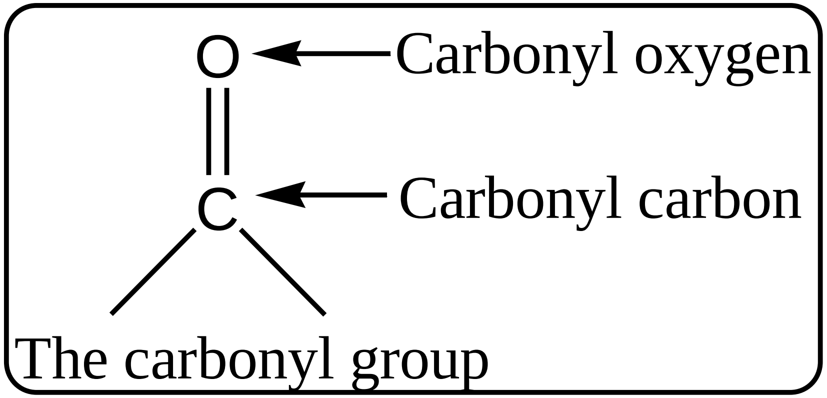
Aldehydes and Ketones:

Nucleophilic Addition Reactions

Aldehydes and Ketones

Aldehydes and ketones are characterized by the carbonyl functional group (C=O)



The compounds occur widely in nature as intermediates in metabolism and biosynthesis

They are also common as chemicals, as solvents, monomers, adhesives, agrichemicals and pharmaceuticals

Naming Aldehydes and Ketones

Aldehydes are named by replacing the terminal -*e* of the corresponding alkane name with –*al*

The parent chain must contain the —CHO group

- The —CHO carbon is numbered as C1

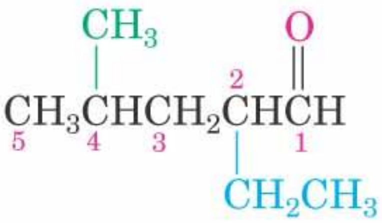
If the —CHO group is attached to a ring, use the suffix See Table 19.1 for common names

$CH_3\overset{\overset{O}{\|}}{C}H$

Ethanal
(Acetaldehyde)

$CH_3CH_2\overset{\overset{O}{\|}}{C}H$

Propanal
(Propionaldehyde)



$\underset{5}{CH_3}\overset{\overset{CH_3}{|}}{\underset{4}{C}}H\underset{3}{CH_2}\overset{2}{\underset{\underset{CH_2CH_3}{|}}{C}}H\overset{\overset{O}{\|}}{\underset{1}{C}}H$

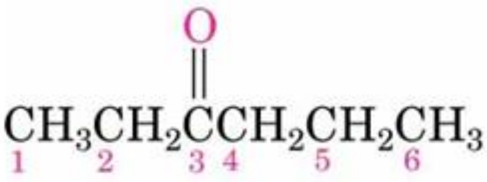
2-Ethyl-4-methylpentanal

Naming Ketones

Replace the terminal -*e* of the alkane name with –*one*

Parent chain is the longest one that contains the ketone group

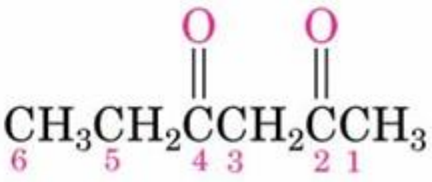
- Numbering begins at the end nearer the carbonyl carbon


$CH_3CH_2\overset{\overset{O}{\|}}{C}CH_2CH_2CH_3$

3-Hexanone

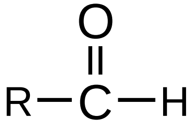

$CH_3CH{=}CHCH_2\overset{\overset{O}{\|}}{C}CH_3$

4-Hexen-2-one


$CH_3CH_2\overset{\overset{O}{\|}}{C}CH_2\overset{\overset{O}{\|}}{C}CH_3$

2,4-Hexanedione

Aldehydes have the general formula.

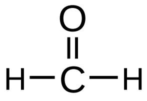
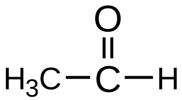
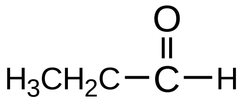
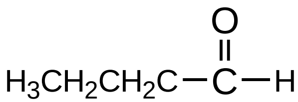

$R-\overset{O}{\overset{\|}{C}}-H$ or RCHO (R = H or C)

Aldehyde function

IUPAC system

Aliphatic aldehydes **are named by dropping the suffix *-e* from the name of the hydrocarbon that has the same carbon skeleton as the aldehyde and replacing it with the suffix *-al.***

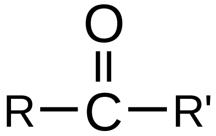
Alkane - e+ *al* = Alkanal

	 $H-\overset{O}{\overset{\|}{C}}-H$	 $H_3C-\overset{O}{\overset{\|}{C}}-H$	 $H_3CH_2C-\overset{O}{\overset{\|}{C}}-H$	 $H_3CH_2CH_2C-\overset{O}{\overset{\|}{C}}-H$
Common name:	Formaldehyde	Acetaldehyde	Propionaldehyde	Butyraldehyde
IUPAC name:	Methanal	Ethanal	Propanal	Butanal

Alkenal in case of double bond, Alkynal in case of triple bond

Ketones: Structure

Ketones have the general formula.

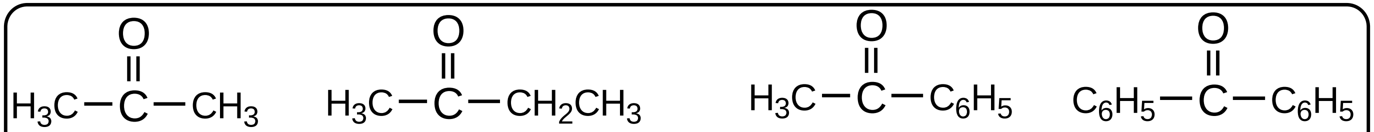


$\mathrm{R-\overset{\overset{O}{\|}}{C}-R'}$

(R and R' = alkyl or aryl)

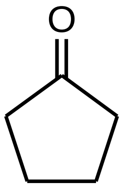
The carbonyl group may appear at any of various positions in the chain, *except at the end.*

The R groups need not be the same; either or both may be aliphatic or aromatic.



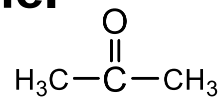
$\mathrm{H_3C-\overset{\overset{O}{\|}}{C}-CH_3}$ $\mathrm{H_3C-\overset{\overset{O}{\|}}{C}-CH_2CH_3}$ $\mathrm{H_3C-\overset{\overset{O}{\|}}{C}-C_6H_5}$ $\mathrm{C_6H_5-\overset{\overset{O}{\|}}{C}-C_6H_5}$

In ketones the carbonyl group may also be part of a cyclic structure.



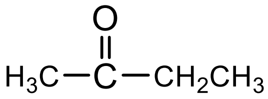
By listing the alkyl substituents attached to the carbonyl group, followed by the word *ketone.*

The simplest alphatic ketone, dimethyl ketone, is usually called acetone.



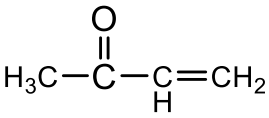
$$H_3C-\overset{\overset{O}{\|}}{C}-CH_3$$

Acetone
(Dimethyl ketone)



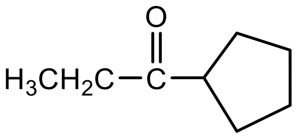
$$H_3C-\overset{\overset{O}{\|}}{C}-CH_2CH_3$$

Methyl ethyl ketone



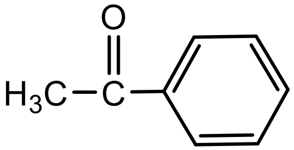
$$H_3C-\overset{\overset{O}{\|}}{C}-\underset{H}{C}=CH_2$$

Methyl vinyl ketone

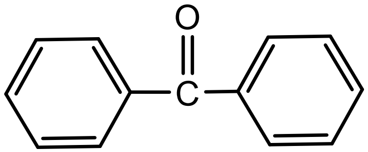


Ethyl cyclopentyl ketone

When the carbonyl group of a ketone is attached to a benzene ring, the ketone may be similarly named, or it may be given a special name.



Methyl phenyl ketone
(Acetophenone)



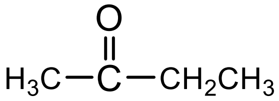
Diphenyl ketone
(Benzophenone)

In the IUPAC system,

ketones named in the usual manner.

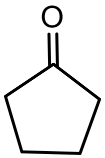
The longest continuous chain *carrying the carbonyl group.*

Name the parent structure by dropping the suffix –*e*, lowest possible number to the C=O group.



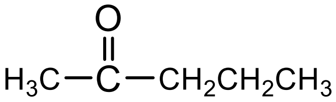
$H_3C-\overset{O}{\overset{\parallel}{C}}-CH_2CH_3$

Butanone



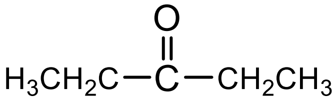
Cyclopentanone

(no number needed, the position of C = O is unambiguous)



$H_3C-\overset{O}{\overset{\parallel}{C}}-CH_2CH_2CH_3$

2-Pentanone
(*not* 4-Pentanone)

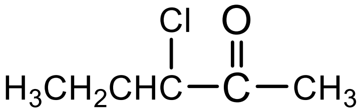


$H_3CH_2C-\overset{O}{\overset{\parallel}{C}}-CH_2CH_3$

3-Pentanone

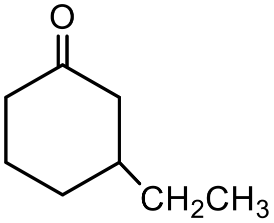
Substituted ketones are named by numbering and listing the substituents alphabetically.

For cyclic ketones, numbering always starts from the C=O group.

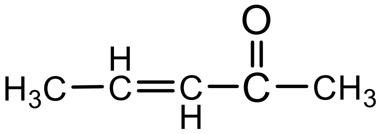


$H_3CH_2CH\overset{Cl}{\overset{|}{C}}-\overset{O}{\overset{\parallel}{C}}-CH_3$

3-Chloro-2-pentanone
(*not* 3-Chloro-4-pentanone)



3-Ethlcyclohexanone
(*not* 5-Methylcyclohexanone)



$H_3C-\overset{H}{C}=\underset{H}{C}-\overset{O}{\overset{\parallel}{C}}-CH_3$

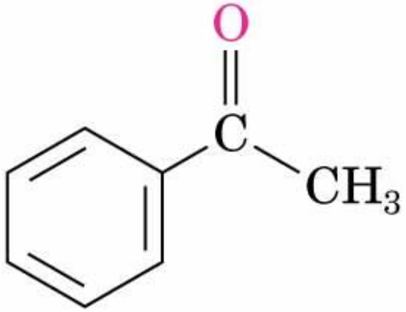
3-Penten-2-one
(*not* 2-Penten-4-one)

Ketones with Common Names

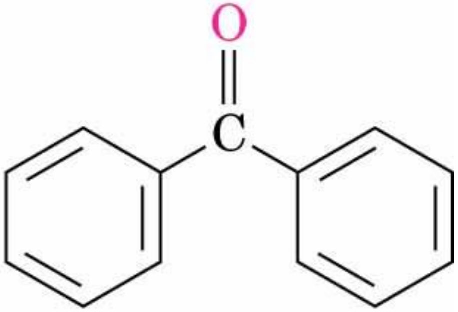
IUPAC retains well-used but unsystematic names for a few ketones

$CH_3\overset{\overset{O}{\|}}{C}CH_3$

Acetone



Acetophenone



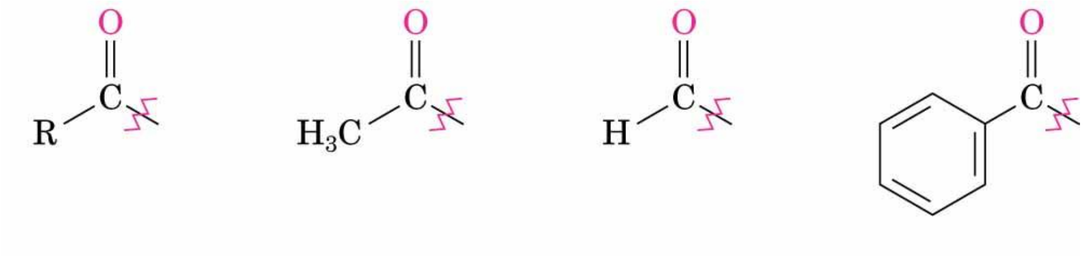
Benzophenone

Ketones and Aldehydes as Substituents

The R–C=O as a substituent is an acyl group is used with the suffix -yl from the root of the carboxylic acid

- CH_3CO: acetyl; CHO: formyl; C_6H_5CO: benzoyl

The prefix *oxo-* is used if other functional groups are present and the doubly bonded oxygen is labeled as a substituent on a parent chain



An acyl group **Acetyl** **Formyl** **Benzoyl**

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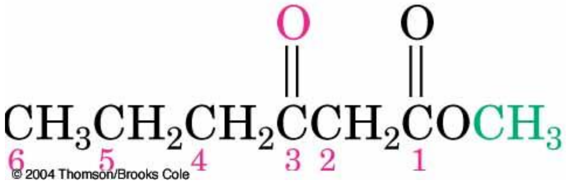

$$CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}CH_2\overset{\overset{O}{\|}}{C}OCH_3$$

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Methyl 3-oxohexanoate

Physical Properties of Aldehydes and Ketones

Boiling Points

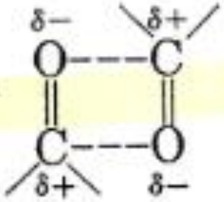
- **Because of the polarity of the carbonyl group,**

  Aldehydes and ketones are polar compounds.

- **The polar character of the molecules gives rise to intermolecular attractions.**

- **These attractive forces, called dipole-dipole attractions.**

  occur between the partial negative charge on the carbonyl oxygen of one molecule and the partial positive charge on the carbonyl carbon of another molecule.



Dipole-dipole attractions among carbonyl compounds

- **Dipole-dipole attractions, although important, are not as strong as interactions due to hydrogen bonding.**

So the boiling points of aldehydes and ketones are

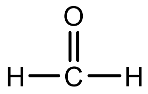
higher than those of nonpolar alkanes, of comparable molecular weights.

lower than those of alcohols, of comparable molecular weights.

CH_3CH_3

Ethane

(mol wt 30; bp -12°C)



$H-\overset{\overset{O}{\|}}{C}-H$

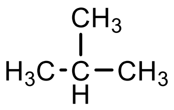
Formaldehyde

(mol wt 30; bp -21°C)

CH_3OH

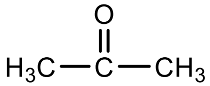
Methyl alcohol

(mol wt 32; bp 64.5°C)



Isobutane

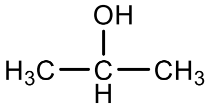
(mol wt 58; bp -12°C)



$H_3C-\overset{\overset{O}{\|}}{C}-CH_3$

Acetone

(mol wt 58; bp 56°C)



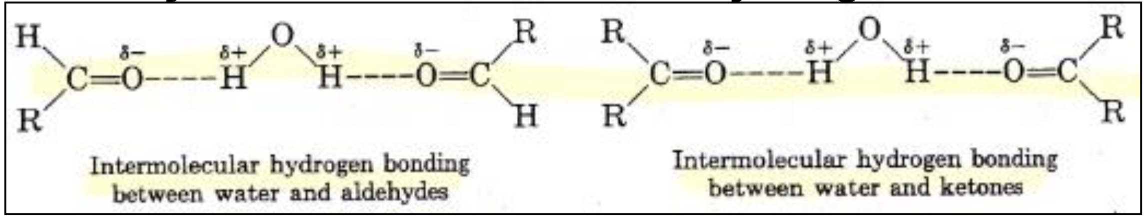
Isopropyl alcohol

(mol wt 60; bp 82.5°C)

Solubility in Water.

The lower aldehydes and ketones are soluble in water.

Because aldehydes and ketones form hydrogen bonds with water.



Intermolecular hydrogen bonding between water and aldehydes

Intermolecular hydrogen bonding between water and ketones

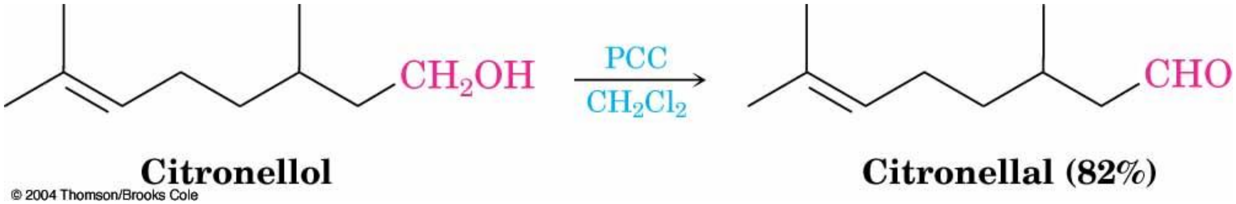
- **As the hydrocarbon portion of the molecule increases, the solubility in water decreases rapidly.**
- **Aldehydes and ketones with more than six carbons are essentially insoluble in water.**

Preparation of Aldehydes and Ketones

Preparing Aldehydes

Oxidize primary alcohols using pyridinium chlorochromate

Reduce an ester with diisobutylaluminum hydride (DIBAH), $LiAlH_4$, or $NaBH_4$



Citronellol → **Citronellal (82%)**

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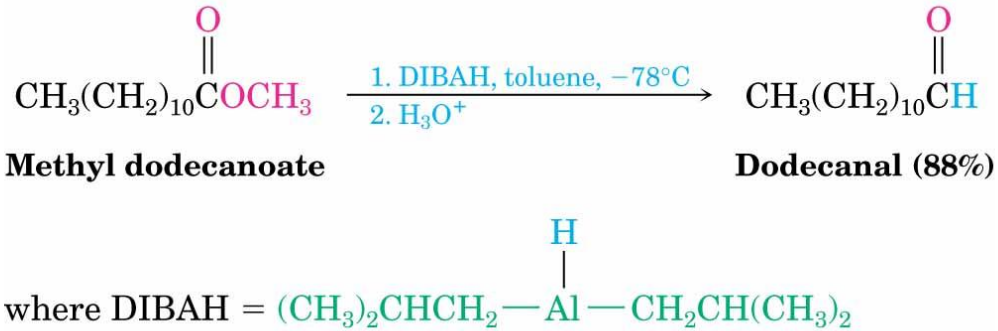

$$CH_3(CH_2)_{10}\overset{\overset{\displaystyle O}{\|}}{C}OCH_3 \xrightarrow[\text{2. } H_3O^+]{\text{1. DIBAH, toluene, −78°C}} CH_3(CH_2)_{10}\overset{\overset{\displaystyle O}{\|}}{C}H$$

Methyl dodecanoate → **Dodecanal (88%)**

$$\text{where DIBAH} = (CH_3)_2CHCH_2-\overset{\overset{\displaystyle H}{|}}{Al}-CH_2CH(CH_3)_2$$

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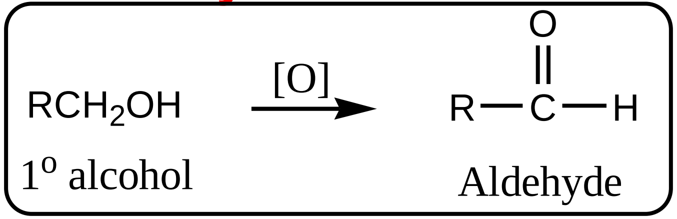
Preparation of Aldehydes and Ketones

Oxidation of Primary and Secondary Alcohols

- **Oxidation of primary alcohols, under controlled conditions, yields aldehydes.**

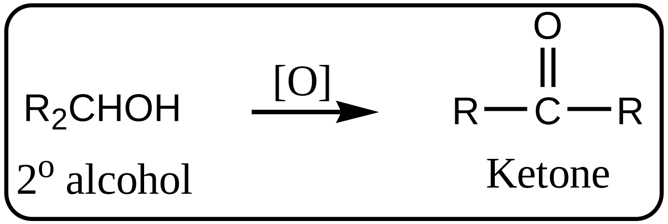


$$RCH_2OH \xrightarrow{[O]} R-\overset{\overset{O}{\|}}{C}-H$$

1^{o} alcohol

Aldehyde

- **Oxidation of secondary alcohols yields ketones.**

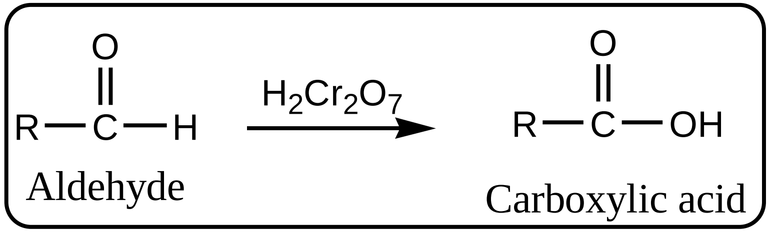


$$R_2CHOH \xrightarrow{[O]} R-\overset{\overset{O}{\|}}{C}-R$$

2^{o} alcohol

Ketone

- **Aldehydes are very easily oxidized to carboxylic acids.**



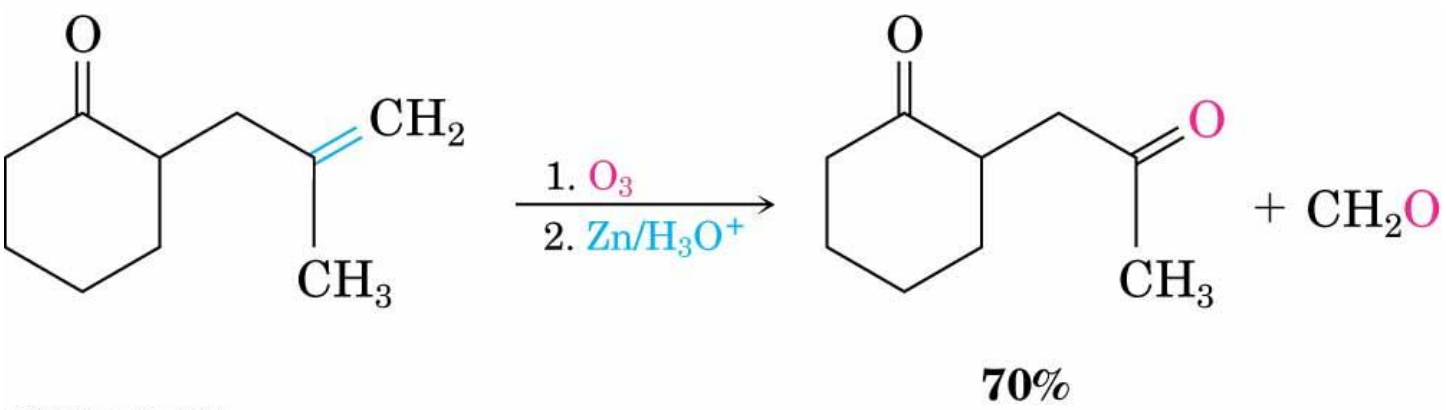
$$R-\overset{\overset{O}{\|}}{C}-H \xrightarrow{H_2Cr_2O_7} R-\overset{\overset{O}{\|}}{C}-OH$$

Aldehyde

Carboxylic acid

Ketones from Ozonolysis

Ozonolysis of alkenes yields ketones if one of the unsaturated carbon atoms is disubstituted



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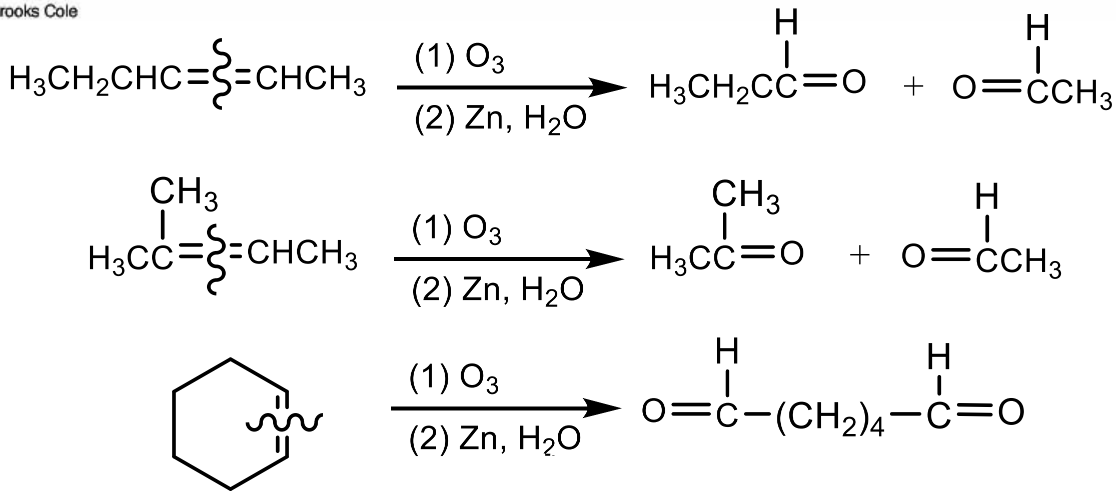
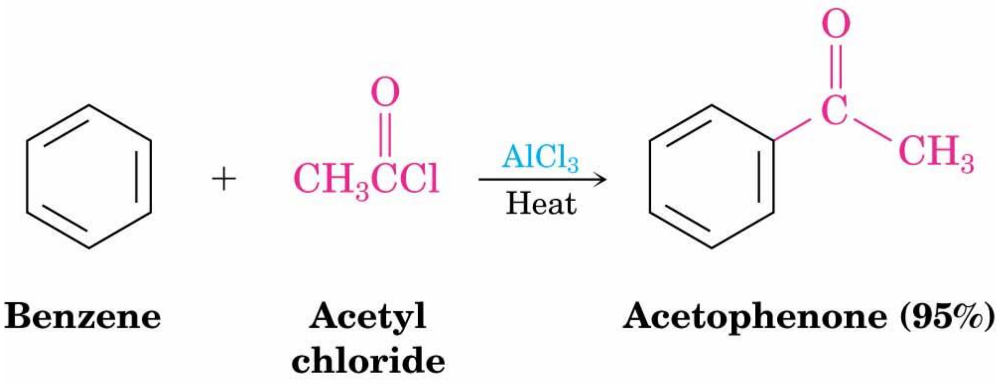
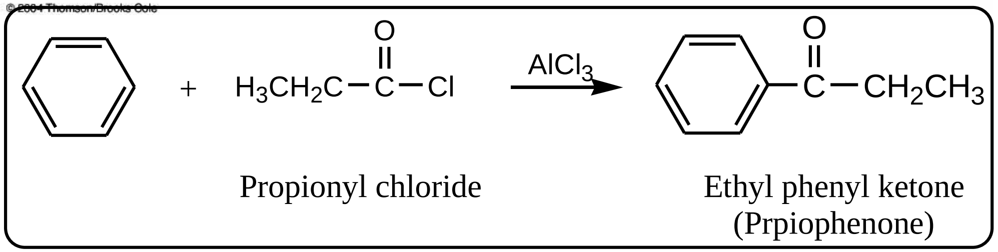
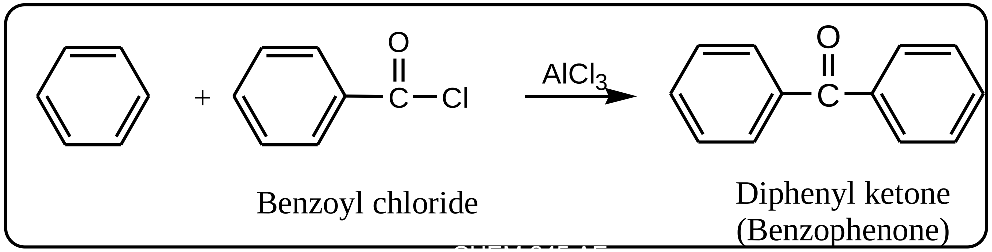


Aryl Ketones by Acylation

Friedel–Crafts acylation of an aromatic ring with an acid chloride in the presence of $AlCl_3$ catalyst



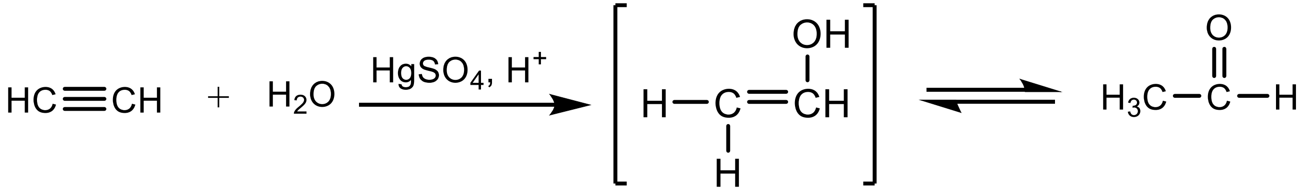




Methyl Ketones by Hydrating Alkynes

Hydration of terminal alkynes in the presence of Hg^{2+}

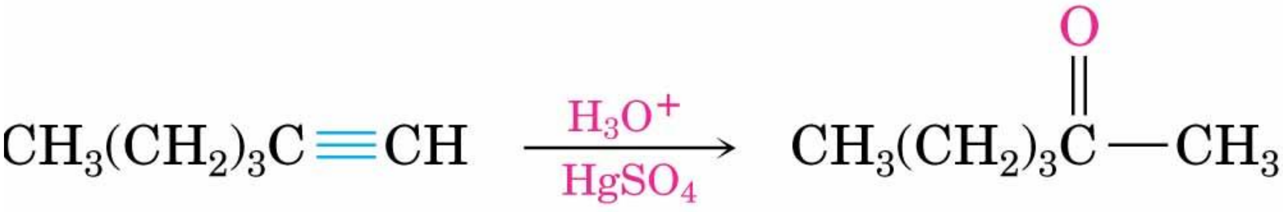
(ALKYNE SECTION)



$$HC{\equiv}CH + H_2O \xrightarrow{HgSO_4,\ H^+} \left[H{-}\underset{\displaystyle H}{C}{=}\overset{\displaystyle OH}{CH} \right] \rightleftharpoons H_3C{-}\overset{\displaystyle O}{\overset{\|}{C}}{-}H$$

Vinyl alcohol
(enol form of acetaldehyde,
unstable) (<1%)

Acetaldehyde
(keto form, stable)
(>99%)



$$CH_3(CH_2)_3C{\equiv}CH \xrightarrow[HgSO_4]{H_3O^+} CH_3(CH_2)_3\overset{\displaystyle O}{\overset{\|}{C}}{-}CH_3$$

1-Hexyne

2-Hexanone (78%)

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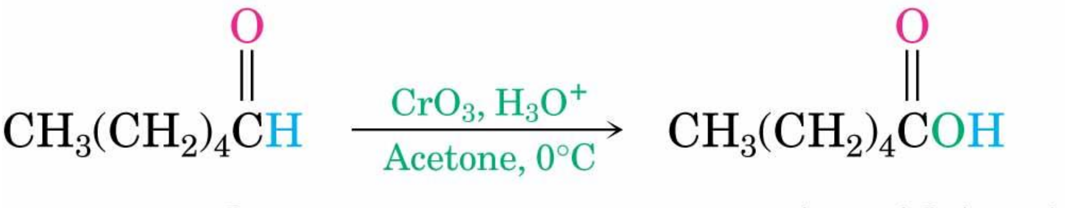
REACTIONS OF ALDEHYDES AND KETONES

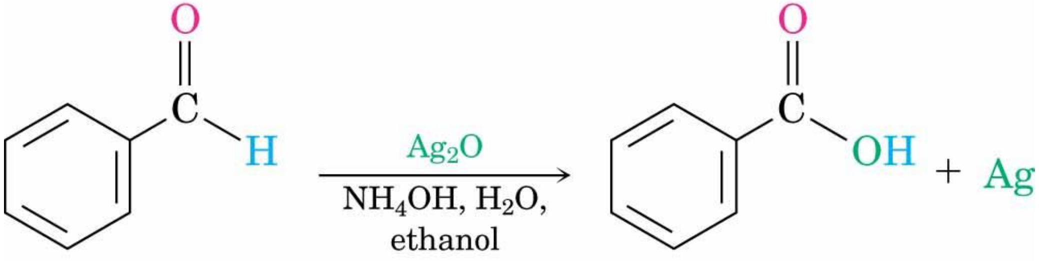
Oxidation of Aldehydes and Ketones

CrO_3 in aqueous acid oxidizes aldehydes to carboxylic acids efficiently

Silver oxide, Ag_2O, in aqueous ammonia (Tollens' reagent) oxidizes aldehydes (no acid)



Hexanal **Hexanoic acid (85%)**



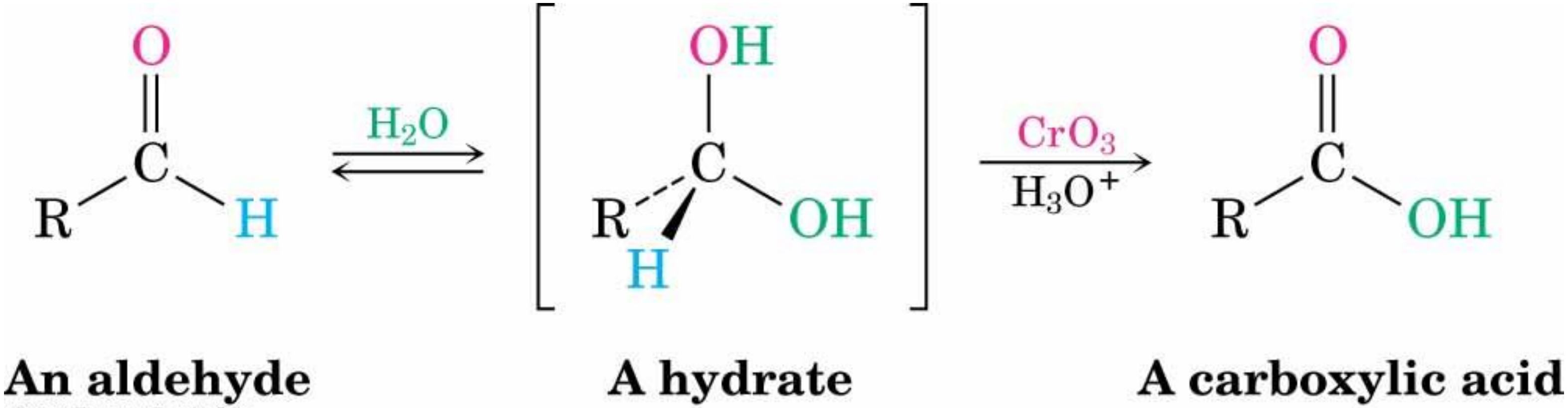
Benzaldehyde **Benzoic acid**

Hydration of Aldehydes

Aldehyde oxidations occur through 1,1-diols (“hydrates”)

Reversible addition of water to the carbonyl group

Aldehyde hydrate is oxidized to a carboxylic acid by usual reagents for alcohols



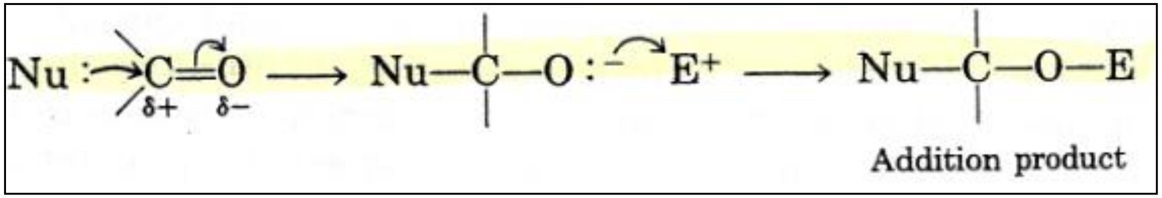
Nucleophilic Addition Reactions of Aldehydes and Ketones

Nucleophific addition reactions to the carbon-oxygen double bond.

In nucleophilic addition reactions

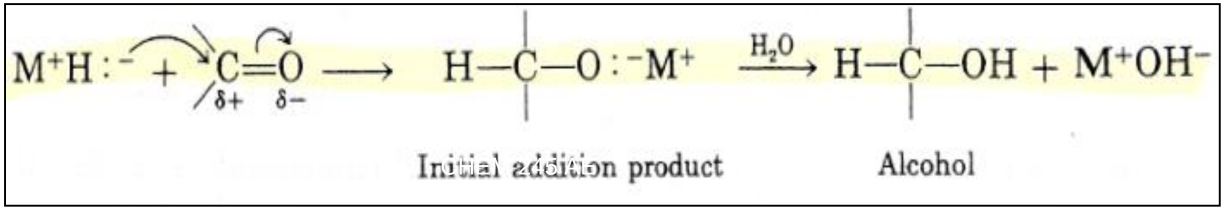
The partially positive carbonyl carbon undergoes attack by electron-rich reagents, or *nucleophiles* (Nu:).

The partially negative carbonyl oxygen is attacked by electron-deficient reagents, or *electrophiles* (E$^+$).



Addition of Metal Hydrides: Formation of Alcohols

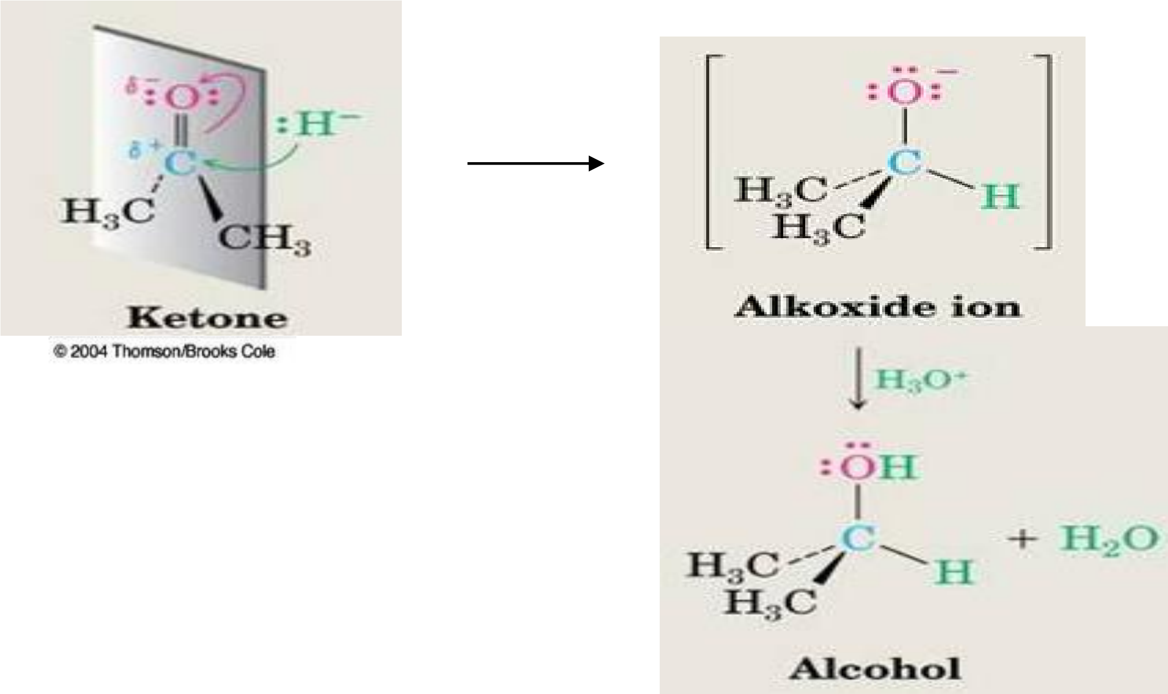
- **Aldehydes can be reduced to primary alcohols.**
- **Ketones can be reduced to secondary alcohols.**
- **The initial addition product, after being hydrolyzed, yields an alcohol.**



Nucleophilic Addition Reactions of Aldehydes and Ketones

Nu^- approaches 45° to the plane of C=O and adds to C

A tetrahedral alkoxide ion intermediate is produced



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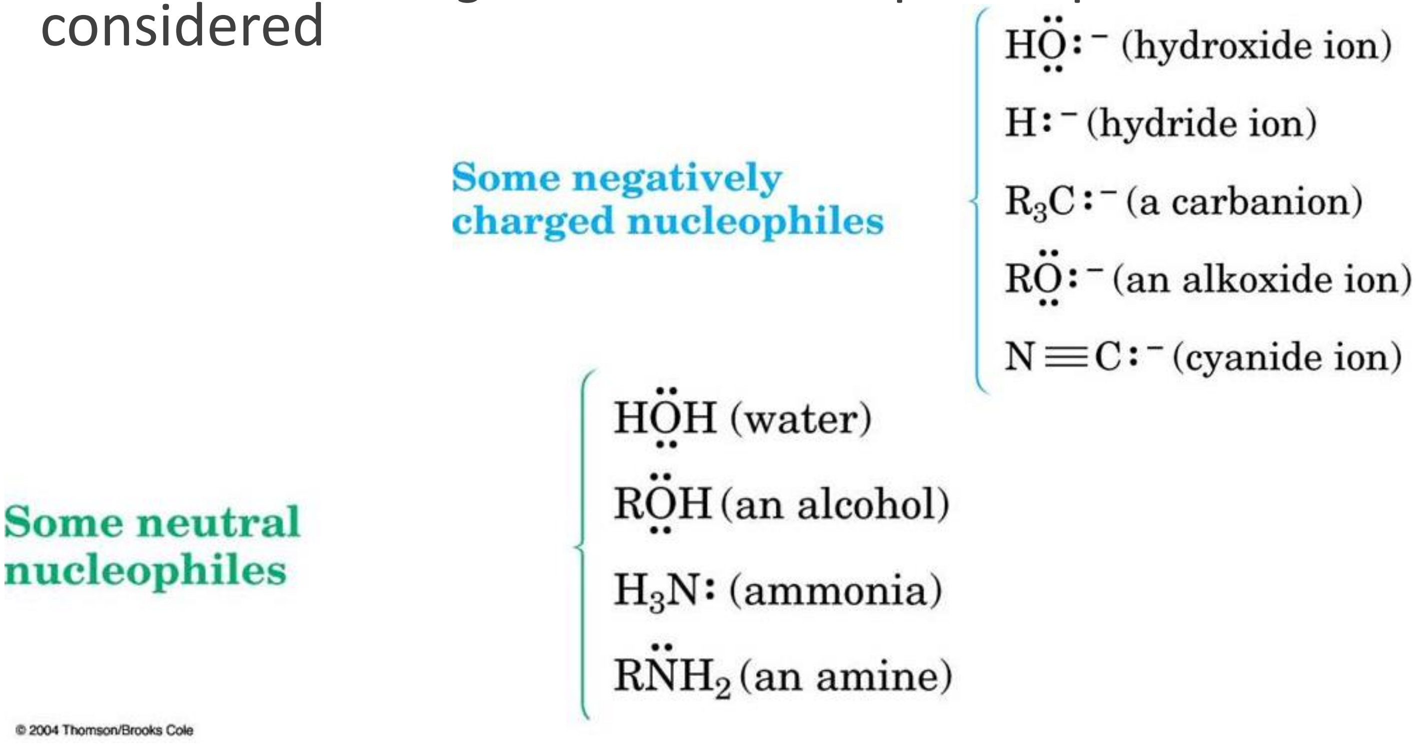
Nucleophiles

Nucleophiles can be negatively charged (: Nu⁻) or neutral (: Nu) at the reaction site

The *overall charge* on the nucleophilic species is not considered



Some negatively charged nucleophiles

- $H\ddot{O}:^-$ (hydroxide ion)
- $H:^-$ (hydride ion)
- $R_3C:^-$ (a carbanion)
- $R\ddot{O}:^-$ (an alkoxide ion)
- $N{\equiv}C:^-$ (cyanide ion)

Some neutral nucleophiles

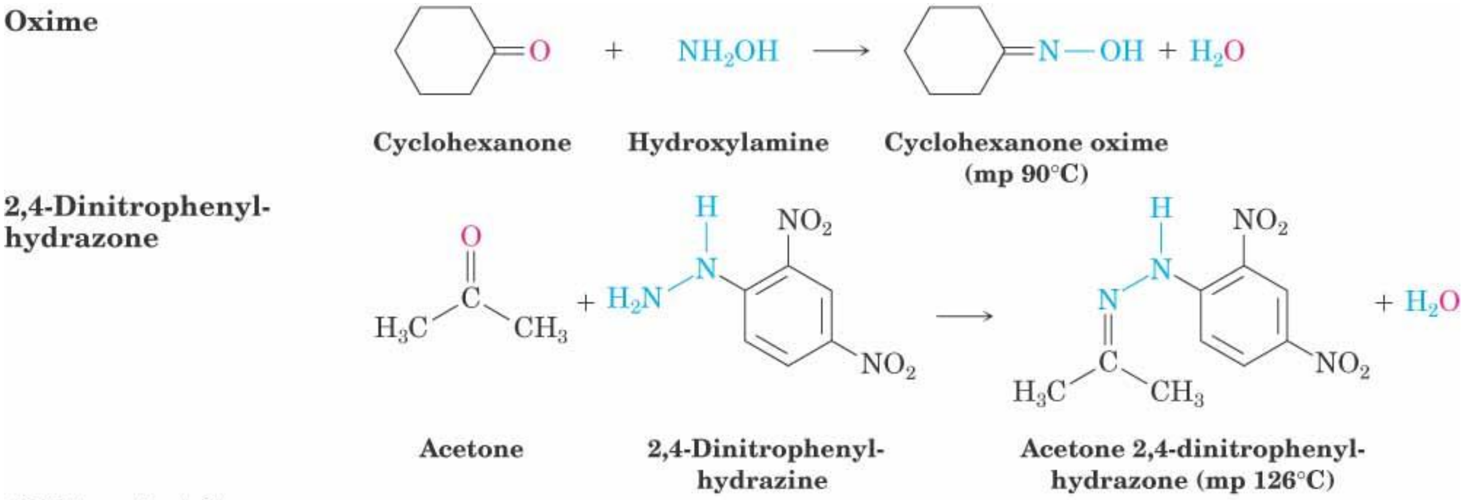
- $H\ddot{O}H$ (water)
- $R\ddot{O}H$ (an alcohol)
- $H_3N:$ (ammonia)
- $R\ddot{N}H_2$ (an amine)

Imine Derivatives

Addition of amines with an atom containing a lone pair of electrons on the adjacent atom occurs very readily, giving useful, stable imines

For example, hydroxylamine forms oximes and 2,4-dinitrophenylhydrazine readily forms 2,4-dinitrophenylhydrazones

- These are usually solids and help in characterizing liquid ketones or aldehydes by melting points

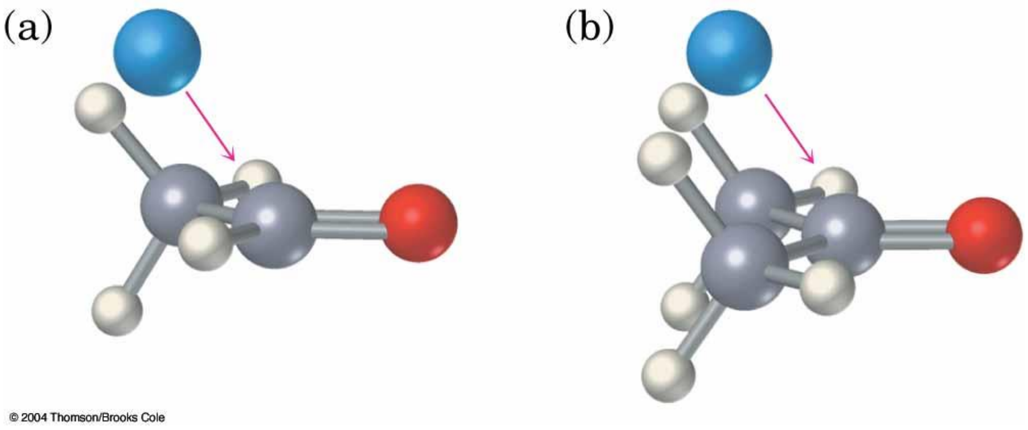


Relative Reactivity of Aldehydes and Ketones

Aldehydes are generally more reactive than ketones in nucleophilic addition reactions

The transition state for addition is less crowded and lower in energy for an aldehyde (a) than for a ketone (b)

Aldehydes have one large substituent bonded to the C=O: ketones have two



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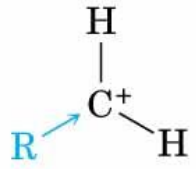
Electrophilicity of Aldehydes and Ketones

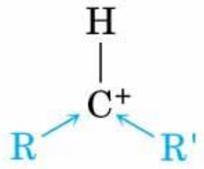
Aldehyde C=O is more polarized than ketone C=O

As in carbocations, more alkyl groups stabilize + character

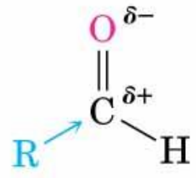
Ketone has more alkyl groups, stabilizing the C=O carbon inductively



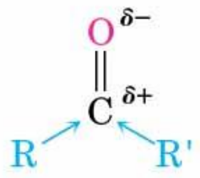
1° carbocation
(less stable, more reactive)



2° carbocation
(more stable, less reactive)



Aldehyde
(less stabilization of δ +, more reactive)

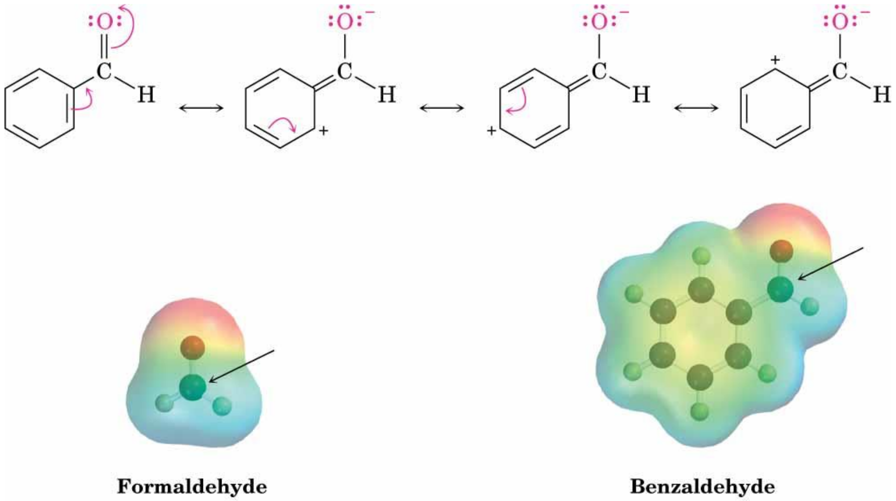


Ketone
(more stabilization of δ +, less reactive)

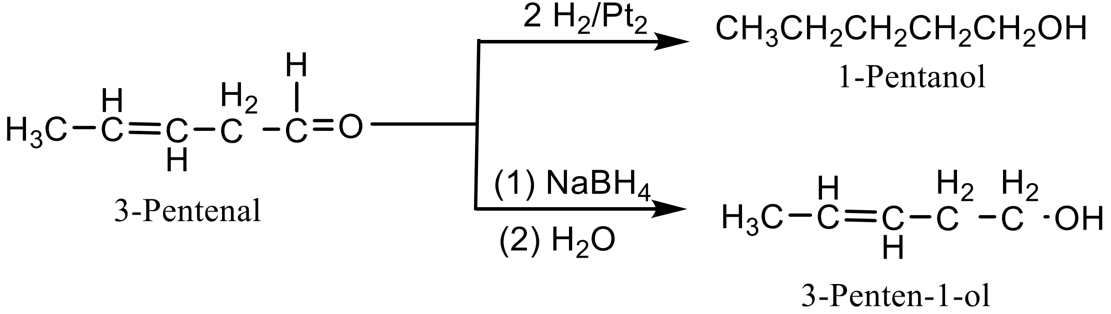
Reactivity of Aromatic Aldehydes

Less reactive in nucleophilic addition reactions than aliphatic aldehydes

Electron-donating resonance effect of aromatic ring makes C=O less reactive electrophilic than the carbonyl group of an aliphatic aldehyde



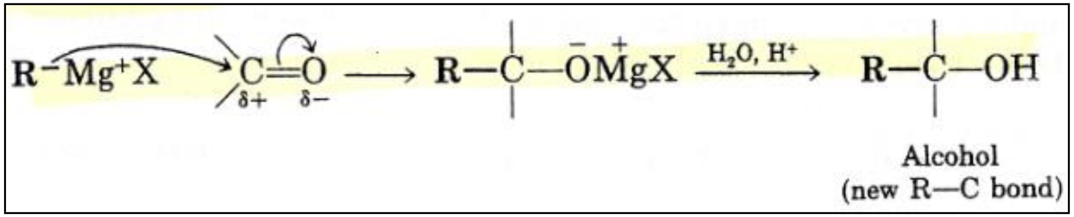
- **Sodium borohydride, $NaBH_4$,** has the advantage of ***selectively*** reducing the carbonyl group of ***non-conjugated*** unsaturated aldehydes or ketones.



Addition of Grignard Reagents: Formation of Alcohols

Addition of Grignard reagents, R^-Mg^+X, to the carbonyl group is used for synthesizing all kinds of alcohols.

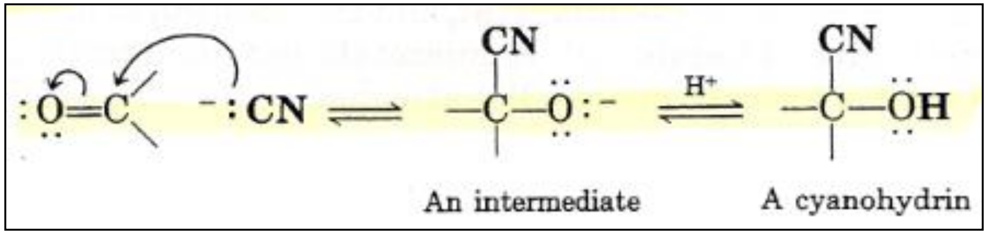
The addition product, after it is formed, is hydrolyzed with aqueous acid to give an alcohol.



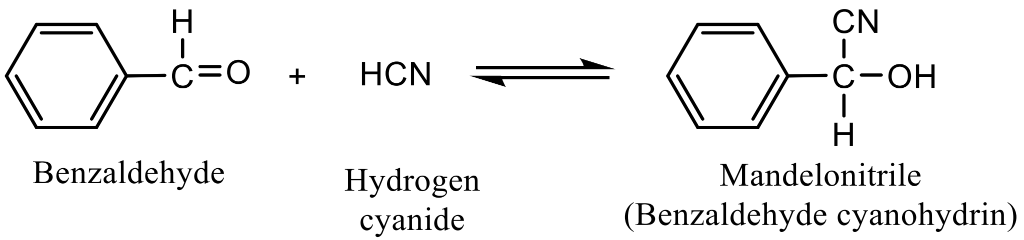
It is possible to prepare 1°, 2°, or 3° alcohols, depending on what kind of carbonyl compound undergoes the addition reaction.

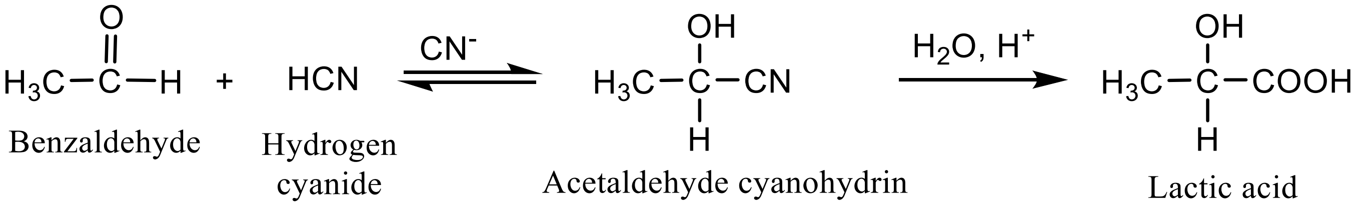
Addition of Hydrogen Cyanide: Formation of Cyanohydrins

- The addition is catalyzed by cyanide ion (good nucleophile).



- **Example**

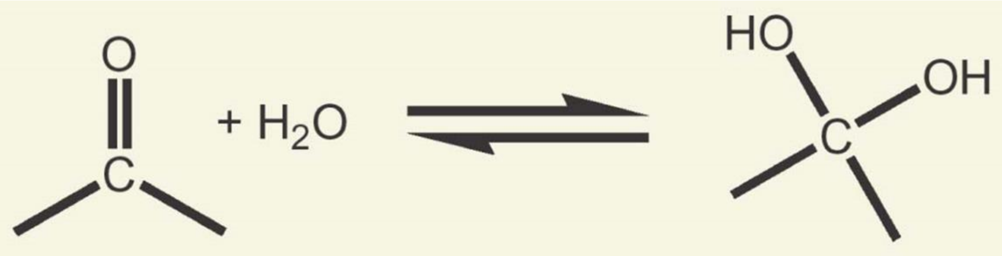




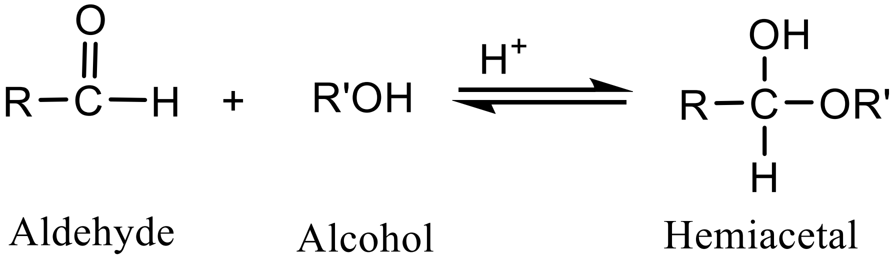
Addition of Alcohols: Formation of Hemiacetals and

A. Hemiacetals (and Hemiketals)

Water and alcohols (weak nucleophiles), can add to the carbonyl group of aldehydes and ketones.



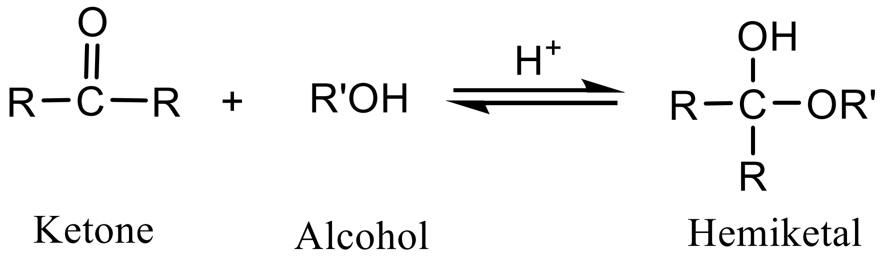
An acid catalyst is required to speed the rate of reaction. The same as in alcohol



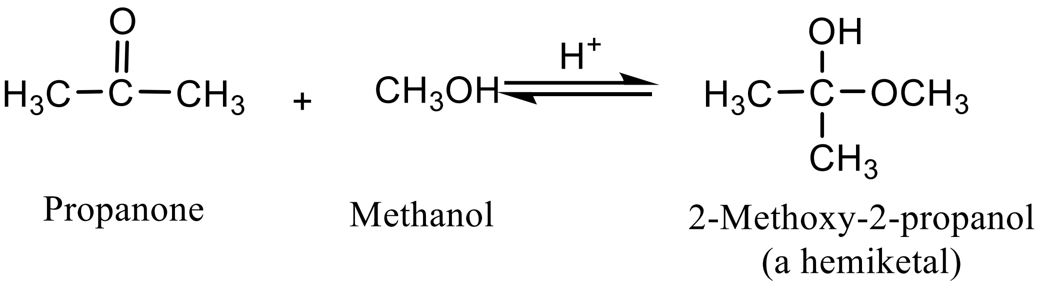
$$R-\overset{\overset{\displaystyle O}{\|}}{C}-H + R'OH \underset{}{\overset{H^+}{\rightleftharpoons}} R-\underset{\underset{\displaystyle H}{|}}{\overset{\overset{\displaystyle OH}{|}}{C}}-OR'$$

The addition of one mole of an alcohol to the carbonyl group of an aldehyde yields a *hemiacetal*.

- The addition of one mole of an alcohol to a ketone gives a ***hemiketal*.**



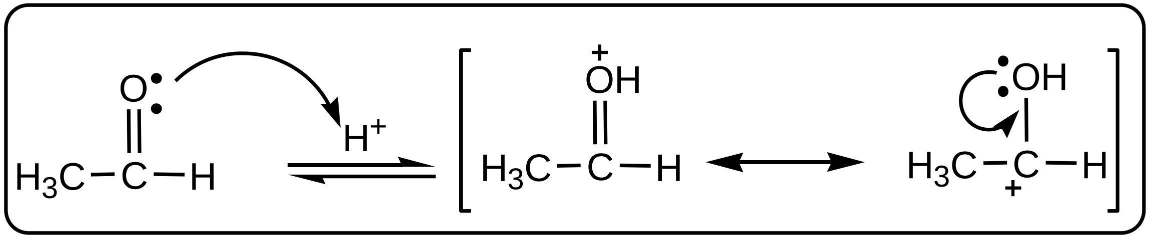
$$R-\overset{O}{\overset{\|}{C}}-R + R'OH \overset{H^+}{\rightleftharpoons} R-\overset{OH}{\underset{R}{C}}-OR'$$



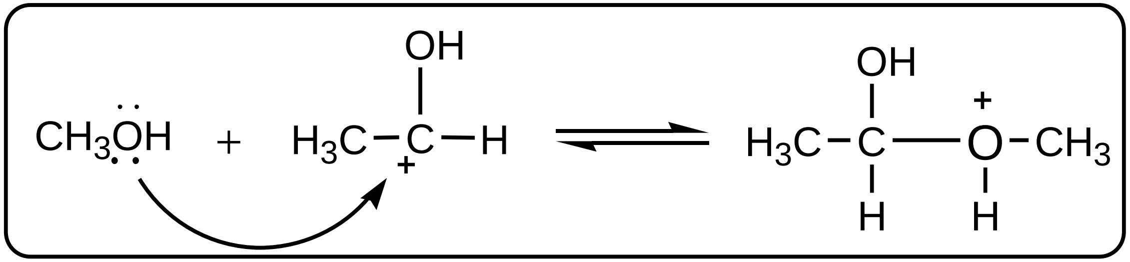
$$H_3C-\overset{O}{\overset{\|}{C}}-CH_3 + CH_3OH \overset{H^+}{\rightleftharpoons} H_3C-\overset{OH}{\underset{CH_3}{C}}-OCH_3$$

Hemiacetals and hemiketals have an alkoxy group (OR) and a hydroxy group (OH) attached to the *same* carbon.

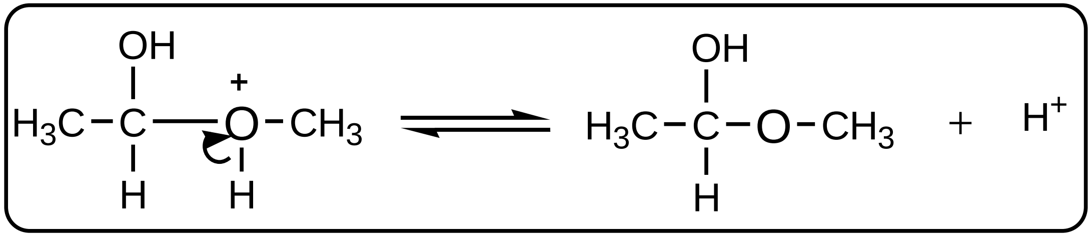
Step 1. Protonation of the carbonyl oxygen:



Step 2. The positively charged carbon is attacked by the weak nucleophile methanol.



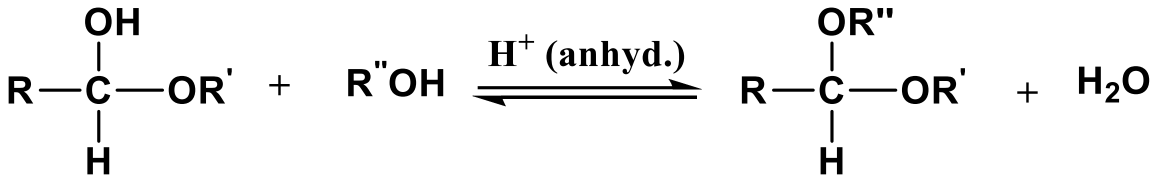
Step 3. The loss of a proton regenerates the acid catalyst and forms the hemiacetal.



B. Acetals

When hemiacetals are treated with an additional mole of alcohol in the presence of anhydrous acid, they are converted to *Acetals*.

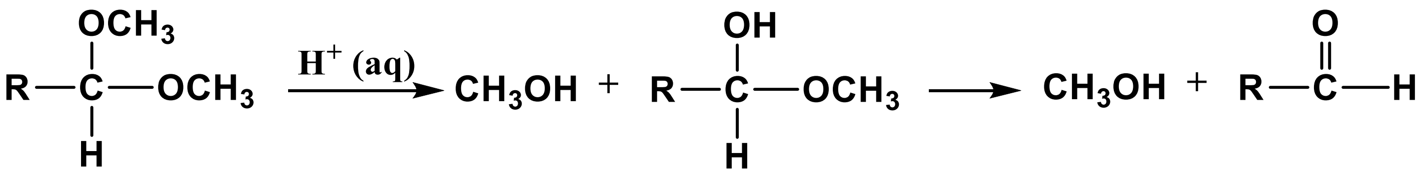
- Acetals have two alkoxy groups (OR) on the *same* carbon.



$$\mathrm{R{-}\overset{OH}{\underset{H}{C}}{-}OR'} + \mathrm{R''OH} \xrightleftharpoons{\mathrm{H^+\ (anhyd.)}} \mathrm{R{-}\overset{OR''}{\underset{H}{C}}{-}OR'} + \mathrm{H_2O}$$

Hemiacetal Alcohol Acetal

- Acetals are stable compounds.
- Acetals, like ethers, do not react with bases, oxidizing agents and reducing agents.

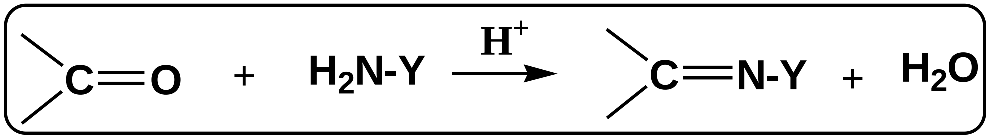


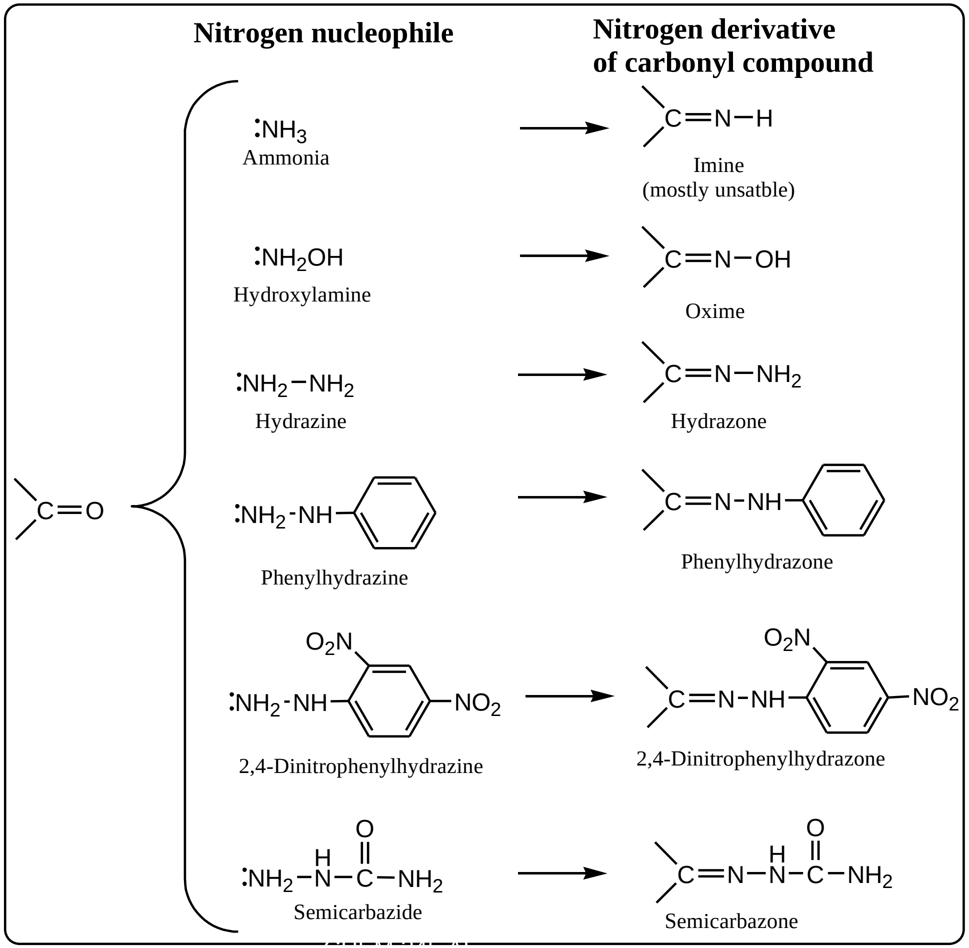
$$\mathrm{R{-}\overset{OCH_3}{\underset{H}{C}}{-}OCH_3} \xrightarrow{\mathrm{H^+\ (aq)}} \mathrm{CH_3OH} + \mathrm{R{-}\overset{OH}{\underset{H}{C}}{-}OCH_3} \longrightarrow \mathrm{CH_3OH} + \mathrm{R{-}\overset{O}{\overset{\|}{C}}{-}H}$$

A dimethyl acetal Hemiacetal Aldehyde

Addition of Ammonia and Ammonia Derivatives

- **The addition of nitrogen nucleophile, such as ammonia(NH_3) an substituted ammonia (NH_2-Y).**





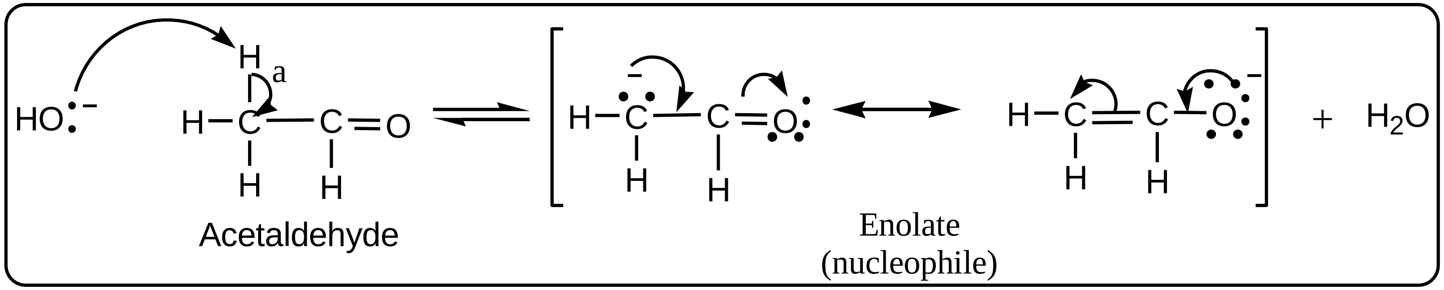
Aldol Condensation

Aldehydes and ketones have α-hydrogens (slightly acidic) in presence of Alkali such as NaOH undergo condensation reaction. Base first abstract the hydrogen from the more acidic one and then it acting as Nucleophiles, which add to the carbonyl group of aldehydes and ketones, a *larger* organic molecule is formed with loss of water.

Example

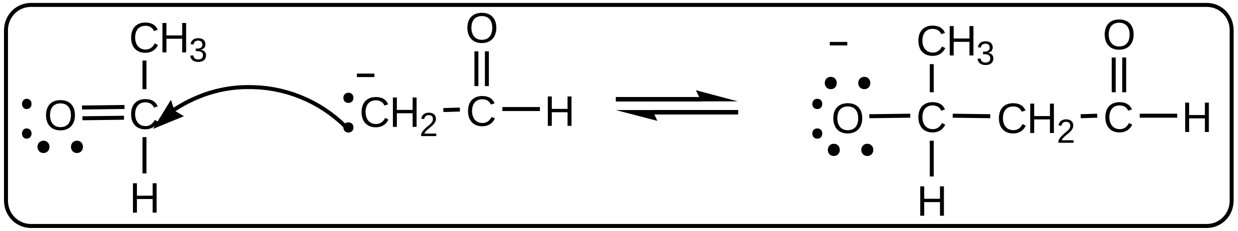
Addition of enolate anion derived from acetaldehyde to the C=O bond of a nonionized acetaldehyde molecule.

Step 1. **When acetaldehyde is treated with dilute sodium hydroxide, A small but significant number of molecules are converted to the enolate anion.**



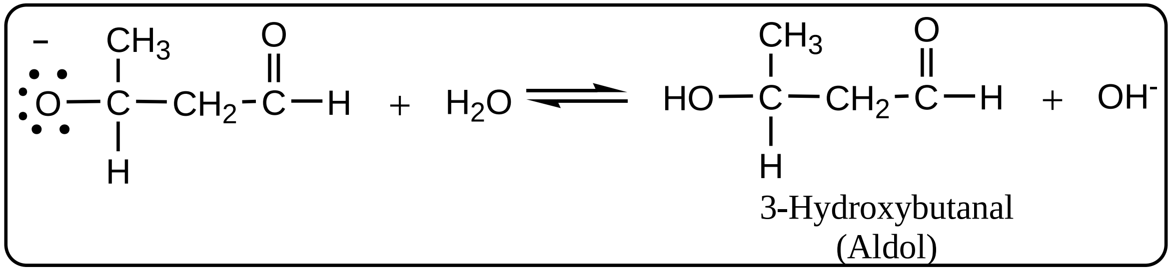
Step 2. **The enolate anion, acting as a nucleophile, adds to the C=O bond of a nonionized acetaldehyde molecule left in solution to give an adduct that carries a negative charge on the oxygen.**

The adduct contains a newly formed carbon-carbon bond.



Step 3. **The negatively charged oxygen abstracts a proton from water.**

to give the final product, 3-hydroxybutanal, commonly known as *aldol*.



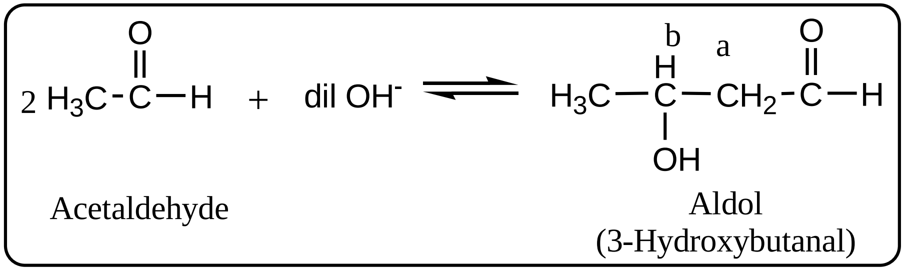
$$^{-}\ddot{\underset{..}{O}}-\underset{H}{\overset{CH_3}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-H + H_2O \rightleftharpoons HO-\underset{H}{\overset{CH_3}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-H + OH^-$$

3-Hydroxybutanal
(Aldol)

- **The term *aldol* is derived from the combination of the words *aldehyde and alcohol*.**

The two functional groups present in the product.

- **The net overall reaction may be written as**

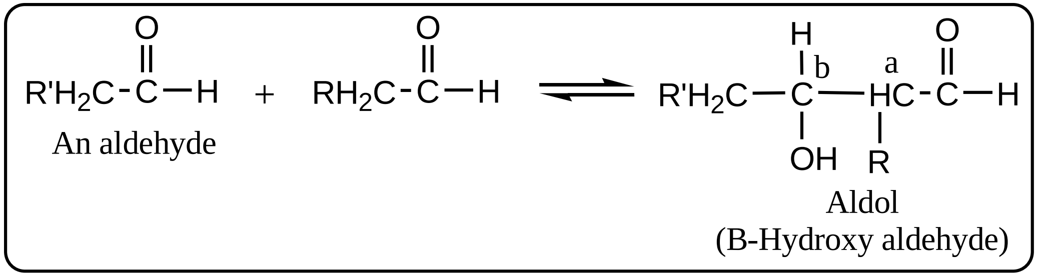


$$2\ H_3C-\overset{O}{\overset{\|}{C}}-H + \text{dil } OH^- \rightleftharpoons H_3C-\underset{OH}{\overset{H}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-H$$

Acetaldehyde

Aldol
(3-Hydroxybutanal)

- **The general overall reaction may be written as**



$$R'H_2C-\overset{O}{\overset{\|}{C}}-H + RH_2C-\overset{O}{\overset{\|}{C}}-H \rightleftharpoons R'H_2C-\underset{OH}{\overset{H}{C}}-\underset{R}{HC}-\overset{O}{\overset{\|}{C}}-H$$

An aldehyde

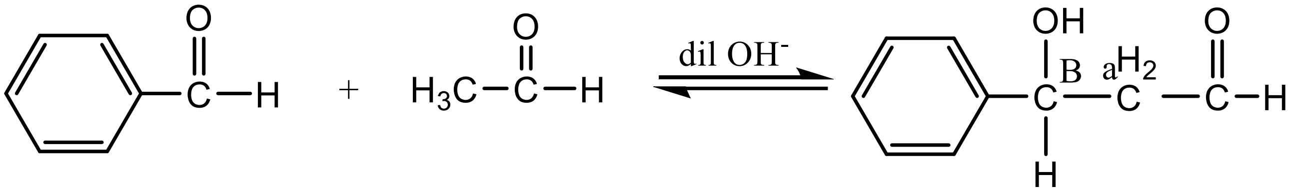
Aldol
(B-Hydroxy aldehyde)

Crossed Aldol Condensation

- **If we subject a mixture of two different aldehydes, each containing a hydrogen, to the aldol condensation,**

For example

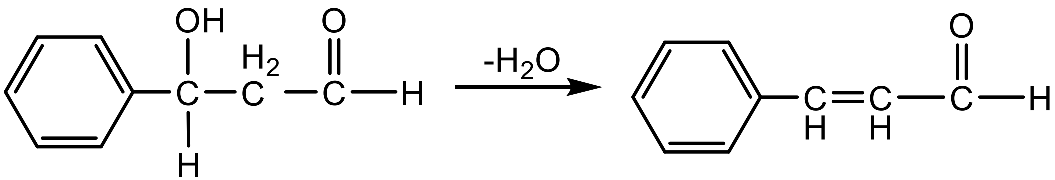
If acetaldehyde is added slowly to an excess of benzaldehyde in the presence of dilute sodium hydroxide,



Benzaldehyde
(excess; no a H)

Acetaldehyde
(source of enolate)

Crossed aldol product

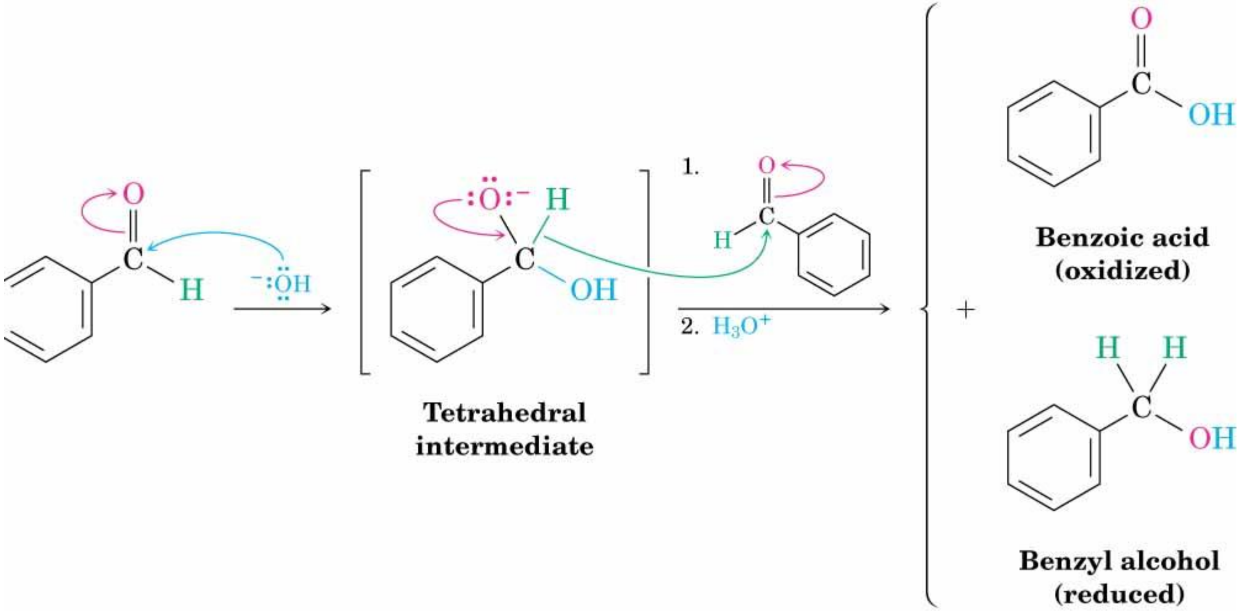


Cinnamaldehyde
(an a,B-unsaturated aldehyde)

The Cannizzaro Reaction

The adduct of an aldehyde and OH⁻ can transfer hydride ion to another aldehyde C=O resulting in a simultaneous oxidation and reduction (*disproportionation)*

It considered as oxidation-reduction reaction



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Summary

Aldehydes are from oxidative cleavage of alkenes, oxidation of 1° alcohols, or partial reduction of esters

Ketones are from oxidative cleavage of alkenes, oxidation of 2° alcohols, or by addition of diorganocopper reagents to acid chlorides.

Aldehydes and ketones are reduced to yield 1° and 2° alcohols , respectively

Grignard reagents also gives alcohols

Addition of HCN yields cyanohydrins

1° amines add to form imines, and 2° amines yield enamines

Reaction of an aldehyde or ketone with Hydrazines form hydrazones

Reaction of an aldehyde or ketone with Hydroxyamine forms oximes

Alcohols add to yield acetals

Reaction of aldehydres and ketones have alpha-hydrogen in presence of alkali undergo **ALDOL REACTION (CODENSATION REACTION**)

Aldehydes or Ketone with **no alpha-hydrogen** in presence of Base undergo **CANNIZARRO's REACTION (OXIDATION-REDUCTION**)