05 Carbonyl Compounds

Introduction:

Organic Compounds having $>C=O$ group are called carbonyl compounds and $>C=O$ group is known as carbonyl or oxo group. It's general formula is $C_n H_{2n}O$ (n = 1, 2, 3.....) Carbonyl compounds are grouped into two categories.

(a) Aldehydes : Aldehyde group is $-\overset{\overset{O}{\|}}{C}-H$ (also known as formyl group). It is a monovalent group

(b) Ketones : The carbonyl group ($>C=O$) is a Ketonic group when it's both the valencies are satisfied by alkyl group. It is a bivalent group Ketones are further classified as :

(i) **Simple or Symmetrical ketones** : Having two similar alkyl groups. $\begin{matrix}R\\R\end{matrix}\!\!>C=O$

(ii) **Mixed or unsymmetrical ketones** : Having two different alkyl groups. $\begin{matrix}R\\R\end{matrix}\!\!>C=O$

Example : (Ketones) :	**Symmetrical**	**Unsymmetrical**
	$\begin{matrix}H_3C\\H_3C\end{matrix}\!\!>C=O$	$\begin{matrix}CH_3CH_2\\H_3C\end{matrix}\!\!>C=O$
	(Acetone or Dimethyl ketone)	(Ethyl methyl ketone)
	2–Propanone	2–Butanone

Special Point : $-\overset{\overset{O}{\|}}{C}-\ddot{O}H$, $-\overset{\overset{O}{\|}}{C}-\ddot{X}:$, $-\overset{\overset{O}{\|}}{C}-\ddot{N}H_2$, $-\overset{\overset{O}{\|}}{C}-\ddot{O}R$

In all the functional group given above, lone pair of electrons and double bond are in conjugation. $\left[-\overset{\overset{O}{\|}}{C}-\ddot{Z}\right]$ so resonance occurs. These functional group have $-\overset{\overset{O}{\|}}{C}-$ group still they are not carbonyl compounds because carbonyl group takes part in resonance with the lone pair of electrons.

- **Structure :**

In $>C=O$ compounds C-atom is sp^2 hybridised which forms two σ bonds with C and (H/C) atom respectively and one σ bond with oxygen atom. The unhybridised atomic orbital of C-atom and the parallel 2p orbital of oxygen atom give the π bond in $>C=O$ group.

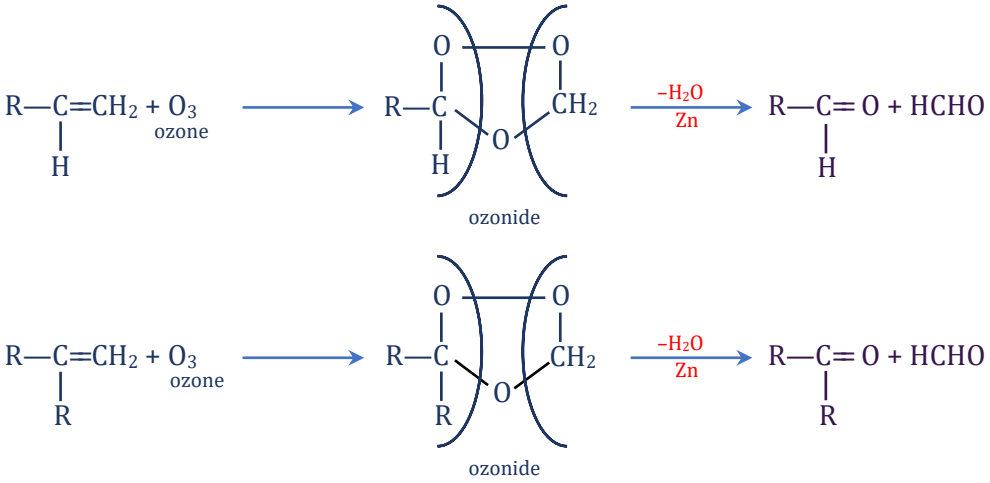
$\left[\begin{matrix}C\\H\end{matrix}\!\!>\overset{sp^2}{C}\overset{\sigma}{=}O\ (\pi)\right]$. The C—C—O and H—C—O bond angles are of approximately 120°.

Due to electro-negativity difference in C & O atoms, the $>C=O$ group is polar, $>\overset{\delta+}{C}=\overset{\delta-}{O}$. Hence aldehydes and Ketones possess dipole moment.

Preparation of carbonyl compound from hydrocarbon:

(1) By Ozonolysis of alkenes :

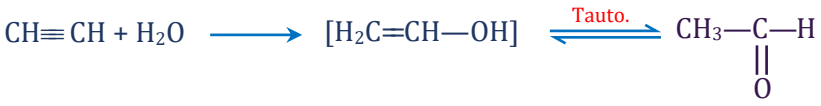
This reaction is used to determine the position of double bond in alkene.



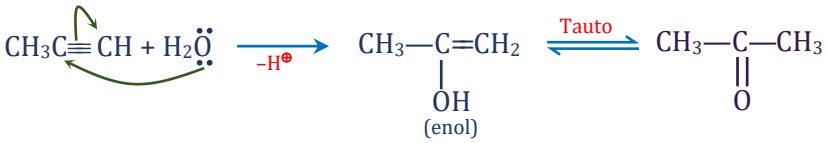
Unbranched alkene	⟶	aldehyde
Branched alkene	⟶	ketone

(2) From Alkyne :

(a) Kucherov reaction (Hydration of alkyne) : With dil H_2SO_4 & 1% $HgSO_4$ at 60-80°C.



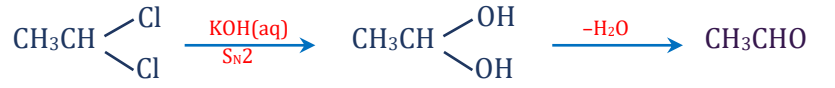
In general other alkynes give ketone :

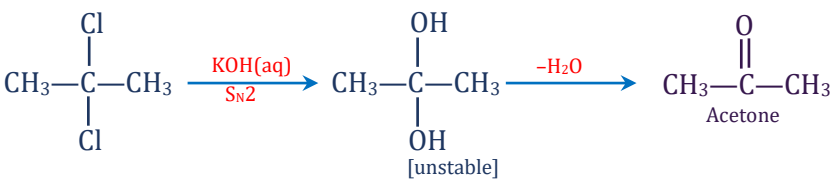


General Methods of Preparation of carbonyl from alcohol :

(1) By Hydrolysis of gem dihalides :

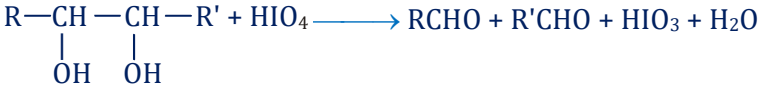
Terminal gem-dihalides on hydrolysis give aldehydes while the non-terminal dihalides give ketone.

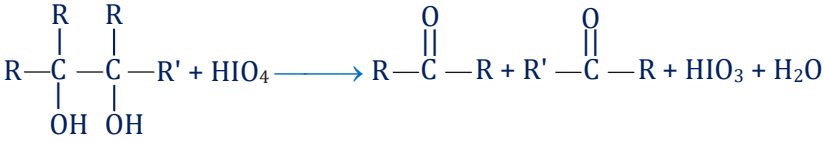




(2) By Oxidation of diols:

With periodic acid (HIO_4) & lead tetraacetate $(CH_3COO)_4Pb$ vicinal diols gets oxidised to form carbonyl compounds





(3) By oxidation of alcohols :

Primary alcohols $\xrightarrow{[O]}$ Aldehydes

For oxidising primary alcohols to aldehydes PCC (Pyridiniumchloro chromate $(C_6H_5NH^{\oplus}CrO_3Cl^{\ominus})$ may be used.

Secondary alcohols $\xrightarrow{[O]}$ Ketones

For oxidising 2° alcohols to ketones $CrO_3/K_2Cr_2O_7$ may be used.

(4) By dehydrogenation of (1° & 2°) alcohols :

Dehydrogenation means removal of hydrogen and reagent used is heated copper or silver. The alcohol vapours are passed over heavy metal catalyst to yield the following products.

1° alcohol $(RCH_2OH) \xrightarrow[-H_2]{Cu/300°C}$ Aldehyde (R–CH=O)

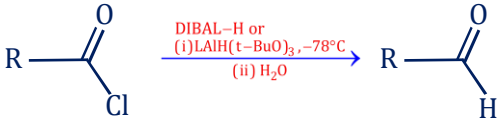
2° alcohol $(R_2CHOH) \xrightarrow[-H_2]{Cu/300°C}$ Ketone $(R_2C=O)$

3° alcohol $\xrightarrow[-H_2]{Cu/300°C}$ Alkene (Dehydration)

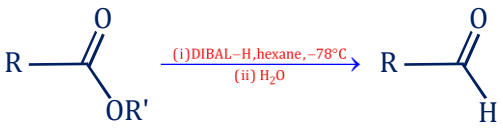
Preparation of aldehyde from reduction:

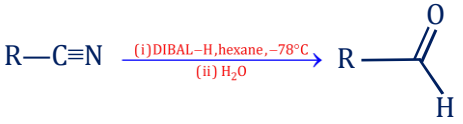
(1) Reduction of acyl halides, esters and nitriles:

(a) Acyl chlorides can be reduced to aldehydes by treating them with lithium-tri-tert butoxyaluminium hydride, $LiAlH[OC(CH_3)_3]_3$ or with DIBAL–H at – 78°C.



(b) Both esters and nitriles can be reduced to aldehydes by DIBAL-H. Reduction must be carried out at low temperatures. Hydrolysis of the intermediates gives the aldehyde.





(2) Rosenmund's reduction :

Quinoline or sulphur act as a poisoned catalyst, controls the further reduction of aldehyde to alcohols.

$$RCOCl + H_2 \xrightarrow[\text{Quinoline or sulphur}]{Pd/BaSO_4} RCHO + HCl$$

This reaction controls further reduction of aldehyde to alcohols.

In case if only Pd is used, formation of alcohol takes place.

$$RCOCl + H_2 \xrightarrow{Pd} RCHO \xrightarrow{H_2/Pd} RCH_2OH$$

Formaldehyde cannot be prepared by this method because HCOCl is highly unstable at room temperature it decompose into CO + HCl.

Example : $C_2H_5COCl + H_2 \xrightarrow[\text{Quinoline or sulphur}]{Pd/BaSO_4} C_2H_5CHO + HCl$

Propionyl chloride — Propanal

$$RMgX + R{-}C{\equiv}N \longrightarrow \underset{\displaystyle R}{R{-}C{=}N{-}MgX} \xrightarrow{H_2O/H^{\oplus}} \underset{\displaystyle O}{\underset{\displaystyle ||}{R{-}C{-}R}} + NH_3 + Mg\begin{matrix}OH\\X\end{matrix}$$

ketone

(3) Stephen's reduction :

Alkyl cyanides are reduced by $SnCl_2$ and HCl.

$$R{-}C{\equiv}N \xrightarrow{SnCl_2/HCl} R{-}CH{=}NH \xrightarrow{H_3O^{\oplus}} RCHO + NH_3\uparrow$$

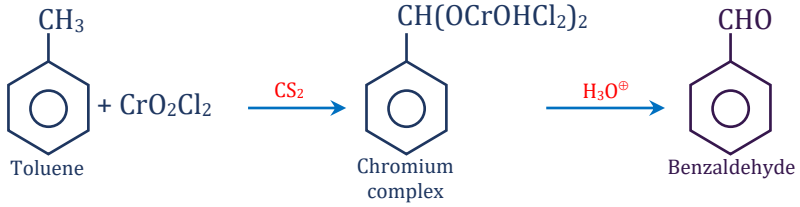
$$C_2H_5{-}C{\equiv}N \xrightarrow{SnCl_2/HCl} C_2H_5CH{=}NH \xrightarrow{H_3O^{\oplus}} C_2H_5CHO + NH_3\uparrow$$

Preparations of Benzaldehyde:

(1) Oxidation of methyl benzene :

Strong oxidising agents oxidise toluene and its derivatives to benzoic acid. So to stop the oxidation at aldehyde stage suitable reagents used.

(a) Etard reactions : with chromyl chloride followed by hydrolysis

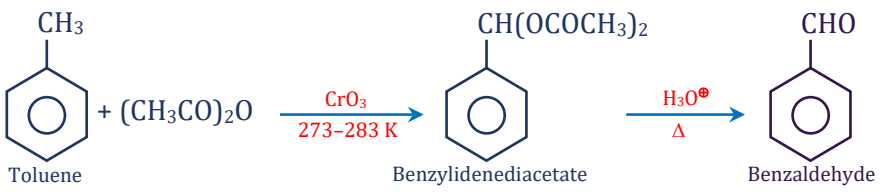


Toluene — Chromium complex — Benzaldehyde

Note:

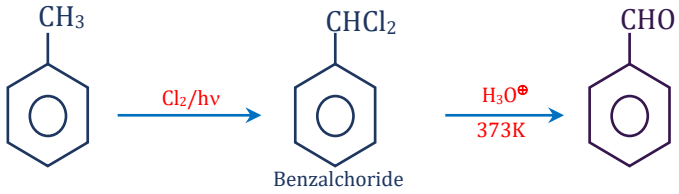
Chromyl chloride (CrO_2Cl_2) oxidises methyl group in methylbenzene to a chromium complex, which on hydrolysis gives corresponding benzaldehyde.

(b) With chromic oxide CrO_3 in acetic anhydride



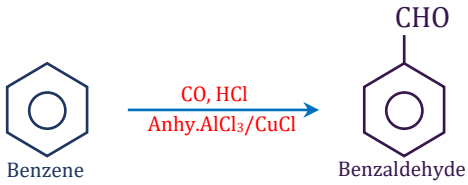
Toluene — Benzylidenediacetate — Benzaldehyde

(2) By side chain chlorination followed by hydrolysis (Commercial Method)



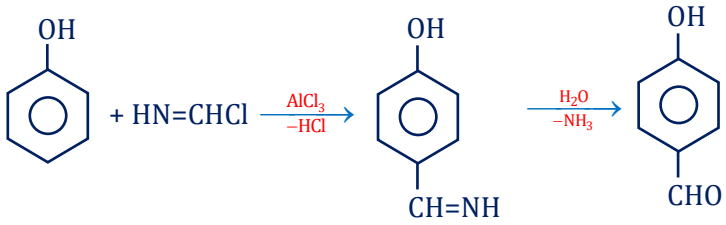
(1) By Gattermann-Koch reaction:

Benzene or its derivative $\xrightarrow[\text{Anhy.AlCl}_3/\text{CuCl}]{\text{CO,HCl}}$ Benzaldehyde or substituted benzaldehyde

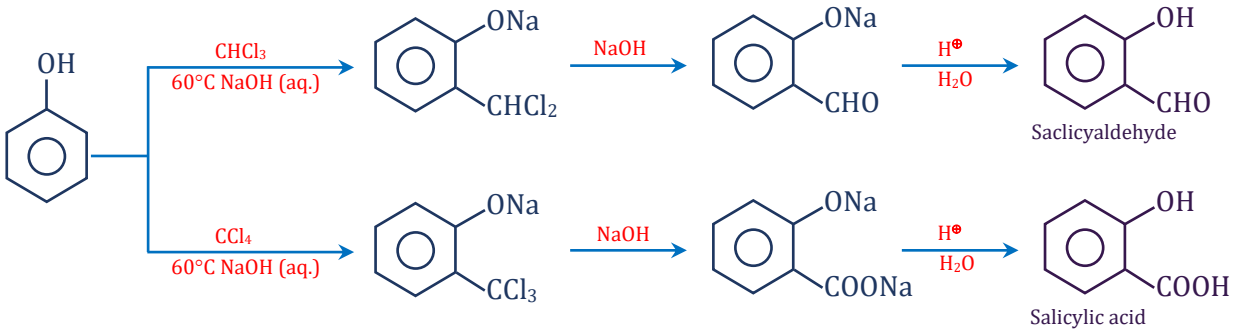


(2) Gattermann aldehyde synthesis: When phenol is treated with liquid HCN and HCl gas in presence of anhydrous $AlCl_3$ it yields mainly p-hydroxybenzaldehyde (formylation)

$$HCl + HCN \xrightarrow{AlCl_3} HN{=}CHCl$$



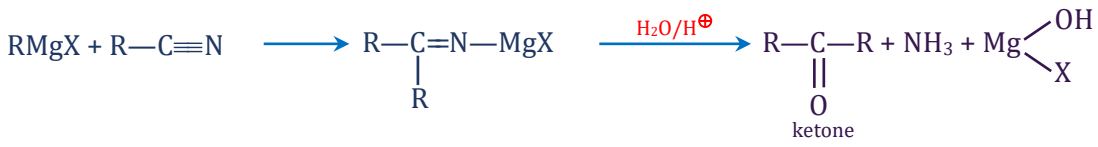
(3) Reimer-Tiemann reaction : Phenol on refluxing with chloroform and NaOH (aqueous) followed by acid hydrolysis yields o–hydroxy benzaldehyde. When CCl_4 is used salicylic acid is formed.



Preparation method for ketone:

(1) From Grignard reagents:

(a) By Cyanides :



(2) From dialkyl Cadmium :

RCdR (dialkyl Cadmium) is a organometallic compound.

$R'COCl + RCdR \longrightarrow RCOR' + RCdCl$

This reaction is superior than Grignard Reaction because the ketones formed, further reacts with Grignard reagent to form 3° alcohols.

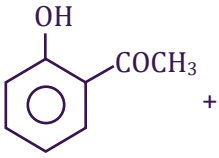
Example : $CH_3COCl + (C_2H_5)_2Cd \rightarrow (CH_3)(C_2H_5)C{=}O + (C_2H_5)ClCd$

(3) Friedel-Craft Acylation Reaction

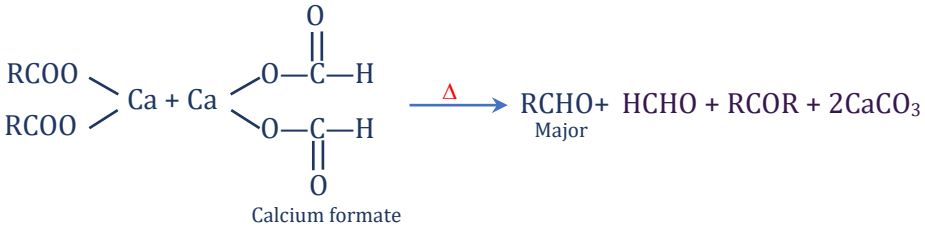
(i) $C_6H_6 + CH_3COCl \xrightarrow[AlCl_3]{Dry} C_6H_5COCH_3 + HCl$
Acetophenone

(ii) $C_6H_6 + C_6H_5COCl \xrightarrow[AlCl_3]{Dry} C_6H_5COC_6H_5 + HCl$
Benzophenone

(iii) $\underset{excess}{C_6H_6} + COCl_2 \xrightarrow[AlCl_3]{Dry} C_6H_5COC_6H_5 + HCl$
Benzophenone

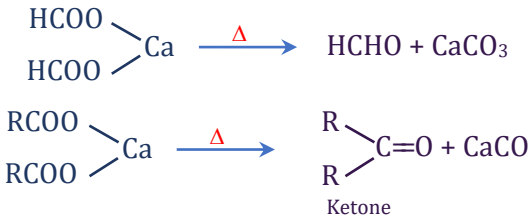
(iv)  $+ CH_3COCl \xrightarrow{Anhydrous\ AlCl_3}$  + 
o–hydroxy acetophenone
p–hydroxy acetophenone

(4) By dry distillation of Ca-salts of carboxylic acid :

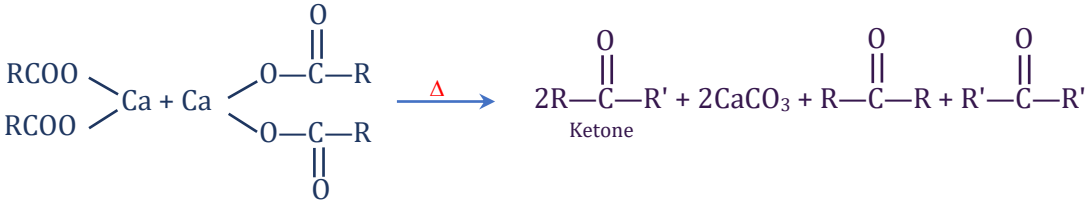


Note :

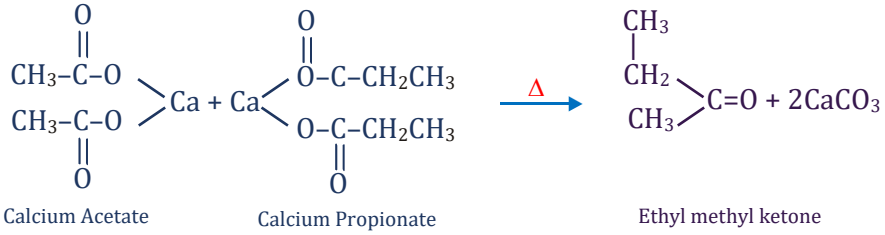
In this reaction mixture of ketones are formed and usually cross product is major product.



Calcium salts of acids other than formic acid on heating together gives ketone



To prepare ethyl methyl ketone Calcium acetate and Calcium propionate are used :



(2) By Thermal decomposition of carboxylic acids:

Vapour of carboxylic acids when passed over MnO/300°C give carbonyl compounds

$$2HCOOH \xrightarrow[300°C]{MnO} HCHO + H_2O + CO_2$$

$$2CH_3COOH \xrightarrow[300°C]{MnO} \underset{H_3C}{\overset{H_3C}{>}}C{=}O + CO_2 + H_2O$$

$$RCOOH + HCOOH \xrightarrow[300°C]{MnO} RCHO + CO_2 + H_2O$$

$$RCOOH + HCOOH \xrightarrow[300°C]{MnO} RCHO + CO_2 + H_2O$$

$$RCOOH + HCOOH \xrightarrow[300°C]{MnO} RCHO + CO_2 + H_2O$$

$$RCOOH + R'COOH \xrightarrow[300°C]{MnO} RCOR' + CO_2 + H_2O$$

Physical Properties :

State :

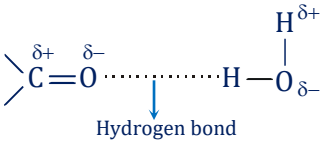
Only formaldehyde is gas, all other carbonyl compounds upto C_{11} are liquids and C_{12} & onwards solid.

Odour :

Lower aldehydes give unpleasant smell, higher aldehydes and all ketones have pleasant smell.

Solubility :

C_1 to C_3 (formaldehyde, acetaldehyde and propionaldehyde) and acetone are freely soluble in water due to polarity of $\overset{\delta+}{C}{=}\overset{\delta-}{O}$ bond and can form hydrogen bond with water molecule. C_5 onwards are insoluble in water.

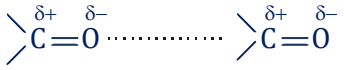


$$\text{Solubility} \propto \frac{1}{\text{Molecular weight}}$$

Boiling point : Boiling point $\propto$ Molecular weight

Boiling point order is - **Alcohol > Carbonyl compounds > Alkane**

This is because in alcohols intermolecular H-bonding is present but in carbonyl compounds H-bonding doesn't exist, instead dipole-dipole vander waal force of attraction is present. Alkanes are non-polar.



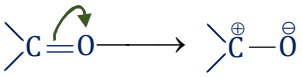
Density : Density of carbonyl compounds is lower than water.

Uses of Aldehydes and Ketones :

- Act as solvents.
- Act as starting materials and reagents for the synthesis of other products.
- Formalin (40% solution of formaldehyde)- Used for preserving biological specimens, bakelite, urea, formaldehyde glues and other polymers products.
- Acetaldehyde used in the manufacture of acetic acid, ethyl acetate, vinyl acetate, polymers and drugs.
- Benzaldehyde used in perfumery and in dye industries.
- Butyraldehyde, vanillin, camphor, etc., are well known for their odours and flavours.
- Acetone and ethyl methyl ketone are common industrial solvents.

Nucleophilic Addition Reaction (NAR) of carbonyl compounds :-

Due to strong electronegativity of oxygen, the mobile π electrons pulled strongly towards oxygen, leaving the carbon atom deficient of electrons.

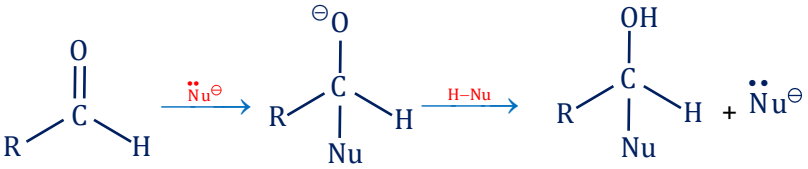


Carbon is thus readily attacked by $\ddot{N}u$. The negatively charged oxygen is attacked by electron deficient (electrophile) E^+, hence carbonyl compound shows Nucleophilic Addition Reaction (NAR).

bond in carbonyl group is stronger than C=C bond in alkanes.

C — O	Bond energy is 84.0 kcal	C — C	Bond energy is 83.1 kcal
C = O	Bond energy is 178 kcal	C = C	Bond energy is 146 kcal

Base catalysed



Acid catalysed :

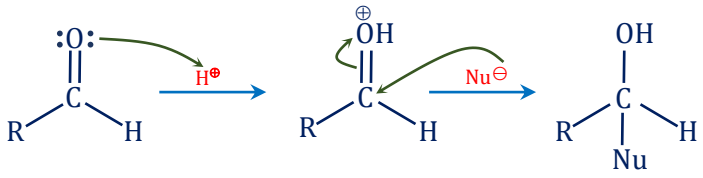
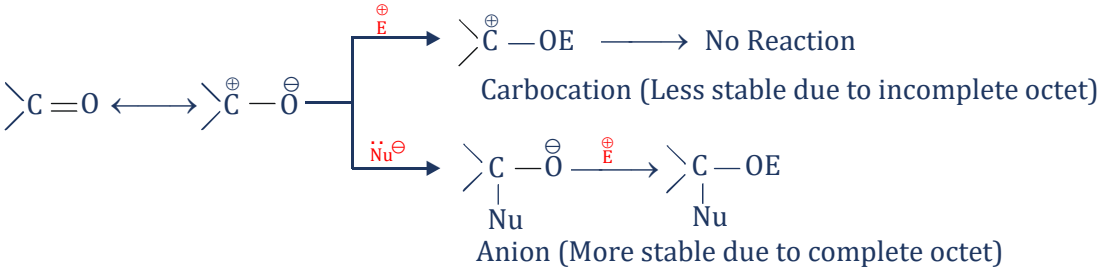


Illustration 1:

Why carbonyl compound gives nucleophilic addition reaction (NAR)?

Solution:



(i) Reactivity of carbonyl group $\propto$ Magnitude of positive charge $\propto$ –I group $\propto$ 1/+ I group at carbonyl carbon

(ii) Reactivity of carbonyl group $\propto \dfrac{1}{\text{Steric Hindrence on carbonyl group}}$

Illustration 2:

Arrange the following for reactivity towards NAR in decreasing order

(A) (I) $\begin{matrix}H\\H\end{matrix}\!\!>\!C=O$ (II) $\begin{matrix}CH_3\\H\end{matrix}\!\!>\!C=O$ (III) $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C=O$

(B) (I) $ClCH_2CHO$ (II) NO_2CH_2CHO (III) CH_3CHO (IV) CH_3CH_2CHO

(C) (I) CH_3CHO (II) $ClCH_2CHO$ (III) Cl_2CHCHO (IV) Cl_3CCHO

(D) (I) $\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>\!C=O$ (II) $\begin{matrix}CH_3CH_2\\CH_3\end{matrix}\!\!>\!C=O$ (III) $\begin{matrix}(CH_3)_2CH\\CH_3\end{matrix}\!\!>\!C=O$ (IV) $\begin{matrix}CCl_3\\CH_3\end{matrix}\!\!>\!C=O$

Ans.

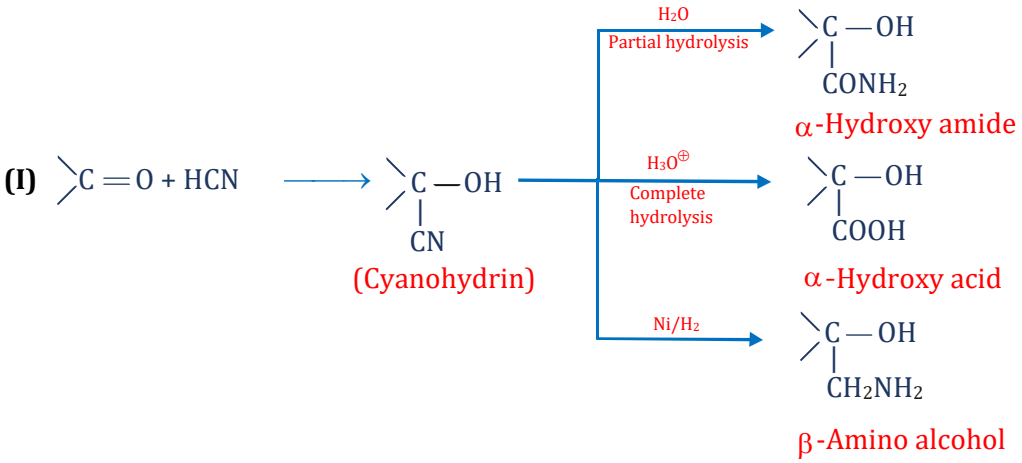
(A) I > II > III ; (B) II > I > III > IV ; (C) IV > III > II > I ; (D) IV > I > II > III

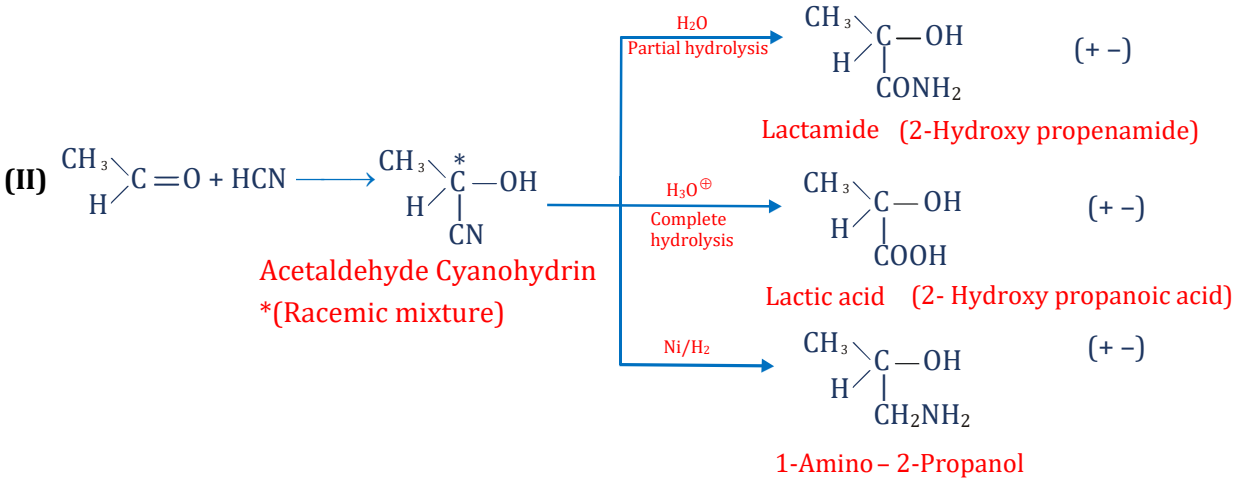
Solution:

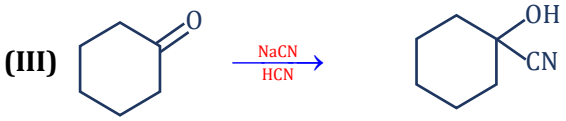
(A) I > II > III ; (B) II > I > III > IV ; (C) IV > III > II > I ; (D) IV > I > II > III

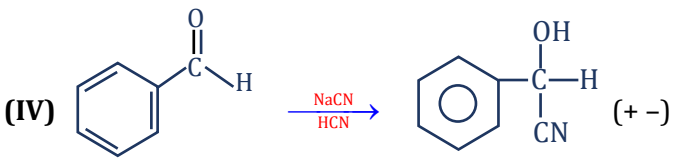
Chemical reaction of Nucleophilic Addition Reaction (NAR):

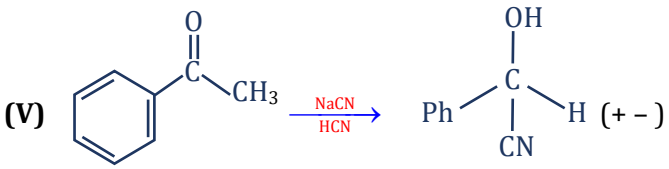
(1) Addition of HCN :





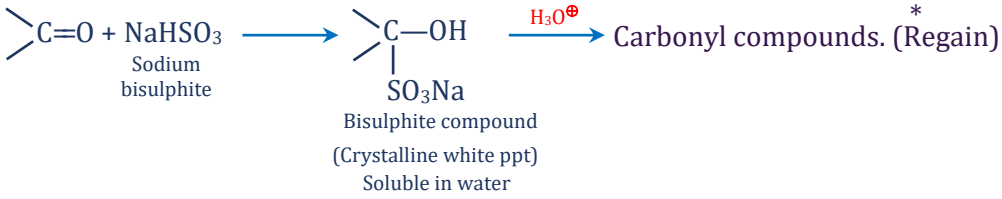




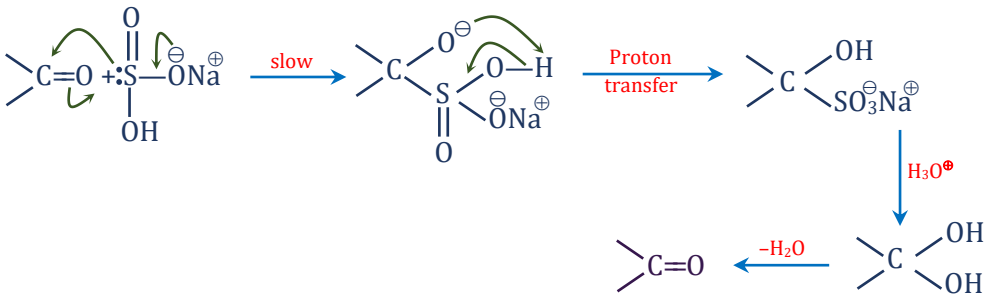


(2) Addition of $NaHSO_3$: (Reaction is useful in POC)

This reaction is utilized for the separation of carbonyl compounds from non - carbonyl compounds.



Mechanism : $NaHSO_3 \rightleftharpoons Na^{\oplus} + HSO_3^{\ominus}$



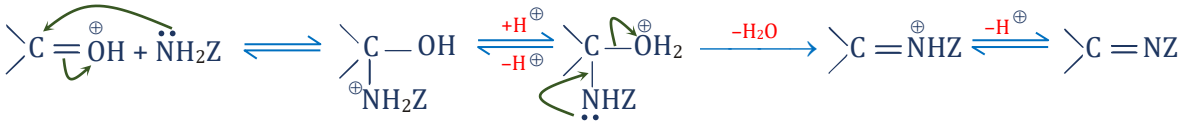
(3) Reaction with ammonia derivatives:

These are condensation or addition elimination reaction. These proceeds well in weakly acidic medium.

$NH_3 + Z \xrightarrow[+Z]{-H} NH_2Z$ (Ammonia derivative)

Addition - elimination (Condensation)

Mechanism :



Ammonia derivatives (NH_2Z) :

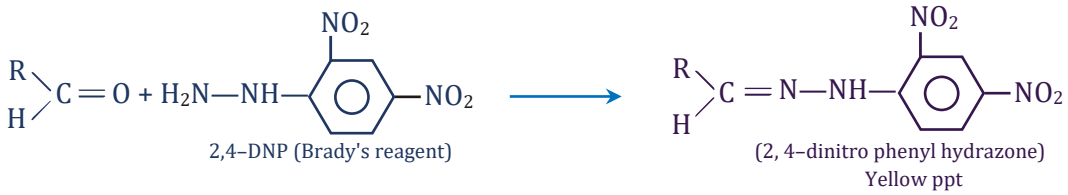
Z = —OH ⟶ NH_2OH (Hydroxyl amine)

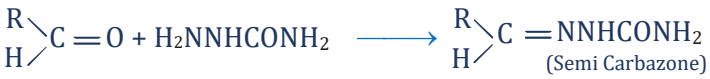
Z = —NH_2 ⟶ NH_2NH_2 (hydrazine)

Z = —NHC_6H_5 ⟶ $NH_2NHC_6H_5$ (Phenyl hydrazine)

Z = —$NHCONH_2$ ⟶ $NH_2NHCONH_2$

Semi Carbazide

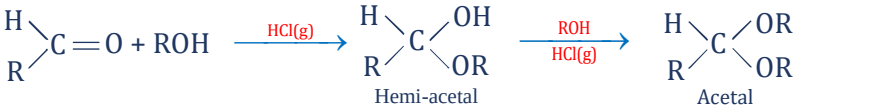


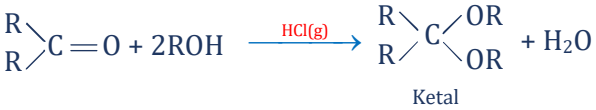


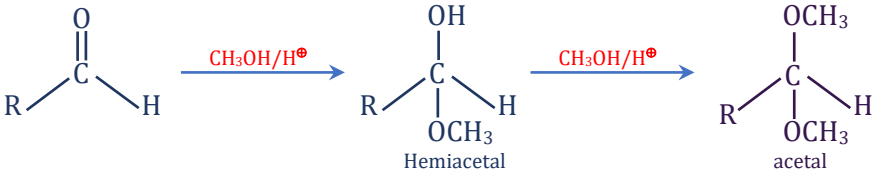
Important note :

1. NH_3 gives imine as product with carbonyl compound.
2. 1° amines (Primary amines) give → N–alkyl imine and 2° amines give → enamine

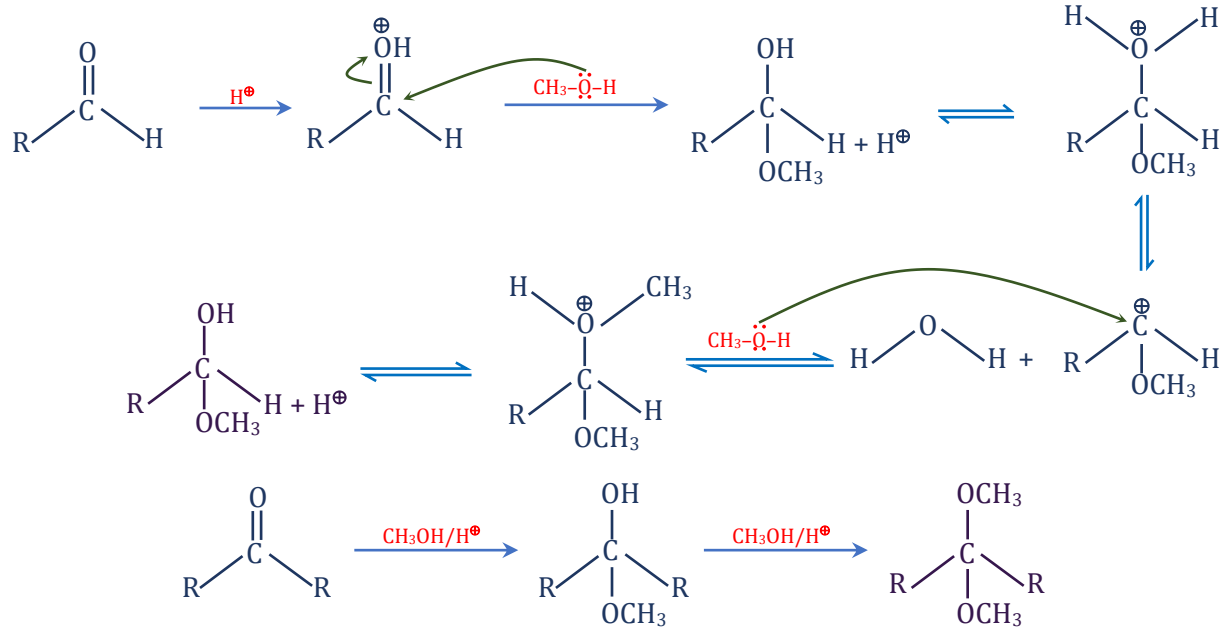
(4) With alcohol :







Mechanism :



(5) Reaction with H_2O : It is a reversible reaction.

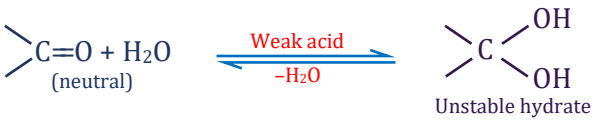


Illustration 3:

Which compound form more stable hydrate with H_2O?

(A) HCHO (B) CH_3CHO (C) CH_3COCH_3 (D) $CH_3COC_2H_5$

Ans. (A)

Solution :

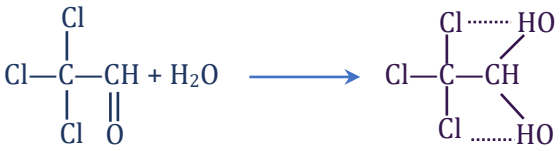
HCHO since it is more reactive towards this reaction.

Illustration 4 :

Which carbonyl compound not gives reversible reaction with water ?

Solution :

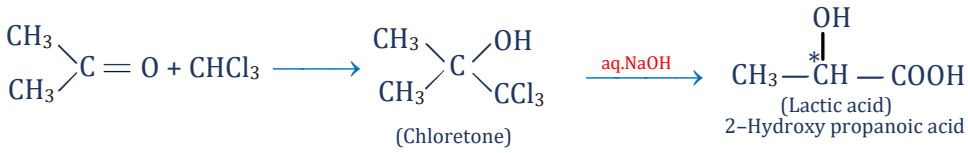
Chloral hydrate.



(Chloral) (Chloral hydrate)

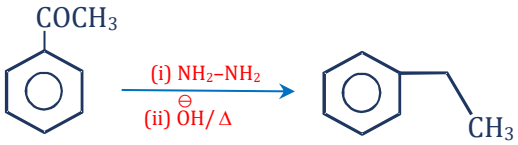
Stable by intramolecular hydrogen bonding.

(6) Reaction with chloroform :



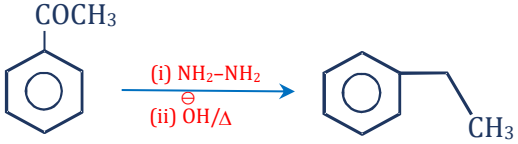
The Wolf Kishner reduction :

When a ketone or an aldehyde is heated in a basic solution of hydrazine, the carbonyl group is converted to a methylene group this process is called Deoxygenation because an oxygen is removed from the reactant. The reaction is known as the Wolf-kishner Reduction.



Clemmensen Reduction :

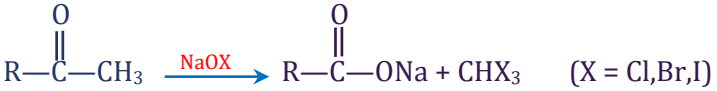
The reduction of carbonyl groups of aldehydes and ketones to methylene groups with amalgamated zinc and concentrated hydrochloric acid is known as Clemmensen reduction.

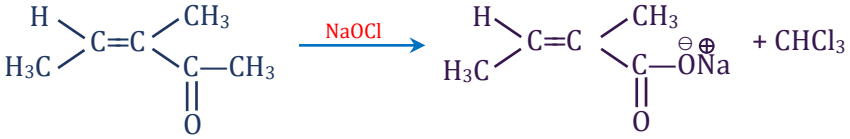


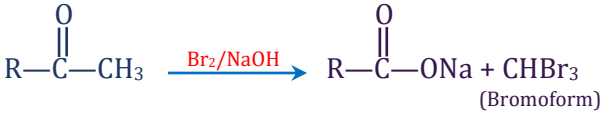
Oxidation :

(i) Haloform reaction :

Acetaldehyde and methylalkyl ketones react rapidly with halogen (Cl_2, Br_2, or I_2) in the presence of alkali to give haloform and acid salt.

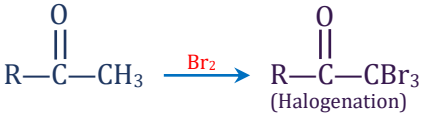




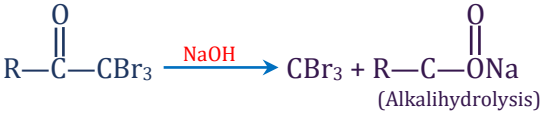


In this reaction $-CH_3$ of $CH_3-\overset{\overset{O}{\|}}{C}-$ group is converted into haloform as it contains acidic hydrogen atom and rest–part of alkyl methyl ketone acid salt having carbon atom corresponding to alkyl ketone. Preparation of haloform from methylketone involves two steps.

(a) Halogenation



(b) Alkalihydrolysis



Oxidation:

(i) Tollen's reagent :

Ammonical silver nitrate (Tollen's reagent) in which the oxidation of the aldehyde is accompanied by reduction of silver ion to free silver appearing in the form of a mirror under the reaction conditions.

$$\underset{\text{Colorless solution}}{RCHO + 2Ag(NH_3)_2OH} \longrightarrow \underset{\text{(Silver mirror)}}{2Ag + RCOONH_4 + H_2O + 3NH_3}$$

Since ketones do not undergo oxidation under mild conditions, Tollen's reagent is for differentiating them from ketones. Tollen's reagent also does not attack carbon–carbon double and hence the reaction provides a valuable method for the synthesis of α, β–unsaturated acids form α, β–unsaturated aldehydes, which are available by the aldol condensation and subsequent dehydration.

(ii) Fehling's solution:

Fehling's solution is an alkaline solution of copper sulphate containing sodium potassium tartrate Rochelle salt) as the complexing agent.

$$R-CHO + 2Cu(OH)_2 + NaOH \longrightarrow \underset{\text{Red precipitate}}{RCOONa + Cu_2O \downarrow + 3H_2O}$$

Ketone are not easily oxidise, thus they do not reduce fehling solution or tollen's reagent. But a hydroxyl ketone readily reduce. The compounds reduce fehiling solution and tollen's are given below

		Fehling solution	Tollen's Reagent
1.	Glucose, Fructose	+	+
2.	α–hydroxy aldehyde	+	+
3.	α–hydroxy ketone	+	+
4.	Formic acid	+	+
5.	Succinaldehyde CH_2—CHO | CH_2—CHO	+	+
6.	Pyruvaldehyde CH_3COCHO	+	+
7.	Glyoxal	–	+
8.	Benzaldehyde and other aromatic aldehyde	–	+
9.	Glyoxylic acid CHO | COOH	–	+

(iii) Benedict's solution :

Benedict's solution is alkaline copper sulphate containing citrate ions as complexing agent. Aldehydes on warning with this solution, give brick red precipitates.

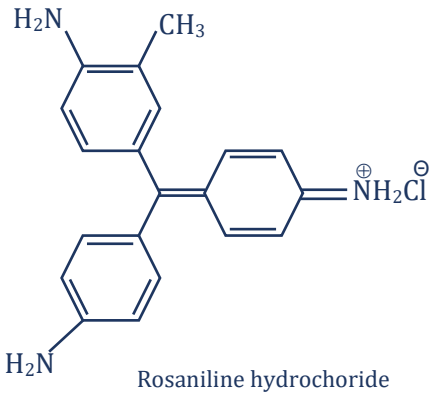
$$RCHO + Cu^{2\oplus}\text{ (complex)} \longrightarrow \underset{\text{Red precipitate}}{Cu_2O\downarrow} + RCOOH$$

Fehling solution and Benedict's solution ate very weak oxidizing agents. These can oxidize only aliphatic aldehydes do not oxidize aromatic aldehydes such as benzaldehyde.

Since Ketones are not oxidized by weak oxidizing agents, such as Tollen's reagent or Fehling solution, therefore, such reagents may be used to distinguish between aldehydes and ketones.

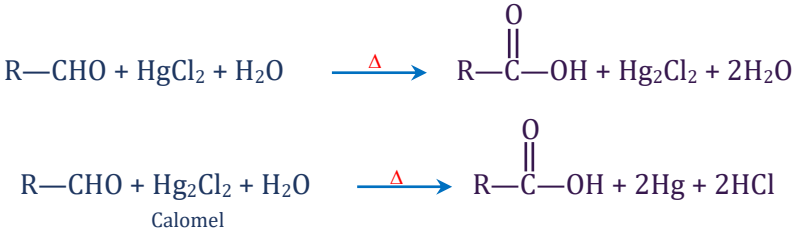
Schiff's Reagent :

Schiff's reagent is an aqueous solution of magenta or pink coloured rosaniline hydrochloride which has been decolourised by passing SO_2.When aldehydes are treated with decolourised solution of Schiff's reagent, its pink or magenta colour is restored. This reaction is used as a test for aldehydes because ketones do not restore the pink colour of Schiff's reagent.



Rosaniline hydrochoride

Oxidation by $HgCl_2/Hg_2Cl_2$:



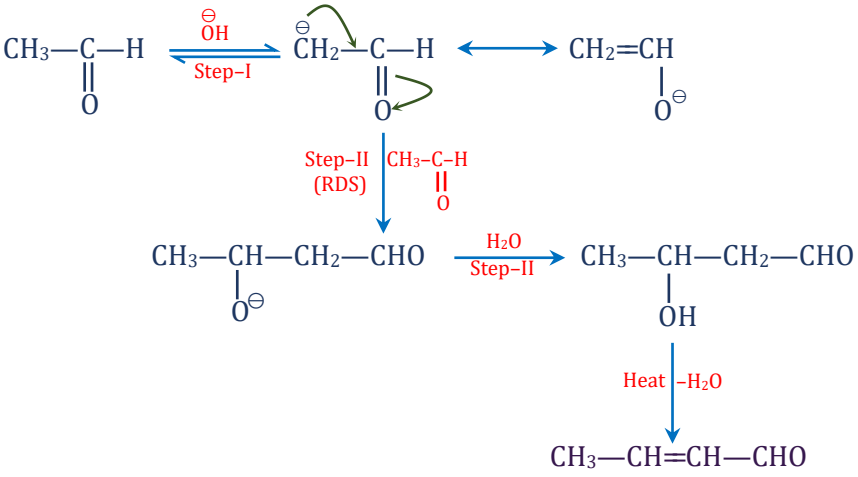
Aldol condensation (or aldol reaction):

Aldehydes and ketones with at least one α-hydrogen undergo a reaction in the presence of dilute alkali as catalyst.

Aldol is derived from two functional groups aldehyde(s) and alcohol.

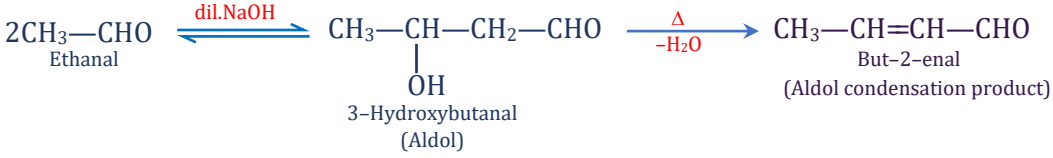
Ketones gives ketols (keto + alcohols) groups. The name aldol condensation still applies to their reactions.

Mechanism :

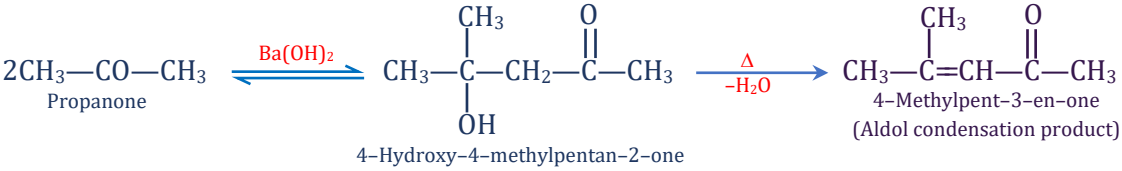


Ex.

(a)



(b)



(I) Cross-Aldol condensation:

On using two types of carbonyl compounds both having α-hydrogen atoms we get a mixture of four condensed product because two types of carbonyl compounds will give two type of carbanions which will be nucleophile for itself and other molecule.

$CH_3CHO + CH_3CH_2CHO \xrightarrow[(ii)\ \Delta]{(i)\ NaOH}$

$CH_3—CH=CH—CHO$ (Simple or self-aldol products)

+

$CH_3—CH_2—CH=\underset{\displaystyle CH_3}{\overset{|}{C}}—CHO$ (Simple or self-aldol products)

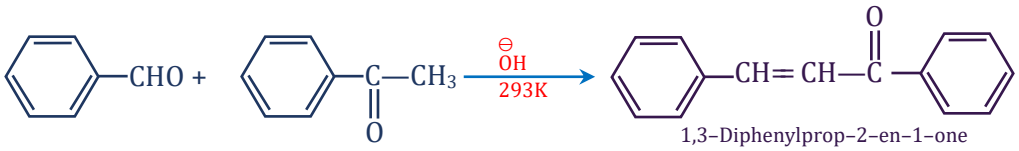
+

$CH_3—CH=\underset{\displaystyle CH_3}{\overset{|}{C}}—CHO$ (Cross aldol products)

+

$CH_3—CH_2—CH=CH—CHO$ (Cross aldol products)

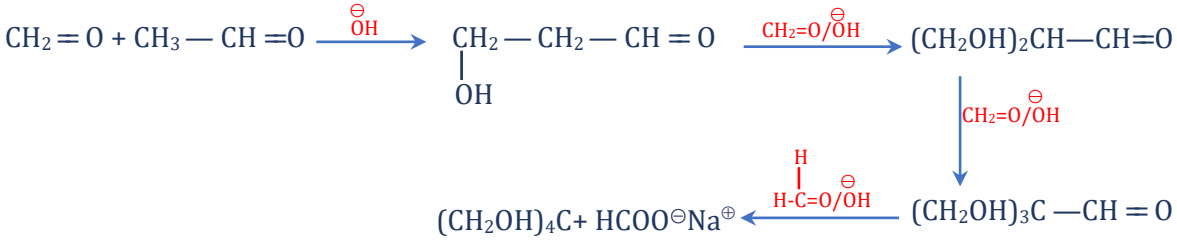
Ketones can also be used as one component in cross-aldol reactions.



1,3–Diphenylprop–2–en–1–one
{Benzalacetophenon}
{Major product}

Note :

On using formaldehyde and acetaldehyde during crossed aldol all the α-hydrogen atom of acetaldehyde are replaced one by one by hydroxymethyl group because of smaller size of formaldehyde to give trihydroxymethylacetaldehyde which undergoes crossed cannizaro's reaction with formaldehyde to give tetrahydroxymethyl methane and formate ion as a final product.

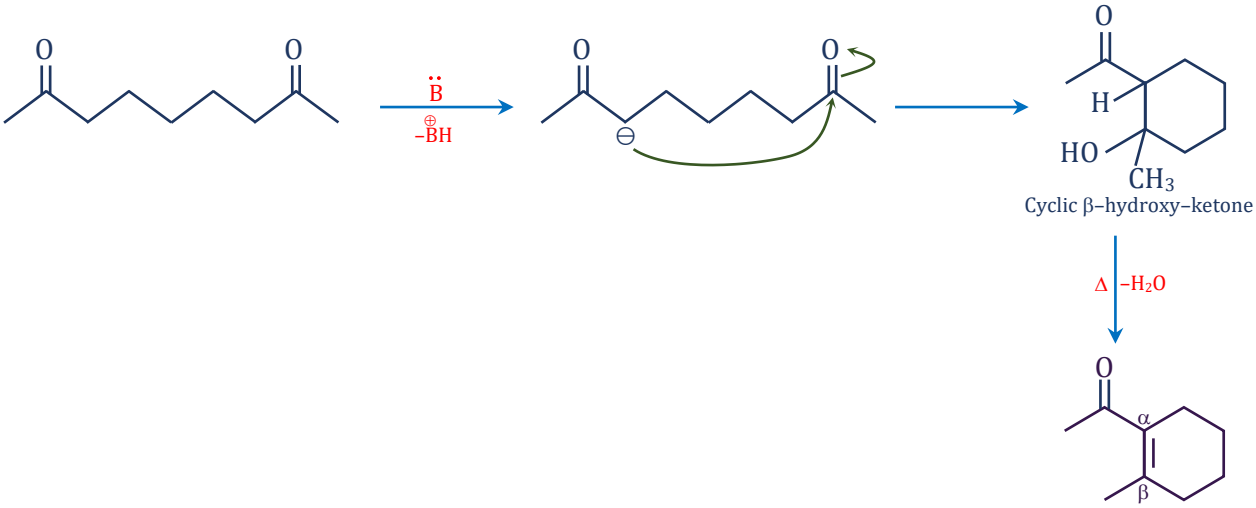


Ex. Show how cinnamaldehyde is prepared by crossed aldol condensation ?

Sol. $C_6H_5HO + CH_3CHO \xrightarrow[(-H_2O)]{\ominus OH} C_6H_5CH=CH—CHO + H_2O$

(II) Intramolecular aldol condensation :

If two carbonyl groups with α-hydrogen atoms are present within the same molecule, then we get cyclic α, β-unsaturated aldehyde/ketones via the formation of cyclic-β-hydroxy aldehyde / ketone in presence of basic medium.



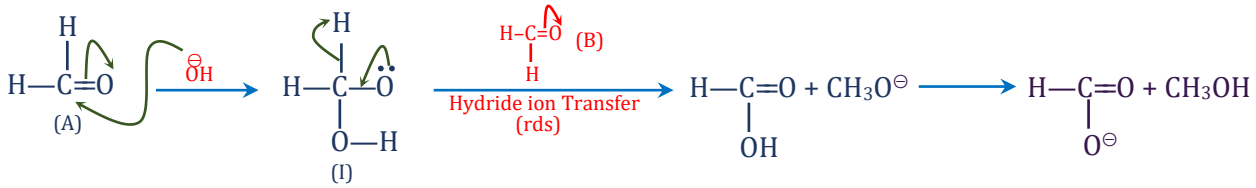
By knowing product we can get reactant as in case of intermolecular aldol condensation :

Cannizzaro reaction:

Aldehydes which do not have an α-hydrogen atom, undergo self oxidation and reduction (disproportionation) reaction on treatment with a concentrated alkali.

Ex :

Mechanism :



By this mechanism it is clear that acid corresponds to that carbonyl compound over which $\overset{\ominus}{O}H$ can attack easily as nucleophile.

Note :

It is observed that hydride ion transfer from (I) to Carbonyl compound (B) is rate determining step.

Crossed Cannizzaro reaction :

On using two types of carbonyl compounds not having α-hydrogen atom, acid salt will be corresponding to that aldehyde over which $\overset{\ominus}{O}H$ will approach without any hinderence.

(i) $\underset{(A)}{H-\overset{H}{\overset{|}{C}}=O} + \underset{(B)}{C_6H_5-CH=O} \xrightarrow{\ominus OH} H-C\begin{matrix}=O\\ -O^{\ominus}\end{matrix} + C_6H_5CH_2OH$

(ii) $\underset{(A)}{(CH_2OH)_3C-CH=O} + \underset{(B)}{H-\overset{H}{\overset{|}{C}}=O} \xrightarrow{\ominus OH} (CH_2OH)_3C-CH_2OH + H-C\begin{matrix}=O\\ -O^{\ominus}\end{matrix}$

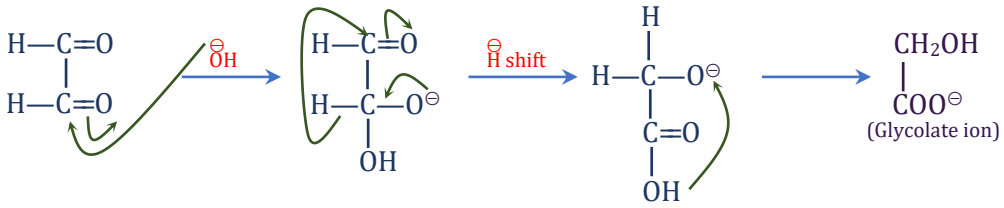
in case (i) $\overset{\ominus}{O}H$ will easily go to (A) and in case (ii) it will go to (B) hence acid salt will be formate ion in both the cases.

Intramolecular Cannizzaro reaction:

Here two carbonyl groups (without α-hydrogen atom) are present within the same molecule.

$\begin{matrix}CH=O\\ |\\ CH=O\end{matrix} \xrightarrow{\ominus OH} \underset{\text{Glycolate ion}}{\begin{matrix}CH_2OH\\ |\\ COO^{\ominus}\end{matrix}}$

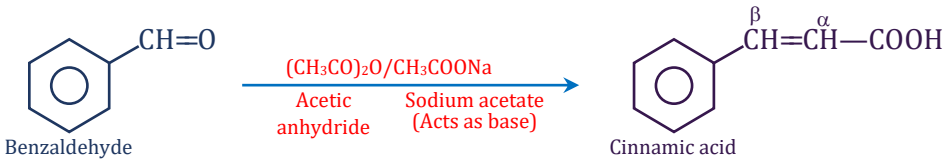
Mechanism :



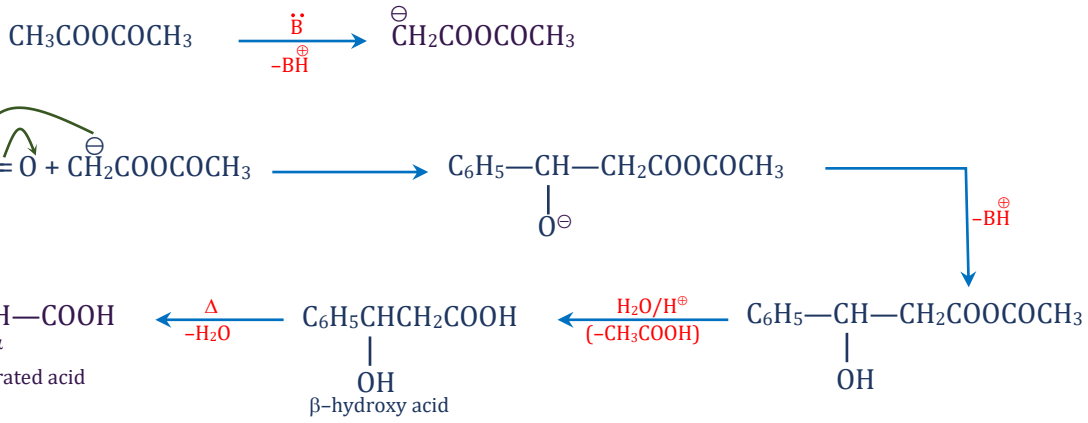
Ex. $\begin{matrix}C_6H_5-C=O\\ |\\ H-C=O\end{matrix} \xrightarrow{\ominus OH} \begin{matrix}C_6H_5-CHOH\\ |\\ COO^{\ominus}\end{matrix}$ (mendalic acid ion)

Perkin reaction :

When aromatic aldehyde like benzaldehyde is treated with anhydride in the presence of sodium salt of acid from which anhydride is derived we get α, β-unsaturated acid.



Mechanism :

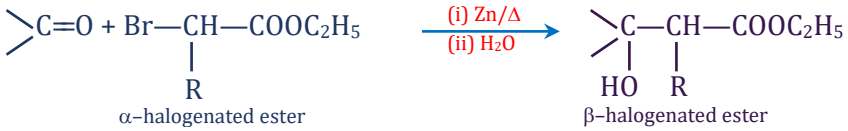


Note :

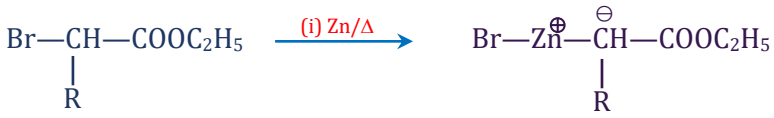
By knowing α,β–unsaturated acid we can get idea about the anhydride used in perkin reaction. This can be done by keeping 'H' at α and –OH at β–carbon atom followed by breaking α,β carbon. By this we can know about acid and it will be anhydride of this acid only.

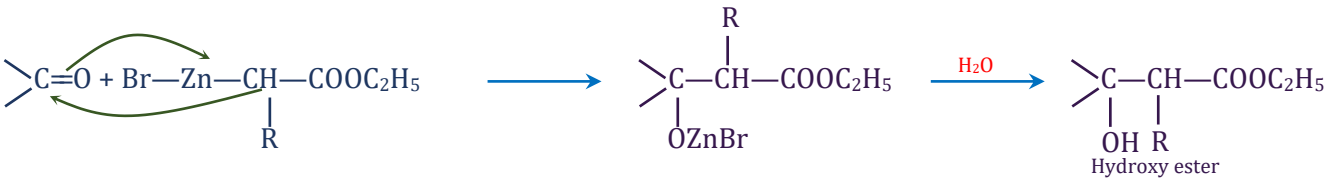
Reformatsky reaction:

When carbonyl compound and α-halogenated ester are heated with zinc followed by treating with water we get β-hydroxyester.



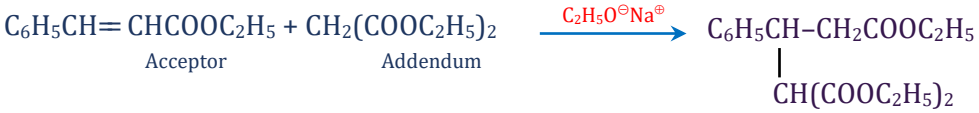
This reaction can be represented as –





Michael Reaction :

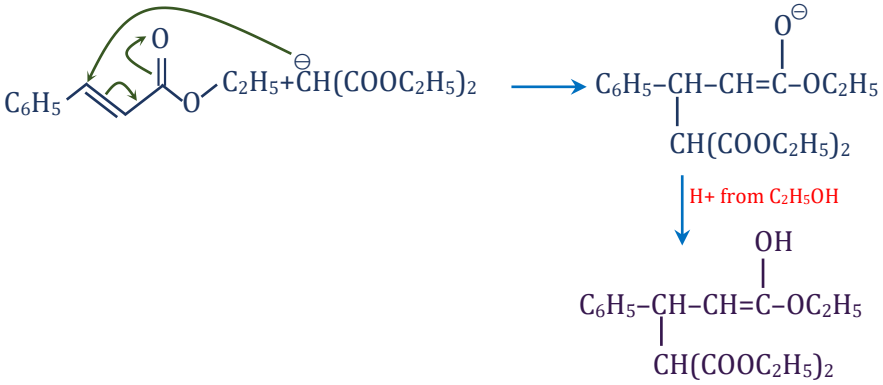
This is the addition reaction between an α, β unsaturated keto compound (acceptor) and with active methylene group (addendum) in presence of base.



Component

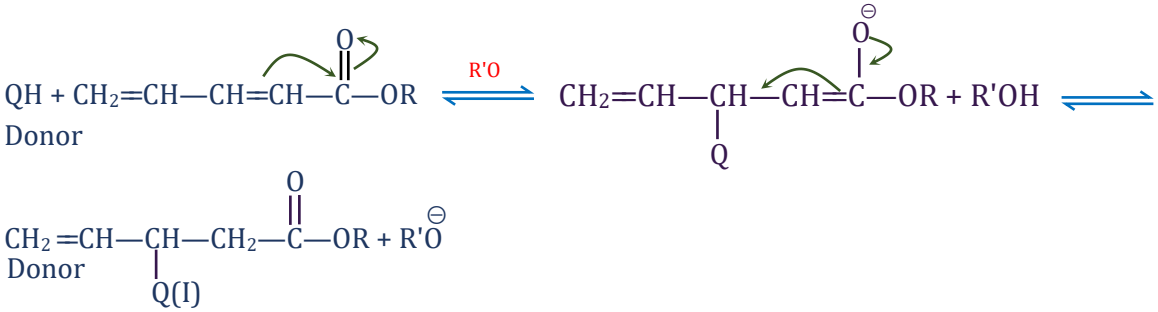
1. Acceptor – All, α, β -unsaturated compounds having a carbonyl or nitrile group in conjugation of double bond. e.g., ketone ester, nitrile (CH_2 = CH – CN), Aldehyde (CH_2 = CH – CHO) etc.
2. Addendum – Compound containing active methylene group which can ionize to a proton and a carbanion. e.g., Malonic acid, benzylcynide, cyclopentadiene etc.
3. Catalyst – Basic catalyst are used e.g. Alcoholic, aq. KOH, C_2H_5ONa etc.
   These catalyst bring about cyclization of the product but when the subsequent cyclization product is to be avoided mild catalyst are used e.g sec. amine, piperdine, pyridine, ter. Amine etc. Acid catalyst such as $AlCl_3$, BF_3, H_2SO_4 etc. can also bring about Michael reaction

Mechanism :

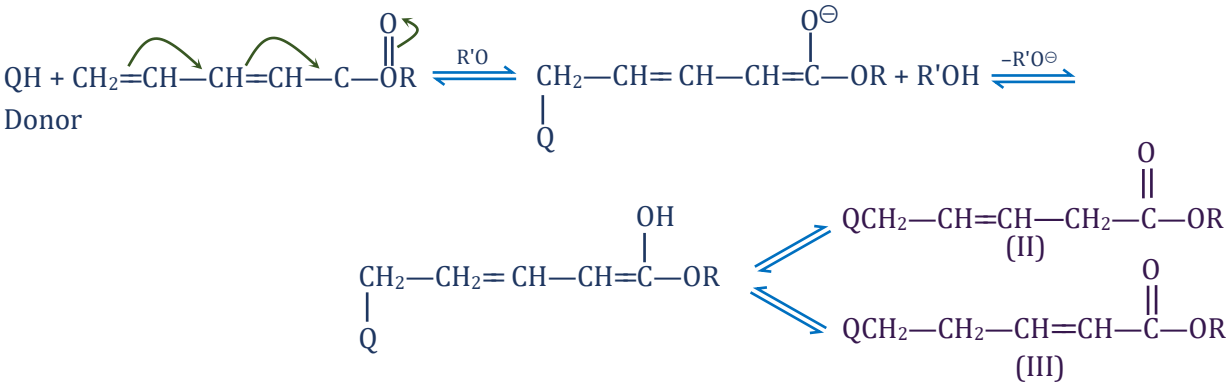
Step – 1	Base facilitates production of anion of compound containing active hydrogen 
Step – 2	Now carbanion react with acceptor and finaly tautomerises to keto form 
Step – 3	

Compounds with two double bonds in conjugation with the electron-withdrawing group may undergo nucleophilic attack at β-carbon or δ-carbon to give three products. Thus :

(a) On attack at β-carbon

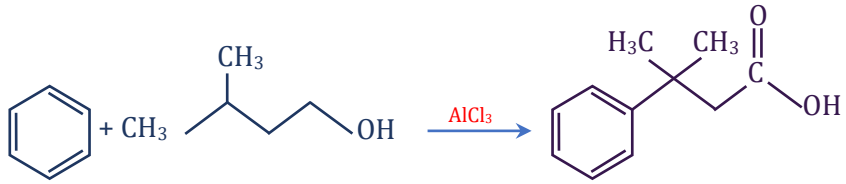


(b) On attack at δ-carbon

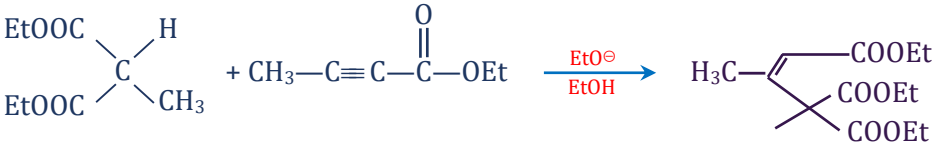


Since the double bond is conjugated in (III), it is the most stable of the three products. Hence it is the predominant product.

Michael acceptors can combine with Lewis acids to generate electrophile, which attacks the benzene ring.



Activated triple bond also acts as acceptor.

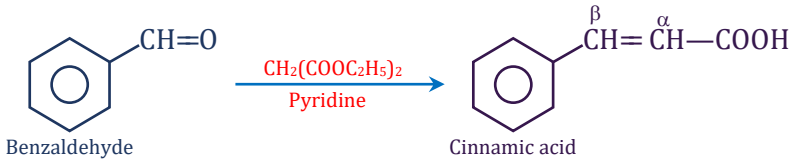


Note :

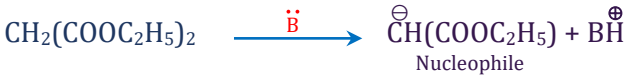
Michael addition preserves the —CO—group, which is strong. Therefore, Michael addition has thermodynamic advantage. The nucleophile pregers to attack the β-site instead of carbonyl group directly.

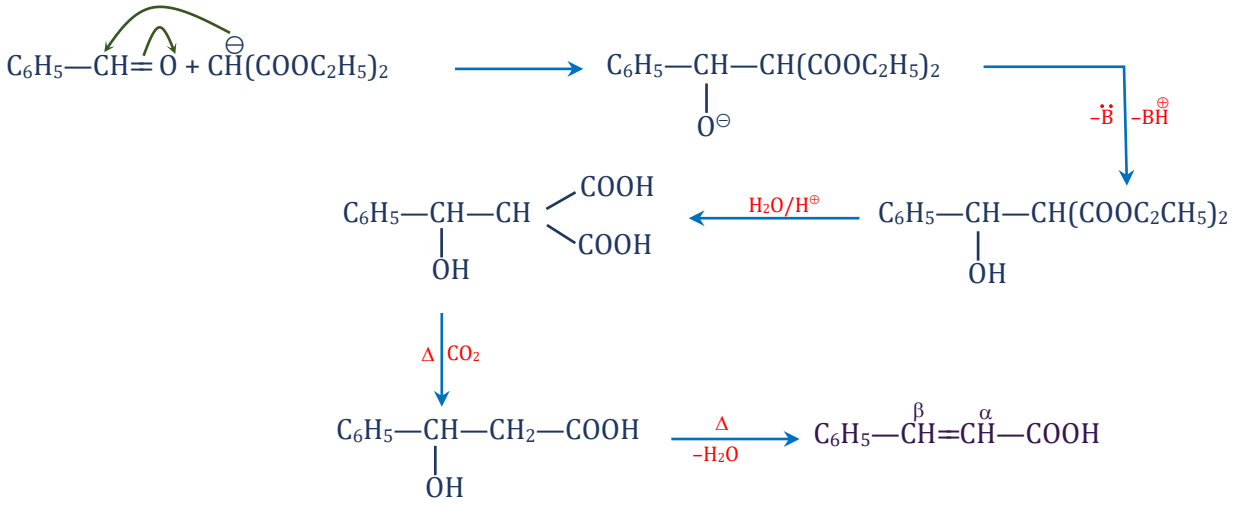
Knoevenagel reaction :

It is preparation of α, β-unsaturated acid with carbonyl compound using malonic ester in the presence of pyridine base.



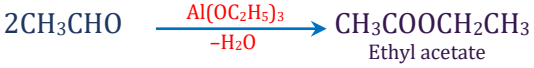
Mechanism :



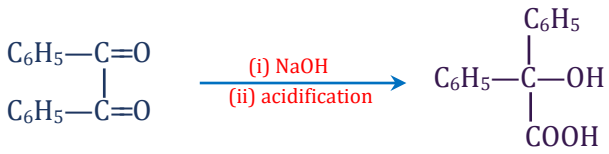


Tischenko Reaction :

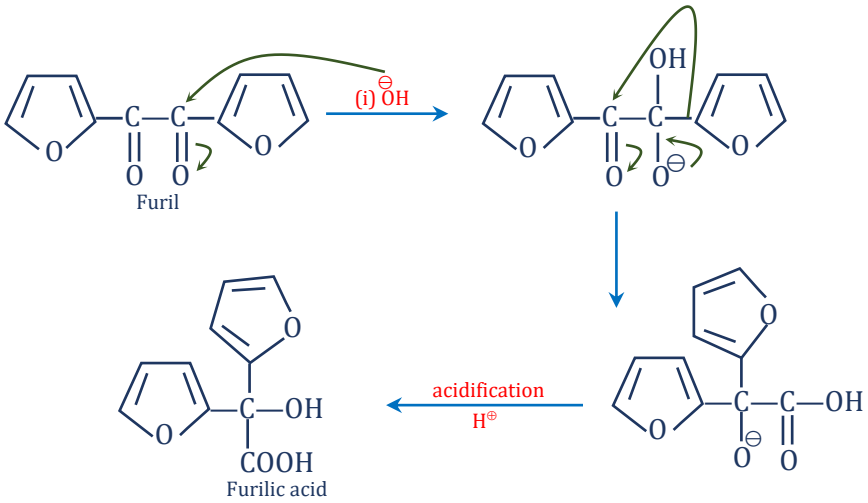
All aldehyde (with or without a-hydrogen) can be made to undergo cannizzaro reaction on treatment with aluminium ethoxide. However under these conditions the alcohol and acid produced as result of cannizzaro combine together to form ester.



Benzil-benzilic acid rearrangement:

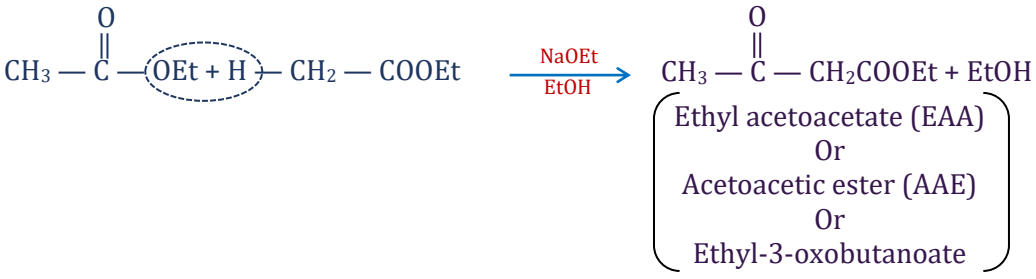


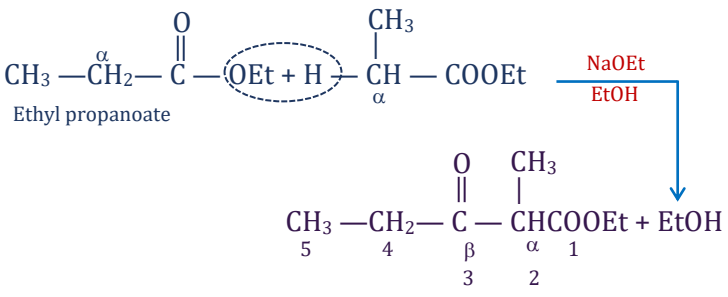
Conversion of furil to furilic acid with mechanism :



Claisen ester condensation:

In Claisen ester condensation, two molecules of an ester containing an α-H atom condense together in the presence of a base such as NaOMe or NaOEt to give a molecule of β-keto ester and a molecule of alcohol. For example.

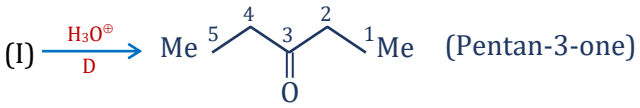
(i) 

(ii) 

Ethyl-2-methyl-3-oxopentanoate

(I)

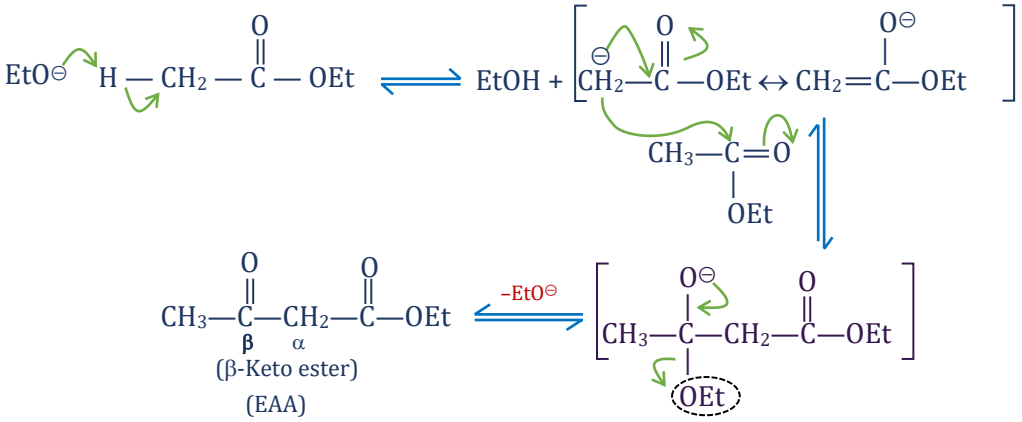
(iii) β-Keto ester on acidic hydrolysis gives β-keto acid which on heating loses CO_2 to give ketone. β-Keto acid on heating undergoes easy decarboxylation.



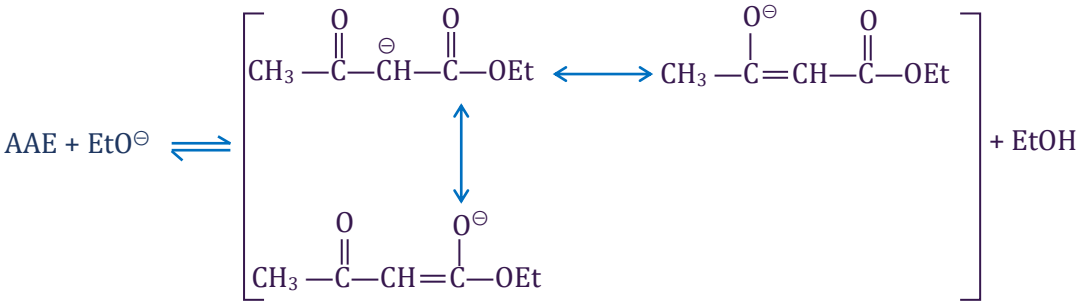
Mechanism :

i. The first step is the formation of α-carbanion which is stabilized through extended π-bonding with (C═O) of (COOR) group.

ii. In the second step, the carbanion adds to (C═O) of another molecule of ester displacing $EtO^{\ominus}$.



The equilibria for two steps are unfavourable for product formation. However, AAE has acidic protons between two (C═O) groups (pK_a of AAE = 11, pK_a of EtOH = 16) and $EtO^{\ominus}$ converts AAE to its conjugate base shifting the reaction for completion.



Mixed or cross claisen condensation

When two molecules of different esters containing α-H atom condense together in the presence of a base such as NaOMe or NaOEt, self- and cross- mixed-condensation products are obtained. The maximum number of cross Claisen ester condensation can be four, two self and two cross products.

For example, in the cross Claisen condensation of CH_3COOEt (I) and CH_3CH_2COOEt, the products formed are as given below:

Table Products of cross Claisen condensation

S.No.	Carbanion source	Acceptor	Product (b-keto ester)	Type
1	$\overset{\ominus}{\underset{\alpha}{CH_2}}COOEt(I)$	$CH_3-\overset{O}{\overset{\|\|}{C}}-OEt(I)$	$CH_3-\overset{O}{\overset{\|\|}{C}}-CH_2-COOEt$ (A)	Self Claisen
2	$\overset{CH_3}{\overset{\ominus}{\underset{\alpha}{CH}}}-COOEt(II)$	$CH_3CH_2-\overset{O}{\overset{\|\|}{C}}-OEt(II)$	$CH_3CH_2-\overset{O}{\overset{\|\|}{C}}-\overset{CH_3}{\overset{\|}{CH}}-COOEt$ (B)	Self claisen
3	$\overset{\ominus}{\underset{\alpha}{CH_2}}COOEt(I)$	$CH_3CH_2-\overset{O}{\overset{\|\|}{C}}-OEt(II)$	$CH_3CH_2-\overset{O}{\overset{\|\|}{C}}-CH_2COOEt$ (C)	Cross claisen
4	$\overset{CH_3}{\overset{\ominus}{\underset{\alpha}{CH}}}-COOEt(II)$	$CH_3-\overset{O}{\overset{\|\|}{C}}-OEt(I)$	$CH_3-\overset{O}{\overset{\|\|}{C}}-\overset{CH_3}{\overset{\|}{CH}}-COOEt$ (D)	Cross claisen

This is not an acceptable synthesis of (A) to (D), since the yield are poor because there are so many products.

Mixed Claisen condensation when one ester has α-H Atom and another Ester Lacks α-H Atom

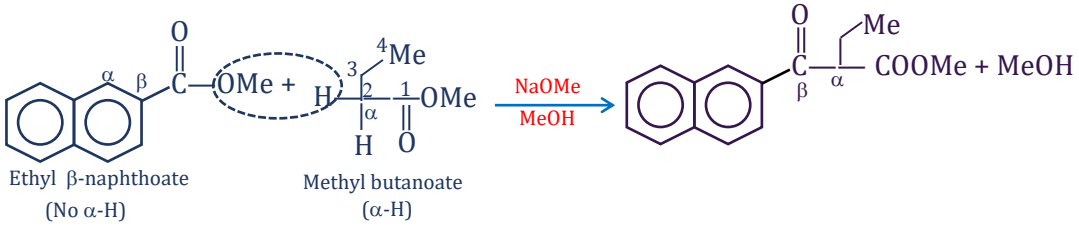
In these reactions, one ester lacking α-H atom as acceptor and ester with α-H atom acts as a carbanion source which adds slowly to the acceptor in an ethanolic solution of NaOEt, thereby discouraging self-condensation. Hence, these syntheses are reasonable for mixed Claisen products, e.g.,

i. $Ph-\overset{O}{\overset{\|\|}{C}}-OEt + H-\overset{\alpha}{CH_2}COOEt \xrightarrow[EtOH]{NaOEt} Ph-\overset{O}{\overset{\|\|}{\underset{\beta}{C}}}-\underset{\alpha}{CH_2}COOEt + EtOH$

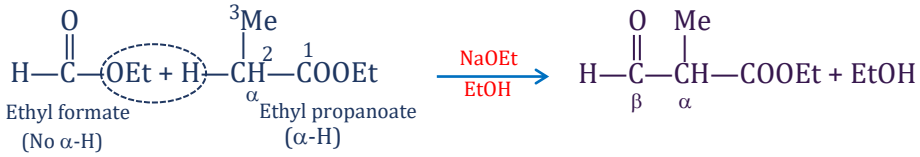
Ethyl benzoate (No α-H); Ethyl acetate (α-H) — Carbanion source; Cross(or) Mixed products

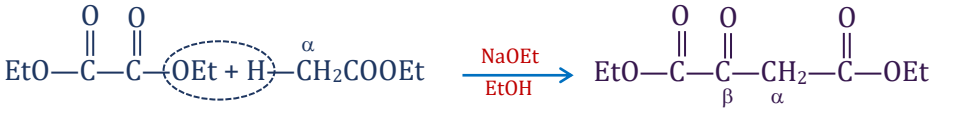
ii. $Me-C_6H_4-\overset{O}{\overset{\|\|}{C}}-OEt + H-\overset{Ph}{\overset{|}{\underset{\alpha}{CH}}}-COOEt \xrightarrow[EtOH]{NaOEt} Me-C_6H_4-\overset{O}{\overset{\|\|}{\underset{\beta}{C}}}-\overset{Ph}{\overset{|}{\underset{\alpha}{CH}}}-COOEt + EtOH$

Ethyl p-methyl benzoate (No α-H); Ethyl phenyl acctate (α-H)

iii. 

Ethyl β-naphthoate (No α-H); Methyl butanoate (α-H)

iv. 

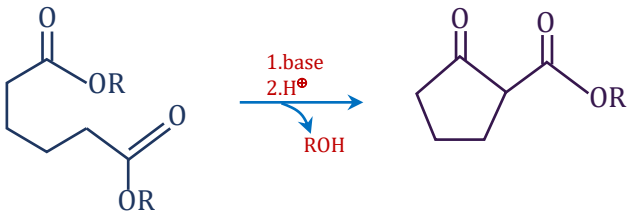
v. 

It does not react with another mole of ester because similar to AAE it forms an unreactive, stable carbanion flanked by two (C=O) groups.

vi. 

It also does not react with another mole of ester as explained above

The Dieckmann condensation is the intramolecular chemical reaction of diesters with base to give β–keto esters.



Mechanism