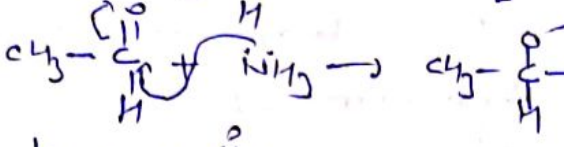
Reaction of Carbonyl Compounds With Nitrogen nucleophile

1 – Rxn with ammonia

The reaction of ammonia with aldehyde/ketone results in the formation of an addition product which readily undergo elimination of water to form an imine.

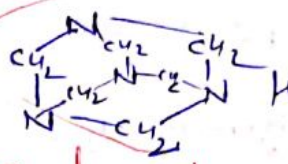
a) $CH_3-\underset{H}{\overset{}{C}}=O + NH_3 \longrightarrow CH_3-CH=NH$ (Imine)



b) $H-\underset{H}{\overset{}{C}}=O + NH_3 \rightarrow CH_2=NH$

$CH_3-CH=NH$

c) $6H-\underset{H}{\overset{}{C}}=O + 4NH_3 \rightarrow$



Hexamethylene tetramine

Reaction with ammonia derivative.

Aldehydes & ketones react with a number of ammonia derivatives such as hydroxylamine (NH_2OH), hydrazine (NH_2NH_2), Phenyl hydrazine ($C_6H_5NHNH_2$), 2,4-dinitrophenyl hydrazine (Brady's Reagent), Semicarbazide ($NH_2-\underset{O}{\overset{}{C}}-NH-NH_2$) in weakly acidic medium to form compounds containing $-C=N$ gp.

Control of pH during addition of ammonia derivative

The addn of ammonia derivatives to the aldehydes & ketones is catalysed by acids. In the acidic medium the oxygen of the carbonyl gp. gets protonated which is in turn by resonance increases the positive charge on the carbonyl carbon. As a result, weak nucleophile like ammonia derivatives readily attack the carbonyl group

$\geq C=\ddot{O}: + H^+ \rightleftharpoons \left[\geq C=\overset{+}{O}H \Rightarrow \geq C-\ddot{O}H\right]$

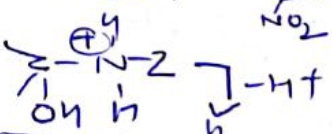
General Rxn

$\geq C=O + H_2\ddot{N}-Z \xrightarrow{H^+} \geq C=N-Z + H_2O$

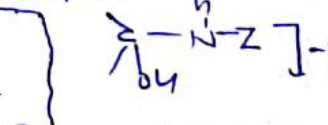
Z = alkyl, $-OH$, $-NH_2$, $-NH-\underset{O}{\overset{}{C}}-NH_2$, $-NH-C_6H_5$, $-NH-C_6H_3(NO_2)_2$

General mechanism

$\geq C=O + H^+ \longrightarrow \geq C^+-OH \xrightarrow{H_2\ddot{N}-Z}$



$\xrightarrow{-H^+}$



$\xrightarrow{-H_2O} \geq C=N-Z$

In case, the medium is too acidic, the ammonia derivative being basic in nature will form their respective ammonium salt

($ZNH_2 + H^+ \rightarrow ZNH_3^+$)

Due to the absence of a lone pair of electrons on the nitrogen atom, these ammonium salt will no longer be nucleophile & hence reaction will not occur. However, if the medium is only very slight acidic, the protonation of carbonyl group will not occur. This in turn will not increase the positive charge on the carbon atom of the carbonyl group and hence weak nucleophile like ammonia derivative will not be able to react. Therefore, to carry out such reactions, an optimum value of pH 3.5 is maintained.

1 Rxn of carbonyl compounds with 1° Amines (formation of Schiff's base)

$CH_3-\underset{H}{C}=O + H_2N-CH_2-CH_3 \xrightarrow{H^+} CH_3-CH=N-CH_2CH_3 + H_2O$

(Imine, Schiff base)

$CH_3-\underset{H}{C}=O + H_2N-C_6H_5 \xrightarrow{H^+} CH_3-CH=N-C_6H_5 + H_2O$

$H-\overset{O}{\overset{\|}{C}}-H + H_2N-CH_2-CH_3 \xrightarrow{H^+} H-CH=N-CH_2CH_3 + H_2O$

$CH_3-\overset{O}{\overset{\|}{C}}-CH_3 + H_2N-CH_3 \xrightarrow{H^+} CH_3-\underset{CH_3}{C}=N-CH_3 + H_2O$

2 With hydroxyl amine (formation of oxime)

$CH_3-\underset{H}{C}=O + H_2N-OH \xrightarrow{H^+} CH_3-CH=N-OH$

Ethanal oxime

$CH_3/H>C=O + H_2NOH \xrightarrow{H^+} CH_3/H>C=NOH + H_2O$

$C_6H_5-CHO + H_2NOH \xrightarrow{H^+} C_6H_5-CH=NOH$

3 With hydrazine (formation of hydrazone)

Aldehyde & ketones react with hydrazine to form hydrazones

$CH_3/H>C=O + H_2N-NH_2 \xrightarrow{H^+} CH_3/H>C=NNH_2 + H_2O$

Hydrazone

$C_6H_5-\overset{H}{\overset{|}{C}}=O + H_2N-NH_2 \xrightarrow{H^+} C_6H_5-CH=N-NH_2 + H_2O$

4 Reaction with Phenyl hydrazine (formation of Phenyl hydrazone)

$R-\underset{H}{C}=O + H_2N-NH-C_6H_5 \xrightarrow{H^+} R-\underset{H}{C}=NNH-C_6H_5 + H_2O$

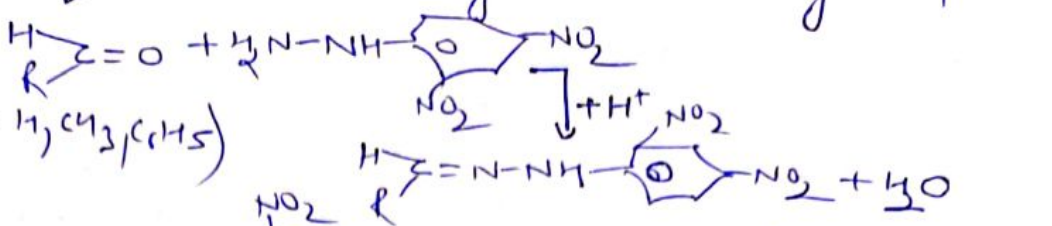
($R = H, -CH_3, -C_6H_5$)

$CH_3>C=O + H_2N-NH-C_6H_5 \xrightarrow{H^+} CH_3>C=N-NHC_6H_5 + H_2O$

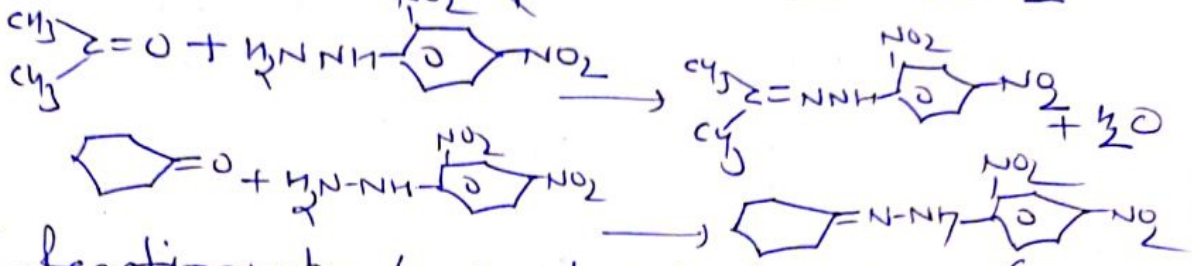
5 Reaction with 2,4-dinitrophenylhydrazine (Brady's Reagent)

Aldehydes & ketones react with 2,4-dinitrophenyl hydrazine (DNP) to form yellow/Orange/Red ppt of 2,4-dinitrophenyl hydrazones (DNP derivatives)

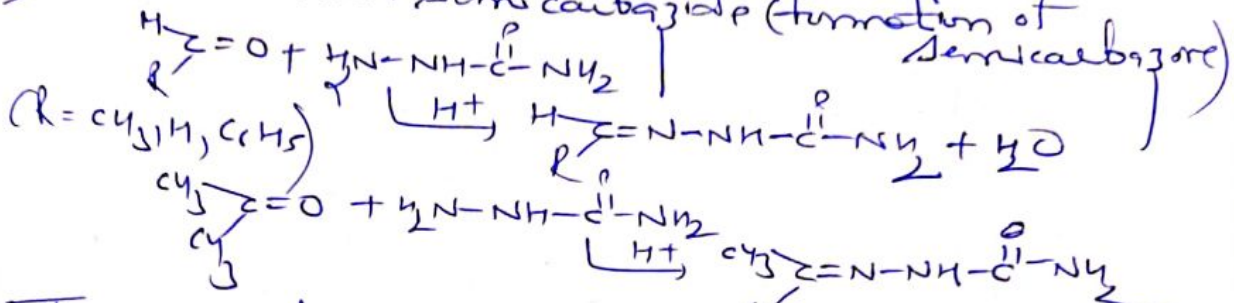
The reaction is of special interest because it is used for the qualitative analysis of carbonyl compounds.



(R = H, CH_3, C_6H_5)

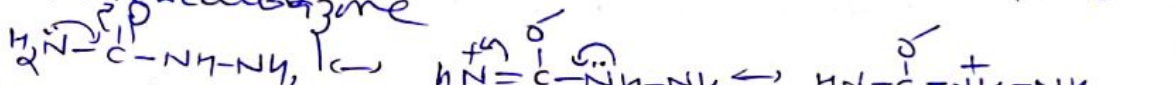


6 Reaction with Semicarbazide (formation of Semicarbazone)



(R = CH_3, H, C_6H_5)

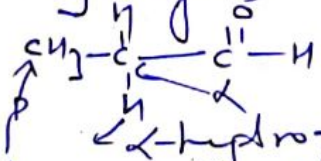
There are two $-NH_2$ groups in semicarbazide. However, only one is involved in the formation of semicarbazone



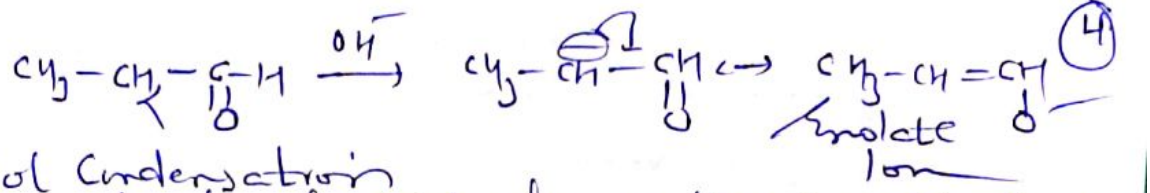
Although semicarbazide has two $-NH_2$ groups but one of them is involved in resonance. As a result, electron density on this $-NH_2$ group decreases & hence it does not act as a nucleophile. In contrast, the lone pair of electrons on the other $-NH_2$ group is not involved in resonance and hence

Reactions involving α-Carbon of Carbonyl Compounds

The carbon adjacent to C=O group also participate in some significant reactions. The carbon adjacent to C=O is known as α-carbon and the hydrogens attached to it are α-hydrogen

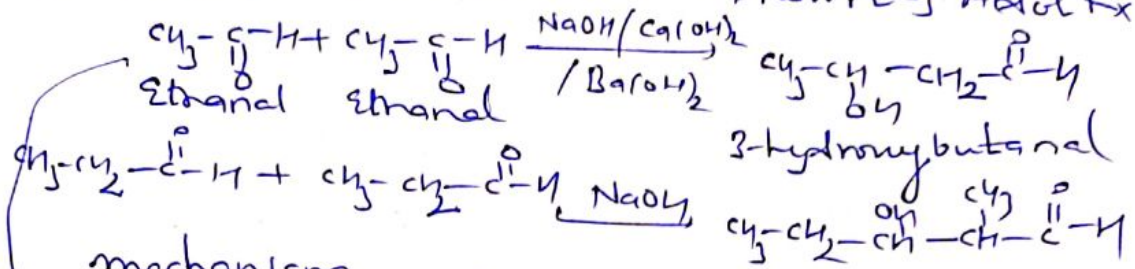


The α-hydrogen of carbonyl compounds is acidic in nature due to E.W. nature of C=O group. The α-hydrogen can be abstracted by a strong base which results in the formation of resonance stabilized carbanion known as Enolate ion



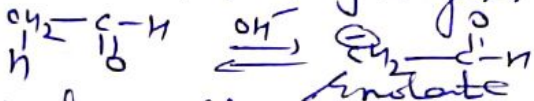
Aldol Condensation

Two molecules of aldehyde containing α-hydrogen undergo self condensation in the presence of dilute base to produce β-hydroxy aldehyde known as aldol & the reaction is known as Aldol Rxn.

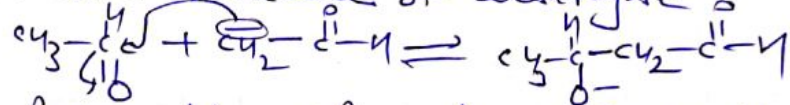


mechanism

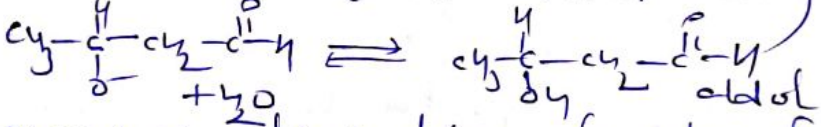
Step1 Abstraction of α-hydrogen of aldehyde



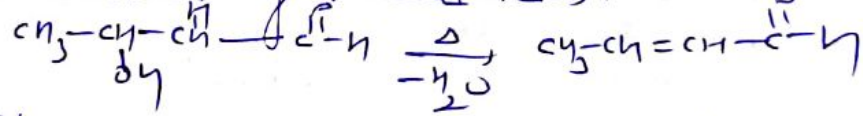
Step2 Nucleophilic attack of carbanion on the second molecule of aldehyde



Step3 Protonation (formation of aldol)

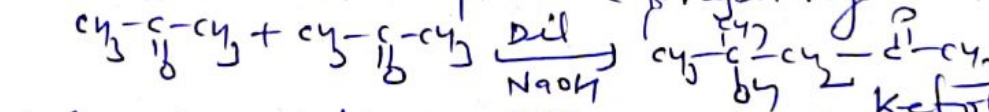


Heating causes elimination of water from aldol to produce α,β-unsaturated aldehyde. Overall reaction is Aldol condensation. Dehydration can also be affected by mineral acids.

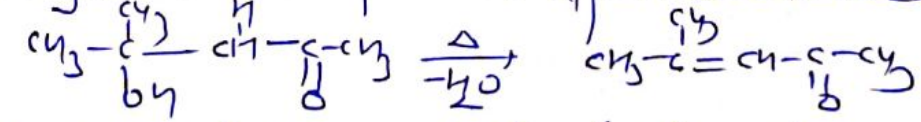


Ketones

The ketones containing α-hydrogen also undergo similar reaction to produce β-hydroxy ketone.



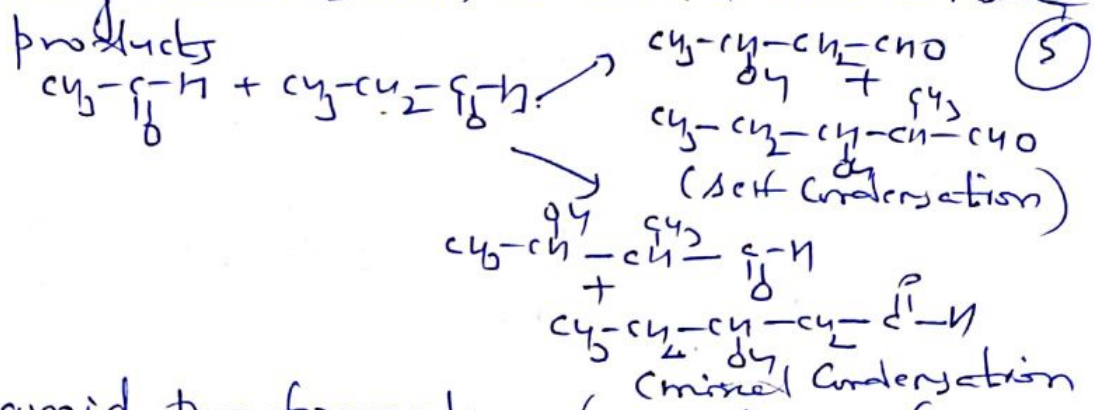
Ketol under acidic conditions or heating undergo dehydration to produce α,β-unsaturated ketones



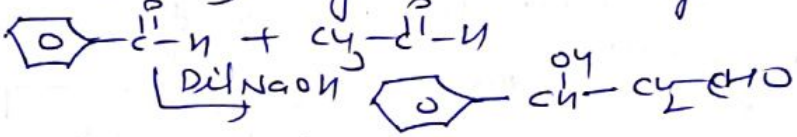
Mixed aldol / Cross aldol condensation

Two diffrent aldehydes / ketones (both having α-hydrogen) may undergo condensation in the presence of base to give a mixture of diffrent β-hydroxy aldehydes / ketones

Eg: Ethanal and propanal in presence of dil alkali undergo condensation to form a mix of four products

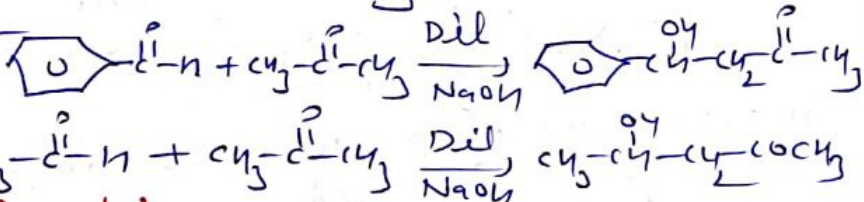


To avoid the formation of mixture of products, the aldol reaction with different aldehydes is carried out in such a way that one aldehyde contains α-hydrogen & other does not have α-hydrogen. During the reaction, carbanion is formed from the α-hydrogen containing aldehyde



Claisen Schmidt Reaction

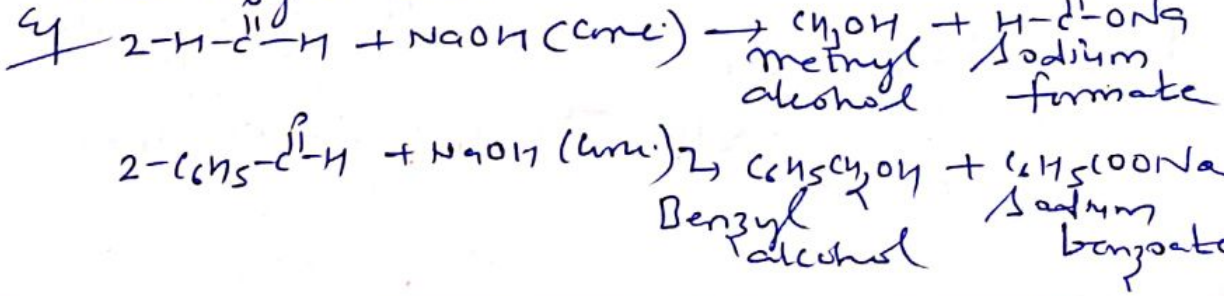
The aldol reaction may occur b/w an aldehyde & a ketone. In a cross aldol condensation, if one of the component is ketone having α-hydrogen & other is aldehyde with no α-hydrogen



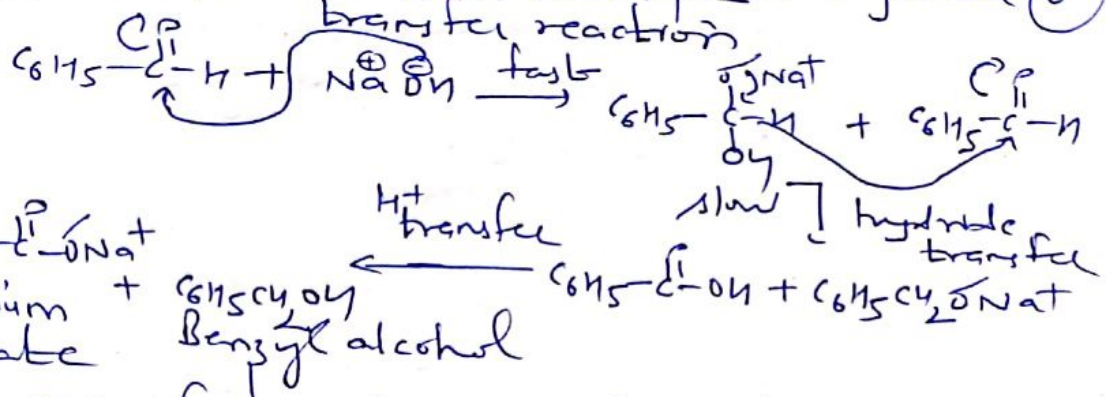
Cannizaro Reaction

(Reaction with Conc. Alkali)

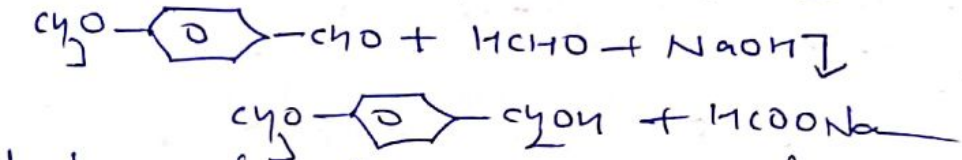
Aldehydes which do not contain an α-hydrogen when treated with conc. alkali undergo disproportionation i.e. self oxidation-reduction. As a result, one molecule of the aldehyde is reduced to the corresponding alcohol and other is oxidised to the corresponding carboxylic acid



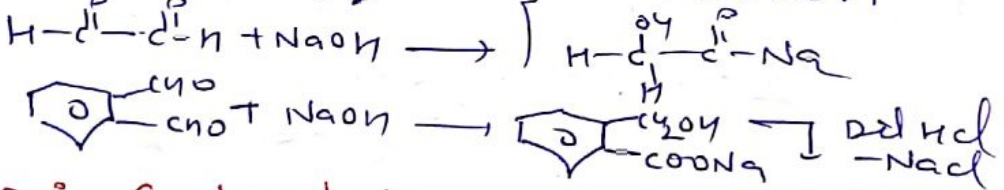
mechanism – It is an example of hydride transfer reaction



In a case of cannizaro reaction, if one of the aldehyde is different from other

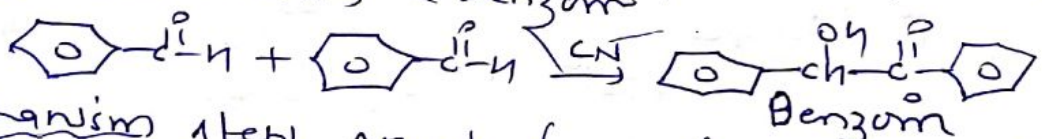


Intramolecular cannizaro reaction

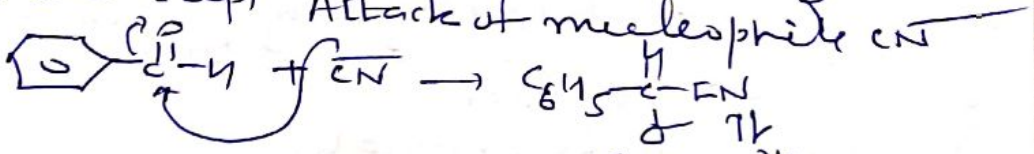


Benzoin Condensation

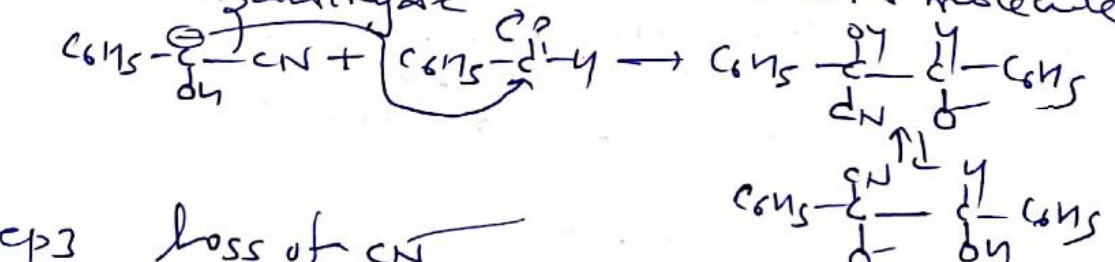
Aromatic aldehydes, in the presence of CN^- undergo to form α-hydroxy ketones. In the case of benzaldehyde, in the presence of CN^- it forms (benzoin)



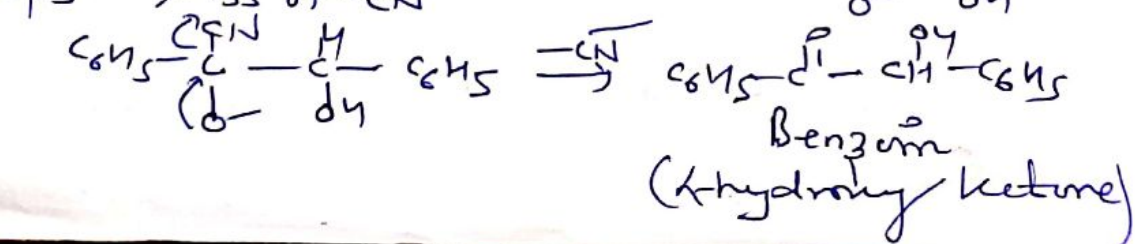
mechanism step1 Attack of nucleophile CN^-



step2 Attack of carbanion to second molecule of benzaldehyde



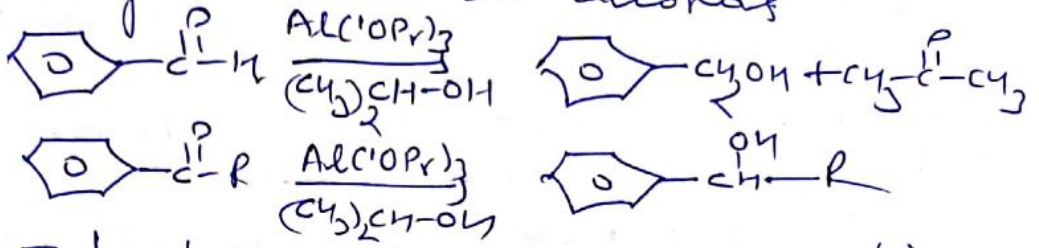
step3 loss of CN^-



Benzoin (α-hydroxy ketone)

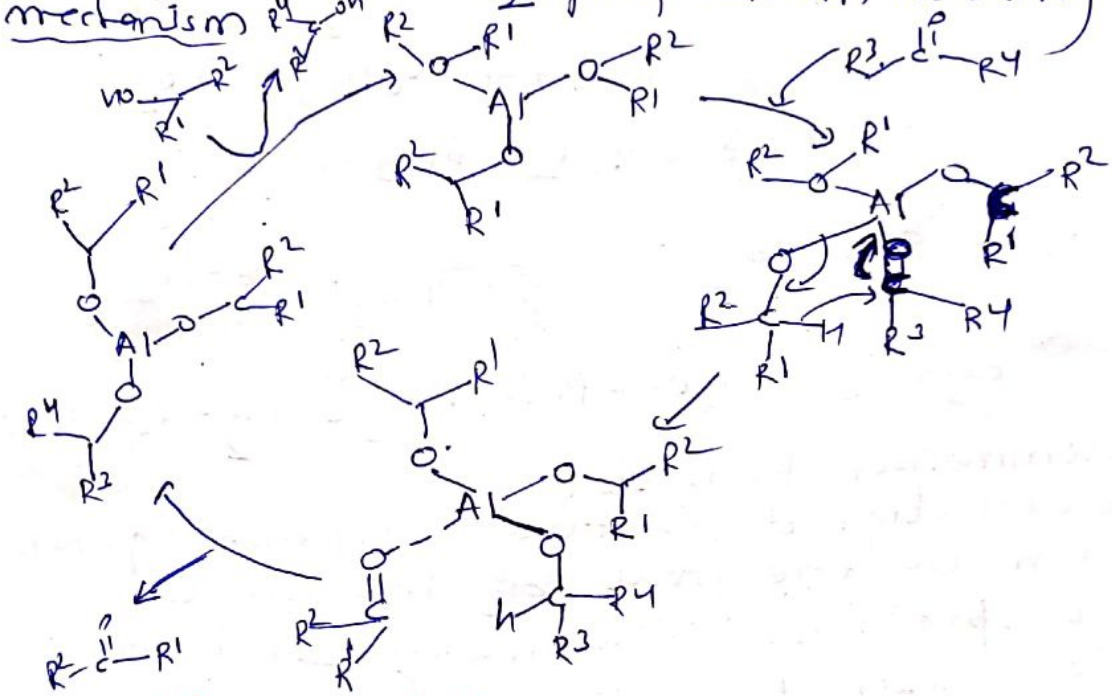
Meerwein-Ponndorf-Verley Reduction (7)

Aromatic carbonyl compounds on treatment with solution of $Al('OPr)_3$ in isopropyl alcohol get reduced to alcohols



(C=C, C≡C bond & $-NO_2$ group remain as such)

mechanism



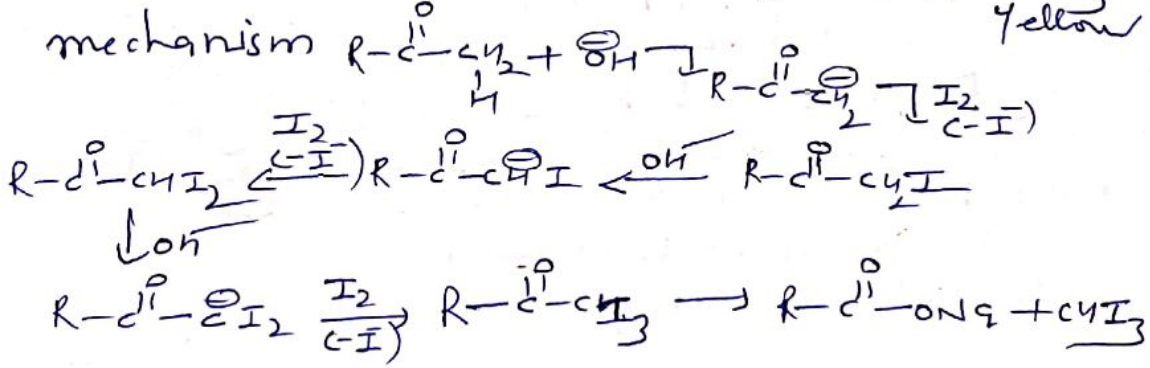
Iodoform test

Iodoform test is used to check the presence of carbonyl compounds with the structure $R-CO-CH_3$ or alcohols with the structure $R-CH(OH)-CH_3$ in a given unknown substance

$$R-C(=O)-CH_3 + NaOH + I_2 \rightarrow R-C(=O)-ONa + CHI_3$$

Yellow

mechanism



Wittig Reaction ($>C=O \rightarrow >CH_2$)

This involves the treatment of aldehyde or ketone with phosphorous ylide

$$>C=O + R_2\overset{\ominus}{C}-\overset{\oplus}{P}(C_6H_5)_3 \longrightarrow >C=CR_2 + (C_6H_5)_3P=O$$

ylide

(Phosphorous ylides are prepared from alkyl halides + triphenyl phosphine)

$$(C_6H_5)_3\ddot{P} + R_2CH-Br \longrightarrow (C_6H_5)_3\overset{\oplus}{P}-CHR_2$$

$\downarrow C_2H_5ONa$

$$C_2H_5OH + (C_6H_5)_3P^+-\overset{\ominus}{C}R_2$$

mechanism step1 $>C=O + R_2\overset{\ominus}{C}-\overset{\oplus}{P}Ph_3 \rightarrow >C(O^-)-C(R_2)-\overset{\oplus}{P}Ph_3$

step2 $>C(O^-)-C(R_2)-\overset{\oplus}{P}Ph_3 \rightarrow >C(O)-C(R_2)-PPh_3 \rightarrow >C=CR_2 + PPh_3=O$

~~step3~~

$$CH_3-\overset{CH_3}{\overset{|}{C}}=O + H_2\overset{\ominus}{C}-\overset{\oplus}{P}Ph_3 \longrightarrow CH_3-\overset{CH_3}{\overset{|}{C}}=CH_2 + (C_6H_5)_3P=O$$

Clemmenson Reduction

The reduction of carbonyl compound / group to methylene group ($>CH_2$) in acidic conditions in the presence of Zinc amalgam is known as clemmenson Reduction

$$CH_3-CH_2-\underset{O}{\overset{||}{C}}-H \xrightarrow[Amg.HCl]{Zn-Hg} CH_3CH_2CH_3$$

$$CH_3-\underset{O}{\overset{||}{C}}-CH_2-CH_3 \xrightarrow[HCl]{Zn-Hg} CH_3CH_2CH_2-CH_3$$

Wolf-kishner Reduction

Wolf kishner Reduction involves hydrazine as reducing agent and reduces carbonyll group of aldehydes & ketones to methylene group Aldehyde / ketone is heated with hydrazine in presence of base such as t-butoxide KOH, $K^+OC_2H_5$, which results in the reduction of carbonyl group to alkane

$$CH_3-\underset{O}{\overset{||}{C}}-H + H_2N-NH_2 \longrightarrow CH_3-CH=NNH_2 \xrightarrow{C_2H_5O^-K^+} CH_3CH_3 + N_2$$

$$CH_3-\underset{O}{\overset{||}{C}}-CH_2-CH_3 + H_2N-NH_2 \xrightarrow{C_2H_5OK^+} CH_3-CH_2-CH_2-CH_3 + N_2$$

It can be used for the reduction of carbonyl compounds which are sensitive to acidic [illegible]