NATIONAL OPEN UNIVERSITY OF NIGERIA

SCHOOL OF SCIENCE AND TECHNOLOGY

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# Module 1: Alcohols and Their Reactions

## Unit 1: Classes, Structures and Naming Of Alcohols

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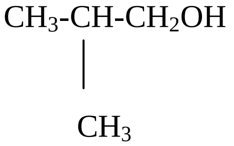
## 1.0 Introduction

Alcohols are compounds in which a hydrogen of an alkane has been replaced by an -OH group. They have –OH group (a hydroxyl) bonded to a saturated alkane like carbon atom R-OH where R is any simple alkyl or substituted alkyl group.

For example:

| | |
|---|---|
| $CH_3OH$ | $CH_3CH_2OH$ |
| methanol | ethanol |



$CH_3\text{-}\underset{\underset{CH_3}{|}}{CH}\text{-}CH_2OH$

2-methyl propan-1-ol

## 2.0 Objectives

At the end of this unit, you should be able to:

(a) Classify alcohols into monohydric, dihydric and polyhydric
(b) Classify monohydric alcohols into primary($1^o$),secondary($2^o$) and tertiary($3^o$) alcohols
(c) Draw the structure of simple alcohols
(d) Give the names of alcohols using the IUPAC system

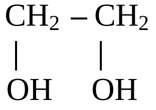
## 3.0 Classes of Alcohols

Alcohols can contain one or more hydroxyl group. It could be:

i. Monohydric – contain only one hydroxyl group. For example, ethanol.

$CH_3\text{-}CH_2\text{-}CH_2\text{-}OH$
Ethanol

ii. Dihydric- contain two hydroxyl groups. For example ethane-1,2-diol.



$\underset{OH}{\underset{|}{CH_2}} - \underset{OH}{\underset{|}{CH_2}}$

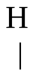
iii. Trihydric- contains three hydroxyl groups. For example, propane-1, 2, 3-triol.

Generally with more than one hydroxyl group, it is said to be **polyhydric**.

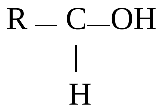
Monohydric alcohols have the general formula $C_nH_{2n+1}OH$. They can be classified into three classes - primary ($1^o$), secondary ($2^o$) and tertiary alcohol ($3^o$) according to the number of alkyl groups attached to the hydroxyl-bonded carbon atom.

(i) Primary alcohol (l°)

It has one alkyl group attached to the hydroxyl bonded carbon atom.

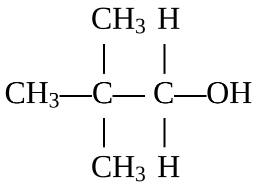


$\overset{H}{|}$



$$\begin{array}{ccccc} \mathrm{R} & - & \mathrm{C} & - & \mathrm{OH} \\ & & | & & \\ & & \mathrm{H} & & \end{array}$$

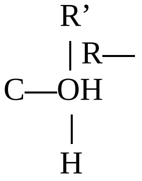
For example, $CH_3OH$ $CH_3CH_2OH$
Methanol Ethanol



$$\begin{array}{ccccccc} & & \mathrm{CH_3} & & \mathrm{H} & & \\ & & | & & | & & \\ \mathrm{CH_3} & - & \mathrm{C} & - & \mathrm{C} & - & \mathrm{OH} \\ & & | & & | & & \\ & & \mathrm{CH_3} & & \mathrm{H} & & \end{array}$$

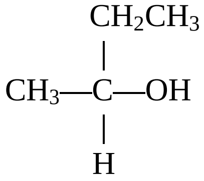
2,2-dimethylpropan-1-ol

Secondary alcohol ($2^o$):
There are two alkyl groups attached to the hydroxyl-bonded carbon atom.



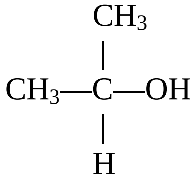
$$\begin{array}{l} \quad \mathrm{R'} \\ \quad | \; \mathrm{R-} \\ \mathrm{C-OH} \\ \quad | \\ \quad \mathrm{H} \end{array}$$

For example:



$$\begin{array}{ccccc} & & \mathrm{CH_2CH_3} & & \\ & & | & & \\ \mathrm{CH_3} & - & \mathrm{C} & - & \mathrm{OH} \\ & & | & & \\ & & \mathrm{H} & & \end{array}$$

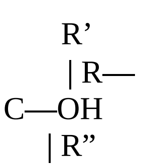
Butan-2-ol



$$\begin{array}{ccccc} & & \mathrm{CH_3} & & \\ & & | & & \\ \mathrm{CH_3} & - & \mathrm{C} & - & \mathrm{OH} \\ & & | & & \\ & & \mathrm{H} & & \end{array}$$

Propan-2-ol

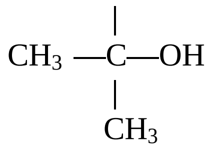
Tertiary ($3^o$):
There are three alkyl groups, but no hydrogen atom directly attached to the hydroxyl-bonded carbon atom.



$$\begin{array}{l} \quad \mathrm{R'} \\ \quad | \; \mathrm{R-} \\ \mathrm{C-OH} \\ \; | \; \mathrm{R''} \end{array}$$

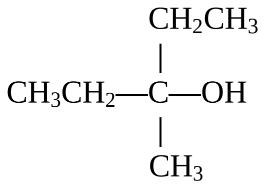
For example:

$CH_3$



$$\begin{array}{ccc} & | & \\ \mathrm{CH_3}\text{—} & \mathrm{C} & \text{—OH} \\ & | & \\ & \mathrm{CH_3} & \end{array}$$

2—methyl propan—2—ol



$$\begin{array}{ccc} & \mathrm{CH_2CH_3} & \\ & | & \\ \mathrm{CH_3CH_2}\text{—} & \mathrm{C} & \text{—OH} \\ & | & \\ & \mathrm{CH_3} & \end{array}$$

3—methylpentan—3—ol

## ACTIVITY A/Self Assessment Exercise

(i) Draw the structure of the following alcohols and classify each as1° 2° or 3° alcohol.

- (i) Butan—1—o1
- (ii) 2—methylpentan—2—ol
- (iii) Pentan—2—ol

## 3.1 Naming Alcohols

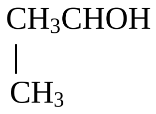
### a. Common names

Simple alcohols are often called by their common names which consists of the name of the alkyl group to which the –OH group is attached followed by the word ‘alcohol’.

For example,

$CH_3OH$
Methyl alcohol

$CH_3CH_2OH$
Ethyl alcohol



$$\begin{array}{l} \mathrm{CH_3CHOH} \\ | \\ \mathrm{CH_3} \end{array}$$

Isopropyl alcohol

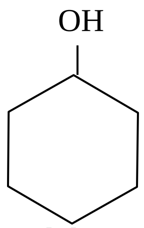
### b. IUPAC names

In the IUPAC system, alcohols are named as alkanols and their names are derived from the parent alkane by replacing the ‘e’ from the parent hydrocarbon and adding the suffix ‘ol’.
For example:

$CH_3CH_2OH$
Ethanol

$CH_3CH_2CH_2OH$
Propanol

For a cyclic alcohol, the –ol ending is added to the parent cycloalkane. For example,

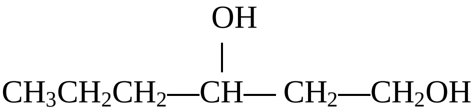


Cyclohexanol

## c. Glycols

Dialcohols or diols are called glycols. They are named as derivatives of the parent hydrocarbon with the –diol name ending added. The –OH groups are added as prefixes.
For example:

$HOCH_2CH_2OH$
1, 2—Ethanediol



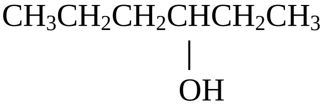
$$CH_3CH_2CH_2\text{—}\overset{\overset{OH}{|}}{C}H\text{—}CH_2\text{—}CH_2OH$$

1, 3—hexanediol

**Activity B/Self Assessment Exercise**

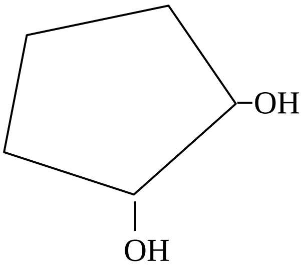
Give systematic names for the following compounds

(i)



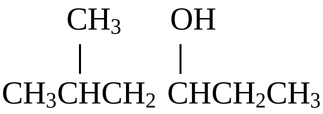
$$CH_3CH_2CH_2\underset{\underset{OH}{|}}{C}HCH_2CH_3$$

(ii)



(iii) $CH_3CHCH_2OH$

(iv)



$$CH_3\overset{\overset{CH_3}{|}}{C}HCH_2\,\overset{\overset{OH}{|}}{C}HCH_2CH_3$$

## 3.2 Physical Properties of Alcohols

3.2.1 Physical Appearance

Most simple alcohols are liquid at room temperature. Alcohols with more than twelve carbon atoms are waxy solid at room temperature.

3.2.2 Melting and boiling point

Like the parent hydrocarbon, the boiling points among the alcohols increase steadily with increase in the number of carbon atoms. The boiling point of alcohols are very high compared with that of the corresponding alkane because of their ability to form hydrogen bond between the hydrogen atom of the hydroxyl group and the oxygen atom of another molecule

The influence of the —OH group however becomes less significant as the carbon skeleton increases.

The order of boiling points of isomeric alcohols is

1° alcohol >2° alcohols >3° alcohols.

3.2.3 Density

The density of alcohols increases with increasing relative molecular mass, however, branching can reduce this effect.

All simple alcohols are less dense than water, but the aromatic homologues are slightly denser than water.

3.2.4 Solubility

Hydrogen bonding in alcohols influences their solubility in water. Alcohols with a relatively short carbon skeleton are soluble in water. For example methane, ethanol, propan-1-o1 and propan-2-o1 are completely miscible with water in all chains increases, the solubility of alcohols drop drastically.

All alcohols are miscible with most organic solvents such as hexane, benzene and ethanol; the smaller ones are useful organic solvents.

## Activity C/Self Assessment Exercise

Arrange the following in increasing order of solubility:
2-methyl propan-1-ol, ethanol, butan-1-ol

## 4.0 Conclusion

Alcohols can be monohydric, dihydric or trihydric.
Monohydric alcohol can be further classified into primary, secondary and tertiary alcohols and the simple ones are miscible with water because of H-bonding.

The names of alcohols are derived from the parent hydrocarbon by replacing the ‘e’ from the name of the parent alkane with ‘-ol’.

## 5.0 Summary

In this unit we have learnt that:

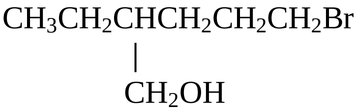
i. Alcohols are compounds in which a hydrogen of alkane has been replaced by an -OH group
ii. Alcohol can be monohydric, dihydric, trihydric or polyhydric
iii. Monohydric alcohols can be classified into $1^o$, $2^o$ and $3^o$ alcohol
iv. In naming alcohols, the ‘e’ from the corresponding alkane is replaced with ‘ol’.

## 6.0 Tutor Marked Assignment

1. Draw the structures of the following alcohols and identify each of the alcohols as primary secondary and tertiary.
   (a) 3-Chloro-1-propanol (b) 2-methyl-4-heptanol (c) 2-Butanol
   (d) 3- methyl-3-pentanol (e) Cyclohexanol

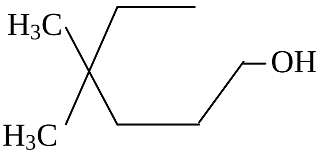
2. Give the IUPAC names for the following compounds:

(a)

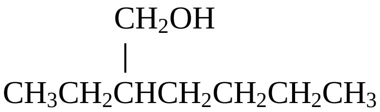


$CH_3CH_2\underset{\underset{CH_2OH}{|}}{CH}CH_2CH_2CH_2Br$

(b)



(b)



$CH_3CH_2\overset{\overset{CH_2OH}{|}}{CH}CH_2CH_2CH_2CH_3$

## 7.0 Further Reading and Other Resources

i. K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry -Third Edition

ii. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry - Sixth Edition

# Unit 2: Preparation of Alcohols

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## 1.0: Introduction

Alcohol may be prepared using the following methods

## 2.0: Objectives

At the end of this unit, you should be able to

(a) List the different methods of preparing alcohols
(b) Discuss using equations, the different methods of preparing alcohols
(c) State the conditions of preparation for the different methods
(d) Discuss the production of alcohol from fermentation

## 3.1 Hydrolysis of halogenoalkanes

This reaction is suitable for the preparation of primary, secondary and tertiary alcohols. All halogenoalkane when heated under reflux with aqueous potassium hydroxide solution are hydrolysed to yield an alcohol

$$RX + KOH \underset{reflux}{\rightleftharpoons} ROH + X^-$$

Where X= $I^-$ , $Br^-$ , $Cl^-$ and R= alkyl group

The ease of reaction of the halogenoalkanes follows the order

$RI > RBr > RCl$

## 3.2 Hydration of alkene

This reaction is simply the addition of water molecule to the alkene to form the corresponding alcohol. It involves the addition of concentrated tetraoxosulphate (VI) acid first to the alkene to give alkyl hydrogen tetraoxosulphate (VI) which when treated with water (hydrolysis), gives an alcohol.

For example, the formation of ethanol:

$$CH_2 = CH_2 + \underset{\text{conc .}}{H_2SO_4} \longrightarrow \underset{\text{ethyl hydrogen tetraoxosulphate (vi)}}{CH_3-CH_2HOSO_3} + H_2$$

$$CH_3-CH_2HOSO_3 + H_2O \longrightarrow \underset{\text{Ethanol}}{CH_3CH_2OH} + H_2SO_4$$

Industrially, hydration of ethane is carried out in the vapour phase using tetraoxophosphate (V) acid supported on silicon (VI) oxide as a catalyst. The reaction is carried out at high temperature and under pressure.

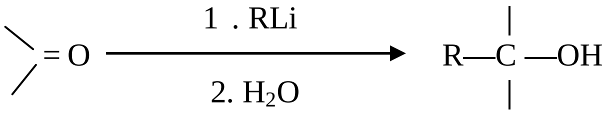
$$CH_2 = CH_2(g) + H_2O(g) \xrightarrow[33^{O}C,\ 60atm]{H_3PO_4 \text{ on } SiO_2} CH_3CH_2OH(g)$$

## 3.3 Reduction of Aldehydes and ketones

### 3.3.1 Addition of organometallic reagents to Aldelydes and ketones

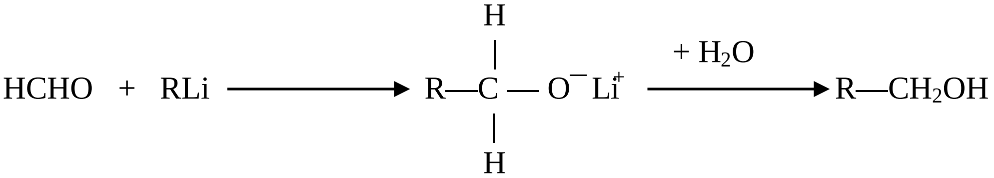
Organometallic reagents (RLI or RMgX) react with aldehydes and ketones to give alcohols.

Use of RLi

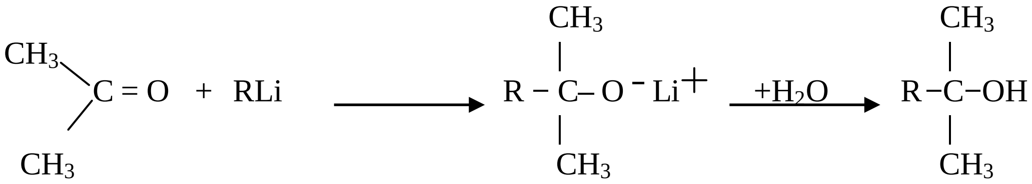


$$>C=O \xrightarrow[2.\ H_2O]{1\ .\ RLi} R-\overset{|}{\underset{|}{C}}-OH$$

This reaction can be used to prepare primary, secondary and tertiary alcohols.
For example:

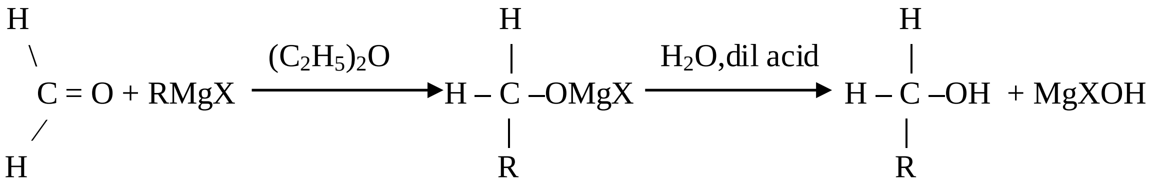


$$HCHO + RLi \longrightarrow R-\overset{H}{\underset{H}{C}}-O^{-}Li^{+} \xrightarrow{+H_2O} R-CH_2OH$$



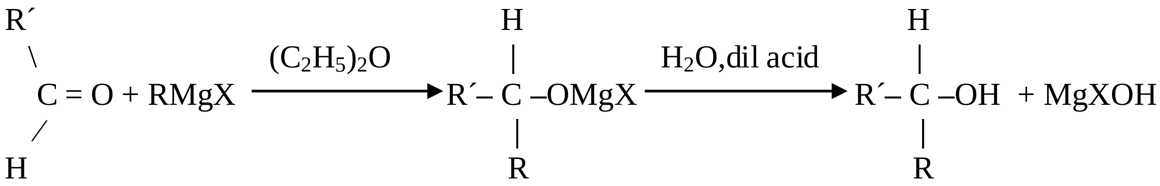
$$(CH_3)_2C=O + RLi \longrightarrow R-\overset{CH_3}{\underset{CH_3}{C}}-O^{-}Li^{+} \xrightarrow{+H_2O} R-\overset{CH_3}{\underset{CH_3}{C}}-OH$$

Reaction with RMgX
In this reaction the intermediate alkylmagnesium halide is hydrolysed using dilute acid or aqueous ammonium chloride in the case of tertiary alcohols



$$H_2C=O + RMgX \xrightarrow{(C_2H_5)_2O} H-\overset{H}{\underset{R}{C}}-OMgX \xrightarrow{H_2O,\text{dil acid}} H-\overset{H}{\underset{R}{C}}-OH + MgXOH$$

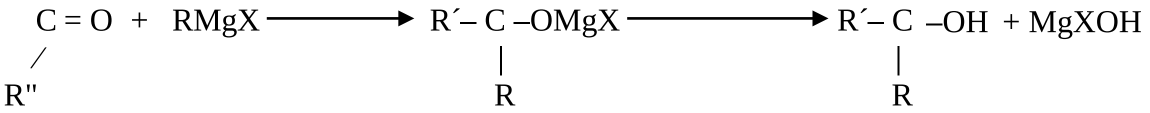
Methanal 1$^o$ alcohol



$$R'HC=O + RMgX \xrightarrow{(C_2H_5)_2O} R'-\overset{H}{\underset{R}{C}}-OMgX \xrightarrow{H_2O,\text{dil acid}} R'-\overset{H}{\underset{R}{C}}-OH + MgXOH$$

Aldehyde 2$^o$ alcohol

$$R' \quad \xrightarrow{(C_2H_5)_2O} \quad \overset{R''}{|} \quad \xrightarrow{H_2O,\text{aq } NH_4Cl} \quad \overset{R''}{|}$$



$$\underset{R''}{C=O} + RMgX \longrightarrow R'-\underset{R}{C}-OMgX \longrightarrow R'-\underset{R}{C}-OH + MgXOH$$

Aldehyde 3° alcohol

## Activity A/Self Assessment Exercise

Predict the product formed from the following reactions:

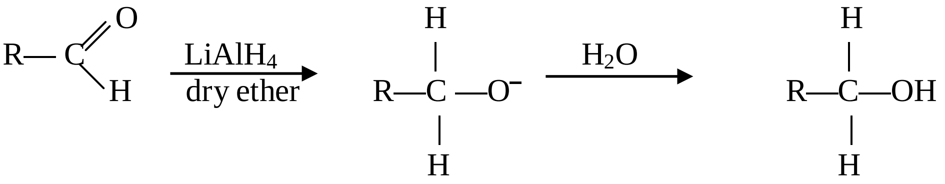
i. $(CH_3)_2C(CH_3)HCH_2CHO + RMgX \longrightarrow$

ii. $C_6H_5CH_2CHO + RMgX \longrightarrow$

### 3.3.2 Use of Lithium tetrahydridoaluminate (III), ( $LiAlH_4$)

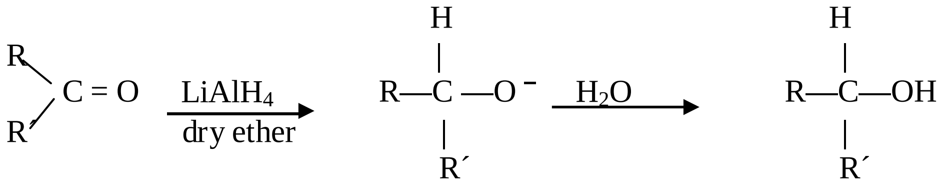
Primary and secondary alcohols can be prepared from the reduction of aldehydes and ketones using Lithium tetrahydridoaluminate (III), $LiAlH_4$ in dry ether.

For example:



$$R-C(=O)H \xrightarrow[\text{dry ether}]{LiAlH_4} R-\overset{H}{\underset{H}{C}}-O^- \xrightarrow{H_2O} R-\overset{H}{\underset{H}{C}}-OH$$

Aldehyde 1°alcohol



$$\begin{matrix}R\\R'\end{matrix}\!\!>C=O \xrightarrow[\text{dry ether}]{LiAlH_4} R-\overset{H}{\underset{R'}{C}}-O^- \xrightarrow{H_2O} R-\overset{H}{\underset{R'}{C}}-OH$$

Ketone 2° alcohol

Lithium tetrahydridoborate (III), $LiBH_4$, in dry ether, a milder reducing agent can also be used as an alternative reagent.

## 3.4 Fermentation of carbohydrates

Industrially, ethanol can be prepared from the fermentation of carbohydrates.

The biological catalysts, enzymes, found in yeast maltase break down the sugar molecules into ethanol to give a yield which is in the region of 95 per cent.

$$\underset{\text{Starch}}{2(C_5H_{10}O_5)n} + nH_2O \xrightarrow[60°C]{\text{diastase}} \underset{\text{maltose}}{nC_{12}H_{22}O_{11}}$$

$$\underset{\text{Maltose}}{C_{12}H_{22}O_{11}} + H_2O \xrightarrow[15°C]{\text{maltase}} \underset{\text{glucose}}{2C_6H_{12}O_6}$$

$$C_6H_{12}O_6 \xrightarrow[15°C]{\text{zymase}} \underset{\text{ethanol}}{2CH_3CH_2OH} + 2CO_2$$

Glucose is rarely used in practice as the initial substrate has some other suitable and cheaper raw materials such as potatoes, cereals and rice are available. The percentage of ethanol can be increased by distillation of the reaction product: to give a mixture containing 95.5 by mass of ethanol and 4.43% water. The mixture is called rectified spirit with a constant boiling point of 78.2°C. Anhydrous calcium chloride cannot be used to remove the residual water because it reacts with alcohols to form compounds of the types $CaCl_2$. $nC_2H_5OH$. On distilling over quicklime, CaO, which reacts with only the water but not with the alcohol, absolute alcohol (99.5% alcohol) is obtained. The last traces of water can be removed from this by refluxing it with metallic calcium and redistilling.

Absolute is ethanol is highly hygroscopic and must be stored away from atmospheric moisture if its purity is to be maintained.

## 4.0 Conclusion

Alcohol can be prepared in the laboratory using diverse methods as discussed above, however fermentation of carbohydrates can be used for the industrial preparation

## 5.0 Summary

In this unit we have learnt that:

(i) alcohols can be prepared from the hydrolysis of halogenoalkanes
(ii) alcohols can be prepared from the hydration of alkene
(iii) alcohols can be prepared from the reduction of aldehydes and ketones using
  - RLi
  - RMgX
  - $LiAlH_4$
  - $LiBH_4$
(iv) alcohols can be prepared from the fermentation of carbohydrates
(v) Rectified Spirit is a mixture of 95.57% ethanol. 4.43% water

## 6.0 Tutor Marked Assignment

a. Outline the steps involve in the preparation of ethanol from fermentation
b. Using equation and stating the conditions of reaction only, explain the production of alcohol using Grignard reagent

## 7.0 Further Reading and Other Resources

a. K.S.TEWARI and N.K. VISHNOI (2006)- A Textbook of Organic Chemistry
-Third Edition

b. Robert Thornton Morrison and Robert Neilson Boyd(2008) – Organic Chemistry
- Sixth Edition

c. W.C.Wong; C.T.Wong; S.O.Onyiruka and L.E.Akpanisi (2001)-University Organic Chemistry-The Fundamentals

# Unit 3: Reactions of Alcohols

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## 1.0 Introduction

Alcohols are neutral to litmus. They undergo diverse reactions depending on the position of cleavage of the bond, RO- H or R-OH forming an alkoxide ion or forming a carbonium ion respectively

## 2.0 Objectives

At the end of this unit, you should be able to:

- (a) Discuss the acidity of alcohol compared with that of water
- (b) Explain the amphoteric nature of alcohols
- (c) Discuss the various reactions of alcohols, stating the necessary conditions of reaction.

## 3.0 Acidity of Alcohols

Alcohols have no effect on pH paper or sodium hydroxide. A measurement of the pH value of ethanol with a pH meter shows that ethanol is neutral.

Alcohols are actually amphoteric in nature. As an acid, it ionizes to form an alkoxide ion ($RO^-$) and hydrogen ion, $H^+$ in the presence of a base.

$$ROH \rightleftharpoons RO^- + H^+$$

The acidic strength of alcohol follow the order: 1° alcohol > 2° alcohol > 3°alcohol.

In the presence of an acid, the alcohol may function as a base; it can accept a proton as shown below:

$$ROH + H^+ \rightleftharpoons ROH^+$$

The basic strength of alcohols follow the order 3° alcohol > 2° alcohol > 1° alcohol

Water is a weak acid, however the acidic strength of alcohols are much weaker than that of water. For example, considering the equilibrium for the ionization of water and the ionization of ethanol:

$$H_2O + H_2O \rightleftharpoons \underset{\text{Hydroxide ion}}{HO^-} + H_3O^+ \quad K\alpha = 1.0 \times 10^{-18}$$

$$CH_3CH_2OH + H_2O \rightleftharpoons \underset{\text{Ethoxide ion}}{CH_3CH_2O^-} + H_3O^+ \quad K\alpha = 1.0 \times 10^{-16}$$

This shows that water is a stronger acid than ethanol.

Aromatic alcohols, for example $C_6H_5CH_2OH$, behave in a similar way as tertiary aliphatic alcohol because of the electron donating properties of the benzene ring.

## Activity A/Self Assessment Exercise

1. Arrange the following in increasing acidic strength
   Methanol, Water, 2-methylpropan-2-ol, ethanol

## 3.1 Reactions of Alcohols

### 3.1.1 Combustion

Alcohols burn in air to give carbon (IV) oxide and water. For example, when ethanol burns in air with a pale blue flame to give carbon (IV) oxide and water.

$$C_2H_5OH + 3O_2 \longrightarrow 2CO_2 + 3H_2O.$$

### 3.1.2 Reactions based on position cleavage of bond in alcohol

Apart from combustion, alcohols undergo many other reactions and the type of reaction depends on the position of cleavage of the bond. There are two likely position of cleavage, giving two categories of reactions

(i) Cleavage of R-OH

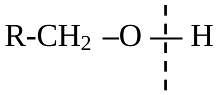
For example: $R\text{-}OH \rightarrow R^+ + OH^-$

(ii) Cleavage of RO-H

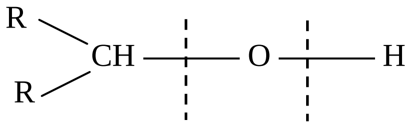
For example: $RO\text{-}H \rightarrow RO^- + H^+$

Either of these reactions may yield the substitution or elimination product and usually a mixture of the two depending mainly on the nature of the alkyl group to which the hydroxyl group is attached.

The preferred position of cleavage for 1°, 2°, and 3° alcohols shown below:

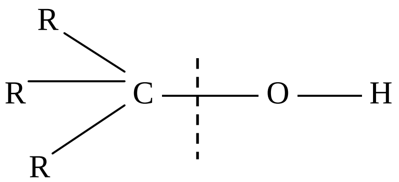


A- Primary alcohol



B- Secondary alcohol

or



C- Tertiary alcohol - - - - - - represents the position of cleavage

In A, the lower +I (I means inductive effect) effect from one alky group favors the formation the alkoxide ion, $RCH_2O^-$ while in C the greater +I effect from three alkyl groups stabilizes the intermediate carbonium ion, $R_3C^+$ .

### 3.1.2.1 Reactions involving R—OH cleavage.

The order of reactivity is as follows 3°alcohol >2°alcohol>1° alcohol.

**a. Halogenations**

The reaction is a nucleophilic substitution reaction.

i. Chlorination (Lucas test for alcohol)

The reaction occurs when concentrated hydrochloric acid is put into absolute alcohol and then refluxed in the presence of an anhydrous zinc chloride as catalyst.

$$R{-}OH + \underset{\text{conc.}}{HCl} \xrightarrow[\text{reflux}]{ZnCl_2\ \text{cat}} R\text{-}Cl + H_2O$$

For example,

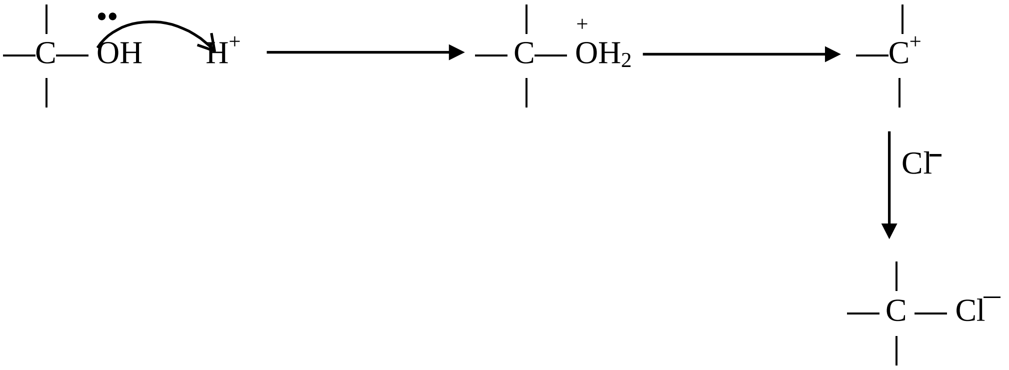
$$CH_3CH_2OH + HCl \xrightarrow[\text{reflux}]{ZnCl_2\ \text{cat}} CH_3CH_2Cl + H_2O.$$

The order of reactivity is as follows 3° > 2° > 1°alcohols.

An insoluble haloalkane will be formed and a cloudy mixture appears. The time it takes for the cloudiness to appear and for separation into two distinct layers indicates the types of alcohol.

For 3° alcohols, two distinct layers are formed immediately, 2° alcohols forms two distinct layers in about 10minutes while for $1^o$ alcohols, a cloudy appearance is noticed after refluxing for a few hours

The reaction is believed to take place via the $SN^1$ mechanism since concentrated hydrochloric acid is used.



The stable the carbonium ion, the faster will the reaction rate be and the quicker is the time for appearance of cloudiness

The stability of the carbonium ion is in the order below:

$R_3C^+ > R_2C^+H > RC^+H_2$

**b. Bromination and iodination**

Different hydrogen halides will require different reagents, for example,

(i) Use of NaX

$$CH_3CH_2OH \xrightarrow[\text{Reflux}]{\text{NaI, Conc } H_3PO_4} CH_3CH_2I + H_2O$$

$$CH_3CH_2OH \xrightarrow[\text{Reflux}]{\text{NaBr, Conc } H_2SO_4} CH_3CH_2Br + H_2O$$

The order of reactivity is as follows HI > HBr > HCl

(ii) Using phosphorus halides ($PCl_5$, $PCl_3$, $PBr_3$ or $PI_3$)

For example, use of phosphorus (V) chloride for chlorination.

This reaction can be carried out by adding solid phosphorus (V) chloride directly into the alcohol in a dry test tube.

For example:

$$CH_3CH_2OH + PCl_5 \longrightarrow CH_3CH_2Cl + POCl_3 + HCl$$

When phosphorus (III) chloride is used instead of phosphorus (V) chloride, the reaction is less vigorous.

$$3CH_3CH_2OH + PCl_3 \longrightarrow 3CH_3CH_2Cl + H_3PO_3$$

(iii) Using sulphur dichloride oxide (thionyl chloride, $SOCl_2$)

Alcohol is refluxed with sulphur dichloride oxide (thionyl chloride) in the presence of a small quantity of pyridine, $C_5H_5N$, which serves to absorb the hydrogen chlorides as it is formed.

For example:

$$CH_3CH_2OH + SOCl_2 \xrightarrow{\text{pyridine}} CH_3CH_2Cl + SO_2 + HCl$$

iv. Using phosphorus trihalide

When alcohols react with phosphorus trihalide under reflux, the product is an haloalkane.

Phosphorus trihalide can be prepared easily by adding red phosphorus and a halogen to the reaction mixture under reflux.The products are obtained by distillation at the end of the reaction.

$$\underset{\text{alcohol}}{ROH} \xrightarrow[\text{reflux}]{\text{red P/X}} \underset{\text{haloalkane}}{RX} + H_3PO_3$$

X = Br or Iodine

For example:

$$CH_3CH_2CH_2OH \xrightarrow[\text{reflux}]{\text{red P/Br}} CH_3CH_2CH_2Br + H_3PO_3$$

propan-1-ol 1-bromopropane

**c.Dehydration**

Dehydration of alcohols can be carried out by using dehydrating agents such as concentrated tetraoxosulphate (VI) acid or aluminum oxide to give the corresponding alkenes.

When alcohol vapour is passed over an aluminium oxide catalyst heated to 350°C or by heating to 170°C with excess concentrated tetraoxosulphate (VI) acid, the corresponding alkene is formed.

For example, the hydration of ethanol gives ethene.

$$CH_3CH_2OH \xrightarrow[170°C]{\text{excess } H_2SO_4} CH_2 = CH_2 + H_2O$$

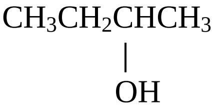
$$CH_3CH_2OH \xrightarrow[350°C]{Al_2O_3} CH_2 = CH_2 + H_2O$$

Mechanism

$$\begin{tikzcd}
CH_3 - CH_2 - OH + H - O_3SOH \arrow[r, shift left] & CH_3CH_2 - OH^+_2 + HSO^-_4 \arrow[l, shift left] \arrow[d, shift left, "-H_2O"] \\
& CH_3 - CH_2^+ \arrow[u, shift left] \arrow[d, shift left, "HSO_4^-"] \\
& CH_2 = CH_2 + H_2SO_4 \arrow[u, shift left]
\end{tikzcd}$$

The reaction above can only take place with alcohols that have at least one hydrogen on the adjacent carbon. For example, methanol cannot undergo dehydration.

When the reaction involves secondary or tertiary alcohols having more than three carbon atoms, the possibility of forming more than one alkene can result from the dehydrated reaction. For example, the dehydration of butan-2-ol gives but-1- ene and but -2- ene



$$\underset{\substack{|\\ OH}}{CH_3CH_2CHCH_3} \xrightarrow{\text{Conc. } H_2SO_4.} \underset{\text{But-1-ene}}{CH_3CH_2CH=CH_2} + \underset{\text{But-2-ene}}{CH_3CH = CHCH_3}$$

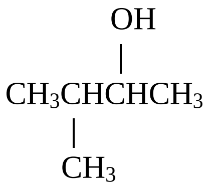
The alkene produced in greater abundance is indicated by Saytzeff's rule.

Saytzeff's rule states that the alkene formed preferentially is the one containing the higher number of alkyl groups. In the dehydration of butan-2-ol, the predominant product is but-2-ene.

## Activity B/Self Assessment Excercise

(a) In the dehydration of the following alkali, state the product(s) formed and indicate the major product when more than one product is possible.

(i)

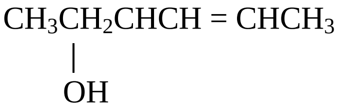


$CH_3CH(CH_3)CH(OH)CH_3$

(ii) $CH_3CH_2CH_2CH_2OH$

(b) What alcohols would yield the following alkenes on dehydration?

(i)



$CH_3CH_2CH(OH)CH = CHCH_3$

(ii) $CH_3CH = CH_2$

**d. Formation of ethers**

When an excess alcohol is heated with concentrated tetraoxosulphate (VI) acid at a lower temperature of about 140°C ether is formed instead of alcohol. The alcohol undergoes intermolecular dehydration forming ether. For example,

Mechanism

$$2CH_3CH_2OH \xrightarrow[140°C]{Conc.\ H_2SO_4} CH_3CH_2OCH_2CH_3 + H_2O$$

ethoxyethane
(ether)

Mechanism

$$CH_3CH_2OH + H \rightleftharpoons CH_3CH_2OH_2^+$$

$$CH_3CH_2OH_2^+ \overset{-H_2O}{\rightleftharpoons} CH_3CH_2^+$$

$$CH_3CH_2^+ + CH_3CH_2OH \rightleftharpoons CH_3CH_2O^+CH_2CH_3 \overset{-H}{\rightleftharpoons} CH_3CH_2OCH_2CH_3$$

**3.1.2.2 Reactions involving cleavage of RO-H**

The rate of reaction follows the order below:

$1^o$ alcohol > $2^o$ alcohol > $3^o$ alcohol

**a. Reaction with reactive metals**

Alcohols react with reactive metals like sodium and potassium to form metal alkoxides and hydrogen gas.

For example:

$$2CH_3CH_2OH + 2Na \longrightarrow 2CH_3CH_2ONa + H_2$$

Sodium ethaoxide

The metal alkoxides are stronger bases than sodium hydroxide; they are commonly used in organic reactions requiring a strong base in a non-aqueous solvent.

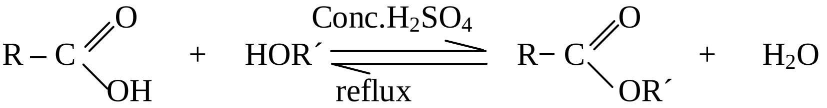
This reaction is similar to the reaction of water with reactive metals, however alcohols reacts more slowly with reactive metals than water

$$2H_2O + 2Na \longrightarrow \underset{\text{Sodium hydroxide}}{2NaOH} + H_2$$

**b.Esterification**

This is a reaction in which an alcohol reacts with carboxylic acid in the presence of concentrated tetraoxosulphate (VI) acid to form esters. For example,the reaction of ethanol with ethanoic acid to form ethyl ethanoate and water.

$$CH_3CH_2OH + CH_3COOH \overset{H+}{\rightleftharpoons} CH_3COOCH_2CH_3 + H_2O$$



$$R-C(=O)OH + HOR' \underset{\text{reflux}}{\overset{\text{Conc.}H_2SO_4}{\rightleftharpoons}} R-C(=O)OR' + H_2O$$

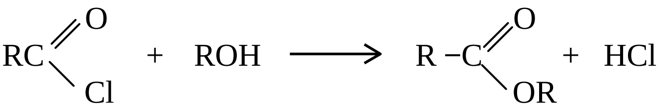
Carboxylic acid alcohol Ester

Esterification reaction is a rather slow reaction even with heating. The reaction is reversible and the yield poor.

The forward reaction is called esterification while the backward reaction is called acid – catalysed hydrolysis of ester. When excess acid or alcohol is added to the reaction mixture, the equilibrium will shift to the right hand side.

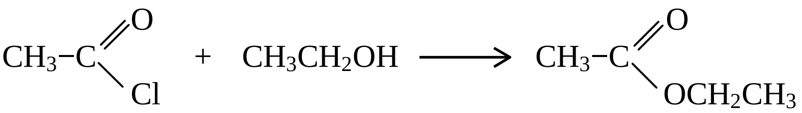
The formation of an ester can also be achieved by reacting with

i. acyl chloride
ii. acid anhydride.

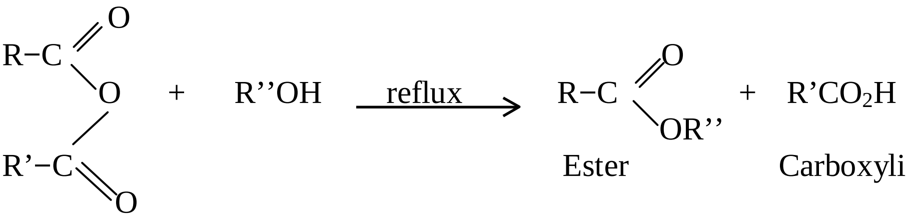


$$RC(=O)Cl + ROH \longrightarrow R-C(=O)OR + HCl$$

For example:



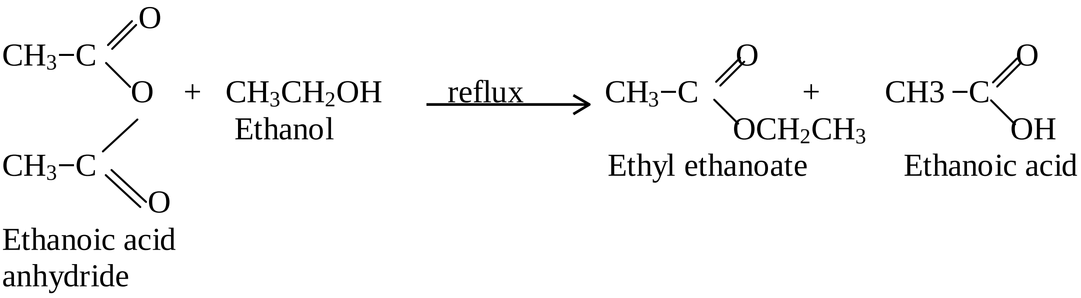
$$CH_3-C(=O)Cl + CH_3CH_2OH \longrightarrow CH_3-C(=O)OCH_2CH_3$$



$$(R-C(=O))O(C(=O)-R') + R''OH \xrightarrow{\text{reflux}} R-C(=O)OR'' + R'CO_2H$$

Ester Carboxylic acid

For example:



**c. Oxidation of alcohols**

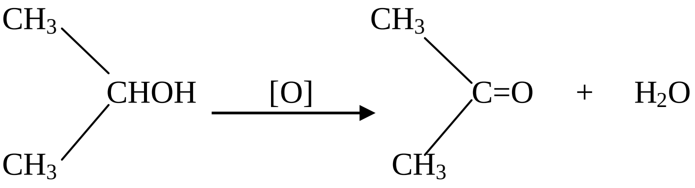
Alcohols can be oxidized by making use of common oxidizing agents such as acidified potassium tetraoxomanganate (VII) or acidified potassium heptaoxodichromate (VI) to give the corresponding carbonyl compound or carboxylic acid.

Primary alcohols are readily oxidized on heating to aldehydes but in the presence of excess of the oxidizing agent the reaction proceeds further to yield the carboxylic acid.

For example:

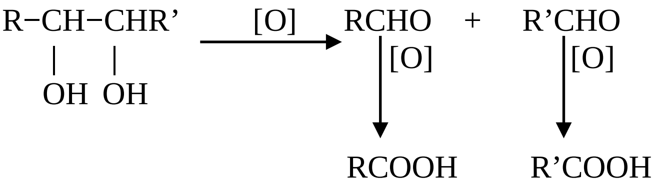
$$CH_3CH_2OH \xrightarrow[\text{From } KMnO_4 \text{ or } K_2Cr_2O_7]{[O]} CH_3\ CHO \xrightarrow{[O]} CH_3COOH$$

Secondary alcohols are oxidized to the corresponding ketone. Ketones are quite resistant to oxidation and do not undergo further reactions unless they are subjected to severe conditions. In that case they are oxidized to a carboxylic acid- a mixture of smaller carboxylic acids will be formed because it involves breaking a carbon – carbon linkage.



Tertiary alcohols are also resistant to oxidation. They are not oxidized at all in neutral or alkaline media.

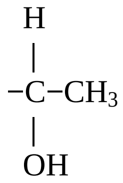
In an acidic medium, tertiary alcohols undergo dehydration to the alkene which can be readily oxidized to the diol and further oxidation yields the oxidation products of primary alcohols.



$$\underset{OH\ \ OH}{R-CH-CHR'} \xrightarrow{[O]} RCHO + R'CHO \xrightarrow{[O]} RCOOH + R'COOH$$

**d. Triiodoform Formation (Iodoform Reaction)**

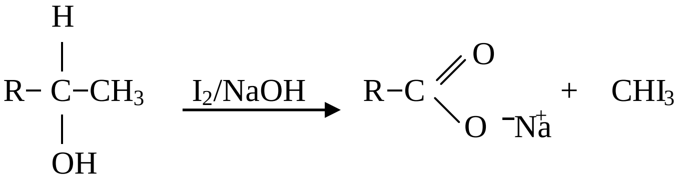
Some alcohols with the structure



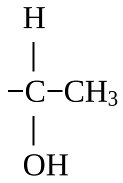
$$-\overset{\displaystyle H}{\underset{\displaystyle OH}{C}}-CH_3$$

react with an iodoform reagent(iodine in the presence of sodium hydroxide), a mild oxidizing agents to give sodium carboxylate and triiodomethane(also called iodoform).

The product, triiodomethane appears as a yellow precipitate in the reaction mixture.



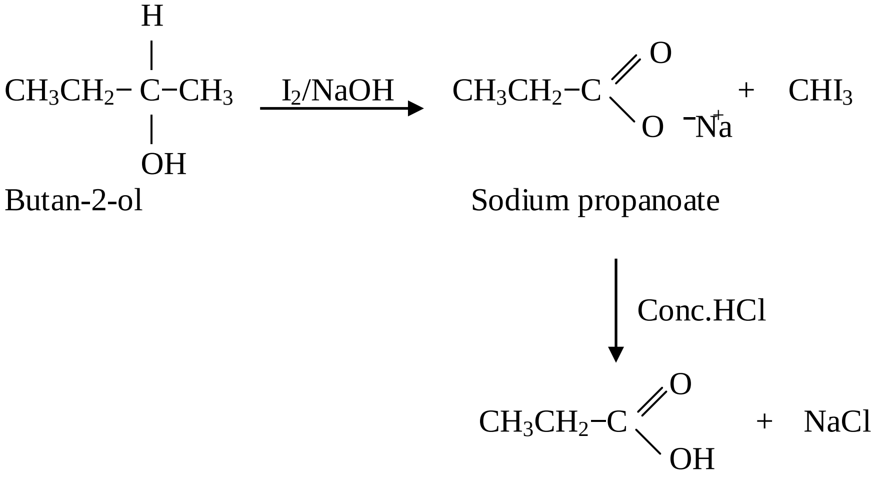
The reaction is a useful reaction for confirming the presence of the group



$$-\overset{\displaystyle H}{\underset{\displaystyle OH}{C}}-CH_3$$

in an alcohol and also a useful means of synthesizing carboxylic acids which will have one carbon less than the parent alcohol.

For example:



Butan-2-ol

Sodium propanoate

Propanoic acid

## Activity C/Self Assessment Exercise

a. Using equations explain how the following compounds can be obtained from alcohols. Name the starting alcohol.

(i) $CH_3CHO$ (ii) $CH_3CH_2CH_2I$ (iii) $CH_3CH_2CH(Cl)CH_3$ (iv) $C_6H_5COOC_2H_5$

b. Which of the following alcohols will be positive to iodoform test?

i. $CH_3CH_2CH(OH)CH_2CH_3$ ii. $CH_3CH(CH_3)CH_2CH(OH)CH_3$

iii. $CH_3CH(OH)(CH_2)_2CH_3$

## 3.2 Distinction between Primary, secondary and tertiary alcohol

i. Lucas Test: To the unknown alcohol, add Lucas reagent- a mixture of concentrated hydrochloric acid and anhydrous zinc chloride in ratio 1:1- at room temperature. The tertiary alcohols reacts with Lucas reagent producing immediate turbidity in the reaction mixture, the secondary alcohols give turbidity within 5 to 10minutes, and the primary alcohols do not give turbidity at all at room temperature.

ii. Oxidation Test: The product formed from the oxidation of alcohols can be used as a test for alcohols.

## 4.0Conclusion

The chemical properties of an alcohol are characterized by the functional group –OH. The reactions of alcohols depend on the position of cleavage of the bond, R-OH or RO-H.

## 5.0Summary

In this unit we have learnt that:

i. Alcohols are neutral to litmus; alcohols have no effect on pH paper or sodium hydroxide.

ii. Alcohols are actually amphoteric in nature. As an acid, it ionizes to form an alkoxide ion ($RO^-$) and hydrogen ion, $H^+$ in the presence of a base.

$$ROH \rightleftharpoons RO^- + H^+$$

The acidic strength of alcohol follow the order: 1° alcohol > 2° alcohol > 3°alcohol.

iii. In the presence of an acid, the alcohol may function as a base; it can accept a proton as shown below:

$$ROH + H^+ \rightleftharpoons ROH^+$$

The basic strength of alcohols follow the order 3° alcohol > 2° alcohol > 1° alcohol

iv. Alcohols are much weaker acids than that of water.

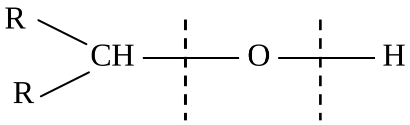
v. Alcohols burn in air to give carbon (IV) oxide and water.

vi. They undergo diverse reactions depending on the position of cleavage of the bond, RO- H or R-OH forming an alkoxide ion or forming a carbonium ion respectively

vii. The preferred position of cleavage for 1°, 2°, and 3° alcohols shown below:

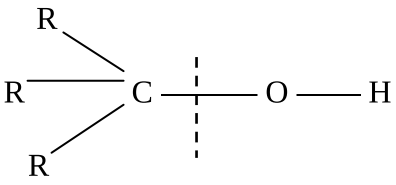
$$R\text{-}CH_2 - O \mid H$$

I- Primary alcohol



II- Secondary alcohol

or



III- Tertiary alcohol ------ represents the position of cleavage

viii. Reactions involving R—OH cleavage

The order of reactivity for reactions involving R—OH cleavage is as follows 3°alcohol >2°alcohol>1° alcohol.
Examples are:
a. Halogenations
I. Chlorination (Lucas test for alcohol)

$$R\text{—}OH + \underset{\text{conc.}}{HCl} \xrightarrow[\text{reflux}]{ZnCl_2 \text{ cat}} R\text{-}Cl + H_2O$$

The order of reactivity is as follows 3° > 2° > 1°alcohols.
The stability of the carbonium ion is in the order below:

$R_3C^+ > R_2C^+H > RC^+H_2$

II. Bromination and iodination
(i) Use of NaX

$$R\text{-}OH \xrightarrow[\text{Reflux}]{NaX, \text{ Conc } H_3PO_4} RX + H_2O$$

The order of reactivity is as follows HI > HBr > HCl

(ii) Using phosphorus halides ($PCl_5$, $PCl_3$, $PBr_3$ or $PI_3$)

$$ROH + PCl_5 \longrightarrow RCl + POCl_3 + HCl$$

$$ROH + PCl_3 \longrightarrow RCl + H_3PO_3$$

(iii) Using sulphur dichloride oxide (thionyl chloride, $SOCl_2$)

$$ROH + SOCl_2 \xrightarrow{\text{pyridine}} RCl + SO_2 + HCl$$

(iv) Using phosphorus

$$\underset{\text{alcohol}}{ROH} \xrightarrow[\text{reflux}]{\text{red P/X}} \underset{\text{haloalkane}}{RX} + H_3PO_3$$

X = Br or Iodine

b. Dehydration

For example, the hydration of ethanol gives ethene.

$$CH_3CH_2OH \xrightarrow[170°C]{\text{excess } H_2SO_4} CH_2{=}CH_2 + H_2O$$

$$CH_3CH_2OH \xrightarrow[350°C]{Al_2O_3} CH_2{=}CH_2 + H_2O$$

c. Formation of ethers

$$2ROH \xrightarrow[140°C]{\text{Conc. } H_2SO_4} \underset{\text{ether}}{ROR} + H_2O$$

ix. For reactions involving cleavage of RO-H, the rate of reaction follow the order below:

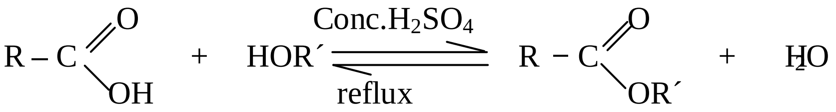
$1^o$ alcohol > $2^o$ alcohol > $3^o$ alcohol

Examples are:

a. Reaction with reactive metals

$$2ROH + 2Na \longrightarrow \underset{\text{Sodium alkoxide}}{2RONa} + H_2$$

b. Esterification



$$R-C(=O)OH + HOR' \underset{\text{reflux}}{\overset{\text{Conc.}H_2SO_4}{\rightleftharpoons}} R-C(=O)OR' + H_2O$$

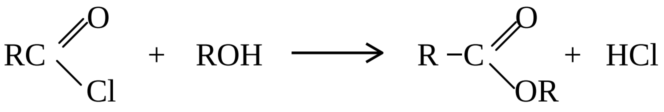
Carboxylic acid alcohol Ester

The reaction is reversible and the yield poor.

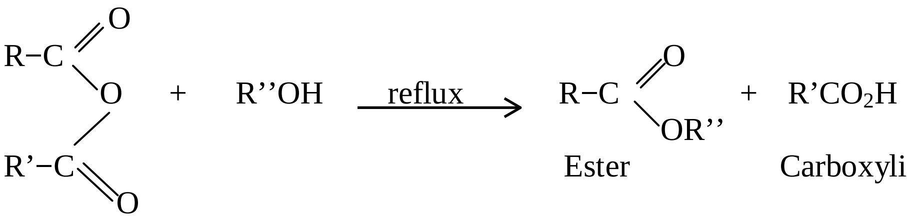
The formation of an ester can also be achieved by reacting with

iii. acyl chloride

iv. acid anhydride.



$$RC(=O)Cl + ROH \longrightarrow R-C(=O)OR + HCl$$



$$(R-C(=O))O(C(=O)-R') + R''OH \xrightarrow{\text{reflux}} R-C(=O)OR'' + R'CO_2H$$

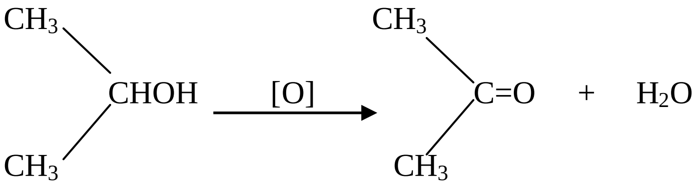
Ester Carboxylic acid

c. Oxidation of alcohols using acidified potassium tetraoxomanganate (VII) or acidified potassium heptaoxodichromate (VI).

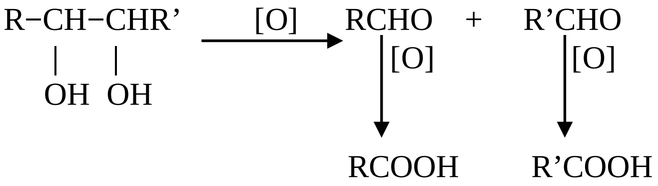
Primary alcohols are readily oxidized on heating to aldehydes and excess of the oxidizing agent it yields the carboxylic acid.

$$CH_3CH_2OH \xrightarrow[\text{From } KMnO_4 \text{ or } K_2Cr_2O_7]{[O]} CH_3\ CHO \xrightarrow{[O]} CH_3COOH$$

Secondary alcohols are oxidized to the corresponding ketone.

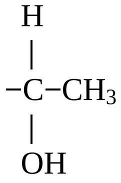


Tertiary alcohols are also resistant to oxidation but they undergo dehydration in acidic medium to the alkene which can be oxidized to the diol and then oxidized to yield the oxidation products of primary alcohols.



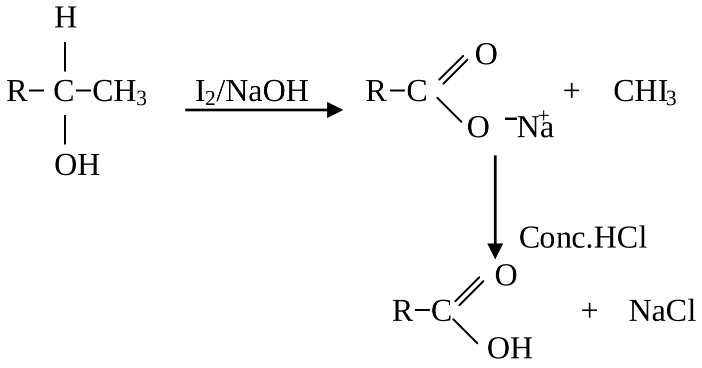
d.Triiodoform Formation (Iodoform Reaction)

Alcohols with the structure



$$-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-CH_3$$

react with an iodoform reagent sodium carboxylate and triiodomethane(also called iodoform). The sodium carboxylate can be hydrolysed to give carboxylic acid.



Carboxylic acids

x. Primary, secondary and tertiary alcohol can be distinguished using

  i. Lucas Test
  ii. Oxidation Test

## 6.0Tutor Marked Assignment

a. Discuss the actions of the following on ethanol:
   - i. Conc.$H_2SO_4$
   - ii. $Cl_2$
   - iii. HCl
   - iv. $PCl_5$
   - v. Na
   - vi. $CH_3COOH$

## 7.0 Further Reading and Other Resources

a. K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry. Third Edition

b. Robert Thornton Morrison and Robert Neilson Boyd(2008) – Organic Chemistry-Sixth Edition

c. W.C.Wong; C.T.Wong; S.O.Onyiruka and L.E.Akpanisi(2001)-University Organic Chemistry-The Fundamentals

# Module 2: Ethers and Epoxides

## Unit 1: Structures and Nomenclature of Ethers and Epoxides

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## 1.0 Introduction

Ethers are a family of organic compounds with the general formula, $C_nH_{2n+2}O$. They are isomeric with the aliphatic monohydric alcohols with the general formula $C_nH_{2n+1}OH$. Epoxides are formed when an oxygen atom is linked to carbon atoms of a carbon chain forming a three membered ring.

## 2.0 Objectives

At the end of this unit you should be able to:

i. Write the general formula of ethers and epoxides
ii. Draw the structures of ethers and epoxides
iii. Distinguish between symmetrical and unsymmetrical ethers
iv. Write the names of ethers using the IUPAC nomenclature
v. State and draw the various isomers of ethers

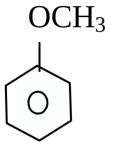
## 3.0 Structures of Ethers

Ethers possess the structure: R − O − R’. R and R’ may be aliphatic or aromatic.

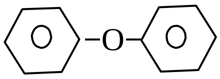
For example:

$CH_3 – O – CH_3$
Methoxymethane (Dimethyl ether)

$CH_3 – O – CH_2CH_3$
Methoxy ethane (Ethyl methyl ether)



Methoxyl benzene
(Anisole)



Phenoxy benzene
(Diphenyl ether)

### 3.1 Symmetrical and Unsymmetrical Ethers

Symmetrical ethers are compounds in which R and R’ are identical, they are also known as simple ethers.

For example:

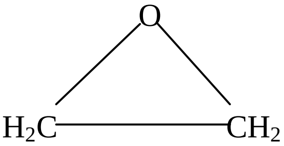
$CH_3 – O – CH_3$ $CH_3CH_2 – O – CH_2CH_3$
Methoxy methane Ethoxy ethane

Unsymmetrical ethers are compounds in which R and R’ are different, they are also known as mixed ethers.

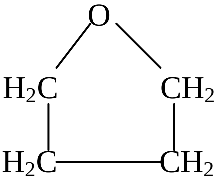
For example:
$CH_3$- O- $CH_2CH_3$
Methoxyethane

## 3.2 Cyclic Ethers

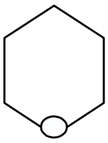
These are compound containing the oxygen atom in a ring. They are heterocyclic compounds.



Epoxyethane
(Ethylene oxide)



Tetrahydrofuran
(Oxalane)



Tetrahydropyran
(Oxane)

The three membered cyclic ethers are known as epoxides. Unlike most ether, epoxides are very reactive substances.

### Activity A/ Self Assessment Exercise

i. Classify the following ethers as symmetrical and asymmetrical
$CH_3CH_2CH_2\text{-}O\text{-}CH_2CH_2CH_3$, $CH_3CH(CH_3)CH_2\text{-}O\text{-}CH_2CH_3$, $CH_3\text{-}O\text{-}CH_2CH_3$
ii. What are epoxides?

## 3.3 Naming Ethers and Epoxides

Ethers can be named using the common system or the IUPAC system

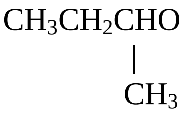
<u>Common System:</u> In the common system, ethers are named by prefixing the names of alkyl radicals attached to oxygen in alphabetical order before the name ether.

For example: $CH_3\text{-}O\text{-}CH_3$ is known as dimethyl ether and $CH_3\text{-}O\text{-}C_2H_5$ is simply ethyl methyl ether (in alphabetical order).

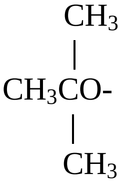
<u>IUPAC System:</u> Using the IUPAC nomenclatures, ethers are named as alkoxy derivatives of alkanes. The prefix ‘–OR’ is composed of the name of the simpler alkyl group in the molecule with the ‘–yl’ ending replaced by the ‘-oxy’. The alkoxy prefix is then followed by the name of the corresponding alkane of the other alkyl group in the molecule.

For example:

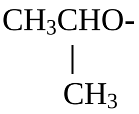
$CH_3O\text{-}$ , $CH_3CH_2O\text{-}$ ,



$\underset{\displaystyle CH_3}{\underset{|}{CH_3CH_2CHO}}$ ,



$\underset{\displaystyle CH_3}{\underset{|}{\overset{\displaystyle CH_3}{\overset{|}{CH_3CO\text{-}}}}}$ ,



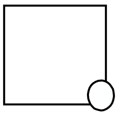
$\underset{\displaystyle CH_3}{\underset{|}{CH_3CHO\text{-}}}$

Methoxy Ethoxy Sec-butoxy Isopropoxy

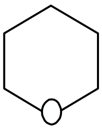
Table 1:1 Structures, IUPAC and Common Names of Ethers

| STRUCTURE | IUPAC | COMMON NAMES |
|---|---|---|
| $CH_3OCH_3$ | Methoxy methane | Dimethyl ether |
| $CH_3CH_2OCH_3$ | Ethoxy ethane | Diethyl ether |
| $CH_3CH_2OCH_3$ | Methoxy ethane | Ethyl methyl ether |
| $CH_3CH_2OCH_2CH_2CH_2Cl$ | 1-Chloro-3-ethoxy propane | 3-Chloropropyl ethyl ether |
| $\underset{\displaystyle OCH_3}{\underset{|}{CH_3CHCH_2CH_3}}$ | 2-Methoxy butane | 2-Buthyl methyl ether |

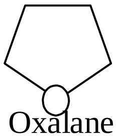
Several cyclic ethers have specific IUPAC name. For example



Oxetane



Oxane
(Tetrahydropyran)

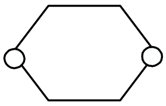


Oxalane
(Tetrahydrofuran)

In each case the ring is numbered starting at the oxygen.
Tetrahydropyran and tetrahydrofuran are acceptable synonyms for oxane and oxalane repectively.

Some substances have more than one ether linkage, for example the diethers, 1,2-dimethoxyethane and 1,4-dioxane and the triether, diglyme.

| | |
|---|---|
| $CH_3OCH_2CH_2OCH_3$ | $CH_3OCH_2CH_2OCH_2CH_2OCH_3$ |
| 1,2-Dimethoxy ethane | Diethylene glycol dimethyl ether<br>(Diglyme) |



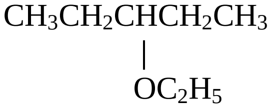
1,4-Dioxane

Compounds that contain several ether functions are referred to as polyethers.

## Activity B/Self Assessment Exercise

1.Draw the structures and write the common names of the following ethers:
  i. Methoxy benzene
  ii. Phenoxy benzene

2. Give the IUPAC name for each of the following ethers
  i. $CH_3OCH_2CH_2CH_2CH_3$
  ii. $CH_3O-C_6H_5$
  iii.



$$\begin{array}{c}CH_3CH_2\underset{\displaystyle OC_2H_5}{\underset{|}{C}}HCH_2CH_3\end{array}$$

## 3.4 Isomerism

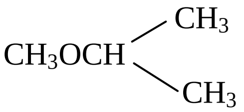
Ethers exhibit the following types of structural isomerism

### 3.4.1 Functional group isomerism

Ethers are isomeric with alcohols as both have the same general formula ($C_nH_{2n+2}O$) but different functional groups. For example, methoxymethane ($CH_3OCH_3$) and ethanol ($CH_3CH_2OH$) have the same molecular formula, $C_2H_6O$.

### 3.4.2 Metamerism

Ethers exhibit metamerism because of the difference in the size of the alkyl groups attached to the oxygen atom. For example, the formula $C_4H_{10}O$ represents three isomeric ethers or metamers.

| | | |
|---|---|---|
| $CH_3OCH_2CH_2CH_3$ | $C_2H_5OC_2H_5$ |  $CH_3OCH(CH_3)_2$ |
| Methoxy propane | Ethoxy ethane | 2-Methoxy propane |

## 4.0 Conclusion

Ethers are compounds having the general formula $C_nH_{2n+2}O$. Epoxides are the three membered cyclic ethers. Ether can be named using common system and the IUPAC system.

## 5.0 Summary

In this unit we have learnt that:

i. Ethers possess the structure: R − O − R'
ii. Ethers are compounds having the general formula $C_nH_{2n+2}O$
iii. Ethers are isomeric with the aliphatic monohydric alcohols with the general formula $C_nH_{2n+1}OH$
iv. Epoxides are the three membered cyclic ethers
v. Symmetrical or simple ethers have R and R' being identical
vi. Unsymmetrical or mixed ethers have R and R' not identical

## 6.0 Tutor Marked Assignment

Write the formula and the names of the various ethers having the formula $C_5H_{12}O$.

## 7.0 Further Reading and Other Resources

a. K.S.TEWARI and N.K. VISHNOI (2006)- A Textbook of Organic Chemistry
-Third Edition

b. Robert Thornton Morrison and Robert Neilson Boyd(2008) – Organic Chemistry- Sixth Edition

c. Organic Chemistry, 4th Edition –Paula Yurkanis Bruice

# Unit 2: Ethers: Preparation and Properties

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## 1.0 Introduction

Ethers can be prepared using the various methods discussed below.

## 2.0 Objectives

At the end of this unit you should be able to:

1. Discuss the various methods of preparing ethers in the laboratory and industrially
2. Explain the various reactions of ethers

## 3.0 General Methods Of Preparation

Ethers can be prepared from the following methods

### a. Dehydration of alcohols

Simple or symmetrical ethers are obtained when excess alcohol is heated with concentrated tetraoxosulphate (VI) acid or tetraoxophosphoric(V) acid. In the process, two molecules of alcohol lose a water molecule amongst themselves to form ethers.

$$ROH + HOR \xrightarrow[heat]{H_2SO_4} ROR + H_2O$$

The method is employed industrially in the preparation of lower ethers. Dehydration of primary alcohols may also be effected by passing alcohol vapour over heated catalysts like alumina at high pressure and temperature.

$$ROH + HOR \xrightarrow[250^{O}C/Pressure]{Al_2O_3} ROR + H_2O$$

When secondary and tertiary alcohols are used under these conditions, alkene is the main product.

### b. Williamson Synthesis

This method is the most important method for laboratory preparation of ethers. It involves heating an alkyl halide with sodium or potassium alkoxides.

$$\underset{\text{Sodium alkoxide}}{RONa} + \underset{\text{alkyl halide}}{R'X} \xrightarrow{heat} \underset{\text{ether}}{ROR'} + Nax$$

For example,

$$\underset{\text{Sodium ethoxide}}{C_2H_5ONa} + \underset{\text{ethyl chloride}}{C_2H_5Cl} \xrightarrow{heat} \underset{\text{Ethoxyethane}}{C_2H_5OC_2H_5} + NaCl$$

The reaction involves nucleophilic substitution of alkoxide ion for halide ion.

$$\underset{Nu^-}{R'O^-} + \underset{\text{substrate}}{R{-}X} \longrightarrow R'O{-}R + \underset{\text{leaving group}}{X^-}$$

It is most suitable for preparing mixed or unsymmentrical ethers.

### c. Heating Alkyl halides with dry silver oxide

Ethers may be prepared by heating alkyl halides with dry silver oxide ($Ag_2O$).

$$2RX + Ag_2O \xrightarrow{heat} R\ O\ R + 2AgX$$

For example:

$$2C_2H_5I + Ag_2O \xrightarrow{heat} C_2H_5OC_2H_5 + 2Ag_2I$$

Mixed ethers can be prepared by taking different alkyl halides in equimolar ratio.

$$2RX + Ag_2O + R'X \xrightarrow{heat} R\ O\ R' + 2AgX$$

$$CH_3I + Ag_2O + C_2H_5I \xrightarrow{heat} CH_3OC_2H_5 + 2Ag_2I$$

### d. Reaction of lower halogenated ethers with Grignard reagents

Higher homologues of ethers can be prepared by the action of Grignard reagent on lower halogenated ethers.

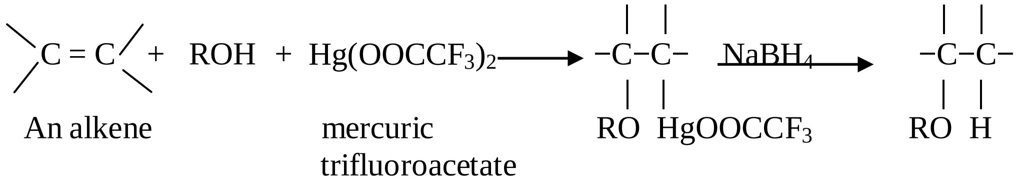
$$\underset{\text{Halogenated Ether}}{ROCH_2X} + \underset{\text{Grignard reagent}}{R'MgX} \longrightarrow \underset{\text{ether}}{ROCH_2R'} + MgX_2$$

For example,

$$\underset{\text{Chloromethoxy Methane}}{CH_3OCH_2Cl} + \underset{\text{ethyl magnesium bromide}}{C_2H_5MgBr} \longrightarrow \underset{\text{methoxy propane}}{CH_3OCH_2C_2H_5} + MgBrCl$$

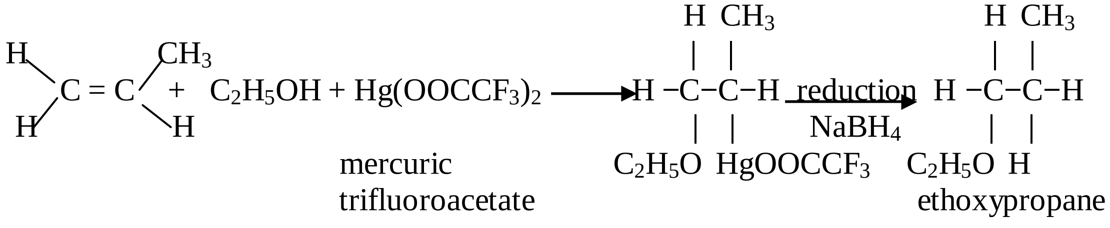
### e. Oxymecuration-demecuration

Alkene reacts with mercuric trifluoroacetate in the presence of alcohol to give alkoxymecurial compound which on reduction gives ether



$$\underset{\text{An alkene}}{>C=C<} + ROH + \underset{\text{mercuric trifluoroacetate}}{Hg(OOCCF_3)_2} \longrightarrow \underset{RO\quad HgOOCCF_3}{-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-} \xrightarrow{NaBH_4} \underset{RO\quad H}{-\overset{|}{\underset{|}{C}}-\overset{|}{\underset{|}{C}}-}$$

For example,



$$\underset{H}{\overset{H}{>}}C=C\underset{H}{\overset{CH_3}{<}} + C_2H_5OH + \underset{\text{mercuric trifluoroacetate}}{Hg(OOCCF_3)_2} \longrightarrow H-\underset{C_2H_5O}{\overset{H}{\overset{|}{\underset{|}{C}}}}-\underset{HgOOCCF_3}{\overset{CH_3}{\overset{|}{\underset{|}{C}}}}-H \xrightarrow[NaBH_4]{reduction} \underset{\text{ethoxypropane}}{H-\underset{C_2H_5O}{\overset{H}{\overset{|}{\underset{|}{C}}}}-\underset{H}{\overset{CH_3}{\overset{|}{\underset{|}{C}}}}-H}$$

### f. Action of diazomethane on alcohols

Methyl ethers may be prepared by the action of diazomethane on alcohols in the presence of catalyst like boron trifluoride or fluoroboric acid.

$$ROH + \underset{\text{Diazomethane}}{CH_2N_2} \xrightarrow{BF_3} ROCH_3 + N_2$$

For example,

$$C_2H_5OH + CH_2N_2 \xrightarrow{BF_3} \underset{\text{Methoxy ethane}}{C_2H_5OCH_3} + N_2$$

**Activity A/Self Assessment Exercise**

Predict the ether formed from the following reactions:

i. $2CH_3OH \xrightarrow[\text{heat}]{H_2SO_4}$

ii. $2CH_3CHI + Ag_2O \xrightarrow{\text{heat}}$

iii. $C_2H_5ONa + C_3H_7Cl \xrightarrow{\text{heat}}$

iv. $CH_2{=}CH_2 + C_2H_5OH \xrightarrow[\text{(ii) NaBH}_4]{\text{(i) Hg(OOCCF}_3)_2}$

## 3.1 General Physical Properties

i. Lower members are gases while higher members are colourless, pleasant smelling, low boiling point, volatile liquids
ii. They are lighter than water
iii. They are sparingly soluble in water but readily soluble in organic solvents like benzene and chloroform. Their solubility increases in the presence of alcohol probably, due to hydrogen bonding.
iv. Ethers are also very important solvents in the laboratory
v. Their boiling points, melting points and specific gravity increases with increase in molecular weight
vi. The boiling points of ethers are much lower than those of isomeric alcohols. The higher boiling points of alcohols are due to the intermolecular hydrogen bonding which is not possible in ethers
vii. Lower ethers acts as anesthetic and their vapour are highly inflammable
viii. Ethers are polar molecules and have definite dipole moments. The value of dipole moment of ethoxy ethane is 1.12D. The C-O-C valency angle in methoxy methane is $111^o$ while that of ethoxy ethane is $118^o$

## 3.2 Chemical Properties Of Ethers

Ethers are comparatively unreactive compounds. The ether linkage is quite stable towards bases, oxidizing agents and reducing agents- they do not react with alkalis, with dilute acids, phosphoric halides etc in the cold. This is because they lack the active hydrogen attached to oxygen as present in alcohol. However, they show reactions due to the presence of:

i. Alkyl radicals: They undergo substitution reactions as in the case of alkanes.
ii. Ethereal oxygen: This coordinate with electron deficient molecules or Lewis acids.
iii. Carbon-oxygen bond: It shows some cleavage reactions similar to carbon-carbon

cleavage. However, the carbon-oxygen linkage is not as stable as the carbon-carbon linkage.

### 3.2.1 Reactions of the alkyl groups: Substitution Reaction

i. Halogenation- Ethers undergo substitution at the alkyl radical when reacted with chlorine or bromine in the absence of sunlight. They form halogen substituted ethers.

$$ROCH_2CH_3 + Cl_2 \xrightarrow{\text{dark}} ROCHClCH_3 + HCl$$

Usually the hydrogen of the α-carbon is substituted most readily.

For example:

$$\underset{}{C_2H_5OC_2H_5} + Cl_2 \xrightarrow[\text{-HCl}]{\text{dark}} \underset{\alpha\text{-monochloroethoxy ethane}}{C_2H_5OCHClCH_3} \xrightarrow[\text{-HCl}]{Cl_2} \underset{\alpha,\alpha\text{-dichloroethoxy ethene}}{CH_3CHCl{-}O{-}CHClCH_3}$$

In sunlight, all the hydrogen is substituted to form perhalo ethers. For example,

$$C_2H_5OC_2H_5 + 10Cl_2 \xrightarrow{\text{light}} \underset{\text{Perchloroethoxy Ethane}}{C_2Cl_5OC_2Cl_5} + 10HCl$$

ii. Combustion: Ethers are volatile and highly inflammable. They burn in air to form carbon(IV) oxide and water.

$$C_2H_5OC_2H_5 + 4O_2 \longrightarrow 4CO_2 + 5H_2O$$

### 3.2.2 Reactions of ethereal oxygen

The oxygen atom in ether has two unshared lone pairs of electrons hence ether behaves like Lewis bases and coordinates with Lewis acids or substances deficient in electrons.

For example:

i. Formation of peroxides

Peroxides are formed when ethers are taken through a prolonged action of atmospheric oxygen or ozonized oxygen due to co-ordination of one lone pair of electrons of the ethereal oxygen with another oxygen atom.

$$R-O-R' + :O: \longrightarrow \underset{\substack{\downarrow \\ :O:}}{R-O-R'}$$

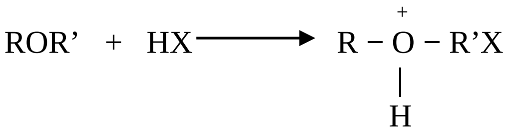
For example:

$$C_2H_5OC_2H_5 + O \longrightarrow (C_2H_5)_2O{\rightarrow}O$$

These peroxides are unstable compounds and decompose violently on heating.

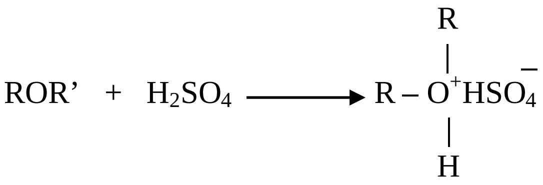
ii. Formation of oxonium salts

Ethers react with strong mineral acids to form oxonium salts which are stable at low temperature in high concentration. The oxonium salts when formed dissolved in solution.



$$ROR' + HX \longrightarrow R-\underset{\underset{H}{|}}{\overset{+}{O}}-R'X$$

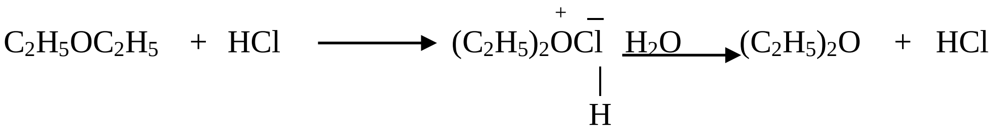
Dialkyl oxonium halide



$$ROR' + H_2SO_4 \longrightarrow R-\underset{\underset{H}{|}}{\overset{\overset{R}{|}}{O^+}}\overset{-}{HSO_4}$$

Dialkyl oxonium hydrogen tetraoxosulphate(VI)

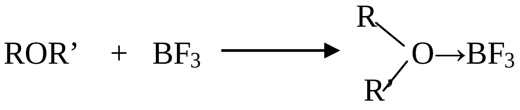
These salts however decompose to yield back ether and acid on dilution with water.



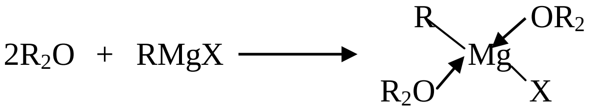
$$C_2H_5OC_2H_5 + HCl \longrightarrow (C_2H_5)_2\underset{\underset{H}{|}}{\overset{+}{O}}\overset{-}{Cl} \xrightarrow{H_2O} (C_2H_5)_2O + HCl$$

Diethyl oxonium chloride

They also form coordination complexes with Lewis acids like $BF_3$, $AlCl_3$, RMgX etc



Boron trifluoride etherate



Ether complex of Grignard reagent

This explains why they are used as solvent for Grignard reagents.

## Activity A/Self Assessment Exercise

Why are ethers useful as solvents in reactions involving the Grignard reagent

### 3.2.3 Reactions involving cleavage of carbon-oxygen bond

i. Hydrolysis: When ethers are boiled with water or treated with steam, they are hydrolysed to form alcohols. The rate of hydrolysis increases in the presence of dilute acid.

ii. Action of tetraoxosulphate (VI) acid: When ethers react with hot tetraxoxsulphate (VI) acid, cleavage of the carbon-oxygen bond occurs.

$$ROR' + H_2SO_4\,(conc.) \xrightarrow{heat} ROH + R'HSO_4$$

For example:

$$C_2H_5OC_2H_5 + H_2SO_4\,(conc.) \xrightarrow{heat} C_2H_5OH + C_2H_5HSO_4$$

Ethanol ethyl hydrogentetraoxosulphate(VI)

iii. Action of hydroboric or hydriodic acid: Ethers react with hydroboric or hydriodic acids in the cold to form an alcohol and alkyl halide. When unsymmentrical ether is used, the halogen attaches itself to the smaller of the two alkyl groups of the ether.

$ROR + 2HI \xrightarrow{Hot} 2RI + H_2O$ $C_2H_5OC_2H_5$

$+ 2HI$ heat $2\xrightarrow{C_2H_5I} + H_2O$ $CH_3OC_2H_5$

$+ 2HI \xrightarrow{heat} CH_3I + C_2H_5I + H_2O$

The order of reactivity of the acids is HI > HBr > HCl

iv. Action of Phosphorus pentachloride ($PCl_5$): Ethers react with hot phosphorus pentachloride, the reaction involve cleavage of carbon-oxygen bond to yield alkyl chlorides.

$ROR' + PCl_5 \longrightarrow RCl + R'Cl + POCl_3$

$C_2H_5OC_2H_5 + PCl_5 \longrightarrow 2C_2H_5Cl + POCl_3$

v. Action of acid derivatives: Ethers reacts with acid chlorides and acid anhydrides in the presence of catalyst like aluminium chloride or zinc chloride to form esters and alkyl halides.

$ROR + R'COCl \xrightarrow{AlCl_3} RCl + R'COOR$
Ester

For example:

$C_2H_5OC_2H_5 + CH_3COCl \xrightarrow{AlCl_3} C_2H_5Cl + CH_3COOC_2H_5$
Acyl chloride Ethyl ethanoate

$C_2H_5OC_2H_5 + (CH_3CO)_2O \xrightarrow{ZnCl_2} CH_3COOC_2H_5$
Ethanoic acid
Anhydride

## Activity B/Self Assessment Exercise

State the product(s) formed from the following reactions of propaoxy propane:

i. $C_3H_7OC_3H_7 + H_2SO_4 \longrightarrow$

ii. $C_3H_7OC_3H_7 + HI \longrightarrow$

iii. $C_3H_7OC_3H_7 + PCl_5 \longrightarrow$

### 3.2.4 Miscellaneous reactions

Apart from the reactions discussed above, ethers also undergo the following reactions:

i. Oxidation: Ethers are oxidized to form aldehydes or acids when treated with strong oxidising agents. For example:

$$C_2H_5OC_2H_5 \xrightarrow[-H_2O]{K_2Cr_2O_7/Acid} \underset{\text{Ethanal}}{2CH_3CHO} \xrightarrow{O} 2CH_3COOH$$

ii. Dehydration: Ethers undergo dehydration to form alkenes when ether vapour is passed over heated alumina.

$$C_2H_5OC_2H_5 \xrightarrow[360^{O}]{Al_2O_3} 2CH_2{=}CH_2 + H_2O$$

iii. Reaction with alkyl metallics: Ethers do not normally react with bases but strong bases like alkali metal alkyls, e.g $CH_3Na$, convert them into alkene and alkoxides.

$$\underset{\substack{\text{Methyl}\\ \text{Sodium}}}{\overset{+}{Na}\overset{-}{CH_3}} + H{-}CH_2CH_2{-}OC_2H_5 \longrightarrow \underset{\text{ethane}}{CH_4} + \underset{\text{ethene}}{CH_2{=}CH_2} + \underset{\substack{\text{sodium}\\ \text{ethoxide}}}{C_2H_5O^-Na^+}$$

iv. Reaction with carbon monoxide: Under suitable conditions ethers react with carbon monoxide to form esters

$$C_2H_5OC_2H_5 + CO \xrightarrow[500\text{ atm.}]{BF_3/150^{O}C} C_2H_5COOC_2H_5$$

## 4.0 Conclusion

Ethers undergo reactions that involve the alkyl group, the ethereal oxygen and the reactions that involve the C-O cleavage. Ethers also undergo reactions like oxidation, dehydration, reaction with alkyl methyl and reaction with carbon (II) oxide.

## 5.0 Summary

In this unit we have learnt that ethers undergo the following reactions:

**a.Reactions of the alkyl groups**: For example

i. Halogenation: $ROCH_2CH_3 + Cl_2 \xrightarrow{\text{dark}} ROCHClCH_3 + HCl$

ii. Combustion: $C_2H_5OC_2H_5 + 4O_2 \longrightarrow 4CO_2 + 5H_2O$

b. **Reaction of ethereal oxygen: For example**

iii. Formation of peroxides

$$R-O-R' + :O: \longrightarrow R-\underset{\substack{\downarrow\\ :O:}}{O}-R'$$

iv. Formation of oxonium salts

$$ROR' + HX \longrightarrow R-\underset{\substack{|\\ H}}{O}-R'X$$

Dialkyl oxonium halide

c. **Reactions involving cleavage of carbon-oxygen bond: For example**

i. Hydrolysis

ii. Action of tetraoxosulphate(vi) acid :

$ROR' + H_2SO_4(Conc.) \xrightarrow{heat} ROH + R'HSO_4$

iii. Action of hydroboric or hydriodic acid

$ROR + 2HI$ Hot $2RI + H_2O$

iv. Action of Phosphorus pentachloride($PCl_5$)

$ROR' + PCl_5 \longrightarrow RCl + R'Cl + POCl_3$

v. Action of acid derivatives

$ROR + R'COCl \xrightarrow{AlCl_3} RCl + R'COOR$

Ester

d. **Miscellaneous reactions of ethers**

i. Oxidation

$$C_2H_5OC_2H_5 \xrightarrow[-H_2O]{K_2Cr_2O_7/Acid} 2CH_3CHO \xrightarrow{O} 2CH_3COOH$$

Ethanal

ii. Dehydration

$$C_2H_5OC_2H_5 \xrightarrow[360^O]{Al_2O_3} 2CH_2{=}CH_2 + H_2O$$

iii. Reaction with alkyl metallics

$$\overset{+}{Na}\overset{-}{C}H_3 + H{-}CH_2CH_2{-}OC_2H_5 \longrightarrow CH_4 + CH_2{=}CH_2 + C_2H_5O^-Na^+$$

Methyl Sodium — ethane — ethene — sodium ethoxide

iv. Reaction with carbon monoxide

$$C_2H_5OC_2H_5 + CO \xrightarrow[500\ atm.]{BF_3/150^OC} C_2H_5COOC_2H_5$$

## 6.0 Tutor Marked Assignment

1. Discuss the reactions of ethoxyethane under the following headings:

- Hydrogenation
-oxidation
-oxonium formation
-reaction with Grignard reagents
-reaction with alkyl metal

## 7.0 Further Reading and Other Resources

K.S.TEWARI and N.K. VISHNOI (2006)- A Textbook of Organic Chemistry. Third Edition

Robert Thornton Morrison and Robert Neilson Boyd(2008) – Organic Chemistry-Sixth Edition

Organic Chemistry, 4th Edition –Paula Yurkanis Bruice

# Unit 3: Epoxides- Preparation and Reactions

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## 1.0 Introduction

When an oxygen atom is linked to carbon atoms of a carbon chain forming a three membered ring, the compound are called epoxides. The naming of epoxide has been discussed earlier (unit 1) in this module.

## 2.0 Objectives

At the end of this unit you should be able to:

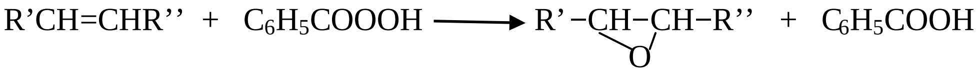
i. Discuss the preparation of epoxides using different methods
ii. Discuss the physical properties of epoxides
iii. Discuss the chemical properties of epoxides

## 3.0 Methods of Formation

Epoxides can be prepared from the following methods:

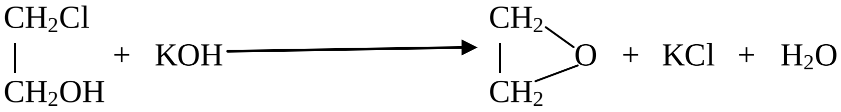
i. Oxidation of alkenes with peroxy acids. Example of peroxy acids are perbenzoic acid ($C_6H_5COOOH$), monoperphthalic acid ($C_6H_5(COOH)_2$) and p-nitrobenzoic acid ( $C_6H_4(NO_2)COOH$).

For example:

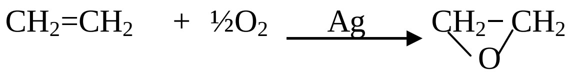


Peroxyfluoroacetic has been found to be a better agent for epoxidation.

ii. Ethylene oxide can be prepared by treating ethylene chlorohydrins with potassium hydroxide.



iii. Ethylene oxide can also be prepared by passing a mixture of ethene and air over silver catalyst under pressure at a temperature of 200-400°C



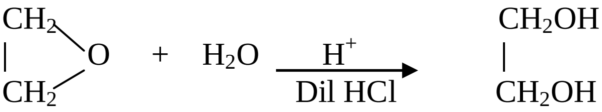
## 3.1 Chemical Properties

Epoxy ethane is a gas at ordinary temperature. They are highly reactive and the ring opens at various reactions.

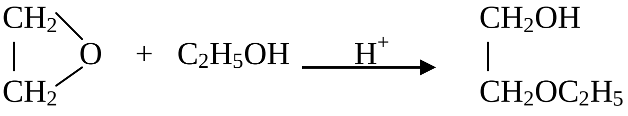
### 3.1.1 Acid catalysed cleavage

i. Convertion to 1,2-diol: When treated with dilute acid solution, epoxides are converted to 1,2-diol.

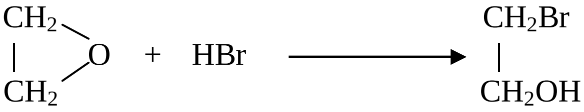
For example:



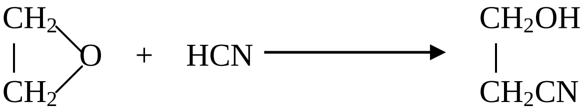
ii. Epoxides react with alcohols in the presence of small amount of acid catalyst to form monoethers.



iii. Epoxides react with concentrated halogen acid solution to form halogenohydrins

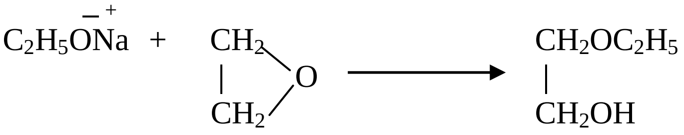


iv. Epoxides react with hydrogen cyanide, HCN, to form ethylene cyanohydrins.



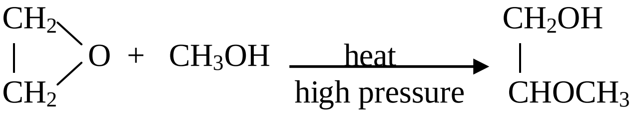
### 3.1.2 Base catalyzed cleavage

i. Reaction with sodium ethoxide. Epoxides react with sodium ethoxide to give 2-ethoxy ethanol (ethyl cellosive).



2-ethoxy ethanol

ii. Epoxides react with methanol under pressure to form 2-methoxy ethanol (methyl cellosolve).



iii. Epoxides react with cellosolves to give carbitols

$$HOCH_2CH_2OCH_3 + C_2H_4O \longrightarrow \underset{\text{Carbitol}}{HOCH_2CH_2OCH_2CH_2OCH_3}$$

iv. Reaction with ammonia: Ammonia reacts with epoxides to give 2-amino ethanol. This reaction usually produces a mixture of three amino acids.

$$C_2H_4O + NH_3 \longrightarrow HOCH_2CH_2NH_2 \xrightarrow{C_2H_4O} (HOCH_2CH_2)_2NH$$

2-amino ethanol

$$\xrightarrow{C_2H_4O} (HOCH_2CH_2)_3N$$

When treated with $RNH_2$ and $R_2NH$, epoxides gives 2(N-Alkyl) amino ethanol and 2- (N,N-Diakyl amino ethanol respectively.

$$C_2H_4O + RNH_2 \longrightarrow HOCH_2CH_2NHR$$

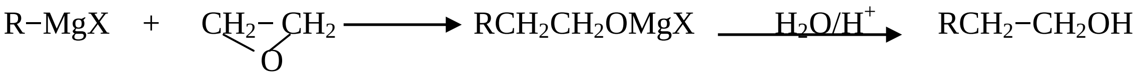
2-(N-alkyl) amino ethanol

$$C_2H_4O + R_2NH \longrightarrow HOCH_2CH_2NR_2$$

2-(N,N-Dialkyl)amino ethanol

### 3.1.3 Reaction with Grignard reagent

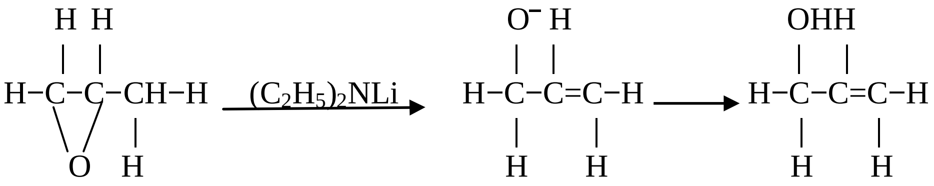
Epoxides react with Grignard reagents with the cleavage of the carbon-oxygen bond to give primary alcohols with a greater number of carbon atoms. The chain is increased by the number of carbon-atoms present in the alkyl radical of the Grignard reagent. For example,



$$R{-}MgX + CH_2{-}CH_2(O) \longrightarrow RCH_2CH_2OMgX \xrightarrow{H_2O/H^+} RCH_2{-}CH_2OH$$

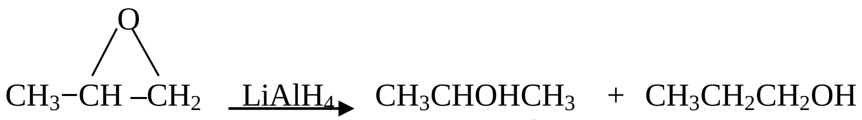
### 3.1.4 Reaction with organolithium compounds

Epoxides when treated with lithium diethylamide are converted to allylic alcohols. For example,



### 3.1.5 Reduction of epoxides

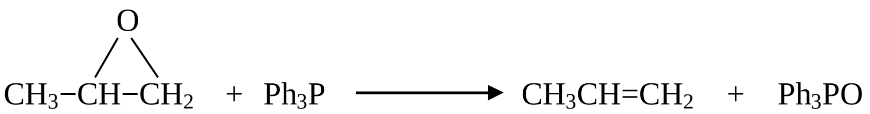
Epoxides can be reduced using lithium aluminium hydride to yield alcohol. Unsymmetrical epoxides give highly substituted alcohols as main product. For example,



$$CH_3{-}CH{-}CH_2(O) \xrightarrow{LiAlH_4} CH_3CHOHCH_3 + CH_3CH_2CH_2OH$$

Main product

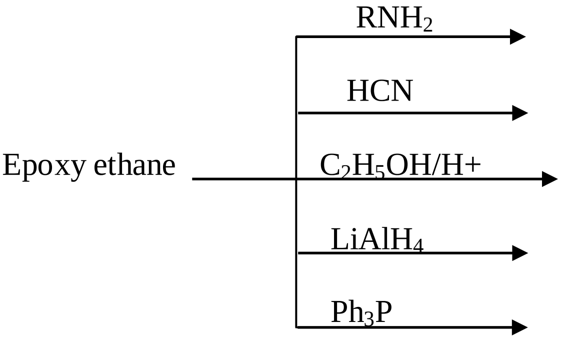
When tertiary phosphine is the reducing agent, epoxides are converted to the corresponding alkenes.



$$CH_3{-}CH{-}CH_2(O) + Ph_3P \longrightarrow CH_3CH{=}CH_2 + Ph_3PO$$

## Activity A/Self Assessment Exercise

Complete the scheme below, by stating the products formed:



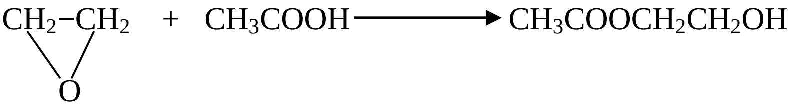
### 3.1.6 Oxidation of epoxides

Epoxides are oxidised to α-hydroxyl ketones by dimethyl sulphoxides.

$$CH_3{-}CH{-}CH{=}CH_2 \quad + \ Me_2SO \xrightarrow{H^+} CH_3CHOHCOCH_3 \quad + \ Me_2S$$

### 3.1.7 Reaction with ethanoic acid

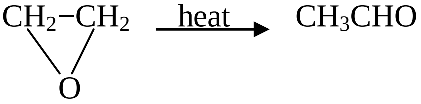
Epoxides react with ethanoic acid to form glycol monoethanoate



$$CH_2{-}CH_2 \ (O) \quad + \quad CH_3COOH \longrightarrow CH_3COOCH_2CH_2OH$$

### 3.1.8 Action of heat

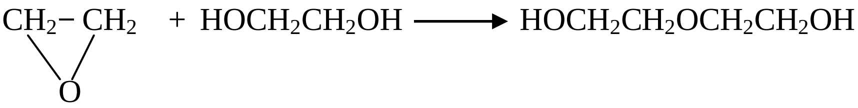
Epoxides undergo rearrangement on heating to form ethanal



$$CH_2{-}CH_2 \ (O) \xrightarrow{heat} CH_3CHO$$

### 3.1.9 Reaction with glycol

When heated with ethane-1,2-diol (ethelene glycol) epoxide forms diethelene glycol.



$$CH_2{-}CH_2 \ (O) \quad + \ HOCH_2CH_2OH \longrightarrow HOCH_2CH_2OCH_2CH_2OH$$

## 3.2 Uses of Epoxides

- Epoxides are used as fumigant and insecticides for grain, tobacco and dried fruits
- They are used in preparation of the glycol ethers used as industrial solvents
- Methyl cellosolve, ethyl cellosolve and butyl cellosolve are used as solvents for cellulose.
- Epoxides are used in the manufacture of non-ionic surface active agents.
- Plyethylene glycols prepared from epoxides are used as industrial solvents.

## 4.0 Conclusion

Ethers can undergo acid and base catalysed cleavage.

## 5.0 Summary

In this unit we have learnt that:

A. Ethers can be prepared from the following methods:

i. Oxidation of alkenes with peroxy acids.

ii. Ethylene oxide can be prepared by treating ethylene chlorohydrins with potassium hydroxide.

iii. Ethylene oxide can also be prepared by passing a mixture of ethene and air over silver catalyst under pressure at a temperature of 200-400$^o$C

B. They are highly reactive and the ring opens at various reactions.

C. They undergo the following reactions:

a. Acid catalysed cleavage, e.g the convertion to 1,2-diol e.g

i. Reaction with alcohols

ii. Epoxides reacts with concentrated halogen acid solution

iii. Epoxides reacts with hydrogen cyanide

b. Base catalysed cleavage e.g

i. Reaction with sodium ethoxide. Epoxides

ii. Reaction of epeoxides with methanol

iii. Epoxides reacts with cellosolves to give carbitols

iv. Reaction with ammonia

c . Reaction with Grignard reagent

c. Reaction with organolithium compounds

e. Reduction of epoxides

f. Oxidation of epoxides

g. Reaction with ethanoic acid

h. Action of heat

i. Reaction with glycol

D. Epoxides are used as fumigant and insecticides; they are used in preparation of the glycol ethers, ethyl cellosolve, ethyl cellosolve, butyl cellosolve and polyethylene glycols. Epoxides are used in the manufacture of non-ionic surface active agents.

## 6.0 Tutor Marked Assignment

1. What are epoxides?
2. Give two methods of preparing epoxides
3. Discuss using equations, their reactions with:

i. Grignard reagent
ii. Dimethyl sulphoxide
iii. Triphenyl phosphine

## 7.0 Further Reading and other Resources

a. K.S.TEWARI and N.K. VISHNOI (2006)- A Textbook of Organic Chemistry
-Third Edition

b. Robert Thornton Morrison and Robert Neilson Boyd(2008) – Organic Chemistry - Sixth Edition

c. Organic Chemistry, 4th Edition –Paula Yurkanis Bruice

# Mobule 3: Carboxylic Acids and Their Derivatives

## Unit 1: Carboxylic Acids and Their Derivatives -Naming and Physical properties

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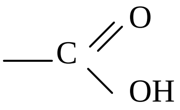
## 1.0 Introduction

Carboxylic acids refers to the class of organic compound with the carboxyl functional group



which contains both a carbonyl and a hydroxyl functional group.

## 2.0 Objectives

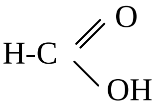
By the end of this unit, you should be able to:

(a) Define carboxylic acids
(b) Give examples of carboxylic acids
(c) Name and draw the structures of simple carboxylic acid
(d) Name and draw structures of carboxylic acid derivatives
(e) Explain the properties of carboxylic acids

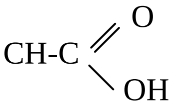
## 3.0 General Formula of Carboxylic Acids

The functional group is attached to an alkyl group or an aromatic ring. The general formula for carboxylic acid is $C_nH_{2n+1}$ COOH ($n \geqslant 1$ or simply R COOH where the R refers to an alkyl – or aryl group.

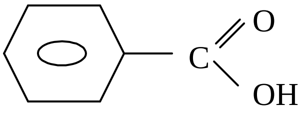
For example,



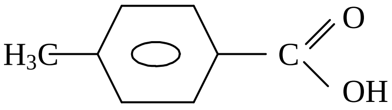
Methanoic acid



Ethanoic acid



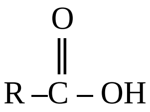
Benzoic acid



4-methylbenzoic acid

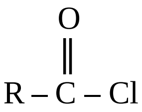
## 3.1 Derivatives of Carboxylic Acids

Carboxylic acid derivatives are the group of compounds in which the –OH group in the acid has been replaced by other groups. Esters have an –OR group, acyl chloride have the –OH replaced with –Cl bonded to the carbonyl carbon atom amides have an $-NH_2$, -NHR or $NR_2$ group bonded to the carbonyl carbon atom while acid anhydrides have the $-O_2$ CR group.



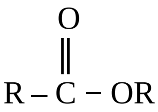
$R-\overset{\overset{O}{\|}}{C}-OH$

Carboxylic acid



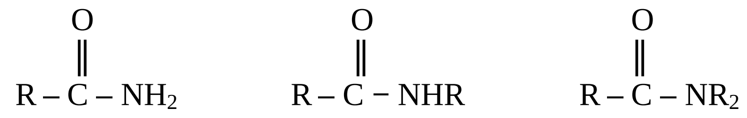
$R-\overset{\overset{O}{\|}}{C}-Cl$

Acyl chloride



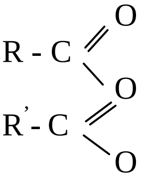
$R-\overset{\overset{O}{\|}}{C}-OR$

Ester



$R-\overset{\overset{O}{\|}}{C}-NH_2$ $R-\overset{\overset{O}{\|}}{C}-NHR$ $R-\overset{\overset{O}{\|}}{C}-NR_2$

Amides



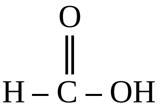
Acid anhydride

## 3.2 Naming Carboxylic Acids and Their Derivatives - IUPAC Nomenclature

### 3.2.1 Carboxylic Acids

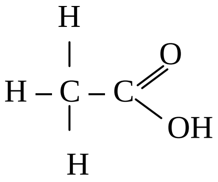
Carboxylic acids are named from the corresponding alkane, by replacing the ending '-e' with the suffix '-oic acid'.

For example

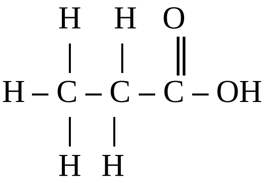


$H-\overset{\overset{O}{\|}}{C}-OH$

Methan**oic acid**

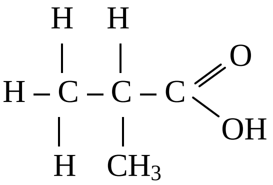


Ethan**oic acid**

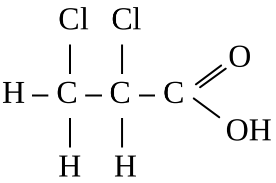


$H-\overset{\overset{H}{|}}{\underset{\underset{H}{|}}{C}}-\overset{\overset{H}{|}}{\underset{\underset{H}{|}}{C}}-\overset{\overset{O}{\|}}{C}-OH$

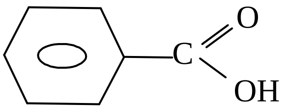
Propan**oic acid**



2-methyl propan**oic acid**



2, 3–Dichloropropan**oic acid**

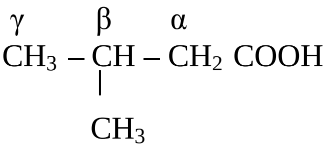


Benz**oic acid**

The numbering of the carbon starts with the carbon atom in the carboxylic acid functional group.

The common names of carboxylic acid are generally derived from the Latin or Greek name of their source of origin. The positions of substitution in the hydrocarbon chain are denoted by the Greek letters α, β, γ and so on, rather than numbers.

For example:



$$\overset{\gamma}{CH_3} - \underset{\underset{CH_3}{|}}{\overset{\beta}{CH}} - \overset{\alpha}{CH_2}\ COOH$$

β - methylvaleric acid

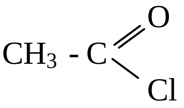
**Table 1.1: IUPAC names, Common names and Sources of Some Carboxylic acids**

| Formula | IUPAC Name | Common Name | Source |
|---|---|---|---|
| $HCOOH$ | Methanoic acid | Formic acid | |
| $CH_3COOH$ | Ethanoic acid | Acetic acid | Vinegar |
| $CH_3CH_2COOH$ | Propanoic acid | Propanionic acid | Plant and Animal Products |
| $CH_3(CH_2)_2COOH$ | Butanoic acid | n-Butyric acid | Rancid butter |
| $CH_3(CH_2)_{14}COOH$ | Hexadecanoic acid | Palmitic acid | |
| $CH_3(CH_2)_{16}COOH$ | Octadecanoic acid | Stearic acid | |

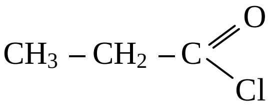
### 3.2.2 Acyl chlorides

Acyl chlorides are named by replacing the ending ‘-e’ from the corresponding alkanes name with ‘-oyl chloride’.

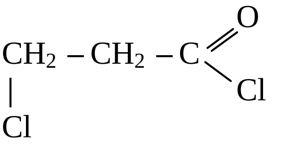
For example,



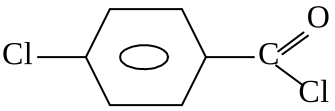
Ethan**oyl chloride**



Propan**oy chloride**



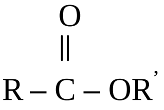
3-Chloropropan**oyl chloride**



4 –Chlorobenz**oyl chloride**

### 3.2.3 Esters

Esters are derivatives of carboxylic acids with the general formula



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

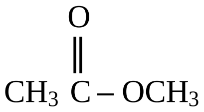
R and R' may be the same or different alkyl groups.

Esters are named as ‘alkyl alkanoate’. The ‘alkyl’ is derived from the original alcohol while the ‘alkanoate’ is derived from the carboxylic acid.

For example:

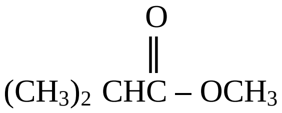
$$H-\overset{\overset{O}{\|}}{C}-OCH_2CH_3$$

Ethyl methanoate



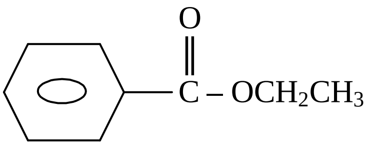
$$CH_3\ \overset{\overset{O}{\|}}{C}-OCH_3$$

Methyl ethanoate

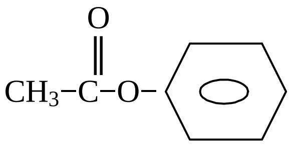


$$(CH_3)_2\ CH\overset{\overset{O}{\|}}{C}-OCH_3$$

Methyl 2-methyl propanoate



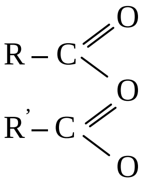
Ethyl benzoate



Phenyl ethanoate

**3.2.4 Acid anhydrides**

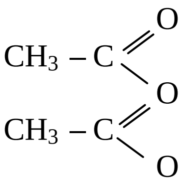
They are derivatives of carboxylic acids with the general formula.



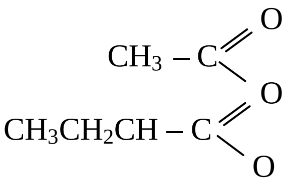
R and R' may be the same or different alkyl groups.

Acid anhydrides are named as carboxylic anhydride with the suffix '-oic anhydride'.

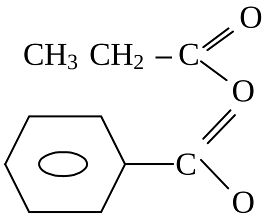
For example:



Ethan**oic anhydride**



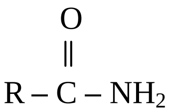
Ethanoic butan**oic anhydride**



Propanoic benzoic anhydride

**3.2.5 Amides**

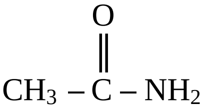
Amides have the general formula



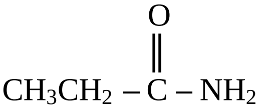
$$R-\overset{\overset{O}{\|}}{C}-NH_2$$

Amides are named from the corresponding alkanes by replacing the 'e' from the alkane with the suffix '- amide'.

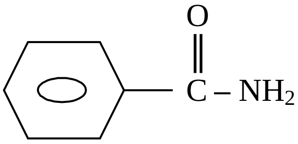
For example:


$CH_3-\overset{\overset{O}{\|}}{C}-NH_2$

Ethanamide


$CH_3CH_2-\overset{\overset{O}{\|}}{C}-NH_2$

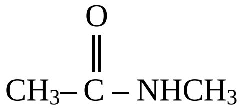
Propanamide



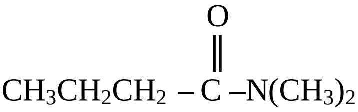
Benzamide

When an amide has substituents on its nitrogen atom, the prefix "N" is used.

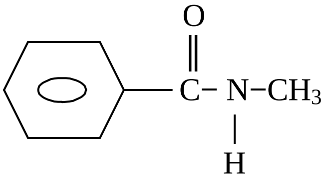
For example,


$CH_3-\overset{\overset{O}{\|}}{C}-NHCH_3$

N – Methyl ethanamide


$CH_3CH_2CH_2-\overset{\overset{O}{\|}}{C}-N(CH_3)_2$

N, N-Dimethyl butanamide

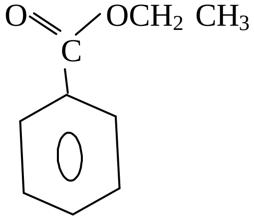


N-Methyl benzamide

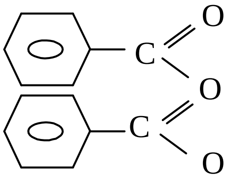
## Activity A/Self Assessment Exercise

(I) Give the IUPAC names of the following compounds.

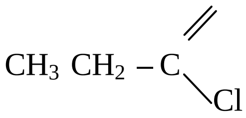
i.



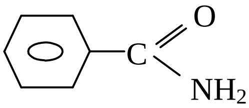
(iv)



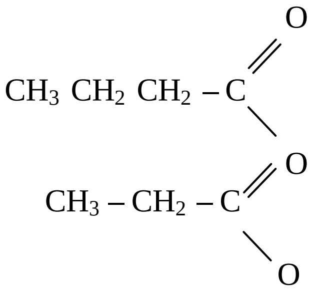
ii.



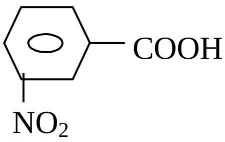
(v)



iii.



(vi)



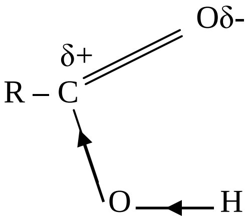
(II) Draw the Structural formulae of the following compounds:

i. Ethanoyl propanoyl anhydride
ii. 3 – Ethyl butanoyl chloride
iii. N, N – Diethylbutanamide

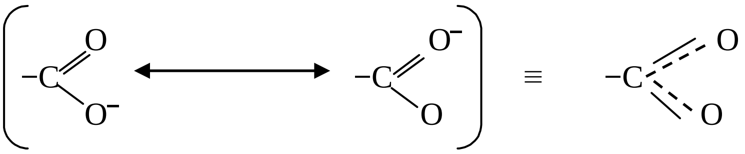
iv. Ethyl 2-methypentanoate
v. 3-hydroxy 1-2-methylbutanoic acid
vi. Benzene- 1,4 –dioic acid

## 3.3 Structure of Carboxylic Acids

In the structure of carboxylic acids, at the carbonyl linkage, there is a mesomeric withdrawal of electrons away from the carbon atom towards the more electronegative atom creating a relative positive charge on the carbon atom. This deficiency of electrons about the carbon atom intensifies the inductive pull of electrons away from the hydrogen atom in the oxygen-hydrogen bond enhancing the stability of the carboxylate anion, $RCOO^-$, and promoting the release of a proton.



The carboxylate anion is a resonance hybrid, the π electrons being delocalize about the two carbon-oxygen bonds, making both bonds equivalent as shown below.



## 3.4 Physical Properties

All simple aliphatic carboxylic acids are liquids at room temperature. They have a characteristic pungent smell and sour taste. Aromatic acids are crystalline solids.

The boiling points of carboxylic acids increases with relative molecular mass and they are higher than those of the corresponding alkanes but lower than that of alcohols. Aromatic acids have higher melting points than their aliphatic counterparts of comparative molecular mass.

The first four aliphatic acids are completely miscible with water due to the ability of the functional group to form hydrogen bonds with the water molecule. However, the higher homologue becomes progressively less soluble in water because of their greater hydrocarbon. Benzoic acid is only slightly soluble in cold water but dissolves reading in hot water. All carboxylic acids can be dissolved in suitable organic solvents.

Generally, density of carboxylic acid decrease with increasing relative molecular mass.

Volatile aldehydes and ketones are flammable. Simple ketones are less toxic than simple aldehydes.

## Activity B/Self Assessment Exercise

Discuss the following physical properties of carboxylic acids:

i. Boiling points
ii. Solubility in water.

## 4.0 Conclusion

Carboxylic acids refer to the class of organic compound with the carboxyl functional group which contains both a carbonyl and a hydroxyl functional group.They are named by replacing the ending ‘e’ from the corresponding alkane with the suffix ‘oic acid’.

Acyl chloride, ester, amides and acid anhydride are derivatives of carboxylic acids

## 5.0 Summary

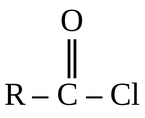
In this unit we have learnt that:

i. Carboxylic acids have both a carbonyl and a hydroxyl functional group.

ii. Carboxylic acids are named from the corresponding alkane, by replacing the ending ‘-e’ with the suffix ‘-oic acid’.

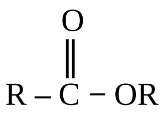
iii. The numbering of the carbon starts with the carbon atom in the carboxylic acid functional group.

iv. The following are derivatives of carboxylic acid.



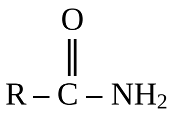
$R-\overset{\overset{O}{\|}}{C}-Cl$

Acyl chloride

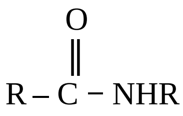


$R-\overset{\overset{O}{\|}}{C}-OR$

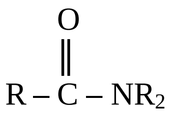
Ester



$R-\overset{\overset{O}{\|}}{C}-NH_2$

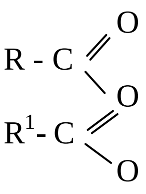


$R-\overset{\overset{O}{\|}}{C}-NHR$



$R-\overset{\overset{O}{\|}}{C}-NR_2$

Amides



Acid anhydride

v. Acyl chlorides are named by replacing the ending ‘-e’ from the corresponding alkanes name with ‘-oyl chloride’.

vi. Esters are named as ‘alkyl alkanoate’.

vii. Acid anhydrides are named as carboxylic anhydride with the suffix '-oic anhydride'.

viii. Amides are named from the corresponding alkanes by replacing the 'e' from the alkane with the suffix '- amide'.

ix. When an amide has substituents on its nitrogen atom, the prefix "N" is used.

x. All simple aliphatic carboxylic acids are liquids at room temperature.

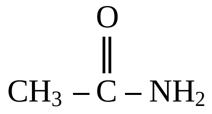
xi. The boiling points of carboxylic acids increases with relative molecule mass
Xii.Solubility in water decreases as molecular mass increase

xiii. Density of carboxylic acid decrease with increasing relative molecule mass.

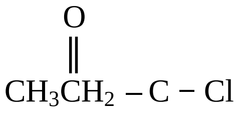
## 6.0 Tutor Marked Assignment

i. Explain why only carboxylic acids with five or fewer carbons are soluble in water.

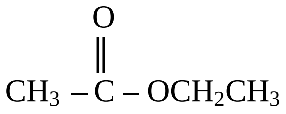
ii. Identify the following carboxylic acid derivatives



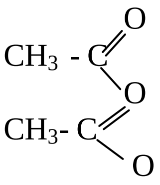
$CH_3 - \overset{\overset{O}{\|}}{C} - NH_2$



$CH_3CH_2 - \overset{\overset{O}{\|}}{C} - Cl$



$CH_3 - \overset{\overset{O}{\|}}{C} - OCH_2CH_3$



## 7.0 Further Readings and other Resources

K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry. Third Edition

Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry- Sixth Edition

Y.C.Wong; C.T.Wong; S.O.Onyiruka and L.E.Akpanisi (2001)-University Organic Chemistry: The Fundamentals

# Unit 2: Preparation of Carboxylic Acids

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## 1.0 Introduction

Carboxylic acids can be prepared using diverse methods.

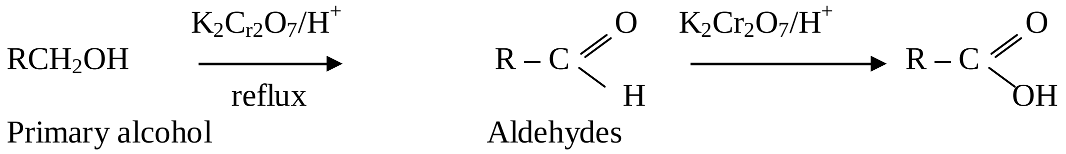
## 2.0 Objectives

At the end of this unit, you should be able to:

i. Prepare carboxylic acids from aldehydes and ketones using oxidation reaction
ii. Explain preparation of carboxylic acids from hydrolysis of nitriles
iii. Explain preparation of carboxylic acids from the hydrolysis

## 3.0 Oxidation of Primary Alcohols and Aldehydes or ketones

Oxidation of primary alcohols and aldehydes or ketones gives carboxylic acids.

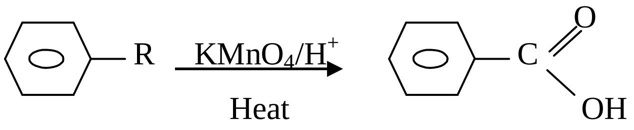


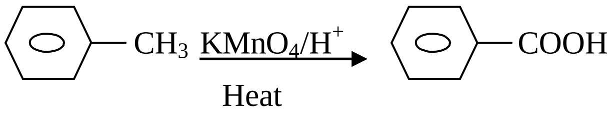
The alcohol is heated under reflux with excess oxidizing potassium dichromate (VI) or manganese (VII). The acid is separated from the reaction mixture.

For example,

$$CH_3\ CH\ OH \xrightarrow[\text{reflux}]{K_2Cr_2O_7/H^+} CH_3\ CHO \xrightarrow[\text{reflux}]{K_2Cr_2O_7/H^+} CH_3COOH$$

Benzoic acid can be prepared from the oxidation of alky benzenes using acidified potassium tetraoxomanganate (vii) as the oxidizing agent.



Example


This reaction will only be possible when R is methyl or other alkyl group but not $3^o$ alkyl groups.

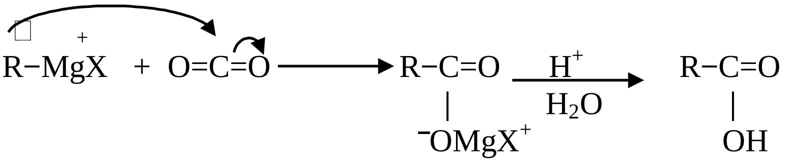
## Activity A/Self Assessment Exercise

1. Predict the acid formed from the following oxidation reactions

    a. $CH_3(CH_2)_3OH + K_2Cr_2O_7 \longrightarrow$
    b. $CH_3CH(CH_3)CH_2OH + K_2Cr_2O_7 \longrightarrow$
    c. $CH_3CHO + K_2Cr_2O_7 \longrightarrow$

## 3.1 From Grignard's Reagent and $CO_2$

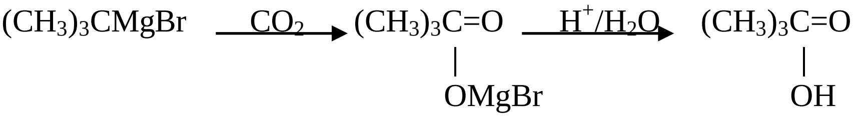
This method is especially used for the preparation of fatty acids.



$$R{-}MgX + O{=}C{=}O \longrightarrow \underset{^{-}OMgX^{+}}{R{-}C{=}O} \xrightarrow[H_2O]{H^+} \underset{OH}{R{-}C{=}O}$$

A carboxylate salt

For example:



$$(CH_3)_3CMgBr \xrightarrow{CO_2} \underset{OMgBr}{(CH_3)_3C{=}O} \xrightarrow{H^+/H_2O} \underset{OH}{(CH_3)_3C{=}O}$$

Tert-Butyl Magnesium

Trimethyl ethanoic acid

## 3.2 Hydrolysis of Nitriles

The hydrolysis of nitriles, R – C = N, in acidic or alkaline medium give carboxylic acids.

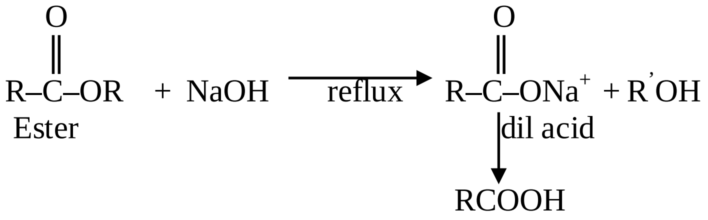
$$R{-}C\equiv N \underset{-H_2O}{\overset{+H_2O}{\rightleftharpoons}} RCONH_2 \underset{-H_2O}{\overset{+H_2O}{\rightleftharpoons}} RCOO^{-}NH_4^{+} \xrightarrow{H^+} RCOOH + NH_3$$

$H^+$

The reaction involves the formation of an amide as the intermediate which is further hydrolyzed into a carboxylate. The carboxylate reacts with a dilute mineral acid to form carboxylic acid.

## 3.3 Hydrolysis of Esters (Saponification)

The hydrolysis of esters may be accomplished by boiling under reflux with concentrated aqueous sodium hydroxide.



$$\underset{\text{Ester}}{R{-}\overset{\overset{O}{\|}}{C}{-}OR} + NaOH \xrightarrow{\text{reflux}} R{-}\overset{\overset{O}{\|}}{C}{-}ONa^{+} + R'OH \quad \xrightarrow{\text{dil acid}} RCOOH$$

## Activity B/Self Assessment Exercise

1. State the conditions necessary for the following reactions to take place:
   i. $CH_3CH_2CH_2OH \longrightarrow CH_3CH_2COOH$
   ii. $(CH_3)_3CH_2CONH_2 \longrightarrow (CH_3)_3CH_2COOH$
   iii. $(CH_3)_2CHMgX \longrightarrow (CH_3)_2COOH$

## 3.4 Cannizzaro Reaction

This reaction is only undergone by aromatic aldehydes and those aliphatic ones containing no α –hydrogen atoms.

For example,

$$2C_6H_5CHO + \underset{40-60\%}{NaOH} \longrightarrow C_2H_5COONa^{+} + C_6H_5CH_2OH$$

If a suitable aldehyde is treated with a concentrated aqueous solution of alkali at room temperature, it undergoes simultaneous oxidation and reduction to yield the appropriate salt of the carboxylic acid and an alcohol.

## 4.0 Conclusion

Carboxylic acids can be prepared from the oxidation of primary alcohol and aldehydes or ketones, reaction of Grignard reagent with carbon (iv) oxide, hydrolysis of nitriles, hydrolysis of esters and Cannizzaro reaction.

## 5.0 Summary

In this unit we have learnt that:

i. Oxidation of primary alcohols and aldehydes or ketones gives carboxylic acids.

ii. Grignard reagents react with $CO_2$ to give carboxylic acids.

ii. The hydrolysis of nitriles, $R - C \equiv N$, in acidic or alkaline medium give carboxylic acids.

iii. The alkali hydrolysis of esters gives carboxylic acid

iv. Cannizzaro reaction- undergone by aromatic aldehydes and those aliphatic ones containing no α –hydrogen atoms gives carboxylic acids.

## 6.0 Tutor Marked Assignment

i. Draw the structure and name the carboxylic acid formed when the following organic compounds undergo oxidation reaction

(i)Ethanol (ii) Butanol (iii) benzaldehyde

ii. Explain the preparation of carboxylic acid from the Cannizzaro reaction

## 7.0 Further Reading and other Resources

a. K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry -Third Edition

b. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry - Sixth Edition

c. Y.C.Wong; C.T.Wong; S.O.Onyiruka and L.E.Akpanisi (2001)-University Organic Chemistry: The Fundamentals

# Unit 4: Reactions of Carboxylic Acids

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## 1.0 Introduction

Carboxylic acids consists of a carboxyl group – COOH group (-C=O and –OH) and an alkyl group. Thus its chemical properties are due to these two groups.

## 2.0 Objectives

At the end of this unit you should be able to:

i. Explain the acidic properties of carboxylic acids
ii. Discuss the reactions of carboxylic acid has an acid
iii. E xplain the following reactions of carboxylic acids
    - Esterification
    - Halogenations
iv. Explain how esters are converted into:
    - Acyl chloride
    - Amide
    - Acid anhydrides
v. Explain the reduction of carboxylic acids

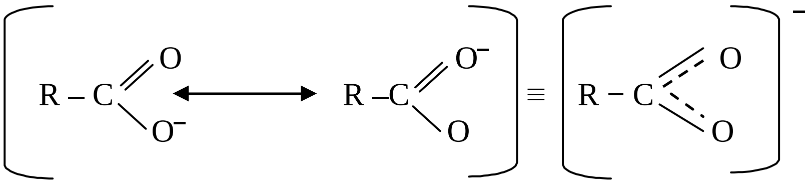
## 3.0 Acidic Properties of Carboxylic Acids

The acidic properties of carboxylic acids are due to their possessing ionizable hydrogen ions ($H^+$), which results in the formation of carboxylates.

$$RCOOH + H_2O \rightleftharpoons RCOO^- + H_3O^+ \qquad K_a = 5$$

Carboxylic acids are only partially ionized in aqueous solution owing to the predominantly covalent nature of the molecule, they are only very weak in comparison with the mineral acids. They are however $10^{10}$ to $10^{11}$ times stronger in acidic strength than alcohols.

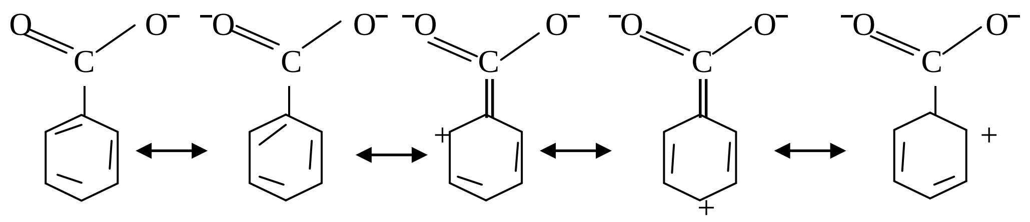
The comparative strengths of carboxylic acids are attributable to the stability of the carboxylic anion which is a resonance hybrid of two canonical forms, A and B below.



A B C

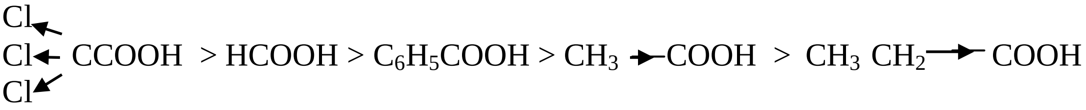
The resonance energy assist the ionization process, hence the released of the proton.
The two canonical forms may be conveniently represented by the single structure C. The structure, C illustrates the equivalence of both carbon-oxygen bonds and also the equal distribution of the negative charge between the oxygen atoms. This effect of charge dispersal results in the stabilization of the carboxylate ion, which enhances the dissociation of the acids.

The effect of charge of dispersal is more significant in benzoic acid and this enhances the stabilization of the carboxylate ion.



Apart from resonance effect, the acidity of a carboxylic acid is affected by the substituent on its hydrocarbon chain. The effect of the substituents on the acidity of carboxylic acids depends on whether the substituents are electron-donating or electron withdrawing. When an electron-donating substituent (+I effect) is attached a carboxylic group, it intensifies the negative charge on the carboxylate ion hence destabilizing the anion making it difficult for the carboxylic acid to form the carboxyl ate and hydrogen ions.

On the contrary, when an electron withdrawing substituent (-I effect), is attached to a carboxylic group, it reduces the negative charge from the carboxylate ion (hence stabilizing the anion. The higher the number of substituent with –I effect, the higher the acidity of the carboxylic acid. The acidic strength decreases in the order.



$$Cl_3CCOOH > HCOOH > C_6H_5COOH > CH_3 \rightarrow COOH > CH_3CH_2 \rightarrow COOH$$

The distance between the substituent and the carboxylic group also has a significant effect on the acidity of carboxylic acid.

## Activity A/Self Assessment Exercise

i. Arrange the following acids in an ascending order of acidity:
$CH_3COOH$, $CHCl_2COOH$, $CH_2Cl_2COOH$, $CCI_3COOH$

## 3.1 Reactions due to Carboxyl Group

As an acid, carboxylic acids undergo ionization into proton and the acid anion.

$$RCOOH \rightleftharpoons RCOO^- + H^+$$

### 3.1.1 Salt Formation

As an acid, carboxylic acids, irrespective of whether they are water soluble or not, liberate hydrogen in the presence of metals and carbon (iv) oxide when added to either sodiumtrioxocarbonate (iv) or hydrogentrioxocarbonate(iv) forming the metal carboxylate in all the reactions. For example,

$$RCOOH + 2Na \longrightarrow 2RCOO^-Na^+ + H_2$$

Sodium Carboxylate

$$2RCOOH + Mg \longrightarrow (RCOO^-)_2Mg^{2+} + H_2$$

Magnesium Carboxylate

$$RCOOH + NaOH \longrightarrow RCOO^-Na + H_2O$$
$$2RCOOH + Na_2CO_3 \longrightarrow 2RCOO^-Na^+ + CO_2 + H_2O$$
$$RCOOH + NaHCO_3 \longrightarrow RCOO^-Na^+ + CO_2 + H_2O$$

The carboxylic acid can be generated by treating the salt with dilute mineral acid.

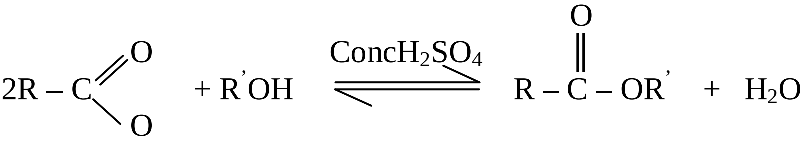
$$RCOONa + HCl \longrightarrow RCOOH + NaCl$$

## 3.2 Reactions involving hydroxyl group

The following reactions involve the hydroxyl group.

### 3.2.1 Esterification

Esters are formed when carboxylic acid reacts with an alcohol in the presence of concentrated tetraoxosulphate (vi) acid as a catalyst.



$$2R-C\overset{O}{\underset{O}{\lessgtr}} + R'OH \underset{}{\overset{ConcH_2SO_4}{\rightleftharpoons}} R-\overset{\overset{O}{\|}}{C}-OR' + H_2O$$

This reaction is slow and reversible and the yield of ester is often low.

Esters are also formed when carboxylic acids react with sulphur dichloride oxide followed by an alcohol.

$$RCOOH \xrightarrow{SOCl_2} RCOCl \xrightarrow{R'OH} RCOOR' + HCl$$

The yield of ester with sulphur dichloride is good.

### 3.2.2 Formation of Acyl Chlorides

Acyl chlorides can be made by reacting carboxylic acids with reagents like phosphorus trichloride, $PCl_3$ , phosphorus pentachloride, $PCl_5$ or sulphur dichloride oxide(thionyl chloride), $SOCl_2$. For example,

$$RCOOH + PCl_3 \longrightarrow RCOCl + H_3PO_3$$

$$RCOOH + PCl_5 \longrightarrow RCOCl + POCl_3 + HCl$$

$$RCOOH + SOCl_2 \longrightarrow RCOCl + HCl + SO_3$$

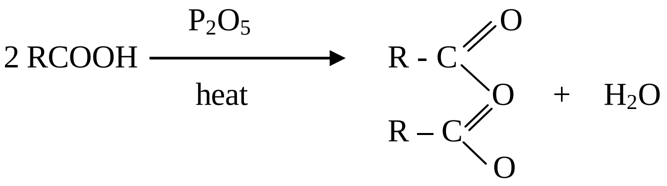
These reactions are examples of substitution reaction.

Sulphur dichloride oxide is particularly convenient of all the reagents because all the products are gaseous except acyl chloride. Also, sulphur dichloride oxide has a low boiling point of 79°C making it easy for the separation of the acyl chloride from excess sulphur dichloride oxide.

The acyl chloride can be hydrolyzed easily in the presence of water to regenerate the carboxylic acids.

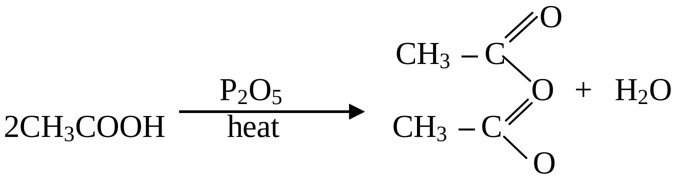
### 3.2.3 Conversion into Acid Anhydrides

Acid anhydrides can be prepared from carboxylic acid by reacting with the dehydrating agent, phosphorus pentaoxide, $P_2O_5$. In the process a molecule of water is eliminated. The reaction is an example of condensation reaction.



Acid anhydride

For example:



Acid anhydrides can also be made via the reaction between an acyl chloride and metal carboxylate.

$$R\,COOH \xrightarrow{SOCl} RCOCl$$

$$2RCOOH + 2Na \longrightarrow 2RCOO^{-}Na^{+} + H_2$$

$$R\,COONa + RCOCl \xrightarrow{heat} (RCO)_2\,O + NaCl$$

### Activity A/Self Assessment Exercise

a. Using relevant examples, explain the chemical properties of carboxylic acids as an acid
b. Use chemical equations to explain the preparation of the following organic compounds from ethanoic acid
    i. $CH_3COCl$
    ii. ii. $CH_3COOC_2H_5$
    iii. iii. $(CH_3CO)_2O$

## 3.3 Reactions of Carboxyl group

### 3.3.1 Reduction by Lithium Tetrahydrido Aluminates

Carboxylic acids are not easily reduced and are immune to most of the common reducing agents. However, Lithium tetrahydrido aluminates, $LiAIH_4$, is a strong reducing agent capable of reducing carboxylic acids to the corresponding alcohols.

$$RCOOH \xrightarrow[\text{2. } H_2O]{\text{1. } LiAlH_4\text{/dry ether}} RCH_2OH$$

## 3.4 Reaction Due to Akyl group

### 3.4.1 Halogenation

When chlorine gas is bubbled through boiling ethanoic acid in the presence of either iodine or red phosphorus in the sunlight, chloroethanoic acid is formed. Chloroethanoic acid is a colourless and corrosive crystalline solid (m.pt. $61^oC$).

$$I_2 + 3Cl_2 \longrightarrow 2ICl_3$$

$$CH_3COOH + ICl_3 \xrightarrow{105\text{-}110^0C} \underset{\text{Chloroethanoic acid}}{CH_2ClCOOH} + ICl + HCl$$

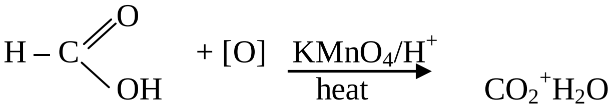
$$ICl + Cl_2 \longrightarrow ICl_3$$

The dichloro and trichloroethanoic acid are obtained by successive substitution of the alkyl hydrogen atoms.

$$CH_2ClCOOH \xrightarrow[\text{elevated temp}]{Cl_2, I_2} \underset{\text{dichloroethanoic acid}}{CHCl_2COOH} \xrightarrow[\text{elevated temp}]{Cl_2, I_2} \underset{\text{trichloromethanoic acid}}{CCl_3COOH}$$

### 3.4.2 Oxidation of Methanoic Acid

Oxidation of methanoic acid using acidified potassium tetraoxomanganate (vii),$KMnO_4$ at elevated temperature gives carbon(IV)oxide, $CO_2$ and water.



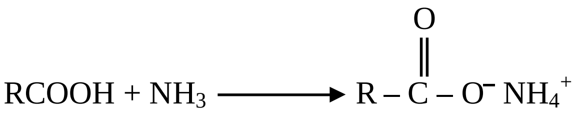
$$H-C\overset{O}{\underset{OH}{\lessgtr}} + [O] \xrightarrow[\text{heat}]{KMnO_4/H^+} CO_2{}^+H_2O$$

This is because it has the – CHO group hence it behaves as a reducing agent similar to aldehydes, unlike other carboxylic acid. This makes methanoic acid positive to Tollen’s and Fehling’s tests and it decolonizes acidified potassium tetraoxomanganate(VII).

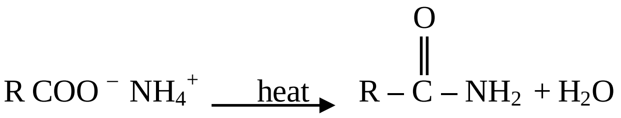
## 3.5. Reaction involving Salts of acids

### 3.5.1 Conversion into Amide

Amide can be made by reacting carboxylic acids with ammonia followed by dehydration of the ammonium salts formed at an elevated temperature.



$$RCOOH + NH_3 \longrightarrow R-\overset{\overset{\displaystyle O}{\|}}{C}-O^- NH_4^+$$



$$R\,COO^- NH_4^+ \xrightarrow{\text{heat}} R-\overset{\overset{\displaystyle O}{\|}}{C}-NH_2 + H_2O$$

Also when sulphur dichloride oxide reacts with carboxylic acids followed by ammonia, amide is formed.

$$R\,COOH \xrightarrow{SOCl_2} RCOCl$$

$$2\,RCOCl_2 + 2NH_3 \longrightarrow RCONH_2 + NH_4Cl$$

**3.5.2 Decarboxylation:** When anhydrous sodium salt of a fatty acid is heated with soda lime, (CaO/NaOH), alkane is produced

$RCOONa + NaOH \longrightarrow RH + Na_2CO_3$

For example $CH_3COONa + NaOH \longrightarrow CH_4 + NaOH$

**3.5.3 Formation of aldehydes and ketones.** When calcium salt of a fatty acid is heated strongly, it gives ketones. However, when it is heated with calcium dicarboxylic acid, it forms an aldehyde.

For example:

$(CH_3COO)_2Ca + (HCOO)_2Ca \longrightarrow 2CH_3CHO + 2CaCO_3$

Calcium ethanoate calcium dicarboxylic acid ethanal

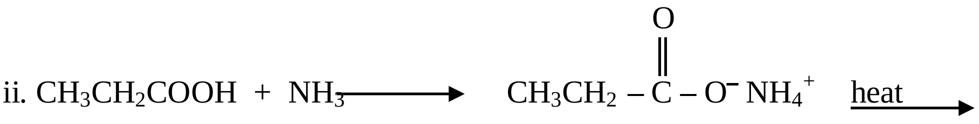
When calcium dicarboxylic acid is heated alone, it forms methanal

$(HCOO)_2Ca \longrightarrow HCHO + CaCO_3$

## Activity B/Self Assessment Exercise

State the product(s) formed from the following reactions:

i. $C_3H_7COOH \xrightarrow[2.\ H_2O]{1.\ LiAlH_4/dry\ ether}$



ii. $CH_3CH_2COOH + NH_3 \longrightarrow CH_3CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-O^-\,NH_4^+ \xrightarrow{heat}$

iii. $CH_3CH(CH_3)CH_2CH_2COONa + NaOH \longrightarrow$

## 4.0 Conclusion

Carboxylic acids are very reactive. Their reaction is due to the presence of the carboxyl group and the alkyl group. Their acidity is due to the presence of ionizable hydrogen ion.

## 5.0 Summary

In this unit, we have learnt that:

i. Carboxylic are acidic, and this property is shown in its reaction with
    - -metals and
    - -sodium hydrogen trioxocarbonates

ii. Carboxylic acids can be converted into:
  - Acyl chlorides
  - Acid anhydrides
  - Amide

iii. Carboxylic acids undergo esterification reaction to form esters

iv. Carboxylic acids can be reduced by Lithium tetrahydridoaluminate in dry ether alcohol.

v. Methanoic acid can be oxidized by acidified $KMnO_4$ to give $CO_2$ and water

## 6.0 Tutor Marked Assignment

Using equations, explain the formation of the following compounds from carboxylic acids. State the conditions of reaction where necessary.

(i) Acyl chlorides
(ii) Esters
(iii) Amide
(iv) Alcohols

## 7.0 Further Reading and Other Resources

a. K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry -Third Edition

b. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry - Sixth Edition

c. Y.C.Wong; C.T.Wong; S.O.Onyiruka and L.E.Akpanisi (2001)-University Organic Chemistry: The Fundamentals

# Unit 5: Derivatives of Carboxylic Acids

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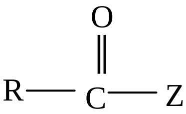
## 1.0 Introduction

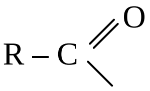
The carboxylic group of the acids has a carbonyl group and a hydroxyl group. The hydroxyl group can be replaced by –Cl, -COCR, $-NH_2$ or -OR' groups giving the compounds known as acyl chloride (acid chloride), acid anhydrides, amides and esters respectively. They can be represented by the general formula



$$R-\overset{\overset{\displaystyle O}{\|}}{C}-Z$$

Where Z represents Cl, OCOR', $NH_2$ or OR'

R and R' may be alkyl or aryl.

The  group, common to all the derivatives is called the **acyl group**

## 2.0 Objectives

At the end of this unit, you should be able to:

- i. Identify the structures of the various derivatives of carboxylic acids
- ii. Compare the properties and reactions of the various derivatives of carboxylic acids
- iii. Explain the reaction of acyl chloride, acid anhydrides, amides and esters

## 3.0 General Comparative Properties

Chlorides, anhydrides and esters have normal boiling points and are similar in value to those of aldehydes and ketones of comparative relative molecular mass. Amides have a higher than expected boiling points and at normal temperatures, they exist as solid because of a fairly high degree of intermolecular hydrogen bonding. The ability of amides to form hydrogen bonds with water molecules allows them to be much more soluble than other derivatives. Simple chlorides and anhydrides undergo spontaneous hydrolysis in water.

## 3.1 Reactivity

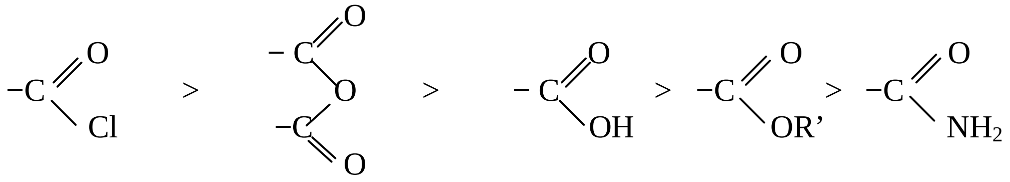
The derivatives of carboxylic acids undergo nucleophilic substitution reactions. This is characterized by nucleophilic substitutions of the halogen, carboxylate, alkoxy or amino groups and the reaction is similar to the condensation reactions of aldehydes and ketones. All the substituent groups possess lone pairs of electrons which are conjugated with the carbonyl group. As the electronegativity of the group increases, the degree of conjugation decreases and the electron availability about the carbonyl oxygen is reduced.

$$R-\overset{\overset{\displaystyle O}{\|}}{C}-Z \quad + Nu^- \longrightarrow R-\overset{\overset{\displaystyle O}{\|}}{C}-Nu \quad + \quad Z$$

The order of electronegativity of the substituent group is as follows

$-Cl > OOCR' > OR' > -NH_2$

The overall polarity of the carbonyl group is enhanced by the more electronegative substituent due to the simultaneous withdrawal of electron away from the carbon atom, making it more susceptible to nucleophilic attack. The decreasing order of reactivity of carboxylic acid itself and its derivatives are as follow:



## Activity A/Self Assessment Exercise

Arrange the following in increasing order of reactivity:
$CH_3COOH$, $CH_3COOC_2H_5$, $CH_3COCl$, $CH_3CONH_2$, $(CH_3CO)_2O$

## 3.2 Acyl Chlorides(Acid Chlorides)

### 3.2.1 General Methods of Formation

**a. From acids**

Acyl chlorides can be made by heating carboxylic acids with phosphorus trichloride, $PCl_3$ or phosphorus pentachloride, $PCl_5$ or sulphur dichloride oxide(thionyl chloride), $SOCl_2$.

$$RCOOH + PCl_3 \longrightarrow RCOCl + H_3PO_3$$

$$RCOOH + PCl_5 \longrightarrow RCOCl + POCl_3 + HCl$$

$$RCOOH + SOCl_2 \longrightarrow RCOCl + HCl + SO_3$$

**b. From the salt of the acids**. Acyl chloride can be prepared by distilling the salts of the acid with phosphorus trichloride, $PCl_3$ or phosphorus trioxychloride, $POCl_3$ or sulphuryl chloride, $SO_2Cl_2$.

$$CH_3COONa + PCl_3 \longrightarrow \underset{\text{Ethanoyl chloride}}{CH_3COCl} + Na_3PO_3$$

$$2CH_3COONa + PCl_5 \longrightarrow 2CH_3COCl + NaCl + NaPO_3$$

$$(CH_3COO)Ca + SO_2Cl_2 \longrightarrow 2CH_3COCl + CaSO_4$$

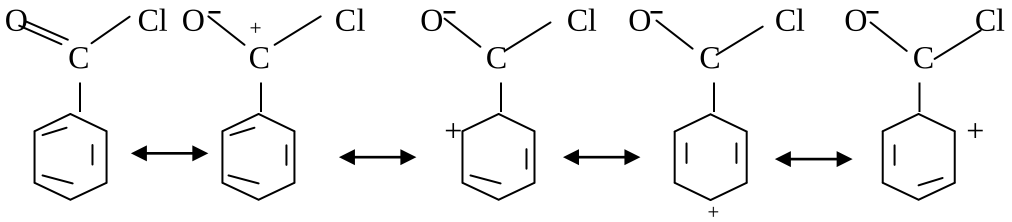
### 3.2.2.Physical Properties

i. The lower members are colourless, volatile liquids with irritating smell.
ii. Their boiling point are much lower than those of acids from which they are obtained. This is due to the absence of intermolecular hydrogen bonding.
iii. . They fume in moist air producing vapours of hydrogen chloride
iv. They are generally insoluble. However they hydrolyse slowly to go into solution.

### 3.2.3 Reactions of Acyl chlorides

The reactions of acyl chlorides are fundamentally similar to those of carboxylic acids. The halogen readily undergoes nucleophilic substitution by – OH – OR', $NH_2$ etc. The mechanism is similar to those of the condensation reactions of aldehydes and ketones.

Benzoyl chloride is much less reactive than any aliphatic acyl chloride due to the reduction in the positive nature of the carbonyl carbon caused by delocalization of electrons between it and the benzene ring (resonance effect), leading to reduction in the strength of the electron deficient nucleophilic site .



**a. Reactions with water (Hydrolysis)**

Acyl chlorides hydrolyse in water to form the parent carboxylic acids and hydrogen chloride.

$RCOCl + H_2O \longrightarrow RCOOH + HCl$

For example,

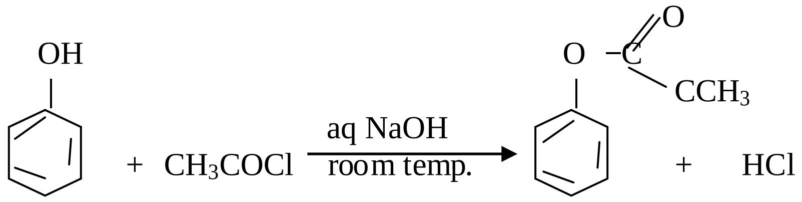
$CH_3COCl + H_2O \longrightarrow CH_3COOH + HCl$

**b. Ester Formation**

Acyl chlorides react with alcohols and phenols to form the corresponding ester and hydrogen chloride.

$RCOCl + R'OH \longrightarrow RCOOR' + HCl$

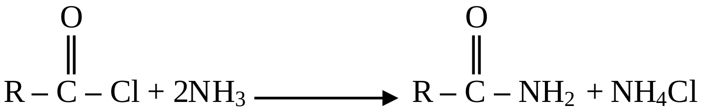
Esterification with phenol requires an alkaline medium.



Phenol Ethanoyl chloride Ester

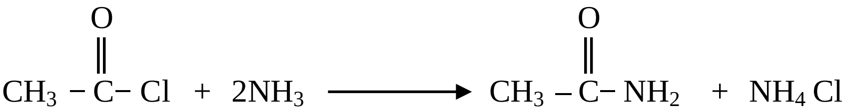
**c. Amide Formation**

Acyl chlorides react with ammonia to give the corresponding amides and ammonium chloride.



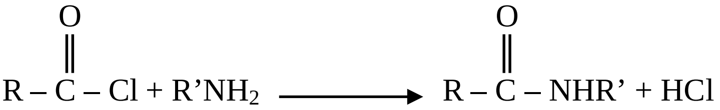
$$R-\overset{\overset{\displaystyle O}{\|}}{C}-Cl + 2NH_3 \longrightarrow R-\overset{\overset{\displaystyle O}{\|}}{C}-NH_2 + NH_4Cl$$

For example,

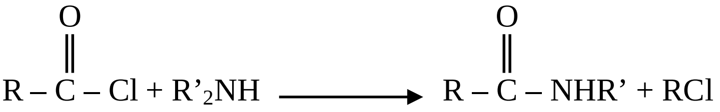


$$CH_3-\overset{O}{\overset{\|}{C}}-Cl + 2NH_3 \longrightarrow CH_3-\overset{O}{\overset{\|}{C}}-NH_2 + NH_4Cl$$

Also, acyl chlorides react with primary and secondary amines ($RNH_2$ and $R_2NH$) to give the corresponding N – substituted amides and hydrogen chloride.

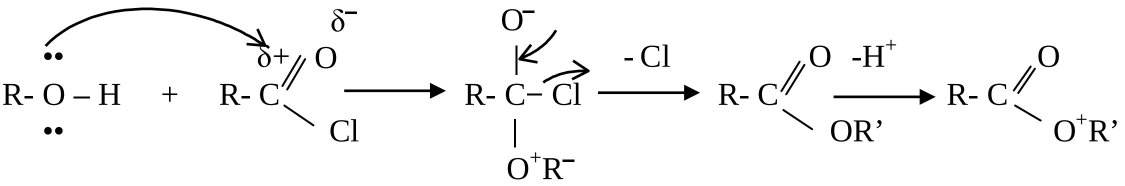


$$R-\overset{O}{\overset{\|}{C}}-Cl + R'NH_2 \longrightarrow R-\overset{O}{\overset{\|}{C}}-NHR' + HCl$$



$$R-\overset{O}{\overset{\|}{C}}-Cl + R'_2NH \longrightarrow R-\overset{O}{\overset{\|}{C}}-NHR' + RCl$$

The mechanism for the condensation reaction of acyl chlorides is described below:



The reaction is similar with $H_2O$, $NH_3$ and $R'_2NH$.

**d. Aldehyde Formation (Rosenmund Reduction)**

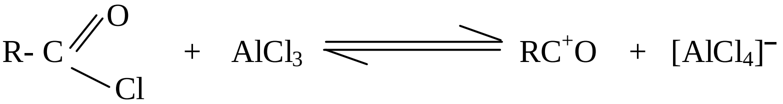
Acyl chlorides are reduced to aldehydes when heated with palladium poisoned with barium tetraoxosulphate (VI). The barium tetraoxosulphate (VI) poison the catalytic activity of the palladium restricting the reduction to aldehyde only. Without the poisonous effect of the barium tetraoxosulphate (VI) the aldehyde might be reduced to alcohol as well

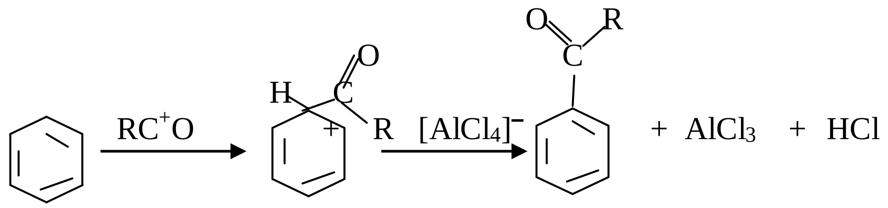
$$RCOCl \xrightarrow[\text{Poisoned Pd/BaSO}_4\text{cat}]{H_2,\ \text{heat}} RCHO + HCl$$

**e. Ketone Formation (Friedel – Crafts acylation)**

Acyl Chlorides reacts with aromatic hydrocarbon in the presence of an anhydrous aluminium chloride- Lewis acid, to give a good yield of the aromatic alkanone.

For example the reaction with benzene, the reaction mixture is refluxed on a water bath at 50°C





**f. Anhydride formation**

Acyl chlorides react with the sodium salts of carboxylic acids at an elevated temperature to give acid anhydrides
For example,

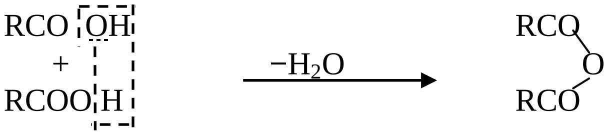
$$CH_3COONa + CH_3COCl \xrightarrow{\text{distil}} (CH_3CO)_2O + NaCl$$

## Activity B/Self Assessment Exercise

Give the structure and the name of the principal product formed when propanoyl chloride reacts with:
i. $H_2O$ ii. $C_2H_5OH$ iii. $C_6H_6(AlCl_3)$ iv. $CH_3NH_2$ v. $NH_3$

## 3.3 Acid Anhydrides

Acid anhydride may be regarded as being derived from acid(s) with the elimination of one molecule of water from two molecules of acids.



### 3.3.1 General Methods of Formation

a. By heating acyl chloride with anhydrous sodium salt of the acid or the acid

$$CH_3COCl + NaOCOCH_3 \longrightarrow CH_3COOCOCH_3 + NaCl$$

$$CH_3COOH + CH_3COCl \xrightarrow{\text{pyridine}} CH_3COOCOCH_3 + HCl$$

b. By treating excess of anhydrous sodium salt of the acid with phosphorus oxy-chloride or thionyl chloride

$$3CH_3COONa + POCl_3 \longrightarrow 3CH_3COCl + Na_3PO_4$$

$$CH_3COCl + NaOCOCH_3 \longrightarrow CH_3COOCOCH_3 + NaCl$$

$$2CH_3COONa + SOCl_2 \longrightarrow CH_3COOCOCH_3 + SO_2 + NaCl$$

c. By the dehydration of anhydrous acids in the presence of suitable dehydrating agent like $P_2O_5$

$$2CH_3COOH \xrightarrow{\text{heat, } P_2O_5} CH_3COOCOCH_3 + H_2O$$

d. Anhydrides of higher acids are obtained by heating their sodium salt of acids with ethanoic anhydride.

$$2RCOONa + (CH_3CO)_2O \longrightarrow RCOOCOR + 2CH_3COONa$$

**3.3.2 Physical Properties**

i. They are colourless liquids or solids with a sharp irritating purgent smell.
ii. They are insoluble in water
iii. Their boiling points are higher than those of the acid from which they are derived because of their large size and greater Van der Wall's interaction.

**3.3.3 Chemical Properties**

Acid anhydrides readily undergo nucleophilic substitution reaction like other carboxylic acid derivatives. The carbonyl carbon is the leaving group.

**a. Hydrolysis**

Acid anhydrides hydrolyses in water to give the parent carboxylic acids

$$(RCO)_2O + H_2O \longrightarrow 2RCOOH$$

For example,

$$(CH_3CO)_2O + H_2O \longrightarrow 2CH_3COOH$$

ethanoic anhydride → ethanoic acid

**b. Ester formation**

Acid anhydrides react with alcohols and phenols to give esters and carboxylic acids. The reaction is irreversible

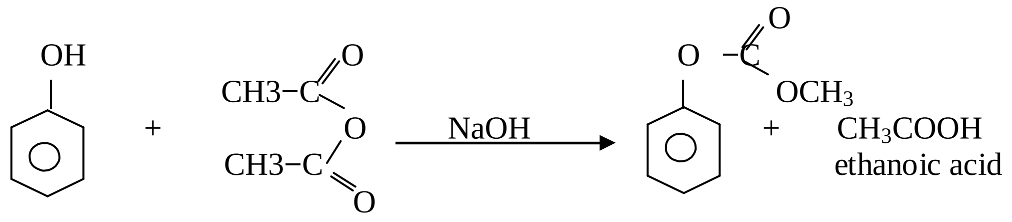
$$(RCO)_2O + R'OH \longrightarrow RCOOR' + RCOOH$$

Ester, Carboxylic acid

For example:

$$(CH_3CO)_2O + CH_3OH \xrightarrow{\text{reflux}} CH_3{-}COOCH_3 + CH_3COOH$$

Ethanoic acid anhydride, methanol, methyl ethanoate, ethanoic acid



Phenol

Phenyl Ethanoate

**c. Amide formation**

Amides are formed when acid anhydride reacts with ammonia, $NH_3$ and primary amine, $R'NH_2$.

$$(RCO)_2O + NH_3 \longrightarrow RCONH_2 + RCOOH$$

ammonia → amide

$$(RCO)_2O + \underset{\text{amine}}{R'NH_2} \longrightarrow \underset{\text{N – substituted amide}}{RCONHR} + R'COOH$$

For example,

$$(CH_3CO)_2\,O + NH_3 \longrightarrow \underset{\text{ethanamide}}{CH_3CONH_2} + \underset{\text{ethanoic acid}}{CH_3COOH}$$

$$\underset{\text{Ethanoic acid}}{(CH_3CO)_2\,O} + \underset{\text{Ethylamine}}{CH_3CH_2NH_2} \longrightarrow \underset{\text{N-ethyl ethanamide}}{CH_3CONHCH_2CH_3} + \underset{\text{ethanoic ac}}{CH_3COOH}$$

**d. Ketone formation: Friedel – Craft acylation**

Acid anhydrides react with benzene in the presence of anhydrous aluminium chloride catalyst to produce aromatic ketone and carboxylic acids.

$$(RCO)_2O + C_6\,H_6 \xrightarrow{AlCl_3\text{ Catalyst}} C_6H_5COR + RCOOH$$

For example,

$$(CH_3CO)_2O + C_6H_6 \xrightarrow{AlCl_3\text{ Catalyst}} C_6H_5COCH_3 + CH_3COOH$$

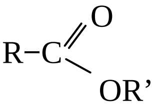
## Activity C/Self Assessment Exercise

Give the products formed when ethanoic acid anhydride reacts with:

i. $H_2O$ ii. $NH_3$ iii. $C_2H_5OH$ iv. $C_6H_6(AlCl_3)$

### 3.4 Esters

Esters have the general formula RCOOR'



### 3.4.1 General Methods of Preparation

a. By direct esterification: Ester are formed by refluxing the acid with alcohols in the presence of small amount of concentrated tetraoxosulphate(vi) acid.

For example: $CH_3COOH + HOC_2H_5 \xrightleftharpoons{H^+} CH_3COOC_2H_5 + H_2O$

b. By the action of alcohols on acyl chloride or anhydrides

For example:

$$CH_3COCl + HOC_2H_5 \longrightarrow CH_3COOC_2H_5 + HCl$$

$$(CH_3CO)_2O + HOC_2H_5 \longrightarrow CH_3COOC_2H_5 + CH_3COOH$$

c. By the action of alkyl halides on silver salts of fatty acids
For example:

$$CH_3COOAg + C_2H_5I \longrightarrow CH_3COOC_2H_5 + AgI$$

d. From diazomethane

For example: $CH_3COOH + \underset{\substack{\text{diazomethane}\\ \text{(ethereal solution)}}}{CH_2N_2} \longrightarrow CH_3COOC_2H_5 + N_2$

e. From Carboxylic acid and alkene; An ester is formed when an acid is treated with an alkene in the presence of boron trifluoride as catalyst.

$$RCOOH + CH_2{=}CH_2 \xrightarrow{BF_3} RCOOC_2H_5$$

f. From ethers and carbon (II) oxide Ethers react with carbon (II) oxide at 125-180°C under 500 atmospheric pressure,in presence of boron trifluoride and little water to form ester.

$$R\text{-}O\text{-}R + CO \xrightarrow[BF_3]{heat} RCOOR$$

**3.4.2 Physical Properties**

i. They are colourless liquids with characteristic sweet odours.

ii. The boiling points of esters are normal, increasing as the relative molecular masses increase. Methyl and ethyl ester however have much lower boiling points than their associated parent acid despite having higher molecular masses.The boiling points of normal-chain esters are higher than those of branched chain isomers.

iii. Methyl methanoate is very soluble in water, but there is a progressive and rapid decrease in solubility of the higher compounds as relative molecular mass increase. Esters of aromatic carboxylic acids are insoluble

## Activity D /Self Assessment Exercise

Arrange the following in increasing order of solubility: $CH_3COOC_2H_5$, $CH_3COOCH_3$, $C_6H_5COOCH_3$

### 3.4.3 Reactions

Esters undergo nucleophilic substitution reactions in which the alky group – OR' is replaced by weak nucleophiles under acid or base catalyzed conditions necessary to enhance the electron deficiency of the carbonyl carbon atom.

**a. Hydrolysis**

Esters hydrolyzed under an acid or base catalyzed condition to form carboxylic acids and alcohols or produce the carboxylates and alcohols respectively. The acid – catalyzed process is the exact opposite of esterification.

Acid catalysed

$$RCOOR' + H_2O \underset{\text{reflux}}{\overset{H+}{\rightleftharpoons}} \underset{\text{Carboxylic Acid}}{RCOOH} + \underset{\text{alcohol}}{R'OH}$$

For example,

$$\underset{\text{Propyl methanoate}}{HCOOCH_2CH_2CH_3} + H_2O \overset{H^+}{\rightleftharpoons} \underset{\text{Methanoic acid}}{HCOOH} + \underset{\text{Propan–1–ol}}{CH_3CH_2CH_2OH}$$

Alkali- catalyzed

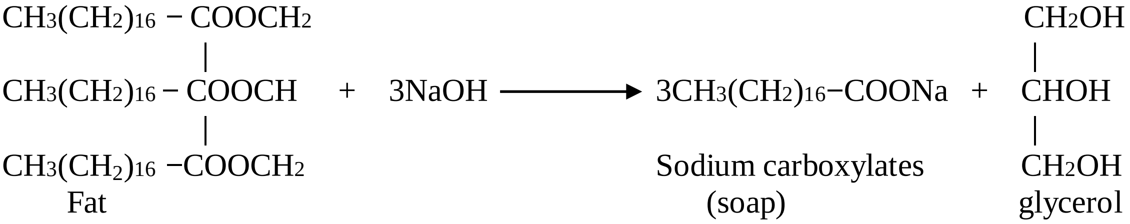
$$RCOOR' + OH^- \rightleftharpoons \underset{\text{Carboxylate}}{RCOO^-} + \underset{\text{alcohol}}{R'OH}$$

For example:

$$CH_3COOCH_2CH_3 + NaOH \rightleftharpoons \underset{\text{Sodium ethanoate}}{CH_3COONa} + \underset{\text{Ethanol}}{CH_3CH_2OH}$$

Hydrolysis under alkaline conditions is referred to as saponification because it is the type of reaction used in soap making process. “Soapy detergents” are alkali metal derivatives of carboxylic acids and they contain between 10 and 18 carbon atoms. Fats and oils (triesters) are hydrolyzed to produce sodium carboxylate (soap).

For example,



$$\underset{\text{Fat}}{\begin{array}{l} CH_3(CH_2)_{16}-COOCH_2 \\ \qquad\qquad\qquad | \\ CH_3(CH_2)_{16}-COOCH \\ \qquad\qquad\qquad | \\ CH_3(CH_2)_{16}-COOCH_2 \end{array}} + 3NaOH \longrightarrow \underset{\text{Sodium carboxylates (soap)}}{3CH_3(CH_2)_{16}-COONa} + \underset{\text{glycerol}}{\begin{array}{c} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array}}$$

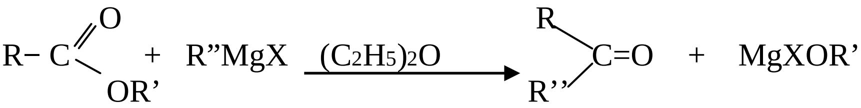
**b. Amide formation**

Esters reacts with ammonia dissolved in an alcoholic medium or alternatively concentrated aqueous ammonia containing dissolved ammonium salts to give amide and alcohol.

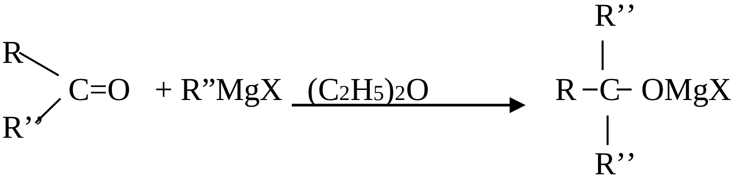
$$R\,COOR + NH_3 \xrightarrow[\text{or } NH^+{}_4 \text{ in conc. Aq. solution}]{RO^- \text{ in alcohol}} \underset{\text{amide}}{RCONH_2} + R'OH$$

**c. Formation of ketones and tertiary alcohols**

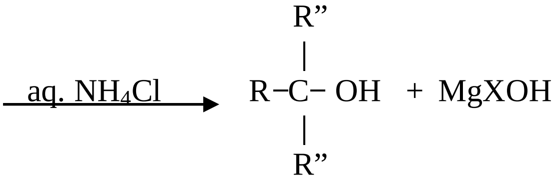
Esters react with Grignard reagent using ether as solvent, the product is a ketone which can react further with Grignard reagent to form tertiary alcohol via hydrolysis of the intermediate alkylmagnesium halide using aqueous ammonium chloride.



$$R-C(=O)OR' + R''MgX \xrightarrow{(C_2H_5)_2O} RR''C=O + MgXOR'$$



$$RR''C=O + R''MgX \xrightarrow{(C_2H_5)_2O} R-C(R'')(R'')-OMgX$$



$$\xrightarrow{aq.\ NH_4Cl} R-C(R'')(R'')-OH + MgXOH$$

**d. Ester Exchange (Transesterification)**

This is the process whereby one alcohol replaces another in an ester. The reaction may be catalyzed by an acid or by the basic alkoxide, $RO^-$

$$RCOOR' + R''OH \xrightleftharpoons{H^+ \text{ or } RO^-} RCOOR'' + R'OH$$

**e. Reduction**

The reduction of esters can be carried out by reacting it with the reagent lithium tetrahydridoaluminate ($LiAIH_4$) and then with water to produce a mixture of two alcohols.

$$RCOOR + 4[H] \xrightarrow[H_2O]{LiAIH_4/(C_2H_5)O} RCH_2OH + R'OH$$

**f. Replacement of the carboxylate group**

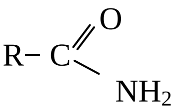
When dry hydrogen bromide, concentrated aqueous hydrogen iodide or concentrated tetraoxosulphate (VI) acid.

## Activity E/Self Assessment Exercise

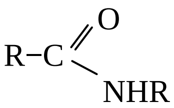
i. List five physical properties of esters
ii. State the products formed from the reaction between ethyl ethanoate and the following compounds:
  - $LiAlH_4$, $H_2O$
  - $CH_3CH_2MgCl$, $H_2O$
  - NaOH
  - $NH_3$

## 3.5 Amides

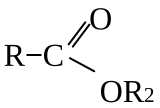
Amides are monoacyl derivates of ammonia. They may be classified as primary, secondary, or tertiary amide based on the number of alkyl groups attached to the nitrogen atom.



$R-C(=O)NH_2$



$R-C(=O)NHR$



$R-C(=O)OR_2$

### 3.5.1 General Methods of Preparation

a. By heating ammonium salts of carboxylic acids.

$$RCOONH_4 \xrightarrow{\text{heat}} RCONH_2 + H_2O$$

b. By ammonolysis of acyl chloride, anhydrides or ester with concentrated ammonia.

$$RCOCl + NH_3 \longrightarrow RCONH_2 + HCl$$

$$(RCO)_2O + NH_3 \longrightarrow RCONH_2 + CH_3COOH$$

$$RCOOR' + NH_3 \longrightarrow RCONH_2 + R'OH$$

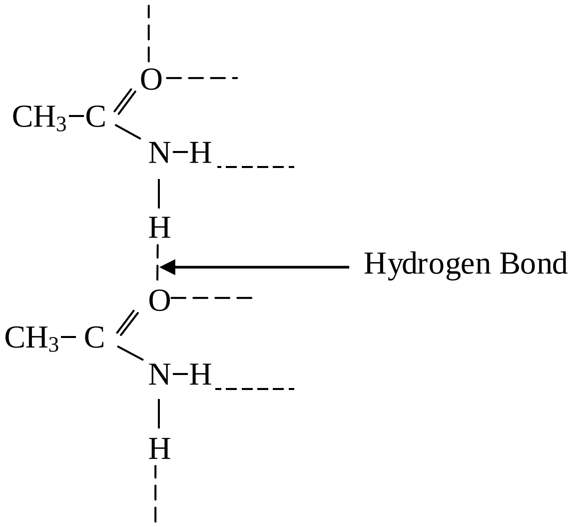
c. By partial hydrolysis of alkyl cyanides with cold concentrated hydrochloric acid, polyphosphoric acid or alkaline hydrogen peroxide.

$$RC \equiv N + H_2O \longrightarrow RCONH_2$$

### 3.5.2 Physical Properties

i. Primary amides, $RCONH_2$ are crystalline solids due to mainly fairly strong intermolecular hydrogen bonding. However methanamide is a liquid at room temperature (melting point $3^OC$).

ii. The melting points of the amides are high for the size of the molecules because they can form hydrogen bonds. The hydrogen atoms in the $NH_2$ group are sufficiently positive to form a hydrogen bond with a lone pair on the oxygen atom of another molecule.



Each molecule has two slightly positive hydrogen atoms hence there is the potential for lots of hydrogen bonds to be formed. These hydrogen bonds need a reasonable amount of energy to break, and so the melting points of the amides are quite high.

iii. The small chain amides are soluble in water because they have the ability to form hydrogen bond with the water molecules.

### 3.5.3 Reactions of amides

Amides are slightly basic in character, because of the lone pair of electrons on the nitrogen atom. Owing to resonance between the two canonical forms of amide, the lone pair of electrons are not readily available for donation as in amines making amides much less basic.

### a. Hydrolysis of amides

Hydrolysis of amide is either acid catalyzed or alkaline catalyzed. The acid hydrolysis involves the use of acids such as dilute hydrochloric acid which acts as a catalyst for the reaction between the amide and water.

$$RCONH_2 \xrightarrow[\text{Heat}]{H_2O,\ H^+} RCOOH + NH_4^+$$

For example,

$$CH_3CONH_2 + H_2O + HCl \longrightarrow CH_3COOH + NH_4^+Cl^-$$

The alkaline hydrolysis involves reaction with hydroxide ions.

$$RCONH_2 \xrightarrow[\text{heat}]{OH^-} RCOO^- + NH_3$$

For example,

$$CH_3CONH_2 + NaOH \longrightarrow CH_3COONa + NH_3$$

The acid catalysed hydrolysis gives carboxylic acids and ammonium salt, while the base catalyzed hydrolysis gives carboxylate and ammonia gas.

### b. Hofmann Degradation

The Hofmann degradation is a reaction between an amide and a mixture of bromine and sodium hydroxide solution in the presence of heat. The overall effect of the reaction is a loss of the carboxyl group of the amide to get a primary amine the original amide.

$$RCONH_2 + Br_2 + 4NaOH \longrightarrow RNH_2 + 2NaBr + Na_2CO_3 + 2H_2O$$

For example,

$$CH_3CONH_2 + Br + 4NaOH \longrightarrow CH_3NH_2 + Na_2CO_3 + 2NaBr + 2H_2O$$

The Hoffmann degradation is used as a way of removing carbon atom out of a chain.

### c. Dehydration

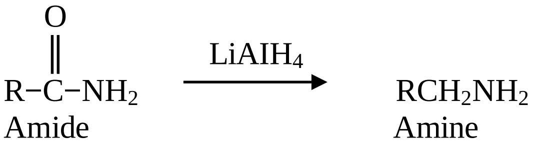
Amides are dehydrated by heating a solid mixture of the amide and phosphorus (v) oxides, $P_2O_5$. Water is removed from the amide group to leave a nitrile group, $^-CN$. The liquid nitrile is collected by simple distillation.

$$RCONH_2 \xrightarrow[\text{heat}]{P_2O_5} RCN + H_2O$$

For example,

$$CH_3CONH_2 \xrightarrow[\text{heat}]{P_2O_5} CH_3CN + H_2O$$

**d. Reduction**
Amides can be reduced by the reagent lithium tetrahydridoaluminate ($LiAIH_4$) to give a primary amine.



$$\underset{\text{Amide}}{R-\overset{\overset{\displaystyle O}{\|}}{C}-NH_2} \xrightarrow{LiAIH_4} \underset{\text{Amine}}{RCH_2NH_2}$$

For example,

$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-NH_2 \xrightarrow{LiAIH_4} CH_3CH_2NH_2$$

## Activity F/Self Assessment Exercise

Give the products formed when propanamide react with the following:
i. NaOH ii. $LiAlH_4$ iii. $P_2O_5$ iv. $Br_2$/NaOH

## 3.6 Uses of carboxylic acids and their derivatives

1. Benzoic acid and its sodium salt are used as food preservative
2. Nylon 6.6 and polymers made from derivatives of carboxylic acids
3. Preparation of soap
4. Liquid esters are widely used as solvents for all purpose adhesives, thinners for paints and nail varnish remover
5. As flavor enhancers in food processing industry

## 4.0 Conclusion

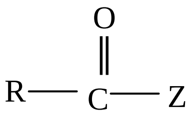
The derivatives of carboxylic acids undergo nucleophilic substitution reactions that is characterized by substitutions of the halogen, carboxylate, alkoxy or amino groups and the reaction is similar to the condensation reactions of aldehydes and ketones

## 5.0 Summary

In this unit we have learnt that:

i. Derivatives of carboxylic acids are formed when the hydroxyl group of the acid is replaced by –Cl, -COCR, -NH2 or -OR’ groups to give compounds known as acyl chloride (acid chloride), acid anhydrides, amides and esters respectively.

ii. Carboxylic acid derivatives can be represented by the general formula

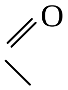


$$R-\overset{\overset{O}{\|}}{C}-Z$$

Where Z represents Cl, OCOR’, $NH_2$ or OR’

R and R’ may be alkyl or aryl.

iii.

The R – C  group, common to all the derivatives is called the **acyl group**

iv. Chlorides, anhydrides and esters have normal boiling points and are similar in value to those of aldehydes and ketones.

v. Amides have a higher than expected boiling points and at normal temperatures,

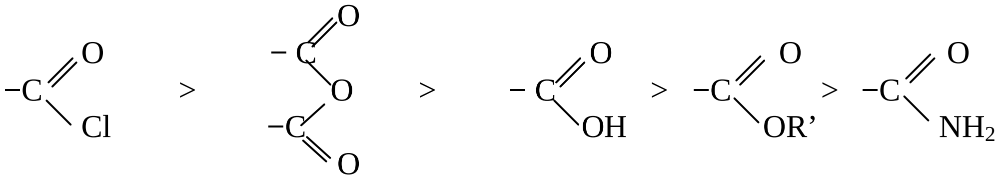
vi. Amides are much more soluble than other derivatives because of the ability to form hydrogen bonds with water molecules

vii. The derivatives of carboxylic acids undergo nucleophilic substitution reactions.

$$R-\overset{\overset{O}{\|}}{C}-Z + Nu^{-} \longrightarrow R-\overset{\overset{O}{\|}}{C}-Nu + Z$$

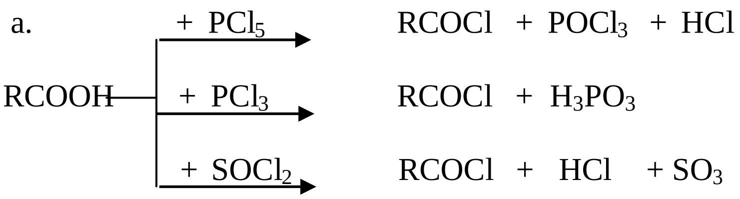
The order of electronegativity of the substituent group is as follows
$-Cl > OOCR' > OR' > -NH_2$

viii. The decreasing order of reactivity of carboxylic acid itself and its derivatives are as follow:



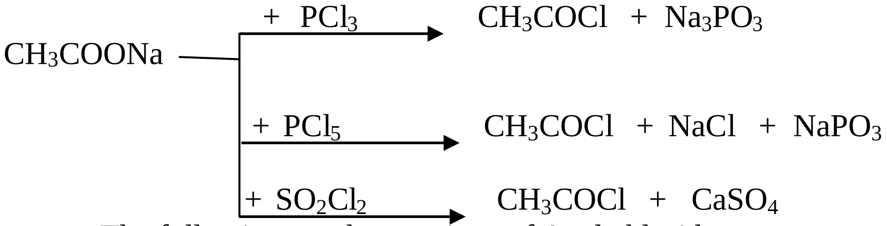
ix. Acyl chlorides are prepare from the following reactions:

a.



$$RCOOH \xrightarrow{+\ PCl_5} RCOCl + POCl_3 + HCl$$
$$RCOOH \xrightarrow{+\ PCl_3} RCOCl + H_3PO_3$$
$$RCOOH \xrightarrow{+\ SOCl_2} RCOCl + HCl + SO_3$$

b. From the salt of the acids.



$$CH_3COONa \xrightarrow{+\ PCl_3} CH_3COCl + Na_3PO_3$$
$$CH_3COONa \xrightarrow{+\ PCl_5} CH_3COCl + NaCl + NaPO_3$$
$$CH_3COONa \xrightarrow{+\ SO_2Cl_2} CH_3COCl + CaSO_4$$

x. The following are the reactions of Acyl chlorides

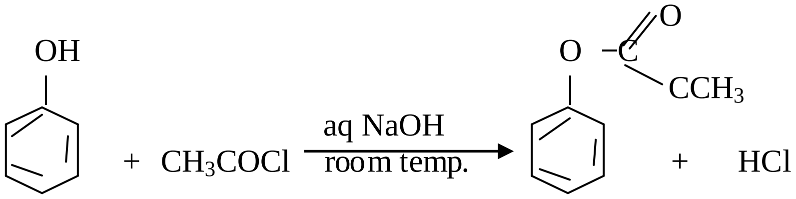
- Reactions with water (Hydrolysis)

$$RCOCl + H_2O \longrightarrow RCOOH + HCl$$

- Ester Formation

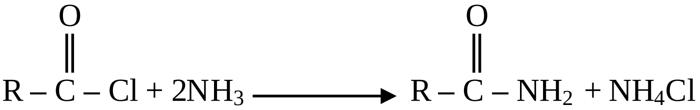
$$RCOCl + R'OH \longrightarrow RCOOR' + HCl$$

Esterification with phenol requires an alkaline medium.



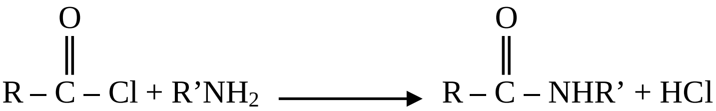
Phenol Ethanoyl Chloride Ester

- Amide Formation

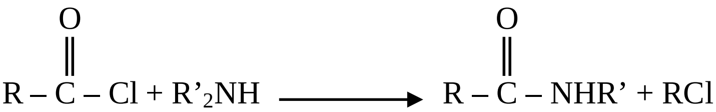


$$R - \overset{\overset{O}{\|}}{C} - Cl + 2NH_3 \longrightarrow R - \overset{\overset{O}{\|}}{C} - NH_2 + NH_4Cl$$

Also, with primary and secondary amines ($RNH_2$ and $R_2NH$) it gives the corresponding N – substituted amides and hydrogen chloride.



$$R - \overset{\overset{O}{\|}}{C} - Cl + R'NH_2 \longrightarrow R - \overset{\overset{O}{\|}}{C} - NHR' + HCl$$

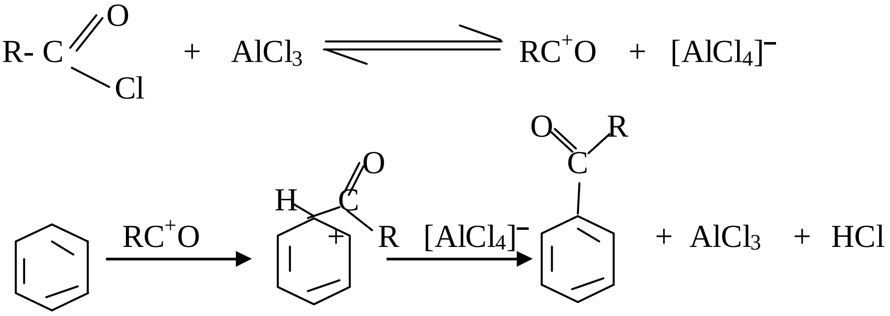


$$R - \overset{\overset{O}{\|}}{C} - Cl + R'_2NH \longrightarrow R - \overset{\overset{O}{\|}}{C} - NHR' + RCl$$

- Aldehyde Formation (Rosenmund Reduction)

$$RCOCl \xrightarrow[\text{Poisoned Pd/BaSO}_4\text{cat}]{H_2,\ \text{heat}} RCHO + HCl$$

- Ketone Formation (Friedel – Crafts acylation)



- Anhydride formation

$$CH_3COONa + CH_3COCl \xrightarrow{\text{distil}} (CH_3CO)_2O + NaCl$$

xi. Acid anhydrides can be prepared the following methods

- By heating acyl chloride with anhydrous sodium salt of the acid or the acid

$$CH_3COCl + NaOCOCH_3 \longrightarrow CH_3COOCOCH_3 + NaCl$$

$$CH_3COOH + CH_3COCl \xrightarrow{\text{pyridine}} CH_3COOCOCH_3 + HCl$$

- By treating excess of anhydrous sodium salt of the acid with phosphorus oxy-chloride or thionyl chloride

$$3CH_3COONa + POCl_3 \longrightarrow 3CH_3COCl + Na_3PO_4$$

$$CH_3COCl + NaOCOCH_3 \longrightarrow CH_3COOCOCH_3 + NaCl$$

$$2CH_3COONa + SOCl_2 \longrightarrow CH_3COOCOCH_3 + SO_2 + NaCl$$

- By the dehydration of anhydrous acids in the presence of suitable dehydrating agent like $P_2O_5$

$$2CH_3COOH \xrightarrow{\text{heat, } P_2O_5} CH_3COOCOCH_3 + H_2O$$

- Anhydrides of higher acids are obtained by heating their sodium salt of acids with ethanoic anhydride.

$$2RCOONa + (CH_3CO)_2O \longrightarrow RCOOCOR + 2CH_3COONa$$

xii. The following are the reactions of acid Anhydrides

- Hydrolysis

$$(RCO)_2O + H_2O \longrightarrow 2RCOOH$$

- Ester formation

$$(RCO)_2O + R'OH \longrightarrow \underset{\text{Ester}}{RCOOR'} + \underset{\text{Carboxylic acid}}{RCOOH}$$

- Amide formation

$$(RCO)_2O + \underset{\text{ammonia}}{NH_3} \longrightarrow \underset{\text{amide}}{RCONH_2} + RCOOH$$

$$(RCO)_2O + \underset{\text{amine}}{R'NH_2} \longrightarrow \underset{\text{N – substituted}}{RCONHR} + R'COOH$$

- Ketone formation: Friedel – Craft acylation

$$(RCO)_2O + C_6H_6 \xrightarrow{AlCl_3 \text{ Catalyst}} C_6H_5COR + RCOOH$$

xiii. Esters can be prepared using the following methods

- By direct esterification

$$CH_3COOH + HOC_2H_5 \overset{H^+}{\rightleftharpoons} CH_3COOC_2H_5 + H_2O$$

- By the action of alcohols on acyl chloride or anhydrides

$$CH_3COCl + HOC_2H_5 \longrightarrow CH_3COOC_2H_5 + HCl$$

$$(CH_3CO)_2O + HOC_2H_5 \longrightarrow CH_3COOC_2H_5 + CH_3COOH$$

- By the action of alkyl halides on silver salts of fatty acids

$$CH_3COOAg + C_2H_5I \longrightarrow CH_3COOC_2H_5 + AgI$$

- From diazomethane

$$CH_3COOH + \underset{\text{diazomethane}}{CH_2N_2} \longrightarrow CH_3COOC_2H_5 + N_2$$

- From Carboxylic acid and alkene

$$RCOOH + CH_2{=}CH_2 \xrightarrow{BF_3} RCOOC_2H_5$$

- From ethers and carbonmonoxide

$$R\text{-}O\text{-}R + CO \xrightarrow[BF_3]{heat} RCOOR$$

xiv. The following are the reactions of esters

- Hydrolysis

Acid catalysed

$$RCOOR' + H_2O \underset{reflux}{\overset{H+}{\rightleftharpoons}} \underset{\text{Carboxylic Acid}}{RCOOH} + \underset{\text{alcohol}}{R'OH}$$

Alkali- catalyzed

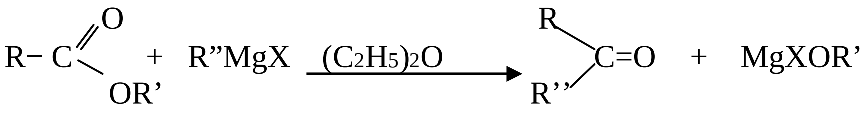
$$RCOOR' + OH^{-} \rightleftharpoons \underset{\text{Carboxylate}}{RCOO^{-}} + \underset{\text{alcohol}}{R'OH}$$

Hydrolysis under alkaline conditions is referred to as saponification.

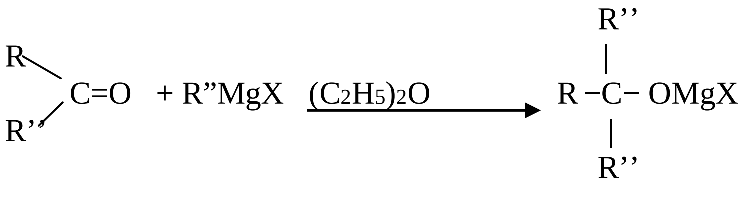
- Amide formation

$$R\,COOR + NH_3 \xrightarrow[\text{or } NH^{+}{}_4 \text{ in conc. Aq. solution}]{RO^{-} \text{ in alcohol}} \underset{\text{amide}}{RCONH_2} + R'OH$$

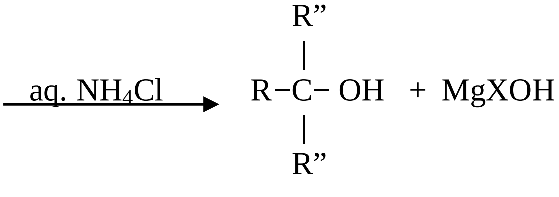
- Formation of ketones and tertiary alcohols



$$R-C(=O)OR' + R''MgX \xrightarrow{(C_2H_5)_2O} RR''C{=}O + MgXOR'$$



$$RR''C{=}O + R''MgX \xrightarrow{(C_2H_5)_2O} R-\underset{R''}{\overset{R''}{C}}-OMgX$$



$$\xrightarrow{aq.\ NH_4Cl} R-\underset{R''}{\overset{R''}{C}}-OH + MgXOH$$

- Ester Exchange(Transesterification)

$$RCOOR' + R''OH \overset{H^+ \text{ or } RO^-}{\rightleftharpoons} RCOOR'' + R'OH$$

- Reduction

$$RCOOR + 4[H] \xrightarrow[H_2O]{LiAIH_4/ (C_2H_5)O} RCH_2OH + R'OH$$

- Replacement of the carboxylate group

When dry hydrogen bromide, concentrated aqueous hydrogen iodide or concentrated tetraoxosulphate (VI) acid.

xv. Amides can be prepared from the following methods

- By heating ammonium salts of carboxylic acids.

$$RCOONH_4 \xrightarrow{heat} RCONH_2 + H_2O$$

- By ammonolysis of acyl chloride, anhydrides or ester with concentrated ammonia.

$$RCOCl + NH_3 \longrightarrow RCONH_2 + HCl$$

$$(RCO)_2O + NH_3 \longrightarrow RCONH_2 + CH_3COOH$$

$$RCOOR' + NH_3 \longrightarrow RCONH_2 + R'OH$$

- By partial hydrolysis of alkyl cyanides with cold concentrated hydrochloric acid, polyphosphoric acid or alkaline hydrogen peroxide.

$$RC \equiv N + H_2O \longrightarrow RCONH_2$$

xvi. Amides undergo the following reactions

- Hydrolysis of amides

$$RCONH_2 \xrightarrow[Heat]{H_2O, H^+} RCOOH + NH_4^+$$

$$RCONH_2 \xrightarrow[heat]{OH^-} RCOO^- + NH_3$$

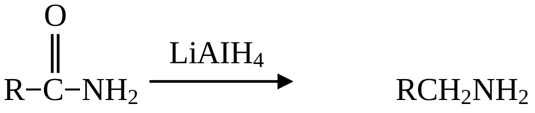
- Hofmann Degradation

$$RCONH_2 + Br_2 + 4NaOH \longrightarrow RNH_2 + 2NaBr + Na_2CO_3 + 2H_2O$$

- Dehydration

$$RCONH_2 \xrightarrow[heat]{P_2O_5} RCN + H_2O$$

- Reduction



$$R{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}NH_2 \xrightarrow{LiAIH_4} RCH_2NH_2$$

Amide Amine

xvii Carboxylic acids and its derivatives are useful in food industries, polymer industries, soap preparation, solvent for paints, thinners and vanish removers.

## 6.0 Tutor Marked Assignment

a. How do you account for the following?
i. ethanoyl chloride has lower boiling point than ethanoic acid
ii. Ethanoyl chloride is more reactive than ethanoic acid anhydride

b. Starting with ethanoic acid, how would you prepare:
i. Ethanoyl chloride
ii. Ethanamide
iii. Ethanoic acid anhydride
iv. Trichloroethanoic acid.

c. Distinguish between ethanoyl chloride, ethanamide and ethanoic acid anhydride in their reactions with the following:
i. $H_2O$ ii. $NH_3$ iii. $LiAlH_4$

## 7.0 Further Reading and Resources

a. K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry -Third Edition

b. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry - Sixth Edition

c. Y.C.Wong; C.T.Wong; S.O.Onyiruka and L.E.Akpanisi (2001)-University Organic Chemistry: The Fundamentals

# Module 4 :Aldehydes and Ketones

## Unit 1: Naming Aldehydes and Ketones, Physical Properties

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3.1.1 Naming Aldehydes……………………………………………………94

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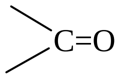
## 1.0 Introduction

Aldehydes and ketones are simple organic compounds called carbonyl compounds. They contain a carbonyl group:



## 3.0 Objectives

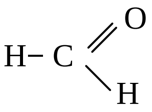
At the end of this unit you should be able:

i. to draw the structure of a simple aldehyde and ketone
ii. Give the names of aldehydes and ketones from the structures
iii. State the physical properties of aldehydes and ketones
iv. Compare the physical properties of the carbonyl compounds

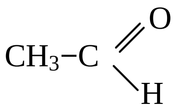
## 4.0 Structures of Aldehyde and Ketones

In aldehydes, the carbonyl group has a hydrogen atom attached to it together with either a second hydrogen atom or a hydrocarbon group which might be an alkyl group or one containing a benzene ring.

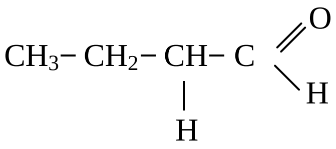
For example:



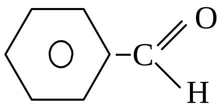
Methanol



Ethanal



2-Methylbutanal

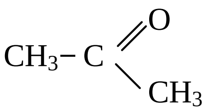


benzaldehyde

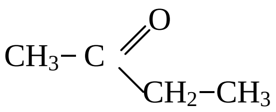
All the structures above have exactly the same end to the molecule; all that differs is the complexity of the other group attached.

In ketones the carbonyl group has two hydrocarbon groups attached. These could either be alkyl group or one containing alkyl group and one aromatic ring or two aromatic rings.

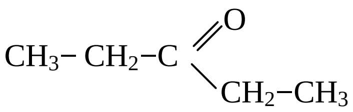
For example:



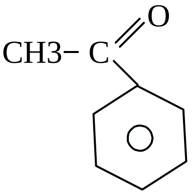
Propanone (Acetone)



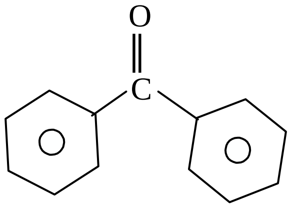
Butanone



Pentan-3-one



Phenyl ethanone

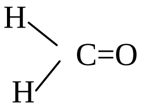


Diphenyl ketone
(benzophenone)

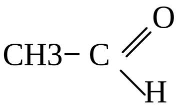
## 3.1 IUPAC Nomenclature of Aldehydes and Ketones

### 3.1.1 Aldehydes

The names of Aldehydes are derived from the root hydrocarbon by adding the suffix ‘-al’ to replace ‘-e’ from the corresponding alkane. For example,



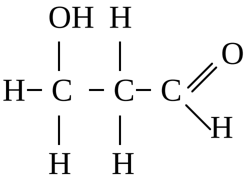
Methanal



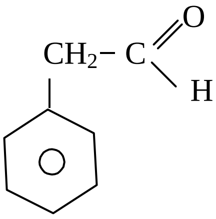
Ethanal

Where there are other substituents on the carbon chain, they are named using prefix (es) with the numbering of carbon from the carbonyl carbon.

For example:



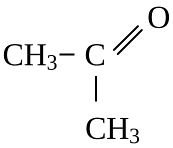
3-hydroxylpropanal



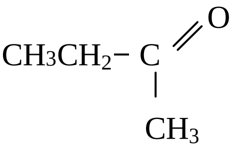
Phenylethanal

### 3.1.2 Ketones

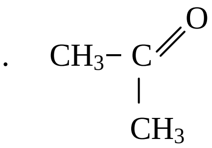
Ketones are named as derivatives of the corresponding alkane with the suffix ‘-one’ replacing the ‘-e’ from the corresponding alkane. For example,



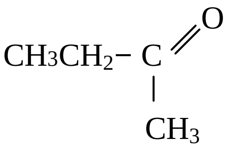
Propanone



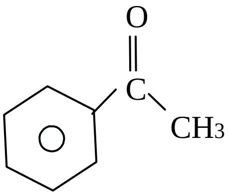
butanone



Pentan -3-one



Pentan-2-one



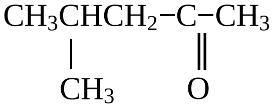
Phenylethanone

The position of the carbonyl group on the carbon chain for isomeric ketones is indicated with numbers, for example Pentan-3-one

## Activity A/ Self Assessment Exercise

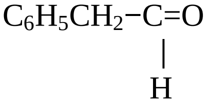
a. Give names to the following carbonyl compounds:

i.



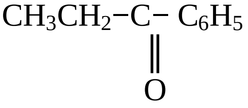
$CH_3\underset{\displaystyle CH_3}{\underset{|}{C}}HCH_2-\underset{\displaystyle O}{\underset{\|}{C}}-CH_3$

ii.



$C_6H_5CH_2-\underset{\displaystyle H}{\underset{|}{C}}=O$

iii.



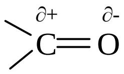
$CH_3CH_2-\underset{\displaystyle O}{\underset{\|}{C}}-C_6H_5$

b. Draw the structures of the following carbonyl compound

i. 3-methyl butanal ii. Benzaldehyde iii. 3-methyl-2-butanone

## 3.2 Bonding and reactivity

The carbon- oxygen double bond is very highly polar. This is because oxygen is far more electronegative than carbon and so has a strong tendency to pull electrons in a carbon-oxygen bond towards itself making it partially negative and the carbon partially positive.



## 3.3 Physical properties

Simple aliphatic aldehydes and ketones are all colourless liquid at 20°C with the exception of methanal which is a gas (boiling point-21°C). Ethanal has a boiling point of 20°C, which means, it boils at close to room temperature. The boiling points increase as the molecules get bigger.

The size of the boiling point is governed by the strength of the Van der Waal's force of attraction which becomes stronger as the molecules get longer and have more electrons. This explains why the boiling point increases as the number of carbon atoms in the chain increases.

The functional group $>C=O$ is polar due to a significant difference in electronegativities of the carbon oxygen atoms. Because of the high polarity in their molecules, carbonyl compounds have higher boiling points than alkanes of similar molecular masses, but much lower than those of alcohols of similar molecular masses because carbonyl compounds unlike alcohols do not have intermolecular hydrogen bonding.

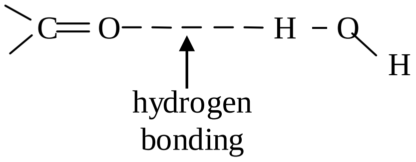
Table 1.1 Boiling Point of Propane, Ethanal and Ethanol

| Molecule | Type | Boiling Point(°C) |
|---|---|---|
| $CH_3CH_2CH_3$ | alkane | -42 |
| $CH_3CHO$ | aldehyde | -21 |
| $CH_3CH_2OH$ | alcohol | 78 |

Notice that in table 1.1 above, the aldehyde (with dipole-dipole attractions as well as Van der Waals forces) has a boiling point higher than the similarly size alkane which only has forces of attraction.

The density of simple aldehydes and ketones are lower than that of water and increases as the relative molecular mass increases. Aromatic aldehydes and ketones are slightly denser than water.

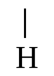
Aldehydes and ketones with short hydrocarbon chains are miscible with water while those with long hydrocarbon chains are insoluble. Lower members of carbonyl compounds can form hydrogen bonds with water molecule and so they have reasonably high solubility in water compared with hydrocarbons of similar molecular masses. Carbonyl compound with carbon atoms of five and above and aromatic compounds which occurs in nature are insoluble in water since the hydrophobic character of the alkyl chains and aromatic rings outweighs the polar character of the carbonyl group.

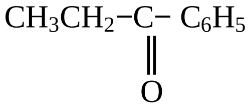


## Activity A/ Self Assessment Exercise

a. Arrange the following in increasing order of:
i. Solubility
ii. Boiling point


$CH_3\underset{\overset{|}{CH_3}}{CH}CH_2-\underset{\overset{\|}{O}}{C}-CH_3$


$C_6H_5CH_2-\underset{\overset{|}{H}}{C}=O$


$CH_3CH_2-\underset{\overset{\|}{O}}{C}-C_6H_5$

## 4.0. Conclusion

Aldehydes and ketones are known as carbonyl compounds. The names of Aldehydes are derived from the root hydrocarbon by adding the suffix “al” to replace “e” from the corresponding alkane while ketones are named as derivatives of the corresponding alkane with the suffix “-one” replacing the “-e” from the corresponding alkane.

## 5.0 Summary

In this unit we have learnt that:

i. Aldehydes and ketones are carbonyl compounds

ii. The contain the carbonyl group $>C=O$

iii. The names of Aldehydes are derived from the root hydrocarbon by adding the suffix “al” to replace “e” from the corresponding alkane

iv. Ketones are named as derivatives of the corresponding alkane with the suffix “-one” replacing the “-e” from the corresponding alkane.

v. Simple aliphatic aldehydes and ketones are all colourless liquid at $20^{o}C$

vi. The boiling points increase as the molecules get bigger.

vii.The carbonyl group is polar

viii. The density of simple aldehydes and ketones are lower than that of water

ix. Aldehydes and ketones with short hydrocarbon chains are miscible with water

x. Carbonyl compound with carbon atoms of five and above and aromatic compounds are insoluble in water.

## 6.0 Tutor Marked Assignment

a. Discuss the physical properties of aldehydes and ketones under the following headings:
i. Boiling point
ii. Solubility
iii. Density

b. Give the IUPAC names of the following carbonyl compounds
i. $CH_3CHO$ ii. $CH_3CH_2CH_2CHClCHO$ iii. $ClCH_2CH_2COCH_3$

## 7.0 Further Reading and other Resources

a. K.S.TEWARI and N.K. VISHNOI (2006)- A Textbook of Organic Chemistry
-Third Edition

b. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry
-Sixth Edition

# Unit: 2 Preparation of Aldehydes and Ketones

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## 1.0 Introduction

Aldehydes and ketones can be prepared as using various methods ranging from oxidation to reduction of suitable compounds.

## 2.0 objectives

At the end of this unit, you should be able to:

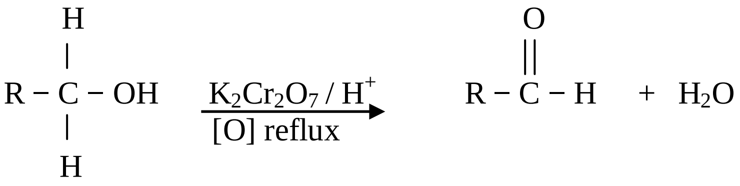
i. Prepare aldehydes and ketones from the dehydration of alcohols
ii. Prepare aldehydes and ketones from oxidation of alcohols
iii. Prepare aldehydes and ketones from the oxidation cleavage of alkene
iv. Prepare aldehydes and ketones from decarbonylation of calcium salts
v. Prepare aldehydes and ketones from the reduction of acyl chloride
vi. Prepare aldehydes and ketones from Friedel Craft acylation reaction

## 3.0 Preparation of Aldehydes and ketones

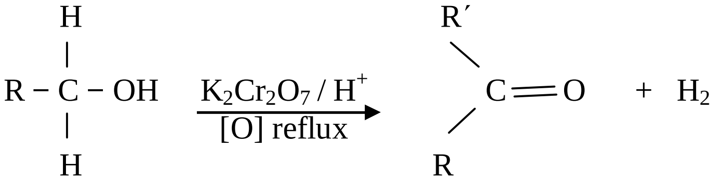
Aldehydes and ketones can be prepared using the various methods discussed below:

### 3.1 Oxidation of primary and secondary alcohols

Aldehydes and ketones are prepared by the oxidation of primary and secondary alcohols respectively using a mild oxidizing agent such as acidified solution of potassium heptadicromate (VI) or tetraoxomanganate (VII)

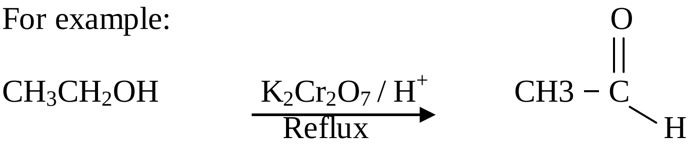


$$R-\underset{H}{\overset{H}{C}}-OH \xrightarrow[\text{[O] reflux}]{K_2Cr_2O_7 / H^+} R-\overset{O}{\overset{\|}{C}}-H \quad + \quad H_2O$$



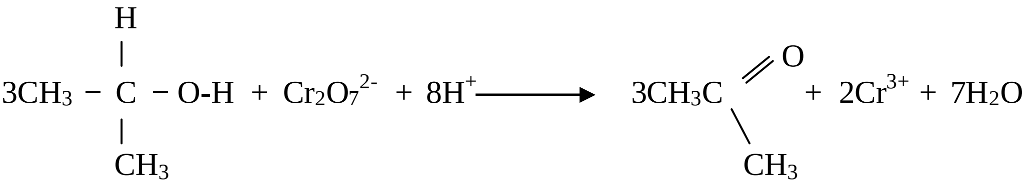
$$R-\underset{H}{\overset{H}{C}}-OH \xrightarrow[\text{[O] reflux}]{K_2Cr_2O_7 / H^+} \begin{matrix} R' & \\ & \diagdown \\ & & C=O \\ & \diagup \\ R & \end{matrix} \quad + \quad H_2$$

For example:



$$CH_3CH_2OH \xrightarrow[\text{Reflux}]{K_2Cr_2O_7 / H^+} CH3-\overset{O}{\overset{\|}{C}}{}_{\diagdown H}$$

$$3CH_3CH_2OH + Cr_2O_7^{2-} + 8H^+ \longrightarrow 3CH_3CHO + 2Cr^{3+} + 7H_2O$$



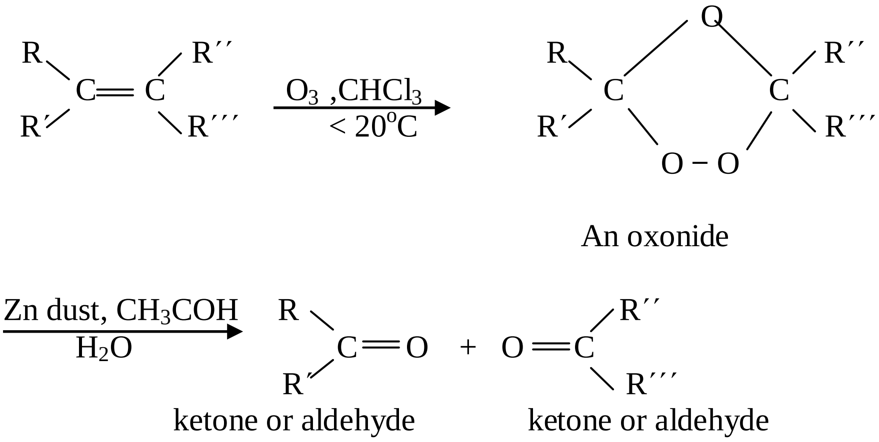
$$3CH_3-\underset{CH_3}{\overset{H}{C}}-O\text{-}H + Cr_2O_7^{2-} + 8H^+ \longrightarrow 3CH_3C\begin{matrix}{}^{\diagup\!\!\diagup O}\\ {}_{\diagdown CH_3}\end{matrix} + 2Cr^{3+} + 7H_2O$$

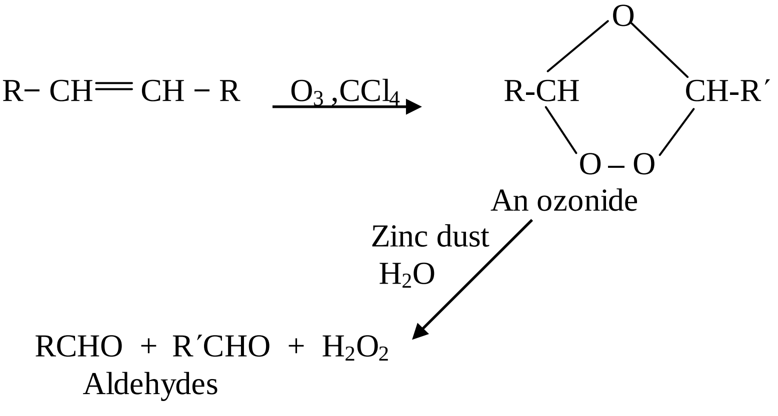
When potassium heptaoxodichromate (VI) acidified with dilute tetraoxosulphate (VI) acid is used, a change in the colour of the solution from the orange solution containing the dichromate (VI) ions is reduced to a green solution containing chromium (III) ions. The net effects is that an oxygen from the oxidizing agent removes one hydrogen atom from the -OH group of the alcohol and another one from the carbon to which it is attached to form water.

However in the oxidation of primary alcohols to form aldehydes, there is a problem. The aldehydes produced can be oxidized further to a carboxylic acid by the acidified dichromate (VI) solution used as the oxidizing agent. This however can be prevented by using excess alcohol and limited oxidizing agent. Also by removing the aldehydes as soon as it is formed, it can be controlled.

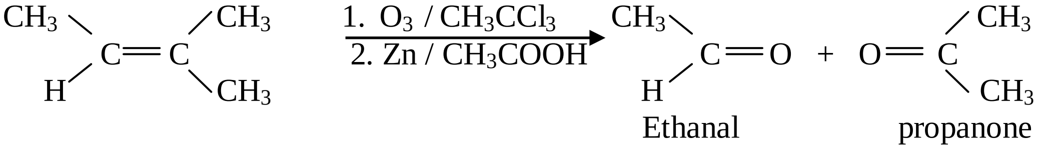
## 3.2 Oxidative cleavage of alkanes (ozonolysis)

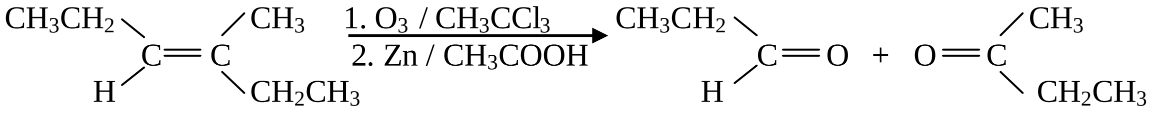
Ozone, when bubbled through a solution of an alkene in 1, 1, 1- trichloromethane, followed by the hydrolysis of the ozonide formed, in the presence of zinc and ethanoic acid gives aldehydes and ketones. The starting alkene determines the product, if aldehydes or ketones.





For example:





Propanal Butan-2-one

## Activity A/Self Assessment Exercise

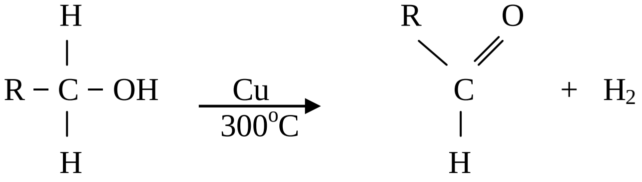
i. Predict the structures of the original hydrocarbon from which the following products of ozonolysis reaction arises:

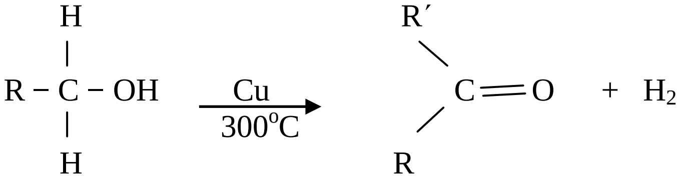
i.

ii.

## 3.3 Dehydration of alcohols

Lower members of aldehydes and ketones are prepared industrially by passing alcohol vapour over hot copper catalyst.



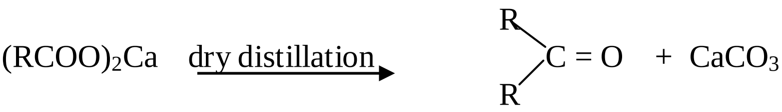


A primary alcohol gives aldehyde while a secondary alcohol gives ketone.

## 3.4 Decarboxylaton of calcium salts

Aldehydes are made by heating a mixture of calcium methanoate and calcium carboxylate at 400°C. If calcium methanaote is not used, then a ketone is formed.

$$(RCOO)_2\ Ca + (HOO)_2Ca \xrightarrow[400^oC]{\text{dry distillation}} \underset{\text{Aldehydes}}{2RCHO} + 2CaCO_3 \longrightarrow$$



Ketone

## 3.5 Reduction of acyl chloride using a ‘poisoned catalyst’

This reaction is known as **Rosenmund Reaction.** It is only suitable for aldehydes.
Acyl chlorides are reduced to aldehydes by treatment with hydrogen in the presence of Palladised barium tetraoxosulphate (VI), poisoned by barium tetraoxosulphate (VI). The catalyst is poisoned to prevent further reduction to the alcohol.

$$RCOCl + H_2 \xrightarrow[\text{heat}]{Pd / BaSO_4} RCHO + HCl$$

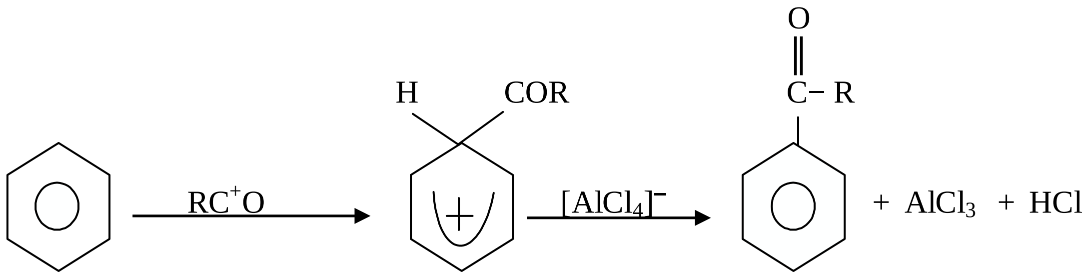
## 3.6 Friedel - Craft acylation

The condensation of benzene with an acyl chloride, RCOCl, or acid anhydride, $(RCO)_2O$, in the presence of anhydrous aluminum chloride-a Lewis acid- gives a good yield of the aromatic ketone. The reaction mixture is refluxed on a water bath at 50°C

$$RCOCl + AlCl_3 \xrightleftharpoons[50^oC]{} RC^+O + [AlCl_4]^-$$

Or when the acid anhydride is used,

$$(RCO)_2O + AlCl_3 \xrightleftharpoons{} RC^+O + [RCOO.\ AlCl_3]^-$$



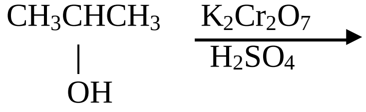
## Activity B/Self Assessment Exercise

Complete the following reactions:

i. $$CH_3CH_2CH_2OH \xrightarrow[H_2SO_4]{K_2Cr_2O_7}$$

ii. $$(C_2H_5COO)_2Ca \xrightarrow{\text{dry distil, } 400^OC}$$

iii.



$$\underset{\displaystyle OH}{\underset{|}{CH_3CHCH_3}} \xrightarrow[H_2SO_4]{K_2Cr_2O_7}$$

## 4.0 Conclusion

Aldehydes and ketones can be prepared from the dehydration of alcohols, oxidation reactions of alcohols, oxidation cleavage of alkenes, decarbonylation of calcium salts, reduction of acyl chloride and from the, Friedel Craft acylation.

## 5.0 Summary

In this unit we have learnt that aldehydes and ketones can be prepare from:

i. The dehydration of alcohols
ii. oxidation reactions of alcohols
iii. oxidation cleavage of alkenes
iv. decarbonylation of calcium salts
v. reduction of acyl chloride and
vi. from the, Friedel Craft acylation.

## 6.0 Tutor Marked Assignment

a. Using equation, explain the preparation of aldehydes and ketone from:
i. Dehydration of alcohols
ii. Oxidation of alcohols
iii. Friedel Craft acylation

## 7.0 Further Reading and other Resources

a. K.S.TEWARI and N.K. VISHNOI (2006)- A Textbook of Organic Chemistry
-Third Edition

b. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry
-Sixth Edition

# Unit 3: Reactions of Aldehydes and Ketones

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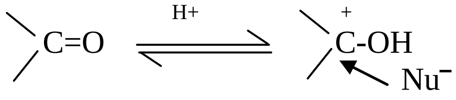
## 1.0 Introduction

Aldehydes and ketones are reactive organic compounds that characteristically undergo nucleophilic addition or condensation reactions. This is due to the difference in electronegative between carbon and oxygen atom. The carbonyl carbon atom is the nucleophilic site since it is electron deficient because of the difference in electronegativity between carbon and oxygen.



## 2.0 Objectives

At the end of this unit, you should be able to:

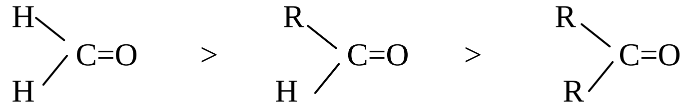
i. Discuss the various reactions of aldehydes and ketones under the following endings
  - Nucleophilic addition reaction
  - Condensation reaction

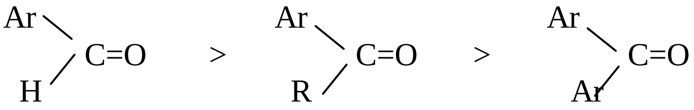
ii. Distinguish between aldehydes and ketones using:
  - Fehling's reaction
  - Schiff reagent
  - Silver mirror test

## 3.0 The Carbonyl Carbon has a nucleophilic site

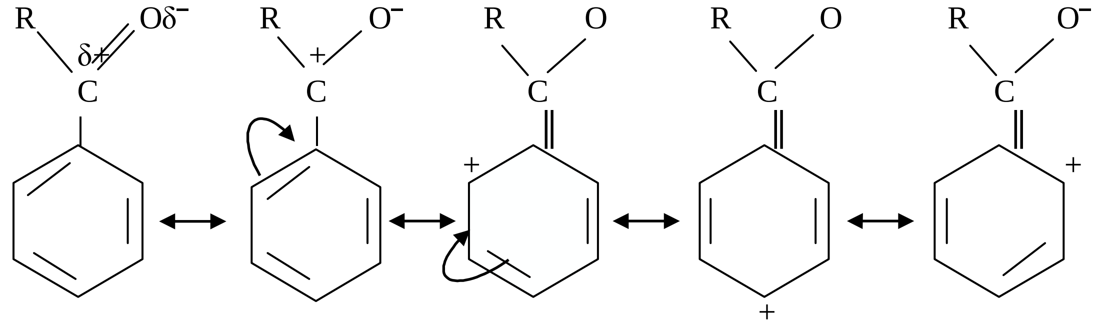
The susceptibility of the carbonyl carbon to nucleophilic attack is reduced by its attachment to electron releasing alkyl or aryl groups, which reduces the degree of positive charge on the carbon. Also, the increase in steric hindrance about the carbon by the bulky hydrocarbon groups hinders the approach of the attacking nucleophile and contributes to the reduction in this reactivity. Hence, aldehydes are more reactive than ketones because they contain only one hydrocarbon group. The carbonyl carbon in the aldehydes is more positive and less sterically hindered than that in ketones, hence more susceptible to nucleophilic attack.

The order of reactivity of carbonyl compounds to nucleophilic attack is as follows.





Alkyl groups donate electrons by inductive effects while aryl (Ar) groups do so by the resonance.



**Activity A/Self Assessment Exercise**

Arrange the following in increasing order of reactivity towards anucleophilic attacks:

$CH_3CH_2COC_6H_5$, $CH_3CH_2CHO$, $CH_3COC_2H_5$, $C_6H_5COC_6H_5$

## 3.1 Nucleophilic Addition

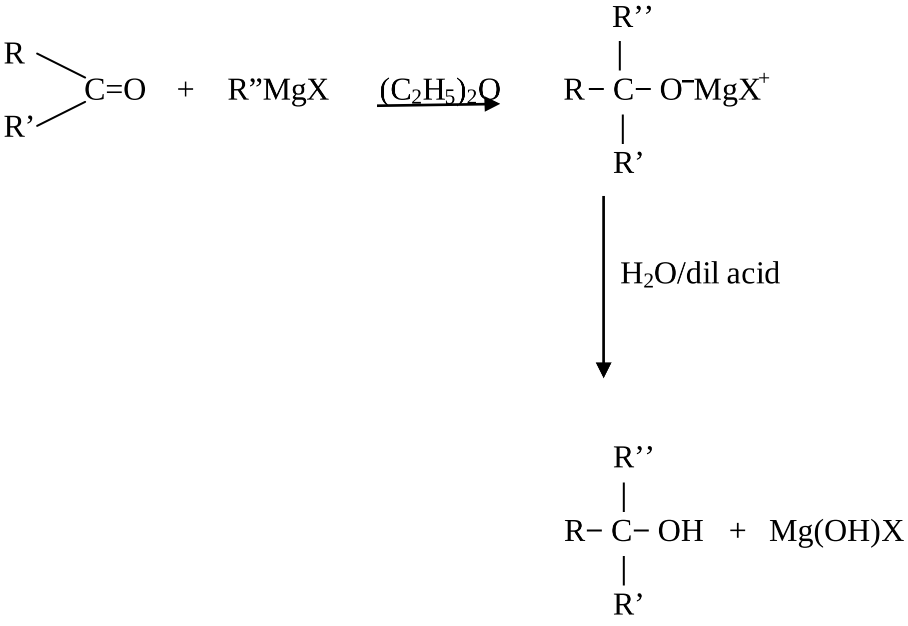
### 3.1.1 Addition of Grignard Reagents

A Grignard reagent has a formula RMgX, where X is a halogen and R is an alkyl or aryl group. For example, $CH_3CH_2MgBr$.

Aldehydes and ketones react with Grignard reagents to form alcohols. This reaction is very useful for preparation all three classes of alcohols. The product formed depends on the starting carbonyl compound as shown below:

Methanal $\longrightarrow$ $1^o$ alcohol
Aldehydes $\longrightarrow$ $2^o$ alcohol
Ketones $\longrightarrow$ $3^o$ alcohol

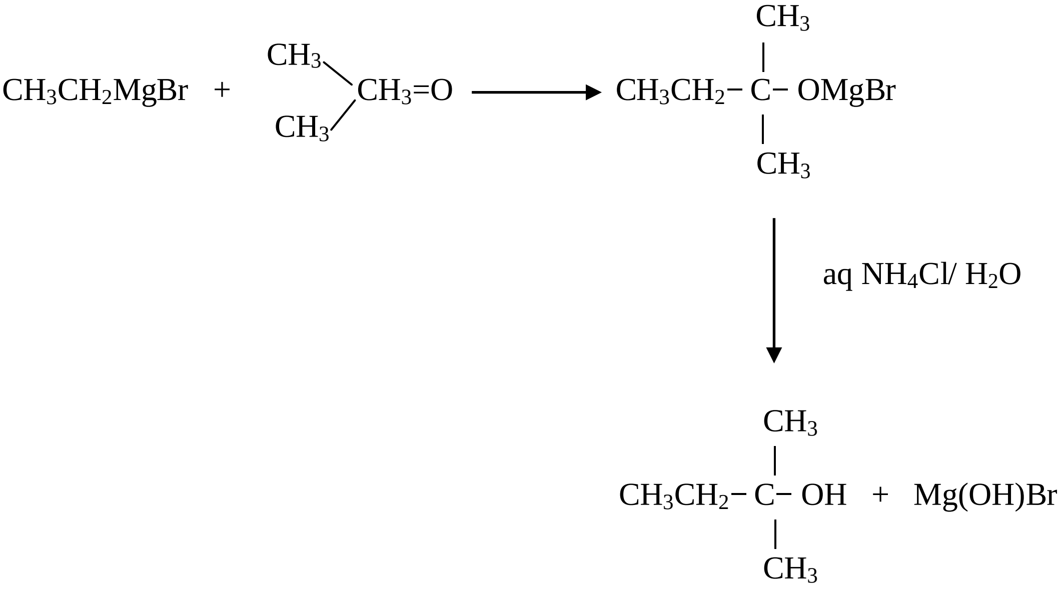
Mechanism:



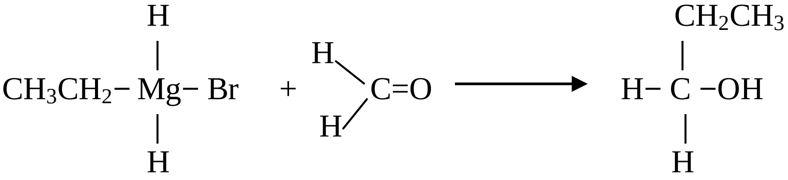
$$\begin{matrix}R\\R'\end{matrix}\!>C{=}O + R''MgX \xrightarrow{(C_2H_5)_2O} R-\underset{R'}{\overset{R''}{C}}-O^-MgX^+ \xrightarrow{H_2O/\text{dil acid}} R-\underset{R'}{\overset{R''}{C}}-OH + Mg(OH)X$$

In the preparation of tertiary alcohols, aqueous ammonium chloride is used for hydrolysis as dilute acid brings about dehydration of the alcohol to yield the alkene which is an elimination product.

For example:

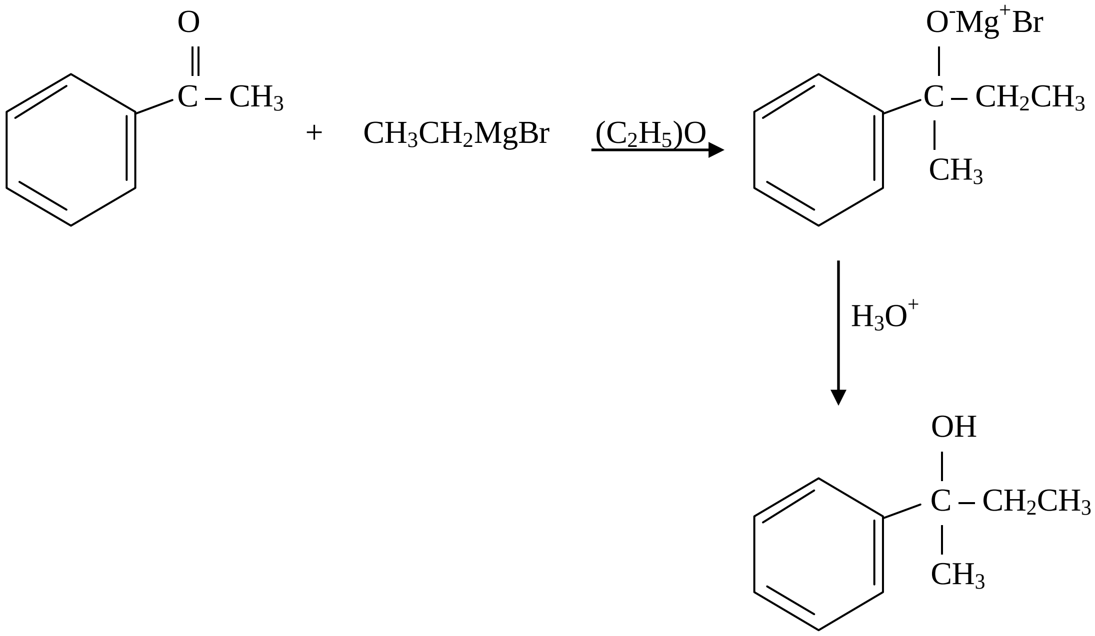


2-Methyl butan-2-ol



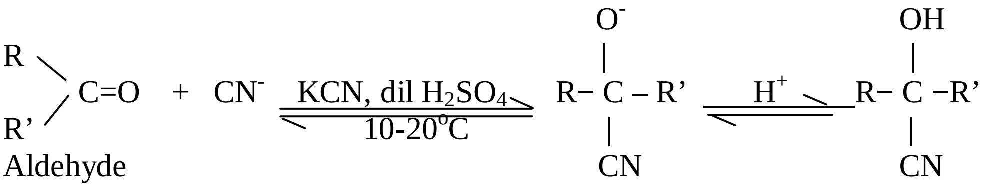
Methanal

Propanol (1° alcohol)



### 3.1.2 Addition of hydrogen cyanide, HCN

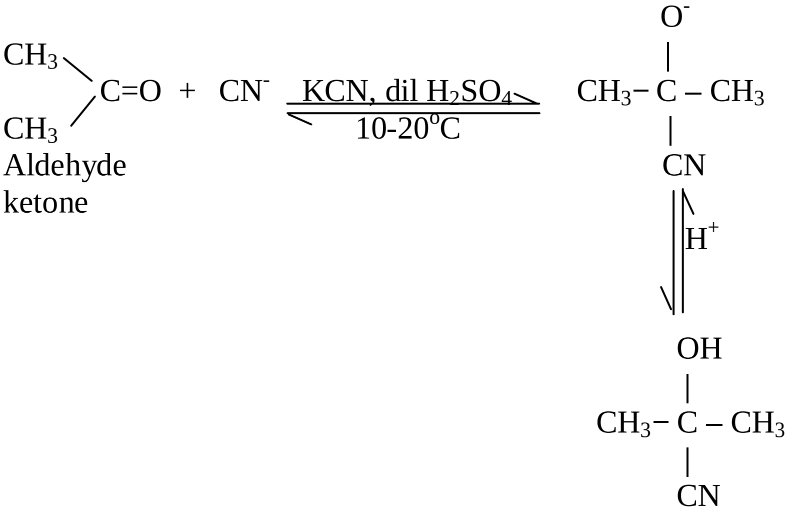
Aldehydes and ketones undergo addition with hydrogen cyanide to yield a class of compounds called 2- hydroxyalkanonitriles (cyanohydrins).



$$\begin{matrix}R\\ \ \ \ \ \ \ >C=O\\ R'\end{matrix} + CN^- \underset{10\text{-}20^oC}{\overset{KCN,\ dil\ H_2SO_4}{\rightleftharpoons}} R-\overset{\overset{O^-}{|}}{\underset{\underset{CN}{|}}{C}}-R' \overset{H^+}{\rightleftharpoons} R-\overset{\overset{OH}{|}}{\underset{\underset{CN}{|}}{C}}-R'$$

Aldehyde
or
ketone

2-Hydroxyalkanonitrile
(cyanohydrin)

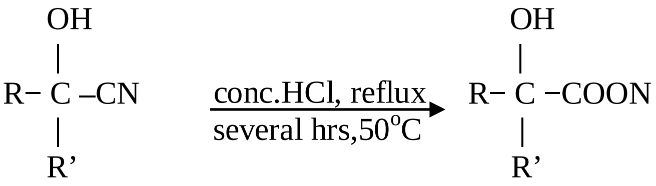


$$\begin{matrix}CH_3\\ \ \ \ \ \ \ >C=O\\ CH_3\end{matrix} + CN^- \underset{10\text{-}20^oC}{\overset{KCN,\ dil\ H_2SO_4}{\rightleftharpoons}} CH_3-\overset{\overset{O^-}{|}}{\underset{\underset{CN}{|}}{C}}-CH_3 \overset{H^+}{\rightleftharpoons} CH_3-\overset{\overset{OH}{|}}{\underset{\underset{CN}{|}}{C}}-CH_3$$

Aldehyde
ketone

2-hydroxy-2-methylpropane nitrile

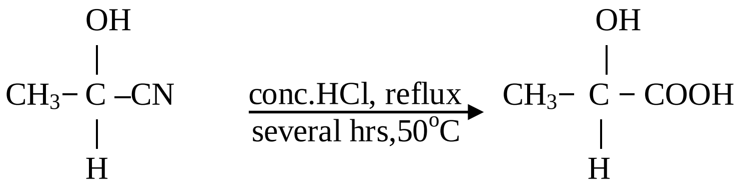
On hydrolysis, 2- hydroxyalkanonitriles-2-hydroxycarboxylic acids are formed.



$$R-\overset{\overset{OH}{|}}{\underset{\underset{R'}{|}}{C}}-CN \xrightarrow[\text{several hrs,}50^oC]{\text{conc.HCl, reflux}} R-\overset{\overset{OH}{|}}{\underset{\underset{R'}{|}}{C}}-COON$$

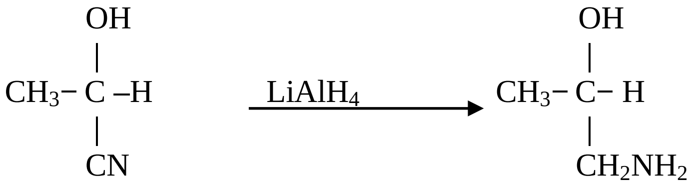
2- or α-hydroxycarboxylic acid

For example:



$$CH_3-\overset{\overset{OH}{|}}{\underset{\underset{H}{|}}{C}}-CN \xrightarrow[\text{several hrs,}50^oC]{\text{conc.HCl, reflux}} CH_3-\overset{\overset{OH}{|}}{\underset{\underset{H}{|}}{C}}-COOH$$

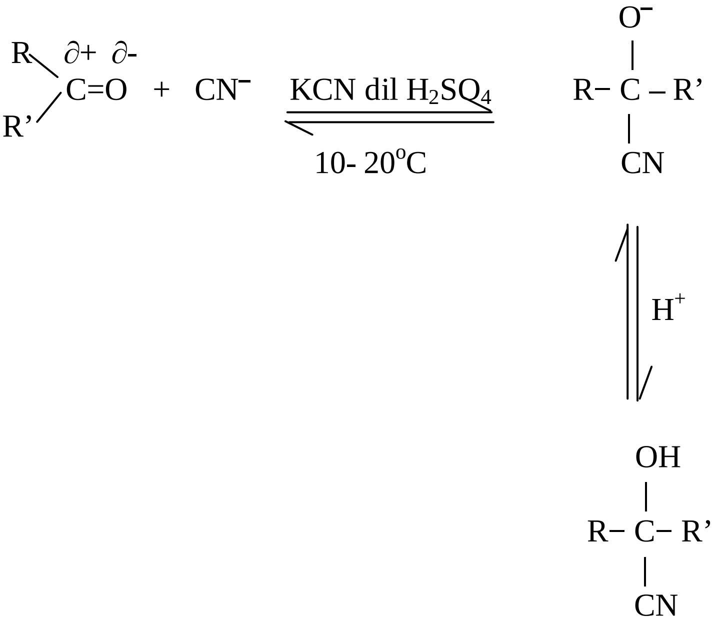
The reduction of 2- hydroxyalkanonitriles form the corresponding amine.



$$CH_3-\overset{\overset{\large OH}{|}}{\underset{\underset{\large CN}{|}}{C}}-H \xrightarrow{LiAlH_4} CH_3-\overset{\overset{\large OH}{|}}{\underset{\underset{\large CH_2NH_2}{|}}{C}}-H$$

2-hydroxypropylamine

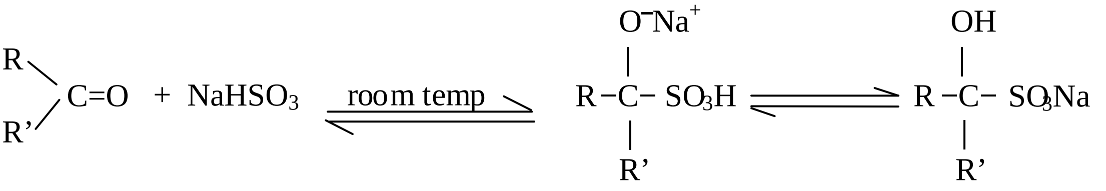
Mechanism



$$\overset{R}{\underset{R'}{}}\!\!\overset{\partial+\ \partial-}{C=O} + CN^- \underset{10-20^oC}{\overset{KCN\ dil\ H_2SO_4}{\rightleftharpoons}} R-\overset{\overset{\large O^-}{|}}{\underset{\underset{\large CN}{|}}{C}}-R' \xrightleftharpoons{H^+} R-\overset{\overset{\large OH}{|}}{\underset{\underset{\large CN}{|}}{C}}-R'$$

### 3.1.3 Addition of sodium hydrogensulphite $NaHSO_3$

Aldehydes and ketones react reversibly with excess 40 percent hydrogensuphite in excess at room temperature to yield the carbonyl hydrogensulphite which is isolated as colourless crystals.

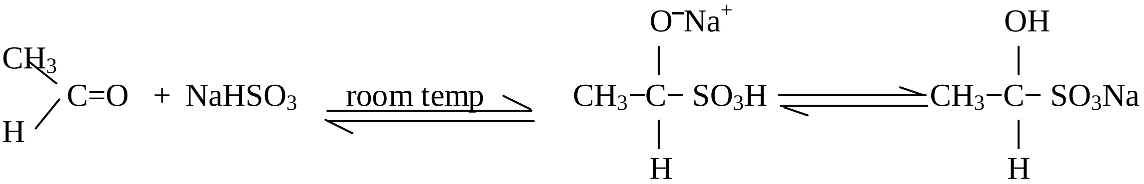


$$\overset{R}{\underset{R'}{}}\!\!C=O + NaHSO_3 \underset{}{\overset{room\ temp}{\rightleftharpoons}} R-\overset{\overset{\large O^-Na^+}{|}}{\underset{\underset{\large R'}{|}}{C}}-SO_3H \rightleftharpoons R-\overset{\overset{\large OH}{|}}{\underset{\underset{\large R'}{|}}{C}}-SO_3Na$$

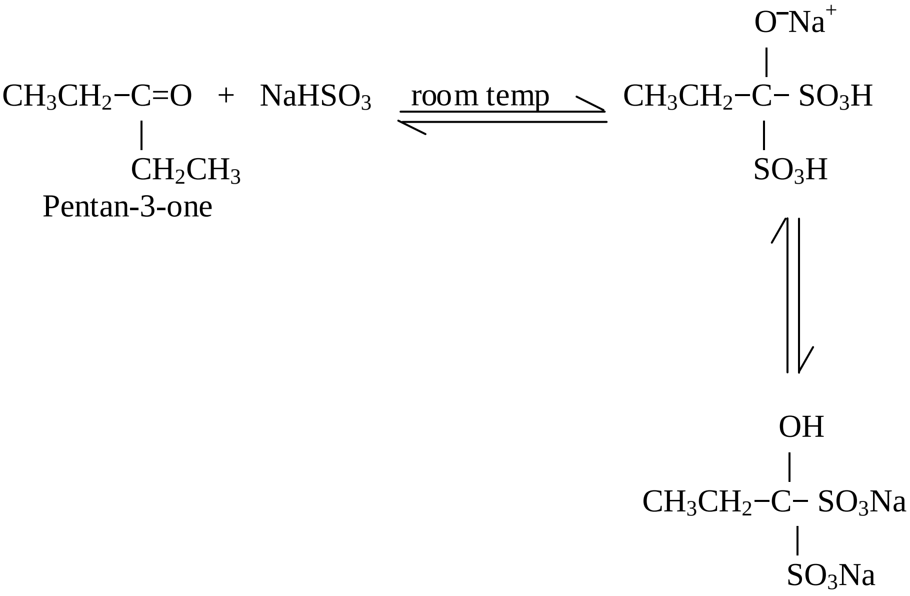
Aldehydes
or ketones

Aldehyde or Ketone
hydrogensulphite

For example



$$\overset{CH_3}{\underset{H}{}}\!\!C=O + NaHSO_3 \overset{room\ temp}{\rightleftharpoons} CH_3-\overset{\overset{\large O^-Na^+}{|}}{\underset{\underset{\large H}{|}}{C}}-SO_3H \rightleftharpoons CH_3-\overset{\overset{\large OH}{|}}{\underset{\underset{\large H}{|}}{C}}-SO_3Na$$



$$CH_3CH_2-\underset{\substack{|\\CH_2CH_3}}{C}=O + NaHSO_3 \xrightleftharpoons{\text{room temp}} CH_3CH_2-\overset{\substack{O^-Na^+\\|}}{\underset{\substack{|\\SO_3H}}{C}}-SO_3H \rightleftharpoons CH_3CH_2-\overset{\substack{OH\\|}}{\underset{\substack{|\\SO_3Na}}{C}}-SO_3Na$$

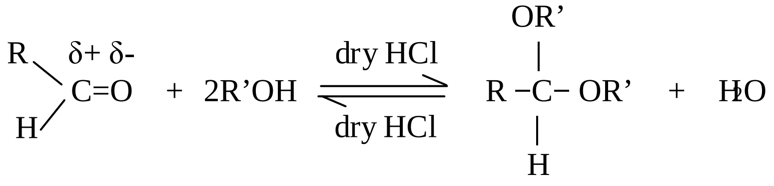
Pentan-3-one

The addition of hydrogensulphite to carbonyl compounds is commonly used to separate carbonyl compounds from a mixture of organic compounds. The carbonyl hydrogensulphite is treated with an acid or an alkali to regenerate the free carbonyl compound. This reaction is a very good method for the purification and seperation of suitable carbonyl compounds from non carbonyl compounds.

The hydrogenosulphate reacts with potassium cyanide or sodium cyanide to give a 2 - hydroxyalkanonitrile.

### 3.1.4 Addition of Alcohols

Aldehydes undergo addition with excess anhydrous alcohol in the presence of a little dry hydrogen chloride catalyst to form 1, 1- dialkoxyl alkanes (Acetals).

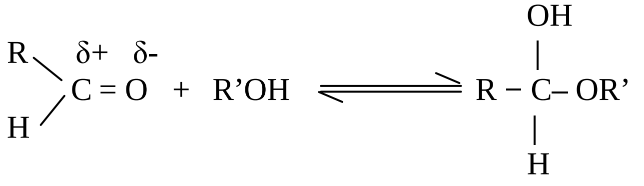


$$\begin{matrix}R\\ \\H\end{matrix}\!>\overset{\delta+}{C}=\overset{\delta-}{O} + 2R'OH \underset{\text{dry HCl}}{\overset{\text{dry HCl}}{\rightleftharpoons}} R-\overset{\substack{OR'\\|}}{\underset{\substack{|\\H}}{C}}-OR' + H_2O$$

1,1- dialkoxyl alkane
(Acetal)

The carbonyl compound (acetal) reacts with two equivalents of an alcohol.

In the absence of a catalyst, the aldehyde and alcohol exist in equilibrium with a type of compound known as 1-alkoxyalcohol (hemiacetal).



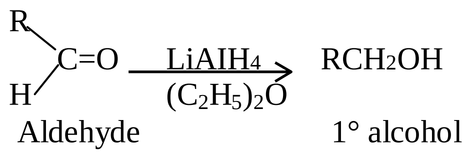
$$\begin{matrix}R\\ \\H\end{matrix}\!>\overset{\delta+}{C}=\overset{\delta-}{O} + R'OH \rightleftharpoons R-\overset{\substack{OH\\|}}{\underset{\substack{|\\H}}{C}}-OR'$$

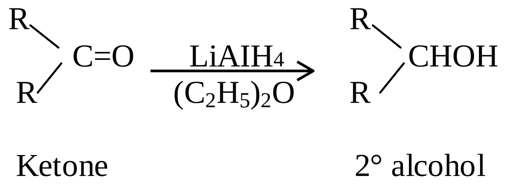
1- alkoxyalcohol
(A hemiacetal)

The Ketone equivalents of these derivatives are known as ketals and they are difficult to prepare via this method.

### 3.1.5 Reduction using Lithium tetrahydridoaluminate (III)

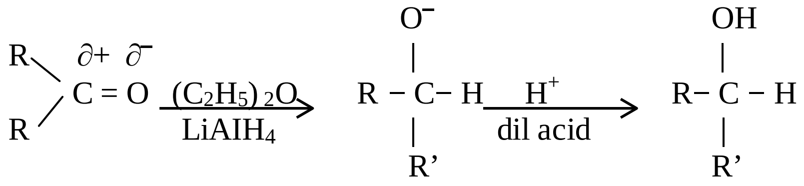
Aldehydes and ketones, when reduced using Lithium tetrahydridoaluminate (III) in ethoxy ethane at 0°C gives primary and secondary alcohols respectively.





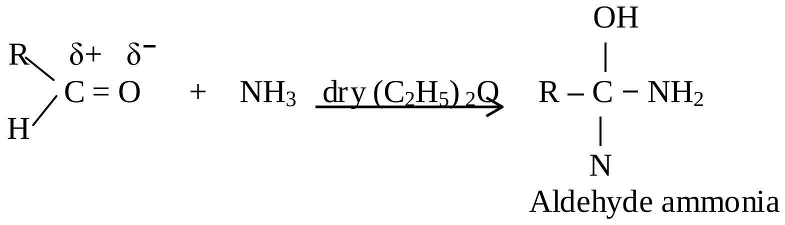
Lithium tetrahydridoborate (III), $LiBH_4$ -a milder reducing agent- in ethoxy ethane or tetra hydrofuran is sometimes used as an alternative reagent.

Also, Sodium tetrahydridoborate (III) $Na^+BH_4^-$, dissolved in water or methanal, because it is insoluble in ethoxy ethane behaves in a similar manner to Lithium tetra hydridoaluminate(III) although it is milder in its action.



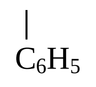
### 3.1.6 Addition of Ammonia

Aliphatic aldehydes react with gaseous ammonia on passing the latter through a dry solution of ethoxy ethane to form a white precipitate of the aldehyde ammonia. Aldehydes ammonia is not stable.



Methanal, aromatic aldehydes and ketones do not undergo this reaction. They however yield complex condensation products.

For example:



$$3C_6H_5CHO + 2NH_3 \longrightarrow C_6H_5CH{=}N{-}\underset{\displaystyle C_6H_5}{\underset{|}{CH}}{-}N{=}CHC_6H_5 + 3H_2O$$

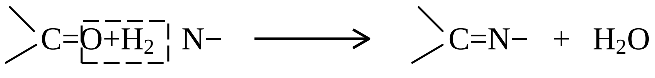
## Activity B/Self Assessment Exercise

Give the structure and the names of the poduct formed when ethanal and propanone react with the following:

i. $CH_3CH_2MgCl$
ii. KCl, dil $H_2SO_4$
iii. $NaHSO_3$
iv. $C_2H_5OH$,dry HCl
v. $LiAlH_4$
vi. $NH_3$

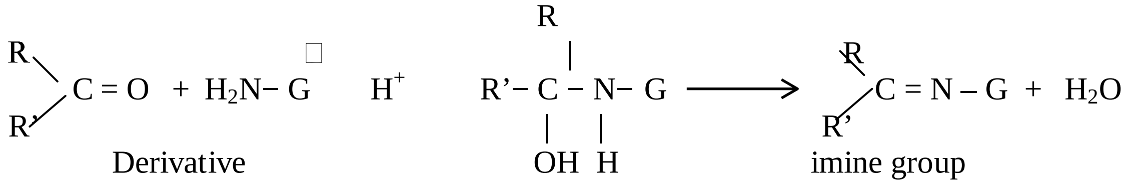
## 3.2 Condensation Reaction (Addition – Elimination Reactions)

Aldehydes and ketones react with derivatives of ammonia such as hydroxlamine, $NH_2OH$, hydrazine, $NH_2NH_2$ or 2, 4 – dinitrophenylhydrazine $C_6H_5N_2H_3$ $(NO_2)_2$ to give a compound containing an imine group, >C=N- with the elimination of water molecules.



Imine group

The general reaction mechanism is as follows:

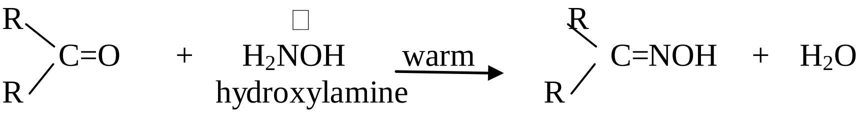


### 3.2.1 Reaction with hydroxylamine, $NH_2OH$

Hydroxylamine in the form of one of its more stable salts, (hydroxylamine hydrochloride $HONH^+_4Cl^-$) reacts with aldehydes and ketones to form OXIMES which are crystalline solids. Free hydroxylamine is liberated by reacting hydroxylamine hydrochloride with sodium hydroxide or sodium ethanate.

$HONH_3^+ Cl^- + NaOH \longrightarrow NH_2OH + NaCl + H_2O$

hydroxylamine chloride → hydroxylamine



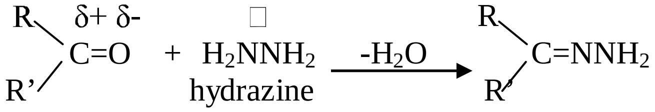
Oxime

For example:

Ethanal
oxime

Propanone oxime

### 3.2.2 Reaction with hydrazine,$NH_2NH_2$



Aldehyde or
Ketone hydrazine

Aldehyde and ketones react with hydrazine in excess to give hydrazone.

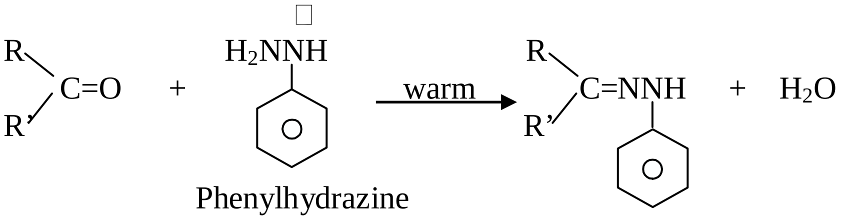
For example,

$CH_3CHO + H_2NNH_2 \longrightarrow CH_3C{=}NNH_2$

Ethanal
hydrazone

### 3.2.3 Reaction with Phenylhydrazine, $C_6H_5NHNH_2$

Phenylhydrazine is a colourless and poisonous liquid that condenses with the carbonyl compound dissolved in aqueous alcohol on warming to give phenyl hydrazones.



Phenylhydrazine

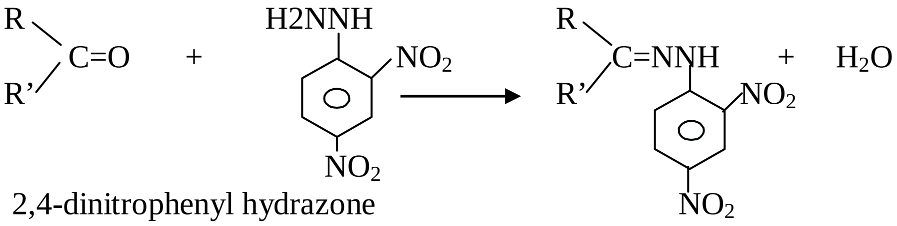
Aldehyde or ketone
Phenyl hydrazone

The phenylhydrazone derivatives of simple aliphatic aldehydes and ketones are oils or solids with low melting points while aromatic carbonyl compounds derivatives are crystalline solids.

### 3.2.4 Reaction with 2,4- dinitrophenyl hydrazine(2,4-$C_6H_3(NO_2)_2NHNH_2$) - Brady's Reagent

Brady's reagent is used for the detection of carbonyl functional group.

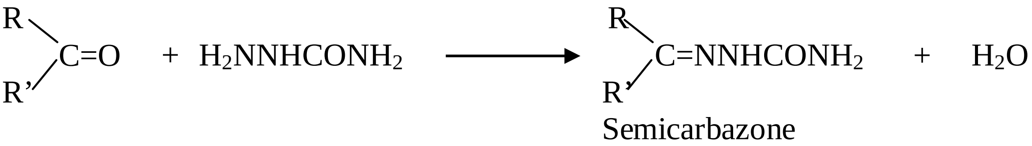
Aldehydes and ketones reacts with 2,4-dinitrophenyl hydrazine to give the 2,4-dinitrophenyl hydrazone derivatives.



2,4-dinitrophenyl hydrazone
(Aldehyde or ketone)

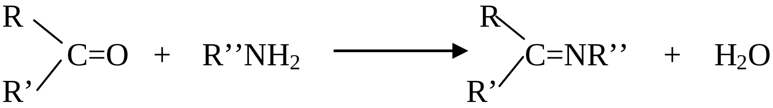
### 3.2.5 Reaction with Semicarbazide- $NH_2NHCONH_2$

Aldehydes and ketones react with an aqeous solution of semicarbazide hydrochloride and sodium ethanoate in the cold to give a colourless crystals-semicarbazone.



### 3.2.6 Reaction with primary amines

Primary amines condense readily with aldehydes and ketones to form **Schiff** bases.



## Activity C/Self Assessment Exercise

Write the formula for the solid derivative formed when an aldehyde or a ketone reacts with each of the following ammonia derivatives:

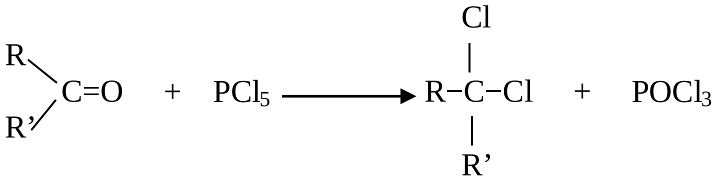
i. $HNOH_2$ ii. $H_2N\text{-}NHC_6H_5$ iii. $H_2NNHCONH_2$

## 3.3 Other reactions of Aldehydes and Ketones

### 3.3.1 Chlorination

(a) With $PCl_5$

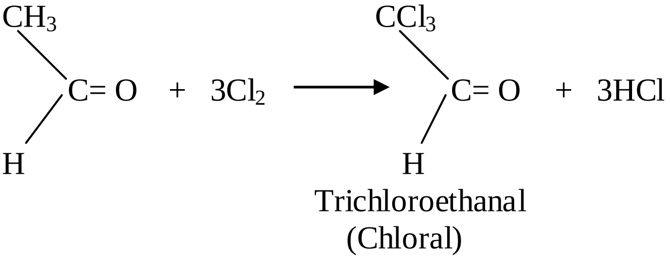
Aliphatic and simple aromatic carbonyl compounds react under dry conditions with $PCl_5$ to form dichlorohydrocarbon. In this reaction the oxygen atom of the carbonyl compound is replaced with two chlorine atoms.



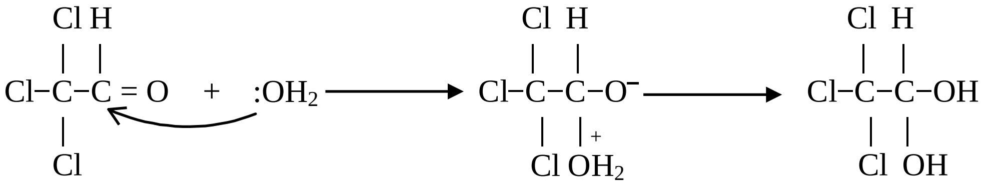
The lower dichlorohydrocarbons are colourless liquids.

(b) With Chlorine gas (Trichloroethanal formation)

When excess chlorine is bubbled through ethanal, the methyl hydrogen atoms are replaced with chlorine to yield a colourless, oily liquid, trichloroethanal known as chloral.



Chloral reacts exothermically with water to form a stable crystalline hydrate.

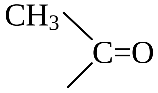


2,2,2-trichloroethanediol
(Chloral hydrate)

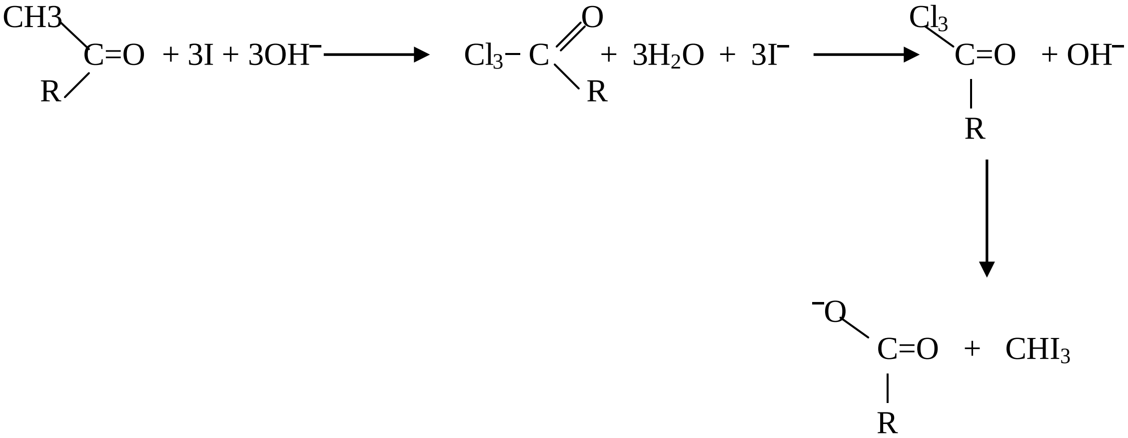
Also, when chlorine is bubbled through warm propanone, successive replacement of the methyl hydrogen occurs, giving a mixture of chloropropanones, e.g.$CH_3COCH_2Cl$, $ClCH_2COCH_2Cl$, $Cl_2CHCOCH_2Cl$ and so on.

### 3.3.2 Trihalomethane (Iodoform) Reaction

Aldehydes or ketones with the structure

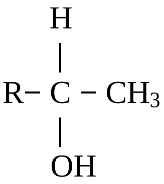


react with iodoform reagent -iodine in aqueous sodium hydroxide solution to give a carboxylate and triiodomethane-a yellow precipitate.



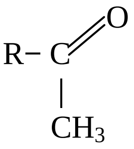
Triiodomethane
(a yellow precipitate)

The reaction is also given by ethanol and secondary alcohols with the structure



$$R-\overset{\displaystyle H}{\underset{\displaystyle OH}{C}}-CH_3$$

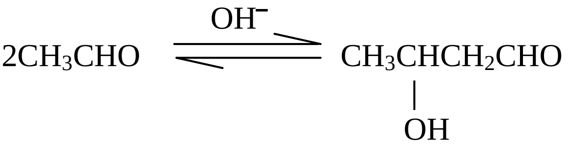
since they can undergo oxidation under a similar condition to form the carbonyl compounds.



### 3.3.3 Aldol Condensation

Aldehydes and ketones containing at least one α-hydrogen atom- the carbon atom attached to the carbonyl carbon must possess at least one hydrogen-undergo aldol condensation reaction.

For example, ethanal, $CH_3CHO$, Methanal, HCHO and benzene carbaldehyde, $C_6H_5CHO$ cannot undergo this reaction because they do not contain α-hydrogen atom. The reaction is base catalysed.

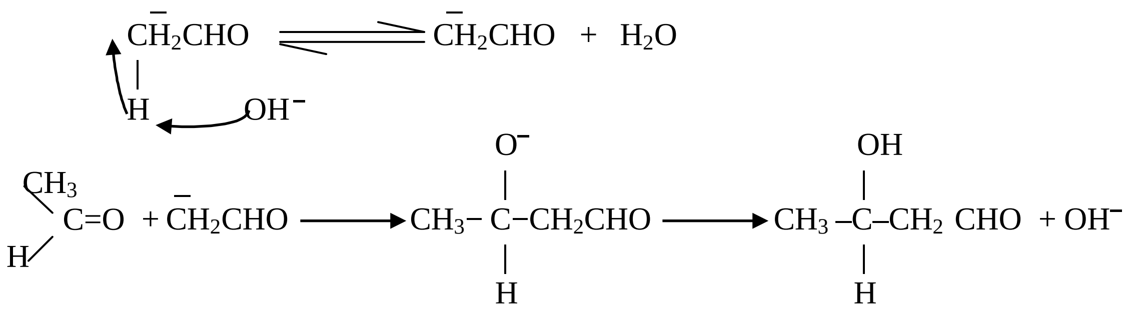


$$2CH_3CHO \overset{OH^-}{\rightleftharpoons} \underset{\substack{|\\ OH}}{CH_3CHCH_2CHO}$$

3-hydroxybutanal
(An aldol)

In the presence of a high concentration of hydroxide ions, the reaction continues to give a polymeric resin.

Mechanism

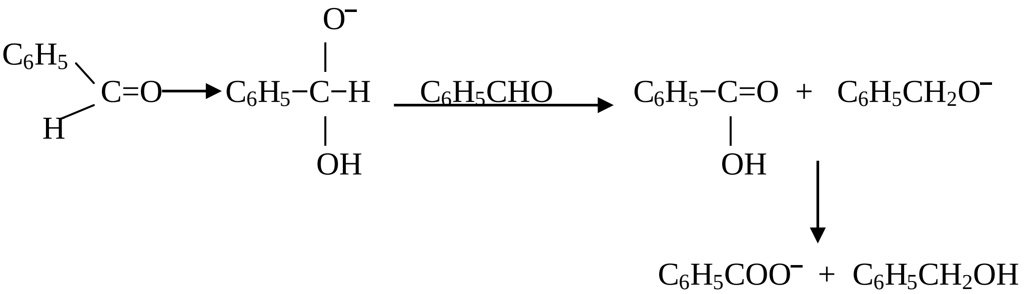


### 3.3.4 Cannizaro Reaction

This reaction is a direct contrast to the aldol condensation. It only applies to carbonyl compounds that do not contain α- hydrogen atoms. It is therefore limited to compounds in which the carbonyl compound is attached to a tertiary alkyl carbon atom. It is also base catalysed. For example, if a suitable aldehyde is treated with a concentrated aqueous solution (40 - 60%) alkali at room temperature, it goes through simultaneous oxidation and reduction to yield the appropriate salt of the carboxylic acid and an alcohol

$$2C_6H_5CHO + NaOH \longrightarrow C_6H_5COONa + C_6H_5CH_2OH$$

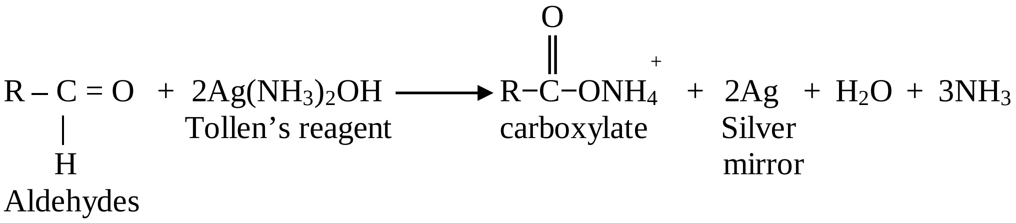
Mechanism



### 3.3.5 Silver mirror Test

Tollen’s reagent- a solution of silver ions in aqueous ammonia is often used as a test for the presence of aldehydes.

Aldehydes are mixed with freshly prepared Tollen’s reagent in a clean test tube and placed in a water bath at 60° C. A ‘silver mirror’ is developed inside the test tube. The aldehydes are oxidized by Tollen’s reagent to give carboxylates

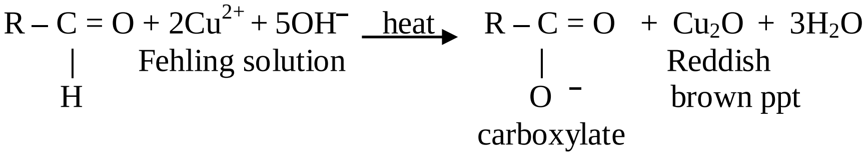


$$\underset{\substack{|\\ H\\ \text{Aldehydes}}}{R-C=O} + \underset{\text{Tollen's reagent}}{2Ag(NH_3)_2OH} \longrightarrow \underset{\text{carboxylate}}{R-\overset{\overset{O}{\|}}{C}-ONH_4^{+}} + \underset{\substack{\text{Silver}\\ \text{mirror}}}{2Ag} + H_2O + 3NH_3$$

### 3.3.6 Fehling’s Test

Fehling’s solution is a mixture of equal volume of copper(II)tetraoxosulphate(VI)solution (Fehling solution A) and sodium hydroxide and potassium sodium tartarate solution (Fehling’s solution B).

Fehling solution is a weak oxidizing agent which reacts with an aldehyde to give a carboxylate.



$$\underset{\substack{|\\ H}}{R-C=O} + \underset{\text{Fehling solution}}{2Cu^{2+} + 5OH^{-}} \xrightarrow{heat} \underset{\text{carboxylate}}{\underset{\substack{|\\ O^{-}}}{R-C=O}} + \underset{\substack{\text{Reddish}\\ \text{brown ppt}}}{Cu_2O} + 3H_2O$$

When an aldehyde is heated with Fehling’s solution, the deep blue solution changes to green and a reddish brown precipitate of copper (I) oxide is obtained

### 3.3.7 Schiff test

Aldehydes restore the red colouration of Schiff reagent, while ketones either causes no colour change at all or only very slowly. Simple aliphatic aldehydes, gives a positive result within one minute, while more complex ones may take thirty minute. A number of aromatic aldehydes give negative result.

### 3.3.8 Disinguishing between Aldehydes and Ketones

The entire test above (3.3.5-3.3.7)can serve as distinguishing test for aldehydes and ketones

### 3.3.9 Uses of Aldehydes and Ketones

1. In making plastics: They are important raw materials for making plastic. For example Urea−methanal. It is white in co lour and it is an excellent electrical insulator which is resistant to chemical attack. It is widely used in electrical industry for making plugs, sockets and casing for electrical appliances. Phenol− methanal is another polymer useful in the plastic industry.

   Propane is used as a raw material for making a plastic commonly called Perspex. Perspex is highly transparent and it is widely used as substitute for glass.

2. Used as solvent
   An example is propane, an important solvent in industries and in the laboratory

3. Used as a preservative.
   In the laboratory 40% methanal aqueous solution is widely used as a preservative for biological specimens.

## Activity D/Self Assessment Exaercise

I. Give the product of reaction for:
a. Benzaldehydes + Tollen,s reagent
b. Cyclohexanone + $HNO_3$, heat
c. Acetalaldehyde + dil. $KMnO_4$

II. Which of the following pair will be positive to Fehling test and Schiff test:
a. Propanone/ Ethanal
b. Glucose/ Fructose

III. Which of the following will be positive to iodoforn test:
a. Propanone b.Ethanal c. butan-1-one d.butan-2-one e. butanal

## 5.0 Conclusion

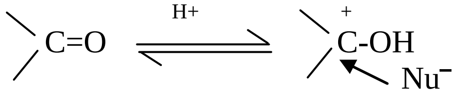
Aldehydes and ketones are very reactive organic compounds. They undergo nuclophilic addition reactions and condensation reactions.

## 6.0 Summary

In this unit we have learnt that:

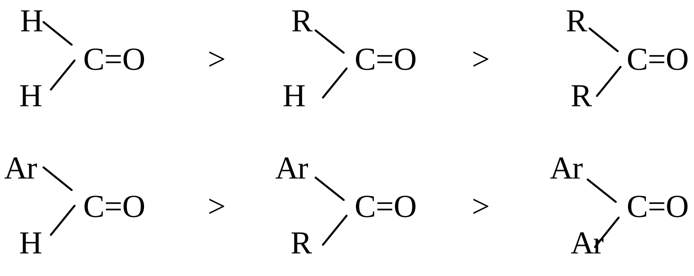
i. Aldehydes and ketones are reactive organic compounds that characteristically undergo nucleophilic addition or condensation reactions.

ii. The carbonyl carbon atom is the nucleophilic site since it is electron deficient because of the difference in electronegativity between carbon and oxygen.



iii. The susceptibility of the carbonyl carbon to nucleophilic attack is reduced by its attachment to electron releasing alkyl or aryl groups.

iv. The order of reactivity of carbonyl compounds to nucleophilic attack is as follows.



v. The following are nucleophilic addition reactions of aldehydes and ketones

a. Aldehydes and ketones react with Grignard reagents to form alcohols.

b. Aldehydes and ketones undergo addition with hydrogen cyanide to yield 2-hydroxyalkanonitriles (cyanohydrins).

- Hydrolysis, 2- hydroxyalkanonitriles-2-hydroxycarboxylic acids are formed.

-The reduction of 2- hydroxyalkanonitriles form the corresponding amine.

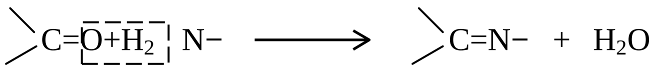
c. Addition of sodium hydrogensulphite $NaHSO_3$

d. Addition of Alcohols

e. Reduction using Lithium tetrahydridoaluminate (III)

f. Addition of Ammonia

vi. Aldehydes and ketones react with derivatives of ammonia such as hydroxlamine, $NH_2OH$, hydrazine, $NH_2NH_2$ or 2, 4 – dinitrophenylhydrazine $C_6H_5N_2H_3$ $(NO_2)_2$ to give a compound containing an imine group, >C=N- with the elimination of water molecules.

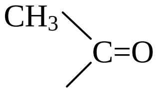


Imine group

vii. Aldehydes and ketones also undergo the following reactions;

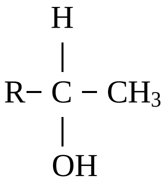
a.Chlorination

b. Aldehydes or ketones with the structure



react with iodoform reagent -iodine in aqueous sodium hydroxide solution to give a carboxylate and triiodomethane-a yellow precipitate.

- The reaction is also given by ethanol and secondary alcohols with the structure



$$R-\overset{\displaystyle H}{\underset{\displaystyle OH}{C}}-CH_3$$

c. Aldehydes and ketones containing at least one α-hydrogen atom undergo aldol condensation reaction.

d. Cannizaro Reaction is a direct contrast to the aldol condensation. It only applies to carbonyl compounds that do not contain α- hydrogen atoms.

e. Silver mirror Test- Tollen's reagent is a solution of silver ions in aqueous ammonia is often used as a test for the presence of aldehydes.

f. Fehling's Test- Fehling's solution (mixture of equal volume of copper(II)tetraoxosulphate(VI)solution -Fehling solution A- and sodium hydroxide and potassium sodium tartarate solution-Fehling's solution B) is a weak oxidizing agent which reacts with an aldehyde to give a carboxylate.

g. Schiff test-Aldehydes restore the red colouration of Schiff reagent.

viii. Silver mirror Test, Fehling's Test and Schiff test can be used to disinguishing between Aldehydes and Ketones.

ix. The following are the uses of Aldehydes and Ketones
-In making plastics e.g Urea−methanal. It is white in colour and it is an excellent electrical insulator which is resistant to chemical attack, Phenol −methanal is a polymer useful in plastic industry.
-Propane is used as a raw material for making Perspex.
-Used as solvent
- Used as a preservative.

## 7.0Tutor Marked Assignment

a. Discuss reactions that can be used to distinguish between aldehydes and ketones
b. Using relevant examples, discuss the nucleophilic addition reactions of aldehydes and ketones
c. Aldehydes and ketones form a number of compounds with ammonia derivatives. Discuss.

## 7.0 Further Reading and other Resources

a. K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry
-Third Edition

b. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry
- Sixth Edition

c. SCHAUM'S OUTLINES- Organic Chemistry(1999-Third Edition

# UNIT 4 Carbanion-Aldol , Wittig Reaction and Claisen Condensation

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## 1.0 Introduction

A carbon atom or radical bearing a negative charge is known as a carbanion.

## 2.0 Objectives

At the end of this unit you should be able to:

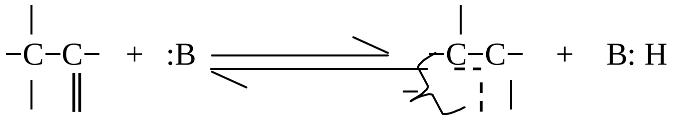
i. Define the carbanion
ii. Explain the formation of the carbanion
iii. Give examples of reactions involving the carbanion
iv. Explain Aldol condensation
v. Explain Cross Aldol condensation
vi. Explain Wittig reaction
vii. Explain Claisen condensation and Cross claisen condensation

## 3.0 Acidity Of α – Hydrogen

In carbonyl compounds, the α- hydrogen is the hydrogen attached to the carbon atom bearing the carbonyl group.

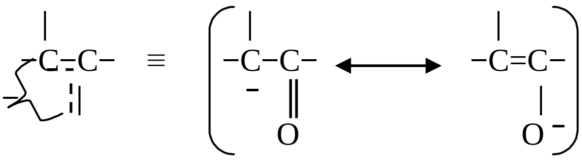
In the study of aldehydes and ketones, the carbonyl group largely determines the chemistry by providing a site at which nucleophilic addition can take place. However one other important role of the carbonyl group not as a functional group but as a substituent is its ability to strengthen the acidity of the hydrogen atoms attached to the α – carbon and by doing this, gives rise to a whole set of chemical reactions.

When the α-hydrogen is ionized it yields a carbanion (I) which is resonance hybrid of two structures.



I

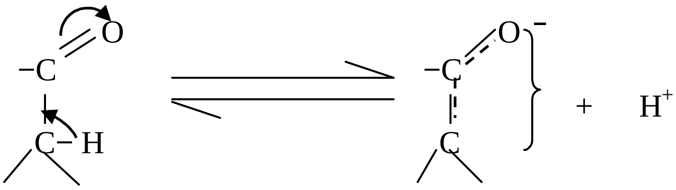
The carbanion is a resonance hybrid of two structures II and III.

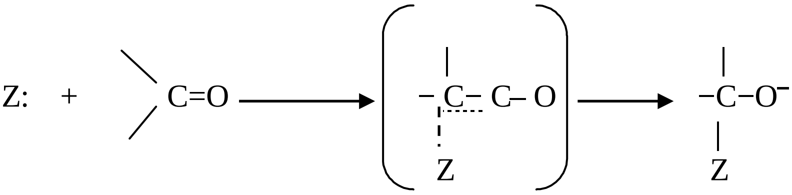


II III

These resonance structures are only possible through the participation by the carbonyl group. Resonance of this kind is not possible for carbanions formed by ionization of β-hydrogens, γ-hydrogen, etc. from saturated carbonyl compounds.

The carbonyl group affects the acidity of α-hydrogens by helping to accommodate the negative change of the anion that develops as a result of attacks.





## 3.1 Reactions Involving Carbanions

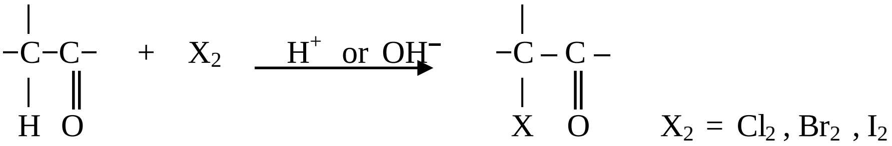
The carbonyl group wherever it is, makes any α-hydrogen acidic and thus aids in formation of carbanions. The carbanions are highly basic and exceedingly reactive particles. In their reactions they behave as nucleophiles.

As nucleophiles, they attack carbon and in so doing form carbon-carbon bonds.

The following are some reactions involving carbanions.

### 3.1.1. Halogenation of ketone

This can take place using an acid or base to speed up the reaction.

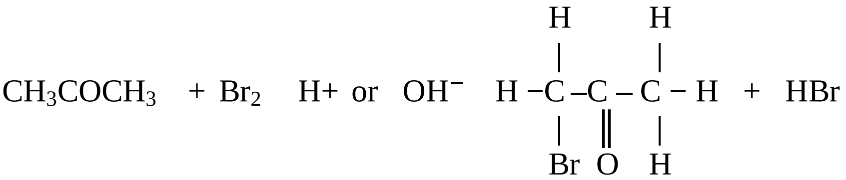


$$-\overset{|}{\underset{\underset{H}{|}}{C}}-\underset{\underset{O}{\|}}{C}- \quad + \quad X_2 \xrightarrow{H^+ \text{ or } OH^-} -\overset{|}{\underset{\underset{X}{|}}{C}}-\underset{\underset{O}{\|}}{C}- \qquad X_2 = Cl_2, Br_2, I_2$$

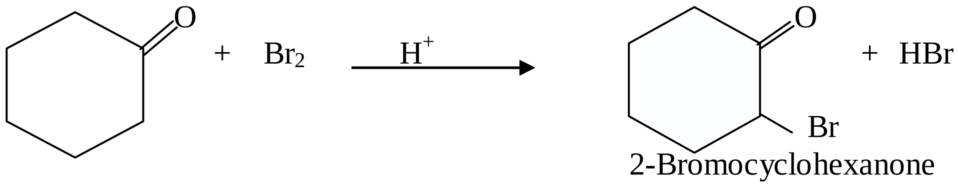
α- Halo ketone

For example, base catalysed halogenations:

Ketones, for example reacts with bromine to form bromopropanone in the presence of a base catalyst (e.g hydroxyl ion, acetate ion, etc.)



$$CH_3COCH_3 \ + Br_2 \quad H+ \text{ or } OH^- \quad H-\overset{\overset{H}{|}}{\underset{\underset{Br}{|}}{C}}-\underset{\underset{O}{\|}}{C}-\overset{\overset{H}{|}}{\underset{\underset{H}{|}}{C}}-H \ + \ HBr$$

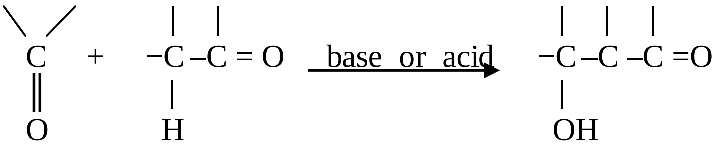


2-Bromocyclohexanone

## 3.1.2. Nucleophilic addition to carbonyl compounds

### a. Aldol condensation

Under the influence of dilute base or dilute acid, two molecules of an aldelyde or a ketone may combine to form a β-hydroxy aldehyde or β-hydroxy ketone. This reaction is called the Aldol condensation.

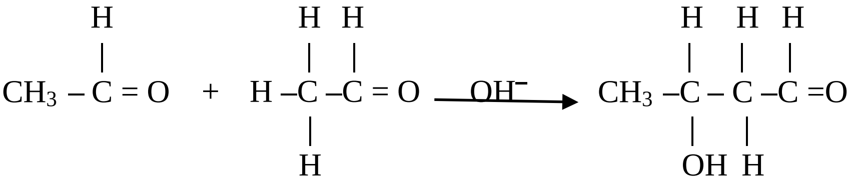


$$\underset{\underset{O}{\|}}{\overset{\diagdown\;\diagup}{C}} + -\overset{|}{\underset{\underset{H}{|}}{C}}-\overset{|}{C}=O \xrightarrow{\text{base or acid}} -\overset{|}{\underset{\underset{OH}{|}}{C}}-\overset{|}{C}-\overset{|}{C}=O$$

An aldol (α, β-hydroxyl carbonyl compound)

The product formed results from the addition of one molecule of aldehyde (or ketone) to a second molecule in such a way that the α-carbon of the first becomes attached to the carbonyl carbon of the second.

For example:



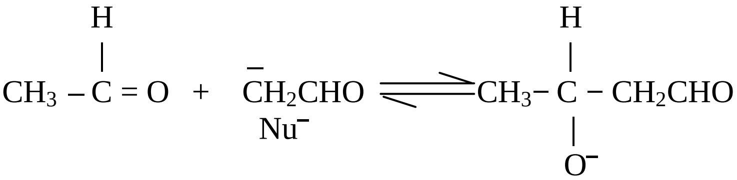
$$CH_3-\overset{\overset{H}{|}}{C}=O + H-\overset{\overset{H}{|}}{\underset{\underset{H}{|}}{C}}-\overset{\overset{H}{|}}{C}=O \xrightarrow{OH^-} CH_3-\overset{\overset{H}{|}}{\underset{\underset{OH}{|}}{C}}-\overset{\overset{H}{|}}{\underset{\underset{H}{|}}{C}}-\overset{\overset{H}{|}}{C}=O$$

If the aldehyde or ketone does not contain an α-hydrogen, a simple Aldol condensation cannot take place.

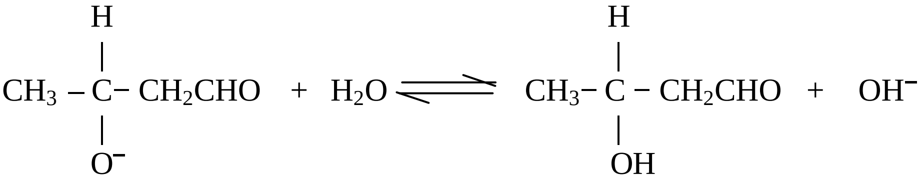
Mechanism

The hydroxide ion donates a lone pair to one of the α-hydrogen to form a water molecule and a carbanion, the later functioning as a nucleophile towards the unionized carbonyl molecule.

$$CH_3CHO + \underset{\text{Base Catalyst}}{OH^-} \rightleftharpoons \overset{-}{C}H_2CHO + H_2O$$



$$CH_3-\overset{\overset{H}{|}}{C}=O + \underset{Nu^-}{\overset{-}{C}H_2CHO} \rightleftharpoons CH_3-\overset{\overset{H}{|}}{\underset{\underset{O^-}{|}}{C}}-CH_2CHO$$



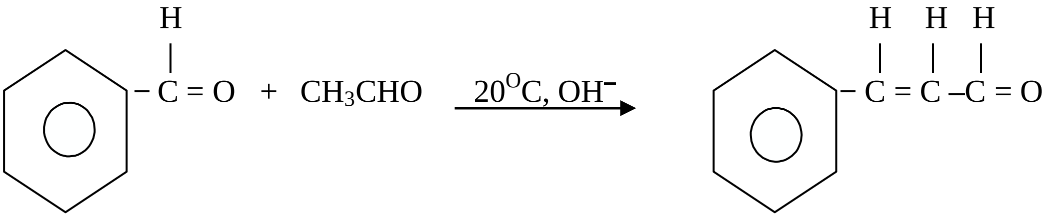
$$CH_3-\overset{\overset{H}{|}}{\underset{\underset{O^-}{|}}{C}}-CH_2CHO + H_2O \rightleftharpoons CH_3-\overset{\overset{H}{|}}{\underset{\underset{OH}{|}}{C}}-CH_2CHO + OH^-$$

Aldol condensation is very useful in the preparation of unsaturated alcohols from an α,β - unsaturated aldehydes or ketones

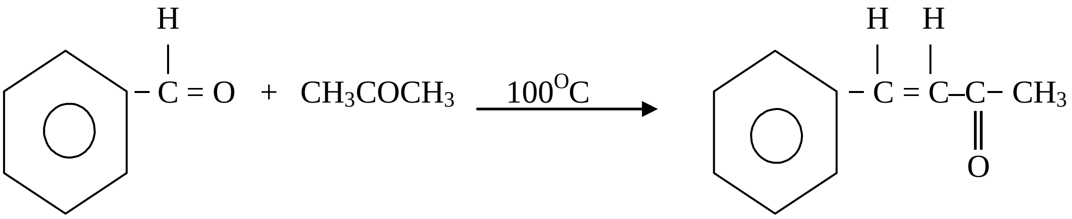
### b. Cross Aldol condensation

This is an Aldol condensation between two different compounds.

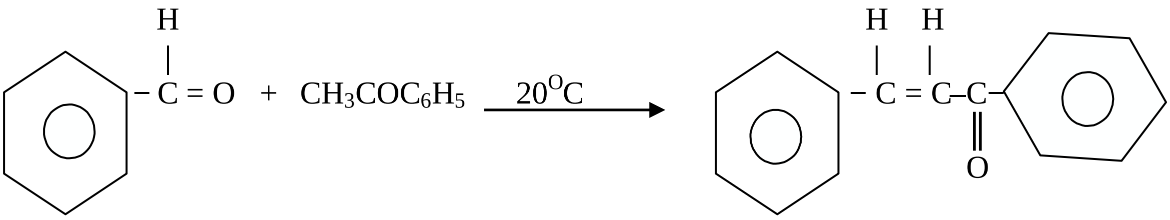
For example:



2-phenyl-2-propenal



4-Phenyl-3-buten-2-one



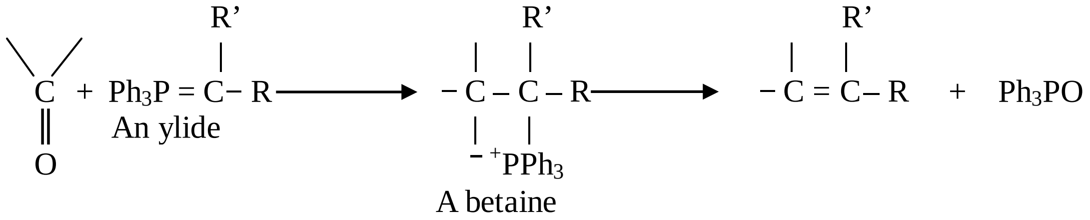
1,3-Diphenyl propenone

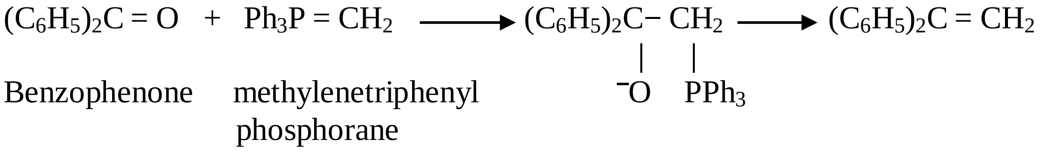
## ACTIVITY A/Self Assess Exercise

a. Which of the following will undergo Aldol condensation? If Aldol condensation is possible, then predict the product formed
   - i. Butanal  ii. Cyclohexanone  iii. Benzaldehyde

### c. Witting reaction

This reaction involves the nucleophilic attack on carbonyl carbon by an ylide to form a betaine which after spontaneously undergoes elimination to yield the product.

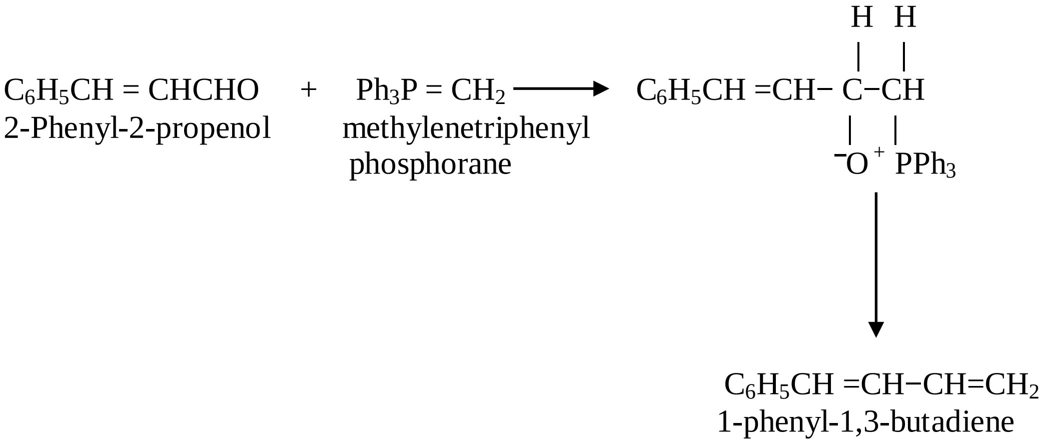




$$(C_6H_5)_2C = O \; + \; Ph_3P = CH_2 \longrightarrow \underset{^-O \quad PPh_3}{(C_6H_5)_2C-CH_2} \longrightarrow (C_6H_5)_2C = CH_2$$

Benzophenone methylenetriphenyl phosphorane

For example:



$$C_6H_5CH = CHCHO \; + \; Ph_3P = CH_2 \longrightarrow C_6H_5CH = CH-\overset{H}{\underset{^-O}{C}}-\overset{H}{\underset{^+PPh_3}{CH}} \longrightarrow C_6H_5CH = CH-CH = CH_2$$

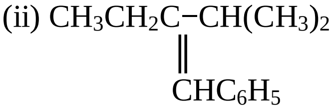
2-Phenyl-2-propenol methylenetriphenyl phosphorane

1-phenyl-1,3-butadiene

## Activity B/Self Assessment Exercise

a. Give structures of the ylide and carbonyl compounds needed to prepare

(i) $C_6H_5CH=CHCH_3$ (ii) $CH_3CH_2C-CH(CH_3)_2$



$$CH_3CH_2\underset{\underset{CHC_6H_5}{\|}}{C}-CH(CH_3)_2$$

## 3.1.3. Nucleophilic Acyl substitution

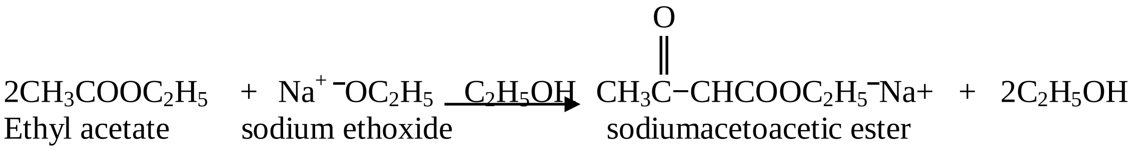
**a. Claisen condensation. Formation of β-Keto esters.**

An α-hydrogen in an ester, like an α hydrogen in an aldehyde or ketone is weakly acidic and for the same reason, through resonance, the carbonyl group helps accommodate the negative charge of the carbanion.

Claisen condensation involves nucleophilic attack by a carbanion on an election deficient carbonyl carbon. It is for esters and it is the exact counterpart of the Aldol condensation.

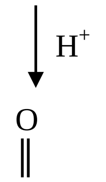
In aldol condensation, nucleophilic attack leads to addition, the typical reaction of aldehydes and ketones while in Claisen condensation, nucleophilic attack leads to substitution, the typical reaction of acyl compounds.

The preparation of ethyl acetoacetate- a β-keto acid illustrates the reaction known as the Claisen condensation. When ethyl acetate is treated with sodium ethoxide and the resulting mixture is acidified, there is obtained ethyl-β- ketobutyrate(ethyl 3-oxobutanoate), generally known as ethyl acetoacetate or acetoacetic ester.



$$2CH_3COOC_2H_5 \; + \; Na^{+}\,{}^{-}OC_2H_5 \xrightarrow{C_2H_5OH} CH_3\overset{\overset{O}{\|}}{C}-CHCOOC_2H_5{}^{-}Na+ \; + \; 2C_2H_5OH$$

Ethyl acetate sodium ethoxide sodiumacetoacetic ester

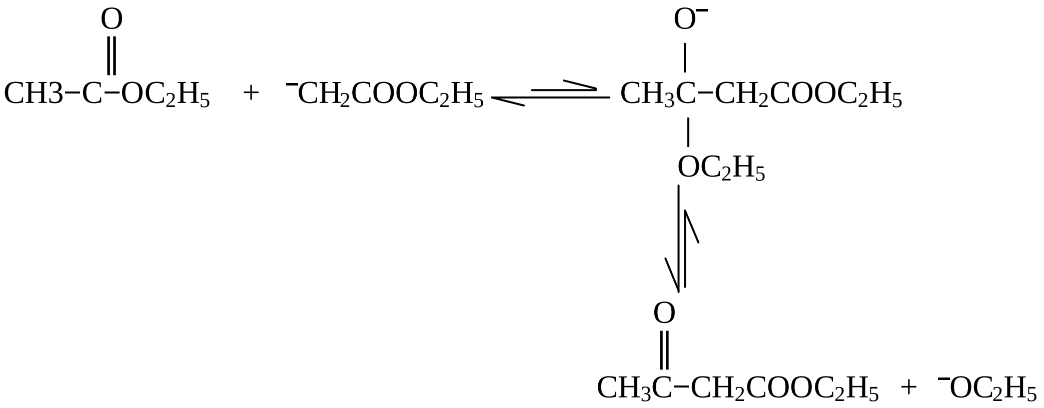


$$\Big\downarrow H^+$$
$$CH_3\overset{\overset{O}{\|}}{C}-CHCOOC_2H_5$$

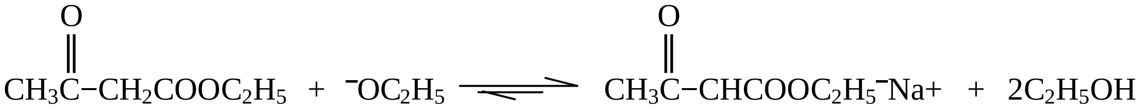
ethyl acetoacetic ester

The acceptable mechanism for Claisen condensation as shown in ethyl acetate is shown below:

$$CH_3COOC_2H_5 + {}^-OC_2H_5 \rightleftharpoons {}^-CH_2COOC_2H_5 + C_2H_5OH$$



$$CH3-\overset{\overset{O}{\|}}{C}-OC_2H_5 + {}^-CH_2COOC_2H_5 \rightleftharpoons CH_3\underset{\underset{OC_2H_5}{|}}{\overset{\overset{O^-}{|}}{C}}-CH_2COOC_2H_5$$
$$\Big\updownarrow$$
$$CH_3\overset{\overset{O}{\|}}{C}-CH_2COOC_2H_5 + {}^-OC_2H_5$$



$$CH_3\overset{\overset{O}{\|}}{C}-CH_2COOC_2H_5 + {}^-OC_2H_5 \rightleftharpoons CH_3\overset{\overset{O}{\|}}{C}-CHCOOC_2H_5{}^-Na+ + 2C_2H_5OH$$

When complicated esters are involved, it yields the products resulting from ionization of an α-hydrogen of the ester. It is always the α-carbon of one molecule that becomes attached to the carbonyl carbon of another.

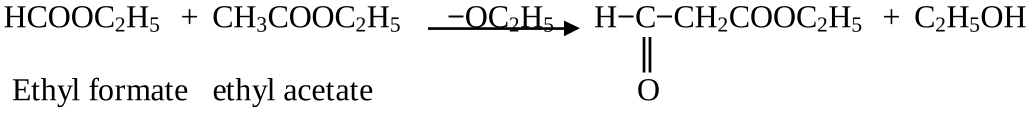
## Activity C/Self Assessment Exercise

a. Write the structural formula of the products from the reaction of $Na^+\,{}^-OC_2H_5$ the following esters:

i. $CH_3COOC_2H_5$
ii. $CH_3CH_2COOC_2H_5$

b .Crossed Claisen condensation

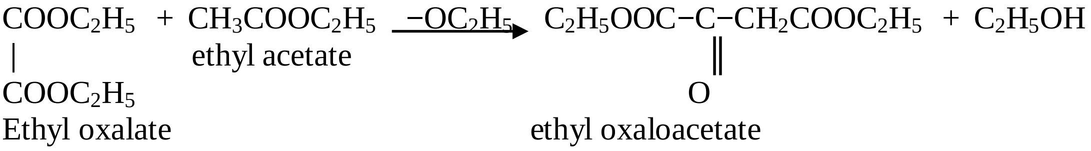
A cross Claisen condensation is generally feasible only when one of the reactants has no α-hydrogen and thus is incapable of undergoing self condensation
For example:



$$HCOOC_2H_5 + CH_3COOC_2H_5 \xrightarrow{-OC_2H_5} H-\underset{\underset{O}{\|}}{C}-CH_2COOC_2H_5 + C_2H_5OH$$

Ethyl formate ethyl acetate

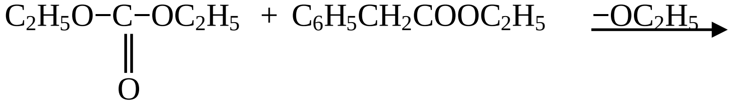
Ethyl formylacetate



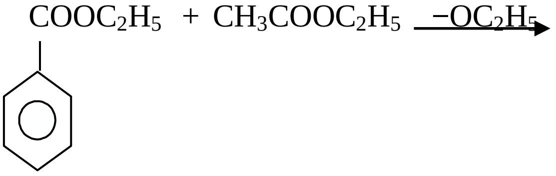
$$\underset{\text{Ethyl oxalate}}{\begin{array}{l}COOC_2H_5\\ |\\ COOC_2H_5\end{array}} + \underset{\text{ethyl acetate}}{CH_3COOC_2H_5} \xrightarrow{^-OC_2H_5} \underset{\text{ethyl oxaloacetate}}{C_2H_5OOC-\underset{O}{\underset{\|}{C}}-CH_2COOC_2H_5} + C_2H_5OH$$

## Activity D/Self Assessment Exercise

Predict the product formed in the following crossed Claisen condensation reactions.

(i) 

$$C_2H_5O-\underset{O}{\underset{\|}{C}}-OC_2H_5 + C_6H_5CH_2COOC_2H_5 \xrightarrow{^-OC_2H_5}$$

(ii) 

## 4.0 Conclusion

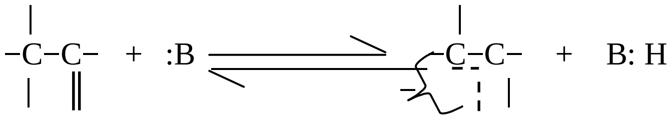
The carbonyl group wherever it is, makes any α-hydrogen acidic and helps in the formation of carbanions. Carbanions are very useful reaction intermediates as examplified in Aldol and Wittig reactions and Claisen condensation.

## 5.0 Summary

In this unit we have learnt that:

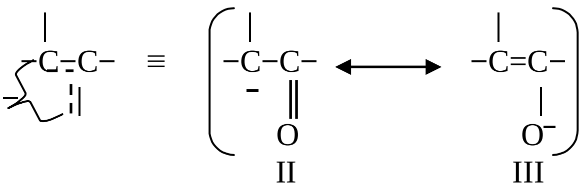
i. A carbon atom or radical bearing a negative charge is known as a carbanion.

ii. Carbanion (I) is a resonance hybrid of two structures.



I

The carbanion is a resonance hybrid of two structures II and III.

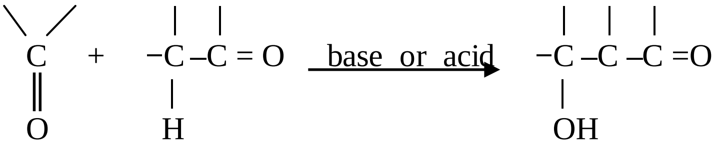


iii. The carbonyl group affects the acidity of α-hydrogens by helping to accommodate the negative change of the anion that develops as a result of attacks.

iv. The following are some reactions involving carbanions.

a.Halogenation of ketone

b. Nucleophilic addition to carbonyl compounds .E.g
-Aldol condensation



$$\underset{\overset{\|}{O}}{\overset{\diagdown\ \diagup}{C}} \quad + \quad -\underset{\overset{|}{H}}{\overset{|}{C}}-\overset{|}{C}=O \xrightarrow{\text{base or acid}} -\underset{\overset{|}{OH}}{\overset{|}{C}}-\overset{|}{C}-\overset{|}{C}=O$$

An aldol (α, β-hydroxyl carbonyl compound)

- Cross Aldol condensation

- Witting reaction

b. Nucleophilic Acyl substitution. E.g

- Claisen condensation.

- Crossed Claisen condensation

## 6.0 Tutor Marked Assignment

Using definite examples distinguish between Aldol condensation and Claisen Condensation reactions

## 7.0 Further Reading and other Resources

a. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry- Sixth Edition

b.K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry -Third Edition

c. SCHAUM’S OUTLINES- Organic Chemistry(1999-Third Edition

# Unit 5: α,β – Unsaturated Carbonyl Compounds

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## 1.0: Introduction

α,β – Unsaturated carbonyl compounds are aldehydes and ketones which are conjugated with a double bond.

## 2.0 Objectives

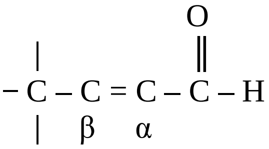
At the end of this unit, you should be able to:

i. Explain the structure and properties of α,β – Unsaturated Carbonyl Compounds
ii. Explain the methods of preparing α,β – Unsaturated Carbonyl Compounds
iii. Explain the reactions of α,β – Unsaturated Carbonyl Compounds
iv. Explain and give examples of Nucleophilic 1,2-addition to α,β – Unsaturated Carbonyl Compounds
v. Explain and give examples of 1,4-addition to α,β – Unsaturated Carbonyl Compounds

## 3.0 Structures and properties

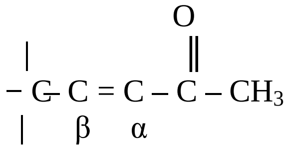
Generally, a compound that contains both a carbon-carbon double bond and a carbon-oxygen double bond has properties that are characteristics of both functional groups. At the carbon-carbon double bond, an unsaturated ester or unsaturated ketone undergoes electrophilic addition of acid and halogen, hydrogenation, hydroxylation and cleavage at the carbonyl group; it undergoes the nucleophilic substitution typical of an ester or the nucleophilic addition typical of ketone.

The carbonyl group of α,β – unsaturated aldehydes and ketones consists of a nucleophilic oxygen and an electrophilic carbon. However, they also have another electrophilic carbon- the β-carbon.



$$-\overset{|}{\underset{|}{C}}-\underset{\beta}{C}=\underset{\alpha}{C}-\overset{\overset{O}{\|}}{C}-H$$

α,β – unsaturated aldehyde



$$-\overset{|}{\underset{|}{C}}-\underset{\beta}{C}=\underset{\alpha}{C}-\overset{\overset{O}{\|}}{C}-CH_3$$

α,β – unsaturated ketone

## 3.1 Preparation

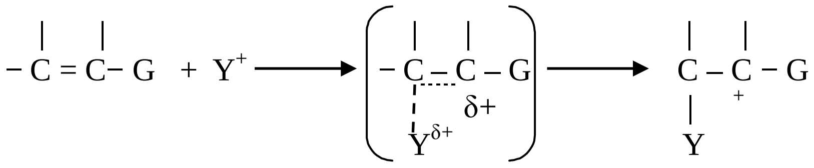
There are several ways to make α,β – unsaturated compounds: aldol condensation for unsaturated aldehydes and ketones; dehydrohalogenation of α – halo acid and the Perkin condensation for unsaturated acids.

## 3.2 Interaction of Functional group

The carbon – carbon double bond normally serve as a source of electrons for the electrophilic reagent. However, the availability of its electrons is determined by the groups attached to it. An electron- releasing substituents stabilizes the transition state leading to the initial carbocation by dispersing the developing positive charge while an electron withdrawing substituents destabilizes the transition state by intensifying the positive charge.

C = O, -COOH, -COOR and –CN groups are powerful electron withdrawing groups and therefore would be expected to deactivate a carbon-carbon double bond toward electrophilic addition. For this reason, α,β – unsaturated ketones, acids ethers are nitriles are generally less reactive than simple alkenes towards reagents like bromine and the hydrogen halides.

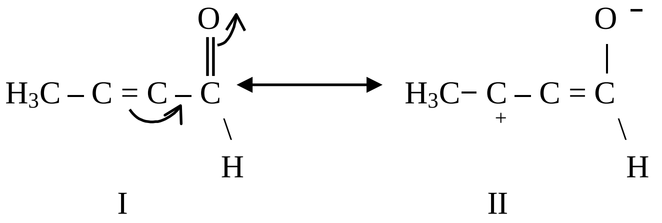
However, these powerful electron withdrawing substituents at the same time activate the carbon-carbon double bond towards electron-rich reagents, hence why α,β – unsaturated ketones , acid, ester and nitriles are susceptible to nucleophilic attack.



$$-\overset{|}{C}=\overset{|}{C}-G + Y^{+} \longrightarrow \left( -\underset{Y^{\delta+}}{\overset{|}{C}}\cdots\overset{|}{\underset{\delta+}{C}}-G \right) \longrightarrow \underset{Y}{\underset{|}{\overset{|}{C}}}-\overset{|}{\underset{+}{C}}-G$$

## 3.3 Nucleophilic and Electrophilic Centres

The carbonyl group of α,β – unsaturatedaldehydes ketones consist of a nucleophilic oxygen and an electrophilic carbon. However, α,β – unsaturated aldehydes and ketones also have another electrophilic carbon – the β – carbon. This is due to the influence of the electronegative oxygen which results in the resonance shown below.



$$\underset{\text{I}}{H_3C-C=C-\underset{\backslash H}{\overset{O}{\overset{\|}{C}}}} \longleftrightarrow \underset{\text{II}}{H_3C-\underset{+}{C}-C=\underset{\backslash H}{\overset{O^{-}}{\overset{|}{C}}}}$$

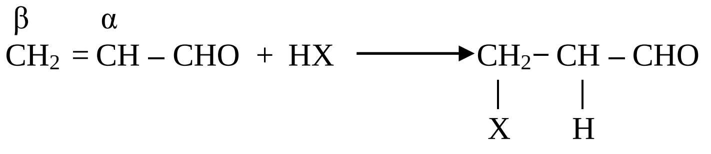
There are therefore two electrophilic centres. Since there are two electrophilic points, there are also two nucleophilic points. If the nucleophile reacts with the carbonyl carbon, this is a normal nucleophilic addition to aldehydes or ketones and it is called 1,2-nucleophilic addition. However, if the nucleophile add to the β – carbon, then it is a 1,4 – nucleophilic addition or a conjugate addition.

## 3.3.1Electrophilic addition

The presence of the carbonyl group lowers the reactivity of the carbon-carbon double bond towards electrophilic addition as well as controlling the orientation of addition.

Generally the addition of an unsymmetrical reagent to an α,β-unsaturated carbonyl compound takes in such a way that hydrogen becomes attached to the α-carbon and the negative group becomes attached to the β-carbon.

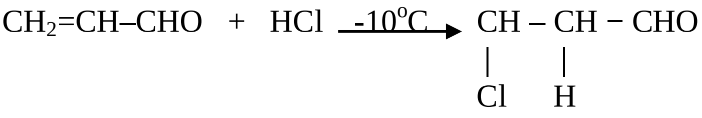
For example:



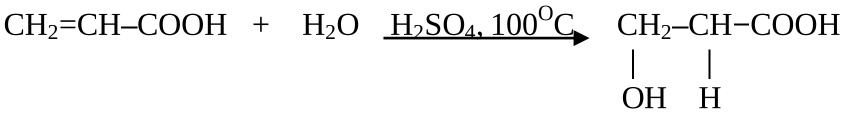
$$\overset{\beta}{CH_2}=\overset{\alpha}{CH}-CHO + HX \longrightarrow \underset{X}{\underset{|}{CH_2}}-\underset{H}{\underset{|}{CH}}-CHO$$

β – Halopropanal

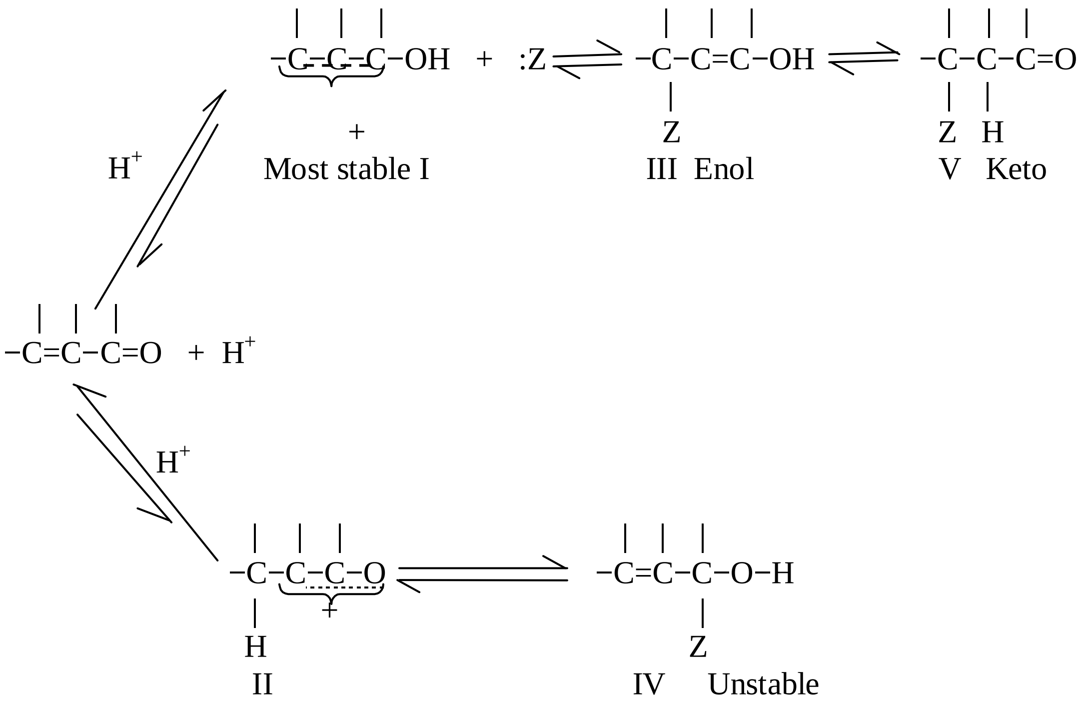
For example:

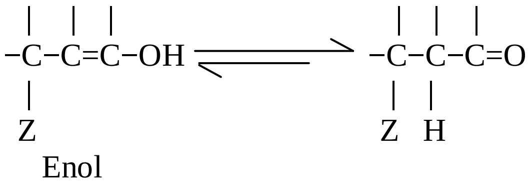


$$CH_2=CH-CHO + HCl \xrightarrow{-10^{o}C} \underset{Cl}{\underset{|}{CH}}-\underset{H}{\underset{|}{CH}}-CHO$$


$$CH_2=CH-COOH \;+\; H_2O \xrightarrow{H_2SO_4,\,100^{O}C} \underset{OH}{CH_2}-\underset{H}{CH}-COOH$$

Addition to α,β- unsaturated carbonyl compounds take place in such a way as to form the most stable intermediate carbocation.



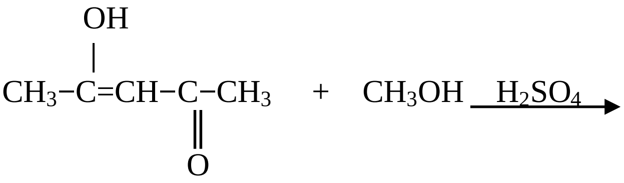


Addition of proton to the compound may take place at either the carbonyl oxygen end giving the cation I or at the β-carbon giving the cation II. Of the two positions, the addition at the carbonyl oxygen gives the more stable cation (I). In cation I, the positive charge is carried by the carbon atoms alone and not partly by the more highly electronegative oxygen atom. The second step of the reaction involves the addition of a negative ion or basic molecule either to the carbonyl carbon or to the β-carbon of the hybrid ion I giving rise to two possibilities- structures III and IV. The addition to the β-carbon is the one that yields a stable product (III) which is the enol form of the saturated carbonyl compound. This will then undergo tautomerization to the keto form to give the observed product (V).

## Activity A/Self Assessment Exercise

Predict the product formed in the following electrophilic addition reactions to α,β-unsaturated carbonyl compound:

i. $CH_3-CH=CH-COOH \;+ \xrightarrow{HBr} 20^{o}C$



$$CH_3-\overset{\overset{OH}{|}}{C}=CH-\underset{\underset{O}{\|}}{C}-CH_3 \quad + \quad CH_3OH \xrightarrow{H_2SO_4}$$

## 3.3.2 Nucleophilic Addition

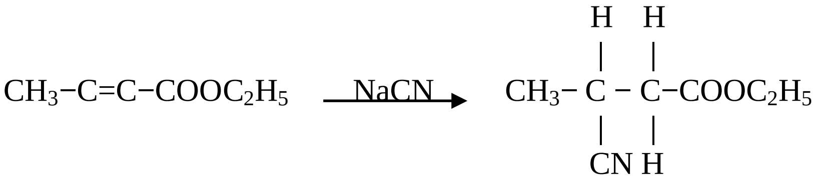
The1,4-nucleophilic addition is going to be the focus here since the 1,2-addition is the normal addition to the carbonyl carbon as observed in aldehydes and ketones.

The following reactions are examples of nucleophilic addition reactions.

**a. Reaction with NaCN (addition of HCN)**

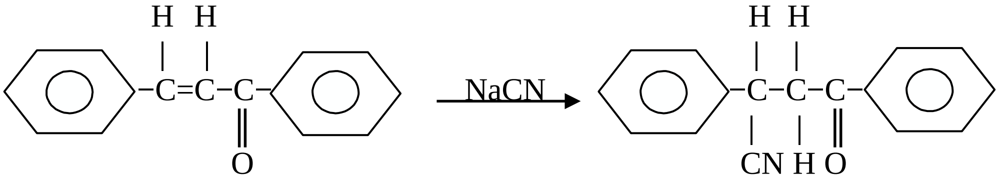
α,β-unsaturated carbonyl compounds are converted to β-cyano carbonyl compounds when they react with aqueous sodium cyanide. The reaction involves the addition of the elements of HCN to the carbon-carbon double bond.

For example:



$$CH_3-C=C-COOC_2H_5 \xrightarrow{NaCN} CH_3-\overset{\overset{H}{|}}{\underset{\underset{CN}{|}}{C}}-\overset{\overset{H}{|}}{\underset{\underset{H}{|}}{C}}-COOC_2H_5$$

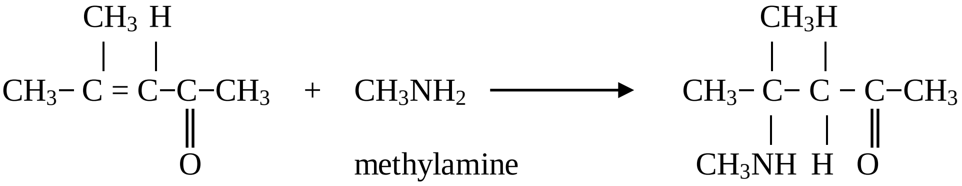
Ethyl β-cyanobutyrate



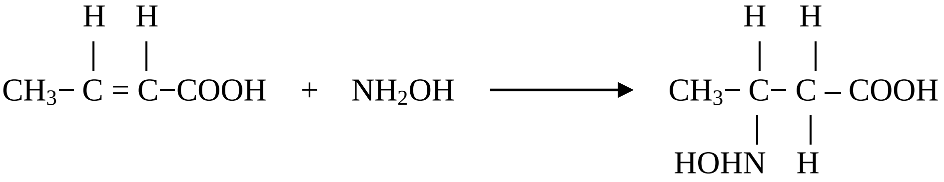
**b. Addition of $NH_3$ and its derivatives**

Ammonia and some derivatives of ammonia like amines, hydroxylamine, phenyl hydrazine, etc ,addd to α,β-unsaturated carbonyl compounds to yield β-amino carbonyl compounds.

For example:

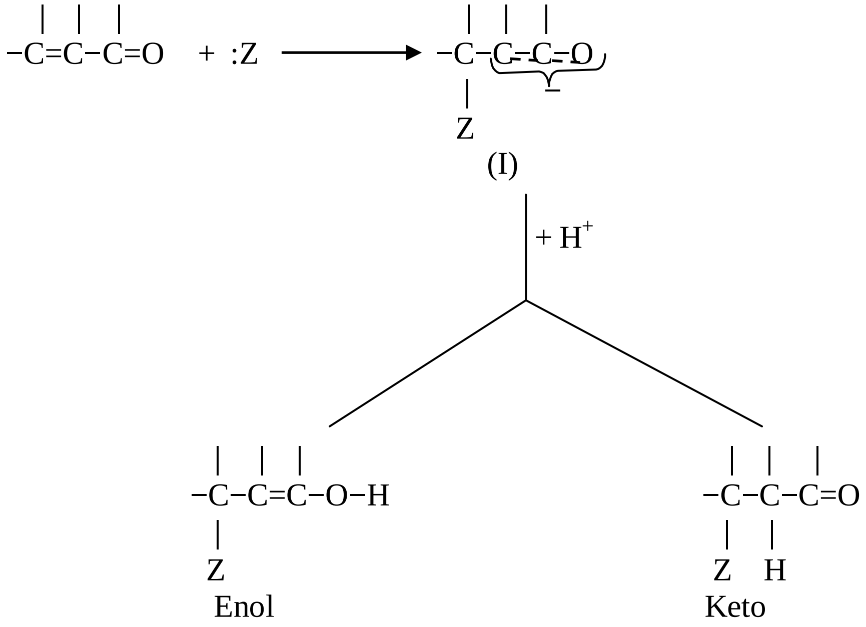


$$CH_3-\overset{\overset{CH_3}{|}}{C}=\overset{\overset{H}{|}}{C}-\underset{\underset{O}{\|}}{C}-CH_3 \quad + \quad \underset{\text{methylamine}}{CH_3NH_2} \longrightarrow CH_3-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3NH}{|}}{C}}-\overset{\overset{H}{|}}{\underset{\underset{H}{|}}{C}}-\underset{\underset{O}{\|}}{C}-CH_3$$



$$CH_3-\overset{\overset{H}{|}}{C}=\overset{\overset{H}{|}}{C}-COOH \quad + \quad NH_2OH \longrightarrow CH_3-\overset{\overset{H}{|}}{\underset{\underset{HOHN}{|}}{C}}-\overset{\overset{H}{|}}{\underset{\underset{H}{|}}{C}}-COOH$$

Mechanism:



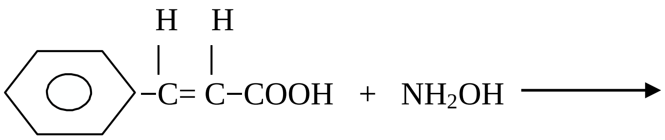
The nucleophilic reagent add to the carbon-carbon double bond of the α,β-unsaturated compound to yield the hybrid anion I which then accept a proton.

## Activity B /Self Assessment Exercise

Predict the product formed from the following reactions

i. Trans HOOCCH= CHCOOH + $NH_3$ $\longrightarrow$

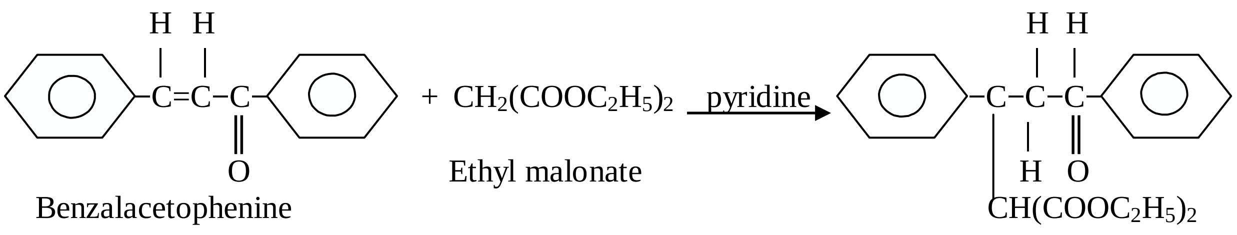
ii.

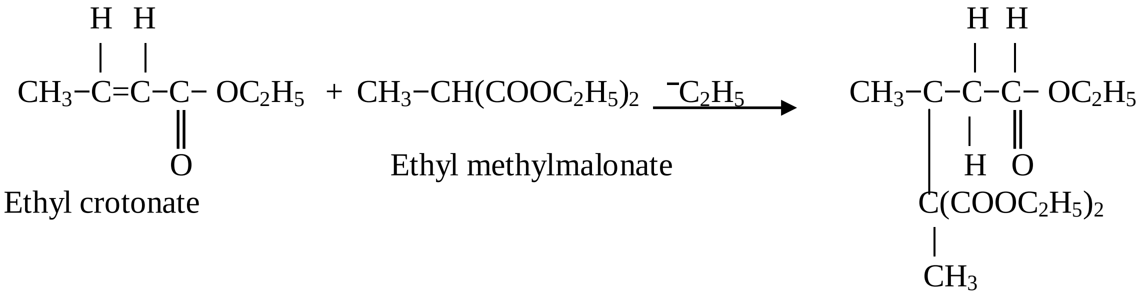


### c. Michael Addtion

This is a special nucleophilic addition to α,β-unsaturated carbonyl compounds. It is of great synthetic importance and it results in the formation of carbon-carbon double bond.

For example:



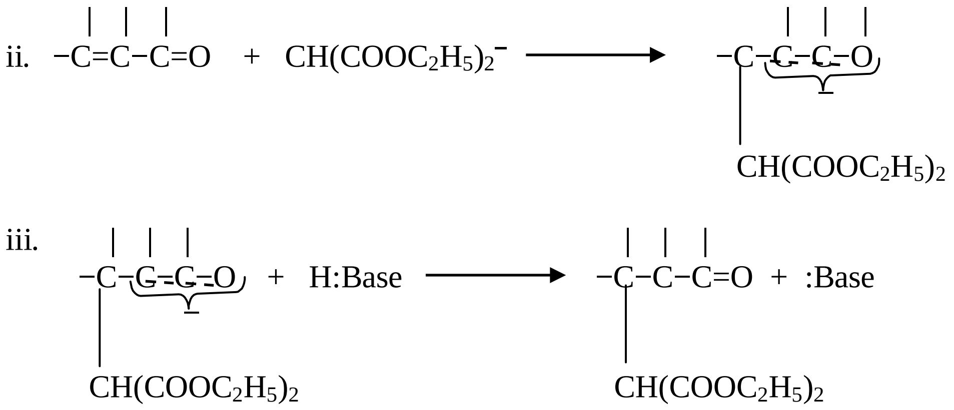


$$CH_3-\overset{H}{C}=\overset{H}{C}-\underset{O}{\overset{\|}{C}}-OC_2H_5 + CH_3-CH(COOC_2H_5)_2 \xrightarrow{^-C_2H_5} CH_3-\underset{\underset{CH_3}{C(COOC_2H_5)_2}}{C}-\underset{H}{\overset{H}{C}}-\underset{O}{\overset{H}{C}}-OC_2H_5$$

Ammonia and primary and secondary amines are powerful catalysts for the Michael addition. They help to abstract a proton from the reagent to generate a carbanion as well as to react with the carbonyl group of the substrate to form an intermediate imine or iminium ion which is very useful towards nucleophilic addition.

The mechanism for Michael addition as shown for malonic ester as shown below:

i. $H-CH(COOC_2H_5)_2 + :Base \longrightarrow H:Base^+ + CH(COOC_2H_5)_2^-$

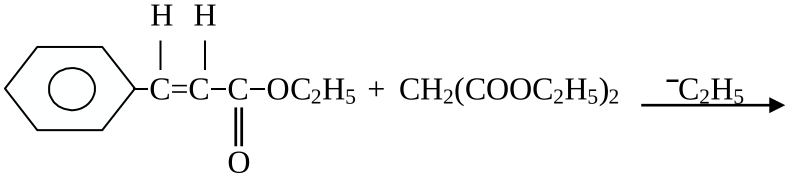


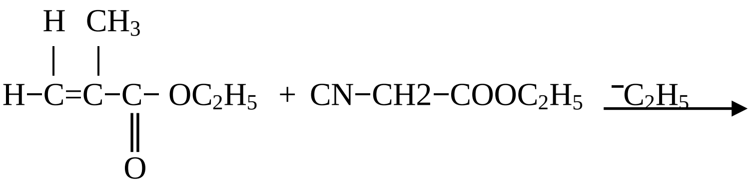
ii. $$-\overset{|}{C}=\overset{|}{C}-\overset{|}{C}=O + CH(COOC_2H_5)_2^- \longrightarrow -\underset{\underset{CH(COOC_2H_5)_2}{|}}{\overset{|}{C}}-\underbrace{\overset{|}{C}-\overset{|}{C}-O}_{-}$$

iii. $$-\underset{\underset{CH(COOC_2H_5)_2}{|}}{\overset{|}{C}}-\underbrace{\overset{|}{C}-\overset{|}{C}-O}_{-} + H:Base \longrightarrow -\underset{\underset{CH(COOC_2H_5)_2}{|}}{\overset{|}{C}}-\overset{|}{C}-\overset{|}{C}=O + :Base$$

## Activity C/Self Assessment Exercise

Predict the product formed from the following reactions:

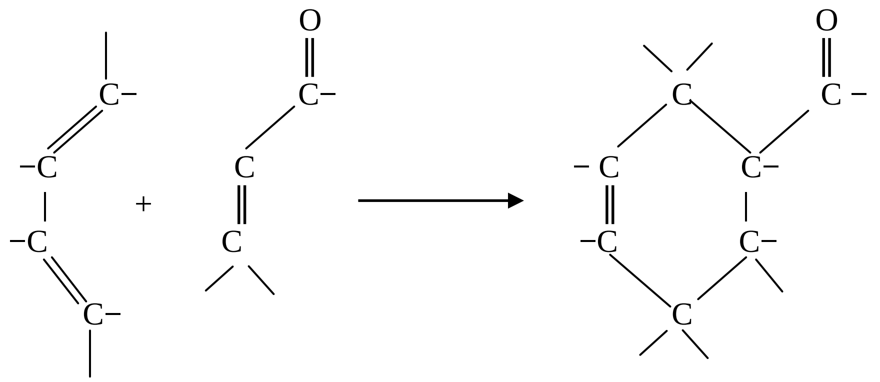




$$H-\overset{H}{C}=\overset{CH_3}{C}-\underset{O}{\overset{\|}{C}}-OC_2H_5 + CN-CH2-COOC_2H_5 \xrightarrow{^-C_2H_5}$$

**d. The Diels-Alder reaction**

This is the reaction between α,β-unsaturated carbonyl compounds with conjugated dienes. It involves the addition of the first and fourth carbon atoms of the conjugated diene system to the doubly bonded carbons of the unsaturated carbonyl compound to form a six membered ring.



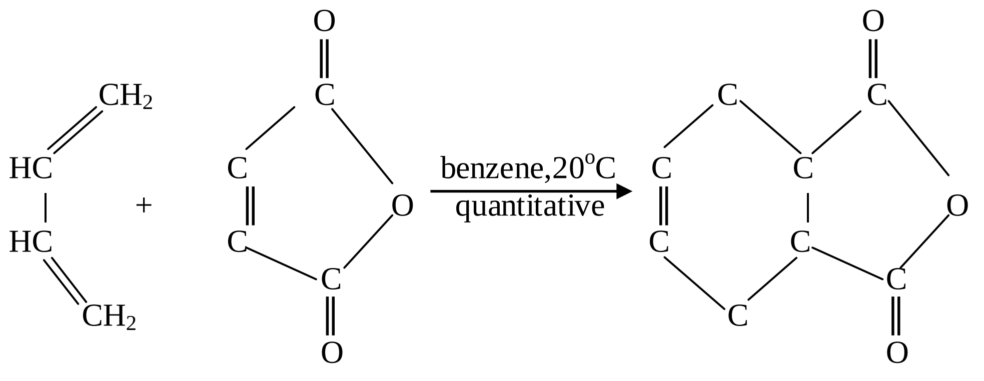
Diene Dienophile (diene-loving) Adduct(six-membered ring)

The reaction involves a concerted single-step mechanism.

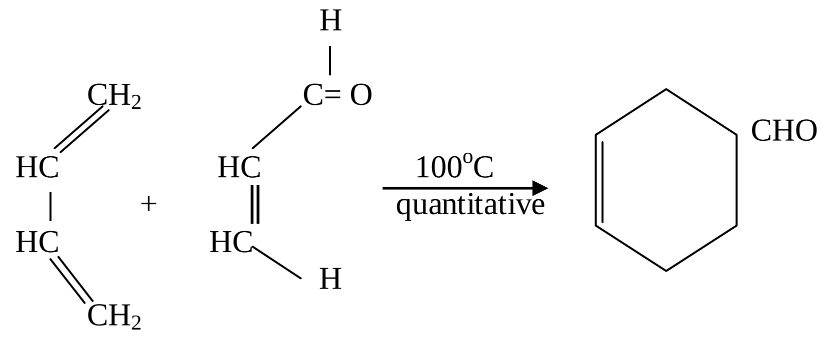
The Diels-Alder reaction is the most important example of cycloaddition. It is known as a[4 + 2] cycloaddition since it involves a system of four π electrons (the diene) and a system of two π electrons(the dienophile).

The Diels-Alder reaction is very useful because it generates a ring and also because it takes place readily for a wide variety of reactants. The reaction is favoured by the electron withdrawing substituents in the dienophile.

For example:



1,3-Butadiene Maleic anhydride Cis-1,2,3,6-tetrahydrophthalic anhydride

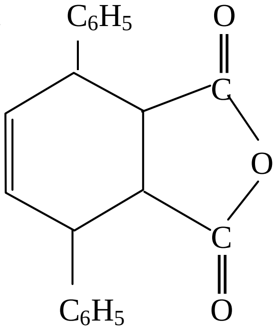


1,3-Butadiene Acrolein 1,2,3,6-tetrahydrobenzaldehyde

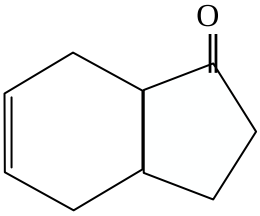
## Activity D /Self Assessment Exercise

Predict the reactants from which the following compounds can be synthesized.

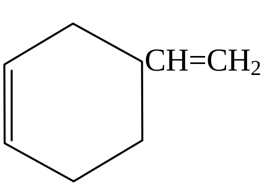
i.



ii.



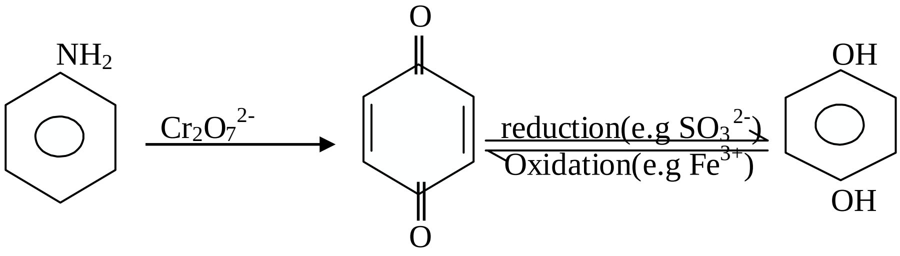
iii.



### e. Quinones

Quinones are special kinds of α,β-unsaturated ketones. They are cyclic diketones with a structure that make them convertible into hydroquinones and phenols by reduction.

Because they are highly conjugated, quinines are coloured. Many properties of quinines result from the tendency to form the aromatic hydroquinone system.



p-Benzoquinone
(yellow colour)
(Quinone)

Hydroquinone

## 4.0 Conclusion

α,β – Unsaturated carbonyl compounds are aldehydes and ketones which are conjugated with a double bond.

The carbonyl group of α,β – unsaturated aldehydes and ketones consists of a nucleophilic oxygen and an electrophilic carbon and they also have another electrophilic carbon- the β-carbon.

The carbon – carbon double bond normally serve as a source of electrons for the electrophilic reagent. Powerful electron withdrawing groups like C = O, -COOH, -COOR and –CN groups deactivates a carbon-carbon double bond toward electrophilic hence, they activate the carbon-carbon double bond towards nucleophilic addition .Hence α,β – unsaturated ketones , acid, ester and nitriles are susceptible to nucleophilic attack.

Michael Addition, Diels-Alder reaction are reactions that involves α,β – Unsaturated carbonyl compounds .Quinones are special kinds of α,β – Unsaturated ketones.

## 5.0 Summary

In this unit, we have learnt the following:

i. α,β – Unsaturated carbonyl compounds are aldehydes and ketones which are conjugated with a double bond.

ii. At the carbon-carbon double bond, an unsaturated ester or unsaturated ketone undergoes electrophilic addition of acid and halogen, hydrogenation, hydroxylation and cleavage at the carbonyl group.

iii. It undergoes the nucleophilic substitution typical of an ester or the nucleophilic addition typical of ketone.

iv. The carbonyl group of α,β – unsaturated aldehydes and ketones consists of a nucleophilic oxygen and an electrophilic carbon, they also have another electrophilic carbon- the β-carbon.

v. α,β – unsaturated compounds can be prepared from aldol condensation, and the Perkin condensation.

vi. The carbon – carbon double bond normally serve as a source of electrons for the electrophilic reagent.

vii. An electron- releasing substituents stabilizes the transition state leading to the initial carbocation while an electron withdrawing groups C = O, -COOH, -COOR and –CN destabilizes the transition state.

viii. Strong electron withdrawing groups like C = O, -COOH, -COOR and –CN deactivate a carbon-carbon double bond toward electrophilic addition but activate the carbon-carbon double bond towards electron-rich reagent.

ix. α,β – unsaturated ketones , acid, ester and nitriles are susceptible to nucleophilic attack.

x. Normal nucleophilic addition to aldehydes or ketones is called 1,2-nucleophilic addition while when it involves nucleophilic addition to the β – carbon, it is a 1,4 – nucleophilic addition or a conjugate addition.

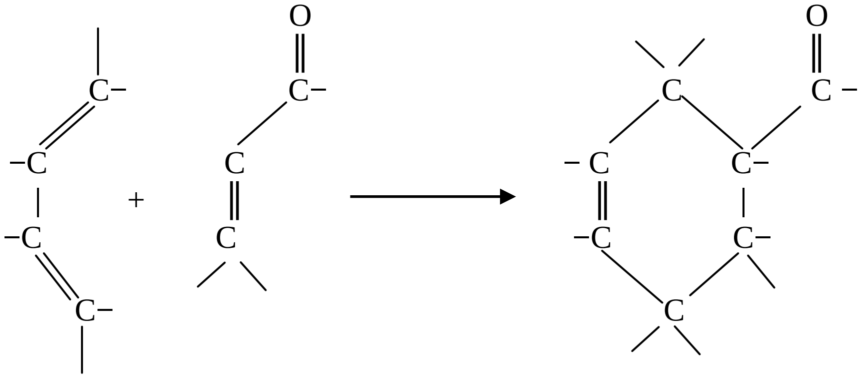
xi. α,β-unsaturated carbonyl compounds are converted to β-cyano carbonyl compounds when they react with aqueous sodium cyanide.

xii. Ammonia and some derivatives of ammonia like amines, hydroxylamine, phenyl hydrazine, etc ,add to α,β-unsaturated carbonyl compounds to yield β-amino carbonyl compounds.

xiii. Michael addition is a special nucleophilic addition to α,β-unsaturated carbonyl compounds.

ivx. Ammonia and primary and secondary amines are powerful catalysts for the Michael addition.

xv. The Diels-Alder reaction is the reaction between α,β-unsaturated carbonyl compounds with conjugated dienes. It involves the addition of the C-1 and C-4 carbon atoms of the conjugated diene system to the doubly bonded carbons of the unsaturated carbonyl compound to form a six membered ring.



Diene Dienophile (diene-loving) Adduct(six-membered ring)

xvi. The Diels-Alder reaction is known as a[4 + 2] cycloaddition since it involves a system of four π electrons (the diene) and a system of two π electrons(the dienophile).

xvii. Quinones are special kinds of α,β-unsaturated ketones.

## 6.0 Tutor Marked Assignment

Give the structures of the organic products expected from the reaction of benzalacetone, $C_6H_5CH{=}CHCOCH_3$, with each of the following:

- i. HCl
- ii. CH3OH
- iii. NaCN
- iv. NH3
- v. Ethyl malonate,base
- vi. 1,3-butadiene

## 7.0 Further Reading and Resources

Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry-Sixth Edition

# Module 5: Heterocyclic Compound

## Unit 1: Classification and Naming Of Heterocyclic Compounds

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## 1.0 Introduction

Heterocyclic compounds are cyclic compounds containing at least one atom other than carbon as a ring member. The most commonly encountered heterocyclic compounds contains only nitrogen, oxygen and sulphur as hetero atom

## 2.0 Objectives

At the end of this unit you should be able to:

i. Define heterocyclic compounds
ii. List classes of heterocyclic compounds
iii. Give examples of five membered, six-membered and condensed heterocyclic compound
iv. Name simple heterocyclic compounds

## 3.0 Occurrences of Heterocyclic Compounds

Heterocyclic compounds have been found to be highly reactive. Heterocyclic intermediates have been used more and more in synthesis as protecting groups. In the biological world,they are everywhere, for example, chlorophyll which makes leaves green in plants and heme which is responsible for making blood red in animals are important heterocyclic compounds. Some heterocyclic rings are however not considered as heterocyclic compounds due to the relatively instability of their ring systems and lack of aromatic character. For example, epoxides and γ- or δ lactones. The introduction of hetero atom in the ring in place of carbon does not alter the strain relationship significantly. The most stable heterocyclic compounds are those having five or six membered rings. Heterocyclic compounds are thus defined as those compounds having five or six membered ring, with at least one hetero atom as the ring member, which are relatively stable and exhibit aromatic character.

## 3.1 Classification

Heterocyclic compounds may be classified into three main categories:

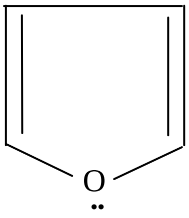
### 3.1.1 Five membered heterocyclics

They are considered as being derived from benzene by replacing a C=C by a hetero atom with an unshared electron pair.

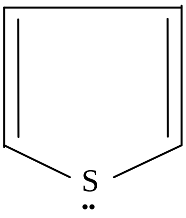
The five membered ring can be further divided into

**a. Compounds having only one hetero atom.**

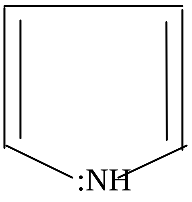
For example, furan, thiophene and pyrrole containg O, S, and N respectively as hetero atoms.



Furan(Oxole)



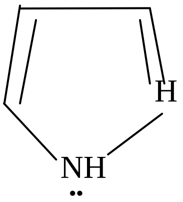
Thiophene(Thiole)



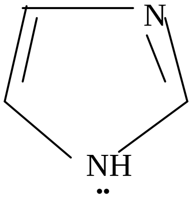
Pyrrole(Azole)

**b. Compounds having more than one hetero atom**

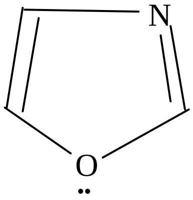
The two hetero atoms may be same, as in pyrazole and imidazone or different, as in thiazole and oxazole.



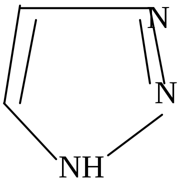
Pyrazole
(1,2-Diazole)



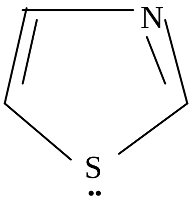
Imidazole
(1,3-Diazole)



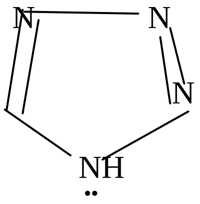
Oxazole
(1,3-Oxazole)



1,2,3-Triazole



Thiazole
(1,3-Thiazole)



Tetrazole

### 3.1.2 Six-memebered heterocyclics

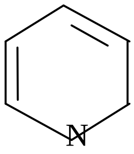
These are formed when a carbon of benzene is replaced by an isoelectric hetero atoms. They may be divided into two types:

**a. Compounds with one hetero atoms**

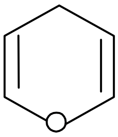
For example, pyridine, pyran, thiopyranetc

**b. Compounds with more than one hetero atom**

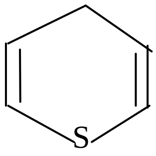
For example, pyrimidine, pyrazine, pyridazine etc



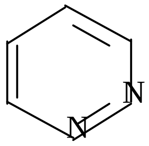
Pyridine
(Azine)



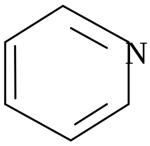
γ-Pyran
(4H-Oxane)



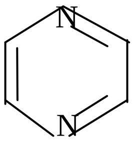
γ-Thiopyran
(4H-Thiane)



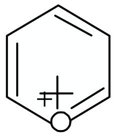
Pyridazine
(1,2-Diazine)



Pyrimidine
(1,3-Diazine)



Pyrazine
(1,4-Diazine)



Pyrilium ion

### 3.1.3 Condensed heterocyclics

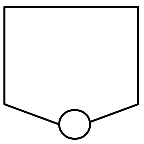
They may consist of two or more fused rings which may be partly carbocyclic and partly heterocyclic, e.g indole, quinoline, carbazole or may be completely heterocyclic eig purine, pteridine etc. They may be classified into two classes based on their properties.

**a. Heteroparaffins**

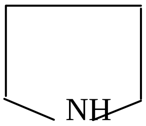
They ressemble paraffin. E.g tetrahydrofuran(THF) , pyrrolidine, piperidine etc

**b. Hetero aromatics**

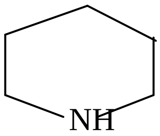
They resemble aromatic compounds. E.g pyrrole, thiophene, furan, pyridine, indole etc.



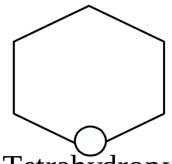
Tetrahydrofuran
THF(Oxalane)



Pyrrolidine
(Azolidine)



Piperidine
(Perhydroazine)



Tetrahydropyrane
(Oxane)

## 3.2 Naming Heterocyclic Compound

Heterocyclic compounds are generally known by their common names. The IUPAC system has accepted most of the common names. However, the IUPAC system of naming is still utilized.

The IUPAC name of heterocyclic is obtained by combining the following prefixes and suffixes in Table 1.1

| Order of seniority | Prefixes | Suffixex |
|---|---|---|
| 1 | oxa for oxygen | -ole 5-membered ring |
| 2 | thia for sulphur | -ine 6-membered ring |
| 3 | aza for nitrogen | -epine 7-membered ring |
| 4 | phospha for phosphorus | |
| 5 | bora for boron | |

Table 1.1
(Source:A Textbook of Organic Chemistry,3rd Edition-By K.S Tewari and N.K.Vishnoi)

The terminal ‘a’ of the prefixes is usually dropped when combing prefixes and suffixes. See the table below:

| No of atoms forming ring | Rings containing nitrogens | | Rings containing nitrogen | |
|---|---|---|---|---|
| | Unsaturated | Saturated | Unsaturated | Saturated |
| 3 | irine | Iridine | Irene | irane |
| 4 | ete | etidine | Ete | etane |
| 5 | ole | olidine | Ole | olane |
| 6 | ine | perhydro Azine | In | ane |

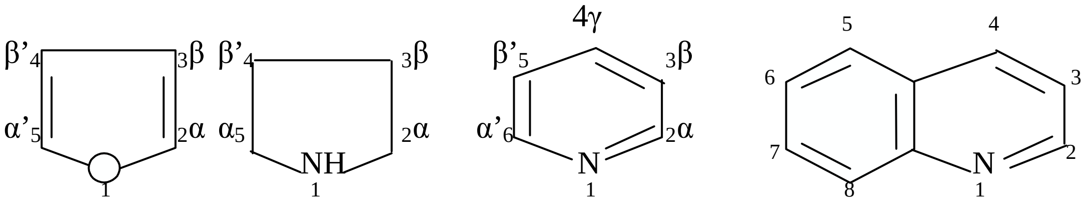
Table 1.2-Suffix used in naming heterocyclic rings
(Source:A Textbook of Organic Chemistry,3rd Edition-By K.S Tewari and N.K.Vishnoi)

If more than one hetero atom is present, the prefixes are placed in order of seniority. i.e ‘oxa-’ first then ‘thia-’, etc.

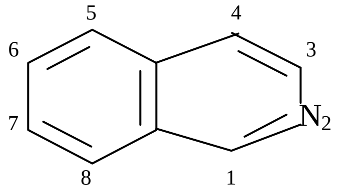
The simple heterocyclics containing one atom are numbered in such a way that the hetero atom gets the lowest possible numbers and the numbering is continued in anti-clockwise direction.

The ring positions are designated by numeral or Greek letters. When Greek letters are used, the position next to the hetero atom is designated as α- followed by β- and so 0n.

For example,



However, in some condensed heterocyclics, the number given to the hetero atom depends on the type of compound. For example, in isoquinoline, ‘N’ does not get the lowest possible number.

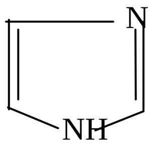


When two or more hetero atoms are present, the numbering is done in such a manner that the hetero atom higher in seniority gets the lowest number . For example ‘O’ takes precedence over ‘S’, and ‘S’ over ‘N’ and the other hetero atoms get the next number. For example

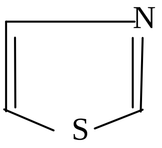
## Activity A/Self Assessment Exercise

Assign number to the heteroatoms and carbon in the following structures

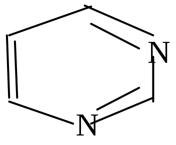
i.



ii.



iii.



## 4.0 Conclusion

Heterocyclic compounds may be five membered, six-membered and condensed heterocyclics.

## 5.0 Summary

In this unit we have learnt that:

1. Heterocyclic compoundare cyclic compounds which contain at least one atom other than carbon as a ring member
2. Heterocyclic compound have at least one hetero atom as a ring member
3. Heterocyclic compounds are relatively stable and exhibit aromatic character
4. Heterocuclic compounds may be divided into three main categories
    - Five membered
    - Six membered
    - Condensed heterocyclics
5. Heterocyclic compounds are known mainly by their common names

## 6.0 Tutor Marked Assignment

- Classify the following into;
    i. What do you understand by the term ‘heterocyclic compounds’?

    ii. Name the three important five membered heterocyclic compounds and draw their structures

## 7.0Further Reading And Other Resourses

a. K.S.TEWARI and N.K. VISHNOI (2006)- A Textbook of Organic Chemistry. Third Edition
b. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry- Sixth Edition

# Unit 2: Five-Membered Heterocyclics

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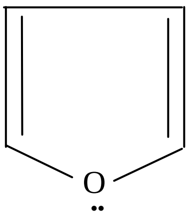
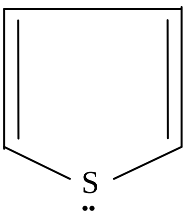
## 1.0 Introduction

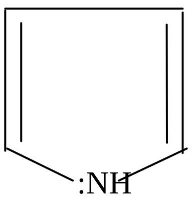
The five membered heterocyclic compounds are very stable and exhibit aromatic character. The important members of this group are thiophene, pyrrole and furan.



Furan(Oxole)



Thiophene(Thiole)



Pyrrole(Azole)

## 2.0 Objectives

At the end of this unit you should be able to:

i. Give examples of five membered heterocyclics
ii. Name simple heterocyclic compounds
iii. Prepare Thiophene, Furan and Pyrrole
iv. State the physical propertoes of Thiophene, Furan and pyrrole
v. Discuss the various chemical properties of Thiophene, Furan and pyrrole
vi Compare the chemical properties of Thiophene, furan and pyrrole

## 3.0 Occurrence

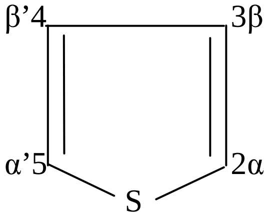
Thiophene and pyrrole occur in coal tar in small amounts. During the fractional distillation of coal tar, thiophene(b.pt 83°C) is collected along with the benzene(b.pt 80°C) hence ordinary benzene always contains about 0.5% of thiophene which must be treated if thiophene free benzene is desired. Thiophene is also present in shale oil and pyrrole in bone oil. Furan is present in the distillate of pine-wood.

The pyrrole ring system occurs in a large number of naturally occurring substances. E.g chlorophyll, haemin,cyanocobalamin(Vitamin B12), auxins, alkaloids etc

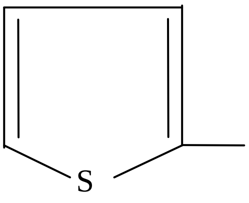
## 3.1 Naming Five Membered Heterocyclics

The nomenclature has been discussed earlier (Unit 1). The ring atoms are numbered such that the hetero atom is given the lowest number or when using the Greek numbering,the carbon atom next to the hetero atom is designated as α- while the next to them is β-carbon atom.

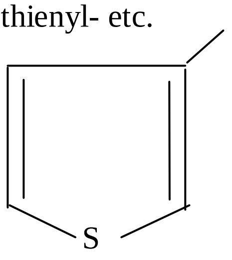
The radicals thienyl-, furyl- and pyrryl- are derived from thiophene, furan and pyrrole respectively by replacing one hydrogen atom. The position of the hydrogen replaced is indicated by the number of carbon atom, e.g 2-thienyl-, or 3-thienyl- etc.



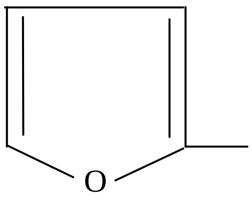
Thiophene



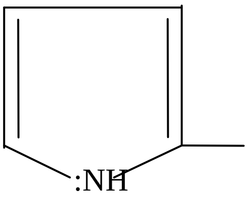
2-Thienyl-



3-Thienyl-

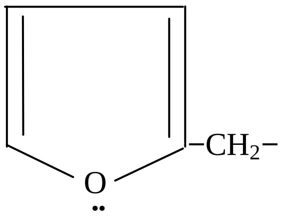


2- Furyl

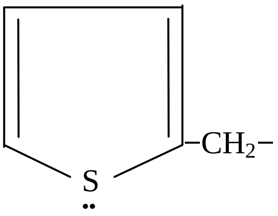


2-Pyrryl

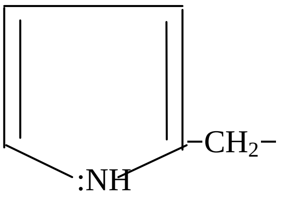
The alkyl derivatives give rise to the corresponding radicals. They are known as thienyl-, furfuryl- and pyrrolyl radicals.



Furfuryl-



Thenyl-

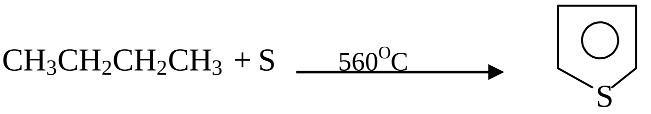


Pyrrolyl-

## 3.2 General Methods of Formation

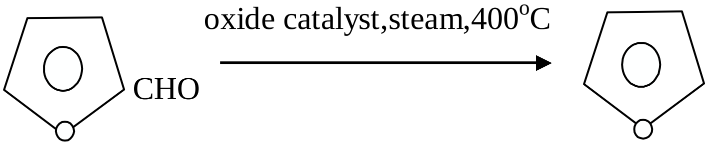
The five membered heterocyclics or their derivatives may be synthesized by the reactions of 1,4-dicarbonyl compounds with an appropriate source of hetero atom.

Thiophene can be synthesized on an industrial scale by the high temperature reaction between n-butane and sulphur.



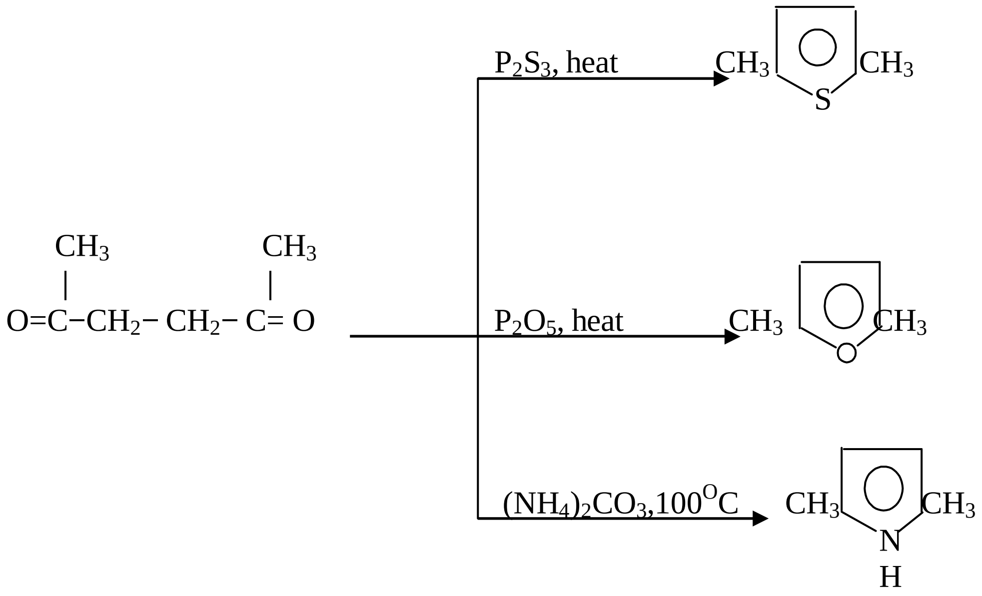
From Coal tar: Thiopene (b.pt 84°C) is collected along with benzene(b.pt.80oC) During the fractional distillation of coal tar. Pyrrole is also found in small amount in coal tar.

Furan is most readily prepared by decarbonylation of furfural



Furfural Furan

Most substituted pyrroles, furan and thiophenes can be prepared from open-chain compounds by ring closure while some are prepared from the parent heterocycles by substitution. For example,



## 3.3 General Characteristics

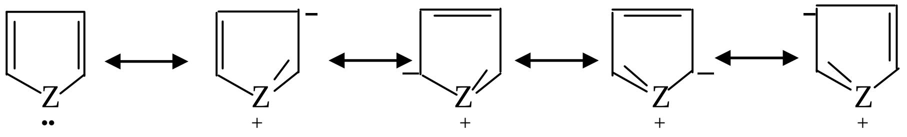
### 3.3.1 Physical Properties

i. They are colourless liquids
ii. The boiling point of furan, thiophene and pyrrole are 32°C, 84°C and 129°C respectively. The relatively high boiling point of pyrrole is due to associated intermolecular H-bonding.

### 3.3.2 Aromatic Character

Like benzene they exhibit aromatic characters and are resonance stabilized. Their resonance energies are however lower than that of benzene and decrease in the order thiophene > pyrrole > furan.

However, unlike benzene, the dipolar structures are important contributing structures to stability.

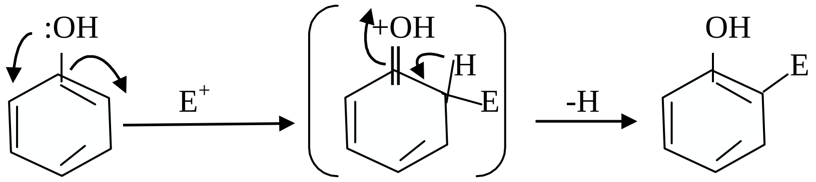


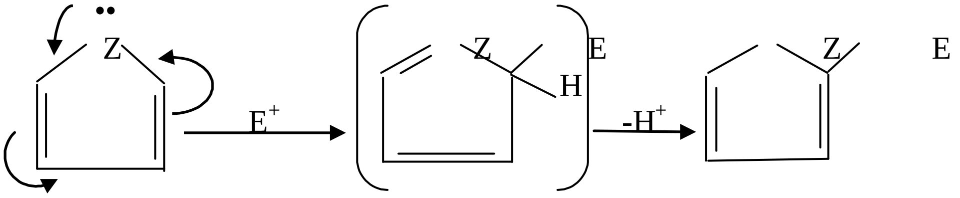
(Z = O, S, or –NH)
Resonance stabilized heterocyclic compounds

Each of the ring atoms is in sp2 hybridization state and the ring is planar. A total of six $\pi$ electrons consisting of two $\pi$ and one lone pair are available for delocalization and hence they exhibit aromatic characters. Because of their aromatic characters, they are resistant to addition reactions like hydrogenation. Their important reactions are electrophilic substitution reactions at carbon.

### 3.3.3 Reactivity

Their electrophilic substitution reactions can be most closely compared to those of phenols.

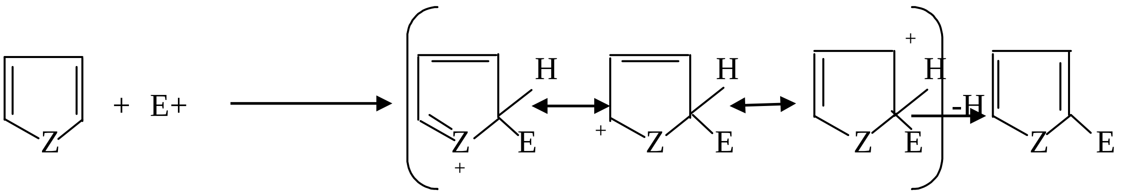




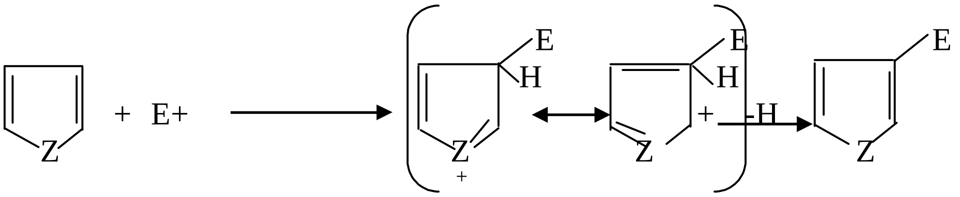
Their reactivity towards electrophiles shows that they are more reactive than benzene. For example, thiophene is 1000times more reactive than benzene. The increasing order of reactivity is:
Benzene < Thiophene < Furan < Pyrrole.

Furan is less reactive than pyrrole because oxygen accommodates a positive charge less readily than nitrogen. Thiophene is less reactive than Furan because the +M effect of sulphur is smaller than that of oxygen. Because of the greater reactivity of these rings systems, they can undergo substitution reactions under milder conditions

The electrophilic substitution occur either at α- or β- position. However, due to a greater stabilization of the intermediate carbocation formed during α- substitution compared to the intermediate carbocation formed in the β- substitution, the former position is preferred.



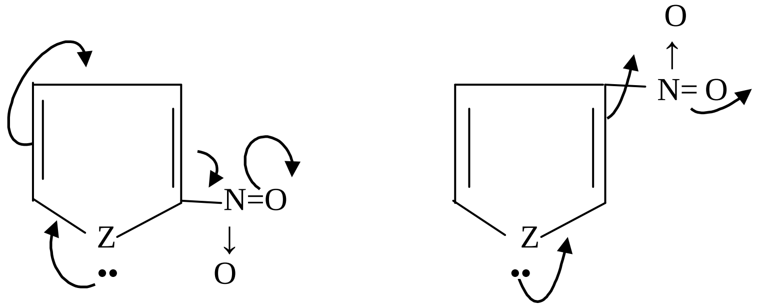
α-Substitution (2- or 5- substitution)



β- Substitution
Z = O, S or NH

Various substituents affect the rate and position of electrophilic attack. For example, electron donating groups increase the reactivity to such an extent that the resultant compounds are highly unstable. Example of electron donating groups are $-NH_2$, $-NR_2$, -OH, -OR.

Electron withdrawing groups such as $–NO_2$, $-SO_3H$, -COOR etc decrease the reactivity and stabilizes the ring by increasing resonance with the hetero atom. Even with electron withdrawing group attached, the incoming substituent enters only 2 or 5 position.



α – substituent β- substituent

Resonance stabilized by electron withdrawing group

Heterocyclics not stabilized by electron withdrawing substituent are thus highly reactive.

## 3.4 Individual Members-Thiophene, Furan, Pyrrole

We are now going to take a closer look at the reactions of the individual members of the five membered heterocyclics

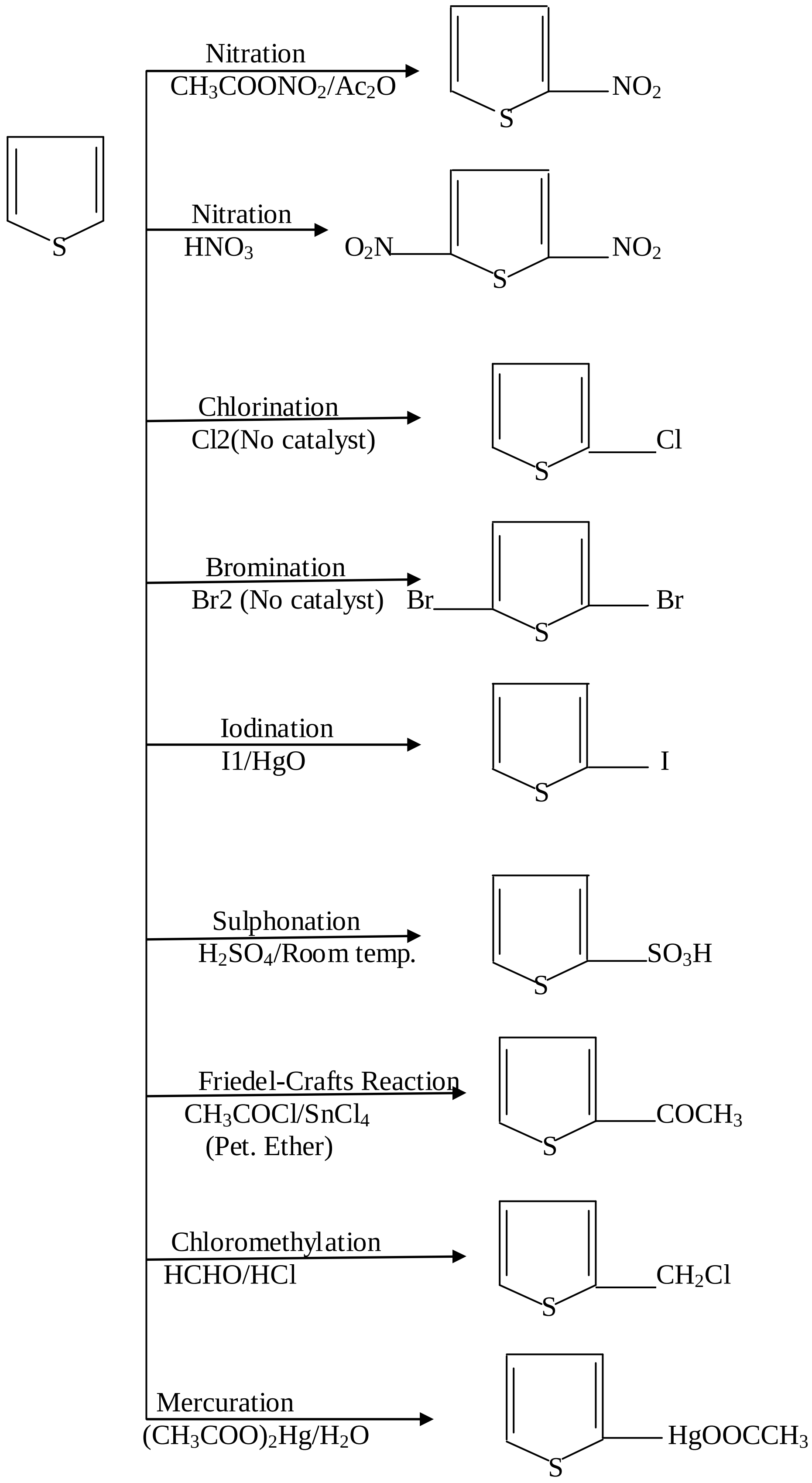
### 3.4.1 Thiophene

a. Physical Properties: It is a colourless liquid with a boiling point of 85°C. It is insoluble in water but soluble in organic solvents.

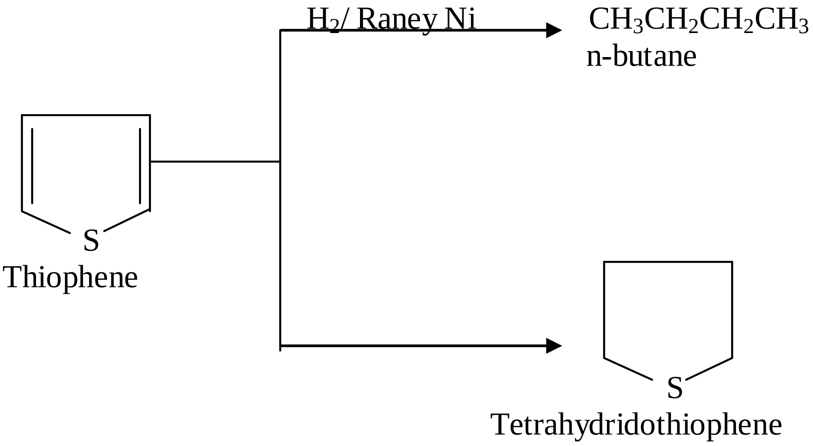
b. Chemical Properties: Thiophene resembles benzene in most of its chemical reactions. This may be because they have similar molecular mass, similar shapes of molecules and especially similar electronic structures.

**i. Electrophilic substitutions**

Thiophene undergoes most of the electrophilic substitution reactions shown by benzene. These reactions are summarised below.

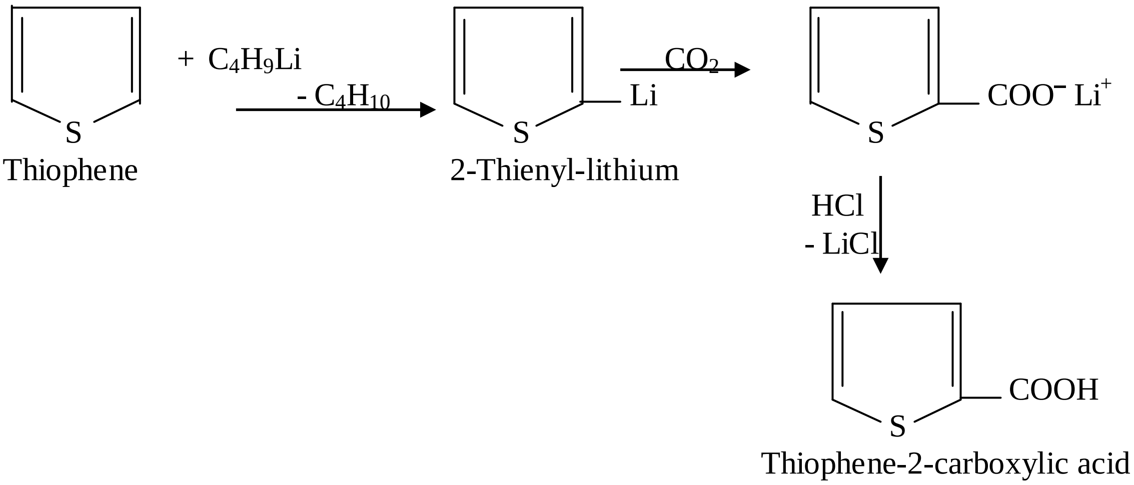

S
Nitration
CH3COONO2/Ac2O
S
NO2
Nitration
HNO3
O2N
S
NO2
Chlorination
Cl2(No catalyst)
S
Cl
Bromination
Br2 (No catalyst)
Br
S
Br
Iodination
I1/HgO
S
I
Sulphonation
H2SO4/Room temp.
S
SO3H
Friedel-Crafts Reaction
CH3COCl/SnCl4
(Pet. Ether)
S
COCH3
Chloromethylation
HCHO/HCl
S
CH2Cl
Mercuration
(CH3COO)2Hg/H2O
S
HgOOCCH3

ii. Addition reactions. Thiophene is catalytically reduced to tetrahydrothiophene . It can be catalytically reduced with hydrogen using Raney nickel as catalyst to give n-butane.



**iii. Reaction with organometallic compounds**

It reacts with butyl-lithium to give 2-thienyl lithium which shows all the usual reactions of organolithium.



**iv. Oxidation**

Thiophene does not get oxidised to sulphoxide or sulphone because it does not form sulphonium salt. However, it reacts with hydrogen peroxide and this leads to the opening of the ring and sulphur is oxidised to tetraoxosulphate (vi) acid. It is decomposed by potassium with the formation of potassium sulphide.

## c. Test For Thiophene

Indophenin reaction: Thiophene when treated with isatin and concentrated tetraoxosulphate (vi) acid produces a blue colour

## Activity A/Self Assessment Exercise

i. Write the structural formulae of thiophene ,pyrrole and furan. How would you test for thiophene?
ii. Using equations, outline five of the substitution reactions of thiophene

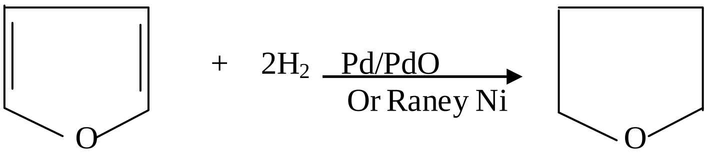
## 3.4.2 Furan

a. Physical Properties: It is a colourless liquid with a boiling point of 31°C. It is almost insoluble in water but soluble in alcohol and ether. It has characteristic chloroform like smell.

b. Chemical Properties: Furan resembles thiophene in its chemical reactions but it is more reactive. It behaves as diene as well as an aromatic compound.

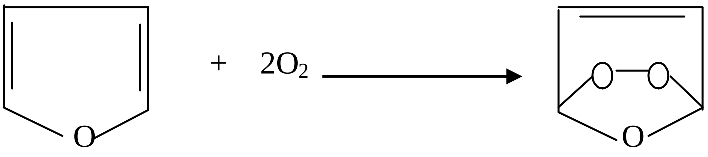
### I. Addition reaction

i. Hydrogenation: It can be catalytically reduced by hydrogen in the presence of lead or Raney nickel catalyst to form a stable saturated cyclic ether known as tetrahydrofuran(THF).



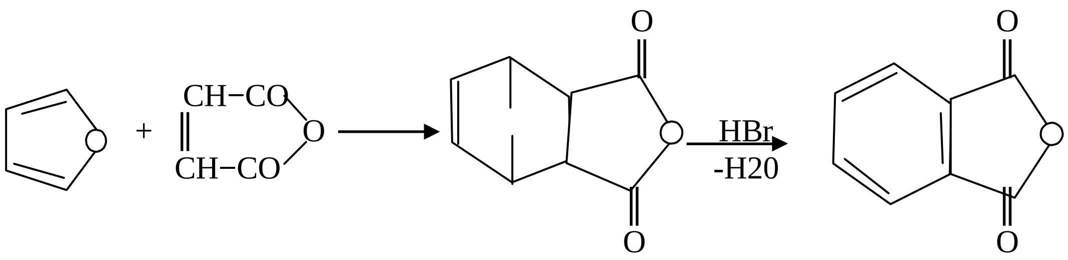
THF

ii. Reaction with oxygen or air
It is unstable in air and it reacts with oxygen to form 2,5-peroxide which readily polymerises.



Furan-2,5-peroxide

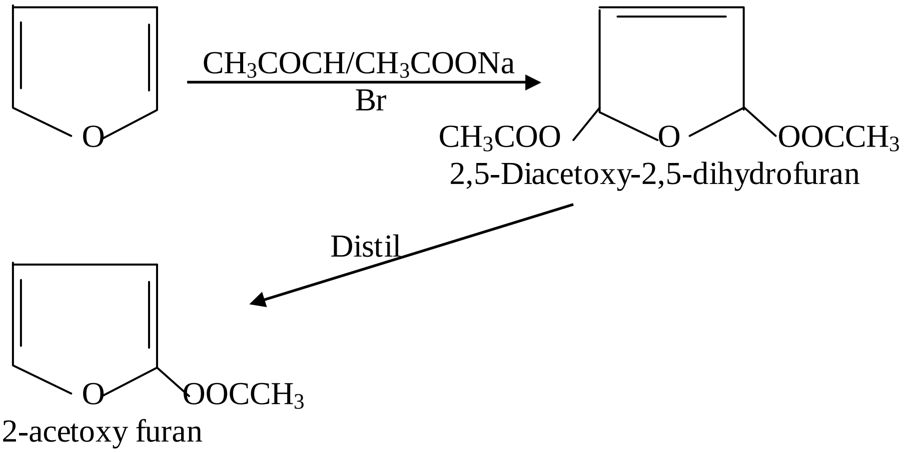
iii. Diel-Alder reaction
It undergoes Diel-Alder reaction because it behaves as diene. For example with maleic anhydride, it forms a 1,4-adduct which on treatment with a mineral acid e.g HBr undergoes dehydration to yield phthalic anhydride.



1,4-Adduct Phthalic anhydride

iv. 2,4-additions

It react with acetic acid in the presence of sodium acetate and bromine to form 2,5-diacetoxy-2,5-dihydrofuran.

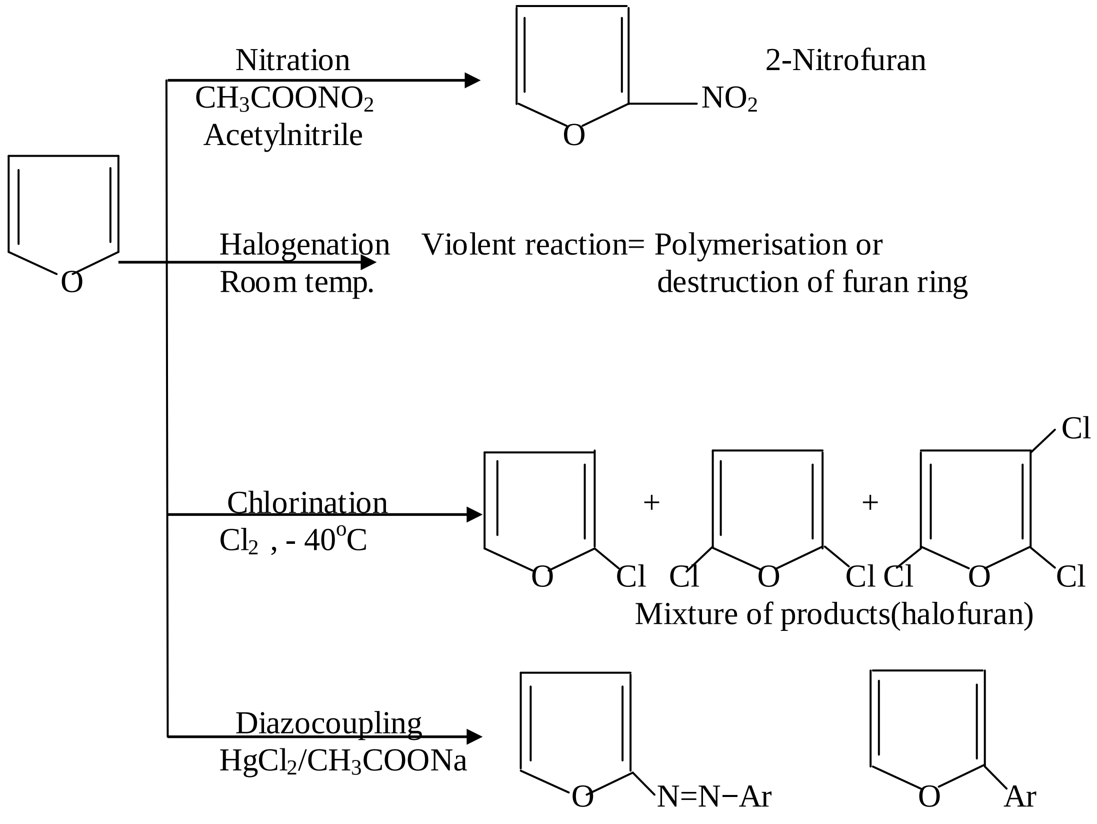


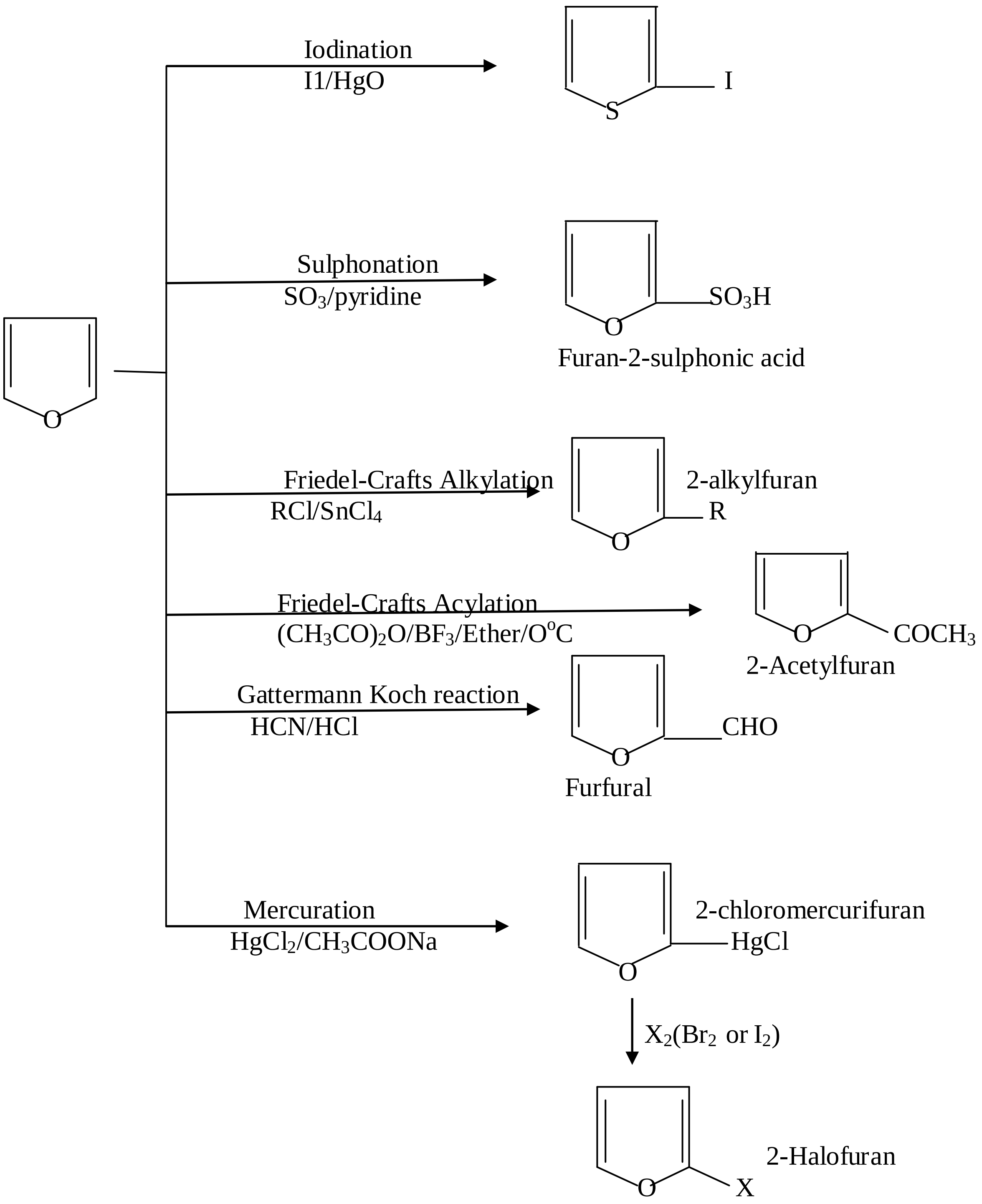
**(II) Electrophilic Substitution reactions**

Furan undergoes electrophilic substitution reactions much more readily than does benzene and thiophene. However, most of these reactions are not of much practical importance because of the following reasons:

(i) It is highly sensitive to strong acids resulting in polymerisation reaction.
(ii) It is highly reactive and form poly substituted product even at low temperature.
(iii)It undergoes 2,5-addition in preference to substitution reactions.

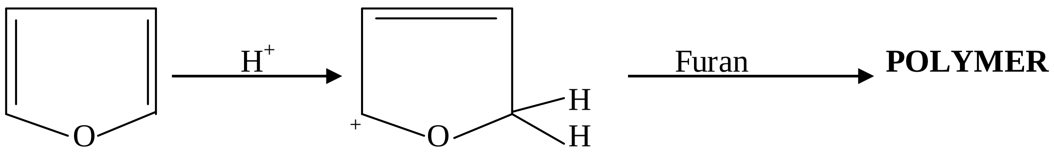
The following reactions are the important electrophilic substitution reactions of furan.





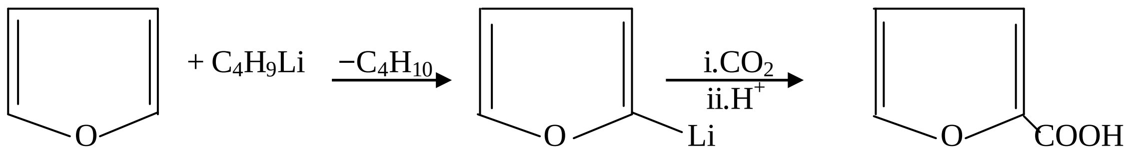
**(III) Polymerisation reaction**

In the presence of strong acids, furan polymerizes to form complex products.



**(IV) Formation of Organometallic compounds**

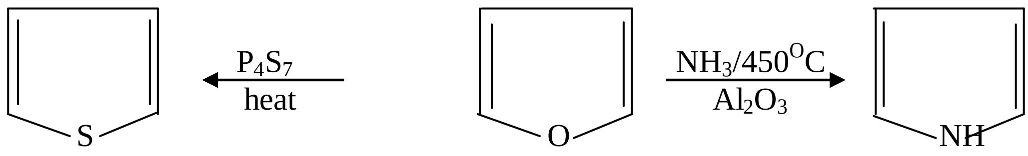
Furan reacts with butyl-lithium to give 2-furyllithium which undergoes the usual reactions of organolithium compounds.



Furan 2-Furyl-lithium Furoic acid

(V) **Formation of pyrrole and thiophene**

Furan reacts with ammonia, $NH_3$ at 450$^O$C in the presence of aluminium to form pyrrole. It also reacts with $P_4S_7$ to give thiophene.



Thiophene Furan Pyrrole

## Activity B/Self Assessment Exercise

Give the products of the reaction of furan with

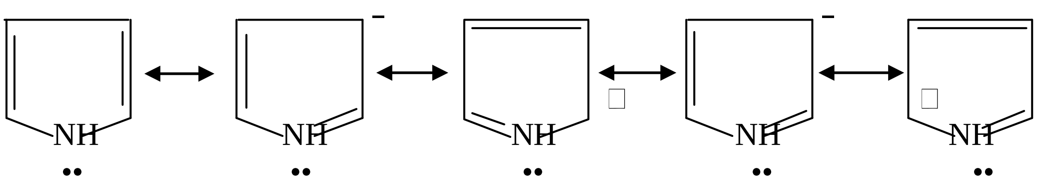
i.$C_4H_9Li$ ii. $NH_3$ iii. $CH_3COCH/CH_3COONa$ iv. $H_2$ v. $O_2$

## 3.4.3 Pyrrole

## Structure

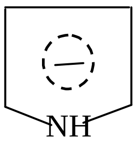
Its molecular formula is $C_4H_5N$. It is the nitrogen analogue of furan and thiophene . It resembles furan and thiophene and its synthesis from succinic acid points to the cyclic structure of furan. The aromatic nature of pyrrole as shown in its resistance to additions and ease of electrophilic substitutions is explained in terms of either resonance or molecular orbital concept

Resonace Concept: It is a resonance hybrid of the following structures:



I

Resonance stabilized pyrrole anion OR



II

Its resonance energy is 21kcal/mol. The double bond shown in its classical structure (I) are not true double bonds, hence it is expected to be resistance to addition reaction. Also the non-availability of the lone pair of electrons at nitrogen explains the lack of basic character.

Molecular orbital Concept: All the carbon and nitrogen atoms in pyrrole are in $sp^2$ hybridization state and form σ bonds with three other atoms by overlap of trigonal $sp^2$ hybrid orbitals. Thus all the C and N lie in the same plane at an angle of 120°C to each other. At each of the carbon there is one unhybridized p-orbital carrying one electron while the unhybridized p-orbital of the nitrogen atom carries the lone pair of electrons.

The p-orbitals are at right angles to the plane of the ring atoms and they overlap with each other to form a delocalised π- molecular orbital electron cloud above and below the plane. This cloud contains six electrons required for aromaticity and thus explains the stability of pyrrole to addition reaction and its tendency to undergo substitution reaction.

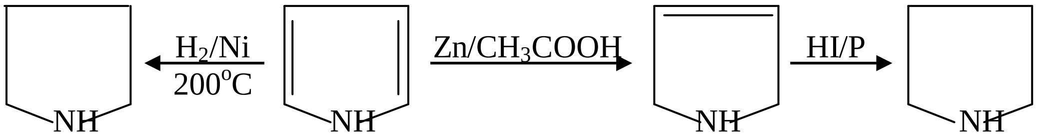
The non-availability of the lone pair of electron of the nitrogen because of its involvement in the π electron cloud, explains the weak basic character of pyrrole.

**Properties of Pyrrole**

a. Physical Properties: It is a colourless liquid with a boiling point of 131°C. It is sparingly soluble in water but fairly soluble in ethanol and ether. It darkens when exposed to air.

b. Chemical Properties: Pyrrole differs markedly in chemical properties from thiophene and furan. However it undergoes usual electrophilic substitution reactions. It has amphoteric properties and behaves like very weak base due to withdrawal of electron density from nitrogen by aromatic sextet and as a weak acid due to greater stabilization by pyrrole.

i. Hydrogenation: Pyrrole on reduction with zinc and acetic acid forms pyrroline(2,5-dihydropyrrole), which on heating with hydriodic acid and red phosphorus yields pyrrolide(tetrahydropyrrole).



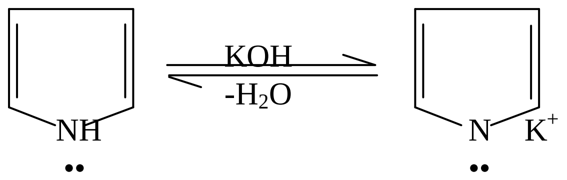
ii. Basic Character: It is a very weak secondary base and dissolves slowly in dilute acids. This is due to the withdrawal of the lone pair of electrons from nitrogen towards aromatic sextet making it available for protonation with acids.

iii. Acidic Character: Pyrrole is weakly acidic in nature unlike furan and thiophenes. It thus reacts with metallic potassium or potassium hydroxide to form potassium salt which can be hydrolysed back to pyrrole on treatment with water.

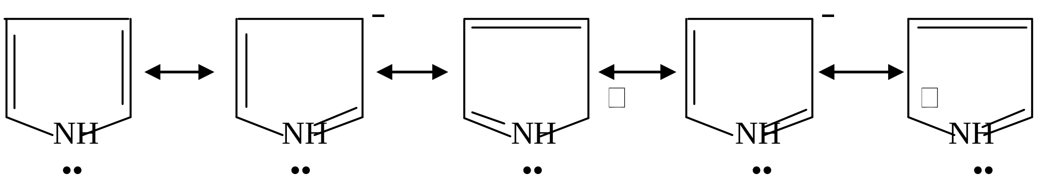
The acidic character of pyrrole is due to two reasons:

- The relatively easy dissociation of proton attached to N

- The greater stability of the pyrrole anion as compared to pyrrole



Potassiopyrrole

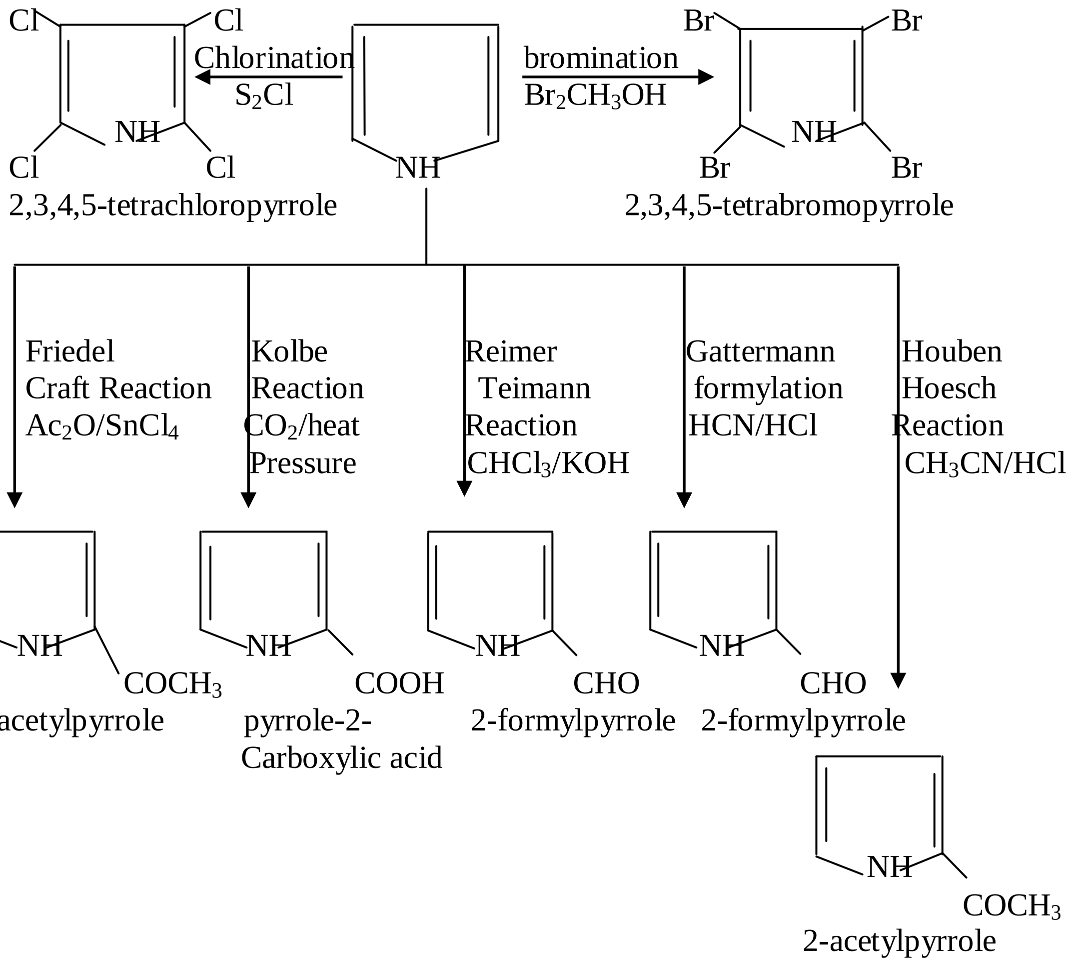


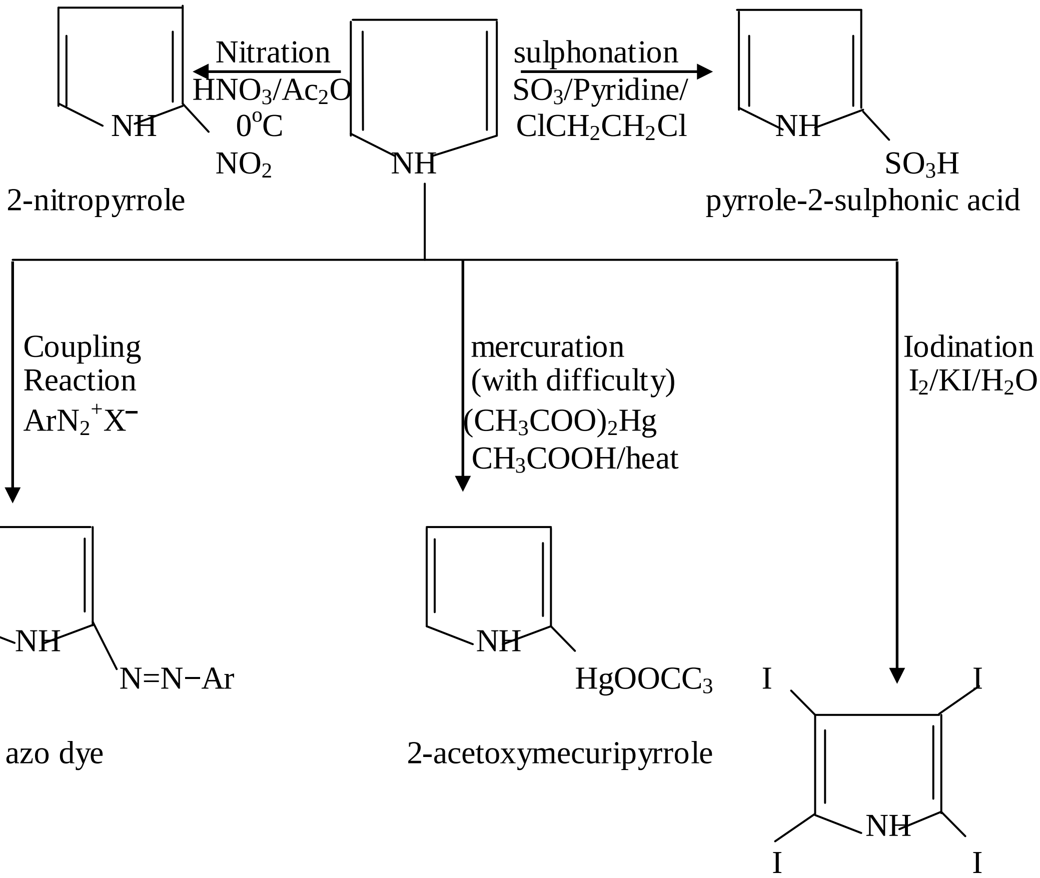
Resonance stabilized pyrrole anion

iv. Electrophilic Substitution reactions

Pyrrole is highly reactive towards electrophilic substitution reactions. It shows striking resemblance to phenol and aromatic amines. It undergoes Kolbe, Reimer-Tiemann, Gattermannformylation, Houben-Hoesch and coupling reactions.

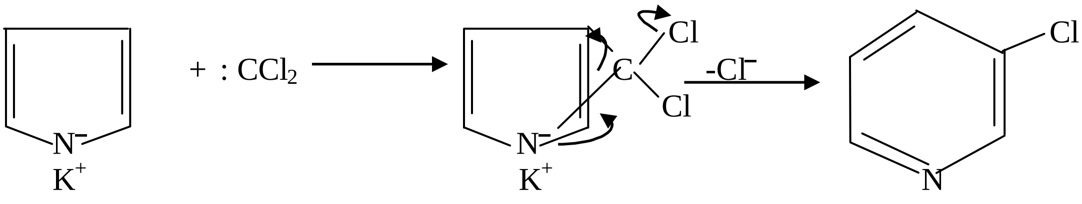
Electrophilic substitution reactions of pyrrole is summarised below:





v. Ring expansion

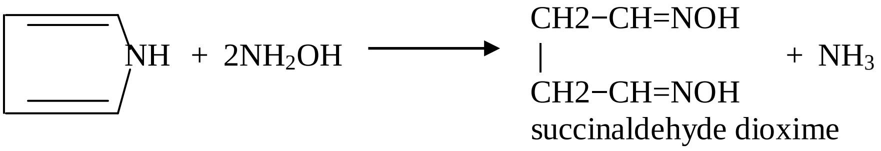
Pyrrole reacts with dichlorocarbene, formed by the interaction of chloroform and sodium ethoxide to give β-chloropyridine through ring expansion.



β-chloropyridine

vi. Ring opening

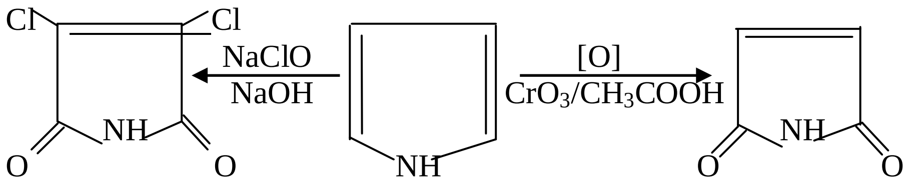
The Pyrrole ring open up to give succinaldehyde dioxime when refluxed with an ethanolic solution of hydroxylamine.



succinaldehyde dioxime

vii. Oxidation

Pyrrole when oxidised by chromium trioxide in acetic acid gives maleinimide while oxidation in alkaline hypochloride yields dichloromaleinimide.

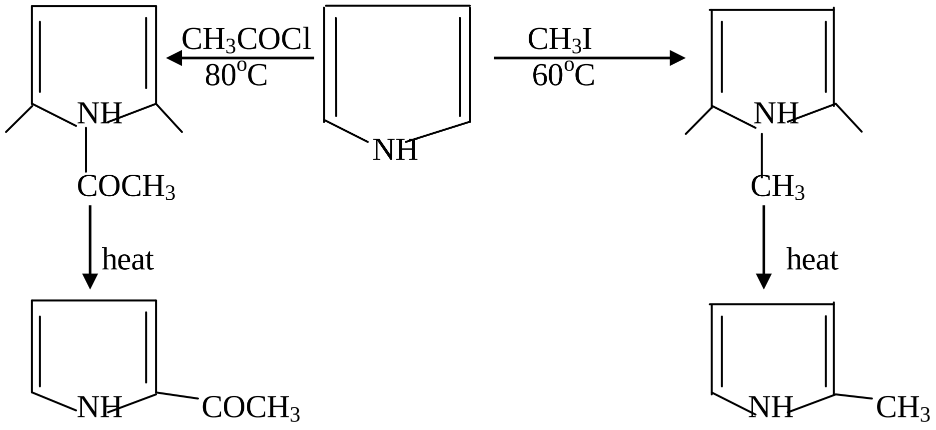


Dichloromaleinimide Pyrrole maleinimide

viii. Resemblance with aromatic amines

Pyrrole behave like phenyl amine (aniline) and phenol by reacting with acid halides like acetyl chloride and methyl iodide.

When it reacts with acetyl chloride at 80°C, it forms N-acetylpyrrole which rearranges on heating to 2-acetylpyrrole. It also reacts with methyl iodide to form N-methylpyrrole which also rearranges to give 2-methylpyrrole.



2-acetylpyrrole 2-methylpyrrole

**Test for Pyrrole** A pine-splint moistened with hydrochloric acid is turned fiery-red by pyrrole vapours.

## Activity C/Self Assessment Exercise

a. i. Explain why pyrrole is not basic
  ii. Explain why pyrrole is more susceptible to substitution reactions and not addition reactions
  iii. Explain using equations, halogenations in pyrrole.

b. Give the products of pyrrole with:
  - $CH_3CN + HCl$, Hydrolysis
  - $CH_3MgI$

## 4.0 Conclusion

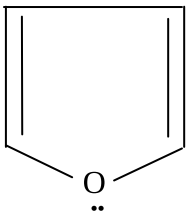
Thiophene, Furan and Pyrrole are examples of five-membered heterocycles and their reactions is more of substitution reaction than addition. The increasing order of their reactivity when compared to benzene is:

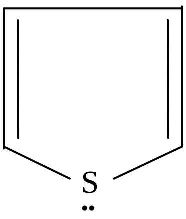
Benzene < Thiophene < Furan < Pyrrole, showing that they are more reactive than benzene.

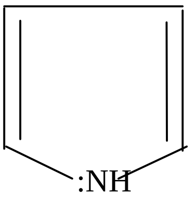
## 5.0 Summary

In this unot we have learnt that:

i. The important members of this group are thiophene, pyrrole and furan


Furan(Oxole)


Thiophene(Thiole)


Pyrrole(Azole)

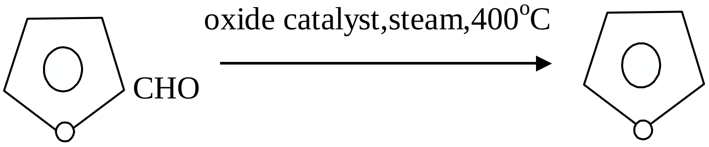
ii. Thiophene and pyrrole occur in coal tar. Thiophene is present in shale oil and pyrrole in bone oil. Furan is in the distillate of pine-wood.The pyrrole ring system occurs in naturally occurring substances like chlorophyll ,haemin, cyanocobalamin (Vitamin B12) , auxins, and alkaloids

iii. The radicals thienyl-, furyl- and pyrryl- are derived from thiophene, furan and pyrrole respectively by replacing one hydrogen atom and position replacement is indicated by the number on carbon atom, e.g 2-thienyl-, or 3-thienyl- etc

iv. Thiophene can be synthesized on an industrial scale by the high temperature reaction between n-butane and sulphur.

Thiopene and Pyrrole is also found in coal tar.

Decarbonylation of furfural gives furan



Furfural Furan

Substituted pyrroles, furan and thiophenes can be prepared from open-chain compounds by ring closure.

v. Generally they are colourless liquids. The boiling point of furan, thiophene and pyrrole are 32$^{O}$C, 84$^{O}$C and 129$^{o}$C respectively

vi. They exhibit aromatic characters like benzene and are resonance stabilized.

vii. Their electrophilic substitution reactions can be most closely compared to those of phenols and they are more reactive than benzene.

viii. The electrophilic substitution occu r either at α- or β- position with the α-substitution preferred due to a greater stabilization of the intermediate carbocation formed during α- substitution compared to the intermediate carbocation formed in the β- substitution

ix. Electron withdrawing groups such as $-NO_2$, $-SO_3H$, -COOR etc decrease the reactivity and stabilizes the ring by increasing resonance with the hetero atom.

x. **Thiophene** is a colourless liquid ,boiling point of 85°C, insoluble in water but soluble in organic solvents.

xi. Thiophene undergoes the following reactions:

- Electrophilic substitutions
- Oxidation

Thiophene reacts with hydrogen peroxide leading to the opening of the ring and sulphur is oxidised to tetraoxosulphate (vi) acid. It is decomposed by potassium with the formation of potassium sulphide.

xii. Thiophene can be tested using Indophenin reaction

xiii. Furan is a colourless liquid with boiling point of 31°C, almost insoluble in water, soluble in alcohol and ether with a characteristic chloroform like smell.

xiv. Furan undergoes the following chemical reactions:

I. Addition reaction
- Hydrogenation
- 2,4-additions

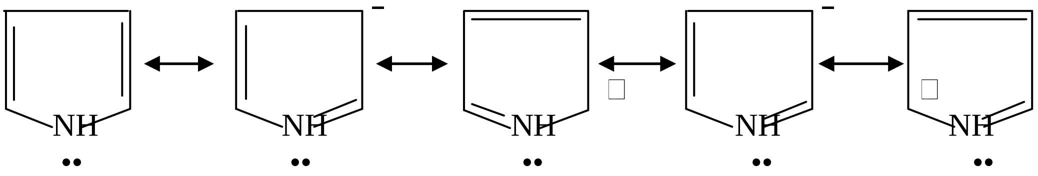
(II) Electrophilic Substitution reactions

(III) Polymerisation reaction

(IV) Formation of Organometallic compounds

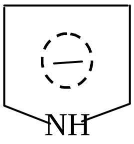
(VI) Formation of pyrrole and thiophene

xv. Pyrrole is a resonance hydride of the following structures:



I

Resonance stabilized pyrrole anion OR



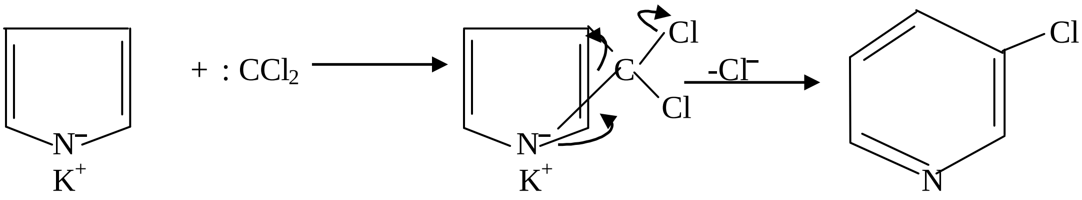
II

xvi. Pyrrole is a colourless liquid, boiling point of 131°C, sparingly soluble in water, fairly soluble in ethanol and ether and it darkens when exposed to air.

xvii. Pyrrole undergoes the following reactions:

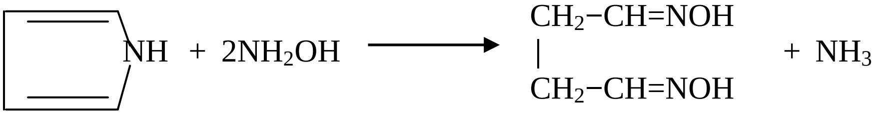
- Hydrogenation

- Pyrrole is a very weak secondary base and dissolves slowly in dilute acids.
- Pyrrole is weakly acidic in nature unlike furan and thiophenes.
- Electrophilic substitution reactions of pyrrole are Friedel Craft Reaction , Kolbe reaction, Reimer Teimann reaction, Gattermann formylation Hoesch Houben .halogenation, Coupling, Nitration, sulphonation and mercuration with difficulty.
- Ring expansion



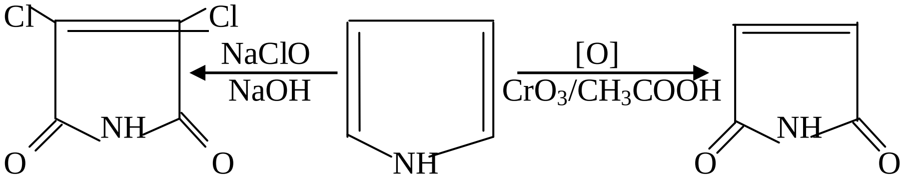
β-chloropyridine

- Ring opening



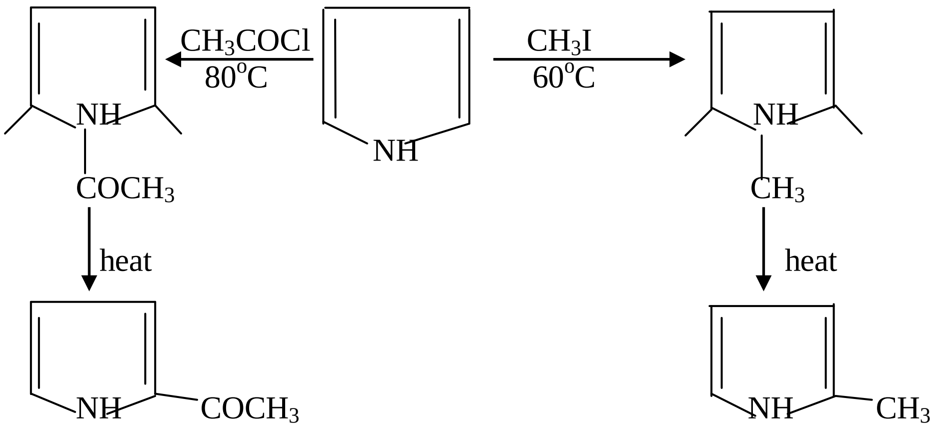
succinaldehyde dioxime

- Oxidation



Dichloromaleinimide Pyrrole maleinimide

- Pyrrole behave like phenyl amine (aniline) and phenol by reacting with acid halides like acetyl chloride and methyl iodide.



xviii. A pine-splint moistened with hydrochloric acid is turned fiery-red by pyrrole vapours.

## 6.0 Tutor Marked Assignment

Discuss the following electrophilic substitution of thiophene, furan and pyrrole:

- Halogenation
- Acylation
- Alkylation
- Nitration

## 7.0 Further Reading and other Resources

a. K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry
-Third Edition

b. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry
- Sixth Edition

c. John McMurry and Mary E.Castellion (1999) Fundamentals of General,Organic, and Biological Chemistry-3rd Edition

d. SCHAUM’S OUTLINES- Organic Chemistry (1999) -Third Edition

# Unit 3 – Six-membered Ring– Pyridine

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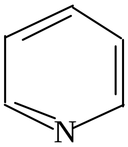
## 1.0: Introduction

The most imprudent member of this class containing one heteroatom is pyridine. It may be considered as derived from benzene by the replacement of a = CH – group by nitrogen atom = N-



## 2.0 Objectives

At the end of this unit you should be able to:

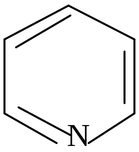
i. Discuss the various methods of preparing pyridine
ii. Name the isomers of pyridine using the IUPAC system
iii. Discuss the basic characters of pyridine
iv. Discuss the electrophilic substitution reaction, nucleophilic substitution reaction and other reactions of pyridine
v. Explain the structure of pyridine compared to benzene
vi. State the uses of pyridine
vii. List some derivatives of pyridine

## 3.0 Occurrences

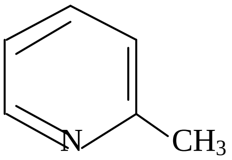
Pyridine occurs in coal tar in about 0.1% form from which it is obtained commercially

## 3.1 Nomenclature and Isomerism

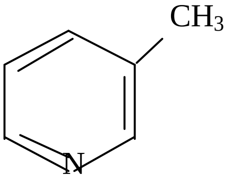
The IUPAC name for pyridine is azine, but it is rarely used. The ring atoms are denoted by numeral or Greek letters as shown below:



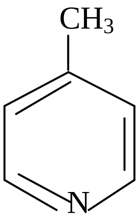
Pyridine



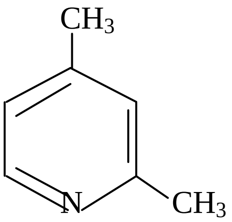
α-picoline
(2-picoline)



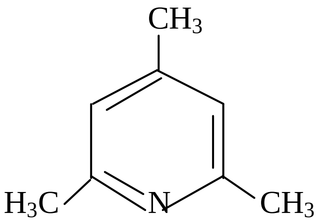
β-picoline
(3-picoline)



γ-picoline
(4-picoline)



2,4-Lutidine

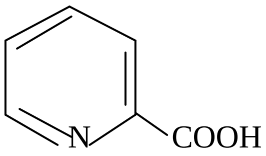


2,4,6-Collidine

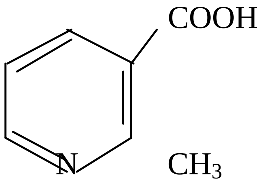
On monosubstitution, pyridine forms three isomer.

There is a need to pay special attention to the nomenclature of the derivatives because the common names are generally used. For example monomethylpyridine are known as picolines, the dimethylpyridines as known as lutidines and trimethylpyridine as collidines.

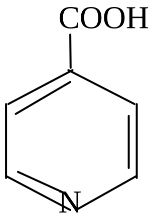
The α-,β-, and γ-pyridine carboxylic acids are referred to as picolinic, nicoctinic and isonicotinic acids respectively.



Picolinic acid
(Pyridine-2-carboxylic acid)



Nicotinic acid
(Pyridine-3-carboxylic acid)



Isonicotinic acid
(Pyridine-4-carboxylic acid)

## 3.2 preparations

a. From coal tar

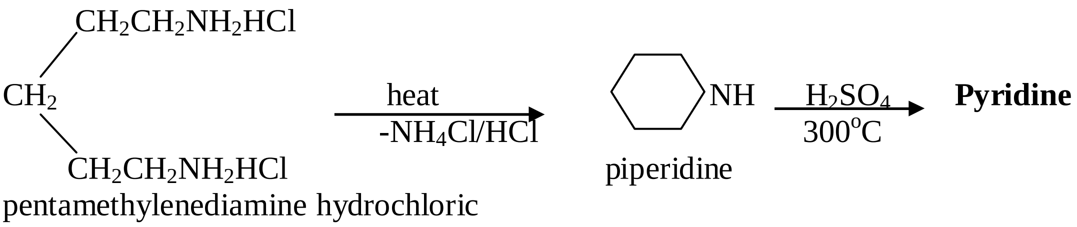
Pyridine can be isolated from the light oil fraction of coal tar. This fraction contains pyridine, alkyl pyridine, aromatic hydrocarbon and phenols. When the oil is treated with dilute tetraoxosulphate (vi) acids, pyridine and other basic substance are dissolved.The aqueous acid layer is neutralized with solium hydroxide when based are liberated as a dark brown oil liquid. The oily layer is seperated and pyridine is obtained by fractional distillation.

b. From ethyne and HCN

By passing through a red hot tube

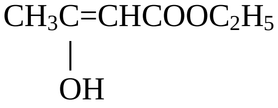
$$\underset{\text{ethyne}}{2CH\equiv CH} + HCN \longrightarrow \underset{\text{pyridine}}{C_6H_5N}$$

c. By heating pentamethylenediamine hydrochloric and oxidizing the product piperidine with concentrated tetraoxosulphate(vi) acid,$H_2S0_4$ at 300°C

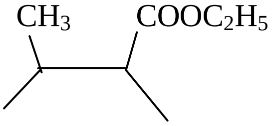


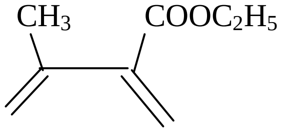
d. Hantzsch synthesis

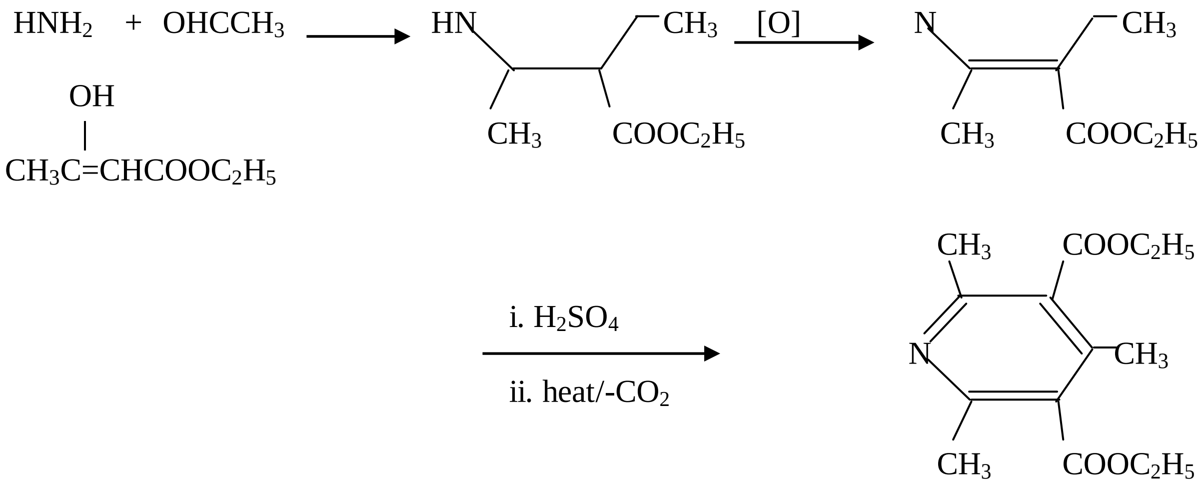
It involves the condensaton of a 3 – dicarbonyl compound (2moles), an aldehyde (I mole) and ammona (I mole) to give a dihydropyndine derivative. This derivative can be oxidised with nitric acid to yield pyridine derivative.



$$\underset{\displaystyle OH}{CH_3C}{=}CHCOOC_2H_5$$





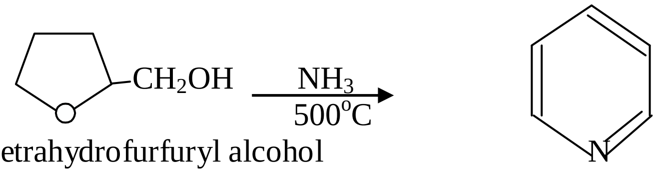


e. When acetylene, formaldehyde hemimetylal and ammonia is passed over alumina – silica catalyst at 500°C, it gives pyridine.

$$2HC{\equiv}CH + 2CH_2(OH)OCH_3 + NH_3 \xrightarrow{Al_2O_3/SiO_2} C_6H_5N + H_2O + 3CH_3OH$$

f. From tetrahydrofurfuryl alcohol

Industrially, pyridine can be obtained from the catalytic reduction of furfuryl alcohol with ammonia at 500°C.



Tetrahydrofurfuryl alcohol

## Activity A/Self Assessment Exercise

a. Explain how pyridine can be prepared from the following:
   i. THF   ii. Pentamethylenediamine   iii. HCN and ethyne   iv. Coal tar.

## 3.3 Properties of Pyridine

a. Physical properties

i. pyridine is a coloniless liquate (b.pt 115$^0$C)
ii. it is miscible with water in all proportion
iii. it is hygroscopic in nature
iv. it has a upbeat small
v. it is a good solvent for many organ and inorganic compounds.

b. Chemical properties

i. Basic Character

Pyridine is a base (pk$_b$ 8.8) of comparable strength with aniline (pk$_b$ 9.4). It is a stronger base than pyrrole (pk$_b$ = 13.6) but much weak than aliphatic tertiary amines (pkb = 4).

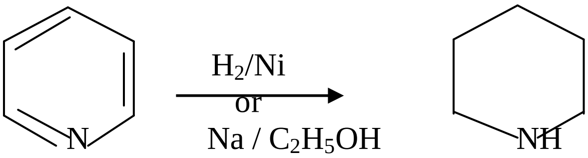
The basic character of pyridine is due to the availability of the lone pair of electrons on hetero atom nitrogen. Thus it reacts with alkyl halide to give quaternary salts.

$$C_5H_5N{:} + CH_3I \longrightarrow C_5H_5\overset{+}{N}CH_3I$$

Pyridine        N – Methyl pyridinium iodide

ii. Reduction

Catalytic hydrogenation of pyridine gives hexa–hydro pyridine known as piperidine. Reduction can also be carried out using Na / $C_2H_5OH$



Pyridine Piperidine

Piperidine($pK_b$ □ 3) is a strong base unlike pyridine .

iii. Addition of halogen

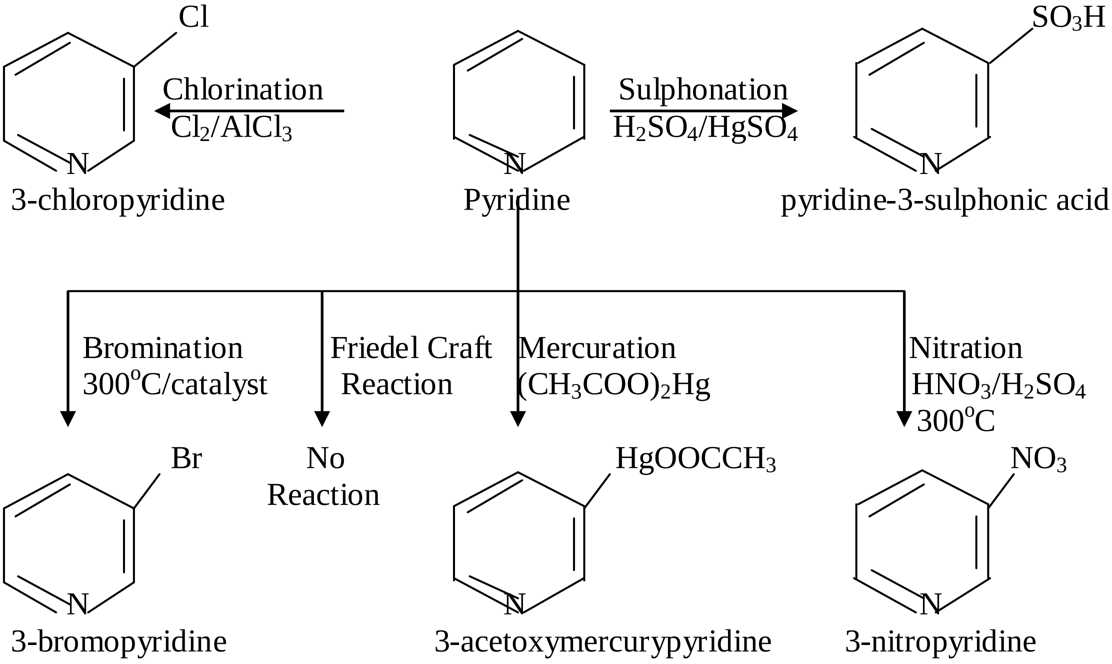
Pyridine add halogen at room temperature in the absence of catalyst to form a dihalide

$$C_5H_5N + Br_2 \longrightarrow C_5H_5\overset{+}{N}BrBr^-$$

iv. Electrophilic substitution reactions

Pyridine behaves as a highly deactivated aromatic nucleus towards electrophilic substitution reaction and vigorous reaction conditions must be employed for these reactions to occur. This low reactively towards electrohilic substitution by pyridine is due to two reasons:

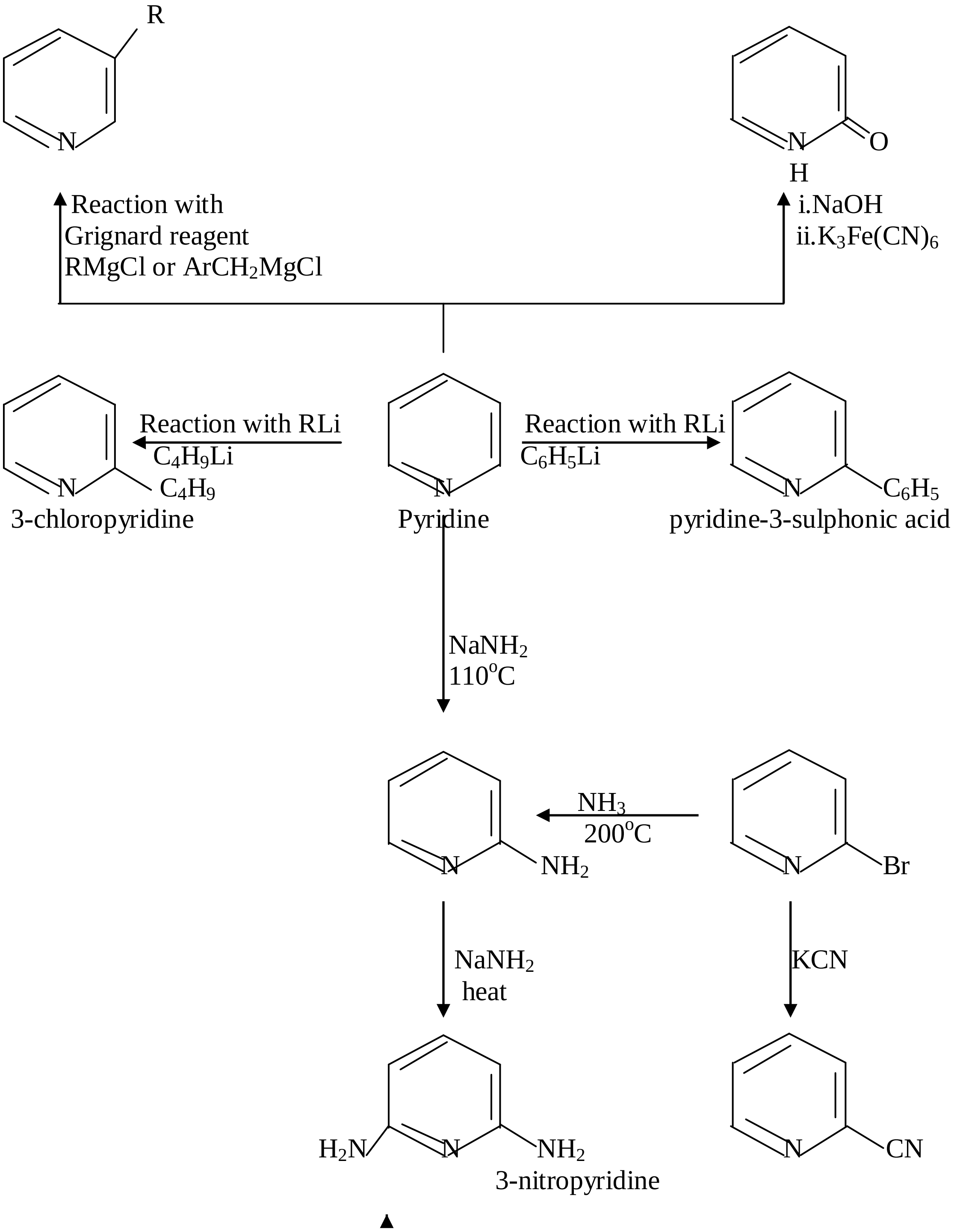
- because of the great electronegativly of nitrogen atom ,it decreases electron atom density of the ring (-I effect), hence deactivating the ring.
- In acidic medium, it forms a pyridine caption with a positive charge at way atom and this nitrogen decreases the election density much move effectively – thus deactivating the ring. The position -3 is however the least effective and is comparatively the position of highest electron density in pyridine.
-



v. Nucleophilic Substitution Reactions

Due to decrease of electron density on ring carbon atoms, pyridine is rendered susceptible to nucleophilic attack. The nucleophilic substitution occur readily at the 2 and 4 positions since these positions are much more electron deficient than position 3. The pyridinium ion is more reactive than pyridine toward nucleophilic substitution owing to the presence of full positive change.

The scheme below summarizes the nucleophilic substitution reaction of pyridine.



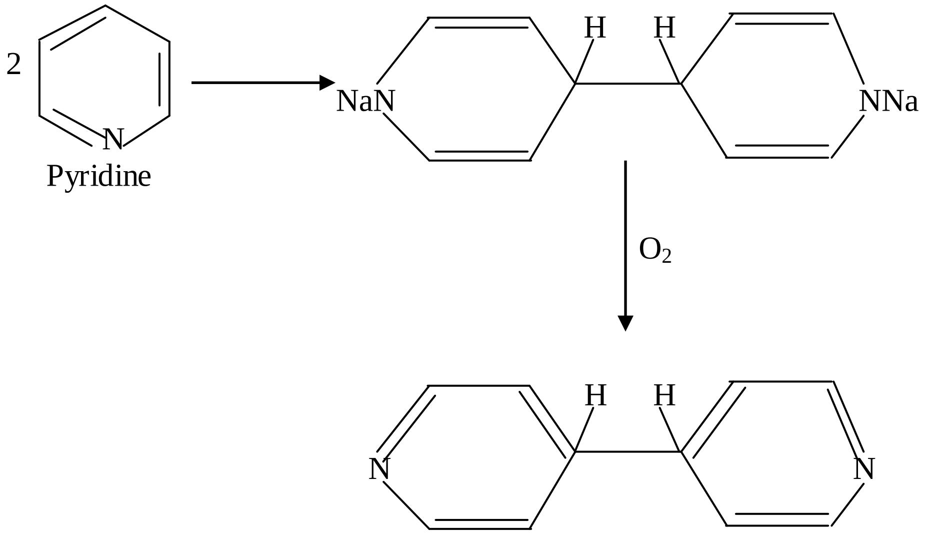
vi. Oxidation

It is oxidized by hydrogen peroxide or per acids to its N-oxide, pyridine-1-oxide is a resonance hybrid and undergoes nitration reaction at 4 – position unlike pyridine

vii. Miscellaneous reactions

a. With $SO_3$ Pyridine form a stable complex with sulphur trioxide. This complex is used in sulphonation of acid sensitive substances.

b. On treatment with sodium, two molecules of pyridine add to form a di-sodio derivative which when exposed to air yields 4,4’-dipyridyl. Small amounts of 2,2’-dipyridyl is also obtained.



4,4’-Dipyridyl

**Activity B/Self Assessment Exercise**

a. Give the products of the reaction of pyridine with:
i. NaOH, $K_3Fe(CN)_6$
ii. $Cl_2/AlCl_3$
iii. $H_2SO_4/HgSO_4$
iv. $CH_3I$
v. $CH_3MgCl$

b. List five physical properties of pyridine

## 3.4 Uses of Pyridine

i. Used as solvent and mild base in many organic reactions
ii. Used as a denaturant for ethyl alcohol
iii. For control of plant pests
iv. Used in the preparation of medicinals like sulphapyridine, isoniazid etc.
v. As catalyst in the preparation of Grignard reagents and in Perkin and Knoevenagel reactions
vi. As a solvent in the estimation of active hydrogen and epimerization
vii. Used in the identification of metals

## 3.5 Structure of Pyridine

a. The molecular formula is $C_5H_5N$.

b. The nature of the nitrogen- Pyridine is a monoacid tertiary base as shown by the following facts:

   i. It is basic in nature and forms quaternary salts with one mole of acid e.g.

$$C_5H_5N + HCl \longrightarrow \underset{\text{Pyridine hydrochloride}}{C_5H_5NHCl}$$

   ii. Its neutralization equivalent shows it is a monoacid

   iii. It does not react with acetyl chloride or $HNO_3$ showing the absence of primary or secondary nitrogen or amino group.

   iv. It reacts with one mole of methyl iodide to form a quaternary ammonium salt N-methylpyridinium iodide.

$$C_5H_5N + CH_3I \longrightarrow C_5H_5\overset{+}{N}CH_3\overset{-}{I}$$

c. The carbon skeleton- It is evidence from the molecular formula that it is highly unsaturated. Like benzene, it is also

   i. Resistant to addition reactions

   ii. Resistant to common oxidizing agents

   iii. Does not decolourise alkaline potassium tetraoxomanganate(vii) solution

Like benzene it undergoes electrophilic substitution reactions despite its unsaturation. So pyridine exhibits aromatic character. Its aromatic nature is further supported by the following:

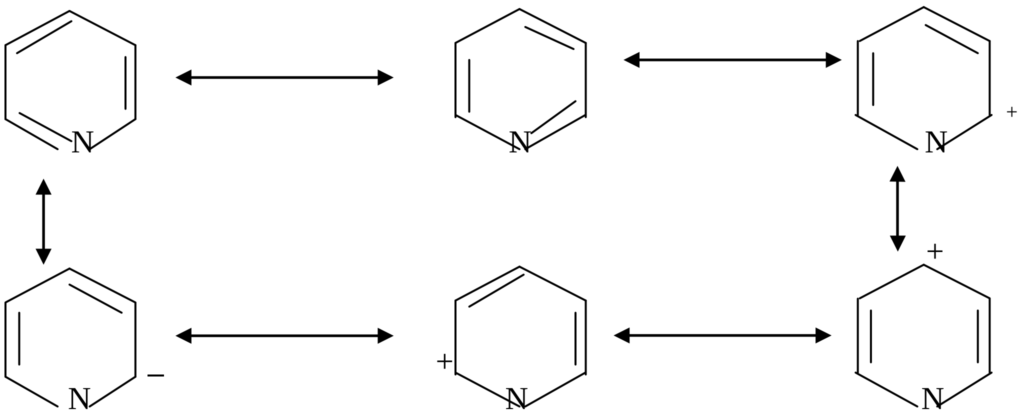
   i. It's alkyl derivatives are readily oxidized to pyridine carboxylic acids

$$\underset{\alpha\text{-, }\beta\text{-, or }\gamma\text{- Picolines}}{H_3CC_5H_4N} \xrightarrow{[O]} \underset{\alpha\text{-, }\beta\text{- or }\gamma\text{-Pyridinecarboxylic acids}}{HOOCC_5H_4N}$$

   ii. The amino derivatives of pyridine can be diazotized and coupled with phenols or amines etc, like aminobenzene

   iii. The halopyridine shows nucleophilic displacement of halogen by –NH2, -OH, -CN etc like the halogen of halonitrobenzenes.

The present day structure shows that pyridine is a resonance structure of the following structures:



Resonance representation of pyridine

- All the carbon, nitrogen and hydrogen atoms lie in the same plane
- The four carbon-carbon bond lengths in pyridine are equal- 1.39Å and the carbon – hydrogen bond length are equal-1.37Å.
- It resists addition due to the absence of true double bonds
- Due to the presence of positive charges at the 2- or 4- position in the contributing structure, it behaves as deactivated system in electrophilic substitution, which occurs at position-3.
- It's resonance energy is 23kcal/mol as compared to -6 kcal/mol in ordinary conjugated trienes.

From the molecular orbital concept, the nitrogen and each of the carbon atoms in pyridine are in the sp2 hybridisation state. They combine together to form a ring utilizing two of their sp2 hybrid trigonal orbitals for forming α-bonds. The remaining sp2 orbital at the five carbon atoms overlap with s-orbital of hydrogen to form σ-bonds while the third sp2 orbital of the nitrogen contains the lone pair of electrons which remains unshared. The unhybridised p orbitals at each of the carbon and nitrogen atom overlaps with each other to form π cloud of electrons below and above the plane of the ring like in benzene.

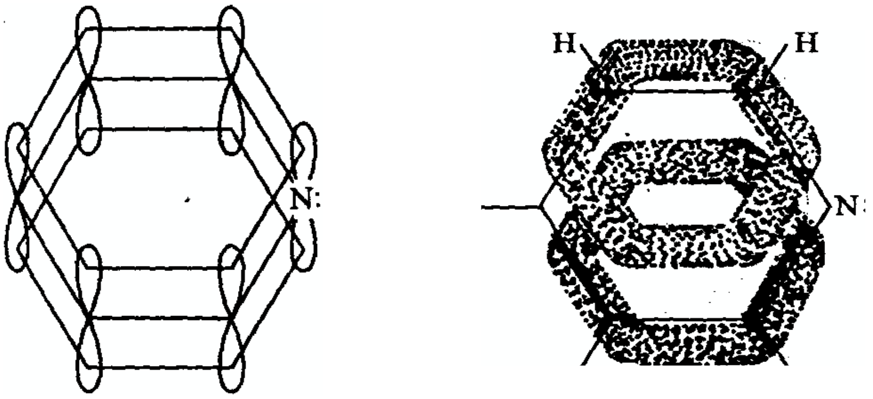
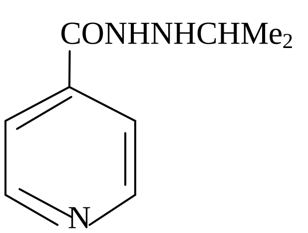


**Fig 1.1 Molecular Orbital Picture of Pyridine**
(Source: A Textbook of Organic Chemistry,3rd Edition-By K.S Tewari and N.K.Vishnoi)

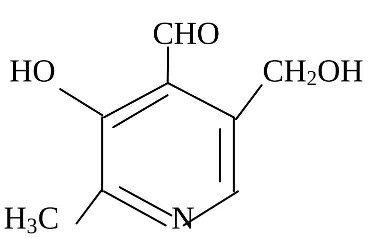
However, due to greater electronegativity of nitrogen, the π- electron cloud is displaced slightly towards nitrogen and the electron density is below unity at all carbon atoms. Position three is the least affected and it is the position with the highest electron density, making it the favoured position for electrophilic substitution.

## 3.6 Derivatives of Pyridine

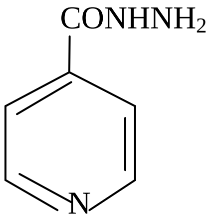
The following are the names and formulae of important derivatives of pyridine that are of physiological and medicinal significance.



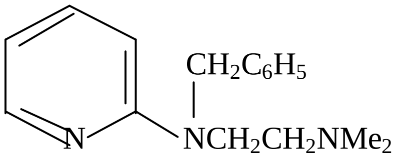
Iproniazid(Psychic stimulant)



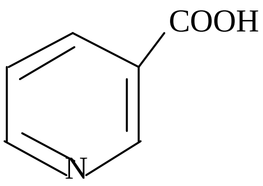
Pyridoxal(Vitamin B6)



Isoniazid
(Antitubercular drug)



Pyribenzamine
( Antihistaminic drug)



Nicotinic acid
(Vitamins)

## Activity C/Self Assessment Exercise

a. Explain why pyridine would rather undergo electrophilic substitution reactions than addition reaction.
b. State some medicinal importance of pyridine

## 4.0 Conclusion

Pyridine is six-membered heterocyclic compound that has basic characters similar to that of aninile. It undergoes mainly electrophilic substitution because of its aromatic characters which shows great resemblance to that of benzene.

## 5.0 Summary

In this unit we have learnt that:
i. The IUPAC name for pyridine is azine,
ii. Pyridine can be prepared from the following

- Coal tar
- Ethyne and HCN
- By heating pentamethylenediamine hydrochloric and oxidizing the product piperidine with concentrated tetraoxosulphate(vi) acid,$H_2S0_4$ at $300^oC$
- Hantzsch synthesis
- When acetylene, formaldehyde hemimetylal and ammonia is passed over alumina – silica catalyst at $500^oC$.
- From tetrahydrofurfuryl alcohol

iii. Pyridine is a colourless liquid (b.pt $115^0C$), miscible with water in all proportion,hygroscopic in nature and it is a good solvent for many organic and inorganic compounds.

iv. Pyridine show the following chemical properties

- Pyridine is a base ($pk_b$ 8.8) of comparable strength with aniline ($pk_b$ 9.4). It is a stronger base than pyrrole ($pk_b$ = 13.6) but much weak than aliphatic tertiary amines (pkb = 4).
- The basic character of pyridine is due to the availability of the lone pair of electrons on hetero atom nitrogen.
- It reacts with alkyl halide to give quaternary salts.

$$C_5H_5N: + CH_3I \longrightarrow C_5H_5\overset{+}{N}CH_3I$$

Pyridine N – Methyl pyridinium iodide

- Reductio- Catalytic hydrogenation of pyridine gives hexa–hydro pyridine known as piperidine. Reduction can also be carried out using Na / $C_2H_5OH$
- Addition of halogen

$$C_5H_5N + Br_2 \longrightarrow C_5H_5NBrBr^-$$

- Electrophilic substitution reactions examples are sulphonation, halogenations, Friedel Craft reaction, nitration etc are possible with pyridine.

- Nucleophilic Substitution Reactions: Reactions with Grignard reagent, NaOH, RLi and $NaNH_2$
- Pyridine form a stable complex with sulphur trioxide

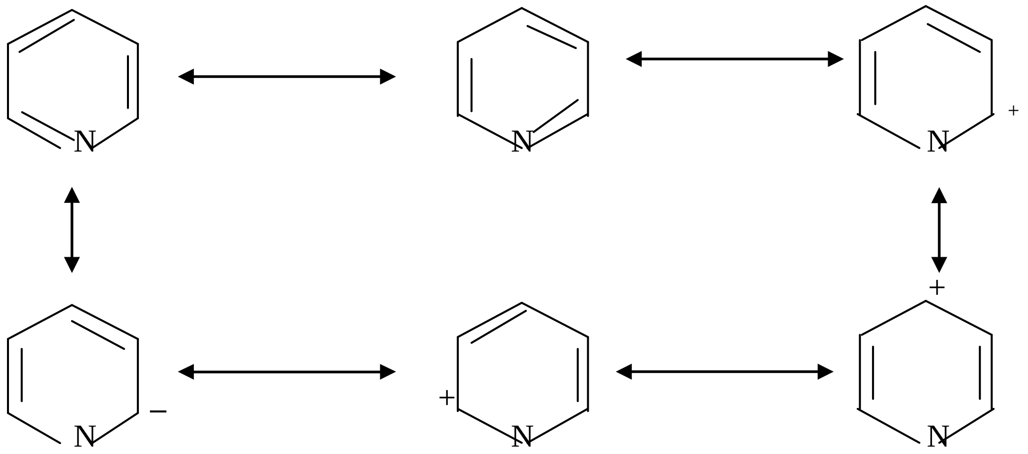
- Two molecules of pyridine with sodium add to form a di-sodio derivative .

v. Some uses of pyridine are :as solvent and mild base in many organic reactions, as a denaturant for ethyl alcohol, for control of plant pests, in the preparstion of medicinals like sulphapyridine, isoniazid etc.,catalyst in the preparation of Grignard reagents and in Perkin and Knoevenagel reactions, a solvent in the estimation of active hydrogen and epimerization and used in the identification of metals

vi . The molecular formula is $C_5H_5N$.

vii. Pyridine is a monoacid tertiary base, highly unsaturated like benzene.

viii. The structure shows that pyridine is a resonance hybride of the following structures:



ix. Iproniazid(Psychic stimulant) , Pyridoxal(Vitamin B6) Isoniazid , Pyribenzamine and Nicotinic acid are important derivatives of pyridine that are of physiological and medicinal significance.

## 6.0 Tutor|Marked Assignment

a. Describe the preparation and synthesis of pyridine

b. Discuss the electrophilic and nucleophilic substitution reactions of pyridine

## 7.0 Further Reading and other Resources

a. K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry
-Third Edition

b.Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry - Sixth Edition

c. John McMurry and Mary E.Castellion (1999) Fundamentals of General,Organic, and Biological Chemistry-3rd Edition

d. SCHAUM'S OUTLINES- Organic Chemistry(1999-Third Edition

# Module 6: Polyfunctional Compounds
# Unit 1: Dicarboxylic Acids and Their Derivatives

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## 1.0 Introduction

As the name suggested, dicarboxylic acids contain two carboxyl groups. They may be saturated and they may be unsaturated. Saturated dicarboxylic acids have the general formula $C_nH_{2n}(COOH)_2$., n may be equal or greater than 0.

## 2.0 Objective

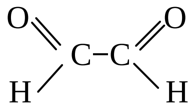
At the end of this unit you should be able to:

- i. Draw the structure of dicarboxylic acids
- ii. Name dicarboxylic acids
- iii. Explain the chemical properties of dicarboxylic acid
- iv. Draw the structure of malonic ester and acetoacetic ester-derivatives of dicarboxylic acid
- v. Explain the chemistry of malonic ester and acetoacetic ester
- vi. Explain the importance of the methylene group in the chemistry of malonic ester and acetoacetic ester
- vii. Describe some synthetic application of malonic ester and acetoacetic ester

## 3.0 Naming Dicarboxylic acids

The saturated dicarboxylic acids are usually named according to the source from which they are obtained. For example, the oxalic acid is obtained from a plant of the oxalis group.

Using the IUPAC system the suffix dioic acid is added to the name of the parent alkane. For example:



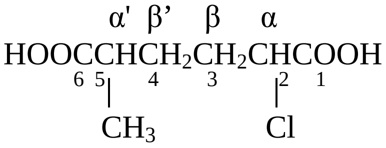
Ethanedioic acid(from ethane)
(Oxalic acid)

TABLE: 1.1 Common and IUPAC names of Important Saturated Dicarboxylic acids

| Formula | Common Name | IUPAC Name |
|---|---|---|
| $(COOH)_2$ | Oxalic acid | Ethanedioic acid |
| $CH_2(COOH)_2$ | Malonic acid | Propanedioic acid |
| $(CH_2)_2(COOH)_2$ | Succinic acid | Butanedioic acid |
| $(CH_2)_3(COOH)_2$ | Glutaric acid | Pentanedioic acid |
| $(CH_2)_4(COOH)_2$ | Adipic acid | Hexanedioic acid |
| $(CH_2)_5(COOH)_2$ | Pinelic acid | Heptanedioic acid |
| $(CH_2)_6(COOH)_2$ | Suberic acid | Octanedioic acid |
| $(CH_2)_7(COOH)_2$ | Azelaic acid | Nonanedioic acid |
| $(CH_2)_8(COOH)_2$ | Sebacic acid | Decanedioic acid |

In the common system, the position of substituents is indicated by Greek letters while in the IUPAC system, it is indicated by numbers.

For example,



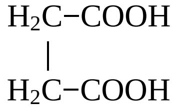
$$\overset{6}{HOOC}\overset{\alpha'}{\underset{\substack{5|\\ CH_3}}{C}H}\overset{\beta'}{\underset{4}{CH_2}}\overset{\beta}{\underset{3}{CH_2}}\overset{\alpha}{\underset{\substack{|2\\ Cl}}{C}H}\underset{1}{COOH}$$

α-chloro-α’-methyladipic acid(common name)
2-chloro-5-methylhexan-1,6-dioic acid(IUPAC name)

## 3.1 Isomerism

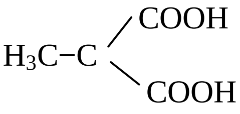
Dicarboxylic acids show position isomerism.

For example,



$$\begin{matrix} H_2C-COOH \\ | \\ H_2C-COOH \end{matrix}$$

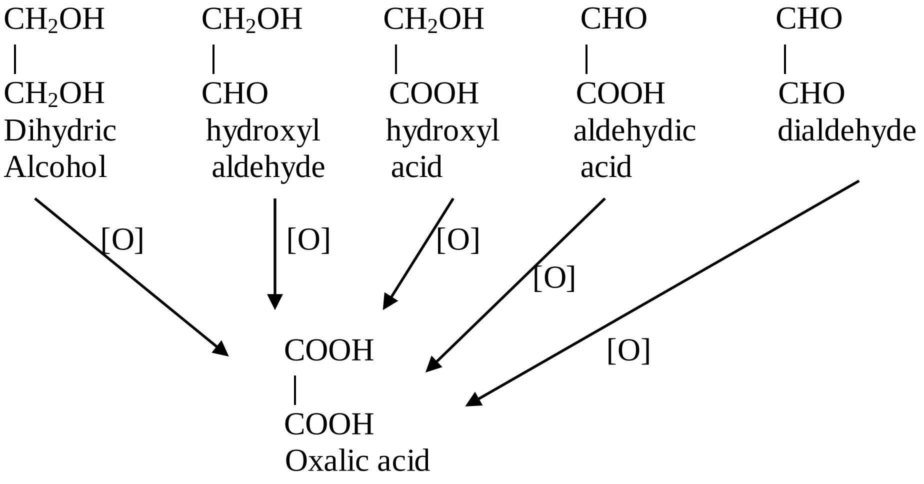
Succinic acid



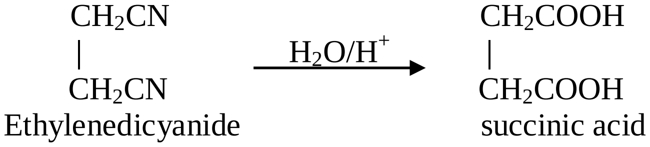
Methylmalonic acid

## 3.2 General Methods of Preparation

i. By oxidation of dihydric alcohols, hydroxyl aldehydes, hydroxy acids, dialdehydes and aldehydic acids with dilute $HNO_3$ or potassium tetraoxomanganate (VII).

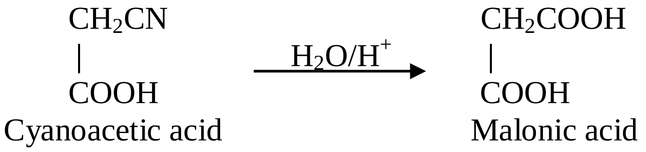


ii. Hydrolysis of dicyanides or cyano acids



$$\begin{matrix} CH_2CN \\ | \\ CH_2CN \end{matrix} \xrightarrow{H_2O/H^+} \begin{matrix} CH_2COOH \\ | \\ CH_2COOH \end{matrix}$$

Ethylenedicyanide succinic acid



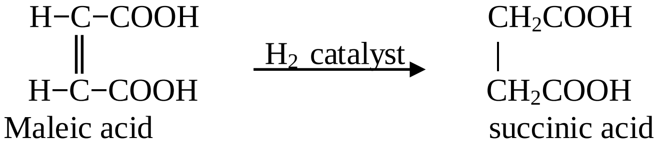
$$\begin{matrix} CH_2CN \\ | \\ COOH \end{matrix} \xrightarrow{H_2O/H^+} \begin{matrix} CH_2COOH \\ | \\ COOH \end{matrix}$$

Cyanoacetic acid Malonic acid

iii. By treating halogen substituted monocarboxylic acid ester with zinc or silver and hydrolysing the ester thus obtained.

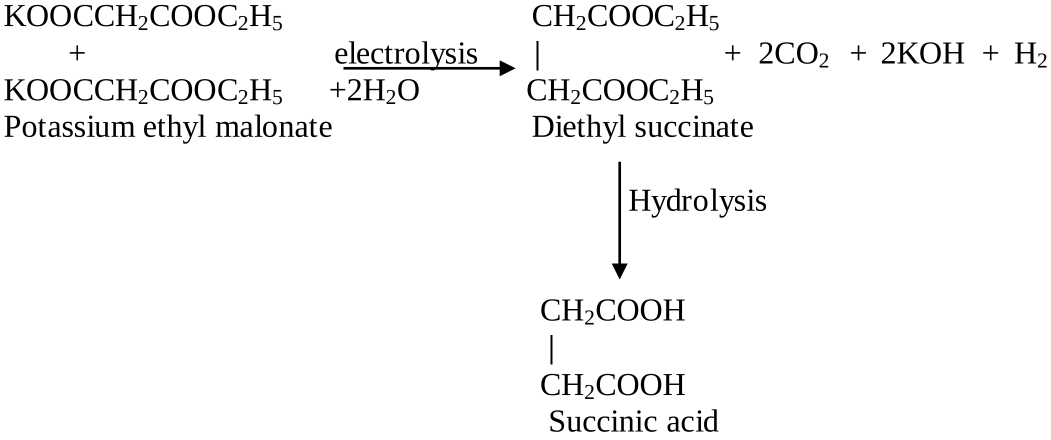
$$\underset{\beta\text{-iodopropionic ester}}{C_2H_5OOCCH_2CH_2I} + 2Ag + ICH_2CH_2COOC_2H_5 \xrightarrow{-2AgI} \underset{\text{diethyl adipate}}{C_2H_5OOC(CH_2)_4COOC_2H_5} \xrightarrow[-2C_2H_5OH]{2H_2O} \underset{\text{Adipic acid}}{HOOC(CH_2)_4COOH}$$

iv. By reduction of unsaturated dicarboxylic acid



$$\underset{\text{Maleic acid}}{\begin{array}{c}H-C-COOH\\ \| \\ H-C-COOH\end{array}} \xrightarrow{H_2\ \text{catalyst}} \underset{\text{succinic acid}}{\begin{array}{c}CH_2COOH\\ | \\ CH_2COOH\end{array}}$$

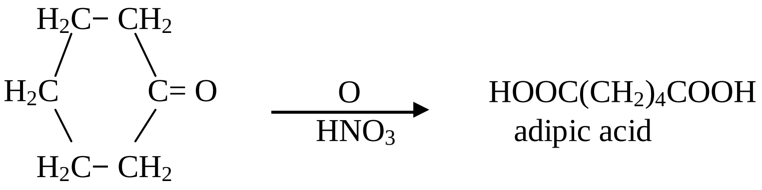
v. By hydrolysis of aqueous solution of potassium alkyl ester of dibasic acid



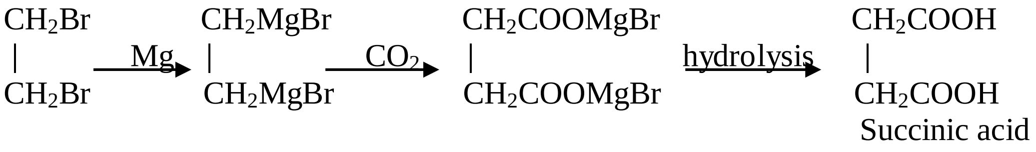
$$\underset{\text{Potassium ethyl malonate}}{\begin{array}{c}KOOCCH_2COOC_2H_5\\ + \\ KOOCCH_2COOC_2H_5\end{array}} \xrightarrow[+2H_2O]{\text{electrolysis}} \underset{\text{Diethyl succinate}}{\begin{array}{c}CH_2COOC_2H_5\\ | \\ CH_2COOC_2H_5\end{array}} + 2CO_2 + 2KOH + H_2$$

$$\xrightarrow{\text{Hydrolysis}} \underset{\text{Succinic acid}}{\begin{array}{c}CH_2COOH\\ | \\ CH_2COOH\end{array}}$$

vi. By oxidation of cyclic ketone



vii. From Grignard reagent of dihaloalkane.

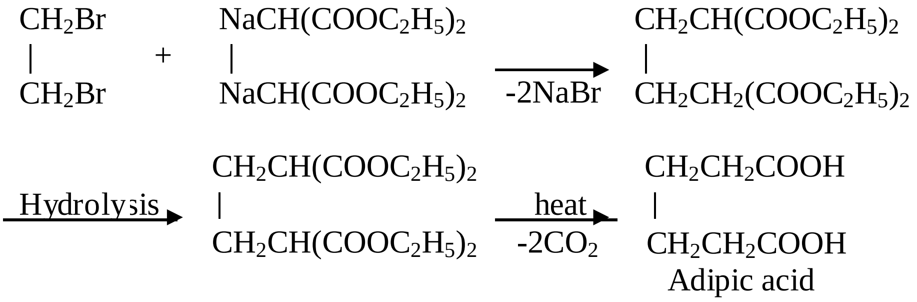


$$\begin{array}{c}CH_2Br\\ | \\ CH_2Br\end{array} \xrightarrow{Mg} \begin{array}{c}CH_2MgBr\\ | \\ CH_2MgBr\end{array} \xrightarrow{CO_2} \begin{array}{c}CH_2COOMgBr\\ | \\ CH_2COOMgBr\end{array} \xrightarrow{\text{hydrolysis}} \underset{\text{Succinic acid}}{\begin{array}{c}CH_2COOH\\ | \\ CH_2COOH\end{array}}$$

viii. By oxidation of unsaturated acids

$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH \xrightarrow{HNO_3} CH_3(CH_2)_7COOH + HOOC(CH_2)_7COOH$

ix. By the action of dihaloalkanes on sodiomalonic ester



$$\begin{matrix} CH_2Br \\ | \\ CH_2Br \end{matrix} + \begin{matrix} NaCH(COOC_2H_5)_2 \\ | \\ NaCH(COOC_2H_5)_2 \end{matrix} \xrightarrow[-2NaBr]{} \begin{matrix} CH_2CH(COOC_2H_5)_2 \\ | \\ CH_2CH_2(COOC_2H_5)_2 \end{matrix}$$

$$\xrightarrow{Hydrolysis} \begin{matrix} CH_2CH(COOC_2H_5)_2 \\ | \\ CH_2CH(COOC_2H_5)_2 \end{matrix} \xrightarrow[-2CO_2]{heat} \begin{matrix} CH_2CH_2COOH \\ | \\ CH_2CH_2COOH \end{matrix}$$

Adipic acid

## ACTIVITY A/Self assessment exercise

Discuss the preparation of oxalic acid by oxidation

## 3.3 General Physical Characteristics

i. State: All dicarboxylic acids are colourless crystalline solids

ii. Solubility: Lower members are soluble in water. Solubility in water decreases as molecular mass increases while in ether the solubility increases as molecular mass increases

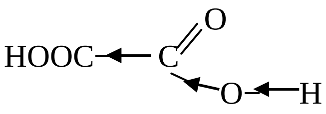
iii. Melting points: Melting points of acids with even number of carbon atoms are higher than those with odd number of carbon atoms. This is because the arrangement of the carbon atoms is zigzag in odd number acids with the two carboxyl groups on the same side, while they are on opposite sides in even number acids.

iv. Acid strength of these acids decrease with increase in molecular weight. Dicarboxylic acids dissociate in two steps:

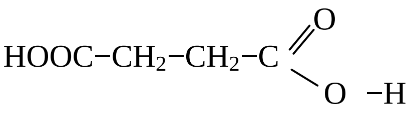
$$HOOC{-}COOH \xrightleftharpoons{K1} {}^{-}OOC{-}COOH + H^+$$

$$^{-}OOC{-}COOH \xrightleftharpoons{K2} {}^{-}OOC{-}COO^{-} + H^+$$

The first dissociation constant K1 is higher than the second dissociation constant K2. It is also higher than that of the corresponding monocarboxylic acid. The higher value of K1 is due to the –I effect of one carboxylic group on the other. This effect becomes weaker due to intervening effect of $-CH_2$ group between two



K1 = 54



K1 = 6.4 × $10^{-5}$

carboxyl groups. The lower value of K2 is due to +I effect of carboxyl group (-COO⁻). Further the electrostatic repulsion due to negative charges at the ends of the dianion (⁻OOC−COO⁻) destabilizes the dianion and reduce the K2 value.

## 3.4 General Chemical Properties

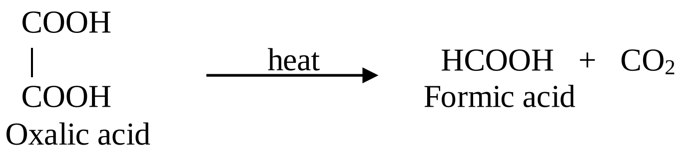
The chemical reactions of dicarboxylic acids are mainly governed by the reactivity of the carboxyl groups. Oxalic acid differs from the other members because it does not contain the hydrocarbon chain and it consists of two carboxyl groups only.

I. Reaction due to carboxyl group: Dicarboxylic acids show the usual reactions of carboxyl group. However, because they have two carboxyl groups they form two series of salts, esters, amides and other acid derivatives. For example, succinic acid form the following derivatives:

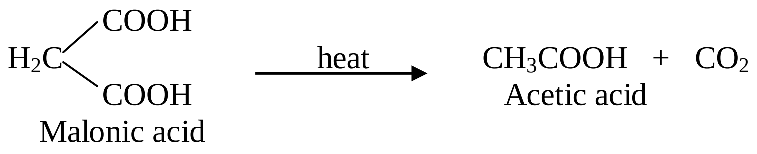
| | | | |
|---|---|---|---|
| $CH_2COONa$<br>\|<br>$CH_2COOH$<br>Acid sodium<br>Succinate | $CH_2COOC_2H_5$<br>\|<br>$CH_2COOH$<br>acid ethyl<br>succinate | $CH_2COCl$<br>\|<br>$CH_2COOH$<br>acid succinyl<br>chloride | $CH_2COONH_2$<br>\|<br>$CH_2COOH$<br>acids succinamide |
| $CH_2COONa$<br>\|<br>$CH_2COONa$<br>Sodium<br>Succinate | $CH_2COOC_2H_5$<br>\|<br>$CH_2COOC_2H_5$<br>Ethyl<br>succinate | $CH_2COCl$<br>\|<br>$CH_2COCl$<br>Succinyl<br>chloride | $CH_2CONH_2$<br>\|<br>$CH_2CONH_2$<br>Succinamide |

II. Action of Heat: The product formed on heating depends on the relative positions of the two carboxyl groups.

   i. When two carboxyl groups are attached to the same carbon, e.g oxalic acid, malonic acids, $CO_2$ is given off:

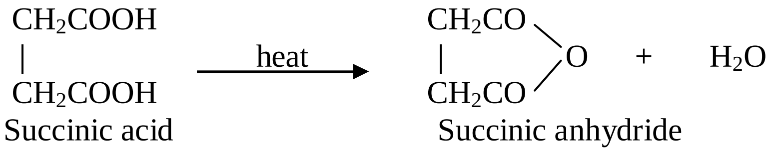


$$\begin{matrix} COOH \\ | \\ COOH \end{matrix} \xrightarrow{heat} HCOOH + CO_2$$

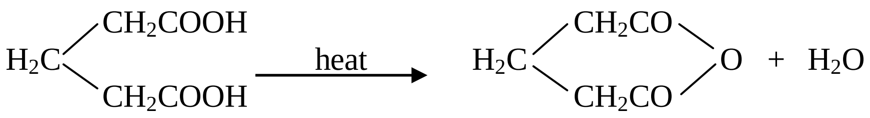


$$H_2C(COOH)_2 \xrightarrow{heat} CH_3COOH + CO_2$$

   ii. Higher acids in which the carboxyl groups are separated by two or three carbon atoms lose a molecule of water on heating or by distilling with acetic anhydride to give the corresponding anhydride.

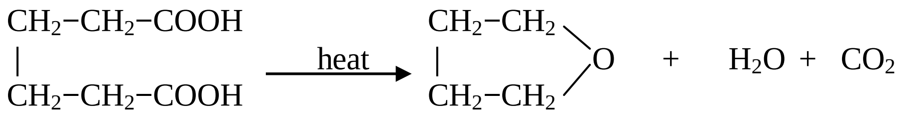


$$\begin{matrix} CH_2COOH \\ | \\ CH_2COOH \end{matrix} \xrightarrow{heat} \begin{matrix} CH_2CO \\ | \\ CH_2CO \end{matrix} \!\!> O + H_2O$$

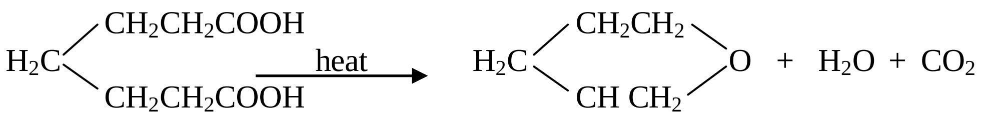


Glutaric acid Glutaric anhydride

iii. When the carboxyl groups are separated by four or more carbon atoms e.g Adipic and pimelic acids, cyclic ketones are formed when distilled with acetic anhydride.

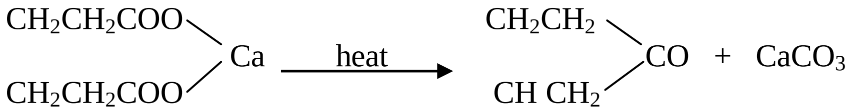


Adipic acid Cyclopentanone



Pimelic acid Cyclohexanone

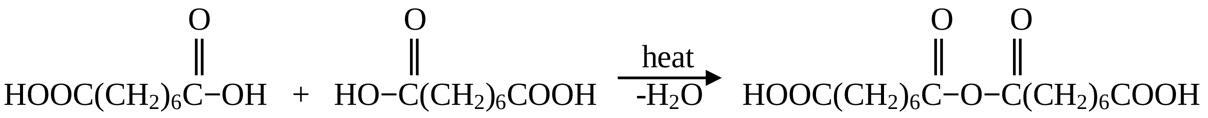
Ketone is formed when the calcium salt of adipic and pimelic acids are heated.



Calcium adipate Cyclopentanone

The products from the action of heat on dicarboxylic acids can be summed up by Blanc's rule that state that on distilling alone or with acetic anhydride at 300$^{O}$C, a dicarboxylic acid may yield an anhydride or a cyclic ketone according to the relative positions of carboxyl groups. 1:4 and 1;5 dicarboxylic acids give anhydride, while 1:6 and 1:7 dicarboxylic acids yield cyclic ketones and 1:8 or higher dicarboxylic acids undergo intermolecular dehydration to form linear polymers.

iv. Higher dicarboxylic acid(1:8 dicarboxylic acids) undergo intermolecular dehydration to form linear polymers.



$$HOOC(CH_2)_6\overset{\overset{O}{\|}}{C}-OH + HO-\overset{\overset{O}{\|}}{C}(CH_2)_6COOH \xrightarrow[-H_2O]{heat} HOOC(CH_2)_6\overset{\overset{O}{\|}}{C}-O-\overset{\overset{O}{\|}}{C}(CH_2)_6COOH$$

Suberic acid Suberic acid Dimer

## Activity B/Self Assessment Exercise

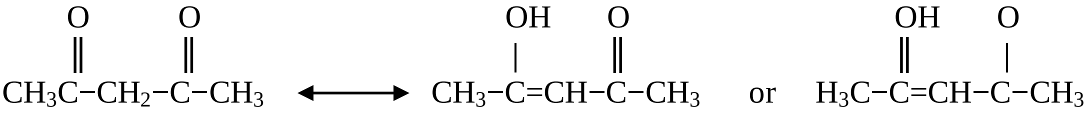
List and name the likely esters, amides and acid derivatives that one would expect adipic acid to form.

## 3.5 Uses of Dicarboxylic acids

Oxalic acid, a common dicarboxylic acid is used in the manufacture of inks, metal polishes, and oxalates. It is also used for textile printing.

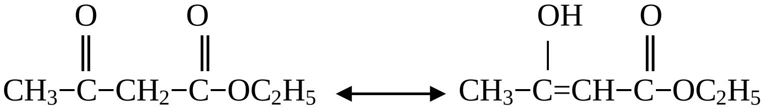
## 3.6 Reactive Methylene Group in reactions

When a methylene group is present between two strongly electronegative (electron attracting) group such as >C=O or −C≡N, the hydrogen atoms of methylene group (called α-hydrogen, being present on carbon atom next to functional groups on either side) become reactive or acidic. Such compounds exist in keto – enol equilibrium. If the compound is symmetrical the hydrogen atom of the methylene group migrates to either of the keto groups but if the compound is unsymmetrical only one form is present exclusively or predominantly and the migration of the hydrogen atom depends upon the inductive effect of the alkyl or other groups present on either side of >$CH_2$ group.



$$CH_3\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-CH_3 \longleftrightarrow CH_3-\overset{\overset{OH}{|}}{C}=CH-\overset{\overset{O}{\|}}{C}-CH_3 \quad \text{or} \quad H_3C-\overset{\overset{OH}{\|}}{C}=CH-\overset{\overset{O}{|}}{C}-CH_3$$

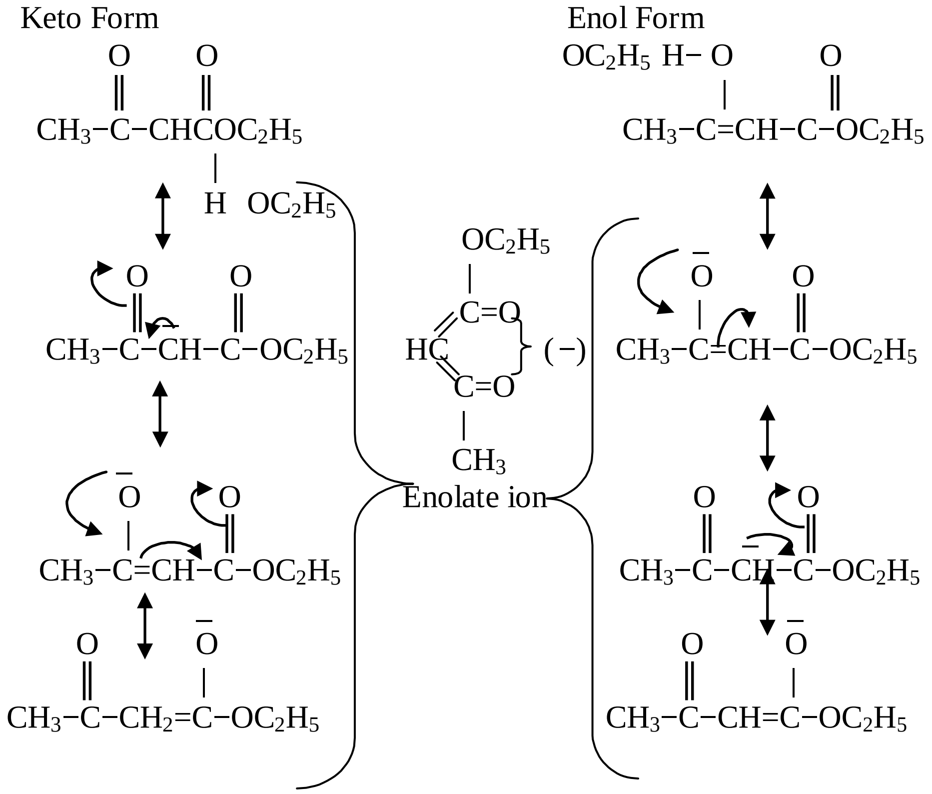
Acetylacetone　　　　　　　Enol form
(unsymmetrical compound)　　(two similar forms)



$$CH_3-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-OC_2H_5 \longleftrightarrow CH_3-\overset{\overset{OH}{|}}{C}=CH-\overset{\overset{O}{\|}}{C}-OC_2H_5$$

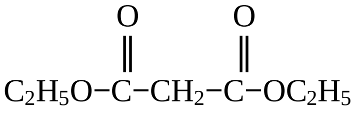
Ethyl acetoacetate　　　　Enol form
(unsymmetrical)　　　　　Only one form

When a compound containing active methylene group reacts with a strong base the proton removal may take place from both, keto and enol forms and the resultant enolate (a carbanion stabilized by an adjacent carbonyl group, is often called an enolate ion) obtained by resonance stabilization is same in both cases.

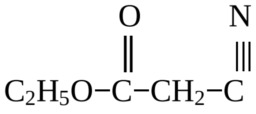


(SOURCE: A Textbook of Organic Chemistry. Third Edition. K.S.Tewari and NK, Vishnoi)

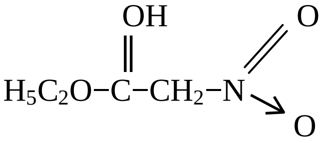
Some other functional groups like nitro, ester etc. also make methylene group reactive. Other such compounds which have an active methylene group are diethylmalonate, ethyl cyanoacetate, ethyl nitroacetate etc.



$C_2H_5O-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-OC_2H_5$



$C_2H_5O-\overset{O}{\overset{\|}{C}}-CH_2-C\equiv N$

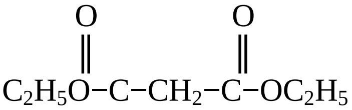


$H_5C_2O-\overset{OH}{\overset{\|}{C}}-CH_2-N\genfrac{}{}{0pt}{}{\nearrow O}{\searrow O}$

In such compound hydrogen of $>CH_2$ group can be easily replaced by sodium or potassium. These sodium derivatives serve as the point for a number of synthetic products.

## 3.7 MALONIC ESTER, DIETHYL MALONATE, $H_2C(COOC_2H_5)_2$

Malonic ester an important synthetic reagent with the formula $H_2C(COOC_2H_5)_2$.



$C_2H_5O-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-OC_2H_5$

Malonic Ester

### 3.7.1 Methods of Preparation

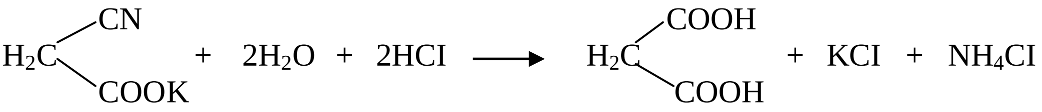
(i) Malonic ester is prepared by passing dry hydrogen chloride gas through a mixture containing absolute alcohol and potassium cyanoacetate, On warming the mxiture the cyanoacetate gets hydrolysed to malonic acid, which gets esterified by alcohol. Potassium cyanoacetate employed is prepared in situ from chloroacetic acid by cyanide synthesis.

$$CH_3COOH \xrightarrow[1_2]{CI_2} CI.CH_2COOH \xrightarrow{K_2CO_3} CI.CH_2COOK$$

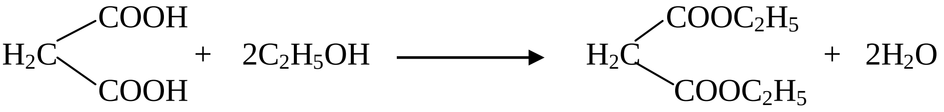
Acetic acid — Monochloroacetic acid — Potassium monochloroacetate

$$\xrightarrow{KNC} CN.CH2COOK$$

Potassium cyanoacetate



Malonic acid



(ii) It may also be prepared in good yield by refluxing cyanoacetic acid with ethylalcohol in the presence of chlorosulphonic acid.

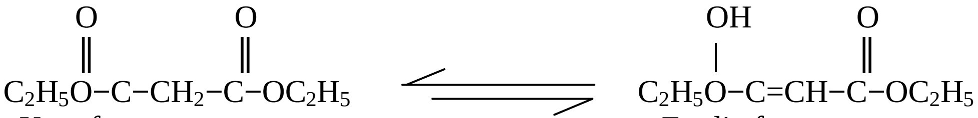
### 3.7.2 General Properties

Physical Properties

i. Malonic ester is a colourless liquid with a pleasant smell
ii. Boiling point is 199°C
iii. It is sparingly soluble in water, but soluble in alcohol, benzene and chloroform

### 3.7.3 Chemical Properties

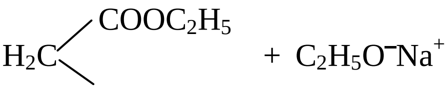
The structure of malonic ester shows the presence of two carbonyl groups, one each on either side of methylene group, this exerts a –I effect. Also Malonic ester is from an anion which is stabilized by resonance since it can exist in two forms - enol and keto forms.The presence of the methylene group, added to the formation of resonance stabilized anion make the hydrogen of the group active (acidic). It exists in following keto-enol tautomeric forms, the enol form being present in much smaller amount.

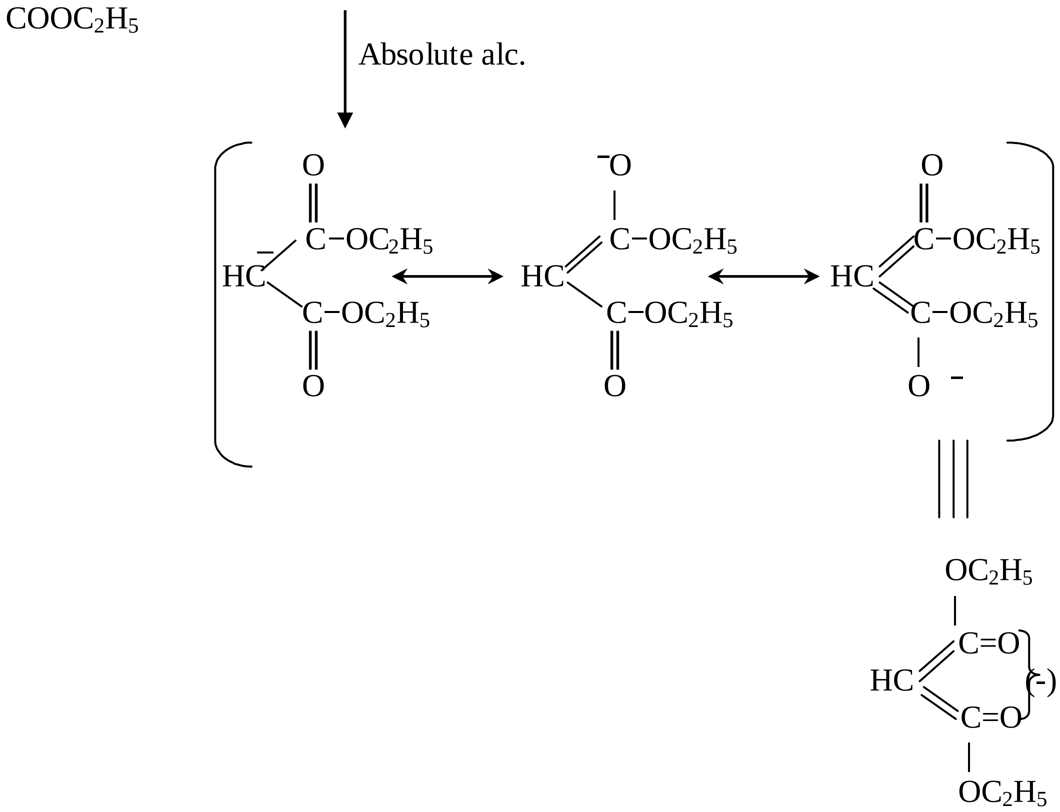


$$C_2H_5O-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-OC_2H_5 \rightleftharpoons C_2H_5O-\overset{\overset{OH}{|}}{C}=CH-\overset{\overset{O}{\|}}{C}-OC_2H_5$$

Keto form — Enolic form

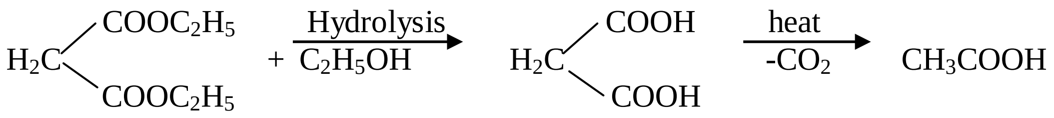
Because of the presence of active methylene group, it behaves as an acid. When it reacts with sodium ethoxide in absolute alcohol, if forms sodio malonic ester, the anion being resonance stabilized.





The anion acts as a nucleophile and can participate intypical nucleophilic substitution reactions to give rise to substituted malonic esters. It is a valuable synthetic reagent. Some of its synthetic applications are mentioned below:

a. Synthesis of monocarboxylic acids. Malonic ester on hydrolysis forms malonic acid which when heated to 150 –200$^0$C , decarboxylates to form acetic acid.



Higher fatty acids can be prepared by treating the sodio derivative of the ester with alkyl halide followed by hydrolysis and decarboxylation. For example N-Butyric acid can be obtained as shown below:

$$CH_2(COOC_2H_5)_2 \xrightarrow[-C_2H_5OH]{NaOC_2H_5} \underset{\text{Sodiomalonic ester}}{NaCH(COOC_2H_5)} \xrightarrow[-NaBr]{C_2H_5Br} \underset{\text{Ethyl malonic ester}}{C_2H_5CH(COOC_2H_5)_2}$$

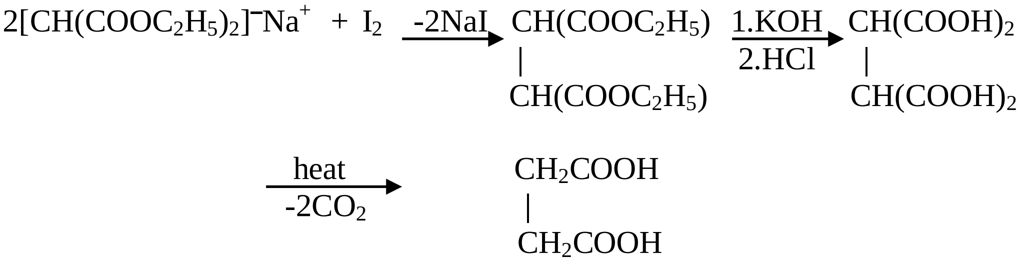
$$\xrightarrow[-2C_2H_5OH]{KOH} C_2H_5CH(COOK)_2 \xrightarrow[-2KCl]{2HCl} C_2H_5CH(COOH)_2 \xrightarrow[150\text{-}200^0C]{heat} \underset{\text{n-Butyric acid}}{C_2H_5CH_2COOH} + CO_2$$

Starting with methyl malonic ester we can prepare dimethyl malonic ester. Its hydrolysis followed by decarboxylation yields dimetylacetic acid (isobutyric acid).

It is not also possible to introduce aryl groups into malonic ester.

b. Synthesis of succinic acid and its homologues. Succinc acid and its homologues can be prepared by the following methods:

i. Monosodio malonic ester with iodine:
Monosodio malonic ester when heated with iodine, followed by hydrolysis and decarboxylation give succinic acid:

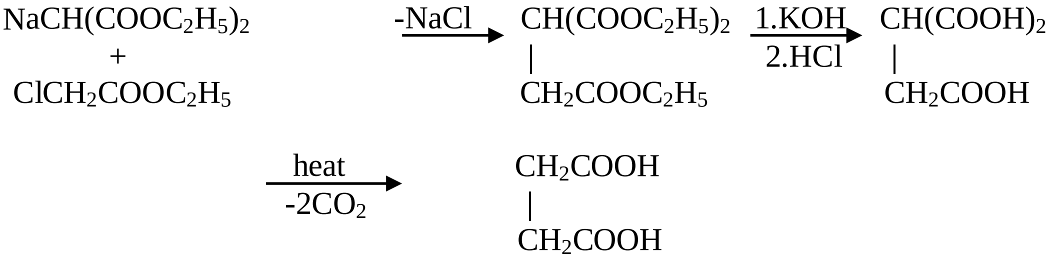


$$2[\mathrm{CH(COOC_2H_5)_2}]^{-}\mathrm{Na}^{+} + \mathrm{I_2} \xrightarrow{-2\mathrm{NaI}} \begin{array}{c}\mathrm{CH(COOC_2H_5)}\\ | \\ \mathrm{CH(COOC_2H_5)}\end{array} \xrightarrow[2.\mathrm{HCl}]{1.\mathrm{KOH}} \begin{array}{c}\mathrm{CH(COOH)_2}\\ | \\ \mathrm{CH(COOH)_2}\end{array} \xrightarrow[-2\mathrm{CO_2}]{\text{heat}} \begin{array}{c}\mathrm{CH_2COOH}\\ | \\ \mathrm{CH_2COOH}\end{array}$$

Succinic acid

If the sodium derivatives of monoalkylmalonic ester is taken, symmetrical dialkylsuccinic acid can be obtained.

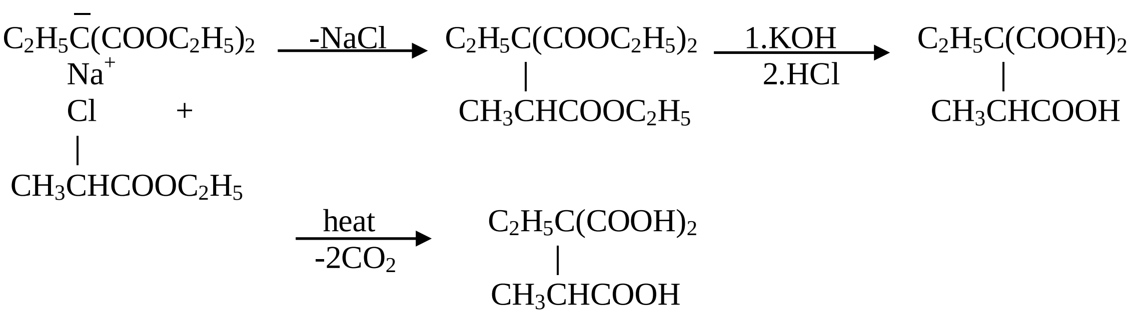
ii. Monosodiomalonic ester when treated with the ester of halogenated carboxylic acid and the product hydrolysed, it forms first a tricarboxylic acid, and then on heating it gives a dicarboxylic acid.



$$\begin{array}{c}\mathrm{NaCH(COOC_2H_5)_2}\\ + \\ \mathrm{ClCH_2COOC_2H_5}\end{array} \xrightarrow{-\mathrm{NaCl}} \begin{array}{c}\mathrm{CH(COOC_2H_5)_2}\\ | \\ \mathrm{CH_2COOC_2H_5}\end{array} \xrightarrow[2.\mathrm{HCl}]{1.\mathrm{KOH}} \begin{array}{c}\mathrm{CH(COOH)_2}\\ | \\ \mathrm{CH_2COOH}\end{array} \xrightarrow[-2\mathrm{CO_2}]{\text{heat}} \begin{array}{c}\mathrm{CH_2COOH}\\ | \\ \mathrm{CH_2COOH}\end{array}$$

Succinic acid

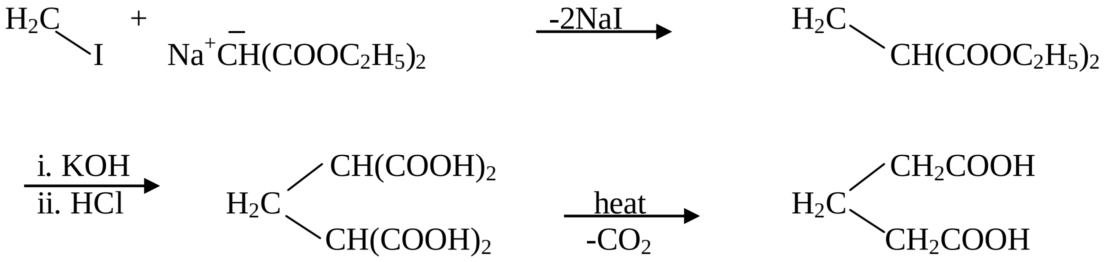
iii. Alkyl succinic acids can be prepared from sodioalkyl malonic ester and mono or dialkyl chloroacetic esters.



$$\begin{array}{c}\mathrm{C_2H_5\overset{-}{C}(COOC_2H_5)_2}\\ \mathrm{Na}^{+}\\ \mathrm{Cl} \quad + \\ | \\ \mathrm{CH_3CHCOOC_2H_5}\end{array} \xrightarrow{-\mathrm{NaCl}} \begin{array}{c}\mathrm{C_2H_5C(COOC_2H_5)_2}\\ | \\ \mathrm{CH_3CHCOOC_2H_5}\end{array} \xrightarrow[2.\mathrm{HCl}]{1.\mathrm{KOH}} \begin{array}{c}\mathrm{C_2H_5C(COOH)_2}\\ | \\ \mathrm{CH_3CHCOOH}\end{array} \xrightarrow[-2\mathrm{CO_2}]{\text{heat}} \begin{array}{c}\mathrm{C_2H_5C(COOH)_2}\\ | \\ \mathrm{CH_3CHCOOH}\end{array}$$

iv. Glutaric acid can be obtained from methylene iodide and mono sodiomalonic ester.

$$\diagup \mathrm{I} \qquad \mathrm{Na^{+}\overset{-}{C}H(COOC_2H_5)_2} \qquad\qquad \diagup \mathrm{CH(COOC_2H_5)_2}$$



Glutaric acid

v. Succinic or alkyl succinic acids can be prepared by the electrolysis of sodiummalonic ester or sodialkylmalonic ester.

$$\begin{array}{c} NaCH(COOC_2H_5)_2 \\ + \\ NaCH(COOC_2H_5)_2 \end{array} \xrightarrow{\text{Electrolysis}} \begin{array}{l} CH(COOC_2H_5)_2 \\ | \\ CH(COOC_2H_5)_2 \end{array} \xrightarrow[\text{heat}]{\text{hydrolysis}} \begin{array}{l} CH_2COOH \\ | \\ CH_2COOH \end{array}$$

(c) Synthesis of α,β - unsaturated acid. Malonic ester condenses with an aldehyde or ketone in the presence of organic bases such as pyridine ,piperidine etc. (Knoevenagel reation). The product on hydrolysis and heating is an unsaturated acid

$$\begin{array}{l} R-C=O \\ \quad | \\ \quad H \end{array} + H_2C(COOC_2H_5)_2 \xrightarrow[-H_2O]{} \begin{array}{l} R-C=O(COOC_2H_5)_2 \\ \quad | \\ \quad H \end{array} \xrightarrow[-2C_2H_5OH]{\text{hydrolysis}} RCH=C(COOH)_2 \xrightarrow[CO_2]{\text{heat}} RCH=CHCOOH$$

α,β - unsaturated acid

Cinnamic acid is obtained when benezaldehyde is condensed with malonic ester.

$$C_6H_5CHO + H_2C(COOC_2H_5)_2 \xrightarrow{-H_2O} C_6H_5CH=C(COOC_2H_5)_2$$

$$\xrightarrow[-C_2H_5OH]{\text{Hydrolysis}} C_6H_5CH=C(COOH)_2 \xrightarrow[-CO_2]{\text{heat}} C_6H_5CH=C(COOH)_2$$

Cinnamic acid

d.Synthesis of keto acids. When sodionalonic ester is treated with an acid chloride, a keto acid is formed by hydrosing and heating the product.

$$CH_3COCI + NaCH(COOC_2H_5) \xrightarrow{-NaCl} CH_3CO.CH(COOC_2H_5)_2$$

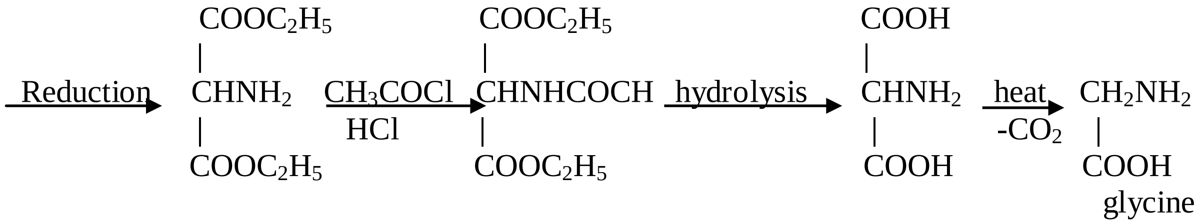
$$\xrightarrow[\text{ii.HCl}]{\text{i.KOH}} CH_3COCH(COOH)_2 \xrightarrow[-CO_2]{\text{heat}} CH_3COCH_2COOH$$

β-Ketobutycic acid
(Acetoacetic acid)

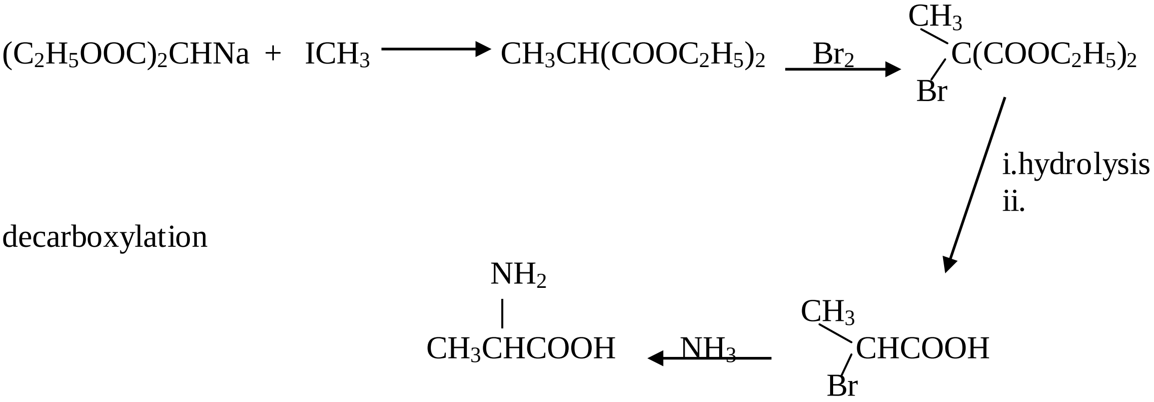
e. Synthesis of α-amino acids. An amino acid can be prepared by the following procedure:

$$\begin{array}{l} COOC_2H_5 \\ | \\ CH_2 \end{array} \xrightarrow{+HNO_2} \begin{array}{l} \quad COOC_2H_5 \\ \quad | \\ H-C-N=O \end{array} \xrightarrow{\text{isomerizes}} \begin{array}{l} COOH \\ | \\ C=N-OH \end{array}$$

Malonic acid

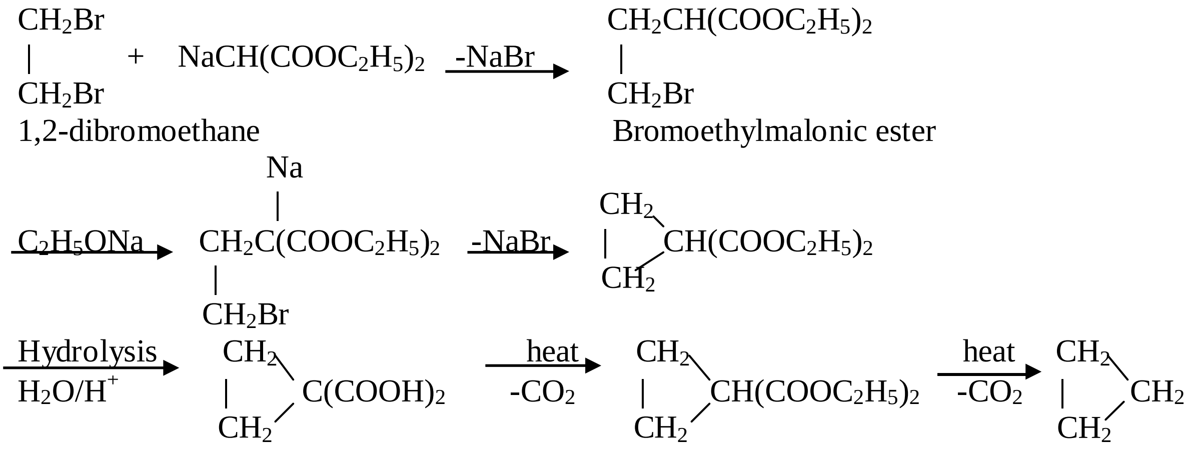


Also starting from sodiomalonic ester, α-amino acids can also be obtained by starting from sodiomalonic ester. For example, preparation of alanine(α-aminopropionic acid).



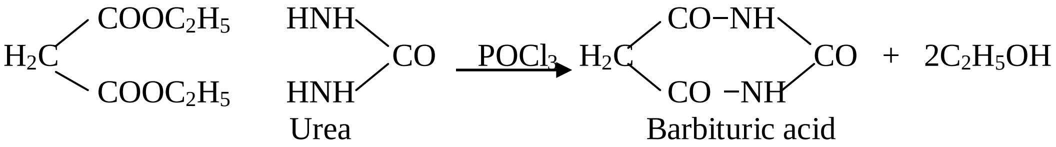
f. Synthesis of alicyclic compounds. This can be carried out by the condensation of alkylene dihalide with sodiomalonic ester. The haloalkylmalonic ester formed, when treated with sodium ethoxide undergoes an intramolecular alkylation reaction to form a cycloalkane carboxylic acid.

For example, preparation of cyclopropane.



Cyclopropane carboxylic acid  Cyclopropane

g. Synthesis of heterocylic compounds. In presence of $POC1_3$, malonic ester condenses with urea to form malonylurea,commonly known as barbituric acid.



h. Synthesis of primary alcohol. When malonic ester is treated with hydrogen in presence of heated cupric chromite, one of the carboethoxy group is reduced to $–CH_2OH$ and the other to $– CH_3$group.

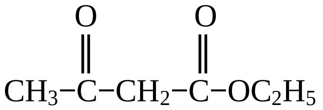
$$H_2C(COOC_2H_5)_2 + 5H_2 \xrightarrow{CuCr_2O_4} CH_3CH_2CH_2OH + H_2O + C_2H_5OH$$

## Activity C/Self Assessment Exercise

What role does the methylene group play in the activities of malonic ester as a synthetic intermediate?

## 3.8 ACETOACETIC ESTER

Acetoacetic ester or ethylacetoacetate is the ethyl ester of acetoacetic acid and may also regarded as acety derivative of ethylacetate . It has the formula $CH_3COCH_2COO_2H_5$.



$$CH_3-\overset{\overset{\displaystyle O}{\|}}{C}-CH_2-\overset{\overset{\displaystyle O}{\|}}{C}-OC_2H_5$$

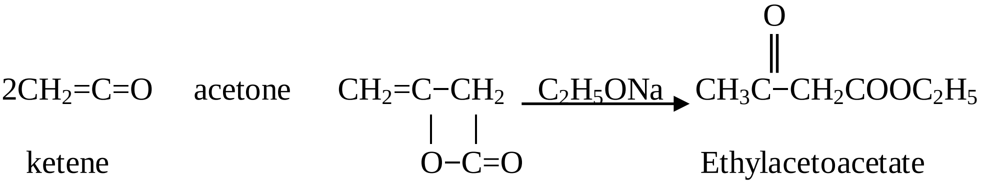
### 3.8.1 Preparation

From Claisen Condensation

It is prepared by the condensation of two molecules of ethylacetate in presence of a base e.g. sodium ethoxide. The reaction is called as Claisen's condensation.

$$CH_3CO\boxed{OC_2H_5 + H}CH_2COOC_2H_5 \xrightarrow{C_2H_5ONa} CH_3COCH_2COOC_2H_5 + C_2H_5OH$$

Ethyl acetoacetate is industrial prepared by polymerising ketene in acetone solution and then treating the diketene with alcohol.

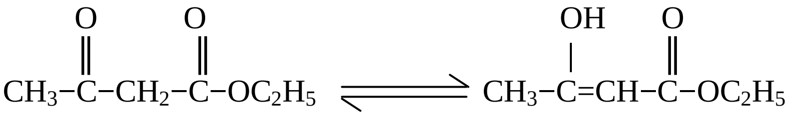


$$\underset{\text{ketene}}{2CH_2{=}C{=}O} \quad \text{acetone} \quad \underset{\substack{| \quad | \\ O-C=O}}{CH_2{=}C-CH_2} \xrightarrow{C_2H_5ONa} \underset{\text{Ethylacetoacetate}}{CH_3\overset{\overset{\displaystyle O}{\|}}{C}-CH_2COOC_2H_5}$$

### 3.8.2 General Properties

a. Physical
   - i. It is a colourless liquid (b.p. 78$^oC$).
   - ii. It has a pleasant smell
   - iii. It decomposes and is, therefore, distilled under reduced pressure.
   - iv. It is sparingly soluble in water but readily soluble in alcohol and ether.
   - v. Though neutral to litmus, it is soluble in dilute sodium hydroxide; it is the enol form which dissolved to give sodium salt.

b. Chemical. Acetoacetic ester behaves a ketone as well as an alcohol which is due to the fact that it exhibits keto-enol-tautomerism



$$\mathrm{CH_3-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-OC_2H_5 \rightleftharpoons CH_3-\overset{\overset{OH}{|}}{C}=CH-\overset{\overset{O}{\|}}{C}-OC_2H_5}$$

Keto form Enol form

The equilibrium mixture contains both forms, however , but the percentage of enol form is very small. At ordinary temperature it is about 7.5 per cent. The degree of enolisation depends on the nature of solvent- for example in acetic acid it is 5 to 7 per cent, while in petroleum ether it is 46.4 per cent.

The reactions of ethylacetoacetate depend on the different forms

**a. Reactions Involving Ketonic Form**

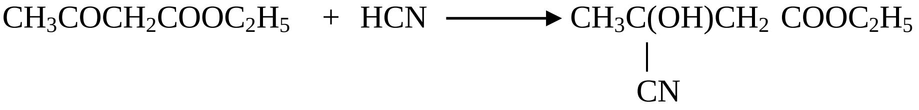
(i) Reduction. This can take place with sodium amalgam and alcohol or with hydrogen in presence of nickel or litium tetrahydridoaluminate(III) in pyridine to give β-hydroxybutyric ester.

$$\mathrm{CH_3COCH_2COOC_2H_5 + 2H \longrightarrow CH_3CHOHCH_2COOC_2H_5}$$

However, with litium tetrahydridoaluminate(III) in absence of pyridine it is reduced to 1,3-butanediol.

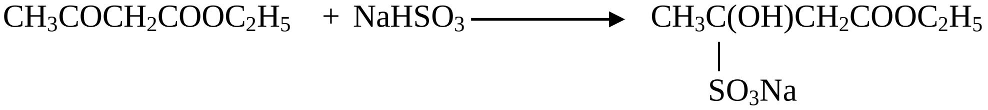
$$\mathrm{CH_3COCH_2COOC_2H_5 + 6H \xrightarrow{LiAlH_4} CH_3CHOHCH_2CH_2OH + C_2H_5OH}$$

(ii) Reaction with hydrogen cyanide. It form cyanohydrins like other ketones.



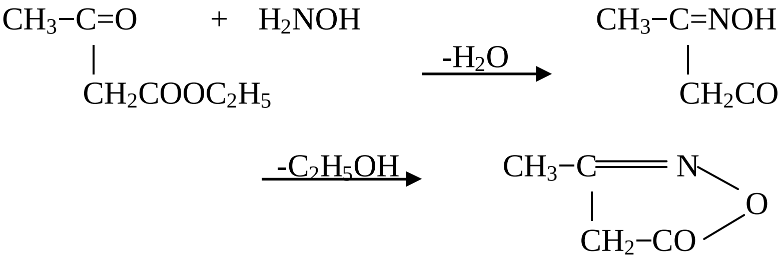
$$\mathrm{CH_3COCH_2COOC_2H_5 + HCN \longrightarrow CH_3\underset{\underset{CN}{|}}{C}(OH)CH_2\ COOC_2H_5}$$

(iii) Reaction with sodium trioxosulohate(VI),$NaHSO_3$. It forms a crystalline addition compound with saturated aqueous solution of sodium trioxosulohate(VI),$NaHSO_3$



$$\mathrm{CH_3COCH_2COOC_2H_5 + NaHSO_3 \longrightarrow CH_3\underset{\underset{SO_3Na}{|}}{C}(OH)CH_2COOC_2H_5}$$

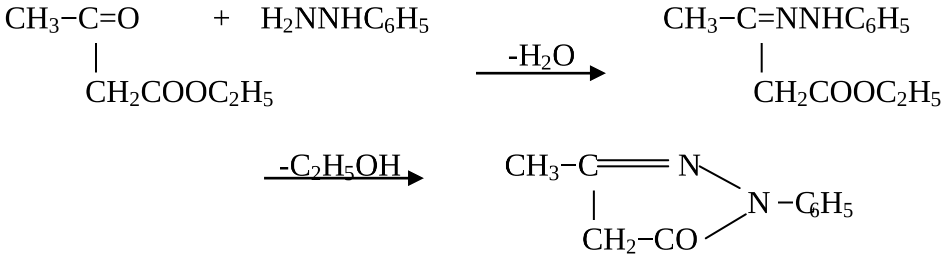
iv. Reaction with hydroxylamine. It form an oxime with hydroxylamine which loses a molecule of alcohol immediately to forms methyl isoxazolone.



$$\mathrm{CH_3-\underset{\underset{CH_2COOC_2H_5}{|}}{C}=O + H_2NOH \xrightarrow{-H_2O} CH_3-\underset{\underset{CH_2COOC_2H_5}{|}}{C}=NOH \xrightarrow{-C_2H_5OH}}$$

Methyl isoxazolone

(v) Action of phenylhydrazine. With phenylhydrazine it first forms phenylhydrazone, which then loses a molecule of alcohol to forms 3-methyl-phenyl-pyrazolone.



$$\underset{CH_2COOC_2H_5}{CH_3-C=O} + H_2NNHC_6H_5 \xrightarrow{-H_2O} \underset{CH_2COOC_2H_5}{CH_3-C=NNHC_6H_5} \xrightarrow{-C_2H_5OH}$$

3-Methyl-1-phenylpyrazolone

v. Hydrolysis. When boiled with dilute aqueous or alcoholic potassium hydroxide, dilute $H_2SO_4$, acetoacetic ester is hydrolysed to form ketone (acetone).

$$CH_3COCH_2COOC_2H_5 \longrightarrow CH_3COCH_3 + CO_2 + C_2H_5OH$$

With 85 per cent solution of phosphoric acid, they yield of ketone may be even up to 95 per cent.

However hydrolysis with concentrated alcoholic potassium hydroxide gives acids.

$$CH_3COCH_2COOC_2H_5 \longrightarrow 2CH_3COOK+C_2H_5OH$$

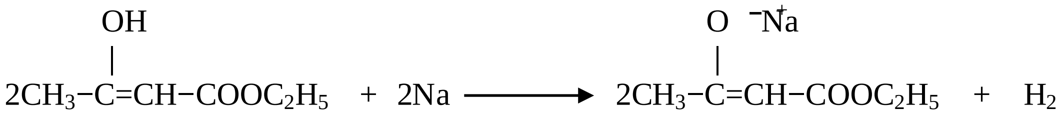
With cold and dilute potassium hydroxide normal hydrolysis takes place resulting in the formulating of potassium acetoacetate.

$$CH_3COCH_2COOC_2H_5 \longrightarrow 2CH_3COOK + C_2H_5OH$$

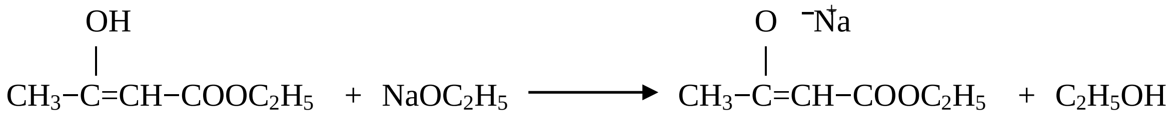
It the solution containing potassium acetoacetate is acidified, extracted with ether and then ether removed carefully under reduced pressure, acetoacatic acid is obtained.
These various hydrolysis are useful in preparing of various acids, ketones etc. form mono and dialkyl derivatives of acetoacetic ester.

**b. Reaction Involving Enolic Form**

(i) Reaction with sodium or sodium ethoxide. With sodium or sodium ethoxide, it forms sodio, derivatives.



$$2CH_3-\overset{\overset{OH}{|}}{C}=CH-COOC_2H_5 + 2Na \longrightarrow 2CH_3-\overset{\overset{O^-Na^+}{|}}{C}=CH-COOC_2H_5 + H_2$$

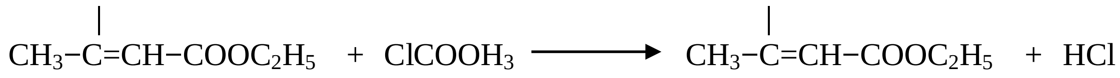


$$CH_3-\overset{\overset{OH}{|}}{C}=CH-COOC_2H_5 + NaOC_2H_5 \longrightarrow CH_3-\overset{\overset{O^-Na^+}{|}}{C}=CH-COOC_2H_5 + C_2H_5OH$$

(ii) Reaction with Iron(III) chloride. Due to the presence of the >C=C−OH group (as in phenol), acetoacetic ester gives a violet colour with Iron(III) chloride.

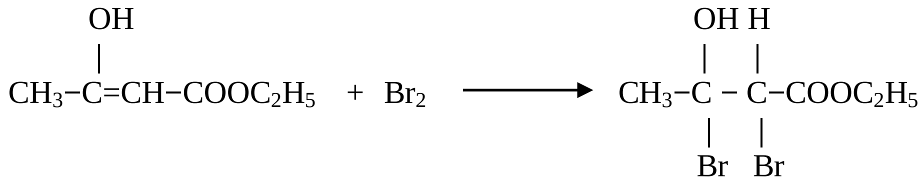
(iii) Acetylation. With acetyl chloride it forms an acetyl derivative.

$$OH \qquad\qquad O-COCH_3$$



$$CH_3-\overset{|}{C}=CH-COOC_2H_5 \;+\; ClCOOH_3 \longrightarrow CH_3-\overset{|}{C}=CH-COOC_2H_5 \;+\; HCl$$

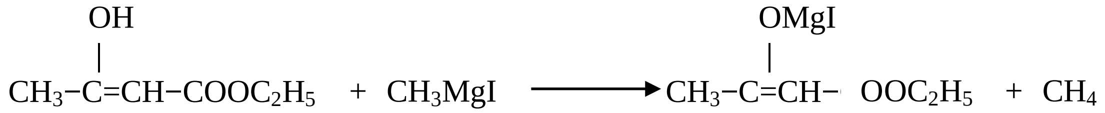
(iv) Reaction with bromine, Due to the presence of C=C linkage it forms addition product with ethanolic bromine solution.



$$CH_3-\overset{OH}{\overset{|}{C}}=CH-COOC_2H_5 \;+\; Br_2 \longrightarrow CH_3-\underset{Br}{\underset{|}{\overset{OH}{\overset{|}{C}}}}-\underset{Br}{\underset{|}{\overset{H}{\overset{|}{C}}}}-COOC_2H_5$$

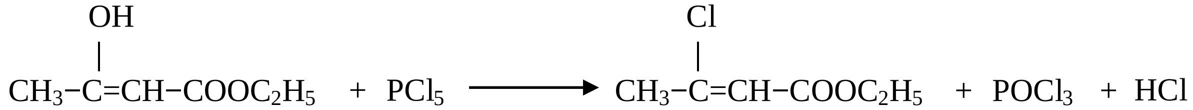
α,β-dibromoacetoacetic acid

(v) Reaction with Grignard reagent. It reacts with Grignard reagent to form hydrocarbon.



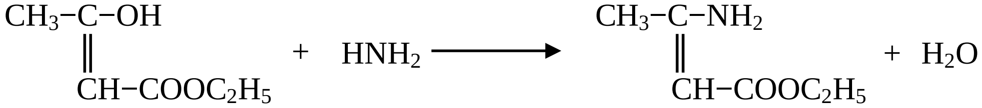
$$CH_3-\overset{OH}{\overset{|}{C}}=CH-COOC_2H_5 \;+\; CH_3MgI \longrightarrow CH_3-\overset{OMgI}{\overset{|}{C}}=CH-\;OOC_2H_5 \;+\; CH_4$$

(vi) Reaction with phosphorus pentachloride, $PCl_5$. It forms β-chlorocrotonic ester.



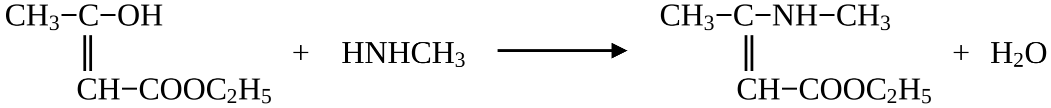
$$CH_3-\overset{OH}{\overset{|}{C}}=CH-COOC_2H_5 \;+\; PCl_5 \longrightarrow CH_3-\overset{Cl}{\overset{|}{C}}=CH-COOC_2H_5 \;+\; POCl_3 \;+\; HCl$$

(vii) Reaction with amine compounds. It reacts with ammonia as well as primary and secondary amines to form β-amino crotonic esters.



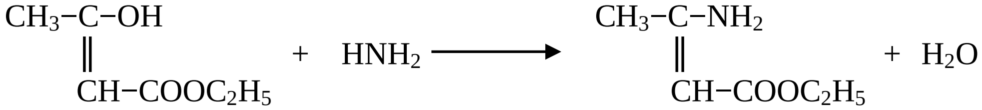
$$\begin{array}{l} CH_3-C-OH \\ \quad\;\; \| \\ \quad\;\; CH-COOC_2H_5 \end{array} \;+\; HNH_2 \longrightarrow \begin{array}{l} CH_3-C-NH_2 \\ \quad\;\; \| \\ \quad\;\; CH-COOC_2H_5 \end{array} \;+\; H_2O$$

B-amino crotonic ester
(β-aminoethyl crotonate)



$$\begin{array}{l} CH_3-C-OH \\ \quad\;\; \| \\ \quad\;\; CH-COOC_2H_5 \end{array} \;+\; HNHCH_3 \longrightarrow \begin{array}{l} CH_3-C-NH-CH_3 \\ \quad\;\; \| \\ \quad\;\; CH-COOC_2H_5 \end{array} \;+\; H_2O$$

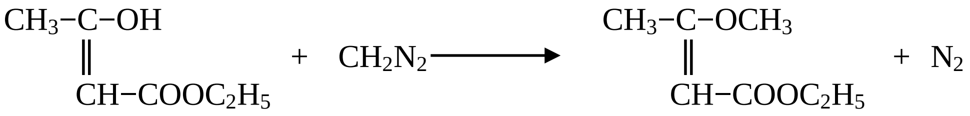
β-Methylamino-ethyl crotonate



$$\begin{array}{l} CH_3-C-OH \\ \quad\;\; \| \\ \quad\;\; CH-COOC_2H_5 \end{array} \;+\; HNH_2 \longrightarrow \begin{array}{l} CH_3-C-NH_2 \\ \quad\;\; \| \\ \quad\;\; CH-COOC_2H_5 \end{array} \;+\; H_2O$$

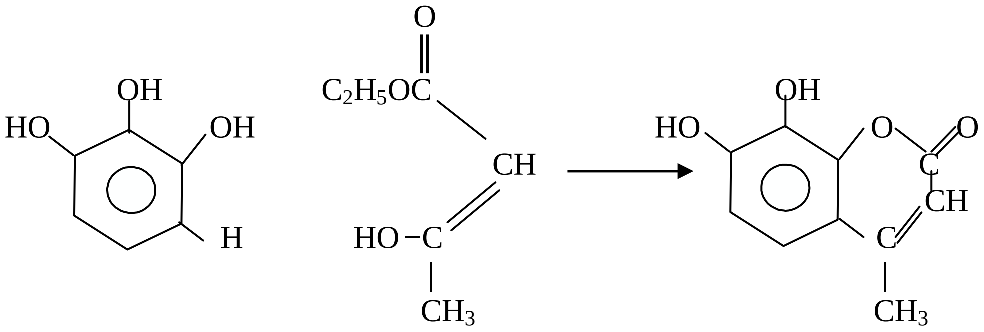
B-dimethylaminoethyl crotonate

(viii) Reaction with diazomethane, with diazomethane it form methyl ether of ethyl crotonate.



$$\begin{matrix}CH_3-C-OH\\ \|\\ CH-COOC_2H_5\end{matrix} + CH_2N_2 \longrightarrow \begin{matrix}CH_3-C-OCH_3\\ \|\\ CH-COOC_2H_5\end{matrix} + N_2$$

(ix) Reaction with pyrogallol. When condensed with pyrogallol in the presence of a dehydrating agent, it form coumarin derivative.



Coumarin 4-methyl-7,8-dihydroxy

## Activity D/Self Assessment Exercise

What are the product formed when acetoacetic acid react with the following:
(i) HCN (ii) $NH_2OH$ (iii) $CH_3MgI$

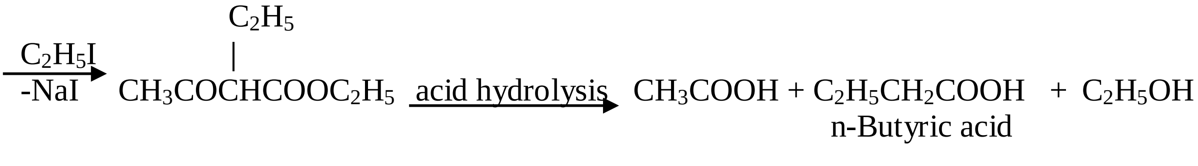
### 3.8.3 Synthetic Applcations

The presence of active methylene group flanked on either side by electron withdrawing carbonyl groups make acetoacetic ester behaves as an acid, forming carbanion, which is resonance stabilized and can undergo typical nucleophilic substitution reactions. This makes it a very useful synthetic tool.

For example, let us consider some synthetic application of the acetoacetic ester in the synthesis of carboxylic acids

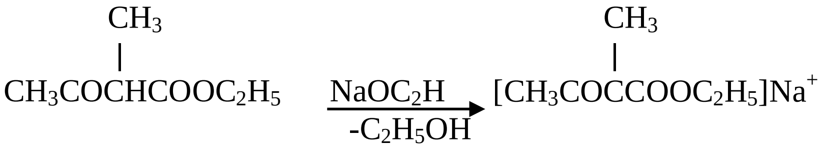
i. **Synthesis of monocarboxylic acid**

$$CH_3COCH_2COOC_2H_5 \xrightarrow[-C_2H_5OH]{NaOC_2H} [CH_3COCHCOOC_2H_5]Na^+$$

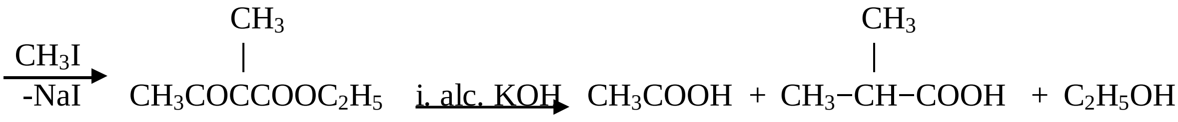


$$\xrightarrow[-NaI]{C_2H_5I} CH_3CO\overset{\overset{C_2H_5}{|}}{C}HCOOC_2H_5 \xrightarrow{\text{acid hydrolysis}} CH_3COOH + C_2H_5CH_2COOH + C_2H_5OH$$

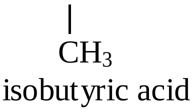
n-Butyric acid



$$CH_3CO\overset{\overset{CH_3}{|}}{C}HCOOC_2H_5 \xrightarrow[-C_2H_5OH]{NaOC_2H} [CH_3CO\overset{\overset{CH_3}{|}}{C}COOC_2H_5]Na^+$$



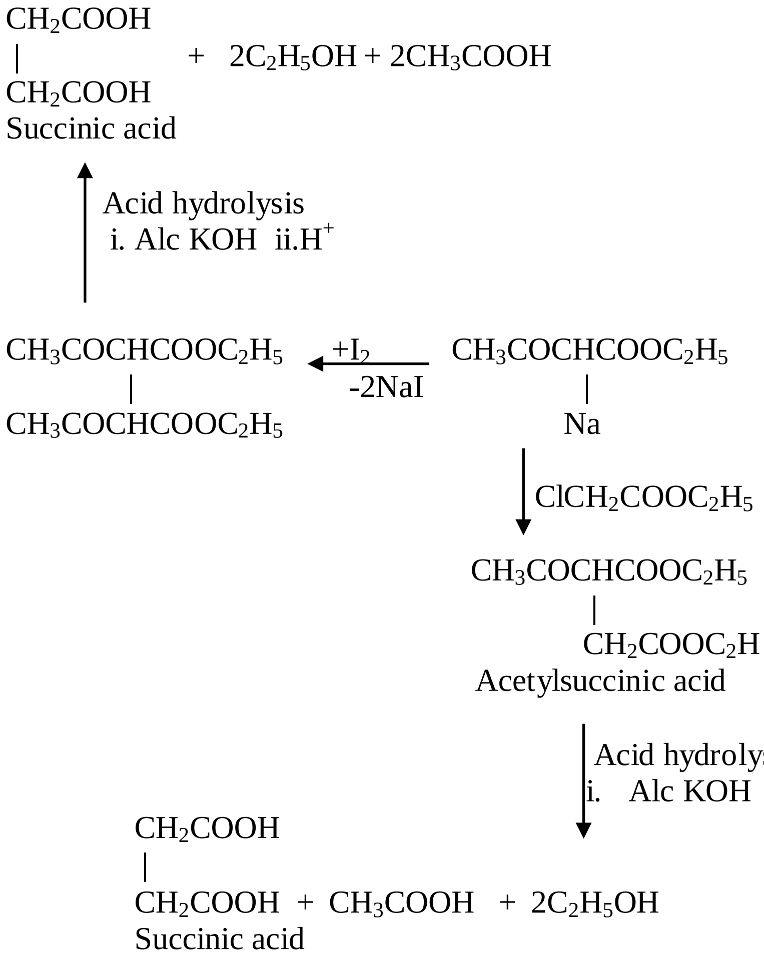
$$\xrightarrow[-NaI]{CH_3I} CH_3CO\overset{\overset{CH_3}{|}}{C}COOC_2H_5 \xrightarrow{\text{i. alc. KOH}} CH_3COOH + CH_3-\overset{\overset{CH_3}{|}}{C}H-COOH + C_2H_5OH$$



$$\begin{matrix} | \\ CH_3 \end{matrix}$$

isobutyric acid

**ii. Synthesis Of Dicarboxylc Acids.E.g Succinic acid**



$$\begin{matrix} CH_3COCHCOOC_2H_5 \\ | \\ CH_3COCHCOOC_2H_5 \end{matrix} \xleftarrow[-2NaI]{+I_2} \begin{matrix} CH_3COCHCOOC_2H_5 \\ | \\ Na \end{matrix} \xrightarrow{ClCH_2COOC_2H_5} \begin{matrix} CH_3COCHCOOC_2H_5 \\ | \\ CH_2COOC_2H \end{matrix}$$

Acetylsuccinic acid

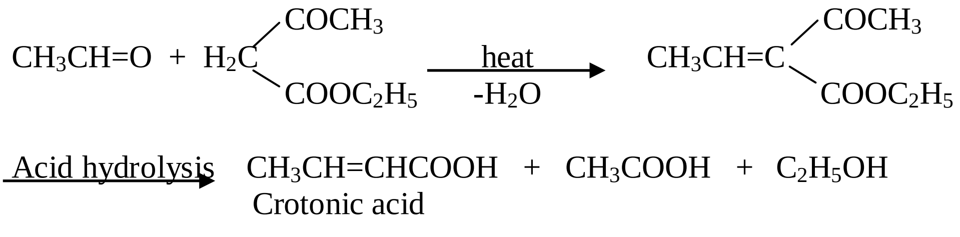
$$\begin{matrix} CH_3COCHCOOC_2H_5 \\ | \\ CH_3COCHCOOC_2H_5 \end{matrix} \xrightarrow[\text{i. Alc KOH ii.}H^+]{\text{Acid hydrolysis}} \begin{matrix} CH_2COOH \\ | \\ CH_2COOH \end{matrix} + 2C_2H_5OH + 2CH_3COOH$$

Succinic acid

$$\begin{matrix} CH_3COCHCOOC_2H_5 \\ | \\ CH_2COOC_2H \end{matrix} \xrightarrow[\text{i. Alc KOH ii.}H^+]{\text{Acid hydrolysis}} \begin{matrix} CH_2COOH \\ | \\ CH_2COOH \end{matrix} + CH_3COOH + 2C_2H_5OH$$

Succinic acid

3. Synthesis of α,β- unsaturated acids. E.g condensation of acetoacetic ester with an aldehyde or ketone

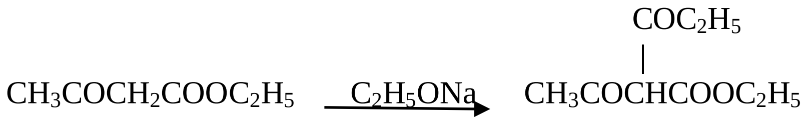


$$CH_3CH{=}O + H_2C\begin{matrix} \diagup COCH_3 \\ \diagdown COOC_2H_5 \end{matrix} \xrightarrow[-H_2O]{heat} CH_3CH{=}C\begin{matrix} \diagup COCH_3 \\ \diagdown COOC_2H_5 \end{matrix}$$

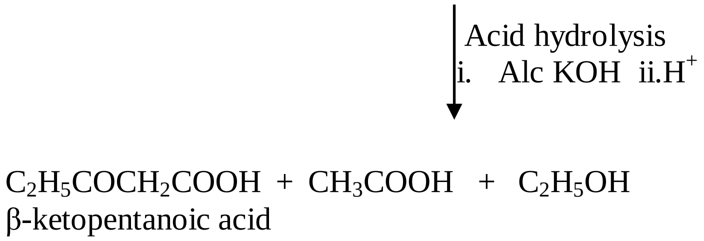
$$\xrightarrow{\text{Acid hydrolysis}} CH_3CH{=}CHCOOH + CH_3COOH + C_2H_5OH$$

Crotonic acid

3. Synthesis of β-Ketone acids. This product formed by condensation of sodioacetic ester with propionul chloride (acy halide) when subjected to acid hydrolysis form B-Ketone acid.



$$CH_3COCH_2COOC_2H_5 \xrightarrow{C_2H_5ONa} \begin{matrix} COC_2H_5 \\ | \\ CH_3COCHCOOC_2H_5 \end{matrix}$$

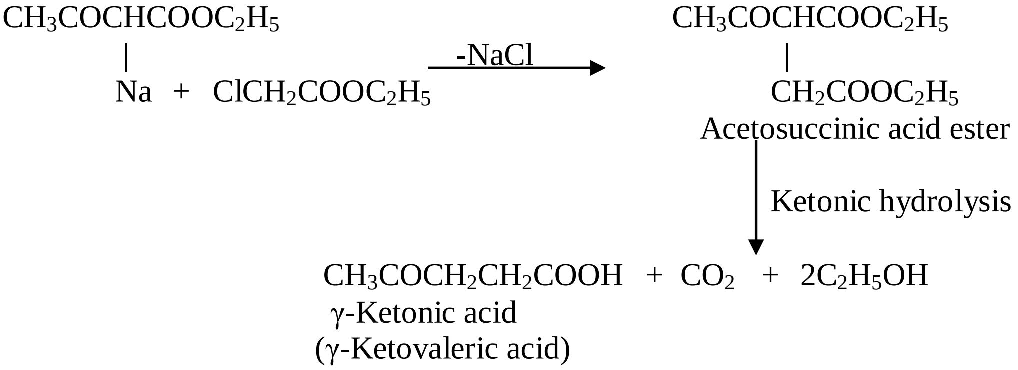


$$\Big\downarrow \text{Acid hydrolysis i. Alc KOH ii.}H^+$$

$$C_2H_5COCH_2COOH + CH_3COOH + C_2H_5OH$$

β-ketopentanoic acid

5. Synthesis of γ-Ketonic acids. For example γ-Ketonic acids from sodio derivative of ester and α-chlorocarboxylic acid ester. The product obtained is subjected to ketonic hydrolysis.



$$\underset{\substack{|\\ Na}}{CH_3COCHCOOC_2H_5} + ClCH_2COOC_2H_5 \xrightarrow{-NaCl} \underset{\substack{|\\ CH_2COOC_2H_5}}{CH_3COCHCOOC_2H_5}$$

Acetosuccinic acid ester

$$\Big\downarrow \text{Ketonic hydrolysis}$$

$$CH_3COCH_2CH_2COOH + CO_2 + 2C_2H_5OH$$

γ-Ketonic acid
(γ-Ketovaleric acid)

## 4.0 Conclusion

Saturated dicarboxylic acids have the general formula $C_nH_{2n}(COOH)_2$ .The chemical reactions of dicarboxylic acids are mainly governed by the reactivity of the carboxyl groups. Functional groups like nitro, ester have methylene group reactive. Examples of compounds which have an active methylene group are malonate ester and acetoacetic ester.

## 5.0 Summary

In this unit we have learnt that:

i. Dicarboxylic acids contain two carboxyl groups.

ii. Dicarboxylic acids may be saturated and they may be unsaturated.

iii. Saturated dicarboxylic acids have the general formula $C_nH_{2n}(COOH)_2$., n may be equal or greater than 0.

iv. In naming dicarboxylic acids using the IUPAC system the suffix dioic acid is added to the name of the parent alkane.

v. In the common system, the position of substituents is indicated by Greek letters while in the IUPAC system, it is indicated by numbers.

vi. Dicarboxylic acids show position isomerism.

vii. General Methods of Preparation are :

- By oxidation of dihydric alcohols.
- Hydrolysis of dicyanides or cyano acids
- By treating halogen substituted monocarboxylic acid ester with zinc or silver and hydrolysing the ester thus obtained.

- By reduction of unsaturated dicarboxylic acid
- By hydrolysis of aqueous solution of potassium alkyl ester of dibasic acid
- By oxidation of cyclic ketone
- From Grignard reagent of dihaloalkane.
- By oxidation of unsaturated acids
- By the action of dihaloalkanes on sodiomalonic ester

viii. All dicarboxylic acids are colourless crystalline solids, Lower members are soluble in water. Solubility in water decreases as molecular mass increases while in ether the solubility increases as molecular mass increases.Melting points of acids with even number of carbon atoms are higher than those with odd number of carbon atoms. Acid strength of these acids decrease with increase in molecular weight.

ix.Dicarboxylic acids dissociate in two steps:

$$\mathrm{HOOC{-}COOH} \overset{K1}{\rightleftharpoons} {}^{-}\mathrm{OOC{-}COOH} + \mathrm{H}^{+}$$

$$ {}^{-}\mathrm{OOC{-}COOH} \overset{K2}{\rightleftharpoons} {}^{-}\mathrm{OOC{-}COO}^{-} + \mathrm{H}^{+}$$

The first dissociation constant K1 is higher than the second dissociation constant K2.

x. The chemical reactions of dicarboxylic acids are mainly governed by the reactivity of the carboxyl groups.

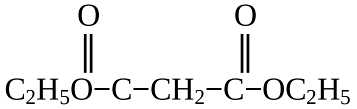
- Dicarboxylic acids show the usual reactions of carboxyl group and they form two series of salts, esters, amides and other acid derivatives because they have two carboxyl groups.
- Action of Heat: The product formed on heating depends on the relative positions of the two carboxyl groups.

xi. When a methylene group is present between two strongly electronegative (electron attracting) group such as >C=O or −C≡N, the hydrogen atoms of methylene group (called α-hydrogen, being present on carbon atom next to functional groups on either side) become reactive or acidic.

x.When a compound containing active methylene group reacts with a strong base the proton removal may take place from both, keto and enol forms and the resultant enolate (a carbanion stabilized by an adjacent carbonyl group, is often called an enolate ion).

xi. Functional groups like nitro, ester etc. also make methylene group reactive.

xii.Malonic ester an important synthetic reagent with the formula.



$$\mathrm{C_2H_5O{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}CH_2{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OC_2H_5}$$

## Malonic Ester

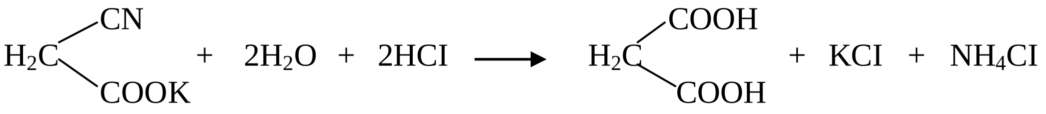
xiii. Methods of preparing Malonic ester are:

a. $CH_3COOH \xrightarrow[1_2]{CI_2} CI.CH_2COOH \xrightarrow{K_2CO_3} CI.CH_2COOK$

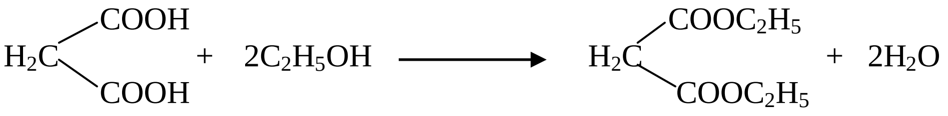
Acetic acid Monochloroacetic acid Potassium monochloroacetate

$\xrightarrow{KNC} CN.CH2COOK$

Potassium cyanoacetate

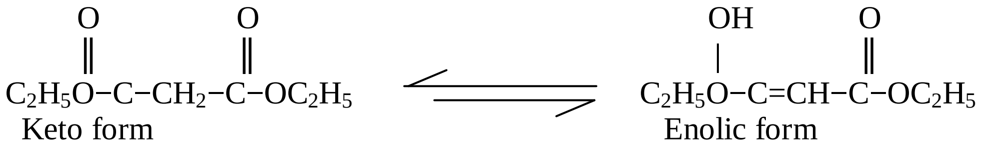


Malonic acid



b. By refluxing cyanoacetic acid with ethylalcohol in the presence of chlorosulphonic acid.

xiv. Malonic ester exists in following keto-enol tautomeric forms, the enol form being present in much smaller amount.



$$C_2H_5O-\overset{\overset{O}{\|}}{C}-CH_2-\overset{\overset{O}{\|}}{C}-OC_2H_5 \rightleftharpoons C_2H_5O-\overset{\overset{OH}{|}}{C}=CH-\overset{\overset{O}{\|}}{C}-OC_2H_5$$

Keto form Enolic form

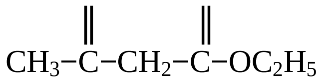
xv. Because of the presence of active methylene group, it behaves as an acid and it is a valuable synthetic reagent.

xvi. Its synthetic applications are :

- Synthesis of monocarboxylic acids.
- Synthesis of succinic acid and its homologues.
- Synthesis of α,β - unsaturated acid.
- Synthesis of keto acids.
- Synthesis of α-amino acids.
- Synthesis of alicyclic compounds.
- Synthesis of heterocylic compounds.
- Synthesis of primary alcohol.

xvii. Acetoacetic ester or ethylacetoacetate is the ethyl ester of acetoacetic acid with the formula

O O



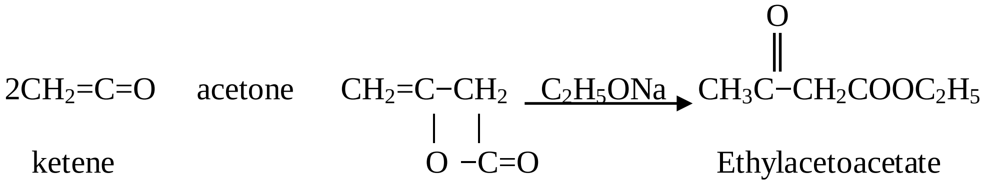
$$CH_3-\overset{\|}{C}-CH_2-\overset{\|}{C}-OC_2H_5$$

xviii. Acetoacetic ester or ethylacetoacetate is prepared from:

- Claisen Condensation

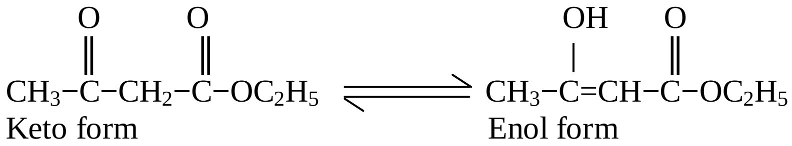
$$CH_3CO\ OC_2H_5 + HCH_2COOC_2H_5 \xrightarrow{C_2H_5ONa} CH_3COCH_2COOC_2H_5 + C_2H_5OH$$

- Ethyl acetoacetate is industrial prepared by polymerising ketene in acetone solution



$$\underset{\text{ketene}}{2CH_2{=}C{=}O} \quad \text{acetone} \quad \underset{O\ -C=O}{\underset{|\quad|}{CH_2=C-CH_2}} \xrightarrow{C_2H_5ONa} \underset{\text{Ethylacetoacetate}}{CH_3\overset{O}{\overset{\|}{C}}-CH_2COOC_2H_5}$$

xix. Chemical. Acetoacetic ester behaves a ketone as well as an alcohol which is due to the fact that it exhibits keto-enol-tautomerism



$$\underset{\text{Keto form}}{CH_3-\overset{O}{\overset{\|}{C}}-CH_2-\overset{O}{\overset{\|}{C}}-OC_2H_5} \rightleftharpoons \underset{\text{Enol form}}{CH_3-\overset{OH}{\overset{|}{C}}=CH-\overset{O}{\overset{\|}{C}}-OC_2H_5}$$

xx.The reactions of ethylacetoacetate depend on the different forms

a.Reactions Involving Ketonic Form

- Reduction- with sodium amalgam and alcohol or with hydrogen in presence of nickel or litium tetrahydridoaluminate(III) in pyridine.

$$CH_3COCH_2COOC_2H_5 + 2H \longrightarrow CH_3CHOHCH_2COOC_2H_5$$

- Reaction with hydrogen cyanide to form cyanohydrins
- Reaction with sodium trioxosulphate(VI),$NaHSO_3$.
- Reaction with hydroxylamine to form an oxime.
- Action of phenylhydrazine forms phenylhydrazone, which then loses a molecule of alcohol to forms 3-methyl-phenyl-pyrazolone.

- Hydrolysis with dilute $H_2SO_4$, form ketone (acetone), with concentrated alcoholic potassium hydroxide gives acids.With cold and dilute potassium hydroxide forms potassium acetoacetate.

If the solution containing potassium acetoacetate is acidified, extracted with ether and then ether removed carefully under reduced pressure, acetoacatic acid is obtained.

b. Reaction Involving Enolic Form

- Reaction with sodium or sodium ethoxide.
- Reaction with Iron(III) chloride.
- Acetylation.
- Reaction with bromine.
- Reaction with Grignard reagent.
- Reaction with phosphorus pentachloride, $PCl_5$.
- Reaction with amine compounds.

- Reaction with diazomethane.
- Reaction with pyrogallol.

xx. The presence of active methylene group flanked on either side by electron withdrawing carbonyl groups make acetoacetic ester behaves as an acid, forming carbanion., makes it a very useful synthetic tool.

xxi. Synthetic application of the acetoacetic ester in the synthesis of carboxylic acids are:

- Synthesis of monocarboxylic acid
- Synthesis of α,β- unsaturated acids
- Synthesis of β-Ketone acids.
- Synthesis of γ-Ketonic acids.

## 6.0 Tutor Marked Assignment

a. Discuss the synthetic application of:
i. Malonic ester
ii. Acetoacetic ester

b. Discuss the action of heat on dicarboxylic acids

## 7.0 Further Reading and other Resources

K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry
-Third Edition

ii. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry
- Sixth Edition

John McMurry and Mary E.Castellion (1999) Fundamentals of General,Organic, and Biological Chemistry-3rd Edition

# Unit 2: Amino acids, Peptides and Proteins

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## 1.0 Introduction

Proteins are macromolecules with very high relative molecular masses. The building units of proteins are called amino acids. The majority of proteins is from some twenty common amino acids, linked up by peptide (amide) bonds in a specific sequence characteristic of the particular protein

## 2.0 Objectives

At the end of this unit you should be able to:

i. Define amino acids-the building unit of proteins
ii. Define α-amino acids and give examples
iii. Differentiate between essential and non-essential amino acids
iv. List the various classes of α-amino acids
v. State the physical properties of α-amino acids
vi. Explain the isoelectric point of amino acids
vii. Discuss the various reactions of amino acids
viii. Distinguish between peptides, polypeptides and protein
ix. Classify proteins
x. Discuss the reactions of proteins
xi. State methods of testing protein
xii. State uses of protein

## 3.0 Amino Acids

Amino acids are the amino substituted acids containing both amino ($-NH_2$) and carbonyl ($-COOH$) group(s). They are the building units of proteins.

## 3.1 Naming Amino acids

The IUPAC names of amino acids are obtained by indicating the position of the amino group by Arabic numeral on the alkyl radical chain of the alkanoic acid, making the carboxylic carbon the number 1 carbon.

Simple amino acids having only one amino and carboxyl groups may be classified as α-, β-, γ- and δ- etc amino acids depending on the position of the amino group with respect to carboxyl group. For example:

α- Amino acids

| | |
|---|---|
| $H_2NCH_2COOH$ | Aminoacetic acid(Glycine) |
| $CH_3CH(NH_2)COOH$ | α-Aminopropionic acid or 2-Aminopropanoic acid(Alanine). |
| $C_6H_5CH_2CH(NH_2)COOH$ | α-Amino-β-phenyl propanoic acid(Phenyl alanine). |

β- Amino acids

| | |
|---|---|
| $H_2NCH_2CH_2COOH$ | β-Aminopropionic acid or 3-Aminopropanoic acid |
| $CH_3CH(NH_2)CH_2COOH$ | β-Aminobutyric acid or 3-Aminobutanoic acid |

γ- Amino acids

| | |
|---|---|
| $NH_2CH_2CH_2CH_2COOH$ | γ-Aminobutyric acid or 4-Aminobutanoic acid |

## 3.1 α-amino acids

The α-amino acids are the most important of all because they are the final products of the hydrolysis of peptides and proteins. Majority of the amino acids obtained in nature are α-

amino acids. They are known as essential amino acids because they are essential in the diet and their absence in human body retards the growth and may even cause death.
Due to the complexity of their systematic names, shorter names are in common use.

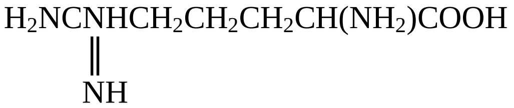
## 3.2 Classes of α-amino acids

They may have one or more than one amino or carboxyl groups and they are classified as follows:

i. Neutral Amino acids: They have equal number of amino acid and carboxyl groups. For example:
   $H_2NCH_2COOH$ Aminoacetic acid (Glycine)
   $HOOCCHH(NH_2)CH_2SSCH_2CH(NH_2)COOH$
   bis-(2-Amino-2-carboxymethyl)disulphide( Cystine)

ii. Basic Amino Acids: They contain more amino groups than carboxyl groups. For example:

   $H_2NCH_2CH_2CH_2CH_2CH(NH_2)COOH$ α,ε-Diaminocaproic acid(lysine)



$$\underset{\displaystyle NH}{\underset{\|}{H_2NC}}NHCH_2CH_2CH_2CH(NH_2)COOH$$

α-Amino-δ-guanidinovalericacid (Arginine).

iii. Acidic Amino Acids: They have more carboxyl group than amino group, e.g.,
   $HOOCCH_2CH(NH_2)COOH$ Aminosuccinic acid(Aspartic acid)

   $HOOCCH_2CH_2CH(NH_2)COOH$ α-Aminoglutaric acid(Glutanic acid)

## 3.3 Configuration of Amino acids

All amino acids obtained by acid or enzymatic hydrolysis of proteins are optically active except glycine, because each one of them have chiral centre which is absent in glycine. Naturally occurring amino acid has been shown through stereochemical studies to have the same configuration about the α-carbon atom and they resembles L(-)-glyceraldehyde.

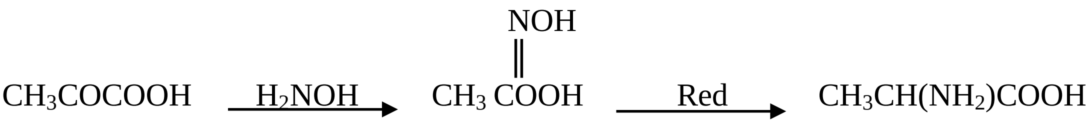
## 3.5 Methods of synthesis of α-amino acids

a. Amination of α-halogenated acids. An α- chloro or bromo substituted acid is treated with concentrated ammonia to gives an α-amino acid.

$$CH_3CHClCOOH + 2NH_3 \longrightarrow CH_3CH(NH_2)COOH + NH_4Cl$$

α-chloropropionic acid α-Aminopropionic acid

b. From Aldehydic and ketonic acids: When the acid is treated with hydroxylamine and the resulting oxime reduced by aluminium amalgam, it gives α-amino acid.



$$CH_3COCOOH \xrightarrow{H_2NOH} CH_3\overset{\overset{\displaystyle NOH}{\|}}{C}OOH \xrightarrow{Red} CH_3CH(NH_2)COOH$$

Pyruvic acid Al-Hg α-amino propionic acid

c. Malonic Ester synthesis: This method can be used to prepare leucine, isoleucine, norleucine, phenyl alanine, methionine and proline. For example in the preparation of leucine:

$$\underset{\text{Isobutyl bromide}}{(CH_3)_2CHCH_2Br} + \underset{\text{sodiomalonic ester}}{NaCH(COOC_2H_5)_2} \xrightarrow{-NaBr} (CH_3)_2CHCH_2CH(COOC_2H_5)_2$$

$$\xrightarrow{\text{(i) KOH (ii) HCl}} (CH_3)_2CHCH_2CH(COOH)_2 \xrightarrow{Br_2} (CH_3)_2CHCH_2CBr(COOH)_2$$

$$\xrightarrow[-CO_2]{\text{Heat}} \underset{\alpha\text{-bromo-idocaproic acid}}{(CH_3)_2CHCH_2CH(Br)COOH} \xrightarrow{NH_3} \underset{\text{Leucine}}{(CH_3)_2CHCH(NH_2)COOH}$$

### 3.5 General Physical Characteristics

i. Amino acids are crystalline solids with fairly high melting points and densities
ii. They are soluble in polar solvents like water
iii. They are insoluble in non-polar solvents like petroleum ether, alcohol and benzene
iv. They all occur in optically active forms except glycine
v. The dipole moments for amino acids are high.
vi. They behave as if they are neither basic nor acidic

These facts point towards their dipolar ion or zwitter ion structure. In solution this zwitter ion is in equilibrium with a little of the covalent form.

$$\begin{tikzcd}
\underset{\text{B}}{H_3N^+CHRCOOH + H_2O} \arrow[d, shift right] & \\
\underset{\substack{\text{zwitter ion}\\ \text{A}}}{H_3N^+CHRCOO^-} \arrow[u, shift right, "H_3O^+"'] \arrow[r, shift left] \arrow[d, shift right] & \underset{\text{amino acid form}}{H_2NCHRCOOH} \arrow[l, shift left] \\
\underset{\text{C}}{H_2NCHRCOO^- + H_2O} \arrow[u, shift right, "^-OH"'] &
\end{tikzcd}$$

When an acid is added to the solution of the amino acid the zwitter ion (A) is converted to the cation B because the stronger acid make a proton available to the carboxylate and a cation results. However, when a strong base is added to the amino acid, the zwitter ion (A) is converted to anion C, because the strong base OH takes away a proton from the ammonium ion forming an anion.

Thus in strongly acid medium the amino acids will migrate towards the cathode in an electric field and in presence of a strong base they will migrate towards the anode. This is exactly what happens to the amino acids in an electric field and hence it further proves the zwitter ion structure of the amino acids.

## Activity A/Self Assessment Exercise

Amino acids behave as if they are neither basic nor acidic. Explain

### 3.5.1 Isoelectric Point

It is possible that at a particular pH the concentration of cation B may be exactly equal to the concentration of anion C and hence at that pH there will be no resultant migration of amino acid in an electric field. Such a pH at which an amino acid does not migrate in an electric field is the 'Isoelectric point' (pI) of that amino acid. At this point the concentration of the zwitter ion is maximum.

The isoelectric point is an individual characteristics of an amino acid and depends on the basicity of the amino group and the acidity of the carboxyl group, which varies with the nature of alkyl group,-R. Thus pI is 6.0 for glycine, 5.5 for phenyl alanine and 3.2 for glutamic acid.

The following equilibrium exists between A, B and C:

$$\underset{B}{H_2NCHRCOO^-} \underset{OH^-}{\overset{H^+}{\rightleftharpoons}} \underset{A}{H_3N^+CHRCOO^-} \underset{OH^-}{\overset{H^+}{\rightleftharpoons}} \underset{C}{H_2NCHRCOOH}$$

An amino acid usually shows its lowest solubility in a solution at the isoelectric point, since at this point, there is the highest concentration of the dipolar ion. This knowledge is of great value in separation of an amino acid from a mixture.

## 3.6 General Chemical Properties

### 3.6.1 Reactions Due to the Amino Group

The amino acid can behave as a base or an acid depending on the pH of the solution. They show the reaction of both the amino and the carbonyl group.

i. They form salt with strong acids.

$$H_2NCHRCOOH + HCl \longrightarrow [H_3\overset{+}{N}CHRCOOH]Cl^-$$

Hydrochloride of α-amino acid

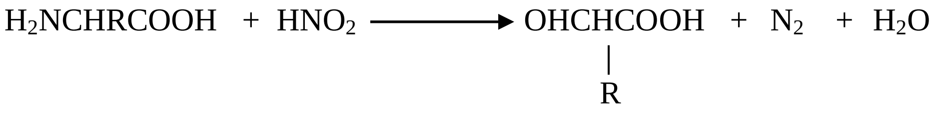
ii. They can be acetylated with ethanoyl chloride or acetic anhydride

$$H_2NCHRCOOH + CH_3COCl \longrightarrow H_3CCOHNCH(R)COOH$$

Acetyl derivative

Benzoylation can also take place by reacting with benzoyl chloride

iii. When treated with dioxonitrate(III) acid,$HNO_2$(nitrous acid), they form α-hydroxy acids.



$$H_2NCHRCOOH + HNO_2 \longrightarrow \underset{\substack{| \\ R}}{OHCHCOOH} + N_2 + H_2O$$

α-hydroxyl acid

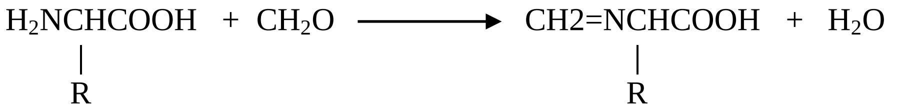
This reaction forms the basis for the determination of free $–NH_2$ groups in amino acids and proteins.

iv. When treated with chloroform and alcoholic solution of potassium hydroxide, they give carbylamines reaction.

$$H_2N\underset{\underset{R}{|}}{C}HCOOH + CH_3Cl + 3KOH \longrightarrow CNC\underset{\underset{R}{|}}{C}HCOOH + 3KCl + 3H_2O$$

Isocyanide derivative

v. When excess of methanal is added the basic function of amino is blocked



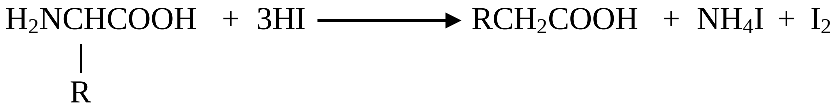
$$H_2N\underset{\underset{R}{|}}{C}HCOOH + CH_2O \longrightarrow CH2{=}N\underset{\underset{R}{|}}{C}HCOOH + H_2O$$

Neutral amino acid Methylene amino acid

However the reaction is more complex in that the main product is the dimethylol derivative of the acid. Since the product formed has a free carboxyl group, it can be titrated using standard alkali and phenolphthalein indicator. It forms the basis of formol titration method.

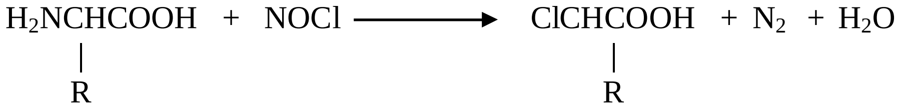
$$H_2NCHRCOOH + 2HCHO \longrightarrow (CH_2OH)_2CHRCOOH$$

vi. When heated with hydrogen iodide, the amino group is knocked off from the molecule resulting in a carboxylic acid



$$H_2N\underset{\underset{R}{|}}{C}HCOOH + 3HI \longrightarrow RCH_2COOH + NH_4I + I_2$$

vii. When treated with nitrosyl chloride, nitrogen is given out with the formation of chloro acid.



$$H_2N\underset{\underset{R}{|}}{C}HCOOH + NOCl \longrightarrow Cl\underset{\underset{R}{|}}{C}HCOOH + N_2 + H_2O$$

viii. Trialkyl derivatives of amino acids are obtained by heating amino acid with alkyl halides in methanolic solution.

$$H_3\overset{+}{N}CH(R)CO\overset{-}{O} + 3CH_3I \xrightarrow{CH_3OH} (CH_3)_3\overset{+}{N}CH_2CO\overset{-}{O} + 3HI$$

### 3.6.2 Reactions Due To Carboxyl Group

i. $H_2NCH(R)COOH + NaOH \longrightarrow H_2NCH(R)COONa + H_2O$

Sodium salt

ii. When treated with $PCl_5$, it yields the hydrochloride of acid chloride.

$$H_2NCH(R)COOH + PCl_5 \longrightarrow H_2NCH(R)COOCl + POCl_3 + HCl$$

$$H_2NCH(R)COOCl \;+\; HCl \longrightarrow [H_3\overset{+}{N}CH(R)COCl]Cl^-$$

iii. When heated with alcohol in the presence of dry hydrogen chloride, amino acids form ester hydrochlorides.

$$H_2NCH(R)COOH \;+ C_2H_5OH \;+\; HCl \longrightarrow \overset{-}{Cl}\,[H_3\overset{+}{N}CH(R)COOC_2H_5] \;+ H_2O$$

The free acid is obtained when the ester is hydrolysed by sodium trioxocarbonate(IV) solution.

iv. The amino acid is decarboxylated when dry distilled or boiled with barium hydroxide.

$$H_2NCH(R)COOH \;+\; Ba(OH)_2 \longrightarrow RCH_2NH_2 \;+\; H_2O + BaCO_3$$

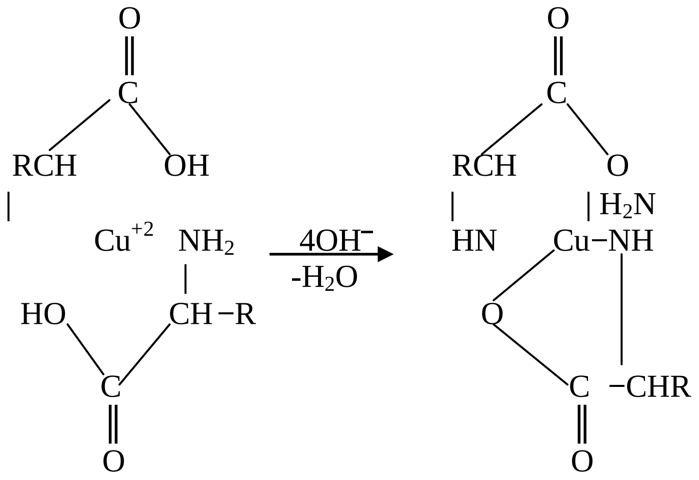
v. They are reduced by lithiumtetrahydridoaluminate(III) to alcohol

$$H_2NCH(R)COOH \xrightarrow{LiAlH_4} H_2NCH(R)CH_2OH$$

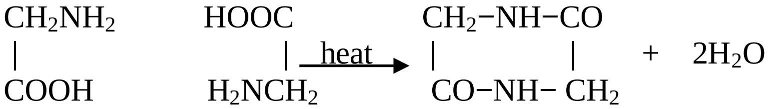
Amino alcohol

### 3.6.3 Reaction Due to Both –$NH_2$ and –COOH groups

i. They form chelate compounds with heavy metal salts. For example when copper(II) oxide is heated with water solution of glycine, a chealate complex in form of deep blue needles is obtained



ii. When amino acids are heated, they lost two molecules of water between two molecules of acids to form diketopiperazines, cyclic diamides



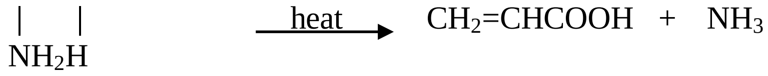
$$\begin{array}{l} CH_2NH_2 \\ | \\ COOH \end{array} \quad \begin{array}{r} HOOC \\ | \\ H_2NCH_2 \end{array} \xrightarrow{heat} \begin{array}{l} CH_2{-}NH{-}CO \\ |\qquad\qquad | \\ CO{-}NH{-}CH_2 \end{array} \;+\; 2H_2O$$

Glycine

2,5-diketopiperazine

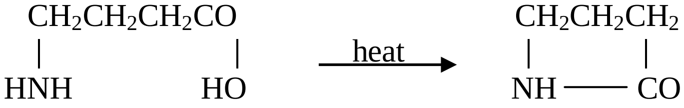
iii. When heated β-amino acid lose a molecule of ammonia to give α,β-unsaturated acid

$CH_2CHCOOH$



$$\underset{NH_2\ \ H}{|\quad|}\ \xrightarrow{heat}\ CH_2{=}CHCOOH + NH_3$$

iv. When heated γ- and δ- amino acids lose a molecule of water by reaction between –NH$_2$ and –COOH group of same molecule to give cyclic amides called lactums



$$\begin{array}{c} CH_2CH_2CH_2CO \\ |\qquad\qquad\quad| \\ HNH\qquad\quad HO \end{array} \xrightarrow{heat} \begin{array}{c} CH_2CH_2CH_2 \\ |\qquad\quad| \\ NH — CO \end{array}$$

v. Ninhydrin test – Amino acids react with ninhydrin (indane-1,2,3-trione hydrate) to form a coloured product.

## Activity B/Self Assessment Exercise

What are the products formed when amino acids react with the following reagents:

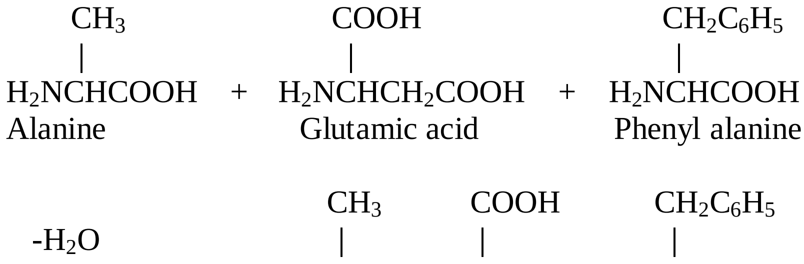
i. PCl$_5$
ii. NaOH
iii. LiAlH4
iv. CH$_3$Cl/alc.KOH
v. CH$_3$COCl

## 3.7 Polypeptides

The α-amino acids obtained from the hydrolysis of proteins contained an amino and a carboxyl group. They are linked through an amide linkage. Chains of amino acid residues, linked through amide linkage formed by the interaction of -COOH group of one and -NH$_2$ group of the another, with elimination of water, are known as peptides and the linkage (-CO.NH-) as peptide linkage.

$$H_2NCH(R')COOH + H_2NCH(R'')COOH \xrightarrow{-H_2O} H_2NCH(R')CONH\ CHR''COOH$$

Dipeptide



$$\underset{Alanine}{\overset{\overset{CH_3}{|}}{H_2NCHCOOH}} + \underset{Glutamic\ acid}{\overset{\overset{COOH}{|}}{H_2NCHCH_2COOH}} + \underset{Phenyl\ alanine}{\overset{\overset{CH_2C_6H_5}{|}}{H_2NCHCOOH}}$$

$$\xrightarrow{-H_2O} \begin{array}{c} CH_3 \qquad COOH \qquad CH_2C_6H_5 \\ |\qquad\quad\ \ |\qquad\qquad\ \ | \\ H_2NCHCONHCHCH_2CONHCHCOOH \end{array}$$

Alanylglutamyphenylalanine
(tripeptide)

When two molecules of amino acids combine in this way, the product is dipeptide. Three or more molecules of same or different acids will give a tripeptide or polypeptide.

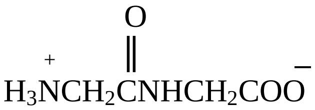
$$H_2NCH(R)CO[HNCH(R')CO]_nNH\ CHR''COOH$$

Polypeptide

If the molecular weight is below 10,000 it is referred to as polypeptide but beyond this it is called a protein

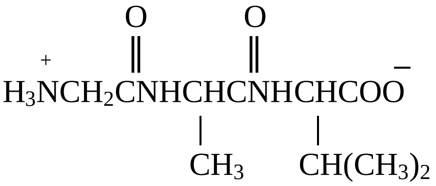
### 3.7.1 Sequence of Amino acids in a Peptide Chain

The $-NH_2$ group end of the peptide chain is called the N-terminal and -COOH group end is called the C-terminal. In writing the sequence of amino acids in a peptide chain the convention is to begin with N-terminal amino acid residue on the left and write the peptide as acylated derivative of C-terminal amino acid on the right.



$$H_3\overset{+}{N}CH_2\overset{\overset{O}{\|}}{C}NHCH_2CO\overset{-}{O}$$

Glycylglycine(Gly.Gly)



$$H_3\overset{+}{N}CH_2\overset{\overset{O}{\|}}{C}NH\underset{\underset{CH_3}{|}}{CH}\overset{\overset{O}{\|}}{C}NH\underset{\underset{CH(CH_3)_2}{|}}{CH}CO\overset{-}{O}$$

Glycyalanylvaline (Gly.Aly.Val)

The symbols of the amino acids are the first three letters of the name but the rule is not adhered to in case of Isoleucine (Ileu), Cysteine (CySH), Cystine (Cy.SSCy), Hydroxy-proline (Hypro), Asparagine ($Asp.NH_2$) AND Glutamine ($GluHN_2$)

## 3.8 Proteins

Proteins are the most important chemical substances that are essential for the growth and maintenance of life. They form an essential part of animal diet. An animal cannot live for long without protein diet though it can without fats and carbohydrates.

### 3.8.1 Occurrences

Proteins occur in the protoplasm of all animal and plant cells. They constitute nearly three fourth of the dry material of most living systems. Plants build up their protein using carbon (IV) oxide, water, nitrates and ammonium salts in presence of energy obtained from the sun, animals and human beings take plant and animal protein in their food which are hydrolysed to amino acids in the system by enzymes. Protein is resynthesised in the animal and human system from these amino acids. They are necessary for growth of the animal body and also for replacing proteins lost in the process of living. Some important sources of proteins and percentage of proteins in them by weight are given in table 1.1 below.

Table 1.1 Percentage protein from different sources of protein

| Source | Protein% | Source | Protein% |
|---|---:|---|---:|
| Soya beans | 43.2 | Groundnut | 26.7 |
| Pea | 28.2 | Cashewnut | 21.2 |
| Milk powder, skimmed | 38 | Almonds | 20.8 |
| Milk powder, whole | 25.2 | Egg yolk | 13.7 |
| Fish | 21.5 | Oat meal | 13.6 |
| Mutton | 18.5 | Wheat | 11.8 |

### 3.8.2 Composition of Proteins

Proteins are complex nitrogenous organic compounds containing carbon, hydrogen, oxygen, sulphur and phosphorus besides nitrogen. Some proteins contain halogens and metals also.

The composition of a protein varies according to the source but an approximation can be as: Carbon 50-55 percent; hydrogen 6-7.5 per cent; nitrogen 15-17 per cent; oxygen 21-24 per cent; sulphur 0.2-2.2 per cent and phosphorous 0.1-1 per cent.

Proteins are built up from α-amino acids units. A protein molecule may have hundreds or thousands of amino acids. There are 23 α-amino acids which by different but precise modes of linking may form an exceedingly large number of different protein molecules. Out of these, ten amino acids are such that they are not synthesized in the human system and are therefore termed as essential. They have to be supplied to the animal system from external sources.

### 3.8.3 Classification of Proteins

Proteins have been classified based on several parameters. According to their solubility and physical properties they are classified into: (a) Simple proteins, (b) Conjugated proteins, and (c) Derived proteins.

a. Simple proteins. These on hydrolysis give only amino acids. For examples:
- Albumis. Serum albumin, egg albumin and lactalbumin.
- Globulins. Serum globulin, tssue globulin and vegetable globulin (in seeds and nuts).
- Prolamines. Zein ( from maize), and gliadin (from wheat).
- Glutelins. Glutenin (from wheat) and oryzenin (from rice).
- Scleroproteins. Keratin (from hair) and fiborin (from silk).
- Histones. Occur in nucleic acids and haemoglobin.
- Protamines. Occur in nucleic acids.

b. Conjugated proteins. These proteins have a non-protein part in their molecule. This non-protein part is also referred to as prosthetic group. It is possible to separate the prosthetic group by careful hydrolysis. Some examples and their prosthetic group are given below:

i. Nucleoproteins. The prosthetic group is nucleic acid and the proteins are found in nucleus of the cell.

ii. Glycoproteins. The non-protein part is a carbohydrate or its derivative. It is found in ‘egg-white’.

iii. Chromoproteins. These have a coloured prosthetic group; especially a pyrrole derivative. The coloured prosthetic groups usually contain a metal e.g., Fe, Cu, Mg etc. Examples are chlorophyll and haemogogbin.

iv. Phosphoproteins. These have a phosphoric acid residue in some form (other than nucleic acids or lipoproteins). Examples are casein (from milk) and viteline (from egg yolk).

v. Lipoproteins These have a lipid such as lecithin, cephalin etc. as prospthetic group.

c. Derived proteins. These are the degradation products, corresponding to various stages, in the hydrolysis of simple or conjugated proteins by acid, alkali or enzymes.

Another classification of proteins into (i) Globular and (ii) fibrous proteins is based on their functions and molecular shapes.

i. Globular proteins. They are nearly spherical in shape, soluble in water and in dilute acids, bases etc. their important function is the maintenance and regulation of life-processes in the living organisms. All enzymes, many hormones, antibodies, haemoglobin etc. are the examples of this class of proteins.

ii. Fibrous proteins. They have a thread like structure and are present in fibre like form. They are soluble in water, dilute acids and bases. They form the main structural material of animal tissues. For example, Keratin (the protein present in skin, hair, nails etc.), myosin (present in muscles), collagen etc.,

### 3.8.4 Physical Characteristics of Proteins

Different proteins have different physical properties but their general physical properties can be summarized as given below:

i. Except chromoproteins, they are colourless, tasteless and odourless. Mostly they are amorphous but some are crystalline when pure. They do not have a sharp melting point.

ii. Most of them are insoluble in alcohol and water but they dissolve in dilute acid and alkalis. Some proteins like those present in skin and hair are, however, insoluble.

iii. They have high molecular weight since the proteins molecules are very complex having thousands of atoms.

iv. They are colloidal in nature. They are hydrophilic colloids which cannot pass through vegetable or animal membrane. Some of the proteins form thick transluscent sols with water which can set to gels on cooling.

v. Reversible precipitation. On addition of sodium chloride, ammonium sulphate, magnesium sulphate and some alkaline earth-salts some proteins are precipitated. The precipitate can be filtered and redissolved in water. This fact can be made use of in separation of some proteins.

vi. Denaturation. When heated or acted upon by reagents like alcohols, heavy metal salts ($HgCl_2$, $CuSO_4$ etc.), picric acid or alkaline earth-salts, proteins are coagulated.

Denaturation occurs most readily at the isoelectric point and is believed to take place because of unfolding of the proteins molecule. During denaturation the secondary and tertiary structure unfolds but the primary structure remains intact. There is loss of biological activity and change in the physical properties during denaturation but the chemical reactivity increases due to opening up of various functional groups.

Denaturation is generally irreversible but there are many examples of reversible nature when it is called renaturation. Gentle treatment of protein with urea or slow cooling help the process of renaturation.

vii. Isoelectric point. Every protein has a characteristic isoelectric point at which its ionization and solubility is minimum. This property is made use of in the isolation and identification of proteins by electrophoretic methods.

## Activity C/Self Assessment Exercise

a. Distinguish between peptise, polypeptide and proteins
b. What are the various classes of proteins?

### 3.8.5 Chemical Characteristics of Proteins

**i.** They are amphoteric nature

Since proteins have free —$NH_2$ and -COOH groups they react with both, the acidic and basic substances.

**ii.** Hydrolysis

Proteins are hydrolysed by dilute acids and alkalis or by enzymes. The products of hydrolysis are proteoses; peptones, polypeptides, simple peptides and α-amino acids.

**iii.** Oxidation

Oxidation of proteins occurs during burning or decay. The products, depending upon the conditions of oxidation, are nitrogen, amines and carbon dioxide. An animal body during decay suffers bacterial oxidation producing all these products and the offensive smell is due to various amines, cyanides etc. produced.

### 3.8.6 Colour Reactions of Proteins

These reactions serve as test for proteins. The entire test may not be positive for every protein but majority of these should be positive for a protein

i. Biuret test

On adding a dilute solution of copper tetraoxosulphate(VI) to alkaline solution of protein, a violet colour may be obtained. This test is on account of the likely formation of biuret ($H_2N.CONH.CONH_2$) as an intermediate.

ii. Xantho-proteic test

When a protein solution is warmed with trioxonitrate (V) acid, a yellow colour is obtained. On making the reaction mixture alkaline with ammonia the colour changes to orange.

iii. Libermann's test

Proteins containing tryptophan on being boiled with concentrated hydrochloric acid followed by the addition of a few drops of sucrose solution give violet colour.

iv. Millon's test

When Millon's reagent (mercurous and mercuric nitrate in $HNO_3$) is added to a protein solution, a white precipitate which turns red on heating may be formed. This is due to a phenolic -OH group in the protein molecule.

v. Nitroprusside test

This test is applicable to certain proteins containing -SH group They produce transient red colour on adding nitroprusside solution.

vi. Lead sulphide test

Proteins containing –S-S- or -SH group when boiled with NaOH and lead acetate produce black precipitate of lead sulphide.

vii. Molisch test

Protein solution is mixed with alcoholic solution of α-naphthol and concentrated $H_2SO_4$ is poured down along the side of the test-tube. Proteins, containing carbohydrate residue give violet colour at the junction of two liquids in the test-tube.

viii. Ninhyrin test

This is a very delicate test and consists in reaction of pyridine solution of a protein with ninhydrin. A deep blue, violet-pink or red colour is indicative of a protein. This test is due to free $-NH_2$ and -COOH groups of protein and is also shown by amino acids

### 3.8.7 Structure of Proteins

The problem of structure of protein has been tackled at different levels. At the first level of a.

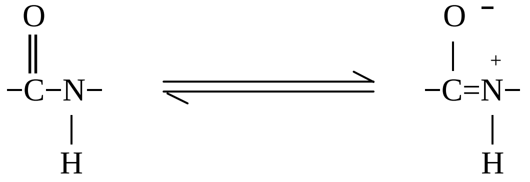
a. Primary Structure

At the level of primary structure determination, the number, nature and sequence of amino acids forming peptide chains of the protein are determined. This can be done by:

i. Isolating the proteins in pure state
ii. Determining the sub-units necessary if results indicate the presence of more than one C or N end groups.
iii. Hydrolysing the proteins to get the amino acids which are identified and extimated quantitatively
iv. Determining the molecular weight by amino acid percentage composition and physical methods
v. Determining the sequence of amino acids by carrying out C-terminal and N-terminal analysis.

b. Secondary Structure

This step deals with the arrangement of the peptide chains in space to form coils, sheet and other structures which are held together by hydrogen bond, electrostatic forces and inter and intramolecular forces. The hydrogen bonds are formed between the carboxylic oxygen and hydrogen of –NH group. The force of electrostatic attraction or repulsion also operates between the charged polar groups. To this is the added influence of the inter and intramolecular bonds like disulphide bond. The α-helix was structure is the generally acceptably structure. In this structure the hydrogen bond occurs between different –CO and –NH group of the same chain which holds helix. Stereochemical study shows that a helix with 3.7 residues per turn is the most stable. Hydrogen bonding exist between the –CO group of one residue and –NH group of the fourth residue in the helix. The stability of the α-helical structure is also due to resonance between the –NH and –CO groups in the peptide chain.



$$-\overset{\overset{O}{\|}}{C}-\underset{\underset{H}{|}}{N}- \rightleftharpoons -\overset{\overset{O^-}{|}}{C}=\underset{\underset{H}{|}}{\overset{+}{N}}-$$

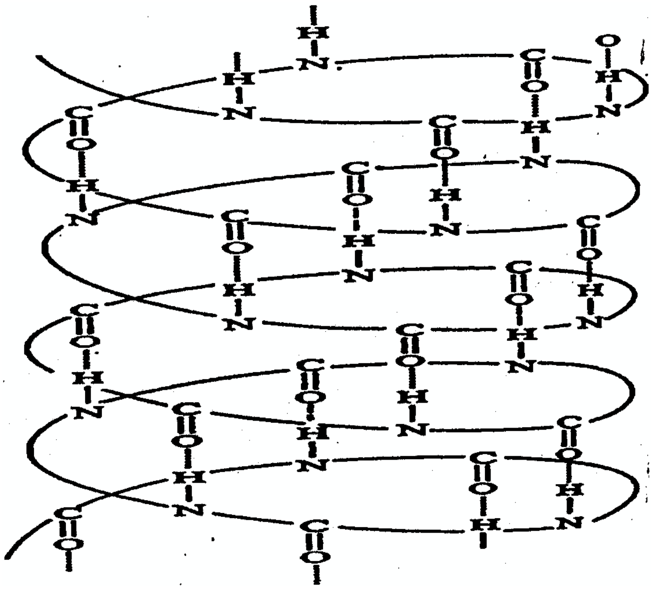


Figure 1.1: Helical structure of protein

c. Tertiary Structure

The coiling or folding of long peptide chains give rise to a three dimensional structure which is called the tertiary structure. It involves hydrogen, ionic inter and intra molecular bonds. Hydrophobic bonds is given rise to by the alkyl side chains of the amino acid which is hydrophobic in character. The polar group with high affinity for water (hydrophilic) tend to take positions on the surface of the globular proteins.

d. Quaternary structure

This arises from the association of various identical or different sub-units. Each sub-unit has its primary, secondary and tertiary structures.

### 3.8.8 Uses of Proteins

i. They are needed as food for animals
ii. Proteins like haemoglobin and various peptides are essential for the system of human being
iii. Various essential enzymes in the human system and in nature are proteins.
iv. Many anti-viral vaccines are protein in denatured form
v. Various amino acids have been obtained from proteins
vi. Wool aand natural silk are proteins
vii. Various useful substances like glue, casein and gelatine are proteins

## 4.0 Conclusion

Amino acids are the building blocks of protein. The α-amino acids are the most important of all because they are the final products of the hydrolysis of peptides and proteins. They are known as essential amino acids because they are essential in the diet.

## 5.0 Summary

In this unit we have learnt that:

i. Proteins are macromolecules with very high relative molecular masses.

ii. Amino acids are the amino substituted acids containing both amino (-$NH_2$) and carbonyl (-COOH) group(s).

iii. The IUPAC names of amino acids are obtained by indicating the position of the amino group by Arabic numeral on the alkyl radical chain of the alkanoic acid, making the carboxylic carbon the number 1 carbon.

iv. Simple amino acids having only one amino and carboxyl groups may be classified as α-, β-, γ- and δ- etc amino acids depending on the position of the amino group with respect to carboxyl group.

v. The α-amino acids are the most important of all because they are the final products of the hydrolysis of peptides and proteins. They are known as essential amino acids because they are essential in the diet.

vi. α-Amino acids are classified into:

- Neutral Amino acids
- Amino Acids:
- Acidic Amino Acids

vii. All amino acids obtained by acid or enzymatic hydrolysis of proteins are optically active except glycine.

viii. α-Amino acids can be prepared from

- Amination of α-halogenated acids.
- From Aldehydic and ketonic acids
- Malonic Ester synthesis

ix Amino acids are crystalline solids with fairly high melting points and densities, soluble in polar solvents like water, insoluble in non-polar solvents like petroleum ether, alcohol and benzene.They all occur in optically active forms except glycine. The dipole moments for amino acids are high.They behave as if they are neither basic nor acidic

x. The pH at which an amino acid does not migrate in an electric field is the 'Isoelectric point' (pI) of that amino acid. The isoelectric point is an individual characteristic of an amino acid and depends on the basicity of the amino group and the acidity of the carboxyl group, which varies with the nature of alkyl group.

xi. The following equilibrium exists between A, B and C:

$$\begin{array}{ccccc} H_2NCHRCOO^- & \underset{OH^-}{\overset{H^+}{\rightleftharpoons}} & H_3N^+CHRCOO^- & \underset{OH^-}{\overset{H^+}{\rightleftharpoons}} & H_2NCHRCOOH \\ B & & A & & C \end{array}$$

xii. An amino acid usually shows its lowest solubility in a solution at the isoelectric point.

xiii.Reactions of amino due to the amino group are:

- They form salt with strong acids.

$$H_2NCHRCOOH + HCl \longrightarrow [H_3\overset{+}{N}CHRCOOH]Cl^-$$

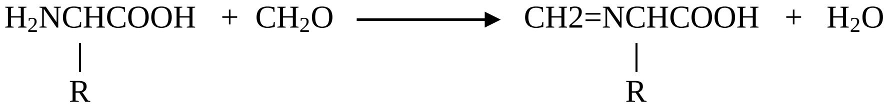
Hydrochloride of α-amino acid

- They can be acetylated with ethanoyl chloride or acetic anhydride

$$H_2NCHRCOOH + CH_3COCl \longrightarrow H_3CCOHNCH(R)COOH$$

Acetyl derivative

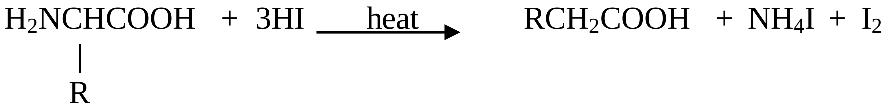
- When treated with dioxonitrate(III) acid,$HNO_2$(nitrous acid), they form α-hydroxy acids.
- When treated with chloroform and alcoholic solution of potassium hydroxide, they give carbylamines reaction.
- When excess of methanal is added the basic function of amino is blocked



$$\underset{\substack{|\\R}}{H_2NCHCOOH} + CH_2O \longrightarrow \underset{\substack{|\\R}}{CH2{=}NCHCOOH} + H_2O$$

Neutral amino acid Methylene amino acid

- When heated with hydrogen iodide, it forms carboxylic acid



$$\underset{\substack{|\\R}}{H_2NCHCOOH} + 3HI \xrightarrow{\text{heat}} RCH_2COOH + NH_4I + I_2$$

xiv. When treated with nitrosyl chloride, nitrogen is given out with the formation of chloro acid.

xv. Trialkyl derivatives of amino acids are obtained by heating amino acid with alkyl halides in methanolic solution.

xvi. The following are reactions due to carboxyl group

- $H_2NCH(R)COOH + NaOH \longrightarrow H_2NCH(R)COONa + H_2O$

  Sodium salt
- $H_2NCH(R)COOH + PCl_5 \longrightarrow H_2NCH(R)COOCl + POCl_3 + HCl$

$$H_2NCH(R)COOCl + HCl \longrightarrow [H_3\overset{+}{N}CH(R)COCl]Cl^-$$

- When heated with alcohol in the presence of dry hydrogen chloride

$$\overset{-}{H}_2NC\overset{+}{H}(R)COOH + C_2H_5OH + HCl \longrightarrow Cl\,[H_3NCH(R)COOC_2H_5] + H_2O$$

- The amino acid is decarboxylated when dry distilled or boiled with barium hydroxide.

$$H_2NCH(R)COOH + Ba(OH)_2 \longrightarrow RCH_2NH_2 + H_2O + BaCO_3$$

- They are reduced by lithiumtetrahydridoaluminate(III) to alcohol

xvii. The following are reactions due to both $–NH_2$ and –COOH groups

- They form chelate compounds with heavy metal salts.
  When amino acids are heated, they lost two molecules of water between two molecules of acids to form diketopiperazines, cyclic diamides

- When heated β-amino acid lose a molecule of ammonia to give α,β-unsaturated acid

- When heated γ- and δ- amino acids lose a molecule of water by reaction between $–NH_2$ and –COOH group of same molecule to give cyclic amides called lactums

- Ninhydrin test – Amino acids react with ninhydrin (indane-1,2,3-trione hydrate) to form a coloured product.

xviii. Chains of amino acid residues, linked through amide linkage formed by the interaction of -COOH group of one and $-NH_2$ group of the another, with elimination of water, are known as peptides and the linkage (-CO.NH-) as peptide linkage.

xix. Two molecules of amino acids is called dipeptide. Three or more molecules of same or different acids will give a tripeptide or polypeptide. Those with molecular weight below 10,000 it is referred to as polypeptide but beyond this it is called a protein

**xx.** In writing the sequence of amino acids in a peptide chain the convention is to begin with N-terminal amino acid residue on the left and write the peptide as acylated derivative of C-terminal amino acid on the right.

xxi. Proteins are complex nitrogenous organic compounds containing carbon, hydrogen, oxygen, sulphur and phosphorus besides nitrogen.

xxii. Proteins are built up from α-amino acids units.

xxiii. Proteins classified according to their solubility and physical properties
(a) Simple proteins,
(b) Conjugated proteins
(c) Derived proteins.

xxiv.Proteins may also be classified into
(i) Globular
(ii) (ii) fibrous proteins is based on their functions and molecular shapes.

xxv. General physical properties can be summarized as given below:

- Except chromoproteins, they are colourless, tasteless and odourless.
- Most of them are insoluble in alcohol and water but they dissolve in dilute acid and alkalies.
- They have high molecular weight
- They are colloidal in nature.

- On addition of sodium chloride, ammonium sulphate, magnesium sulphate and some alkaline earth-salts some proteins are precipitated.
- When heated or acted upon by reagents like alcohols, heavy metal salts ($HgCl_2$, $CuSO_4$ etc.), picric acid or alkaline earth-salts, proteins are coagulated.

xxvi. Chemical Characteristics of Proteins are:
- They are amphoteric nature
- Proteins are hydrolysed by dilute acids and alkalis or by enzymes.
- Oxidation of proteins occur during burning or decay.

xxvii. Colour reactions of proteins serve as test for proteins, and they are:
- Biuret test
- Xantho-proteic test
- Libermann’s test
- Millon’s test
- Nitroprusside test
- Lead sulphide test
- Molisch test
- Ninhyrin test

xxviii. The structure of protein can be determined at the following levels:
- Primary Structure
- Secondary Structure
- Tertiary Structure
- Quaternary structure

xxix. Proteins are needed as food for animals.Proteins like haemoglobin and various peptides are essential for the system of human being.Essential enzymes in the human system, anti-viral vaccines, Wool and natural silk and useful substances like glue, casein and gelatine are proteins.

## 6.0 Tutor Marked Assignment

a. Discuss the effect of heat on α-amino acid.
b. What are the various ways protein can be tested for?
c.Discuss isoelectric point in amino acids.

## 7.0 Further Reading and other resources

a. K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry -Third Edition

b. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry - Sixth Edition

c. John McMurry and Mary E.Castellion (1999) Fundamentals of General,Organic, and Biological Chemistry-3rd Edition

# Unit 3: Fats and Oil

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## 1.0: Introduction

Fats and oils are esters of glycerol with higher fatty acids and are called glycerides. They are obtained by the combination of propane-1,2,3-triol with fatty acid, which are long chain carboxylic acids.

## 2.0 Objectives

At the end of this unit you should be able to:

- i. Distinguish between fats and oil
- ii. Give examples of natural sources of fats and oil
- iii. Distinguish between saturated and unsaturated fatty acids
- iv. Describe a method of preparing oil
- v. Discuss the physical properties of fats and oil
- vi. Describe the results of drying, hydrogenation, hydrolysis and hydrogenolysis in fats and oil
- vii. Distinguish acid hydrolysis and alkali hydrolysis fats and oils
- viii. Define physical and chemical methods of determining the composition and purity of fats and oil
- ix. Define acid value, saponification, iodine value, R.M value, Acetyl value and Polenske value
- x. State uses of fats and oils
- xi. Describe the structure of soap
- xii. Describe the cleaning action of soap
- xiii. Distinguish between soapy and soapless detergents.

## 3.0 Occurrence and Composition of Fats

Fats are the main constituents of the storage fat cells in animals and plants and they are one of the important food reserves of living organism. These plant and animal fats can be extracted. Liquid fats are often referred to as oils.

Carboxylic acids found in natural fats and oils are mainly unbranched. They can be divided into two groups: saturated and unsaturated.

Saturated carboxylic acids have single bonds in their hydrocarbon chains only and they are found in animals, while unsaturated carboxylic acids contain at least one C=C double in their chains and they are obtained in plants. Carboxylic acids with more than one C=C double bonds are known as polyunsaturated.

Saturated carboxylic acids are solids at room temperature. This is because the regular nature of their aliphatic chains allows the molecules to be packed in a close, parallel alignment. Unsaturated carboxylic acids are liquids at room temperature. It is because the double bonds in the hydrocarbon chains interrupt the regular packing.

Thus the important difference between oils and fats is that oils are liquids at ordinary temperature while fats are solids.

|  | **Saturated Fatty ACID(%)** |  |  | **Unsaturated Fatty Acid(%)** |  |  |
|---|---|---|---|---|---|---|
| **Source** | **C12 Lauric** | **C14 Myristic** | **C16 Palmitic** | **C18 Stearic** | **C18 Oleic** | **C18 Linoleic** |
| **Animal Fat** |  |  |  |  |  |  |
| Lard Butter |  | 1 | 25 | 15 | 50 | 6 |
| Human Fat | 2 | 10 | 25 | 10 | 25 | 5 |
|  | 1 | 3 | 25 | 8 | 46 | 10 |
| **Vegetable Oil** Corn |  |  |  |  |  |  |
| Olive |  |  |  |  |  |  |
| Peanut |  | 1 | 8 | 4 | 46 | 42 |
| Soybean |  | 1 | 5 | 5 | 83 | 7 |
|  |  |  | 7 | 5 | 60 | 20 |
|  |  |  | 7 | 4 | 34 | 53 |

**Figure 1.0 Approximate Composition of Common Fats and Oil**

(Source: Fundamentals of General,Organic, and Biological Chemistry,3rd Edition By John McMurry and Mary E.Castellion)

## Activity A/Self Assessment Exercise

a. Distinguish between fats and oil
b. What are the differences between saturated and unsaturated fatty acids

## 3.1 Formation of Fats and Oils

When a molecule of glycerol, i.e propane-1,2,3-triol, reacts with a molecule of stearic acid, glyceryl monostearate is formed.

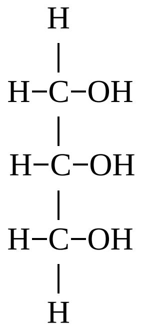
The product formed may then react with another molecule of stearic acid to form glyceryl distearate, which further reacts to give glyceryl tristearate.

The glyceryl tristearate formed is a solid. It is a fat. If glycerol reacts with other fatty acids to form a liquid product, then it is oil.

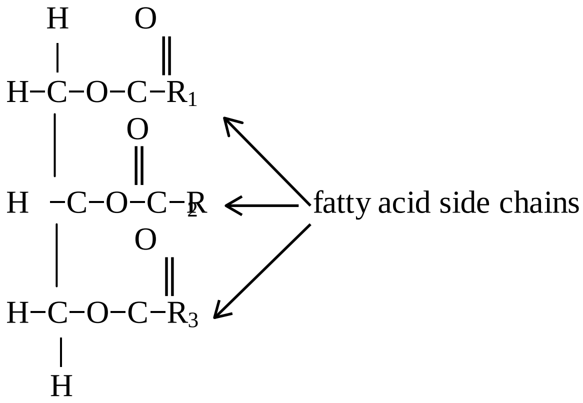
In fact, most natural fats and oils are mixed glycerides. They are esters formed from propane-1,2,3-triol and a mixture of different long chain carboxylic acids, such as linoleic, stearic and oleic acids.

## 3.2 Structure of Fats and Oils

Fats and oils are obtained by the combination of propane-1,2,3-triol with fatty acids, which are long chain carboxylic acids.



$$\begin{array}{c} H \\ | \\ H-C-OH \\ | \\ H-C-OH \\ | \\ H-C-OH \\ | \\ H \end{array}$$



$$\begin{array}{l} H \quad\quad O \\ | \quad\quad\ \| \\ H-C-O-C-R_1 \\ | \quad\quad\ \ O \\ | \quad\quad\ \ \| \\ H\ -C-O-C-R_2 \\ | \quad\quad\ \ O \\ | \quad\quad\ \ \| \\ H-C-O-C-R_3 \\ | \\ H \end{array}$$

Propane-1,2,3-triol
(glycerol)

general structure
of a triglyceride

## 3.3 General Properties

| Name | Typical Source | Structure | Meltin Point (oC) |
|---|---|---|---|
| **Saturated** | | | |
| Lauric | Coconut oil | $CH_3(CH_2)_{10}COOH$ | 44 |
| Myristic | Butter fat | $CH_3(CH_2)_{12}COOH$ | 58 |
| Palmitic | Most fats and oil | $CH_3(CH_2)_{14}COOH$ | 63 |
| stearic | Most fats and oil | $CH_3(CH_2)_{16}COOH$ | 70 |
| **unsaturated** | | | |
| Oleic | Olive oil | $CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$ | 4 |
| Linoleic | Vegetable oils | $CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$(Cis) | -5 |
| Linolenic | Soybeans and canola oil | $CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$(Cis) | -11 |
| Arachidonic | Lard | $CH_2(CH_2)_4(CH{=}CHCH_2)_4CH_2CH_2COOH$ | -50 |

**Figure 1.1 Structures Of Some Common Fatty Acids**(Source: Fundamentals of General,Organic, and Biological Chemistry,3rd Edition By John McMurry and Mary E.Castellion)

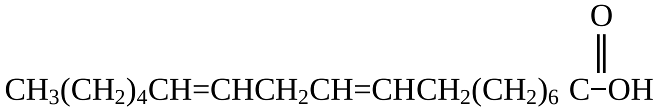
### 3.3.1 General Physical Properties

i. Oils and fats are colourless liquids or solids(may be yellow or brown due to impurities).
ii. Vegetable oils have lower boiling points than animal fats because they generally have a higher proportion of unsaturated fatty acids. The more highly unsaturated the acyl group in a triglyceride, the lower it's melting point.
iii. The are lighter than water.
iv. The are immiscible with water.

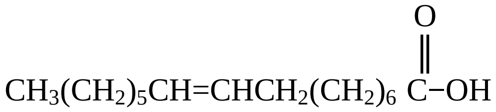
v. They are freely soluble in organic solvents such as benzene, petroleum ether etc.
vi. They are non-volatile.
vii. The decomposes on strong heating giving irritating odour of acrolein
viii. They readily form emulsions when agitated with water in the presence of soap,gelatine or other emulsifiers.

## Activity B/Self Assessment Exercise

Which of the following fatty acids has the highest melting points?

a. 

$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2(CH_2)_6\overset{\overset{O}{\|}}{C}{-}OH$

b. 

$CH_3(CH_2)_5CH{=}CHCH_2(CH_2)_6\overset{\overset{O}{\|}}{C}{-}OH$

### 3.3.2 General Chemical Properties

a. Drying

Some oils containing glycerides of unsaturated acids with two or three double bonds have the property of slowly absorbing oxygen from the air and then polymerises to form a hard transparent coating used in making paints and oil cloth. This process is known as drying and the oils as drying oil. Examples of these oils are linoleic, eleostearic and licanic acids.

Drying take place much more readily if the acids contains conjugated system of double bonds e.g in eleostearic and licanic acids unlike in acids containing non-conjugated double bonds.

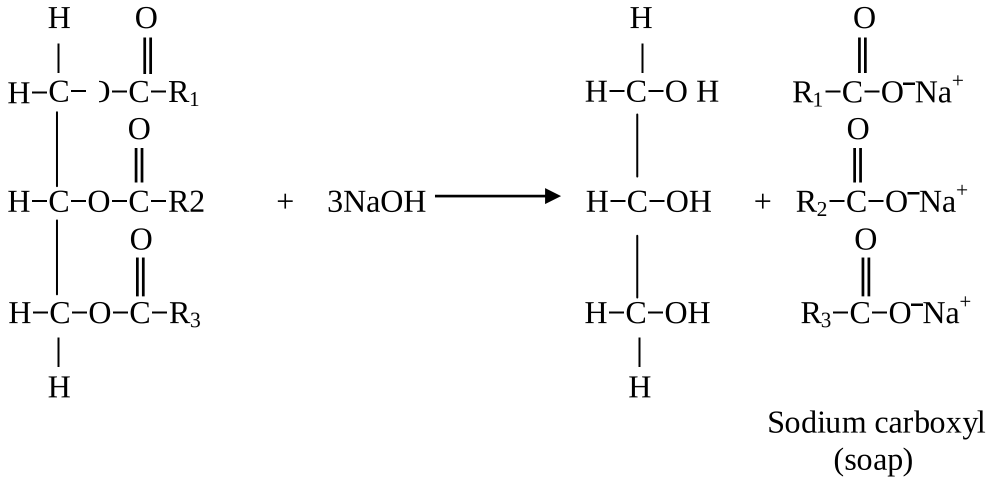
b. Rancidification

Oils and fats, when exposed to air and moisture for a long time during storage undergo slow decomposition and develop unpleasant smell. The process is known as rancidification.

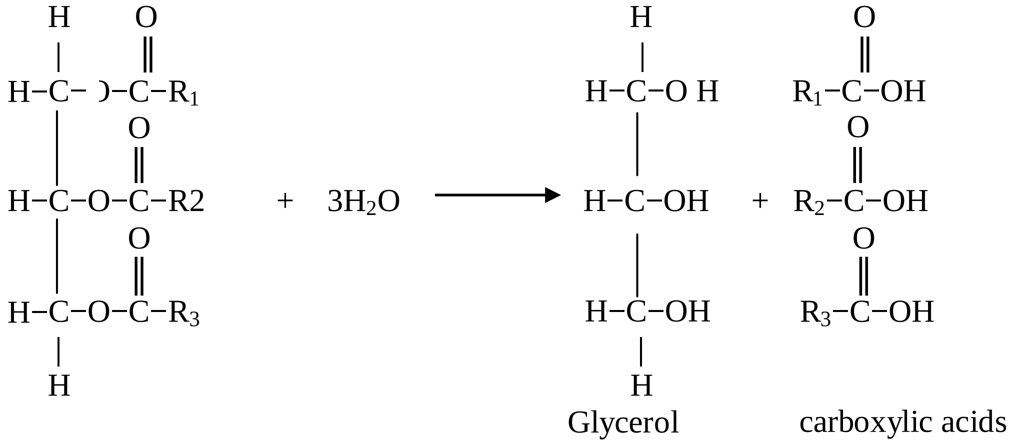
c. Hydrolysis of Fats and Oils

Oils and fats can be hydrolysed to glycerol and the fatty acids by dilute acids, alkalis or superheated steam. Hydrolysis may also be brought about by enzymes.

Hydrolysis carried out in an alkaline medium is more practical and the reaction is irreversible. Such process is called saponification. The reaction can be catalysed by sodium hydroxide. Propane-1,2,3-triol and mixture of sodium salts of carboxylic acids, called soap, are then produced.

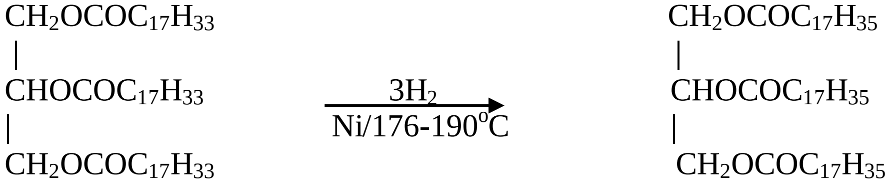


Fats and oils ingested into our bodies are hydrolysed into carboxylic acids and glycerol. These substances are then used as fuel in our body, in building cell membranes or are stored up as fatty tissues. Some fats also provide essential carboxylic acids to our body.



d. Hydrogenation

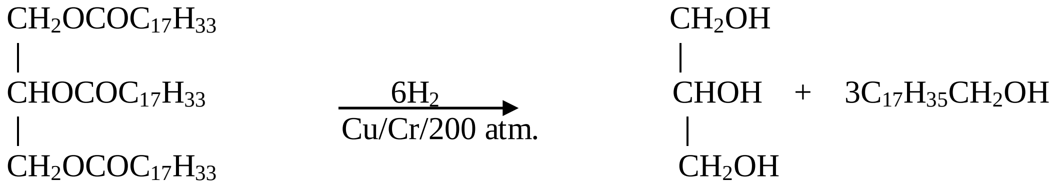
Oil contains more of unsaturated glycerides than fats and so are liquids ordinarily. When hydrogen is passed them under pressure in the presence of finely divided nickel or Raney nickel, the unsaturated glycerides becomes saturated and the oil becomes solid or semi-solid. This process is known as hydrogenation and the solid oil is known as margarine.It improves the colour,odour and taste of oils.



$$\begin{array}{l}CH_2OCOC_{17}H_{33}\\ |\\ CHOCOC_{17}H_{33}\\ |\\ CH_2OCOC_{17}H_{33}\end{array} \xrightarrow[Ni/176\text{-}190^{o}C]{3H_2} \begin{array}{l}CH_2OCOC_{17}H_{35}\\ |\\ CHOCOC_{17}H_{35}\\ |\\ CH_2OCOC_{17}H_{35}\end{array}$$

e. Hydrogenolysis

This process of splitting a compound by means of hydrogen. When excess hydrogen is passed through oil or fat under pressure in the presence of copper chromium catalyst, it splits up into glycerol and higher aliphatic alcohols.



$$\begin{array}{l} CH_2OCOC_{17}H_{33} \\ | \\ CHOCOC_{17}H_{33} \\ | \\ CH_2OCOC_{17}H_{33} \end{array} \xrightarrow[\text{Cu/Cr/200 atm.}]{6H_2} \begin{array}{l} CH_2OH \\ | \\ CHOH \\ | \\ CH_2OH \end{array} + 3C_{17}H_{35}CH_2OH$$

## Activity C/Self Assessment Exercise

i. Draw the structure of the triglyceride whose components are glycerol and three oleic acid acyl groups

ii. Take the triglyceride in (a) above through acid and alkali hydrolysis and predict the products formed

## 3.4 Analysis of Fats and Oils

The value of a particular oil depends on it's composition and purity. Some of the usual physical tests to determine the purity of fats and oil are melting point, specific gravity, refractive index and viscosity.

Some of the chemical tests are:

i. Acid value: It indicates the amounts of free fatty acids present in an oil or fat. It is the number of milligrams of potassium hydroxide required to neutralise the free organic acids present in 1gm of fat or oil. It is determined by dissolving a weighed quantity of oil or fat in alcohol and titrating against standard alkali, using phenolphthalein as indicator.

   A high acid value indicates a stale oil or fat.

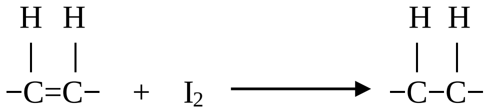
ii. Saponification : This is the number of milligrams of potassium hydroxide required to completely saponify 1gm of fat or oil- or completely neutralise the fatty acids resulting from complete hydrolysis of 1gm fat or oil.

   Saponification gives an idea about the molecular weight of fats or oil. The smaller the saponification value , the higher the molecular weight. It is also useful in calculating the amount of alkali needed to convert a definite amount of fat or iol into soap and in detecting the alteration of a fat or oil by one of lower or higher saponification value.

   The difference between saponification value and acid value is known as ester value of the fat or oil.

iii. Iodine Value

   One structural difference between fats and oils is the degree of unsaturation. Solid animal fats contain mainly saturated carboxylic acids while vegetable oils contain large amounts of unsaturated carboxylic acids. As unsaturated carboxylic acids cannot be synthesized by our body, they are essential in the diet. Therefore, it is useful to have a quantitative measure of the degree of unsaturation in fats and oils. A convenient reference for the purpose is the iodine value. Its determination is based on the reaction between iodine and the carbon-carbon double bond in fats and oils. In practice, the more reactive iodine monochloride is used.



$$\begin{array}{c}H\ \ H\\ |\ \ \ |\\ -C{=}C-\end{array} + I_2 \longrightarrow \begin{array}{c}H\ \ H\\ |\ \ \ |\\ -C-C-\end{array}$$

Unsaturated fats and oil combine with iodine readily, whereas saturated fats and oils do not. The more unsaturated the fats and the oil is, the more iodine it will react with.

The iodine value of fats or and oil is defined as the number of grams of iodine that reacts with 100g of the fat or oil. The higher the iodine value, the greater is the degree of unsaturation of the fat or oil. It also gives an idea of the drying character of the fat or oil.

Generally, vegetable oils have higher values than animal fats. This shows that vegetable oils are more unsaturated. It has been found that animal fats have iodine values less than 70, while vegetable oils are more than 70.

iv. Reichert-Meissi(R.M.)Value: It measure the volatile fatty acids present as glycerides in oil or fats. It is defined as the number of ml of 0.1N potassium hydroxide solution required to neutralise the distillate of 5g of hydrolysed fat or oil.

v. Acetyl Value: It is defined as the number of milligrams of potassium hydroxide required to neutralise acetic acid liberated by the saponification of one gram of completely acetylated oil or fat. the distillate of 5g of hydrolysed fat or oil.

It measures the alcoholic group present in oil or fat.

vi. Polenske value: t is defined as the number of ml of 0.1N potassium hydroxide solution required to neutralise the steam volatile, but water insoluble fatty acids obtained from the distillate of 5g of hydrolysed fat or oil.

## Activity D/Self Assessment Exercise

Write the equation for the complete hydrogenation of the fatty acid, you drew in activity C(i) above.

## 3.5 Uses of Fats and Oil

i. Used as food
ii. Used in the manufacture of soap.alycerol,candle, margarine, hair creams etc
iii. Long chain alcohols prepared from fats and oils are used in the preparation of synthetic detergents
iv. Used in the manufacture of paints and vanishes
v. Used in the manufacture of oil cloth and linoleum

## 3.6 Soaps

Soaps are metallic salts of higher fatty acids such as stearic, palmitic and oleic acids. They are manufactured by cold , semi-boiled or boiled processes. Ordinary soap today is a mixture of sodium salts of long-chain fatty acids because the fat from which it is made is a mixture.

Soap may vary in composition and methods of processing; it may be Castile soap, if made from olive oil; alcohol may be added to make it transparent; air may be beaten into it to make it float; perfumes,dyes,and germicides may be added; if a potassium salt instead of a sodium salt, it is soft soap.

In solution, soap is dispersed in spherical clusters called micelles, each of which may contain hundreds of soap molecules. A soap molecule has a polar end, $-COO^{-}Na^{+}$, and a non-polar end, the long carbon chain of 12-18 carbons. The polar end is water soluble-hydrophilic while the non-polar end is hydrophobic or lipophilic.

Molecules that have both polar and non-polar end and are are big enough for each end to display its own solubility behaviour are called amphipathic. In solution, the polar ends projects towards the polar solvent-water, while the non –polar end seeks for a non-polar environment – the non-polar ends of other soap molecules.

### 3.6.1 Cleaning action of soap

The problem in cleaning is the fat and grease that make up and contain dirt. Water alone cannot dissolve these hydrophobic substances because when oil substance is in contact with water, it tends to coalesce so that there is a water layer and an oil layer. However, the presence of soap changes the situation. The non-polar ends of soap molecules dissolves in the oil droplet, leaving the carboxylate ends projecting into the surrounding water layer . Repulsion between similar charges keeps the oil droplets from coalescing; a stable emulsion of oil and water forms and can be removed from the surface being cleaned.

Hard water contains calcium and magnesium salts which reacts with soap to form insoluble calcium and magnesium carboxylates.

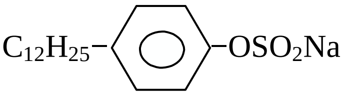
### 3.6.2.Synthetic Detergents

They are called soapless detergents or syndets. They are more resistant to hard water than soaps. Like soaps the contain both hydrophilic-water soluble and hydrophobic –oil soluble part. They have replaced soap to large extent.

| | |
|---|---|
| $C_{12}H_{25}$ ———— $OSO_3Na$ | $C_{15}H_{31}$ ———— $COOCNa$ |
| Hydrophobic Part   Hydrophilic part | Hydrophobic part   Hydrophilic part |
| Soapless detergent-synthetic detergent<br>(sodium lauryl sulphate) | soap(Sodium palmitate) |

Examples are:

| | |
|---|---|
| $C_{12}H_{25}-O-OSO_2Na$ | $C_{16}H_{33}-O-SO_2-ONa$ |
| Sodium lauryl sulphate | sodium cetyl sulphate |



Sodium p-dodecyl-benzenesulphonate

Synthetic detergents may be anionic surface active, cationic surface active or non-ionic surface active agents.

## Activity E/Self Assessment Exercise

i. Describe the structure of the soap.
ii. Soap may vary in composition and in methods of processing. Explain

## 4.0 Conclusion

Fats and oils are esters of glycerol with higher fatty acids and are called glycerides. Saturated carboxylic acids contain single bond and they are solids at room temperature while unsaturated carboxylic acids contain at least one C=C and they are liquids at room temperature. The important difference between oils and fats is that oils are liquids at ordinary temperature while fats are solids.

Soaps are metallic salts of higher fatty acids such as stearic, palmitic and oleic acids. Synthetic detergents like soaps, contain both hydrophilic and hydrophobic end.

## 5.0 Summary

In this unit we have learnt that:

i. Fats and oils are esters of glycerol with higher fatty acids and are called glycerides. Fats are the main constituents of the storage fat cells in animals and plants and they are one of the important food reserves of living organism. These plants and animal fats can be extracted. Liquid fats are often referred to as oils.

ii. Carboxylic acids found in natural fats and oils can be divided into two groups-saturated and unsaturated.

iii. Saturated carboxylic acids have single bonds in their hydrocarbons,they are found in animals, while unsaturated carboxylic acids contain at least one C=C, they obtained in plants.

iv. Saturated carboxylic acids are solids at room temperature while unsaturated carboxylic acids are liquids at room temperature.

v. Oils are liquids at ordinary temperature while fats are solids.

vi. When a molecule of glycerol, i.e propane-1,2,3-triol, reacts with a molecule of stearic acid, glyceryl monostearate is formed.

vii. Oils and fats are colourless liquids or solids, lighter than water, immiscible with water, freely soluble in organic solvents such as benzene, petroleum ether, are non-volatile, they decomposes on strong heating and they readily form emulsions when agitated with water in the presence of soap,gelatine or other emulsifiers.

viii. Fats and oil undergo the following reactions
    ii. Drying
    iii. Rancidification
    iv. Hydrolysis of Fats and Oils

v. Hydrogenation
vi. Hydrogenolysis

ix. Hydrolysis carried out in an alkaline medium is called saponification.
x. Physical tests to determine the purity of fats and oil are melting point, specific gravity, refractive index and viscosity.

xi. The following chemical test can be used to determine the composition and purity of fats and oils:
vii. Acid value- the number of milligrams of potassium hydroxide required to neutralise the free organic acids present in 1gm of fat or oil.
viii. Saponification -the number of milligrams of potassium hydroxide required to completely saponify 1gm of fat or oil- or completely neutralise the fatty acids resulting from complete hydrolysis of 1gm fat or oil.
ix. Iodine Value- iodine value of fats or and oil is defined as the number of grams of iodine that reacts with 100g of the fat or oil.
x. Reichert-Meissi(R.M.)Value- the number of ml of 0.1N potassium hydroxide solution required to neutralise the distillate of 5g of hydrolysed fat or oil.

xi. Acetyl Value- the number of milligrams of potassium hydroxide required to neutralise acetic acid liberated by the saponification of one gram of completely acetylated oil or fat. the distillate of 5g of hydrolysed fat or oil.

xii. Polenske value- the number of ml of 0.1N potassium hydroxide solution required to neutralise the steam volatile, but water insoluble fatty acids obtained from the distillate of 5g of hydrolysed fat or oil.

x. The following are the uses of fats and oil:
- as food
- in the manufacture of soap.alycerol,candle, margarine, hair creams etc
-Long chain alcohols prepared from fats and oils are used in the preparation of synthetic detergents
- in the manufacture of paints and vanishes
- in the manufacture of oil cloth and linoleum

xi. Soaps are metallic salts of higher fatty acids such as stearic, palmitic and oleic acids.

xii. In solution, soap is dispersed in spherical clusters called micelles,
xiii. A soap molecule has a polar end, $-COO^{-}Na^{+}$, and a non-polar end, the long carbon chain of 12-18 carbons.
xiv. The polar end is water soluble-hydrophilic while the non-polar end is hydrophobic or lipophilic.

xv. Amphipathic molecules that have both polar and non-polar end and are big enough for each end to display its own solubility behaviour.

xvi. In cleaning, the non-polar ends of soap molecules dissolves in the oil droplet, leaving the carboxylate ends projecting into the surrounding water layer

xvii. Hard water contains calcium and magnesium salts which reacts with soap to form insoluble calcium and magnesium carboxylates.

xviii. Synthetic detergents are called soapless detergents or syndets.

xix. Like soaps the contain both hydrophilic-water soluble and hydrophobic –oil soluble part. They have replaced soap to large extent.

xx. Synthetic detergents may be anionic surface active, cationic surface active or non-ionic surface active agents

## 6.0 Tutor Marked Assignment

a. Explain the differences the following
- oils and fats
- soap and synthetic detergent
- hard soap and soft soap

b. Write short notes on the following:
-Rancidification
- Saponification
-Cleaning action of soap.

## 7.0 Further Reading and other Resources

i. K.S.TEWARI and N.K. VISHNOI (2006) - A Textbook of Organic Chemistry
-Third Edition

ii. Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry
- Sixth Edition

John McMurry and Mary E.Castellion (1999) Fundamentals of General,Organic, and Biological Chemistry-3rd Edition

# Unit 2: Carbohydrates

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## 1.0 Introduction

Carbohydrates are a large class of naturally occurring polyhydroxy aldehydes and ketones or compounds that yield polyhydroxyl aldehydes or ketones on hydrolysis. They contain carbon, hydrogen and oxygen atoms only. They have the general formula $C_xH_{2y}O_z$.

Simple carbohydrates are mainly synthesized by chlorophyll containing plants through photosynthesis.

## 2.0 Objectives

At the end of this unit you should be able to:

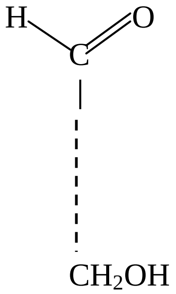
i. Name the classes of carbohydrate
ii. Distinguish between monosaccharides, disaccharides and polysaccharides
iii. Give examples of monosaccharides, disaccharides and polysaccharides
iv. Name simple monosaccharide
v. Distingiush between glucose-an aldohexose and fructose-ketohexose
vi. Draw the structures of glucose and fructose
vii. Explain the properties of glucose-an example of aldohexose
viii. Explain the properties of fructose-an example of ketohexose
ix. Disinguish between reducing sugar and non-reducing sugar
x. Distinguish between, maltose,lactose and sucrose from their physical and chemical properties
xi. Distinguish between starch and cellulose-examples of polysaccharide

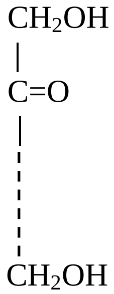
## 3.0 Classification of Carbohydrates

Depending on the size of the molecules, carbohydrates may be divided into three groups, namely monosaccharides, disaccharides and Polysaccharides

Monosaccharides are the simplest carbohydrates and they are known as simple sugars. They have the general formula $C_6H_{12}O_6$ . They cannot be hydrolysed to simpler compounds.They are the basic unit of carbohydrates.They have three to seven carbon atoms, and each has one aldehyde or one ketone functional group. The aldehyde group is always at the end of the carbon chain; the ketone group is always on the second carbon of the chain. In either case, there is a –$CH_2OH$ group at the other end of the chain.

There are hydroxyl groups on all the carbon atom and the –$CH_2OH$ at the other end, and on the end carbon next to the ketone group.





$$\begin{array}{c} CH_2OH \\ | \\ C=O \\ | \\ \vdots \\ CH_2OH \end{array}$$

Disaccharides consist of two monosaccharide units joined together by a glycosidic bond. Their general formula is $C_{12}H_{22}O_{11}$. E.g sucrose, maltose and lactose. When one molecule of disaccharides is taken through acid hydrolysis, it yields two monosaccharide molecules.

Polysaccharides are condensation polymers of monosaccharides, they contain thousands of monosaccharide units in their structures. They have the general formula $(C_6H_{10}O_5)_n$, where n is a very large number. On acid hydrolysis polysaccharides yield a large number of monosaccharide molecules, e.g. cellulose, starch, inulin and glycogen. Polysaccharides are futher subdivided into homopolysaccharides and heteropolysaccharide. The homopolysaccharides on hydrolysis produce the same molecule while heteropolysaccharides produce different monosaccharides. Starch and cellulose are homopolysaccharides while inulin is a heteropolysaccharide.

Carbohydrates that reduces Fehling's (or Benedict's) or Tollens' reagent are known as reducing sugars. All monosaccharides whether aldose or ketose, are reducing sugars. Most disaccharides are reducing sugars. Sucrose however is a non-reducing sugar.

| Carbohydrate | | Molecular Formula | Source or Origin | Monosacchar Produced on hydrolysis |
|---|---|---|---|---|
| Monosaccharide | Glucose(also known as blood sugar, grape sugar and dextrose) | $C_6H_{12}O_6$ | Blood, plant sap, fruit, honey | |
| | Fructose(also known as levulose) | $C_6H_{12}O_6$ | Plants, fruit, honey | |
| | Galactose | $C_6H_{12}O_6$ | From the hydrolysis of lactose | |
| Disaccharide | Sucrose(also known as table sugar, beet sugar and cane sugar) | $C_{12}H_{22}O_{11}$ | Sugar cane, sugar beets, maple syrup, and various fruits and vegetables | Glucose and fructose |
| | Maltose(also known as malt sugar) | $C_{12}H_{22}O_{11}$ | Partial hydrolysis of starch | Glucose |
| | Cellobiose | $C_{12}H_{22}O_{11}$ | Partial hydrolysis of cellulose | |
| | Lactose(also known as milk sugar) | $C_{12}H_{22}O_{11}$ | Makes up about 5% of milk | Glucose and galactose |
| Polysaccharide | Starch | $(C_6H_{10}O_5)n$ | Potatoes, corn, various grains | Glucose |
| | Cellulose | $(C_6H_{10}O_5)n$ | Cell walls of plants | Glucose |

Classes of Carbohydrates with examples

## Activity A/Self Assessment Exercise

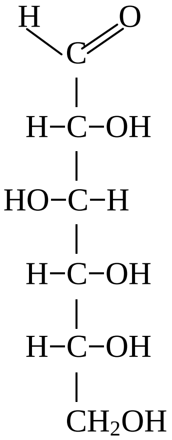
a. Classify the following into reducing and non-reducing sugar
   i. Fructose    ii. Galactose    iii. Maltose    iv. Sucrose   v. Glucose

## 3.1 Monosaccharides

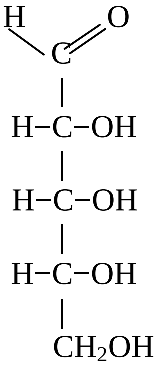
Monossaccharides may be an aldose or a ketose. An aldose is a monosaccharide with an aldehyde carbonyl group while a ketose contains a ketone structure.

### 3.1.1 Naming Monosaccharides

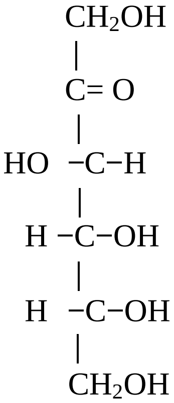
The family name ending '–ose' indicates a carbohydrate, and simple sugars are known by common names like glucose, ribose, and fructose rather than systematic names. The number of carbon atoms in an aldose or ketose can be specified by one of the prefixes bi-,tri-,tetr-, pent-, hex-,hept-. Thus, glucose is an aldohexose( aldo- = aldehyde; hex- = six carbons; -ose = sugar); fructose is a ketohexose( a six-carbon ketone sugar); and ribose is an aldopentose(a five-carbon aldehyde sugar). Most naturally occurring simple sugars are aldehydes with either five or six carbons.



Glucose
(An aldohexose)



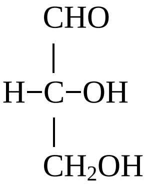
Ribose
(An aldoPentose)



Fructose
(A ketohexose)

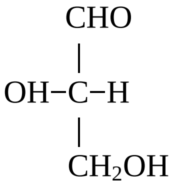
i. Biose ($C_2H_4O_2$) . Glycolaldehyde($CH_2OHCHO$) is the simplest hydroxyl aldehyde. It is regarded as an aldobiose. It is not optically active because it does not contain an asymmetric carbon.

ii. Trioses($C_3H_6O_3$): Glyceraldehyde is the only aldotriose known. It possesses an asymmetric carbon aton an exists in two optically active forms.



$$\begin{array}{c} CHO \\ | \\ H-C-OH \\ | \\ CH_2OH \end{array}$$

D(+) Glyceraldehyde

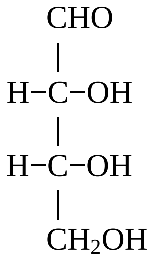


$$\begin{array}{c} CHO \\ | \\ OH-C-H \\ | \\ CH_2OH \end{array}$$

L(-) Glyceraldehyde

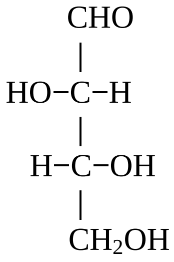
iii. Tetroses($C_4H_8O_2$): An aldotetroroses has the formula $CH_2OHCHOHCHOHCHO$; it has two asymmetrical carbon atoms. It is therefore capable of four optically active forms- D- and L- erythrose and D- and L- threose.

A ketose has only one asymmetric carbon atom and hence exixts in only two optically active forms- D- and L-erythrulose.



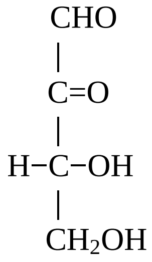
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

D-Erythrose



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HO-C-H} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

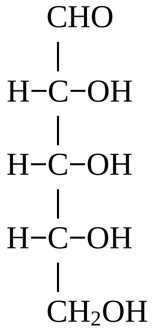
D-Threose



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{C=O} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

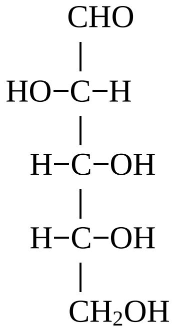
D-Erythrulose

iv. Pentoses($C_5H_{10}O_5$): Aldopentoses has 3 asymmetric carbon atoms and therefore exists in 8 optically active forms- D- and L- forms of ribose, arabinose, xylose and lyxose, D-ribose,L- arabinose, D-xylose and- lyxose occur in nature while the others are synthetic.



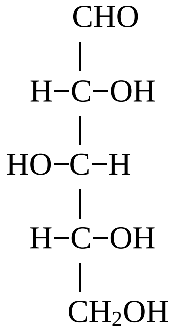
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

D-ribose



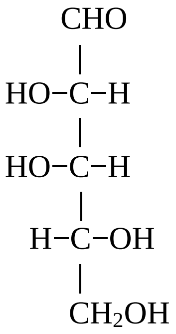
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HO-C-H} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

D-arabinose



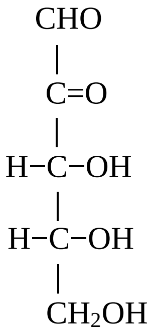
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{HO-C-H} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

D-xylose



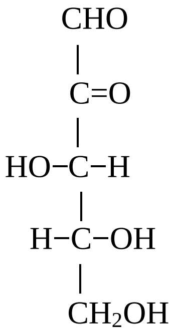
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HO-C-H} \\ | \\ \mathrm{HO-C-H} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

D-Lyxose



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{C=O} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

D-Ribulose



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{C=O} \\ | \\ \mathrm{HO-C-H} \\ | \\ \mathrm{H-C-OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

D-Xylulose

v. Hexoses: Aldo hexoses have four asymmetric carbon atoms. They have the formula $CH_2OHCHOHCHOHCHOHCHOHCHO$; hence they exist in sixteen optically active forms- D- and L- forms of glucose, mannose, allose, altrose, gulose, idose, galactose, talose.

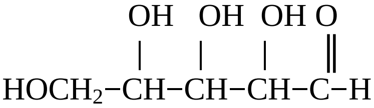
Ketohexoses have 3 asymmetric carbon atoms and they have the formula $CH_2OHCOCHOHCHOHCHOHCH_2OH$. They exist in eight optically active forms of which only six- D- and L-fructose, D- and L-sorbose, D-tagalose and L-psicose- occurs in nature.

Also there are sugars containing heptoses (7-carbon atoms), octoses (8 carbon atoms) and so on.

## Activity B/Self Assessment Exercise

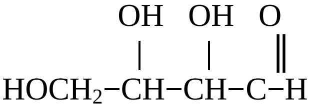
Classify each of the following monosaccharides as an aldose or ketose, and name each according to the number of carbon atoms:

(a)



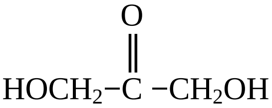
$$\mathrm{HOCH_2{-}\overset{OH}{\overset{|}{C}H}{-}\overset{OH}{\overset{|}{C}H}{-}\overset{OH}{\overset{|}{C}H}{-}\overset{O}{\overset{\|}{C}}{-}H}$$

(b)



$$\mathrm{HOCH_2{-}\overset{OH}{\overset{|}{C}H}{-}\overset{OH}{\overset{|}{C}H}{-}\overset{O}{\overset{\|}{C}}{-}H}$$

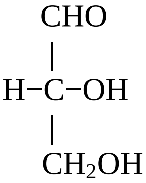
(b)



$$\mathrm{HOCH_2{-}\overset{O}{\overset{\|}{C}}{-}CH_2OH}$$

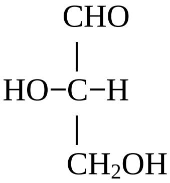
### 3.1.2 Configuration

Glyceraldehyde contains a central chiral carbon atom. For each of its optical isomers the (+) and(-) signs indicating dextrorotatory and laevorotatory respectively, specifying the direction in which each one rotates plane polarized light, give no indication of the way in which the groups are attached to the chiral carbon. The absolute configuration of the two is therefore shown by placing a D or L in front of the name



$$\begin{array}{c}\mathrm{CHO}\\ |\\ \mathrm{H{-}C{-}OH}\\ |\\ \mathrm{CH_2OH}\end{array}$$

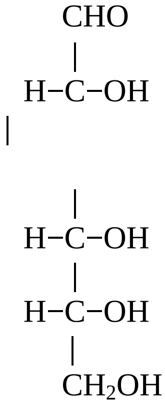
D-Glyceraldehyde



$$\begin{array}{c}\mathrm{CHO}\\ |\\ \mathrm{HO{-}C{-}H}\\ |\\ \mathrm{CH_2OH}\end{array}$$

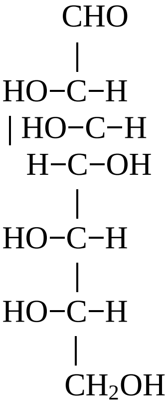
L- Glyceraldehyde

Since all monosaccharides are in effect higher homologue og one of the enantiomers of glyceraldehydes, they are called D-compound if they are related to D- glyceraldehydes and L-compounds if related to L- glyceraldehydes. The comparism to glyceraldehydes is done by considering the lowest chiral carbon atom.For example,



$$\begin{array}{c}\mathrm{CHO}\\ |\\ \mathrm{H{-}C{-}OH}\\ |\\ \\ |\\ \mathrm{H{-}C{-}OH}\\ |\\ \mathrm{H{-}C{-}OH}\\ |\\ \mathrm{CH_2OH}\end{array}$$

D-Glucose

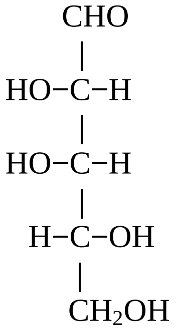


$$\begin{array}{c}\mathrm{CHO}\\ |\\ \mathrm{HO{-}C{-}H}\\ |\ \mathrm{HO{-}C{-}H}\\ \mathrm{H{-}C{-}OH}\\ |\\ \mathrm{HO{-}C{-}H}\\ |\\ \mathrm{HO{-}C{-}H}\\ |\\ \mathrm{CH_2OH}\end{array}$$

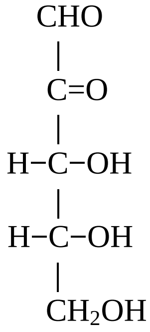
L-Glucose

## Activity C/Self Assessment Exercise

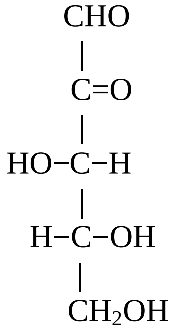
a. Classify the following monosaccharides into D- and L- sugars



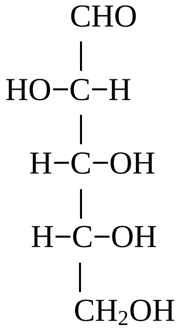
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$



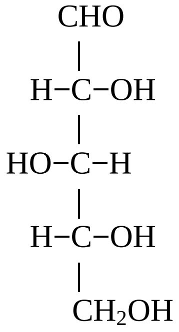
$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{C{=}O} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{C{=}O} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

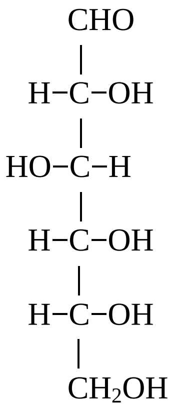
### 3.1.3 Occurrence

Many monosaccharides exist in nature and most of the others have been synthetically prepared.

### 3.1.4 General physical characteristics

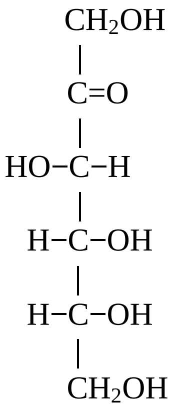
i. They are colourless compounds
ii. They are soluble in water but insoluble in ether and other organic compounds
iii. They have sweet taste
iv. They char on heating giving a characteristic smell
v. They are optically active

Two important monosacharides are glucose and fructose. They are hexoses and commonly found in fruit juice and honey and are the major constituents of many disaccharides and polysaccharides.



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

Glucose

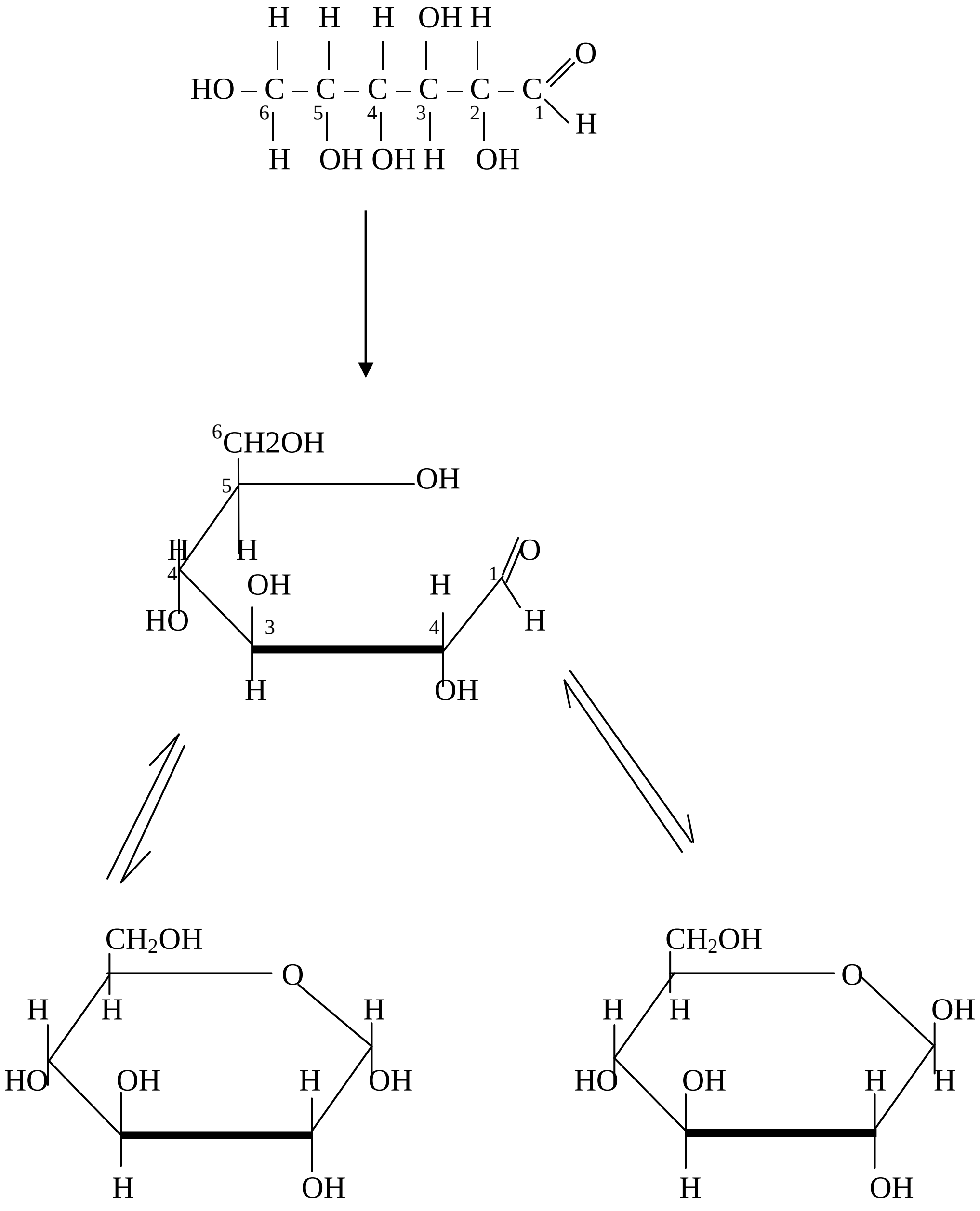


$$\begin{array}{c} \mathrm{CH_2OH} \\ | \\ \mathrm{C{=}O} \\ | \\ \mathrm{HO{-}C{-}H} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{H{-}C{-}OH} \\ | \\ \mathrm{CH_2OH} \end{array}$$

Fructose

## 3.2 Glucose

Glucose is the most important and the most abundant monosaccharide. It is the unit of which starch, cellulose, and glycogen are made up and it has special role in biological processes. It can exist in acyclic and cyclic forms. It is an aldohexose since it contain an aldehyde in its open chain structure.



α- glucose β-glucose

These monosaccharides form rings through the addition of an –OH group of one of their chiral carbons to the carbonyl group of aldose.

Six-membered rings are chemically more stable than the straight chains of the monosaccharides. The direction from which the –OH adds on to the carbonyl group determines which one of the two possible cyclic structures forms(α- and β-glucose)

Most of what we need to know about monosaccharides can be learnt from the study of glucose. As an aldohexose, it undergoes the following reactions as shown below:

### 3.2.1 Physical Properties of Glucose

i. Glucose posses a sweet taste but this is not quite so immediately distinctive in that of fructose and sucrose.

ii. Glucose is extremely soluble in water
iii. It is insoluble in alcohol
iv. When crystallized from warm solution at $98^{o}$C, it yields anhydrous crystals with melting point $146^{o}$C, but from cold solution, it forms a monohydrate with melting point $86^{o}$C.

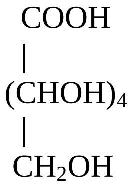
### 3.2.2 Reactions of Glucose

Glucose undergoes many of the reactions typical of carbonyl compounds. As a reducing sugar it reacts with Fehling solution and Tollen's reagent and the formation of osazones provides a useful means of characterization and identification.

Generally the reactions of sugars provide a considerable amount of information about the structure of the molecules and this clearly exemplified by glucose in its ability to form α- and β- cyclic glucosides.

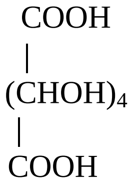
**a. Oxidation**

Glucose, like aldehydes and ketones on warming readily reduces Fehling solution, ammoniacal silver(i) nitrate and Tollen's reagent. It can also be oxidised by bromine water to gluconic acid. However a more powerful oxidizing agent like trioxonitrate(v) acid will oxidize it to the dicarboxylic acid, glycaric acid.



$$\begin{array}{c}\mathrm{COOH}\\|\\\mathrm{(CHOH)_4}\\|\\\mathrm{CH_2OH}\end{array}$$

Gluconic acid

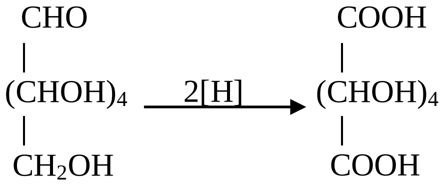


$$\begin{array}{c}\mathrm{COOH}\\|\\\mathrm{(CHOH)_4}\\|\\\mathrm{COOH}\end{array}$$

Glycaric acid(Saccharic acid)

**b. Reduction**

Glucose react with hydrogen and nickel catalyst or sodium tetrahydridoborate(III) or sodium amalgam and water to yields hexahydric alcohol, sorbitol.



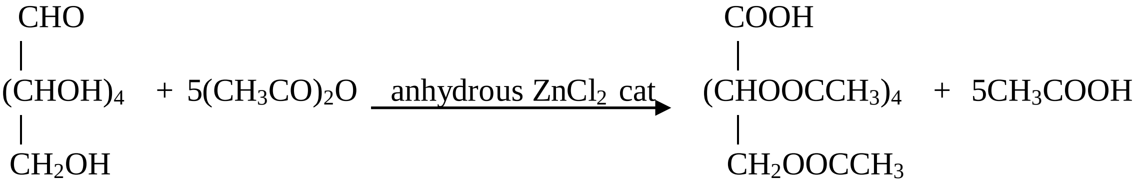
$$\begin{array}{c}\mathrm{CHO}\\|\\\mathrm{(CHOH)_4}\\|\\\mathrm{CH_2OH}\end{array}\xrightarrow{2[H]}\begin{array}{c}\mathrm{COOH}\\|\\\mathrm{(CHOH)_4}\\|\\\mathrm{COOH}\end{array}$$

Sorbitol

Glucose can also be reduced by hydrogen iodide and red phosphorus at 100oC to give hexane. This reaction confirms the existence of a straight chain structure for glucose.

**c. Acylation**

Glucose reacts with excess ethanoic anhydride or ethanoyl chloride in the presence of an anhydrous zinc chloride catalyst to yield pentaethanoyl derivative. This reaction indicates the presence of five hydroxyl groups in glucose.

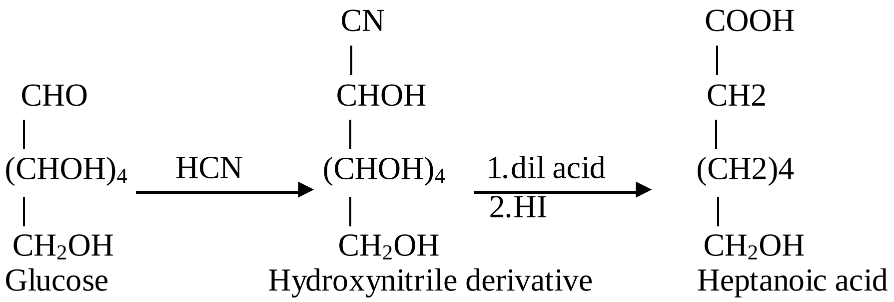


$$\begin{array}{c}\mathrm{CHO}\\|\\\mathrm{(CHOH)_4}\\|\\\mathrm{CH_2OH}\end{array} + 5\mathrm{(CH_3CO)_2O}\xrightarrow{\text{anhydrous } \mathrm{ZnCl_2} \text{ cat}}\begin{array}{c}\mathrm{COOH}\\|\\\mathrm{(CHOOCCH_3)_4}\\|\\\mathrm{CH_2OOCCH_3}\end{array} + 5\mathrm{CH_3COOH}$$

### d. Addition Reaction of the carbonyl group

i. Reaction with HCN

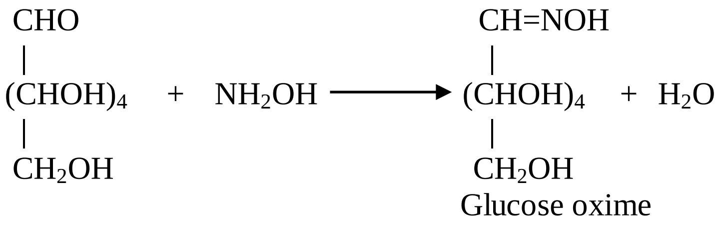
Glucose react with HCN to give hydroxynitrile (cyanohydrins) But do not react with sodium hydrogen sulphite. When the hydroxylnitrile formed is taken through acid hydrolysis followed by reduction with hydriodic acid, heptanoic acid is formed. This reaction also indicates the existence of a straight chain structure.



$$\begin{array}{c} \\ \\ \mathrm{CHO} \\ | \\ \mathrm{(CHOH)_4} \\ | \\ \mathrm{CH_2OH} \\ \text{Glucose} \end{array} \xrightarrow{\mathrm{HCN}} \begin{array}{c} \mathrm{CN} \\ | \\ \mathrm{CHOH} \\ | \\ \mathrm{(CHOH)_4} \\ | \\ \mathrm{CH_2OH} \\ \text{Hydroxynitrile derivative} \end{array} \xrightarrow[\text{2.HI}]{\text{1.dil acid}} \begin{array}{c} \mathrm{COOH} \\ | \\ \mathrm{CH2} \\ | \\ \mathrm{(CH2)4} \\ | \\ \mathrm{CH_2OH} \\ \text{Heptanoic acid} \end{array}$$

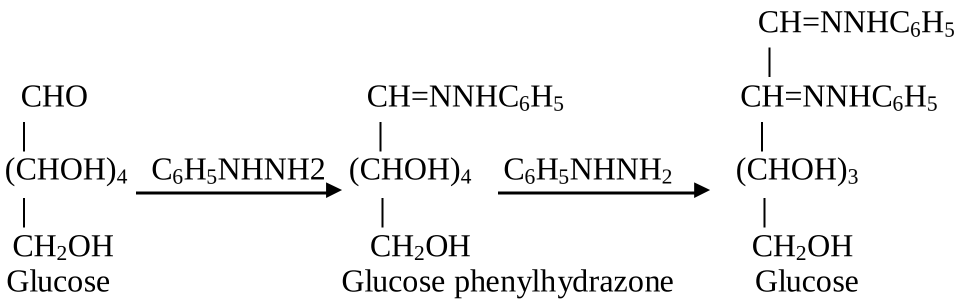
ii. Condensation reactions of the carbonyl group

Hydroxylamine and hydrazine condenses with glucose to form an oxime and a hydrazone respectively.



$$\begin{array}{c} \mathrm{CHO} \\ | \\ \mathrm{(CHOH)_4} \\ | \\ \mathrm{CH_2OH} \\ \\ \end{array} + \mathrm{NH_2OH} \longrightarrow \begin{array}{c} \mathrm{CH{=}NOH} \\ | \\ \mathrm{(CHOH)_4} \\ | \\ \mathrm{CH_2OH} \\ \text{Glucose oxime} \end{array} + \mathrm{H_2O}$$

Also at room temperature, phenylhydrazine reacts with glucose to form the phenylhydrazone. The phenylhydrazone remains in solution, however on warming to 100$^{O}$C in the presence of a large excess of phenylhydrazine, a yellow precipitate of glucose phenylosazone is formed. The formation of phenylosazone is very useful for characterisation and identification purpose.

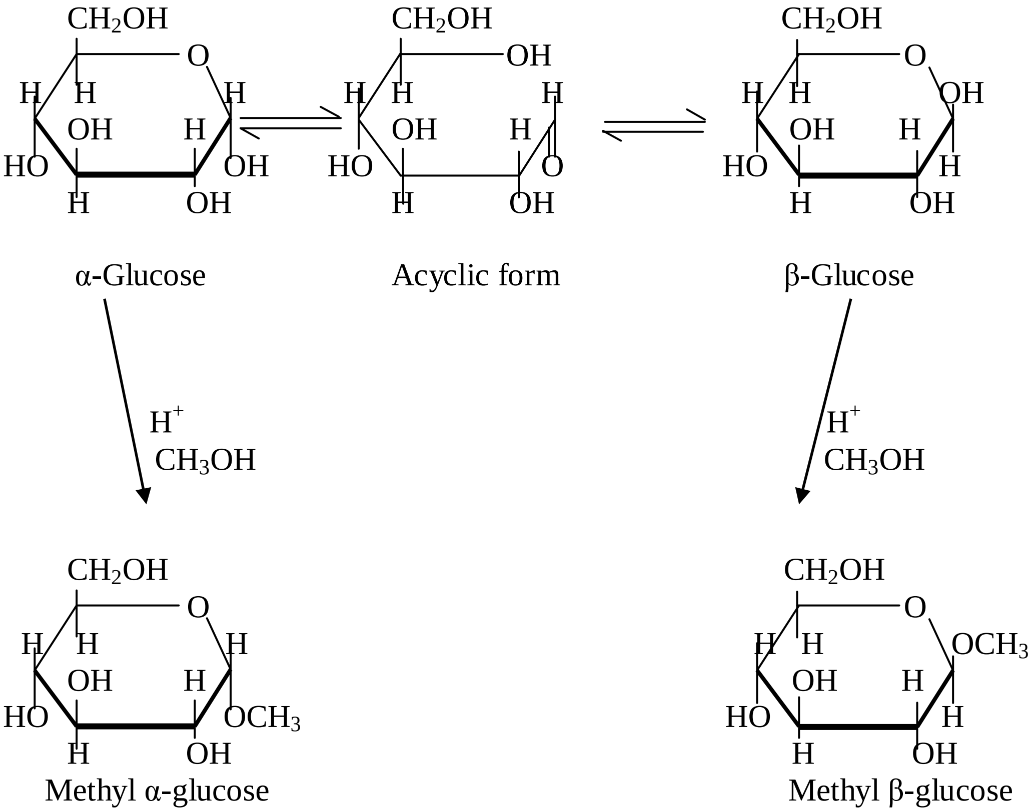


$$\begin{array}{c} \\ \\ \mathrm{CHO} \\ | \\ \mathrm{(CHOH)_4} \\ | \\ \mathrm{CH_2OH} \\ \text{Glucose} \end{array} \xrightarrow{\mathrm{C_6H_5NHNH2}} \begin{array}{c} \\ \\ \mathrm{CH{=}NNHC_6H_5} \\ | \\ \mathrm{(CHOH)_4} \\ | \\ \mathrm{CH_2OH} \\ \text{Glucose phenylhydrazone} \end{array} \xrightarrow{\mathrm{C_6H_5NHNH_2}} \begin{array}{c} \mathrm{CH{=}NNHC_6H_5} \\ | \\ \mathrm{CH{=}NNHC_6H_5} \\ | \\ \mathrm{(CHOH)_3} \\ | \\ \mathrm{CH_2OH} \\ \text{Glucose} \end{array}$$

### e. Glucoside Formation

Glucose reacts with methanol to form a crystalline solid which contains only one methyl group. This compound formed does not contain aldehyde group as it does not reduce Fehling solution or form oxazone with phenylhydrazine and it exist in two anomeric forms.

This behaviour of glucose can only be accounted for in terms of the α- and β- cyclic structures being in dynamic equilibrium.



This reaction is unlike that of aldehydes with alcohol in the presence of an acid catalyst hemiacetals(1-alkoxyalcohols) and acetal(1,1-dialkoxyalcohol).

**f. Fermentation**

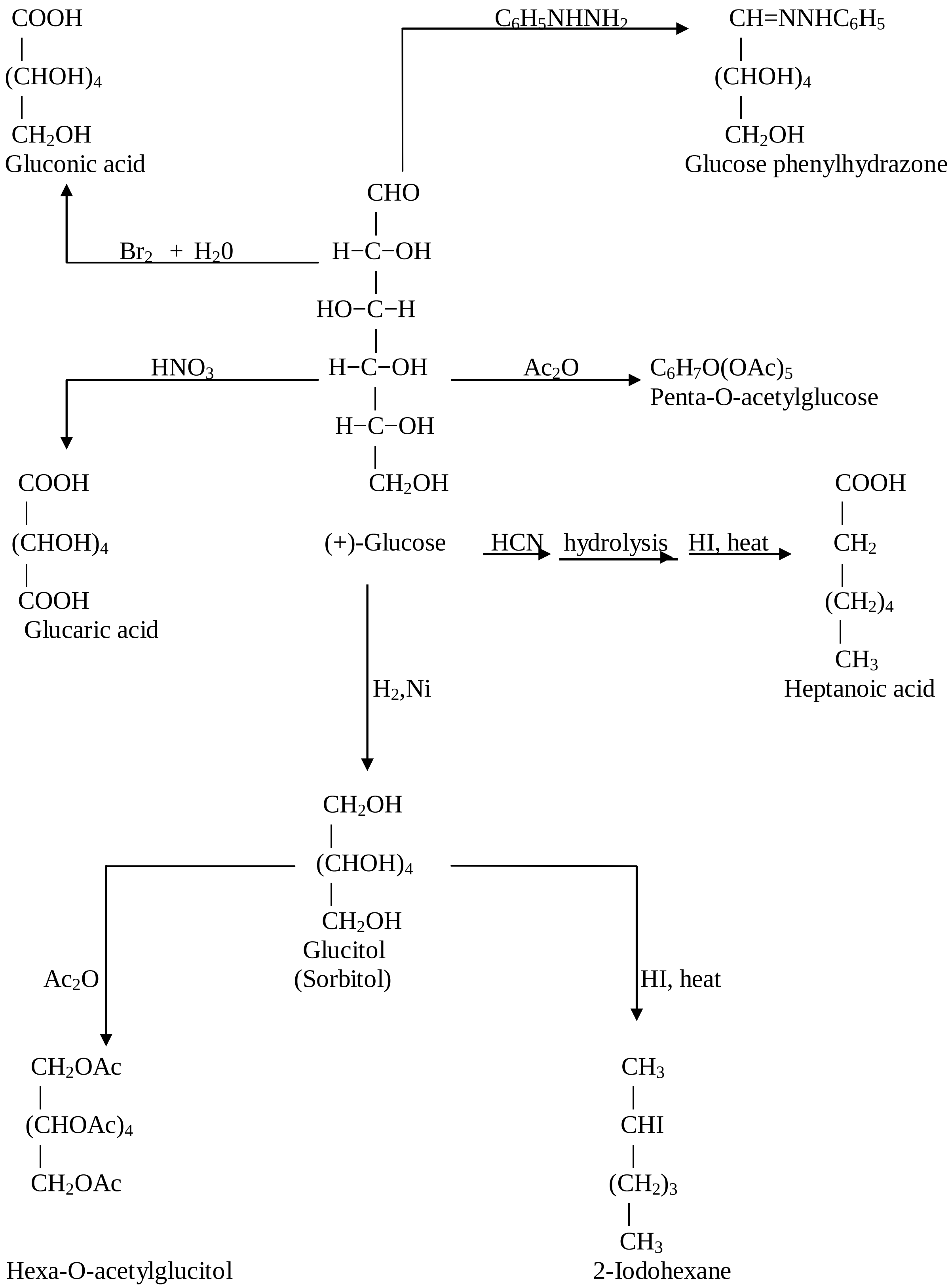
Glucose, during fermentation react with the enzyme zymase from yeast at 15Oc to form ethanol and carbon(iv)oxide

$$C_6H_{12}O_6 \xrightarrow[15^{O}C]{zymase} 2CH_3CH_2OH + 2CO_2$$

**g. Dehydration**

Glucose, when strongly heated chars and leave a black carbon residue. Alternatively when treated with concentrated tetraoxosulphate (vi) acid, it sugar charcoal.

$$\underset{\text{Glucose}}{C_6H_{12}O_6} \xrightarrow[-\ H_2O]{conc.\ H_2SO_4} \underset{\text{Sugar charcoal}}{6C}$$



Summary of the reactions of glucose

## Activity D/Self Assessment Exercise

Using equations and stating the conditions of reactions only, explain the reactions of glucose with:

i. Ethanoic anhydride
ii. $HNO_3$
iii. Phenylhydrazine

## 3.3 Fructose

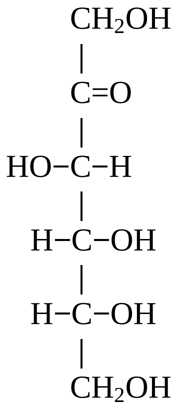
Fructose occurs widely in fruits and combined with glucose, in the disaccharide, sucrose. It is often called fruit sugar.

### 3.3.1 Physical Properties of Fructose

i. It is the more soluble in water than glucose
ii. It is the sweetest among all sugars, approximately twice as sweet as glucose
iii. It is reasonably soluble in alcohol unlike glucose. This property can be utilized in separating it from glucose.
iv. It is a colourless crystals with the melting point of 95°C

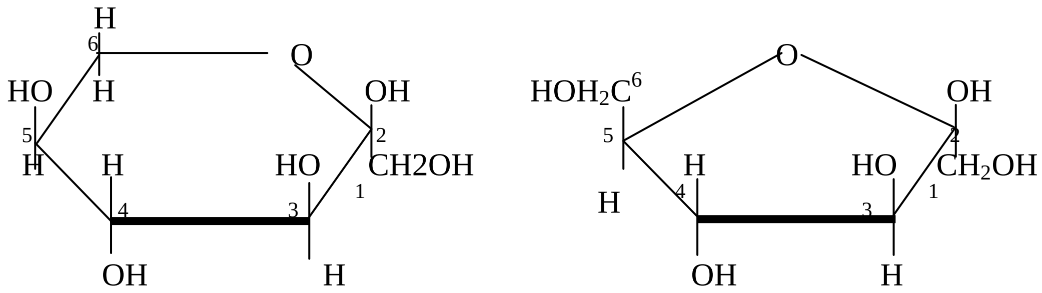
### 3.3.2 Structures of Fructose

Fructose can exist with an acyclic as well as with cyclic structures of six-membered ring and five membered rings. It is a ketohexose as it contains a keto group in its open chain structure.



$$\begin{array}{c} CH_2OH \\ | \\ C{=}O \\ | \\ HO{-}C{-}H \\ | \\ H{-}C{-}OH \\ | \\ H{-}C{-}OH \\ | \\ CH_2OH \end{array}$$

Fructose



A six membered cyclic form (β-fructopyranose)

A five membered cyclic form (β-fructofuranose)

Structures of Fructose

In the crystalline form, only one form of fructose is known- the six membered,cyclic, β-isomer.

In solution, the β-isomer exists in equilibrium with the cyclic α-isomer, with the open-chain structure and also with a five membered ring structure. The α- and β- isomer differs in configuration of the C-2 atom, i.e at the carbonyl atom of the acyclic structure. This phenomenon is known as epimerism and the isomers are known as epimers.

The six membered ring structure is known as a fructopyranose while the five membered ring is known as a fructofuranose.
Generally, sugars which contain a six-membered ring structure including the oxygen atom referred to as pyranose compounds and those containing a five-membered ring structure are called furanose compounds.

### 3.3.3 Reactions of Fructose

Fructose undergoes reactions that are similar to those of glucose

i. Oxidation: Fructose like glucose reduces Fehling's solution, ammoniacal silver(I) nitrate and Tollen's reagent. It is not however not oxidised by bromine water indicating the absence of an aldehyde group.

ii. Reduction: Fructose like glucose is also reduced to sorbitol

iii. Acylation: Fructose undergoes acylation as decribed in glucose to yield pentaethanoyl derivative, indicating the presence of five hydroxyl groups in the molecule.

iv. Addition and Condensation Reactions of the carbonyl group: Like glucose, fructose forms hydroxylnitrile (cyanohydrin) with hydrogen cyanide and condenses with hydroxylamine and hydrazine. When Fructose is warmed with excess phenylhydrazine, it yields an osazone, fructose phenyl osazone which is similar to the glucose derivative.

v. Fermentation and Dehydration
Fermentation and dehydration of fructose is similar to that of glucose.

## 3.4 Disaccharides

Disaccharides are carbohydrates that are made up of two monosaccharide units They have the molecular formula $C_{12}H_{22}O_{11}$. On hydrolysis a molecule of disaccharide yields two molecules of monosaccharide. Common examples are sucrose(cane or beet sugar), maltose(malt sugar) and lactose(milk sugar).

Sucrose is made up of a glucose molecule and a fructose molecule, a maltose consist of two glucose molecules while lactose is made up of one glucose molecule and one galactose molecule.

### 3.4.1 Natural Sources of Disaccharides

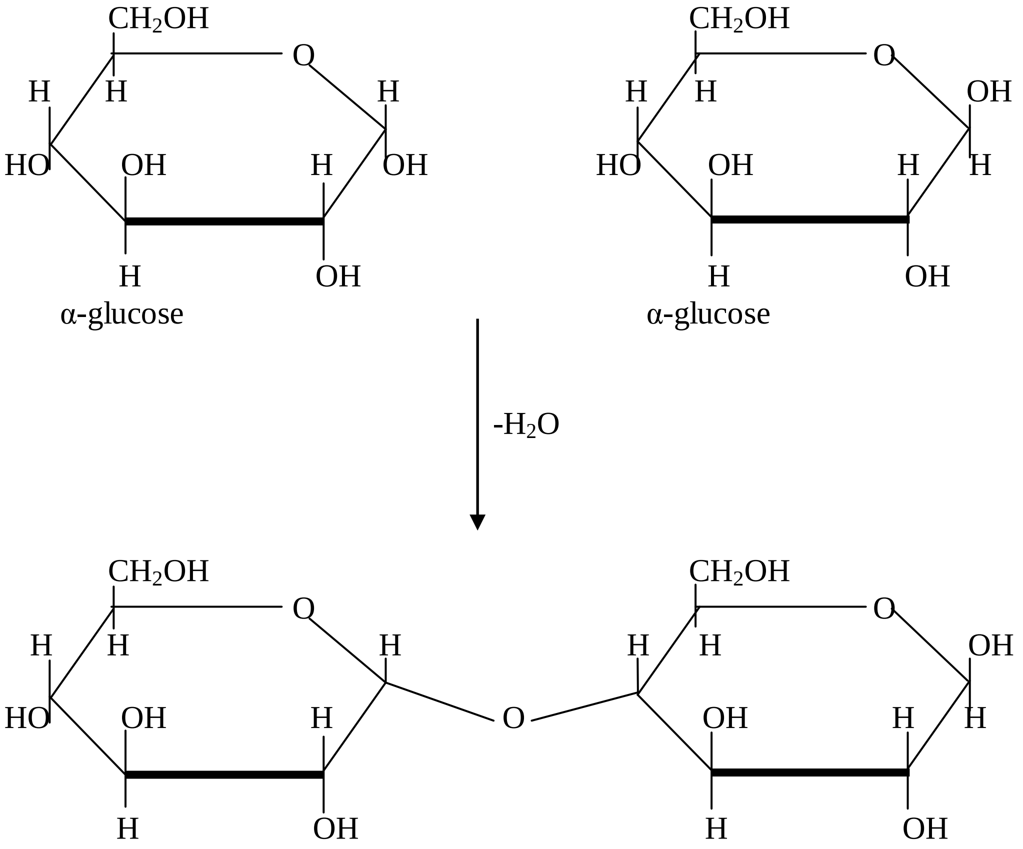
Surcose occurs in as much as 15% in cane and beet sugar which is the principal source. Apart from cane and beet sugar, it occurs naturally in fruit and plants. Maltose is formed as an intermediate in the fermentation of starch while lactose is present in the milk of mammal in about 5%.

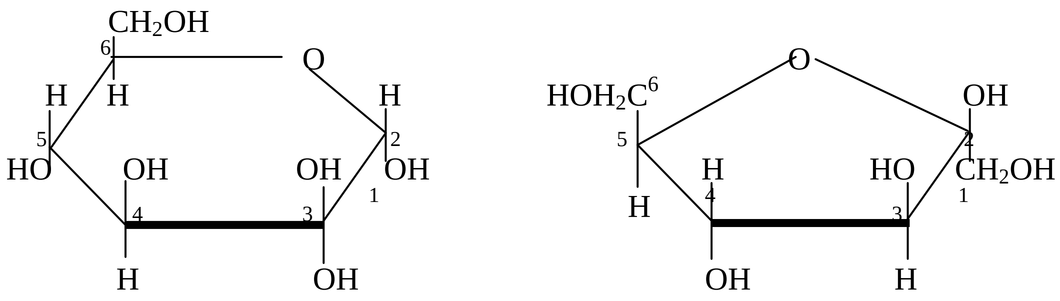
### 3.4.2 Structure and Constitution of Disaccharides

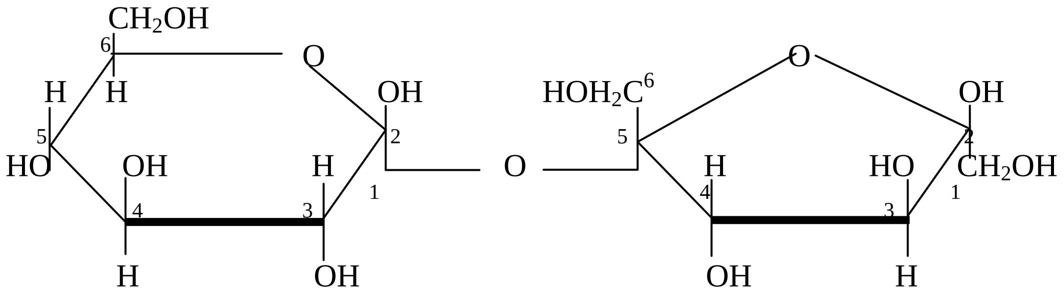
The bond formed between two monosaccharides is called a glycosidic linkage. It is formed from a condensation reaction between two hydroxyl groups.

Disaccharides are glycosides in which the alcohol substituent is replace by another monosaccharide which is attached via one of its hydroxyl groups. Sucrose is made up of a glucose molecule and a fructose molecule with the elimination of a water molecule- a pyranose and a furanose ring. A maltose molecule is built up from two glucose molecules with the elimination of a water molecule- two hexose (pyranose).

Maltose and lactose molecules consist of two hexose (or pyranose) units while sucrose has a hexose-pyranose, i.e pyranose-furanose structure.







Sucrose

Maltose and lactose exist in α- and β- forms and they undergo mutarotation in solution, while sucrose does not exist in anomeric forms. Maltose and lactose are capable of reducing Fehling solution and forming osazones indicating that the structures of the molecules contain a potentially ‘free’ carbonyl group and a hemiacetal ring structure while sucrose is a non-reducing sugar, indicating the absence of a ‘free’ carbonyl group.

### 3.4.3 Physical Properties of Disaccharides

i. Sucrose, maltose and lactose are readily soluble in water

ii. They are virtually insoluble in alcohol

iii. Sucrose, maltose and lactose are dextrorotatory and are used as foodstuffs.

iv. If sucrose is heated above $160^{o}C$ (its melting point), and cooled, it re-solidify to form a solid mass known as ‘barley sugar’. On raising the temperature to about $200^{o}C$, it lost some water molecule to form ‘caramel’- a softer, brownish substance.

### 3.4.4 Reactions

Considering the common examples, many of their reactions are useful means of distinguishing between them.

i. Hydrolysis: All disaccharides are hydrolysed by dilute mineral acid into the constituent monosaccharides. Maltose gives glucose only, lactose gives glucose and galactose while sucrose gives glucose and fructose.

$$\begin{array}{llll} C_{12}H_{22}O_{11} + H_2O & \xrightarrow[\text{Or maltase}]{\text{dil.acid}} & 2C_6H_{12}O_6 & \\ \text{Maltose} & & \text{Glucose} & \end{array}$$

$$\begin{array}{llll} C_{12}H_{22}O_{11} + H_2O & \xrightarrow[\text{Or lactase}]{\text{dil.acid}} & C_6H_{12}O_6 & + C_6H_{12}O_6 \\ \text{lactose} & & \text{Glucose} & \text{Galactose} \end{array}$$

$$\begin{array}{llll} C_{12}H_{22}O_{11} + H_2O & \xrightarrow[\text{Or invertase}]{\text{dil.acid}} & C_6H_{12}O_6 & + C_6H_{12}O_6 \\ \text{sucrose} & & \text{Glucose} & \text{Fructose} \end{array}$$

Sucrose which is dextrorotary on hydrolysis gives an equal proportion of (+)-glucose and (-)-fructose with specific rotations $+52.7^{o}$ and $-92.4^{o}$ respectively. Since the the laevorotatory power of fructose is greater than the dextrorotatory power of glucose, the overall mixture formed is therefore laevorotatory.Hence the rotation of plane polarised light changes from positive to negative when sucrose is hydrolysed. This is known as the inversion of (+)-sucrose.

$$\text{(+)-Sucrose} \xrightarrow[\text{invertase}]{\text{H+ or}} \text{(+)-glucose} + \text{(-)-fructose}$$

$$[\alpha]_D = +66.5^O \qquad [\alpha]_D = +52.7^O \quad [\alpha]_D = -92.4^O$$

$$[\alpha]_D = -19.9^O$$

ii Oxidation

Maltose and lactose are affected by Fehling's solution, ammoniacal silver(I) nitrate and bromine water while sucrose is not. This is because sucrose has no 'free' carbonyl group. Bromine water oxidise maltose and lactose to maltobiotic acid and lactobiotic acid respectively.

However, when sucrose is warmed with more powerful oxidising agent like dilute trioxonitrate(V) acid, it is oxidised to ethanedioic acid(oxalic acid).

iii. Acylation

Sucrose, maltose and lactose react with ethanoic anhtdride on heating to yield an octaethanoyl derivative. This reaction confirm the presence of eight hydroxyl groups

iv. Condensation: Maltose and lactose reacts with phenylhydrazine to form phenylhydrazone. Sucrose does not undergo this reaction because it lack reducing power and has no carbonyl group.

v. Dehydration: All disaccharides yields sugar charcoal when heated above their melting points or when they are warmed with concentrated tetraoxosulphate(VI) acid.

$$C_{12}H_{22}O_{11} \xrightarrow[-11H_2O]{\text{conc.}H_2SO_4} 12C$$

## Activity E/Self Assessment Exercise

Distinguish between maltose and sucrose using the following reactions of disaccharides:

- i. Oxidation
- ii. Hydrolysis
- iii. Condensation

# 3.5 Polysaccharides

Polysaccharides are high relative molecular mass condensation polymers of monosaccharides. They have the general formula $(C_6H_{10}O_5)n$, where n is a large number. They contain a large number of monosaccharide units linked together in the same way as disaccharides by means of a common linking oxygen atom.

Generally polysaccharides are tasteless and amorphous compounds. They are generally insoluble in water and organic solvents. Many of them form colloidal solution. When they are hydrolysed with dilute acids or enzymes they yield monosaccharides.

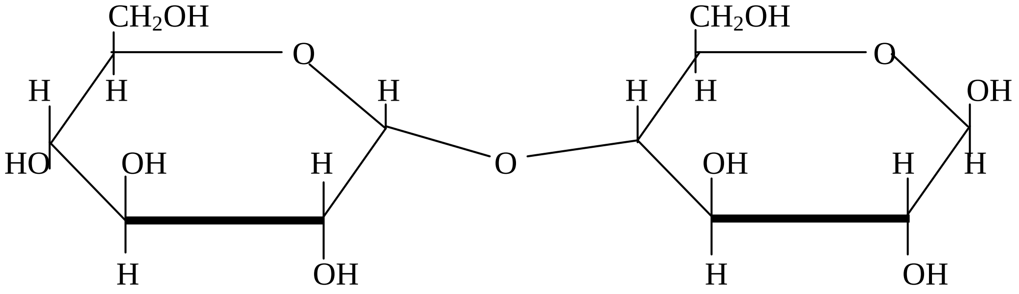
Common examples of polysaccharides are starch and cellulose. Inulin and glycogen are also known polysaccharides.

### 3.5.1 Starch

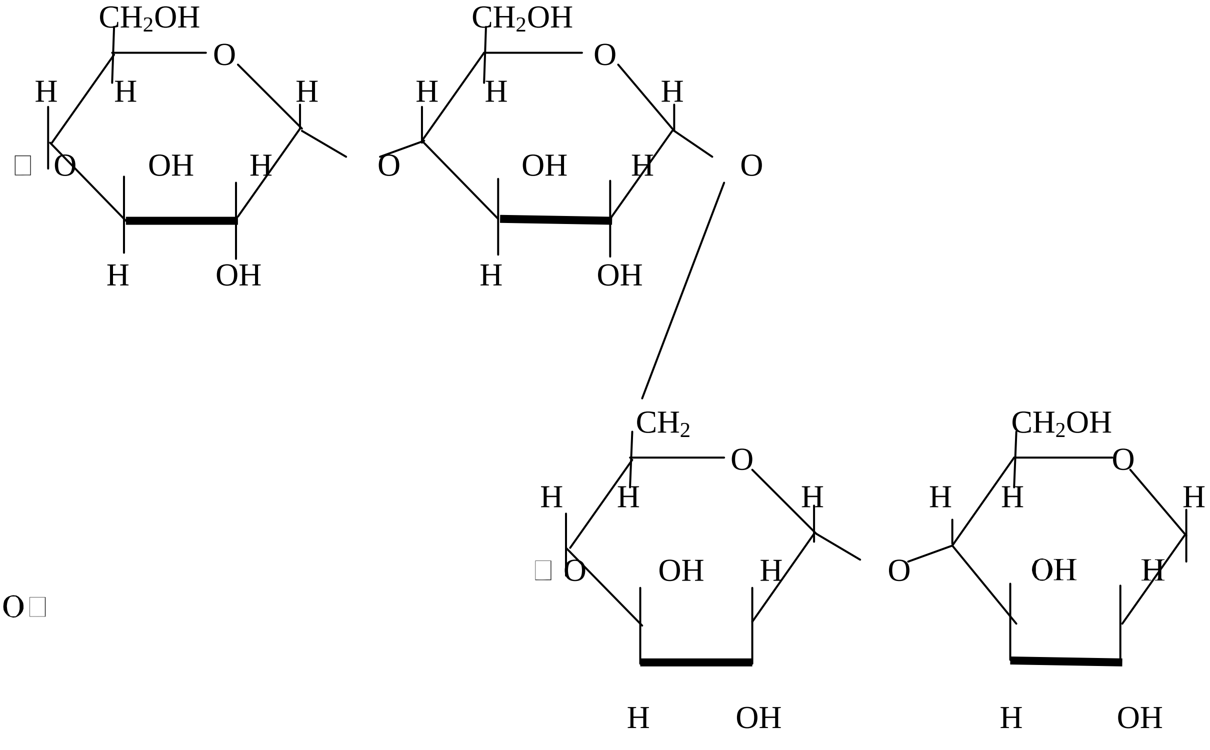
Starch is a polyglucose found in potatoes, wheat, maize, rice, barley and generally in green plants. In nature it is transformed into complex polysaccharides like gums and cellulose.It can also be transformed into simpler mono- and disaccharides by enzymic actions.

The exact chemical nature of starch varies from source to source. Starch obtained from the same ssource has been found to consist of two fractions: amylase and amylopectin.

Amylose is a linear polymer containing α-D-glucopyranose units joined by 1,4-α-glycosidic linkages while amylopectin is a highly branched polymer. The branches of amylopectin consist of 20 to 25 glucose units joined by 1,4-α- linkages and joined to each other by 1,6-α-glycosidic linkages.



α- Amylase



Amylopectin

A. General Properties

a. Physical Properties

- i. Starch is a white amorphous substance
- ii. It has no taste or odour
- iii. It is insoluble in water

iv. When added to boiling water, the starch granules swells and burst forming colloidal transluscent suspension

b. Chemical Properties

i. Action of heat

When starch is heated to a temperature between 200 and 250Oc, it changes to dextrin- a gum like substance. At higher temperature, charring take place.

ii.Hydrolysis

When starch is boiled with dilute acid, all the glycosidic linkages are broken and it untimately yields glucose.

$$\underset{\text{Starch}}{(C_6H_{10}O_5)_n} + nH_2O \xrightarrow{H^+} \underset{\text{glucose}}{nC_6H_{12}O_6}$$

However when hydrolysed with diastase, maltose is formed. On further treatment of the maltose with a dilute acid or an enzyme maltase, glucose is obtained.

$$\underset{\text{Starch}}{2(C_6H_{10}O_5)_n} + nH_2O \xrightarrow{\text{diastase}} \underset{\text{maltose}}{nC_{12}H_{22}O_{11}}$$

$$C_{12}H_{22}O_{11} \xrightarrow{H^+ \text{ or maltase}} \underset{\text{Glucose}}{2\ C_6H_{12}O_6}$$

iii. Action of iodine solution

When a drop of iodine solution is added to starch solution, it gives a blue colour. The blue colour disappears on heating and reappers on cooling. This reaction serves as a test for starch.

iv. Action of a mixture of Concentrated tetraoxosulphate (VI) acid and trioxonitrate (V)acid

When starch is heated with a mixture of concentrated tetraoxosulphate (VI) acid and trioxonitrate(V)acid, it gives nitrostarch.

B. Uses

i. Use as food. It forms the omportant part of daily diet like bread, rice, potatoesetc
ii. It is used in the manufacture of starch jelly and adhesives
iii. It is a valuable source of glucose and alcohol
iv. Used in laundaries
v. Used in paper and textile industries
vi. Used in the preparation of starch acetate, nitro-starch, soluble starch
vii. Used as an indicator for iodometric titration
viii. Dextrins obtained from starch are used in sizing paper and in adhesives

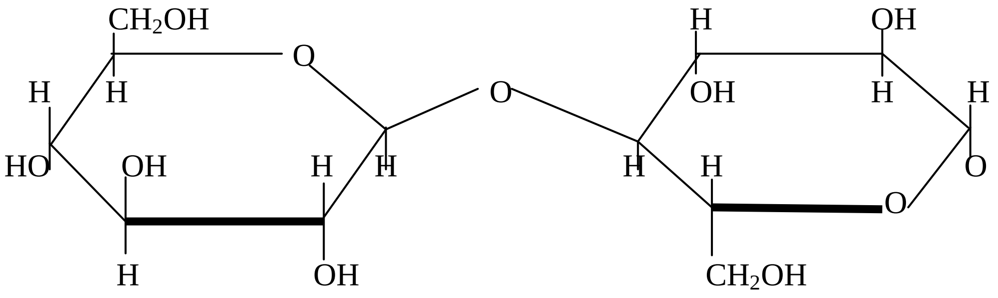
## Activity F/Self Assessment Exercise

How can starch be tested for in the laboratory?

### 3.5.2 Cellulose

It is the principal structural component of the cell walls of plant. Like starch, it is a polyglucose containing 1000-1500 glucose units. It is obtained from the cotton plant, wood, straw etc.

Cellulose plays a very important role in the polymer industry



Cellulose

Like starch the structure of cellulose varies with the source.

Cellulose is a linear polymer having β-D-glucopyranose units joined by 1,4-β-linkages.

On complete hydrolysis it yields glucose but unlike starch it is present in cellulose as β-D-glucopyranose unit. Enzymatic hydrolysis yields a disaccharide cellobiose having the glucose linked through 1,4-β-glycosidic linkages.

A. Properties of Cellulose
i.Cellulose is acolourless amorphous substance with organised fibrous structure
ii. It is insoluble in water but dissolves in ammoniacal solution of copper(II) hydroxide. It also dissolves in a solution of zinc chloride in hydrochloric acid.

iii. Cellulose form a starch like substance amyloid: It is treated with concentrated tetraoxosulphate (VI) acid in cold to form a solution. The solution formed then dilute with water to form amyloid.

iv. When boiled with dilute teraoxosulphate (VI) acid, it is completely hydrolused to glucose.

v. When treated with 20% caustic acids, it becomes smooth and lustrous in appearance

vi. When treated with a mixture of concentrated tetraoxosulphate (VI) acid and trioxonitrate v. acid, it forms mono-,di-,and tri-nitrates of cellulose. Cellulose of nitrates are used in the preparation of explosives.

$$(C_6H_{10}O_5)n \xrightarrow{HNO_3/H_2SO_4} \underset{\text{Mono- nitrate}}{[C_6H_9O_4(O.NO_2)]n}, \underset{\text{di- nitrate}}{[C_6H_8O_3(O.NO_2)_2]n}, \underset{\text{Tri-nitrate}}{[C_6H_7O_2(O.NO_2)_3]n}$$

vi. When treated with o mixture of acetic acid and acetic anhydride, cellulose gives a mixture of di- and tri-acetates. Cellulose acetates are used in the manufacture of synthetic fibres and paints.

$\underset{\text{di-acetate}}{[C_6H_8O_3(O.Ac)_2]n}$ and $\underset{\text{tri-acetate}}{[C_6H_7O_2(O.Ac)_3]n}$

B. Uses of Cellulose

i. Used in the manufacture of paper and cloth
ii. Cellulose nitrates are used in the manufacture of explosives
iii. Cellulose nitrates with camphor gives celluloid which is used in the manufacture of toys.
iv. Cellulose acetate is used in the manufacture of rayon and plastics

## Activity G/Self Assessment Exercise

What are the differences in the structures of starch and cellulose?

## 4.0 Conclusion

Carbohydrates are a large class of naturally occurring polyhydroxy aldehydes and ketones that contain carbon, hydrogen and oxygen atoms only. They have the general formula $C_xH_{2y}O_z$.

Carbohydrates may be divided into three groups, namely monosaccharides, disaccharides and Polysaccharides. Monosaccharides are the simplest carbohydrates known as simple sugars. Disaccharides consist of two monosaccharide units joined together by a glycosidic bond. Polysaccharides are condensation polymers of monosaccharides.

Carbohydrates that reduces Fehling's (or Benedict's) or Tollens' reagent are known as reducing sugars.

Glucose and fructose are common monosaccharides. Maltose, lactose and sucrose are common examples of disaccharides while starch and cellulose are polysaccharides.

## 5.0 Summary

i. Carbohydrates contain carbon, hydrogen and oxygen atoms only with the general formula $C_xH_{2y}O_z$.

ii. carbohydrates may be divided into three groups, monosaccharides, disaccharides and Polysaccharides

iii. Monosaccharides have the general formula $C_6H_{12}O_6$ .

iv. Disaccharides consist of two monosaccharide units joined together by a glycosidic bond with general formula is $C_{12}H_{22}O_{11}$.

v. Polysaccharides are condensation polymers of monosaccharides, they have the general formula $(C_6H_{10}O_5)_n$, where n is a very large number.

vi. Carbohydrates that reduces Fehling's (or Benedict's) or Tollens' reagent are known as reducing sugars. All monosaccharides and most disaccharides are reducing sugars. Sucrose however is a non-reducing sugar.

vii. An aldose is a monosaccharide with an aldehyde carbonyl group while a ketose contains a ketone structure.

viii. The family name ending '–ose' indicates a carbohydrate.

ix. Glucose can exist in acyclic and cyclic forms.

**x.** Generally the reactions of sugars provide information about the structure of the molecules .

xi. Glucose undergo thw following reactions

-Oxidation

-Reduction

- Acylation
- Addition Reaction of the carbonyl group
- Reaction with HCN

Condensation reactions of the carbonyl group

- Glucoside Formation
- Fermentation
- Dehydration

xii. Fructose is a ketohexose and can exist with an acyclic as well as with cyclic structures of six-membered ring and five membered rings.

xiii. The six membered ring structure is known as a fructopyranose while the five membered ring is known as a fructofuranose.

xiv. Fructose undergoes reactions that are similar to those of glucose

xv. Disaccharides are glycosides in which the alcohol substituent is replace by another monosaccharide which is attached via one of its hydroxyl groups.

xvi. Polysaccharides are high relative molecular mass condensation polymers of monosaccharides. They have the general formula $(C_6H_{10}O_5)n$, where n is a large number.

xvii. Common examples of polysaccharides are starch ,cellulose, Inulin and glycogen .

xviii. Hydrolysis of starch gives glucose

xix. Cellulose is a linear polymer having β-D-glucopyranose units joined by 1,4-β-linkages.

## 6.0 Tutor Marked Assignment

a. Discuss the following reactions of glucose:
i.Condensation
ii.Oxidation
iii. Reduction
iv.Acylation.

b. Distinguish between starch and cellulose
c. What is mutarotation

## 7.0 Further Readings and other Resources

K.S.TEWARI and N.K. VISHNOI (2006)- A Textbook of Organic Chemistry. Third Edition
Robert Thornton Morrison and Robert Neilson Boyd (2008) – Organic Chemistry- Sixth Edition