ALDEHYDES AND KETONES

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Nomenclature

Carbonyl compounds have H, R, or Ar groups attached to the carbonyl group.
\[ \text{C} \equiv \text{O} \]
Aldehydes have at least one H bonded to the carbonyl group; ketones have only R’s or Ar’s.

Aldehydes

Common names replace the suffix –ic and the word acid of the corresponding carboxylic acids by –aldehyde. Locations of substituent groups are designated by Greek letters, e.g.
\[ \text{C} \equiv \text{O} \]
IUPAC names use the longest chain with \[ \text{C} \equiv \text{O} \] and replace e of alkane by the suffix –al.
The C of CHO is number 1. – CHO is also called the formyl group.

Ketones

Common names use the names of R or Ar as separate words, along with the word ketone. The IUPAC system replaces the e of the name of the longest chain by the suffix –one.
In molecules with functional groups, such as \(-\text{COOH}\), that have a higher naming priority, the carbonyl group is indicated by the prefix \textit{keto-}. Thus, \(\text{CH}_3\text{–CO–CH}_2\text{–CH}_2\text{–COOH}\) is 4-ketopentanoic acid.

**Common and IUPAC names for some simple molecules**

**Examples:**

<table>
<thead>
<tr>
<th>Molecule</th>
<th>Common name</th>
<th>IUPAC name</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) CH(_3)CHO</td>
<td>acetaldehyde (from acetic acid)</td>
<td>ethanal</td>
</tr>
<tr>
<td>(b) (CH(_3))(_2)CHCH(_2)CHO</td>
<td></td>
<td>β-methylbutyraldehyde</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3-methylbutanal</td>
</tr>
<tr>
<td>c (\text{CH}_3\text{CH}_2\text{CH}_2\text{CHClCHO})</td>
<td>α-chlorovaleraldehyde</td>
<td>2-chloropentanal</td>
</tr>
<tr>
<td>d ((\text{CH}_3)_2\text{CHCOCH}_3)</td>
<td>methyl isopropyl ketone</td>
<td>3-methyl-2-butnone</td>
</tr>
<tr>
<td>e (\text{CH}_3\text{CH}_2\text{COC}_6\text{H}_5)</td>
<td>ethyl phenyl ketone (propiophenone)</td>
<td>1-phenyl-1-propanone</td>
</tr>
<tr>
<td>f (\text{H}_2\text{C} \rightleftharpoons \text{CHCOCH}_3)</td>
<td>methyl vinyl ketone</td>
<td>3-buten-2-one</td>
</tr>
<tr>
<td></td>
<td></td>
<td>The (\text{C} = \text{O}) group has numbering priority over the (\text{C} = \text{C}) group</td>
</tr>
<tr>
<td>g ((\text{CH}_3)_3\text{CCHO})</td>
<td>(\alpha,\alpha)-dimethylpropionic aldehyde or trimethylacetaldehyde</td>
<td>2,2-dimethylpropanal</td>
</tr>
<tr>
<td>h (\text{C}_6\text{H}_5\text{CH} \equiv \text{CH} \equiv \text{CHO})</td>
<td>Cinnamaldehyde</td>
<td>3-phenyl-propenal</td>
</tr>
<tr>
<td>i (\text{HOCH}_2\text{CH}_2\text{CH} \equiv \text{O})</td>
<td>β-hydroxypropionic aldehyde</td>
<td>3-hydroxypropanal</td>
</tr>
<tr>
<td>j ((\text{CH}_3)_2\text{C} \equiv \text{CHCOCH}_3)</td>
<td>mesityl oxide</td>
<td>4-methyl-3-penten-2-one</td>
</tr>
</tbody>
</table>
Structural formulas from names

Examples:

<table>
<thead>
<tr>
<th>Name</th>
<th>Structural formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Methyl isobutyl ketone</td>
<td>CH₃—C—CH₂CH₂CH₃</td>
</tr>
<tr>
<td></td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>CH₃</td>
</tr>
<tr>
<td>(b) Phenylacetaldehyde</td>
<td>C₆H₅CH₂—C═O</td>
</tr>
<tr>
<td></td>
<td>H</td>
</tr>
<tr>
<td>(c) 2-methyl-3-pentanone</td>
<td>CH₃CH₂—C—CH₂CH₃</td>
</tr>
<tr>
<td></td>
<td>O</td>
</tr>
<tr>
<td></td>
<td>CH₃</td>
</tr>
<tr>
<td>(d) 3-hexenal</td>
<td>CH₃CH₂CH═CH₂C═O</td>
</tr>
<tr>
<td></td>
<td>H</td>
</tr>
<tr>
<td>(e) β-chloropropionaldehyde</td>
<td>ClCH₂CH₂C═O</td>
</tr>
</tbody>
</table>

Methods of preparation

*Aldehydes*

**Oxidation of alcohols or alkyl halides**

A. 1-propanol with

<table>
<thead>
<tr>
<th></th>
<th>Produces</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) Alkaline aq. KMnO₄ solution during distillation</td>
<td>CH₃CH₂CHO. Since aldehydes are oxidized further under these conditions, CH₃CH₂COOH is also obtained.</td>
</tr>
<tr>
<td>(b) Hot Cu shavings</td>
<td>CH₃CH₂CHO. The aldehyde can’t be oxidized further.</td>
</tr>
</tbody>
</table>

B. 1° Alkyl halides with dimethyl sulfoxide in base

$$
\text{CH}_3(\text{CH}_{2})_6\text{I} + \text{CH}_3\text{SCH}_3 \xrightarrow{\text{HCO}_3^-} \text{CH}_3(\text{CH}_{2})_5\text{CHO} + \text{CH}_3\text{SCH}_3
$$
C. ArCH₃ to ArCHO

(i) \[ \text{RCHO} \longrightarrow \text{NH₂} \]

(ii) \[ \text{NH₂} \longrightarrow \text{RCH(OH)₂} \]

gem-diacetate

Strecker synthesis

The Strecker amino acid synthesis is a series of chemical reactions that synthesize an amino acid from an aldehyde (or ketone). The aldehyde is condensed with ammonium chloride in the presence of potassium cyanide to form an α-aminonitrile, which is subsequently hydrolyzed to give the desired amino-acid.

Use of ammonium salts gives unsubstituted amino acids. Primary and secondary amines also successfully give substituted amino acids. Likewise, the use of ketones, instead of aldehydes, gives α,α-disubstituted amino acids.

Mechanism

Reaction type: Nucleophilic Addition followed by Nucleophilic Acyl Substitution

The reaction is promoted by acid, and HCN must be supplied or generated in situ from cyanide salts - in the latter case, one equivalent of acid is consumed in the reaction.

\[ \text{NH}_4\text{Cl} + \text{NaCN} \rightleftharpoons \text{NH}_2 + \text{HCN} + \text{NaCl} \]

The steps may be identified as follows:

1. The first step is probably the condensation of ammonia with the aldehyde to form an imine,

2. The cyanide adds as a nucleophile to the imine carbon, generating the α-aminonitrile,
3. This product may be hydrolysed to the corresponding $\alpha$-aminoacid:

![Mechanistic steps for Strecker Synthesis](image)

Fig-: Mechanistic steps for Strecker Synthesis

D. (Oxidation of) vinylboranes from alkynes
With dialkylacetylenes, the products of oxidation are ketones.

2. Reduction of Acyl chlorides  
   (R—C—Cl)

A. \[ R\text{—C—Cl} + \text{LiAl}[\text{(CH}_3\text{)}_3\text{CO}]_3\text{H} \rightarrow R\text{—C—H} + \text{LiCl} + \text{Al}[\text{OC(CH}_3\text{)}_3\text{]}_3 \]
   Lithium aluminum tri-\(\text{t}\)-butoxyhydride

B. \[ \text{RCOCl or ArCOCl} + \text{H}_2/\text{Pd(BaSO}_4\text{)} \rightarrow \text{RCH—O or ArCH—O} + \text{HCl} \]
   moderated catalyst

3. Introduction of CHO (Formylation)

A. \[ \text{C}_6\text{H}_5\text{CH(CH}_3\text{)}_2 + \text{CO} \xrightarrow{\text{HCl, AlCl}_3} p-(\text{CH}_3)_2\text{CHC}_6\text{H}_4\text{CHO} \]
   (Gatterman-Koch Reaction)
   \(p\)-Isopropylbenzaldehyde

B. \[ \text{activated ring} + \text{HCN} + \text{HCl} \xrightarrow{1. \text{ZnCl}_2, \text{ether}} \text{OH} + \text{NH}_4\text{Cl} \xrightarrow{2. \text{H}_2\text{O}} \text{OH} \]
   (Gatterman Reaction)
C.  \[ \text{ArH} + \text{H} = \text{C} \equiv \text{N(CH}_3\text{)}_2 \xrightarrow[\text{POCl}_3]{\text{\textbullet}} \text{ArCHO} + (\text{CH}_3)_2\text{NH} \]

Ketones

1. Oxidation of 2° ROH

Ketones are oxidation products of 2° alcohols.

\[ \text{C}_6\text{H}_5\text{CH}-\text{CH}_3 \xrightarrow[\text{K}_2\text{Cr}_2\text{O}_7]{\text{H}^+} \text{C}_6\text{H}_5\text{C} = \text{CH}_3 \]

1-Pheny ethanol  \hspace{1cm}  Acetophenone

Q. Write formula for an alcohol used in, and identify reagents/ reaction conditions for the preparation of \( \text{C}_6\text{H}_5\text{COCH}_3 \)

2. Acylation of aromatic rings

\[ \text{ArH} + \text{RCOCl} \xrightarrow[\text{AlCl}_3]{\text{\textbullet}} \text{ArCOR} + \text{HCl} \]

3. Acylation of alkenes

\[ \text{RC} \xrightarrow[\text{Cl}]{\text{H}_2\text{C} = \text{CHR'}} \xrightarrow{\text{HCl}} \text{R} = \text{C} \equiv \text{CH}_2 = \text{CHCl} \rightarrow \text{R} = \text{C} \equiv \text{CH} = \text{CHR'} \]

This is a Markownikov addition initiated by \( \text{RC}^+ \) acylonium cation

4. With Organometallics

A. \[ 2\text{R} = \text{C} \equiv \text{Cl} + \text{R'}\text{Cd} \rightarrow 2\text{R} = \text{C} \equiv \text{R'} + \text{CdCl}_2 \quad (\text{R'} = \text{Ar or 1° alkyl}) \]

\( \text{R'}\text{Cd} \) is prepared from \( \text{R'}\text{MgX} \): \[ 2\text{R'}\text{MgX} + \text{CdCl}_2 \rightarrow \text{R'}\text{Cd} + 2\text{MgXCl} \].
5. **General properties and reactions of aldehydes and ketones**

H-bonding between alcohol molecules is responsible for the higher boiling point, e.g., n-Butyl alcohol boils at 118°C and n-butyraldehyde boils at 76°C, yet their molecular weights are 74 and 72, respectively.

1. **Tollens’ Reagent**

   A specific oxidant for RCHO is \([\text{Ag(NH}_3\text{)}_2]^+\).

   \[
   \text{RCHO} + 2\text{[Ag(NH}_3\text{)}_2]^+ + 3\text{OH}^- \rightarrow \text{RCOO}^- + 2\text{H}_2\text{O} + 4\text{NH}_3 + 2\text{Ag} \quad \text{(mirror)}
   \]

2. **Strong Oxidants**

   Ketones resist mild oxidation, but with strong oxidants at high temperature they undergo cleavage of C–C bonds on either side of the carbonyl group.

   \[
   \text{RCH}_2\text{C} \overset{(a)}{\text{CH}_2\text{R}} \overset{\text{Oxid.}}{\rightarrow} \text{RCOOH} + \text{R'CH}_2\text{COOH} + \text{RCH}_2\text{COOH} + \text{R'COOH}
   \]

   from cleavage of bond (a) from cleavage of bond (b)

3. **Haloform Reaction**

   Methyl ketones, \(\text{CH}_3\text{C} \overset{\text{O}}{\rightarrow} \), are readily oxidized by \(\text{NaOI (NaOH + I}_2\) to iodoform, \(\text{CH}_3\text{I}\) and \(\text{RCOO}^-\text{Na}^+\).
6. Addition reactions

Reactions of the carbonyl group

- Dipole moment measurements of carbonyl compounds have shown that there is an uneven distribution of charge.

- Electron donation to the electron-deficient carbon atom may be provided by:
  (a) an external Nu⁻
  (b) by an adjacent lone pair
  (c) by an adjacent anion

Acidic Hydrogens
The O atom is basic and reacts with electrophiles, such as proton and Lewis acids.

Protonation of the O makes C more electron deficient. Hence many addition reactions of the carbonyl group are acid catalysed.

Carbonyl gr has an influence on the chemistry of substituents:

- Electron donation from lone pairs on O and N in esters and amides diminishes the reactivity of carbonyl group towards Nu⁻ and also reduces the basicity of O and N atoms.

- Electron withdrawing effect of carbonyl gr makes H atoms, attached to the neighboring atoms, acidic. Once anion is formed, it stabilizes by delocalization over the carbonyl groups.

There is a tautomeric relationship between the carbonyl compound and the corresponding enol.

a. - The enol possesses an electron rich alkene
   - The H atom of the enolic –OH is acidic and in presence of base forms an anion

b. - Protonation of enolate anion may take place on O or C to regenerate either the enol or the corresponding carbonyl compound.
   - The existence of electron rich enolic form leads to the position adjacent to a carbonyl group being sensitive to electrophilic attack.

c. The electron withdrawing effect of the carbonyl group may be relayed through a conjugated system.
   \[ \text{the } \overset{\text{E}}{\text{E}} \text{-unsaturated ketone is susceptible to nucleophilic attack} \]
An –OH attached to this carbon is acidic and the anion is stabilized by delocalization.

The enolate of a \( \beta \)-dicarbonyl compound is acidic. The resultant anion is neutralized by reaction with an electrophile either on the central carbon or on an oxygen atom.

This reactivity of \( \beta \)-dicarbonyl compounds makes them extremely useful in synthesis.

- The addition of a nucleophile to the carbonyl group involves the conversion of a planar sp\(^2\) centre to a tetrahedral sp\(^3\) with an increase in the steric bulk of the intermediate. The preferred direction of approach of the nucleophile to the carbonyl carbon is along an axis through C and O atoms and at an angle of 108° to the plane of the carbonyl group.

6.1 Addition of Oxygen Nucleophiles

- Quite easily – under acid catalysed conditions
• O atom of the carbonyl group is protonated to produce an electron deficient C; initial addition takes place to form a **hemi-acetal**.

• In the presence of acid, water is lost, carbocation is formed which is stabilized by the lone pairs on O.

• Further addition of R\_OH then takes place to give **acetal**.

• Due to increasing steric congestion, dimethyl acetals are less readily formed by ketones.

![Hemiacetal and dimethyl acetal](image)

• Ethane-1,2-diol reacts with aldehydes and ketones under these conditions to form ethylene acetals.

![Ethylene acetal](image)

• These compounds no longer possess the electron-deficient carbon of carbonyl group, and therefore these acetals function as protecting groups for the carbonyl group.

• The O nucleophile may be that of a peroxo acid such as perbenzoic acid. A rearrangement may occur under acidic conditions
  - This takes place with the expulsion of benzoate and insertion of an O atom adjacent to the carbonyl group.

  The reaction is known as **Baeyer-Villiger** rearrangement.

  Thus, ketone is converted to an ester, or a cyclic ketone to a lactone (cyclic ester)
6.2 Addition of S nucleophiles (addition of NaHSO₃)
- Addition of NaHSO₃ to carbonyl/ aldehydic carbon gives solid adduct; these are sulfonates that are water soluble.
- Only RCHO, methyl ketones, and cyclic ketones react.
- Carbonyl compounds can be regenerated on treating the adduct with acid or base.

\[
\begin{align*}
R\text{–}\text{C–}O + \text{NaHSO}_3 & \rightarrow R\text{–}\text{C–}OH + \text{SO}_3\text{Na}^+ \\
\text{C – S bond is formed because S is a more nucleophilic site than O.}
\end{align*}
\]

- \(\text{C – S bond is formed because S is a more nucleophilic site than O.}\)
- \(\text{SO}_3\text{ is a large ion and reacts only if RCHO is not sterically hindered.}\)
- The reaction can be used to separate RCHO from non-carbonyl compounds such as RCH₂OH.

\[
\begin{align*}
R\text{–C–SO}_3\text{Na}^+ & \rightarrow \text{SO}_2 + \text{SO}_3^- \\
\text{Formation of thioacetals from aldehydes and ketones involves the reaction with thiol such as ethane-1,2-dithiol in the presence of a Lewis acid catalyst such as BF}_3\text{ etherate.}
\end{align*}
\]

- Formation of thioacetals from aldehydes and ketones involves the reaction with thiol such as ethane-1,2-dithiol in the presence of a Lewis acid catalyst such as BF₃ etherate.
- The C– bonds of cyclic thioketals/ thioacetals prepared from HSCH₂CH₂SH are reduced with Ni to

\[
\begin{align*}
\text{C–O} + \text{HSCH}_2\text{CH}_2\text{SH} & \rightarrow \text{C–S–CH}_2 + \text{CH}_3\text{CH}_3 + \text{H}_2\text{S} + \text{CH}_3\text{CH}_3
\end{align*}
\]

thus \(\text{C–O}\) is converted to \(\text{CH}_3\text{CH}_3\).

6.3 Addition to N nucleophiles

When an aldehyde or ketone reacts with the following ammonia derivatives:

(a) \(\text{H–N–OH}\)  
(b) \(\text{H–N–NH}_2\)  
(c) \(\text{H–N–NHCONH}_2\)

[Product : oxime  Ph - hydrazone  Semicarbazide]

addition is followed by dehydration.
These derivatives are crystalline compounds and their melting points are used to identify carbonyl compounds.

Oximes are planar, and show geometrical isomerism. They undergo Beckmann rearrangement.

Rearrangement involving migration of R from C to an electron deficient N, occurs, the group trans to the –OH migrates.

Thus, a ketone is converted to amide.

6.4 Carbon Nucleophiles

The reaction of carbon nucleophiles with electron deficient carbon of a carbonyl group represents one of the major ways of making C–C bonds.

The addition of HCN to acetone to form cyanohydrin was one of the first reactions to be studied mechanistically.

CN may be hydrolysed to –COOH, or reduced to amine.

(i) Treatment with aq. NH₄Cl and NaCN
Hydrolysis of –CN in the amino nitrile gives α-amino acid. It is known as Strecker synthesis. (e.g. DL-alanine)

(ii) \[ \text{Me}_2\text{CHCH}_2\text{C} = \text{O} \xrightarrow{\text{HCN}, \text{NH}_3} \text{Me}_2\text{CHCH}_2\text{CH}_{\text{CN}} \xrightarrow{\text{H}^+} \text{Leu} \]

A carbanion C can form a p–d π bond with an adjacent P or S. The resulting charge delocalization is especially effective if P or S furnishing the empty d orbital, also has a + charge. Carbanions with these characteristics are called ylides.

- P-ylides change O of the carbonyl group to

\[ \text{C} \xrightarrow{\text{R'}} \text{R} \]

and the reaction is known as Wittig Reaction

- The ylide is prepared in two steps from RX.

\[ \text{Ph}_3\text{P} + \text{RCH}_2\text{X} \xrightarrow{\text{SN}_2} [\text{Ph}_3\text{PCH}_2\text{R}]^- \xrightarrow{\text{BuLi}} \text{Ph}_3\text{PCHR} + \text{C}_4\text{H}_{10} + \text{LiX}^- \]

- The carbanion formed (i.e., ylide) is due to elimination of a hydrogen halide from a phosphonium salt by a strong base, such as NaOH, BuLi, etc.

- The addition of these carbanions to a carbonyl group generates a dipolar intermediate, a betaine.

- Decomposition of this adduct with the formation of triphenyl phosphine oxide, brings about the regiospecific formation of an alkene from a carbonyl group.

- The P ylide may be obtained from a wide range of different halides, and thus ketones may be converted into a range of unsaturated compounds.
A useful reaction with the methoxymethylene Wittig reagent leads, via the acid-labile enol ether, to an aldehyde.

\[ \text{Ph}_3\text{P} + \text{CHO}_\text{Me} \rightarrow \text{HCl} \]

6.5 Reduction

- Aldehydes and ketones are reduced to corresponding 1° or 2° alcohol by LiAlH₄, NaBH₄, Na/EtOH or H₂/Pt.
- (a) Zn amalgam/conc. HCl reduce acetone to methylene (called as **Clemmensen Reduction**).
- (b) Use of hydrazone with alkali reduces ketone to – CH₂ group (called **Wolf-Kishner reduction**).
- Reagents such as Mg, or low valency states of Ti dissolving in acid – donate an electron to the carbonyl group to form a radical anion. The reductive process may be completed by the dimerization of these radicals to form 1,2-diols (pinacols) in case of Mg, or alkenes in case of Ti.

(c) **Meerwein – Pondorf Reduction**

- Al-tri-isopropoxide – is the reagent
- Transfer of hydride from isopropanol takes place.
Finally, all the three iso-propanol molecules are used to transfer one hydride each. Thus, three molecules of $2^\circ$ alcohol corresponding to original ketone are produced. Three molecules of acetone are produced corresponding to three molecules of iso-propyl alcohol attached to Al. Acetone is removed from the reaction to keep the equilibrium to RHS.

- The reverse reaction, i.e., conversion of i-PrOH to acetone is known as Oppenauer oxidation.

(d) Cannizzaro Reaction

Non-enolizable aldehydes (i.e., aldehydes having no $\alpha$-hydrogen), under alkaline conditions give this reaction where one molecule gets reduced and the other is oxidised. Thus, transfer of hydride from one molecule to the other takes place.

Formaldehyde makes a good hydride donor in a cross Cannizzaro reaction, e.g.

$$
\text{HCHO} + \text{CH}_2\text{CHO} \rightarrow \text{H}_2\text{C}+\text{H}_2\text{C} = \text{CHO}
$$

The product, pentaerythritol, may further react with one molecule of HCHO (work out the product).

6.6 Reactions of enolate anions

- An $\alpha$-carbanion is a nucleophile that can add to the carbonyl group of its parent compound.
- These reactions are **aldol condensations** leading to $\beta$-hydroxycarbonyl compounds.
- Aldol condensations are reversible.
- With ketones, the equilibrium is unfavourable for the condensation product – due to inductive/ steric effects.
To effect condensations of ketones, the product is continuously removed from the basic catalyst.

- β-hydroxycarbonyl compounds are readily dehydrated to give α-β-unsaturated carbonyl compounds.
- With Ar on the β-carbon, only the dehydrated product is isolated
- Aldol condensation is one of the most important methods of C – C bond formation.

\[
\begin{align*}
\text{Me} & \quad \text{H} \\
\text{CH}_2 & \quad \text{C} \\
\text{O} & \quad \text{H}
\end{align*}
\]

- Depending on the base, elimination of water may also take place to give an unsaturated ketone. This is an example of base catalysed dehydration.

\[
\begin{align*}
\text{Me} & \quad \text{C} \quad \text{CH}_2 \quad \text{CHO} \\
\text{H} & \quad
\end{align*}
\]

- A second condensation may also take place, for example:

\[
\begin{align*}
2\text{Me} & \quad \text{C} \quad \text{CH}_3 \\
\text{Ba(OH)}_2 & \quad
\end{align*}
\]

- If the carbonyl components are esters rather than ketones, stronger bases (e.g., sodium ethoxide) are required to generate the carbanions. This is known as **Claisen condensation**, and the product is a β-keto ester.
6.7 Other similar reactions

- There are large a number of variations on this general theme, in which both the source of the carbanion and the carbonyl recipient have been varied.
- The preparation of Cinnamic acid and its ester from benzaldehyde exemplify some of these reactions.

(a) Doebner-Knoevenagel condensation

(b) Perkin condensation

(i) Doebner-Knoevenagel condensation

(ii) Perkin condensation

(i) Perkin condensation
Perkin reaction requires:
- an aromatic aldehyde
- an aliphatic anhydride along with sodium or potassium salt of the corresponding carboxylic acid.

7. Properties of β-ketoesters

1. Acidity: Carbanion formation
   a resonance stabilized carbanion

\[
\text{CH}_3\text{C}\equiv\text{C}\equiv\text{C}\text{OC}_2\text{H}_5 + \text{NaOEt} \rightarrow \text{CH}_3\text{C}\equiv\text{C}\equiv\text{C}\text{OC}_2\text{H}_5
\]

2. Alkylation, either one or two \(R\)'s can be introduced

\[
\text{Na (CH}_3\text{COCH C OOC}_2\text{H}_5) + \text{RX} \rightarrow \text{CH}_3\text{COCH COOC}_2\text{H}_5 \rightarrow \text{CH}_3\text{COCH COOC}_2\text{H}_5 - \text{OEt}
\]

3. Hydrolysis and decarboxylation
   Dilute acid or base hydrolyses the \text{COOC}_2\text{H}_5 group

\[
\text{CH}_3\text{C}\equiv\text{C}\equiv\text{C}\text{OC}_2\text{H}_5 + \text{H}_3\text{O}^+ \rightarrow \text{C}_2\text{H}_5\text{OH} + \text{CH}_3\text{C}\equiv\text{C}\equiv\text{C}\text{O}\text{H}
\]

\[
\text{CH}_3\text{C}\equiv\text{C}\equiv\text{C}\text{H} + \text{CO}=\text{O}
\]

8. SUMMARY

1. The Chemistry of the carbonyl group is dominated by the electron deficiency of the carbon and its sensitivity to nucleophilic attack.
Protonation of the carbonyl oxygen increases the electron deficiency and thus many reactions are carried out with acid catalysis.

2. There is a tautometric relationship between carbonyl compounds and electron-rich enols that are susceptible to electrophilic attack.

3. O, S, N and C nucleophiles add to the carbonyl group to form acetals, thioketals, imines, and new C–C bonds.

4. Aldehydes may be distinguished from ketones by their ease of oxidation to acids.

5. The carbonyl group renders the hydrogen of an attached O–H, N–H or C–H acidic. The resultant anion is stabilized by resonance and acts as a nucleophile.

6. Tetrahedral intermediates are involved in the formation and reactions of esters and amides.

7. The acidity of C–H lying between two carbonyl groups leads to synthetically useful carbanions.

8. The aldol condensation involves the reaction between a carbanion from an aldehyde or ketone and a second carbonyl component and leads to a β-hydroxy ketone.

The claisen condensation between two molecules of an ester leads to a β-keto ester.

9. The reactions of nitriles, imines, nitroso, and nitro compounds show some parallels to carbonyl chemistry.

9. **Examples of carbonyl function reactions (Questions and answers)**

1. General reactions (reagents, conditions and products)

(a) Benzaldehyde + Tollen’s reagent  \[ \text{CH}_3\text{C}=-\text{O} + \text{NH}_2\text{Ag}^{+} \rightarrow \text{CH}_3\text{COO}^{-} \text{NH}_4^{+} \text{Ag} \]

(b) \[ \text{CH}_3\text{C}=-\text{O} + \text{HNO}_3 \xrightarrow{\Delta} \text{HOOC(CH}_2\text{)}_4 \text{COOH} \]

(c) \[ \text{CH}_3\text{CHO} + \text{dil. KmnO}_4 \rightarrow \text{CH}_3\text{COOH} \]

(d) \[ \text{C}_6\text{H}_5\text{CH}_2\text{CHO} + \text{LiAlH}_4 \rightarrow \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OH} \]

(e) methyl vinyl ketone + H_2/ Ni \[ \text{CH}_3\text{C}(-=\text{O})\text{HCH}=\text{CH}_2 \text{CH}_2\text{OH} \xrightarrow{\Delta} \text{CH}_3\text{CH}-\text{CH}-\text{CH}_2\text{OH} \text{ C}(-=\text{O}) \text{ reduced} \]

(f) methyl vinyl ketone + NaBH_4 \[ \text{CH}_3\text{C}(-=\text{O})\text{HCH}=\text{CH}_2 \text{CH}_2\text{OH} \xrightarrow{\Delta} \text{CH}_3\text{CH}-\text{CH}-\text{CH}_2\text{OH} \text{ (only }\text{C}(-=\text{O})\text{ reduced}) \]
2. Carbonyl protection by acetal formation

\[ \text{CH}_3\text{C}==\text{O} + \text{KMnO}_4 \rightarrow \text{CO}_2 + \text{CH}_3\text{CH}_2\text{COOH} + \text{CH}_3\text{COOH} \]

The –CHO is protected as an acetal and then generated. e.g.

\[ \text{H}_2\text{C}==\text{C}==\text{O} + \text{H}_2\text{N.NH} \rightarrow \text{C}==\text{NH} \]

3. Write structures for the cyclic ketals or acetals prepared from

(a) butanal + 1,3-propanediol (b) cyclohexanone + ethylene glycol
4. The bonds of cyclic thioketals prepared from HS.CH₂CH₂SH are reduced with Ni to \( \text{CH}_2 + \text{H}_2\text{Sg} \).

\[
\begin{array}{c}
\text{C}=\text{O} + \text{HS.CH}_2\text{CH}_2\text{SH} \xrightarrow{\text{ZnCl}_2} \text{C}-\text{S}-\text{C} \\
\xrightarrow{\text{H}_2/\text{Ni}} \text{CH}_3\text{CH}_3 + \text{H}_2\text{S} + \text{C}\\n\end{array}
\]

5. Synthesis of cyclo-octyne from \( (\text{CH}_2)_6 \text{COOC}_2\text{H}_5 \) and \( \text{C}_2\text{H}_5\text{O} \).

\[
\begin{array}{c}
\text{C}_2\text{H}_5\text{O} - \text{C} - (\text{CH}_2)_6 - \text{C} - \text{OC}_2\text{H}_5 \\
\xrightarrow{\text{Na}} \text{an acyloan} \\
\xrightarrow{\text{Zn-Hg, H}_3\text{O}^+} \text{cyclo-octanone} \\
\text{1,2-cyclooctadiene} \\
\text{1,8-diester} \\
\text{cyclo-octyne} \\
\text{an allene} \\
\end{array}
\]

The 1,8-diester is converted to an 8-membered ring acyloan, which is then changed to alkyne.

6. Answer the following based on the concepts of carbonyl group chemistry.

Q.1(a) Why is \(+\) PhCH(CH₃)CHO racemized by base?

(b) Why is \(+\) Ph—C—C—Ph.CH₂CH₃ is not racemized by base?

Ans (a) Base removes the \( \alpha\)-H to form an anion. The \( \alpha\)-C of the anion is no longer chiral. Return of an \( \text{H}^+ \) gives a racemic keto form.
(b) This ketone has no $\alpha$–H, and cannot form anion.

Q.2 Explain why formation of oximes and other ammonia derivatives requires slightly acidic media (pH $\approx$ 3.5) for maximum rate, while basic or strong acid conditions lower the rate.

Ans. Weak acidic media: $\overset{\oplus}{C} = O$ the caronyl group becomes more electrophilic and reactive.

Strongly acidic media: the electron pair on N is protonated to give $\overset{\oplus}{H_3N}$– which cannot react.

In basic media: there is no protonation of $\overset{\ominus}{C} = O$

Q.3 Symmetric ketones, $R_2C = O$, form a single oxime, but aldehydes and unsymmetric ketones may form two isomeric oximes. Explain.

Ans. The $\pi$ bond in $\overset{\ominus}{C} = N$ prevents free rotation, and therefore geometric isomerism occurs if the groups on the C are dissimilar.

Q.4 Why are oximes more acidic than hydroxylamine?

Ans. Loss of $H^+$ from $H_2NOH$ gives the conjugate base, $H_2NO^–$ with the charge localized on O. Delocalization of charge by extended $\pi$ bonding can occur in the conjugate base on the oxime.

Q.5 Devise a mechanism for the Cannizzaro reaction -

(i) $2 \text{ArCDO} \xrightarrow{\overset{\ominus}{\text{OH}}} \overset{\ominus}{\text{H}_2\text{O}} \text{ArCOO}^– + \text{ArCD}_2\text{OH}$

(ii) $2 \text{ArCHO} \xrightarrow{\overset{\ominus}{\text{OD}}} \overset{\ominus}{\text{D}_2\text{O}} \text{ArCOO}^– + \text{ArCH}_2\text{OH}$

Ans. The D’s from OD– and D$_2$O (solvent) are not found in the products. The molecule of ArCDO that is oxidized must transfer its D to the molecule that is reduced.
Q. 6. Which alkenes are formed from the following ylide carbonyl pairs?

<table>
<thead>
<tr>
<th>Ylide carbonyl pairs</th>
<th>Alkenes (products)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) 2-butanone and CH₃CH₂CH₂CH₂ = Pφ₃</td>
<td>CH₃CH₂CH=C(CH₂CH₃)</td>
</tr>
<tr>
<td>(b) Acetophenone and φ₃P = CH₂</td>
<td>C₆H₅CH=CH₂</td>
</tr>
<tr>
<td>(c) Benzaldehyde and C₆H₅–CH = Pφ₃</td>
<td>C₆H₅COCH=C₆H₅</td>
</tr>
<tr>
<td>(d) Cyclohexanone and (C₆H₅)₃P = C(CH₃)₂</td>
<td></td>
</tr>
</tbody>
</table>

The boxed portions come from the ylide.

Q. 7. Give structures of the ylide and carbonyl compound needed to prepare

- (a) φ–CH=CHCH₃
- (b) \[
\begin{array}{c}
\text{CH} \\
\text{H}
\end{array}
\]
- (c) CH₃CH₂C=CH(CH₃)₂
- (d) \[(\text{CH₃})₂C\text{O} \]

Ans

- (a) \[\phi₃P\text{CH}H \text{CH}_3 + \phi \text{CHO} \quad \text{or} \quad \phi₃P\text{CH}_6\text{H}_5 + \text{CH}_3\text{C}=\text{O}\]

The cis- and trans- geometry of the alkene is influenced by the nature of the substituents, solvents, and dissolved salts. Polar protic or aprotic solvents favor the cis-isomer.
10. Revision

Copy this revision chart showing the relationship between aldehydes and ketones and other functional groups, and fill in the relevant reagents and conditions for the inter-relationships beside the arrows.