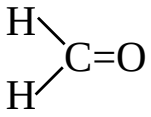
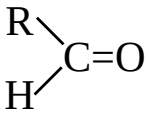
Introduction

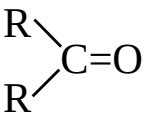
Aldehydes and ketones both possess a carbonyl group ($>C=O$) and therefore are called carbonyl compounds. Formaldehyde is the simplest aldehyde, bonded to two hydrogens. In all other aldehydes, the carbonyl group is bonded to a hydrogen and to an alkyl (or an aryl) group. The carbonyl group of a ketone is bonded to two alkyl (or aryl) groups.



Formaldehyde



An aldehyde



A ketone

Aldehydes and ketones undergo two types of characteristic reactions.

(a) Nucleophilic addition reactions:

The carbonyl compounds can be readily attacked by nucleophiles due to the presence of electrophilic carbon. In the overall reaction, nucleophilic addition takes place and not the nucleophilic substitution as aldehydes and ketones possess very poor leaving groups, R^- and H^- respectively.

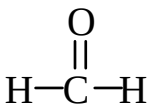
(b) Reactions due to acidity of α–hydrogen atoms:

Carbonyl compounds with α–hydrogen atoms can loose H^+ to a base to give carbanion, which is resonance stabilized. This carbanion acts as nucleophile and can add to the electrophilic carbon of same or different carbonyl compound to give final product.

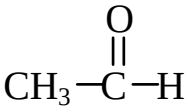
IUPAC Nomenclature Of Aldehydes & Ketones

The IUPAC name of an aldehyde is obtained by removing ‘e’ from the alkane name and adding ‘al’. The position of the aldehyde group is not necessarily designated since it is always at the terminal and is thus always at the number one position.

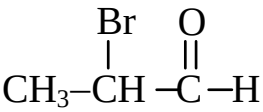
The common name of an aldehyde is same as the common name of the corresponding carboxylic acid, except that 'aldehyde' is substituted for 'ic acid' (or 'oic acid'). When common names are used, the position of a substituent is designated by a lowercase Greek letter. The carbonyl carbon is not given a designation, the carbon adjacent to the carbonyl carbon is the α–carbon.



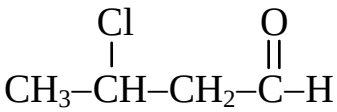
IUPAC name: Methanal
Common name: Formaldehyde



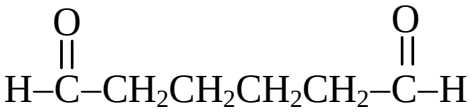
IUPAC name: Ethanal
Common name: Acetaldehyde



IUPAC name: 2–Bromopropanal
Common name: α–bromopropionaldehyde

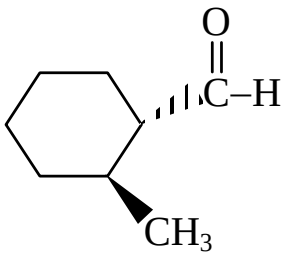


IUPAC name: 3–chlorobutanal
Common name: β–chlorobutyraldehyde

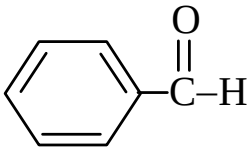


IUPAC name: Hexanedial
Common name: —

If the aldehyde group is attached to a ring, the aldehyde is named by adding "carbaldehyde" to the name of the cyclic compound.

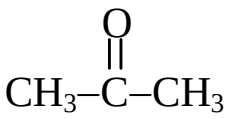


IUPAC name: trans–2–methylcyclohexane cycarbaldehyde
Common name: —

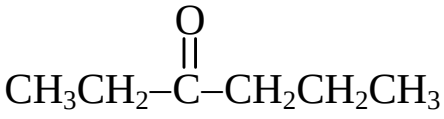


IUPAC name: Benzene carbaldehyde or phenylmethanal
Common name: Benzaldehyde

Ketones are named according to the IUPAC system by removing "e" from the alkane name and adding "one". The chain is numbered from that end, which gives smaller number to the carbonyl group. In case of cyclic ketones, numbering is not necessary because the carbonyl group is assumed to be at number 1 position. For ketones, derived names are also used. In derived names, the substituents attached to the carbonyl group are cited in alphabetical order followed by "ketone".

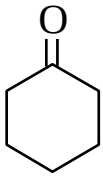


IUPAC name: Propanone
Common name: Acetone
Derived name: Dimethyl ketone

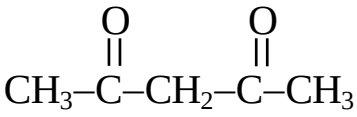


IUPAC name: 3–hexanone
Common name: ——
Derived name: Ethyl propyl ketone

IUPAC name: 6–methyl–2–heptanone
Common name: ——
Derived name: Isohexyl methyl ketone.



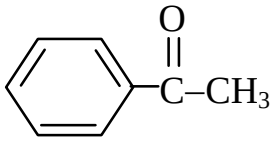
IUPAC name: Cyclohexanone
Common name: ——



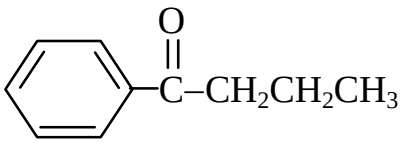
IUPAC name: 2, 4–pentanedione
Common name: Acetylacetone

IUPAC name: 4–hexen–2–one
Common name: ——

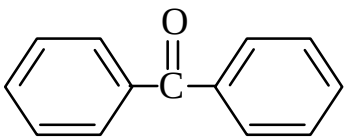
Common names are also used for some phenyl substituted ketones, the number of carbons (other than those of the phenyl group) is indicated by the common name of the corresponding carboxylic acid substituting "ophenone" for "ic acid".



IUPAC name: Acetophenone
Common name: Methyl phenyl ketone



IUPAC name: Butyrophenone
Common name: Phenyl propyl ketone



IUPAC name: Benzophenone
Common name: Diphenyl ketone

Methods Of Preparation Of Aldehydes & Ketones

By Oxidation Of Alcohols:

The oxidation of an alcohol involves the loss of one or more α–hydrogen atoms from the carbon bearing –OH group. The kind of product formed depends upon how many of these α–hydrogen atoms the alcohol contains, i.e. whether the alcohol is primary or secondary.

A primary alcohol (which has 2 α–hydrogens) can lose one of the hydrogen to form an aldehyde whereas secondary alcohol can lose its only α–hydrogen to form a ketone.

$$RCH_2OH \xrightarrow[KMnO_4 \text{ or Aqueous acidic } K_2Cr_2O_7]{\text{Aqueous acidic}} RCHO + MnO_2 \text{ or } Cr^{3+}$$

The reagents employed here are not highly selective since aldehyde can further be easily oxidised to carboxylic acids, so isolation of aldehydes in this reaction is troublesome. Thus, for the convenient and selective conversion of primary alcohol to aldehyde, pyridinium chlorochromate (PCC, $C_5H_5NH^+CrO_3Cl^-$) is used, which is formed by the reaction between chromic acid and pyridinium chloride.

$$RCH_2OH \xrightarrow[\text{or } CrO_3 \text{ in glacial acetic acid}\\ \text{or } CrO_3 \text{ in pyridine}]{\overset{\oplus}{C_5H_5NH}\overset{\ominus}{CrO_3Cl}\text{(PCC)}} RCHO + Cr^{3+}$$

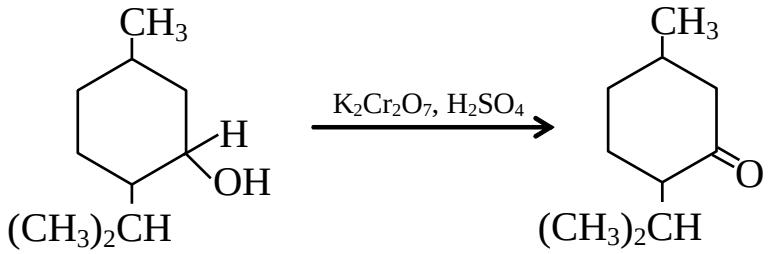
$$R_2CHOH \xrightarrow[\text{or Aqueous acidic } K_2Cr_2O_7\\ \text{or } CrO_3 \text{ in glacial acetic acid or}\\ CrO_3 \text{ in pyridine}]{\text{Aqueous acidic } KMnO_4} R_2CO + MnO_2 \text{ or } Cr^{3+}$$

Secondary alcohols can also be oxidised by aluminium t–butoxide, $[(CH_3)_3CO]_3Al$ in acetone. The reaction is called Oppenauer oxidation. In presence of p–benzoquinone solvent 1° alcohol can also be oxidised to aldehyde on distillation.

$$R_2CHOH \xrightarrow[\text{in acetone}]{[(CH_3)_3CO]_3Al} R_2CO + (CH_3)_2CHOH$$

For example,

$$CH_3CH_2CH_2OH \xrightarrow[CH_2Cl_2]{\text{PCC in}} CH_3CH_2CHO + Cr^{3+}$$



By Heating Calcium Or Barium Salts Of Carboxylic Acids:

When calcium salt of formic acid is dry distilled, formaldehyde is obtained. If a mixture of calcium salt of formic acid and any of its higher homologues is used, then aldehydes other than formaldehyde are obtained while when only calcium salt of monocarboxylic acid (other than formic acid) is dry distilled, the product obtained is a ketone.

$$(HCO_2)_2Ca \xrightarrow{\text{Dry distillation}} HCHO + CaCO_3$$

$$(HCO_2)_2Ca + (RCO_2)_2Ca \xrightarrow{\text{Dry distillation}} 2RCHO + CaCO_3 + RCOR + HCHO$$

$$(RCO_2)_2Ca \xrightarrow{\text{Dry distillation}} R_2CO + CaCO_3$$

If a mixture of calcium salts of acids is used, mixed ketones along with simple ketones are obtained.

$$(RCO_2)_2Ca + (R'CO_2)_2Ca \xrightarrow[\text{distillation}]{\text{Dry}} RCOR' + R_2CO + R'_2CO + CaCO_3$$

Using Acid Chloride:

Acid chlorides can be reduced to aldehydes, only by the use of a bulky hydride reducing agent, tri–t–butoxy lithium aluminium hydride. If $LiAlH_4$ is used as a reducing agent, the product isolated is an alcohol and not an aldehyde.

$$R–COCl \text{ or } Ar–COCl \xrightarrow{LiAlH(OBu-t)_3} R–CHO \text{ or } Ar–CHO$$

Acid chlorides can also be reduced to aldehydes by H_2 gas in the presence of Pd supported on $BaSO_4$ in xylene, poisoned with quinoline and sulphur. This reaction is called Rosenmund's reduction, which is applicable for the preparation of aliphatic as well as aromatic aldehydes.

$$R–COCl \text{ or } Ar–COCl \xrightarrow[\text{Poisoned with quinoline \& S}]{H_2/Pd-BaSO_4} R–CHO \text{ or } Ar–CHO + HCl$$

Acid chlorides on reaction with lithium organocuprates, R_2CuLi or Ar_2CuLi yields ketones. Here, the R part of organocopper compound acts as nucleophile and displaces Cl of acid chloride to undergo nucleophilic substitution.

$$R'X \text{ or } ArX \xrightarrow[-LiX]{2\,Li} R'Li \text{ or } ArLi \xrightarrow[-LiX]{CuX} R'_2CuLi \text{ or } Ar_2CuLi$$

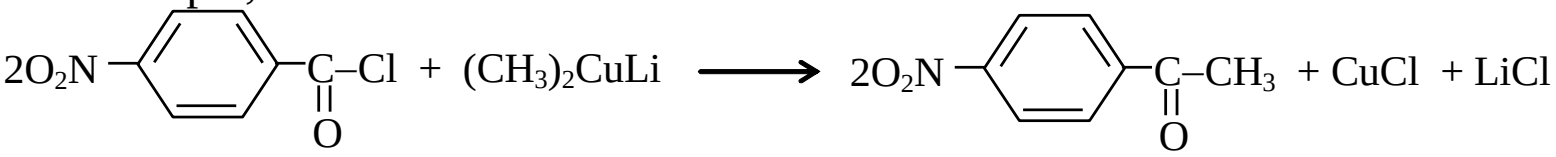
$$R'_2CuLi + 2RCOCl \longrightarrow 2RCOR' + CuCl + LiCl$$

(Note: R and R′ may be alkyl or aryl).

Grignard reagents can also react with acid chlorides, but the product is tertiary alcohols because the ketone produced reacts with additional RMgX. This shows that organocopper reagents are less reactive than Grignard reagents towards the carbonyl group of ketones and the reaction stops at the ketone formation stage.

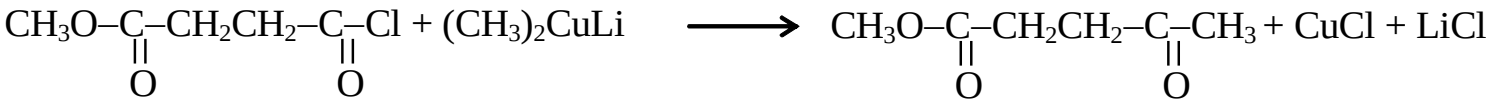
This low reactivity of organocopper compounds is useful in the light that it do not react with the functional groups with which organomagnesium and organolithium reagents react. Thus, the presence of some functional groups (like $-NO_2$, $-CN$, $-CO-$, $-CO_2R$ etc.) does not interfere with the synthesis of ketones.

For example,



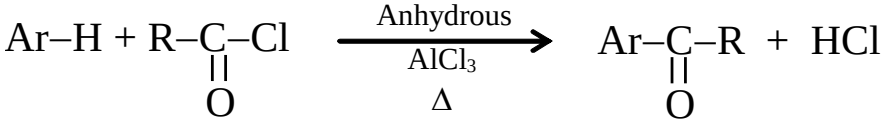
p–nitrobenzoyl chloride

p–nitro acetophenone

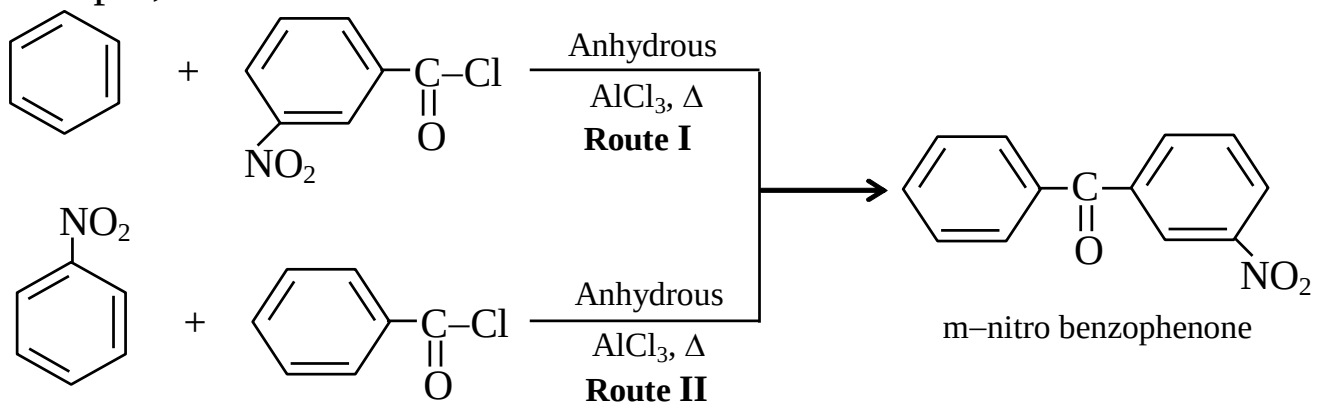


methyl–4–oxopentanoate

Aromatic ketones can be synthesized using acid chlorides and benzene via Friedel–Crafts acylation.



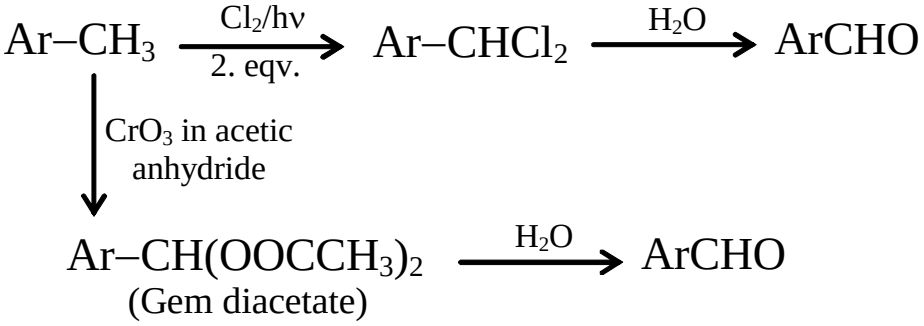
For example,



There seems to be two possible routes to get m–nitro benzophenone using Friedel–Crafts acylation. Route II is not feasible because nitrobenzene does not participate in Friedel–Crafts reaction, as $-NO_2$ is a strongly deactivating group. Thus, route I is the only feasible pathway to get m–nitro benzophenone.

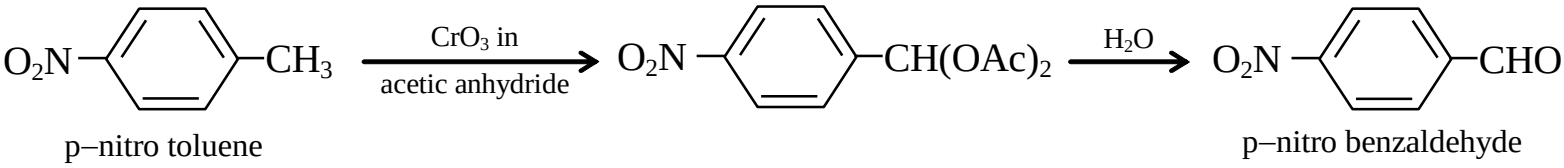
By Oxidation Of Methyl Benzenes (For Aromatic Aldehydes Only):

Methyl benzene on treatment with either Cl_2 in presence of ultraviolet light or CrO_3 in acetic anhydride gives $Ar–CHCl_2$ or $Ar–CH(OOCH_3)_2$. Both these compounds on decomposition with water gives benzaldehyde.



Overall reaction is the oxidation of methyl benzene to benzaldehyde. Oxidation of methyl benzene to benzaldehyde by CrO_3 in acetic anhydride is a better route than chlorination because the gem diacetate formed is not further oxidisable while $ArCHCl_2$ can further chlorinate to give $ArCCl_3$, which on hydrolysis finally gives $ArCO_2H$.

For example,

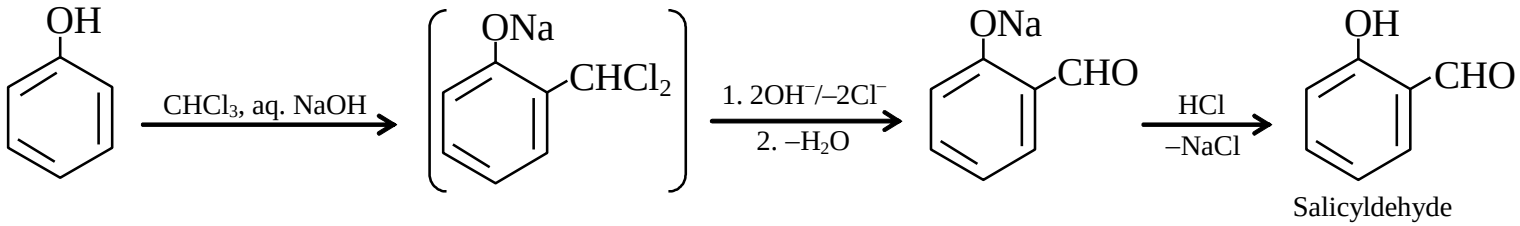


p–nitro toluene

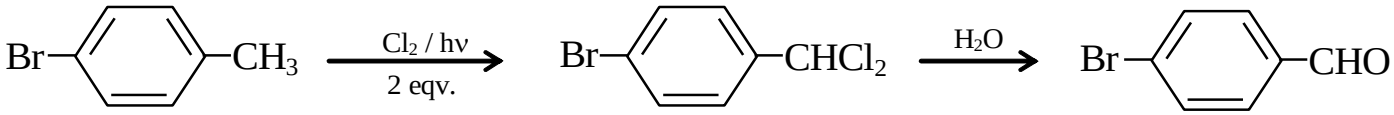
p–nitro benzaldehyde

Reimer–Tiemann Reaction (For Phenolic Aldehydes Only):

When phenol is treated with chloroform and aqueous NaOH/KOH, an aldehyde group is introduced in the aromatic ring, generally at the ortho position.



Salicyldehyde

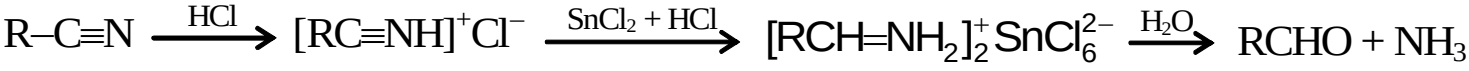


p–bromo toluene

p–bromo benzaldehyde

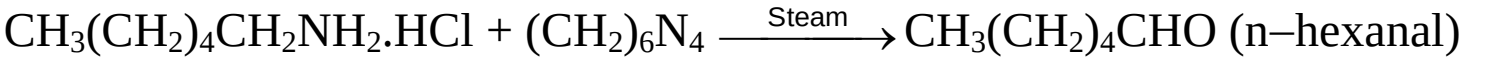
Stephen's Method (Only For Aldehydes):

An alkyl or aryl cyanide dissolved in ether is reduced with stannous chloride and HCl to give aliphatic or aromatic aldehydes. The reaction proceeds by the formation of aldimine hydrochloride (present as stannichloride), which are not stable and hydrolyse to give aldehydes.

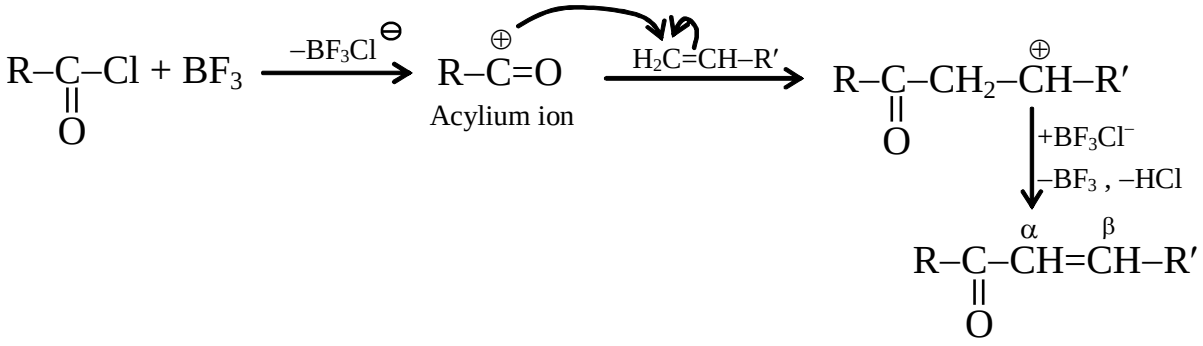


Sommelet Reaction (Only For Aldehydes):

When an aqueous solution of n–hexylamine hydrochloride is reacted with hexamethylene tetramine in acetic acid and steam is passed into it, n–hexanal is produced. This reaction is called Sommelet reaction.



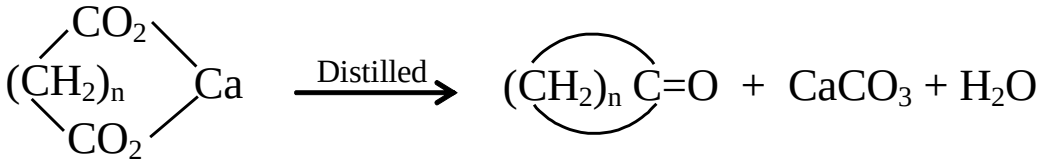
Acylation Of Alkenes (Only For Ketones):



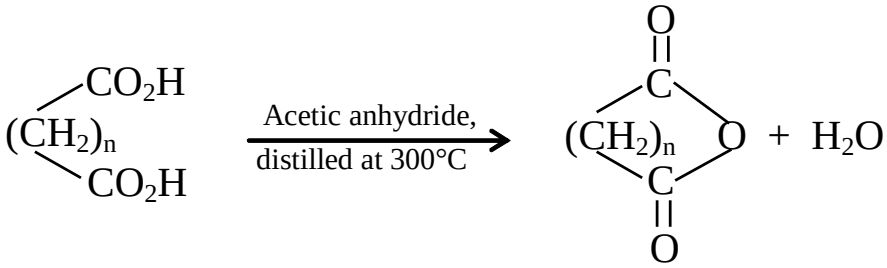
In this reaction, alkenes act as nucleophiles and cause nucleophilic substitution of Cl of RCOCl to give α, β–unsaturated ketone.

Ring Ketones From Dicarboxylic Acids:

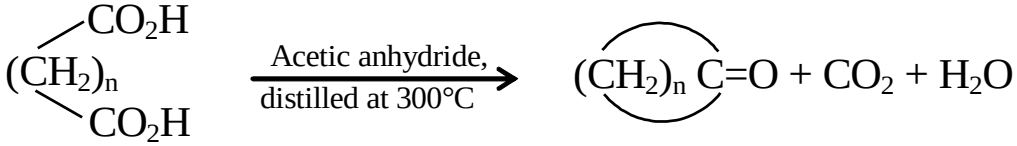
When the calcium, barium or thorium salts of the carboxylic acids are distilled, cyclic ketones (cycloalkanones) are produced.



When the 'n' value is 4, the product is cyclopentanone and when it is 5, the product is cyclohexanone. Also, when dicarboxylic acids are heated with acetic anhydride and then distilled at 300°C, cyclic anhydrides or cyclic ketones are formed depending on the relative positions of two carboxyl groups.



[n can be 2 or 3 i.e. the acid is 1, 4 or 1, 5–dicarboxylic acid].



[n can be 4 or 5 i.e. the acid is 1, 6 or 1, 7–dicarboxylic acid].

By Passing Vapours Of Carboxylic Acids Over MnO:

Aldehydes can be prepared by passing vapours of formic acid and any one of its homologue over manganous oxide as catalyst at 300°C.

$$RCO_2H + HCO_2H \xrightarrow{\Delta, MnO} RCHO + CO_2 + H_2O$$

Here, HCHO and R_2CO are the by–products in this reaction.

When vapours of any monocarboxylic acid other than formic acid are passed over manganous oxide at 300°C, ketones are formed.

$$2RCO_2H \xrightarrow{\Delta, MnO} R_2CO + CO_2 + H_2O$$

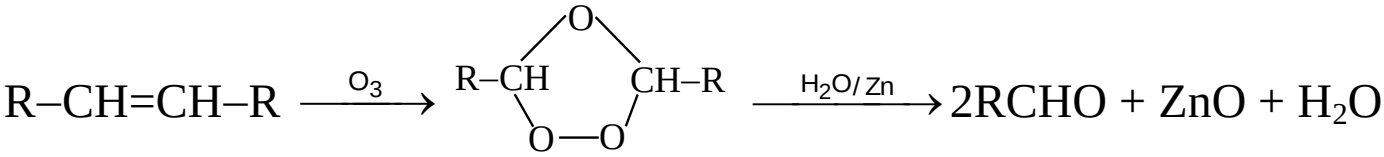
A mixture of monocarboxylic acids when passed over MnO at 300°C gives mixed ketones.

$$RCO_2H + R'CO_2H \xrightarrow{\Delta, MnO} RCOR' + CO_2 + H_2O$$

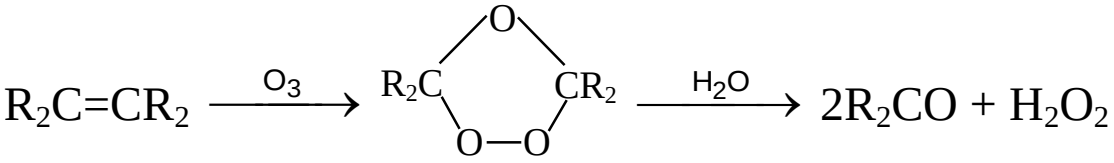
In this case, R_2CO and R'_2CO are obtained as by–products.

By Ozonolysis:

Aldehydes can be prepared by the ozonolysis of alkenes of the type R–CH=CH–R in presence of Zn (reductive ozonolysis).



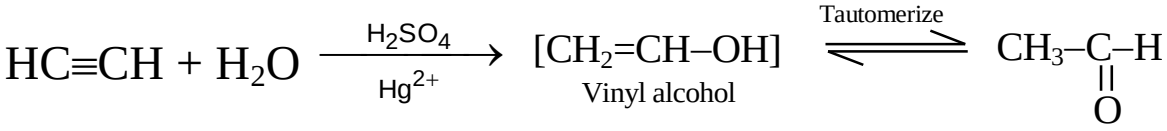
Ketones can also be prepared by the ozonolysis of alkenes of the type $R_2C=CR_2$.



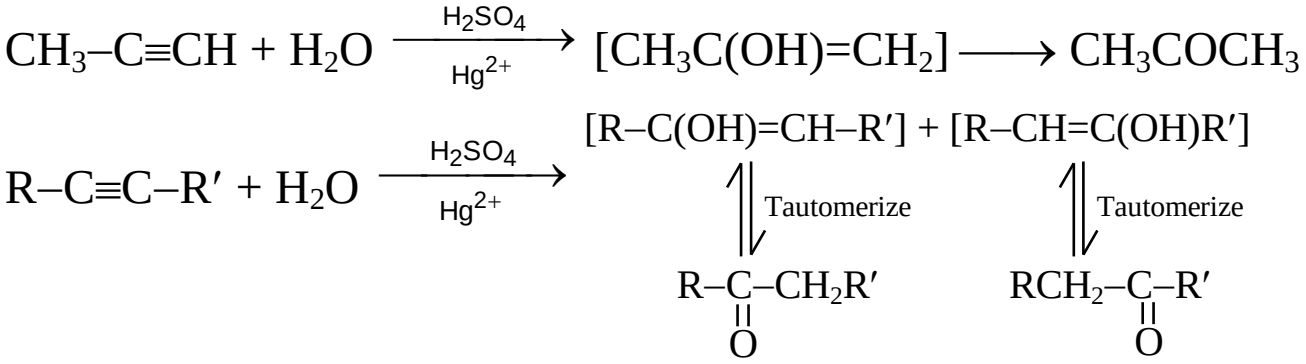
This oxidation of alkenes can also be achieved by Lemieux reagent, which is an aqueous solution of sodium periodate and a trace of potassium permanganate.

From Alkynes (For Ketones Mostly):

Acetylene gas when passed into hot dilute sulphuric acid in the presence of mercuric sulphate as catalyst, is converted into acetaldehyde.

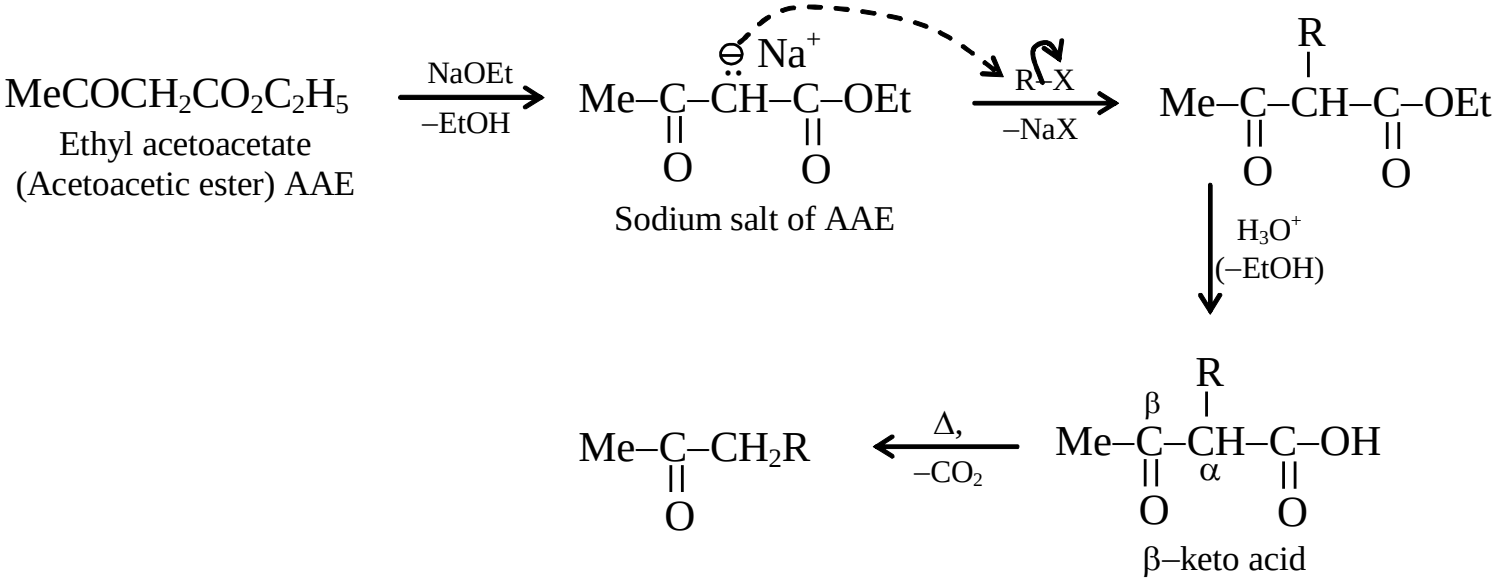


Homologues of acetylene form ketones when hydrated. For example, propyne gives acetone.



Acetoacetic Ester Synthesis (For Ketones Only):

This synthesis is used for preparing ketones only and is based on the fact that active methylene group (which is sandwiched between two strongly electron–withdrawing groups) have more acidic hydrogen than other α–hydrogens.



In the last step, β–keto acid undergoes ready decarboxylation even on slightest warming to form ketones.

General Physical Properties Of Aldehydes & Ketones

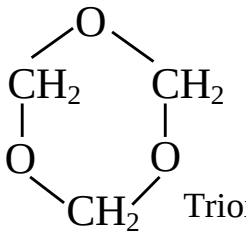
The polar carbonyl group makes aldehydes and ketones polar in nature and thus they have higher boiling points than non–polar compounds having comparable molecular weights. Their boiling points are less than the comparable alcohols or carboxylic acid as they do not form intermolecular hydrogen bond.

The lower members of the aldehydes & ketones are appreciably soluble in water because of hydrogen bonding between water and aldehydes or ketones. The solubility in water decreases as the number of carbon atoms increases. The aldehydes and ketones are soluble in usual organic solvents.

Formaldehyde is a gas (boiling point –21°C) and is normally used either as an aqueous solution (formalin, 40% aqueous solution of formaldehyde) or as its solid polymer, paraformaldehyde $(CH_2O)_n$ or trioxane, $(CH_2O)_3$. Formaldehyde is obtained by heating paraformaldehyde or trioxane.

$$-CH_2OCH_2OCH_2O-$$

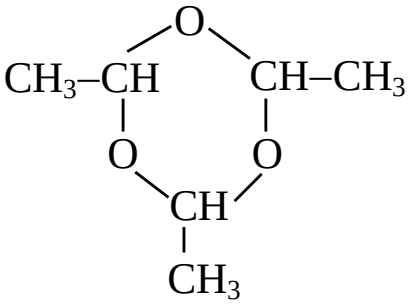
Paraformaldehyde



Trioxane

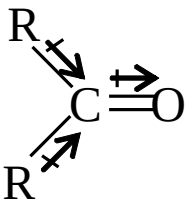
Acetaldehyde (boiling point 20°C) is generated from its high boiling trimer by heating it with acid.

$$3CH_3CHO \xrightleftharpoons{H^+}$$



Paraldehyde
(B. P. 125°C)

Carbonyl compounds exhibits some net dipole moment because of the polarization of $>C=O$ bond and the bond moments of R–C and $>C=O$ bonds acting in the same direction.



General Chemical Properties Of Aldehydes & Ketones

Oxidation:

Aldehydes are easily oxidised to carboxylic acids but ketones are not. Aldehydes are oxidised not only by the same reagents, which oxidizes primary and secondary alcohols (like acidified $KMnO_4$, $K_2Cr_2O_7$) but also by mild oxidising agents like Tollen's reagent, Fehling's solution and Benedict's solution. Aldehydes are very easily oxidised and thus are very powerful reducing agents.

Tollen's reagent contains diamminesilver(I) ion, which is obtained through ammoniacal $AgNO_3$ solution. Tollen's reagent oxidises aldehydes to acid salt and they reduces to free silver in the form of silver mirror.

$$\underset{\text{Colourless Solution}}{RCHO + 2Ag(NH_3)_2^+ + 3OH^-} \longrightarrow \underset{\text{Silver mirror}}{RCO_2^- + 2Ag\downarrow} + 4NH_3 + 2H_2O$$

Tollen's reagent is useful in differentiating aldehydes from ketones because ketones do not react with them. Tollen's reagent is a mild and selective oxidising agent, attacking only aldehydic group, keeping other groups untouched. Unsaturated aldehydes can be converted to unsaturated acid using Tollen's reagent.

$$\underset{\alpha,\ \beta\text{–unsaturated aldehyde}}{R\text{–}\overset{\beta}{C}H=\overset{\alpha}{C}H\text{–}CH=O} \xrightarrow[\text{reagent}]{\text{Tollen's}} \underset{\alpha,\ \beta\text{–unsaturated acid salt}}{R\text{–}\overset{\beta}{C}H=\overset{\alpha}{C}H\text{–}CO_2^-} + Ag\downarrow$$

Aldehydes are easily oxidised, thus they also reduce Fehling's solution (an alkaline solution containing a complex of copper tartarate) to red cuprous oxide. Aldehydes also reduce Benedict's solution (an alkaline solution containing a complex of copper citrate) to red precipitate of cuprous oxide.

$$R{-}CHO + 2CuO \longrightarrow RCOO^- + Cu_2O\downarrow \text{ (Fehling's and Benedict's test)}$$
(Red)

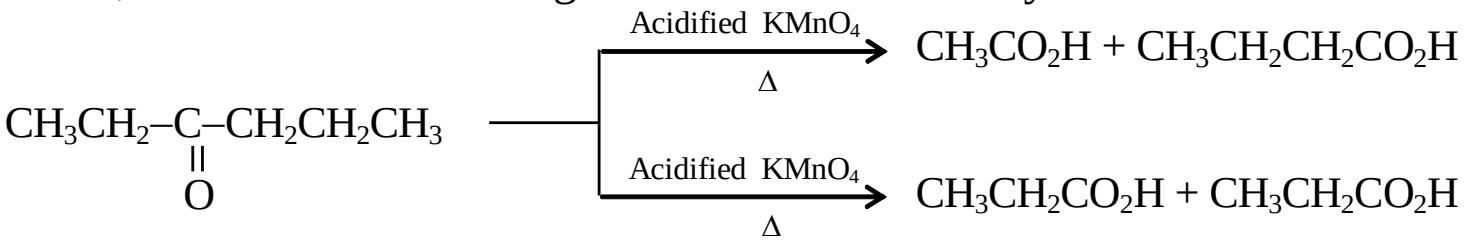
Ketones are not easily oxidised, thus they do not reduce Fehling's solution or Tollen's reagent. But α–hydroxy ketones (compounds containing the unit $-CH(OH)-\overset{\overset{O}{\|}}{C}-R$) readily reduce The compounds which respond to the test with Fehling's solution and ammoniacal silver nitrate are given below in the tabulated manner.

Name of the compounds	Fehling's test	Tollen's Test
Glucose, Fructose	✓	✓
α–hydroxy ketone	✓	✓
α–hydroxy aldehyde	✓	✓
Glyoxal (OHC.CHO)	×	✓
Benzaldehyde & other aromatic aldehydes	×	✓
Formic acid	✓	✓
Glyoxylic acid ($OHC.CO_2H$)	×	✓
Succinaldehyde ($OHCCH_2CH_2CHO$)	✓	✓
Pyruvaldehyde (CH_3COCHO)	✓	✓

Aldehydes restore the magenta colour of the Schiff's reagent (rosaniline hydrochloride is dissolved in H_2O and SO_2 is passed till the magenta colour is decolourised). Ketones do not restore the colour of Schiff's reagent except acetone, which restores the colour very slowly.

Oxidation of ketones requires breaking of carbon–carbon bonds, which requires vigorous conditions. Cleavage involves the double bond of the enol form and

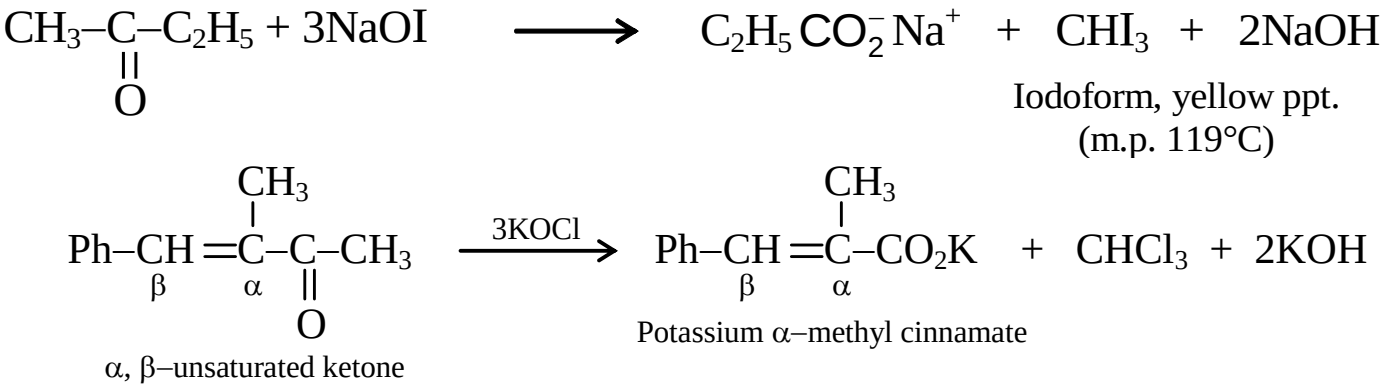
wherever the structure permits, occurs on both sides of carbonyl group. Thus, in general, ketones on oxidation give a mixture of carboxylic acids.



3–Hexanone gives a mixture of carboxylic acids because it can form two enols, $CH_3CH{=}C(OH)CH_2CH_2CH_3$, which on cleavage gives CH_3CO_2H & $CH_3CH_2CH_2CO_2H$ and $CH_3CH_2C(OH){=}CHCH_2CH_3$, which on oxidation gives 2 moles of $CH_3CH_2CO_2H$.

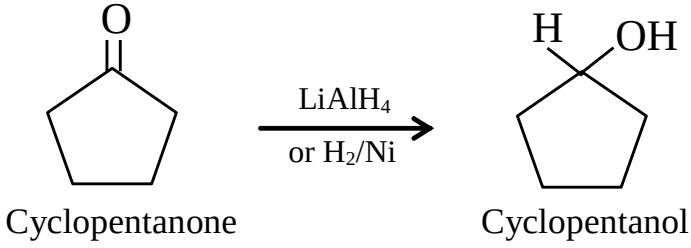
Methyl ketones can be conveniently oxidised by hypohalite in the haloform reaction. Hypohalite is a selective oxidising agent, used for detecting methyl ketones as well as it do not attack carbon–carbon double bonds.

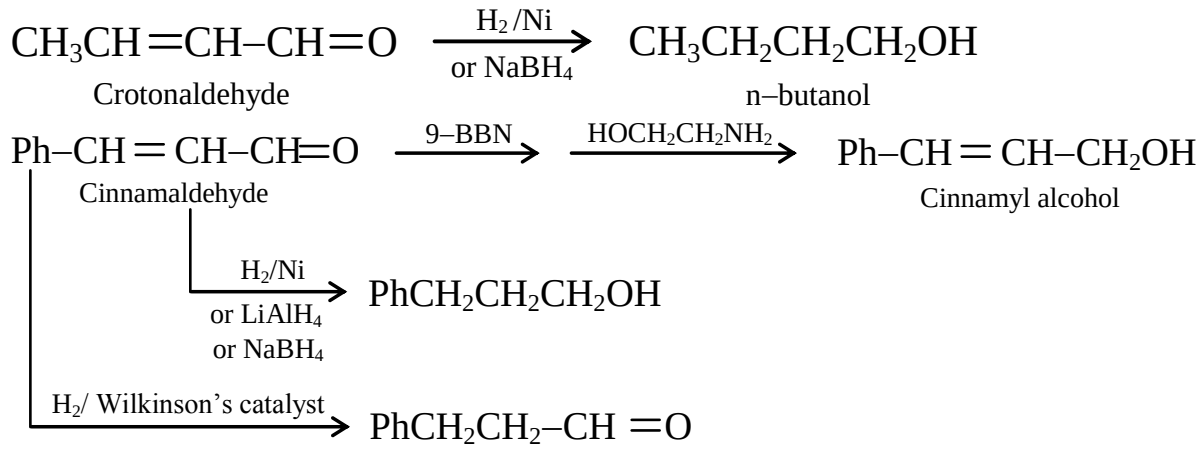
For example,



Reduction:

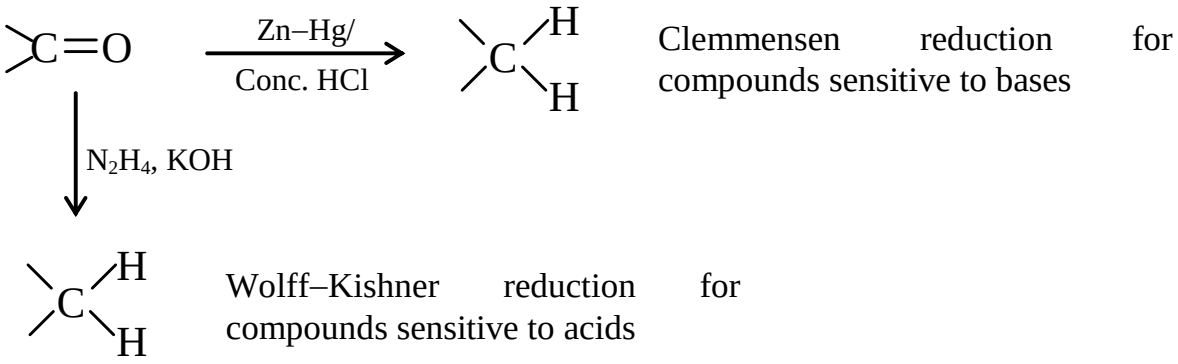
Aldehydes can be reduced to primary alcohols and ketones to secondary alcohols, either by catalytic hydrogenation or by $LiAlH_4$. For example,





To reduce a carbonyl group that is conjugated with a carbon–carbon bond without reducing the carbon–carbon double bond requires a regioselective reducing agent. One such reagent is 9–BBN, 9–Borabicyclo[3.3.1]nonane. This reduction can also be achieved by $LiAlH_4$ but not by $NaBH_4$, which reduces carbon–carbon double bond as well as the carbonyl group. While carbon–carbon double bond can be selectively reduced without affecting carbonyl group by hydrogenation in presence of Wilkinson's catalyst. $LiAlH_4$ reduces the carbon–carbon double bond, which is in conjugation with carbonyl group only when the β–carbon bears an aryl group.

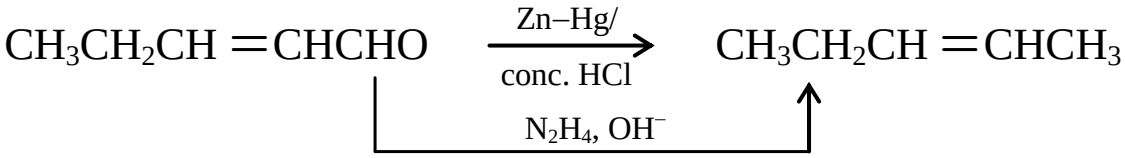
Aldehydes & ketones can be reduced to hydrocarbons by the action of (a) amalgamated zinc and concentrated hydrochloric acid (Clemmensen reduction) or (b) hydrazine (N_2H_4) and a strong base like KOH or potassium tertiary butoxide (Wolff–Kishner reduction).



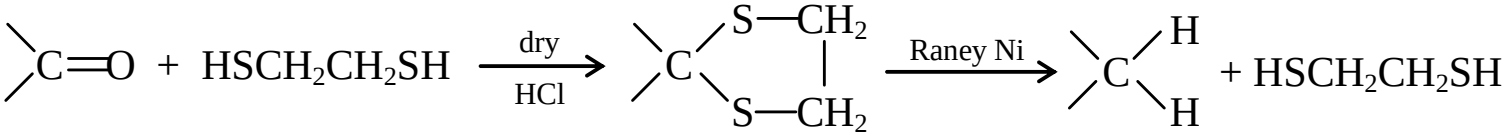
Clemmensen reduction for compounds sensitive to bases

Wolff–Kishner reduction for compounds sensitive to acids

For example,

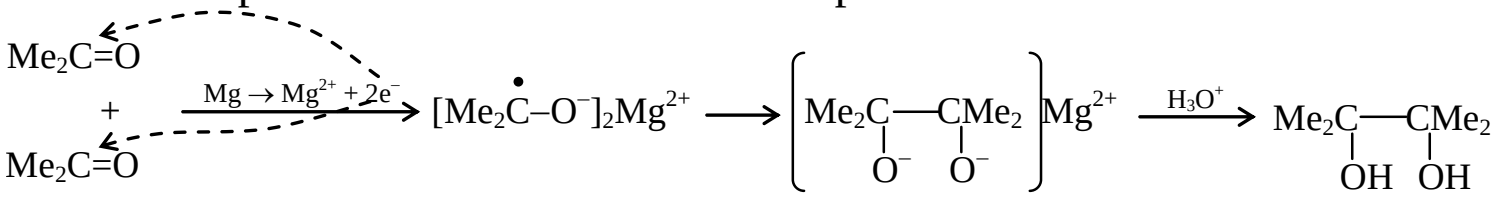


Raney nickel desulfurization is also used for reducing carbonyl compounds to hydrocarbons. Raney nickel has adsorbed hydrogen.



Cyclic thioacetal

Ketones are reduced catalytically or by dissolving metals in alkaline solutions to alcohols but reduction by dissolving metals in neutral or acid solution gives 1, 2–glycols. For example, acetone with magnesium–amalgam gives pinacol. The reaction proceeds via a free radical and polar mechanism.



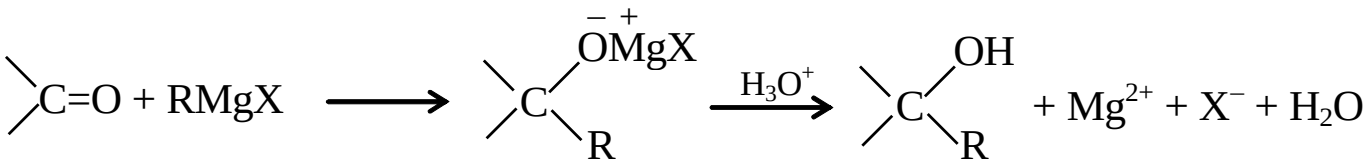
Pinacol

Nucleophilic Addition Reactions:

Due to the difference in electronegativity between carbon and oxygen, the π–electrons shift towards oxygen creating partial positive charge on carbon and making it electrophilic. So, this electrophilic carbon can be attacked by different nucleophiles.

Addition of Grignard reagents:

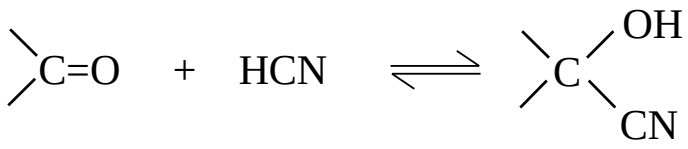
Aldehydes and ketones add on a molecule of a Grignard reagent to give an adduct, which on decomposition by aqueous acid gives an alcohol.



The product is a primary alcohol, if carbonyl compound is formaldehyde. An aldehyde (other than formaldehyde) gives secondary alcohol and a ketone leads to the formation of tertiary alcohol.

Addition of hydrogen cyanide:

Aldehydes and ketones add on hydrogen cyanide to form addition product, cyanohydrin.



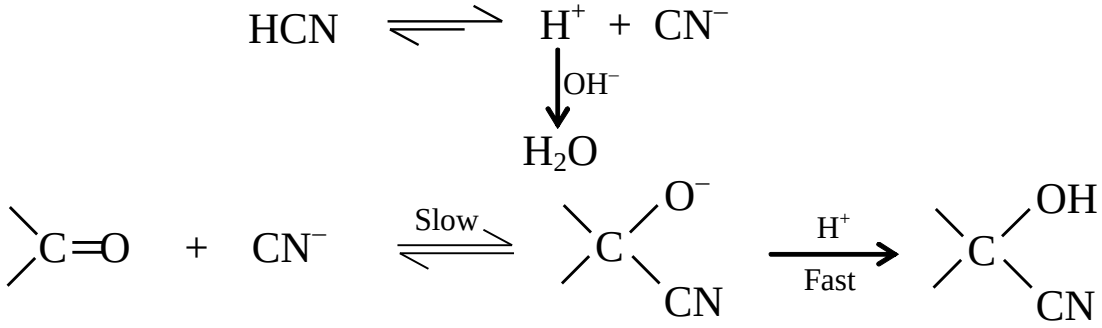
Cyanohydrin

HCN is not the nucleophile in this reaction. Infact the nucleophile is CN^-, which is more nucleophilic than HCN. The rate law for the reaction is

$$\text{Rate} = k\ [>C=O]\ [CN^-]$$

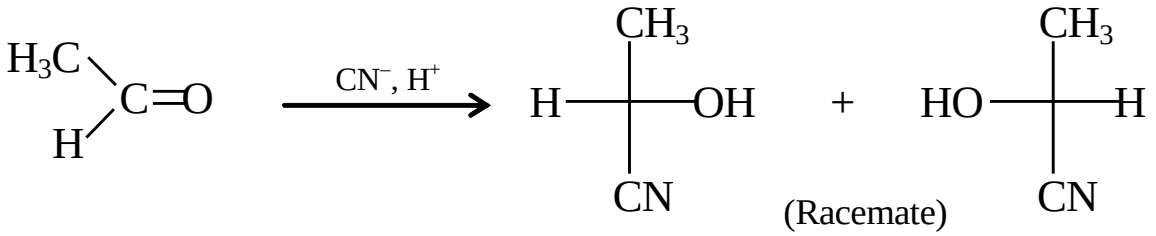
The addition of HCN to carbonyl compounds is base catalysed, which can lead to the generation of more nucleophilic CN^-.

Mechanism:

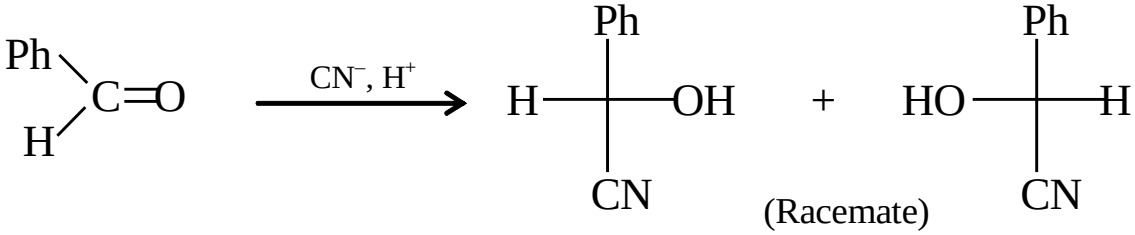


The addition of CN^- is reversible and the equilibrium lies in the direction of carbonyl compound. The presence of a proton donor shifts the equilibrium in the forward direction by converting into cyanohydrin. The RDS of the reaction is attack by CN^- while proton transfer is a rapid step. The rate of reaction of HCN with aldehydes, simple aliphatic and cyclic ketones are fast but slow with ArCOR and reaction does not take place at all with ArCOAr.

The CN^- ion may attack from front side or back side as carbonyl group is planar to give enantiomeric pair (provided the groups attached to carbonyl group are different).



(Racemate)



(Racemate)

The cyanohydrins can be readily hydrolysed to give α–hydroxy acids.

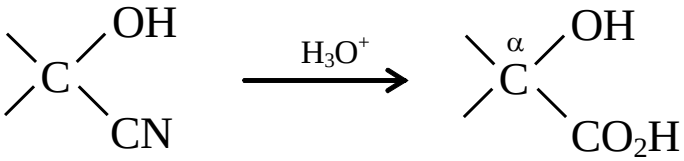


Illustration 1.

Write structures for (A) through (D) in the given reaction sequence.

$$Me_2C{=}O + HCN \longrightarrow (A) \xrightarrow{H_3O^+} (B) \xrightarrow[\Delta]{H_2SO_4} (C) \xrightarrow[2.\ H_2O_2\ /\ OH^-]{1.\ B_2H_6\ /\ THF} (D).$$

Product (D) is optically active.

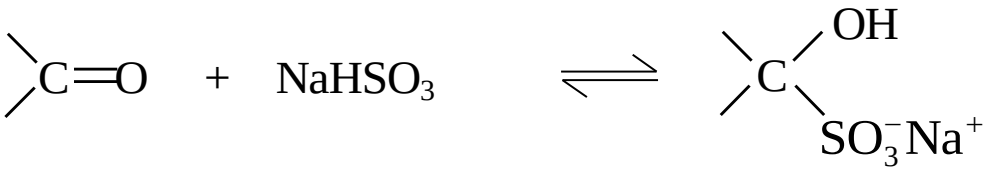
Solution:

(A) $CH_3{-}\underset{\displaystyle CH_3}{\overset{\displaystyle OH}{\overset{|}{\underset{|}{C}}}}{-}CN$ (B) $CH_3{-}\underset{\displaystyle CH_3}{\overset{\displaystyle OH}{\overset{|}{\underset{|}{C}}}}{-}CO_2H$ (C) $CH_2{=}\underset{\displaystyle CH_3}{\overset{|}{C}}{-}CO_2H$ (D) $HOCH_2{-}\underset{\displaystyle CH_3}{\overset{|}{\overset{*}{C}}}H{-}CO_2H$

(D) is optically active due to the absence f symmetry elements.

Addition of sodium bisulphite

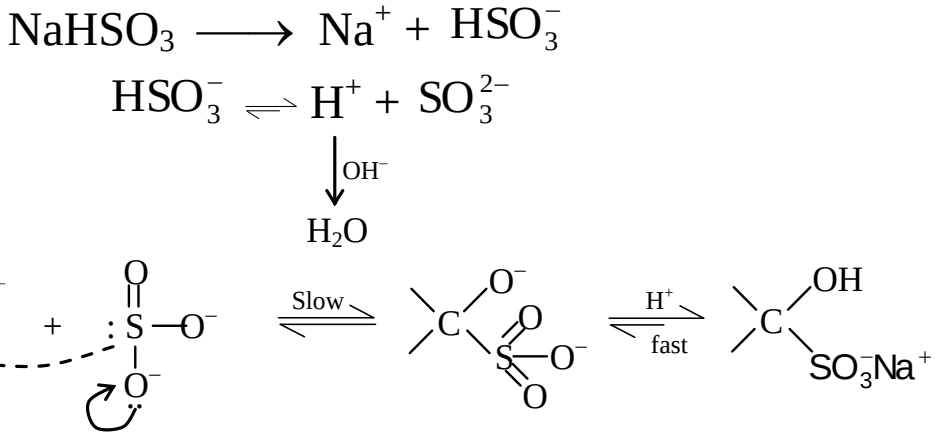
Aldehydes and ketones add on sodium hydrogen sulphite to form bisulphite compounds.



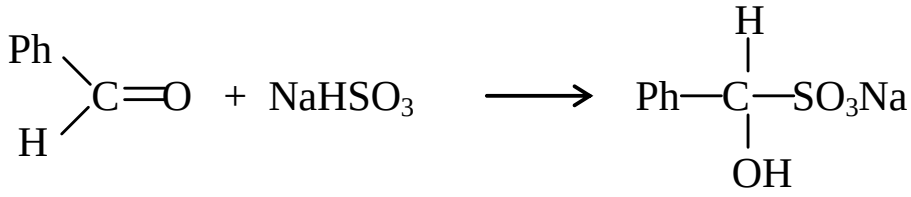
This bisulphite formation is confined to aldehydes, methyl ketones and some cyclic ketones. Those carbonyl compounds, which form bisulphite adduct can be separated from mixtures as they are crystalline solids, insoluble in $NaHSO_3$ solution and / or purified by isolation, purification and subsequent decomposition of these adducts in dilute acids.

Mechanism:

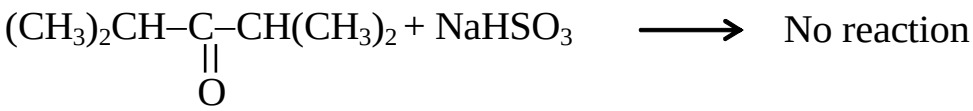
The effective nucleophile of the reaction is SO_3^{2-} ion rather than HSO_3^- and formation of SO_3^{2-} is achieved in slightly basic solution.



For example,



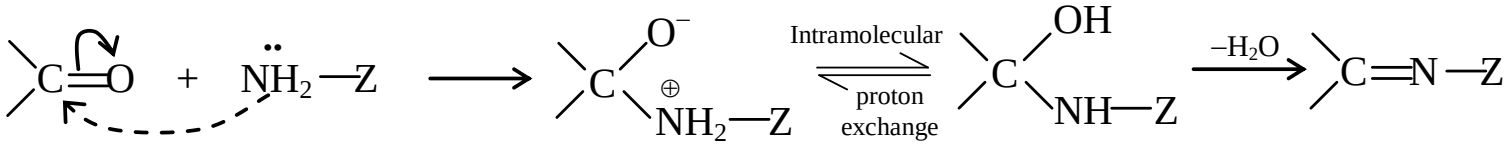
Benzaldehyde bisulphite adduct



Hindered ketones like di–isopropyl ketone, di–t–butyl ketone does not undergo any reaction with $NaHSO_3$.

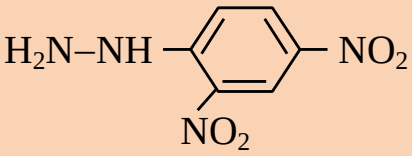
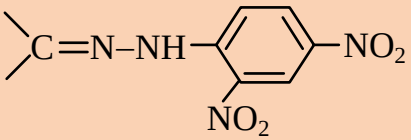
Addition of ammonia derivatives:

Aldehydes and ketones combine with a variety of ammonia derivatives of the type $NH_2–Z$ (where Z = –OH, $–NH_2$, $–NHC_6H_5$, $–NHCONH_2$ etc). The general reaction is shown as



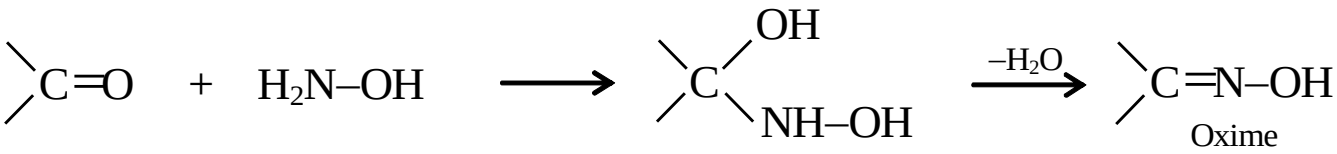
(I) (II) (III)

The various ammonia derivatives and their products are indicated in the following table.

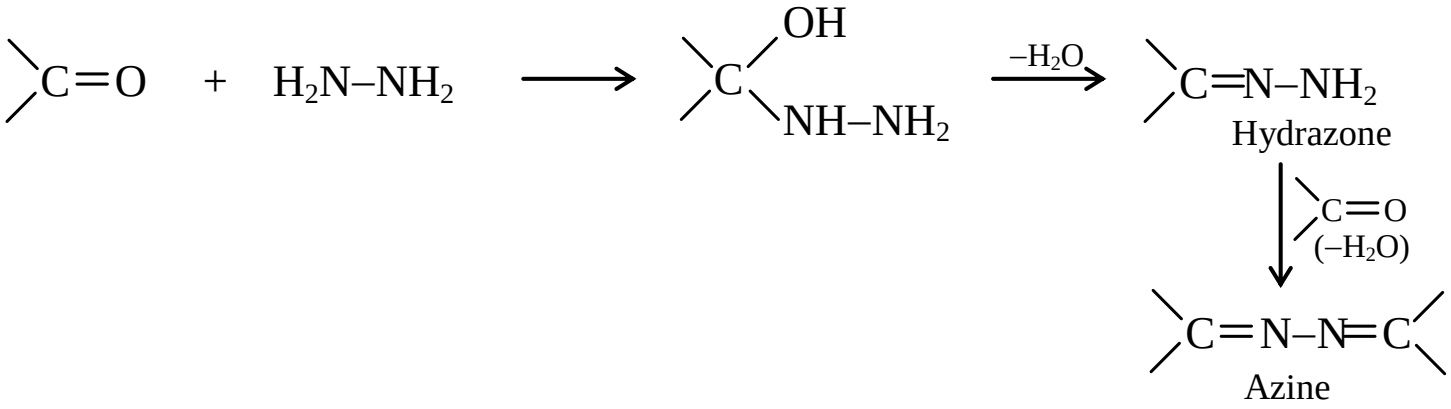
$H_2N–Z$	Product structure	Name of the product
$H_2N–OH$, Hydroxylamine	$>C=N–OH$	Oxime (crystalline solid)
$H_2N–NH_2$, Hydrazine	$>C=N–NH_2$	Hydrazone (crystalline solid)
$H_2N–NHPh$, Phenyl hydrazine	$>C=N–NH–Ph$	Phenyl hydrazone (crystalline solid)
$H_2N–NHCONH_2$, Semicarbazide	$>C=N–NHCONH_2$	Semicarbazone (crystalline solid)
 2, 4–Dinitro phenyl hydrazine (Brady's reagent)		2, 4–Dinitro phenyl hydrazone (yellow crystalline solid used for identification of aldehydes & ketones)

Brady's regent with carbonyl compounds gives 2, 4–dinitro phenyl hydrazone, which is obtained as a yellow crystalline solid. It is thus used for the identification of aldehydes and ketones.

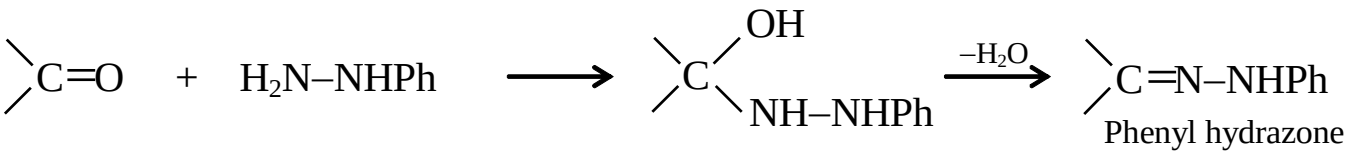
Oximes are obtained with hydroxylamine.



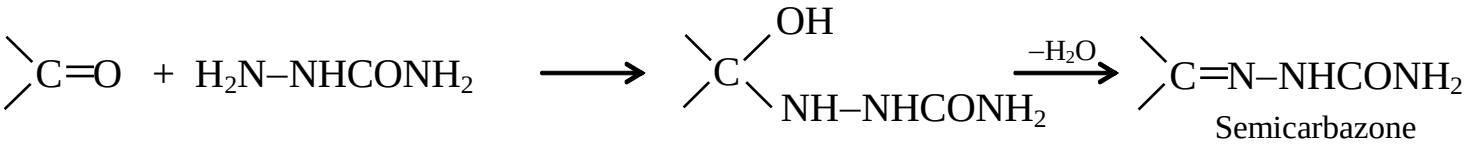
With hydrazine, hydrazones and azines are formed.



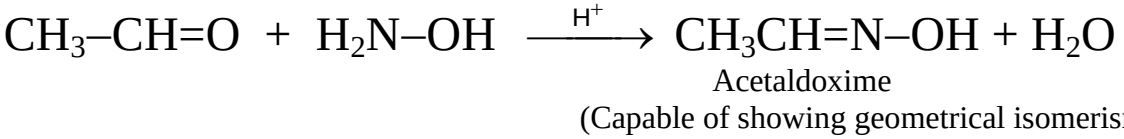
Phenyl hydrazine forms phenyl hydrazones.

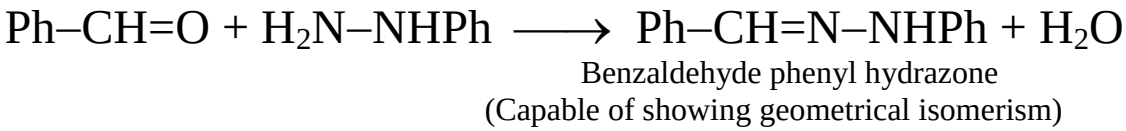


Semicarbazide forms semicarbazones.

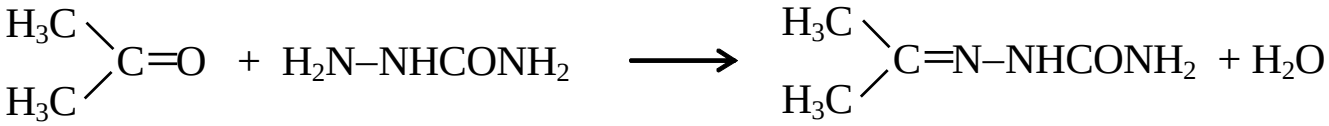


The rate of such reaction is maximum at some particular pH. These reactions are catalysed by the presence of slightly acidic conditions. In slightly acidic conditions, dehydration step is the RDS, whose rate is increased by the protonation of OH, leading to overall increase in rate of the reaction. But, when the acidity increases, the rate of addition step decreases because concentration of $NH_2–Z$ reduces due to its conversion to conjugate acid, $NH_3^+–Z$ (which can not function as a nucleophile because of absence of lone pair). Thus, at low pH or more acidity, the addition step becomes the RDS. For example,





Benzaldehyde phenyl hydrazone
(Capable of showing geometrical isomerism)



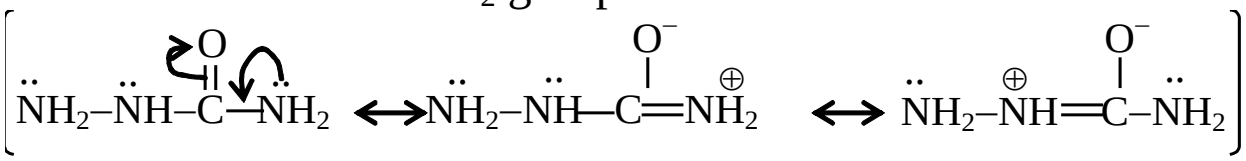
Acetone semicarbazone

Illustration 2.

There are two NH_2 groups in semicarbazide that might react with a ketone or an aldehyde. Explain why the reaction occurs with one of the terminal NH_2.

Solution:

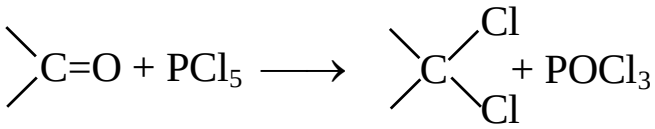
The NH_2 group closer to the carbonyl group is deactivated due to resonance stabilization,
as compared to the other end NH_2 group.



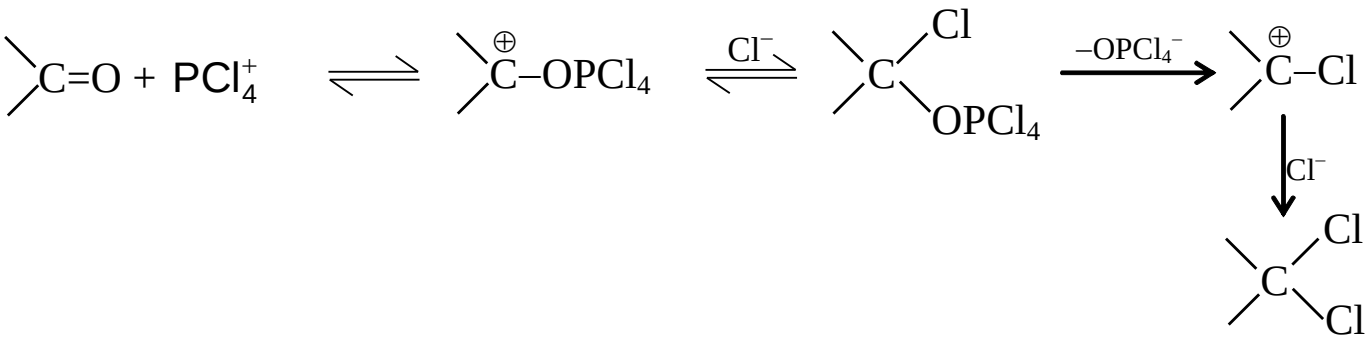
The electron pair availability is more on the terminal nitrogen, thus making it more nucleophilic and semicarbazone is formed through its attack.

Reaction With PCl_5:

Phosphorous pentachloride reacts with simple carbonyl compounds to give 1, 1–dichlorides (gem dichloride).



The possible mechanism of the reaction is



The reaction is initiated by the attack of PCl_4^+ (solid PCl_5 is $PCl_4^+\ PCl_6^-$) and the chloride ions are obtained from PCl_6^-.

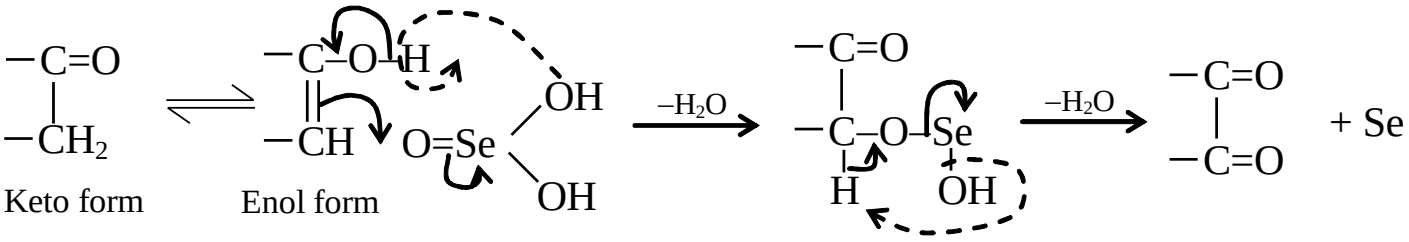
Reaction With SeO_2:

Aldehydes and ketones with a methyl or methylene group adjacent to the carbonyl group are oxidised by selenium dioxide in acetic acid at room temperature to dicarbonyl compounds. For example, acetaldehyde forms glyoxal and acetone forms methyl glyoxal.

$$CH_3CHO + SeO_2 \xrightarrow[\text{acid}]{\text{Acetic}} OHC{-}CHO + Se + H_2O$$

$$CH_3COCH_3 + SeO_2 \xrightarrow[\text{acid}]{\text{Acetic}} CH_3COCHO + Se + H_2O$$

The actual reagent of the reaction is selenous acid (H_2SeO_3) and the probable mechanism is



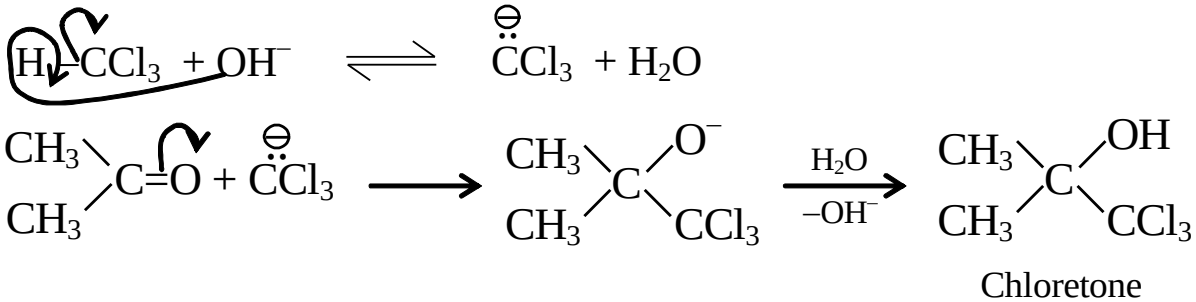
Reaction With Chloroform:

Ketones condense with chloroform in the presence of potassium hydroxide to give chloretone, which is used as a hypnotic drug.

$$CH_3COCH_3 + CHCl_3 \xrightarrow{KOH} (CH_3)_2C(OH)CCl_3$$

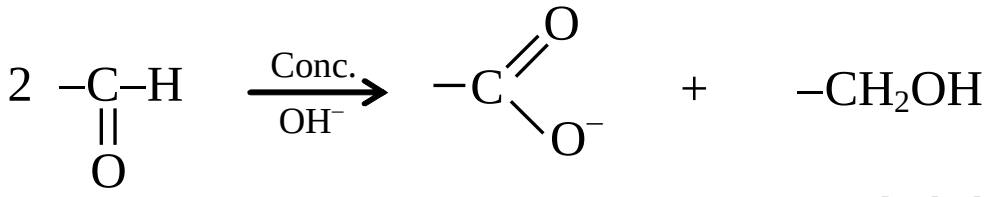
Chloretone

The reaction proceeds as



Cannizaro Reaction:

Those aldehydes (aliphatic or aromatic), which do not have α–hydrogen atom on treatment with strong base undergoes a reaction involving its 2 moles, one getting oxidised to yield acid salt and the other getting reduced to primary alcohol. The important condition is that there should not be a good leaving group attached to the carbonyl group.



(Aldehyde with no α–H atom) Acid salt Alcohol

This reaction is an example of organic disproportionation.

Mechanism:

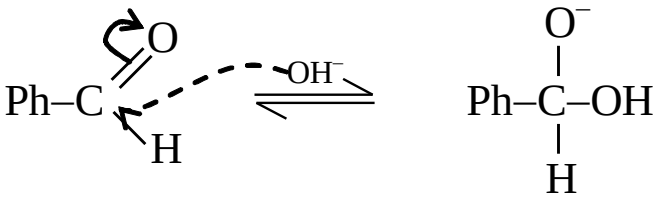
The first step of the mechanism involve reversible attack of OH^- on an aldehyde molecule to give hydroxy alkoxide. This hydroxy alkoxide in the subsequent step transfer hydride ion to second molecule of either same aldehyde (simple Cannizaro) or different aldehyde (crossed Cannizaro). The hydroxy alkoxide on transferring hydride becomes carboxylic acid molecule while second aldehyde molecule becomes alkoxide. The carboxylic acid and alkoxide then undergoes proton exchange to form carboxylate and alcohol respectively.

The reaction requires presence of strong bases and the rate law with PhCHO is of the type

$$\text{Rate} = k[\text{PhCHO}]^2[OH^-]$$

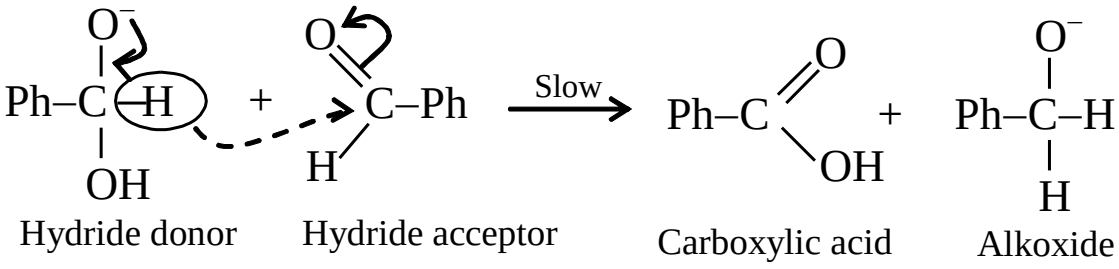
The slowest (rate–determining) step of the reaction is transfer of hydride ion.

Step (I):



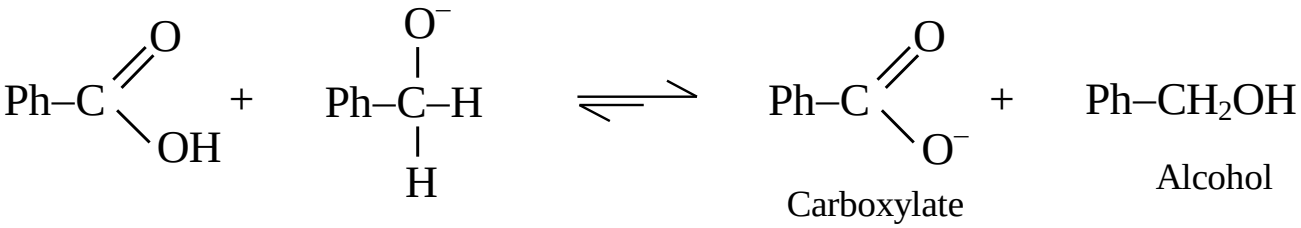
Hydroxy alkoxide

Step (II):



Hydride donor | Hydride acceptor | Carboxylic acid | Alkoxide

Step (III):



Carboxylate (More resonance stabilized) | Alcohol

It is evident from the mechanism that the species acting as hydride donor finally forms acid salt while the one, which accepts hydride will form primary alcohol.

When crossed Cannizaro reaction is carried out between formaldehyde and benzaldehyde, formaldehyde always forms formate salt while benzaldehyde yields benzyl alcohol.

$$HCHO + PhCHO \xrightarrow{50\%\,NaOH} HCO_2^-Na^+ + PhCH_2OH$$

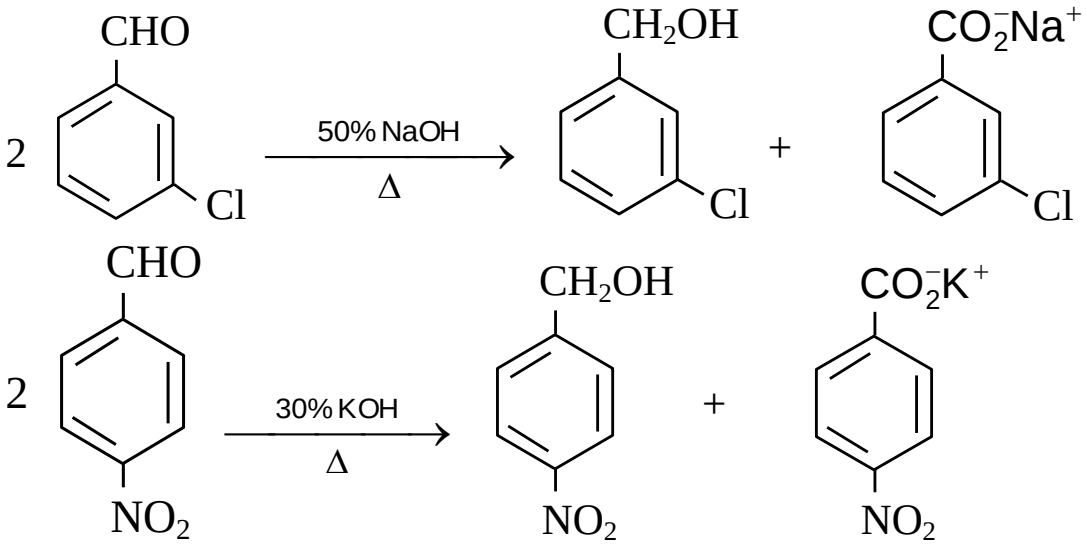
This is because carbonyl carbon of formaldehyde is more electrophilic than that of benzaldehyde. So, OH^- initially attacks at formaldehyde (due to electronic, statistical and steric factors) to form hydroxy alkoxide, which acts as hydride donor to finally form carboxylate while benzaldehyde accepts hydride to form alcohol finally.

The presence of electron withdrawing substituent increases the rate of Cannizaro reaction while electron releasing substituent decreases the rate.

For example,

$$2HCHO \xrightarrow[\Delta]{50\%\,NaOH} CH_3OH + HCO_2^-Na^+$$

$$2PhCHO \xrightarrow[\Delta]{50\%\,NaOH} PhCH_2OH + PhCO_2^-Na^+$$



$$PhCHO + HCHO \xrightarrow[\Delta]{50\%KOH} PhCH_2OH + HCO_2^-K^+$$

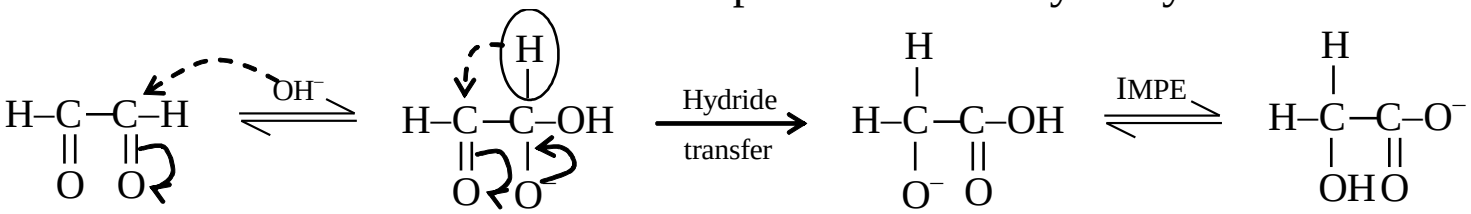
$$(CH_3)_2CHCHO \xrightarrow[\Delta]{50\%KOH} (CH_3)_2CHCOO^-Na^+ + (CH_3)_2CHCH_2OH$$

The above exception may be due to the fact that stability of α–carbanion is less & attack of this carbanion to the carbonyl carbon is difficult because of the steric crowding hence, aldol condensation is not feasible.

$$(CH_3)_3CCHO + HCHO \xrightarrow[\Delta]{50\%NaOH} (CH_3)_3CCH_2OH + HCO_2^-Na^+$$

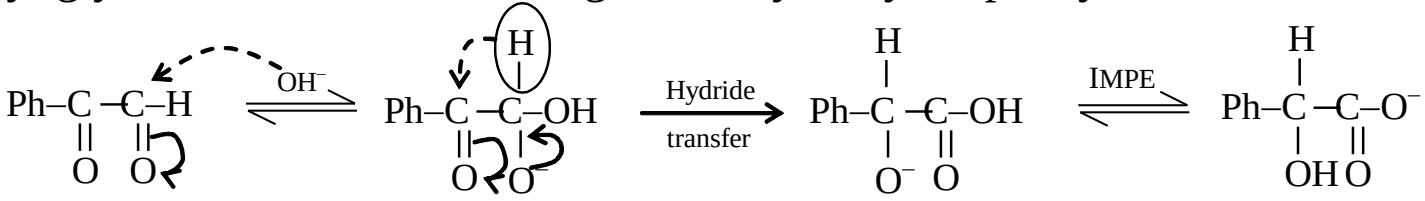
Intramolecular Cannizaro:

Glyoxal on reaction with concentrated NaOH gives 2–hydroxy ethanoate by intramolecular Cannizaro reaction. The product is a α–hydroxy acid.



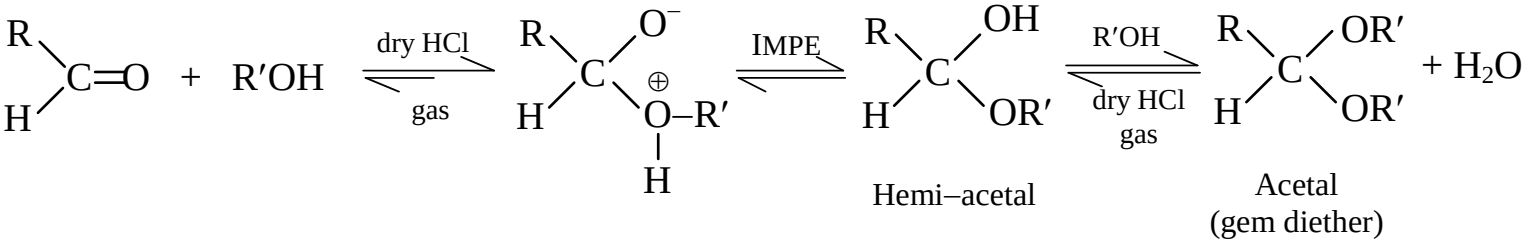
IMPE: Intramolecular proton exchange

Phenyl glyoxal on similar reaction gives 2–hydroxy–2–phenyl ethanoate.



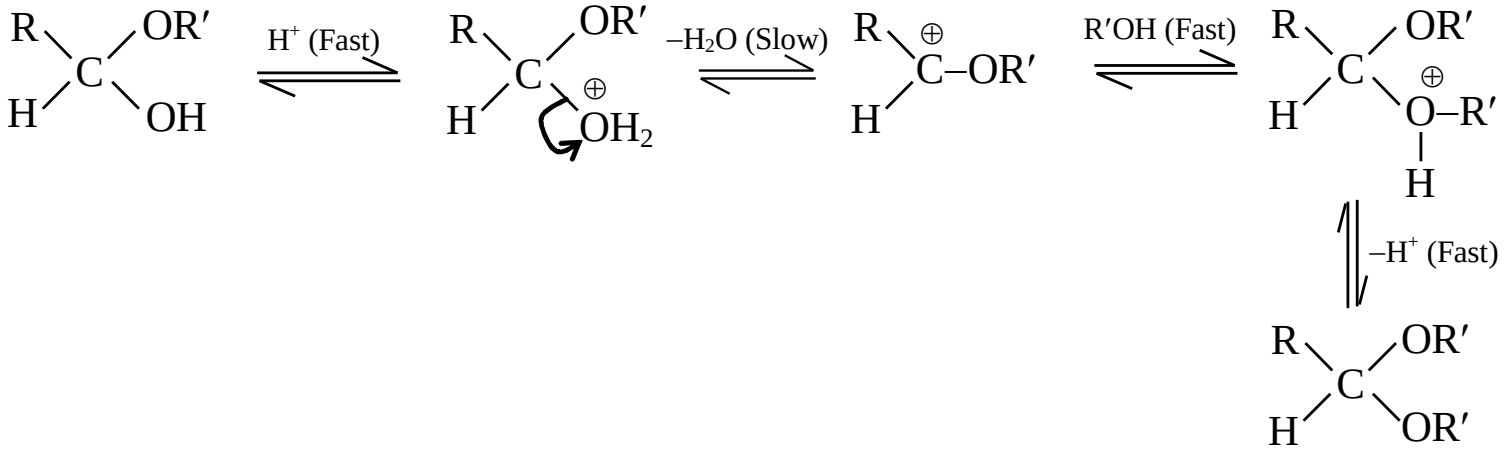
Addition Of Alcohols:

Carbonyl compounds add on one mole of alcohol to give hemi–acetals and hemi–ketals while addition of two moles of alcohols give acetals and ketals.

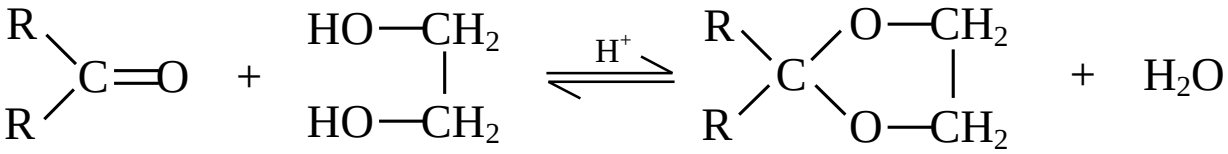


Generally, hemi–acetals and hemi–ketals are not isolated while isolable products are acetals and ketals.

Conversion of hemi–acetal to acetal is a specific acid catalysis reaction. Hemi–acetal is first protonated, which then loses H_2O molecule to give carbocation. Formation of this carbocation is the rate limiting step. Carbocation is then attacked by neucleophile to give final product, acetal.

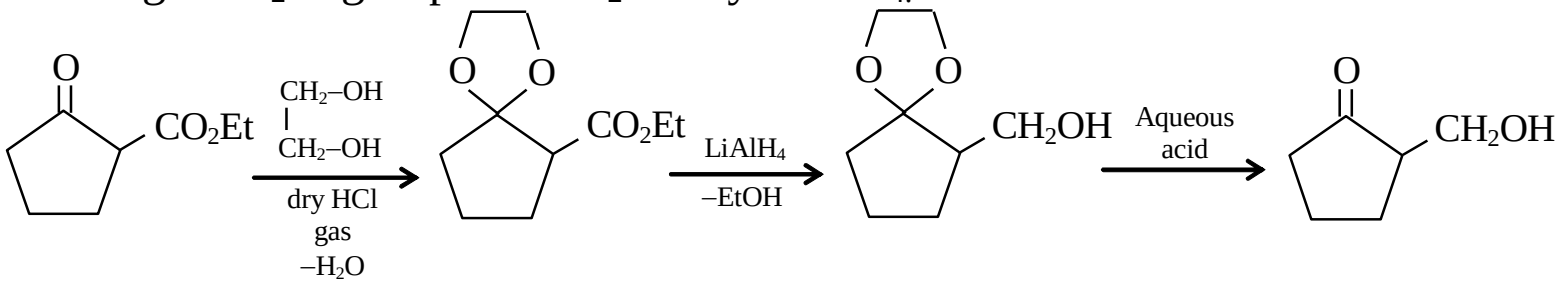


This reaction is not so favourable with ketones under these conditions (with simple alcohols) but reaction can be favoured if 1, 2 or 1, 3–diols are used. With diols, cyclic ketals are formed. The reaction with simple alcohols was not favourable because entropy decreases (ΔS = –ve) as 3 molecules give 2 molecules on reaction while with diols, entropy change is zero, so reaction becomes favourable.



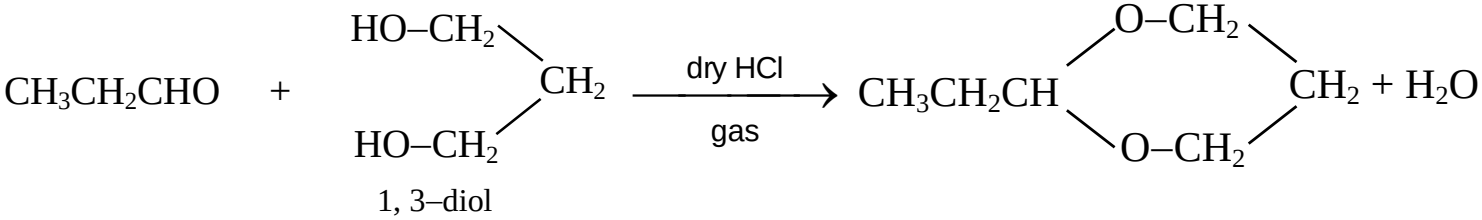
Ketals are formed only by unhindered ketones.

Acetals or ketals are stable in neutral or basic conditions but in acidic medium, they undergo acid catalysed cleavage similar to that of ethers to regenerate carbonyl compounds. Thus, this reaction is used to protect carbonyl groups. For example, we want to convert 2–carbethoxy cyclopentanone to 2–hydroxy methyl cyclopentanone. This can be achieved by protecting keto group and reducing $-CO_2Et$ group to $-CH_2OH$ by $LiAlH_4$.



For example,

$$CH_3–CH=O + 2C_2H_5OH \xrightarrow[\text{gas}]{\text{dry HCl}} CH_3CH(OC_2H_5)_2 + H_2O$$



1, 3–diol

Halogenation Of Ketones:

Ketones can be halogenated (chlorinated, brominated or iodinated) to form α–haloketone in the presence of either base or an acid catalyst. So the reaction is referred as base–promoted halogenation and acid–catalysed halogenation of ketones. For example,

$$CH_3COCH_3 + Br_2 \xrightarrow[\text{acid}]{\text{base or}} CH_3COCH_2Br + HBr$$

Rate of this reaction (in presence of acid or base both) depends upon the concentration of acetone and of base/acid but is independent of bromine concentration.

Rate = k[Acetone] [Base] or Rate = k′[Acetone] [Acid]

The mechanism of base–promoted halogenation is given as

Step I: $CH_3–\underset{\underset{O}{||}}{C}–CH_3 + B^- \underset{(slow)}{\overset{RDS}{\rightleftharpoons}} \overset{\ominus}{\underset{\cdot\cdot}{CH_2}}–\underset{\underset{O}{||}}{C}–CH_3 + B–H$

Step II: $CH_3–\underset{\underset{O}{||}}{C}–\overset{\ominus}{\underset{\cdot\cdot}{CH_2}} + Br–Br \xrightarrow{fast} CH_3–\underset{\underset{O}{||}}{C}–CH_2Br + Br^{\ominus}$

For a given [Acetone] and [Base], the bromination, chlorination and iodination proceed at identical rates because value of rate constant (K) for the step I is same regardless of which halogen is involved.

The mechanism of acid–catalysed halogenation involves formation of enol in two step. The first step is reversible protonation of the carbonyl oxygen while second step is slow loss of α–hydrogen, which is the rate–limiting step. The enol in third step reacts rapidly with bromine to give α–haloketone in last step.

Step I: $CH_3–\underset{\underset{O}{||}}{C}–CH_3 + HX \overset{Fast}{\rightleftharpoons} CH_3–\underset{\underset{:\overset{\oplus}{O}–H}{||}}{C}–CH_3 + X^-$

Step II: $CH_3–\underset{\underset{:\overset{\oplus}{O}–H}{||}}{C}–CH_3 + X^{\ominus} \xrightarrow{Slow} CH_3–\underset{\underset{OH}{|}}{C}=CH_2 + HX$

Step III: $CH_3–\underset{\underset{:OH}{|}}{C}=CH_2 + Br_2 \xrightarrow{Fast} CH_3–\underset{\underset{:\overset{\oplus}{O}–H}{||}}{C}–CH_2Br + Br^{\ominus}$

Step IV: $CH_3–\underset{\underset{:\overset{\oplus}{O}–H}{||}}{C}–CH_2Br + X^{\ominus} \overset{Fast}{\rightleftharpoons} CH_3–\underset{\underset{O}{||}}{C}–CH_2Br + HX$

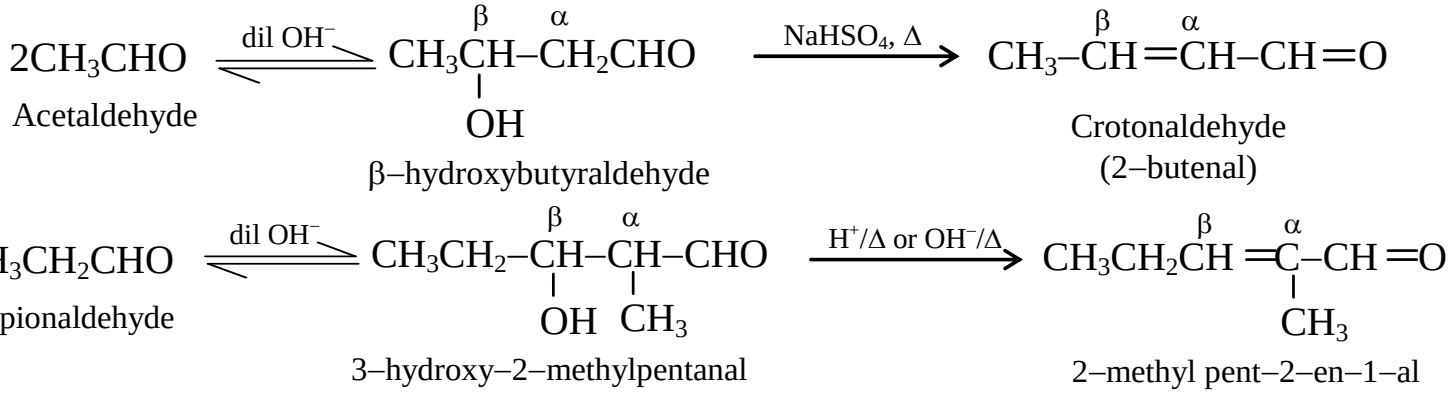
Aldol Condensation:

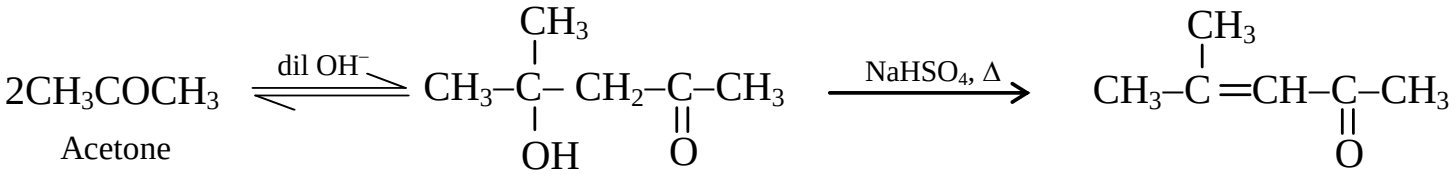
Under the influence of dilute base, two molecules of an aldehyde or a ketone may combine to form a β–hydroxy aldehyde or β–hydroxy ketone. This reaction is called the aldol reaction because product of reaction of 2 moles of aldehyde is called aldol ("ald" for aldehyde and "ol" for alcohol). In every case, the product results from addition of one molecule of aldehyde (or ketone) to a second molecule in such a manner that the α–carbon of the first becomes attached to the carbonyl carbon of the second. Because the addition reaction is reversible, good yields of the addition product are obtained only if it is removed from the solution as it is formed.

The aldol reaction in more favourable for aldehydes than for ketones because of more acidic α–hydrogen atoms and more electrophilic carbon.

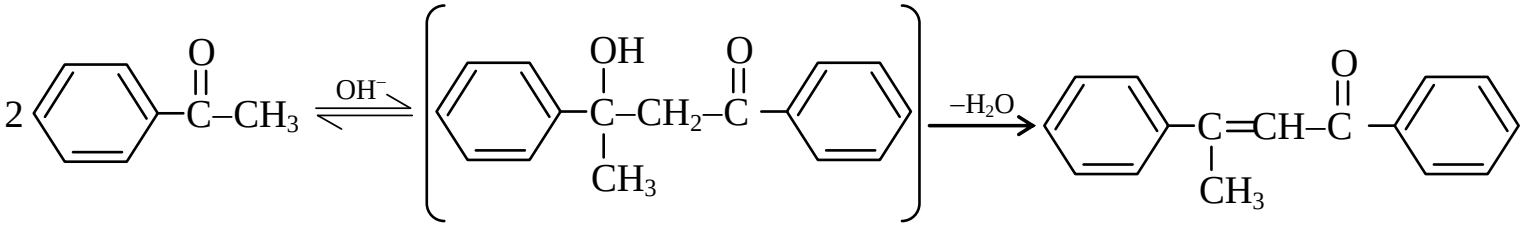
Heating the aldol product in either acid or base leads to dehydration because the double bond generated is in conjugation with the carbonyl group (making it more stable). If the product of an aldol addition is dehydrated, the overall reaction is called an aldol condensation.

The dehydration product is α, β–unsaturated carbonyl compound. When the aldol product contains an aryl (or phenyl) group at the β–position, dehydration occurs under the conditions in which the aldol addition is carried out, without additional heating. This is because the double bond formed is conjugated not only with the carbonyl group but also with the aryl group. This makes the product a very stable compound and is therefore easy to form. For example,





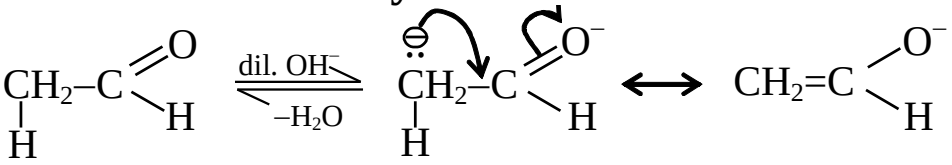
Acetone — 4–hydroxy–4–methyl–2–pentanone — Mesityl oxide



The carbonyl group plays two important roles in the aldol condensation. First, it makes α–hydrogens acidic enough for carbanion formation to take place and secondly, it provides the unsaturated linkage at which nucleophilic addition takes place.

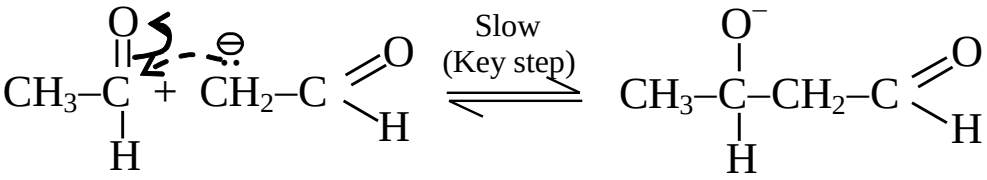
Aldol Condensation in Acetaldehyde:

Step I:

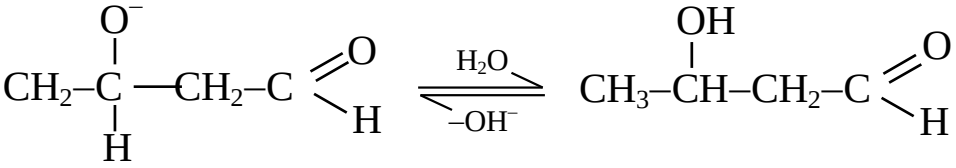


Carbanion — Enolate ion

Step II:

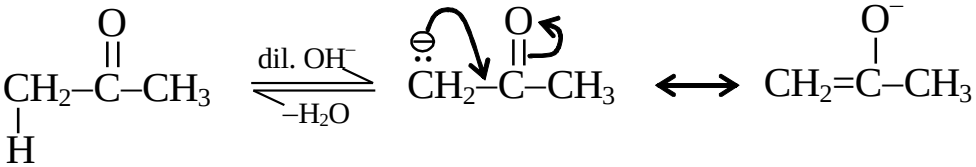


Step III:

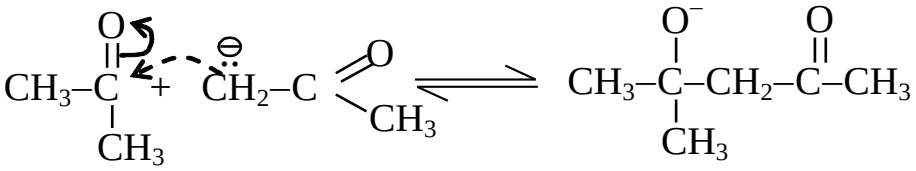


Aldol Condensation in Acetone:

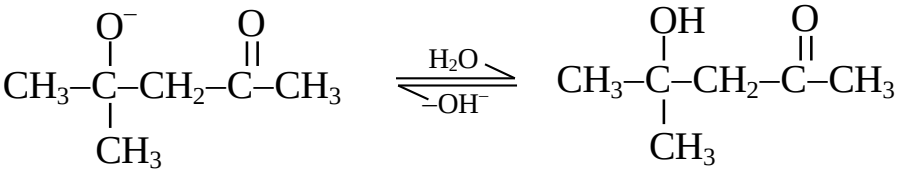
Step I:



Step II:

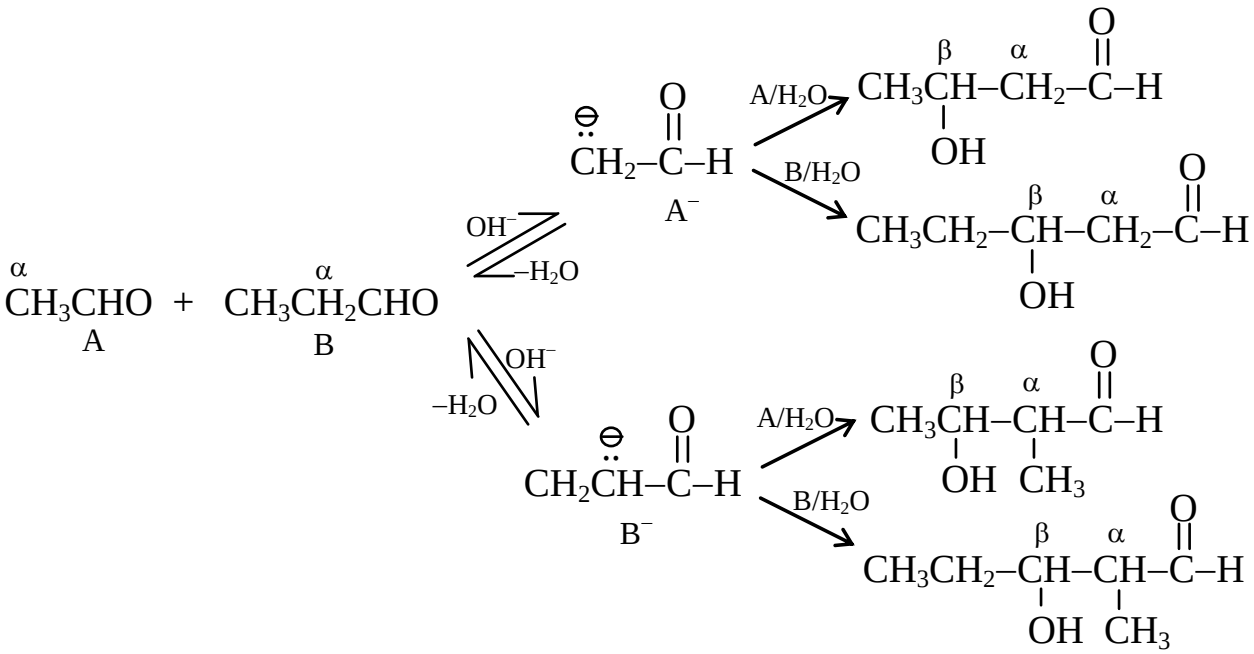


Step III:

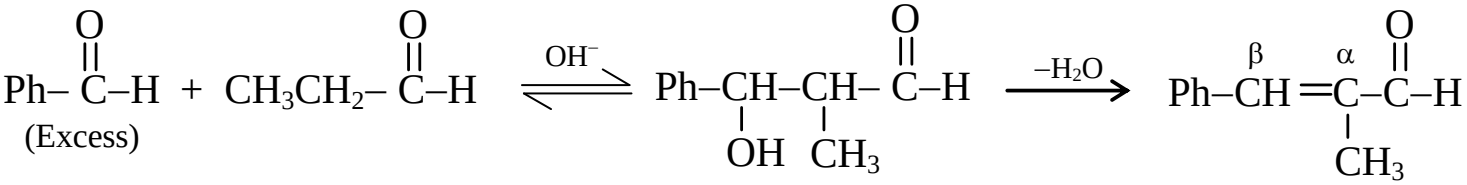


Crossed aldol condensation:

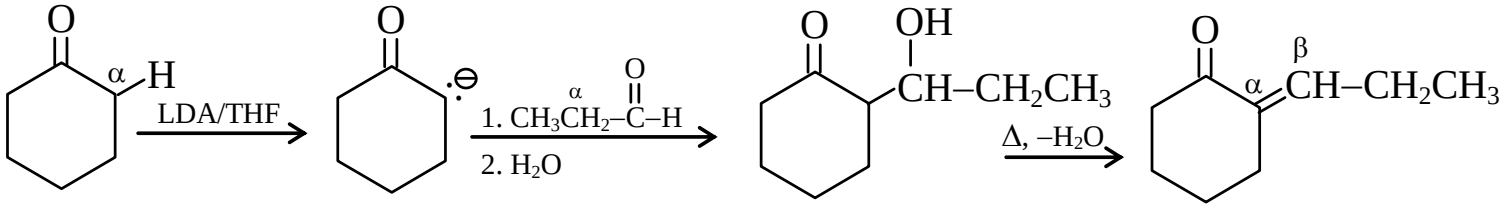
When two different carbonyl compounds (with α–H atoms) are used in an aldol condensation, four products are formed because each carbonyl compound can react with itself (self aldol) as well as with the other carbonyl compound (crossed aldol). For example, when two carbonyl compounds, A and B are treated with dil OH^-, both can lose a proton from the α–carbon to form carbanion (acting as nucleophiles) A^- and B^- respectively. A^- can either react with A or B and B^- can react with either B or A. The reaction of A^- with B or B^- with A is called crossed aldol addition. All the four products have similar physical properties, making them difficult to separate. Consequently, crossed aldol addition is not a useful synthetic preparation.



All the four products are β–hydroxy carbonyl compounds. Under certain conditions, a mixed aldol reaction can lead primarily to one product. When one of the carbonyl compound does not have any α–hydrogen, it cannot form carbanion and number of possible products reduces to two. A greater amount of one of the two products will be formed if the compound without α–hydrogen is present in excess. The carbanion will be more likely to attack the carbonyl compound without α–hydrogen because there is more of it in the solution.



Another way to obtain a single aldol product is to convert one carbonyl compound completely into carbanion. This cannot be done by using a weaker base (dil. OH^-). To achieve this, we make use of a much stronger base like LDA (lithium diisopropyl amide). Thus, this carbanion attacks over other carbonyl compound to give only one product. For example,



LDA = $[(CH_3)_2CH]_2NLi$

Note that when mixture of an aldehyde and a ketone with α–hydrogen atom are used, the carbanion is exclusively formed by ketone and the carbanion generated attacks the carbonyl carbon of aldehyde (as it is more electrophilic).

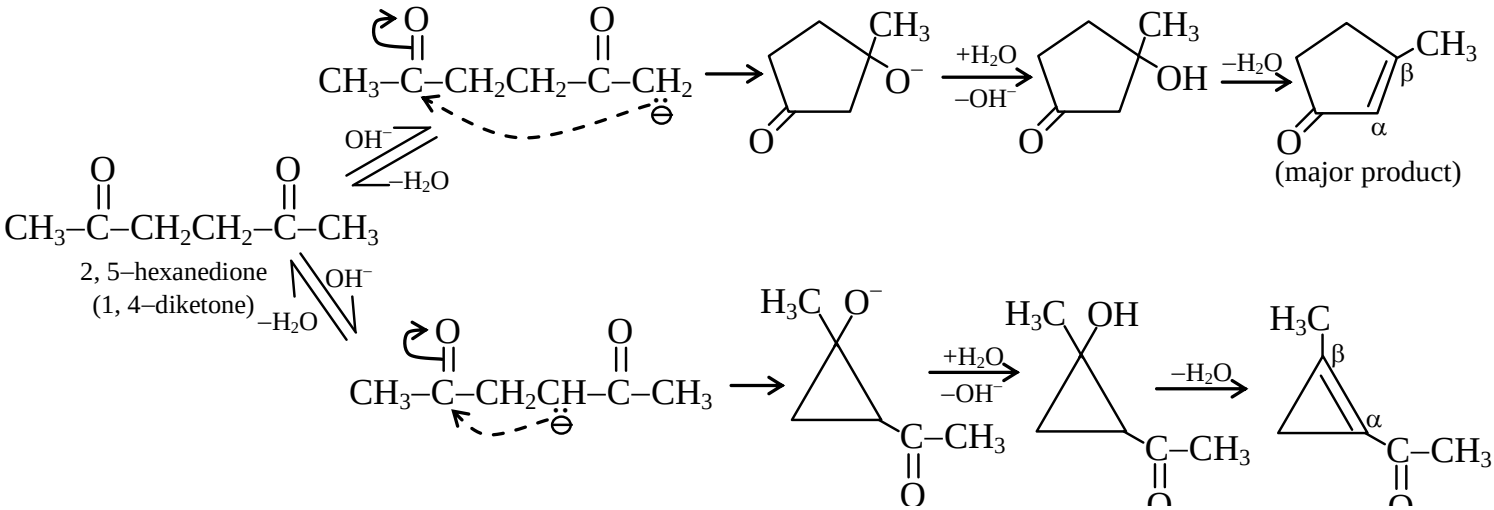
Intramolecular aldol condensation:

When a compound has two carbonyl groups, it can undergo intramolecular aldol condensation in the presence of dilute base (if α–H atoms are present in the compound).

An intramolecular reaction is readily favoured if the reaction leads to the formation of a 5 or 6–membered ring. When one of carbonyl group is an

aldehyde and other is a ketone, it's the ketone, which forms carbanion and this carbanion attack the carbonyl group of an aldehyde in such a manner that 5 or 6–membered ring is formed.

For example, 2, 5–hexanedione in presence of dilute OH^- undergoes intramolecular aldol condensation to give 2 set of products as there are 2 different types of α–hydrogens. One of the product has a 5–membered ring and the other has a 3–membered ring. The major product of the reaction is a 5–membered ring compound as 5–membered ring has greater stability than 3–membered ring.



When 6–oxoheptanal is treated with dilute base, a mixture of three products is formed, of which one of the product is major while other two are minor products.

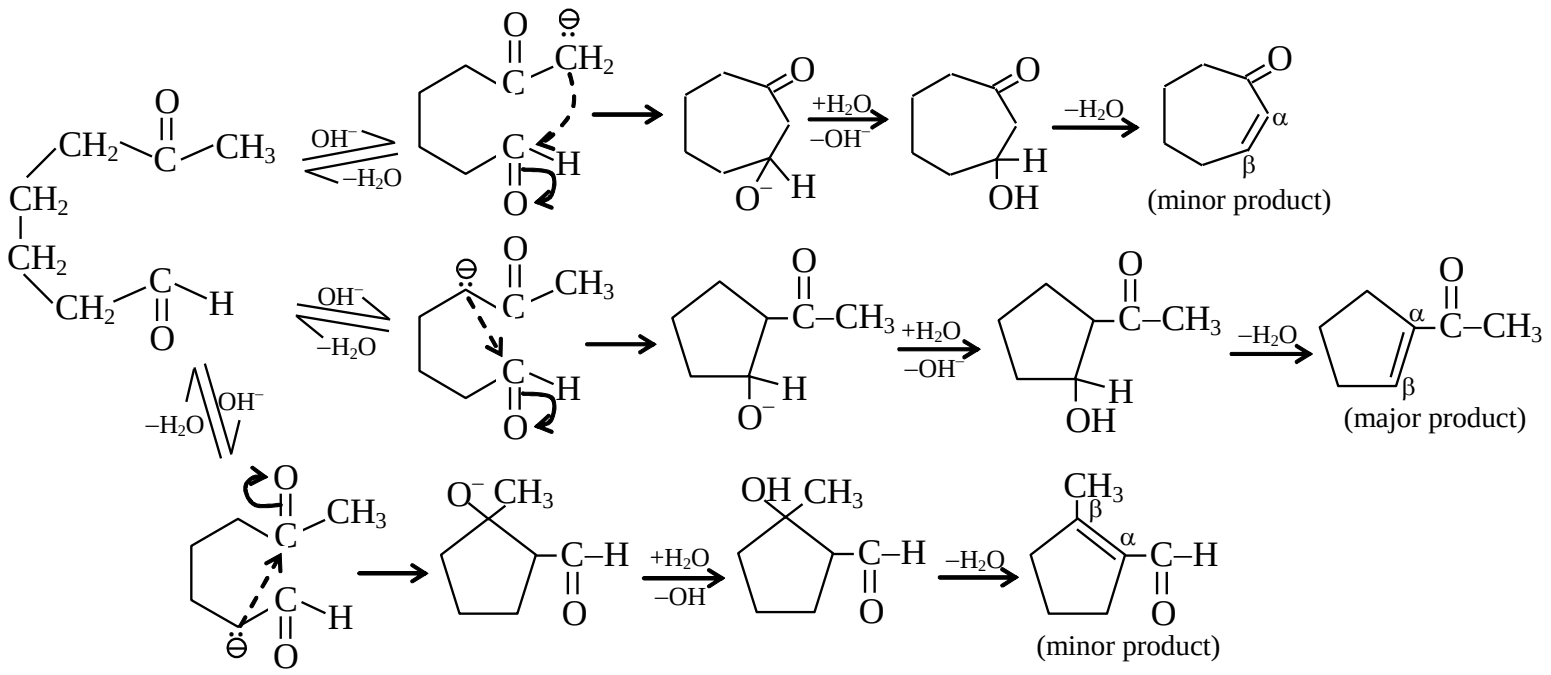
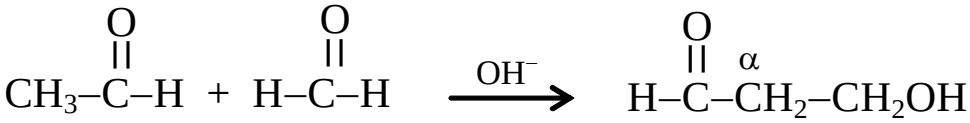


Illustration 3.

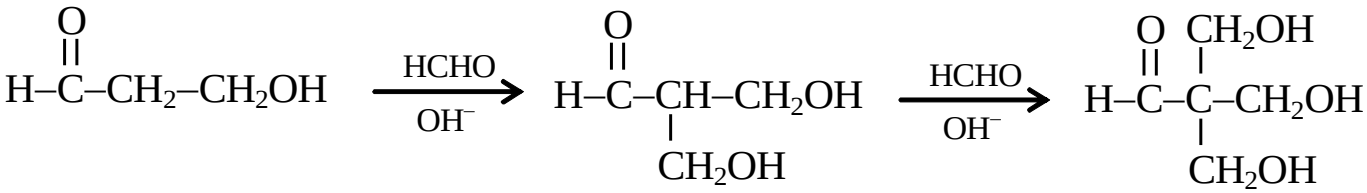
The compound, pentaerythritol $C(CH_2OH)_4$, used in making explosives is obtained from the reaction of acetaldehyde and excess of formaldehyde in the presence of calcium hydroxide. Outline the probable steps in this synthesis.

Solution:

First a crossed aldol condensation takes place between CH_3CHO and HCHO. This converts HCHO into methylol group ($-CH_2OH$).

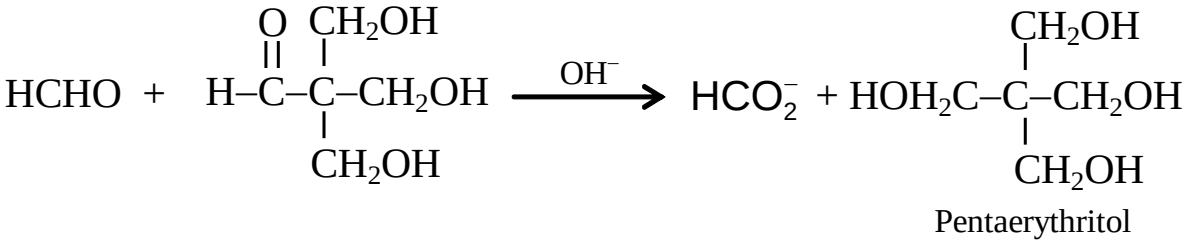


Since the product has 2 more α–hydrogens, so two more such conversions gives a tri–methylol compound.



Now crossed Cannizzaro reaction takes place, as no α–hydrogens are now available.

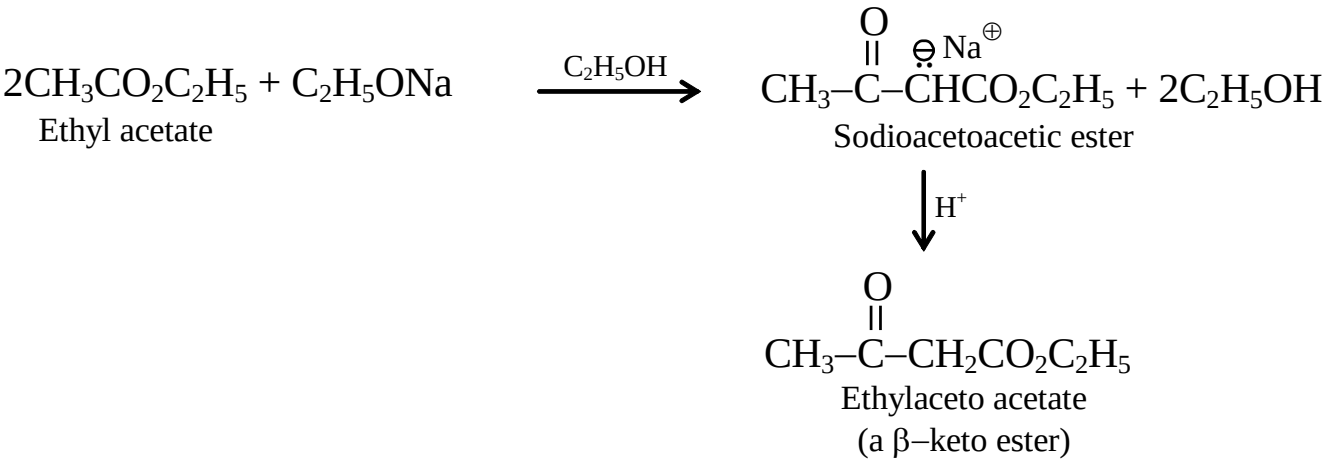
In this reaction, HCHO gets oxidised to formate while the other compound gets reduced to pentaerythritol.



Pentaerythritol

Claisen Condensation:

When ethyl acetate is treated with sodium ethoxide and the resulting mixture is acidified, then ethyl β–ketobutyrate (ethyl 3–oxobutanoate), generally known as ethyl acetoacetate or acetoacetic ester is obtained.



Ethyl acetate

Sodioacetoacetic ester

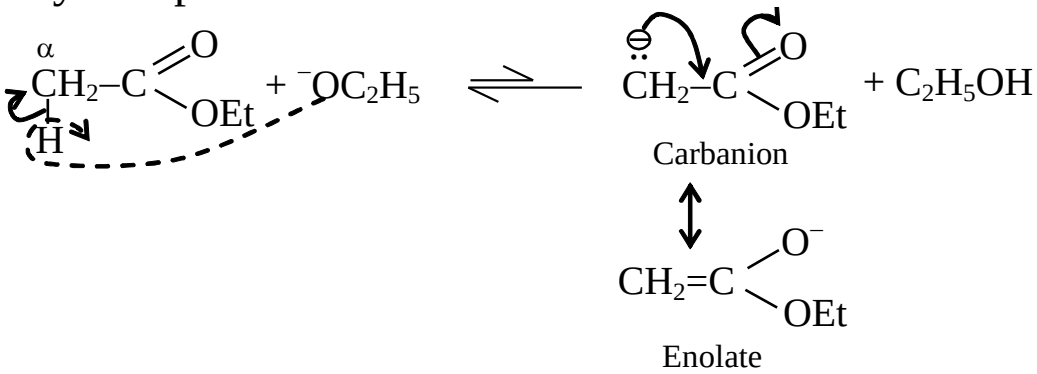
Ethylaceto acetate
(a β–keto ester)

The reaction is similar to aldol condensation i.e involving nucleophilic attack by a carbanion on an electron–deficient carbonyl carbon, but with two differences. First difference is that the α–hydrogen of an ester is less acidic than that of aldehydes or ketones, became of conjugation occur in $-C(=O)OC_2H_5$ group, so dilute OH^- is not the base employed here. We need a much stronger base than OH^-, that's why sodium ethoxide is used as a base. The second difference is that in aldol condensation, nucleophilic attack leads to addition but in Claisen condensation, nucleophilic attack leads to substitution (typical reaction of acyl compounds).

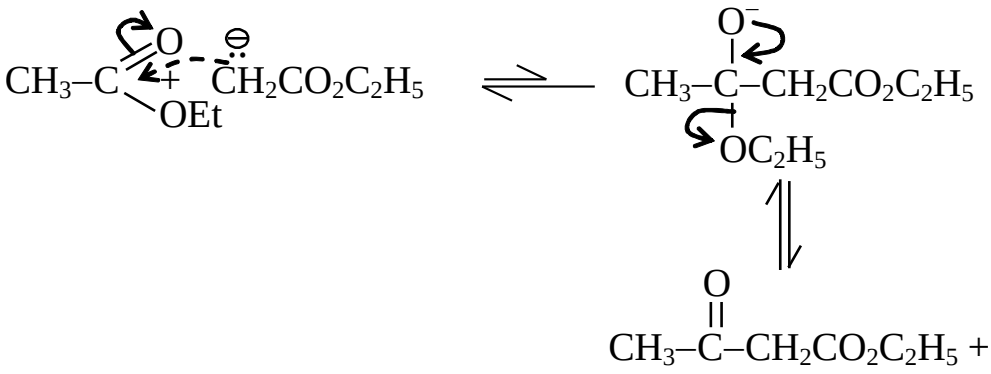
Mechanism:

The generally accepted mechanism for the Claisen condensation is

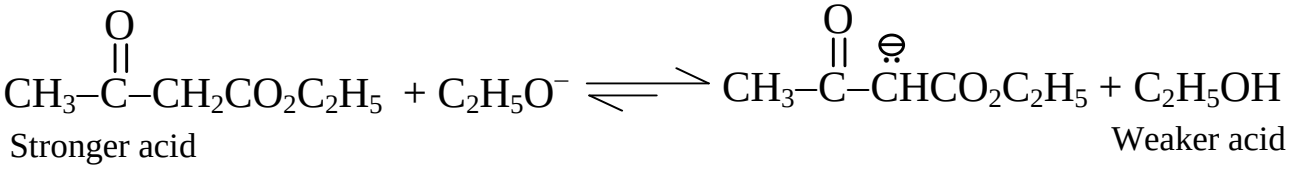
Step I:



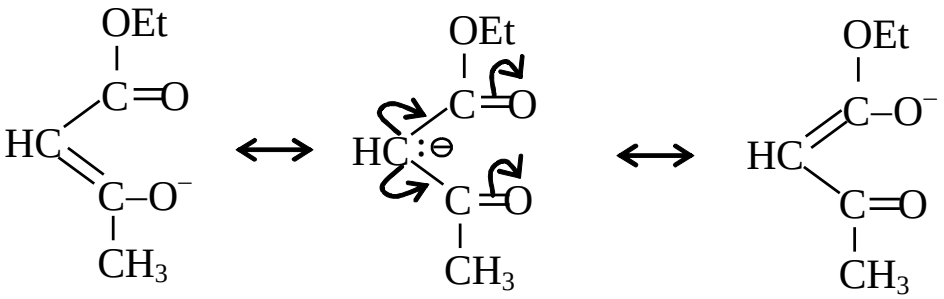
Step II:



Step III:



Ethoxide ion in the first step abstracts a hydrogen ion from the α–carbon of the ester to form carbanion, which in the next step undergoes nucleophilic attack on the carbonyl carbon of second molecule of ester to displace ethoxide ion and finally give β–keto ester. But the product isolated is not a β–keto ester, it is sodium salt of β–keto ester. This is because acetoacetic ester (having α–hydrogens between two carbonyl groups) is much stronger acid than ethyl alcohol. So, acetoacetic ester reacts with ethoxide ion to form ethyl alcohol and the anion of sodio acetoacetic ester. The salt is readily stabilized by resonance.

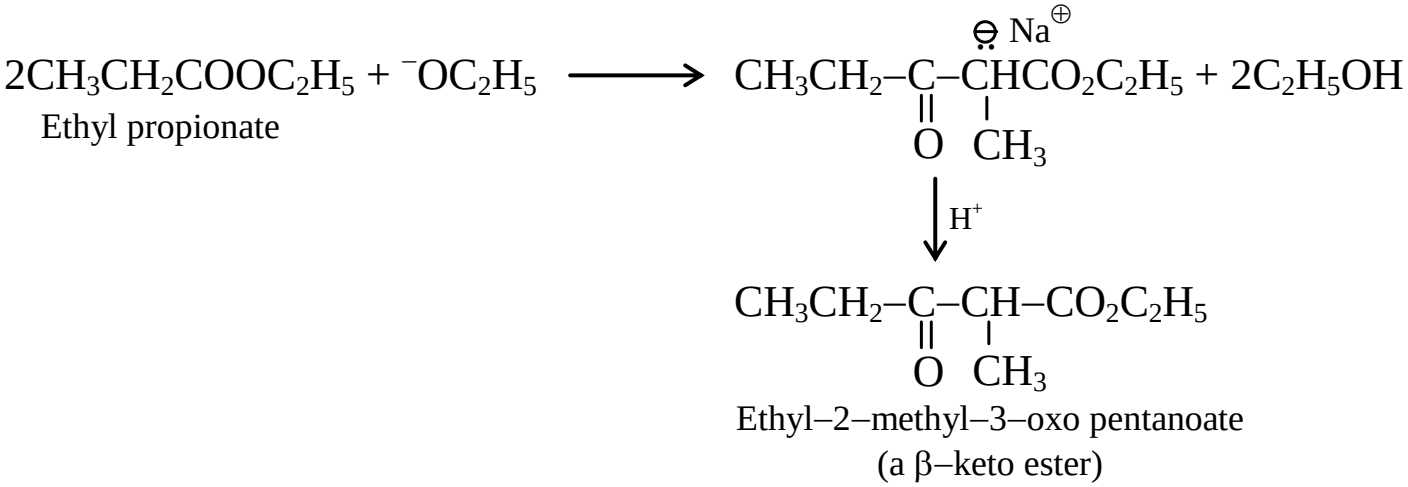


Anion of sodioaceto acetic ester

Claisen condensation can be driven to completion by removing a proton from the β–keto ester. This is easy to achieve as α–carbon of the β–keto ester is flanked by two electron withdrawing groups, making its hydrogen more acidic than the α–hydrogen of the reacting ester.

Successful Claisen condensation requires an ester with two α–hydrogens and an equivalent amount of base rather than a catalytic amount of base.

While drawing the product of Claisen condensation directly (without writing the mechanism), we should remember to form carbanion (mentally) from α–carbon of the ester and attach it to the carbonyl carbon of other molecule of ester by ejecting ethoxide ion. The final product should be sodium salt of β–keto ester. For example,

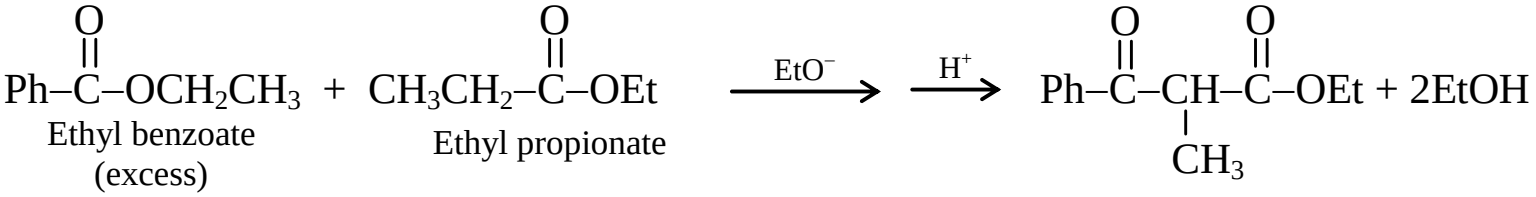


Ethyl propionate

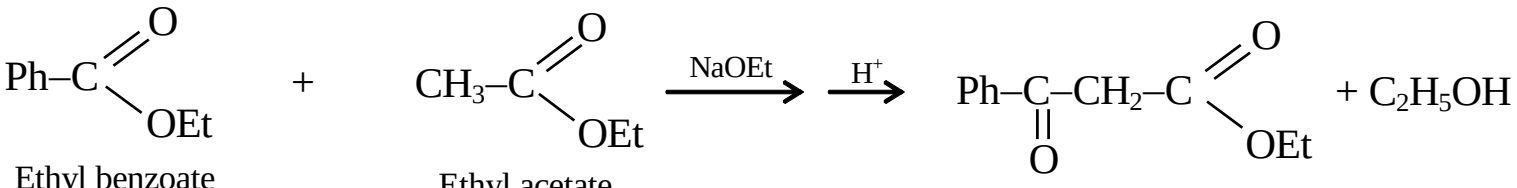
Ethyl–2–methyl–3–oxo pentanoate
(a β–keto ester)

Mixed Claisen condensation:

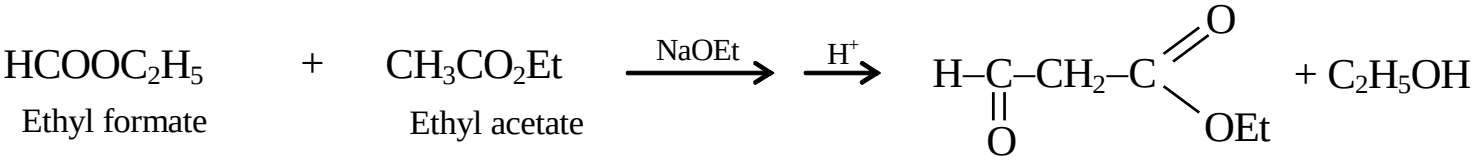
Mixed Claisen condensation is a condensation reaction between two different esters. Like mixed aldol condensation, a mixed Claisen condensation will be useful only when it is carried under conditions that allows the formation of primarily one product, other wise, the result is a mixture of products that are difficult to separate. Only one product will be formed when one of the ester has no α–hydrogen and is taken in excess while the other ester is added slowly to the reaction mixture.



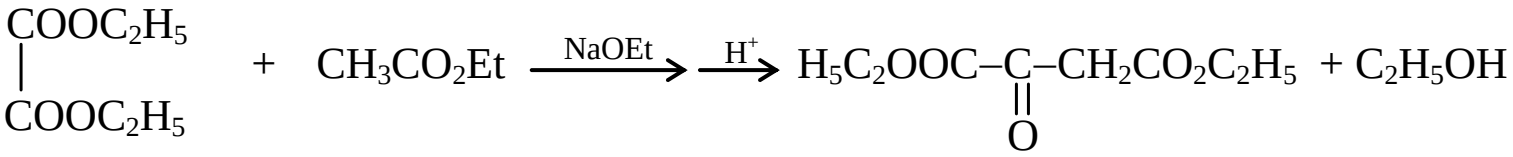
Ethyl benzoate (excess) — Ethyl propionate



Ethyl benzoate — Ethyl acetate — Ethyl benzoylacetate

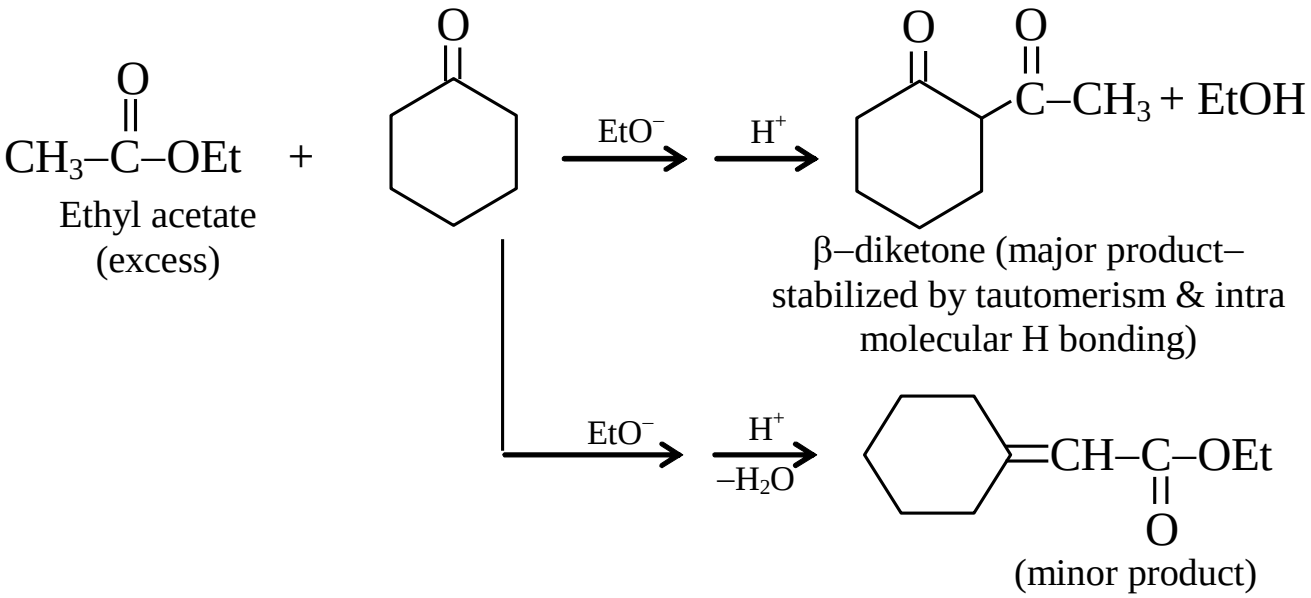


Ethyl formate — Ethyl acetate — Ethyl formylacetate



Ethyl oxalate — Ethyl oxaloacetate

A reaction similar to mixed Claisen condensation is the condensation of a ketone (but not aldehydes) and an ester (taken in excess). As α–hydrogens of ketones are more acidic than that of esters, so carbanion is formed by ketones, which attacks the electrophilic carbon of ester to finally give a product, β–diketone (stabilized by intramolecular hydrogen bonding in the enol form).



$$CH_3COCH_3 + CH_3CO_2C_2H_5 \xrightarrow{NaOC_2H_5} \xrightarrow{H^+} CH_3COCH_2COCH_3 + C_2H_5OH$$

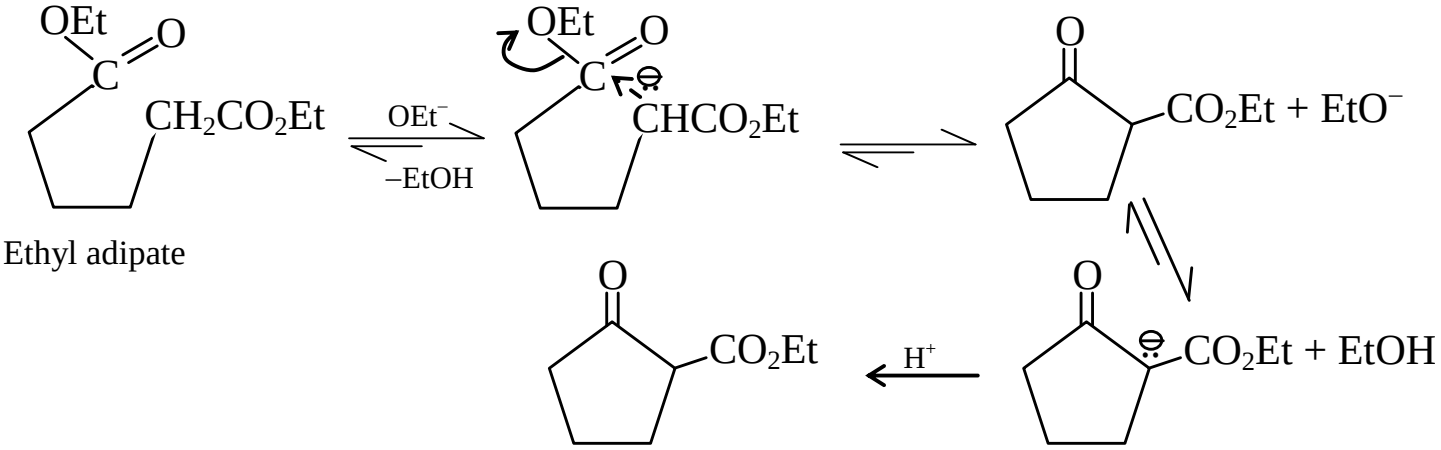
2, 4–pentanedione

$$CH_3COPh + Ph–CO_2Et \xrightarrow{NaOEt} \xrightarrow{H^+} Ph–C(=O)–CH_2–C(=O)–Ph + C_2H_5OH$$

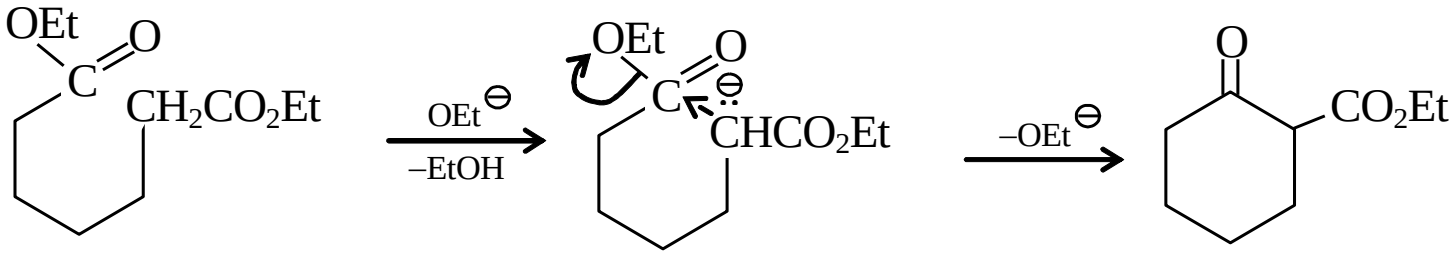
Dibenzoyl methane

Dieckmann Condensation:

Intramolecular Claisen condensation of esters with α–hydrogen atoms in the presence of sodium ethoxide leading to cyclization is called Dieckmann condensation. When ethyl adipate is treated with sodium ethoxide, followed by acidification gives 2–carbethoxy cyclopentanone (a cyclic β–keto ester).



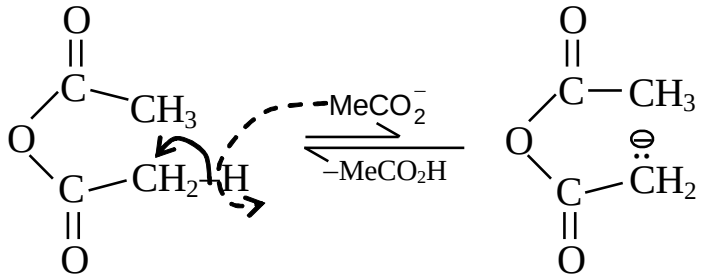
Ethyl pimelate on treatment with sodium ethoxide gives 2–carbethoxy cyclohexanone.



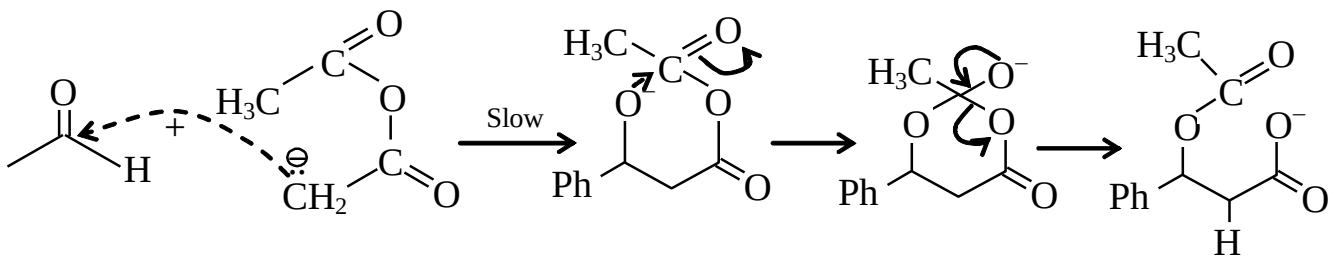
Perkin Reaction:

The reaction between aromatic aldehydes and alkanoic anhydrides in presence of alkanoate is called Perkin reaction. The reaction is similar to aldol condensation. In this reaction, the carbanion is obtained by the removal of an α–hydrogen atom from acid anhydride by carboxylate (anion of the corresponding acid of the acid anhydride). The carbanion then attacks the aromatic aldehyde to yield alkoxide anion. The transfer of acetyl group then takes place from the carboxyl oxygen to alkoxy oxygen via a cyclic intermediate to give a more stable anion. Removal of an α–hydrogen from this anion by carboxylate results in the loss of good leaving group from the β–position to give anion of the α, β–unsaturated acid. This on acidification gives α, β–unsaturated acid. For example, PhCHO on reaction with excess acetic anhydride in presence of sodium acetate followed by acidification gives cinnamic acid (3–phenyl propenoic acid).

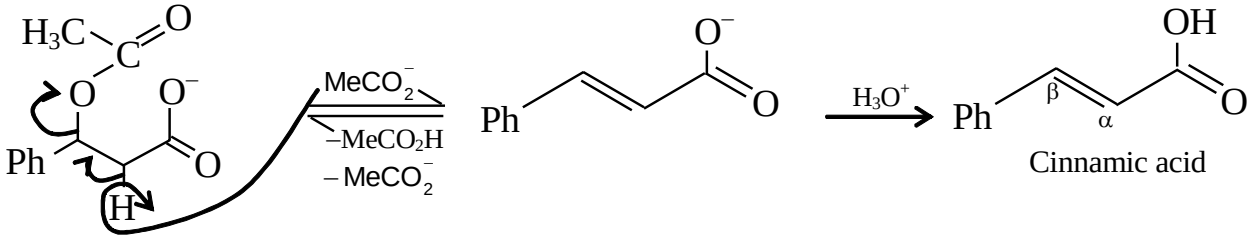
Step I:



Step II:



Step III:



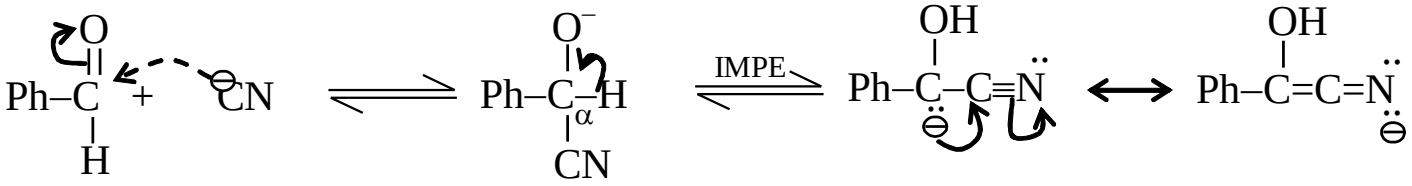
Benzoin Condensation:

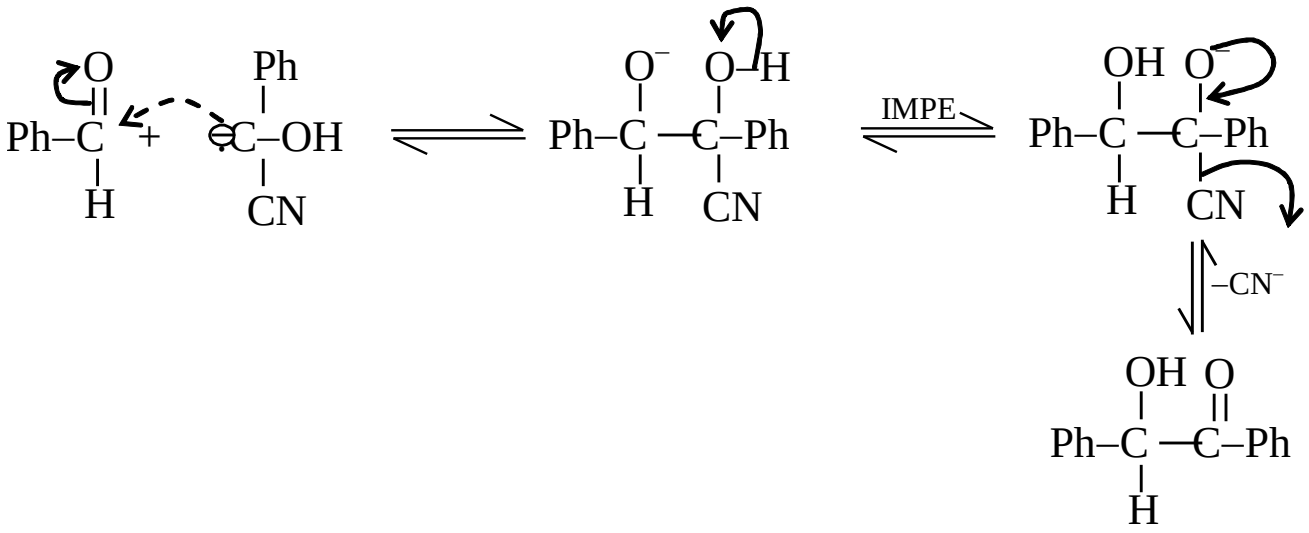
$$2PhCHO \xrightarrow[KCN]{\text{Alcoholic}} PhCH(OH)COPh$$

Benzoin

When aromatic aldehyde is treated with alcoholic KCN, the product is not a cyanohydrin but α–hydroxy aromatic ketone called benzoin. The product of aromatic aldehydes with KCN is different than aliphatic aldehydes because after the attack of CN^-, the intermediate (I) in aromatic aldehyde has sufficient acidity (due to – I effect of Ph) so that intramolecular proton exchange takes place to form a carbanion, which is resonance stabilized. This carbanion then attacks another molecule of aromatic aldehyde, which undergoes intramolecular proton exchange and then ejection of CN^- to give final product i.e. benzoin. The rate–limiting step of the reaction is attack of carbanion on second molecule of aromatic aldehyde.

Mechanism:



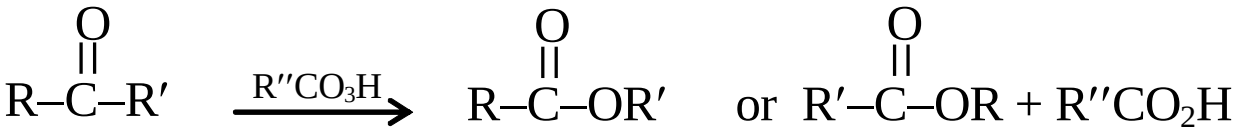


IMPE = Intra molecular proton exchange

Benzoin

Baeyer–Villiger Oxidation:

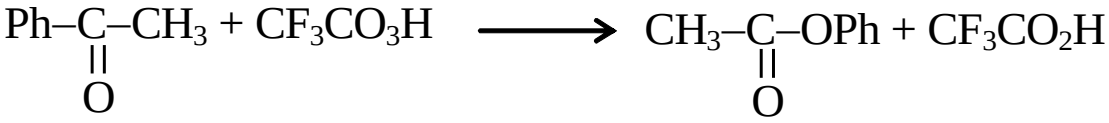
The reaction of oxidation of ketones to esters by peroxy acids (CF_3COOOH) or BF_3/H_2O_2 or H_2O_2/Base is called Baeyer–Villiger oxidation.



(I) (II)

Product (I) is formed when migratory aptitude of R′ is greater than that of R and if it is greater for R, then product (II) is produced.

For example, acetophenone on treatment with peroxy trifluoro acetic acid gives phenyl acetate and not methyl benzoate. This reflects phenyl group has a greater migrating tendency than methyl group.

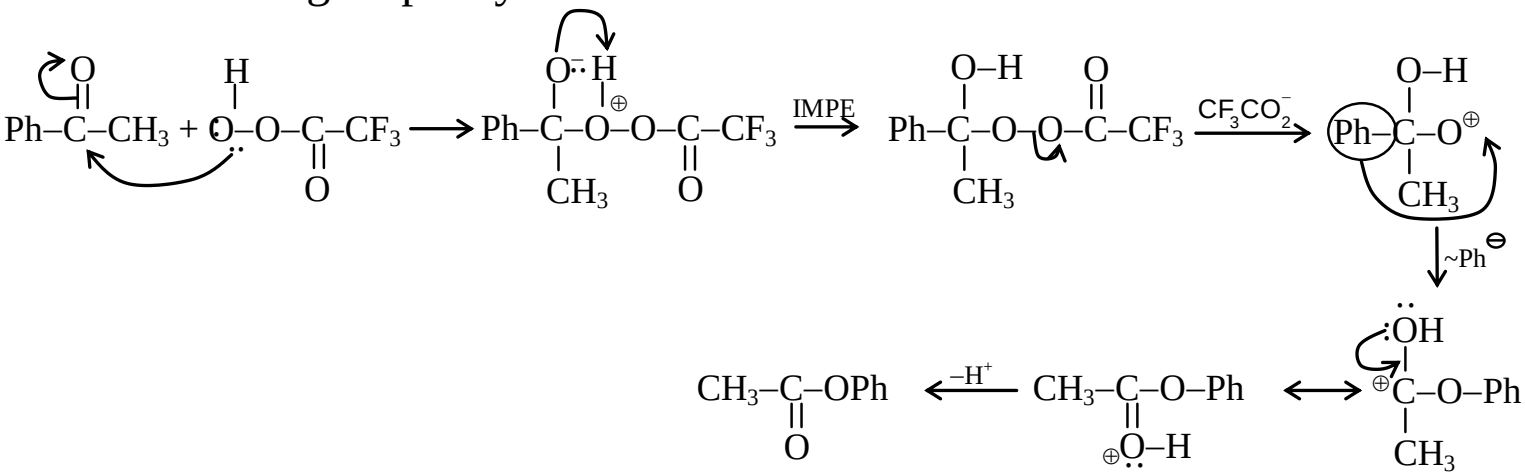


Phenyl acetate

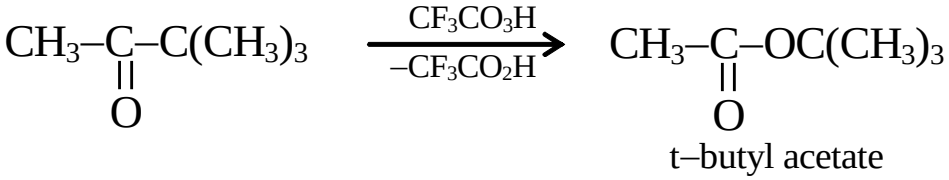
The overall reaction is an insertion of oxygen atom between the carbonyl group and the group that has greater migrating tendency.

Mechanism:

The proposed mechanism involves transfer of acidic hydrogen from peroxy acid to carbonyl oxygen and attack of $CF_3CO_3^-$ on carbonyl carbon of acetophenone. As O–O linkage is weak, it cleaves to release $CF_3CO_2^-$ (which is a good leaving group) and oxygen becomes electron deficient. On electron deficient oxygen, phenyl group migrates from the adjacent carbon to give a carbocation, which then loses H^+ to give phenyl acetate.

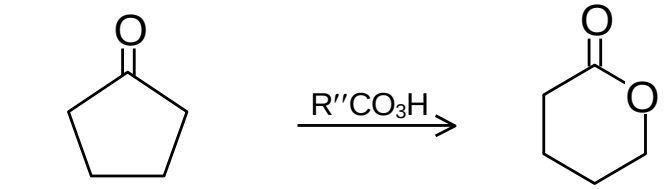


Thus, the reaction establishes the migratory aptitude of various alkyl groups and H as $H^{\ominus} > 3°R^{\ominus} > 2°R^{\ominus} > 1°R^{\ominus} > CH_3^{\ominus}$ and that of aryl groups as p–anisyl > p–tolyl > phenyl > p–chloro phenyl > p–nitro phenyl. In case of alkyl aryl ketones, it is the aryl group which migrates (except in case of $(CH_3)_3C$ group. For example,



t–butyl acetate

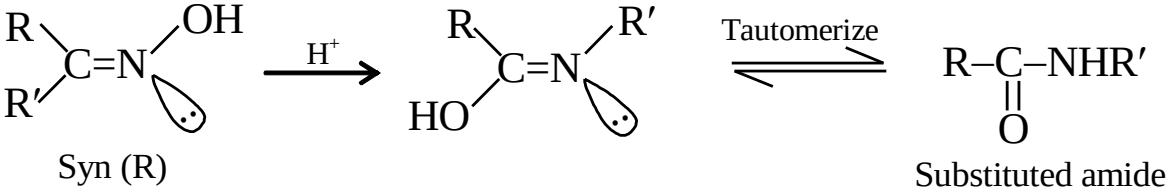
Cyclic ketones get converted to lactones with ring expansion on treatment with peroxy acids.

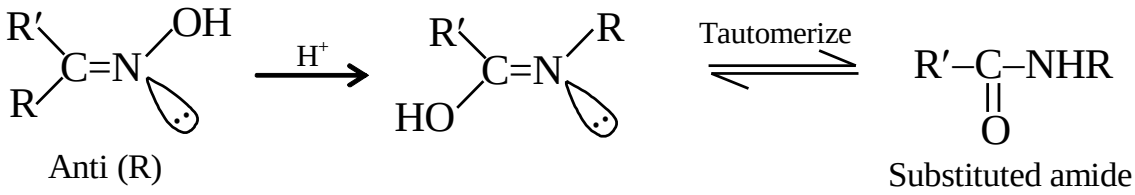


Cyclopentanone δ–lactone

Beckmann Rearrangement:

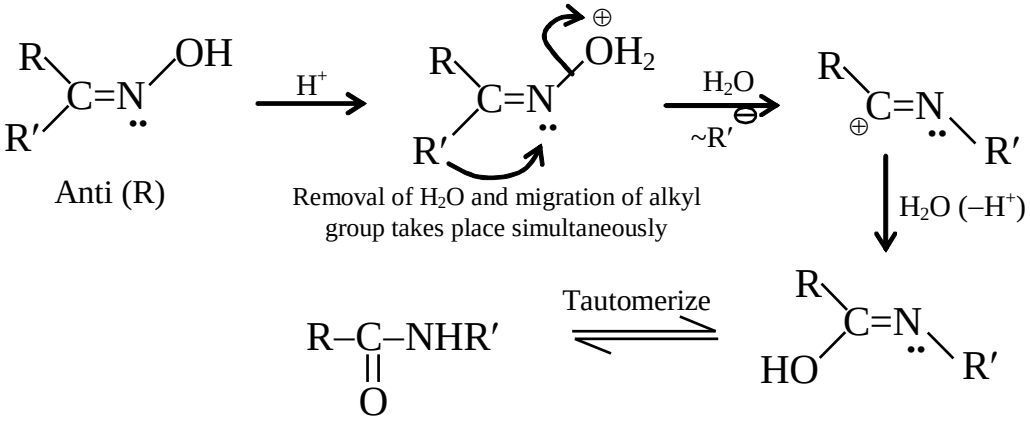
When oximes (especially ketoximes) are treated with acidic catalyst like H^+, PCl_5, $SOCl_2$, SO_3, P_2O_5 etc., they are transformed into substituted amides. The structure of the substituted amide depends on the structure of ketoxime as the migration of the groups does not depend on their migratory aptitude but on the group that is at trans position to the hydroxyl group.



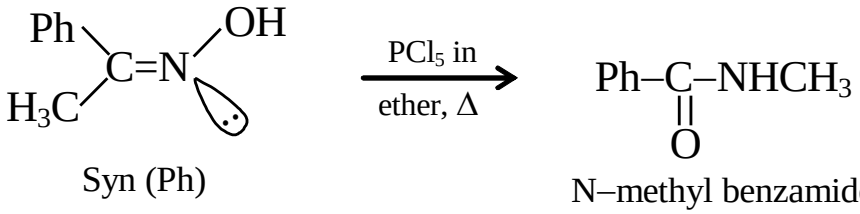


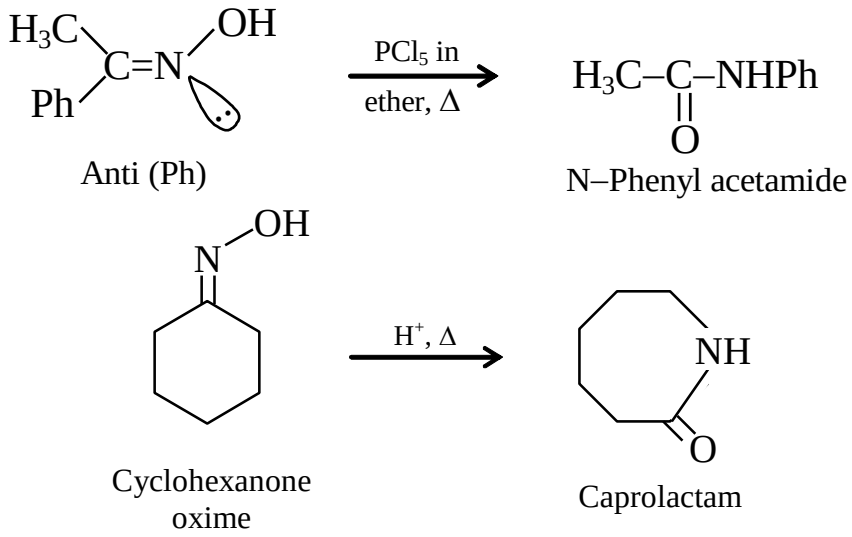
Mechanism:

The given reaction adopts following mechanism, in which group that migrates is anti to the –OH group.



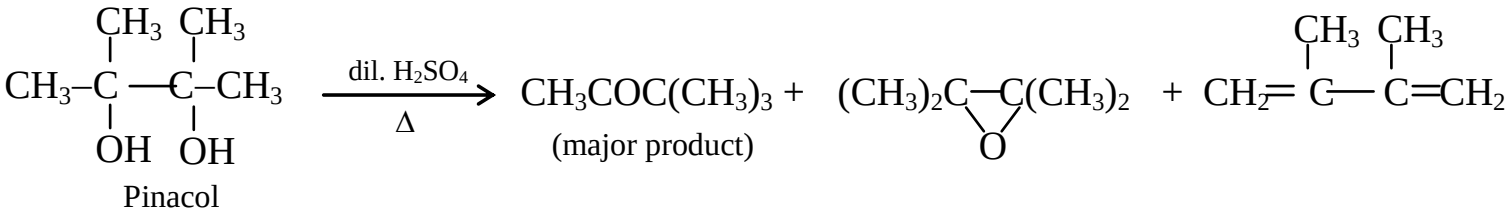
For example,





Pinacol – Pinacolone Rearrangement:

Pinacol (a vicinal diol) on treatment with hot and dilute sulphuric acid undergoes dehydration with rearrangement to give aldehydes or ketones as the major product depending upon the structure of diol. With pinacol, a major product is pinacolone.



For a symmetrical 1, 2 –diol, any of the –OH group can be protonated but for an unsymmetrical 1, 2 –diol, that–OH group is protonated whose loss as H_2O can form a stable carbocation. Although the initially formed carbocation is 3° (or some other type of carbocation), it rearranges by alkyl or aryl shift to give a secondary carbocation. This secondary carbocation formed as a result of rearrangement is more stable than the initially formed carbocation because of lone pair delocalization, it gives a resonating form in which octet of every atom is complete, except hydrogen, which has a duplet only. The group that migrates is the one that has a higher migratory aptitude. The rearranged carbocation then loses a proton to the base to give final product.

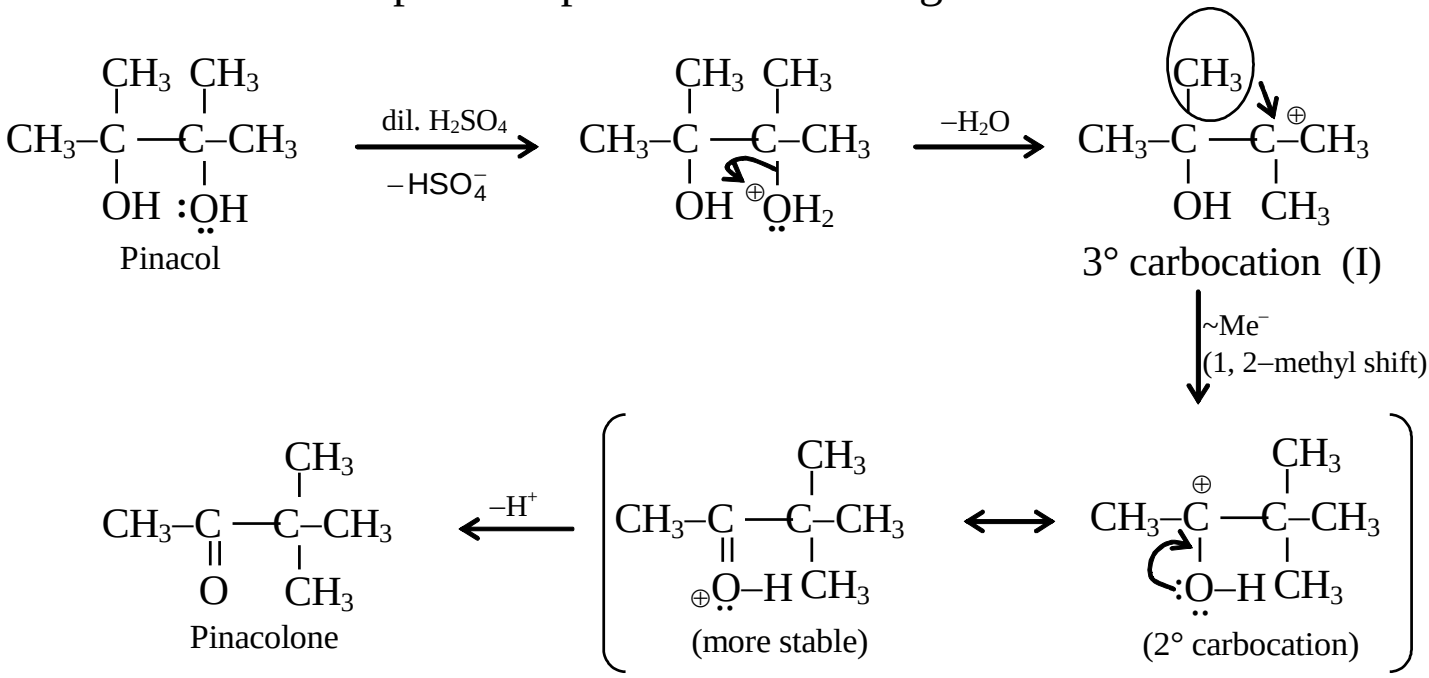
Some of the order of migratory aptitude of groups are

(i) Aryl > hydrogen > alkyl

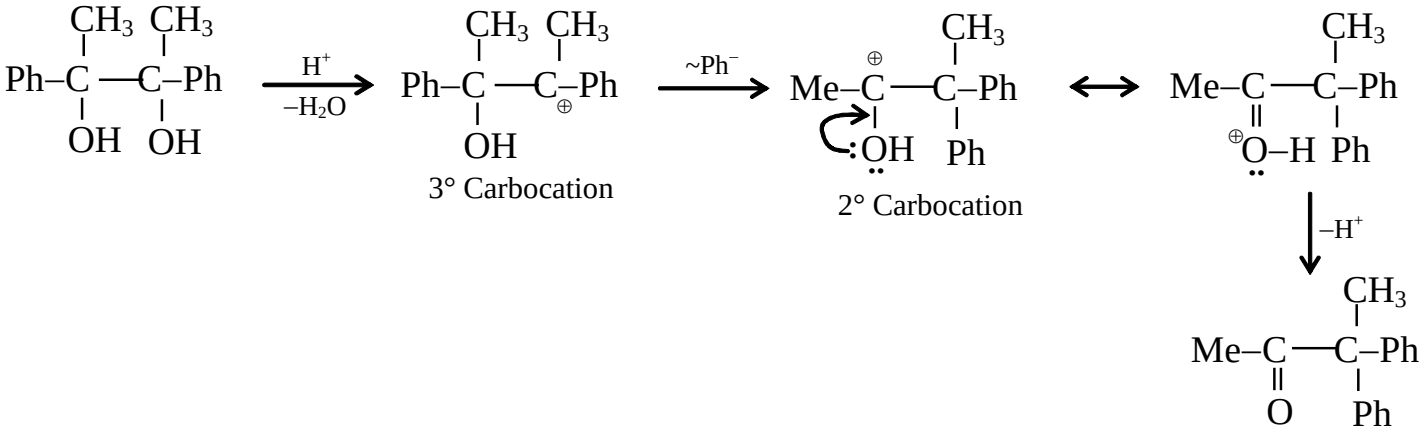
(ii) p–anisyl > p–tolyl > m–tolyl > m–anisyl > phenyl > p–chlorophenyl > o–anisyl > o–tolyl

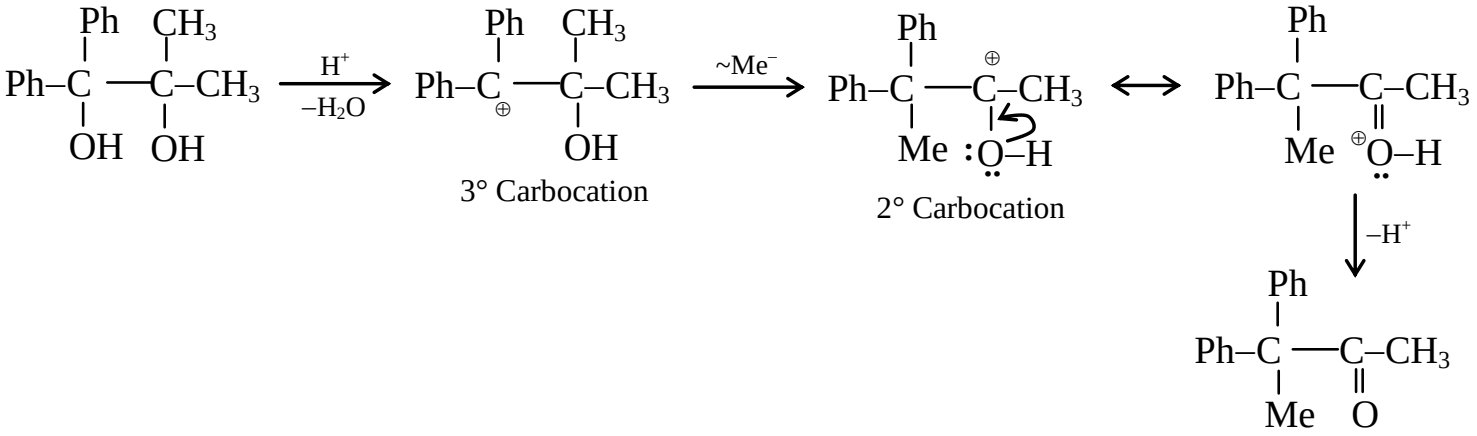
(iii) Me_3C(3° alkyl) > Me_2CH (2° alkyl) > $MeCH_2$ (1° alkyl) > Me

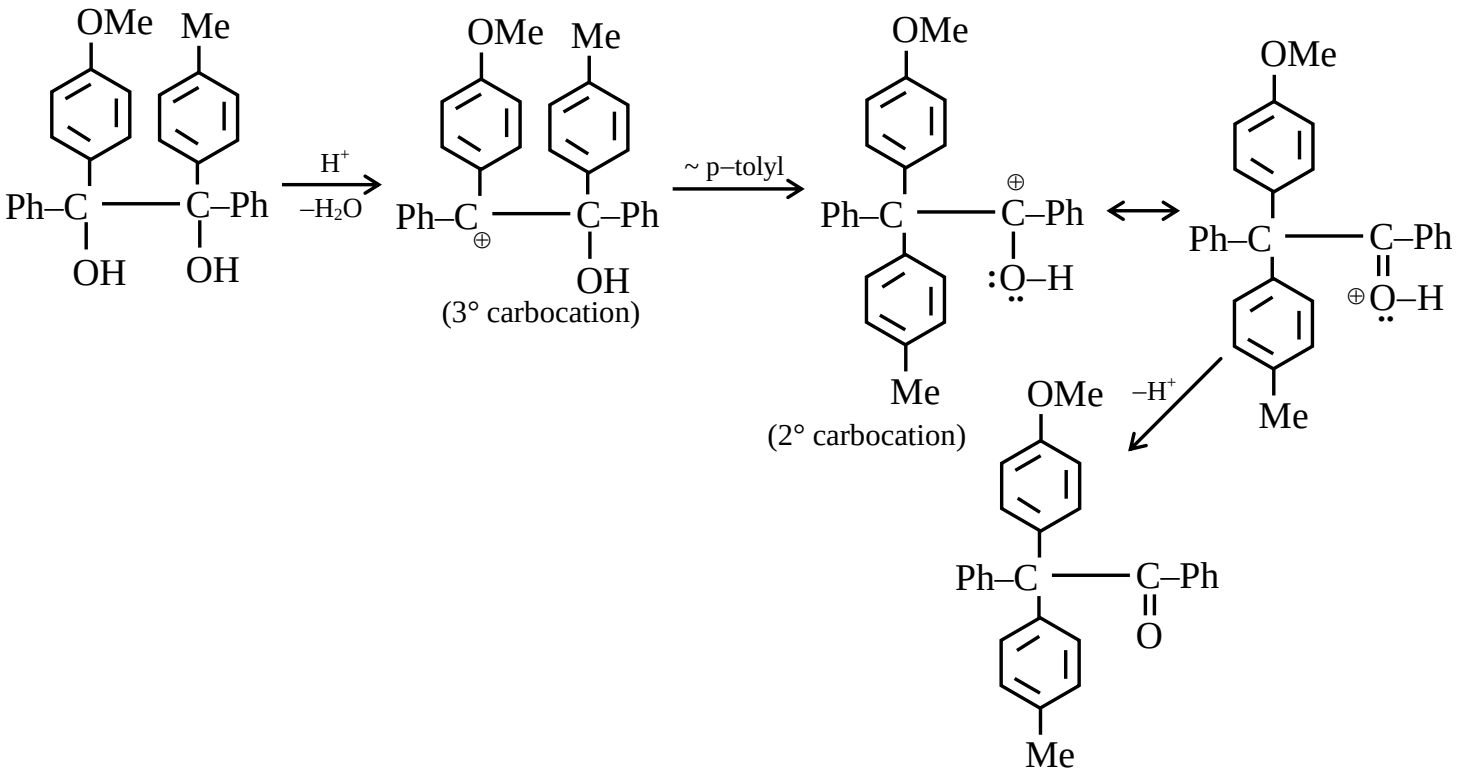
Let us see some cases of pinacol–pinacolone rearrangement.



The conjugated alkene product would be obtained when intermediate (I) loses another OH as H_2O to give a dication, which then loses 2 protons from α–positions. The epoxide product would be obtained when in intermediate (I), OH attacks $C^{\oplus}$ through its lone pair to form a three–membered ring, which finally loses H^+. But diene is a minor product as the dication formed is not stable due to the presence of positive charges on adjacent carbanions. Epoxide is also not the stable product as it gets cleaved in acidic medium to give back (I).


CH3 CH3
Ph–C —C–Ph
OH OH
H+
–H2O
3° Carbocation
~Ph–
2° Carbocation
–H+


Ph CH3
Ph–C —C–CH3
OH OH
H+
–H2O
3° Carbocation
~Me–
2° Carbocation
–H+


OMe Me
Ph–C —C–Ph
OH OH
H+
–H2O
(3° carbocation)
~ p–tolyl
Me
(2° carbocation)
–H+
O–H

Bicyclic 1,2–diols also undergo pinacol–pinacolone type mechanism with the ring expansion/ring contraction depending on the ring sizes.

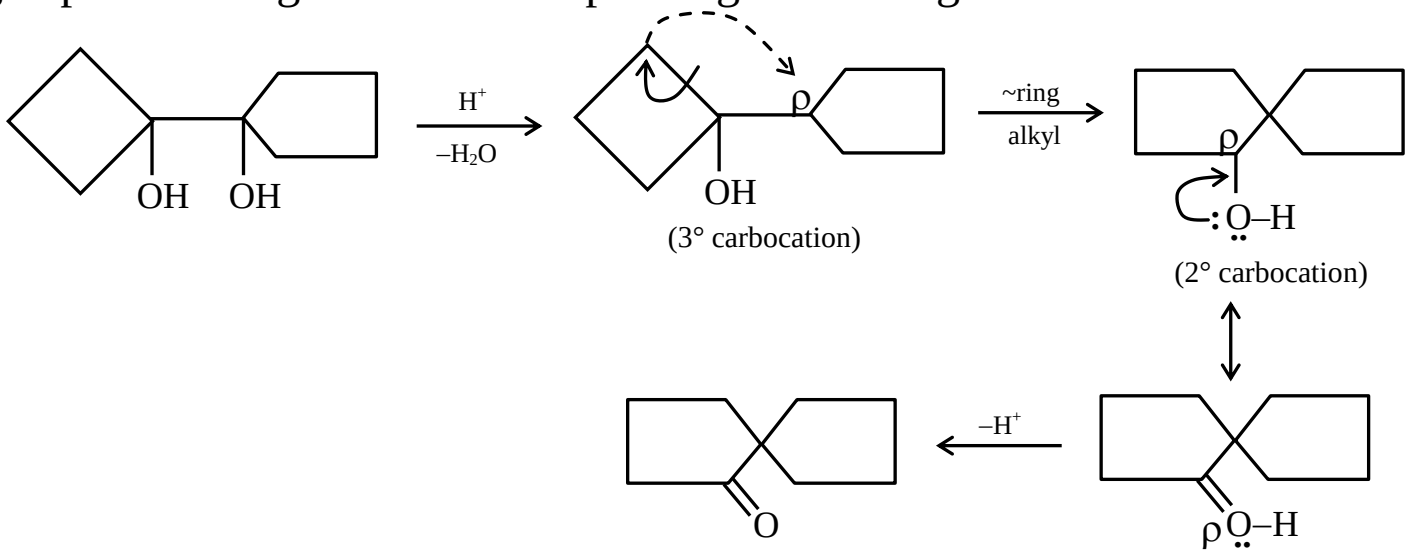
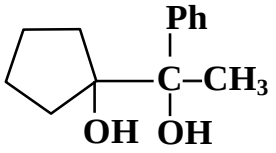
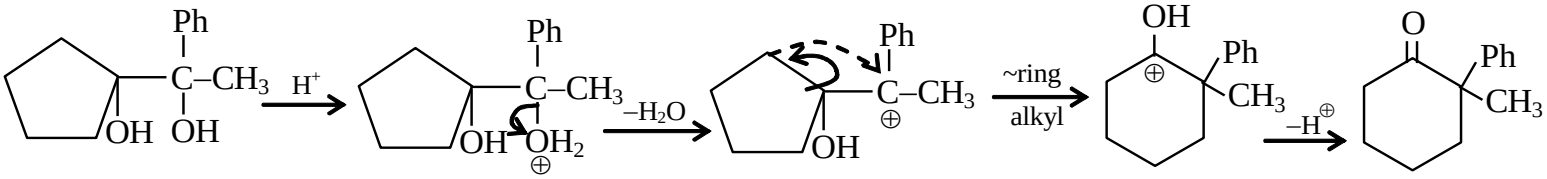


Illustration 4.

Give the product of the rearrangement of the cyclopentyl glycol, 

and show how it is formed.

Solution:



Meerwein–Ponndorf–Verley Reduction:

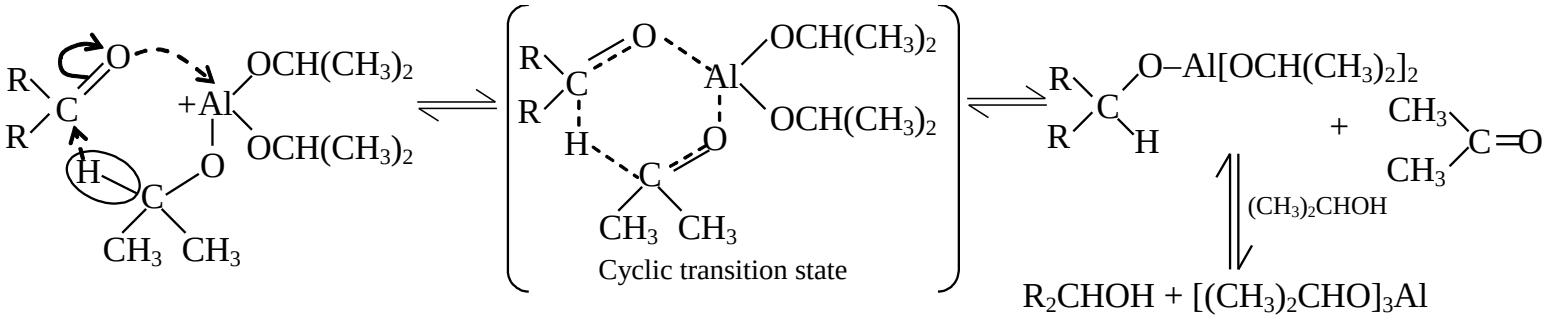
When carbonyl compounds are heated with aluminium isopropoxide in isopropanol solution, they are reduced to alcohols and isopropoxide is oxidised to acetone, which can be easily removed by distillation. Aldehydes are reduced to primary alcohols and ketones to secondary alcohols. This method is generally used for the reduction of ketones to secondary alcohols. The reducing agent employed in the reaction is a specific reagent, used for reducing ketones or aldehydes in presence of reducible functional groups like double bond, nitro

group etc. This reagent reduces only the carbonyl group, keeping other groups untouched.

$$R_2CO + [Me_2CHO]_3Al \rightleftharpoons R_2CHOAl[OCHMe_2]_2 + MeCOMe$$

$$R_2CHOAl[OCHMe_2]_2 \xrightarrow{\text{dil. } H_2SO_4} R_2CHOH$$

Mechanism:



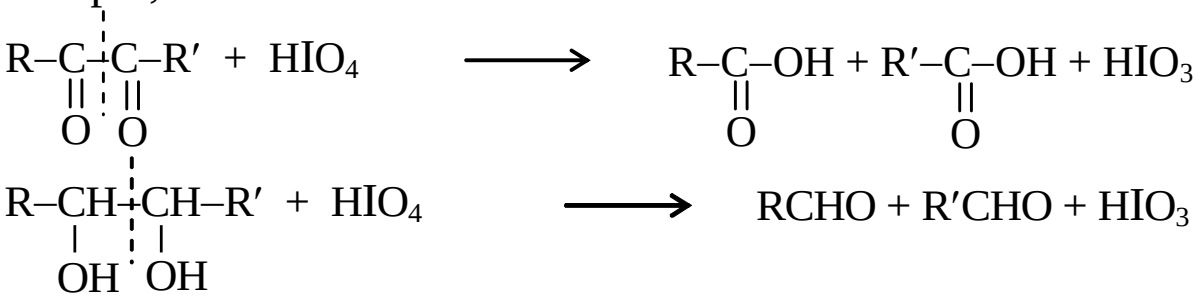
$$R_2CHOH + [(CH_3)_2CHO]_3Al$$

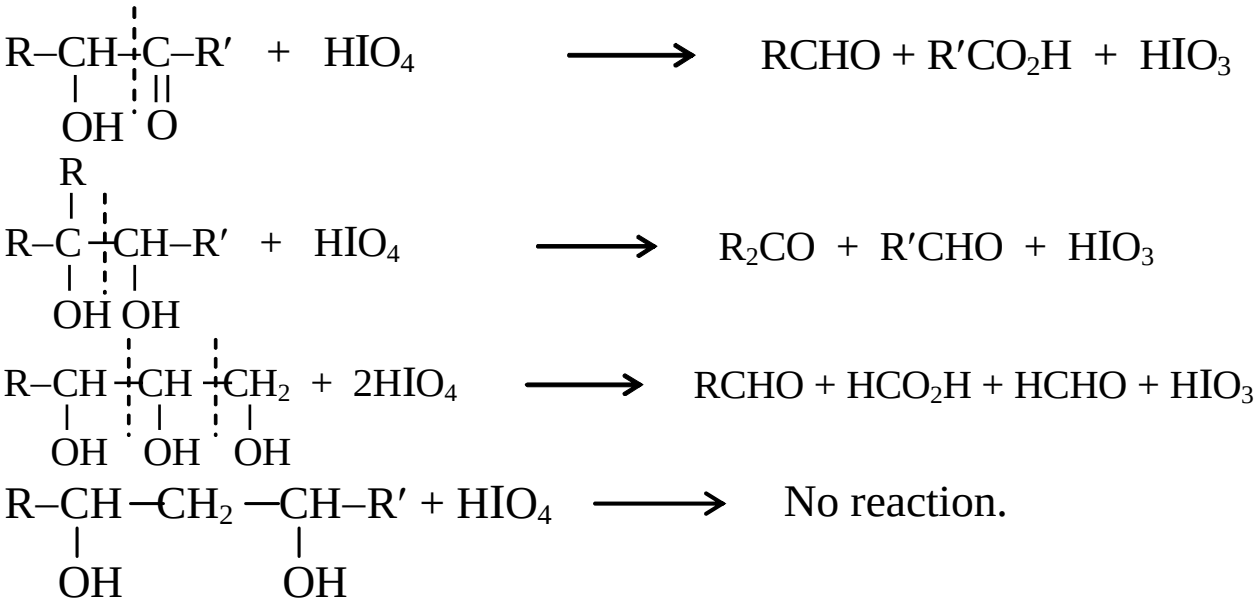
The reverse of this reaction is called Oppenauer oxidation, in which alcohols are oxidised to carbonyl compounds. Primary alcohols are oxidised to aldehydes and ketones are obtained from secondary alcohols.

Periodic Acid Oxidation:

Compounds containing two or more $>C=O$ or –OH groups attached to adjacent carbon atoms undergo oxidation by HIO_4 (periodic acid), resulting in the cleavage of carbon–carbon bonds. Oxidation products can be drawn by cleaving carbon–carbon bond of any two adjacent carbons having –OH groups or oxo groups and supplying each carbon with OH group and then deriving the final product from it.

For example,

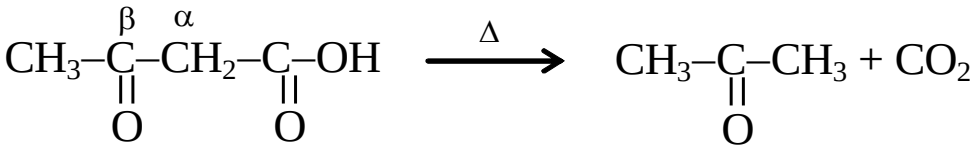




The oxidation is particularly useful in determination of the structure of α–hydroxy ketones or α–hydroxy aldehydes or 1, 2–dialdehydes or 1, 2–diketones or 1, 2–keto aldehydes. Qualitatively, oxidation by HIO_4 is indicated by the formation of white precipitate ($AgIO_3$) upon addition of silver nitrate. The nature and amounts of the products and the quantity of periodic acid consumed gives valuable information regarding the structure of the compound.

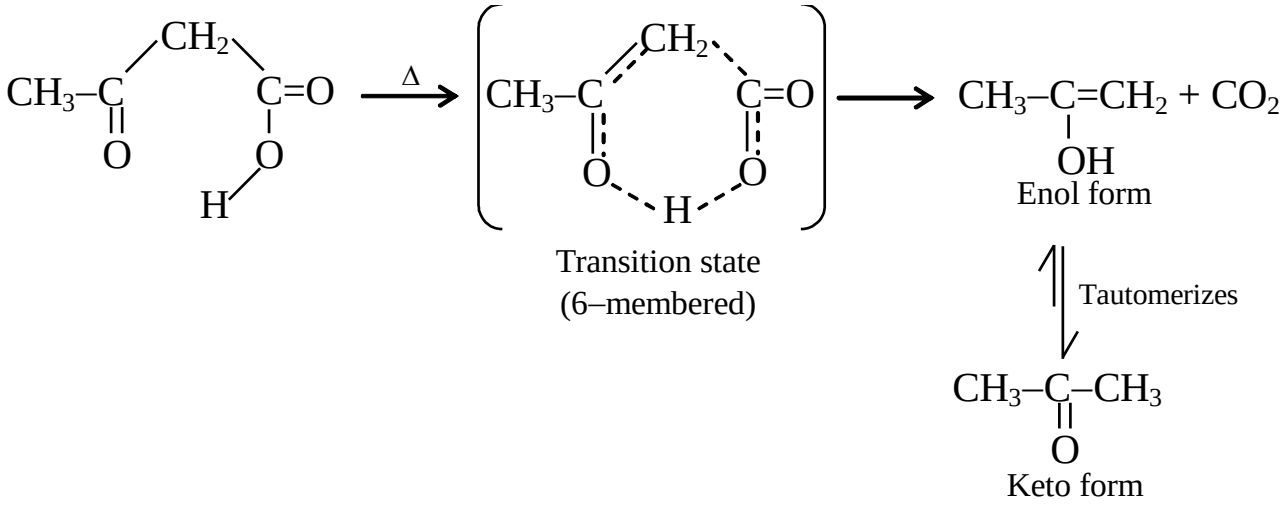
Decarboxylation Of β–Keto Carboxylic Acids:

β–keto acids on slightest warming alone or in presence of a base undergoes ready removal of CO_2. The process of loss of CO_2 is called decarboxylation. For example,

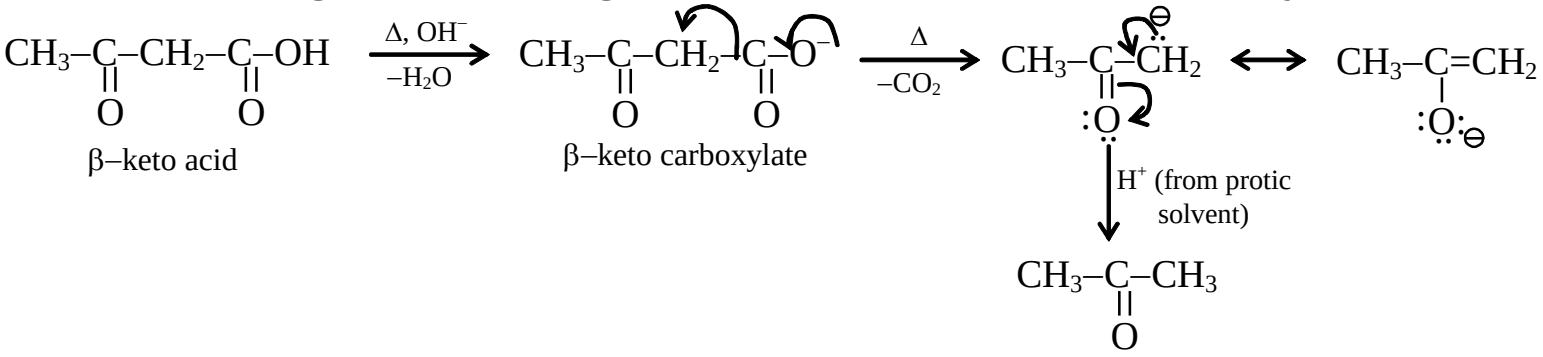


The reaction occurs readily as the transition state involved is 6–membered. Decarboxylation is catalysed by an intramolecular transfer of a proton from the carboxyl group to the carbonyl group with the simultaneous ejection of CO_2. The initial product of the reaction is an enol, which then tautomerizes to keto form.

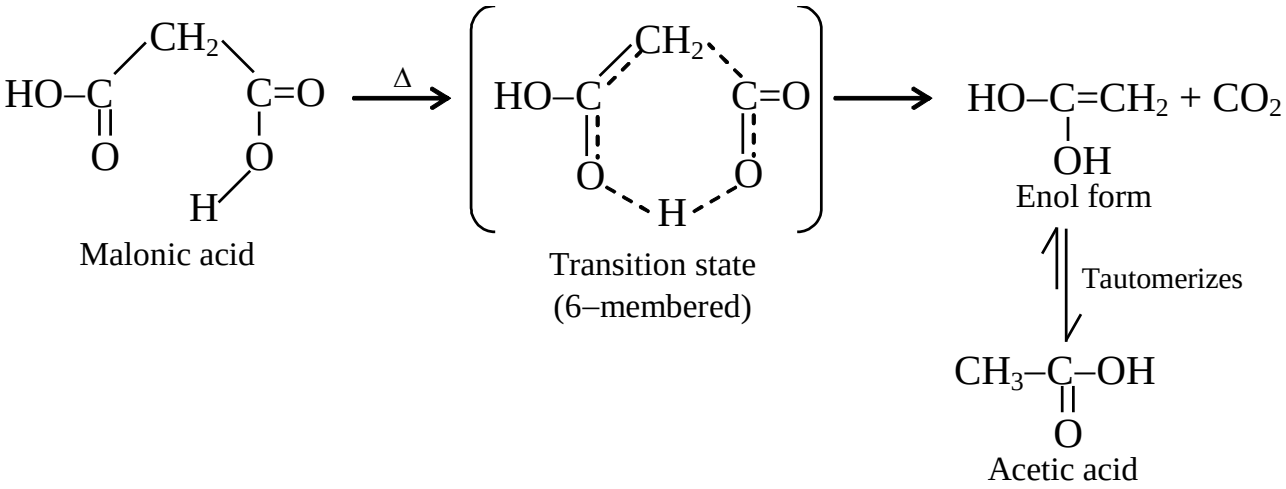
Mechanism:



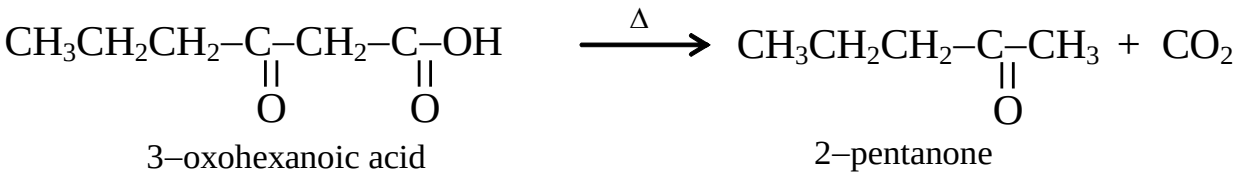
In the presence of a base, β–keto acid is converted into β–keto carboxylate, which on heating loses CO_2 to give a carbanion, that is stabilized by resonance.

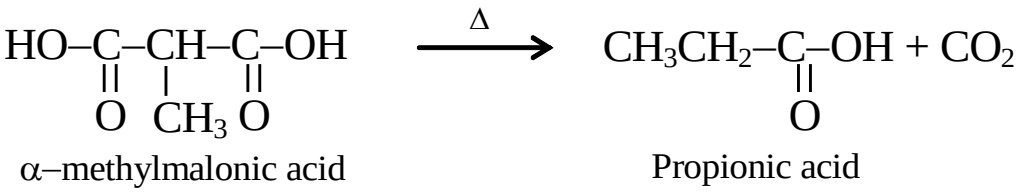


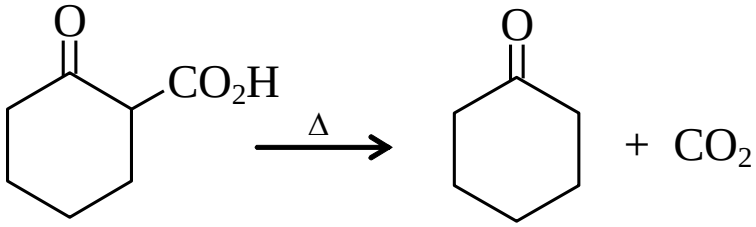
When a compound carrying two carboxyl groups on the same carbon is heated at about 150°C, it also undergoes decarboxylation, in a manner similar to β–keto acids. But higher temperature is required to decarboxylates a β–dicarboxylic acid than to decarboxylates a β–keto acid as carbonyl oxygen is more basic than carboxyl oxygen.



For example,







Analysis Of Aldehydes & Ketones

Aldehydes and ketones are characterized by the addition of nucleophilic reagents (especially ammonia derivatives) to the carbonyl group. For example, all aldehydes or ketones will react with 2, 4–dinitrophenylhydrazine to form an insoluble yellow or red solid of 2, 4–dinitro phenyl hydrazone.

Aldehydes are characterized and in particular are differentiated from ketones through their ease of oxidation: aldehydes give a positive test with Tollen's reagent while most of the ketones do not.

Aldehydes are also oxidized by many other oxidizing agents: cold, dilute, neutral $KMnO_4$ and by CrO_3 in H_2SO_4.

A highly sensitive test for aldehydes is the Schiff's test. An aldehyde reacts with the fuschin aldehyde reagent to form a characteristic magenta colour.

Aldehydes and ketones are generally identified through the melting points of derivatives like 2, 4–dinitrophenylhydrazones, oximes and semicarbazones.

Methyl ketone is characterized through the iodoform test.

Aldehydes can be oxidised by Fehling's solution.

Fehling's solution, an alkaline solution of cupric ion complexed with tartarate ion (or Benedict's solution, in which complexing is with citrate ion); the deep–blue colour of the solution is discharged, and red cuprous oxide precipitates.

Fehling's solution is made by mixing, Fehling A solution, which contains copper sulphate and Fehling B solution, which contains sodium hydroxide and Rochelle salt (Sodium Potassium Tartarate). During the oxidation of aldehydes to acids, the cupric ions are reduced to cuprous ions, which are precipitated as red cuprous oxide.

$$RCHO + 2Cu^{2+} + 3OH^- \longrightarrow RCO_2^- + 2Cu^+ + 2H_2O$$

$$2Cu^+ + 2OH^- \longrightarrow Cu_2O\downarrow + H_2O$$

Cuprous oxide (red)

Illustration 5.

Give simple chemical tests to distinguish between the compounds in each of the following pairs.

(a) $PhCH=CHCH_2OH$ and $PhCH=CHCHO$

(b) $CH_3CH_2CH_2CH_2CHO$ and $CH_3CH_2COCH_2CH_3$

(c) $PhCH_2COCH_2CH_3$ and $PhCH(OH)CH_2CH_2CH_3$

(d) $PhCH_2CHO$ and $PhCOCH_3$

Solution:

(a) and (b): The aldehydes give a positive Tollen's test with $Ag(NH_3)_2^+$. Also in (a), only the aldehyde gives a precipitate with either H_2NOH or $PhNHNH_2$.

(c): Only the alcohol is oxidised by CrO_3 (colour change from orange–red to green). Alternatively, the ketone gives a solid oxime or phenyl hydrazone with H_2NOH or $PhNHNH_2$ respectively.

(d): Only the aldehyde gives a positive Tollen's test and the given ketone gives a positive iodoform test.

Fundamental Solved Examples

Example 1.

Synthesize the following compounds, starting with cyclopentane (C_5H_{10}), alcohols of three or fewer carbons, H_2CO and inorganic reagents.

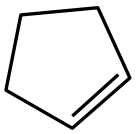
(a) Cyclopentane carbaldehyde

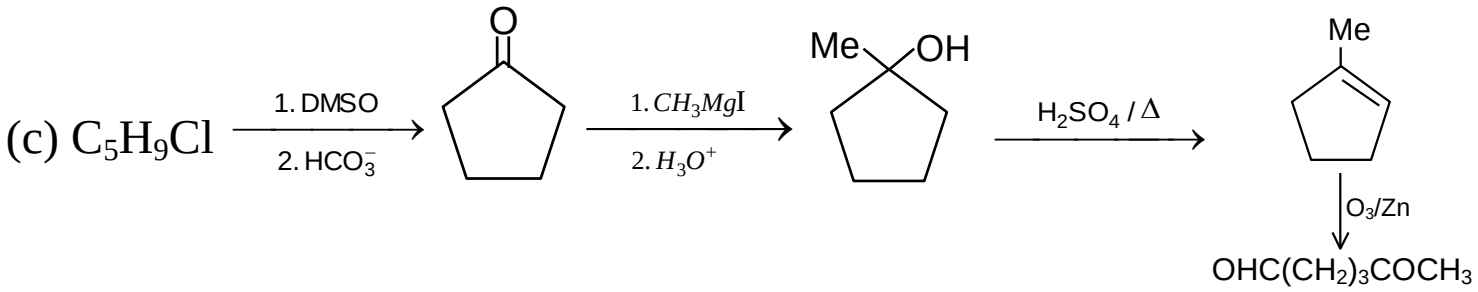
(b) 1, 5–pentanedial and

(c) 5–oxohexanal.

Solution:

(a) $C_5H_{10} \xrightarrow{Cl_2\,/\,h\nu} C_5H_9Cl \xrightarrow{Mg\,/\,Dry\ ether} C_5H_9MgCl \xrightarrow[H_3O^+]{H_2CO} C_5H_9{-}CH_2OH \xrightarrow{CrO_3/Py} C_5H_9{-}CHO$

(b) $C_5H_9Cl \xrightarrow[EtOH]{KOH}$  $\xrightarrow{O_3\,/\,Zn} OHC(CH_2)_3CHO$



Example 2.

Write structures for (A) and (B) in the following reactions.

$$(A) \xleftarrow[0^\circ C]{LBAH} CH_3CH(CH_3)COCl \xrightarrow{LiAlH_4} (B)$$

where LBAH is lithium tri–t–butoxyaluminium hydride. Also account for the different products.

Solution:

(A): $CH_3CH(CH_3)CHO$ (B): $CH_3CH(CH_3)CH_2OH$

LBAH is a less reactive reducing agent than $LiAlH_4$ because of its bulky alkoxide groups, which reduces its ability to donate hydride ion.

Example 3.

The reaction of R′COCl with R_2CuLi gives a ketone, but with RMgX gives a 3° alcohol, $R_2R'COH$. Explain why the latter reaction does not give a ketone.

Solution:

With RMgX, initially a ketone is formed.

$$R'COCl + RMgX \longrightarrow R'COR + MgX(Cl)$$

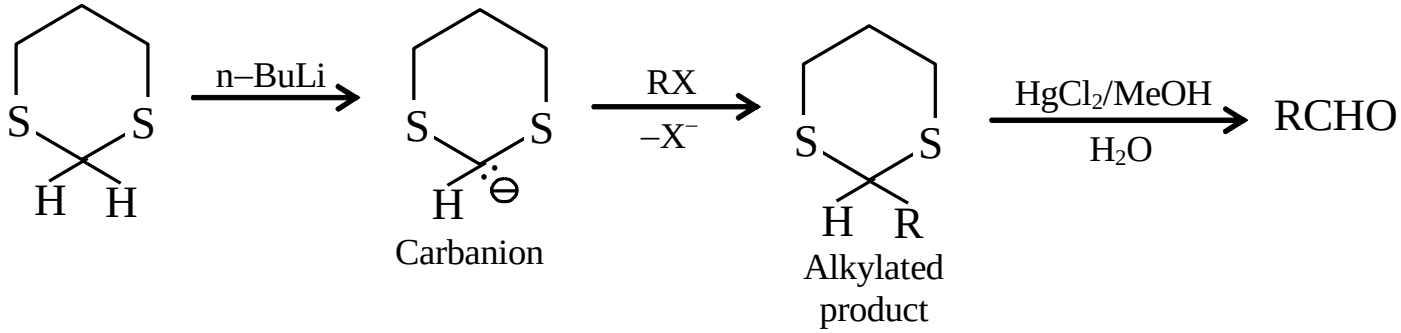
But since the ketone is more reactive than R′COCl, it reacts further with RMgX to form 3° alcohol. R_2CuLi reacts with the less reactive R′COCl but not with the more reactive R′COR. This is because they do not react by typical nucleophilic addition of R^- to $\diagdown C{=}O$. Instead Cu complexes with the Cl of R′COCl as $\left[R'—\overset{\delta+}{\underset{\underset{O}{\|}}{C}}\cdots Cl\cdots\overset{\delta-}{CuLiR_2} \right]$, producing an acylium like ion with greater δ+ on the carbon. This strongly electrophilic carbon can form a bond with even less nucleophilic R^- of R_2CuLi.

Example 4.

Prepare (a) $(CH_3)_2CHCH_2CHO$ (b) $PhCH_2CHO$ (c) cyclopentyl carbaldehyde from 1, 3–dithiane.

Solution:

Aldehydes are prepared by alkylating 1, 3–dithiane at C^2 and by hydrolyzing the resulting thioacetal. The product RCHO has one more carbon from C^2 of dithiane. The general equation of preparation of aldehyde from dithiane is



To get $(CH_3)_2CHCH_2CHO$, alkylate with $(CH_3)_2CHCH_2Cl$.

To prepare $PhCH_2CHO$, alkylate with $PhCH_2Br$

To get cyclopentyl carbaldehyde, alkylate with cyclopentyl chloride.

Example 5.

Compare the acidity of hydroxylamine and oximes and explain the difference.

Solution:

Loss of a proton from $H_2N–OH$ gives a conjugate base, $H_2N–O^-$, in which the negative charge is localized on oxygen. Loss of H^+ from oxime, $\rangle C=N–OH$ gives conjugate base $\left[\rangle C=N–O^- \leftrightarrow \rangle C–N=O\right]$.

The conjugate base of oxime is stabilized by lone pair–pπ delocalization. Thus, $\rangle C=N–O^-$ is a weaker base than $H_2N–O^-$ and consequently, oximes become more acidic than hydroxylamine.

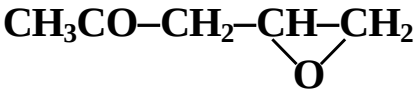
Example 6.

Select the best way for reducing the $\rangle c=o$ group in each of the following:

(a) $BrCH_2CH_2CHO$

(b) $(CH_3)_2C(OH)CH_2CH_2COCH_3$

(c) $PhCH(OH)CH_2COCH_2CH_3$

(d) 

Solution:

(a) Clemmensen reduction is used for reducing it. Strong base causes dehydrohalogenations. $HSCH_2CH_2CH_2SH$ can displace Br^-.

(b) and (c) require Wolff–Kishner reduction or desulfurization. In (b), the 3° alcohol is dehydrated in acid.

In (c), the 2° alcohol is easily dehydrated because the C = C formed is conjugated with the benzene ring.

(d) None. All methods lead to opening of the epoxide ring.

Example 7.

How can we convert $PhCH=CHCOCH_3$ to

(a) $PhCH=CHCOOH$ (b) $PhCH=CHCH(OH)CH_3$

(c) $PhCH_2CH_2COCH_3$ (d) $PhCH=CHCH_2CH_3$

(e) $Ph(CH_2)_3CH_3$?

Solution:

(a) Cl_2 in NaOH (haloform reaction)

(b) $[Me_2CHO^-]_3Al^{3+}$ in Me_2CHOH (Meerwein–Ponndorf reduction) or $LiAlH_4$.

(c) To reduce only C=C of α, β–unsaturated carbonyls use dissolving metal conditions (Birch reduction), Li in liq. NH_3, ether.

(d) H_2NNH_2, OH^- (Wolff–Kishner reduction)

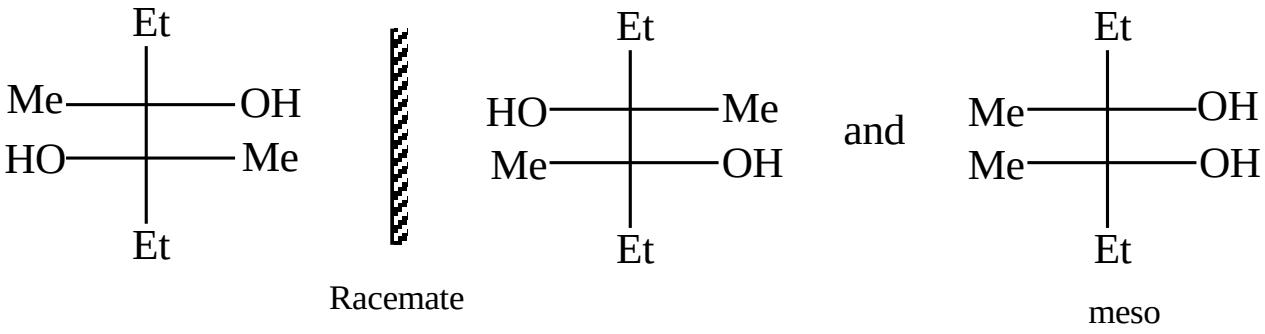
(e) Reduce the compound in (d) with H_2/Pt or reduce the compound in (c) by Clemmensen or Wolff–Kishner method.

Example 8.

Two isomers are formed from the reaction of butanone with Mg/Hg. Write their structures.

Solution:

Two chiral carbons are formed in this reaction leading to a racemate and a meso structures.

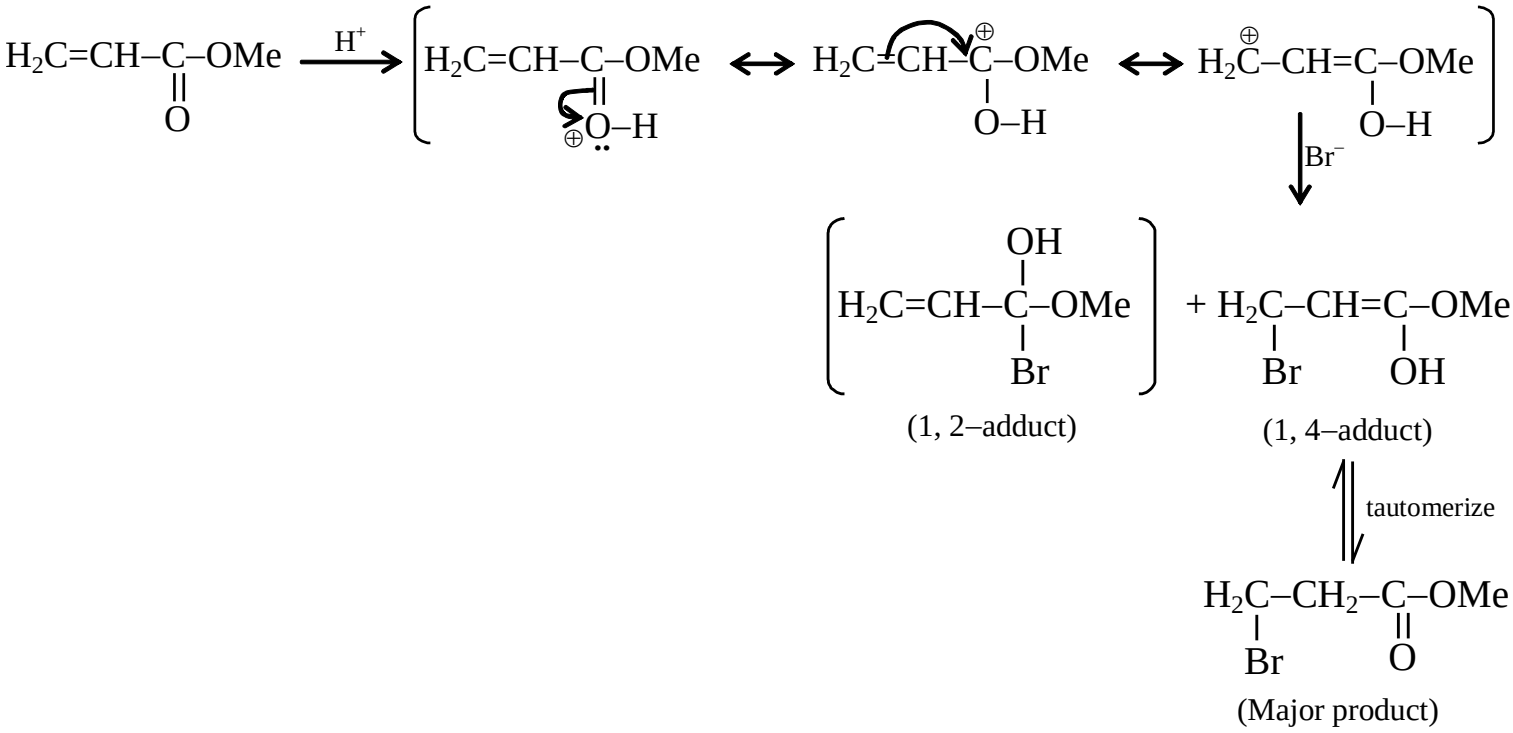


Example 9.

Give the product from the addition of HBr to methyl acrylate, $CH_2=CHCO_2Me$ and the mechanism for its formation.

Solution:

Initially H^+ adds to the $>C=O$ and not to $>C=C<$, to give a resonance stabilised cation.



Example 10.

Give the aldol products and the corresponding alkenes (aqueous NaOH or KOH used, 100°C) from

(a) 2, 5–hexanedione

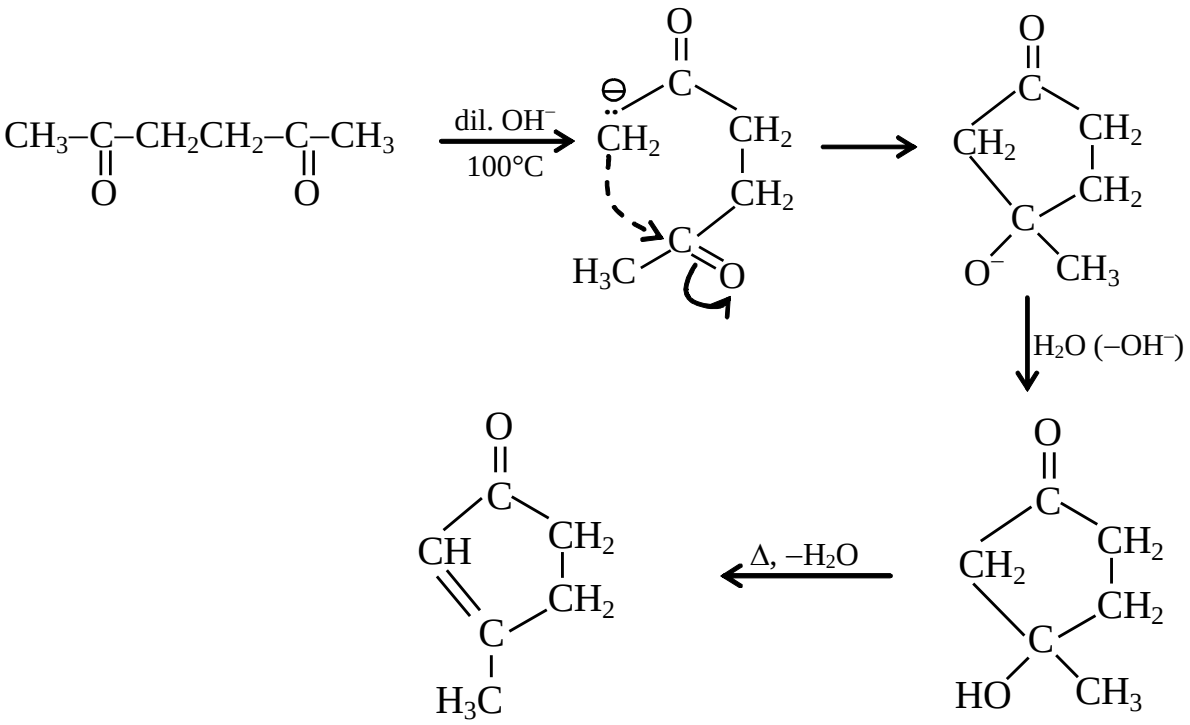
(b) 2, 7–octanedione

(c) 2, 8–nonanedione and

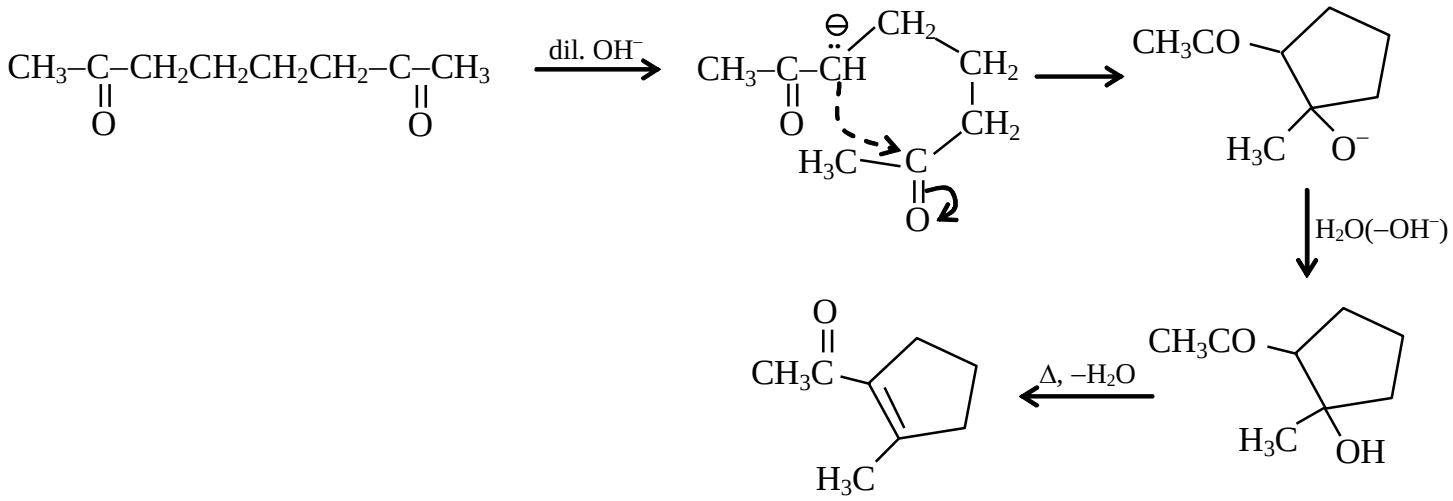
(d) 2, 4–pentanedione

Solution:

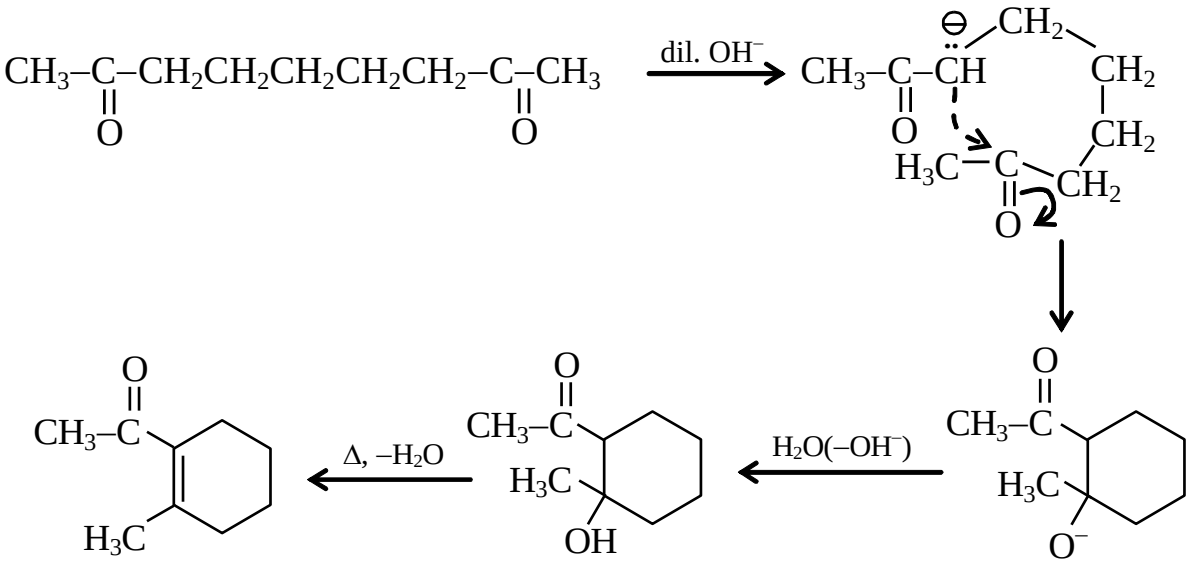
(a)



(b)



(c)



(d)