary alkyl halide which provides greater steric hindrance to back-side attack. Therefore, there will be greater competition from the E2 reaction that will form an elimination product, reducing the yield of the desired substitution product.

28.

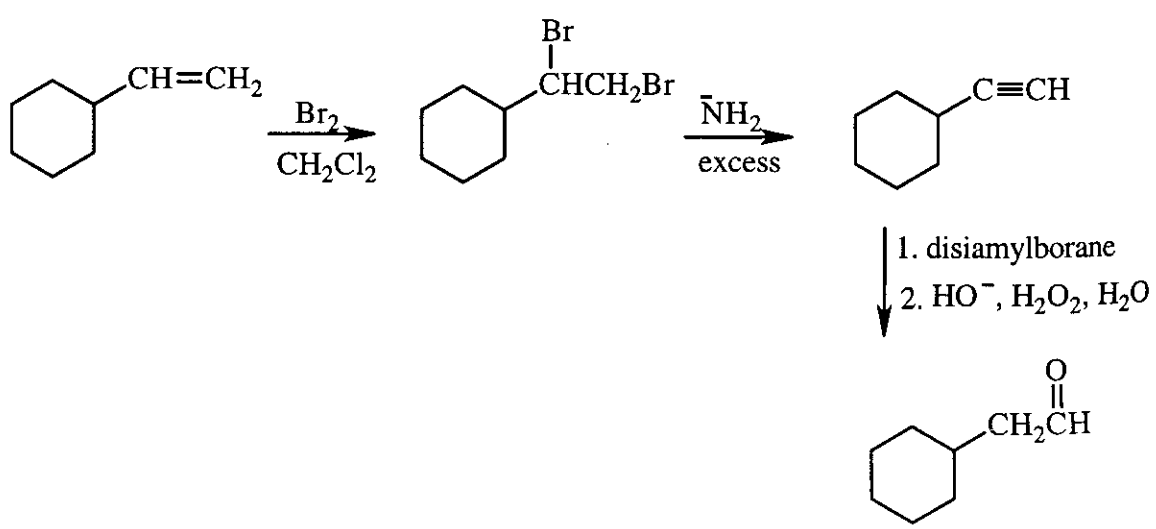
a.



b.



c.

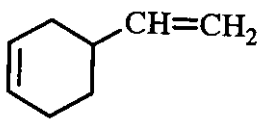


d. $CH_3CH_2CH_2CH_2Br \xrightarrow{tert\text{-}BuO^-} CH_3CH_2CH{=}CH_2 \xrightarrow{Br_2} CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_2Br$

(Notice that a bulky base is used to encourage elimination over substitution.)

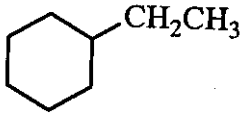
$\downarrow \; {}^-NH_2$ excess

$CH_3CH_2C{\equiv}CH \xrightarrow[2.\ CH_2CH_2Br]{1.\ {}^-NH_2} CH_3CH_2C{\equiv}CCH_2CH_3 \xrightarrow[H_2SO_4]{H_2O} CH_3CH_2\overset{\displaystyle O}{\overset{\|}{C}}CH_2CH_2CH_3$

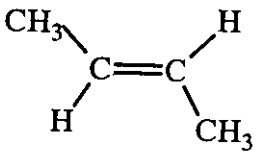
e. $BrCH_2CH_2CH_2CH_2Br \xrightarrow[\text{excess}]{tert\text{-}BuO^-} CH_2{=}CHCH{=}CH_2 \xrightarrow{\Delta}$ 

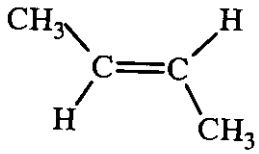
(1,3-butadiene is both the diene and the dienophile)

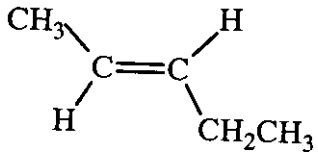
H_2 | Pd/C



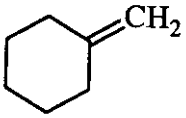
29.

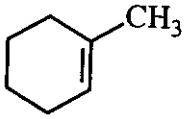
a. 

b. 

c. 

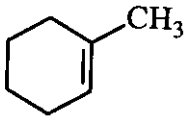
d. 

e. 

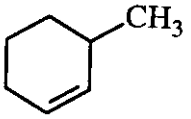
f. 

g. The product depends on the configuration of the reactant, which has not been specified.

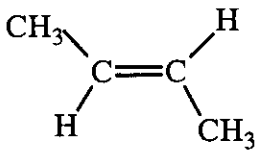
If the reactant is cis.

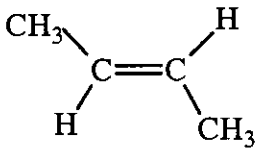


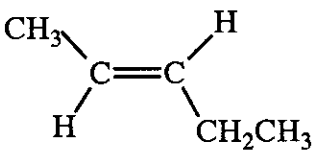
If the reactant is trans.



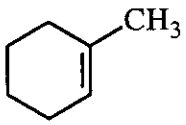
30.

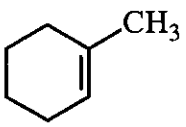
a. 

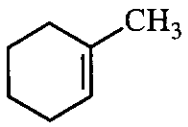
b. 

c. 

d. 

e. 

f. 

g. 

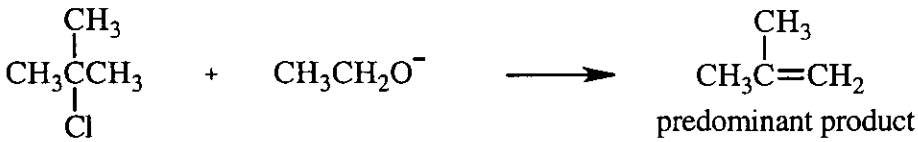
31. **a.**

1. $3° > 2° > 1°$
2. An E1 reaction is not affected by the strength of the base, but a weak base favors an E1 reaction by disfavoring an E2 reaction.
3. An E1 reaction is not affected by the concentration of the base, but a low concentration of a base favors an E1 reaction by disfavoring an E2 reaction.
4. An aprotic polar solvent favors an E1 reaction if the reactant is charged.
   A protic polar solvent favors an E1 reaction if the reactant is not charged.

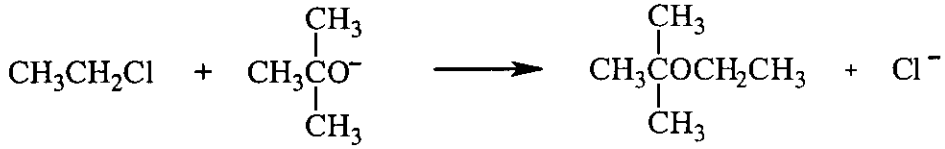
b.

1. $3° > 2° > 1°$
2. A strong base favors an E2 reaction.
3. A high concentration of a base favors an E2 reaction.
4. An aprotic polar solvent favors an E2 reaction if either of the reactants is charged.
   A protic polar solvent favors an E2 reaction if neither of the reactants is charged.

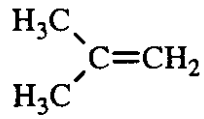
32. The predominant product is the elimination product because tertiary alkyl halides react with nucleophiles to form an elimination product and little substitution product.



Rather than a tertiary alkyl halide and a primary alkoxide ion, he should have used a primary alkyl halide and a tertiary alkoxide ion.

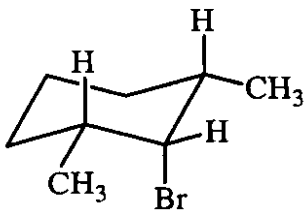


33.

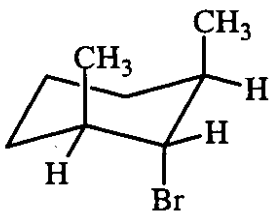
a. $(CH_3)_3Cl \xrightarrow[H_2O]{HO^-}$  + I^-

Because I^- is a better leaving group than Cl^-.

b.

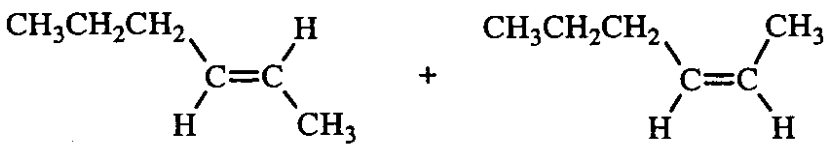


This compound is the only one that can undergo an E2 elimination reaction because the other compound does not have a hydrogen trans to the Br.

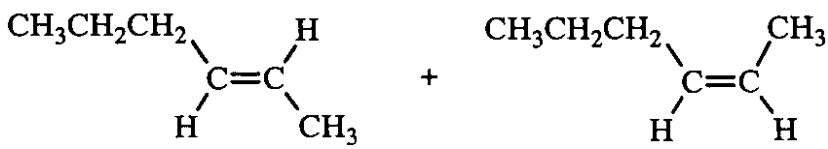


This compound will undergo an elimination reaction more slowly because it can react only by an E1 pathway.

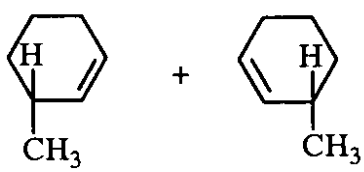
34. The very minor products that would be obtained from "anti-Zaitsev" elimination (i.e., the less substituted alkenes) are not shown.

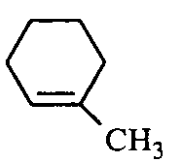
a. 

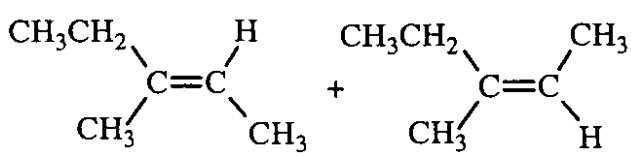
minor

b. 

minor

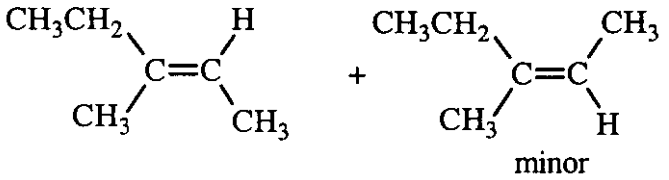
c. 

d. 

e. 

minor

f.



minor

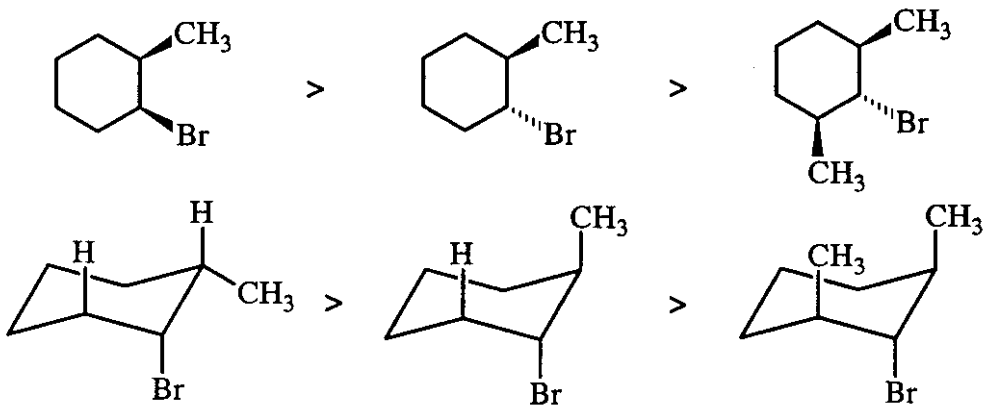
35. **a.** ethoxide ion because elimination is favored by the bulkier base, and *tert*-butoxide ion is bul than ethoxide ion

b. $^-$SCN because elimination is favored by the stronger base, and $^-$OCN is a stronger base th $^-$SCN

c. Br^- because elimination is favored by the stronger base, and Cl^- is a stronger base than Br

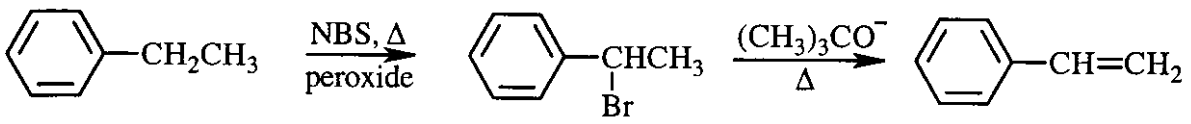
d. CH_3S^- because elimination is favored by the stronger base, and CH_3O^- is a stronger base CH_3S^-

36. The first compound has two axial hydrogens adjacent to Br, the second has one axial hydroge adjacent to Br but it cannot form the more substituted (more stable) alkene that can be formed the first compound. The last compound cannot undergo an E2 reaction because it does not ha axial hydrogen adjacent to Br.



37.

a.

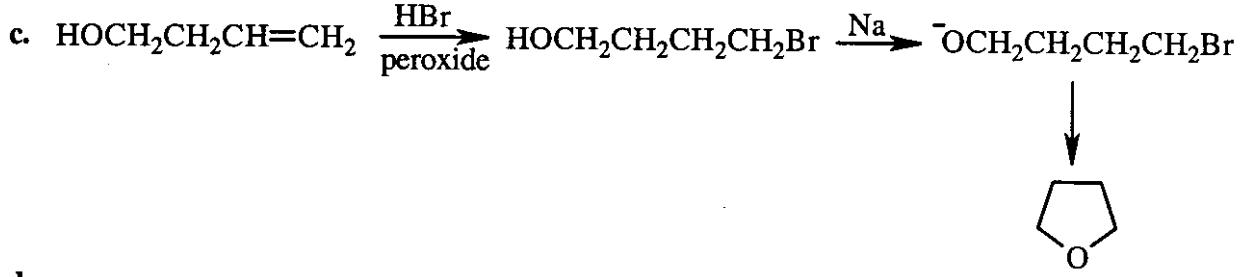


Notice that a bulky base and heat are used in the last step to encourage elimination over substitution.

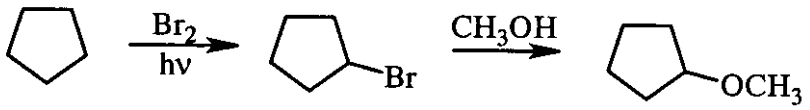
b. $CH_3CH_2CH{=}CH_2 \xrightarrow[\text{peroxide}]{HBr} CH_3CH_2CH_2CH_2Br \xrightarrow[2.\ HO^-]{1.\ NH_3} CH_3CH_2CH_2CH_2NH_2$

After the S_N2 reaction with NH_3, the solution is made basic so the final amine product is in its basic form.

c.

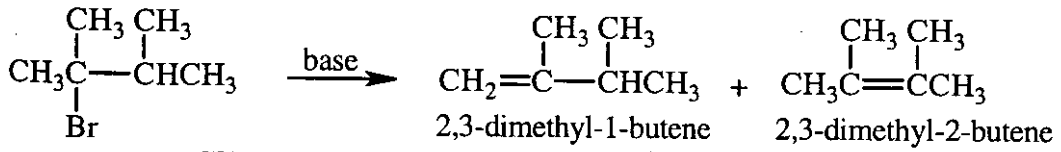


d.



e. $CH_3CH_2CH{=}CH_2 \xrightarrow[\text{peroxide}]{NBS,\ \Delta} CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH{=}CH_2 \xrightarrow[\Delta]{(CH_3)_3CO^-} CH_2{=}CHCH{=}CH_2$

38.



a. $CH_3CH_2\underset{\displaystyle CH_2CH_3}{\underset{|}{C}}O^-$

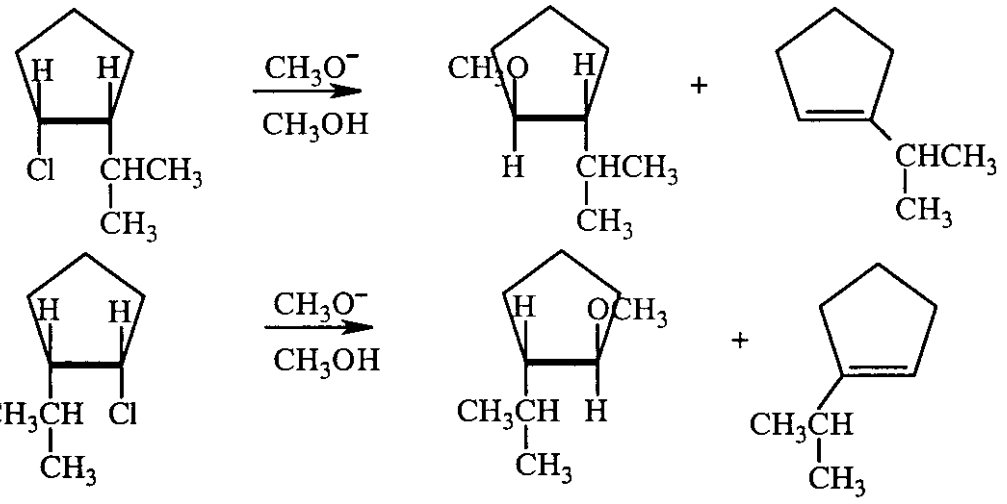
Because it is the most sterically hindered base, it gives the highest percentage of the 1-alkene.

b. $CH_3CH_2O^-$

Because it is the least sterically hindered base, it gives the highest percentage of the 2-alkene.

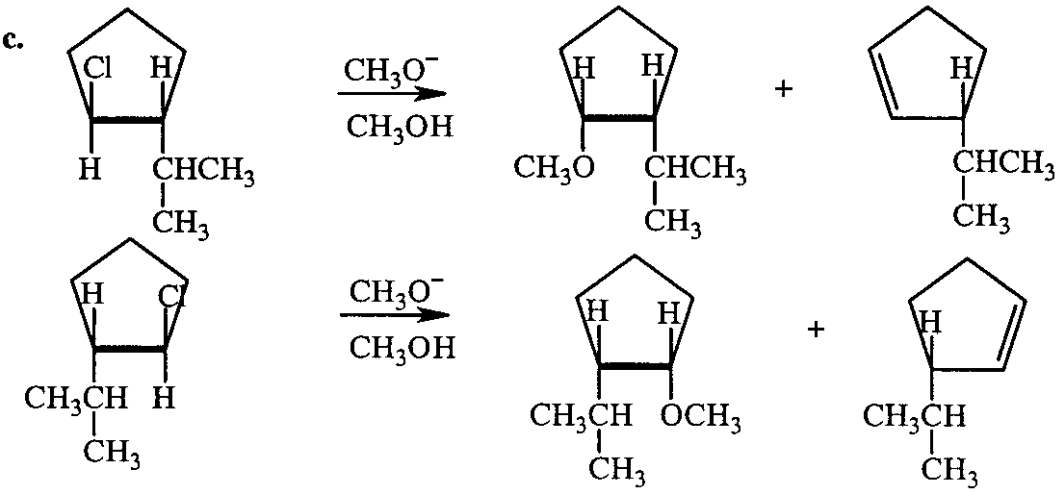
39.

a. These are $S_N2/E2$ reactions.



b. Only the substitution products are optically active.

c.



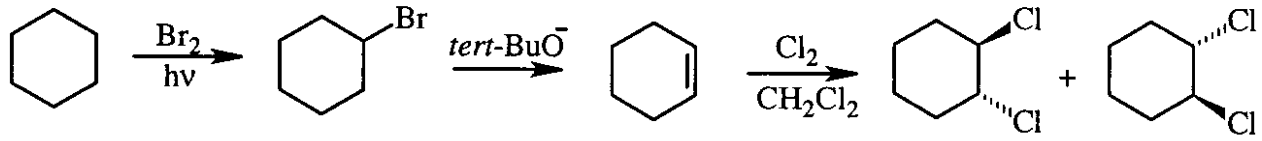
Yes, all the products are optically active.

d. The cis enantiomers form the substitution products more rapidly because there is less steric hindrance from the adjacent substituent.

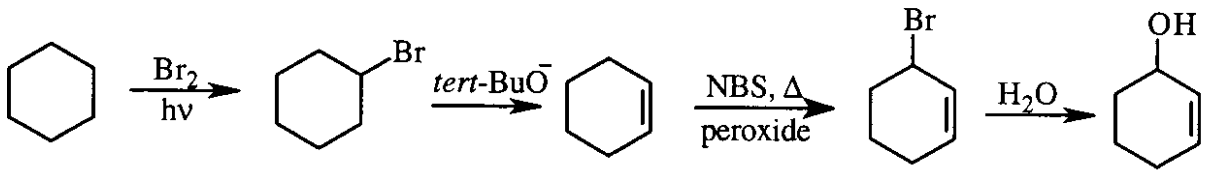
e. The cis enantiomers form the elimination products more rapidly because the alkenes formed from the cis enantiomers are more substituted and, therefore, more stable. The more stable th alkene, the lower the energy of the transition state leading to its formation.

40.

a.



b.



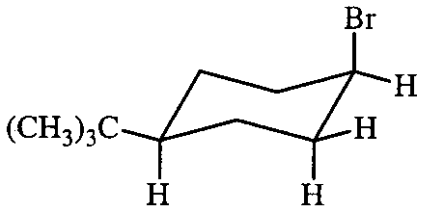
41. The number of atoms in the ring is given by *n*. Three and four membered rings have strain, so they are harder to make than 5 and 6 membered rings. The three-membered ring is formed faster than the four-membered ring because the compound leading to the three-membered ring has one less carbon-carbon single bond that can rotate to give a conformer in which the reacting groups are positioned too far from one another for reaction.



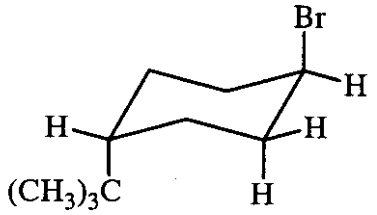
Even though the compound that forms the five-membered ring has one more bond that can rotate to give a conformer in which the reacting groups are positioned too far from one another for reaction than the compound that forms the four-membered ring, the five-membered ring is formed faster because it is relatively strain free. So lack of strain more than makes up for the lower probability of having the reacting groups in the proper position for reaction.

Now the rate of the ring-forming reaction gets slower as the size of the ring being formed gets larger, because the reactant has more bonds that can rotate to give conformers in which the reacting groups are positioned too far from one another for reaction.

42. In an E2 reaction, both groups to be eliminated must be in axial positions.
When the bromine is in the axial position in the cis isomer, the *tert*-butyl substituent is in the mo stable equatorial position.
When the bromine is in the axial position in the trans isomer, the *tert*-butyl substituent is in the l stable axial position.
Thus, elimination takes place via the most stable conformer in the cis isomer and via a less stable chair conformer in the trans isomer, so the cis isomer undergoes elimination more rapidly.

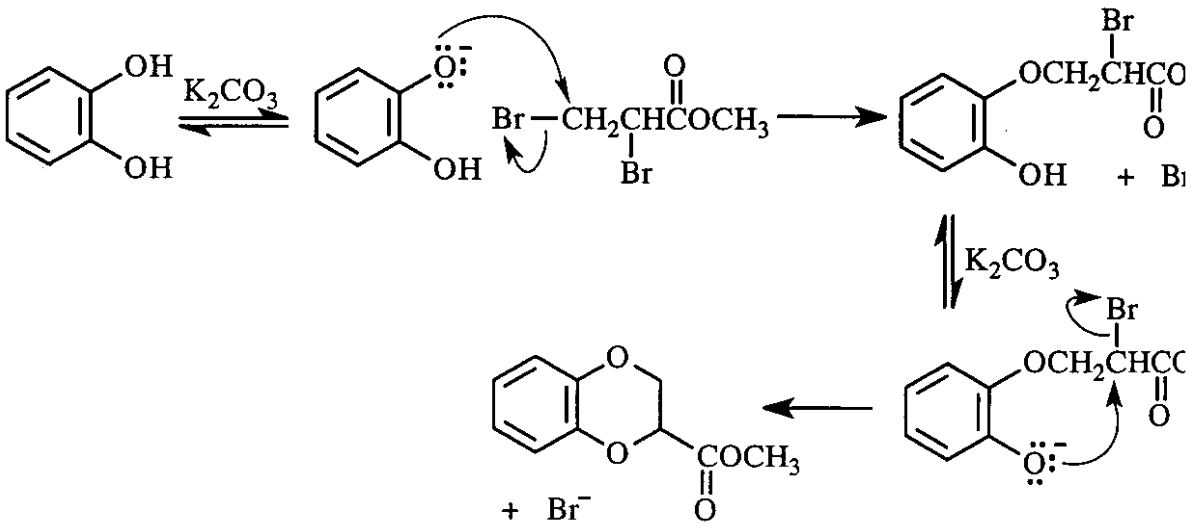


cis-1-bromo-4-*tert*-butylcyclohexane



trans-1-bromo-4-*tert*-butylcyclohexane

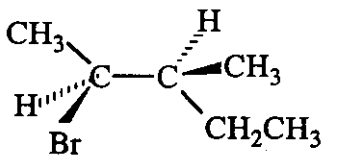
43.



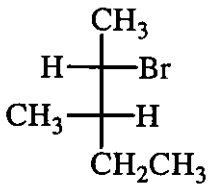
44. Because the β-carbon from which the hydrogen is to be removed is bonded to only one hydroge the configuration of the reactant determines the configuration of the E2 elimination product.

To determine the configuration of the product, convert the prospective formula of the Fischer projection to a staggered a Newman projection, in which the groups (H and Br) that are to be eliminated anti to one another. (Remember that the Fischer projection of the reactant shows the molecule in an eclipsed conformation, since both horizontal bonds are pointing toward the viewe Thus the elimination product formed from (2*S*,3*S*)-2-chloro-3-methypentane is the *E* isomer.

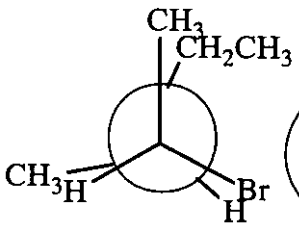
a.

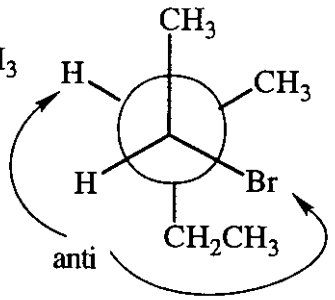


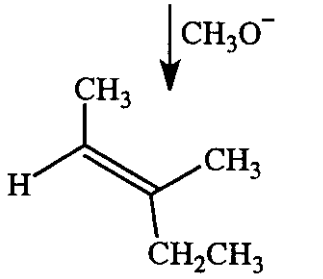
or



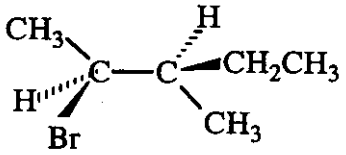
(2*S*,3*S*)-2-chloro-
3-methylpentane



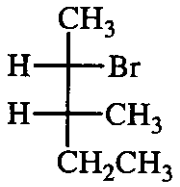




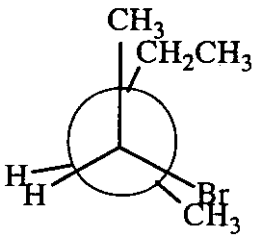
b.

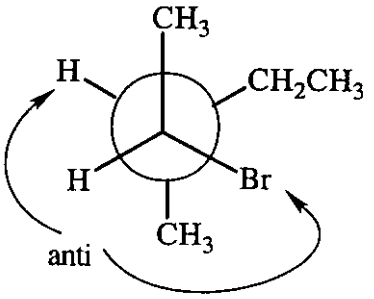


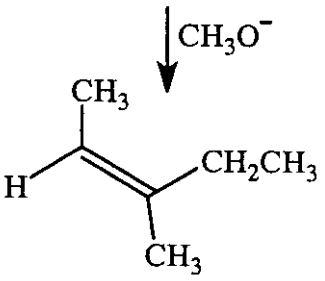
or



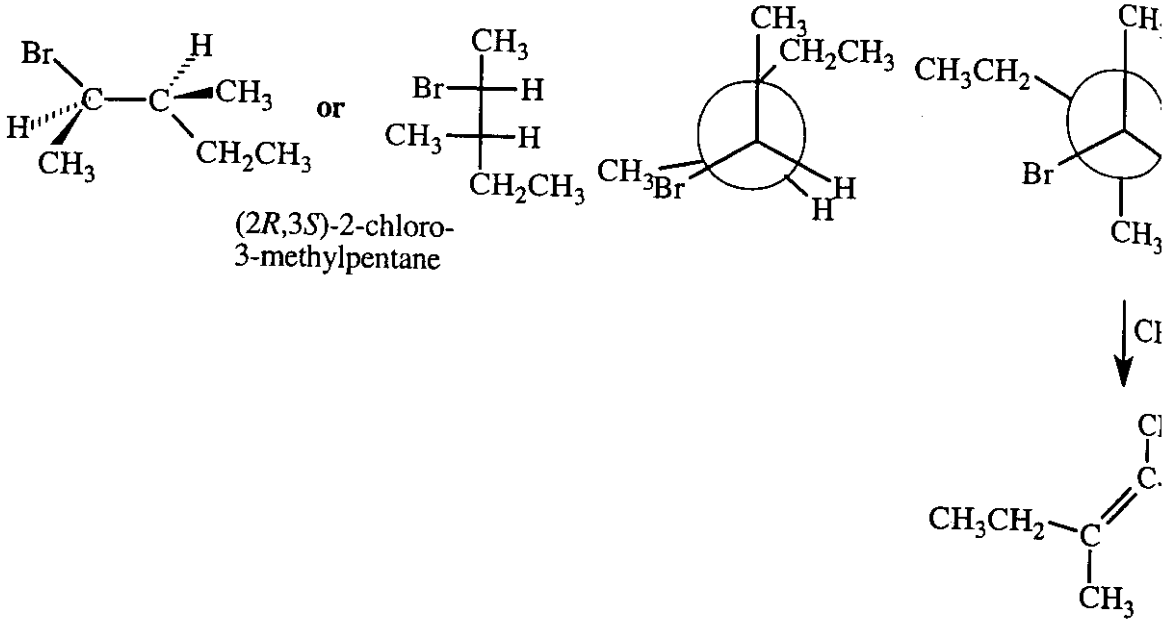
(2*S*,3*R*)-2-chloro-
3-methylpentane





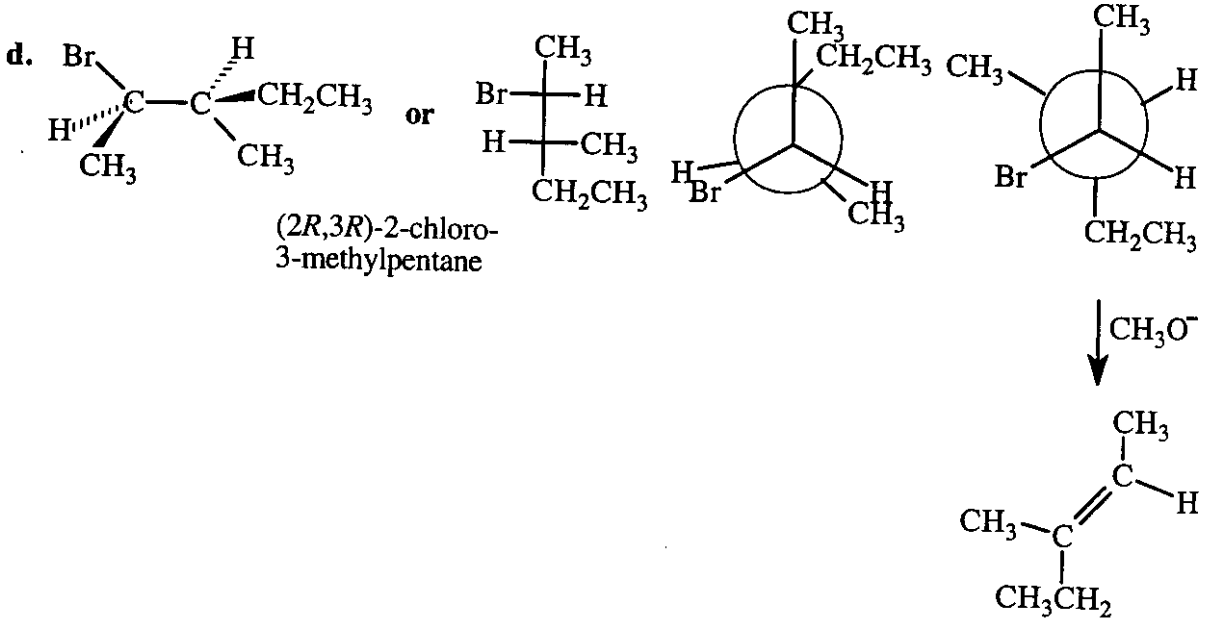


c.



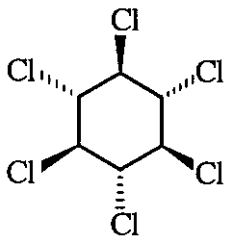
(2*R*,3*S*)-2-chloro-3-methylpentane

d.

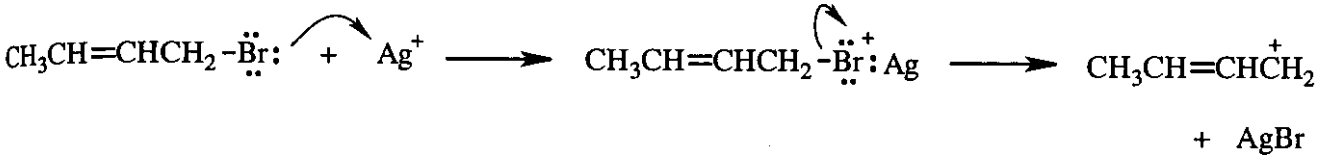


(2*R*,3*R*)-2-chloro-3-methylpentane

45. In order to undergo an E2 reaction, a chlorine and a hydrogen on an adjacent carbon must be trans to one another so they can both be in the required axial positions. Every Cl in the following compound has a Cl trans to it so no Cl has a hydrogen trans to it.

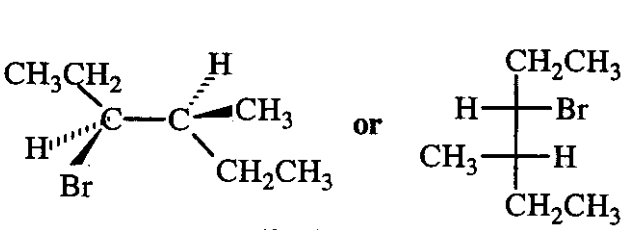


46. The silver ion increases the ease of departure of the halogen atom.



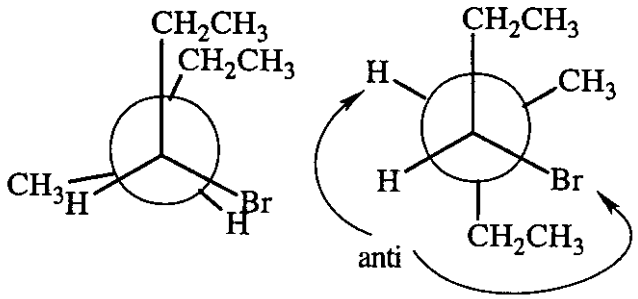
47. For a description of how to do this problem, see Problem 44.

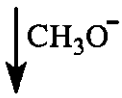
a.

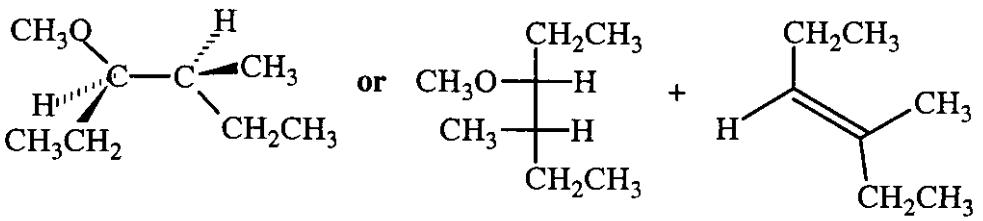


or

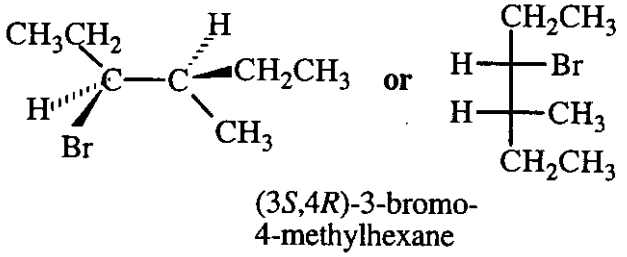
(3*S*,4*S*)-3-bromo-4-methylhexane





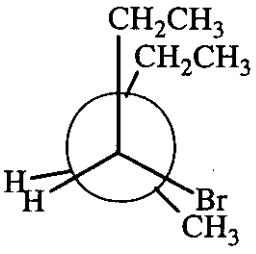


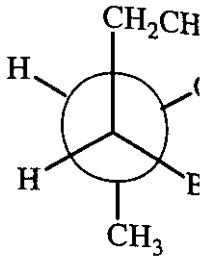
b.

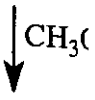


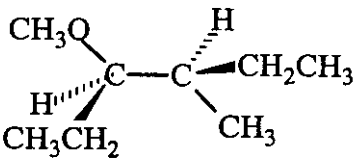
or

(3*S*,4*R*)-3-bromo-
4-methylhexane

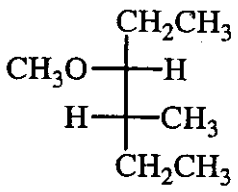




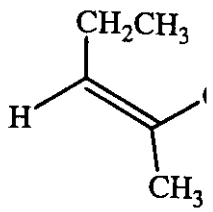




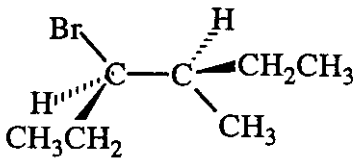
or



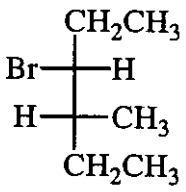
+



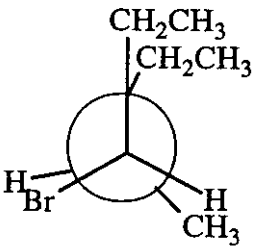
c.

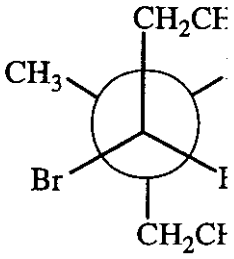


or

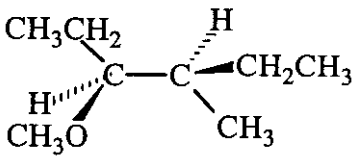


(3*R*,4*R*)-3-bromo-
4-methylhexane

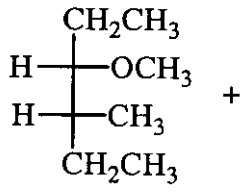




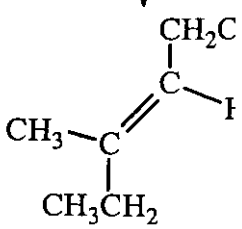




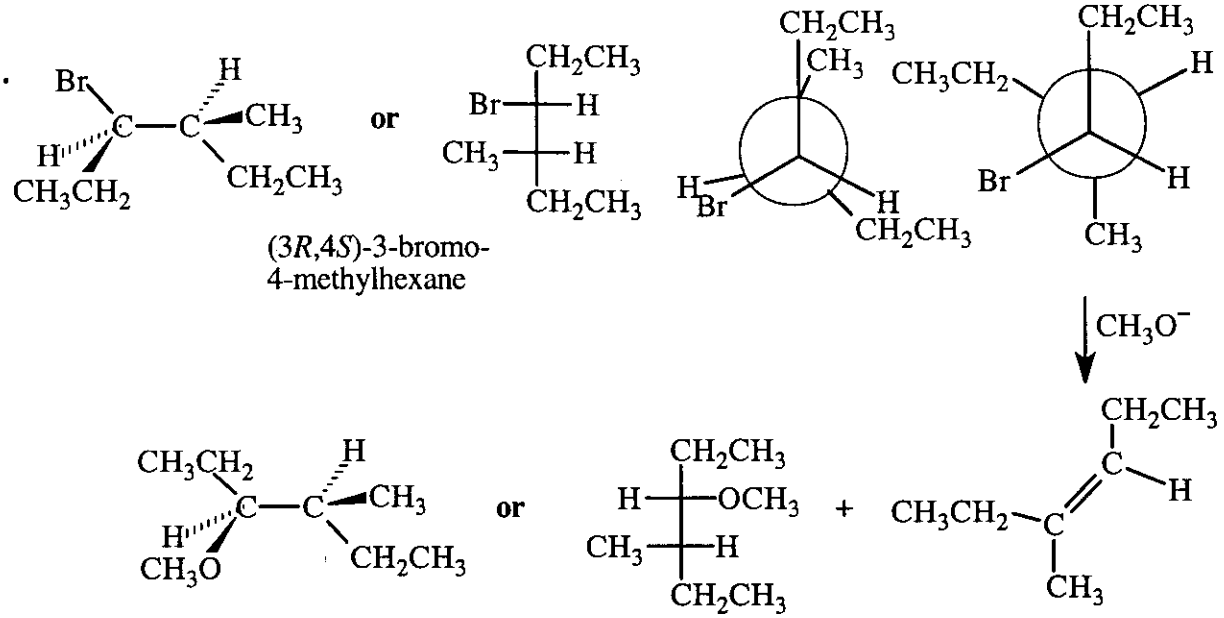
or



+



d.

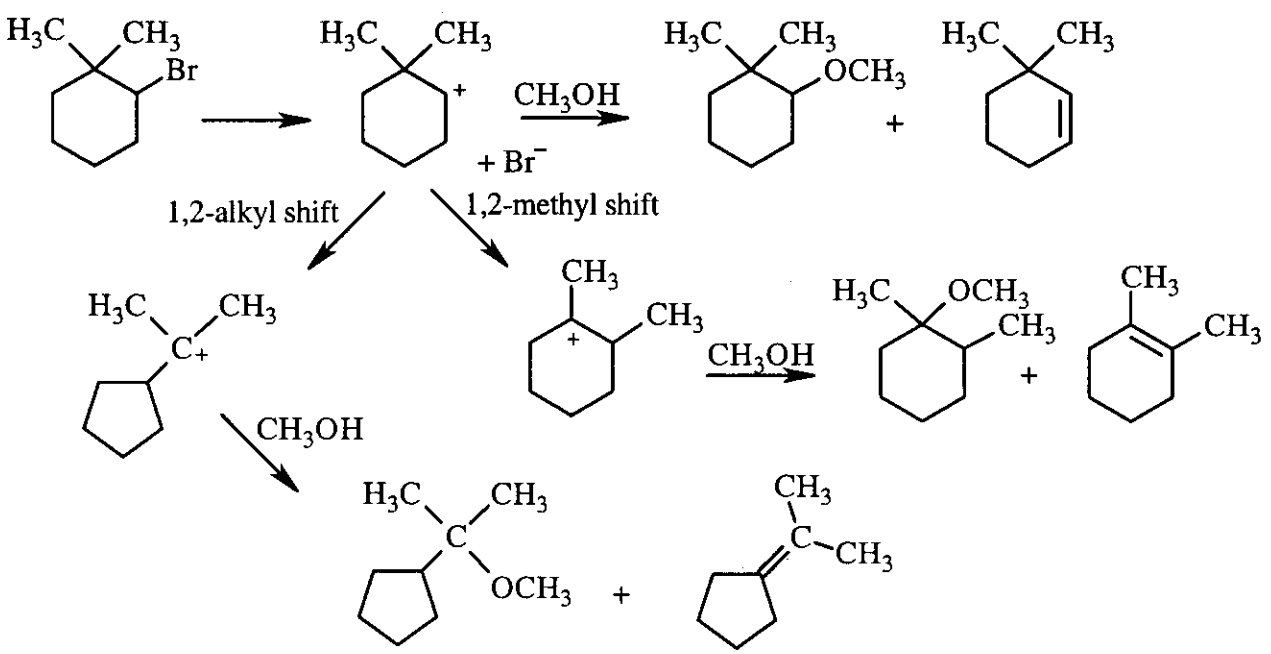


48.

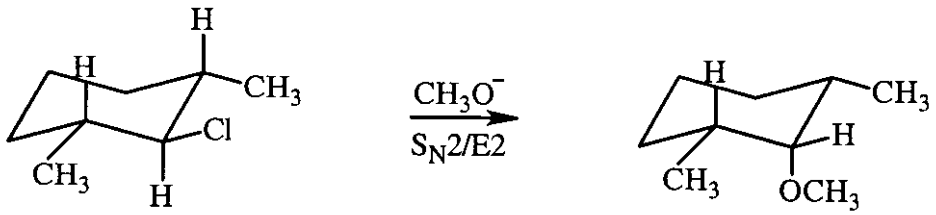
a. $CH_3CH_2CD{=}CH_2$ and $CH_3CH_2CH{=}CH_2$

b. The deuterium-containing compound results from elimination of HBr, while the non-deuterium-containing compound results from elimination of DBr. The deuterium-containing compound will be obtained in greater yield because a C—H bond is easier to break than a C—D bond.

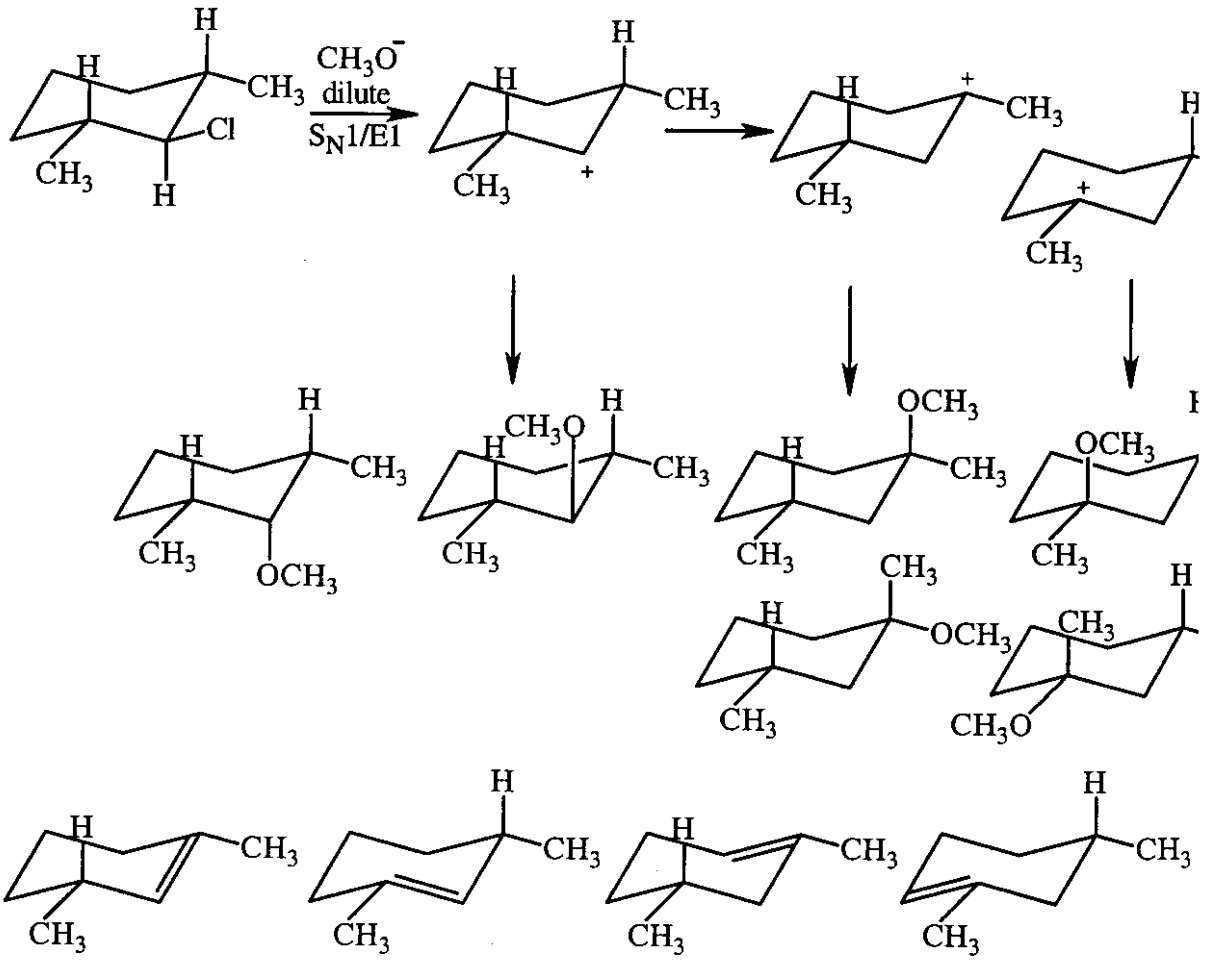
49.



50.

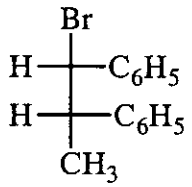


There is only a substitution product.
The reactant does not undergo elimination be
when Cl is in an axial position, there is not ar
adjacent hydrogen in an axial position.



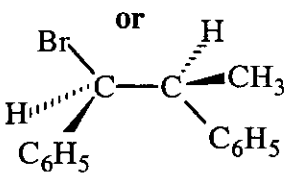
51.

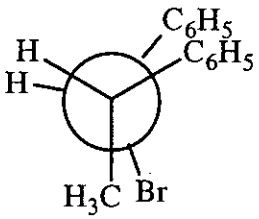
a.

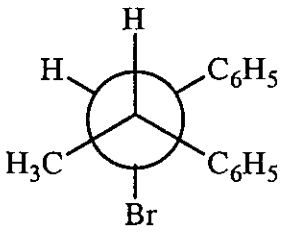


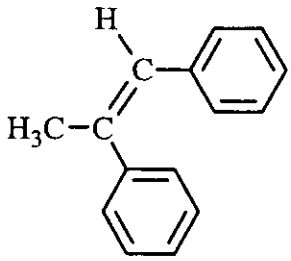
1*S*,2*S*

or

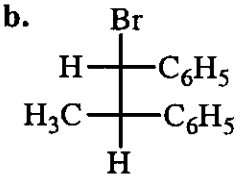






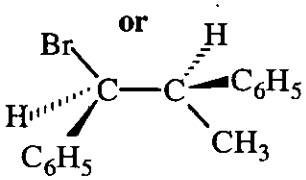


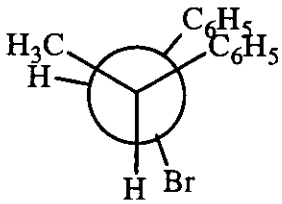
b.

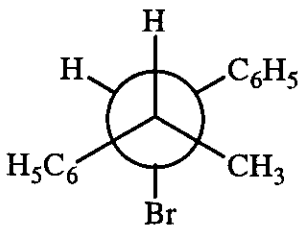


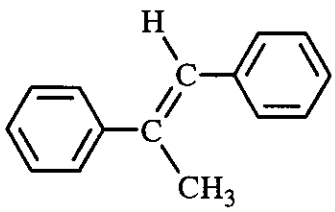
1*S*,2*R*

or



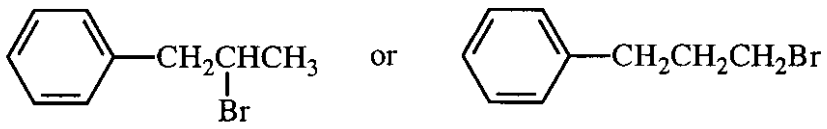






Chapter 11 Practice Test

1. Which of the following is more reactive in an E2 reaction?

a. 

b. $CH_3CH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$ or $CH_2{=}CHCH_2\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$

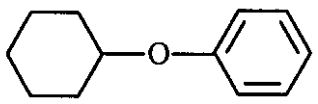
2. Which of the following compounds would give the greater amount of substitution product under conditions that would give an $S_N2/E2$ reaction?

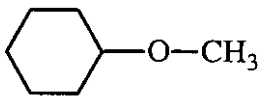
$$\begin{array}{l} CH_3 \\ | \\ CH_3CBr \\ | \\ CH_3 \end{array} \quad \text{or} \quad \begin{array}{l} CH_3 \\ | \\ CH_3CHBr \end{array}$$

3. What products are obtained when (*R*)-2-bromobutane reacts with CH_3O^-/CH_3OH under conditions that favor S1/E1 reactions? Include the configuration of the products.

4. What alkoxide ion and what alkyl bromide should be used to synthesize the following ethers?

a. $CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}OCH_2CH_2CH_3$

b. 

c. 

5. For each of the following pairs of E2 reactions, indicate the one that occurs with the greater rate constant:

a. $CH_3CH_2CH_2Cl + HO^-$ or $CH_3\underset{\displaystyle Cl}{\underset{|}{C}}HCH_3 + HO^-$

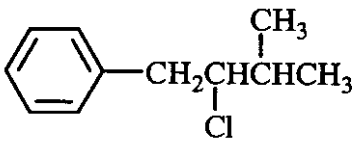
b. $CH_3CH_2CH_2Cl + HO^-$ or $CH_3CH_2CH_2I + HO^-$

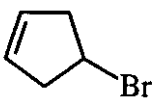
c. $CH_3CH_2CH_2Br + HO^-$ or $CH_3CH_2CH_2Br + H_2O$

d. $CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH_3 \xrightarrow[H_2O/CH_3OH]{CH_3O^-}$ or $CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH_3 \xrightarrow[CH_3OH]{CH_3O^-}$

e. $CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH_3 + HO^-$ or $CH_3\overset{\displaystyle CH_3}{\overset{|}{\underset{\displaystyle Br}{\underset{|}{C}}}}CH_3 + HO^-$

6. Give the major product of an E2 reaction of each of the following compounds with hydroxide ion:

a. 

b. 

c. $CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH(CH_3)_2$

d. $CH_3\underset{\displaystyle F}{\underset{|}{C}}HCH(CH_3)_2$

7. a. Which would be more reactive in an E2 reaction, *cis*-1-bromo-2-methylcyclohexane or *trans*-1-bromo-2-methylcyclohexane?

b. Which would be more reactive in an E1 reaction, *cis*-1-bromo-2-methylcyclohexane or *trans*-1-bromo-2-methylcyclohexane?

CHAPTER 12

Reactions of Alcohols, Ethers, Epoxides, and Sulfur-Containing Compounds • Organometallic Compounds

Important Terms

alcohol	an organic compound with an OH functional group (ROH).
alkyl tosylate	an ester of *para*-toluenesulfonic acid.
alkyl triflate	an ester of trifluoromethanesulfonic acid.
antibiotic	a compound that interferes with the growth of a microorganism.
arene oxide	an aromatic compound that has had one of its double bonds converted epoxide.
coupling reaction	a reaction that joins two carbon-hydrogen cintaining groups groups.
crown ether	a cyclic molecule that possesses several ether linkages.
crown-guest complex	the complex formed when a crown ether binds a substrate.
dehydration	loss of water.
epoxide (oxirane)	an ether in which the oxygen is incorporated into a three-membered ri
ether	a compound containing an oxygen bonded to two carbons (ROR).
Gilman reagent	a dialkylcopper reagent used to replace a halogen with an alkyl group.
Grignard reagent	the compound that results when magnesium is inserted between the ca and halogen of an alkyl halide (RMgBr, RMgCl).
Heck reaction	couples an aryl, benzyl, or vinyl halide or triflate with an alkene.
inclusion compound	a compound that specifically binds a metal ion or an organic molecule
mercapto group	an SH group.
molecular recognition	the recognition of one molecule by another as a result of specific interactions.
organocuprate	$(R)_2CuLi$; prepared by treating an organolithium reagent with cuprous iodide.
organolithium compound	RLi; prepared by adding lithium to an alkyl halide.
organomagnesium compound	RMgBr; prepared by adding an alkyl halide to magnesium shavings.
organometallic compound	a compound with a carbon-metal bond.
oxirane (epxoide)	an ether in which the oxygen is incorporated into a three-membered ri

phase-transfer catalyst	a compound that carries a polar reagent into a nonpolar phase.
ring-expansion rearrangement	rearrangement of a carbocation in which the positively charged carbon is bonded to a cyclic compound, and as a result of rearrangement, the size of the ring increases by one carbon.
Stille reaction	couples an aryl, benzyl, or vinyl halide or triflate with a stannane.
sulfonate ester	the ester of a sulfonic acid (RSO_2OR).
sulfonium salt	$(R)_3\,S^+\ X^-$
Suzuki reaction	couples an aryl, benzyl, or vinyl halide or triflate with an organoborane.
thioether (sulfide)	the sulfur analog of an ether (RSR).
thiol (mercaptan)	the sulfur analog of an alcohol (RSH).
transmetallation	metal exchange.
vicinal diol (vicinal glycol)	a compound with OH groups bonded to adjacent carbons.

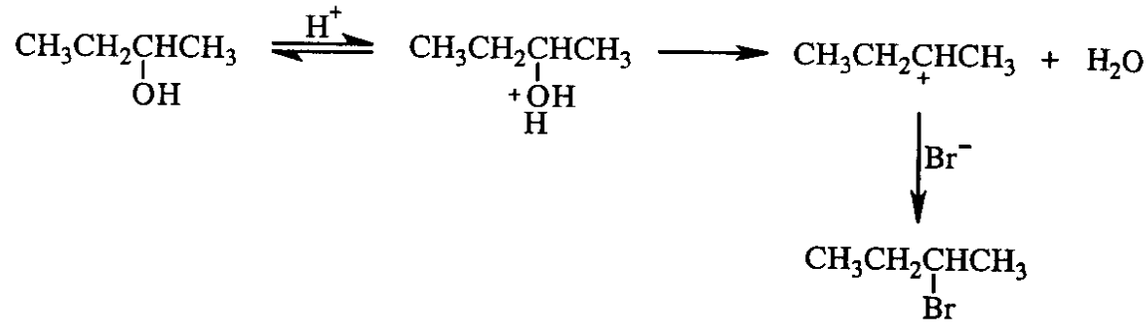
Solutions to Problems

1. The relative reactivity would be: tertiary > primary > secondary.

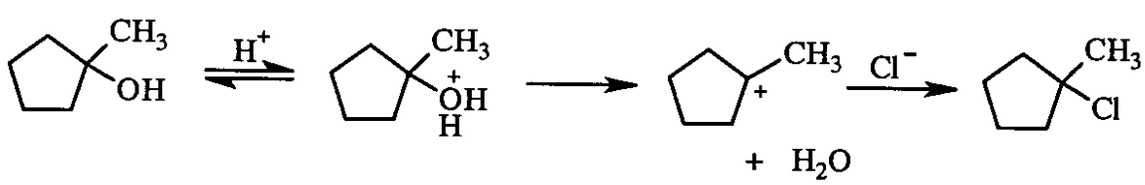
If secondary alcohols reacted by an S_N2 mechanism, they would be less reactive than primary alcohols because they are more sterically hindered than primary alcohols.

2. All four alcohols react by an S_N1 mechanism because they are either secondary or tertiary alcohols.

a.

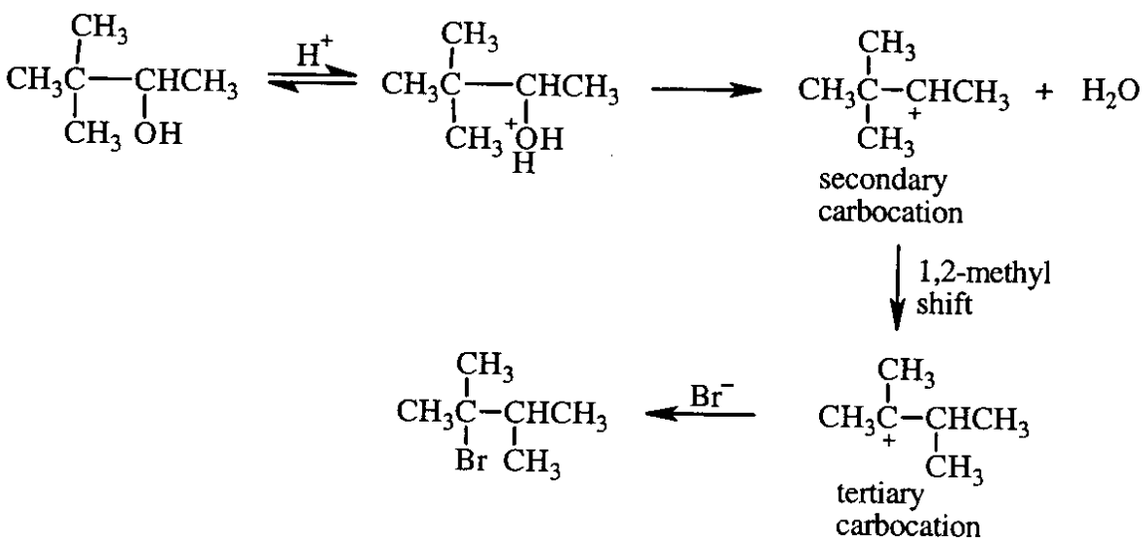


b.

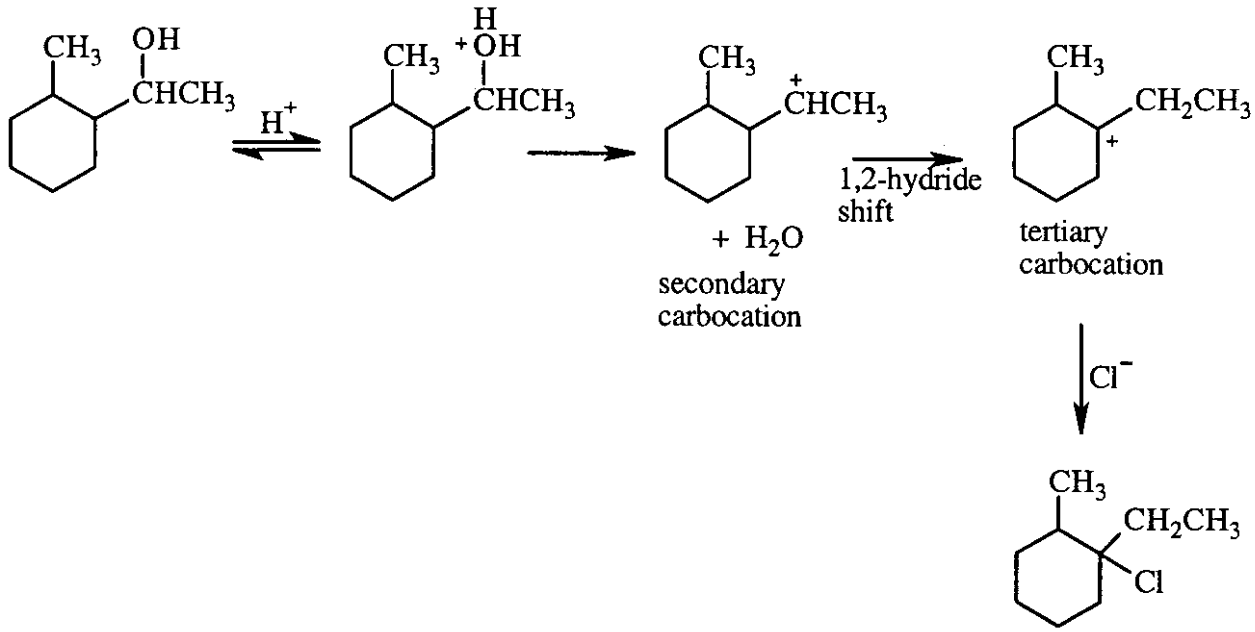


The carbocation that is initially formed in **c** and the carbocation that is initially formed in **d** rearrange in order to form more stable carbocations.

c.



d.



3. The stronger the base, the more difficult it is to displace.

Water is a stronger base by about 7 pK_a units than Br^-;

(the pK_a of HBr = – 9; the pK_a of $CH_3OH_2^+$ = -1.7).

$$Br^- + CH_3\overset{+}{O}H_H \xrightarrow{\Delta} CH_3Br + H_2O$$

Ammonia is a stronger base by about 18 pK_a units than Br^- ;

(the pK_a of HBr = – 9; the pK_a $CH_3NH_3^+$ = 9.4).

Thus, ammonia is far too basic to be displaced by Br^-.

$$Br^- + CH_3\overset{+}{N}H_3 \xrightarrow{\Delta} \text{no reaction}$$

4. Solved in the text.

5. All the syntheses below are shown to be accomplished by converting the alcohol into a sulfonate ester and then treating the sulfonate ester with the desired nucleophile:

a could also have been carried out by converting the alcohol directly into the alkyl bromide with HBr;

b-f could have been carried out by converting the alcohol into an alkyl halide and then adding the desired nucleophile.

a. $CH_3CH_2CH_2CH_2OH \xrightarrow[2.\ KBr]{1.\ TsCl} CH_3CH_2CH_2CH_2Br$

b. $CH_3CH_2CH_2CH_2OH \xrightarrow[2.\ CH_3CH_2C(=O)O^-]{1.\ TsCl} CH_3CH_2CH_2CH_2OC(=O)CH_2CH_3$

c. $CH_3CH_2CH_2CH_2OH \xrightarrow[2.\ CH_3O^-]{1.\ TsCl} CH_3CH_2CH_2CH_2OCH_3$

d. $CH_3CH_2CH_2CH_2OH \xrightarrow[2.\ CH_3CH_2NH_2]{1.\ TsCl} CH_3CH_2CH_2CH_2\overset{+}{N}H_2CH_2CH_3 \xrightarrow{HO^-} CH_3CH_2CH_2CH_2NHCH_2CH_3$

Notice that in "**d**" a neutral amine ($CH_3CH_2NH_2$) is used instead of $CH_3CH_2NH^-$, because the weaker base ($CH_3CH_2NH_2$) favors the desired substitution reaction, while the stronger base ($CH_3CH_2NH^-$) would favor elimination at the expense of substitution (Section 11.8).

e. $CH_3CH_2CH_2CH_2OH \xrightarrow[2.\ H_2S]{1.\ TsCl} CH_3CH_2CH_2CH_2\overset{+}{S}H_2 \xrightarrow{HO^-} CH_3CH_2CH_2CH_2SH$

f. $CH_3CH_2CH_2CH_2OH \xrightarrow[2.\ {}^-C\equiv N]{1.\ TsCl} CH_3CH_2CH_2CH_2C\equiv N$

6. The product of each reaction is an alkene.

$$CH_3CH_2\underset{OH}{CH}CH_3 \underset{\Delta}{\overset{H_2SO_4}{\rightleftharpoons}} CH_3CH_2\underset{{}^+OH\ H}{CH}CH_3 \longrightarrow CH_3CH_2\underset{+}{C}HCH_3 + H_2O$$

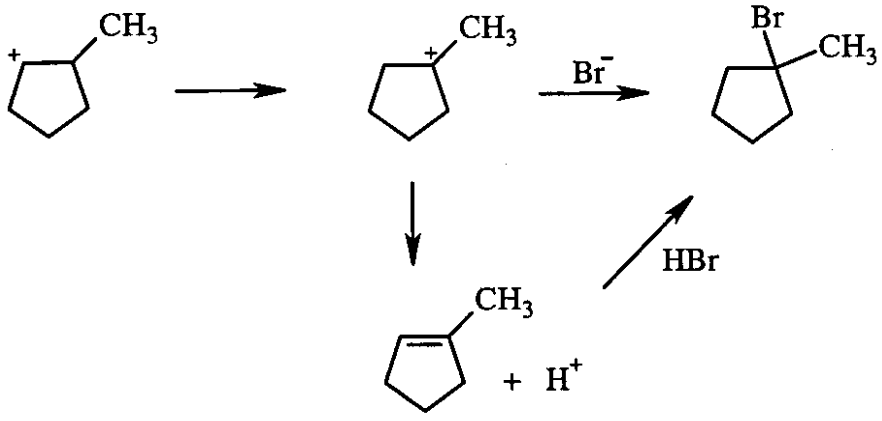
$$CH_3CH_2\underset{+}{C}HCH_3 \longrightarrow CH_3CH{=}CHCH_3 + H_3O^+$$

$$CH_3CH_2\underset{Br}{CH}CH_3 \xrightarrow{HO^-} CH_3CH{=}CHCH_3 + H_2O + Br^-$$

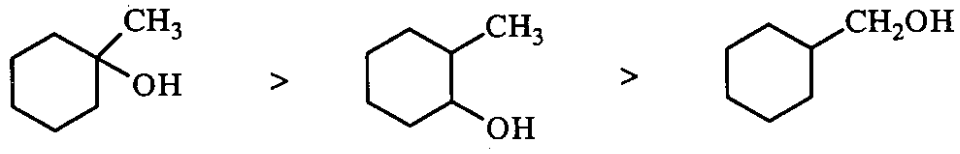
Recall that alkenes undergo electrophilic addition reactions, and the first step in an electrophilic addition reaction is addition of an electrophile to the alkene. The acid-catalyzed dehydration reaction is reversible because the electrophile (H^+) needed for the first step of the reverse electrophilic addition reaction is available.

Base-promoted elimination reaction of a hydrogen halide is not reversible because an electrophile is not available to react with the alkene.

7. 1-Bromo-1-methylcyclopentane would be formed because Br^- would react with the carbocation. If the carbocation were able to lose a proton before it reacts with Br^-, HBr could add to the resulting alkene, thereby forming the same alkyl halide as would be formed by addition of Br^- to the carbocation.



8.



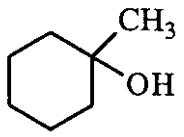
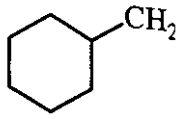
9. **a.** In order to synthesize an unsymmetrical ether (ROR') by this method, two different alcohols (ROH and R'OH) would have to be heated with sulfuric acid. Therefore, three different ethers would be obtained as products. Consequently, the desired ether would account for considerably less than half of the total amount of ether that is synthesized.

$$\text{ROH} + \text{R'OH} \xrightarrow[\Delta]{H_2SO_4} \text{ROR} + \text{ROR'} + \text{R'OR'}$$

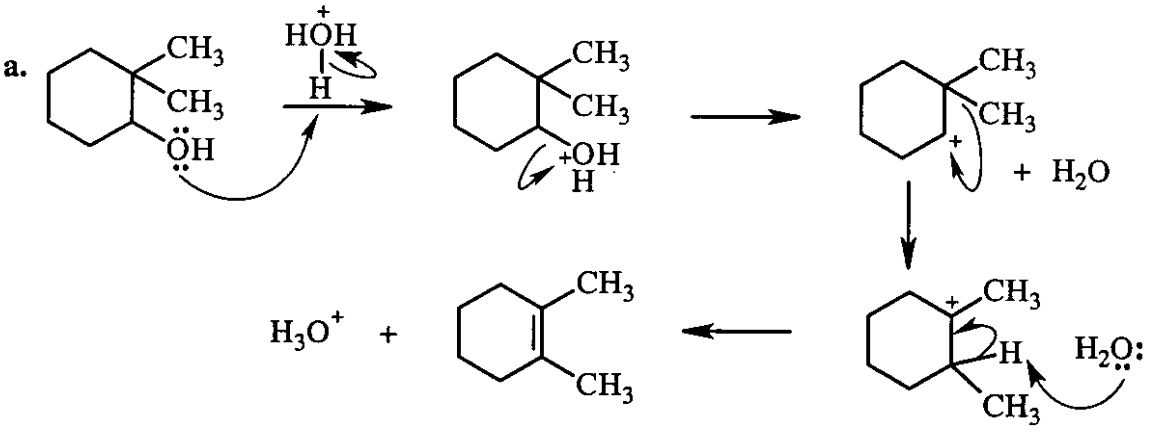
b. It could be synthesized by a Williamson ether synthesis. (See Section 11.9 on page 425 of the text.)

$$CH_3CH_2CH_2OH \xrightarrow{Na} CH_3CH_2CH_2O^- \xrightarrow{CH_3CH_2Br} CH_3CH_2CH_2OCH_2CH_3 + Br^-$$

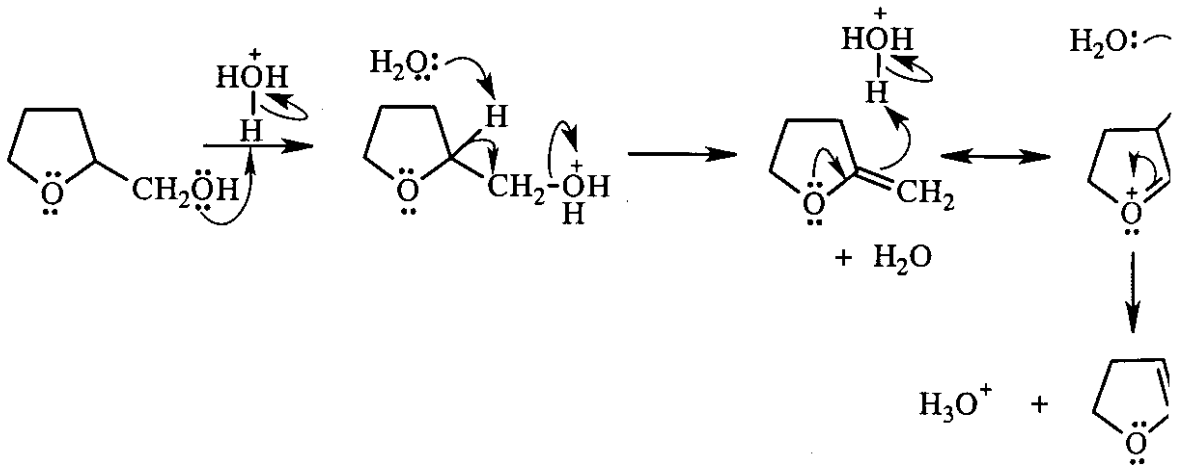
10.

a. $CH_3CH_2\underset{\displaystyle CH_3}{\overset{|}{C}}HCH_2OH$ **b.**  **c.** $CH_3CH_2\underset{\displaystyle OH}{\overset{|}{C}}HCH_2CH_3$ **d.** 

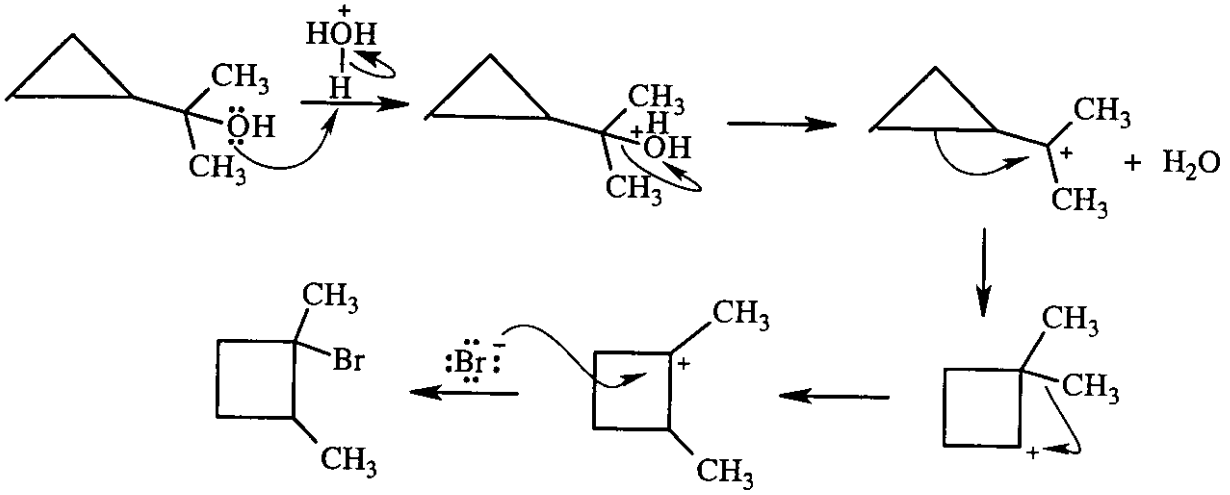
11.

a. 

b. Because of the difficulty of forming a primary carbocation, dehydration is an E2 reaction. The alkene that results is protonated and the proton that is removed is the one that results in formation of the most stable alkene.

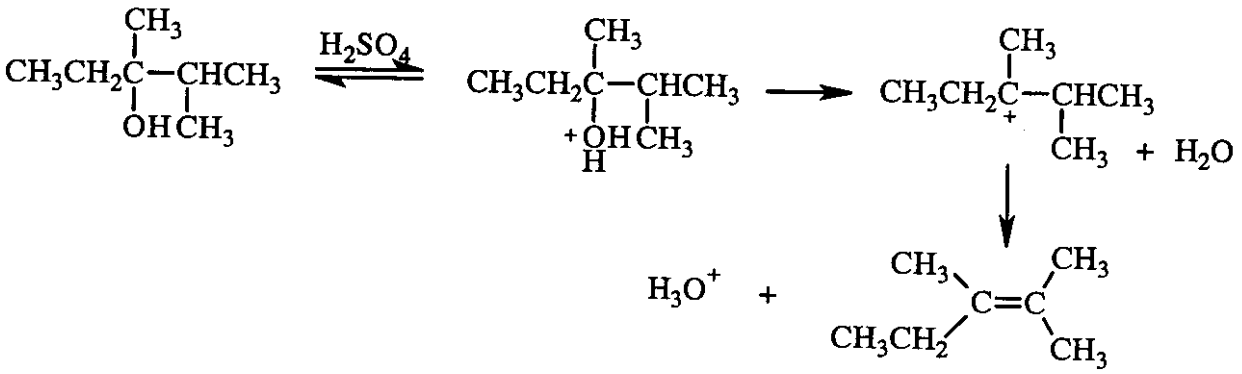


c.

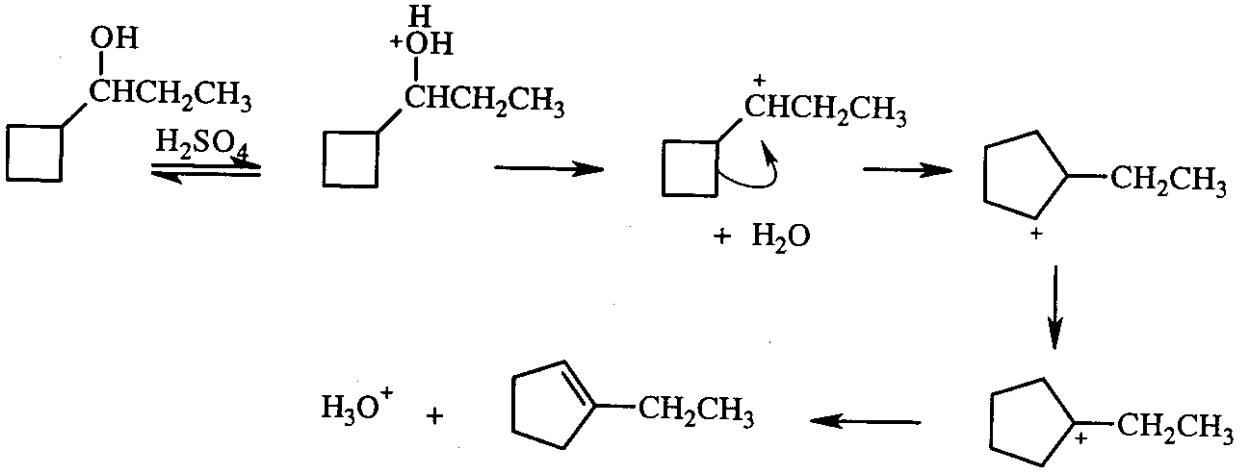


12.

a.

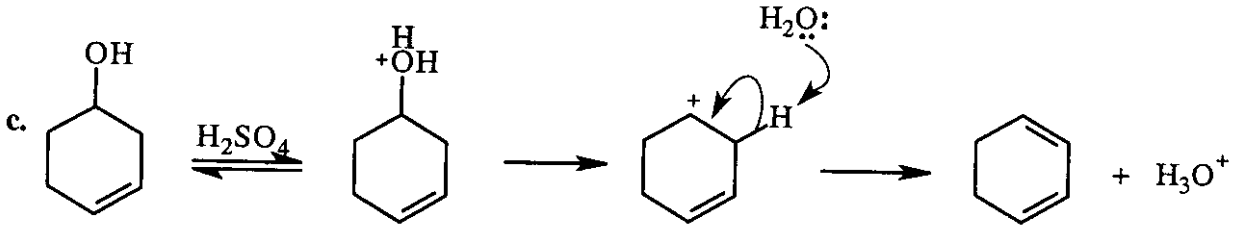


b.



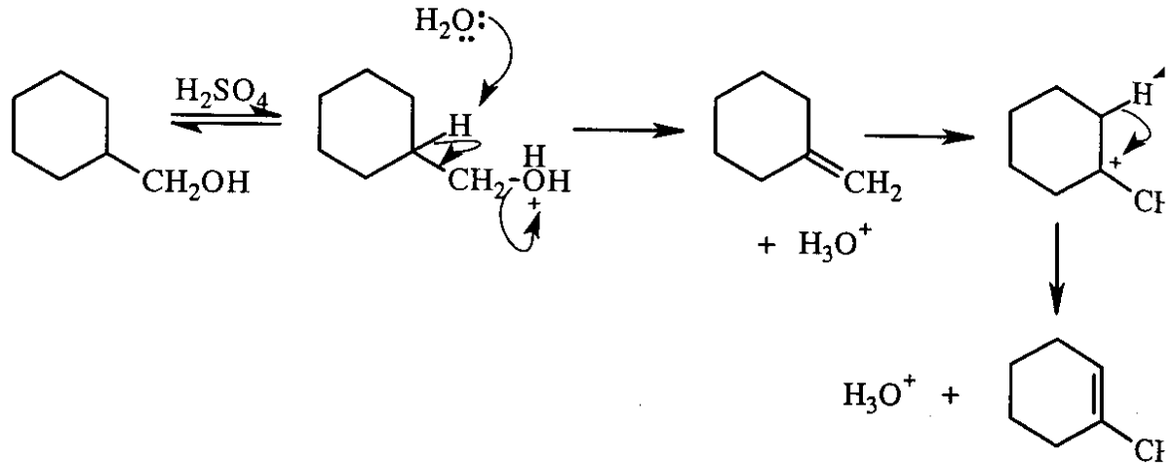
Loss of any one of four hydrogens leads to this product.

c.

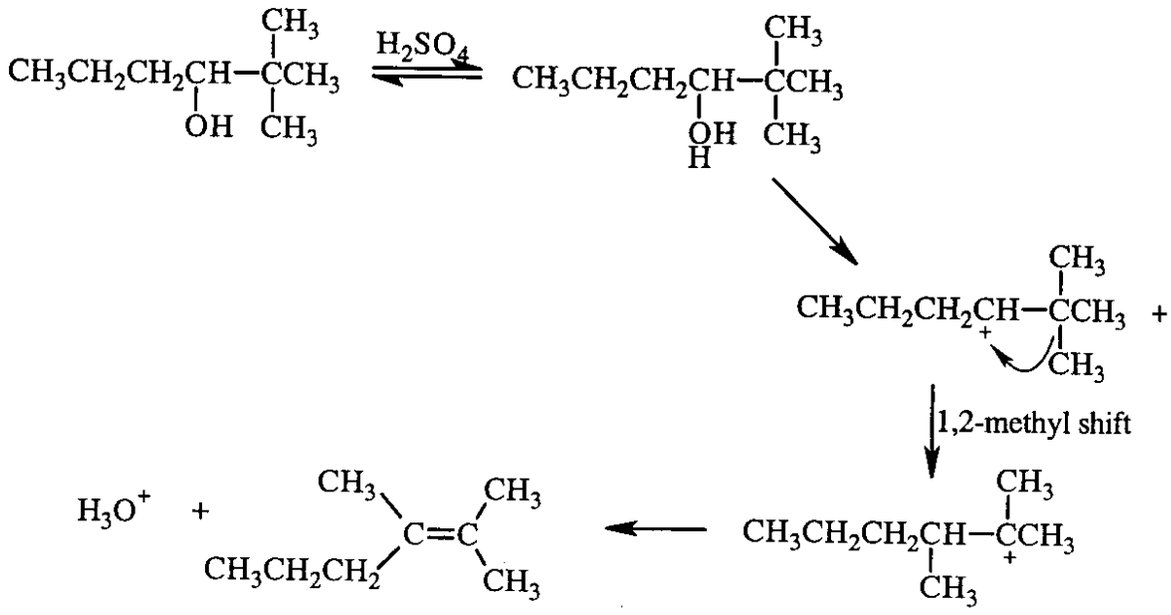


In "**d**" and "**f**", the reactant is a primary alcohol. Therefore, elimination of water takes place by an E2 mechanism.
Because the dehydration reaction is being carried out in an acidic solution, the alkene that is formed initially is protonated to form a carbocation. The proton that is then lost from the carbocation is the one that results in formation of the most stable alkene.

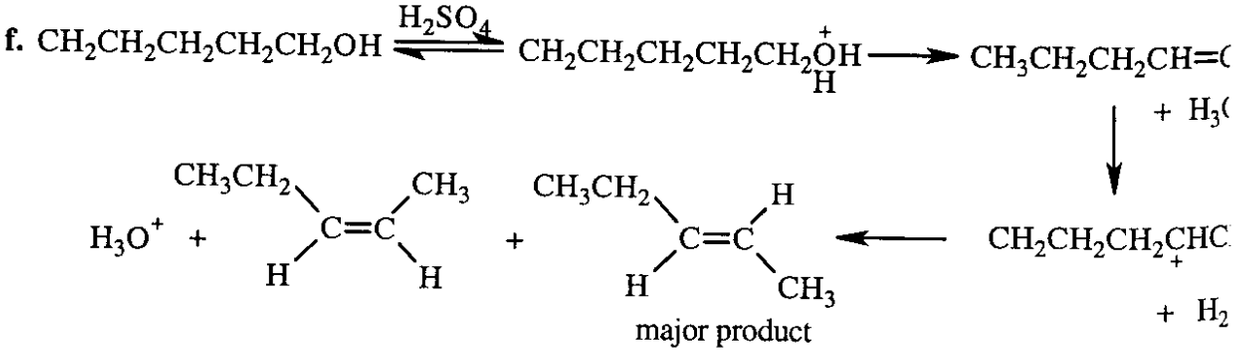
d.



e.



f.



13. In the presence of excess HI, the alcohol that is formed when the ether is cleaved is subsequently converted into an alkyl iodide.

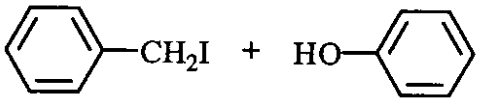
$$CH_3OCH_2CH_2CH_3 \xrightarrow[\Delta]{HI} CH_3I + CH_3CH_2CH_2OH \xrightarrow[\Delta]{HI} CH_3CH_2CH_2I + H_2O$$

14. We saw that HCl does not cleave ethers, because Cl^- is not a strong enough nucleophile. F^- is an even weaker nucleophile, so HF cannot cleave ethers. Therefore, ethers can be cleaved only with HBr or HI.

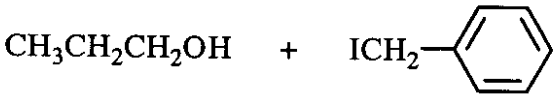
15. Notice that if there is excess concentrated HI, the initially formed alcohol can be converted to an alkyl iodide in c, d, and f.

a. Solved in the text.

b. Cleavage occurs by an S_N1 pathway because the benzyl carbocation that is formed is relatively stable; I^- will attack the benzyl carbocation.

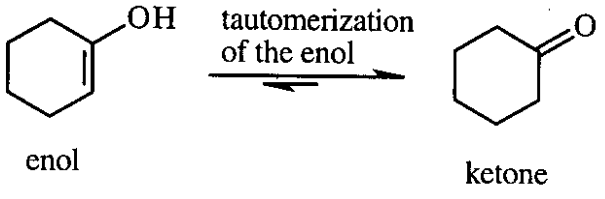


c. Cleavage occurs by an S_N1 pathway because the benzyl carbocation that is formed is relatively stable; I^- will attack the benzyl carbocation.



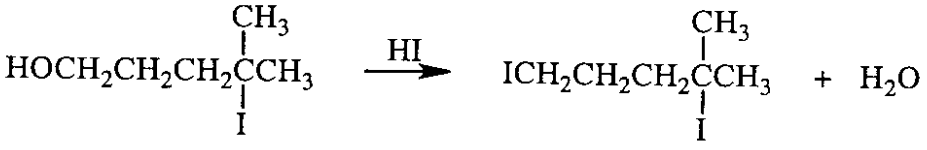
d. $HOCH_2CH_2CH_2CH_2CH_2I \xrightarrow{HI} ICH_2CH_2CH_2CH_2CH_2I + H_2O$

e. CH_3I +

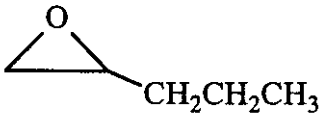


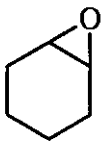
enol ketone

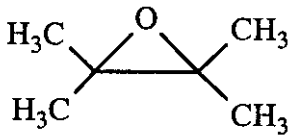
f. Cleavage will occur by an S_N1 pathway because the tertiary carbocation that is formed is relatively stable; I^- will attack the tertiary carbocation.

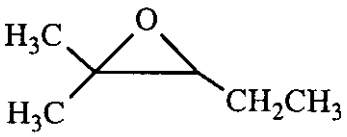


16.

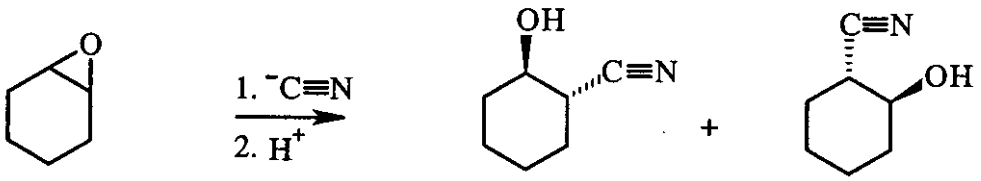
a. 

b. 

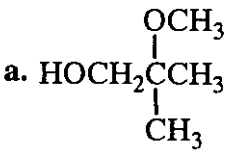
c. 

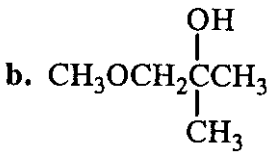
d. 

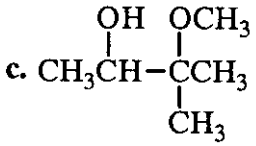
17. Two stereoisomers will be formed because the cyano group can attack either of the carbons that are bonded to the oxygen from the backside.

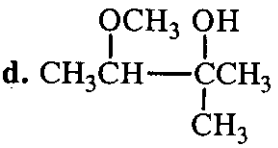


18.

a. 

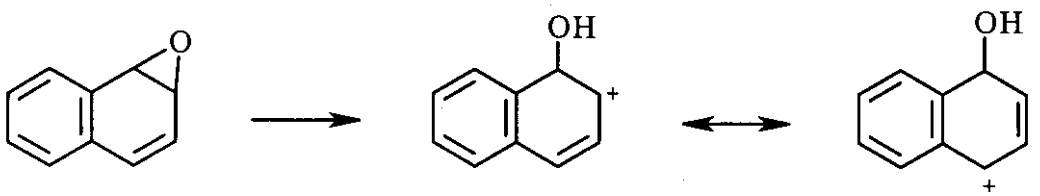
b. 

c. 

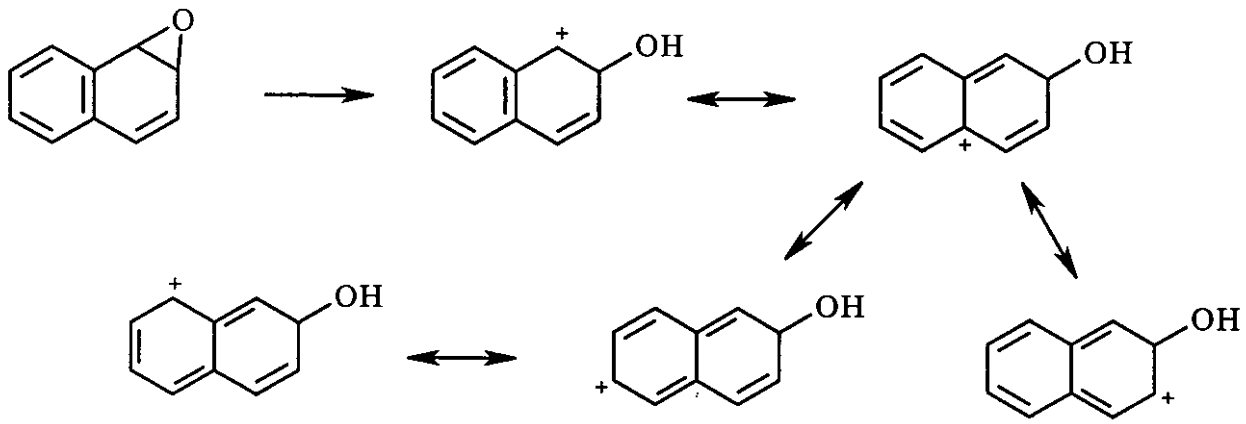
d. 

19. The reactivity of tetrahydrofuran is more similar to a noncyclic ether because the five-membere ring does not have the strain that makes the epoxide reactive.

20. The carbocation leading to 1-naphthol can be stabilized without destroying the aromaticity of the intact benzene ring. The carbocation leading to 2-naphthol can be stabilized only by destroying the aromaticity of the intact benzene ring. therefore, the carbocation leading to 1-naphthol is more stable.



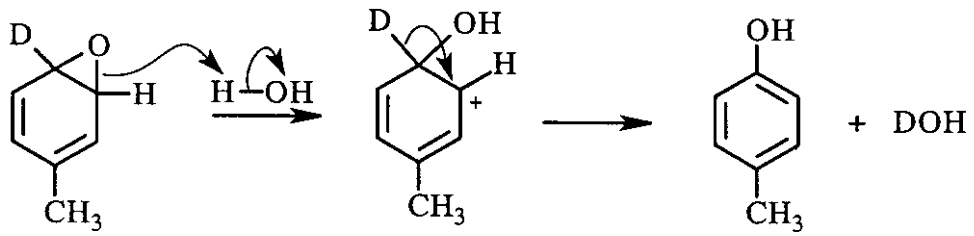
carbocation that leads to 1-naphthol



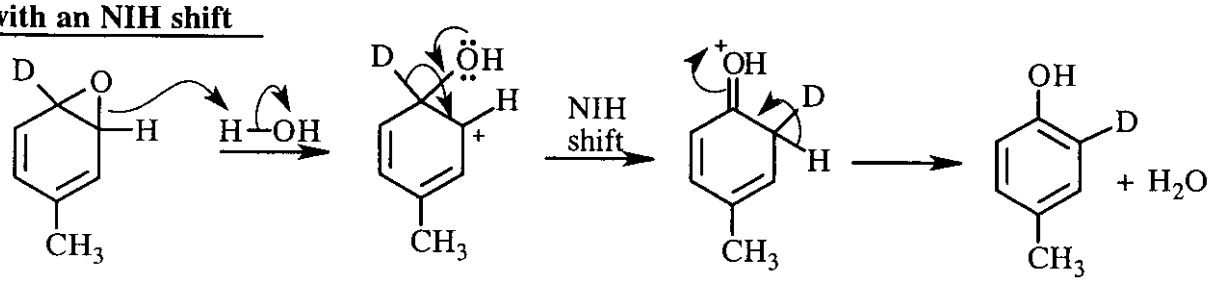
carbocation that leads to 2-naphthol

21.

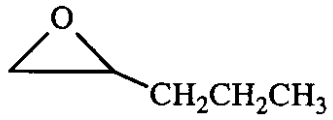
without an NIH shift

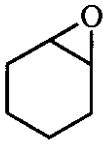


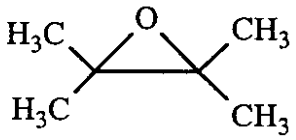
with an NIH shift

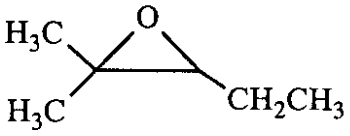


16.

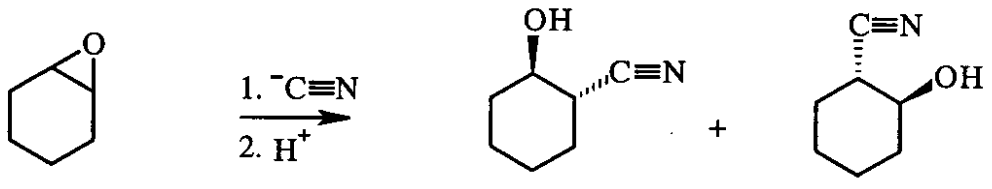
a. 

b. 

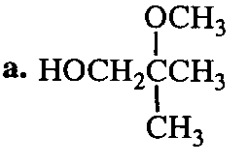
c. 

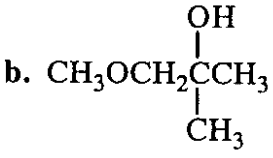
d. 

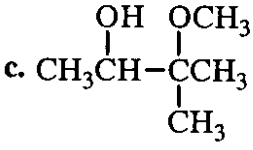
17. Two stereoisomers will be formed because the cyano group can attack either of the carbons that are bonded to the oxygen from the backside.

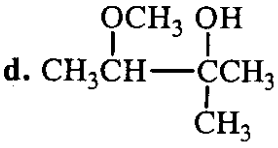


18.

a. 

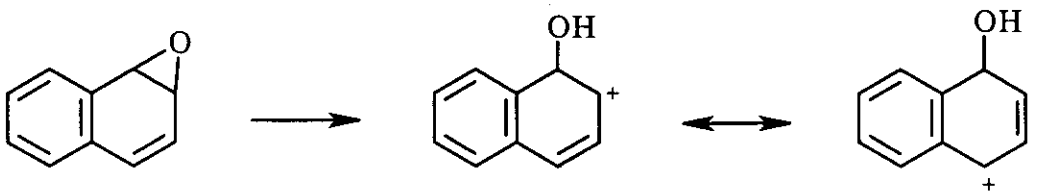
b. 

c. 

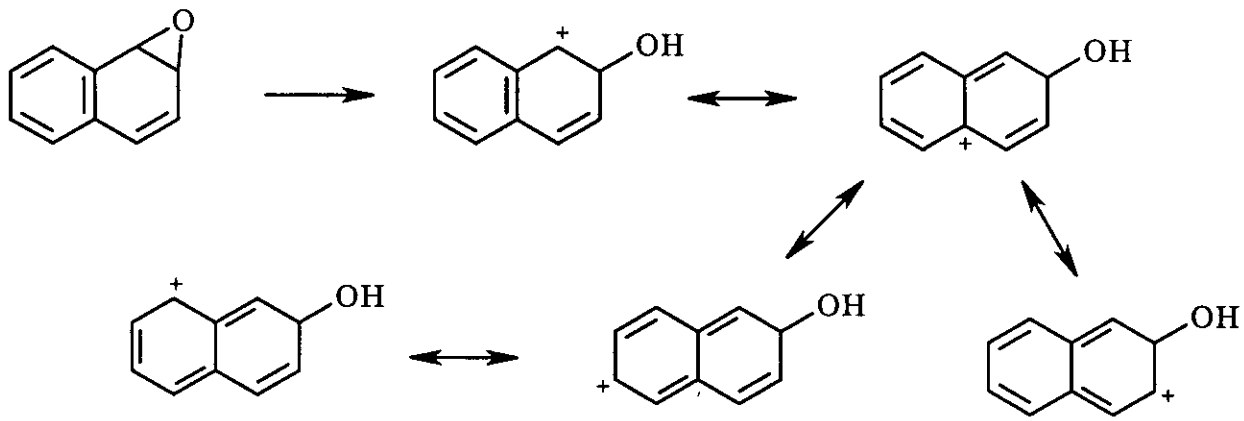
d. 

19. The reactivity of tetrahydrofuran is more similar to a noncyclic ether because the five-membered ring does not have the strain that makes the epoxide reactive.

20. The carbocation leading to 1-naphthol can be stabilized without destroying the aromaticity of the intact benzene ring. The carbocation leading to 2-naphthol can be stabilized only by destroying the aromaticity of the intact benzene ring. therefore, the carbocation leading to 1-naphthol is more stable.



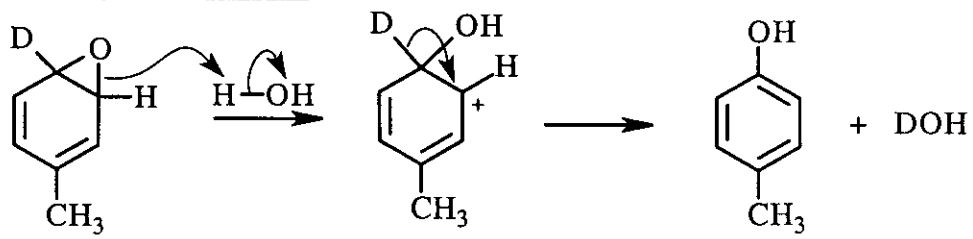
carbocation that leads to 1-naphthol



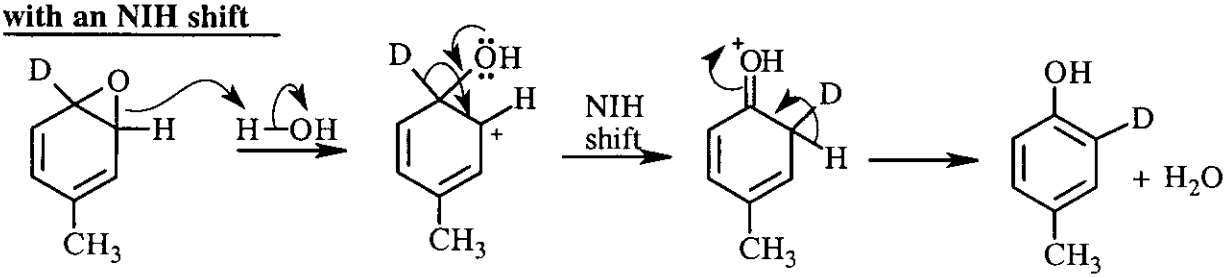
carbocation that leads to 2-naphthol

21.

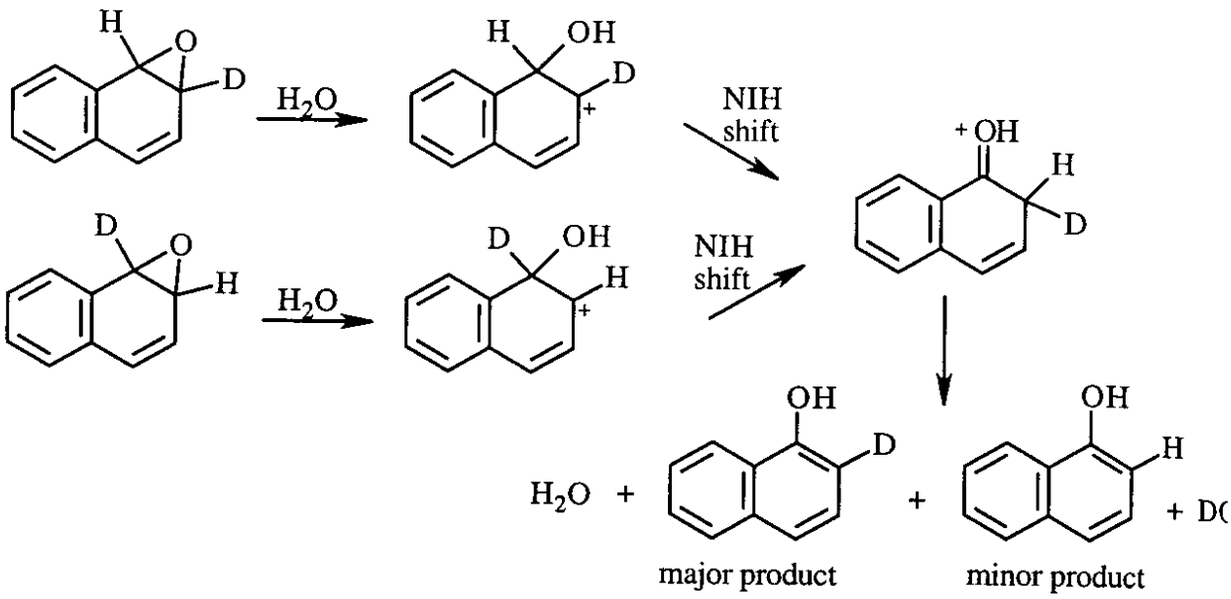
without an NIH shift



with an NIH shift

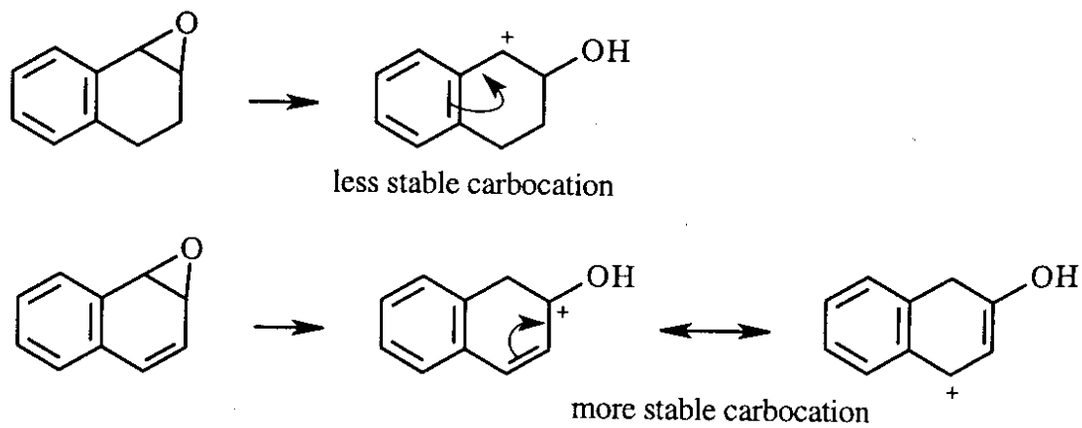


22. The epoxide opens in the direction that will give the most stable carbocation. The carbocation undergoes an NIH shift and, as a result of the NIH shift, both reactants form the same ketone intermediate. Because they form the same intermediate, they form the same products. The deuterium-containing product is the major product because in the last step of the reaction it is easier to break a carbon-hydrogen bond than a carbon-deuterium bond.

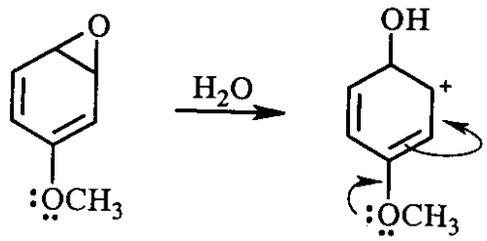


23. **a.** Solved in the text.

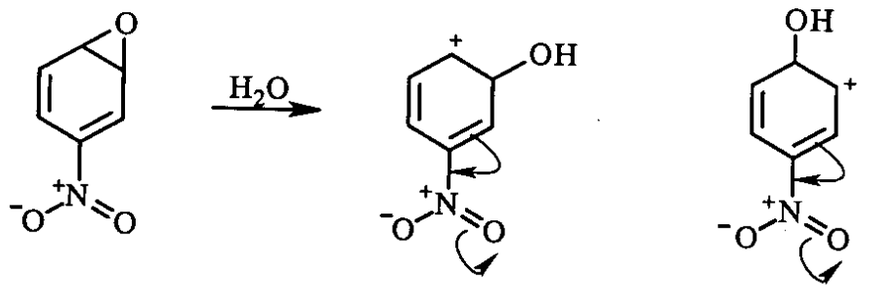
b. The compound without the double bond in the second ring is more apt to be carcinogenic. It opens to form a less stable carbocation than the other compound because it can be stabilized by electron delocalization only if the aromaticity of the benzene ring is destroyed. Because the carbocation is less stable, it is formed more slowly, giving the carcinogenic pathway a better chance to compete with ring-opening.



24. Each arene oxide will open in the direction that forms the most stable carbocation. Thus, the arene oxide opens so the positive charge can be stabilized by electron delocalization from the methoxide group.

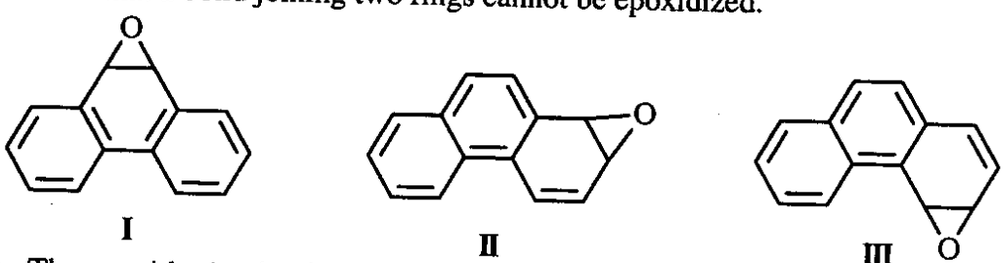


The arene oxide opens to form the most stable carbocation intermediate, which is the one where the positive charge is father away from the electron-withdrawing NO_2 group.



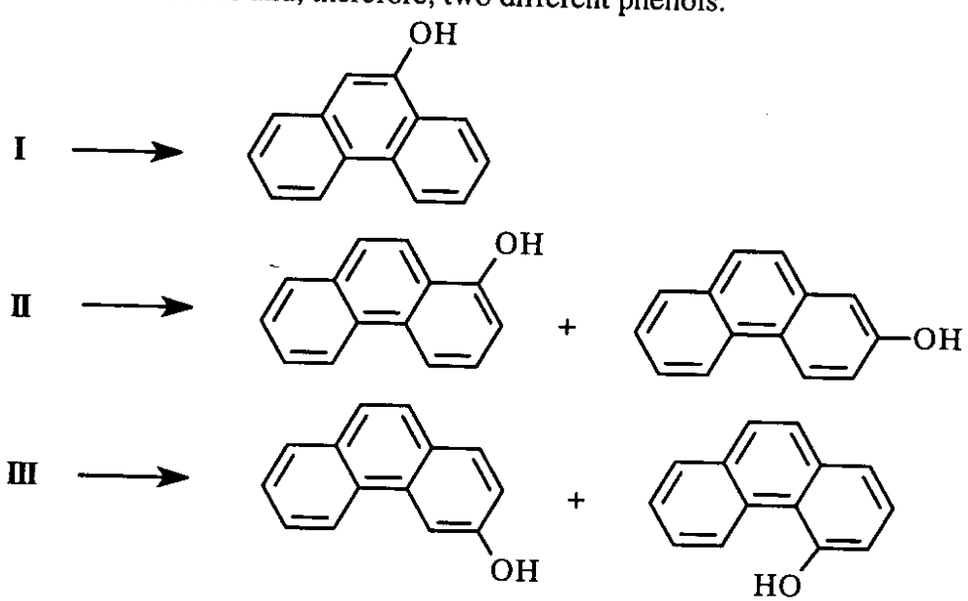
more stable less stable

25. **a.** Note that a bond joining two rings cannot be epoxidized.

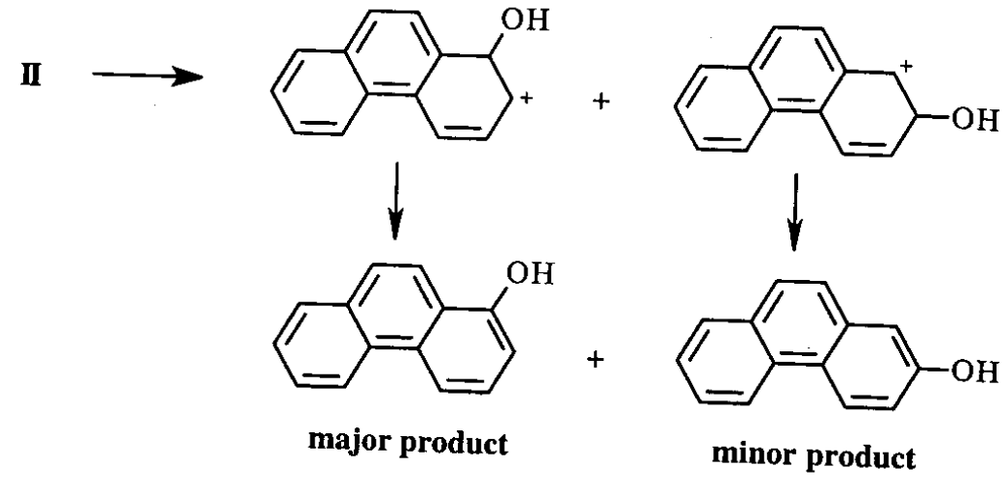


I II III

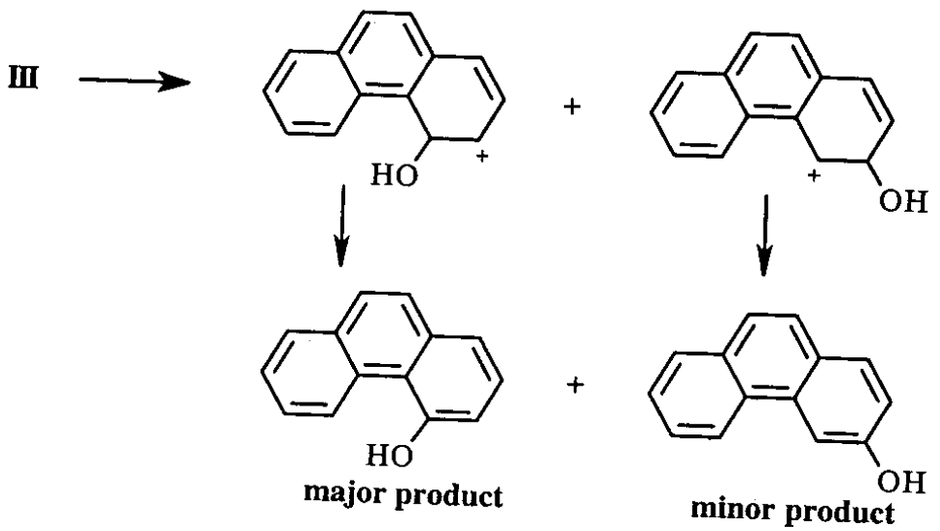
b. The epoxide ring in phenanthrenes II and III can open in two different directions to give two different carbocations and, therefore, two different phenols.



c. The two different carbocations formed by phenanthrenes II and III differ in stability. One carbocation is more stable than the other because it can be stabilized by resonance without disrupting the aromaticity of the adjacent ring. The more stable carbocation leads to the major product.



major product **minor product**



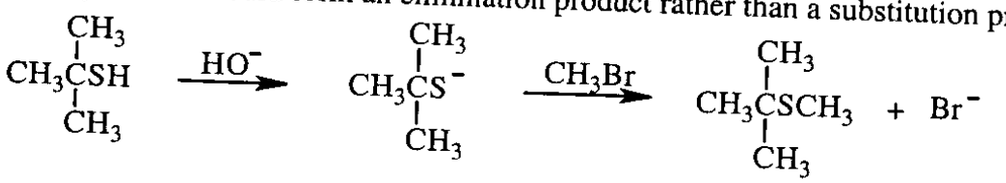
major product **minor product**

d. Phenanthrene oxide I is the most carcinogenic because it is the only one that opens to form a carbocation that cannot be stabilized without disrupting the aromaticity of the other ring(s).

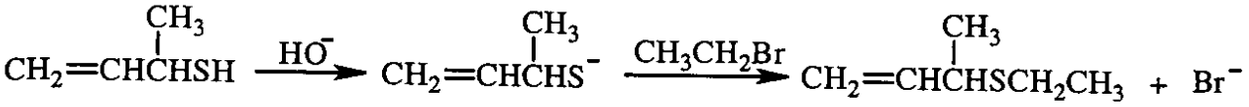
26.

a. $CH_3CH_2SH \xrightarrow{HO^-} CH_3CH_2S^- \xrightarrow{CH_3CH_2Br} CH_3CH_2SCH_2CH_3 + Br^-$

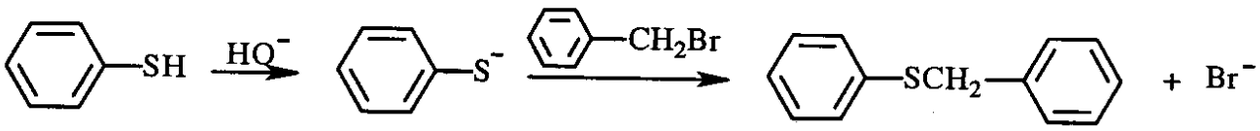
b. The reaction cannot be done with methanethiol and *tert*-butyl bromide, because a tertiary alkyl halide would form an elimination product rather than a substitution product.



c. The highest yield is obtained by having the less substituted of the two R groups of the thioether be the alkyl halide and the more substituted be the thiol.

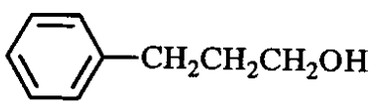
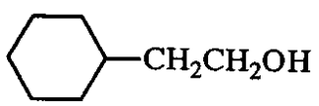


d. The synthesis must be done this way because the sp^2 carbon of the benzene ring cannot undergo backside attack.

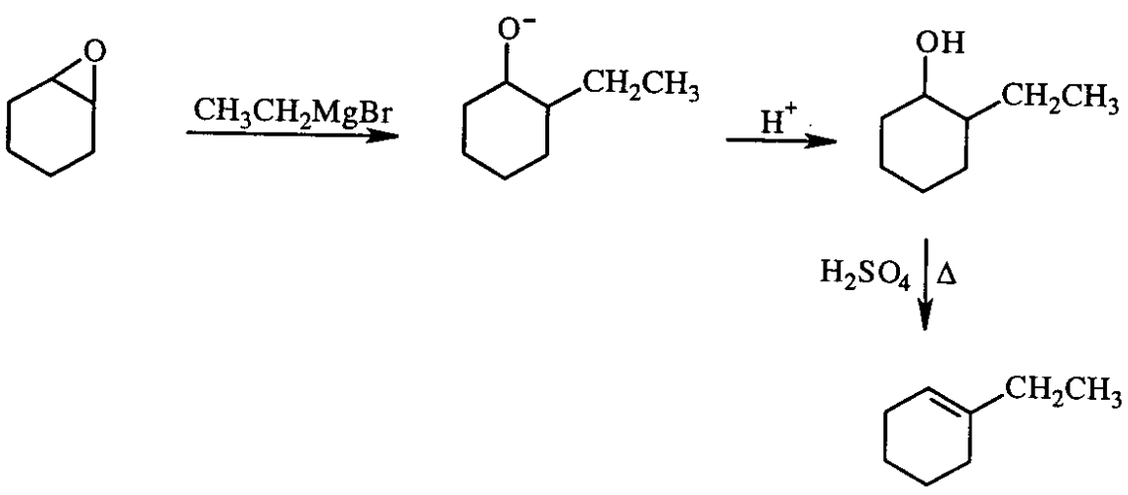


27. The first compound is too insoluble.
The second compound is too reactive.
The third compound is more soluble than the first because of the oxygen-containing substituent.
The third compound is less reactive than the second because the lone pair can be delocalized into the benzene ring, so the lone pair is less apt to displace a chloride ion.

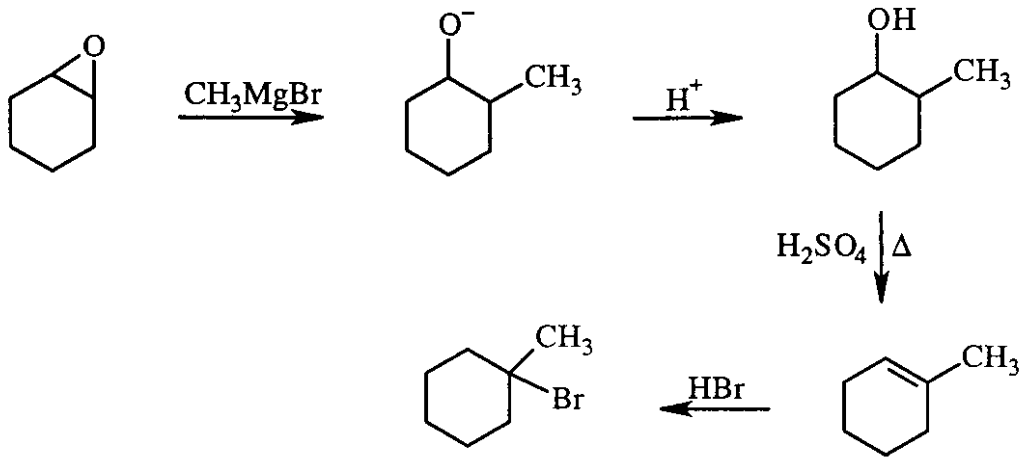
28.

a. $CH_3CH_2CH_2CH_2CH_2OH$ **b.**  **c.** 

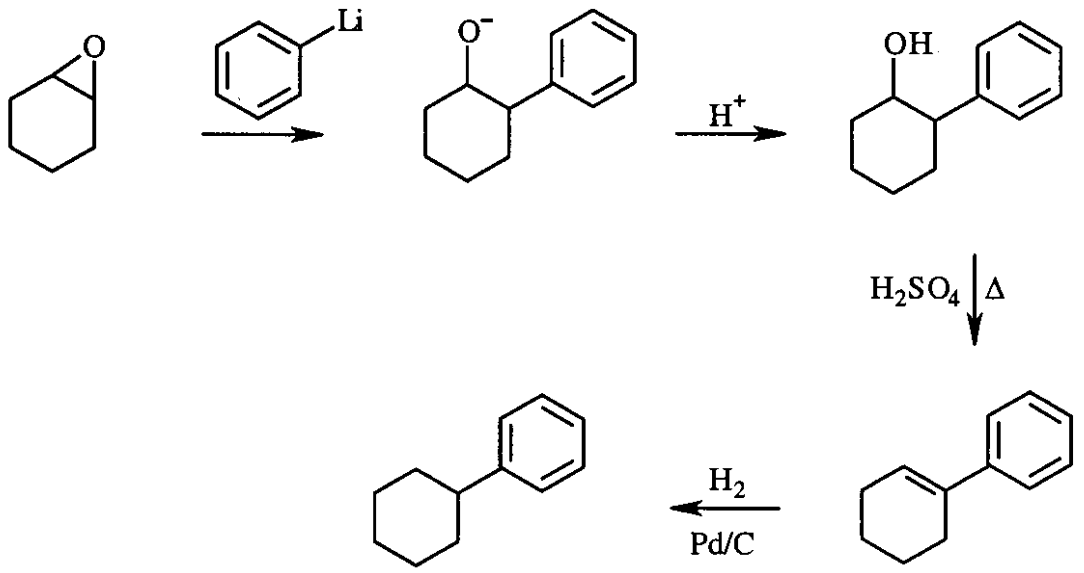
29.

a. 

b.



c.



30. Solved in the text.

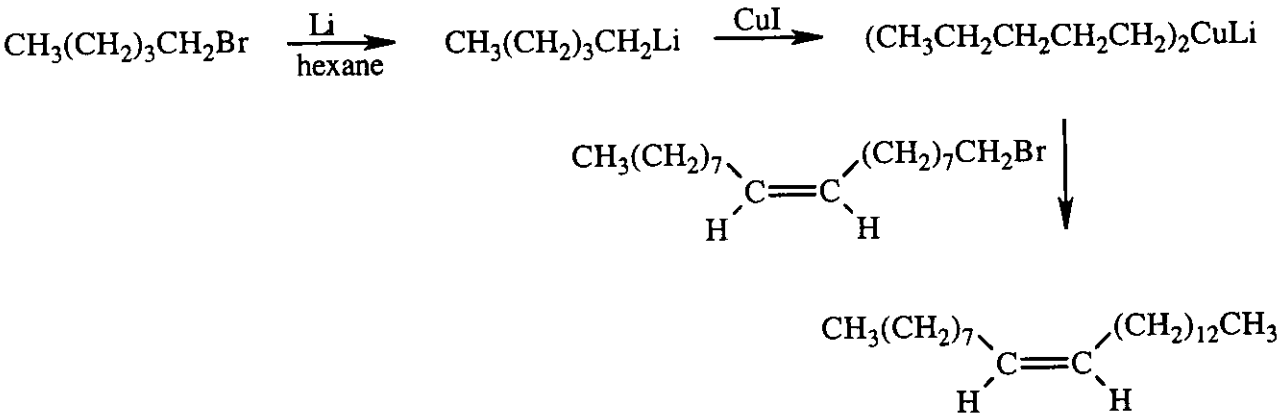
31. All the reactions occur because, in each case, the reactant acid is a stronger acid than the product acid (methane, $pK_a = 50$).

32. Because silicon is more electronegative than magnesium, transmetallation will occur.

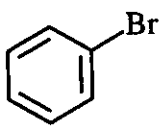
$$4\ CH_3MgCl + SiCl_4 \longrightarrow (CH_3)_4Si + 4\ MgCl_2$$

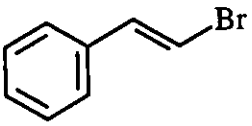
33. Because the alkyl halide will undergo an elimination reaction instead of the alkyl group of the Gilman reagent substituting for the halogen.

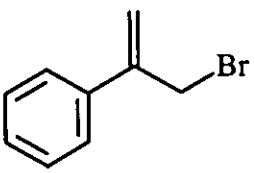
34.



35.

a. 

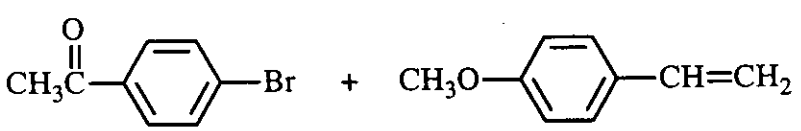
b. 

c. 

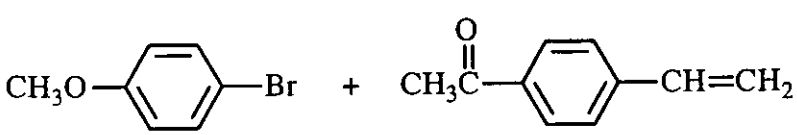
36.

$CH_3CH_2CH_2C{\equiv}CH$

37.



or



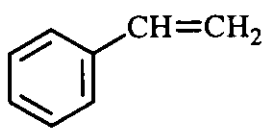
38.

a. $CH_3CH_2CH_2O\overset{\overset{O}{\|}}{C}CH_3$

b. $CH_3CH_2CH_2CH_2Br$

c. $CH_3\underset{\underset{CH_3}{|}}{C}HCH_2CH_2O-C_6H_5$

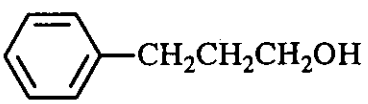
d. $CH_3CH_2\underset{\underset{OH}{|}}{C}H-\overset{\overset{CH_3}{|}}{\underset{\underset{OCH_3}{|}}{C}}CH_3$

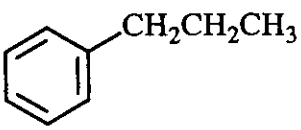
e. 

f. $CH_3CH_2\underset{\underset{CH_3O}{|}}{C}H-\overset{\overset{CH_3}{|}}{\underset{\underset{OH}{|}}{C}}CH_3$

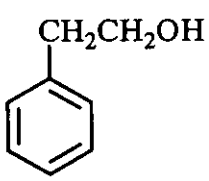
g. $CH_3CH{=}CHCH_3$

h. $CH_3\underset{\underset{CH_3}{|}}{C}HCH_2CH_2Cl$

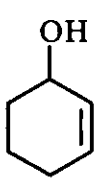
i. 

j. 

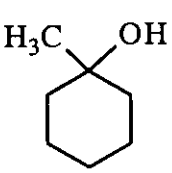
39.

a. 

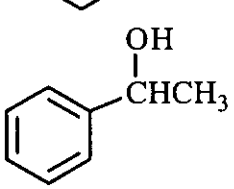
The other alcohol cannot undergo dehydration because its β-carbon is not bonded to a hydrogen.

b. 

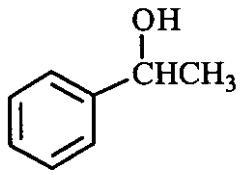
A secondary allylic carbocation is more stable than a secondary carbocation.

c. 

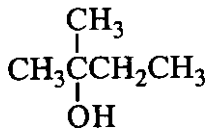
A tertiary carbocation is more stable than a secondary carbocation.

d. 

The rate-limiting step in both dehydrations is carbocation formation: a secondary benzylic carbocation is more stable than a secondary carbocation and, therefore, easier to form.

e. 

Secondary alcohols undergo dehydration faster than primary alcohols.

f. 

A tertiary carbocation is more stable than a secondary carbocation.

40. **c** is the only one that can be used to form a Grignard reagent.

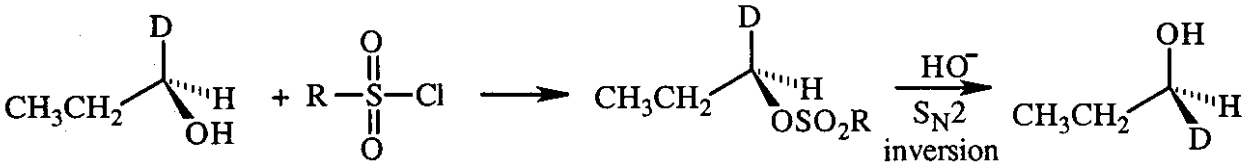
The Grignard reagent formed from **a** will be destroyed by reacting with the proton of the alcohol group.

The Grignard reagent formed from **b** will be destroyed by reacting with the proton of the carboxylic acid group.

The Grignard reagent formed from **d** will be destroyed by reacting with a proton of the amino group.

41. Only one S_N2 reaction takes place in reactions "**a**" and "**b**", so the product has the inverted configuration compared to the configuration of the reactant.

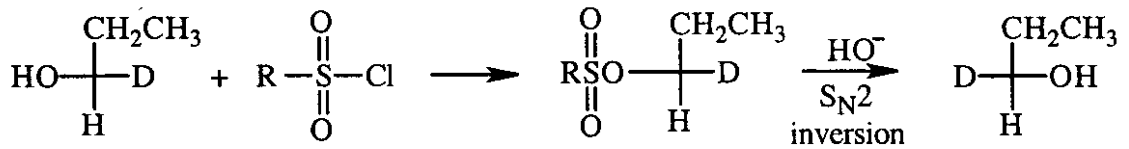
Two S_N2 reactions take place in reaction "**c**", so the product has the same configuration compared to the configuration of the reactant.

a. 

(*R*)-1-deuterio-1-propanol

(*S*)-1-deuterio-1-propanol

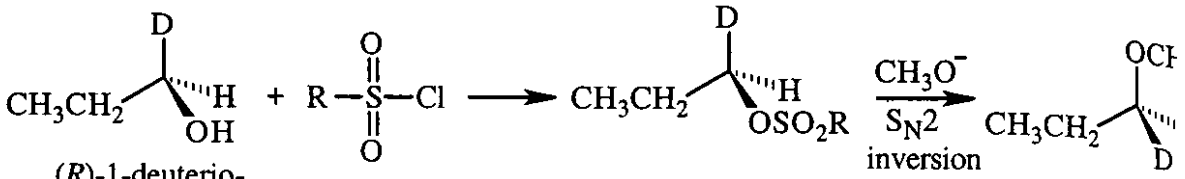
or



(*R*)-1-deuterio-1-propanol

(*S*)-1-deuterio-1-propanol

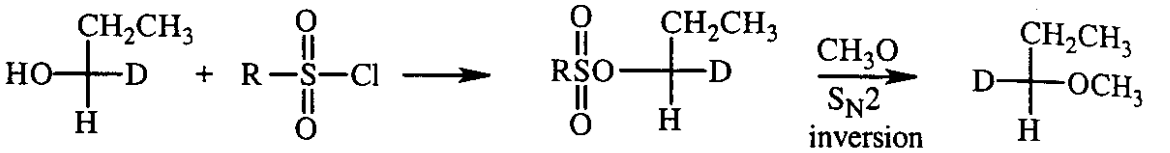
b.



(*R*)-1-deuterio-1-propanol

(*S*)-1-deuteric 1-methoxypr

or

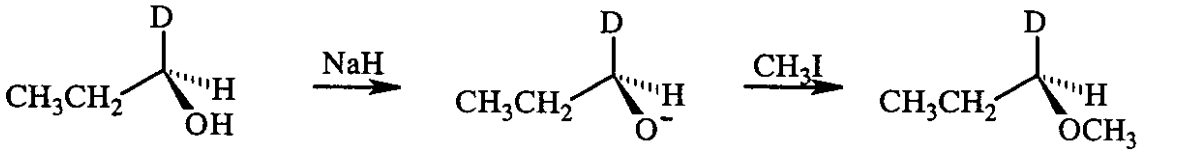


(*R*)-1-deuterio-1-propanol

(*S*)-1-deuterio-1-methoxypropa

c. Since the desired product has the same configuration as the starting material, it can be synthesized using two consecutive reactions that each involves inversion of configuration. For example, treating the starting material with PBr_3 forms (*S*)-1-bromo-1-deuteriopropane followed by reaction of the alky halide with methoxide ion.

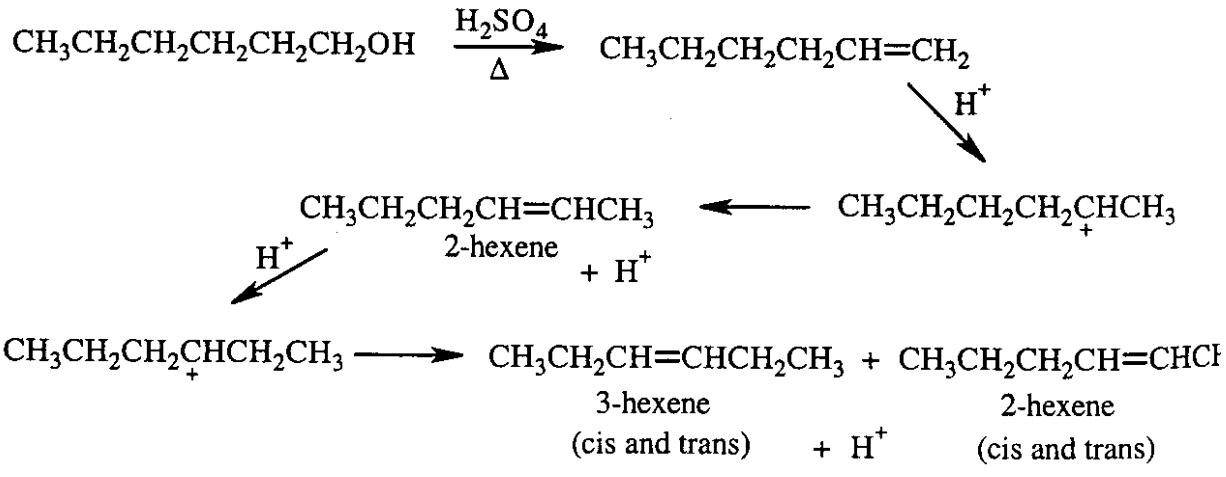
An easier way to prepare the desired compound is to use reactions that don't break any of th bonds to the asymmetric carbon.



(*R*)-1-deuterio-1-propanol

(*R*)-1-deuterio-1-methoxypropane

42. 2-hexene and 3-hexene

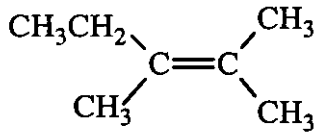


43.

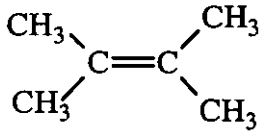
a. $(CH_3)_3CBr + CH_3CH_2OH$

b. $CH_3CH(CH_3)CH_2OH + CH_3I$

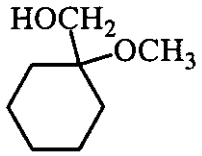
c.



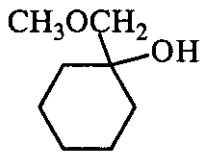
d.



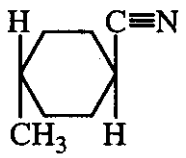
e.



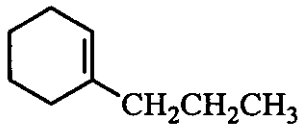
f.



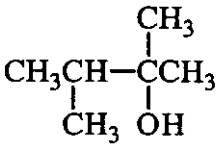
g.



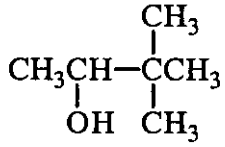
h.



44. 2,3-Dimethyl-2-butanol will dehydrate faster because it is a tertiary alcohol, while 3,3-dimethyl-2-butanol is a secondary alcohol.



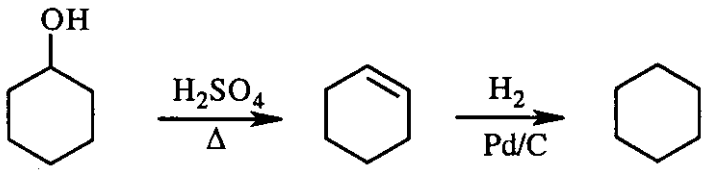
2,3-dimethyl-2-butanol
a tertiary alcohol



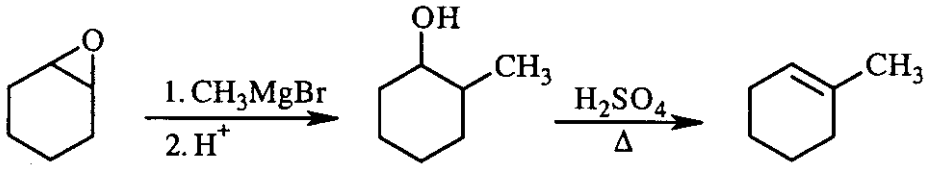
3,3-dimethyl-2-butanol
a secondary alcohol

45.

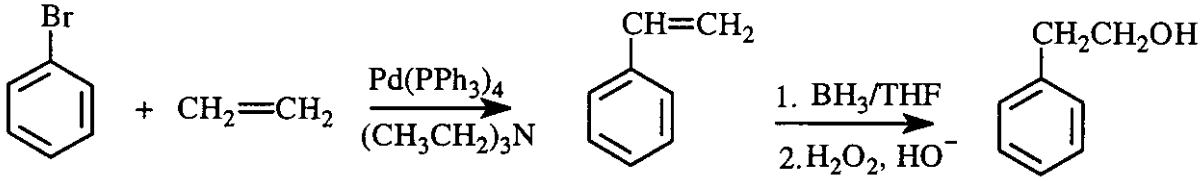
a.



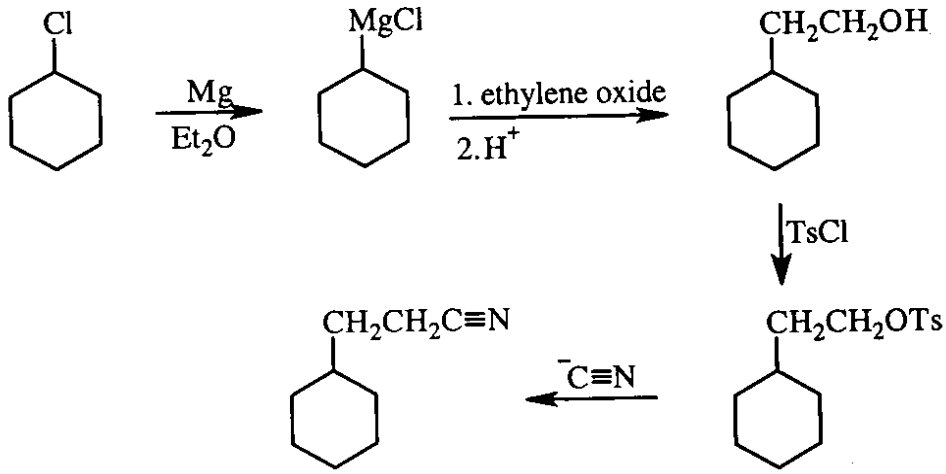
b.



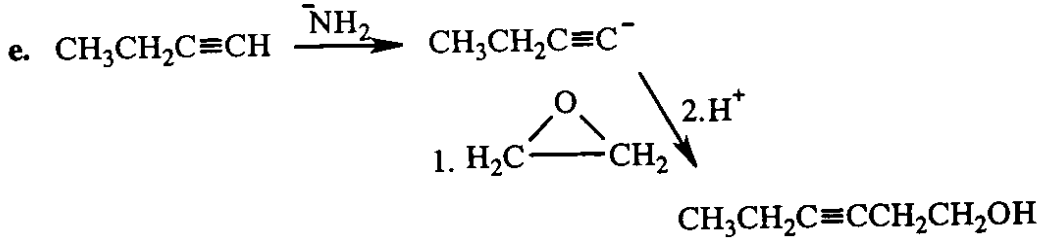
c.



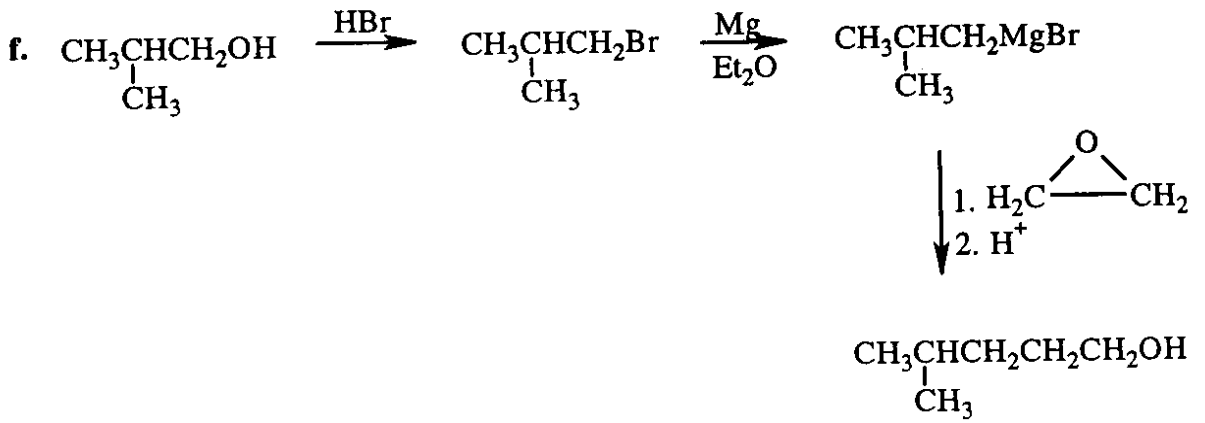
d.


Cl
Mg
Et_2O
MgCl
1. ethylene oxide
2. H^+
CH_2CH_2OH
TsCl
CH_2CH_2OTs
$^-C{\equiv}N$
$CH_2CH_2C{\equiv}N$

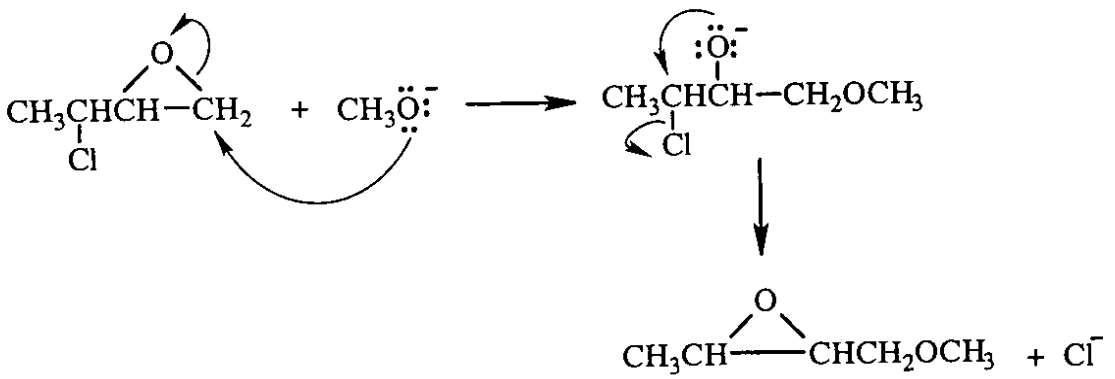
e.


$CH_3CH_2C{\equiv}CH$
$^-NH_2$
$CH_3CH_2C{\equiv}C^-$
1. H_2C—CH_2 (O)
2. H^+
$CH_3CH_2C{\equiv}CCH_2CH_2OH$

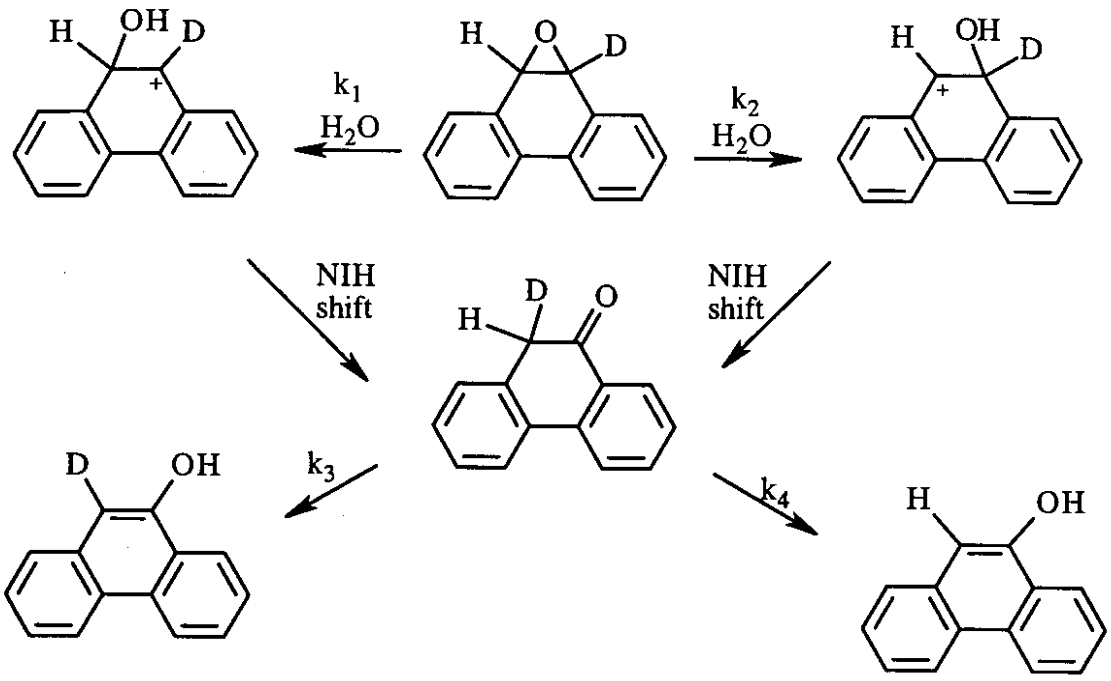
f.


CH_3CHCH_2OH
CH_3
HBr
CH_3CHCH_2Br
CH_3
Mg
Et_2O
CH_3CHCH_2MgBr
CH_3
1. H_2C—CH_2 (O)
2. H^+
$CH_3CHCH_2CH_2CH_2OH$
CH_3

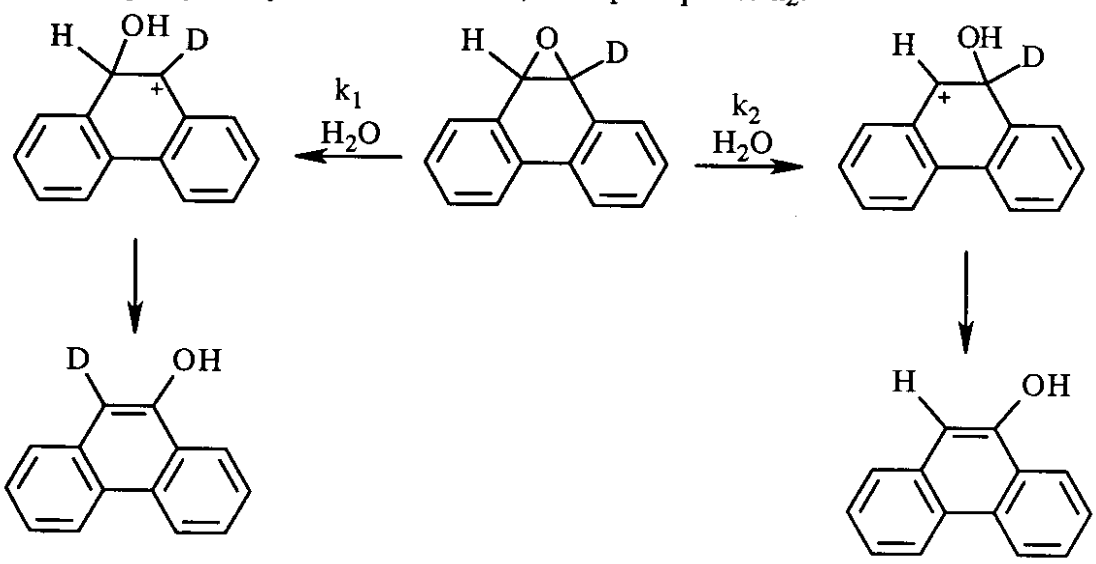
46.


$CH_3CHCH{-}CH_2$ (O)
Cl
+ CH_3O^-
$CH_3CHCH{-}CH_2OCH_3$
$:O^-$
Cl
CH_3CH—$CHCH_2OCH_3$ (O)
+ Cl^-

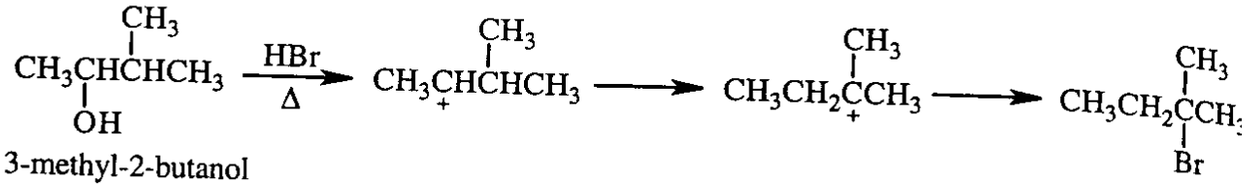
47. **a.** If an NIH shift occurs, both carbocations will form the same keto-intermediate. Because it is about four times easier to break a C—H bond (k_3) compared with a C—D bond (k_4), about 80% of the deuterium will be retained.



b. If an NIH shift does not occur, 50% of the deuterium will be retained because the epoxide can open equally easily in either direction, and k_1 is equal to k_2.

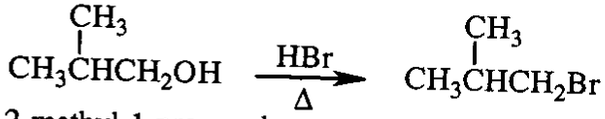


48. 3-Methyl-2-butanol is a secondary alcohol and, therefore, will undergo an S_N1 reaction. The carbocation intermediate that is formed rearranges to a more stable tertiary carbocation.



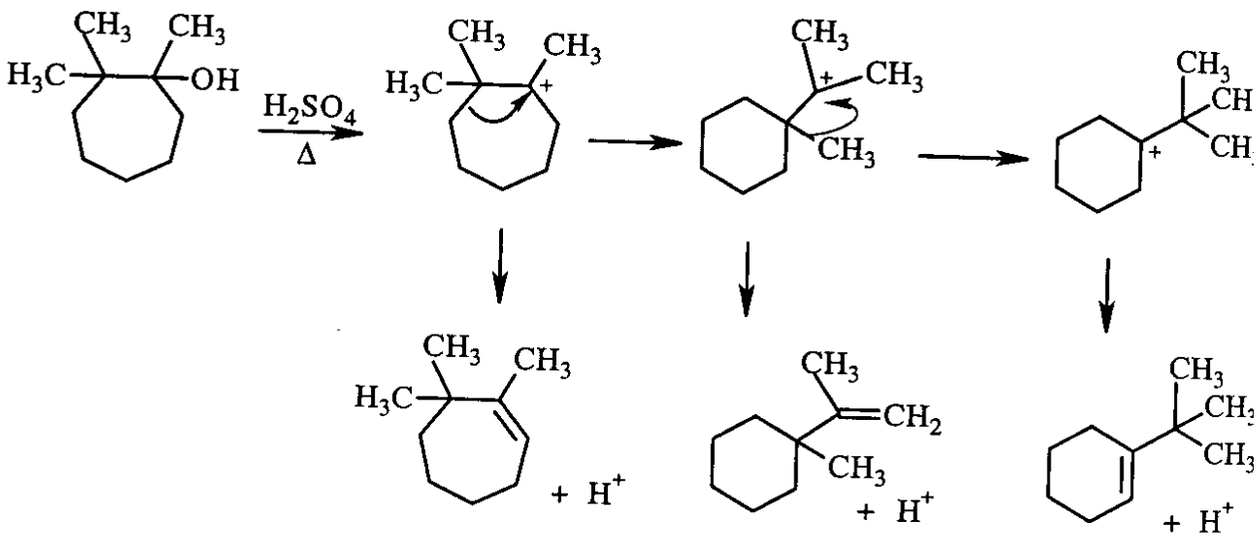
3-methyl-2-butanol

2-Methyl-1-propanol is a primary alcohol and therefore will undergo an S_N2 reaction. Because carbocations are not formed in S_N2 reactions, carbocation rearrangement cannot occur.

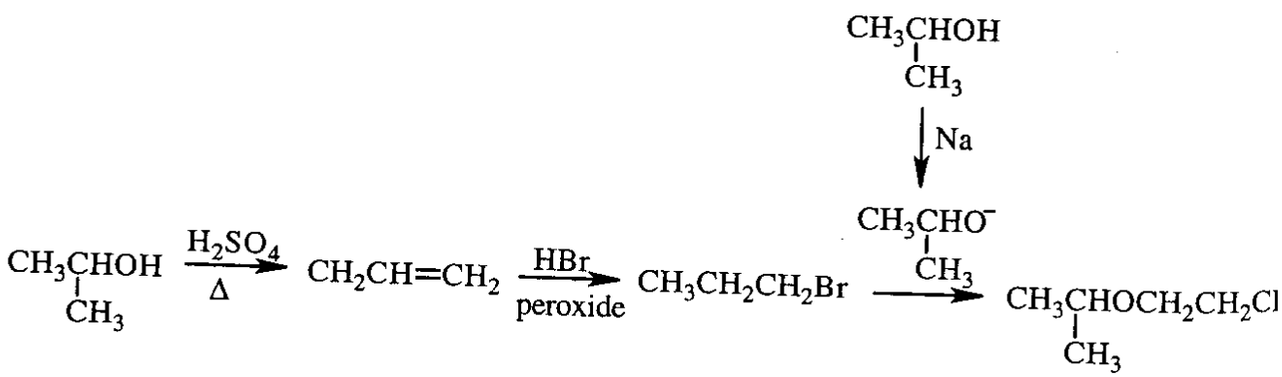


2-methyl-1-propanol

49.



50.



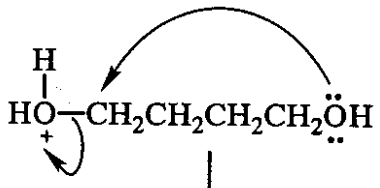
isopropyl propyl eth

51. Cyclopropane does not react with HO^-, because cyclopropane does not contain a leaving group; a carbanion is far too basic to serve as a leaving group. Ethylene oxide reacts with HO^- because ethylene oxide contains an RO^- leaving group.

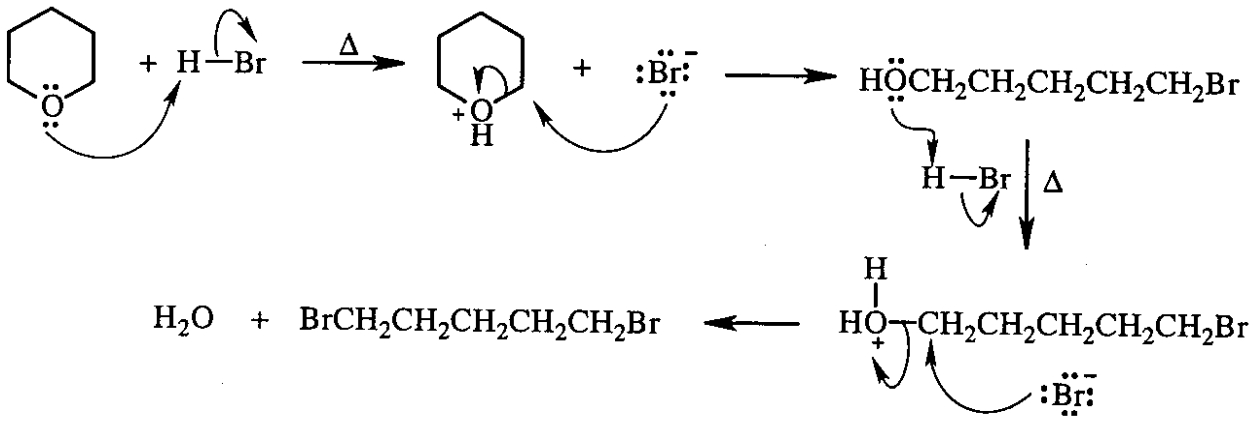
52. **Diethyl ether** is the ether that would be obtained in greatest yield, because it is a symmetrical ether. Since it is symmetrical, only one alcohol is used in its synthesis. Therefore, it is the only ether that would be formed.

The synthesis of an unsymmetrical ether requires two different alcohols. Therefore, the asymmetrical ether is one of three different ethers that can be formed.

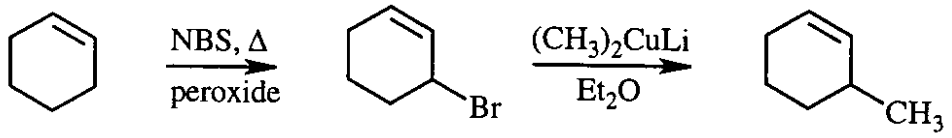
53.

a. $HOCH_2CH_2CH_2CH_2OH \xrightleftharpoons{H^+}$ 



b. 

54.

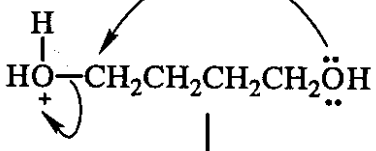
a. 

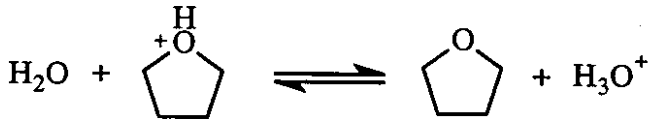
51. Cyclopropane does not react with HO^-, because cyclopropane does not contain a leaving group; a carbanion is far too basic to serve as a leaving group. Ethylene oxide reacts with HO^- because ethylene oxide contains an RO^- leaving group.

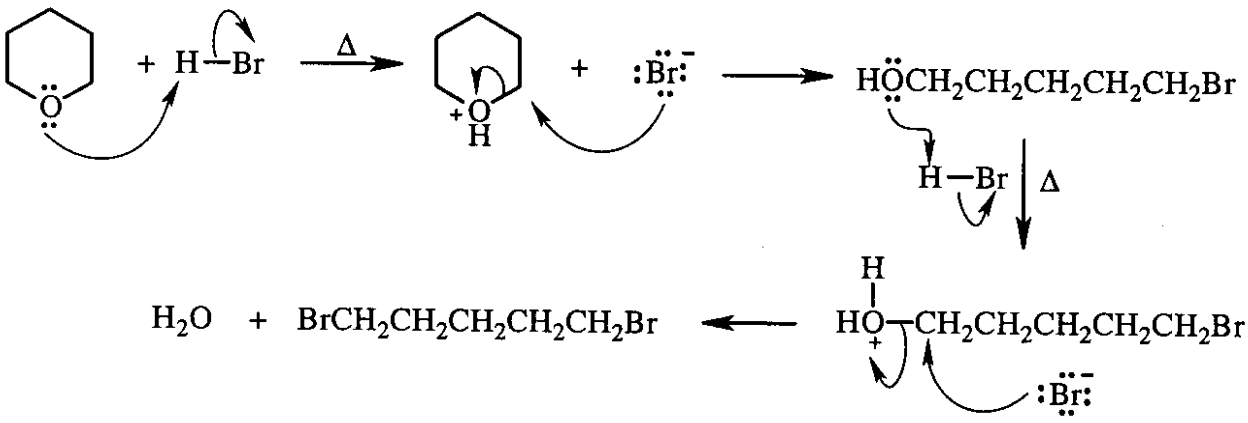
52. **Diethyl ether** is the ether that would be obtained in greatest yield, because it is a symmetrical ether. Since it is symmetrical, only one alcohol is used in its synthesis. Therefore, it is the only ether that would be formed.

The synthesis of an unsymmetrical ether requires two different alcohols. Therefore, the asymmetrical ether is one of three different ethers that can be formed.

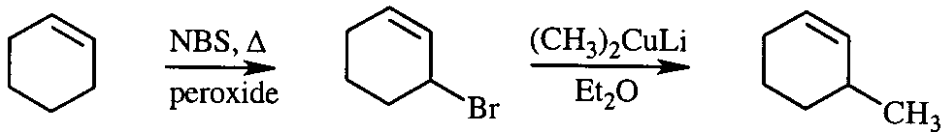
53.

a. $HOCH_2CH_2CH_2CH_2OH \xrightleftharpoons{H^+}$ 

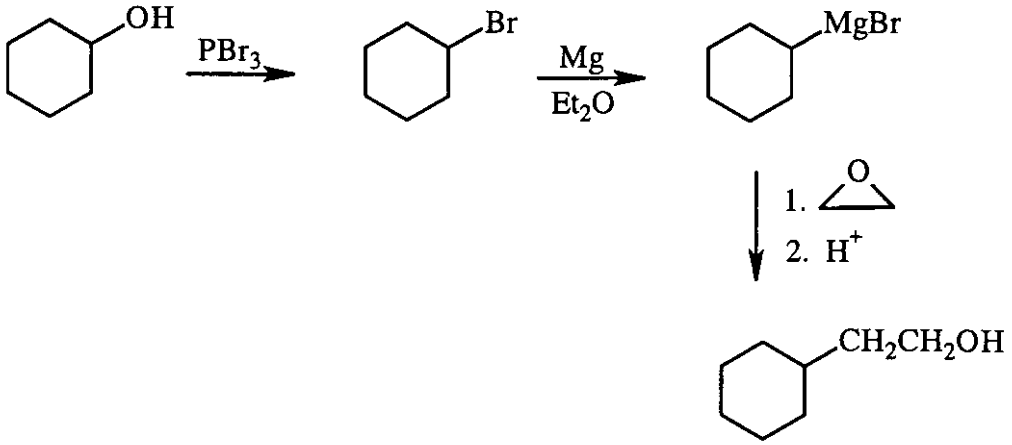


b. 

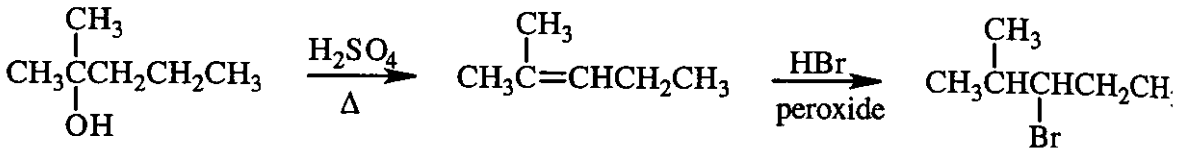
54.

a. 

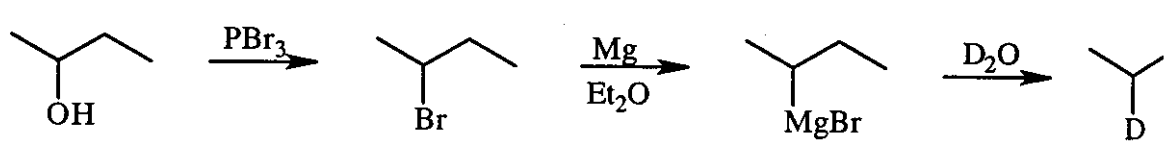
b.


OH
PBr3
Br
Mg
Et2O
MgBr
1.
O
2. H+
CH2CH2OH

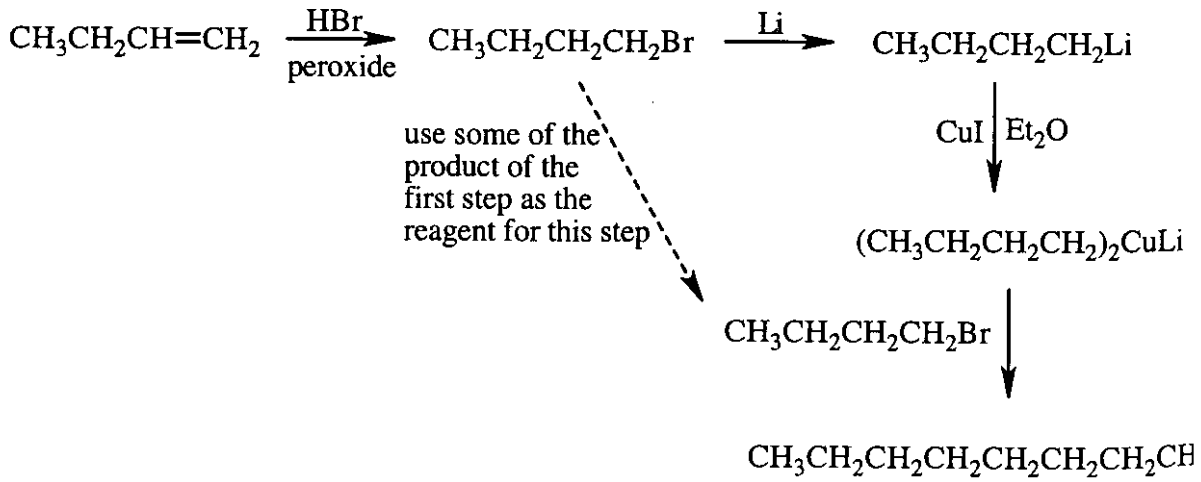
c.


CH3
CH3CCH2CH2CH3
OH
H2SO4
Δ
CH3
CH3C=CHCH2CH3
HBr
peroxide
CH3
CH3CHCHCH2CH
Br

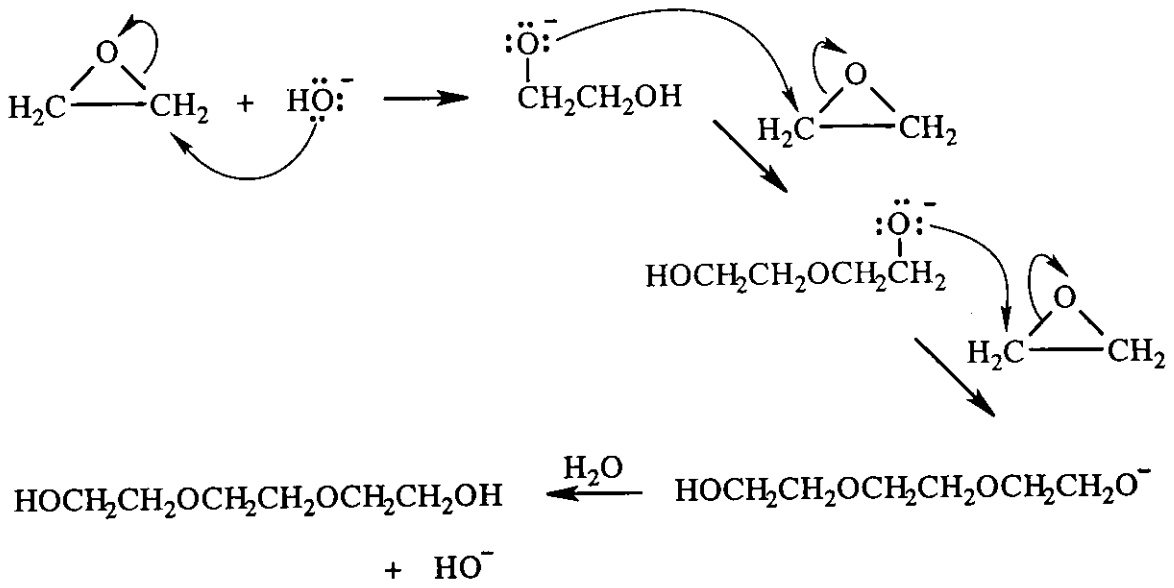
d.


OH
PBr3
Br
Mg
Et2O
MgBr
D2O
D

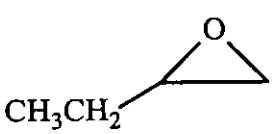
e.


CH3CH2CH=CH2
HBr
peroxide
CH3CH2CH2CH2Br
Li
CH3CH2CH2CH2Li
use some of the product of the first step as the reagent for this step
CuI
Et2O
(CH3CH2CH2CH2)2CuLi
CH3CH2CH2CH2Br
CH3CH2CH2CH2CH2CH2CH2CH

55.



56.



2-ethyloxirane

a. $CH_3CH_2\underset{\underset{OH}{|}}{C}HCH_2OH$

0.1 M HCl is a dilute solution of HCl in water

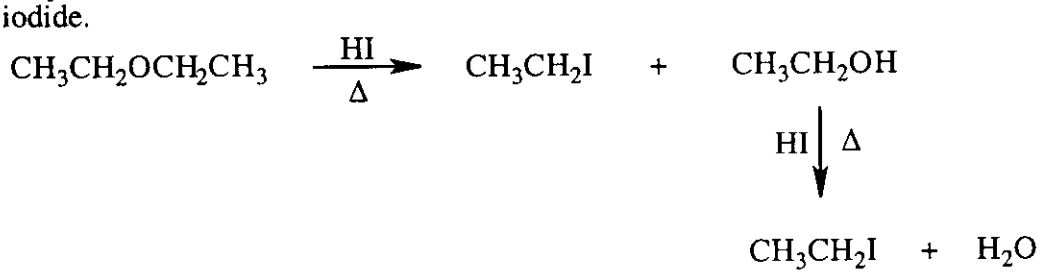
b. $CH_3CH_2\underset{\underset{OCH_3}{|}}{C}HCH_2OH$

c. $CH_3CH_2\underset{\underset{OH}{|}}{C}HCH_2CH_2CH_3$

d. $CH_3CH_2\underset{\underset{OH}{|}}{C}HCH_2OH$

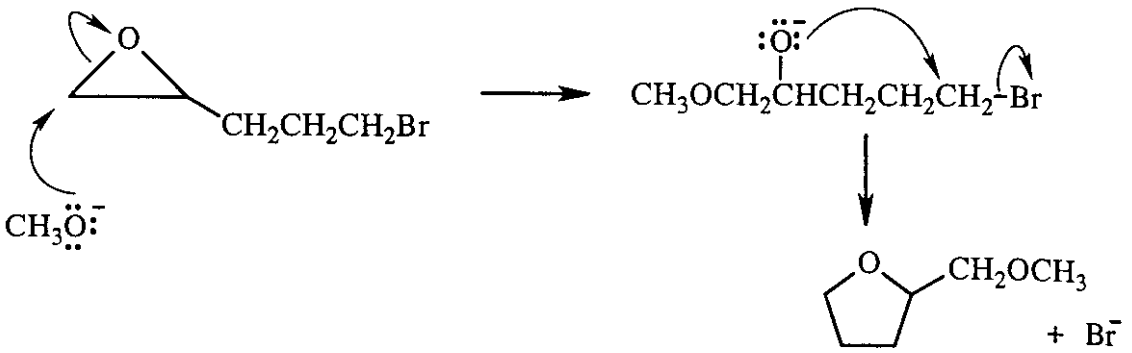
e. $CH_3CH_2\underset{\underset{OH}{|}}{C}HCH_2OCH_3$

57. Ethyl alcohol is not obtained as a product, because it reacts with the excess HI and forms ethyl iodide.

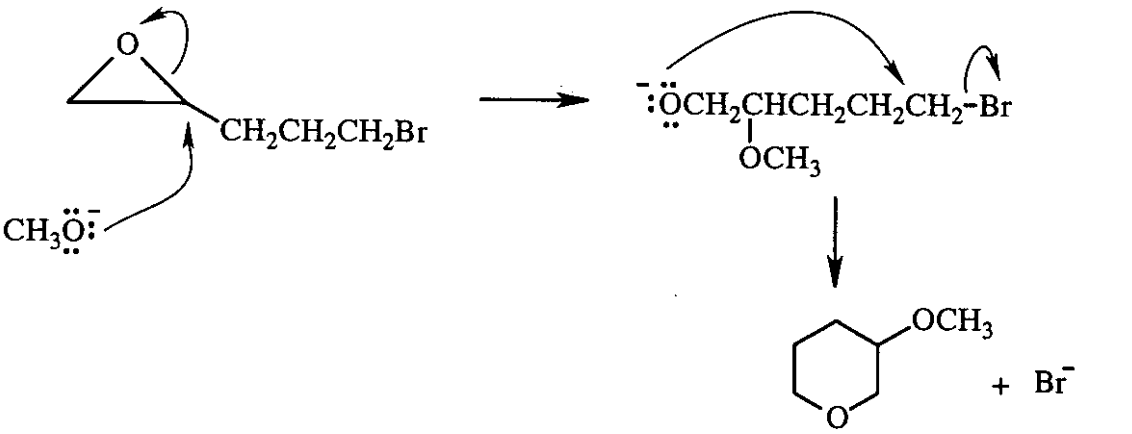


58.

a.



b.

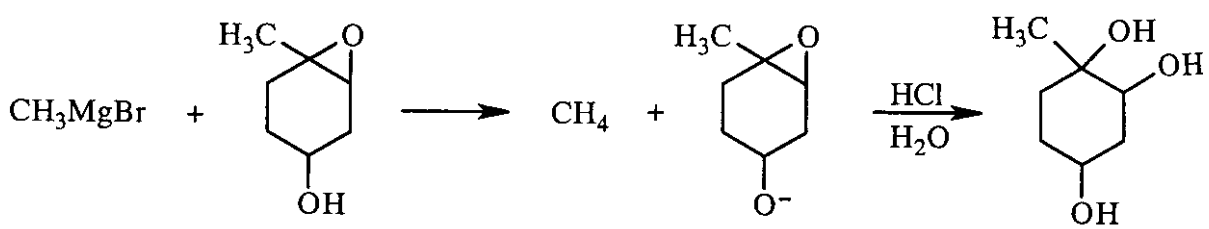


c. The six-membered ring is formed by attack on the more sterically hindered carbon of the epoxide. Attack on the less sterically hindered carbon is preferred.

59.

A = Mg
B = diethyl ether
C = CH_3MgBr
D = ethylene oxide
E = H^+
F = Na
G = ethylene oxide
H = H^+

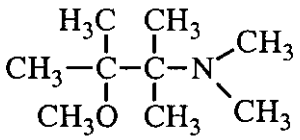
60. Greg did not get any of the expected product, because the Grignard reagent reacted with the hydrogen of the alcohol group. Addition of HCl/H_2O protonated the alkoxide ion and opened the epoxide ring.



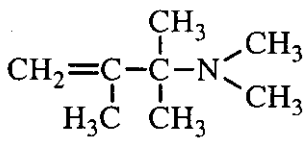
61. **A** is the substitution product that is formed by methoxide ion attacking a carbon of the three-membered ring and eliminating the amino group, thereby opening the ring.

B is the product of a Hofmann elimination reaction: methoxide ion removes a proton from a methyl group bonded to a carbon, eliminating the amino group. The red color disappears when Br_2 is added to **B**, because Br_2 adds to the double bond.

When the aziridinium ion reacts with methanol, only the substitution product is formed.

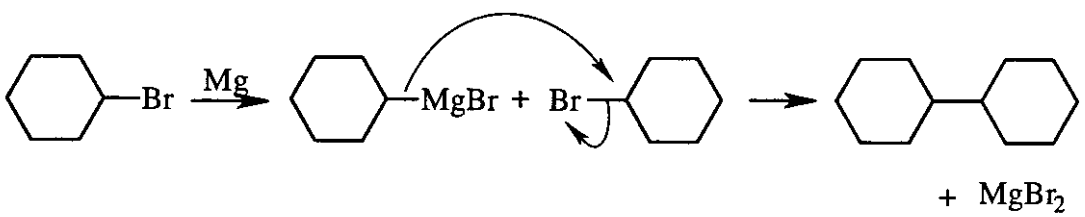


A

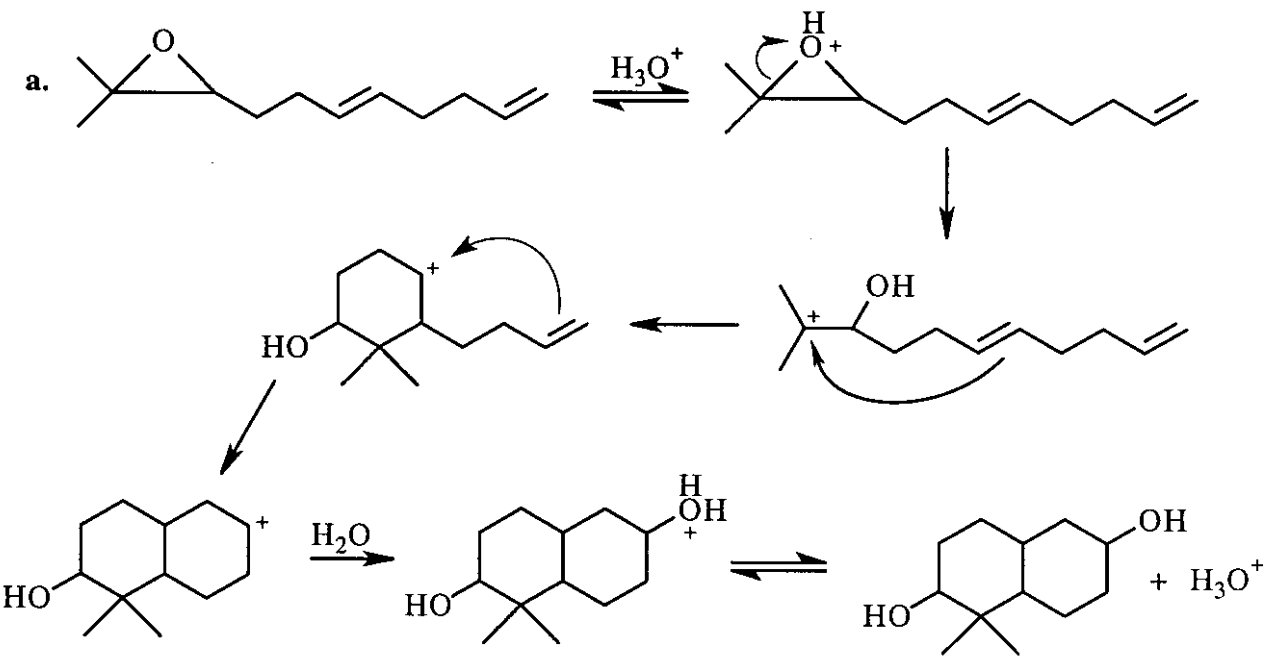


B

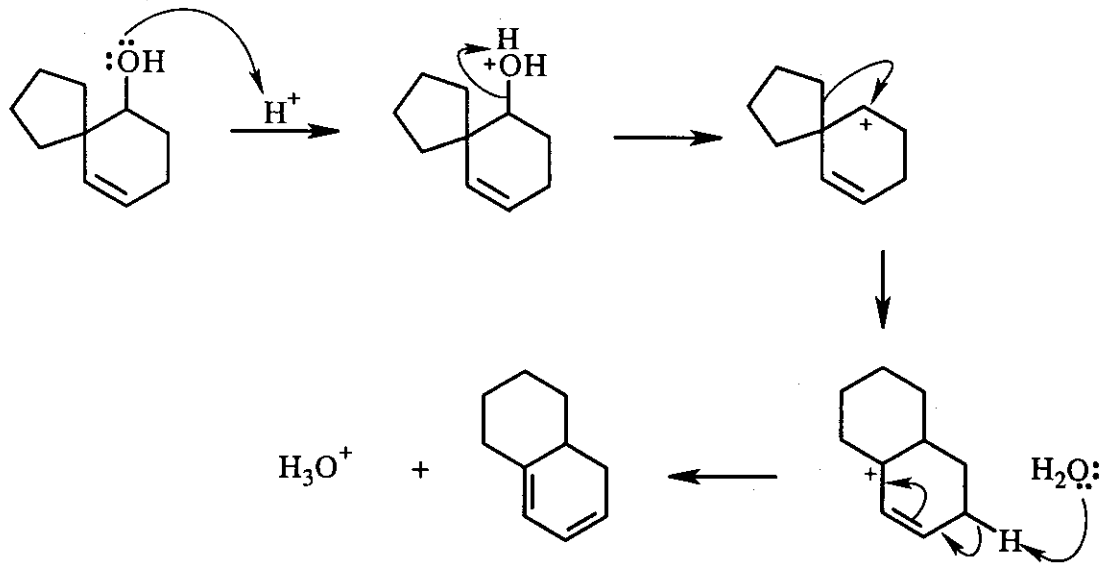
62.



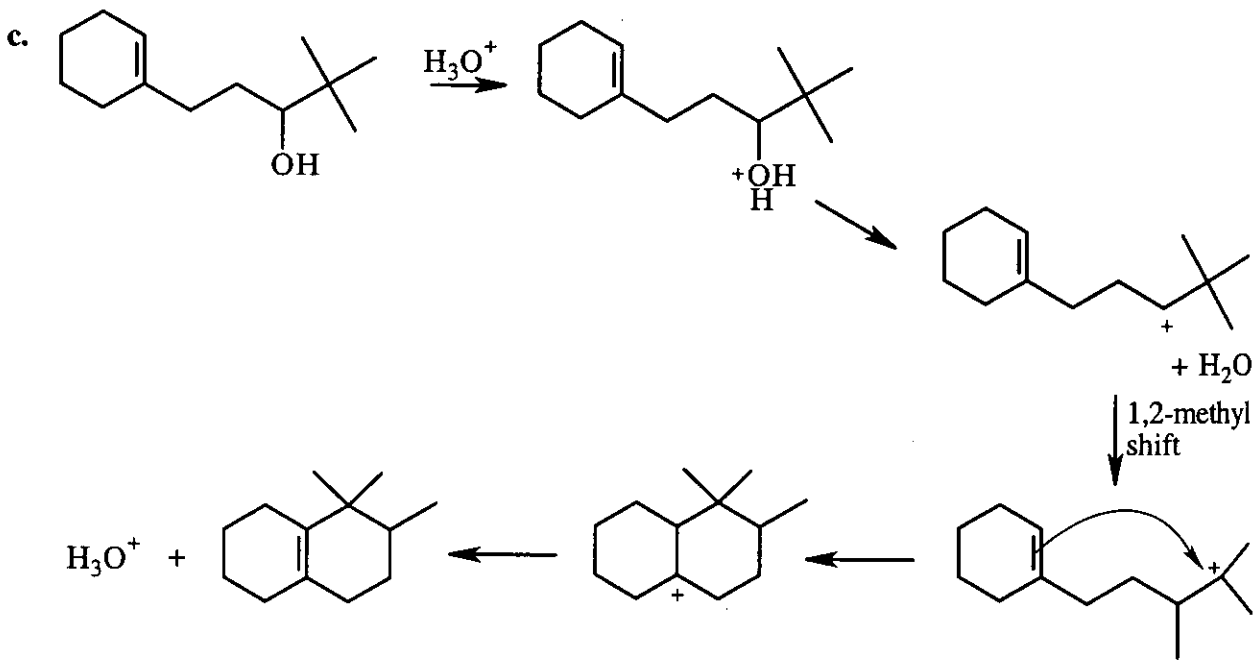
63.



b.

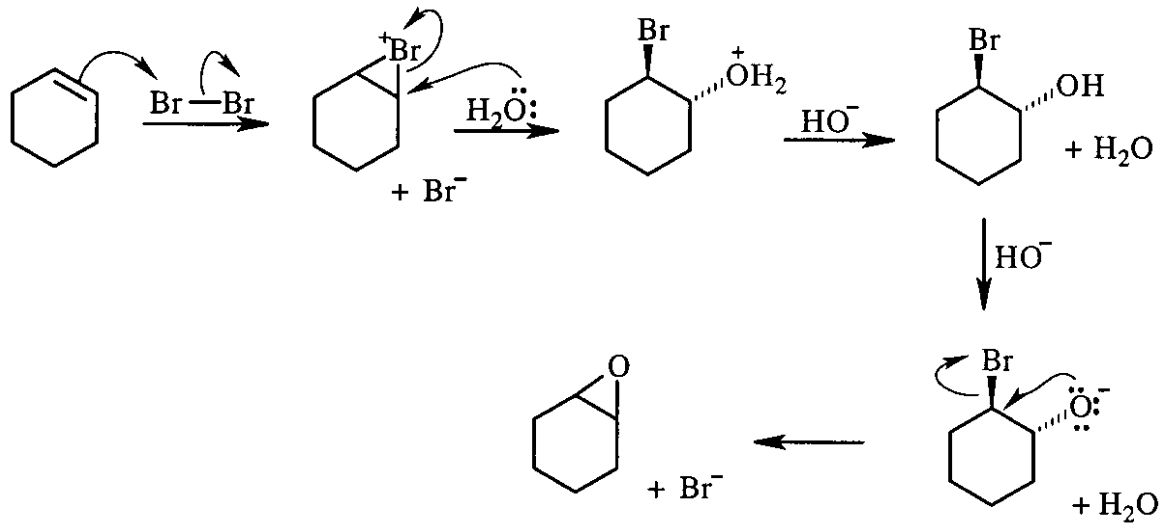


c.

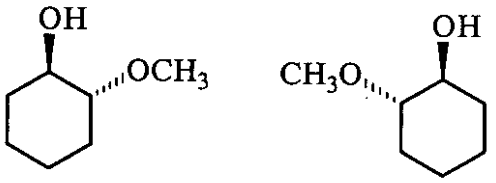


64.

a.

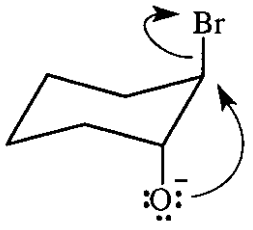


b. Only the trans isomers will be formed because the epoxide undergoes backside attack by methoxide ion.



65. **b** is the fastest reaction; **a** is the slowest reaction

In order to form the epoxide, the alkoxide ion must attack the backside of the carbon that is bonded to Br. This means that the OH and Br substituents must both be in axial positions. To be diaxial, they must be trans to each other.

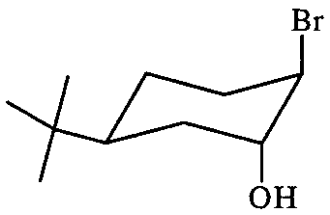


a does not form an epoxide, because the OH and Br substituents are cis to each other.

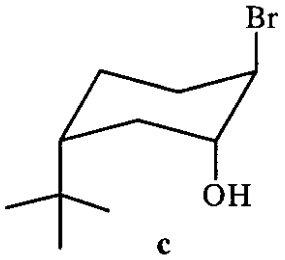
b and **c** can form epoxides because the OH and Br substituents are trans to each other.

The rate of formation of the epxoide is given by $k'K_{eq}$, where k' is the rate constant for the substitution reaction, and K_{eq} is the equilibrium constant for the equatorial/axial conformers.

When the OH and Br substituents are in the required diaxial position, the large *tert*-butyl substituent is in the equatorial position in **b** and in the axial position in **c**.

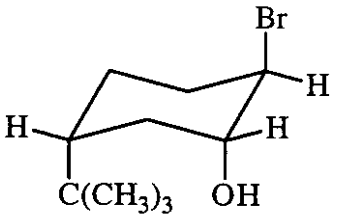


b

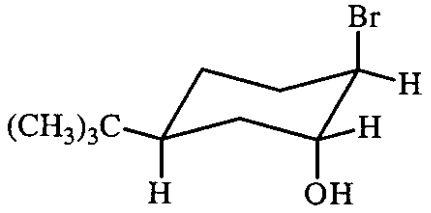


c

Because the more stable conformer is the one with the large *tert*-butyl group in the equatorial position, the more stable conformer of **b** has the OH and Br substituents in the required diaxial position (K_{eq} is large), while the OH and Br substituents in **c** are in the required diaxial position in its less stable conformer (K_{eq} is small). Therefore, **b** reacts faster than **c**.

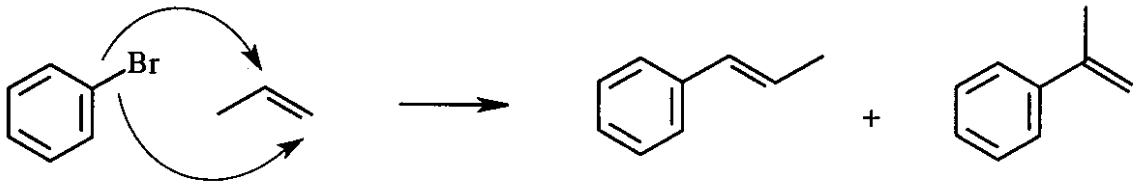


b

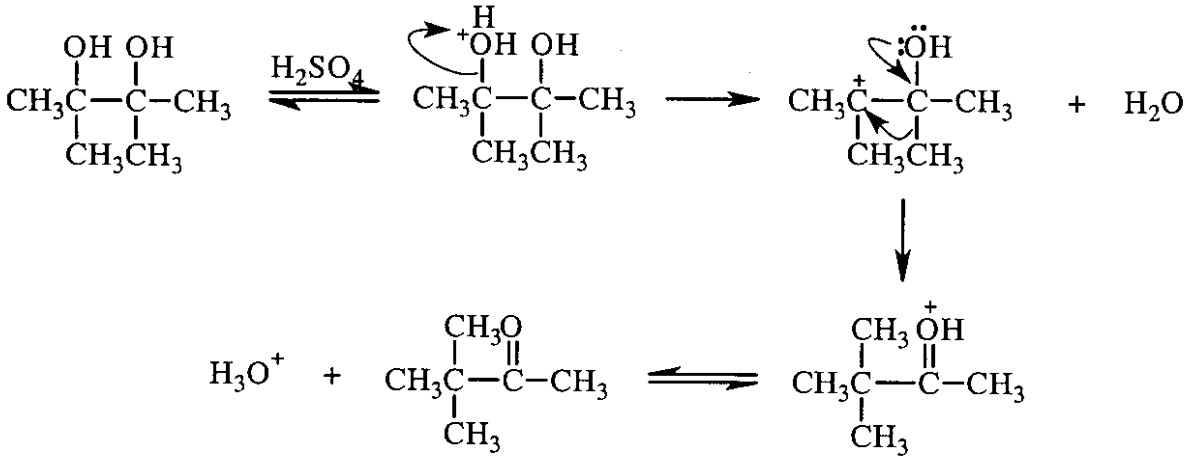


c

66. The benzene ring can become attached to either of the sp^2 carbons of the alkene, resulting in the formation of a pair of constitutional isomers.

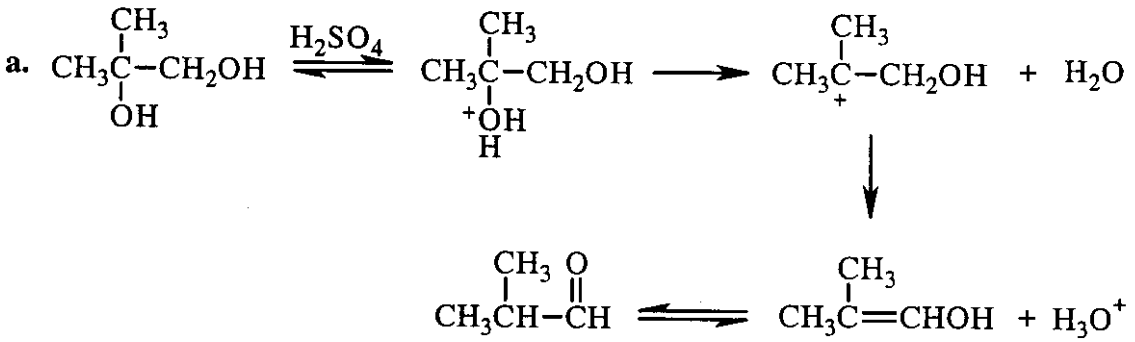


67.



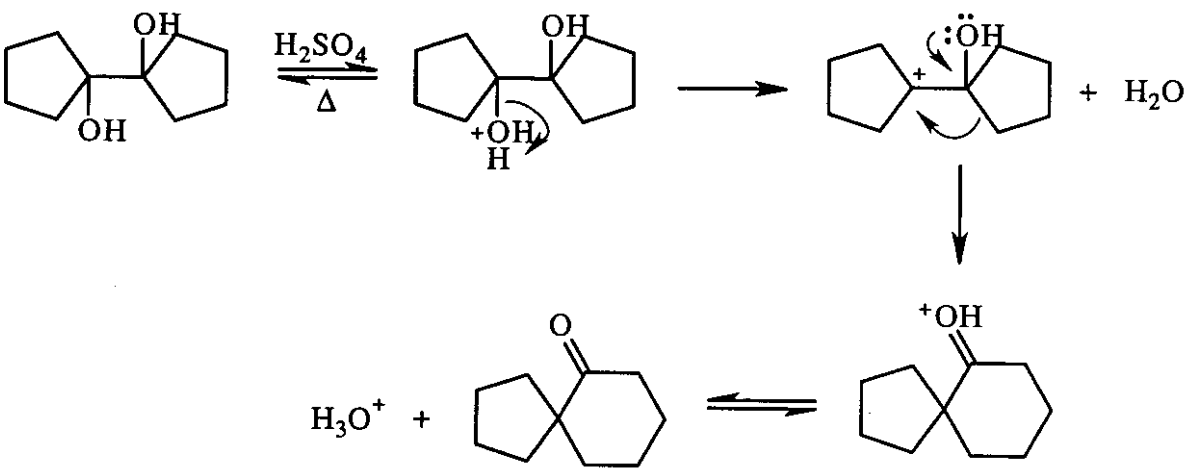
68.

a.

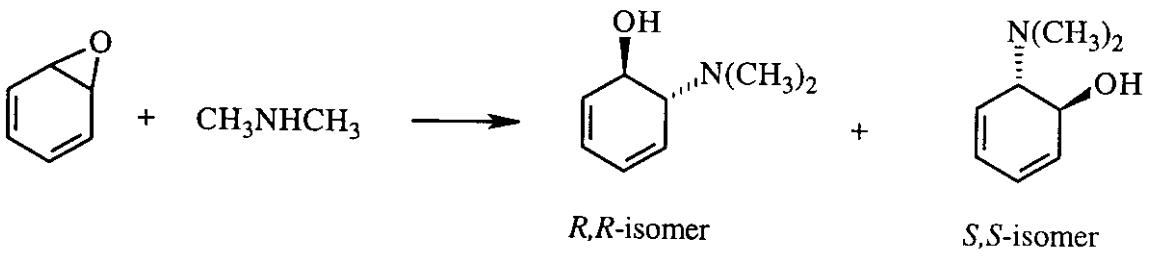


b. Dehydration of the primary alcohol group cannot occur because it cannot lose water via an E1 pathway, because a primary carbocation cannot be formed. It cannot lose water via an E2 pathway, because the β-carbon is not bonded to a hydrogen.

69.



70.

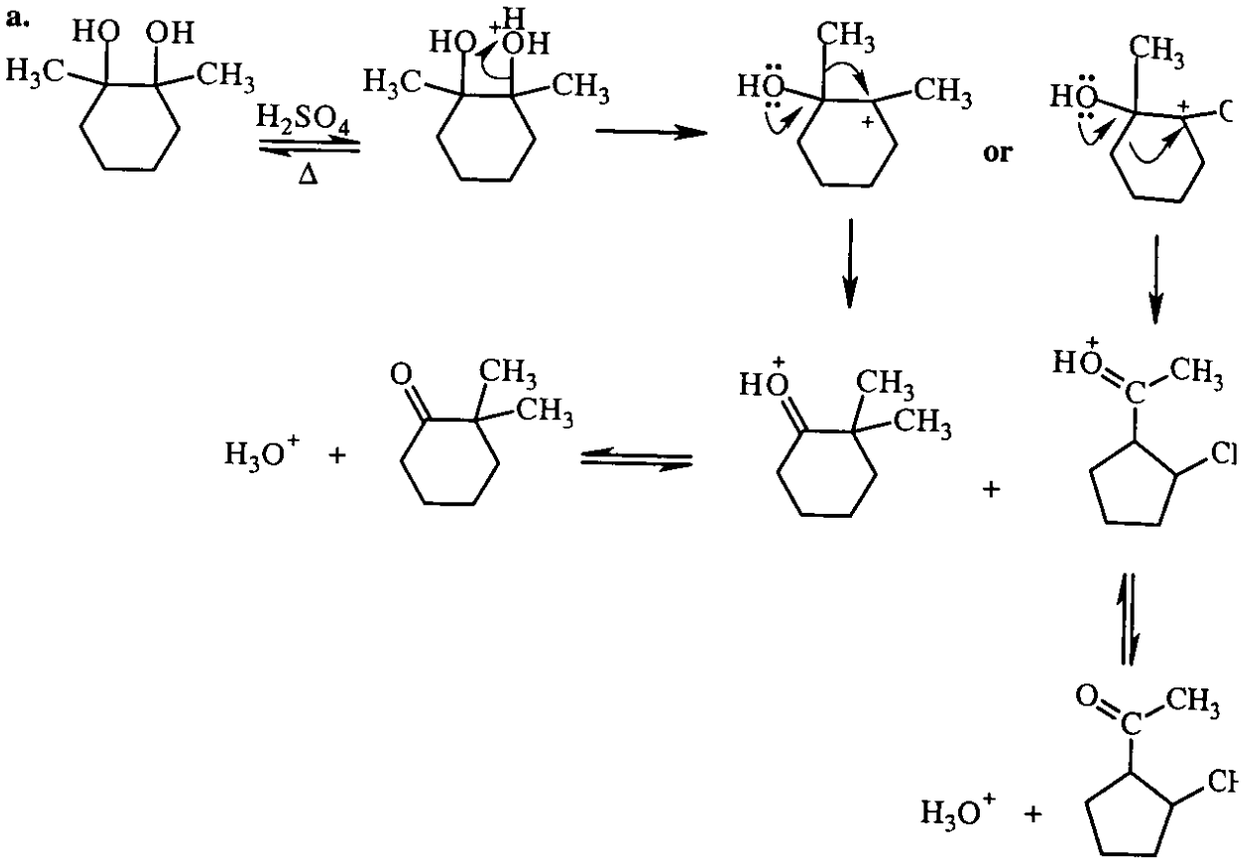


R,R-isomer

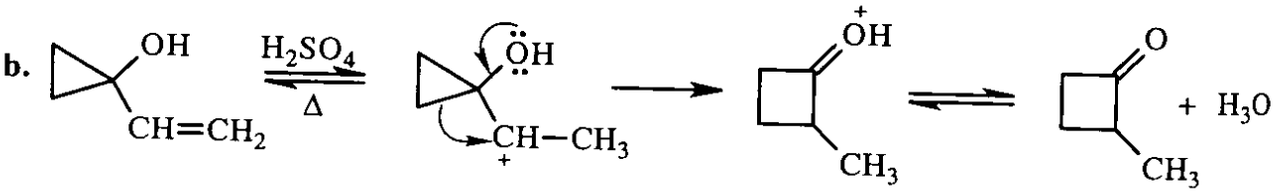
S,S-isomer

71.

a.


HO OH
H3C CH3
H2SO4
Δ
HO H OH
H3C CH3
CH3
HO
CH3
or
CH3
HO
C
O CH3
CH3
H3O+ +
HO+ CH3
CH3
+
HO+ CH3
C
CH3
Cl
O CH3
C
CH3
Cl
H3O+ +

b.


OH
CH=CH2
H2SO4
Δ
OH
CH–CH3
+
OH+
CH3
O
CH3
+ H3O

Chapter 12 Practice Test

1. Which of the following reagents is the best one to use in order to convert methyl alcohol into methyl bromide?

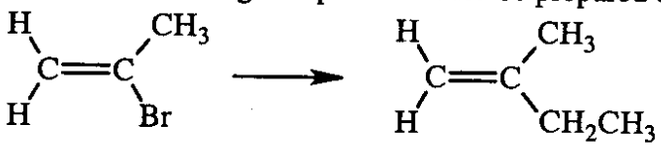
Br^- HBr Br_2 NaBr Br^+

2. Which of the following reagents is the best one to use in order to convert methyl alcohol into methyl chloride?

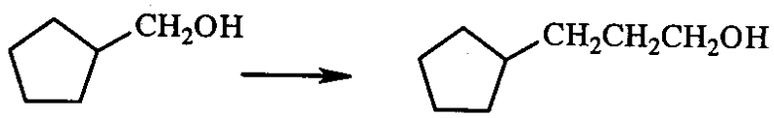
Cl_2/CH_2Cl_2 $Cl_2/h\nu$ Cl^- $SOCl_2$ NaCl

3. Indicate how the following compounds could be prepared using the given starting material:

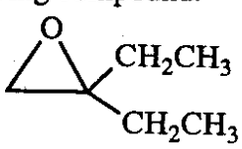
a.



b.



4. Give two names for the following compound:

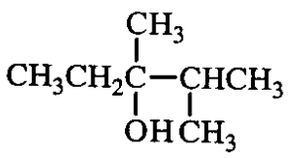


5. **a.** What would be the major product obtained from the reaction of the epoxide in the above problem in methanol containing O.1 M HCl?

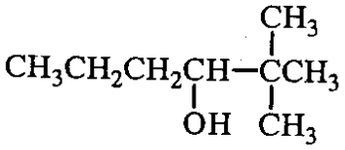
b. What would be the major product obtained from the reaction of the epoxide in the above problem in methanol containing O.1 M $NaOCH_3$?

6. Give the major product that is obtained when each of the following alcohols is heated in the presence of H_2SO_4.

a.

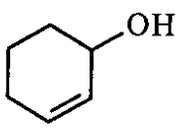


b.



c. $CH_3CH_2CH_2CH_2CH_2OH$

d.



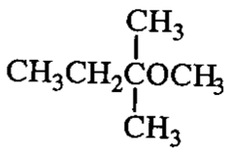
7. Indicate whether the following statements are true or false:

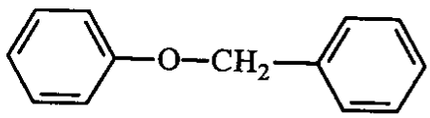
a. Tertiary alcohols are easier to dehydrate than secondary alcohols. T F

b. Alcohols are more acidic than thiols. T F

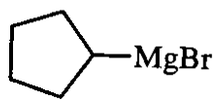
c. Alcohols have higher boiling points than thiols. T F

8. What products would be obtained from heating the following ethers with one equivalent of HI?

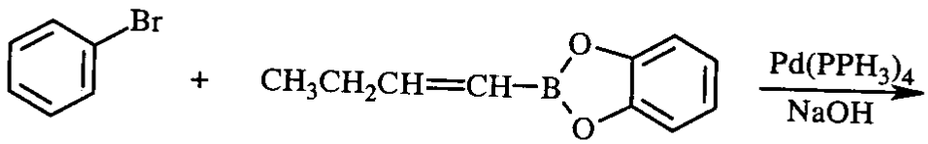
a. 

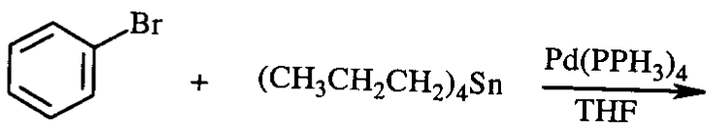
b. 

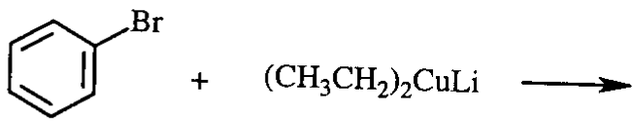
9. What alcohols would be formed from the reaction of ethylene oxide with the following Grignard reagents?

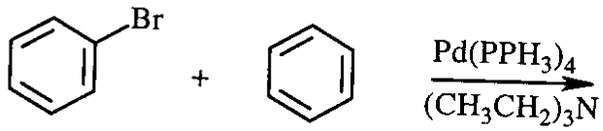
a. $CH_3CH_2CH_2MgBr$ **b.** 

10. Give the major product of each of the following reactions:

a. 

b. 

c. 

d. 

CHAPTER 13
Mass Spectrometry and Infrared Spectroscopy

Important Terms

absorption band	a peak in a spectrum that occurs as a result of absorption of energy.
base peak	the peak in a mass spectrum with the greatest intensity.
bending vibration	a vibration that does not occur along the line of the bond.
α cleavage	homolytic cleavage of an alpha substituent.
electromagnetic radiation	radiant energy that displays wave properties.
fingerprint region	the right-hand third of an IR spectrum where the absorption bands are characteristic of the compound as a whole.
frequency	the velocity of a wave divided by its wavelength. (It has units of cycles/second.)
functional group region	the left-hand two thirds of an IR spectrum, where most functional groups show absorption bands.
Hooke's law	an equation that describes the motion of a vibrating spring.
infrared radiation	electromagnetic radiation familiar to us as heat.
infrared spectroscopy	spectroscopy that uses infrared energy to provide a knowledge of the functional groups in a compound.
infrared spectrum (IR spectrum)	a plot of relative absorption versus wavenumber (or wavelength) of absorbed infrared radiation.
mass spectrometry	provides a knowledge of the molecular weight and certain structural features of a compound.
mass spectrum	a plot of the relative abundance of the positively charged fragments produced in a mass spectrometer versus their *m/z* values.
McLafferty rearrangement	rearrangement of the molecular ion of a ketone that contains a γ-hydrogen; the bond between the α- and β-carbons breaks, and a γ-hydrogen migrates to the oxygen.
molecular ion (M)	the radical cation formed by removing one electron from a molecule.
nominal molecular mass	mass to the nearest whole number.
radical cation	a species with a positive charge and an unpaired electron.
spectroscopy	study of the interaction of matter and electromagnetic radiation.
stretching frequency	the frequency at which a stretching vibration occurs.

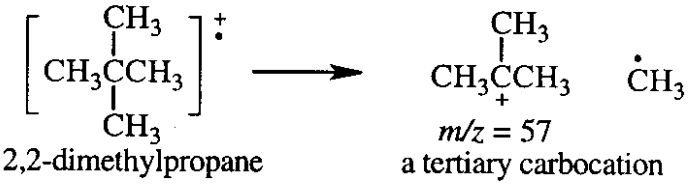
stretching vibration a vibration occurring along the line of the bond.

wavelength distance from any point on one wave to the corresponding point on the next wave.

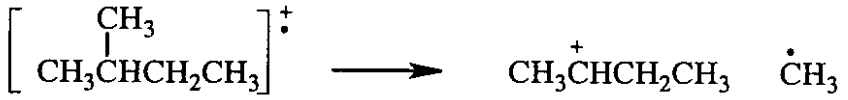
wavenumber the number of waves in one centimeter.

Solutions to Problems

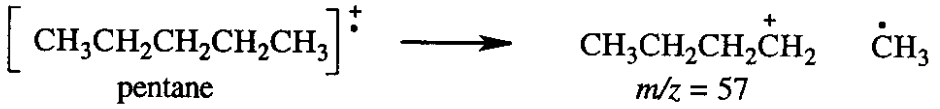
1. The peak at $m/z = 57$ will be more intense for 2,2-dimethylpropane than for 2-methylbutane or for pentane because the peak at $m/z = 57$ is due to loss of a methyl group: loss of a methyl group from 2,2-dimethylpropane results in the formation of a tertiary carbocation, whereas loss of a methyl group from 2-methylbutane and pentane results in the formation of a secondary and primary carbocation, respectively.



2,2-dimethylpropane — $m/z = 57$, a tertiary carbocation



2-methylbutane — $m/z = 57$, a secondary carbocation

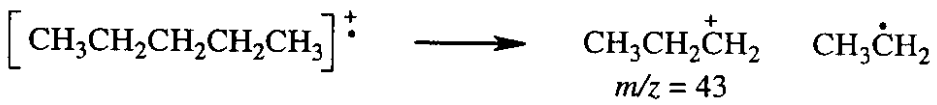


pentane — $m/z = 57$, a primary carbocation

Note that the mass spectrum of 2-methylbutane can be distinguished from those of the other isomers by the peak at $m/z = 43$. The peak at $m/z = 43$ will be most intense for 2-methylbutane because such a peak is due to loss of an ethyl group, which results in the formation of a secondary carbocation. Pentane gives a less intense peak at $m/z = 43$ because loss of an ethyl group from pentane forms a primary carbocation. 2,2-Dimethylpropane cannot form a peak at $m/z = 43$, because it does not have an ethyl group.

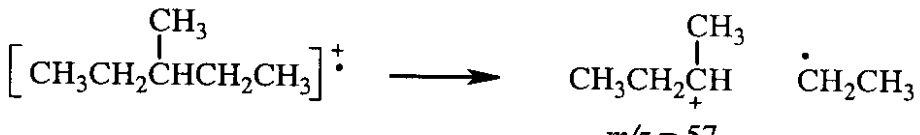


$m/z = 43$

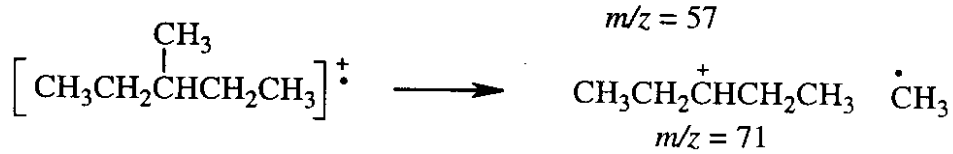


$m/z = 43$

2. Peaks should occur at $m/z = 57$ for loss of an ethyl group (86-29), and at $m/z = 71$ for loss of a methyl group (86-15).



$m/z = 57$



$m/z = 71$

A secondary carbocation is formed in both cases. Because an ethyl radical is more stable than a methyl radical, the base peak will most likely be at $m/z = 57$.

3. Solved in the text.

4. **a.** **1.** $15 + (3 \times 14) + 16 = 73$ **2.** $16 + (3 \times 14) + 16 = 74$

b. An alkane has an even-mass molecular ion. If a CH_2 group (14) of an alkane is replaced by an NH group (15), or if a CH_3 group (15) of an alkane is replaced by an NH_2 group (16), the molecular ion will have an odd mass.
A second nitrogen in the molecular ion will cause it to have an even mass.
Thus, for a molecular ion to have an odd mass, an odd number of nitrogens must be present.

c. An even-mass molecular ion either has no nitrogens or has an even number of nitrogens.

5.

$$\text{number of carbon atoms} = \frac{\text{relative intensity of M + 1 peak}}{0.011 \times \text{relative intensity of M peak}}$$

$$= \frac{3.81}{0.011 \times 43.27} = \frac{3.81}{0.467} = 8 \text{ carbon atoms}$$

6. The calculated exact masses show that only C_6H_{14} has an exact mass of 86.10955.

C_6H_{14}

$$\begin{aligned} 6(12.00000) &= 72.00000 \\ 14(1.007825) &= \underline{14.10955} \\ & 86.10955 \end{aligned}$$

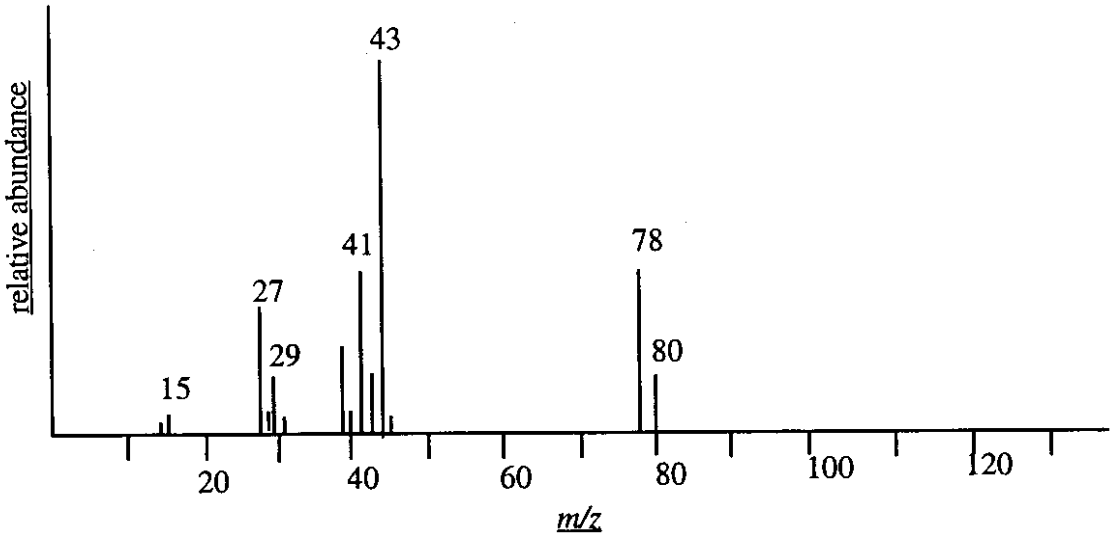
$C_4H_{10}N_2$

$$\begin{aligned} 4(12.00000) &= 48.00000 \\ 10(1.007825) &= 10.07825 \\ 2(14.0031) &= \underline{28.0064} \\ & 86.08465 \end{aligned}$$

$C_4H_6O_2$

$$\begin{aligned} 4(12.00000) &= 48.00000 \\ 6(1.007825) &= 6.04695 \\ 2(15.9949) &= \underline{31.9898} \\ & 86.03675 \end{aligned}$$

7. Because the compound contains chlorine, the M + 2 peak is one third the size of the M peak. Loss of a chlorine atom from either the M + 2 peak (80 – 37) or the M peak (78 – 35) gives a peak with $m/z = 43$.

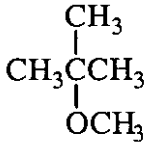


Mass spectrum of 1-chloropropane

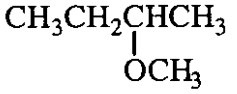
8. The base peak at $m/z = 73$, due to loss of a methyl group (88 – 15), indicates that Figure 13.7a is the mass spectrum of **2-methoxy-2-methylpropane**.

The base peak at $m/z = 59$ (88 – 29), due to loss of an ethyl group, indicates that Figure 13.7b is the mass spectrum of **2-methoxybutane**.

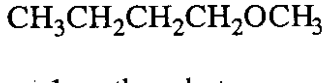
The base peak at $m/z = 45$ (88 – 43), due to loss of a propyl group, indicates that Figure 13.7c is the mass spectrum of **1-methoxybutane**.



2-methoxy-2-methylpropane

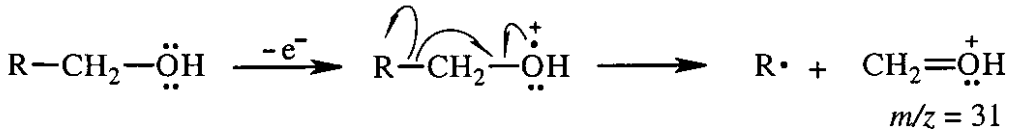


2-methoxybutane



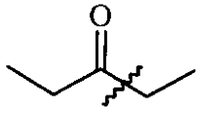
1-methoxybutane

9.



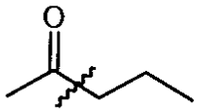
10. All ketones will have molecular ions with $m/z = 86$.

3-pentanone



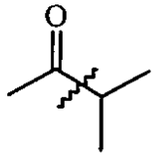
86 - 29 = 57

2-pentanone



86 - 41 = 43

3-methyl-2-butanone



86 - 41 = 43

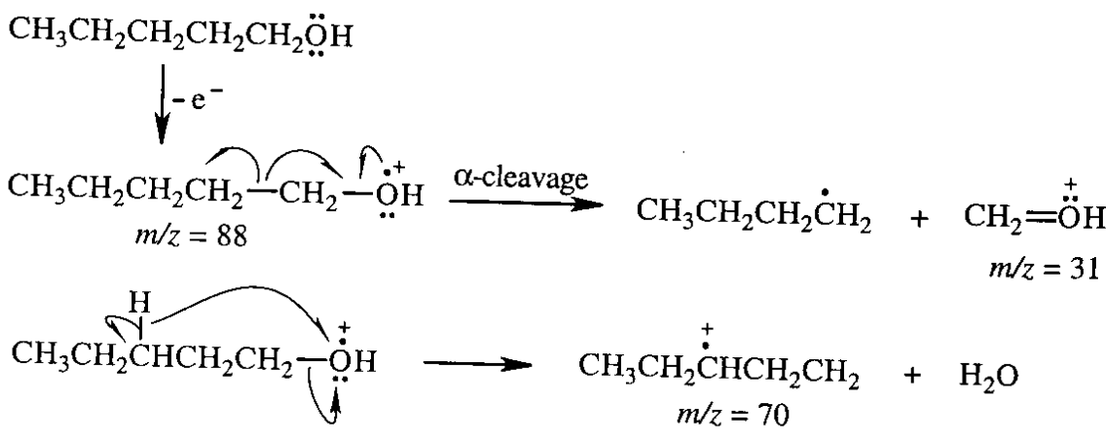
3-Pentanone will have a base peak at $m/z = 57$, whereas the other two ketones will have base peaks at $m/z = 43$.
2-Pentanone will have a peak at at $m/z = 58$ due to a McLafferty rearrangement.
3-Methyl-2-butanone does not have any γ-hydrogens. Therefore, it can't undergo a McLafferty rearrangement so it will not have a peak at at $m/z = 58$.

11. The fact that Figure 13.9a shows a peak at $m/z = 43$ for loss of a propyl group (86 – 43) indicates that it is the mass spectrum of either 2-pentanone or 3-methyl-2-butanone, since each of these has a propyl group.
The fact that the spectrum has a peak at $m/z = 58$, indicating loss of ethene, indicates that the compound has a γ-hydrogen that enables it to undergo a McLafferty rearrangement.
Therefore, it must be 2-pentanone, since 3-methyl-2-butanone does not have a γ-hydrogen.

The fact that Figure 13.9b shows a peak at $m/z = 57$ for loss of an ethyl group (86 – 29), indicates that it is the mass spectrum of 3-pentanone.

12.

a.



b. $CH_3\overset{\overset{\cdot\cdot}{O}:}{\overset{\|}{C}}CH_2CH_2CH_2CH_3$

$\downarrow -e^-$

$CH_3\overset{\overset{\cdot+}{O}:}{\overset{\|}{C}}CH_2CH_2CH_2CH_3 \xrightarrow{\alpha\text{-cleavage}} CH_3CH_2CH_2CH_2\overset{+}{C}\equiv\ddot{O} + \dot{C}H_3$

$m/z = 100$ $\qquad$ $m/z = 85$

$CH_3\overset{\overset{+\cdot}{O}:}{\overset{\|}{C}}CH_2CH_2CH_2CH_3 \xrightarrow{\alpha\text{-cleavage}} CH_3C\equiv\overset{+}{O}: + CH_3CH_2CH_2\dot{C}H_2$

$m/z = 43$

$CH_3\overset{\overset{+\cdot}{O}:}{\overset{\|}{C}}CH_2-CH_2-\overset{H}{\underset{|}{C}}HCH_3 \xrightarrow[\text{rearrangement}]{\text{McLafferty}} \overset{+}{O}H\overset{\|}{C}CH_2 + CH_2{=}CHCH_3$

$m/z = 58$

c. $CH_3CH_2\underset{:\ddot{O}H}{\underset{|}{C}}HCH_2CH_2CH_2CH_3$

$\downarrow -e^-$

$CH_3CH_2-\underset{+\cdot\ddot{O}H}{\underset{|}{C}}HCH_2CH_2CH_2CH_3 \xrightarrow{\alpha\text{-cleavage}} CH_3CH_2CH_2CH_2CH{=}\overset{+}{O}H + CH_3\dot{C}H_2$

$m/z = 116$ $\qquad$ $m/z = 87$

$CH_3CH_2CH-CH_2CH_2CH_2CH_3 \xrightarrow{\alpha\text{-cleavage}} CH_3CH_2CH{=}\overset{+}{O}H + CH_3CH_2CH_2\dot{C}H_2$

$\underset{+\cdot\ddot{O}H}{\underset{|}{C}}$

$m/z = 59$

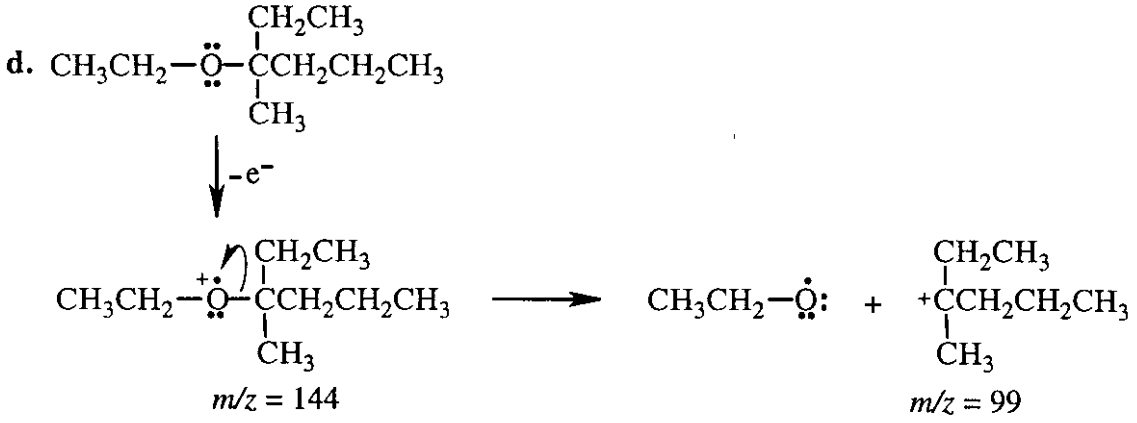
$CH_2CH_2\underset{H}{\underset{|}{C}}HCH_2CH_2CH_2CH_3 \longrightarrow \dot{C}H_2CH_2\overset{+}{C}HCH_2CH_2CH_2CH_3 + H_2O$

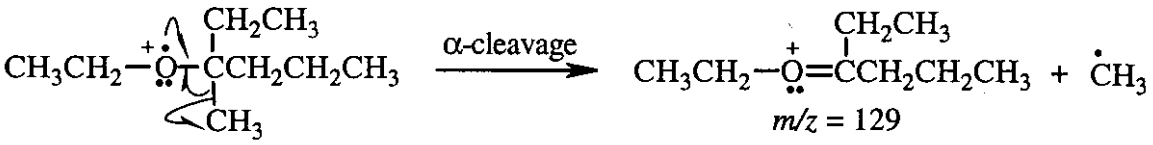
$\underset{+\cdot\ddot{O}H}{\underset{|}{C}}$

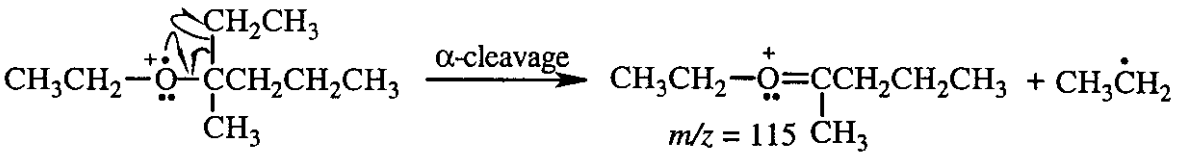
$m/z = 98$

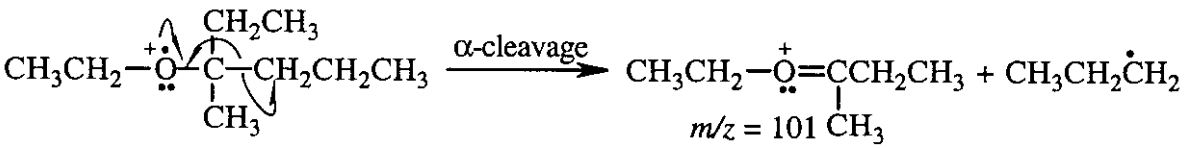
$CH_3CH_2\underset{+\cdot\ddot{O}H}{\underset{|}{C}}HCH_2\underset{H}{\underset{|}{C}}HCH_2CH_3 \longrightarrow CH_3CH_2\overset{+}{C}HCH_2\dot{C}HCH_2CH_3 + H_2O$

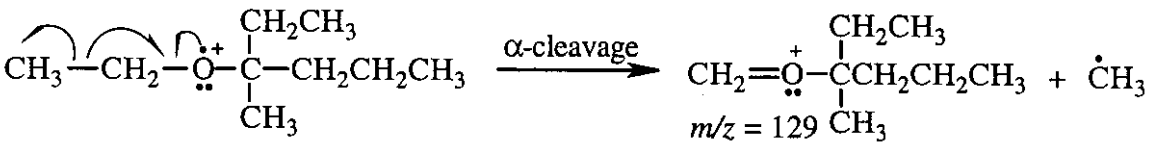
$m/z = 98$

d. 
CH3CH2—O—CCH2CH2CH3
CH2CH3
CH3
-e⁻
CH3CH2—O—CCH2CH2CH3
m/z = 144
CH3CH2—O:
+CCH2CH2CH3
m/z = 99


CH3CH2—O—CCH2CH2CH3
CH2CH3
CH3
α-cleavage
CH3CH2—O=CCH2CH2CH3 + ·CH3
m/z = 129


CH3CH2—O—CCH2CH2CH3
CH2CH3
CH3
α-cleavage
CH3CH2—O=CCH2CH2CH3 + CH3·CH2
m/z = 115
CH3


CH3CH2—O—C—CH2CH2CH3
CH2CH3
CH3
α-cleavage
CH3CH2—O=CCH2CH3 + CH3CH2·CH2
m/z = 101
CH3


CH3—CH2—O—C—CH2CH2CH3
CH2CH3
CH3
α-cleavage
CH2=O—CCH2CH2CH3 + ·CH3
m/z = 129
CH3

e. $CH_3CH_2\underset{\underset{CH_3}{|}}{CH}\ddot{Cl}: \xrightarrow{-e^-} CH_3CH_2\underset{\underset{CH_3}{|}}{CH}-\ddot{Cl}: \longrightarrow CH_3CH_2\overset{+}{C}H + :\dot{Cl}:$

$m/z = 92$ and 94 $\qquad$ $m/z = 57$

$CH_3CH_2CH-\ddot{Cl}: \xrightarrow{\alpha\text{-cleavage}} CH_3CH_2CH=\overset{+}{\ddot{Cl}}: + \dot{C}H_3$

$m/z = 77$ and 79

$CH_3CH_2-CH-\ddot{Cl}: \xrightarrow{\alpha\text{-cleavage}} CH_3CH=\overset{+}{\ddot{Cl}}: + CH_3\dot{C}H_2$

$m/z = 63$ and 65

f. $CH_3CH_2\underset{\underset{CH_3}{|}}{\overset{CH_3}{\overset{|}{C}}}-\ddot{Br}: \xrightarrow{-e^-} CH_3\underset{\underset{CH_3}{|}}{\overset{CH_3}{\overset{|}{C}}}-\ddot{Br}: \longrightarrow CH_3\underset{\underset{CH_3}{|}}{\overset{CH_3}{\overset{|}{C}}}{}^{+} + :\dot{Br}:$

$m/z = 136$ and 138 $\qquad$ $m/z = 57$

13. When (*Z*)-2-pentene reacts with water and an acid catalyst, 3-pentanol and 2-pentanol are formed. Both alcohols have a molecular weight of 88. (Notice that the first step in solving this problem is to use chemical knowledge to identify the products.) The absence of a molecular ion peak is consistent with the fact that the compounds are alcohols.

$$\underset{\text{(Z)-2-pentene}}{H_3C(H)C{=}C(H)CH_2CH_3} + H_2O \xrightarrow{H_2SO_4} \underset{\text{3-pentanol}}{CH_3CH_2\underset{\underset{OH}{|}}{C}HCH_2CH_3} + \underset{\text{2-pentanol}}{CH_3\underset{\underset{OH}{|}}{C}HCH_2CH_2CH_3}$$

Figure 13.10a shows a base peak at $m/z = 59$ due to loss of an ethyl group (88 – 29), indicating that it is the spectrum of 3-pentanol.

Figure 13.10b shows a base peak at $m/z = 45$ due to loss of a propyl group (88 – 43), indicating that it is the spectrum of 2-pentanol.

14. **a.** 2000 cm^{-1} (The greater the wavenumber, the higher the energy.)

b. 8 μm (The smaller the wavelength, the higher the energy.)

c. 2 μm, because 2 μm = 5000 cm^{-1} (5000 cm^{-1} is a greater wavenumber than 3000 cm^{-1})

15.

the equation used for these calculations: $\tilde{\nu}\,(\text{cm}^{-1}) = \dfrac{10{,}000}{\lambda\,(\mu\text{m})}$

a. $\tilde{\nu}\,(\text{cm}^{-1}) = \dfrac{10{,}000}{4\,(\mu\text{m})} = 2500\ \text{cm}^{-1}$

b. $200\,(\text{cm}^{-1}) = \dfrac{10{,}000}{\lambda\,(\mu\text{m})}$

$$\lambda\,(\mu\text{m}) = \frac{10{,}000}{200\,(\text{cm}^{-1})}$$

$$\lambda\,(\mu\text{m}) = 50\ \mu\text{m}$$

16. The stretching vibration of a C=O bond will be more intense because the vibration is associated with a greater change in dipole moment than the dipole moment associated with the stretching vibration of a C=C bond.

17.

a. **1.** C≡C stretch — A triple bond is stronger than a double bond, so it takes more energy to stretch a triple bond.

2. C—H stretch — It requires more energy to stretch a bond than to bend it.

3. C=N stretch — A double bond is stronger than a single bond, so it takes more energy to stretch a double bond.

b. **1.** C—O — Vibrations of lighter atoms occur at larger wavenumbers.

2. C—C — Vibrations of lighter atoms occur at larger wavenumbers.

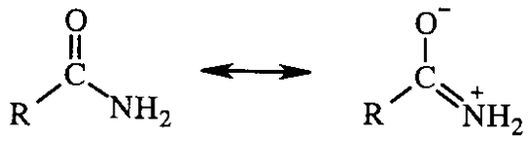
18. **a.** The carbon-nitrogen stretch of an amide because it has partial double-bond character as a result of electron delocalization.



b. The carbon-oxygen stretch of phenol because it has partial double-bond character as a result of electron delocalization.

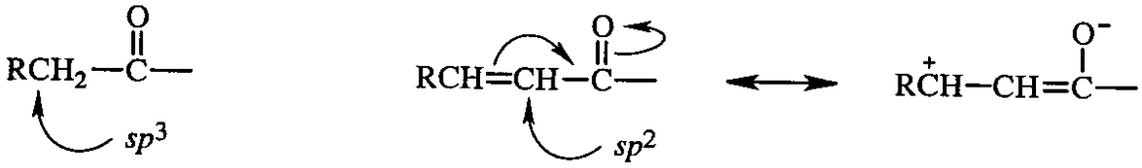


c. The carbon-oxygen double-bond stretch of a ketone because it has more double-bond character. The double bond character of the amide is reduced by electron delocalization.

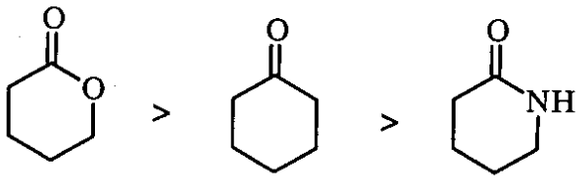


d. The C—O stretch, because a bond stretches at a higher frequency than it bends.

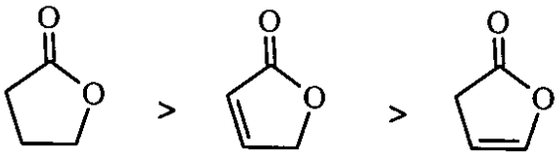
19. A carbonyl group bonded to an sp^3 hybridized carbon will exhibit an absorption band at a higher frequency because a carbonyl group bonded to an sp^2 hybridized carbon will have greater single-bond character as a result of electron delocalization.



20. **a.** The C=O absorption band of an ester occurs at the highest frequency because an ester has the most double bond character since the predominant effect of the ester oxygen atom is inductive electron withdrawal.
The C=O absorption band of an amide occurs at the lowest frequency because an amide has the least double bond character since the predominant effect of the amide nitrogen atom is electron donation by resonance.

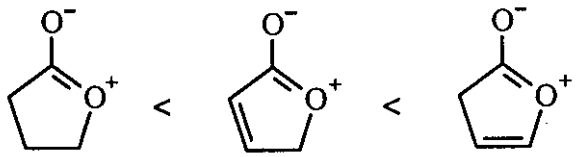


b. The C=O absorption band of the three compounds decreases in the following order.



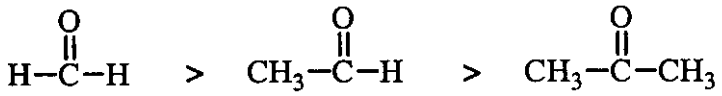
To explain the relative frequency of the C=O absorption, we need to look at the relative stabilities of the resonance contributors because the more stable the resonance contributor with a carbon-oxygen single bond, the lower the carbonyl absorption frequency will be. The resonance contributor without a conjugated double bond is the least stable, and the compound with a π cloud extending over five atoms is the most stable.

relative stabilities of the resonance contributors



least stable **most stable**

c. Because alkyl groups are more electron-donating than a hydrogen, the absorption band for the carbonyl group bonded to two relatively electron-withdrawing hydrogens has the greatest frequency, while the absorption band for the carbonyl group bonded to two alkyl groups has the lowest frequency.



21. Ethanol dissolved in carbon disulfide will show the oxygen-hydrogen stretch at a greater wavenumber because there is extensive hydrogen bonding in the undiluted alcohol, and an oxygen-hydrogen bond is easier to stretch if it is hydrogen bonded.

22. **a.** Because oxygen is more electronegative than nitrogen, the O—H stretching vibration is associated with a greater change in dipole moment.

b. The O—H group of a carboxylic acid can form both intermolecular and intramolecular hydrogen bonds, while an alcohol can form only intermolecular hydrogen bonds. Therefore, the extent of hydrogen bonding is greater in a carboxylic acid, and hydrogen bonded OH groups have broader absorption bands.

23. The absorption band at 1100 cm^{-1} would be less intense if it were due to a C—N bond because smaller change in dipole moment is associated with a C—N bond compared to the change in dipole moment associated with the stretch of a C—O bond.

24. **a.** The absorption band at 1700 cm^{-1} indicates that the compound has a carbonyl group.

The absence of an absorption band at 3300 cm^{-1} indicates that the compound is not a carboxylic acid.

The absence of an absorption band at 2700 cm^{-1} indicates that the compound is not an aldehyde.

The absence of an absorption band at 1100 cm^{-1} indicates that the compound is not an ester an amide.

The compound, therefore, must be a **ketone**.

b. The absence of an absorption band at 3400 cm^{-1} indicates that the compound does not have an N—H bond.
The absence of an absorption band between 1700 cm^{-1} and 1600 cm^{-1} indicates that the compound is not an amide.
The compound, therefore, must be a **tertiary amine**.

25. **a.** An aldehyde would show absorption bands at 2820 and 2720 cm^{-1}. A ketone would not have these absorption bands.

b. A straight-chain ketone would have a methyl substituent and therefore an absorption band at 1385-1365 cm^{-1} that a cyclic ketone would not have.

c. Cyclohexene would show an sp^3 C—H stretch slightly to the left 3000 cm^{-1}. Benzene would not show an absorption band in this region.

d. The cis isomer would show a carbon-hydrogen bending vibration at 730-675 cm^{-1}, while the trans isomer would show a carbon-hydrogen bending vibration at 960-980 cm^{-1}.

e. Cyclohexene would show a carbon-carbon double-bond stretching vibration at 1680-1600 cm^{-1} and a carbon-hydrogen stretching vibration at 3100-3020 cm^{-1}. Cyclohexane would not show these absorption bands.

f. A primary amine would show a nitrogen-hydrogen stretch at 3500-3300 cm^{-1}, and a tertiary amine would not have this absorption band.

26. **a.** An absorption band at 1150-1050 cm^{-1} would be present for the ether and absent for the alkane.

b. An absorption band at 3300-2500 cm^{-1} would be present for the carboxylic acid and absent for the ester.

c. An absorption band at 1780-1650 cm^{-1} would be present for the carboxylic acid and absent for the alcohol.

d. Only the terminal alkyne would show an absorption band at 3300 cm^{-1}.

e. An absorption band at 1385-1365 cm^{-1} would be present for methylcyclohexane and absent for cyclohexane.

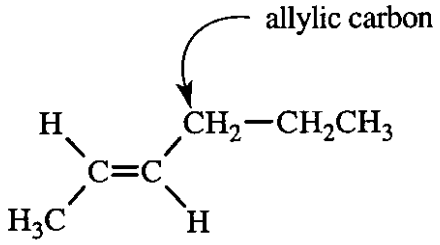
f. An absorption band 2960-2850 cm^{-1} would be present for cyclohexene and absent for benzene. (Also, an absorption band at 1500 cm^{-1} would be present for benzene and absent for cyclohexene.)

27. 2-butyne, H_2, Cl_2, ethene

28. The absorption bands in the vicinity of 3000 cm^{-1} indicate that the compound has hydrogens attached to both sp^2 and sp^3 hybridized carbons. The lack of absorption at 1600 cm^{-1} and 1500 cm^{-1} indicates the compound does not have a benzene ring. The sp^2 hydrogens, therefore, must be those of an **alkene**.

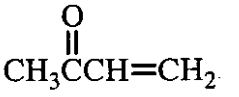
The lack of significant absorption at 1600 cm^{-1} indicates it must be an alkene with a relatively small (if any) dipole moment change when the vibration occurs. The absorption band at 965 cm^{-1} indicates the compound is a ***trans*-alkene**.

The molecular ion with $m/z = 84$ suggests the compound has a molecular formula of C_6H_{12}. The base peak with $m/z = 55$ indicates the compound most easily loses an ethyl group (84 - 29 = 55), but it can also lose a methyl group ($m/z = 69$) or a propyl group ($m/z = 41$). Because it most easily loses an ethyl group, the ethyl group must be attached to an allylic carbon. The compound, therefore, is ***trans*-2-hexene**.



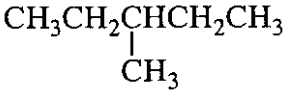
trans-2-hexene

29. The absorption band at ~1700 cm^{-1} indicates the compound has a carbonyl group, and the absorption band at ~1600 cm^{-1} indicates the compound has a carbon-carbon double bond. The absorption bands in the vicinity of 3000 cm^{-1} indicate that the compound has hydrogens attached to both sp^2 and sp^3 hybridized carbons. The absorption band at ~1380 cm^{-1} indicates th compound has a methyl.
Because the compound has only four carbons and one oxygen, it must be **methyl vinyl ketone**.



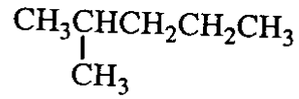
30. The molecular ion peak for these compounds is $m/z = 86$; the peak at $m/z = 57$ is due to loss of an ethyl group (86 – 29), and the peak at $m/z = 71$ is due to loss of a methyl group (86 – 15).

a. 3-Methylpentane will be more apt to lose an ethyl group (forming a secondary carbocation and a primary radical) than a methyl group (forming a secondary carbocation and a methyl radical), so the peak at $m/z = 57$ would be more intense than the peak at $m/z = 71$.



3-methylpentane

b. 2-Methylpentane has two pathways to lose a methyl group (forming a secondary carbocation and a methyl radical in each pathway), and it cannot form a secondary carbocation by losing an ethyl group. (Loss of an ethyl group would form a primary carbocation and a primary radical.) Therefore, it will be more apt to lose a methyl group than an ethyl group, so the peak at $m/z = 71$ would be more intense than the peak at $m/z = 57$.



2-methylpentane

31. 1. the change in the dipole moment when the bond stretches or bends
2. the number of bonds that give rise to the absorption band
3. the concentration of the sample

32. **a.** An absorption band at ~1250 cm^{-1} would be present for the ester and absent for the ketone.

b. An absorption band at 720 cm^{-1} would be present for heptane and absent for methylcyclohexane.

c. Absorption bands at 990 cm^{-1} and 910 cm^{-1} would be present for the terminal alkene and absent for the internal alkene.

d. The secondary alcohol would have an absorption band at 1385-1365 cm^{-1} for the methyl group. The primary alcohol does not have a methyl group, so it would not have this absorption band.

e. The C=O absorption band will be at a higher wavenumber for the ester (1740 cm^{-1}) than for the ketone (1720 cm^{-1}).

f. The alkene would have an absorption band at 1680-1600 cm^{-1} and 3100-3020 cm^{-1} that the alkyne would not have. The alkyne would have an absorption band at 2260-2100 cm^{-1} that the alkene would not have.

g. An absorption band at ~2700 cm^{-1} would be present for the aldehyde and absent for the ketone.

h. The C=O absorption band will be at a higher wavenumber for the β,γ-unsaturated ketone (1720 cm^{-1}) than for the α,β-unsaturated ketone since the double bonds in the latter are conjugated (1680 cm^{-1}).

i. The trans isomer would have an absorption band at 980-960 cm^{-1}, while the cis isomer would have an absorption band at 730-675 cm^{-1}. In addition, an absorption band at 1680-1600 cm^{-1} would be present for the cis isomer and absent for the trans isomer.

j. An absorption band at 3650-3200 cm^{-1} would be present for the alcohol and absent for the ether.

k. An absorption band at 3500-3300 cm^{-1} would be present for the amide and absent for the ester.

l. Absorption bands at 1600 cm^{-1} and 1500 cm^{-1} and at 3100-3020 cm^{-1} would be present for the compound with the benzene ring and absent for the compound with the cyclohexane ring An absorption band at 2960-2850 cm^{-1} would be present for the compound with the cyclohexane ring and absent for the compound with the benzene ring.

33. **a.** If the reaction had occurred, the intensity of the absorption bands at ~1700 cm^{-1} (due to the carbonyl group) and ~2700 cm^{-1} (due to the aldehyde hydrogen) of the reactant would have decreased. If all the aldehyde had reacted, these absorption bands would have disappeared.

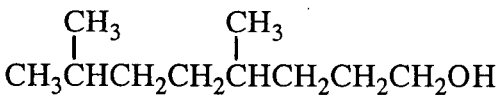
b. If all the NH_2NH_2 had been removed, there would be no N—H absorption at ~ 3400 cm^{-1}.

34. The compound would have an M and an M + 4 peak of equal intensity, and there would be an M + 2 peak of twice the intensity of the M peak.

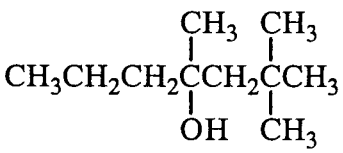
35. If the force constants are approximately the same, the lighter atoms absorb at higher frequenci

$$C{-}C \quad > \quad C{-}N \quad > \quad C{-}O$$

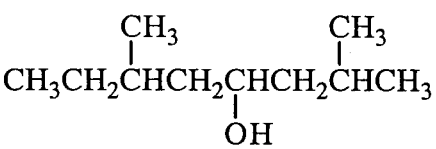
36. The molecular weight of each of the alcohols is 158. The peak at $m/z = 140$ is due to loss of water (158 − 18); each of the alcohols could show such a peak. The peaks at $m/z = 87$, 115, an 143 are due to loss of a group with five carbons, a group with three carbons, and a methyl grou respectively. Only 2,2,4-trimethyl-4-heptanol would lose all three groups.



4,7-dimethyl-1-octanol



2,2,4-trimethyl-4-heptanol



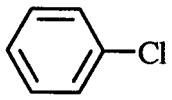
2,6-dimethyl-4-octanol

$CH_2{=}CHCH_2CH_2CH{=}CH_2$ $CH_3CH{=}CHCH{=}CHCH_3$

1,5-hexadiene 2,4-hexadiene

The easiest way to distinguish the two compounds is by the presence or absence of an absorption band at ~1370 cm^{-1} due to the methyl group that 2,4-hexadiene has but that 1,5-hexadiene does not have. In addition, 2,4-hexadiene has conjugated double bonds, and therefore its double bonds have some single-bond character due to resonance. Consequently, they are easier to stretch than the isolated double bonds of 1,5-hexadiene. Thus, the carbon-carbon double bond stretch of 2,4-hexadiene will be at a lower wavenumber than the carbon-carbon double-bond stretch of 1,5-hexadiene.

38. The fact that the abundance of the M+2 peak is 30% of the abundance of the M peak indicates that the compound has one chlorine atom. The peak at $m/z = 77$ is due to loss of the chlorine atom (112 – 35 = 77). The peak at m/z value of 77 and fact that the this peak does not fragment, indicates it is a benzene ring. The compound is chlorobenzene.



39. A hydrocarbon with eight carbons (C_nH_{2n+2}) has a molecular formula of C_8H_{18} and a molecular weight of 114. Since the molecular ion is 112, the compound must be a hydrocarbon with eight carbons and one double bond or one ring. Possible compounds are cyclooctane, methylcycloheptane, all the dimethylcyclohexanes, ethylcyclohexane, propylcyclopentane, isopropylcyclopentane, all the ethylmethyl cyclopentanes, all the trimethylcyclopentanes, all octenes, all methylheptenes, all ethylhexenes, etc.

40.

3600 cm^{-1}	3000	1800	1400	1000
OH 3300-3000	sp^3 CH 2950	C=O 1700	C–O 1250-1050	
NH 3600-3200	O ‖ RCH 2700	C=C 1600	C–N 1230-1030	
sp CH 3300	C≡C 2100	 1500		
sp^2 CH 3050	C≡N 2250			

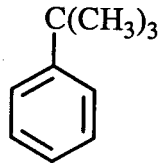
41. **a.** The absorption band at ~2100 cm^{-1} indicates a carbon-carbon triple bond, and the absorption band at ~3300 cm^{-1} indicates a hydrogen bonded to an *sp* hybridized carbon.

$$CH_3CH_2CH_2CH_2C{\equiv}CH$$

b. The absence of an absorption band at ~2700 cm^{-1} indicates that the compound is not an aldehyde, and the absence of a broad absorption band in the vicinity of 3000 cm^{-1} indicates that the compound is not a carboxylic acid. The ester and the ketone can be distinguished by the absorption band that is present at ~1200 cm^{-1} that indicates the carbon-oxygen single bond of an ester.

$$CH_3CH_2\overset{\overset{O}{\|}}{C}OCH_2CH_3$$

c. The absorption band at ~1360 cm^{-1} indicates the presence of a methyl group.



42. 4-Methyl-2-pentanone would show peaks at $m/z = 85$ (loss of a methyl group) and at $m/z = 43$ (loss of an isobutyl group) and a peak at $m/z = 58$ due to a McLafferty rearrangement.

$$CH_3\overset{\overset{O}{\|}}{C}CH_2\underset{\underset{CH_3}{|}}{C}HCH_3$$

4-methyl-2-pentanone

2-Methyl-3-pentanone would show peaks at $m/z = 71$ (loss of an ethyl group) and at $m/z = 57$ (loss of an isopropyl group). Because it doesn't have a γ-hydrogen, it cannot undergo a McLafferty rearrangement.

$$CH_3\underset{\underset{CH_3}{|}}{C}H\overset{\overset{O}{\|}}{C}CH_2CH_3$$

2-methyl-3-pentanone

The absorption bands at ~2700 cm^{-1} for the aldehydic hydrogen and at ~1380 cm^{-1} for the methyl group would distinguish the compounds.

A would have the band at ~2700 cm^{-1} but not the one at ~1380 cm^{-1}.
B would have the band at ~1380 cm^{-1} but not the one at ~2700 cm^{-1}.
C would have the both the band at ~2700 cm^{-1} and the one at ~1380 cm^{-1}.

44. 1-Hexyne will show absorption bands at ~3300 cm^{-1} for a hydrogen bonded to an *sp* hybridized carbon and at ~2100 cm^{-1} for the triple bond.

$$CH_3CH_2CH_2CH_2C{\equiv}CH$$
1-hexyne

2-Hexyne will show the absorption band at ~2100 cm^{-1} but not the one at ~3300 cm^{-1}.

$$CH_3CH_2CH_2C{\equiv}CCH_3$$
2-hexyne

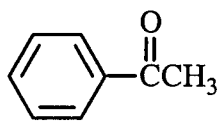
3-Hexyne will show neither the absorption band at ~3300 cm^{-1} nor the one at ~2100 cm^{-1} (there is no change in dipole moment).

$$CH_2CH_2C{\equiv}CCH_2CH_3$$
3-hexyne

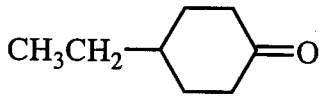
45. **a.** The broad absorption band at ~3300 cm^{-1} is characteristic of the oxygen-hydrogen stretch of an alcohol, and the absence of absorption bands at ~1600 cm^{-1} and ~3100 cm^{-1} indicates that it is not the alcohol with a carbon-carbon double bond.

$$CH_3CH_2CH_2CH_2OH$$

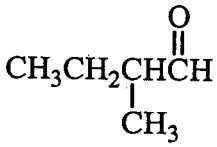
b. The absorption band at ~1685 cm^{-1} indicates a carbon-oxygen double bond. The absence of a strong and broad absorption band at ~3000 cm^{-1} rules out the carboxylic acid, and the absence of an absorption band at ~2700 cm^{-1} rules out the aldehyde. Thus, it must be the ketone.



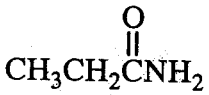
c. The absorption band at ~1700 cm^{-1} indicates a carbon-oxygen double bond. The absence of an absorption band at ~1600 cm^{-1} rules out the ketones with the benzene or cyclohexene rings. The absence of absorption bands at ~2100 cm^{-1} and ~3300 cm^{-1} rules out the ketone with the carbon-carbon triple bond. Thus, it must be 4-ethylcyclohexanone.



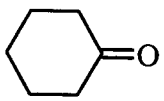
46. **a.** The absorption band at ~2700 cm^{-1} indicates that the compound is an aldehyde (carbon-hydrogen stretch of an aldehyde hydrogen). The absence of an absorption band at ~1600 cm^{-1} rules out the aldehyde with the benzene ring. Thus, it must be the other aldehyde.



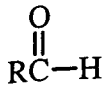
b. The absorption bands at ~3350 cm^{-1} and ~3200 cm^{-1} indicate that the compound is an amide (nitrogen-hydrogen stretch). The absence of an absorption band at ~3050 cm^{-1} indicates that the compound does not have hydrogens bonded to sp^2 carbons. Therefore, it is not the amide that has a benzene ring.



c. The absence of absorption bands at ~1600 cm^{-1} and ~1500 cm^{-1} indicates that the compound does not have a benzene ring. Thus, it must be the ketone. This is confirmed by the absence of an absorption band at ~1380 cm^{-1}, indicating that the compound does not have a methyl group. (Notice the first fundamental of the 1700 cm^{-1} absorption band at 3400 cm^{-1}.)



47.

a.  2700

 1700

C=C 1600

b.  1700

 1500, 1600

C–O ~1250, ~1050

c.  1700

C–N ~1030

N–H 3500-3300

d. C–O ~1050

O–H 3600-3200 (broad)

e.

sp CH 3300 (narrow)

C≡C 2100

f.  1700

 ~3000 (broad)

C–O ~1250

48. Calculating the term in Hooke's law that depends on the masses of the atoms joined by a bond for a C—H bond and for a C—C bond shows why smaller atoms give rise to greater wavenumbers.

<u>for a carbon-hydrogen bond</u>

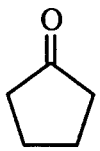
$$\frac{m_1 + m_2}{m_1 \times m_2} = \frac{12 + 1}{12 \times 1} = \frac{13}{12} = 1.08$$

<u>for a carbon-carbon bond</u>

$$\frac{m_1 + m_2}{m_1 \times m_2} = \frac{12 + 12}{12 \times 12} = \frac{24}{144} = 0.17$$

49. The absorption band at ~1700 cm^{-1} indicates that the compound has a carbonyl group, and the absence of an absorption band at ~1380 cm^{-1} indicates that it has no methyl groups. The absence of an absorption band at ~1600 cm^{-1} indicates the compound does not have a carbon-carbon double bond, and the absence of an absorption band at ~3050 cm^{-1} indicates the compound does not have hydrogens bonded to sp^2 carbons.

From the molecular formula you can deduce that the compound is **cyclopentanone**.



50. The broad absorption band at ~3300 cm^{-1} indicates that the compound has an OH group. The absorption bands at ~2900 cm^{-1} indicate that the compound has hydrogens attached to an sp^3 hybridized carbon. The compound, therefore, is **benzyl alcohol**.

51. The broad absorption band at ~3300 cm^{-1} indicates that the compound has an OH group. The absence of absorption at ~2950 cm^{-1} indicates the compound does not have any hydrogens bonded to sp^3 hybridized carbons. Therefore, the compound is phenol.

52. The M peak at 100 indicates that the compound has a molecular weight of 100, and the relative intensities of the M and M + 1 peaks indicate that the compound has seven carbons. When $n = 7$, $(C_nH_{2n+2}) = C_7H_{16}$. A compound with that molecular formula has a molecular weight of 100.

$$\text{number of carbon atoms} = \frac{M+1}{0.011 \times M} = \frac{2.10}{0.011 \times 27.32} = \frac{2.10}{0.301} = 7$$

53.

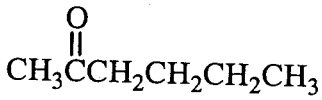
$$\tilde{\nu} = \frac{1}{2 \times 3.1416 \times 3 \times 10^{10}\ \text{cm s}^{-1}} \sqrt{\frac{10 \times 10^{5}\ \text{g s}^{-2} \left(\frac{12}{6.02} + \frac{12}{6.02}\right) \times 10^{-23}}{\frac{12}{6.02} \times 10^{-23}\ \text{g} \times \frac{12}{6.02} \times 10^{-23}\ \text{g}}}$$

$$\tilde{\nu} = \frac{1}{18.85 \times 10^{10}} \sqrt{10.0 \times 10^{28}}$$

$$\tilde{\nu} = \frac{1}{18.85 \times 10^{10}} \times 3.16 \times 10^{14}$$

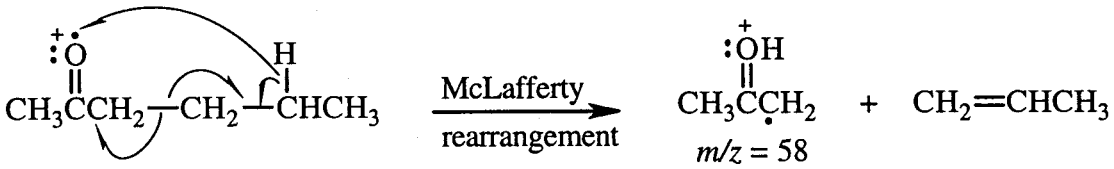
$$\tilde{\nu} = 1676\ \text{cm}^{-1}$$

54. **a.** The IR spectrum indicates that the compound is an aliphatic ketone with at least one methyl group. The M peak at $m/z = 100$ indicates that the ketone is a hexanone. The peak at 43 (100 – 57) for loss of a butyl group and the peak at 85 for loss of a methyl group (100 – 15) suggest that the compound is **2-hexanone**.

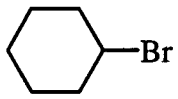


2-hexanone

This is confirmed by the peak at 58 for loss of propene (100 – 42) as a result of a McLafferty rearrangement.

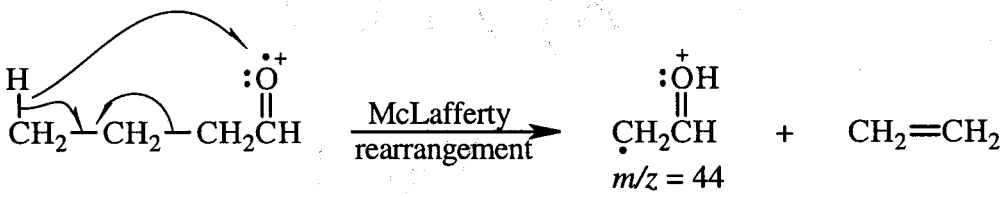


b. The equal heights of the M and M + 2 peaks at 162 and 164 indicate that the compound contains bromine. The peak at $m/z = 83$ (162 – 79) is for the carbocation that is formed when the bromine atom is eliminated. The IR spectrum does not indicate the presence of any functional groups, and it shows that there are no methyl groups present. The m/z peak = 83 indicates a carbocation with a molecular formula of C_6H_{11}. The fact that the compound does not contain a methyl group indicates that the compound is **bromocyclohexane**.

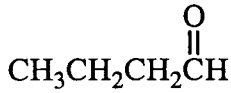


bromocyclohexane

c. The absorption bands at ~1700 cm^{-1} and ~2700 cm^{-1} indicate that the compound is an aldehyde. The molecular ion peak at $m/z = 72$ indicates that the aldehyde contains four carbons. The peak at $m/z = 44$ for loss of a group with molecular weight 28 indicates that 0ethene has been lost as a result of a McLafferty rearrangement.



A McLafferty rearrangement can occur only if the aldehyde has a γ-hydrogen. The only four-carbon aldehyde that has a γ-hydrogen is **butanal**.



butanal

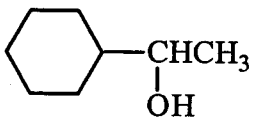
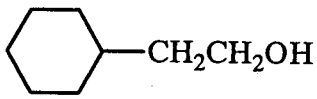
Chapter 13 Practice Test

1. Give one IR absorption band that could be used to distinguish each of the following pairs of compounds. Indicate the compound for which the band would be present.

a. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H$ and $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}CH_3$

b. $CH_3CH_2\overset{O}{\overset{\|}{C}}NH_2$ and $CH_3CH_2\overset{O}{\overset{\|}{C}}OCH_3$

c. $CH_3CH_2CH_2CH_2OH$ and $CH_3CH_2CH_2OCH_3$

d.  and 

e. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_3$ and $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}CH_3$

f. $CH_3CH_2CH{=}CHCH_3$ and $CH_3CH_2C{\equiv}CCH_3$

g. $CH_3CH_2C{\equiv}CH$ and $CH_3CH_2C{\equiv}CCH_3$

2. Indicate whether each of the following is true or false.

a. The O—H stretch of a concentrated solution of an alcohol occurs at a higher frequency than the O—H stretch of a dilute solution. T F

b. Light of 2 μm is of higher energy than light of 3 μm. T F

c. It takes more energy for a bending vibration than for a stretching vibration. T F

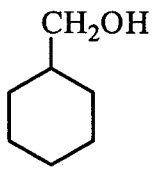
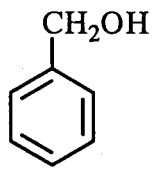
d. Propyne will not have an absorption band at 3100 cm^{-1} because there is no change in the dipole moment. T F

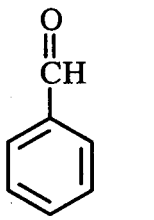
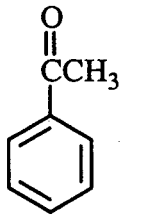
e. Light of 8 μm has the same energy as light of 1250 cm^{-1}. T F

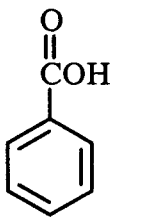
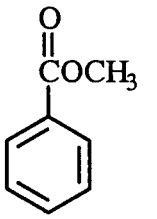
f. The M + 2 peak of an alkyl chloride is half the height of the M peak. T F

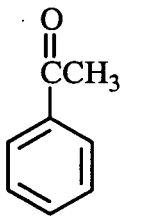
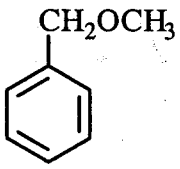
3. The major peaks shown in the mass spectrum of a tertiary alcohol are at m/z = 73, 87, 98, and 101. Identify the alcohol.

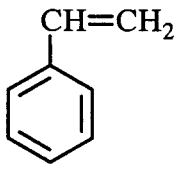
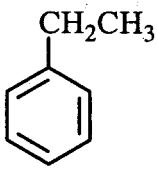
4. How could you distinguish between the IR spectra of the following compounds?

a.  and 

b.  and 

c.  and 

d.  and 

e.  and 

CHAPTER 14
NMR Spectroscopy

Important Terms

applied magnetic field — the externally applied magnetic field.

chemically equivalent protons — protons with the same connectivity relationship to the rest of the molecule.

chemical shift — location of a signal occurring in an NMR spectrum. It is measured downfield from a reference compound (most often TMS).

^{13}C NMR — nuclear magnetic resonance that shows carbon (^{13}C) nuclei.

COSY spectrum — a 2-D NMR spectrum showing ^{1}H-^{1}H correlations.

coupled protons — protons that split each other. Coupled protons have the same coupling constant.

coupling constant — the distance (in hertz) between two adjacent peaks of a split NMR signal.

DEPT ^{13}C NMR spectrum — a group of four ^{13}C NMR spectra that distinguish CH_3, CH_2, and CH groups.

diamagnetic anisotropy — the term used to describe the greater freedom of π electrons to move in response to a magnetic field as a consequence of their greater polarizability compared with σ electrons.

diamagnetic shielding — shielding by the local magnetic field that opposes the applied magnetic field.

2-D NMR — two-dimensional nuclear magnetic resonance.

doublet — an NMR signal split into two peaks.

doublet of doublets — an NMR signal split into four peaks of approximately equal height. Caused by splitting a signal into a doublet by one hydrogen and into another doublet by another (nonequivalent) hydrogen.

downfield — father to the left-hand side of the spectrum.

effective magnetic field — the magnetic field that a nucleus "senses" through the surrounding cloud of electrons.

Fourier transform NMR (FT-NMR) — a technique in which all the nuclei are excited simultaneously by an rf pulse, their relaxation monitored, and the data mathematically converted to a spectrum.

geminal coupling — the mutual splitting of two nonidentical protons bonded to the same carbon.

gyromagnetic ratio — the ratio of the magnetic moment of a rotating charged particle to its angular momentum.

COR spectrum — a 2-D NMR spectrum showing ^{13}C-^{1}H correlations.

MR — nuclear magnetic resonance that shows hydrogen nuclei.

-resolution NMR troscopy — NMR spectroscopy that uses a spectrometer with a high operating frequency.

g-range coupling — splitting of a proton by a proton more than 3 σ bonds away.

gnetic resonance aging (MRI) — NMR used in medicine. The difference in the way water is bound in different tissues produces the signal variation between organs as well as between healthy and diseased states.

ethine hydrogen — a tertiary hydrogen.

RI scanner — an NMR spectrometer used in medicine for whole-body NMR.

ultiplet — an NMR signal split by two non-equivalent sets of protons.

ultiplicity — the number of peaks in an NMR signal.

***N* + 1 rule** — an ^{1}H NMR signal for a hydrogen with N equivalent hydrogens bonded to an adjacent carbon is split into $N + 1$ peaks. A ^{13}C NMR signal for a carbon bonded to N hydrogens is split into $N + 1$ peaks.

NMR spectroscopy — the absorption of electromagnetic radiation to determine the structural features of an organic compound. In the case of ^{1}H NMR spectroscopy, it determines the carbon-hydrogen framework.

operating frequency — the frequency at which an NMR spectrometer operates.

proton exchange — the transfer of a proton from one molecule to another.

quartet — an NMR signal split into four peaks.

reference compound — a compound added to the sample whose NMR spectrum is to be taken. The position of the signals in the NMR spectrum are measured from the position of the signal given by the reference compound.

rf radiation — radiation in the radiofrequency region of the electromagnetic spectrum.

shielding — caused by electron donation to the environment of a proton. The electrons shield the proton from the full effect of the applied magnetic field. The more a proton is shielded, the farther to the right its signal appears in an NMR spectrum.

singlet — an unsplit NMR signal.

spin-coupled ^{13}C NMR spectrum — a ^{13}C NMR spectrum in which each signal for a carbon is split by the hydrogens bonded to that carbon.

spin-coupling — coupling between the carbon nucleus and certain nearby atoms.

spin-spin coupling	the splitting of a signal in an NMR spectrum described by the $N + 1$ rule.
α-spin state	nuclei in this spin state have their magnetic moments oriented in the same direction as the applied magnetic field.
β-spin state	nuclei in this spin state have their magnetic moments oriented opposite to the direction of the applied magnetic field.
splitting diagram (splitting tree)	a diagram that describes the splitting of a set of protons.
triplet	an NMR signal split into three peaks.
upfield	farther to the right-hand side of the spectrum.

Solutions to Problems

1.

$$\nu = \frac{\gamma}{2\pi} B_o$$

$$= \frac{26.75 \times 10^7 \text{ rad T}^{-1} \text{ sec}^{-1} \times 1.0 \text{ T}}{2(3.1416) \text{ rad}}$$

$$= 43 \times 10^6 \text{ sec}^{-1}$$

$$= 43 \times 10^6 \text{ Hz} = 43 \text{ MHz}$$

2. **a.**

$$\nu = \frac{\gamma}{2\pi} B_o$$

$$B_o = \frac{\nu \times 2\pi}{\gamma}$$

$$B_o = \frac{360 \times 10^6 \times 2(3.1416)}{26.75 \times 10^7}$$

$$B_o = \frac{226.2}{26.75}$$

$$B_o = 8.46 \text{ T}$$

b.

$$B_o = \frac{\nu \times 2\pi}{\gamma}$$

$$B_o = \frac{500 \times 10^6 \times 2(3.1416)}{26.75 \times 10^7}$$

$$B_o = \frac{314.2}{26.75}$$

$$B_o = 11.75 \text{ T}$$

From these calculations, you can see that the greater the operating frequency of the instrument (360 MHz versus 500 MHz), the more powerful the magnet (8.46 T versus 11.75 T) required to operate it.

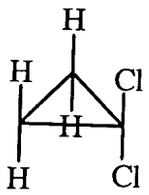
3.

a. 2	**e.** 3	**i.** 5	**m.** 3
b. 1	**f.** 4	**j.** 4	**n.** 1
c. 3	**g.** 3	**k.** 2	**o.** 3
d. 4	**h.** 3	**l.** 3	

4. **a** would give two signals, **b** would give one signal, and **c** would give three signals.

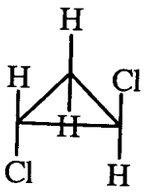
5.

#1



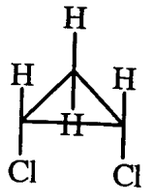
All the H's are equivalent.

#2



The H's attached to the front of the molecule are equivalent, and the methylene H's are equivalent.

#3



The H's attached to the fron of the molecule are equivale and the methylene H's are n equivalent.

6.

a. $\frac{600 \text{ Hz}}{300 \text{ MHz}} = 2.0 \text{ ppm}$

b. The answer would still be 2.0 ppm because the chemical shift is independent of the operatin frequency of the spectrometer.

c. $\frac{x \text{ Hz}}{100 \text{ MHz}} = 2.0 \text{ ppm}$

$x = 200$

200 Hz downfield from TMS

7. **a.** The chemical shift is independent of the operating frequency. Therefore, if the two signals differ by **1.5 ppm** in a 300-MHz spectrometer, they will still differ by **1.5 ppm** in a 100-M spectrometer.

b. $\frac{\text{Hz}}{\text{MHz}} = \text{ppm}$

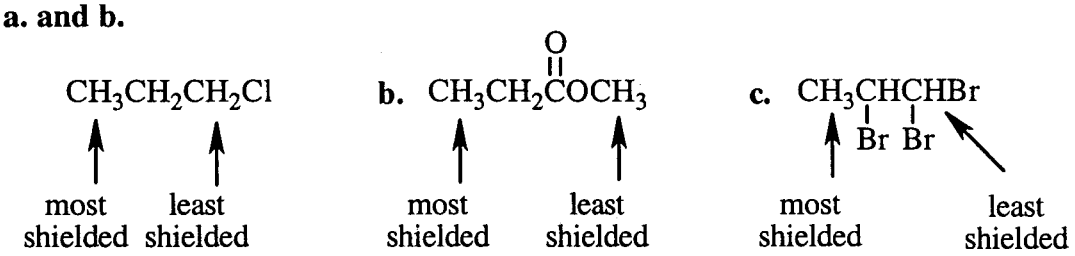
$\frac{90 \text{ Hz}}{300 \text{ MHz}} = 0.3 \text{ ppm}$

$\frac{x \text{ Hz}}{100 \text{ MHz}} = 0.3 \text{ ppm}$

$x = 30 \text{ Hz}$

8. Magnesium is less electronegative than silicon. (See Table 12.3 on page 467 of the text.) Therefore, the peak for $(CH_3)_2Mg$ would be upfield from the TMS peak.

a. and b.



10. The signal farthest downfield in both spectra is the signal for the hydrogens bonded to the carbon that is also bonded to the halogen. Because chlorine is more electronegative than iodine, the farthest downfield signal should be farther downfield in the ^{1}H NMR spectrum for 1-chloropropane than in the ^{1}H NMR spectrum for 1-iodopropane.
Therefore, the **first spectrum** in Figure 14.6 is the ^{1}H NMR spectrum for **1-iodopropane**, and the **second spectrum** in Figure 14.6 is ^{1}H the NMR spectrum for **1-chloropropane**.

11.

a. $CH_3\underline{C}H(Br)\underline{C}HBr$ **c.** $CH_3\underline{C}H_2CH(Cl)CH_3$ **e.** $CH_3CH_2CH{=}\underline{C}H_2$

b. $CH_3\underline{C}H(CH_3)O\underline{C}H_3$ **d.** $CH_3\underline{C}H(CH_3)C(=O)\underline{C}H_2CH_3$

12.

a. $CH_3CH_2\underline{C}H_2Cl$ **b.** $CH_3CH_2\underline{C}H(Cl)CH_3$ **c.** $CH_3CH(=O)\underline{C}H$

13.

a. $\overset{\mathbf{a}}{C}H_3\overset{\mathbf{b}}{C}H_2\overset{\mathbf{c}}{C}H(=O)$

b. $\overset{\mathbf{a}}{C}H_3\overset{\mathbf{c}}{C}H_2\overset{\mathbf{e}}{C}H(\overset{\mathbf{d}}{O}CH_3)\overset{\mathbf{b}}{C}H_3$

c. $\overset{\mathbf{b}}{Cl}\overset{\mathbf{a}}{C}H_2\overset{\mathbf{b}}{C}H_2Cl$

d. $\overset{\mathbf{a}}{C}H_3\overset{\mathbf{b}}{C}H_2\overset{\mathbf{c}}{C}H_2\overset{\mathbf{d}}{C}(=O)OCH_3$

e. $\overset{\mathbf{a}}{C}H_3\overset{\mathbf{b}}{C}H_2\overset{\mathbf{d}}{C}H(\overset{\mathbf{c}}{O}CH_3)\overset{\mathbf{b}}{C}H_2\overset{\mathbf{a}}{C}H_3$

f. $\overset{\mathbf{a}}{C}H_3\overset{\mathbf{c}}{C}H_2\overset{\mathbf{d}}{C}H_2\overset{\mathbf{e}}{O}\overset{\mathbf{b}}{C}H(\overset{\mathbf{b}}{C}H_3)CH_3$

g. $\overset{\mathbf{a}}{C}H_3\overset{\mathbf{b}}{C}H_2\overset{\mathbf{d}}{C}H_2\overset{\mathbf{c}}{C}(=O)CH_3$

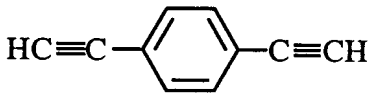
h. $\overset{\mathbf{a}}{C}H_3\overset{\mathbf{b}}{C}H(\overset{\mathbf{a}}{C}H_3)\overset{\mathbf{d}}{C}H_2OCH_3$

i. $\overset{\mathbf{a}}{C}H_3\overset{\mathbf{c}}{C}H(Cl)\overset{\mathbf{d}}{C}H\overset{\mathbf{b}}{C}H_3$ ($\overset{\mathbf{a}}{C}H_3$)

14. Each of the compounds would show two signals, but the ratio of the integrals for the two sign would be different for each of the compounds. The ratio of the integrals for the signals given l the first compound would be 2 : 9 (or 1 : 4.5), the ratio of the integrals for the signals given b the second compound would be 1 : 3, and the ratio of the integrals for the signals given by the third compound would be 1 : 2.

15. Solved in the text.

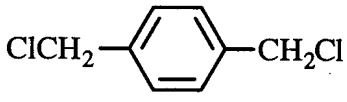
16. The heights of the integrals for the signals in the spectrum shown in Figure 14.8 are about 3.5 and 5.2. The ratio of the integrals, therefore, is 5.2/3.5 = 1.5. This matches the ratio of the integrals calculated for **1,4-dimethyl benzene**. (Later we will see that a signal at ~7 ppm is characteristic of a benzene ring.)



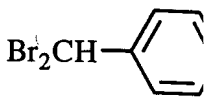
$\frac{2}{4} = 0.5$



$\frac{6}{4} = 1.5$



$\frac{4}{4} = 1.0$

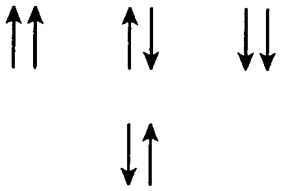


$\frac{2}{4} =$

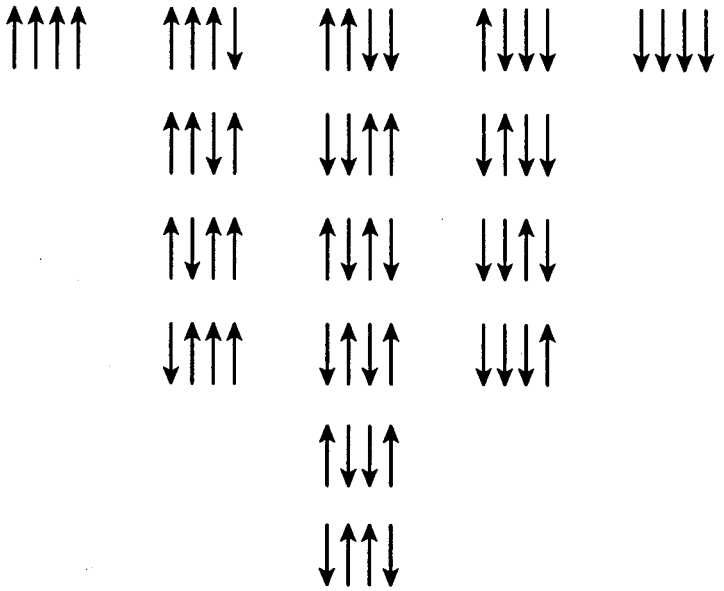
17. From the direction of the electron flow around the benzene ring pictured in Figure 14.9 on pa 541 of the text, you can see that the magnetic field induced in the region of the hydrogens tha protrude out from the compound shown in this problem is in the same direction as the applied magnetic field, whereas the magnetic field induced in the region of the hydrogens that protruc into the center of the compound is in the opposite direction of the applied magnetic field.

Thus, the signal at 9.25 ppm is for the hydrogens that protrude out because they need a smalle applied magnetic field to come into resonance due to the fact that the induced and applied magnetic fields are in the same direction. The signal at -2.88 ppm is for the hydrogens that protrude inward because a greater applied field is necessary to make up for the magnetic field that is induced in the opposite direction.

18. **a.** A triplet is caused by two equivalent protons on an adjacent carbon. The two protons can l aligned in three different ways: both with the field, one with the field and one is against th field, or both against the field. That is why the signal is a triplet. There is only one way to align two protons that are with the field or two protons that are against the field. However, there are two ways to align two protons if one is with and one against the field: with and against or against and with. Consequently, the peaks in a triplet have relative intensities of 1 : 2: 1.



b. A quintet is caused by four equivalent protons on adjacent carbons. The four protons can be aligned in five different ways. The following possible arrangements for the alignment of four protons explain why the relative intensities of a quintet are 1: 4 : 6 : 4 : 1.



CHB

19. The signal between 10-12 indicates that the compound is a carboxylic acid. From the molecular formula and the splitting patterns of the signals, the spectra can be identified as the ^{1}H NMR spectrum of:

a. $CH_3\underset{\displaystyle Cl}{\underset{|}{C}}HC(=O)OH$ **b.** $ClCH_2CH_2C(=O)OH$

20.

a. 3 signals

$ICH_2CH_2CH_2Br$

triplet triplet multiplet

b. 2 signals

$ClCH_2CH_2CH_2Cl$

triplet quintet

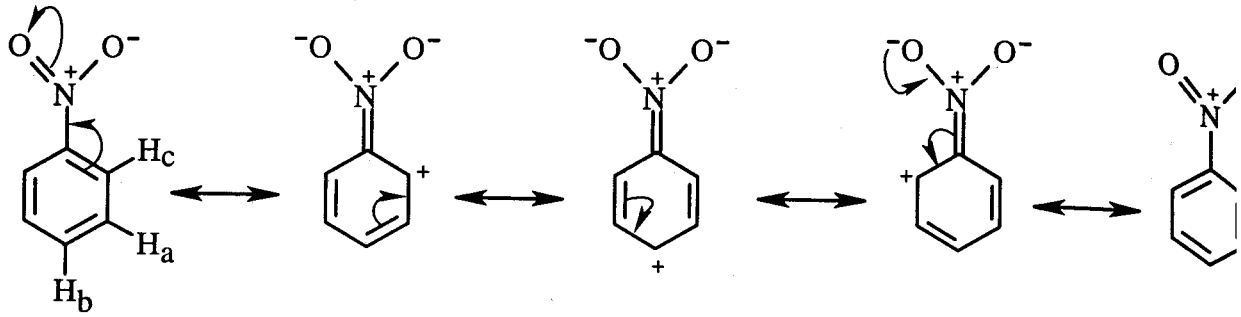
c. 3 signals

$ICH_2CH_2CHBr_2$

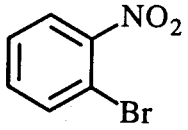
triplet triplet multiplet

21. The contributing resonance structures show that the nitro group's ability to withdraw electrons by resonance causes the C-2 and C-4 positions of the resonance hybrid (the actual structure of the compound) to have a partial positive charge. The nitro group's ability to withdraw electrons inductively (through the sigma bonds) causes the partial positive charge to be greater at C-2 than at C-4. Therefore, the H_c proton has the least electron dense (less shielded) environment, so its signal appears at the highest frequency. The C-3 position does not have a partial positive charge.

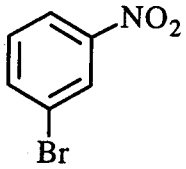
Therefore, the H_a proton has the most electron dense (most shielded) environment, so its signal appears at the lowest frequency.



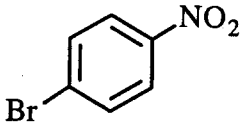
22. Each compound will have two doublets. In addition, **A** will have 2 doublet of doublets, **B** will have one doublet of doublets and a singlet, and **C** will have no other signals.



4 signals
(2 doublets and
2 doublet of doublets)

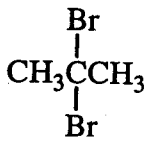


4 signals
(1 singlet,
2 doublets and,
1 doublet of doublets)

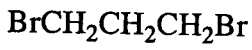


2 signals
(2 doublets)

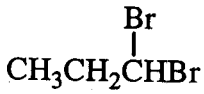
23.



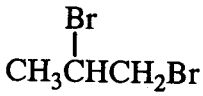
1 signal



2 signals

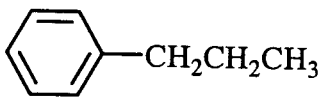


3 signals
2 triplets and a multiplet

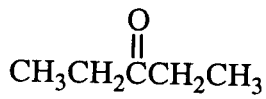


3 signals
2 doublets and a multiplet

24. **a.** The signal at ~7.2 ppm indicates the presence of a benzene ring. If the ring has a single substituent, it has a molecular formula of C_6H_5. Subtracting C_6H_5 from the molecular formula of the compound ($C_9H_{12} - C_6H_5$) gives a substituent with a molecular formula of C_3H_7. The triplet at ~0.9 ppm indicates a methyl group adjacent to a methylene group. The identical integration under the signals at 1.6 ppm and 2.6 ppm indicate two methylene groups. Thus, the compound is propyl benzene.

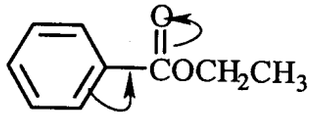


b. The triplet and quartet indicate a CH_3CH_2 group bonded to an atom that is not bonded to any hydrogens. The molecular formula of $C_5H_{10}O$ indicates that the compound is diethyl ketone.



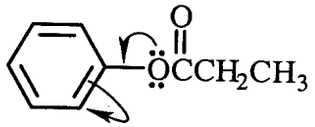
c. The signals between ~7-8 ppm indicate the presence of a benzene ring. The observation that there are 3 benzene rings signals indicates the compound has a mono-substituted benzene ring or a 1,3-disubstituted benzene ring. Since none of the 3 benzene ring signals is a singlet, we know that the compound has a mono-substituted benzene ring. Subtracting C_6H_5 from the molecular formula of the compound ($C_9H_{10}O_2 - C_6H_5$) shows that the substituent has a molecular formula of $C_3H_5O_2$.

The triplet and quartet suggest a CH_3CH_2 group. Therefore, we can conclude that the compound is one of the following.



A

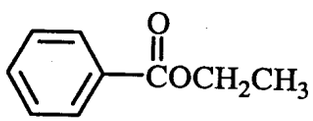
or



B

Compound **A** withdraws electrons from the benzene ring, whereas compound **B** donates electrons into the benzene ring. Because one of the peaks of the benzene ring signal is at a higher frequency (farther downfield) than usual (> 8 ppm) suggests that an electron-withdrawing substituent is present on the benzene ring.

This is confirmed by the signal for the CH_2 group at 3.8 ppm, indicating that the methylene group is adjacent to the electron-withdrawing oxygen. Thus, the compound is compound **A**.

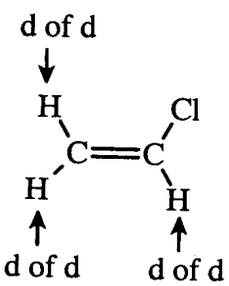


25.

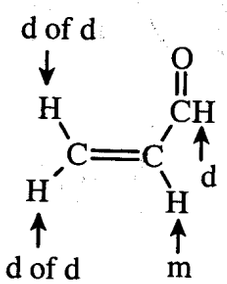
a. $CH_3\underset{\text{t}}{CH_2}\underset{\text{q}}{CH_2}CH_3$

b. $Br\underset{\text{s}}{CH_2}CH_2Br$

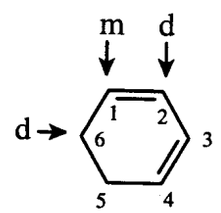
c.



d.



e.

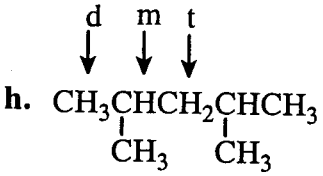


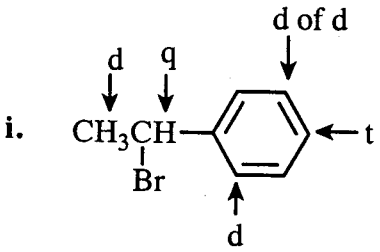
The H on C-2 will not be split by the H on C-3, since they are equivalent.

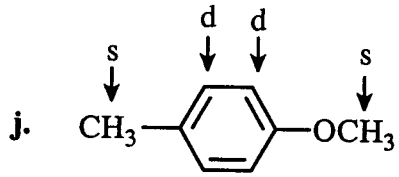
The H's on C-6 will not be split by the H's on C-5, since the H's on C-5 and C-6 are equivalent.

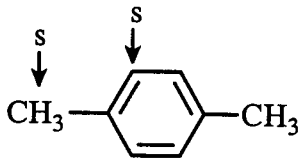
f. $CH_3\underset{\text{t}}{CH_2}\underset{\text{m}}{CH_2}\underset{\text{t}}{C}\underset{\text{s}}{CH_3}$ (O)

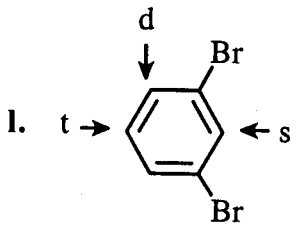
g. $CH_3CH_2\underset{\text{quin}}{\underset{|}{\underset{\text{Cl}}{CH}}}\underset{\text{m}}{CH_2}\underset{\text{t}}{CH_3}$

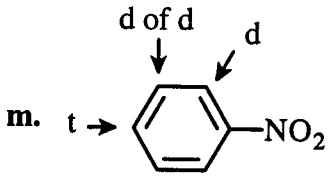
h. 

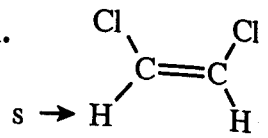
i. 

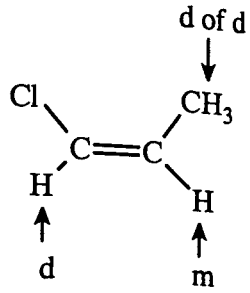
j. 

k. 

l. 

m. 

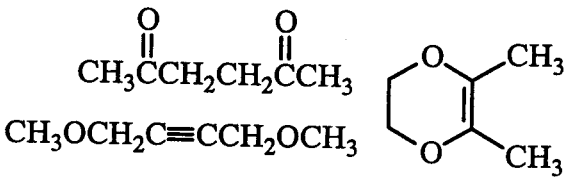
n. 

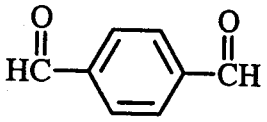
o. 

26.

a. $CH_3OCH_2CH_2OCH_3$

b. There are 3 possibilities.



c. 

27. Each spectrum is described going from left to right.

a. $BrCH_2CH_2CH_2CH_2Br$ triplet triplet $BrCH_2CH_2CH_2Br$ triplet quintet $BrCH_2CH_2Br$ singlet

b. two triplets (close to each other) singlet multiplet
(Appendix VI on page A-20 of the text indicates that a methylene adjacent to an RO and a methylene adjacent to a Br appear at about the same place.)

c. singlet (Equivalent H's do not split each other.)

d. quartet singlet triplet

e. three singlets

f. three doublets of doublets

g. quartet triplet

h. singlet quartet triplet

i. doublet multiplet doublet

j. triplet quintet

k. triplet doublet of doublets multiplet doublet

l. triplet singlet quintet

m. singlet (Equivalent H's do not split each other.)

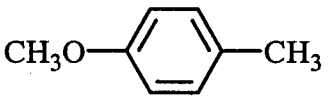
n. singlet (Equivalent H's do not split each other.)

o. singlet

28. There is no coupling between H_a and H_b because they are separated by four σ bonds.

There is no coupling between H_b and H_c because they are separated by four σ bonds and one π bond.

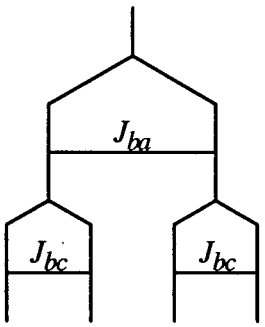
29. The IR spectrum indicates a benzene ring (1600 cm^{-1} and 1500^{-1}) with hydrogens on sp^2 carbons, and no carbonyl group. The absorption bands in the 1250^{-1} -1000^{-1} region suggests there are two
C-O single bonds, one with no double bond character and one with some double bond character. The two singlets in the ^1H NMR spectrum with about the same integration suggest two methyl groups, one of which is adjacent to an oxygen. That the benzene ring protons (6.7-7.1 ppm) consist of two doublets indicates a 1,4-disubstituted benzene ring.



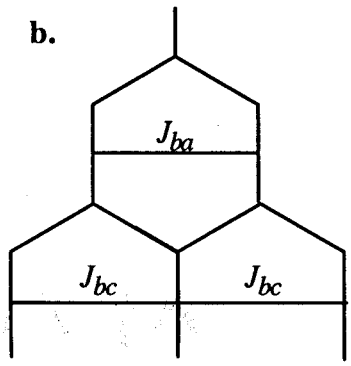
30. Solved in the text.

31.

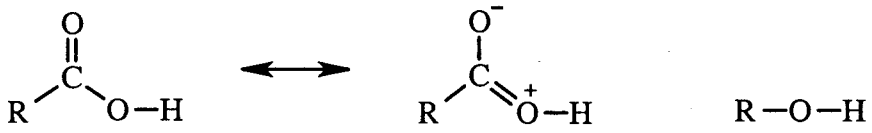
a.



b.

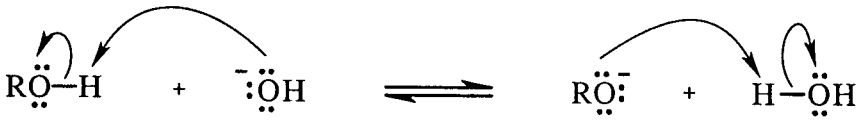


32. The H of a carboxylic acid is more deshielded than the H of an alcohol as a result of electron delocalization.

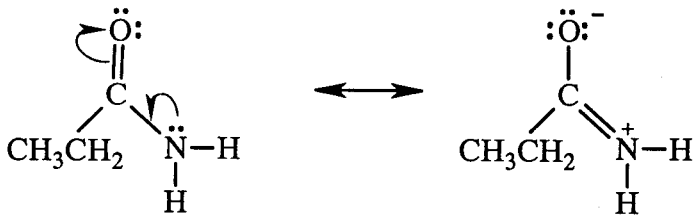


33. The greater the extent of hydrogen bonding, the greater the chemical shift. Therefore, the ^1H NMR spectrum of pure ethanol would have the signal for the OH proton at a greater chemical shift because it would be hydrogen bonded to a greater extent.

34.



35. Figure 14.29 is the ^1H NMR spectrum of propanamide. Notice that the signals for the N-H protons are unusually broad. Because of the partial double bond character of the C-N bond, the two N-H protons are not chemically equivalent. The quartet and triplet are characteristic of an ethyl group.



36. **a.**

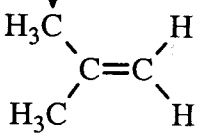
1. 3	**5.** 3	**8.** 3
2. 3	**6.** 3	**9.** 3
3. 3	**7.** 4	**10.** 2
4. 2		

An arrow is drawn to the carbon that gives the signal at the lowest frequency.

b.

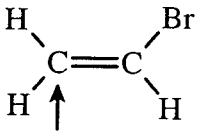
1. $CH_3CH_2CH_2Br$

2.



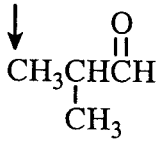
3. $CH_3CH_2OCH_3$

4.

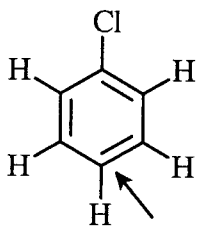


5. $CH_3CH_2COCH_3$

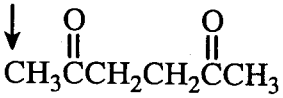
6.



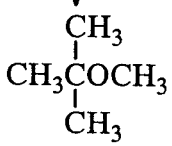
7.



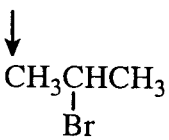
8.



9.



10.



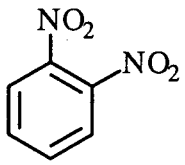
37. Each spectrum is described going from left to right.

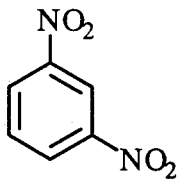
1. triplet triplet quartet

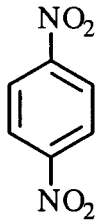
3. triplet quartet quartet

5. singlet quartet triplet quartet

38.

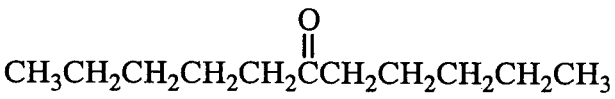




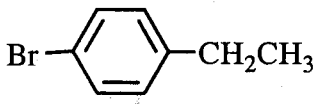


a. ^{1}H NMR	2 signals	3 signals	1 signal
b. ^{13}C NMR	3 signals	4 signals	2 signals

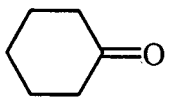
39. **a.** The signal at 210 is for a carbonyl carbon. There are ten other carbons in the compound and five other signals. That suggests the compound is a ketone with identical five-carbon alkyl groups.



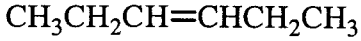
b. Because there are only four signals for the six carbons of the benzene ring, the compound must be a 1,4-disubstituted benzene.



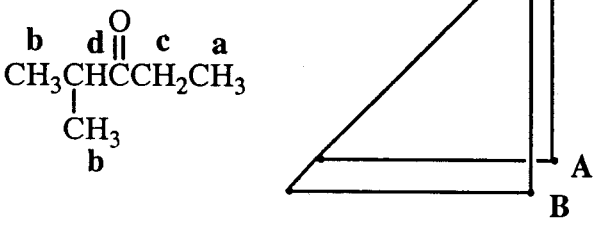
c. The signal at 212 is for a carbonyl carbon. There are five other carbons in the compound and three other signals. That suggests the compound is a cyclic ketone.



d. The molecular formula indicates the compound has one double bond. Each of the two sp^2 carbons must be bonded to the same groups because the six carbons only exhibit three signals. Whether the compound is *cis*-3-hexene or *trans*-3-hexene cannot be determined from the spectrum. The coupling constants in an ^{1}H NMR spectrum could distinguish the compounds because the coupling constant for trans protons is greater than the coupling constant for cis protons.



40.



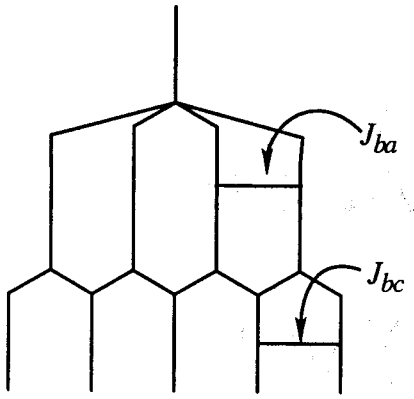
Point **A** shows that the "**a**" protons are split by the "**c**" protons.
Point **B** shows that the "**b**" protons are split by the "**d**" protons.

41.

	a.		**b.**	
1.	5	**4.** 2	7	**4.** 2
2.	5	**5.** 3	7	**5.** 2
3.	4	**6.** 3	5	**6.** 4

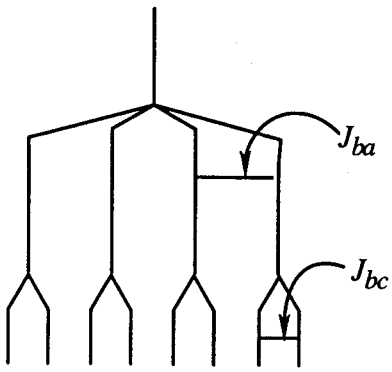
42.

a.



5 peaks

b.



8 peaks

43.

a. d septet

a b

CH_3CHNO_2

CH_3

a

d. t m t s

a b c d

$CH_3CH_2CH_2CCH_2Cl$

O

b. $CH_3CH_2CH_2OCH_3$ (t, m, t, s; a, b, d, c)

c. $CH_3CHCCH_2CH_2CH_3$ (d, septet, t, m, t; b, e, d, c, a; CH_3 b)

e. $ClCH_2CCHCl_2$ (s, s; a, b, c; CH_3 a)

f. $ClCH_2CH_2CH_2CH_2CH_2Cl$ (t, m, quintet; c, b, a, b, a)

44. **a.** The spectrum must be that of **2-bromopropane** because the NMR spectrum has two signals and the signal farthest upfield is a doublet.

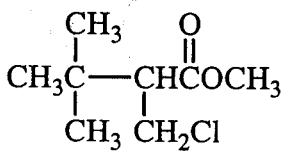
b. The spectrum must be that of **1-nitropropane** because the NMR spectrum has three signals and the signals farthest upfield and farthest downfield are triplets.

c. The spectrum must be that of **ethyl methyl ketone** because the NMR spectrum has three signals and the signals are a triplet, a singlet, and a quartet.

45. By dividing the value of the integration steps by the smallest one, the ratios of the hydrogens are found to be 3 : 2 : 1 : 9.

$$\frac{40.5}{13} = 3.1 \qquad \frac{27}{13} = 2.1 \qquad \frac{13}{13} = 1 \qquad \frac{118}{13} = 9.1$$

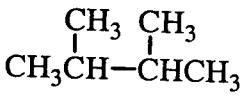
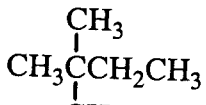
Assuming that the ratios are given in the downfield to upfield direction, a possible compound could be the following ester.



46.

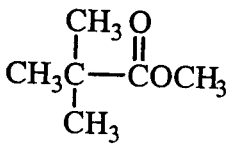
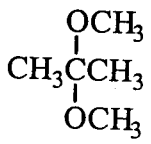
a. $CH_3CH_2CH_2OCH_3$ (4 signals) and $CH_3CH_2OCH_2CH_3$ (2 signals)

b. $BrCH_2CH_2CH_2Br$ (2 signals) and $BrCH_2CH_2CH_2NO_2$ (3 signals)

c.  and 

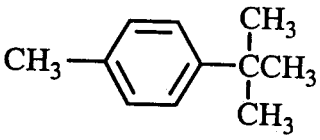
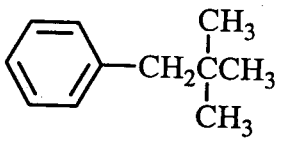
2 signals

3 signals

d.  and 

2 signals with integration 3 : 1

2 signals with integration 1 : 1

e.  and 

3 signals with integration 9 : 4 : 3

3 signals with integration 9 : 5 : 2

f.  and 

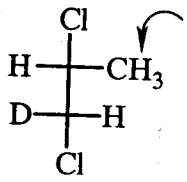
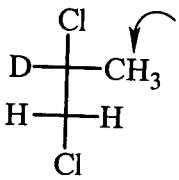
2 signals

3 signals

g. $CH_3CHClCH_3$ and $CH_3CDClCH_3$

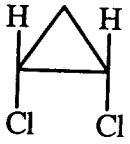
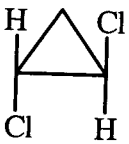
2 signals

1 signal

h.  and 

signal farthest upfield = doublet

signal farthest upfield = singlet

i.  and 

3 signals

2 signals

47. **a.** Chemical shift in ppm is independent of the operating frequency.

b. Chemical shift in hertz is proportional to the operating frequency.

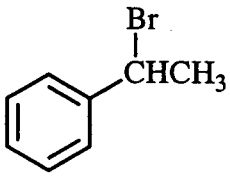
c. The coupling constant is independent of the operating frequency.

d. The frequency required for NMR is lower than that required for IR, which is lower than that required for UV/Vis.

48.

a. $CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HBr$ **b.** $CH_3CH_2CH_2CH_2Br$ **c.** $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2Br$

49.

a. $CH_3\underset{\displaystyle Br}{\underset{|}{C}}CH_2Br$ **b.**  **c.** $CH_3CH_2\overset{\displaystyle O}{\overset{\|}{C}}OCH_2CH_3$

50. The singlet at 210 indicates a carbonyl group. The splitting of the other two signals indicates an isopropyl group. The molecular formula indicates that it must have two isopropyl groups.

$$CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}H\overset{\displaystyle O}{\overset{\|}{C}}\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_3$$

51.

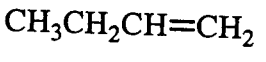
$CH_3\underset{\displaystyle Cl}{\underset{|}{C}}CH_3$
tert-butyl chloride
Compound A

$CH_3\underset{\displaystyle Cl}{\underset{|}{C}}HCH_2CH_3$
sec-butyl chloride
Compound B

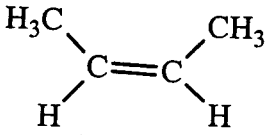
52.

a. $CH_3\overset{\displaystyle O}{\overset{\|}{C}}CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}CH_3$ **b.** $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}H\overset{\displaystyle O}{\overset{\|}{C}}CH_2CH_2CH_3$ **c.** $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}H\overset{\displaystyle O}{\overset{\|}{C}}\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_3$

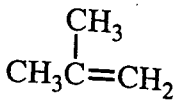
53.



1-butene



cis-2-butene

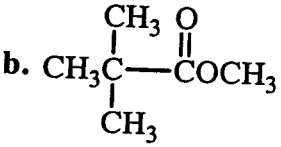


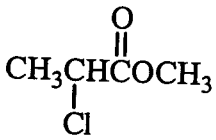
2-methylpropene

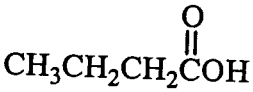
It would be better to use ^{13}C NMR because you would only have to look at the number of signals in each spectrum: 1-butene will show four signals, *cis*-2-butene will show two signals, and 2-methylpropene will show three signals. (In the ^{1}H NMR spectrum, 1-butene will show four signals, and *cis*-2-butene and 2-methylpropene will both show two signals.)

54.

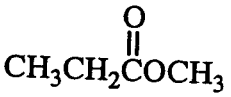
a. $CH_3CH_2CH_2CH_2OCH_3$

b. 

c. 

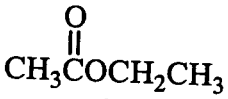
d. 

55.



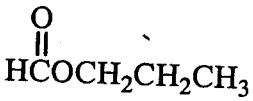
A

3 signals
singlet, quartet, triplet
(singlet farthest downfield)



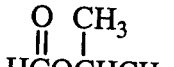
B

3 signals
singlet, quartet, triplet
(quartet farthest downfield)



C

4 signals
singlet, triplet
multiplet, triplet



D

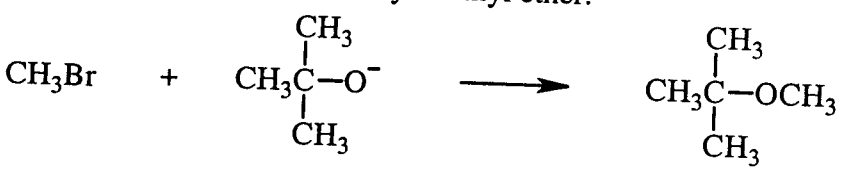
3 signals
singlet, septet
doublet

C can be distinguished from **A**, **B**, and **D** because **C** has 4 signals and the others have 3 signals.

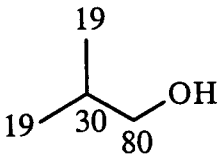
D can be distinguished from **A** and **B** because the 3 signals of **D** are a singlet, a septet, and a doublet, whereas the 3 signals of **A** and **B** are a singlet, a quartet, and a triplet.

A and **B** can be distinguished because the signal farthest downfield in **A** is a singlet, whereas the signal farthest downfield in **B** is a quartet.

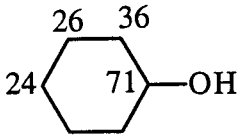
56. It is the ^{1}H NMR spectrum of *tert*-butyl methyl ether.



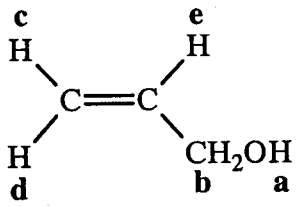
a.



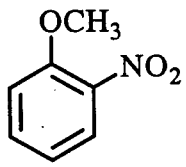
b.



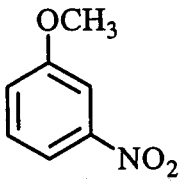
58. The broad signal at ~2.9 ppm is for the H_a proton that is bonded to the oxygen. The signal for the H_b protons is split into a doublet by the H_e proton. The H_c proton and the H_d are each split by the H_e proton; the coupling constant is greater for the trans protons. The H_e proton is split by the H_b protons and by the H_c proton and the H_c protons.



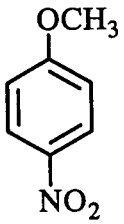
59. Each compound will have a singlet for the methoxy substituent and two doublets. In addition, **A** will have 2 doublet of doublets, **B** will have one doublet of doublets and a second singlet, and **C** will have no other signals.



5 signals
(1 singlet,
2 doublets and
2 doublet of doublets)

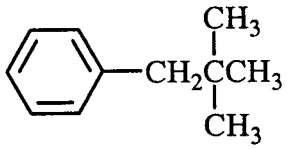


5 signals
(2 singlets,
2 doublets and,
1 doublet of doublets)



3 signals
(1 singlet and
2 doublets)

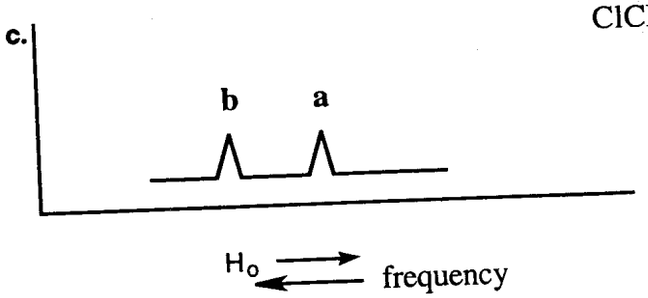
60. **a.** The signals at ~7.2 ppm indicate that the compounds whose spectra are shown in **a** and **b** both contain a benzene ring. From the molecular formula, you know that there are five additional carbons in **a**, and the hydrogens on these carbons must all be accounted for by two singlets with integral ratios of ~ 1 : 4.5, indicating that the compound is **2,2-dimethyl-1-phenylpropane**.



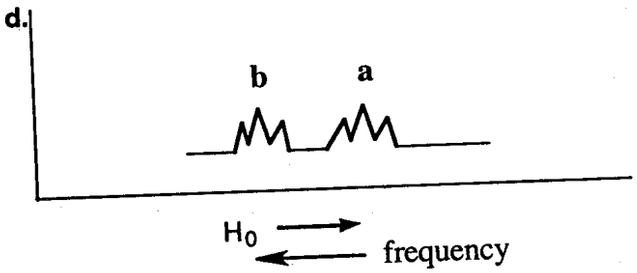
2,2-dimethyl-1-phenylpropane

$\overset{\mathbf{a}\quad\mathbf{b}}{ClCH_2CH_2OH}$

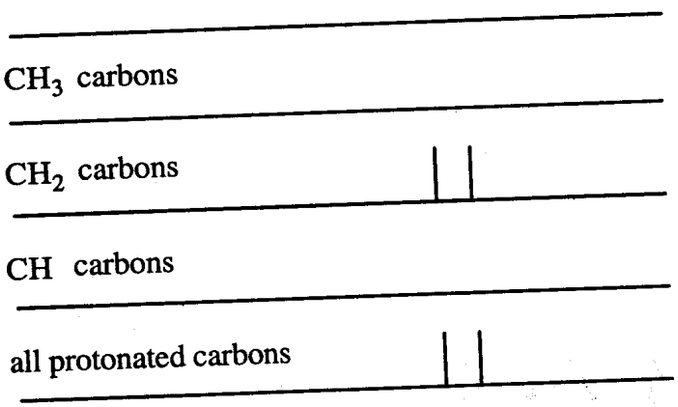
c.



d.



e.

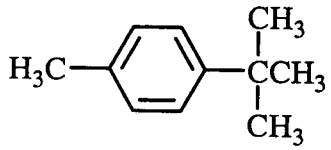


63. If addition of HBr to propene follows the rule that says the electrophile adds to the sp^2 carbon that is bonded to the greater number of hydrogens, the product of the reaction will give an NMR spectrum with two signals (a doublet and a septet). If addition of HBr does not follow the rule, the product will give an NMR spectrum with three signals (two triplets and a multiplet).

$$CH_3CH{=}CH_2 + HBr \longrightarrow \underset{\text{follows the rule}}{\overset{\quad\quad Br}{\overset{\quad\quad |}{CH_3CHCH_3}}} \qquad \underset{\text{does not follow the rule}}{CH_3CH_2CH_2Br}$$

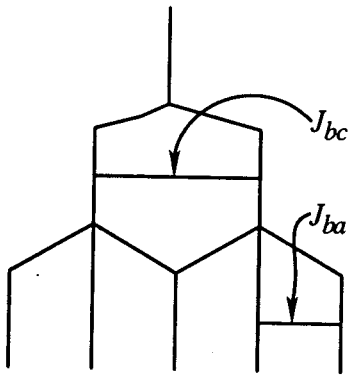
2 signals **3 signals**

b. The two singlets have integral ratios of ~ 1 : 3, indicating a methyl substituent and a *tert*-butyl substituent. The signals at ~7.1 and ~7.3 ppm indicate that the benzene ring has two kinds of hydrogens. Thus, the compound is **4-methyl-1-*tert*-butylbenzene**.



4-methyl-1-*tert*-butylbenzene

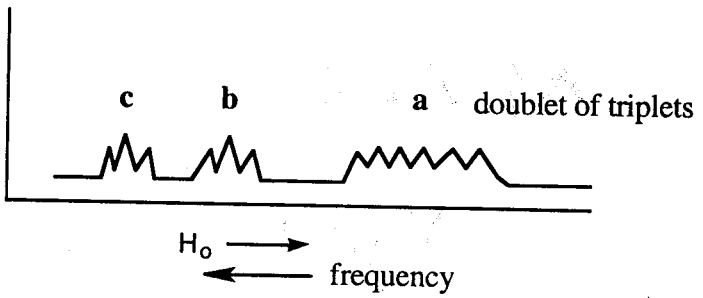
61.



5 signals

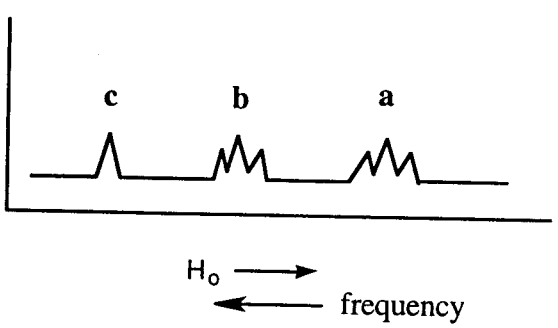
62.

a.



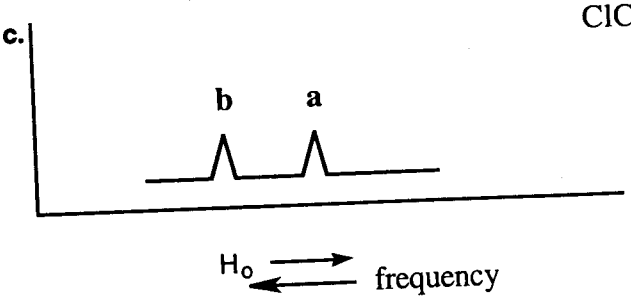
b a c
$ClCH_2CH_2OH$

b.

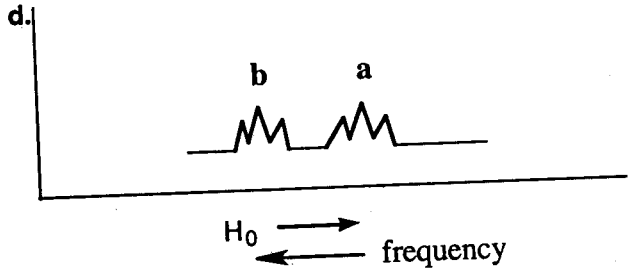


$\overset{a}{Cl}CH_2\overset{b}{C}H_2OH$

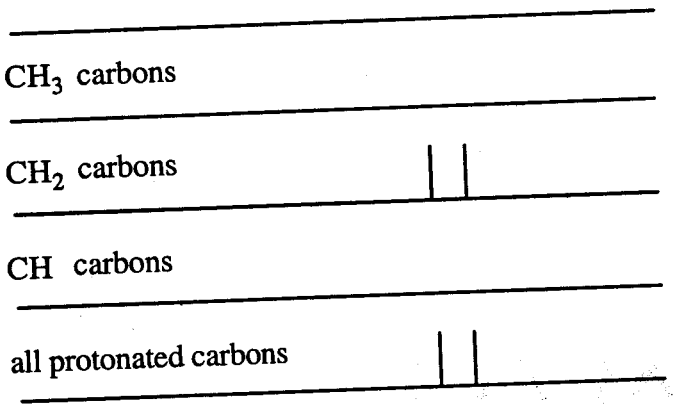
c.



d.



e.

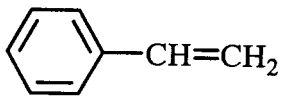


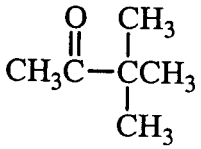
63. If addition of HBr to propene follows the rule that says the electrophile adds to the sp^2 carbon that is bonded to the greater number of hydrogens, the product of the reaction will give an NMR spectrum with two signals (a doublet and a septet). If addition of HBr does not follow the rule, the product will give an NMR spectrum with three signals (two triplets and a multiplet).

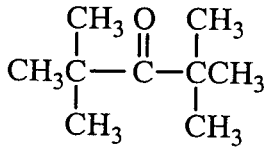
$$CH_3CH{=}CH_2 + HBr \longrightarrow \underset{\text{follows the rule}}{\overset{Br}{\overset{|}{CH_3CHCH_3}}} \qquad \underset{\text{does not follow the rule}}{CH_3CH_2CH_2Br}$$

2 signals **3 signals**

64.

a. 

b. 

c. 

d. $CH_2{=}CHOCH_2CH_3$

65. Methyl bromide gives a signal at 2.7 ppm for its three methyl protons, and 2-bromo-2-methylpropane gives a signal at 1.8 ppm for its nine methyl protons. If equal amounts of each were present in solution, the ratio of the hydrogens (and, therefore, the ratio of the relative integrals) would be 3 : 1. Because the relative integrals are 1 : 6, there must be an 18-fold greater concentration of methyl bromide in the mixture.

$$\frac{CH_3CCH_3 \\ | \\ Br}{CH_3Br} = \frac{3}{1} \times \frac{1}{18} = \frac{1}{6}$$

66. Using the formula given on page 528 of the text:

$$\Delta E = h\nu = \frac{h\gamma}{2\pi} B_o$$

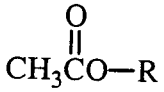
Given: Planck's constant = h = 6.626×10^{-34} Js (page 140 in the text)
1 cal = 4.184 J (page 127 in the text)
60 MHz = 1.4092 T (page 528 in the text)
γ for ^1H = 2.675×10^8 T^{-1} s^{-1}

$$\Delta E = \frac{h\gamma}{2\pi} B_o$$

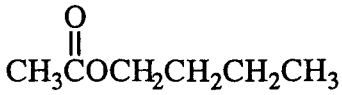
$$= \frac{6.626 \times 10^{-34} \text{ Js} \times 2.675 \times 10^8 \text{ T}^{-1} \text{ s}^{-1}}{2\,(3.1416)} \times 1.4092 \text{ T} \times \frac{1 \text{ cal}}{4.184 \text{ J}}$$

$$= 9.50 \times 10^{-27} \text{ cal}$$

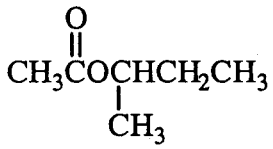
67. All four spectra show a singlet at ~2.0 ppm suggesting they are all esters with a methyl group attached to the carbonyl group. So now the problem becomes determining the nature of the group attached to the oxygen.



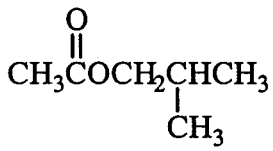
a. The signal farthest downfield in the first spectrum is a triplet, indicating that the carbon attached to the oxygen is bonded to a CH_2 group. The signal farthest upfield is also a triplet, indicating that it too is attached to a CH_2 group. The presence of two multiplets confirms the structure.



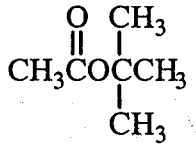
b. The signal farthest downfield in the second spectrum is a multiplet, indicating that the carbon attached to the oxygen is attached to two non-equivalent carbons bonded to hydrogens. The signal farthest upfield is a triplet, indicating that it is attached to a CH_2 group. The doublet at ~1.2 ppm is a methyl group attached to a carbon bonded to a one hydrogen.



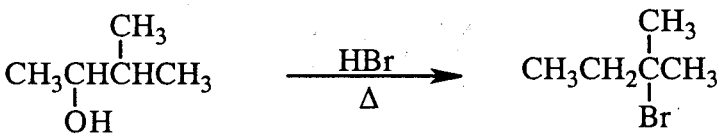
c. The signal farthest downfield and the signal farthest upfield in the third spectrum are doublets, indicating that the carbon attached to the oxygen and the terminal carbon of the group are both attached to a CH group.



d. The group attached to the oxygen in the fourth spectrum has only one kind of hydrogen.

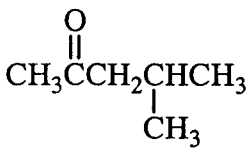


68.

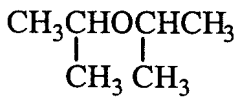


compound A compound B

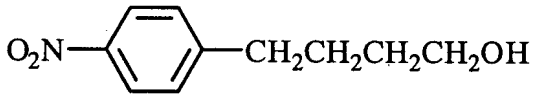
69. **a.** The IR spectrum indicates that the compound is a ketone. The doublet in the NMR spectrum at ~0.9 ppm suggests an isopropyl group. There is a singlet at ~2.1 ppm on top of a multiplet, and a doublet at ~2.2 ppm. Knowing that the compound contains 6 carbons helps in the identification.



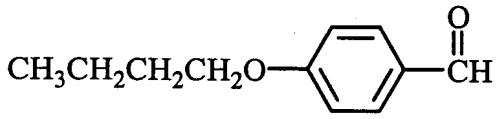
b. The IR spectrum indicates that this oxygen-containing compound is not a carbonyl compound or an alcohol; the absorption band at ~1000 cm^{-1} suggests that it is an ether. The doublet at ~1.1 ppm suggests an isopropyl group. Since there is only one other signal in the NMR spectrum, the compound must be a symmetrical ether. The compound is diisopropyl ether.



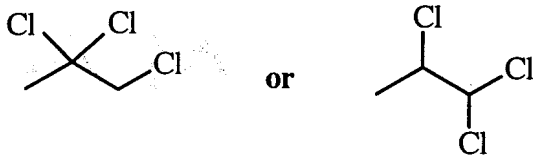
c. The absorption band at ~3400 cm^{-1} indicates an alcohol. The two signals at 7.3 and 8.1 ppm indicate a 1,4-substituted benzene ring with a strongly electron-withdrawing substituent. The two triplets indicate that the four-carbon substituent is not branched.



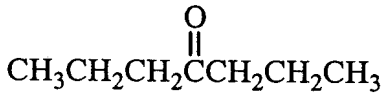
d. The absorption bands at ~1700 cm^{-1} and 2700 cm^{-1} indicate the compound is an aldehyde. The two doublets at ~7.0 and 7.8 ppm indicate a 1,4-disubstituted benzene ring. That none of the NMR signals is a doublet suggests that the aldehyde group is attached directly to the benzene ring. The two triplets and two multiplets indicate an unbranched substituent. The triplet at ~ 4.0 ppm indicates that the group giving this signal is next to an electron-withdrawing group.



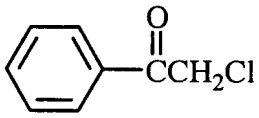
70. Since each of the three carbons is in a different environment, the compound must be 1,1,2-trichloropropane.



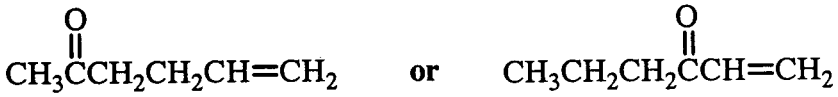
71. **a.** The IR spectrum indicates it is a ketone; the mass spectrum tells you it is a ketone with 7 carbons. The fact that there are only 3 signals in the NMR spectrum suggests it is a symmetrical ketone. The splitting pattern confirms the structure.



b. The M + 2 peak tells you the compound contains chlorine; the IR spectrum indicates it is a ketone; the NMR spectrum indicates it has a monosubstituted benzene ring. The singlet at ~4.7 indicates that the group giving this signal is in a strongly electron-withdrawing environment. The integration tells you that the two kinds of hydrogens are in a 2.5 : 1 ratio.

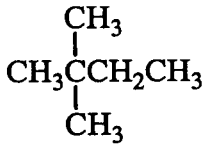


72. The DEPT ^{13}C NMR spectrum indicates that the compound has five carbons bonded to hydrogens. The molecular formula tells us that the compound has six carbons and an oxygen. The sixth carbon is not bonded to a hydrogen, suggesting a ketone. The following ketone has the single CH_3 group, the single CH group, and the three CH_2 groups indicated by the DEPT spectrum.



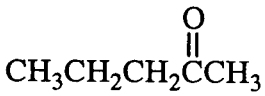
or

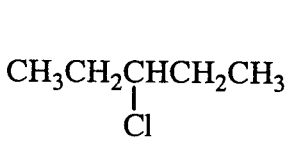
73. There is a singlet for the three methyl groups that are attached to the quaternary carbon. The singlet is on top of the triplet for the other methyl group. The methylene group shows the expected quartet.

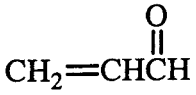


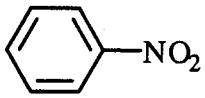
Chapter 14 Practice Test

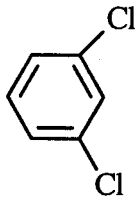
1. How many signals would you expect to see in the ^1H NMR spectrum of each of the following compounds?

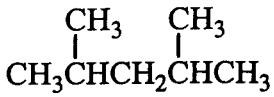




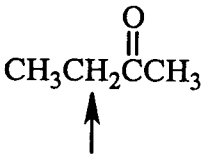


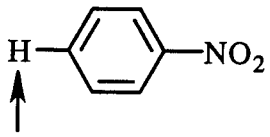


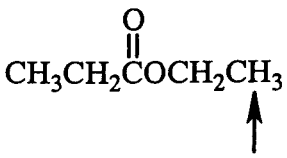


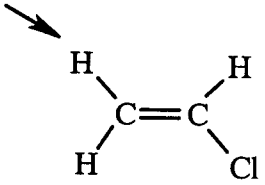


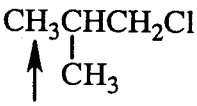
2. Indicate the multiplicity of each of the indicated sets of protons. (i.e., indicate whether it is a singlet, doublet, triplet, quartet, quintet, multiplet, or doublet of doublets.)

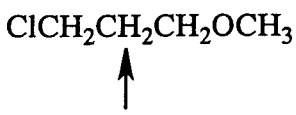


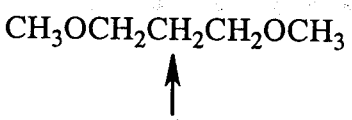


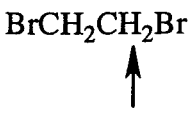






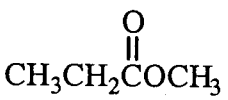






3. How could you distinguish the following compounds using ^1H NMR spectroscopy?





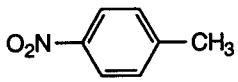


4. Indicate whether each of the following statements is true or false:

a. The signals on the right of an NMR spectrum are deshielded compared to the signals on the left. T F

b. Dimethyl ketone has the same number of signals in its ^{1}H NMR spectrum as in its ^{13}C NMR spectrum. T F

c. In the ^{1}H NMR spectrum of the compound shown below, the lowest frequency signal (the one farthest upfield is a singlet and the signal farthest downfield is a doublet. T F



d. The greater the frequency of the signal, the greater its chemical shift in ppm. T F

5. For each compound:

a. Indicate the number of signals you would expect to see in ^{1}H NMR spectrum.
b. Indicate the hydrogen or set of hydrogens that would give the highest frequency (farthest downfield) signal.
c. Indicate the multiplicity of that signal.
d. Indicate the relative integrals going from left to right across the spectrum.

a. $CH_3CH_2CH_2Cl$ **b.** $CH_3CH_2\overset{\overset{O}{\|}}{C}OCH_3$ **c.** $CH_3\underset{\underset{Br}{|}}{C}HCH_3$

6. For each compound of Problem 5:

a. Indicate the number of signals you would expect to see in its proton-decoupled ^{13}C NMR spectrum.
b. Indicate the carbon that would give the highest frequency (farthest downfield) signal.
c. Indicate the multiplicity of that signal in a spin-coupled ^{13}C NMR spectrum.

CHAPTER 15
Aromaticity • Reactions of Benzene

Important Terms

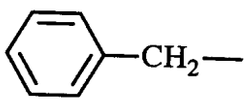
aliphatic compound — an organic compound with a higher hydrogen-to-carbon ratio than an aromatic compound.

annulene — a monocyclic hydrocarbon with alternating double and single bonds.

antiaromatic compound — a cyclic and planar compound with an uninterrupted cloud of electrons containing an even number of pairs of π electrons.

aromatic compound — a cyclic and planar compound with an uninterrupted cloud of electrons containing an odd number of pairs of π electrons.

benzyl group



Clemmensen reduction — a reaction that reduces the carbonyl group of a ketone to a methylene group using Zn(Hg)/HCl.

electrophilic aromatic substitution reaction — a reaction in which an electrophile substitutes for a hydrogen of an aromatic ring.

Friedel-Crafts acylation — an electrophilic substitution reaction that puts an acyl group on a benzene ring.

Friedel-Crafts alkylation — an electrophilic substitution reaction that puts an alkyl group on a benzene ring.

Gatterman-Koch reaction — a reaction that uses a high-pressure mixture of carbon monoxide and HCl to form benzaldehyde.

halogenation — reaction with halogen (Br_2, Cl_2).

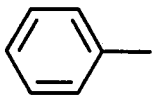
heteroatom — an atom other than a carbon atom or a hydrogen atom.

heterocyclic compound (heterocycle) — a cyclic compound in which one or more of the atoms of the ring are heteroatoms.

Hückel's rule or the $4n + 2$ rule — the number of π electrons in a cyclic uninterrupted π cloud that a cyclic and planar compound must have in order to be aromatic.

nitration — substitution of a nitro group (NO_2) for a hydrogen of a benzene ring.

henyl group



C_6H_5—

principle of microscopic reversibility states that the mechanism for a reaction in the forward direction has the same intermediates and the same transition states as the mechanism for the reaction in the reverse direction.

sulfonation substitution of a hydrogen of a benzene ring with a sulfonic acid group (SO_3H).

Wolff-Kishner reduction a reaction that reduces the carbonyl group of a ketone to a methylene group using NH_2NH_2/HO^-.

Solutions to Problems

1. **a.** In the case of 9 pairs of π electrons, there are 18 electrons. Therefore, $4n + 2 = 18$ and $n = 4$.

b. Because it has an odd number of pairs of π electrons, it will be aromatic if it is cyclic, planar, and if every atom in the ring has a *p* orbital.

2. **b, c, e,** and **g** are aromatic.

b is aromatic, because it is cyclic, planar, every atom in the ring has a *p* orbital, and it has seven pairs of π electrons.

c is aromatic, because it is cyclic, planar, every atom in the ring has a *p* orbital, and it has three pairs of π electrons.

e is aromatic, because it is cyclic, planar, every atom in the ring has a *p* orbital, and it has nine pairs of π electrons.

g is aromatic, because it is cyclic, planar, every atom in the ring has a *p* orbital, and it has five pairs of π electrons.

a is not aromatic, because it has two pairs of π electrons.

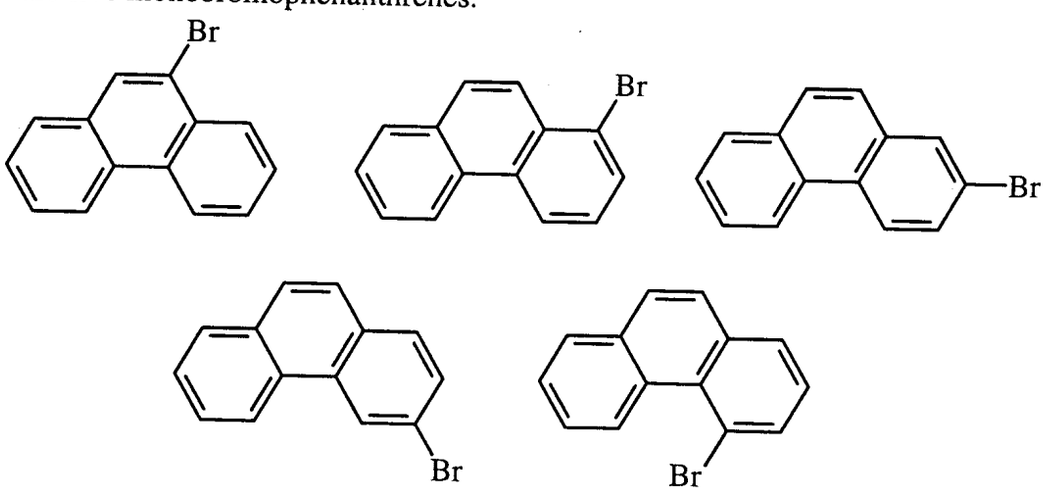
d is not aromatic, because it has two pairs of π electrons and every atom in the ring does not have a *p* orbital

f is not aromatic, because it has two pairs of π electrons and every atom in the ring does not have a *p* orbital

h is not aromatic, because it is not cyclic.

3. **a.** Solved in the text.

b. There are five monobromophenanthrenes.

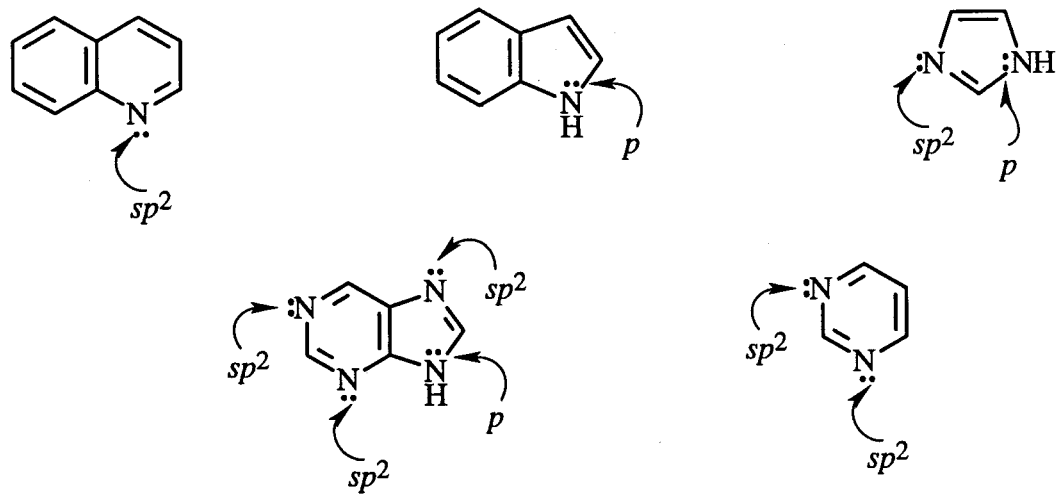


4. To be aromatic, a compound must be cyclic and planar, every atom in the ring must have a *p* orbital, and the π cloud must contain an odd number of pairs of π electrons.

[10]-Annulene is cyclic, every atom in the ring has a *p* orbital, and it has the correct number of π electrons to be aromatic (five pairs). Knowing it is not aromatic, we can conclude that it is not planar.

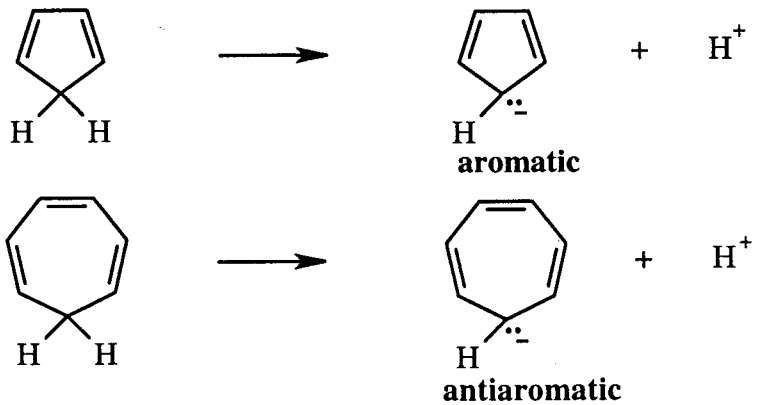
[12]-Annulene has an even number of pairs of π electrons (six pairs) in its π cloud, so it cannot be aromatic.

5.



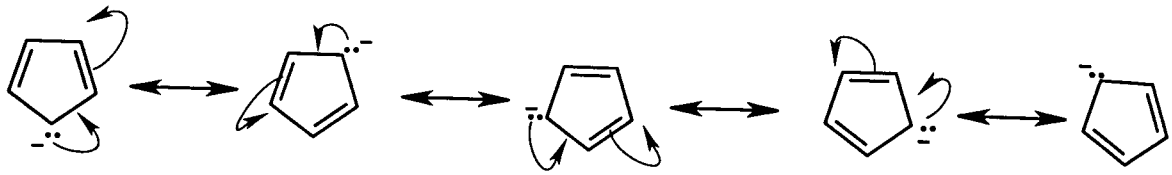
6. **a.** The nitrogen atom (the atom at the bottom of the epm) in pyrrole has a partial positive charge because it donates electrons by resonance into the ring.
b. The nitrogen atom (the atom at the bottom of the epm) in pyridine has is the most electronegative atom in the molecule.
c. The relatively electronegative nitrogen atom in pyridine withdraws electrons from the ring.

7. Cyclopentadiene has a lower pK_a. When cyclopentadiene loses a proton, a relatively stable aromatic compound is formed. When cycloheptatriene loses a proton, an unstable antiaromatic compound is formed (Section 15.5). It is, therefore, easier to lose a proton from cyclopentadiene.

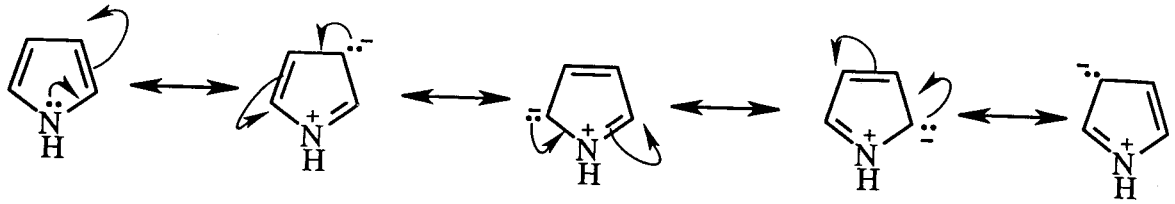


8.

a. **1.** Notice that each resonance contributor has a charge of −1.



2. Notice that each resonance contributor has a net charge of 0.

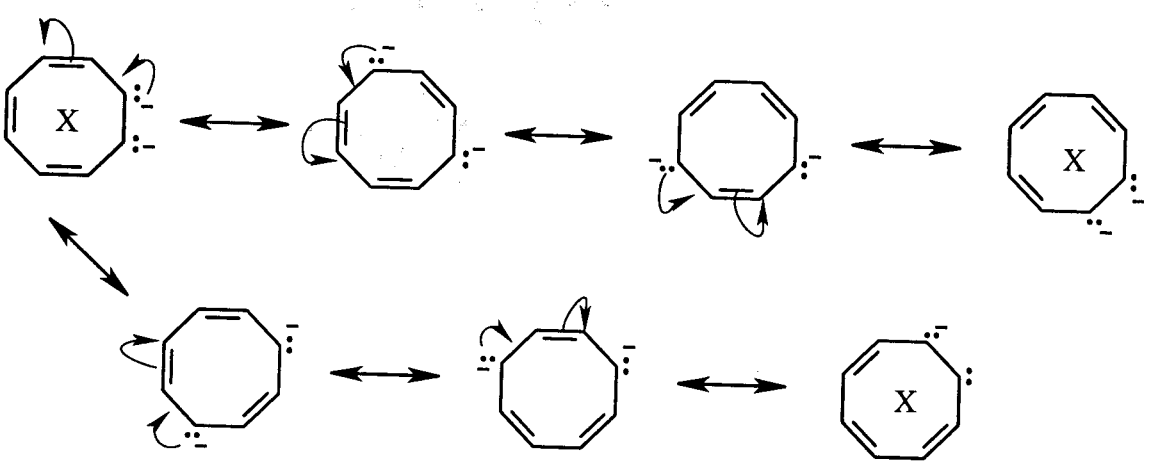


b. **1.** five ring atoms

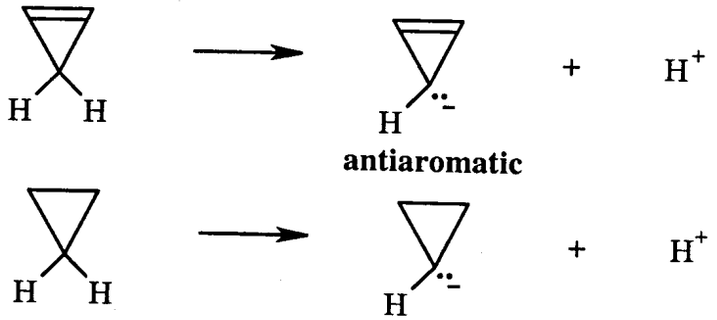
2. four ring atoms

9. **a.** The three resonance contributors marked with an X are the least stable because in these contributors the two negative charges are on adjacent carbons.

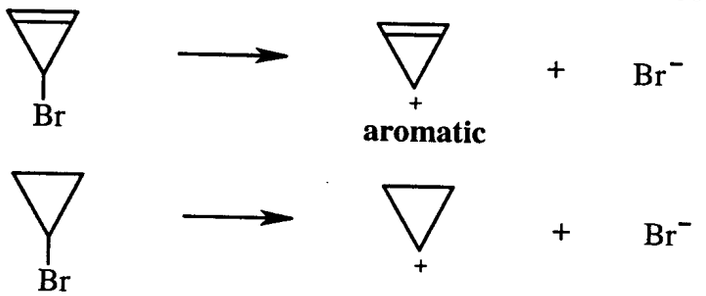
b. Because these contributors are the least stable, they make the smallest contribution to the hybrid.



10. **a.** Cyclopropane has a lower pK_a because an antiaromatic compound is formed when cyclopropene loses a proton.



b. 3-Bromocyclopropene is more soluble in water, because it is more apt to ionize since heterolytic cleavage of its carbon-bromine bond forms an aromatic compound.



11. **a** is antiaromatic because it is cyclic, planar, every atom in the ring has a *p* orbital, and it has two pairs of π electrons.

When you did Problem 2, you found that **b**, **c**, **e**, and **g** are aromatic.

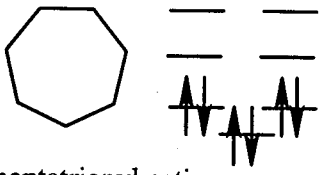
d, **f**, and **h** are neither aromatic nor antiaromatic. **d** and **f** have ring atoms that do not have *p* orbitals, and **h** is not cyclic.

12. Cyclobutadiene has 1 bonding molecular orbital, 2 nonbonding molecular orbitals, and 1 antibonding molecular orbital.

Because each of its four atoms has a *p* atomic orbital, it has 4 π electrons; 2 π electrons are in the bonding π molecular orbital, and each of the two nonbonding molecular orbitals contains one π electron.

13. No. To be aromatic, all the bonding molecular orbitals must be filled and there must be no partially filled orbitals. Each orbital contains two electrons. Since a radical has an unpaired electron, there will be an orbital with a single electron (a partially filled molecular orbital). A radical, therefore, cannot be aromatic.

14. The compounds with completely filled bonding orbitals and electrons in no other orbitals are aromatic (the cycloheptatrienyl cation and the cylopropenyl cation).

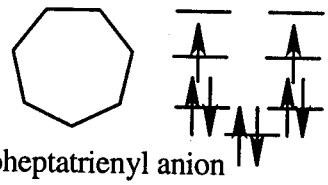


cycloheptatrienyl cation



cyclopropenyl cation

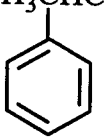
The compound with unpaired electrons in degenerate orbitals is antiaromatic (the cycloheptatrienyl anion).



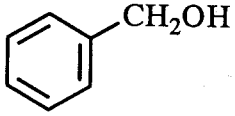
cycloheptatrienyl anion

15.

a. $CH_3CHCH_2CH_2CH_2CH_3$

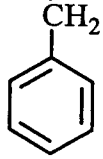


b.

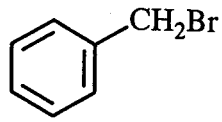


c. $CH_3CH_2CHCH_2CH_3$

CH_2



d.

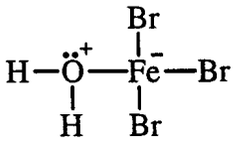


16. Because benzene is an aromatic molecule, it is particularly stable. Therefore, electrophilic addition to benzene is an endergonic reaction because benzene is more stable than the non-aromatic addition product. (See Figure 15.4 on page 606 of the text.)

An alkene is much less stable than benzene because it does not have any delocalized electrons. Electrophilic addition to an alkene is an exergonic reaction because an alkene is less stable than the addition product. (The overall reaction trades a σ bond and a π bond into two σ bonds; a σ bond is stronger and, therefore, of lower energy than a π bond.)

17. The two compounds undergo electrophilic aromatic substitution at the same rate. Breaking the C—H or C—D bond occurs is a fast step after the rate-determining step. Therefore, the difference in the rate of breaking a C—H or C—D bond will not affect the rate of electrophilic aromatic substitution.

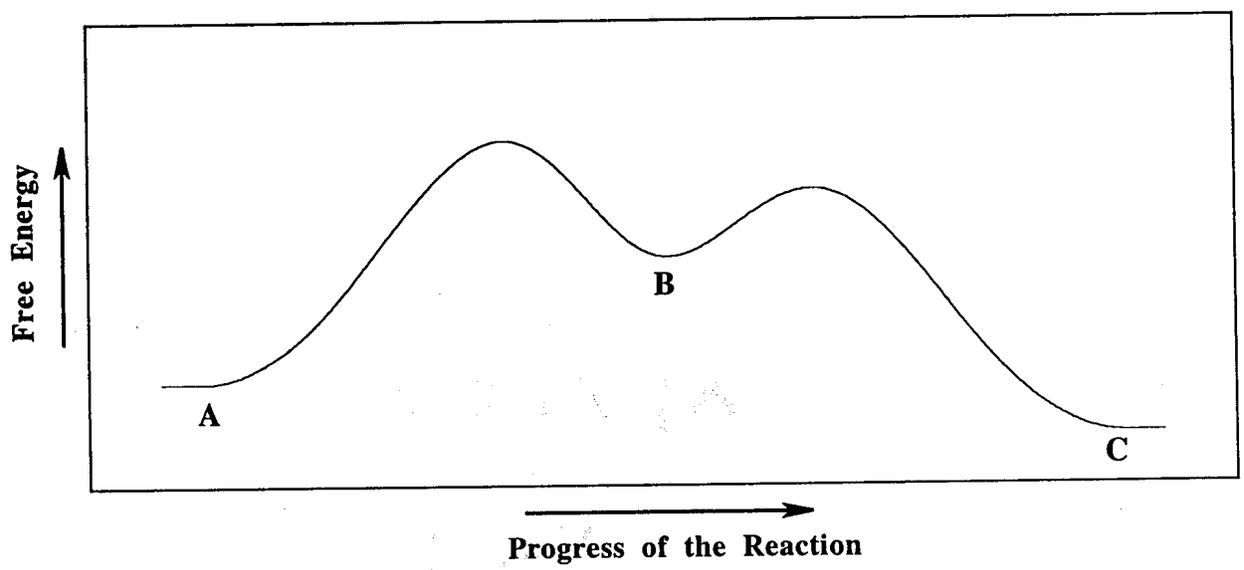
18. Hydrated ferric bromide cannot activate Br_2 for nucleophilic attack by accepting a pair of electrons from it, because it has already accepted a pair of electrons from water.



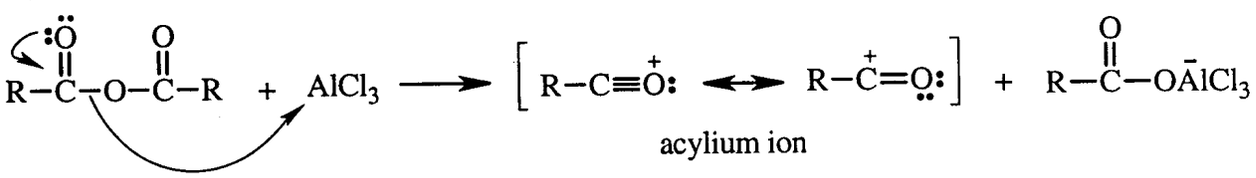
19. In sulfonation, **A** to **B** has a smaller rate constant (a higher energy hill and, therefore, a slower reaction) than **B** to **C**; **A** to **B** is the rate-determining step.

In desulfonation (the reverse reaction), **C** to **B** has a smaller rate constant than **B** to **A**, but **B** to **A** is the rate-determining step. That is because once **B** is formed, it is easier for it to go back to **C** than to proceed to **A**, so **B** to **A** is the bottleneck (or rate-determining) step.

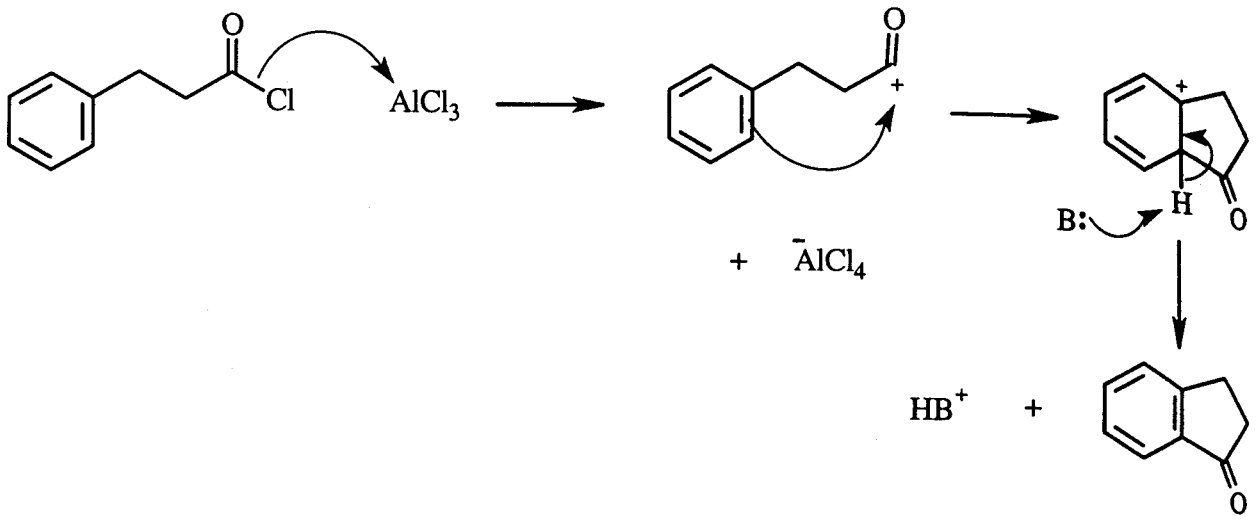
This example shows that the rate-determining step of a reaction is not necessarily the step with the smallest rate constant; it is the step that has the transition state with the highest energy on the reaction coordinate.



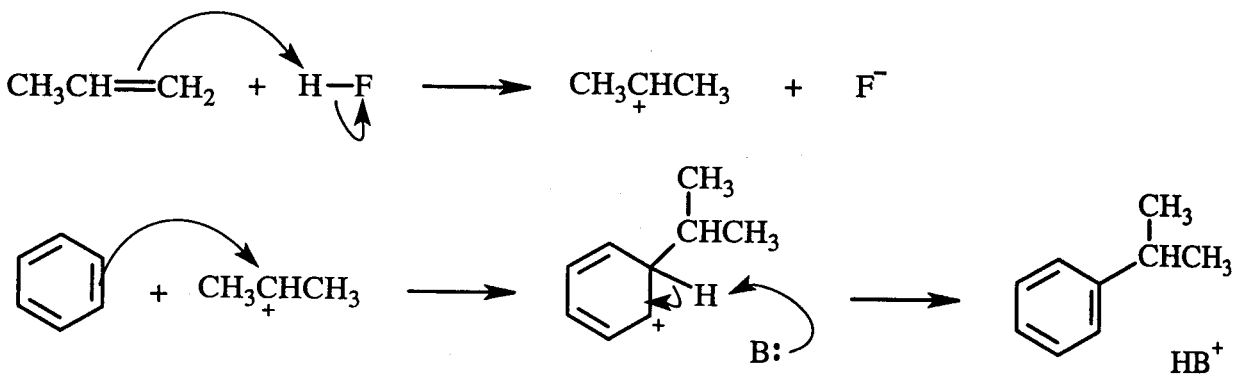
20.



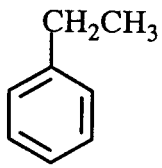
21.

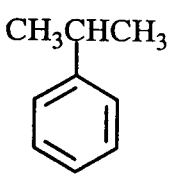


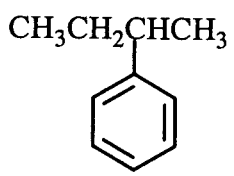
22.

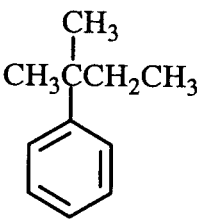


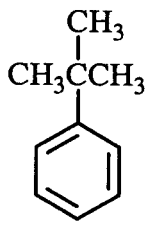
23.

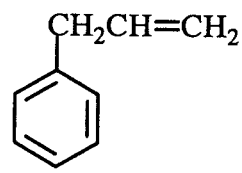
a. 

b. 

c. 

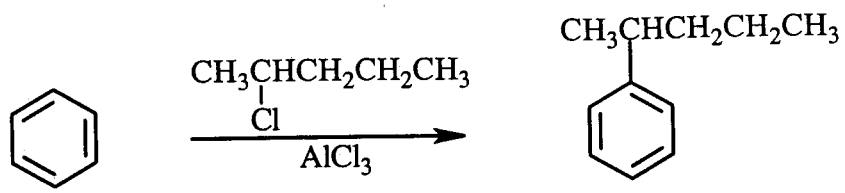
d. 

e. 

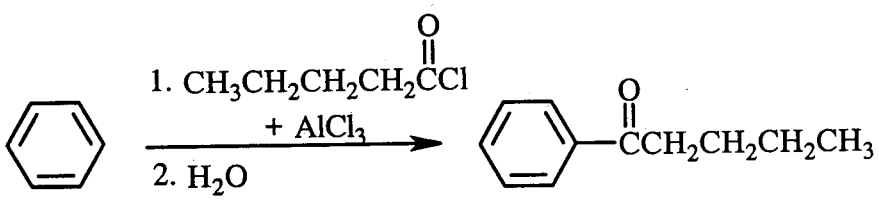
f. 

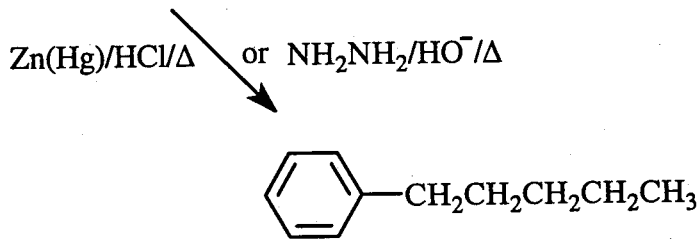
24.

a.

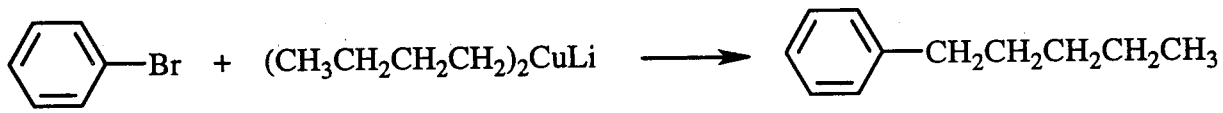


b.

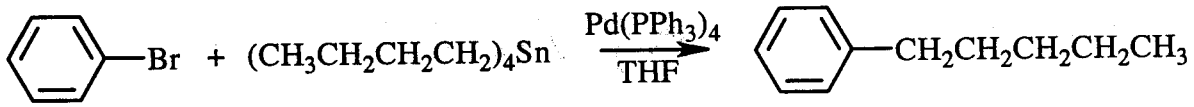




or

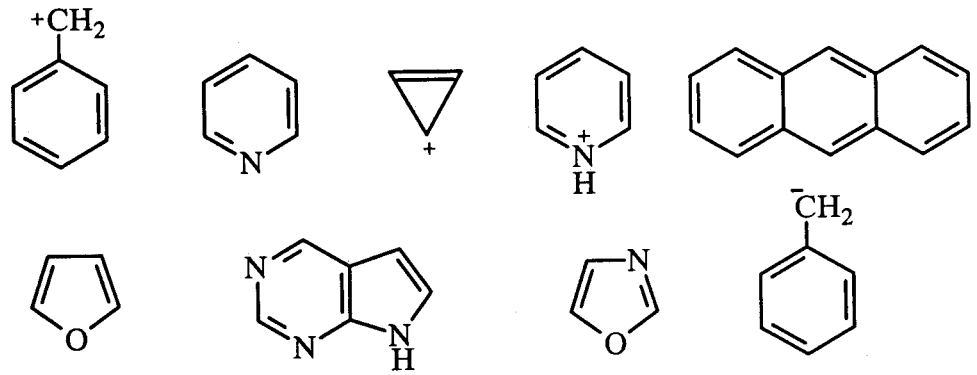


or



25.

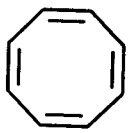
aromatic



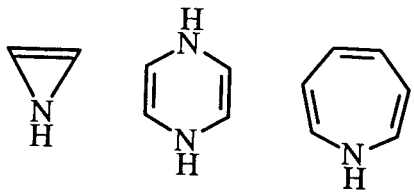
antiaromatic



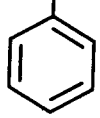
By not being flat, cyclooctatetraene avoids being antiaromatic.

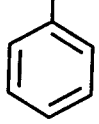


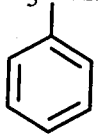
Notice that the nitrogen atoms in compounds such as those to the right are sp^3 hybridized, because if they were sp^2 hybridized, the compounds would be unstable antiaromatic compounds.

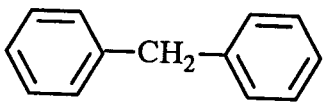


26.

a. CH_3CCH_3 (with CH_3) 

b. CH_3CHCH_3 

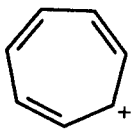
c. $CH_3CCH_2CH_3$ (with CH_3) 

d. 

27.

a. 

It is aromatic.

b. 

It is aromatic.

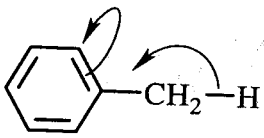
c. 

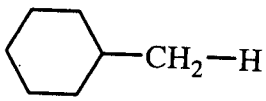
It is aromatic.

d. 

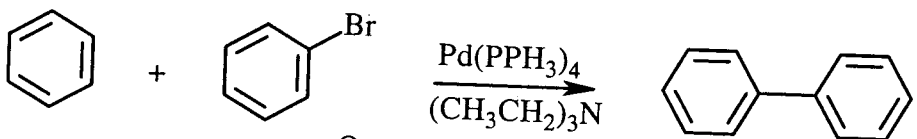
It is not antiaromatic.

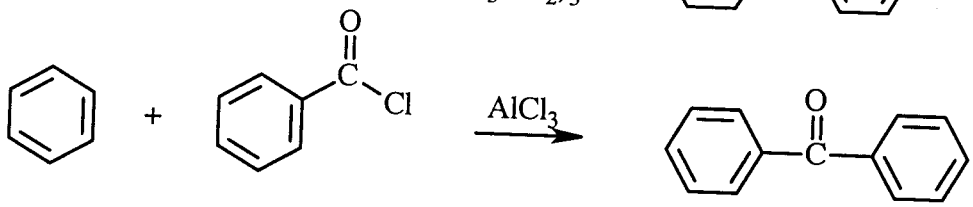
28. The methyl group on benzene can lose a proton easier than the methyl group on cyclohexane because the electrons left behind in the former can be delocalized by resonance into the benzene ring.



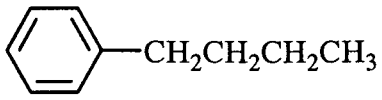


29.

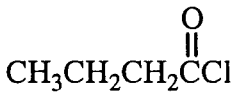
a. 

b. 

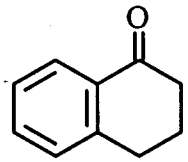
30. The ^{1}H NMR spectrum is the spectrum of 1-phenylbutane: the benzene ring protons show a signal at ~ 7.2 ppm. The two triplets and two multiplets indicate a butyl substituent.

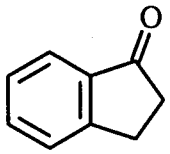


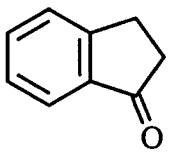
Therefore, the acyl chloride has a straight chain propyl group and a carbonyl group that will be reduced to a methylene group.

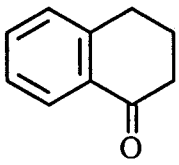


31.

a. 

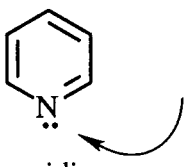
b. 

c. 

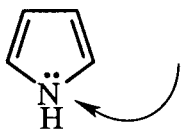
d. 

32. **a.** Pyridine is a stronger base because its nonbonding electrons are not part of the π cloud. Thus, when it is protonated, it is still aromatic.

The nonbonding electrons of pyrrole are part of the π electron cloud, so when pyrrole is protonated, it loses its aromaticity.

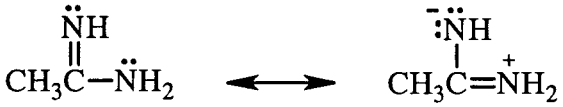


pyridine

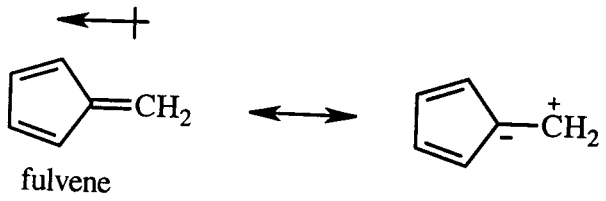


pyrrole

b. The compound with the carbon-nitrogen double bond is a stronger base because it has increased electron density on one of the nitrogens as a result of resonance.

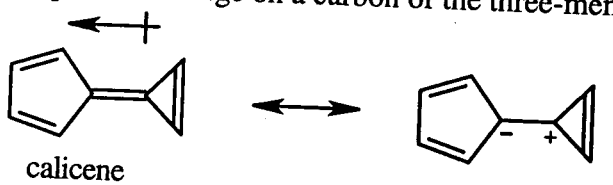


33. **a.** In fulvene, the electrons move toward the five-membered ring because the resonance contributor that has a negative charge on a ring carbon is aromatic.



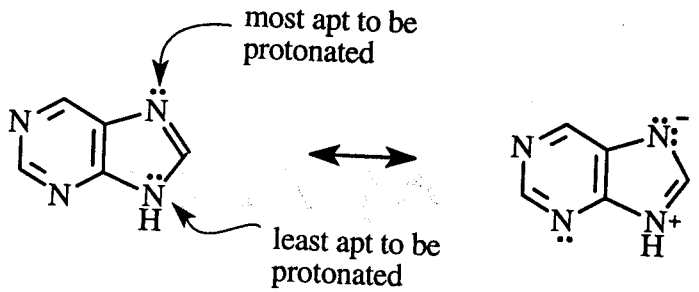
fulvene

b. In calicene, the electrons move toward the five-membered ring because both rings are aromatic in the resonance contributor that has a negative charge on a carbon of the five-membered ring and a positive charge on a carbon of the three-membered ring.



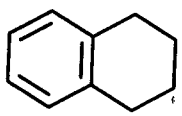
calicene

34. The contributing resonance structure that is shown indicates which nitrogen is most apt to be protonated and which nitrogen is least apt to be protonated.

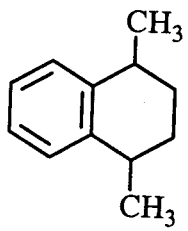


35.

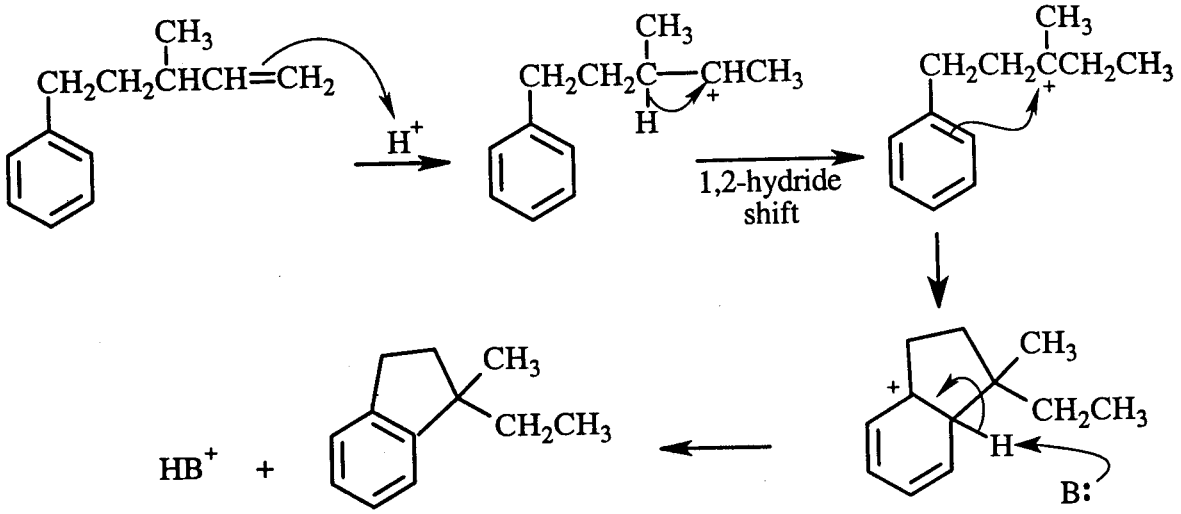
a.



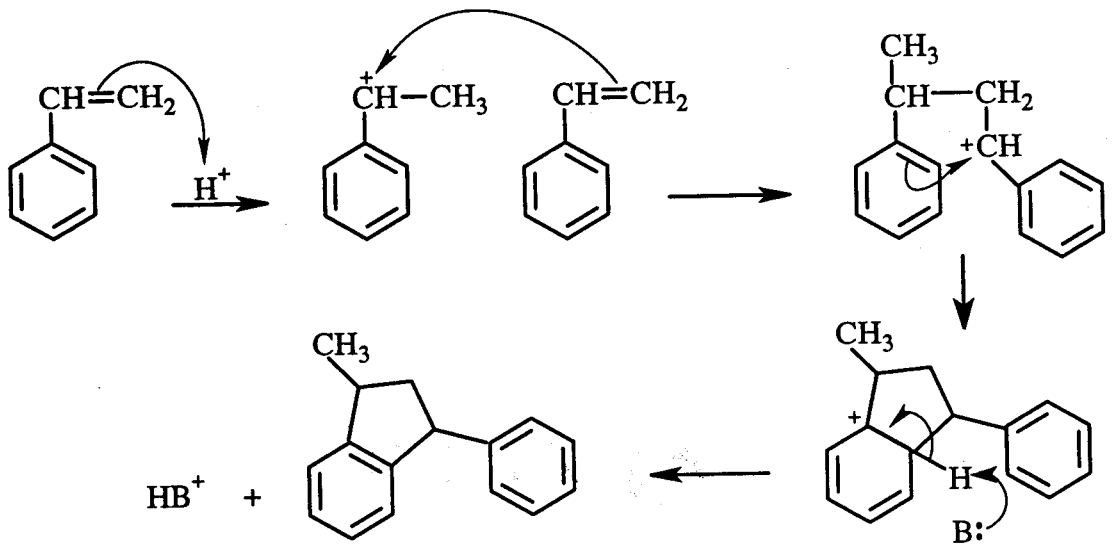
b.



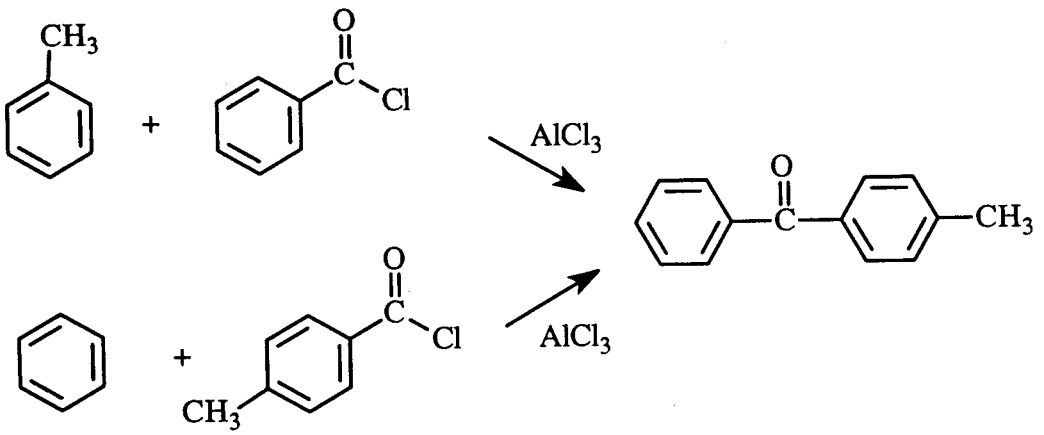
a.


CH3
CH2CH2CHCH=CH2
H+
CH3
CH2CH2C—CHCH3
H
1,2-hydride shift
CH3
CH2CH2CCH2CH3
CH3
CH2CH3
HB+ +
CH3
CH2CH3
H
B:

b.

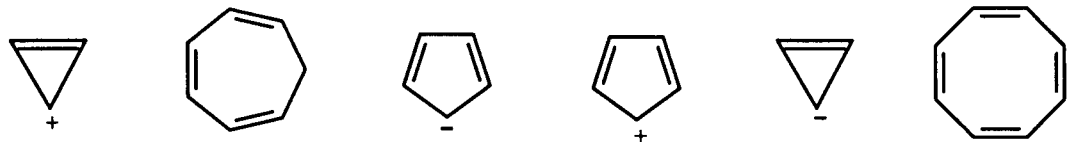

CH=CH2
H+
CH—CH3
CH=CH2
CH3
CH—CH2
CH
HB+ +
CH3
H
B:

37.

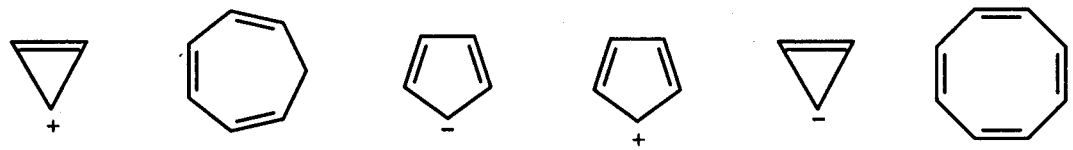

CH3
+
O
C
Cl
AlCl3
O
C
CH3
+
O
C
Cl
CH3
AlCl3

Chapter 15 Practice Test

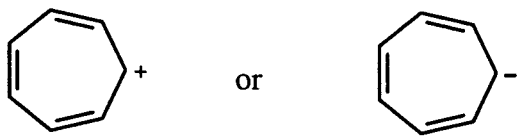
1. Which are aromatic compounds?



2. Which are antiaromatic compounds?

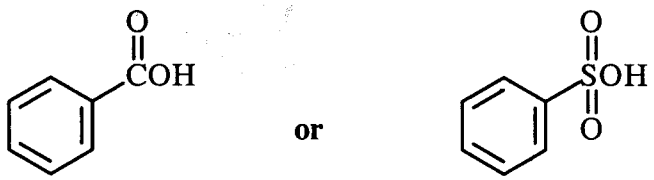


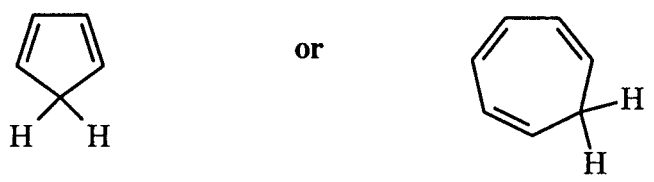
3. Which compound has the greater resonance energy?



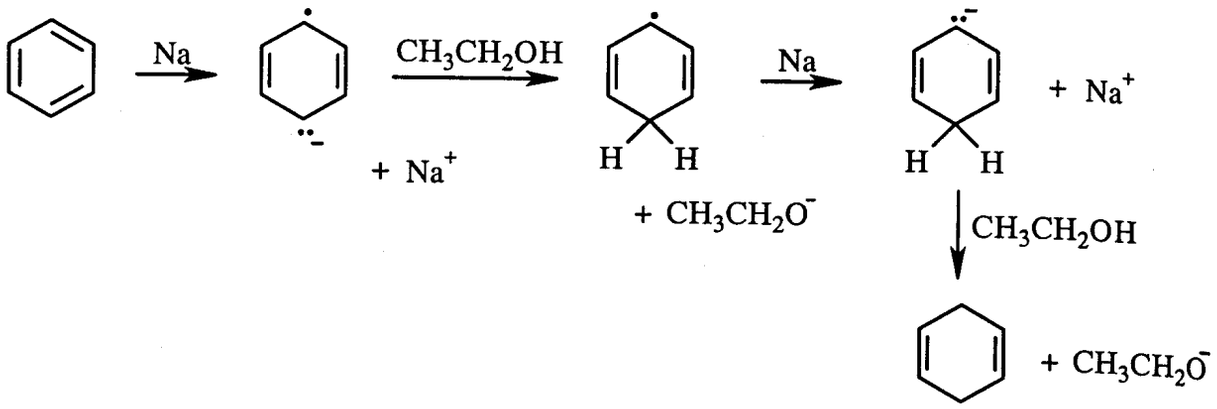
4. Draw the resonance contributors for the carbocation intermediate that is formed when benzene reacts with an electrophile (Y^+).

5. Which of the following is a stronger acid?

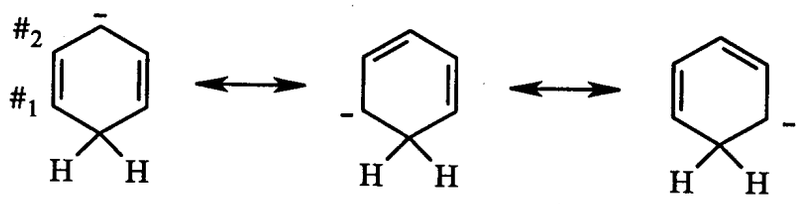




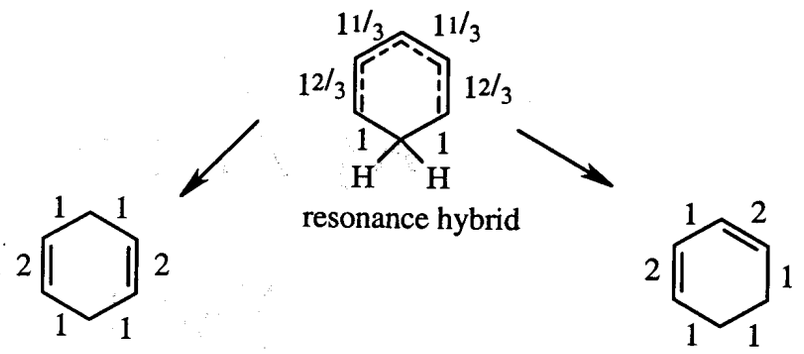
38.



39. From the three resonance structures for the cyclohexadienyl anion, the bond orders in the resonance hybrid can be calculated. (For example, the C1-C2 bond is represented by a single bond in one resonance structure and by a double bond in two resonance structures, which gives i a bond order 1+ 2/3 in the hybrid.)



contributing resonance structures



resonance hybrid

1,4-cyclohexadiene

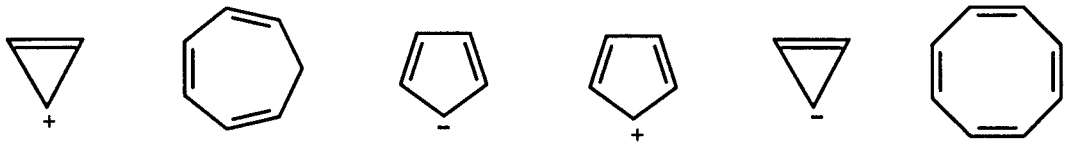
1,3-cyclohexadiene

Comparing the bond order difference in each bond in the anion and in the corresponding bond in the possible products, there is a (1/3 + 1/3 + 1/3 + 1/3 = 4/3) 4/3 difference in bond order when 1,4-cyclohexadiene is formed and a (1/3 + 1/3 + 2/3 + 2/3 = 6/3) 6/3 difference in bond order when 1,3-cyclohexadiene is formed. Thus, the principle of least motion predicts that 1,4-cyclohexadiene will be the major product, since its formation from the anion involves less of a change in electronic configuration.

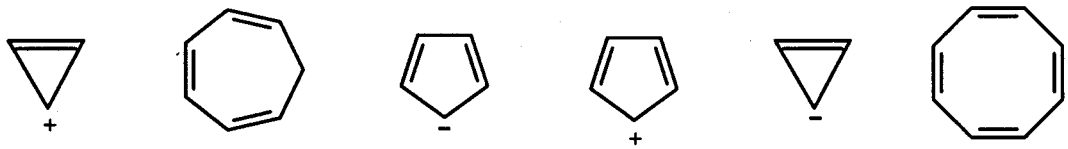
40. The observation that cyclobutadiene is rectangular and the observation that there are two different 1,2-dideutrio-1,3-cyclobutaidenes both indicate that the π electrons are localized rather than delocalized. Localization of the π electrons prevents the compound from being antiaromatic

Chapter 15 Practice Test

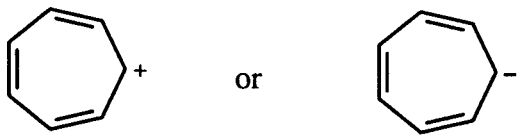
1. Which are aromatic compounds?



2. Which are antiaromatic compounds?

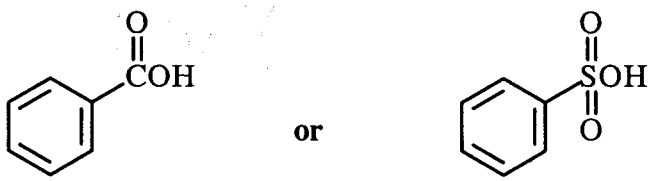


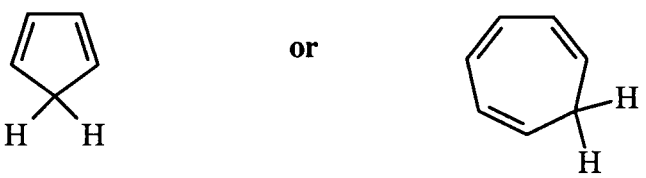
3. Which compound has the greater resonance energy?



4. Draw the resonance contributors for the carbocation intermediate that is formed when benzene reacts with an electrophile (Y^+).

5. Which of the following is a stronger acid?

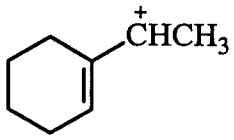
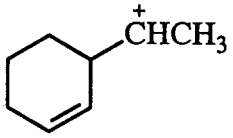




6. Give two alkyl halides, two alkenes, and two alcohols that could be used in a reaction with benzene to form 2-phenylbutane.

7. What acid anhydride would you use in a synthesis of 1-phenylpropane?

8. Which in each of the following pairs is more stable?

a.  or 

b. $CH_3\overset{+}{C}HCH_2CH_3$ or $CH_3\overset{+}{C}HCH{=}CH_2$

c. $CH_3\bar{C}HCH_2\overset{O}{\overset{\|}{C}}CH_3$ or $CH_3\bar{C}H\overset{O}{\overset{\|}{C}}CH_3$

9. Give the mechanism for formation of the nitronium ion from nitric acid and sulfuric acid.

CHAPTER 16
Reactions of Substituted Benzenes

Important Terms

activating substituent — a substituent that increases the reactivity of an aromatic ring. Electron-donating substituents activate aromatic rings toward electrophilic attack, and electron-withdrawing substituents activate aromatic rings toward nucleophilic attack.

arenediazonium salt — $ArN\equiv N^{+}\ X^{-}$

azo linkage — an -N=N- bond.

benzyne intermediate — a compound with a triple bond in place of one of the double bonds of benzene.

cine substitution — substitution at the carbon adjacent to the carbon that was bonded to the leaving group.

deactivating substituent — a substituent that decreases the reactivity of an aromatic ring. Electron-withdrawing substituents deactivate aromatic rings toward electrophilic attack, and electron-donating substituents deactivate aromatic rings toward nucleophilic attack.

direct substitution — substitution at the carbon that was bonded to the leaving group.

donate electrons by resonance — donation of electrons through *p* orbital overlap with neighboring π bonds.

fused rings — rings that share two adjacent carbons.

inductive electron donation — donation of electrons through a σ bond.

inductive electron withdrawal — withdrawal of electrons through a σ bond.

meta director — a substituent that directs an incoming substituent meta to an existing substituent.

nitrosamine — an amine with a nitroso (-N=O) substituent bonded to its nitrogen atom.

***N*-nitroso compound** — an amine with a nitroso (-N=O) substituent bonded to its nitrogen atom.

nucleophilic aromatic substitution	a reaction in which a nucleophile substitutes for an atom or group bonded to a benzene ring.
ortho-para director	a substituent that directs an incoming substituent ortho and para to an existing substituent.
resonance electron donation	donation of electrons through *p* orbital overlap with neighboring π bonds.
resonance electron withdrawal	withdrawal of electrons through *p* orbital overlap with neighboring π bonds.
Sandmeyer reaction	the reaction of an arenediazonium ion with a cuprous salt.
Schiemann reaction	the reaction of an arenediazonium ion with HBF_4.
S_NAr reaction	a nucleophilic aromatic substitution reaction.
withdraw electrons by resonance	withdrawal of electrons through *p* orbital overlap with neighboring π bonds.

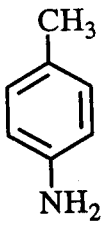
Solutions to Problems

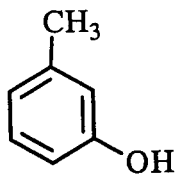
1. **a.** *ortho*-ethylphenol or 2-ethylphenol

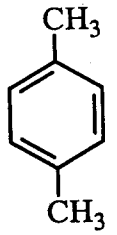
   b. *meta*-bromochlorobenzene or 3-bromochlorobenzene

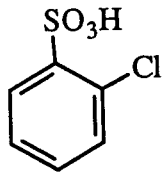
   c. *meta*-bromobenzaldehyde or 3-bromobenzaldehyde

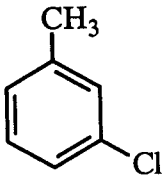
   d. *ortho*-ethyltoluene or 2-ethyltoluene

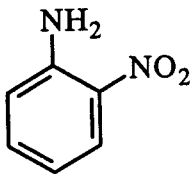
2. **a.** 

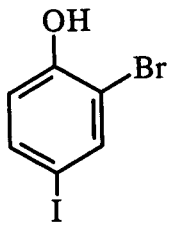
   b. 

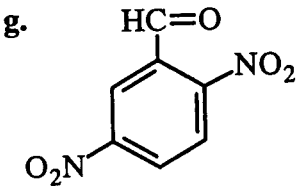
   c. 

   d. 

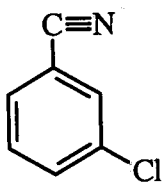
3. **a.** 

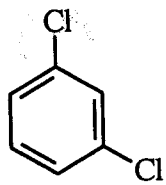
   c. 

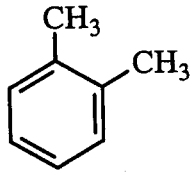
   e. 

   g. 

   b. 

   d. 

   f. 

   h. 

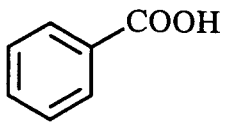
4. **a.** 1,3,5-tribromobenzene

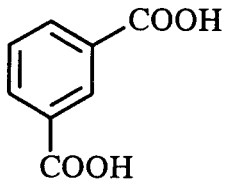
   b. *meta*-nitrophenol or 3-nitrophenol

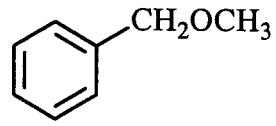
   c. *para*-bromotoluene or 4-bromotoluene

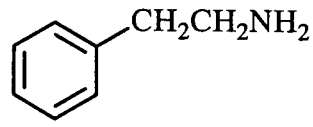
   d. *ortho*-dichlorobenzene or 1,2-dichlorobenzene

5.

a. 

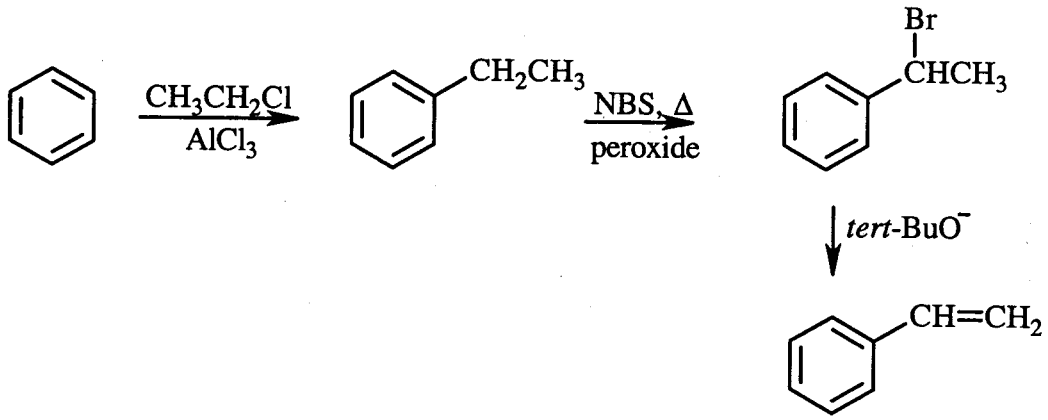
b. 

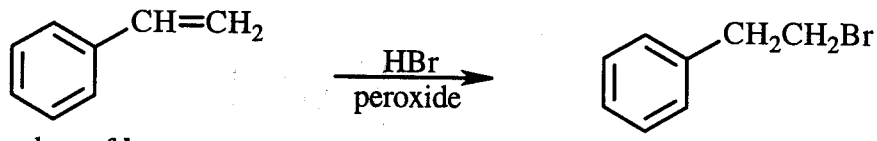
c. 

d. 

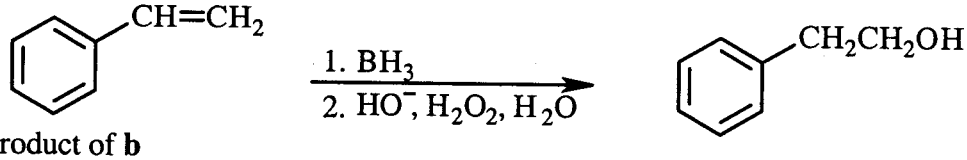
6. **a.** Solved in the text.

A more direct method that can be used to synthesize benzaldehyde from benzene is via the Gattterman-Koch reaction (see p. 613 of the text).

b. 

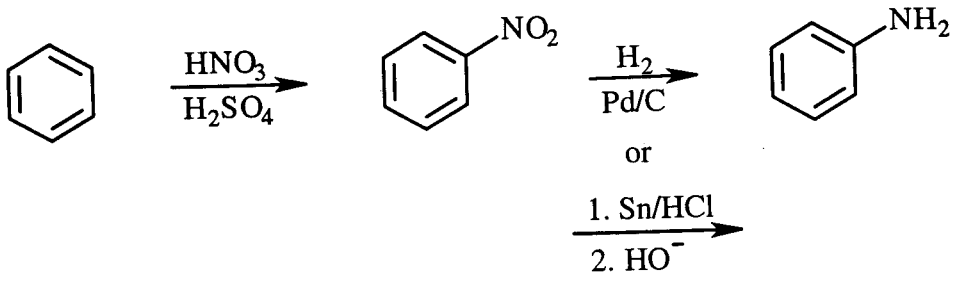
c. 

product of **b**

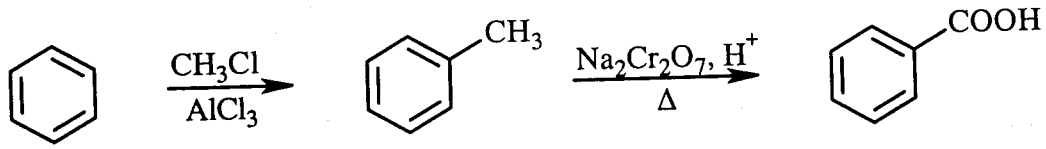
d. 

product of **b**

e.



f.



7. **a.** donates electrons by resonance and withdraws electrons inductively

b. donates electrons inductively

c. withdraws electrons by resonance and withdraws electrons inductively

d. donates electrons by resonance and withdraws electrons inductively

e. donates electrons by resonance and withdraws electrons inductively

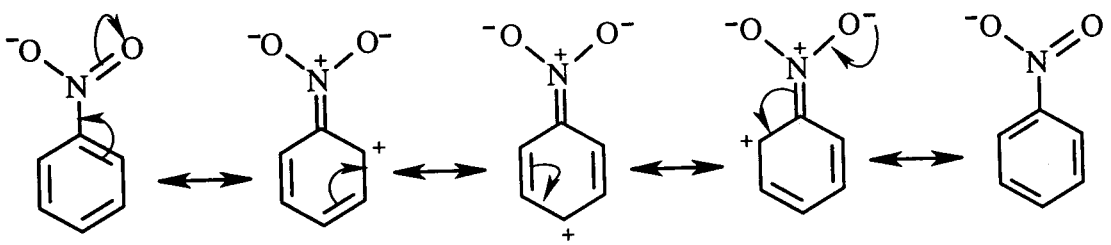
f. withdraws electrons inductively

8. **a.** phenol > toluene > benzene > bromobenzene > nitrobenzene

b. toluene > chloromethylbenzene > dichloromethylbenzene > difluoromethylbenzene

9. Solved in the text.

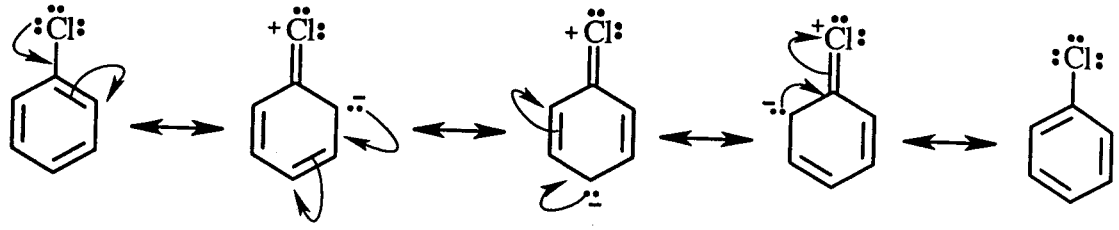
10. **a.**



The above resonance structures show there is positive charge density on the ortho and para positions, so an incoming electrophile will avoid those positions.

By drawing the resonance structures for the carbocation intermediates formed by putting a substituent at various positions, you will see that the most stable carbocation is obtained when the substituent is placed in the meta position.

b.

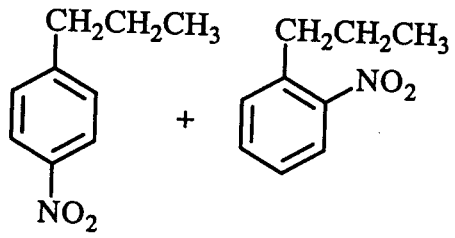


Resonance electron donation increases the electron density at the ortho and para positions, so an incoming nucleophile will be attracted to those positions.

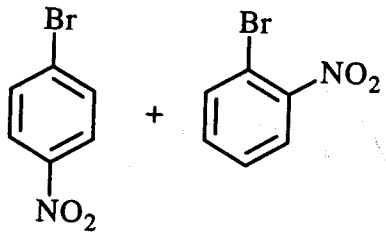
By drawing the resonance structures for the carbocation intermediates formed by putting a substituent at various positions, you will see that the most stable carbocation is obtained when the substituent is placed in the ortho or para position.

11.

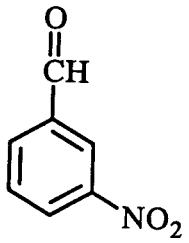
a.



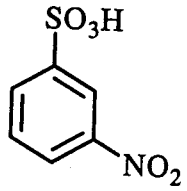
b.



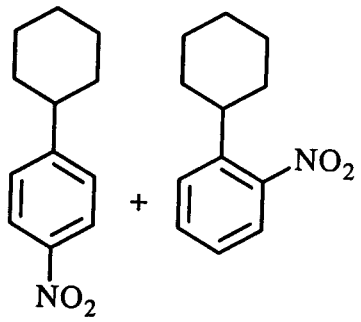
c.



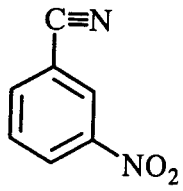
d.



e.

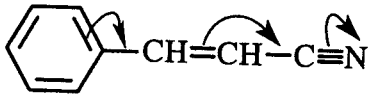


f.



12. They are all meta directors:

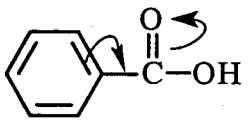
a. this group withdraws electrons by resonance from the ring. The relatively electronegative nitrogen atom causes it to withdraw electrons inductively from the ring.



b. NO_2 withdraws electrons inductively and withdraws electrons by resonance.

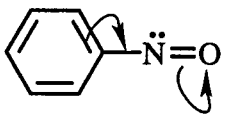
c. CH_2OH withdraws electrons inductively from the ring.

d. COOH withdraws electrons inductively and withdraws electrons by resonance.

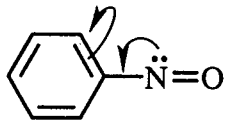


e. CF_3 withdraws electrons inductively from the ring.

f. N=O withdraws electrons inductively and withdraws electrons by resonance.
You could draw resonance contributors for electron donation into the ring by resonance. However, the most stable resonance contributors are obtained by electron flow out of the benzene ring toward oxygen, the most electronegative atom in the compound.



resonance electron withdrawal out of the ring



resonance electron donation into the ring

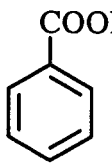
13.

a. $ClCH_2COH$

b. O_2NCH_2COH

c. $H_3\overset{+}{N}CH_2COH$

d.



e. $HOCCH_2COH$

The negatively charged compound has a greater amount of electron donation by resonance.

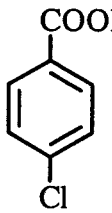
f. $HCOH$

A hydrogen is electron-withdrawing compared to a methyl group.

g. FCH_2COH

Fluorine is more electronegative than chlorine.

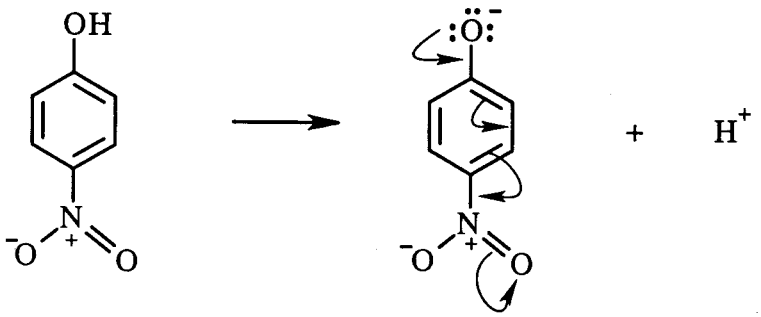
h.



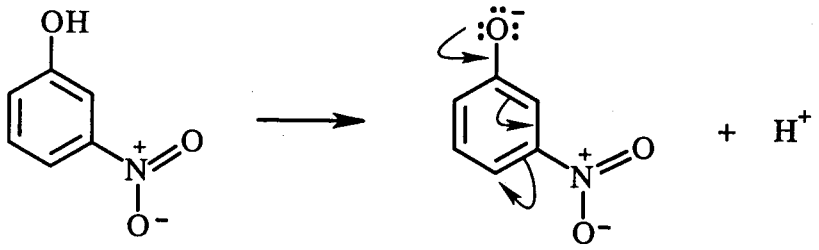
We know that F withdraws electrons inductively more than Cl does, because F is more electronegative than Cl.
We know that F donates electrons by resonance better than Cl does, because F donation involves $2p$-$2p$ overlap, while Cl donation involves $3p$-$2p$ overlap.

Because Table 16.1 on page 632 of the text shows that F is more activating than Cl, we know that overall F donates electrons better than Cl. Thus resonance electron donation is more important than inductive electron withdrawal.

14. When *para*-nitrophenol loses a proton, the electrons that held the proton can be delocalized by resonance onto the nitro substituent. Therefore, the *para*-nitro substituent decreases the pK_a by resonance electron withdrawal and by inductive electron withdrawal.



When *meta*-nitrophenol loses a proton, the electrons that held the proton cannot be delocalized by resonance onto the nitro substituent. Therefore, the *meta*-nitro substituent can decrease the pK_a only by inductive electron withdrawal. Therefore, the para isomer has a lower pK_a.

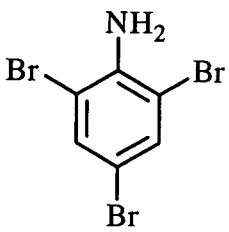


15. No reaction will occur in **a** and **c**, because a Friedel-Crafts reaction cannot be carried out on a ring that possesses a meta director.

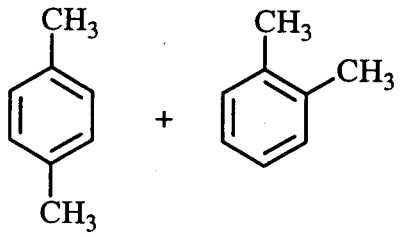
a. no reaction

c. no reaction

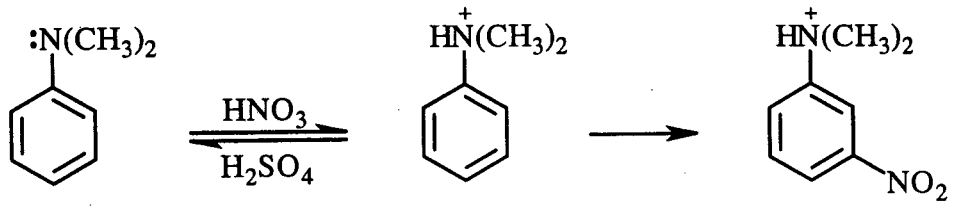
b.



d.

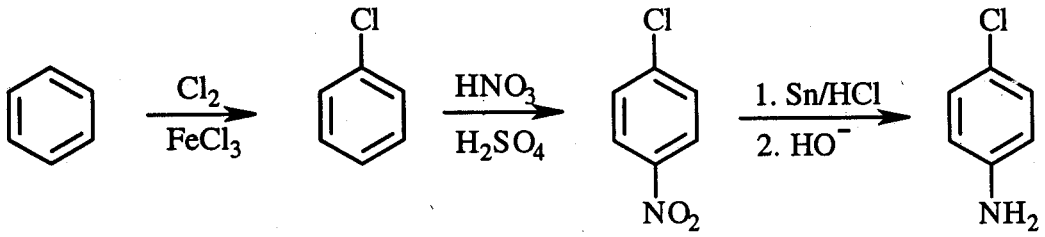


16. In acid solution, some of the amine is protonated, and the protonated substituent is a meta director. Because a greater percentage of the compound is protonated at pH = 3.5 than at pH = 4.5, more of the meta isomer is formed at pH = 3.5.

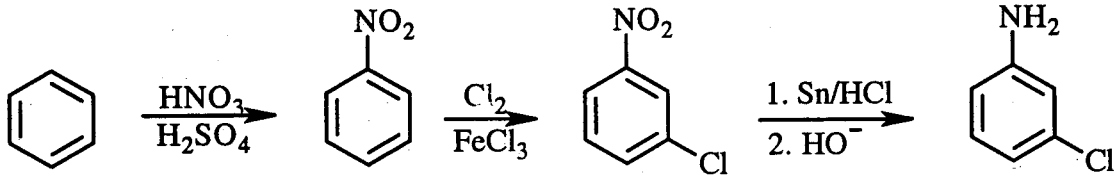


17.

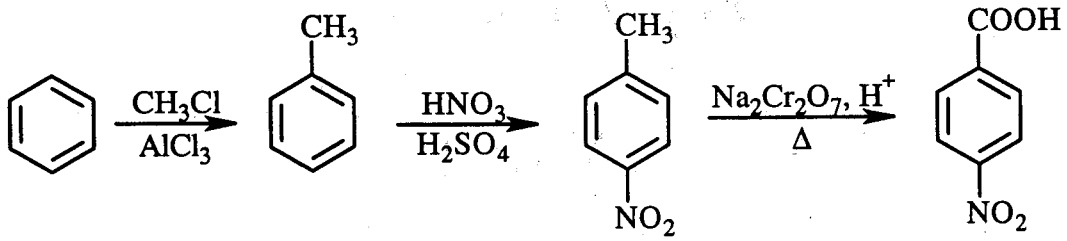
a.



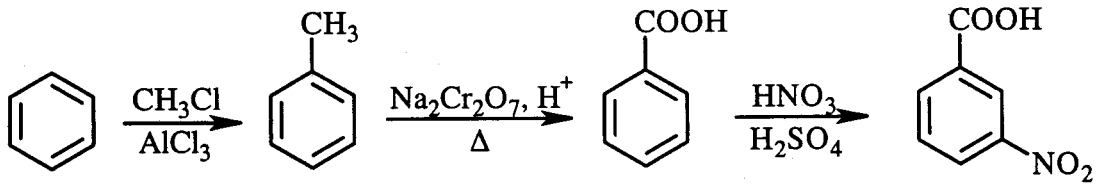
b.



c.

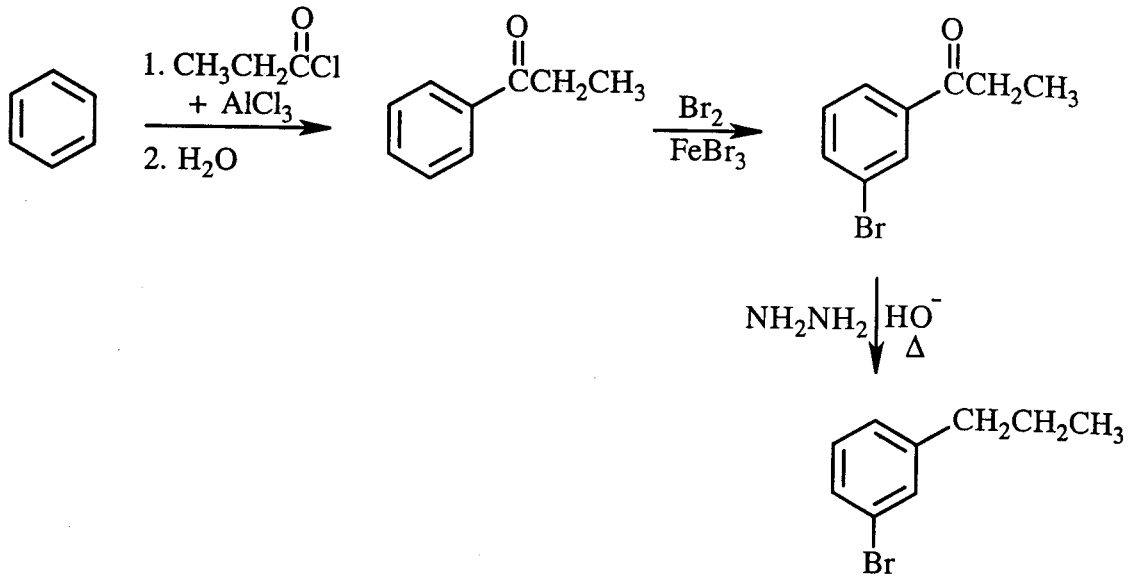


d.

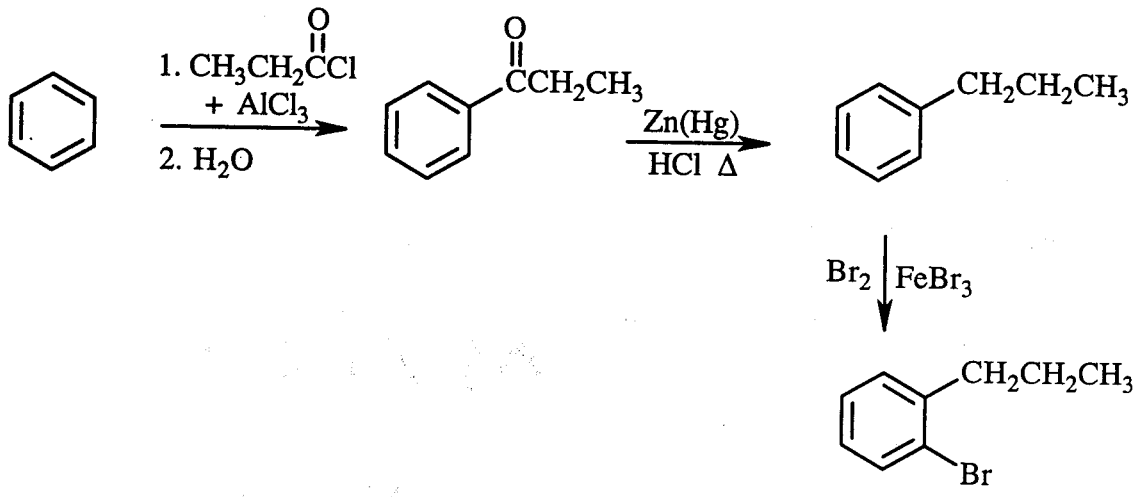


In the next two problems ("**e**" and "**f**"), the carbonyl group can be converted to a methylene group by either a Wolff-Kishner reduction (as is used in "**e**") or a Clemmensen reduction (as is used in "**f**").

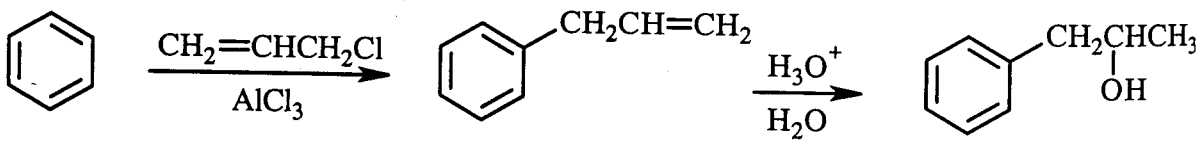
e.



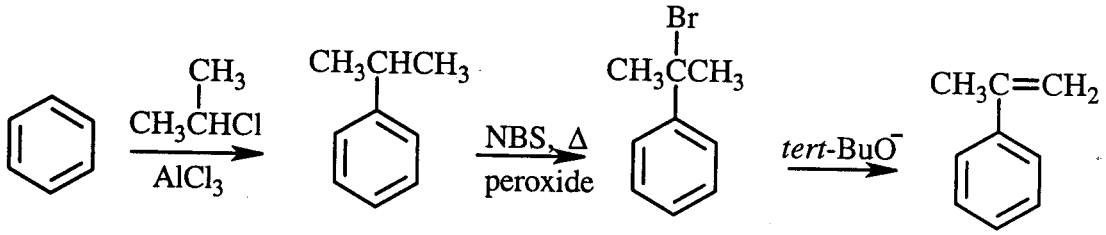
f.



g.

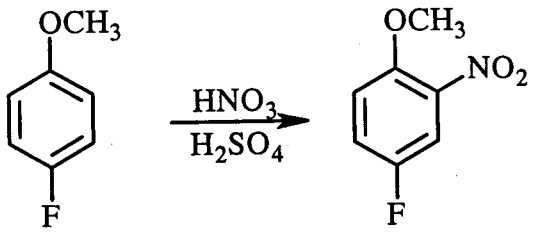


h.



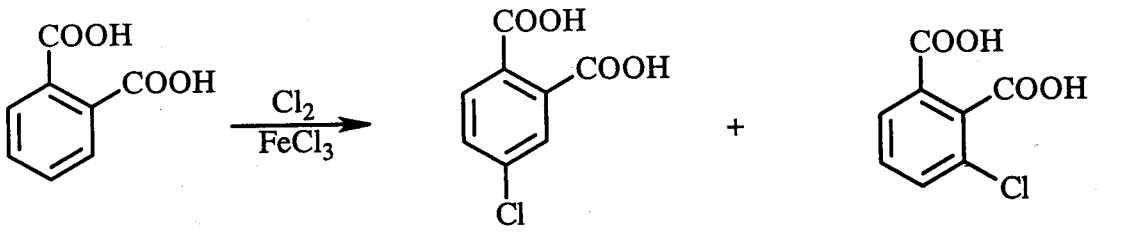
18.

a.



A methoxy substituent is strongly activating, whereas a fluorine substituent is deactivating, so the methoxy substituent will do the directing.

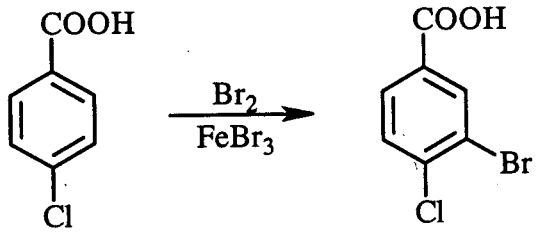
b.



COOH directs to the meta position. The same product will be obtained regardless of which COOH is chosen to be the director.

Less of this compound will be obtained because of steric hindrance.

c.



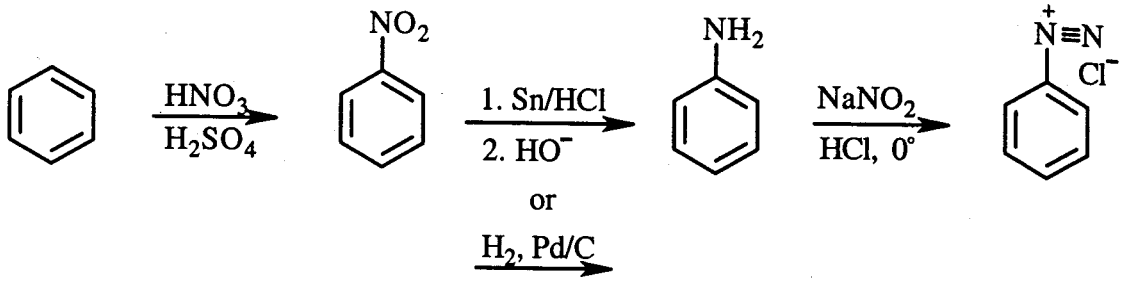
COOH directs to its meta position and Cl directs to its ortho position, so they both direct to the same position on the ring.

19. Solved in the text.

20. Because a diazonium ion is electron withdrawing, it deactivates the benzene ring. A deactivated benzene ring would be too unreactive to undergo an electrophilic substitution reaction at the cold temperature necessary to keep the benzenediazonium from decomposing.

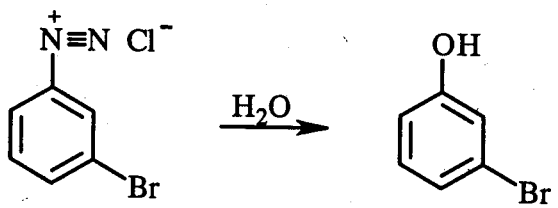
21. More of the desired bromo-substituted compound will be obtained if the ions in solution are $Cu^+ + Br^-$ than if they are $Cu^+ + Br^-$ and Cl^-.

22.

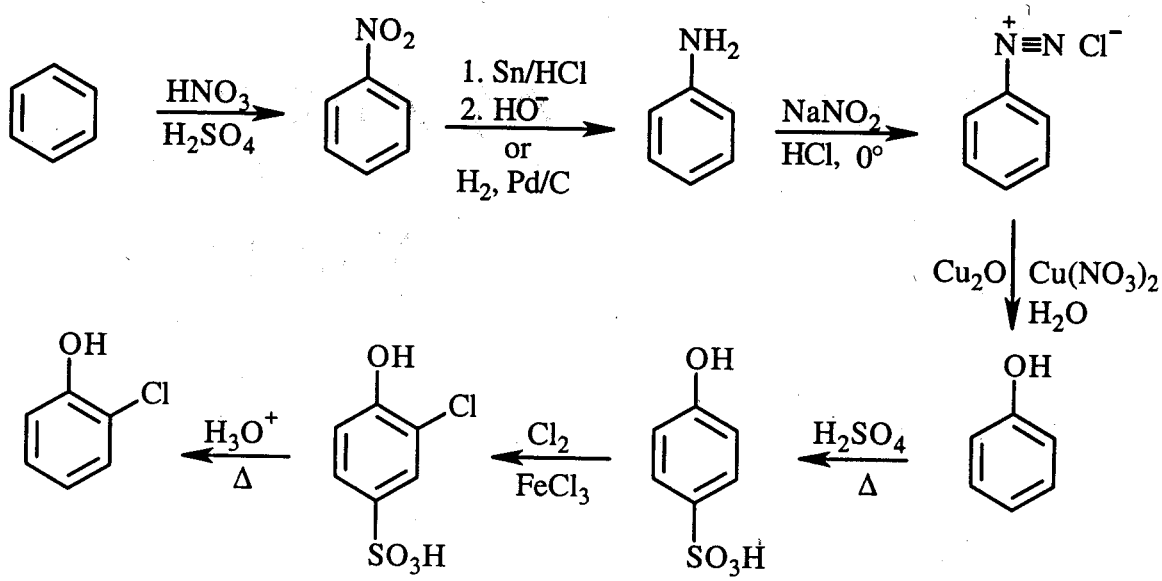


23. **a.** Solved in the text.

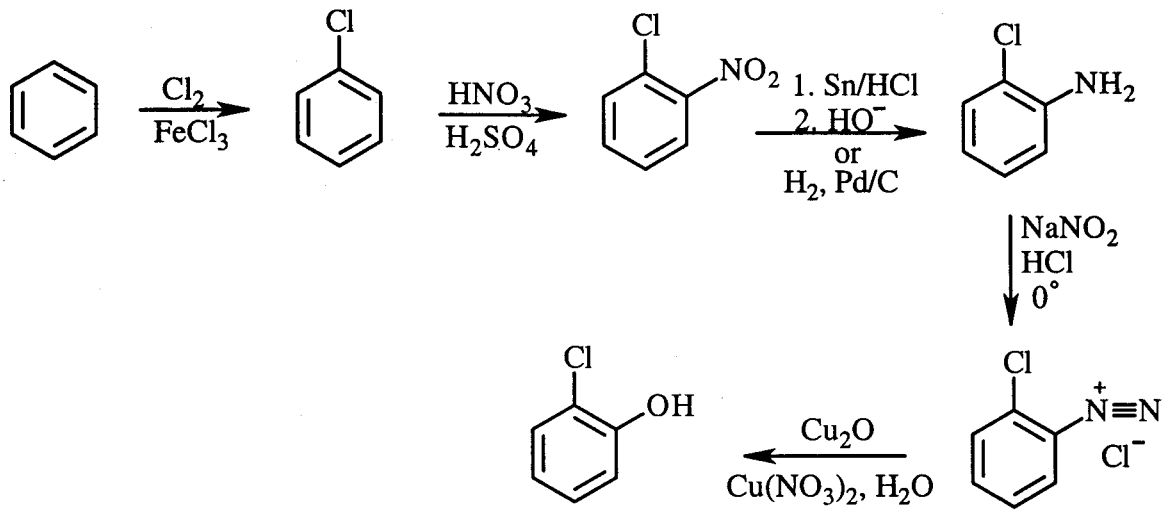
b. The reaction steps are the same as those in **a** (answered on page 649 of the text) except for the last step. In the last step the meta-bromo-substituted ion should undergo reaction with water rather than with CuBr.



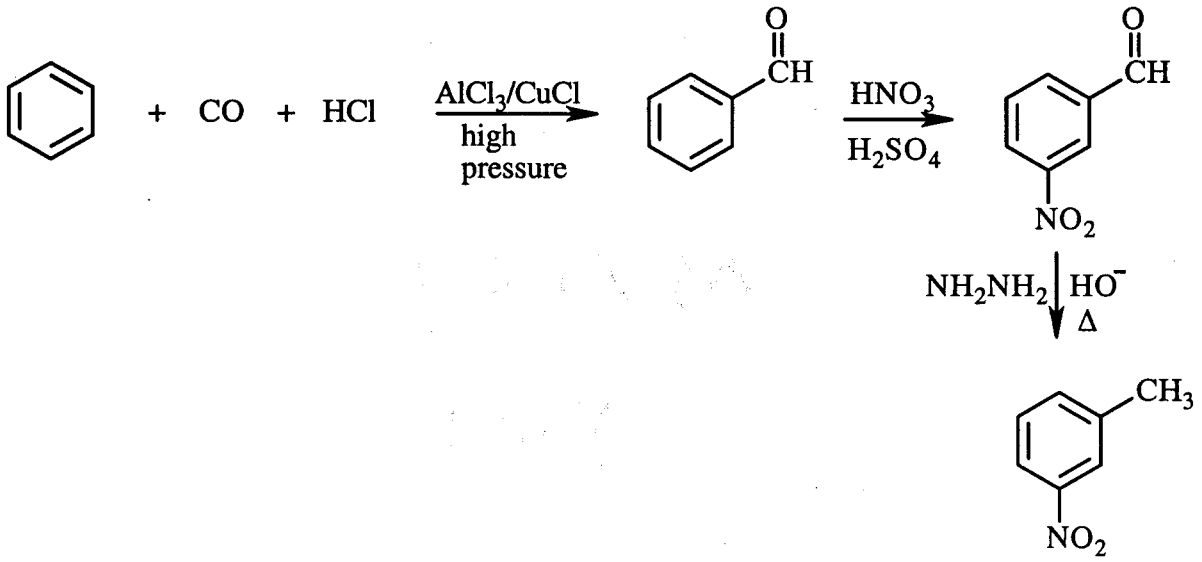
c.



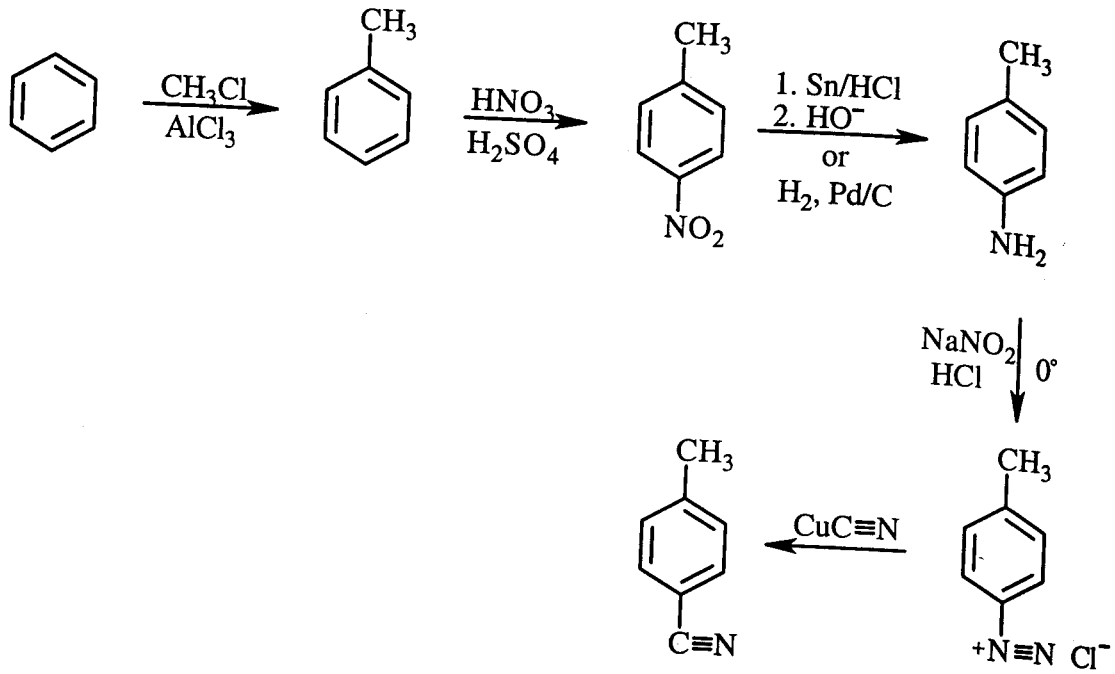
or



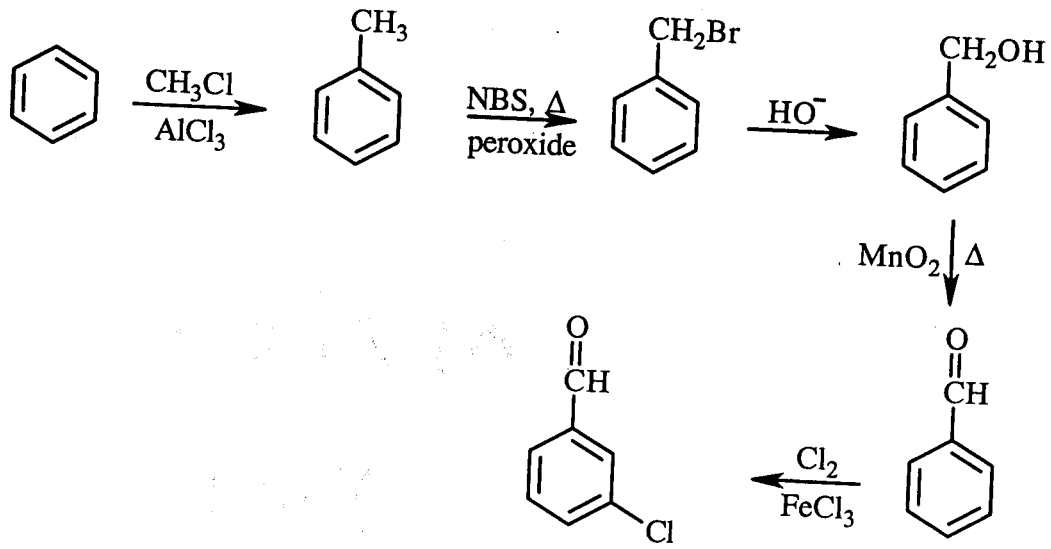
d. The nitro group cannot be placed on the benzene ring first, because a Friedel-Crafts reaction cannot be carried out on a ring with a meta director. Because formyl chloride is too unstable to be purchased, benzaldehyde is prepared by the Gatterman-Koch reaction p. 613 in the text).



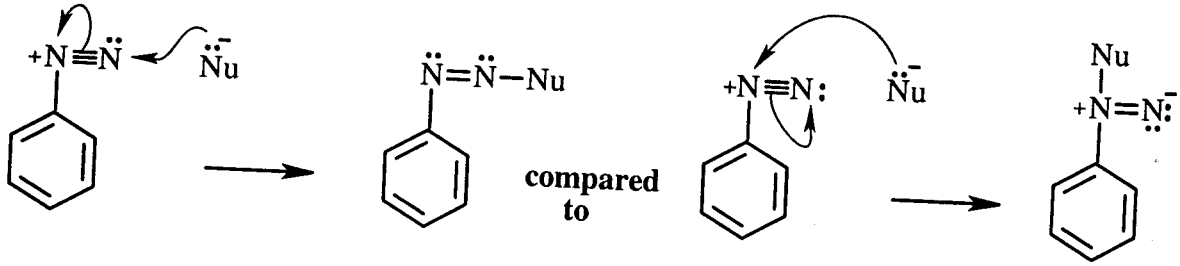
e.



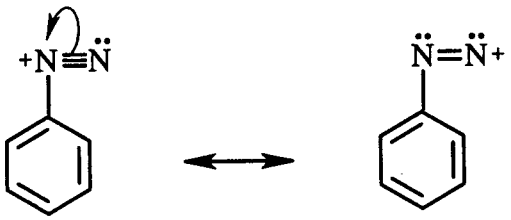
f.



24. You can see why nucleophilic attack occurs on the neutral nitrogen if you compare the products of nucleophilic attack on the two nitrogens. Nucleophilic attack on the neutral nitrogen forms a stable product, whereas nucleophilic attack on the positively charged nitrogen would form an unstable compound with two charged nitrogen atoms.

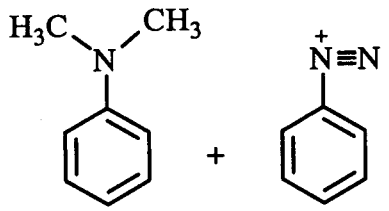


The terminal nitrogen is electrophilic because of electron withdrawal by the positively charged nitrogen. If you draw the resonance contributors, you can see that the "neutral" nitrogen is electron deficient.



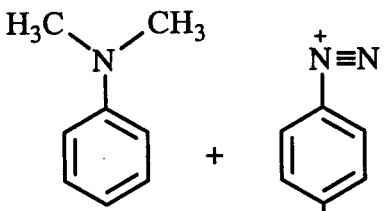
5.

a.

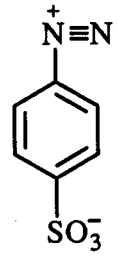


activated ring diazonium ion

b.

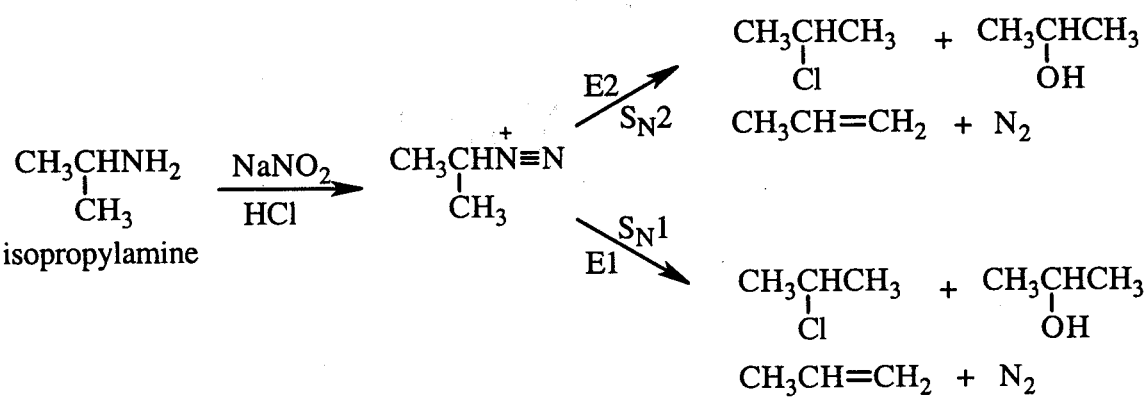


activated ring

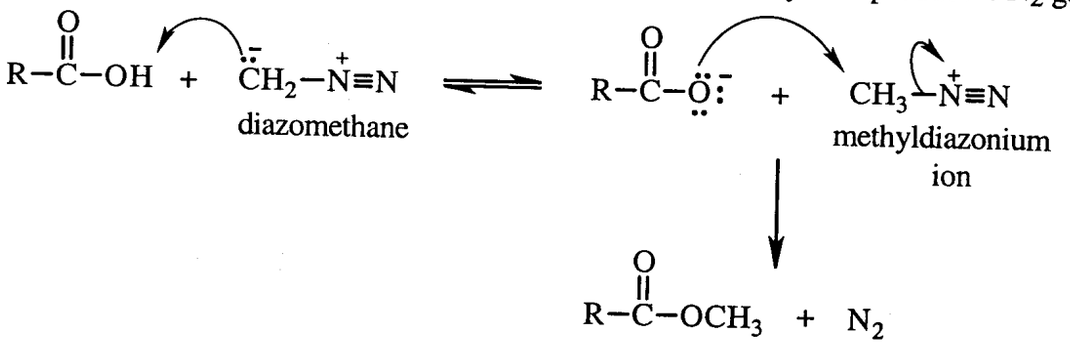


diazonium ion

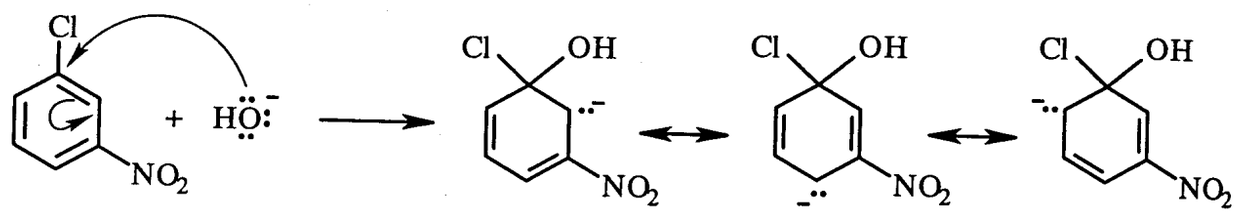
26. The reaction of an amine with sodium nitrite and HCl converts the amino group into an excellent leaving group. Substitution and elimination reactions can then occur by both S_N1/E1 and S_N2/E2 pathways. The same products are obtained by both pathways. Because the reaction is carried out in an aqueous solution, the nucleophiles are Cl^- and H_2O.



27. The first step in the reaction is formation of the methyldiazonium ion as a result of abstraction of a proton from the carboxylic acid by diazomethane. Diazomethane is both explosive and toxic, so it should be synthesized only in small amounts by experienced laboratory workers.
In the second step of the reaction, the carboxylate ion displaces nitrogen from the methyldiazonium ion. High yields are obtained, since the only side product is N_2 gas.



28. From the resonance contributors, you can see that the reason that *meta*-chloronitrobenzene does not react with hydroxide ion is because the negative charge that is generated on the benzene ring cannot be delocalized onto the nitro substituent.
Electron delocalization onto the nitro substituent can occur only if the nitro substituent is ortho or para to the site of nucleophilic attack.



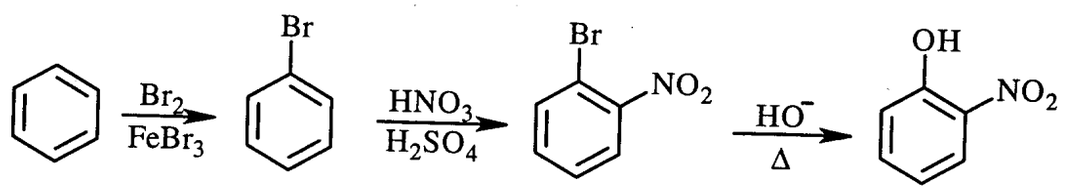
29.

a. 1-chloro-2,4-dinitrobenzene > *p*-chloronitrobenzene > chlorobenzene

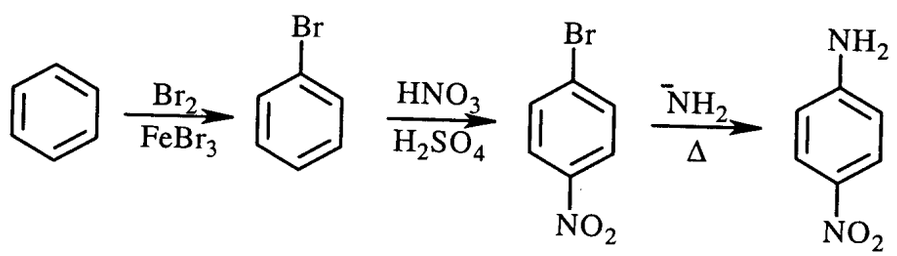
b. chlorobenzene > *p*-chloronitrobenzene > 1-chloro-2,4-dinitrobenzene

30.

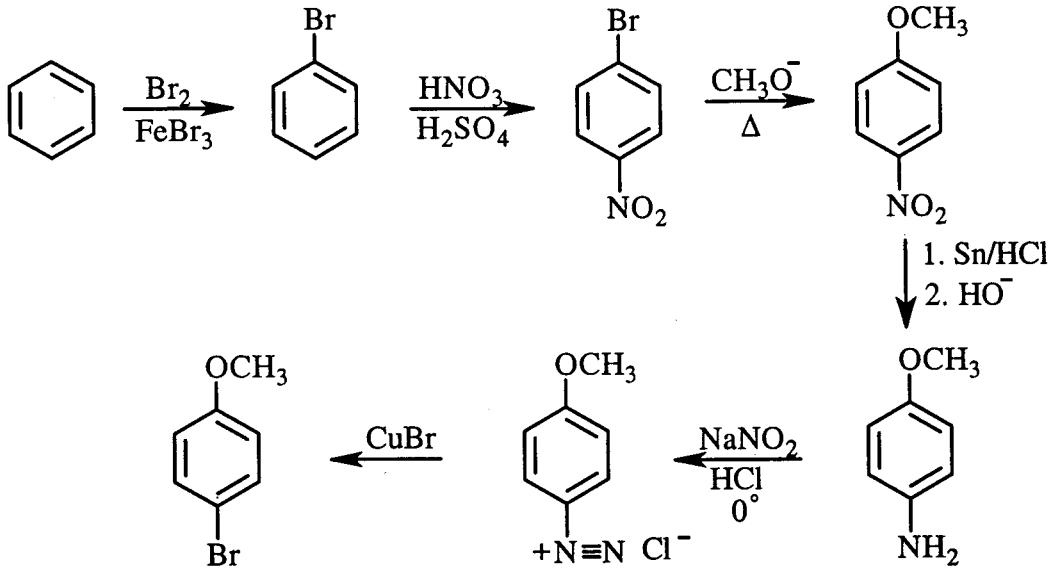
a.



b.

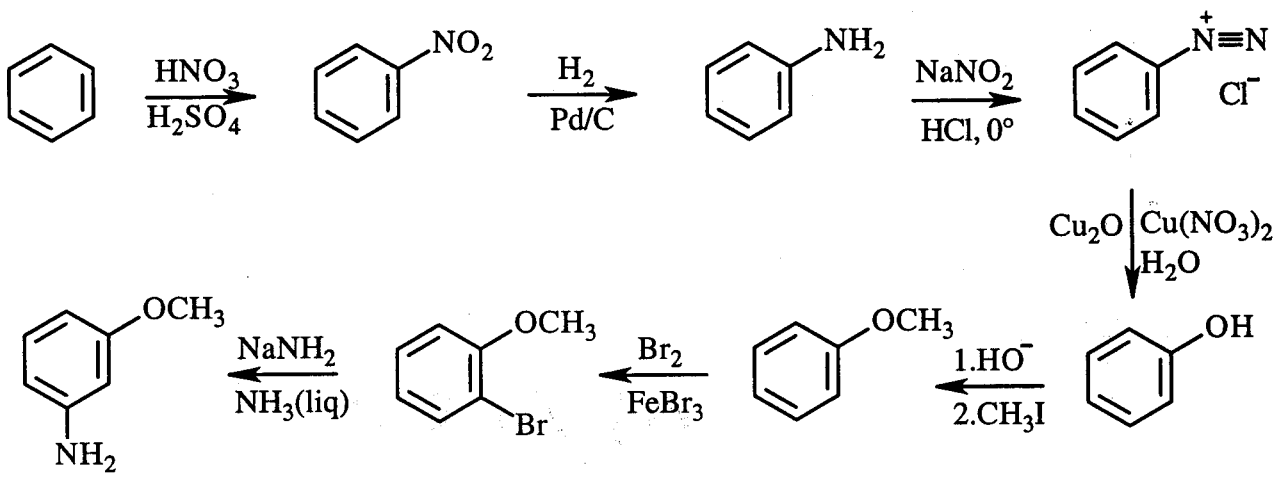


c.

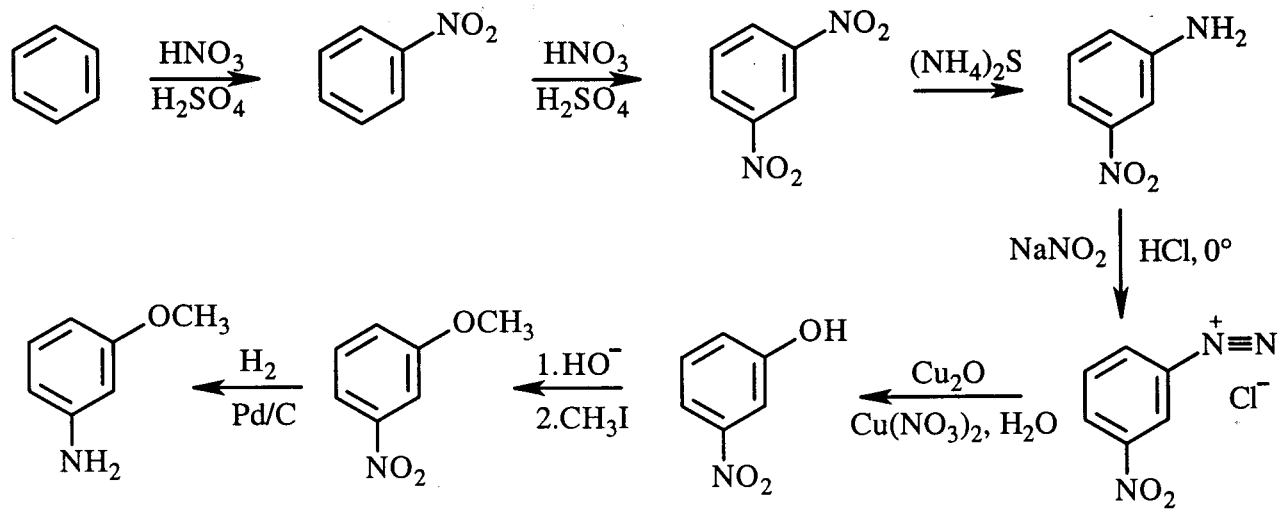

Br
Br2
FeBr3
HNO3
H2SO4
Br
NO2
CH3O−
Δ
OCH3
NO2
1. Sn/HCl
2. HO−
OCH3
NH2
NaNO2
HCl
0°
OCH3
+N≡N Cl−
CuBr
OCH3
Br

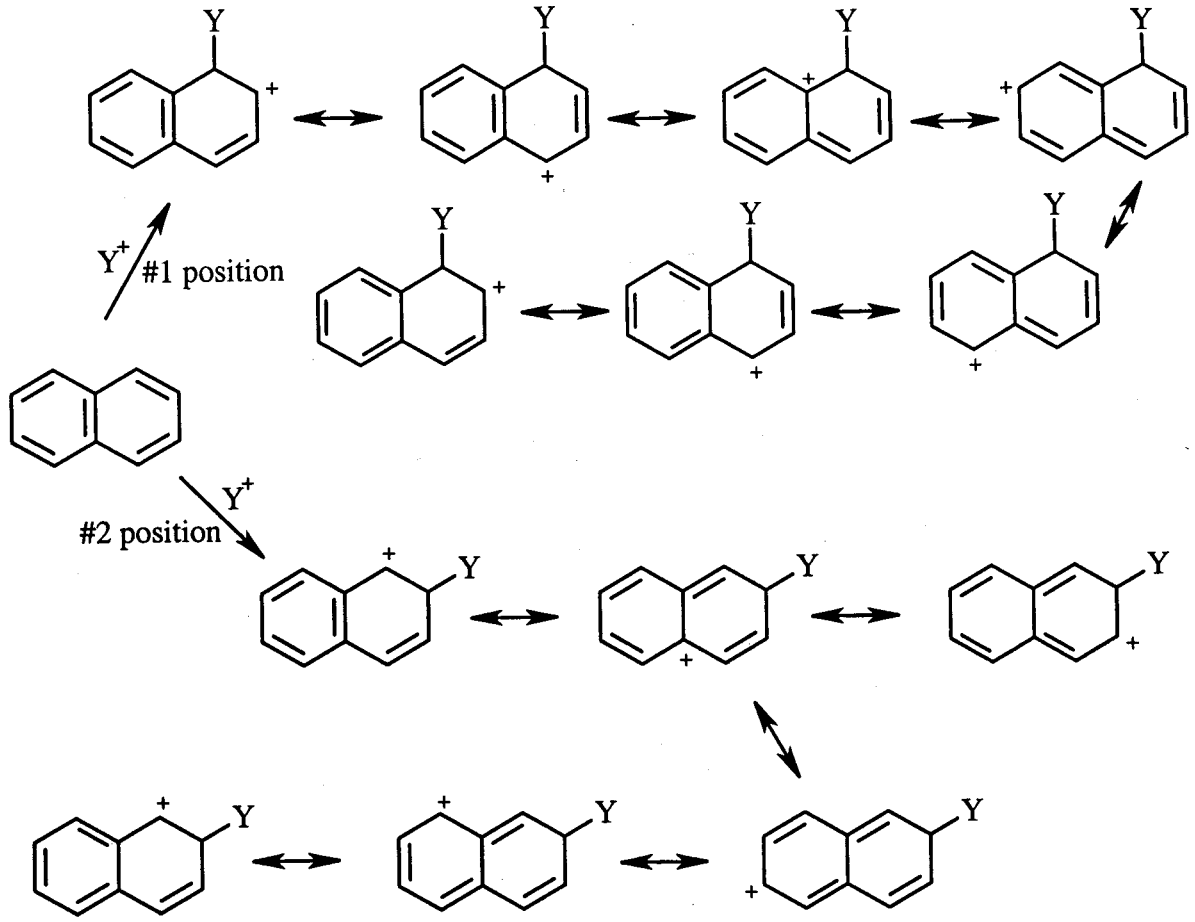
31.

a.


HNO3
H2SO4
NO2
H2
Pd/C
NH2
NaNO2
HCl, 0°
+N≡N
Cl−
Cu2O
Cu(NO3)2
H2O
OH
1.HO−
2.CH3I
OCH3
Br2
FeBr3
OCH3
Br
NaNH2
NH3(liq)
OCH3
NH2

b.


HNO3
H2SO4
NO2
HNO3
H2SO4
NO2
NO2
(NH4)2S
NH2
NO2
NaNO2
HCl, 0°
+N≡N
Cl−
NO2
Cu2O
Cu(NO3)2, H2O
OH
NO2
1.HO−
2.CH3I
OCH3
NO2
H2
Pd/C
OCH3
NH2



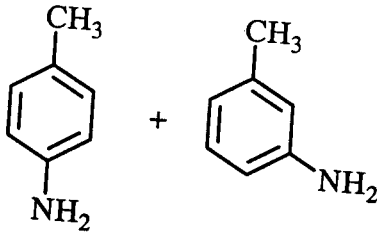
Substitution at the 1-position leads to a carbocation with seven resonance contributors; substitution at the 2-position leads to a carbocation with six resonance contributors.

Of the seven resonance contributors obtained from substitution at the 1-position, four are more stable than the others because they have an intact benzene ring.

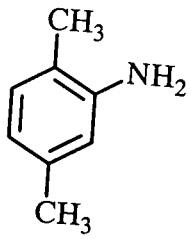
Of the six resonance contributors obtained from substitution at the 2-position, only two have an intact benzene ring. Substitution, therefore, is favored at the 1-position because the intermediate carbocation is more stable.

32.

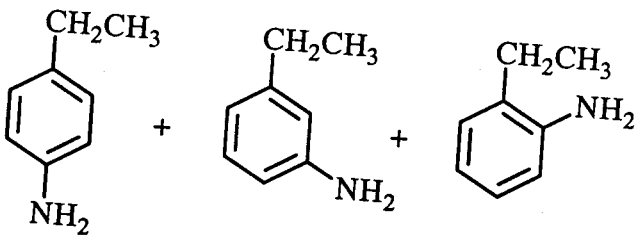
a.



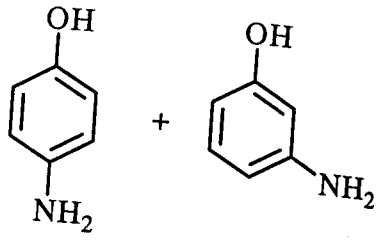
c.



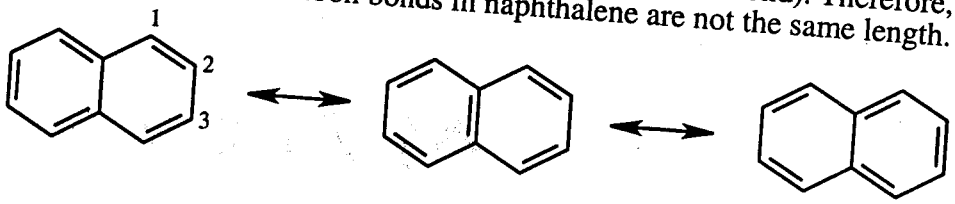
b.

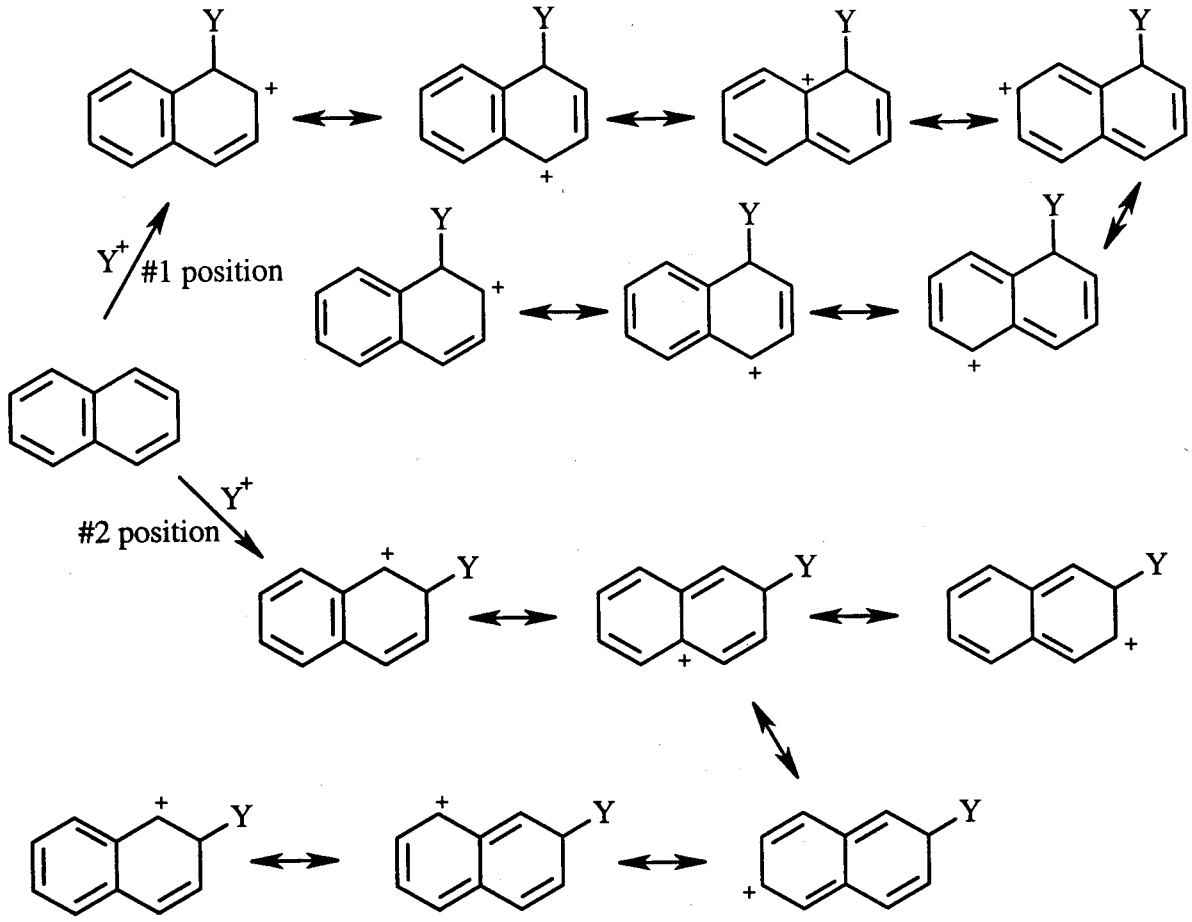


d.



33. From the resonance contributors, you can see that some bonds are approximated by *two double* bonds and *one single* bond (for example, the C1-C2 bond), whereas some are approximated by *one double* bond and *two single* bonds (for example, the C2-C3 bond). Therefore, we can conclude that all the carbon-carbon bonds in naphthalene are not the same length.

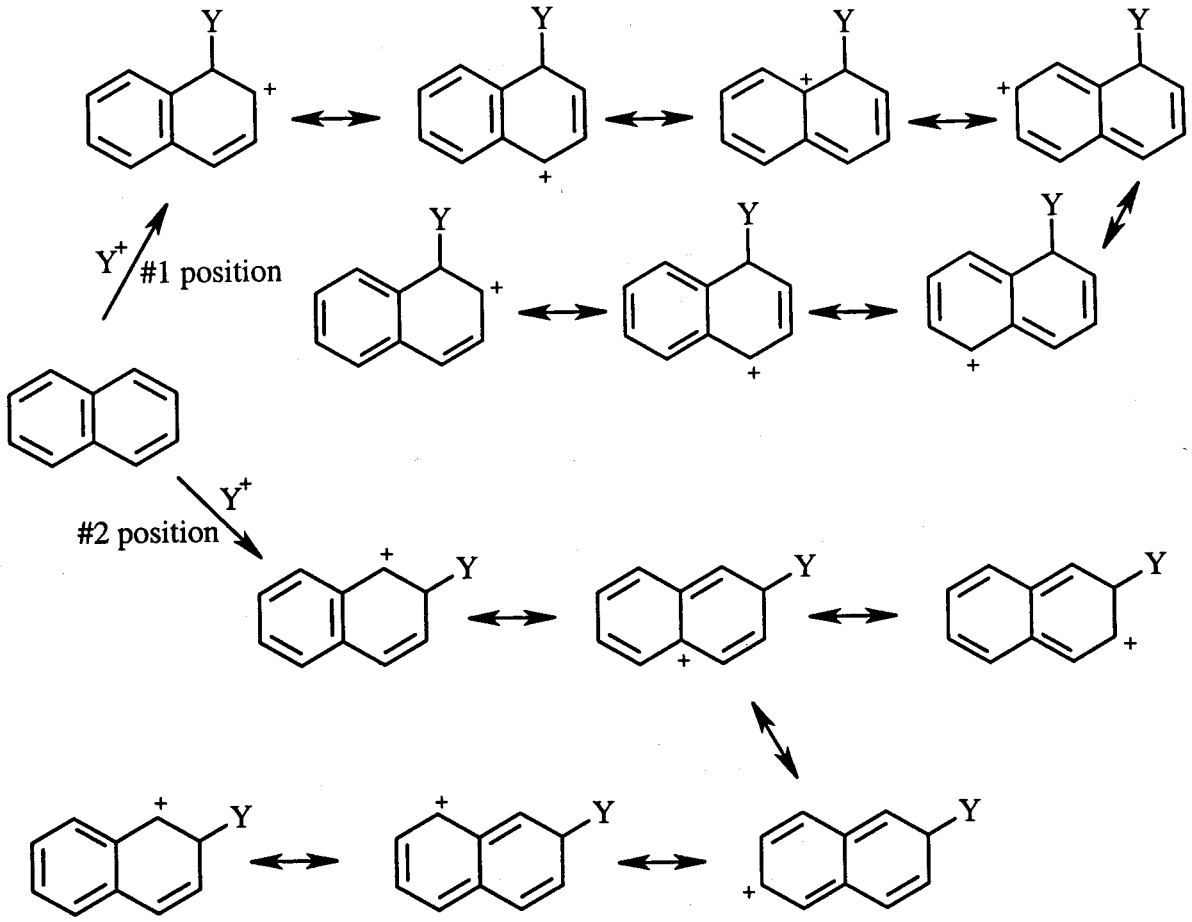




Substitution at the 1-position leads to a carbocation with seven resonance contributors; substitution at the 2-position leads to a carbocation with six resonance contributors.

Of the seven resonance contributors obtained from substitution at the 1-position, four are more stable than the others because they have an intact benzene ring.

Of the six resonance contributors obtained from substitution at the 2-position, only two have an intact benzene ring. Substitution, therefore, is favored at the 1-position because the intermediate carbocation is more stable.



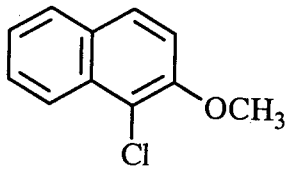
Substitution at the 1-position leads to a carbocation with seven resonance contributors; substitution at the 2-position leads to a carbocation with six resonance contributors.

Of the seven resonance contributors obtained from substitution at the 1-position, four are more stable than the others because they have an intact benzene ring.

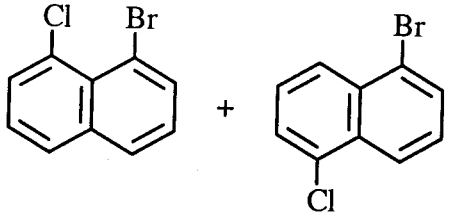
Of the six resonance contributors obtained from substitution at the 2-position, only two have an intact benzene ring. Substitution, therefore, is favored at the 1-position because the intermediate carbocation is more stable.

35.

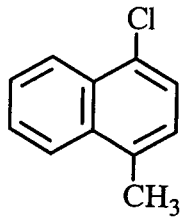
a.



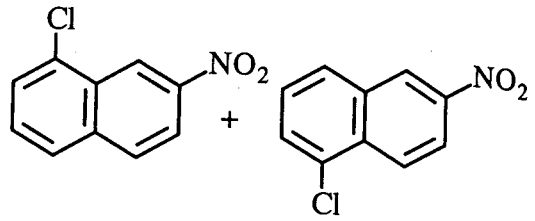
b.



c.

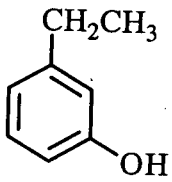


d.

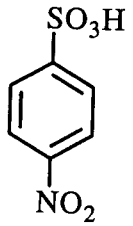


36.

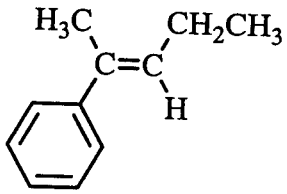
a.



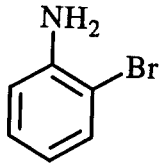
b.



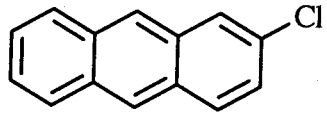
c.



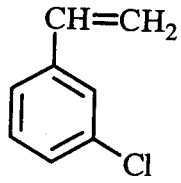
d.



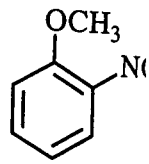
e.



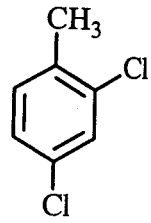
f.



g.

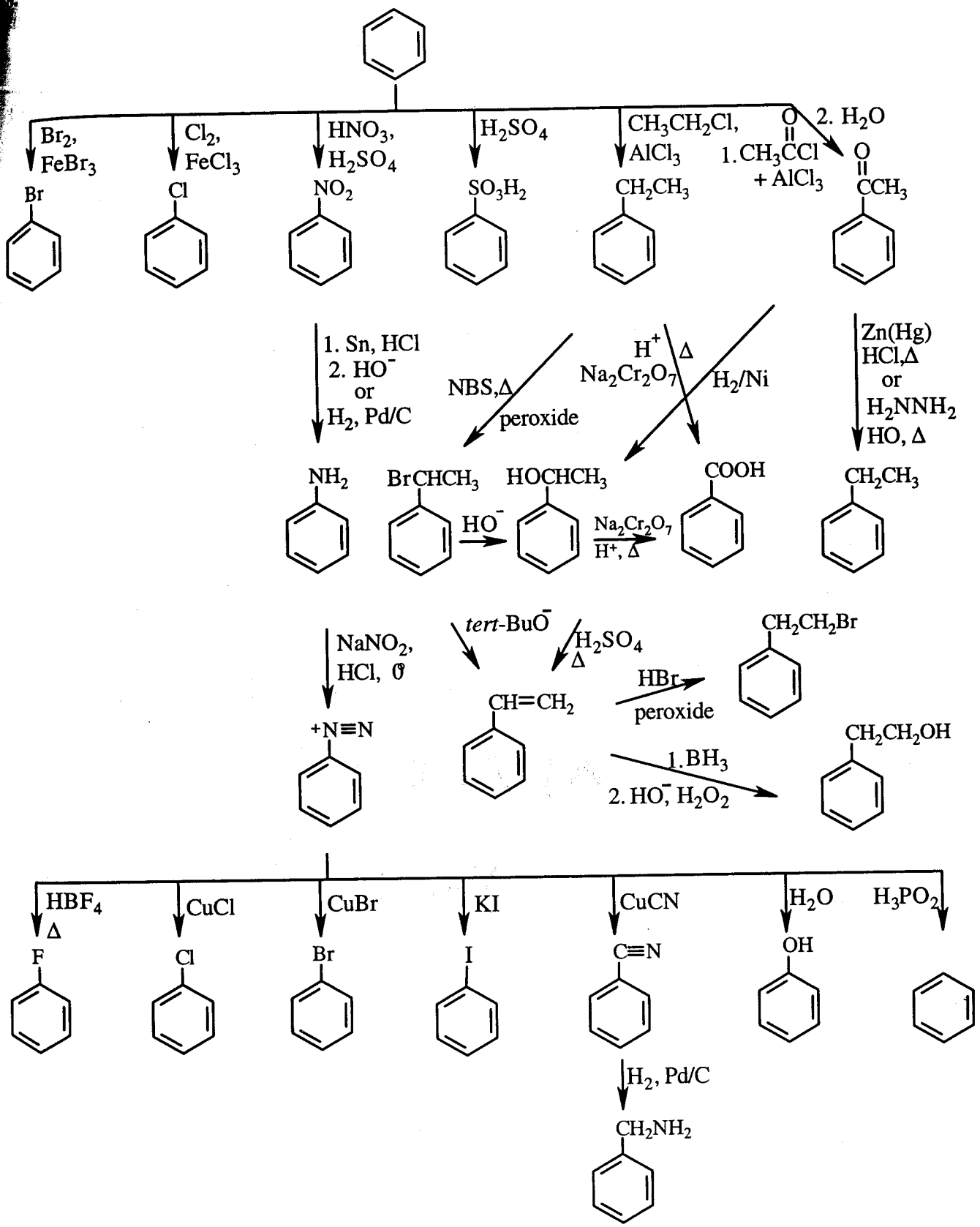


h.



37.

a. *m*-bromobenzoic acid
b. 1,2,4-tribromobenzene
c. 2,6-dimethylphenol
d. *p*-nitrostyrene
e. *m*-ethylanisole
f. 3,5-dichlorobenzenesulfonic acid
g. *o*-bromotoluene
h. *p*-cyclohexyltoluene
i. 2-chloro-4-ethylazobenzene


Br2, FeBr3
Cl2, FeCl3
HNO3, H2SO4
H2SO4
CH3CH2Cl, AlCl3
1. CH3CCl + AlCl3
2. H2O
Br
Cl
NO2
SO3H2
CH2CH3
CCH3
1. Sn, HCl
2. HO⁻
or
H2, Pd/C
NBS, Δ
peroxide
H+
Na2Cr2O7
Δ
H2/Ni
Zn(Hg)
HCl, Δ
or
H2NNH2
HO, Δ
NH2
BrCHCH3
HOCHCH3
HO⁻
Na2Cr2O7
H+, Δ
COOH
CH2CH3
NaNO2,
HCl, 0°
tert-BuO⁻
H2SO4
Δ
CH=CH2
HBr
peroxide
CH2CH2Br
+N≡N
1. BH3
2. HO⁻, H2O2
CH2CH2OH
HBF4
Δ
CuCl
CuBr
KI
CuCN
H2O
H3PO2
F
Cl
Br
I
C≡N
OH
H2, Pd/C
CH2NH2

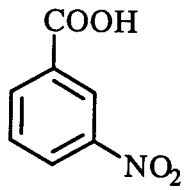
39. The chloro substituent primarily withdraws electrons inductively. (It only minimally donates electrons by resonance.) The closer it is to the COOH group, the more it can withdraw electrons from the OH bond and the stronger the acid.

The nitro substituent withdraws electrons inductively. It also withdraws electrons by resonance if it is ortho or para to the COOH group. Therefore, the ortho and para isomers are the strongest acids, and the ortho isomer is a stronger acid than the para isomer because of the greater inductive electron withdrawal from the closer position.

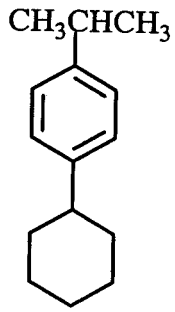
The amino substituent primarily donates electrons by resonance, but it can donate electrons by resonance to the COOH group only if it is ortho or para to it. From the pK_a values it is apparent that resonance electron donation to the COOH group is more efficient from the ortho position.

40.

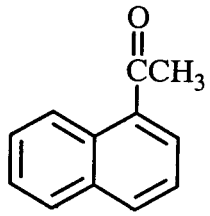
a.



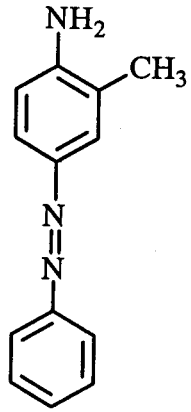
b.



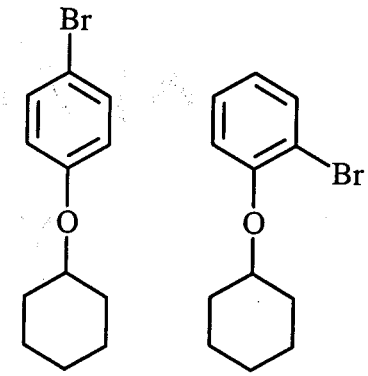
c.



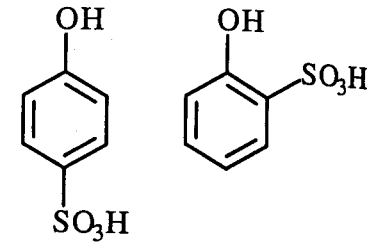
d.



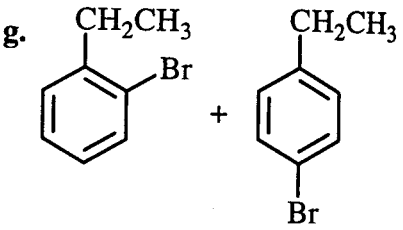
e.



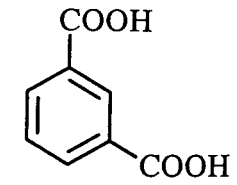
f.



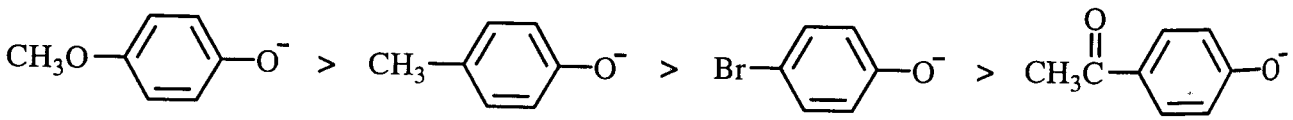
g.



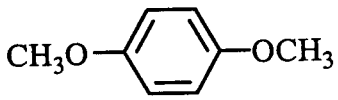
h.



41.

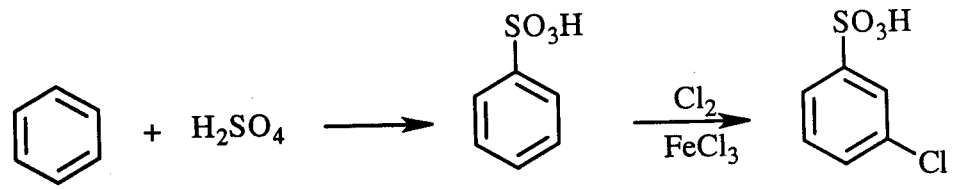


42.

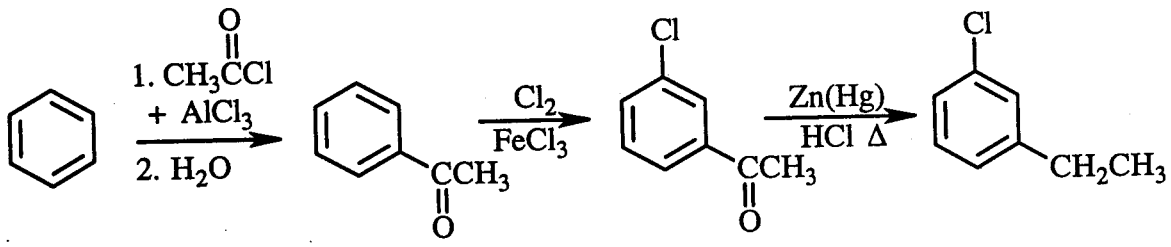

CH3O
OCH3

43.

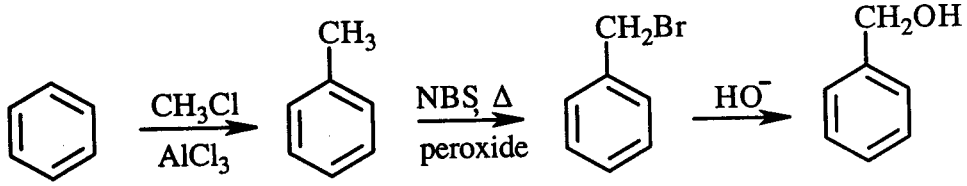
a.


+ H2SO4
SO3H
Cl2
FeCl3
SO3H
Cl

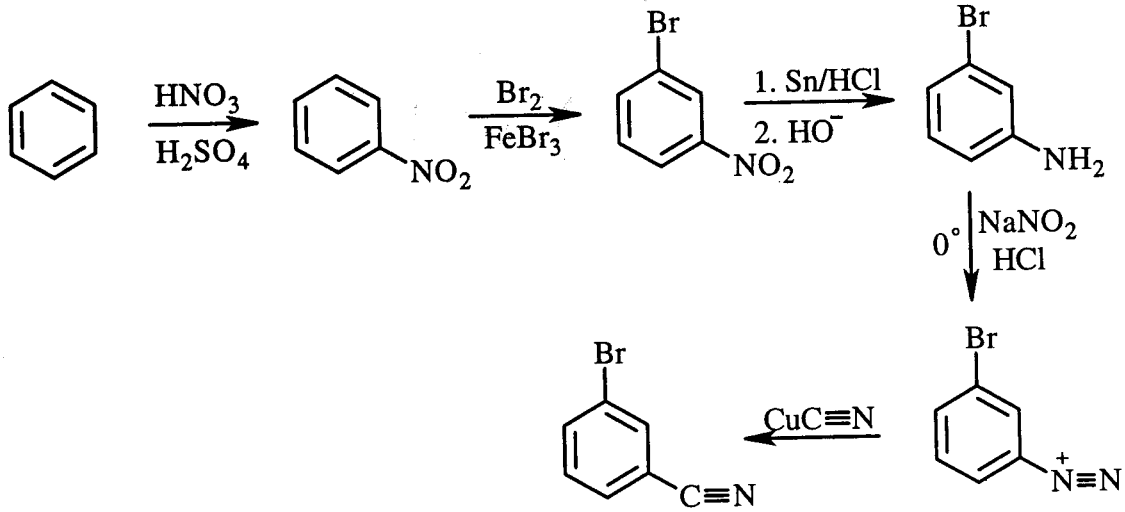
b.


O
1. CH3CCl
+ AlCl3
2. H2O
CCH3
O
Cl2
FeCl3
Cl
CCH3
O
Zn(Hg)
HCl Δ
Cl
CH2CH3

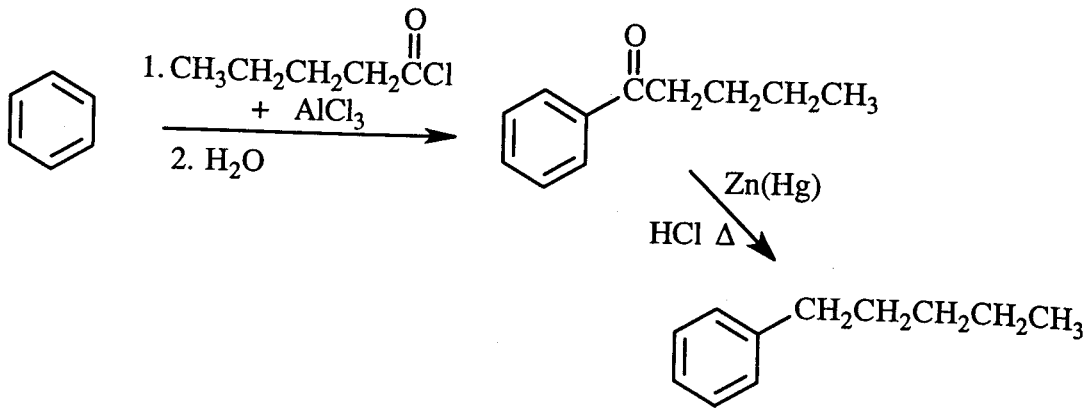
c.


CH3Cl
AlCl3
CH3
NBS, Δ
peroxide
CH2Br
HO⁻
CH2OH

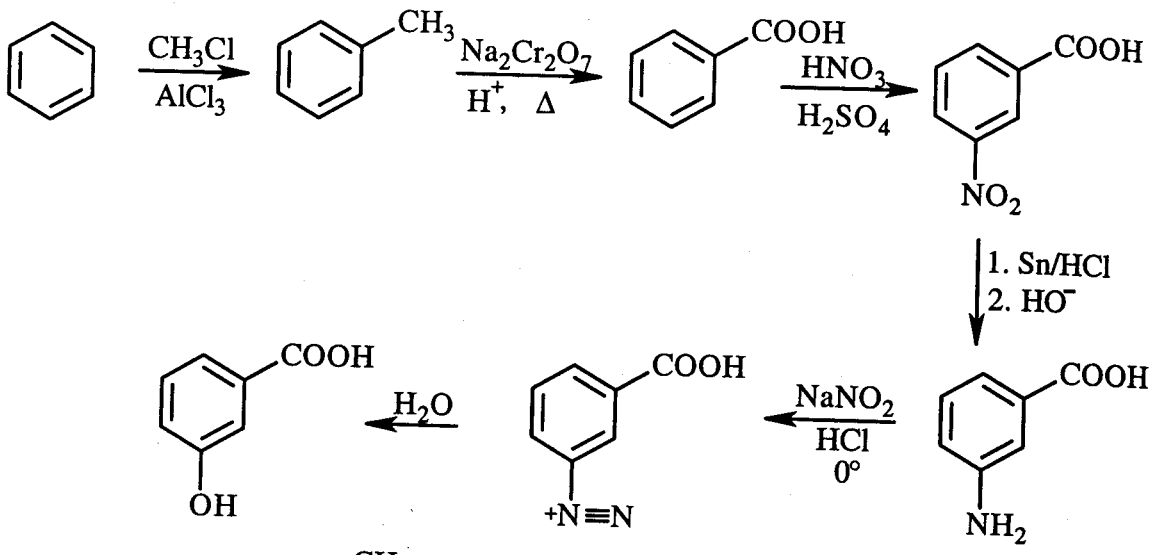
d.


HNO3
H2SO4
NO2
Br2
FeBr3
Br
NO2
1. Sn/HCl
2. HO⁻
Br
NH2
0°
NaNO2
HCl
Br
+
N≡N
CuC≡N
Br
C≡N

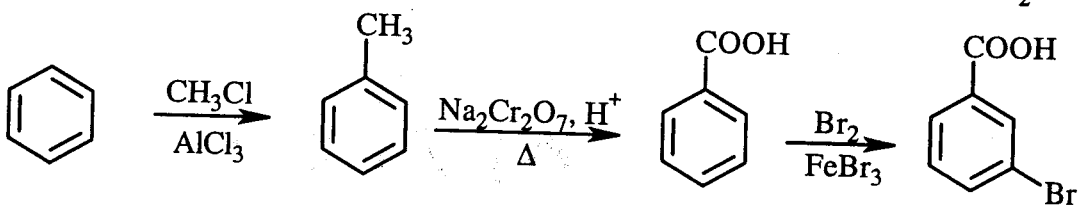
e.


1. CH3CH2CH2CH2CCl
+ AlCl3
2. H2O
CCH2CH2CH2CH3
Zn(Hg)
HCl Δ
CH2CH2CH2CH2CH3

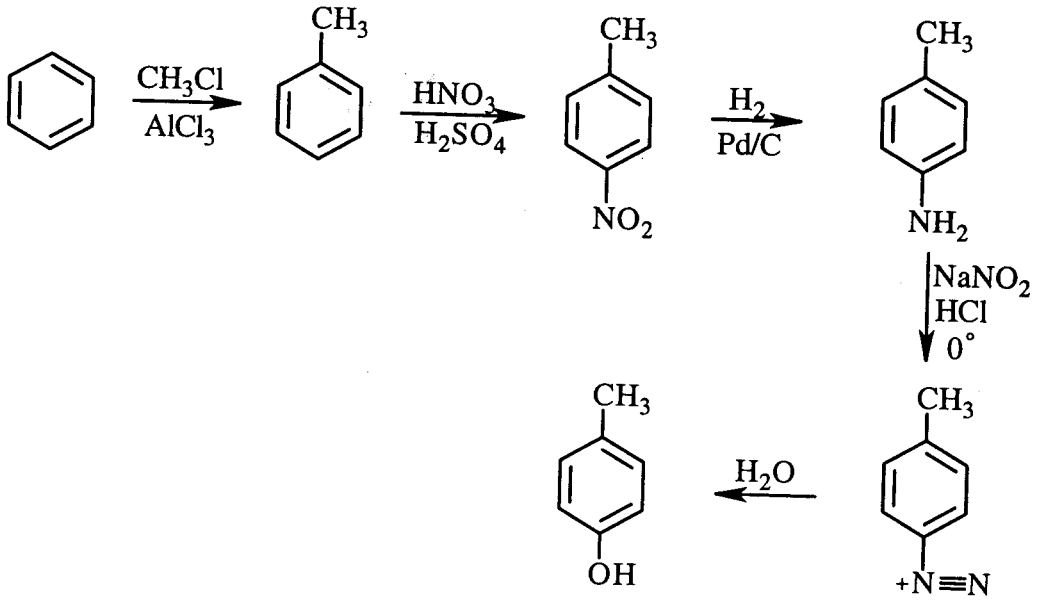
f.


CH3Cl
AlCl3
CH3
Na2Cr2O7
H+, Δ
COOH
HNO3
H2SO4
NO2
1. Sn/HCl
2. HO-
NH2
NaNO2
HCl
0°
+N≡N
H2O
OH

g.

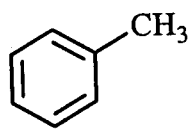

CH3Cl
AlCl3
CH3
Na2Cr2O7, H+
Δ
COOH
Br2
FeBr3
Br

h.

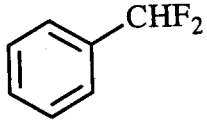

CH3Cl
AlCl3
CH3
HNO3
H2SO4
NO2
H2
Pd/C
NH2
NaNO2
HCl
0°
H2O
OH
+N≡N

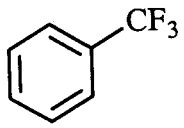
44.

1.



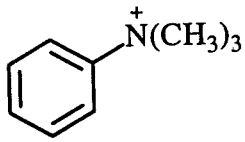
most reactive



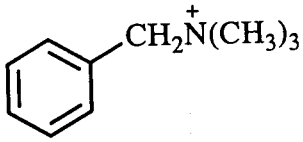


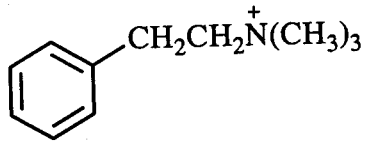
least reactive
highest % meta product

2.



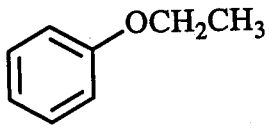
least reactive
highest % meta product



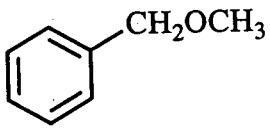


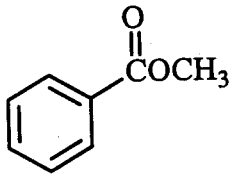
most reactive

3.



most reactive





least reactive
highest % meta product

45. **a.** anisole > ethylbenzene > benzene > chlorobenzene > nitrobenzene

b. 2,4-dinitrophenol > 2,4-dinitrotoluene > 1-chloro-2,4-dinitrobenzene

c. *p*-cresol > *p*-xylene > toluene > benzene

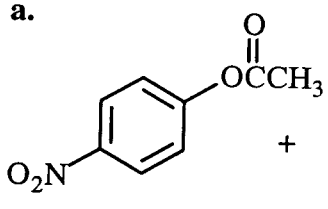
d. phenol > propylbenzene > benzene > benzoic acid

e. *p*-chlorotoluene > *p*-nitrotoluene > 2-chloro-4-nitrotoluene > 2,4-dinitrotoluene

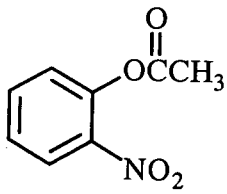
f. fluorobenzene > chlorobenzene > bromobenzene > iodobenzene

46.

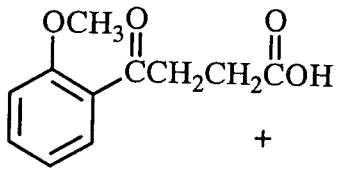
a.



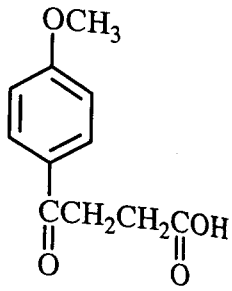
+



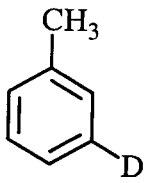
c.



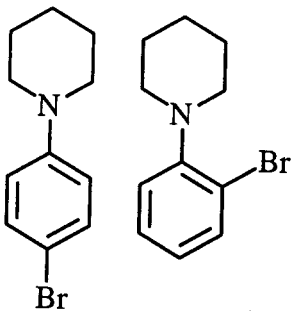
+



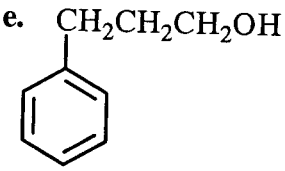
b.



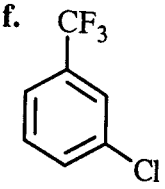
d.



e.



f.



47. **a.** CH_2CH_3 donates electrons inductively but does not donate or withdraw electrons by resonance.

b. NO_2 withdraws electrons inductively and withdraws electrons by resonance.

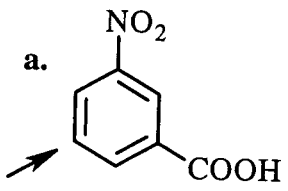
c. Br deactivates the ring and directs ortho/para.

d. OH withdraws electrons inductively, donates electrons by resonance, and activates the ring.

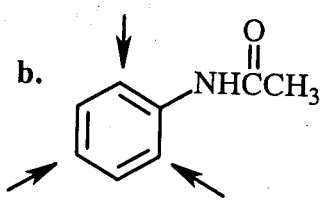
e. $^+NH_3$ withdraws electrons inductively but does not donate or withdraw electrons by resonance.

48.

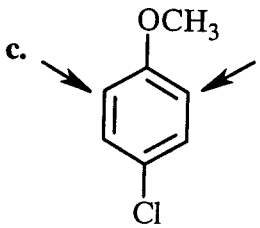
a.



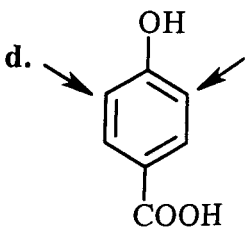
b.



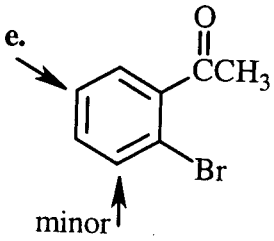
c.



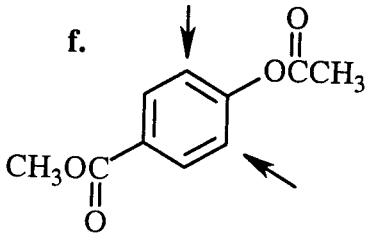
d.



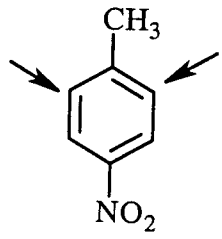
e.



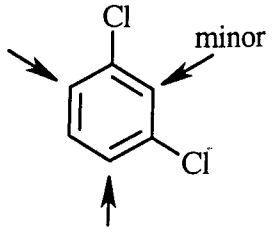
f.

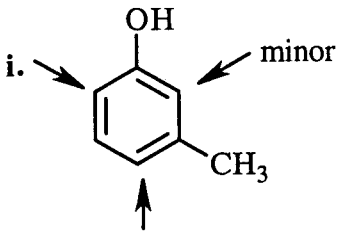


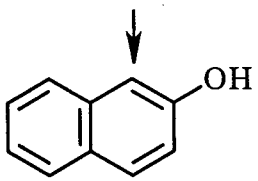
g.

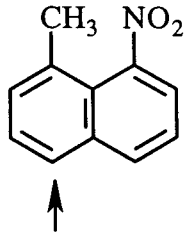


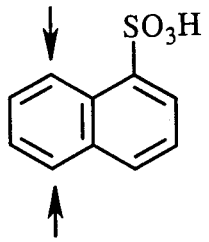
h.



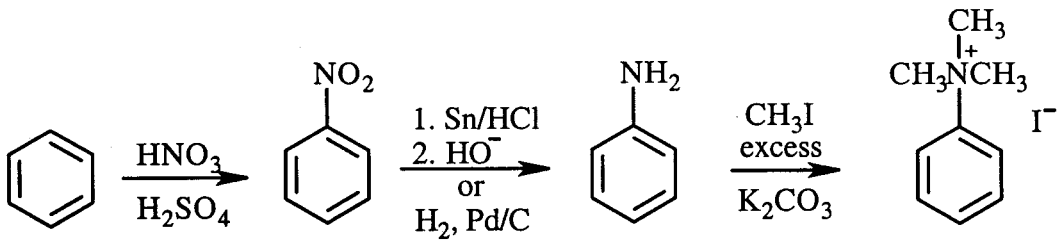
i. 
OH
minor
CH3

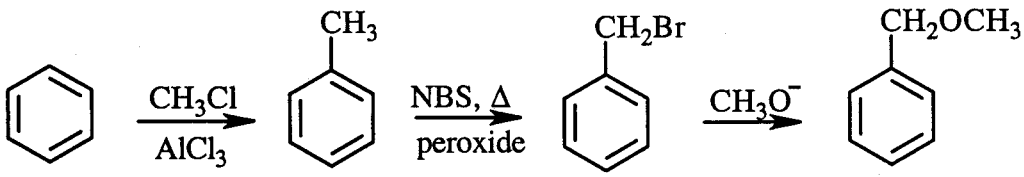
j. 
OH

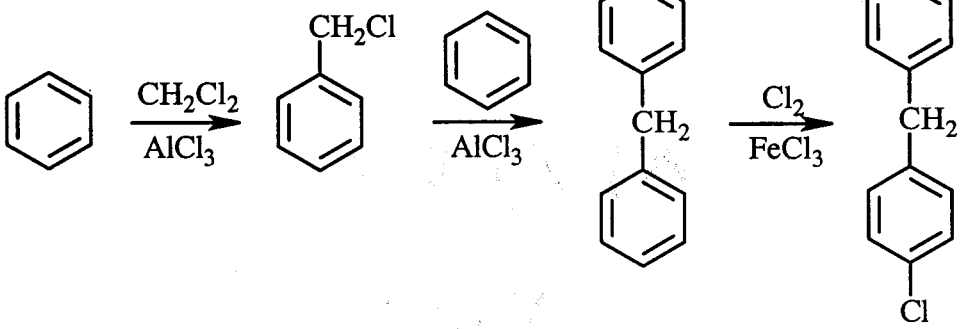
k. 
CH3
NO2

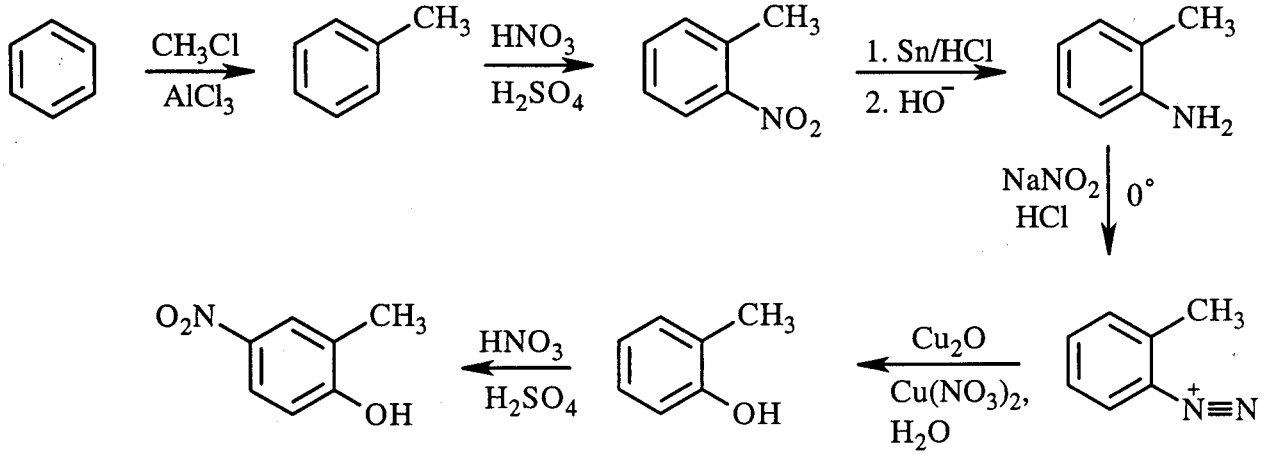
l. 
SO3H

49.

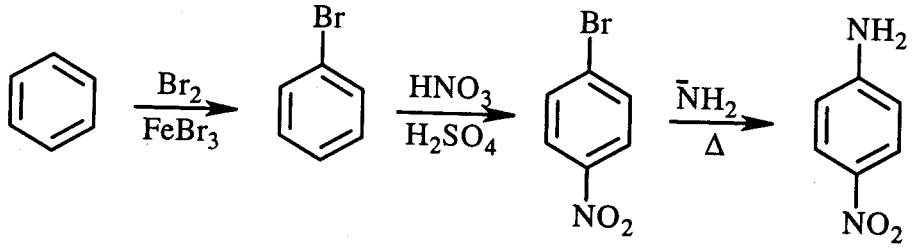
a. 
HNO3
H2SO4
NO2
1. Sn/HCl
2. HO−
or
H2, Pd/C
NH2
CH3I
excess
K2CO3
CH3
CH3NCH3
I−

b. 
CH3Cl
AlCl3
CH3
NBS, Δ
peroxide
CH2Br
CH3O−
CH2OCH3

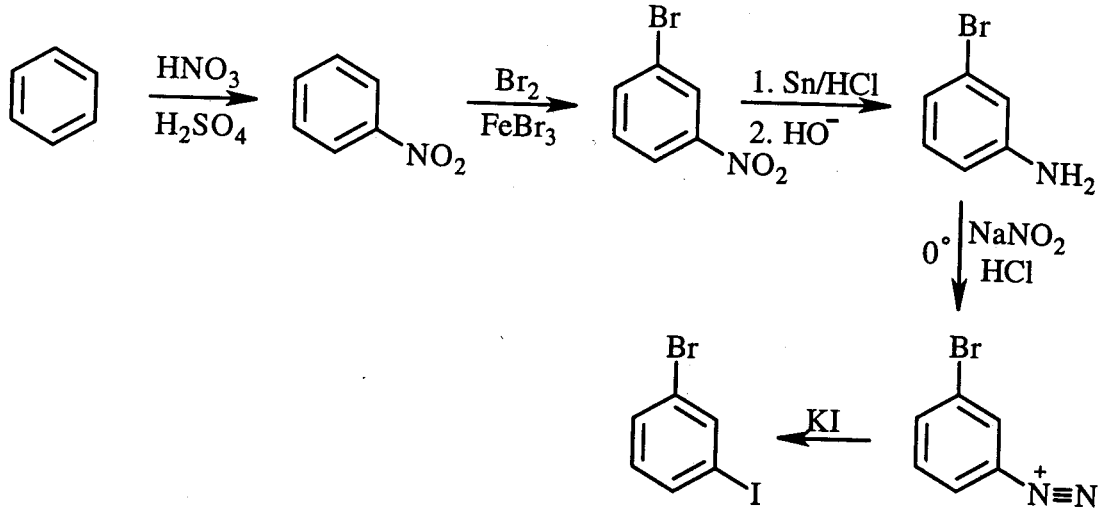
c. 
CH2Cl2
AlCl3
CH2Cl
AlCl3
CH2
Cl2
FeCl3
CH2
Cl

d. 
CH3Cl
AlCl3
CH3
HNO3
H2SO4
CH3
NO2
1. Sn/HCl
2. HO−
CH3
NH2
NaNO2
HCl
0°
CH3
N≡N
Cu2O
Cu(NO3)2,
H2O
CH3
OH
HNO3
H2SO4
O2N
CH3
OH

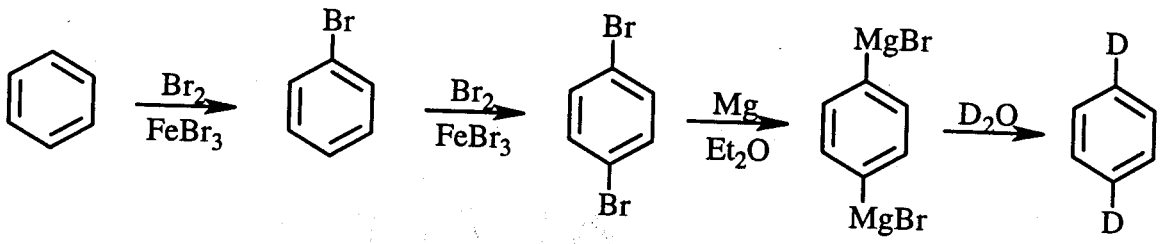
e.



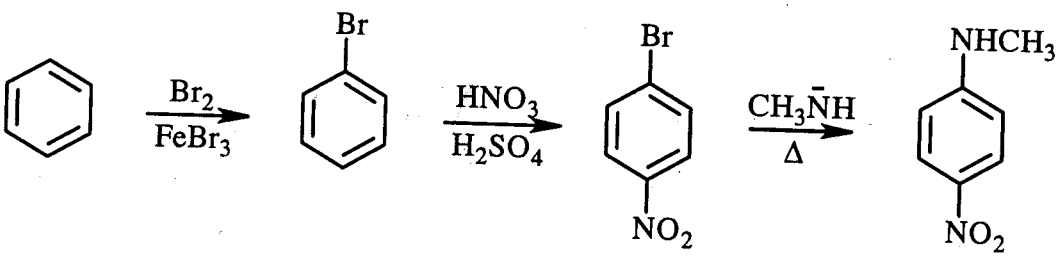
f.



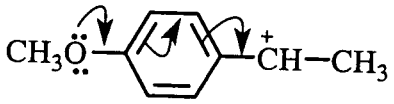
g.



h.

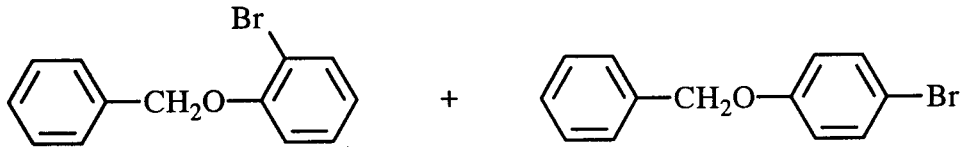


50. The compound with the methoxy substituent is the more reactive because it forms the more stable carbocation intermediate. The carbocation intermediate is stabilized by resonance electron donation.

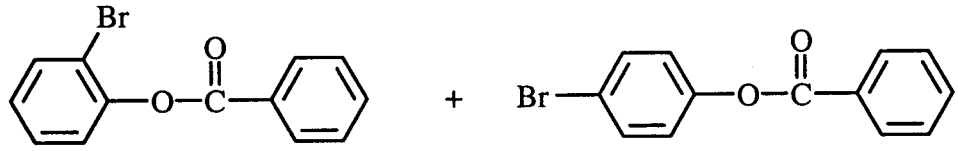


51. For each compound, determine which benzene ring is more highly activated. For example, in "**a**", the ring on the left is deactivated by the oxygen because it withdraws electrons inductively, whereas the ring on the right is activated by the oxygen because it donates electrons by resonance. Therefore, the ring on the right is more highly activated so it is the one that undergoes aromatic electrophilic substitution.

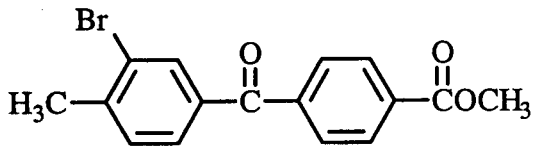
a.



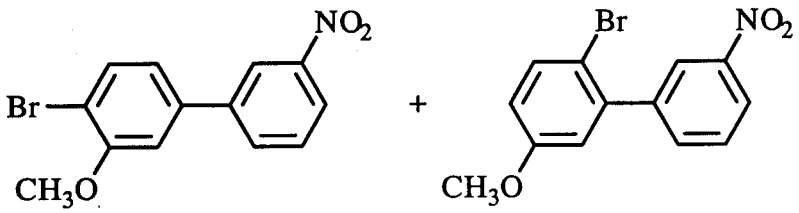
b.



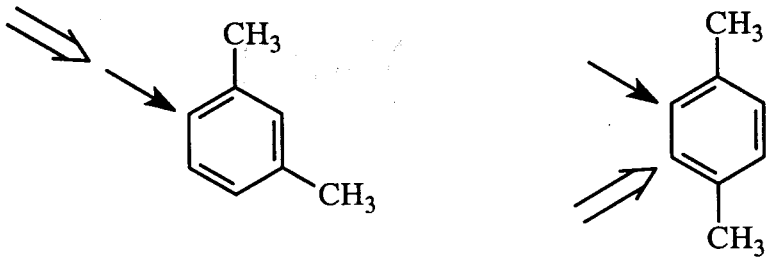
c.



d.

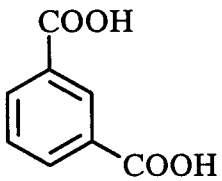


52. *Meta*-xylene will react more rapidly. In *meta*-xylene both methyl groups activate the same position, while in *para*-xylene each methyl group activates a different position.

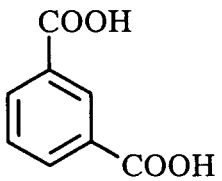


53.

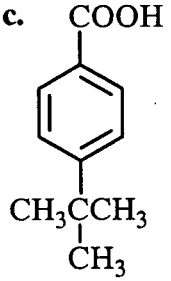
a.



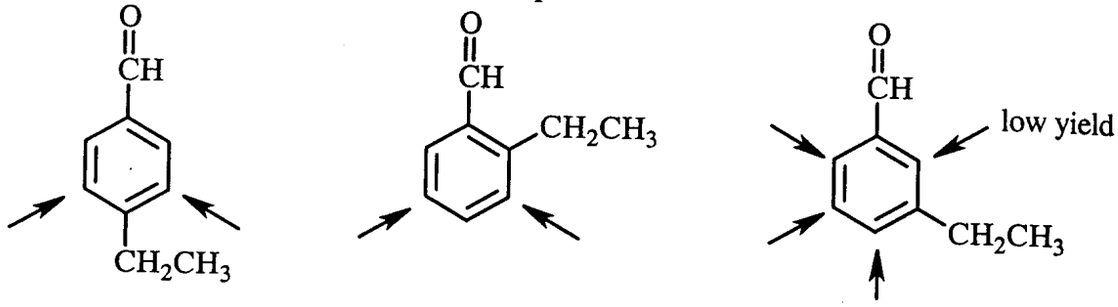
b.



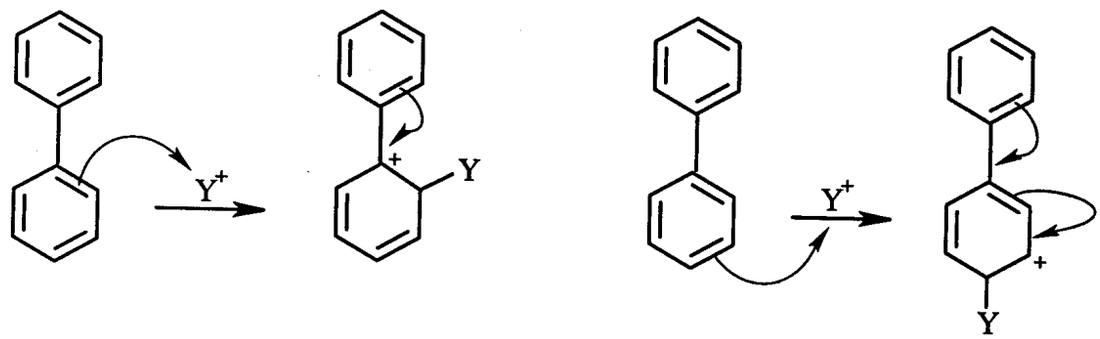
c.



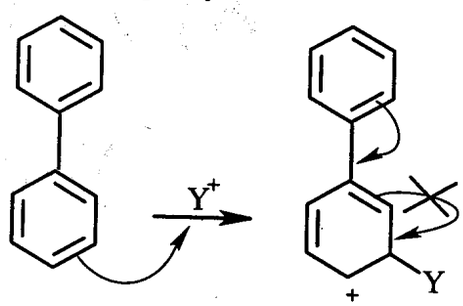
54. Yes, the advice is sound. The para isomer will form one product, because the formyl and ethyl groups direct to the same two positions and both positions result in the same product. The ortho isomer will form two products, because the formyl and ethyl groups direct to the same two positions but different products are obtained from each position. The meta isomer will form as many as four products, because the formyl and ethyl groups direct to four different positions and a different product is obtained from each position.



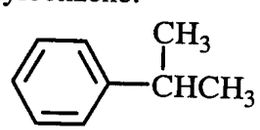
55. The carbocation formed by putting an electrophile at the ortho or para positions can be stabilized by resonance electron donation from the phenyl substituent.



The carbocation formed by putting an electrophile at the meta position cannot be stabilized by resonance electron donation from the phenyl substituent.



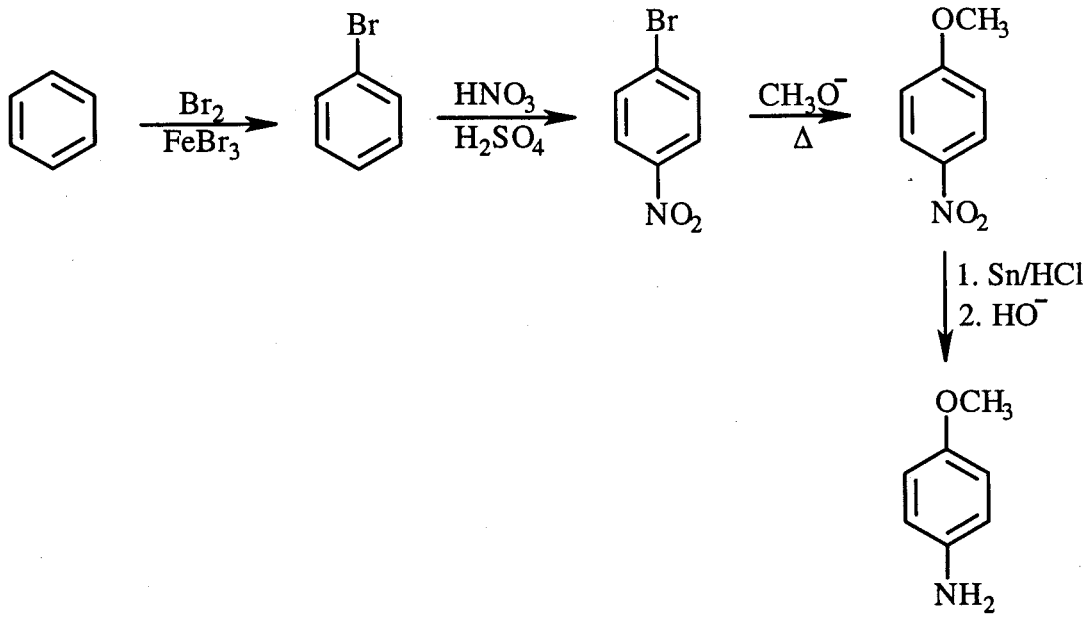
56. The spectrum indicates that the benzene ring has a substituent with two different kinds of hydrogens. The doublet and multiplet indicate that the substituent is an isopropyl group. Therefore, Compound A is isopropylbenzene.



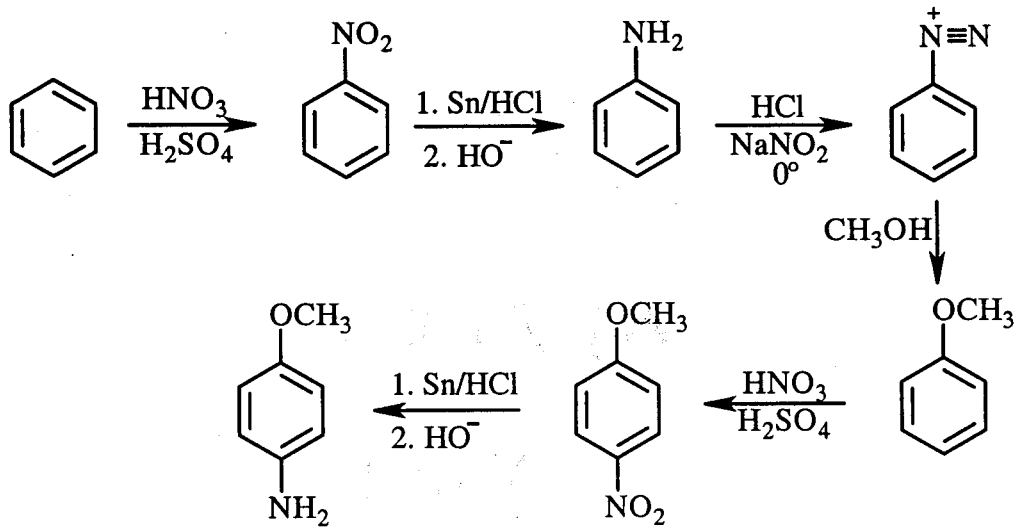
isopropylbenzene

57.

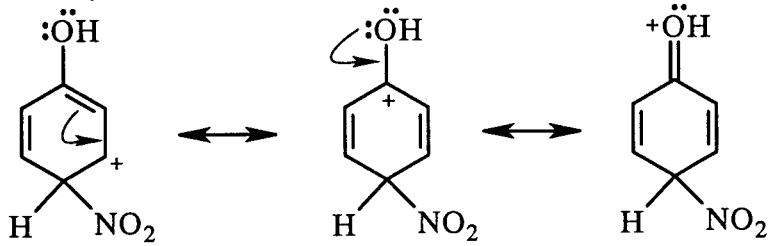
1.



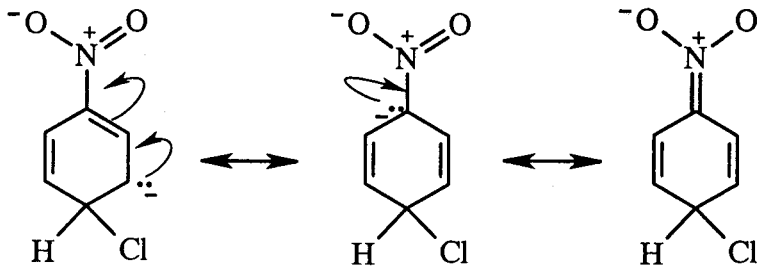
2.



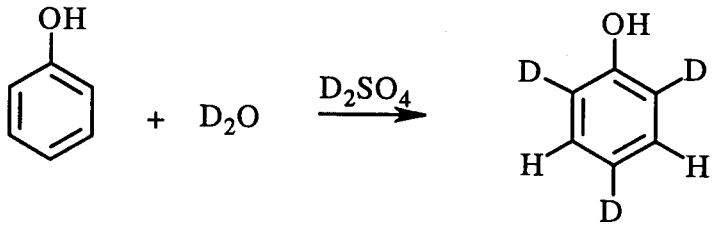
58. **a.** The hydroxy-substituted carbocation intermediate is more stable because the positive charge can be stabilized by resonance electron donation from the OH group.



b. The carbanion with the negative charge meta to the nitro group is more stable because a negative charge in the meta position can be delocalized onto the nitro group but a negative charge in the ortho position cannot.

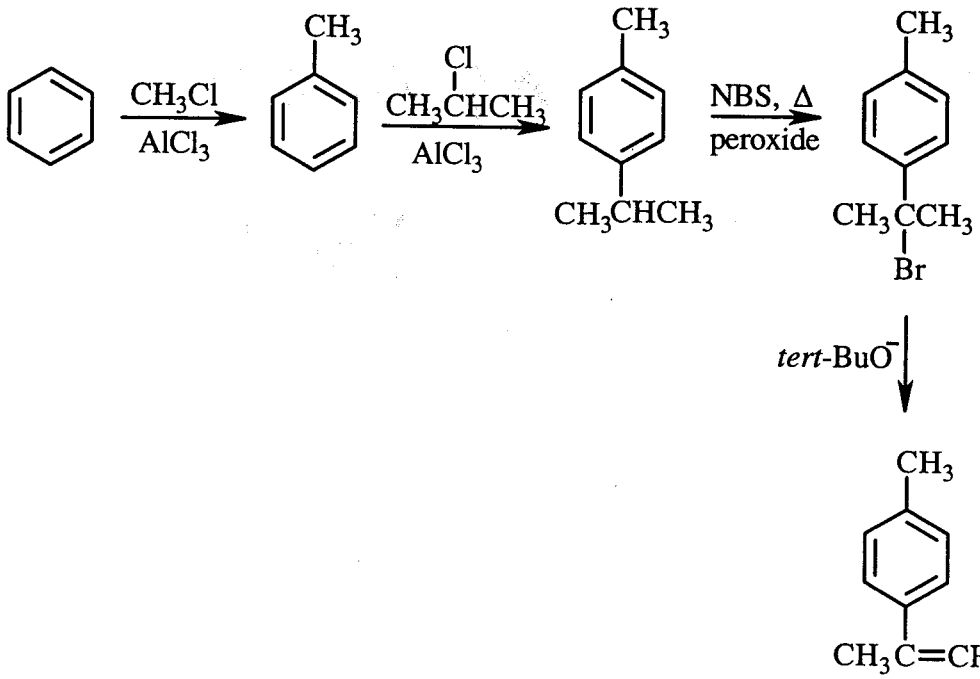


59. Phenol will undergo electrophilic aromatic substitution (D+ is the electrophile) primarily at the ortho and para positions.

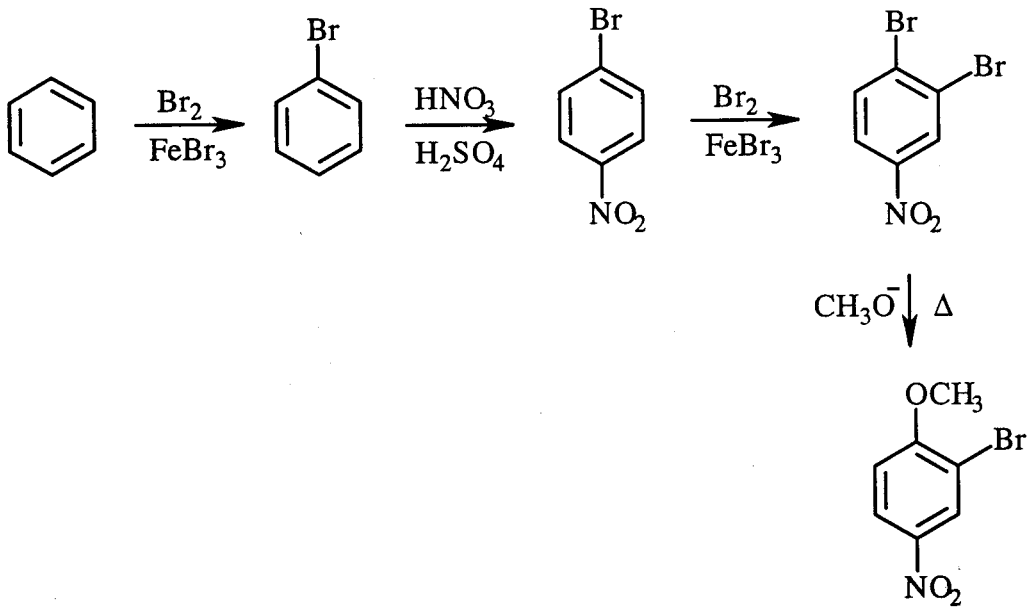


60.

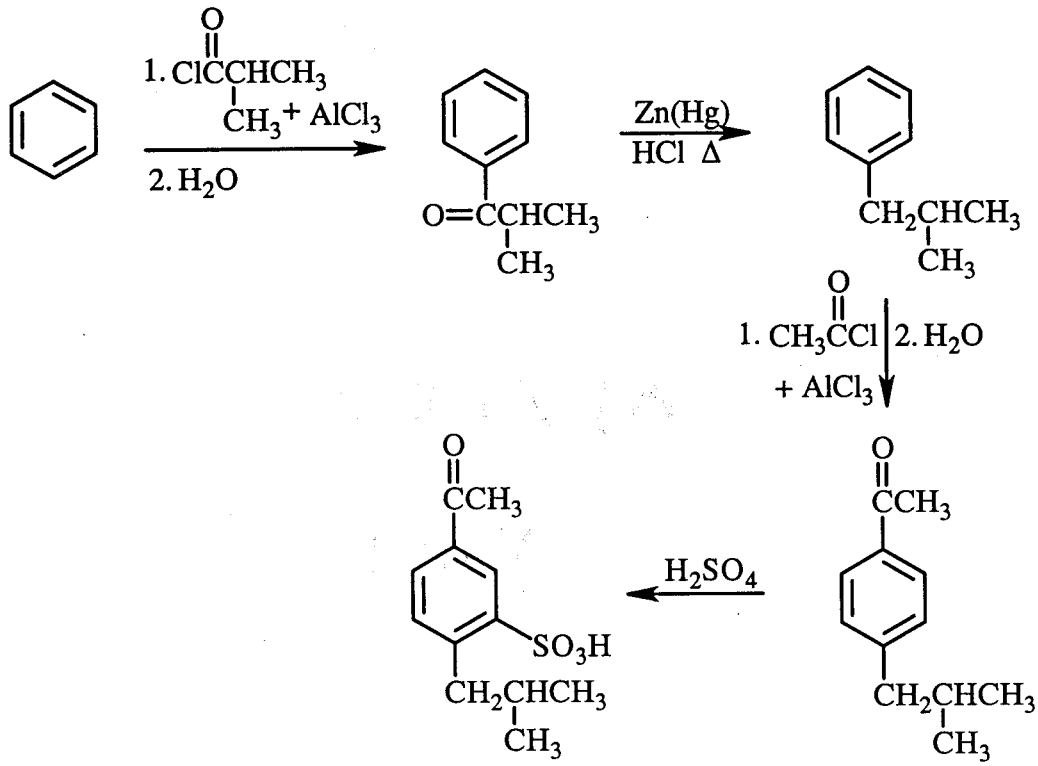
a.



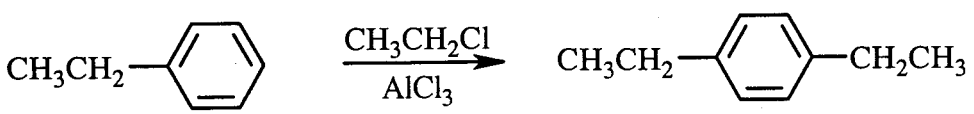
b.



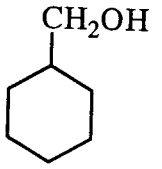
c.



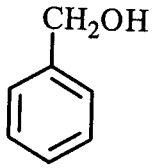
61. The unsplit signal at ~ 7.1 ppm suggests that all the hydrogens of the benzene ring in the product are chemically equivalent.



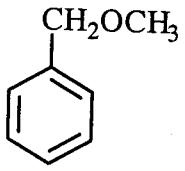
62. **a.** The first three compounds will not show a carbonyl stretch at 1700 cm^{-1} and the bottom four will show this absorption band. The first three can be differentiated from one another by the presence or absence of the indicated absorption bands.



band at 3300
no band at 1600

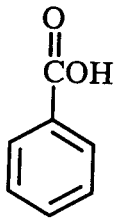


band at 3300
band at 1600

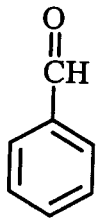


no band at 3300
band at 1600

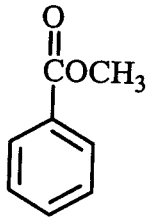
The last four compounds all have an absorption band at 1700 cm^{-1}.
They can be differentiated by the presence or absence of the indicated absorption bands.



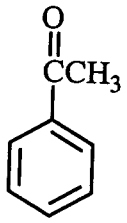
large band at ~3000
band at 1250
no band at 2700



no band at ~3000
no band at 1250
band at 2700

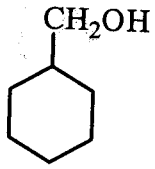


no band at ~3000
band at 1250
no band at 2700

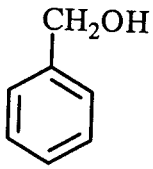


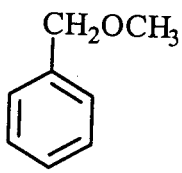
no band at ~3000
no band at 1250
no band at 2700

b. This is the only compound without the characteristic benzene ring hydrogens at ~ 7-8 ppm

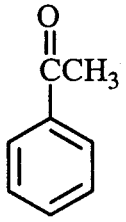


Only two compounds will have two signals other than the signals for the benzene ring hydrogens. They can be distinguished by integration (3:2 versus 2:1), or by the two sharp singlets for the ester, versus the somewhat broader singlet for the hydrogen bonded to oxygen.

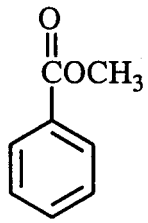




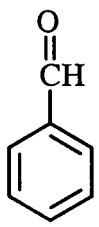
Each of the following four compounds has only one signal (a singlet) in addition to the benzene ring hydrogens. The four can be identified by the positions of the signals.



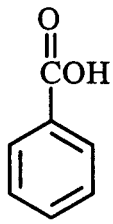
~ 2 ppm



~ 4 ppm

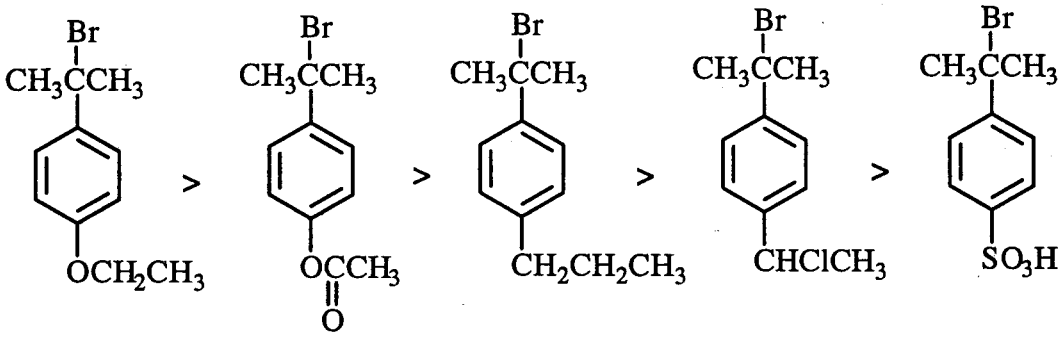


~ 9-10 ppm



~ 10-12 ppm

63. The rate-determining step in the S_N1 reaction is the formation of the tertiary carbocation. An electron-donating substituent will stabilize the carbocation and cause it to be more easily formed. An electron-withdrawing substituent will destabilize the carbocation and cause it to be less easily formed.

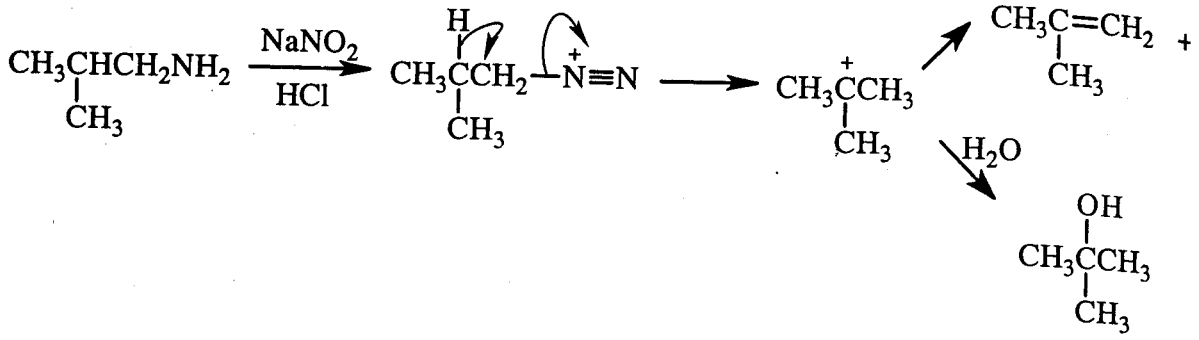


64. A fluoro substituent is more electronegative than a chloro substituent. Therefore, nucleophilic attack on the carbon bearing the fluoro substituent will be easier than nucleophilic attack on the carbon bearing the chloro substituent.

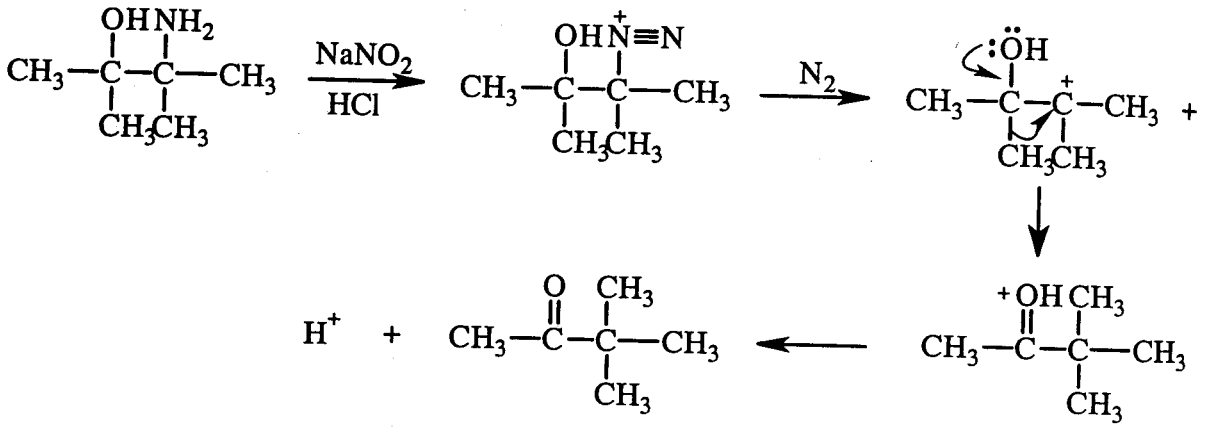
A fluoro substituent is a stronger base than a chloro substituent, so elimination of the halogen in the second step of the reaction will be harder for a fluoro-substituted benzene than for a chloro-substituted benzene.

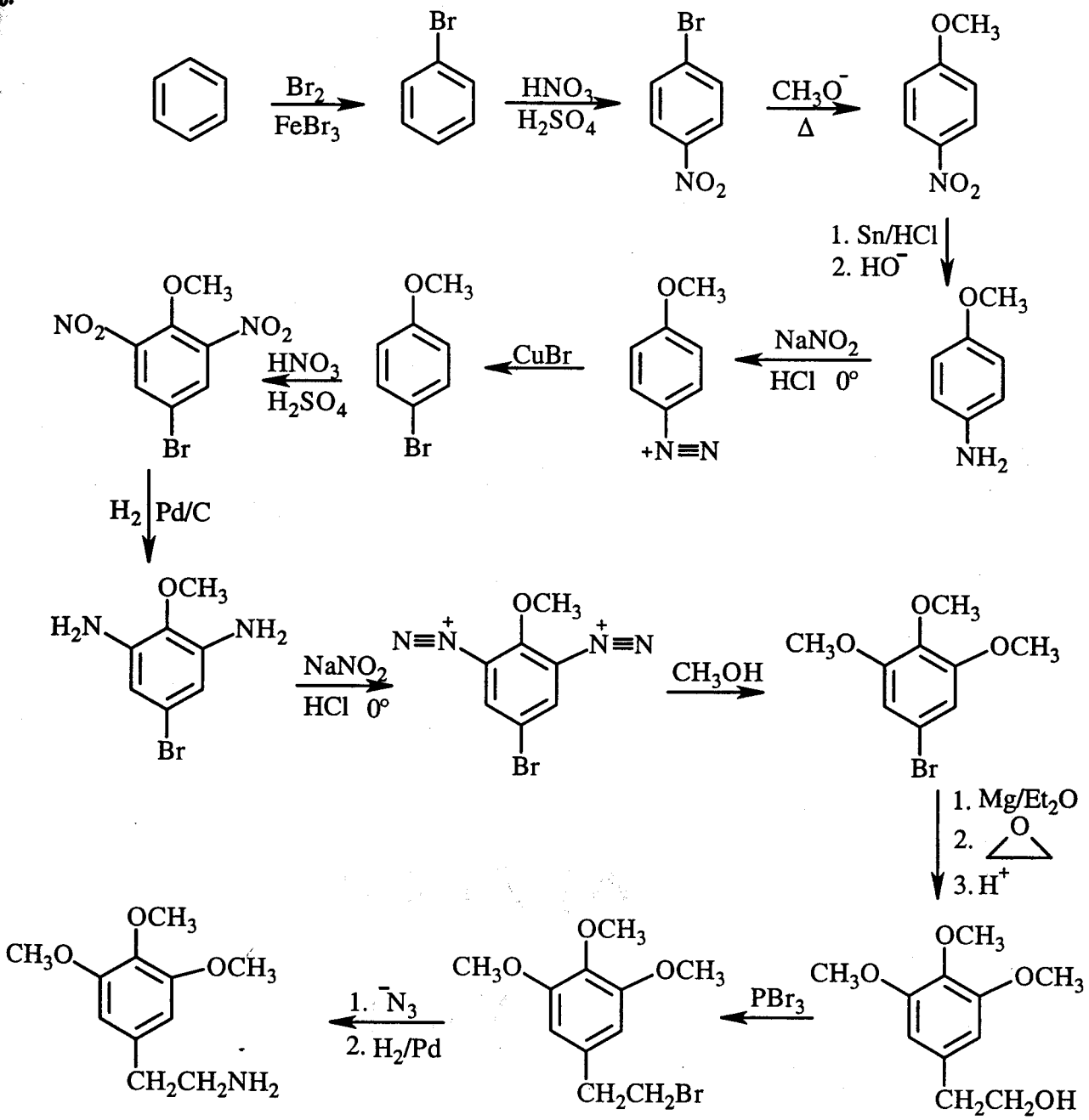
The fact that the fluoro-substituted compound is more reactive tells you that attack of the nucleophile on the aromatic ring is the rate-determining step of the reaction.

65. **a.** The alkyl diazonium ion is very unstable. Loss of N_2 and a 1,2-hydride shift forms a *tert*-butyl carbocation, which can undergo either substitution or elimination.

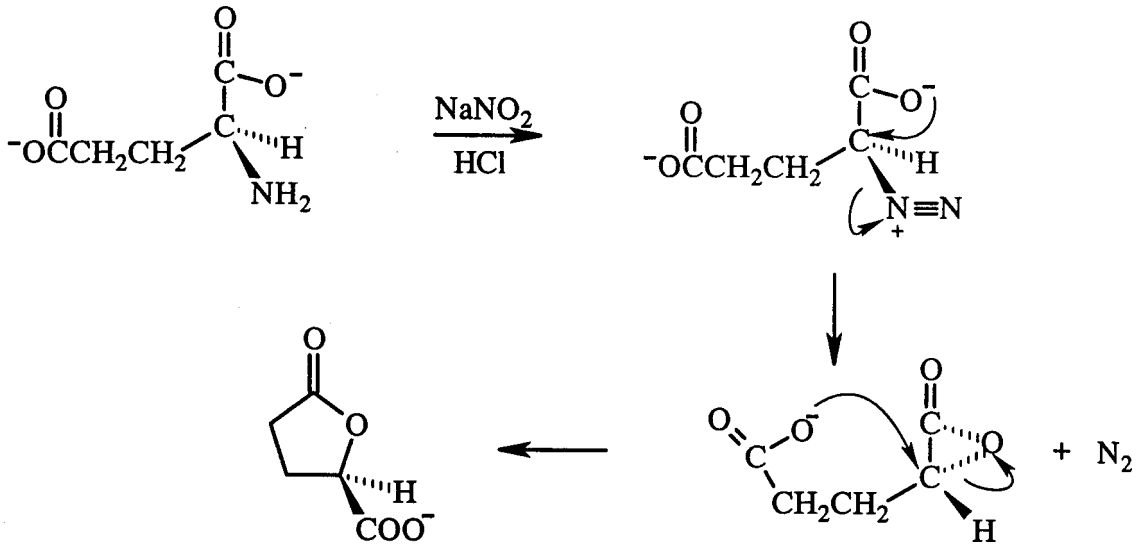


b. The cation formed from the diazonium ion will undergo a pinacol rearrangement.

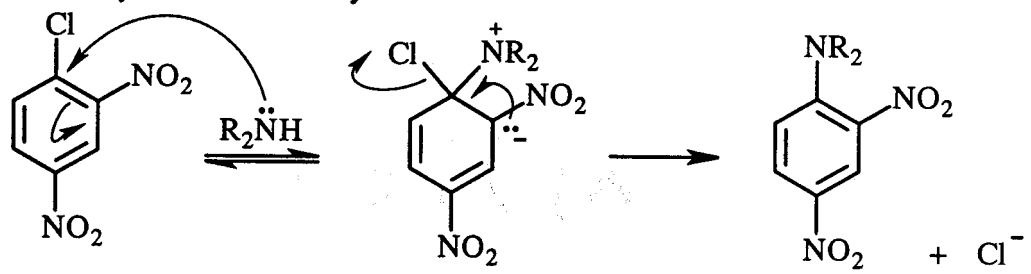



Br2
FeBr3
HNO3
H2SO4
CH3O-
Δ
OCH3
NO2
Br
1. Sn/HCl
2. HO-
NH2
NaNO2
HCl 0°
+N≡N
CuBr
HNO3
H2SO4
H2 Pd/C
NH2
H2N
1. -N3
2. H2/Pd
CH2CH2NH2
PBr3
CH2CH2Br
1. Mg/Et2O
2.
3. H+
CH2CH2OH
CH3O

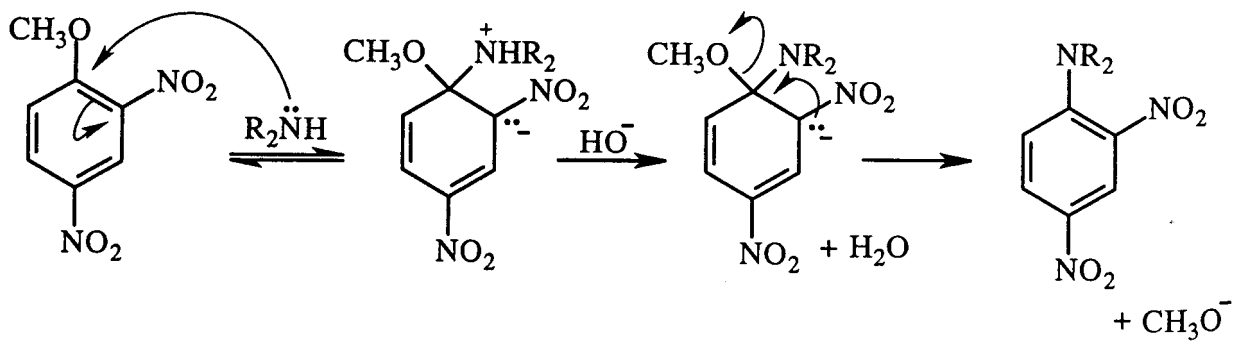
67. The configuration of the chirality center in the reactant will be retained only if the chirality center undergoes two successive S_N2 reactions.



68. A chloro group is a better leaving group than the ammonium group, so the product is formed without hydroxide ion catalysis.

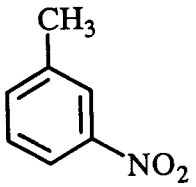


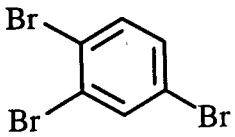
A methoxy group is a poorer leaving group than the ammonium group, so the ammonium group is eliminated, reforming starting materials. By removing a proton, hydroxide ion converts the ammonium group into an amino group. Since the amino group is a poorer leaving group than the methoxy group, the methoxy group is eliminated.

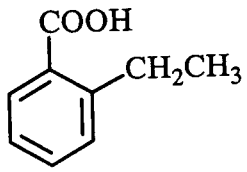


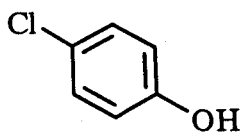
Chapter 16 Practice Test

1. Give one name for each of the following.

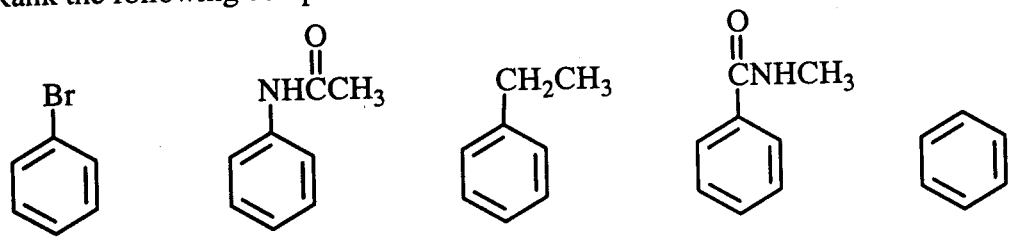
a. 

b. 

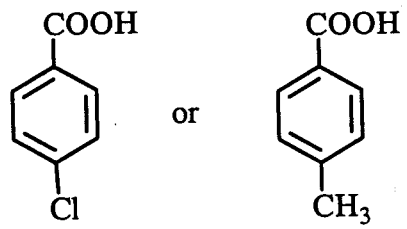
c. 

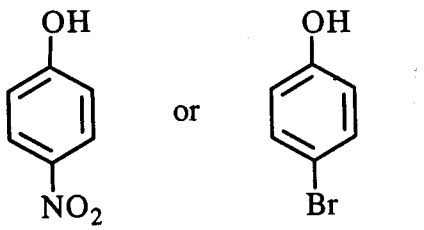
d. 

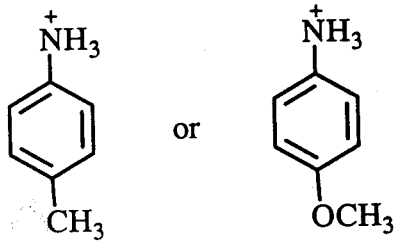
2. Rank the following compounds in order of decreasing reactivity toward $Br_2/FeBr_3$.

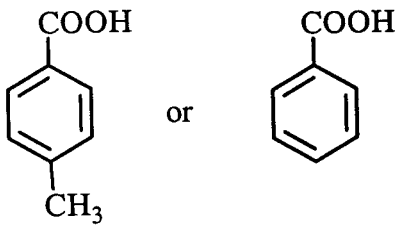


3. For each pair of compounds, indicate the one that is the stronger acid.

a. 

b. 

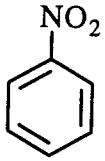
c. 

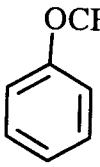
d. 

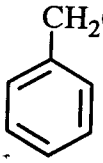
4. **a.** Which is more reactive in a nucleophilic substitution reaction, *para*-bromonitrobenzene or *para*-bromoethylbenzene?

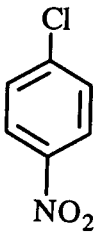
b. Which is more reactive in an electrophilic substitution reaction, *para*-bromonitrobenzene or *para*-bromoethylbenzene?

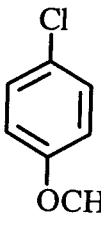
5. Give the major product(s) of each of the following reactions.

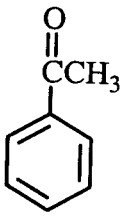
a.  + H_2SO_4 ⟶

b.  + CH_3Cl $\xrightarrow{AlCl_3}$

c.  $\xrightarrow[H^+,\ \Delta]{Na_2Cr_2O_7}$

d.  + CH_3O^- $\xrightarrow{\Delta}$

e.  + HNO_3 $\xrightarrow{H_2SO_4}$

f.  + Cl_2 $\xrightarrow{AlCl_3}$

6. Indicate whether each of the following statements is true or false.

a. Benzoic acid is more reactive than benzene towards electrophilic substitution. T F

b. *para*-Chlorobenzoic acid is more acidic than *para*-methoxybenzoic acid. T F

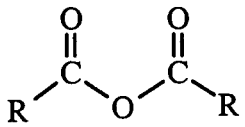
c. A —CH=CH_2 group is a meta director. T F

d. *para*-Nitroaniline is more basic than *para*-chloroaniline. T F

CHAPTER 17
Carbonyl Compounds I: Nucleophilic Acyl Substitution

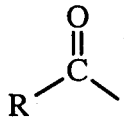
Important Terms

acid anhydride

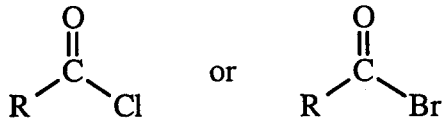


acyl adenylate a carboxylic acid derivative with AMP as the leaving group.

acyl group



acyl halide



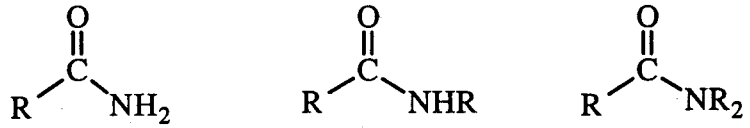
acyl phosphate a carboxylic acid derivative with a phosphate leaving group.

acyl pyrophosphate a carboxylic acid derivative with a pyrophosphate leaving group.

acyl transfer reaction a reaction that transfers an acyl substituent from one group to another.

alcoholysis reaction with an alcohol that converts one compound into two compounds.

amide



amino acid an α-amino carboxylic acid.

aminolysis reaction with an amine that converts one compound into two coompounds.

biosynthesis synthesis in a biological system.

α-carbon a carbon adjacent to a carbonyl group.

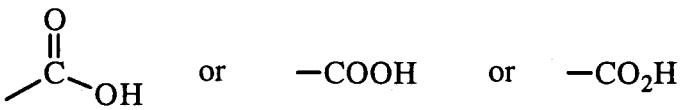
carbonyl carbon the carbon of a carbonyl group.

carbonyl compound a compound that contains a carbonyl group.

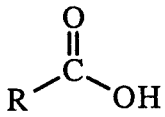
carbonyl group a carbon doubly bonded to an oxygen.

carbonyl oxygen the oxygen of a carbonyl group.

carboxyl group



carboxylic acid



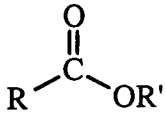
carboxylic acid derivative a compound that is hydrolyzed to a carboxylic acid.

carboxyl oxygen the single-bonded oxygen of a carboxylic acid or ester.

catalyst a species that increases the rate of a reaction without being consumed in th reaction.

detergent a salt of a sulfonic acid.

ester



fat a triester of glycerol that exists as a solid at room temperature.

fatty acid a long-chain carboxylic acid.

Fischer esterification reaction reaction of a carboxylic acid with excess alcohol and an acid catalyst.

Gabriel synthesis a method used to convert an alkyl halide into a primary amine.

hydrolysis reaction with water that converts one compound into two compounds.

hydrophobic interactions the attractive forces of hydrocarbon chains in water.

imide a compound with two acyl groups bonded to a nitrogen.

lactam a cyclic amide.

lactone a cyclic ester.

micelle a spherical aggregation of molecules, each with a long hydrophobic tail an a polar head, arranged so the polar head points to the outside of the sphere

mixed anhydride an acid anhydride with two different R groups.

neurotransmitter a compound that transmits nerve impulses across the synapses between nerve cells.

nitrile a compound that contains a carbon-nitrogen triple bond.

$$R{-}C{\equiv}N$$

nucleophilic acyl substitution reaction a reaction in which a group bonded to an acyl group is substituted by another group.

oil a triester of glycerol that exists as a liquid at room temperature.

phosphoanhydride bond the bond holding two phosphoric acid molecules together.

Ritter reaction the reaction of a nitrile with a secondary or tertiary alcohol to form a secondary amine.

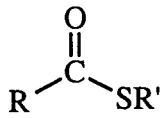
saponification hydrolysis of a fat under basic conditions.

soap a sodium or potassium salt of a fatty acid.

symmetrical anhydride an acid anhydride with identical R groups.

tetrahedral intermediate the intermediate formed in a nucleophilic acyl substitution reaction.

thioester the sulfur analog of an ester.



transesterification reaction the reaction of an ester with an alcohol to form a different ester.

Solutions to Problems

1. The lactone would be a three-membered ring, which is too strained to form.

2.

a. butanenitrile
propyl cyanide

b. ethanoic propanoic anhydride
acetic propionic anhydride

c. potassium butanoate
potassium butyrate

d. pentanoyl chloride
valeryl chloride

e. isobutyl butanoate
isobutyl butyrate

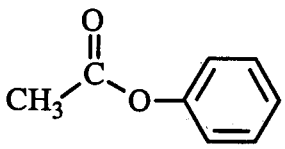
f. *N,N*-dimethylhexanamide

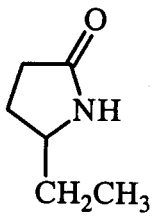
g. γ-butyrolactam or
2-azacyclopentanone

h. cyclopentanecarboxylic acid

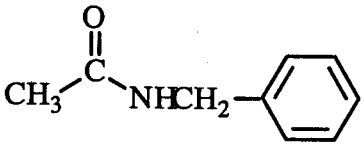
i. β-methyl-δ-valerolactone or
5-methyl-2-oxacyclohexanone

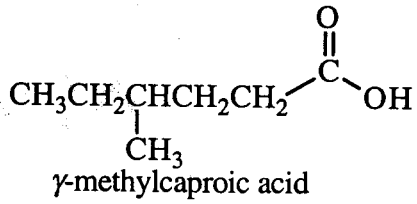
3.

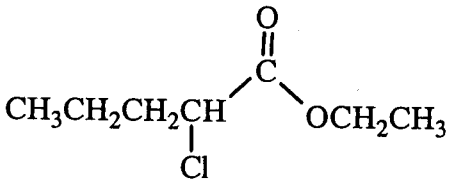
a. 

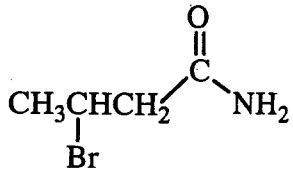
b. 

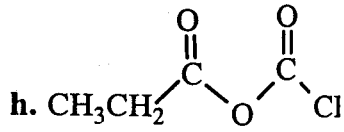
c. $CH_3CH_2CH_2C{\equiv}N$

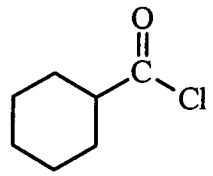
d. 

e. 
γ-methylcaproic acid

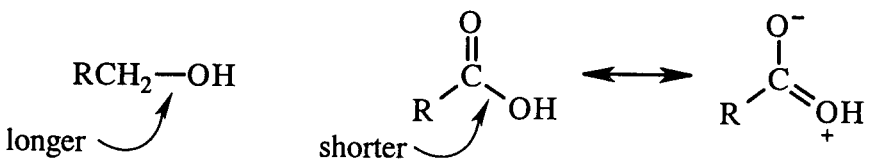
f. 

g. 

h. 

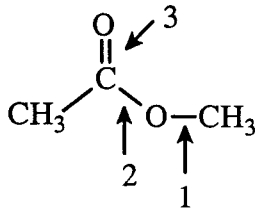
i. 

4. The carbon-oxygen single bond in an alcohol is longer because, as a result of resonance, the carbon-oxygen single bond in a carboxylic acid has some double-bond character.



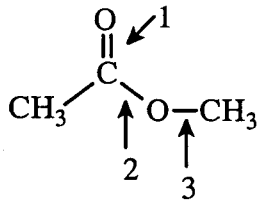
a. The bond between oxygen and the methyl group is the longest because it is a pure single bond, whereas the other two carbon-oxygen bonds have some double-bond character.

The bond between carbon and the carbonyl oxygen is the shortest because it has the most double bond character.



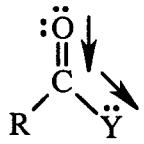
1 = longest
3 = shortest

b. Notice that the longer the bond, the lower its IR stretching frequency.

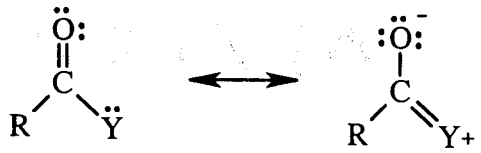


1 = highest frequency
3 = lowest frequency

6. The more electronegative the base (Y) attached to the carbonyl carbon, the greater the double bond character of the C=O bond.



The weaker the base (Y) attached to the carbonyl carbon the less well it shares it electrons. When Y shares its electrons, it decreases the double bond character of the C=O bond, making it easier to stretch.



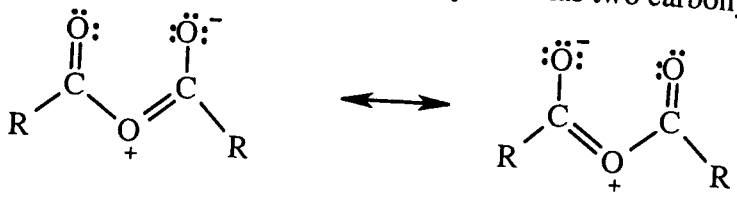
Therefore, the compounds have the indicated carbonyl IR absorption bands.

The carbonyl group of the acyl chloride stretches at the highest frequency because the chlorine atom is the most electronegative atom and the weakest base.

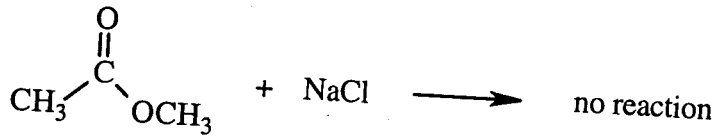
The carbonyl group of the amide stretches at the lowest frequency because the nitrogen atom is the least electronegative atom and the strongest base.

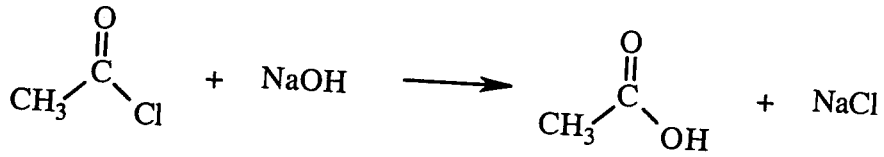
acyl chloride	~ 1800 cm^{-1}
acid anhydride	~ 1800 and 1750 cm^{-1}
ester	~ 1730 cm^{-1}
amide	~ 1640 cm^{-1}

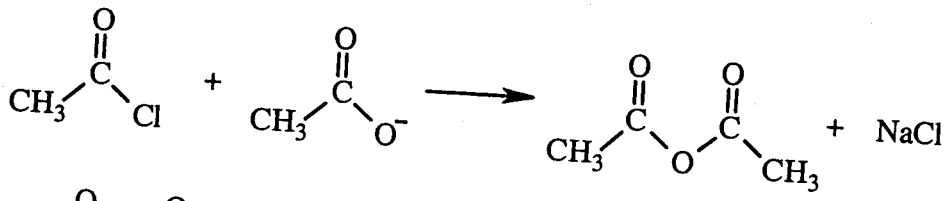
The resonance contributors show why the acid anhydride has two carbonyl IR absorption banc

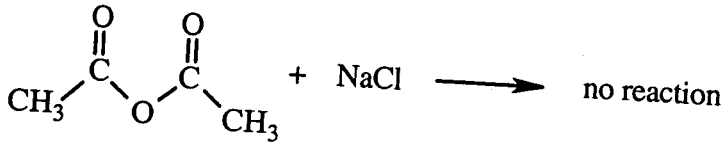


7.

a. 

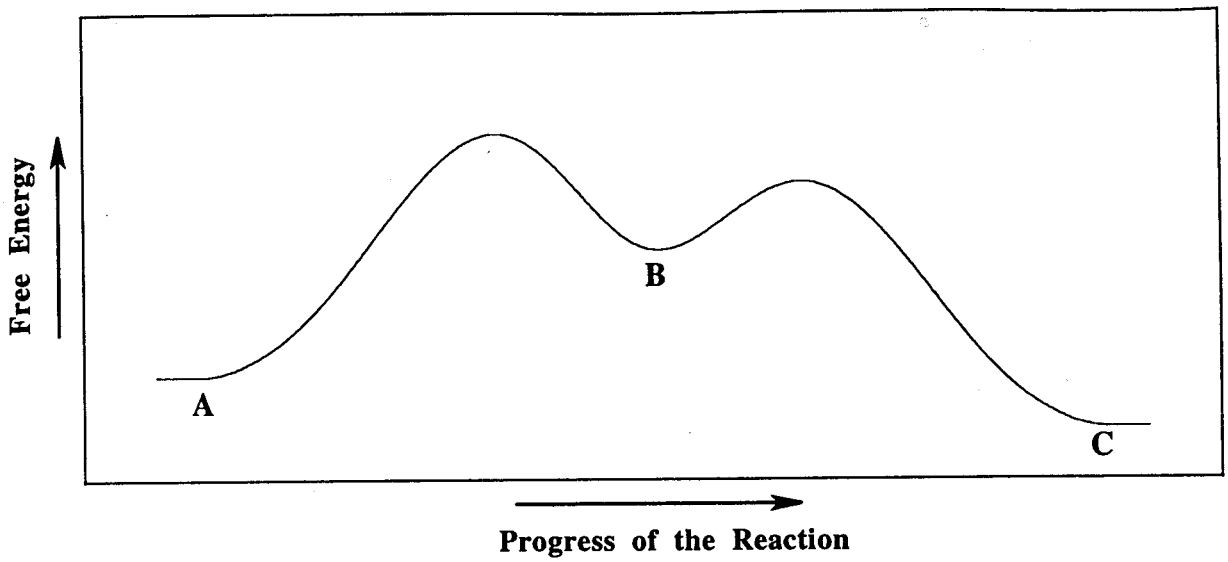
b. 

c. 

d. 

8. It is a true statement.

If the nucleophile is the stronger base, it will be harder to eliminate the nucleophile from the tetrahedral intermediate (**B**) than to eliminate the group attached to the acyl group in the reactant. In other words, the hill that has to be climbed from the intermediate (**B** to **A**) back to the reactants is higher than the hill that has to be climbed from the intermediate (**B** to **C**) to the products. Since the transition state with the highest energy is the transition state of the rate-limiting step, the first step is the rate-limiting step.



a. a new carboxylic acid derivative

b. no reaction

c. a mixture of two carboxylic acid derivatives

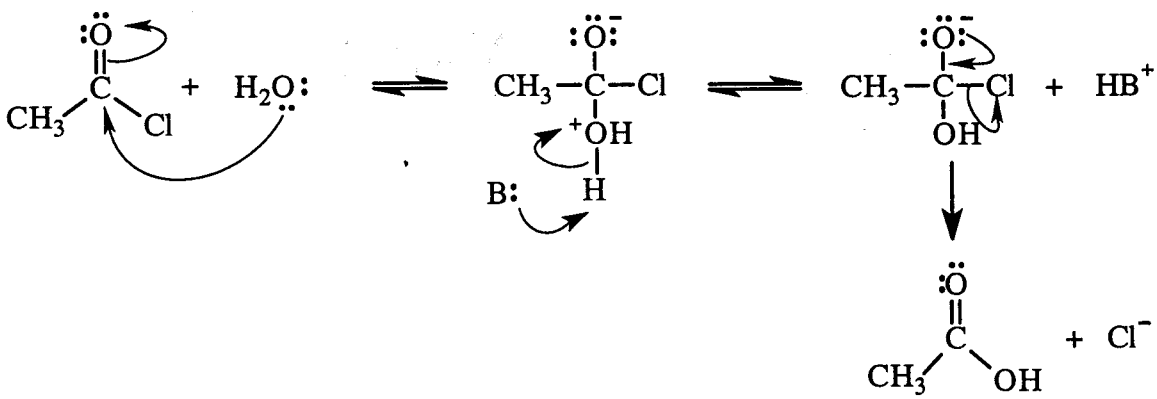
10. Solved in the text.

11. A protonated amine has a pK_a ~ 11. Therefore, the amine will be protonated by the acid that is produced in the reaction, and a protonated amine is not a nucleophile. Excess amine is used in order to have some unprotonated amine available to react as a nucleophile.

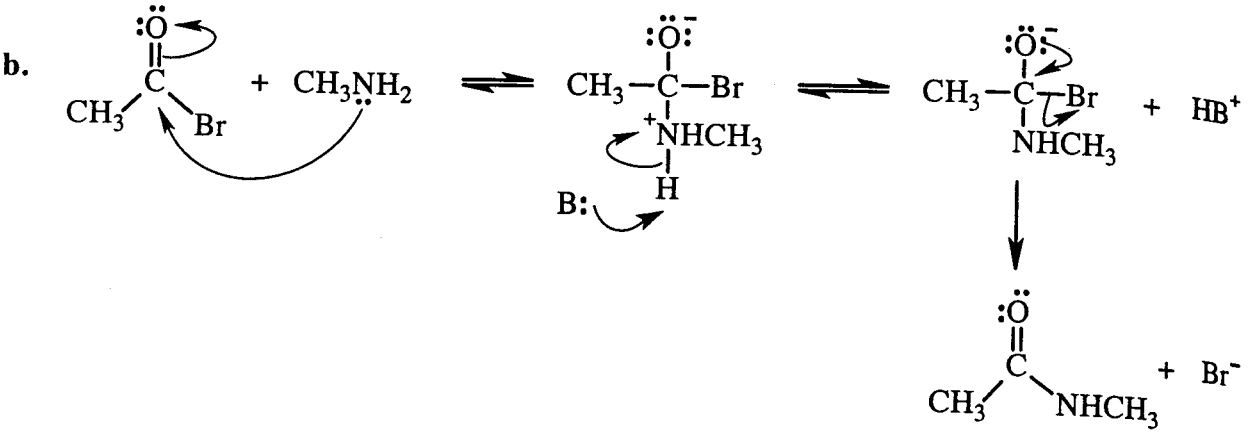
A protonated alcohol has a pK_a ~ −2. Therefore, the alcohol will not be protonated by the acid that is produced in the reaction.

12.

a.



b.



13.

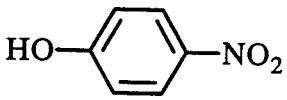
a. $CH_3CH_2CH_2OH$

b. $CH_3CH_2NH_2$

c. $(CH_3)_2NH$

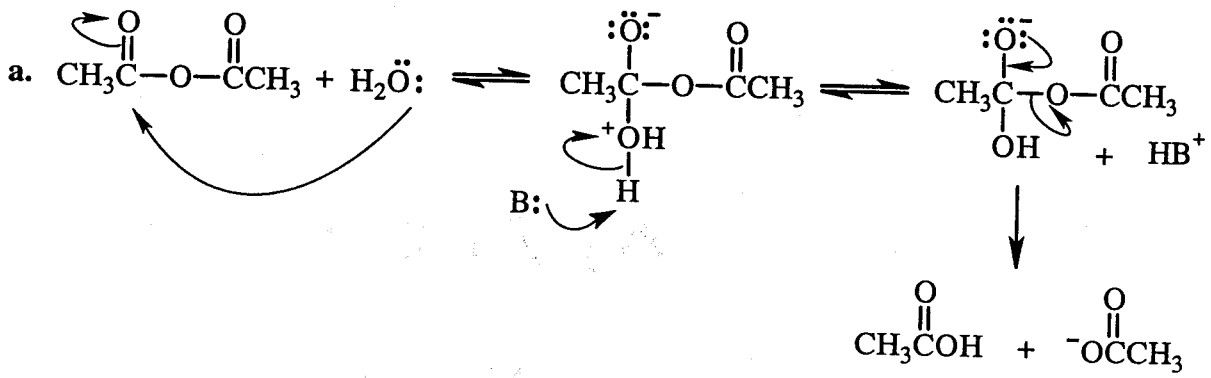
d. H_2O

e. CH_3CO^-

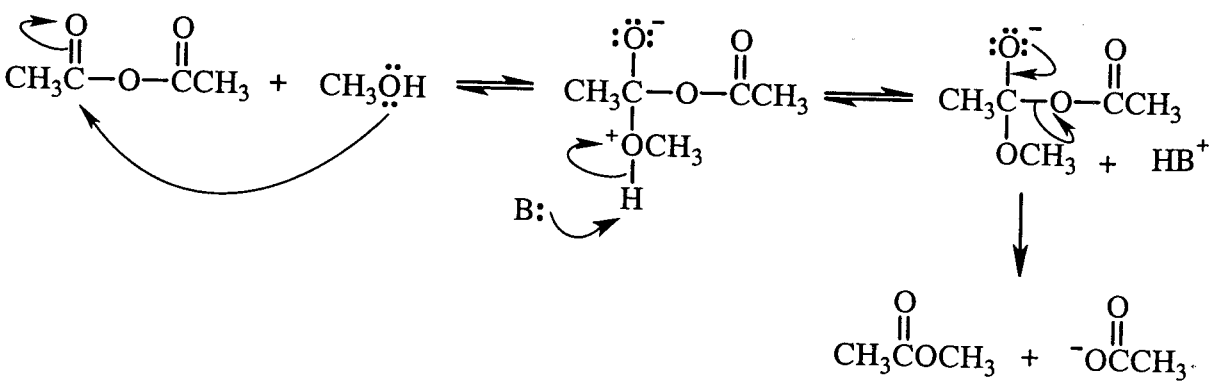
f. 

14.

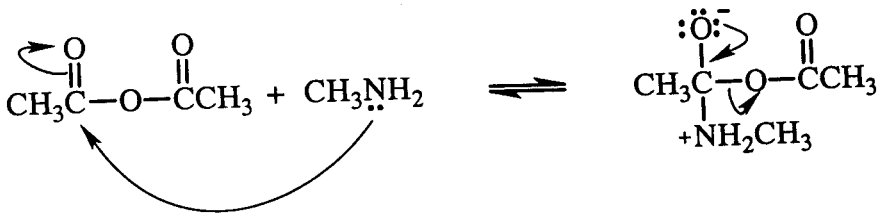
a.



b. The mechanisms are exactly the same.

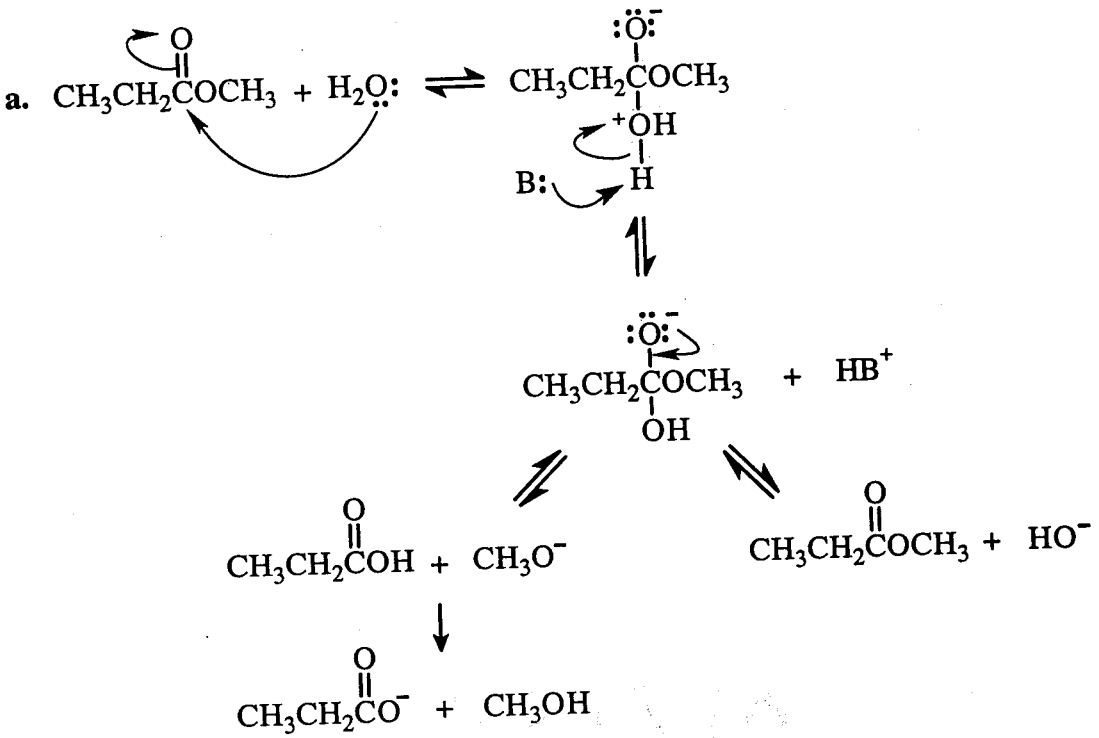


When an acid anhydride reacts with an amine, the tetrahedral intermediate does not have to lose a proton before it eliminates the carboxylate ion, because the carboxylate ion is a weaker base (pK_a of its conjugate acid is ~ 5) than an amine (pK_a of its conjugate acid is ~ 10).

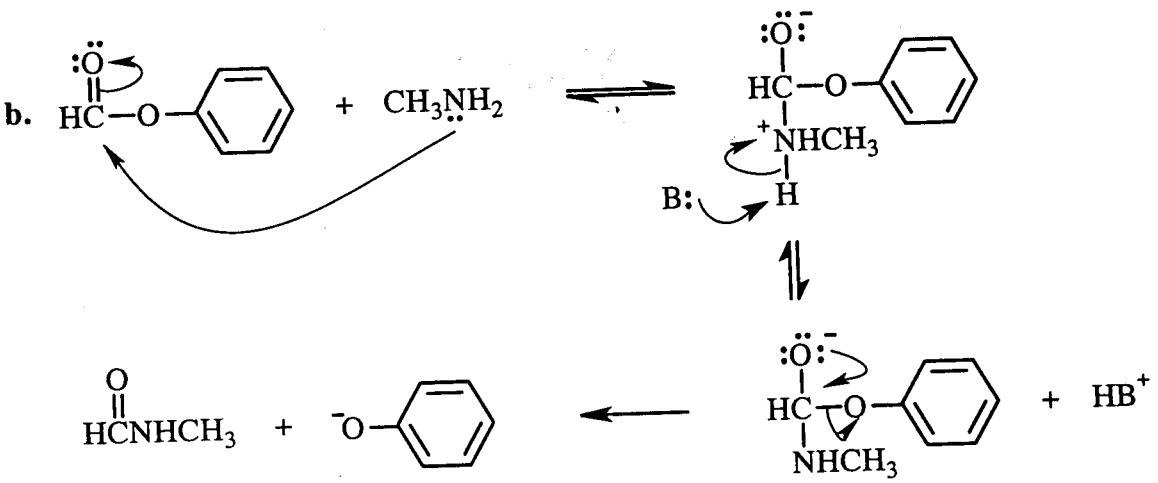


16.

a.



b.

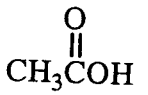
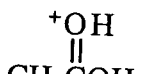
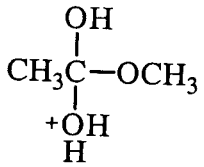
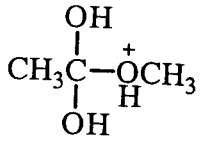


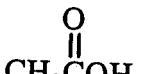
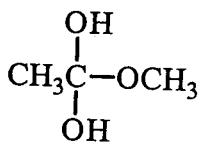
17. **a.** **1.** The carbonyl group of an ester is a weak electrophile.
2. Water is not a very strong nucleophile.
3. $^{-}OCH_3$ is a strong base and, therefore, a poor leaving group.

b. Aminolysis is faster.

18. Solved in the text.

19.

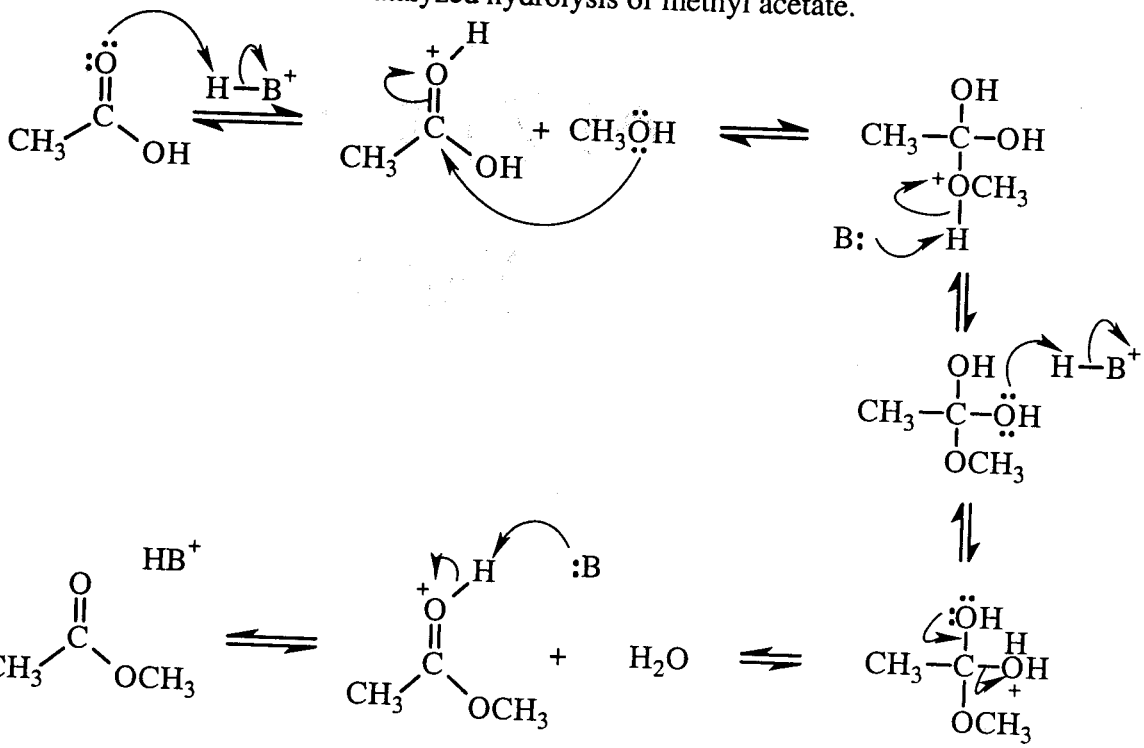
a. H_3O^+ $CH_3\overset{+}{O}H_2$    

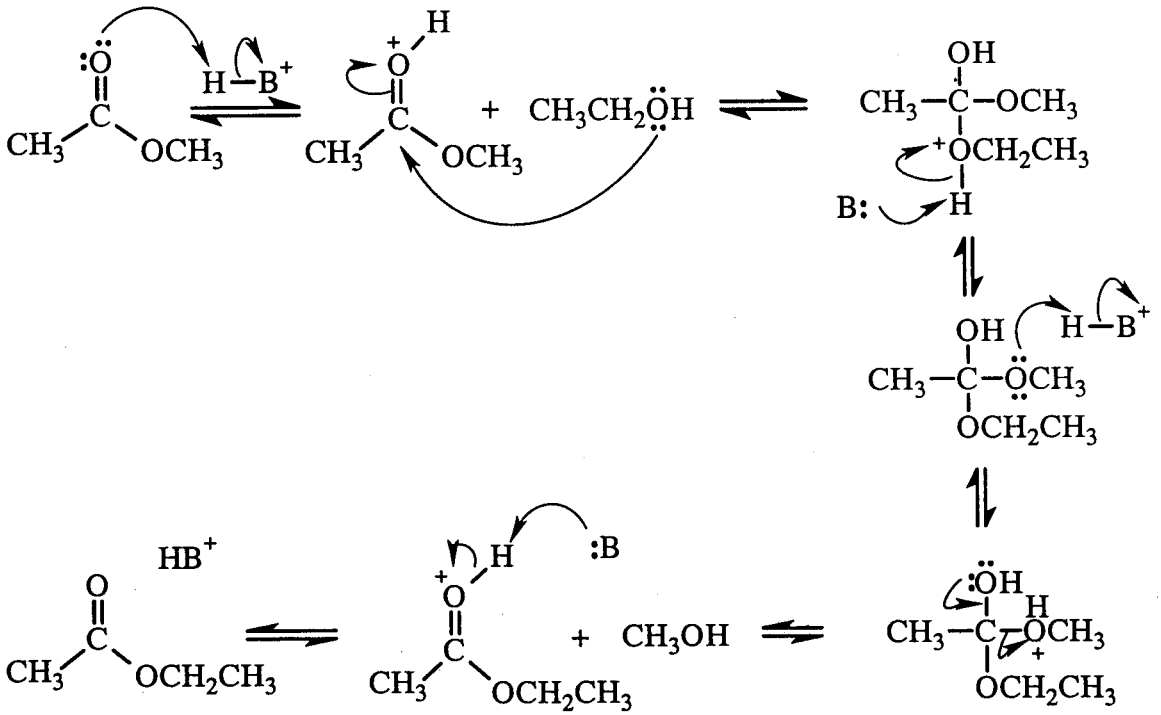
b. H_2O CH_3OH   Cl^-

c. H_3O^+

d. H_3O^+ if excess water is used, $CH_3\overset{+}{O}H_2$ if not

20. The mechanism for the acid-catalyzed reaction of acetic acid and methanol is the exact reverse of the mechanism for the acid-catalyzed hydrolysis of methyl acetate.





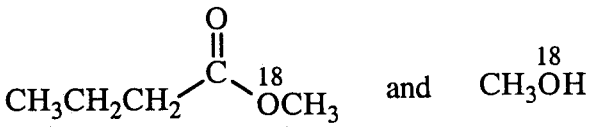
22. **a.** The conjugate base ($CH_3CH_2CH_2O^-$) of the reactant alcohol ($CH_3CH_2CH_2OH$) can be used to catalyze the reaction.

b. If H^+ is used as a catalyst, the amine will be protonated in the acidic solution and, therefore, will not be able to react as a nucleophile.

If HO^- is used as a catalyst, HO^- will be the strongest nucleophile present in solution, so it will attack the ester, and the product of the reaction will be a carboxylic acid rather than an amide.

If RO^- is used as a catalyst, RO^- will be the nucleophile, and the product of the reaction will be an ester rather than an amide.

23.



24. **a.** The alcohol (CH_3CH_2OH) contained the ^{18}O label.

b. The carboxylic acid would have contained the ^{18}O label.

25. Solved in the text.

26. Solved in the text.

27.

a. $CH_3CH_2CH_2COH \xrightarrow{SOCl_2} CH_3CH_2CH_2CCl \xrightarrow{CH_3OH} CH_3CH_2CH_2COCH_3$

$CH_3CH_2CH_2CO^- \xrightarrow{CH_3Br} CH_3CH_2CH_2COCH_3$

b. $CH_3COH \xrightarrow{SOCl_2} CH_3CCl \xrightarrow{CH_3CH_2CH_2OH} CH_3COCH_2CH_2CH_3$

$CH_3CO^- \xrightarrow{CH_3CH_2CH_2Br} CH_3COCH_2CH_2CH_3$

c. $CH_3CH_2CH_2COH \xrightarrow{SOCl_2} CH_3CH_2CH_2CCl \xrightarrow{CH_3CH_2OH} CH_3CH_2CH_2COCH_2CH_3$

$CH_3CH_2CH_2CO^- \xrightarrow{CH_3CH_2Br} CH_3CH_2CH_2COCH_2CH_3$

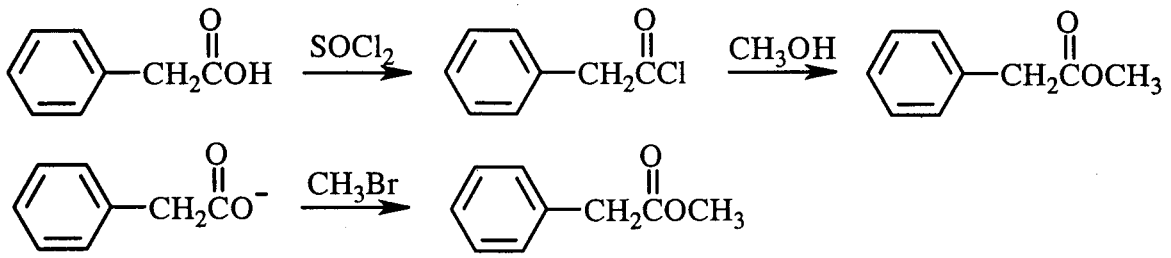
d. $CH_3COH \xrightarrow{SOCl_2} CH_3CCl \xrightarrow{CH_3(CH_2)_7OH} CH_3CO(CH_2)_7CH_3$

$CH_3CO^- \xrightarrow{CH_3(CH_2)_7Br} CH_3CO(CH_2)_7CH_3$

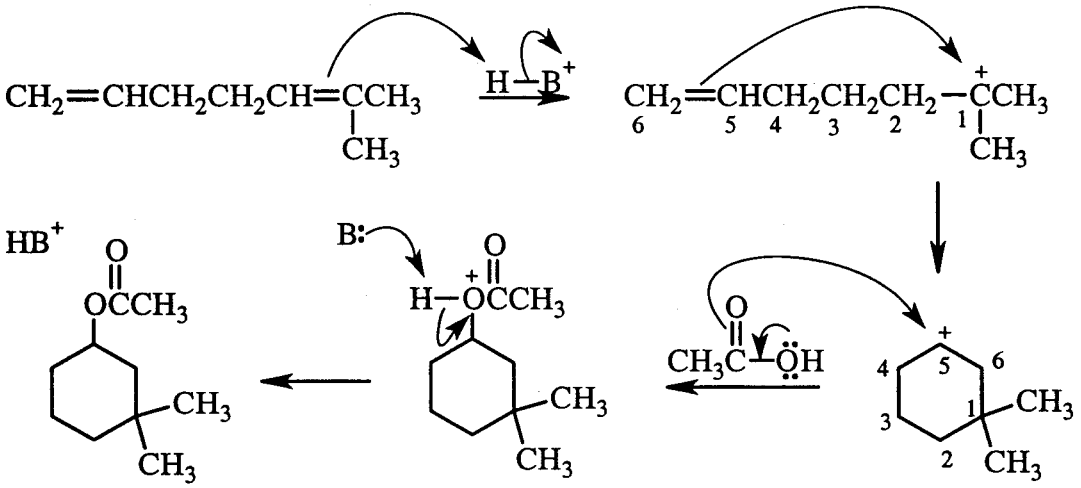
e. $CH_3COH \xrightarrow{SOCl_2} CH_3CCl \xrightarrow{(CH_3)CH(CH_2)_2OH} CH_3CO(CH_2)_2CH(CH_3)_2$

$CH_3CO^- \xrightarrow{(CH_3)CH(CH_2)_2Br} CH_3CO(CH_2)_2CH(CH_3)_2$

f.



28. In the first step, protonation occurred to give the most stable carbocation (a tertiary carbocation).

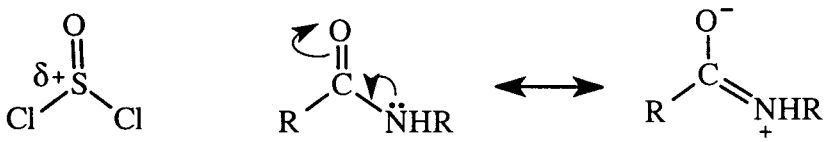


29. **a.** #2 and #5 will form amides

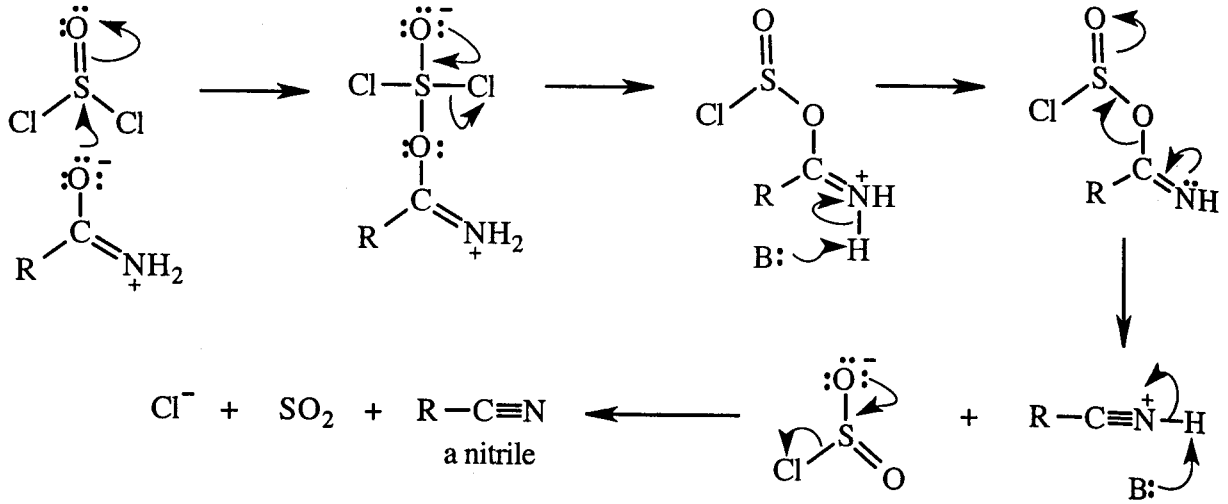
b. For #2: if the nucleophile were CH_3NH^- instead of CH_3NH_2, the better nucleophile will increase the rate of amide formation.

For #5: using two equivalents of methylamine will increase the yield of the product. The second equivalent will ensure that there is sufficient nucleophile present to react with the acyl halide.

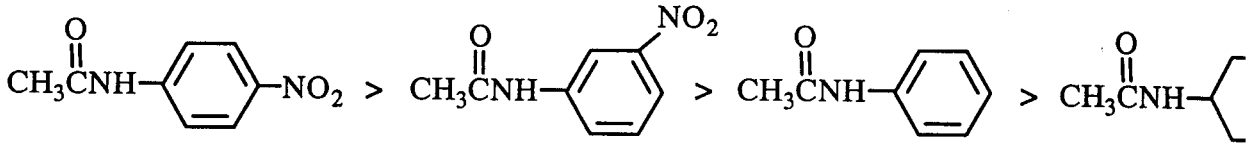
30. We know that the electrophile is thionyl chloride and that its electrophilic site is the sulfur atom.
We know that the amide is the nucleophile and its nucleophilic site is the oxygen atom.



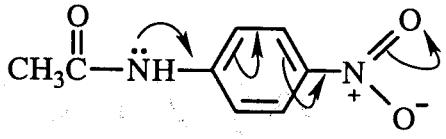
Therefore, we should let the nucleophile attack the electrophile and then see if that product helps us figure out how we can arrive at the given product (the nitrile).



31. The relative reactivities of the amides depend on the basicities of their leaving groups: the weaker the base, the more reactive the amide.

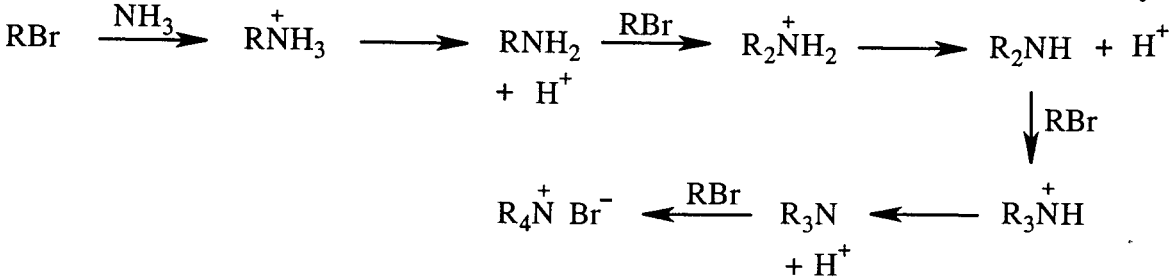


A *para*-nitro-substituted aniline is less basic than a *meta*-substituted aniline because when the nitro group is in the para position, electrons can be delocalized onto the nitro group.



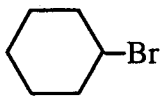
32. **a.** pentyl bromide **b.** isohexyl bromide **c.** benzyl bromide **d.** cyclohexyl bromide

33. The reaction of an alkyl halide with ammonia leads to primary, secondary, and tertiary amines, and even quaternary ammonium ions. Thus, the yield of primary amine could be relatively low.

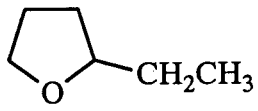


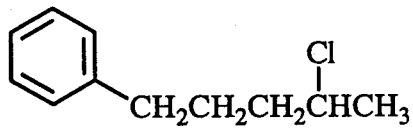
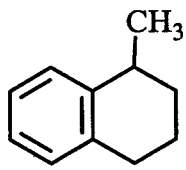
In contrast, the Gabriel synthesis forms only primary amines. The reaction of an alkyl halide with azide ion also forms only primary amines because the compound formed from the initial reaction of the two reagents is not nucleophilic, so polyalkylation does not occur.

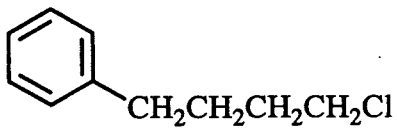
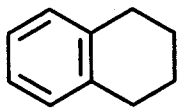
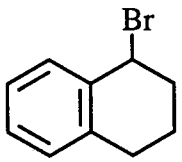
34.

a. $CH_3CH_2CH_2Br$ **b.** CH_3CHCH_2Br (CH$_3$ branch) **c.** 

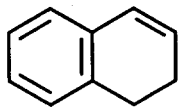
35.

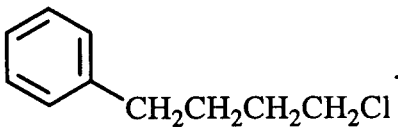
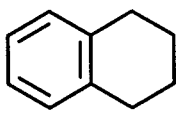
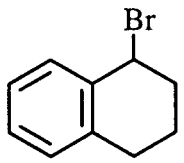
a. $BrCH_2CH_2CH_2CHCH_2CH_3$ (OH branch) $\xrightarrow{Na}$ 

b.  $\xrightarrow{AlCl_3}$ 

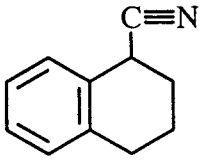
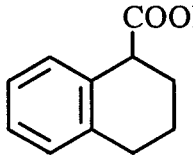
c.  $\xrightarrow{AlCl_3}$  $\xrightarrow[\text{peroxide}]{NBS,\ \Delta}$ 

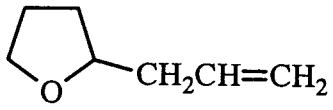
$\downarrow KOH$

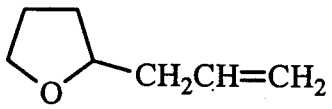


d.  $\xrightarrow{AlCl_3}$  $\xrightarrow[\text{peroxide}]{NBS,\ \Delta}$ 

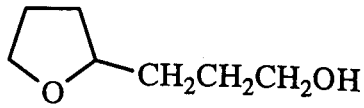
$\downarrow {}^{-}C{\equiv}N$

 $\xrightarrow[\Delta]{H_2O,\ HCl}$ 

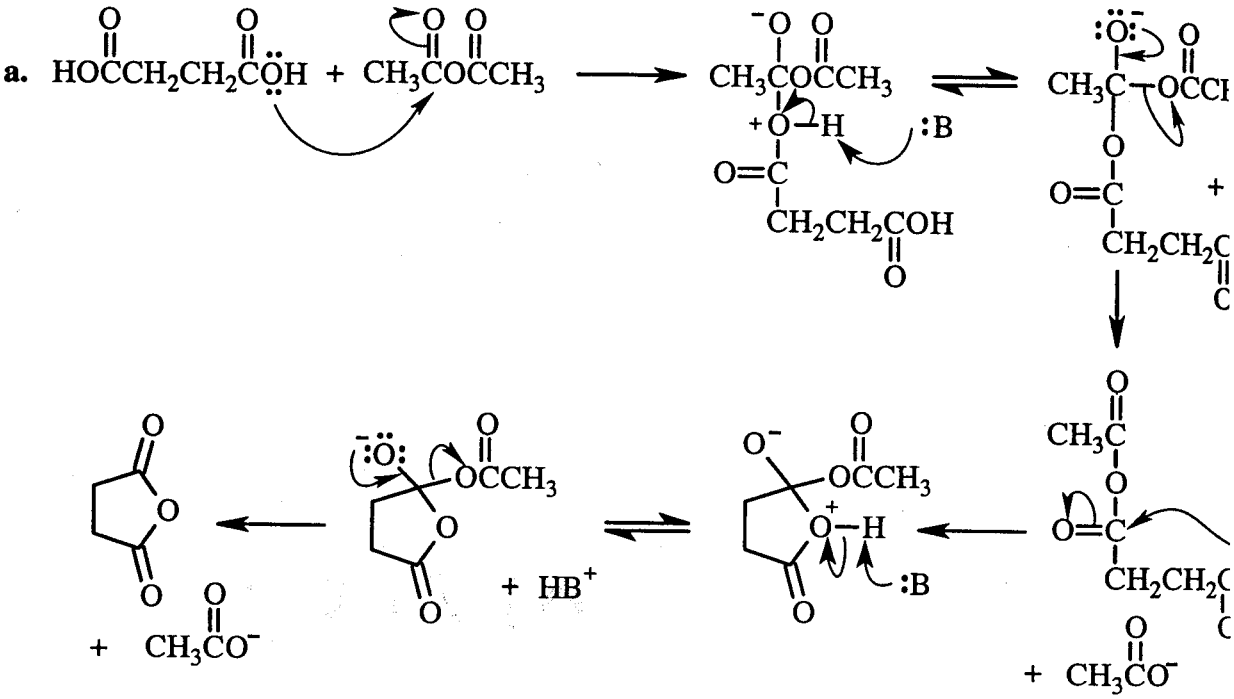
e. $BrCH_2CH_2CH_2\underset{\displaystyle OH}{\underset{|}{C}}HCH_2CH{=}CH_2 \xrightarrow{Na}$ 

f. 

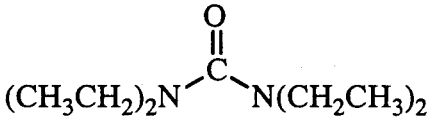
product of **e**

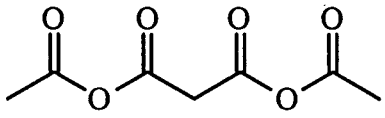
$\xrightarrow[2.\ HO^-,\ H_2O_2,\ H_2O]{1.\ BH_3}$ 

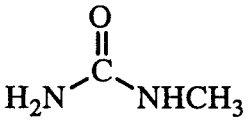
36.

a. 

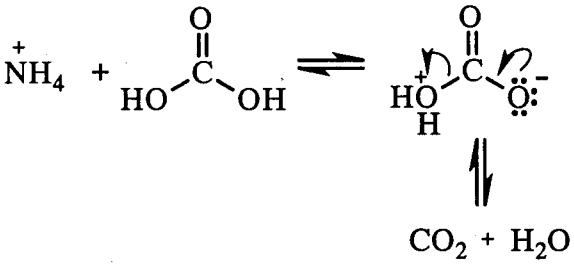
b. Without acetic anhydride, the leaving group would be hydroxide ion. Acetic anhydride causes the reaction to take place via two successive acyl substitution reactions. In both reactions the leaving group is acetate ion, which is much less basic than hydroxide ion.

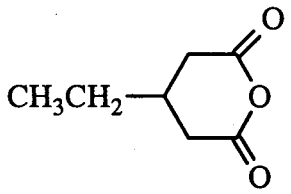
a. 

b. 

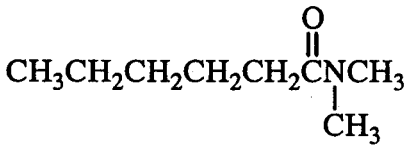
c. 

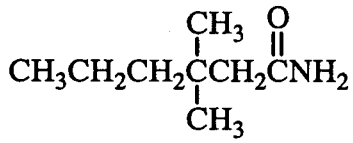
d. no reaction

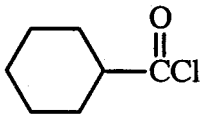
e. 

f. 

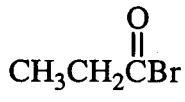
38.

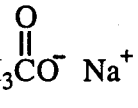
a. 

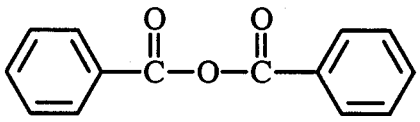
b. 

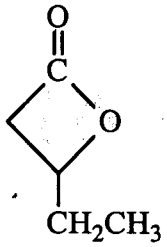
c. 

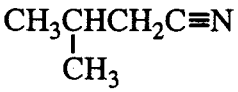
d. $CH_3CH_2C{\equiv}N$

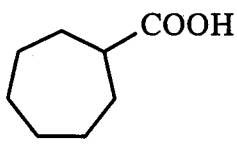
e. 

f. 

g. 

h. 

i. 

j. 

39. **a.** 5-ethylheptanoic acid

b. propyl propanoate
propyl propionate

c. pentanenitrile
butyl cyanide

d. propanoic anhydride
propionic anhydride

e. *N,N*-dimethylbutanamide
N,N-dimethylbutyramide

f. pentanoyl chloride
valeryl chloride

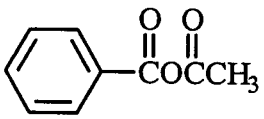
g. acetic benzoic anhydride

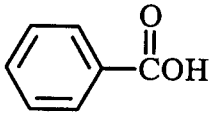
h. *N*-methyl-3-butenamide

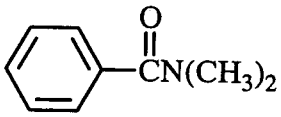
i. (*S*)-3-methylpentanoic acid
(*S*)-β-methylvaleric acid

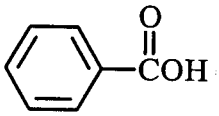
j. (*R*)-3-methylhexanenitrile

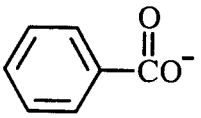
40.

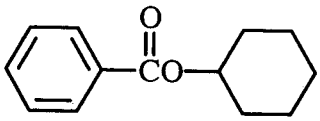
a. 

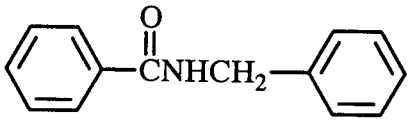
b. 

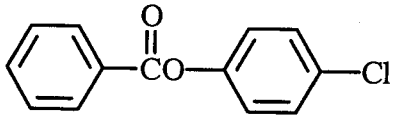
c. 

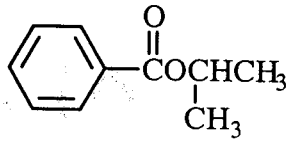
d. 

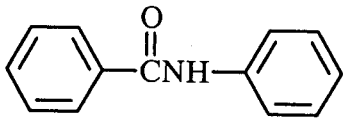
e. 

f. 

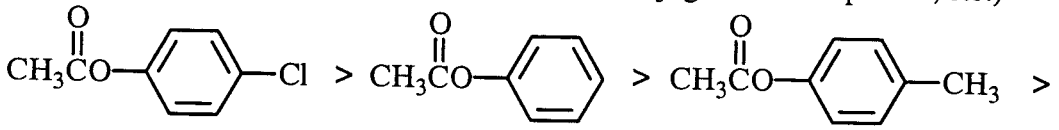
g. 

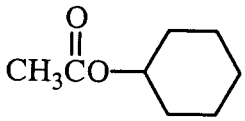
h. 

i. 

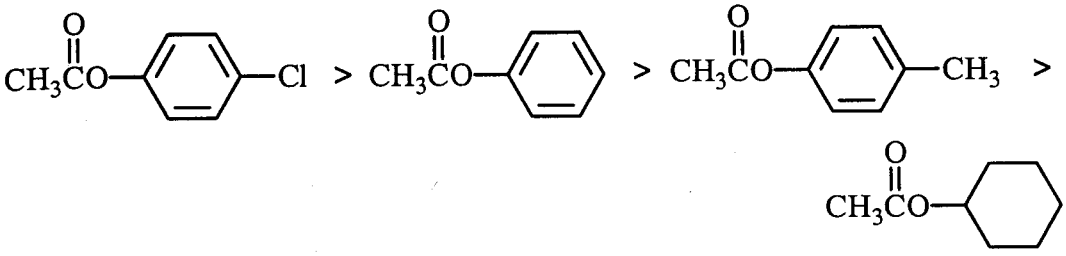
j. 

41. **a.** The weaker the base attached to the acyl group, the easier it is to form the tetrahedral intermediate. (*para*-Chlorophenol is a stronger acid than phenol so the conjugate base of *para* chlorophenol is a weaker base than the conjugate base of phenol, etc.)

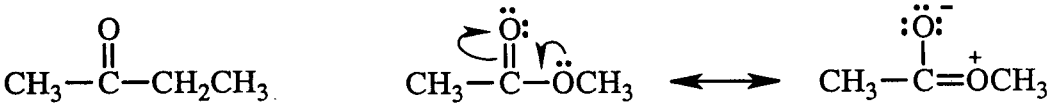




b. The tetrahedral intermediate collapses by eliminating the $^-$OR group of the tetrahedral intermediate. The weaker the basicity of the $^-$OR group, the easier it is to eliminate it. Thus, the rate of both formation of the tetrahedral intermediate and collapse of the tetrahedral intermediate is decreased by increasing the basicity of the $^-$OR group.

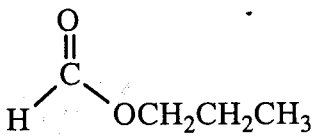


42. **a.** Methyl acetate has a resonance contributor that butanone does not have, and this resonance contributor causes methyl acetate to be more polar than butanone. Because butanone is less polar, it has the lower dipole moment.

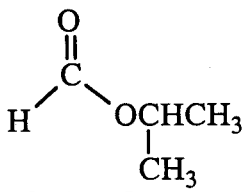


b. Because it is more polar, the intermolecular forces holding methyl acetate molecules together are stronger, so we would expect methyl acetate to have a higher boiling point.

43. Propyl formate is easy to distinguish because it is the only ester that will show four signals. The other three esters show three signals. Isopropyl formate can be distinguished by its unique splitting pattern: a singlet, a doublet, and a septet. The splitting patterns of the other two esters are the same: a singlet, a triplet, and a quartet. They can be distinguished because the peak farthest downfield in ethyl acetate is a quartet, whereas the peak farthest downfield in methyl propionate is a singlet.

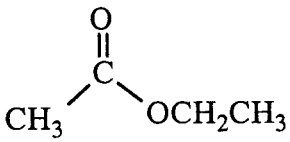


4 signals



3 signals

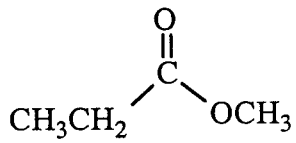
singlet, doublet, septet



3 signals

singlet, triplet, quartet

The peak farthest downfield is a quartet.

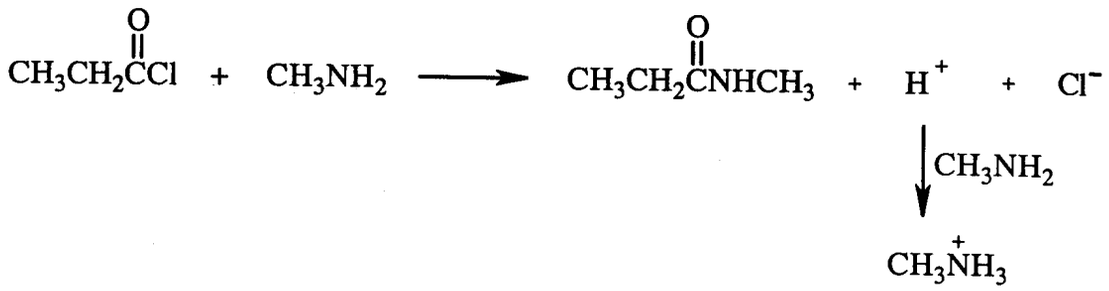


3 signals

singlet, triplet, quartet

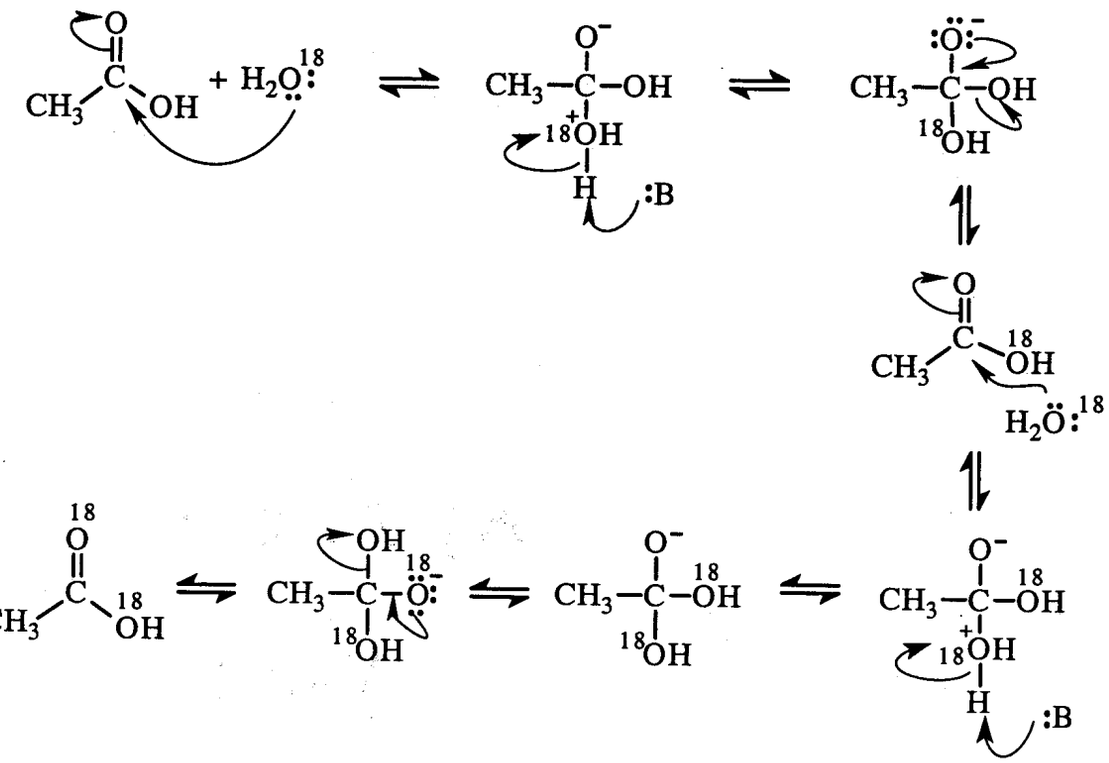
The peak farthest downfield is a singlet.

44. The reaction of methylamine with propionyl chloride generates a proton that will protonate unreacted amine, thereby destroying its nucleophilicity. If two equivalents of CH_3NH_2 are used one equivalent will remain unprotonated and be able to react with propionyl chloride to form *N*-methylpropanamide.

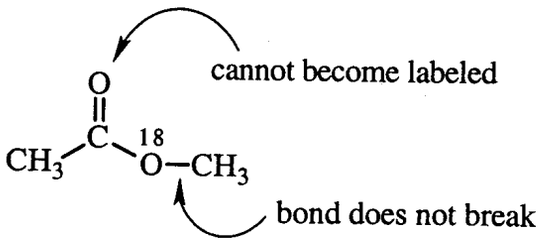


45.

a.



b. Only one isotopically labeled oxygen can be incorporated into the ester because the bond between the methyl group and the labeled oxygen does not break, so there is no way for the carbonyl oxygen to become labeled.



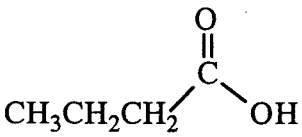
46. **a.** isopropyl alcohol and HCl

b. aqueous sodium hydroxide

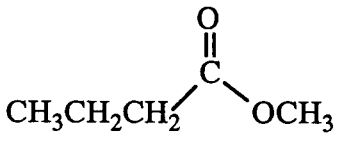
c. ethylamine

d. water and HCl

47. The offset in the NMR spectrum shows that there is a signal at ~ 10 ppm, which is where the proton of a COOH group shows a signal. The two triplets and the multiplet are characteristic of a propyl group. The compound is butanoic acid.

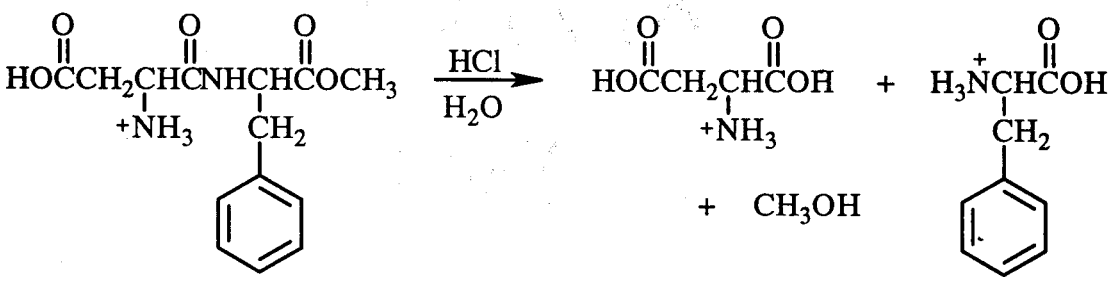


The molecular formula shows that the unknown compound has one more carbon atom than butanoic acid. Since butanoic acid is formed from acid hydrolysis of the compound, the compound must be the methyl ester of butanoic acid.



$C_5H_{10}O_2$

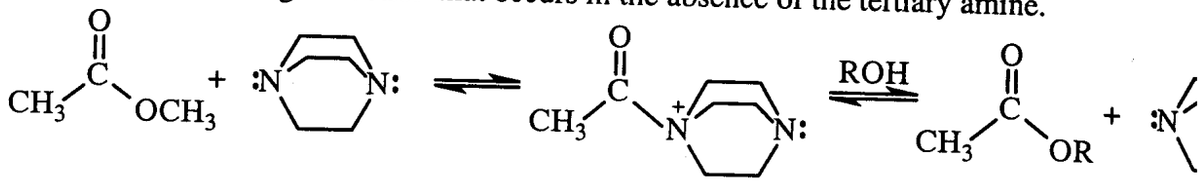
48. Aspartame has an amide group and an ester group that will be hydrolyzed in an aqueous solution of HCl. Because the hydrolysis is carried out in an acidic solution, the carboxylic acid groups and the amino groups will be in their acidic forms.



49. **a.** 1, 3, 4, 6, 7, 9 will not form the indicated products under the given conditions.

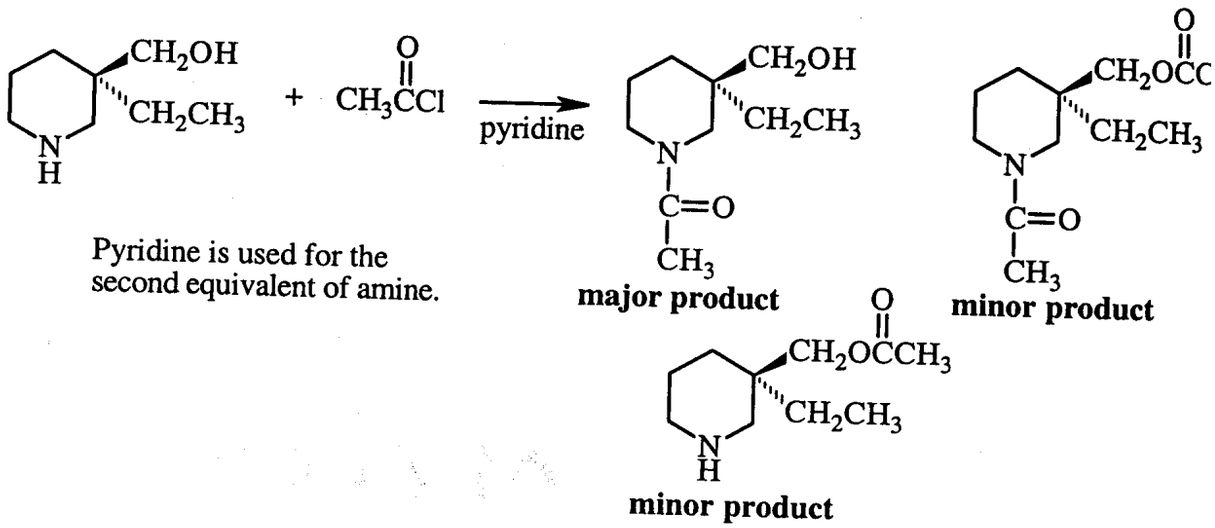
b. 9 will form the product shown in the presence of an acid catalyst.

50. The tertiary amine is a stronger nucleophile than the alcohol, so formation of the charged ami will be faster than formation of the new ester would have been. The charged amide is more reactive than an ester, so formation of the new ester by reaction of the alcohol with the charg amide will be faster than formation of the ester by reaction of the alcohol with the starting est would have been. In other words, both reactions that occur in the presence of the tertiary ami are faster than the single reaction that occurs in the absence of the tertiary amine.



+ CH_3OH

51. The amine is a stronger nucleophile than the alcohol, but since the acyl chloride is very reacti it can react easily with both nucleophiles. Therefore, steric hindrance will be the most importa factor in determining the products. The amino group is less sterically hindered than the alcoh group so that will be the group most easily acetylated.



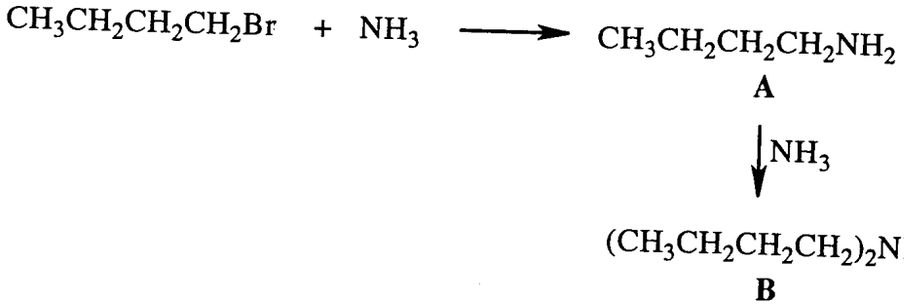
Pyridine is used for the second equivalent of amine.

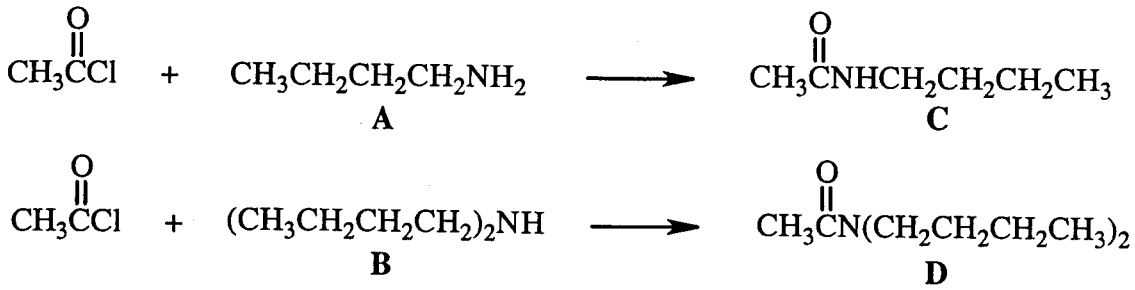
major product

minor product

minor product

52. Bromobutane undergoes an S_N2 reaction with NH_3 to form butylamine **(A)**. Bromobutane can then react with butylamine to form dibutylamine **(B)**. The amines each form an amide upon reaction with acetyl chloride. The IR spectrum of **C** exhibits an NH stretch at about 3300 cm^{-1} while the IR spectrum of **D** does not exhibit this absorption band, because the nitrogen in **D** is not bonded to a hydrogen.

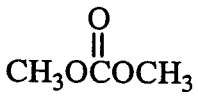
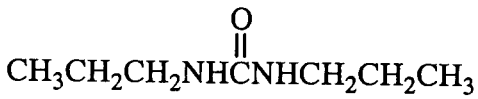
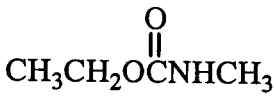




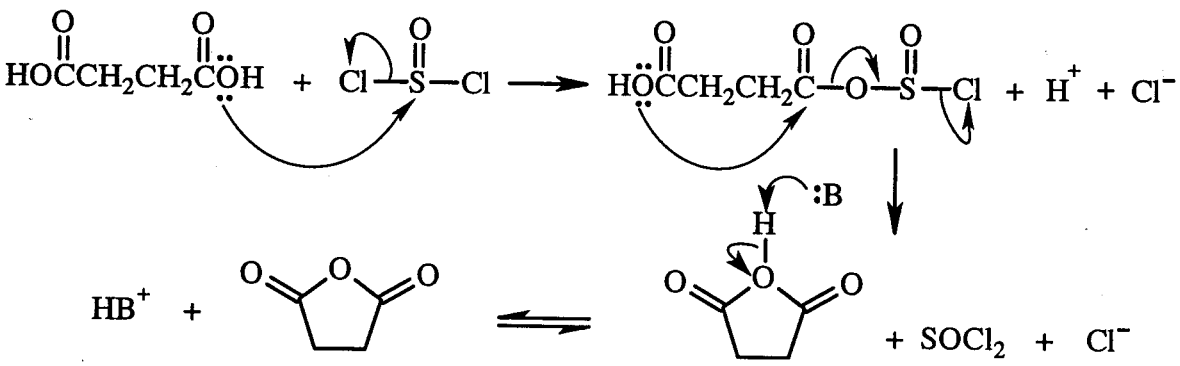
A **C**

B **D**

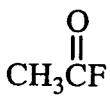
53.

1. 
2. 
3. 
4. 

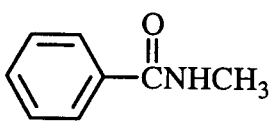
54.

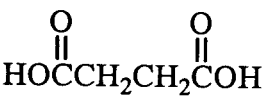


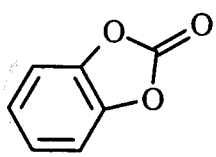
55.

a. 

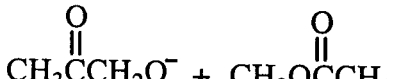
b. 

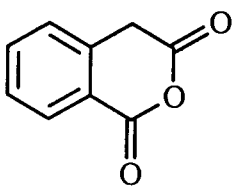
c. 

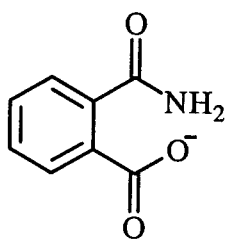
d. 

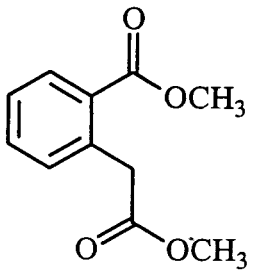
e. 

f. 

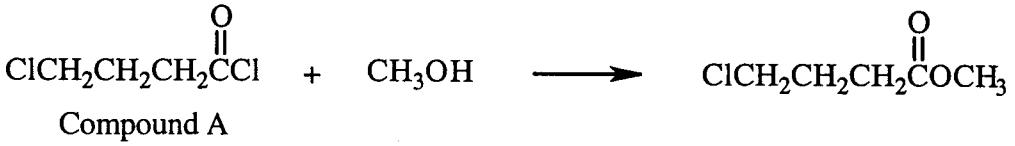
g. 

h. 

i. 

j. 

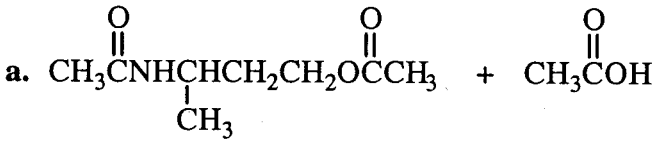
56.



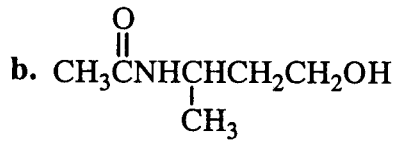
Compound A

57.

a.

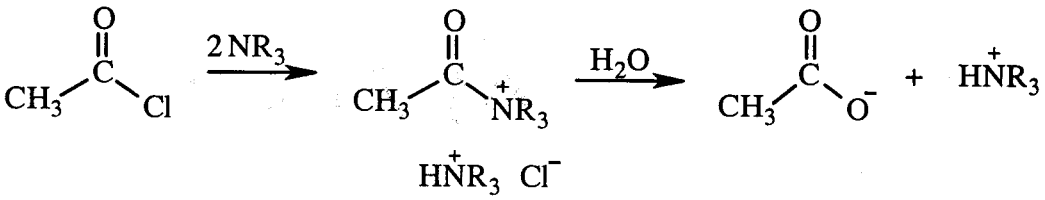


b.



Because the amino group is a stronger nucleophile than the OH group, the predominant product will be the amide if the reaction is stopped prematurely.

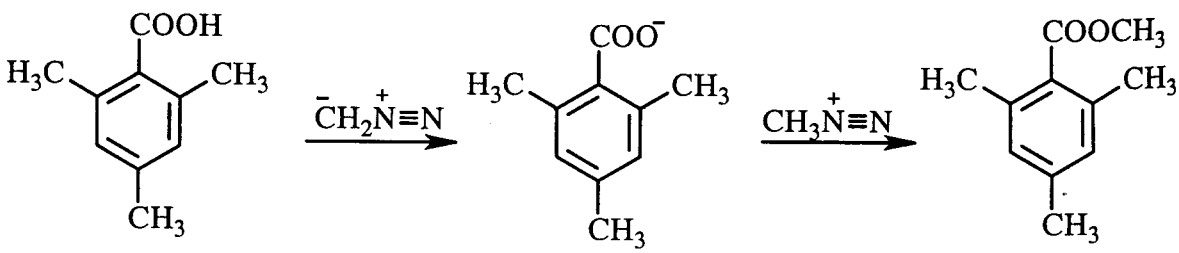
58. If the amine is tertiary, the nitrogen atom in the amide cannot get rid of its positive charge by losing a proton. An amide with a positively charged amino group is very reactive because the positively charged amino group is a weak base and, therefore, an excellent leaving group. Water will immediately react with the amide, and because the positively charged amine is a better leaving group than the OH group, the amine will be expelled and the product will be a carboxylic acid.



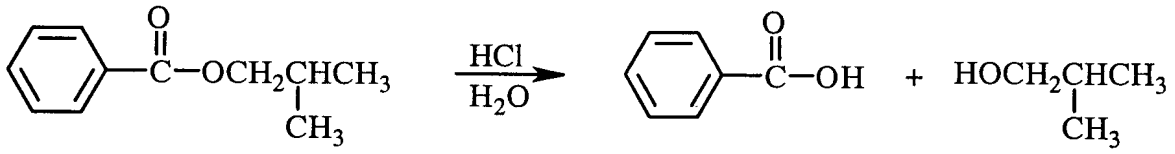
59. **a.** The steric hindrance provided by the methyl groups prevents methyl alcohol from attacking the carbonyl carbon.

b. No, because there would be no steric hindrance.

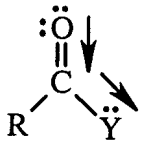
c.



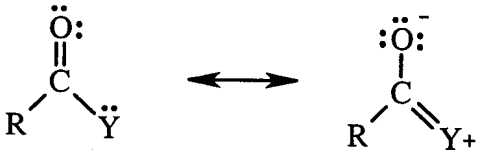
60. The spectrum shows that the compound has four different kinds of hydrogens with relative ratios 2 : 1 : 1 : 6. The doublet at 0.9 ppm and the ratio of 6 hydrogens suggests that the compound has an iso group. The signal at 3.4 ppm indicates hydrogens on a carbon that is attached to an oxygen atom. The shape of the signal at 2.4 ppm suggests an OH group. We can conclude that the spectrum is a spectrum of isobutyl alcohol. The molecular formula indicates the compound that undergoes hydrolysis is an ester. Subtracting the atoms due to the isobutyl group lets us identify the ester as isobutyl benzoate.



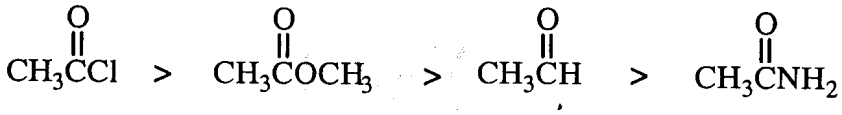
61. The more electronegative the base (Y) attached to the carbonyl carbon, the greater the double bond character of the C=O bond.



The weaker the base (Y) attached to the carbonyl carbon the less well it shares it electrons. when Y shares its electrons, it decreases the double bond character of the C=O bond, making it easier to stretch.



Therefore, the carbonyl IR absorption band decreases in the order:



The carbonyl group of the acyl chloride stretches at the highest frequency because the chlorine atom is the most electronegative atom and the weakest base.

The predominant effect of the oxygen of an ester is inductive electron withdrawal, so its carbonyl group stretches at a higher frequency than the carbonyl group of the aldehyde.

The carbonyl group of the amide stretches at the lowest frequency because the nitrogen atom is the strongest base, so it is best at sharing its electrons.

62. **a.**

$$4.02 = \frac{x^2}{(1-x)^2}$$

$$2.00 = \frac{x}{(1-x)}$$

$$2 - 2x = x$$

$$2 = 3x$$

$$x = 0.667$$

[ethyl acetate] = 0.667 times the concentration of acetic acid used

b.

$$4.02 = \frac{x^2}{(10-x)(1-x)}$$

$$x = 0.974$$

[ethyl acetate] = 0.974 times the concentration of acetic acid used

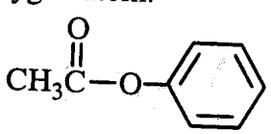
c.

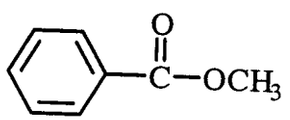
$$4.02 = \frac{x^2}{(100-x)(1-x)}$$

$$x = 0.997$$

[ethyl acetate] = 0.997 times the concentration of acetic acid used

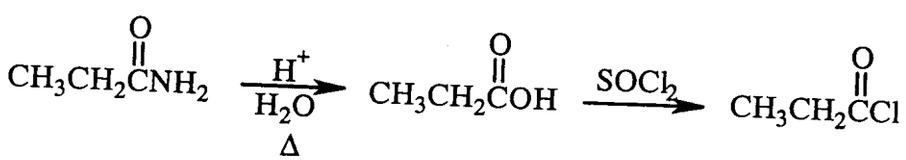
63. Each of the NMR spectra has signals between about 7-8 ppm, indicating that the compound has a benzene ring with one substituent (the benzene ring has hydrogens in three different environments) and one additional signal that is a singlet. From the molecular formulas it can be determined that the esters have the following structures. The singlet in each spectrum is due to a methyl group. Because the methyl group is farther downfield in the spectrum on the right, it is the spectrum of the compound on the right, since its methyl group is adjacent to an electron-withdrawing oxygen atom.





The ester on the left will hydrolyze faster because phenol is a much weaker base than methyl alcohol.

64.

a. 

b. $CH_3CH_2CH_2CH_2OH \xrightarrow{SOCl_2} CH_3CH_2CH_2CH_2Cl \xrightarrow{^-C\equiv N} CH_3CH_2CH_2CH_2C\equiv N$

$CH_3CH_2CH_2CH_2C\equiv N \xrightarrow[H_2O,\ HCl,\ \Delta]{} {}^+NH_4 + CH_3CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

c. $CH_3(CH_2)_{10}\overset{O}{\overset{\|}{C}}OH \xrightarrow{SOCl_2} CH_3(CH_2)_{10}\overset{O}{\overset{\|}{C}}Cl \xrightarrow[2.\ H_2O]{1.\ \bigcirc,\ AlCl_3} CH_3(CH_2)_{10}\overset{O}{\overset{\|}{C}}\bigcirc$

$CH_3(CH_2)_{10}\overset{O}{\overset{\|}{C}}\bigcirc \xrightarrow[HCl,\ \Delta]{Zn(Hg)} CH_3(CH_2)_{11}\bigcirc \xrightarrow[\Delta]{H_2SO_4} CH_3(CH_2)_{11}\bigcirc\!\!-\!\!SO_3H$

$CH_3(CH_2)_{11}\bigcirc\!\!-\!\!SO_3H \xrightarrow{NaOH} CH_3(CH_2)_{11}\bigcirc\!\!-\!\!SO_3^-\ Na^+$

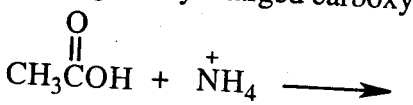
d. $CH_3\bigcirc \xrightarrow[H^+,\ \Delta]{Na_2Cr_2O_7} \overset{O}{\overset{\|}{C}}OH\bigcirc \xrightarrow{SOCl_2} \overset{O}{\overset{\|}{C}}Cl\bigcirc \xrightarrow{excess\ CH_3NH_2} \overset{O}{\overset{\|}{C}}NHCH_3\bigcirc$

e. $NH_2\bigcirc \xrightarrow[pyridine]{CH_3\overset{O}{\overset{\|}{C}}Cl} NH\overset{O}{\overset{\|}{C}}CH_3\bigcirc \xrightarrow[2.\ H_2O]{1.\ CH_3\overset{O}{\overset{\|}{C}}Cl,\ AlCl_3} NH\overset{O}{\overset{\|}{C}}CH_3\bigcirc\!\!-\!\!\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[2.\ HO^-]{1.\ HCl,\ H_2O,\ \Delta} NH_2\bigcirc\!\!-\!\!\overset{O}{\overset{\|}{C}}CH_3$

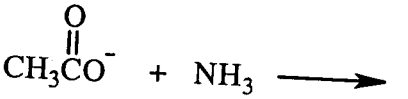
f. $CH_3\bigcirc \xrightarrow[peroxide]{NBS\ \Delta} CH_2Br\bigcirc \xrightarrow{^-C\equiv N} CH_2C\equiv N\bigcirc \xrightarrow[HCl\ \Delta]{H_2O} CH_2COOH\bigcirc$

65. The acid-catalyzed hydrolysis of acetamide forms acetic acid and ammonium ion. It is ar irreversible reaction, because the pK_a of a acetic acid is less than the pK_a of the ammoni Therefore, it is impossible to have the carboxylic acid in its reactive acidic form and amn its reactive basic form.

If the solution is sufficiently acidic to have the carboxylic acid is in its acidic form, amm also be in its acidic form so it will not be a nucleophile. If the pH of the solution is suffici basic to have ammonia in its nucleophilic basic form, the carboxylic acid will also be its b form; a negatively charged carboxylic acid is not attacked by nucleophiles



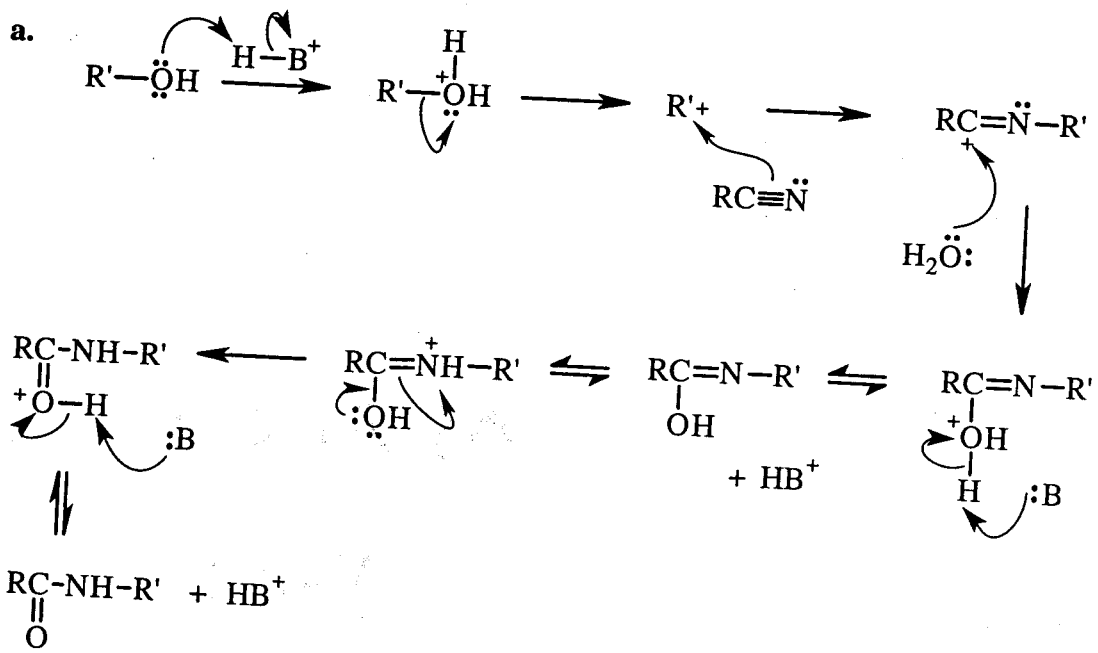
no reaction
The ammonium ion is not nucleophilic.



no reaction
The carboxylate ion is not attacked by nucleophiles.

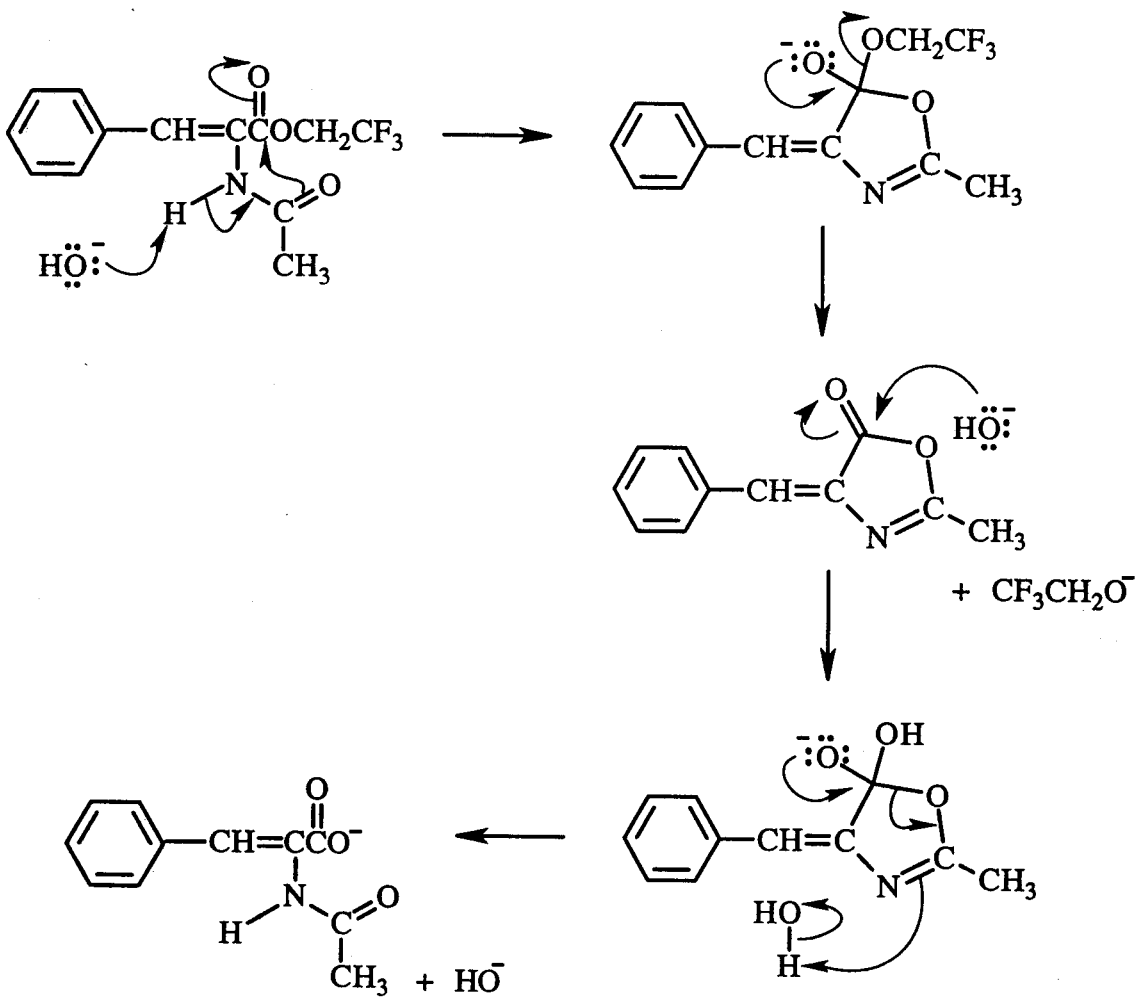
66.

a.



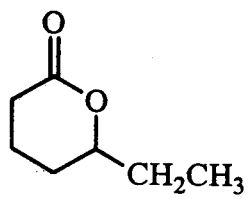
b. The Ritter reaction does not work with primary alcohols, because primary alcohols do not form carbocations.

c. The only difference in the two reactions is the electrophile that attaches to the nitrogen of tl nitrile: it is a carbocation in the Ritter reaction and a proton in the acid-catalyzed hydrolysis of a nitrile.

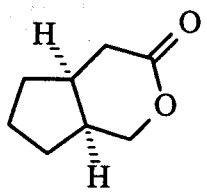


68.

a.

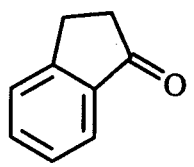


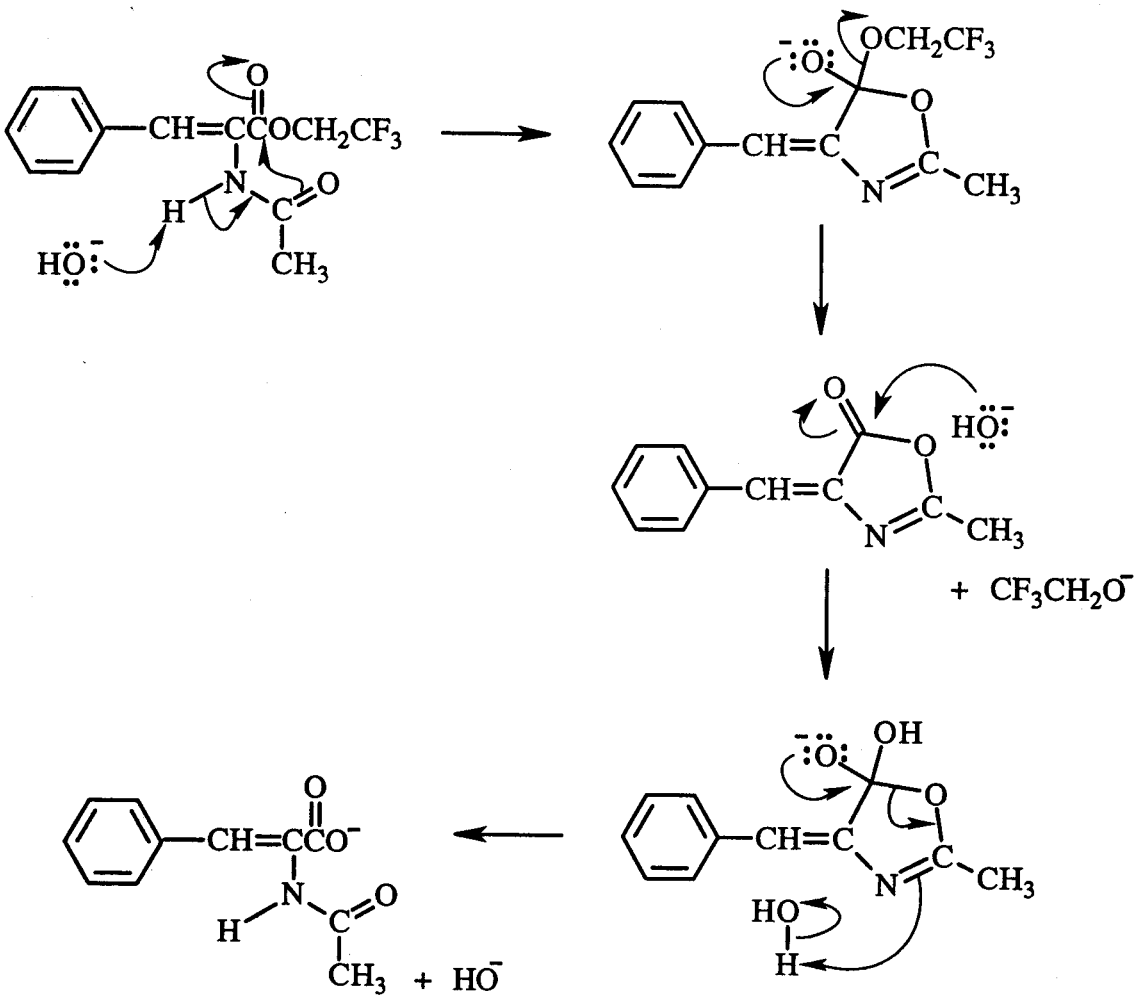
b.



+ CH_3CH_2OH

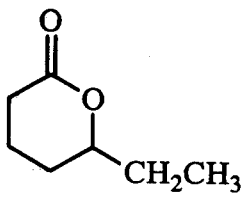
c.



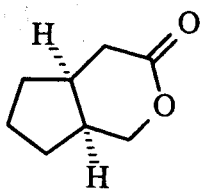


68.

a.

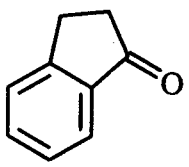


b.

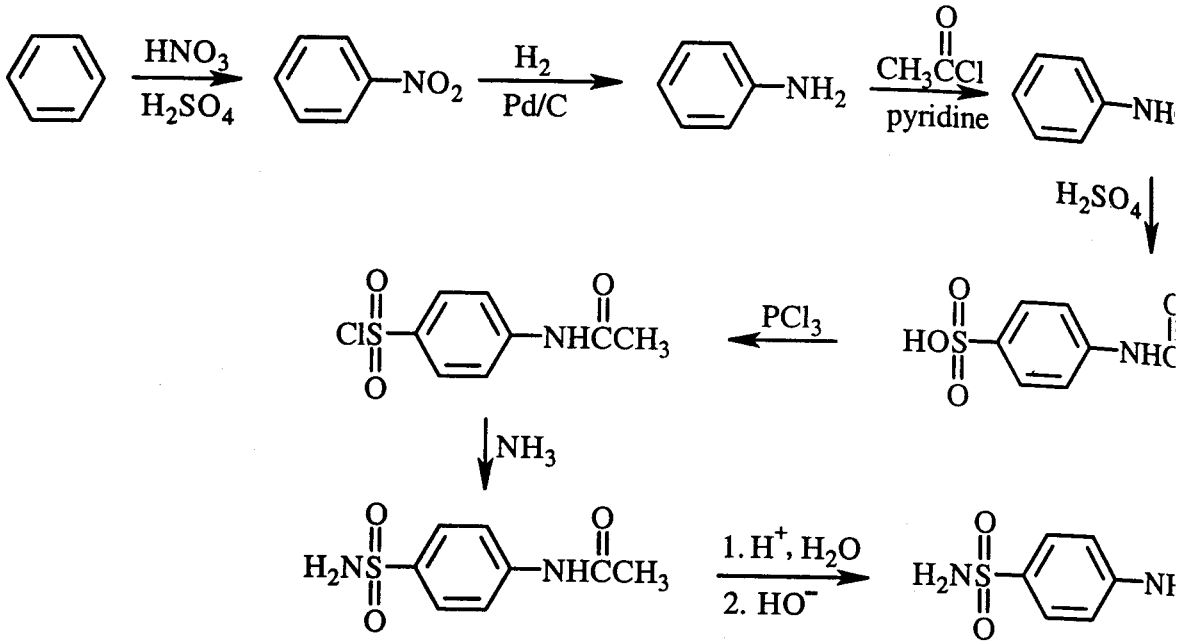


+ CH_3CH_2OH

c.

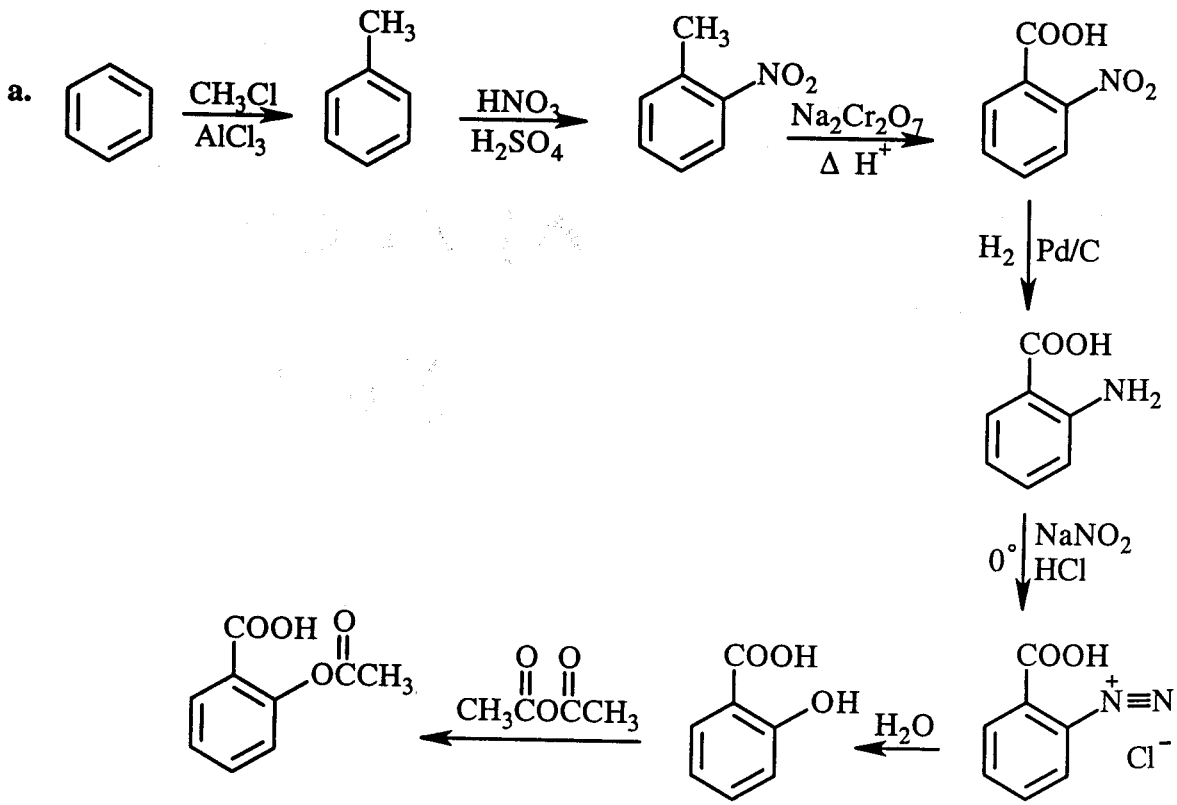


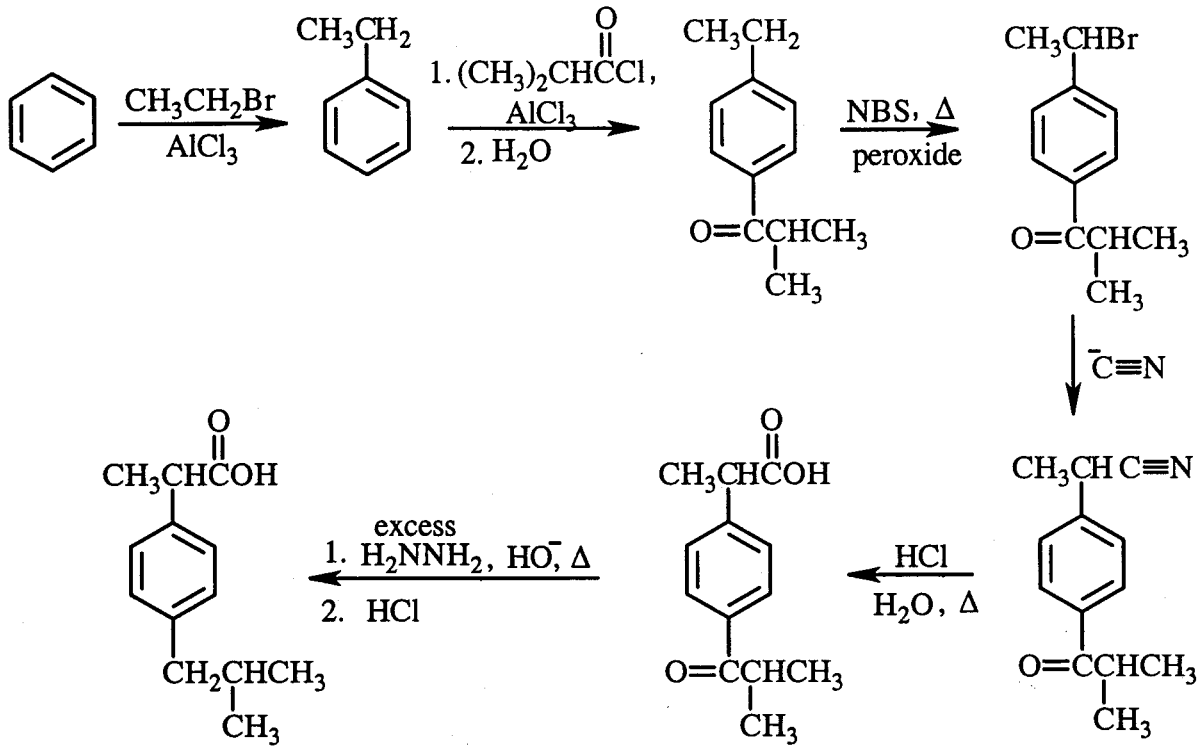
69.



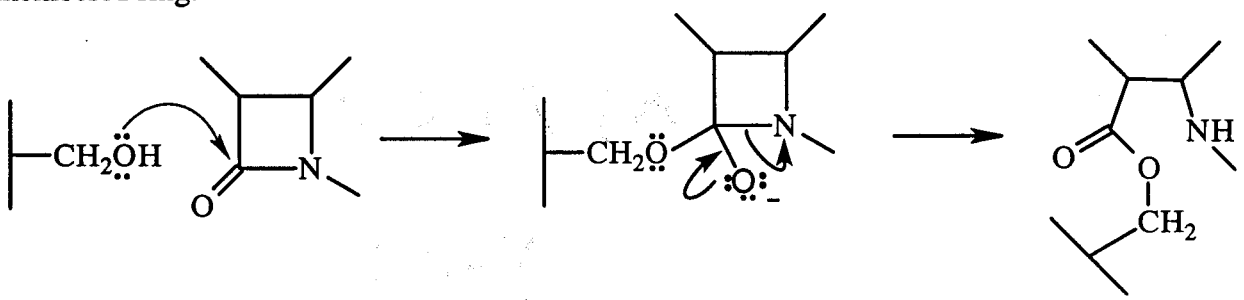
70.

a.

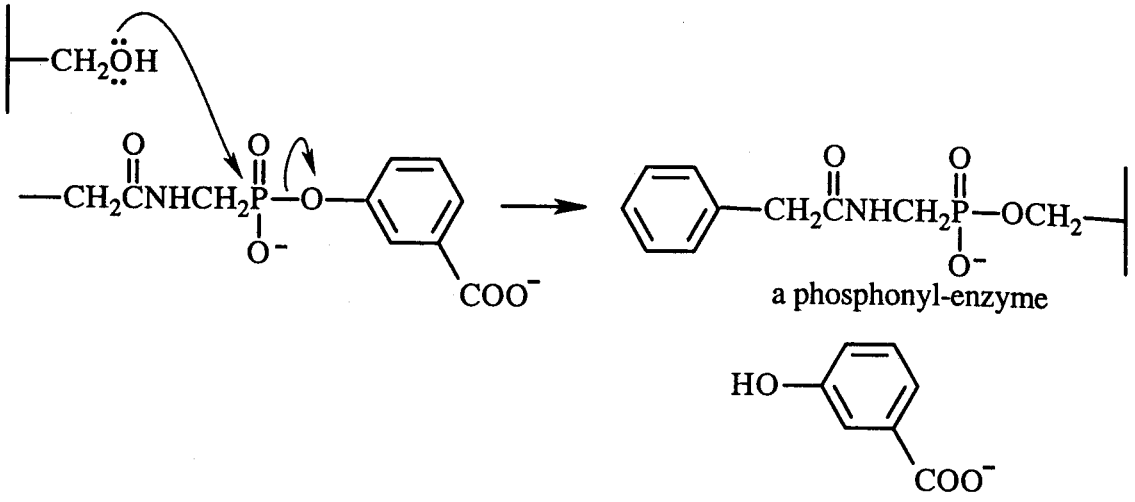


b. 

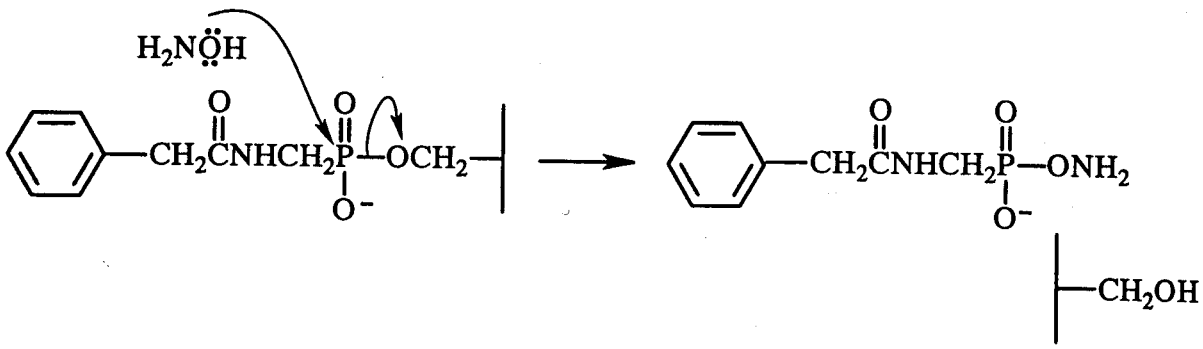
71. A β-lactamase enzyme provides resistance to penicillin by reacting with it, opening the four-membered ring.



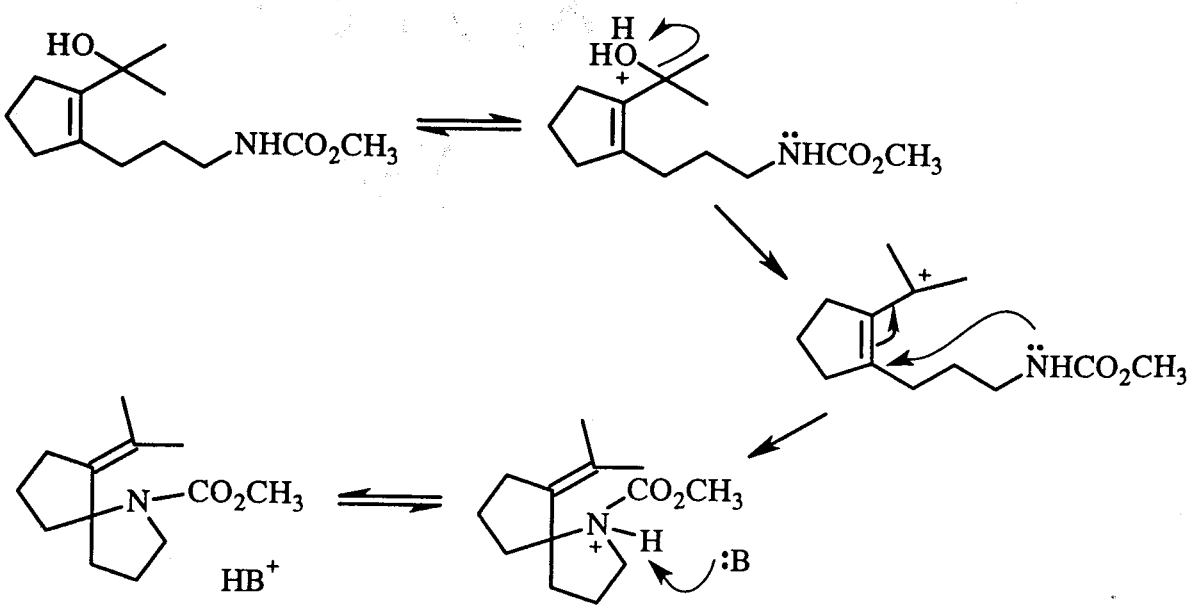
The inhibitor of the β-lactamase enzyme has an excellent leaving group, so it is readily attacked by nucleophiles. When the enzyme attacks the inhibitor, a relatively stable phosphonyl-enzyme is formed, so its OH group is no longer available to react with penicillin.



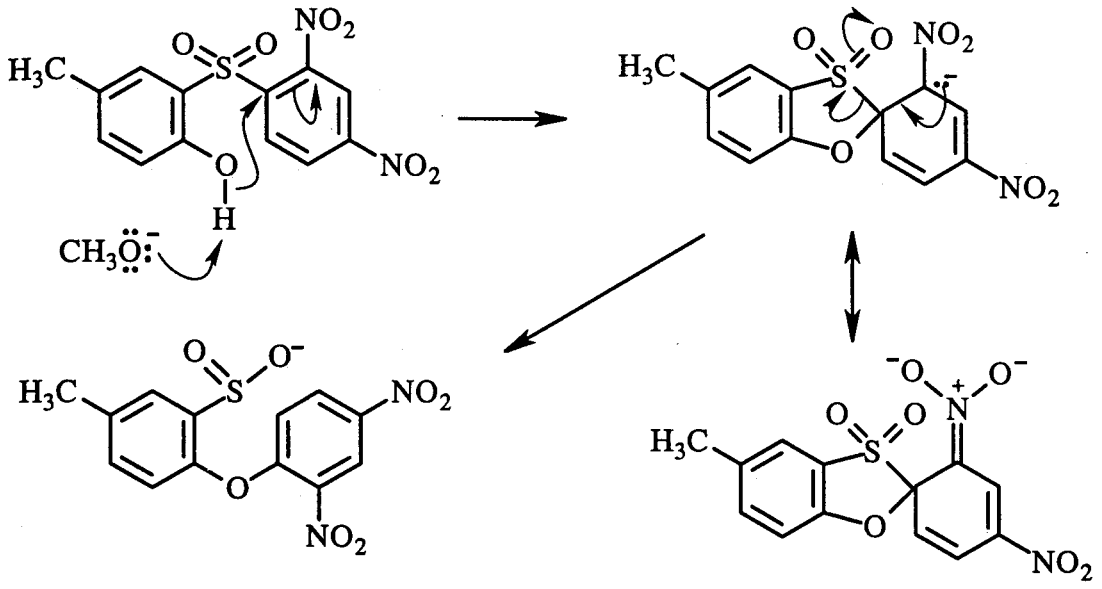
Hydroxylamine (H_2NOH) reactivates the enzyme by liberating the enzyme from the phosphonyl-enzyme.



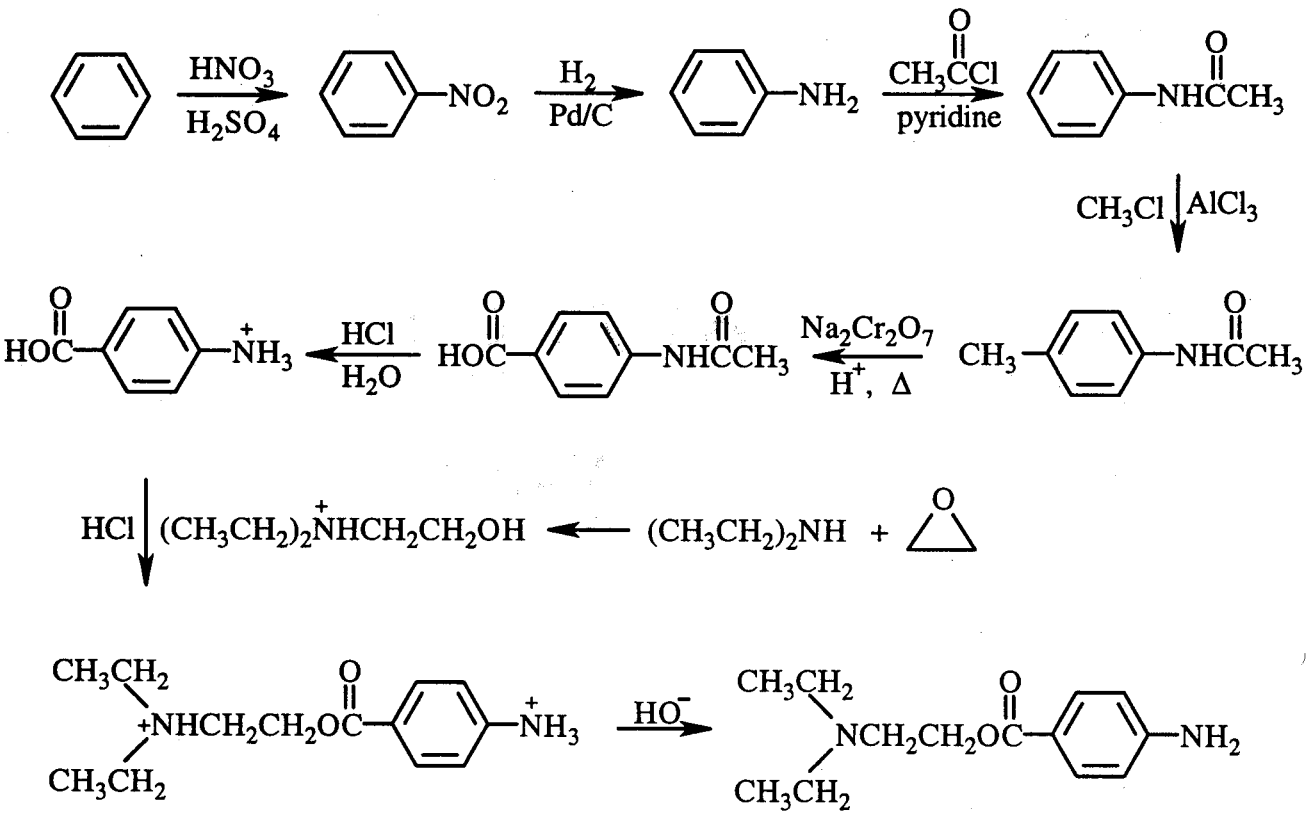
72. a.



b.

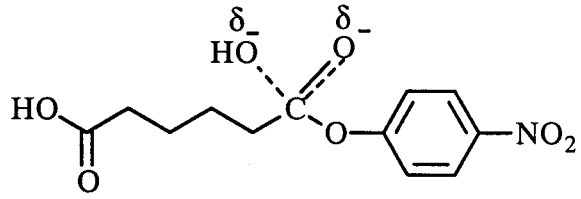


73.

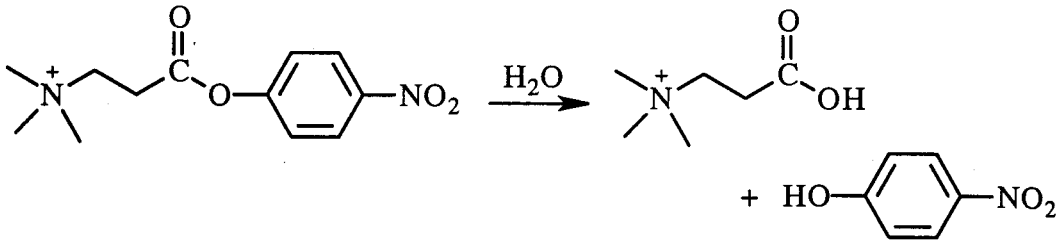


74.

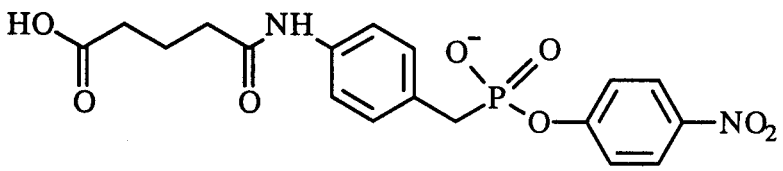
a.



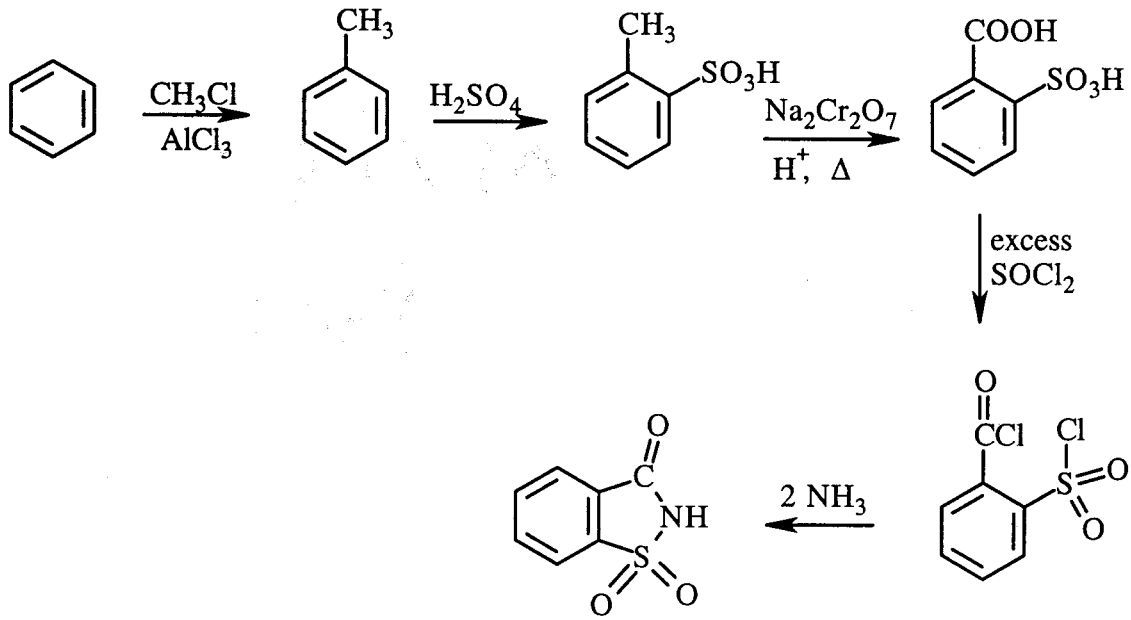
b.



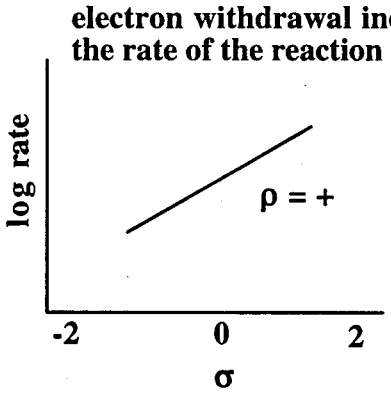
c.

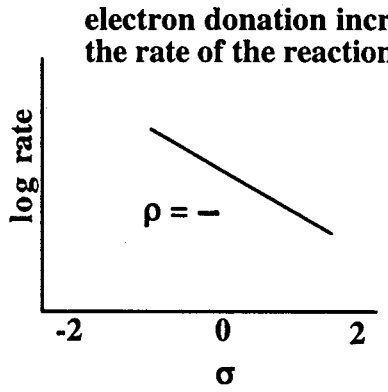


75.

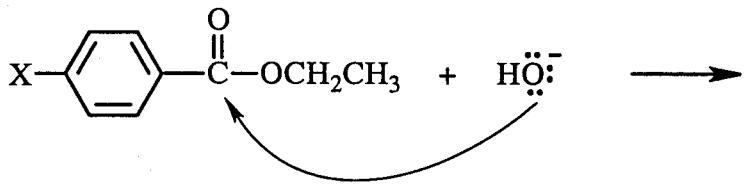


76. Because electron-withdrawing substituents have positive substituent constants and electron-donating substituents have negative substituent constants, a reaction with a positive ρ value is one in which compounds with electron-withdrawing substituents react more rapidly than compounds with electron-donating substituents, and a reaction with a negative ρvalue is one in which compounds with electron-donating substituents react more rapidly than compounds with electron-withdrawing substituents.

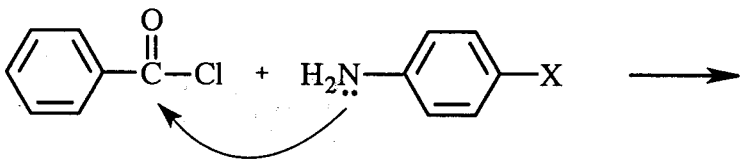




a. In the hydroxide-ion-promoted hydrolysis of a series of ethyl benzoates, electron-withdrawing substituents will increase the rate of the reaction by increasing the amount of positive charge on the carbonyl carbon, thereby making it more readily attacked by hydroxide ion. The ρ value for this reaction is, therefore, positive.



In amide formation with a series of anilines, electron donation will increase the rate of the reaction by increasing the nucleophilicity of the aniline. The ρ value for this reaction is, therefore, negative.

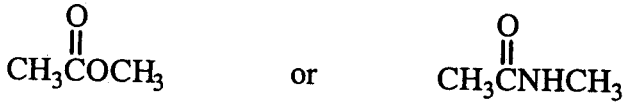


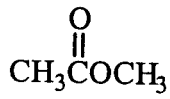
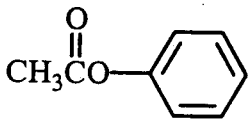
b. Because ortho substituents are close to the site of the reaction, they introduce steric factors into the rate constant for the reaction. In other words, the presence of an ortho substituent can slow a reaction down, not because it can donate or withdraw electrons but because it can get in the way of the reactants. Therefore, any change in the rate is due to a combination of steric effects and the electron-donating or electron-withdrawing ability of the substituent. Because the change in rate cannot be attributed solely to the electron-donating or electron-withdrawing ability of the substituent, ortho-substituted compounds were not included in the study.

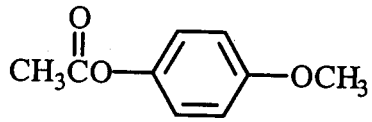
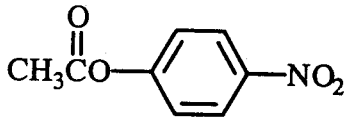
c. An electron-withdrawing substituent will make it easier for benzoic acid to lose a proton, so ionization will show a positive ρ value.

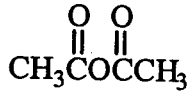
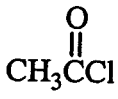
Chapter 17 Practice Test

1. Circle the compound in each pair that is more reactive toward nucleophilic acyl substitution.

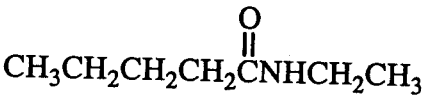
a.  or

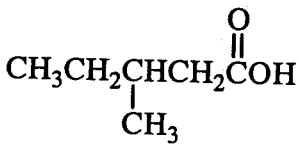
b.  or 

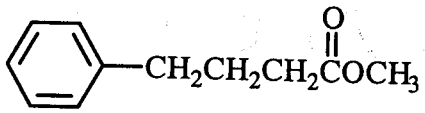
c.  or 

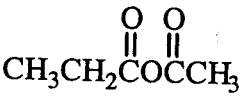
d.  or 

2. Give the systematic name for each of the following:

a. 

b. 

c. 

d. 

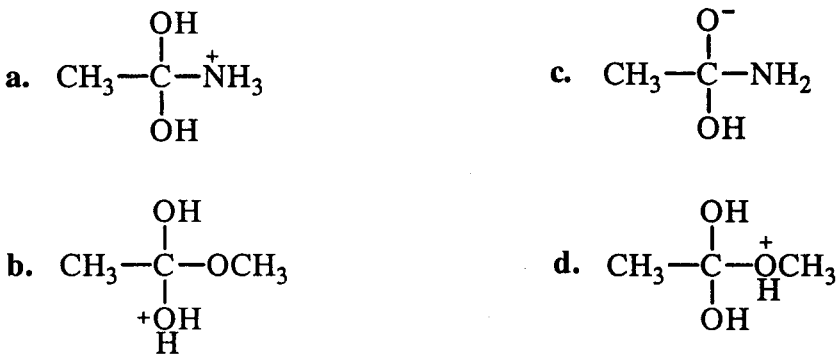
3. Give an example of each of the following:

a. a symmetrical anhydride

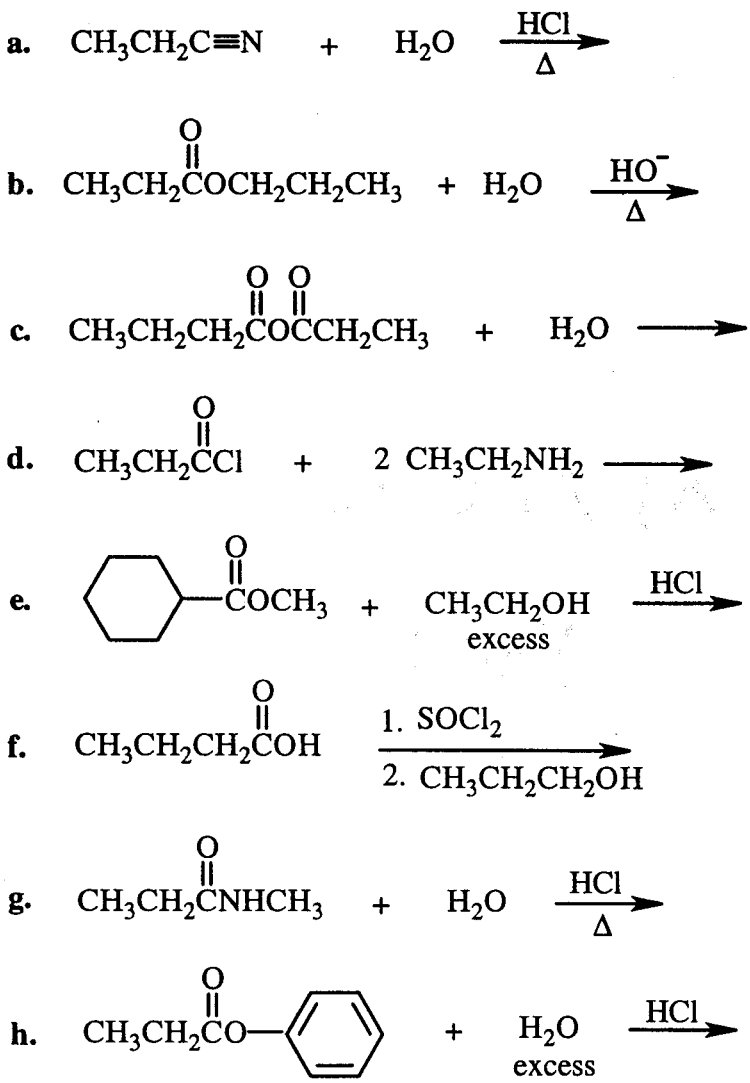
b. a hydrolysis reaction

c. a transesterification reaction

4. What carbonyl compound would be obtained from collapse of each of the following tetrahedral intermediates?



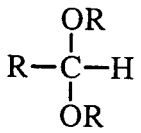
5. Give the product of each of the following reactions.



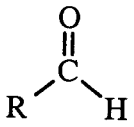
CHAPTER 18
Carbonyl Compounds II: Nucleophilic Acyl Addition, Nucleophilic Acyl Substitution, and Nucleophilic Addition-Elimination • Reactions of α,β-Unsaturated Carbonyl Compounds

Important Terms

acetal

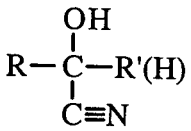


aldehyde



conjugate addition nucleophilic addition to the β-carbon of an α,β-unsaturated carbonyl compound.

cyanohydrin



deoxygenation removal of an oxygen from a reactant.

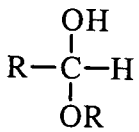
***gem*-diol (hydrate)** a molecule with two OH groups on the same carbon.

direct addition nucleophilic addition to the carbonyl carbon.

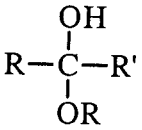
disconnection breaking a bond to carbon, in a retrosynthetic analysis, to give a simpler molecule.

enamine an α,β-unsaturated tertiary amine.

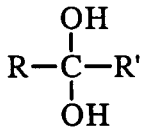
hemiacetal



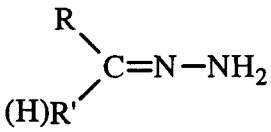
hemiketal



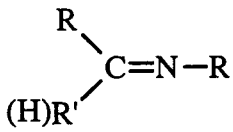
hydrate (*gem*-diol) a compound with two OH groups on the same carbon.



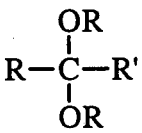
hydrazone



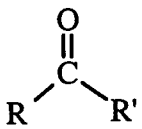
imine (Schiff base)



ketal



ketone

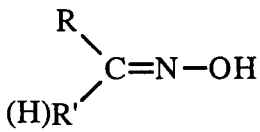


nucleophilic acyl substitution reaction a reaction in which a group bonded to an acyl group is substituted by another group.

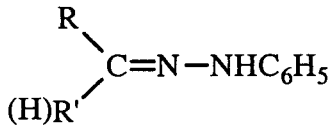
nucleophilic addition-elimination reaction a nucleophilic addition reaction that is followed by an elimination reaction. Imine formation is an example: an amine adds to the carbonyl carbon, and water is eliminated.

nucleophilic addition reaction a reaction that involves the addition of a nucleophile to a reagent.

oxime



phenylhydrazone



pH-rate profile a plot of the rate constant of a reaction versus the pH of the reaction mixture.

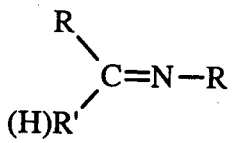
prochiral carbonyl carbon — a carbonyl carbon that will become a chirality center if it is attacked by a group unlike any of the groups already bonded to it.

protecting group — a reagent that protects a functional group from a synthetic operation that would otherwise not survive.

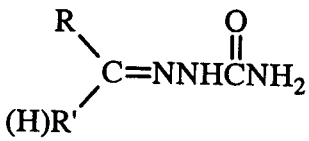
reduction reaction — a reaction in which a molecule gains electrons. In the case of an organic molecule, a reaction in which the number of C-H bonds is increased or the number of C-O, C-N, or C-X (X = halogen) bonds is decreased

reductive amination — the reaction of an aldehyde or a ketone with ammonia or with a primary amine in the presence of a reducing agent (H_2/Raney Ni).

Schiff base (imine)



semicarbazone



synthetic equivalent — the reagent actually used as the source of a synthon.

synthon — a fragment of a disconnection.

target molecule — the desired end product of a synthesis.

Wittig reaction — the reaction of an aldehyde or a ketone with a phosphonium ylide, resulting in formation of an alkene.

ylide — a compound with opposite charges on adjacent, covalently bonded atoms with complete octets.

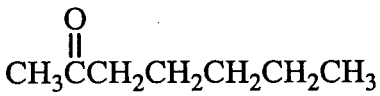
Solutions to Problems

1. If the ketone functional group were anywhere else in these compounds, they would not be ketones and, therefore, would not have the "one" suffix.

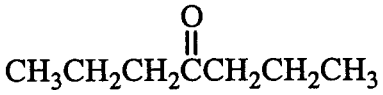
2.
a. 3-methylpentanal, β-methylvaleraldehyde
b. 4-heptanone, dipropyl ketone
c. 2-methyl-4-heptanone, isobutyl propyl ketone
d. 4-phenylbutanal, γ-phenylbutyraldehyde
e. 4-ethylhexanal, γ-ethylcaproaldehyde
f. 1-hepten-3-one, butyl vinyl ketone

3. **a.** 6-hydroxy-3-heptanone **b.** 2-oxocyclohexylmethanenitrile **c.** 3-formylpentanamide

4. **a.** 2-Heptanone is more reactive because it has less steric hindrance. There is little difference in the amount of steric hindrance provided at the carbonyl carbon (the site of nucleophilic attack) by a pentyl and a propyl group because they differ at a point somewhat removed from the site of nucleophilic attack. The difference in size between a methyl group and a propyl group is significant at the site of nucleophilic attack.

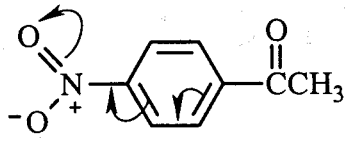


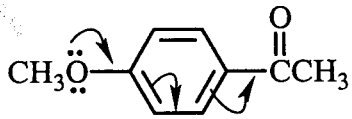
2-heptanone



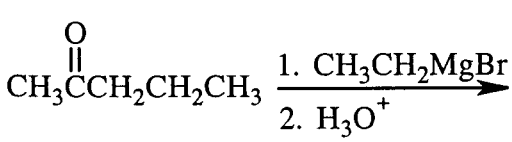
4-heptanone

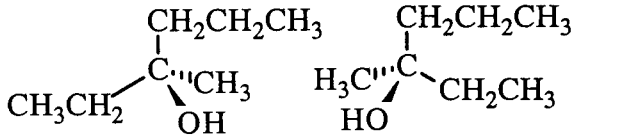
b. *para*-Nitroacetophenone is more reactive because the electron-withdrawing nitro group makes the carbonyl carbon more susceptible to nucleophilic attack compared with an electron-donating methoxy group.





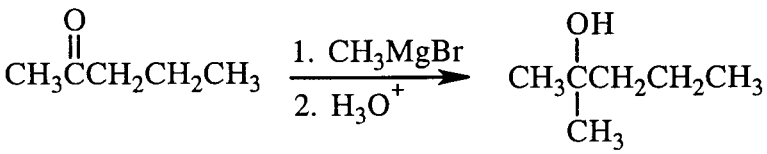
5. **a.** Two isomers are obtained because the reaction creates an asymmetric carbon in the product.



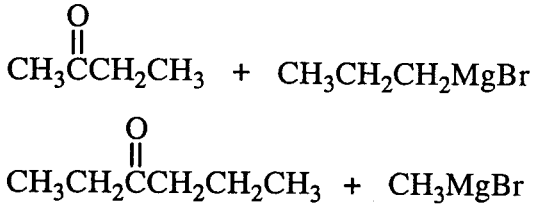


(*S*)-3-methyl-3-hexanol (*R*)-3-methyl-3-hexanol

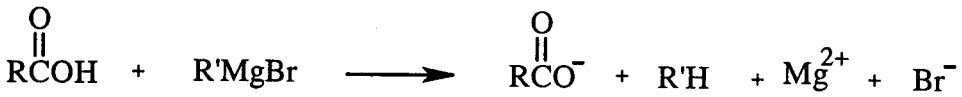
b. Only one compound is obtained because the product does not have an asymmetric carbon.



6.



7. The Grignard reagent will react with the proton from the carboxylic acid, forming an alkane and a carboxylate ion.

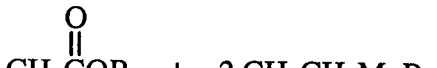


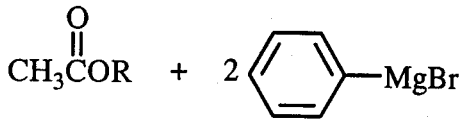
8. **a.** Solved in the text.

b.

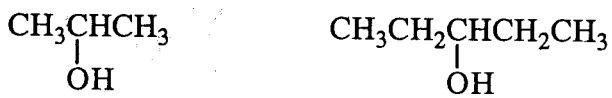
1. 

2. Solved in the text.

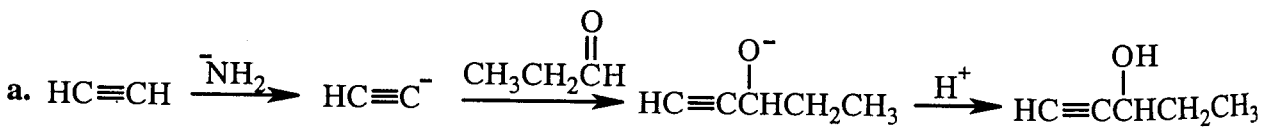
4. 

6. 

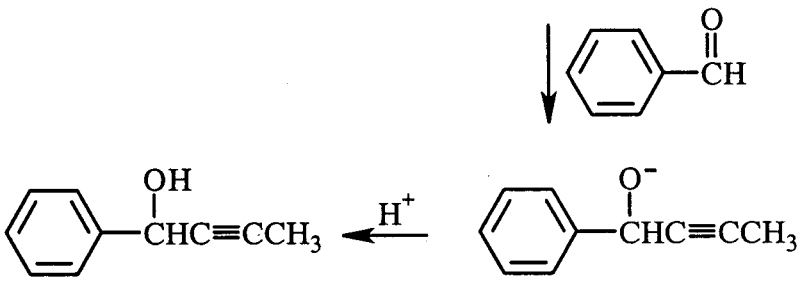
9. If a secondary alcohol is formed from the reaction of a formate ester with excess Grignard reagent, the two alkyl substituents of the alcohol will be identical because they both come from the Grignard reagent. Therefore, only the following two alcohols can be prepared that way.



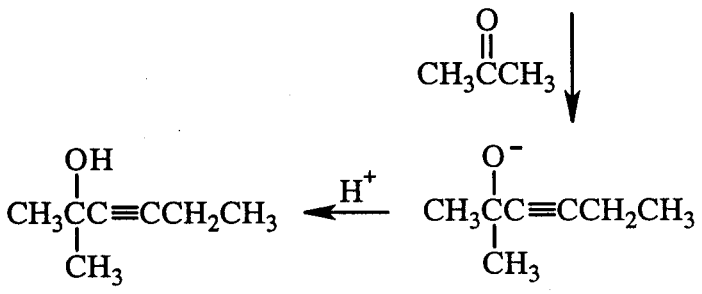
10. If the compound is alkylated after nucleophilic attack, the alkylation on oxygen will compete with alkylation on carbon.

a. 

b. $HC{\equiv}CH \xrightarrow{\bar{N}H_2} HC{\equiv}C^- \xrightarrow{CH_3Br} HC{\equiv}CCH_3 \xrightarrow{\bar{N}H_2} \bar{C}{\equiv}CCH_3$



c. $HC{\equiv}CH \xrightarrow{\bar{N}H_2} HC{\equiv}C^- \xrightarrow{CH_3CH_2Br} HC{\equiv}CCH_2CH_3 \xrightarrow{\bar{N}H_2} \bar{C}{\equiv}CCH_2CH_3$



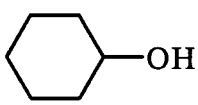
11. No, an acid must be present in the reaction mixture in order to protonate the oxygen of the cyanohydrin. Otherwise the cyano group will be eliminated and the reactants will be reformed.

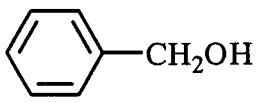
12. Strong acids like HCl and H_2SO_4 have very weak conjugate bases (Cl^- and HSO_4^-), which are excellent leaving groups. When these bases add to the carbonyl group, they are readily eliminated, reforming the starting materials. Cyanide ion is a strong enough base, so it is not eliminated unless the oxygen in the product is negatively charged.

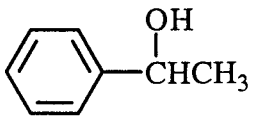
13. Solved in the text.

14.

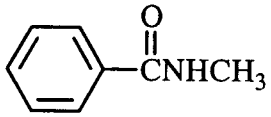
a. CH_3CHCH_2OH (with CH_3 branch)

b. 

c. 

d. 

15.

a. 

b. CH_3CNH_2 **c.** $CH_3CNHCH_2CH_3$ **d.** $CH_3CN(CH_2CH_3)_2$

16.

a. 1. $LiAlH_4$ 2. H_2O

b. HCl, H_2O, Δ

c. 1. HCl, H_2O, Δ 2. $SOCl_2$ 3. $LiAlH[OC(CH_3)_3]_3$, – 80 °C 4. H_2O

d. 1. HCl, H_2O, Δ 2. $LiAlH_4$ 3. H_3O^+

17. For the derivations of the equations used to calculate the amount of a compound that is present in either its acidic or basic form, see page 42.

a. fraction present in the acidic form $= \dfrac{[H^+]}{K_a + [H^+]}$

$$\frac{[H^+]}{K_a + [H^+]} = \frac{3.2 \times 10^{-5}}{3.2 \times 10^{7} + 3.2 \times 10^{-5}}$$

$$= \frac{3.2 \times 10^{-5}}{3.2 \times 10^{7}}$$

$$= 1 \times 10^{-12}$$

b. fraction present in the acidic form $= \dfrac{[H^+]}{K_a + [H^+]}$

$$\frac{[H^+]}{K_a + [H^+]} = \frac{3.2 \times 10^{-2}}{3.2 \times 10^{7} + 3.2 \times 10^{-2}}$$

$$= \frac{3.2 \times 10^{-2}}{3.2 \times 10^{7}}$$

$$= 1 \times 10^{-9}$$

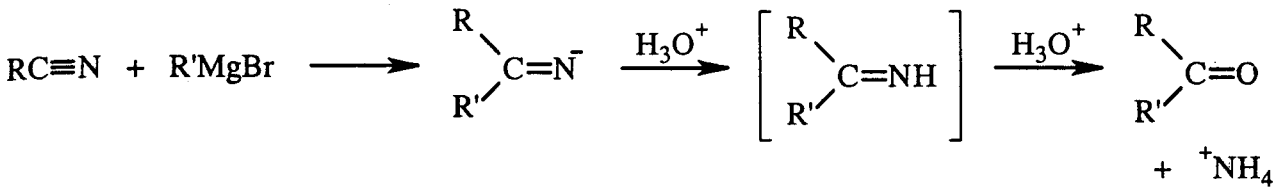
c. fraction present in the basic form $= \dfrac{K_a}{K_a + [H^+]}$

$$\frac{K_a}{K_a + [H^+]} = \frac{1.0 \times 10^{-6}}{1.0 \times 10^{-6} + 3.2 \times 10^{-2}}$$

$$= \frac{1.0 \times 10^{-6}}{3.2 \times 10^{-2}}$$

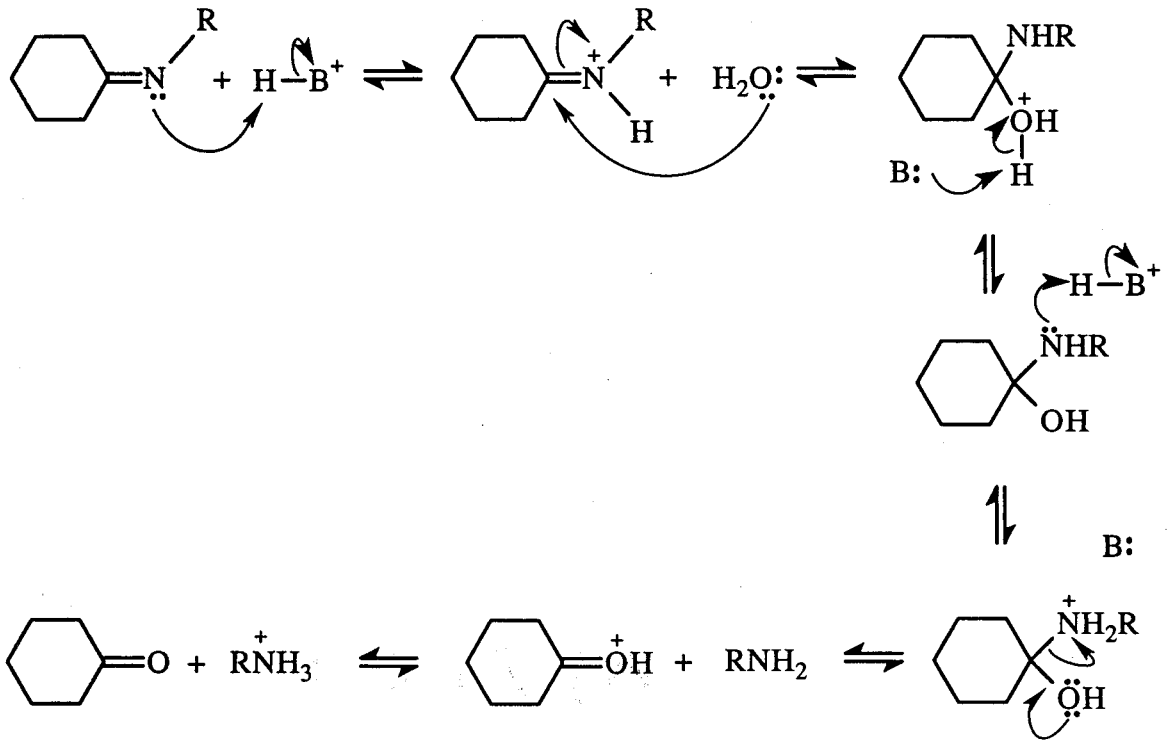
$$= 3.1 \times 10^{-3}$$

18. The nitrile reacts with the Grignard reagent to form an imine which could then be hydrolyzed to a ketone.

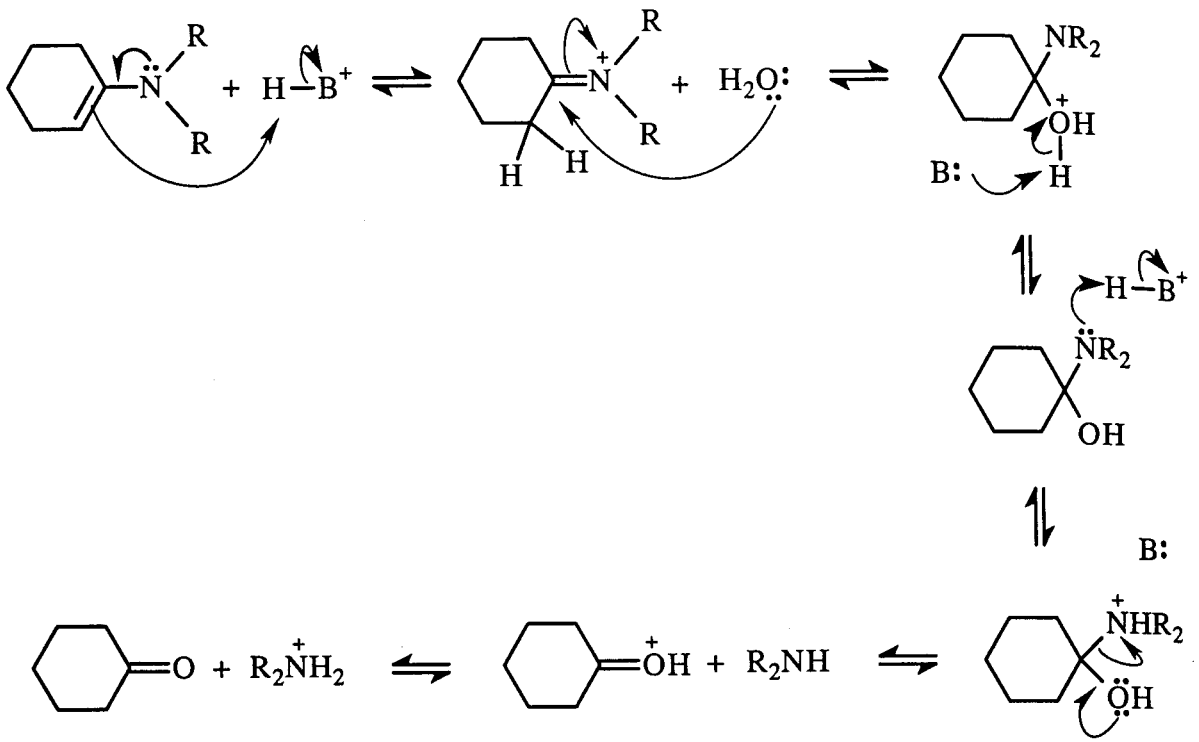


19. **a.**

1.



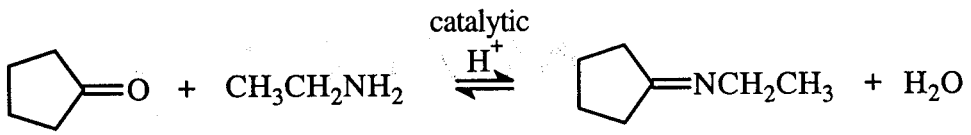
2.



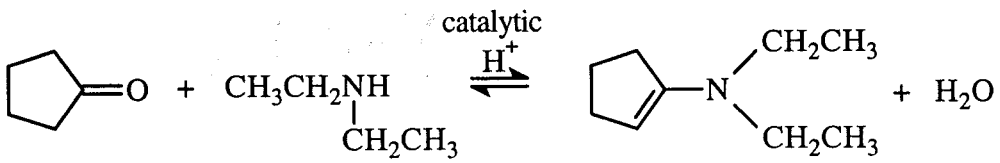
b. The only difference is in the first step of the mechanism: in imine hydrolysis the acid protonates the nitrogen; in enamine hydrolysis, the acid protonates the β-carbon.

20.

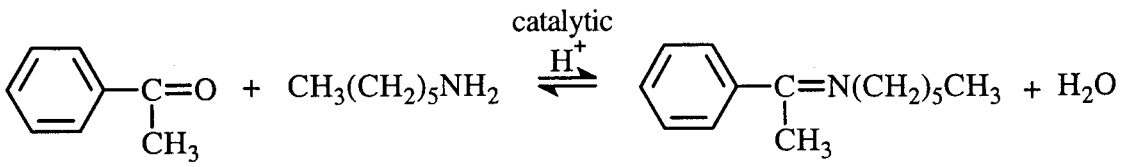
a.



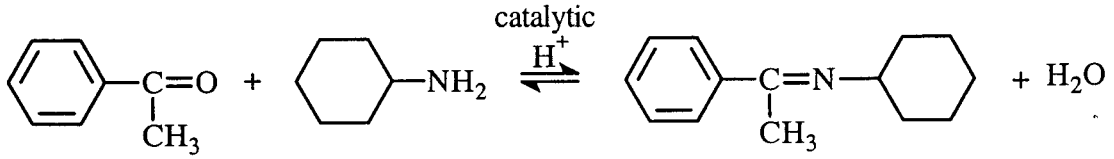
b.



c.

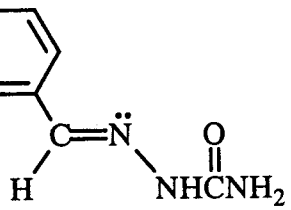


d.

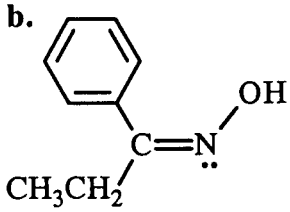


21.

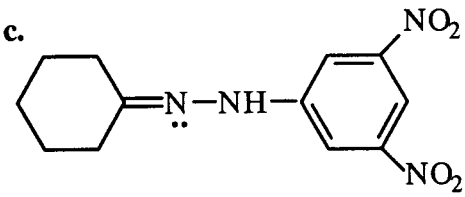
a.



b.

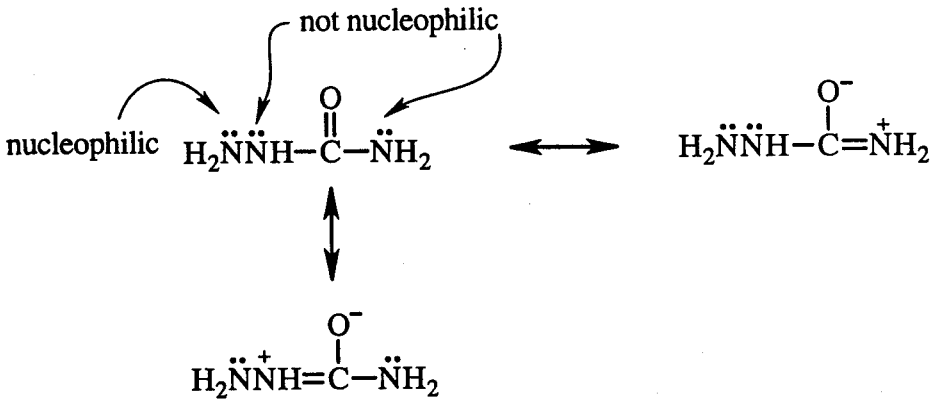


c.

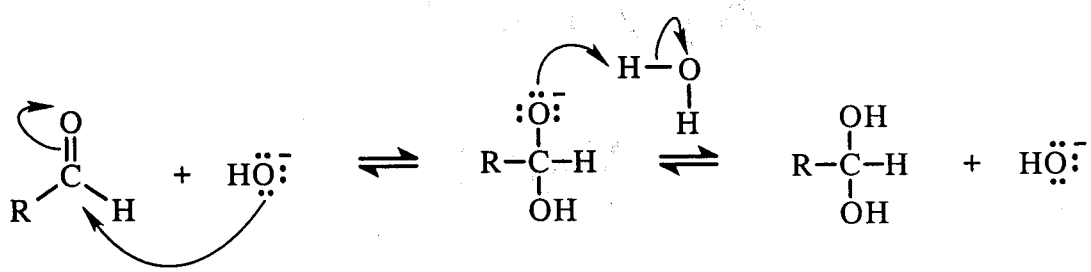


Because the ketone is symmetrical, *E* and *Z* isomers are not possible for this compound.

22. The lone pair on the nitrogen that is attached to the carbonyl carbon is in resonance with the carbonyl group. This nitrogen, therefore, cannot act as a nucleophile since its lone pair is not available for nucleophilic attack.



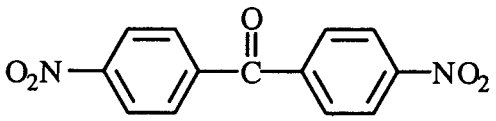
23.



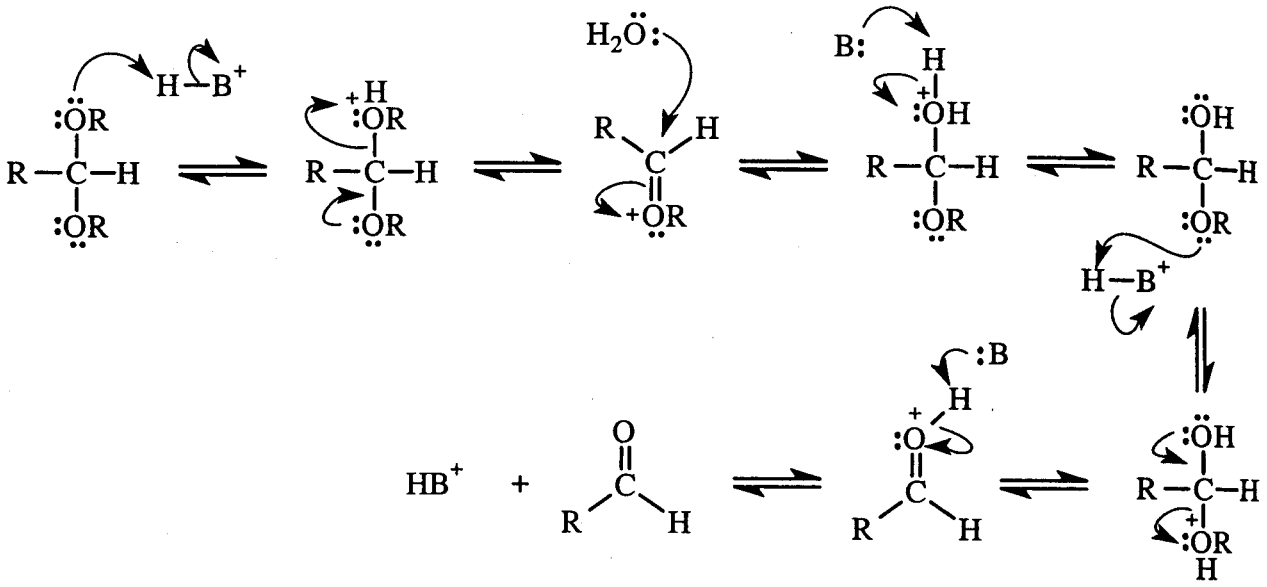
24. Electron-withdrawing groups decrease the stability of the aldehyde and increase the stability of the hydrate. Therefore, the three electron-withdrawing chlorines cause trichloroacetaldehyde to have a large equilibrium constant for hydrate formation.

$$K_{eq} = \frac{[\text{hydrate}]}{[\text{aldehyde}]\,[H_2O]}$$

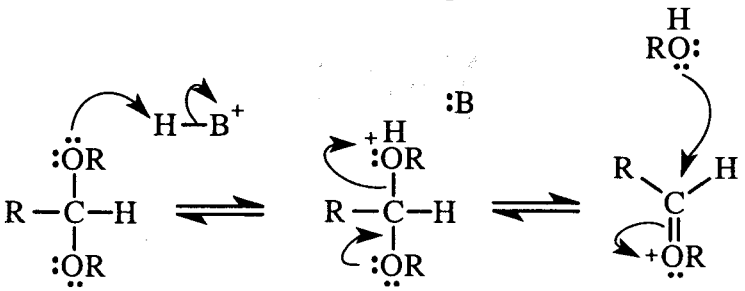
25. Because an electron-withdrawing substituent decreases the stability of a ketone and increases the stability of a hydrate, the compound with the electron-withdrawing *para*-nitro substituents has the largest equilibrium constant for addition of water.

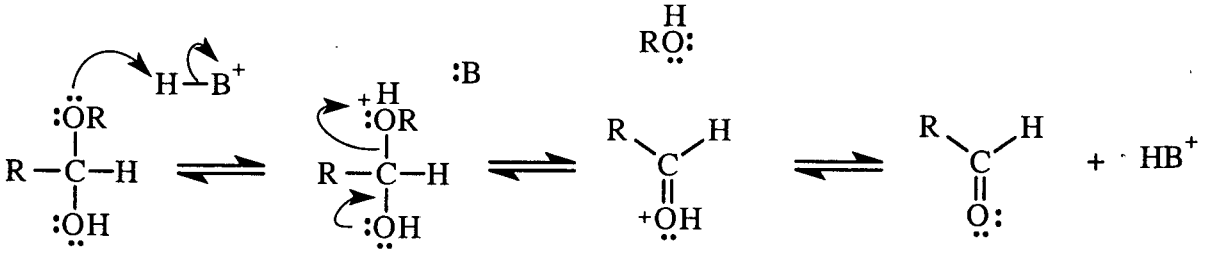


26.

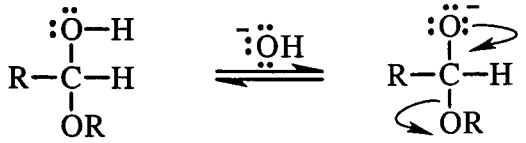


27. When a tetrahedral intermediate collapses, the intermediate that is formed is very unstable because of the positive charge on the sp^2 oxygen atom. In the case of an acetal or ketal, the only way to form a neutral species is to reform the acetal or ketal. In the case of a hydrate, a neutral species can be formed by loss of a proton.

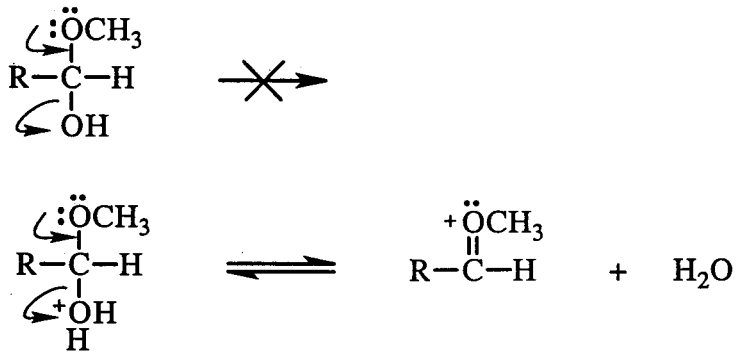




28. **a.** Hemiacetals are unstable in basic solution because the base can remove a proton from an OH group, thereby providing an oxyanion that has sufficient driving force to expel the basic $^-$OR group.

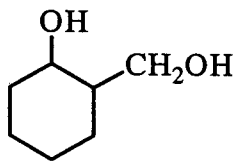


b. In order for an acetal to form, the CH_3O group in the hemiacetal must eliminate an $^-$OH group. Hydroxide ion is too basic to be eliminated by a CH_3O group, but water can be eliminated by a CH_3O group. Since the OH group must be protonated before it can be eliminated, acetal formation must be carried out in an acidic solution.

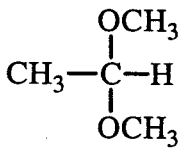


c. Hydrate formation can be catalyzed by hydroxide ion because a group does not have to be eliminated after hydroxide ion attacks the aldehyde or ketone.

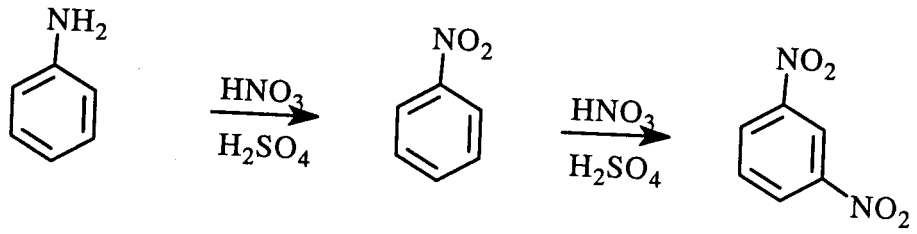
29.

a.  **b.** $NaBH_4$

30. An acetal has a very poor leaving group (CH_3O^-).



31. Nitric acid is an oxidizing agent and primary amines are easily oxidized. So one product would nitrobenzene. If excess nitric acid is present, nitrobenzene can be converted to *meta*-dinitroben



32.

a. A → B → C → D → E → F →

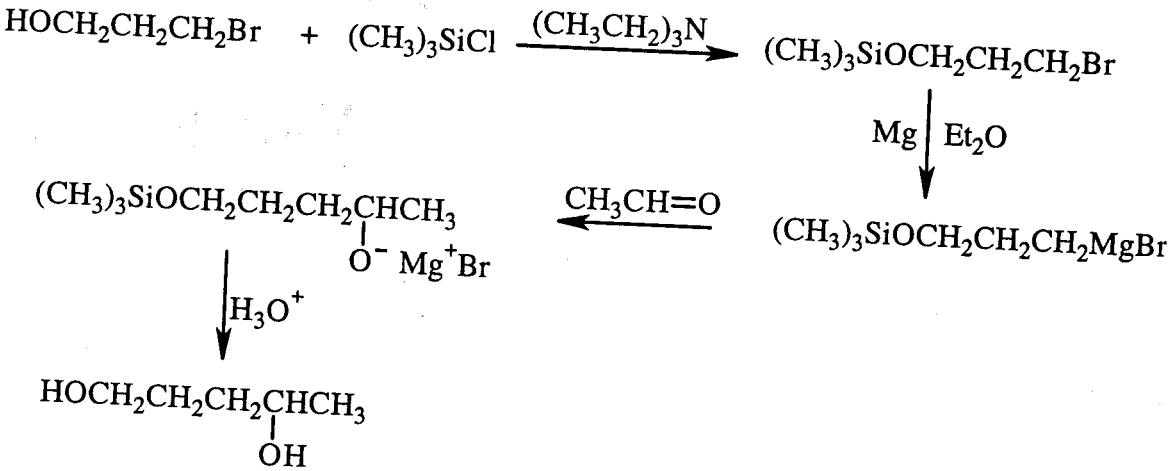
80% 0.80 x 0.80 = 64% 0.80 x 0.64 = 51% 0.80 x 0.51 = 41% 0.80 x 0.41 = 33%

b. G → H → I

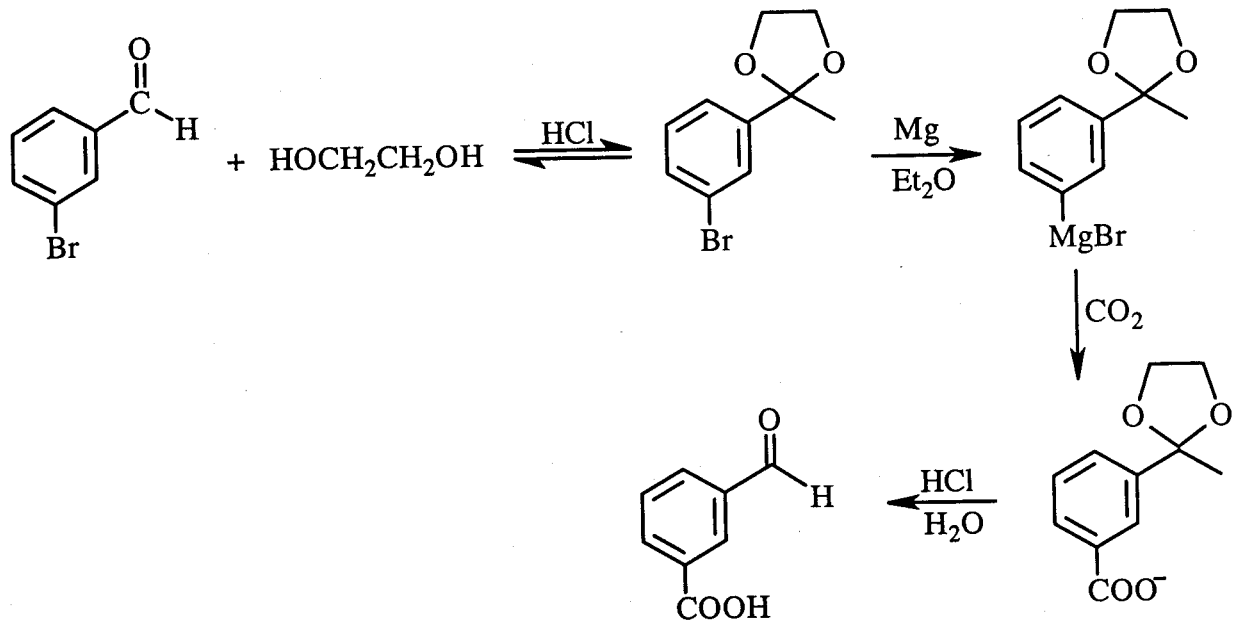
26% 0.80 x 0.26 = 21% 0.80 x 0.21 = 17%

33.

a.



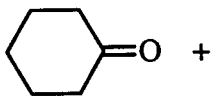
b.

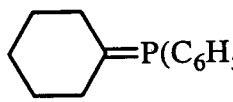


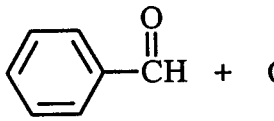
34.

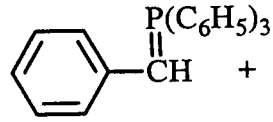
a.

1. Solved in the text.

2.  + $CH_3CH_2CH{=}P(C_6H_5)_3$

or  + $CH_3CH_2CH{=}O$

3.  + $CH_2{=}P(C_6H_5)_3$

or  + $CH_2{=}O$

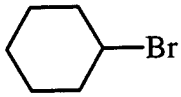
4. $(C_6H_5)_2C{=}O + CH_3CH{=}P(C_6H_5)_3$

or $(C_6H_5)_2C{=}P(C_6H_5)_3 + CH_3CH{=}O$

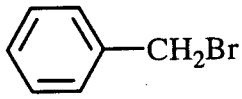
b.

1. Solved in the text.

2. $CH_3CH_2CH_2Br$

or 

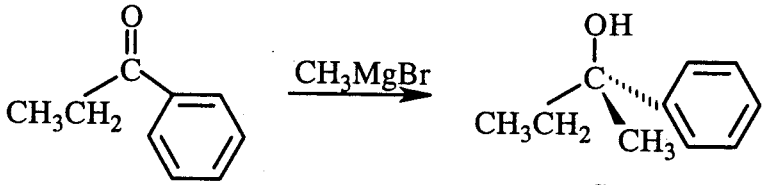
3. CH_3Br

or 

4. CH_3CH_2Br or $(C_6H_5)_2CHBr$

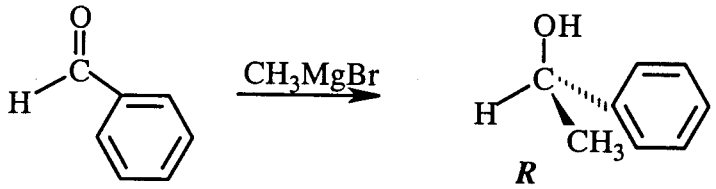
35. To review how to determine whether an asymmetric carbon has the *R* or *S* configuration, see Section 5.6.

a.



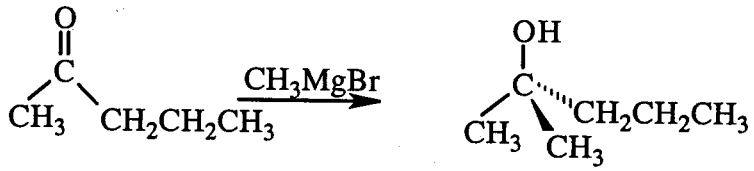
S

b.



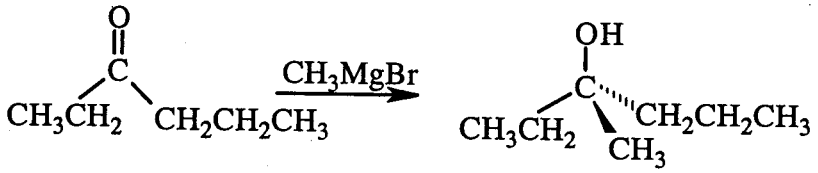
R

c.



No enantiomers are possible because the compound does not have an asymmetric carbon.

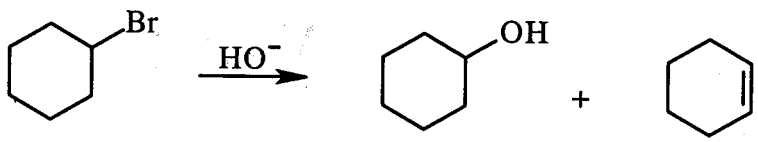
d.



S

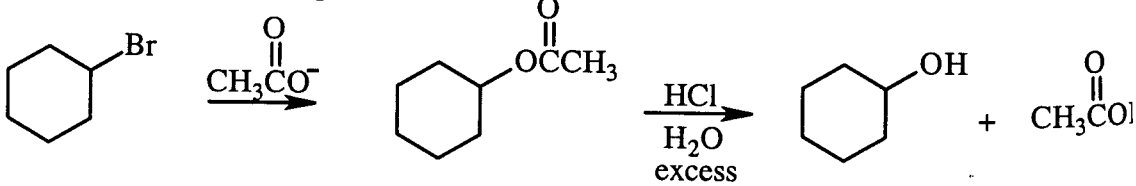
36.

a.

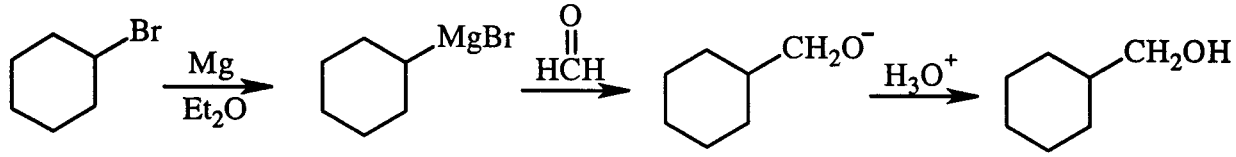


The above synthesis will also form an elimination product (cyclohexene).

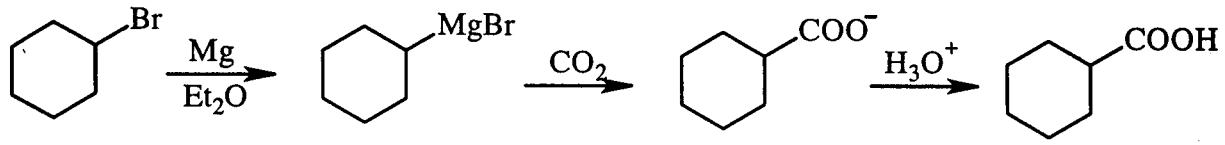
The following procedure will give a greater yield of the target molecule because the substitution product is favored by a weak base (see page 423 of the text), and the substitution product can b hydrolyzed to the target compound.



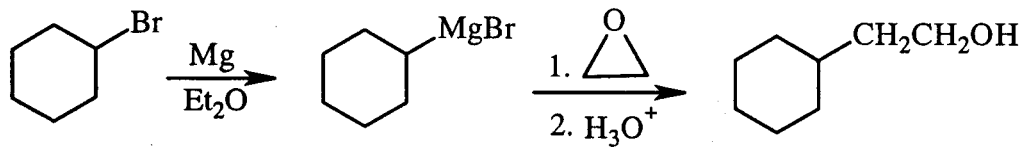
b.


Br
Mg
Et_2O
MgBr
O
HCH
CH_2O^-
H_3O^+
CH_2OH

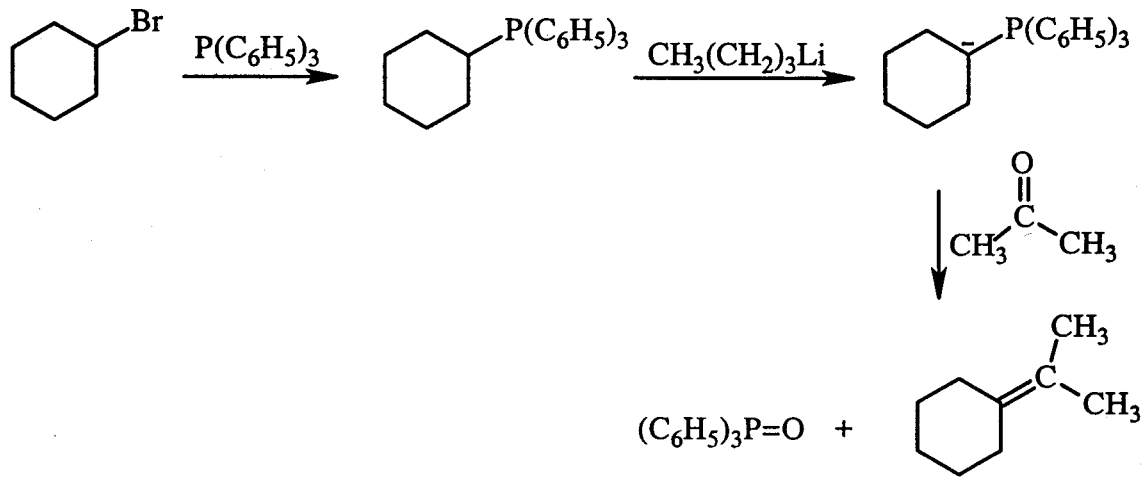
c.


Br
Mg
Et_2O
MgBr
CO_2
COO^-
H_3O^+
COOH

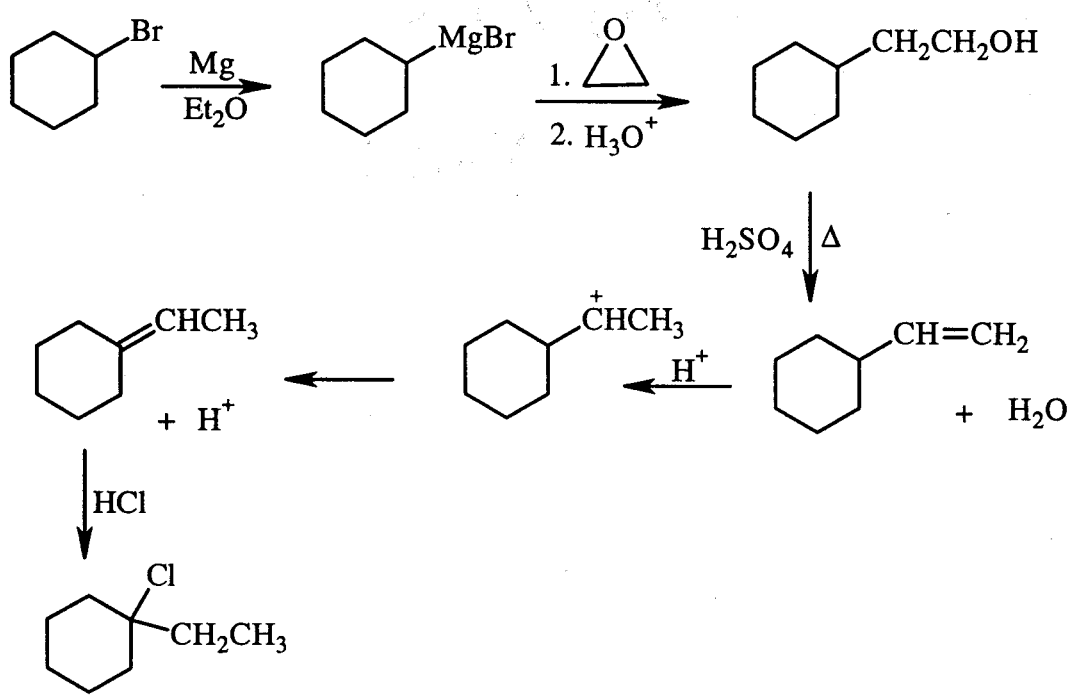
d.


Br
Mg
Et_2O
MgBr
O
1.
2. H_3O^+
CH_2CH_2OH

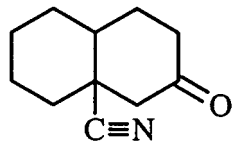
e.

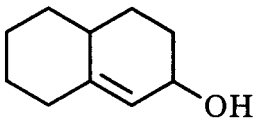

Br
$P(C_6H_5)_3$
$P(C_6H_5)_3$
$CH_3(CH_2)_3Li$
$P(C_6H_5)_3$
O
C
CH_3
CH_3
CH_3
C
CH_3
$(C_6H_5)_3P=O$ +

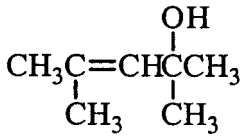
f.

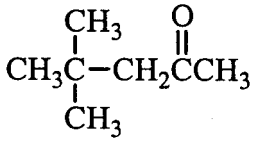

Br
Mg
Et_2O
MgBr
O
1.
2. H_3O^+
CH_2CH_2OH
H_2SO_4
Δ
$CH=CH_2$
+ H_2O
H^+
$\overset{+}{C}HCH_3$
$CHCH_3$
+ H^+
HCl
Cl
CH_2CH_3

37.

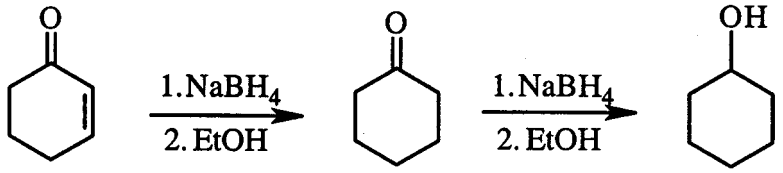
a. 

b. 

c. 

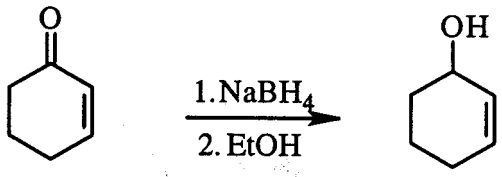
d. 

38. If the initial reaction of the α,β-unsaturated ketone with sodium borohydrate is *conjugate* addition, a ketone will be formed, which is then reduced to a saturated alcohol.



a saturated alcohol

If the initial reaction of the α,β-unsaturated ketone with sodium borohydrate is *direct* addition, the final product will be an α,β-unsaturated alcohol, which won't be further reduced.

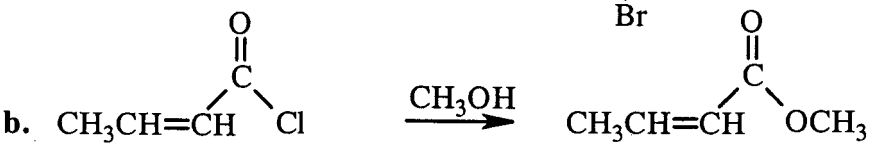


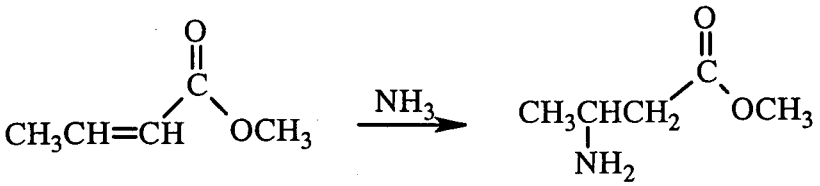
unsaturated alcohol

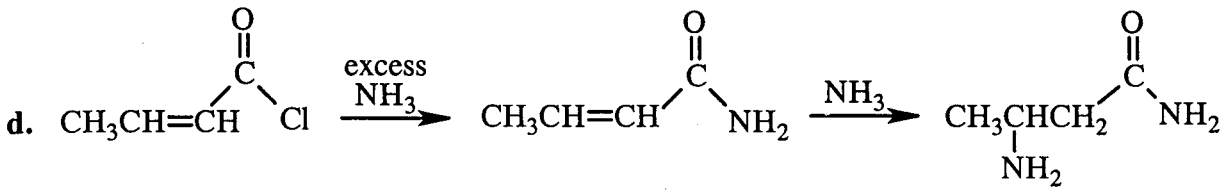
A sterically hindered ketone will be less likely to undergo direct addition and, therefore, more likely to undergo conjugate addition, the pathway that does not form an unsaturated alcohol. Thus, the nonsterically hindered ketone will give a higher yield of unsaturated alcohol.

39.

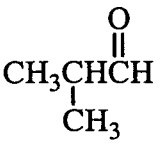
a. 

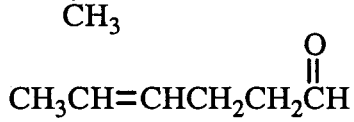
b. 

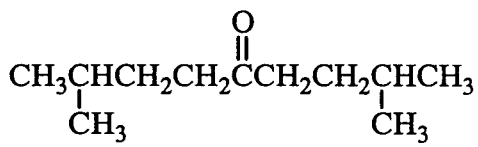
c. 

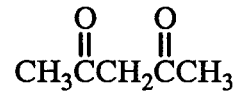
d. 

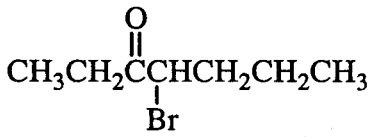
40.

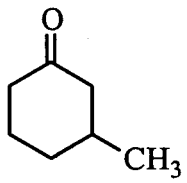
a. 

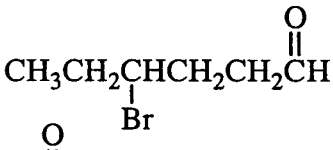
b. 

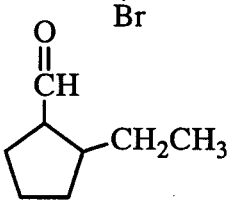
c. 

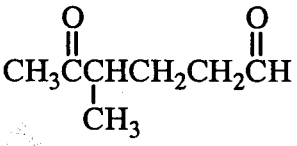
e. 

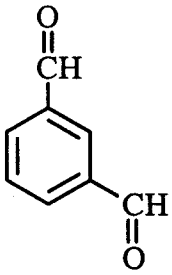
f. 

d. 

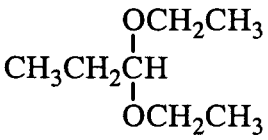
g. 

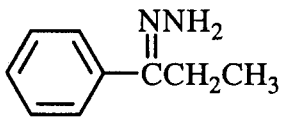
h. 

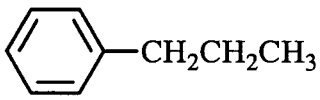
i. 

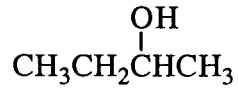
j. 

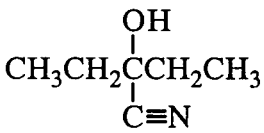
41.

a. 

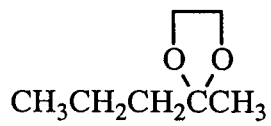
b. 

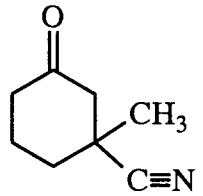
c. 

d. 

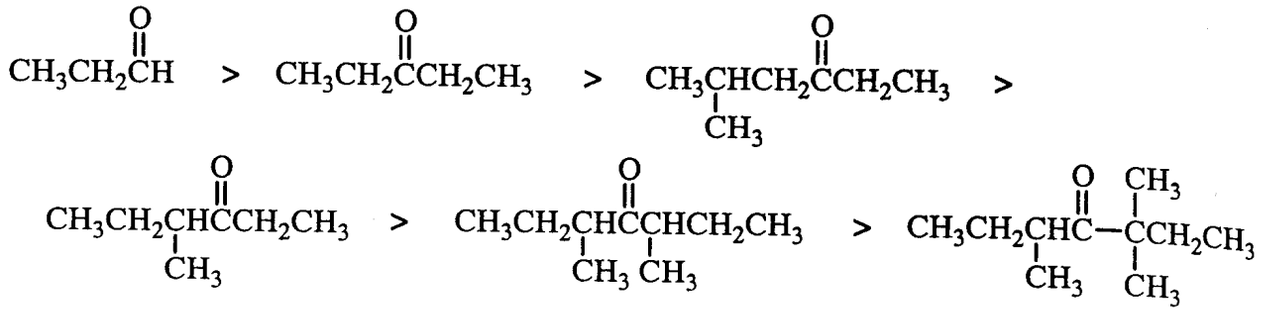
e. 

f. $CH_3CH_2CH_2CH_2OH + CH_3CH_2OH$

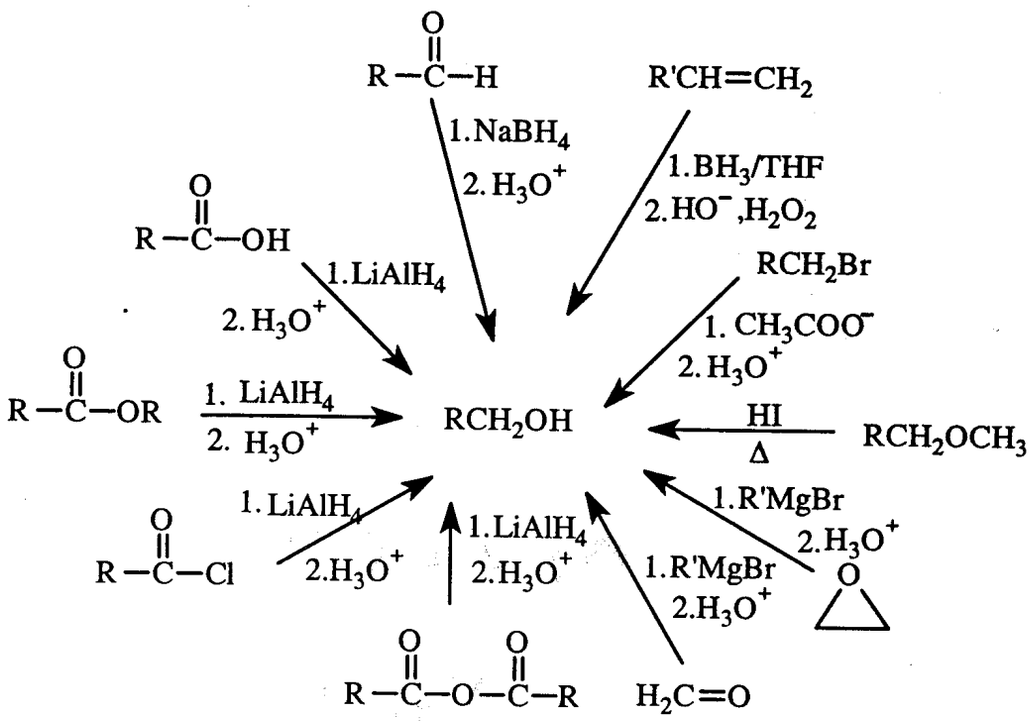
g. 

h. 

42.



43. **a.**

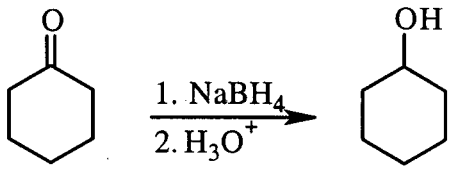


b. The reaction of a Grignard reagent with an epoxide.

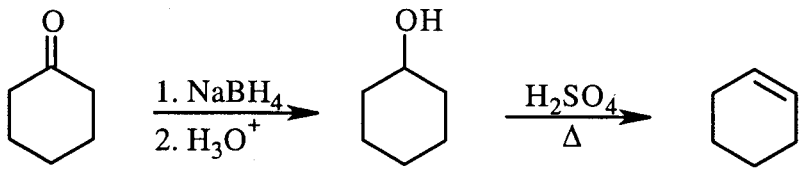
c. The reaction of a Grignard reagent with an epoxide and the reaction of a Grignard reagent with formaldehyde. In each of these reactions, a new carbon-carbon bond is formed.

44.

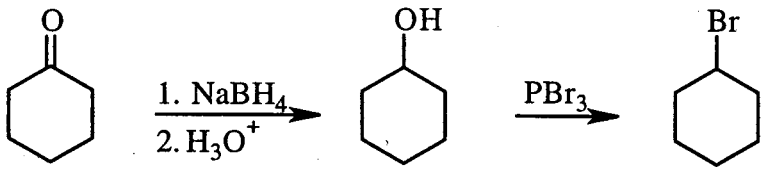
a.



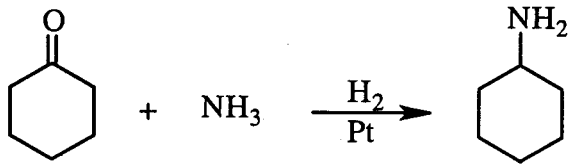
b.



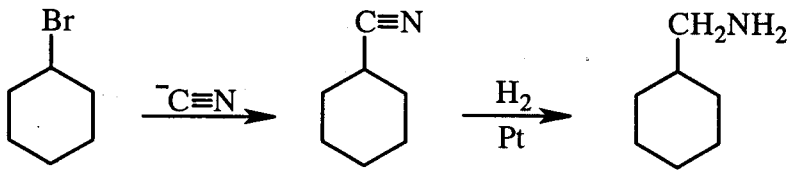
c.



d.

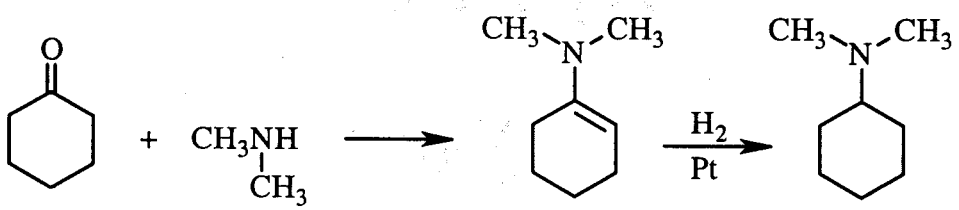


e.

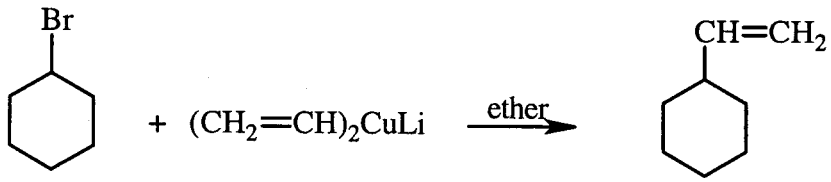


product of **c**

f.

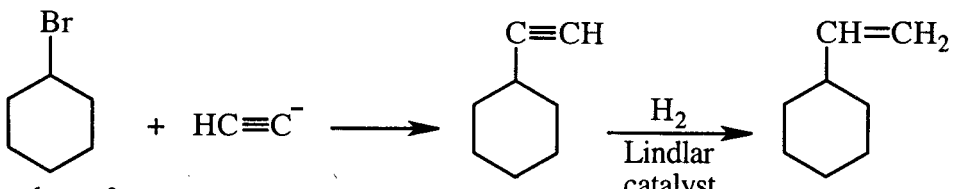


g.



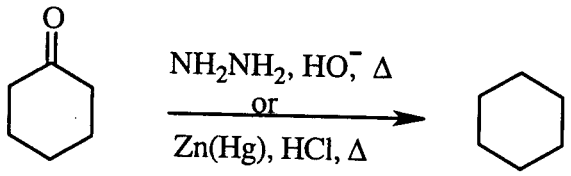
product of **c**

or

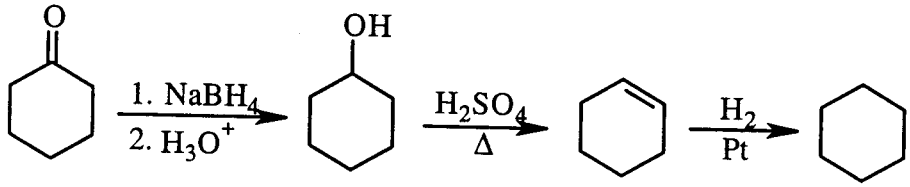


product of **c**

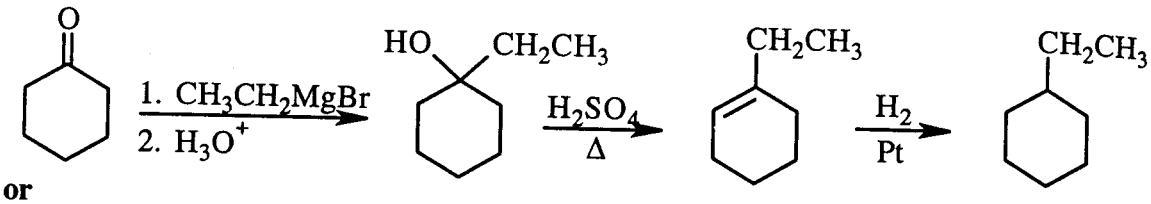
h.



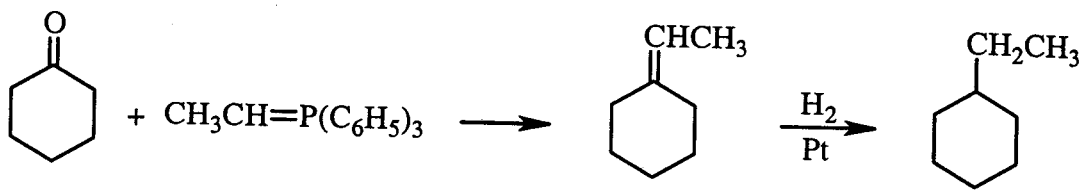
or



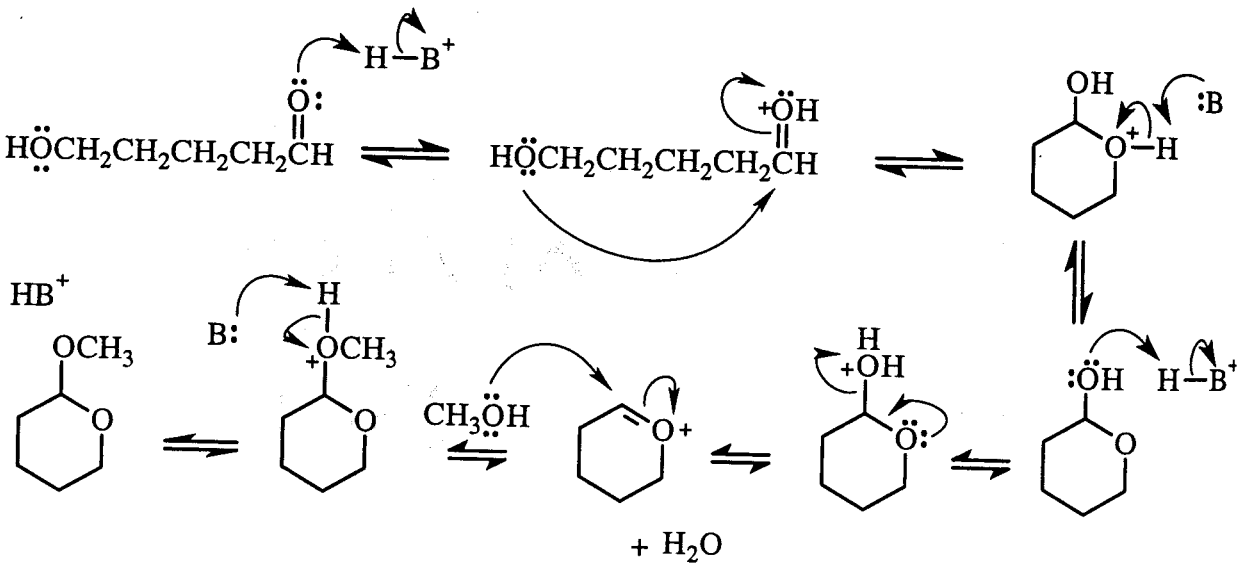
i.



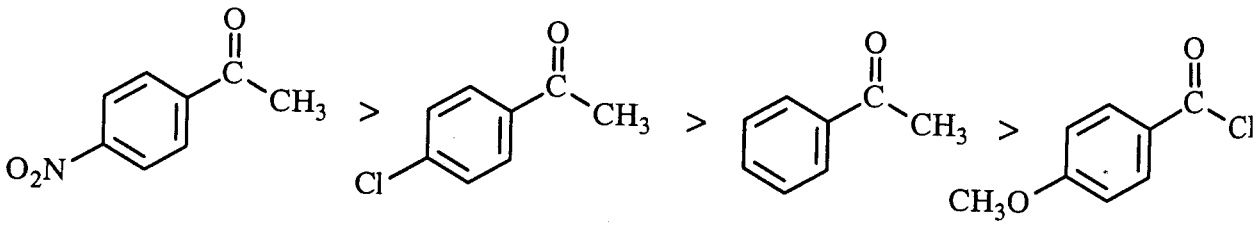
or



45.



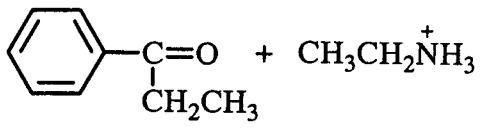
46. The greater the electron-withdrawing ability of the para substituent, the greater the K_{eq} for hydrate formation.

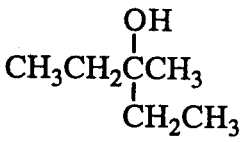


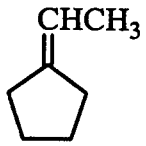
a. $CH_3OH \xrightarrow{PBr_3} CH_3Br \xrightarrow[Et_2O]{Mg} CH_3MgBr \xrightarrow[2.\ H^+,\ H_2O]{1.\ H_2C{=}O} CH_3CH_2OH$

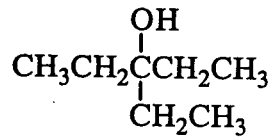
b. $CH_4 \xrightarrow[h\nu]{Br_2} CH_3Br \xrightarrow[Et_2O]{Mg} CH_3MgBr \xrightarrow[2.\ H^+,\ H_2O]{1.\ \text{ethylene oxide}} CH_3CH_2CH_2OH$

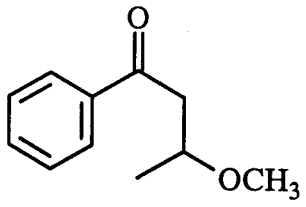
48.

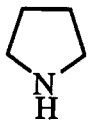
a. 

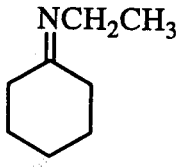
b. 

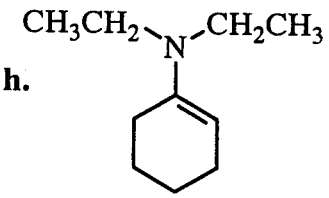
c. 

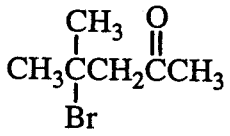
d. 

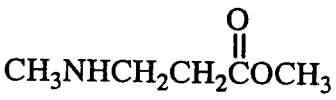
e. 

f. 

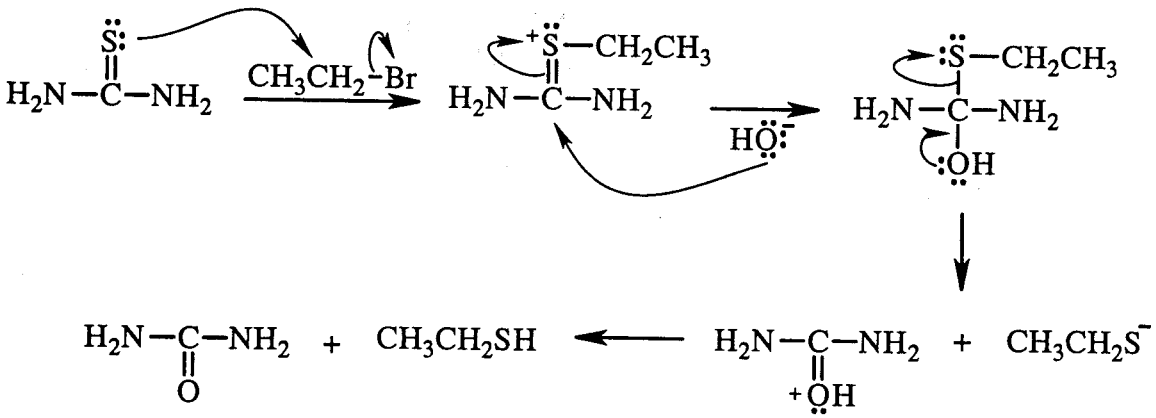
g. 

h. 

i. 

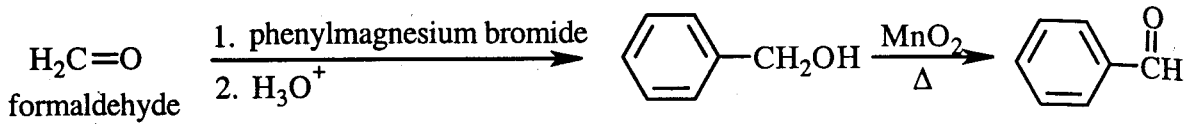
j. 

49. **a.**



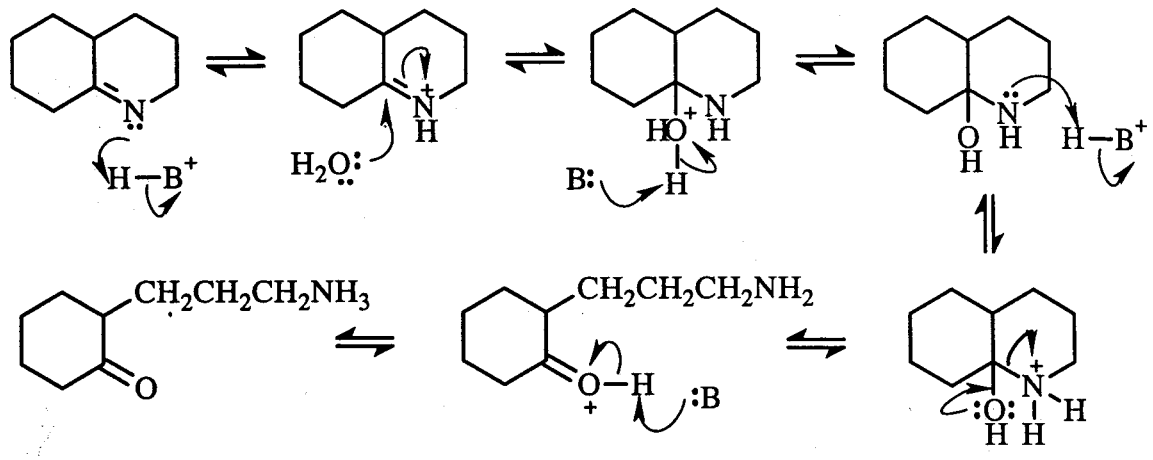
b. $CH_3CH_2CH_2CH_2CH_2SH$

50. The offset shows there is a signal at ~11.8 ppm, indicating an aldehyde. The ^{1}H NMR spectrum is that of benzaldehyde. Phenylmagnesium bromide, therefore, must react with a compound with one carbon atom to form an alcohol that can be oxidized by the mild oxidizing agent (MnO_2) to benzaldehyde. Therefore, Compound Z must be formaldehyde.

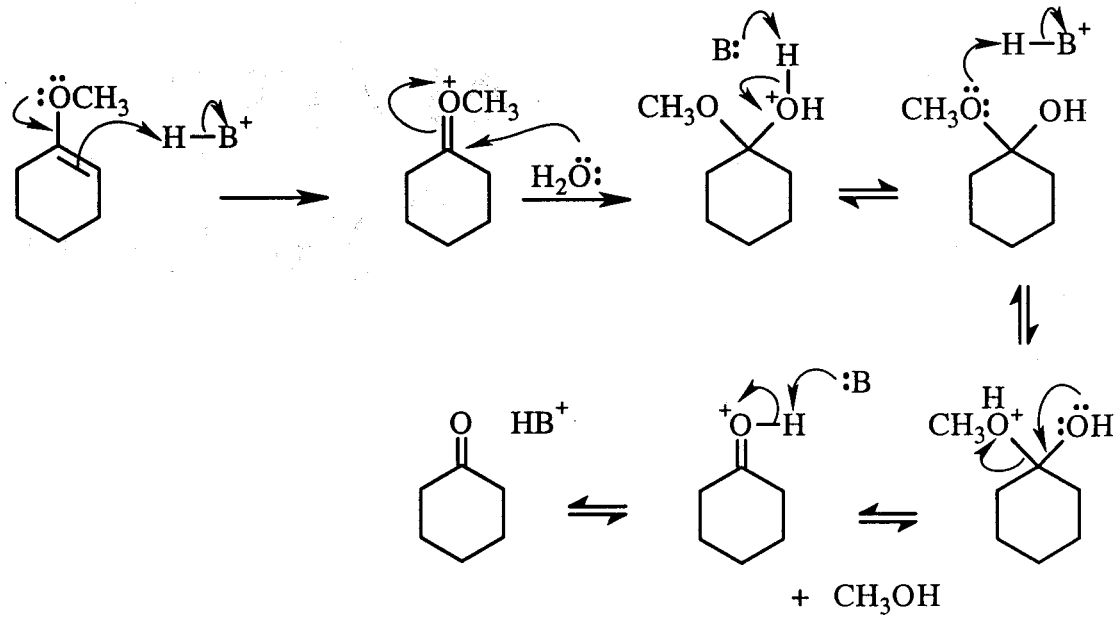


51.

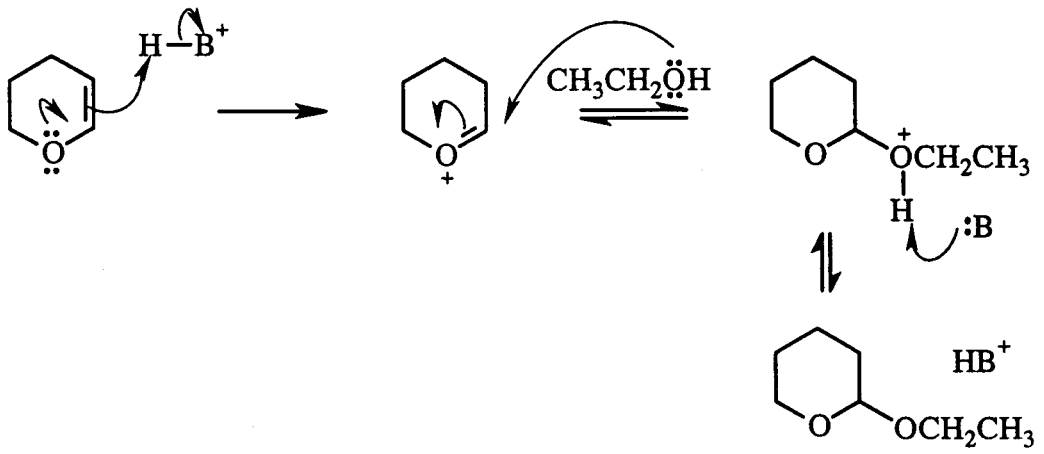
a.



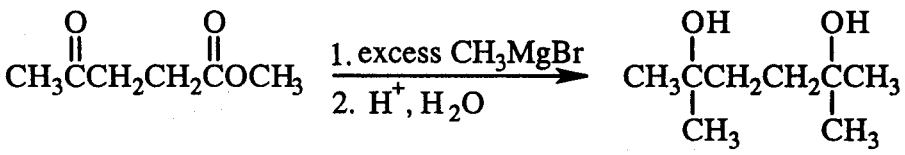
b.



c.

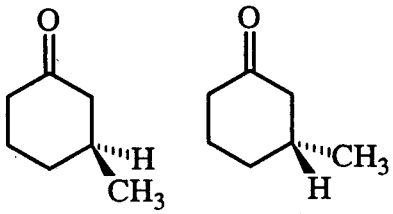


52. **a.** three signals in the ^1H NMR spectrum **b.** three signals in the ^{13}C NMR spectrum

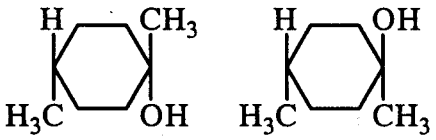


53.

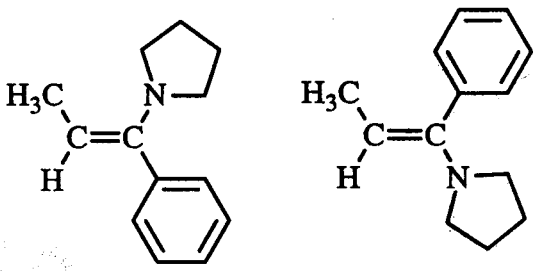
a.



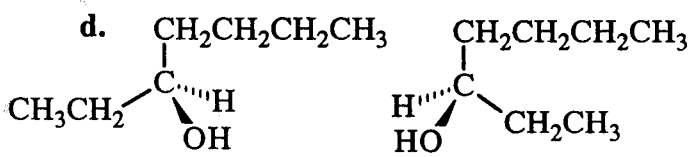
b.



c.

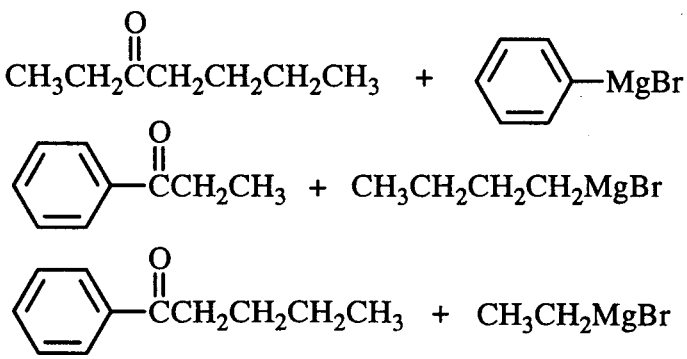


d.



54.

a.

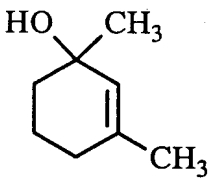


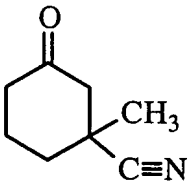
b. $CH_3CH_2\overset{O}{\overset{\|}{C}}CH_2CH_2CH_3 + CH_3CH_2MgBr$

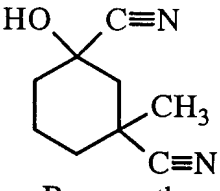
$CH_3CH_2\overset{O}{\overset{\|}{C}}CH_2CH_3 + CH_3CH_2CH_2MgBr$

$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3 + 2\ CH_3CH_2MgBr$

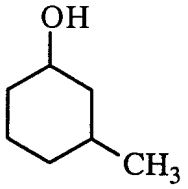
55.

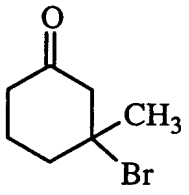
a. 

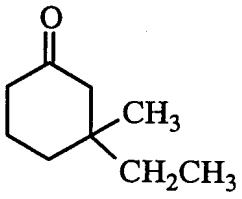
b. 

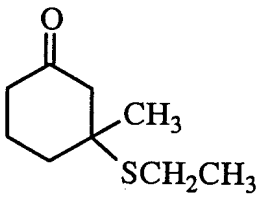


Because there is excess cyanide ion.

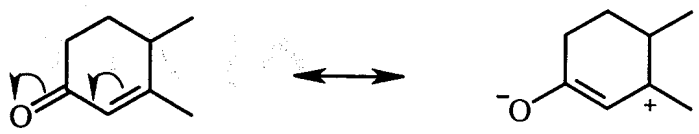
c. 

d. 

e. 

f. 

56. Enovid would have its carbonyl stretch at a higher frequency. The carbonyl group in Norlutin has some single-bond character because of the conjugated double bonds. This causes the carbon oxygen bond to be easier to stretch than the carbon-oxygen bond in Enovid that is not involved in resonance.

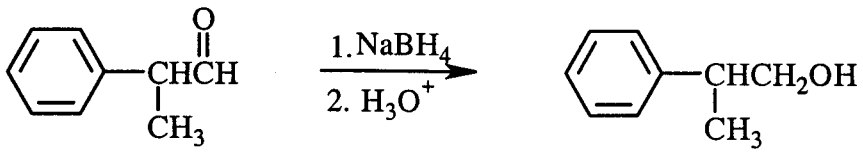


Norlutin

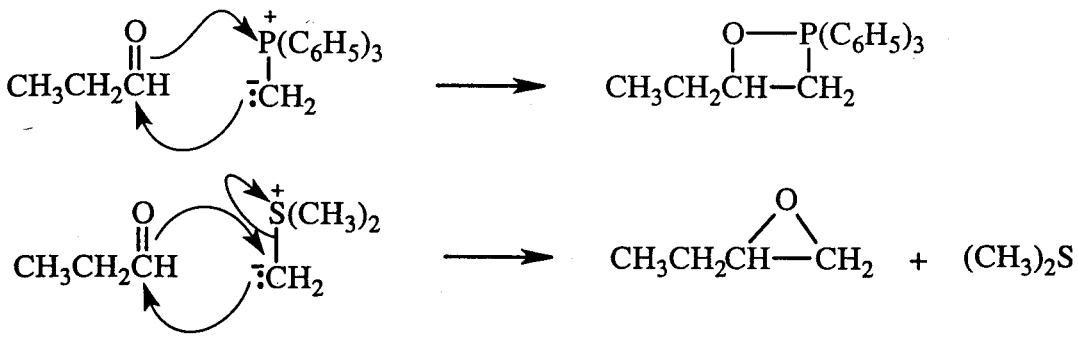
57. The absorption bands at 1600 cm^{-1}, 1500 cm^{-1}, and > 3000 cm^{-1} in the IR spectrum indicate the compound has a benzene ring. The absorption band 1720 cm^{-1} suggests it is a ketone with the carbonyl group not conjugated with the benzene ring.

The broad signal at 1.8 ppm in the ^1H NMR spectrum indicates an OH group. We also see there are three different kinds of hydrogens (other than the OH group and the benzene ring hydrogens The doublet at 1.2 ppm indicates a methyl group adjacent to a carbon bonded to one hydrogen, and the doublet at 3.6 ppm are due to protons on a carbon that has the carbon bonded to one hydrogen on one side of it and the electron-withdrawing OH group on the other side.

The IR spectrum is the spectrum of 2-phenylpropanal and the ^1H NMR spectrum is the spectrun of 2-phenyl-1-propanol.

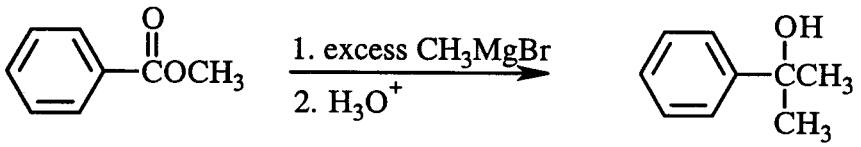


The difference in the two reactions is a result of the difference in the leaving ability of a sulfonium group and a phosphonium group. Because the sulfonium group is a weaker base, it is a better leaving group. Therefore, it is eliminated by the oxyanion.

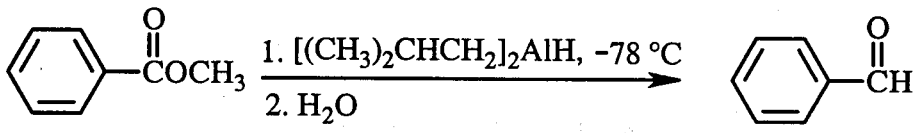


59.

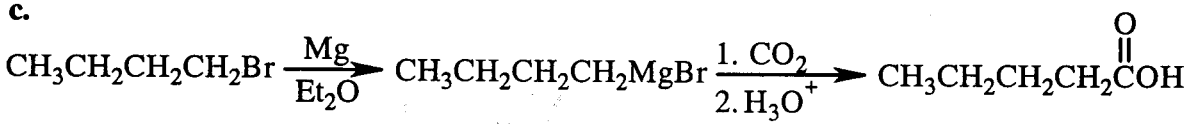
a.



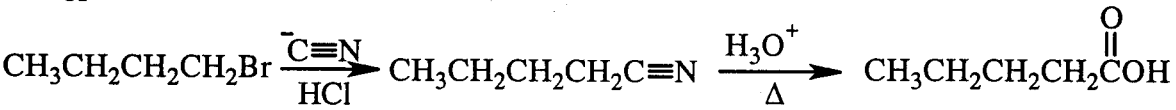
b.



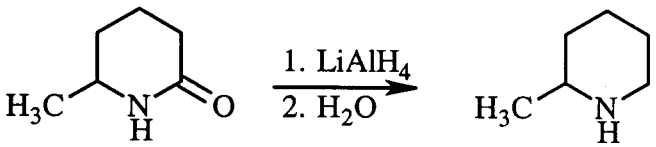
c.



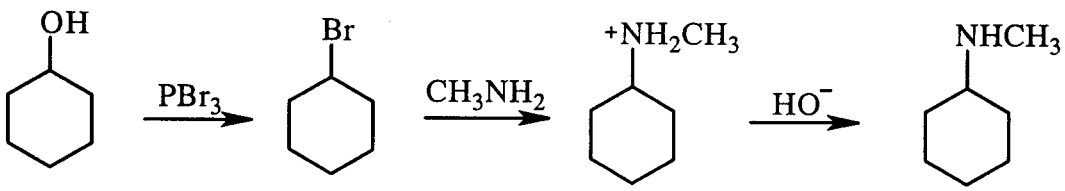
or



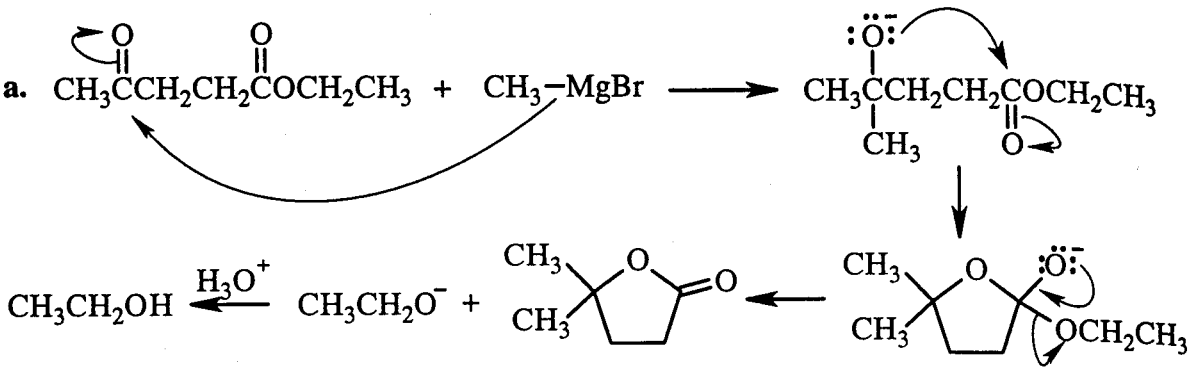
d.

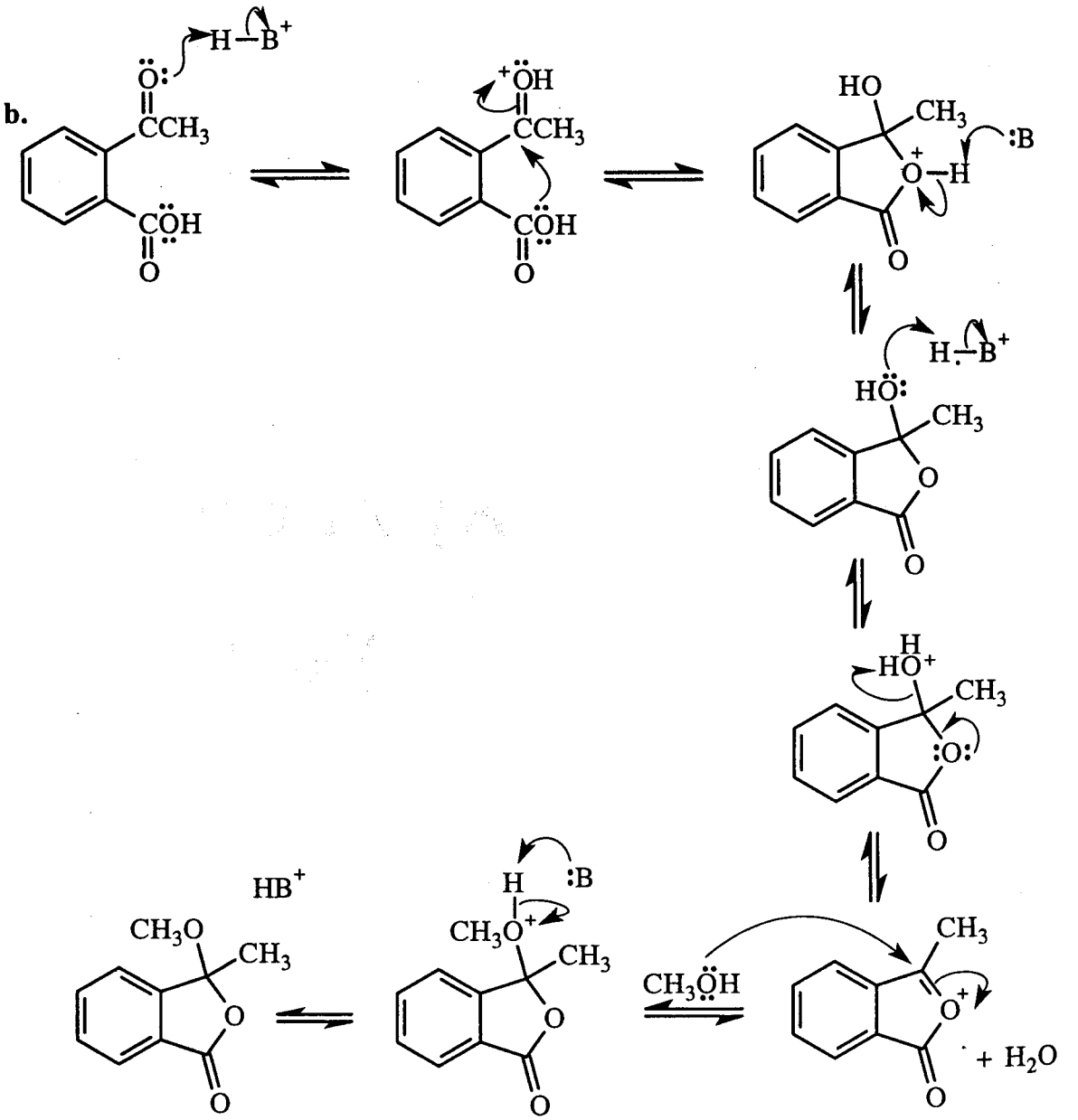


e.

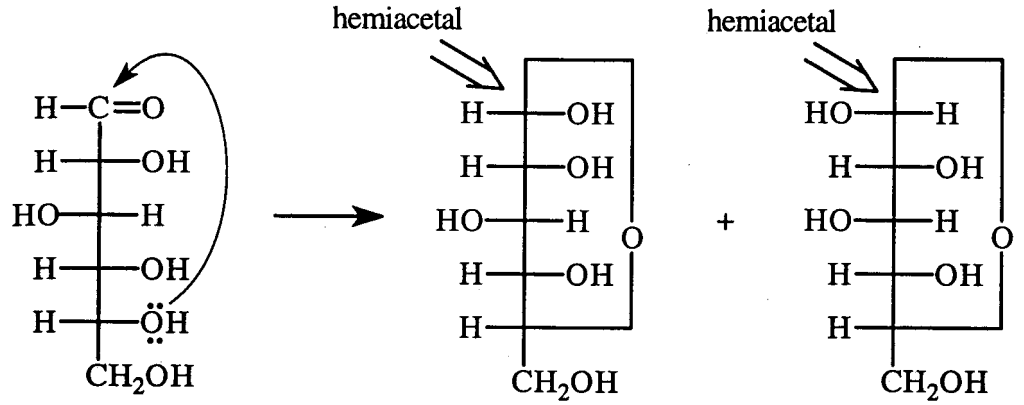


60.

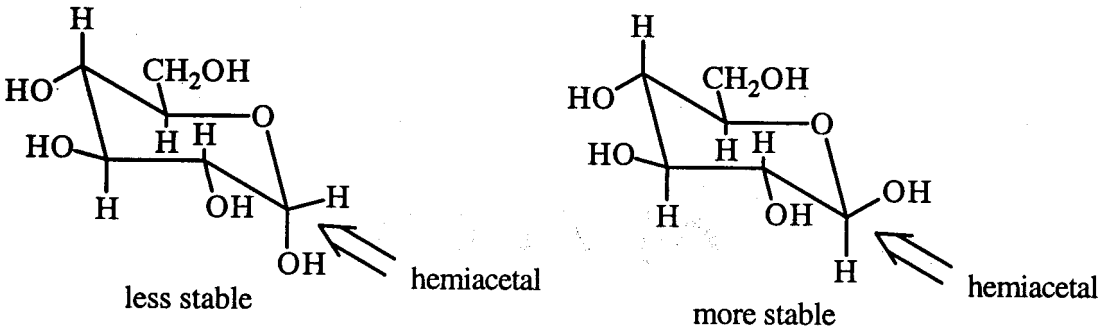




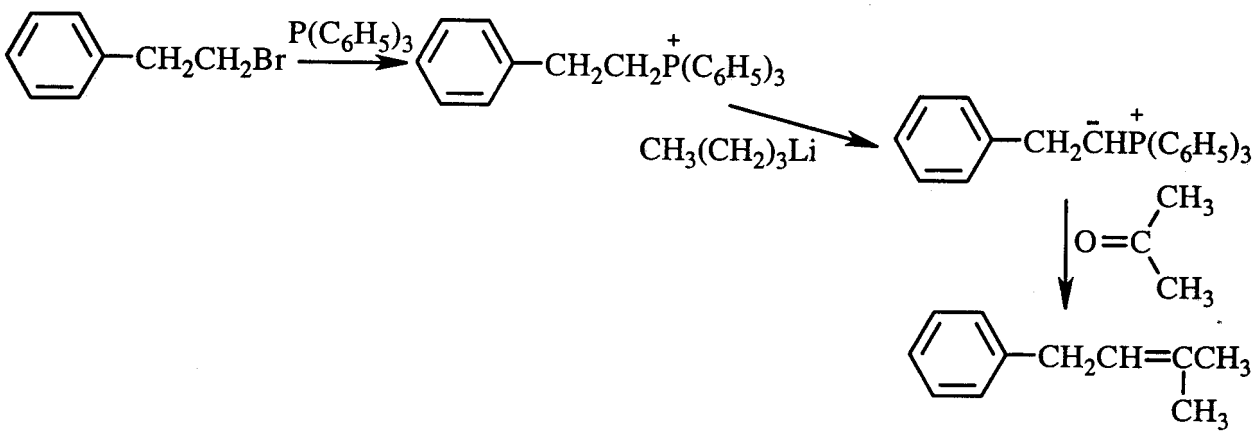
a. The OH group on C-5 of glucose reacts with the aldehyde group in an intramolecular reaction, forming a cyclic hemiacetal. Because the reaction creates a new asymmetric carbon, two cyclic hemiacetals can form, one with the *R* configuration at the new asymmetric carbon and one with the *S* configuration.



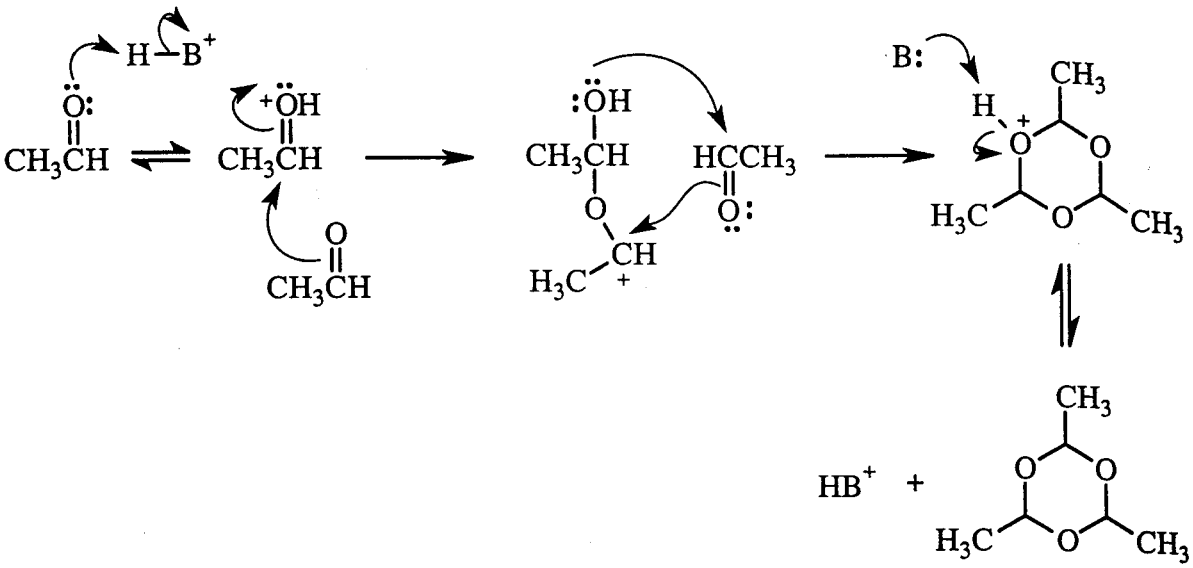
b. The two products can be drawn in their chair conformations by putting the largest group (CH_2OH) in the equatorial position and then putting the other groups in axial or equatorial positions depending on whether they are cis or trans to one another. The hemiacetal on the left has all but one of its OH groups in the more stable equatorial position, while the hemiacetal on the right has all its OH groups in the equatorial position. Therefore, the hemiacetal on the right is more stable.



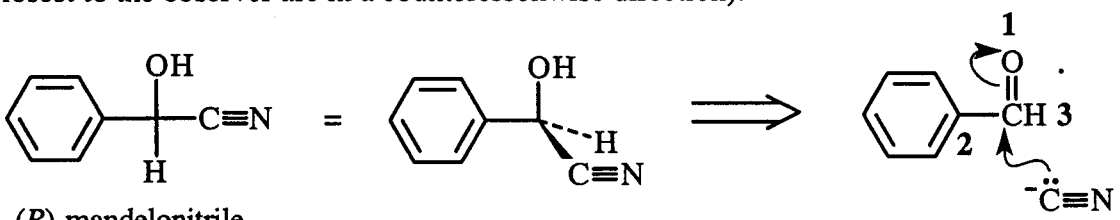
62.



63.

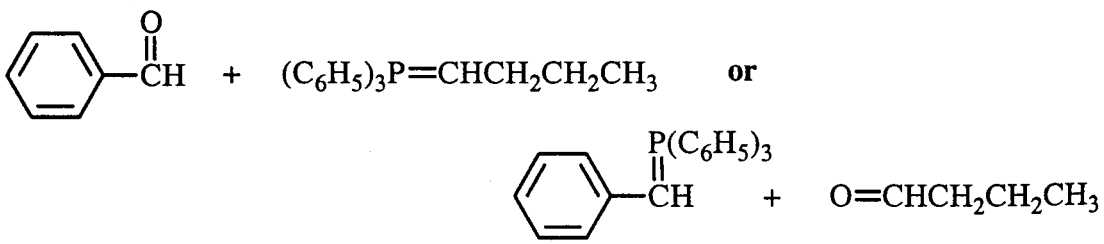


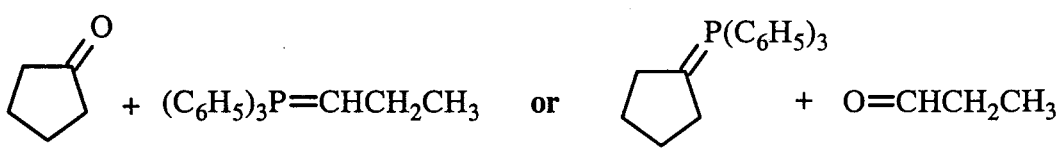
64. Converting the Fischer projection of (*R*)-mandelonitrile into a wedge-and-dash structure allows you to see that attack of cyanide ion occurred on the *Si* face (decreasing priorities on the face closest to the observer are in a counterclockwise direction).

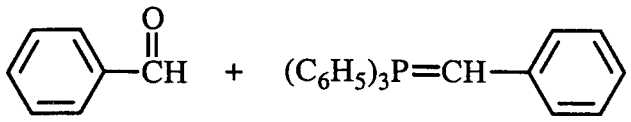


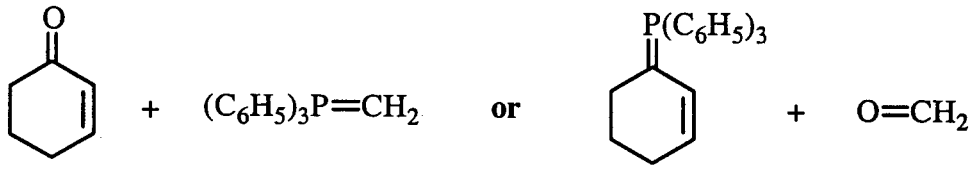
(*R*)-mandelonitrile

65.

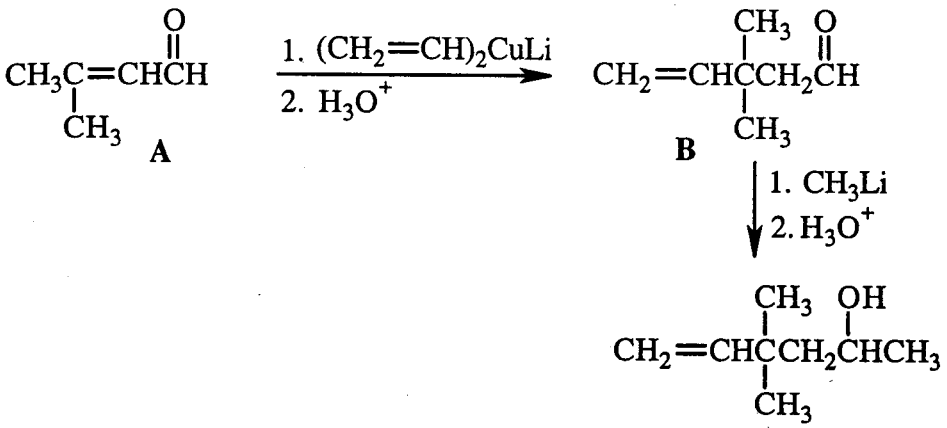
a. 

b. 

c. 

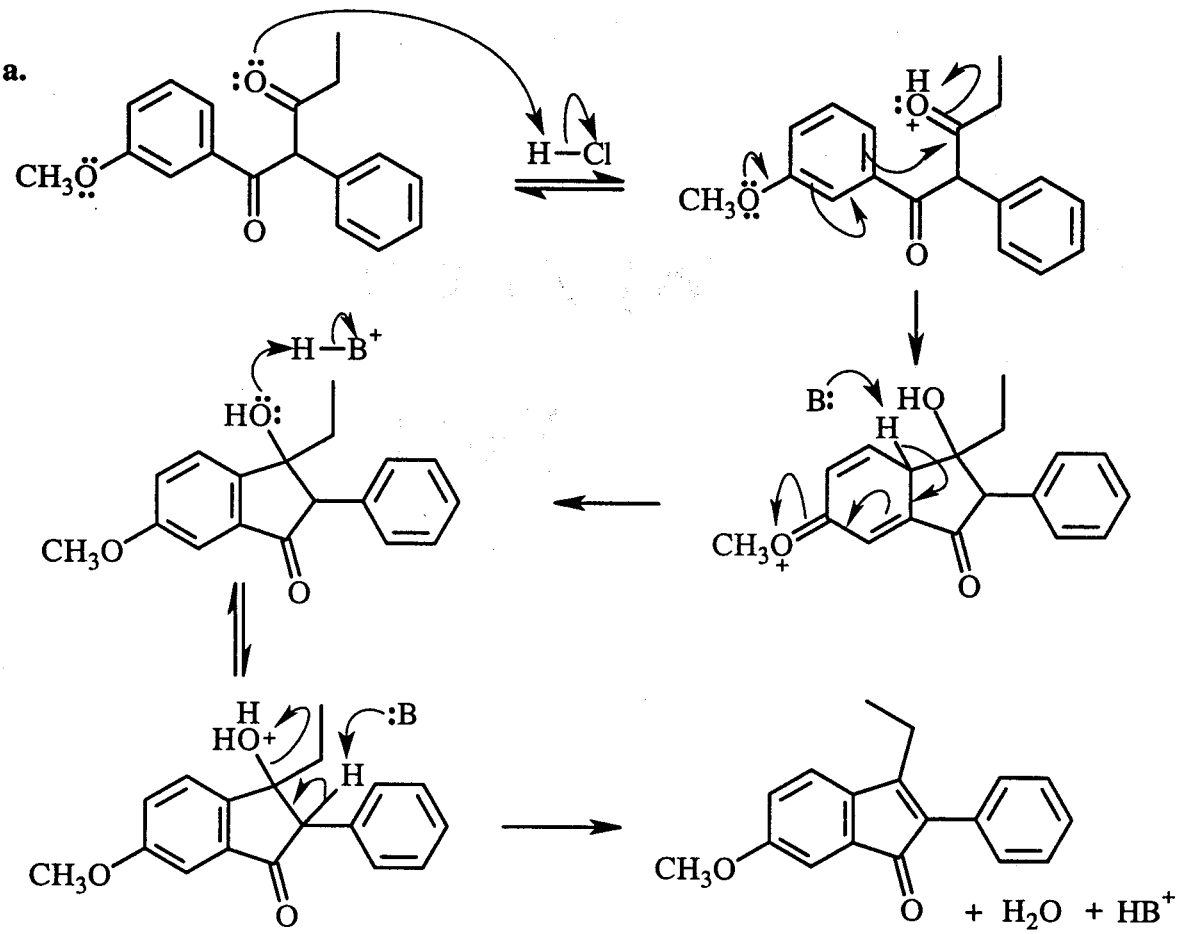
d. 

66.

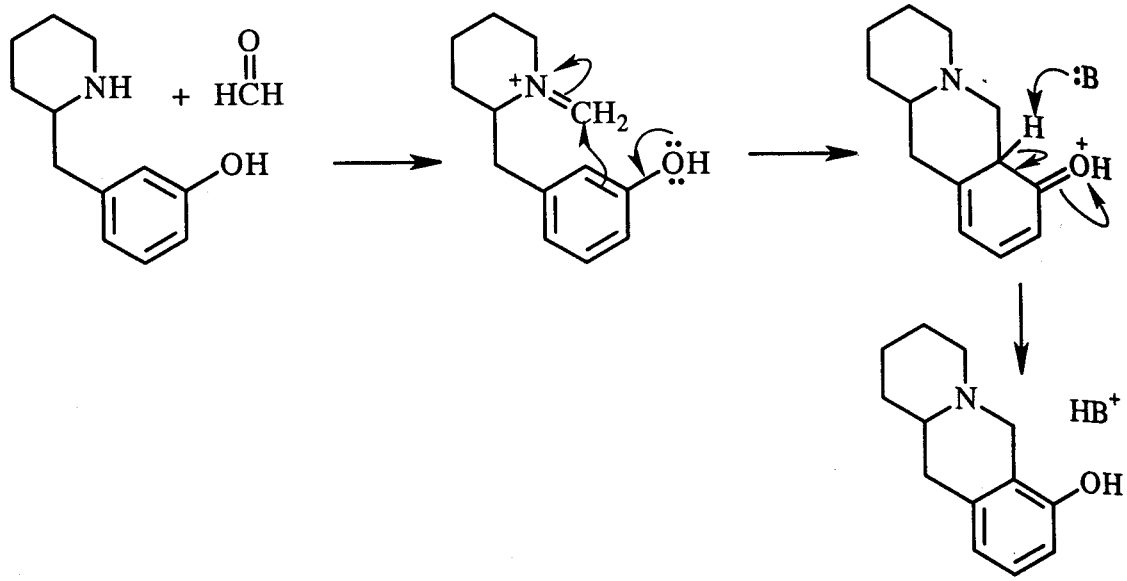


67.

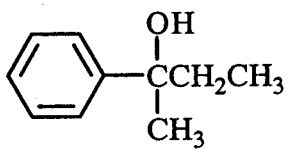
a.



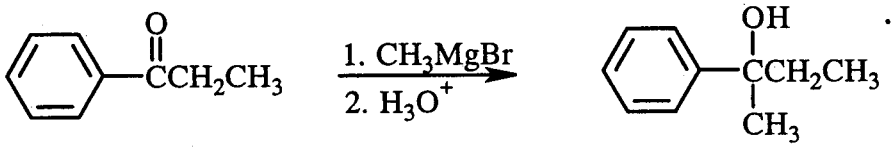
b.



68. The compound that gives the ^{1}H NMR spectrum is 2-phenyl-2-butanol.

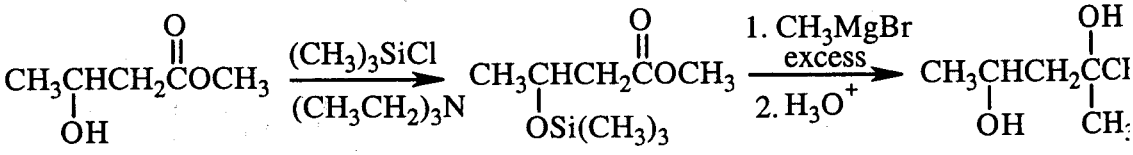


Therefore, the compound that reacts with methylmagnesium bromide is 1-phenyl-1-propanol

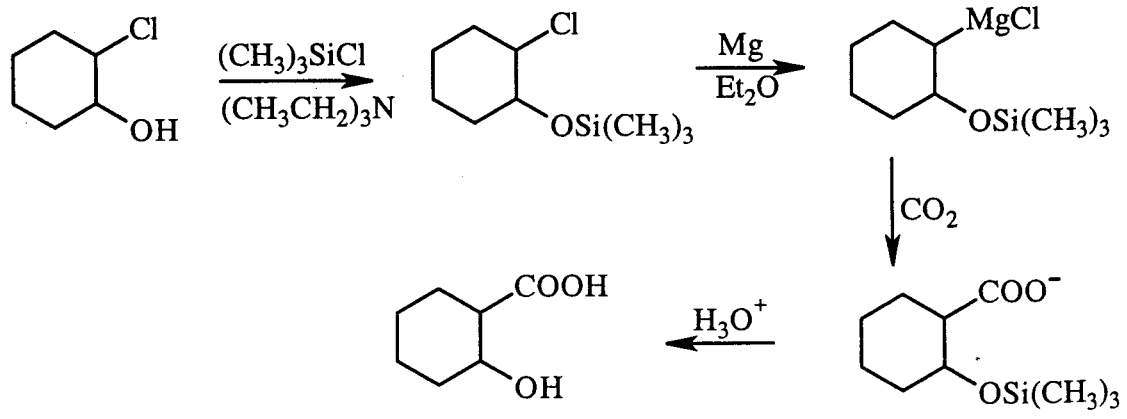


69.

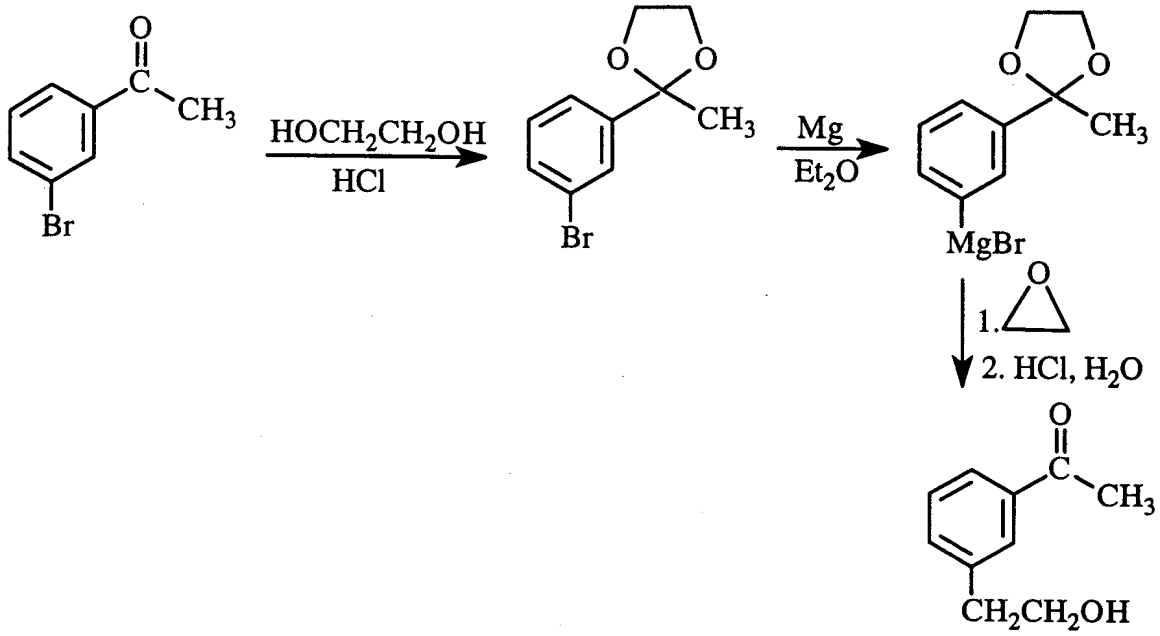
a.



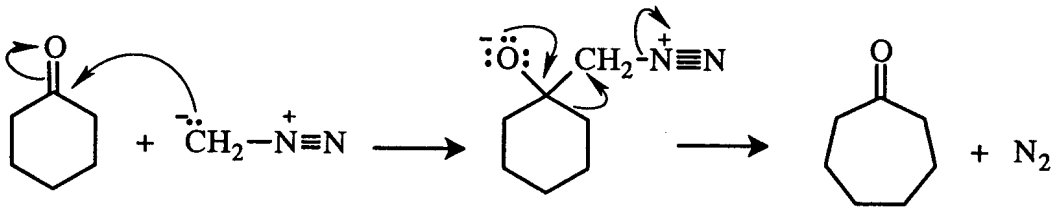
b.



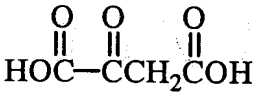
c.



70.

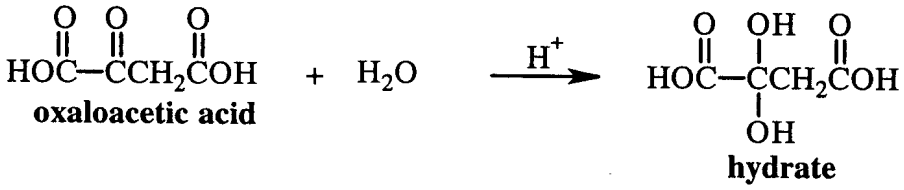


71. **a.** The COOH group that is closest to the electron-withdrawing keto group is the more acidic COOH group.



$pK_a = 2.22$ $pK_a = 3.98$

b. The data show that the amount of hydrate decreases with increasing pH until about pH = 6 and that increasing the pH beyond 6 has no effect on the amount of hydrate.

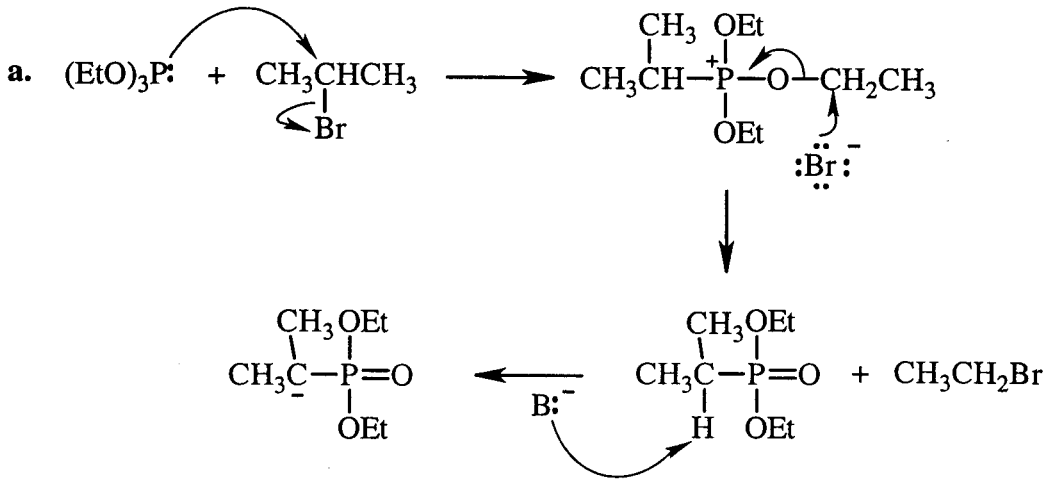


oxaloacetic acid **hydrate**

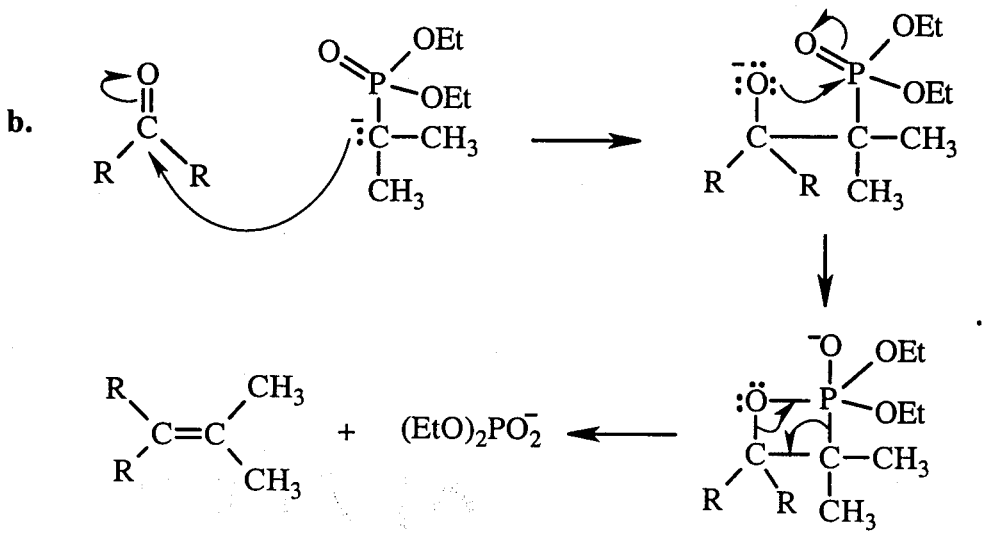
A hydrate is stabilized by electron-withdrawing groups. A COOH group is electron withdrawing, but a COO^- group is much less so. In acidic solutions, where both carboxylic acid groups are in their acidic (COOH) forms and, therefore, stabilize the hydrate, the compound exists as essentially all hydrate. As the pH of the solution increases and the COOH groups become COO^- groups, the amount of hydrate decreases. Above pH = 6, where both carboxyl groups are in their basic (COO^-) forms, there is only a small amount of hydrate.

72.

a.

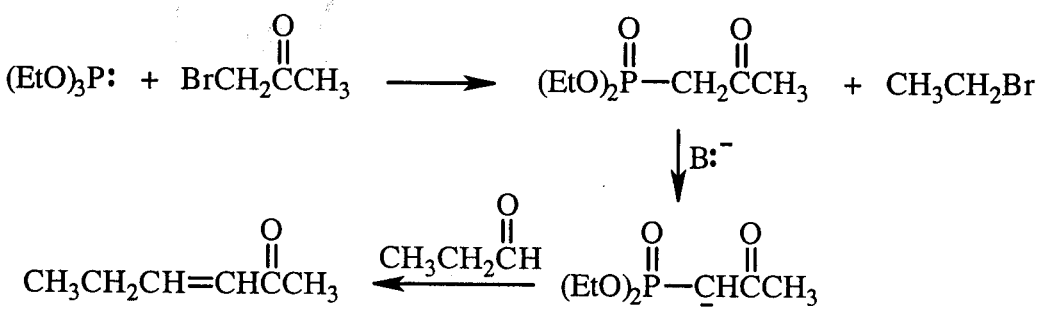


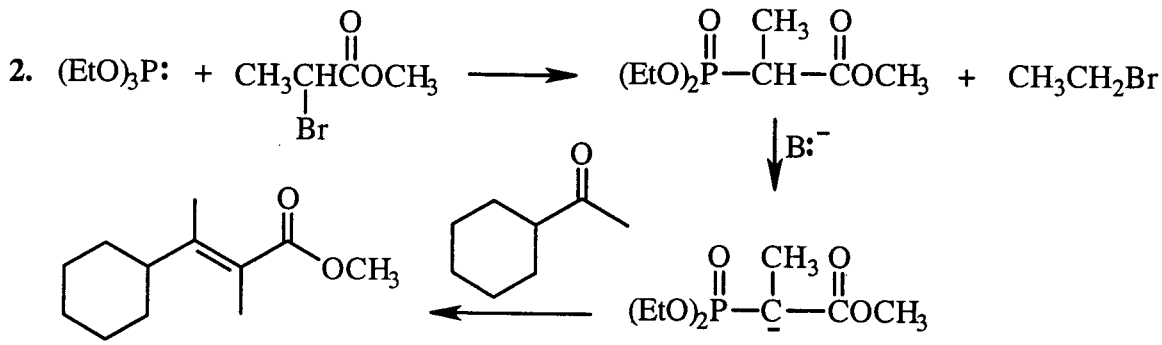
b.

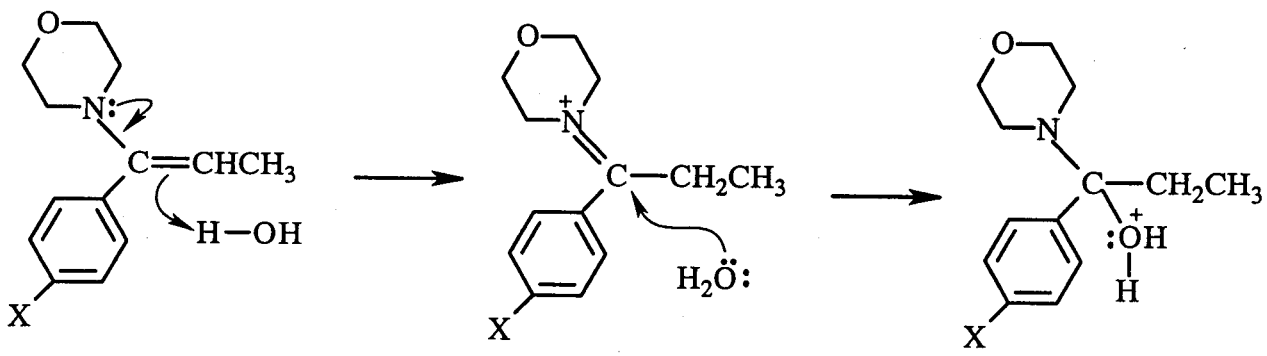


c.

1.



2. 

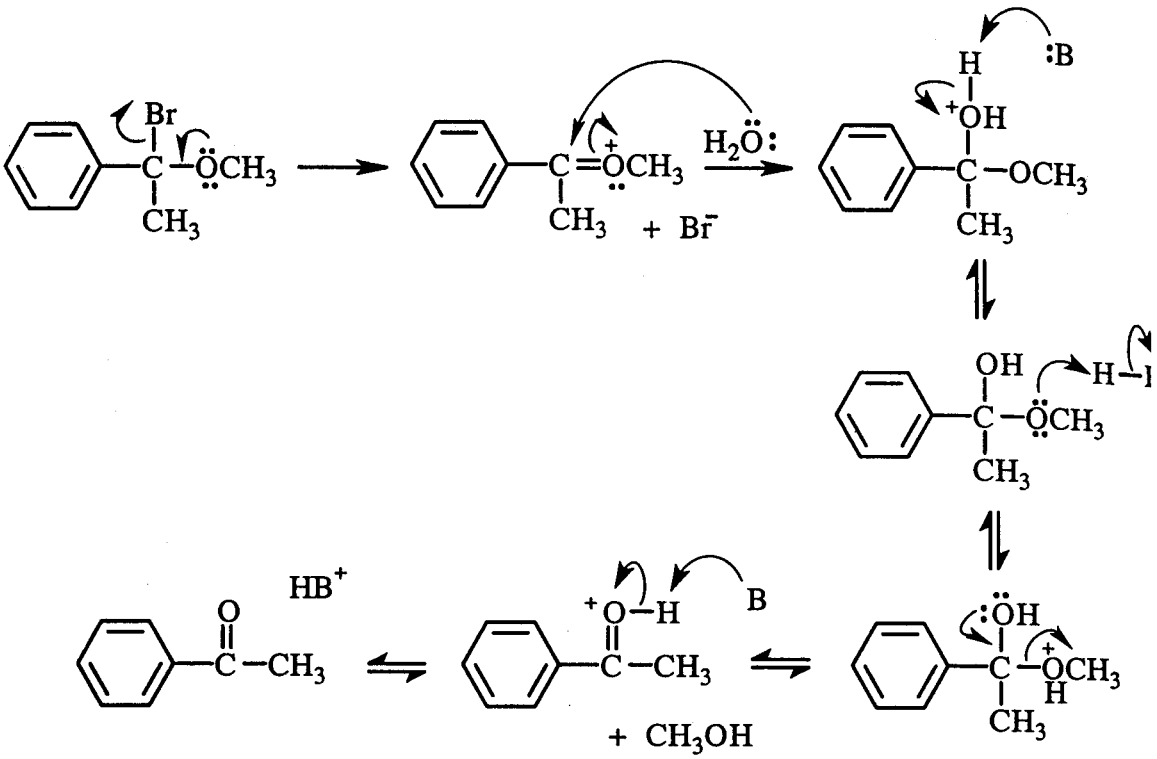
73. 

a. The negative ρ value obtained when hydrolysis is carried out in a basic solution indicates that electron-donating substituents increase the rate of the reaction. This means that the rate-determining step must be protonation of the carbon (the first step), because the more electron-donating the substituent, the greater the negative charge on the carbon and the easier it will be to protonate.

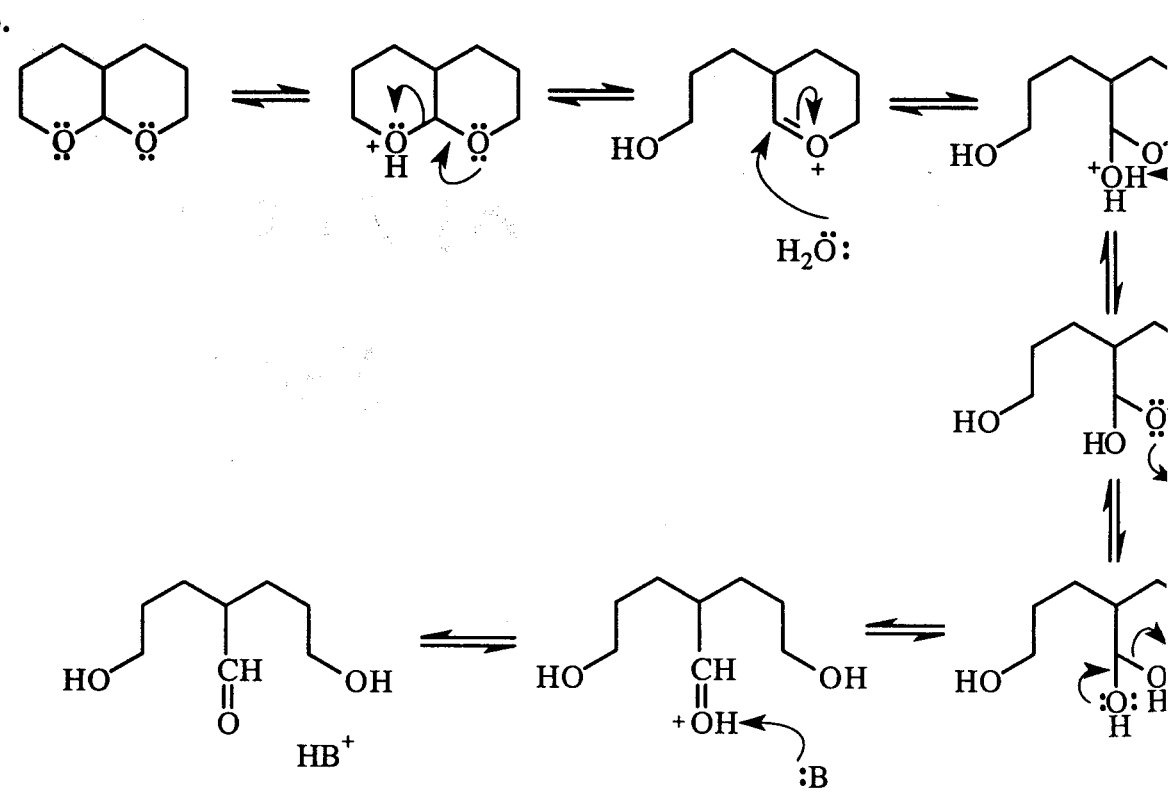
b. The positive ρ value obtained when hydrolysis is carried out in an acidic solution indicates that electron-withdrawing substituents increase the rate of the reaction. This means that the rate-determining step must be attack of water on the imine carbon to form the tetrahedral intermediate, because electron withdrawal increases the electrophilicity of the imine carbon, making it more susceptible to nucleophilic attack.

74.

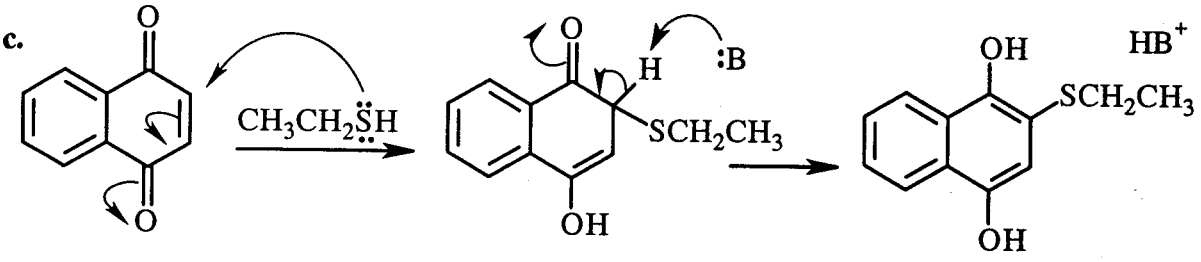
a.



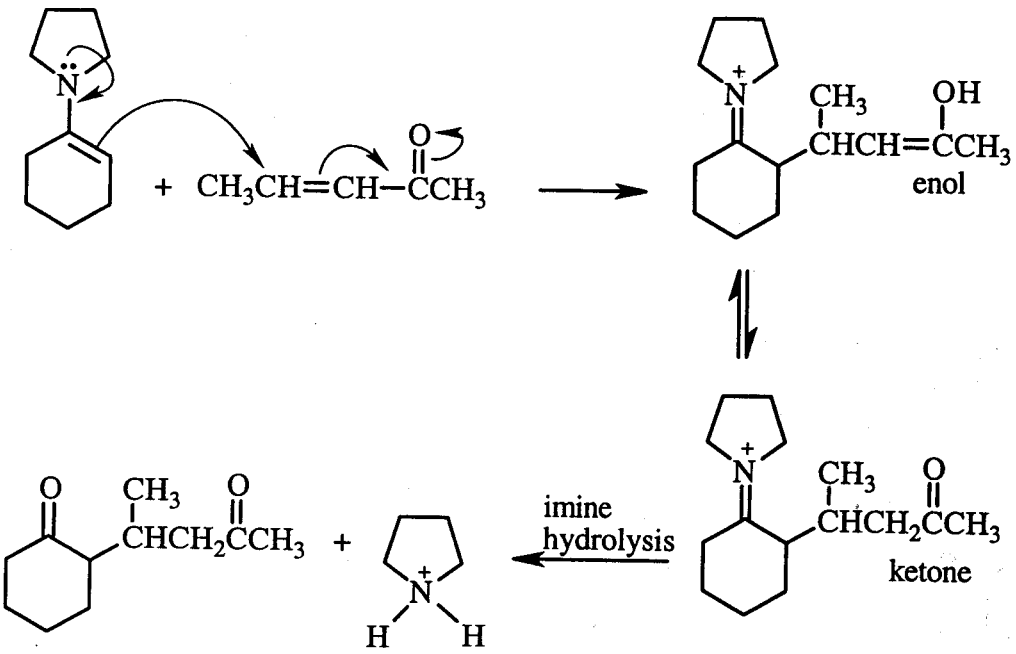
b.



c.


O
O
CH3CH2SH
O
H
:B
SCH2CH3
OH
OH
HB+
SCH2CH3
OH

d.

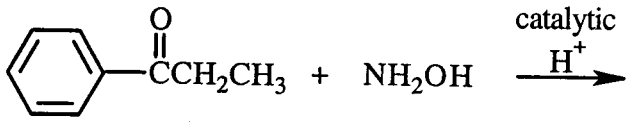

N
+ CH3CH=CH–CCH3
O
N+
CH3
OH
CHCH=CCH3
enol
N+
CH3
O
CHCH2CCH3
ketone
imine
hydrolysis
O
CH3
O
CHCH2CCH3
+
N+
H
H

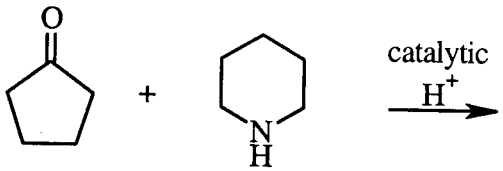
B

-B+

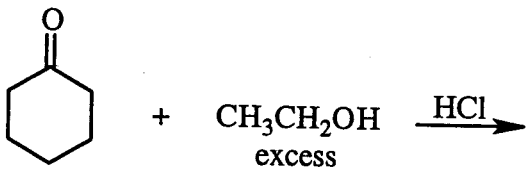
Chapter 18 Practice Test

1. Give the product of each of the following reactions.

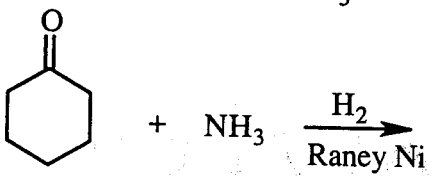
a. 

b. 

c. $CO_2 \xrightarrow[2.\ H_3O^+]{1.\ CH_3CH_2CH_2MgBr}$

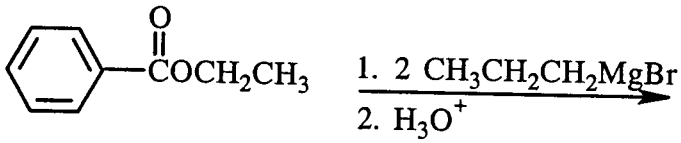
d. 

e. $CH_3CH_2\overset{\overset{O}{\|}}{C}CH_2CH_3 \xrightarrow[2.\ H_3O^+]{1.\ CH_3MgBr}$

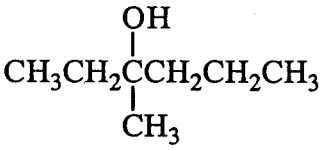
f. 

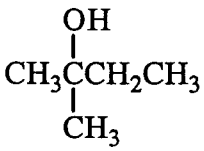
g. $CH_3CH_2\overset{\overset{O}{\|}}{C}CH_2CH_3 \xrightarrow[HCl]{^-C\equiv N}$

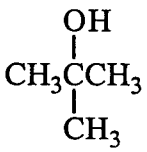
h. $CH_3CH{=}CH\overset{\overset{O}{\|}}{C}CH_3 \xrightarrow[2.\ H_3O^+]{1.\ LiAlH_4}$

i. 

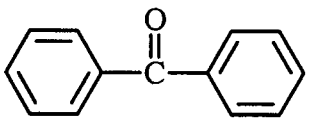
Which of the following alcohols cannot be prepared by the reaction of an ester with excess Grignard reagent?

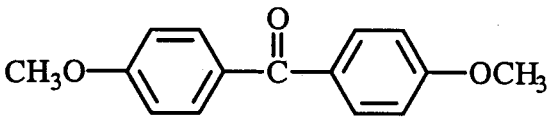


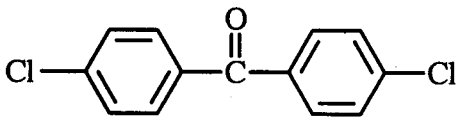




Which of the following ketones would form the greatest amount of hydrate in an aqueous solution?







4. Give an example of each the following:

a. an enamine

b. an acetal

c. an imine

d. a hemiacetal

e. a phenylhydrazone

5. Which is more reactive toward nucleophilic addition?

a. butanal or methyl propyl ketone

b. 4-heptanone or 3-pentanone

6. Indicate how the following compound could be prepared using the given starting material.



CHAPTER 19
Carbonyl Compounds III: Reactions at the α-Carbon

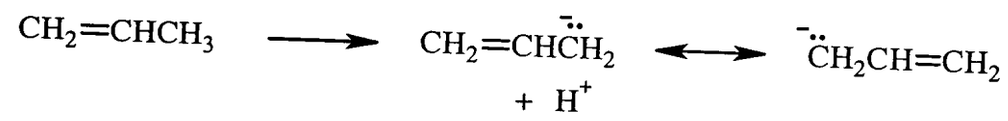
Important Terms

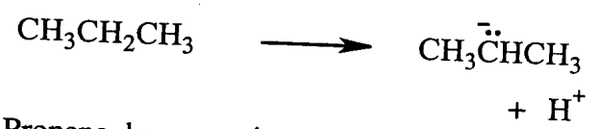
acetoacetic ester synthesis	synthesis of a methyl ketone using ethyl acetoacetate as the starting material.
aldol addition	a reaction between two molecules of an aldehyde (or two molecules of ketone) that connects the α-carbon of one with the carbonyl carbon of t other.
aldol condensation	an aldol addition followed by elimination of water.
ambident nucleophile	a nucleophile with two nucleophilic sites.
annulation reaction	a ring-forming reaction.
α-carbon	a carbon adjacent to a carbonyl carbon.
carbon acid	a compound that contains a carbon bonded to a relatively acidic hydrog
Claisen condensation	a reaction between two molecules of an ester that connects the α-carbon of one with the carbonyl carbon of the other and eliminates an alkoxide
condensation reaction	a reaction combining two molecules while removing a small molecule (usually water or an alcohol).
crossed aldol addition (mixed aldol addition)	an aldol addition in which two different carbonyl compounds are used.
decarboxylation	loss of carbon dioxide.
Dieckmann condensation	an intramolecular Claisen condensation.
β-diketone	a ketone with a second ketone carbonyl group at the β-position.
enolization	keto-enol interconversion.
gluconeogenesis	the synthesis of D-glucose from pyruvate.
glycolysis	the breakdown of D-glucose into two molecules of pyruvate.
haloform reaction	the conversion of a methyl ketone to a carboxylic acid and haloform.
Hell-Volhard-Zelinski (HVZ) reaction	conversion of a carboxylic acid into an α-bromocarboxylic acid using $PBr_3 + Br_2$.
Hundsdiecker reaction	conversion of a carboxylic acid into an alkyl halide by heating a heavy metal salt of the carboxylic acid with bromine or iodine.
α-hydrogen	a hydrogen bonded to the carbon adjacent to a carbonyl carbon.

...o-enol tautomerism (...o-enol interconversion)	interconversion of keto and enol tautomers.
...eto ester	an ester with a ketone carbonyl group at the β-position.
...lbe-Schmidt ...boxylation reaction	reaction of a phenolate ion with carbon dioxide under pressure.
...alonic ester synthesis	synthesis of a carboxylic acid using diethyl malonate as the starting material.
...ichael reaction	the addition of an α-carbanion to the β-carbon of an α,β-unsaturated carbonyl compound.
...ixed aldol addition (crossed aldol addition)	an aldol addition in which two different carbonyl compounds are used.
...ixed Claisen condensation	a Claisen condensation in which two different esters are used.
Robinson annulation	a Michael reaction followed by an intramolecular aldol condensation.
Stork enamine reaction	uses an enamine as a nucleophile in a Michael reaction.
α-substitution reaction	a reaction that puts a substituent on an α-carbon in place of an α-hydrogen.
tautomers	isomers that differ in the location of a double bond and a hydrogen.

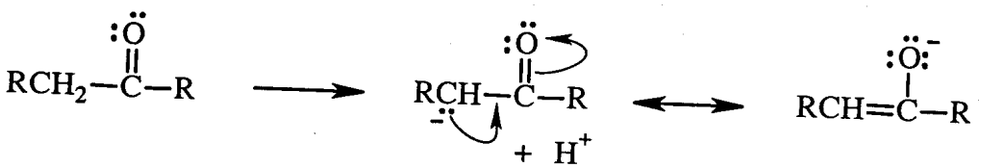
Solutions to Problems

1. The electrons left behind when a proton is removed from propene are delocalized—they are shared by two carbon atoms. In contrast, the electrons left behind when a proton is removed fro an alkane are localized—they belong to a single (carbon) atom. The base with delocalized electrons is more stable so it has the stronger conjugate acid; i.e. propene is a stronger acid than an alkane.





Propene, however, is not as acidic as the carbon acids in Table 19.1, because the electrons left behind when a proton is removed from these carbon acids are delocalized onto an oxygen or a nitrogen, which are more electronegative atoms than carbon and, therefore, better able to accommodate the electrons.



2.

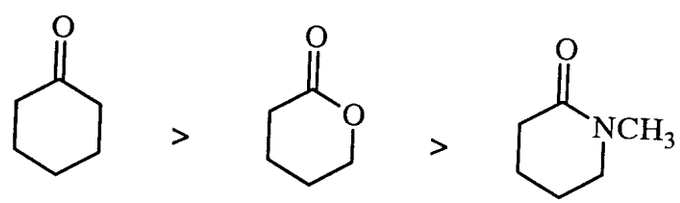
a. $CH_3CCH_2C{\equiv}N$ (a β-keto nitrile)

b. $CH_3OCCH_2COCH_3$ (a β-diester)

3.

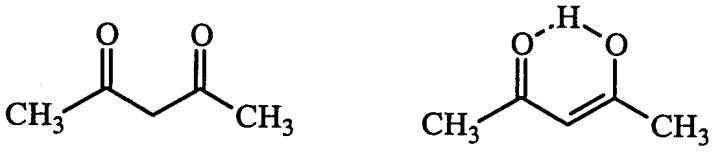
a. CH_3CH > $HC{\equiv}CH$ > $CH_2{=}CH_2$ > CH_3CH_3

b. $CH_3CCH_2CCH_3$ > $CH_3CCH_2COCH_3$ > $CH_3OCCH_2COCH_3$ > CH_3CCH_3

c. 

The ketone is the strongest acid because there is no competition for delocalization of the electrons that are left behind when the α-hydrogen is removed. The lactam is the weakest acid because nitrogen, being less electronegative, can better accommodate a positive charge and, therefore, is better than oxygen at delocalizing its lone pair onto the carbonyl oxygen. Therefore, nitrogen is better at competing with the electrons left behind when an α-hydrogen is removed for delocalization onto the carbonyl oxygen.

Both the keto and enol tautomers of 2,4-pentanedione can form hydrogen bonds with water. Neither the keto nor the enol tautomer can form hydrogen bonds with hexane. However, the enol tautomer can form an intramolecular hydrogen bond. This intramolecular hydrogen bonding stabilizes the enol tautomer. Thus, the enol tautomer is more stable relative to the keto tautomer in hexane than in water.

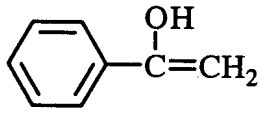


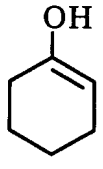
keto tautomer enol tautomer

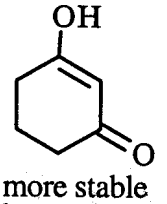
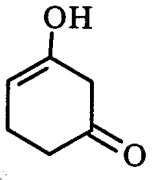
2,4-pentanedione

5.

a. $CH_3CH{=}C(OH)CH_2CH_3$

b. 

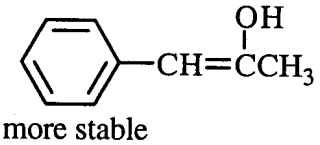
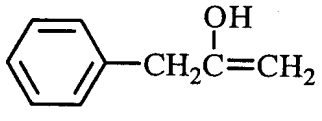
c. 

d.  and 

more stable
because the double bonds are conjugated

e. $CH_3CH_2C(OH){=}CHC(=O)CH_2CH_3$ $CH_3CH{=}C(OH)CH_2C(=O)CH_2CH_3$

more stable
because the double bonds are conjugated

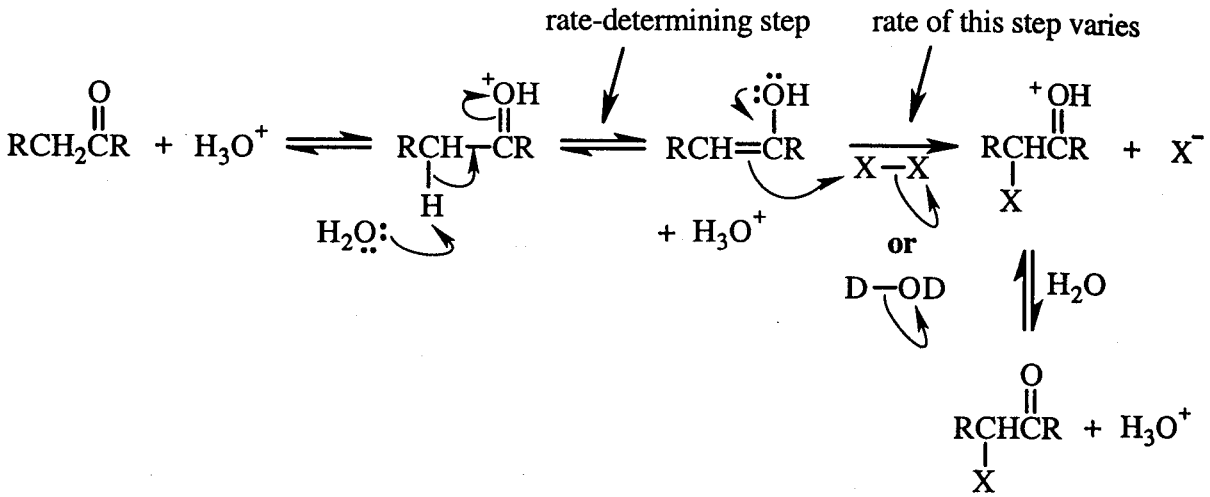
f.  and 

more stable
because the double bond is conjugated with the benzene ring

6. The aldehyde hydrogen cannot be removed by ^-OD. The aldehyde hydrogen is not acidic, because the electrons left behind if it were to be removed cannot be delocalized.

7. The haloform reaction requires that a group be created that is a weaker base than hydroxide ion so that hydroxide ion is not the group eliminated from the tetrahedral intermediate. For an alkyl group to be the weaker base, it must be bonded to three halogen atoms. The only alkyl group tha fulfills this requirement is a methyl group.

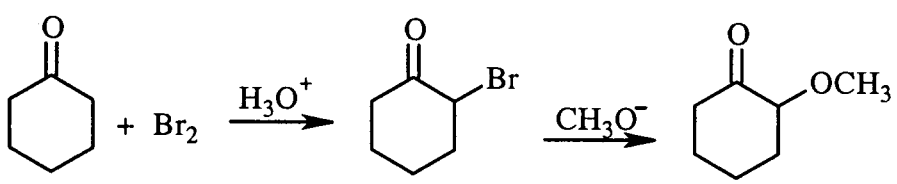
8. A Br—Br bond is weaker and easier to break than a Cl—Cl bond, which in turn is weaker and easier to break than a D—O bond. Because the rates of bromination, chlorination, and deuterium exchange are about the same, you know that breaking the Br—Br, Cl—Cl, or D—O bond takes place after the rate-determining step. Therefore, the rate-determining step must be removal of th proton from the α-carbon of the ketone.

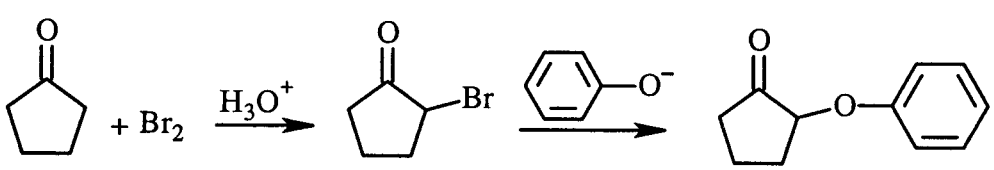


9.

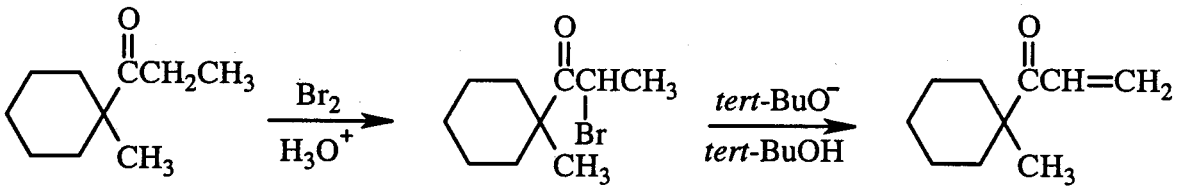
a. $CH_3CH_2CH + Br_2 \xrightarrow{H_3O^+} CH_3CHCH \xrightarrow{CH_3NHCH_3} CH_3CHCH$ (Br; $N(CH_3)_2$)

b. $CH_3CH_2CH + Br_2 \xrightarrow{H_3O^+} CH_3CHCH \xrightarrow{HO^-} CH_3CHCH$ (Br; OH)

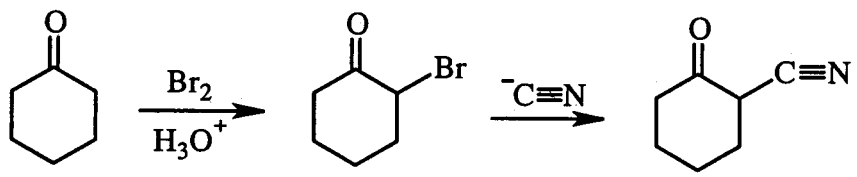
c. 

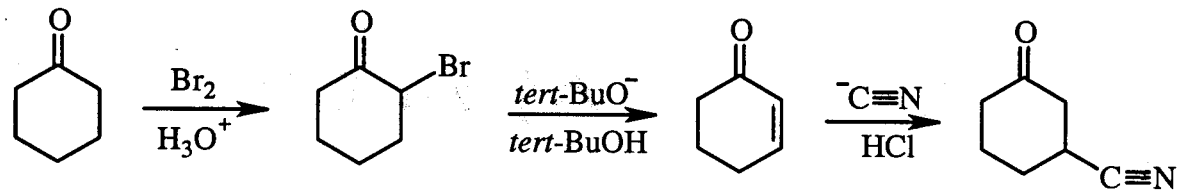
d. 

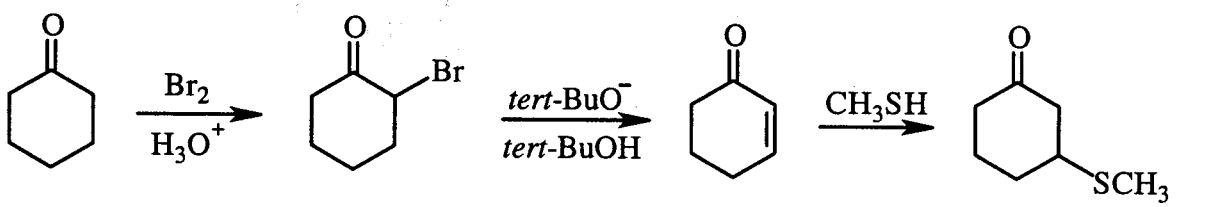
a. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}CH_2CH_2CH_3 \xrightarrow[H_3O^+]{Br_2} CH_3CH_2\underset{Br}{\overset{O}{\overset{\|}{C}}}HCCH_2CH_2CH_3 \xrightarrow[tert\text{-}BuOH]{tert\text{-}BuO^-} CH_3CH{=}CH\overset{O}{\overset{\|}{C}}CH_2CH_2CH_3$

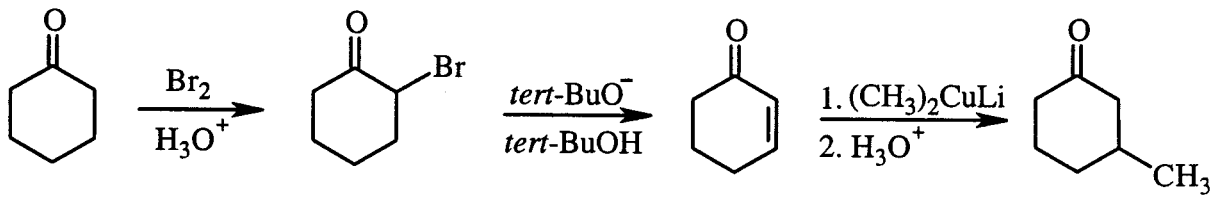
b. 

11.

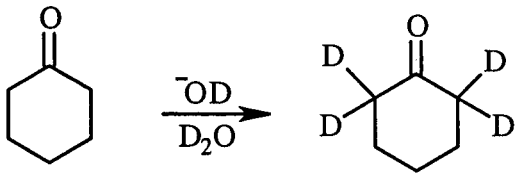
a. 

b. 

c. 

d. 

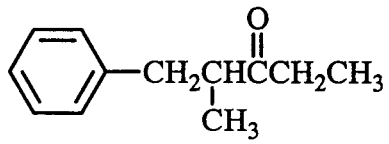
12.



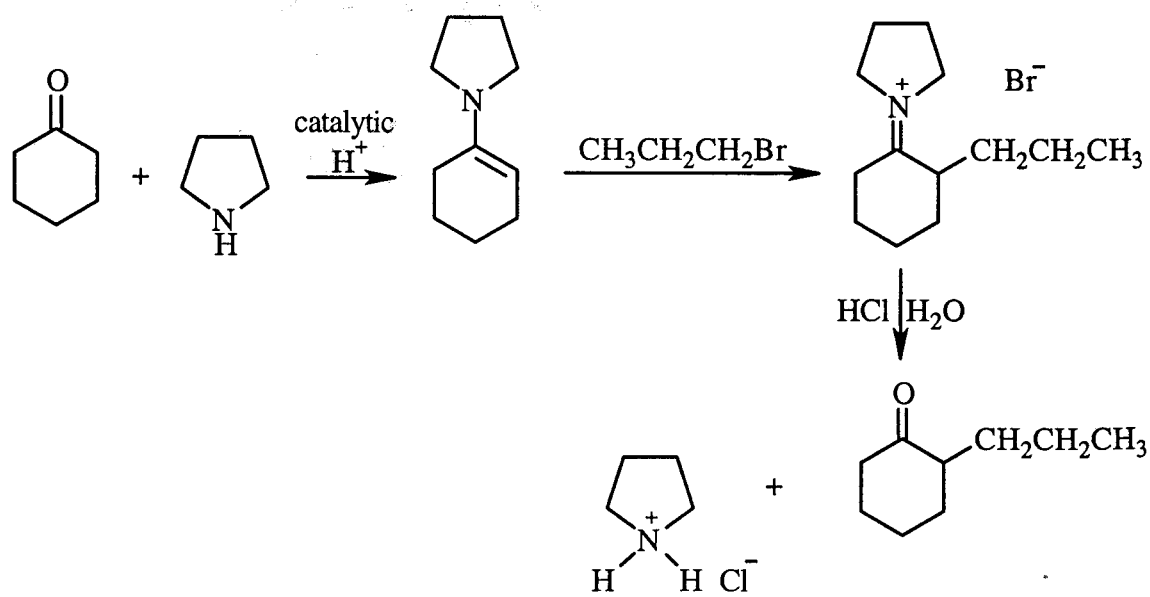
13. Alkylation of an alpha carbon is an S_N2 reaction. S_N2 reactions work best with primary alkyl halides because there is less steric hindrance in a primary alkyl halide than in a secondary alkyl halide. S_N2 reactions don't work at all with tertiary alkyl halides because they are the most sterically hindered of the alkyl halides. Therefore, in the case of tertiary alkyl halides, the S_N2 reaction cannot compete with the E2 elimination reaction.

14.

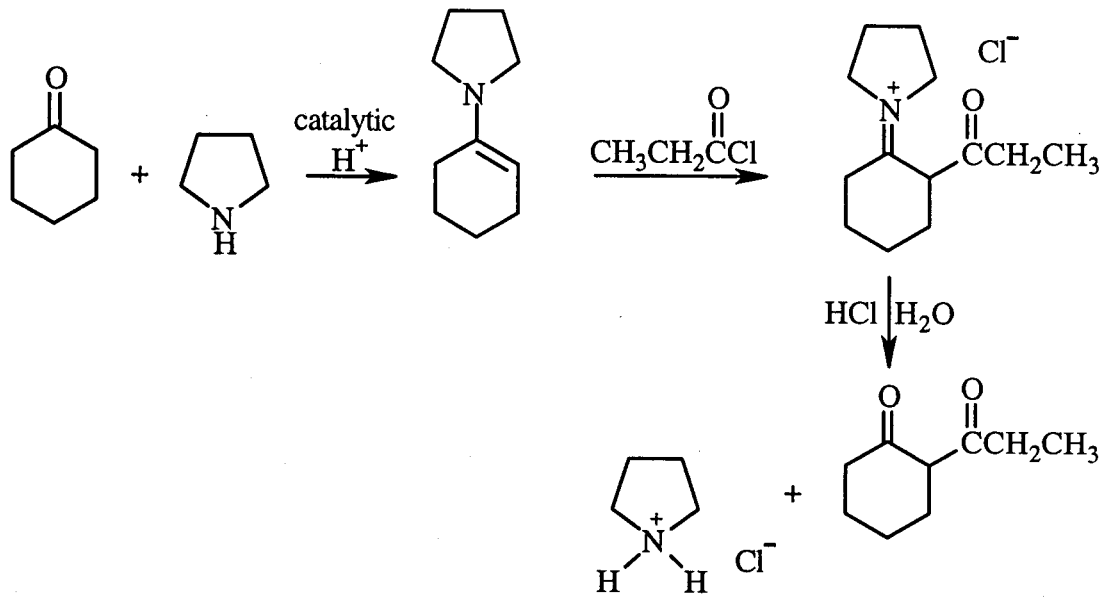
a. $CH_3\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow[2.\ ICH_2CH{=}CH_2]{1.\ LDA/THF} CH_3\overset{O}{\overset{\|}{C}}CH_2CH_2CH{=}CH_2$

b. $CH_3CH_2\overset{O}{\overset{\|}{C}}CH_2CH_3 \xrightarrow[2.\ \text{C}_6\text{H}_5\text{CH}_2\text{Br}]{1.\ LDA/THF}$ 

15.

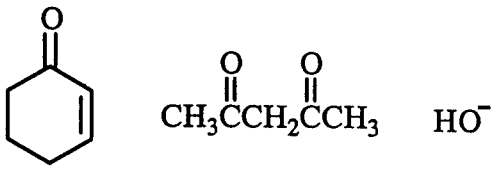
a. 

b.

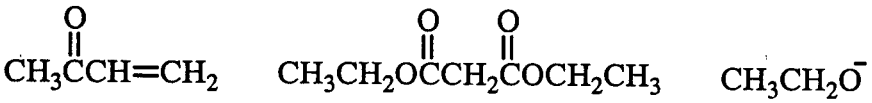


16.

a.

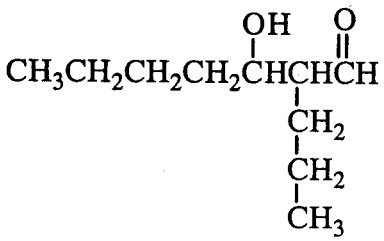


b.

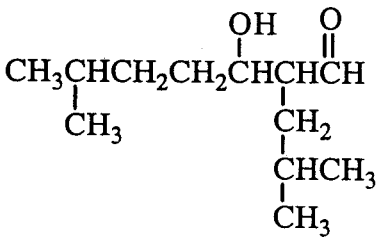


17.

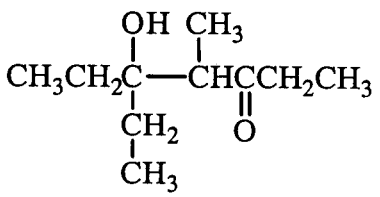
a.



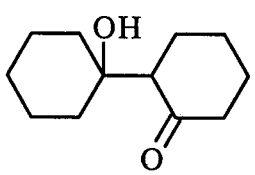
b.



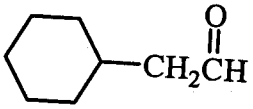
c.



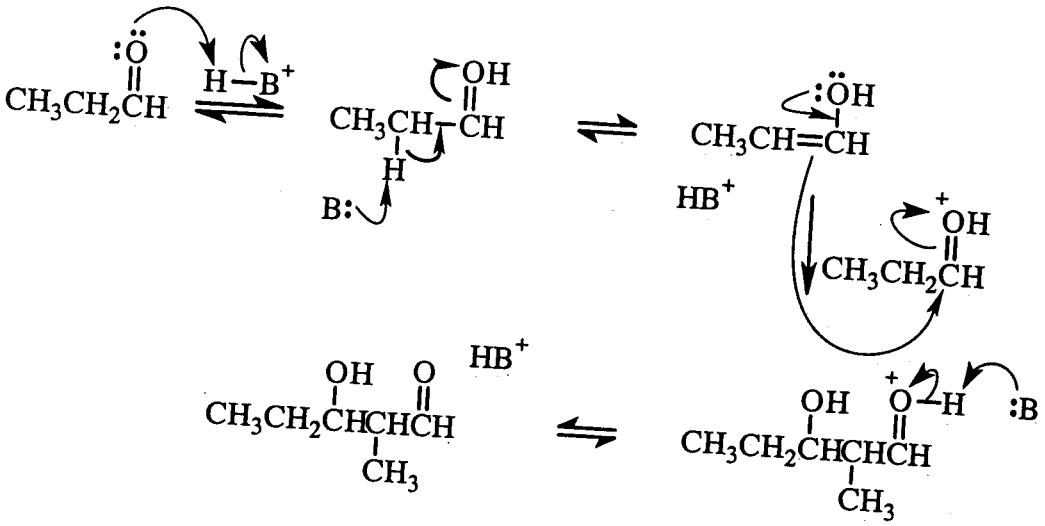
d.



18.

a. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H$ **b.** $CH_3\overset{O}{\overset{\|}{C}}CH_3$ **c.**  **d.** $CH_3CH_2\overset{O}{\overset{\|}{C}}CH_2CH_3$

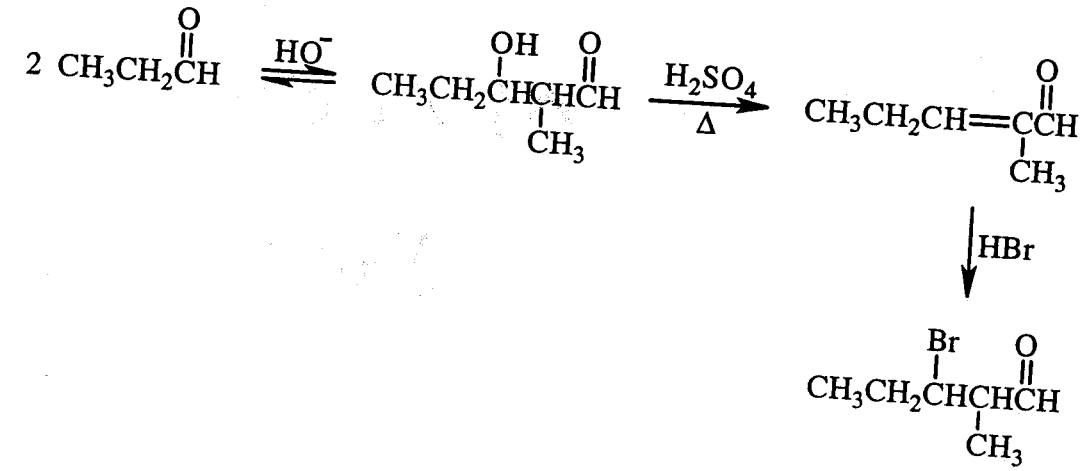
19.



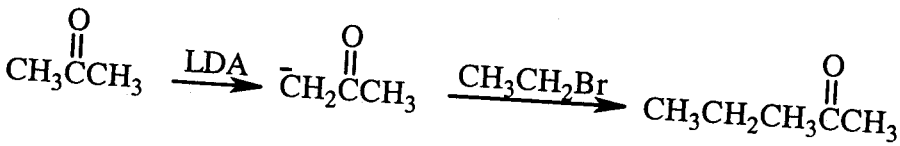
20.

a. Solved in the text.

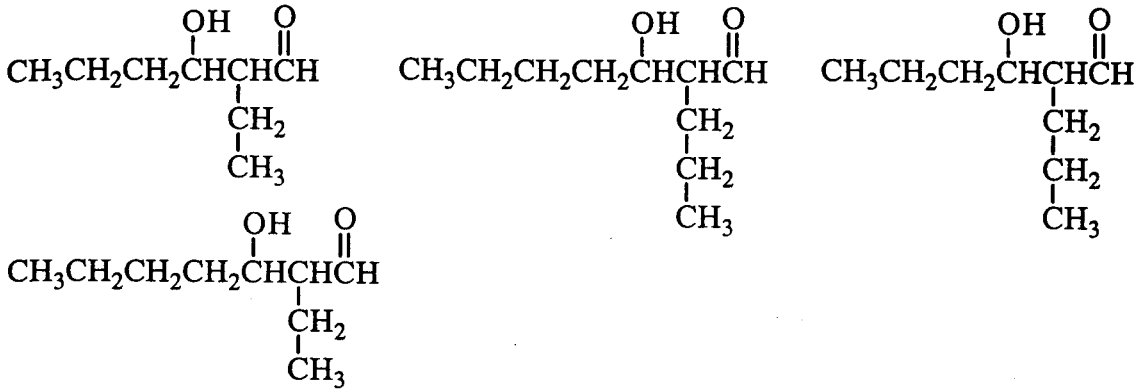
b.



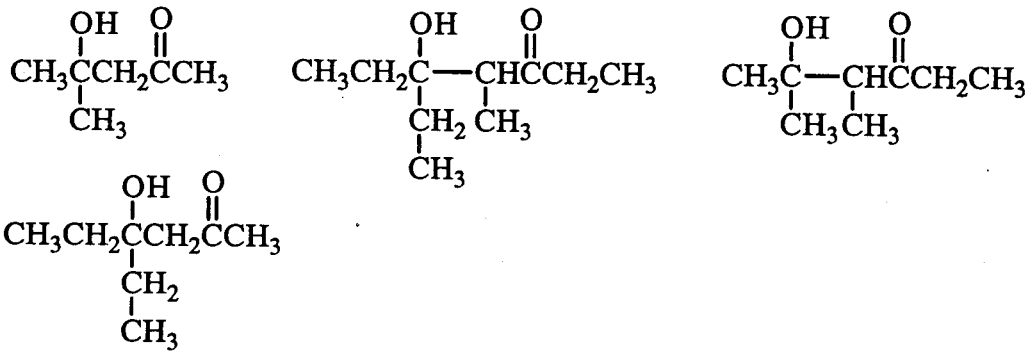
c.



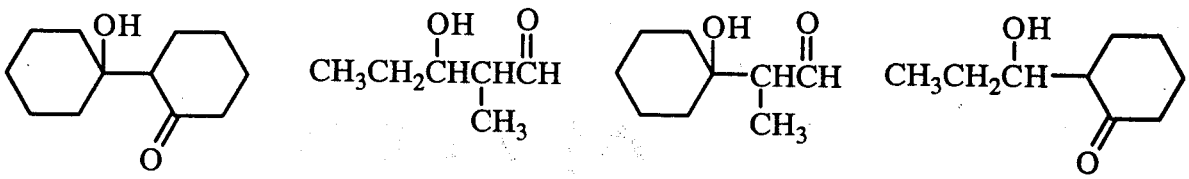
a.



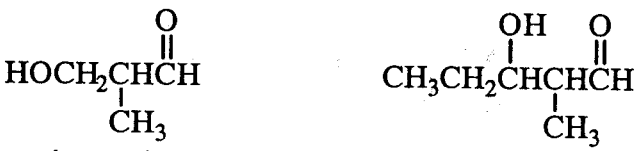
b.



c.



d.

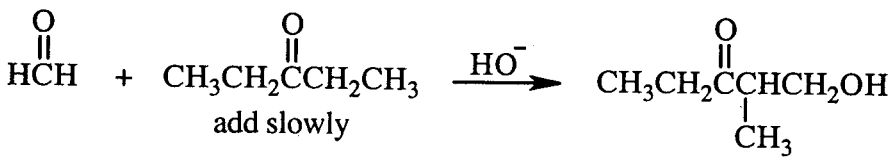


major product

minor product

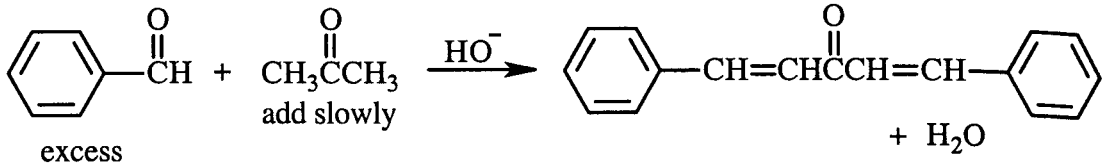
22.

a.

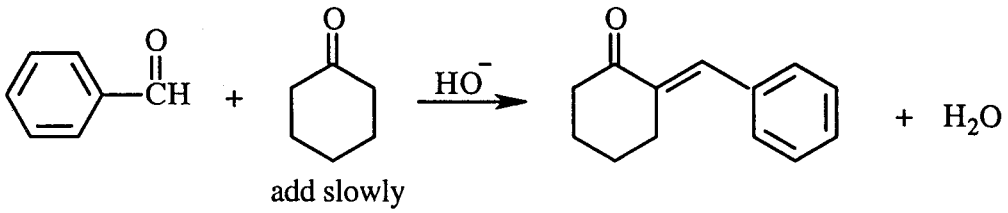


add slowly

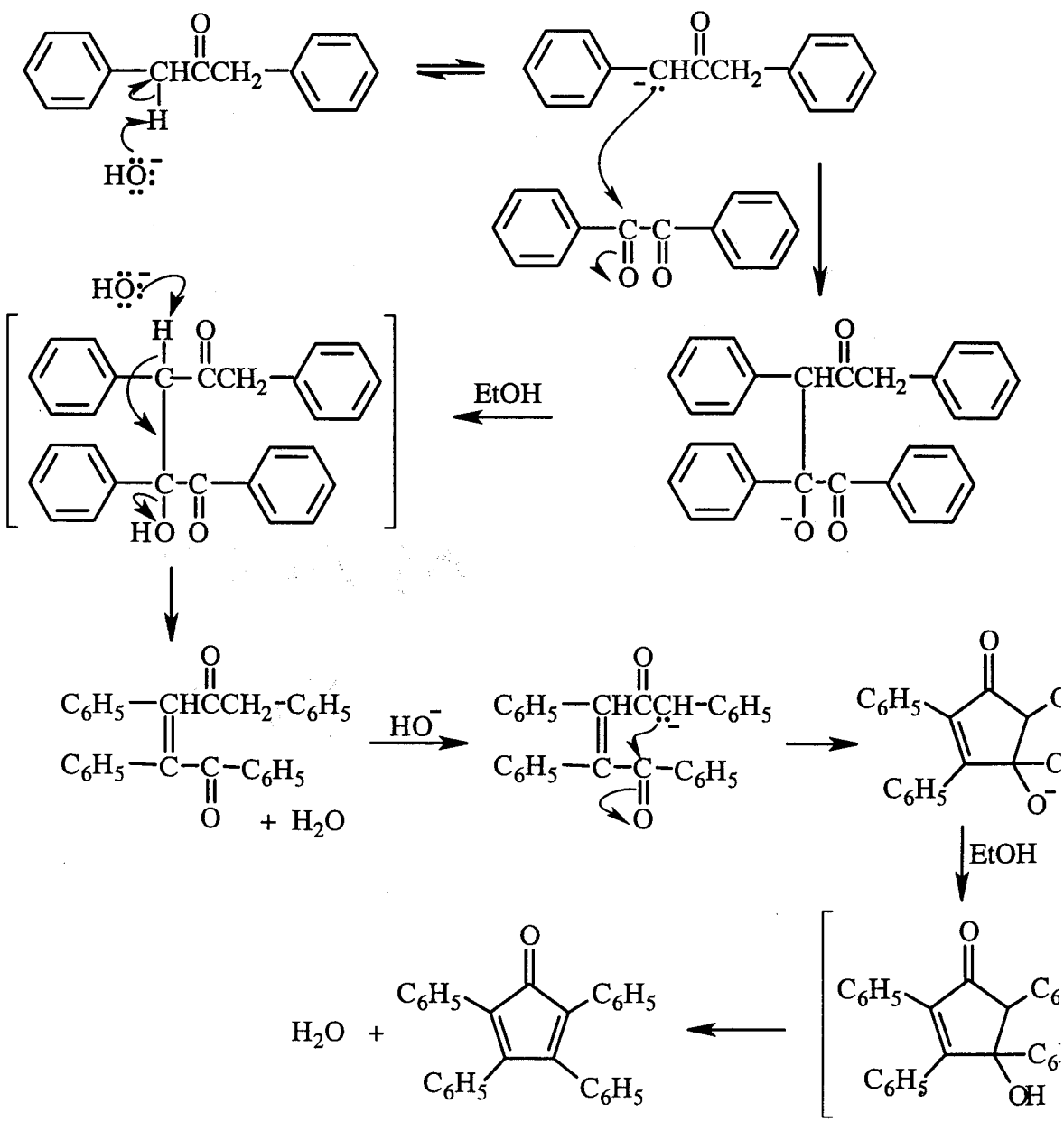
b.


CH
+
CH_3CCH_3
add slowly
excess
HO^-
CH=CHCCH=CH
+ H_2O

c.


CH
+
add slowly
HO^-
+ H_2O

23.


$CHCCH_2$
HO^-
EtOH
C_6H_5—$CHCCH_2$-C_6H_5
C_6H_5—C—C—C_6H_5
+ H_2O
HO^-
C_6H_5—$CHCCH$-C_6H_5
EtOH
H_2O +

24.

a. $CH_3CH_2CH_2C(=O)CH(CH_2CH_3)C(=O)OCH_3$

b. $CH_3CH(CH_3)CH_2C(=O)CH(CH(CH_3)_2)C(=O)OCH_2CH_3$

25. An α-hydrogen has to be removed from the condensation product in order to drive the reaction toward completion. If the original ester had only one α-hydrogen, the condensation product would not have an α-hydrogen, so the reaction cannot be driven to completion.

$$2\ CH_3CH(CH_3)C(=O)OCH_3 \xrightarrow{CH_3O^-} CH_3CH(CH_3)C(CH_3)(C(=O)OCH_3)C(=O)CH(CH_3)CH_3 \xrightarrow{CH_3O^-}\ \not\rightarrow$$

26.

a. $CH_3CH_2C(=O)CH(CH_3)C(=O)OCH_3$ $CH_3C(=O)CH_2C(=O)OCH_3$ $CH_3CH_2C(=O)CH_2C(=O)OCH_3$ $CH_3C(=O)CH(CH_3)C(=O)OCH_3$

b. $C_6H_5C(=O)CH_2C(=O)C_6H_5$

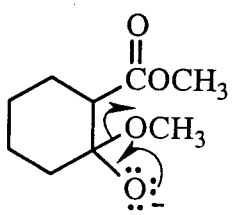
c. $HC(=O)CH(CH_2CH_3)C(=O)OCH_3$

d. $CH_3CH_2OC(=O)CH(CH_3)C(=O)OCH_2CH_3$

27. Solved in the text.

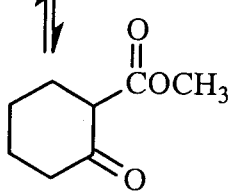
28.

$$CH_2CH_2C(=O)OCH_3,\ CH_2,\ CH_2CH_2C(=O)OCH_3,\ C(=O) \xrightleftharpoons{CH_3O^-} CH_2CHC(=O)OCH_3,\ CH_2,\ CH_2CH_2C(=O)OCH_3,\ C(=O) \rightleftharpoons$$



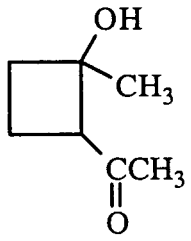
$$+\ CH_3OH$$

$$CH_3O^- + \rightleftharpoons$$

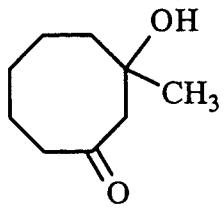


29.

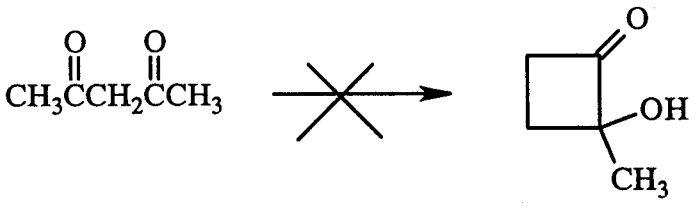
a.



b.



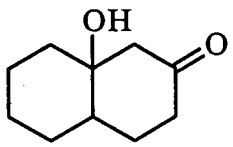
30. No, because an intramolecular reaction would lead to a strained four-membered ring. Therefore the intermolecular reaction will be preferred.



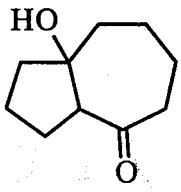
31. Solved in the text.

32.

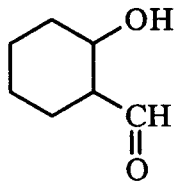
a.



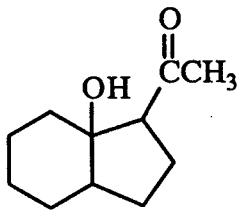
b.



c.

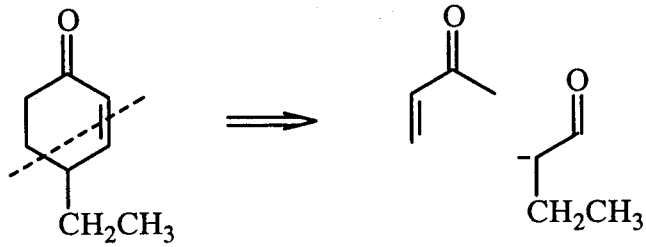


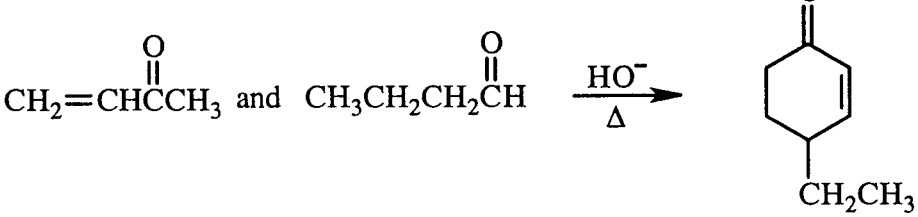
d.



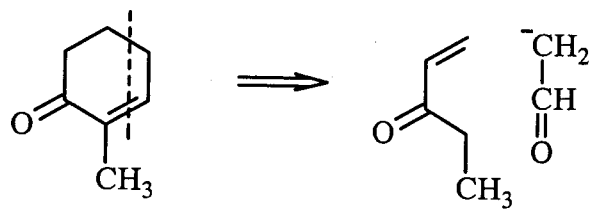
33.

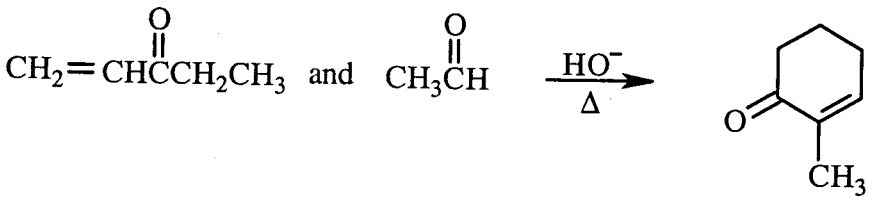
a.



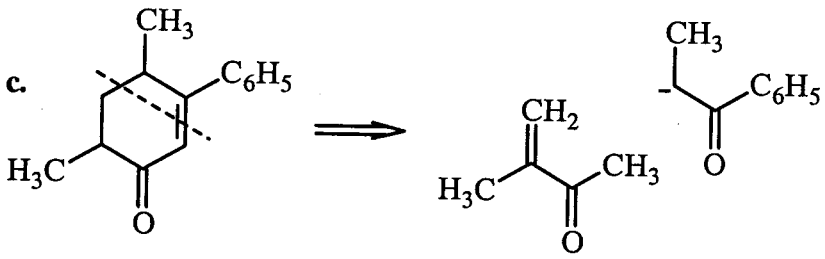


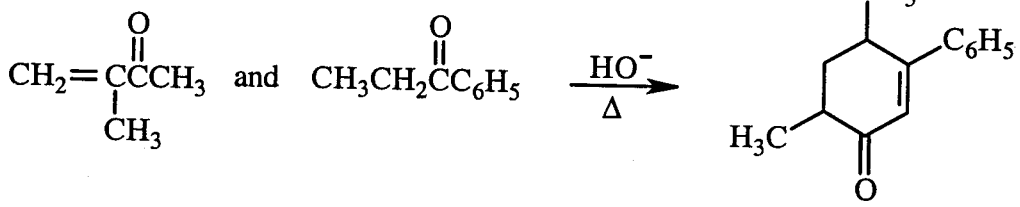
b.



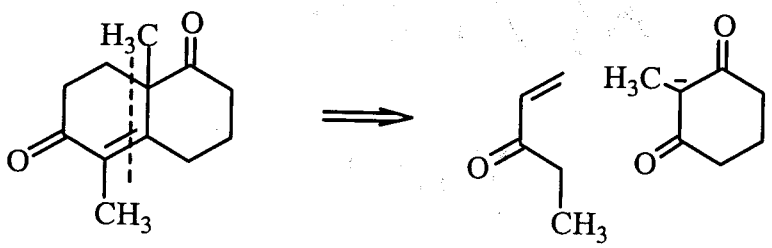


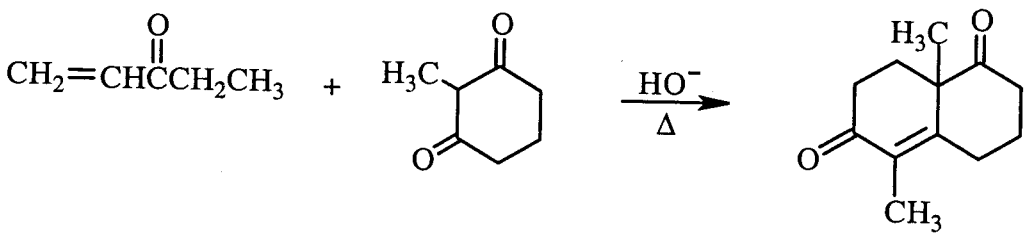
c.





d.





34. **a** and **d** can be decarboxylated.
b can't be decarboxylated, because it doesn't have a carboxyl group.
The electrons left behind if **c** were decarboxylated cannot be delocalized onto an oxygen.

35. **a.** methyl bromide
b. methyl bromide (twice)
c. benzyl bromide
d. isobutyl bromide

36. **a.** An S_N2 reaction cannot be done on bromobenzene. (Section 10.8 of the text.)

b. An S_N2 reaction cannot be done on vinyl bromide. (Section 10.8 of the text.)

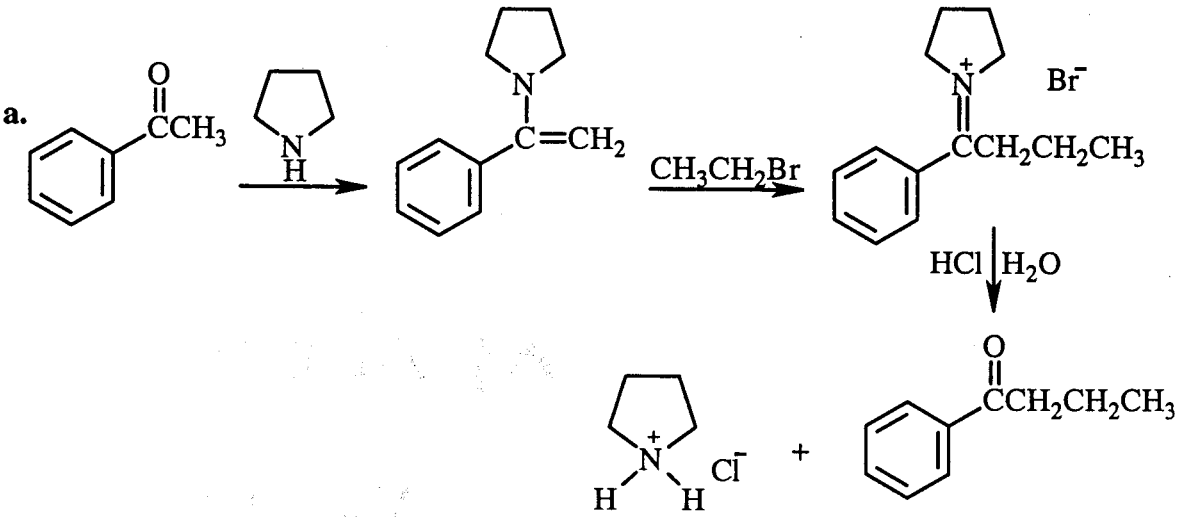
c. An S_N2 reaction cannot be done on a tertiary alkyl halide. (Only elimination occurs; Section 11.8 of the text.)

37. Solved in the text.

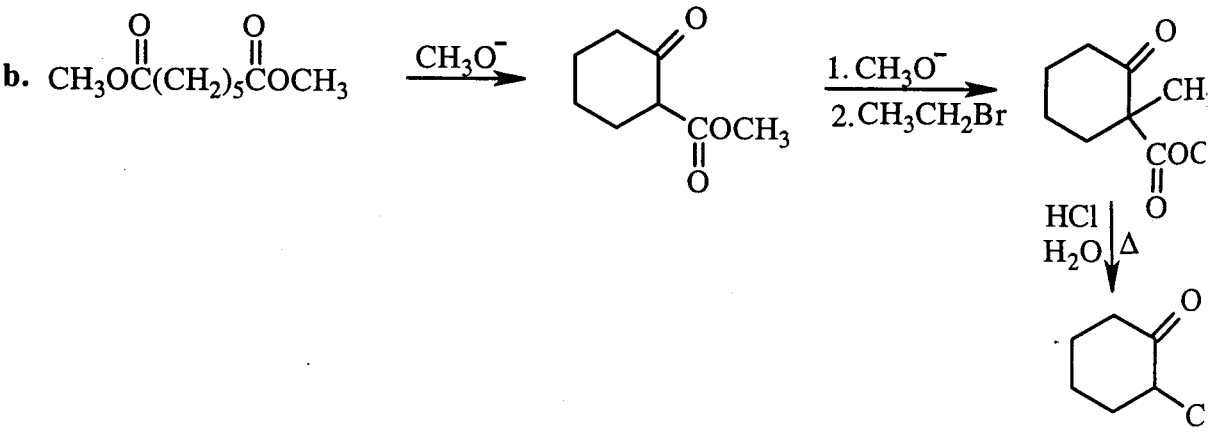
38. **a.** ethyl bromide **b.** pentyl bromide **c.** benzyl bromide

39.

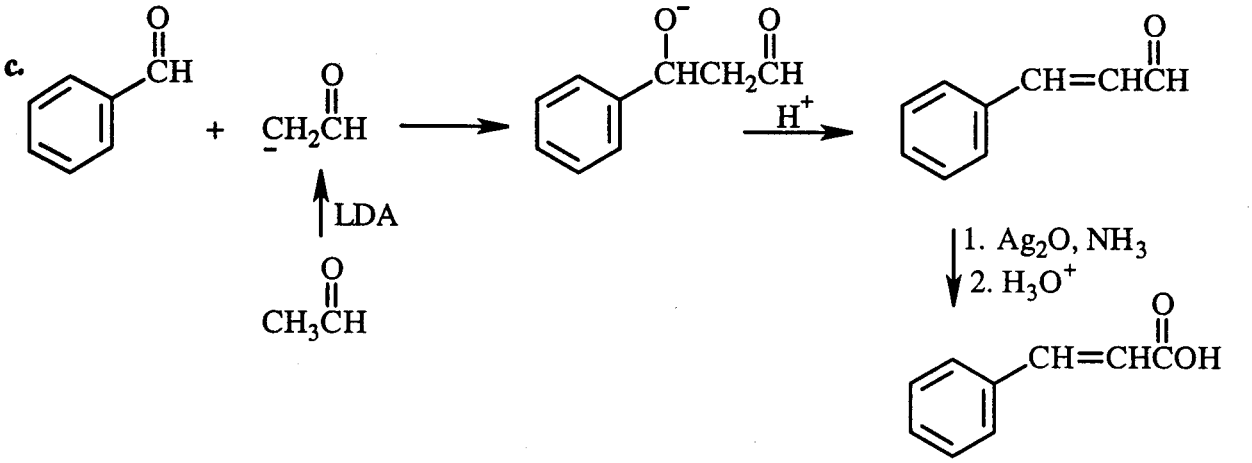
a.



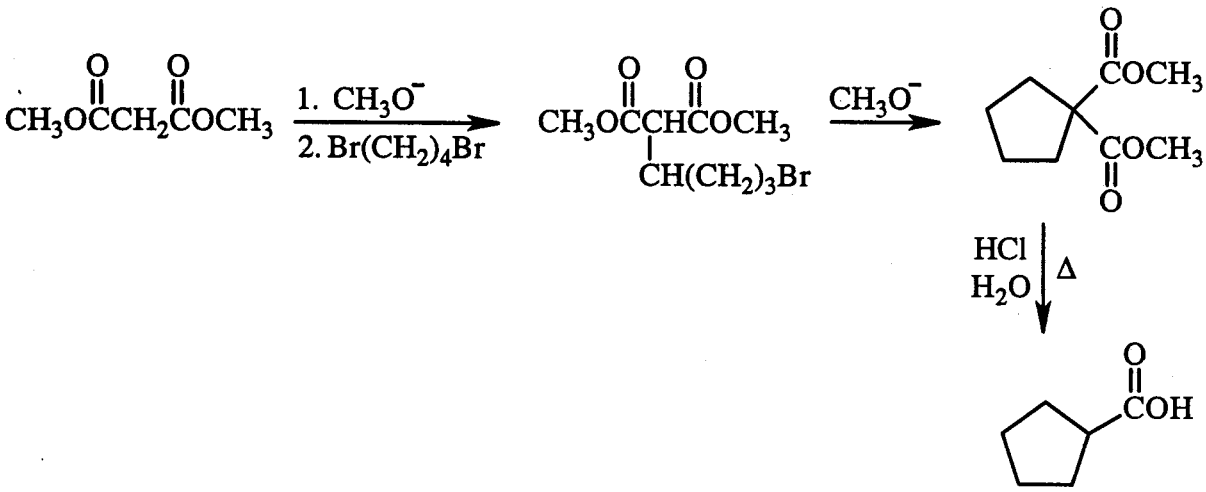
b.



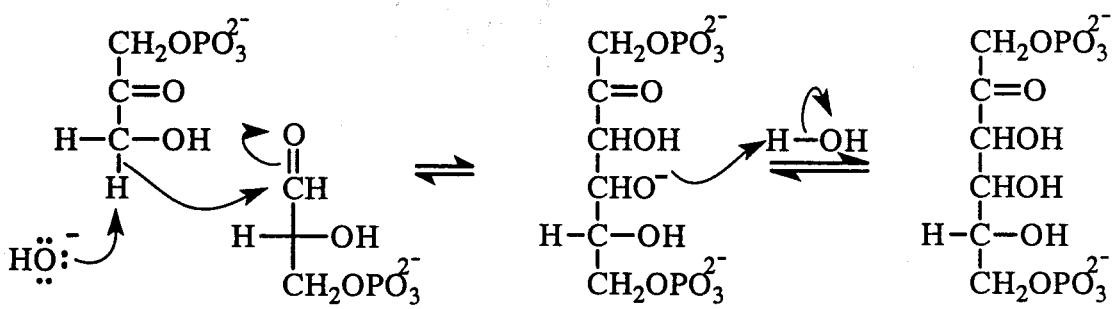
c.



d.



40. Because the catalyst is hydroxide ion rather than an enzyme, four stereoisomers will be formed since two chirality centers are created in the product. One of the four is fructose.

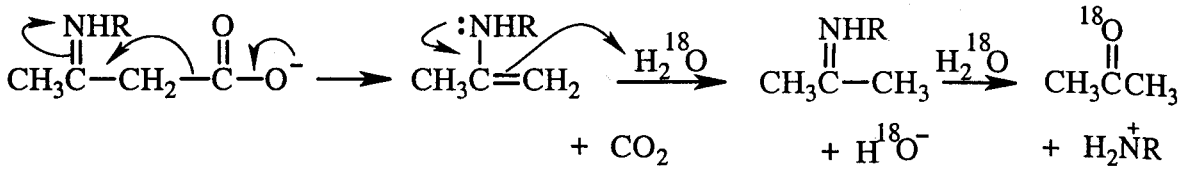


41. **Seven** moles. The first two carbons in the fatty acid come from acetyl CoA. Each subsequent two-unit piece comes from malonyl CoA. Because this amounts to fourteen carbons for the synthesis of the 16-carbon fatty acid, seven moles of malonyl CoA are required.

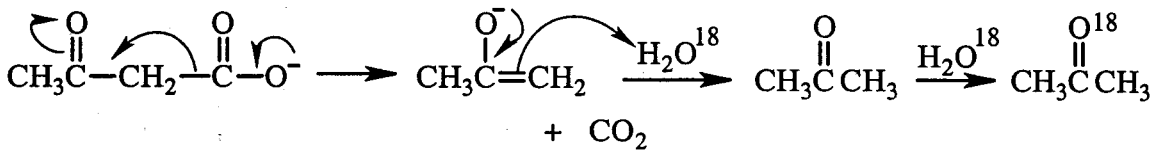
42. **a.** **Three** deuteriums would be incorporated into palmitic acid because only one CD_3COSR is used in the synthesis.

b. **Seven** deuteriums would be incorporated into palmitic acid because seven $^-OOCCD_2COSR$ are used in the synthesis (for a total of 14 D's), and each $^-OOCCD_2COSR$ loses one deuterium in the dehydration step (14 D's - 7 D's = 7 D's).

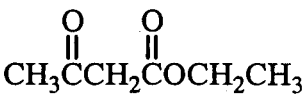
43. It tells you that an imine is formed as an intermediate. Because an imine is formed, the only source of oxygen for acetone formation is $H_2{}^{18}O$.

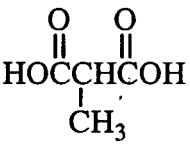


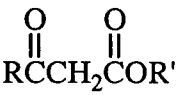
If decarboxylation occurred without imine formation, acetone would contain ^{16}O and some ^{18}O from a hydration-dehydration equilibrium.

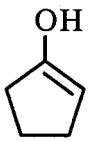


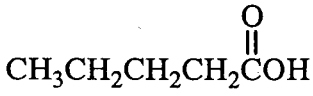
44.

a. 

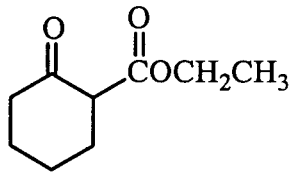
b. 

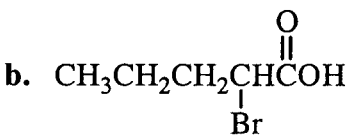
c. 

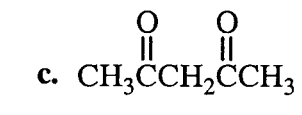
d. 

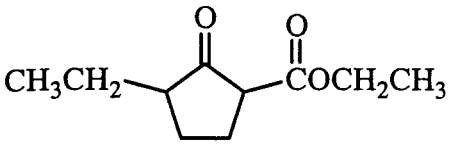
e. 

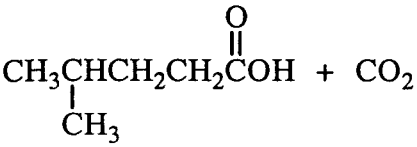
45.

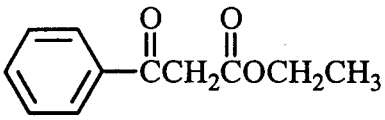
a. 

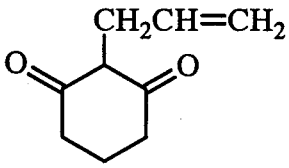
b. 

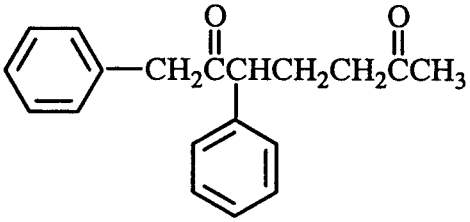
c. 

d. 

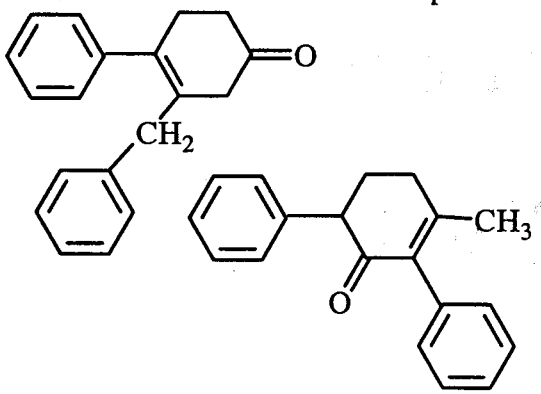
e. 

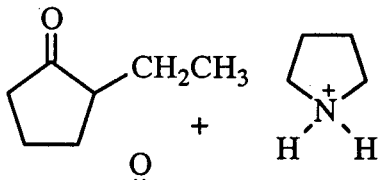
f. 

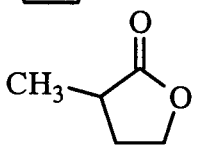
g. 

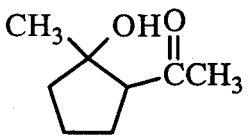
h. 

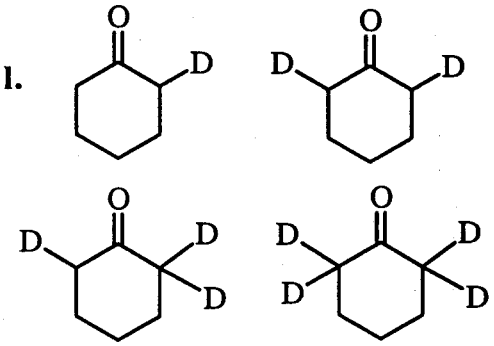
The two compounds below are formed by a Robinson annulation of the above product.

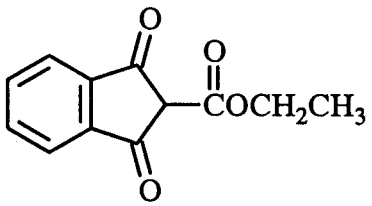


i. 

j. 

k. 

l. 

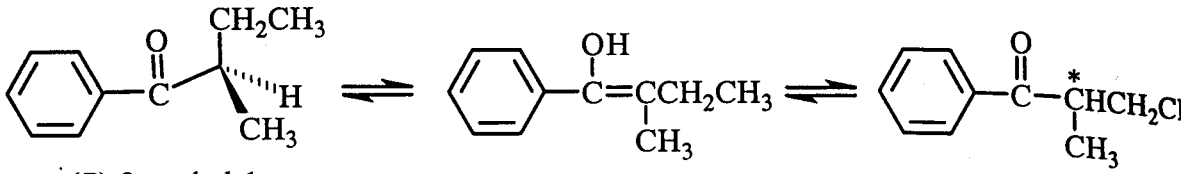
m. 

46. The electron withdrawing nitro group will cause the signal to occur at a higher frequency (will have a larger chemical shift). The more acidic the hydrogen, the greater the chemical shift.

CH_3NO_2	$CH_2(NO_2)_2$	$CH(NO_2)_3$
δ 4.33	δ 6.10	δ 7.52

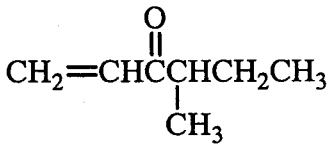
47. **a.** When the ketone enolizes, the chirality center is lost.

When the enol reforms the ketone, it can form the *R* and *S* enantiomer equally as easily, so a racemic mixture is obtained.

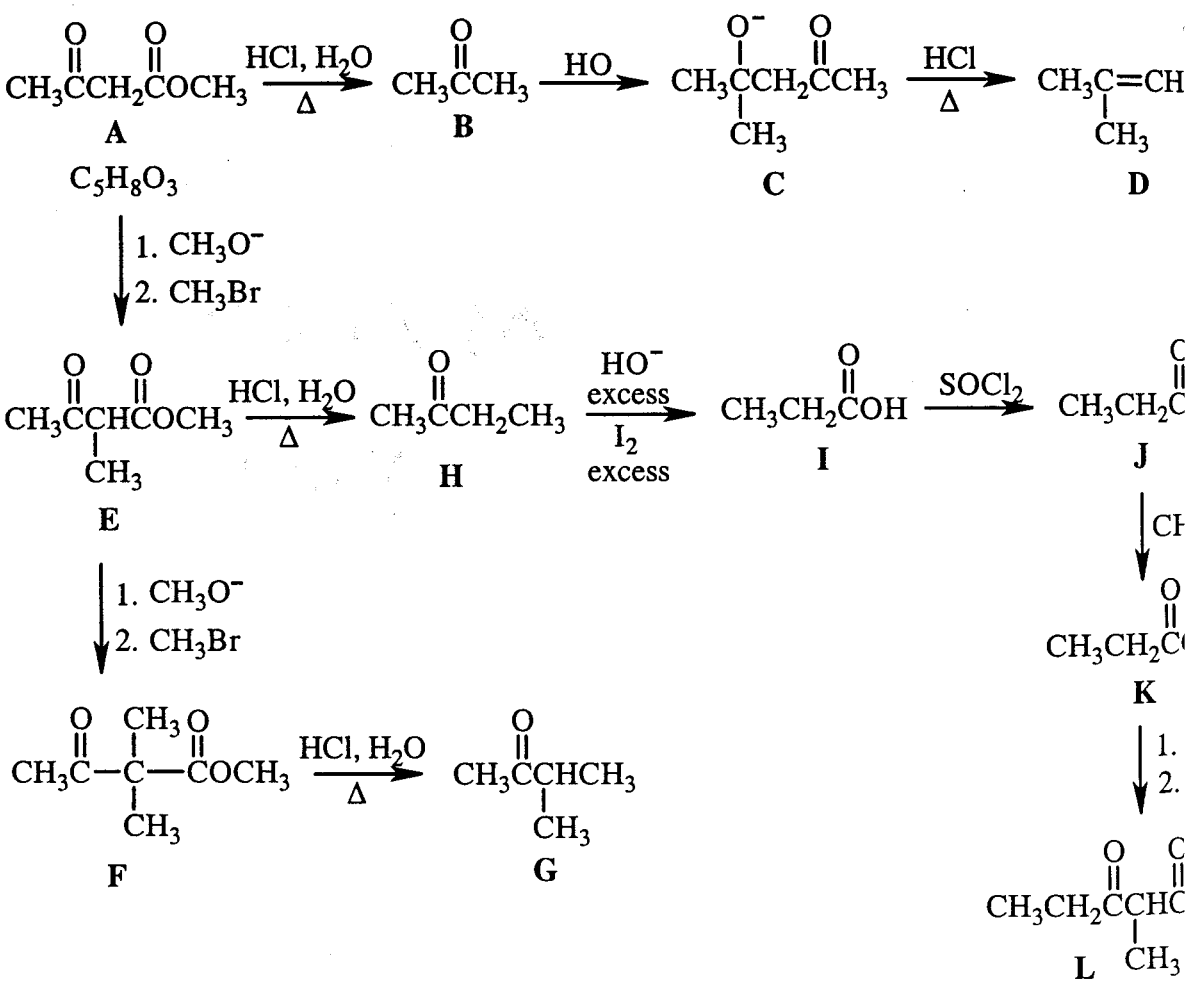


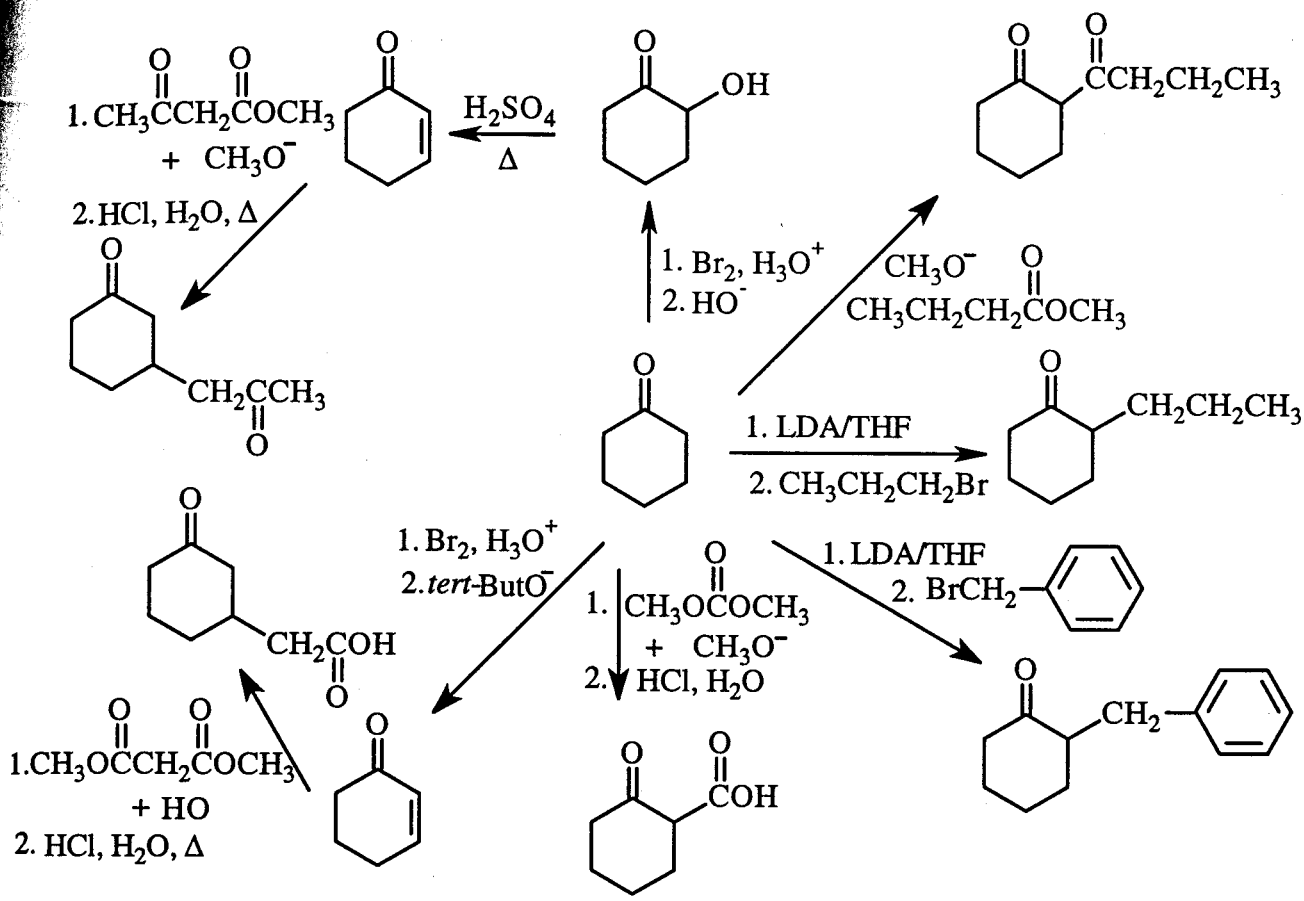
(*R*)-2-methyl-1-phenyl-1-butanone

b. You need a ketone that has an α-carbon that is an asymmetric carbon. Racemization will occur when an α-hydrogen is removed from the asymmetric carbon. If you don't want racemization to have to compete with removal of a hydrogen from a second α-carbon, it is best to chose a compound that can form only one enol.



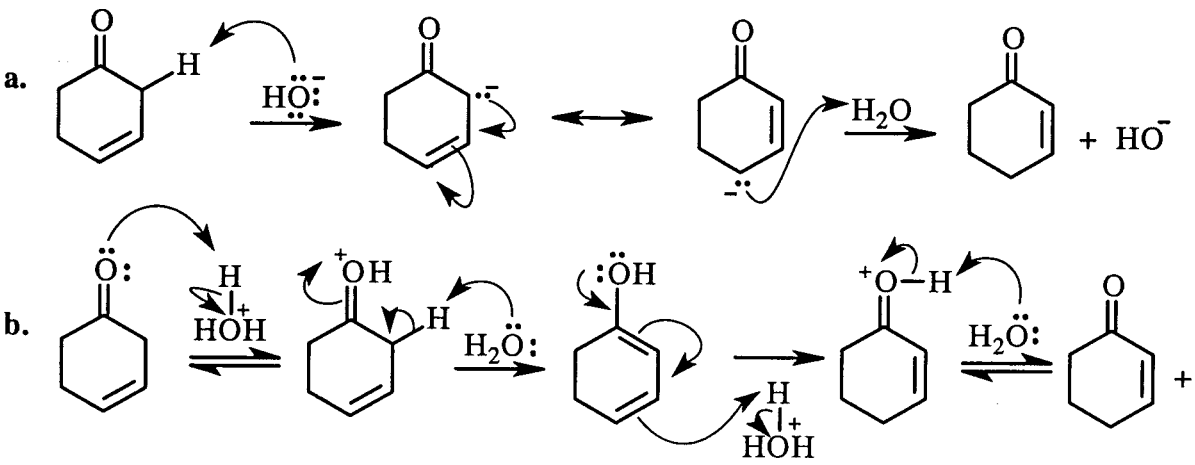
48.





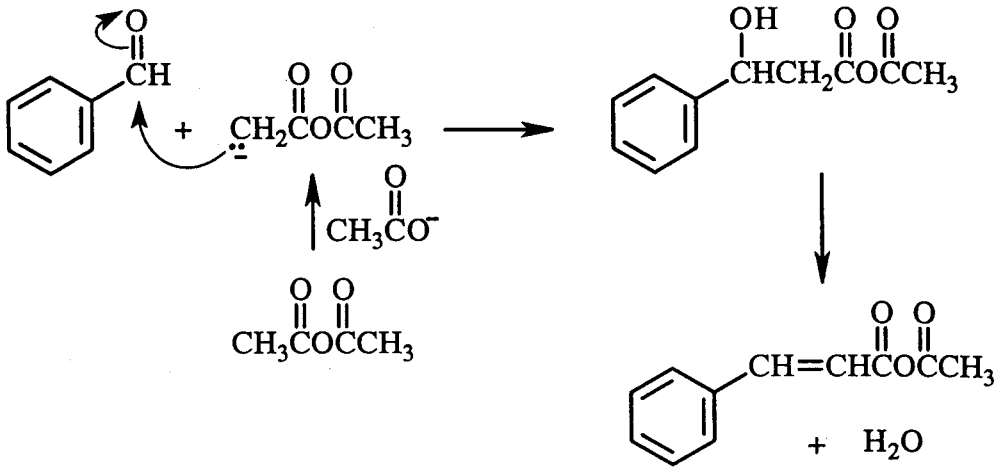
Notice that the β-substituted compounds are prepared via an α,β-unsaturated ketone, which can prepared in two different ways—either by dehydrohalogenation of α-bromocyclohexanone or by dehydration of α-hydroxycyclohexanone.

50. Remember that there are no positively charged organic reactants, intermediates, or products in a basic solution, and no negatively charged organic reactants, intermediates, or products in an acidic solution.

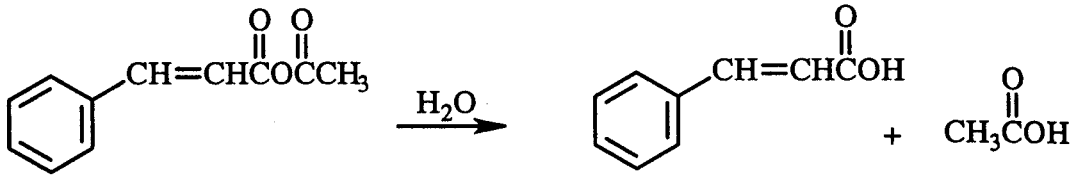


51.

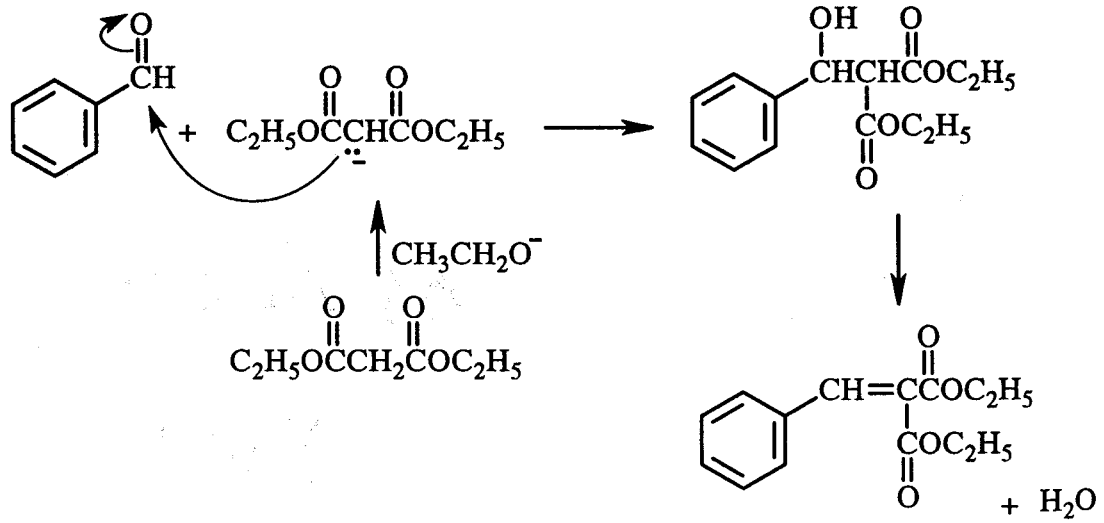
a.



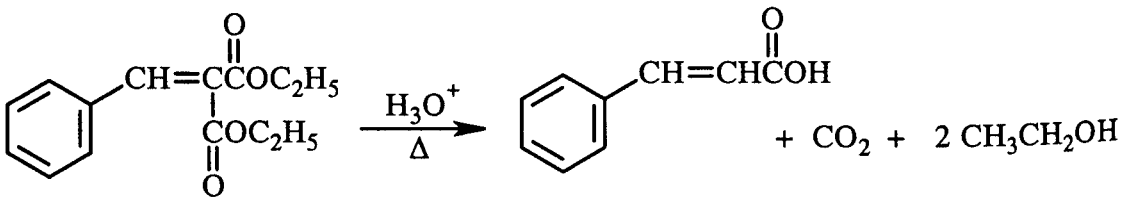
b.



c.



d.



52.

a. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H + BrCH_2\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow[2.\ H_2O]{1.\ Zn} CH_3CH_2CH_2\underset{OH}{CH}CH_2\overset{O}{\overset{\|}{C}}OCH_3$

b. $CH_3CH_2\overset{O}{\overset{\|}{C}}H + CH_3CH_2\underset{Br}{CH}\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow[2.\ H_2O]{1.\ Zn} CH_3CH_2\underset{OH}{CH}\underset{CH_2CH_3}{CH}\overset{O}{\overset{\|}{C}}OCH_3$

$\xrightarrow[\text{excess}]{H^+,\ H_2O}$

$CH_3CH_2\underset{OH}{CH}\underset{CH_2CH_3}{CH}\overset{O}{\overset{\|}{C}}OH$

c. $CH_3CH_2\overset{O}{\overset{\|}{C}}H + CH_3\underset{Br}{CH}\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow[2.\ H_2O]{1.\ Zn} CH_3CH_2\underset{OH}{CH}\underset{CH_3}{CH}\overset{O}{\overset{\|}{C}}OCH_3$

$\xrightarrow[\text{excess}]{H^+,\ H_2O}$

$CH_3CH_2\underset{OH}{CH}\underset{CH_3}{CH}\overset{O}{\overset{\|}{C}}OH \xrightarrow[\Delta]{H_2SO_4} CH_3CH_2CH{=}\underset{CH_3}{C}\overset{O}{\overset{\|}{C}}OH$

d. $CH_3CH_2\overset{O}{\overset{\|}{C}}CH_2CH_3 + BrCH_2\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow[2.\ H_2O]{1.\ Zn} CH_3CH_2\underset{OH}{\underset{CH_2CH_3}{C}}CH_2\overset{O}{\overset{\|}{C}}OCH_3$

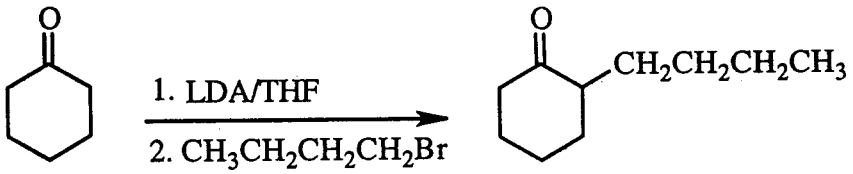
53. The ketone is 2-hexanone. Therefore, the alkyl halide is a propyl halide (propyl bromide, propyl chloride, or propyl iodide).

$CH_3\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2CH_3$

This part comes from acetoacetic ester.

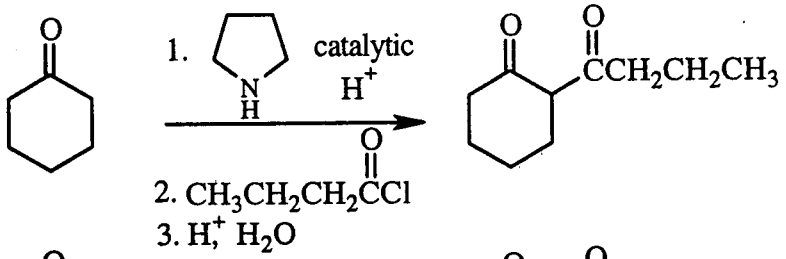
54.

a.

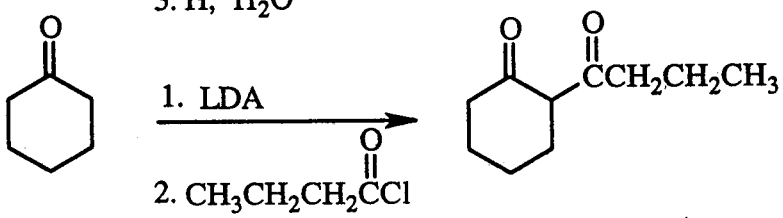

1. LDA/THF
2. CH3CH2CH2CH2Br
CH2CH2CH2CH3

b.

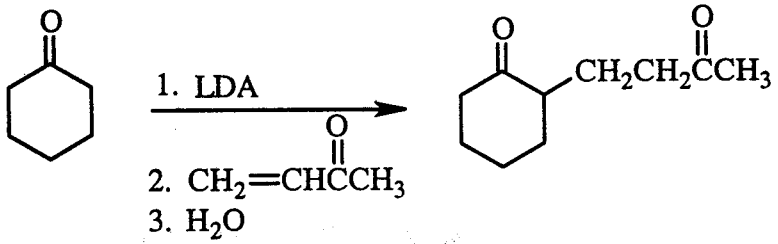
1.


1.
catalytic
H+
2. CH3CH2CH2CCl
3. H+, H2O
CCH2CH2CH3

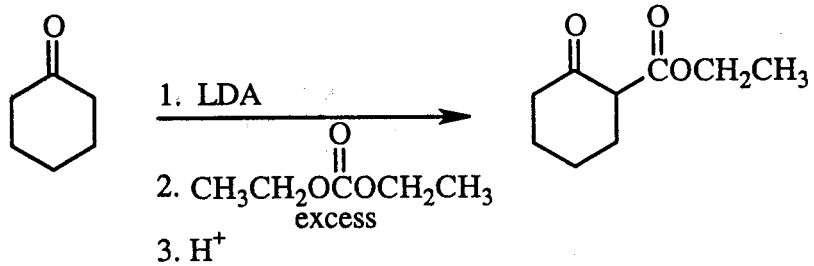
2.


1. LDA
2. CH3CH2CH2CCl
CCH2CH2CH3

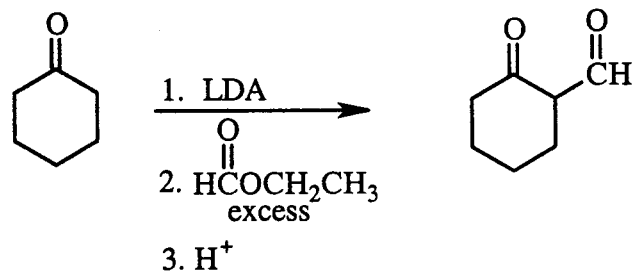
c.


1. LDA
2. CH2=CHCCH3
3. H2O
CH2CH2CCH3

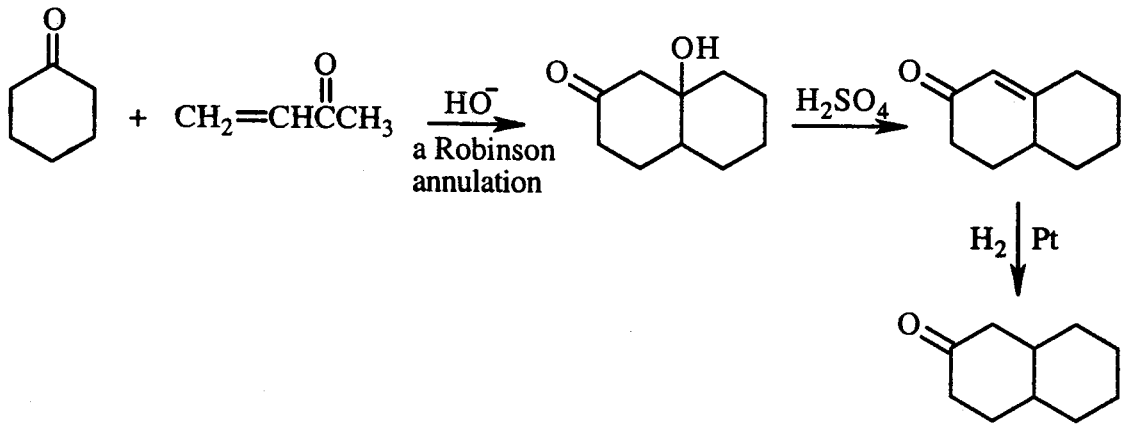
d.


1. LDA
2. CH3CH2OCOCH2CH3
excess
3. H+
COCH2CH3

e.

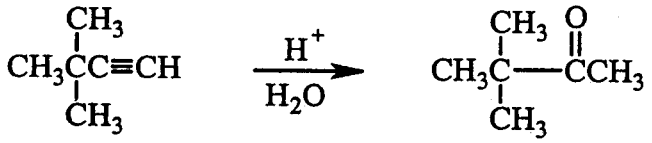

1. LDA
2. HCOCH2CH3
excess
3. H+
CH

f.



55. The positive iodoform test indicates that the compound with two singlets with a ratio of 3 : 1 is a methyl ketone.

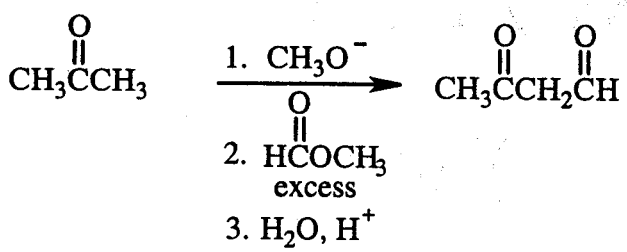
3,3-Dimethyl-1-butyne will show two singlets with a ratio of 9 : 1, and when it adds water, it will form a methyl ketone with two singlets with a ratio of 3 : 1.



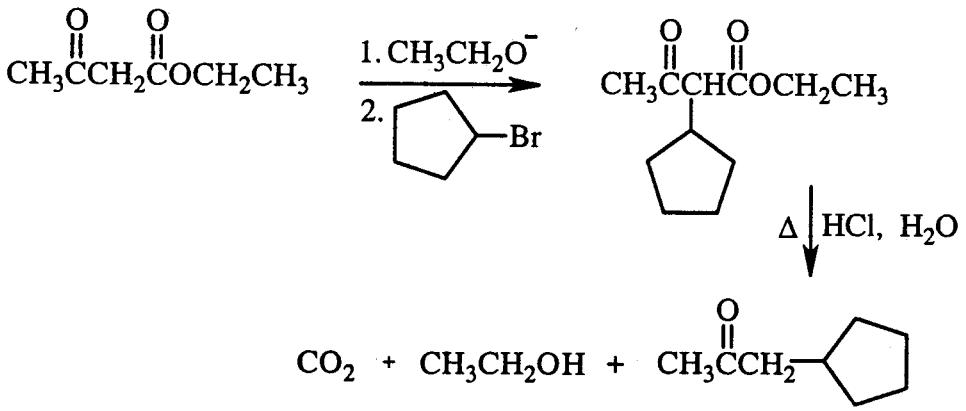
2 singlets (9 : 1) **2 singlets** (3 : 1)

56.

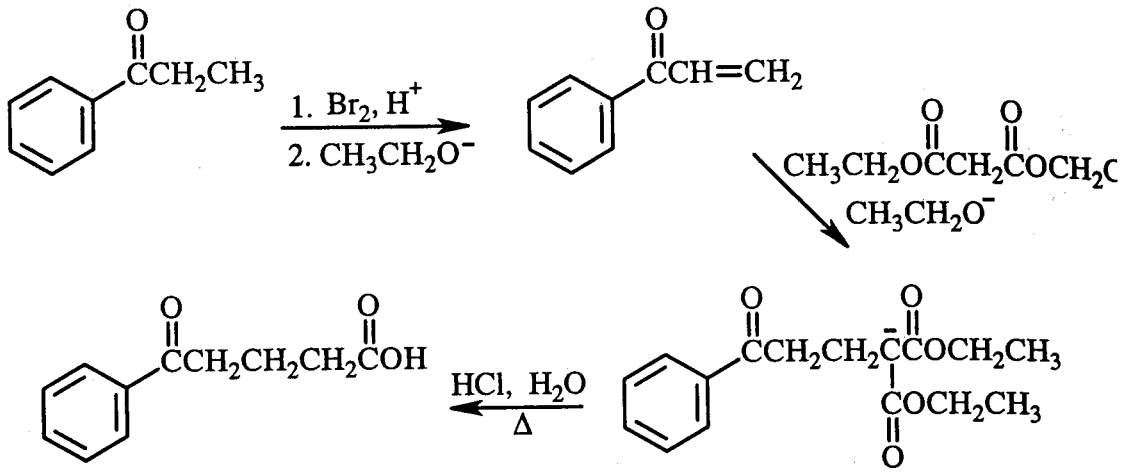
a.



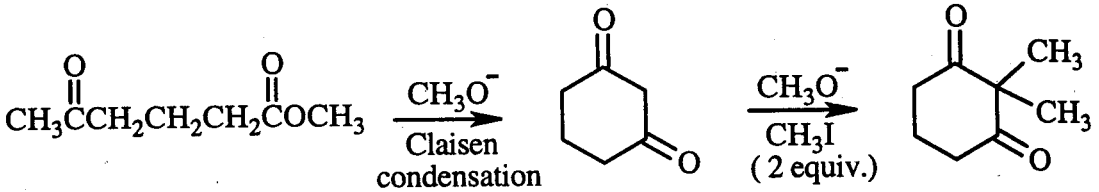
b.



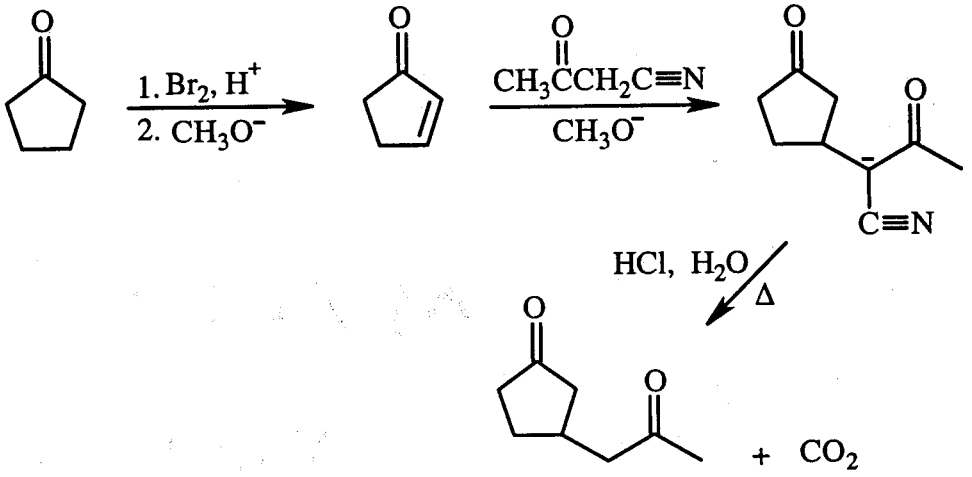
c.


1. Br2, H+
2. CH3CH2O−
CH3CH2O−
HCl, H2O
Δ

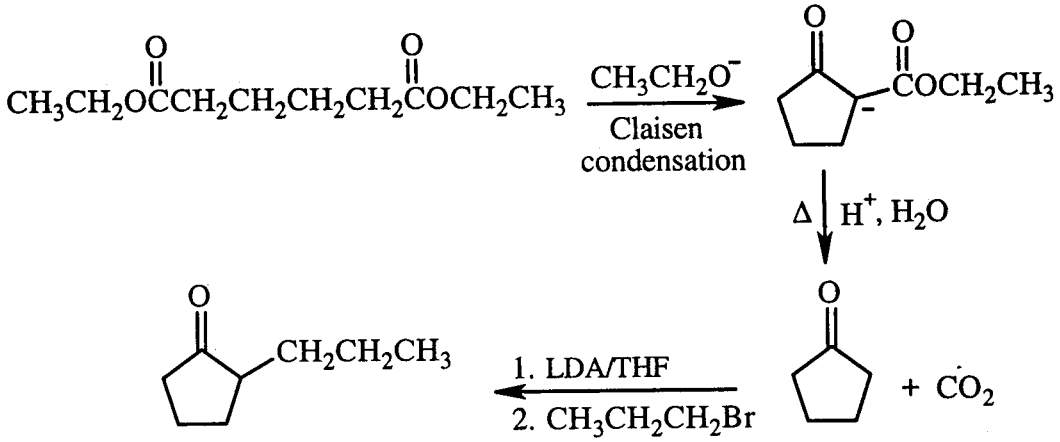
d.

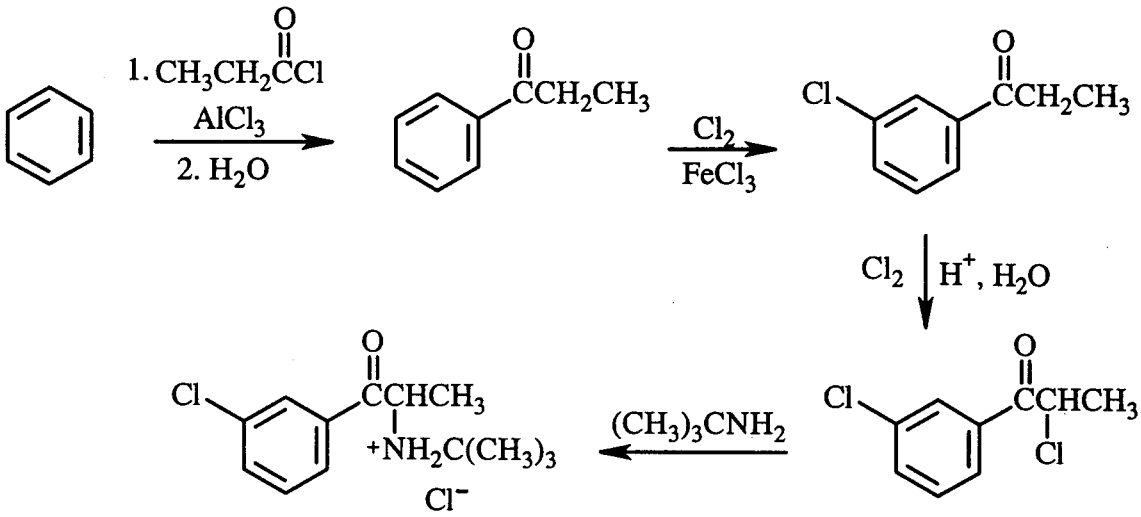

CH3O−
Claisen
condensation
CH3O−
CH3I
(2 equiv.)

e.

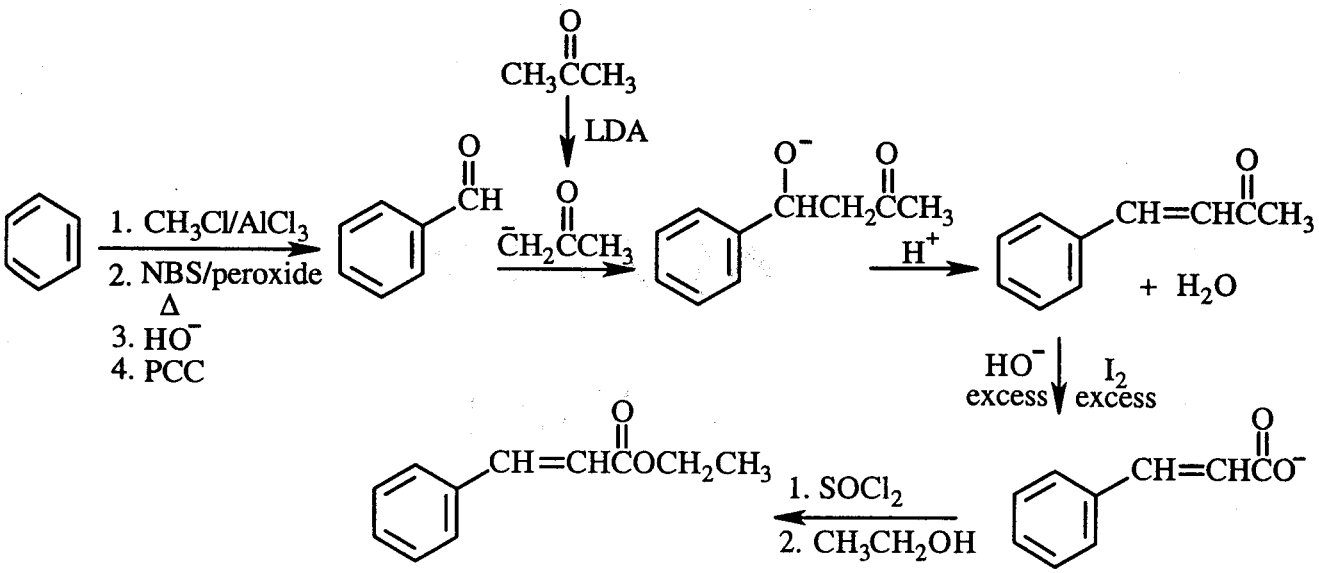

1. Br2, H+
2. CH3O−
CH3O−
HCl, H2O
Δ
+ CO2

f.

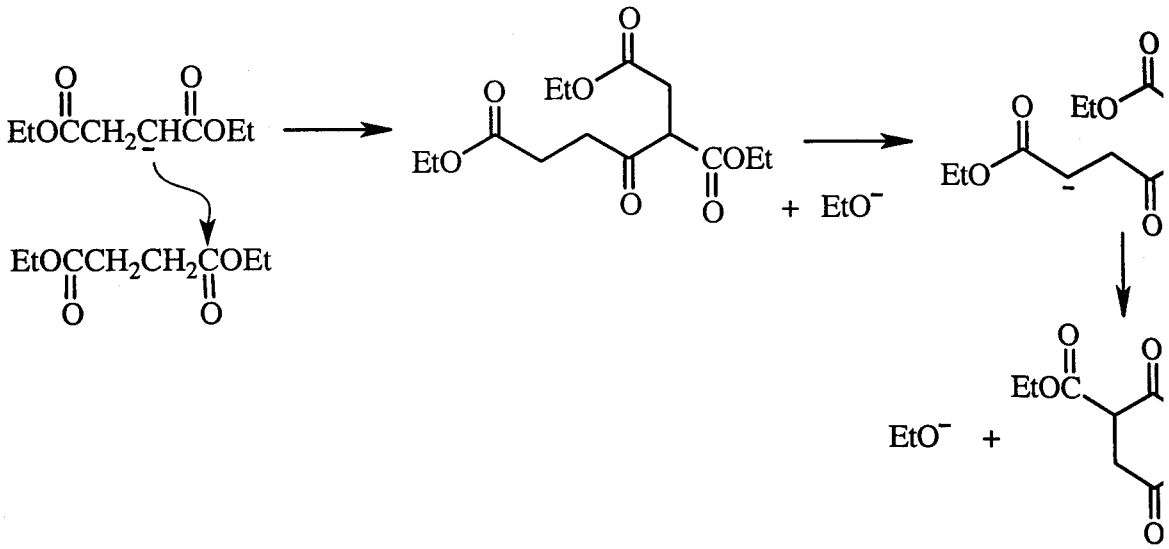

CH3CH2O−
Claisen
condensation
Δ
H+, H2O
1. LDA/THF
2. CH3CH2CH2Br
+ CO2



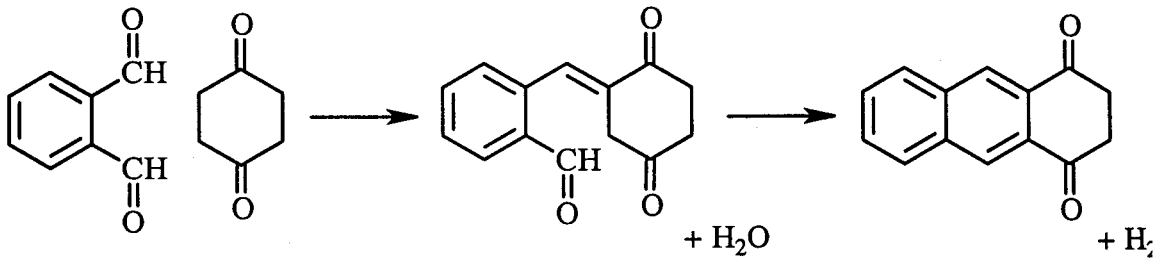
58. Synthesizing benzaldehyde from benzene would be easy if a one carbon acyl chloride could be used, but there is no such compound. The only way a single carbon can be placed on a benzene ring is via a Friedel-Crafts alkylation.



59. **a.** The first reaction is an intermolecular Claisen condensation. The base then removes a hydrogen from the α-carbon that has two α-hydrogens, and an intramolecular Claisen condensation occurs.



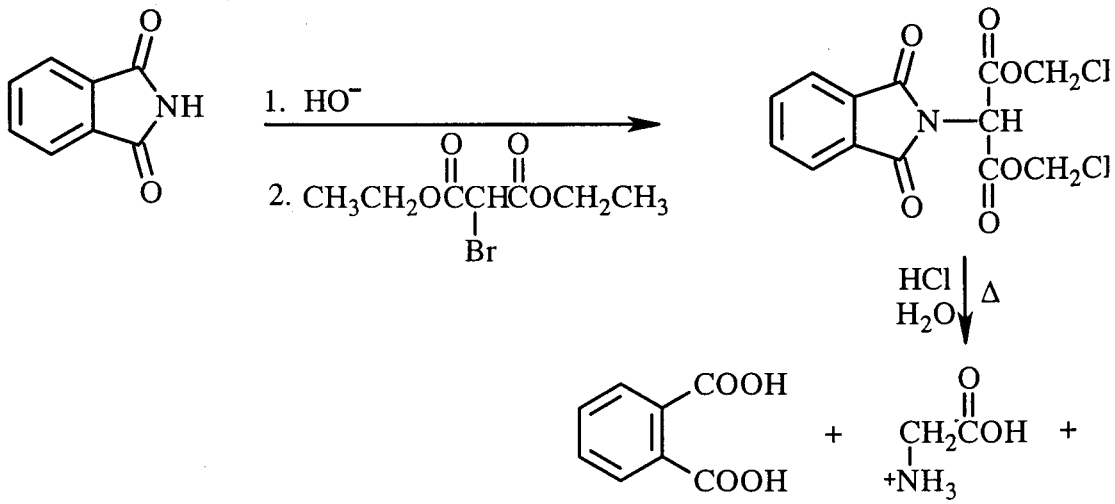
b. The reaction involves two successive aldol condensations.



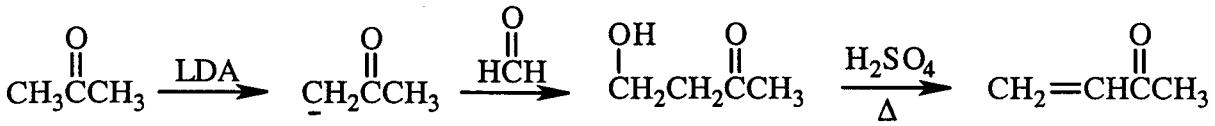
60.

a. $CH_3CH_2COH \xrightarrow[2.\ H_3O^+]{1.\ Br_2,\ PBr_3} CH_3CHCOH \xrightarrow[2.H_3O^+]{\text{excess } 1.\ NH_3} CH_3CHCOH$ (Br; $^+NH_3$)

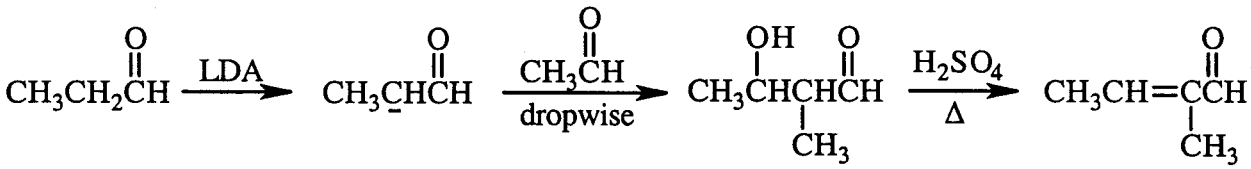
b.



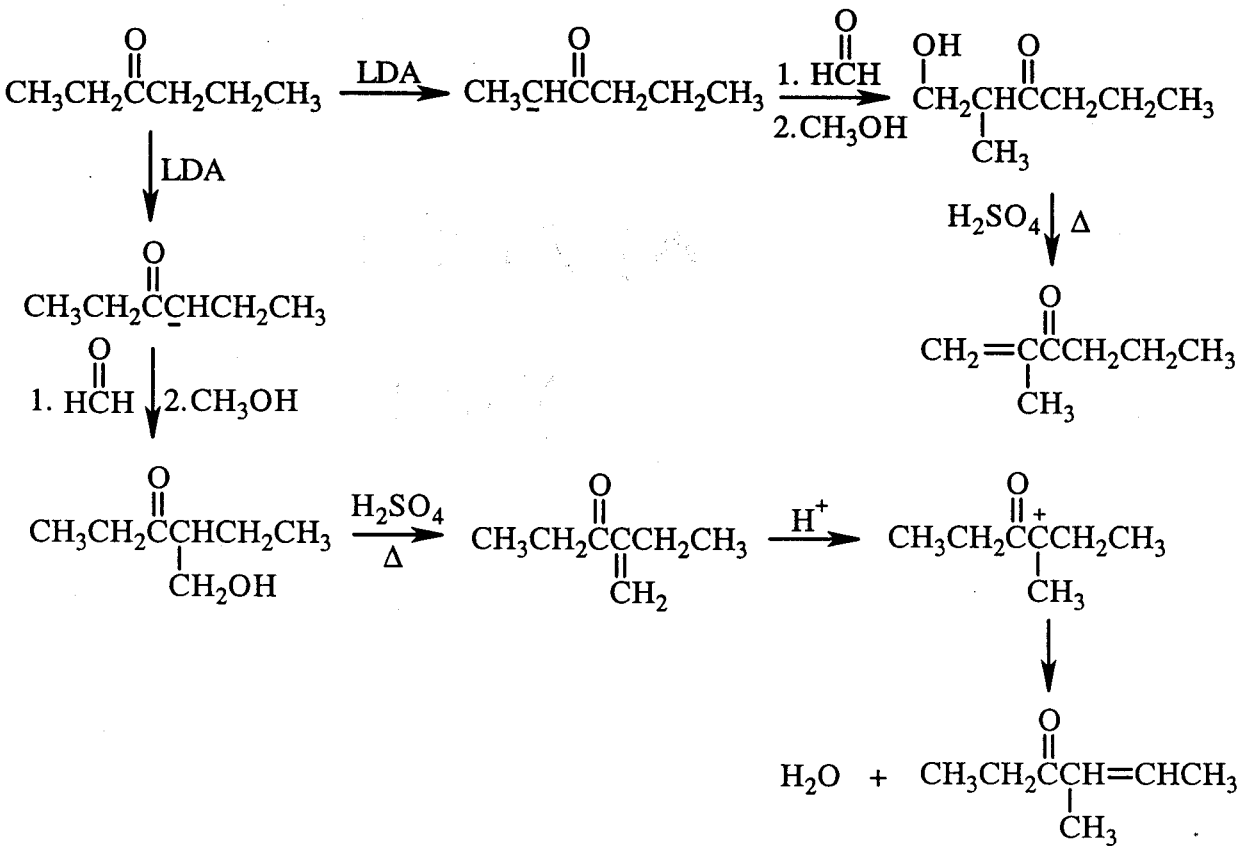
a can be prepared by removing an α-hydrogen from acetone with LDA and then adding formaldehyde, followed by dehydration.



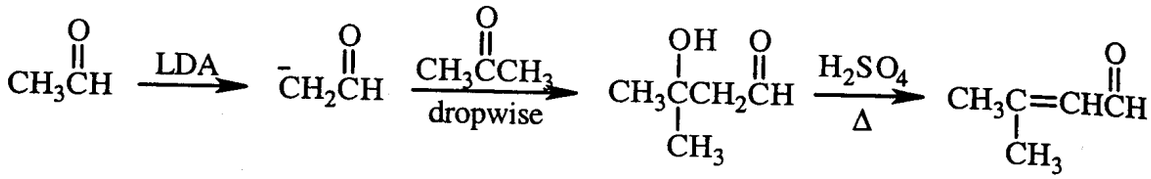
b can be prepared by removing an α-hydrogen from propionaldehyde with LDA and then slowly adding acetaldehyde, followed by dehydration.



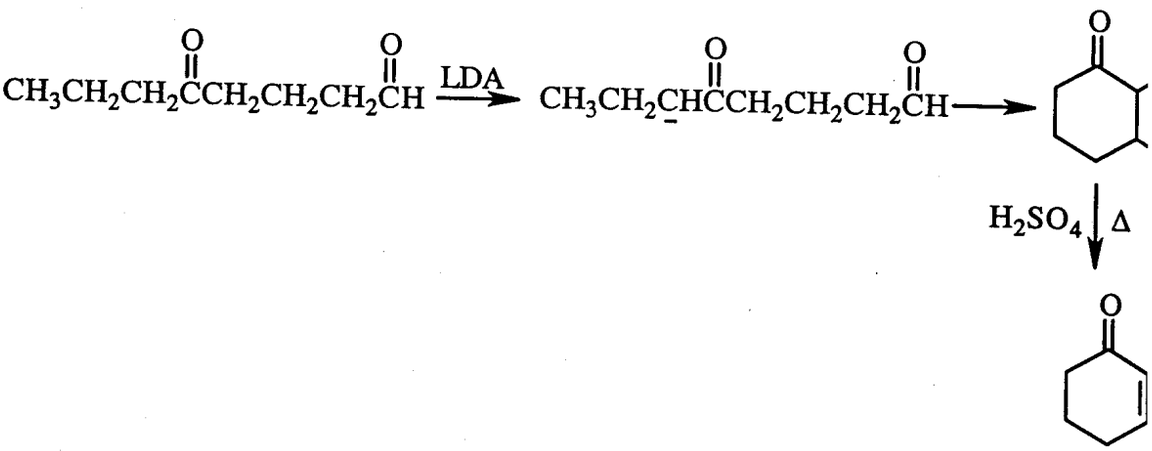
c can be prepared by removing an α-hydrogen from 3-hexanone with LDA and then adding formaldehyde, followed by dehydration. The yield is poor because 3-hexanone is an asymmetrical ketone therefore, two different α-carbanions are formed that lead to two different α,β-unsaturated ketones.



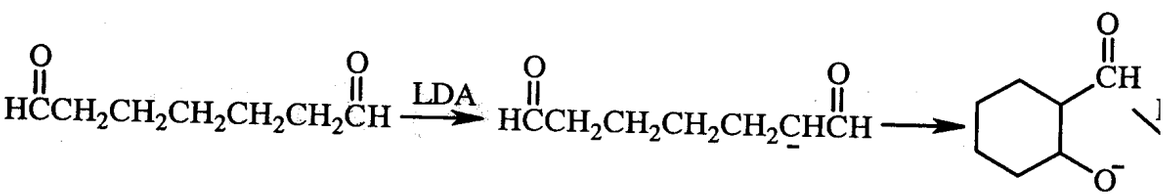
d can be prepared by removing an α-hydrogen from acetaldehyde with LDA and then slo adding acetone, followed by dehydration.



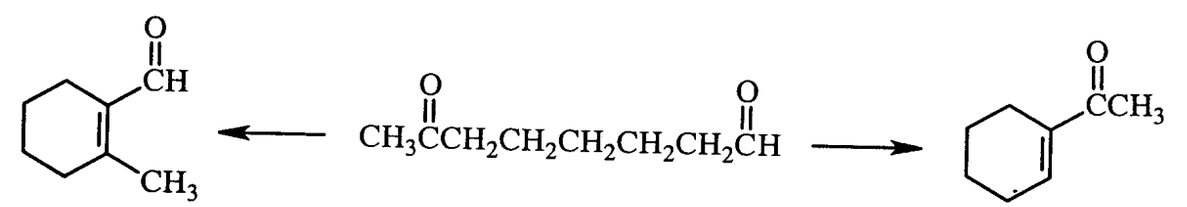
e cannot be prepared by a mixed aldol condensation. It can be prepared via an intramolecu aldol condensation using 5-oxooctanal, followed by dehydration.



f cannot be prepared by a mixed aldol condensation. It can be prepared via an intramolecu aldol condensation using 1,7-heptanedial, followed by dehydration.

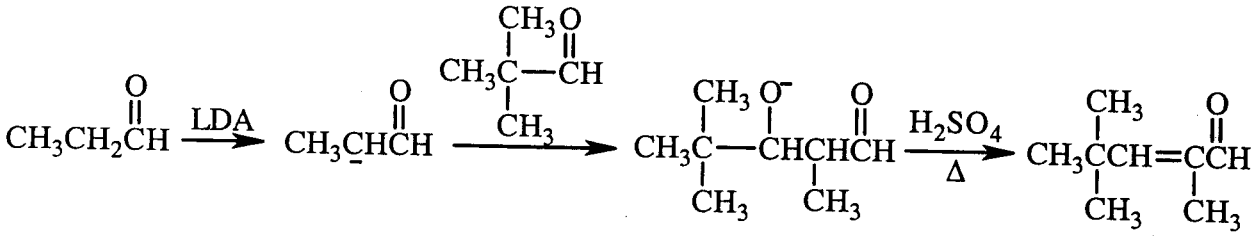


g cannot be prepared by a mixed aldol condensation. A small amount of **g** can be formed v an intramolecular aldol condensation using 7-oxooctanal, but this compound can form two different α-carbanions that can react with a carbonyl group to form a six-membered ring. Because an aldehyde is more reactive than a ketone, the desired compound will be formed as a minor product.

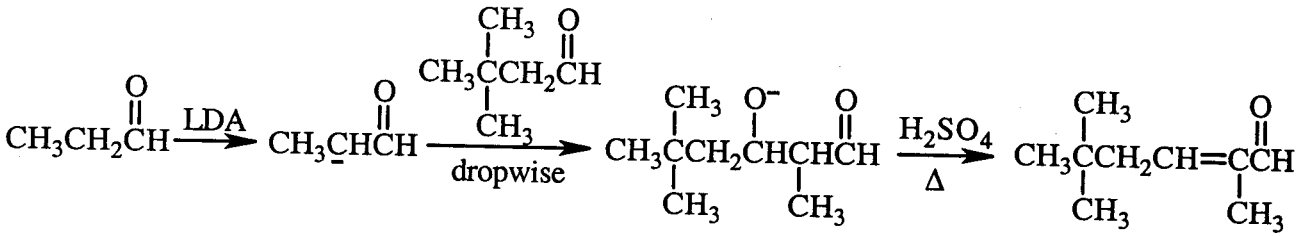


minor product **major product**

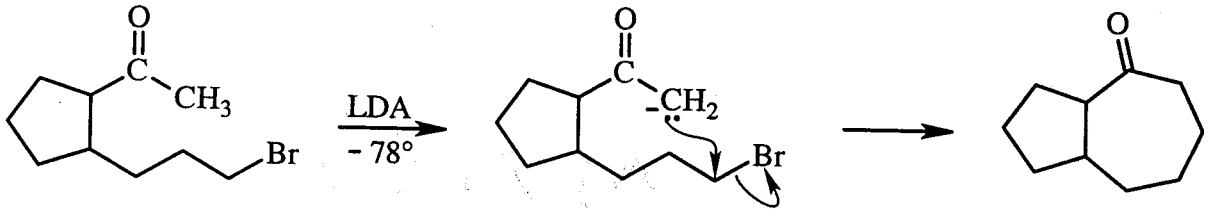
Theoretically **h** can be prepared by a mixed aldol condensation. However, because of steric hindrance, the reaction of propanal with dimethylpropanal to form the desired product would be very slow.



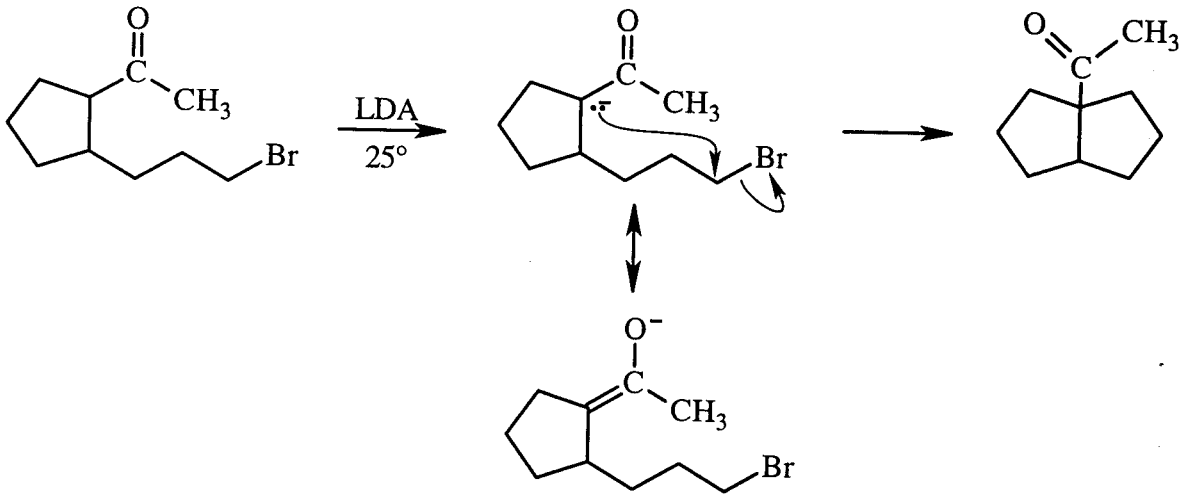
i can be prepared was using propanal and 3,3-dimethylbutanal.



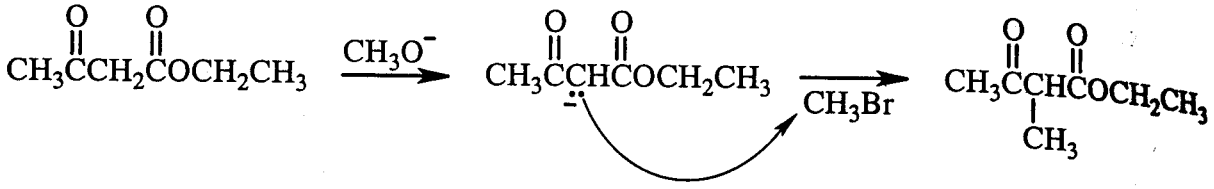
62. At low temperatures (– 78°), the proton will be more apt to be removed from the methyl group because its hydrogens are the most accessible and are slightly more acidic.



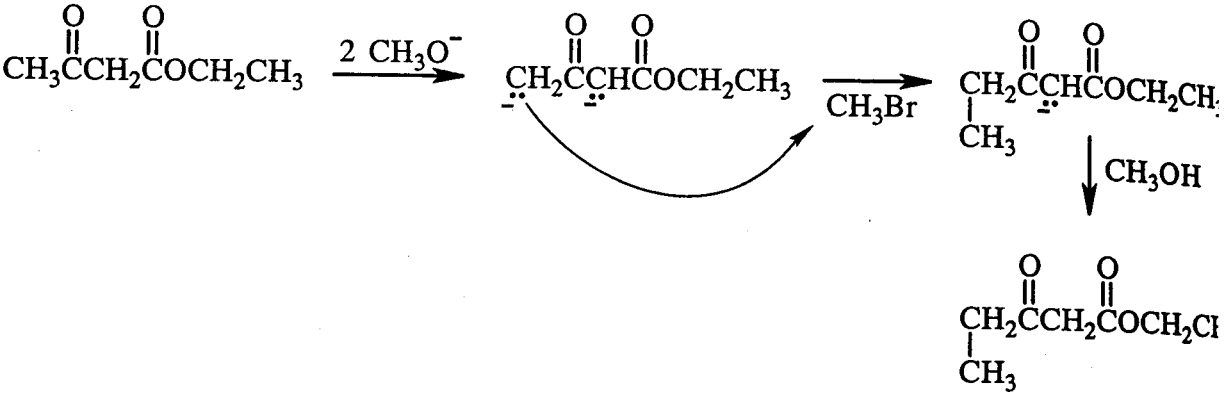
At higher temperatures (25°), the proton will be more apt to be removed from the more substituted α-carbon because in that way the more stable enolate is formed (the one with the more stable double bond).



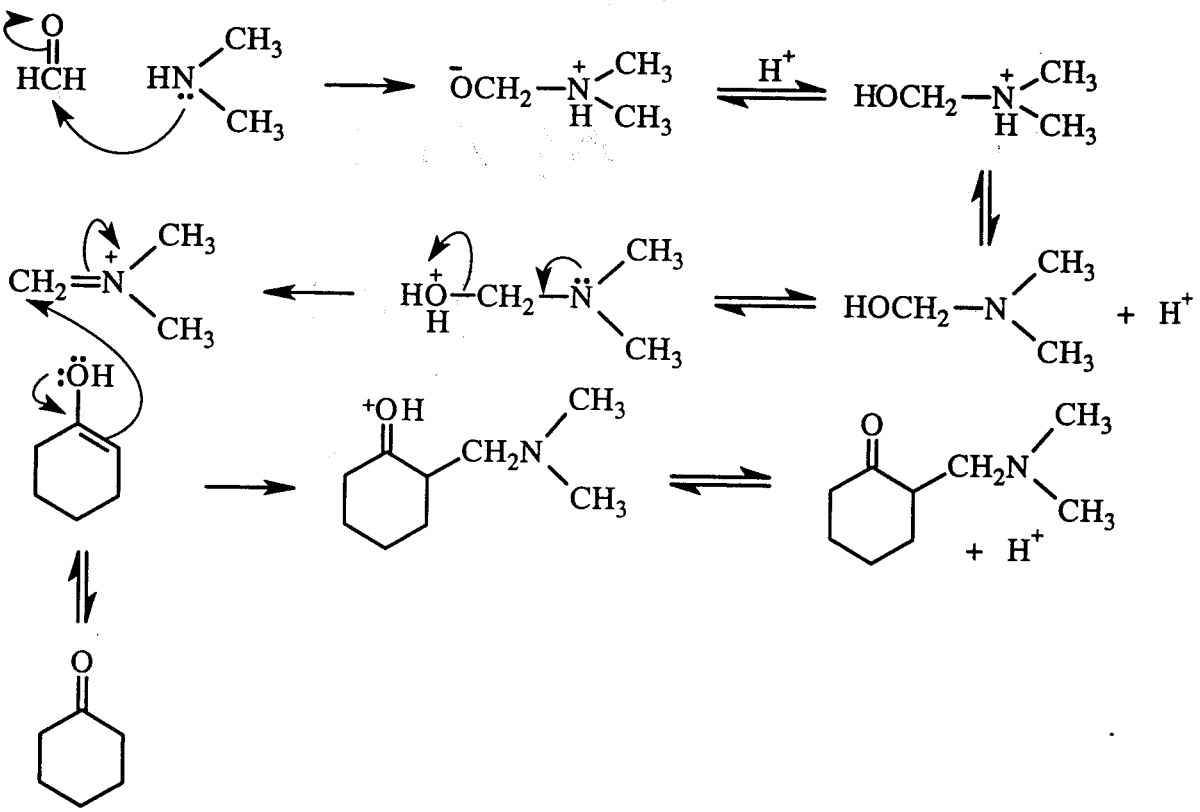
63. The single equivalent of base removes the most acidic proton (from a carbon flanked by two carbonyl groups), and alkylation takes place at that position.



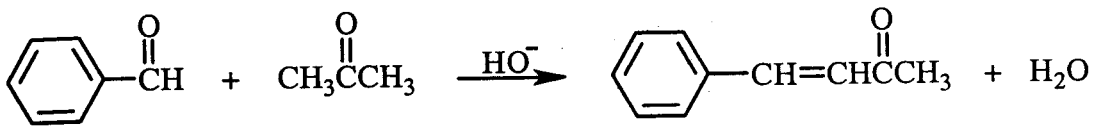
The second equivalent of base removes a proton from the methyl group. Since the methyl group is a weaker acid than the methylene group, the conjugate base of the methyl group is the stronger base and alkylation takes place at that position.



64.

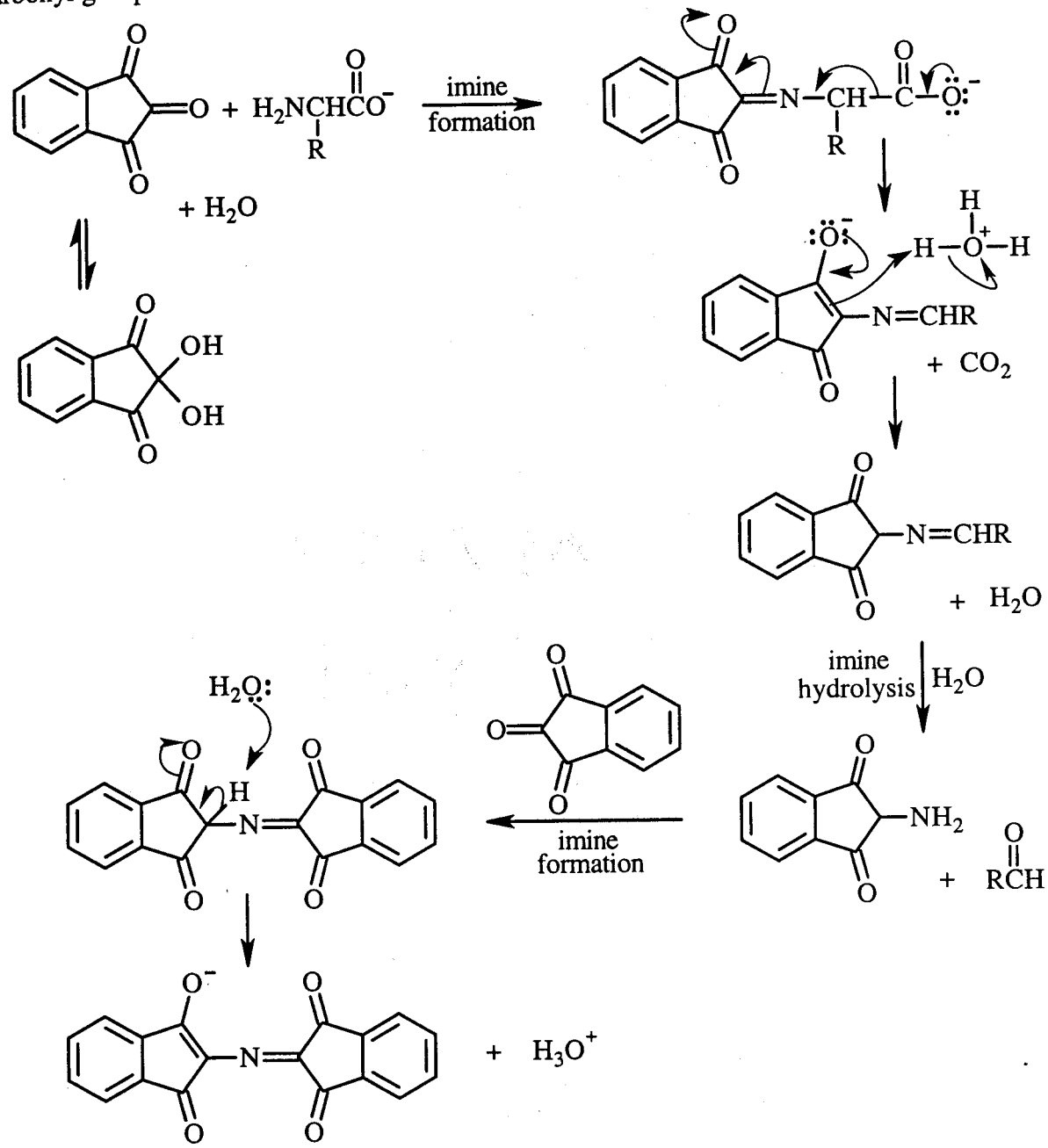


The compound that gives the ^{1}H NMR spectrum is 4-phenyl-3-propen-2-one. The singlet at 2.3 ppm is the methyl group, the doublet at ~ 6.7 ppm and the doublet buried under the benzene ring protons are the hydrogens bonded to the sp^2 carbons. The compounds that would form this compound (via an aldol condensation) are benzaldehyde and acetone.

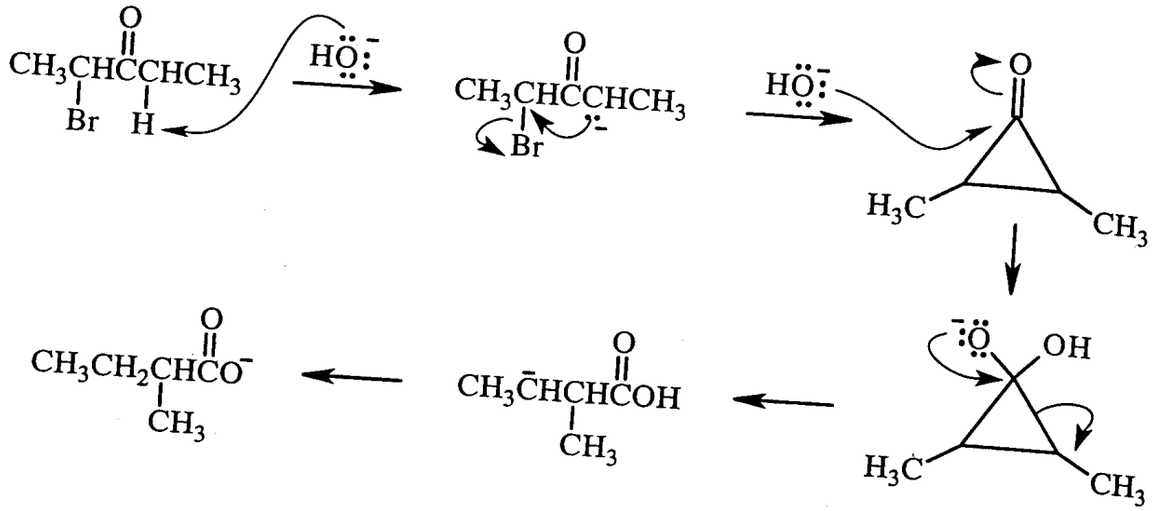


4-phenyl-3-buten-2-one

66. The middle carbonyl group is hydrated because it is stabilized by the electron-withdrawing carbonyl groups on either side of it.

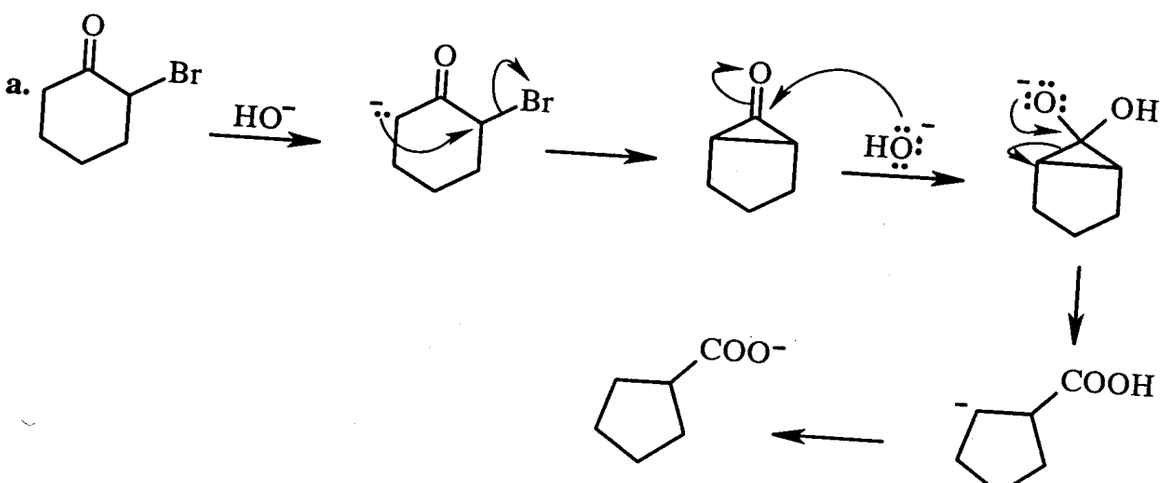


67.

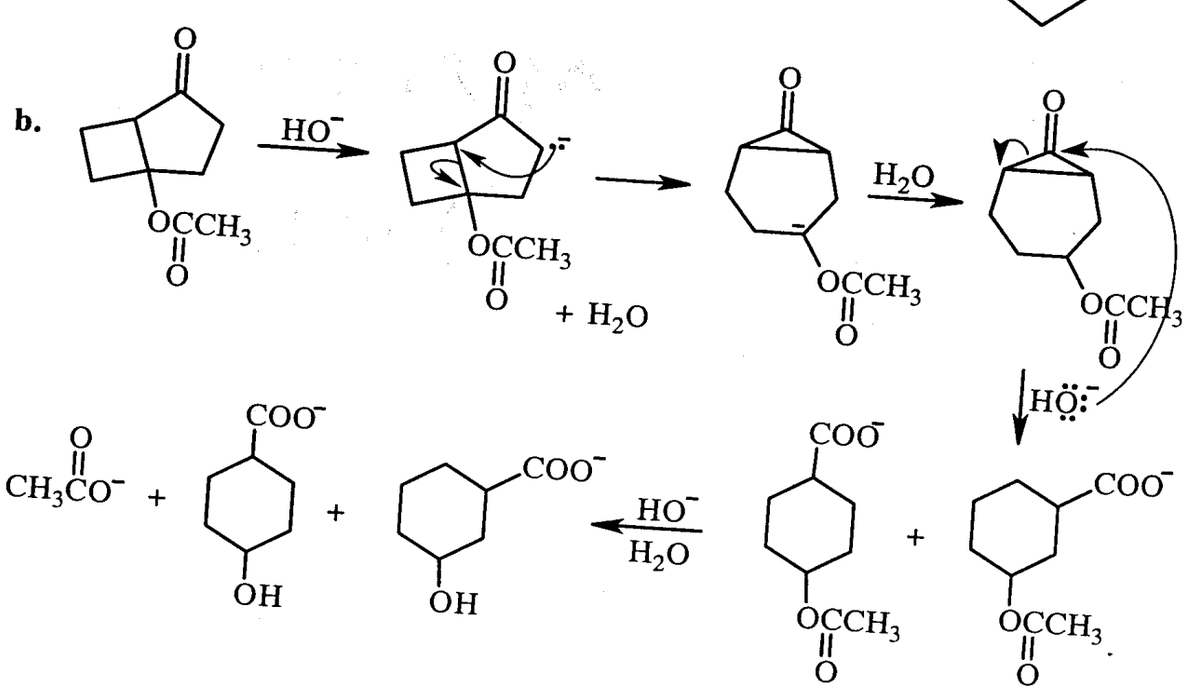


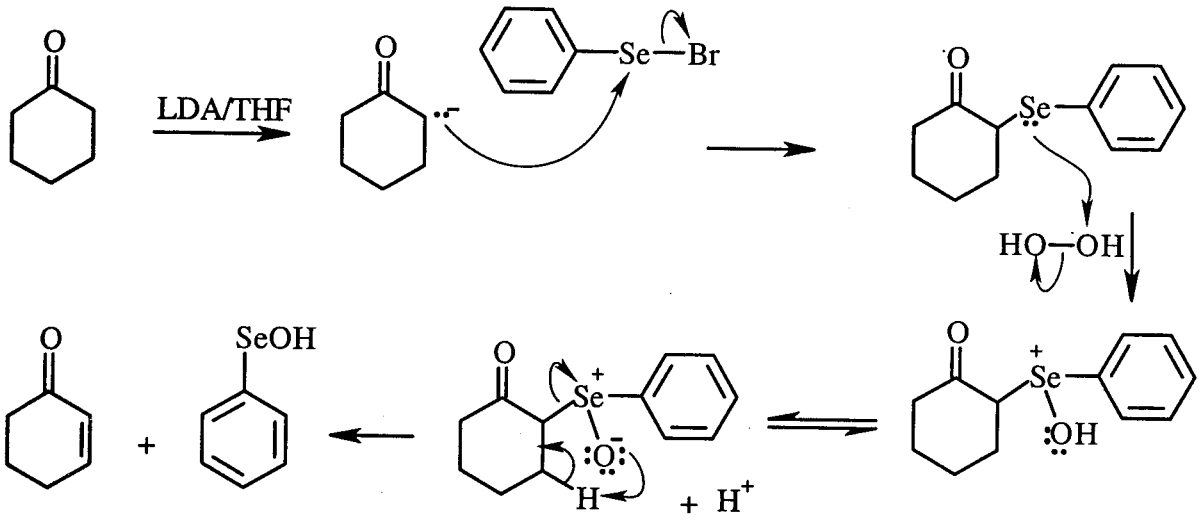
68.

a.



b.





70.

a. $CH_3CH_2OCCH_2COCH_2CH_3$ $\xrightarrow[2.\ Br(CH_2)_5Br]{1.\ CH_3CH_2O^-}$ $CH_3CH_2OCCH(CH_2CH_2CH_2CH_2CH_2Br)COCH_2CH_3$

$\xrightarrow{CH_3CH_2O^-}$

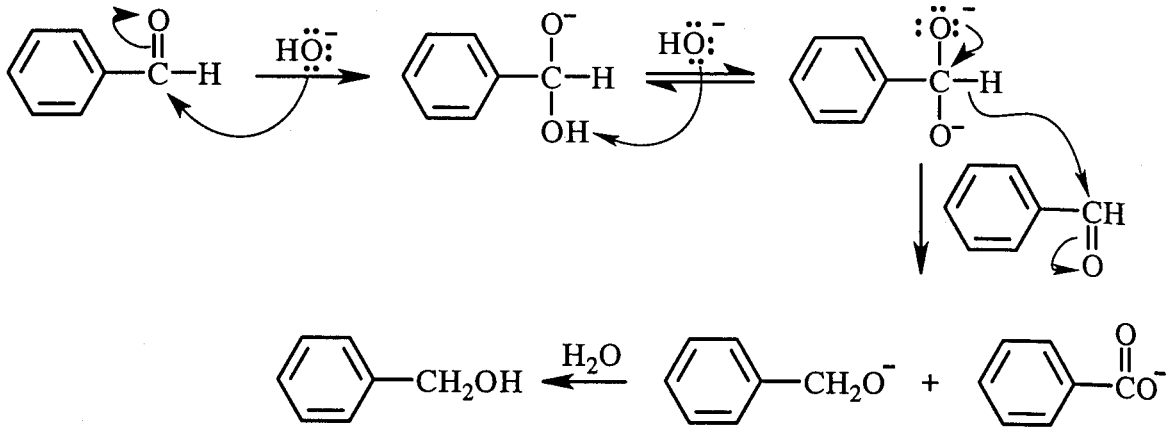
$\xrightarrow[\Delta]{HCl,\ H_2O}$ $C_6H_{10}(COH)_2$

b. $CH_3CH_2OCCH_2COCH_2CH_3$ $\xrightarrow[2.\ Br(CH_2)_5Br]{1.\ CH_3CH_2O^-}$ $CH_3CH_2OCCH(CH_2CH_2CH_2CH_2CH_2Br)COCH_2CH_3$

$\xrightarrow[CH_3CH_2O^-]{\text{malonic ester}}$

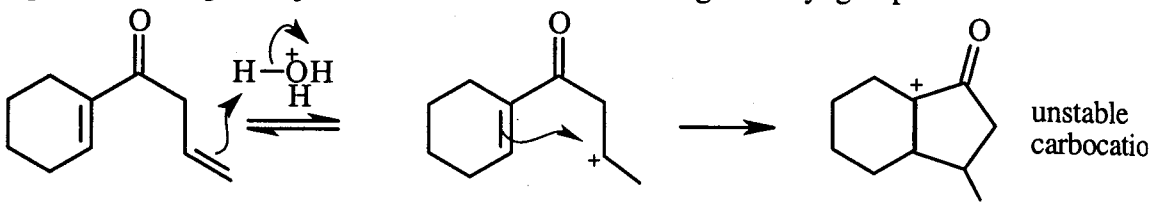
$\xrightarrow[\Delta]{HCl,\ H_2O}$ $HOCCH_2CH_2CH_2CH_2CH_2CH_2CH_2COH$

71.

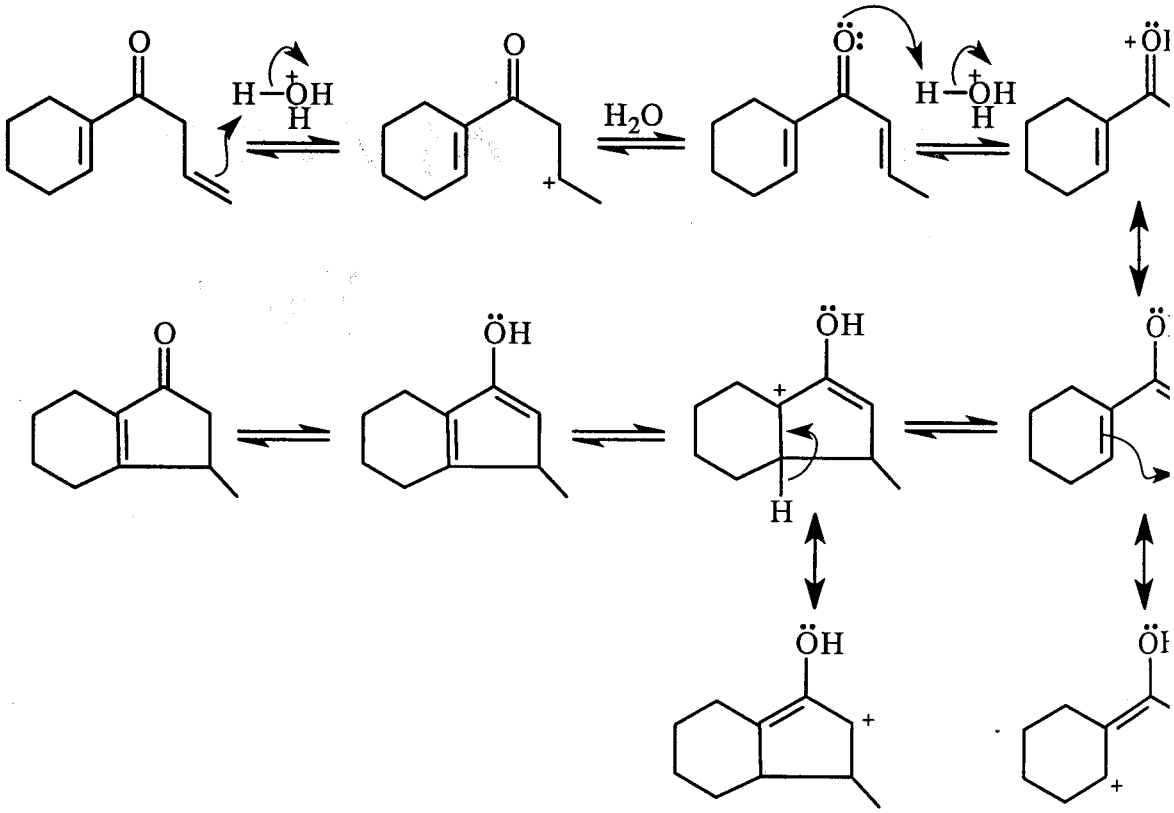


72. **a.** Generally the carbonyl group is the group that is protonated, but this does not lead a productive reaction.

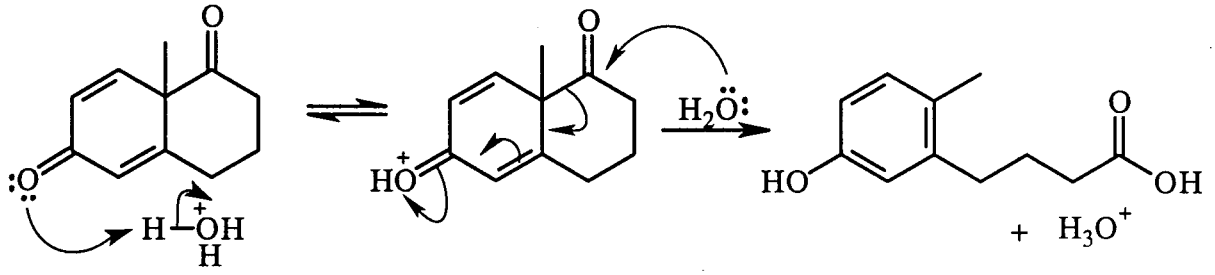
The most obvious way to work out the mechanism leads to an unstable carbocation, since the positive chanrge is adjacent to an electron-withdrawing carbonyl group.



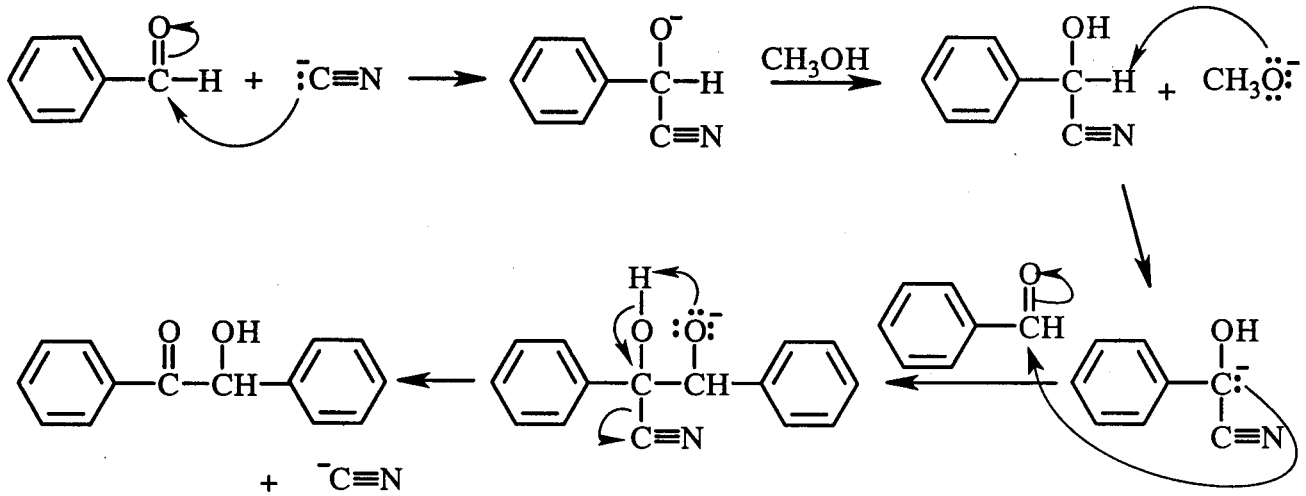
The following mechanism avoids the formation of the unstable carbocation.



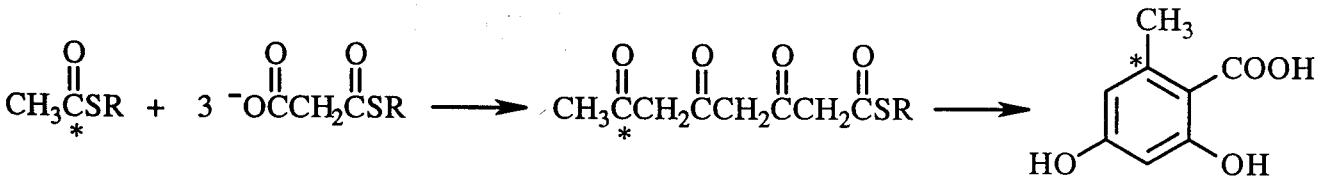
b. The carbonyl group on the left is protonated because electron delocalization causes it to be more basic than the other carbonyl group.



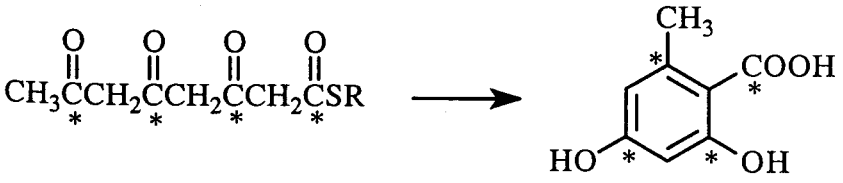
73. Hydroxide ion cannot be used in place of cyanide ion because the aldehydic hydrogen cannot be removed unless the electrons left behind can be delocalized onto an electronegative atom. The nitrogen of the cyano group serves that purpose.



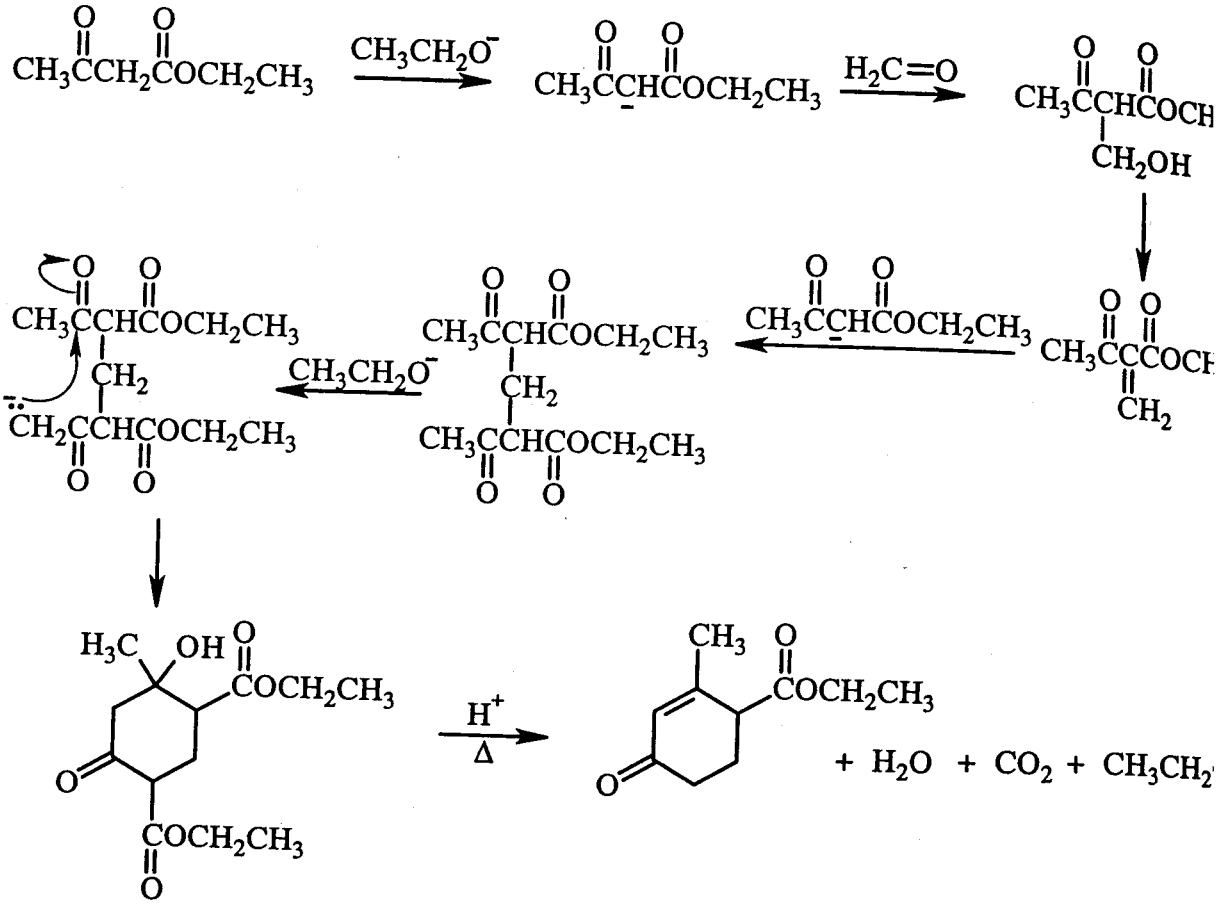
74. To arrive at the final product, three equivalents of malonyl thioester are needed. (See page 828 in the text.)



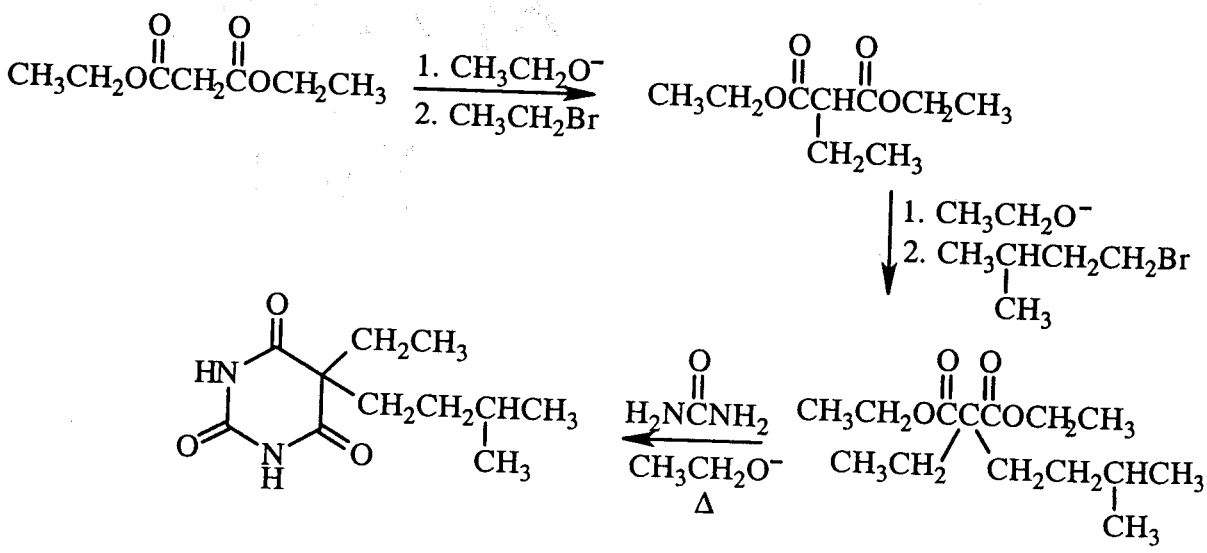
In Chapter 25, you will see that malonyl thioester is synthesized from acetyl thioester. So if the lichen is not fed unlabeled malonyl thioester, its malonyl thioester will also be labeled, and the product will have labels in the indicated positions.



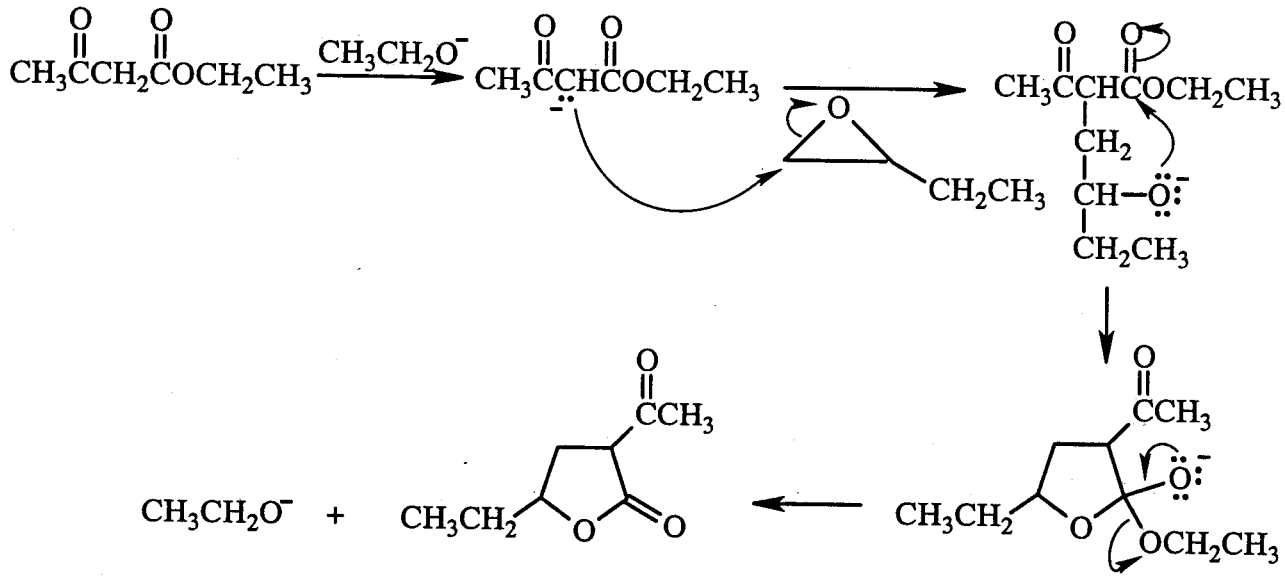
75.



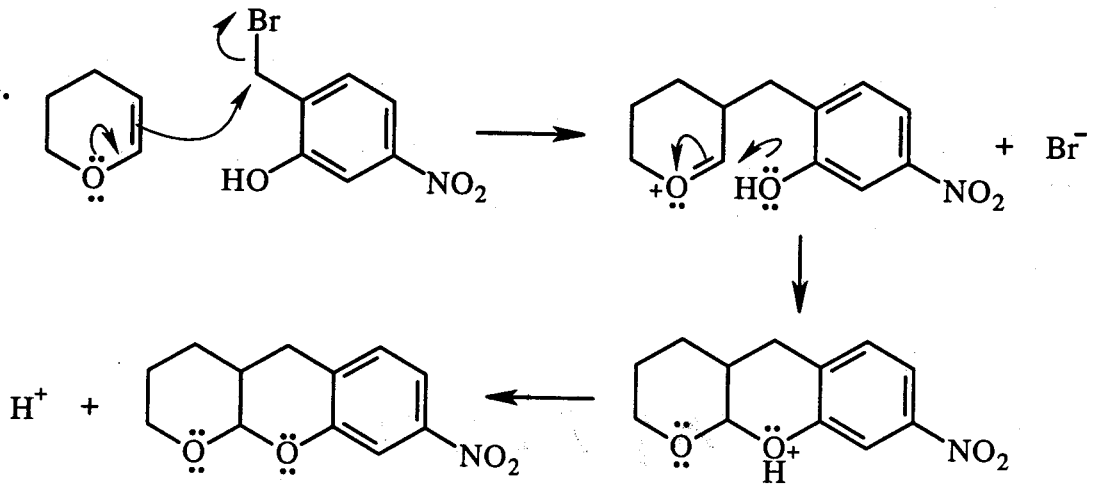
76.



a.

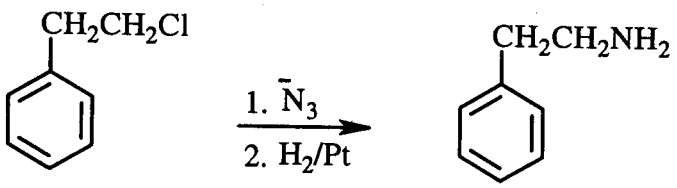


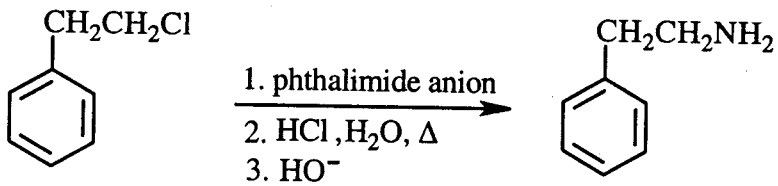
b.



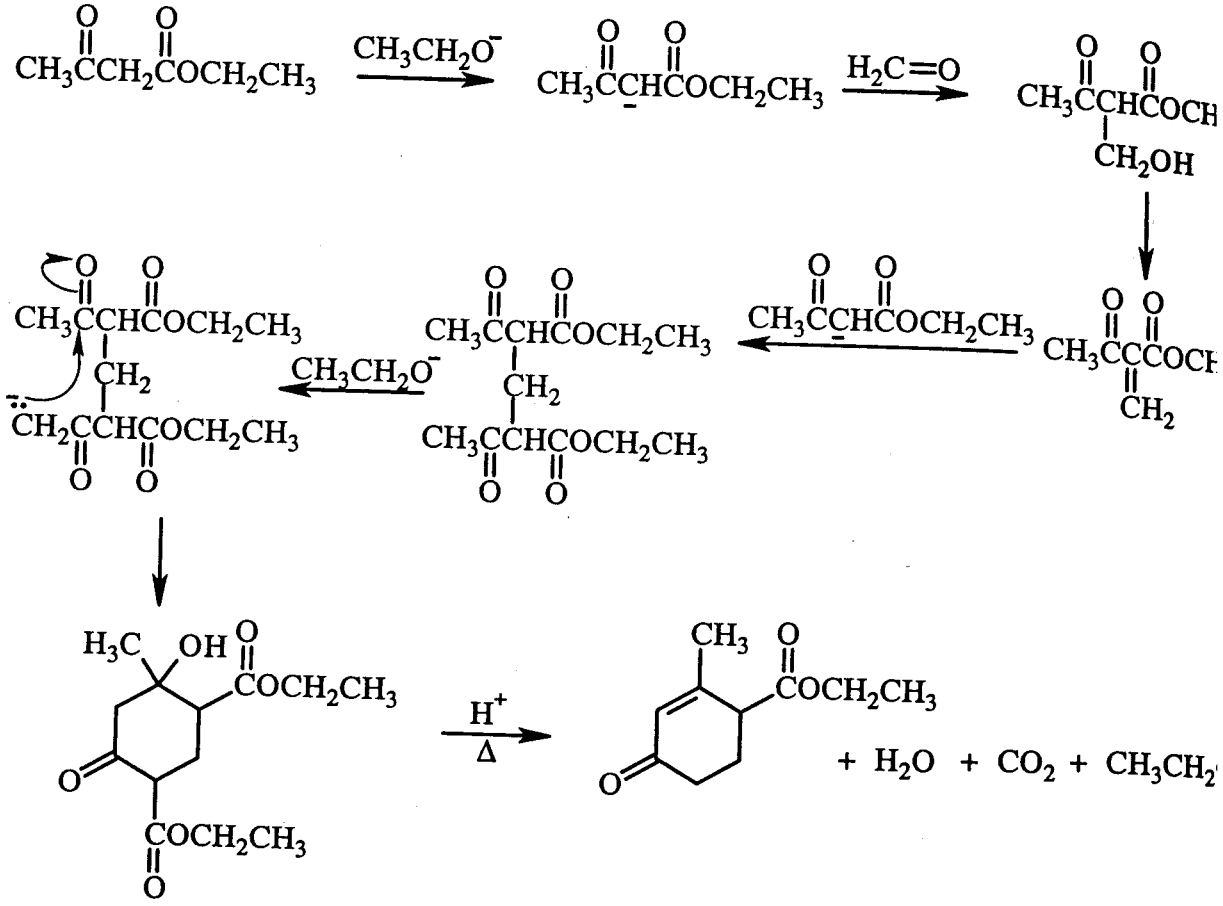
78.

a.

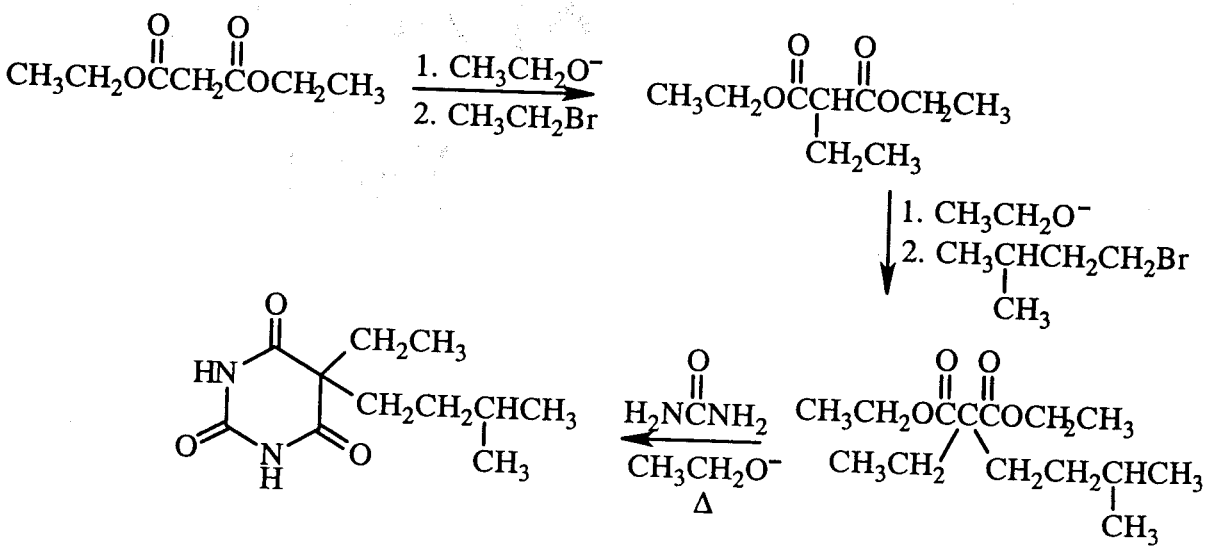




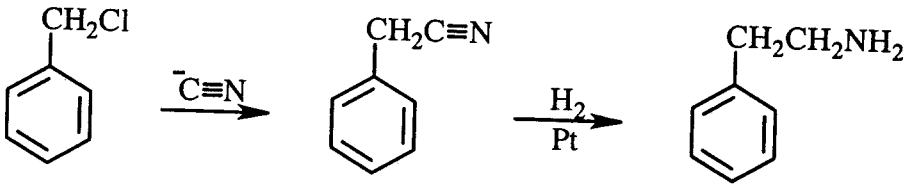
75.



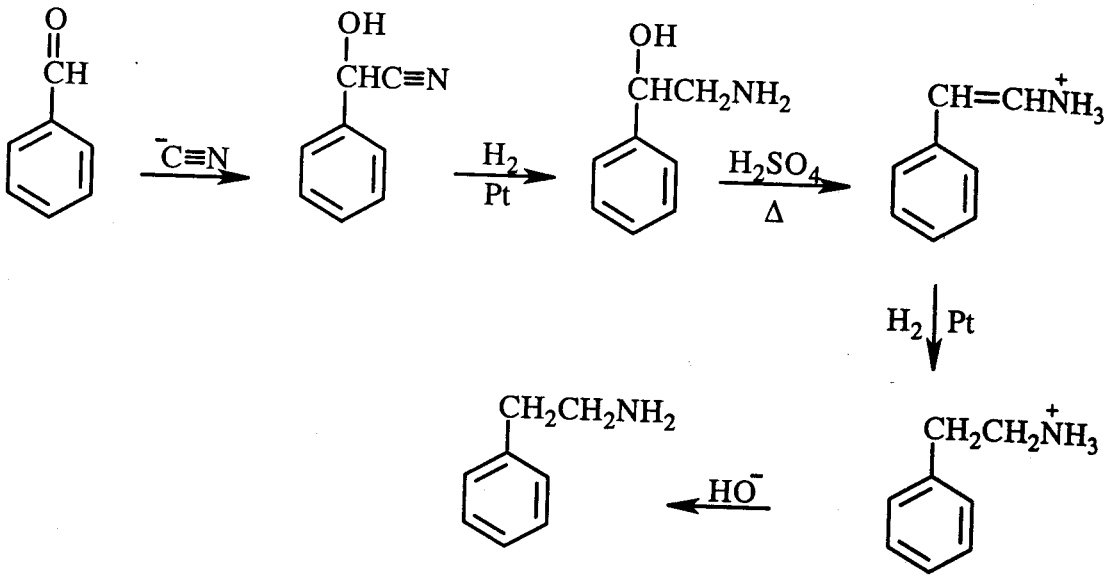
76.



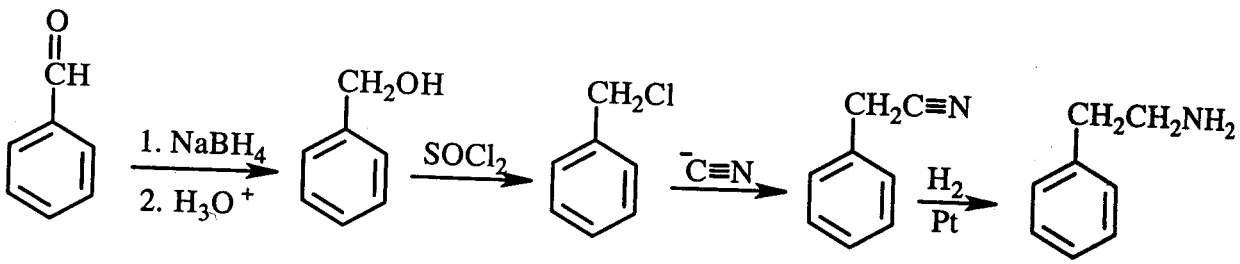
b.


CH2Cl
⁻C≡N
CH2C≡N
H2
Pt
CH2CH2NH2

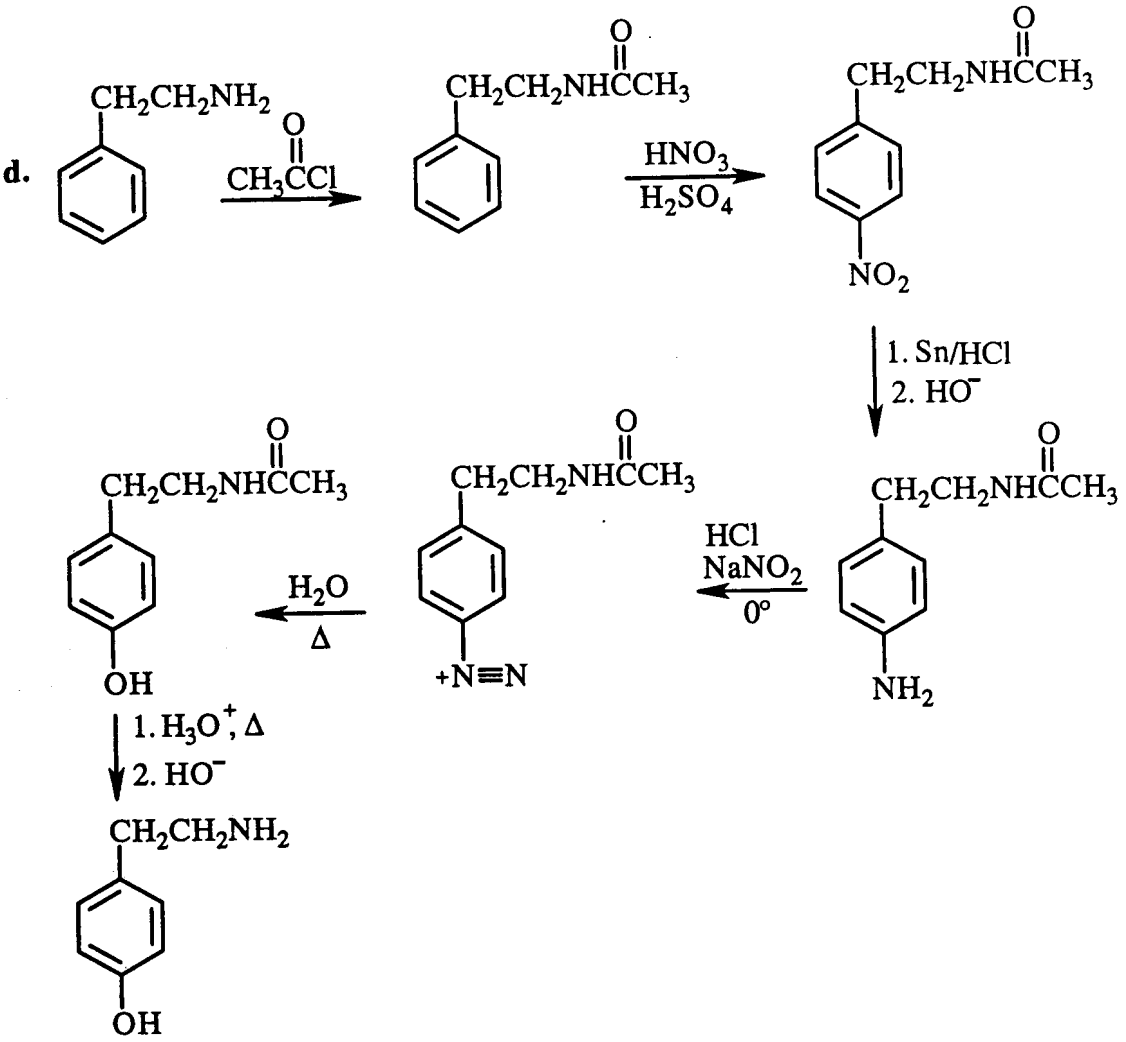
c.


O
CH
⁻C≡N
OH
CHC≡N
H2
Pt
OH
CHCH2NH2
H2SO4
Δ
CH=CHNH3
H2
Pt
CH2CH2NH2
CH2CH2NH3
HO⁻

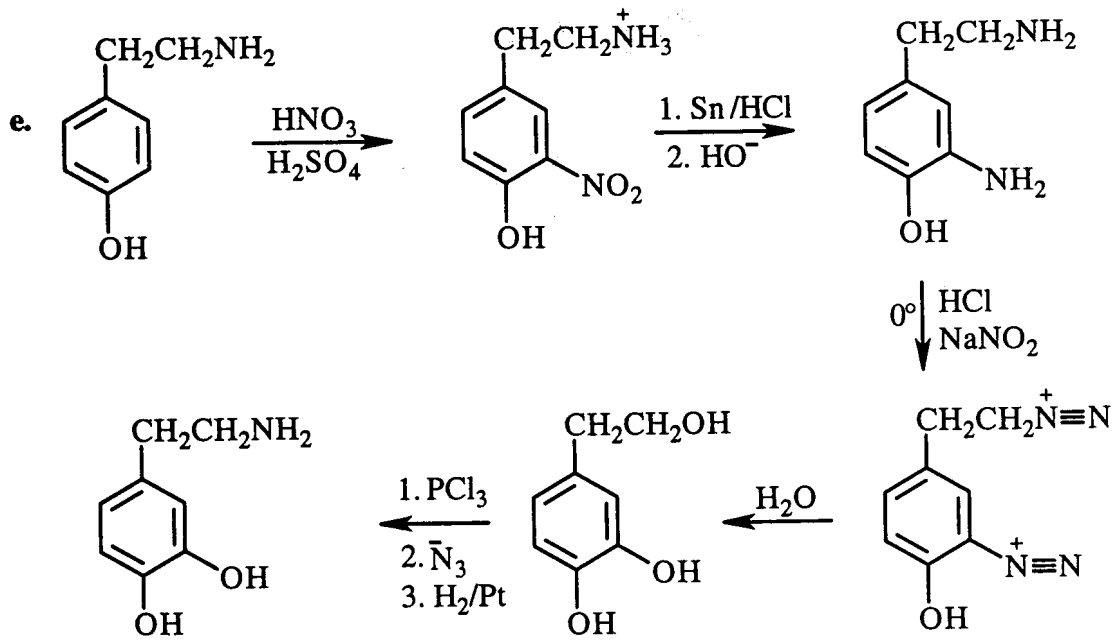
or


O
CH
1. NaBH4
2. H3O+
CH2OH
SOCl2
CH2Cl
⁻C≡N
CH2C≡N
H2
Pt
CH2CH2NH2

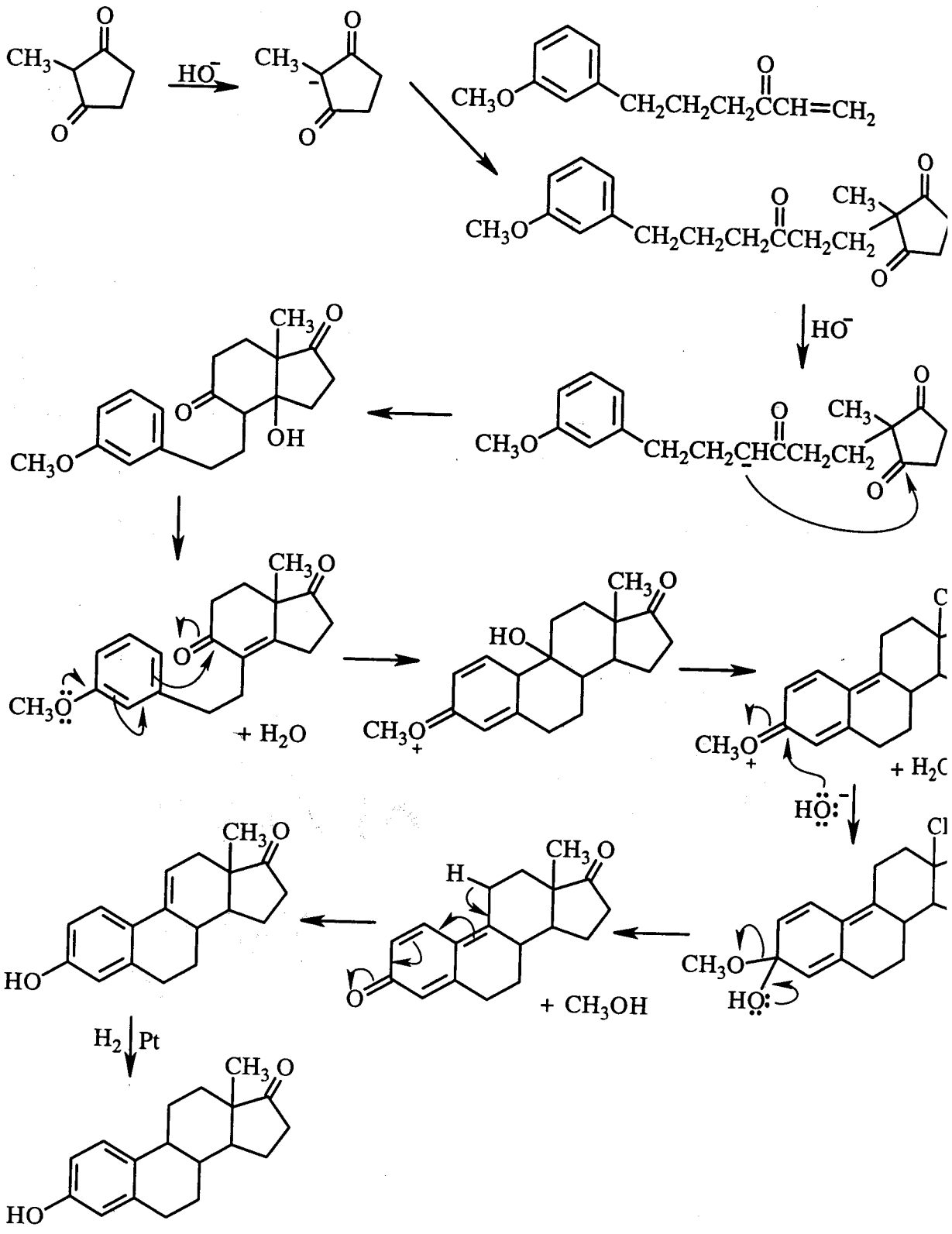
d.


CH2CH2NH2
CH3CCl
O
CH2CH2NHCCH3
HNO3
H2SO4
NO2
1. Sn/HCl
2. HO⁻
NH2
HCl
NaNO2
0°
+N≡N
H2O
Δ
OH
1. H3O⁺, Δ
2. HO⁻

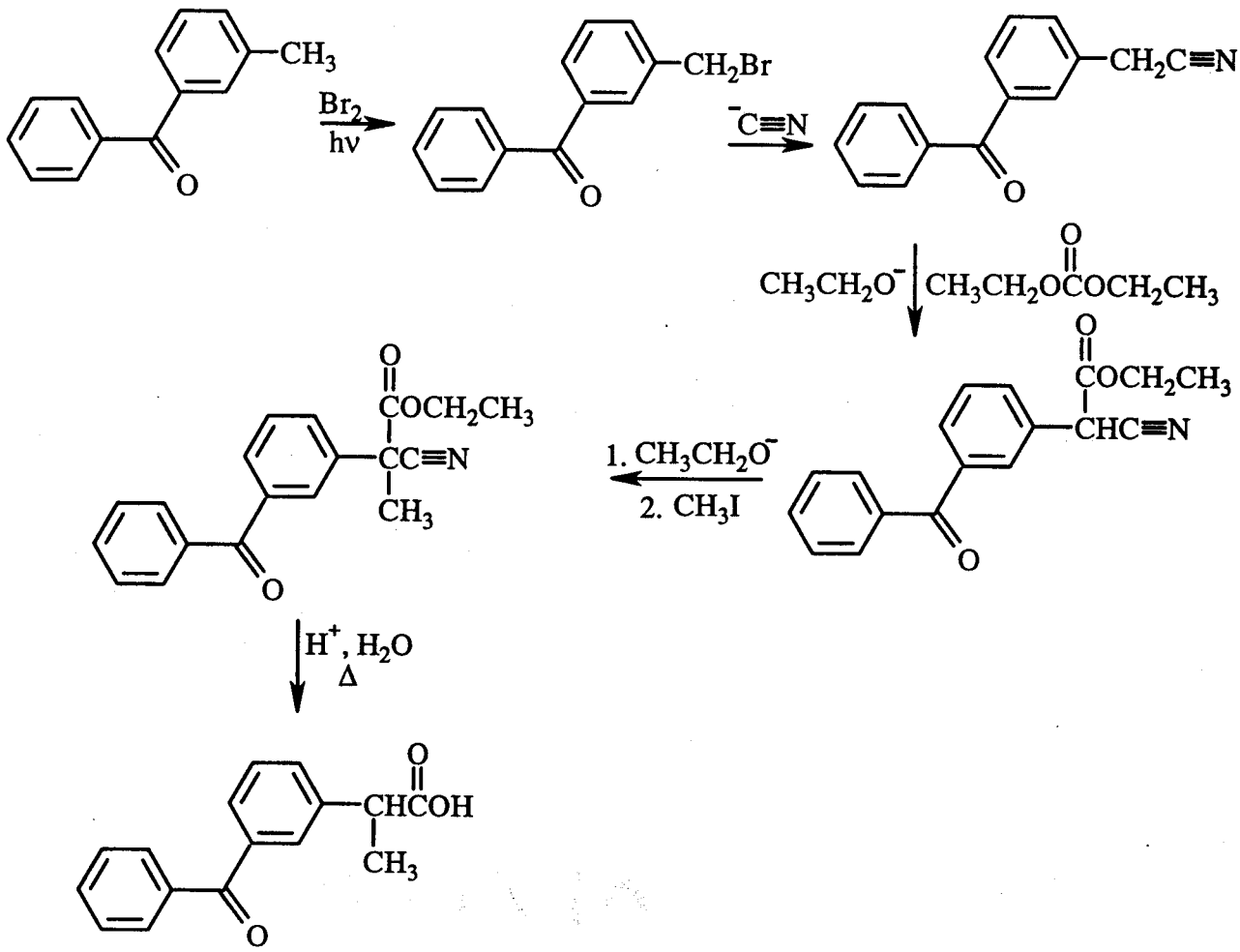
e.


CH2CH2NH2
HNO3
H2SO4
CH2CH2NH3⁺
NO2
OH
1. Sn/HCl
2. HO⁻
NH2
0°
HCl
NaNO2
CH2CH2N≡N⁺
1. PCl3
2. N3⁻
3. H2/Pt
H2O
CH2CH2OH

79.

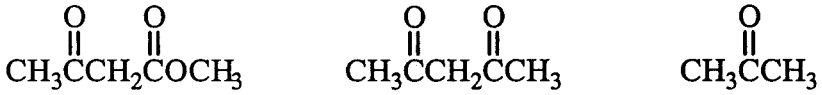

CH3
HO-
CH3O
CH2CH2CH2CCH=CH2
CH3
CH2CH2CH2CCH2CH2
HO-
OH
CH3O
CH2CH2CHCCH2CH2
+ H2O
HO
+ H2O
HO:-
+ CH3OH
H
HO
H2
Pt
HO

80. The substituent in ibuprofen is placed on the ring by a Friedel-Crafts acylation reaction. A Friedel-Crafts reaction cannot be done in the synthesis of ketoprofen because the benzene rings are deactivated and deactivated rings cannot undergo Friedel-Crafts reactions.



Chapter 19 Practice Test

1. Rank the following compounds in order of decreasing acidity. (Label the most acidic #1.)

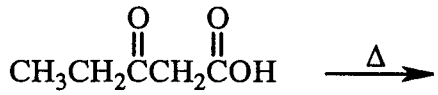


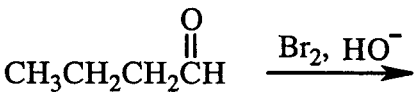
2. Give a structure for each of the following:

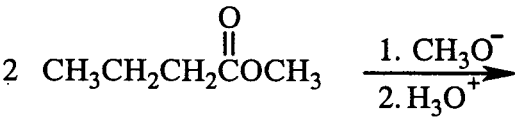
a. the most stable enol tautomer of 2,4-pentanedione

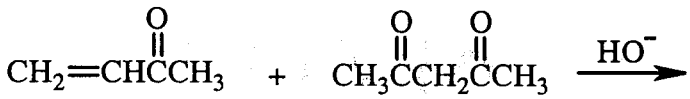
b. a β-keto ester

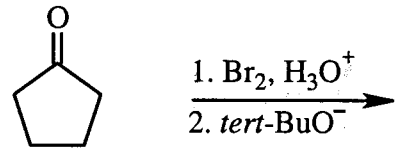
3. Give the product of each of the following reactions.

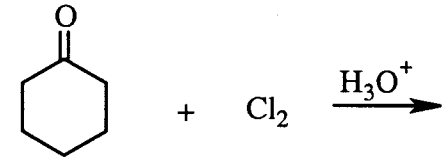
a. 

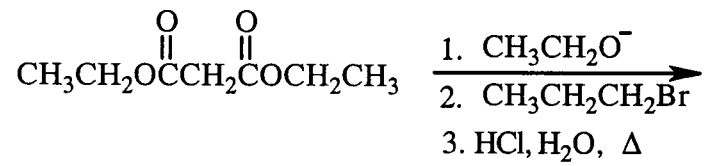
b. 

c. 

d. 

e. 

f. 

g. 

4. Give an example of each of the following:

a. an aldol addition

b. an aldol condensation

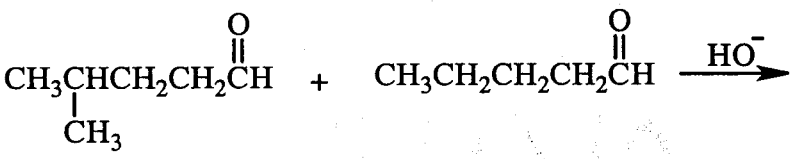
c. a Claisen condensation

d. a Dieckmann condensation

e. a malonic ester synthesis

f. an acetoacetic ester synthesis

5. Give the products of the following crossed aldol addition:



CHAPTER 20
More About Oxidation-Reduction Reactions

Important Terms

Baeyer-Villiger oxidation	oxidation of aldehydes or ketones with H_2O_2 to form carboxylic acids o esters, respectively.
catalytic hydrogenation	addition of hydrogen to a double or triple bond in the presence of a met catalyst.
chemoselective reaction	a reaction in which a reagent reacts with one functional group in prefere to another.
dissolving metal reduction	a reduction using sodium or lithium metal dissolved in liquid ammonia.
enantioselective reaction	a reaction that forms an excess of one enantiomer.
epoxidation	formation of an epoxide.
functional group interconversion	a reaction that converts one functional group into another.
glycol	a compound containing two or more OH groups.
metal hydride reduction	a reduction using a metal-containing reagent that delivers a hydride ion.
molozonide	an unstable intermediate containing a five-membered ring with three oxygens in a row that is formed from the reaction of an alkene with ozo
oxidation	loss of electrons by an atom or molecule.
oxidation-reduction reaction	a reaction that involves the transfer of electrons from one atom or mole to another.
oxidation state	the oxidation state of a carbon is given by the number of C—Z bonds, where Z = oxygen, nitrogen, or halogen.
oxidative cleavage	an oxidation reaction that cleaves the reactant into two or more compou
oxidizing agent	the compound that is reduced in a redox reaction as it oxidizes the othe compound.
ozonide	a five-membered ring compound formed as a result of rearrangement o molozonide.
ozonolysis	reaction of a carbon-carbon double or triple bond with ozone.
peroxyacid	a carboxylic acid with an OOH group instead of an OH group.
redox reaction	an oxidation-reduction reaction.
reducing agent	the compound that is oxdized in a redox reaction as it reduces the othe compound.

reduction	gain of electrons by an atom or molecule.
Rosenmund reduction	the reduction of an acyl chloride to an aldehyde using H_2/Lindlar catalyst.
Swern oxidation	uses dimethyl sulfoxide, oxalyl chloride, and triethylamime to oxidize primary alcohols to aldehydes and secondary alcohols to ketones.
Tollens test	a test to determine the presence of an aldehyde. A positive result is indicated by the formation of a silver mirror.
vicinal diol (vicinal glycol)	a 1,2-diol.

Solutions to Problems

1.

a. reduction

b. neither

c. oxidation

d. oxidation

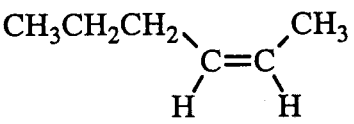
e. reduction

f. neither

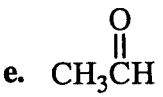
2.

a. $CH_3CH_2CH_2CH_2CH_2OH$

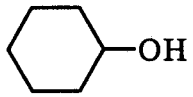
b. $CH_3CH_2CH_2CH_2NH_2$

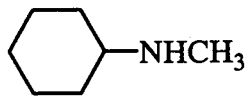
c. 

d. no reaction

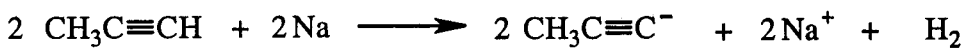
e. 

f. CH_3CH_2OH

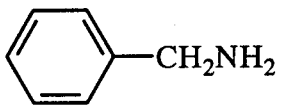
g. 

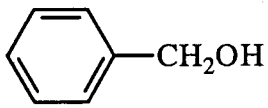
h. 

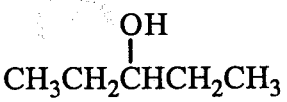
3. A terminal alkyne cannot be reduced by Na, because Na donates an electron to the terminal *sp* carbon, causing a hydrogen atom to be removed.

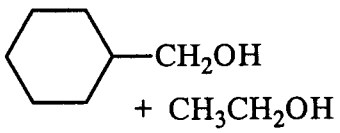


4.

a. 

b. 

c. 

d. 

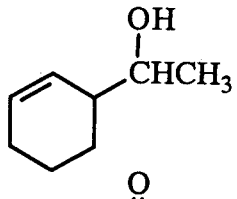
e. $CH_2CH_2CH_2NHCH_2CH_3$

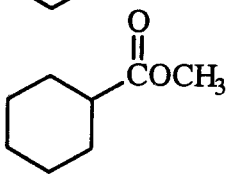
f. $CH_3CH_2CH_2CH_2OH$

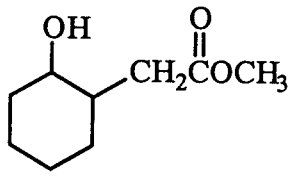
5. Carbon-nitrogen double and triple bonds can be reduced by $LiAlH_4$ because the bonds are pol
The hydride ion will be attracted to the partially positively charged carbon.

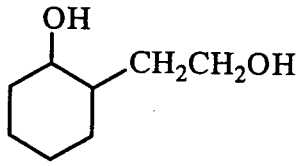


6.

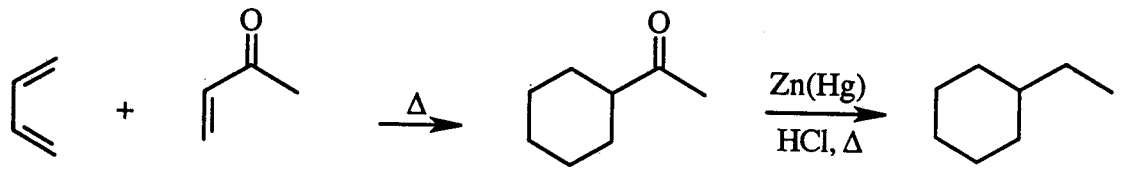
a. 

b. 

c. 

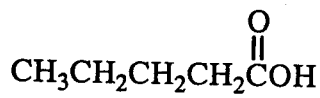
d. 

7. **a.** solved in the text.

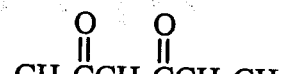
b. 

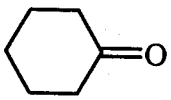
8.

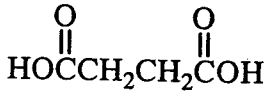
a. **1.** 

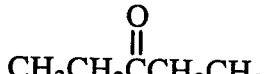
2. 

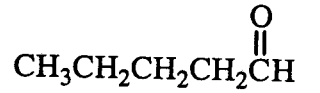
3. A tertiary alcohol is not oxdized to a carbonyl compound.

4. 

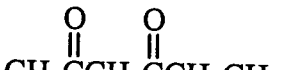
5. 

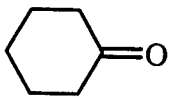
6. 

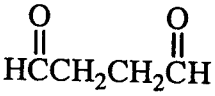
b. **1.** 

2. 

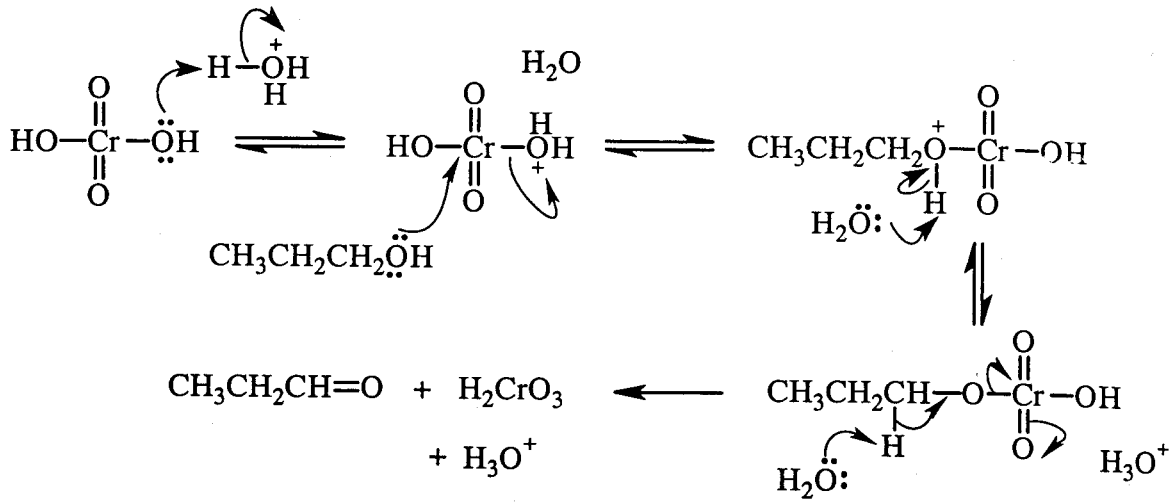
3. A tertiary alcohol is not oxdized to a carbonyl compound.

4. 

5. 

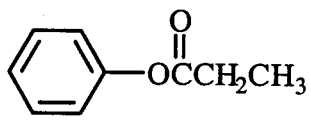
6. 

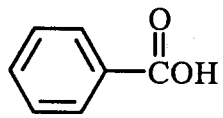
9. Chromic acid needs to be protonated to convert a poor leaving group (^-OH) into a good leaving group (H_2O). The alcohol displaces water to form a protonated chromate ester, which loses a proton. The aldehyde is then formed in an elimination reaction.

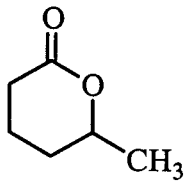


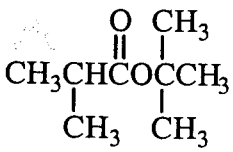
10. Solved in the text.

11.

a. 

b. 

c. 

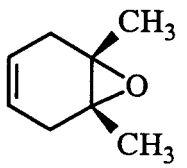
d. 

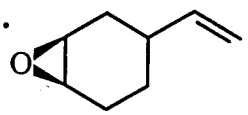
e. 

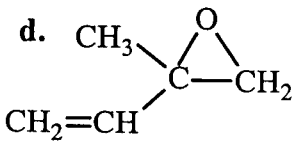
f. no reaction

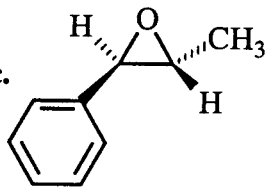
12. **a.** cyclohexene **b.** 1-butene **c.** *trans*-2-pentene **d.** *cis*-2-pentene

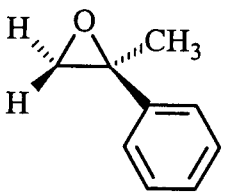
13.

a. 

b. 

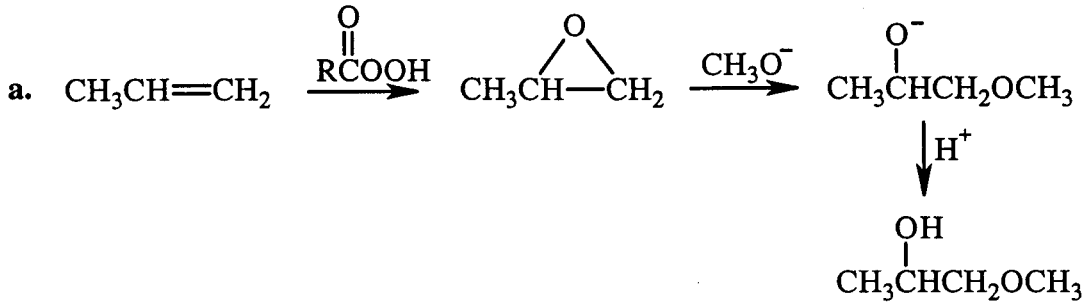
d. 

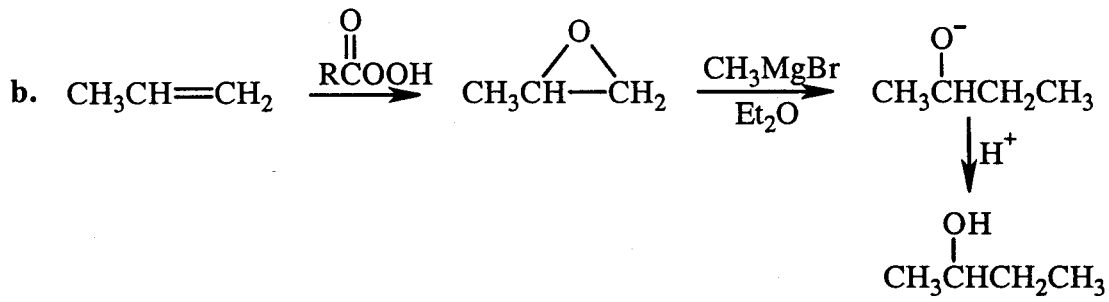
c. 

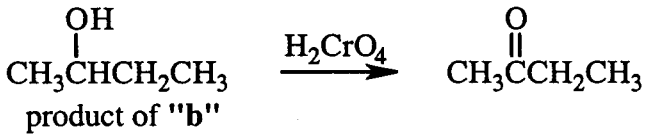


The reaction forms a product with two new asymmetric carbons. Because only syn addition occurs, only two of the four possible stereoisomers are formed.

14.

a. 

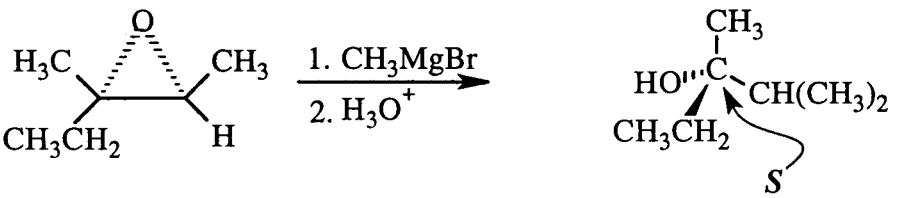
b. 

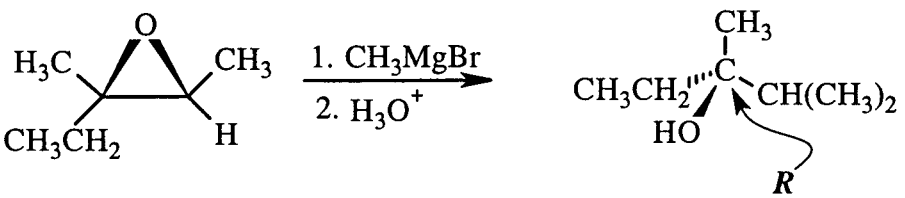
c. 
product of "b"

15. The bromonium ion is much less stable than an epoxide, because the C—Br bond of a bromonium ion is a much weaker bond than the C—O bond of an epoxide, and a weaker bond is easier to break.

The difference in the strength of the bonds can be understood by comparing the pK_a of HBr (– 9) and the pK_a of an alcohol such as CH_3OH (15.5). Thus, HBr is a much stronger acid than CH_3OH, which means that Br^- is a much weaker base than $^-OCH_3$. Being a weaker base, Br^- shares its electrons less well (is a better leaving group). The difference in basicity is even greater than this when comparing the leaving group in a bromonium ion and an epoxide, because the leaving group in a bromonium ion is a neutral bromine, which is a weaker base than Br^-.

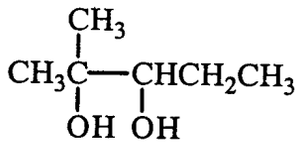
16. The major product results from attack of the Grignard reagent on the less sterically hindered carbon of the epoxide (the one bonded to a hydrogen and to a methyl group).
It will be easier to answer this question if you use molecular models.

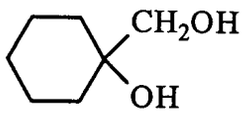




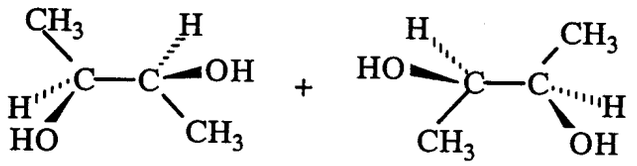
17. The addition of Br_2 to an alkene is a stereoselective reaction because not all possible stereoisomers are formed: the trans-alkene forms the erythro pair of enantiomers, whereas the cis-alkene forms the threo pair of enantiomers.
It is a stereospecific reaction because a cis-alkene leads to a different set of products than doe trans-alkene.
It is not enantioselective, because if an asymmetric carbon is created, both enantiomers are obtained in equal amounts, and if two asymmetric carbons are created, two pairs of enantiome (or a meso form and a pair of enantiomers) are obtained.

18.

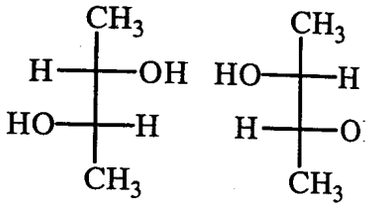
a. 

b. 

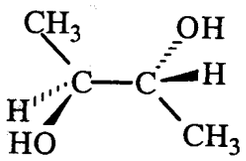
19. **a.** Syn addition to the trans isomer forms the threo pair of enantiomers. (See Section 5.19)



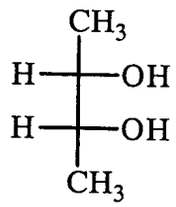
or



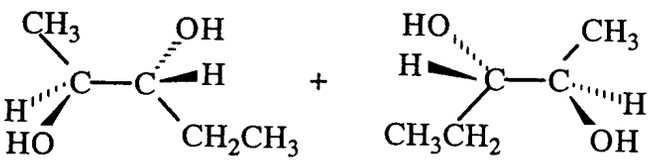
b. Syn addition to the cis isomer forms the erythro pair of enantiomers. In this case, the prod is a meso compound because each asymmetric carbon is bonded to the same four substitue so only one stereoisomer is formed.



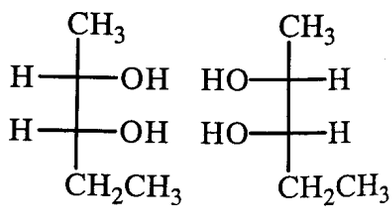
or



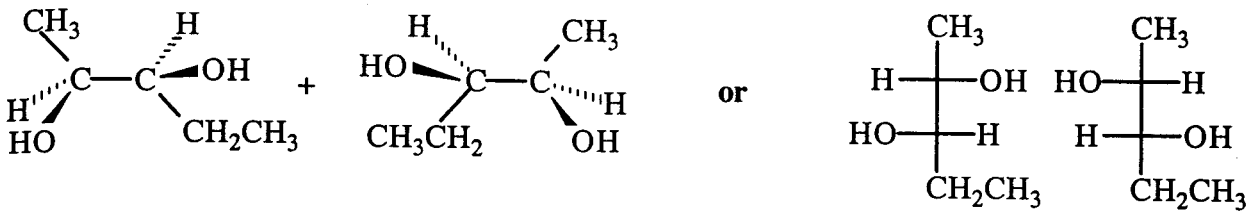
c. Syn addition to the cis isomer forms the erythro pair of enantiomers.



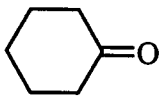
or



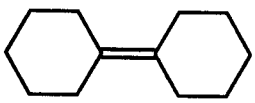
d. Syn addition to the trans isomer forms the threo pair of enantiomers.



20. The fact that only one ketone is obtained means that the alkene must be symmetrical. The cyclic ketone that is obtained is

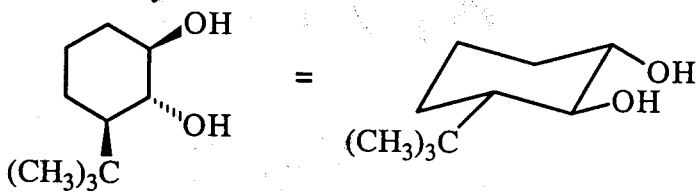


Therefore, the alkene is

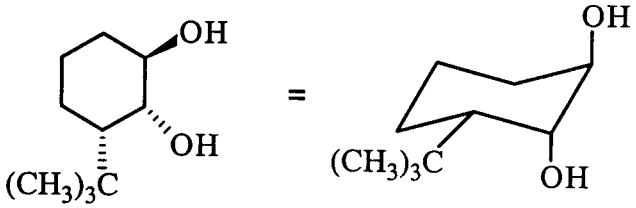


21.

a. The compound on the left is more reactive because when the bulky *tert*-butyl group is in the more stable equatorial position, the two OH groups are in equatorial positions. In the other compound, the two OH groups are in axial positions and, therefore, are too far away one another to form the cyclic intermediate.

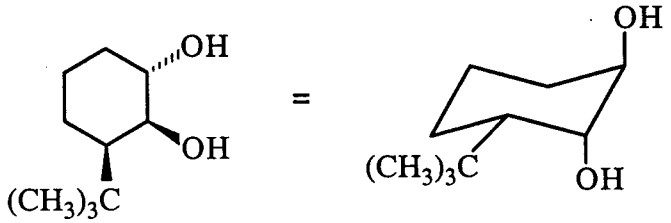


more reactive

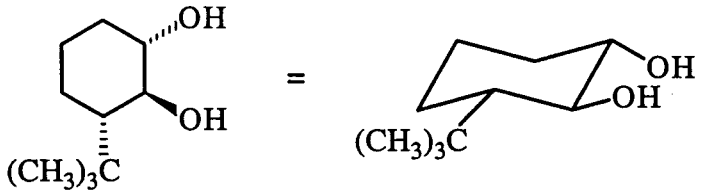


less reactive

b. The compound on the right is more reactive because when the bulky *tert*-butyl group is in tl more stable equatorial position, the two OH groups are in equatorial positions. In the other compound, the two OH groups are in axial positions and, therefore, cannot form the cyclic intermediate.

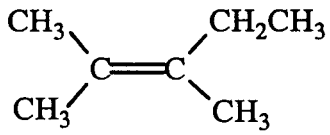


less reactive



more reactive

22. Any alkene that forms two ketones when it is cleaved will form the same products when the ozonide is worked up under reducing conditions as it forms when it is worked up under oxi conditions. In other words, each sp^2 carbon must be bonded to two alkyl groups.



23.

1. a. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}CH_3 + CH_3\overset{O}{\overset{\|}{C}}H$

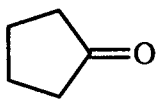
b. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}CH_3 + CH_3\overset{O}{\overset{\|}{C}}OH$

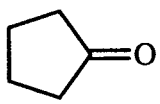
2. a. $H\overset{O}{\overset{\|}{C}}H + CH_3CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}H$

b. $H\overset{O}{\overset{\|}{C}}OH + CH_3CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

3. a. $CH_3\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}H$

b. $CH_3\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

4. a. $H\overset{O}{\overset{\|}{C}}H +$ 

b. $H\overset{O}{\overset{\|}{C}}OH +$ 

5. a. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H$
(2 equivalents)

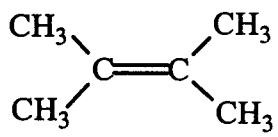
b. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OH$
(2 equivalents)

6. a. $CH_3\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}H + H\overset{O}{\overset{\|}{C}}CH_2CH_2\overset{O}{\overset{\|}{C}}H$

b. $CH_3\overset{O}{\overset{\|}{C}}-\overset{O}{\overset{\|}{C}}OH + HO\overset{O}{\overset{\|}{C}}CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

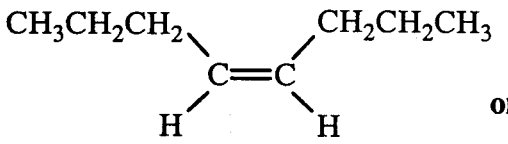
24.

a.



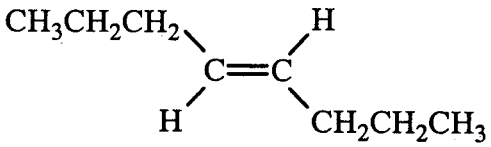
2,3-dimethyl-2-butene

b.



cis-4-octene

or



trans-4-octene

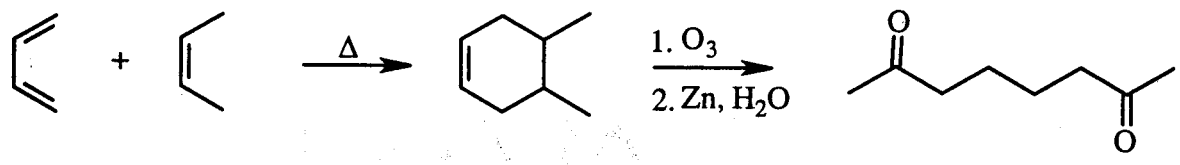
25. Solved in the text.

26. It does not tell you whether the double bond has the cis or the trans configuration.

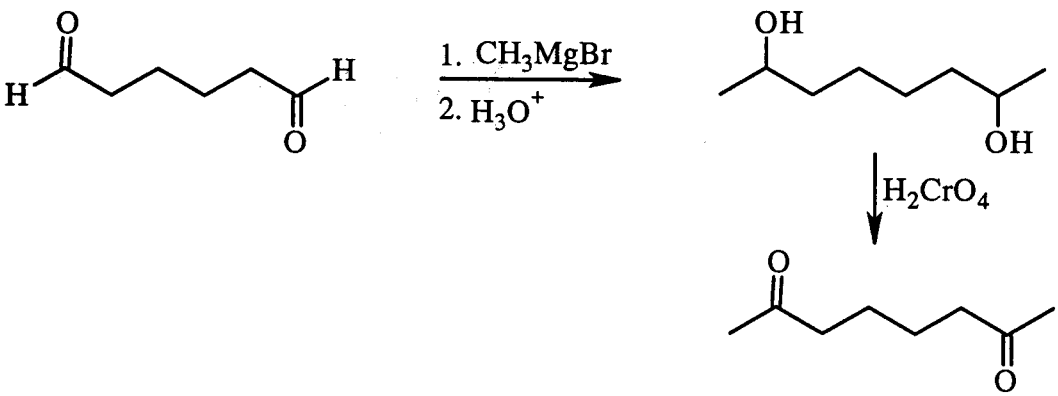
27. Solved in the text.

28.

a.

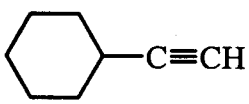


b.



29.

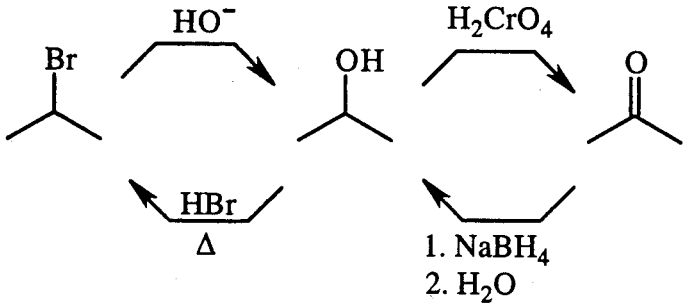
a.



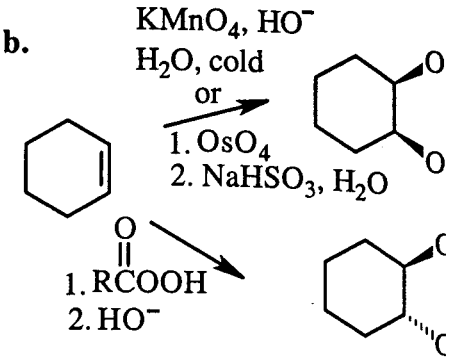
b. $CH_3CH_2C{\equiv}CCH_2CH_2CH_2C{\equiv}CCH_2CH_3$

30.

a.



b.



31.

a.

1. $CH_3CH_2Br \xrightarrow[Et_2O]{Mg} CH_3CH_2MgBr \xrightarrow{H_2C{=}O} CH_3CH_2CH_2O^- \xrightarrow{H_3O^+} CH_3CH_2CH_2($

2. $CH_3CH_2Br \xrightarrow[Et_2O]{Mg} CH_3CH_2MgBr \xrightarrow{CO_2} CH_3CH_2\overset{O}{\overset{\|}{C}}O^- \xrightarrow[2.\ H_3O^+]{1.\ LiAlH_4} CH_3CH_2CH_2$

3. $CH_3CH_2Br \xrightarrow[HCl]{^-C{\equiv}N} CH_3CH_2C{\equiv}N \xrightarrow[\Delta]{H_3O^+} CH_3CH_2\overset{O}{\overset{\|}{C}}OH$

or $\xrightarrow[\Delta]{^-OH,\ H_2O} CH_3CH_2\overset{O}{\overset{\|}{C}}O^- \xrightarrow[2.\ H_3O^+]{1.\ LiAlH_4} CH_3CH_2CH$

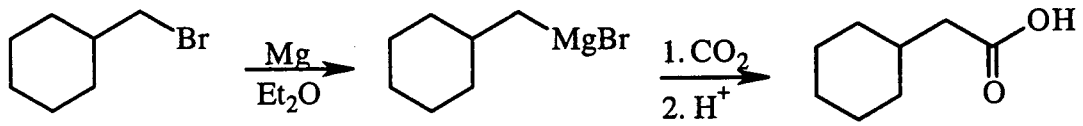
b. $CH_3CH_2Br \xrightarrow{^-C{\equiv}N} CH_3CH_2C{\equiv}N \xrightarrow[Pd/C]{H_2} CH_3CH_2CH_2NH_2$

c. $CH_3CH_2CH_2Br \xrightarrow{tert\text{-}BuO^-} CH_3CH{=}CH_2 \xrightarrow[2.\ Zn,\ H_2O]{1.\ O_3} CH_3CH{=}O \xrightarrow[2.\ H_2]{1.\ NH_3} CH_3CH$

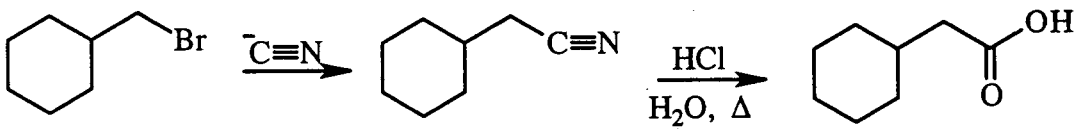
Raney Nickel

32.

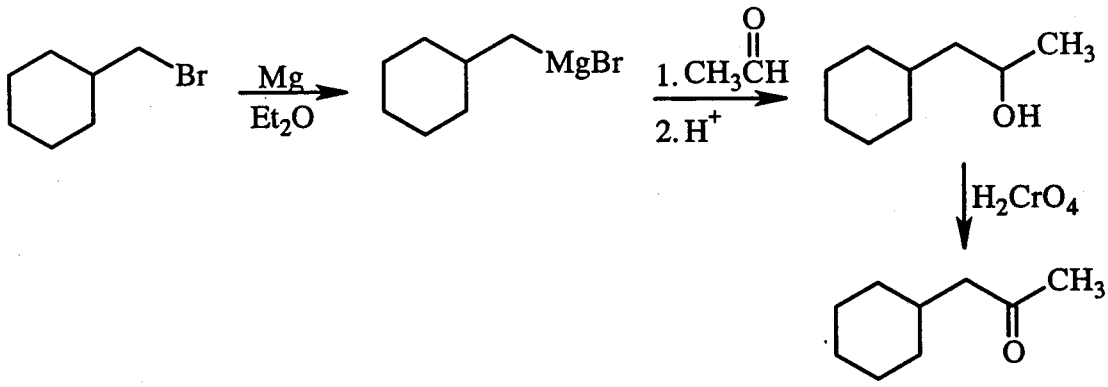
a.



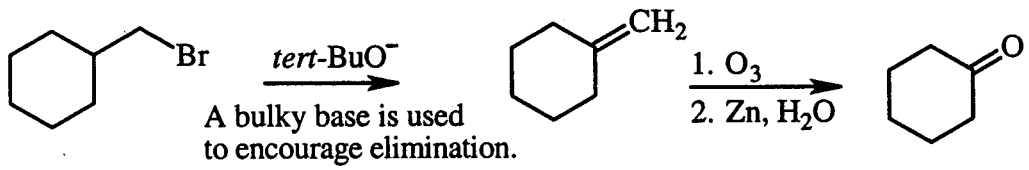
or



b.

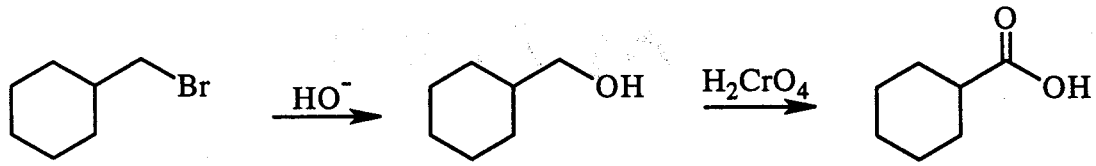


c.



A bulky base is used to encourage elimination.

d.



33.

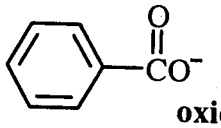
aldehyde	acyl halide	alkyl halide
carboxylic acid	acid anhydride	ether
ester	alkene	epoxide

34.

a. oxidized	**c.** reduced	**e.** oxidized	**g.** reduced
b. reduced	**d.** oxidized	**f.** oxidized	

35.

a. $CH_3CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OH$
oxidation

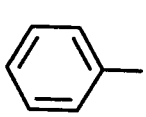
b.  + CO_2
oxidation

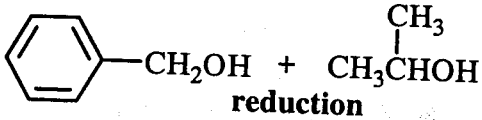
c. $CH_3CH_2CH_2CH_2OH$ **reduction**

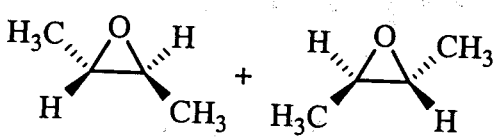
d. $CH_3CH_2CH_2CH_2OH$
Formation of the aldehyde after steps 1 and 2 is neither oxidation or reduction.
Formation of the alcohol after steps 3and 4 is a **reduction**.

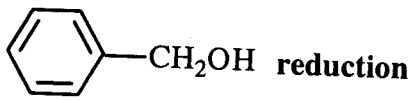
e. $CH_3CH_2\overset{O}{\overset{\|}{C}}H$ **oxidation**

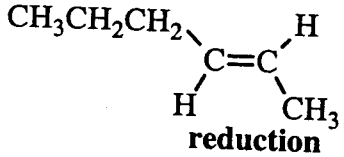
f. $CH_3CH_2CH_2CH_2NHCH_3$
reduction

g.  **oxidation**

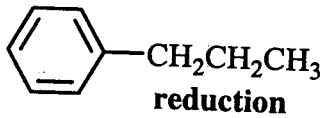
h. 
reduction

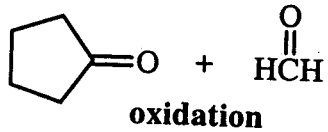
i. 
oxidation

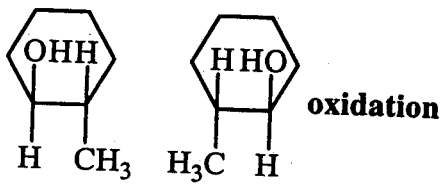
j.  **reduction**

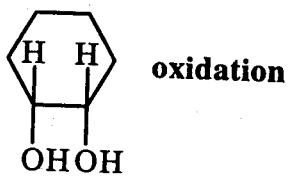
k. 
reduction

l. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OH + CH_3\overset{O}{\overset{\|}{C}}OH$
oxidation

m. 
reduction

n. 
oxidation

o. 
oxidation

p. 
oxidation

q. $^{-}O\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}O^{-}$
oxidation

r. $HO\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}OH$ **oxidation**

36.

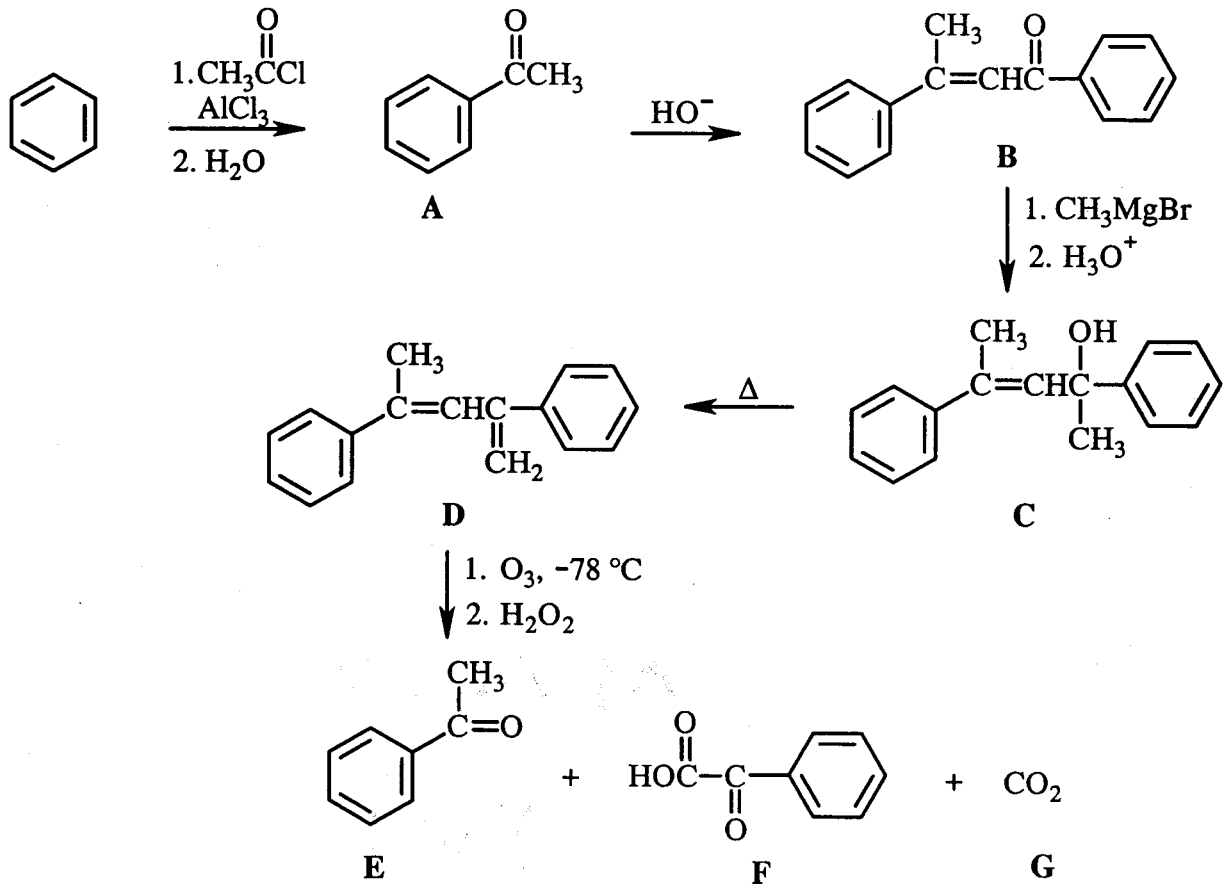
a. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H \xrightarrow{H_2CrO_4} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

b. $CH_3CH_2CH_2CH_2OH \xrightarrow{H_2CrO_4} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

c. $CH_3CH_2CH_2CH_2Br \xrightarrow{HO^-} CH_3CH_2CH_2CH_2OH \xrightarrow{H_2CrO_4} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

d. $CH_3CH_2CH{=}CH_2 \xrightarrow[2.\ HO^-, H_2O_2]{1.\ BH_3} CH_3CH_2CH_2CH_2OH \xrightarrow{H_2CrO_4} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

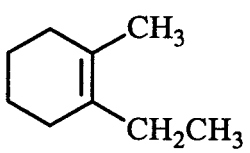
37.



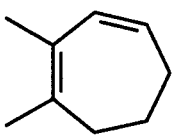
38.

a. $CH_3CH_2CH_2CH{=}C(CH_3)_2$

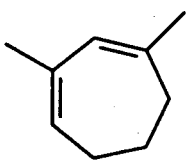
b.



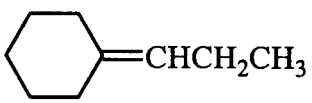
c.



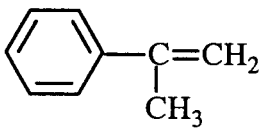
or



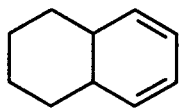
d.



e.



f.



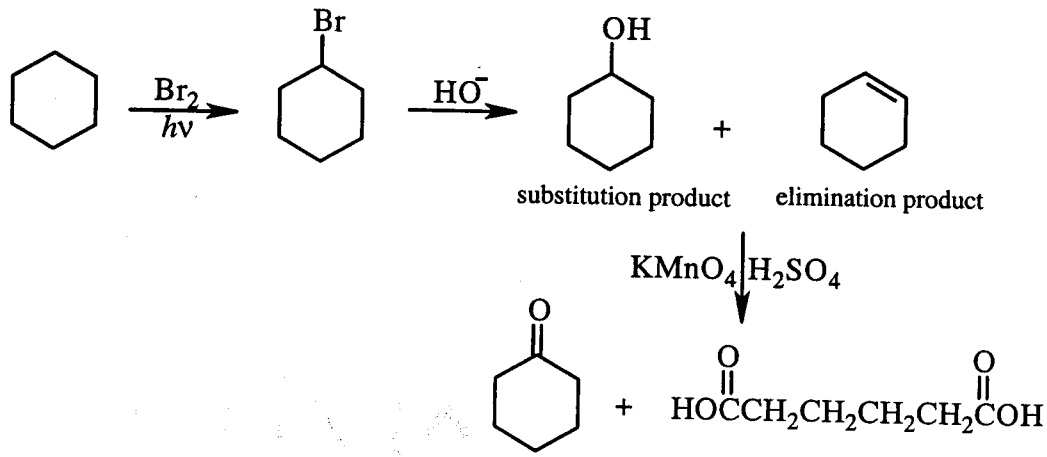
39.

a. $CH_3CH_2CH{=}CH_2 \xrightarrow[2.\ H_2O_2,\ HO^-]{1.\ BH_3} CH_3CH_2CH_2CH_2OH$

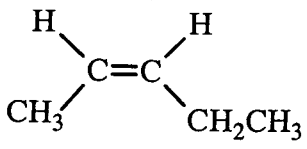
$CH_3CH_2CH_2CH_2OH \underset{\Delta}{\overset{H_2SO_4}{\rightleftharpoons}} CH_3CH{=}CHCH_3 + H_2O$

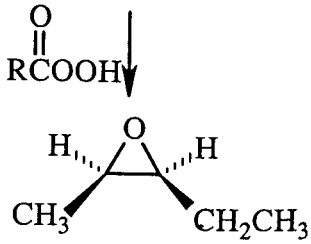
$CH_3CH{=}CHCH_3 \xrightarrow[H_2SO_4]{KMnO_4} 2\ CH_3\overset{O}{\overset{\|}{C}}OH$

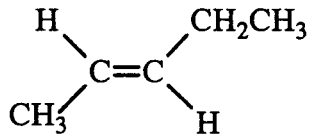
b. $CH_3CH_2Br \xrightarrow[Et_2O]{Mg} CH_3CH_2MgBr \xrightarrow[2.\ H_3O^+]{1.\ \text{epoxide}} CH_3CH_2CH_2CH_2OH \xrightarrow{PCC} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H$

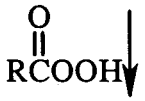
c. 

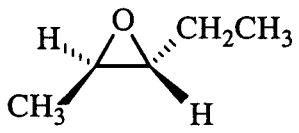
40.

a. $HC{\equiv}CCH_2CH_3 \xrightarrow[2.\ CH_3Br]{1.\ \bar{N}H_2} CH_3C{\equiv}CCH_2CH_3 \xrightarrow[\text{Lindlar catalyst}]{H_2}$ 



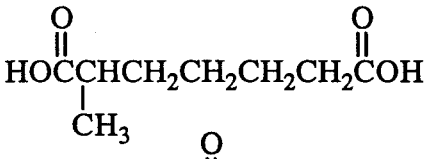
b. $HC{\equiv}CCH_2CH_3 \xrightarrow[2.\ CH_3Br]{1.\ \bar{N}H_2} CH_3C{\equiv}CCH_2CH_3 \xrightarrow[NH_3]{Na}$ 

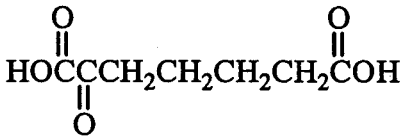


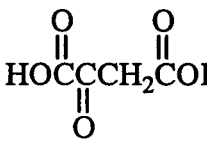
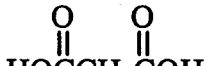


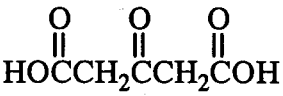
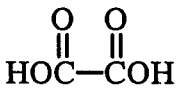
41.

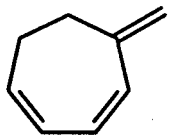
a. 1. 

2. 

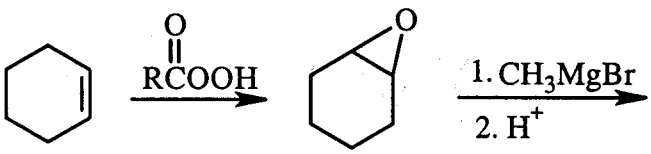
3. CO_2 + 

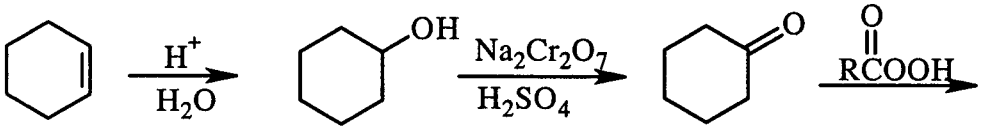
4. CO_2 +  + 

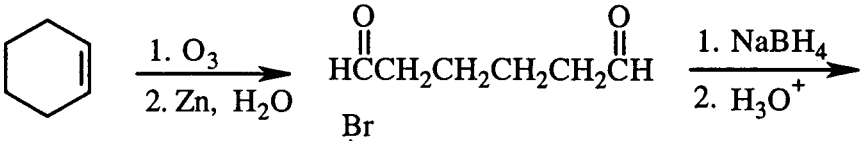
5. CO_2 +  + 

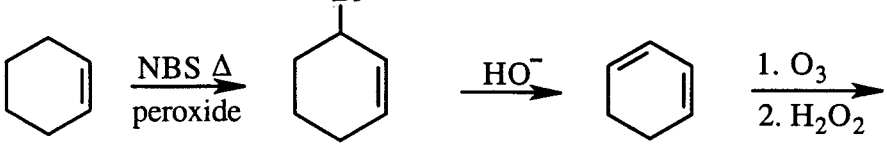
b. 

42.

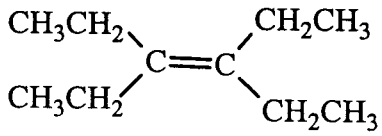
a. 

b. 

c. 

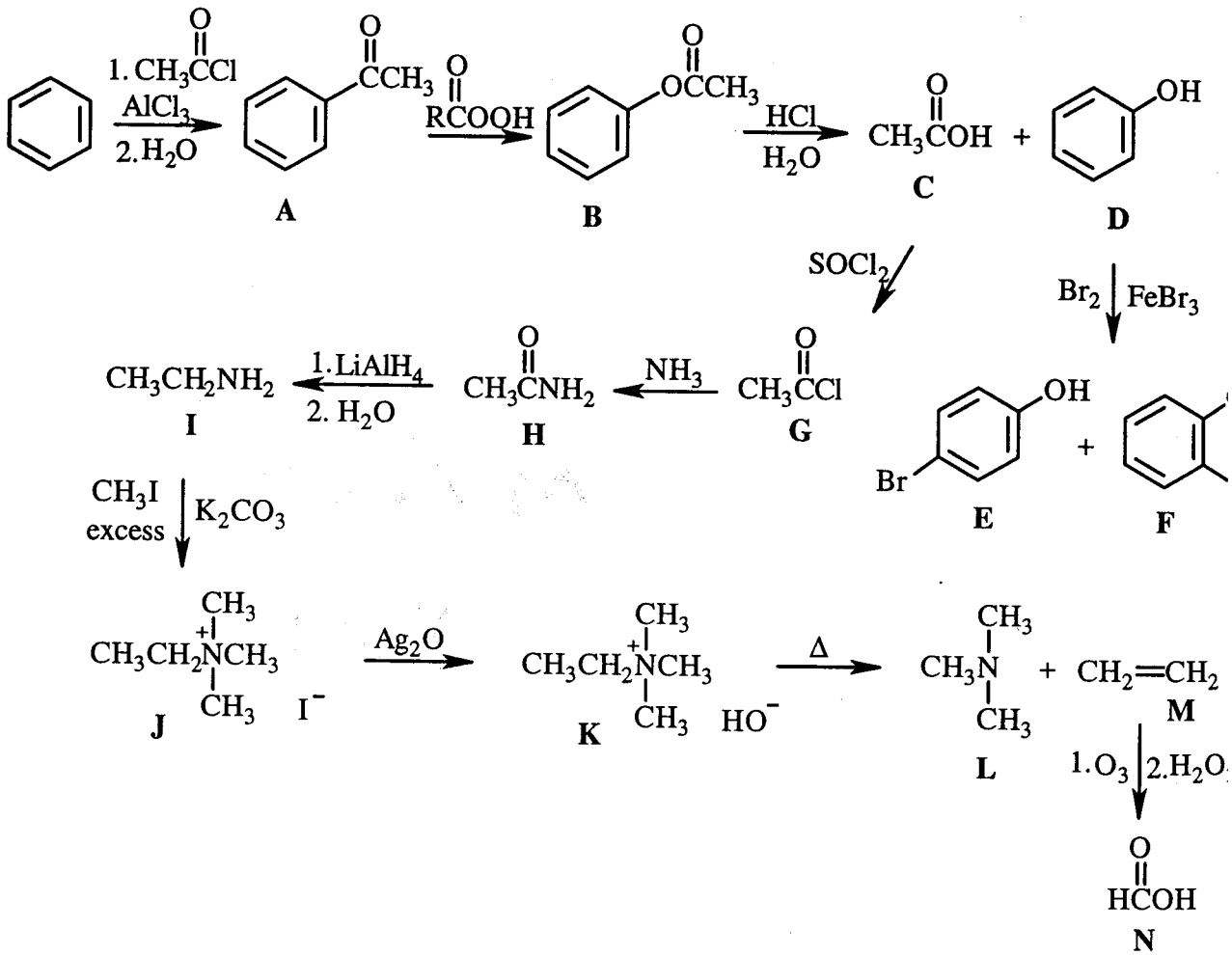
d. 

43. Because the compound is produced as a result of ozonolysis of an alkene under oxidizing conditions, it must be a ketone or a carboxylic acid. Since there is no signal for an OH group, compound must be a ketone. The NMR spectrum shows two signals with splitting that is characteristic of an ethyl group. Therefore, the compound produced as a result of ozonolysis must be 3-pentanone. The alkene that underwent ozonolysis, therefore, must be 3,4-diethyl-3-hexene.

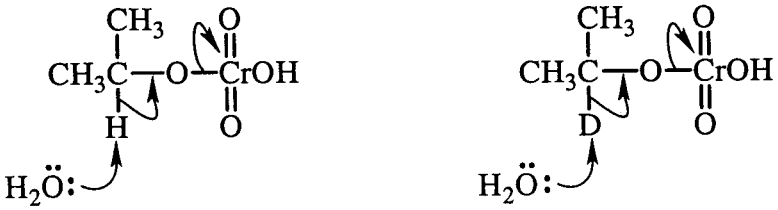


3,4-diethyl-3-hexene

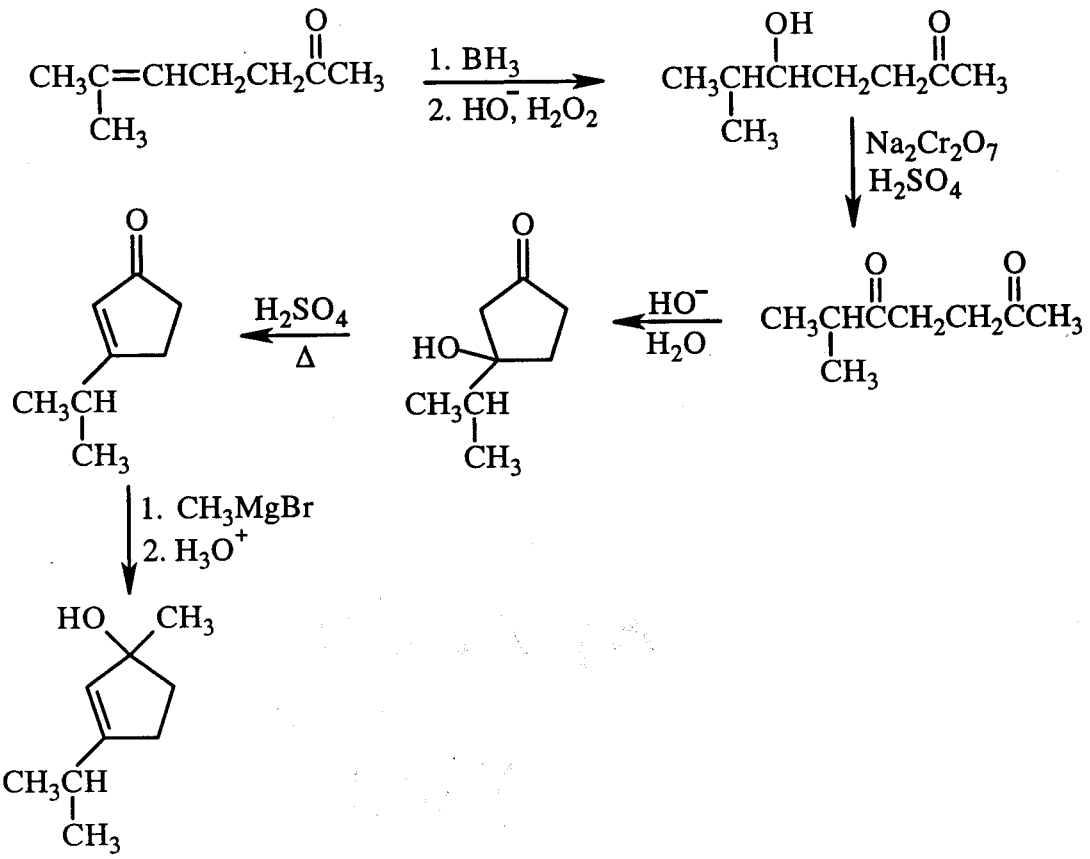
44.



45. The rate-determining step in the chromic acid oxidation of an alcohol is the E2 elimination reaction of the chromate ester. 2-Propanol is oxidized more rapidly than 2-deuterio-2-propanol because it is easier to break the carbon-hydrogen bond than the carbon-deuterium bond.

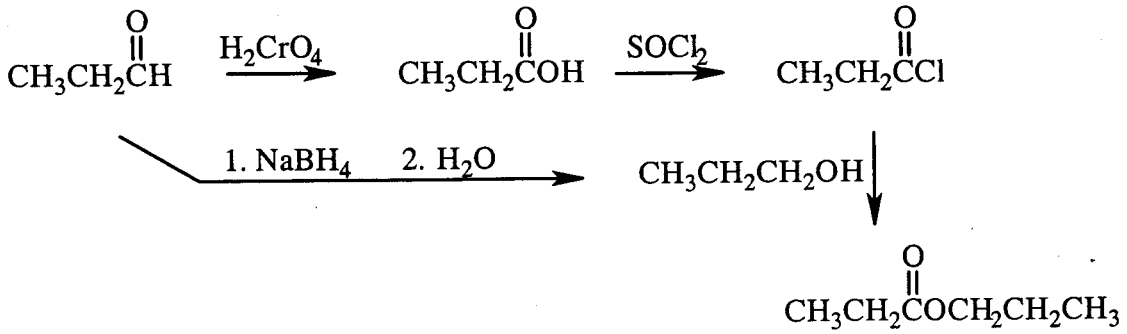


46.



47.

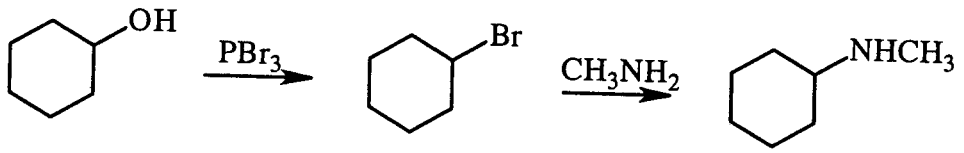
a.

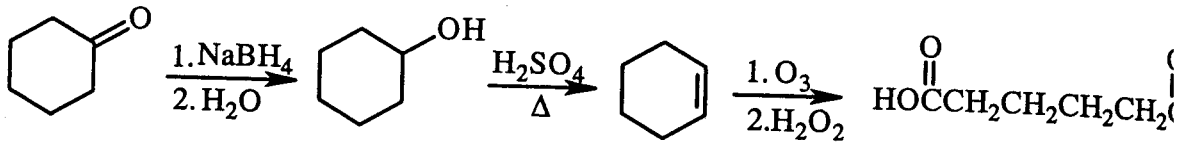


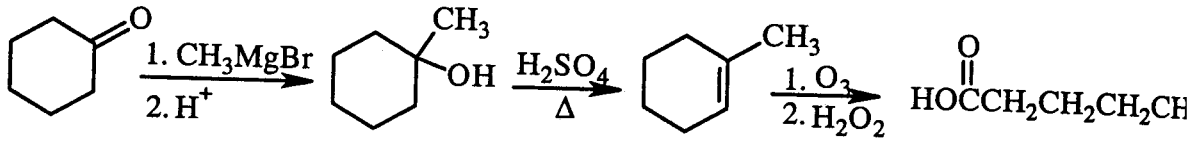
b. $CH_3CH_2CH_2CH_2OH \xrightarrow{PCC} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H \xrightarrow[2.\ H_2O]{1.\ CH_3CH_2MgBr} CH_3CH_2CH_2\overset{OH}{\overset{|}{C}}HCH$

$\xrightarrow{H_2CrO_4}$

$CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}CH_2($

c. 

d. 

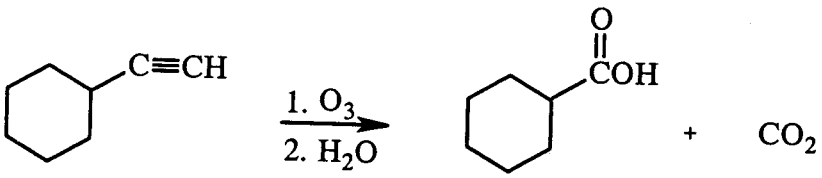
e. 

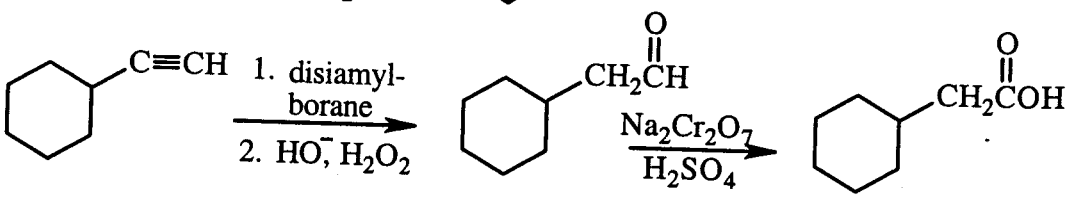
48.

$CH_3CH_2\overset{CH_3}{\overset{|}{C}}=CH_2$

49. A cyclic intermediate is formed when HIO_4 cleaves a 1,2-diol. It is easier to form a cyclic intermediate if the two OH groups are on the same side of the molecule. Therefore, **A** is cleaved more easily because it is a cis diol, while **B** is a trans diol.

50.

a. 

b. 

a. $CH_3CH_2CH_2OH \xrightarrow{PCC} CH_3CH_2\overset{O}{\overset{\|}{C}}H \xrightarrow[H_2O]{HO^-} CH_3CH_2\underset{CH_3}{\overset{OH}{C}}H\overset{O}{\overset{\|}{C}}H$

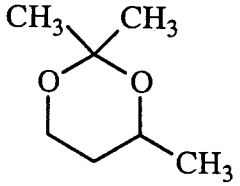
$\xrightarrow[\Delta]{H_2SO_4} CH_3CH_2CH=\underset{CH_3}{\overset{O}{\overset{\|}{C}}}H \xrightarrow[Pd/C]{H_2} CH_3CH_2CH_2\underset{CH_3}{CH}CH_2OH$

b. $CH_3\underset{CH_3}{CHOH} \xrightarrow[H_2SO_4]{Na_2Cr_2O_7} CH_3\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow{HO^-} CH_3\underset{CH_3}{\overset{OH}{C}}CH_2\overset{O}{\overset{\|}{C}}CH_3$

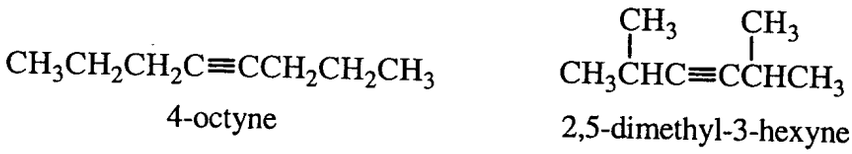
$\xrightarrow[2.\ H_3O^+]{1.\ NaBH_4} CH_3\underset{CH_3}{\overset{OH}{C}}H\underset{CH_3}{\overset{OH}{C}}HCH_3 \xrightarrow[\Delta]{H_2SO_4}$ $\begin{cases} CH_3\underset{CH_3}{C}=CHCH=CH_2 \\ CH_2=\underset{CH_3}{C}CH=CHCH_3 \end{cases}$ $\xrightarrow[Pd/C]{H_2} CH_3\underset{CH_3}{CH}CH_2CH_2CH_3$

c. $CH_3CH_2OH \xrightarrow{PCC} CH_3\overset{O}{\overset{\|}{C}}H \xrightarrow[2.\ CH_3\overset{O}{\overset{\|}{C}}H]{1.\ LDA/THF} CH_3\underset{CH_3}{\overset{OH}{C}}H\overset{O}{\overset{\|}{C}}H \xrightarrow[2.\ H_3O^+]{1.\ NaBH_4} CH_3\underset{CH_3}{\overset{OH}{C}}HCH_2CH_2OH$

$CH_3\underset{CH_3}{CHOH} \xrightarrow[H_2SO_4]{Na_2Cr_2O_7} CH_3\overset{O}{\overset{\|}{C}}CH_3 \xrightarrow{HCl}$



52. The compound is either **4-octyne** or **2,5-dimethyl-3-hexyne**.



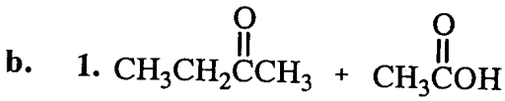
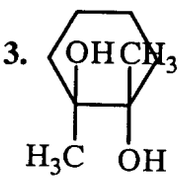
4-octyne

2,5-dimethyl-3-hexyne

Because oxidative cleavage formed only one four-carbon carboxylic acid, you know the compound is either a symmetrical eight-carbon alkene or a symmetrical eight-carbon alkyne. Therefore, the compound has a molecular formula of C_8H_{14} or C_8H_{16} and, consequently, a molecular weight of 110 or 112.

0.5 g of the hydrocarbon was hydrogenated; this corresponds to 0.0045 mol (0.5/112 = 0.0045, 0.5/110 = 0.0045). The key here is to remember from general chemistry that 1 mol of a gas has volume of 22.4 liters at standard temperature and pressure. Knowing this, it can be calculated that 0.0045 mol of H_2 = 100 mL H_2. Since about 200 mL of H_2 were consumed, the compound must have two π bonds. Thus, the unknown compound is an alkyne.

53. **a.** None was successful.

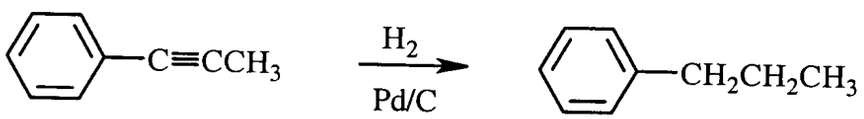
b. **1.**  **2.** no reaction **3.** 

c. **1.** $\xrightarrow[2.\ H_2O]{1.\ KMnO_4,\ HO^-,\ cold}$ **or** $\xrightarrow[2.\ H_2O_2]{1.\ OsO_4}$ **2.** $\xrightarrow[2.\ H_3O^+]{1.\ LiAlH_4}$ **3.** $\xrightarrow[2.\ H_2O]{1.\ KMnO_4,\ HO^-,\ cold}$ **or** $\xrightarrow[2.\ H_2O_2]{1.\ OsO_4}$

54. The absorption bands at 1600 cm^{-1}, 1500 cm^{-1}, and > 3000 cm^{-1} in the IR spectrum indicate the compound has a benzene ring. The absorption band 2250 cm^{-1} indicates the compound has a triple bond, and the absence of an absorption band 3200 cm^{-1} tells you that it is not a terminal alkyne.

The two triplets and the multiplet in the ^1H NMR spectrum indicate a propyl group.

Compound **A** is 1-phenyl-1-propyne and compound **B** is propylbenzene.



A **B**

55. Diane has enough information to identify diols **A**, **C**, **E**, and **F**, but not enough information to distinguish between diols **B** and **D**.

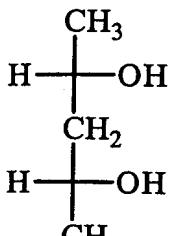
Only the 4th compound will form two products upon cleavage with periodic acid. So it must be **F**.

The 1st and 5th compounds will not react with periodic acid. Because the 1st compound is optically inactive and the 5th compound is optically active, the 1st compound must be **C** and the 5th compound must be **E**.

The 3rd compound is the only optically active compound that forms one compound with periodic acid. Therefore, it must be **A**.

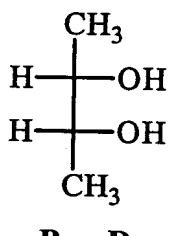
Diane could distinguish between **B** and **D** if she analyzed the products obtained from the reaction of **B** and **D** with periodic acid. **B** will form acetaldehyde (a 2-carbon aldehyde), while **D** will form propanal (a 3-carbon aldehyde).

1



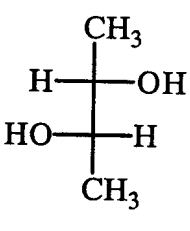
C

2



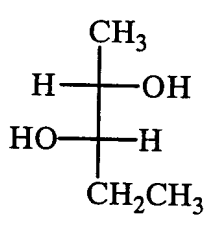
B or D

3



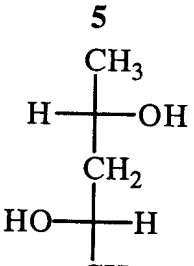
A

4



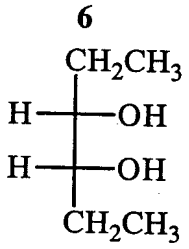
F

5



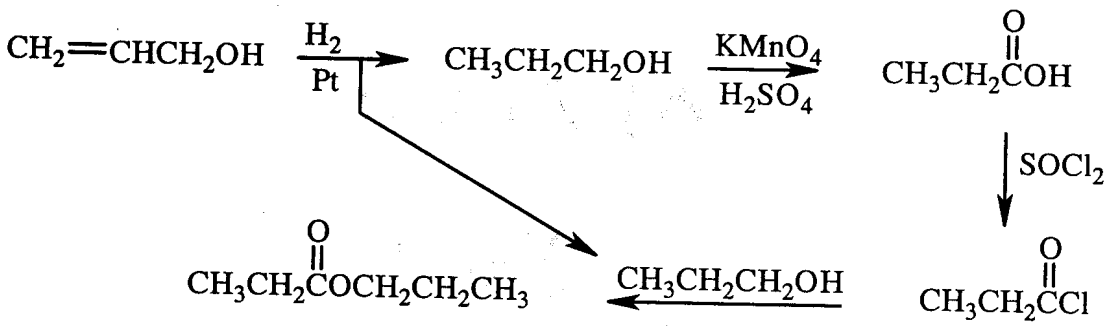
E

6

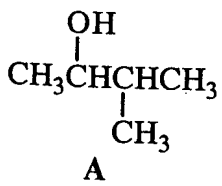


B or D

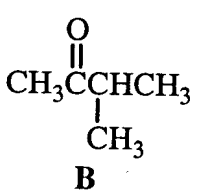
56.



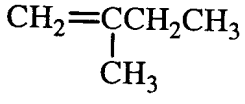
57.



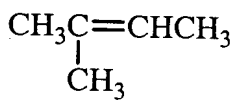
A



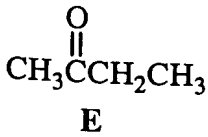
B



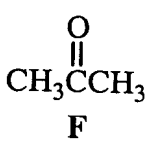
C



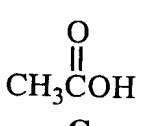
D



E



F

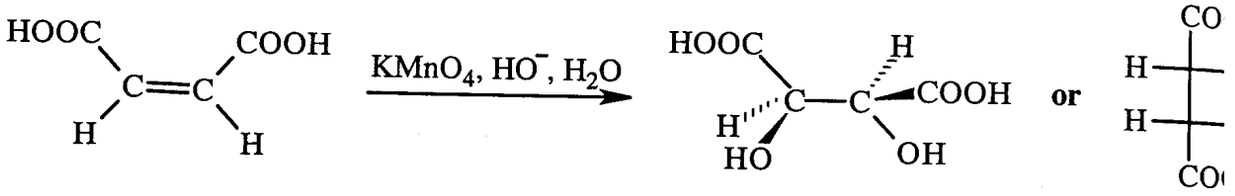


G

58.

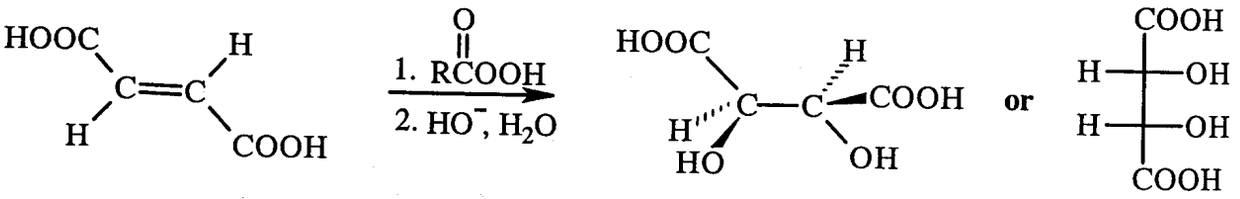


59. **a.** (2*R*,3*S*)-Tartaric acid is a meso compound. It will be formed by syn addition to the cis isom
Syn addition of two OH groups can be carried out using a cold, basic solution of potassium
permanganate or using osmium tetroxide followed by an aqueous solution of sodium bisulfi



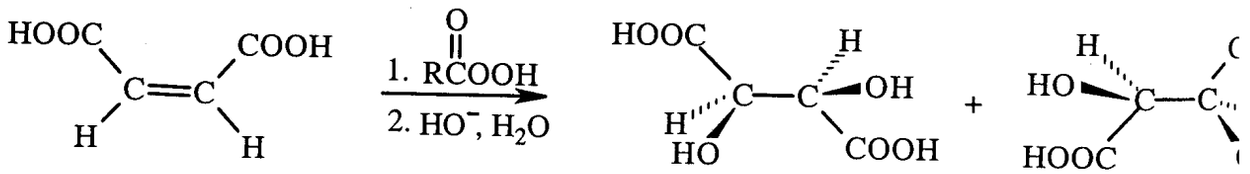
(2*R*,3*S*)-tartaric acid

b. (2*R*,3*S*)-Tartaric acid can also be formed by anti addition to the trans isomer. Anti addition o
two OH groups can be carried out by first forming an epoxide and then treating the epoxide
with an aqueous solution of hydroxide.



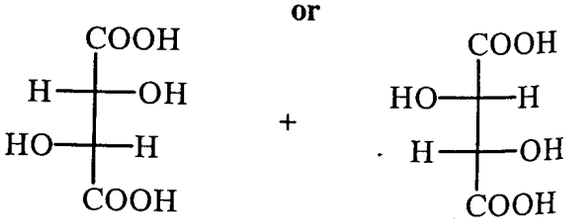
(2*R*,3*S*)-tartaric acid

c. (2*R*,3*R*)-Tartaric acid and (2*S*,3*S*)-tartaric acid are the threo isomers. They will be formed by
anti addition to the cis isomer.

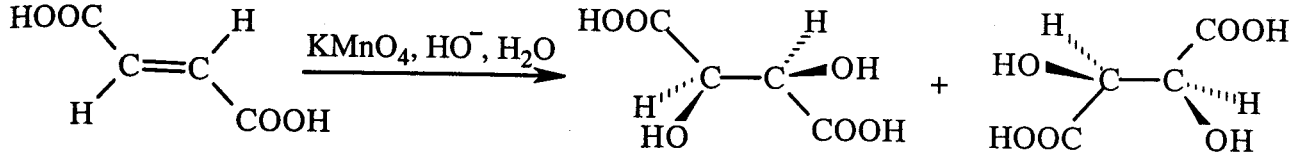


(2*R*,3*R*)-tartaric acid (2*S*,3*S*)-tartaric a

or

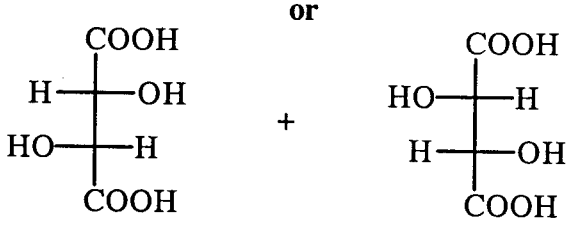


d. The threo isomers can also be formed by syn addition to the trans isomer.

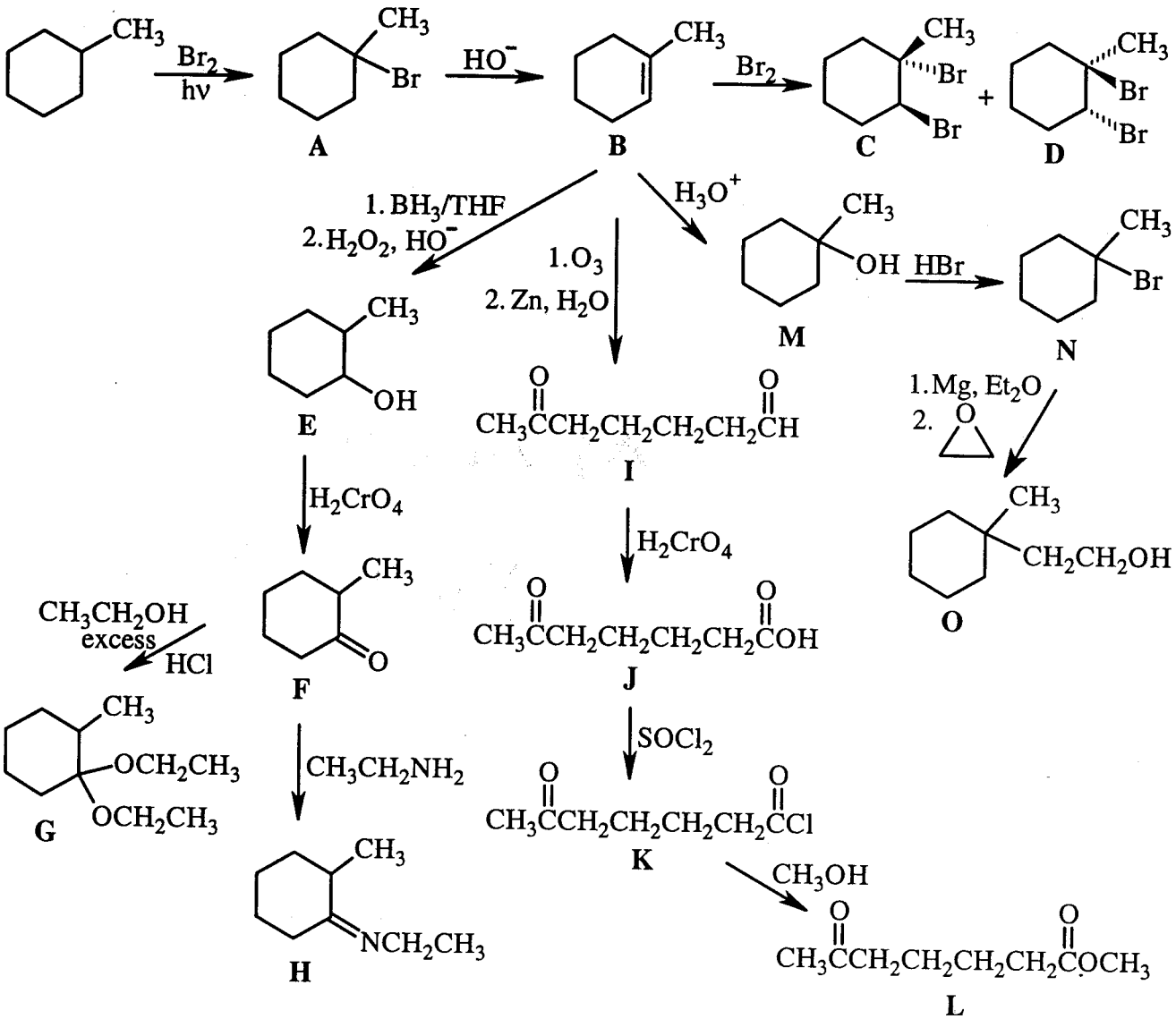


(2*R*,3*R*)-tartaric acid (2*S*,3*S*)-tartaric acid

or



60.



61.

a. CH_3CHCH_3 (CH_3) $\xrightarrow[h\nu]{Br_2}$ CH_3CCH_3 (Br, CH_3) $\xrightarrow{HO^-}$ $CH_3C{=}CH_2$ (CH_3) $\xrightarrow[2.\ H_2O_2]{1.\ O_3}$ CH_3CCH_3 (=O)

b. Note that 2-bromopropane (obtained from the first step) is divided into two portions; one portion is used to form propene, and the other is used to form the Grignard reagent.

$CH_3CH_2CH_3 \xrightarrow[h\nu]{Br_2}$ CH_3CHCH_3 (Br) $\xrightarrow{HO^-}$ $CH_3CH{=}CH_2$

CH_3CHCH_3 (Br) $\xrightarrow{Mg\,|\,Et_2O}$ CH_3CHCH_3 ($MgBr$)

$CH_3CH{=}CH_2 \xrightarrow[2.\ Zn,\ H_2O]{1.\ O_3}$ CH_3CH (=O)

CH_3CHCH_3 ($MgBr$) + CH_3CH (=O) $\longrightarrow$ $CH_3CHCHCH_3$ (O^-, CH_3)

$CH_3CHCHCH_3$ (O^-, CH_3) $\xrightarrow{H_2SO_4\,|\,\Delta}$ $CH_3CH{=}CCH_3$ (CH_3)

c. $CH_3CH_2CH_3 \xrightarrow[h\nu]{Br_2}$ CH_3CHCH_3 (Br) $\xrightarrow[Et_2O]{Mg}$ CH_3CHCH_3 ($MgBr$) $\xrightarrow[2.\ H^+]{1.\ CH_3CH(=O)}$ $CH_3CHCHCH_3$ (OH, CH_3)

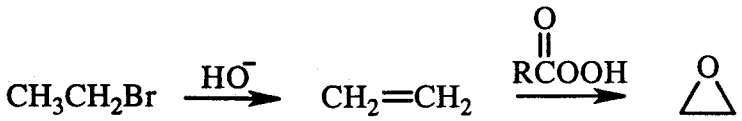
$CH_3CHCHCH_3$ (OH, CH_3) $\xrightarrow[H_2SO_4]{Na_2Cr_2O_7}$ CH_3CHCCH_3 (=O, CH_3)

d. $CH_3CH_3 \xrightarrow[h\nu]{Br_2}$ $CH_3CH_2Br \xrightarrow[Et_2O]{Mg}$ $CH_3CH_2MgBr \xrightarrow[2.\ H^+]{1.\ \text{epoxide}}$ $CH_3CH_2CH_2CH_2OH$

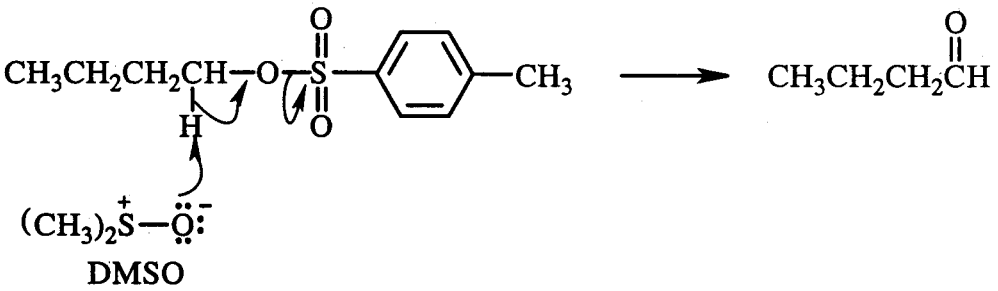
$CH_3CH_2CH_2CH_2OH \xrightarrow{PBr_3}$ $CH_3CH_2CH_2CH_2Br$

$CH_3CH_2CH_2Br \xrightarrow{HO^-}$ $CH_3CH_2CH{=}CH_2 \xrightarrow[2.\ Zn,\ H_2O]{1.\ O_3}$ CH_3CH_2CH (=O) + HCH (=O)

The ethylene oxide needed for the reaction can be obtained from some of the bromoethane prepared in the first step.

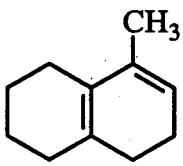


62.

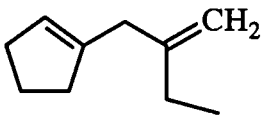


63.

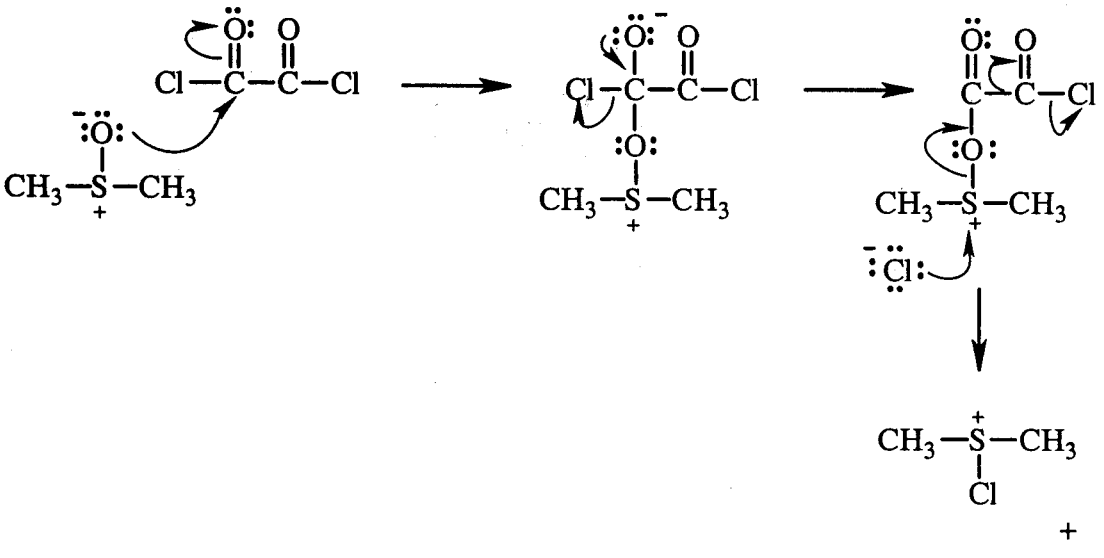
a.



b.

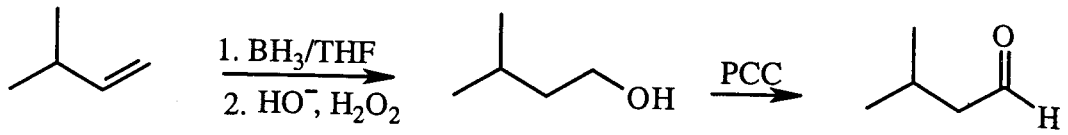


64.

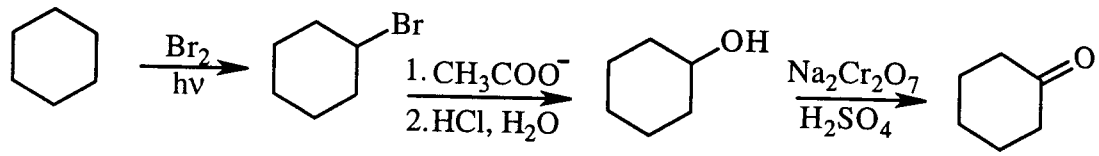


65.

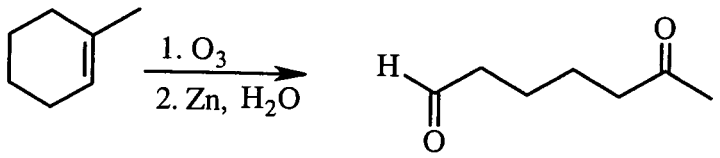
a.


1. BH3/THF
2. HO⁻, H2O2
OH
PCC
O
H

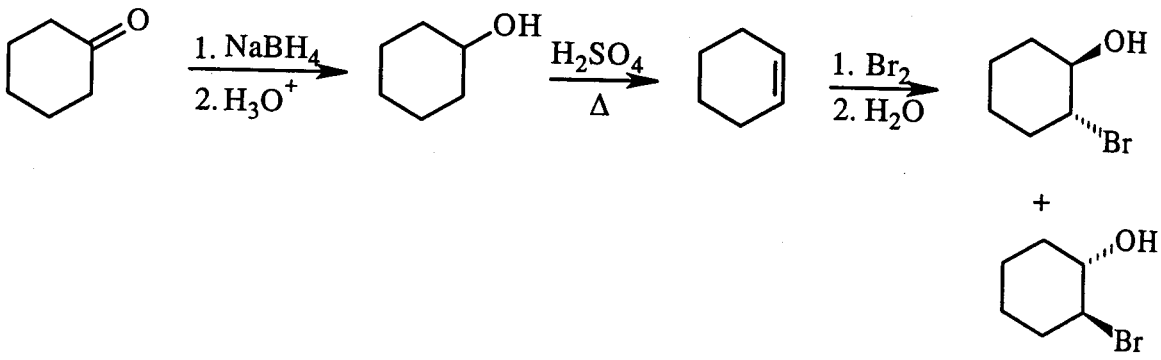
b.


Br2
hν
Br
1. CH3COO⁻
2. HCl, H2O
OH
Na2Cr2O7
H2SO4
O

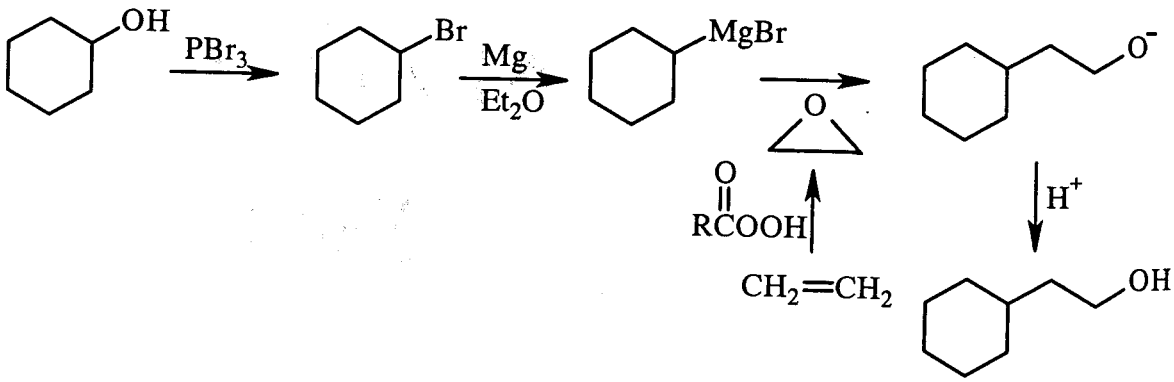
c.


1. O3
2. Zn, H2O
H
O
O

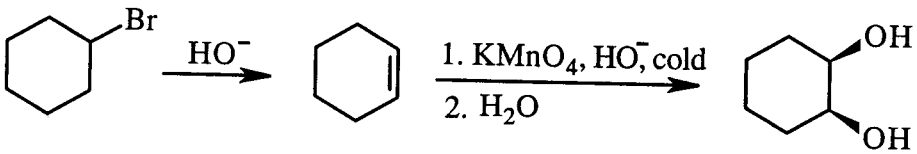
d.


O
1. NaBH4
2. H3O+
OH
H2SO4
Δ
1. Br2
2. H2O
OH
Br
+
OH
Br

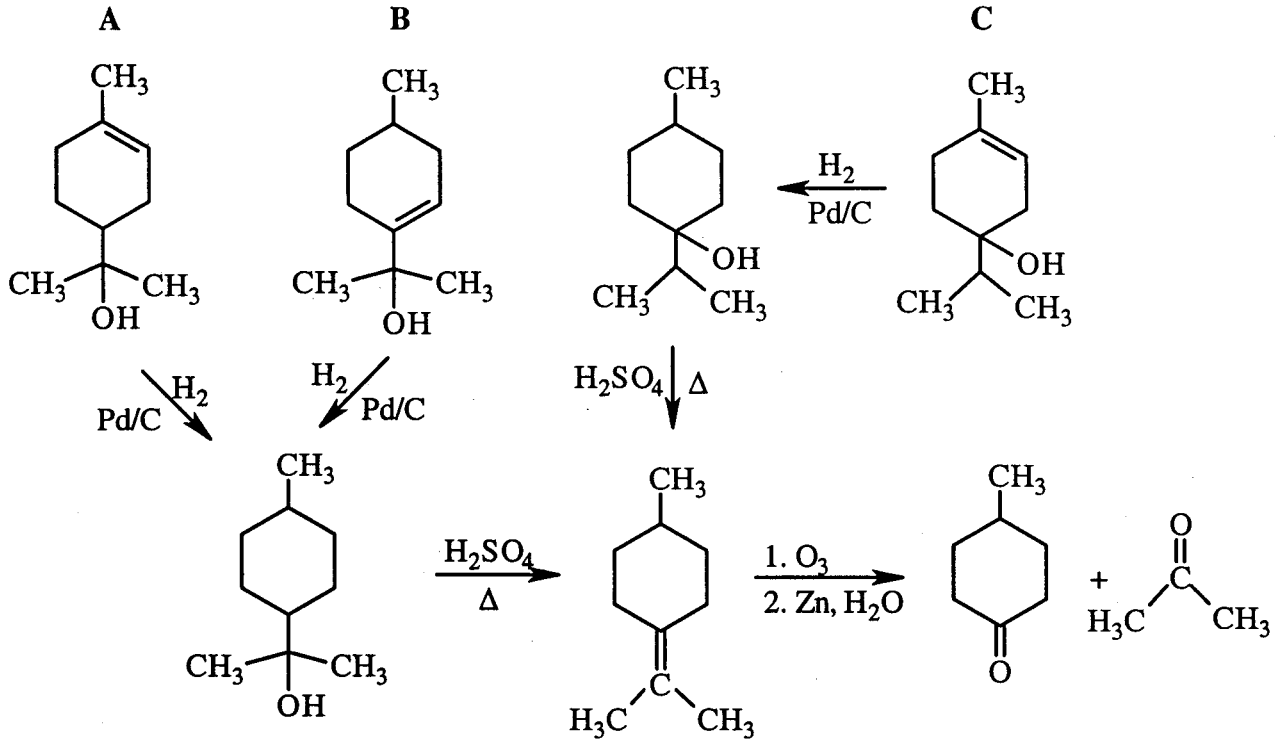
e.


OH
PBr3
Br
Mg
Et2O
MgBr
O
O⁻
O
RCOOH
H+
CH2=CH2
OH

f.


Br
HO⁻
1. KMnO4, HO⁻, cold
2. H2O
OH
OH

66. Three structures (**A**, **B**, **C**) fit the data given. Terpineol is actually **C**.



67. The fact that the HO substituent ends up on the least substituted sp^2 carbon of the double bond indicates that oxygen is the first species to add to the double bond. That H_2O_2 is one of the reagents suggests that the alkene reacts with H_2O_2, forming an epoxide. Br^- attacks the epoxide from the backside with the result that the OH and Br substituents form an anti addition product. The fact that Br^- attacks the most substituted carbon of the epoxide suggests that there is an acid catalyst at the surface of the enzyme that causes the epoxide to open to give the more stable partial carbocation.

Chapter 20 Practice Test

1. Indicate whether each of the following reactions is an oxidation, a reduction, or neither:

a. $CH_3CH_2\overset{\overset{O}{\|}}{C}CH_3 \longrightarrow CH_3CH_2\overset{\overset{OH}{|}}{C}HCH_3$

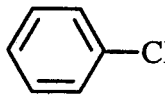
b. $CH_3CH_2\overset{\overset{O}{\|}}{C}H \longrightarrow CH_3CH_2\overset{\overset{O}{\|}}{C}OH$

2. Give the product of each of the following reactions, or if no reaction will occur, so state:

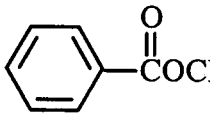
a. $CH_3CH_2CH_2CH_2OH \xrightarrow[H_2SO_4]{Na_2Cr_2O_7}$

b. $CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}OCH_3 \xrightarrow[Pt]{H_2}$

c. $CH_3CH_2\overset{\overset{O}{\|}}{C}NHCH_2CH_3 \xrightarrow[2.\ H_2O]{1.\ LiAlH_4}$

d.  $+ \ H_2 \xrightarrow{Pt}$

e. $CH_3CH_2CH_2CH_2\overset{\overset{O}{\|}}{C}H + R\overset{\overset{O}{\|}}{C}OOH \longrightarrow$

f.  $\xrightarrow[2.\ H_3O^+]{1.\ LiAlH_4}$

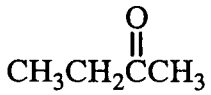
g. $CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}CH_2CH_3 \xrightarrow[2.\ H_3O^+]{1.\ NaBH_4}$

h. $CH_3CH_2CH_2\overset{\overset{CH_3}{|}}{C}{=}CHCH_2CH_3 \xrightarrow[2.\ H_2O_2]{1.\ O_3}$

3. Which of the following reagents **cannot** be used to convert an aldehyde into an alcohol?

H_2/Pt 1. $NaBH_4$ 2. H_3O^+ 1. $LiAlH_4$ 2. H_3O^+ 1. Ag_2O/NH_3 2. H_3O^+ H_2/Raney Nickel

4. Two alkenes, when treated with ozone and then with $(CH3)_2S$, both form only the ketone shown below. Identify the alkenes.



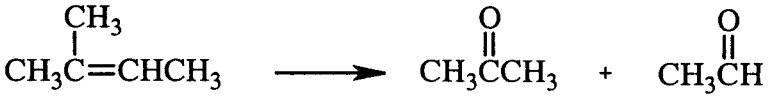
5. Indicate whether each of the following statements is true or false:

a. $NaBH_4$ is a weaker reducing agent than $LiAlH_4$.	T	F
b. Esters are easier to reduce than ketones.	T	F
c. In an oxidation-reduction reaction the oxidizing agent is oxidized.	T	F
d. Ketones are reduced to primary alcohols.	T	F
e. Aldehydes are oxidized to carboxylic acids.	T	F
f. Acyl halides are oxidized to aldehydes.	T	F
g. Alkenes cannot be reduced with $NaBH_4$.	T	F

6. Describe how the following compound can be prepared from the given starting material:



7. Which pair of reagents could be used to carry out the following reaction?



a. 1. O_3 2. Zn, H_2O and 1. O_3 2. H_2O_2

b. 1. OsO_4 2. H_2O_2 and $KMnO_4/H^+$

c. 1. O_3 2. Zn, H_2O and 1. O_3 2. $(CH_3)_2S$

CHAPTER 21
More About Amines • Heterocyclic Compounds

Important Terms

alkaloid	a natural product with a nitrogen heteroatom found in the leaves, bark, or seeds of plants.
Cope elimination reaction	elimination from an amine oxide.
corrin ring system	the ring system found in vitamin B_{12}. It is similar to the porphyrin ring system, but one of the methine bridges of the porphyrin ring system is missing.
deamination	loss of ammonia.
exhaustive methylation	reaction of an amine with excess methyl iodide, resulting in the formation of a quaternary ammonium iodide.
furan	a five-membered ring aromatic compound containing an oxygen heteroatom.
heteroatom	an atom other than a carbon atom or a hydrogen atom.
heterocyclic compound (heterocycle)	a cyclic compound in which one or more of the atoms of the ring are heteroatoms.
Hofmann elimination (anti-Zaitsev elimination)	a hydrogen is removed from the β-carbon bonded to the most hydrogens.
Hofmann elimination reaction	elimination of a proton and a tertiary amine from a quaternary ammonium hydroxide.
imidazole	a five-membered ring compound with two nitrogen heteroatoms and two double bonds.
iron protoporphyrin IX	the porphyrin ring system of heme ligated to an iron atom.
ligation	sharing of nonbonded electrons with a metal.
natural product	a product synthesized in nature.
phase transfer catalysis	catalysis of a reaction by providing a way to bring a polar reagent into a nonpolar phase so that the reaction between a polar and a nonpolar compound can occur.
phase transfer catalyst	a compound that carries a polar reagent into a nonpolar phase.
porphyrin ring system	consists of four pyrrole rings joined by one carbon bridge.
protoporphyrin IX	the porphyrin ring system of heme.
purine	a pyrimidine ring fused to an imidazole ring.

pyrimidine	a benzene ring with nitrogens at the 1- and 3-positions.
pyrrole	a five-membered ring aromatic compound containing a nitrogen heteroatom.
quaternary ammonium ion	a cation containing a nitrogen bonded to four alkyl groups (R_4N^+).
reductive amination	the reaction of an aldehyde or a ketone with ammonia or with a primary amine in the presence of a reducing agent (H_2/Raney Ni).
saturated heterocycle	a heterocyclic compound with no double bonds.
thiophene	a five-membered ring aromatic compound containing a sulfur heteroatom.

Solutions to Problems

1.

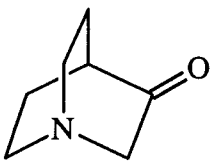
a. 2,2-dimethylaziridine
b. 4-ethylpiperidine
c. 3-methylazacyclobutane
d. 2-methylthiacyclopropane
e. 2,3-dimethyltetrahydrofuran
f. 2-ethyloxacyclobutane

2. The electron-withdrawing oxygen atom of morpholine stabilizes the conjugate base, making protonated morpholine the stronger acid.

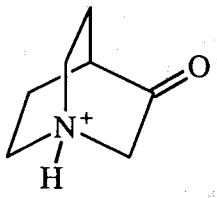


pK_a = 9.28 morpholine pK_a = 11.12 piperidine

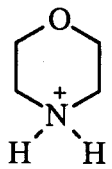
3. **a.**



b. The conjugate acid of 3-quinuclidinone has a lower pK_a than the conjugate acid of morpholine (pK_a = 9.28) because the electron-withdrawing oxygen atom in 3-quinuclidinone is closer to the nitrogen atom.

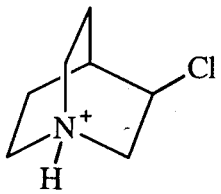


conjugate acid of 3-quinuclidinone

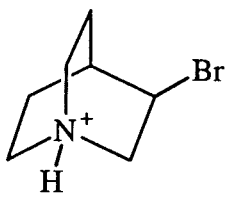


conjugate acid of morpholine

c. The conjugate acid of 3-chloroquinuclidine has a lower pK_a than the conjugate acid of 3-bromoquinuclidine because chlorine is more electronegative than bromine. This means that 3-bromoquinuclidine is a stronger base than 3-chloroquinuclidine.

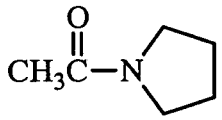


conjugate acid of 3-chloroquinuclidine



conjugate acid of 3-bromoquinuclidine

4. The leaving group of a protonated primary alcohol is a much weaker base (better leaving group) than the leaving group of a protonated primary amine.

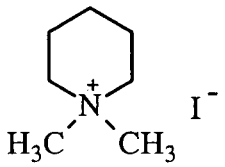
a. 

b. $HOCH_2CH_2CH_2CH_2CH_2I$

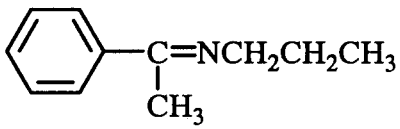
↓ if excess HI is used

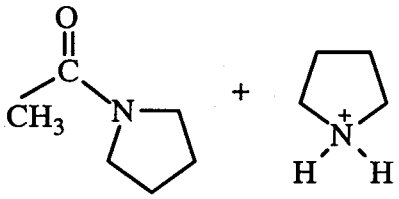
$ICH_2CH_2CH_2CH_2CH_2I$

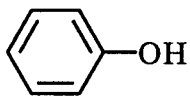
c. $HOCH_2CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

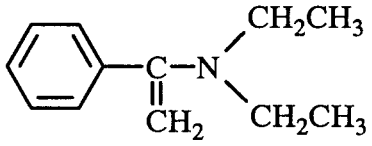
d. 

5.

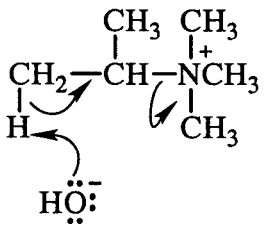
a. 

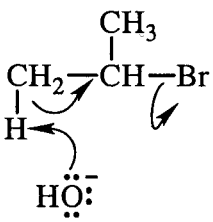
b. 

c. 

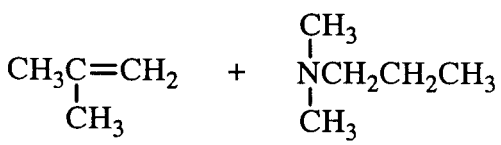
d. 

6. The only difference is the leaving group.





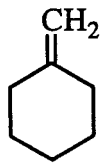
7.



8. In each case, a proton is removed from the β-carbon that is bonded to the greater number of hydrogens.

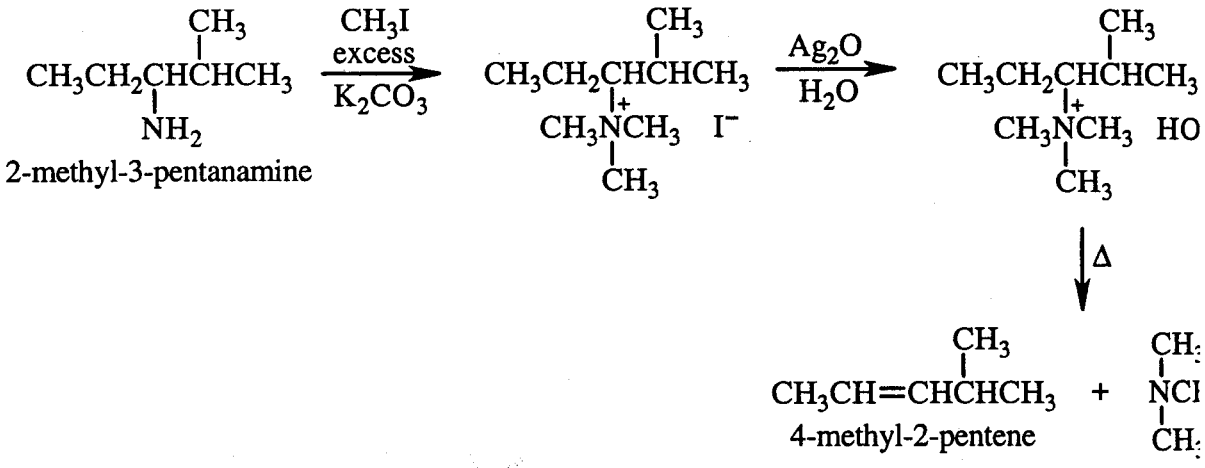
a. $CH_3CH{=}CH_2 + (CH_3)_3N$

b. $CH_2{=}CHCH(CH_3)CH_2CH_2N(CH_3)_2$

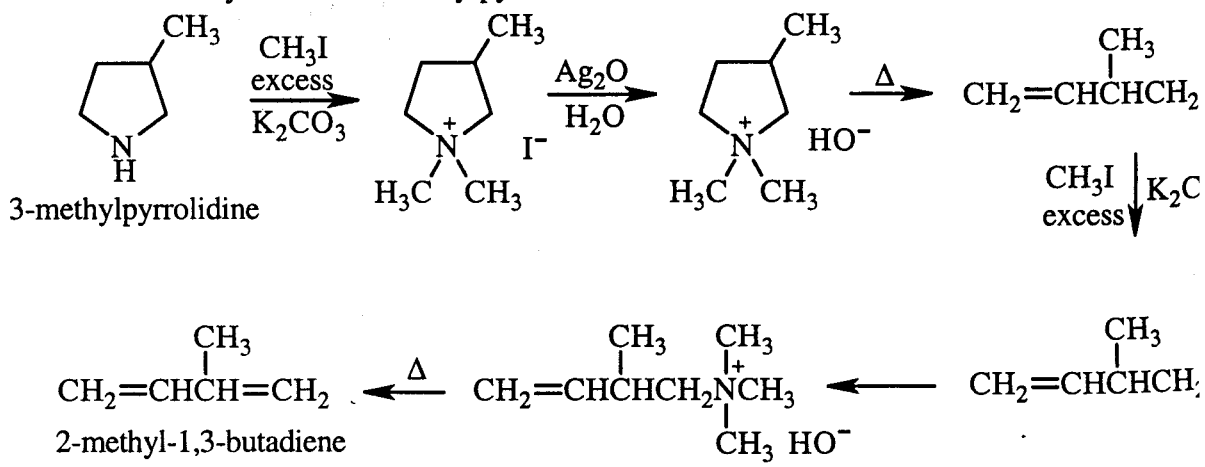
c.  $+ N(CH_3)_3$

d. $CH_3N(CH_3)CH_2CH(CH_3)CH_2CH{=}CH_2$

9. **a.** The primary amine is 2-methyl-3-pentanamine.

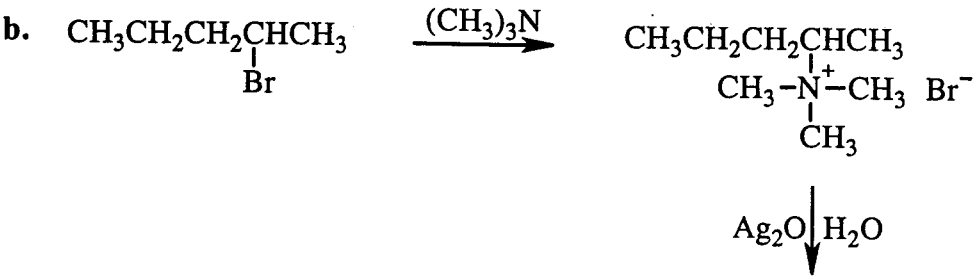


b. The secondary amine is 3-methylpyrrolidine.

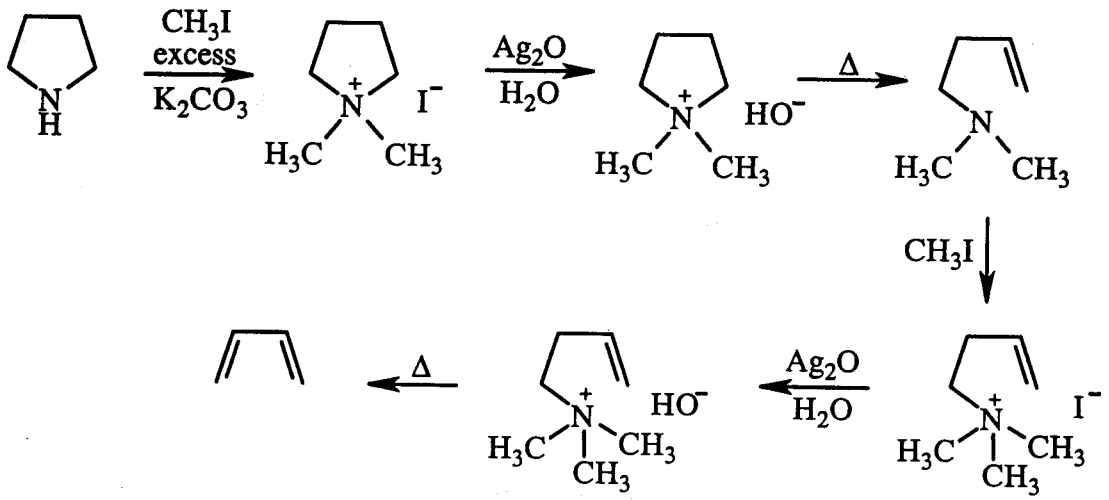


10. **a.** Solved in the text.

b.



c.

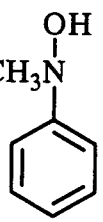


11. Because the major product is the one obtained by removing a proton from the β-carbon bonded to the most hydrogens, we can conclude that the Cope elimination has a "carbanion-like" transition state.

12.

a. $CH_3N(CH_3)OH + CH_2{=}CHCH_3$

b.

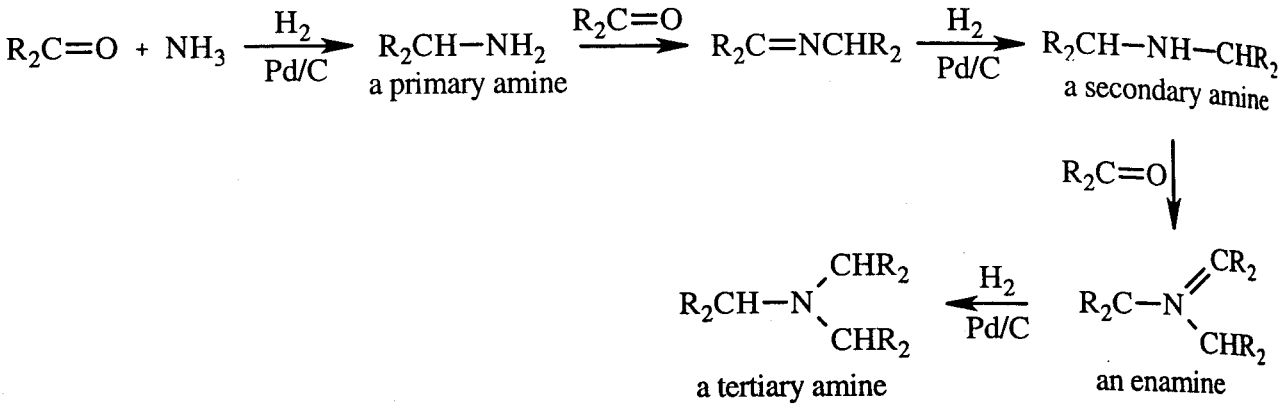


c. $CH_2{=}CH_2 + CH_3N(CH_3)CH_2CH(CH_3)OH$

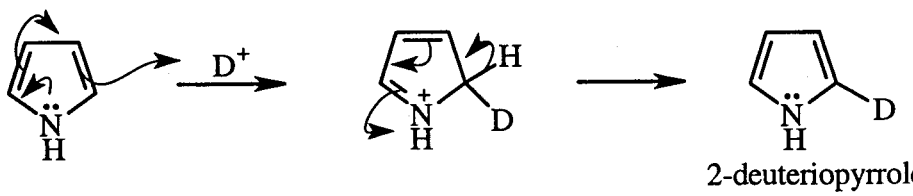
d. $CH_2{=}CHCH_2CH_2CH_2CH_2N(CH_3)OH$

Notice that the methyl group is the β-carbon with the greatest number of hydrogens.

13. Both a secondary amine and a tertiary amine could be obtained. The secondary amine will be obtained because the primary amine synthesized in the first part of the reaction will react with the excess carbonyl compound, forming an imine that will be reduced to a secondary amine. The secondary amine (if steric hindrance does not prevent the reaction) will then react with the carbonyl compound, forming an enamine that will be reduced to a tertiary amine.



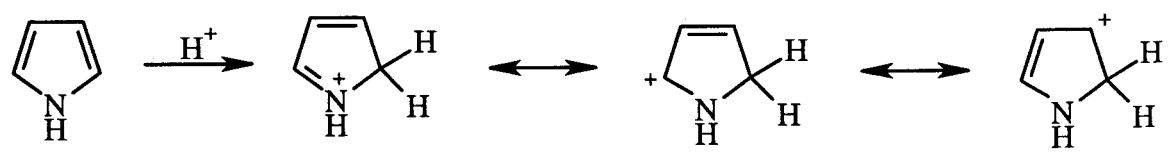
14.



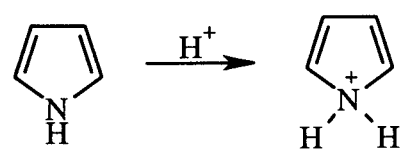
2-deuteriopyrrole

15. Protonation on C-2 leads to a cation with three resonance contributors. Protonation on nitrogen leads to a cation with no resonance contributors. (The positively charged nitrogen cannot accept electrons by resonance, because that would put ten electrons around the nitrogen.)

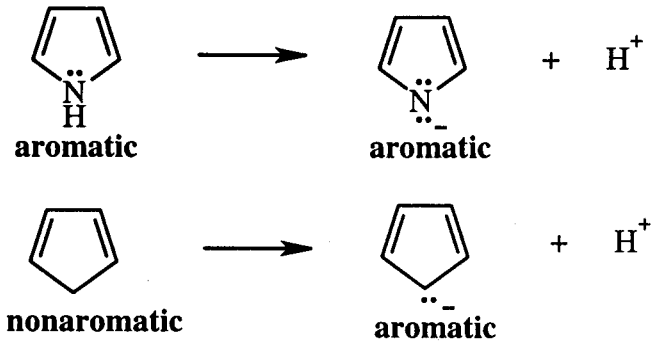
protonation on C-2



protonation on nitrogen

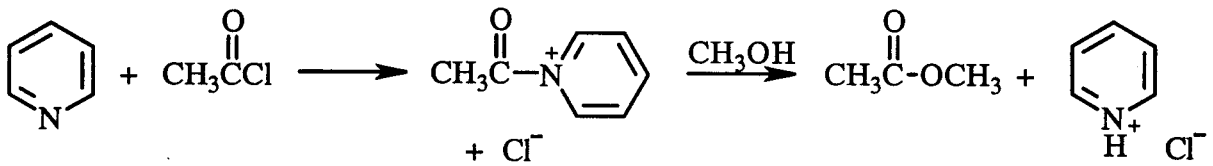


16. Pyrrole is aromatic in both its acidic and basic forms. Cyclopentadiene does not become aromatic until it loses a proton. It is the drive to become a stable aromatic compound that causes cyclopentadiene to be more acidic than pyrrole.

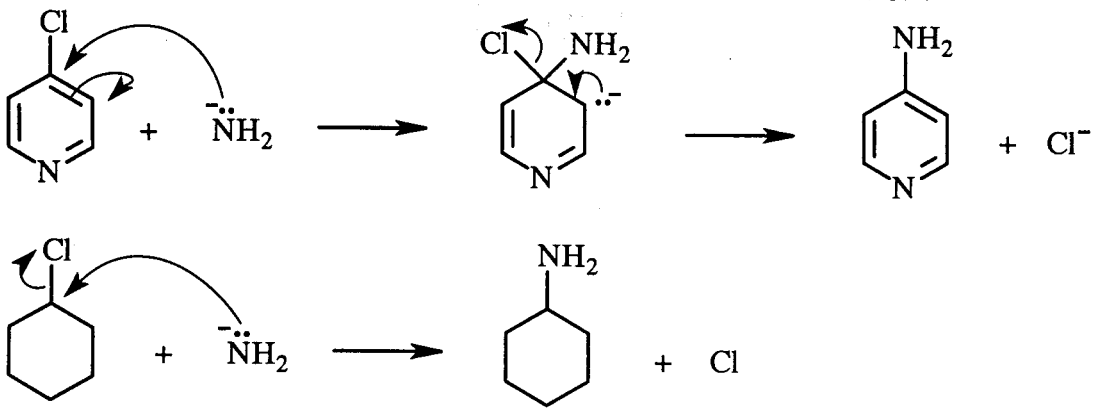


17. Solved in the text.

18. Pyridine will act as an amine with the acid chloride. However, the amide that is formed is very reactive because of its positively charged nitrogen atom. Therefore, it will undergo a nucleophilic acyl substitution reaction with methanol, forming an ester as the final product of the reaction.

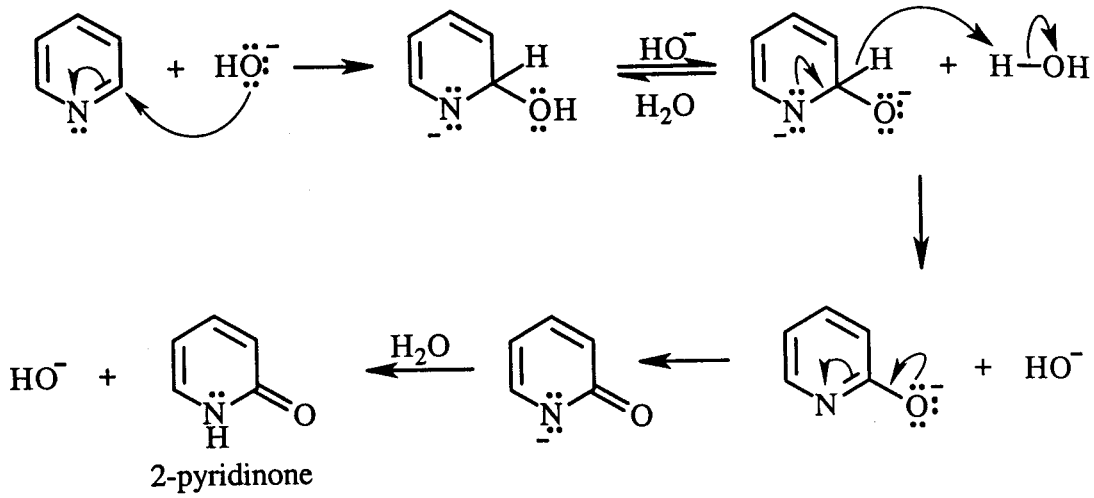


19. The first reaction is a two-step nucleophilic aromatic substitution reaction (S_NAr). The second reaction is a one-step nucleophilic substitution reaction (S_N2).



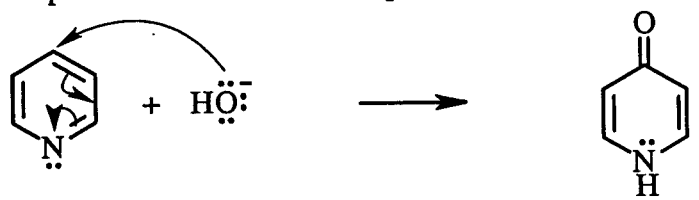
20.

a.



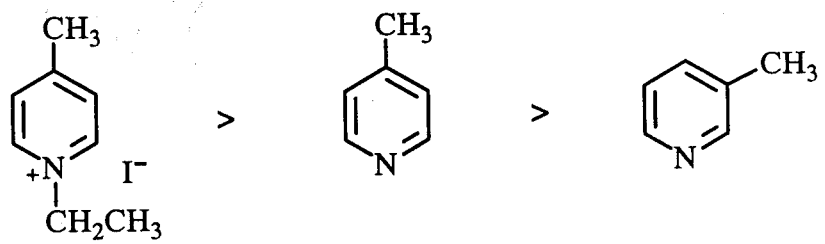
2-pyridinone

b. 4-Pyridinone is also formed because nucleophilic attack by hydroxide ion can take place at the 4-position as well as at the 2-position.



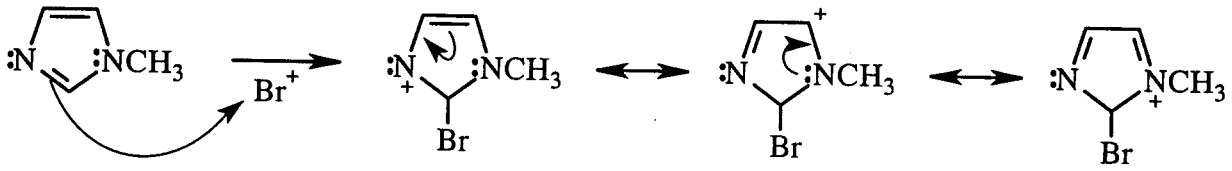
4-pyridinone

21. It is easiest to remove a proton from the *N*-alkylated pyridine because the electrons left behind when the proton is removed can be delocalized onto the positively charged nitrogen atom. It is easier to remove a proton from 4-methylpyridine than from 3-methylpyridine because in the former, the electrons left behind when the proton is removed can be delocalized onto the electronegative nitrogen atom. In 3-methylpyridine, the electrons can be delocalized only onto carbon atoms.

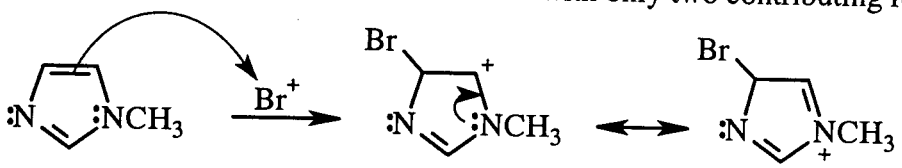


22. There are three possible sites for electrophilic substitution: C-2, C-4, and C-5. To determine the major product, compare the relative stabilities of the carbocations formed in the first step of the reaction.

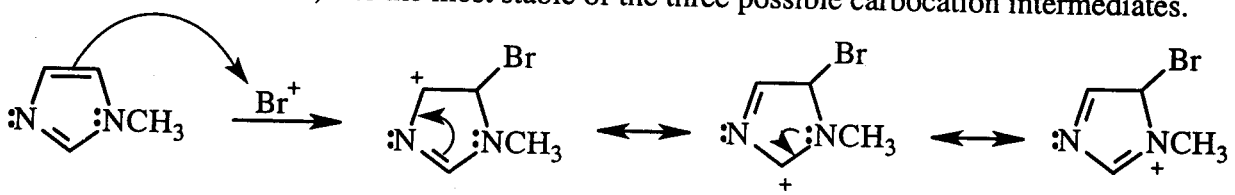
Substitution at C-2 leads to a carbocation with three contributing resonance structures. One of them is particularly unstable, because the positive charge is on a nitrogen atom that does not have a complete octet.



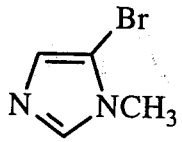
Substitution at C-4 leads to a carbocation with only two contributing resonance structures.



Substitution at C-5 leads to a carbocation with three contributing resonance structures. Because none of them are as unstable as one of the contributing resonance structures obtained from substitution at C-2, it is the most stable of the three possible carbocation intermediates.

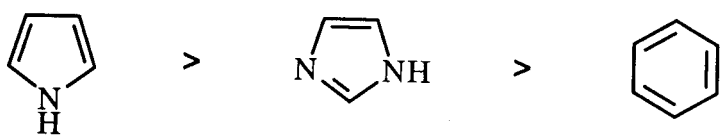


Therefore, the major product of the reaction is 5-bromo-*N*-methylimidazole.

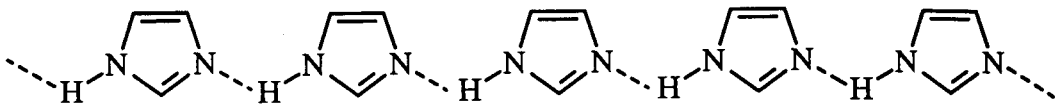


5-bromo-*N*-methylimidazole

23. Pyrrole and imidazole are more reactive than benzene because each has a carbocation intermediate that can be stabilized by resonance electron donation into the ring by a nitrogen atom.
Pyrrole is more reactive than imidazole because the second nitrogen atom of imidazole cannot donate electrons into the ring by resonance but can only withdraw electrons from the ring inductively.



24. Imidazole forms intermolecular hydrogen bonds, whereas *N*-methylimidazole cannot form hydrogen bonds. Because the hydrogen bonds have to be broken in order for the compound to boil, imidazole has a higher boiling point.





This compound cannot form hydrogen bonds, because it does not have a hydrogen bonded to a nitrogen.

25.

$$\text{fraction of imidazole in the acidic form} = \frac{[H^+]}{K_a + [H^+]}$$

$$pH = 7.3;\ [H^+] = 5.0 \times 10^{-8}$$

$$pK_a = 6.8;\ K_a = 1.58 \times 10^{-7}$$

$$\text{fraction of imidazole in the acidic form} = \frac{5.0 \times 10^{-8}}{1.58 \times 10^{-7} + 5.0 \times 10^{-8}}$$

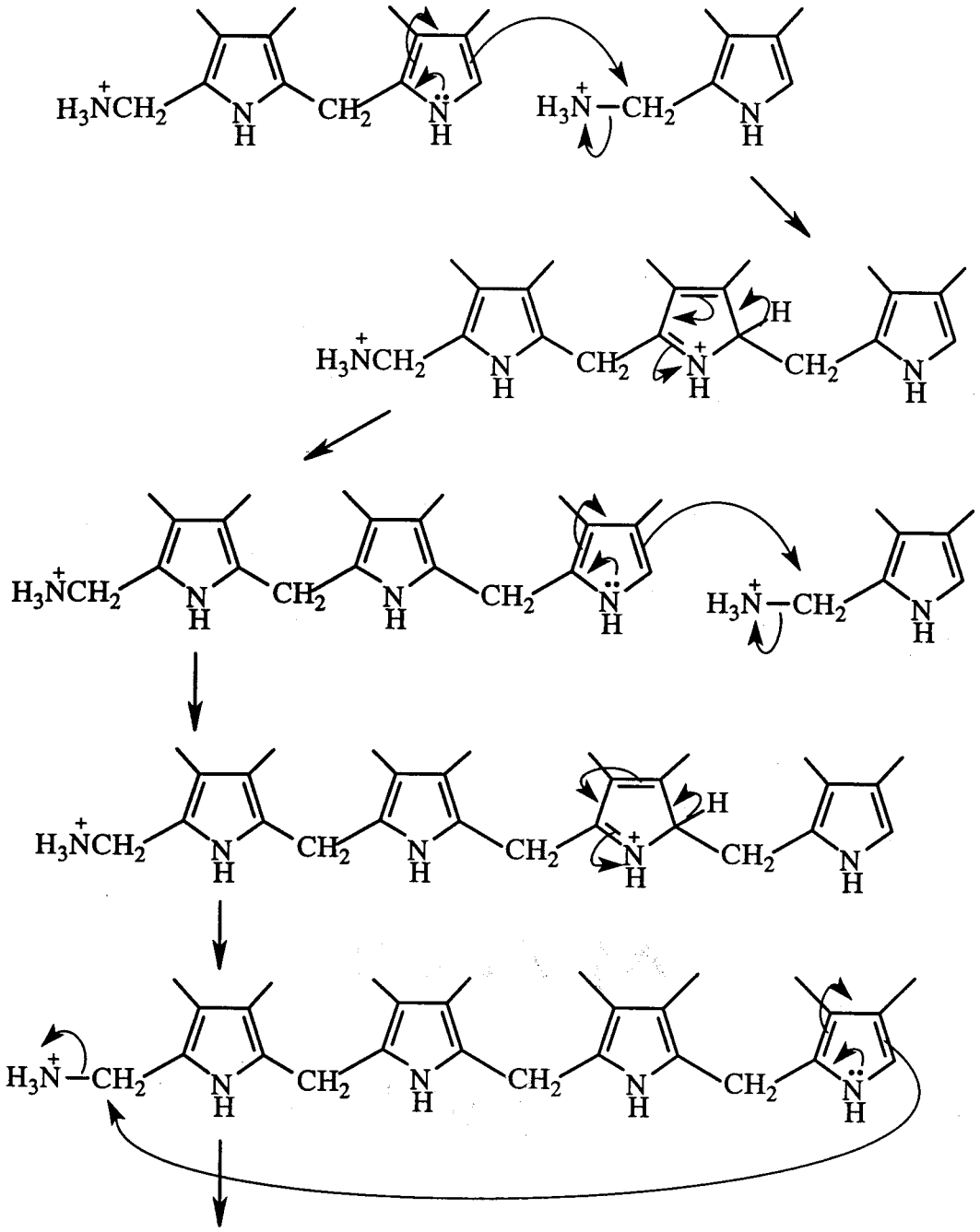
$$= \frac{5.0 \times 10^{-8}}{2.08 \times 10^{-7}}$$

$$= 0.24$$

$$\text{percent of imidazole in the acidic form} = 24\%$$

26. Yes, porphyrin is aromatic, because it fulfills the two requirements for aromaticity. It has an uninterrupted ring of *p* orbital-bearing atoms (it is cyclic and planar), and the π cloud contains an odd number of pairs (thirteen pairs) of π electrons.

27.

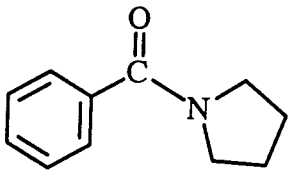


A proton is lost in the next step, which restores the aromaticity of the right-hand ring. Subsequent oxidation results in the formation of porphyrin.

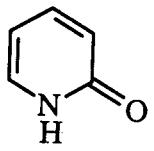
28. **a.** 2-methylazacyclobutane
b. 2,3-dimethylpiperidine
c. 3-chloropyrrole
d. 2-ethyl-5-methylpiperidine

29.

a.

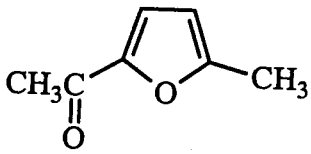


b.

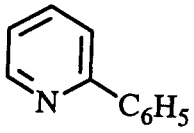


c. $CH_3CH_2CH_2CH_2CH_2NH_2$

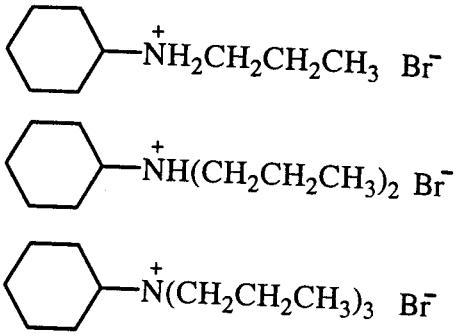
d.



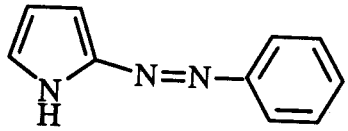
e.



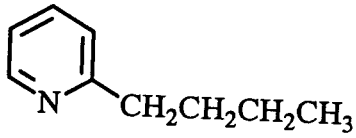
f.



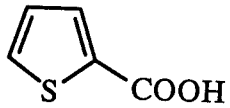
g.



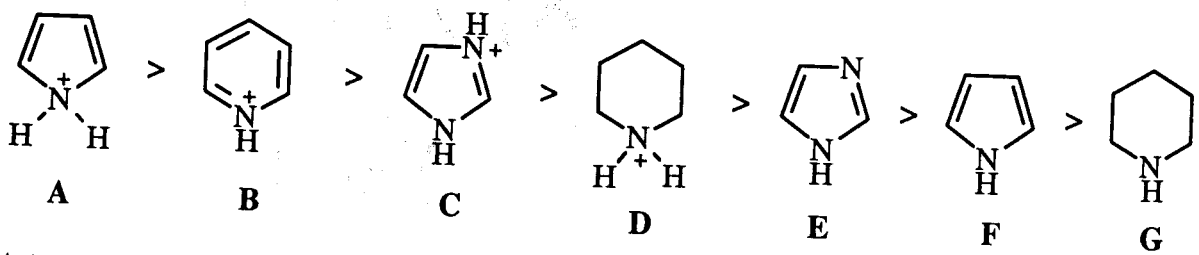
h.



i.



30.



A **B** **C** **D** **E** **F** **G**

A is the most acidic because it becomes aromatic when it loses a proton.

B, **C**, and **D** are the next most acidic because in all three, the proton is bonded to a positively charged nitrogen atom.

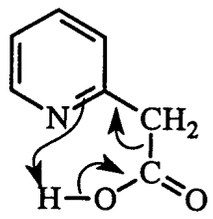
B and **C** are more acidic than **D** because in **B** and **C** the proton to be lost is bonded to an sp^2 hybridized nitrogen atom, which is more electronegative than the sp^3 hybridized nitrogen atom in **D**.

B is more acidic than **C** because the uncharged nitrogen atom in **C** can donate electrons by resonance to the positively charged nitrogen atom.

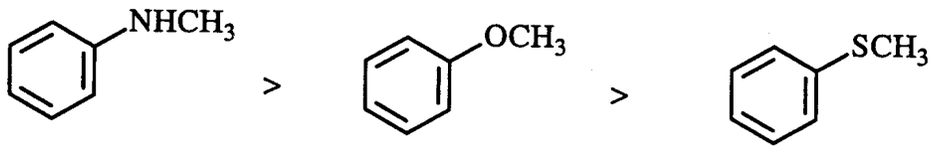
Neutral compounds **E**, **F**, and **G** are the least acidic, with **E** and **F** more acidic than **G**, because **E** and **F** lose a proton from an sp^2 nitrogen atom, while a proton is lost from a less electronegative sp^3 nitrogen atom in **G**.

E is more acidic than **F** because of the electron-withdrawing second nitrogen in **E**.

31. The compound on the right (shown below) is easier to decarboxylate because the electrons left behind when CO_2 is removed can be delocalized onto nitrogen and stabilized by accepting a proton from oxygen. The electrons left behind when the other compound loses CO_2 cannot be delocalized.



32.



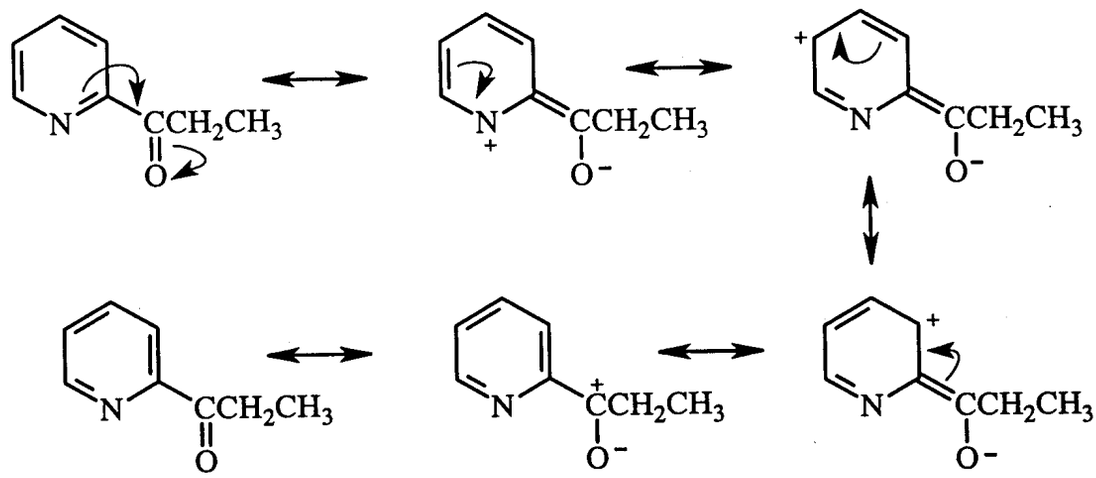
The *N*-, *O*-, and *S*-substituted benzenes have the same relative reactivity toward electrophilic aromatic substitution as the *N*-, *O*-, and *S*-containing five-membered heterocyclic rings and for the same reason.

The *N*-substituted benzene is more reactive than the *O*-substituted benzene, because nitrogen is more effective than oxygen at donating electrons into the benzene ring, since it is less electronegative than oxygen. (Recall that electrophilic substitution is aided by electron donation into the ring.)

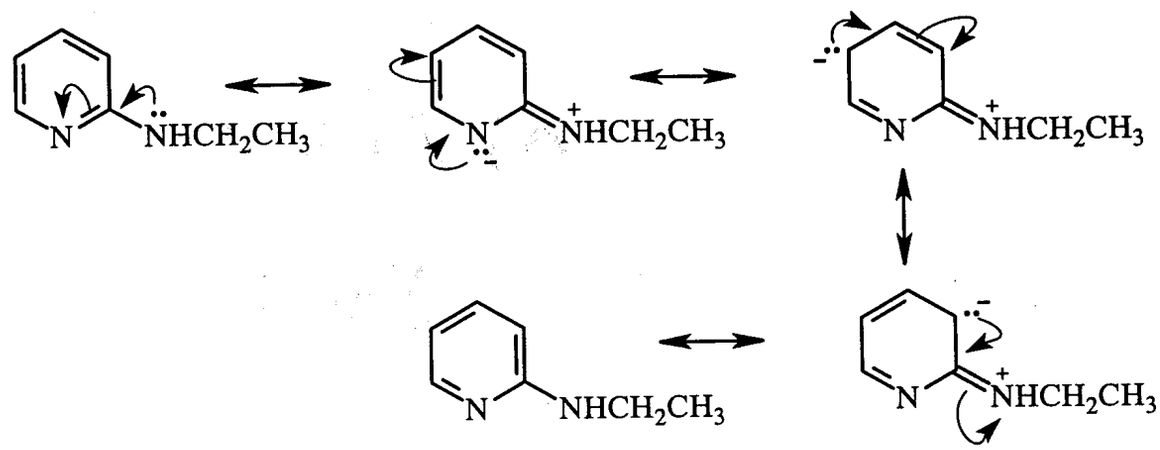
The *S*-substituted benzene is the least reactive because the lone-pair electrons of sulfur are in a 3*p* orbital, whereas the nonbonding electrons of nitrogen and oxygen are in a 2*p* orbital. The overlap of a 3*p* orbital with the 2*p* orbitals of carbon is less effective than the overlap of a 2*p* orbital with the 2*p* orbitals of carbon.

33. Because the slow step in aromatic electrophilic substitution is getting the electrophile onto the ring, electrophilic substitution will take place at the ring position with the greatest electron density.

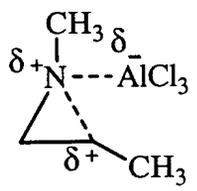
The ketone substituent withdraws electrons by resonance, putting a partial positive charge on the #1, #3, and #5 positions. Therefore, electrophilic substitution will take place at the #4 and #6 positions, since they are more electron dense than the positions with partial positive charges.



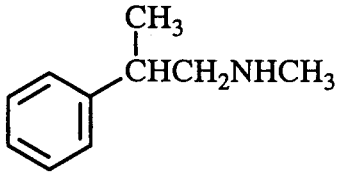
The amino substituent donates electrons into the ring by resonance. The resonance structures show that the extra electron density resides on the #3 and #5 positions. Since these positions are the most electron dense, this is where electrophilic substitution will take place.



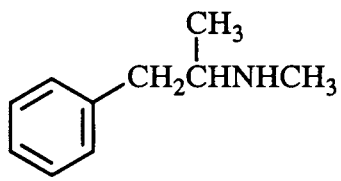
34. **a.** The Lewis acid, $AlCl_3$, complexes with nitrogen, causing the aziridine ring to open when it attacked by the nucleophilic benzene ring. The ring will open in the direction that puts the partial positive charge on the more substituted carbon (more stable carbocation).



The major and minor products are those shown.



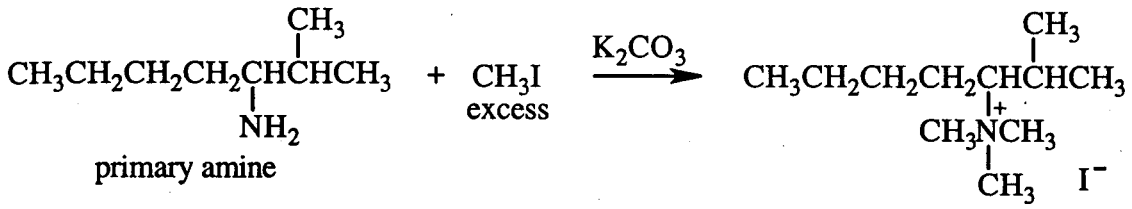
major

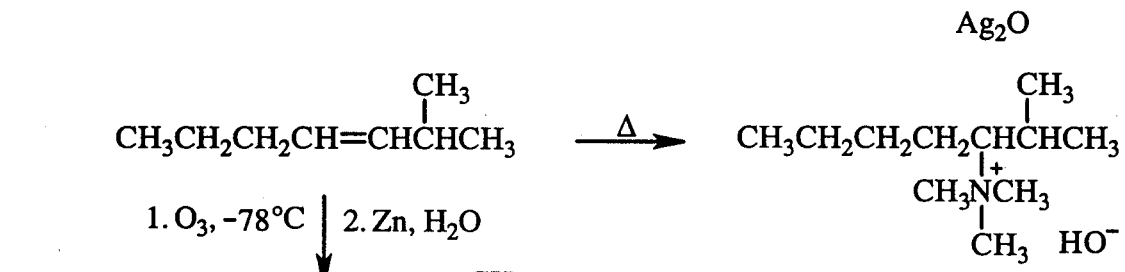


minor

b. Yes, epoxides can undergo similar reactions.

35.





36. Oxygen is the negative end of the dipole in both compounds. Tetrahydrofuran has the greater dipole moment because in furan the effect of the electron-withdrawing oxygen is mitigated by the ability of oxygen to donate electrons by resonance into the ring.

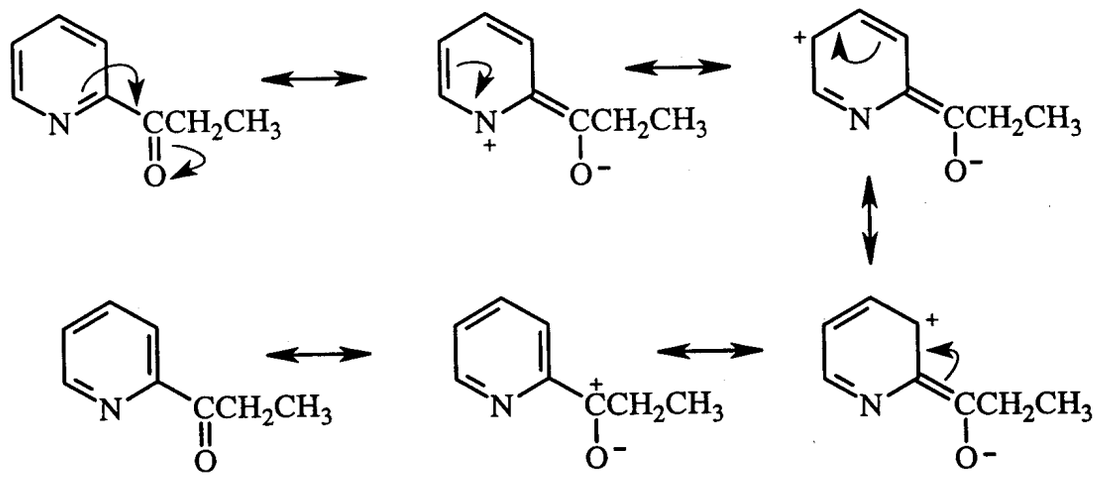


tetrahydrofuran
1.73 D

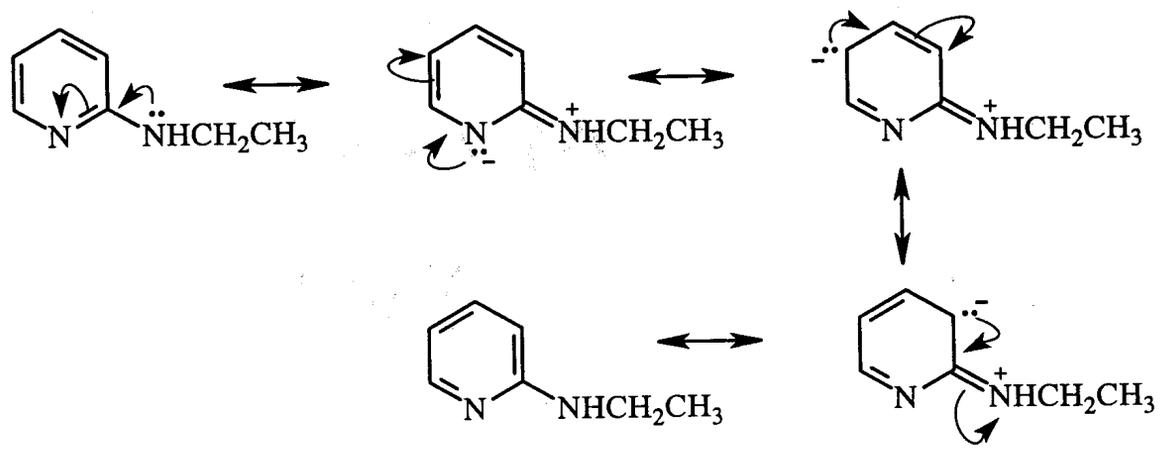
furan
0.70 D

33. Because the slow step in aromatic electrophilic substitution is getting the electrophile onto the ring, electrophilic substitution will take place at the ring position with the greatest electron density.

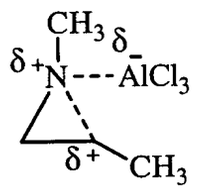
The ketone substituent withdraws electrons by resonance, putting a partial positive charge on the #1, #3, and #5 positions. Therefore, electrophilic substitution will take place at the #4 and #6 positions, since they are more electron dense than the positions with partial positive charges.



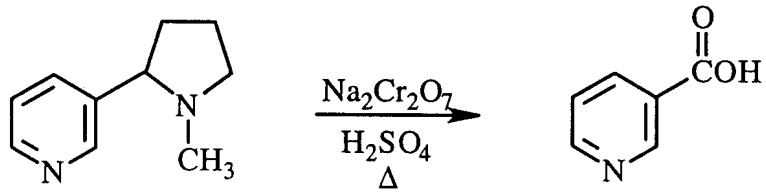
The amino substituent donates electrons into the ring by resonance. The resonance structures show that the extra electron density resides on the #3 and #5 positions. Since these positions are the most electron dense, this is where electrophilic substitution will take place.



34. **a.** The Lewis acid, $AlCl_3$, complexes with nitrogen, causing the aziridine ring to open when it attacked by the nucleophilic benzene ring. The ring will open in the direction that puts the partial positive charge on the more substituted carbon (more stable carbocation).



37. We saw in Section 16.2 of the text that an alkyl substituent bonded to a benzene ring can be oxidized to a carboxylic acid substituent. Similarly, an alkyl substituent bonded to a pyridine ring can be oxidized to a carboxylic acid substituent. Nicotine is an alkaloid found in tobacco leaves. It is used in agriculture as an insecticide.

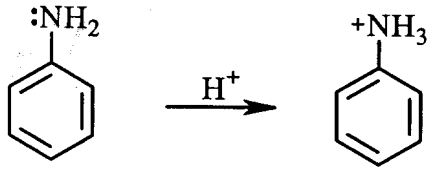


nicotine niacin

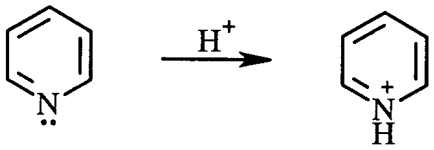
38. Pyrrolidine is a saturated nonaromatic compound, whereas pyrrole and pyridine are unsaturat aromatic compounds. The C-2 hydrogens of pyrrolidine are at δ 2.82, about where one would expect the signal for hydrogens bonded to an sp^3 carbon adjacent to an electron-withdrawing amino group.

The C-2 hydrogens of pyrrole and pyridine are expected to be farther downfield because of magnetic anisotropy. Because the nitrogen of pyrrole donates electrons into the ring and the nitrogen of pyridine withdraws electrons from the ring, the C-2 hydrogens of pyrrole are in a environment with a greater electron density, so they should show a signal upfield relative to C-2 hydrogens of pyridine. Thus, the C-2 hydrogens of pyrrole are at δ 6.42, and the C-2 hydrogens of pyridine are at δ 8.50.

39. A UV spectrum results from the π electron system. The lone-pair electrons on the nitrogen atom in aniline is delocalized into the benzene ring and, thus, is part of the π system. Protonation of aniline removes two electrons from the π system, which has a significant effe its UV spectrum.



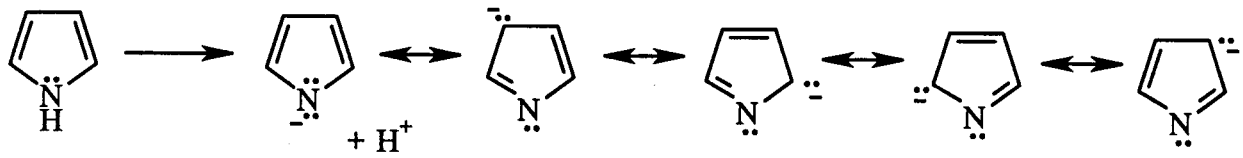
The lone-pair electrons on the nitrogen atom in pyridine are sp^2 electrons and thus are not pa of the π system. Protonation of pyridine, therefore, does not remove any electrons from the π system and has only a minor effect on the UV spectrum.



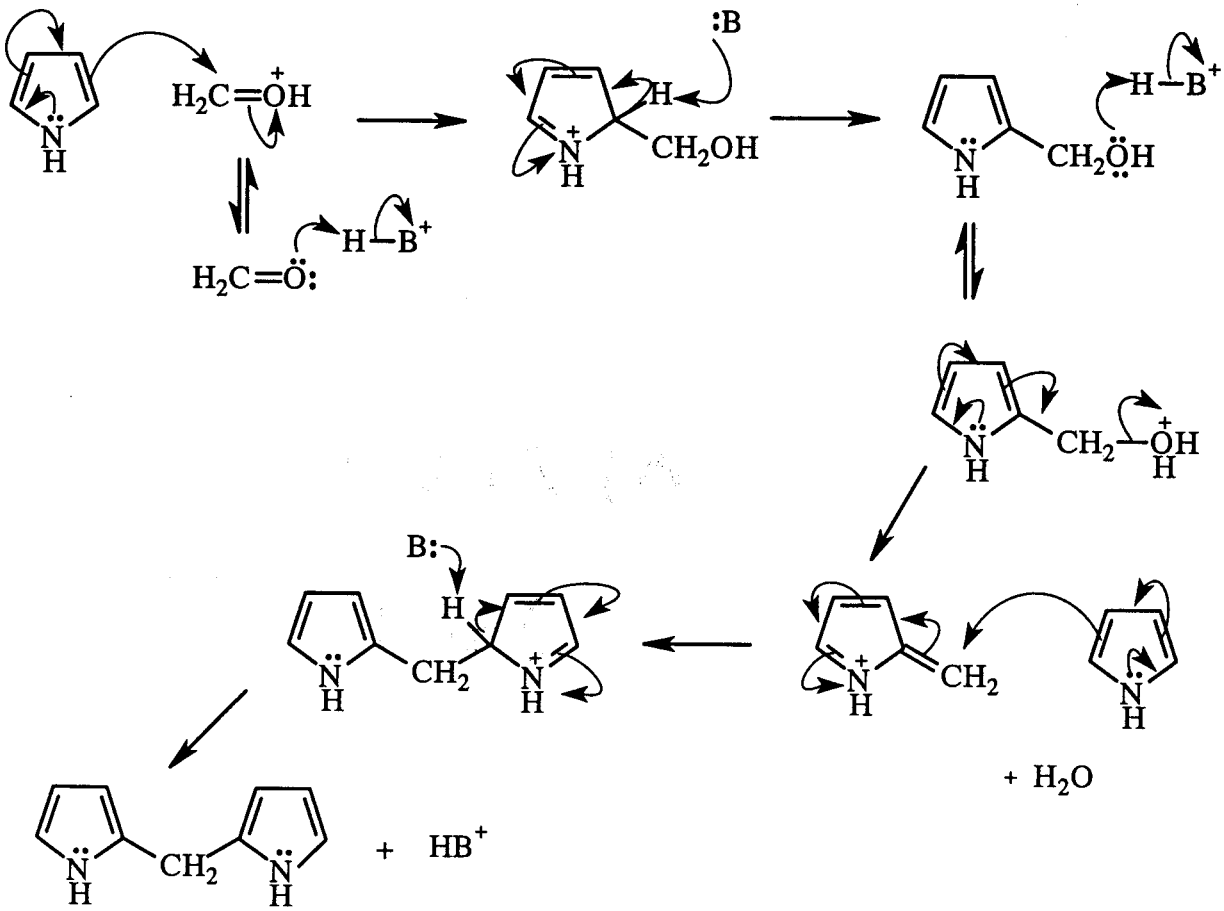
40. When ammonia loses a proton, the electrons left behind remain on nitrogen.



When pyrrole loses a proton, the electrons left behind can be delocalized onto the four ring carbons. Electron delocalization stabilizes the anion and makes it easier to form.

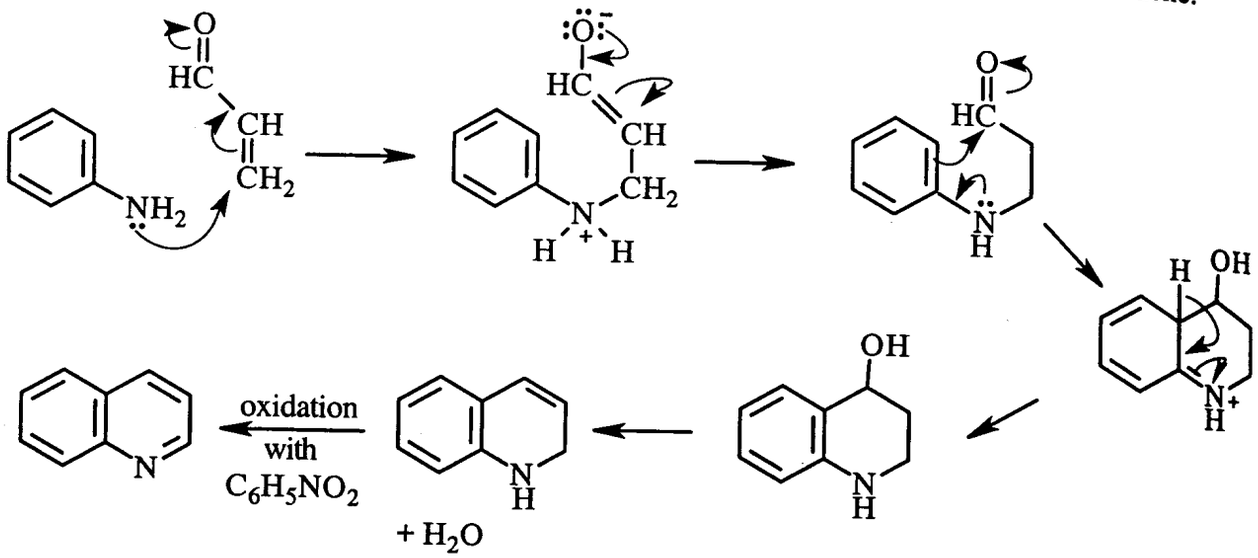


41.

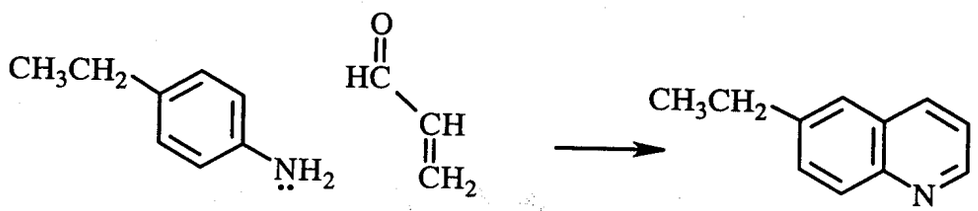


42. Before we can answer the questions, we must figure out the mechanism of the reaction. Once the mechanism is known, it will be easy to determine how a change in a reactant will affect the product. The mechanism is shown below:

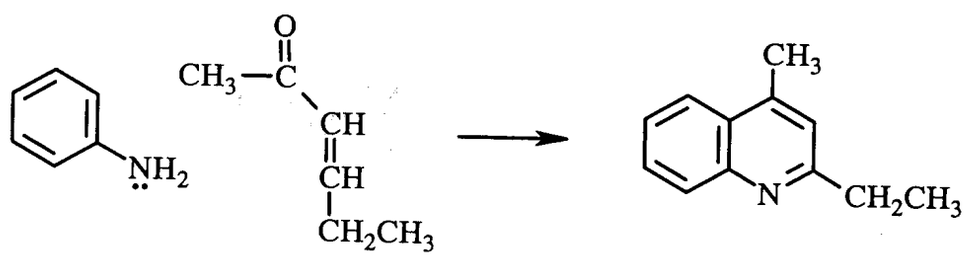
Propenal, an α,β-unsaturated aldehyde, undergoes a conjugate addition reaction with aniline. This is followed by an intramolecular electrophilic aromatic substitution reaction. Dehydration of the alcohol results in 1,2-dihydroquinoline, which is oxidized to quinoline by nitrobenzene.



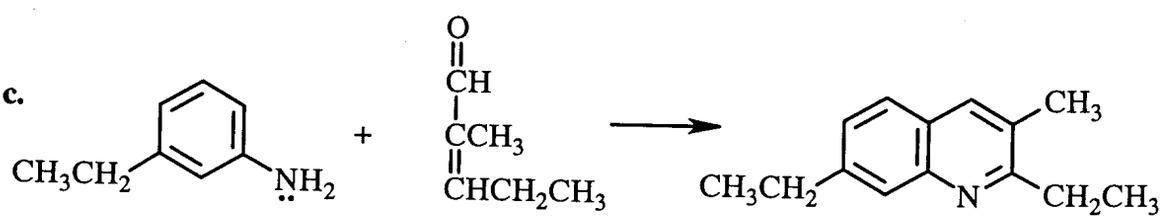
a.



b.



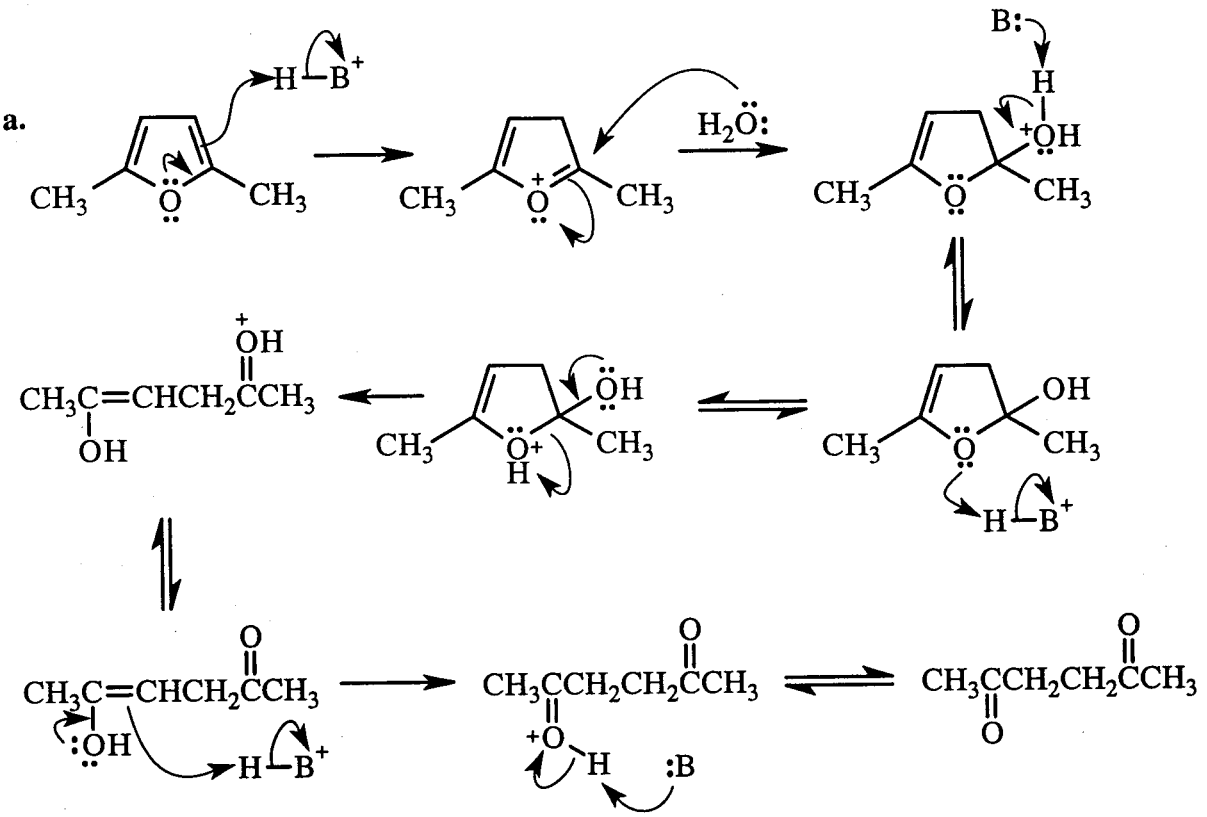
c.



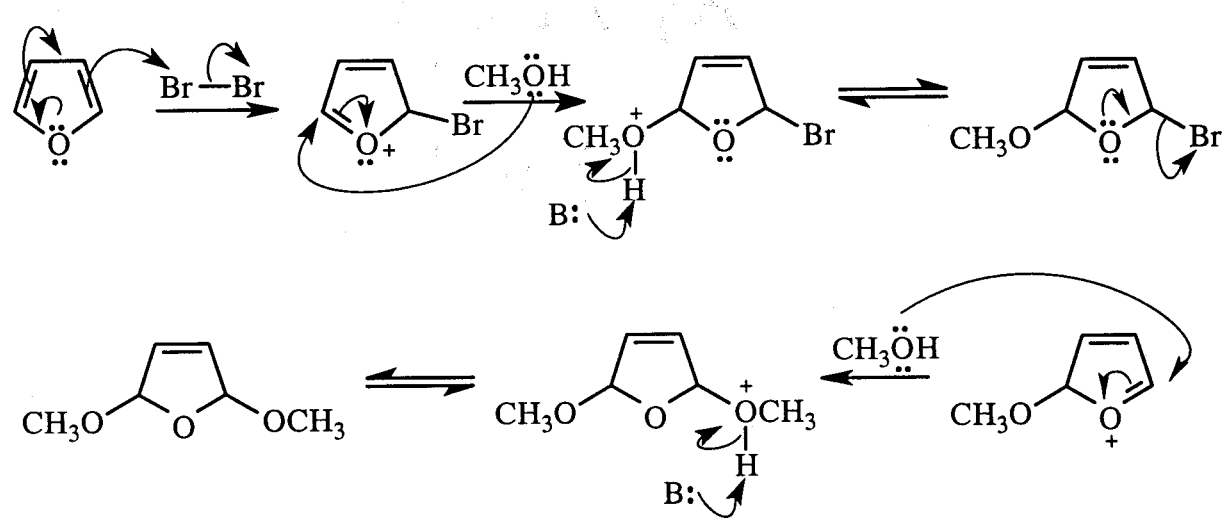
meta-ethylaniline + 2-methyl-2-pentenal → 2,7-diethyl-3-methylquinoline

3.

a.

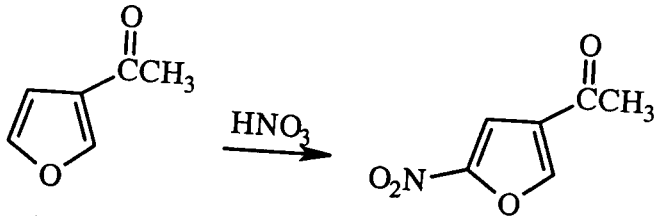


b.

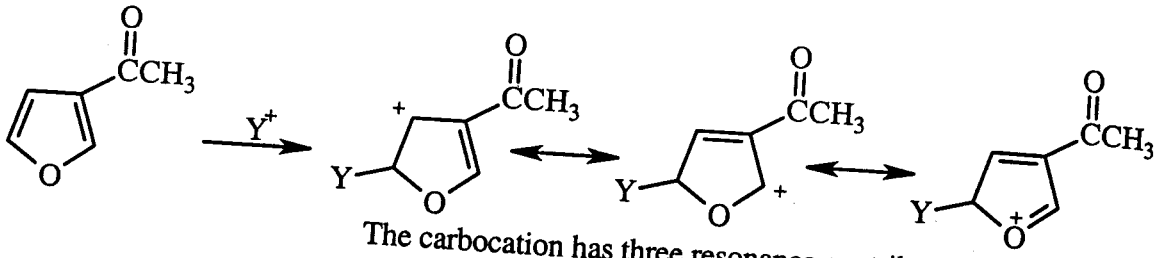


44.

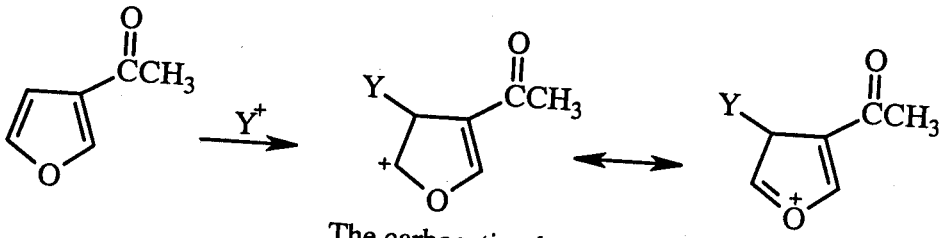
a.



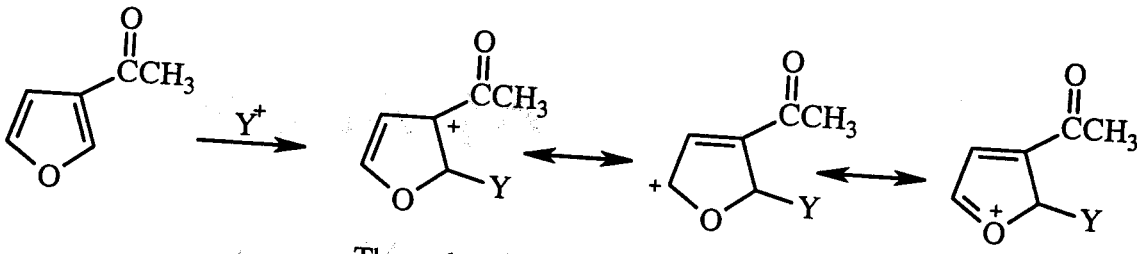
You can see why the nitro substituent goes to this position by examining the relative stabilities of the possible carbocation intermediates.



The carbocation has three resonance contributors.

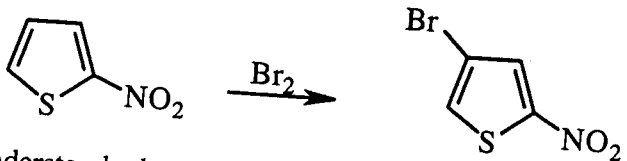


The carbocation has two resonance contributors.

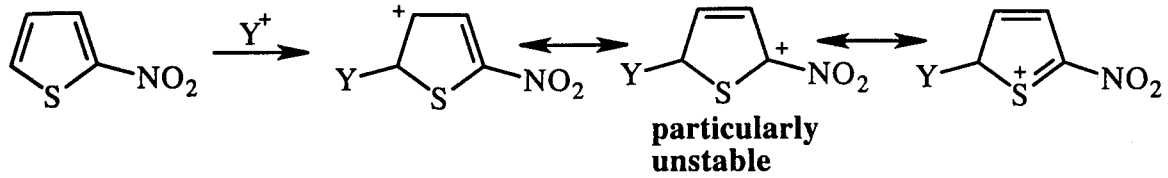


The carbocation has three resonance contributors, but the first one is relatively unstable because the positive charge is on the carbon attached to the electron-withdrawing substituent.

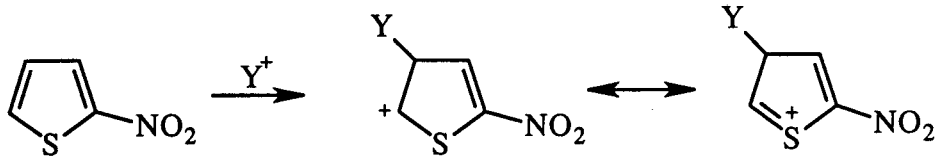
b.

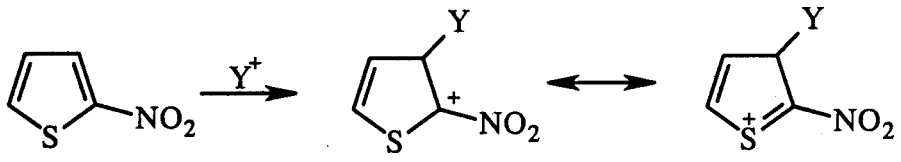


You can understand why the bromo substituent goes to this position by examining the relative stabilities of the possible carbocation intermediates.



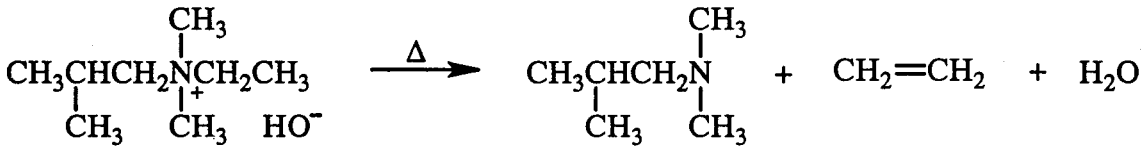
particularly unstable



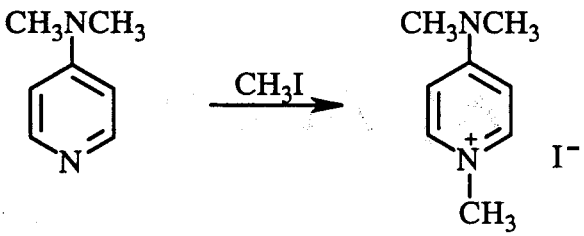


particularly unstable

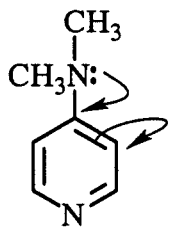
c.



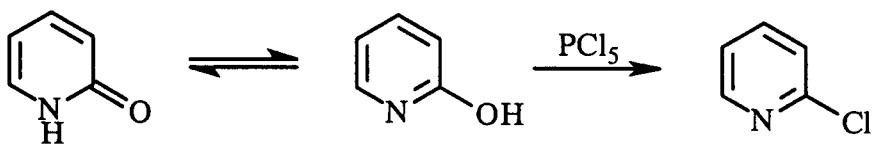
d.



The other nitrogen is not alkylated, because its lone pair is delocalized into the pyridine ring, so it are not available to react with the alkyl halide.

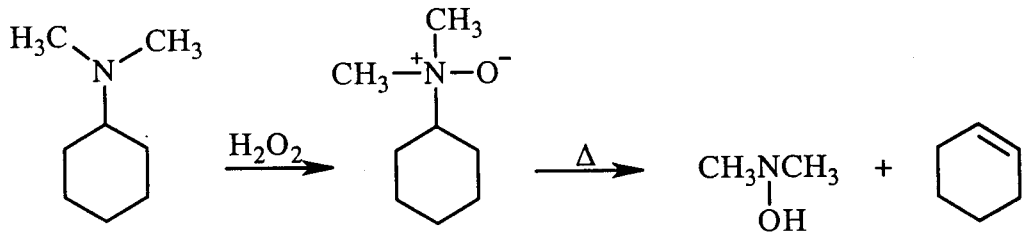


e.

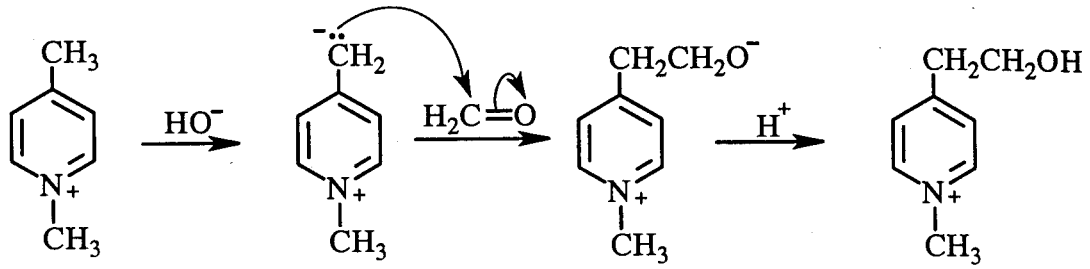


PCl_5 substitutes a Cl for an OH, as it does in alcohols and carboxylic acids.

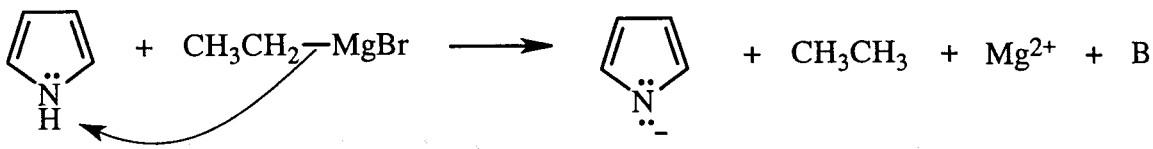
f.



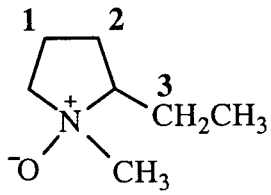
g. In the first step, hydroxide ion removes the most acidic hydrogen from the compound. A hydrogen bonded to the C-4 methyl group is the most acidic hydrogen because the electron left behind when the proton is removed can be delocalized into the pyridinium ring. In contrast, the electrons left behind when a proton is removed from the N-methyl group cannot be delocalized.

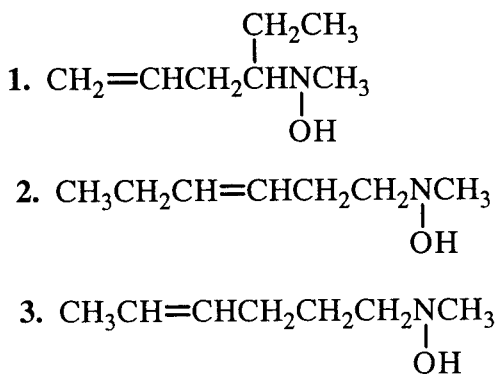


h.

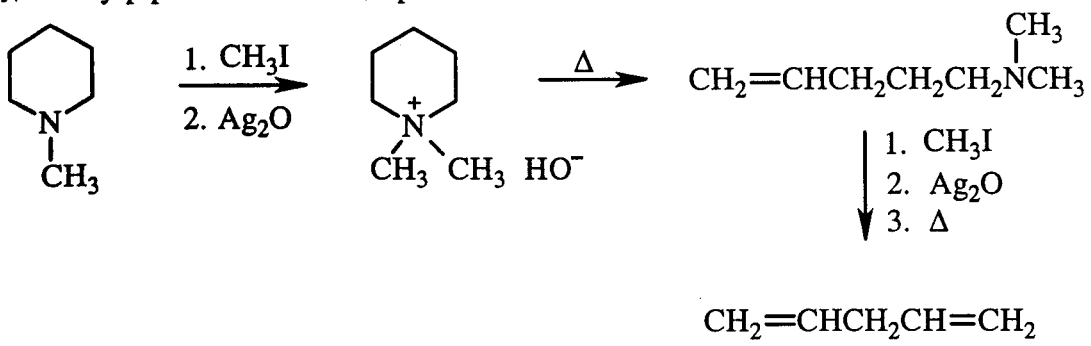


i. The tertiary amine oxide will have a proton removed from the β-carbon that is bonded to the greater number of hydrogens. Each of the three β-carbon atoms of this tertiary amine oxide is attached to two hydrogens, so three products will be formed.

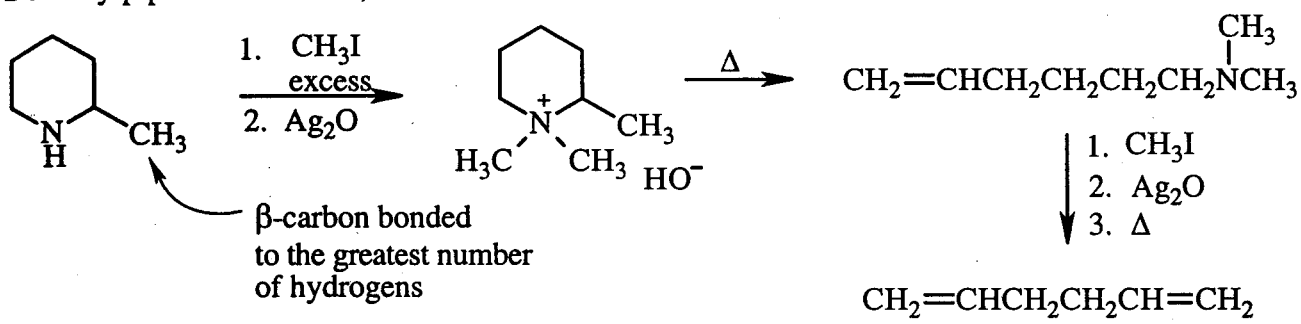




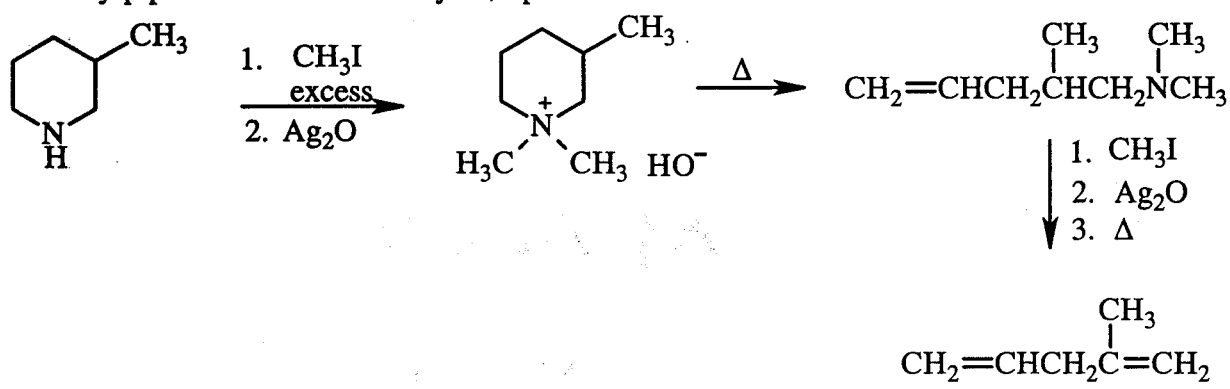
45. *N*-Methylpiperidine forms 1,4-pentadiene.



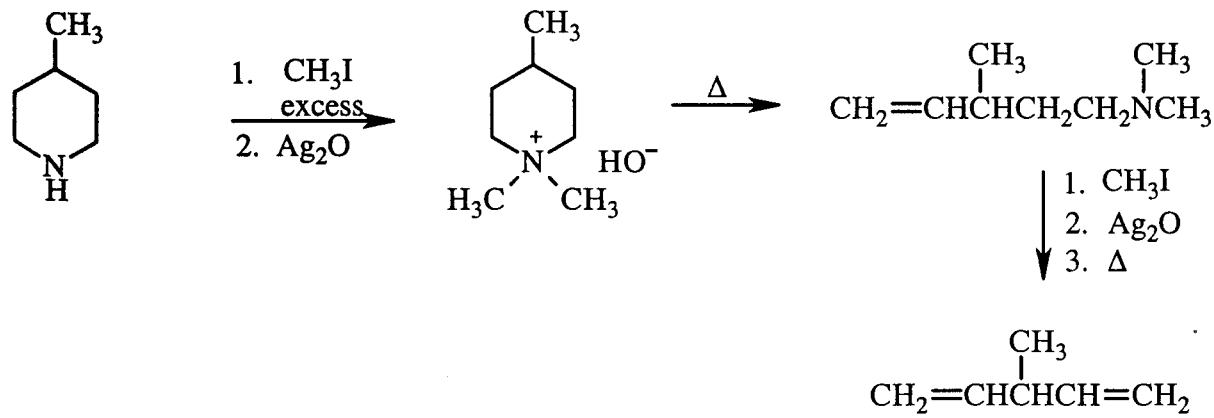
2-Methylpiperidine forms 1,5-hexadiene.



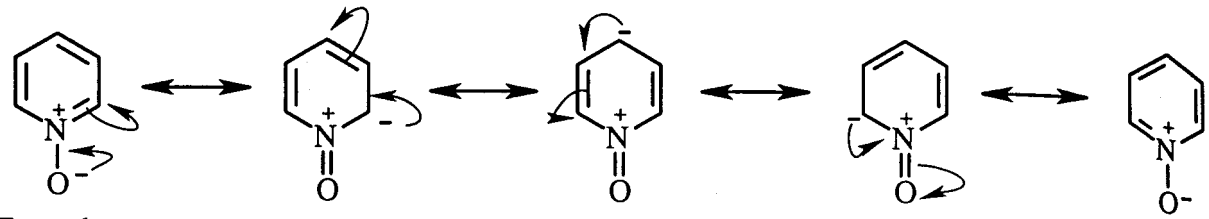
3-Methylpiperidine forms 2-methyl-1,4-pentadiene.



4-Methylpiperidine forms 3-methyl-1,4-pentadiene.

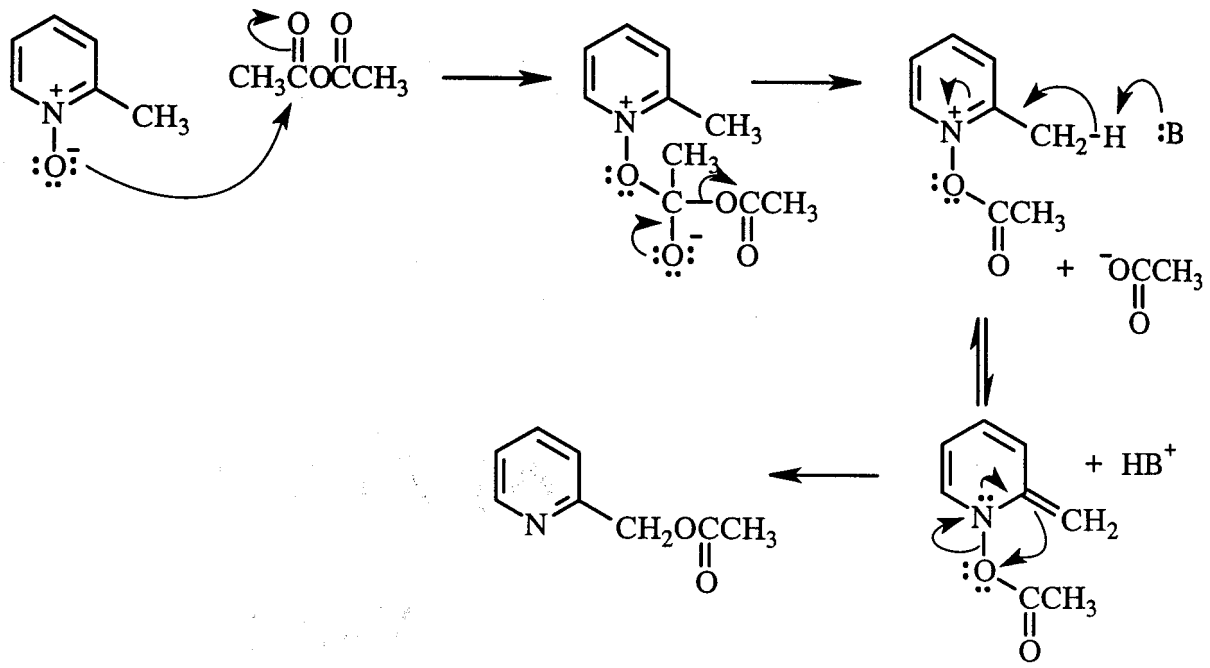


46. The increase in the electron density of the ring as a result of resonance donation of electrons by oxygen causes pyridine-*N*-oxide to be more reactive toward electrophilic substitution than pyridine.



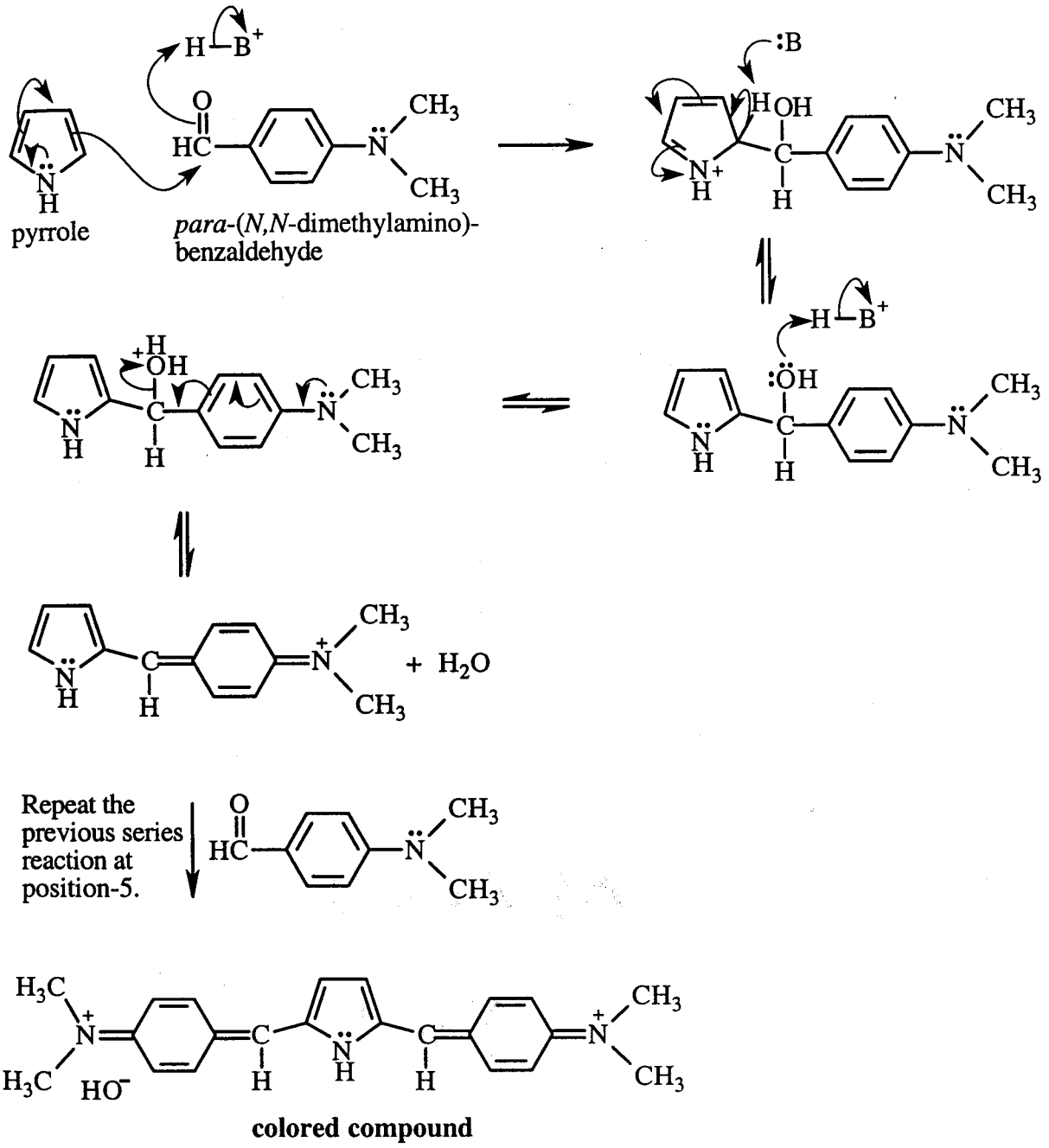
From the resonance structures you can see that the increased electron density is at the 2- and 4-positions. Because the 2-position is somewhat sterically hindered, pyridine-*N*-oxide undergoes electrophilic substitution primarily at the 4-position.

47.



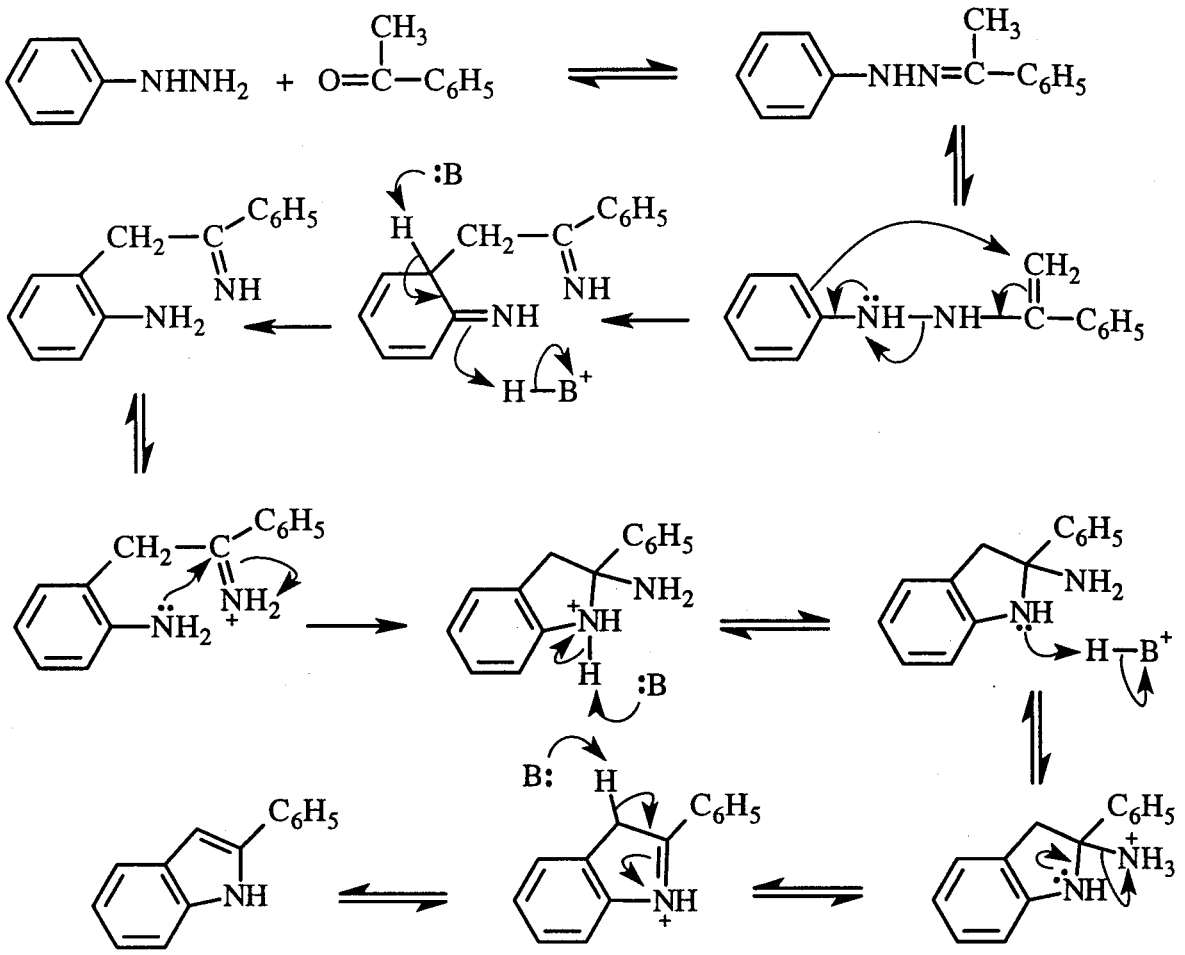
48. The C—N—C internal bond angle of the aziridinium ion is smaller than usual because of the three-membered ring. This causes the external bond angles to be somewhat larger than usual. The larger external bond angles cause the orbital that nitrogen uses to overlap the orbital of hydrogen to have more *s* character than a typical sp^3 orbital. The greater *s* character makes the nitrogen more electronegative which lowers the pK_a

49.

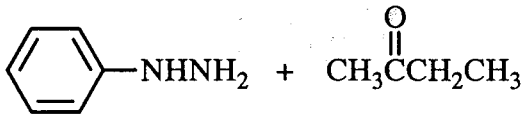


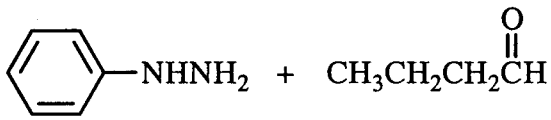
colored compound

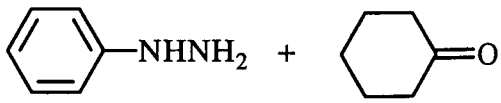
50.



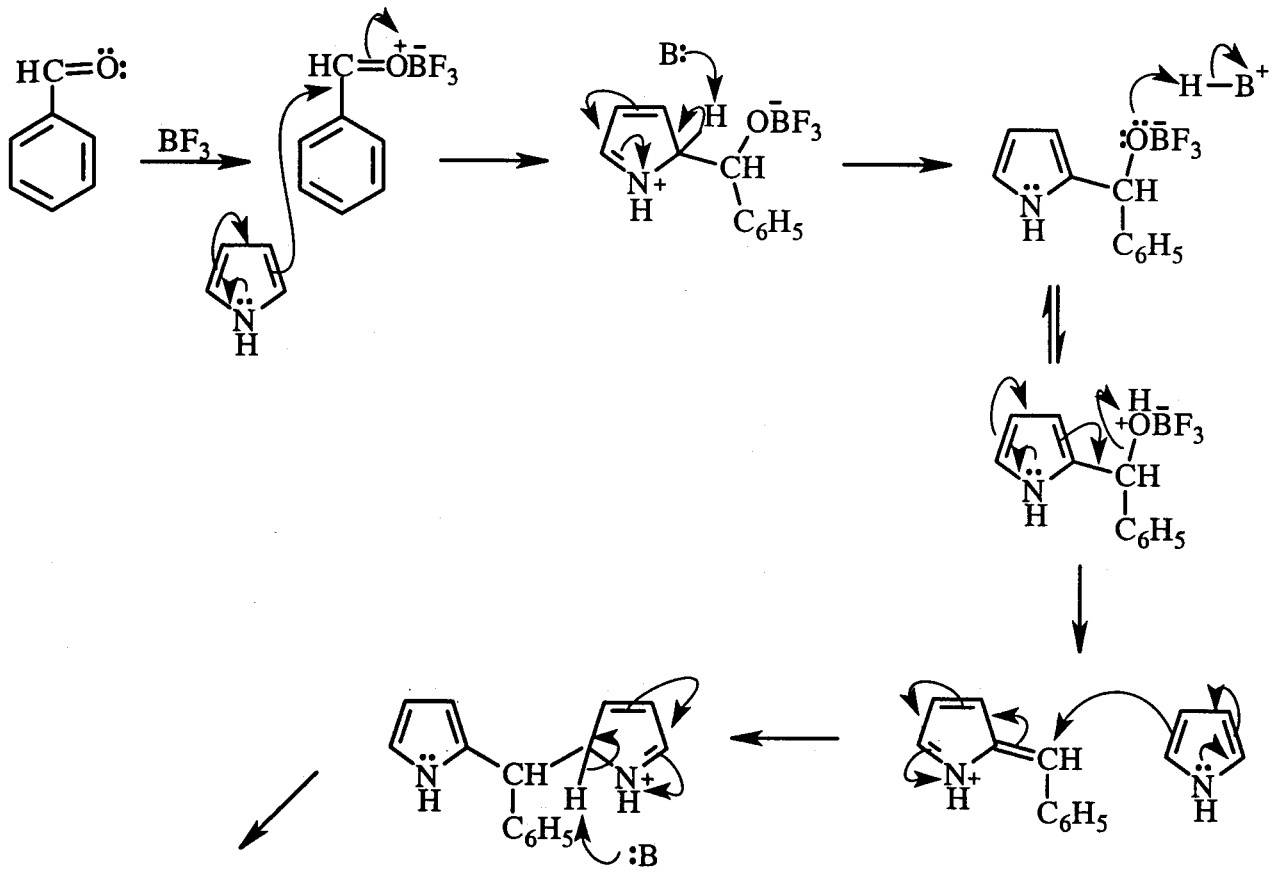
51.

a. 

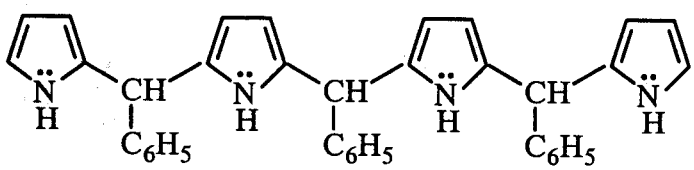
b. 

c. 

52.

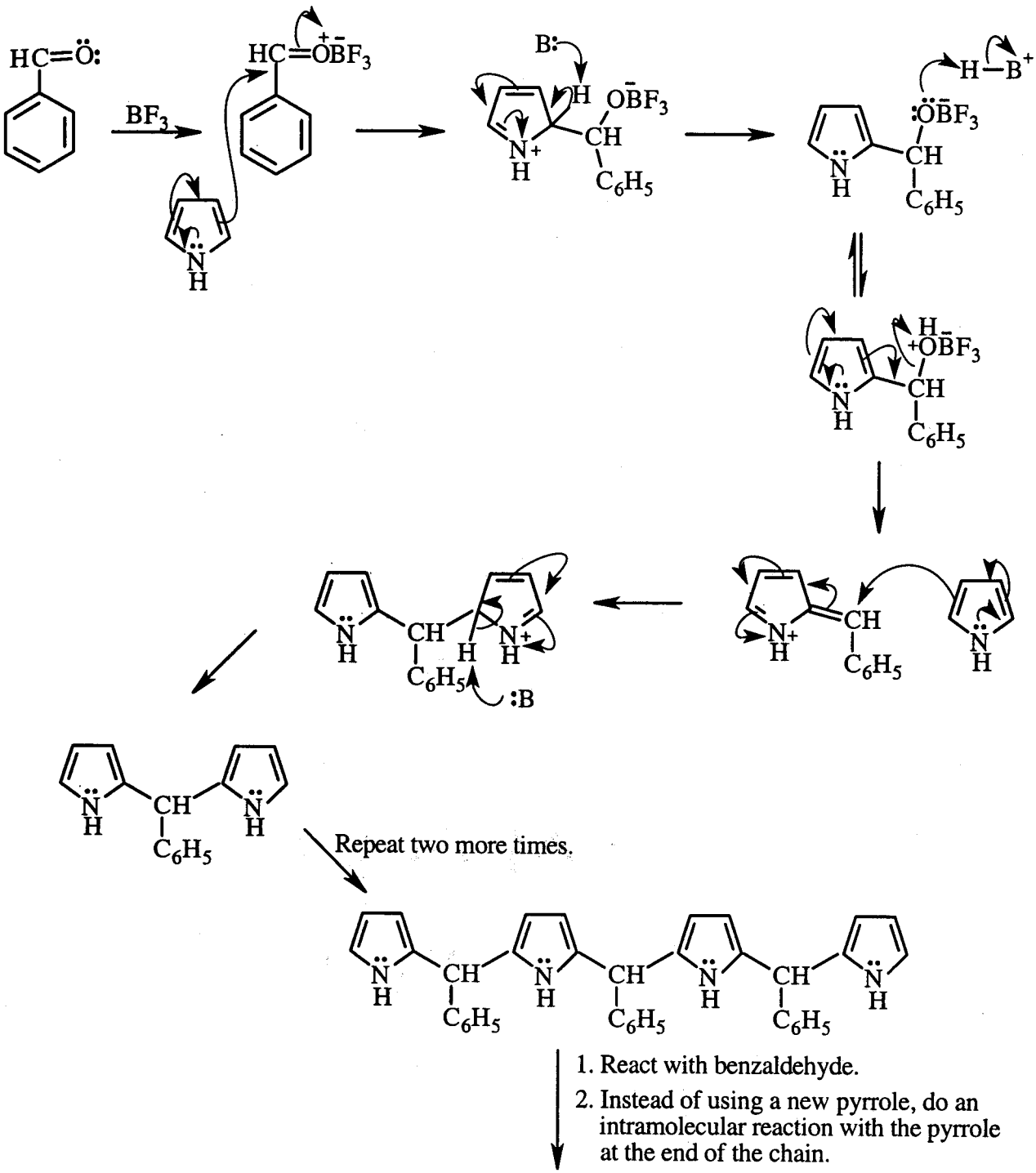


Repeat two more times.

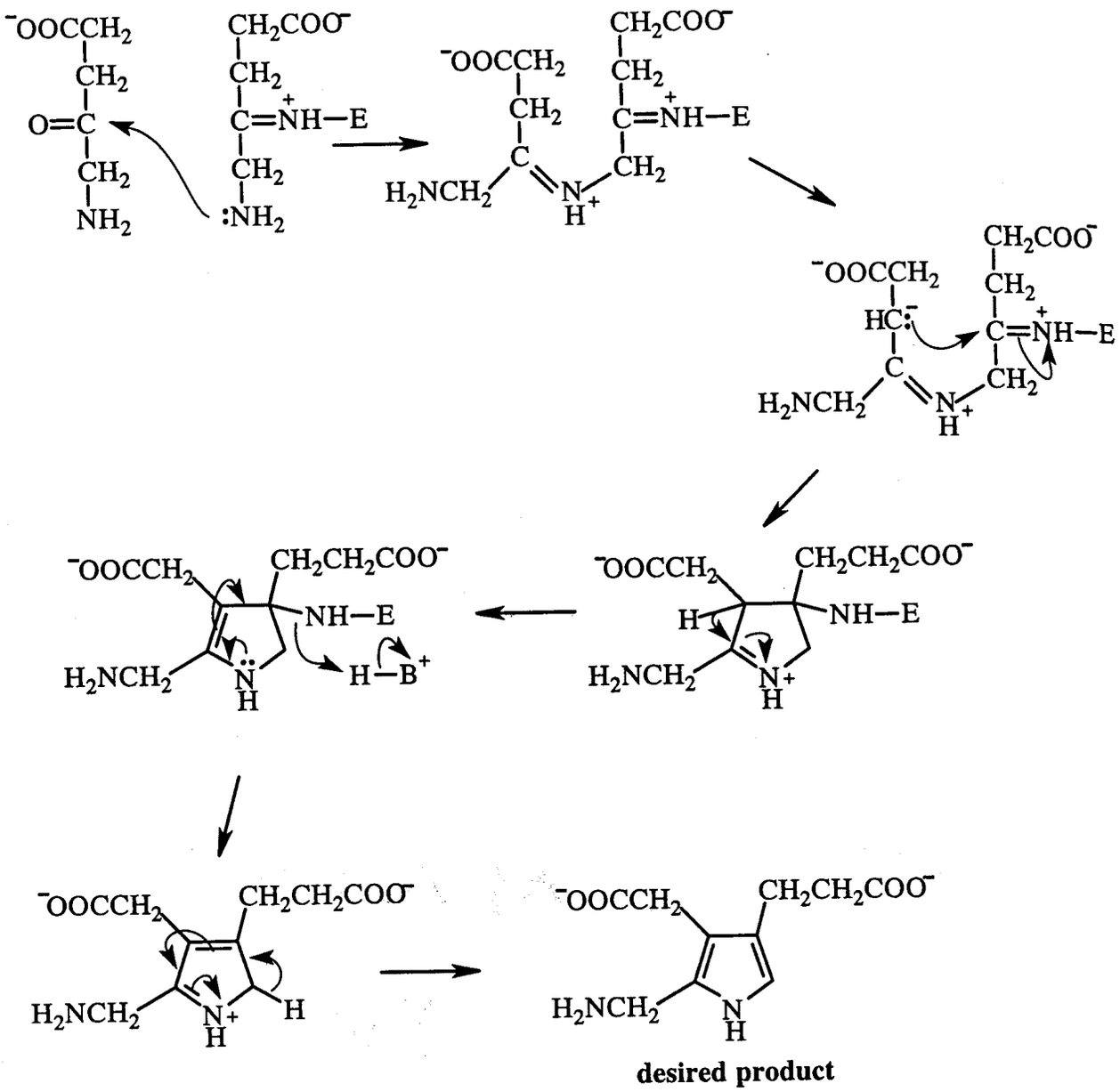


1. React with benzaldehyde.
2. Instead of using a new pyrrole, do an intramolecular reaction with the pyrrole at the end of the chain.

52.


HC=Ö:
BF3
HC=OBF3
B:
H OBF3
CH
C6H5
N+
H
H—B+
:ÖBF3
CH
C6H5
N
H
H
+OBF3
CH
C6H5
N
H
CH
C6H5
N+
H
N
H
N
H
CH
H
N+
H
C6H5
:B
N
H
CH
C6H5
N
H
Repeat two more times.
N
H
CH
C6H5
1. React with benzaldehyde.
2. Instead of using a new pyrrole, do an intramolecular reaction with the pyrrole at the end of the chain.

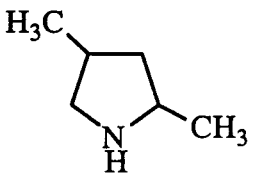
53.

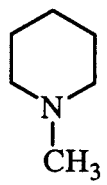


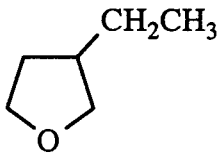
desired product

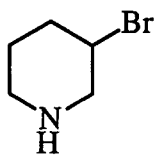
Chapter 21 Practice Test

1. Give two names for each of the following compounds:

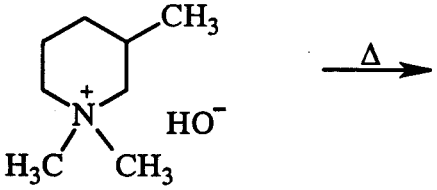
a. 

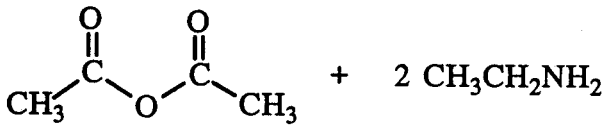
b. 

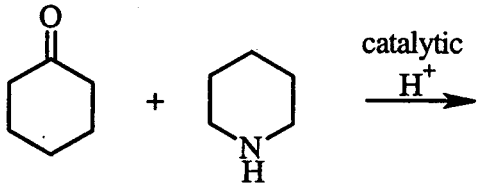
c. 

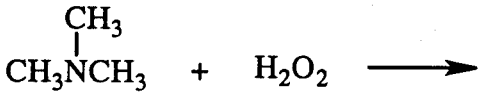
d. 

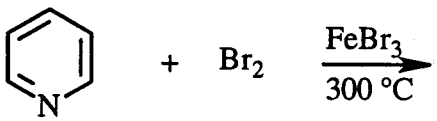
2. Give the product of each of the following reactions:

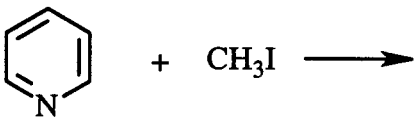
a. 

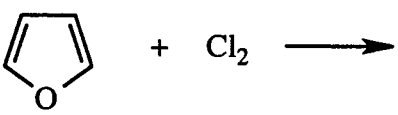
b. 

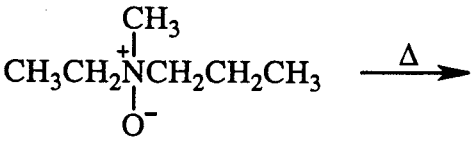
c. 

d. 

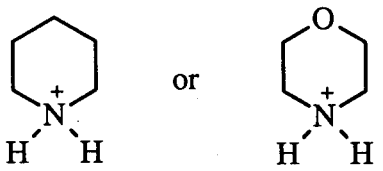
e. 

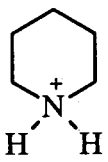
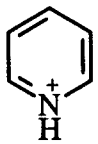
f. 

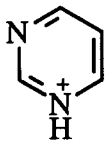
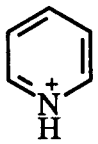
g. 

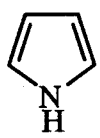
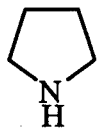
h. 

3. Which is a stronger acid?

a.  or

b.  or 

c.  or 

d.  or 

4. Indicate whether each of the following is true or false:

a. Pyridine is more reactive towards nucleophilic aromatic substitution than is pyrrole.
T F

b. Pyrrole is more reactive towards electrophilic aromatic substitution than is furan.
T F

c. Pyrrole is more reactive towards electrophilic aromatic substitution than is benzene
T F

d. Pyridine is more reactive towards electrophilic aromatic substitution than is benzene.
T F

CHAPTER 22
Carbohydrates

Important Terms

aldaric acid	a dicarboxylic acid with an OH group bonded to each carbon. Obtained by oxidizing the aldehyde and primary alcohol groups of an aldose.
alditol	a compound with an OH group bonded to each carbon. Obtained by reducing an aldose or a ketose.
aldonic acid	a carboxylic acid with an OH group bonded to each carbon. Obtained by oxidizing the aldehyde group of an aldose.
aldose	a polyhydroxyaldehyde.
amino sugar	a sugar in which one of the OH groups is replaced by an NH_2 group.
anomeric carbon	the carbon in a cyclic sugar that is the carbonyl carbon in the straight-chain form.
anomeric effect	preference for the axial position by certain substituents bonded to the anomeric carbon.
anomers	two cyclic sugars that differ in configuration only at the carbon that is the carbonyl carbon in the straight-chain form.
antibody	a compound that recognizes foreign particles in the body.
antigen	a compound that can generate a response from the immune system.
bioorganic compound	an organic compound that is found in a biological system.
carbohydrate	a sugar, a saccharide. Naturally occurring carbohydrates have the D-configuration.
complex carbohydrate	contains two or more sugar molecules linked together; it can be hydrolyzed to simple sugars.
deoxy sugar	a sugar in which one of the OH groups has been replaced by a hydrogen.
disaccharide	a compound containing two sugar molecules linked together.
epimers	monosaccharides that differ in configuration at only one carbon.
furanose	a five-membered ring sugar.
furanoside	a five-membered ring glycoside.
glycoprotein	a protein that is covalently bonded to a polysaccharide.
glycoside	the acetal of a sugar.
***N*-glycoside**	a glycoside with a nitrogen instead of an oxygen at the glycosidic linkage.

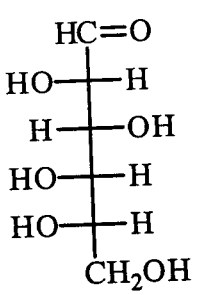
Ruff degradation	a method used to shorten an aldose by one carbon.
simple carbohydrate	a single sugar molecule.
tetrose	a monosaccharide with four carbons.
triose	a monosaccharide with three carbons.

glycosidic bond	the bond between the anomeric carbon and the alcohol residue in a glycoside.
α-1,4'-glycosidic linkage	a glycosidic linkage between the C-1 of one sugar and the C-4 of a second sugar with the oxygen atom at C-1 in the axial position.
α-1,6'-glycosidic linkage	a glycosidic linkage between the C-1 of one sugar and the C-6 of a second sugar with the oxygen atom at C-1 in the axial position.
β-1,4'-glycosidic linkage	a glycosidic linkage between the C-1 of one sugar and the C-4 of a second sugar with the oxygen atom at C-1 in the equatorial position.
Haworth projection	a way to show the structure of a sugar in which the five- and six-membered rings are represented as being flat.
heptose	a monosaccharide with seven carbons.
hexose	a monosaccharide with six carbons.
ketose	a polyhydroxyketone.
Kiliani-Fischer synthesis	a method used to increase the number of carbons in an aldose by one, resulting in the formation of a pair of C-2 epimers.
molecular recognition	the ability of molecules to recognize one another.
monosaccharide	a single sugar molecule.
mutarotation	a slow change in optical rotation to an equilibrium value.
nonreducing sugar	a sugar that cannot be oxidized by reagents such as Ag^+ and Cu^+. Nonreducing sugars are not in equilibrium with the open-chain aldose or ketose.
oligosaccharide	three to ten sugar molecules linked by glycosidic bonds.
osazone	the product obtained by reacting an aldose or a ketose with excess phenylhydrazine. An osazone contains two imine bonds.
oxocarbenium ion	an ion in which the positive charge is shared by a carbon and an oxygen.
pentose	a monosaccharide with five carbons.
photosynthesis	the synthesis of glucose and O_2 from CO_2 and H_2O.
polysaccharide	a compound containing ten or more sugar molecules linked together.
pyranose	a six-membered ring sugar.
pyranoside	a six-membered ring glycoside.
reducing sugar	a sugar that can be oxidized by reagents such as Ag^+ and Cu^+. Reducing sugars are in equilibrium with the open-chain aldose or ketose.

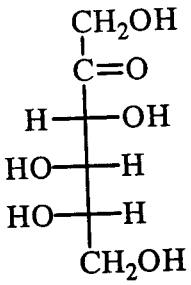
Solutions to Problems

1. D-Ribose is an aldopentose.
D-Sedoheptulose is a ketoheptose.
D-Mannose is an aldohexose.

2.

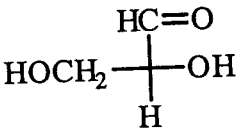


L-glucose

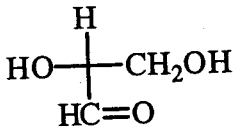


L-fructose

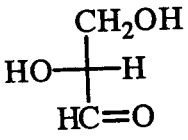
3.



L-glyceraldehyde



L-glyceraldehyde



D-glyceraldehyde

4. **a.** enantiomers

b. diastereomers

5. **a.** D-ribose **b.** L-talose **c.** L-allose

6. **a.** D-glucose = (2*R*,3*S*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexanal

b. L-Glucose is the mirror image of D-glucose, so each carbon in D-glucose has the opposit configuration in L-glucose.
L-glucose = (2*S*,3*R*,4*S*,5*S*)-2,3,4,5,6-pentahydroxyhexanal

c. D-Galactose is the C-4 epimer of D-glucose. Therefore, each of its carbon atoms, except has the same configuration as it has in D-glucose.
D-galactose = (2*R*,3*S*,4*S*,5*R*)-2,3,4,5,6-pentahydroxyhexanal

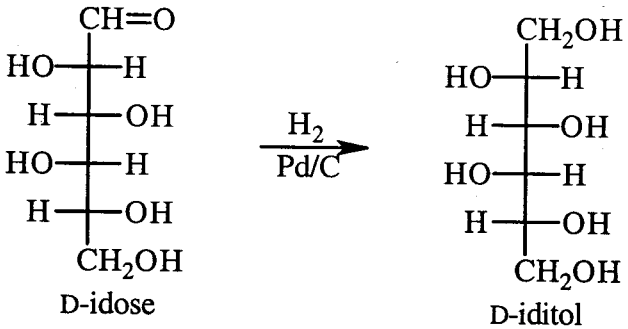
7. D-psicose

8. **a.** A ketoheptose has four asymmetric carbons ($2^4 = 16$ stereoisomers).

b. An aldoheptose has five asymmetric carbons ($2^5 = 32$ stereoisomers).

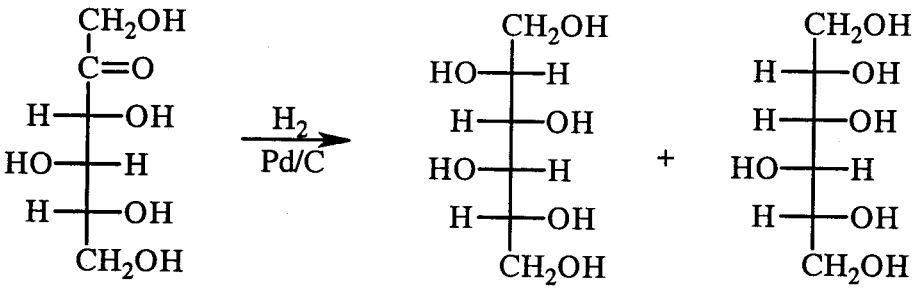
c. A ketotriose has no asymmetric carbons; therefore, it has no stereoisomers.

9. **a.** When D-idose is reduced, D-iditol is formed.



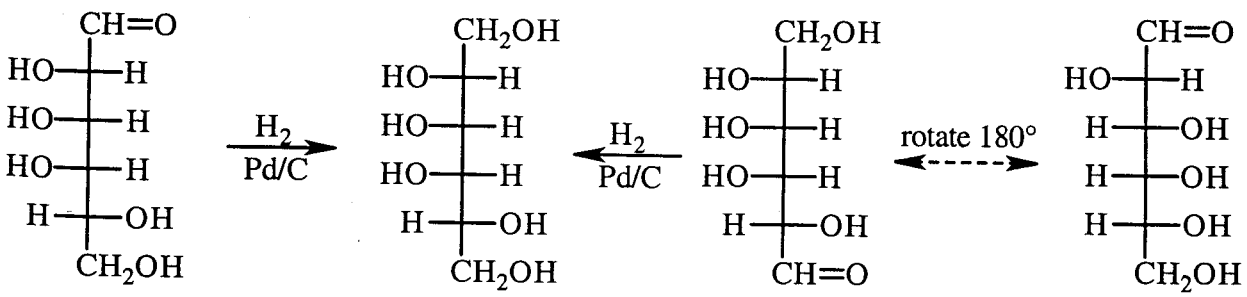
D-idose D-iditol

b. When D-sorbose is reduced, C-2 becomes an asymmetric carbon, so both D-iditol and the C-2 epimer of D-iditol (D-gulitol) are formed.



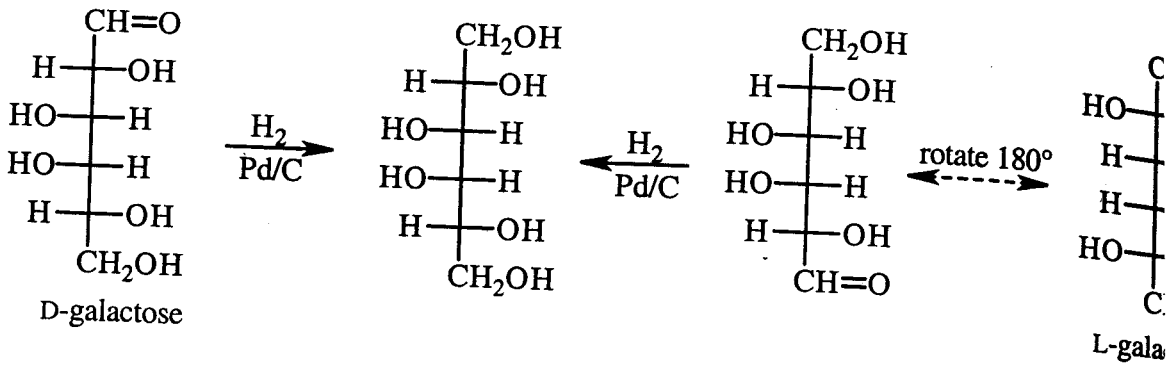
D-sorbose D-iditol D-gulitol

10. **a.** **1.** D-Altrose is reduced to the same alditol as D-talose.
The easiest way to answer this question is to draw D-talose and its alditol. Then draw the monosaccharide with the same configuration at C-2, C-3, C-4, and C-5 as D-talose, reversing the functional groups at C-1 and C-6. (Put the alcohol group at the top and the aldehyde group at the bottom.) The resulting Fischer projection can be rotated 180° in the plane of the paper, and the monosaccharide can then be identified.

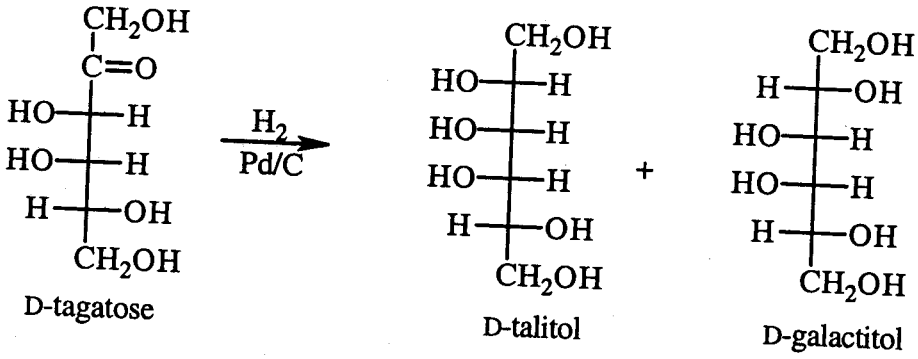


D-talose D-altrose

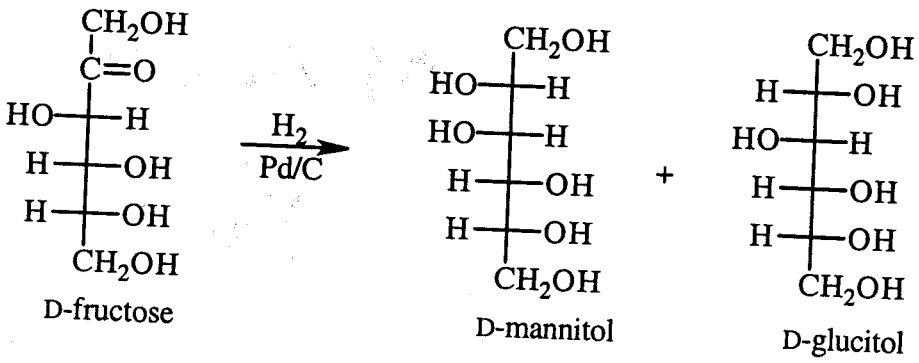
2. L-Galactose is reduced to the same alditol as D-galactose.



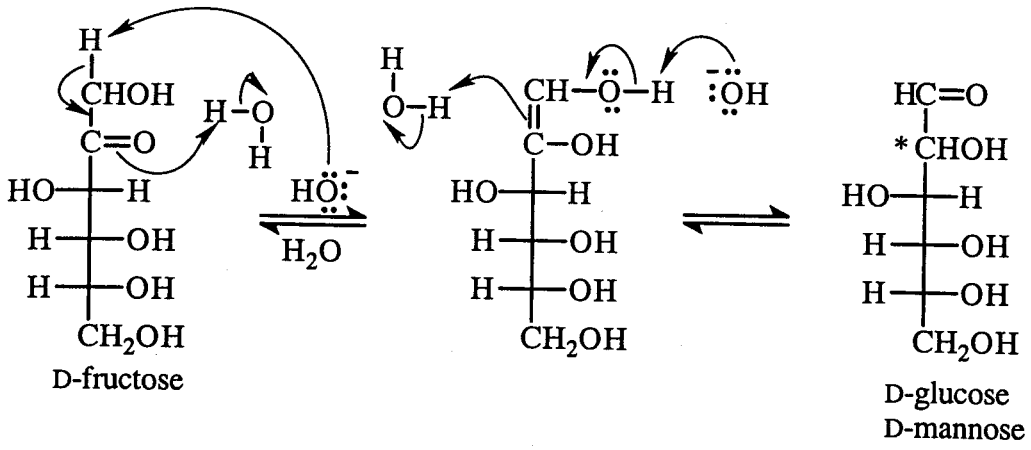
b. **1.** The ketohexose (D-tagatose) with the same configuration at C-3, C-4, and C-5 as D-ta will give the same alditol as D-talose. The other alditol is the one with the opposite configuration at C-2.



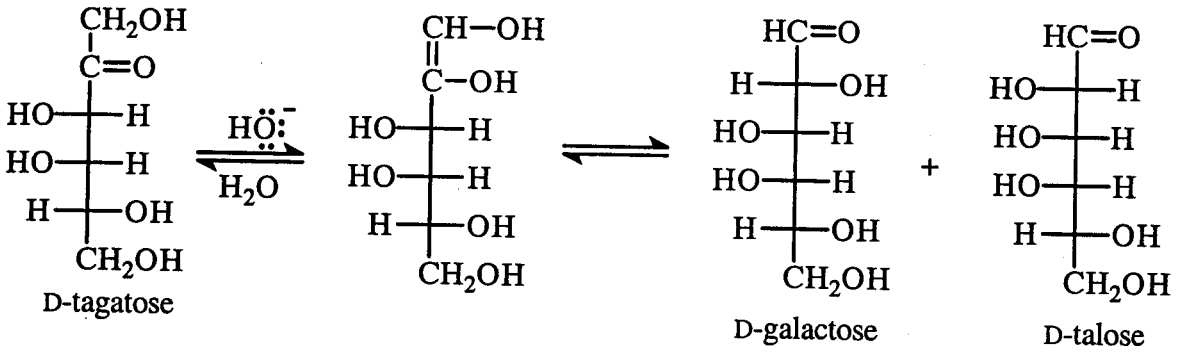
2. D-fructose



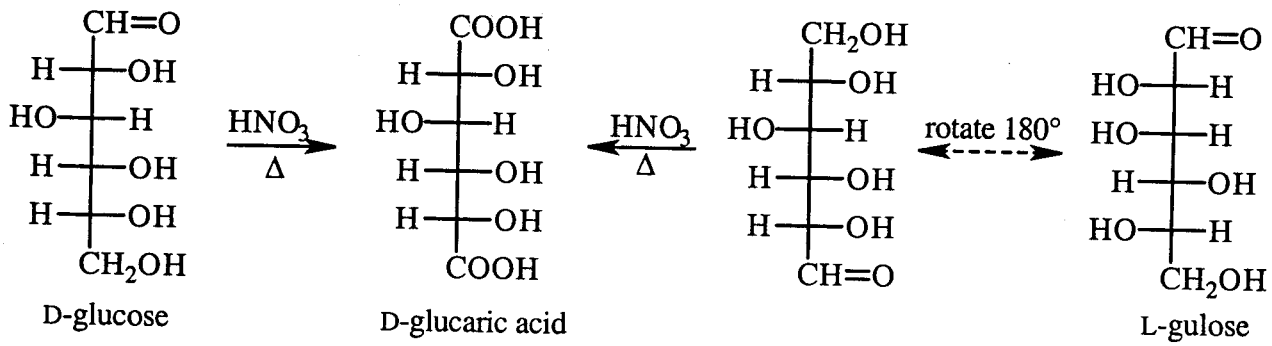
Removal of an α-hydrogen creates an enol that can enolize back to the ketone (using the OH at C-2) or can enolize to an aldehyde (using the OH at C-1). The aldehyde has a new asymmetric carbon; one of the epimers is D-glucose, and the other is D-mannose.



12. D-tagatose, D-galactose, and D-talose



13. **a.** L-gulose



b. L-Gularic acid, because it is also the oxidation product of L-gulose.

c. D-allose and L-allose, D-altrose and D-talose, L-altrose and L-talose, D-galactose and L-galactose

14. **a.** D-arabinose and D-ribulose

b. D-allose and D-psicose

c. L-gulose and L-sorbose

d. D-talose and D-tagatose

15. D-gulose and D-idose

16. **a.** D-gulose and D-idose

b. L-xylose and L-lyxose

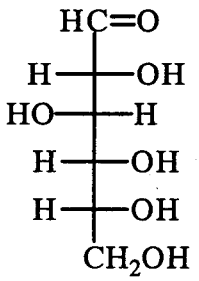
17. **a.** D-glucose and D-mannose

b. D-erythrose and D-threose

c. L-allose and L-altrose

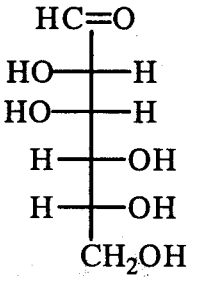
18. Solved in the text.

19.



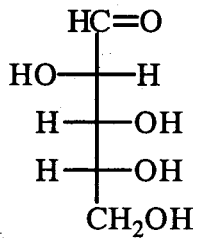
D-glucose

A



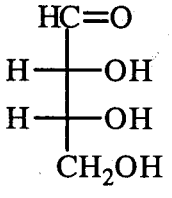
D-mannose

B



D-arabinose

C

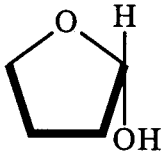


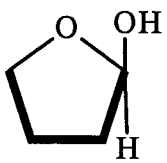
D-erythrose

D

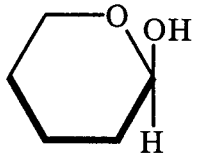
20. The hemiacetals in **a** and **b** have one chirality center; therefore, each has two stereoisomers. The hemiacetals in **c** and **d** have two chirality centers; therefore, each has four stereoisomers.

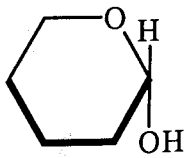
a.



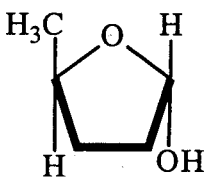


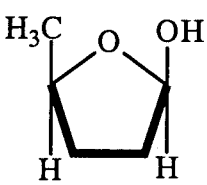
b.

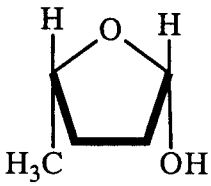


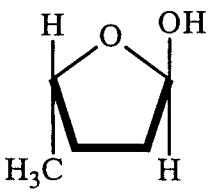


c.

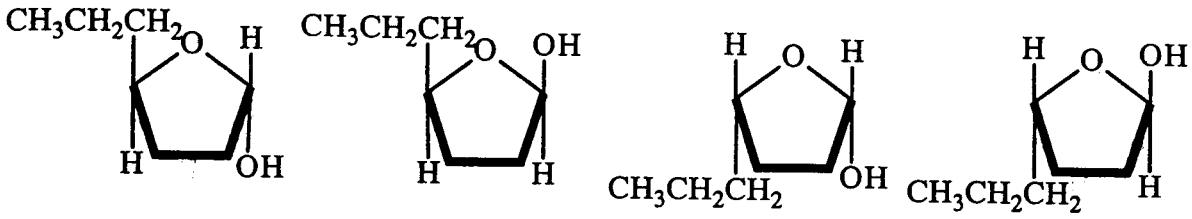






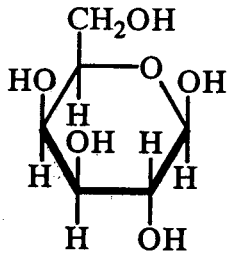


d.



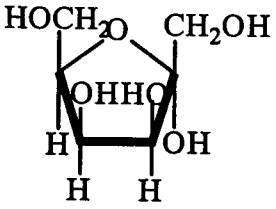
21.

a.

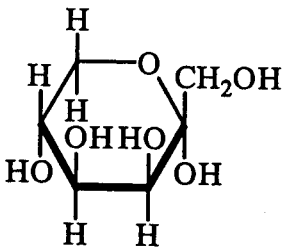


β-D-galactose

b.

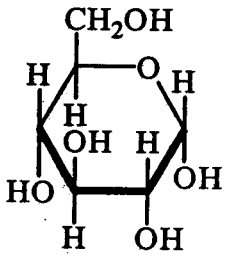


α-D-tagatose
furanose form

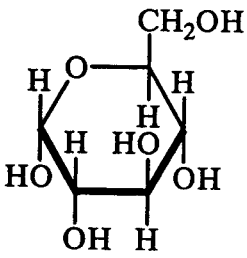


α-D-tagatose
pyranose form

c.

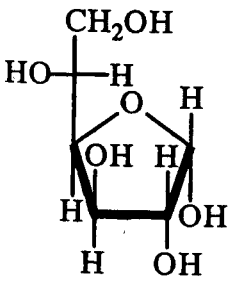


α-D-glucose



α-L-glucose
the mirror image of α-D-glucose

22.



23. First recall that in the more stable chair conformation: an α-anomer has the anomeric carbon in the axial position, whereas a β-anomer has the anomeric carbon in the equatorial position. Then recall that glucose has all its OH groups in equatorial positions. Now this question can be answered easily.

a. Mannose is a C-2 epimer of glucose. Therefore, the OH group at C-2 in β-D-mannose is in the axial position.

b. Idose differs in configuration from glucose at C-2, C-3, and C-4. Therefore, the OH groups at C-2, C-3, and C-4 in β-D-idose are in the axial position.

c. Allose is a C-3 epimer of glucose. Therefore, the OH group at C-3 is in the axial position and, since it is the α-anomer, the OH group at C-1 (the anomeric carbon) is in the axial position.

24. If more than a trace amount of acid is used, the amine that acts as a nucleophile when it forms the *N*-glycoside becomes protonated, and a protonated amine is not nucleophilic.

25. **a.** Solved in the text.

b. methyl α-D-galactoside	(nonreducing)
c. α-D-idose	(reducing)
d. ethyl β-D-psicosideside	(nonreducing)

26. an L-aldohexose

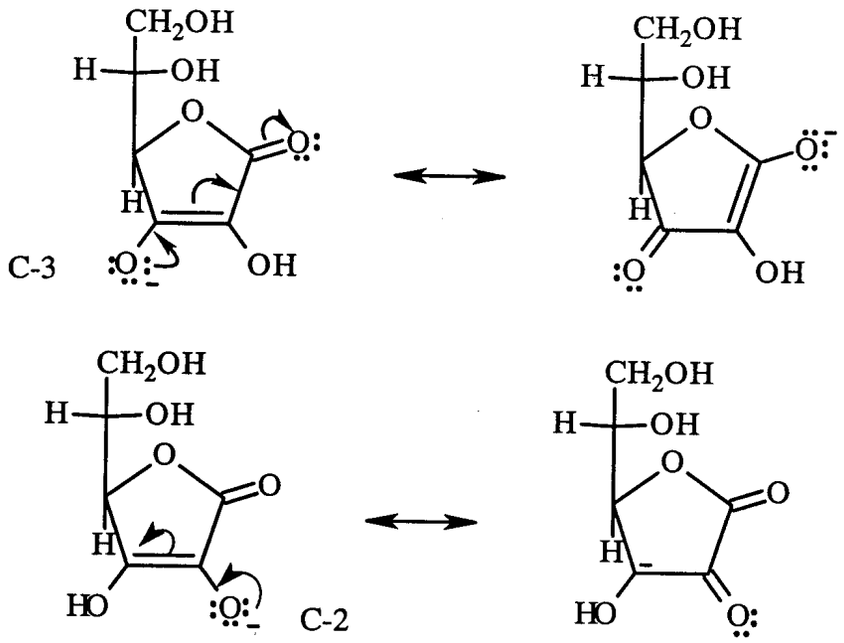
27. **a.** Amylose has α-1,4'-glycosidic linkages, whereas cellulose has β-1,4'-glycosidic linkages.

b. Amylose has α-1,4'-glycosidic linkages, whereas amylopectin has both α-1,4'-glycosidic linkages and α-1,6'-glycosidic linkages.

c. Glycogen and amylopectin have the same kind of linkages, but glycogen has a higher frequency of α-1,6'-glycosidic linkages.

d. Cellulose has a hydroxyl at C-2, whereas chitin has an *N*-acetylamino group at that position.

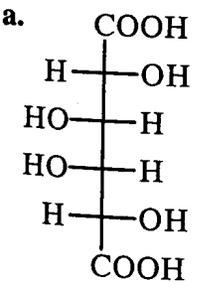
28. A proton is more easily lost from the C-3 OH group because the anion that is formed when the proton is removed is more stable than the anion that is formed when a proton is removed from the C-2 OH group. When a proton is removed from the C-3 OH group, the electrons that are left behind can be delocalized onto another oxygen atom. When a proton is removed from the C-2 OH group, the electrons that are left behind are delocalized onto a carbon atom. Because oxygen is more electronegative than carbon, a negatively charged oxygen is more stable than a negatively charged carbon.

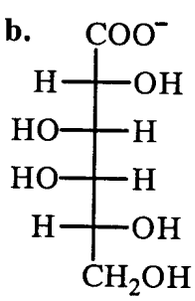


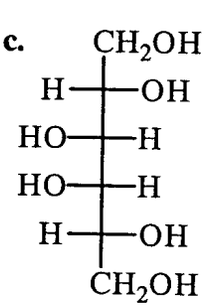
29. **a.** People with Type O blood can receive blood only from other people with Type O blood, because Type A, B, and AB blood have sugar components that Type O blood does not have.

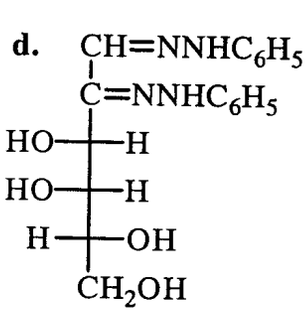
b. People with Type AB blood can give blood only to other people with Type AB blood, because Type AB blood has sugar components that Type A, B, or O blood does not have.

30.

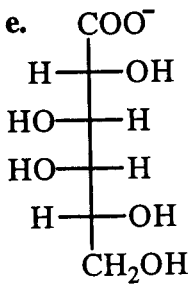
a.


b.


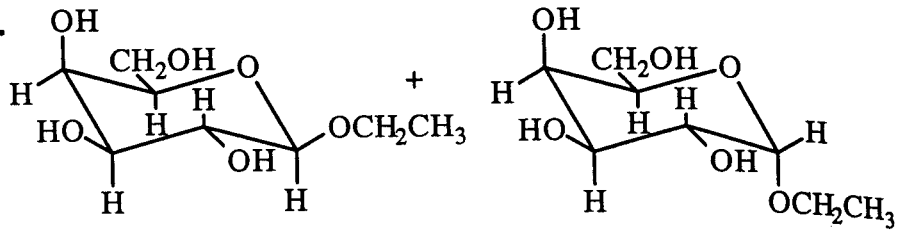
c.


d.


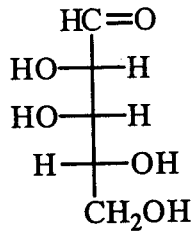
e.



f.



g.



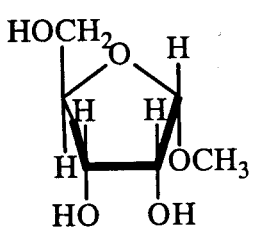
31. **a.** D-lyxose **b.** D-tagatose **c.** D-talose **d.** D-psicose

32. **a.** D-ribose and L-ribose, D-arabinose and L-arabinose, D-xylose and L-xylose, D-lyxose and L-lyxose

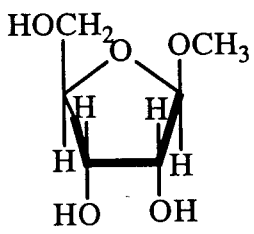
b. D-ribose and D-arabinose, L-ribose and L-arabinose, D-xylose and D-lyxose, L-xylose and L-lyxose

c. D-arabinose, L-arabinose, D-lyxose, and L-lyxose

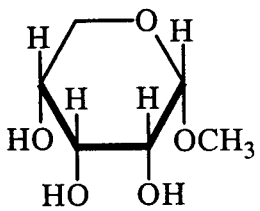
33.



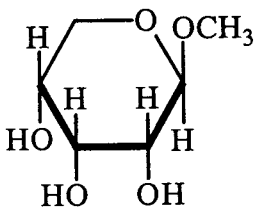
methyl α-D-ribofuranose



methyl β-D-ribofuranose



methyl α-D-ribopyranose

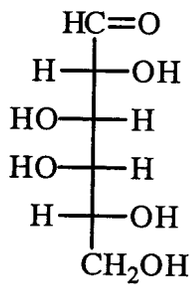


methyl β-D-ribopyranose

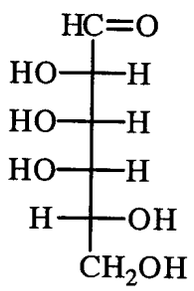
34. 1. As Fischer did, we can narrow our search to eight 6-carbon sugars, since there are eight pairs of enantiomers. First we need to find an aldopentose that forms (+)-galactose as a product of a Kiliani-Fischer synthesis. That sugar is the one known as (−)-lyxose. The Kiliani-Fischer synthesis on (−)-lyxose yields two sugars with melting points that show them to be the sugars known as (+)-galactose and (+)-talose. Now we know that (+)-galactose and (+)-talose are C-2 epimers. They are sugars 1 and 2, 3 and 4, 5 and 6, or 7 and 8. (See page 932 of the text.)

2. When (+)-galactose and (+)-talose react with HNO_3, (+)-galactose forms an optically inactive product and (+)-talose forms an optically active product. Thus, (+)-galactose and (+)-talose are sugars 1 and 2 or 7 and 8. Since (+)-galactose is the one that forms the optically inactive oxidation product, it is either sugar 1 or 7.

3. To determine the structure of (+)-galactose, we can go back to (−)-lyxose, the sugar that forms sugars 7 and 8 by a Kiliani-Fischer synthesis, and oxidize it with HNO_3. Finding that the aldaric acid is optically active allows us to conclude that (+)-galactose is sugar 7, because the aldopentose that leads to sugars 1 and 2 would give an optically inactive aldaric acid.

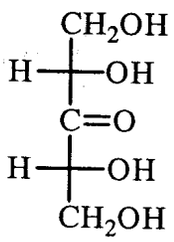


7
D-galactose



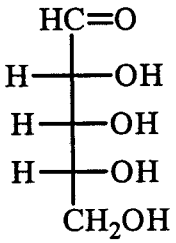
8
D-talose

35. A monosaccharide with a molecular weight of 150 must have five carbons (five C's = 60, five O's = 80, and 10 H's = 10 for a total of 150). All aldopentoses are optically active. Therefore, the compound must be a ketopentose. The following is the only ketopentose that would not be optically active.



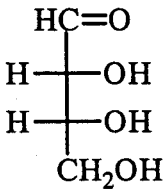
36. The hydrogen that is bonded to the anomeric carbon will be the hydrogen that is farthest downfield, because it is the only hydrogen that is bonded to a carbon that is bonded to two electronegative oxygen atoms. So the two anomeric hydrogens, one on the α-anomer and one on the β-anomer, are responsible for the two low-field doublets.

37.



D-ribose

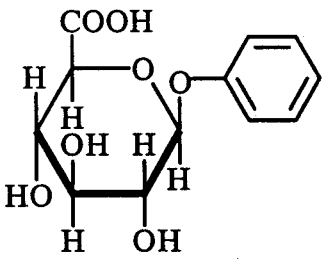
A



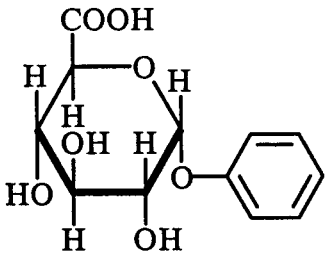
D-erythrose

B

38.

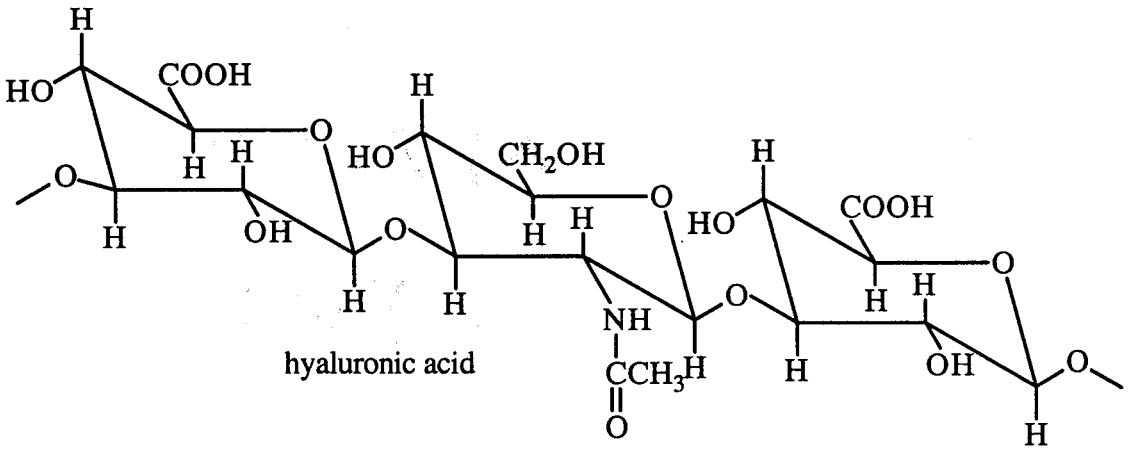


the β-D-glucuronide



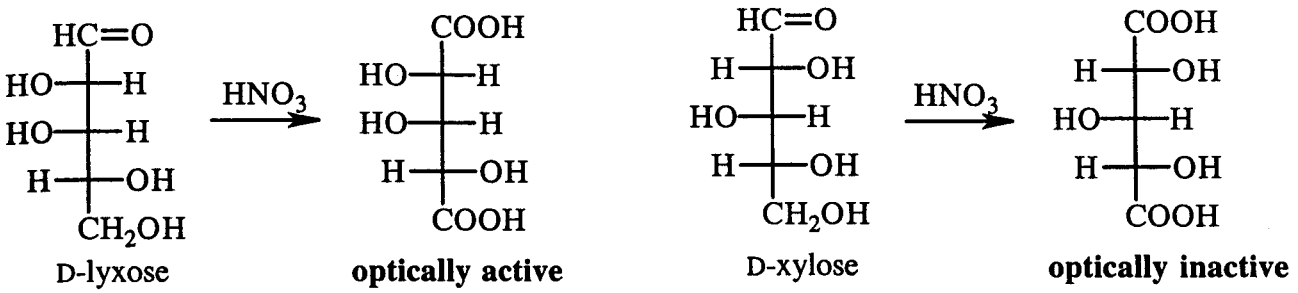
the α-D-glucuronide

39.

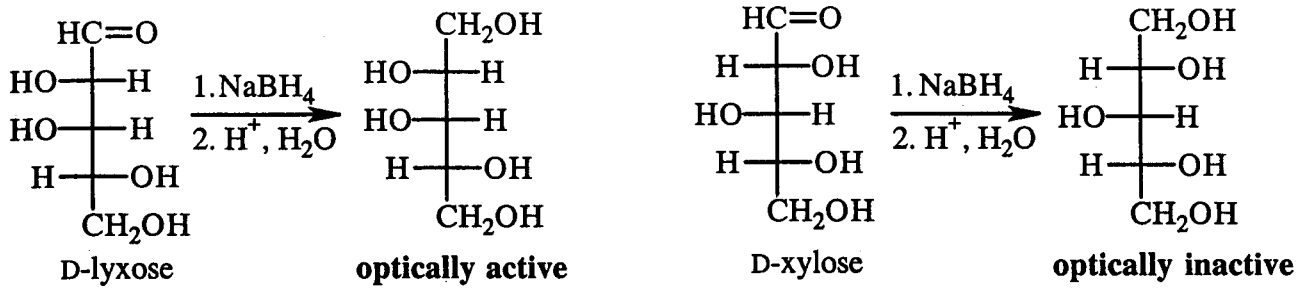


hyaluronic acid

40. She can take a sample of one of the sugars and oxidize it with nitric acid to an aldaric acid or reduce it with sodium borohydride to an alditol. If the product is optically active, the sugar was D-lyxose. If the product is not optically active, the sugar was D-xylose; if the product is optically active, the sugar was D-lyxose.

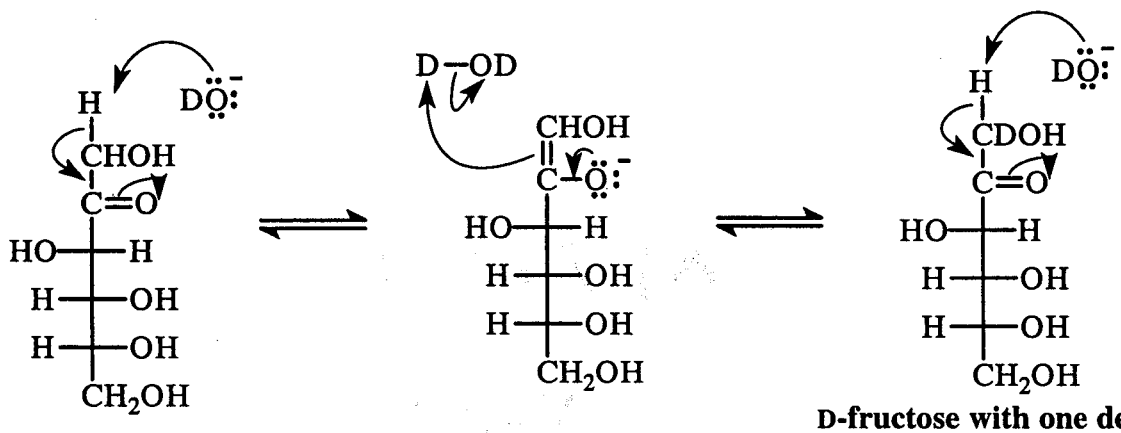


D-lyxose **optically active** D-xylose **optically inactive**

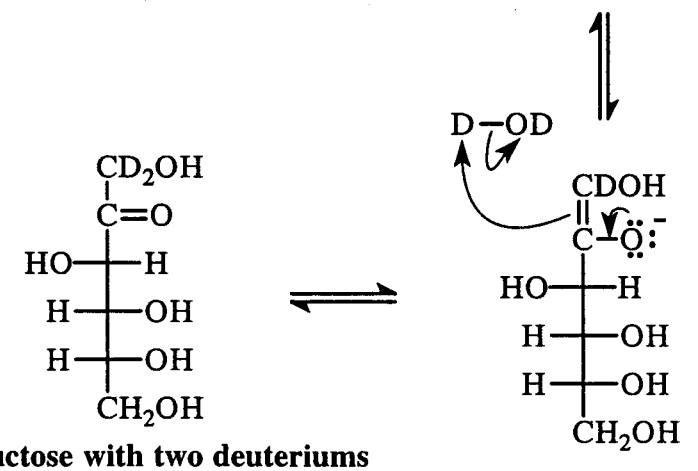


D-lyxose **optically active** D-xylose **optically inactive**

41.



D-fructose with one deuterium



D-fructose with two deuteriums

42. **D-arabinose.** The only D-aldopentoses that are oxidized to optically active aldaric acids are D-arabinose and D-lyxose.

A Ruff degradation of D-arabinose forms D-erythrose, whereas a Ruff degradation of D-lyxose forms D-threose. Since D-erythrose forms an optically inactive aldaric acid but D-threose does not, the D-aldopentose is D-arabinose.

43. **10** aldaric acids

Each of the following pairs forms the same aldaric acid:

D-allose and L-allose	L-altrose and L-talose
D-galactose and L-galactose	D-glucose and L-gulose
D-altrose and D-talose	L-glucose and D-gulose

Thus twelve aldohexoses form six aldaric acids. The other four aldohexoses each form a distinctive aldaric acid, and (6 + 4 = 10).

44. Let A = the fraction of glucose in the α-form and B = the fraction of glucose in the β-form.

$A + B = 1$

$B = 1 - A$

specific rotation of A = 112.2°
specific rotation of B = 18.7°
specific rotation of the equilibrium mixture = 52.7°

specific rotation of the mixture = specific rotation of A x fraction of glucose in the α-form + specific rotation of B x fraction of glucose in the β-form

$52.7 = 112.2\,A + (1 - A)\,18.7$

$52.7 = 112.2\,A + 18.7 - 18.7\,A$

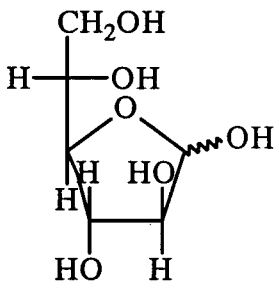
$34.0 = 93.5\,A$

$A = 0.36$

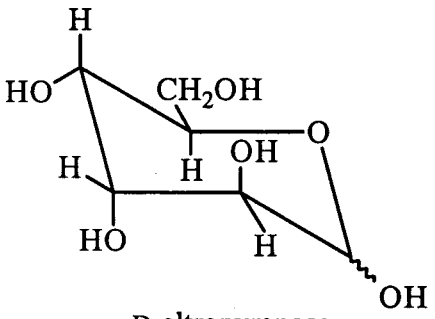
$B = 0.64$

This calculation shows that 36% is in the α-form and 64% is in the β-form.

45. D-Altrose will most likely exist as a furanose because
(1) the furanose is particularly stable, because all the large substituents are trans to each other, and
(2) the pyranose has two of its OH groups in the unstable axial position.

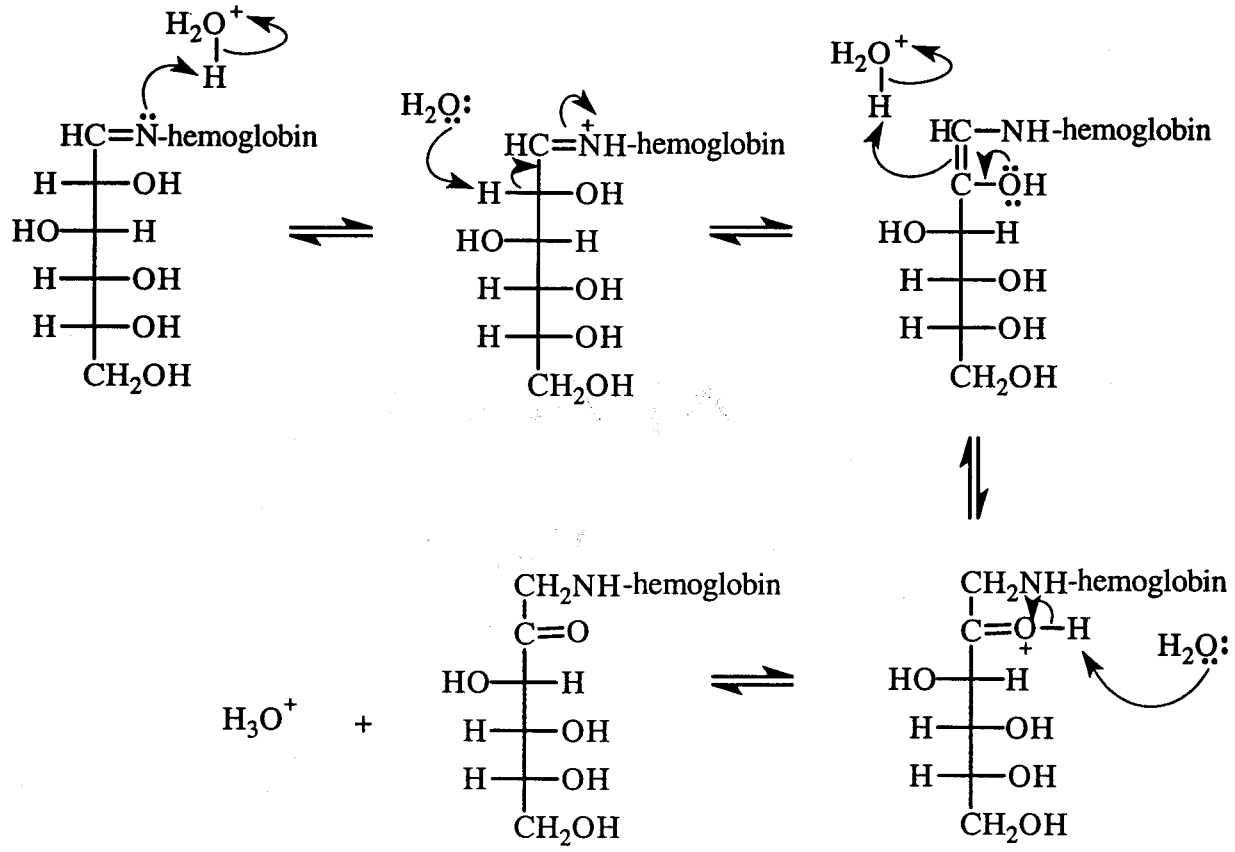


D-altrofuranose

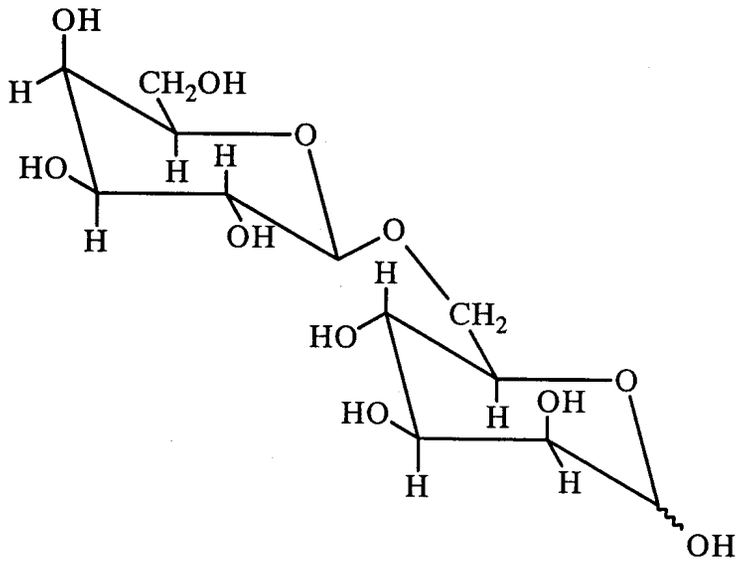


D-altropyranose

46.

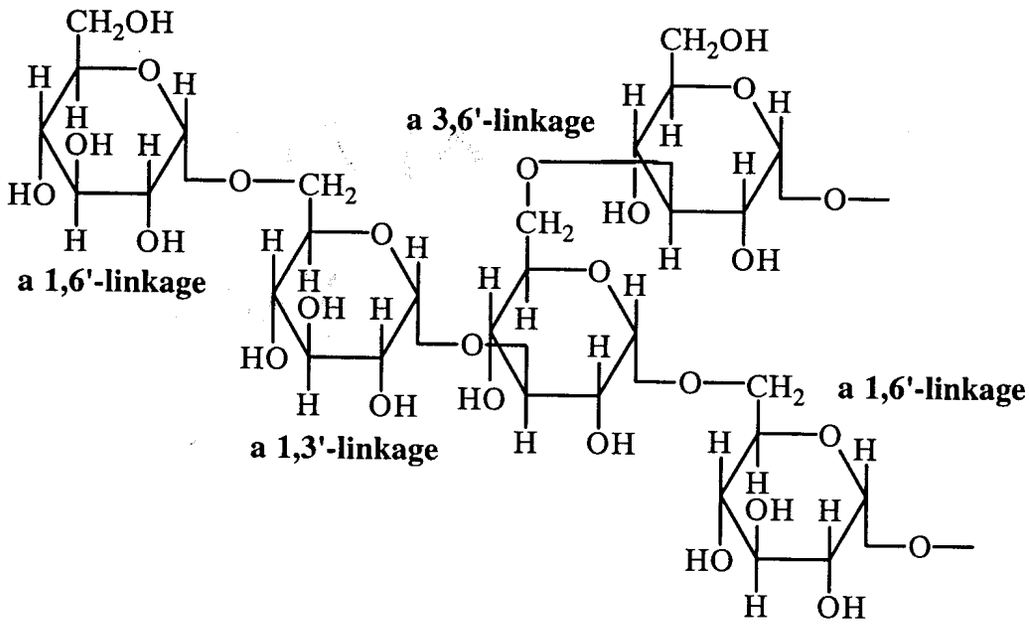


47. **a.** Because mannose is missing the methyl substituent on the oxygen at C-6, the disaccharide must be formed using the C-6 OH group of mannose and the anomeric carbon of galactose.



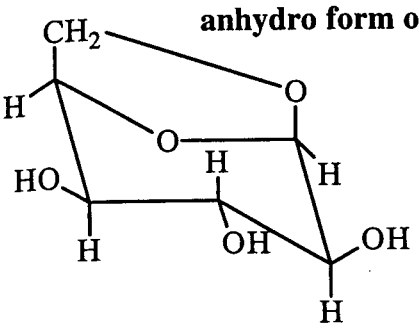
b. Silver oxide increases the leaving tendency of the iodide ion from methyl iodide, thereby allowing the nucleophilic substitution reaction to take place with the weakly nucleophilic alcohol groups.

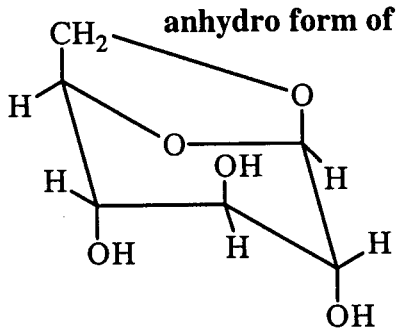
48. Because all the glucose units have six-membered rings, the 5-position is never methylated.
2,3,4,6-tetra-*O*-methyl-D-glucose has only its 1-position in an acetal linkage.
2,3,6-tri-*O*-methyl-D-glucose has its 1-position and its 3-position in an acetal linkage.
2,3,4-tri-*O*-methyl-D-glucose has its 1-position and its 6-position in an acetal linkage.
2,4-di-*O*-methyl-D-glucose has its 1-position, its 3-position, and its 6-position in an acetal linkage.



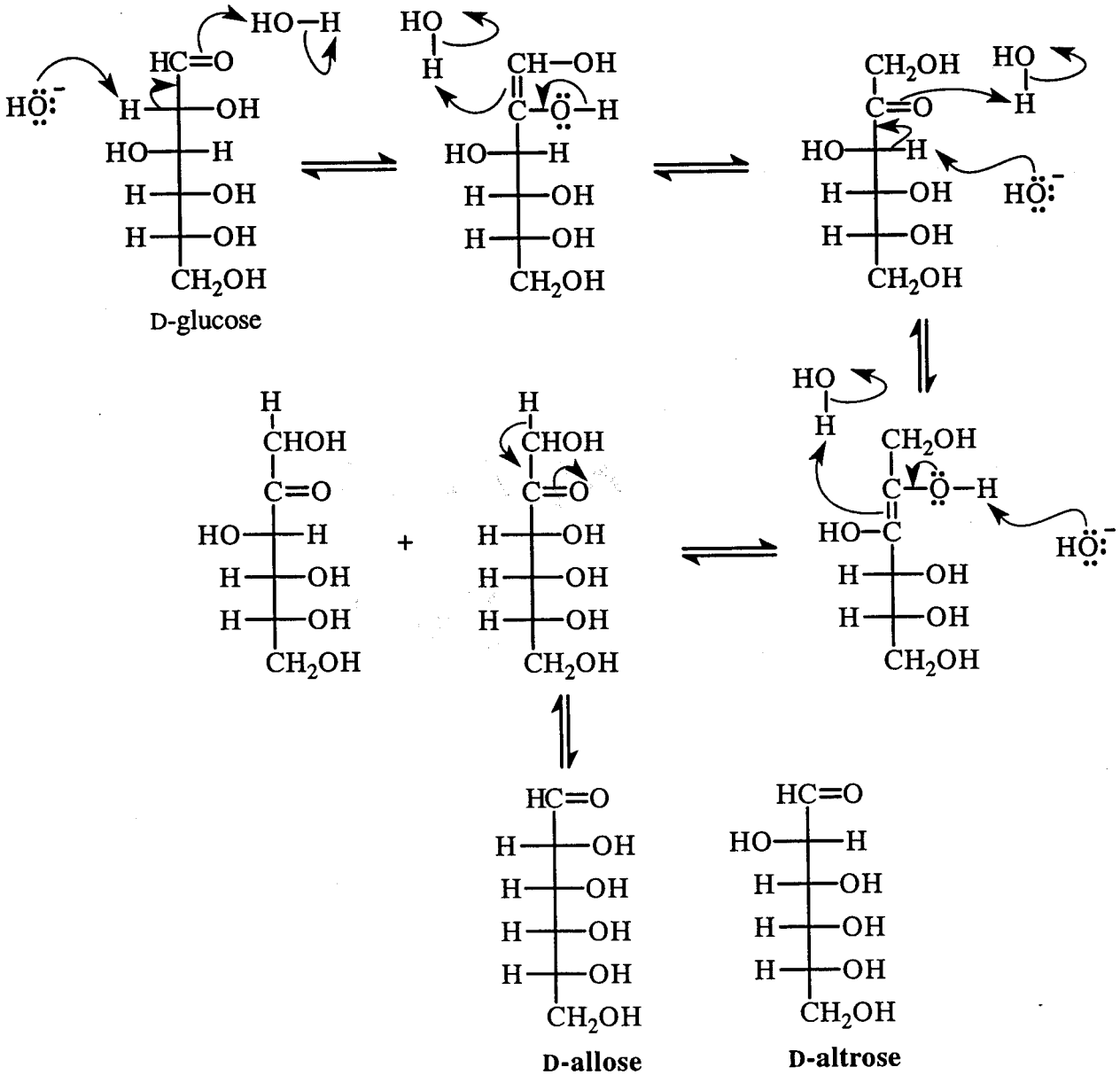
49. In the case of D-idose, the chair conformer with the OH substituents at C-1 and C-5 in the axial position (which is necessary for formation of the anhydro form) has the OH substituents at C-2, C-3, and C-4 all in equatorial positions. Thus, this is a preferred conformer, since three of the five large substituents are in the more stable equatorial position.

In the case of D-glucose, the chair conformer with the OH substituents at C-1 and C-5 in the axial position has the OH substituents at C-2, C-3, and C-4 all in axial positions. This is a relatively unstable conformer, since all the large substituents are in less stable axial positions.





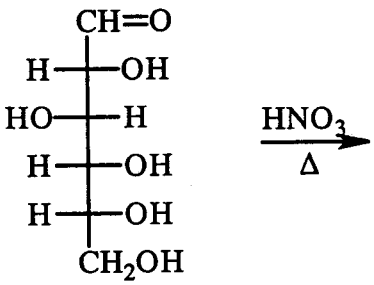
50.



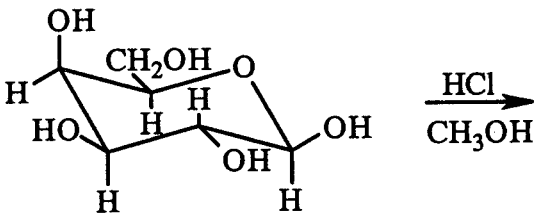
Chapter 22 Practice Test

1. Give the product(s) of each of the following reactions:

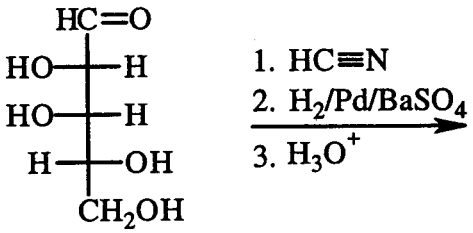
a.



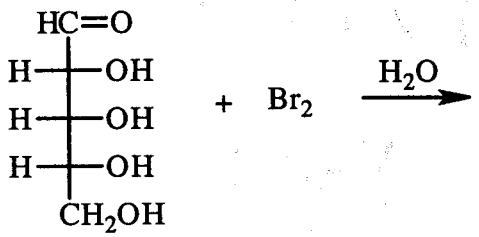
b.



c.



d.



2. Indicate whether the following statements are true or false:

a. Glycogen contains α-1,4'- and β-1,6'-glycosidic linkages. T F

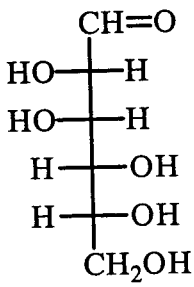
b. D-Mannose is a C-1 epimer of D-glucose. T F

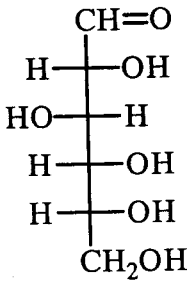
c. D-Glucose and L-glucose are anomers. T F

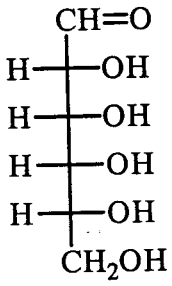
d. D-Erythrose and D-threose are diastereomers. T F

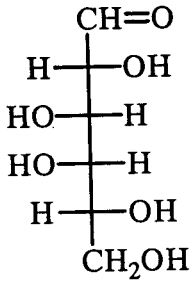
e. Ruff degradations of D-glucose and D-gulose form the same aldopentose. T F

3. Which of the following sugars will form an optically active aldaric acid?









4. When crystals of D-fructose are dissolved in a basic aqueous solution, two aldohexoses are obtained. Identify the aldohexoses.

5. A sugar forms the same osazone as D-galactose but is not oxidized by an aqueous solution of Br_2. Identify the sugar.

6. D-Talose and _____ are reduced to the same alditol.

7. What is the main structural difference between amylose and cellulose?

8. What aldohexoses are formed from a Kiliani-Fischer synthesis starting with D-xylose?

9. What aldohexose is the C-3 epimer of D-glucose?

10. Draw the most stable chair conformer of β-D-allose, a C-3 epimer of β-D-glucose.

CHAPTER 23
Amino Acids, Peptides, and Proteins

Important Terms

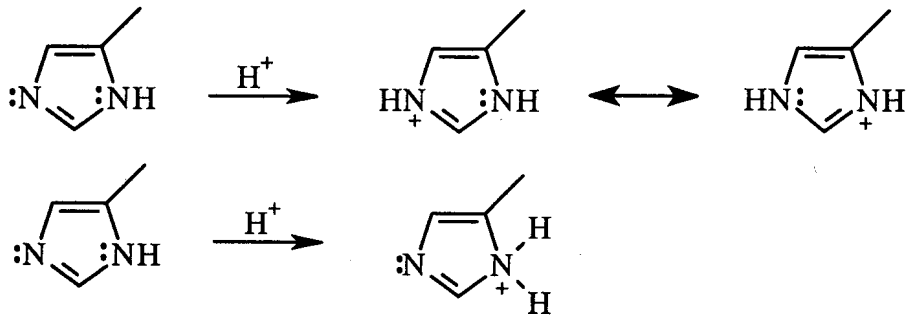
amino acid	an α-aminocarboxylic acid. Naturally occurring amino acids have the L-configuration.
D- amino acid	the configuration of an amino acid drawn in a Fischer projection such that the carboxyl group is on top, the hydrogen is on the left, and the amino group is on the right.
L-amino acid	the configuration of an amino acid drawn in a Fischer projection such that the carboxyl group is on top, the hydrogen is on the right, the amino group is on the left.
amino acid analyzer	an instrument that automates the ion-exchange separation of amino acids.
amino acid residue	a monomeric unit of a peptide or protein.
anion-exchange resin	a resin that binds anions.
antiparallel β-pleated sheet	the adjacent hydrogen-bonded peptide chains in a β-pleated sheet run in opposite directions.
automated solid-phase peptide synthesis	an automated technique that synthesizes a peptide while its C-terminal amino acid is attached to a solid support.
cation-exchange resin	a resin that binds cations.
coil conformation (loop conformation)	that part of a protein that is highly ordered but not in an α-helix or a β-sheet.
denaturation	destruction of the highly organized tertiary structure of a protein.
dipeptide	two amino acids linked together by an amide bond.
disulfide	a compound with an -S—S- bond.
disulfide bridge	a disulfide (-S—S-) bond in a peptide or protein.
Edman's reagent	phenyl isothiocyanate. A reagent used to determine the N-terminal amino acid of a polypeptide.
electrophoresis	a technique that separates amino acids on the basis of their pI values.
endopeptidase	an enzyme that hydrolyzes a peptide bond that is not at the end of a peptid chain.
enkephalin	a pentapeptide synthesized by the body to control pain.
enzyme	a protein that is a catalyst.

essential amino acid	an amino acid that humans must obtain from their diet because they either cannot synthesize it at all or they cannot synthesize it in adequate amounts.
exopeptidase	an enzyme that hydrolyzes a peptide bond at the end of a peptide chain.
fibrous protein	a water insoluble protein that has its polypeptide chains arranged in bundles.
globular protein	a water soluble protein that tends to have a roughly spherical shape.
α-helix	the backbone of a polypeptide coiled in a right-handed spiral with hydrogen bonding occurring within the helix.
hydrophobic interactions	interactions between nonpolar groups. They increase stability by decreasing the amount of structured water (increasing entropy).
interchain disulfide bridge	a disulfide bridge between two cysteine residues in different peptide chains.
intrachain disulfide bridge	a disulfide bridge between two cysteine residues in the same peptide chain.
ion-exchange chromatography	a technique that uses a column packed with an insoluble resin to separate compounds on the basis of their charge and polarity.
isoelectric point (pI)	the pH at which there is no net charge on an amino acid.
kinetic resolution	separating enantiomers based on the difference in their rate of reaction with an enzyme.
oligomer	a protein with more than one peptide chain.
oligopeptide	three to ten amino acids linked by amide bonds.
paper chromatography	a technique that separates amino acids based on polarity.
parallel β-pleated sheet	the adjacent hydrogen-bonded peptide chains in a β-pleated sheet run in the same direction.
partial hydrolysis	a technique that hydrolyzes only some of the peptide bonds in a polypeptide.
peptide	polymer of amino acids linked together by amide bonds.
peptide bond	the amide bond that links the amino acids in a peptide or protein.
β-pleated sheet	the backbone of a polypeptide is extended in a zigzag structure with hydrogen bonding between neighboring chains.
polypeptide	many amino acids linked by amide bonds.
primary structure	the sequence of amino acids in a protein.
protein	polymer of amino acids linked together by amide bonds.

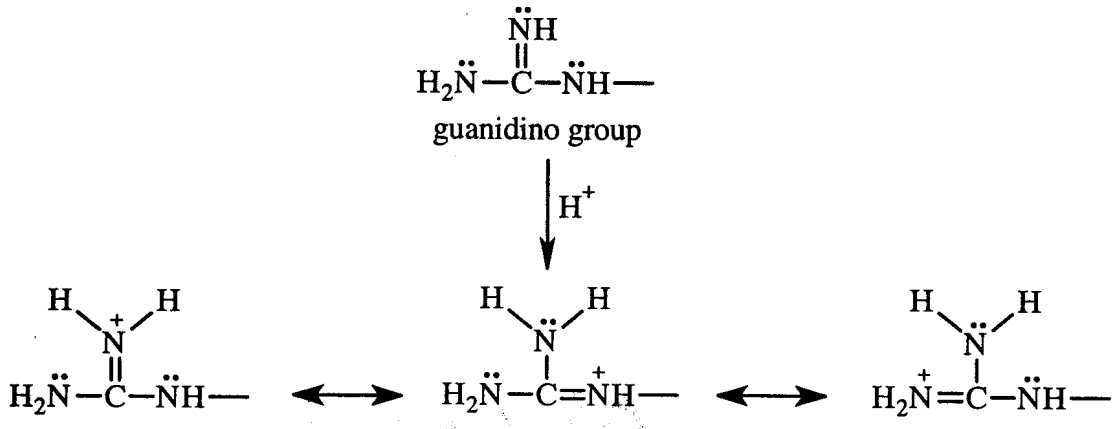
quaternary structure	a description of the way the individual polypeptide chains of a protein are arranged with respect to one other.
random coil	the conformation of a totally denatured protein.
secondary structure	a description of the conformation of the backbone of a protein.
structural protein	a protein that gives strength to a biological structure.
subunit	an individual chain of an oligomer.
C-terminal amino acid	the terminal amino acid of a peptide (or protein) that has a free carboxyl group.
N-terminal amino acid	the terminal amino acid of a peptide (or protein) that has a free amino group.
tertiary structure	a description of the three-dimensional arrangement of all the atoms in a protein.
thin-layer chromatography	a technique that separates compounds on the basis of their polarity.
tripeptide	three amino acids linked by amide bonds.
zwitterion	a compound with a negative charge and a positive charge on nonadjacent atoms.

Solutions to Problems

1. **a.** Protonation of the doubled-bonded nitrogen forms a conjugate acid that is stabilized by electron delocalization. Protonation of the other nitrogen forms a conjugate acid that is not stabilized by electron delocalization. The resonance-stabilized conjugate acid is the one that is more readily formed.



b. Protonation of the doubled-bonded nitrogen forms a conjugate acid that is stabilized by electron delocalization. Protonation of either of the other nitrogen atoms forms a conjgate acid that is not stabilized by electron delocalization. The resonance-stabilized conjugate acid is the one that is more readily formed.



2. **a.** (*R*)-alanine

b. (*R*)-aspartate

c. The α-carbons of all the D-amino acids except cysteine have the *R*-configuration.

Similarly, the α-carbon of all the L-amino acids except cysteine has the *S*-configuration.
(In all the amino acids except cysteine, the amino group has the highest priority and the carboxyl group has the second-highest priority. In cysteine, the thiomethyl group has a higher priority than the carboxyl group because sulfur has a greater atomic number than oxygen.)

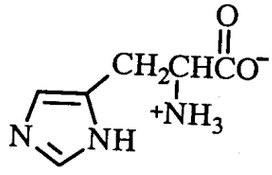
3. isoleucine and threonine
naturally occurring L-isoleucine is (2*S*,3*S*)-isoleucine
naturally occurring L-threonine is (2*S*,3*R*)-threonine

4. The electron-withdrawing $^{+}NH_3$ substituent on the α-carbon increases the acidity of the carboxyl group.

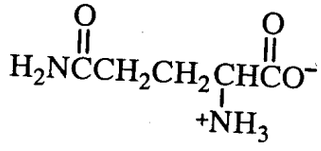
5.

a. Solved in the text.

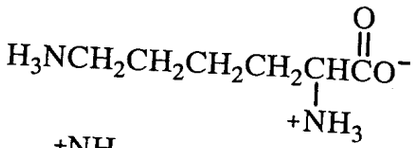
b.



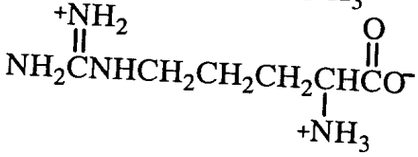
c.



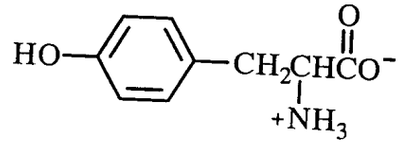
d.



e.

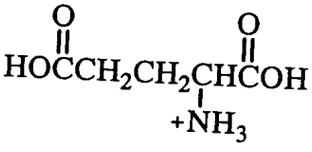


f.

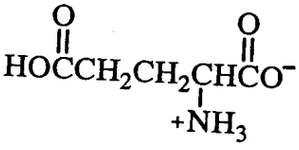


6.

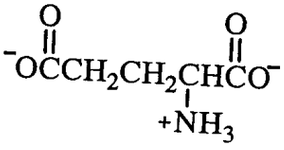
a.



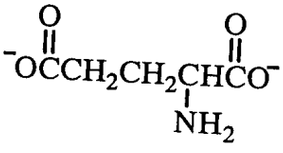
b.



c.



d.



7. **a.** The carboxyl group of the aspartic acid side chain is a stronger acid than the carboxyl group of the glutamic acid side chain because the aspartic acid side chain is closer to the electron-withdrawing protonated amino group.

b. The lysine side chain is a stronger acid that the arginine side chain. The arginine side chain has less of a tendency to lose a proton because the positive charge is delocalized over three nitrogen atoms.

8. In order for the amino acid to have no net charge, the two amino groups must have a +1 charge between them in order to cancel out the -1 charge of the carboxylate group. Because they are positively charged in their acidic forms and neutral in their basic forms, the sum of their charges will be +1 at the midpoint of their pK_a values.

a. asparagine $pI = \frac{2.02 + 8.84}{2} = \frac{10.86}{2} = 5.43$

b. arginine $pI = \frac{9.04 + 12.48}{2} = \frac{21.52}{2} = 10.76$

c. serine $pI = \frac{2.21 + 9.15}{2} = \frac{11.36}{2} = 5.68$

d. aspartate $pI = \frac{2.09 + 3.86}{2} = \frac{5.95}{2} = 2.98$

10. **a.** Asp (pI = 2.98)

b. Arg (pI = 10.76)

c. Asp

d. Met, because at pH = 6.20 Met is farther away from the pH at which it has no net charge (pI of Met = 5.75, pI of Gly = 5.97).

11. Tyrosine and cysteine each have two groups that are neutral in their acidic forms and negatively charged in their basic forms. Unlike other amino acids that have similarly ionizing groups, the pK_a values of the two similarly ionizing groups in tyrosine and cysteine are not close in value and quite different from the pK_a of the group that ionizes differently. Therefore, the third group cannot be ignored in calculating the pI.

12. Leucine and isoleucine both have butyl side chains and, therefore, have the same polarity. Consequently, the spots for both amino acids appear at the same place on the chromatographic plate.

13. Because the amino acid analyzer contains a cation-exchange resin (it binds cations), the less positively charged the amino acid, the less tightly it is bound to the column. Using buffer solutions of increasingly higher pH to elute the column causes the amino acids bound to the column to become increasingly less positively charged, so they can be released from the column.

14. Cation-exchange chromatography releases amino acids in order of their pI values. The amino acid with the lowest pI is released first because at a given pH it will be the amino acid with the highest concentration of negative charge, and negatively charged molecules are not bound by the negatively charged resin. The relatively nonpolar resin will release polar amino acids before nonpolar amino acids.

a. Asp (pI = 2.98) is more negative than Ser (pI = 5.68).
b. Gly is more polar than Ala.
c. Val is more polar than Leu.
d. Tyr is more polar than Phe.

15. A column containing an anion-exchange resin releases amino acids in reverse order of their pI values. The amino acid with the highest pI is released first, because at a given pH it will be the amino acid with the highest concentration of positive charge.

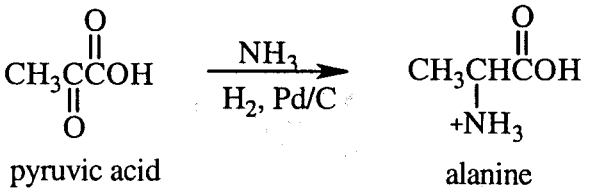
His > Val > Ser > Asp

16. The first equivalent of ammonia will react with the acidic proton of the carboxylic acid to form ammonium ion, which is not nucleophilic and, therefore, cannot substitute for Br. A second equivalent of ammonia therefore is needed for the desired nucleophilic substitution reaction.

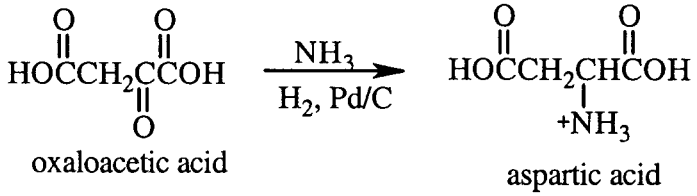
17. Convert the amino acids into esters using $SOCl_2$ followed by ethanol. The products obtained after treatment with pig liver esterase will be an L-amino acid and unreacted ester of the D-amino acid. These compounds can be readily separated, and the D-amino acid can be obtained by acid-catalyzed hydrolysis of the ester. This technique is called a *kinetic resolution*. If the difference in the rate of the enzyme-catalyzed reaction with the two enantiomers is greater than about 3 kcal/mol, a kinetic resolution will be successful.

18. **a.** The reactions below show that pyruvic acid forms alanine, oxaloacetic acid forms aspartic acid, and α-ketoglutarate forms glutamic acid. If reductive amination (p. 896) is carried out in the cell, only the L-isomer of each amino acid will be formed.

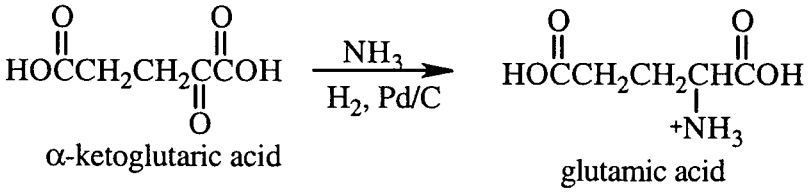
b. If reductive amination is carried out in the laboratory, both the D- and L-isomer of each amino acid will be formed.



pyruvic acid — alanine

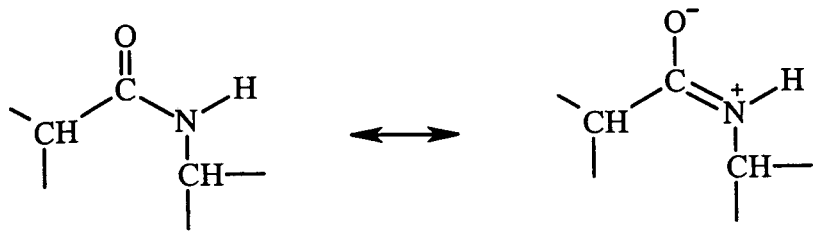


oxaloacetic acid — aspartic acid



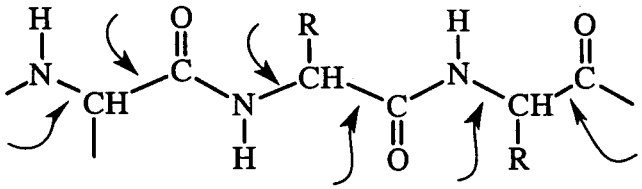
α-ketoglutaric acid — glutamic acid

19.

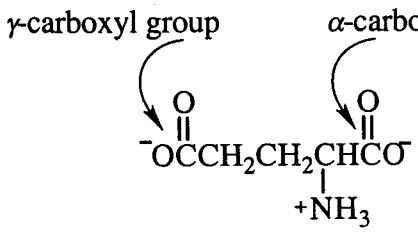


20. **a.** $20^8 = 25{,}600{,}000{,}000$ **b.** 20^{100}

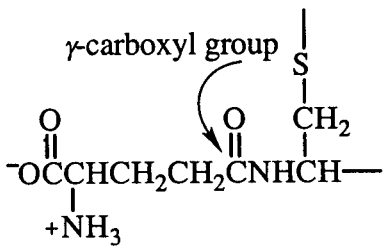
21. The bonds on either side of the α-carbon can freely rotate. In other words, the bond between the α-carbon and the carbonyl carbon and the bond between the α-carbon and the nitrogen (the bonds indicated by arrows) can freely rotate.



22. In forming the amide linkage, the amino group of cysteine reacts with the γ-carboxyl group rather than with the α-carboxyl group of glutamic acid.

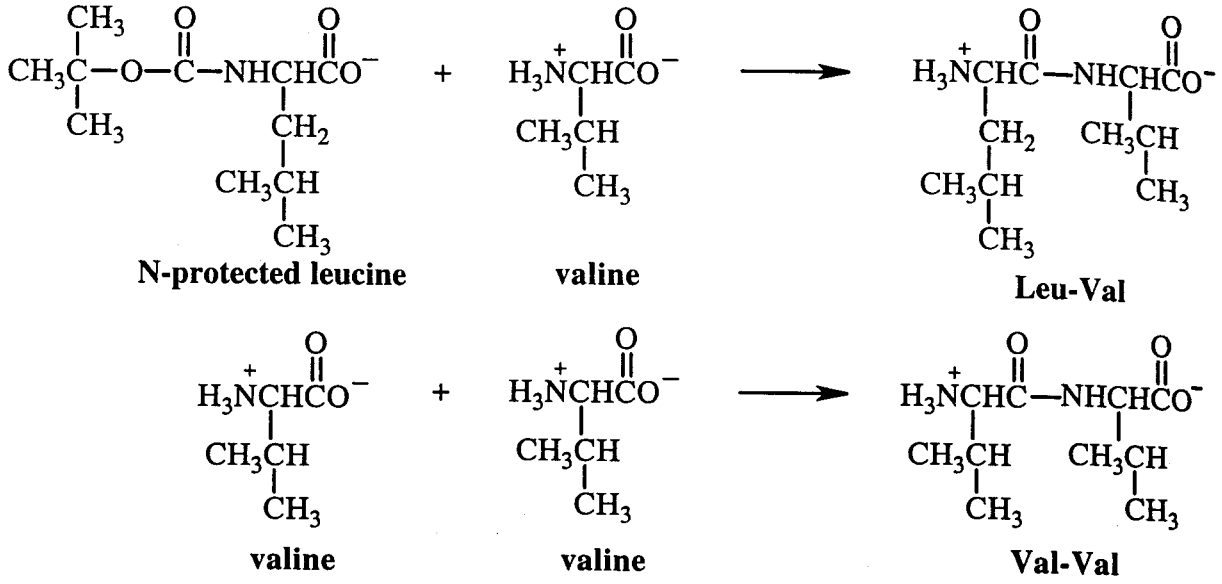


glutamate

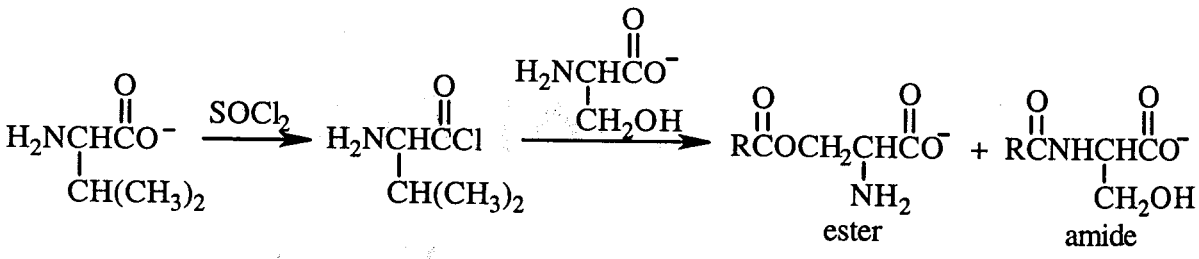


a segment of glutathione

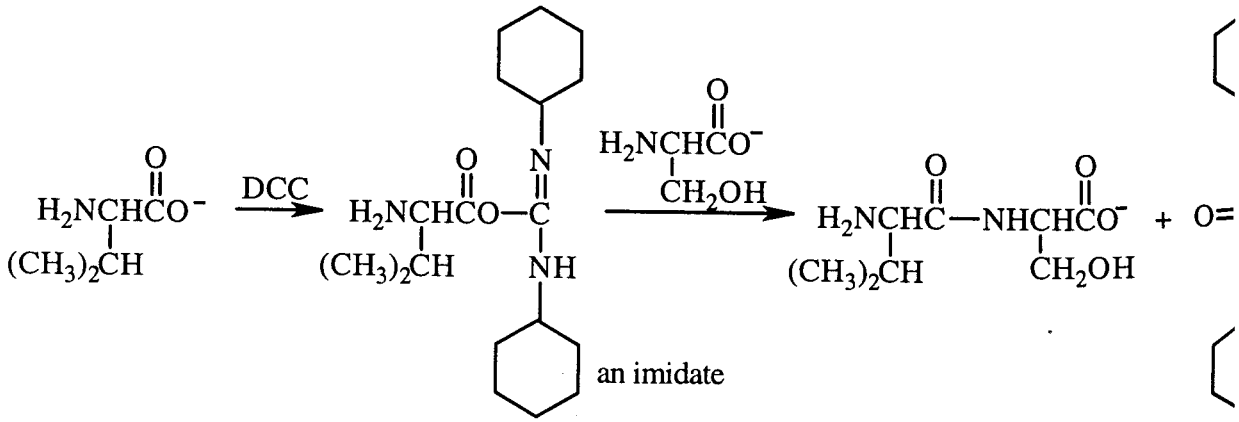
23. **Leu-Val** and **Val-Val** will be formed because the amino group of leucine is not reactive (so leucine could not be the C-terminal amino acid) but the amino group of valine would react equally easily with the carboxyl group of leucine and the carboxyl group of valine.

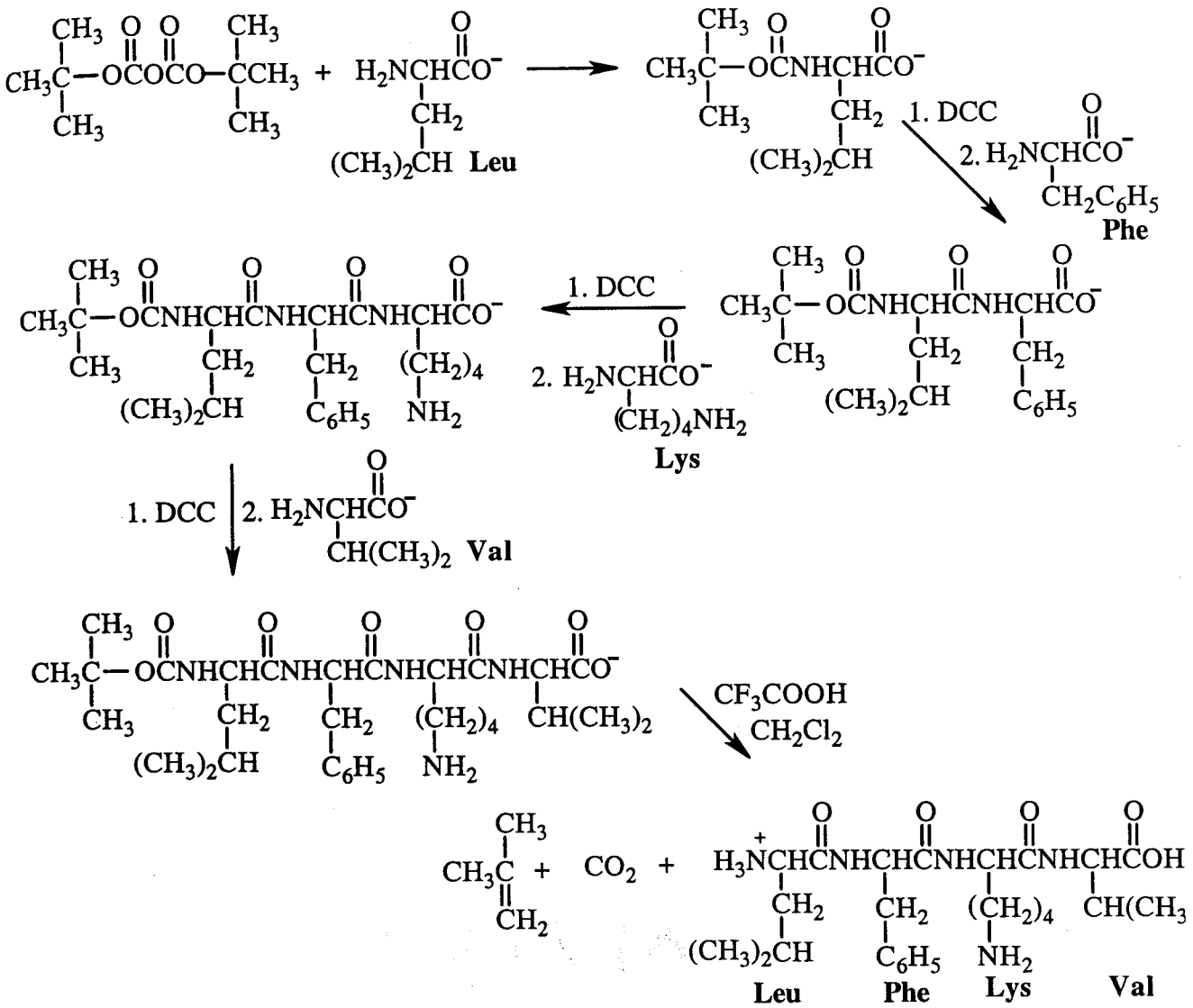


24. If valine's carboxyl group is activated with thionyl chloride, the OH group of serine, as well as the NH_2 group of serine, would react readily with the very reactive acyl halide, forming both an ester and an amide.



If valine's carboxyl group is activated with DCC, an imidate will be formed. Because an imidate is less reactive than an acyl chloride, the imidate will react with the more reactive NH_2 group in preference to the OH group.





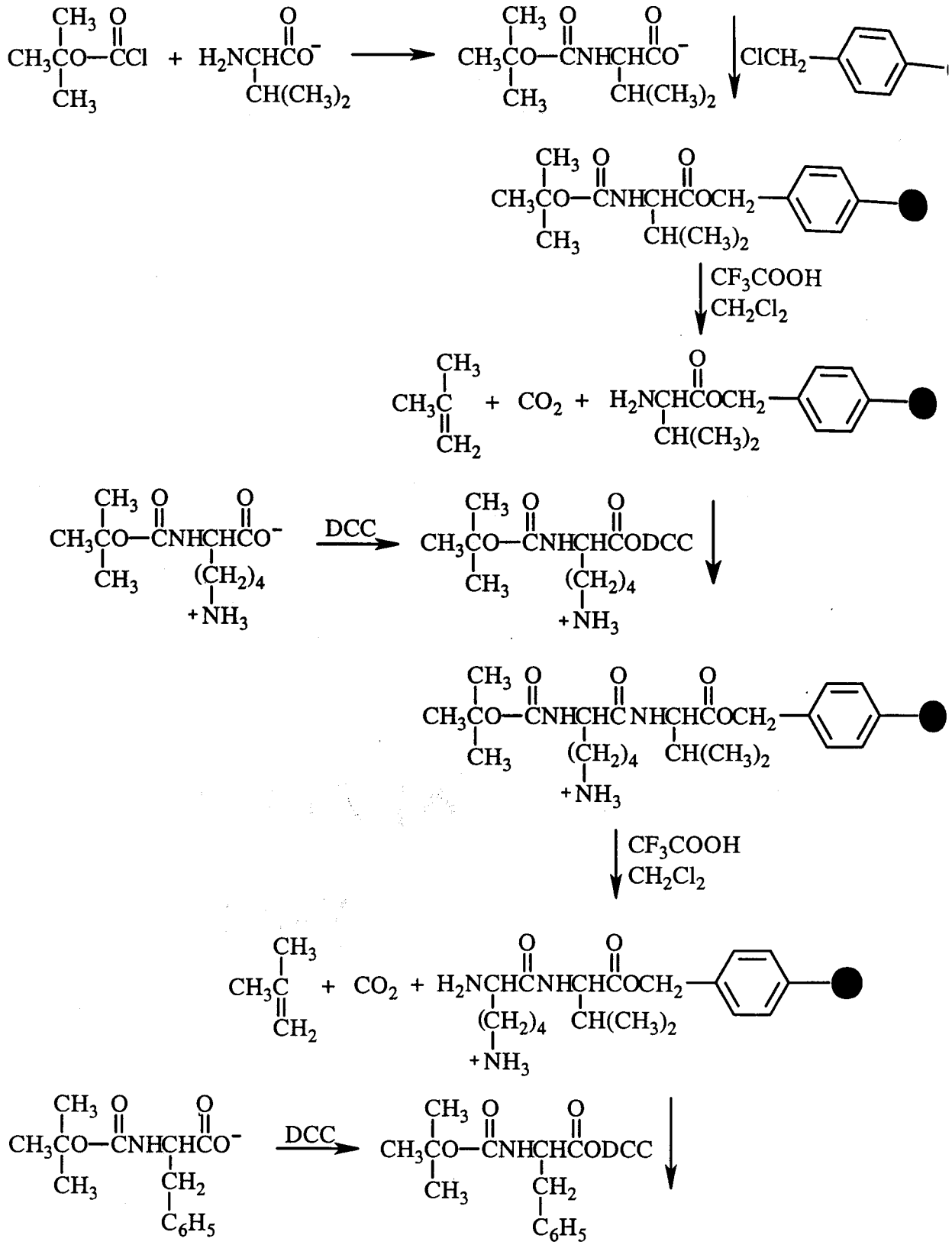
26. **a.** 5.8%

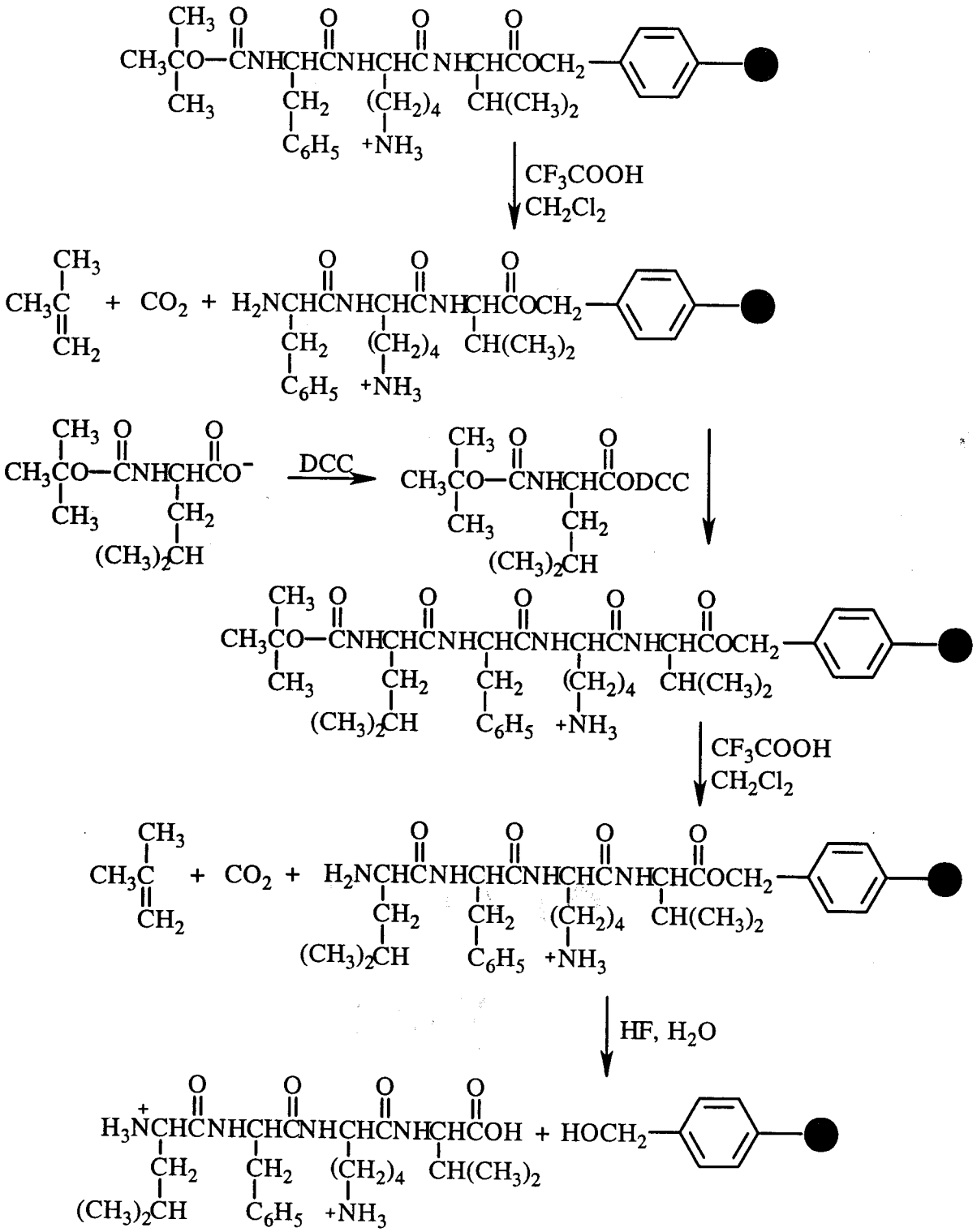
2	3	4	5	6	7	8	9
70%	49%	34%	24%	17%	12%	8.2%	5.8%

b. 4.4%

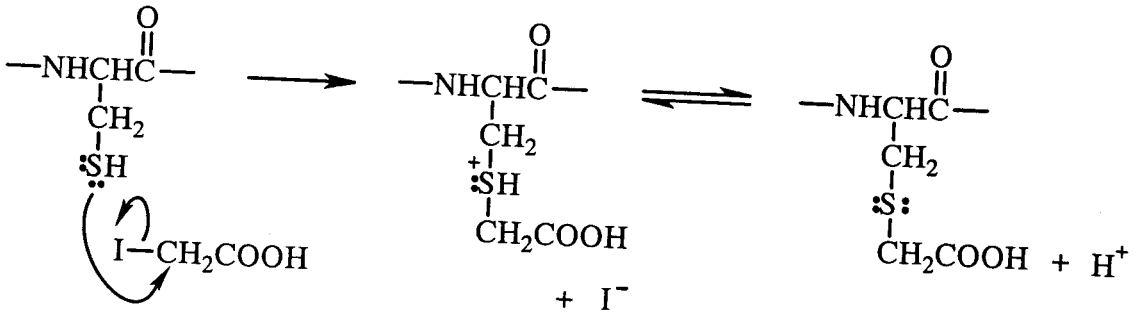
2	3	4	5	6	7	8	9	10	11	12	13	14	15
80%	64%	51%	41%	33%	26%	21%	17%	13%	11%	8.6%	6.9%	5.5%	4.4%

27.




CF3COOH
CH2Cl2
DCC
CF3COOH
CH2Cl2
HF, H2O

28.



29. Knowing that the N-terminal amino acid is Gly, look for a peptide fragment that contains Gly.

"f" tells you that the 2nd amino acid is Arg

"e" tells you the next two are Ala-Trp or Trp-Ala. **"d"** tells you that Glu is next to Ala, so 3 and must be Trp-Ala and the 5th is Glu

"g" tells you the 6th amino acid is Leu

"h" tells you the next two are Met-Pro or Pro-Met. **"c"** tells you that Pro is next to Val, so 7 and must be Met-Pro and the 9th is Val

"b" tells you the last amino acid is Asp

Gly-Arg-Trp-Ala-Glu-Leu-Met-Pro-Val-Asp

30. Cysteine can react with cyanogen bromide, but the lactone will not be formed, because it would be a strained four-membered-ring lactone and the sulfur would not be positively charged, causing it to be a poor leaving group. Without lactone formation, cleavage cannot occur.

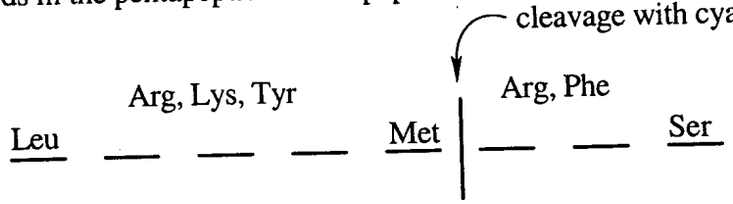
31. Treatment with Edman's reagent would release two PTH-amino acids in approximately equal amounts.

32. Solved in the text.

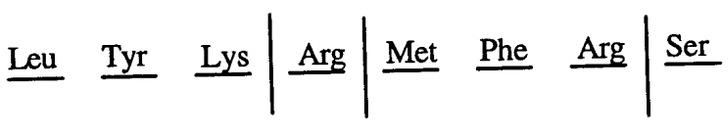
33. The data from treatment with Edman's reagent and carboxypeptidase A identify the first and last amino acids.

Leu ___ ___ ___ ___ ___ ___ Ser

The data from cleavage with cyanogen bromide identify the position of Met and identify the other amino acids in the pentapeptide and tripeptide but not their order.



The data from treatment with trypsin put the remaining amino acids in the correct position.



34. 74 amino acids/ 3.6 amino acids per turn = 20.6 turns of the helix
20.6 x 5.4 Å = **110 Å** in an α-helix

74 amino acids x 3.5 Å = **260 Å** in a straight chain

35. It would fold so that its nonpolar residues are on the outside of the protein in contact with the nonpolar membrane and its polar residues are on the inside of the protein.

36. **a.** A cigar-shaped protein has the greatest surface area to volume ratio, so it has the highest percentage of polar amino acids.

b. A subunit of a hexamer would have the smallest percentage of polar amino acids because part of the surface of the subunit can be on the inside of the hexamer and, therefore, have nonpolar amino acids on its surface.

37. An amino acid is insoluble in diethyl ether (a relatively nonpolar solvent) because an amino acid exits as a zwitterion at neutral pH. In contrast, carboxylic acids and amines have a single charge at neutral pH and, therefore, are less polar.

38.

a. His-Lys Leu-Val-Glu-Pro-Arg Ala-Gly-Ala

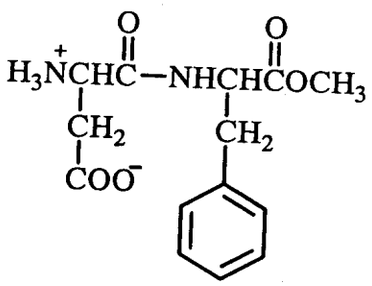
b. Leu-Gly-Ser-Met-Phe-Pro-Tyr Gly-Val

c. Val-Arg-Gly-Met-Arg-Ala Ser

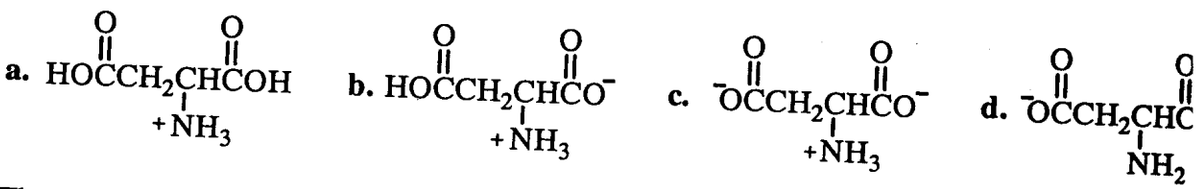
d. Ser-Phe-Lys-Met Pro-Ser-Ala-Asp

e. Arg Ser-Pro-Lys Lys Ser-Glu-Gly

39.

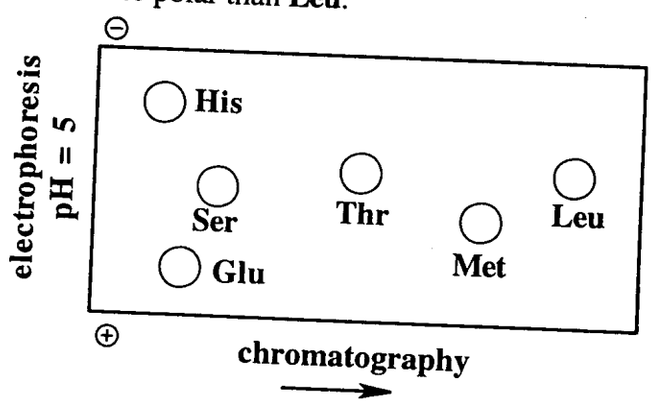


40.

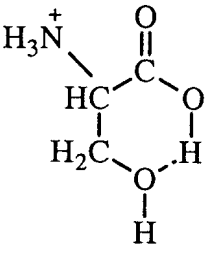


41. The student is correct. At the pI the total of the positive charges on the tripeptide's amino grou must be 1 to balance the one negative charge of the carboxyl group. When the pH of the solutic is equal to the pK_a of a lysine residue, the three lysine groups each have one-half a positive cha for a total of one and one-half positive charges. Thus, the solution must be more basic than this order to have just one positive charge.

42. Since the mixture of amino acids is in a solution of pH = 5, **His** will have an overall positive charge and **Glu** will have an overall negative charge. **His**, therefore, will migrate to the cathode, and **Glu** will migrate to the anode. **Ser** is more polar than **Thr** (both have OH groups, but **Thr** has an additional carbon); **Thr** is more polar than **Met** (**Met** has S instead of O and an additiona carbon); and **Met** is more polar than **Leu**.



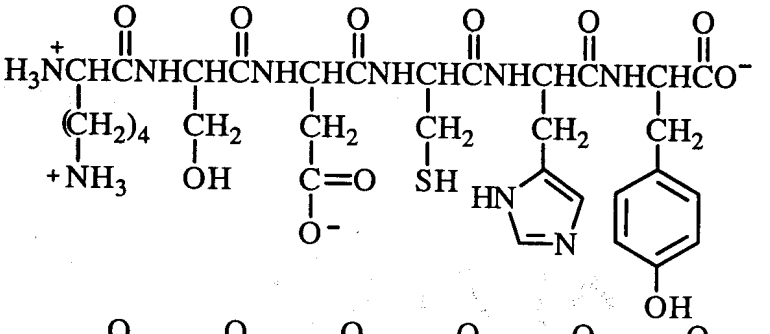
43. You would expect serine and cysteine to have lower pK_a's than alanine since a hydroxymethyl and a thiomethyl group are more electron withdrawing than a methyl group. Because oxygen is more electronegative than sulfur, one would probably expect serine to have a lower pK_a than cysteine. The fact that cysteine has the lower pK_a can be explained by stabilization of serine's carboxyl proton by hydrogen bonding to the β-OH group of serine, which causes it to have less of a tendency to be removed by base.



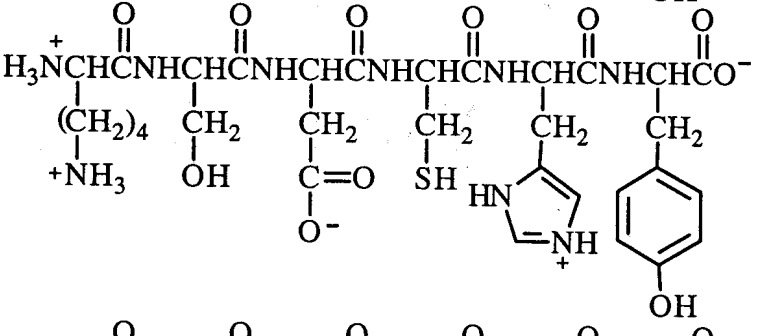
44. Each compound has two groups that can act as a buffer, one amino group and one carboxyl group. Thus, the compound in higher concentration (0.2 M glycine) will be a more effective buffer.

45.

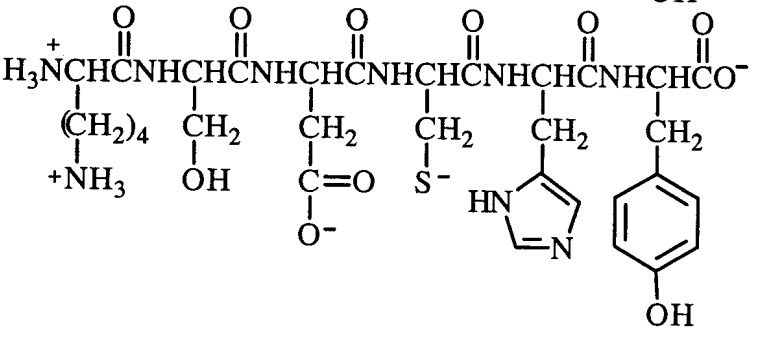
a.



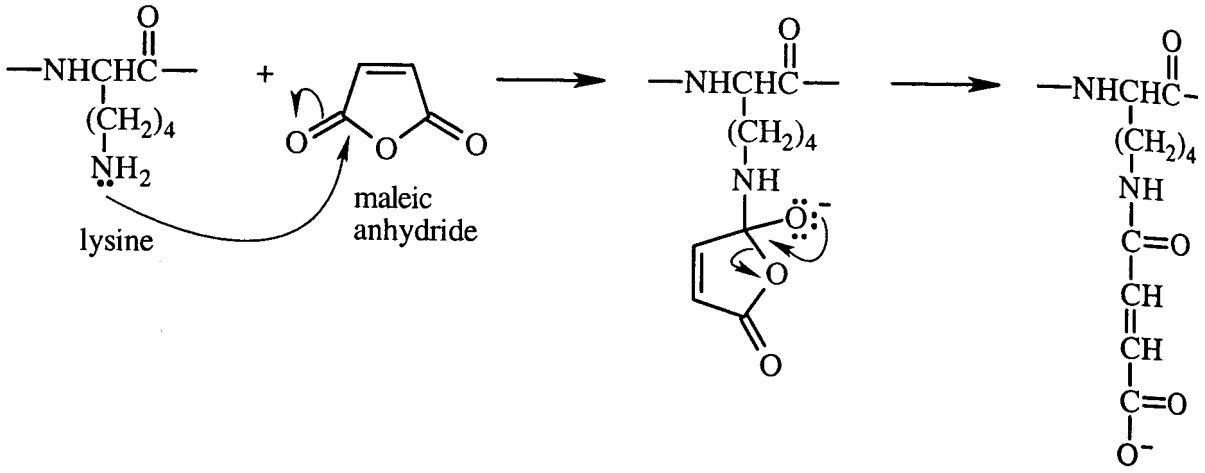
b.



c.



46. **a.** When the polypeptide is treated with maleic anhydride, lysine reacts with maleic anhydride, bu the amino group of arginine is not sufficiently nucleophilic to react. Therefore, trypsin will cleave only at arginine residues, since it will no longer recognize lysine residues. Trypsin also will not cleave the Arg-Pro bond.



b. The N-terminal end of each fragment will be positively charged because of the $^{+}NH_3$ group, the C-terminal end will be negatively charged because of the COO^- group; arginine residues will be positively charged; aspartate and glutamate residues will be negatively charged, and lysine residues will be negatively charged because they are attached to the maleic acid group.

A Gly-Ser-Asp-Ala-Leu-Pro-Gly-Ile-Thr-Ser-Arg — overall charge = 0
+ - + -

B Asp-Val-Ser-Lys-Val-Glu-Tyr-Phe-Glu-Ala-Gly-Arg — overall charge = –3
+ - - - - + -

C Ser-Glu-Phe-Lys-Glu-Pro-Arg — overall charge = –2
+ - - - + -

D Leu-Tyr-Met-Lys-Val-Glu-Gly-Arg-Pro-Val-Ser-Ala-Gly-Leu-Trp — overall charge = –1
+ - - + -

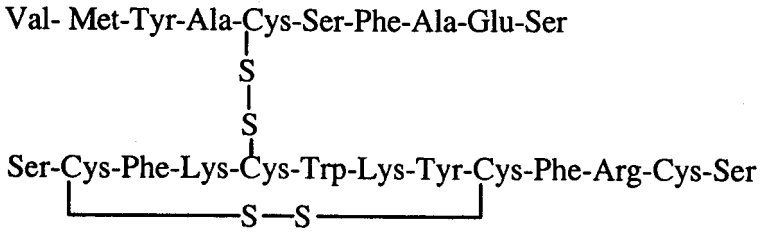
c. Elution order: **A > D > C > B**

47. First mark off where the chains would have been cleaved by chymotrypsin (C-side of Phe, Trp, Tyr).

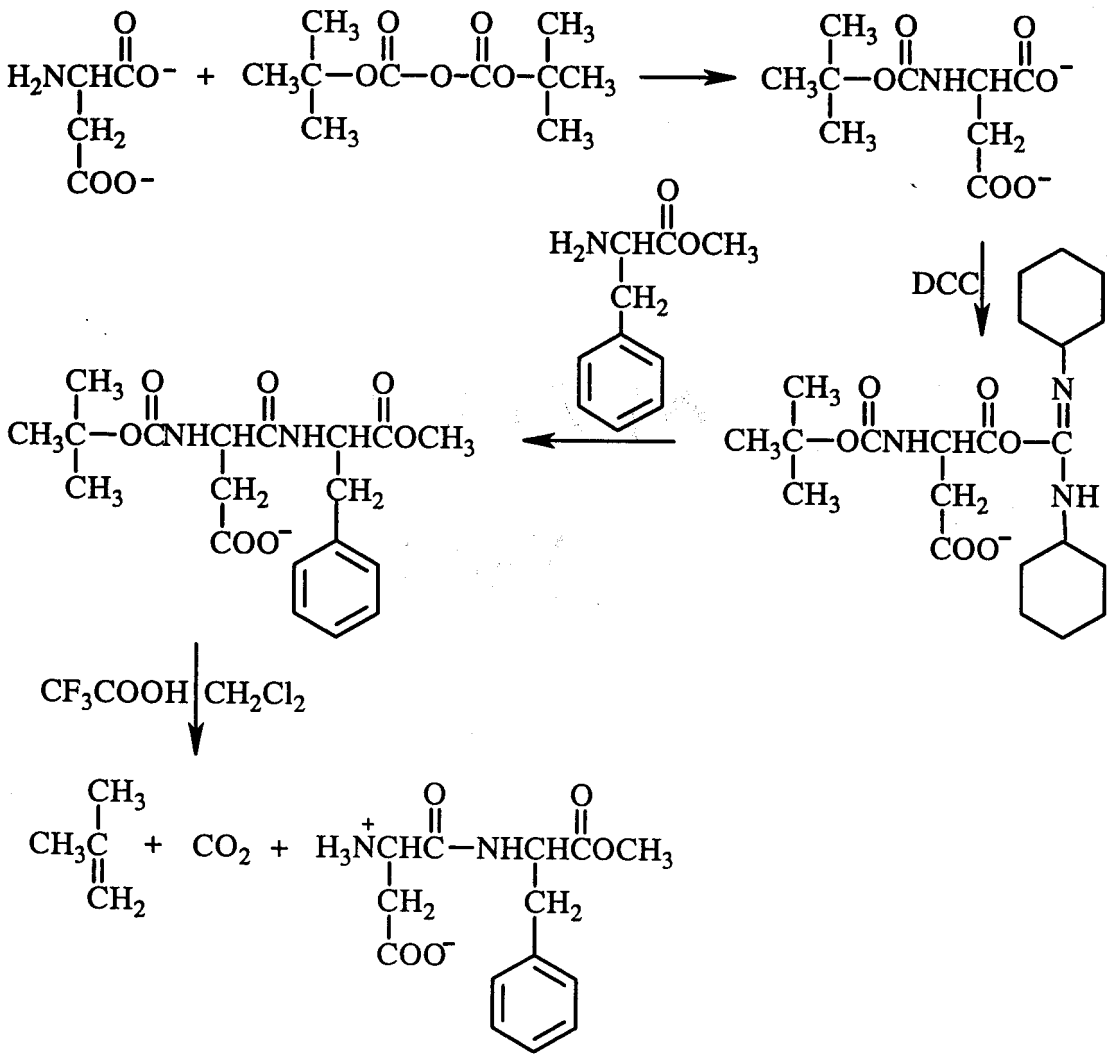
Val-Met-Tyr|Ala-Cys-Ser-Phe|Ala-Glu-Ser

Ser-Cys-Phe|Lys-Cys-Trp|Lys-Tyr|Cys-Phe|Arg-Cys-Ser

Then, from the pieces given, you can determine where the disulfide brides are.



48. The methyl ester of phenylalanine rather than phenylalanine itself should be added in the peptide bond-forming step because if esterification is done after amide bond formation, both carboxyl groups could be esterified. Some product will be obtained in which the amide bond is formed with the γ-carboxyl group of aspartate rather than with the α-carboxyl group.



49. Ser-Glu-Leu-Trp-Lys-Ser-Val-Glu-His-Gly-Ala-Met

From the experiment with carboxypeptidase, we know the C-terminal amino acid is Met.

"l" tells us the amino acid adjacent to Met is Ala

"e" tells us the next amino acid is Gly

"b" tells us the next amino acid is His

"g" tells us the next amino acid is Glu

"j" tells us the next amino acid is Val

"c" tells us the next amino acid is Ser

"i" tells us the next amino acid is Lys

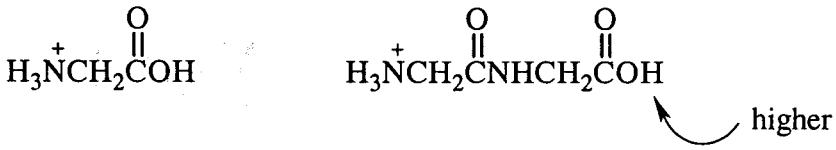
"a" tells us the next amino acid is Trp

"h" tells us the next amino acid is Leu

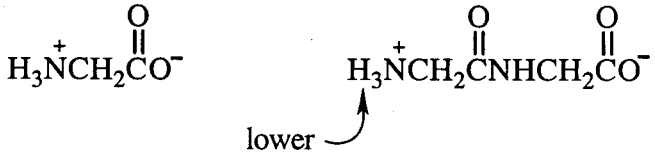
"k" tells us the next amino acid is Glu

"k" tells us the next (first) amino acid is Ser

50. The pK_a of the carboxylic acid of the dipeptide is higher than the pK_a of the carboxylic acid of the amino acid because the positively charged amino group of the amino acid is more strongly electron withdrawing than the amide group of the peptide. This causes the amino acid to be a stronger acid and have a lower pK_a.

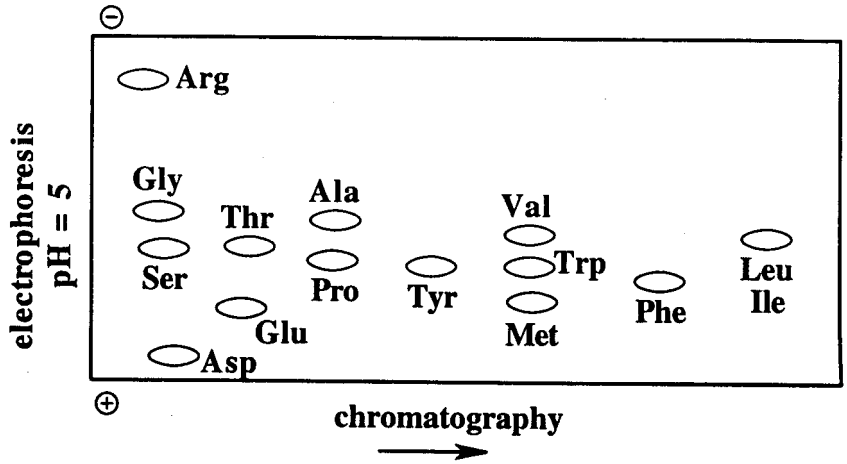


The pK_a of the amino group of the peptide is lower than the pK_a of the amino group of the amino acid because the amide group of the peptide is more strongly electron withdrawing than the carboxylate group of the amino acid.

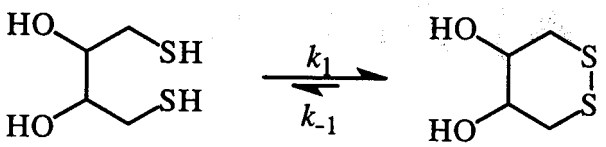


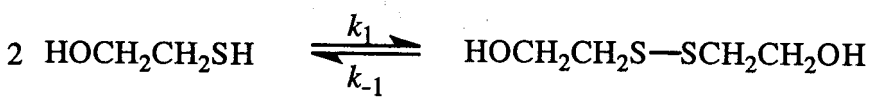
51. Finding that there is one less spot than the number of amino acids tells you that the spots for two of the amino acids superimpose. Since leucine and isoleucine have identical polarities, they are good candidates for being the amino acids that migrate to the same location.

Val (pI = 5.97), Trp (pI = 5.89), and Met (pI = 5.75) can be ordered based on their pI values because the one with the greatest p*I* will be the one with the greatest amount of positive charge at pH = 5.



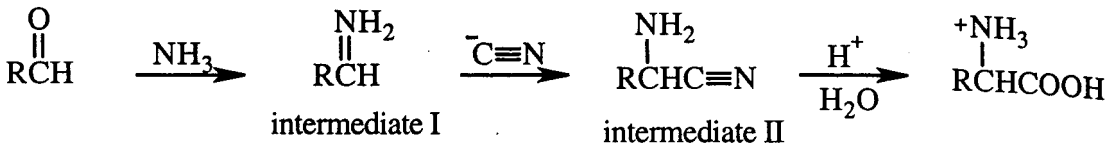
52. Oxidation of dithiothreitol is an intramolecular reaction so it occurs with a larger rate constant than the oxidation of 2-mercaptoethanol, which is an intermolecular reaction. The reverse reduction reaction should occur with about the same rate constant in both cases. Increasing the rate of the oxidation reaction while keeping the rate of the reduction reaction constant is responsible for the greater equilibrium constant, since $K_{eq} = k_1/k_{-1}$.



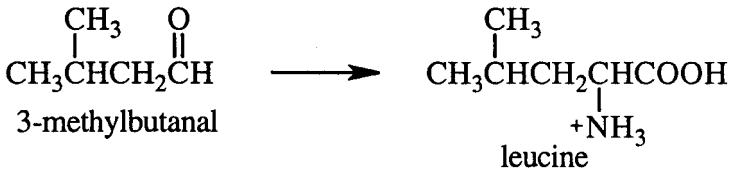


53.

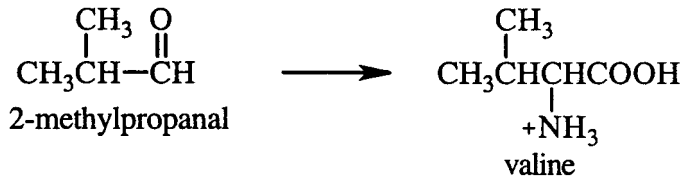
a.



b.



c.

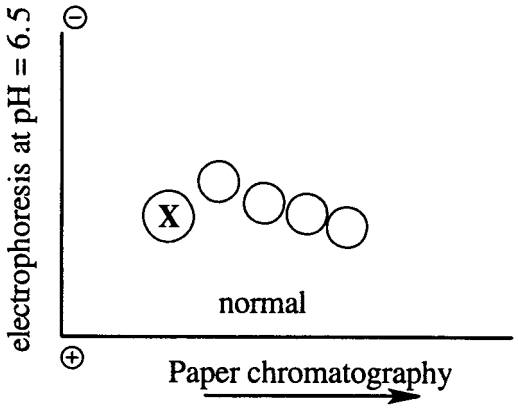


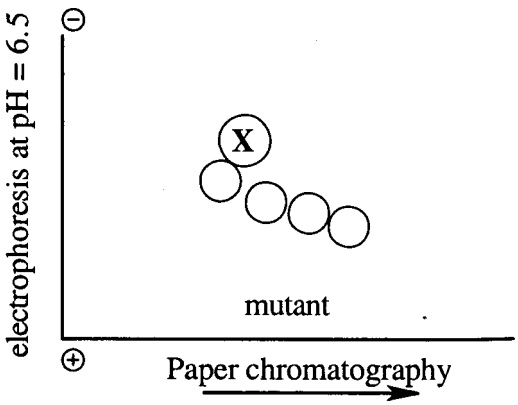
54.

amino acid	Absorbance at 280 nm	molar absorptivity = absorbance/concentration
tryptophan	0.61	610
tyrosine	0.15	150
phenylalanine	0.01	1

55. The spot marked with an **X** is the peptide that is different in the normal and mutant polypeptide. The spot is closer to the cathode, indicating that the substituted amino acid in the mutant has a higher pI and is less polar.

The fingerprints are those of hemoglobin (normal) and sickle-cell hemoglobin (mutant). In sickle-cell hemoglobin, a glutamate in the normal polypeptide is substituted with a valine. This agrees with our observation that the substituted amino acid is less negative and more nonpolar. (See the discussion of sickle cell anemia on page 1131 of the text.)





56.

a. Acid-catalyzed hydrolysis indicates the peptide contains 12 amino acids.

___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___

b. Treatment with Edman's reagent indicates that Val is the N-terminal amino acid.

Val ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___

c. Treatment with carboxypeptidase A indicates that Ala is the C-terminal amino acid.

Val ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ ___ Ala

d. Treatment with cyanogen bromide indicates that Met is the 5th amino acid with Arg, Gly, Ser in an unknown order in positions 2, 3, and 4.

Val ___ ___ ___ Met ___ ___ ___ ___ ___ ___ Ala

Arg, Gly, Ser

e. Treatment with chymotrypsin indicates that Tyr is the 6th amino acid, Phe is the 10th, and Ser the 11th .

Val ___ ___ ___ Met Tyr ___ ___ ___ Phe Ser Ala

Arg, Gly, Ser

The tetrapeptide that contains Phe, also contains Pro and 2 Lys. Cleavage would not have occurred at Tyr if it had been adjacent to Pro. Therefore, the 7th amino acid is Lys.

Val ___ ___ ___ Met Tyr Lys ___ ___ Phe Ser Ala

Arg, Gly, Ser Pro, Lys

f. Treatment with trypsin indicates that Arg is the 3rd amino acid, and Ser is 2nd and Gly 4th.

Val Ser Arg Gly Met Tyr Lys ___ ___ Phe Ser Ala

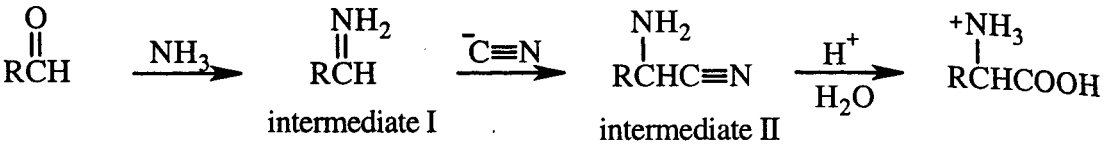
Pro, Lys

Since trypsin catalyzed cleavage between the 7th and 8th amino acids, Lys must be the 8th amino acid, since cleavage would not have occurred at Pro.

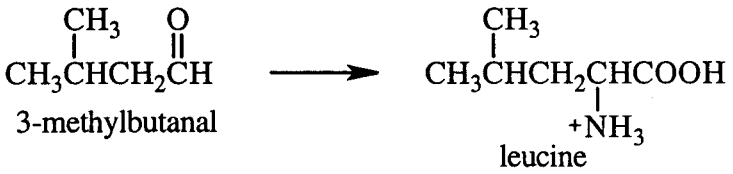
Val Ser Arg Gly Met Tyr Lys Lys Pro Phe Ser Ala

53.

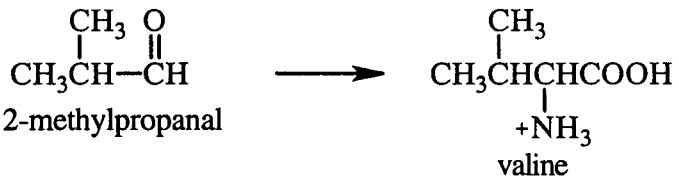
a.



b.



c.

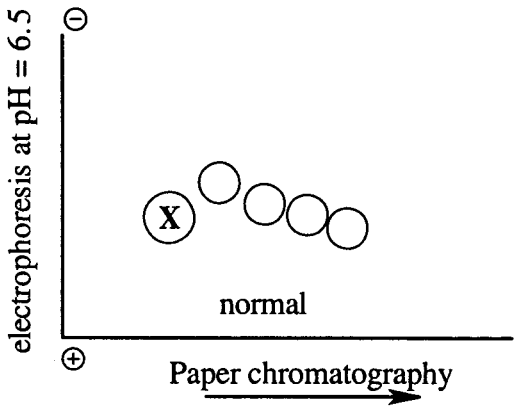


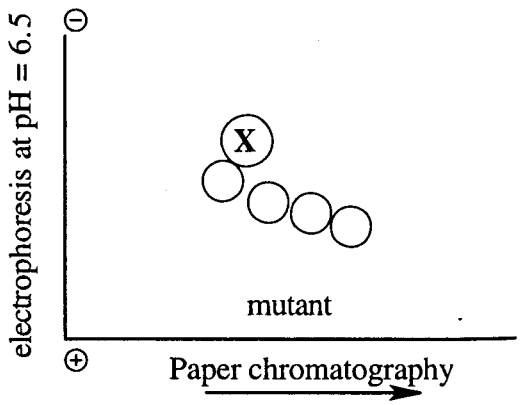
54.

amino acid	Absorbance at 280 nm	molar absorptivity = absorbance/concentration
tryptophan	0.61	610
tyrosine	0.15	150
phenylalanine	0.01	1

55. The spot marked with an **X** is the peptide that is different in the normal and mutant polypeptide. The spot is closer to the cathode, indicating that the substituted amino acid in the mutant has a higher pI and is less polar.

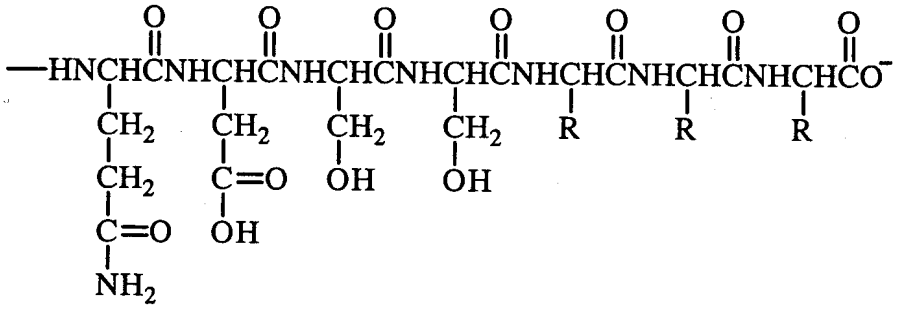
The fingerprints are those of hemoglobin (normal) and sickle-cell hemoglobin (mutant). In sickle-cell hemoglobin, a glutamate in the normal polypeptide is substituted with a valine. This agrees with our observation that the substituted amino acid is less negative and more nonpolar. (See the discussion of sickle cell anemia on page 1131 of the text.)





57. **a.** The C-terminal end of the protein contains 3 nonpolar amino acids and 4 polar amino acids. Each of the seven amino acids has two atoms that can form hydrogen bonds for a total of 14 atoms that can form hydrogen bonds. Gln and Asp each have two additional groups, and each serine one additional group that can form hydrogen bonds. Thus, the terminal end of the protein has 3 hydrophobic groups and can form 20 hydrogen bonds. So there are 20 hydrogen bonds formed between protein groups and water that must be broken before the protein groups can hydrogen bond to each other. So 20 hydrogen bonds are broken and 20 hydrogen bonds are formed (10 hydrogen bonds from 20 atoms involved in intramolecular hydrogen bonds, and 10 hydrogen bonds from 20 liberated water molecules forming hydrogen bonds with each other). Thus ΔG° comes only from removing the three hydrophobic groups from water (3 x –4) = **–12 kcal/mol.**

b. If two of the polar groups do not form intramolecular bonds in the interior of the protein, 20 hydrogen bonds will be broken, but only 19 will be formed, so $\Delta G^\circ = -12 + 3 =$ **–9 kcal/mol.**



58. Because the native enzyme has four disulfide bridges, the denatured enzyme has eight cysteine residues. The first cysteine has a 1 in 7 chance of forming a disulfide bridge with the correct cysteine. The first cysteine of the next pair has a 1 in 5 chance, and the first cysteine of the third pair has a 1 in 3 chance.

$$\frac{1}{7} \times \frac{1}{5} \times \frac{1}{3} = 0.0095$$

If disulfide bridge formation were entirely random, the recovered enzyme should have 0.95% of its original activity. The fact that the enzyme Professor Gold recovered had 80% of its original activity proves her hypothesis that disulfide bridges form after the minimum energy conformation of the protein has been achieved. In other words, disulfide bridge formation is not random but is determined by the tertiary structure of the protein.

Chapter 23 Practice Test

1. Give the structure of the following amino acids at pH = 7:

   a. glutamic acid **b.** lysine **c.** isoleucine **d.** arginine **e.** asparagine

2. Draw the form of histidine that predominates at:

   a. pH = 1 **b.** pH = 4 **c.** pH = 8 **d.** pH = 11

3. Answer the following:

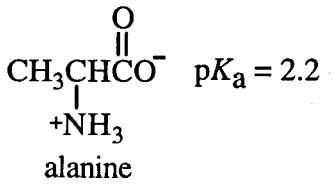
   a. Alanine has a pI = 6.02 and serine has a pI = 5.68. Which would have the highest concentration of positive charge at pH = 5.50?

   b. Which amino acid is the only one that does not have a chirality center?

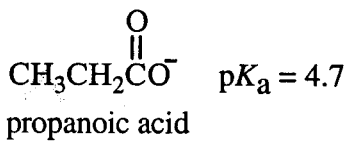
   c. Which are the two most nonpolar amino acids?

   d. Which amino acid has the lowest pI?

4. Why does the carboxyl group of alanine have a lower pK_a than the carboxyl group of propanoic acid?



alanine, $pK_a = 2.2$



propanoic acid, $pK_a = 4.7$

5. Indicate whether each of the following is true or false:

   a. A cigar-shaped protein has a greater percentage of polar residues than a spherical protein. T F

   b. Naturally occurring amino acids have the L-configuration. T F

   c. There is free rotation about a peptide bond. T F

6. Give the compound obtained from mild oxidation of cysteine.

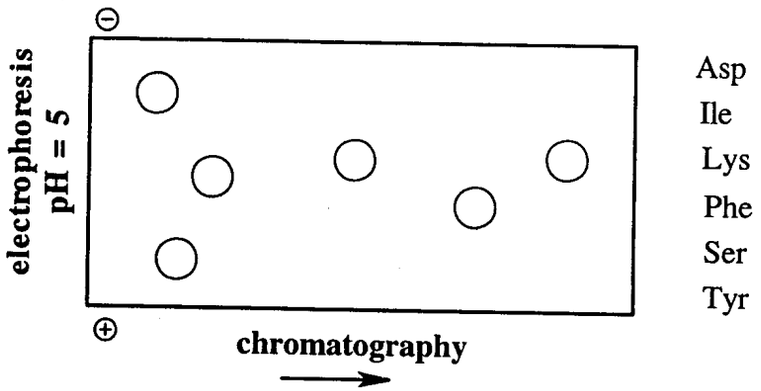
7. Define the following:

a. the primary structure of a protein

b. the tertiary structure of a protein

c. the quaternary structure of a protein

8. Identify the spots.



9. Calculate the pI of each of the following amino acids:

a. phenylalanine (pK_a's = 2.16, 9.18)

b. arginine (pK_a's = 2.17, 9.04, 12.48)

10. From the following information, determine the primary sequence of the decapeptide:

a. Acid hydrolysis gives: Ala, 2 Arg, Gly, His, Ile, Lys, Met, Phe, Ser
b. Reaction with Edman's reagent liberated Ala
c. Reaction with carboxypeptidase A liberated Ile

d. Reaction with cyanogen bromide (cleaves on the C-side of Met)
1. Gly, 2 Arg, Ala, Met, Ser
2. Lys, Phe, Ile, His

e. Reaction with trypsin (cleaves on the C-side of Arg and Lys)
1. Arg, Gly
2. Ile
3. Phe, Lys, Met, His
4. Arg, Ser, Ala

f. Reaction with thermolysin (cleaves on the N-side of Leu, Ile, Phe, Trp, Tyr)
1. Lys, Phe
2. 2 Arg, Ser, His, Gly, Ala, Met
3. Ile

CHAPTER 24
Catalysis

Important Terms

acid catalyst	a catalyst that increases the rate of a reaction by donating a proton.
active site	a pocket or cleft in an enzyme where the substrate is bound.
acyl-enzyme intermediate	an amino acid residue of an enzyme that has been acylated while catalyzing a reaction.
anchimeric assistance (intramolecular catalysis)	catalysis in which the catalyst that facilitates the reaction is part of the molecule undergoing reaction.
base catalyst	a catalyst that increases the rate of a reaction by removing a proton.
catalyst	a substance that increases the rate of a reaction without itself being consumed in the overall reaction.
catalytic antibody	a compound that facilitates a reaction by forcing the conformation of the substrate in the direction of the transition state.
covalent catalysis (nucleophilic catalysis)	catalysis that occurs as a result of a nucleophile forming a covalent bond with one of the reactants.
effective molarity	the concentration of the reagent that would be required in an intermolecular reaction for it to have the same rate as an intramolecular reaction.
electrophilic catalyst	an electrophile that facilitates a reaction.
electrostatic catalysis	stabilization of a charge by an opposite charge.
enzyme	a protein that is a catalyst.
***gem*-dialkyl effect**	two alkyl groups on a carbon whose effect is to increase the probability that the molecule will be in the proper conformation for ring closure.
general-acid catalysis	catalysis in which a proton is transferred to the reactant during the slow step of the reaction.
general-base catalysis	catalysis in which a proton is removed from the reactant during the slow step of the reaction.
induced fit model	a model that describes the specificity of an enzyme for its substrate: the shape of the active site does not become completely complementary to the shape of the substrate until after the enzyme has bound the substrate.
intramolecular catalysis (anchimeric assistance)	catalysis in which the catalyst that facilitates the reaction is part of the molecule undergoing reaction.
lock-and-key model	a model that describes the specificity of an enzyme for its substrate: the substrate fits the enzyme like a key fits into a lock.
metal-ion catalysis	catalysis in which the species that facilitates the reaction is a metal ion.

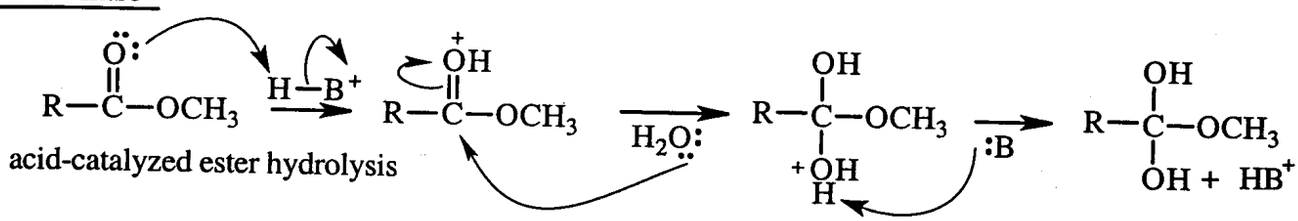
molecular recognition	the recognition of one molecule by another as a result of specific interactions; for example, the specificity of an enzyme for its subst
nucleophilic catalysis (covalent catalysis)	catalysis that occurs as a result of a nucleophile forming a covalent with one of the reactants.
nucleophilic catalyst	a catalyst that increases the rate of a reaction by acting as a nucleop
oxocarbenium ion	an ion in which the positive charge is shared by a carbon and an ox
pH-activity profile or pH-rate profile	a plot of the activity of an enzyme as a function of the pH of the rea mixture.
relative rate	obtained by dividing the actual rate constant by the rate constant of slowest reaction in the group being compared.
site-specific mutagenesis	a technique that substitutes one amino acid of a protein for another.
specific-acid catalysis	catalysis in which the proton is fully transferred to the reactant befo slow step of the reaction.
specific-base catalysis	catalysis in which the proton is completely removed from the reacta before the slow step of the reaction.
substrate	the reactant of an enzyme-catalyzed reaction.
transition-state analog	a compound that is structurally similar to the transition state of an e catalyzed reaction.

...tions to Problems

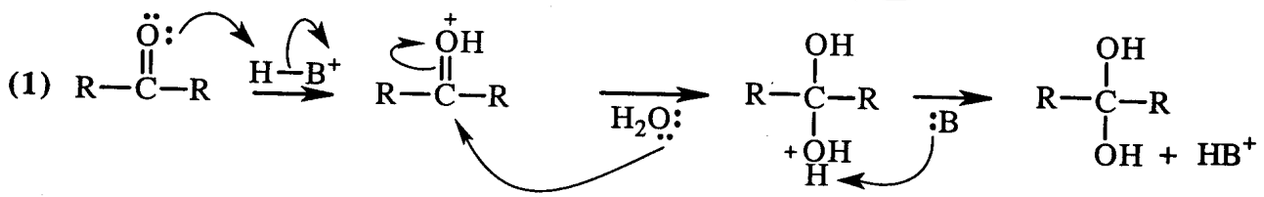
$\Delta H^{\dagger}$, E_a, $\Delta S^{\dagger}$, $\Delta G^{\dagger}$, k_{rate} (These are the parameters that measure the difference in energy between the reactant and the transition state.)

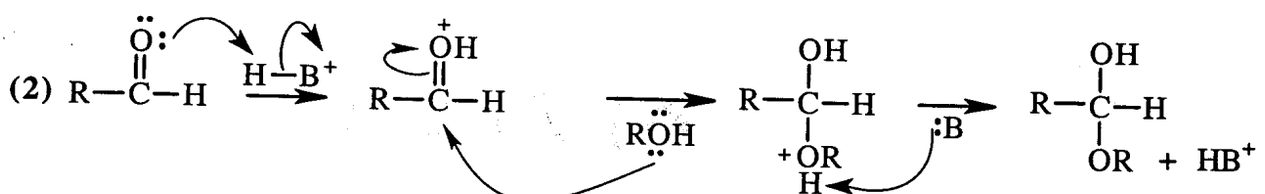
Note that **(1)** and **(2)** have only the first phase (because the final product of the reaction is a tetrahedral intermediate), **(3)** has only the second phase (because the initial reactant is a tetrahedral intermediate) and **(4)** has both the first and second phases.

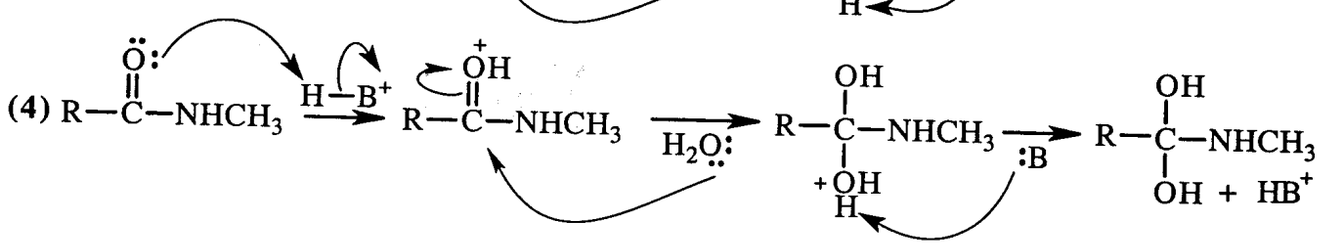
First Phase



acid-catalyzed ester hydrolysis



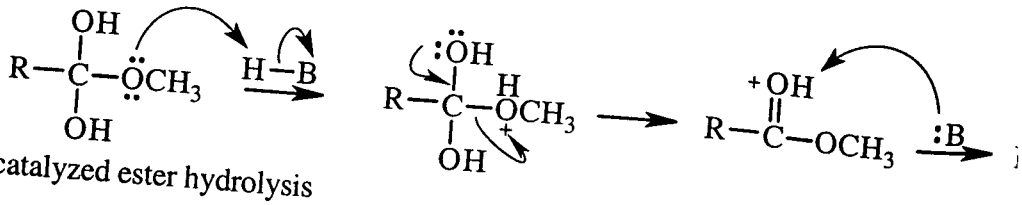




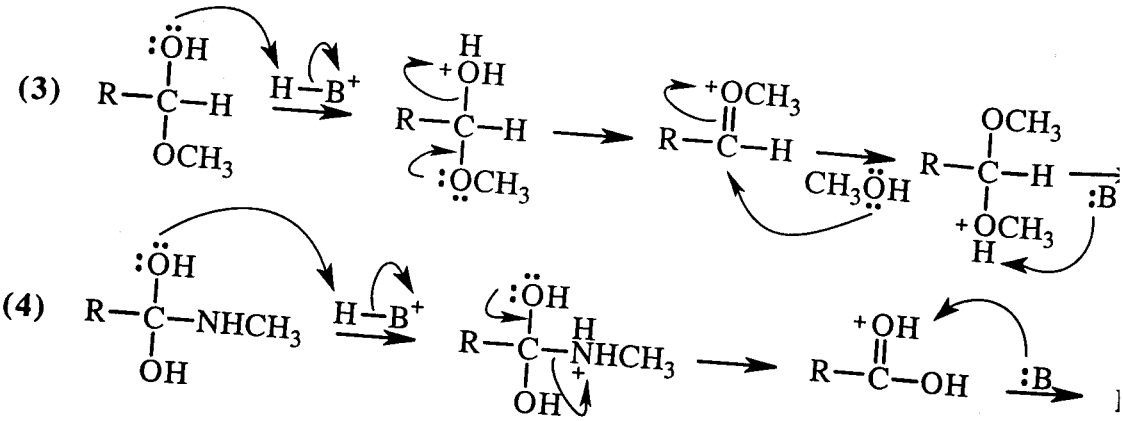
a. similarities: the first step is protonation of the carbonyl compound, the second step is attack of a nucleophile on the protonated carbonyl compound, and the third step is loss of a proton.

b. differences: the carbonyl compound that is used as the starting material, and the nucleophile that is used in **(2)** is an alcohol rather than water.

Second Phase



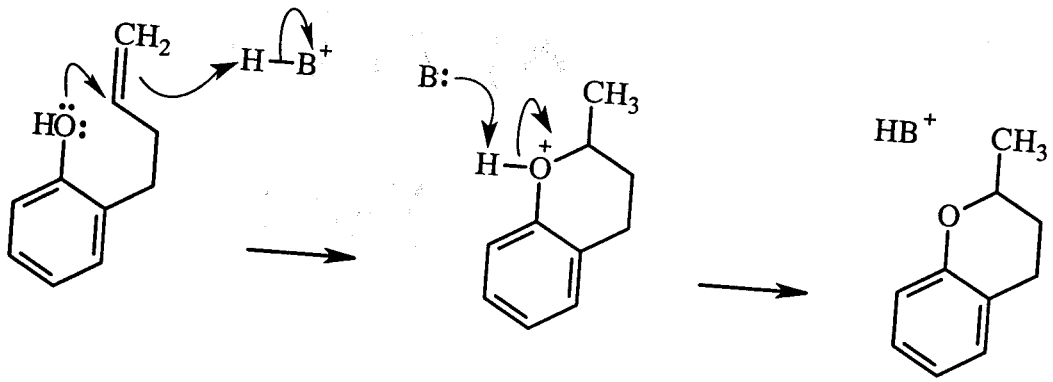
acid-catalyzed ester hydrolysis



a. similarities: the first step is protonation of the tetrahedral intermediate, and the secon elimination of a group from the tetrahedral intermediate. In two of the three reactions third step is loss of a proton.

b. differences: the nature of the group that is eliminated from the tetrahedral intermediat acetal formation, the third step is not loss of a proton because the intermediate does no proton to lose. Instead, the third step is attack of a nucleophile, and the fourth step is lo proton.

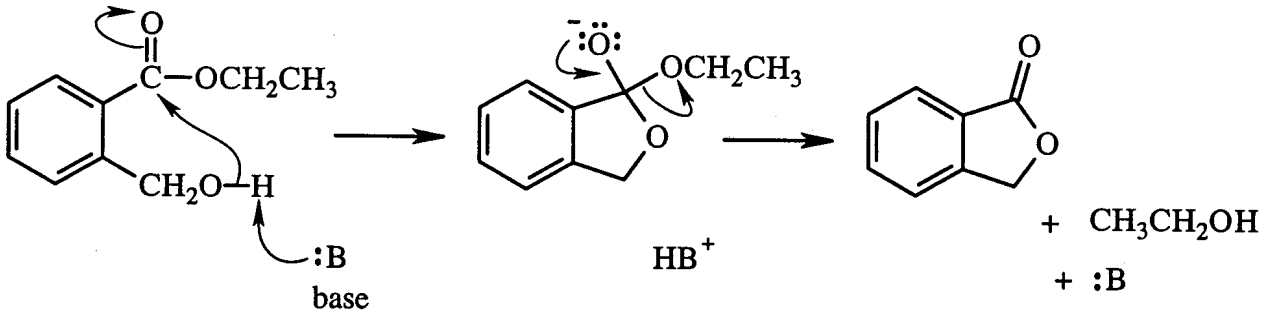
3.



4. Solved in the text.

5. Hydroxide ion catalyzes formation of the tetrahedral intermediate by acting as a nucleophilic catalyst. (It is a better nucleophile than water.) Hydroxide ion catalyzes collapse of the tetrahedral intermediate by acting as a specific-base catalyst. It removes a proton from the neutral tetrahedral intermediate, creating a negatively charged oxygen. It is easier for a negatively charged oxygen to expel a leaving group because the transition state is more stable than the transition state formed from a neutral oxygen, which would have a partial positive charge on the oxygen.

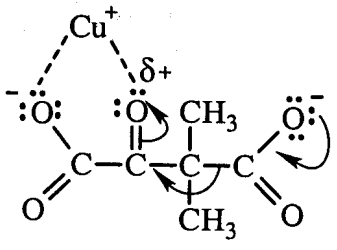
6.



7.

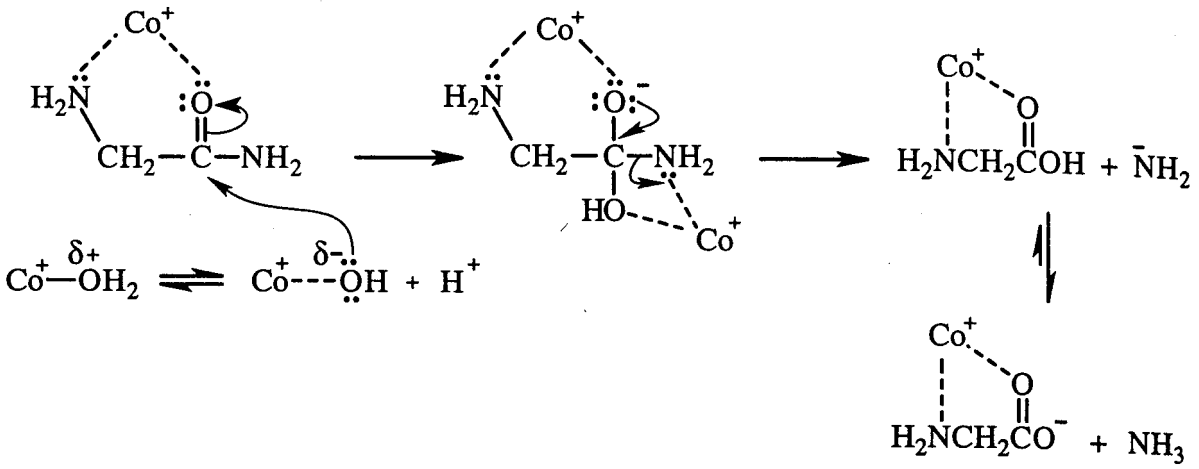
$$\frac{1.5 \times 10^6\ s^{-1}M^{-1}}{0.6\ s^{-1}M^{-1}} = 2.5 \times 10^6$$

8. The metal ion catalyzes the decarboxylation reaction by complexing with the negatively charged oxygen of the carboxyl group and carbonyl oxygen of the β-keto group, thereby making it easier for the carbonyl oxygen to accept the electrons that are left behind when CO_2 is eliminated.

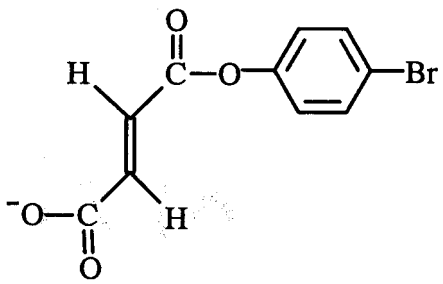


Because acetoacetate and the monoethyl ester of dimethyloxaloacetate do not have a negatively charged oxygen on one carbon and a carbonyl group on an adjacent carbon with which to form a complex, a metal ion does not catalyze decarboxylation of these compounds.

9. Co^{2+} can catalyze the reaction in three different ways. It can complex with the reactant, increasing the susceptibility of the carbonyl group to nucleophilic attack. It can also complex with water, increasing the tendency of water to lose a proton, resulting in a stronger nucleophile for hydrolysis. And it can complex with the leaving group, decreasing its basicity and thereby making it a better leaving group.

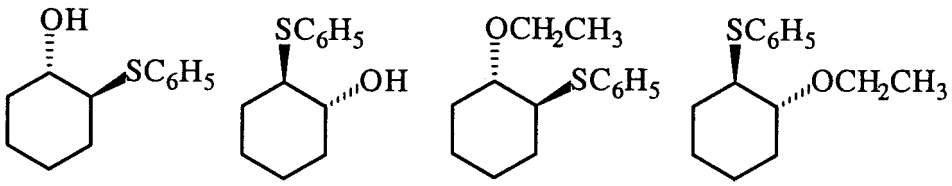


10. Because the reacting groups in the trans isomer are pointed in opposite directions, they cannot react in an intramolecular reaction. Because they can only react via an intermolecular pathway, they will have approximately the same rate of reaction as they would have if the reacting groups were in separate molecules. Consequently, the relative rate would be expected to be close to one.



11. **a.** The nucleophile can attack the back side of either of the two ring carbons to which the sulfur is bonded, thereby forming two trans products. There are two nucleophiles (water and ethanol), so a total of four products will be formed.

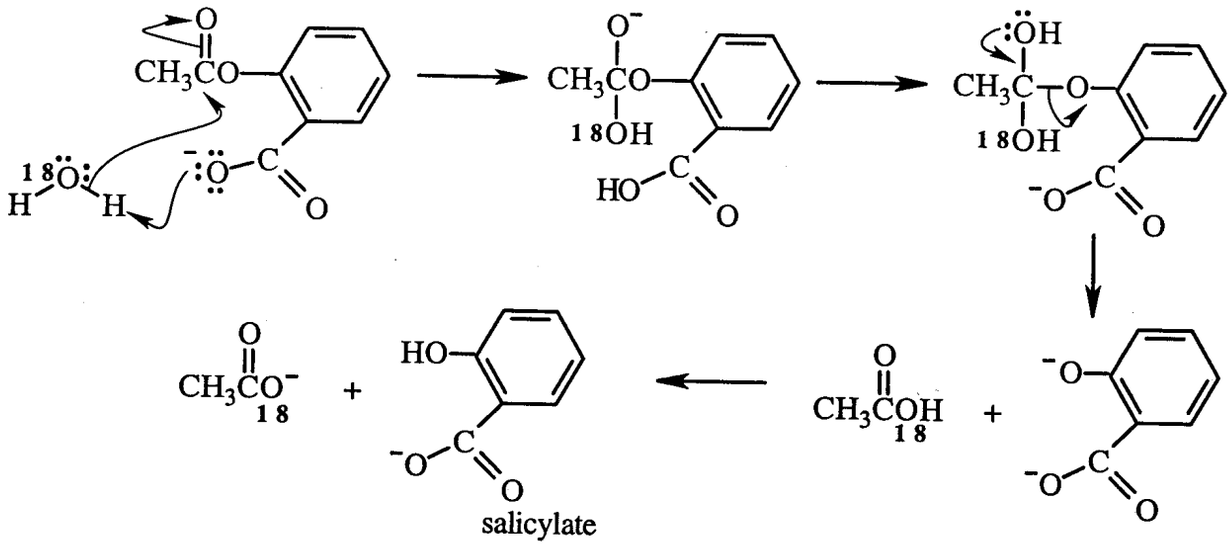
b.



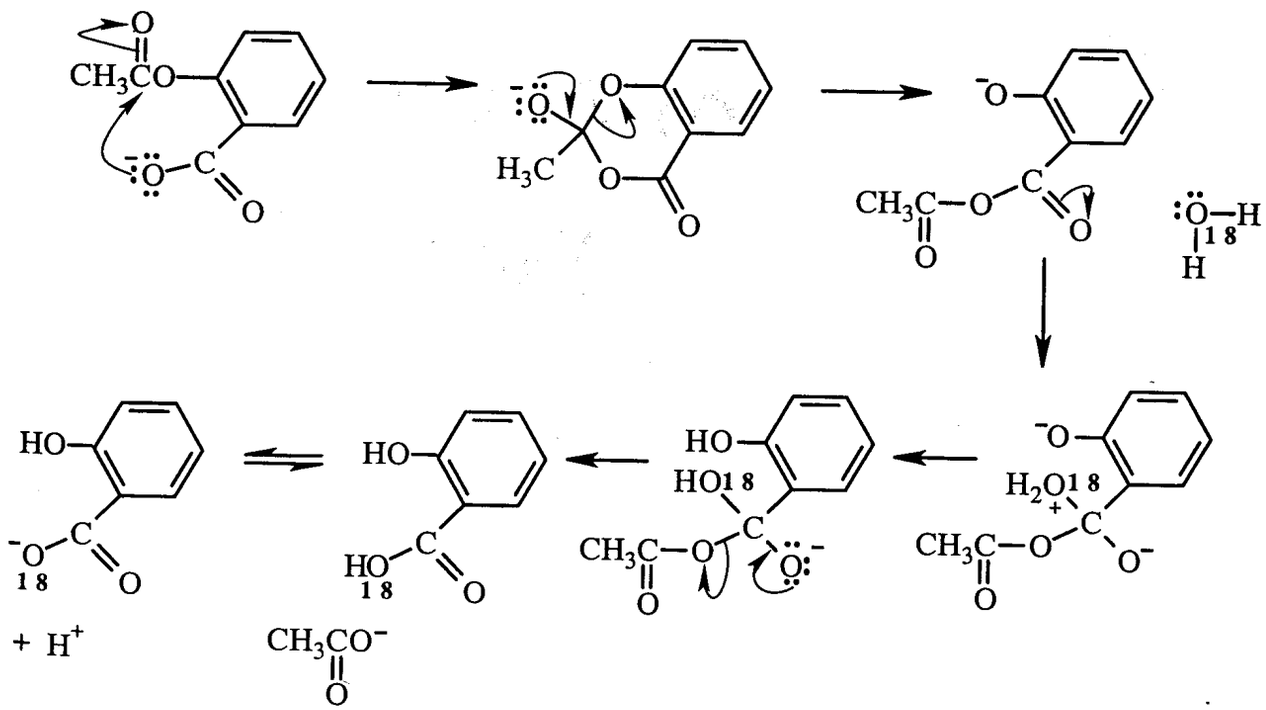
12. Solved in the text.

13. The tetrahedral intermediate has two leaving groups, a carboxylate ion and a phenolate ion. The carboxylate ion is a weaker base (a better leaving group) than the phenolate ion, so the tetrahedral intermediate re-forms **A**. The 2,4-dinitrophenoxide ion is a weaker base (better leaving group) than the carboxylate ion, so the tetrahedral intermediate forms **B**.

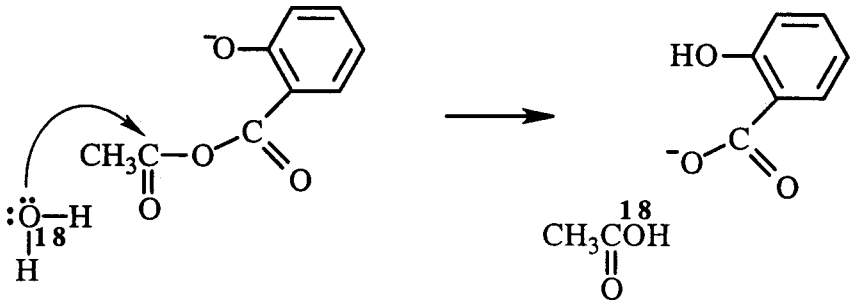
14. If the *ortho*-carboxyl substituent acts as an intramolecular general-base catalyst, ^{18}O would not be incorporated into salicylic acid.



If the *ortho*-carboxyl substituent acts as an intramolecular nucleophilic catalyst, ^{18}O would be incorporated into salicylic acid.

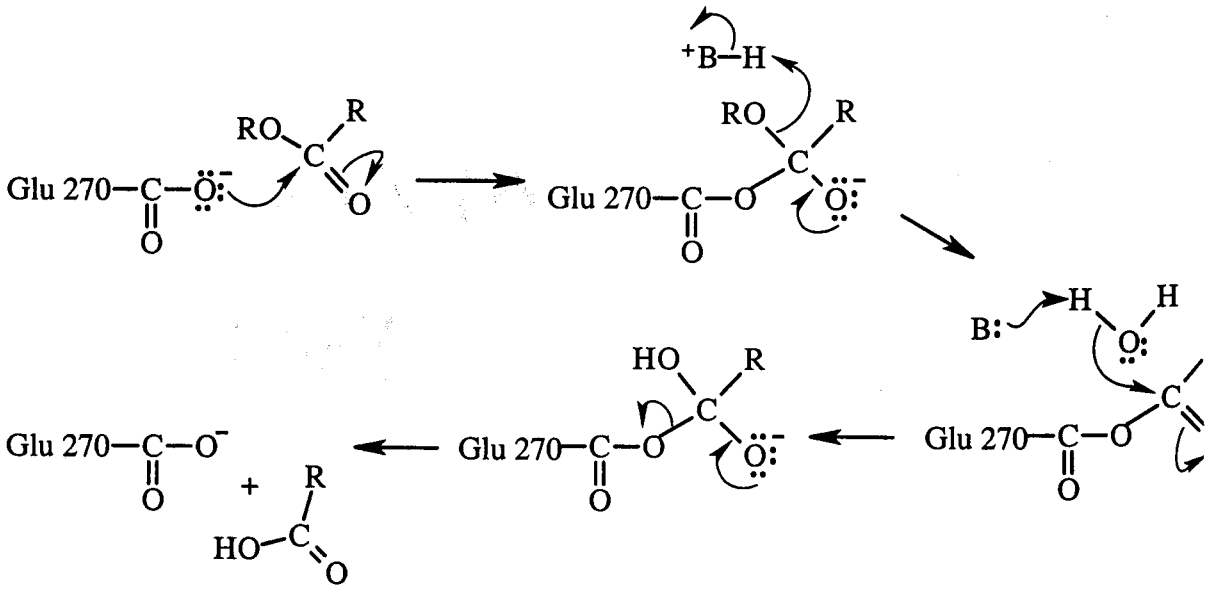


Not all the salicylic acid would contain ^{18}O, because the anhydride intermediate can be hydrolyzed in two different ways.

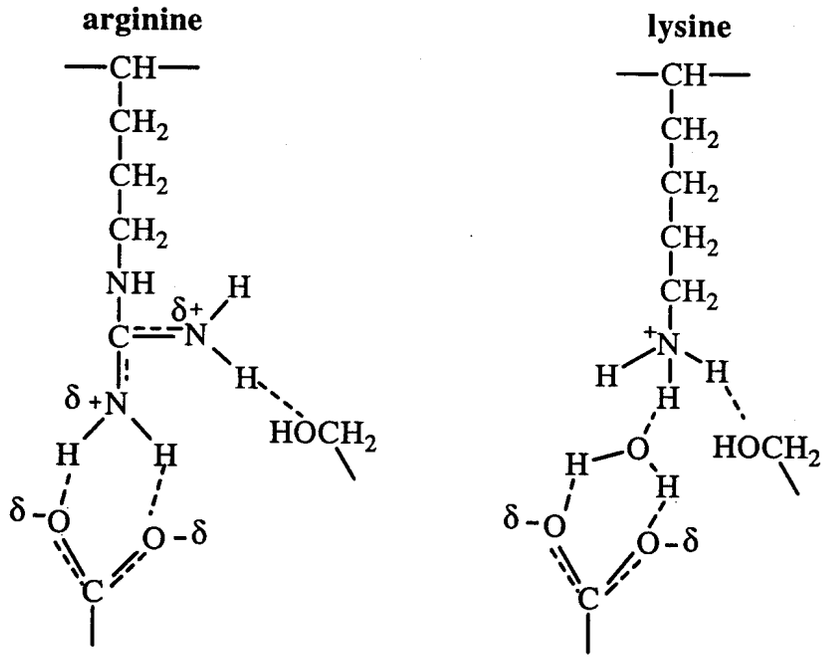


15. Ser-Ala-Phe would be more readily cleaved by carboxypeptidase A because the phenyl substituent of phenylalanine would be more attracted to the hydrophobic pocket of the enzyme than would the negatively charged substituent of aspartate.

16. Glu 270 attacks the carbonyl group of the ester, forming a tetrahedral intermediate. Collapse c the tetrahedral intermediate is most likely catalyzed by a general-acid group of the enzyme in order to increase the leaving ability of the RO group. (Perhaps the HO substituent of tyrosine i close enough in the esterase to act as the catalyst.) The group that donates the proton can then act as a general-base catalyst to remove a proton from water as it hydrolyzes the anhydride.

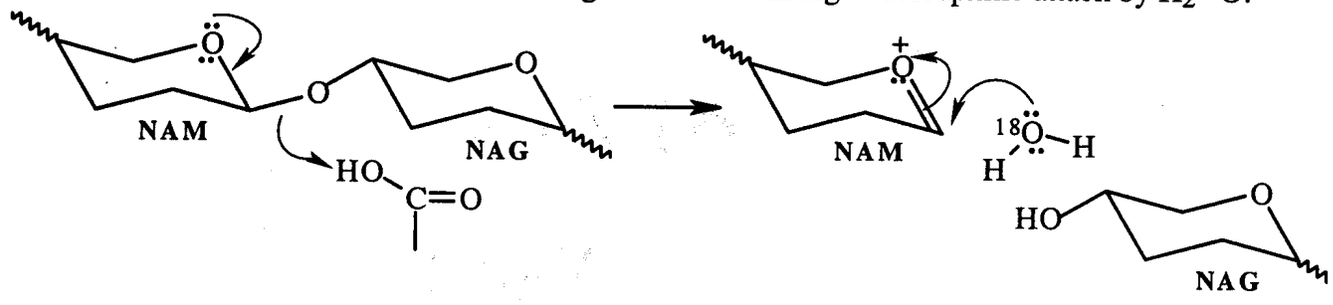


17. Because arginine extends farther into the binding pocket, it must be the one that forms direct hydrogen bonds. Lysine, which is shorter, needs the mediation of a water molecule in order to engage in bond formation with aspartate.



18. The side chains of D-Arg and D-Lys are not positioned to bind correctly at the active site.

19. NAM would contain ^{18}O because it is the ring that would undergo nucleophilic attack by $H_2{}^{18}O$.



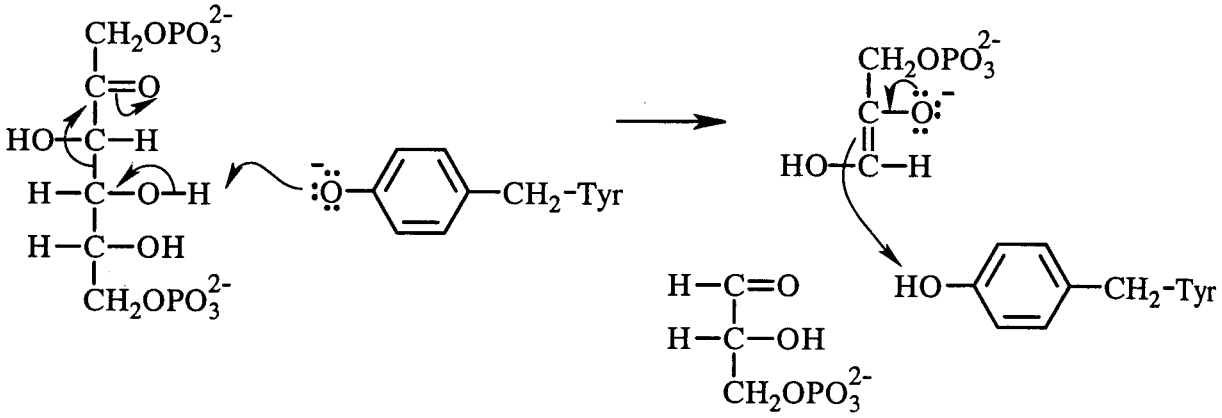
20. Lemon juice contains citric acid. Some of the side chains of an enzyme will become protonated in an acidic solution. This will change the charge of the group (for example a negatively charged aspartate, when protonated, becomes neutral), and because the shape of an enzyme is determined by the interaction of the side chains, changing the charges of the side chains will cause the enzyme to undergo a conformational change that leads to denaturation. When the enzyme is denatured, it loses its ability to catalyze the reaction that causes apples to turn brown.

21. In the absence of imine formation, D-fructose isomerizes to D-glucose and D-mannose (an equilibrium is set up between D-fructose, D-glucose, and D-mannose) because a new asymmetric carbon is formed at C-2 and it can have either the *R* or the *S* configuration. Enzyme catalyzed reactions are enantioselective—the enzyme catalyzes the formation of a single enantiomer of a pair. Thus D-fructose isomerizes only to D-glucose.

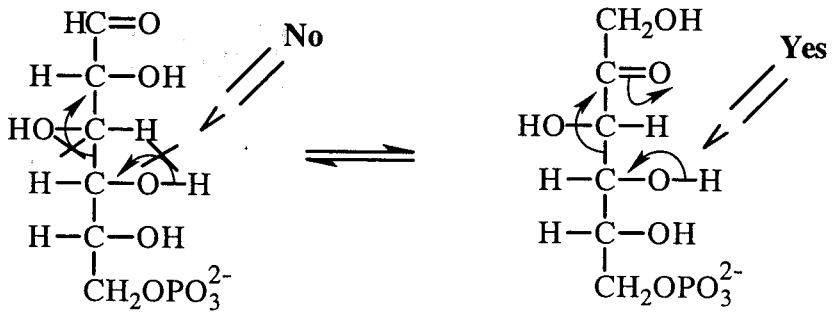
22. It could be lysine (pK_a = 10.79), tyrosine (pK_a = 10.07), or cysteine (pK_a = 8.33). The fact that the pK_a is given by a descending leg means that the side chain of the amino acid is functioning as a general-acid catalyst.

23. The positively charged nitrogen atom of the imine serves as an electron sink to accept the electrons that are left behind when the C3-C4 bond breaks.

In the absence of the imine, the electrons would be delocalized onto a neutral oxygen. The neutral oxygen is not as electron withdrawing as the positively charged nitrogen. In other words, the electron sink that is present as a result of imine formation makes it easier to break the C—C bond.

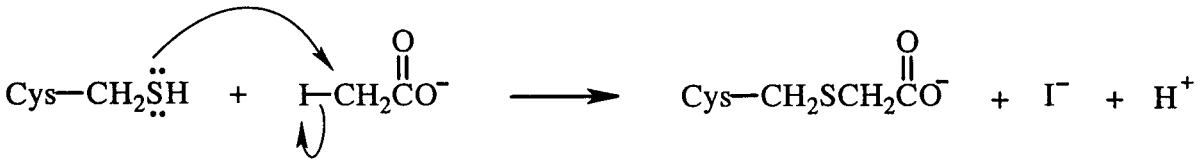


24. In order to break the C3-C4 bond, the carbonyl group has to be at the 2-position as it is in fructose, so it can accept the electrons; the carbonyl group at the 1-position in glucose cannot serve as an electron sink. Therefore, glucose must isomerize to a ketose, so the carbonyl group will be at the 2-position.

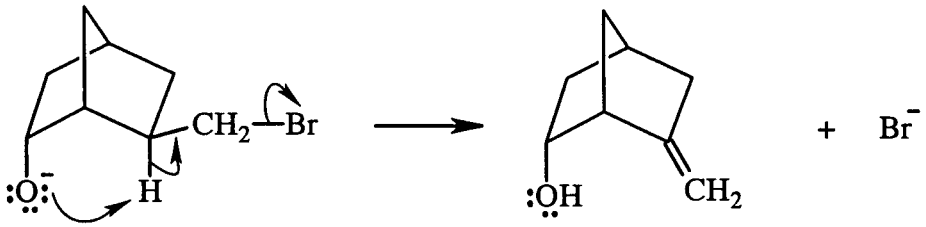


glucose-6-phosphate fructose-6-phosphate

25. Cysteine residues are known to react with iodoacetic acid. If a cysteine residue is at the active site of the enzyme, adding a substituent to the sulfur atom could interfere with the enzyme's being able to bind the substrate or it could interfere with positioning the tyrosine residue that is involved in catalyzing the reaction. Adding a substituent to cysteine might also cause a conformational change in the enzyme that could destroy its activity

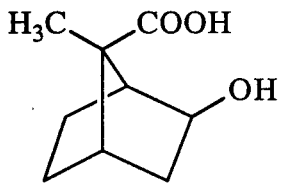


26. The following compound will lose HBr more rapidly because the negatively charged oxygen is in position to act as an intramolecular general-base catalyst.

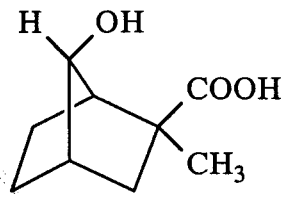


27. The compounds shown below will be the more reactive because the methyl substituent causes the reacting groups (COOH and OH) to stay in a more favorable conformation for reaction.

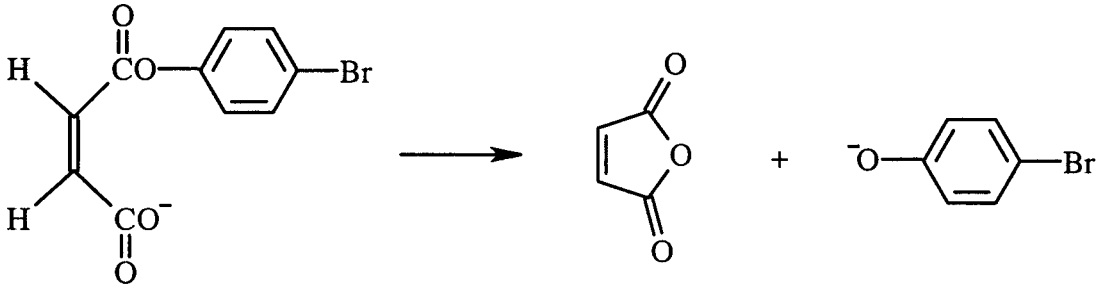
a.



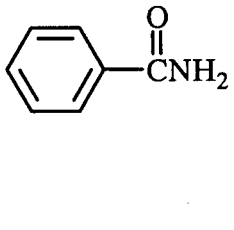
b.

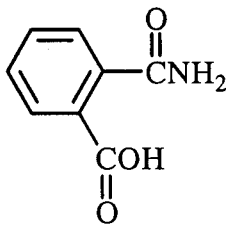


28. The compound shown below will form a lactone more rapidly because it forms a five-membered-ring lactone, which is less strained and than the seven-membered-ring lactone formed by the other compound. The greater stability of the five-membered-ring product will cause the transition state leading to its formation to be more stable than the transition state leading to the seven-membered-ring product.

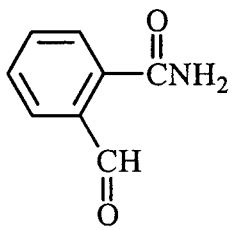


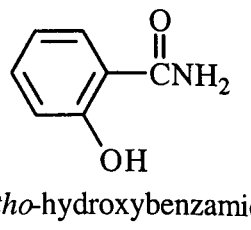
29. In order to hydrolyze an amide, the NH_2 group in the tetrahedral intermediate has to leave in preference to the less basic OH group. This can happen if the NH_2 group is protonated because $^+NH_3$ is a weaker base and, therefore, easier to eliminate than OH. Of the four compounds, two have substituents that can protonate the NH_2 by acting as general-acid catalysts, *ortho*-carboxybenzamide and *ortho*-hydroxybenzamide.





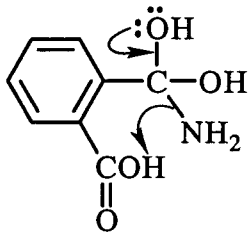
ortho-carboxybenzamide

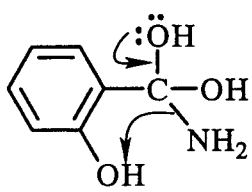




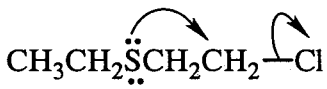
ortho-hydroxybenzamide

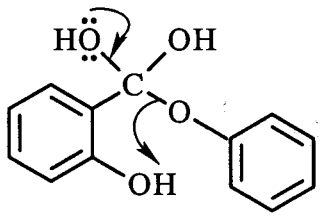
Because the carboxy group is electron-withdrawing and the phenolic OH group is electron-donating, formation of the tetrahedral intermediate will be faster for *o*-carboxybenzamide. Because the carboxy group is a stronger acid than the phenolic OH group, the tetrahedral intermediate of *o*-carboxybenzamide will collapse to products faster. Therefore, the *o*-carboxybenzamide has the faster rate of hydrolysis.





30.

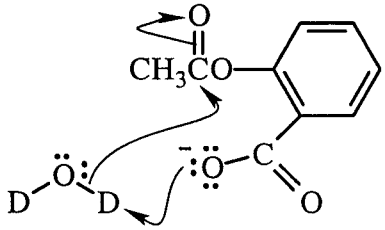
a.  intramolecular nucleophilic catalysis

b. 

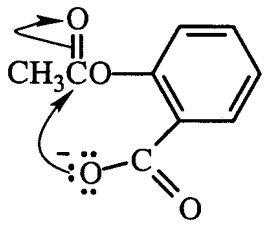
intramolecular general-acid catalysis

The OH substituent is protonating the leaving group as it departs, causing it to be a weaker base and, thus, a better leaving group.

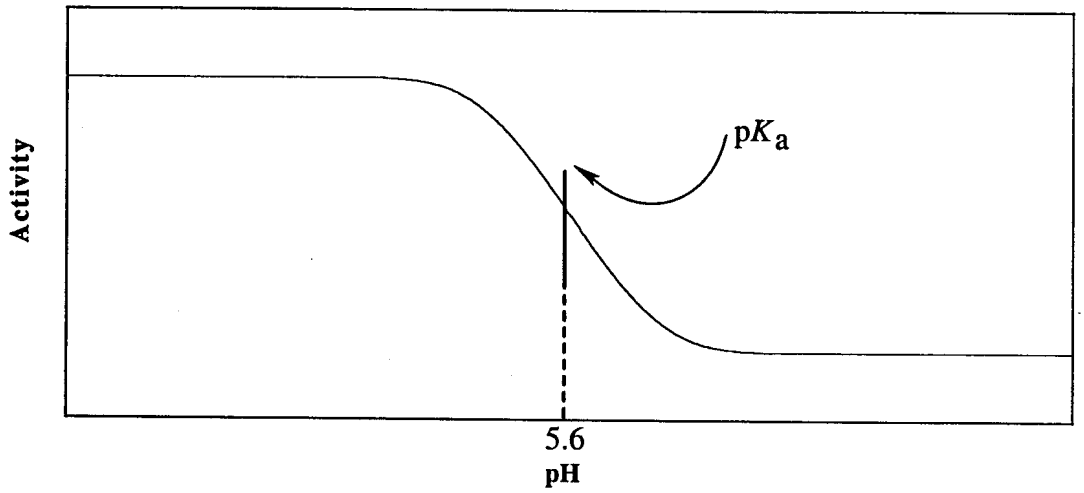
31. If the *ortho*-carboxy substituent is acting as a general-base catalyst, the kinetic isotope effect will be greater than 1.0 because an OH (or OD) bond is broken in the slow step of the reaction.



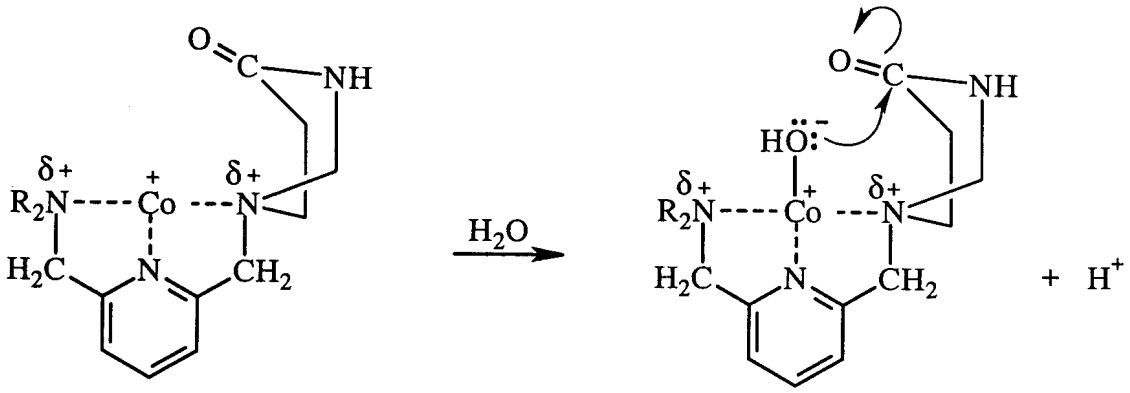
If the *ortho*-carboxyl substituent is acting as a nucleophilic catalyst, the kinetic isotope effect will be about 1.0 because an OH (or OD) bond is not broken in the slow step of the reaction.



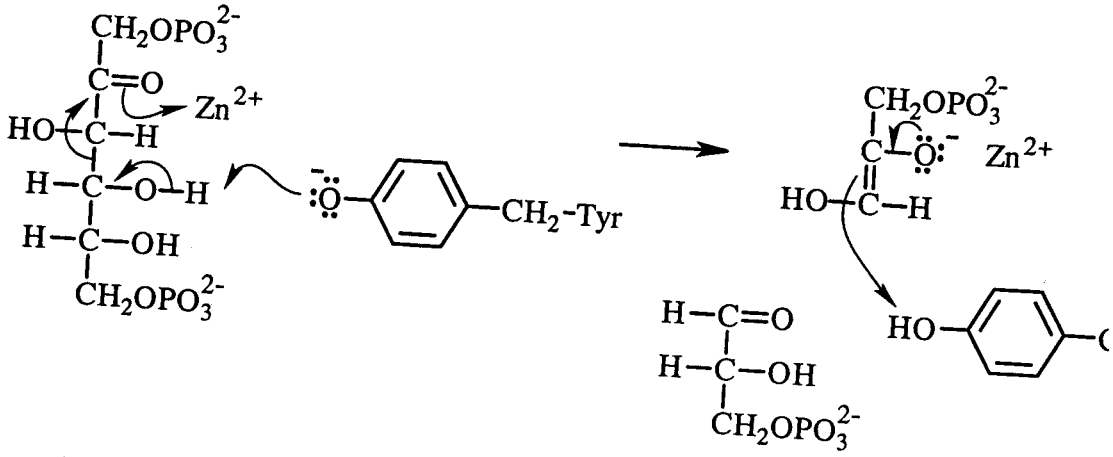
32. Because the catalytic group is a general-acid catalyst, it will be active in its acidic form and inactive in its basic form. The pH at the midpoint of the curve corresponds to the pK_a of the group responsible for the catalysis.



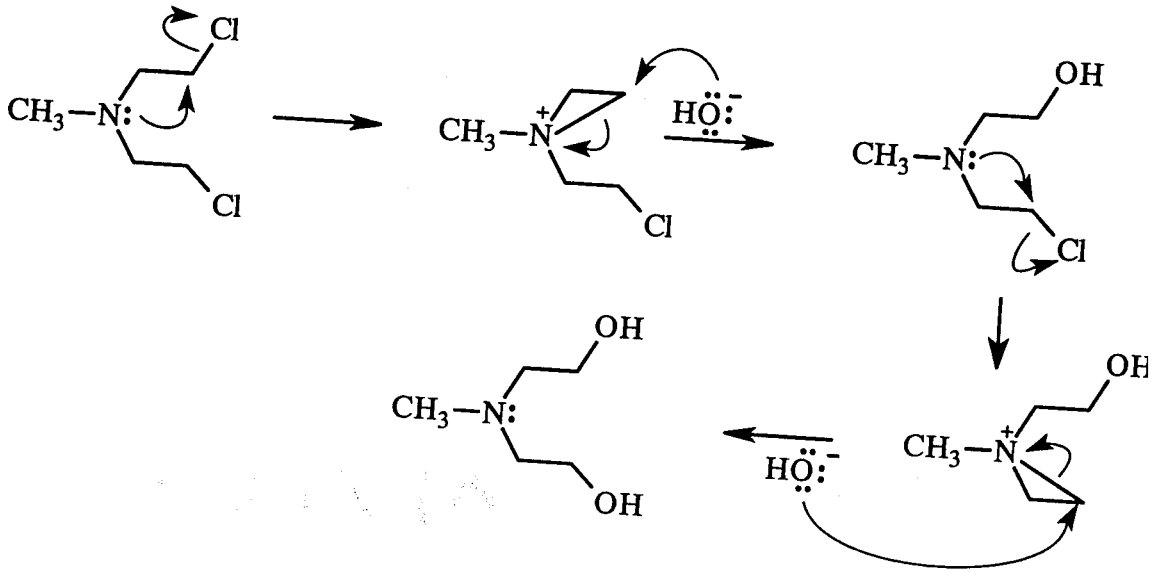
33. Co^{2+} can catalyze the hydrolysis reaction by complexing with three nitrogen atoms in the substrate as well as with water. Complexation increases the acidity of water, thereby providing a stronger nucleophile for the hydrolysis reaction. Complexation with the substrate locks the nucleophile into the correct position for attack on the carbonyl carbon.



34.



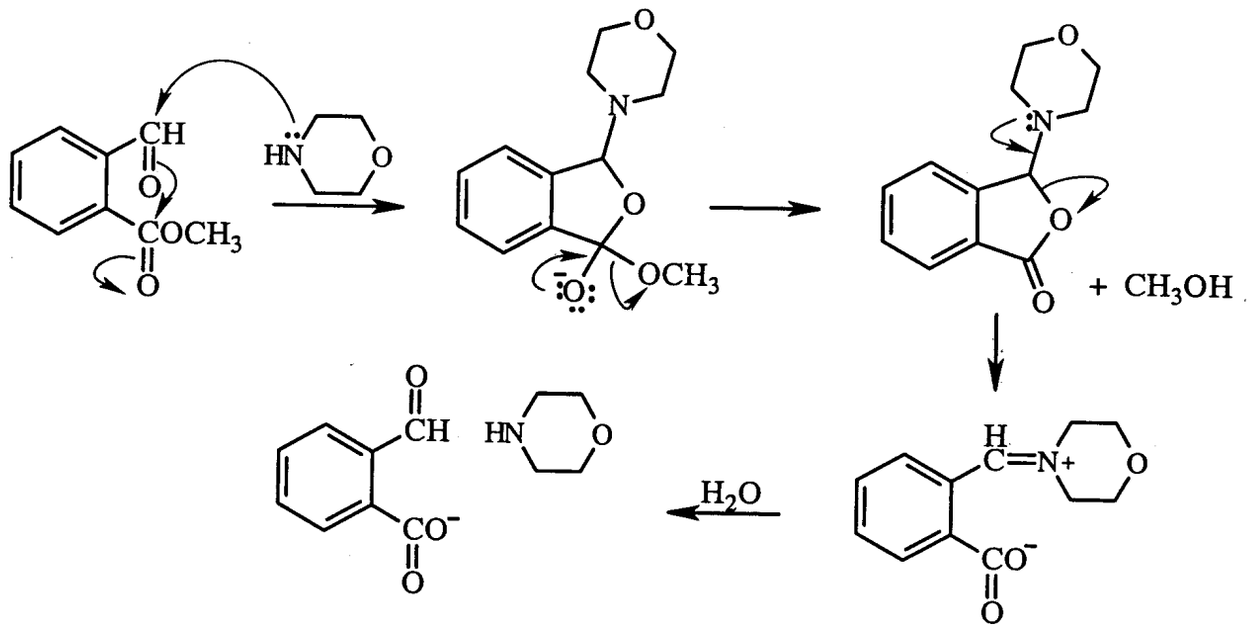
35.



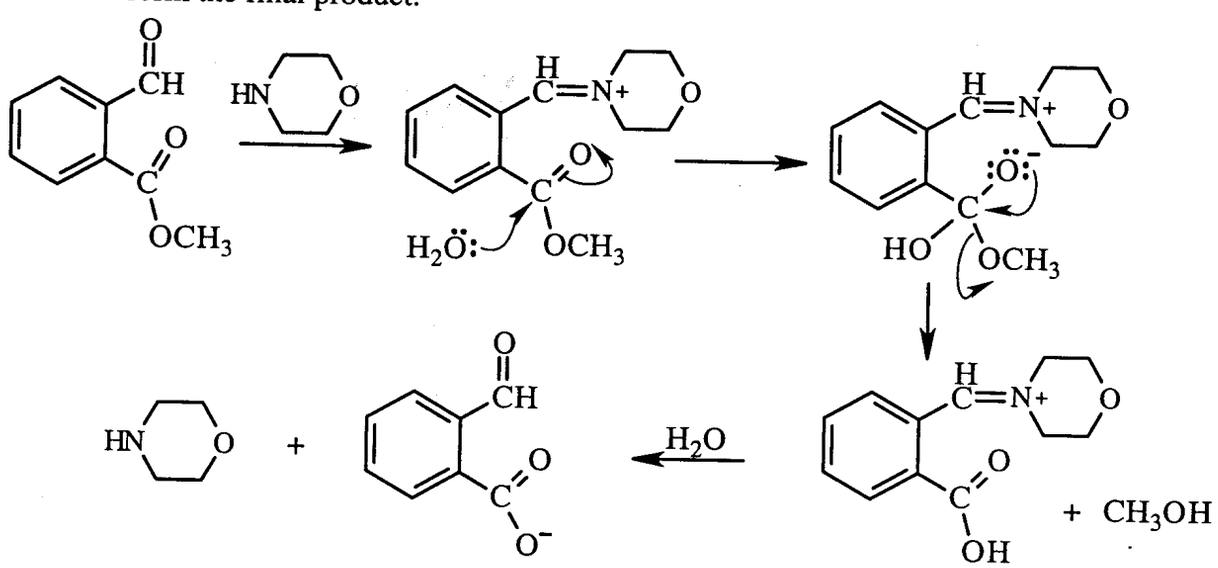
36. There are two possible mechanisms that involve morpholine as a nucleophilic catalyst that can account for the observed catalysis by morpholine. In the absence of morpholine, the first step in the reaction is attack of water on the ester. In the presence of morpholine, the first step in the reaction (in both mechanisms) is attack of morpholine on the aldehyde, which is a faster reaction because morpholine is a stronger nucleophile than water and an aldehyde is more susceptible to nucleophilic attack than an ester.

-Tyr

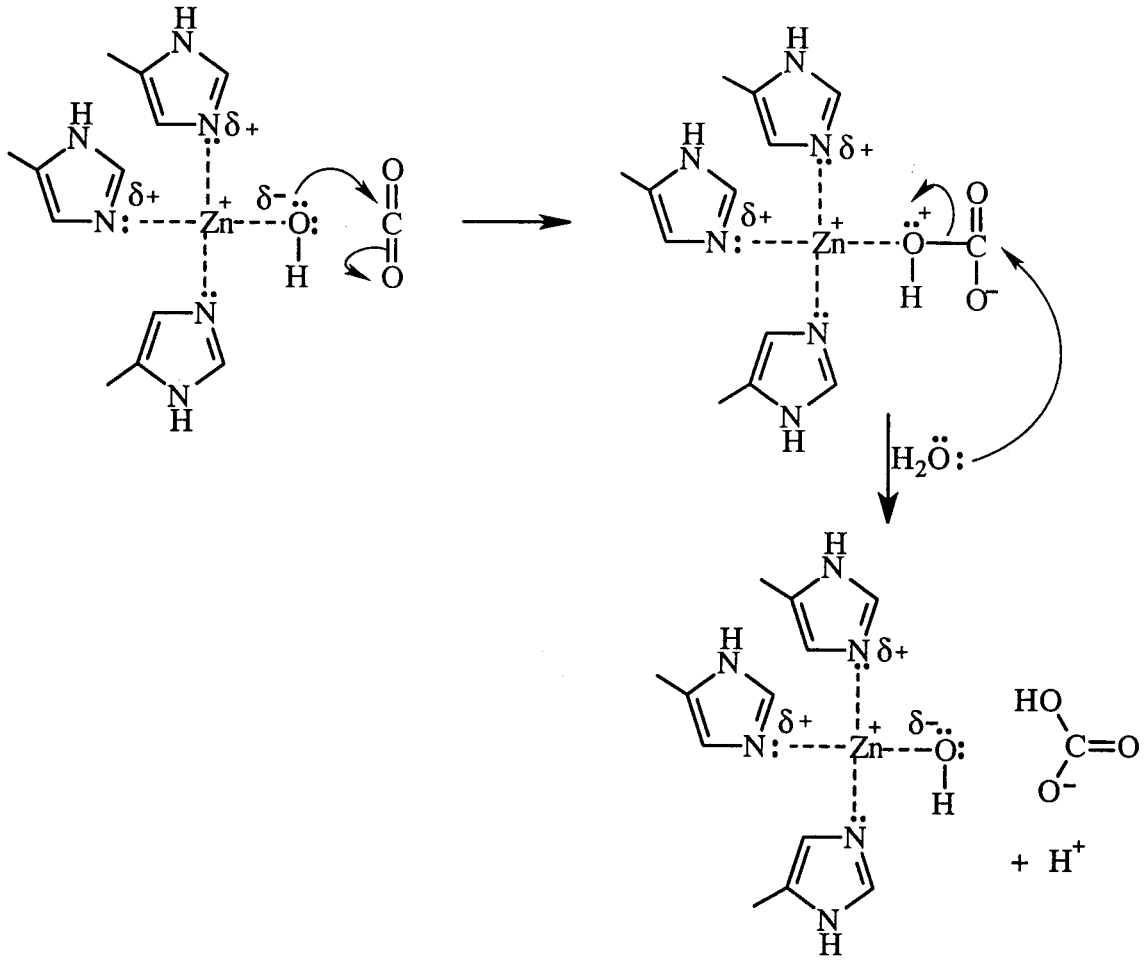
In one mechanism, the negatively charged aldehyde oxygen (which is a much stronger nucleophile than water) is then the nucleophile that attacks the ester. The tetrahedral intermediate collapses to form a lactone. Imine formation followed by imine hydrolysis gives the final product.



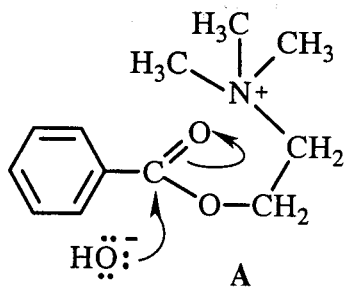
In the other mechanism, the reaction of morpholine with the aldehyde forms an imine. The positively charged imine makes it easier for water to attack the ester by stabilizing the negative charge that develops on the oxygen. Collapse of the tetrahedral intermediate and hydrolysis of the imine form the final product.



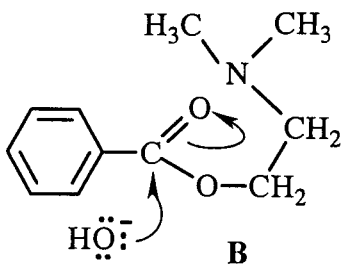
37.



38. At pH = 12, the nucleophile is hydroxide ion. Attack of hydroxide ion on the carbonyl group is faster in **A** because the negative charge that is created in the tetrahedral intermediate is stabilized by the positively charged nitrogen.

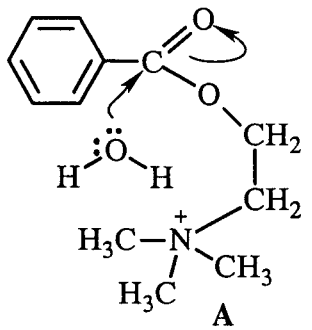


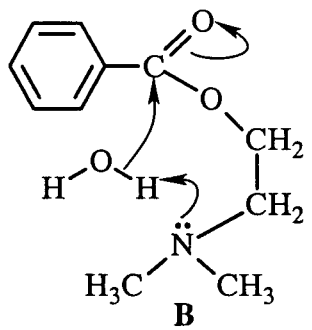
A



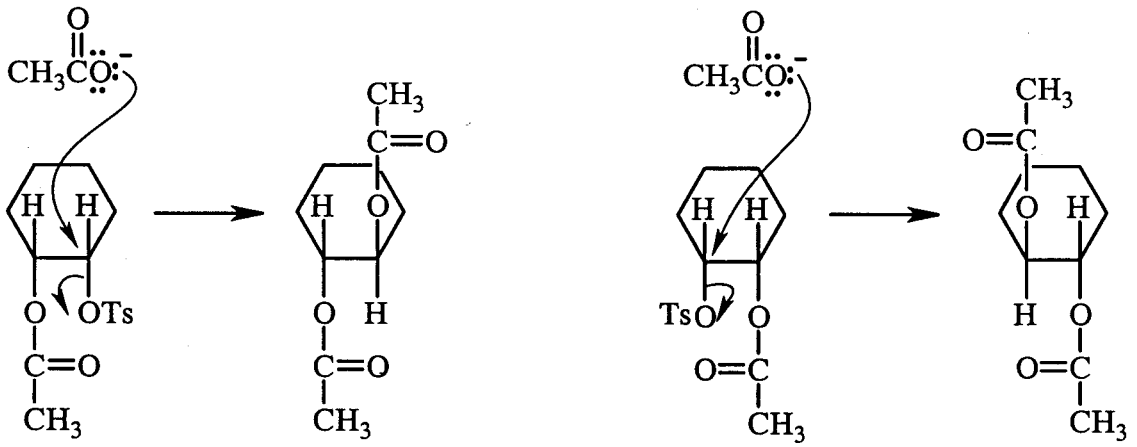
B

At pH = 8, the nucleophile is water. Attack of water on the carbonyl group is faster in **B** because the amino group can act as a general-base catalyst to make water a better nucleophile.

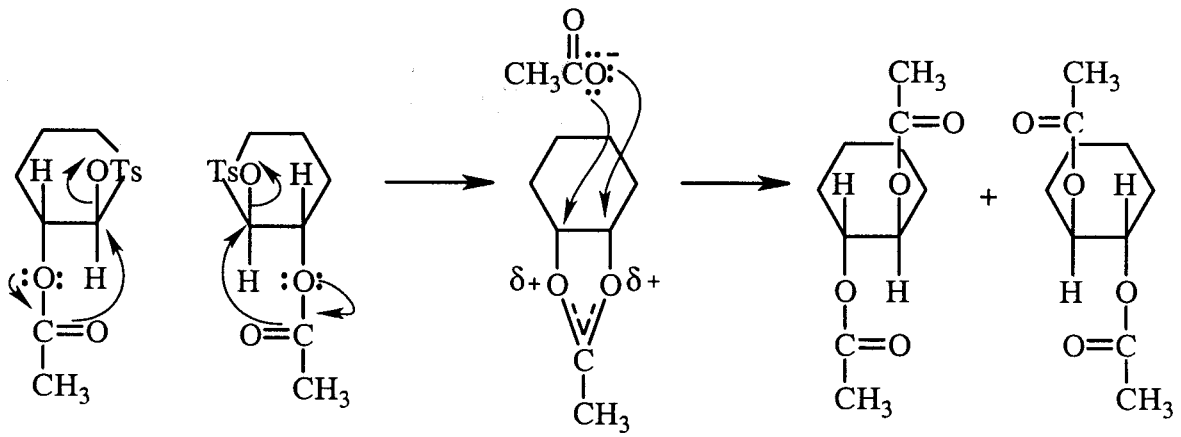

A


B

39. **a.** The cis reactants each undergo a direct S_N2 reaction. Because the acetate displaces the tosyl group by backside attack, each cis reactant forms a trans product.

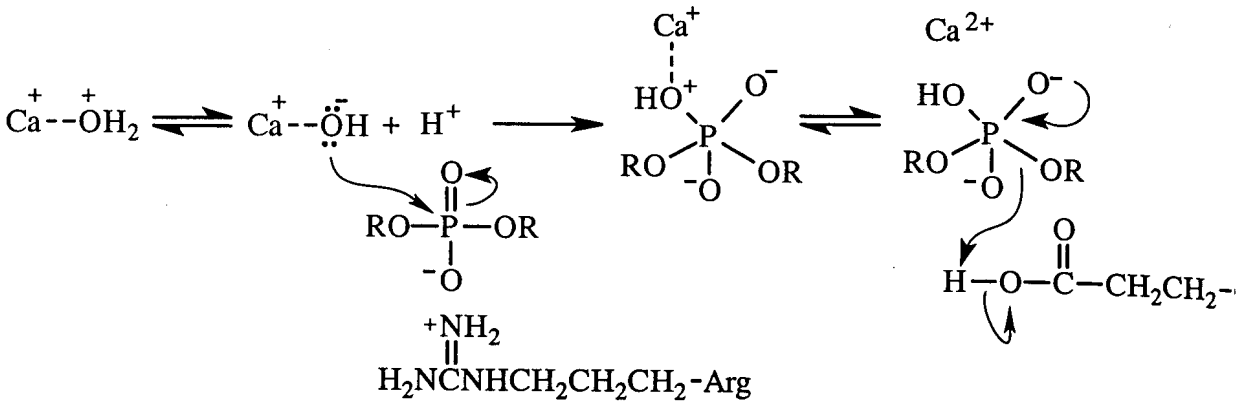


b. The acetate group in a trans reactant is positioned to be able to displace the tosyl leaving group by an intramolecular S_N2 reaction. Acetate ion then attacks in a second S_N2 reaction from the backside of the group it displaces, so trans products are formed. Because both trans reactants form the same intermediate, they both will form the same product. Because the acetate ion can attack either of the carbons in the intermediate equally as easily, a racemic mixture will be formed.

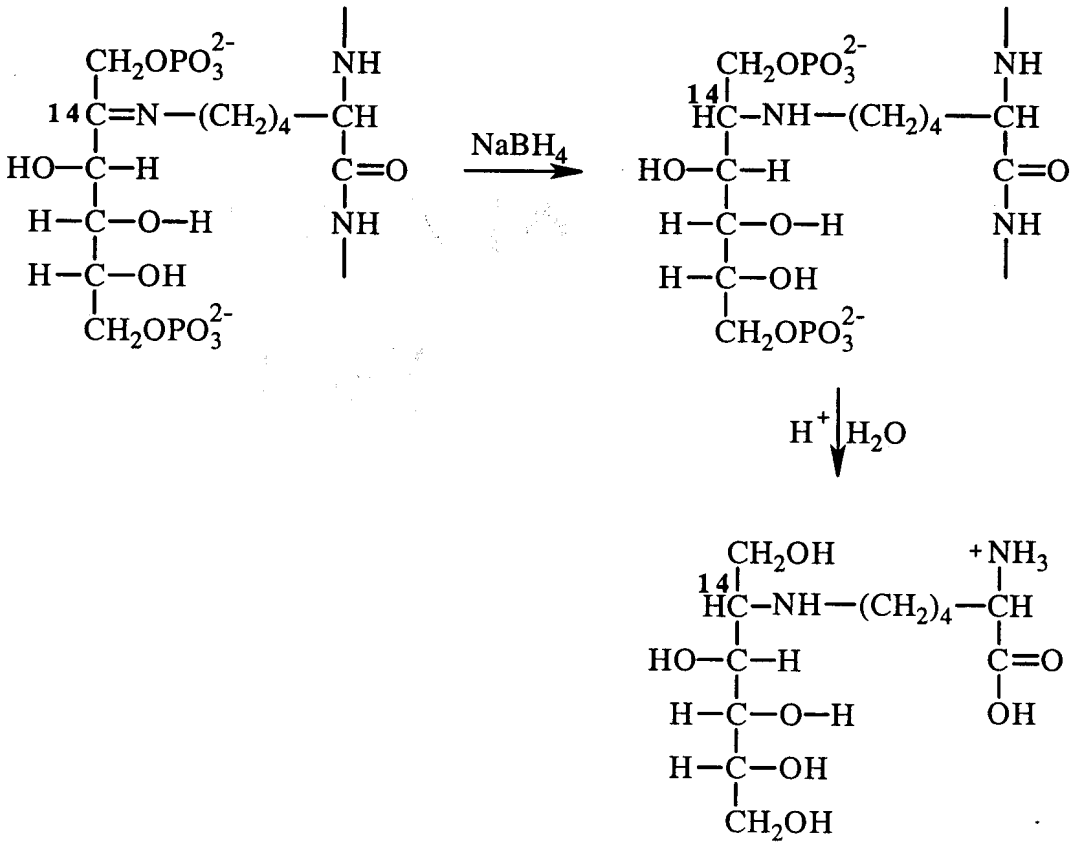


c. The trans reactant is more reactive because the tosyl leaving group is displaced in an intramolecular reaction, forming a positively charged cis intermediate that is considerably more reactive than the neutral cis isomer.

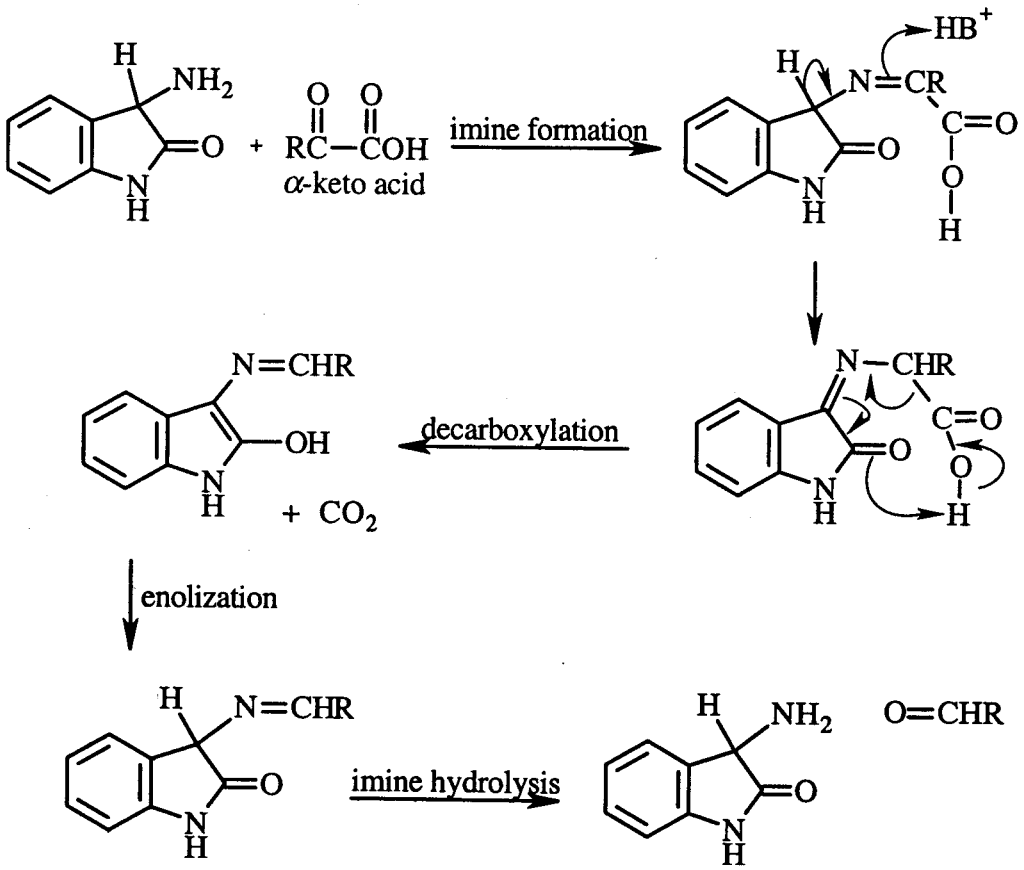
40. A possible mechanism for hydrolysis of the phosphodiester is for Arg to neutralize the negative charge on the phosphate group so a negatively charged nucleophile can approach it. (See Figure 27.5 on page 1117 of the text.) Ca^{2+} increases the acidity of water, forming metal-bound hydroxide ion that is a stronger nucleophile than water. Glu can function as a general-acid catalyst, donating a proton to the leaving group, thereby decreasing its basicity and making it a better leaving group.



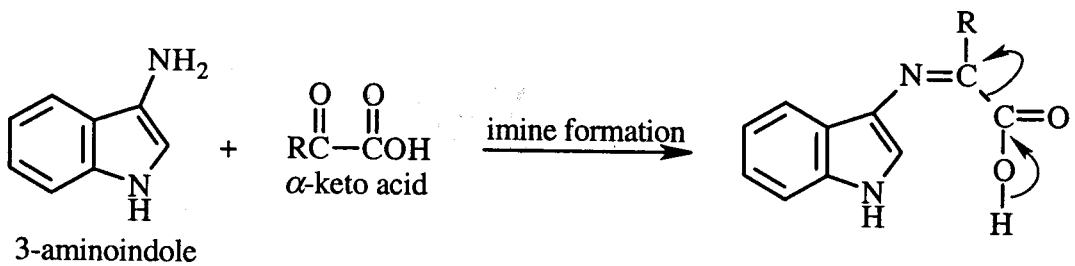
41. Reduction of the imine linkage with sodium borohydride causes fructose to become permanently attached to the enzyme because the hydrolyzable imine bond has been lost. Acid-catalyzed hydrolysis removes the phosphate groups and hydrolyzes the peptide bonds, so the radioactive fragment that is isolated after hydrolysis is the lysine residue (covalently attached to fructose) of the enzyme that originally formed the imine.



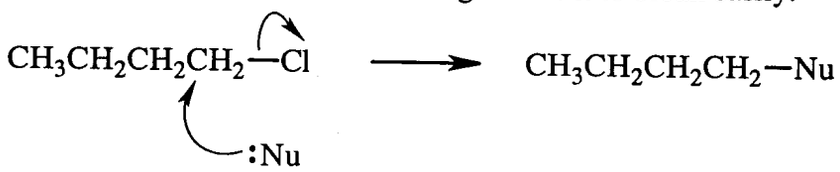
42. **a.** 3-Amino-2-oxindole catalyzes the decarboxylation of an α-keto acid by first forming an imine that is followed by a prototropic shift.

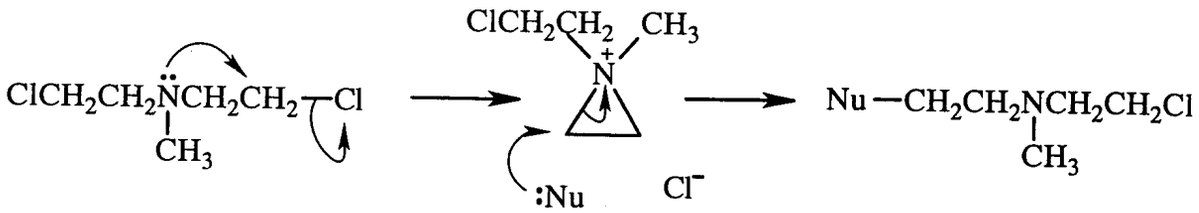


b. 3-Aminoindole would not be as effective a catalyst, because the electrons left behind when CO_2 is eliminated cannot be delocalized onto an electronegative atom.

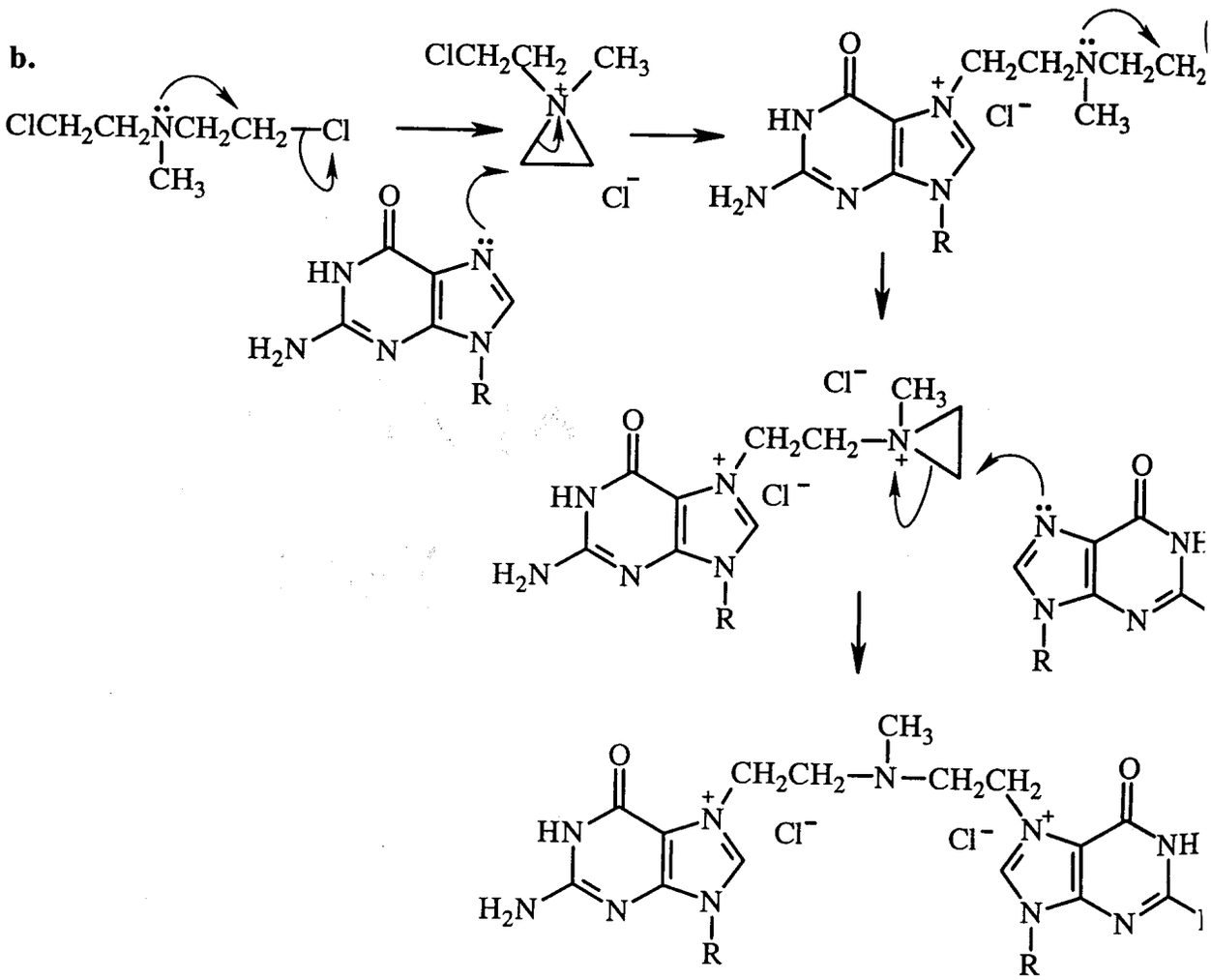


43. **a.** Intramolecular nucleophilic attack on an alkyl halide occurs more rapidly than intermolecular attack on an alkyl halide, because the reacting groups are tethered together in the former. The intramolecular reaction is followed by another relatively rapid reaction, because the strain in the three-membered ring causes it to break easily.

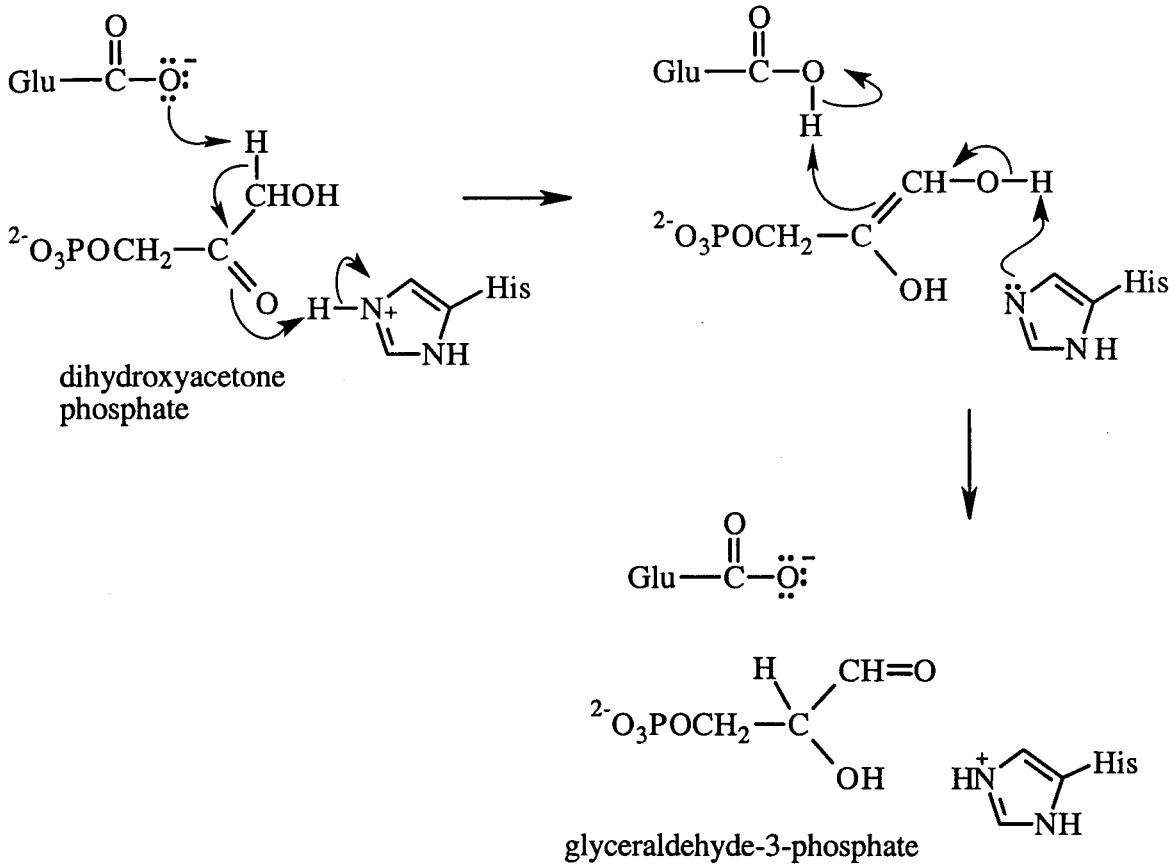




b.



44.


Glu—C—O
H
CHOH
2-O3POCH2—C
O
H—N+
His
NH
dihydroxyacetone phosphate
Glu—C—O
H
CH—O—H
2-O3POCH2—C
OH
N
His
NH
Glu—C—O
H
CH=O
2-O3POCH2—C
OH
HN+
His
NH
glyceraldehyde-3-phosphate

CHAPTER 25
The Organic Mechanisms of the Coenzymes • Metabolism

Important Terms

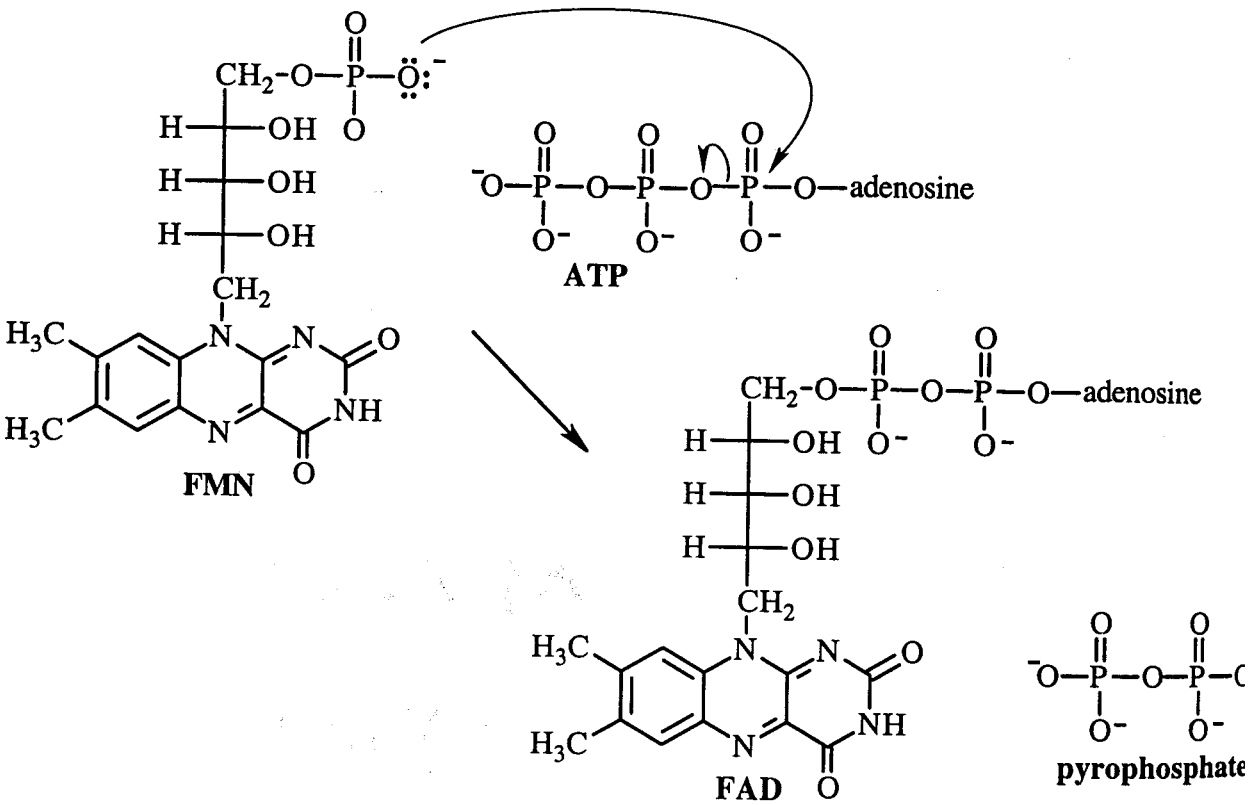
anabolism	the reactions living organisms carry out that result in the synthesis of complex biomolecules from simple precursor molecules.
apoenzyme	an enzyme without its cofactor.
biotin	the coenzyme required by enzymes that catalyze carboxylation of a car adjacent to an ester or a keto group.
catabolism	the reactions living organisms carry out to provide energy and simple precursor molecules for synthesis.
coenzyme	a cofactor that is an organic molecule.
coenzyme A	a thiol used by biological organisms to form thioesters.
coenzyme B_{12}	the coenzyme required by enzymes that catalyze certain rearrangement reactions.
cofactor	an organic molecule or a metal ion that an enzyme needs in order to catalyze a reaction.
competitive inhibitor	a compound that inhibits an enzyme by competing with the substrate fo binding at the active site.
dehydrogenase	an enzyme that carries out an oxidation reaction by removing hydrogen from the substrate.
electron sink	a site to which electrons can be delocalized.
flavin adenine dinucleotide (FAD)	a coenzyme required in certain oxidation reactions. It is reduced to FAD which is a coenzyme required in certain reduction reactions.
flavin mononucleotide (FMN)	a coenzyme required in certain oxidation reactions. It is reduced to $FMNH_2$, which is a coenzyme required in certain reduction reactions.
heterocycle	a cyclic compound in which one or more of the ring atoms is an atom otl than carbon.
holoenzyme	an enzyme plus its cofactor.
lipoate	a coenzyme required in certain oxidation reactions.
mechanism-based inhibitor	an inhibitor that inactivates an enzyme by undergoing part of the normal catalytic mechanism.
metabolism	reactions living organisms carry out in order to obtain the energy they ne and to synthesize the compounds they require.
metalloenzyme	an enzyme that has a tightly bound metal ion.

nicotinamide adenine dinucleotide (NAD^+)	a coenzyme required in certain oxidation reactions. It is reduced to NADH, which is a coenzyme required in certain reduction reactions.
nicotinamide adenine dinucleotide phosphate ($NADP^+$)	a coenzyme required in certain oxidation reactions. It is reduced to NADPH, which is a coenzyme required in certain reduction reactions.
nucleotide	a heterocycle attached in the β-position to a phosphorylated ribose.
pyridoxal phosphate	the coenzyme required by enzymes that catalyze certain transformations of amino acids.
suicide inhibitor (mechanism-based inhibitor)	a compound that inactivates an enzyme by undergoing part of its normal catalytic mechanism.
tetrahydrofolate (THF)	the coenzyme required by enzymes that catalyze a reaction that donates a group containing a single carbon to its substrate.
thiamine pyrophosphate (TPP)	the coenzyme required by enzymes that catalyze a reaction that transfers a two-carbon fragment to its substrate.
transamination	a reaction in which an amino group is transferred from one compound to another.
transimination	the reaction of a primary amine with an imine to form a new imine and a primary amine derived from the original imine.
vitamin	a substance needed in small amounts for normal body function that the body cannot synthesize or cannot synthesize in adequate amounts.
vitamin KH_2	the coenzyme required by the enzyme that catalyzes the carboxylation of glutamate side chains.

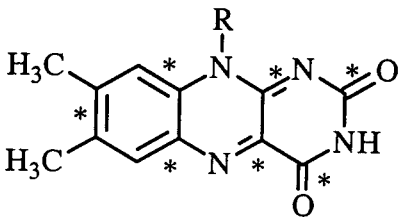
Solutions to Problems

1. The metal ion (Zn^{2+}) makes the carbonyl carbon more susceptible to nucleophilic attack, increases the nucleophilicity of water by making it more like a hydroxide ion, and stabilizes the negative charge on the transition state.

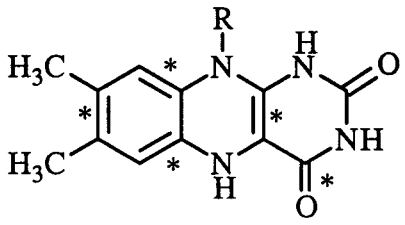
2. FAD contains a diphosphate linkage. One of the phosphate groups comes from FMN and the other comes from ATP. Since ATP uses only one of its three phosphate groups in forming FAD, the other product of the reaction must be pyrophosphate to account for loss of the two phosphate groups. In other words, the phosphate group of FMN must attack the α-phosphorus of ATP, eliminating pyrophosphate. (See pages 714 and 1114 of the text.)



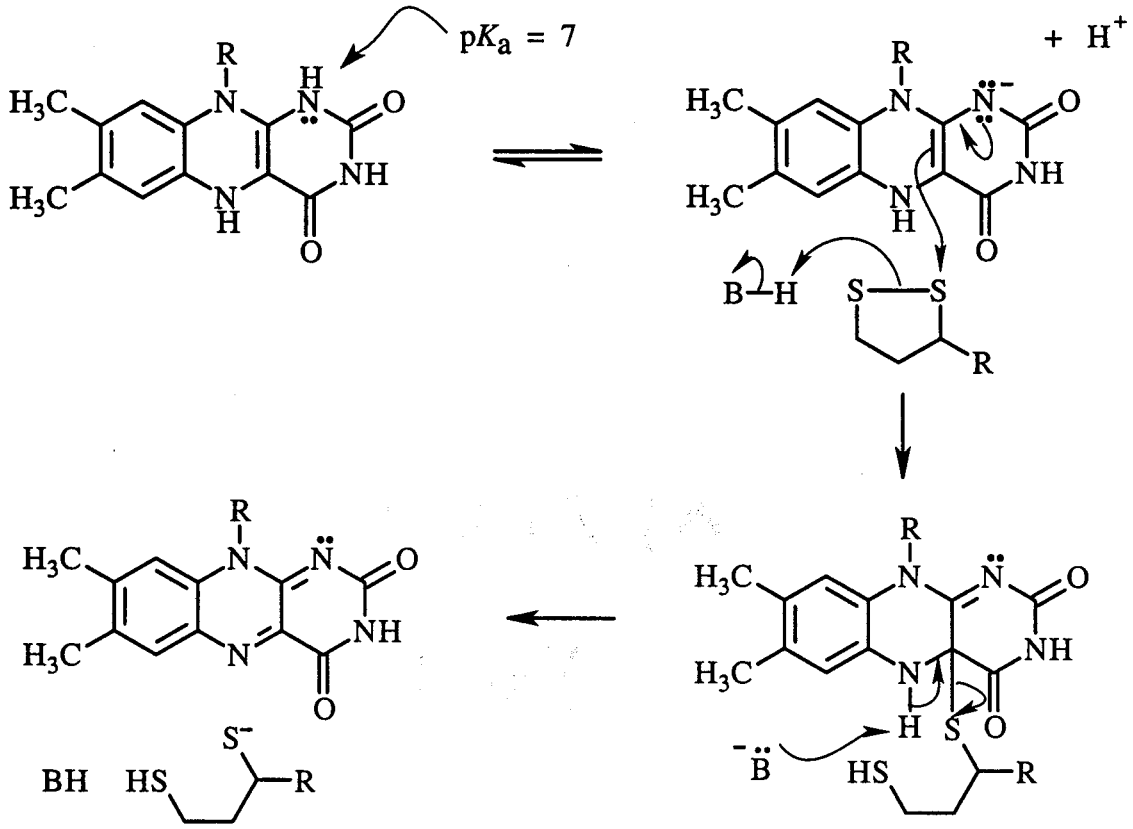
3. **a.** FAD has seven conjugated double bonds. (The conjugated double bonds are indicated *.)



b. $FADH_2$ has three conjugated double bonds. It also has two conjugated double bonds that are isolated from the other three.

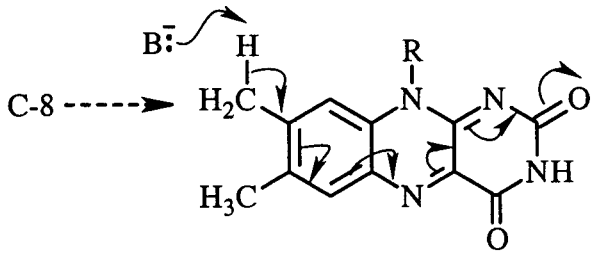


4. The mechanism for reduction of lipoate by $FADH_2$ is the reverse of the mechanism for oxidation of dihydrolipoate by FAD. Because the pK_a of the N-1 hydrogen is 7, $FADH_2$ is present in both the acidic and basic forms at physiological pH (7.3).



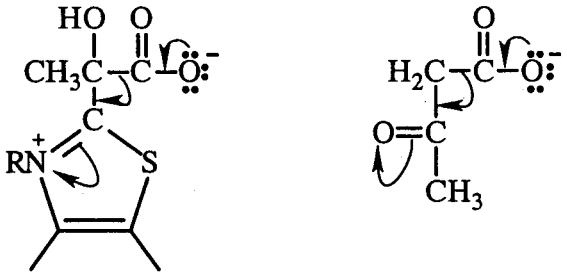
5. Solved in the text.

6. When a proton is removed from the methyl group at C-8, the electrons that are left behind can be delocalized onto the oxygen at the 2-position or onto the oxygen at the 4-position.

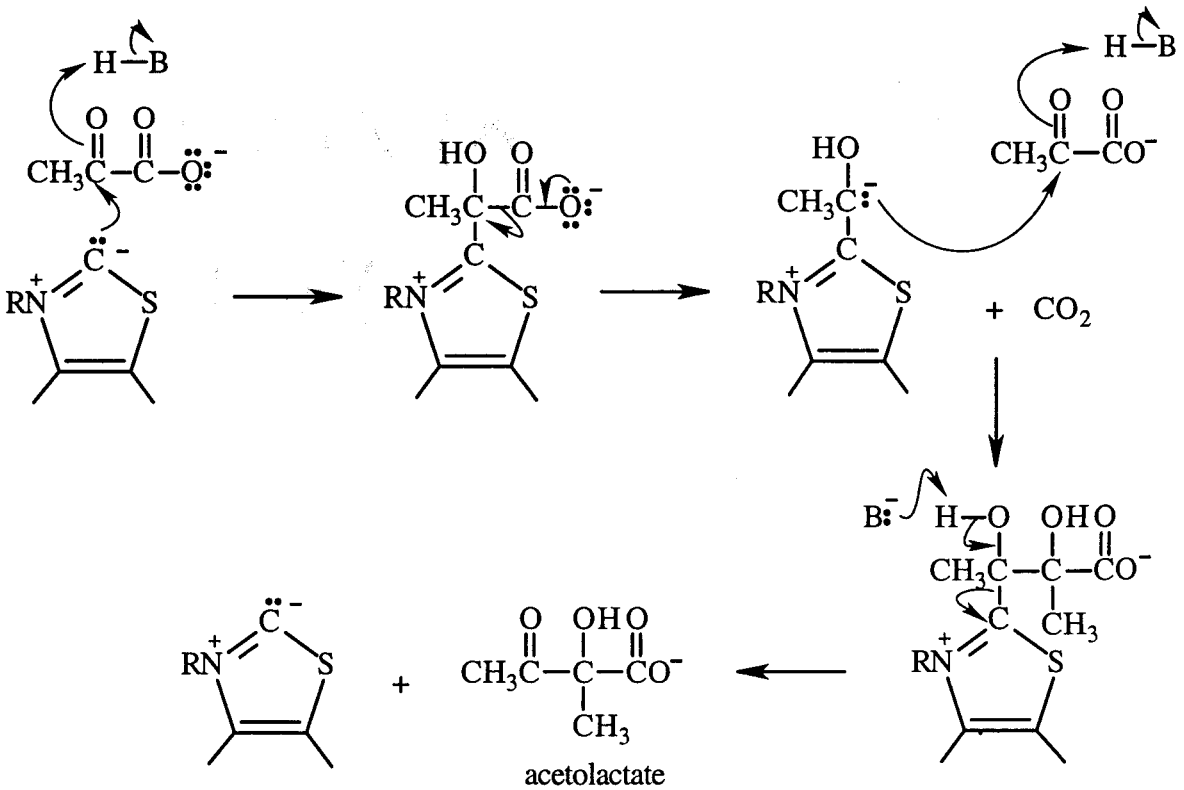


When a proton is removed from the methyl group at C-7, the electrons that are left behind can delocalized only onto carbon atoms that, being less electronegative than oxygen atoms, are less able to accommodate the electrons. (Try pushing electrons to prove to yourself that this is so.)

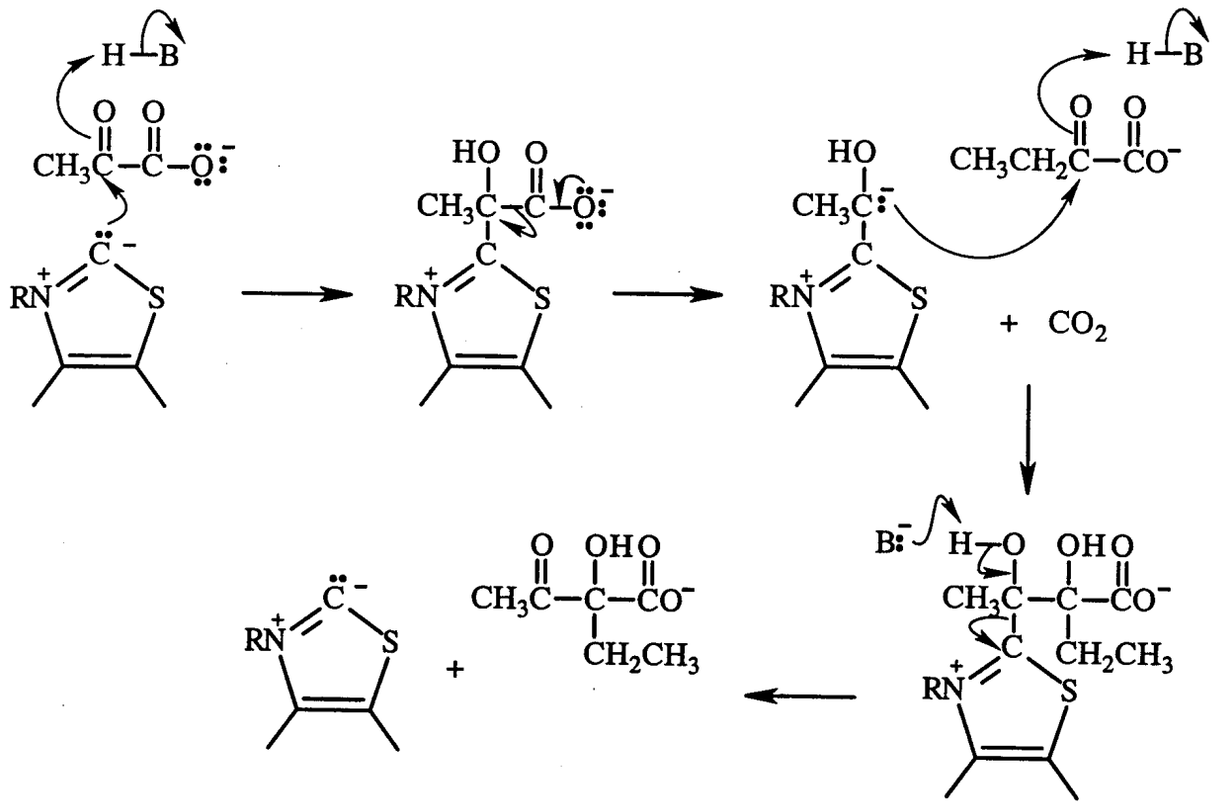
7.



8. The only difference in the mechanisms of pyruvate decarboxylase and acetolactate synthase is the species the two-carbon fragment (the carbanion) is transferred to: a proton in the case of pyruvate carboxylase and pyruvate in the case of acetolactate synthase.



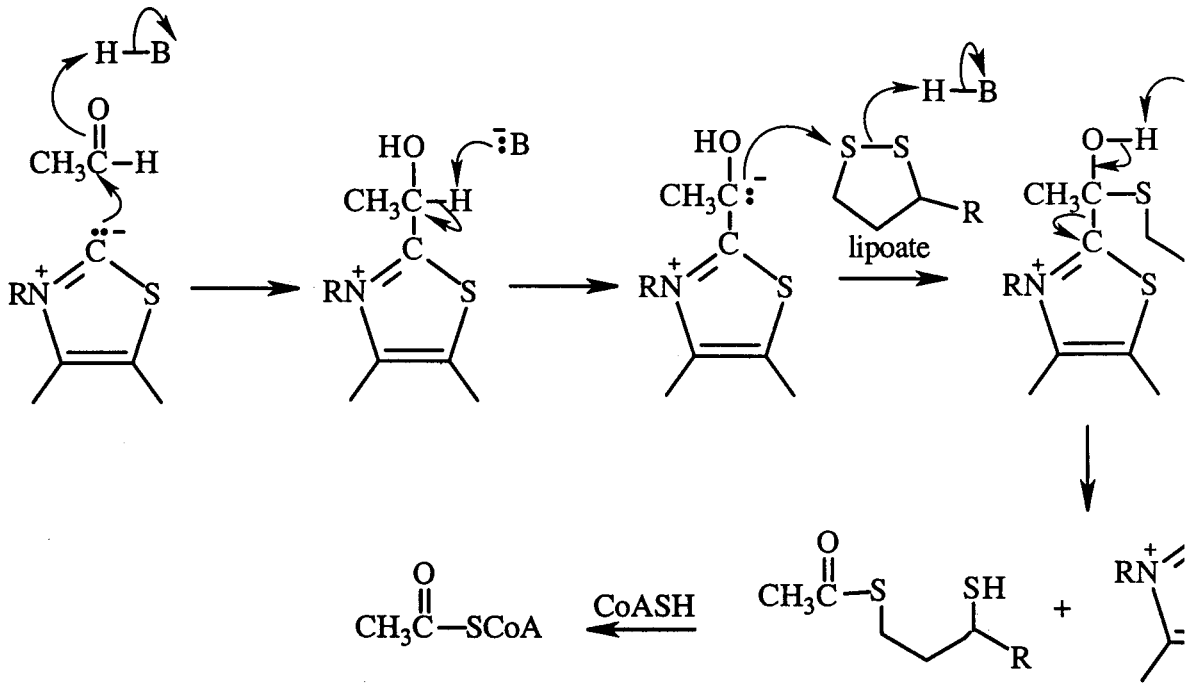
9. Notice that the only difference in this reaction and that in Problem 8 is that the species to which the two-carbon fragment is transferred has an ethyl group in place of the methyl group.



10. Solved in the text.

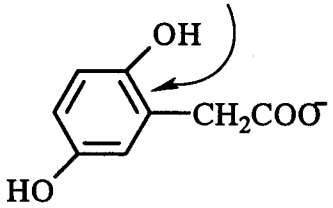
11. Acetaldehyde is responsible for the physiological effects known as a hangover. A way to "cure" a hangover, therefore, is to get rid of the acetaldehyde that is formed from the oxidation of ethanol. Thiamine pyrophosphate (the coenzyme form of vitamin B_1) can convert acetaldehyde into acetyl-CoA. It does this by attacking the carbonyl carbon of acetaldehyde to form an intermediate. Loss of a proton from the intermediate forms the carbanion that is the reactive intermediate in the reaction catalyzed by the pyruvate dehydrogenase system. The final product of this pathway is acetyl-CoA.

Notice that, except for the second step of the reaction, the reaction is the same as the reaction catalyzed by the pyruvate dehydrogneanse system. In the second step of reaction catalyzed by the pyruvate dehydrogenase system, CO_2 is removed from the carbon that formerly was the carbonyl carbon; in this reaction it is a proton rather than CO_2 that is removed in that step.



12. **a.** coenzyme = pyridoxal phosphate; other organic compound = α-ketoglutarate

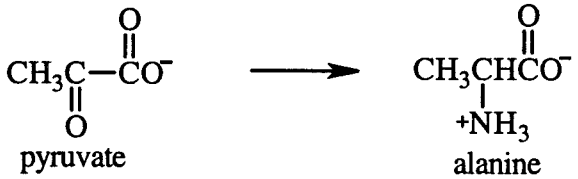
b. This is the bond that breaks.



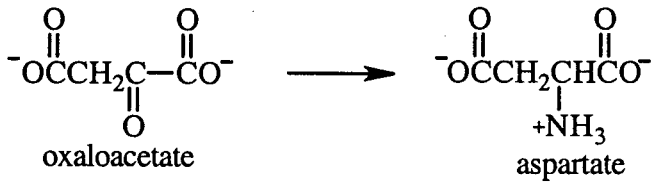
c. *S*-adenosylmethionine

13. The α-keto group that accepts the amino group from pyridoxamine is converted into an amir group.

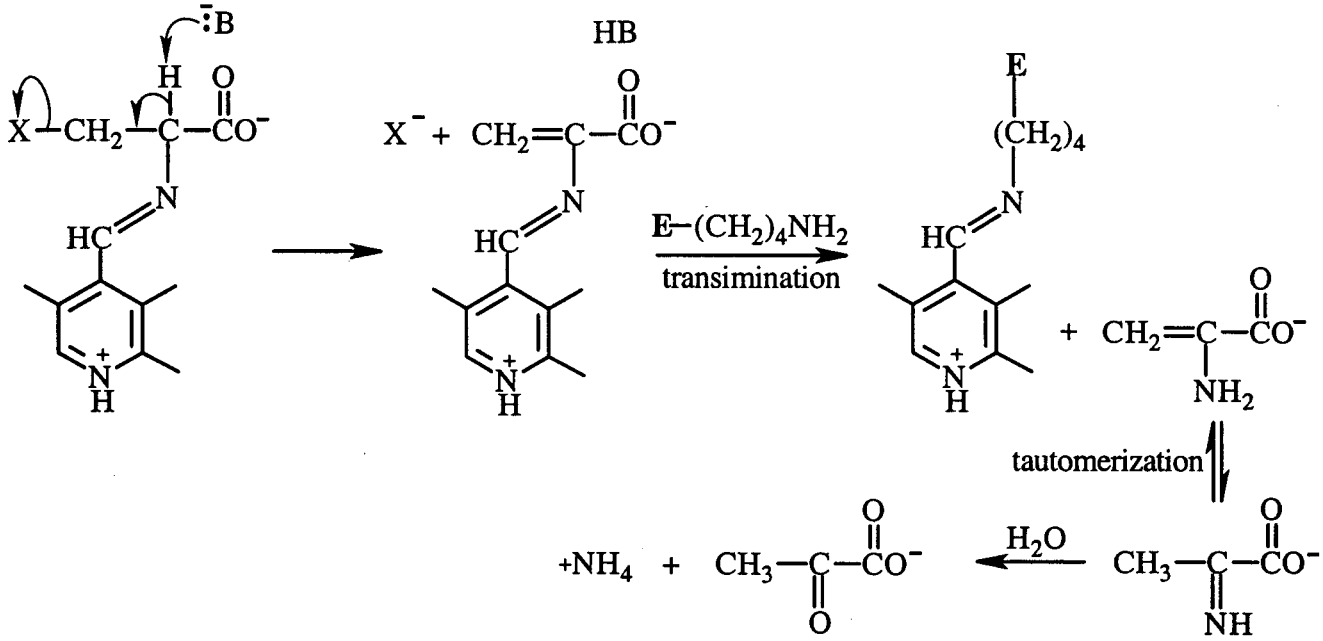
a.



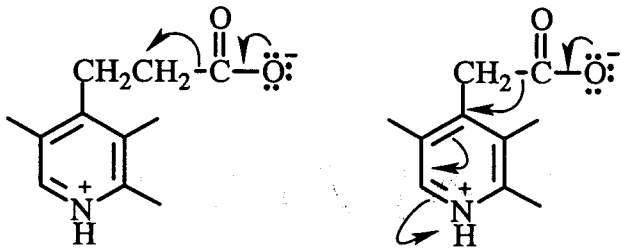
b.



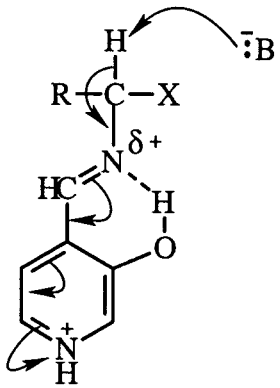
14. In the first step, a proton is removed from the α-carbon, and the electrons left behind expel the leaving group from the β-carbon. Hydrolysis of the imine regenerates pyridoxal and produces an enamine. The enamine tautomerizes to an imine that is hydrolyzed to the final product.



15. The compound on the right is more easily decarboxylated because the electrons left behind when CO_2 is eliminated are delocalized onto the positively charged nitrogen of the pyridine ring.

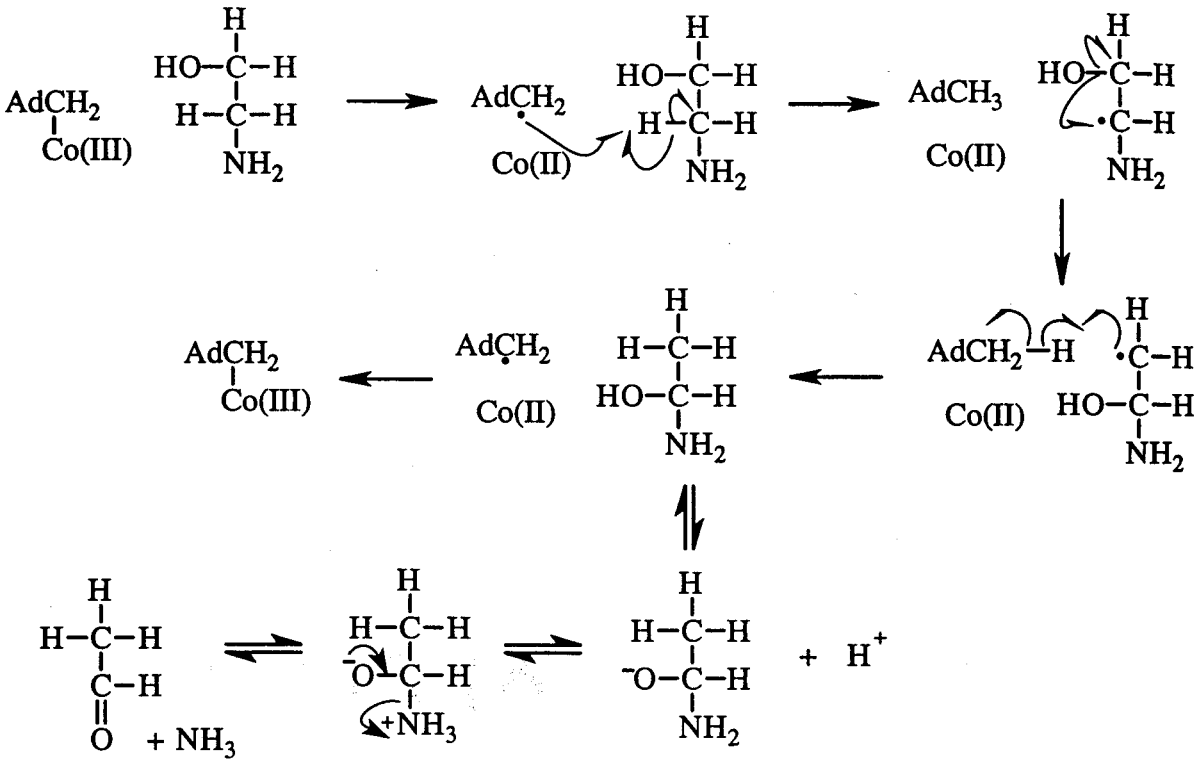


16. The first step in all amino acid transformations is removal of a substituent from the α-carbon of the amino acid. The electrons left behind when the substituent is removed are delocalized onto the positively charged nitrogen of the pyridine ring. If the ring nitrogen were not protonated, it would be less attractive to the electrons. In other words, it would be a less effective electron sink.

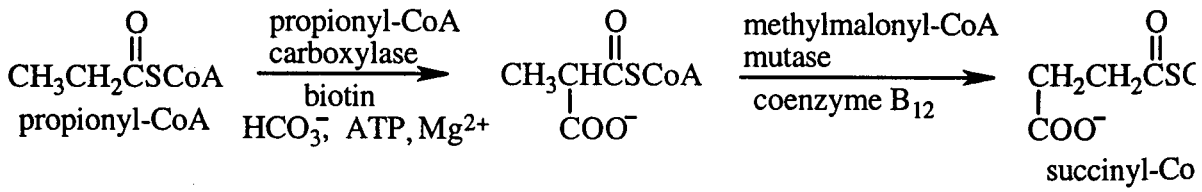


17. The hydrogen of the OH substituent forms a hydrogen bond with the nitrogen of the imine linkage (see above structure). This puts a partial positive charge on the nitrogen, which makes it easier for the amino acid to attack the imine carbon in the transimination reaction that attach the amino acid to the coenzyme. It also makes it easier to remove a substituent from the α-carbon of the amino acid. If the OH substituent is replaced by an OCH_3 substituent, there is no longer a proton available to form the hydrogen bond.

18. The mechanism is the same as that shown in the text for dioldehydrase. The tetrahedral intermediate that is formed as a result of the coenzyme B_{12}-catalyzed isomerization is unstable and loses ammonia to give acetaldehyde, the final product of the reaction.



19.



20. The methyl group in thymidine comes from the methylene group of N^5,N^{10}-methylene-THF. The methylene group of N^5,N^{10}-methylene-THF comes from the CH_2OH group of serine by means of a PLP-catalyzed C_α-C_β cleavage.

21. Two thiol groups are necessary for each of the two oxidations in the conversion of vitamin K epoxide to vitamin KH_2. Since lipoate has two thiol groups, each oxidation involves an intramolecular reaction. When thiols such as ethanethiol or propanethiol are used, the oxidation involves an intermolecular reaction. These thiols react more slowly than lipoate because the two thiol groups are not in the same molecule. Therefore, they have to find each other in order to react.

22. **a.** NAD^+, $NADP^+$, FAD, FMN, lipoate, vitamin K epoxide

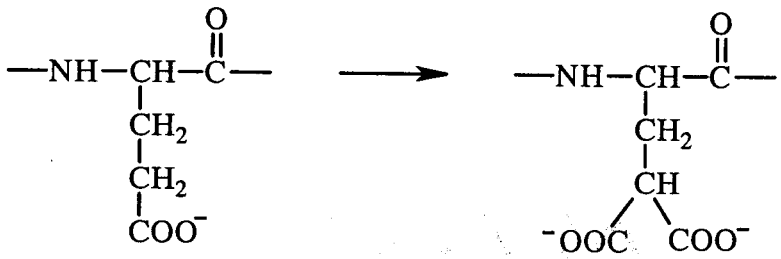
b. N^5-methyl-THF, N^5,N^{10}-methylene-THF, N^5,N^{10}-methenyl-THF, N^5-formyl-THF, N^{10}-formyl-THF, N^5-formimino-THF, *S*-adenosylmethionine
One could include biotin and vitamin KH_2; they accept a one carbon group (from HCO_3^- and CO_2, respectively) and transfer it to the substrate.

c. $-CH_3$ $-CH_2-$ $-\overset{\overset{O}{\|}}{C}H$

d. FAD oxidizes dihydrolipoate back to lipoate.

e. NAD^+ oxidizes $FADH_2$ back to FAD.

f.



g. thiamine pyrophosphate and pyridoxal phosphate

h. Thiamine pyrophosphate is used for the decarboxylation of α-keto acids.
Pyridoxal phosphate is used for the decarboxylation of amino acids.

i. biotin and vitamin KH_2

j. Biotin carboxylates a carbon adjacent to a carbonyl group.
Vitamin KH_2 carboxylates the γ-carbon of a glutamate.

23. **a.** NAD^+, $NADP^+$, FAD, FMN, thiamine pyrophosphate, carboxybiotin, pyridoxal phosphate

b. All coenzymes that bind the substrate do so to activate it for some kind of further reaction. So all the coenzymes can be considered to activate substrates for further reaction except those that directly deliver an atom or group to the substrate or directly receive an atom or group from the substrate without binding it, such as NAD^+, $NADP^+$, NADH, NADPH, and the tetrahydrofolate coenzymes that deliver a one-carbon fragment in one step such as N^5-methyl-THF. In other words, the answers are: FAD, FMN, $FADH_2$, $FMNH_2$, thiamine pyrophosphate, biotin, pyridoxal phosphate, coenzyme B_{12}, some tetrahydrofolate coenzymes, and vitamin KH_2.

c. thiamine pyrophosphate

d. vitamin KH_2

24. **a.** acetyl-CoA carboxylase, biotin

b. dihydrolipoyl dehydrogenase, FAD

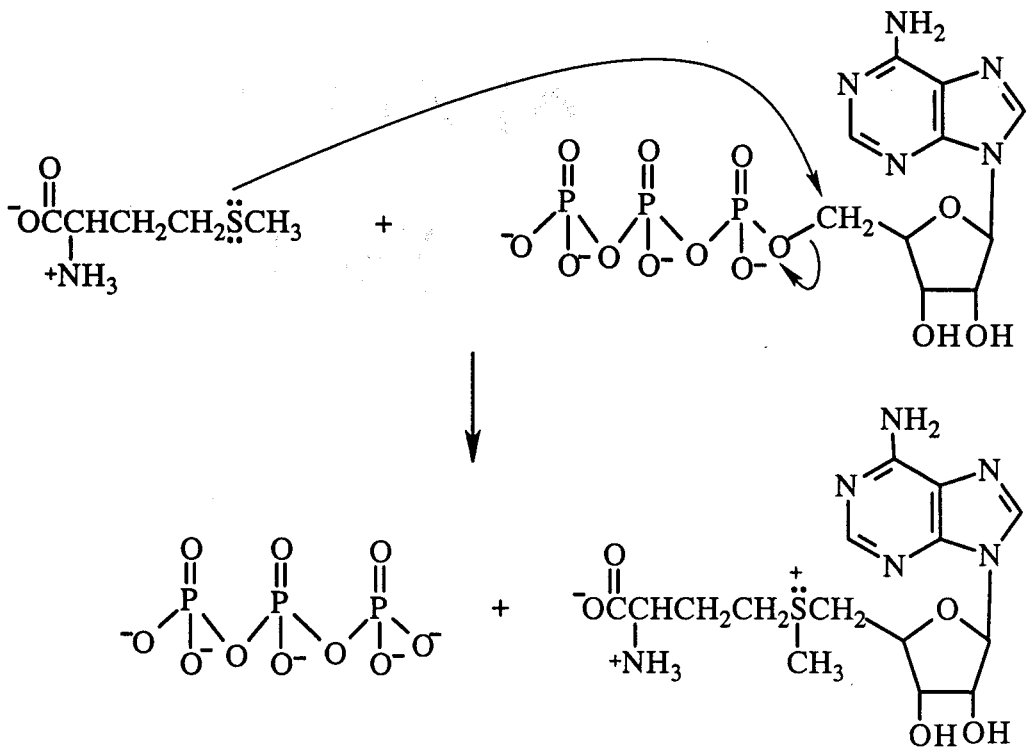
c. methylmalonyl-CoA mutase, coenzyme B_{12}

d. lactate dehydrogenase, NADH

e. aspartate transaminase, pyridoxal phosphate

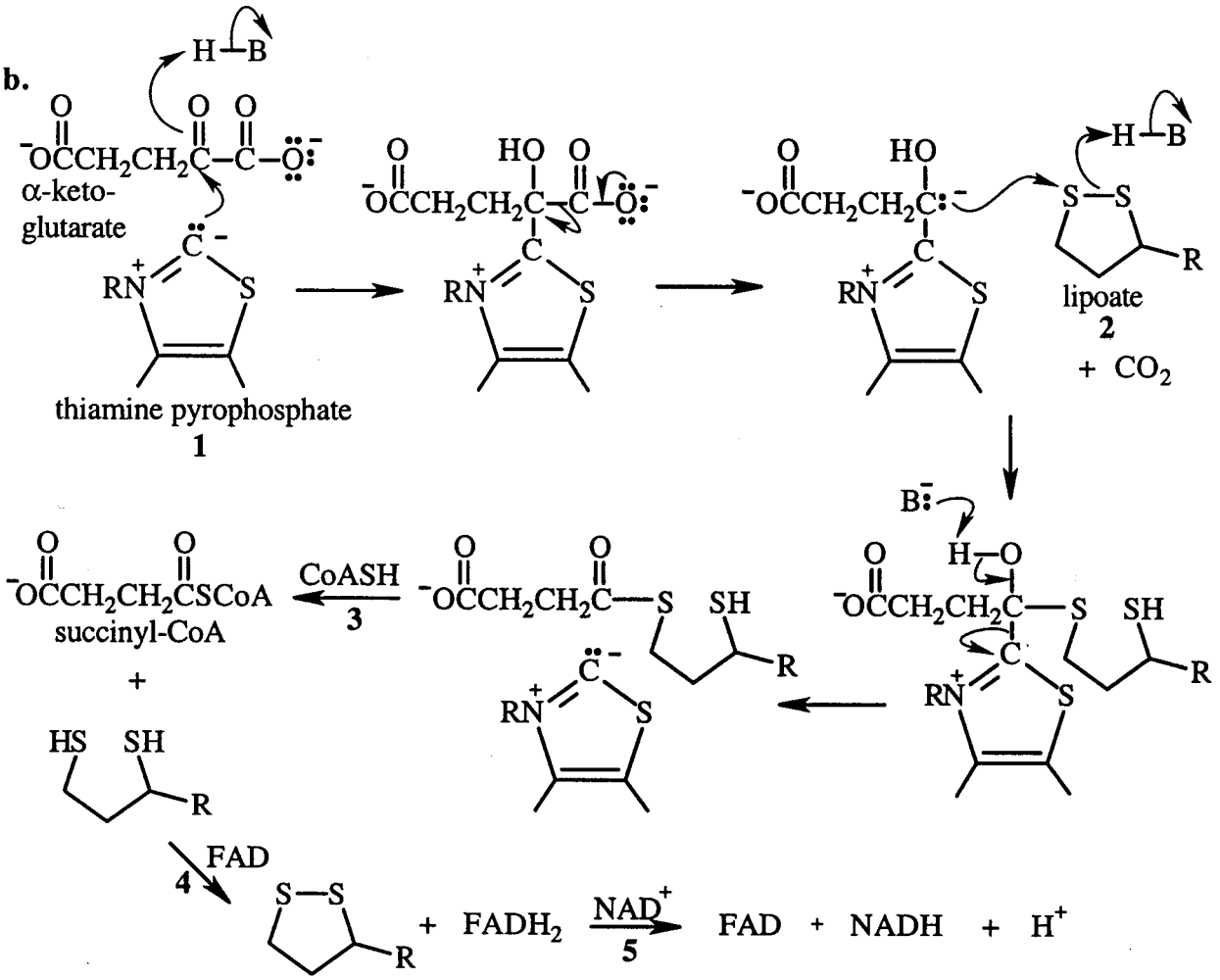
f. propionyl-CoA carboxylase, biotin

25.

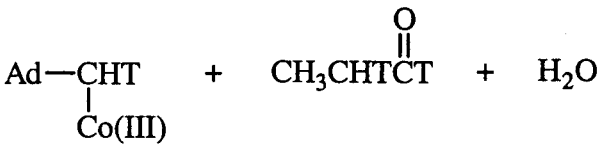


26. **a.** thiamine pyrophosphate, lipoate, coenzyme A, FAD, NAD^+

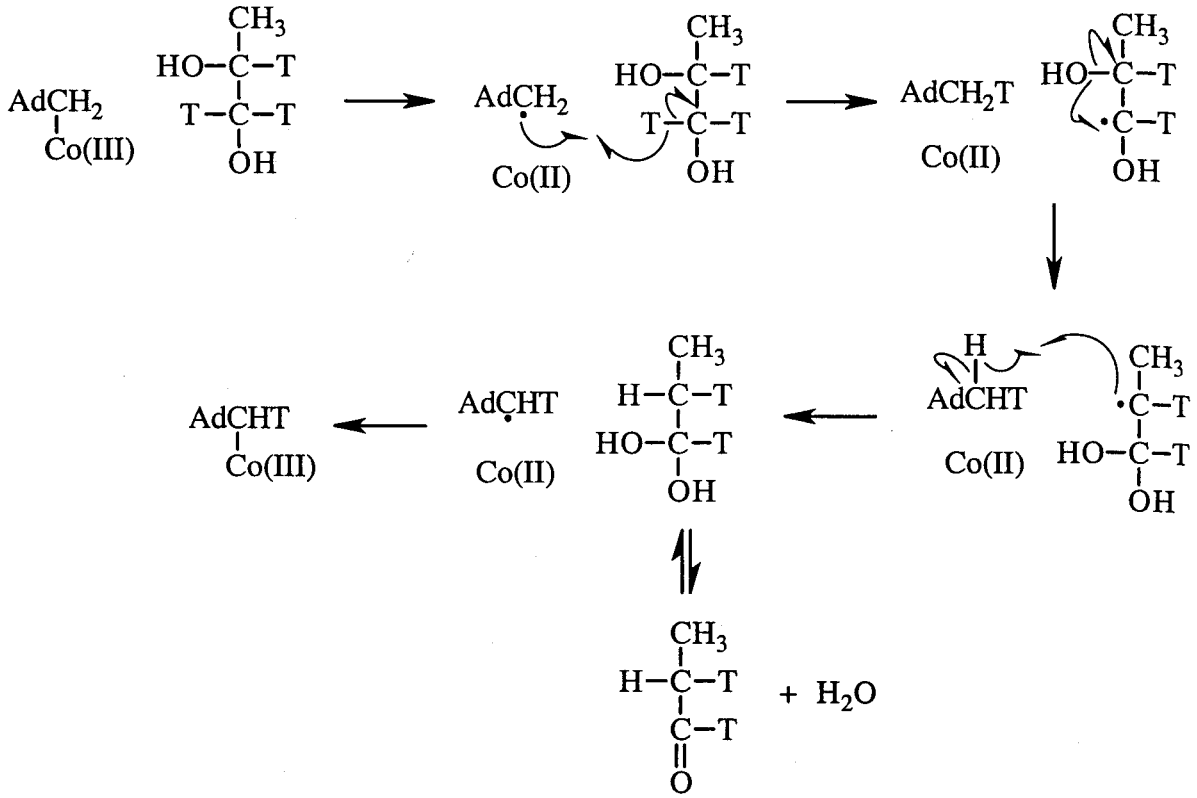
b.



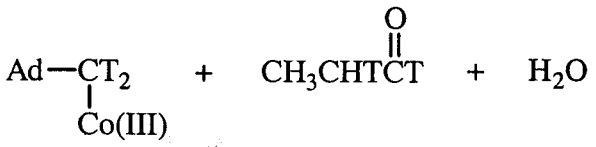
27. The products of the reaction are shown below.



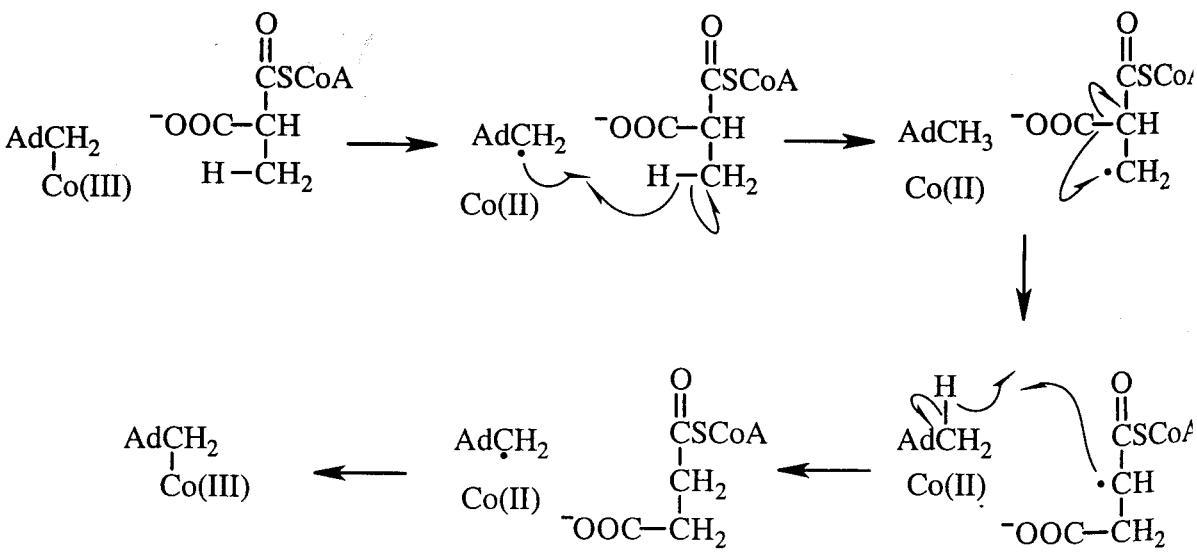
The following mechanism explains the products.



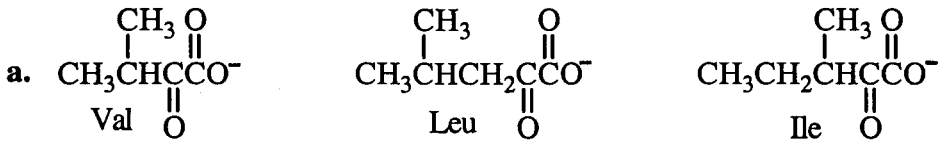
If there is only a limited amount of coenzyme, the second H of the coenzyme will be replaced T in a subsequent round of catalysis, which means that the final product will be:

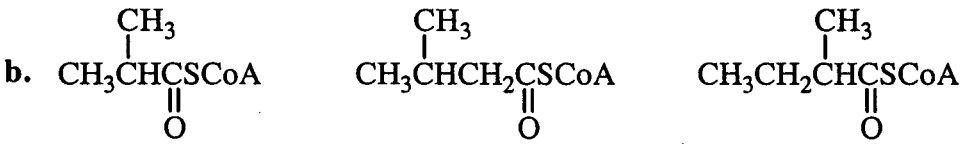


28.



29.

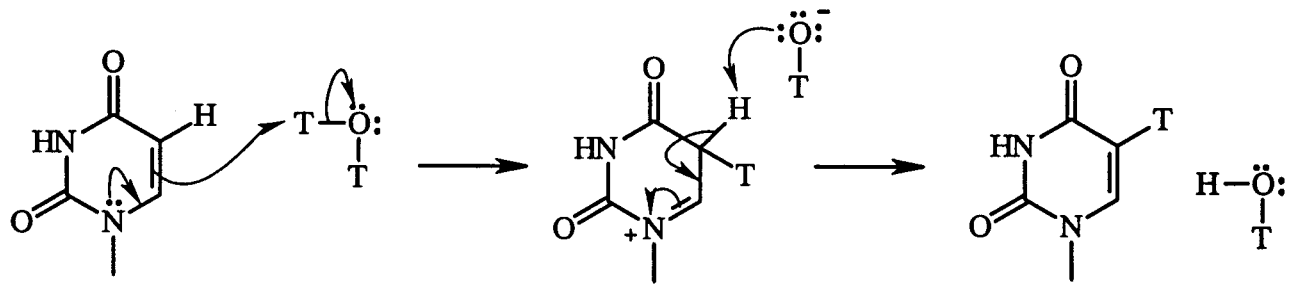
a. 

b. 

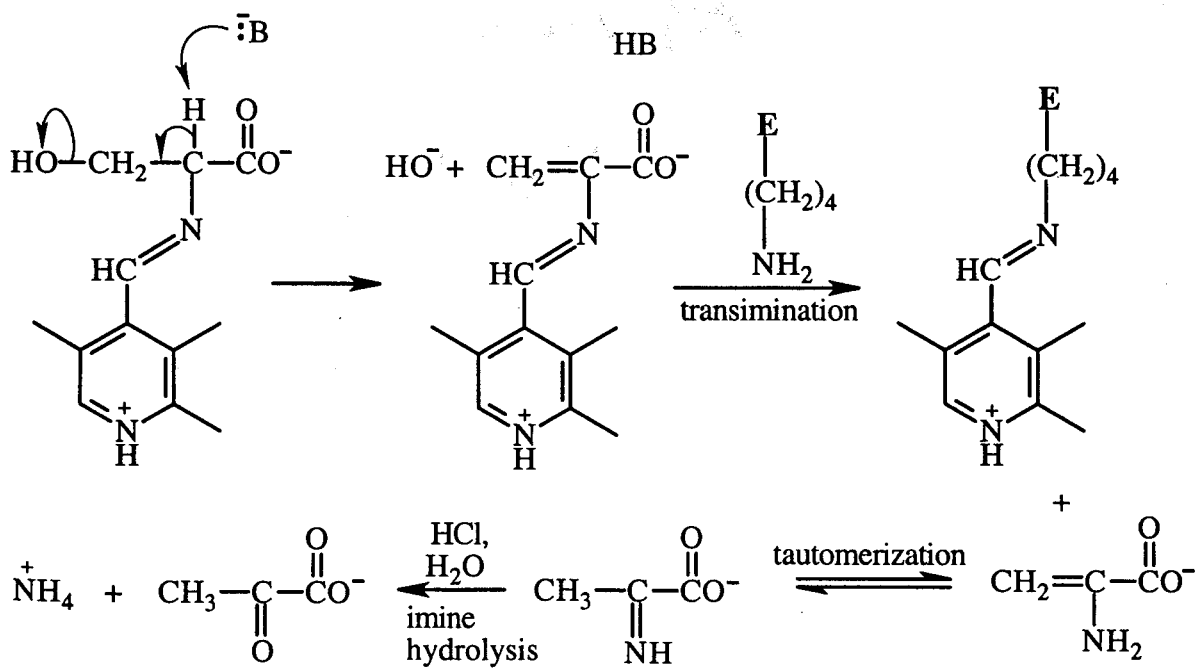
c. thiamine pyrophosphate, lipoate, coenzyme A, FAD, NAD^+

d. The disease can be treated by a diet low in branched-chain amino acids.

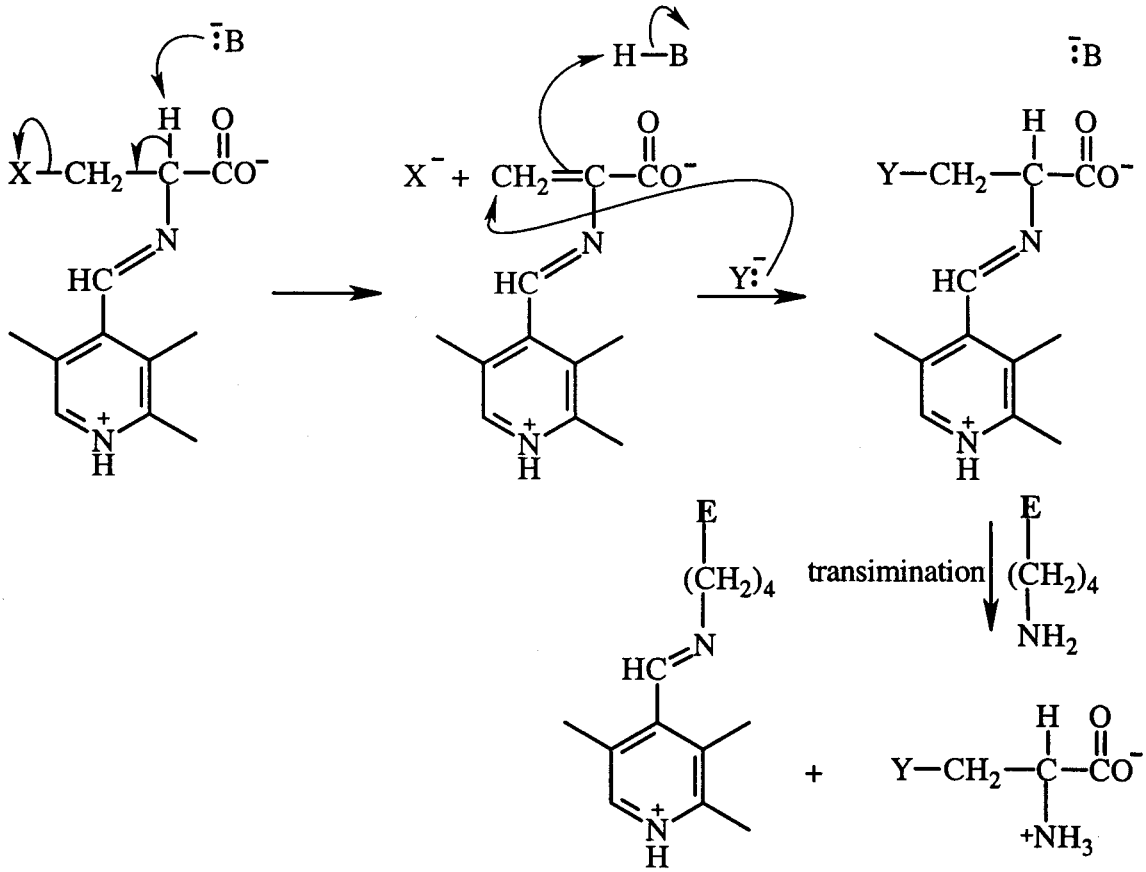
30.



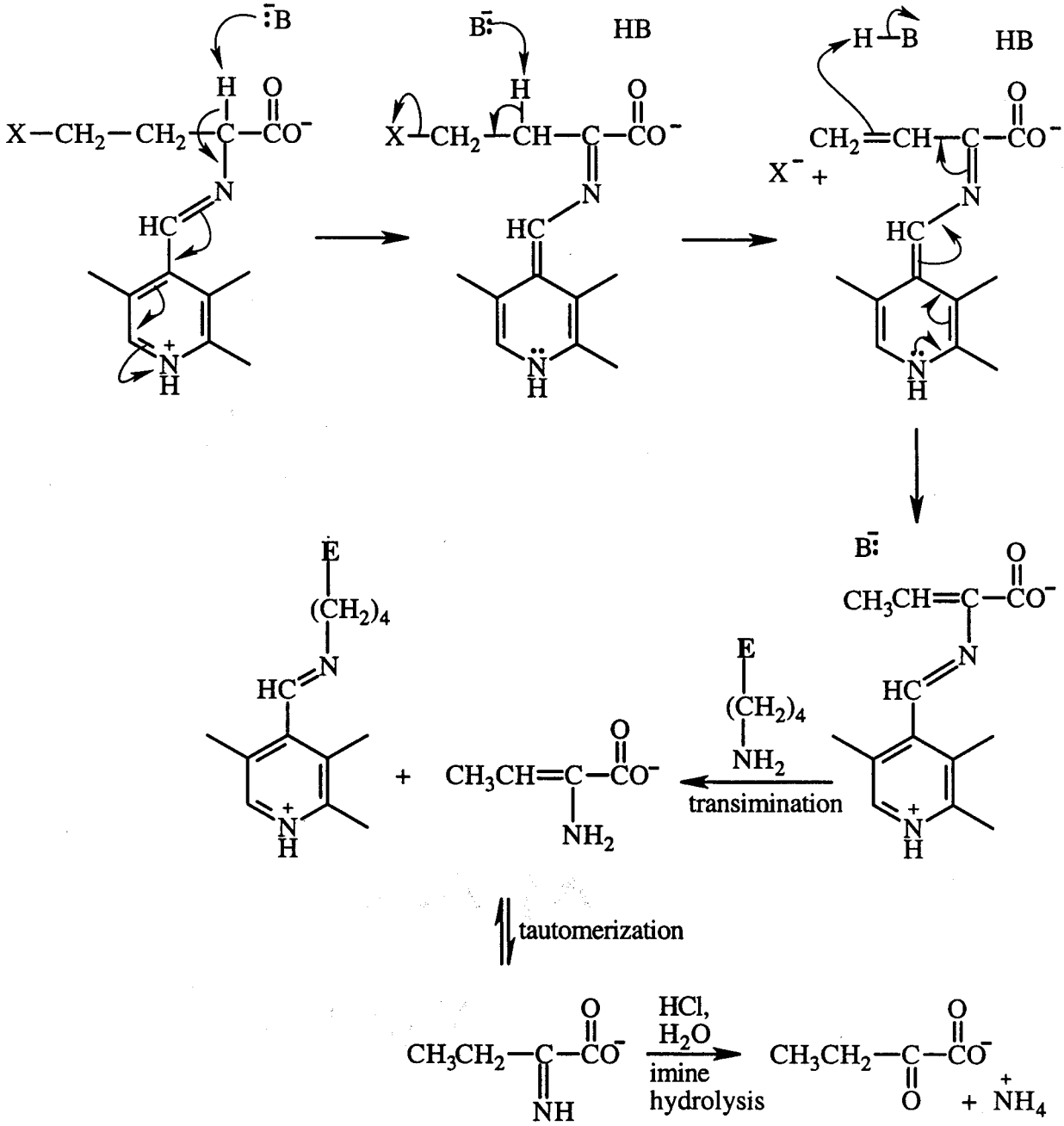
31.



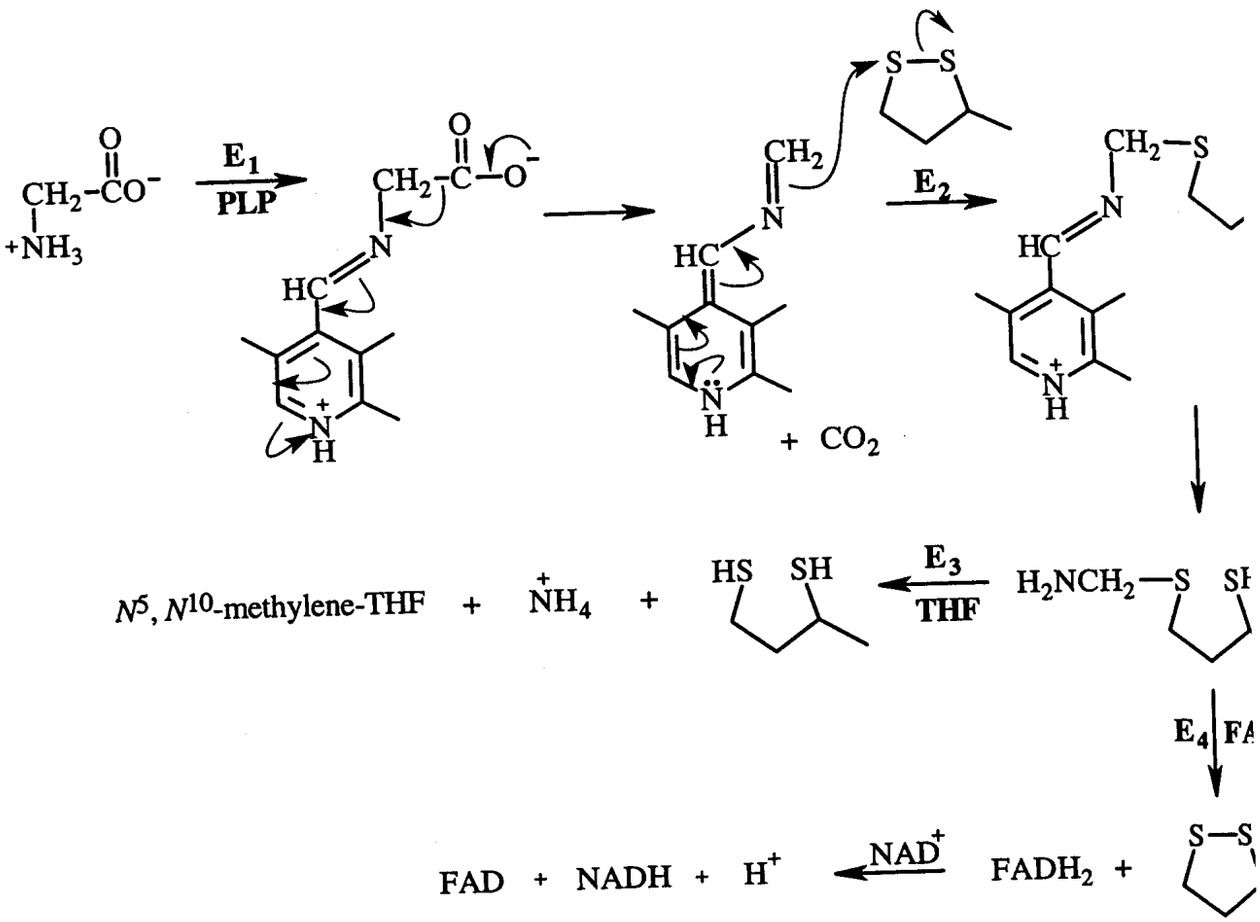
32.



33.


transimination
tautomerization
HCl,
H_2O
imine
hydrolysis

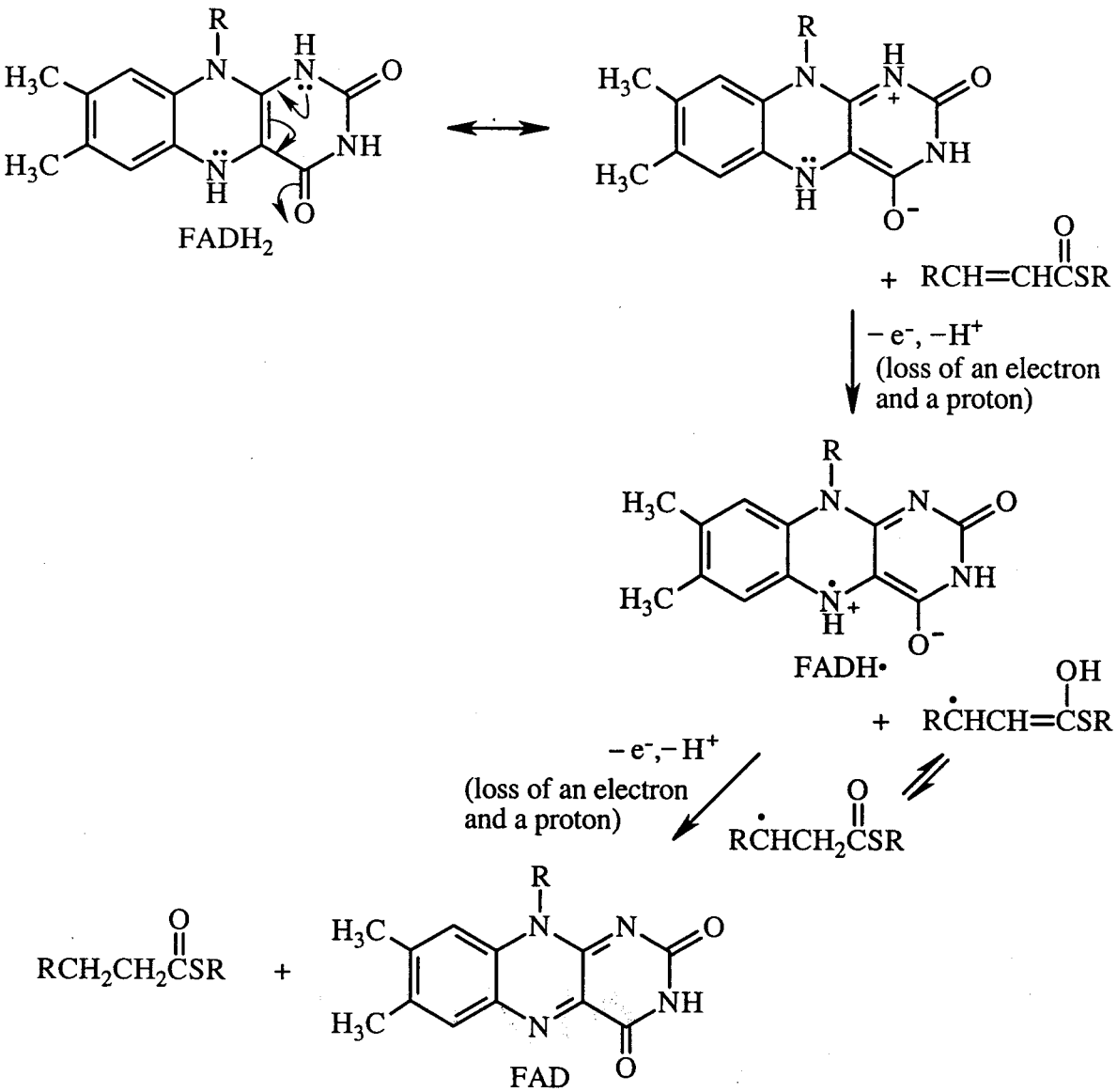
34.



35. Nonenzyme-bound FAD has a greater oxidation potential than NAD^+. Consequently, FAD oxidizes NADH to NAD^+. When the enzyme binds FAD, it changes its oxidation potential, causing it to become less than that of NAD^+. Consequently, NAD^+ oxidizes enzyme-bound $FADH_2$ to FAD. In addition, there will be much more NAD^+ relative to enzyme-bound $FADH_2$ in the mitochondria (where the oxidation of $FADH_2$ by NAD^+ takes place). Therefore, the equilibrium favors the oxidation of $FADH_2$ by NAD^+ (Le Châtelier's principle).

$$\text{E-FADH}_2 + \underset{\text{excess}}{\text{NAD}^+} \rightleftharpoons \text{E-FAD} + \text{NADH} + \text{H}^+$$

36.


FADH2
+ RCH=CHCSR
– e–, –H+
(loss of an electron
and a proton)
FADH•
+ RĊHCH=CSR
– e–,– H+
(loss of an electron
and a proton)
RĊHCH2CSR
RCH2CH2CSR +
FAD

CHAPTER 26
Lipids

Important Terms

adrenal cortical steroids	steroids synthesized in the adrenal cortex.
anabolic steroids	steroids that aid in the development of muscle.
androgens	steroids responsible for the development of male secondary sex characteristics.
angular methyl group	a methyl substituent at the 10- or 13-position of a steroid ring system.
carotenoid	a class of compound (a tetraterpene) responsible for the red and orange colors of fruits, vegetables, and fall leaves.
cephalin	a phosphoacylglycerol in which the second OH group of phosphate has formed an ester with ethanolamine.
cerebroside	a sphingolipid in which the primary OH group of sphingosine is bonded to a sugar residue.
cholesterol	a steroid that is the precursor of all other steroids.
cis fused	two rings fused together such that if one ring is considered to be two substituents of the other ring, the substituents would be on the same side of the first ring.
essential oil	fragrances and flavorings isolated from plants that do not leave a residue when they evaporate. Most are terpenes.
estrogens	steroids responsible for the development of female secondary sex characteristics.
fat	a triester of glycerol that exists as a solid at room temperature.
fatty acid	a carboxylic acid with a long hydrocarbon side chain.
hormone	an organic compound synthesized in a gland and delivered by the bloodstream to its target tissue.
isoprene rule	head-to-tail linkage of isoprene units.
lecithin	a phosphoacylglycerol in which the second OH group of phosphate has formed an ester with choline.
leukotriene	compounds that induce contraction of the muscle that lines the airways to the lungs.
lipid	a water-insoluble compound found in a living system.
lipid bilayer	two layers of phosphoacylglycerols arranged so that their polar heads are on the outside and their nonpolar fatty acid chains are on the inside.

membrane the material the surrounds the cell in order to isolate its contents.

mixed triacylglycerol a triacylglycerol in which the fatty acid components are different.

monoterpene a terpene that contains 10 carbons.

oil a triester of glycerol that exists as a liquid at room temperature.

phosphatidic acid a phosphoacylglycerol in which only one of the OH groups of phosphate is in an ester linkage.

phosphoacylglycerol (phosphoglyceride) formed when two OH groups of glycerol form esters with fatty acids and the terminal OH group forms a phosphate ester.

phospholipid a lipid that contains a phosphate group.

polyunsaturated fatty acid a fatty acid with more than one double bond.

progestins a class of steroid hormones.

prostacyclin a compound that dilates blood vessels and inhibits platelet aggregation.

prostaglandin a carboxylic acid, derived from arachidonic acid, that is responsible for a variety of physiological functions.

sesquiterpene a terpene that contains 15 carbons.

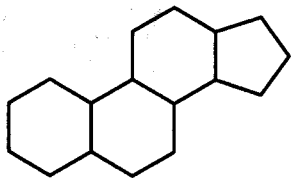
simple triacylglycerol a triacylglycerol in which the fatty acid components are the same.

sphingolipid a lipid that contains sphingosine.

sphingomyelin a sphingolipid in which the primary OH group of sphingosine is bonded to a phosphocholine or to a phosphoethanolamine.

squalene a triterpene that is a precursor of steroid molecules.

steroid a class of compounds that contains a steroid ring system.



steroid ring system

α-substituent a substituent on the opposite side of a steroid ring system as the angular methyl groups.

β-substituent a substituent on the same side of a steroid ring system as the angular methyl groups.

terpene a lipid isolated from a plant that contains carbon atoms in multiples of five.

terpenoid a terpene that contains oxygen.

tetraterpene a terpene that contains 40 carbons.

thromboxane a compound that constricts blood vessels and stimulates platelet aggregation.

trans fused two rings fused together such that if one ring is considered to be two substituents of the other ring, the substituents would be on opposite sides o the first ring.

triacylglycerol the compound formed when the three OH groups of glycerol are esterified with fatty acids.

triterpene a terpene that contains 30 carbons.

wax an ester formed from a long-chain carboxylic acid and a long-chain alcohol.

Solutions to Problems

1. **a.** Stearic acid has the higher melting point because it has two more methylene groups (giving it a greater surface area) than palmitic acid.

b. Palmitic acid has the higher melting point because it does not have any carbon-carbon double bonds, whereas palmitoleic acid has a cis double bond that prevents the molecules from packing closely together.

c. Oleic acid has the higher melting point because it has one double bond, while linoleic acid has two double bonds, which give greater interference to close packing of the molecules.

2.

$$CH_3CH_2CH_2CH_2CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH_2CH_2COOH$$

$$\downarrow \begin{matrix}1.\ \text{excess } O_3\\ 2.\ H_2O_2\end{matrix}$$

$CH_3CH_2CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OH$ hexanoic acid

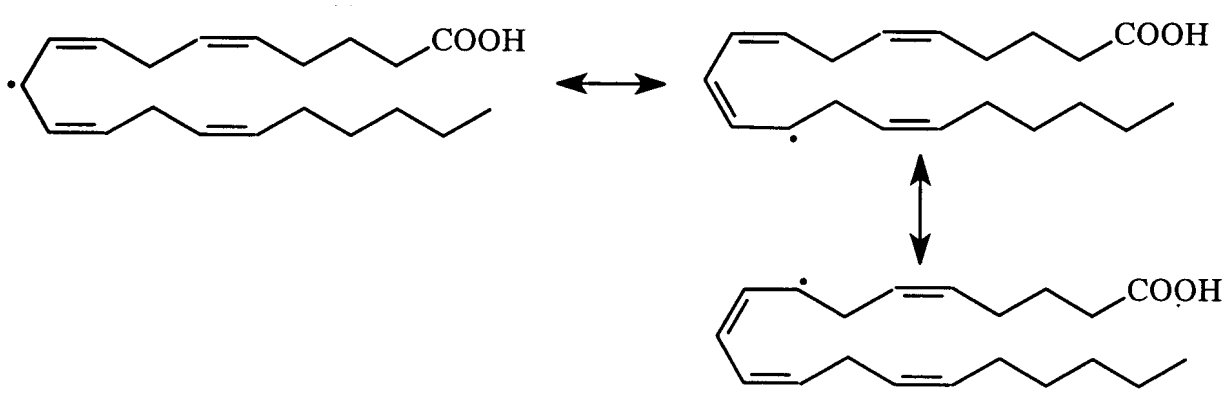
$3\ HO\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}OH$ 3 malonic acids

$HO\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OH$ glutaric acid

3. All triacylglycerols do not have the same number of chirality centers. If the carboxylic acid components at C-1 and C-3 of glycerol are not identical, the triacylglycerol has one chirality center (C-2). If the carboxylic acid components at C-1 and C-3 of glycerol are identical, the triacylglycerol has no chirality centers.

4. Glyceryl tripalmitate has a higher melting point because the carboxylic acid components are saturated and can, therefore, pack more closely together than the unsaturated carboxylic acid components of glyceryl tripalmitoleate.

5.

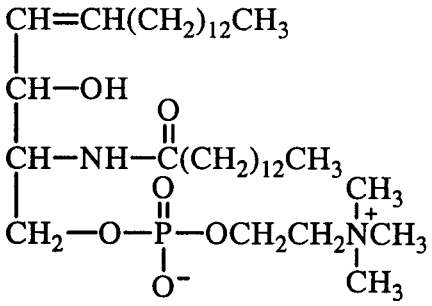


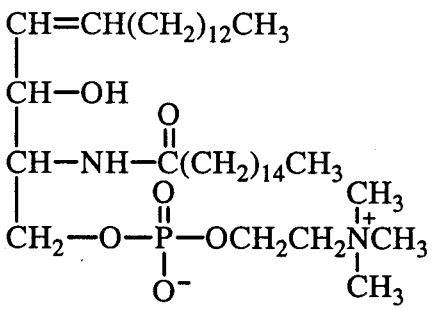
6. Because the interior of a membrane is nonpolar and the surface of a membrane is polar, integral proteins will have a higher percentage of nonpolar amino acids.

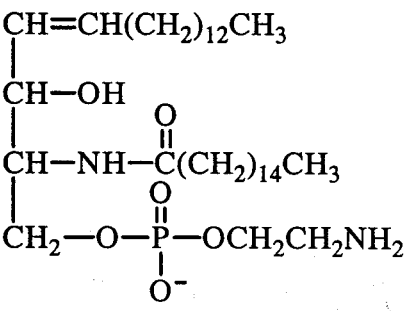
7. The bacteria could synthesize phosphoacylglycerols with more saturated fatty acids because these triacylglycerols would pack more tightly in the lipid bilayer and, therefore, would have higher melting points and be less fluid.

8. The sphingomyelins can differ in the fatty acid component of the amide and have either choline or ethanolamine attached to the phosphate group.

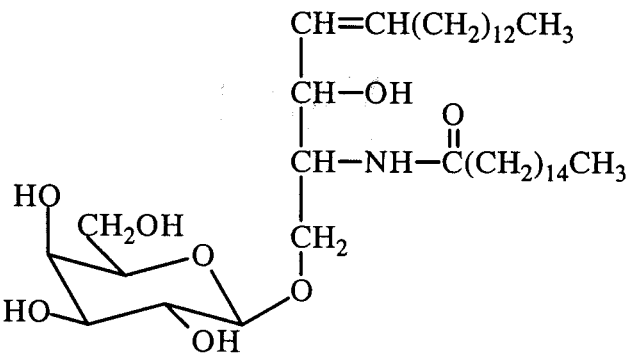
a.





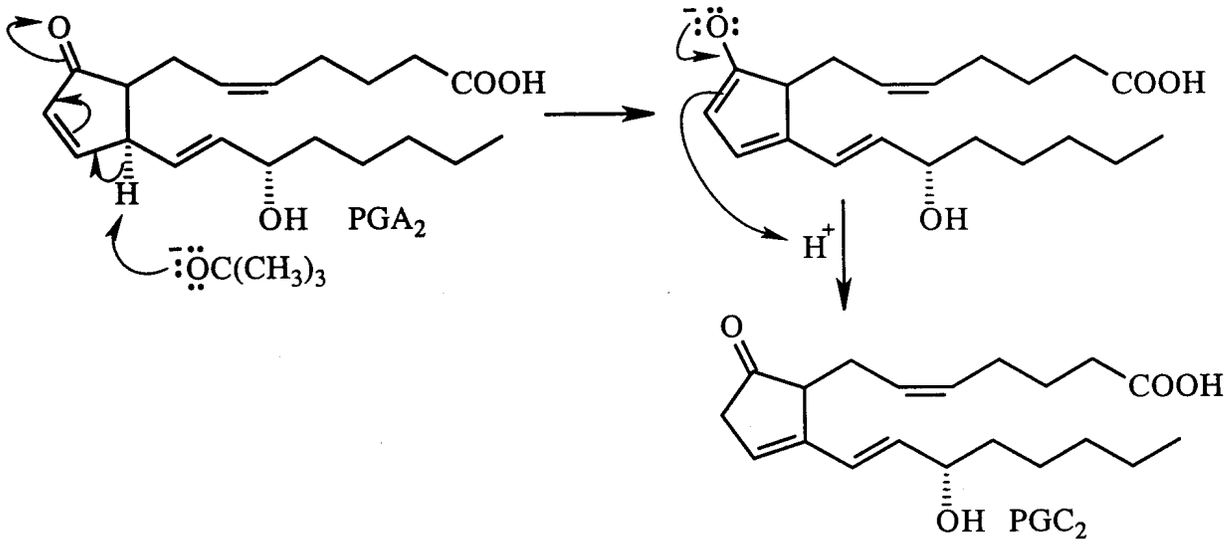


b.

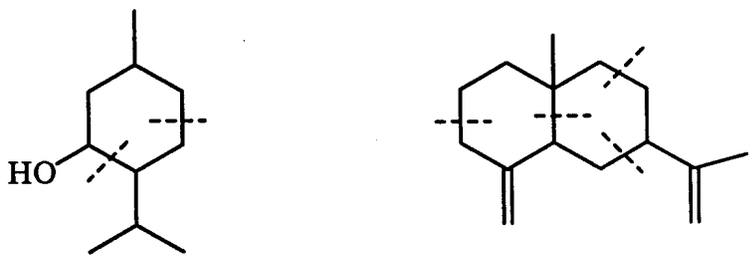


9. Membranes must be kept in a semifluid state in order to allow transport across them. Cells closer to the hoof of an animal are going to be in a colder average environment than cells closer to the body. Therefore, the cells closer to the hoof have a higher degree of unsaturation to give them a lower melting point so the membranes will not solidify at the colder temperature.

10.

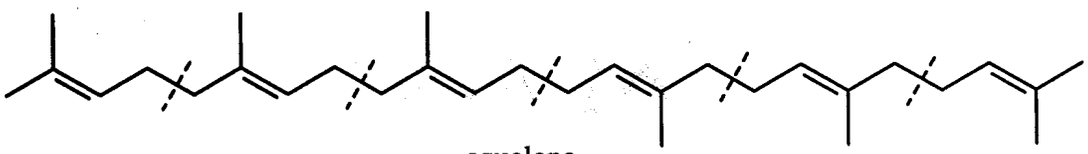


11.



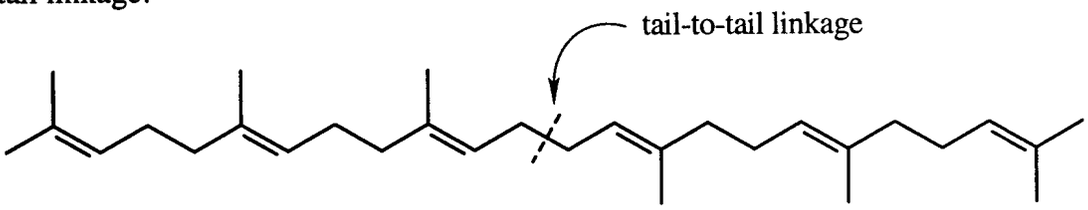
menthol

β-selinene

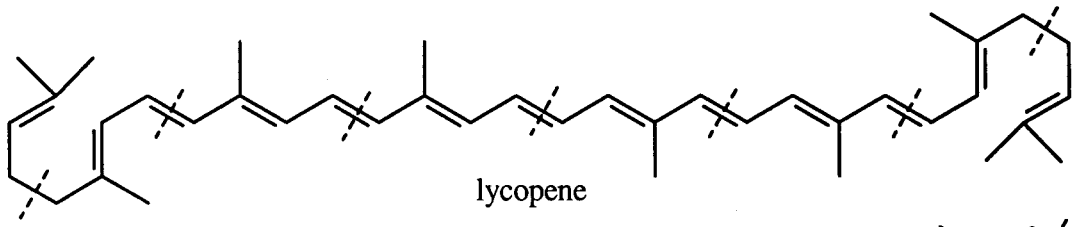


squalene

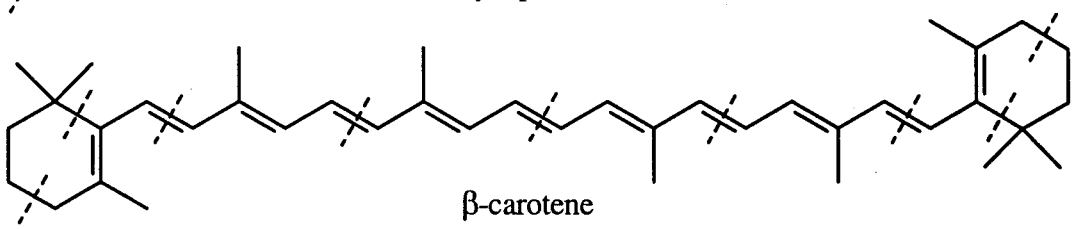
12. The fact that the tail-to-tail linkage occurs in the exact center of the molecule indicates that the two halves are synthesized (in a head-to-tail fashion) and then joined together in a tail-to-tail linkage.



13. Squalene, lycopene, and β-carotene are all synthesized in the same way. In each case, two halves are synthesized (in a head-to-tail fashion) and then joined together in a tail-to-tail linkage.



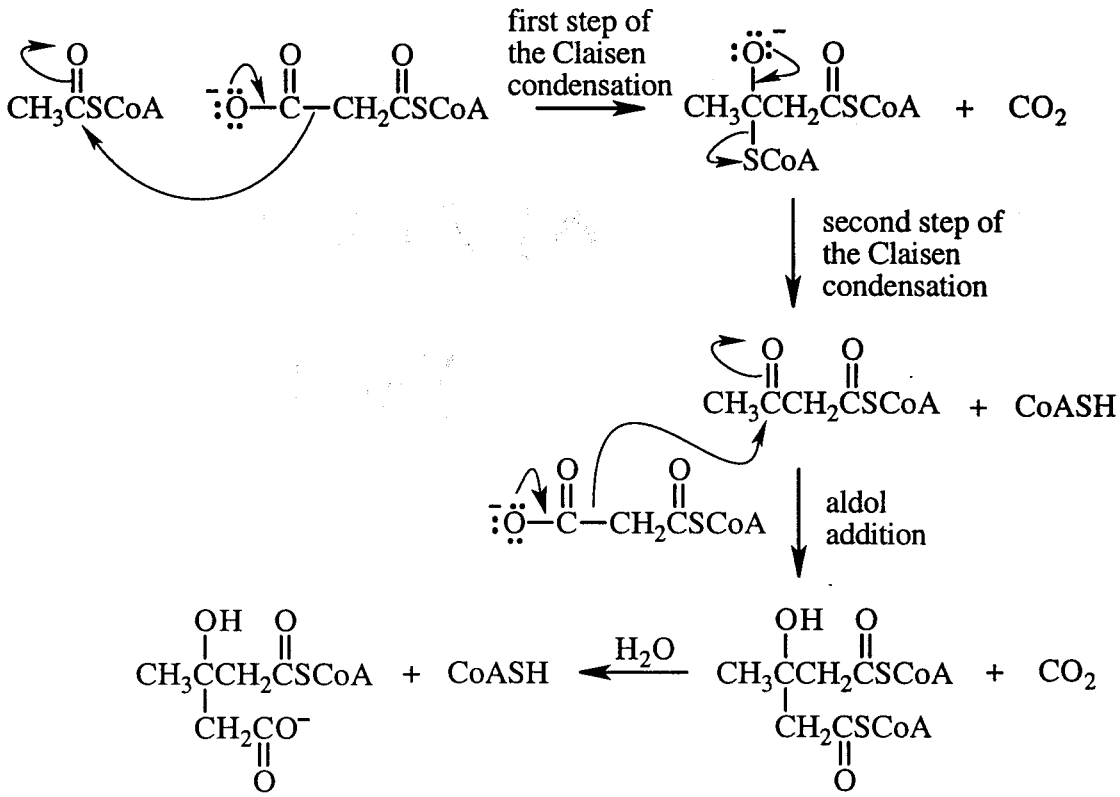
lycopene



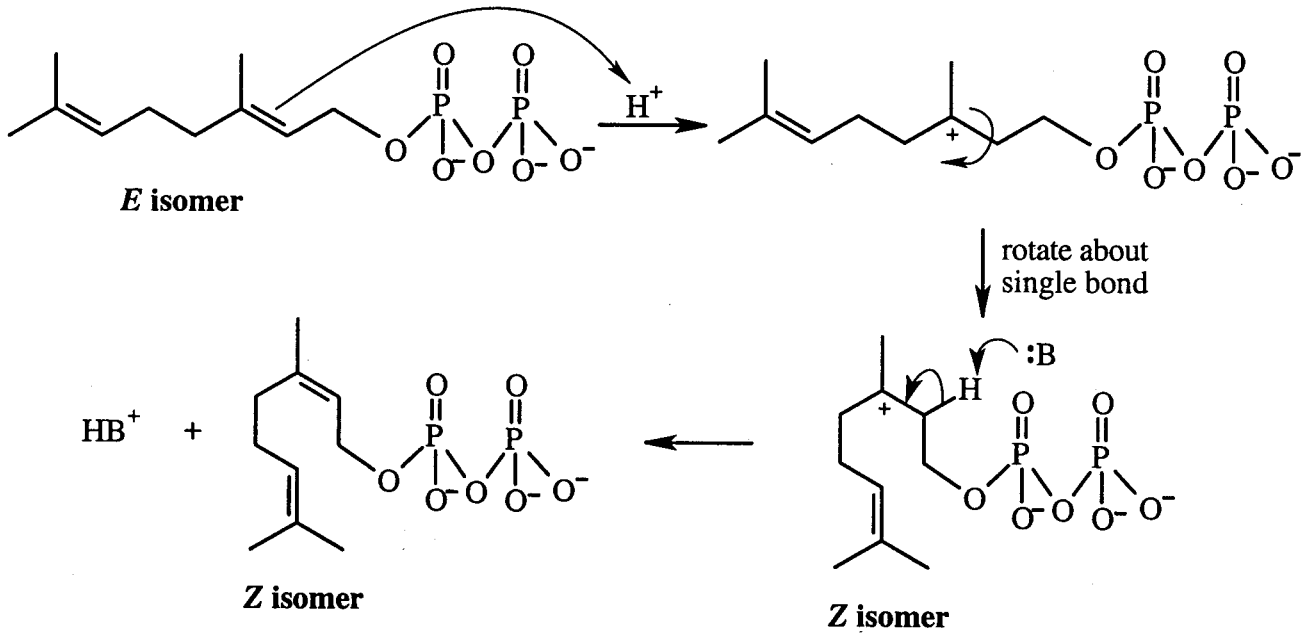
β-carotene

14. Solved in the text.

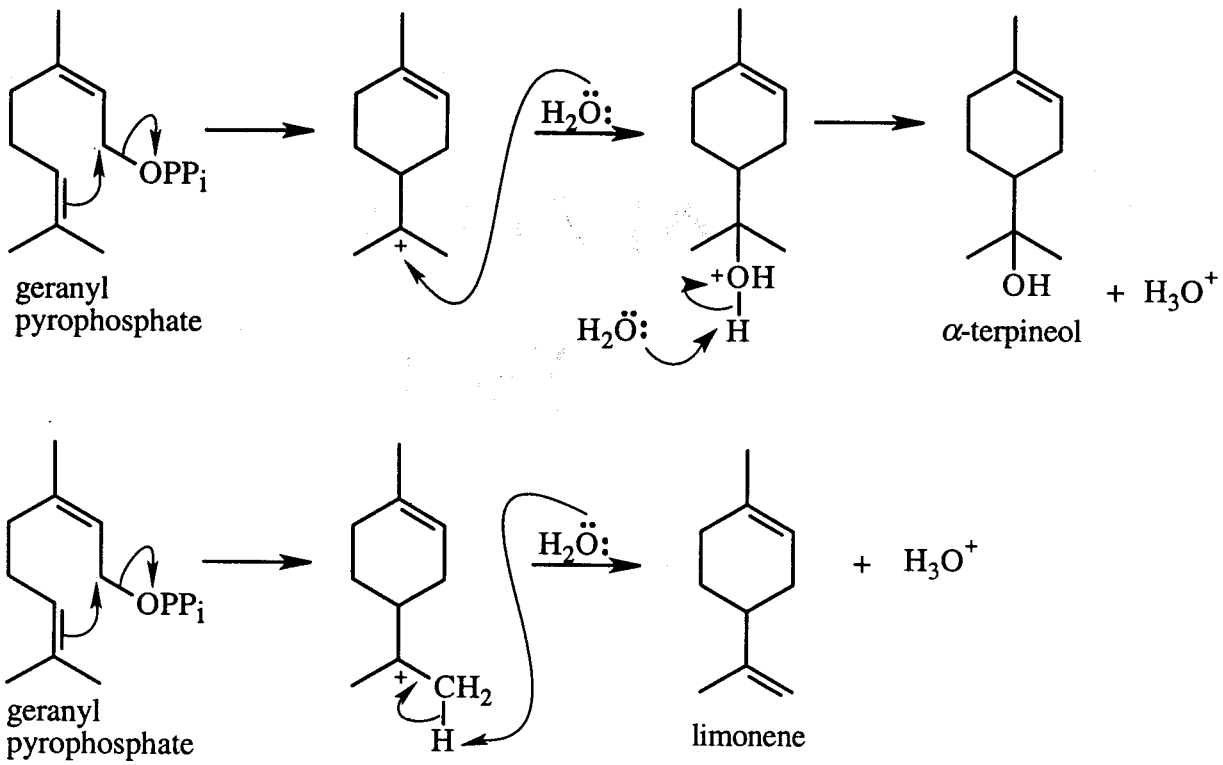
15.



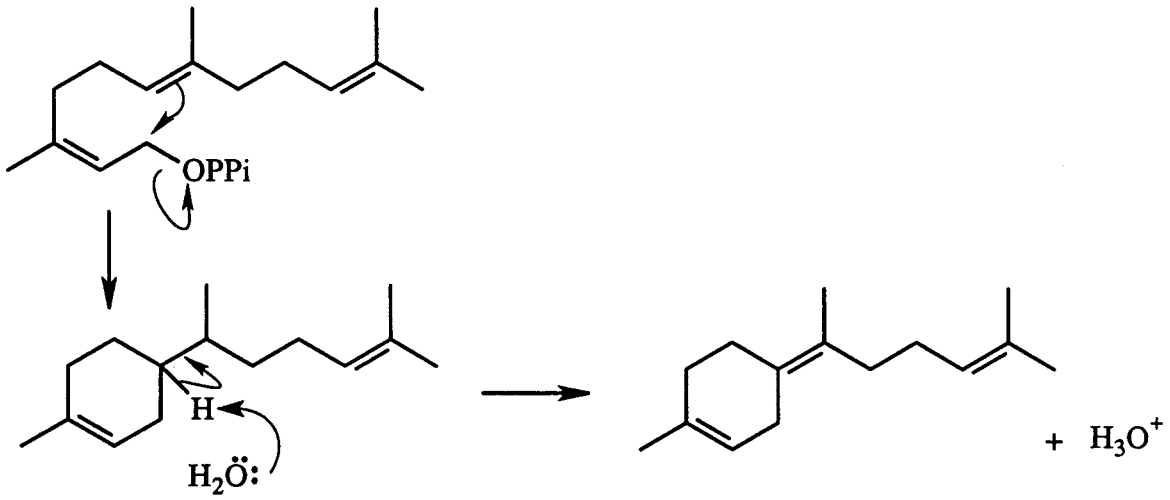
16.


E isomer
H+
rotate about
single bond
:B
H
HB+ +
Z isomer
Z isomer

17.


OPPi
geranyl
pyrophosphate
H2Ö:
+OH
H2Ö:
H
OH
α-terpineol
+ H3O+
OPPi
geranyl
pyrophosphate
H2Ö:
CH2
H
limonene
+ H3O+

18.

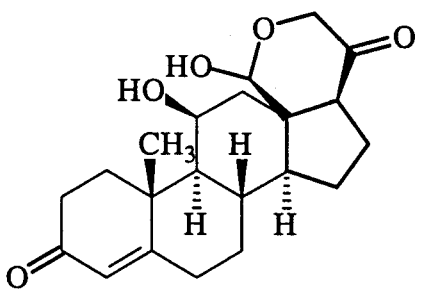


19. Solved in the text.

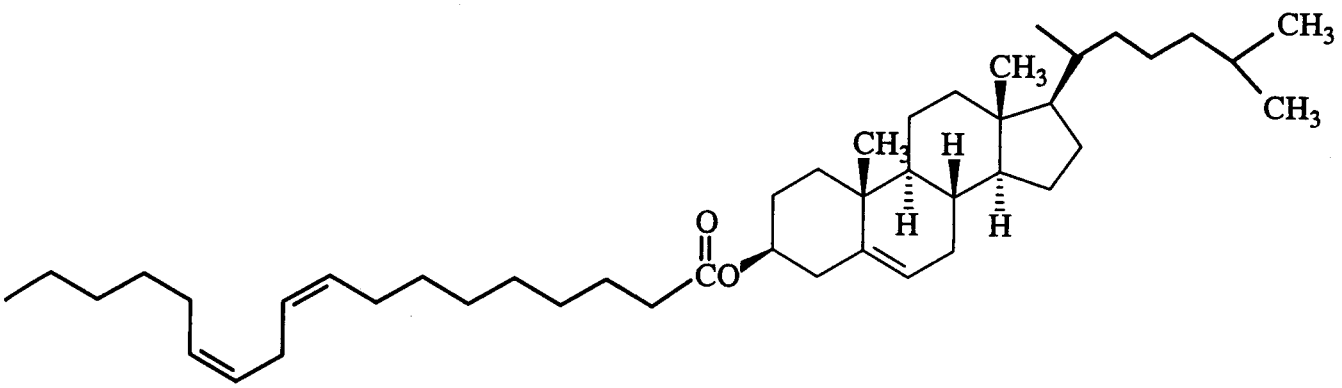
20. A **β-hydrogen** at C-5 means that the A and B rings are **cis** fused, whereas an **α-hydrogen** at C-5 means that the A and B rings are **trans** fused.

21. Because the OH substituent is on the **same side** of the steroid ring system as the angular methyl groups, it is a **β-substituent.**

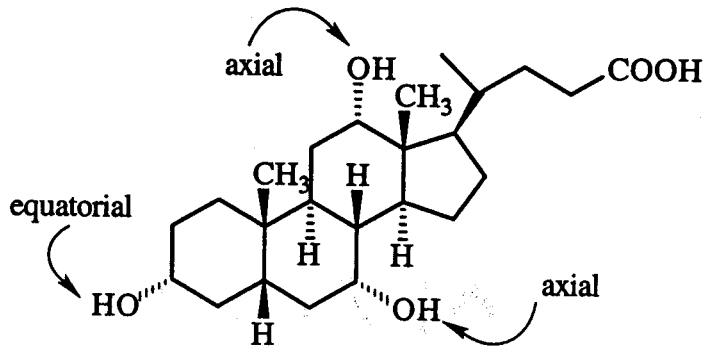
22. The hemiacetal is formed by reaction of the primary alcohol with the aldehyde.



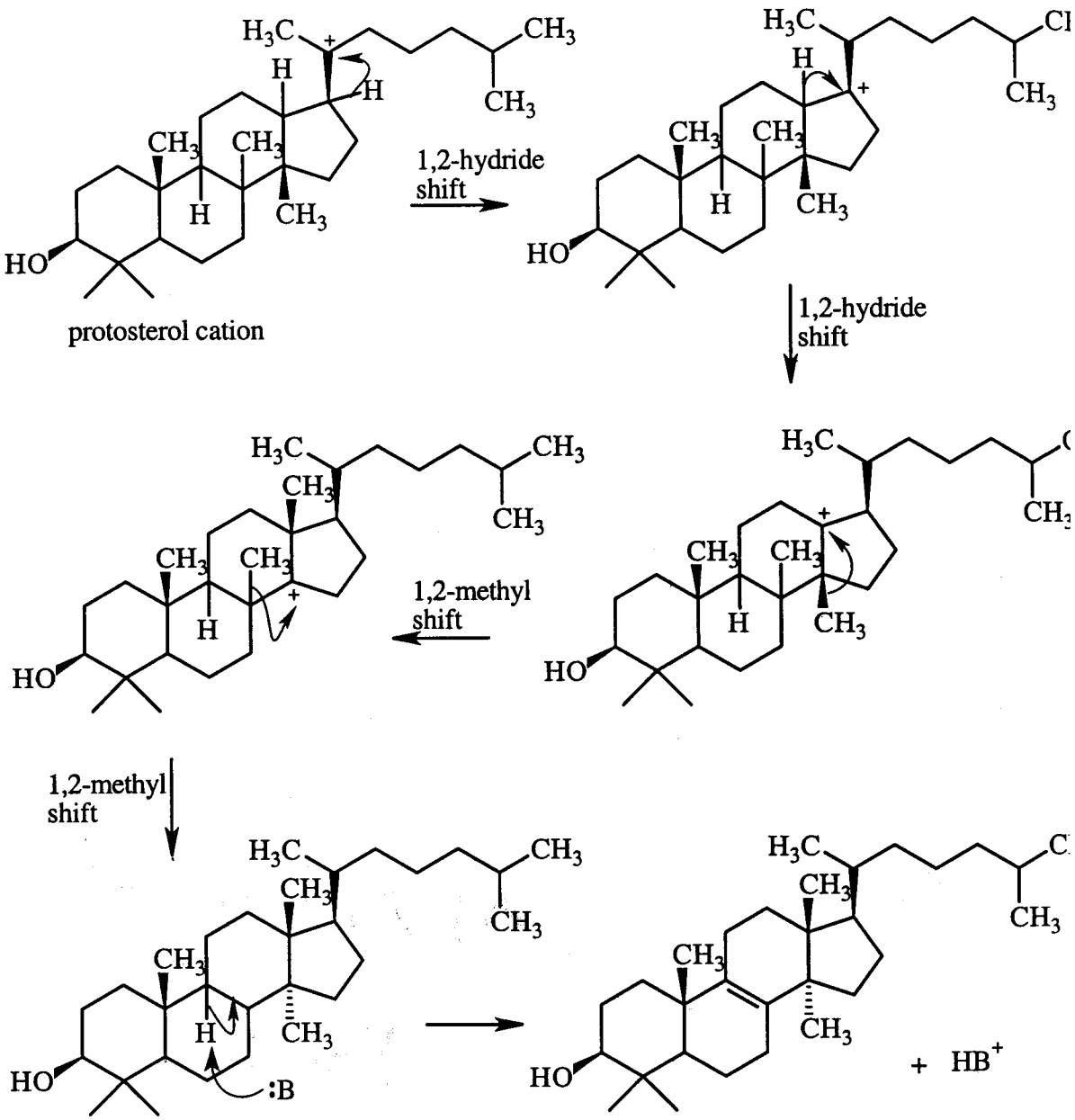
23.



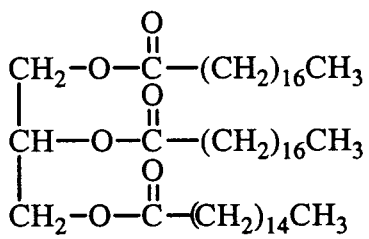
24. Because the three OH substituents of cholic acid are on the **opposite side** of the steroid ring system as the angular methyl groups, they are all **α-substituents**. Two of the OH substituents are axial substituents and one is an equatorial substituent.



25. There are two hydride shifts and two methyl shifts. The last step is elimination of a proton.

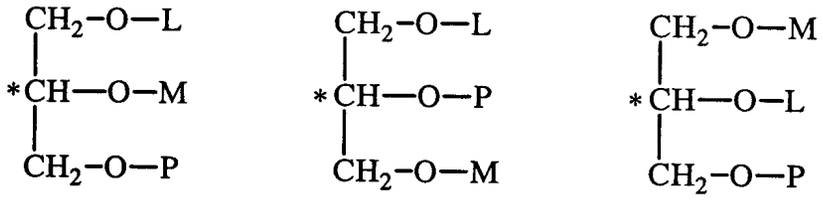


26. If stearic acid were at C-1 and C-3, the fat would not be optically active. Therefore, stearic acid must be at C-1 and C-2 (or C-2 and C-3).

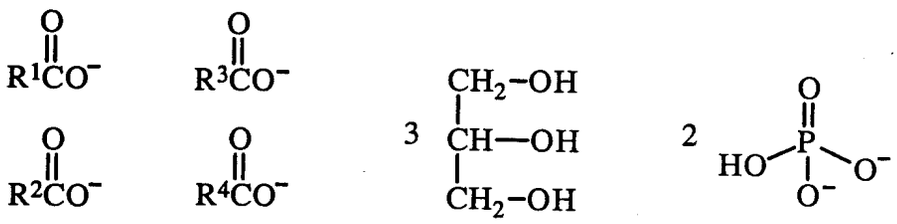


27. **a.** There are three triacylglycerols in which one of the fatty acid components is lauric acid and two are myristic acid. Myristic acid can be at C-1 and C-3 of glycerol, in which case the triacylglycerol does not have any chirality centers. If myristic acid is at C-1 and C-2 of glycerol, C-2 is an asymmetric carbon, and consequently, two enantiomers are possible for the compound.

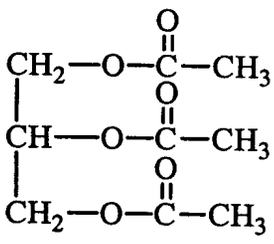
b. There are six triacylglycerols in which one of the fatty acid components is lauric acid, one is myristic acid, and one is palmitic acid. The three possible arrangements are shown below (with the fatty acid components abbreviated as L, M, and P). Since each has an asymmetric carbon, each can exist as a pair of enantiomers for a total of six triacylglycerols.



28.



29.



The structure at left has a molecular formula = $C_9H_{14}O_6$ and a molecular weight = 218.

Subtracting 218 from the total molecular weight gives the molecular weight of the methylene (CH_2) groups in the triacylglycerol.

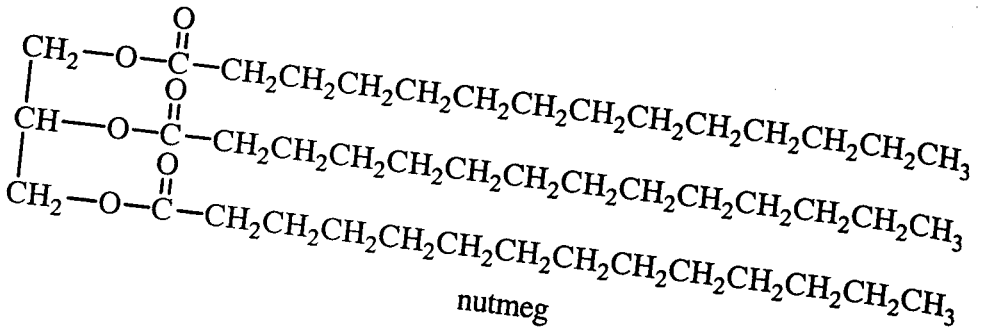
$$722 - 218 = 504$$

Dividing 504 by the molecular weight of a methylene group (14) will give the number of methylene groups.

$$\frac{504}{14} = 36$$

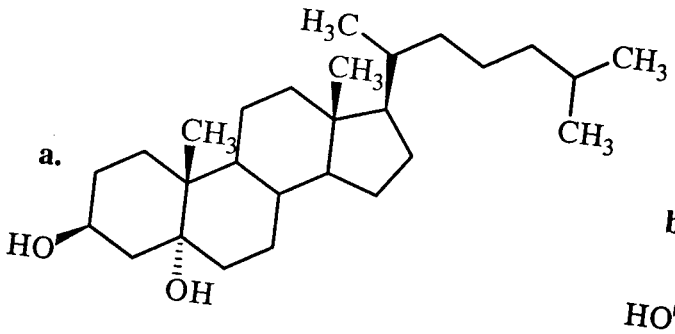
Since there are 36 methylene groups, each fatty acid in the triacylglycerol has 12 methylene groups.

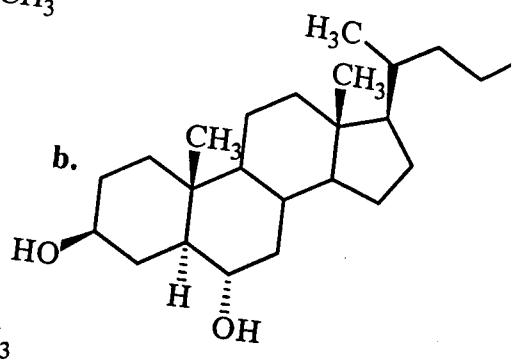
25.

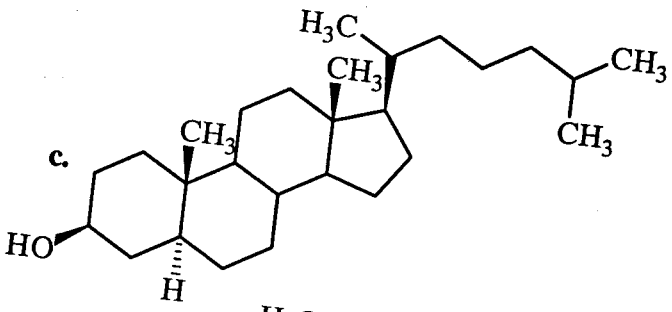


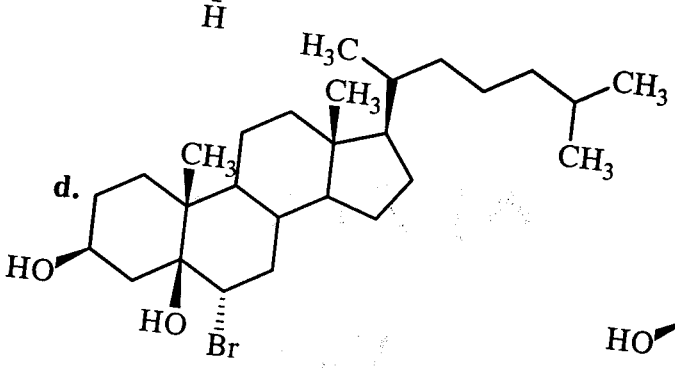
nutmeg

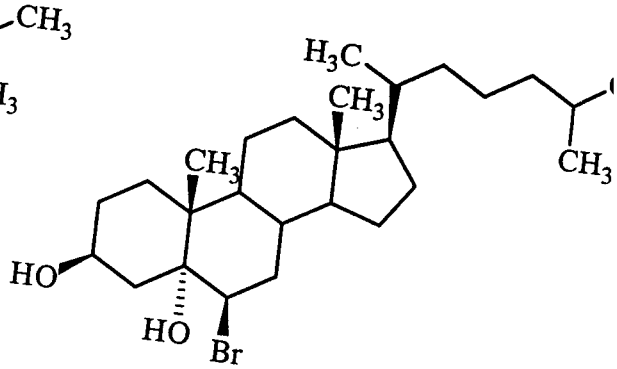
30.

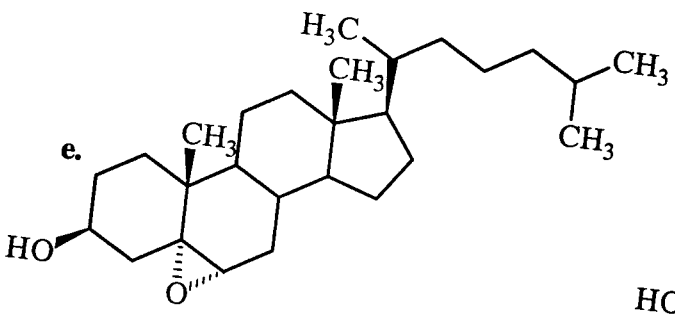

a.
H3C
CH3
CH3
CH3
CH3
HO
OH

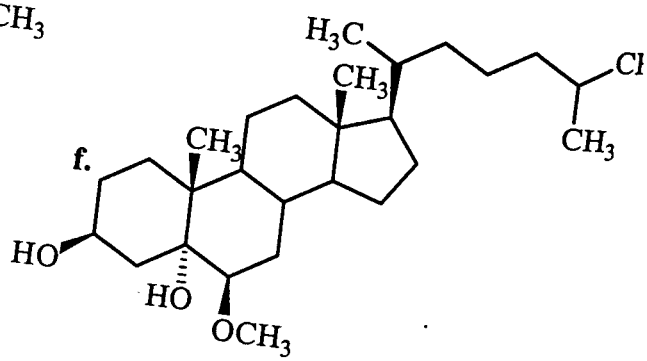

b.
H3C
CH3
CH3
HO
H
OH


c.
H3C
CH3
CH3
CH3
HO
H

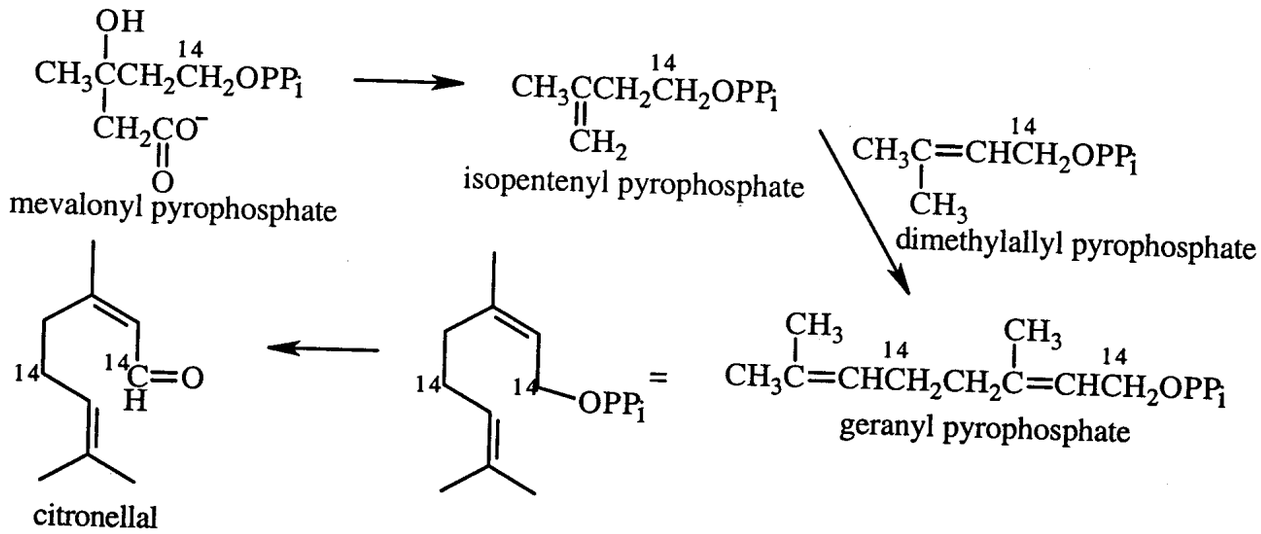

d.
H3C
CH3
CH3
CH3
HO
HO
Br


H3C
CH3
CH3
CH3
HO
HO
Br

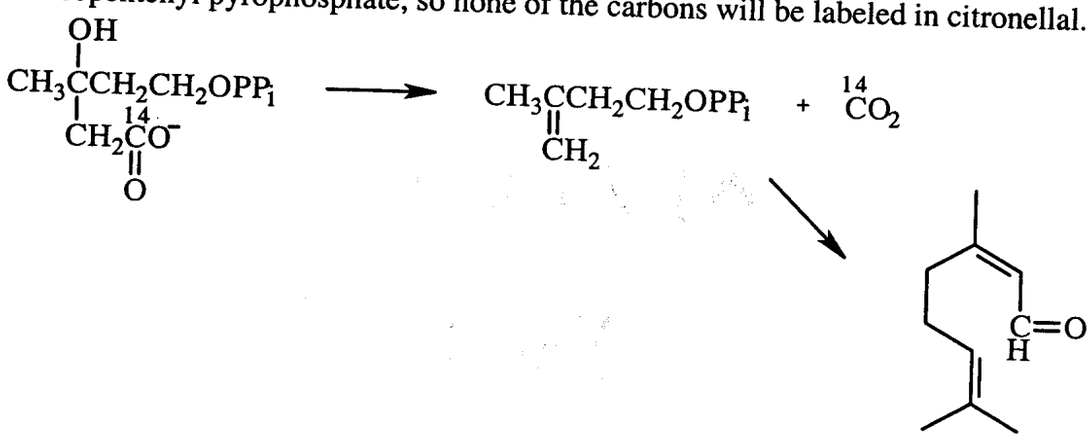

e.
H3C
CH3
CH3
CH3
HO
O


f.
H3C
CH3
Cl
CH3
CH3
HO
HO
OCH3

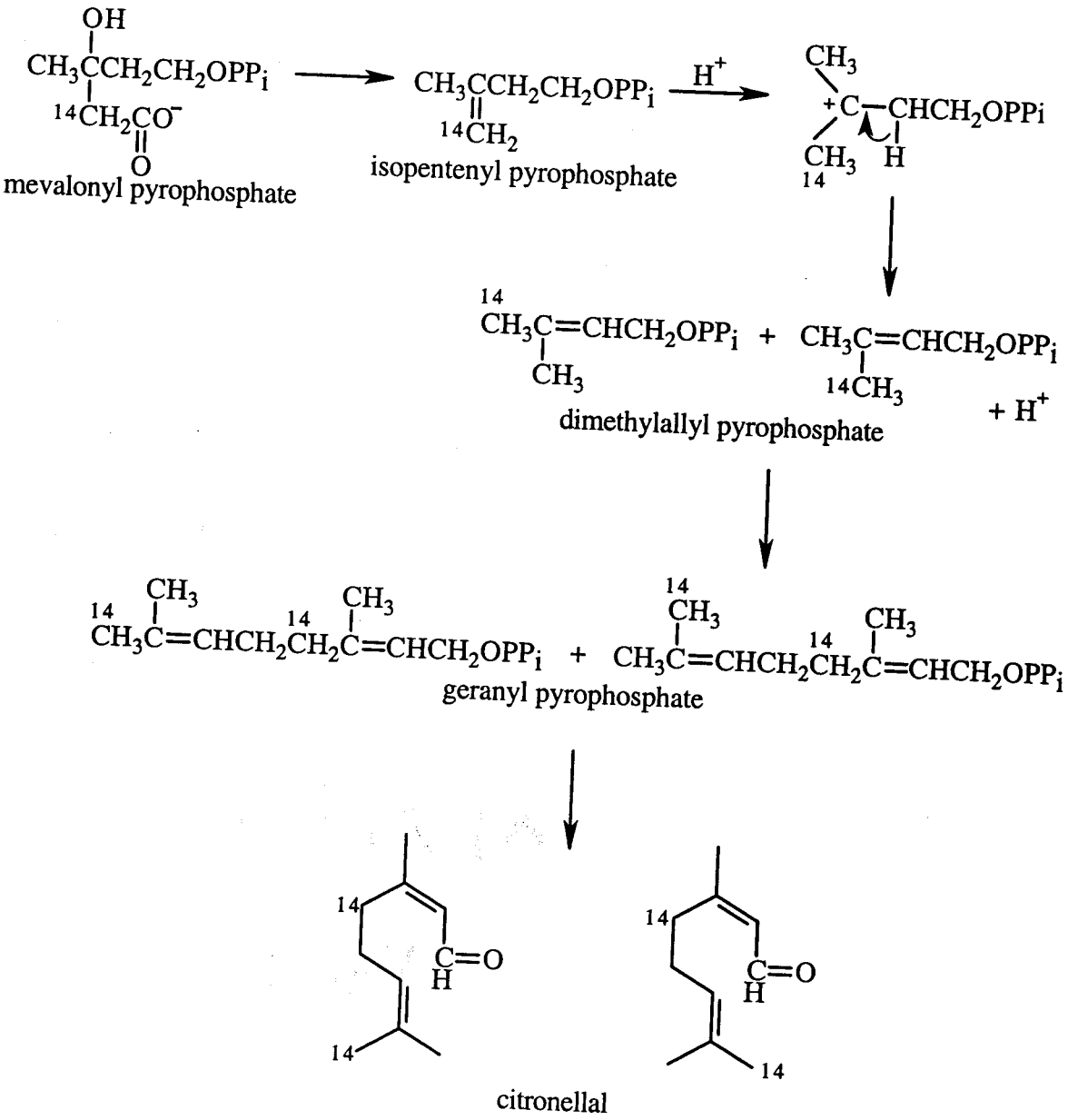
31. **a.** Starting with mevalonyl pyrophosphate, you can trace the location of the label in the compounds that lead to the formation of geranyl pyrophosphate, and geranyl pyrophosphate is converted to citronellal.



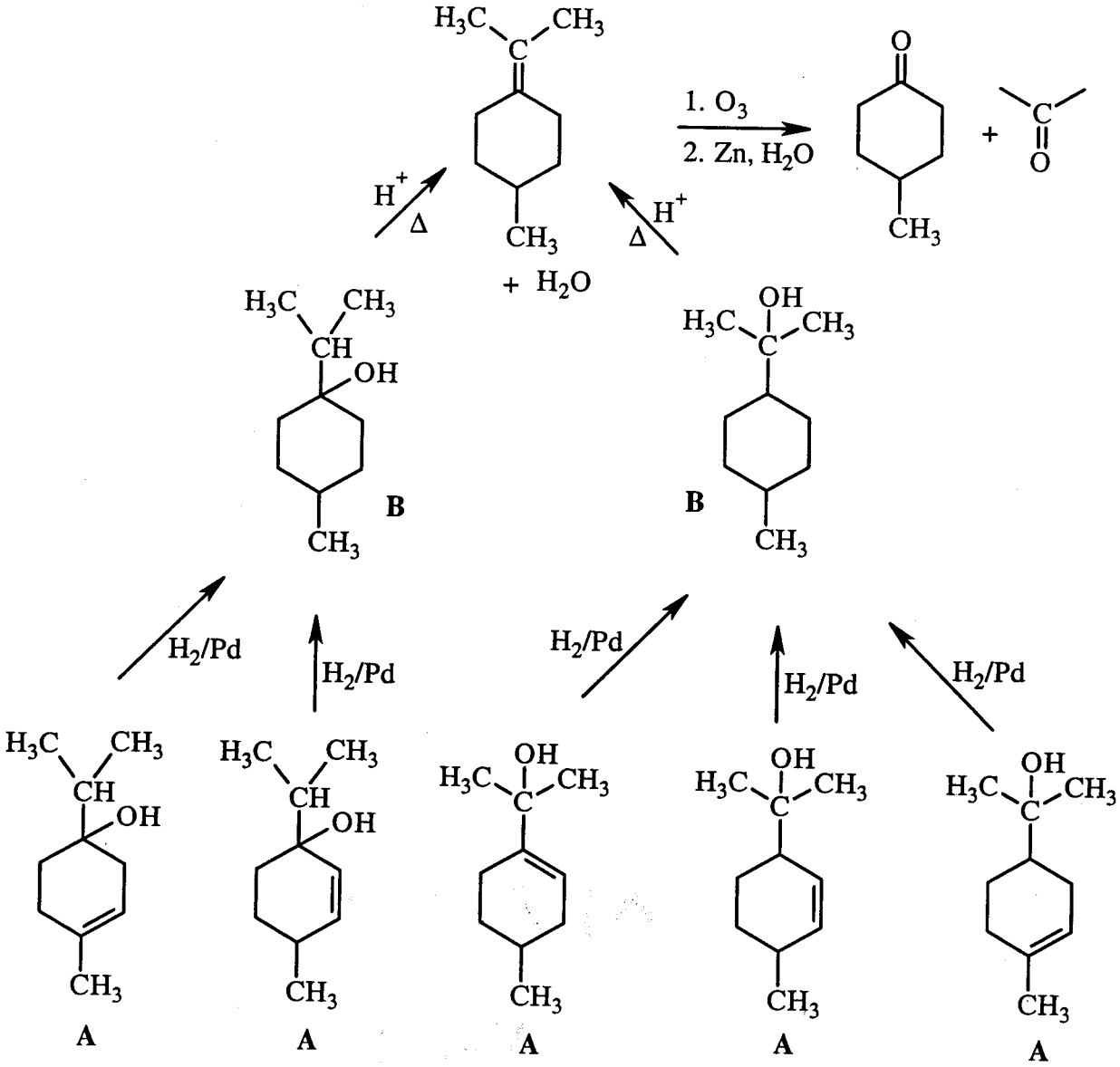
b. The label is lost from sample B when mevalonic pyrophosphate loses CO_2 to form isopentenyl pyrophosphate, so none of the carbons will be labeled in citronellal.



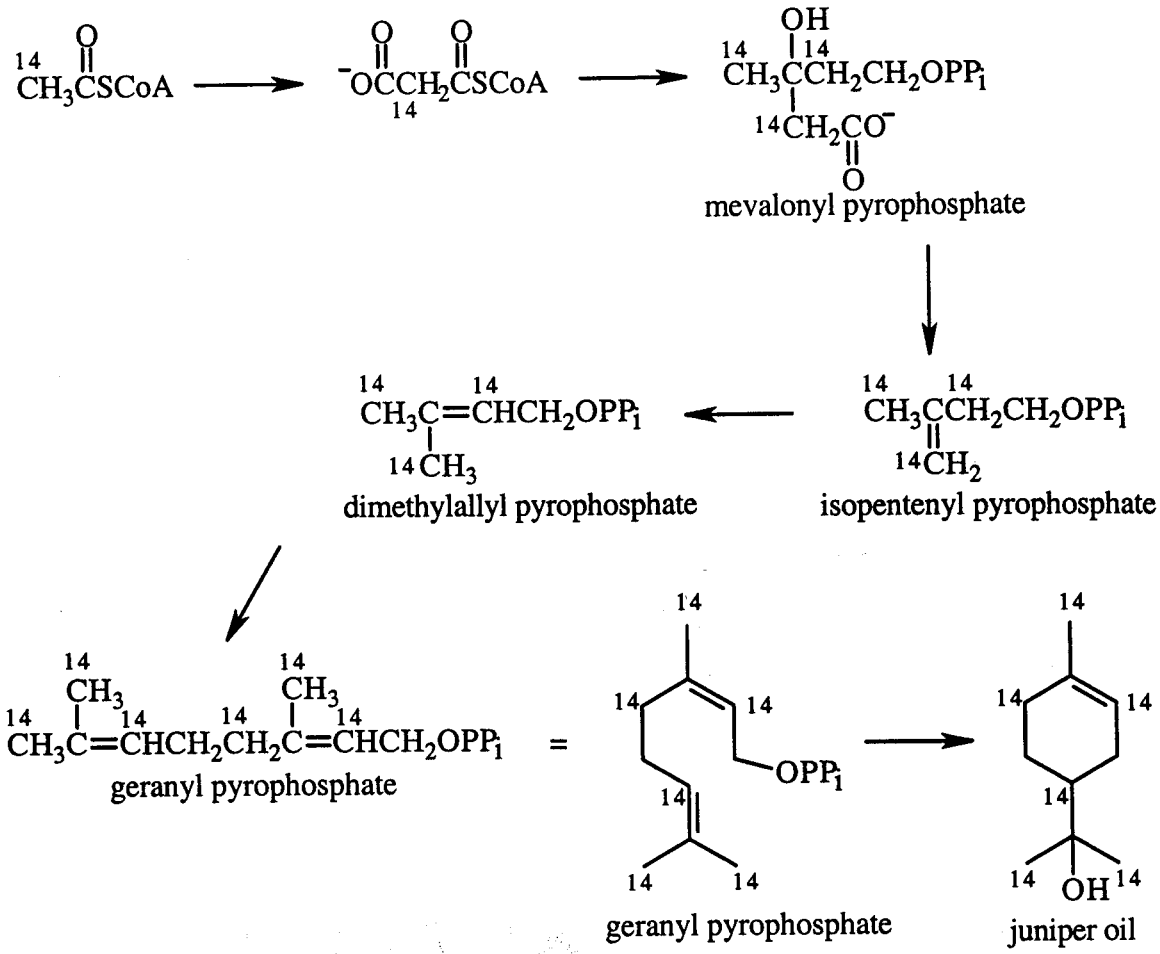
c. Because the methyl groups are equivalent in the carbocation that is formed as an intermedi when isopentenyl pyrophosphate is converted to dimethylallyl pyrophosphate, either of the methyl groups can be labeled in dimethylallyl pyrophosphate. This means that either of the two methyl groups can be labeled in geranyl pyrophosphate and in citronellal.



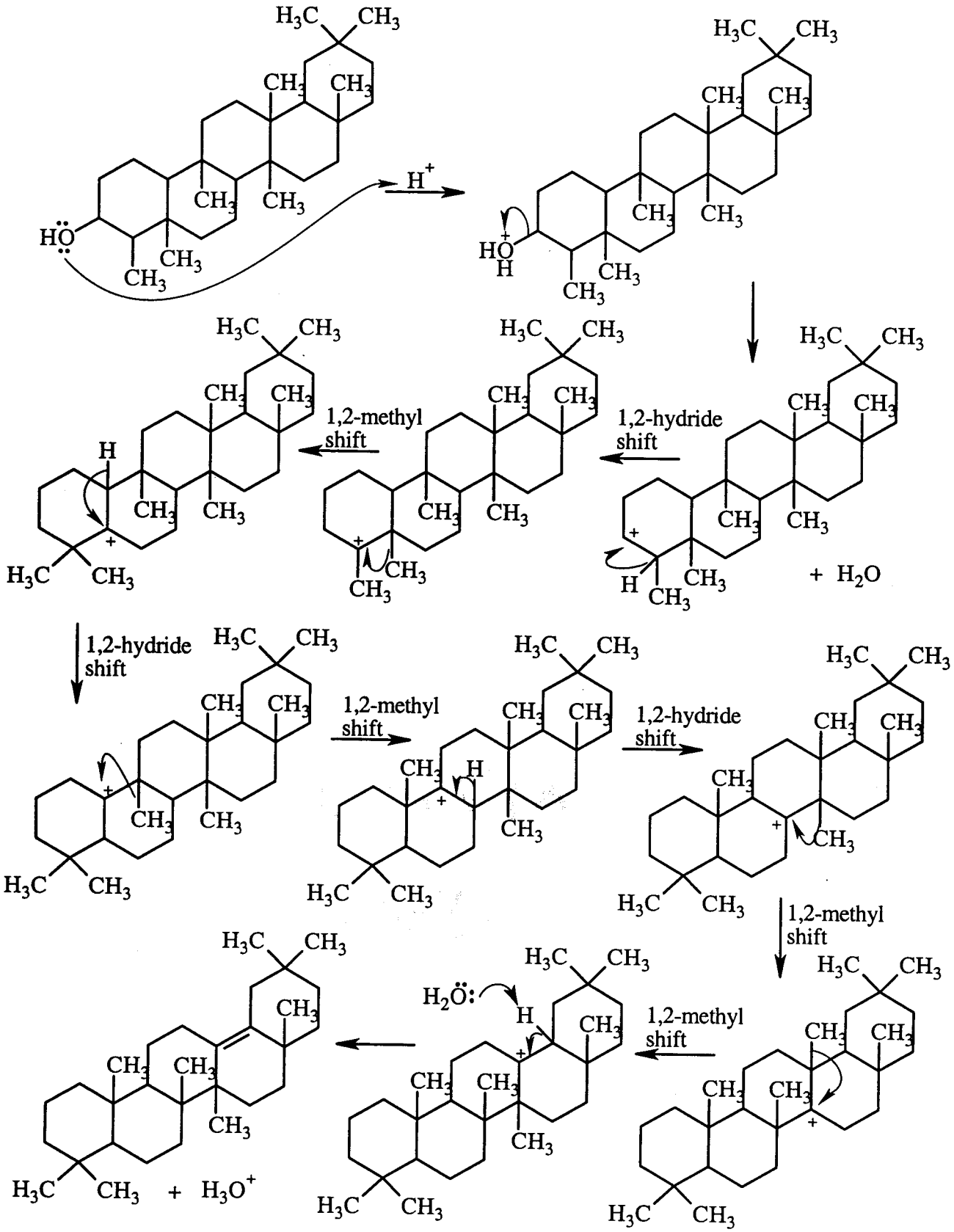
32. There are five possible structures for compound A, and two possible structures for compound B.



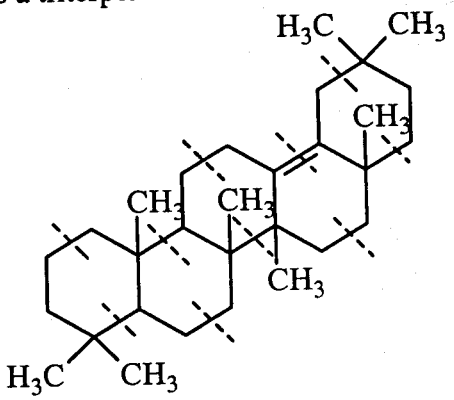
33. Because acetyl-CoA is converted into malonyl-CoA (see Section 26.8), mevalonyl pyrophosphate will contain three labeled carbons, which means that juniper oil will contain six labeled carbons.



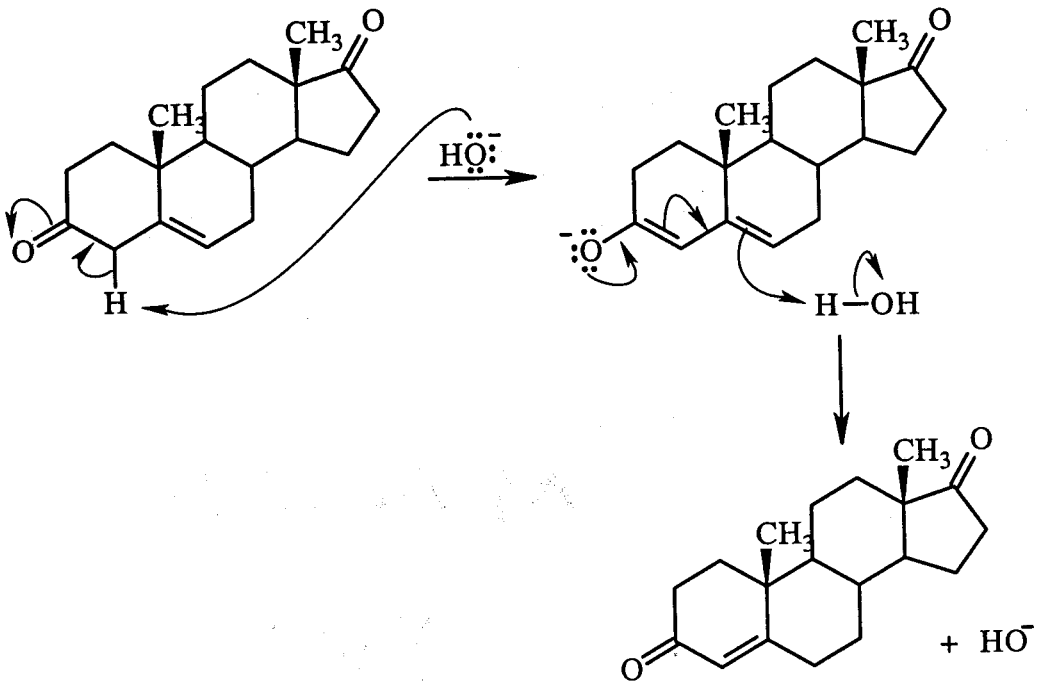
34. a.


1,2-methyl shift
1,2-hydride shift
1,2-hydride shift
1,2-methyl shift
1,2-hydride shift
1,2-methyl shift
+ H2O
+ H3O+

b. It has 30 carbons, so it is a triterpene.



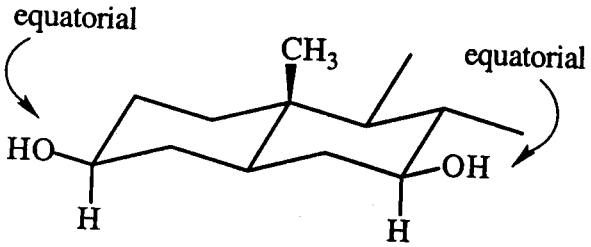
35.



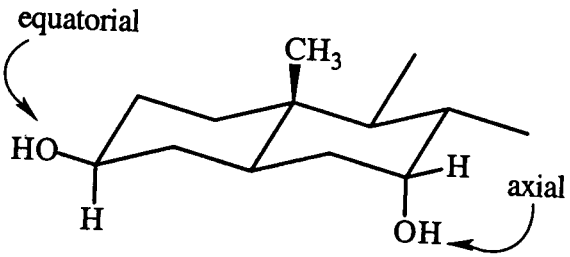
36. The OH groups will react only if they are in equatorial positions, because introduction of bulky axial substituents would decrease the stability of the molecule.

In the case of 5α-cholestane-3β,7β-diol, the two OH groups are on the same side of the ring system as the angular methyl group, which means that they are in equatorial positions. Both OH groups react with ethyl chloroformate.

In the case of 5α-cholestane-3β,7α-diol, only one of the OH groups is on the same side of the ring system as the angular methyl group. The other is on the opposite side of the ring, which means that it is in an axial position. Only the OH group that is in the equatorial position reacts with ethyl chloroformate.

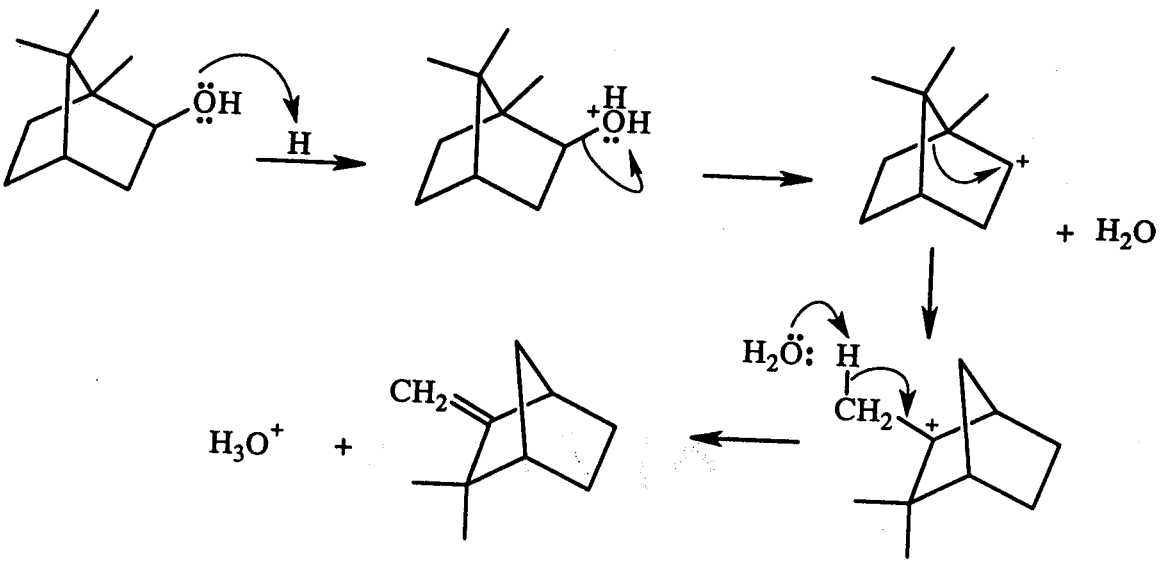


5α-cholestane-3β,7β-diol

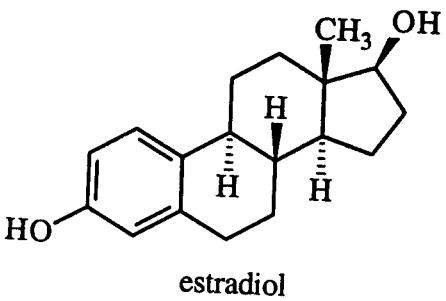


5α-cholestane-3β,7α-diol

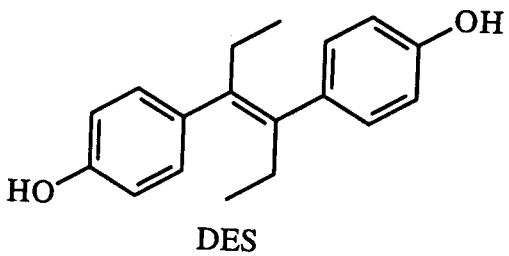
37.



38.



estradiol

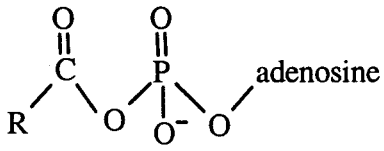


DES

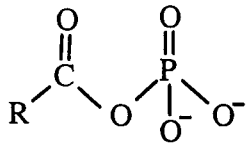
CHAPTER 27
Nucleosides, Nucleotides, and Nucleic Acids

Important Terms

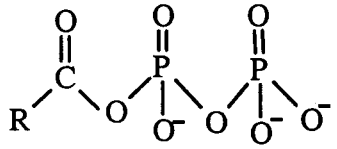
acyl adenylate



acyl phosphate



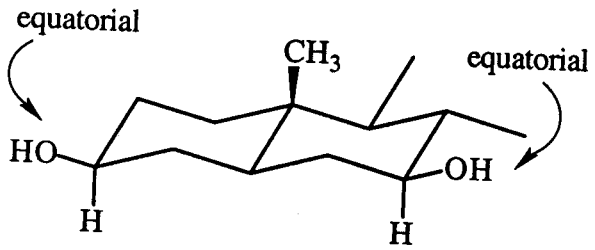
acyl pyrophosphate



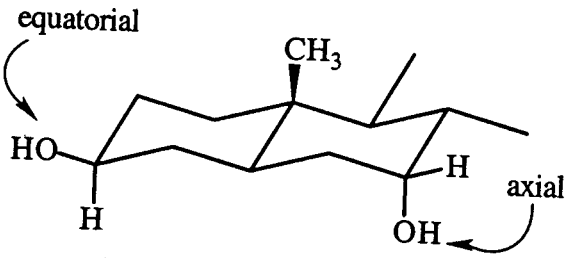
anticodon	the three bases at the bottom of the middle loop in a tRNA.
antigene agent	a polymer designed to bind to DNA at a particular site.
antisense agent	a polymer designed to bind to mRNA at a particular site.
antisense strand (template strand)	the strand in DNA that is read during transcription.
autoradiograph (autorad)	the exposed photographic plate obtained in autoradiography.
autoradiography	a technique used to determine the base sequence of DNA.
base	a heterocyclic compound (a purine or a pyrimidine) in DNA and RNA.
codon	a sequence of three bases of mRNA that specifies the amino acid to be incorporated into a protein.
deamination	a hydrolysis reaction that results in removal of ammonia.
deoxyribonucleic acid (DNA)	a polymer of deoxyribonucleotides.
deoxyribonucleotide	a nucleotide where the sugar component is D-2-deoxyribose.
dideoxy method	a method used to determine the sequence of bases in DNA.

dinucleotide	two nucleotides linked by phosphodiester bonds.
double helix	the term used to describe the secondary structure of DNA.
eukaryotic organism	an organism with cells that contain a nucleus.
exon	a stretch of bases in DNA that are a portion of a gene.
gene	a segment of DNA.
gene therapy	a technique that inserts a synthetic gene into the DNA of an organism defective in that gene.
genetic code	the amino acid specified by each three-base sequence of mRNA.
high-energy bond	a bond that releases a great deal of energy when it is broken.
Hoogsteen base pairing	the pairing between a base in a synthetic strand of DNA with a base pair in double-stranded DNA.
human genome	the total DNA of a human cell.
informational strand (sense strand)	the strand in DNA that is not read during transcription; it has the same sequence of bases as the synthesized mRNA strand (with Us in place of Ts).
in-line displacement mechanism	nucleophilic attack on a phosphorus concerted with breaking a phosphoanhydride bond.
intron	a stretch of bases in DNA that contain no genetic information.
major groove	the wider and deeper of the two alternating grooves in DNA.
minor groove	the narrower and more shallow of the two alternating grooves in DNA.
nucleic acid	the two kinds of nucleic acids are DNA and RNA.
nucleoside	a heterocyclic base (purine or pyrimidine) bonded to the anomeric carbon of a sugar (D-ribose or D-2-deoxyribose).
nucleotide	a nucleoside with one of its OH groups bonded to phosphoric acid in an ester linkage.
oligonucleotide	three to ten nucleotides linked by phosphodiester bonds.
phosphoanhydride bond	the bond holding two phosphoric acid molecules together.
phosphoryl transfer reaction	the transfer of a phosphate group from one compound to another.
polynucleotide	many nucleotides linked by phosphodiester bonds.
primary structure	the sequence of bases in the nucleic acid.

In the case of 5α-cholestane-3β,7α-diol, only one of the OH groups is on the same side of the ring system as the angular methyl group. The other is on the opposite side of the ring, which means that it is in an axial position. Only the OH group that is in the equatorial position reacts with ethyl chloroformate.

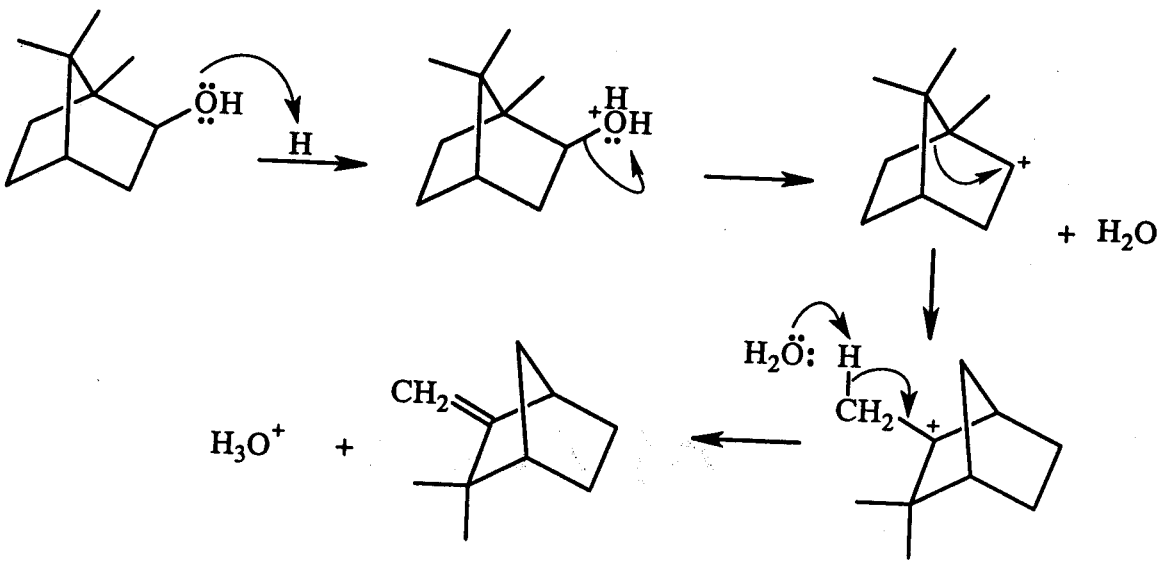


5α-cholestane-3β,7β-diol

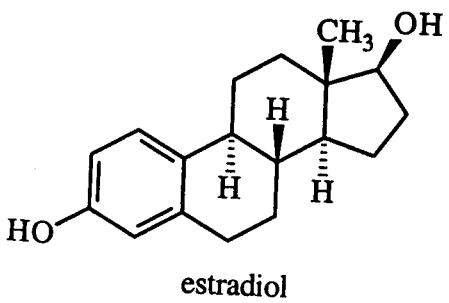


5α-cholestane-3β,7α-diol

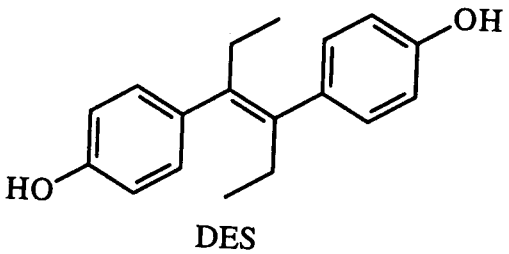
37.



38.



estradiol

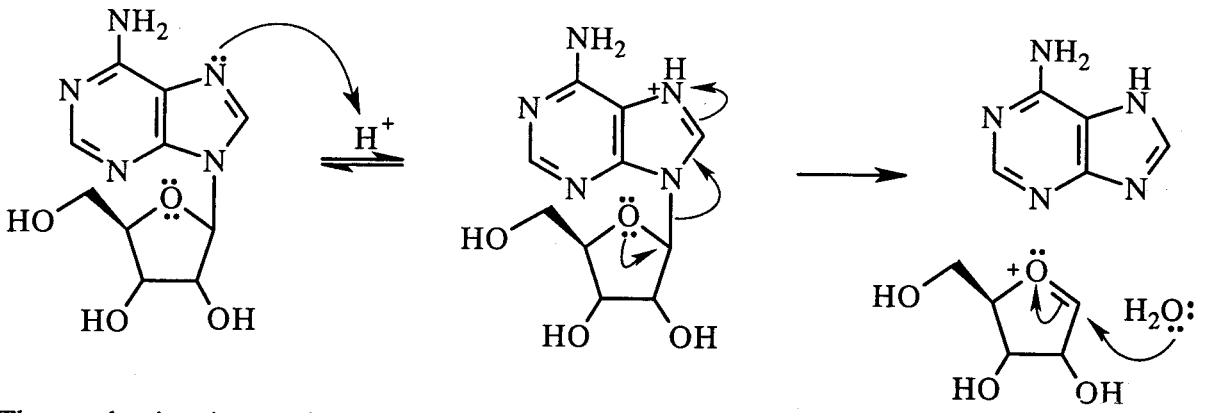


DES

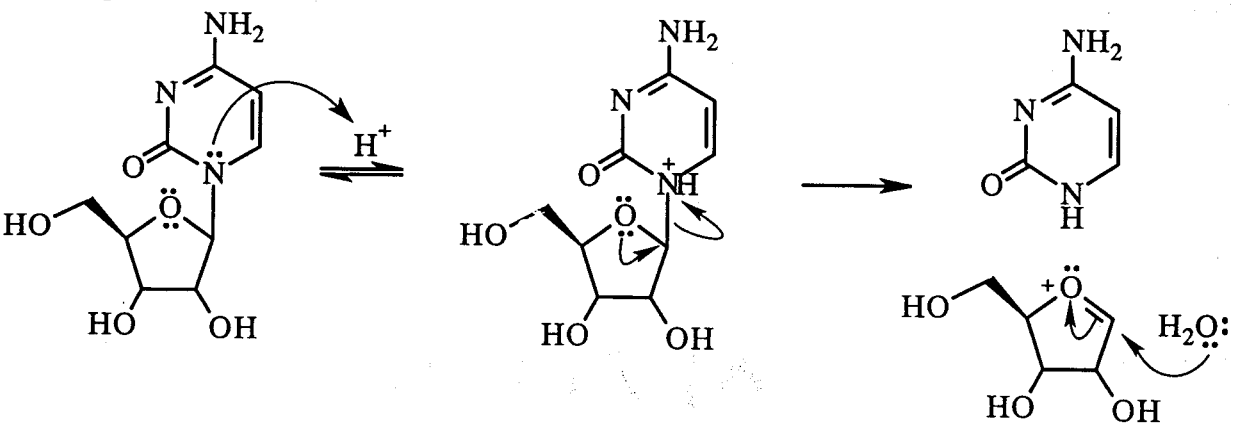
prokaryotic organism	a unicellular organism without a nucleus.
promoter site	a short sequence of bases at the beginning of a gene.
rational drug design	designing drugs with a particular structure to achieve a specific purpose.
replication	the synthesis of identical copies of DNA.
replication fork	the position on DNA where replication begins.
restriction endonuclease	an enzyme that cleaves DNA at a specific base sequence.
restriction fragment	a fragment that is formed when DNA is cleaved by a restriction endonuclease.
retrovirus	a virus whose genetic information is stored in its RNA.
ribonucleic acid (RNA)	a polymer of ribonucleotides.
ribonucleotide	a nucleotide where the sugar component is D-ribose.
ribosome	a particle composed of about 40% protein and 60% RNA on which protein biosynthesis takes place.
ribozyme	an RNA molecule that acts as a catalyst.
RNA splicing	the step in RNA processing that cuts out nonsense bases and splices informational pieces together.
sedimentation constant	designates where a species sediments in an ultracentrifuge.
semiconservative replication	the mode of replication that results in a daughter molecule of DNA having one of the original DNA strands plus a newly synthesized strand.
sense strand (informational strand)	the strand in DNA that is not read during transcription; it has the same sequence of bases as the synthesized mRNA strand (with Us in place of Ts).
site-specific recognition	recognition by a molecule of a specific site on another molecule.
stacking interactions	van der Waals interactions between the mutually induced dipoles of adjacent pairs of bases in DNA.
stop codon	a codon that says "stop protein synthesis here."
template strand	the strand in DNA that is read during transcription.
transcription	the synthesis of mRNA from a DNA blueprint.
translation	the synthesis of a protein from a mRNA blueprint.

Solutions to Problems

1. The ring is protonated at its most basic position. In the case of a purine, this is the 7-position. In the next step, the bond between the heterocyclic base and the sugar breaks, with the anomeric carbocation being stabilized by the ring oxygen's nonbonding electrons.

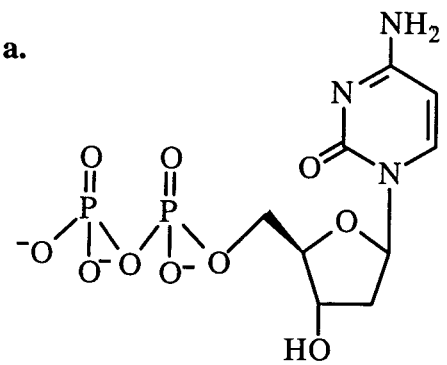


The mechanism is exactly the same for pyrimidines except that the initial protonation takes place at the 1-position.



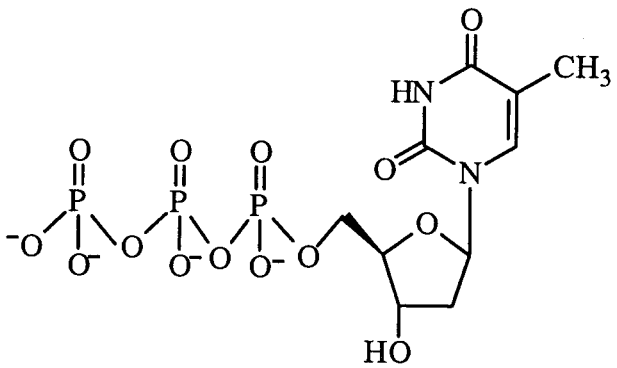
2.

a.



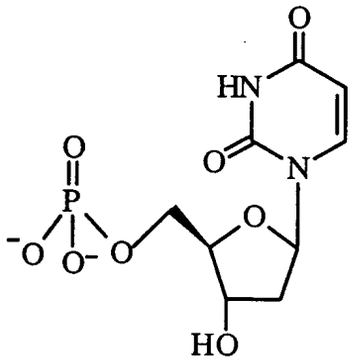
dCDP

b.



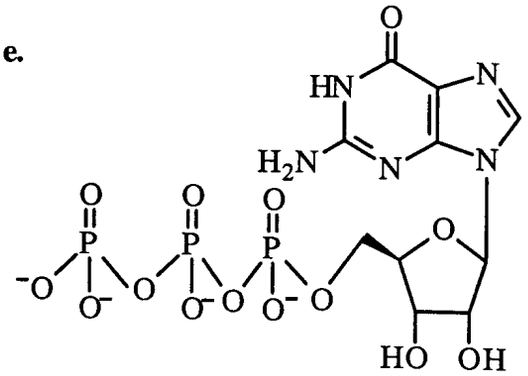
dTTP

c.



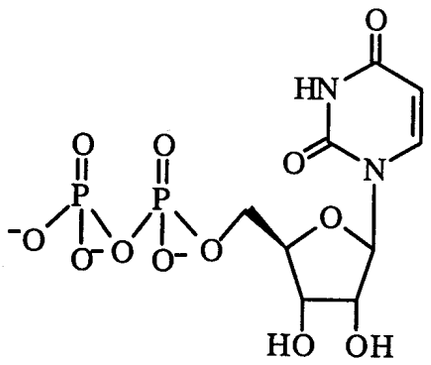
dUMP

e.



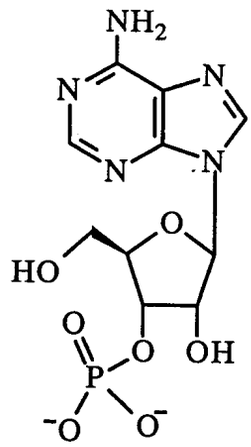
guanosine 5'-triphosphate
GTP

d.



UDP

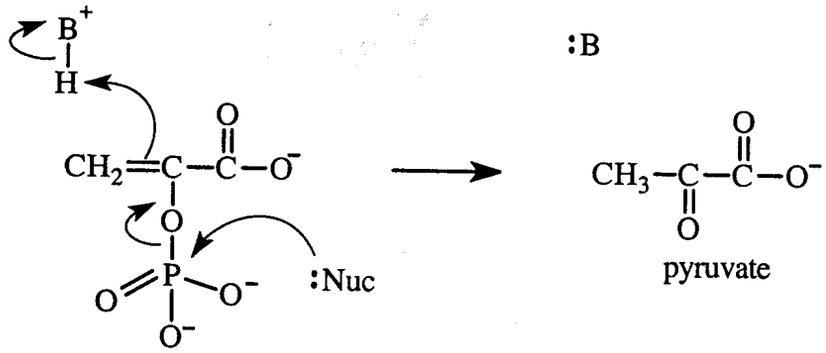
f.



adenosine 3'-monophosphate

3. Solved in the text.

4. Pyruvate is a good leaving group because the electrons left behind when the P—O bond breaks can be delocalized, resulting in the formation of a relatively stable keto group.



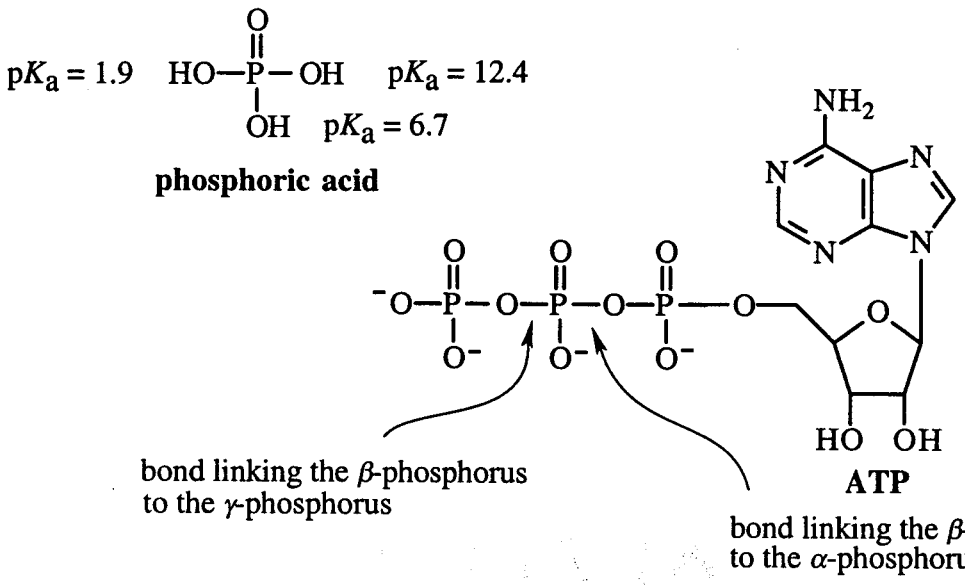
5. The $\Delta G°$ for formation of ATP is + 7.3 kcal/mol. This means that for a compound to drive the formation of ATP, it must hydrolyze with a $\Delta G°$ that is more negative than – 7.3 kcal/mol. Phosphocreatine is the only one of the four compounds that hydrolyzes with sufficient energy.

6. Phosphoric acid has three pK_a's: the first OH group to lose a proton has a pK_a of 1.9, the second OH group has a pK_a of 6.7, and the third OH group a pK_a of 12.4.

When the bond linking the β-phosphorus to the α-phosphorus breaks, the phosphorus leaving group attains its second negative charge which means that the pK_a of the conjugate acid of the leaving group is ~ 7.0.

When the bond linking the β-phosphorus to the γ-phosphorus breaks, the phosphorus leaving group attains its third negative charge, which means that the pK_a of the conjugate acid of the leaving group is ~ 12.4.

Consequently, the bond to the γ-phosphorus never breaks because the leaving group is a much stronger base than the leaving group that leaves when the bond to the α-phosphorus breaks.



7. **a.** Solved in the text.

b. Because pH 7.3 is much more basic than the pK_a values of the first two ionizations of ADP, these two groups will be in their basic forms at that pH, giving ADP two negative charges. We can determine the fraction of the group with pK_a of 6.8 that will be in its basic form at pH 7.3 using the method shown in part **a**.

$$\frac{K_a}{K_a + [H^+]} = \frac{1.6 \times 10^{-7}}{1.6 \times 10^{-7} + 5.0 \times 10^{-8}}$$

$$= \frac{1.6 \times 10^{-7}}{1.6 \times 10^{-7} + 0.5 \times 10^{-7}} = 0.8$$

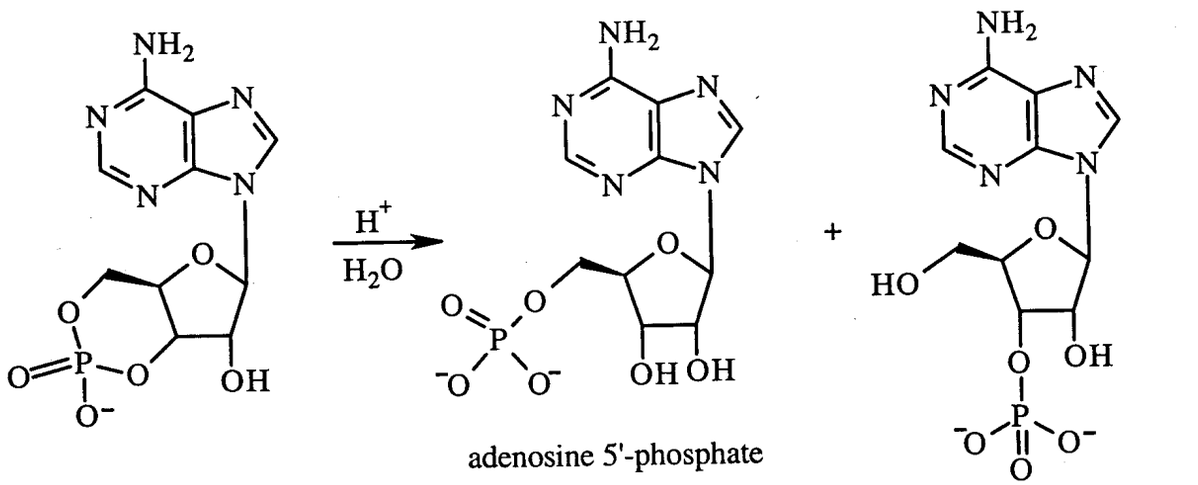
total negative charge on ADP = 2.0 + 0.8 = 2.8

c. At pH 7.3 the OH group with a pK_a of 1.9 will account for one negative charge and the OH group with a pK_a of 12.4 will have no negative charge. We need to calculate the fraction of the group with a pK_a value of 6.7 that will be negatively charged at pH 7.3.

$$\frac{K_a}{K_a + [H^+]} = \frac{2.0 \times 10^{-7}}{2.0 \times 10^{-7} + 0.5. \times 10^{-7}} = 0.8$$

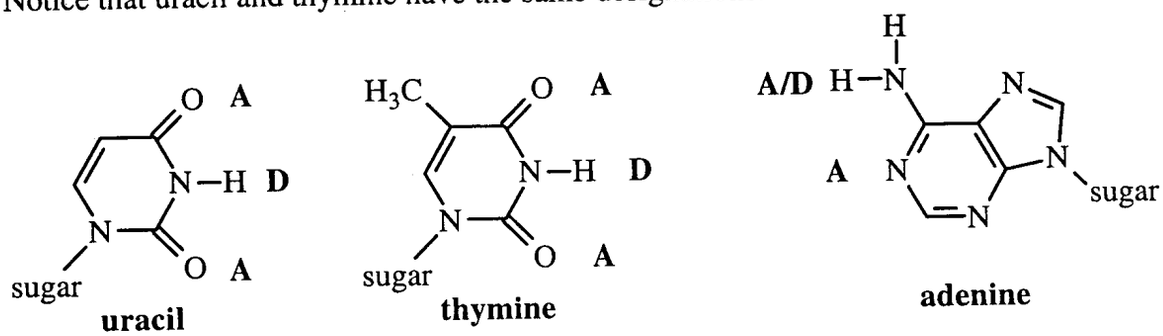
total negative charge on phosphate = 1.0 + 0.8 = 1.8

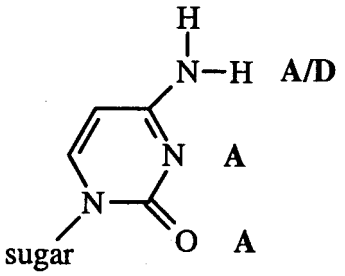
8. The hydrolysis of cyclic AMP forms adenosine 5'-phosphate and adenosine 3'-phosphate.



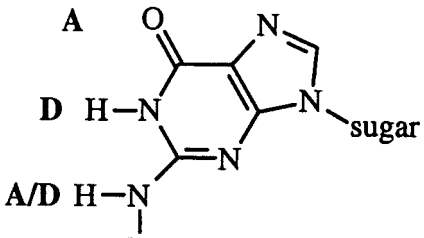
9. The NH_2 groups could serve either as hydrogen bond acceptors, using the nonbonding electron on nitrogen, or as hydrogen bond donors, using the hydrogen bonded to the nitrogen.

The **A**, **D**, and **A/D** designations show that the maximum number of hydrogen bonds that can form are two between thymine and adenine and three between cytosine and guanine. Notice that uracil and thymine have the same designations.





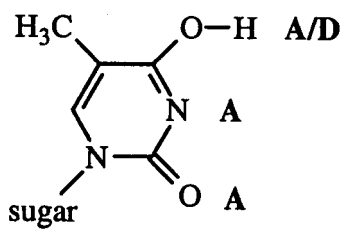
cytosine



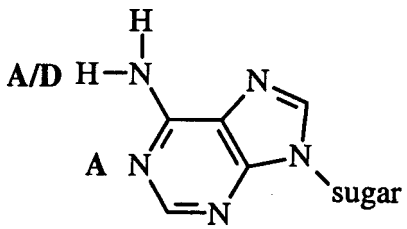
guanine

10. If the bases existed in the enol form, the OH groups and NH_2 groups could act either as hydrogen bond acceptors or as hydrogen bond donors.

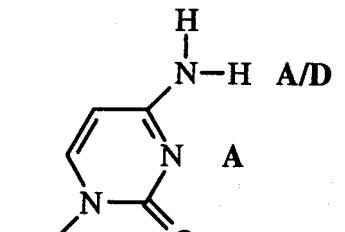
The maximum number of hydrogen bonds that could form is one between thymine and adenine and two between cytosine and guanine.



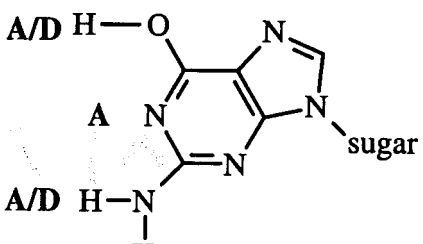
thymine



adenine

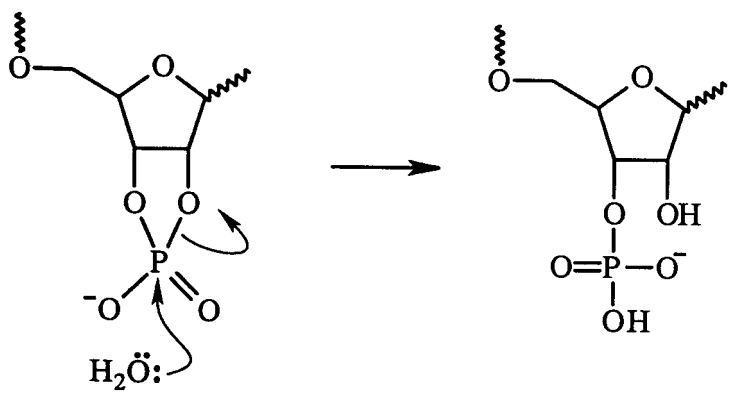


cytosine

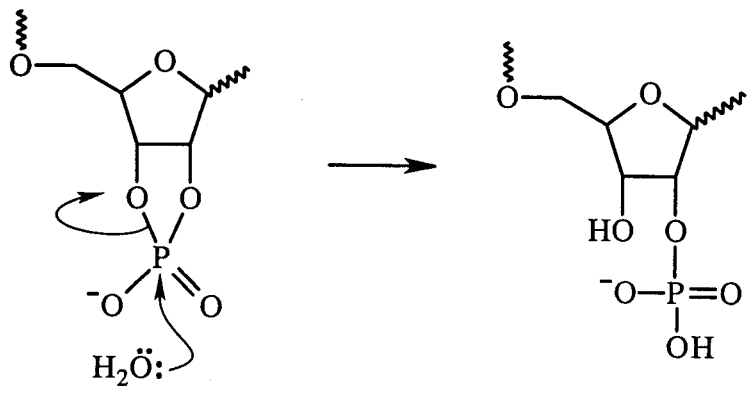


guanine

11.



or



12.

a. 3'—C—C—T—G—T—T—A—G—A—C—G— 5'

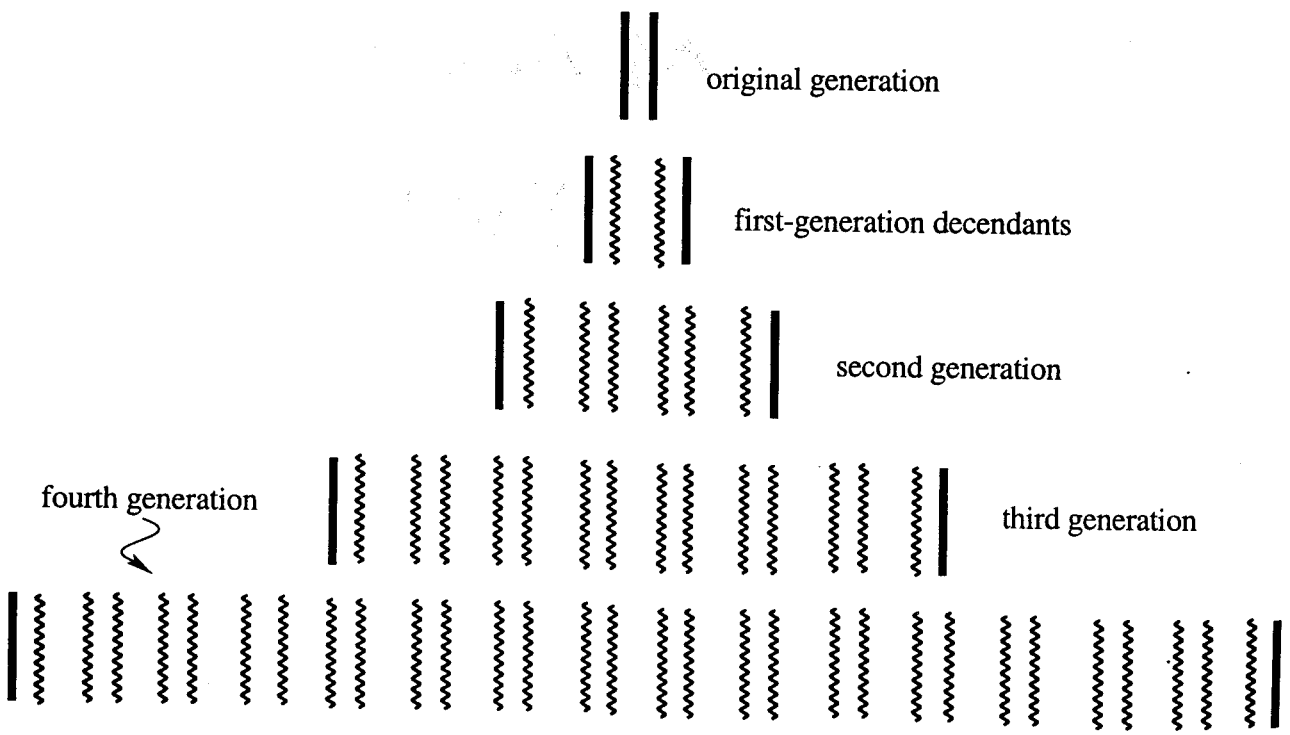
b. guanine

13. **a.** Eleven base pairs per turn: (11 x 2.3 Å = 25 Å).

b. Ten base pairs per turn: (10 x 3.4 Å = 34 Å).

c. Twelve base pairs per turn: (12 x 3.8 Å = 46 Å).

14.



15. The rise per turn in B-DNA (the form found in living organisms) is 34 Å, and there are 10 base pairs per turn:

$$3{,}100{,}000{,}000 \times 3.4\ Å = 3.1 \times 10^9 \times 3.4\ Å = 10^{10}\ Å$$

16. It requires energy to break the hydrogen bonds that hold the two chains together, so an enormous amount of energy would be required to unravel the chain completely. However, as the new nucleotides that are incorporated into the growing chain form hydrogen bonds with the parent chain, energy is released, and this energy can be used to unwind the next part of the double helix.

17. Thymine and uracil differ only in that thymine has a methyl substituent that uracil does not have. (Thymine is 5-methyluracil.) Because they both have the same groups in the same positions that can participate in hydrogen bonding, they will both call for the incorporation of the same purine. Because thymine and uracil form one hydrogen bond with guanine and two with adenine, they will incorporate adenine in order to maximize hydrogen bonding.

18. Because methionine is known to be the first base incorporated into the heptapeptide, the mRNA sequence is read beginning at AUG, since that is the only codon that codes for methionine.

Met-Asp-Pro-Val-Ile-Lys-His

19. Met-Asp-Pro-Leu-Leu-Asn

20. It does not cause protein synthesis to stop, because the sequence UAA does not occur within a triplet. The reading frame causes the triplets to be AUU and AAA.

21. The sequence of bases in the template strand of DNA specify the sequence of bases in mRNA, so the bases in the template strand and the bases in mRNA are complementary. Therefore, the sequence of bases in the sense strand of DNA are identical to the sequence of bases in mRNA, except wherever there is a U in mRNA, there is a T in the sense strand of DNA.

5' —— G-C-A-T-G-G-A-C-C-C-C-G-T-T-A-T-T-A-A-A-C-A-C —— 3'

22.

	Met	Asp	Pro	Val	Ile	Lys	His
codons	AUG	GAU	CCU	GUU	AUU	AAA	CAU
		GAC	CCC	GUC	AUC	AAG	CAC
			CCA	GUA	AUA		
			CCG	GUG			

anticodons

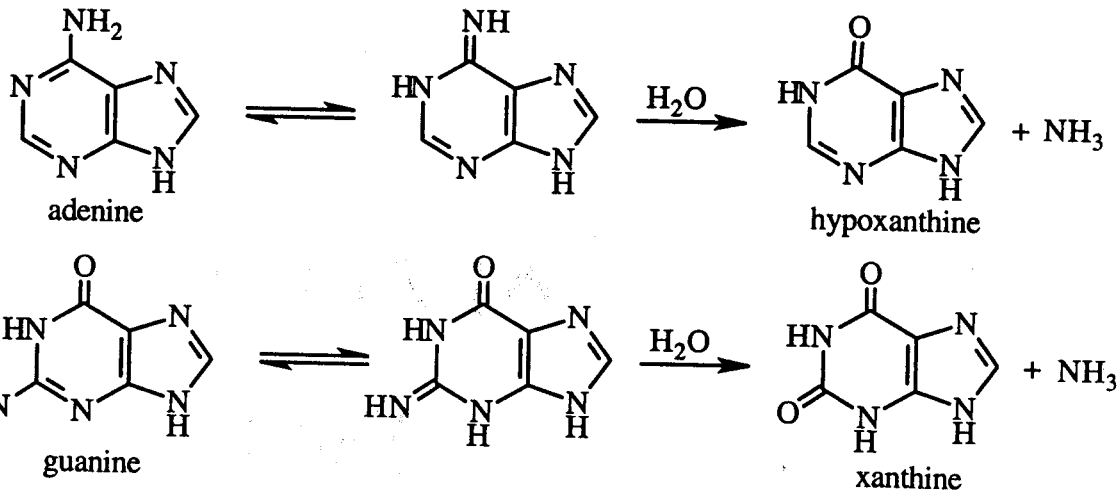
Note that the anticodons are stated in the 5' → 3' direction. For example, the anticodon of AUG is stated as CAU (not UAC).

codon 5' AUG 3'

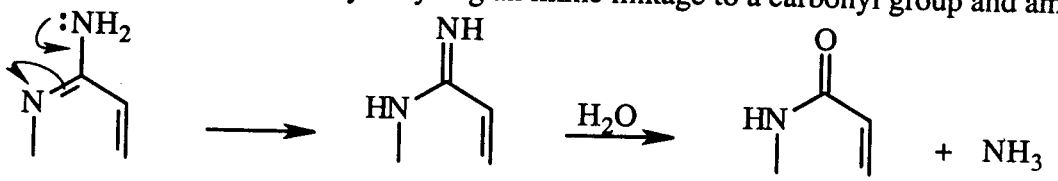
anticodon 3' UAC 5'

CAU	AUC	AGG	AAC	AAU	UUU	AUG
	GUC	GGG	GAC	GAU	CUU	GUG
		UGG	UAC	UAU		
		CGG	CAC			

23.



24. Thymine does not have an amino substituent on the ring, which means that it cannot form an imine. Deamination involves hydrolyzing an imine linkage to a carbonyl group and ammonia.



25. **a** is the only sequence that has a chance of being recognized by a restriction endonuclease because it is the only one that has the same sequence of bases in the 5' → 3' direction that the complementary strand has in the 5' → 3' direction.

ACGCGT

ACGCGT

26. All the fragments will end in "G".

^{32}P—TCCGAGGTCACTAGG

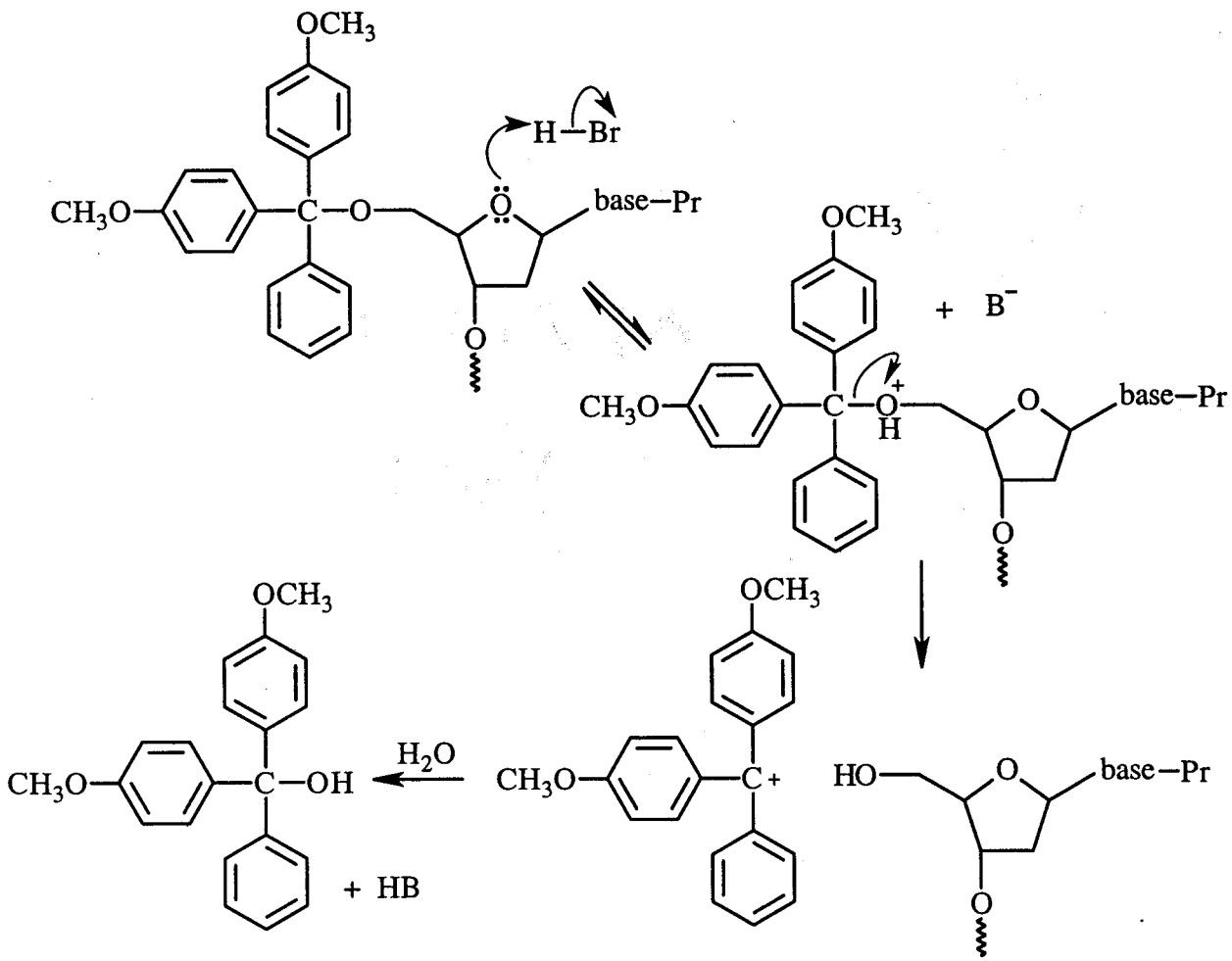
^{32}P—TCCGAGGTCACTAG

^{32}P—TCCGAGG

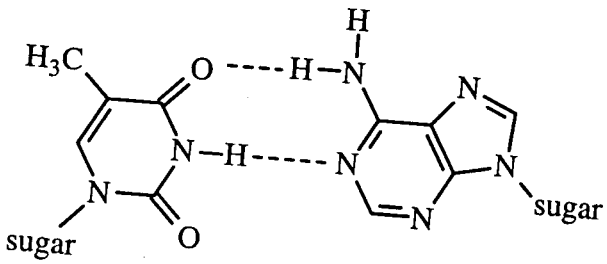
^{32}P—TCCGAG

^{32}P—TCCG

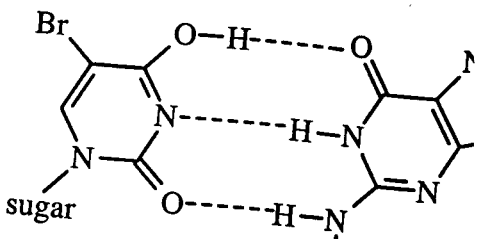
27.



28. 5-Bromouracil is incorporated into DNA in place of thymine because of their similar si
Thymine pairs with adenine via two hydrogen bonds. 5-Bromouracil exists primarily in
form. The enol can form only one hydrogen bond with adenine, but it can form three hy
bonds with guanine. Therefore, 5-bromouracil pairs with guanine. Because 5-bromoura
causes guanine to be incorporated instead of adenine into newly synthesized DNA stran
causes mutations.



thymine **adenine**



5-bromouracil **guanine**

29. **a.** guanosine 3'-monophosphate

b. cytidine 5'-diphosphate

c. 2'-deoxyadenosine 5'-monophosphate

d. 2'-deoxythymidine

30. Lys-Val-Gly-Tyr-Pro-Gly-Met-Val-Val

31. The third base in each codon has some variability.

mRNA 5'-GG(UCA or G)UC(UCA or G)CG(UCA or G)GU(UCA or G)CA(U or C)GA(A or G)-3
or AG(U or C) AG(A or G)

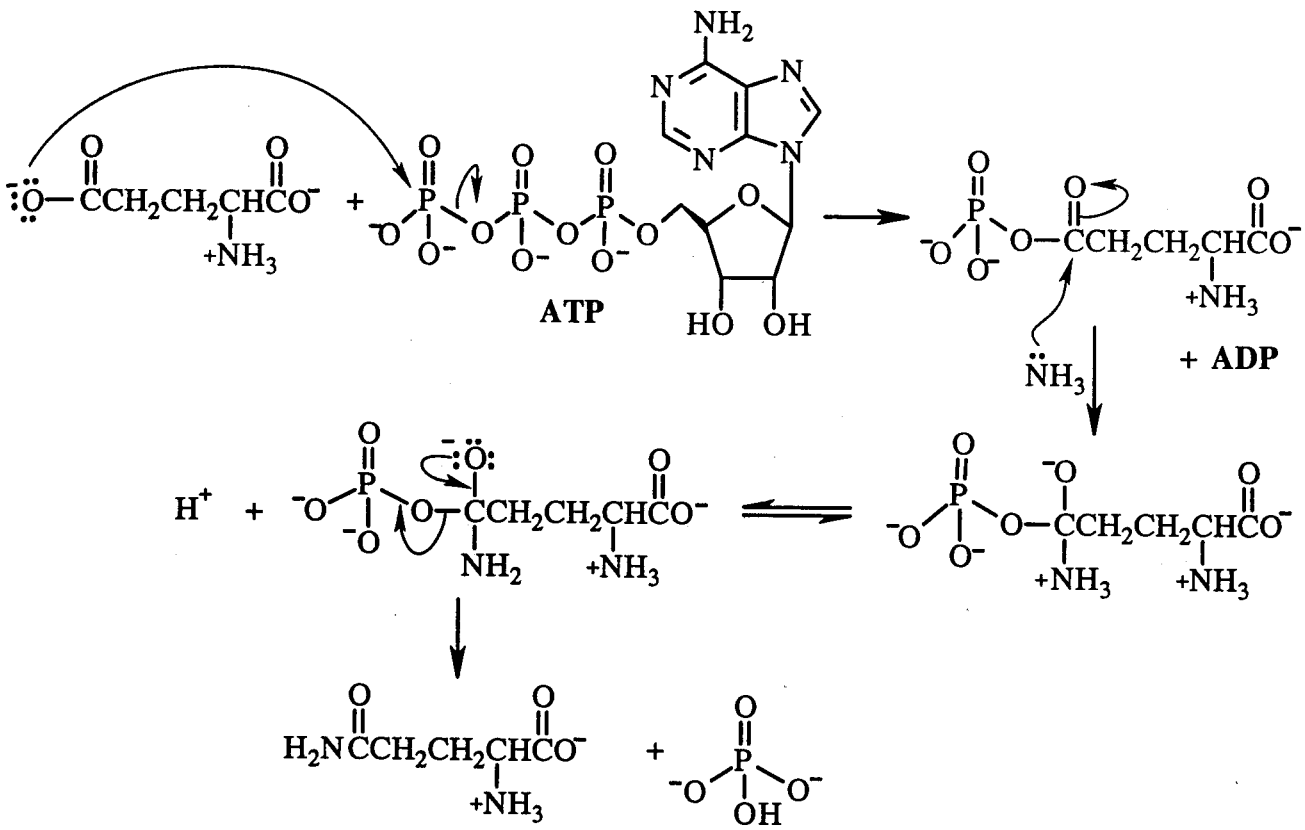
DNA

template 3'-CC(AGT or C)AG(AGT or C)GC(AGT or C)CA(AGT or C)GT(A or G)CT(T or C)-5'
or TC(A or G) TC(T or C)

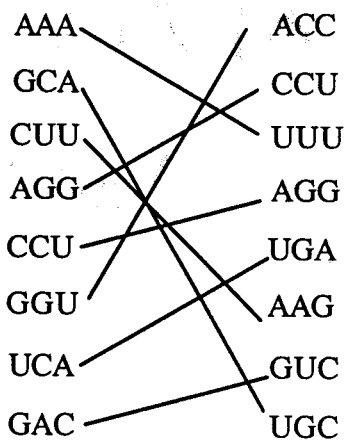
sense 5'-GG(TCA or G)TC(TCA or G)CG(TCA or G)GT(TCA or G)CA(T or C)GA(A or G)-3'
or AG(T or C) AG(A or G)

Notice that Ser and Arg are two of three amino acids that can be specified by six different codons.

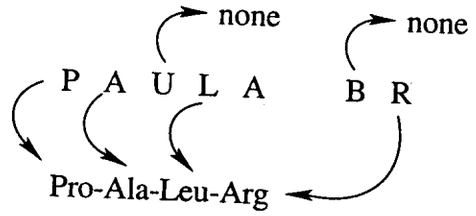
32.


ATP
+ ADP

33.


AAA
GCA
CUU
AGG
CCU
GGU
UCA
GAC
ACC
CCU
UUU
AGG
UGA
AAG
GUC
UGC

34.



mRNA CC(UCA or G)GC(UCA or G)CU(UCA or G)CG(UCA or G)
UU(A or G) AG(A or G)

DNA (sense strand) CC(TCA or G)GC(TCA or G)CT(TCA or G)CG(TCA or G)
TT(A or G) AG(A or G)

Note that because mRNA is complementary to the template strand of DNA, which is complementary to the sense strand, the sense strand of DNA and mRNA have the same sequence of bases (except DNA has a T where RNA has a U).

Also note that Leu and Arg are specified by six codons.

35. **a.** CC and GG **c.** CA and TG

CA and TG are formed in equal amounts, since A pairs with T and C pairs with G. (Remember that the dinucleotides are written in the 5' → 3' direction.)

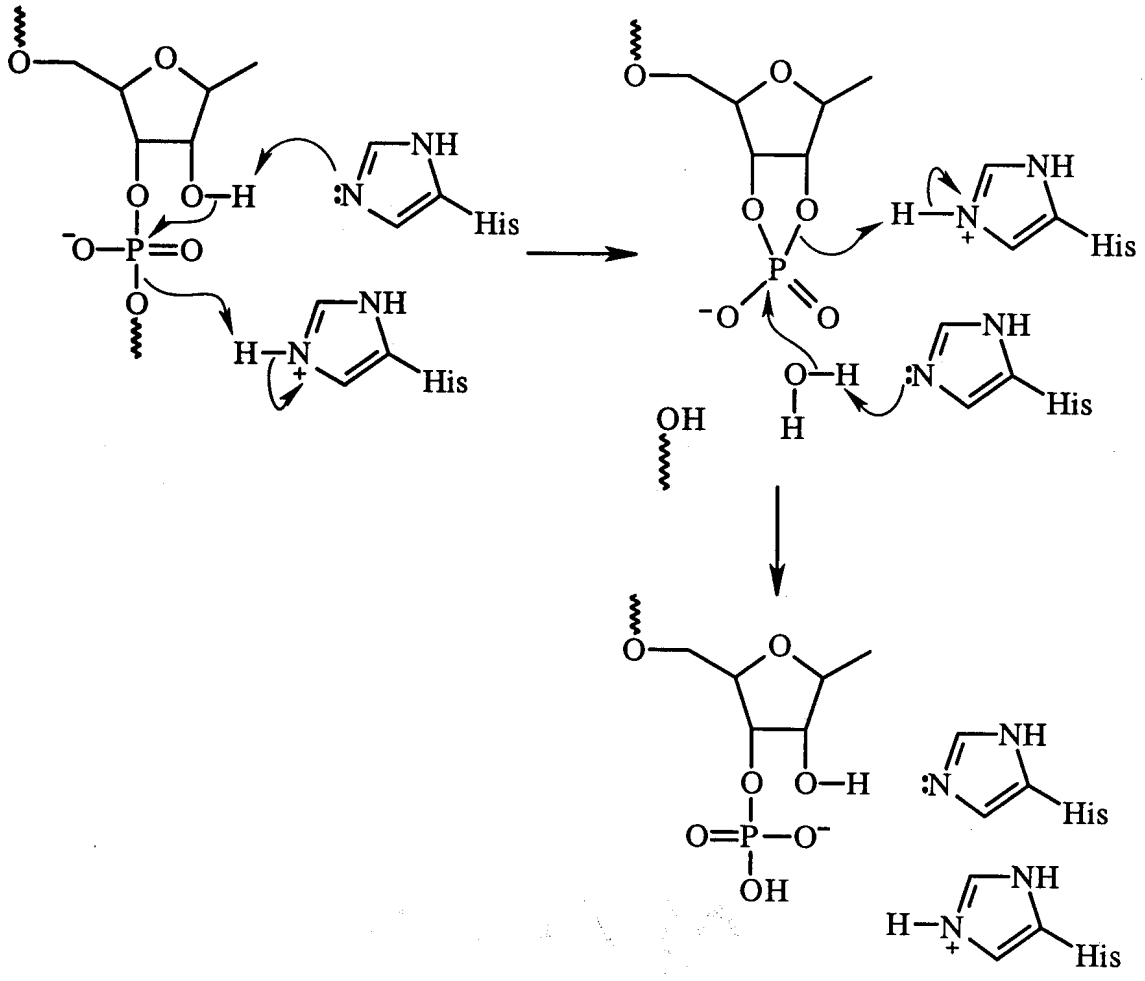
5' CA 3'
3' GT 5'

36. The number of different possible codons using four nucleotides is $(4)^n$ where n is the number of letters (nucleotides) in the code.

for a two-letter code: $(4)^2 = 16$
for a three-letter code: $(4)^3 = 64$
for a four-letter code: $(4)^4 = 256$

Since there are 20 amino acids that must be specified, a two-letter code would not provide an adequate number of codons.
A three-letter code provides enough codes for all the amino acids and also provides the necessary stop codons.
A four-letter code provides many more codes than would be needed.

37. In the first step of the reaction, the imidazole ring of one histidine acts as a general-base catalyst, removing a proton from the 2-OH group to make it a better nucleophile. The imidazole ring of the other histidine acts as a general-acid catalyst, protonating the leaving group to make it a weaker base and therefore a better leaving group. In the second step of the reaction the roles of the two imidazole rings are reversed.



38. The normal and mutant peptides would have the following base sequence in their mRNA.

normal: CA(AG) UA(UC) GG(UCAG) AC(UCAG) CG(UCAG) UA(UC) GU(UCAG)

mutant: CA(AG) UC(UCAG) GA(AG) CC(UCGA) GG(UCGA) AC(UCAG)

a. The middle nucleotide (A) in the second triplet was deleted. This means that an A was deleted in the sense strand of DNA or a T was deleted in the template strand of DNA.

b. The mRNA for the mutant peptide has an unused 3'-terminal two-letter code, U(UCGA). The last amino acid in the octapeptide of the normal fragment is leucine, so its last triplet is UU(AG) or CU(UCAG).

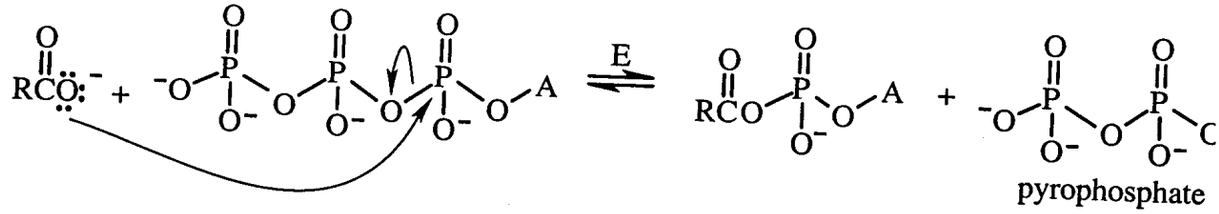
This means that the triplet for the last amino acid in the mutant is U(UCGA)(UC) and that the last amino acid in the mutant is one of the following: Phe, Ser, Tyr, or Cys.

39. Because the compound that will react in the second step with the activated carboxylic acid gr is excluded from the incubation mixture, the reaction between the carboxylate ion and ATP w come to equilibrium.

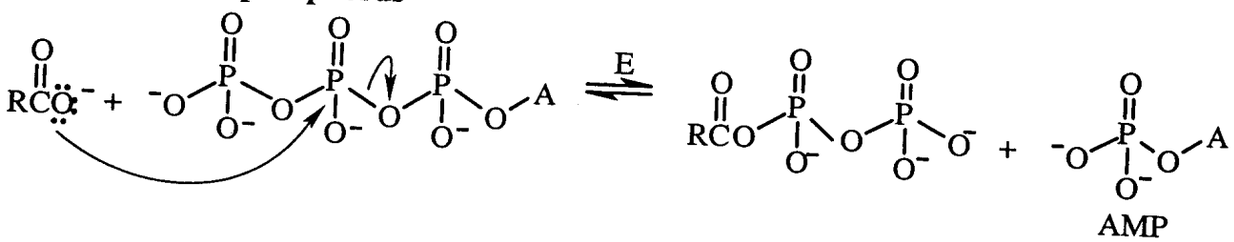
If radioactively labeled pyrophosphate is put into the incubation mixture, ATP will become radioactive if the mechanism involves attack on the α-phosphorus, because ATP is formed fro the reverse reaction between the activated carboxylate ion and pyrophosphate.

ATP will not become radioactive if the mechanism involves attack on the β-phosphorus because ATP is formed from reaction between the activated carboxylate ion and AMP. (In other words, because pyrophosphate is not a product of the reaction, it cannot become incorporated into ATP in the reverse reaction.)

attack on the α-phosphorus



attack on the β-phosphorus



40. If radioactive AMP is added to the reaction mixture, the results will be opposite.
If the mechanism involves attack on the α-phosphorus, ATP will not become radioactive.
If the mechanism involves attack on the β-phosphorus, ATP will become radioactive.

41. If deamination does not occur, the mRNA sequence will be:

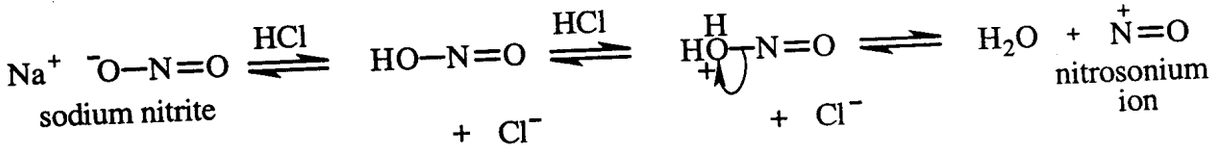
AUG-UCG-CUA-AUC which will code for the following tetrapeptide
Met - Ser - Leu - Ile

Deamination of a cytosine results in a uracil.
If the cytosines are deaminated, the mRNA sequence will be:

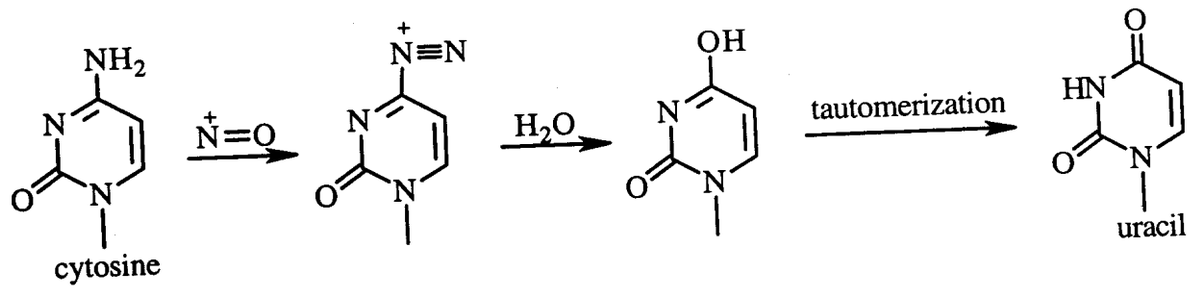
AUG-UUG-UUA-AUU which will code for the following tetrapeptide
Met - Leu - Leu - Ile

The only cytosine that will change the particular amino acid that is incorporated into the peptide is the first one. Therefore, this is the cytosine that could cause the most damage to an organism if it were deaminated.

42. In an acidic environment, nitrite ion is protonated to nitrous acid. We have seen that the nitrosonium ion is formed from nitrous acid (Section 15.11).



The nitrosonium ion reacts with a primary amino group to form a diazonium ion, which can be displaced by water (Section 15.10).



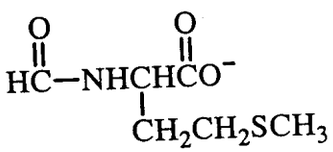
43. The smaller subunit of a prokaryotic ribosome (30S) contains a binding site for the growing peptide chain and a binding site for the next amino acid to be incorporated into the chain.



peptide binding site amino acid binding site

All peptide bonds are formed by the reaction of an amino acid with a peptide, except formation of the first peptide bond, which has to be formed by the reaction of two amino acids. Therefore, in the synthesis of the first peptide bond, one of the amino acids has to be a peptide that will fit into the peptide binding site.

The formyl group of *N*-formylmethionine will provide the peptide group that will be recognized by the peptide binding site, and the second amino acid will be bound in the amino acid binding site.



N-formylmethionine

CHAPTER 28
Synthetic Polymers

Important Terms

addition polymer (chain-growth polymer)	made by adding monomers to the growing end of a chain.
alpha olefin	a monosubstituted olefin.
alternating copolymer	a copolymer in which two monomers alternate.
anionic polymerization	chain-growth polymerization where the initiator is a nucleophile; the propagation site, therefore, is an anion.
aramide	an aromatic polyamide.
atactic polymer	a polymer in which the substituents are randomly oriented on the extended carbon chain.
biodegradable polymer	a polymer that can be broken into small segments by an enzyme-catalyzed reaction.
biopolymer	a polymer that is synthesized in nature.
block copolymer	a copolymer in which there are blocks of each kind of monomer.
cationic polymerization	chain-growth polymerization where the initiator is an electrophile; the propagation site, therefore, is a cation.
chain-growth polymer (addition polymer)	made by adding monomers to the growing end of a chain.
chain transfer	a growing polymer chain reacts with a molecule XY in a manner that allows X to terminate the chain, leaving behind Y· to initiate a new chain.
condensation polymer (step-growth polymer)	made by combining two molecules while removing a small molecule (usually water or an alcohol).
conducting polymer	a polymer that can conduct electricity down its backbone.
copolymer	a polymer formed using two or more different monomers.
cross-linking	connecting polymer chains by intermolecular bond formation.
crystallites	regions of a polymer in which the chains are highly ordered.
elastomer	a polymer that can stretch and then revert back to its original shape.
epoxy resin	formed by mixing a low molecular weight prepolymer with a compound that forms a cross-linked polymer.
graft copolymer	a copolymer that contains branches of a polymer of one monomer grafted onto the backbone of a polymer made from another monomer.

head-to-tail addition	the head of one molecule is added to the tail of another molecule.
homopolymer	a polymer that contains only one kind of monomer.
isotactic polymer	a polymer in which all the substituents are on the same side of the fully extended carbon chain.
living polymer	a nonterminated chain-growth polymer that remains active. Therefore, the polymerization reaction can continue upon addition of more monomer.
materials science	the science of creating new materials to take the place of known materials such as metal, glass, wood, cardboard, and paper.
monomer	a repeating unit in a polymer.
oriented polymer	a polymer obtained by stretching out polymer chains and putting them back together in a parallel fashion.
plasticizer	an organic molecule that dissolves in a polymer and allows the polymer chains to slide by each other.
polyamide	a polymer with many amide groups.
polycarbonate	a step-growth polymer in which the dicarboxylic acid is carbonic acid.
polyester	a polymer with many ester groups.
polymer	a large molecule made by linking monomers together.
polymer chemistry	the field of chemistry that deals with synthetic polymers; part of the larger discipline known as materials science.
polymerization	the process of linking up monomers to form a polymer.
polyurethane	a polymer with many urethane groups.
propagating site	the reactive end of a chain-growth polymer.
radical polymerization	chain-growth polymerization where the initiator is a radical; the propagation site, therefore, is a radical.
random copolymer	a copolymer with a random distribution of monomers.
ring-opening polymerization	a chain-growth polymerization that involves opening the ring of the monomer.
step-growth polymer (condensation polymer)	made by combining two molecules while removing a small molecule (usually water or an alcohol).
syndiotactic polymer	a polymer in which the substituents regularly alternate on both sides of the fully extended carbon chain.
synthetic polymer	a polymer that is not synthesized in nature.

thermoplastic polymer	a polymer that has both ordered crystalline regions and amorphous non-crystalline regions.
thermosetting polymer	cross-linked polymers that, after they are hardened, cannot be re-melted b heating.
urethane	a compound with a carbonyl group that is both an amide and an ester.
vinyl polymer	a polymer in which the monomer is ethylene or a substituted ethylene.
vulcanization	increasing the flexibility of rubber by heating it with sulfur.
Ziegler-Natta catalyst	an aluminum-titanium initiator that controls the stereochemistry of a polymer.

Solutions to Problems

1.

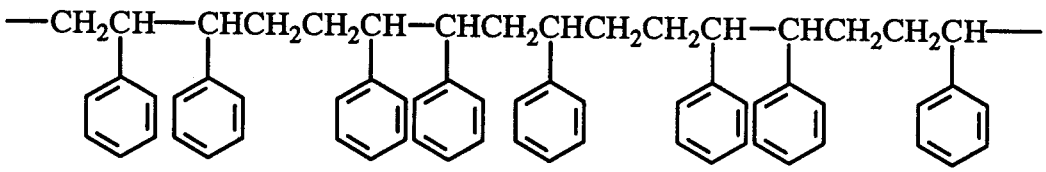
a. $CH_2=CHCl$

b. $CH_2=C(C=O)(OCH_3)CH_3$

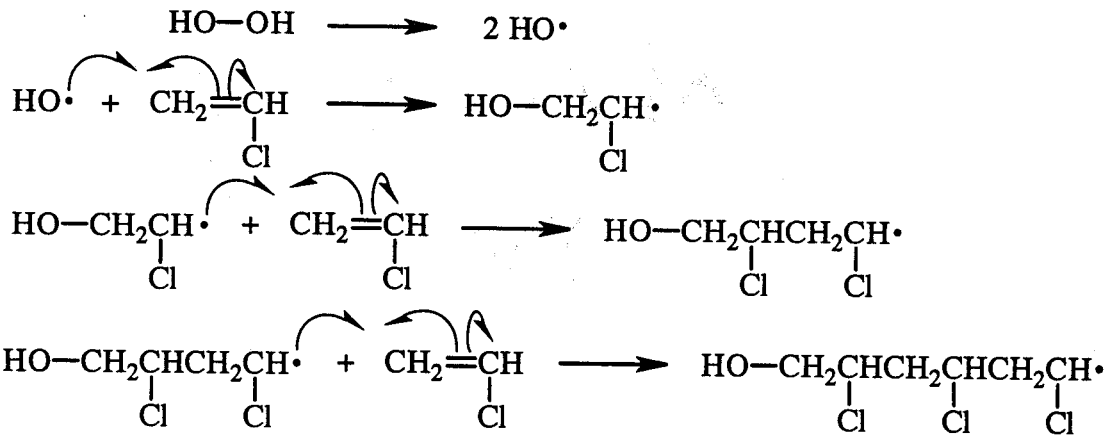
c. $CF_2=CF_2$

2. Poly(vinyl chloride) would be more apt to contain head-to-head linkages because a chloro substituent is less able (compared with a phenyl substituent) to stabilize the growing end of the polymer chain by resonance.

3.

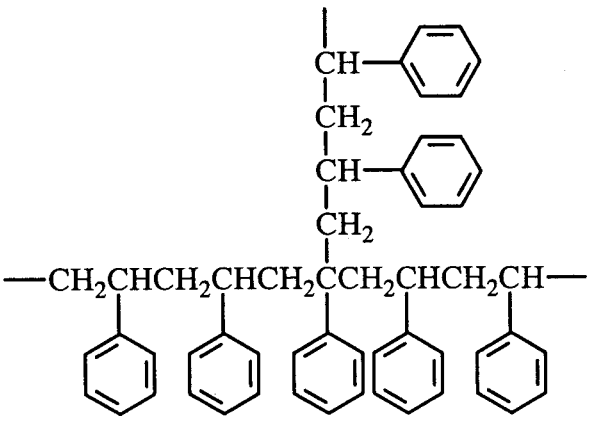


4.



5. Since branching increases the flexibility of the polymer, beach balls are made from more highly branched polyethylene.

6.



7. Decreasing ability to undergo cationic polymerization is in the same order as decreasing stability of the carbocation intermediate. (Electron donation increases the stability of the carbocation.)

a. $CH_2{=}CH$ (OCH$_3$) > $CH_2{=}CH$ (CH$_3$) > $CH_2{=}CH$ (NO_2)

donates electrons by resonance — **withdraws electrons by resonance**

b. $CH_2{=}CHOCCH_3$ (O) > $CH_2{=}CHCH_3$ > $CH_2{=}CHCOCH_3$ (O)

donates electrons by resonance — **withdraws electrons by resonance**

c. $CH_2{=}CCH_3$ > $CH_2{=}CH$

A tertiary benzylic carbocation is more stable than a secondary benzylic carbocation.

8. Decreasing ability to undergo anionic polymerization is in the same order as decreasing stability of the carbanion intermediate. (Electron withdrawal increases the stability of the carbanion.)

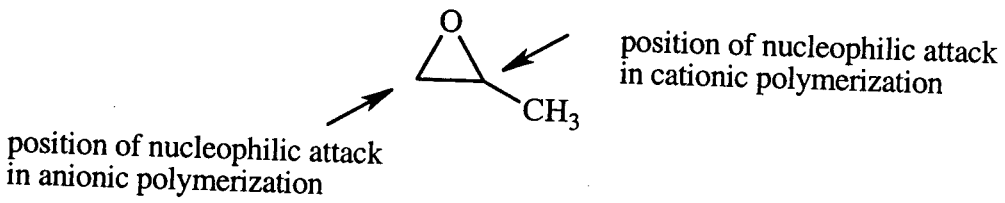
a. $CH_2{=}CH$ (NO_2) > $CH_2{=}CH$ (CH$_3$) > $CH_2{=}CH$ (OCH$_3$)

withdraws electrons by resonance — **donates electrons by resonance**

b. $CH_2{=}CHC{\equiv}N$ > $CH_2{=}CHCl$ > $CH_2{=}CHCH_3$

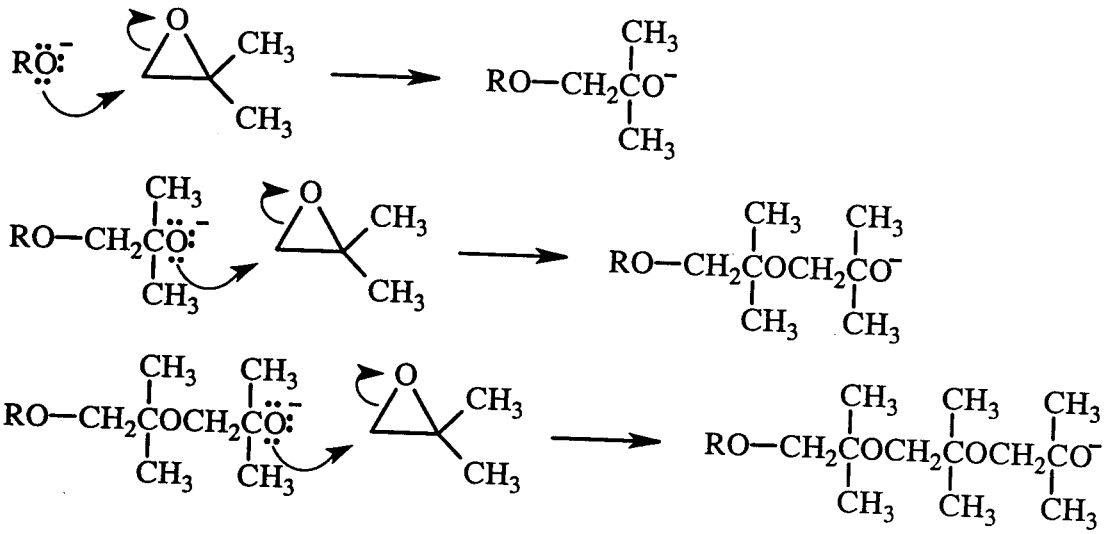
withdraws electrons by resonance

9. In anionic polymerization, nucleophilic attack occurs at the less substituted carbon because it is the less sterically hindered (Section 12.7). In cationic polymerization, nucleophilic attack occurs at the more substituted carbon, because the ring opens to give the more stable partial carbocation.

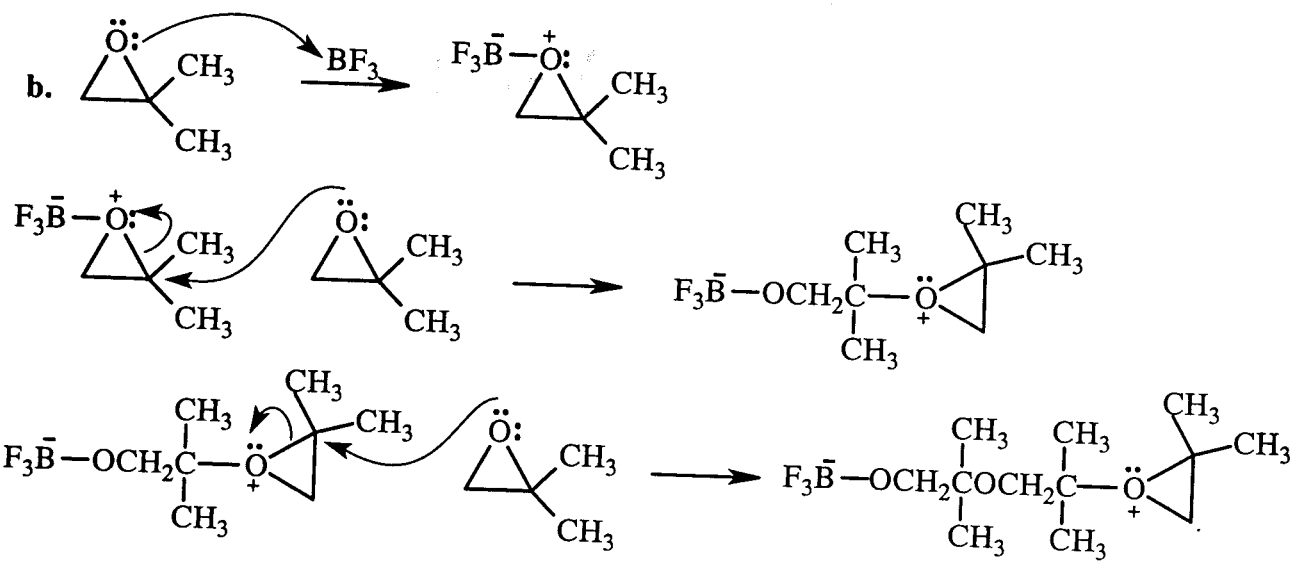


10.

a.

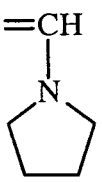


b.

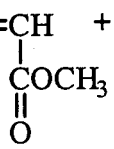


11.

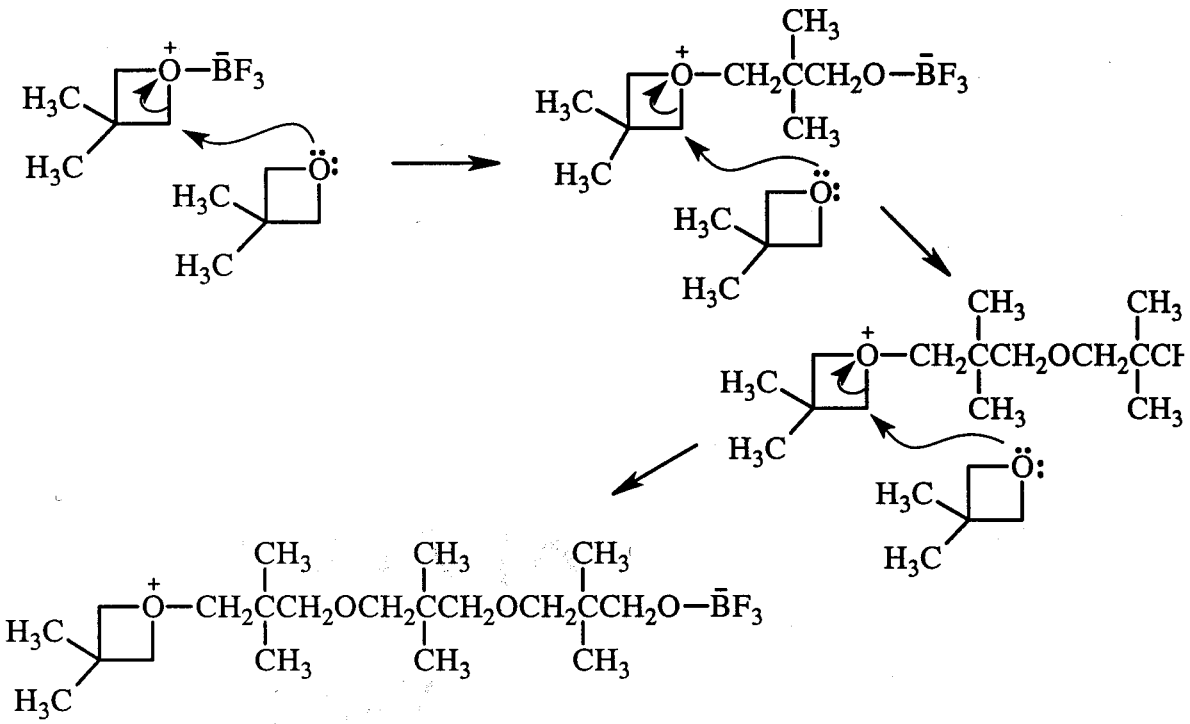
a. $CH_2{=}C(CH_3)CH_3 + BF_3$

b. 

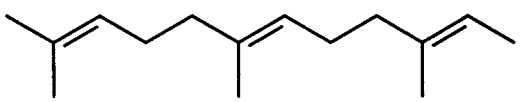
c.  $+ CH_3O^-$

d. 

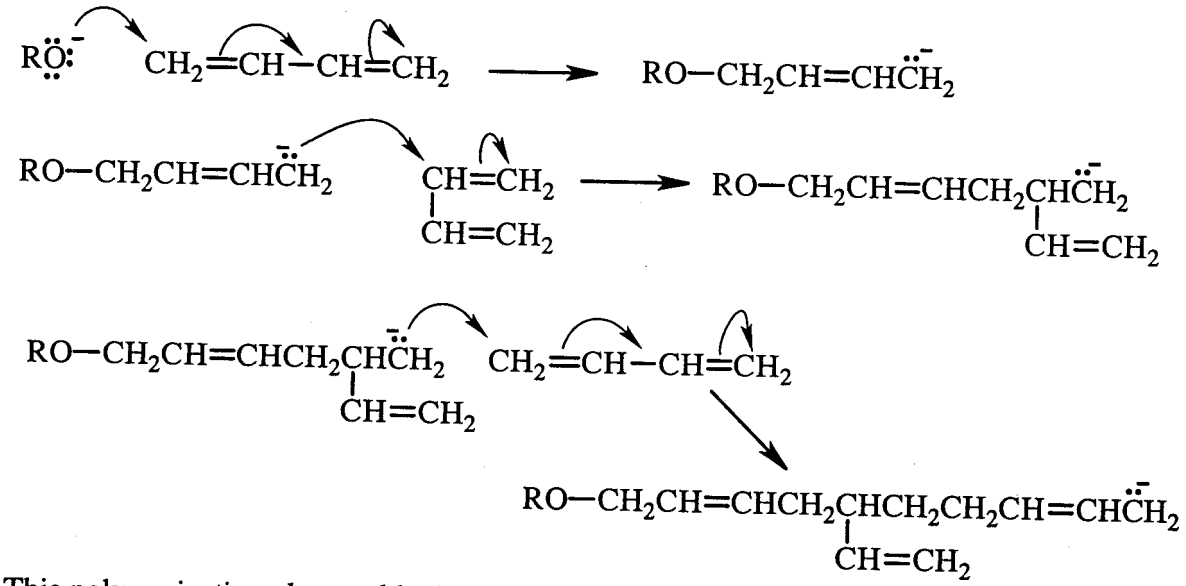
12. 3,3-Dimethyloxacyclobutane undergoes cationic polymerization by the following mechanism



13.



14. Notice that a branch occurs as a result of nucleophilic attack on C-3 instead of on C-1.

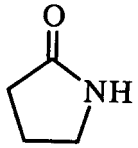


This polymerization also could take place by a radical mechanism or by a cationic mechanism.

15.

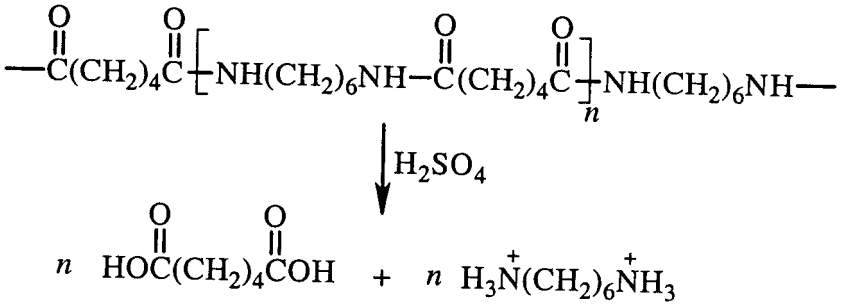
a. $-NHCH_2CH_2CH_2\overset{\overset{O}{\|}}{C}NHCH_2CH_2CH_2\overset{\overset{O}{\|}}{C}-$

b.

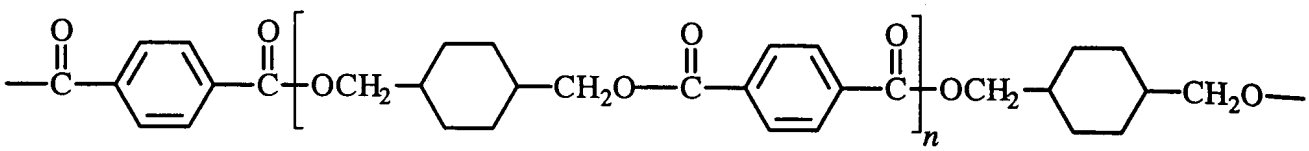


c. $-NH(CH_2)_4NH\overset{\overset{O}{\|}}{C}CH_2CH_2\overset{\overset{O}{\|}}{C}NH(CH_2)_4NH\overset{\overset{O}{\|}}{C}CH_2CH_2\overset{\overset{O}{\|}}{C}-$

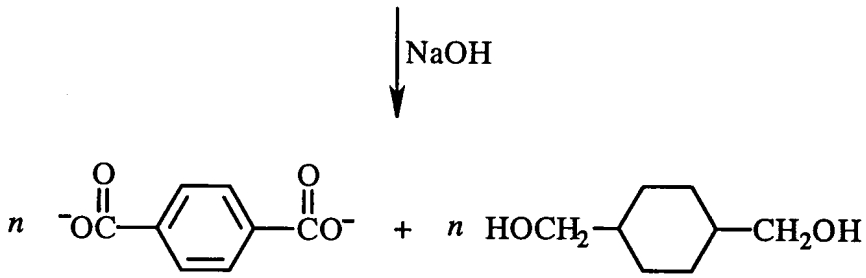
16.

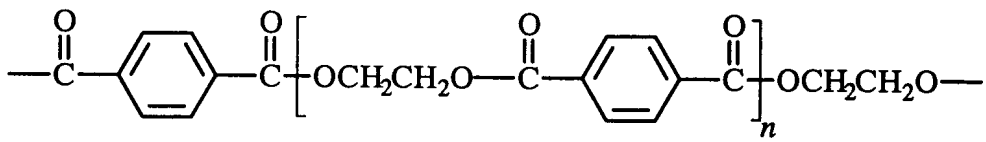


17. They hydrolyze to give monomers of dicarboxylic acids and diols.

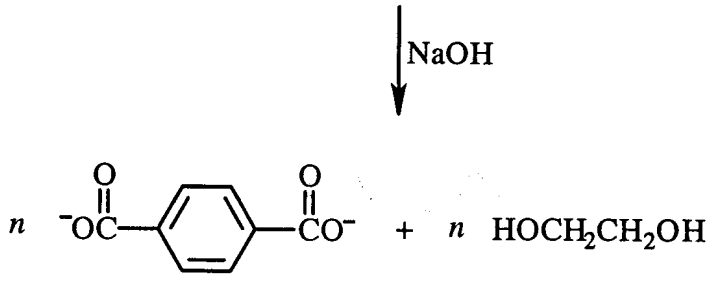


Kodel



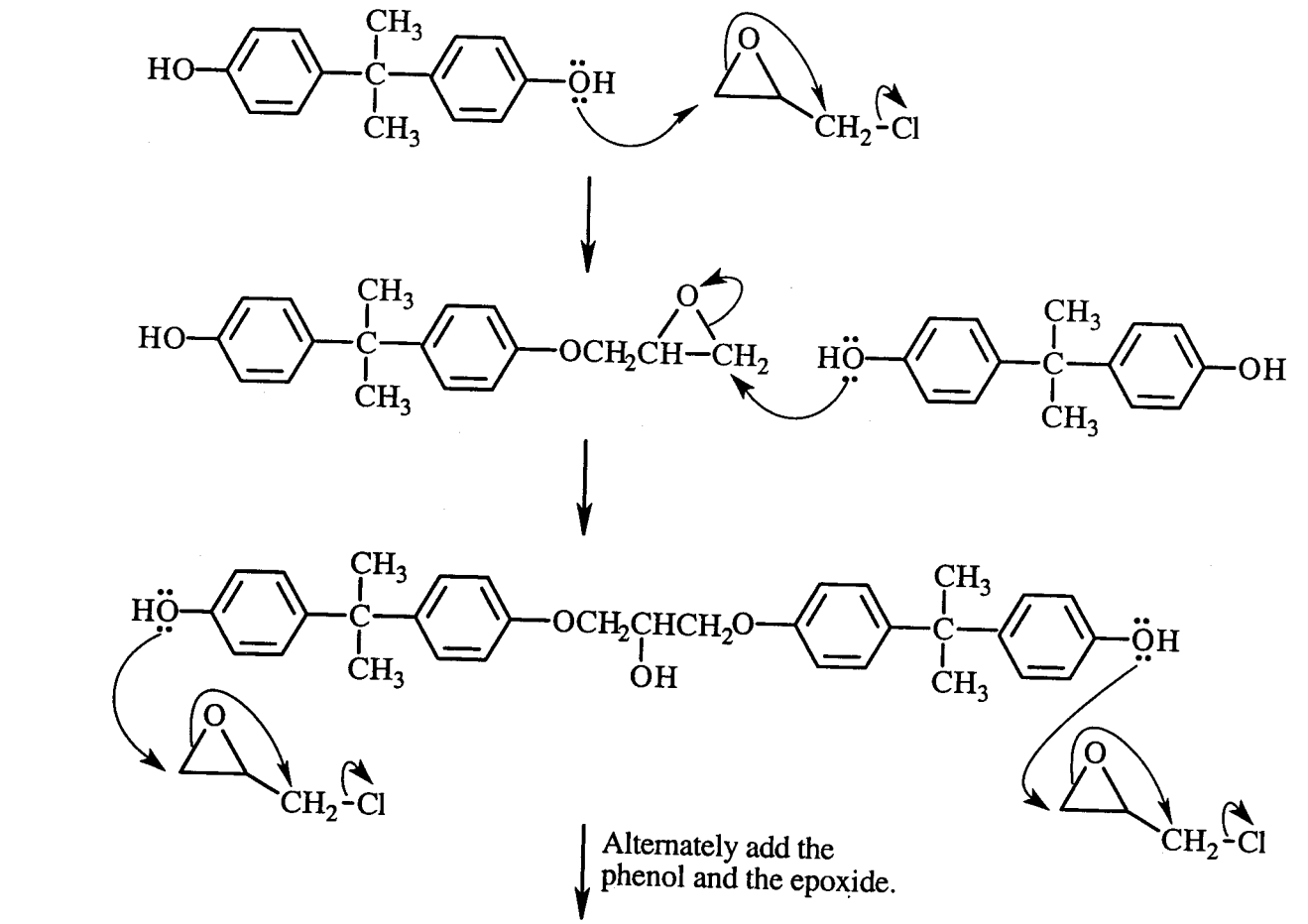


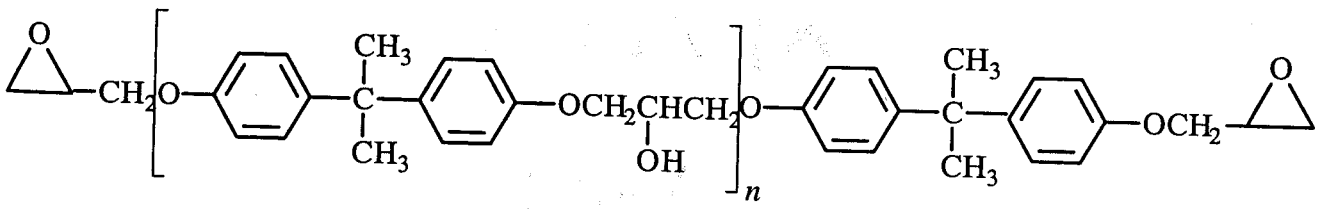
Dacron



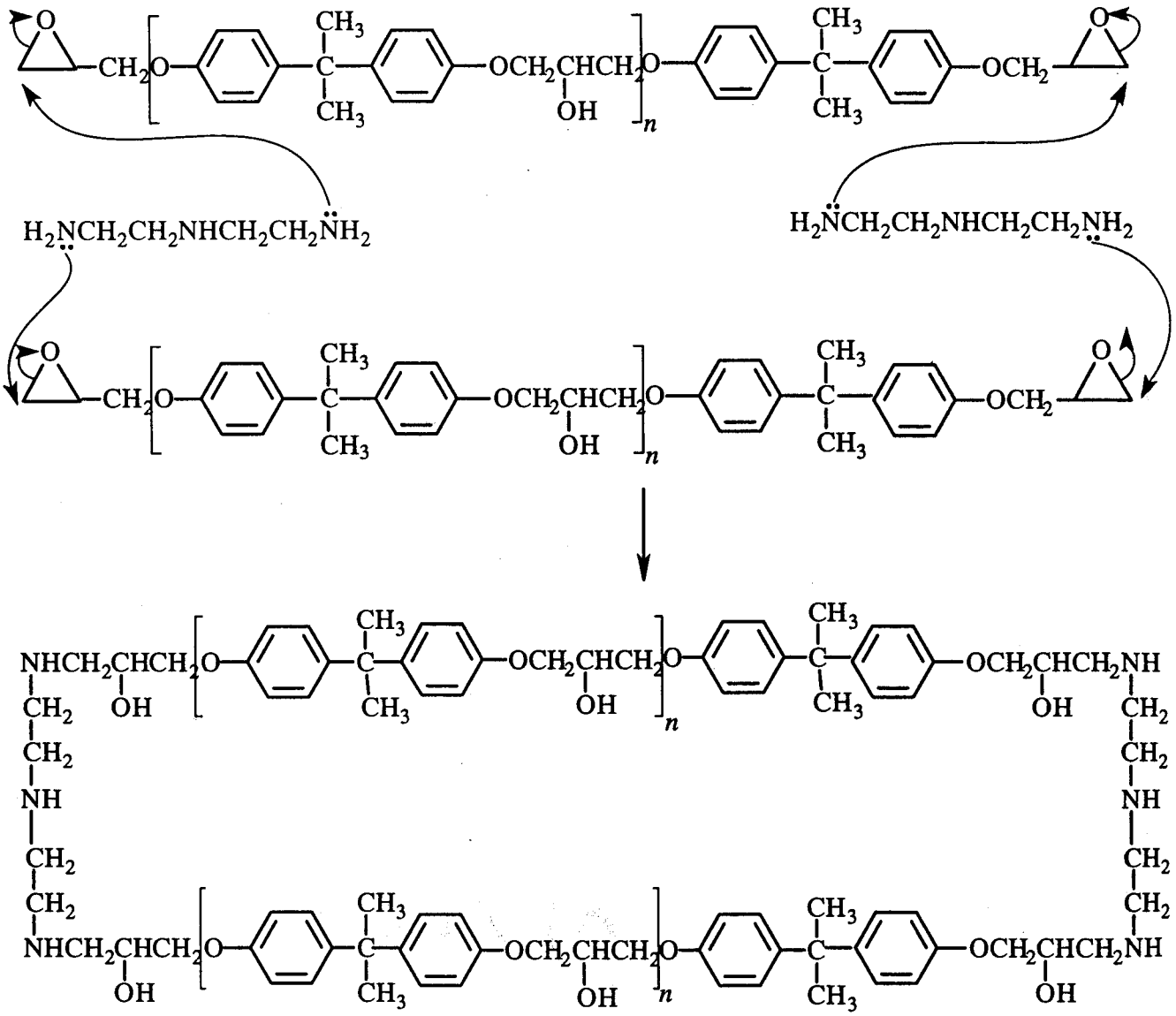
18.

a.

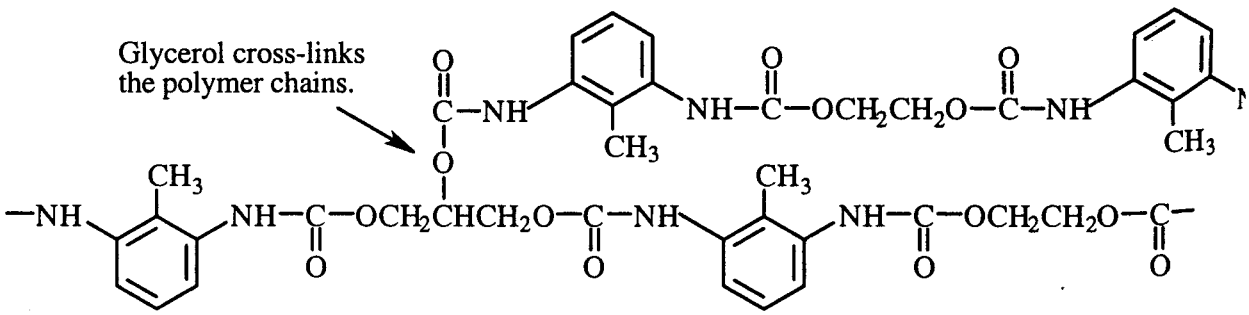




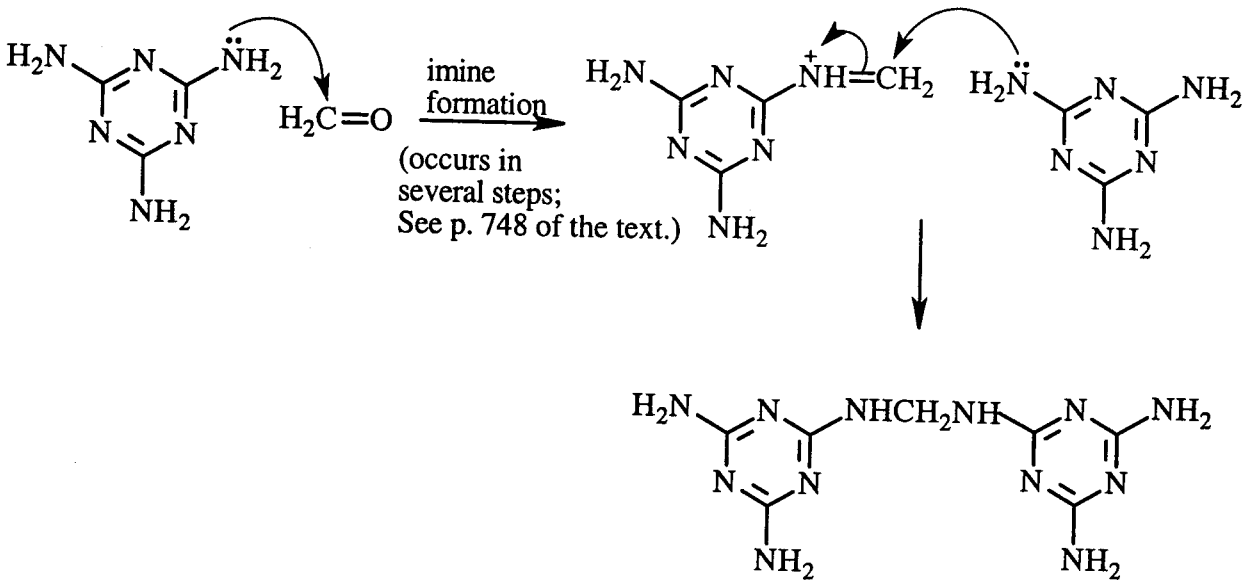
b.



19.

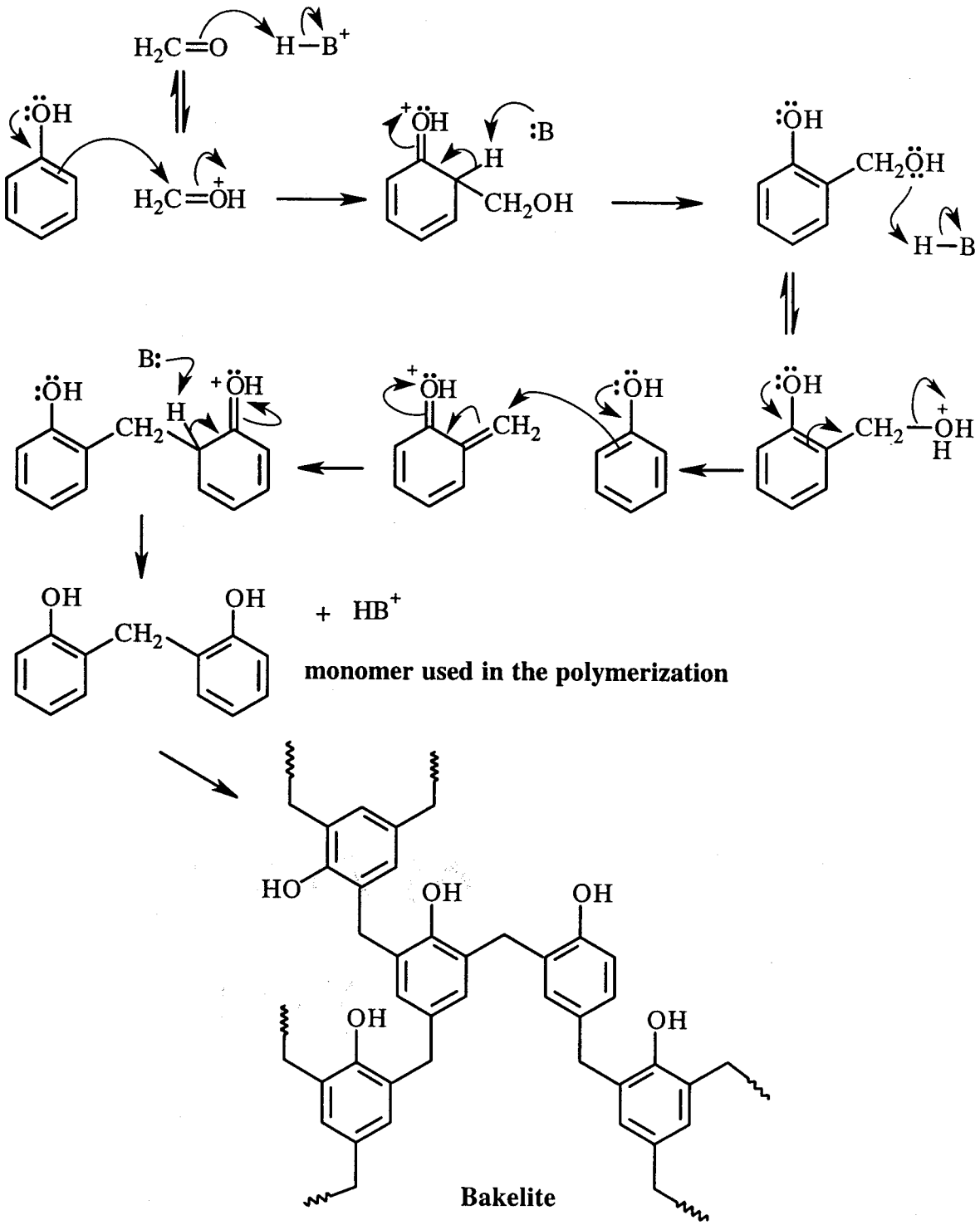


20. Formation of an imine between formaldehyde and one amino group, followed by reaction of the imine with a second amino group, accounts for formation of the linkage that holds the monomers together.

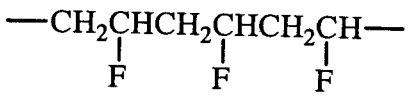


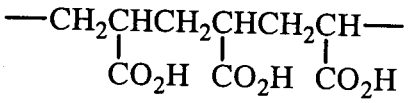
a dimer of Melmac

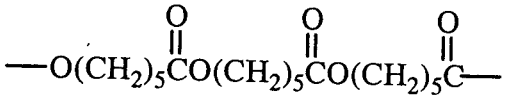
21.

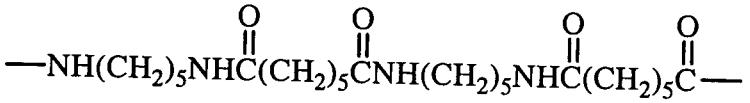


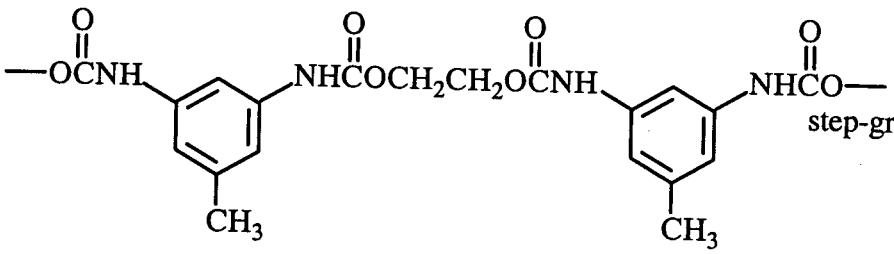
22.

a.  chain-growth polymer

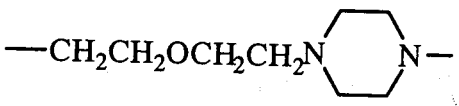
b.  chain-growth polymer

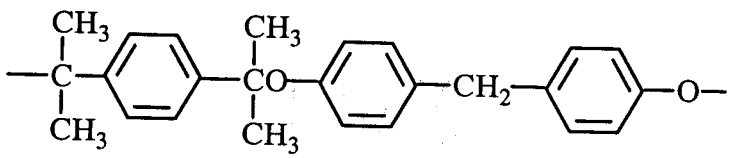
c.  step-growth polymer

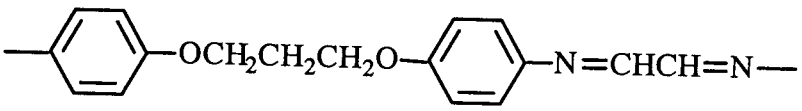
d.  step-growth polymer

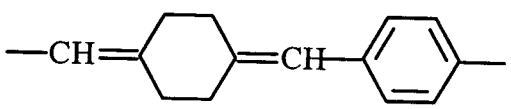
e.  step-growth polymer

23.

a. 

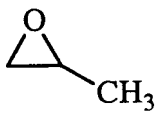
b. 

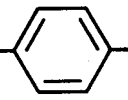
c. 

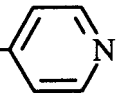
d. 

24.

a. $CH_2{=}CHCH_2CH_3$

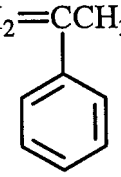
b. 

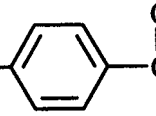
c. $ClSO_2$–  –$SO_2Cl + H_2N(CH_2)_6NH_2$

d. $CH_2{=}CH$– 

e. $CH_2{=}C(CH_3)CH{=}CH_2$

f. $HO(CH_2)_4COH$

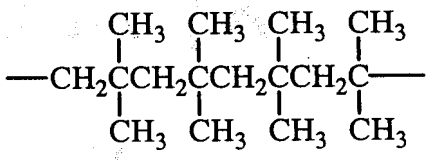
g. $CH_2{=}CCH_3$ 

h. HOC–  –$COH + HOCH_2CH_2OH$

a, **b**, **d**, **e**, and **g** are chain-growth polymers.

c, **f**, and **h** are step-growth polymers.

25. Whether a polymer is isotactic, syndiotactic, or atactic depends on whether the substituents are all on one side of the carbon chain, alternate on both sides of the chain, or are random with respect to the chain. Because a polymer of isobutylene has two identical substituents at each carbon in the chain, different configurations are not possible.



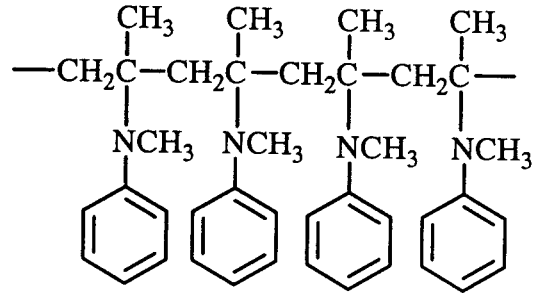
polymer of isobutylene

26.

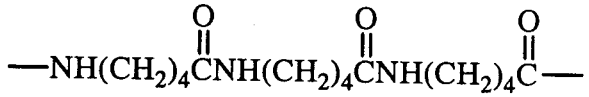
a. $CH_3OCH_2CH(CH_3)OCH_2CH(CH_3)OCH_2CH(CH_3)OCH_2CH(CH_3)O-$

b. $CH_3CH_2CH_2CH_2CH_2CH(Cl)CH_2CH(Cl)CH_2CH(Cl)CH_2CH(Cl)-$

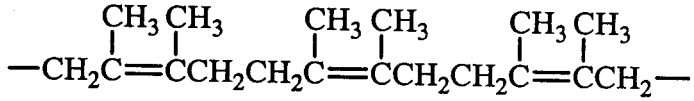
c.



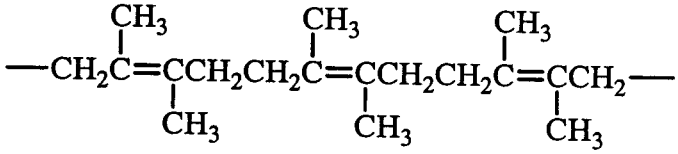
d.



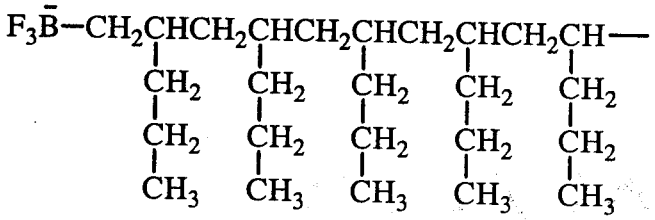
e. Depending on the particular Ziegler-Natta catalyst used, the double bonds can be either cis or trans.



or



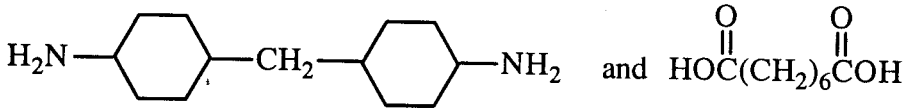
f.



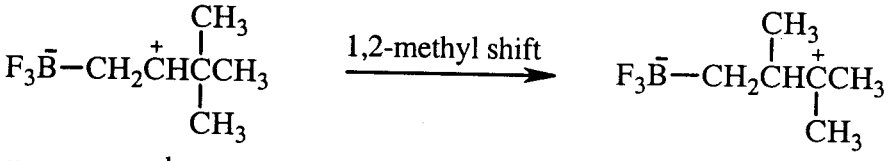
27.

a. Because it is a polyamide (and not a polyester), it is a nylon.

b.



28. A copolymer is a polymer composed of more than one kind of monomer. Because the initially formed carbocation can rearrange, two different monomers are involved in formation of the polymer.



unrearranged monomer

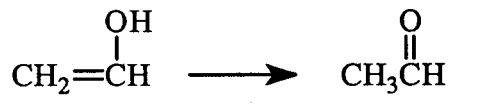
rearranged monomer

29. The polymer in the flask that contained a high molecular weight polymer and little material of intermediate molecular weight was formed by a chain-growth mechanism, whereas the polymer in the flask that contained mainly material of intermediate molecular weight was formed by a step-growth mechanism.

In a chain-growth mechanism, monomers are added to the growing end of a chain. This means that at any one time there will be polymeric chains and monomers.

Step-growth polymerization is not a chain reaction; any two monomers can react. Therefore, high molecular weight material will be formed by the reaction of two pieces of intermediate molecular weight.

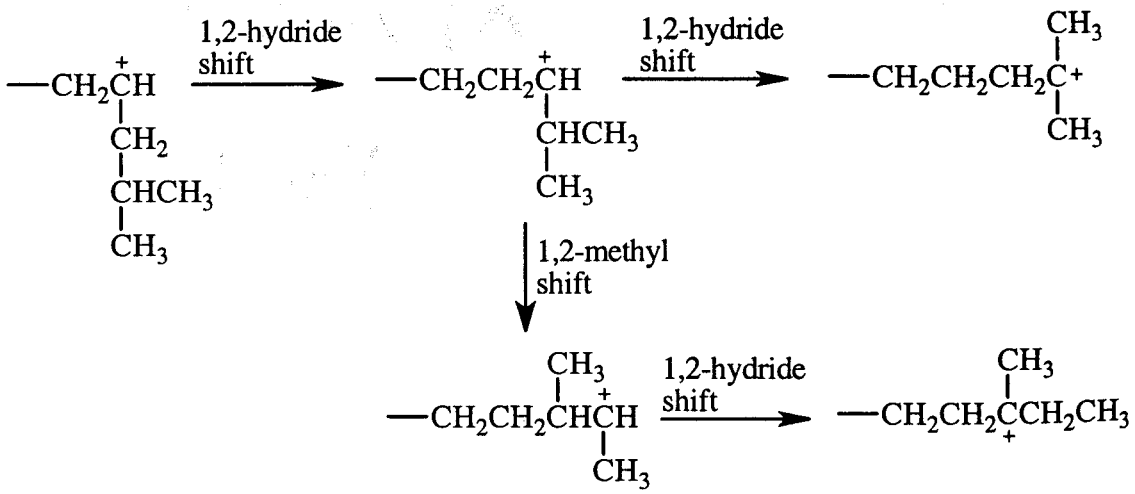
30. **a.** Vinyl alcohol is unstable, it tautomerizes to acetaldehyde.



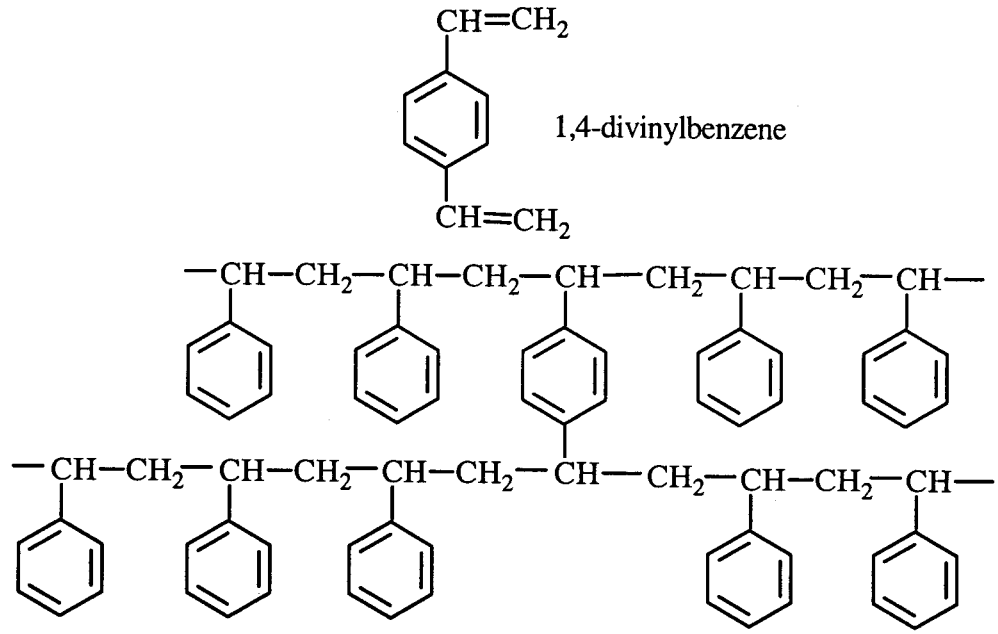
vinyl alcohol acetaldehyde

b. It is not a true polyester. It has ester groups as substituents **on** the backbone of the chain so it does have "polyester" groups, but it does not have ester groups **within** the backbone of the polymer chain. A true polyester has ester groups in the backbone of the polymer chain.

31. Each of the five carbocations shown below can add the growing end of the polymer chain.

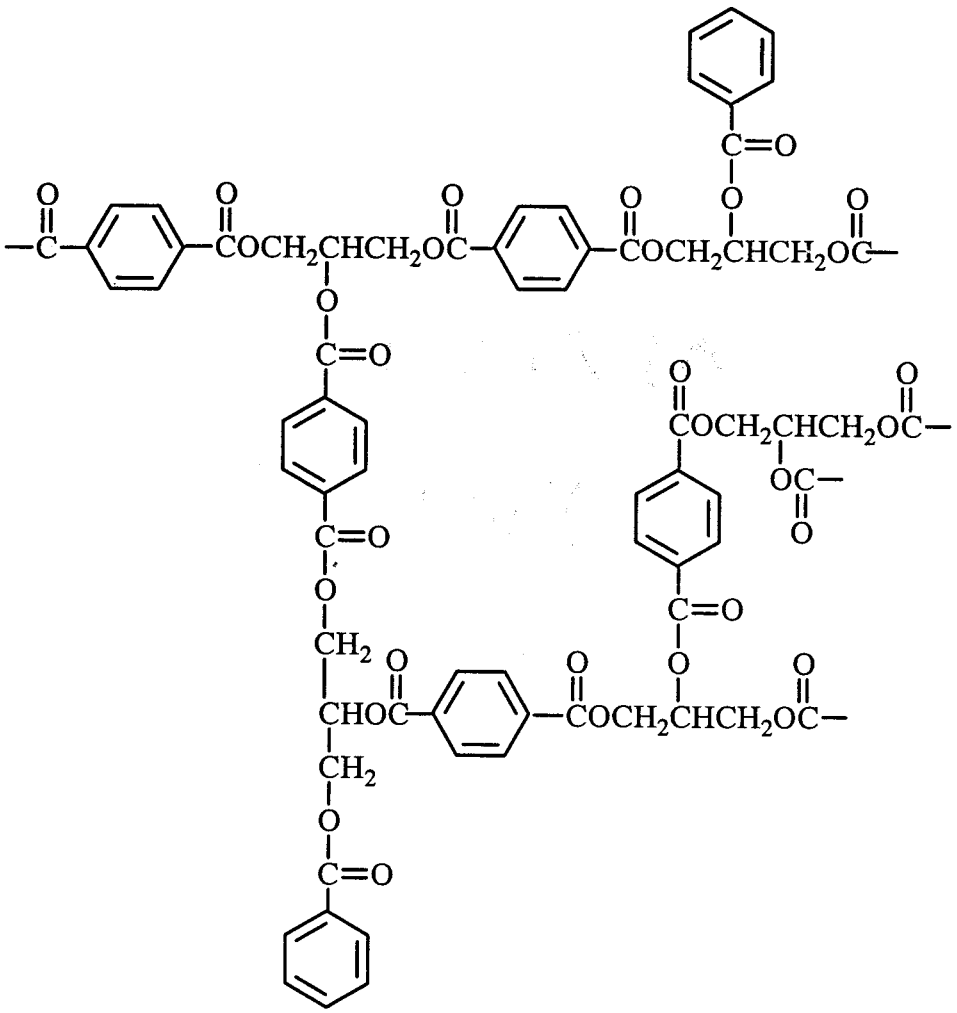


32. Because 1,4-divinylbenzene has substituents on both ends of the benzene ring that can engage in polymerization, the polymer chains can become cross-linked, which increases the rigidity of the polymer.

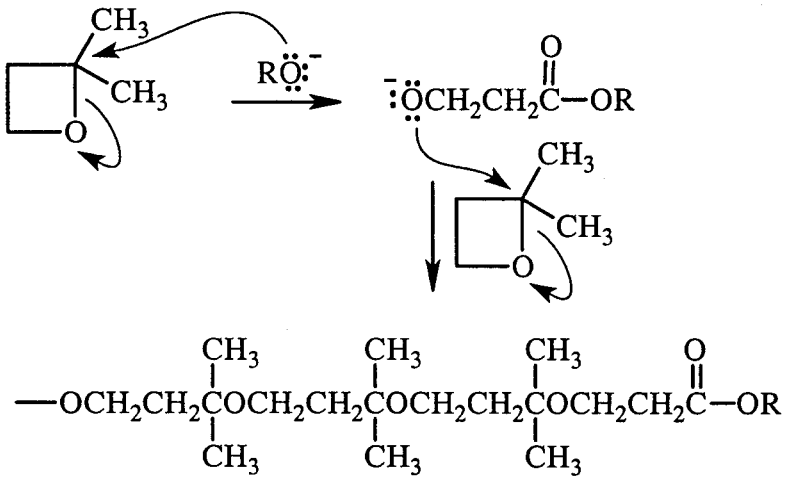


1,4-divinylbenzene

33. Glyptal gets its strength from cross-linking.

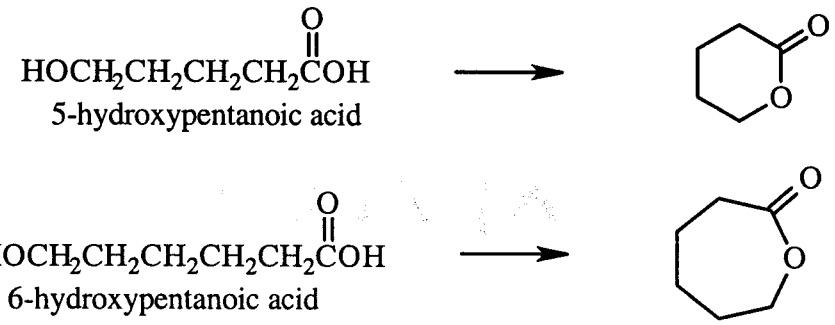


34.



35. Both compounds can form esters via intramolecular or intermolecular reactions. The product of the intramolecular reaction is a lactone; the intermolecular reaction leads to a polymer.

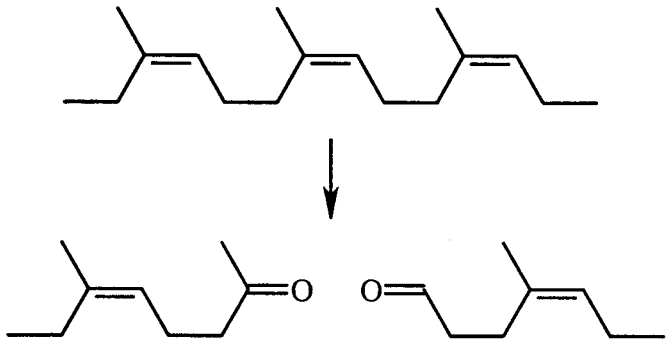
5-Hydroxypentanoic acid reacts intramolecularly to form a six-membered-ring lactone, whereas 6-hydroxyhexanoic acid reacts intramolecularly to form a seven-membered-ring lactone.



The compound that forms the most polymer will be the one that forms the least lactone, because the two reactions compete with one another.

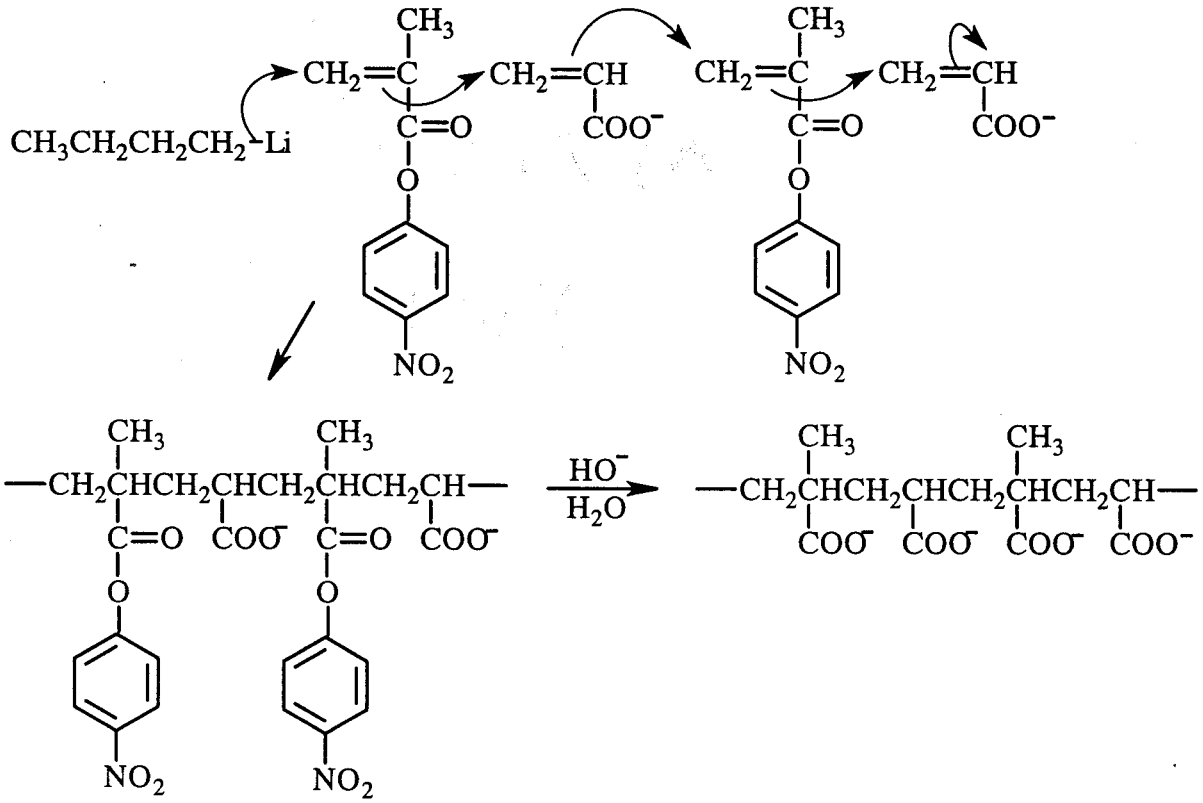
The six-membered-ring lactone is more stable and so is the transition state for its formation, compared to a seven-membered ring lactone. Since it is easier for 5-hydroxypentanoic acid to form the six-membered ring lactone, than for 6-hydroxyhexanoic acid to form the seven-membered ring lactone, **6-hydroxypentanoic acid** will form more polymer.

36. Rubber contains cis double bonds. Ozone, which is present in the air, oxidizes double bonds to carbonyl groups, destroying the polymer chain. Polyethylene does not contain double bonds, so it is not air-oxidized.

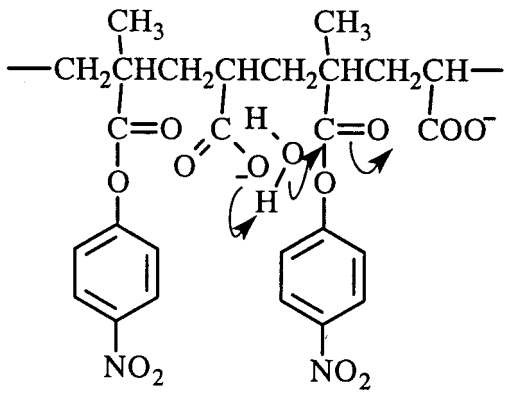


37. The plasticizer that keeps vinyl soft and pliable can vaporize over time, causing the polymer to become brittle. For this reason, high boiling materials are preferred over low boiling materials as plasticizers.

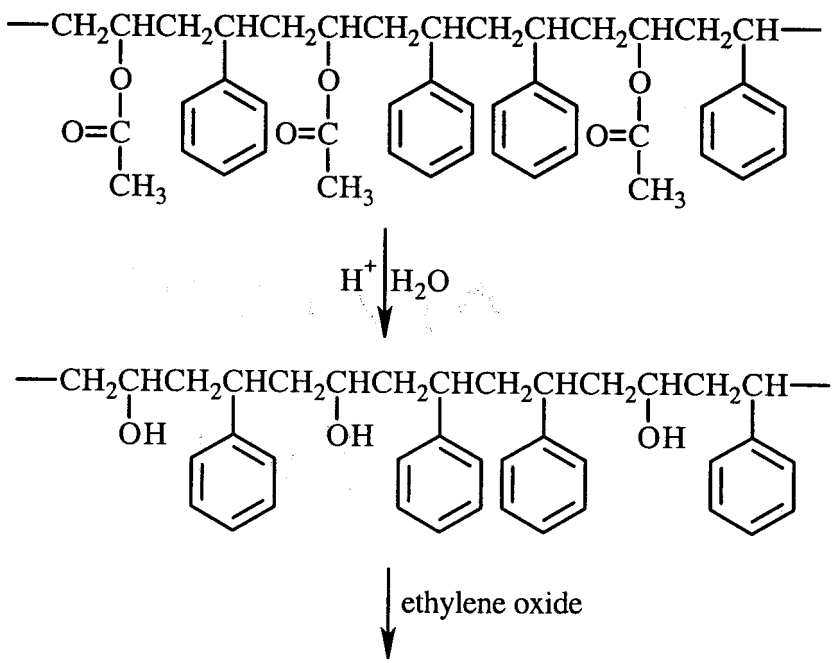
38. **a.** Because the negative charge on the propagation site can be delocalized onto the carbonyl oxygen, the polymer is best prepared by anionic polymerization.

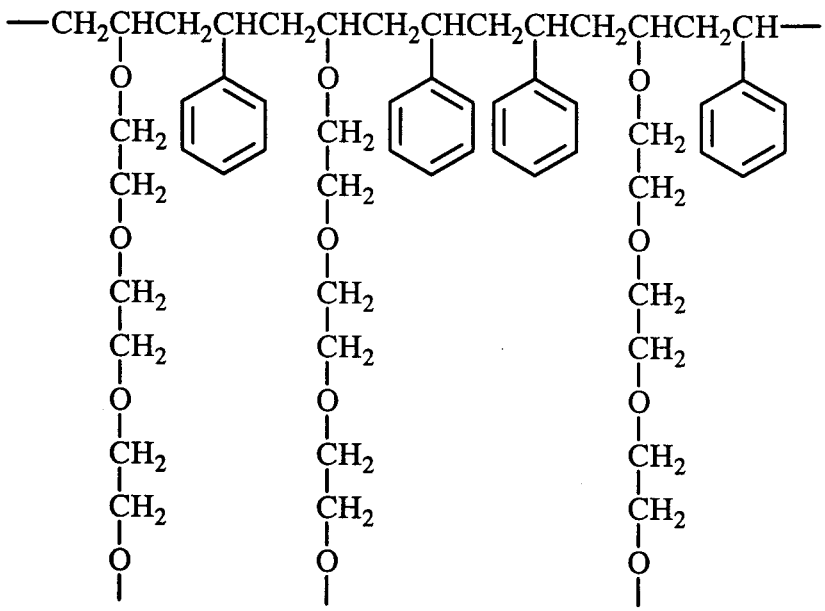


b. The carboxyl substituent is in position to remove a proton from water, making water a stronger nucleophile. (See page 1013 of the text.)



39. Hydrolysis converts the ester substituents into alcohol substituents, which can react with ethylene oxide to graft a polymer of ethylene oxide onto the backbone of the random polymer of styrene and vinyl acetate.

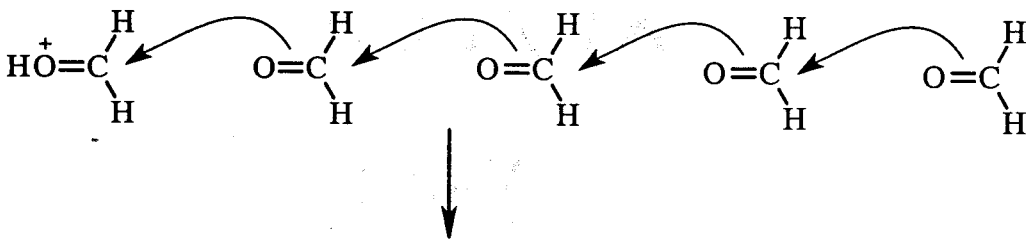




40. The desired polymer is an alternating copolymer of ethylene and 1,2-dibromoethylene.



41. **a.**



Delrin

b. Delrin is a chain-growth polymer,

CHAPTER 29
Pericyclic Reactions

Important Terms

antarafacial bond formation	formation of two σ bonds from opposite sides of the π system.
antarafacial rearrangement	a rearrangement where the migrating group moves to the opposite face the π system.
antibonding π molecular orbital	a molecular orbital that results when two parallel atomic orbitals with opposite signs interact. Electrons in an antibonding orbital decrease bor strength.
asymmetric molecular orbital	a molecular orbital in which the left half is not a mirror image of the rig half.
bonding π molecular orbital	a molecular orbital that results when two parallel atomic orbitals with th same sign interact. Electrons in a bonding orbital increase bond strength
Claisen rearrangement	a [3,3] sigmatropic rearrangement of an allyl vinyl ether.
conrotatory ring closure	achieves head-to-head overlap of π orbitals by rotating the orbitals in th same direction.
conservation of orbital symmetry theory	a theory that explains the relationship between the structure and stereochemistry of the reactant, the conditions under which a pericyclic reaction takes place, and the stereochemistry of the product.
Cope rearrangement	a [3,3] sigmatropic rearrangement of a 1,5-diene.
cycloaddition reaction	a reaction in which two π-bond-containing molecules react to form a cyc compound.
disrotatory ring closure	achieves head-to-head overlap of π orbitals by rotating the orbitals in opposite directions.
electrocyclic reaction	a reaction in which a π bond in the reactant is lost so that a cyclic compound with a new σ bond can be formed.
excited state	a description of which orbitals the electrons of an atom or molecule occup when an electron in the ground state has been moved to a higher energy orbital.
frontier orbital analysis	determining the outcome of a pericyclic reaction using frontier molecular orbitals.
frontier orbitals	the HOMO and the LUMO.
frontier orbital theory	a theory that, like the conservation of orbital symmetry, explains the relationship between reactant, product, and reaction conditions in a pericyclic reaction.

ground state	a description of which orbitals the electrons of an atom or molecule occupy when they are all in their lowest energy orbitals.
highest occupied molecular orbital (HOMO)	the molecular orbital of highest energy that contains an electron.
linear combination of atomic orbitals (LCAO)	the combination of atomic orbitals to produce a molecular orbital.
lowest unoccupied molecular orbital (LUMO)	the molecular orbital of lowest energy that does not contain an electron.
molecular orbital (MO) theory	describes a model in which the electrons occupy orbitals as they do in atoms but with the orbitals extending over the entire molecule.
pericyclic reaction	a reaction that occurs as a result of a cyclic reorganization of electrons.
photochemical reaction	a reaction that takes place when a reactant absorbs light.
polar reaction	the reaction between a nucleophile and an electrophile.
radical reaction	a reaction in which a new bond is formed using one electron from one reagent and one electron from another reagent.
selection rules	the rules that determine the outcome of a pericyclic reaction.
sigmatropic rearrangement	a reaction in which a σ bond is broken in the reactant, a new σ bond is formed in the product, and the π bonds rearrange.
suprafacial bond formation	formation of two σ bonds from the same side of the π system.
suprafacial rearrangement	a rearrangement where the migrating group remains on the same face of the π system.
symmetric molecular orbital	a molecular orbital in which the left half is a mirror image of the right half.
symmetry-allowed pathway	a pathway that leads to overlap of in-phase orbitals.
symmetry-forbidden pathway	a pathway that leads to overlap of out-of-phase orbitals.
thermal reaction	a reaction that takes place without the reactant having to absorb light.
Woodward-Hoffmann rules	a series of selection rules for pericyclic reactions.

Solutions to Problems

1. **a.** electrocyclic reaction **c.** cycloaddition reaction

b. sigmatropic rearrangement **d.** cycloaddition reaction

2. **a.** bonding orbitals = ψ_1, ψ_2, ψ_3; antibonding orbitals = ψ_4, ψ_5, ψ_6

b. ground-state HOMO = ψ_3; ground-state LUMO = ψ_4

c. excited-state HOMO = ψ_4; excited-state LUMO = ψ_5

d. symmetric orbitals = ψ_1, ψ_3, ψ_5; asymmetric orbitals = ψ_2, ψ_4, ψ_6

e. The HOMO and LUMO have opposite symmetries.

3. **a.** 8 π molecular orbitals **b.** ψ_4 **c.** 8 nodes (includes the node that passes through the centers of the *p* orbitals).

4. **a.** 1,3-Pentadiene has two conjugated π bonds, so it has the same π molecular orbital description as 1,3-butadiene, a compound that also has two conjugated π bonds. (See Figure 29.2 on page 1180 of the text.)

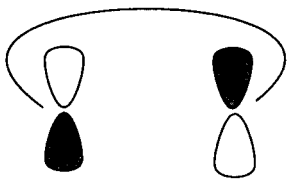
b. The π bonds in 1,4-pentadiene are isolated, so its π molecular orbital description is the same as ethene, a compound with an isolated π bond. (See Figure 29.1 on page 1179 of the text.)

c. 1,3,5-Heptatriene has three conjugated π bonds, so it has the same π molecular orbital description as 1,3,5-hexatriene, a compound that also has three conjugated π bonds. See Figure 29.3 on page 1181 of the text.)

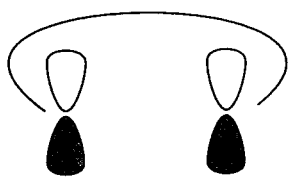
d. 1,3,5,8-Nonatetraene has three conjugated π bonds and an isolated π bond. The three conjugated π bonds are described by Figure 29.3 and the isolated π bond by Figure 29.1.

5. **a.**

2, 4, or 6 conjugated double bonds



3, 5, or 7 conjugated double bonds



6. **a.** (2*E*,4*Z*,6*Z*,8*E*)-Decatetraene has an even number of conjugated π bonds (4). Therefore, under thermal conditions, ring closure will be conrotatory.

b. The substituents point in opposite directions, and conrotatory ring closure of such substituents will cause them to be trans in the ring-closed product.

c. Under photochemical conditions, a compound with four conjugated π bonds will undergo disrotatory ring closure.

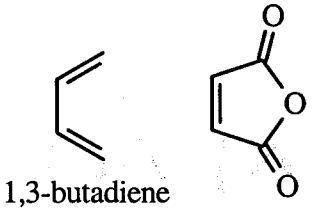
d. Because ring closure is disrotatory and the substituents point in opposite directions, the product will have the cis configuration.

7. **a.** correct **b.** correct **c.** correct

8. **1.** **a.** conrotatory
b. trans

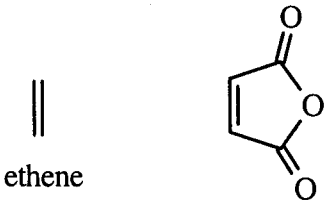
2. **a.** disrotatory
b. cis

9. The reaction of maleic anhydride with 1,3-butadiene involves three π bonds in the reacting system, and such a reaction under thermal conditions involves suprafacial ring closure.



1,3-butadiene

The reaction of maleic anhydride with ethylene involves two π bonds in the reacting system, and such a reaction under thermal conditions involves antarafacial ring closure, which cannot occur with a four-membered ring.

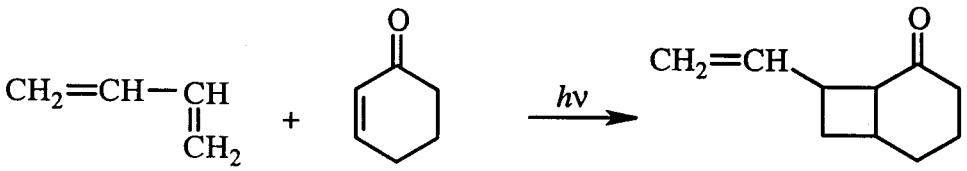


ethene

10. Solved in the text.

807

Since we are dealing with formation of a small ring, ring closure will have to be suprafacial. photochemical conditions, suprafacial ring closure requires an even number of π bonds in cting system. Thus, a concerted reaction will occur but it will use only one of the π bonds 1,3-butadiene.



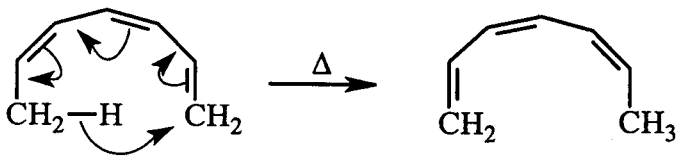
12. **a.** **1.** [1,7] sigmatropic rearrangement

2. [1,5] sigmatropic rearrangement

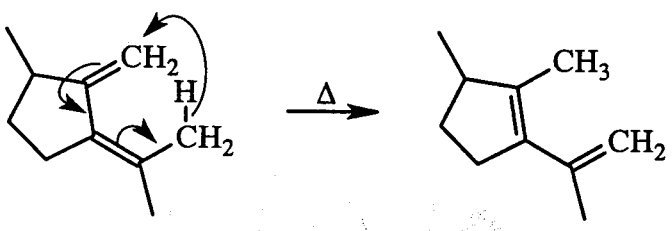
3. [5,5] sigmatropic rearrangement

4. [3,3] sigmatropic rearrangement

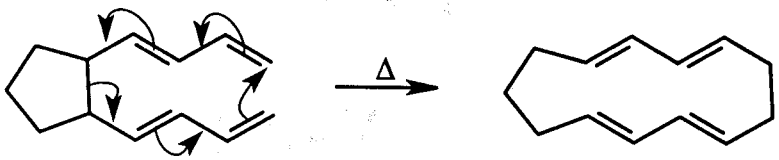
b. **1.**



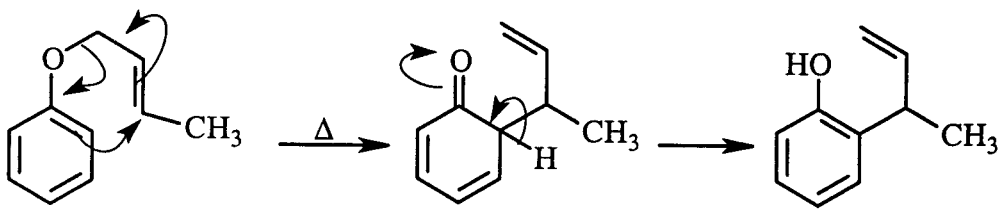
2.



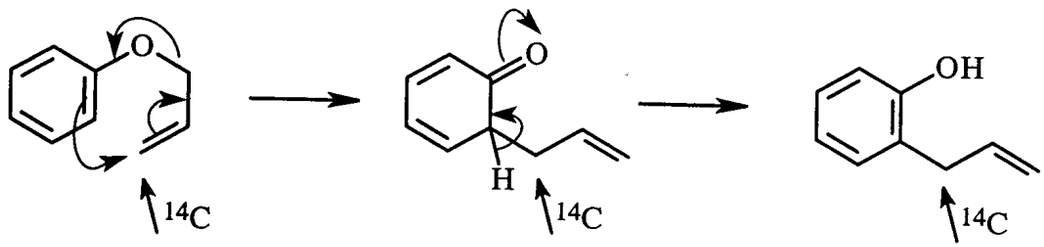
3.



4.

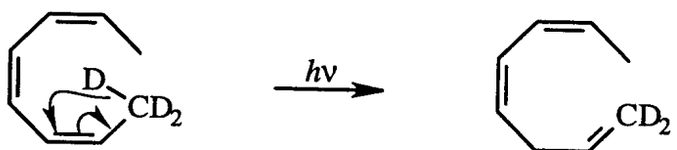


13.



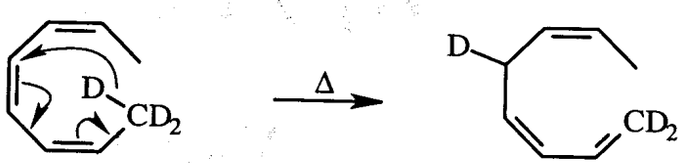
14. If a nondeuterated reactant had been used, the product would have been identical to the reactant. Therefore, the rearrangement would not have been detectable.

15. A suprafacial rearrangement can take place under photochemical conditions if there are an even number of electrons in the reacting system. Therefore, a 1,3-hydrogen shift occurs.



a [1,3] sigmatropic migration of deuterium

A suprafacial rearrangement can take place under thermal conditions if there are an odd number of electrons in the reacting system. Therefore, a 1,5-hydrogen shift occurs.



a [1,5] sigmatropic migration of deuterium

16. Solved in the text.

17. [1,3] Sigmatropic migrations of hydrogen cannot occur under thermal conditions, because the four-membered transition state does not allow the required antarafacial rearrangement.

[1,3] Sigmatropic migrations of carbon can occur under thermal conditions because carbon can achieve the required antarafacial rearrangement by using both of its lobes when it migrates.

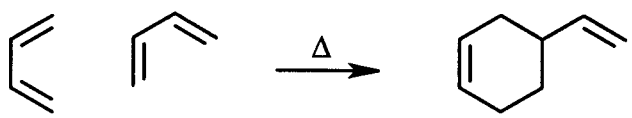
18. **a.** Because 1,3-migration of carbon requires carbon to migrate using both of its lobes (it involves an even number of pairs of electrons, so it takes place by an antarafacial pathway), migration will occur with inversion of configuration.

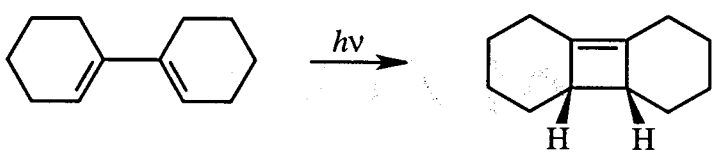
b. Because 1,5-migration of carbon requires carbon to migrate using only one of its lobes (it involves an odd number of pairs of electrons, so it takes place by a suprafacial pathway), migration will occur with retention of configuration.

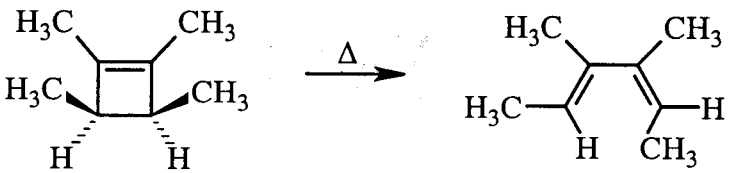
19. Because the [1,7] sigmatropic rearrangement takes place under thermal conditions and involves an even number (4) of pairs of electrons, migration of hydrogen involves antarafacial rearrangement.

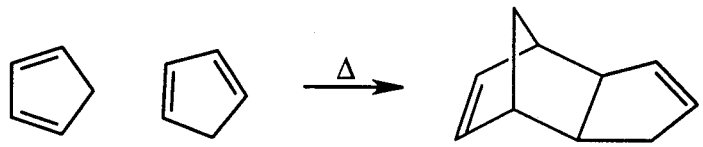
20. Because the reactant (provitamin D_3) has an odd number (3) of conjugated π bonds and reacts under photochemical conditions, ring closure is conrotatory. The methyl and hydrogen substituents point in opposite directions in provitamin D_3. Conrotatory ring closure will cause substituents that point in opposite directions in the reactant to be trans in the product.

21.

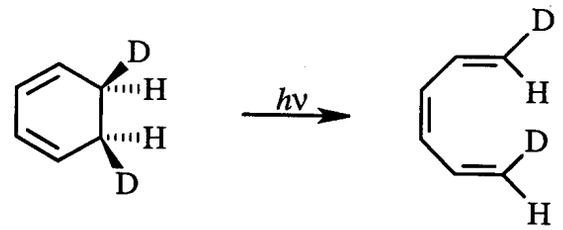
a. 

b. 

c. 

d. 

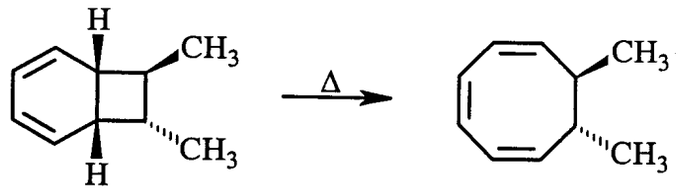
e.



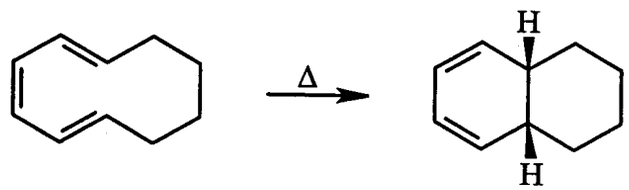
f.



g.



h.

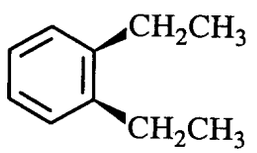


22. Because the compound has an odd number of π bonds, it will undergo disrotatory ring closure under thermal conditions and conrotatory ring closure under photochemical conditions.

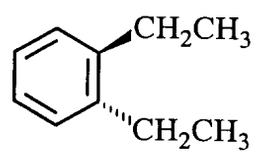
In the compounds in which the two methyl substituents point in opposite directions, they will be cis in the ring-closed product when ring closure is disrotatory and trans in the ring-closed product when ring closure is conrotatory.

In the compounds in which the two methyl substituents point in the same direction, they will be trans in the ring-closed product when ring closure is disrotatory and cis in the ring-closed product when ring closure is conrotatory.

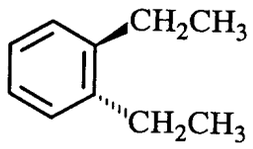
a.



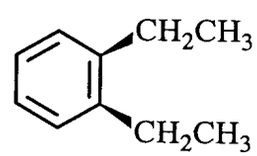
c.



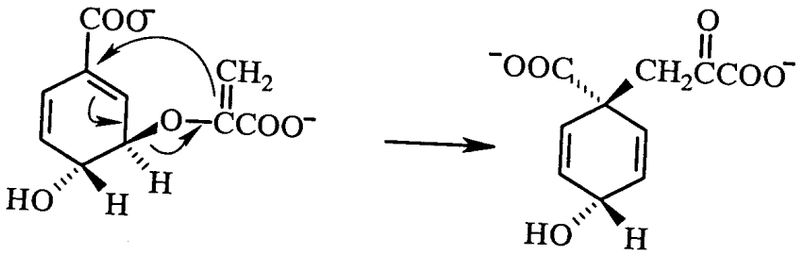
b.



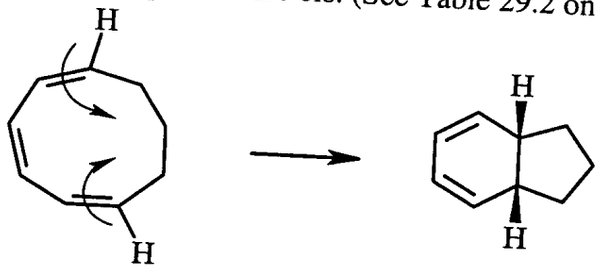
d.



23. Chorismate mutase catalyzes a [3,3] sigmatropic rearrangement.



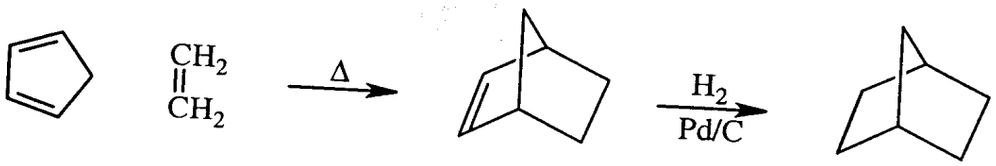
24. The hydrogens that end up at the ring juncture in the first reaction point in opposite directions in the reactant. Because ring closure is disrotatory (odd number of π bonds, thermal conditions), the hydrogens in the ring-closed product are cis. (See Table 29.2 on page 1188 of the text.)



The hydrogens that end up at the ring juncture point in the same directions in the reactant. Ring closure is still disrotatory, so the hydrogens in the ring-closed product are trans.

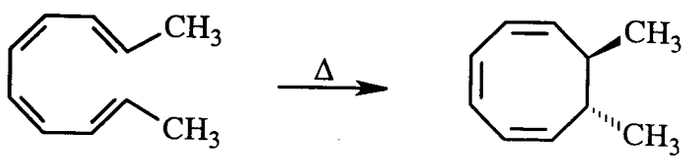


25.

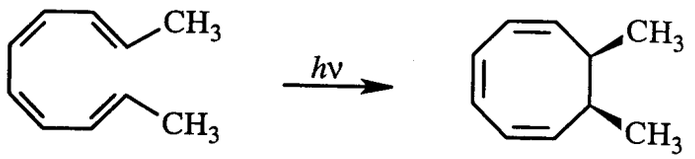


26. **1.** Because the compound has an even number of π bonds, it will undergo conrotatory ring closure under thermal conditions and disrotatory ring closure under photochemical conditions. Because the two methyl substituents point in opposite directions, they will be trans in the ring-closed product when ring closure is conrotatory and cis in the ring-closed product when ring closure is disrotatory.

a.

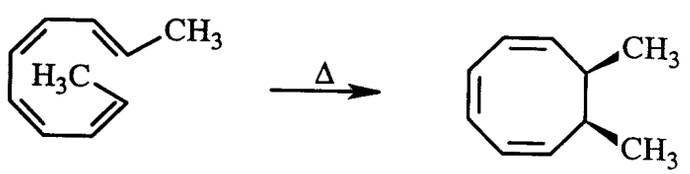


b.

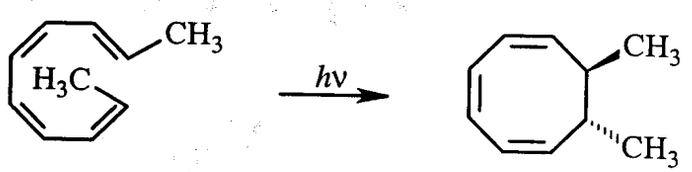


2. Because the compound has an even number of π bonds, it will undergo conrotatory ring closure under thermal conditions and disrotatory ring closure under photochemical conditions. Because the two methyl substituents point in the same direction, they will be cis in the ring-closed product when ring closure is conrotatory and trans in the ring-closed product when ring closure is disrotatory.

a.

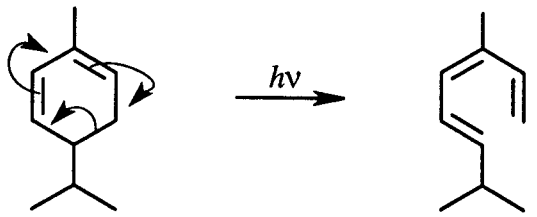


b.

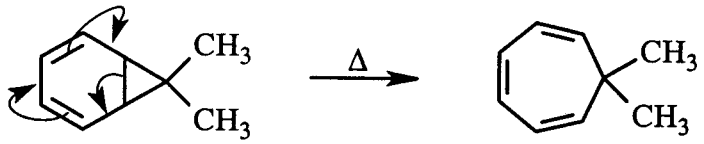


27.

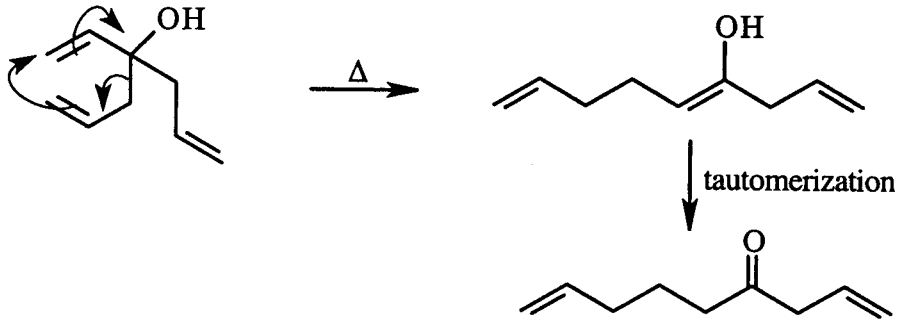
a.


hν

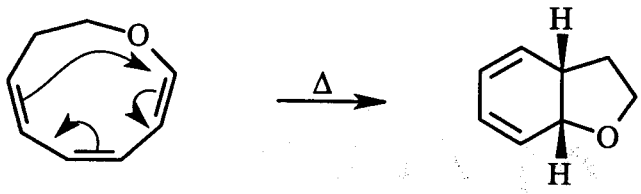
b.


CH3
CH3
Δ
CH3
CH3

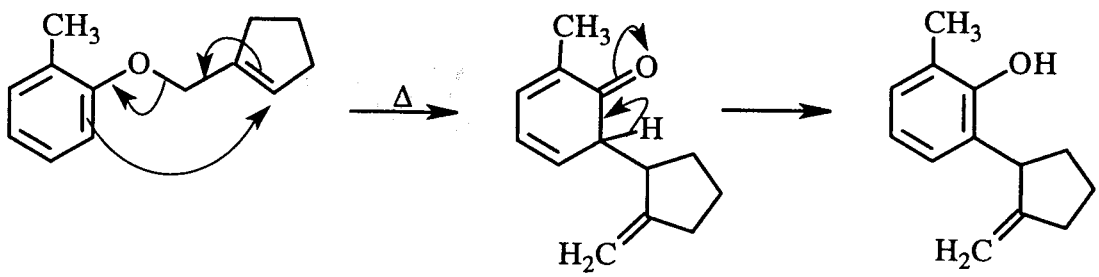
c.


OH
Δ
OH
tautomerization
O

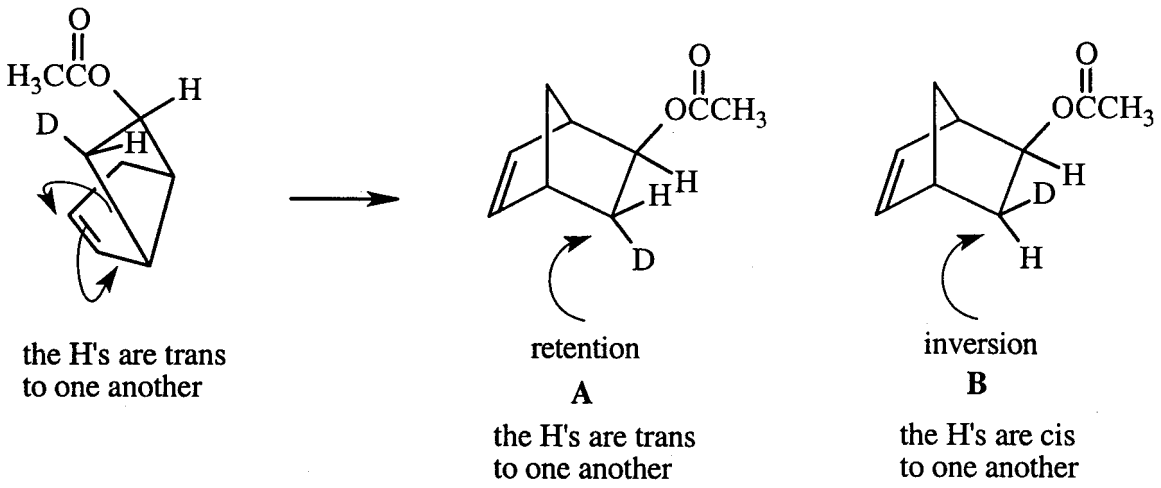
d.


O
Δ
H
O
H

e.


CH3
O
Δ
CH3
O
H
H2C
CH3
OH
H2C

28. **B** is the product. Because the reaction is a [1,3] sigmatropic rearrangement, antarafacial ring closure is required. Carbon, therefore, must migrate using both of its lobes. This means that the configuration of the migrating carbon will undergo inversion. The configuration of the migrating carbon has been inverted in **B** (the H's are cis to one another but were trans to one another in the reactant) and retained in **A**.



the H's are trans to one another

retention

A

the H's are trans to one another

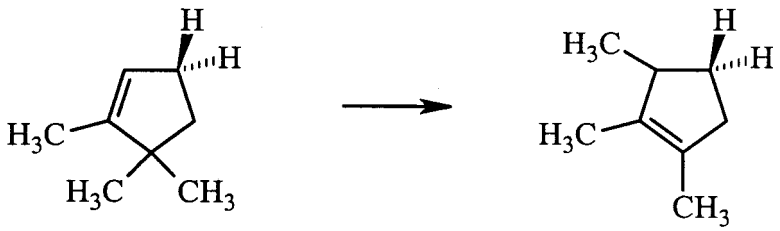
inversion

B

the H's are cis to one another

29. At first glance it is surprising that the isomerization of Dewar benzene (a highly strained and unstable molecule) to benzene (a stable aromatic compound) is so slow. However, the isomerization requires conrotatory ring-opening, which is symmetry-forbidden under thermal conditions. The reaction, therefore, cannot take place by a concerted pathway and has to take place by a much slower stepwise process.

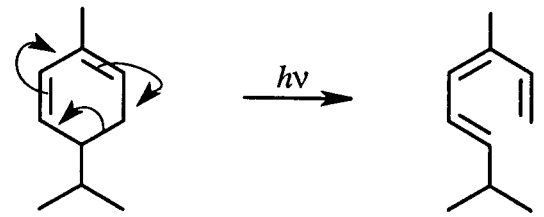
30. Hydrogen cannot undergo a [1,3] sigmatropic rearrangement, because it cannot migrate by a suprafacial pathway since its HOMO is asymmetric. Carbon can undergo a [1,3] sigmatropic rearrangement because it can migrate by a suprafacial pathway if it uses both of its lobes. So, the first compound can undergo only a 1,3-methyl group migration.



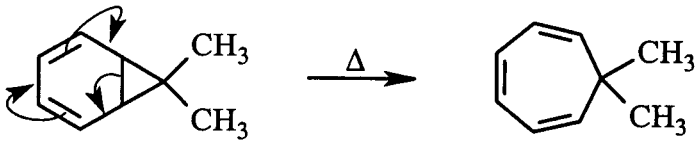
The second compound can under the 1,3-methyl group migration that the first compound undergoes, and the *sec*-butyl group can also undergo a [1,3] sigmatropic rearrangement. The migrating *sec*-butyl group will have its configuration inverted.

27.

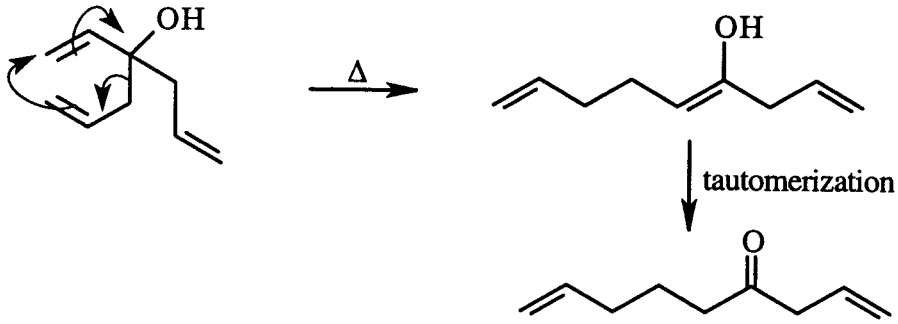
a.


hν

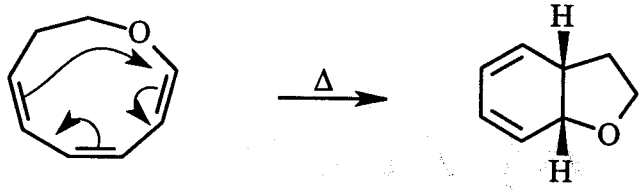
b.


CH3
CH3
Δ
CH3
CH3

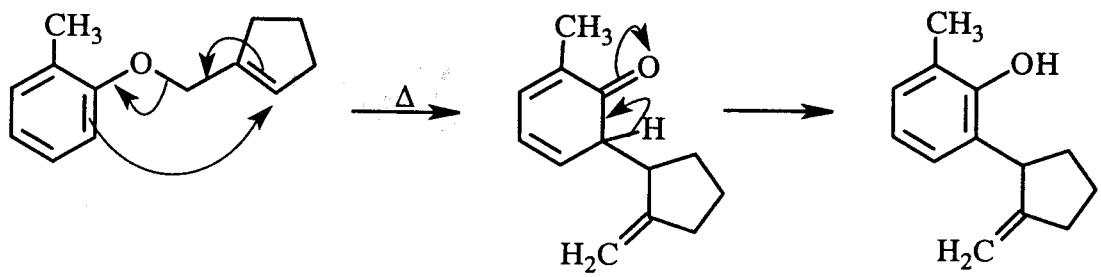
c.


OH
Δ
OH
tautomerization
O

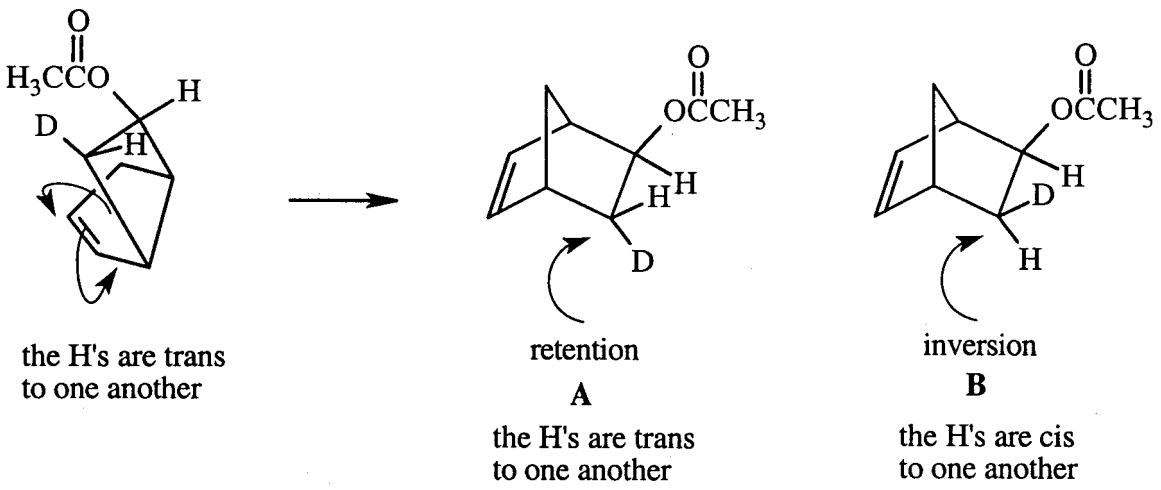
d.


O
Δ
H
O
H

e.


CH3
O
Δ
CH3
O
H
H2C
CH3
OH
H2C

28. **B** is the product. Because the reaction is a [1,3] sigmatropic rearrangement, antarafacial ring closure is required. Carbon, therefore, must migrate using both of its lobes. This means that the configuration of the migrating carbon will undergo inversion. The configuration of the migrating carbon has been inverted in **B** (the H's are cis to one another but were trans to one another in the reactant) and retained in **A**.



the H's are trans to one another

retention

A

the H's are trans to one another

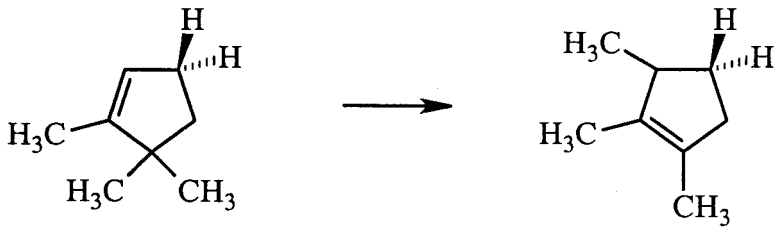
inversion

B

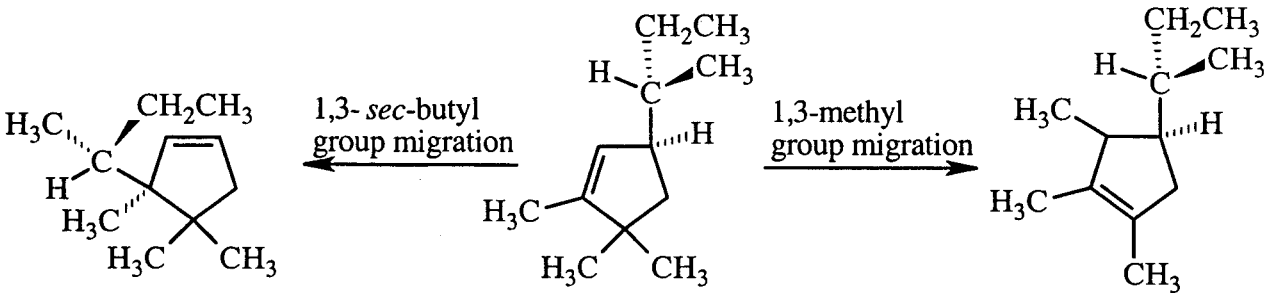
the H's are cis to one another

29. At first glance it is surprising that the isomerization of Dewar benzene (a highly strained and unstable molecule) to benzene (a stable aromatic compound) is so slow. However, the isomerization requires conrotatory ring-opening, which is symmetry-forbidden under thermal conditions. The reaction, therefore, cannot take place by a concerted pathway and has to take place by a much slower stepwise process.

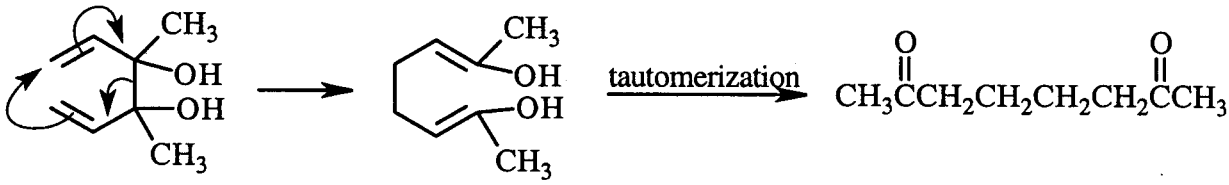
30. Hydrogen cannot undergo a [1,3] sigmatropic rearrangement, because it cannot migrate by a suprafacial pathway since its HOMO is asymmetric. Carbon can undergo a [1,3] sigmatropic rearrangement because it can migrate by a suprafacial pathway if it uses both of its lobes. So, the first compound can undergo only a 1,3-methyl group migration.



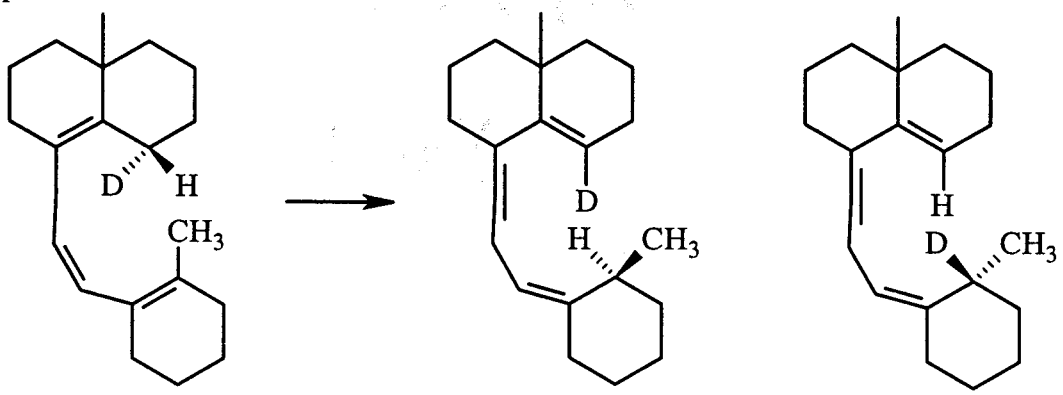
The second compound can under the 1,3-methyl group migration that the first compound undergoes, and the *sec*-butyl group can also undergo a [1,3] sigmatropic rearrangement. The migrating *sec*-butyl group will have its configuration inverted.

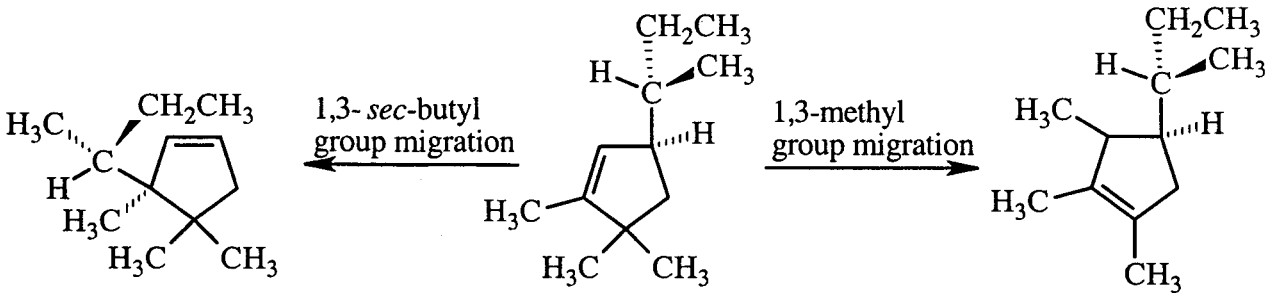


31. An infrared absorption band is indicative of a carbonyl group. A [3,3] sigmatropic rearrangement of the reactant leads to a compound with two enolic groups. Tautomerization of the enols results in keto groups. The ketone carbonyl groups are what give the absorbance at 1715 cm^{-1}.

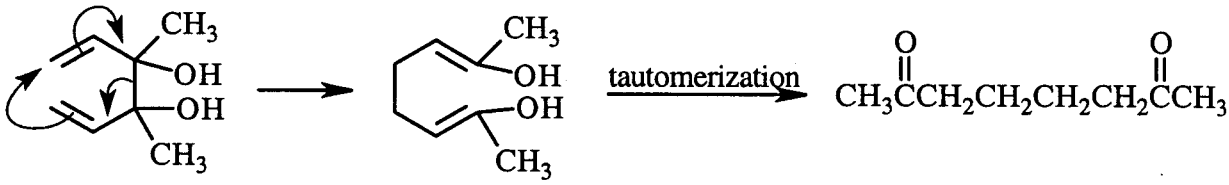


32. The reaction is a [1,7] sigmatropic rearrangement. Since the reaction involves four pairs of electrons, antarafacial rearrangement occurs. Thus, when H migrates, because it is above the plane of the reactant molecule, it ends up below the plane of the product molecule. When D migrates, because it is below the plane of the reactant molecule, it ends up above the plane of the product molecule.

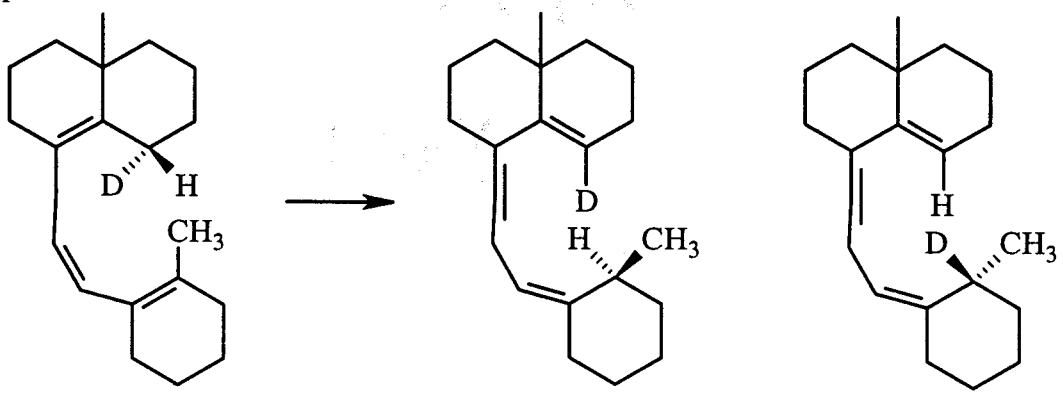




31. An infrared absorption band is indicative of a carbonyl group. A [3,3] sigmatropic rearrangement of the reactant leads to a compound with two enolic groups. Tautomerization of the enols results in keto groups. The ketone carbonyl groups are what give the absorbance at 1715 cm^{-1}.

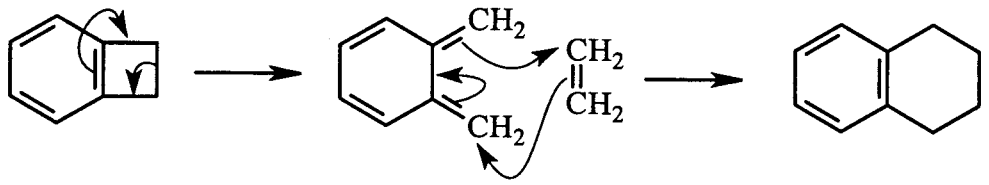


32. The reaction is a [1,7] sigmatropic rearrangement. Since the reaction involves four pairs of electrons, antarafacial rearrangement occurs. Thus, when H migrates, because it is above the plane of the reactant molecule, it ends up below the plane of the product molecule. When D migrates, because it is below the plane of the reactant molecule, it ends up above the plane of the product molecule.

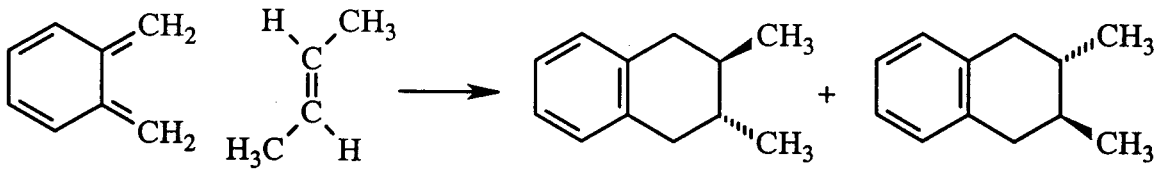


33.

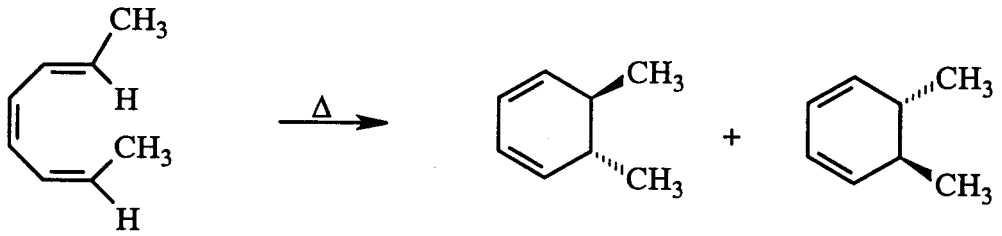
a.



b.

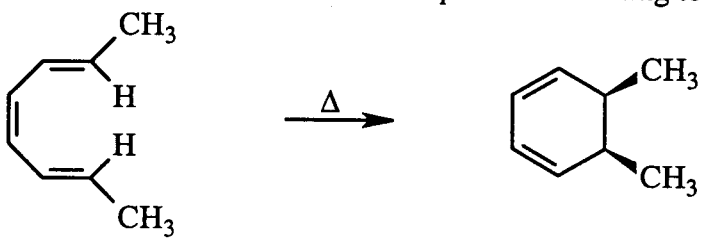


34. Disrotatory ring closure of (2*E*,4*Z*,6*Z*)-octatriene leads to the trans isomer, which can exist as a pair of enantiomers. One enantiomer is formed if the "top lobes" of the *p* orbitals rotate toward one other , and the other enantiomer is formed if the "bottom lobes" of the *p* orbitals rotate toward one other.



(2*E*,4 *Z*,6 *Z*)-octatriene

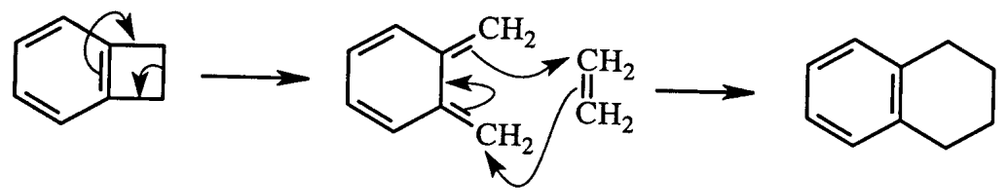
In contrast, disrotatory ring closure of (2*E*,4*Z*,6*E*)-octatriene leads to the cis isomer, which is a meso compound and, consequently, does not have a nonsuperimposable mirror image. Therefore, the same compound is formed from the "top lobes" of the *p* orbitals rotating toward one other and from the "bottom lobes" of the *p* orbitals rotating toward one other.



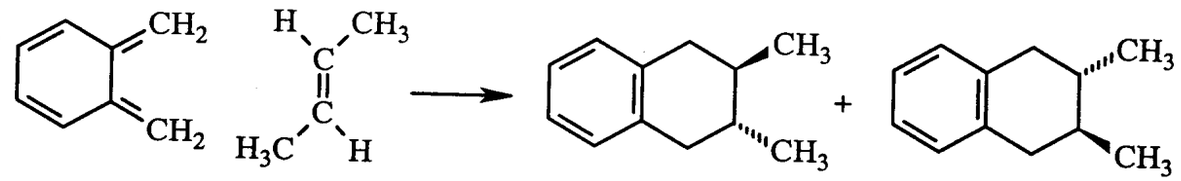
(2*E*,4 *Z*,6 *E*)-octatriene

33.

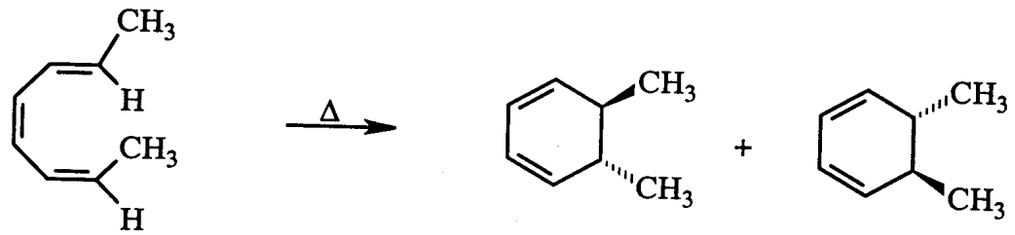
a.



b.

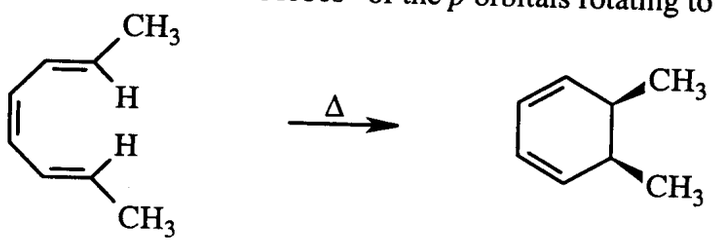


34. Disrotatory ring closure of (2*E*,4*Z*,6*Z*)-octatriene leads to the trans isomer, which can exist as a pair of enantiomers. One enantiomer is formed if the "top lobes" of the *p* orbitals rotate toward one other , and the other enantiomer is formed if the "bottom lobes" of the *p* orbitals rotate toward one other.



(2*E*,4 *Z*,6 *Z*)-octatriene

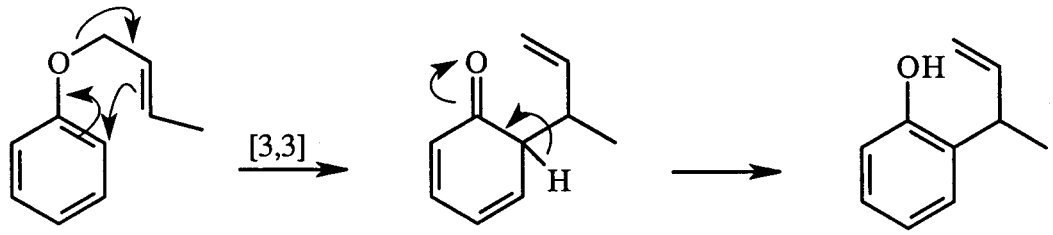
In contrast, disrotatory ring closure of (2*E*,4*Z*,6*E*)-octatriene leads to the cis isomer, which is a meso compound and, consequently, does not have a nonsuperimposable mirror image. Therefore, the same compound is formed from the "top lobes" of the *p* orbitals rotating toward one other and from the "bottom lobes" of the *p* orbitals rotating toward one other.



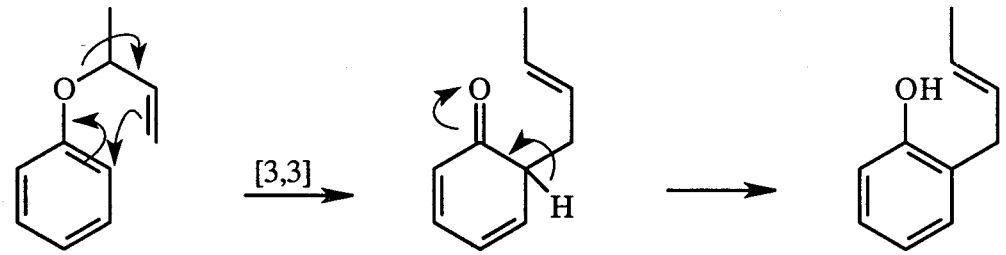
(2*E*,4 *Z*,6 *E*)-octatriene

35.

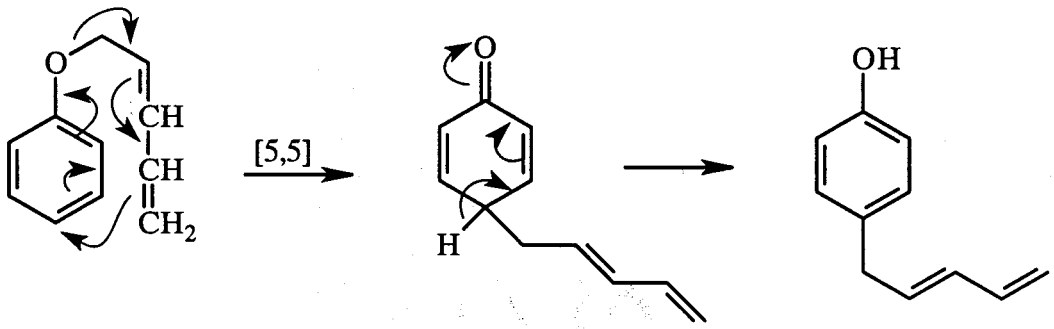
a.



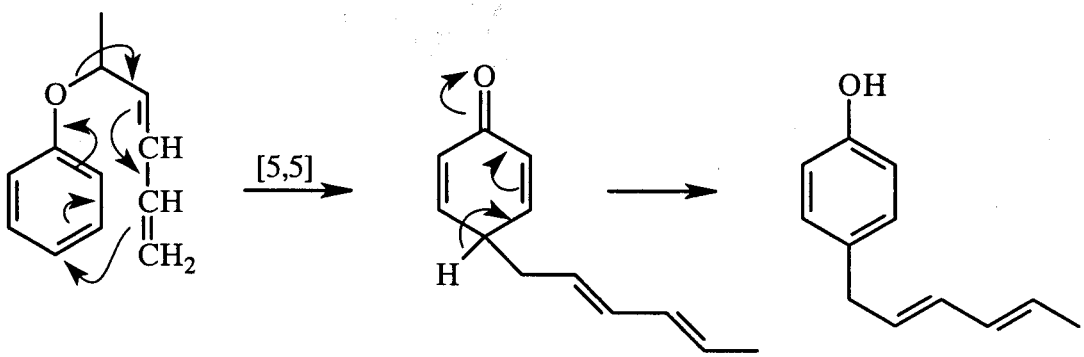
b.



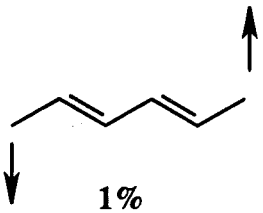
c.



d.

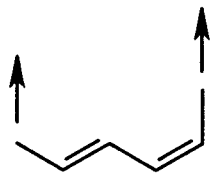


36. Under thermal conditions a compound with two π bonds undergoes conrotatory ring closure. Conrotatory ring closure that results in a ring-closed compound with the substituents cis to one another requires that the substituents point in the same direction in the reactant. Therefore, the product with the methyl substituents pointing in the same direction is obtained in 99% yield.



1%

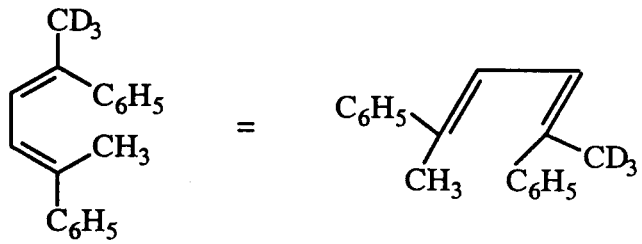
methyl groups point in opposite directions



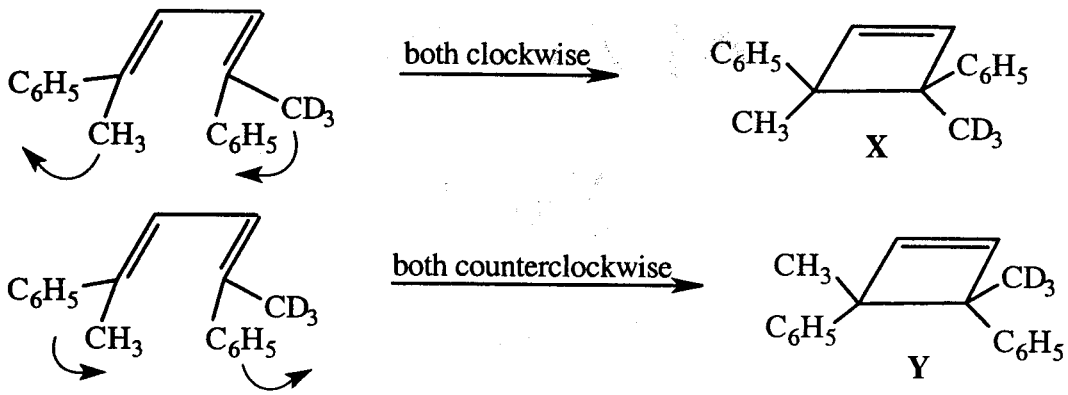
99%

methyl groups point in the same direction

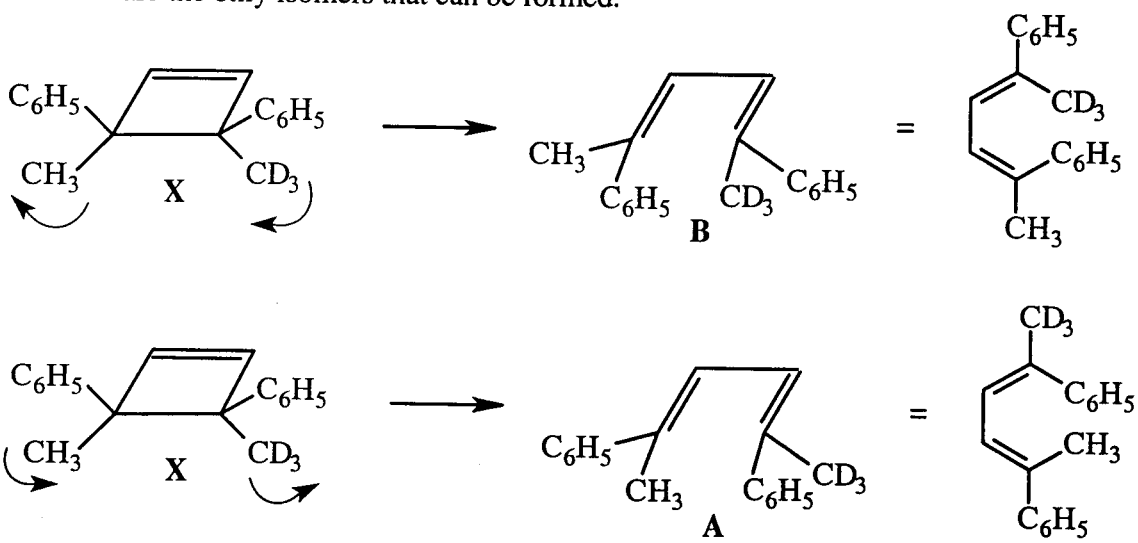
37.

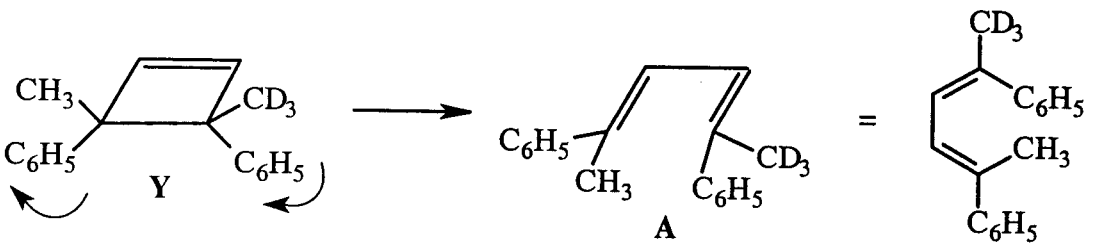


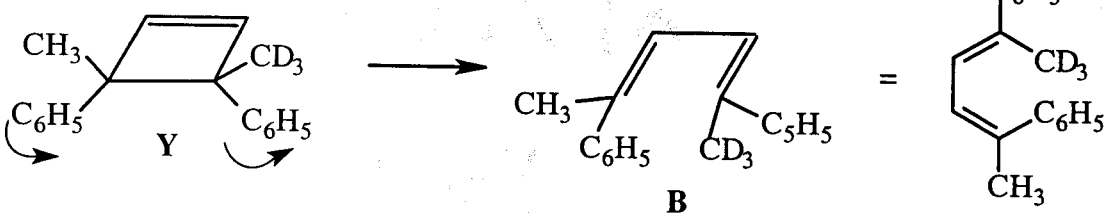
Because the reactant has two π bonds, ring closure is conrotatory.
Two different compounds, **X** and **Y**, can be formed because conrotatory ring closure can occur in either a clockwise or a counterclockwise direction.



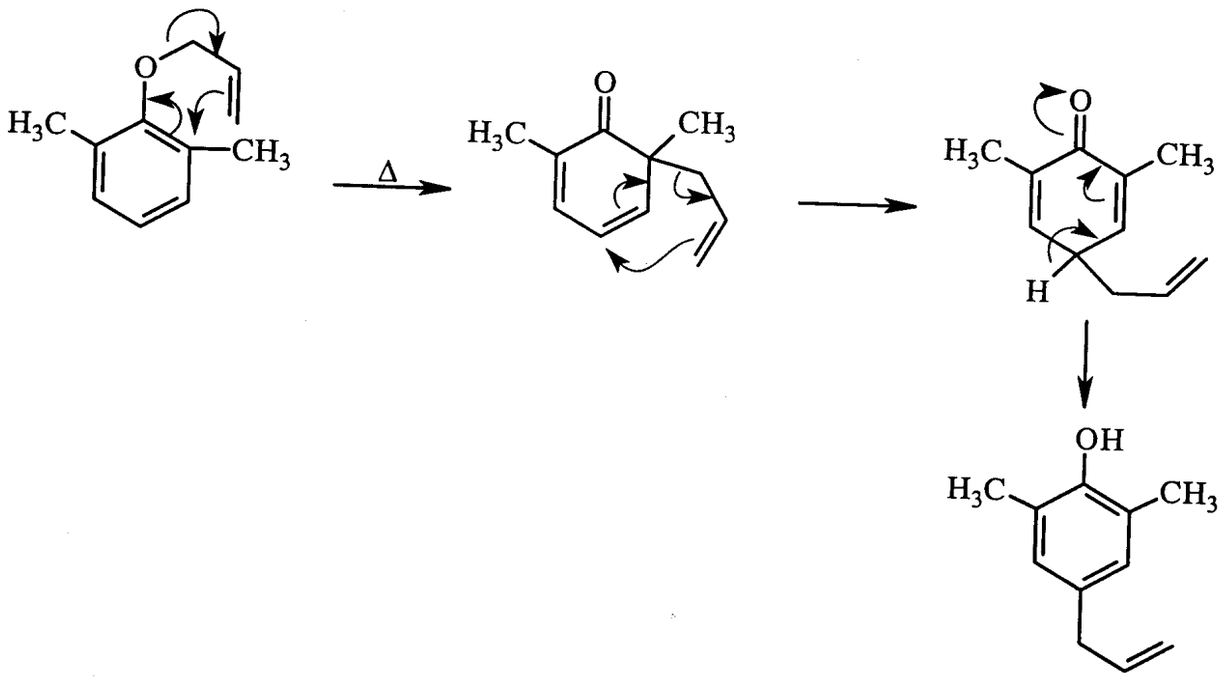
Each of the compounds (**X** and **Y**) can undergo a conrotatory ring-opening reaction in either a clockwise or a counterclockwise direction to form either **A** or **B**.
A and **B** are the only isomers that can be formed.







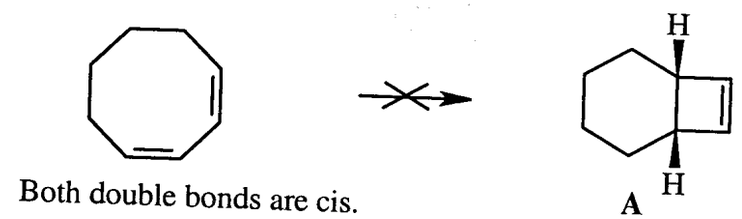
38.



39. Because the compounds that undergo ring closure to give **A** and **B** have two π bonds, ring opening of **A** and **B** under thermal conditions will be conrotatory. Because the hydrogens in **A** and **B** are cis, they must point in the same direction in the ring-opened product. To have the two hydrogens pointing in the same direction, one of the double bonds in the ring-opened compound must be cis and the other must be trans.

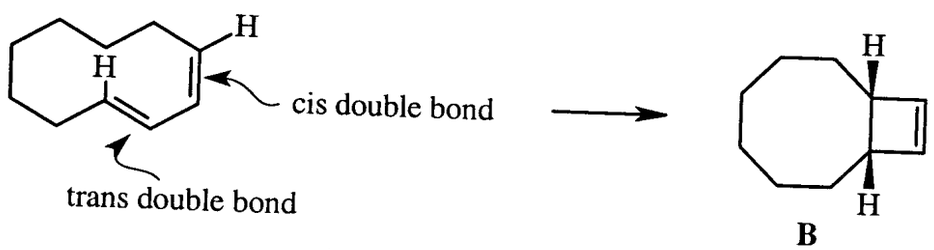
An eight-membered ring is too small to accommodate cojugated double bonds with one cis and the other trans, so **A** will not be able to undergo a ring-opening reaction under thermal conditions.

A ten-membered ring can accommodate a trans double bond, so **B** will be able to undergo a ring-opening reaction under thermal conditions.



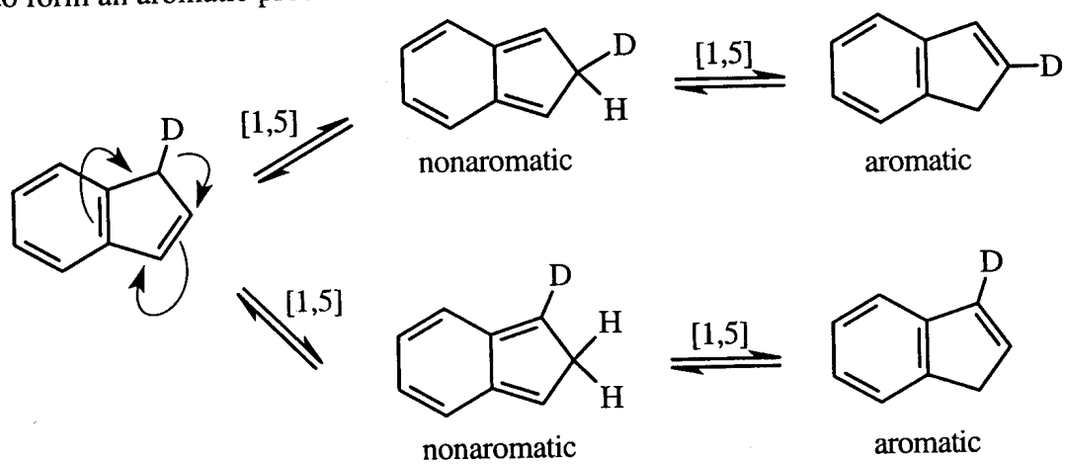
Both double bonds are cis.

A

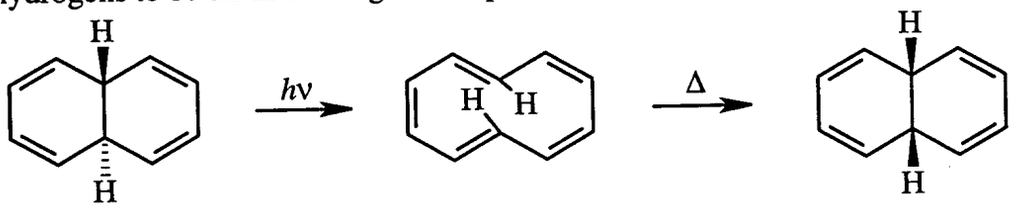


B

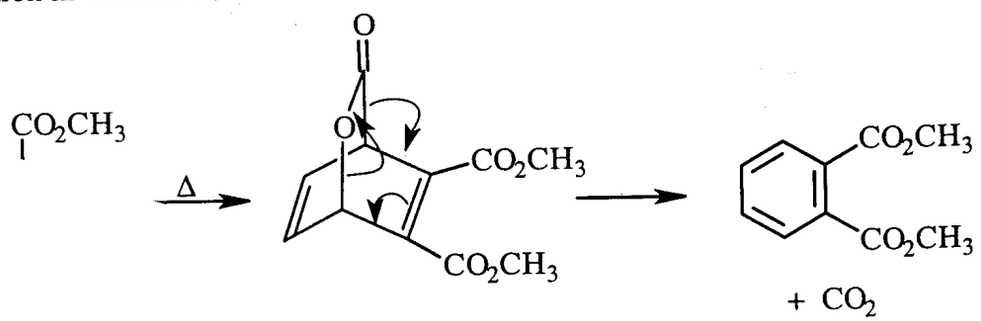
40. The compound undergoes a 1,5-hydrogen shift of D or a 1,5-hydrogen shift of H. In each case, an unstable nonaromatic intermediate is formed that undergoes a subsequent 1,5-hydrogen shift to form an aromatic product.



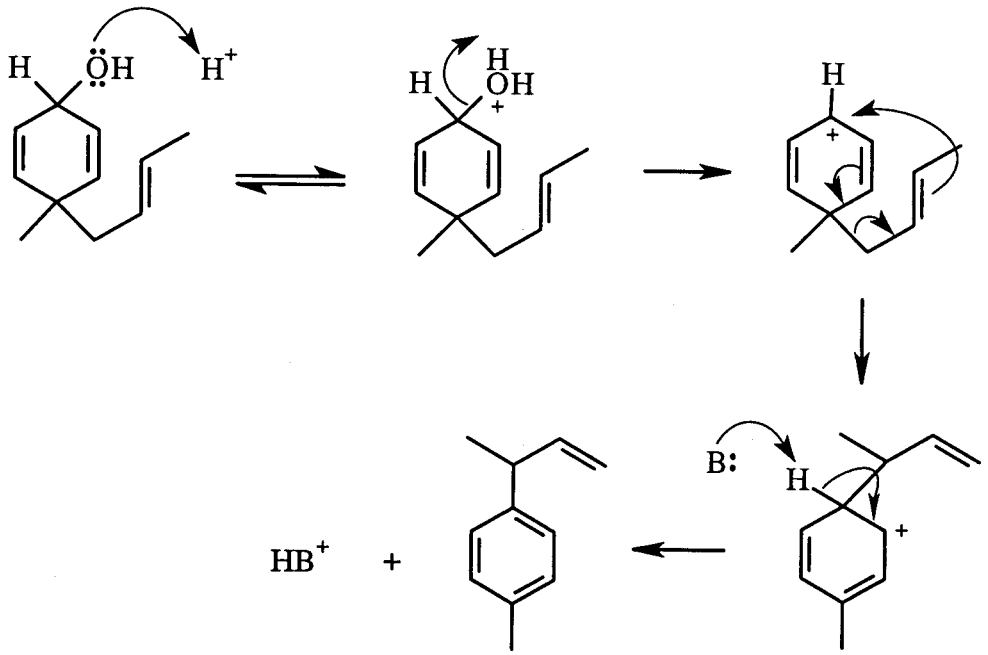
41. Because the reacting system of the ring-opened compound has three conjugated π bonds involved in the reaction, conrotatory ring closure will occur under photochemical conditions, and trans hydrogens require that the hydrogens point in the opposite direction in the ring-opened compound. Thermal ring closure of a three π bond system is disrotatory, and disrotatory ring closure of a compound with hydrogens that point in opposite directions will cause those hydrogens to be cis in the ring-closed product.



42. A Diels-Alder reaction is followed by an extrusion reaction that eliminates CO_2. An extrusion reaction is a reaction in which a neutral molecule is eliminated from a molecule.



43.



CHAPTER 30
The Organic Chemistry of Drugs: Discovery and Design

Important Terms

antiviral drug	a drug that interferes with DNA or RNA synthesis in order to prevent a virus from replicating.
bactericidal drug	a drug that kills bacteria.
bacteriostatic drug	a drug that inhibits the further growth of bacteria.
blind screen (random screen)	the search for a pharmacologically active compound without any information about what chemical structures might show activity.
brand name (proprietary name, trade name)	identifies a commercial product and distinguishes it from other products. It can be used only by the owner of the registered trademark.
combinatorial organic synthesis	the synthesis of a library of compounds by covalently connecting sets of building blocks of varying structure.
distribution coefficient	the ratio of the amount of a compound dissolving in each of two solvents.
drug	a compound that reacts with a biological molecule, triggering a physiological effect.
drug resistance	resistance to a particular drug.
drug synergism	when the effect of two drugs used in combination is greater than the sum of the effects obtained when administered individually.
generic name	a name for a drug that anyone can manufacture.
lead compound	the prototype in a search for other biologically active compounds.
molecular modeling	computer-assisted design of a compound with a structure similar to that of a compound with the desired activity.
molecular modification	changing the structure of a lead compound.
orphan drug	a drug for a disease or condition that affects fewer than 200,000 people.
proprietary name	identifies a commercial product and distinguishes it from other products. It can be used only by the owner of the registered trademark.
quantitative structure-reactivity relationship (QSAR)	the relation between a particular property of a series of compounds and their biological activity.
random screen (blind screen)	the search for a pharmacologically active compound without any information about what chemical structures might show activity.
receptor	the site where a drug binds in order to exert its physiological effect.

suicide inhibitor a compound that inactivates an enzyme by undergoing part of the normal catalytic mechanism.

therapeutic index the ratio of the lethal dose of a drug to the therapeutic dose.

trademark a registered name, symbol, or picture.

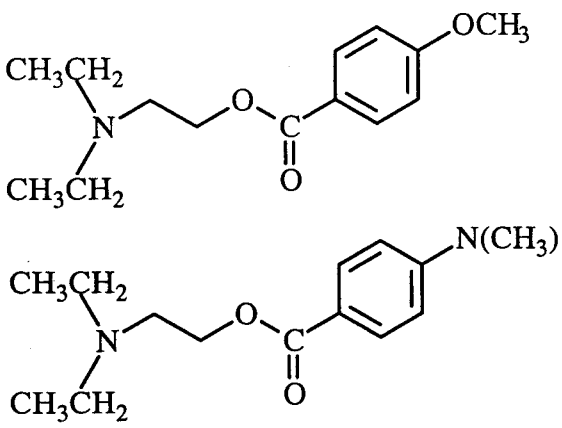
trade name identifies a commercial product and distinguishes it from other products. It can be used only by the owner of the registered trademark.

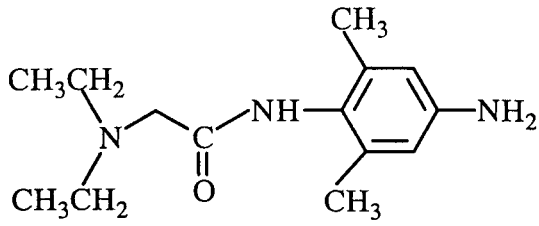
Solutions to Problems

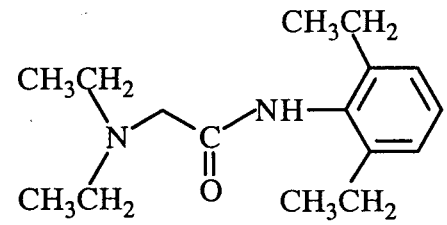
1. **a.** ethyl *para*-aminobenzoate **b.** 2-(*N*,*N*-diethyl)ethyl *para*-aminobenzoate

2.

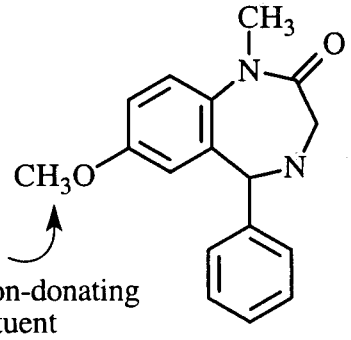
There are many possibilities. The following are just a few of them.



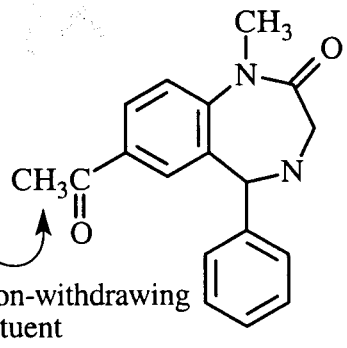




3. The compound on the left has an electron-donating substituent, while the compound on the right has an electron-withdrawing substituent in the same position. Because the compounds known to be effective tranquilizers have an electron-withdrawing substituent in that position (Cl or NO_2), the compound on the right is more likely to show activity as a tranquilizer.



electron-donating substituent

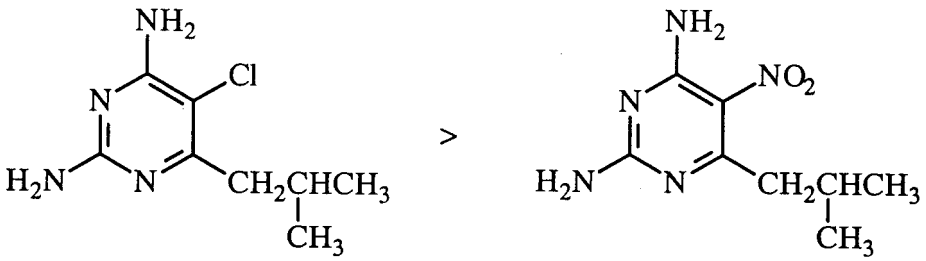


electron-withdrawing substituent

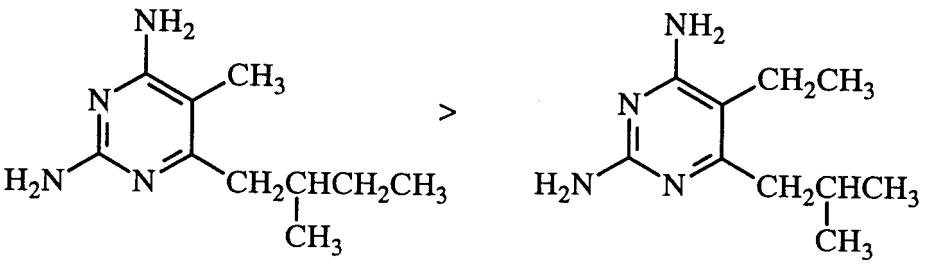
4. Anesthetics have been found to have similar distribution coefficients, which means that they have similar polarities. Since diethyl ether is a known anesthetic, ethyl methyl ether with a polarity similar to that of diethyl ether is more apt to be a general anesthetic than propanol, which is considerably more polar.

5. The electron-withdrawing SO_2 group is weakly basic and, therefore, an excellent leaving group. The weak carbon-sulfur bond aids imine formation.

6. **a.** The chloro-substituted compound would be expected to be a more potent inhibitor because potency increases with the ability of the substituents to donate electrons.



b. The compound with the pentyl substituent would be expected to be a more potent inhibitor because potency increases with increasing hydrophobicity of one of the substituents.



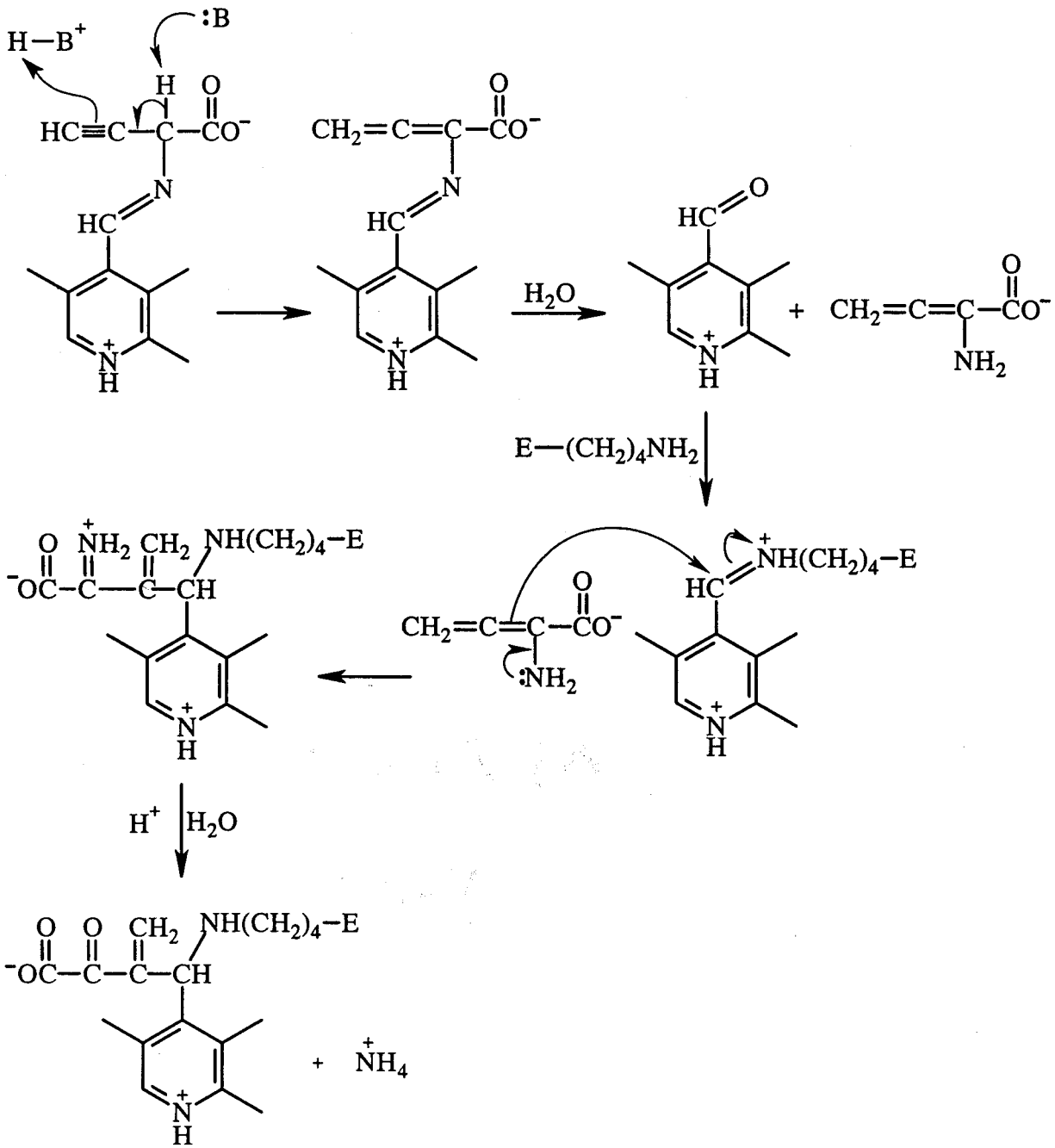
7. Tetrahydrocannabinol is a safer drug because it has a higher therapeutic index.

$$\text{therapeutic index} = \frac{\text{lethal dose}}{\text{therapeutic dose}}$$

$$\text{tetrahydrocannabinol} = \frac{2.0\ \text{g/kg}}{20\ \text{mg/kg}} = \frac{2000\ \text{mg/kg}}{20\ \text{mg/kg}} = 100$$

$$\text{sodium pentothal} = \frac{100\ \text{mg/kg}}{30\ \text{mg/kg}} = 3.3$$

8. Hydrolysis frees the coenzyme and forms a reactive α,β-unsaturated amino acid that can react with the coenzyme bound to its enzyme. This reaction causes the imine linkage to be converted into an amine linkage that cannot be hydrolyzed to release the enzyme. In this way the enzyme is deactivated.



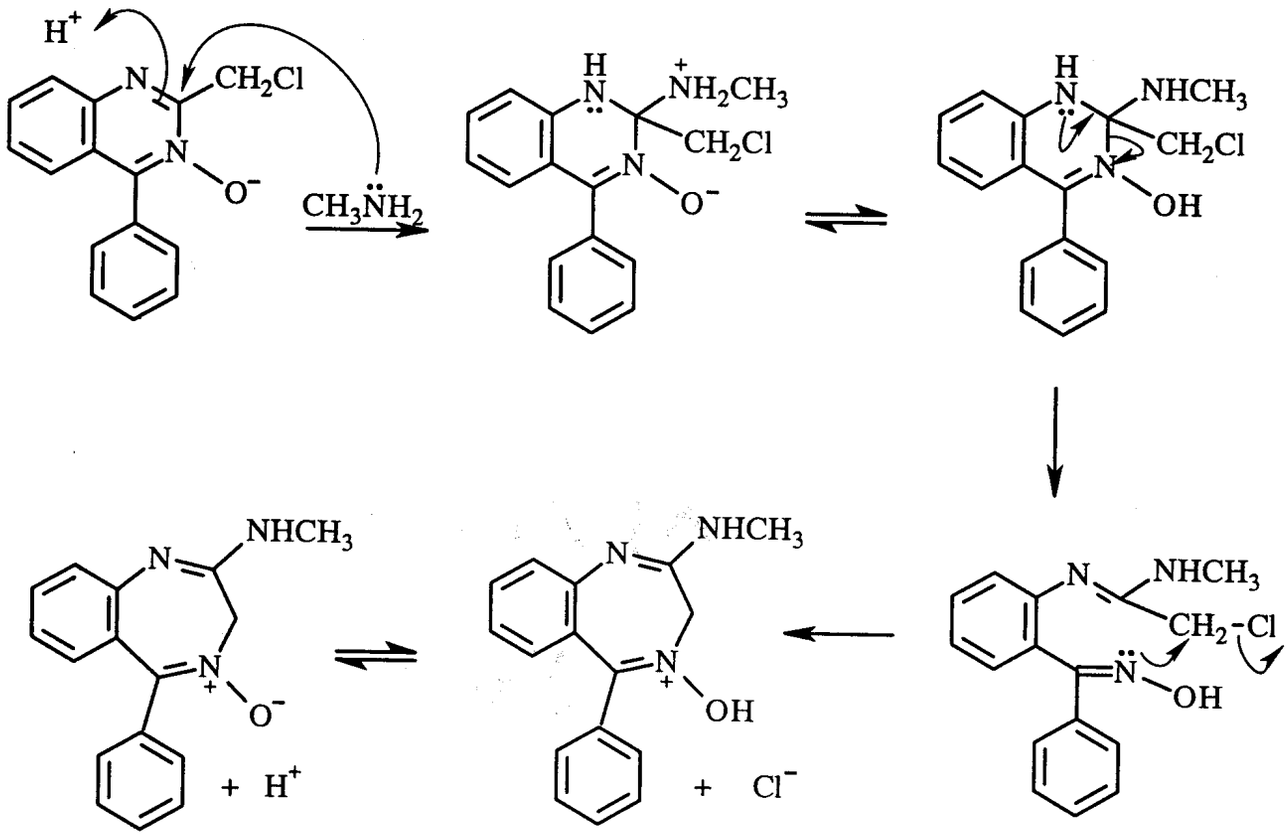
9. Aclovir differs from guanosine in that it has a hydroxy-ether substituent rather than a ribose.

Cytosar differs from cytidine in that it has the 2'-OH group in the β-position.

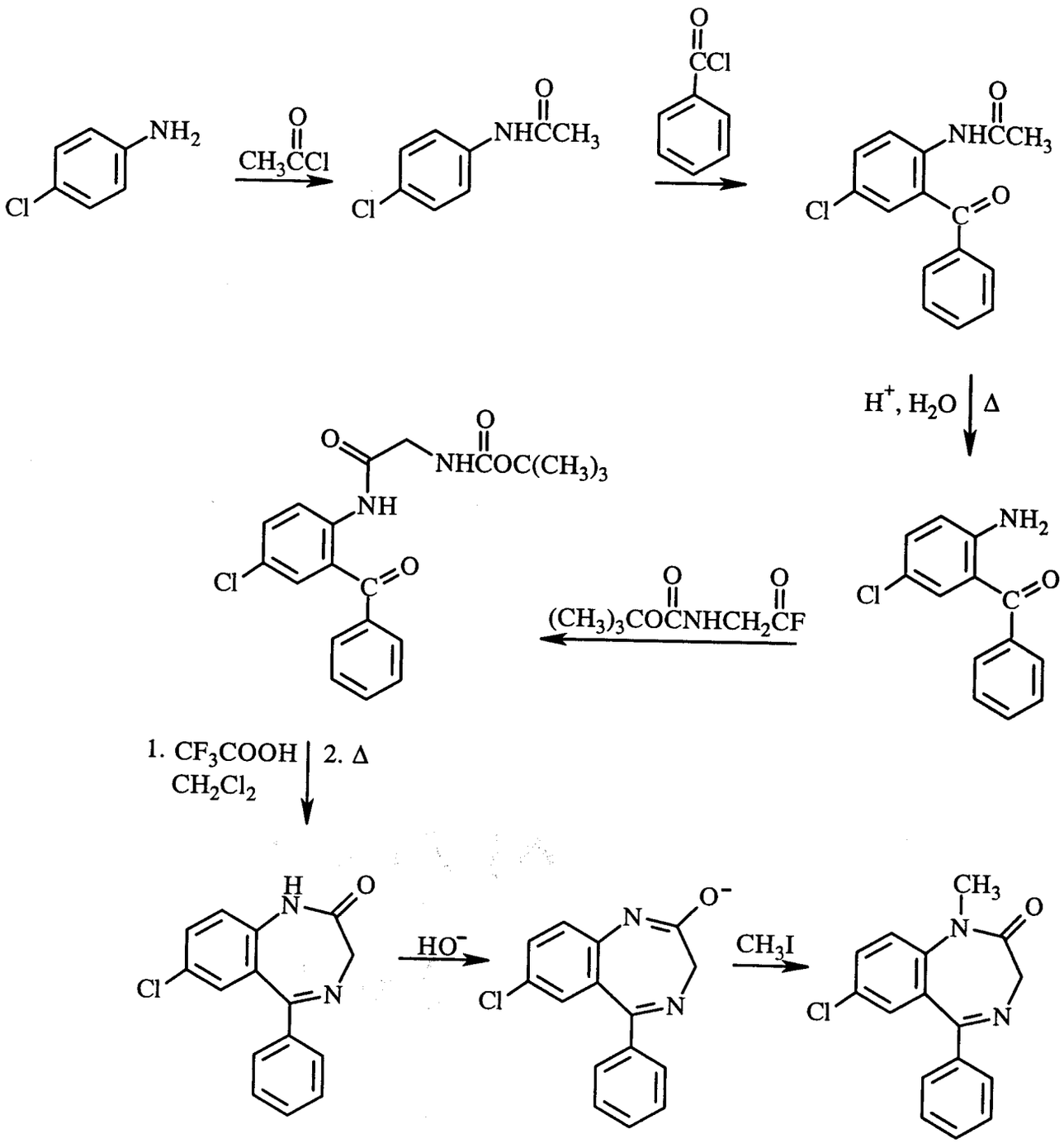
Viramid has an unusual heterocyclic base attached to ribose.

Herplex differs from 2'-deoxyuridine in that it has an iodo substituent in the 5-position.

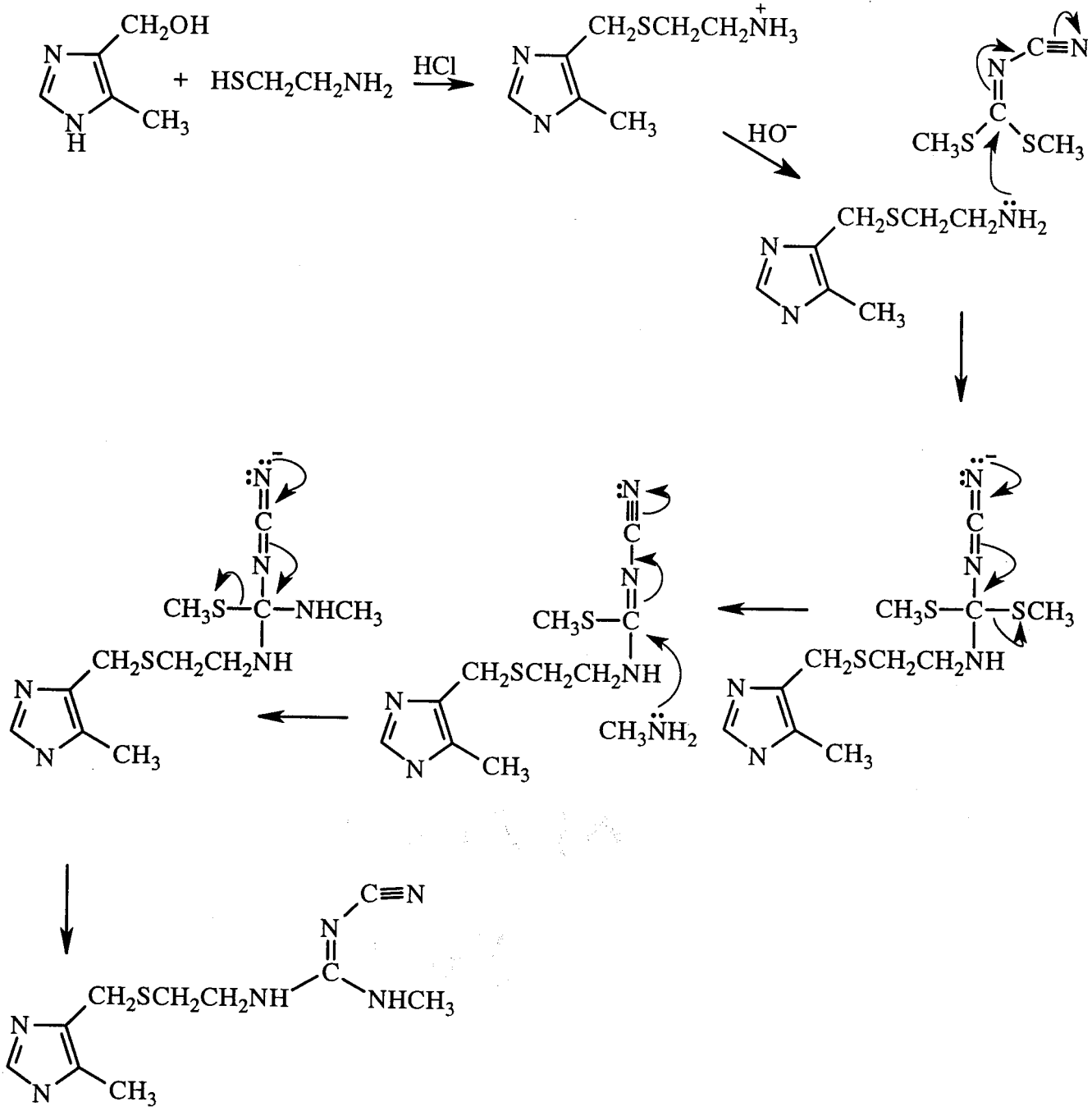
10.



11.


NH2
Cl
CH3CCl
O
NHCCH3
CCl
H+, H2O
Δ
NHCOC(CH3)3
NH
(CH3)3COCNHCH2CF
1. CF3COOH
CH2Cl2
2. Δ
HO-
CH3I
O-
CH3
N

12.

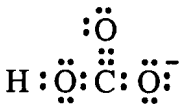


Tagamet

Answers to Chapter 1 Practice Test

1. **a.** HBr **b.** NH_3 **c.** a carbon-fluorine bond **d.** CCl_4

2. $\overset{+}{C}H_3$ sp^2 $\overset{-}{C}H_3$ sp^3 $\overset{\cdot}{C}H_3$ sp^2

3. 

4. CH_3COO^- CH_3CH_2OH CH_3OH $CH_3CH_2\overset{+}{N}H_3$

5. $^+NH_4$ **6.** $^-NH_2$

7. $CH_3CH_2CH_2CH{=}CH_2$ **or** $CH_3CH_2CH{=}CHCH_3$ **or** $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCH{=}CH_2$

8. **a.** $CH_3OH + \overset{+}{N}H_4 \rightleftharpoons CH_3\overset{+}{\underset{H}{O}}H + NH_3$ **b.** reactants

9. **a.** $1s^2\ 2s^2\ 2p_x\ 2p_y$ **b.** $1s^2\ 2s\ 2p_x\ 2p_y\ 2p_z$

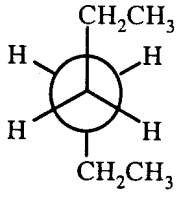
10. $CH_3CH_2\underset{\displaystyle Cl}{\underset{|}{C}}HCOOH$

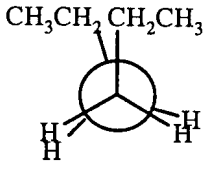
11. $O{=}C{=}O$ (*sp*) $HC(=O)OH$ (*sp*^{2}) $HC{\equiv}N$ (*sp*) CH_3OCH_3 (*sp*^{3}) $CH_3CH{=}CH_2$ (*sp*^{3})

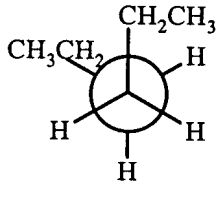
12.
a. A pi bond is stronger than a sigma bond. F
b. A triple bond is shorter than a double bond. T
c. The oxygen-hydrogen bonds in water are formed by the overlap of an sp^2 orbital of oxygen with an *s* orbital of hydrogen. F
d. HO^- is a stronger base than $^-NH_2$. F
e. A double bond is stronger than a single bond. T
f. A tetrahedral carbon has bond angles of 107.5°. F
g. A Lewis acid is a compound that accepts a share in a pair of electrons. T

Answers to Chapter 2 Practice Test

1. 3-methyloctane

2. **a.** 

b. 

c. 

3. **a.** *sec*-butyl chloride, 2-chlorobutane
b. isohexyl alcohol, 4-methyl-1-pentanol
c. cyclopentyl bromide, bromocyclopentane

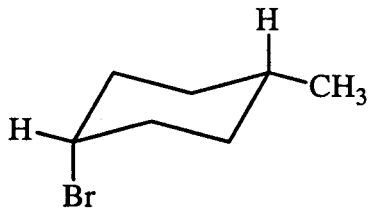
4. a. $CH_3CH_2CH_2CH_2CH_2Br$ (1) $CH_3CH_2CH_2Br$ (3) $CH_3CH_2CH_2CH_2Br$ (2)

b. $CH_3CH_2CH_2CH_2CH_3$ (3) $CH_3CH_2CH_2CH_2OH$ (1) $CH_3CH_2CH_2CH_2Cl$ (2)

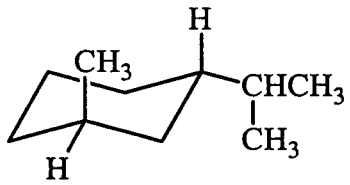
c. $(CH_3)_2C(CH_3)C(CH_3)_3$ (3) $CH_3CH_2CH_2CH_2CH_2CH_2CH_2CH_3$ (1) $CH_3CH(CH_3)CH_2CH_2CH_2CH_2CH_3$ (2)

5.
a. 6-methyl-3-heptanol
b. 3-ethoxyheptane
c. 1-bromo-3-methylcyclopentane
d. 1,4-dichloro-5-methylheptane

6.



7.



8.
a. butyl alcohol
b. 1-butanol
c. hexane
d. pentylamine
e. ethyl alcohol

9.
a. 1-bromo-3-methylbutane
isopentyl bromide
b. 3-methyl-1-butanol
isopentyl alcohol
c. 3-methyl-1-butanamine
isopentylamine

10.
a. a staggered conformer
b. the chair conformer of methylcyclohexane with the methyl group in the equatorial position
c. cyclohexane

11. a. $CH_3CH(Br)CH_3$ **d.** $CH_3CH(CH_3)CH_3$ **e.** $CH_3CH_2CH_2OH$ $CH_3CH(CH_3)OH$ $CH_3CH_2OCH_3$

b. $CH_3CH_2NHCH_3$

c. $CH_3CH(CH_3)CH_3$ **or** $CH_3C(CH_3)_2CH_3$ **or** CH_4 **or** $CH_3C(CH_3)_2C(CH_3)_3$

Answers to Chapter 3 Practice Test

1. a. 4-methyl-1-hexene
b. 4-bromocyclopentene
c. 7-methyl-3-nonene
d. 4-chloro-3-m3thylcyclohexene

2. $-CCH_3$ (O) (2) $-CH=CH_2$ (4) $-Cl$ (1) $-C\equiv N$ (3)

3.
a. 2-pentene
b. 3-methyl-1-hexene
c. 3-methyl-2-pentene
d. 1-methylcyclohexene

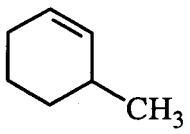
4.

a.	Increasing the energy of activation, increases the rate of the reaction.	F
b.	Decreasing the entropy of the products compared to the entropy of the reactants makes the equilibrium constant more favorable.	F
c.	An exergonic reaction is one with a $-\Delta G°$.	T
d.	An alkene is an electrophile.	F
e.	The higher the energy of activation, the more slowly the reaction will take place.	T
f.	Another name for *trans*-2-butene is *Z*-2-butene.	F
g.	*trans*-2-Butene has a dipole moment of zero.	T
h.	A reaction with a negative $\Delta G°$ has an equilibrium constant greater than one.	T

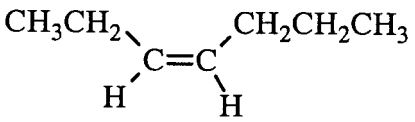
5. **a.** Z **b.** Z

6. **a.** $CH_2{=}CHCH_2OH$

b.



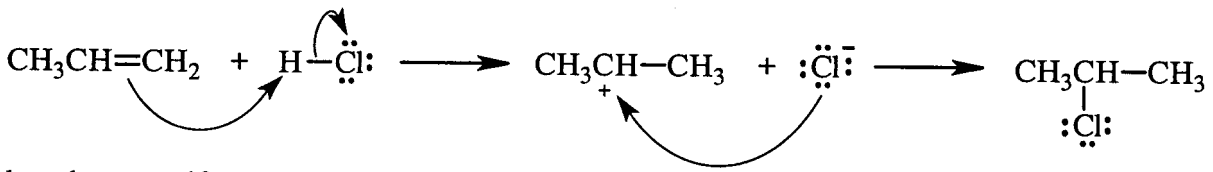
c.



d. $CH_2{=}CHBr$

7. 5

8.



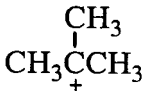
9. b and c

10. **a.** 4 kcal/mol **b.** 35 °C **c.** one reactant forms two products

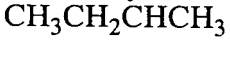
Answers to Chapter 4 Practice Test

1.

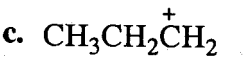
a.



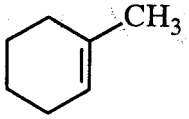
b.



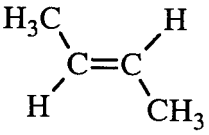
c.



d.



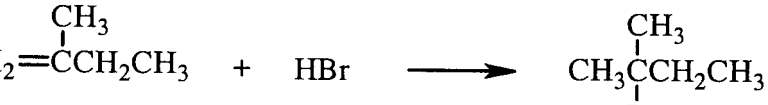
e.



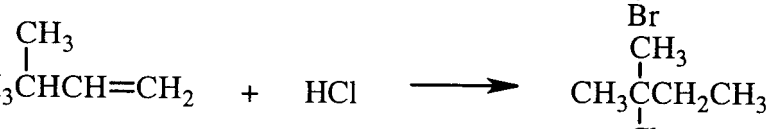
2. $CH_3CH_2CH_2CH{=}CH_2$ **3.** **B**

4.

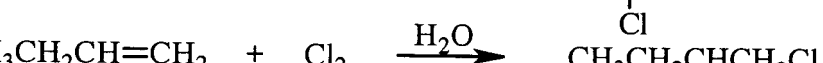
a.



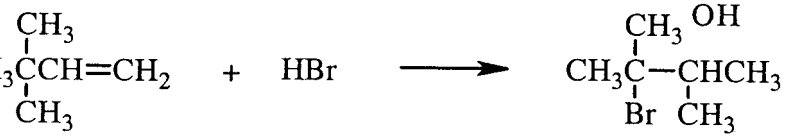
b.



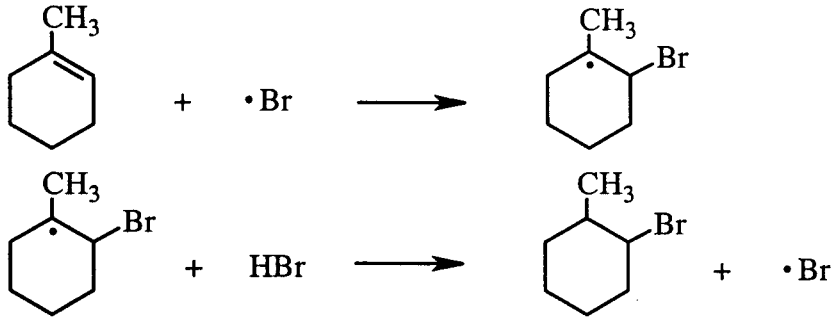
c.



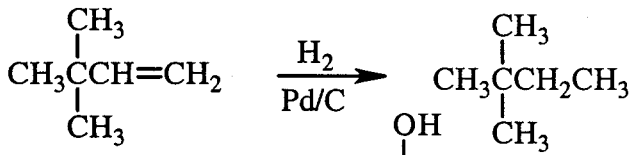
d.



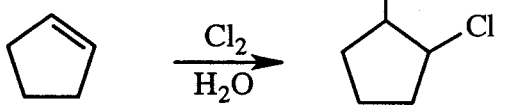
5.



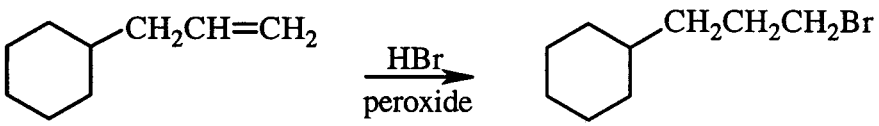
6. a.



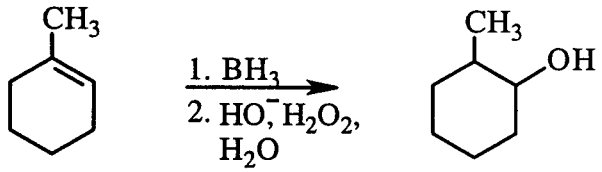
b.



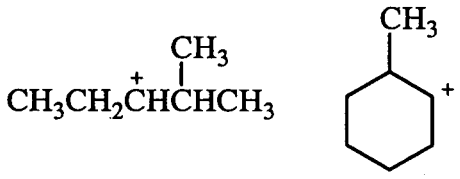
c.



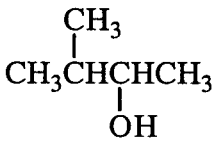
d.



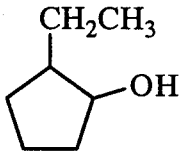
7.



8. a.



b.



9.

a. The addition of Br_2 to 1-butene to form 1,2-dibromobutane is a concerted reaction. F

b. The reaction of 1-butene with HCl will form 1-chlorobutane as the major product if hydrogen peroxide is added to the reaction mixture. F

c. 2,3-Dimethyl-2-pentene is more stable than 3,4-dimethyl-2-pentene. T

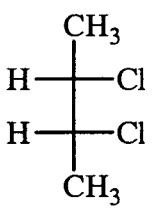
d. The reaction of HBr with 3-methylcyclohexene is more highly regioselective than the reaction of HBr with 1-methylcyclohexe. F

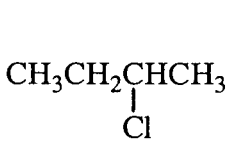
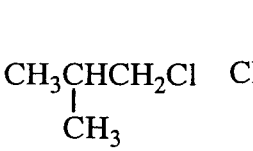
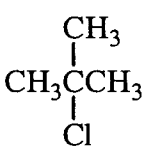
Answers to Chapter 5 Practice Test

1. a pair of enantiomers

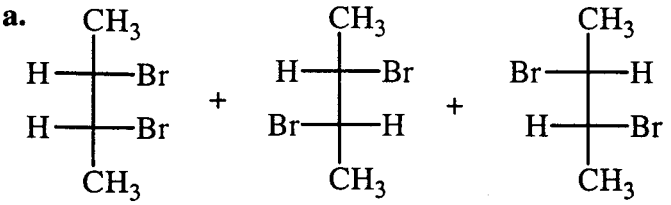
2. -3.0°

3.

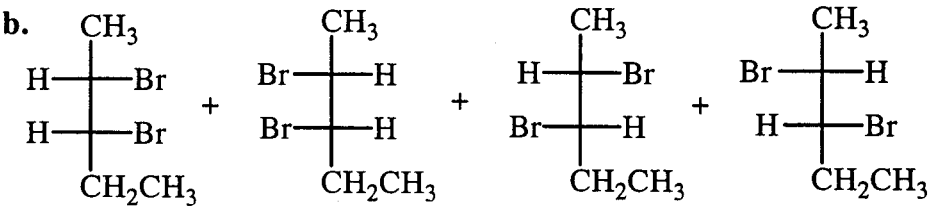


4. $CH_3CH_2CH_2CH_2Cl$   

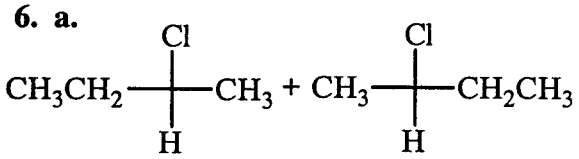
5. a.



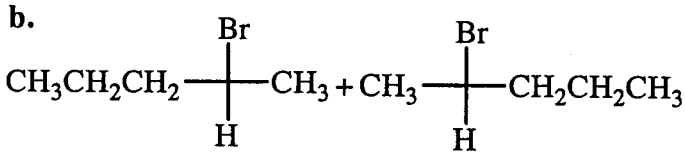
b.



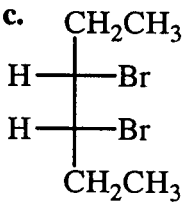
6. a.



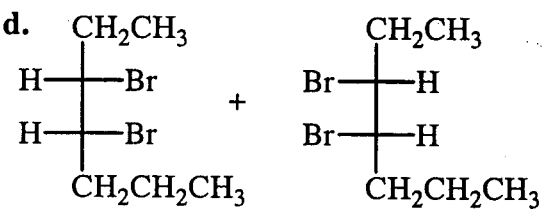
b.



c.

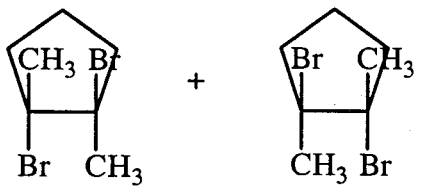


d.

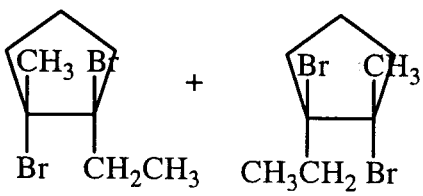


7. (−)-2-Methylbutanoic acid has the *S* configuration.

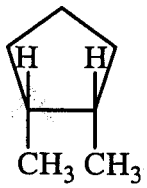
8. a.



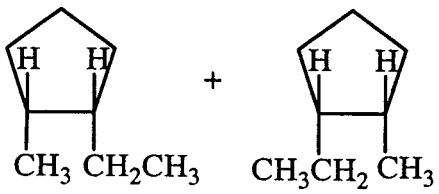
b.



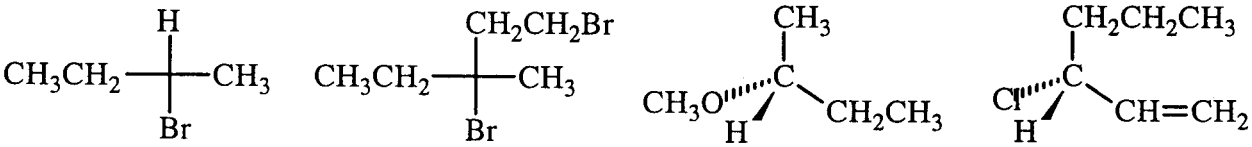
c.



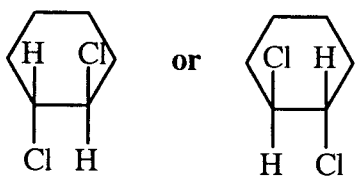
d.



9.



10.

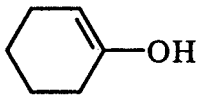


11.
a. Diastereomers have the same melting points. F
b. The addition of HBr to 3-methyl-2-pentene is stereospecific. F
c. The addition of HBr to to 3-methyl-2-pentene is stereoselective. F
d. The addition of HBr to to 3-methyl-2-pentene is regioselective. T
e. Meso compounds do not rotate polarized light. T
f. 2,3-Dichloropentane has a stereoisomer that is a meso compound. F
g. All compounds with the *R* configuration are dextrorotatory. F
h. A compound with three asymmetric carbons can have a maximum of nine stereoisomers. F

Answers to Chapter 6 Practice Test

1. **a.** 1. disiamylborane 2. HO^-, H_2O_2, H_2O

b. H_2/Lindlar catalyst

2. 

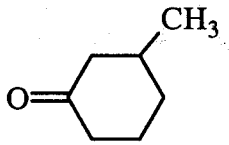
3. $CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HC{\equiv}CCH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_3$

4. **a.** A terminal alkyne is more stable than an internal alkyne. F
b. Propyne is more reactive than propene toward reaction with HBr. F
c. 1-Butyne is more acidic than 1-butene. T
d. An sp^2 hybridized carbon is more electronegative than an sp^3 hybridized carbon. T

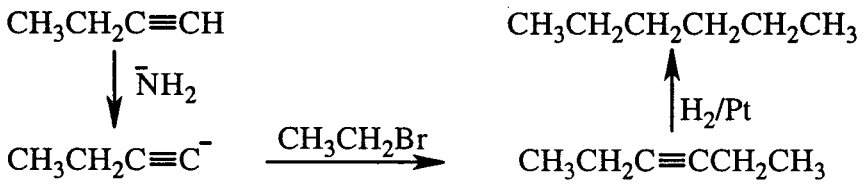
5. 1-bromo-5-methyl-3-hexyne

6. $CH_3CH_2CH_2C{\equiv}CH$

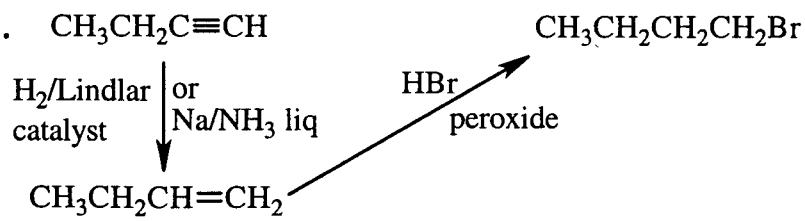
7. NH_3 (3) $CH_3C{\equiv}CH$ (2) CH_3CH_3 (5) H_2O (1) $CH_3CH{=}CH_2$ (4)

8. $CH_3CH_2CH_2\overset{\displaystyle O}{\overset{\|}{C}}CH_2CH_3$ 

9. **a.**

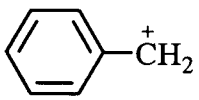


b.



c. $CH_3CH_2C{\equiv}CH$ → ($\bar{N}H_2$) → $CH_3CH_2C{\equiv}C^-$ → (CH_3CH_2Br) → $CH_3CH_2C{\equiv}CCH_2CH_3$ → (H_2O, H_2SO_4) → $CH_3CH_2\overset{O}{\overset{\|}{C}}CH_2CH_2CH_3$

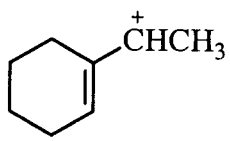
Answers to Chapter 7 Practice Test

1. a. 

b. $CH_3\bar{C}HC{\equiv}CH$

c. $CH_3\bar{C}H\overset{O}{\overset{\|}{C}}CH_3$

d. $CH_2{=}CH\overset{+}{C}H_2$

e. 

2. a. $CH_3CH{=}CH{-}\ddot{\underset{\cdot\cdot}{O}}CH_3 \longleftrightarrow CH_3\bar{C}H{-}CH{=}\overset{+}{O}CH_3$

b. $CH_3CH{=}CH{-}CH{=}CH{-}\overset{+}{C}H_2 \longleftrightarrow CH_3CH{=}CH{-}\overset{+}{C}H{-}CH{=}CH_2$

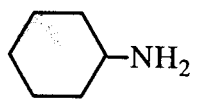
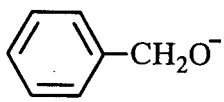
$\updownarrow$

$CH_3\overset{+}{C}H{-}CH{=}CH{-}CH{=}CH_2$

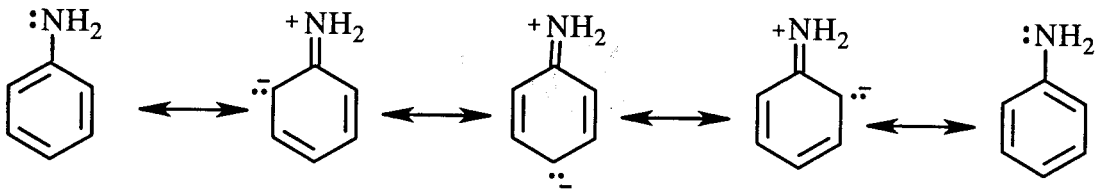
c. $\bar{C}H_2{-}CH{=}CH{-}\overset{O}{\overset{\|}{C}}H \longleftrightarrow CH_2{=}CH{-}\bar{C}H{-}\overset{O}{\overset{\|}{C}}H \longleftrightarrow CH_2{=}CH{-}CH{=}\overset{O^-}{\overset{|}{C}}H$

3. $CH_3\overset{CH_3}{\overset{|}{\underset{+}{C}}}CH_2CH{=}CH_2$ $CH_2{=}CHCH_2CH{=}CH_2$ $CH_3CH_2NHCH_2CH{=}CHCH_3$ 

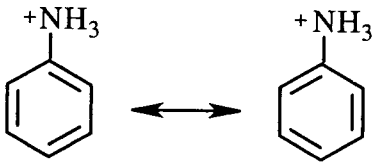
4. c. $CH_3\overset{O}{\overset{\|}{C}}OH$ and $CH_3\overset{O^-}{\overset{|}{C}}{=}\overset{+}{O}H$

5.  

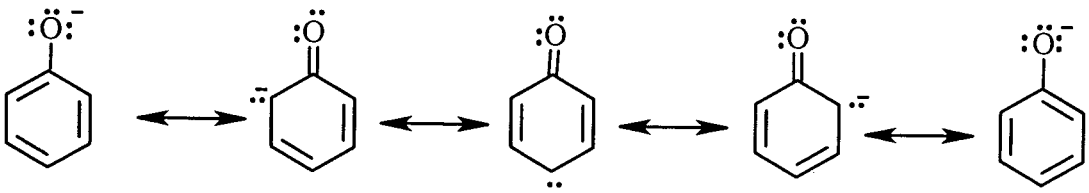
6. a.

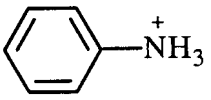


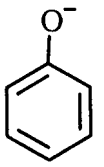
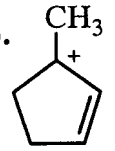
b.



c.



7. a.  **b.** $CH_3CH{=}CH_2$ **c.** 

8. a.  **b.** 

9. Indicate whether the following statements is true or false:

a. A compound with four conjugated double bonds will have four molecular orbitals. F

b. ψ_1 and ψ_2 are symmetric molecular orbitals. F

c. If ψ_3 is the HOMO in the ground state, ψ_4 will be the HOMO in the excited state. T

d. If ψ_3 is the LUMO, ψ_4 will be the HOMO. F

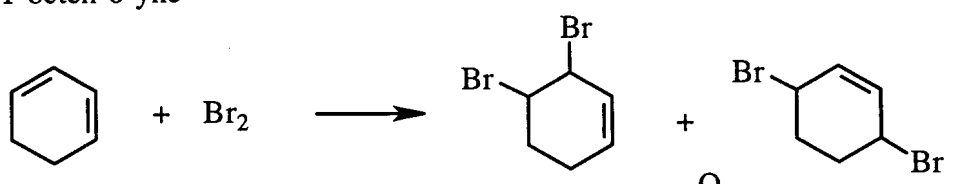
e. If the ground-state HOMO is symmetric, the ground-state LUMO will be asymmetric. T

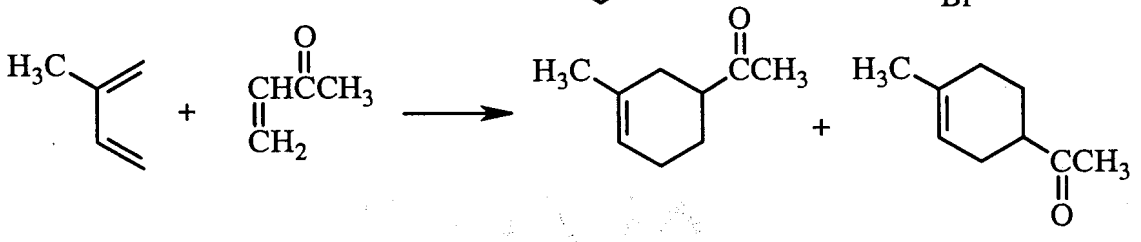
10. $CH_3CH{=}CH\overset{+}{C}HCH_3 > CH_3CH{=}CH\overset{+}{C}HCH_3 > CH_3CH{=}CH\overset{+}{C}H_2 > CH_3CH{=}CH\overset{+}{C}HCH_2$

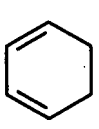
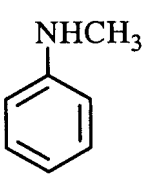
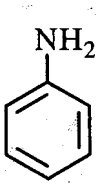
Answers to Chapter 8 Practice Test

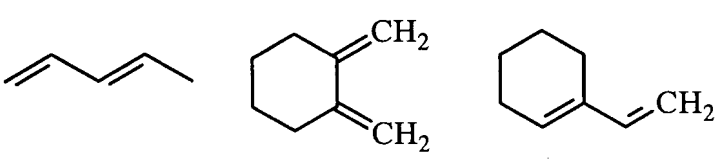
1. **a.** 5-chloro-1,3-cyclohexadiene **c.** 4-methyl-2-cyclohexen-1-ol

b. 1-octen-6-yne

2. a. 

b. 

3. a.  **b.**  **c.** 

4. 

5. molar absorbtivity = 19.7

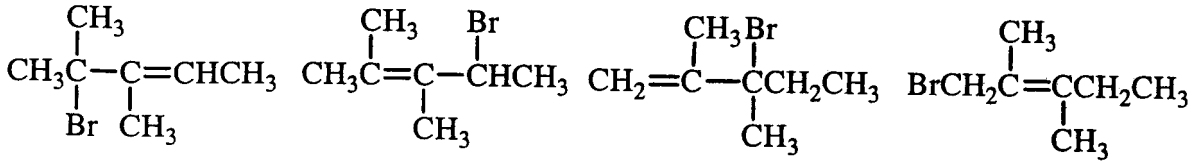
6. **a.** A conjugated diene is more stable than an isomeric isolated diene. T

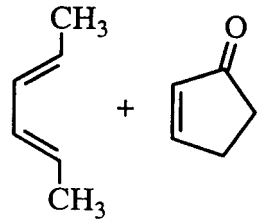
b. A single bond formed by an sp^2—sp^2 overlap is longer than a single bond formed by an sp^2—sp^3 overlap. F

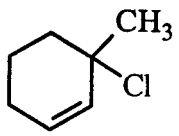
c. The thermodynamically controlled product is the major product obtained when the reaction is carried out under mild conditions. F

d. 1,3-Hexadiene is more stable than 1,4-hexadiene. T

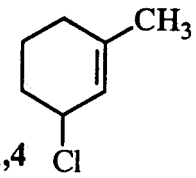
e. A chromophore that exhibits both $n \rightarrow \pi^*$ and $\pi \rightarrow \pi^*$ transitions will have the $n \rightarrow \pi^*$ transition at a longer wavelength. T

7. 

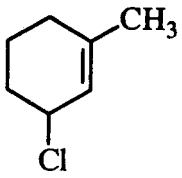
8. 

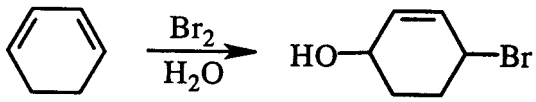
9. a. 

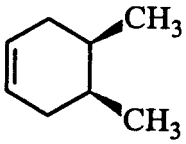
1,2

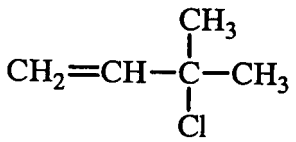


1,4

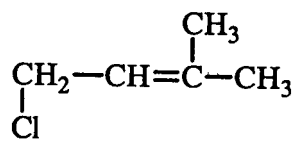
b. 

10. 

11. 

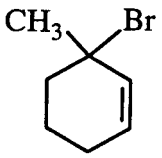
12. a. 

product of kinetic control

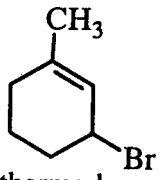


product of thermodynamic control

13. 6.3×10^{-4} M

b. 

product of kinetic control

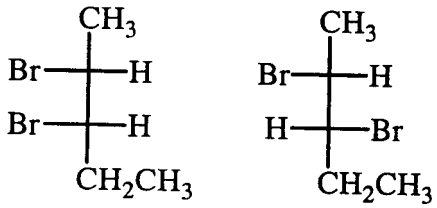


product of thermodynamic control

Answers to Chapter 9 Practice Test

1. 3

2. $CH_3CH_3 + {}^{\bullet}Cl \longrightarrow CH_3\dot{C}H_2 + HCl$

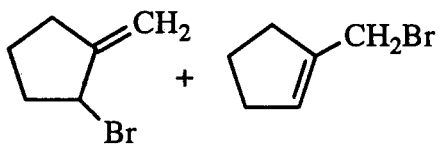
3. 

4. $CH_3CH_3 + Cl^{\bullet} \longrightarrow CH_3\dot{C}H_2 + HCl \quad \Delta H^\circ = 101 - 103 = -2$

$CH_3\dot{C}H_2 + Cl_2 \longrightarrow CH_3CH_2Cl + Cl^{\bullet} \quad \Delta H^\circ = 58 - 85 = -27$

5. $\overset{\bullet}{C}H_2CH_2CH_2CH{=}CH_2$ (3) $\quad CH_3CH_2\overset{\bullet}{C}HCH{=}CH_2$ (1)

$CH_3CH_2CH_2CH{=}\overset{\bullet}{C}H$ (4) $\quad CH_3\overset{\bullet}{C}HCH_2CH{=}CH_2$ (2)

6. a. 

b. $CH_3\underset{\displaystyle Br}{\underset{|}{C}}HCH{=}CH_2 + CH_3CH{=}CHCH_2Br$

7. a. $CH_3CCH_2CH_2CHCH_3$ (CH₃ on C2, CH₃ on C5, CH_2Cl on C2)

$CH_3C(CH_3)(Cl)$—$CHCH_2CHCH_3$ (CH₃ on C5)

$CH_3CCH_2CHCHCH_3$ (CH₃ on C2, Cl on C3, CH₃ on C4)

$CH_3CCH_2CH_2CCH_3$ (CH₃ on C2, CH₃ on C5, Cl on C5)

$CH_3CCH_2CH_2CHCH_2Cl$ (CH₃ on C2, CH₃ on C5, CH_2Cl on C6)

b. $CH_3CCH_2CH_2CHCH_3$ (CH_2Cl on C2)

c. $CH_3CCH_2CH_2CCH_3$ (CH₃ on C2, CH₃ on C5, Br on C5)

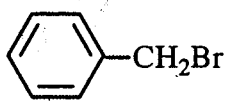
8. 23%

Answers to Chapter 10 Practice Test

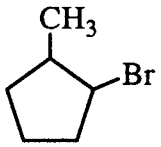
1. a. $CH_3CH_2CH_2CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HBr$

b. $CH_3CH{=}CH\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$

2. a. $CH_3CH_2\underset{\displaystyle CH_3}{\underset{|}{C}}HBr$

b. 

3. $CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}H\underset{\displaystyle Br}{\underset{|}{C}}HCH_3$



4.

a. Increasing the concentration of the nucleophile favors an S_N1 reaction over an S_N2 reaction. F

b. Ethyl iodide is more reactive than ethyl chloride in an S_N2 reaction. T

c. In an S_N1 reaction, the product with the retained configuration is obtained in greater yield. F

d. The rate of a substitution reaction in which none of the reactants is charged will increase if the polarity of the solvent is increased. T

e. An S_N2 reaction is a two-step reaction. F

f. The pK_a of a carboxylic acid is greater in water than it is in a mixture of dioxane and water. F

5. **a.** CH_3O^- **b.** CH_3S^-

6. **a.** $CH_3CH_2CH_2Cl + HO^-$

b. $CH_3CH_2CH_2I + HO^-$

c. $CH_3CH_2CH_2Br + HO^-$

d. $CH_3\underset{\underset{Br}{|}}{C}HCH_3 \xrightarrow[CH_3OH]{CH_3O^-}$

e. $BrCH_2CH_2CH_2CH_2NHCH_3$

7. All are aprotic solvents except ethanol.

8. **a.** The rate of the reaction would increase.

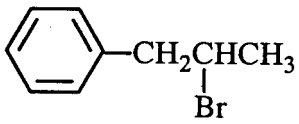
b. The rate of the reaction would increase.

c. The rate of the reaction would decrease.

d. The pK_a would decrease.

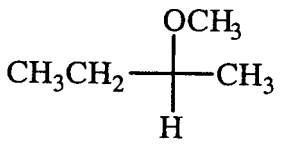
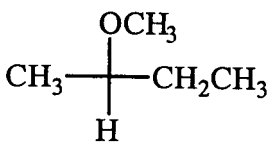
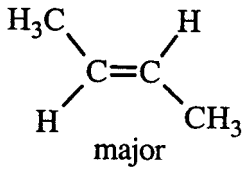
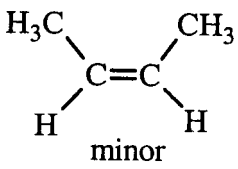
e. The pK_a would decrease.

Answers to Chapter 11 Practice Test

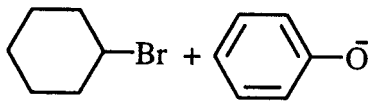
1. **a.** 

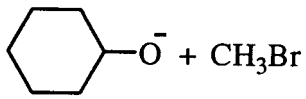
b. $CH_2{=}CHCH_2\underset{\underset{Br}{|}}{C}HCH_3$

2. $CH_3\underset{\underset{CH_3}{|}}{C}HBr$

3. 


major

minor

4. **a.** $CH_3CH_2\underset{\underset{CH_3}{|}}{\overset{\overset{CH_3}{|}}{C}}O^- + CH_3CH_2CH_2Br$

b. 

c. 

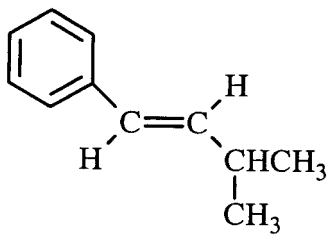
5. **a.** $CH_3\underset{\underset{Cl}{|}}{C}HCH_3 + HO^-$

b. $CH_3CH_2CH_2I + HO^-$

c. $CH_3CH_2CH_2Br + HO^-$

d. $CH_3\underset{\underset{Br}{|}}{C}HCH_3 \xrightarrow[CH_3OH]{CH_3O^-}$

e. $CH_3\underset{\underset{Br}{|}}{\overset{\overset{CH_3}{|}}{C}}CH_3 + HO^-$

6. **a.** 

b. 

c. $CH_3CH{=}\overset{\overset{CH_3}{|}}{C}CH_3$

d. $CH_2{=}\overset{\overset{CH_3}{|}}{C}HCH_3$

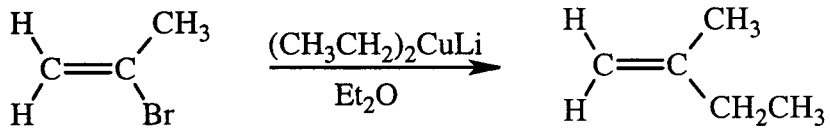
7. **a.** *cis*-1-bromo-2-methylcyclohexane

b. The cis and trans isomers react at about the same rate.

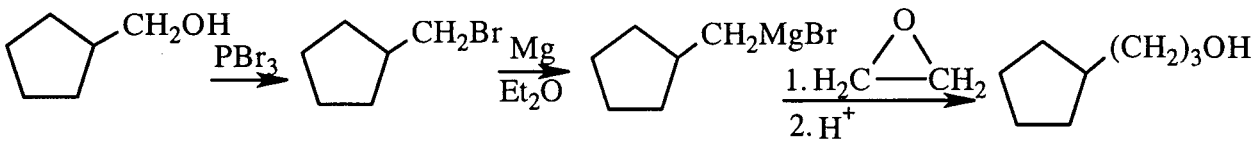
Answers to Chapter 12 Practice Test

1. HBr **2.** $SOCl_2$

3. a.



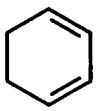
b.



4. 2,2-diethyloxirane or 1,2-epoxy-2-ethylbutane

5. a. $HOCH_2C(CH_2CH_3)(OCH_3)CH_2CH_3$ **b.** $CH_3OCH_2C(CH_2CH_3)(OH)CH_2CH_3$

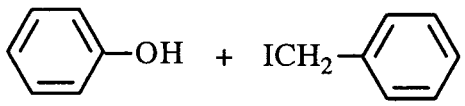
6. a. $CH_3CH_2C(CH_3)=CCH_3(CH_3)$ **b.** $CH_3CH_2CH_2C(CH_3)=CCH_3(CH_3)$ **c.** $CH_3CH_2CH=CHCH_3$ **d.**



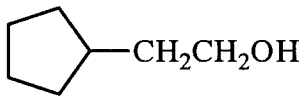
7.

a. Tertiary alcohols are easier to dehydrate than secondary alcohols.	T
b. Alcohols are more acidic than thiols.	F
c. Alcohols have higher boiling points than thiols.	T

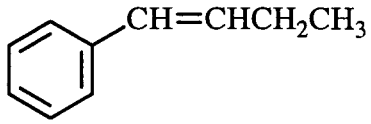
8. a. $CH_3CH_2C(CH_3)(CH_3)—I + CH_3OH$ **b.**



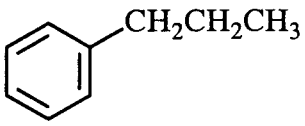
9. a. $CH_3CH_2CH_2CH_2CH_2OH$ **b.**



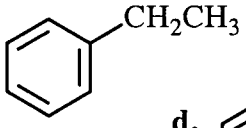
10. a.



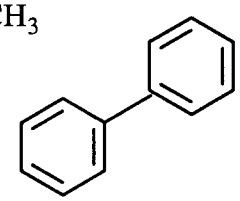
b.



c.



d.



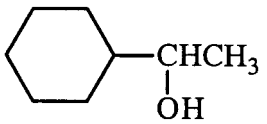
Answers to Chapter 13 Practice Test

1.

a. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}H$ ~2700 cm^{-1}

b. $CH_3CH_2\overset{O}{\overset{\|}{C}}NH_2$ ~3300 cm^{-1}

c. $CH_3CH_2CH_2CH_2OH$ ~3600-3200 cm^{-1}

d.  ~1380 cm^{-1}

e. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_3$ ~1050 or ~1250 cm^{-1}

f. $CH_3CH_2CH{=}CHCH_3$ ~1600 cm^{-1}, ~3100 cm^{-1} $\quad$ $CH_3CH_2C{\equiv}CCH_3$ ~2100 cm^{-1}

g. $CH_3CH_2C{\equiv}CH$ ~3300 cm^{-1}

2.

a. The O-H stretch of a concentrated solution of an alcohol occurs at a higher frequency than the O-H stretch of a dilute solution. F

b. Light of 2 μm is of higher energy than light of 3 μm. T

c. It takes more energy for a bending vibration than for a stretching vibration. F

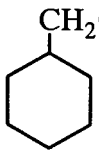
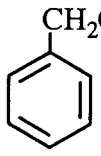
d. Propyne will not have an absorption band at 3100 cm^{-1} because there is no change in the dipole moment. F

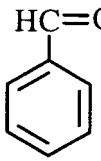
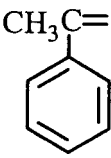
e. Light of 8 μm has the same energy as light of 1250 cm^{-1}. T

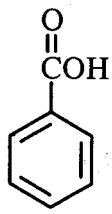
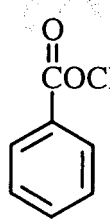
f. The M + 2 peak of an alkyl chloride is half the height of the M peak. F

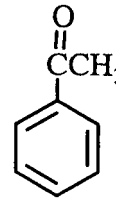
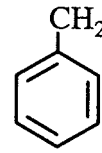
3. $CH_3CH_2\overset{\overset{CH_3}{|}}{\underset{\underset{OH}{|}}{C}}CH_2CH_2CH_3$

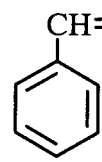
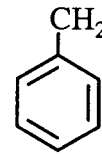
4.

a.   ~ 3100 cm^{-1}, ~ 1500 cm^{-1}

b.  ~ 2700 cm^{-1}  ~ 2900 cm^{-1}, ~ 1380 cm^{-1}

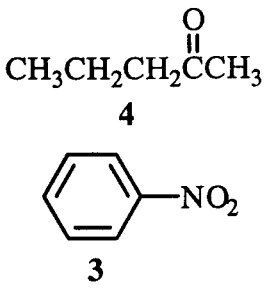
c.  ~ 3300-2500 cm^{-1}  ~ 2900 cm^{-1}, ~ 1380 cm^{-1}, ~ 1050 cm^{-1}

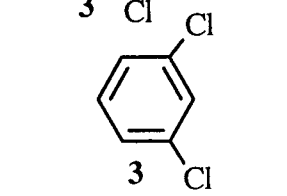
d.  ~ 1700 cm^{-1}  ~ 1050 cm^{-1}

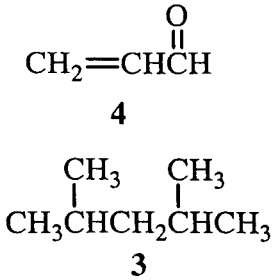
e.  ~ 3100 cm^{-1}  ~ 2900 cm^{-1}, ~ 1380 cm^{-1}

Answers to Chapter 14 Practice Test

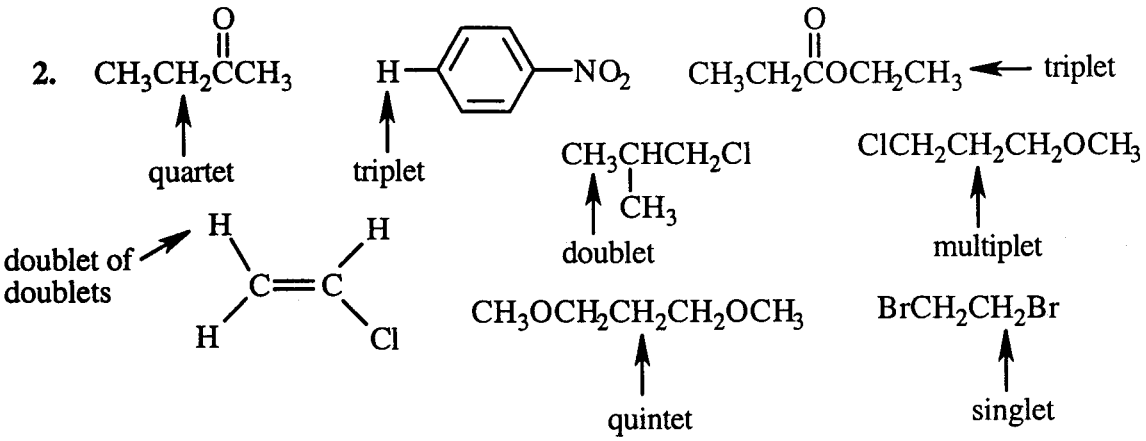
1.



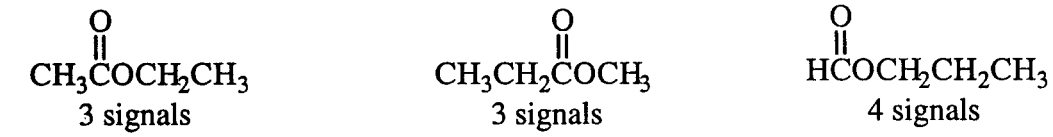




2.



3.



The signal at the highest frequency (farthest downfield) is a quartet.

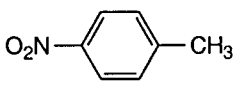
The signal at the highest frequency (farthest downfield) is a signal.

4.

a. The peaks on the right of an NMR spectrum are deshielded compared to the peaks on the left. F

b. Dimethyl ketone has the same number of signals in its ^{1}H NMR spectrum as in its ^{13}C NMR spectrum. F

c. In the ^{1}H NMR spectrum of the compound shown below, the signal farthest upfield is a singlet and the signal farthest downfield is a doublet. T



d. The greater the frequency of the signal, the greater its chemical shift in ppm. T

5. **a.** $CH_3CH_2CH_2Cl$ — triplet, 3 signals

b. $CH_3CH_2\overset{O}{\overset{\|}{C}}OCH_3$ — singlet, 4 signals

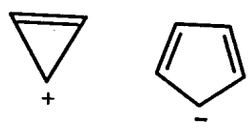
c. $CH_3\underset{Br}{\overset{\text{doublet}}{CH}}CH_3$ — 2 signals

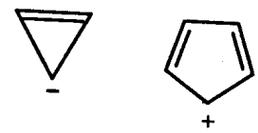
6. **a.** $CH_3CH_2CH_2Cl$ — 3 signals, triplet

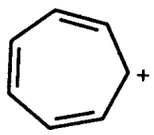
b. $CH_3CH_2\overset{O}{\overset{\|}{C}}OCH_3$ — 4 signals, quartet

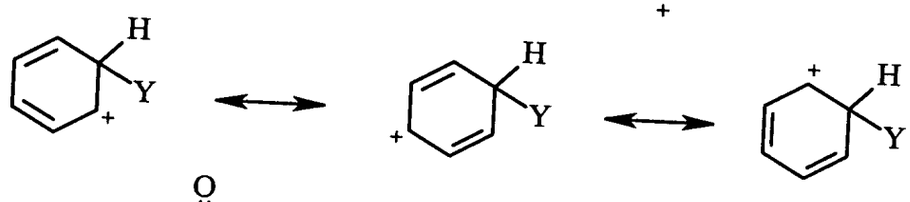
c. $CH_3\underset{Br}{CH}CH_3$ — 3 signals, doublet

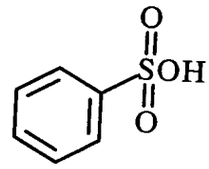
Answers to Chapter 15 Practice Test

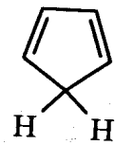
1. 

2. 

3. 

4. 

5. 



6. $CH_3CH_2CH_2CH_2Cl$

$CH_3CH=CHCH_3$

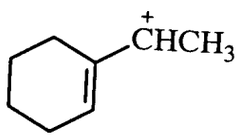
$CH_3CH_2CH_2CH_2OH$

$CH_3CH_2\underset{Cl}{CH}CH_3$

$CH_2=CHCH_2CH_3$

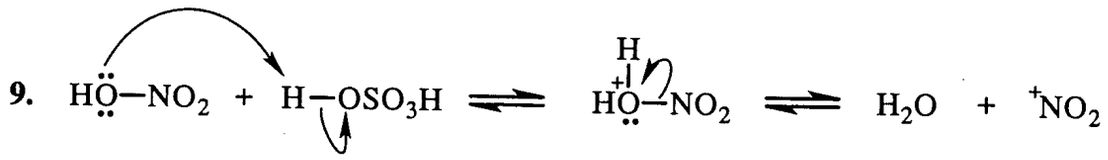
$CH_3CH_2\underset{OH}{CH}CH_3$

7. $CH_3CH_2\overset{O}{\overset{\|}{C}}O\overset{O}{\overset{\|}{C}}CH_2CH_3$

8. **a.** 

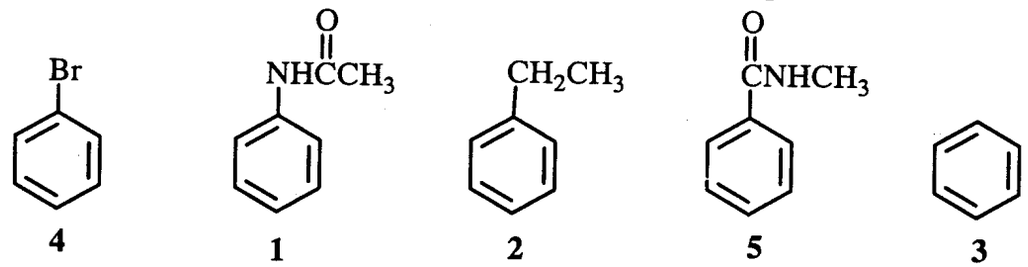
b. $CH_3\overset{+}{C}HCH=CH_2$

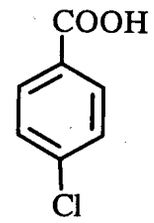
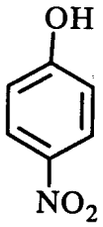
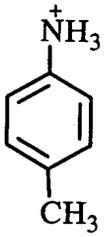
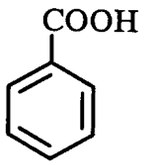
c. $CH_3\overset{-}{C}H\overset{O}{\overset{\|}{C}}CH_3$

9. 

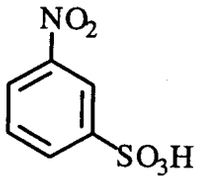
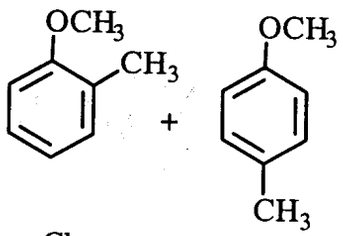
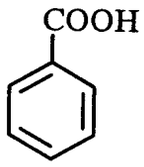
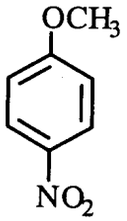
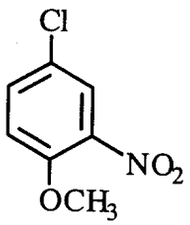
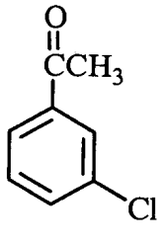
Answers to Chapter 16 Practice Test

1. **a.** *meta*-nitrotoluene
   3-nitrotoluene
   b. 1,2,4-tribromobenzene
   c. *ortho*-ethylbenzoic acid
   2- ethylbenzoic acid
   d. *para*-chlorophenol
   4-chlorophenol

2. 
   4 1 2 5 3

3. **a.**  **b.**  **c.**  **d.** 

4. **a.** *para*-bromonitrobenzene **b.** *para*-bromoethylbenzene

5. **a.**  **b.**  **c.** 
   d.  **e.**  **f.** 

6. **a.** Benzoic acid is more reactive than benzene towards electrophilic substitution. F
   b. *para*-Chlorobenzoic acid is more acidic than *para*-methoxybenzoic acid. T
   c. A $-CH=CH_2$ group is a meta director. F
   d. *para*-Nitroaniline is more basic than *para*-chloroaniline. F

Answers to Chapter 17 Practice Test

1. **a.** CH_3COCH_3 **b.** CH_3CO–C$_6$H$_5$ **c.** CH_3CO–C$_6$H$_4$–NO_2 **d.** CH_3CCl

2.
a. *N*-ethylpentanamide
b. 3-methylpentanoic acid
c. methyl 4-phenylbutanoate
d. ethanoic propanoic anhydride

3. **a.** $CH_3CH_2CO(O)CCH_2CH_3$

b. $CH_3CCl + H_2O \longrightarrow CH_3COH + HCl$

Any reaction in which one of the reactants is cleaved as a result of reaction with water.

c. $CH_3COCH_3 + CH_3CH_2OH \overset{H^+}{\rightleftharpoons} CH_3COCH_2CH_3 + CH_3OH$

4. **a.** CH_3COOH **b.** CH_3COCH_3 **c.** CH_3CONH_2 **d.** CH_3COOH

5. **a.** $CH_3CH_2COH + NH_4^+$

b. $CH_3CH_2CO^- + CH_3CH_2CH_2OH$

c. $CH_3CH_2CH_2COH + CH_3CH_2COH$

d. $CH_3CH_2CNHCH_2CH_3 + Cl^-$

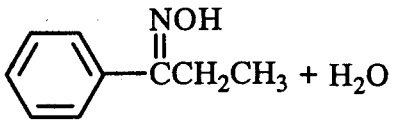
e. C$_6$H$_5$–$COCH_2CH_3 + CH_3OH$

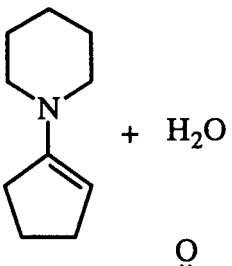
f. $CH_3CH_2CH_2COCH_2CH_2CH_3$

g. $CH_3CH_2COH + CH_3NH_3^+$

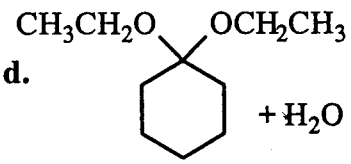
h. $CH_3CH_2COH +$ HO–C$_6$H$_5$

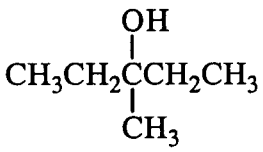
Answers to Chapter 18 Practice Test

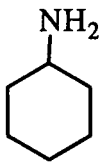
1. a. 

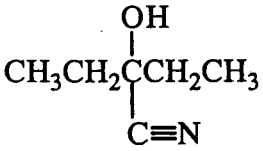
b. 

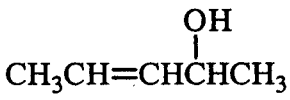
c. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

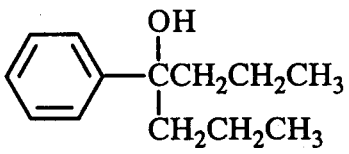
d. 

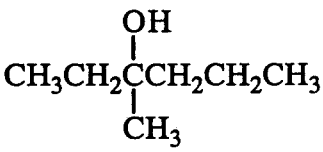
e. 

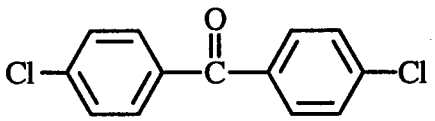
f. 

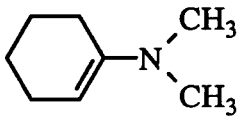
g. 

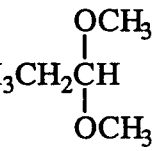
h. 

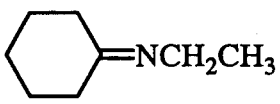
i. 

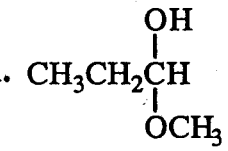
2. 

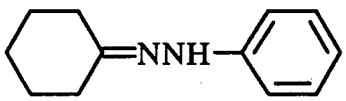
3. 

4. a. 

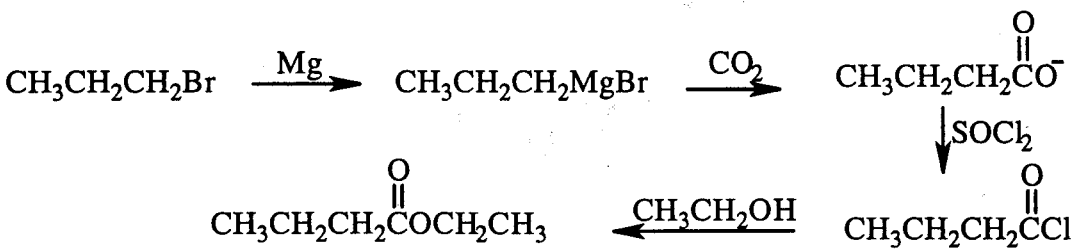
b. 

c. 

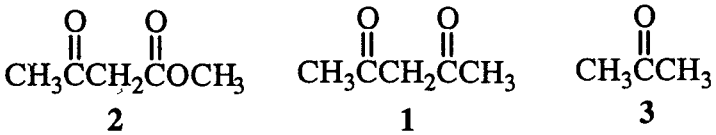
d. 

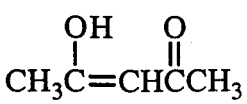
e. 

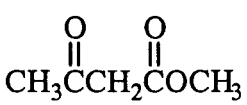
5. **a.** butanal **b.** 3-pentanone

6. 

Answers to Chapter 19 Practice Test

1. 

2. a. 

b. 

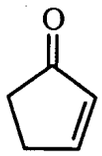
3. a. $CH_3CH_2\overset{O}{\overset{\|}{C}}CH_3 + CO_2$

b. $CH_3CH_2\overset{Br}{\underset{Br}{C}}(\overset{O}{\overset{\|}{C}}H) + 2\ Br^-$

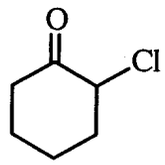
c. $CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}\overset{CH_2CH_3}{\overset{|}{C}}H\overset{O}{\overset{\|}{C}}OCH_3$

d. $CH_3\overset{O}{\overset{\|}{C}}\overset{CH_2CH_2\overset{O}{\overset{\|}{C}}CH_3}{\overset{|}{C}}H\overset{O}{\overset{\|}{C}}CH_3$

e.



f.



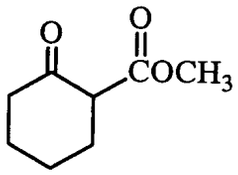
g. $CH_3CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

4. a. $2\ CH_3CH_2\overset{O}{\overset{\|}{C}}H \xrightarrow{HO^-} CH_3CH_2\overset{OH}{\underset{}{C}}H\overset{O}{\overset{\|}{C}}\overset{CH_3}{\overset{|}{C}}H$

b. $2\ CH_3CH_2\overset{O}{\overset{\|}{C}}H \xrightarrow{HO^-} CH_3CH_2\overset{OH}{\underset{}{C}}H\overset{O}{\overset{\|}{C}}\overset{CH_3}{\overset{|}{C}}H \xrightarrow[\Delta]{H_2SO_4} CH_3CH_2CH{=}\overset{O}{\overset{\|}{C}}\overset{CH_3}{\overset{|}{C}}H$

c. $2\ CH_3CH_2\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow{CH_3O^-} CH_3CH_2\overset{O}{\overset{\|}{C}}\overset{CH_3}{\overset{|}{C}}H\overset{O}{\overset{\|}{C}}OCH_3 + CH_3OH$

d. $CH_3O\overset{O}{\overset{\|}{C}}CH_2CH_2CH_2CH_2CH_2\overset{O}{\overset{\|}{C}}OCH_3 \xrightarrow{CH_3O^-}$



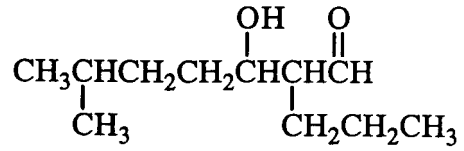
e. $CH_3CH_2O\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3 \xrightarrow[2.\ CH_3CH_2Br]{1.\ CH_3CH_2O^-} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}OH$

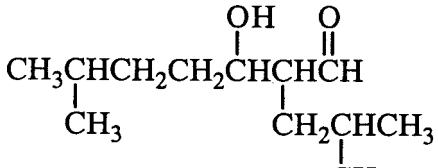
3. H^+, H_2O, Δ

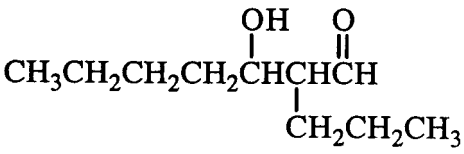
f. $CH_3\overset{O}{\overset{\|}{C}}CH_2\overset{O}{\overset{\|}{C}}OCH_2CH_3 \xrightarrow[2.\ CH_3CH_2Br]{1.\ CH_3CH_2O^-} CH_3CH_2CH_2\overset{O}{\overset{\|}{C}}CH_3$

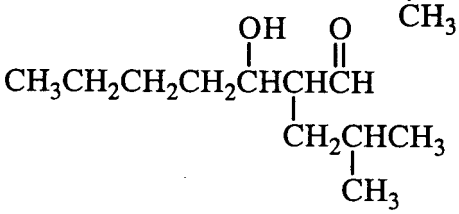
3. H^+, H_2O, Δ

5.



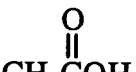




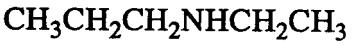


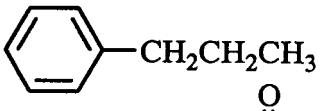
Answers to Chapter 20 Practice Test

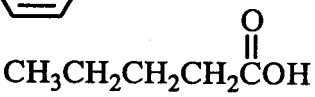
1. **a.** reduction **b.** oxidation

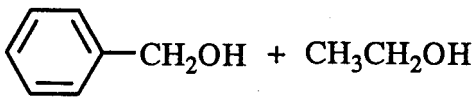
2. **a.** 

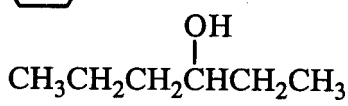
b. no reaction

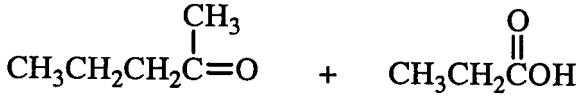
c. 

d. 

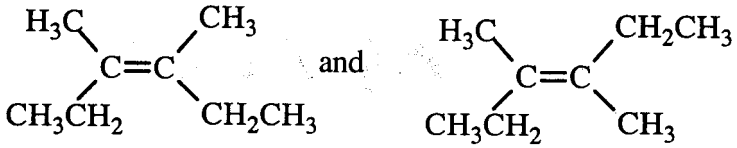
e. 

f. 

g. 

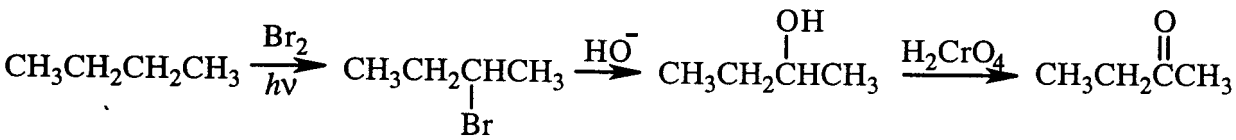
h. 

3. 1. Ag_2O/NH_3
2. H_3O^+

4. 

5.

a.	$NaBH_4$ is a weaker reducing agent than $LiAlH_4$.	T
b.	Esters are easier to reduce than ketones.	F
c.	In an oxidation-reduction reaction the oxidizing agent is oxidized.	F
d.	Ketones are reduced to primary alcohols.	F
e.	Aldehydes are oxidized to carboxylic acids.	T
f.	Acyl halides are oxidized to aldehydes.	F
g.	Alkenes cannot be reduced with $NaBH_4$.	T

6. 

7. **c.** 1. O_3 2. Zn, H_2O or 1. O_3 2. $(CH_3)_2S$

Answers to Chapter 21 Practice Test

1.

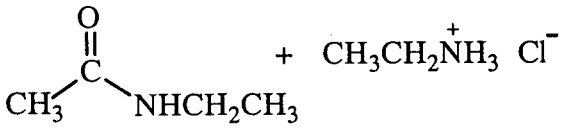
a. 2,4-dimethyl pyrrolidine
2,4-dimethylazacyclopentane

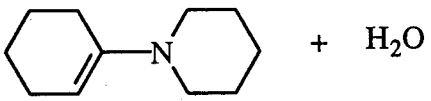
b. *N*-methylpiperidine
N-azacyclohexane

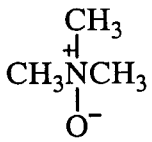
c. 3-ethyltetrahydrofuran
3-ethyloxacyclopentane

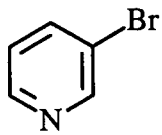
d. 3-bromopiperidine
3-bromoazacyclohexane

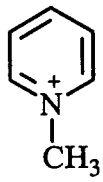
2. a. $CH_2{=}CHCH_2\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{\underset{|}{\overset{|}{C}}}}HCH_2\underset{\displaystyle CH_3}{\overset{\displaystyle CH_3}{|}}NCH_3$

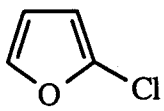
b. 

c. 

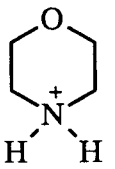
d. 

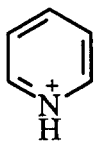
e. 

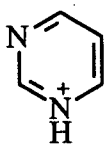
f. 

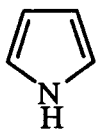
g. 

h. $CH_2{=}CH_2 + \underset{\displaystyle OH}{\overset{\displaystyle CH_3}{\underset{|}{\overset{|}{N}}}}CH_2CH_2CH_3$

3. a. 

b. 

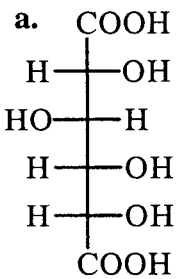
c. 

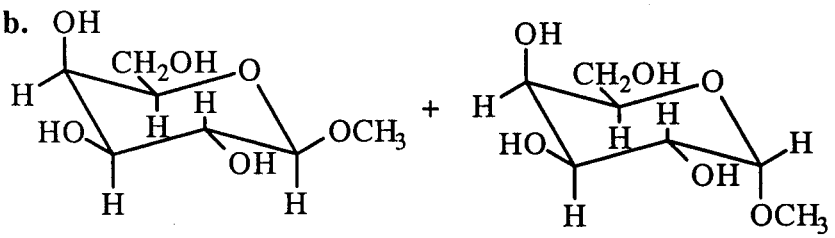
d. 

4.

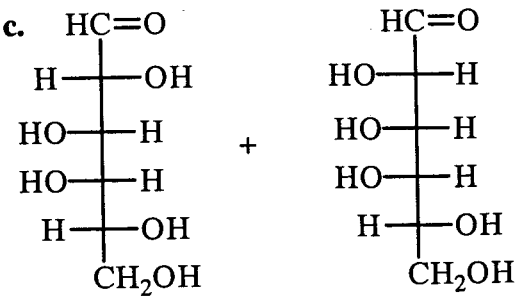
a. Pyridine is more reactive towards nucleophilic aromatic substitution than is pyrrole. T
b. Pyrrole is more reactive towards electrophilic aromatic substitution than is furan. T
c. Pyrrole is more reactive towards electrophilic aromatic substitution than is benzene T
d. Pyridine is more reactive towards electrophilic aromatic substitution than is benzene. F

Answers to Chapter 22 Practice Test

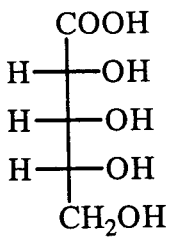
1. a. 

b. 

c.

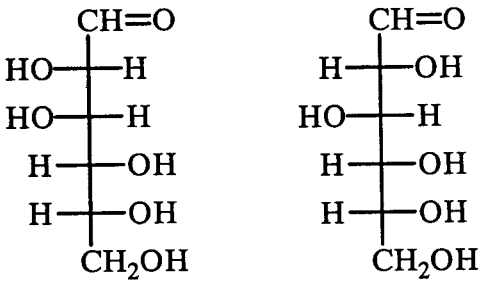


d.



2. **a.** Glycogen contains α-1,4' and β-1,6'-glycosidic linkages. F
b. D-Mannose is a C-1 epimer of D-glucose. F
c. D-Glucose and L-glucose are anomers. F
d. D-Erythrose and D-threose are diastereomers. T
e. Ruff degradations of D-glucose and D-gulose form the same aldotetrose. F

3.

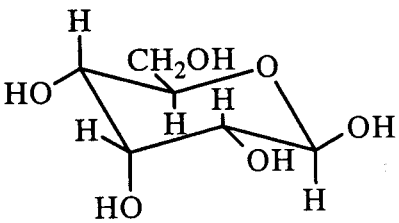


4. D-mannose and D-glucose **5.** D-tagatose **6.** D-altrose

7. Amylose has α-1,4'-glycosidic linkages, while cellulose has β-1,4'-glycosidic linkages.

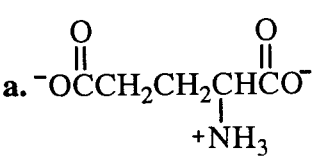
8. D-gulose and D-idose **9.** D-allose

10.

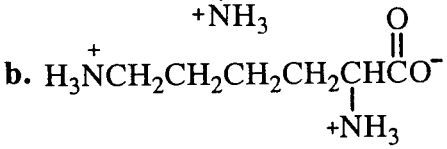


Answers to Chapter 23 Practice Test

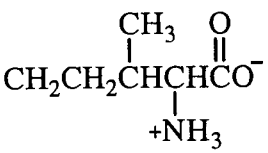
1. **a.**



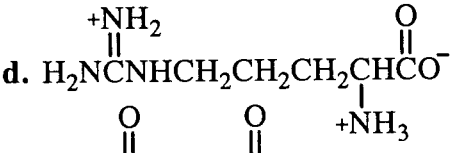
b.



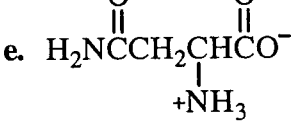
c.

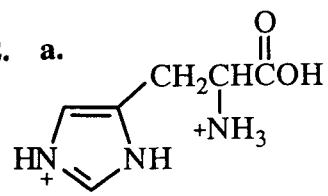


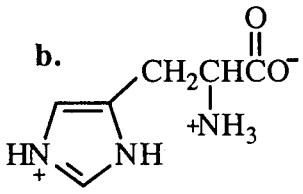
d.

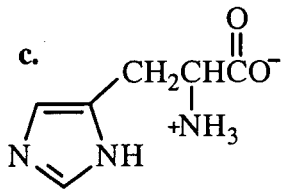


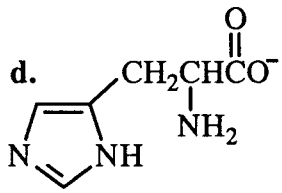
e.



2. **a.** 

b. 

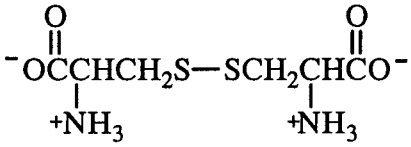
c. 

d. 

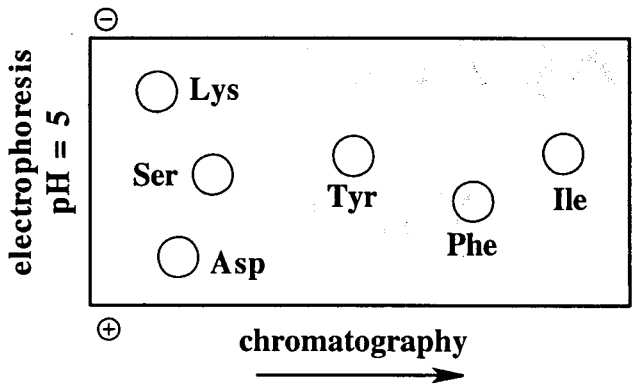
3. **a.** Alanine, because it is farther away from its pI.
b. glycine
c. leucine and isoleucine
d. aspartic acid

4. The electron-withdrawing protonated amino group causes the carboxyl group of alanine to have a lower pK_a.

5.
a. A cigar shaped protein has a greater percentage of polar residues than a spherical protein. T
b. Naturally occurring amino acids have the L-configuration. T
c. There is free rotation about a peptide bond. F

6. 

7.
a. The sequence of the amino acids in the protein chain.
b. The three-dimensional arrangement of all the atoms in the protein.
c. A description of the way the subunits of an oligomer are arranged in space.

8. 

9. **a.** $\frac{2.16 + 9.18}{2} = \frac{11.34}{2} = 5.67$ **b.** $\frac{9.04 + 12.48}{2} = \frac{21.52}{2} = 10.76$

10. Ala Ser Arg Gly Arg Met His Phe Lys Ile



An indispensable resource for the student of organic chemistry

This ***Study Guide and Solutions Manual***, written by Paula Bruice to support the fourth edition of her book, **ORGANIC CHEMISTRY**, is a critical resource for students seeking additional opportunities to test their understanding of key organic chemistry topics. This supplement includes the following features:

- Full solutions to all problems in **ORGANIC CHEMISTRY**, fourth edition, with explanations.
- Special exercises with solutions on pH, pK_a, and buffers.
- Special exercises with solutions on drawing curved arrows ("pushing electrons").
- Special exercises with solutions on kinetics.
- Model-building exercises.
- Twenty-one practice tests.

PEARSON
Prentice Hall

Upper Saddle River, NJ 07458
http://www.prenhall.com/bruice

ISBN 0-13-141010-5
90000
9 780131 410107



An indispensable resource for the student of organic chemistry

This ***Study Guide and Solutions Manual***, written by Paula Bruice to support the fourth edition of her book, **ORGANIC CHEMISTRY**, is a critical resource for students seeking additional opportunities to test their understanding of key organic chemistry topics. This supplement includes the following features:

- Full solutions to all problems in **ORGANIC CHEMISTRY**, fourth edition, with explanations.
- Special exercises with solutions on pH, pK_a, and buffers.
- Special exercises with solutions on drawing curved arrows ("pushing electrons").
- Special exercises with solutions on kinetics.
- Model-building exercises.
- Twenty-one practice tests.

PEARSON
Prentice Hall

Upper Saddle River, NJ 07458
http://www.prenhall.com/bruice

ISBN 0-13-141010-5
90000
9 780131 410107