Organic Chemistry

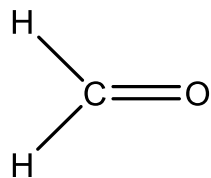## Aldehydes and Ketones

2nd Stage

Dr. Munther A. M. Ali
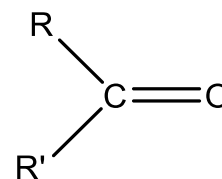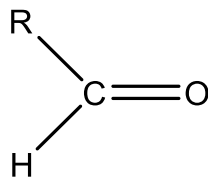
Part I

ALDYHYDES AND KETONES

Aldehydes are compounds of the general formula RCHO

Ketones are compounds of the general formula RR'CO

Aldehydes   A ketone

Both aldehydes and ketones contain the carbonyl group, C=O

This difference in structure affects their properties in two ways:
(a) Aldehydes are quite easily oxidized, whereas ketones are oxidized only with difficulty.
(b) Aldehydes are usually more reactive than ketones toward nucleophilic addition, the characteristic reaction of carbonyl compounds.

The structure of the carbonyl group

Carbonyl carbon is joined to three other atoms by bonds; since these bonds utilize *sp2* orbitals, they lie in a plane, and are 120 apart.

The remaining *p* orbital of the carbon overlaps a *p* orbital of oxygen to form a π bond; carbon and oxygen are thus joined by a double bond.

C–H σ bonds   C–O σ bond

lone pairs

C–O π bond

carbon and the oxygen are both sp^2
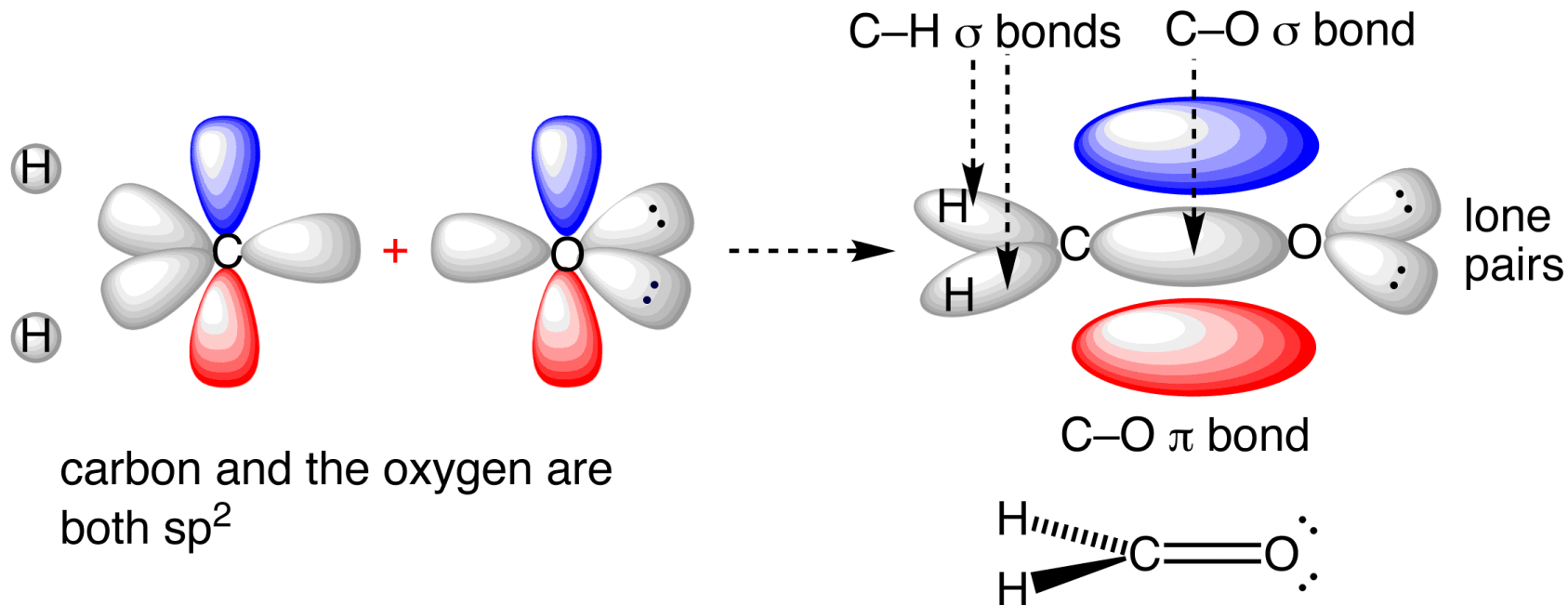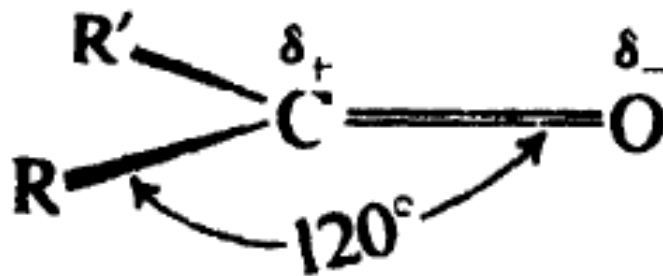
The electrons of the carbonyl double bond hold together atoms of quite different electronegativity, and hence the electrons are not equally shared; in particular, the mobile π cloud is pulled strongly toward the more electronegative atom, oxygen.
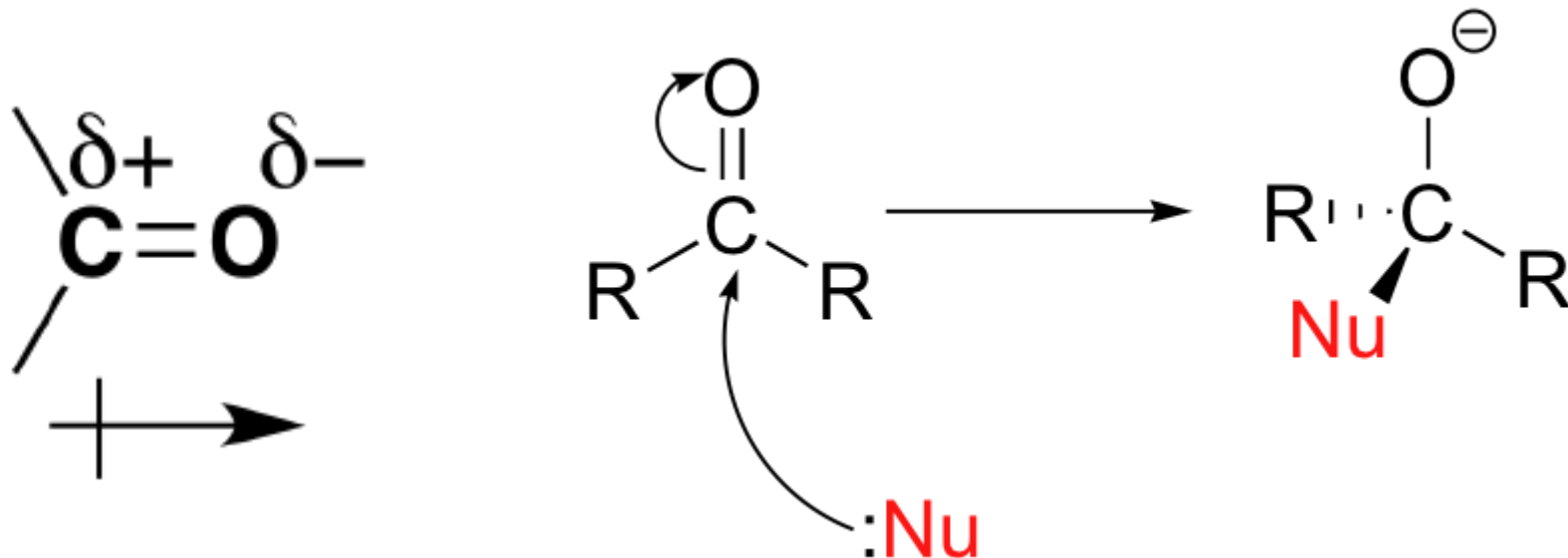
Nomenclature

Aldehydes

The common names of aldehydes are derived from the names of the corresponding carboxylic acids by replacing *-ic* add by *-aldehyde*.

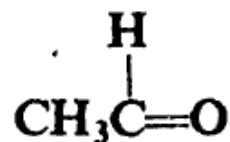| Common name of carboxylic acid	Formula	Common name of aldehydes	Formula
Form**ic** acid	HCOOH	Form**aldehyde**	HCHO
Acet**ic** acid	CH_3COOH	Acet**aldehyde**	CH_3CHO
Propion**ic** acid	CH_3CH_2COOH	Propio**aldehyde**	CH_3CH_2CHO

The IUPAC names of aldehydes:

The longest chain carrying the CHO group is considered the parent structure and is named by replacing the *-e* of the corresponding alkane by *-al.*

The position of a substituent is indicated by a number, the carbonyl carbon always being considered as C-l. Here we notice that C-2 of the IUPAC name corresponds to *alpha* α of the common name.
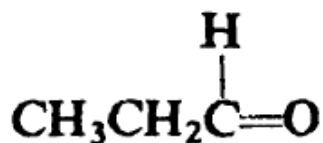
Formula	Common Name	Aldehyde	IUPAC Name
HCO_2H	formic acid	Formaldehyde	methanoic acid
CH_3CO_2H	acetic acid	Acetaldehyde	ethanoic acid
$CH_3CH_2CO_2H$	propionic acid	Propionaldehyde	propanoic acid
$CH_3(CH_2)_2CO_2H$	butyric acid	Butyraldehyde	butanoic acid
$CH_3(CH_2)_3CO_2H$	valeric acid	Veleraldehyde	pentanoic acid
$CH_3(CH_2)_4CO_2H$	caproic acid	Caproaldehyde	hexanoic acid
$CH_3(CH_2)_5CO_2H$	enanthic acid	Enanthaldehyde	heptanoic acid
$CH_3(CH_2)_6CO_2H$	caprylic acid	Caprylaldehyde	octanoic acid
$CH_3(CH_2)_7CO_2H$	pelargonic acid	Pelargonaldehyde	nonanoic acid
$CH_3(CH_2)_8CO_2H$	capric acid	Capraldehyde	decanoic acid

$$H-\overset{\overset{\displaystyle H}{|}}{C}=O$$
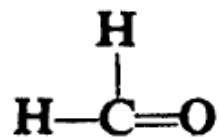
Formaldehyde
Methanal

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

Acetaldehyde
Ethanal

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

Propionaldehyde
Propanal

$$CH_3CH_2CH_2\overset{\overset{\displaystyle H}{|}}{C}=O$$

n-Butyraldehyde
Butanal

$$CH_3CH_2CH_2\overset{\alpha}{C}H\overset{\overset{\displaystyle H}{|}}{C}=O$$
$$\overset{\displaystyle |}{CH_3}$$
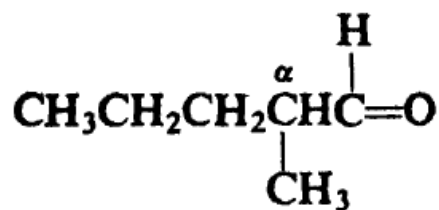
α-Methylvaleraldehyde
2-Methylpentanal

$$CH_3CH_2\overset{\beta}{C}HCH_2\overset{\overset{\displaystyle H}{|}}{C}=O$$
$$\overset{\displaystyle |}{CH_3}$$
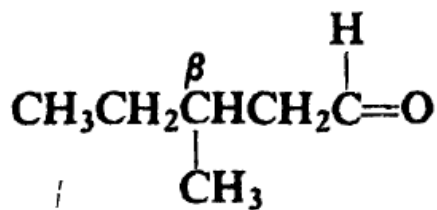
β-Methylvaleraldehyde
3-Methylpentanal

$$CH_3\overset{\gamma}{C}HCH_2CH_2\overset{\overset{\displaystyle H}{|}}{C}=O$$
$$\overset{\displaystyle |}{CH_3}$$
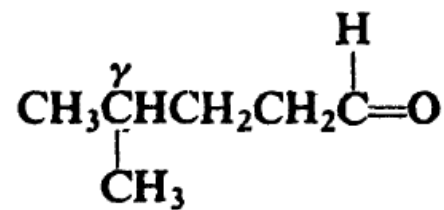
Isocaproaldehyde
γ-Methylvaleraldehyde
4-Methylpentanal

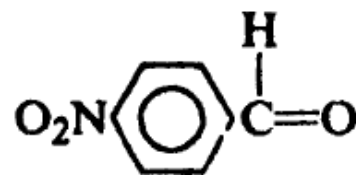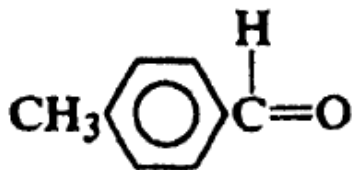❖ Aromatic aldehyde: derived from simplest benzaldehyde
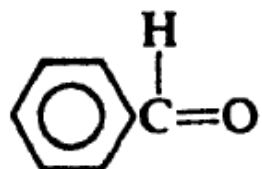
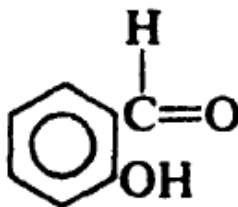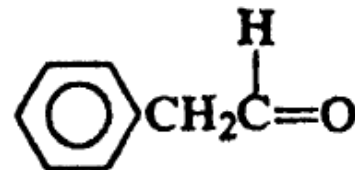
Benzaldehyde

p-Nitrobenzaldehyde

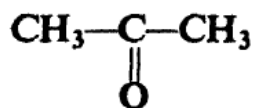p-Tolualdehyde

Salicylaldehyde
(o-Hydroxybenzaldehyde)

Phenylacetaldehyde
(Phenylethanal)

Ketones

❖ The simplest aliphatic ketone has the common name of acetone, CH_3COCH_3.

For most other aliphatic ketones we name the two groups that are attached to carbonyl carbon, and follow these names by the word ketone.

❖ According to the IUPAC system,

the longest chain carrying the carbonyl group is considered the parent structure, and is named by replacing the *-e* of the corresponding alkane with *-one*.

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

Acetone
Propanone

$$CH_3CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3$$
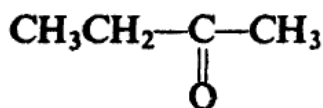
Methyl ethyl ketone
Butanone

$$CH_3CH_2CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3$$
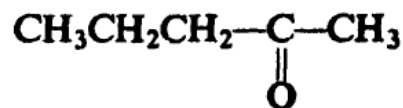
Methyl *n*-propyl ketone
2-Pentanone

$$CH_3CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-CH_2CH_3$$
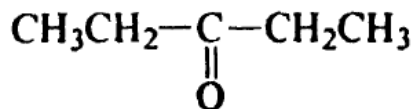
Ethyl ketone
3-Pentanone

$$CH_3\overset{\overset{\displaystyle CH_3}{|}}{CH}-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3$$
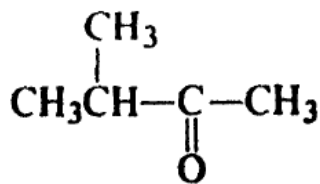
Methyl isopropyl ketone
3-Methyl-2-butanone

$$\text{⬡}CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-CH_3$$
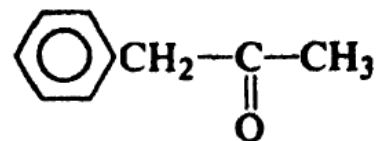
Benzyl methyl ketone
1-Phenyl-2-propanone

A ketone in which the carbonyl group is attached to a benzene ring is named as a *–phenone*.
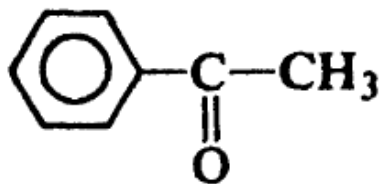
Acetophenone
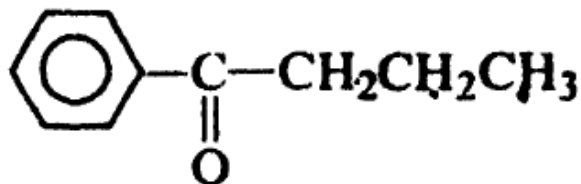
n-Butyrophenone
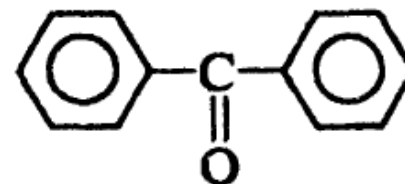
Benzophenone
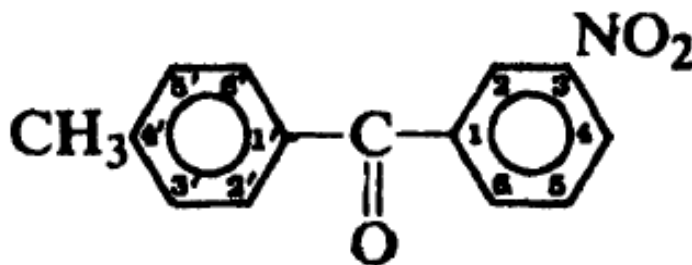
3-Nitro-4.'-methylbenzophenone

Physical properties

➢ The polar carbonyl group makes aldehydes and ketones polar compounds, and hence they have higher boiling points than non-polar compounds of comparable molecular weight.

For example; compare n-butyraldehyde (b.p, 76) and methyl ethyl ketone (b.p. 80) with n-pentane (b.p. 36).

➢ They are not capable of intermolecular hydrogen bonding; as a result they have lower boiling points than comparable alcohols or carboxylic acids.

For example; compare n-butyraldehyde (b.p, 76) and methyl ethyl ketone (b.p. 80) with n-butyl alcohol (b.p. 118) and propionic acid (b.p. 141).

➢ The lower aldehydes and ketones are appreciably soluble in water, borderline solubility is reached at about five carbons. Aldehydes and ketones are soluble in the usual organic solvents.

➢ Formaldehyde is a gas (b.p. -21), and is handled either as an aqueous solution (Formalin 37%), or as one of its solid polymers: paraformaldehyde $(CH_2O)n$, or trioxane, $(CH_2O)_3$.

~$CH_2OCH_2OCH_2O$~
Paraformaldehyde

Trioxane
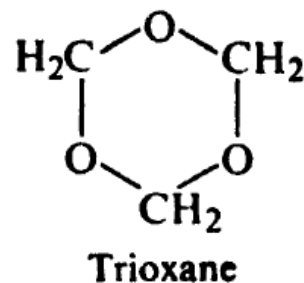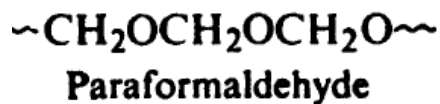
Preparation

Preparation of aldehydes

1. Oxidation of primary alcohols.

$$RCH_2OH \xrightarrow{K_2Cr_2O_7} R-\overset{\overset{\displaystyle H}{|}}{C}=O$$
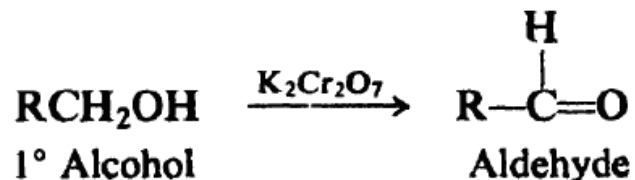
1° Alcohol   Aldehyde

Aldehydes may prepare by oxidation of primary alcohol by acidic dichromate, but the aldehydes are easily oxidized to carboxylic acids by the same reagent, therefore, the aldehyde must remove as fast as it is formed.

Specific reagent may be used to yield aldehyde without further oxidation reaction, as pyridinium chlorochromate.

Pyridinium chlorochromate

$CH_3CH_2CH_2CHO$ $\xrightarrow{\text{Pyridinium chlorochromate}}$ $CH_3CH_2CH_2CH_2OH$

n-Butyl alcohol   n-Butyraldehyde

1-Butanol   Butanal

2. Oxidation of methylbenzenes.

Oxidation of the side chain can be interrupted by trapping the aldehyde in the form of a non-oxidizable derivative, the gem-diacetate, which is isolated and then hydrolyzed.

$$ArCH_3 \xrightarrow[\text{CrO}_3, \text{ acetic anhydride}]{\text{Cl}_2, \text{ heat}} \begin{array}{c} ArCHCl_2 \xrightarrow{\text{H}_2\text{O}} \\ \text{gem-diacetate} \\ ArCH(OOCCH_3)_2 \xrightarrow{\text{H}_2\text{O}} \end{array} ArCHO$$

Examples:

$$Br\text{—}C_6H_4\text{—}CH_3 \xrightarrow{\text{Cl}_2, \text{ heat, light}} Br\text{—}C_6H_4\text{—}CHCl_2 \xrightarrow{\text{CaCO}_3, \text{ H}_2\text{O}} Br\text{—}C_6H_4\text{—}CHO$$

p-Bromotoluene   1-Bromo-4-dichloromethyl-benzene·   *p*-Bromobenzaldehyde

$$O_2N\text{—}C_6H_4\text{—}CH_3 \xrightarrow{\text{CrO}_3, \text{ Ac}_2\text{O}} O_2N\text{—}C_6H_4\text{—}CH(OAc)_2 \xrightarrow{\text{H}_2\text{O}, \text{ H}_2\text{SO}_4} O_2N\text{—}C_6H_4\text{—}CHO$$

p-Nitrotoluene   *p*-Nitrobenzaldehyde

3. Reduction of acid chlorides.

$$\text{RCOCl} \quad \text{or} \quad \text{ArCOCl} \xrightarrow{\text{LiAlH(Bu-}t)_3} \text{RCHO} \quad \text{or} \quad \text{ArCHO}$$

Acid chloride   Aldehyde

Examples:

$$O_2N\text{—}C_6H_4\text{—}\text{COCl} \xrightarrow{\text{LiAlH(Bu–}t)_3} O_2N\text{—}C_6H_4\text{—}\text{CHO}$$

p-Nitrobenzoyl chloride   *p*-Nitrobenzaldehyde
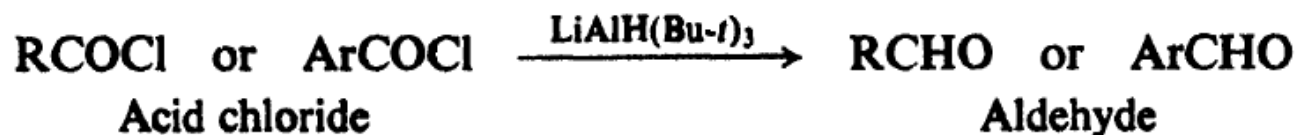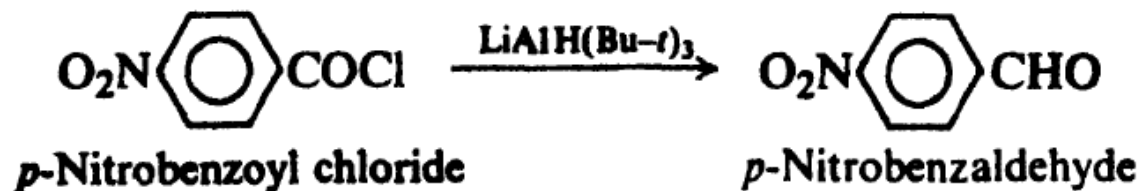
LiAlH(Bu-*t*)$_3$ = Lithium tri-t-butoxy aluminum hydride , reducing agent

4. Reimer-Tiemann reaction. Phenolic aldehydes.
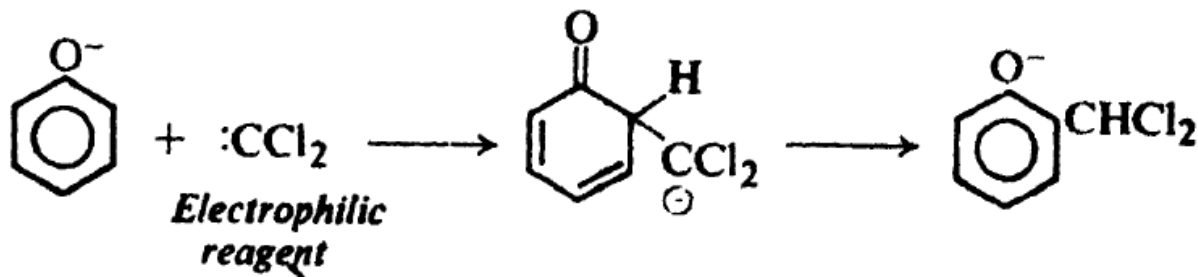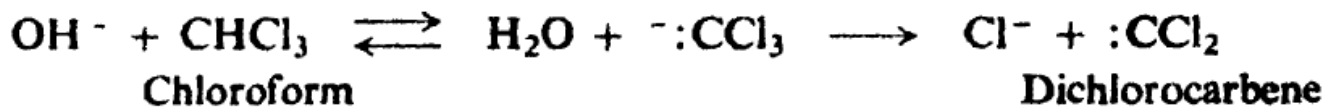
Treatment of a phenol with chloroform and aqueous hydroxide introduces an aldehyde group, -CHO, into the aromatic ring, generally ortho to the -OH. For example:
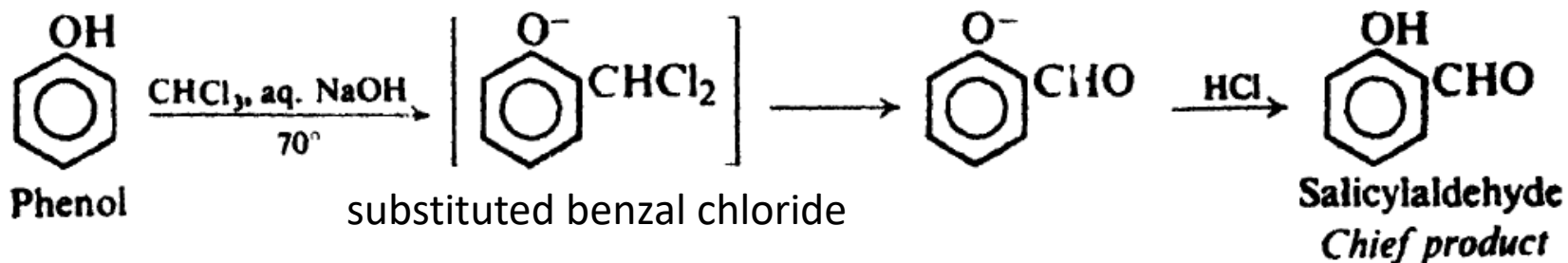
The Reimer-Tiemann reaction involves electrophilic substitution on the highly reactive phenoxide ring. The electrophilic reagent is dichlorocarbene, :CCl$_2$, generated from chloroform by the action of base.

$$OH^- + CHCl_3 \rightleftharpoons H_2O + {}^-:CCl_3 \longrightarrow Cl^- + :CCl_2$$

Chloroform   Dichlorocarbene

1   KOH   **2**   **3**

4   KOH   **5**   **3**   **6**

9   **8**   KOH   **7**
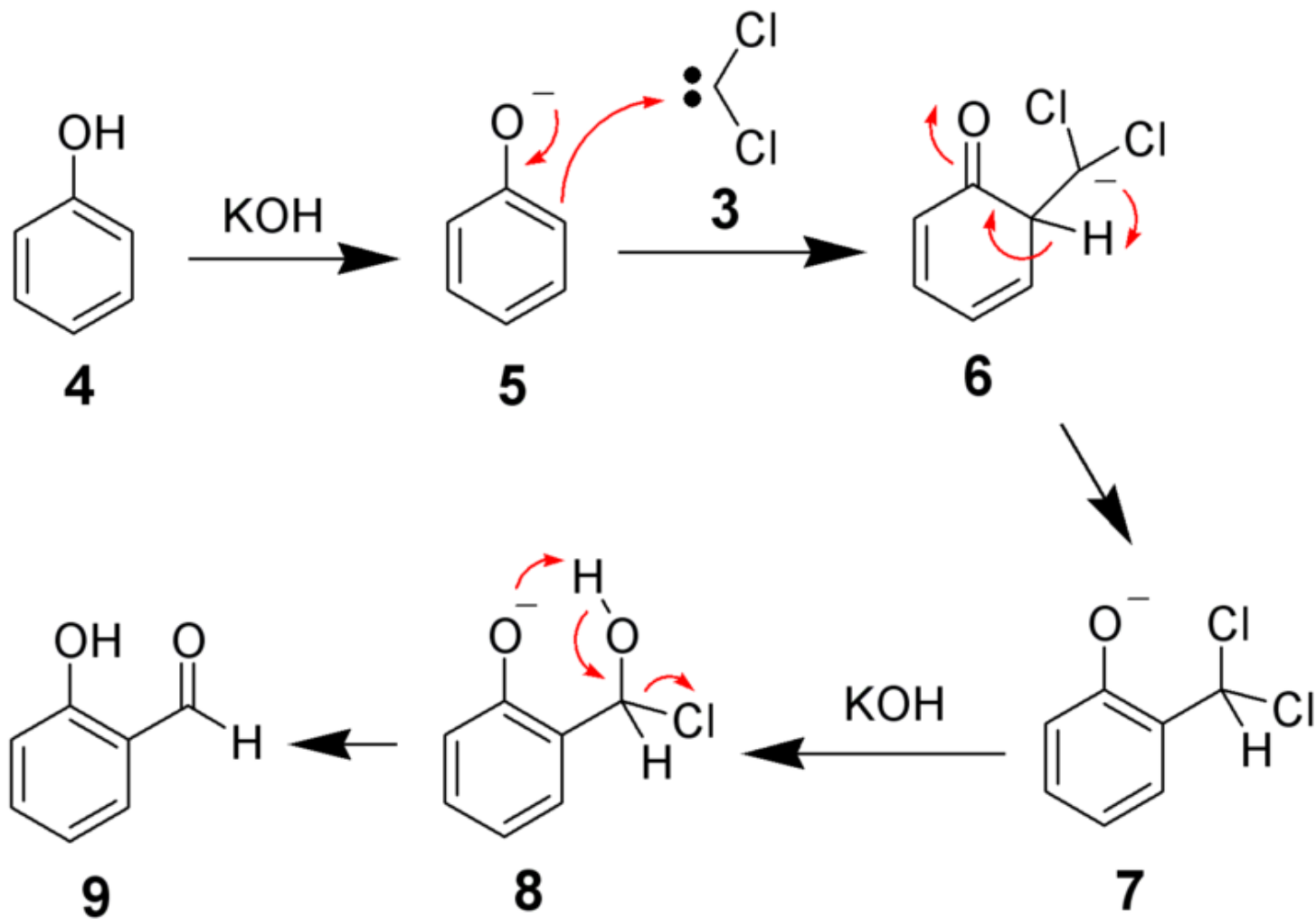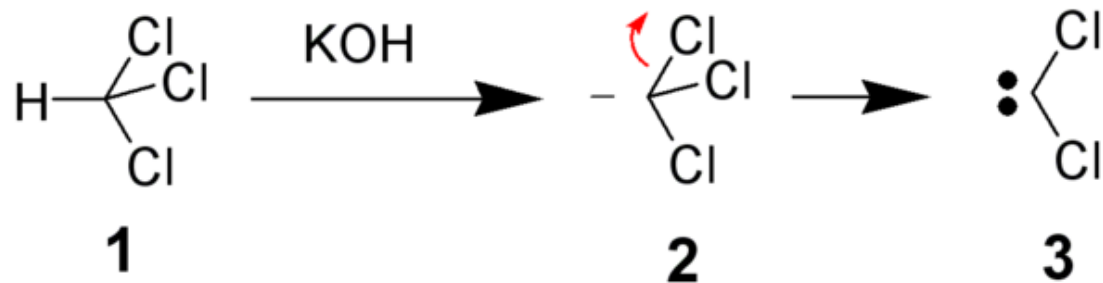
Preparation of ketones

1. Oxidation of secondary alcohols.

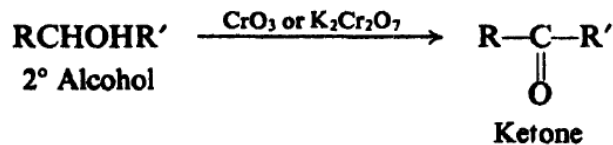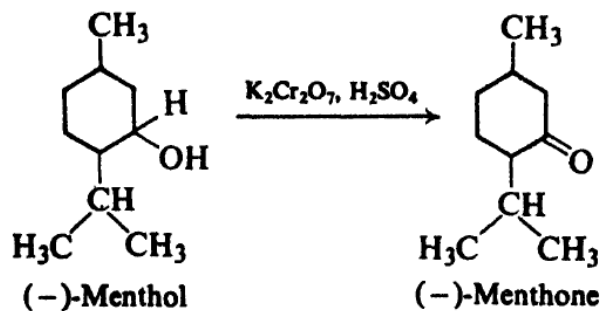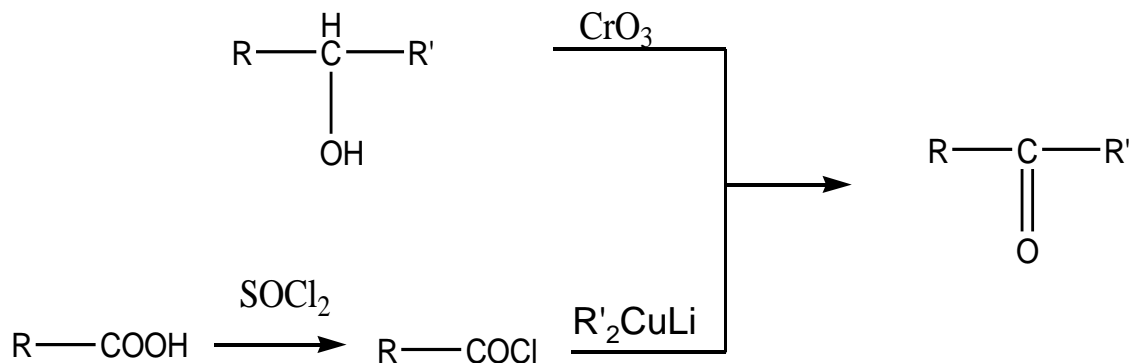Aliphatic ketones are readily prepared from the corresponding secondary alcohols.
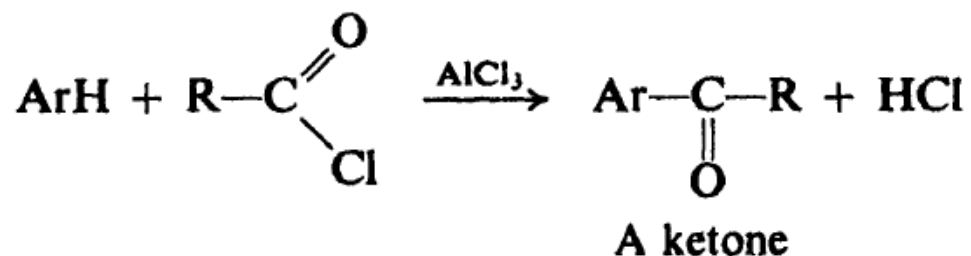

More complicated aliphatic ketones can be prepared by the reaction of acid chlorides with organocopper compounds.

2. Friedel-Crafts acylation.

An acyl group, RCO-, becomes attached to the aromatic ring, thus forming a ketone; the process is called **acylation**.
As usual for the Friedel-Crafts reaction catalysis by aluminum chloride or another Lewis acid is required.

$$ArH + R-C\overset{\displaystyle O}{\underset{\displaystyle Cl}{\big<}} \xrightarrow{AlCl_3} Ar-\underset{\displaystyle O}{\overset{}{C}}-R + HCl$$

$$A\ ketone$$

The most likely mechanism for Friedel-Crafts acylation and involves the following steps:

(1) $RCOCl + AlCl_3 \longrightarrow RC\overset{\oplus}{\equiv}O + AlCl_4^-$

(2) $ArH + RC\overset{\oplus}{\equiv}O \longrightarrow Ar\overset{\displaystyle H}{\underset{\displaystyle COR}{\big<}}$

(3) $\overset{\oplus}{Ar}\overset{\displaystyle H}{\underset{\displaystyle COR}{\big<}} + AlCl_4^- \longrightarrow Ar-\underset{\displaystyle O}{\overset{}{C}}-R + HCl + AlCl_3$
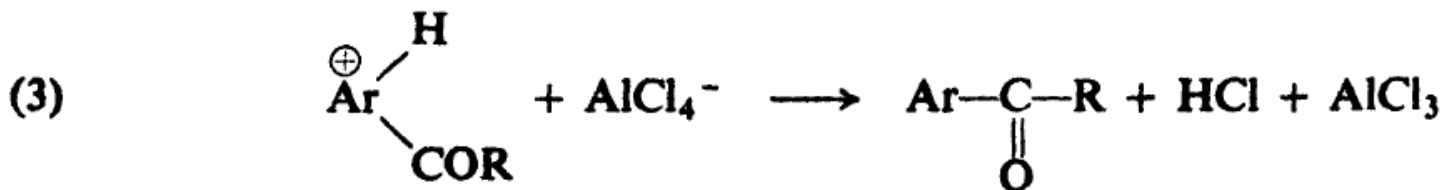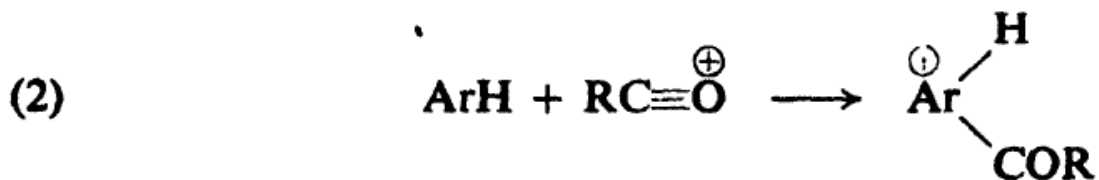
MECHANISM FOR THE FRIEDEL-CRAFTS ACYLATION OF BENZENE

Step 1:
The acyl halide reacts with the Lewis acid to form a complex.

Step 2:
Loss of the halide to the Lewis acid forms the electrophilic acylium ion.
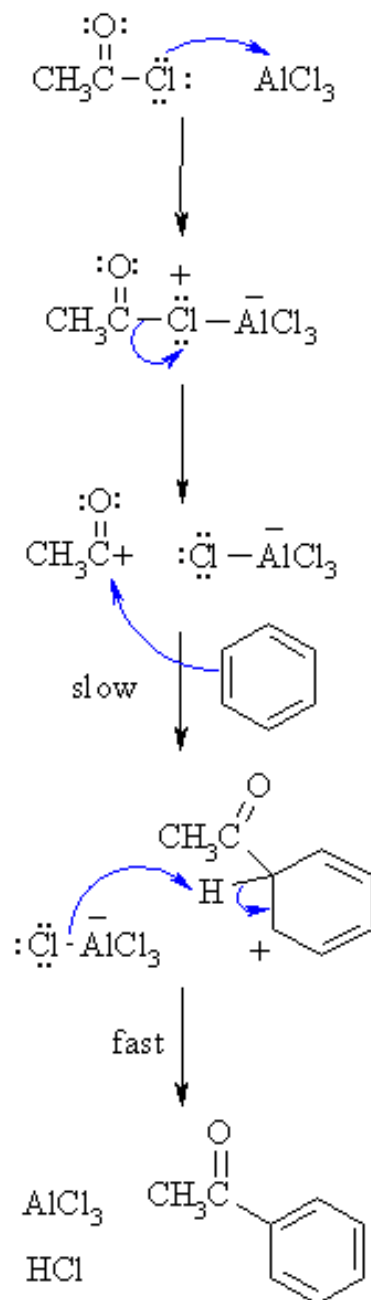
Step 3:
The p electrons of the aromatic **C=C** act as a nucleophile, attacking the electrophilic C+. This step destroys the aromaticity giving the cyclohexadienyl cation intermediate.

Step 4:
Removal of the proton from the sp^3 C bearing the acyl- group reforms the **C=C** and the aromatic system, generating HCl and regenerating the active catalyst.

$$CH_3C-Cl: \quad AlCl_3$$

$$CH_3C-Cl-\bar{A}lCl_3$$

$$CH_3C+ \quad :Cl-\bar{A}lCl_3$$

slow

$$:Cl-\bar{A}lCl_3$$

fast

$$AlCl_3 \quad CH_3C$$

$$HCl$$

In the preparation of m-nitrobenzophenone, for example, the nitro group can be present in the acid chloride but not in the ring undergoing substitution, since as a strongly deactivating group it prevents the Friedel-Crafts reaction.
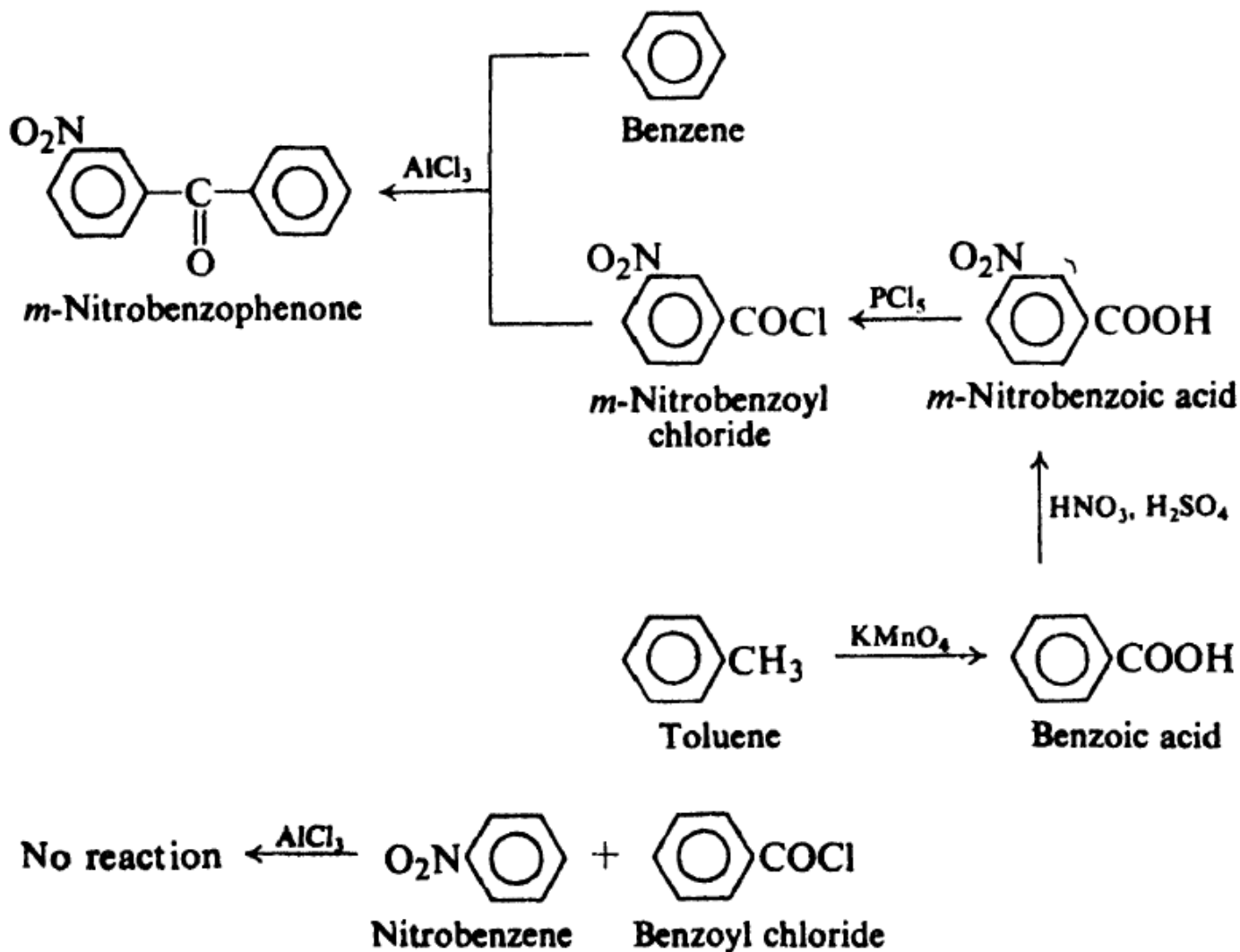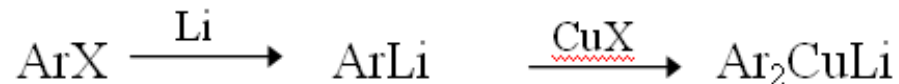
3. Reaction of acid chlorides with organocopper compounds.

Treatment of alkyl or aryl halides with lithium metal gives organolithium compounds which on treatment with a cuprous halides form lithium organocuprates, **R$_2$CuLi** or **Ar$_2$CuLi**.

$$RX \xrightarrow{\text{Li}} RLi \xrightarrow{\text{CuX}} R_2CuLi$$

$$ArX \xrightarrow{\text{Li}} ArLi \xrightarrow{\text{CuX}} Ar_2CuLi$$

Lithium organocuprates react readily with acid chlorides to yield ketones:

An acid chloride   A ketone
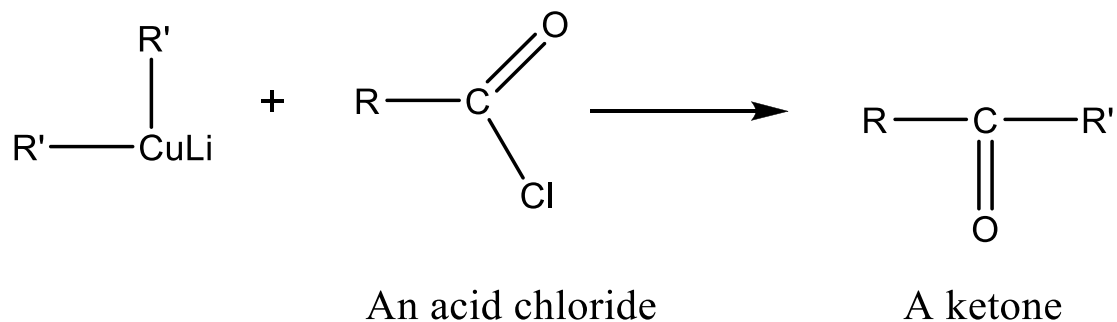
4. Acetoacetic ester synthesis.

using of ethyl acetoacetate (acetoacetic ester), $CH_3COCH_2COOC_2H_5$.
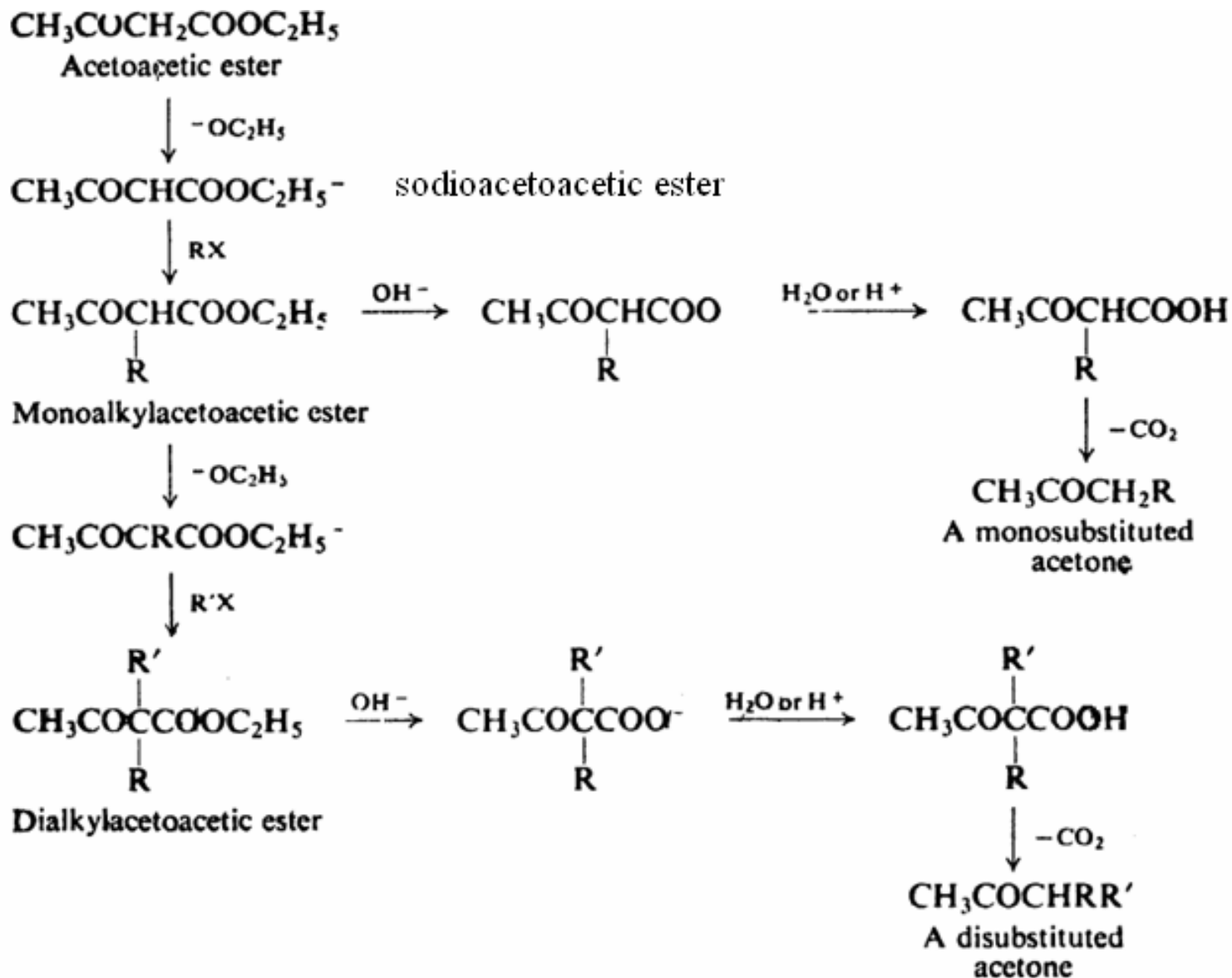

$CH_3COCH_2COOC_2H_5$
Acetoacetic ester

↓ $^-OC_2H_5$

$CH_3COCHCOOC_2H_5^-$ sodioacetoacetic ester

↓ RX

$CH_3COCHCOOC_2H_5$ $\xrightarrow{OH^-}$ $CH_3COCHCOO$ $\xrightarrow{H_2O\,or\,H^+}$ $CH_3COCHCOOH$
|R |R |R
Monoalkylacetoacetic ester

↓ $^-CO_2$

CH_3COCH_2R
A monosubstituted acetone

↓ $^-OC_2H_5$

$CH_3COCRCOOC_2H_5^-$

↓ R'X

R'   R'   R'
| | |
$CH_3COCCOOC_2H_5$ $\xrightarrow{OH^-}$ $CH_3COCCOO^-$ $\xrightarrow{H_2O\,or\,H^+}$ $CH_3COCCOOH$
|R |R |R
Dialkylacetoacetic ester

↓ $^-CO_2$

$CH_3COCHRR'$
A disubstituted acetone

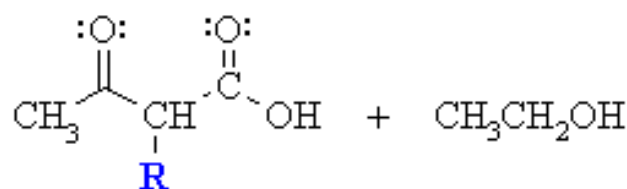# OVERVIEW OF ACETOACETIC ESTER SYNTHESIS

Step 1:
First, an acid-base reaction. Ethoxide functions as a base and removes the acidic α-hydrogen giving the reactive enolate which is then alkylated.
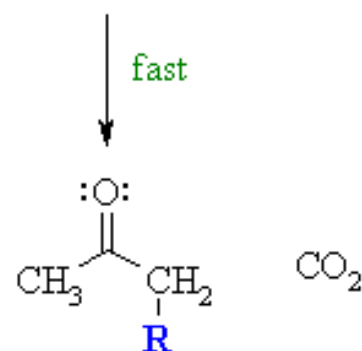
1. NaOEt
2. R–X
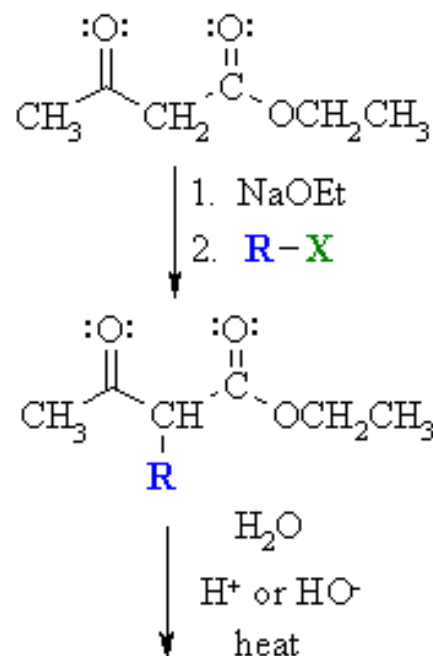
Step 2:
Acid or base catalysed hydrolysis of the ester to the parent carboxylic acid.
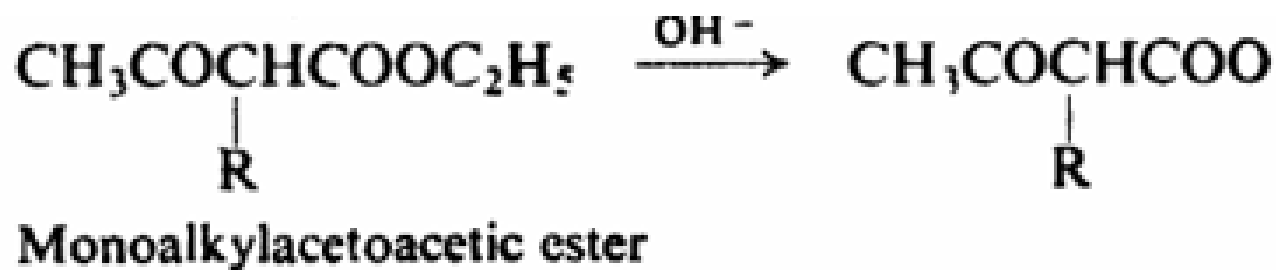
H_2O
H^+ or HO^-
heat

fast

Step 3:
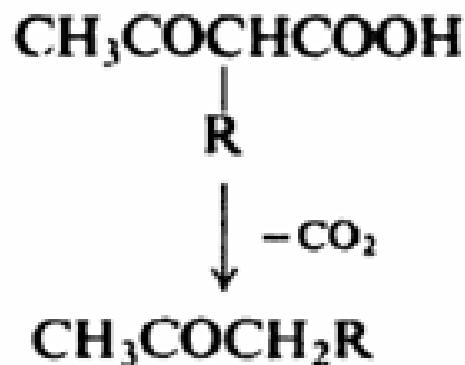Loss of CO_2 = decarboxylation, readily occurs giving a substituted ketone.

In the acetoacetic ester synthesis, give the mechanism of the following:

1- Hydrolysis of ester in the alkaline condition.

$$CH_3COCHCOOC_2H_5 \xrightarrow{OH^-} CH_3COCHCOO$$

$$\underset{R}{\mid} \qquad\qquad \underset{R}{\mid}$$

Monoalkylacetoacetic ester

2- Thermal decarboxylation

$$CH_3COCHCOOH$$
$$\underset{R}{\mid}$$
$$\downarrow -CO_2$$
$$CH_3COCH_2R$$

3- Use acetoacetic ester method to prepare ethyl methyl ketone.