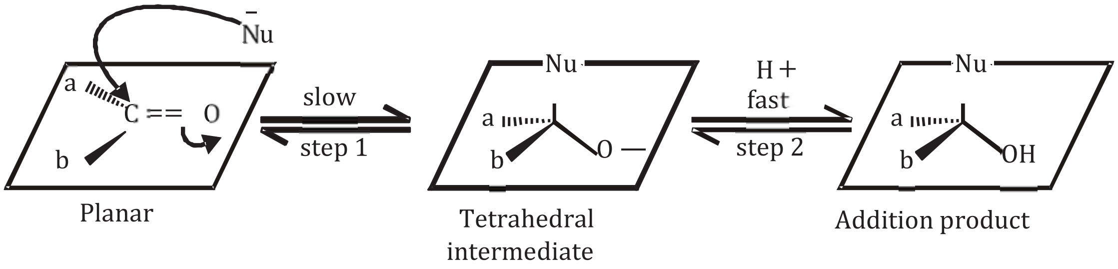
CHEMICAL REACTIONS

In general, carbonyl compounds undergo nucleophilic addition reactions, which involve the addition of both a nucleophile and a proton across the carbon-oxygen double bond ($C = O$). The reactivity of the carbonyl group is a consequence of the oxygen atom's electronegativity, which results in the polarization of the carbon-oxygen double bond. The electrophilic carbon atom in the carbonyl group is sp^2 hybridized and possesses a flat geometry, making it relatively unobstructed and susceptible to attack from either side of the double bond.

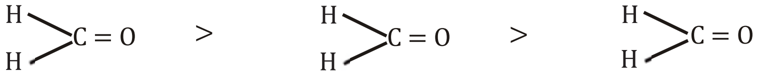
Mechanism



The nucleophile (Nu^-) approaches the carbonyl group in a direction perpendicular to the plane of the sp^2 hybridized orbitals of the carbonyl carbon.

During this process, the carbon's hybridization shifts from sp^2 to sp^3. This results in the formation of a tetrahedral alkoxide intermediate.

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



$$\begin{matrix} H \\ H \end{matrix}\!>\!C = O \;>\; \begin{matrix} H \\ H \end{matrix}\!>\!C = O \;>\; \begin{matrix} H \\ H \end{matrix}\!>\!C = O$$

There are two factors which influence the reactivity of ketone and aldehyde.

(i) Inductive effect

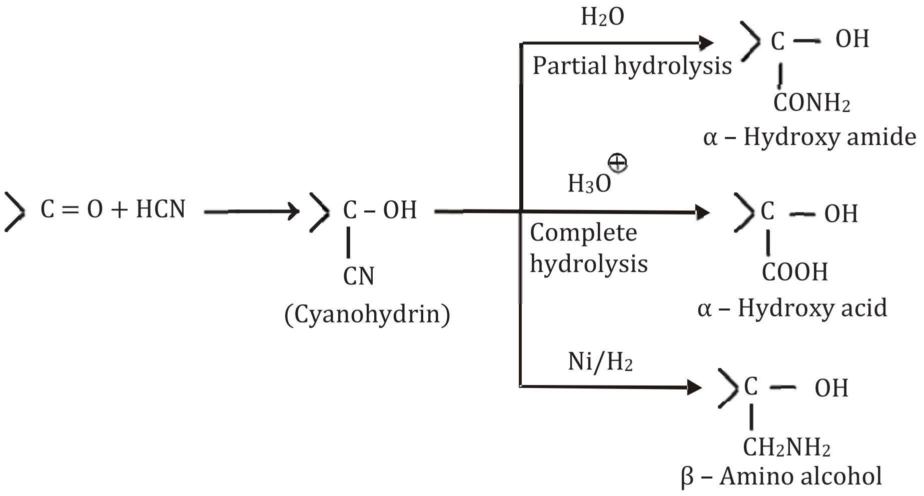
(ii) Steric factor

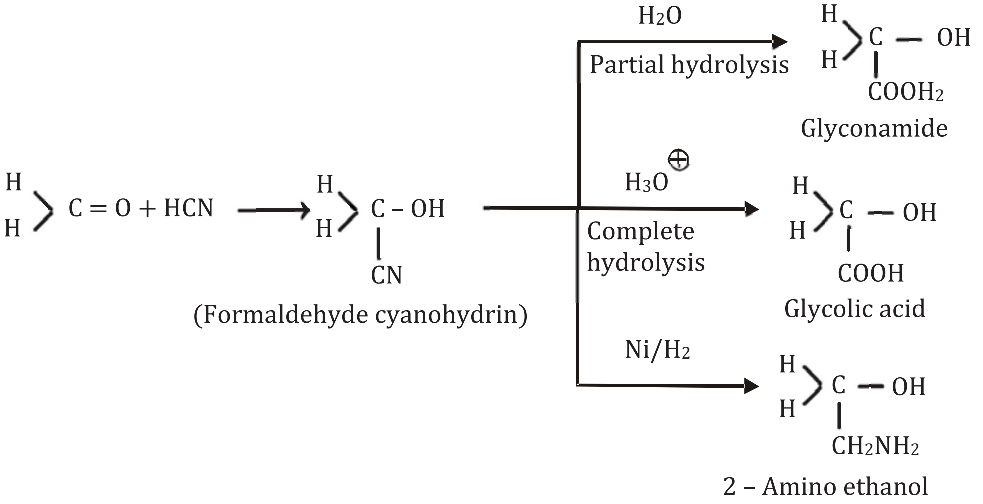
(i) + I effect of alkyl group decrease the amount of charge on C^+ ($C^+ - O^-$). in ketones.

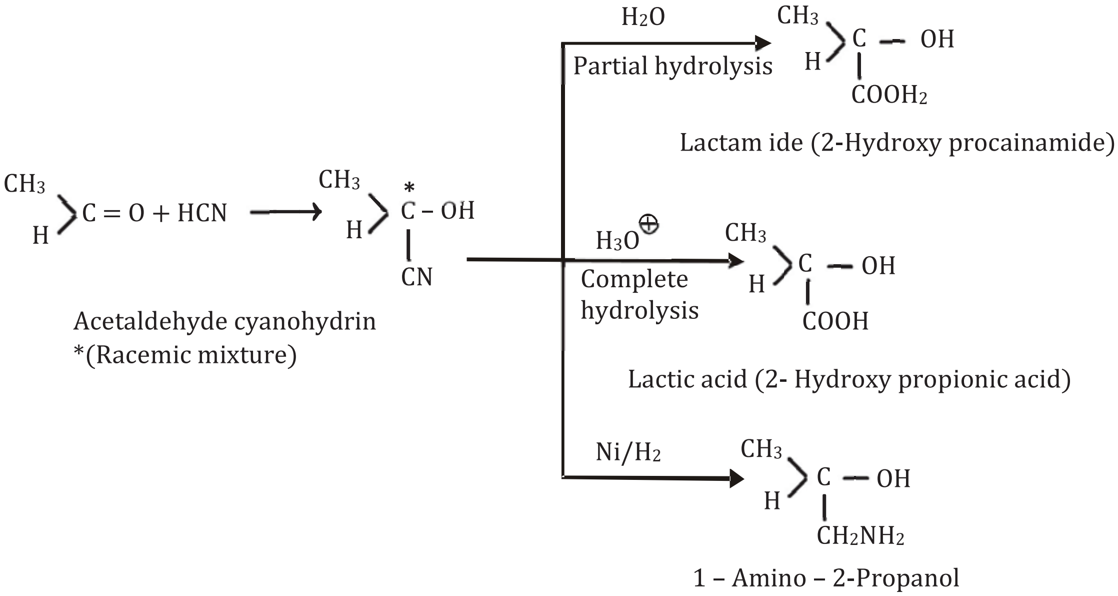
(ii) Steric effect also causes the less reactivity of carbonyl group.

Nucleophilic addition reactions

(1) Addition of HCN

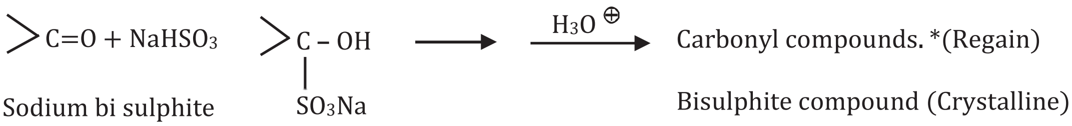






(2) Addition of $NaHSO_3$

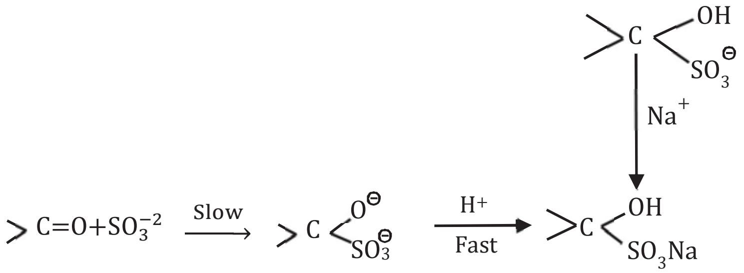
This reaction is employed to isolate carbonyl compounds from substances that do not contain carbonyl groups.



Mechanism

$NaHSO_3 \leftrightarrow Na^+ + HS\overline{O}_3$

$HS\overline{O}_3 \leftrightarrow H^+ + SO_3^{-2}$



(3) Reaction with ammonia derivatives

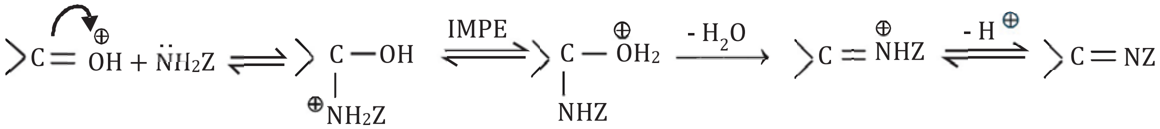
These reactions are either condensation or addition-elimination reactions, and they progress effectively in a mildly acidic environment.

$$NH_3 \longrightarrow H_2Z \text{ (Ammonia derivative)}$$

$$> C = O + H_2N - Z \xrightarrow[+Z]{-H} \; > C = N - Z + H_2O$$

Addition - elimination (Condensation)

Mechanism



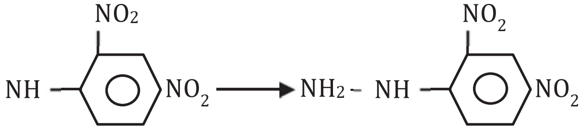
Ammonia derivatives (NH_2Z)

Z = OH ⟶ NH_2OH (Hydroxyl amine)

Z = NH_2 ⟶ NH_2NH_2 (hydrazine)

Z = NHC_6H_5 ⟶ $NH_2NHC_6H_5$ (Phenyl hydrazine)

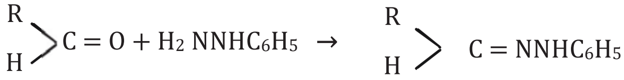
Z =



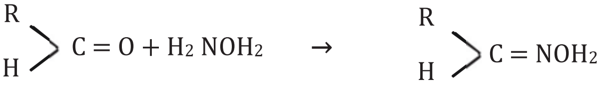
2, 4–Dinitro phenyl hydrazine (DNP) Brady's reagent.

Z = $NHCONH_2$ ⟶ $NH_2NHCONH_2$

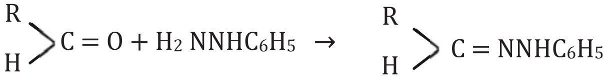
Semi Carbazide.



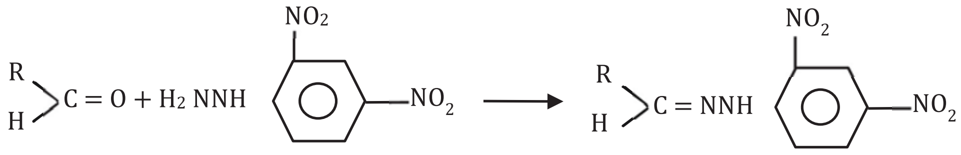
$$\begin{matrix}R\\H\end{matrix}\!\!>C = O + H_2\,NNHC_6H_5 \rightarrow \begin{matrix}R\\H\end{matrix}\!\!> C = NNHC_6H_5 \qquad \text{(Aldoxime)}$$



$$\begin{matrix}R\\H\end{matrix}\!\!> C = O + H_2\,NOH_2 \rightarrow \begin{matrix}R\\H\end{matrix}\!\!> C = NOH_2 \qquad \text{(Hydrazone)}$$



$$\begin{matrix}R\\H\end{matrix}\!\!>C = O + H_2\,NNHC_6H_5 \rightarrow \begin{matrix}R\\H\end{matrix}\!\!> C = NNHC_6H_5 \qquad \text{(Phenyl hydrazone)}$$

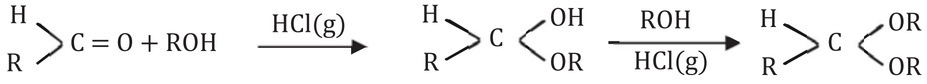


2,4-DNP (Brady's reagent)

(2,4-dinitro phenyl hydrazine)

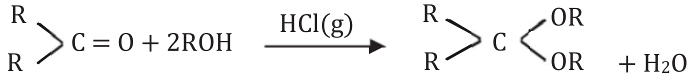
(Semi Carbazone)

(4) With alcohol and thioalcohol



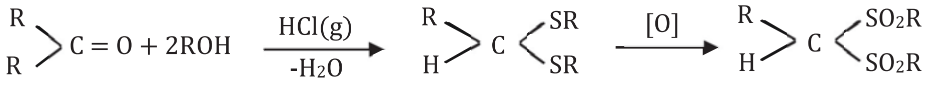
Hemi - acetal

Aceta



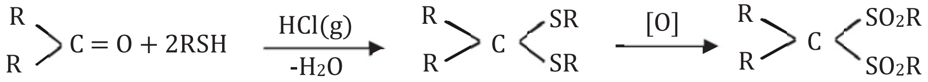
Ketal

Tri ethoxy methane [$HC(OC_2H_5)_3$] remove the water formed during the reaction and so the reaction proceeds in forward direction.



Thioalcohol

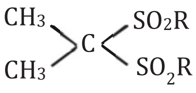
Mercaptan



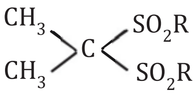
Mercaptan (Thio Ketal)

Sulphones Compound

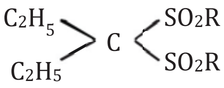
All sulphones' compounds are hypnotic compounds.



Sulphonal

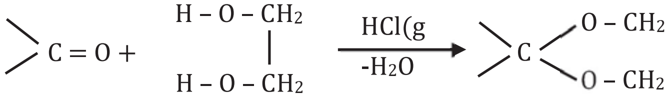


Trional



Tetronal

(5) Reaction with glycol (group protection)

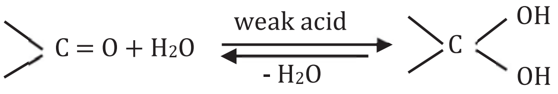


(neutral)

Cyclic acetal/ketal

(6) Reaction with H_2O

It is a reversible reaction.



(neutral) unstable hydrate

Ex. Which compound form more stable hydrate with H_2O?

(A) HCHO (B) CH_3CHO

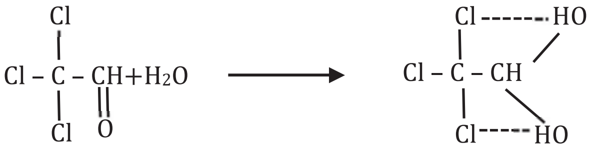
(C) CH_3COCH_3 (D) $CH_3COC_2H_5$

[**Hint:** HCHO since it is more reactive towards this reaction.]

Ans. (A)

Ex. Which carbonyl compound not gives reversible reaction with water?

Sol. Chloral hydrate.



(Chloral) (Chloral hydrate)

Stable by intra molecular hydrogen bonding.

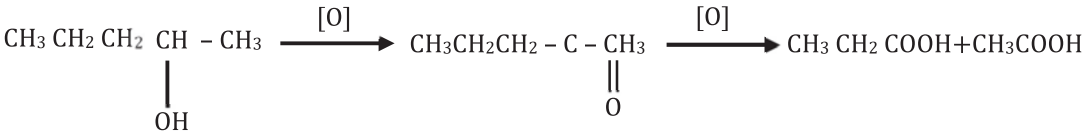
Oxidation Reactions

By $K_2Cr_2O_7/H_2SO_4$

When primary alcohols are oxidized with $K_2Cr_2O_7/H_2SO_4$, they initially form aldehydes. Further oxidation of the aldehyde results in the formation of an acid containing the same number of carbon atoms. In contrast, secondary alcohols, when oxidized, yield ketones. Subsequent oxidation of the ketone leads to the production of an acid with fewer carbon atoms.

$$R—CH_2OH \xrightarrow{[O]} R—CHO \xrightarrow{[O]} R—COOH$$

(1° alcohol)



$$CH_3\,CH_2\,CH_2\,\underset{\displaystyle OH}{\underset{|}{CH}} - CH_3 \xrightarrow{[O]} CH_3CH_2CH_2 - \underset{\displaystyle O}{\underset{\|}{C}} - CH_3 \xrightarrow{[O]} CH_3\,CH_2\,COOH + CH_3COOH$$

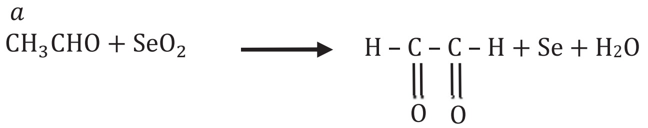
2° alcohol

(i) 3° alcohol is not oxidised within 2 or 3 minutes.

(ii) 1° and 2° alcohol convert orange colour of $K_2Cr_2O_7$ to green in 2-3 minutes.

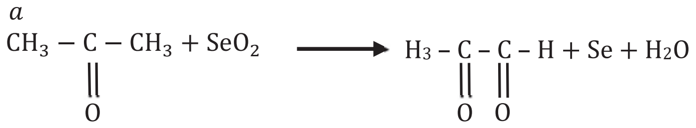
SeO_2 (Selenium Oxide)

Oxidation of ketones or aldehydes using SeO2 results in the formation of dicarbonyl compounds. This reaction occurs exclusively in compounds that contain an α-carbon. Notably, formaldehyde (HCHO) does not exhibit this reaction.



$$\overset{a}{CH_3}CHO + SeO_2 \longrightarrow H-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-H + Se + H_2O$$

Glyoxal



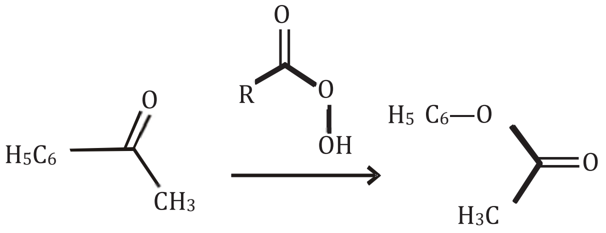
$$\overset{a}{CH_3}-\underset{\underset{O}{\|}}{C}-CH_3 + SeO_2 \longrightarrow H_3-\underset{\underset{O}{\|}}{C}-\underset{\underset{O}{\|}}{C}-H + Se + H_2O$$

Methyl Glyoxal (Pyruvaldehyde)

Baeyer's Villiger Oxidation

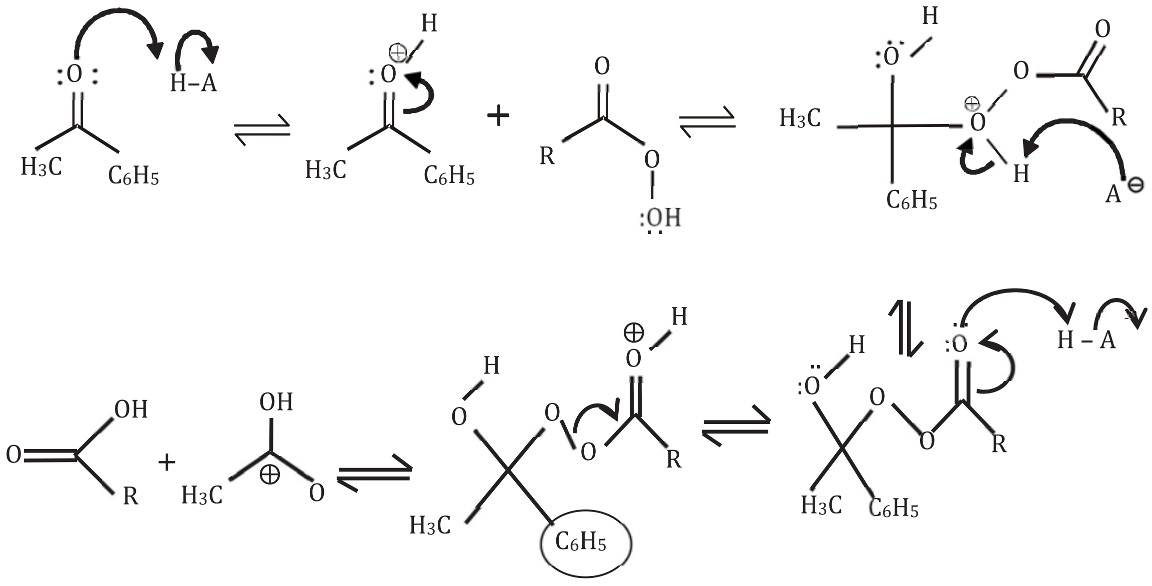
Peroxy acids can oxidize both aldehydes and ketones. This chemical transformation, referred to as the Baeyer-Villiger oxidation, is particularly effective when applied to ketones, as it leads to the conversion of ketones into carboxylic esters.

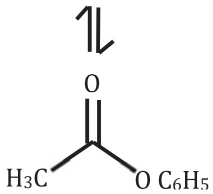
For example, when acetophenone is exposed to a peroxy acid, it is transformed into the ester known as phenyl acetate.



phenyl acetate

Mechanism:





The outcome of this reaction demonstrates that a phenyl group exhibits a higher inclination to migrate than a methyl group. If it were otherwise, the product would have been $C_6H_5COOCH_3$ instead of $CH_3COOC_6H_5$. This propensity for a group to migrate is referred to as migratory aptitude.

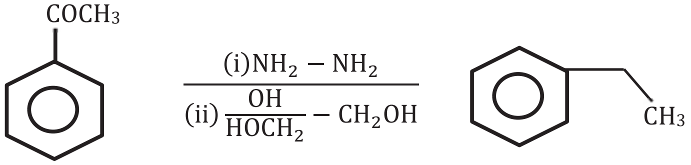
Studies of the Baeyer-villager oxidation and other reaction have shown that the migratory aptitude of groups H > phenyl > 3° alkyl > 2° alkyl 1° alkyl > methyl. In all cases, this order is for groups migrating with their electron pairs, that is, as anions.

Other Reactions of Aldehyde and Ketones

Reduction

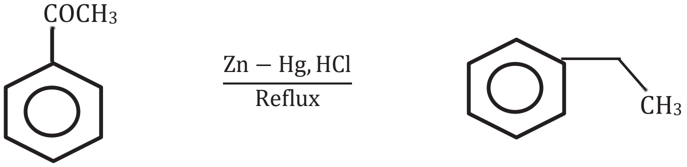
The wolf kirshner reduction

Heating a ketone or aldehyde in a basic hydrazine solution result in the transformation of the carbonyl group into a methylene group. This chemical alteration is referred to as deoxygenation since it involves the removal of an oxygen atom from the reactant. The specific reaction is recognized as the Wolf-Kishner Reduction.



Clemmensen Reduction

The process of converting the carbonyl groups in aldehydes and ketones into methylene groups using amalgamated zinc and concentrated hydrochloric acid is commonly referred to as Clemmensen reduction.



The nature of product depends upon the reducing agent used. It can be summarized as.

(i) $>C=O \longrightarrow >CH_2$

Reducing agents are

— Red P/HI at 150°C

— Zn-Hg/HCl [Clemensen's reduction]

$—NH_2—NH_2/C_2H_5OH, OH^1$

[Wolff Kirshner's reduction]

(ii) $>C=O \longrightarrow >CHOH$

Reducing agents are

— $LiAlH_4$ (Nice Tron brown)

— Na/C_2H_5OH (Bouveault blank)

— NaH/Benzene (Darzen reaction)

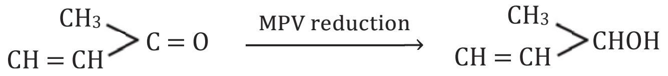
— $[(CH_3)_2CHO]_3Al$

(Aluminium isopropoxide)

— $(CH_3)_2$ CHOH (Isopropyl alcohol)

The reduction of a compound using aluminum isopropoxide in an excess of isopropanol is termed MPV (Meerwein-Ponndorf-Verley) reduction. This method selectively reduces specific functional groups, leaving other reducible groups unaffected. $—NO_2$, $—CHCH_2$, —CC—.

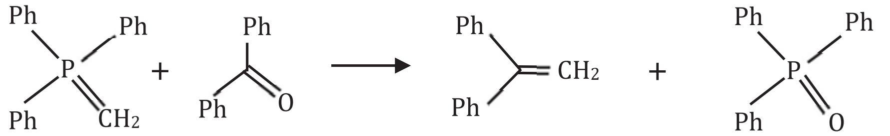
Example:



$$\begin{matrix}CH_3\\CH=CH\end{matrix}\!\!>C=O \xrightarrow{\text{MPV reduction}} \begin{matrix}CH_3\\CH=CH\end{matrix}\!\!>CHOH$$

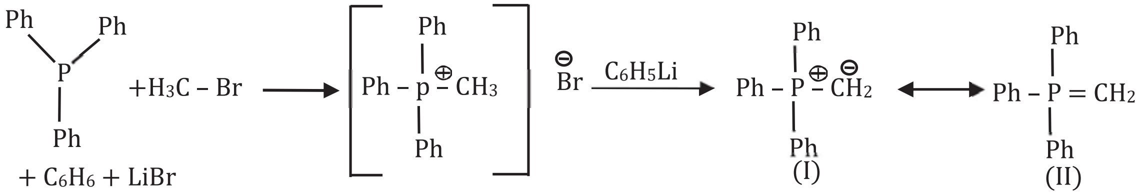
Wittig Reaction

The Wittig reaction offers a significant and valuable approach to synthesize alkenes. It involves treating aldehydes or ketones with alkylidene phosphoranes, also known as phosphorene's, typically represented as $Ph_3P = CR_2$.



(1-phenylvinyl) benzene Triphenylphosphine oxide

The Wittig reagent, also known as alkylidene triphenyl phosphorane or ylide, is created by reacting a trialkyl or triaryl phosphine, often the latter, with an alkyl halide,



typically, in a solution. The resulting phosphonium salt is then subjected to a strong base, such as C_6H_5Li, BuLi, $NaNH_2$, NaH, C_2H_5ONa, and so on.

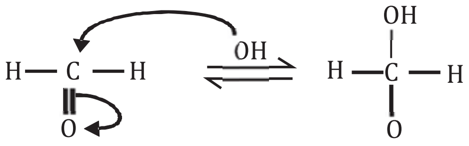
Cannizaro's Reaction

Aldehydes lacking a hydrogen atom are capable of undergoing this reaction when treated with concentrated NaOH or KOH. The resulting products consist of the salt of a carboxylic acid and an alcohol. In this reaction, one molecule of the carbonyl compound is oxidized to form an acid, while the other is reduced to produce an alcohol. Reactions of this kind are referred to as disproportionation reactions, which are a type of redox reaction.

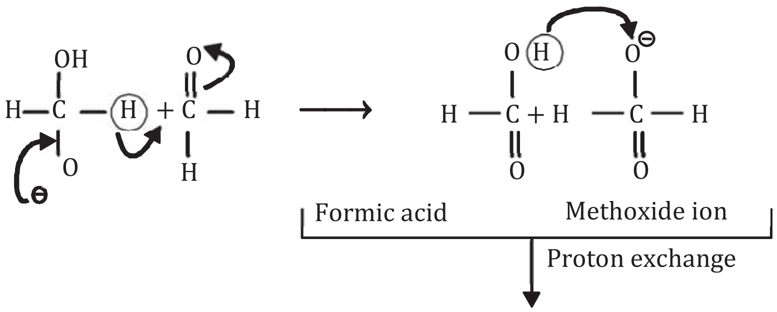
$$HCHO + HCHO \xrightarrow[\text{NaOH}]{\text{conc.}} HCOONa + CH_3OH$$

Mechanism: (Cannizaro reaction)

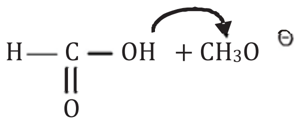
(a) Rapid reversible addition of $\overline{O}H$ to one molecule of HCHO.



(b) Transfer of hydride ion to second molecule of HCHO



(c) Proton exchange



$$H-\underset{\underset{O}{\|}}{C}-OH + CH_3O^{\ominus} \longrightarrow HCOO^{1} + CH_3OH$$

$$HCOO^{1} + Na^{\oplus} \longrightarrow HCOONa$$

When molecules are same ------→ Simple cannizaro reaction

Two different molecules ------→ Mixed cannizaro reaction

In a mixed or crossed Cannizaro reaction, the more reactive aldehyde undergoes oxidation, while the less reactive aldehyde experiences reduction.

$$HCHO + C_6H_5CHO \xrightarrow{NaOH} HCOONa + C_6H_5CH_2OH$$

Oxidized	Reduced
(Sodium format)	(Benzyl alcohol)

Ex: $CH_3CHO + HCHO \xrightarrow{Ca(OH)_2} C(CH_2OH)_4 + (HCOO)_2$ Ca, explain mechanism?

2, 2-Dihydroxy methyl –1, 3–propane diol. (Penta erythritol)

Tishchenko Reaction

It is a modified Cannizaro reaction. All aldehydes undergo this reaction in presence of $(C_2H_5O)_3Al$, to form ester.

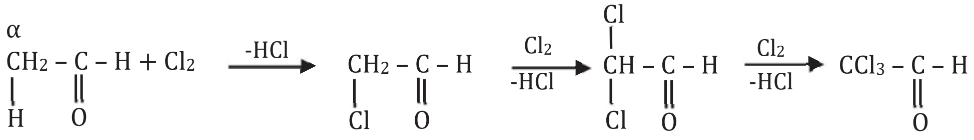
$$2RCHO \xrightarrow[\Delta]{(R'O)_3A} RCH_2-O-\overset{\overset{O}{\|}}{C}-R$$

Ester

Reaction With Halogen

Replacement of α-H atoms

Formaldehyde (HCHO) does not exhibit this reaction because it lacks alpha-hydrogen atoms, and enolization does not occur in HCHO.



$$\underset{\underset{H}{|}}{\overset{\alpha}{CH_2}}-\underset{\underset{O}{\|}}{C}-H + Cl_2 \xrightarrow{-HCl} \underset{\underset{Cl}{|}}{CH_2}-\underset{\underset{O}{\|}}{C}-H \xrightarrow[-HCl]{Cl_2} \overset{\overset{Cl}{|}}{\underset{\underset{Cl}{|}}{CH}}-\underset{\underset{O}{\|}}{C}-H \xrightarrow[-HCl]{Cl_2} CCl_3-\underset{\underset{O}{\|}}{C}-H$$

Chloral

Replacement of O-atom of $>C=O$ group: It takes place by PCl_5 or $SOCl_2$.

$$>C=O + PCl_5 \longrightarrow >C{<}^{Cl}_{Cl} + POCl_3$$

Phosphorus Penta chloride

$$>C=O + SOCl_2 \longrightarrow >C{<}^{Cl}_{Cl} + SO_2$$

Thionyl chloride

Haloform Reactions

Chlorine or bromine can substitute one or more alpha-hydrogen atoms in aldehydes and ketones. For example, acetone can undergo bromination in glacial acetic acid to yield Mon bromoacetone.

$$CH_3COCH_3 + Br_2 \rightarrow CH_3COCH_2Br + HBr \ (43–44\%)$$

Halogenation of carbonyl compounds can be catalyzed by both acids and bases. For instance, let's examine the case of acetone. In an alkaline solution, we can isolate tribromo acetone and bromoform. Interestingly, the addition of a second and a third bromine atom occurs more rapidly than the first. When using aqueous sodium hydroxide, it has been demonstrated that the reaction rate is unaffected by the concentration of bromine but follows a first-order relationship with respect to both acetone and the base, meaning the rate depends on the concentration of these two reactants.

$$\text{Rate} = k\,[\text{acetone}]\,[OH^1]$$

Aldol Condensation

When a base is present, two molecules of an aldehyde or a ketone can combine in a condensation reaction to form a β-hydroxy aldehyde or a β-hydroxy ketone. This chemical process is known as aldol condensation. In general, carbonyl compounds that have alpha-hydrogen atoms can undergo aldol condensation when treated with dilute NaOH. The resulting compound, known as an aldol, contains both an alcoholic (-OH) and a carbonyl group.

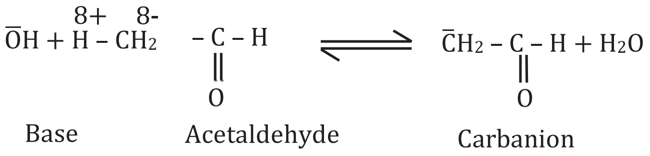
Mechanism of Aldol Condensation

This process occurs in two sequential stages:

- Generation of a carbanion.
- The carbanion then combines with another aldehyde molecule.

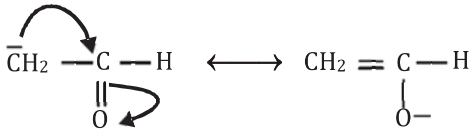
Formation of Carbanion

α-H atom of group is quite acidic which can be removed easily as proton, by a base.



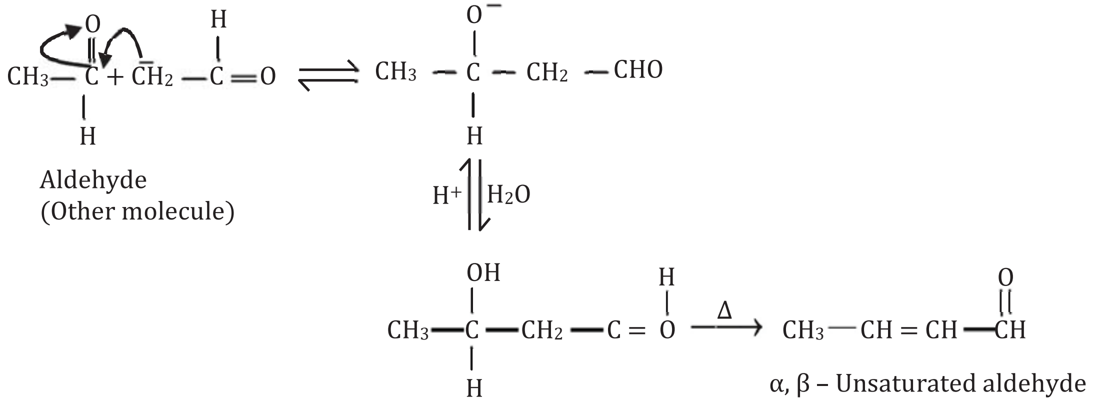
$$\overline{O}H + \overset{8+}{H} - \overset{8-}{CH_2} - \underset{\underset{O}{\|}}{C} - H \rightleftharpoons \overline{C}H_2 - \underset{\underset{O}{\|}}{C} - H + H_2O$$

Carbanion thus formed is stable because of resonance –



$$\overline{C}H_2 - \underset{\underset{O}{\|}}{C} - H \longleftrightarrow CH_2 = \underset{\underset{O-}{|}}{C} - H$$

Combination of carbanion with other aldehyde molecule



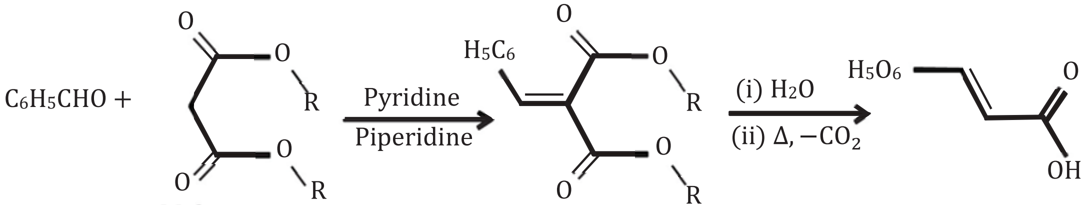
Aldehyde
(Other molecule)

Aldol

α, β – Unsaturated aldehyde

Knoevenagel Reaction

The Knoevenagel Reaction refers to the condensation of aldehydes and ketones with substances containing an active methylene group in the presence of a basic catalyst. This reaction leads to the formation of α, β-unsaturated compounds. The basic catalyst can be ammonia or one of its derivatives. Various amines, including primary, secondary, and tertiary amines such as aniline, di- or tri-alkyl amines, pyridine, or piperidine, are commonly employed in this process.

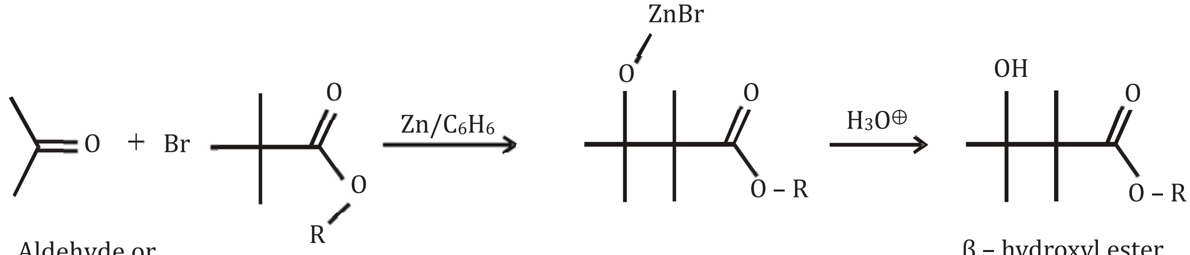


Malonic Ester

Cinnamic acid

Reformat Sky Reaction

A reaction similar to the addition of organometallic compounds to carbonyl compounds is the incorporation of an organozinc reagent into the carbonyl group of an aldehyde or ketone. This chemical process is known as the Reformat sky reaction, and it leads to the extension of the carbon skeleton of an aldehyde or ketone, resulting in the production of β-hydroxy esters. In this reaction, an aldehyde or ketone is treated with an α-bromo ester in the presence of zinc metal, with benzene being the commonly used solvent. The initial product formed is a zinc alkoxide, which must be subjected to hydrolysis to yield the β-hydroxy ester.



Aldehyde or ketone

a – Bromo ester

β – hydroxyl ester

Uses of Aldehydes and Ketones

Aldehydes and ketones find extensive applications across various industries, serving as solvents, raw materials, and reagents for synthesizing a wide array of products. Here's a detailed breakdown of their diverse uses:

1. Formaldehyde, commonly known as 40% aq. HCHO or formalin, plays a crucial role in preserving biological specimens due to its ability to fix tissues effectively.
2. Additionally, formaldehyde serves as a disinfectant owing to its strong antimicrobial properties.
3. In the realm of manufacturing, formaldehyde (HCHO) is indispensable for producing synthetic polymers like Bakelite, contributing to the production of durable and versatile materials.
4. Acetaldehyde finds application in the process of silvering mirrors, a crucial step in mirror production that enhances their reflective properties.
5. Benzaldehyde adds distinct flavor notes in the perfume industry, acting as a key flavoring agent to enhance fragrances.
6. Acetone, a ketone compound, serves as a versatile solvent in both industrial settings and laboratory environments due to its ability to dissolve a wide range of substances effectively.
7. Furthermore, acetone is a common ingredient in nail polishes, contributing to their formulation and facilitating smooth application.
8. Various other aldehydes and ketones, such as butyraldehyde, vanillin, acetophenone, and camphor, are renowned for their characteristic odors and flavors, lending their unique aromatic profiles to a plethora of products ranging from perfumes to food additives.