Organic Reaction Mechanisms-I

(Chemical properties of Aldehydes, Ketones, Carboxylic acid and Acid derivatives)

Section (A) : Reagents, solvents and leaving group

An organic reaction can be represented as

_____solvent

Reactant (substrate) + Reagent Conditions Product

(a) Types of Bond dissociation :

All reactions are initiated with bond dissociation. There are two types of bond dissociation.

(i) **Homolytic bond dissociation :** A bond dissociation in which a bond pair electron is equally distributed to the bonding atoms.

e.g., $A-B \longrightarrow A^{\cdot} + B^{\cdot}$

(ii)

A homolytic bond dissociation generates radicals.

Hetrolytic bond dissociation : A bond dissociation in which a bond pair electron is shifted to one atom only.

e.g., $A-B \longrightarrow A^{\oplus} + B^{\Theta}$

A hetrolytic bond dissociation always generate a cation and an anion.

(b) Types of Reagents :

Reagents are of two types : (i) Electrophiles (ii) Nucleophiles

(i) Electrophiles :

Electrophiles are electron deficient species and having empty p and d-orbitals. All electrophiles are always behave like lewis-acid.

 Ex.1 R⁺, Cl⁺, Br⁺, I⁺, NO₂⁺ (positively charged species), PCl₅, SO₂, SO₃, BeCl₂, BF₃, AlCl₃, :CCl₂, species with vacant orbital at central atom. (H₃O⁺ & NH₄⁺ do not act as electrophile).

(ii) Nucleophiles and their nucleophilicity :

Nucleophile is a specie having negative charge or lone pair of electrons. They are electron rich species. All nucleophiles are always behave like lewis base.

Ex.2 H₂O, NH₃, R-NH₂ (l.p. on central atom) and R⁻, Cl⁻, Br⁻, I⁻, CN⁻, RS⁻ (negaively charged species)

Note : Carbene (:CCl₂, :CH₂) is not a nucleophile because it is electron deficient specie and acts as electrophile.

Negative ions are more nucleophilic than their neutral species

 $OH^{\Theta} > H_2O, NH_2^{\Theta} > NH_3, \qquad \overset{\heartsuit}{OR} > ROH$

• Down the group nucleophilicity increases because the more polarizable donor atom is better nucleophile.

(Polarizability \propto size of donor atom)

 $F^{\Theta} < CI^{\Theta} < Br^{\Theta} < I^{\Theta}$. $OH^{\Theta} < SH^{\Theta}$

Across the period nucleophilicity decreases.

$$CH_3^{\Theta} > NH_2^{\Theta} > OH^{\Theta} > F^{\Theta}$$

• Bulky base has less nucleophilic character due to steric reason.

$$CH_{3} - C - O^{\Theta}$$

$$CH_{3} - C - O^{\Theta}$$

$$CH_{3} - CH_{2} - O^{\Theta}$$

• Effect of solvent : In case of polar aprotic solvents nucleophilicity order of halides is just reversed.

 $F^{\Theta} > Cl^{\Theta} > Br^{\Theta} > I^{\Theta}$

(iii) Bases and their basicity :

Bases are the species which accept the proton or which donates l.p. of electron to proton.

- Basicity decreases down the group while nucleophilicity increases $F^- > CI^- > Br^- > I^-$
- Nucleophilicity and basicity order will be same across the period.
- For the same donor atom nucleophilicity and basicity order will be same

(c) Leaving group ability :

- Weaker base is better leaving group.
- More resonance stabilised ion will be better leaving group.
- Weaker the carbon-leaving group bond better will be the leaving ability.
- If activation energy of a reaction is low then reaction will be fast and leaving group will be better.



Note : More stable anions are weak bases & hence better leaving group.



S.N.	Solvent	Polar	Nonpolar	Protic	Aprotic
1.	CH₃ COOH	\checkmark	×	\checkmark	×
2.	H – C – OCH ²	\checkmark	×	×	\checkmark
З.	H₂O	\checkmark	×	\checkmark	×
4.	ROH	\checkmark	×	\checkmark	×
5.	CH ₃ — CH ₃	\checkmark	×	×	\checkmark
6.	CH ₃ CH ₃ S = O	\checkmark	×	×	\checkmark
7.	R – O – R	\checkmark	×	×	\checkmark
8.	\bigcirc	×	\checkmark	×	\checkmark
9.	DMF	\checkmark	×	×	\checkmark
10.	DMA	\checkmark	×	×	\checkmark

Note : If H-atom is attached to oxgyen, nitrogen or sulphur then it is said to be protic solvent.

Section (B) : Reactions of acidic hydrogen

(i) Reaction with metals and metal hydride :

All active-H (attached with O, S, X, C_{sp} and active methylene) gives H₂ gas with Na or K.

 $CH_3COOH + Na \longrightarrow CH_3COONa + \frac{1}{2}H_2$

 $CH_{3}COOH + NaH \longrightarrow CH_{3}COONa + H_{2}$

(ii) Reaction with alkalies :

All active-H(equal or more acidic than H₂O) reacts with NaOH

 $CH_3COOH + NaOH \longrightarrow CH_3COONa + H_2O$

 $CH \equiv CH + NaOH \longrightarrow No reaction.$

(iii) Reaction with sodium bicarbonate :

Acids more acidic than H_2CO_3 give this reaction and release $CO_2\,\text{gas}$

 $CH_{3}COOH + NaHCO_{3} \longrightarrow CH_{3}COONa + CO_{2} \uparrow + H_{2}O$

PhOH + NaHCO₃ —→ No reaction

(iv) Reaction with Grignard reagent :

Compounds having reactive or acidic hydrogen give acid base reaction with grignard reagent.

 $Z - H + R - MgX \longrightarrow R - H + Z - MgX$

Note : If $R = CH_3$ in R-Mg-Br then methane gas is released.

The reaction is used for estimation of active hydrogen atoms present in a molecule. The method is called **Zerewitinoff method** for estimation of active hydrogen atoms.

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Reactivity order with respect to X (For preparation of RMgX)

$$R - I > R - Br > R - CI > R - F$$

Most
commonly (No G.R. formation)

R – X : used

Examples of Grignard's reagent :

1. Saturated Aliphatic Grignard's reagent R – MgX (Alkylmagnesium halide)

 $CH_3 - MgI$ (Methylmagnesium iodide)

2. Unsaturated Aliphatic Grignard's reagent

(i) Alkenyl Grignard's reagent : $CH_2 = CH - CH_2 - MgX$ (Allylmagnesium halide) (ii) Alkynyl Grignard's reagent : $CH_3-C\equiv C-MgX$

3. Alicyclic Grignard's reagent

4. Aromatic Grignard's reagent

lgX (Phenylmagnesium halide) C6H5CH2MgCI (Benzylmagnesium halide)

Structural stability of G.R.

If the alkyl part has more stable negative charge, then RMgX is more stable and it will be less reactive.

Ex.5 Reactivity order : Stability order :

(1) CH_3 - CH_2 -MqX; (2) CH_2 =CH-MqX1 > 2 > 31 < 2 < 3

; (3) CH₃C=C-MqX

(b) Reactivity of Grignard Reagent :

It has been found out by estimation that there is approx 35% ionic character in carbon-magnesium bond of Grignard's reagent. Therefore, there is a tendency of forming carbanion by heterolysis of this polar bond as follows.

$$\mathsf{R} \not\leftarrow \overset{\mathfrak{G}}{\mathsf{Mg}} \overset{\mathfrak{G}}{X} \longrightarrow \overset{\mathfrak{G}}{\mathsf{R}} \overset{\mathfrak{G}}{\cdot} \overset{\mathfrak{G}}{\mathsf{Mg}} \overset{\mathfrak{G}}{X}$$

If Grignard reagent is regarded as the attacking reagent, then the nucleophilic carbanion of Grignard's reagent will attack on the other compound taken as substrate.

$$\stackrel{\Theta}{R:} + \sum C \stackrel{\frown}{=} \stackrel{O}{O} \longrightarrow \stackrel{R-\stackrel{I}{C} - \stackrel{\Theta}{O:} }{|}$$

(c) Reactivity order of Grignard's reagent

On having same hydrocarbon radical, the order of reactivity of Grignard's reagent will be as follows :

- * RMgI > RMgBr > RMgCl
- Reactivity order with different alkyl part is

* RMaX : $3^{\circ} > 2^{\circ} > 1^{\circ} > CH_{3} > C=C > C=C$

Reactivity order with respect to different reactants (Substrate)

* Acidic hydrogen > - CHO > R - CO - R > R - COOR' > R - X

Except X (halogen) all other functional groups must be absent in the alkyl group otherwise G.R. will be Note : destroyed by internal reactions. [- NO₂, - CN must also be absent]

(d) Synthesis of other organometallic compounds

$$R-Mg-X + ZnCl_2 \longrightarrow R_2Zn + MgX(Cl)$$

+ HgCl₂
$$\longrightarrow$$
 R₂Hg + MgX(Cl)

+ SnCl₄
$$\longrightarrow$$
 R₄Sn + MgX(Cl)

+
$$PbCl_4 \longrightarrow R_4Pb + MgX(Cl)$$

 \rightarrow R₂Cd + MgX(Cl) + CdCl₂-

Section (C) : Nucleophilic addition reaction of Aldehydes and Ketones

Addition of a nuceophile and a proton across the carbonyl (C=O) double bond. The reactivity of the carbonyl group arises from the electronegativity of the oxygen atom and the resulting polarization of the carbon-oxygen double bond. The electrophilic carbonyl carbon atom is sp² hybridized and flat, leaving it relatively unhindered and open to attack from either face of the double bond.



Mechanism :

Nucleophile (Nu⁻) attacks the carbonyl group perpendicular to the plane of sp² hybridised orbitals of carbonyl carbon.

In the process, hybridisation of carbon changes from sp² to sp³. A tetrahedral alkoxide is formed as intermediate.

Reactivity: Aldehydes are more reactive than ketones in nucleophilic addition reactions generally.

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Note : (i) Product is cyanohydrin.

(ii) Cyanohydrin on acid hydrolysis gives α -hydroxy acid.

(iii) Cyanohydrin on treating with NH₃(ℓ) followed by acid hydrolysis gives α -amino acid.

Tetrahedral

intermediate

(iv) In case of ketone cyanohydrin formation is reversible due to bulky group of ketone which hinder the formation.

Cvanohvdrin

(II) Addition of sodium hydrogen sulphite (NaHSO₃)



Bisulphite salt on hydrolysis gives carbonyl compounds again, this reaction is used to separate the aldehydes from mixture.

$$\begin{array}{c} \searrow C - OH \\ I \\ SO_3Na \xrightarrow{H_2O} OH \end{array} \xrightarrow{I} OH \xrightarrow{-H_2O} \searrow C = O \end{array}$$

(III) Addition of alcohols (ROH) :

Reagents : (i) Alcohol + dry HCl or HCl gas or H⁺

Note : In cyclic vicinal diol only cis-isomer are used for acetal & ketal formation.



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Note: (i) Acetal or ketal is formed to protect aldehydes or ketones for a long time.

(ii) Acetal formed can be decomposed to original aldehyde by dilute acid.

(iii) On treating with ethyleneglycol we get cyclic acetal or ketal.

(iv) Acetal formation is found to be more favourable than ketal formation if both the carbonyl groups are present within the molecule.

(IV) Addition of water :

Aldehyde or ketone reacts with water to form gem-diols. This reaction is generally reversible and equilibrium shift towards backward direction, but the rate of reaction can be increased by adding an acid catalyst.

Mechanism:



(V) Nucleophilic addition reaction of Grignard reagent : (i) Reaction with aldehyde and ketones (Preparation of alcohol)

Substrate	Product
Formaldehyde	Primary alcohols
Aldehydes other than formaldehyde	Secondary alcohols
Ketones	Tertiary alcohols



Ex.11 R-MgX + R'' $R'' \to R'' \to R'' \to R'' \to R'' \to R''$ (3° alcohol) **(ii) Reaction with Carbon dioxide and carbon disulphide** A carboxylic acid is formed on hydrolysis of the adduct formed by passing carbon dioxide in the etherial solution of a Grignard's reagent. $R - C - OMgX \to R'' \to R'' \to R''$

$$\begin{array}{c} O=C=O \\ R-MgX + Dry ice \end{array} \xrightarrow{ether} H^{+} \xrightarrow{H^{+}} O \\ (1) O \end{array} \xrightarrow{H^{+}} Alkanonic acid \end{array}$$

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An analogous reaction of Grignard reagent is observed with carbon disulphide to give alkanedithionic acid.



 $R-MgX + O=O \longrightarrow R-O-O-MgX$

 $R-O-O-MgX + R-MgX \longrightarrow 2R-O-MgX$

$$R-O-MgX + HOH \longrightarrow R-O-H + Mg(OH)X$$

Primary, secondary and tertiary alcohols can be obtained by above reaction.

Phenol is obtained on hydrolysis of the product obtained by reaction of arylmagnesium bromide with oxygen.

 $C_6H_5MgBr + O=O \longrightarrow C_6H_5O-OMgBr$

 $C_6H_5O-OMgBr + C_6H_5MgBr \longrightarrow 2C_6H_5-OMgBr$

 $C_6H_5-OMgBr + H_3O^+ \longrightarrow C_6H_5-OH + Mg(OH)Br$

Other phenols can be prepared by taking any aryl (Ar) group in place of phenyl group.

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For example, on taking p-toluenemagnesium bromide p-cresol is formed.



Applications : G.R. is used to prepare alcohols or phenol from those alkyl halides / aryl halides which do not give normal S_N reactions



Section (D) : Addition elimination reactions



Z	Reagent name	Carbonyl derivative	Product name
-H	Ammonia	C=NH	Imine
–R	Amine	C=NR	Substituted imine (Schiffs base)
–OH	Hydroxylamine	С=N-ОН	Oxime
-NH2	Hydrazine		Hydrazone
-NH-	Phenylhydrazine	C=N-NH-	Phenylhydrazone
	2,4-Dinitrophenyl- hydrazine		2,4-Dinitrophenyl- hydrazone
O II –NH–C–NH ₂	Semicarbazide	O II C=N–NH–C–NH ₂	Semicarbazone

⁴ 2,4-Dinitrophenylhydrazine or 2,4-DNP (Brady's reagent) 2,4-DNP-derivatives are yellow-orange or red solids. It is useful for lab test of aldehydes and ketones.

Beckmann rearrangement in Oximes:



Ex.1

Ex.1

Ex.1

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Carboxylic acid derivative will undergo a nucleophilic acyl substitution reaction if the incoming nucleophile on the sp² "c" is a stronger base than the leaving group attached to the sp² "c". If the incoming nucleophile and the leaving group attached to the acyl group in the starting material have identical basicities, then the tetrahedral intermediate can expell either of the two with similar ease and a mixture of starting material and substitution product will result.

(i) L must be better leaving group than Nu^{θ} , i.e., basicity of Nu^{θ} should be more than that of L^{θ} .

(ii) Nu⁰ must be enough strong to attack
(iii) Carbonyl carbon must be enough electrophilic to react with Nu⁰.
Reactivity order:
$$R - C - CI > R - C - O - C - R > R - C - O R > R - C - NH_2$$

Note :- Rate = Nucleophilic Addition > S_N2Th Reaction
Acid derivatives gives S_N2Th reaction with grignard reagent first.
 $R - C - G + R'MgX \rightarrow R - C - R' + MgXG$
1eq.
Ex.17 $R - C - OH + CH_3OH - H^- \rightarrow R - C - OCH_3 + H_2O$
 $R - C - G + R'MgX \rightarrow R - C - R' + MgXG$
1eq.
Ex.18 $R - C - CI + OH^- - \rightarrow R - C - OH + CI^-$
 $Ex.19 C_0H_5 - C - OCH_3 + NH_3 - \rightarrow C_0H_5 - C - NH_2 + CH_3O^-$
 $Ex.20 CH_3 - C - OCH_3 + H_2O - H^- \rightarrow 2CH_3 - C - OH$
(a) Su2Th Poaction of carboxylic acid :

(a) S_N2Th Reaction of carboxylic acid :

(i) Formation of acid chlorides : $\xrightarrow{\text{PCI}_{5}} \text{R-C-CI} + \text{POCI}_{3} + \text{HCI}$ R-COOH-PCl₃ Pyridine $CI + H_3PO_3$ SOCI, + SO₂ + HCI

(ii) Fisher's Esterification :

Carboxylic acids reacts with alcohol to form esters through a condensation reaction known as esterification.

General Reaction :
$$\begin{array}{c} O \\ \parallel \\ -C-OH + R' - OH \end{array} \xrightarrow{\oplus} \begin{array}{c} O \\ + \\ -C-OR' + H_2O \end{array}$$

Specific Examples: $\begin{array}{c} O \\ -C+OH + CH_3CH_2-OH \end{array} \xrightarrow{\oplus} \begin{array}{c} O \\ + \\ -C-OC_2H_5 + H_2O \end{array}$

$$C_{6}H_{5}-C-OH_{+}CH_{3}-OH \xleftarrow{\oplus}{H} C_{6}H_{5}-C-OCH_{3}+H_{2}O$$

Mechanism : (Acid catalysed esterification)



If we follow the forward reactions in this mechanism, we have the mechanism for the acid catalysed esterification of an acid. If however, we follow the reverse reactions, then it is mechanism for the acid catalysed hydrolysis of an ester.

Acid catalysed ester hydrolysis.

$$\begin{array}{c} O \\ \parallel \\ R-C-OR' + H_2O \end{array} \xrightarrow{H_3O} \begin{array}{c} O \\ \parallel \\ R-C-OH + R'-OH \end{array}$$

The results obtain will depend on the conditions we choose. If we want to esterify an acid, use an excess of alcohol and, if possible remove the water as it is formed. If we want to hydrolyse an ester, use excess of water (that is we reflux the ester with dilute aqueous HCl or dilute aqueous H_2SO_4 .)



In fact amides can not be prepared from carboxylic acids and amines unless the ammonium salt is heated strongly to dehydrate it. This is usually not a good method of preparing amides.

(iv) Formation of acid anhydride :



Ex.21 CH_3 -COOH + HOOC- $CH_3 \xrightarrow{P_2O_5} CH_3$ - CH_3 - CH_3 - H_2O (b) S_N2Th Reaction of acid derivatives :

(i) Conversion of acid derivatives to other acid derivatives.



Exception : Acid halides give final product ketone with R2Cd, because it is less reactive than grignard reagent.

$$R - C - X \xrightarrow{1eq, R'_{2}Cd}_{S_{n}2Th} R - C - R'$$

$$R - C - R'$$

Ex.31

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Ex.34

