Pharmacy Exam Guide

Step I

PHARMACEUTICAL CHEMISTRY-I

-1st Edition
(P1C2)

PHARMACY EXAM GUIDE
STEP I
PHARMACEUTICAL CHEMISTRY-I (ORGANIC-I)
1^{ST} EDITION
(P1C2)

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DEDICATED TO OUR PARENTS

AND TEACHERS

ACKNOWLEDGEMENT

The future belongs to those who believe in the beauty of their dreams.

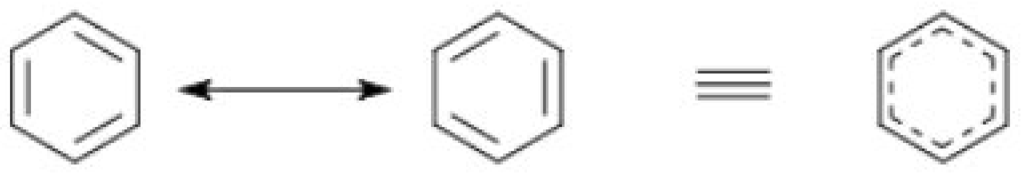
The preparation of this book "**Pharmacy Exam Guide**" was just a dream of some students of **Doctor of Pharmacy, University of Central Punjab**, which could not be fulfill without the help and support of our teachers and parents.

We appreciate the tireless efforts of ***Our Teachers*** who encouraged us always to achieve our endeavor, no matter, how hard they can be.

We are much indebted to ***Our Parents*** for inspiring and motivating us to achieve the great goals in life.

Chapter 1 **Conjugation**

- ❖ Electron density shifts from one place to another



- ❖ Delocalization of electron is the shifting of electron density. It is done to make a molecule more stable.

Shelf Life: Shelf Life is the time interval between date of manufacturing of a drug and the date of expiry of that drug.
It is increased to keep the medicine available for use for a longer period of time.

- ➢ Molecules possessing $CH_2= CH_2$ (multiple bond/degree of unsaturation), conjugation occurs.
  $CH_2= CH_2$ (have got one sigma and one pi-bond) → sp^2 hybridization.
- ➢ This electron density cannot shift because electronegativity difference between both the carbons is same.
- ➢ Pi bonds are formed because half electron density is above and half is below.
- ➢ If electron density shifts then it is called "delocalized" and if it cannot shift then it is called as "localized"

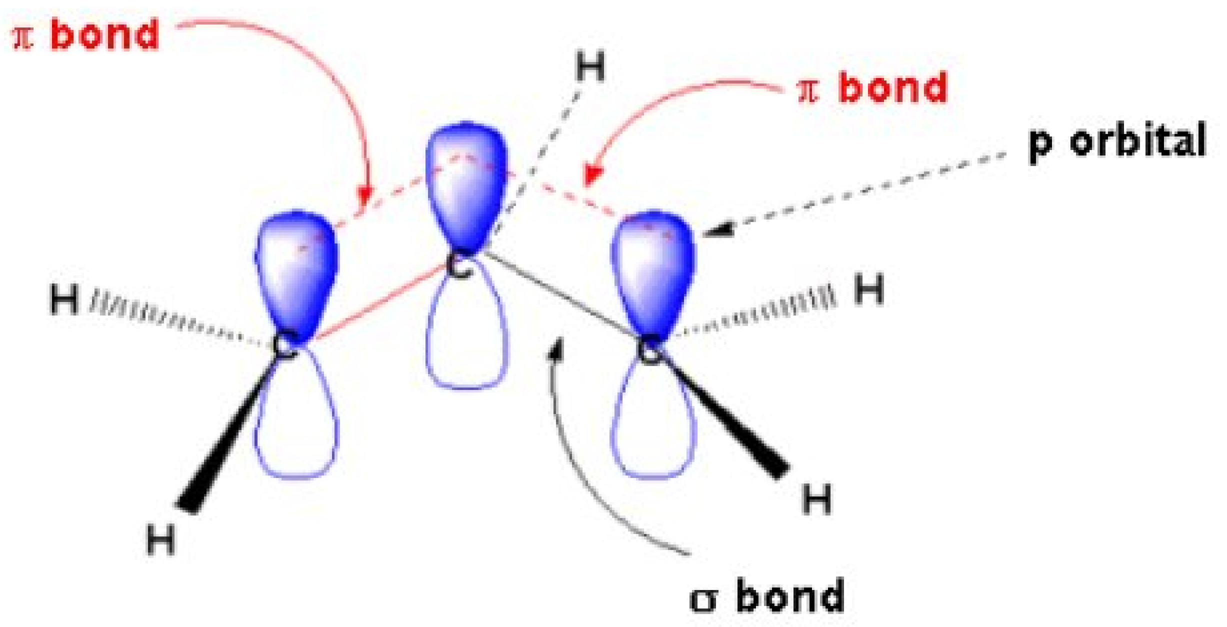
DEFINITION

- ➢ The process of electron density shifting from one place to another is known as conjugation in which electron density decreases at one place and increases correspondingly at some other place.

1.1 EXPLANATION

- ➢ In case of sigma bond, the electron pair is shared between the two nuclei while in pi-bond the electron density exists above and below the bond axis. If it is not able to shift it is called "localized" e.g. Ethene ($CH_2 = CH_2$). While in compounds having more than 3-p orbitals on adjacent atoms, may cause electron shifting as in allyl radical or benzene.

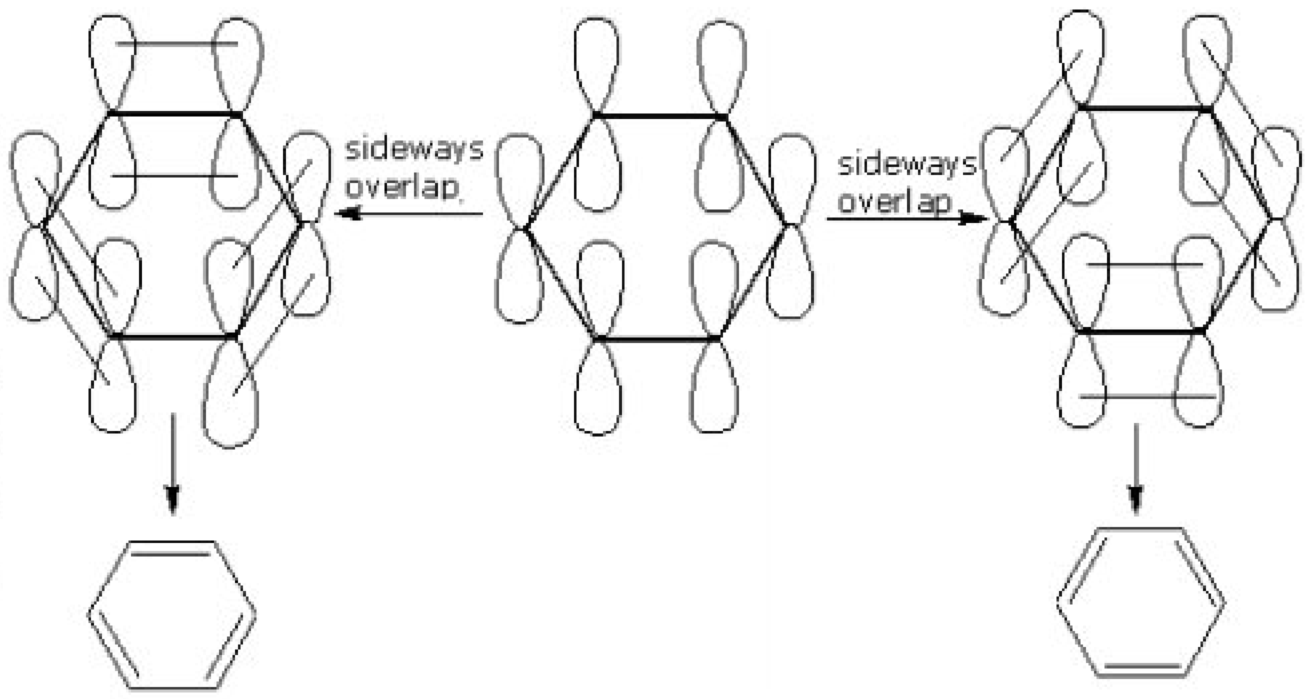
Radical: Radical is a specie available for attachment or reaction
$CH_2 = CH$- (Vinyl radical)
$CH_2 = CH_2$-CH_2- (Allyl radical)



- ➢ Each carbon atom have p-orbitals, electrons are in motion. They make bonds by jumping. Thus electron density may increase or decrease around the three carbon atoms. So molecule may become like - $CH_2 – CH = CH_2$ Similarly, in benzene, each carbon atom is sp^2 hybridized and it's structure is planar (one at specific angle)

Each carbon atom in Benzene is "planar"

- ➢ If angles are not specific then electron density cannot shift. Each carbon atom forms 3 sigma bonds, 2 with adjacent carbons and one with hydrogen and it also possess one unhybridized p-orbital. Since all six carbon atoms possess six unhybridized p-orbitals, two forms are possible.



CONDITIONS FOR CONJUGATION

1) There must be p-orbitals on 3 adjacent atoms
2) The atoms having p-orbitals must be in same plane

CHARACTERISTICS

- The conjugated ion, radical and molecule are more stable than non-conjugated system.
- The difference in energy between conjugated molecule and theoretical unconjugated molecule (analogue) is called "delocalized or resonance energy"
- The molecule in which conjugated orbital is linear are said to be "linear conjugated"

molecule while in which it’s branched is called “cross conjugated”

Chapter 2 Hyper Conjugation

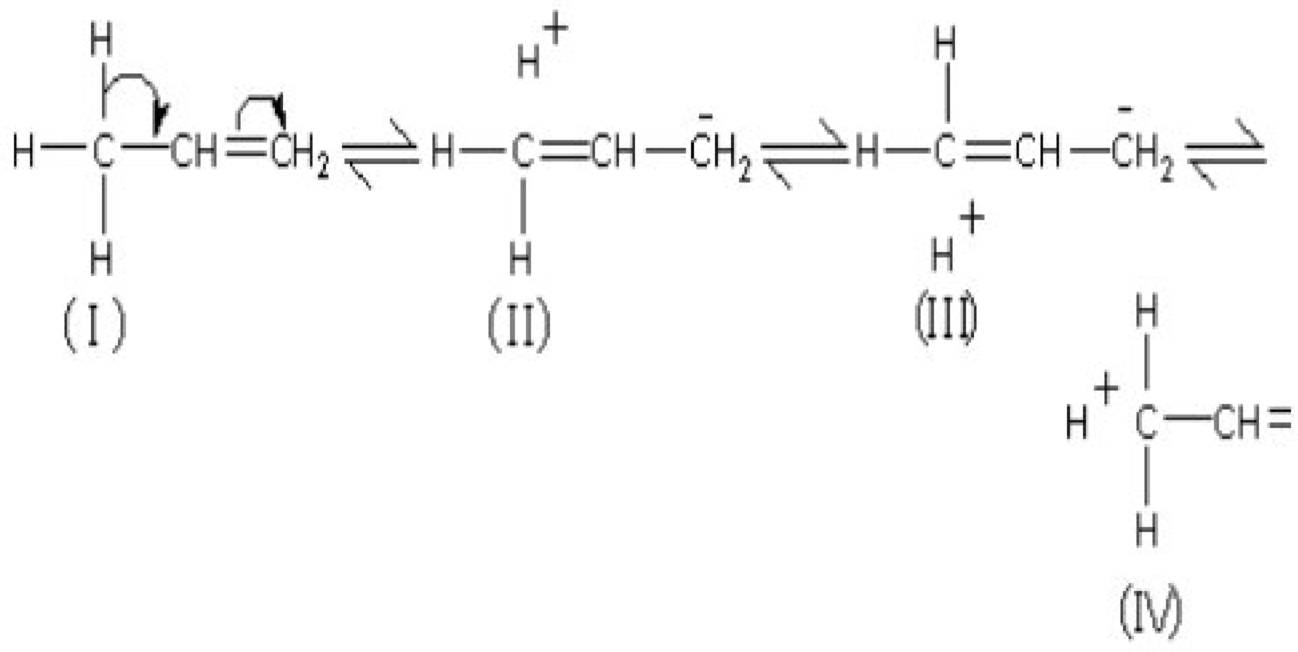
- Process in which pi and sigma bonds, both contribute in shifting of electron density.

DEFINITION

- The delocalization of sigma electrons with pi electrons of adjacent double bond is called hyper conjugation.

2.1 EXPLANATION

- When carbon to hydrogen bond (C-H) is attached to an unsaturated carbon atom the electrons of carbon to hydrogen bond (C-H) become less localized by entering into partial conjugation with attached unsaturated system. It is also mentioned as sigma to pi conjugation. Thus conjugation between electrons of sigma bong and those multiple bond is called hyper conjugation.



- Above conjugation is also called “no bond resonance”
- In canonical forms (all resonance hybrids) where no bond is indicated between carbon and hydrogen doesn’t mean that there is no bond. Actually it is weaker than usual carbon to hydrogen bond and it is proved by experimental bond length.

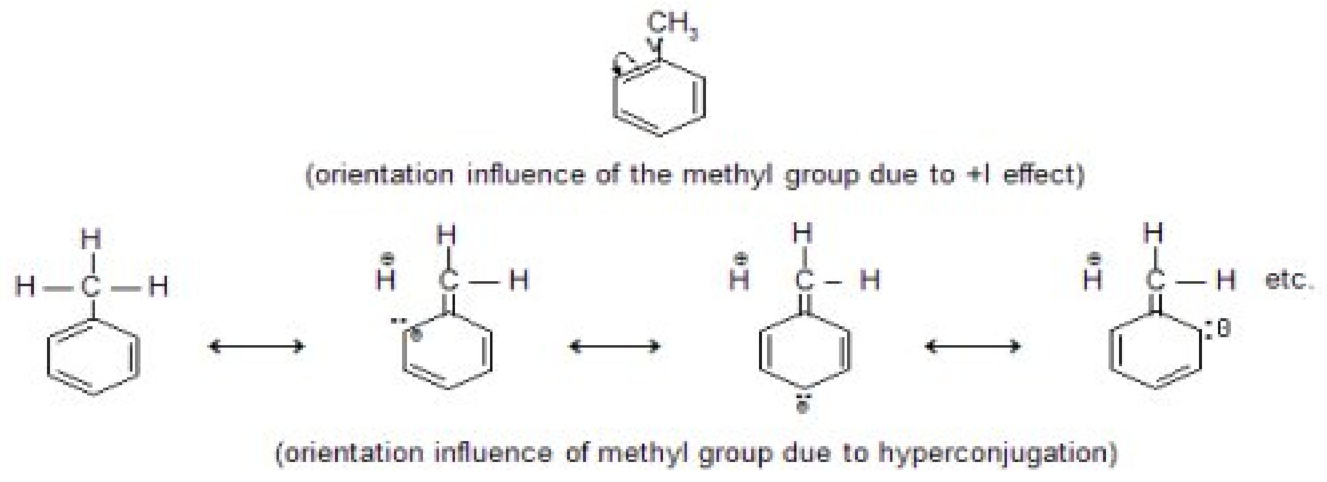
As the number of bond increases the bond length decreases

CH_3 – CH_3 = 1.54 A^0

CH_2 = CH_2 = 1.34 A^0

C ≡ C = 1.23 A^0

- Single bond while attached to with double bond is undergoing the process of hyperconjugation.
- Methyl is a nucleophile


(orientation influence of the methyl group due to +I effect)

(orientation influence of methyl group due to hyperconjugation)

- The order of electron donation in hyper conjugation is as such

CH_3- > $MeCH_2$ > Me_2CH > Me_3C

Methyl is rich in alpha hydrogen, it is rich in electron

- The reason is that, hyper conjugation depends upon hydrogen attached to the α-carbon of saturated system. It is minimum in tertiary methyl.

Chapter 3 **Steric Effect**

3.1 DEFINITION

- Effective delocalization via pi orbitals to make a specific geometrical shape or figure which allows the molecule to undergo a specific reaction is called “Steric Effect”

3.2 EXPLANATION

- Effect arise in the molecule due to its geometry that whether a molecule may react or not
- When the carbon is blocked by all the four sides the reaction cannot occur. If we ionize the molecule, then the reaction may occur as the molecule was blocked from all possible sides.
- If atoms are not bulky then they can move within a molecule to allow reaction.
- So geometry is the only thing that allows the reaction.
- Conjugation, Hyper conjugation, Inductive Effect and Mesomeric Effect can be modifies and enhanced in intensity by Steric Effect.
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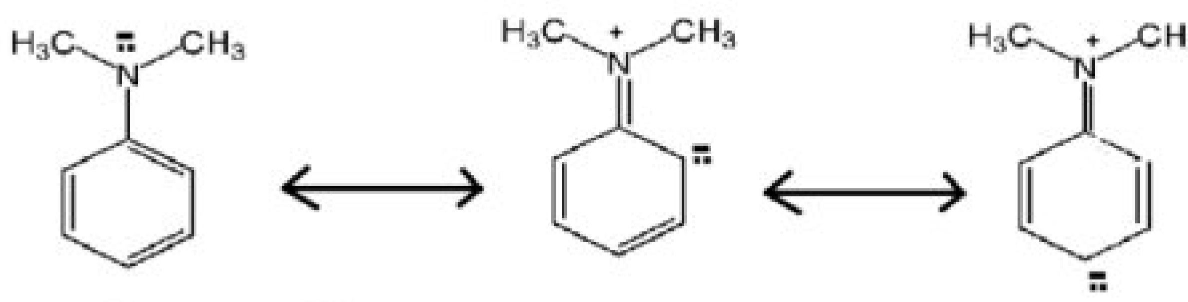
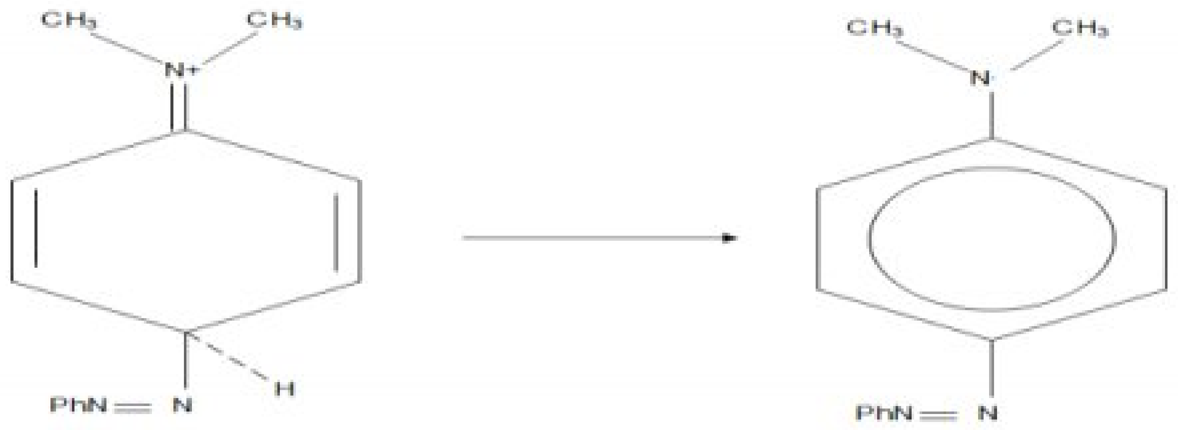
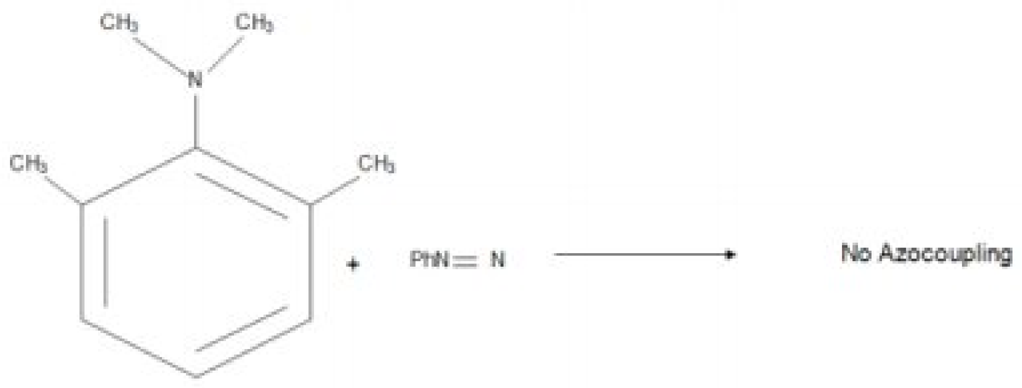




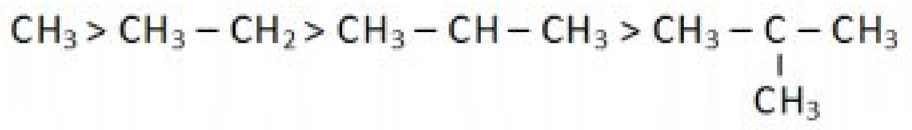
- Negative charges are generated at position number 2, 4 & 6.
- Asocoupling means that nitrogenous molecule is being attached with some other molecule.

  $$Ph - N = N^+$$

- N is making double bond but it can make triple bond, positive charge comes over it.
- Ph – N = N$^+$ may attach at position number 2, 4 and 6. So Aso may be attached only at ortho and para. These molecules are thus undergoing reaction because of their geometry, allows them to react. So there is no steric effect.



- Effective delocalization is not allowed due to geometry of the molecule. This is due to Steric Effect.
- If N-N$^-$ dimethylaniline –N(CH_3) dimethyl amine group is electron donating to the benzene ring and activates it towards attack by dizonium cation (Ph-N=N+). Ph is Phenyl (C_6H_5) for Asocoupling but its 2,6 dimethyl derivative doesn’t undergo asocoupling due to steric effect. Since methyl group is at ortho position, doesn’t allow effective delocalization of electrons and phenyl dizonium cation can’t attack at ortho and para place. However, the most common steric effect is the classic effect/hindrance of SN-reactions in which bulk of groups influence the reactivity of compound inhibiting approach of a reagent to reacting site.
- e.g. Alkyl halide, shows following order of reaction



$$CH_3 > CH_3 - CH_2 > CH_3 - CH - CH_3 > CH_3 - \underset{\displaystyle CH_3}{\underset{|}{C}} - CH_3$$

- Tertiary Alkyl halides have more steric effect
- Reactivity is inversely proportional to Steric Effect
- Methyl halide is more reactive because steric hindrance is less around electrophilic carbon since carbon atom is surrounded by three hydrogen while in tertiary alkyl halide carbon atom is surrounded by 3 bulky groups and steric effect is high.

Chapter 4 INDUCTIVE EFFECT

- Only involves sigma bond ---- charge penetrates, but with decreased effect

4.1 Definition

- Inductive effect may be defined as Polarization of a bond induced by adjacent polar bond and is denoted by Inductive Effect. All this happens due to sigma bond.

4.2 EXPLANATION

- Inductive Effect refers to the polarity produced in a molecule as a result of difference in electronegativity of different atoms as compared to one another. In single covalent bond between unlike atoms, the electron pair (sigma bond) is attached more towards more electronegative atoms
- E.g. Alkyl chloride, electron density tends to be greater near chlorine because chlorine is more electronegative than carbon and represented as

$$-\overset{\delta+}{C}-\overset{\delta-}{Cl} \quad \text{Or} \quad -C \rightarrow Cl$$

- If carbon atom is bonded to chlorine is itself attached to further carbon atom, the effect can be transmitted resulting in polarization of next bond with a slight positive charge on next carbon atom.

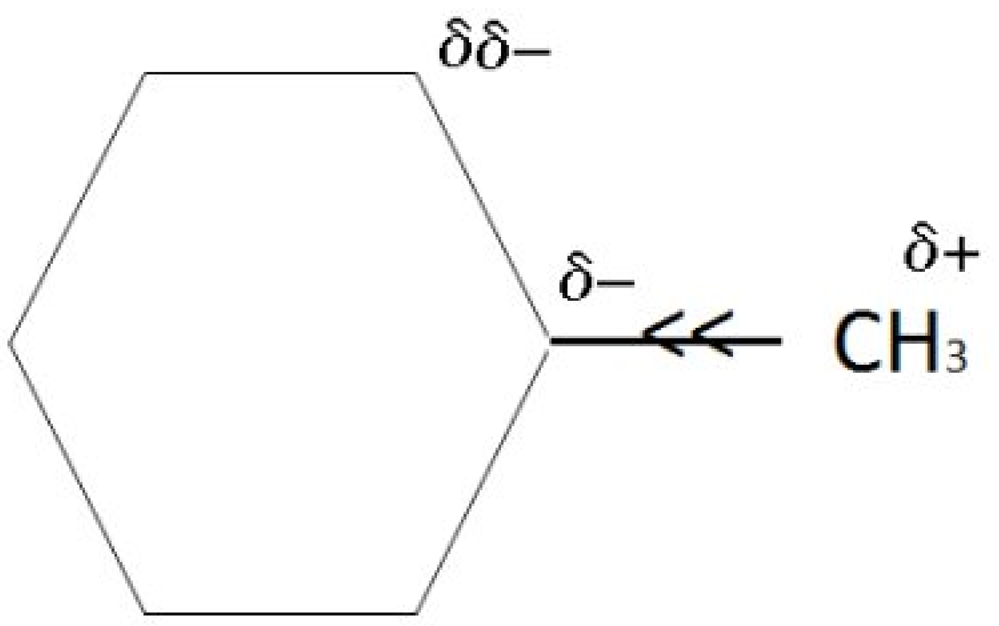
$$-C-\overset{\delta++}{C}-\overset{\delta+}{C}-\overset{\delta-}{Cl} \quad \text{Or} \quad -C-C \rightarrow C \twoheadrightarrow Cl$$

- Inductive Effect involves sigma electrons only. It may be operated in opposite direction depending upon nature of functional group

$$CH_3 \leftarrow CH_2 \twoheadleftarrow O^-$$

- (as O^- is electron donating being rich in electrons)

➤



- CH_3 may donate electrons from either side in a ring as its density shifts equally from both sides). Para side is least affected by opposite charge and it is more stable. Thus Inductive Effect may be considered as dipole-dipole interaction.
- The effect operates through bonds and is greater for adjacent bonds, decreasing rapidly with the distance so that in most cases it causes very little effect on a bond that is four bonds away.
The functional group responsible for producing Inductive Effect can be classified into two groups. These are as such

1) ELECTRON WITHDRAWING GROUPS (ELECTROPHILE) → -VE INDUCTIVE EFFECT

the more electronegative atom may withdraw the electrons from carbon atoms

$$O^-,\ CO_2^-,\ CR_3^-,\ CH_3^-\ \text{etc.}$$

2) ELECTRON DONATING GROUPS (NUCLEOPHILE) → +VE INDUCTIVE EFFECT

they are less electronegative atoms and withdraw electrons towards carbon

$$I \leftarrow CH \leftarrow COO$$

Iodoacetic acid is more acidic than acetic acid:

More acidity of Iodoacetic acid than acetic acid is because of Inductive Effect as the negative charge of carboxylate ion is stabilized by Iodine.

CH_3 – COOH

I - CH_2 – COOH

And hydrogen ions are allowed to disperse in solution, making it more acidic as compared to acetic acid.

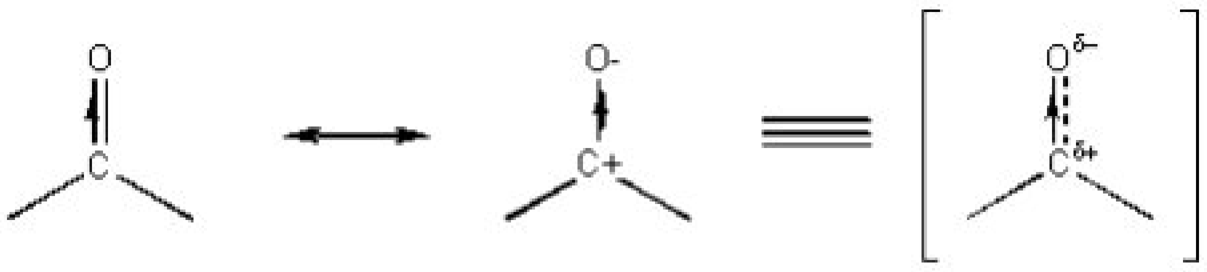
Inductive Effect always occurs in saturated compounds

Acetic Acid is less acidic than Formic Acid?? Yes or No

Hint: Inductive Effect (elaborate for your convenience)

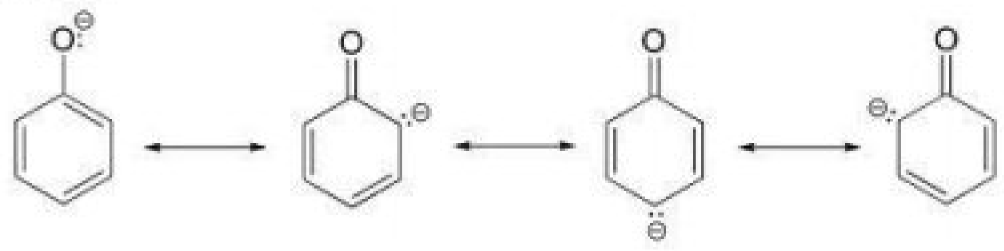
Chapter 5 MESOMERIC EFFECT

- Involves only pi bond
- It is easy to shift electrons of double bond rather than single bond because electron density in single bond lies between two nuclei.



5.1 DEFINITION

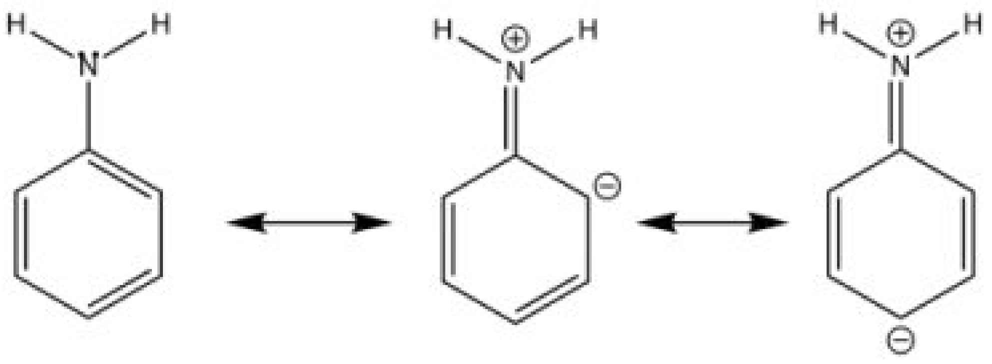
- It refers to the polarity produced in the molecule as a result of interaction between two pi bond electrons & a pi-bond and a lone pair.
- It involves pi electrons and is transmitted in the molecule in similar way as Inductive Effect.



- This effect also affects others having pi electrons.

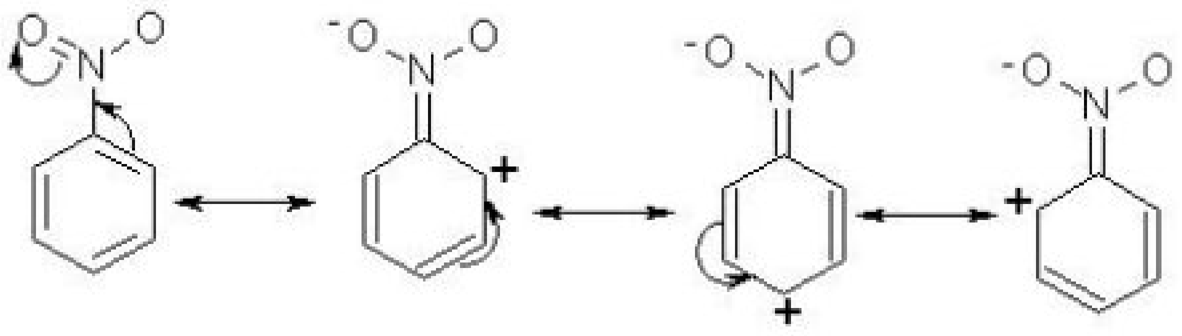
5.2 EXPLANATION

- Consider a carbonyl group. The oxygen atom is more electronegative than carbon atom and attracts the pi bond electrons towards it and creates a partial positive and partial negative charge on concerned atoms. If this carbonyl group is conjugated with unsaturated system, the above polarization will transmit further to the molecule as shown above.
- Ammonia does not resonate and give any canonical form because it doesn't have any unsaturated system attached. In aniline, N has a lone pair that can be given to the unsaturated system.



Resonance Forms of Aniline

- So we see that lone pair and pi bond electrons are interacting.
- Ammonia does not give any canonical form. However if one hydrogen of NH3 is replaced by Benzene ring, it may show mesomeric effect in which electron pair of nitrogen delocalizes over entire ring of benzene ring as mentioned above.
- Similarly in nitrobenzene,



- incoming group can come over meta group but not at ortho and para group because they are deficient in electron. So nitro group is also called as metadirecting group. Two types of groups are involved.

Depending on the groups it is classified into two types:

1) NEGATIVE MESOMERIC EFFECT

- It is represented by group which withdraw the electrons from the molecule e.g. Nitro group, Cyanide, Carbonyl.

2) POSITIVE MESOMERIC EFFECT

- It is shown by molecules which donates electrons to the molecules. E.g. –NH2 , -NR2 , -SH , -OH

PRACTICAL APPLICATION

$$H_3C-CH_2-OH \rightleftharpoons H_3C-CH_2-O^- + H_3O^+$$

- In ethanol reversible reaction is feasible and H+ is able to rejoin but in phenol there is mesomeric effect (have degree of unsaturation) and reversible reaction is not feasible so H+ are difficult to rejoin. So it retains its antiseptic character. That's why phenol is more acidic then ethanol.

Chapter 6 HYDROGEN BONDING

6.1 DEFINITION

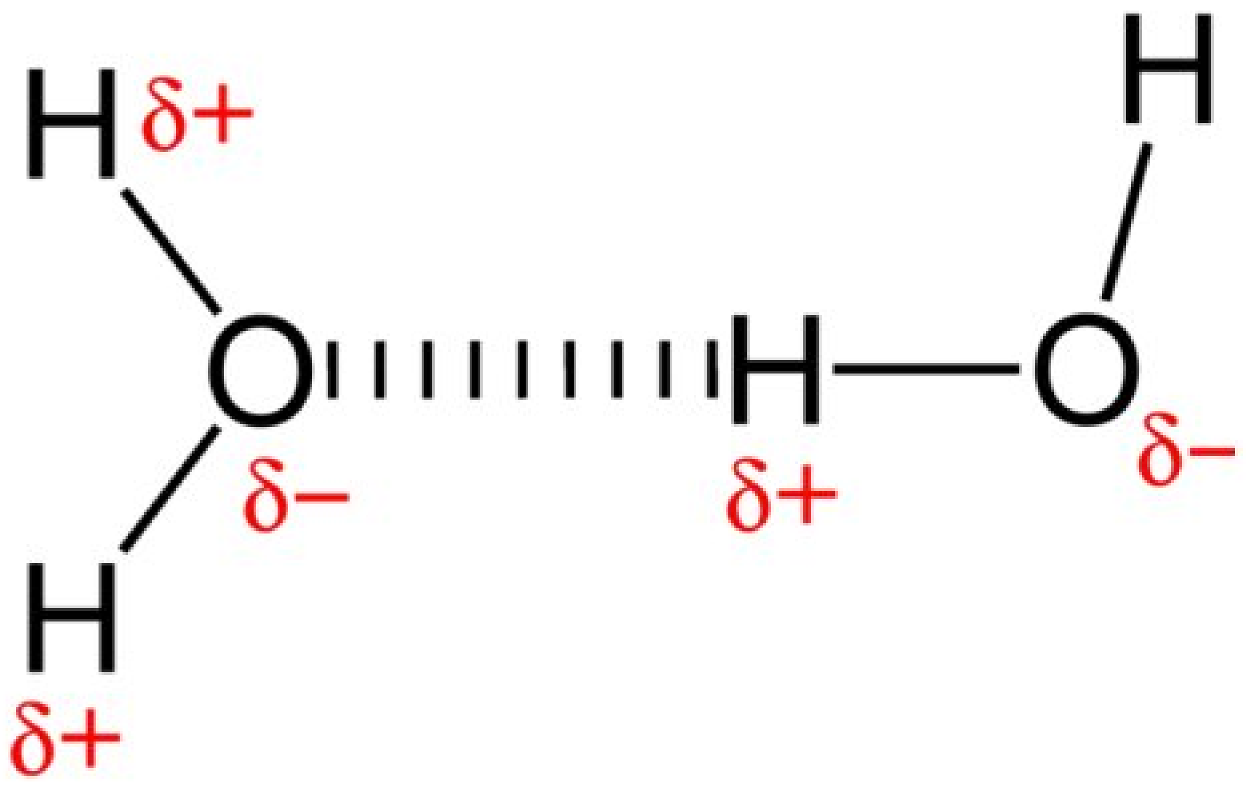
- The hydrogen bond is an attractive interaction between a hydrogen atom from a molecule or a molecular fragment X–H in which X is more electronegative than H, and an atom or a group of atoms in the same or a different molecule, in which there is evidence of bond formation.
  (Definition by IUPAC Published in "Pure and Applied Chemistry")

OR

- A chemical bond in which a hydrogen atom of one molecule is attracted to an electronegative atom; especially nitrogen, oxygen or fluorine atom; usually of another molecule.
  (The American Heritage® Dictionary)

6.1.1 EXAMPLE

- Hydrogen bonding is present in water molecule. Hydrogen of one molecule is interacted by the oxygen atom of the other molecule through Hydrogen Bonding.



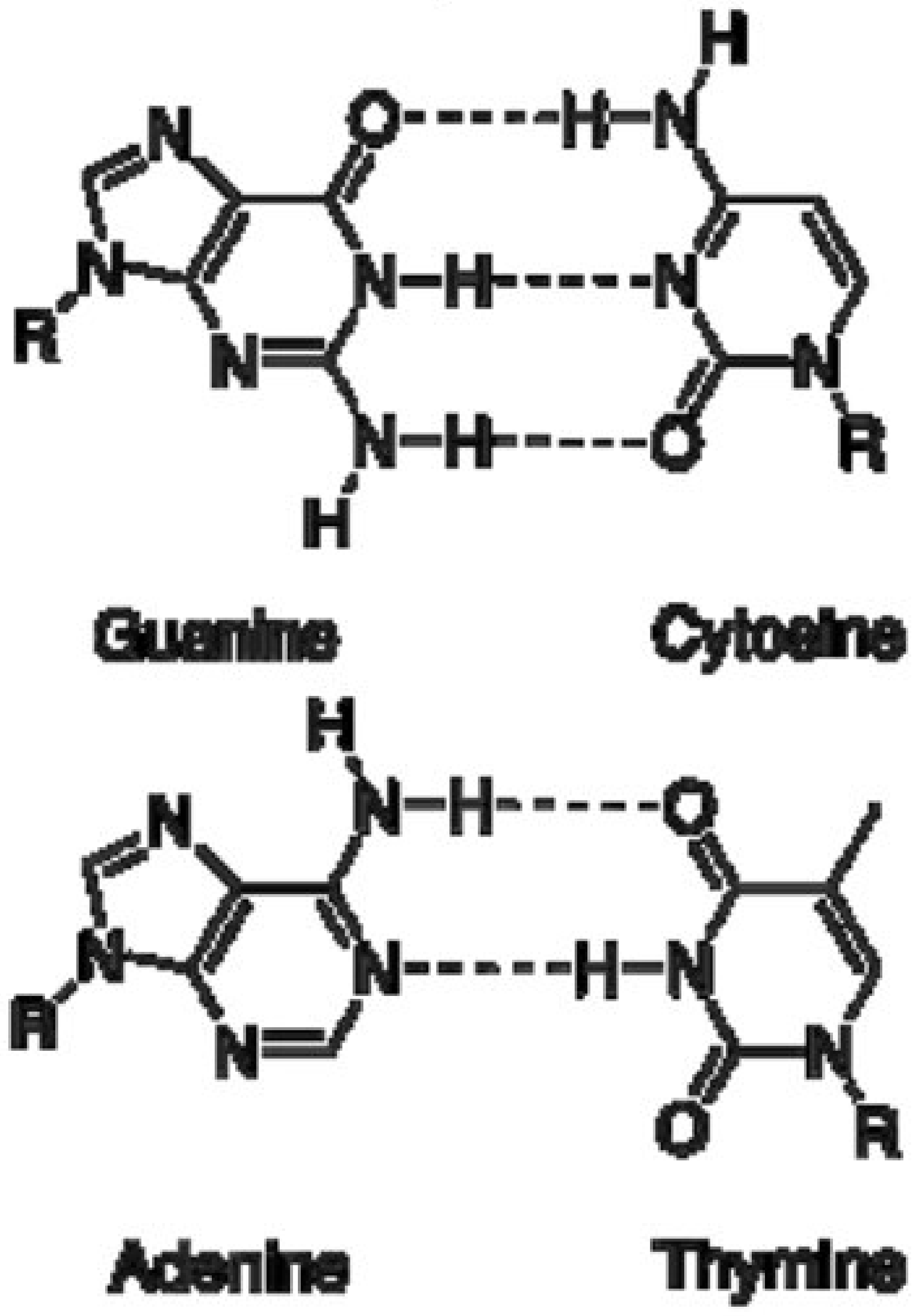
6.2 APPLICATION OF HYDROGEN BONDING

6.2.1 HYDROGEN BONDING IN PROTEINS

- Hydrogen bonding helps in determining the three-dimensional structures that are adapted by proteins. Proteins fold in specific shape which indeed is responsible for its physiological and biochemical role.
- In Secondary Structure of Proteins Hydrogen bonding is formed between the backbone oxygen and the amide hydrogen. In this way the two strands of amino acids are combined together to build a secondary structure of proteins. The hydrogen bonding between N-H and O-C group of amino acid after every four residues make up the alpha helix structure of the proteins, while if the spacing is less than the structure is refer as beta sheet.

6.2.2 HYDROGEN BONDING IN DNA

- The double helical structure of the DNA is due largely to hydrogen bonding present between the base pairs. The base pair link the two strands together by the help of hydrogen bonding. During replication the hydrogen bonding present between the two molecules break down and the strands are separated. Nitrogenous base pair presents in DNA molecule includes Guanine, Cytosine, Adenine and Thymine. Three Hydrogen bonds are present in bonding between Guanine and Cytosine i.e. between two molecules of H-O bonds and one molecule of H-N. Two Hydrogen bonds are present between the Adenine and Thymine i.e. between an H-O and H-N molecules. Hydrogen helps us in understanding the Watson-Crick Model of DNA molecule and process of replication.

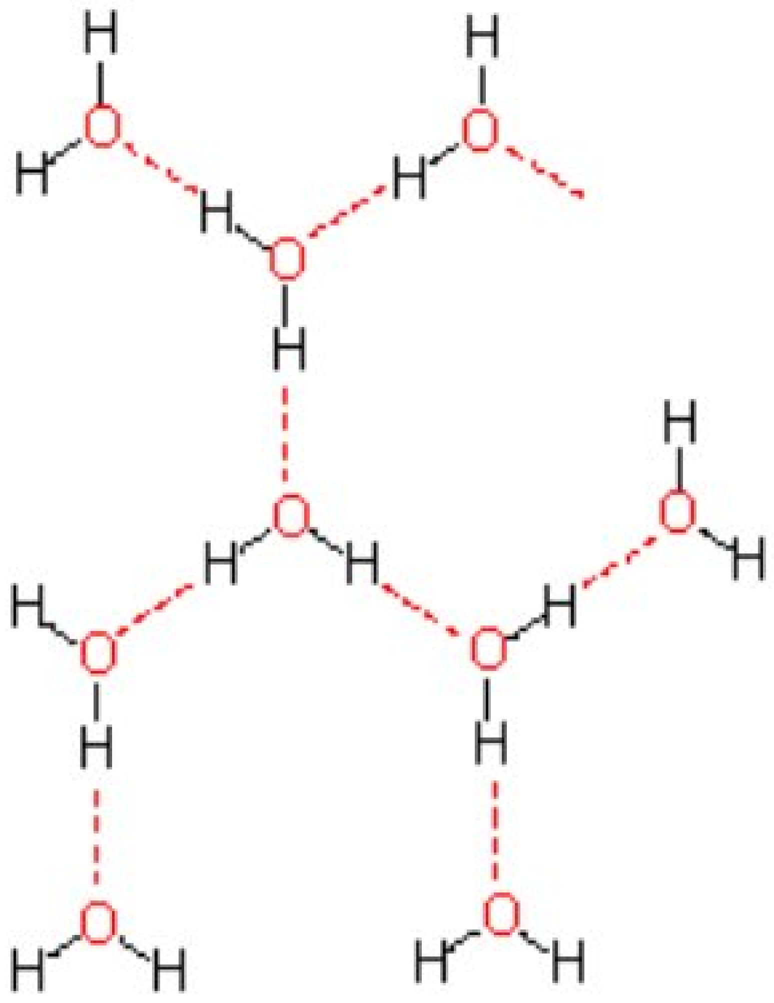


6.2.3 HYDROGEN BONDING IN CARBOHYDRATES

- Carbohydrates (or saccharides) are the most abundant biological molecules; cellulose is said alone to account for more than half of the carbon found in the biosphere. The intermolecular interactions of carbohydrates are dominated by extensive and cooperative O H --- O hydrogen bond networks and C H --- O hydrogen bonds are also formed in large numbers.

6.2.4 HYDROGEN BONDING IN WATER MOLECULES

- The most ubiquitous, and perhaps simplest, example of a hydrogen bond is found between water molecules. In a discrete water molecule, there are two hydrogen atoms and one oxygen atom.
- The oxygen of one water molecule has two lone pairs of electrons, each of which can form a hydrogen bond with hydrogen on another water molecule. This can repeat such that every water molecule is H-bonded with up to four other molecules, as shown in the figure (two through its two lone pairs, and two through its two hydrogen atoms).



6.2.4.1 Why ice floats on water?

- Water molecules are also attracted to each other by weaker chemical bonds (hydrogen bonds) between the positively-charged hydrogen atoms and the negatively-charged oxygen atoms of neighboring water molecules. As water cools below 4°C, the hydrogen bonds adjust to hold the negatively charged oxygen atoms apart. This produces a crystal lattice, which is commonly known as 'ice'. Ice floats because it is about 9% less dense than liquid water. In other words, ice takes up about 9% more space than water, so a liter of ice weighs less than liter water.

6.2.5 Carboxylic Acid

- Hydrogen bonding accounts for several properties of carboxylic acids. Carboxylic acids contain a polar –COOH region, where the carbon has a double bond to one oxygen and a single bond to another. The oxygen in the single bond is bonded to a hydrogen atom. In a sample of a carboxylic acid, individual molecules associate into hydrogen bonded couples called carboxylic acid dimers.

6.2.6 Movement of Water Molecules In the Vascular System of Plants

- Hydrogen bonding is partially responsible for the movement of water molecules in the vascular system of plants. Basically water is pulled up from through the stems to the top of a tree (or other vascular plant) by a combination of factors including evaporation and differential pressure inside and outside of the plant tissue. As one molecule of water moves upward, it tugs on a molecule below it, with which it shares a hydrogen bond.

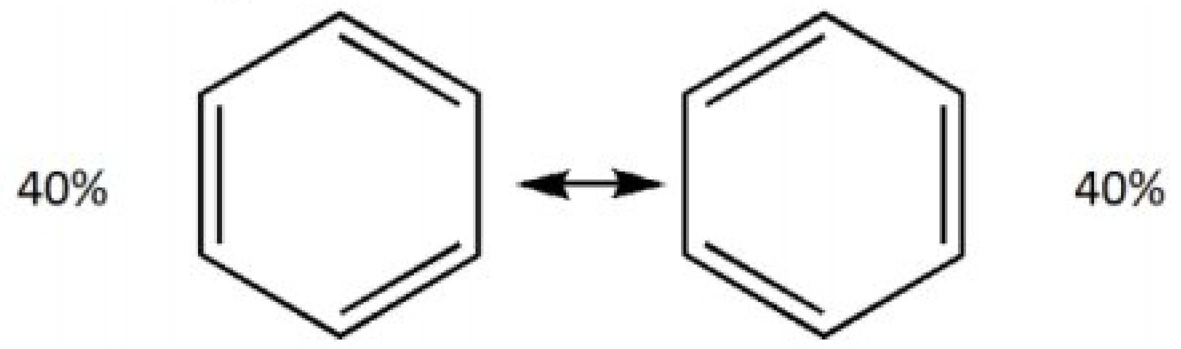
6.2.7 Protic Bond

- Hydrogen bonding is also useful in performing certain chemical reactions to make new products. For some starting materials and reactions, using a hydrogen-bonding solvent speeds up the reaction, while for others it slows it down. This has to do with how the products, reactants and chemical intermediates interact with the solvent. Hydrogen bonding solvents are called protic solvents. Some of the most common protic solvents in an organic chemistry lab are water, methanol and ethanol.

Chapter 7 THEORY OF RESONANCE

Q: Why benzene does not show colorless appearance?
Ans: It is due to delocalization of pi bond. We see it in theory of resonance.

- Resonance occurs in molecules having alternate single and double bond and can be interconverted
  e.g. Benzene



- In the structures of Benzene bond distance between carbon to carbon (C-C) is same i.e. 1.39A^{O} (1A^{O} = 10^{-10} m) while in actual the bond length of carbon to carbon single bond (C-C) is 1.54A^{O} and for carbon to carbon double bond (C=C) is 1.33A^{O}. That is not true in case of benzene. It is because of shifting of electron density between two canonical forms. So the phenomena in which two or more structures can be written for a compound having identical position of atoms is called "Resonance". The alternative (interconvertable) forms are called resonance structures or canonical forms and are actual structures of the molecule and a resonance hybrid is said to possess all these canonical forms.

Kekule structure contribute 40% and Dewar structures contribute 20%

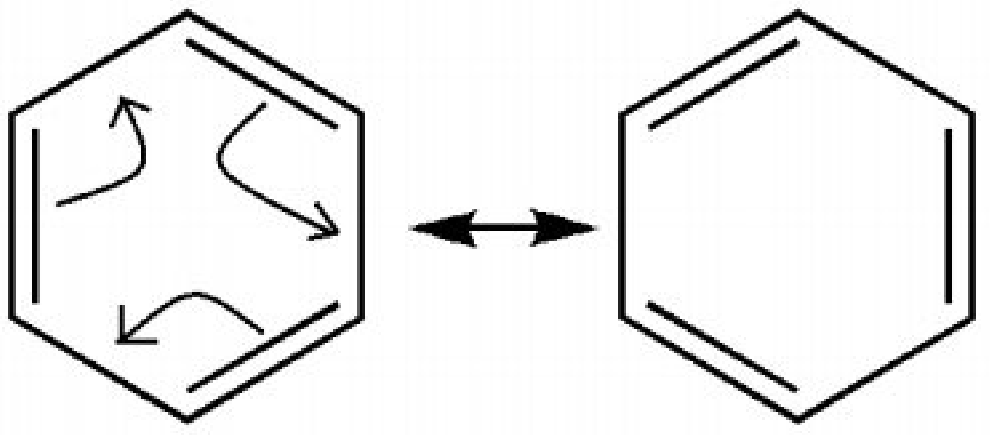
- The canonical forms are represented by a double headed arrow " ↔ " and resonance hybrid is more stable than any of the canonical forms.
- The difference in energy between the hybrid and most stable resonance form is called "Resonance Energy"

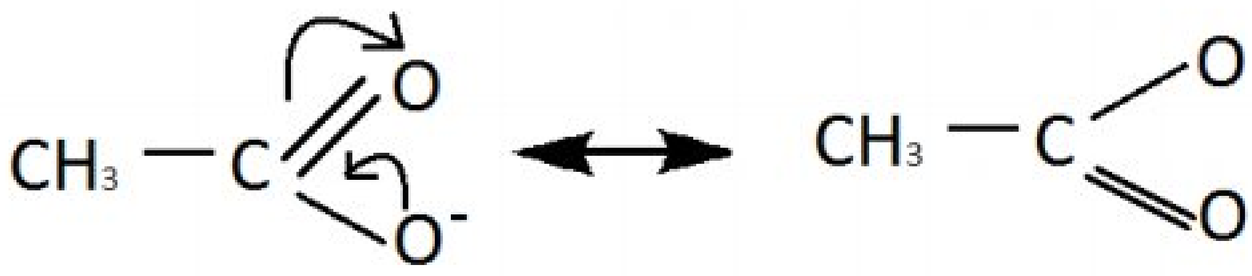
7.1

RULES OF RESONANCE

1) Resonance involves only delocalization of electrons. Whenever a molecule is to be represented by two or more structures, they differ only in arrangement of electrons not atoms.

2) Resonance structures are interconvertable by a series of electron shift.





3) Resonance hybrid possesses all characters of Canonical forms.

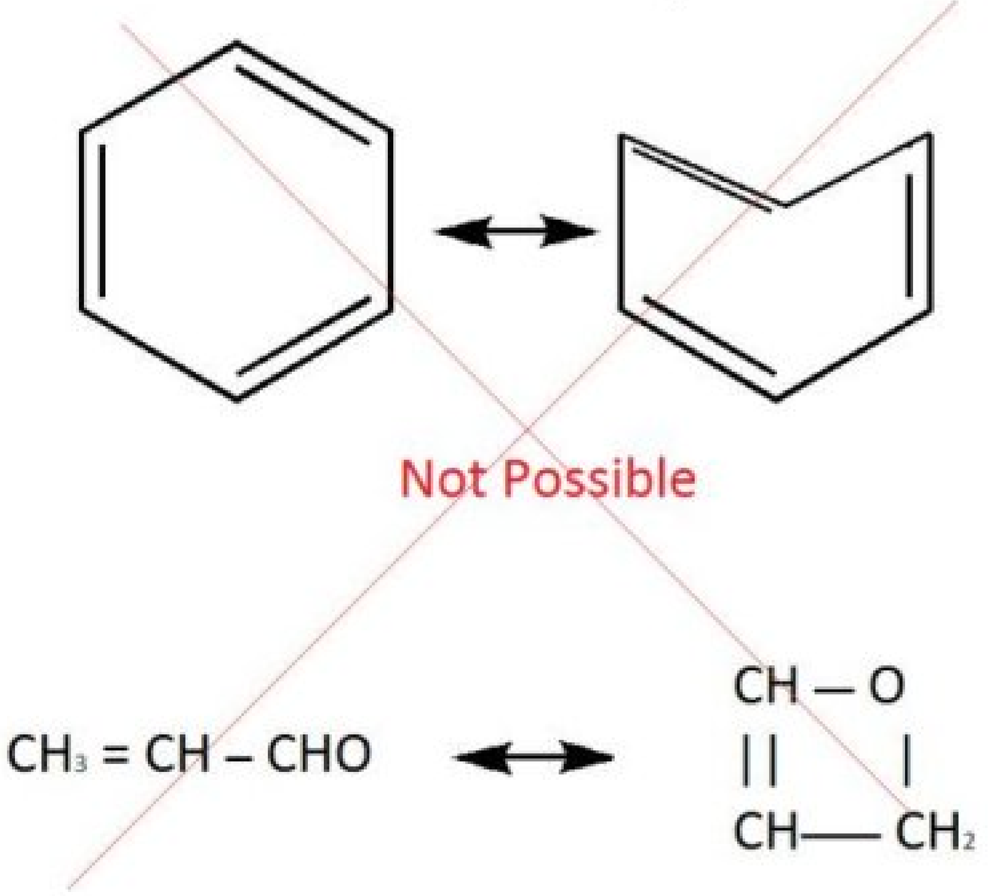
4) Resonance structures are represented by a double headed arrow " ↔ "

5) Resonance hybrid is more stable than any of the contributing form.

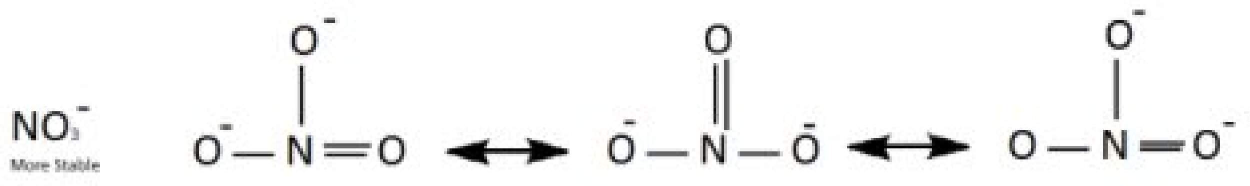
6) Resonance always increases stability of molecule and decreases reactivity.

7) Number of unpaired electrons should be same in all canonical forms.

8) Structures with distorted bond length or angles will not contribute towards resonance hybrids.



9) Compounds with larger number of canonical forms or significant structures has greater resonance energy and are more stable while the one with less canonical forms is less stable. That is why NO_3^- is more stable (less reactive)

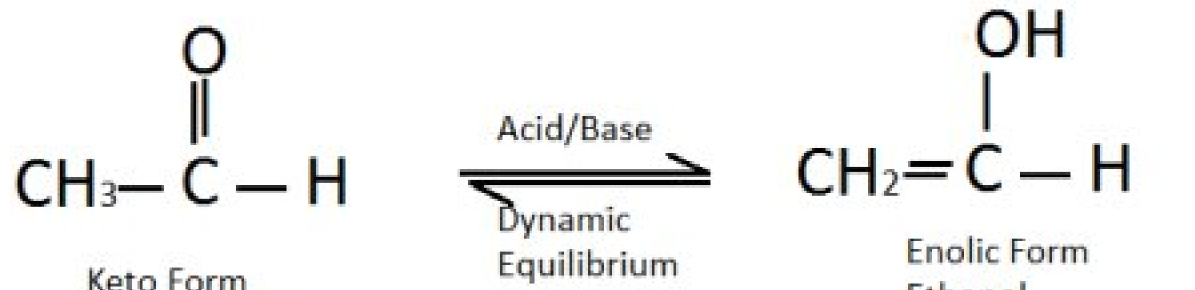


10) Structures in which bond angles and bond lengths closely resembles with resonance hybrid are more stable than those with bonds of distorted angle.

Chapter 8 KETO-ENOL TAUTOMERISM

8.1 DEFINATION

- A type of isomerism in which two functional groups of isomers exists together in solution and is in dynamic equilibrium is called tautomerism. In case of Keto-Enol tautomerism, a rapid equilibrium is established between aldehyde and ketone and their isomeric Enolic form in presence of acid or base catalyst.

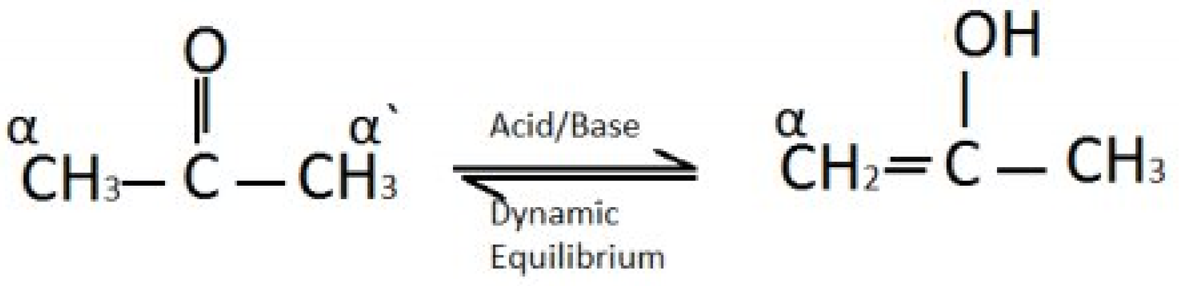


$$CH_3-\overset{\overset{O}{\|}}{C}-H \xrightleftharpoons[\text{Dynamic Equilibrium}]{\text{Acid/Base}} CH_2=\overset{\overset{OH}{|}}{C}-H$$

Keto Form
Acetaldehyde

Enolic Form
Ethenol

Keto-Enol tautomers are formed by transfer of α-proton (α-hydrogen).

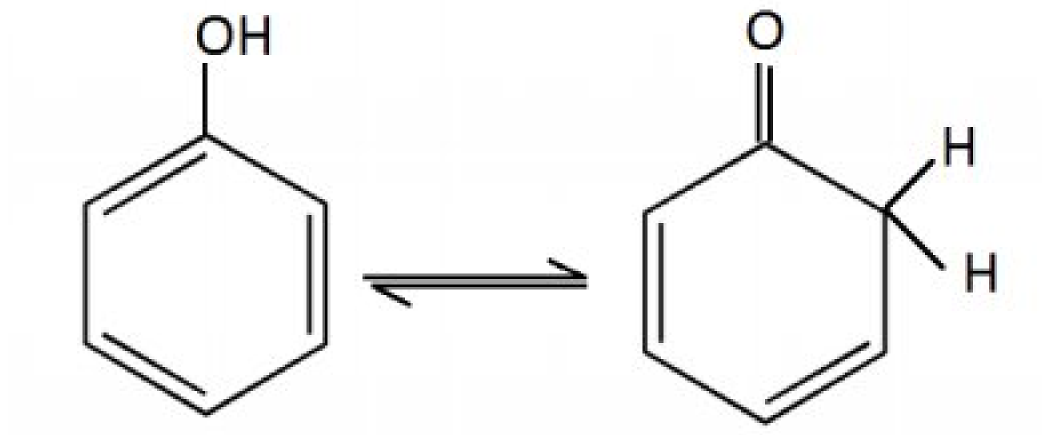


$$\overset{\alpha}{CH_3}-\overset{\overset{O}{\|}}{C}-\overset{\alpha`}{CH_3} \xrightleftharpoons[\text{Dynamic Equilibrium}]{\text{Acid/Base}} \overset{\alpha}{CH_2}=\overset{\overset{OH}{|}}{C}-CH_3$$

Benaldehyde and Formadehyde etc. cannot possess tautomers as they do not possess α-hydrogen.

8.2 EXPLANATION

- Above mentioned isomers are calledtautomers and they differs essentially in position of α-hydrogen (adjacent to carbonyl carbon). Keto form is of low energy than enolic form and is more stable. They exist in dynamic equilibrium in solution form. It was first observed by K.Mayer in ethyl esterof 3-oxo-butanoic acid (ethyl acetoacetate). White ring chain tautomers were recognized by Emil Fischer. They are classified as Constitutional Isomers.
- Generally carbonyl compounds are more stable than corresponding enol, never the less some enol are more stable ketonic form because of delocalized benzene ring (resonance).



Phenol
(enolic form)

Ketonic Form

- For the compound to undergo the process of Keto-Enol tautomerism it must possess α-hydrogen.
- Therefore compounds like Acetophenone first undergoes the process of tautomerism

Chapter 9 SN REACTION

$$R — Y + X^- \longrightarrow R—X + Y^-$$

9.1 PURPOSE

- Meant for improvement of drug properties, to introduce good drugs and to eliminate bad/adverse effects.

9.2 DEFINITION

- The reaction in which one nucleophile replaces another nucleophile is known as nucleophilic substitution reaction or simply SN-reaction.

$$\mathbf{R\text{-}Y + X^- \rightarrow R\text{-}X + Y^-}$$

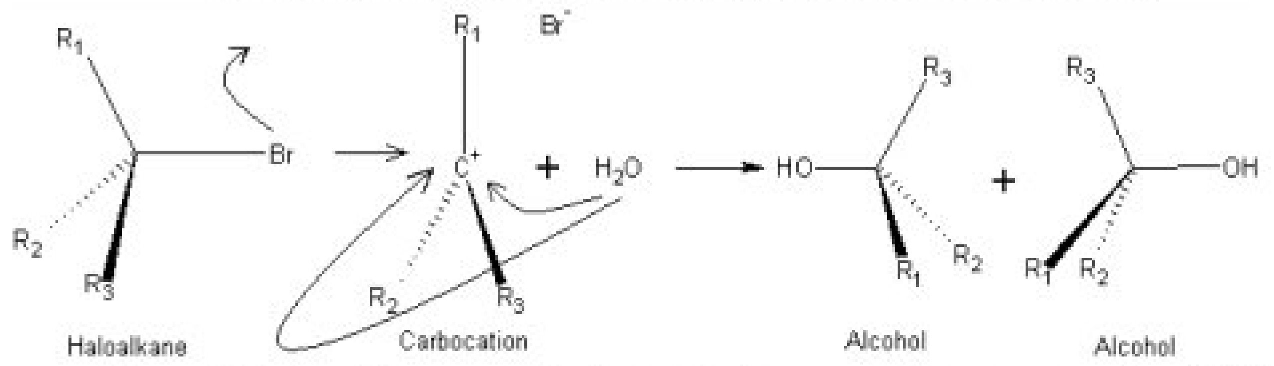
- The incoming nucleophile is called "attacking nucleophile" which should be stronger than leaving nucleophile. Compound containing electrophilic carbon is called "substrate"

9.3 TYPES OF REACTIONS

There are two types of SN-reactions:
1) SN_1
2) SN_2

9.4 SN_1 REACTION

- Nucleophile can attack from either side of carbonium ion and forms a Recimic Mixture if we start with optically active compounds.



- All tertiary alkyl halides undergo only SN_1 reactions while primary alkyl halides undergo SN_2 reactions only. Secondary alkyl halide may opt SN_1 or SN_2 depending upon following conditions.

1) Nature of alkyl halide
2) nature of attacking nucleophile
3) nature of solvent

Chapter 10 Electrophilic Substitution Reaction

- ❖ One electrophile is replaced by another electrophile

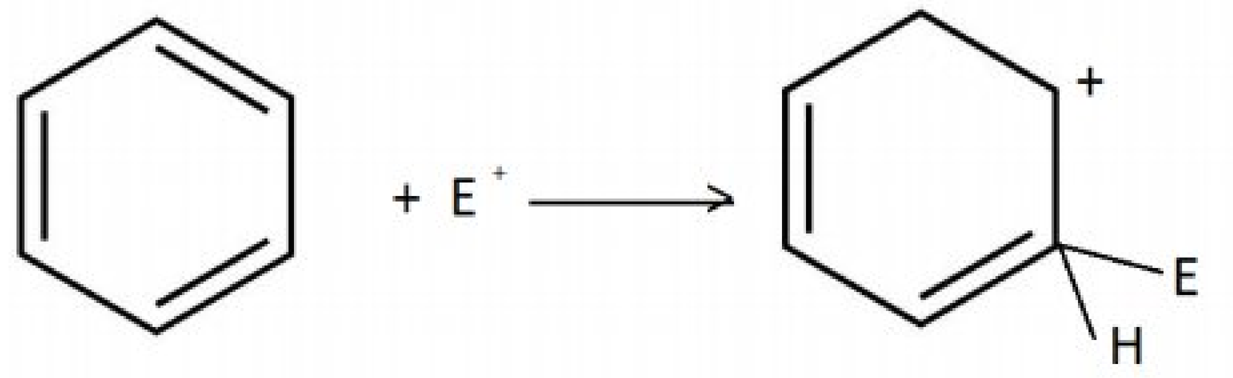
> Remember: Benzene do not give addition reaction due to "Stability/Resonance"
>
> Hydrogen of benzene is positively charged. If it is removed then another positively charged
>
> Species comes and attaches i.e. an electrophile replaces another.

10.1 Definition

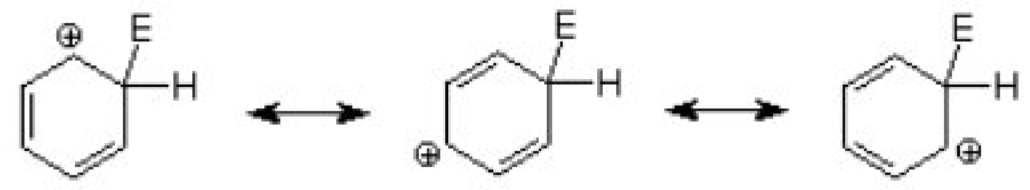
- ➢ When a substitution reaction of aromatic system involves the attack by an electrophile, the reaction is called as electrophilic Substitution Reaction.

10.2 Explanation

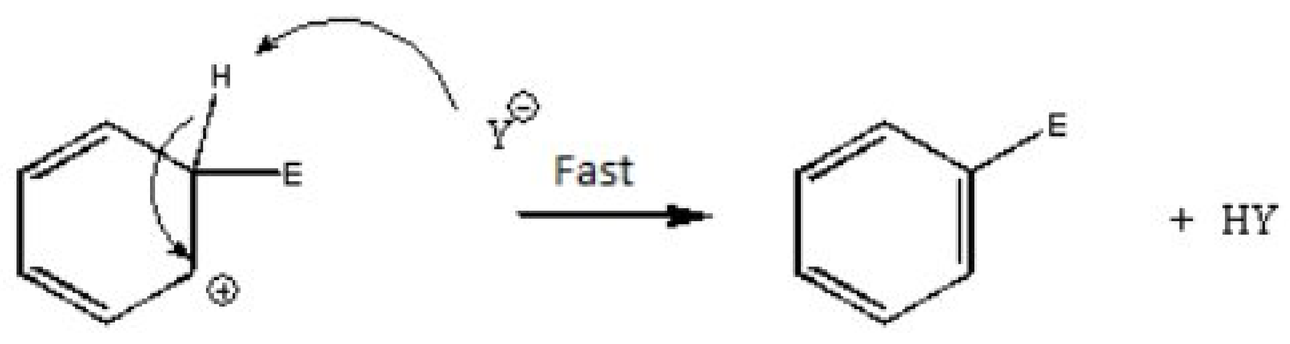
- ➢ All aromatic electrophilic substitution reactions involve two steps.



- ➢ In first step, an electrophile attacks the pi-bond system of aromatic ring to form a sigma bond with one of the carbon of aromatic ring. This intermediate is called "Arenium Ion" or "Sigma Complex".
- ➢ In arenium ion carbon atom to which electrophile is attached becomes sp^3 hybridized and benzene ring is left with 2 delocalized pair of electrons hence its stability decreases.

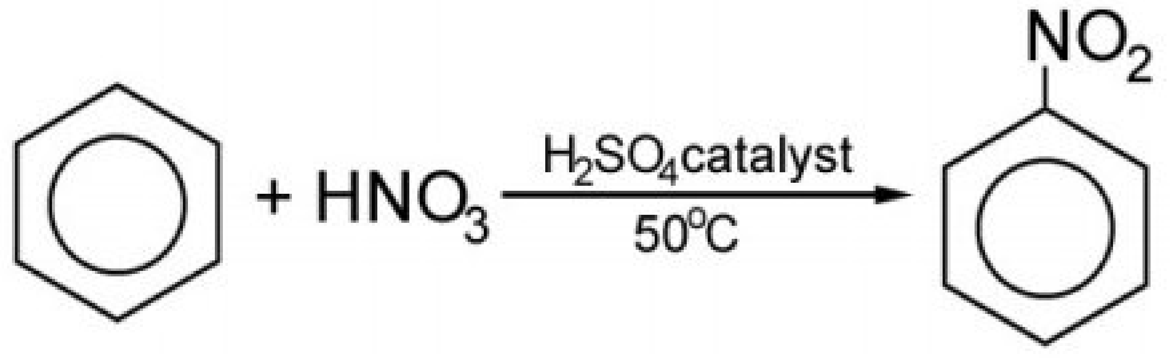


- ➢ In second step, the intermediate Arenium Ion rapidly loses proton from carbon atom and assumes sp^2 hybridized state again and contribute towards stability of the compound.



- ➢ The first step is rate determining step since it depends upon 2 molecules, hence it is bimolecular.

10.3 Nitration

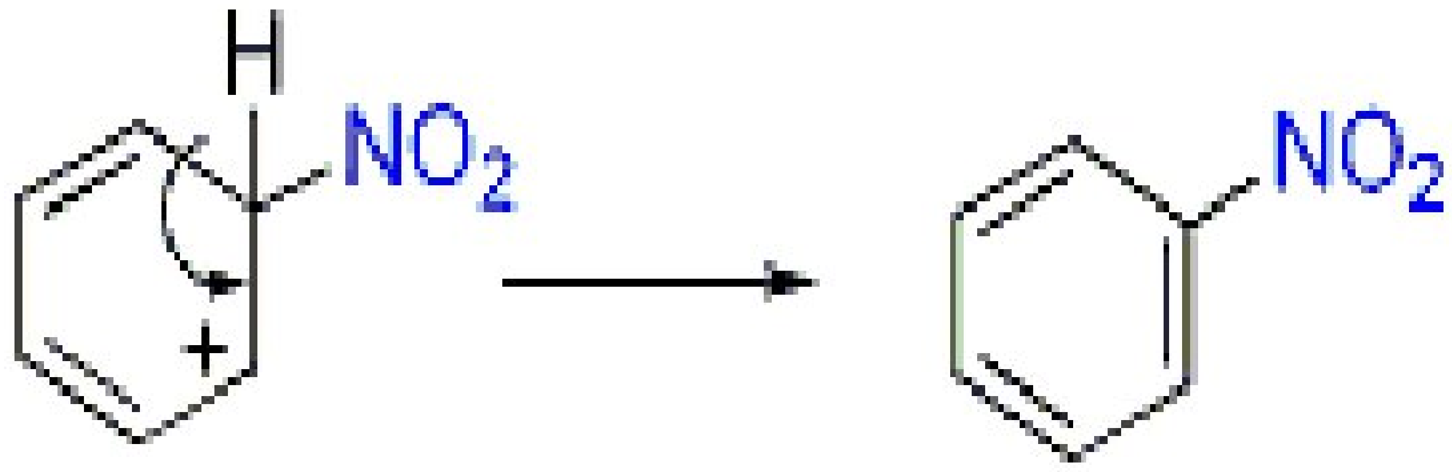


10.3.1 Step 1: Formation of an Electrophile

$$HNO_3 + 2H_2SO_4 \longrightarrow \overset{+}{NO_2} + 2HSO_4 + \overset{+}{H_3O}$$

10.3.2 Step 2: Attack of an Electrophile

10.3.3 Step 3: Formation of Chlorobenzene

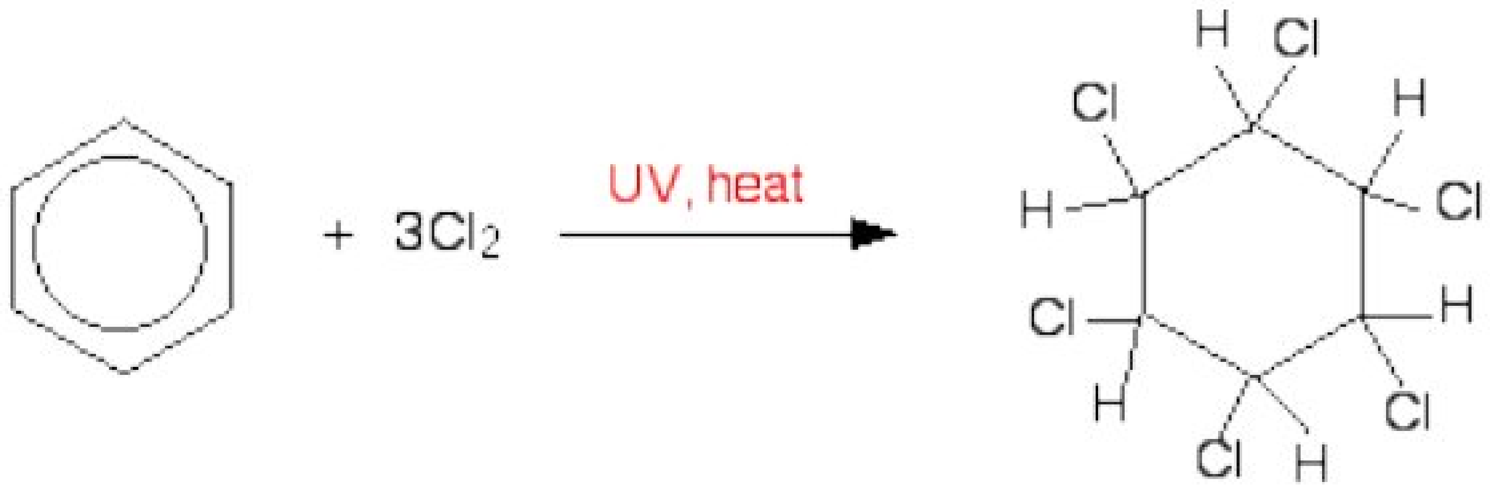


10.3.4 Step 4: Restoration of Catalyst

$$\overset{+}{H} + HSO_4 \longrightarrow H_2SO_4$$

- ❖ Bromine reacts in similar way but using a different catalyst $FeBr_3$.

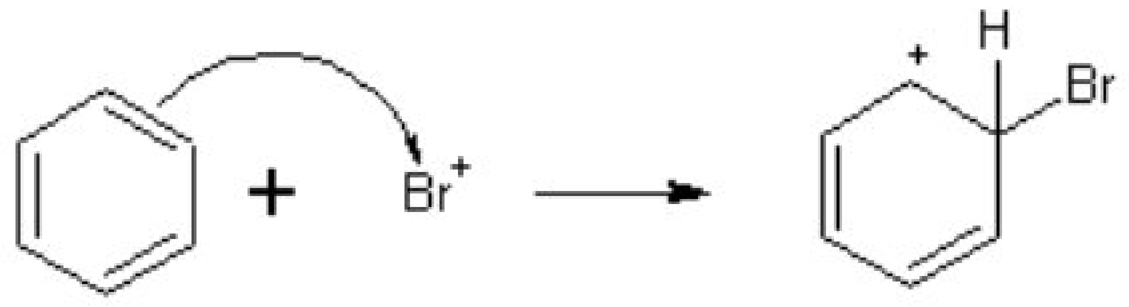
10.4 Halogenation



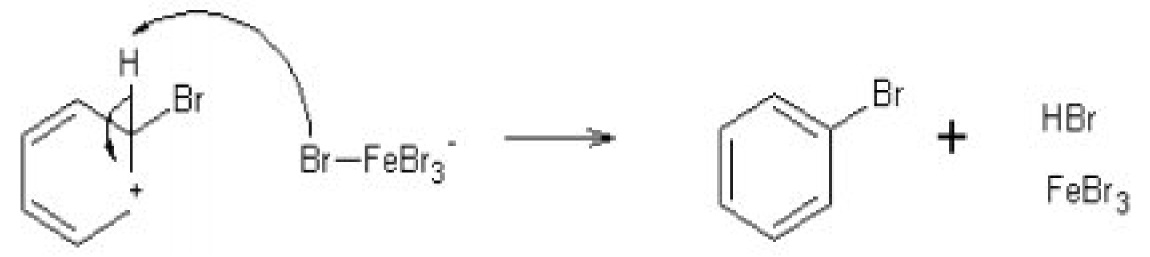
- ➢ In case of photochemical activation, there is addition instead of substitution. In case of substitution a radical ferric chloride ($FeCl_3$) or ($AlCl_3$) reacts with benzene to form chlorobenzene. The mechanism involves following steps:

Step 1: Formation of an electrophile [redacted]

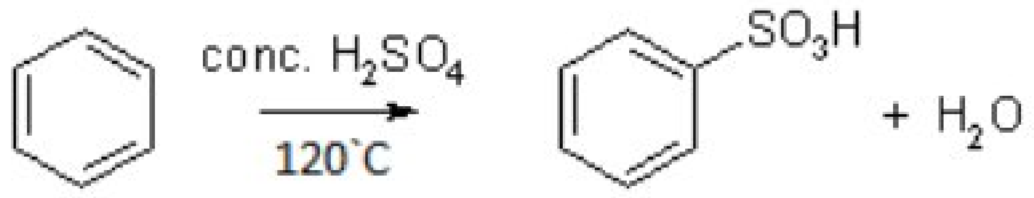
Step 2: Attack of an Electrophile (Formation of Arenium Ion)



Step 3: Loss of Proton & Restoration of Catalyst



10.5 Sulphonation

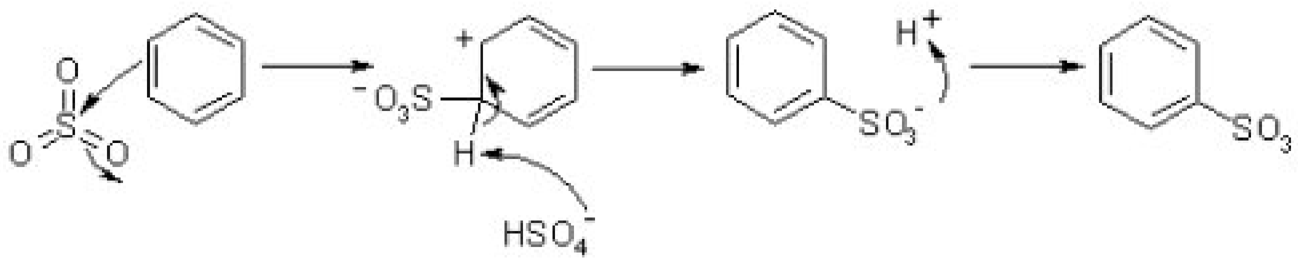


- Benzene reacts with conc.H_2SO_4 at 120 ^{0}C or fuming H_2SO_4 at room temperature to give benzenesulphonic acid
- The mechanism involves following steps

Mechanism

$$2H_2SO_4 \rightleftharpoons H_3O^{+} + HSO_4^{-} + SO_3$$

- Electrophile is sulphurtrioxide (SO_3) .So in fuming H_2SO_4 this step is not important since SO_3 is already present and it is generated as

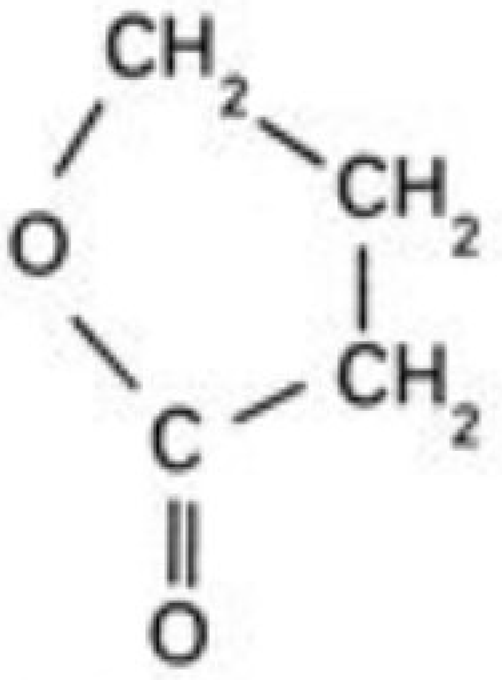


Chapter 11 BAEYER VILLIGER

- Esters constitute most important class of carboxylic acid derivative. They occur widely and are responsible for fragrance of fruits and flowers

e.g. Apple = Methyl butyrate
Orange =Octyl acetate
Pears = n-Amyl acetate
Rum = Ethyl formate

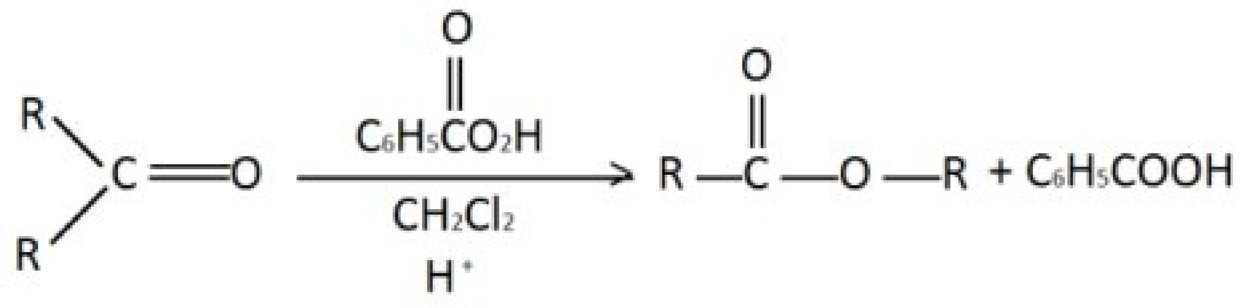
Cyclic esters are called "Lactones"



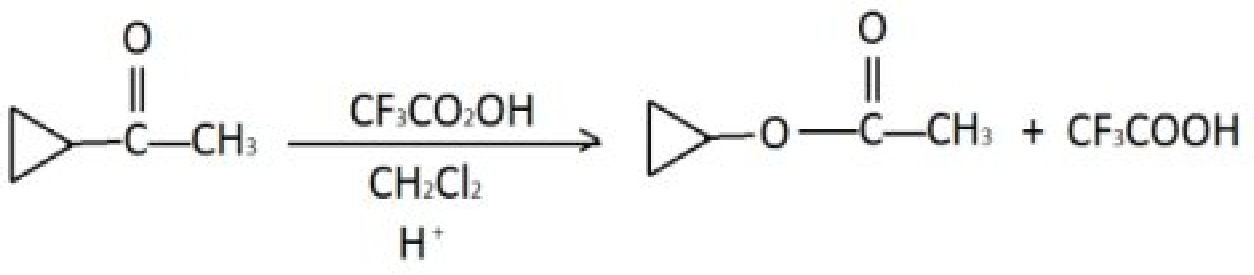
γ-lactone
(γ-butyrolactone)

11.1 DEFINITION

- Treatment of ketones with per-oxy acids such as per oxybenzoic acid, per oxytriflouro acetic acid (per-mono sulphuric acid) in the presence of an acid catalyst converts/makes an ester. The reaction is called Baeyer Villiger oxidation reaction.



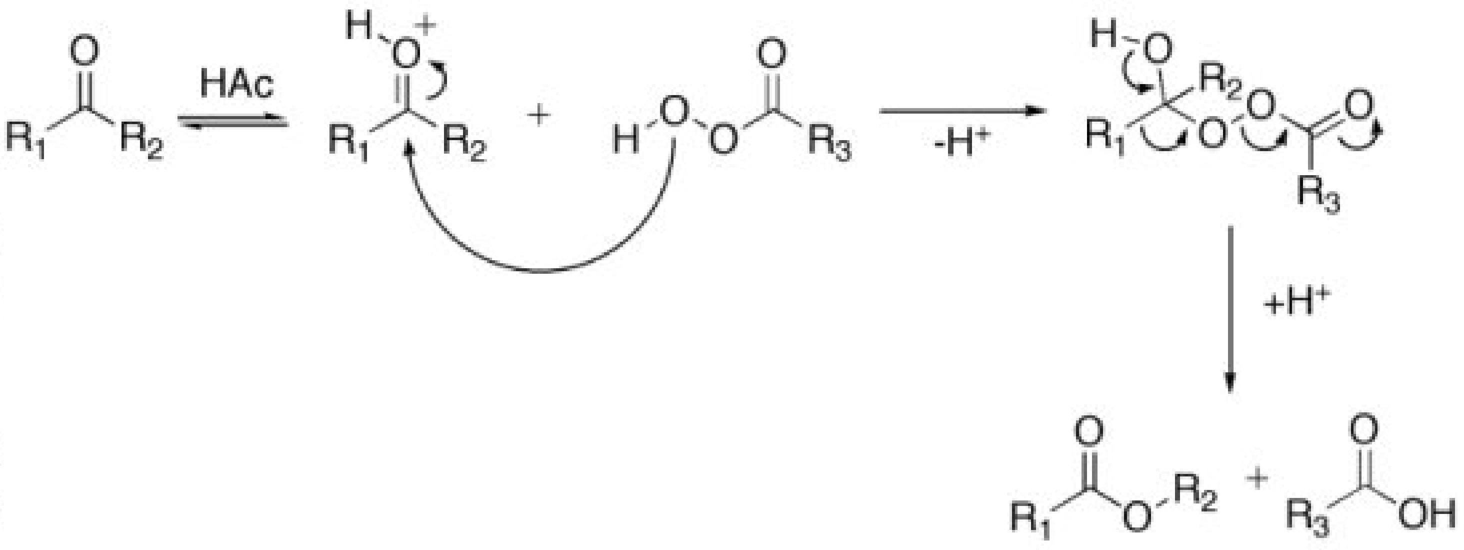
$$R_2C{=}O \xrightarrow[\substack{CH_2Cl_2 \\ H^+}]{C_6H_5CO_2H} R-\overset{O}{\overset{\|}{C}}-O-R + C_6H_5COOH$$



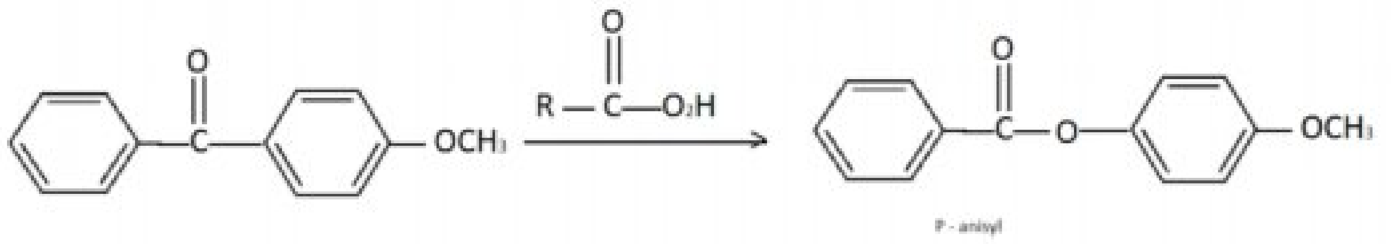
$$\triangleright-\overset{O}{\overset{\|}{C}}-CH_3 \xrightarrow[\substack{CH_2Cl_2 \\ H^+}]{CF_3CO_2OH} \triangleright-O-\overset{O}{\overset{\|}{C}}-CH_3 + CF_3COOH$$

11.2 MECHANISM

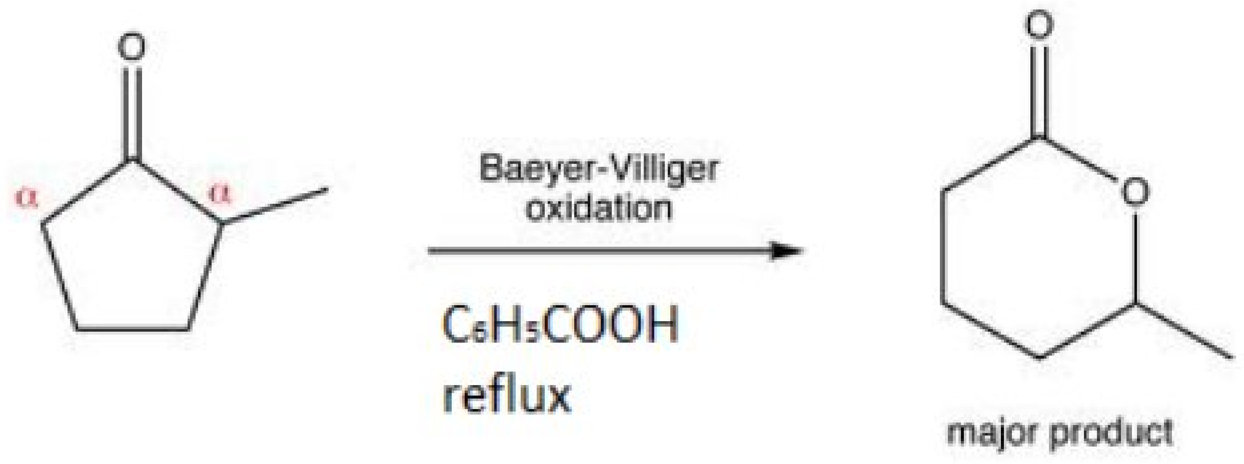
- Initially, carbonyl oxygen is protonated; the specie is attacked by per benzoate ion to give an additional intermediate.

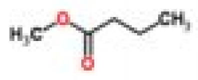
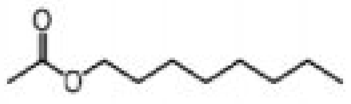
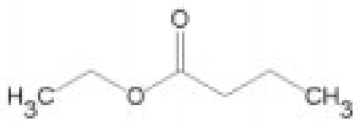
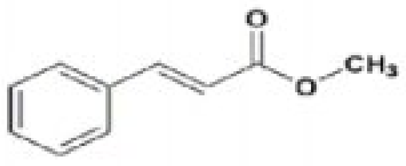
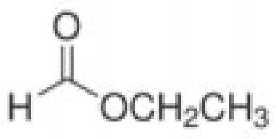


- Alkyl migration from carbon to oxygen with simultaneous release of acetate ion takes place. Finally a proton transfer leads to an ester. The group that is rich in electron migrates preferentially.



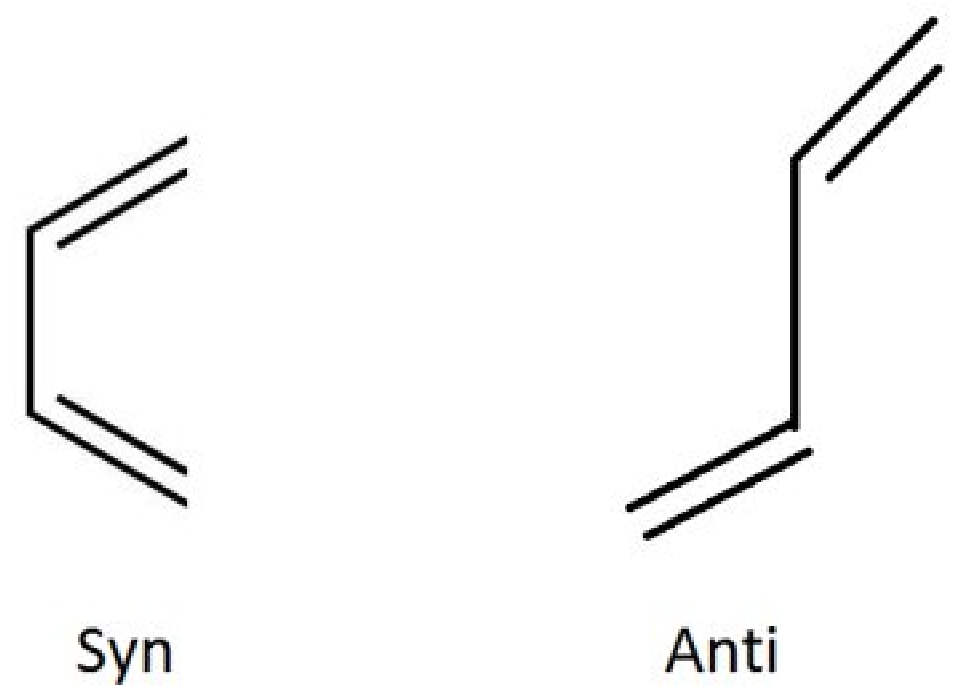
- Expansion of the ring takes place in Baeyer Villiger oxidation as in case of cyclic ketones.

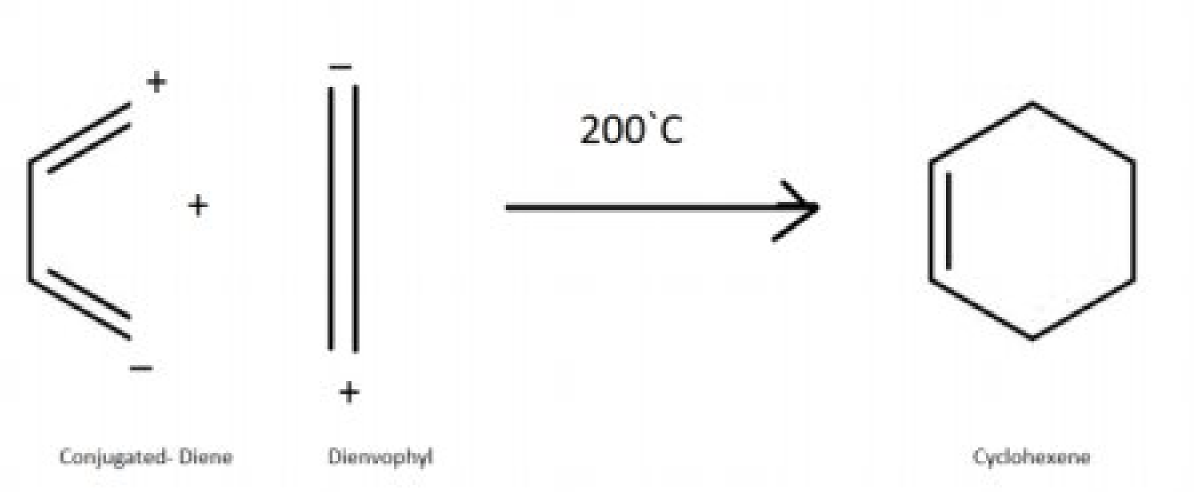


Name	Flavour	Structure
Methylbutyrate	Apple	
Octylacetate	Orange	
Ethylbutyrate	Pineapple	
n- Amylacetate	Pears	
Methyltrans-cinamate	Stawbery	
Ethyl Formate	Rum	

Chapter 12 DIEL- ALDER REACTION

- ❖ Acyclic to Cyclic



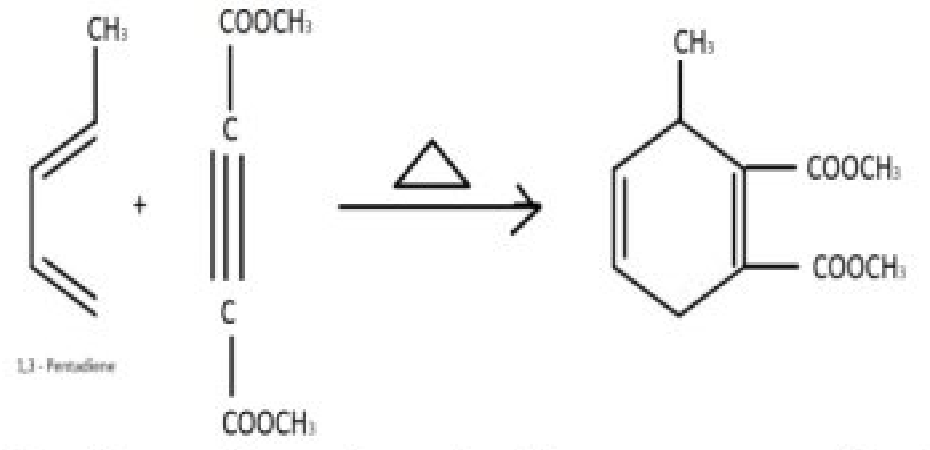


12.1 DEFINITION

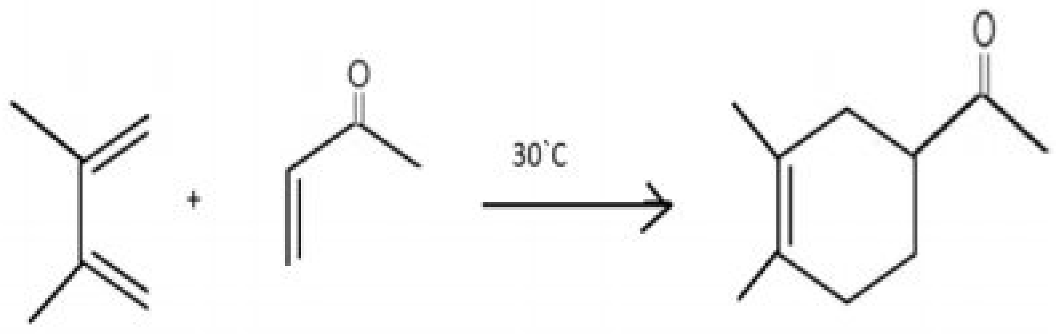
- ➢ An important reaction for preparation of cyclic compounds in which two unsaturated molecules unite to form a cyclic molecule. The process is called Diel-Alder reaction.

12.2 EXPLANATION

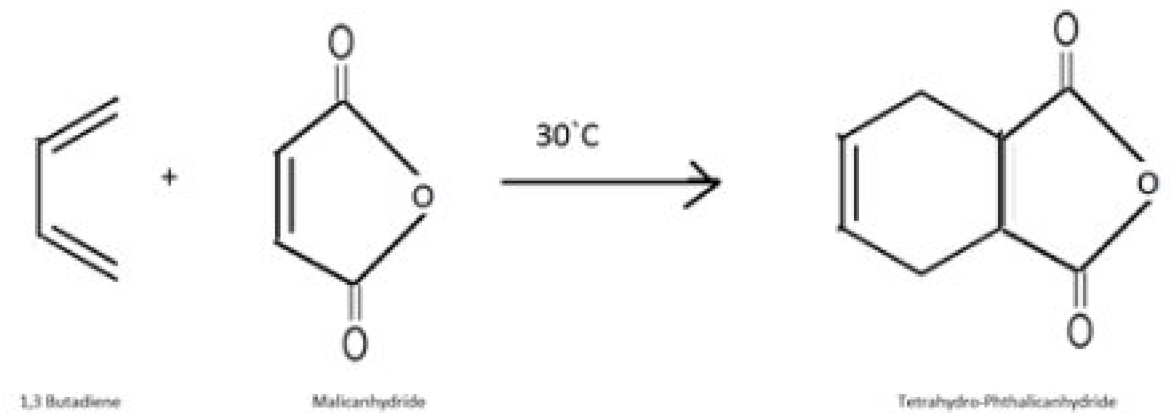
- ➢ The reaction involves a conjugated diene and a dienophyle. Diene can have two planar forms, either Syn or Anti. Diel-Alder reaction is an example of 1,4 cyclo addition reaction and the product of it is called **"Adduct"**
- ➢ Presence of electron withdrawing groups such as Acetyl, Carboxylic acid, Nitrile, Cyanide activates the dienophyle and accelerates the rate of reaction i.e. being shown by following reaction.



- ➢ On the other hand, dienes are activated by presence of electron donating group such as methyl methoxy trimethyl amine.



- ➢ Diel-Alder reaction takes place in single step without formation of intermediates. Therefore, addition of diene to dienophyle takes place in Syn manner.



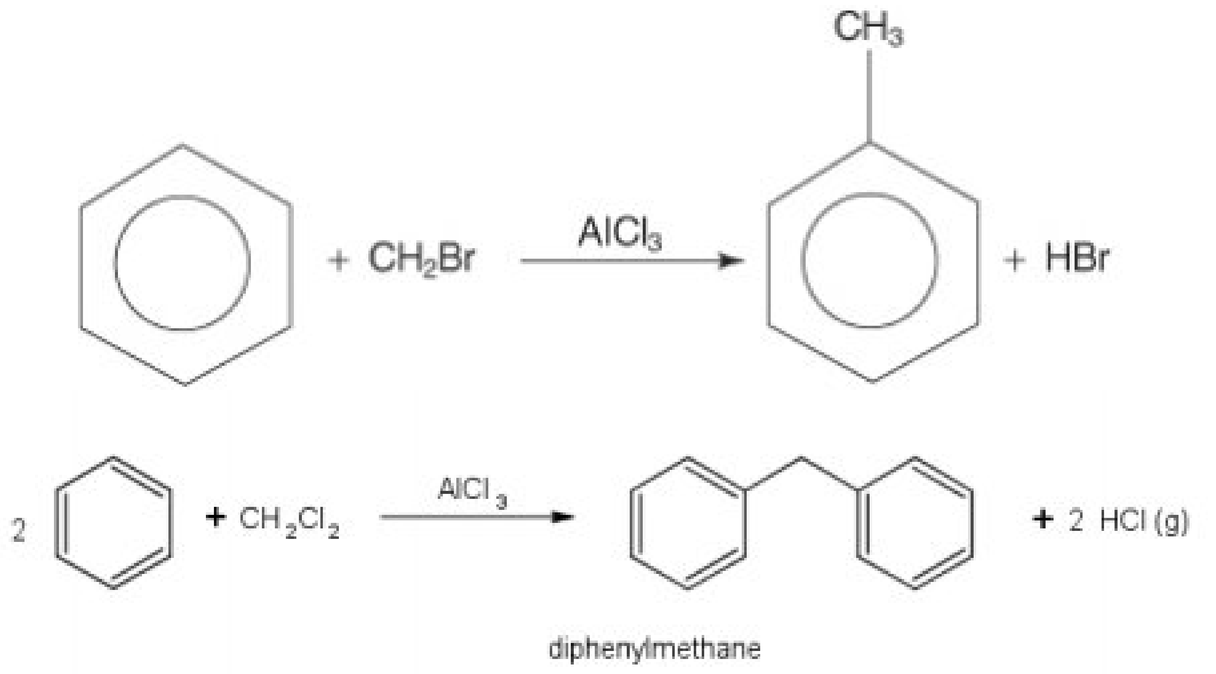
Chapter 13 FREDEL CRAFT REACTION

- Alkyl group (CH_{3-}) is highly lipid permeable and useful in our body during Chemotherapy. These drugs penetrate into the body more and more and target the place.
- Drug is more targets oriented due to introduction of Alkyl group.

Alkylating Agents
- Cis-Platin & Carbo-platin =pair the cell division and normal growth of cell is disturbed. They form covalent bond.
- Alkyl groups come under category of antineoplastic drugs.

13.1 DEFINITION

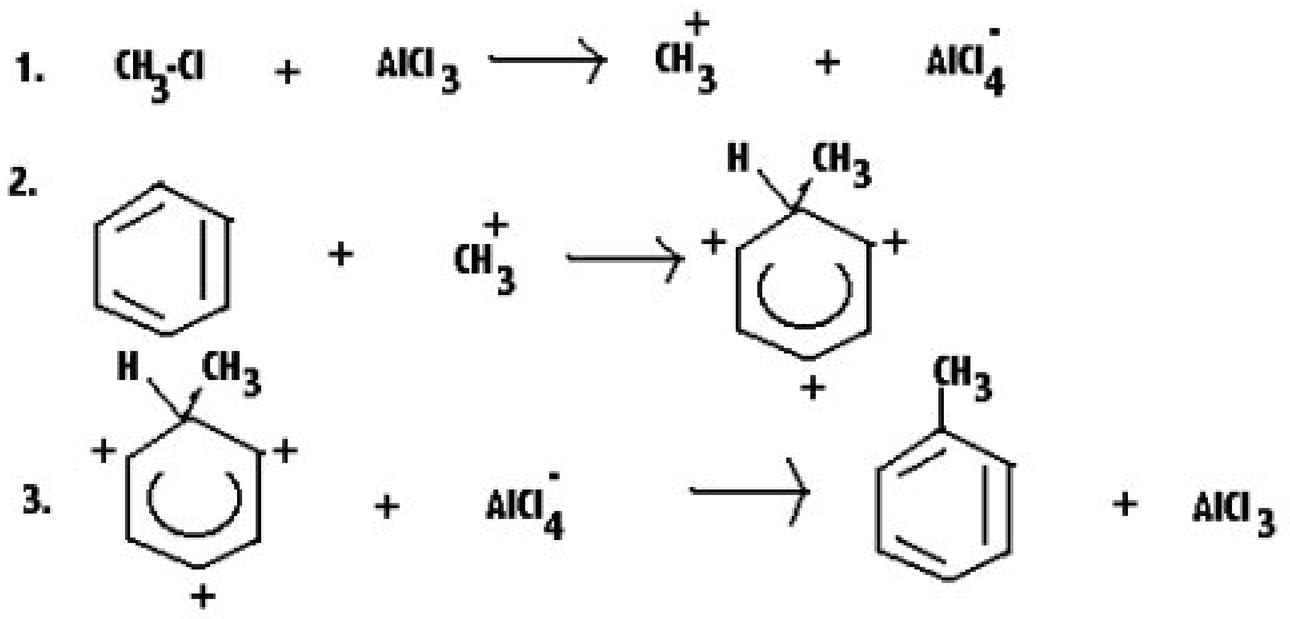
- It is an important reaction for preparation of benzene derivatives and allows an alkyl group to attach directly to benzene ring. $AlCl_3$ is used as catalyst and aromatic hydrocarbon is taken in excess (because aromatic compounds are highly volatile)



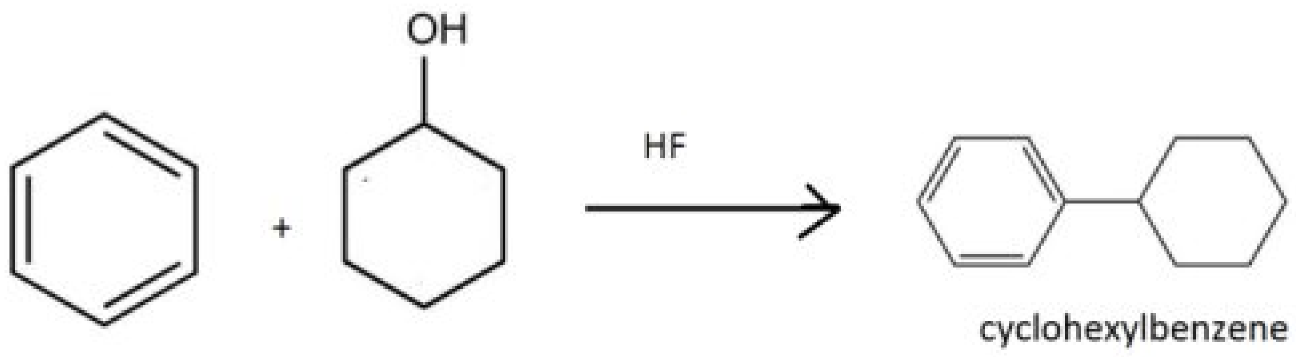
- No reaction would occur in case of nitrobenzene because it creates positive centers. Nitro group deactivatesnthe ring at ortho and para place for an alkyl group to attack.

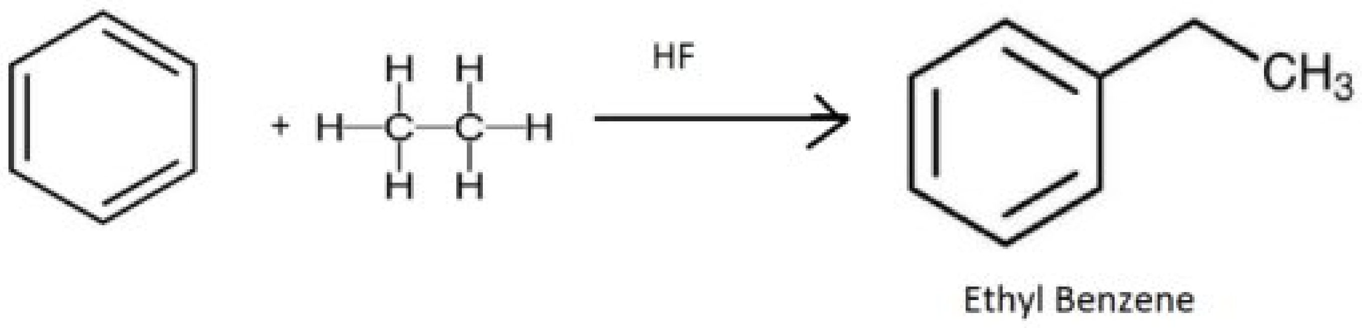
13.2 MECHANISM

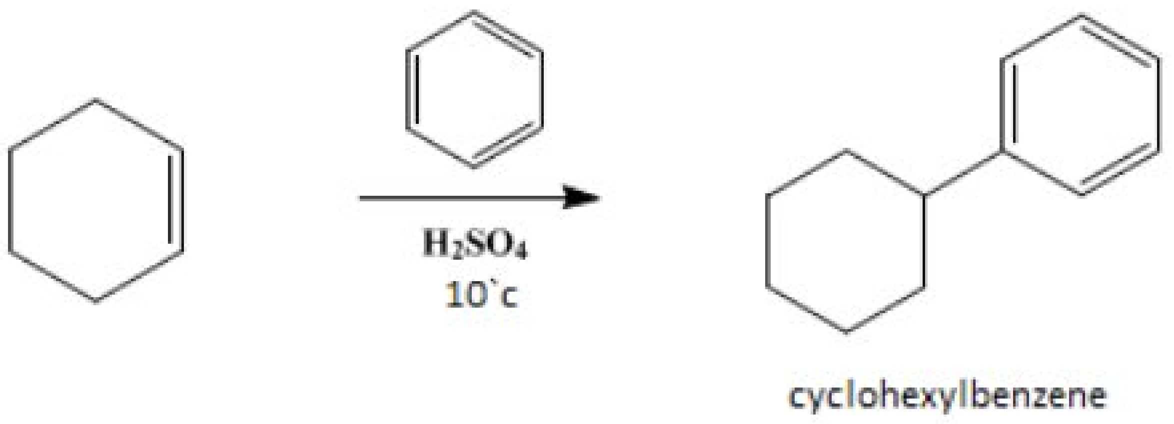
- It is an electrophilic substitution reaction. An alkyl group reacts with $AlCl_3$ to generate an electrophile which subsequently attacks benzene ring.



- Since positive specie attacks the aromatic ring, presence of electron withdrawing group such as nitro group, cyanide group on aromatic ring retards the rate of reaction. That is why nitrobenzene doesn't undergo alkylation.
- Certain electron donating group such as an NH_2 and OH^- also deactivate the ring toward electrophilic substitution reaction. These groups makes complex with the catalyst and diminish the electron density.
- The choice of alkylating agent is quite unique as protonated alcohols and alkenes also provide carbocations.







Chapter 14 METAL HYDRIDE REDUCTION

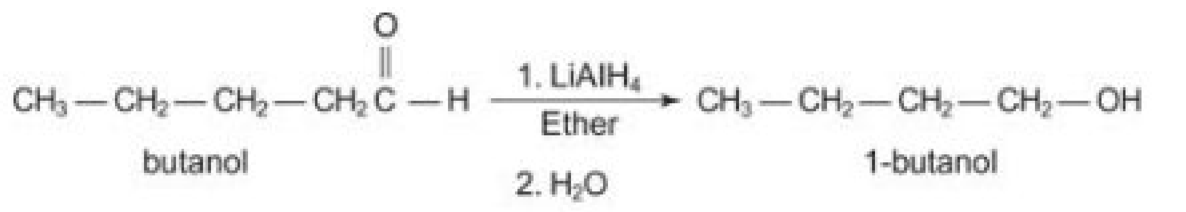
Hydride = hydrogen with a negative charge
Examples: $LiAlH_4$, $NaBH_4$, H_2/catalyst
We use H_2/catalyst whenever there is a degree of unsaturation e.g. in case of alkenes.

14.1 DEFINITION

- Metal hydrides such as $LiAlH_4$, $NaBH_4$, H_2/catalyst are used for reduction of carbonyl compounds and most of the other functional groups.

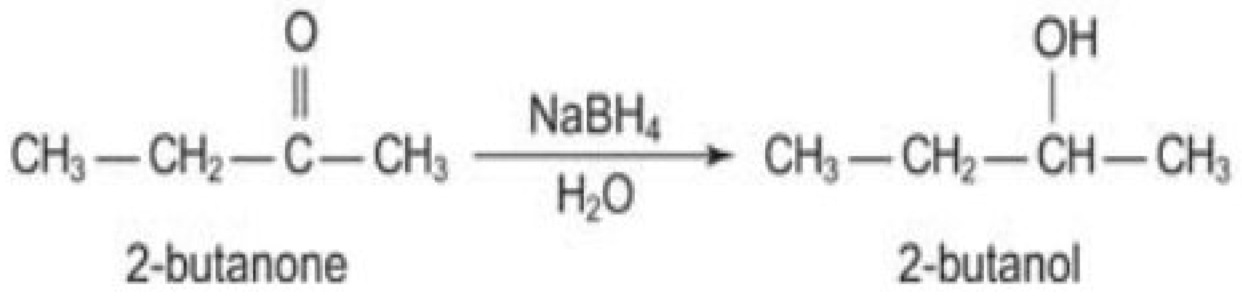
$$R\overset{O}{\overset{\|}{C}}OR' \xrightarrow[2.\ H_2O]{1.\ LiAlH_4,\ ether} RCH_2OH + R'OH$$

- If we take aldehydes, it converts into Primary Alcohol
- If we take ketones, it converts into Secondary Alcohol
- $LiAlH_4$ is sufficient to convert 4 moles of carbonyl groups. So catalyst is in excess.
- For the reaction of 4 moles of ketones 1 mole of $LiAlH_4$ is consumed.
- Carboxylic acids, esters and aldehydes after reduction with $LiAlH_4$ gives primary alcohol.

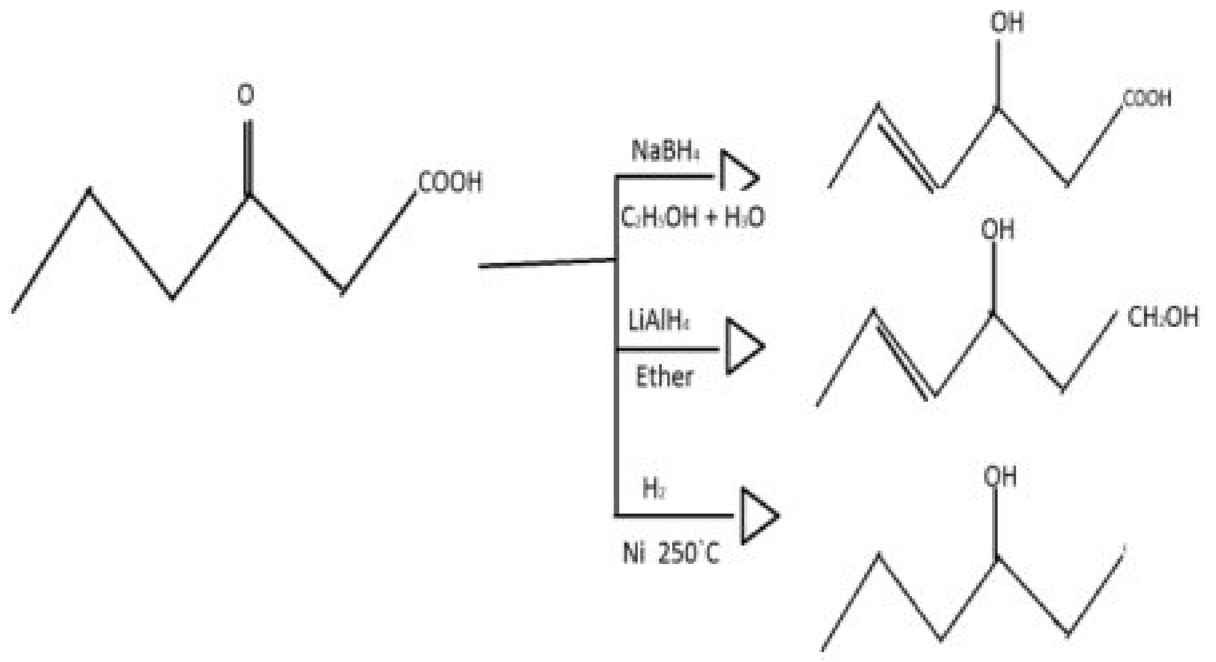


$$\underset{\text{butanol}}{CH_3-CH_2-CH_2-CH_2\overset{O}{\overset{\|}{C}}-H} \xrightarrow[2.\ H_2O]{1.\ LiAlH_4\ \text{Ether}} \underset{\text{1-butanol}}{CH_3-CH_2-CH_2-CH_2-OH}$$

- $NaBH_4$ reduces aldehyde and ketone to the corresponding without affecting other functional groups such as carboxylic, nitro, cyanide groups and esters.

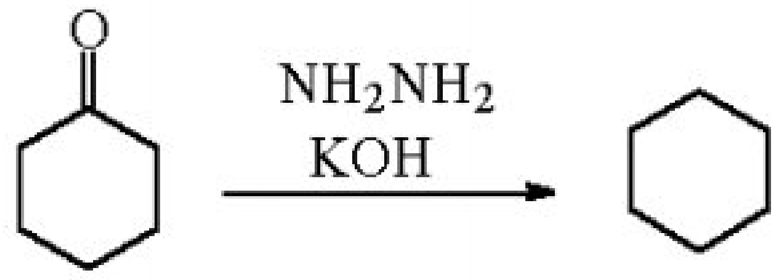


$$\underset{\text{2-butanone}}{CH_3-CH_2-\overset{O}{\overset{\|}{C}}-CH_3} \xrightarrow[H_2O]{NaBH_4} \underset{\text{2-butanol}}{CH_3-CH_2-\overset{OH}{\overset{|}{CH}}-CH_3}$$



Chapter 15 Wolf Kishner Reduction

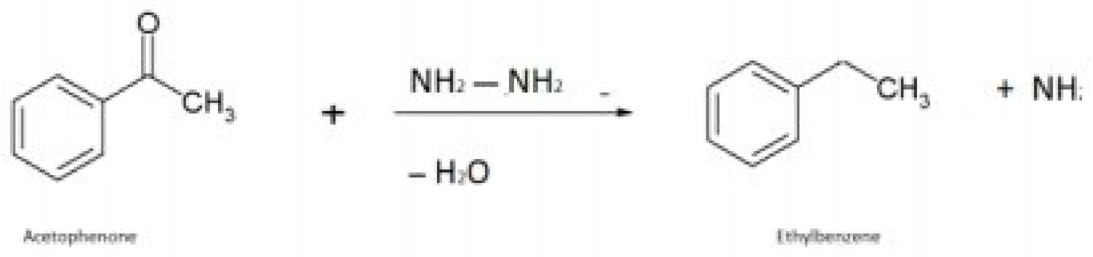
- ❖ Carbonly group getting changed into methylene
- ➢ So this is one type of rearrangement of Carbonyl group



- ➢ Here ketonic group is changed into normal alkane (Cyclo octanone to Cyclo octane)
- ➢ It is one of the process in which ketones are directly changed into alkane.
- ➢ Reduction of carbonyl group leads to alcohol but special methods can be used to convert it to methylene.

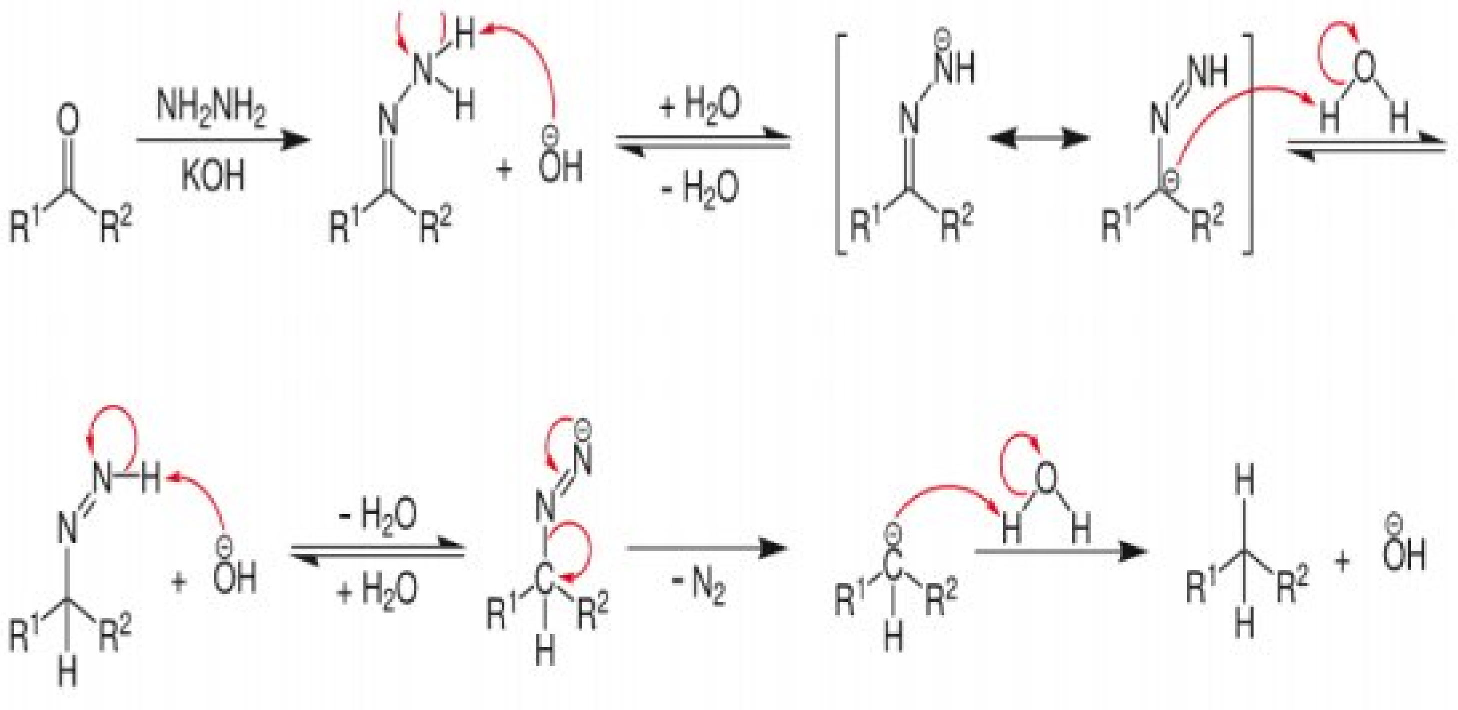
15.1 Definition

- ➢ When an aldehyde or ketone is heated with hydrazine and a strong base (in presence of diethylene glycol as solvent) the carbonyl group is reduced to methylene group. It is called as Wolf Kishner Reduction.
- ➢ This reaction is useful for direct conversion of carbonyl to methylene to bypass several intermediates.



15.2 Mechanism

- ➢ The process consist of conversion of ketone to hydrazoneon treatment with hydrazine and intermediate is being formed which picks up proton from the solvent and nitrogen is being eliminated to form the finalized product i.e. methylene/alkane (reduced product).



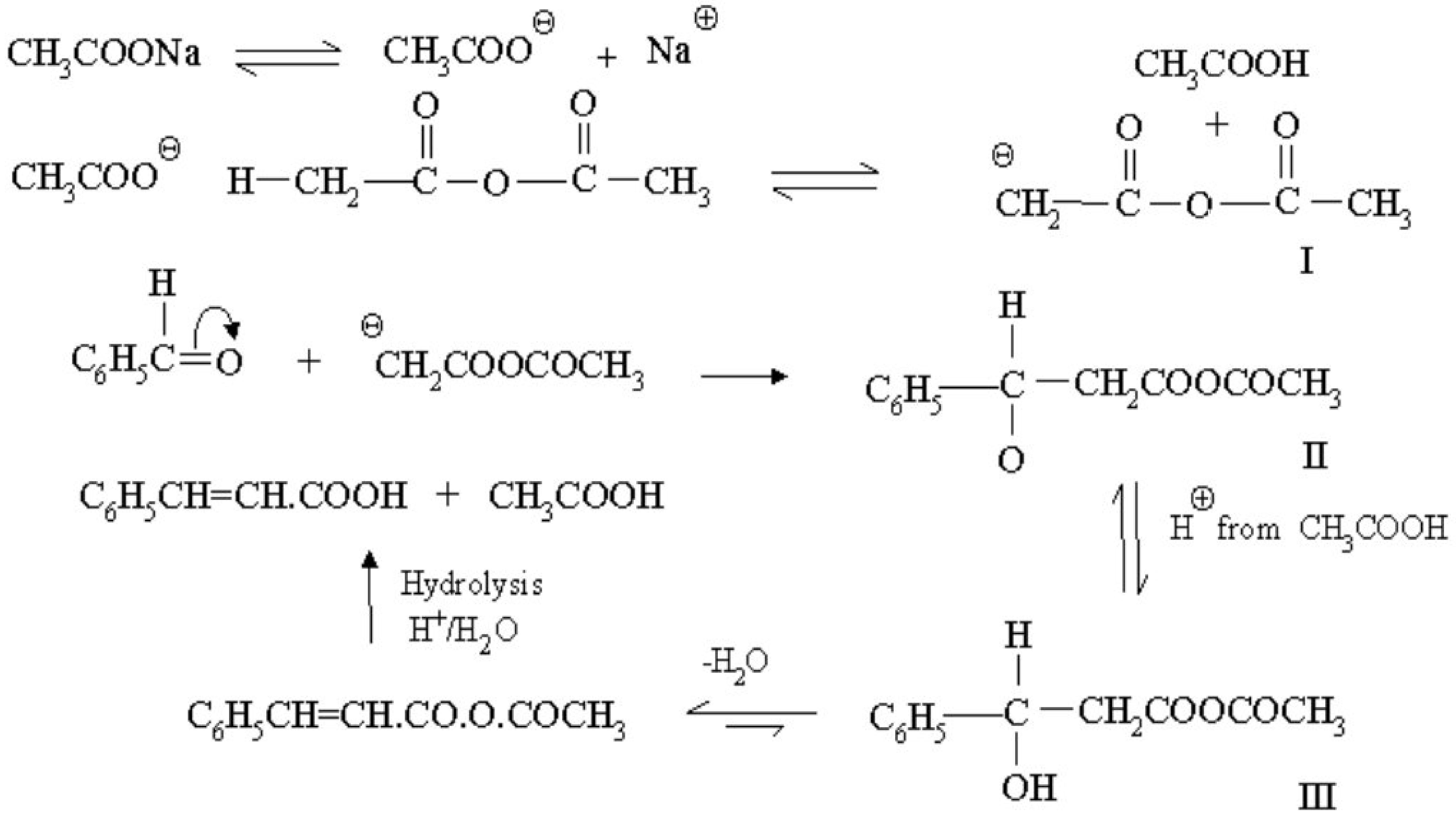
Chapter 16 PERKIN CONDENSATION

- Perkin condensation is the condensation of an aromatic aldehyde and acetic anhydride producing α-β unsaturated product.
- E.g. Benzaldehyde reacts with acetic anhydride in presence of sodium acetate at 180 °C to form Cinnamic Acid.

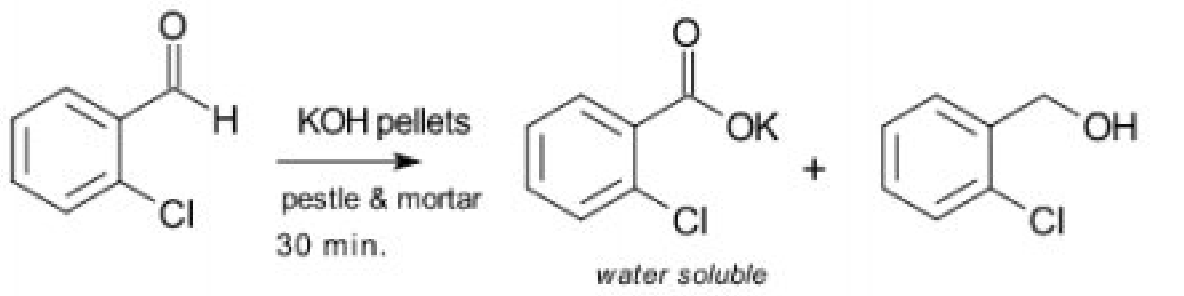
$$C_6H_5CHO + (CH_3CO)_2O \xrightarrow[170-175^0C]{CH_3COONa} C_6H_5CH{=}CHCOOH$$

16.1 MECHANISM

The Perkin reaction consists of following steps:



Chapter 17 CANNIZARO REACTION

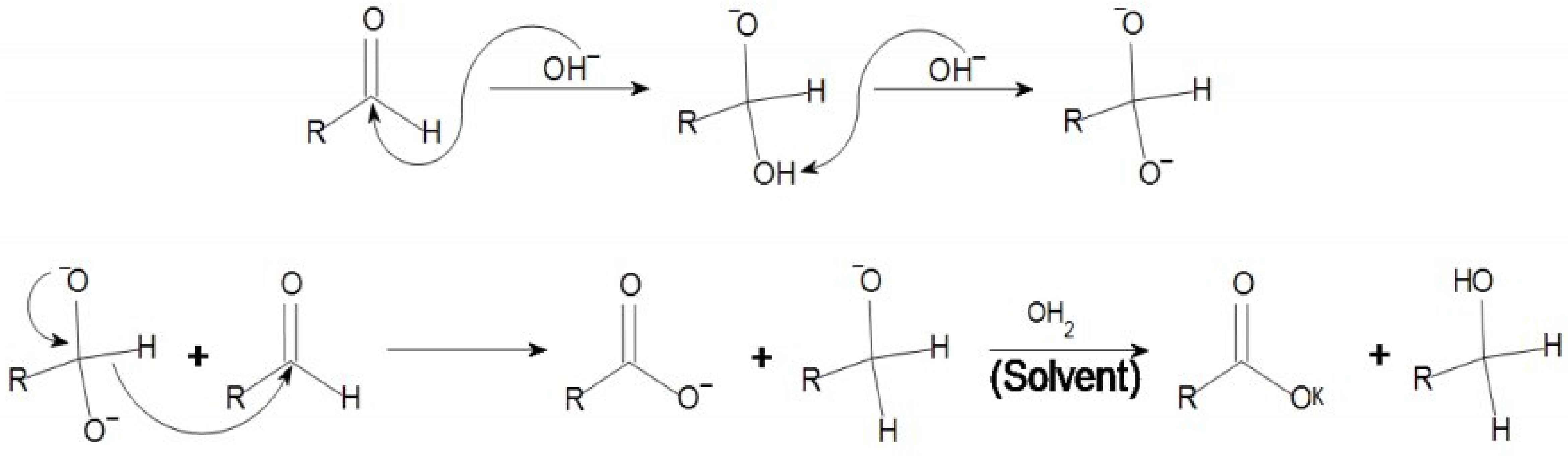


17.1 DEFINITION

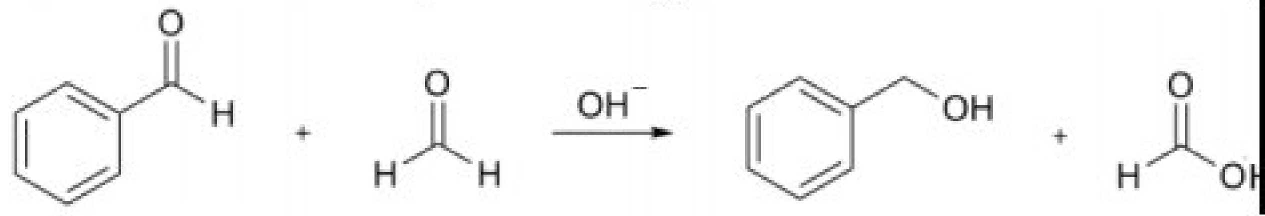
- An aliphatic or aromatic aldehyde possessing no α-hydrogen when treated with conc.soln of a base undergoes an oxidation reduction reaction referred as Canizarro's reaction where one molecule is reduced to alcohol while other is oxidized to carboxylic acid.

17.2 MECHANISM

- OH^- ions make nucleophilic attack at carbonyl carbon atom in the first step forming oxyanion which loses a hydride ion i.e. transferred intermolecular to another aldehyde. This slow step is very difficult and does not make good synthetic product.

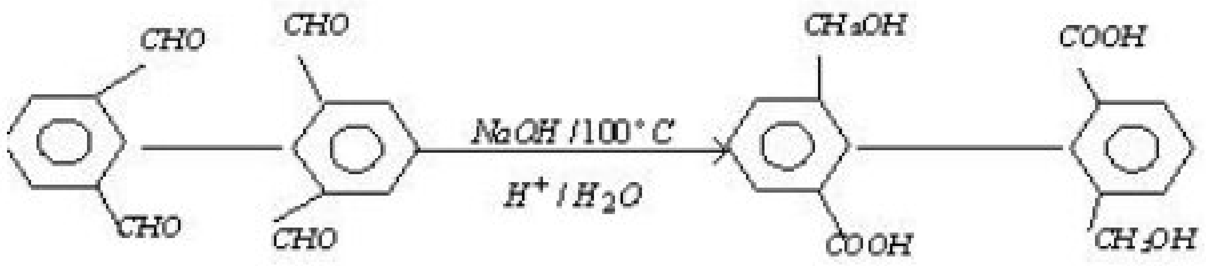


- Acetaldehyde and Ketones do not undergo this reaction because both have α-hydrogen. When a benzaldehyde is treated with formaldehyde in aqueous base, formaldehyde undergoes oxidation.



[redacted]

- This is known as cross canizarro's reaction and formaldehyde reacts as reducing agent.



Chapter 18 ORGANOMETALLIC COMPOUND

18.1 DEFINITION

- Organometallic compounds are those in which a metal atom is linked directly to an organic compound.

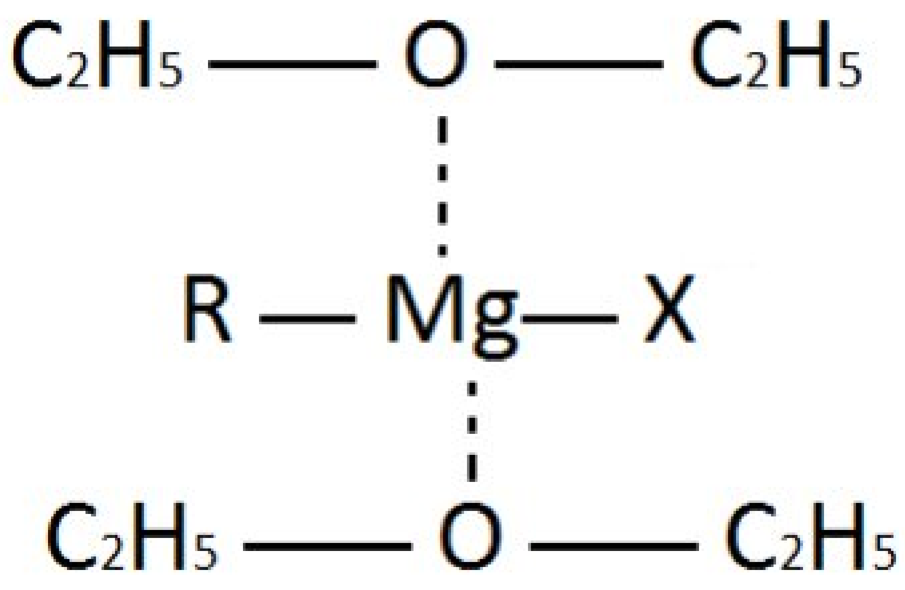
18.2 EXPLANATION

- They have a high degree of Ionic character because metals are electropositive in nature.

  e.g. CH_3Li , $(CH_3)_3Al$, $(CH_3CH_2)_2$, $(CH_3CH_2)Zn$, $(C_6H_5)_3CNa$
- Organometallic compounds with a general formula R^--Mg^+-X are known as "Grignard Reagent" after the scientist Grignard, a noble prize winner in chemistry.

$$R{-}X + Mg \xrightarrow{\text{Dry Ether}} \overset{\delta-}{R}-\overset{\delta+}{Mg}-\overset{\delta-}{X}$$

- The reaction is carried out by heating Mg turnings with an organic halide in dry ether with exclusion of moisture.
- Ethyl ether is most frequently used solvent. Other solvents such as diethyl glycol or tetrahydro furan can be used. Small amount of Iodine or ethylene bromide is added to initiate the reaction.
- X-ray diffraction analysis has shown that two ether molecules are attached with Grignard Reagent



Reaction with Hydrogen Free Compound/ Compound having active H⁺

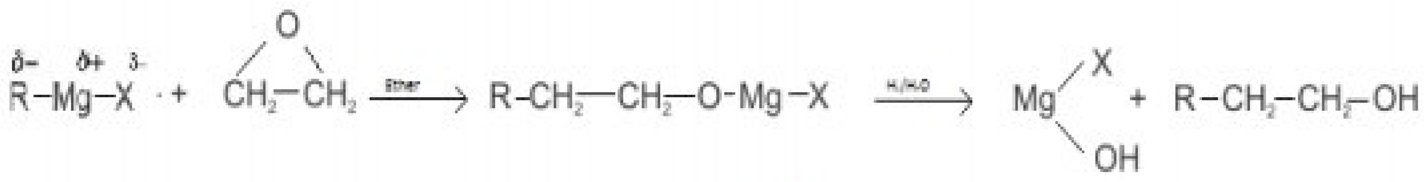
$$\overset{\delta-}{R}-\overset{\delta+}{Mg}-\overset{\delta-}{X} + H{-}OH \xrightarrow{Ether} R{-}H + Mg(OH)X$$

$$\overset{\delta-}{R}-\overset{\delta+}{Mg}-\overset{\delta-}{X} + C_2H_5OH \xrightarrow{Ether} R{-}H + Mg(OC_2H_5)X$$

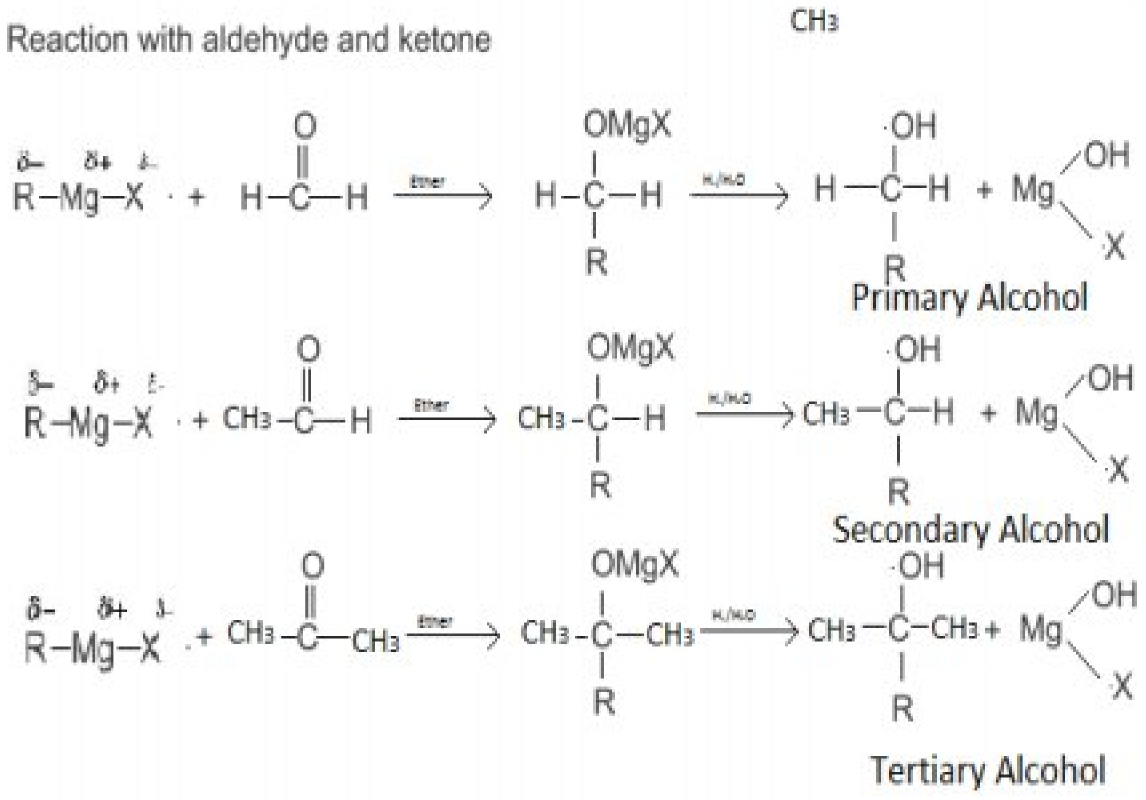
Reaction with Alkyl Halide

$$R{-}X + \overset{\delta-}{R}-\overset{\delta+}{Mg}-\overset{\delta-}{X} \xrightarrow{Ether} MgX_2 + R{-}R$$

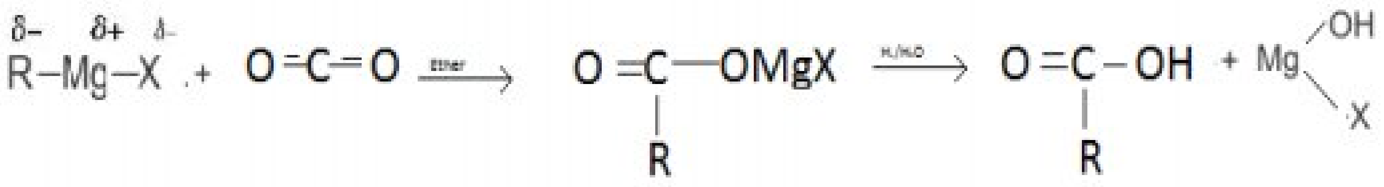
Reaction with ethylene oxide



Reaction with aldehyde and ketone

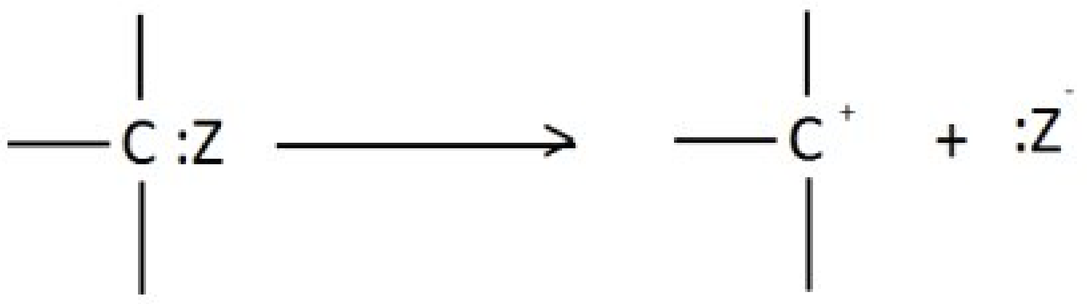


Reaction with carbon dioxide



Chapter 19 CARBONIUM IONS

- Organic ions with a positively charge carbon atom are called carbocation or carbonium ions, they are formed by heterolytic fission.



$$-\overset{|}{\underset{|}{C}}:Z \longrightarrow -\overset{|}{\underset{|}{C}}^{+} + :Z^{-}$$

- Where Z is more electronegative than carbon
- Carbonium ions are named after parent alkyl group and adding the word carbonium ion.

$CH_3—CH_2^{+}$

Ethyl carbonium ion

$\overset{+}{CH_3}$

Methyl carbonium Ion

- The positively charged carbonium atom in carbonium ion uses sp2 hybridization for hybridizing orbitals. 1 empty p orbital extent to above or below the plane of sigma bond. This carbonium ion can combine with any substance which can donate a pair of electron.

19.1 CARBONIUM ION REARRANGEMENT

- Migration of alkyl, eryl or hydrogen atom along with its electron towards the positive center is called carbonium ion rearrangement. It is of two types

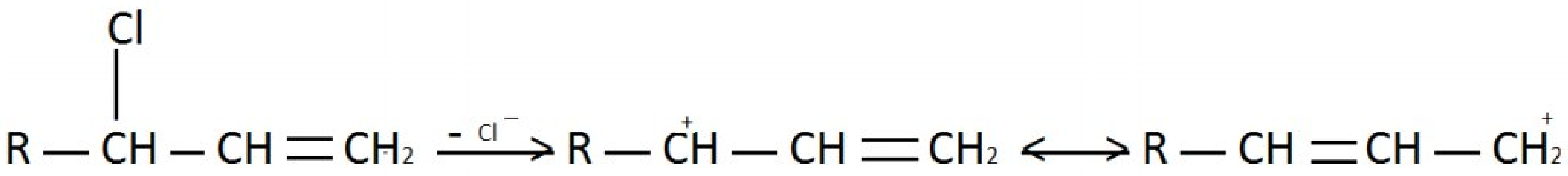
19.1.1 WITHOUT CHANGE IN CARBON SKELETON

A Proton is being shifted

$$CH_3—CH_2—\overset{+}{CH_2} \longleftrightarrow CH_3—\overset{+}{CH}—CH_3$$

1- propyl carbonium ion 2- propyl carbonium ion

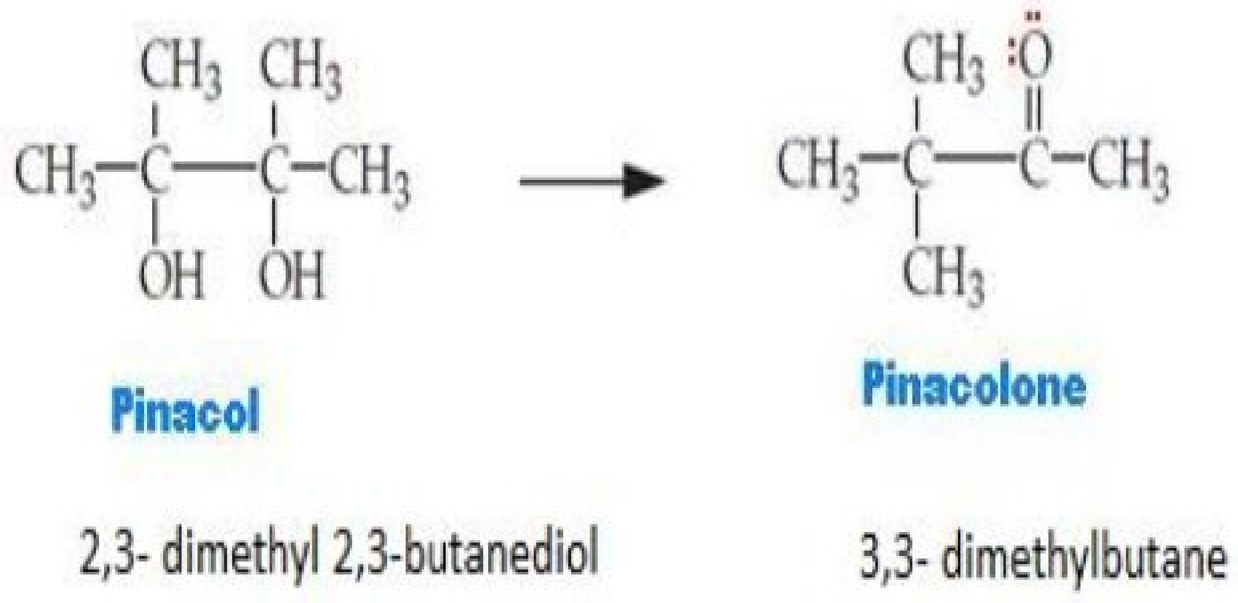
A pair of electron is being shifted



$$R—\overset{Cl}{\overset{|}{CH}}—CH=CH_2 \xrightarrow{-Cl^{-}} R—\overset{+}{CH}—CH=CH_2 \longleftrightarrow R—CH=CH—\overset{+}{CH_2}$$

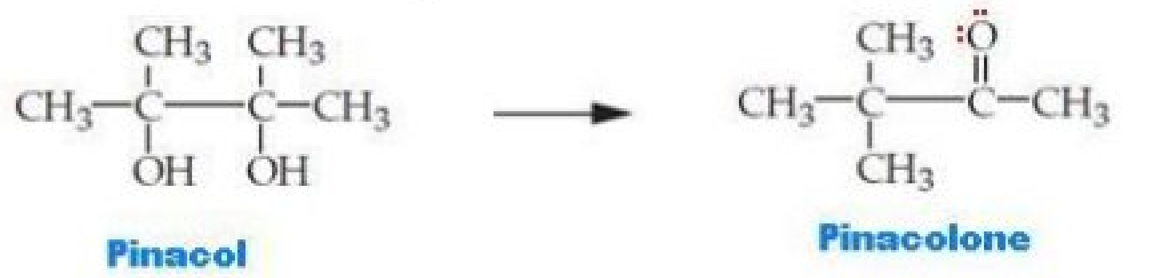
19.1.2 WITH CHANGE IN CARBON SKELETON

Pinacol- Pinacolone Rearrangement is an example of with change in carbon skeleton.



Chapter 20 PINACOL-PINACOLONE REARRANGEMENT

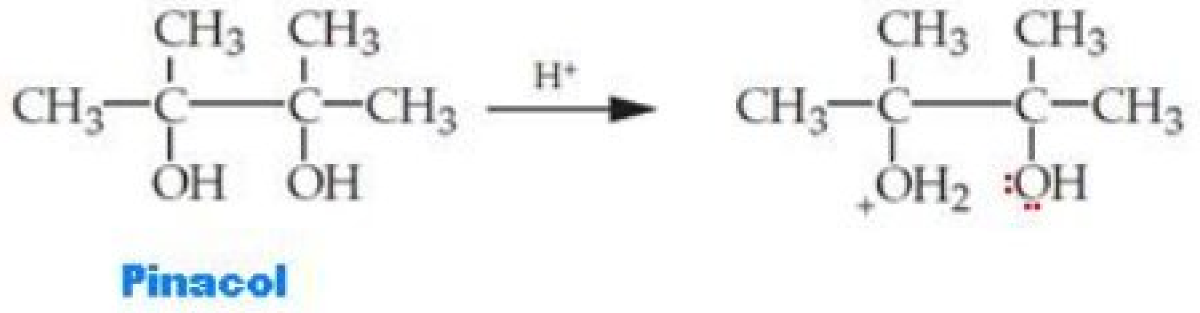
Completely substituted 2-3 dimethyl 2-3 butane diols are called pinacols, on treatment with mineral acid (HCl) they undergo dehydration and rearrangement to form ketones and this reaction is called pinacole pinacolone rearrangement.



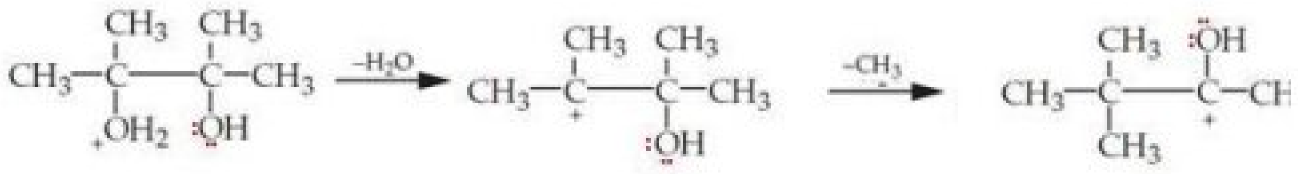
2,3- dimethyl 2,3-butanediol   3,3- dimethylbutane

20.1 MECHANISM

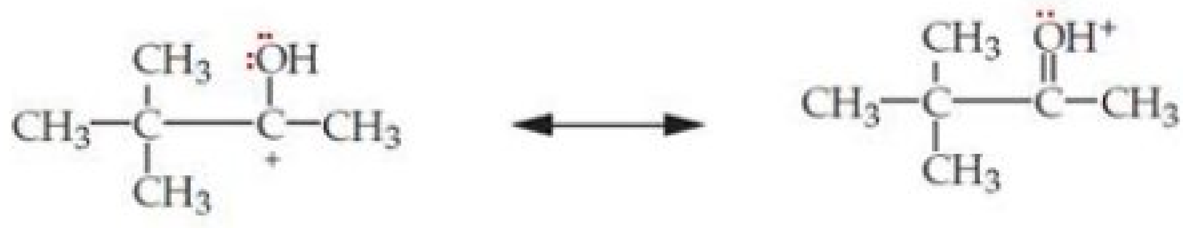
20.1.1 PROTONATION OF DIOLE



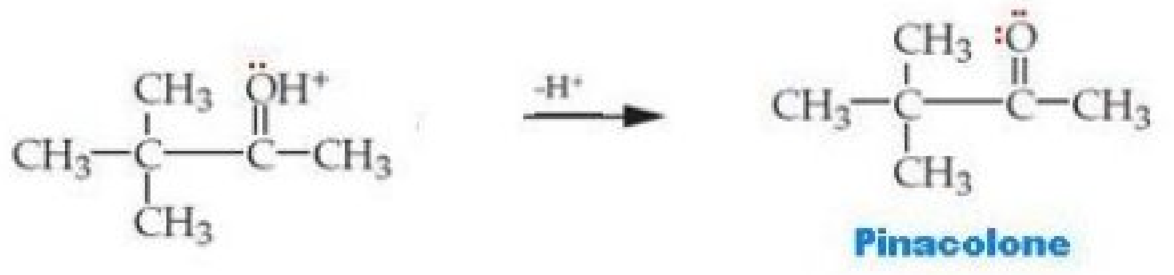
20.1.2 DEHYDRATION AND FORMATION OF CARBONIUM ION



20.1.3 REARRANGEMENT OF CARBONIUM ION

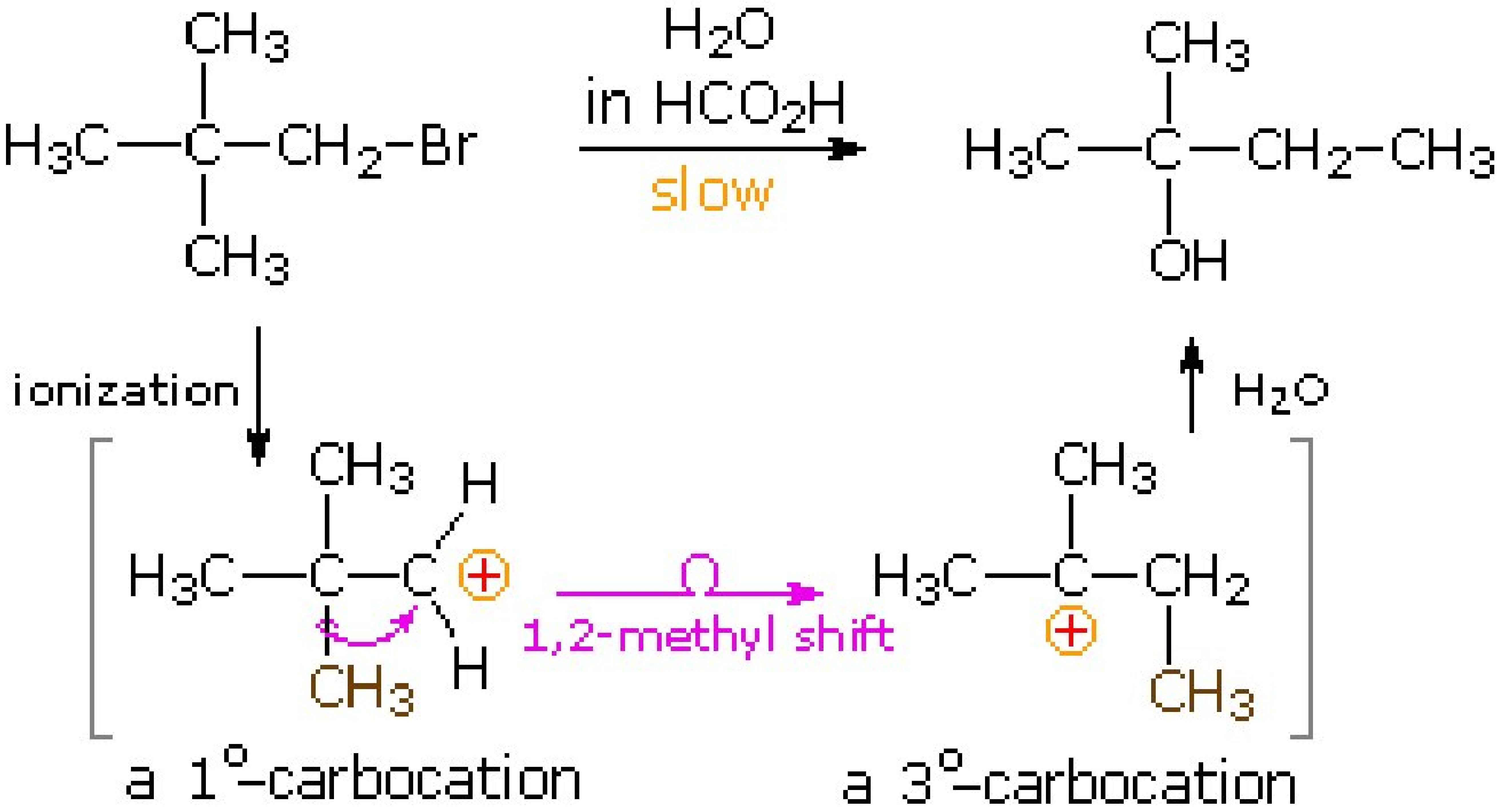


20.1.4 FORMATION OF KETONE



Chapter 21 WAGER-MERWEIN REARRANGEMENT

- **Neopentyl Rearrangement**
- This arrangement is a class of carbocation rearrangement in which hydrogen, alkyl or aryl migrates from one carbon to the neighboring to produce more stable products. This rearrangement was first discovered in bicyclic terpenes present in Camphor. Currently they are used in skeletal rearrangement of certain medicinal compounds

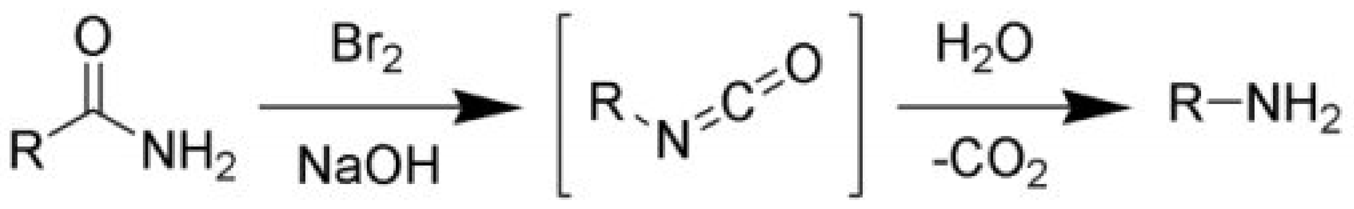


Chapter 22 HOFFMAN'S REARRANGEMENT

- ❖ A process in which amide is converted to amine
- ➢ As amide is converted to amine so it is one of the reductive processes.
- ➢ If hydrogen of ammonia is replaced by such specie which is electron deficient, is called "Amide"
  e.g. $NaNH_2$ (Soda Amide)
- ➢ $R\text{-}NH_2$
  "R" is electron donating specie. So amine is one in which hydrogen is replaced by a nucleophile (electron donating group)

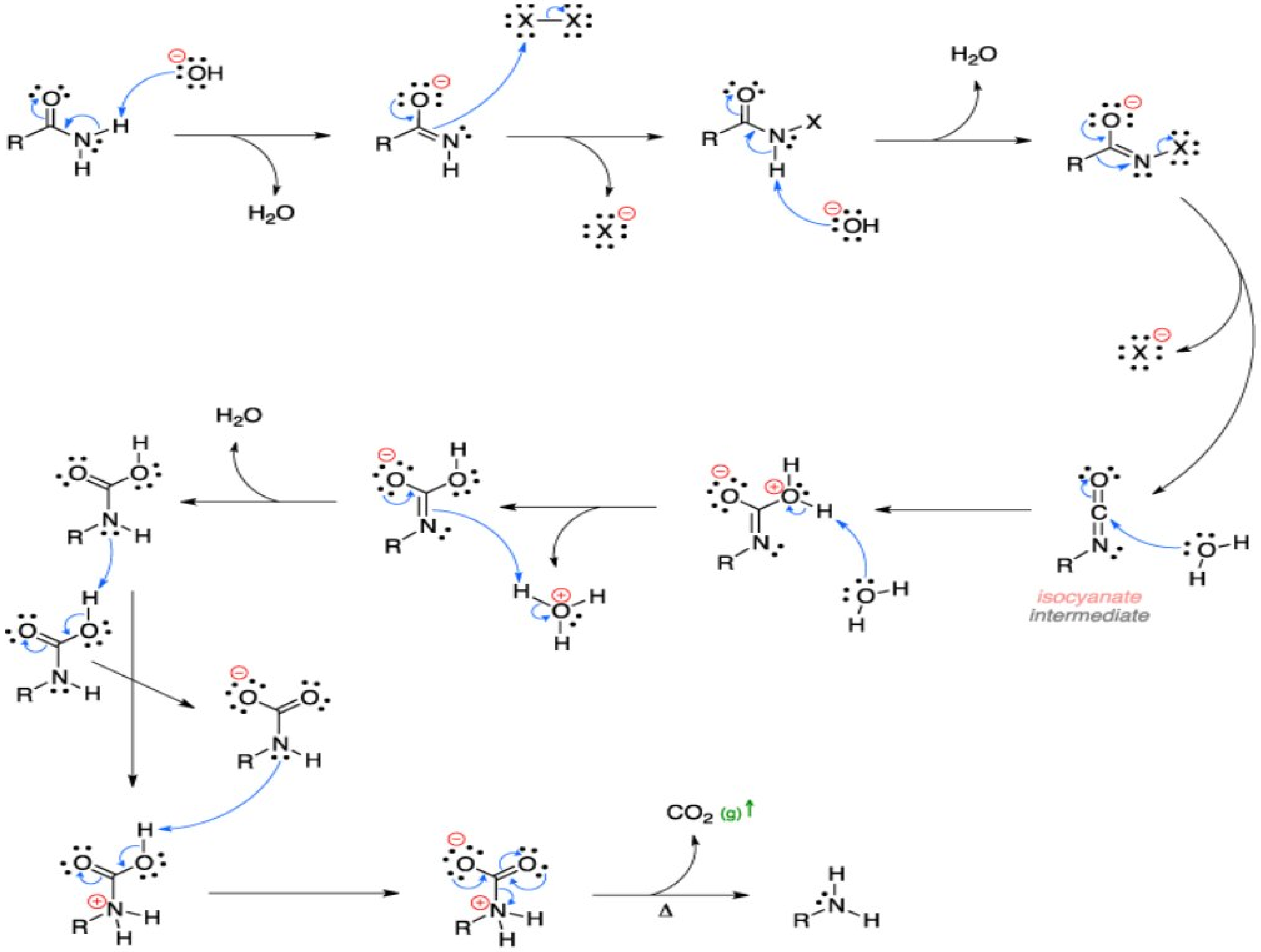
22.1 DEFINITION

A primary amide on treatment with Bromine in presence of an aqueous base undergoes rearrangement to form amine. This reaction is called Hoffman's Rearrangement or Hoffman's hypo bromide reaction.



22.2 MECHANISM

First two steps are base catalyzed for bromination of Amide than this base catalyzed product is stabilized by Resonance and forms stable product.



- ➢ Resulting Amine has 1 carbon less than starting Amide and lowest number of Amide which can give this reaction is "Acetamide".

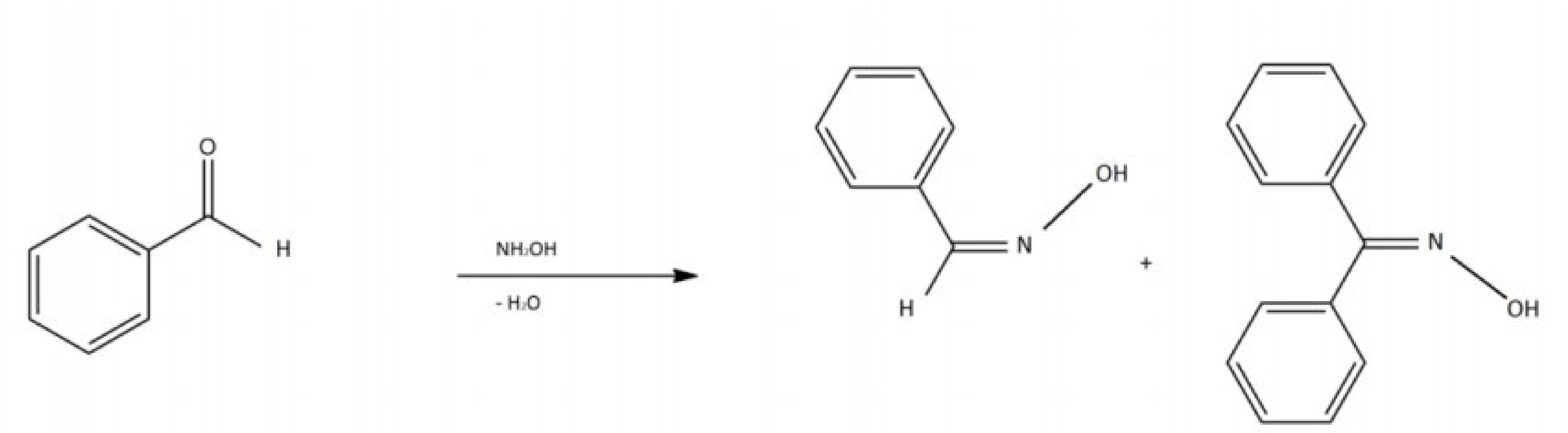
And MIC is deadly poisonous because of high solubility in lipids.

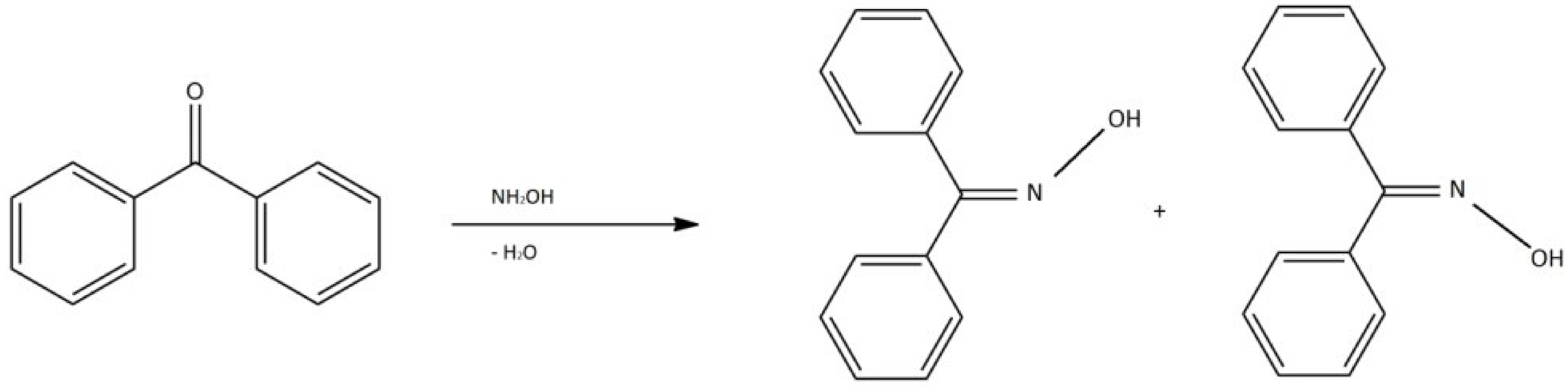
Chapter 23 Beckmann Rearrangement

- This process is important in metabolism/anabolism of Proteins. Ultimately some amides/artificial amino acids/proteins are produced that are required by the body and in TPN.
- If oxygen of carbonyl group is replaced by hydroxyl amine, it is called "oxime"
- Ketones and hydroxyl amines combine to form oxyme.
- By rearrangement we convert oxime to Amides.
- If double bond is not there, molecule may rotate but in this case double bond cannot rotate. They may form 2 types of Configuration.

  1) Cis or Syn
  2) Trans or Anti

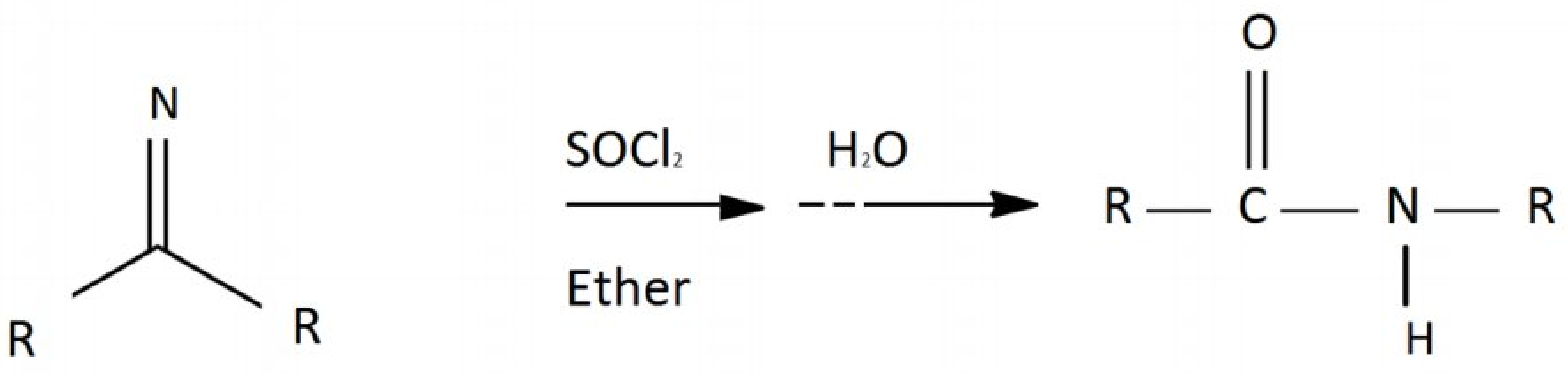
  - two heavy groups on the same side or the two light groups on the same side = Cis
  - if two heavy groups on opposite sides or two light groups on opposite sides = Trans
- Aldehydes and Ketones react with hydroxyl amine to form aldo-oxyme or keto-oxyme. Since there is no
- free rotation around C=N so two geometric forms are possible.



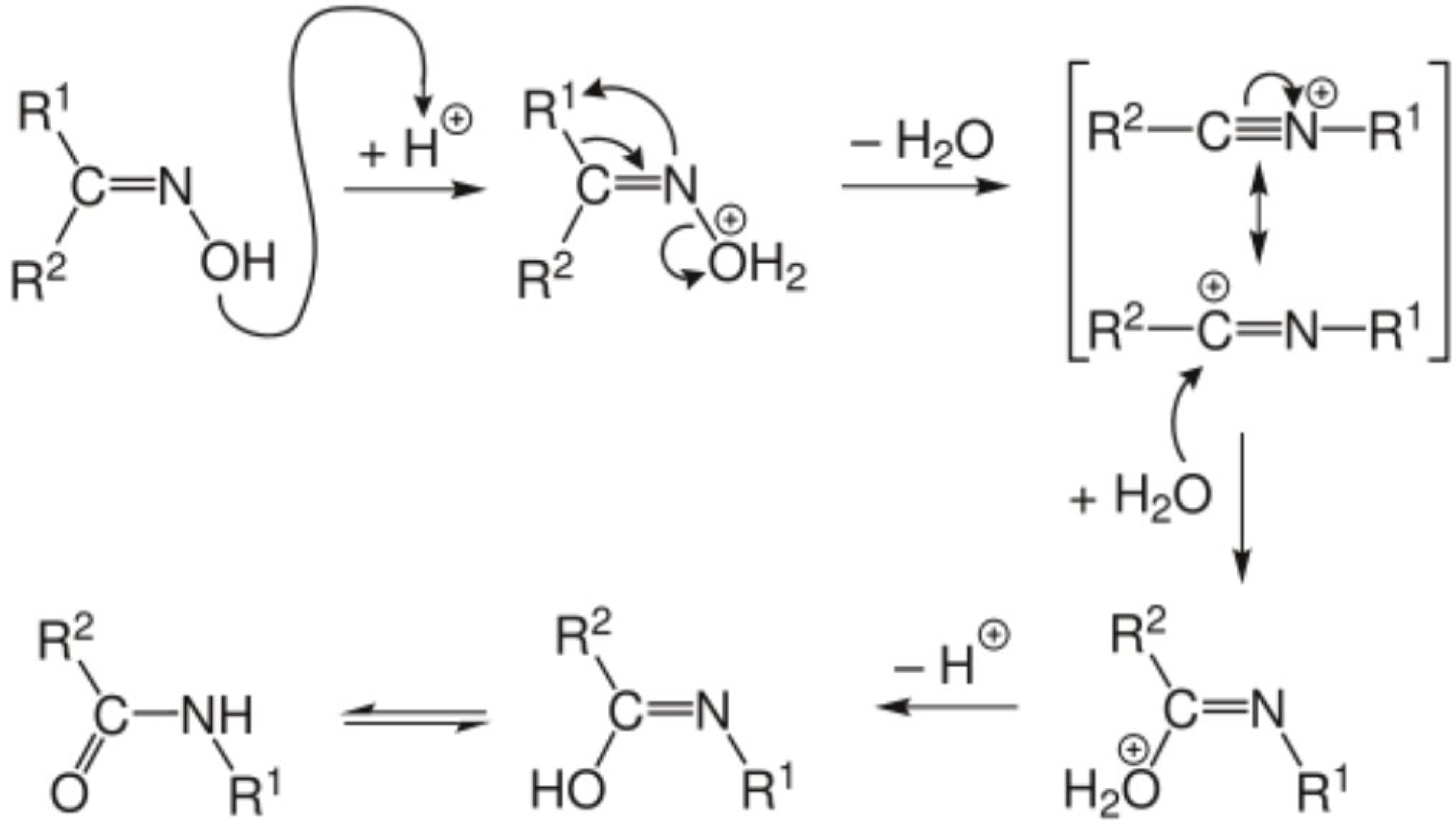


DEFINITION

- The keto oxyme are transferred into substituted amides on treatment with strong acid (H_2SO_4 , PCl_5 , $SOCl_2$). This reaction is known as Beckmann's Rearrangement.



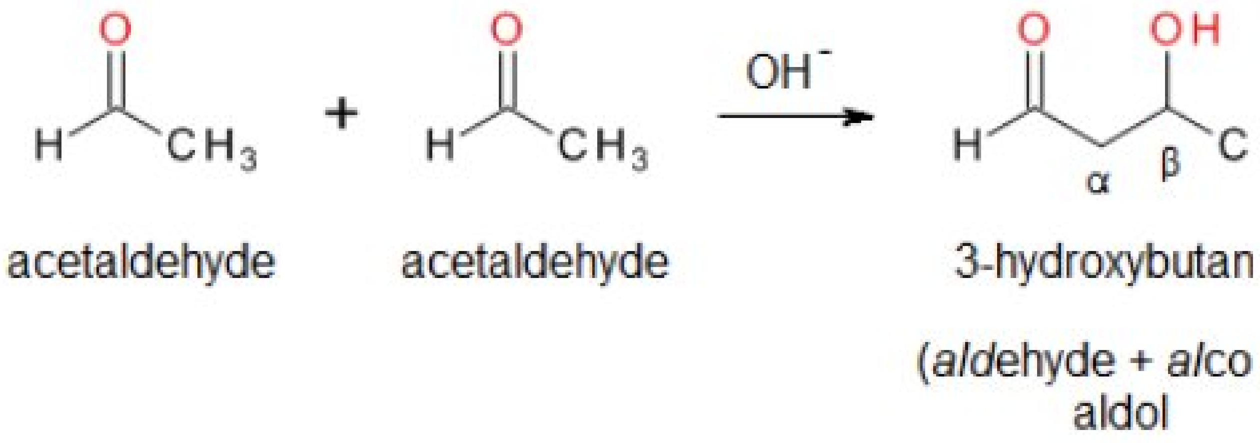
MECHANISM


+ H⊕
− H₂O
+ H₂O
− H⊕

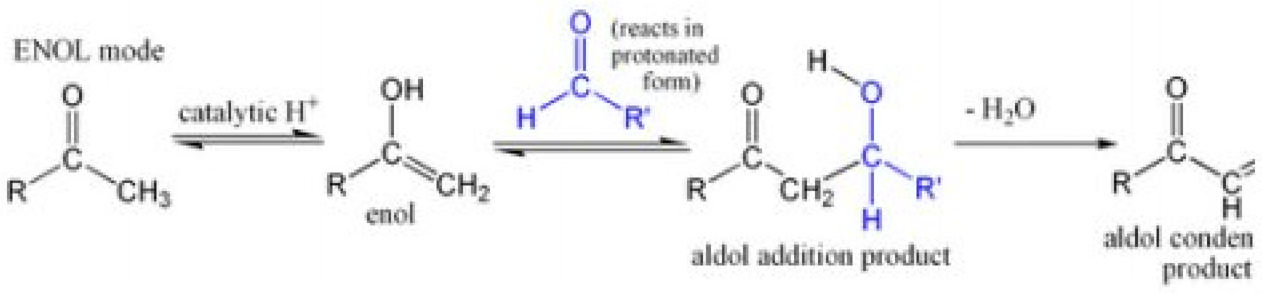
Chapter 24 ALDOL CONDENSATION

24.1 DEFINITION

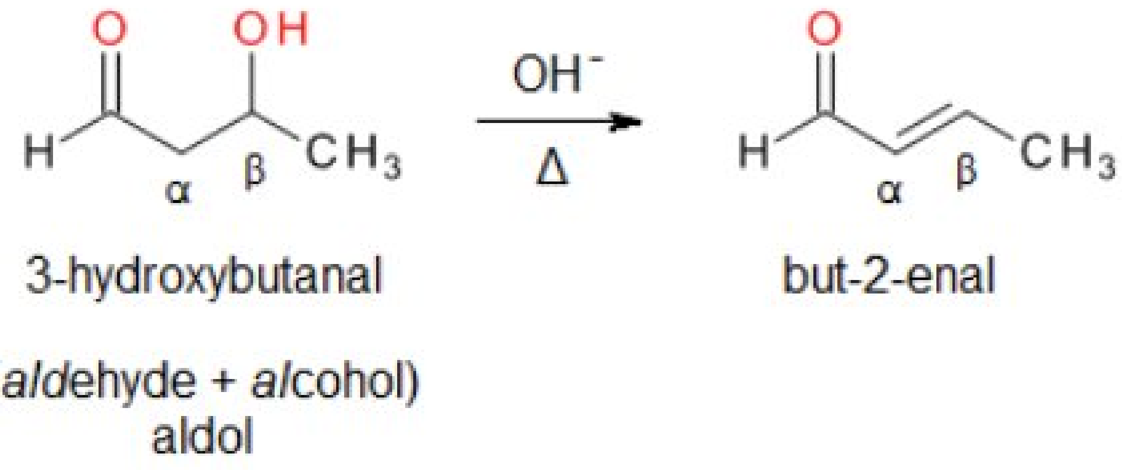
- Aldehyde containing alpha-hydrogen (hydrogen attach to alpha carbon) undergoes addition in the presence of base to form product called aldol and the reaction is called aldol condensation.



24.2 MECHANISM

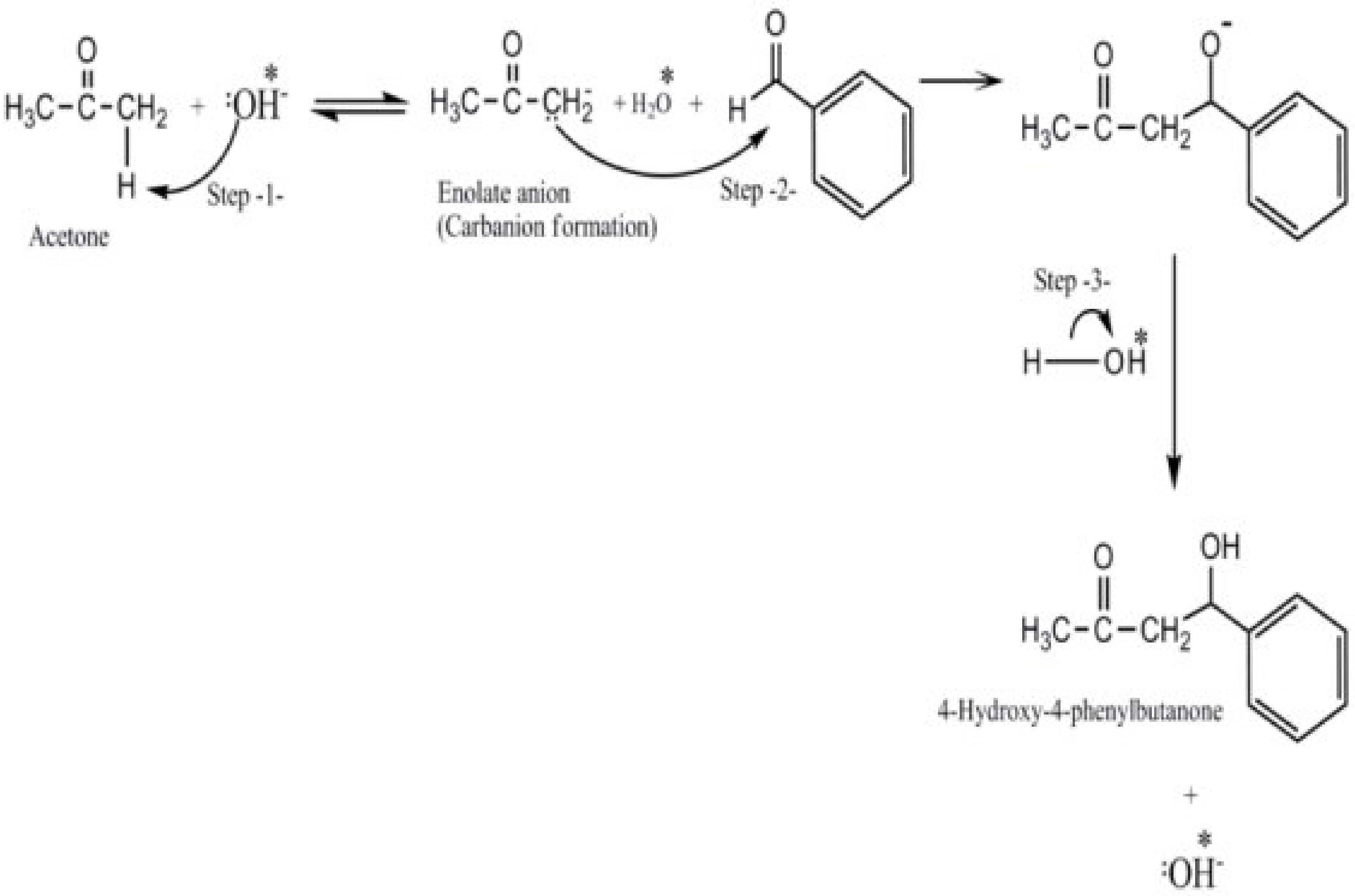


24.3 DEHYDRATION



24.4 CROSS OR MIX ALDOL CONDENSATION

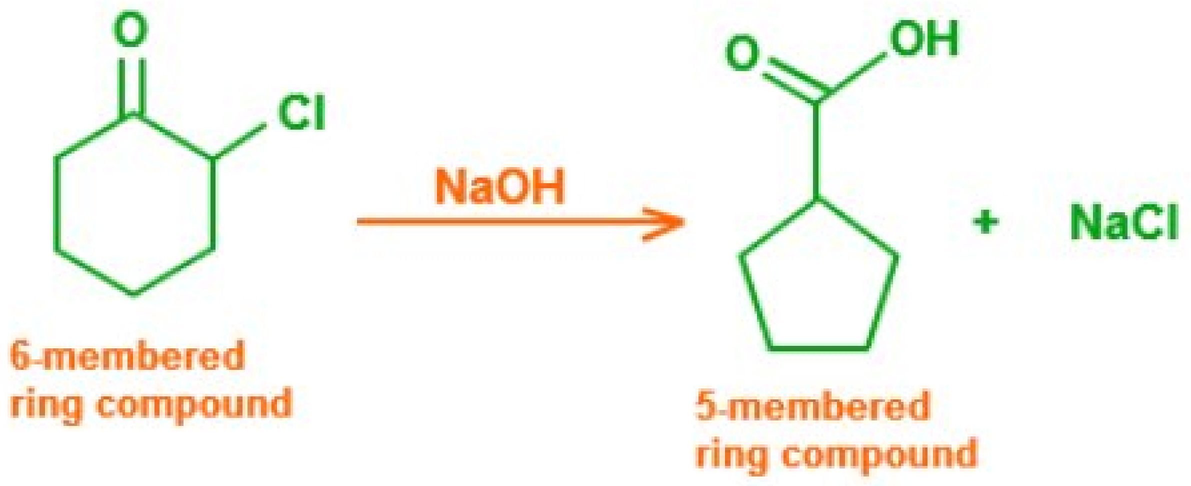
- An aldol condensation between two different aldehyde containing at least one alpha hydrogen is called cross or mix condensation.



Chapter 25 Favorskii Rearrangement

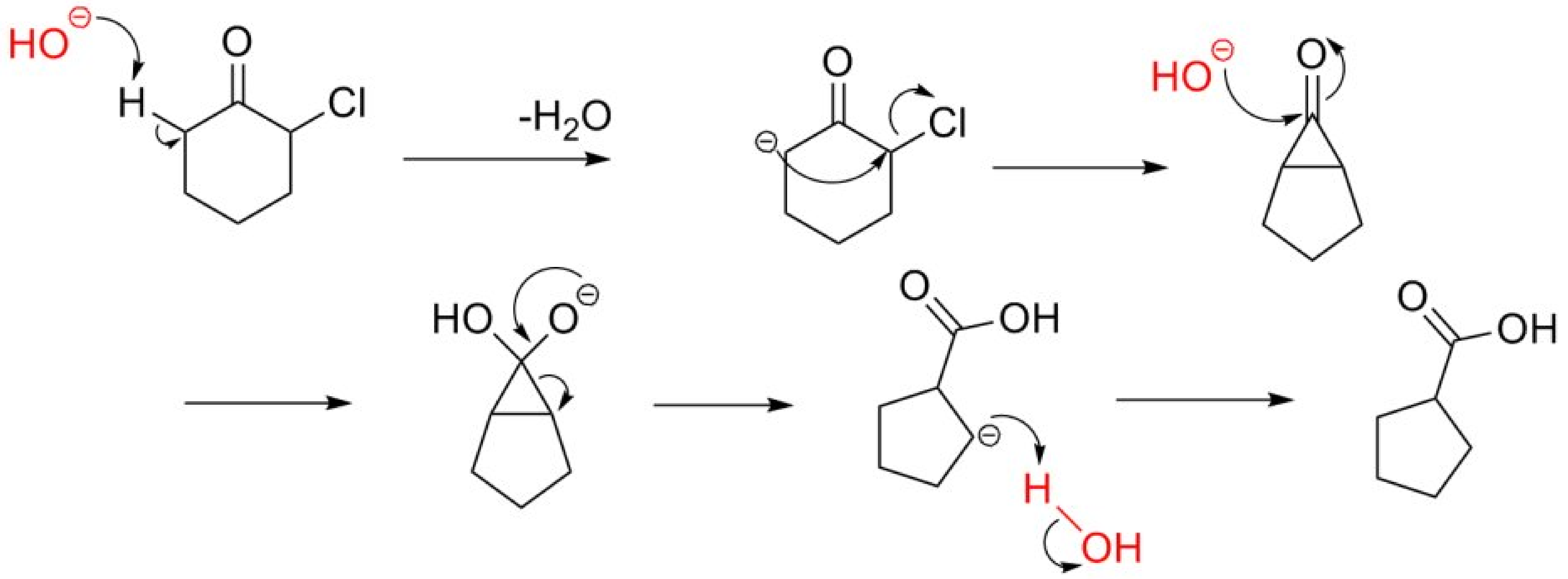
25.1 DEFINITION

- The Favorskii rearrangement is principally the rearrangement of cyclopropanone and α-haloketones which leads to the carboxylic acid derivatives. This rearrangement takes place in presence of a base to yield carboxylic acid.



25.2 MECHANISM

- The reaction is thought to involve the formation of an enolate on the side of ketone away from chlorine atom. This enolate cyclizes to cyclopropanone intermediate which is then, attacked by a nucleophile.



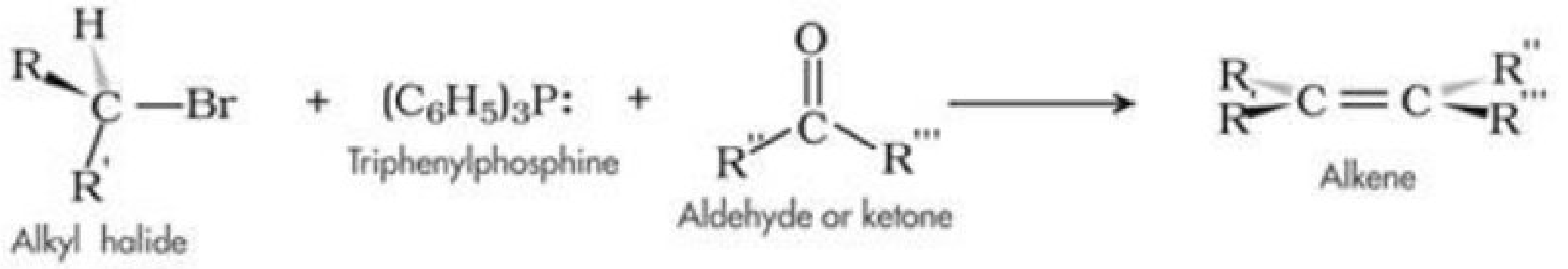
- This rearrangement leads to the ring contraction; cyclopropanone intermediate is symmetrical in nature, so that product is same whatever bond breaks after nucleophile attacks.

Chapter 26 WITTING REACTION

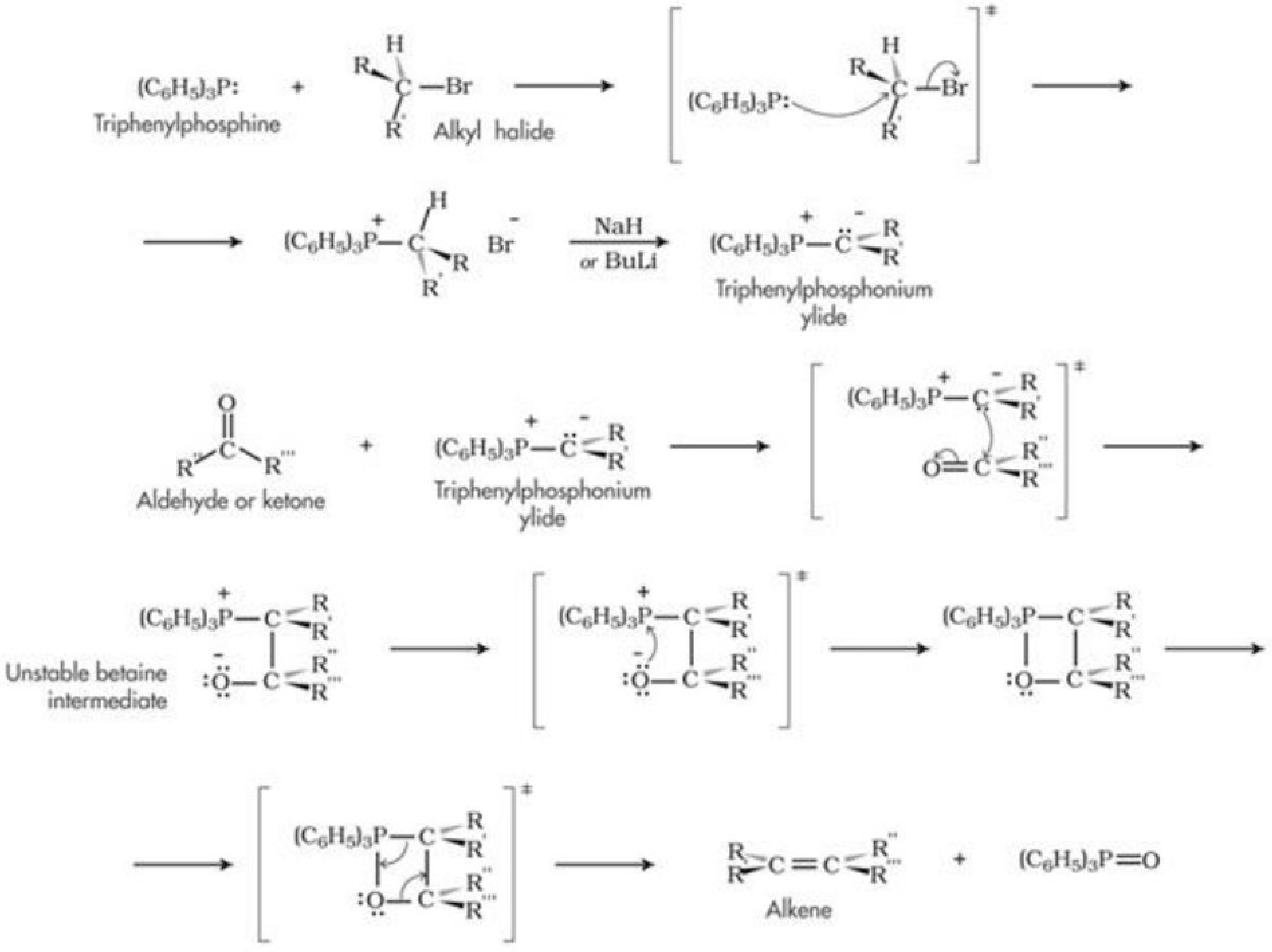
- An important method for preparing alkenes from aldehyde and ketones

26.1 DEFINITION

- Trialkyl and Triphenyl phosphorous compounds (phosphines) can be alkylated to undergo the said reaction.
  A ylid is a strong nucleophile and can be condensed with an aldehyde or ketone with the resultant formation of alkene. The reaction thus provides a versatile means for synthesis of alkenes as in given example.



Mechanism



Chapter 27 STEREOCHEMISTRY

27.1 ISOMERS

The molecules having same molecular formula but different structural formula are called isomers.

27.2 ISOMERISM

The molecules having same molecular formula but different structural formula are called isomers, and This phenomenon is called isomerism.

There are two types of isomerism

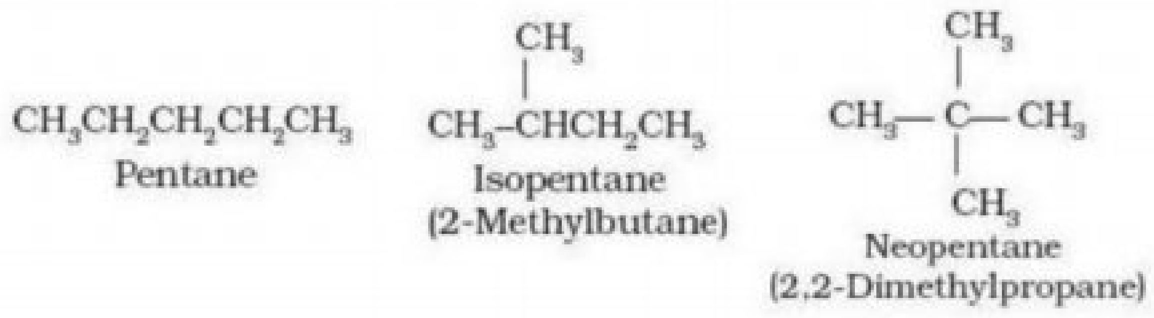
1. Structural or Constitutional isomerism
2. Stereoisomerism

27.3 STRUCTURAL ISOMERISM

When isomerism is due to difference in arrangement of atoms within the molecule without any reference to space; the phenomena is called structural isomerism. It is of 5 types:

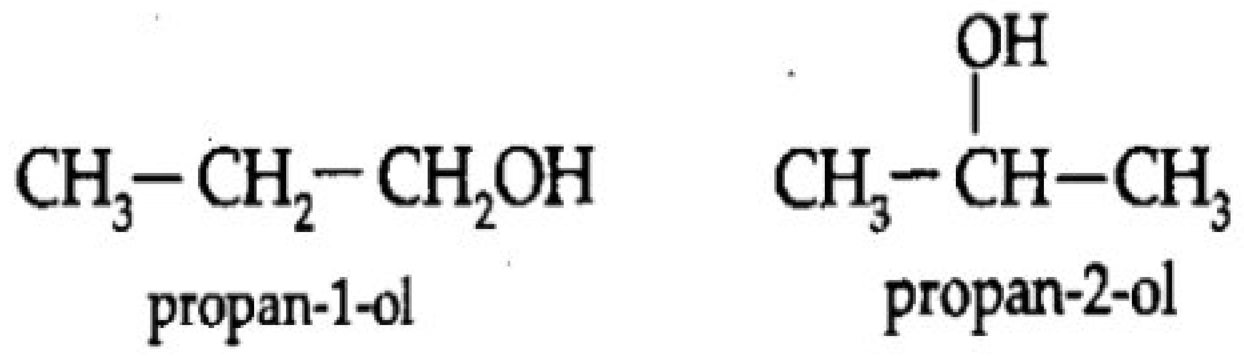
27.3.1 CHAIN ISOMERISM

Type of isomerism arises due to different in nature of carbon chain



27.3.2 POSITION ISOMERISM

Isomerism arises due to different in position of same function group.



$CH_3-CH_2-CH_2OH$

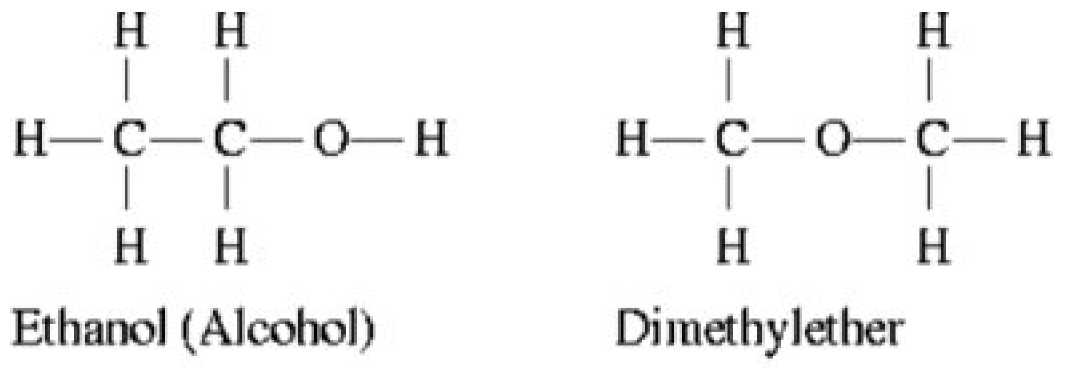
propan-1-ol

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

propan-2-ol

27.3.3 FUNCTIONAL GROUP ISOMERISM

Compounds having same molecular formula but different functional group

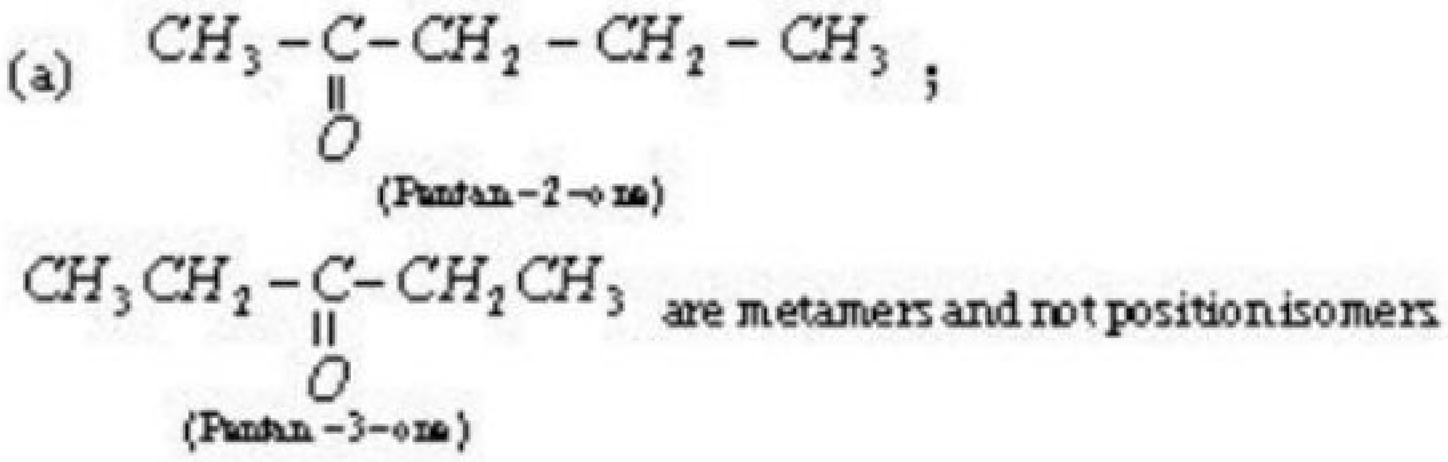


Ethanol (Alcohol)

Dimethylether

27.3.4 METAMERISM

Isomerism that arises due to unequal distribution of carbon atom on either side of the functional group.

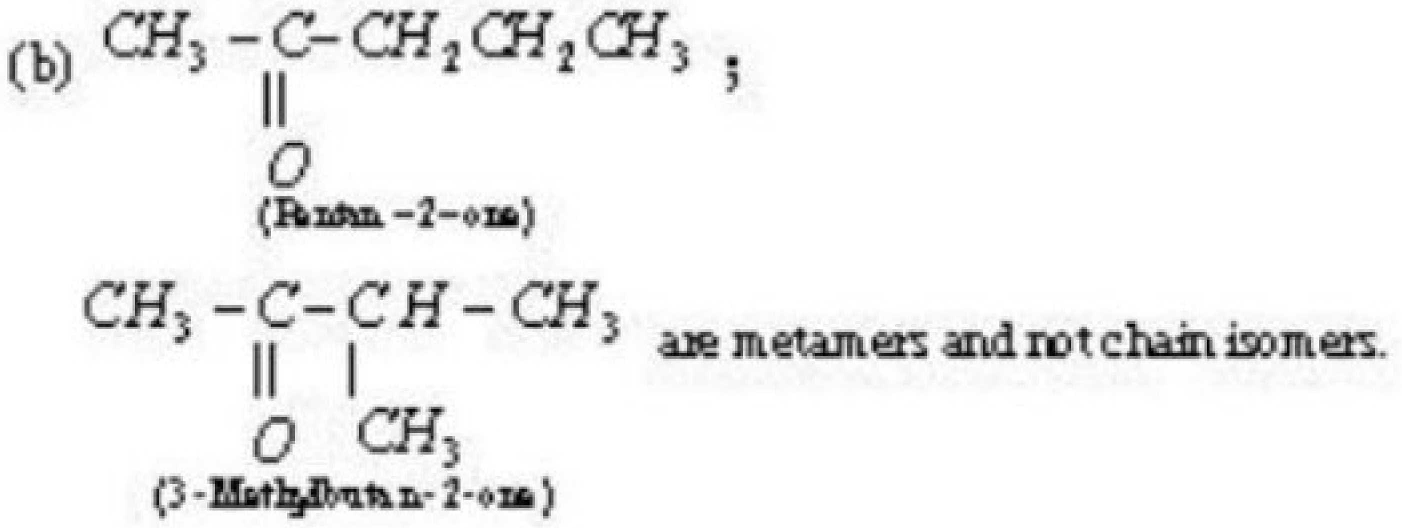


(a) $CH_3-\underset{O}{\underset{\|}{C}}-CH_2-CH_2-CH_3$;

(Pentan-2-one)

$CH_3CH_2-\underset{O}{\underset{\|}{C}}-CH_2CH_3$ are metamers and not position isomers

(Pentan-3-one)



(b) $CH_3-\underset{O}{\underset{\|}{C}}-CH_2CH_2CH_3$;

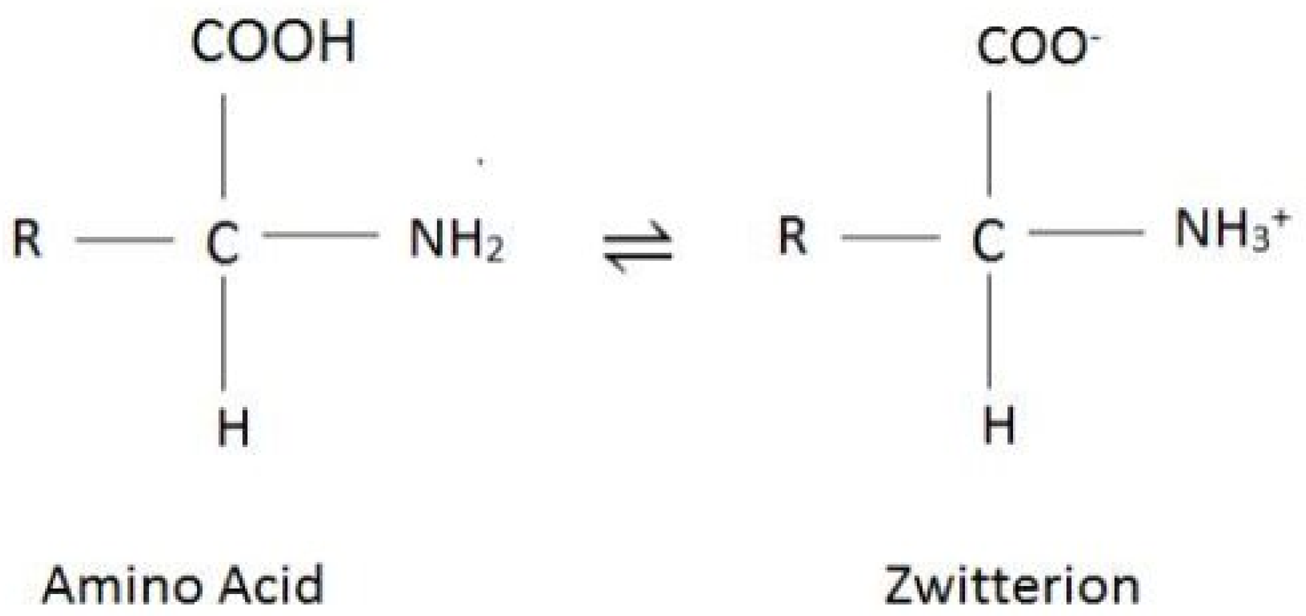
(Pentan-2-one)

$CH_3-\underset{O}{\underset{\|}{C}}-\underset{CH_3}{\underset{|}{C}H}-CH_3$ are metamers and not chain isomers.

(3-Methylbutan-2-one)

27.3.5 TAUTOMERISM

Type of isomerism arises due to shifting of proton from one atom to other in the same molecule



27.4 STEREOISOMERISM

When isomerism is due to difference in arrangement of atoms within the molecule with special reference to space (i.e. different in configuration), the phenomena is called stereoisomerism.

There are two types of stereoisomerism:

1. Geometric Isomerism
2. Optical isomerism

- ❖ Configuration exists in double bond
- ❖ Confirmation exists in single bond

27.5 GEOMETRIC ISOMERISM

Geometric Isomerism results from restriction in rotation about double bond in acyclic compound or about single bond in cyclic compound.

27.6 RESTRICTION

The carbon atom of double bonded molecule are sp^2 hybridized since it consists of one σ and one π bond therefore presence of π bond blocks the molecule in one position and rotation around double bond is not possible because rotation will break the molecule.

This restriction of rotation of carbon to carbon double bond is responsible for geometric isomerism, while in cyclic compound this restriction lies in carbon to carbon single bond because rotation will break the ring

Types of Geometrical Isomerism

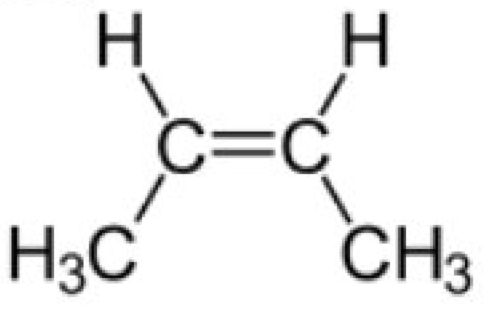
1. Cis
2. Trans

27.7 CIS ISOMERS

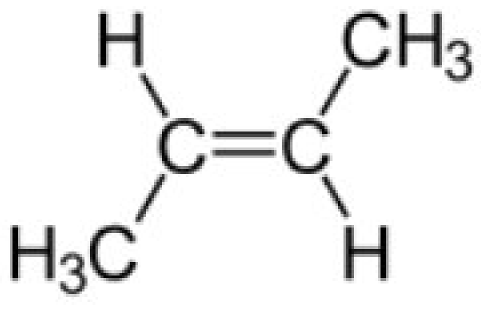
The geometrical Isomer in which two similar groups are on same sides of double bond is called as cis isomer. Cis is a Latin word which means on this side.

27.8 TRANS ISOMERS

The geometrical isomerism in which two similar groups are on opposite side of double bond is called Trans isomer. Trans is a Latin word which mean across.



cis-2-Buten



trans-2-Buten

27.9 E/Z SYSTEM

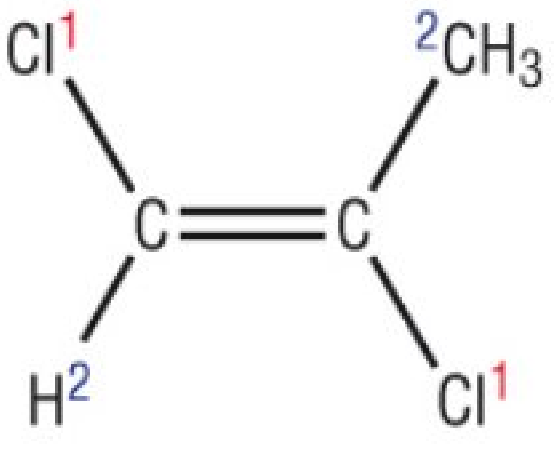
When there is same substituent attached to the double bonded carbon as in above example it is quite straight forward to desiccate Cis and Trans. However if there are more than one different group or atoms present as in following example the situation become complicated.

To simplify this situation, E/Z system is used for naming geometrical isomerism Z stands for Gerthan Zusamenn (same side) while E for German Entgegen (on opposite side).

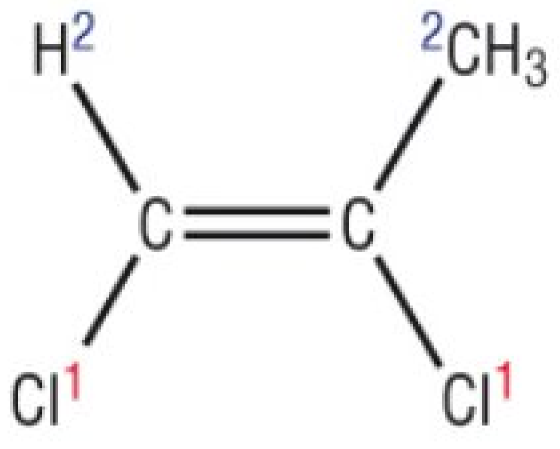
F>Cl>Br>I

27.9.1 IN E/Z SYSTEM FOLLOWING RULES ARE FOLLOWED

- On each carbon atom of double bond we have to assign priority of atoms bonded e.g. F>Cl>Br>I
- If two higher priority groups of two carbon atoms are on the same side it is called Z isomer
- If two higher priority groups are on opposite side of double it is called E isomer.

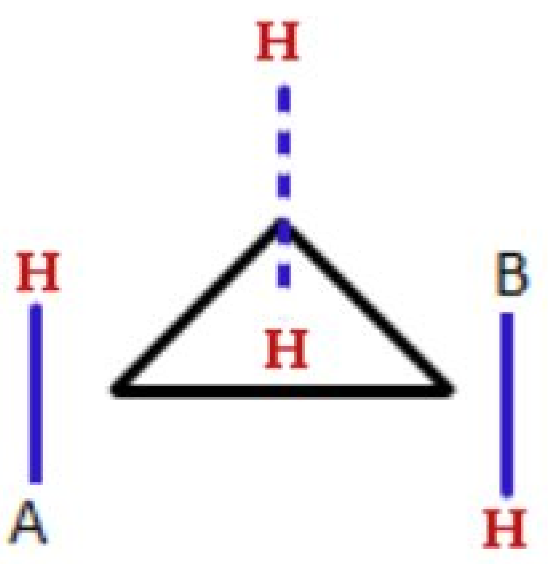


E isomer

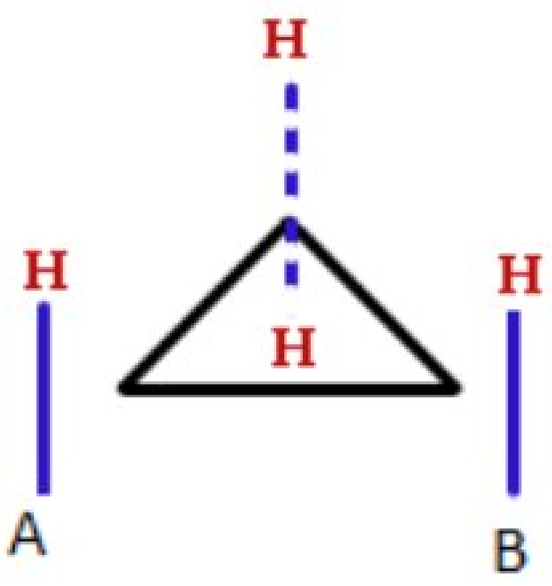


Z isomer

Now let's look on cyclic compound, we can use this E/Z system for a cyclic compound, when two or more than two groups are attached to a ring e.g.



E- System

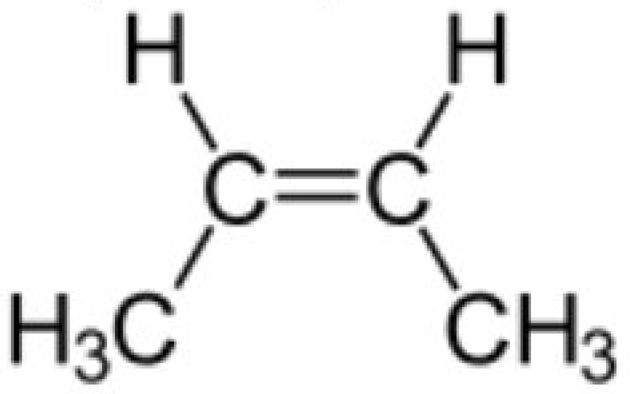


Z- System

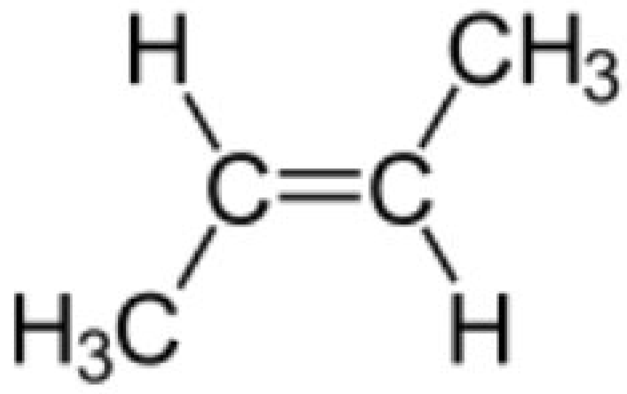
27.10 PROPERTIES OF GEOMETRICAL ISOMERISM

27.10.1 STABILITY

Trans isomers are more stable than cis isomers this because in cis isomers like groups are on same side and steric repulsion of the group makes the cis isomers less stable than trans isomer in which bulky group are far apart.



cis-2-Buten



trans-2-Buten

27.10.2 INTER-CONVERSION

Conversion of cis into Trans or vice versa is only possible, if either isomer is heated to high temperature or it absorbs light. The heat supplies energy 62 calories/mole to break pi-bond so that rotation about the σ bond is possible on cooling reformation take place giving a mixture of cis and trams.

27.10.3 PHYSICAL AND CHEMICAL BEHAVIOR

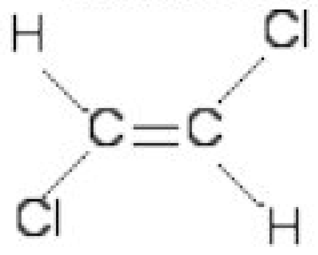
Geometrical isomerism differs in all physical properties and some chemical properties.

27.10.4 SEPARATION

They can be separated by conventional technique like fractional distillation and gas chromatography etc.

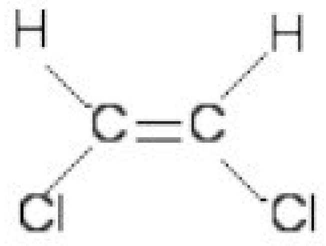
27.11 Example of Geometrical Isomerism

27.11.1 Alkene and other straight chain compound



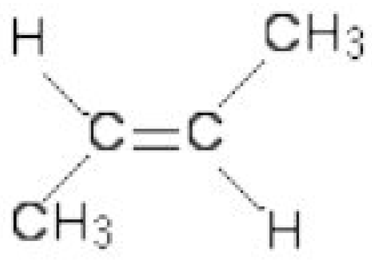
trans-1,2-dichloroethene

(E)-1,2-dichloroethene



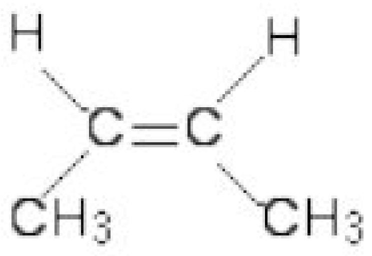
cis-1,2-dichloroethene

(Z)-1,2-dichloroethene



trans-but-2-ene

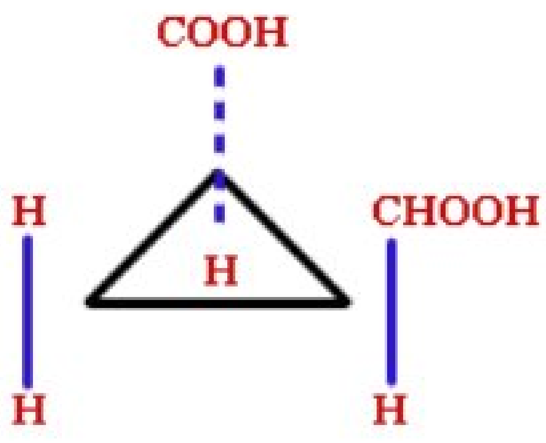
(E)-but-2-ene



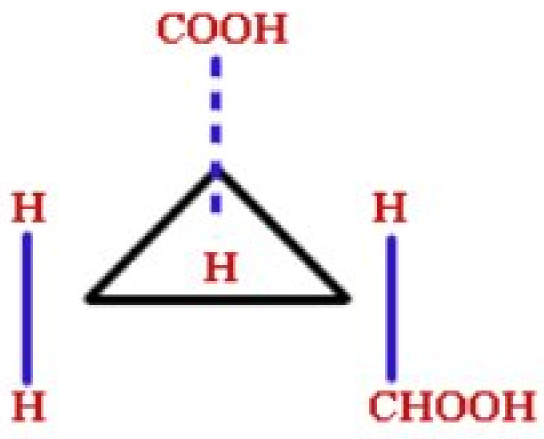
cis-but-2-ene

(Z)-but-2-ene

27.11.2 Cyclic Compound



Cis-form

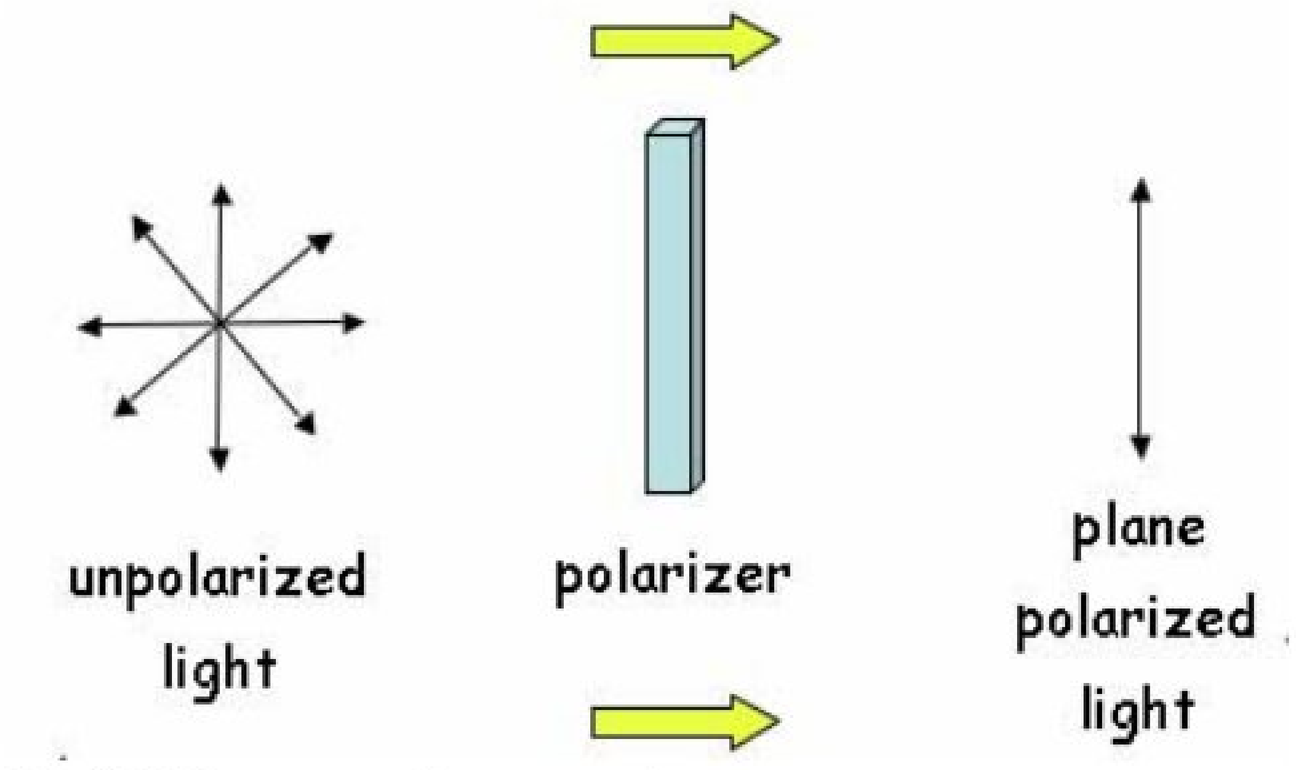


trans-form

27.12 Optical Isomerism

27.12.1 Plane polarized light

Light of ordinary lamp is composed of waves moving in all possible directions, when this light is passed through Nichole-prism made up of calcite ($CaCO_3$) or polarized lens, it is found to vibrate in only one phase and is called as plane polarized light.



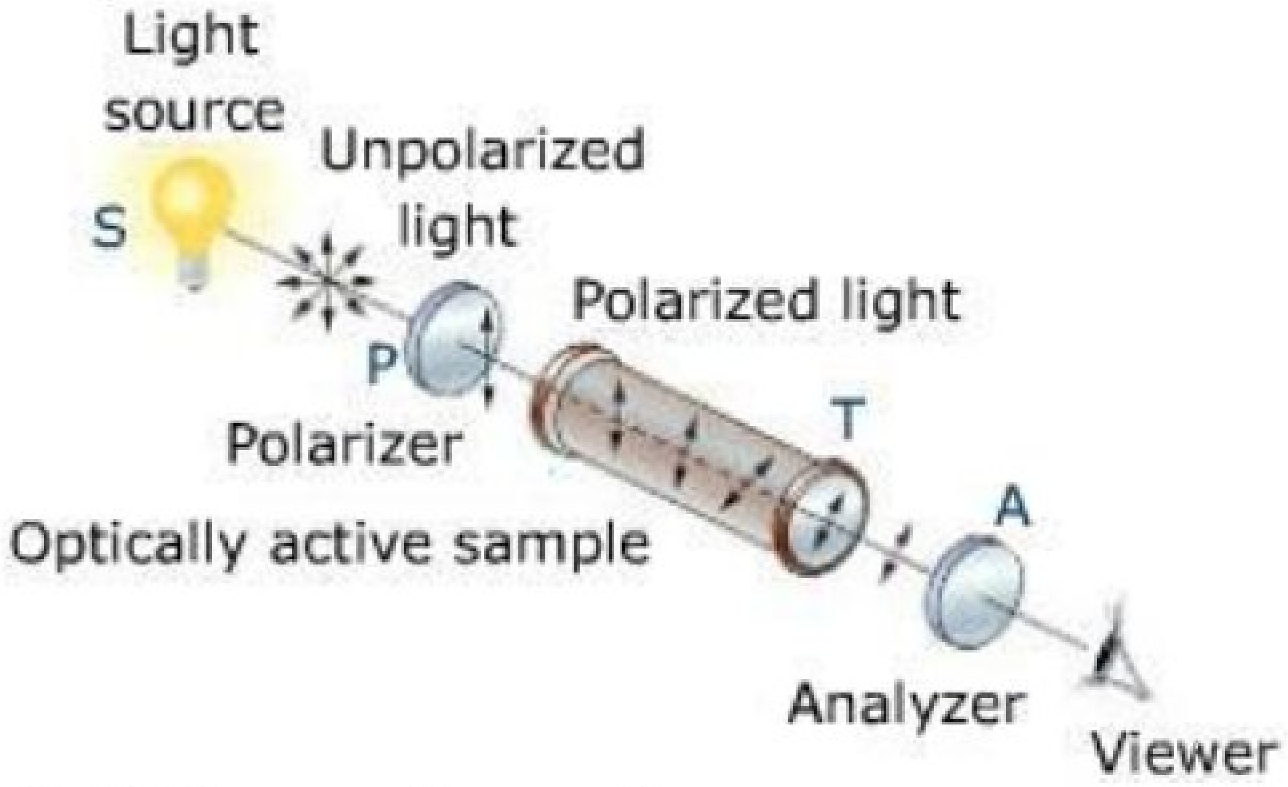
27.12.2 Optical Activity

The ability of an organic substance/compound to rotate plane of polarized light which is passed through it, is called optical activity and these compounds are called optically active compound.

27.13 Optical Rotation

The angle to which a beam of plain polarized light is rotated is known as optical rotation and magnitude of this rotation is also called as observed rotation and is donated by α.

Optical Activity of a compound is measure by Polarimeter which consists of fixed polarize and moveable analyzer.



27.13.1 Specific Rotation

The degree of rotation depends upon number of molecule of the compound encountered by light along its path so it is necessary to introduce some standard by which the rotating powers of different compound may be comparing.

It is defined as rotation produce by a solution of 10 cm and unit conc. (1g/ml) for a given wavelength of light at a given temperature.

Consider a system in which plain of polarized light is rotated through α-degree at a specific temperature using sodium-D-lines (a constant wave length) as a source and specific rotation can be calculated by given formula.

l= length of tube in decimeter

C = Concentration of solution

t= temperature

D= wavelength of light source

$$[\propto]_D^t = \frac{100\ \propto}{l\ c}$$

27.13.2 PLANE OF SYMMETRY

The plane which divide an object into two equal parts/ symmetrical halves is said to be plane of symmetry. E.g. human being possesses a plane of symmetry. E.g. tartaric acid (Meso-compound).

This plane divides the molecule in such a way that atoms or groups of atoms on the side of plane are mirror images of each other and are supper imposable.

Only Meso compounds possess plane of symmetry.

Meso compound possess plane of symmetry and the two equal parts are super imposable.

27.13.3 DEXTRO ROTATORY

The compound which rotates the plane of polarized light to right (clockwise) is said to be dextro rotatory. It is indicated by d or (+).

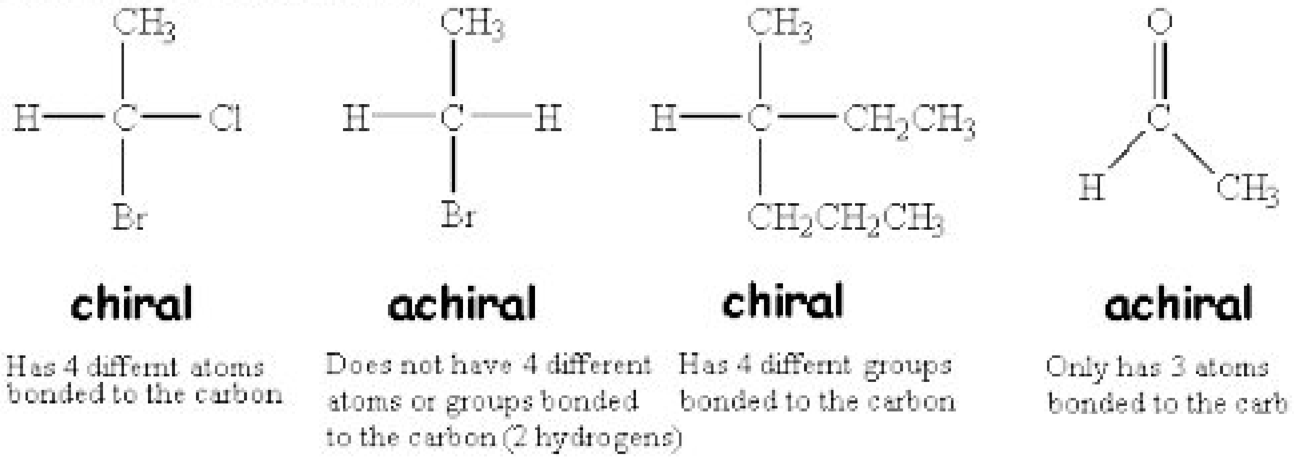
27.13.4 LEVO ROTATORY

Compound which rotates the plane of polarized light to the left (anti- clockwise) is said to be levo rotatory. It is indicated by l or (-).

There is no co-relation between D and (+) rotation and similarly L isomer does not have necessarily (-) rotation

27.14 ASYMMETRIC CARBON ATOM/CHIRAL CARBON ATOM

A carbon atom which is bounded to four different atoms or groups of atoms is called asymmetric carbon atom for example.



- ❖ 2^n= total possible isomers (where n is the number of chiral carbon)

27.15 CONFORMATIONAL ISOMERS

Conformational isomers differ from each other only in there arrangement of their atoms in space and can be converted from one form into other since there is only single bond (σ bond) which can be rotated.

27.16 OPTICAL ISOMERISM

The phenomena in which optically active substance/compound rotate plane of polarized light in either direction is known optical isomerism

Optical Rotatory powers of dextro and levo are equal in magnitude but opposite in direction.

An equimolar mixture of two isomers will not rotate plane of polarized light and is said to be racemic mixture.

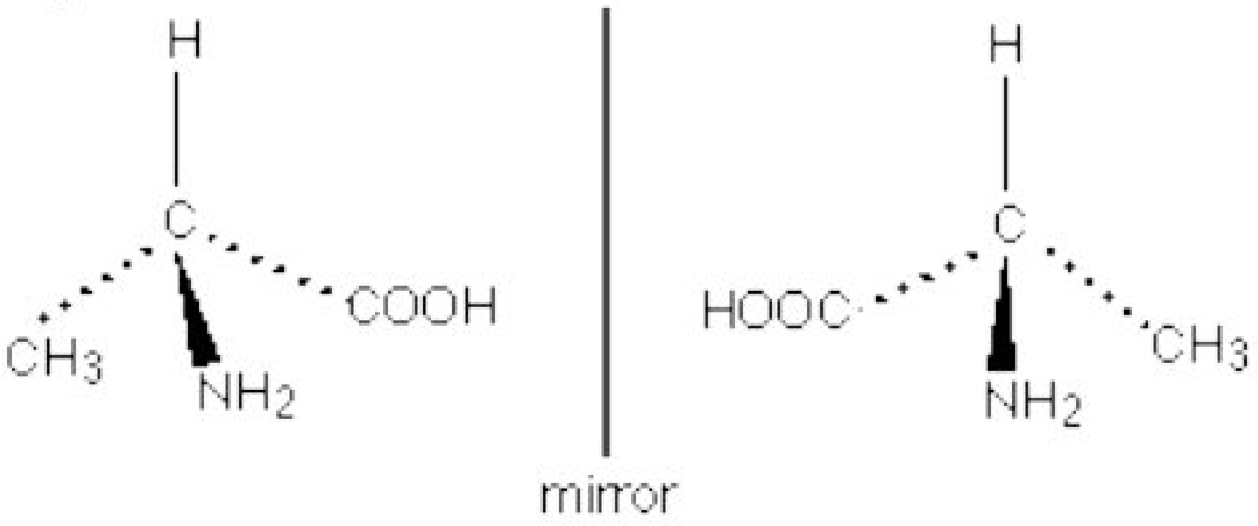
27.16.1 CONDITION FOR OPTICAL ISOMERISM

The necessary condition for a molecule to exhibit optical isomerism is that it should be asymmetric/dissymmetric or chiral carbon atom.

It means that molecule should not be super-impossible on its mirror image this chirality is based upon actual arrangement of atoms in the molecule.

27.16.2 DIAGRAM

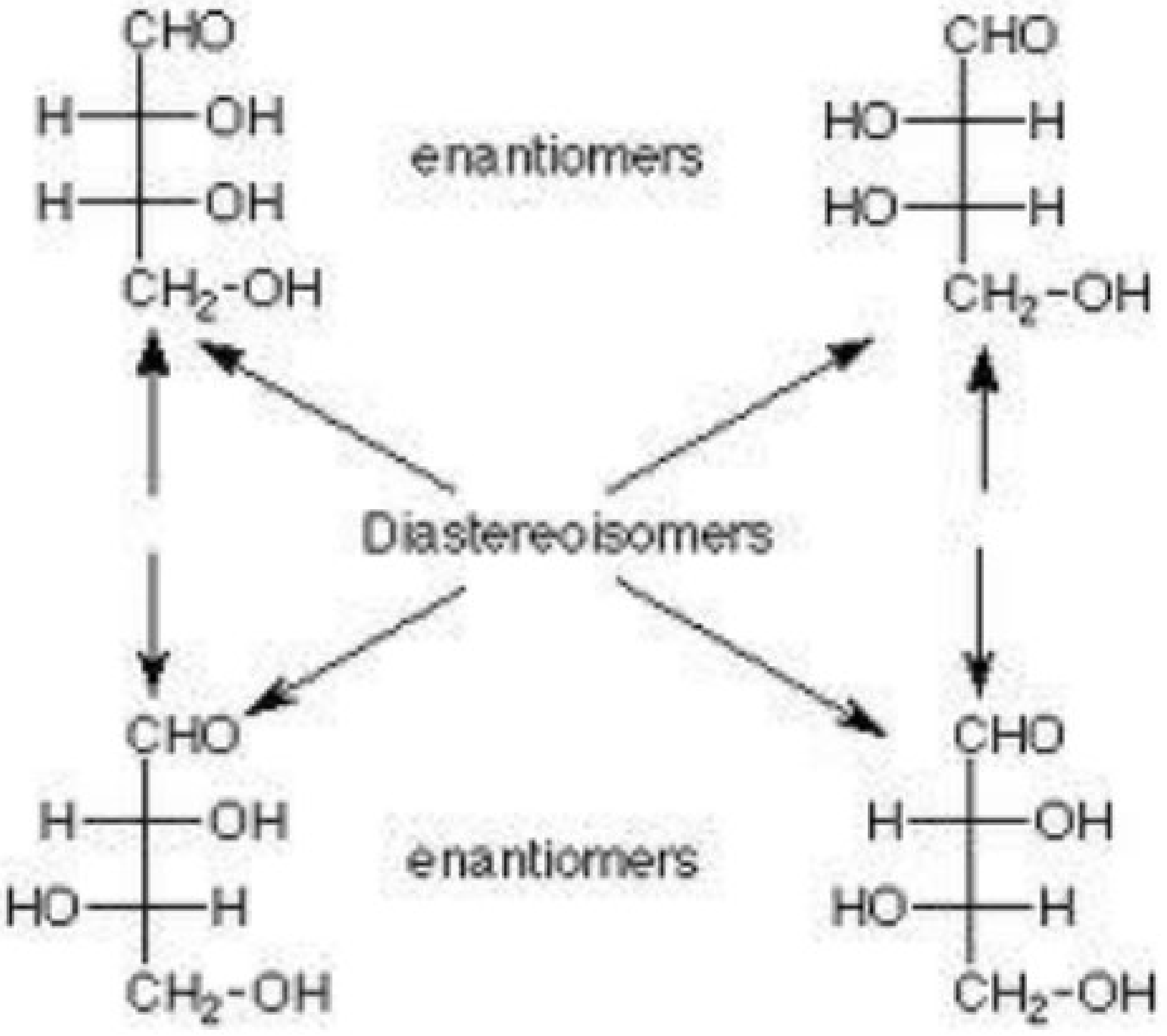
They are mirror image of one another but not super imposable.



27.17 ENANTIOMERS

The Greek word "enatio" mean "opposite". These optical isomers that are mirror images and non-superimposable are called as enantiomers.

When one arrangement rotates the plane of polarized light to one side while other arrangement rotates plane of polarized light to opposite direction and both arrangement are mirror images of each other, these are called enantiomers.



27.18 Properties of Enantiomers

- They always exist in discrete pair.
- They are always mirror image of each other
- They are stable, isolable (can be isolated) compound that differ from one another 3 dimensional special arrangement
- They cannot be interconverted under ordinary condition
- They have same properties which the exception of interaction with plane of polarized light as both rotate plane of polarized light in opposite direction but with same magnitude.
- Equimolar mixture of two enantiomers is called racemic mixture.

27.19 Diastereomers

Optical isomers that are not mirror images of each other are called diastereomers OR stereoisomers that not enantiomers are diastereomers.

27.20 Erythrose

Isomers having two like groups on same side in projection formula are called erythrose form.

27.21 Threose

Isomer having two like groups on opposite side in projection formula is called threose.

27.22 Meso-compound

A compound with two or more asymmetric carbon atoms possessing a plane of symmetry is called Meso-compound, one half is the mirror image of the other and they are optically inactive due to internal compensation.

27.23 CIP (Cahn-Ingold-Prelog)

The priority rules are been involved to confer many situation and these are as such

$$I > Cl > C > H$$

Consider the first atom of each part of the molecule, this atoms is given the highest priority

If the first atom of two groups is same, consider the second atom; if this does not give the priority consider the next until there is a difference.

$$-C(CH_3) > -CH(CH_3)_2 > -CH_2CH_3 > CH_3$$

27.24 R-S System

R-S rotation use CIP Priority rules for assignment of absolute configuration, around a stereo-center.

- First assign priority as describe above to each bonded group i.e. 1 – highest to 4 lowest
- Point the lowest priority (4) group away from you and follow the direction of the remaining 3
- from highest to lowest priority.
- Anticlockwise Sinister (S) and a clockwise is R (rectus)

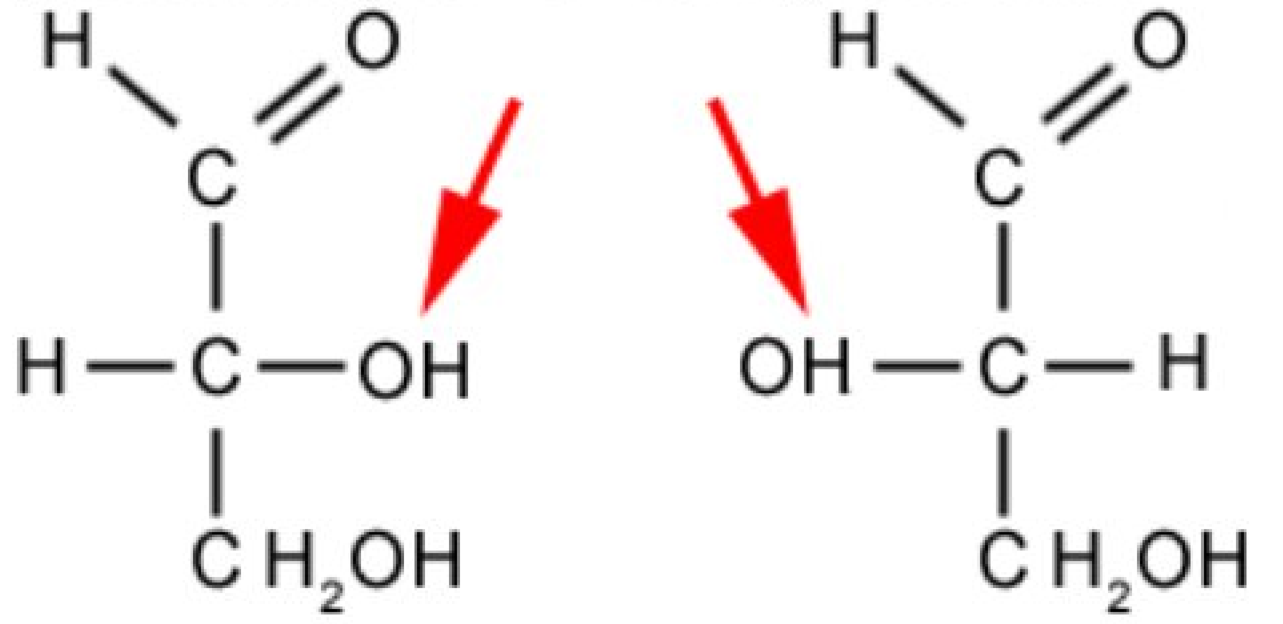
27.24.1 Clockwise (R-) & Anti-Clockwise (S-)

If more OH groups are on one side than it is erythrose but if they are present across then threose.

27.25 D-L Rotation

Emil Fischer used Glyceraldehyde as as standard for D-L rotation. He randomly took positive (+) glyceraldehyde and name it as D-glyceraldehyde and the other was designed as L-glyceraldehyde, the only difference in these two structure is orientation of OH group at chiral center. In this case if OH group is on right side, it is D form while OH group is on left side, its L-form.

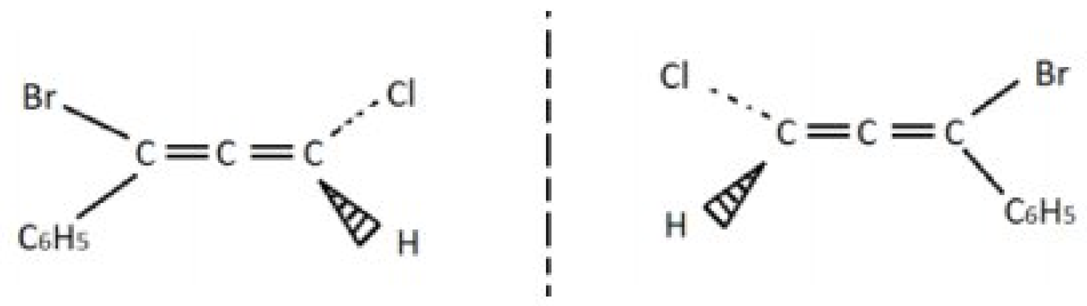
The structure are similar to glyceraldehyde are compared and are given D or L naming nomenclature.



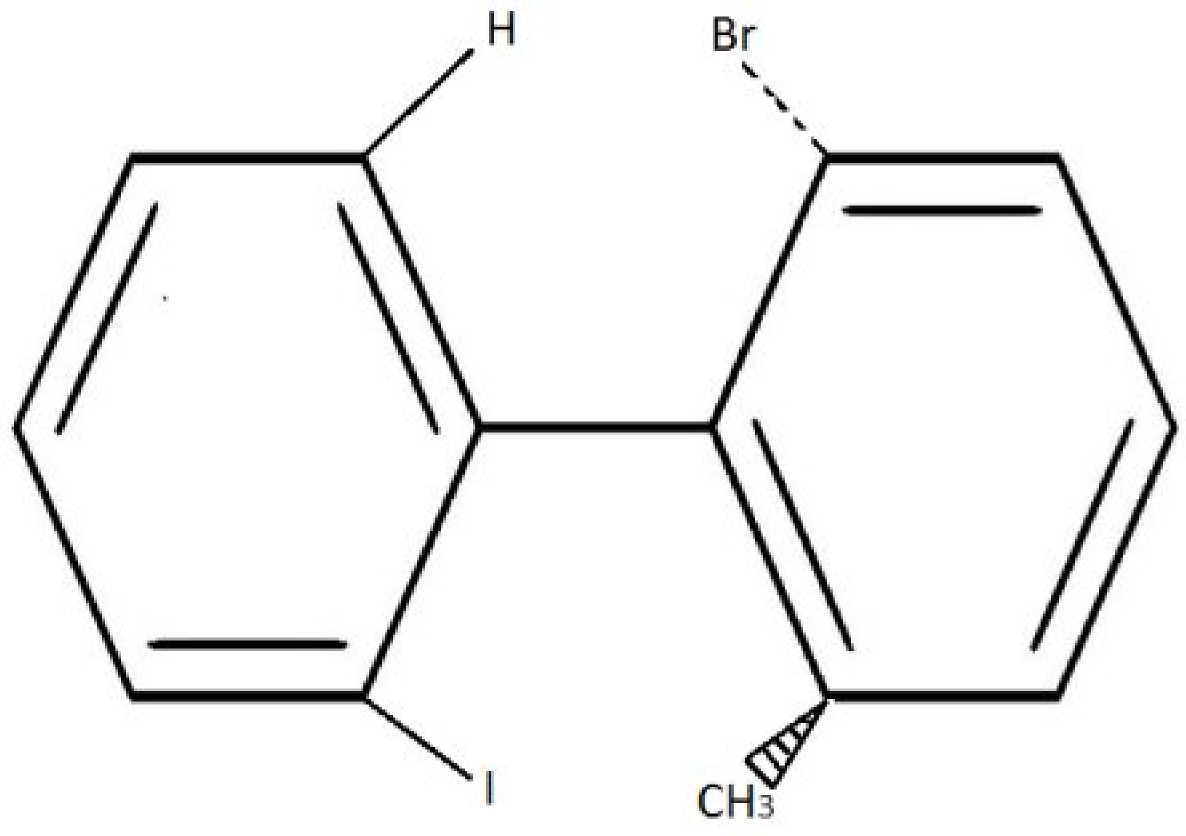
D-Glyceraldehyde L-Glyceraldehyde

27.26 Containing No Asymmetric Carbon but are Optically Active

27.26.1 Structure of Alkene Derivatives



27.26.2 BIPHENYL DERIVATIVES



27.27 RACEMIC MIXTURE

An equimolar mixture of pair of enantiomers is called racemic mixture. It is expressed by (+-) dl and this mixture does not show any optically activity.

We make racemic mixture to store molecule, it increases stability.

27.28 METHOD OF FORMATION OF RACEMIC FORMATION

27.28.1 MIXING OF ENANTIOMER

In this process mixing of exactly equal amounts of two enantiomer (+-) take place. This process is associated with entropy and this entropy is positive because this mixing leads from an organized system to random one.

27.28.2 SYNTHESIS

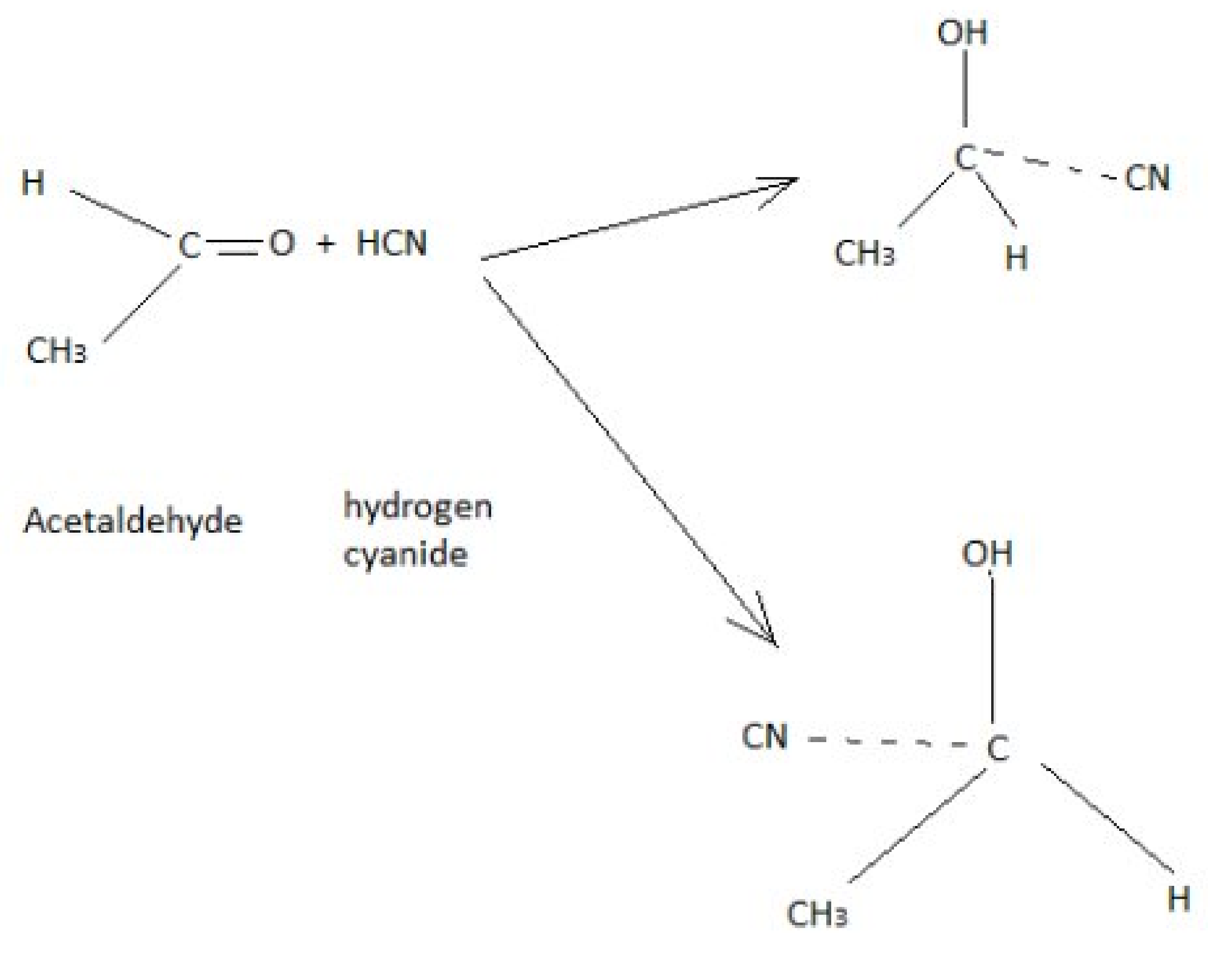
A synthesis of asymmetric molecules from symmetric molecule always results in racemic mixture provided the reaction is carried out in absence of optically active reagent or catalyst or any other physical influence.

27.28.3 BY ADDITION

Formulation of lactonitrile by the addition of hydrogen cyanide to acetaldehyde.

- ❖ Measure of order or disorderness of a system is called entropy

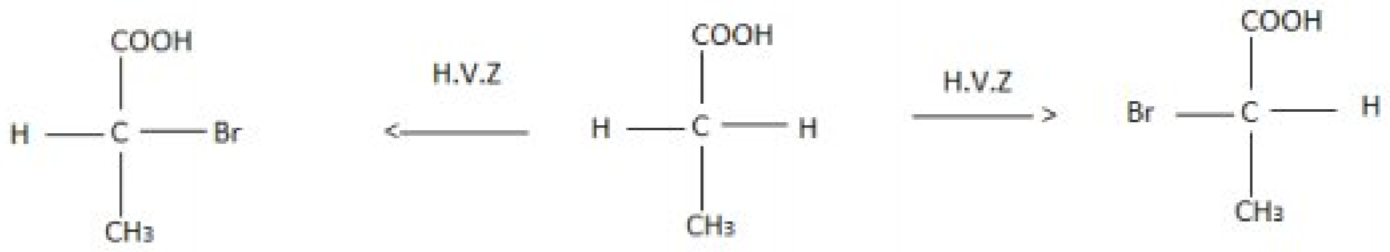
The cyanide group approaches to the positively charged carbon atom from front or back which results in formation of racemic mixture.



Lactonitrile

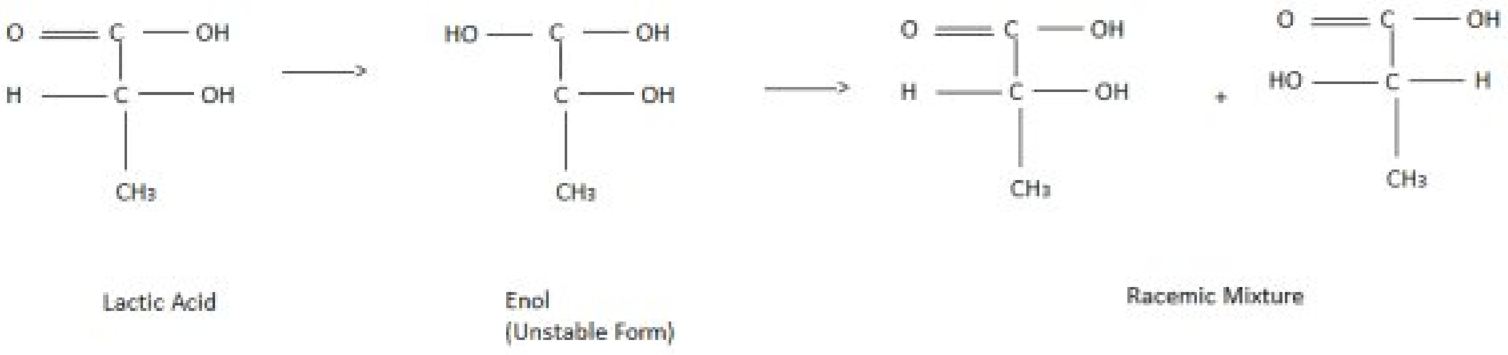
27.28.4 BY DISPLACEMENT

The formation of alpha bromo proponic acid take place by Hell-Volhord-Zelinsky



27.28.5 RACEMIZATION

Conversion of optically active compound into an equimolar mixture of an enantiomer is called as racemization.



Most of the enantiomers are capable of undergoing the process of racemization under the influence of heat light or chemical agent such compound are called optically labile and are sore in a specific container.

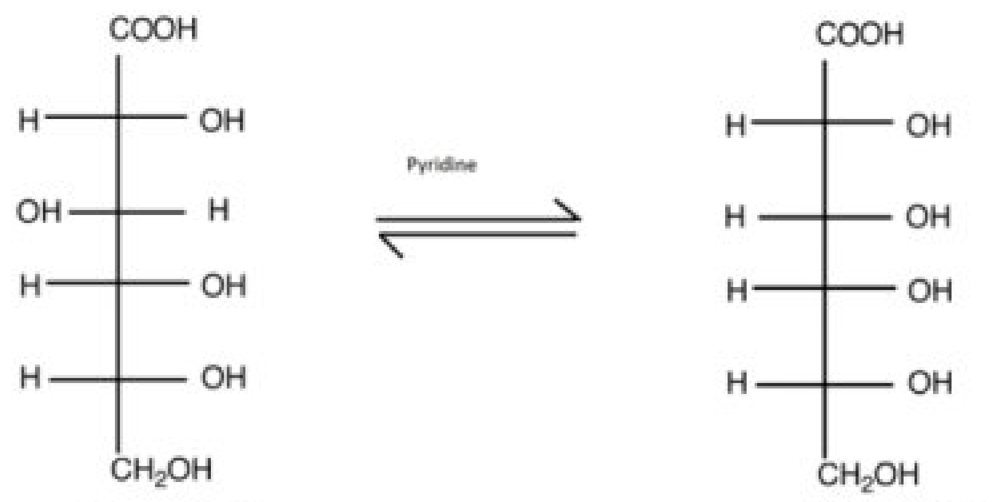
27.29 EPIMERS

27.29.1 EPIMERIZATION

Epimerization is a closely related to racemization and is defined as inversion of configuration at one of the several center of asymmetry /Chirality.

For Example Epimerization of mannonic acid to gluconic acid in the presence of pyridine

Alpha- hydrogen is displaced



Mannonic Acid Glucconic Acid

And these two are called epimer of each other.

27.30 Racemic Modification

Mixing, addition, substitution, synthesis, racemization and epimerization are the process of racemic modification.

27.31 Properties of Racemic Mixture

Racemic Modification may exists in any three different form of matter

27.31.1 In Solid State

Racemic Mixture: It is simply a mechanical mixture of two forms dextro and levo. They are known as conglomerates

It is two phase system. The melting point of racemic mixture is lower than individual enantiomers

27.31.2 Racemic Compounds

The molecule of one enantiomer have greater affinity for the opposite enantiomer this pair unite to form a molecule called as racemic compound and is represent one phase system. The physical properties differ from the constituent enantiomers

In solution form it dissociates into (+) and (-) form.

27.31.3 Racemic Solid Solution (Pseudo Racemic Compound)

This is known as pseudo racemic compound as there is a tendency of enantiomers to crystalize together due to their isomorphic form. They are also 1 phase system. The arrangement of molecules in the sold is random and racemic sold solution is obtained.

27.32 Resolution of Racemic Mixture

The separation of racemic mixture into two optically active components is called resolution and these individual forms are pure when isolated. The following are the method adapted

- Mechanical Separation
- Biochemical Separation
- Selective Adsorption (Chromatography)
- Kinetic Separation
- Conversion into Diastereomers

27.32.1 Mechanical Separation

This method is only applicable to those racemic mixtures whose crystals are non-enatiomorphs (not isomorphs) and hence are non-identical in appearance.

Pasteur separated crystals of racemic sodium ammonium tartrate by hand picking the crystals with the help of twizzer under lens.

This method is of limited application because very few compounds crystalize in this manner.

27.32.2 Biochemical Separation

Certain Bacteria and molds of chiral nature when grows in a dilute solution of a racemic, destroy one enantiomer more rapidly than the other. E.g.When Penicillium glaucum (mold Fungus) is grown in a solution of a racemic ammonium tartrate the solution becomes levo rotatory because the mold has preferentially destroy the dextro form.

This method is of limited use because one form is destroyed.

27.32.3 Selective Adsorption

An optically active substance of limited solubility such as starch sometimes acts as selective adsorbent towards racemic mixture.

When a solution of racemic mixture is poured into the top of chromatography column the enantiomer moves along the column at a different rate.

The enantiomers with less adsorbing rate will be rich at the bottom while the other is rich at the top.

Racemic mandelic acid has been completely separated by this method.

27.32.4 Kinetic Separation

Enantiomers react with chiral compound at different rate and it is sometime possible to separate them by using limited amount of reagent which specifically reacts with only one of the two enantiomers or by stopping the reaction before completion. E.g racemic mandelic acid has been resolved by using (-) menthol which reacts faster with (+) mandelic acid.

- ❖ Alkaloid
    - ○ Natural origin
    - ○ Contains nitrogenous compound
    - ○ Specific pharmaceutical activity
    - ○ E.g. brucine from Nux Vomica

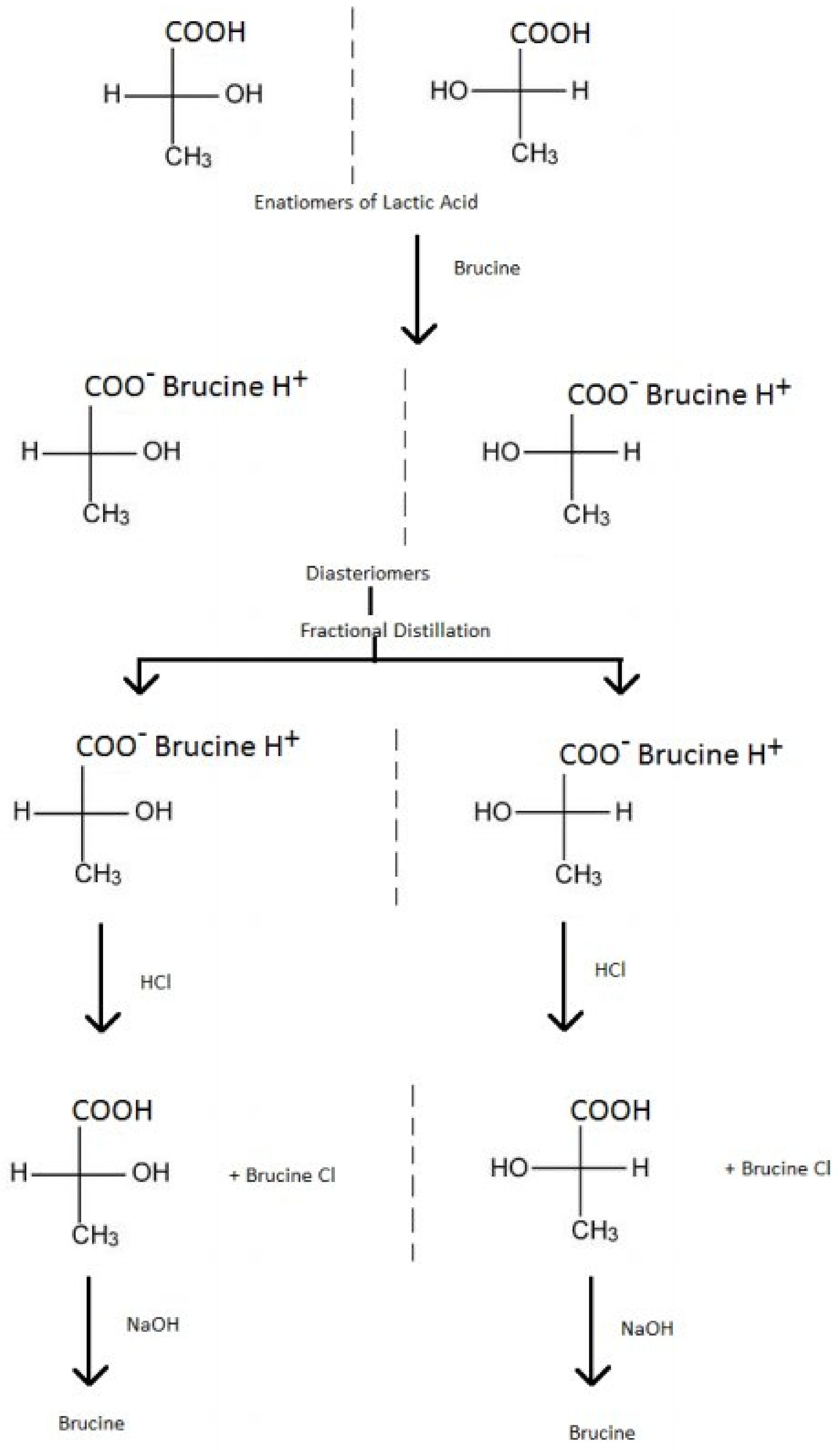
27.32.5 Conversion into Diastereomers

The fact that diastereomers differs in physical properties from the basis of this method. The racemic mixture of enantiomer is reacted with optically active base like brucine which naturally occurring alkaloid to form a salt.

The product is allowed to crystalize taking the advantage of difference in their solubility. Less soluble diastereomers precipitate out rapidly and separated.

We may use fractional distillation

Once the two diastereomers have been separated they are hydrolyzed to regenerate original form.

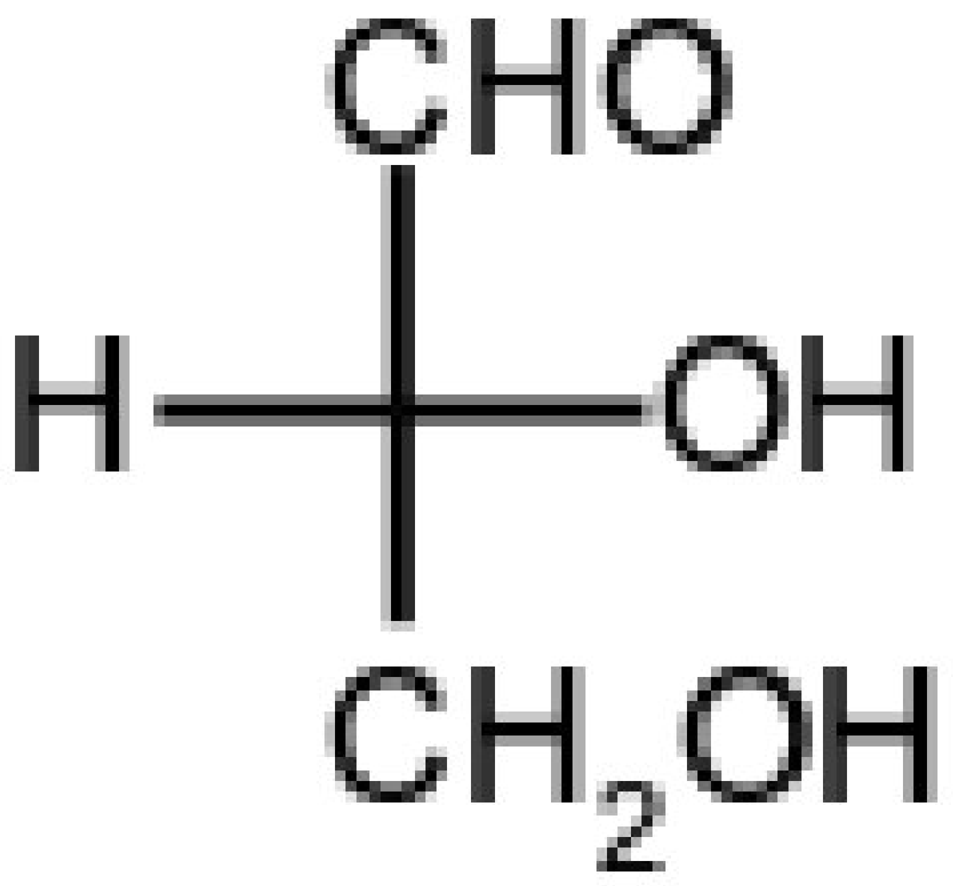


27.33 FISCHER'S PROJECTION

This projection was devised by German chemist Emil Fischer, it provide a convenient way to draw 3D molecule on paper. The rules are as such

- Carbon chain of the compound is arranged vertically with the most oxidized carbon at top or given carbon no. 1 position.
- Asymmetric carbon atom is represented by intersection of cross line.
- Group attached to the vertical lines are understood to be going back behind the planes of paper and asymmetric carbon atom is present in the pane.
- Groups attach to horizontal lines are understood to be coming forward out of the paper toward observer.

For example the Fischer's projection of glyceraldehyde is given as:-



27.34 ECLIPSE CONFORMATION

The conformation in which asymmetric carbon atoms are so arranged with respect to each other that groups attached to them are as close as possible and crowning between the substituent is maximum making the molecule unstable by steric repulsion.

27.35 STAGGERED CONFORMATION

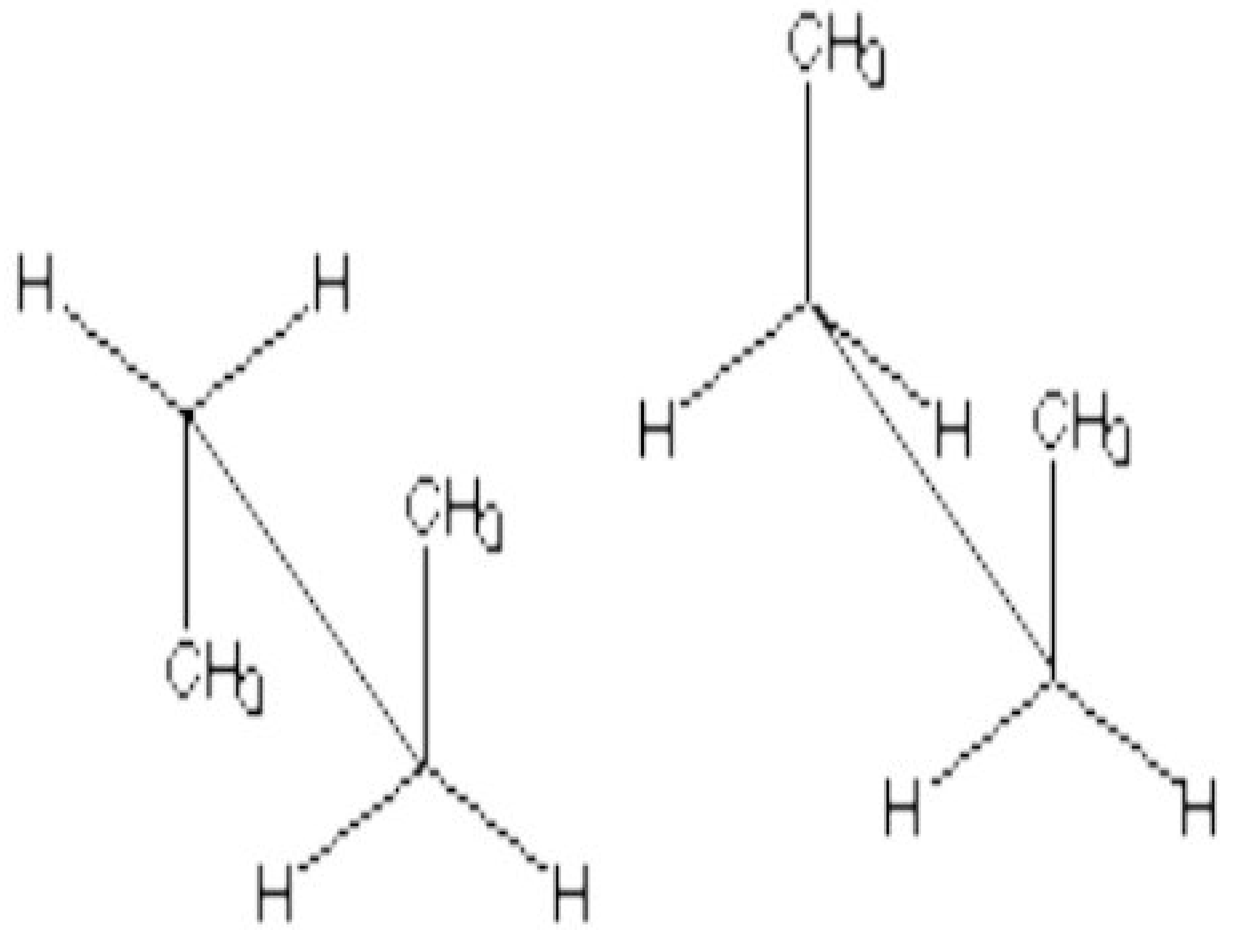
The conformation in which asymmetric carbon atoms are so rotated/arranged with respect to each other that groups attached to them are as far as possible and crowding between the substituent is minimum. In staggered conformation, substituent is maximum distance apart which makes them to be most stable.
These two extreme forms can be represented by following projections:-

27.36 SAWHORSE PROJECTION

In sawhorse projection, the molecule is simply drawn in 3D and the bond between asymmetric carbon atoms is oriented diagonally backward and somewhat exaggerated in length.

27.37 NEWMANN PROJECTION

In Newmann Projection we imagine ourselves receiving the molecule from one end the front carbon atom is represent by a dot from where the three remaining bond emerge while rare carbon atom represented by a circle and its bonds are emerging from the edge of the circle.
The high potential energy of eclipse is due to repulsive interaction of electrons on adjacent carbon atom and this distance is minimum in eclipse and makes them unstable.
While in staggered conformation groups are so arranged that there is stability in the molecule



Sawhorse structures

Chapter 28 Free Radical

28.1 Definition

Free radicals are atoms or molecules possessing odd or unpaired electrons. These unpaired electrons are highly reactive and make the free radical to participate in chemical reaction extensively/fastly. They play a very important role in combustion, atmospheric chemistry, polymerization, plasma chemistry, biochemistry and many other chemical processes including human physiology.

The first organic free radical (triphenylmethyl free radical) was identified by Moses, Gomberg in 1900 in Michigan University. They were formed by hemolytic fission.

A hemolytic fission is the one in which two participants have the same electronegativity values and the radical formed is electrically neutral and carries no charge and are named after parent alkyl group by adding the word "free radical". E.g. methyl free radical, ethyl free radical

28.2 Properties of Free Radicals

1. They are electrically neutral, carries no charge.
2. They are highly reactive.
3. They are paramagnetic.
4. The carbon atom in free radical is sp^2 hybridized, remaining one free p-orbital extends above or below the bond axis (sigma bond axis).
5. They have transition resistance.
6. All the free radicals show addition reactions.
7. They are stabilized by resonance.
8. Like carbonium ion, tertiary free radicals are stable than secondary free radicals due to stearic hindrance.

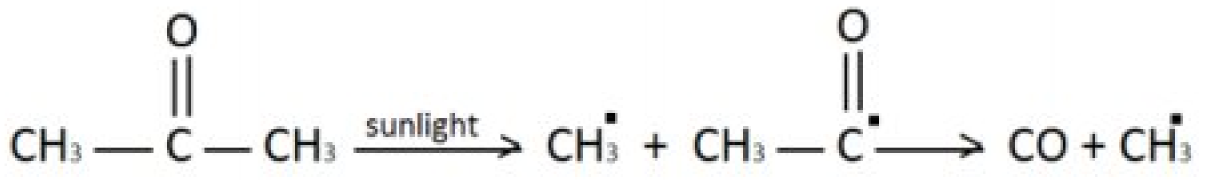
28.3 Radical Formation

There are number of ways by which radicals may be generated. The most important are as such:

1. Photolysis
2. Thermolysis
3. Hemolysis
4. From other free radicals
5. Redox reactions

28.3.1

28.3.2 Photolysis: *Acetone in vapour state is decomposed by light having a wavelength of about 320.*



$$CH_3-\overset{\overset{O}{\|}}{C}-CH_3 \xrightarrow{\text{sunlight}} CH_3^{\bullet} + CH_3-\overset{\overset{O}{\|}}{C}^{\bullet} \longrightarrow CO + CH_3^{\bullet}$$

$$Cl : Cl \xrightarrow{\text{sunlight}} Cl^{\bullet} + Cl^{\bullet}$$

$$RO-Cl \xrightarrow{\text{sunlight}} RO^{\bullet} + Cl^{\bullet}$$

Thermolysis: Compounds containing weak bonds often produce free radicals when subjected to heat.

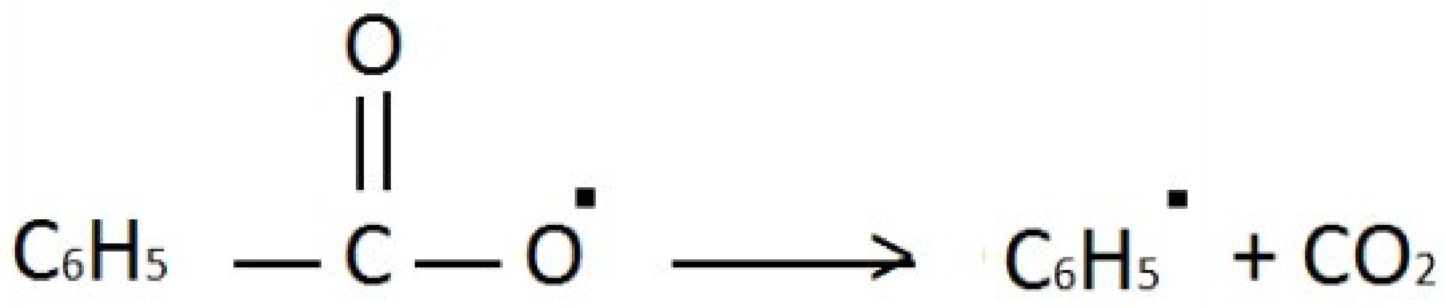
$$(C_2H_5)_4\,Pb \xrightarrow{\Delta} Pb^{\bullet\bullet} + 4C_2H_5^{\bullet}$$

Homolysis of Covalent Bond: Free radicals are formed by hemolytic cleavage of single covalent bond. Energy required for this process is called as bond dissociation energy.

$$C_6H_5-\overset{\overset{O}{\|}}{C}-O-O-\overset{\overset{O}{\|}}{C}-C_6H_5 \longrightarrow C_6H_5-\overset{\overset{O}{\|}}{C}-O^{\bullet}$$

From other free radicals: Free radicals are formed by reaction between a free radical and a molecule to generate or form another free radical.

$$Cl^{\bullet} + CH_4 \longrightarrow CH_3^{\bullet} + HCl$$



$$C_6H_5-\overset{\overset{O}{\|}}{C}-O^{\bullet} \longrightarrow C_6H_5^{\bullet} + CO_2$$

Redox Reaction: In these reactions inorganic ions that can change their valence state by gain or loss of electron can be used to generate free radicals.

$$H_2O_2 + Fe^{+2} \longrightarrow OH^{\bullet} + Fe^{+3} + OH^{-}$$

Hydroxide free radical

28.4 Free Radical Mechanism:

Mechanism of Free Radical

a) Initiation Step

$$\underset{\text{Chlorine Molecule}}{Cl : Cl} \xrightarrow{\text{sunlight}} \underset{\text{Chlorine Free Radical}}{Cl^{\bullet} + Cl^{\bullet}}$$

b) Propogation Step

$$Cl^{\bullet} + CH_4 \longrightarrow \underset{\text{Methyl Free Radical}}{CH_3^{\bullet}} + HCl$$

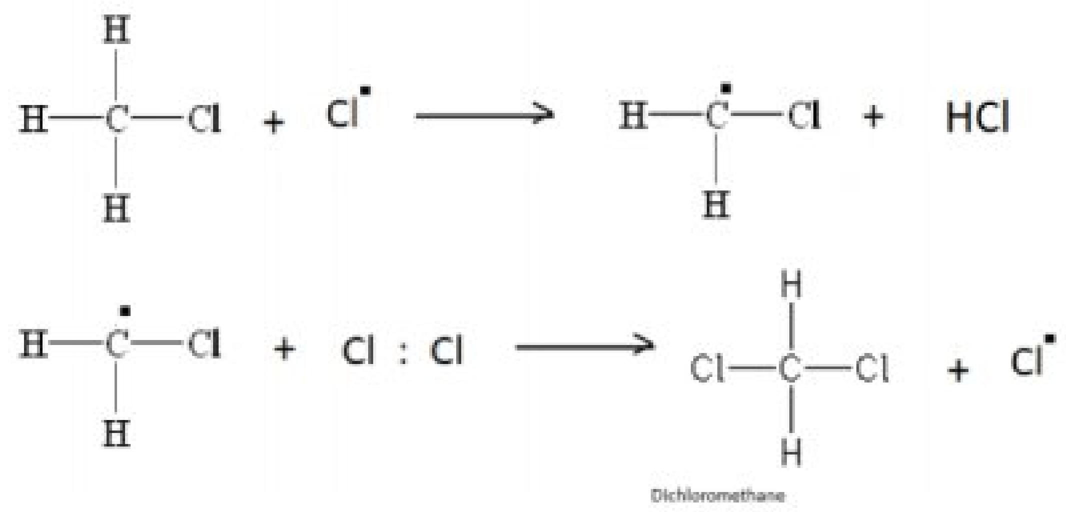
$$CH_3^{\bullet} + Cl : Cl \longrightarrow \underset{\text{Methyl Chloride}}{CH_3Cl} + \underset{\text{Chlorine Free Radical}}{Cl^{\bullet}}$$

c) Termination

$$CH_3^{\bullet} + Cl^{\bullet} \longrightarrow \underset{\text{Methyl Chloride}}{CH_3Cl}$$

Further Substitution of Hydrogen

i)



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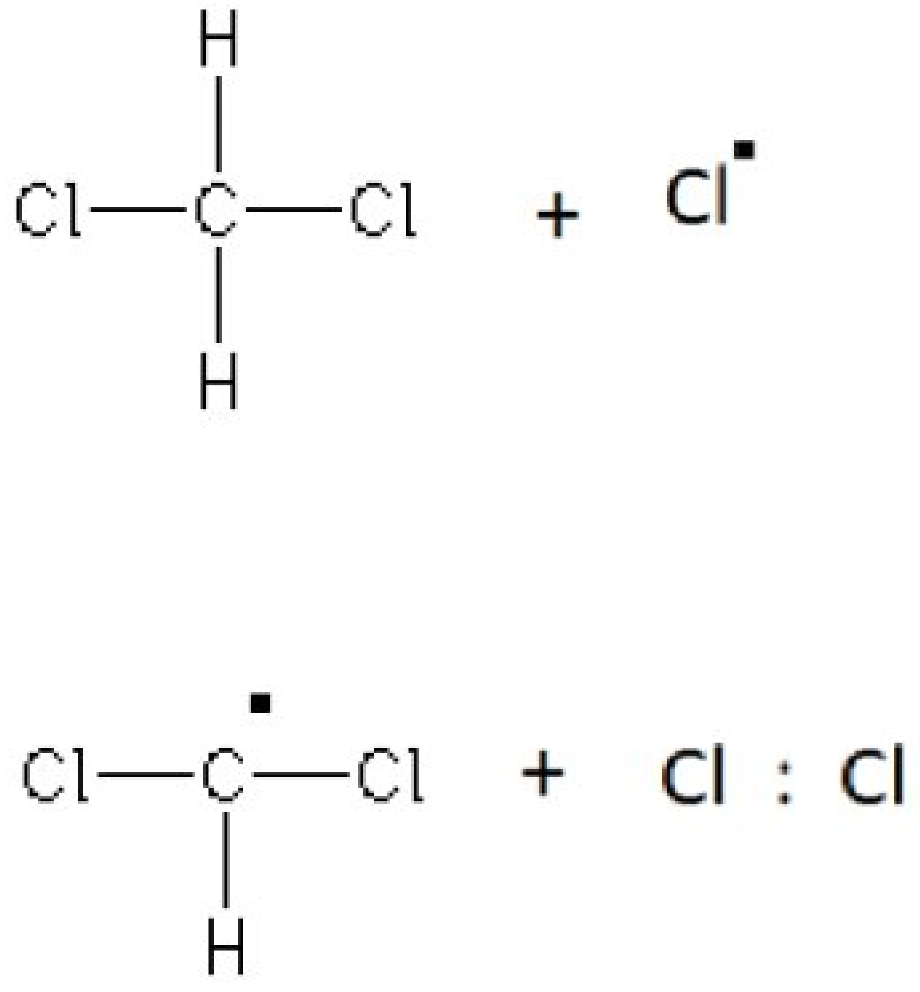
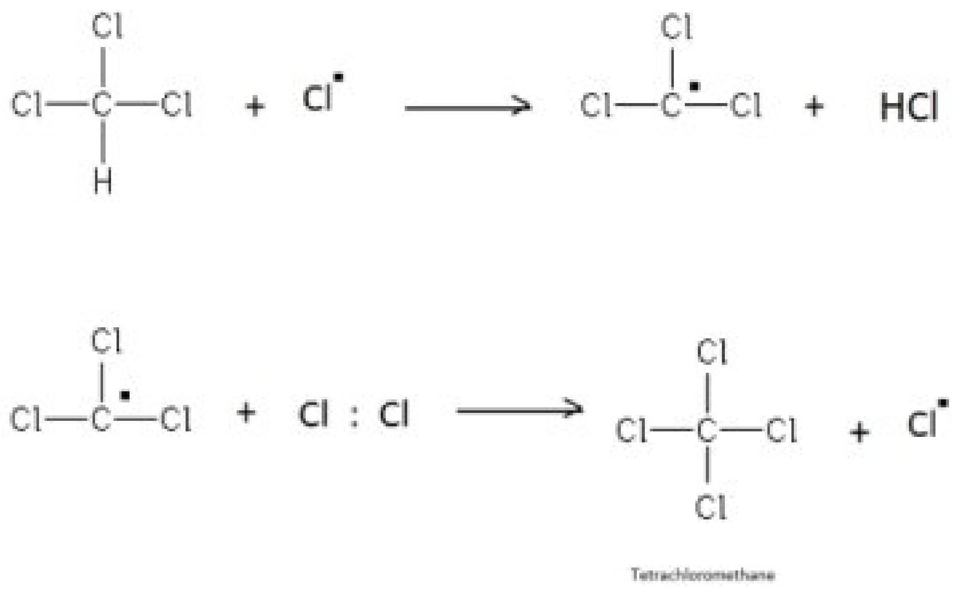


iii)



28.5 REACTION OF FREE RADICALS:

Free Radicals show two types of Reactions:

- Long Life Free Radical Reactions
- Short Life Free Radical Reactions

28.5.1 LONG LIFE FREE RADICAL REACTIONS:

Triphenylmethyl free radical is long life free radical since it produce a lot more other free radicals before the termination.

28.5.2 SHORT LIFE FREE RADICAL REACTIONS:

I. COUPLING REACTION (TERMINATION): two similar or dissimilar free radicals combine to give a stable product e.g.

II. PROPAGATION REACTION: in these reactions free radicals attack the substrate to form another free radical. The types are given as:

   a) DISPLACEMENT REACTION: It is that reaction in which a free radical displaces one atom to form or generate another free radical.

   b) ADDITION REACTION: Addition of a free radical to an unsaturated compound or that compound which can absorb the free radical.

   c) REARRANGEMENT: The rearrangement of a free radical gives another free radical.

   d) FRAGMENTATION: It gives another free radical.

28.6 APPLICATIONS/ IMPORTANCE:

- Free radical polymerization is a key synthesis route for obtaining a wide variety of different polymers and material composites.
- Antioxidants are molecules which can safely interact with free radicals and terminate the chain reaction before vital molecules are damaged.

Chapter 29 ALCOHOL, PHENOL AND ETHERS

All three molecules are derivatives of water

Alcohol, Phenol and Ethers are regarded as derivatives of water and are produced by replacing hydrogen with Aryl or Alkyl groups. Alcohol and Phenol are regarded as hydroxyl derivatives of Aliphatic or Aromatic hydrocarbons.

Chapter 30 ALCOHOL

30.1.1 NOMENCLATURE

Number of 'C' atoms	Word root	IUPAC name	Structure	Molecular formula
1	Meth	Methane	CH_4	CH_4
2	Eth	Ethane	$CH_3—CH_3$	C_2H_6
3	Prop	Propane	$CH_3—CH_2—CH_3$	C_3H_8
4	But	Butane	$CH_3—(CH_2)_2—CH_3$	C_4H_{10}
5	Pent	Pentane	$CH_3—(CH_2)_3—CH_3$	C_5H_{12}
6	Hex	Hexane	$CH_3—(CH_2)_4—CH_3$	C_6H_{14}
7	Hept	Heptane	$CH_3—(CH_2)_5—CH_3$	C_7H_{16}
8	Oct	Octane	$CH_3—(CH_2)_6—CH_3$	C_8H_{18}
9	Non	Nonane	$CH_3—(CH_2)_7—CH_3$	C_9H_{20}
10	Dec	Decane	$CH_3—(CH_2)_8—CH_3$	$C_{10}H_{22}$

30.2 COMMON NAMES

Chemical Formula	IUPAC Name	Common Name
Monohydric alcohols		
CH_3OH	Methanol	Wood alcohol
C_2H_5OH	Ethanol	Alcohol
C_3H_7OH	Isopropyl alcohol	Rubbing alcohol
C_4H_9OH	Butyl alcohol	Butanol
$C_5H_{11}OH$	Pentanol	Amyl alcohol
$C_{16}H_{33}OH$	Hexadecan-1-ol	Cetyl alcohol
Polyhydric alcohols		
$C_2H_4(OH)_2$	Ethane-1,2-diol	Ethylene glycol
$C_3H_6(OH)_2$	Propane-1,2-diol	Propylene Glycol
$C_3H_5(OH)_3$	Propane-1,2,3-triol	Glycerol
$C_4H_6(OH)_4$	Butane-1,2,3,4-tetraol	Erythritol, Threitol
$C_5H_7(OH)_5$	Pentane-1,2,3,4,5-pentol	Xylitol
$C_6H_8(OH)_6$	Hexane-1,2,3,4,5,6-hexol	Mannitol, Sorbitol
$C_7H_9(OH)_7$	Heptane-1,2,3,4,5,6,7-heptol	Volemitol
Unsaturated aliphatic alcohols		
C_3H_5OH	Prop-2-ene-1-ol	Allyl alcohol
$C_{10}H_{17}OH$	3,7-Dimethylocta-2,6-dien-1-ol	Geraniol
C_3H_3OH	Prop-2-in-1-ol	Propargyl alcohol
Alicyclic alcohols		
$C_6H_6(OH)_6$	Cyclohexane-1,2,3,4,5,6-hexol	Inositol
$C_{10}H_{19}OH$	2 - (2-propyl)-5-methyl-cyclohexane-1-ol	Menthol

30.3 PREPARATION:

HYDROLYSIS OF ALKYL HALIDE

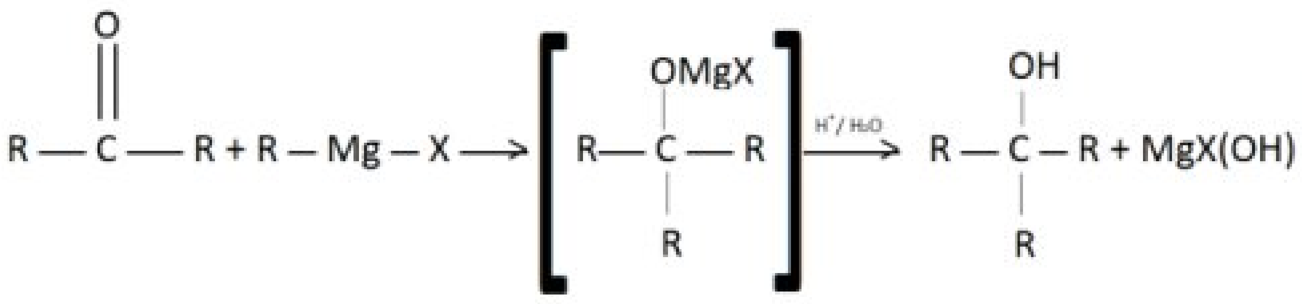
$$R — X + NaOH \xrightarrow[\triangle]{H_2O} R — OH + NaX$$

$$CH_3 — Cl + NaOH \xrightarrow[\triangle]{H_2O} CH_3 — OH + NaCl$$

HYDRATION OF ALKENES

$$CH_2 = CH_2 + H_2O \xrightarrow{H_2SO_4} CH_3 — CH_2 — OH$$

GRIGNARD REAGENT



$$R — \overset{\overset{O}{\|}}{C} — R + R — Mg — X \longrightarrow \left[R — \underset{R}{\overset{OMgX}{\overset{|}{\underset{|}{C}}}} — R \right] \xrightarrow{H^+/H_2O} R — \underset{R}{\overset{OH}{\overset{|}{\underset{|}{C}}}} — R + MgX(OH)$$

30.4 Properties:

30.4.1.1 Physical

- Lower alcohols are colourless, toxic liquids. They have characteristic smell.
- Boiling Point increase with increase in number of carbon atoms and decreases as branch increases.

30.4.1.2 Chemical

30.4.2 Reaction with Active Metals

$$R-OH + 2Na \longrightarrow RONa + H_2$$

30.4.3 Reaction with Phosphorous Pentahalide

$$R-OH + PX_5 \longrightarrow R-X + POX_3 + HX$$

30.4.4 Reaction with Phosphorous Trihalide

$$3R-OH + PX_3 \longrightarrow 3R-X + H_3PO_3$$

30.4.5 Reaction with Thionyl Chloride

$$R-OH + SOCl_2 \longrightarrow R-Cl + SO_2 + HCl$$

30.4.6 Dehydration of Alcohol

$$CH_3-CH_2-OH + OH-CH_2-CH_3 \xrightarrow[H_2SO_4]{140^\circ C} CH_3-CH_2-O-C_2H_5$$

30.4.7 Test for OH (Lucas Test)

$$R-OH + HCl \xrightarrow{ZnCl_2} R-Cl + H_2O$$

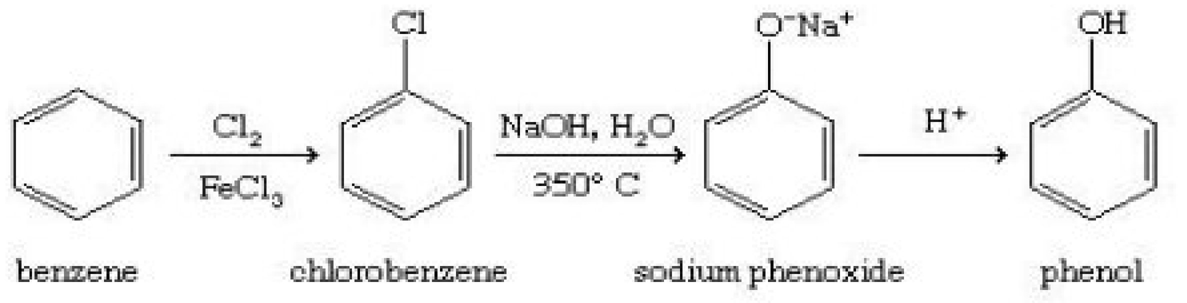
30.5 Uses of Alcohol

- Methyl alcohol is used in making of alcoholic beverage, industrial solvents, manufacturing of drugs, flavouring extracts and perfumes.
- It is used as anti-septic and anti-freeze in automobile radiators.
- Liquor in varnish
- As a fuel (Methanol again burns to form carbon dioxide and water)

Chapter 31 PHENOL

PREPARATION:

DOW'S METHOD:



FROM COAL TAR: Coal Tar provides a natural source of phenol and also contains naphthalene.

STEP 1: $C_6H_5OH + NaOH \rightarrow C_6H_5ONa + H_2O$

STEP 2: $C_6H_5ONa + CO_2 + H_2O \rightarrow C_6H_5OH + Na_2CO_3$

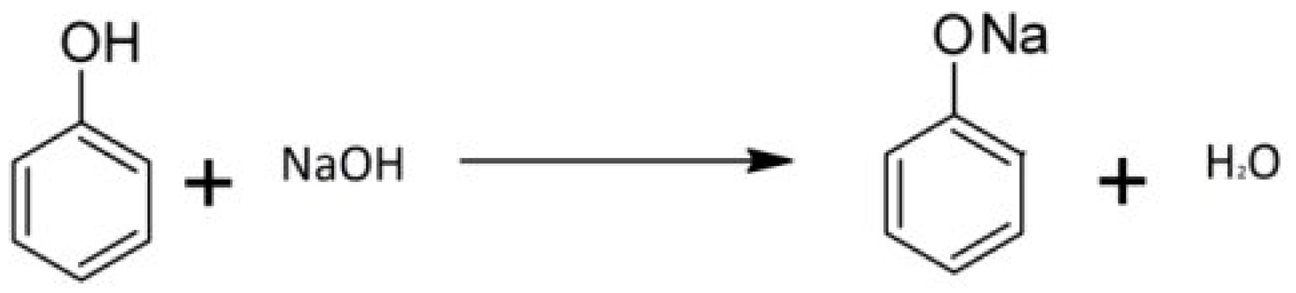
31.1.1 PROPERTIES

PHYSICAL PROPERTIES:

- Colourless, hygroscopic, crystalline solid and 5% sol. Of it is called as "Carbolic Acid" and it turns pink on exposure to air and light.

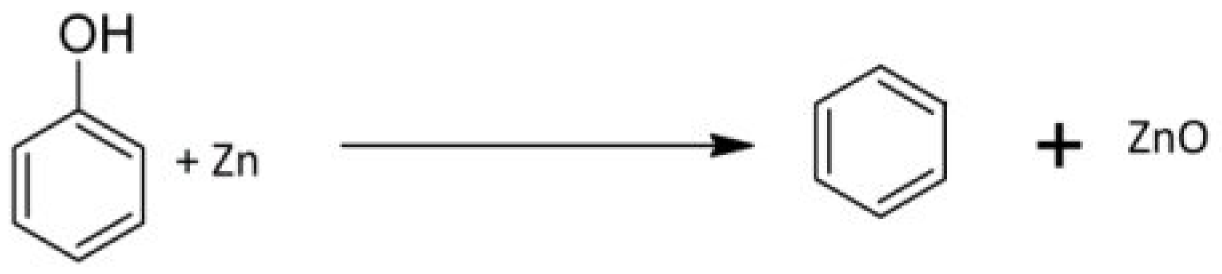
31.1.2 CHEMICAL PROPERTIES:

SALT FORMATION:

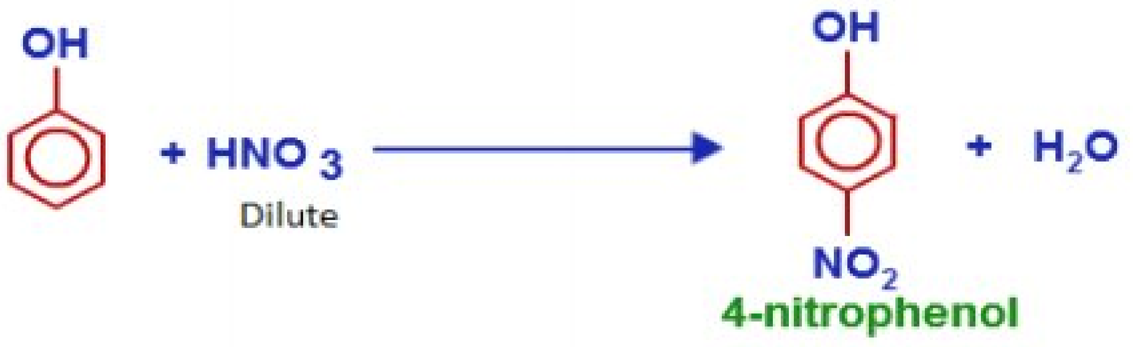


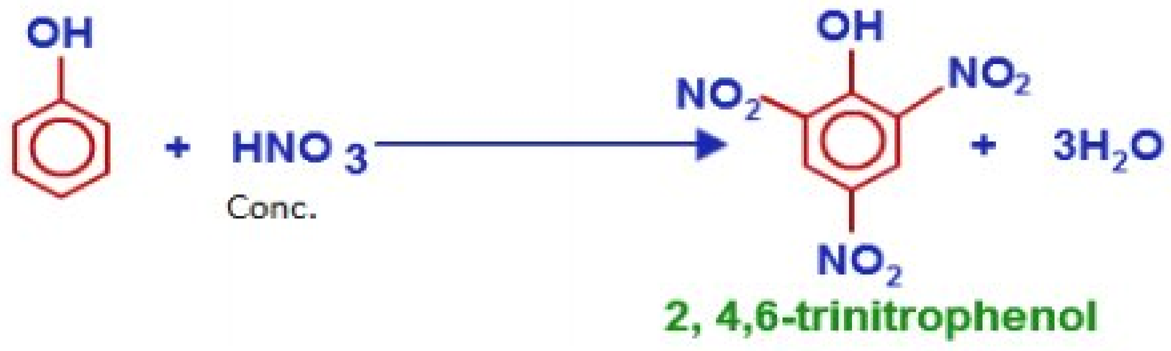
REACTION WITH FECL3: Phenol gives purple colouration with one or two drops of natural ferric chloride soln. to form complex

REACTION WITH ZNO:



31.1.5 NITRATION:

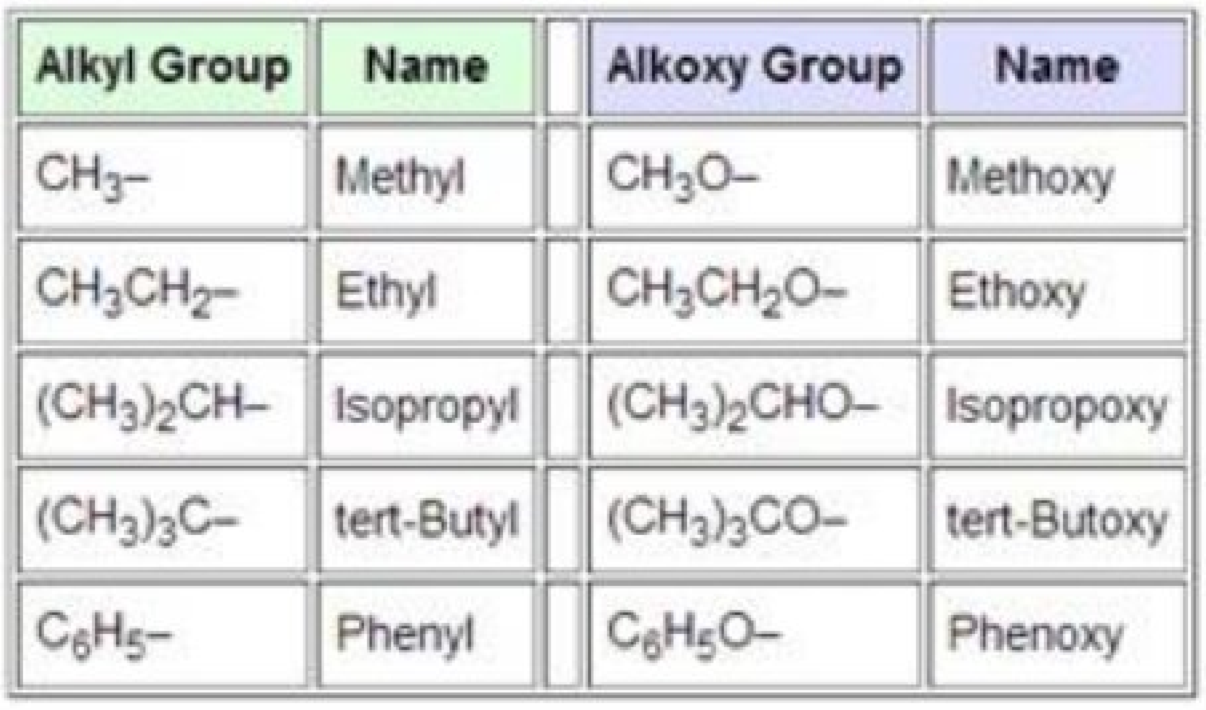




31.1.6 USES:

- Phenol formaldehyde resin is called Backelite
- Starting drug for Aspirin exclusive picric acid
- Wood preservative
- Herbicid

Chapter 32 ETHERS



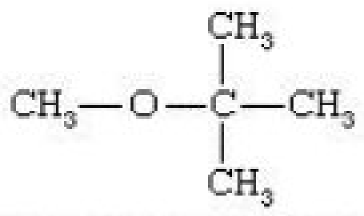
Alkyl Group	Name		Alkoxy Group	Name
$CH_3–$	Methyl		$CH_3O–$	Methoxy
$CH_3CH_2–$	Ethyl		$CH_3CH_2O–$	Ethoxy
$(CH_3)_2CH–$	Isopropyl		$(CH_3)_2CHO–$	Isopropoxy
$(CH_3)_3C–$	tert-Butyl		$(CH_3)_3CO–$	tert-Butoxy
$C_6H_5–$	Phenyl		$C_6H_5O–$	Phenoxy

$CH_3CH_2—O—CH_2CH_3$

common name: diethyl ether
(ethyl ether or "ether")
IUPAC name: ethoxyethane

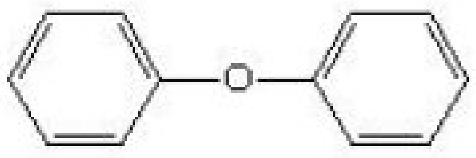
$CH_3—O—CH_2CH_3$

methyl ethyl ether
or ethyl methyl ether
methoxyethane



$CH_3—O—C(CH_3)_2—CH_3$

common name: methyl-*t*-butyl ether
(MTBE)
IUPAC name: 2-methoxy-2-methylpropane



diphenyl ether
or phenyl ether
phenoxybenzene

32.1 PREPARATION

32.1.1 DEHYDRATION OF ALCOHOL

$$R–OH + OH–R \xrightarrow[H_2SO_4]{140^\circ C} R–O–R + H_2O$$

$$CH_3–CH_2–OH + OH–CH_2–CH_3 \xrightarrow[H_2SO_4]{140^\circ C} CH_3–CH_2–O–C_2H_5$$

32.1.2 WILLIAMSON SYNTHESIS

$$RO^-Na^+ + R'X \xrightarrow{-NaX} R–O–R'$$

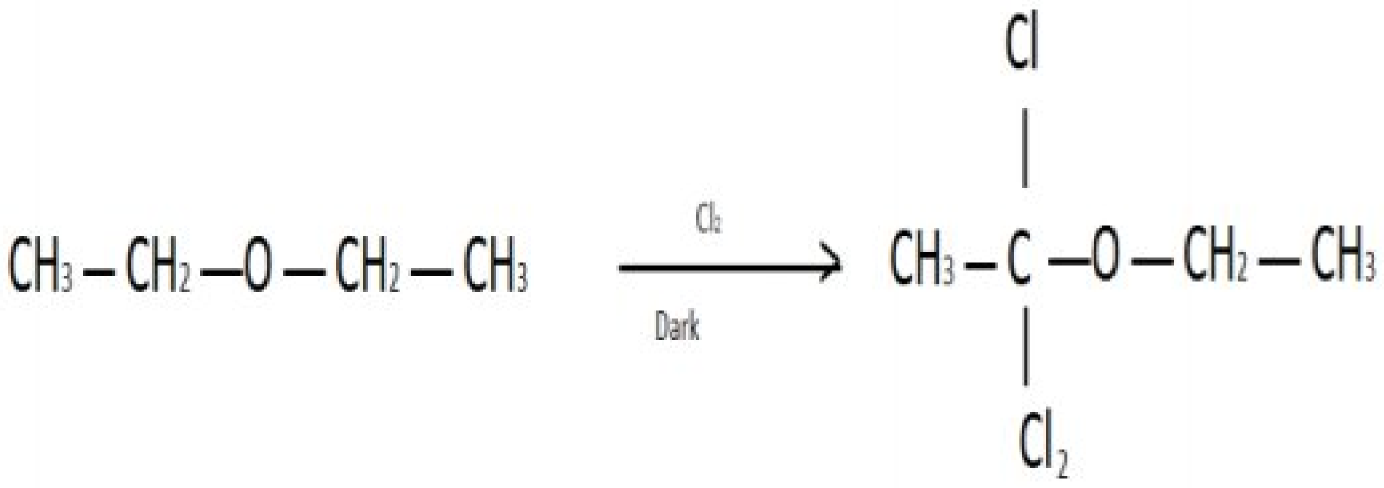
PROPERTIES:

PHYSICAL PROPERTIES:

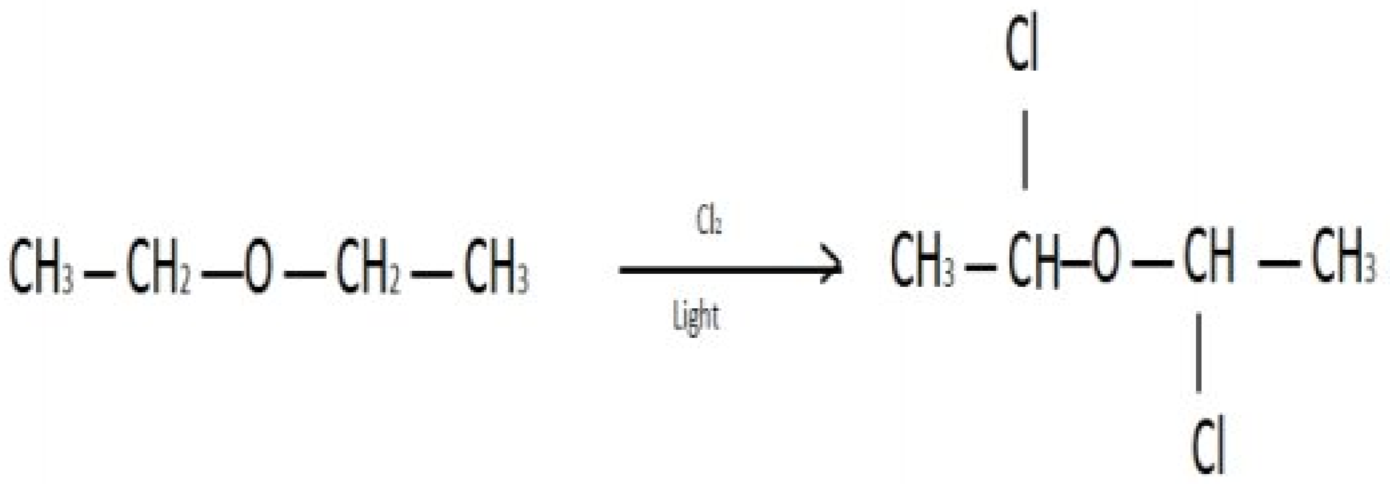
- Dimethyl ether, Ethyl methyl ether are gas and other ethers are highly volatile and gas.
- Slightly soluble in water

32.2 CHEMICAL PROPERTIES:

HALOGENATION: Halogenation is frequently taking place at α-carbon

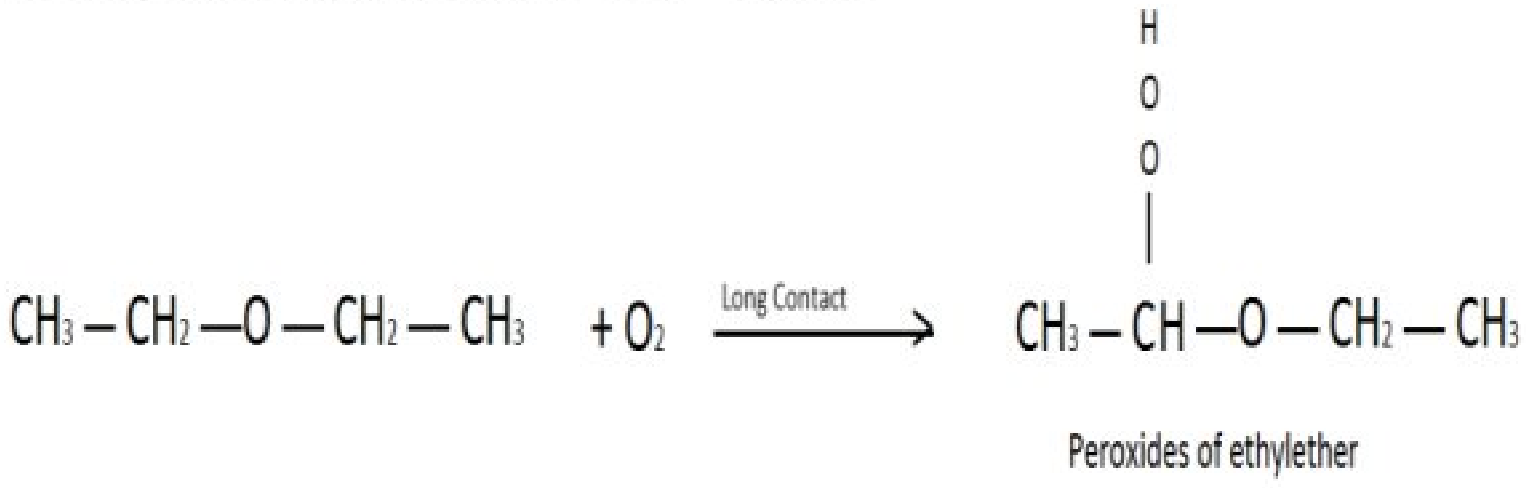


$$CH_3–CH_2–O–CH_2–CH_3 \xrightarrow[Dark]{Cl_2} CH_3–\underset{Cl_2}{\overset{Cl}{C}}–O–CH_2–CH_3$$



$$CH_3–CH_2–O–CH_2–CH_3 \xrightarrow[Light]{Cl_2} CH_3–\overset{Cl}{CH}–O–\underset{Cl}{CH}–CH_3$$

32.2.1 Formation of per-oxide



$$CH_3–CH_2–O–CH_2–CH_3 + O_2 \xrightarrow{Long\ Contact} CH_3–\overset{HOO}{CH}–O–CH_2–CH_3$$

Peroxides of ethylether

32.2.2 HYDROLYSIS

$$CH_3–CH_2–O–C_2H_5 + H_2O \xrightarrow[\Delta]{H^+} 2\,CH_3–CH_2–OH$$

32.2.3 USES

- Diethyl ether is used as general anesthesia but it is replaced by Halothane.
- It is used as a solvent in Grignard Reagent

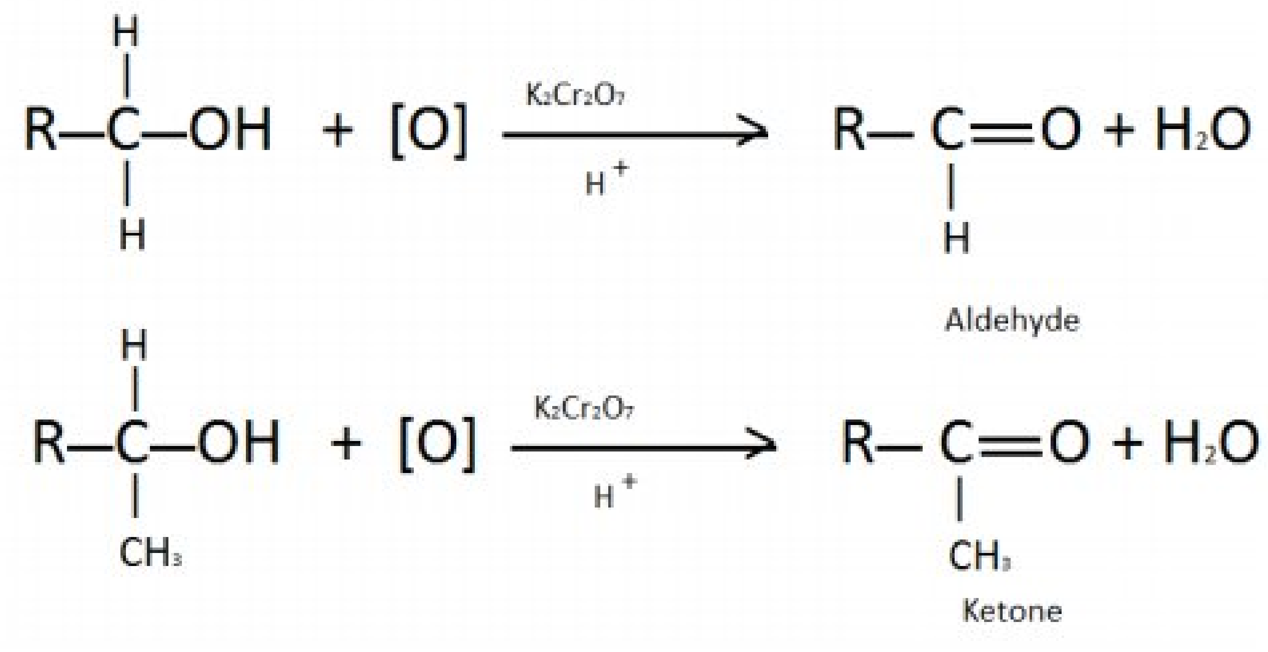
Chapter 33 ALDEHYDE AND KETONES

Aldehyde and Ketone possess a carbon to oxygen double bond; this unit is referred to as carbonyl group. They are collectively called as carbonyl compounds.

In aldehyde, carbonyl group is added to alkyl while in ketone, carbonyl group is added to two alkyl groups on both sides.

33.1 METHODS OF PREPARATION

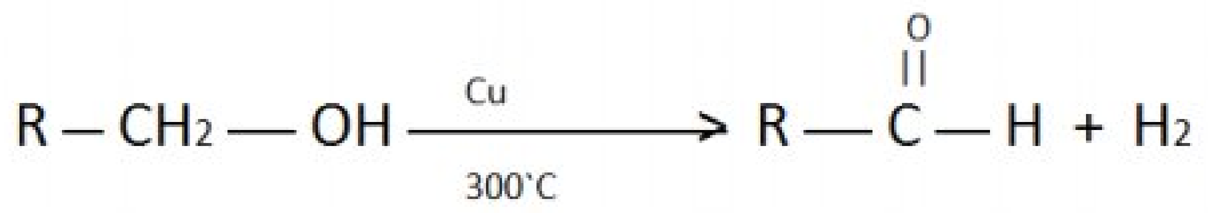
OXIDATION OF ALCOHOL:



$$R-\underset{H}{\overset{H}{C}}-OH + [O] \xrightarrow[H^+]{K_2Cr_2O_7} R-\underset{H}{C}{=}O + H_2O$$

$$R-\underset{CH_3}{\overset{H}{C}}-OH + [O] \xrightarrow[H^+]{K_2Cr_2O_7} R-\underset{CH_3}{C}{=}O + H_2O$$

33.2 CATALYTIC REHYDRATION OF ALCOHOL:



$$R-CH_2-OH \xrightarrow[300^{\circ}C]{Cu} R-\overset{O}{\overset{\|}{C}}-H + H_2$$

33.3 HYDRATION OF ALKYNE:

$$HC{\equiv}CH + HOH \xrightarrow[H_2SO_4]{HgSO_4} CH_2{=}CH{-}OH \rightarrow CH_3CHO$$

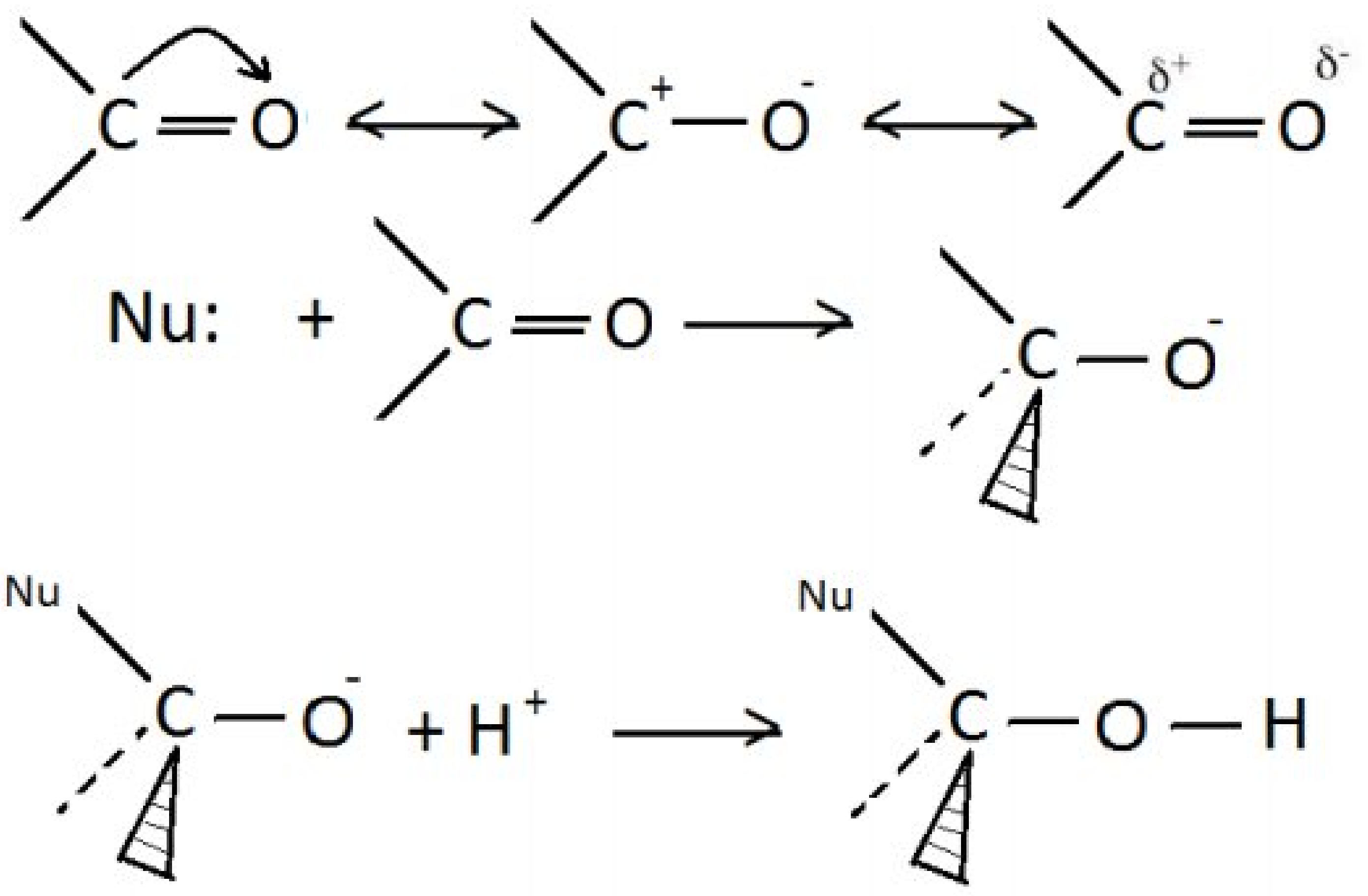
33.4 PROPERTIES

33.4.1 PHYSICAL PROPERTIES:

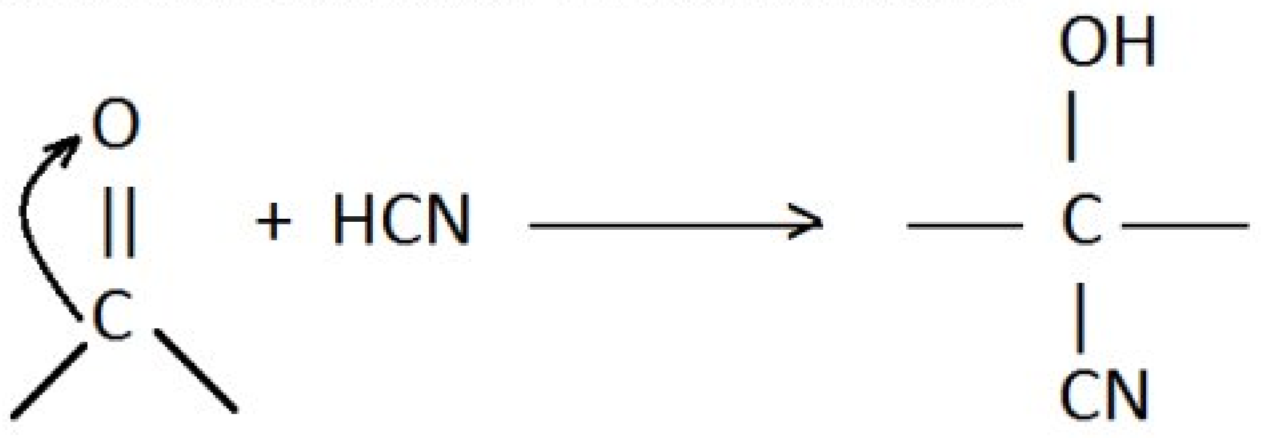
- Formaldehyde is a gas at room temperature
- Acetaldehyde boils at 20 ^{0}C
- Density of these two are less than water

33.4.2 CHEMICAL PROPERTIES

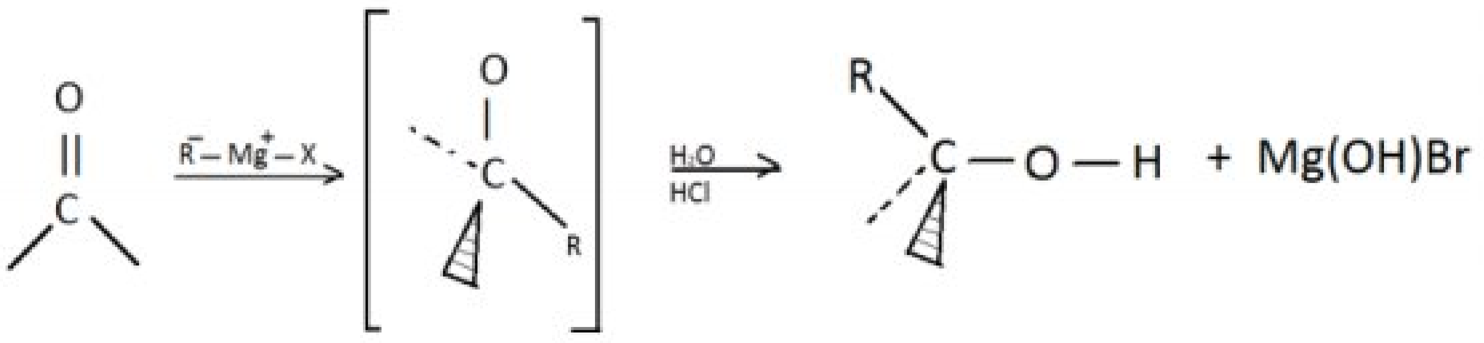
33.4.2.1 NUCLEOPHILIC ADDITION REACTION



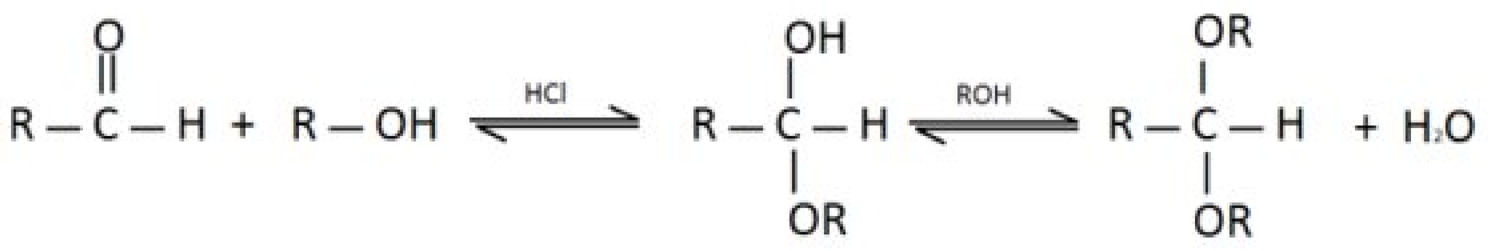
33.4.2.2 ADDITION OF HYDROGENCYANIDE



33.4.2.3 REACTION WITH GRIGNARD REAGENT



33.4.2.4 ADDITION OF ALCOHOL



$$R-\overset{O}{\overset{\|}{C}}-H + R-OH \overset{HCl}{\rightleftharpoons} R-\underset{OR}{\overset{OH}{C}}-H \overset{ROH}{\rightleftharpoons} R-\underset{OR}{\overset{OR}{C}}-H + H_2O$$

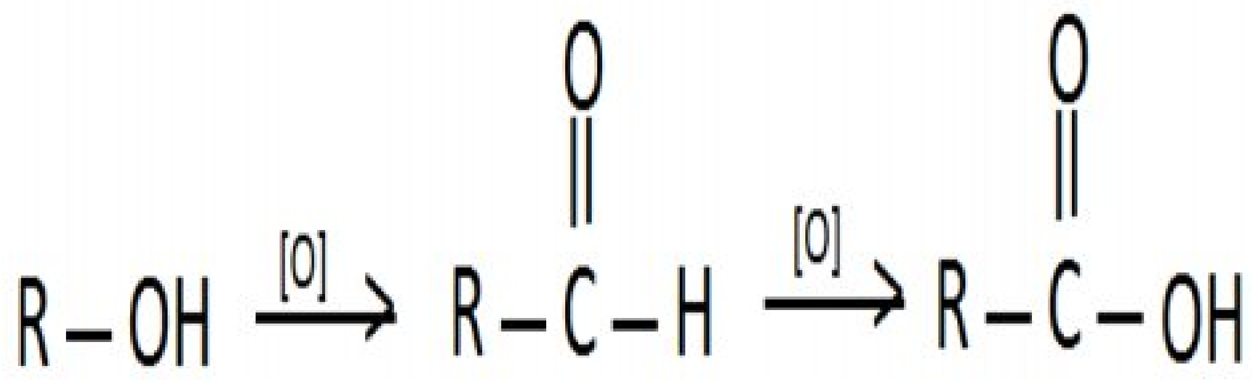
33.4.3 USES

- Formalin is used as general antiseptic and is made by 40% soln. of formaldehyde
- Acetaldehyde is used in the manufacturing of acetic acid, acetanhydride and dyes while acetone is used as a solvent for acetylene, cellulose derivative, varnish and resin.

Chapter 34 CARBOXYLIC ACID

34.1 PREPARATION:

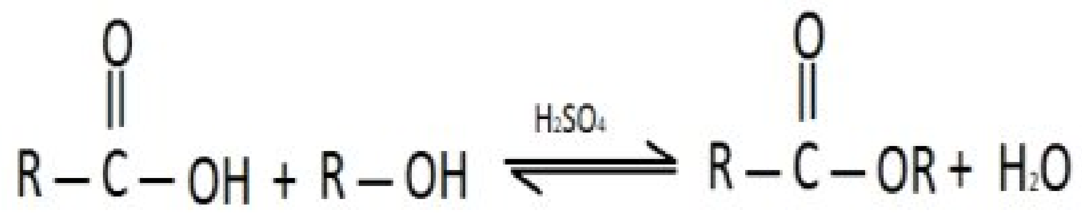
34.1.1 OXIDATION OF ALCOHOL



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

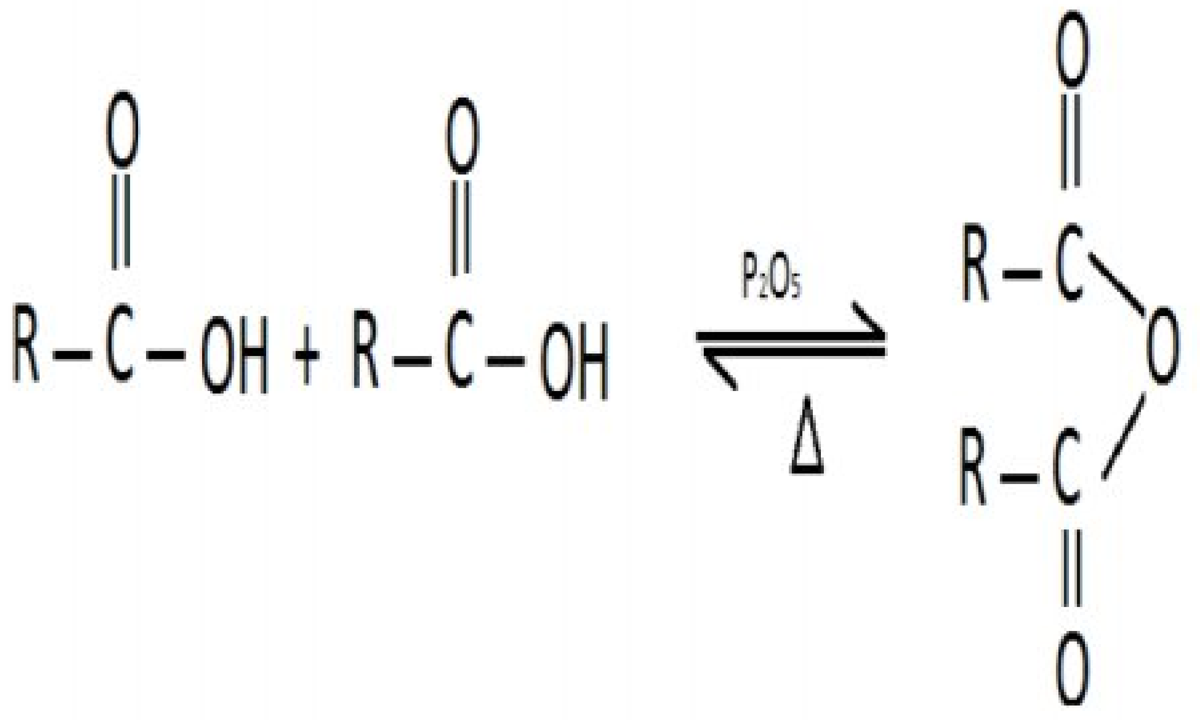
34.2 REACTION

34.2.1 ESTERIFICATION



$$R-\overset{\overset{O}{\|}}{C}-OH + R-OH \overset{H_2SO_4}{\rightleftharpoons} R-\overset{\overset{O}{\|}}{C}-OR + H_2O$$

34.2.1.1 FORMATION OF ANHYDRIDES



$$R-\overset{\overset{O}{\|}}{C}-OH + R-\overset{\overset{O}{\|}}{C}-OH \underset{\Delta}{\overset{P_2O_5}{\rightleftharpoons}} \begin{array}{l} R-\overset{\overset{O}{\|}}{C}\searrow \\ \qquad O \\ R-\underset{\underset{O}{\|}}{C}\nearrow \end{array}$$

34.3 USES

- Formic Acid is used as textile dying
- Coagulant for rubber
- Leather tanning
- The treatment of Gout (arthritic type)
- Acetic acid is used in manufacturing of white vinegar, cellulose acetate and polyvinyl acetate.

Chapter 35 AMIDE AND AMINE

35.1 AMINE

Amines are derivatives of Ammonia in which one or more hydrogen have been replaced by alkyl or aryl group. They are classified as primary, secondary or tertiary depending upon the number of groups attached to the nitrogen atom.

35.1.1 PRIMARY:

$$CH_3I + NH_3 \longrightarrow CH_3NH_2$$

35.1.2 SECONDARY:

$$CH_3NH_2 + CH_3I \longrightarrow (CH_3)_2NH$$

35.1.3 TERTIARY:

$$(CH_3)_2NH + CH_3I \longrightarrow (CH_3)_3N:$$

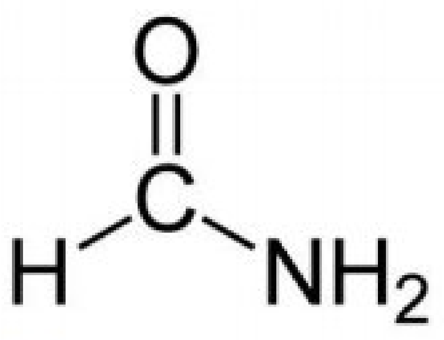
35.1.4 QUATERNARY:

$$(CH_3)_3N: + CH_3I \longrightarrow [(CH_3)_4N^+]I^-$$

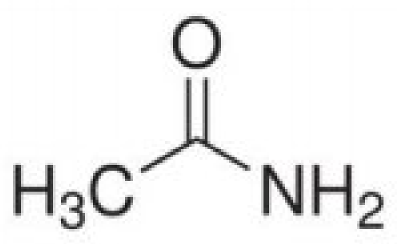
Quaternary Salt/Amine
Tetramethylammonium iodide

35.2 AMIDES

Amides are derivatives of Ammonia in which one or more hydrogen is replaced by electron deficient group (electrophile)



formamide



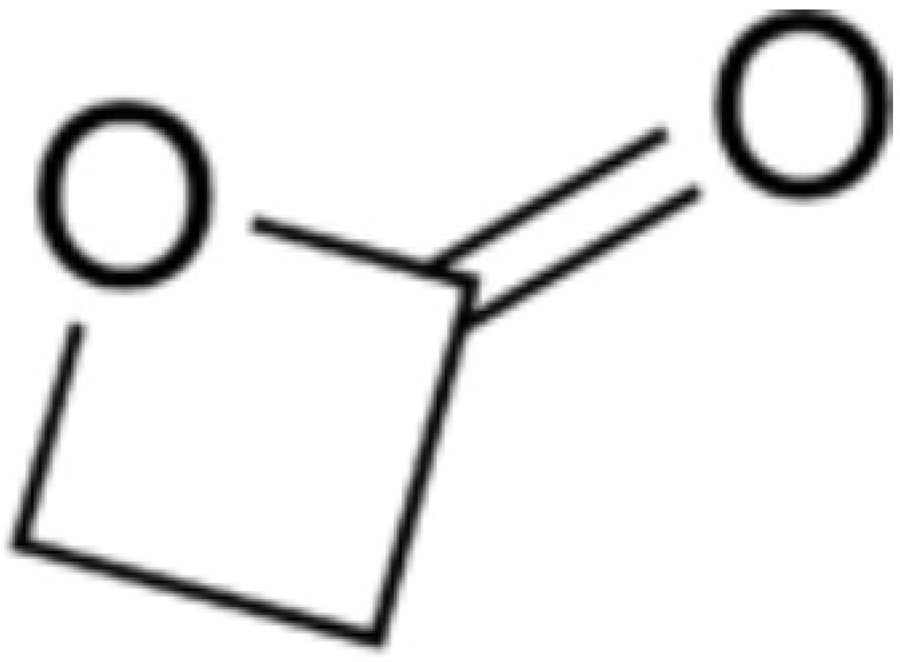
acetamide

Chapter 36 LACTONES

Cyclic ketones give cyclic esters which are called as Lactones.

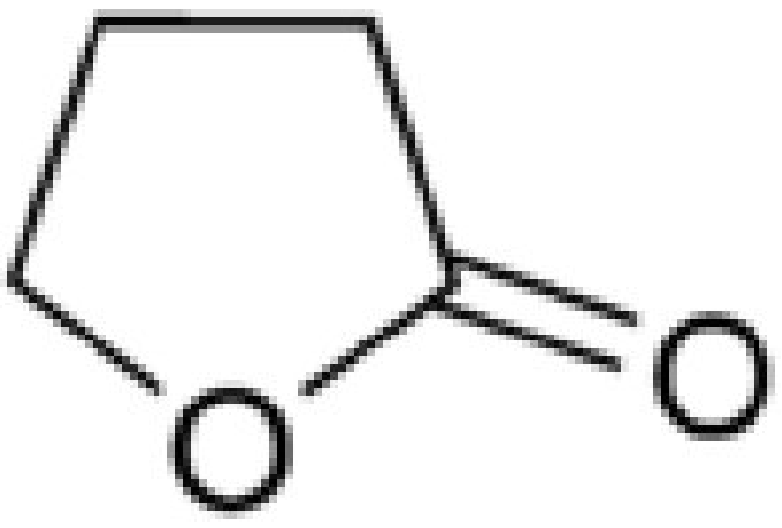
36.1 EXAMPLES:

1)



β-propiolactone

2)



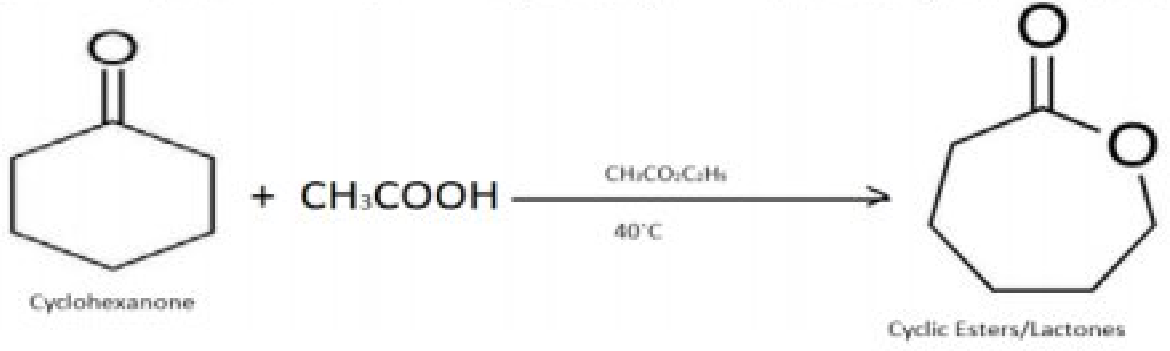
γ-butyrolactone

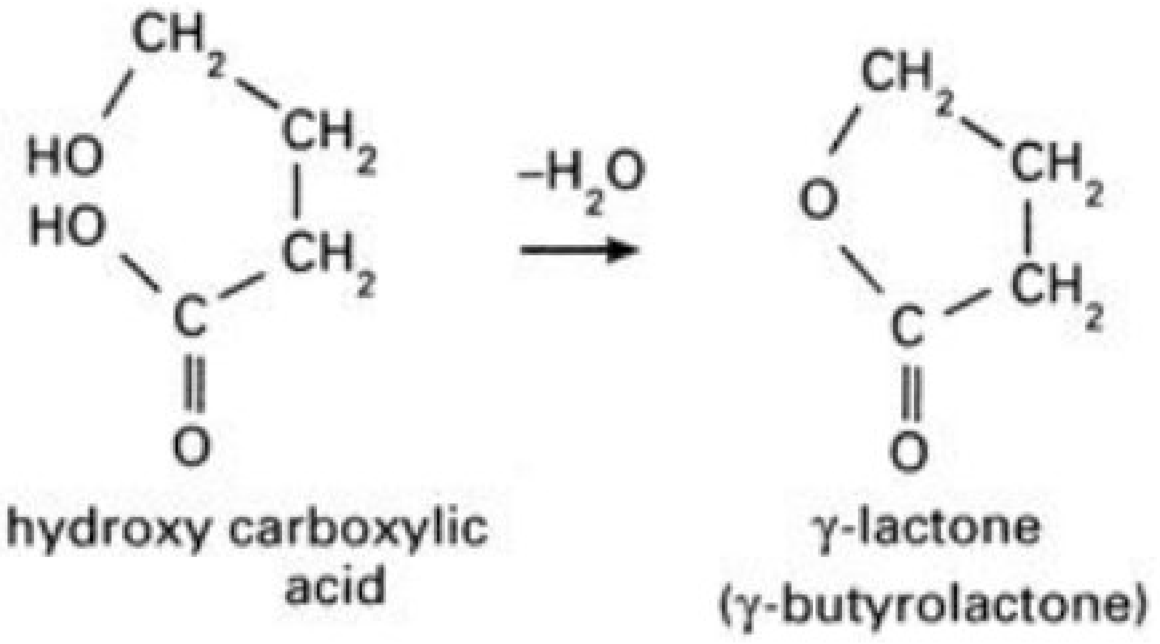
36.2 NATURAL SOURCES

Lactones (specifically 3-methyl-4-octanolide) are found in oak trees as well as many other plants, and impart flavour to whiskey and some red wines.

If both hydroxyl and carboxyl group are present in the same molecule and are substituted with respect to each other, the molecule undergoes intramolecular modification to form cyclic esters, commonly known as Lactones. The most common lactones are with 5 or 6 members.

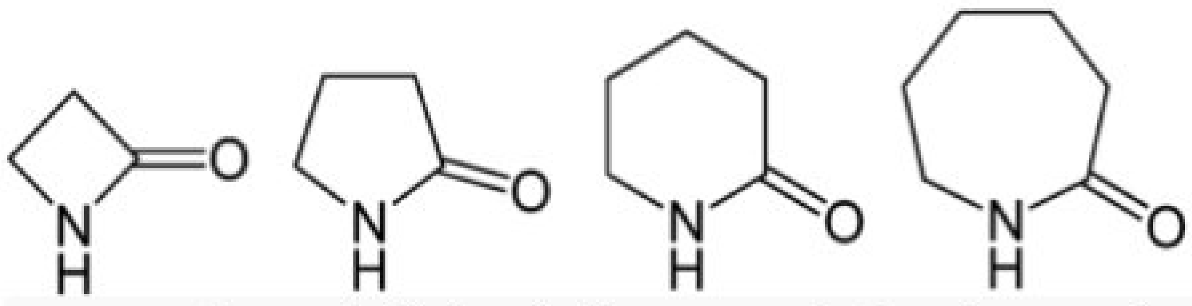
Lactones are hydrolysed by aqueous base to yield open chain of hydroxyl carboxylic acid.





Chapter 37 LACTAM

A lactam is a cyclic amide. Prefixes indicate how many carbon atoms (apart from the carbonyl moiety) are present in the ring: β-lactam (2 carbon atoms outside the carbonyl, 4 ring atoms in total), γ-lactam (3 and 5 total), δ-lactam (4 and 6 total).



From left to right, general structures of a β-lactam, a γ-lactam, a δ-lactam and an ε-lactam.

Chapter 38 DIAZONIUM ION & DIAZONIUM SALT

38.1 DEFINITION:

It is an important class of compound i.e characterized by presence of dizonium ion (+N≡N) i.e directly bounded to alkyl (R-) or Aryl (Ar-). These alkyl or aryl diazonium ion forms a salt with anions such as halogens (X^{-}). These species are called as diazonium salt (which is a stable salt).

DIAZOTIZATION:

The reaction of primary amine with nitrous acid to form a diazonium salt is called "Diazotization"

38.2 CONDITIONS FOR DIAZOTIZATION:

This reaction is carried out in the absence of light at a temperature of 0-5 °C.

38.3 MECHANISM:

38.3.1 1: FORMATION OF NITROUS ACID:

Nitrous Acid is prepared is prepared in reaction mixture by treating sodium nitrate by aqueous solution of strong acid.

$$\mathrm{NaO-N{=}O + HCl \longrightarrow NaCl + \underset{\text{Nitrous acid}}{H-O-N{=}O}}$$

38.3.2 2: REACTION WITH AMINES:

Primary Amines react with Nitrous Acid to form Diazonium salt.

$$\mathrm{2R-NH_2 + HNO_2 \longrightarrow R-N^{+}{\equiv}N + 2H_2O}$$

38.3.3 OVERALL REACTION:

$$\mathrm{R-NH_2 + NaNO_2 + 2HCl \longrightarrow R-N^{+}{\equiv}NCl + 2H_2O + NaCl}$$

38.4 PREPERATION OF DIAZONIUM SALT:

The primary aliphatic amines react with nitrous acid to give unstable aliphatic diazonium salt. Nitrous acid is weak and unstable acid prepared during the reaction to react with primary amine.

DEGRADATION: Aliphatic diazonium salt is very unstable and decomposes rapidly into carbonium ion and nitrogen molecule.

$$\mathrm{CH_3-CH_2-N^{+}{\equiv}NCl \longrightarrow CH_3-CH_2^{+} + Cl^{\cdot} + N_2}$$

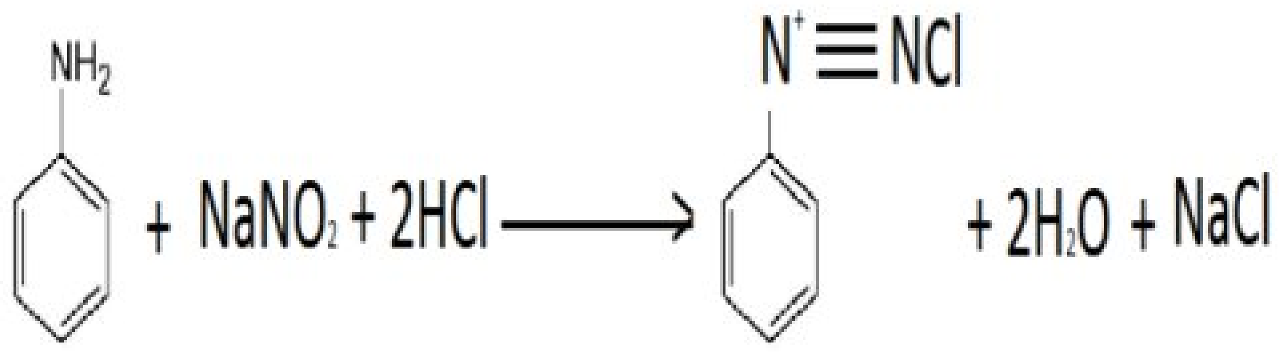
$$\mathrm{CH_3-CH_2^{+} + H_2O \longrightarrow CH_3-CH_2-OH + H^{+}}$$

$$\mathrm{CH_3-CH_2^{+} + Cl^{\cdot} \longrightarrow CH_3-CH_2-Cl}$$

The carrbonium ion may make an alcohol or alkyl halide depending upon its reaction with water or halogens.

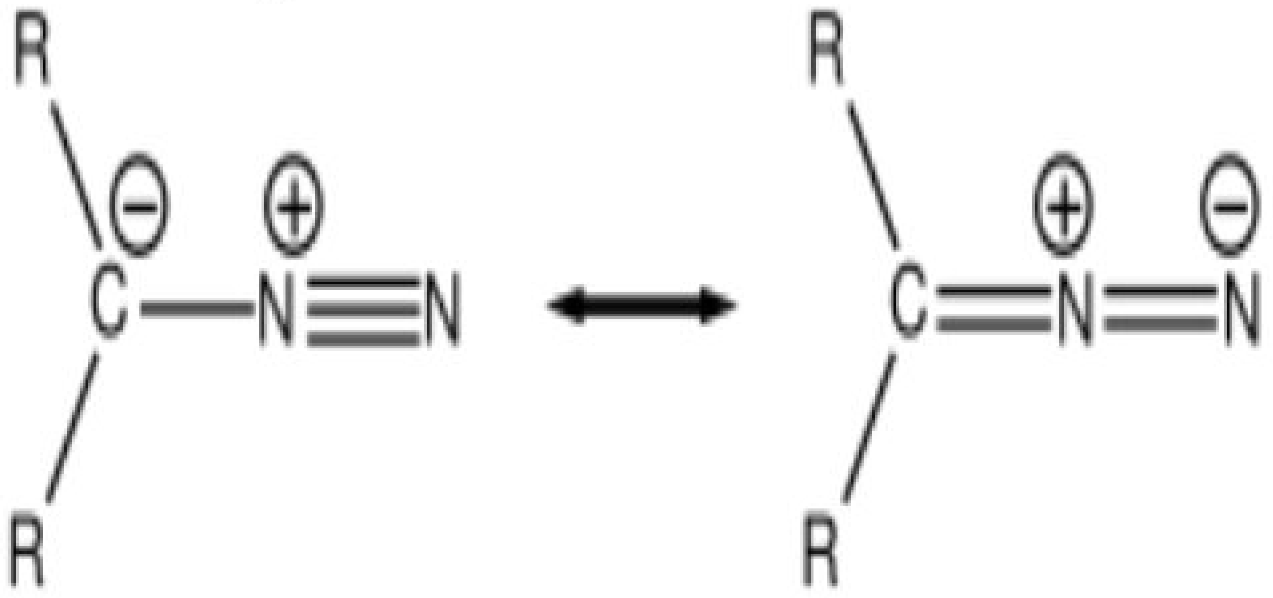
ARYL DIAZONIUM SALT: are prepared by the action of aromatic primary amines (e.g. Aniline) with nitrous acid at 0-5 °C. The nitrous acid forms nitronium ion which reacts with Primary amine to form Diazonium cation.

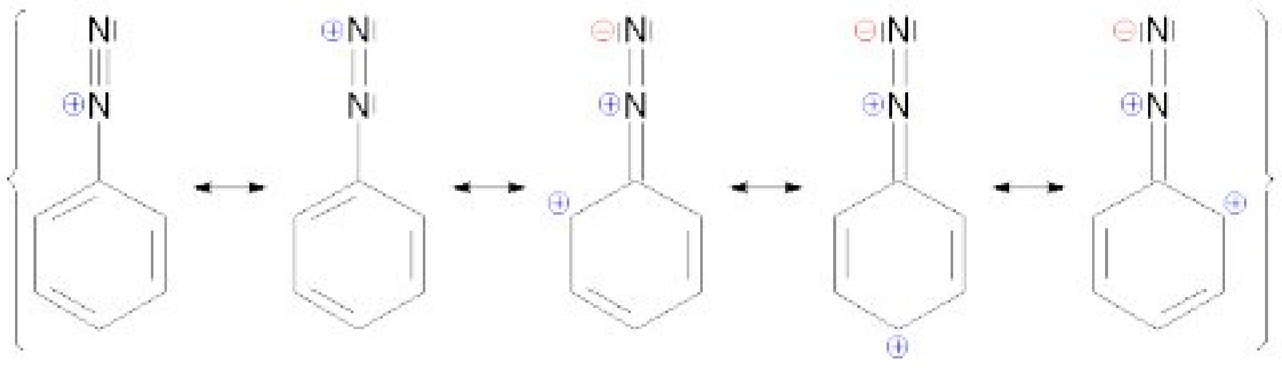
Benzene diazonium salt is prepared by a reaction of aniline with sodium nitrite and HCl at a very low temperature.



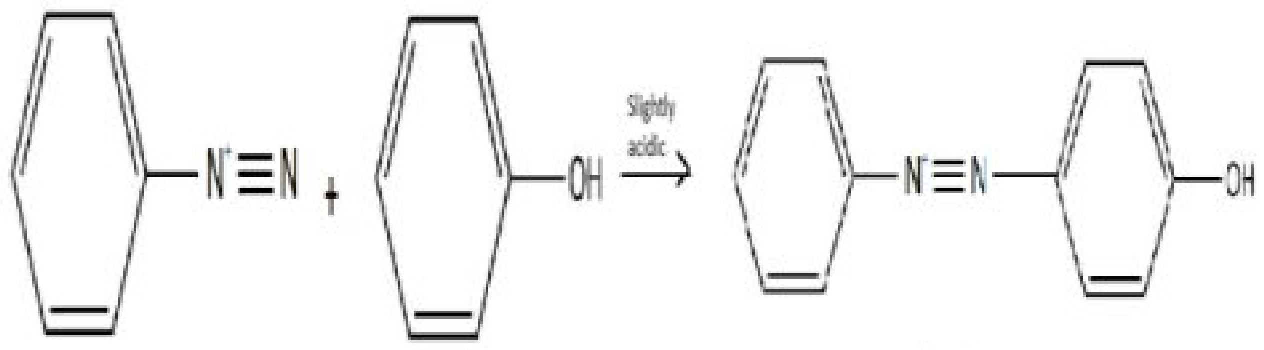
STABILITY: Aromatic diazonium salt is more stable than aliphatic diazonium salt. The relative stability is due to the large number of contributing structures of Resonance hybrid.

e.g. Aliphatic diazonuim salt has only two contributing forms while aromatic has a large number of contributing forms.

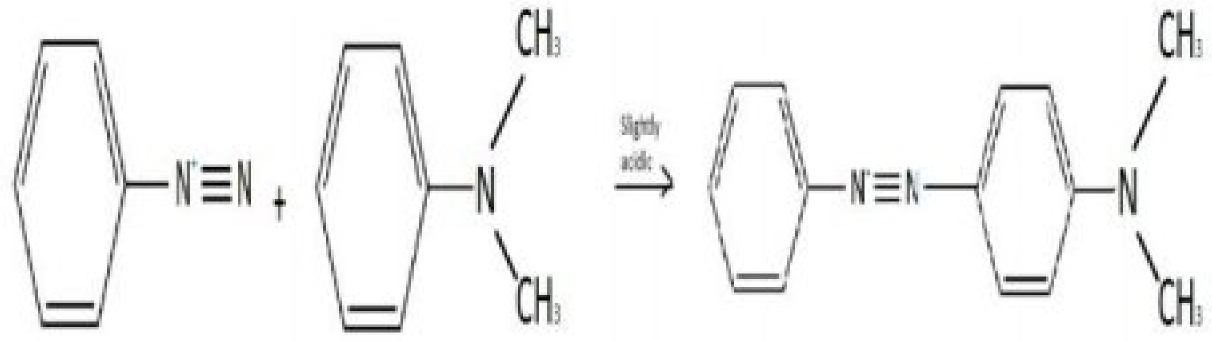




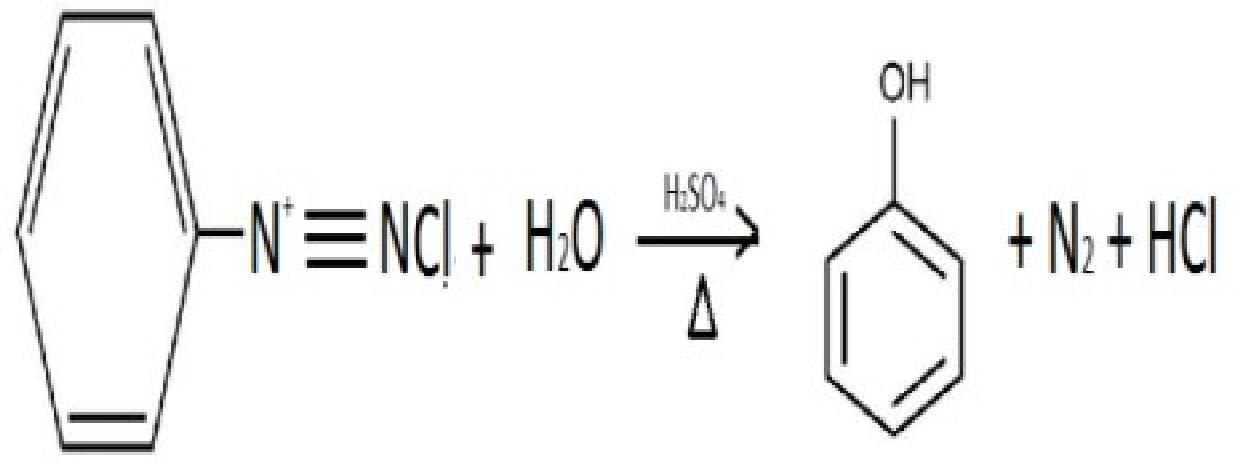
38.5 REACTIONS:



P- Hydroxyazobenzene



P- Dimethylaminoazobenzene



Chapter 39 HETEROCYCLIC COMPOUNDS

39.1 *DEFINITION*

The cyclic organic compounds in which one or more ring atom is/are other than carbon are called Heterocyclic compounds. Nitrogen (N) , Oxygen (O) , Sulphur (S) are most common hetero atoms. Heterocyclic compounds may be classified as Aliphatic or Aromatic. The aliphatic heterocyclic compounds are cyclic analogues of amines, ethers, thioethers, amides etc. While in the aromatic heterocyclic compounds, a hetero atom is fused in the ring and behaves in a similar manner to benzene in most of the properties.

IMPORTANCE

In pharmaceuticals most of the drugs are made up of heterocyles e.g. Penicillin, Quinolone, Ciprofloxacin.

Vitamins also contain Heterocyclic rings e.g. .Ascorbic acid (vitamin C), Pyridoxine(Vitamin B6), Riboflavin (vitamin B2)

Almost all alkaloids are hetero cyclic compounds e.g. Indole alkaloids, Quinine, Phenazine, Cinnoline.

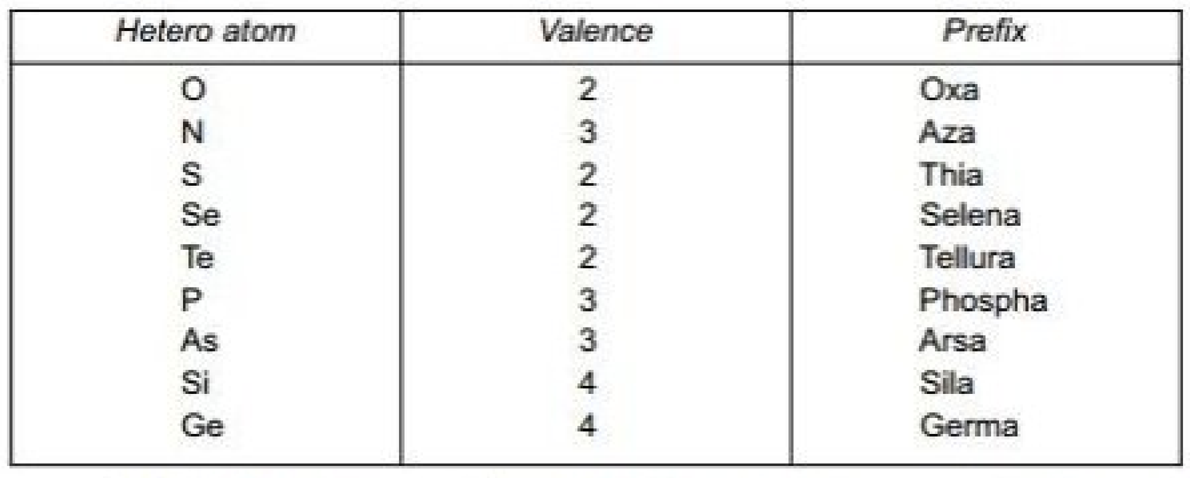
Dyes and ink are made up of substituted pyridine dyes, quinophthalone dyes, tartrazine dyes which are also heterocyclic compounds.

Bases in DNA are one of the factors responsible for genetic intelligence. All these bases are heterocyclic compound which is responsible for genetic character and intelligence.

Hemoglobin (blood) is a metalloprotein which helps in oxygen transport. It contains a quaternary structure with four globular protein subunits. Single globular protein subunit contains iron held in heterocyclic rings called porphyrin ring and imidazole ring.

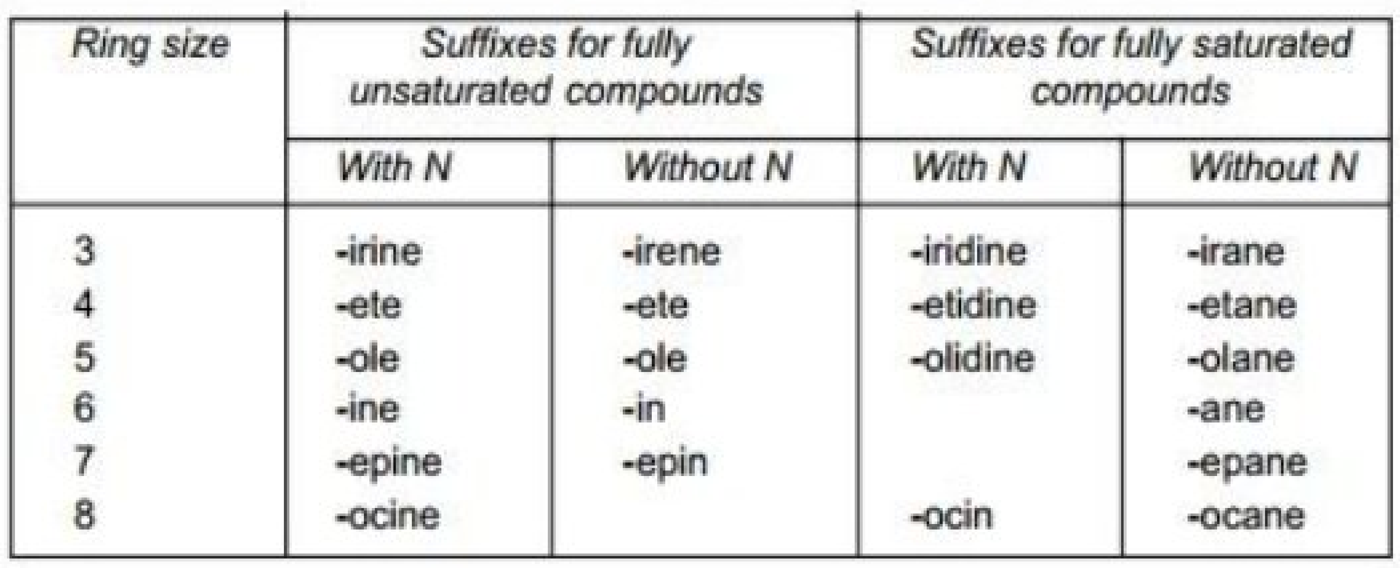
39.2 NOMENCLATURE

Table 1.1 Prefix for Hetero Atoms



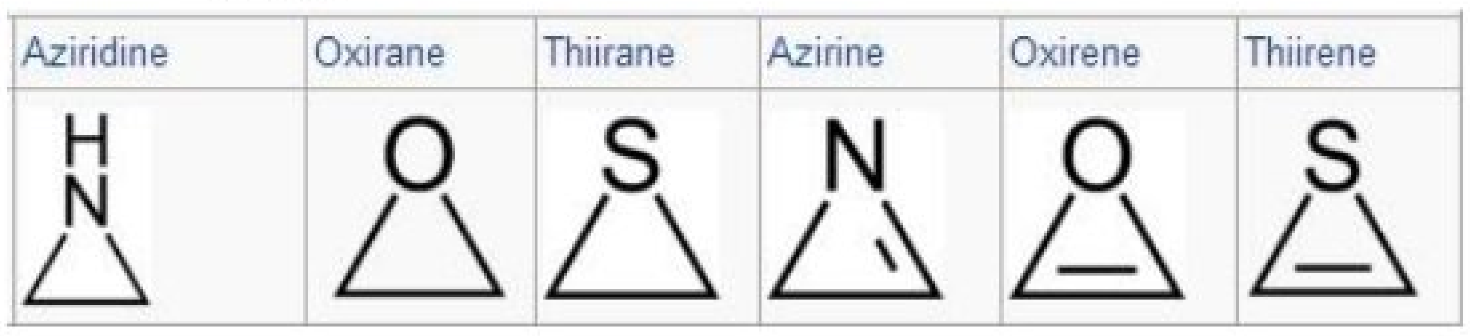
Hetero atom	*Valence*	*Prefix*
O	2	Oxa
N	3	Aza
S	2	Thia
Se	2	Selena
Te	2	Tellura
P	3	Phospha
As	3	Arsa
Si	4	Sila
Ge	4	Germa

Table 1.2 Common Name Endings for Heterocyclic Compounds

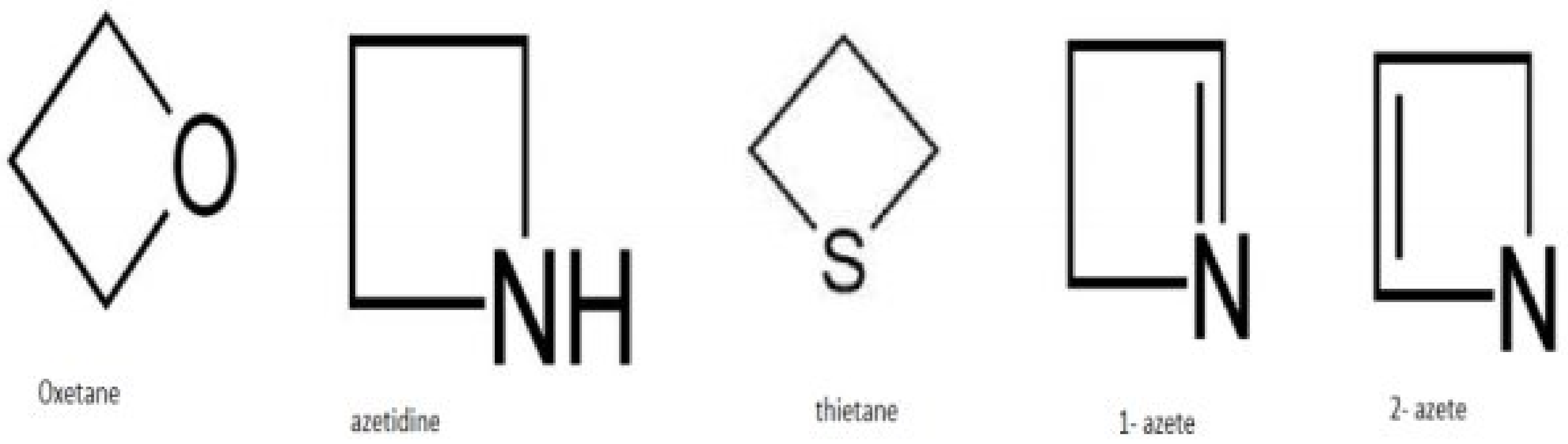


Ring size	*Suffixes for fully unsaturated compounds*		*Suffixes for fully saturated compounds*	
	With N	*Without N*	*With N*	*Without N*
3	-irine	-irene	-iridine	-irane
4	-ete	-ete	-etidine	-etane
5	-ole	-ole	-olidine	-olane
6	-ine	-in		-ane
7	-epine	-epin		-epane
8	-ocine		-ocin	-ocane

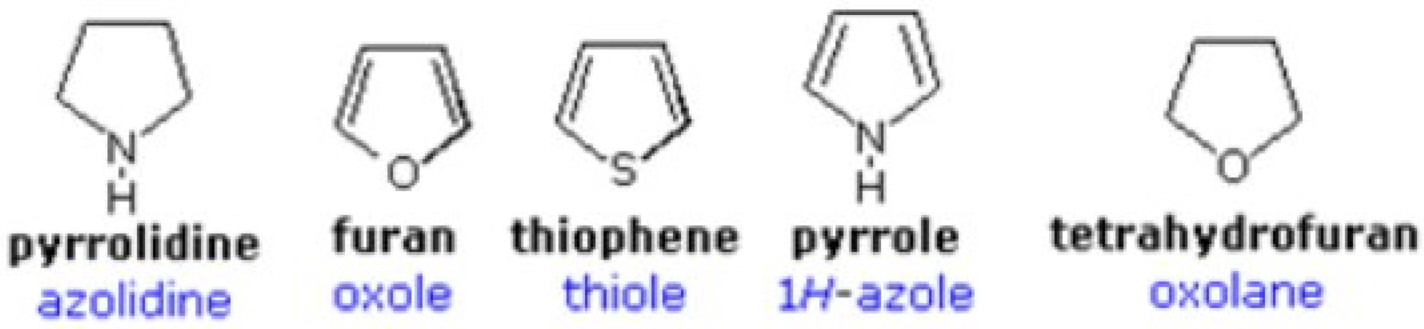
39.2.1 3-MEMBERED RINGS WITH ONE HETERO ATOM



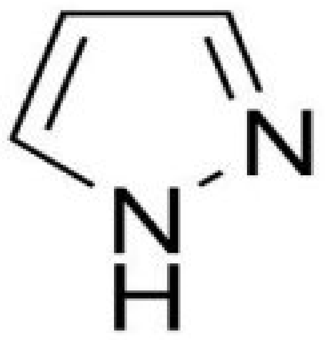
39.2.2 4-MEMBERED RINGS WITH ONE HETERO ATOM



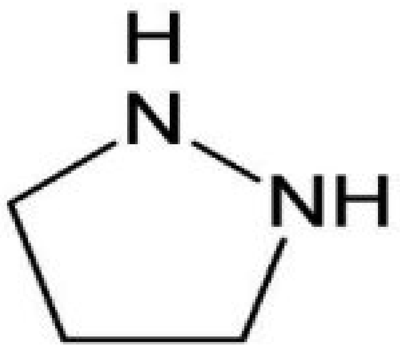
39.2.3 5-MEMBERED RINGS WITH ONE HETERO ATOM



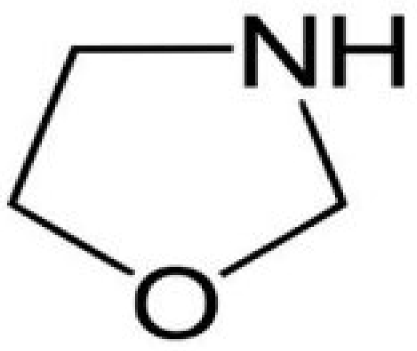
39.2.4 5-MEMBERED RINGS WITH TWO HETERO ATOM



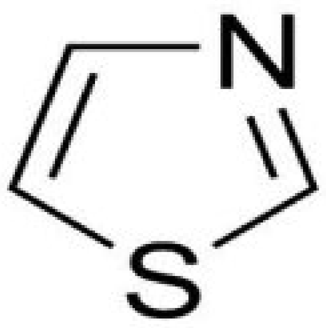
Pyrazole



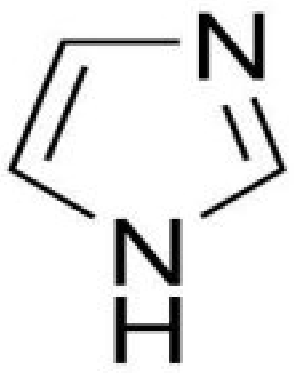
Pyrazolidine



Oxazolidine

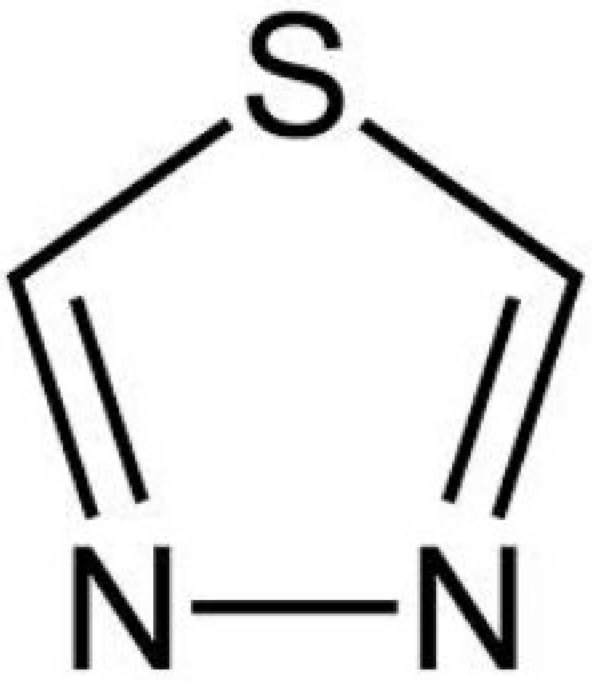


Thiazole



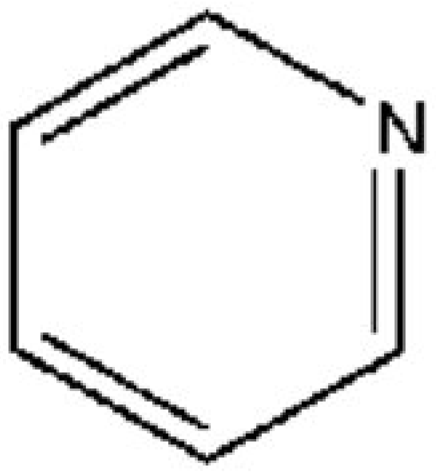
Imidazole

39.2.5 5-MEMBERED RINGS WITH THREE HETERO ATOM

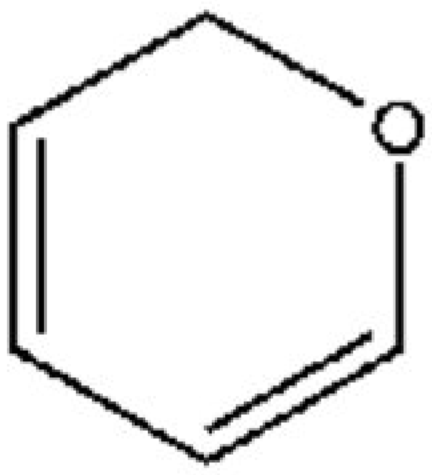


Thiadiazole

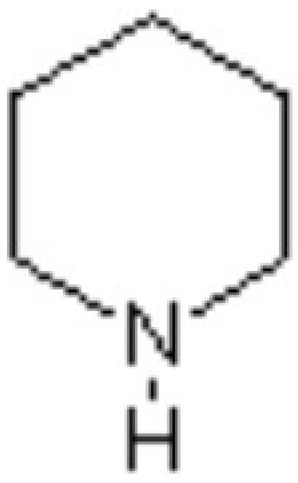
39.2.6 6-MEMBERED RINGS WITH ONE HETERO ATOM



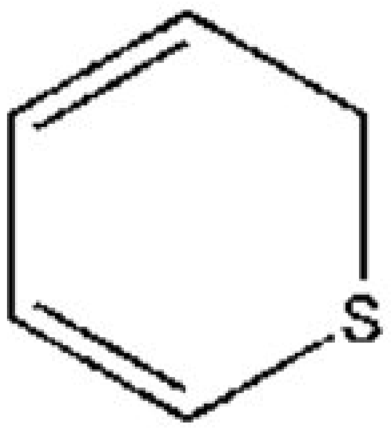
pyridine



pyran

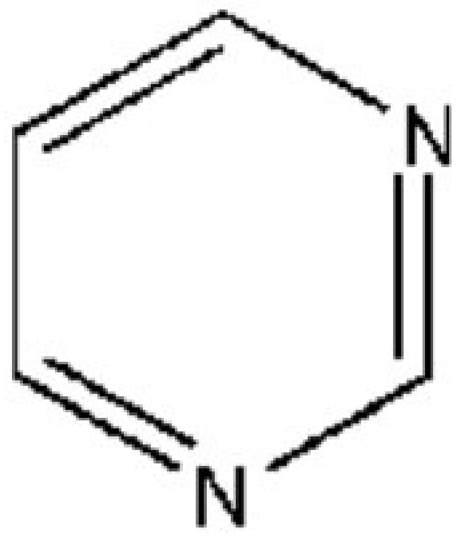


piperidine
perhydropyridine

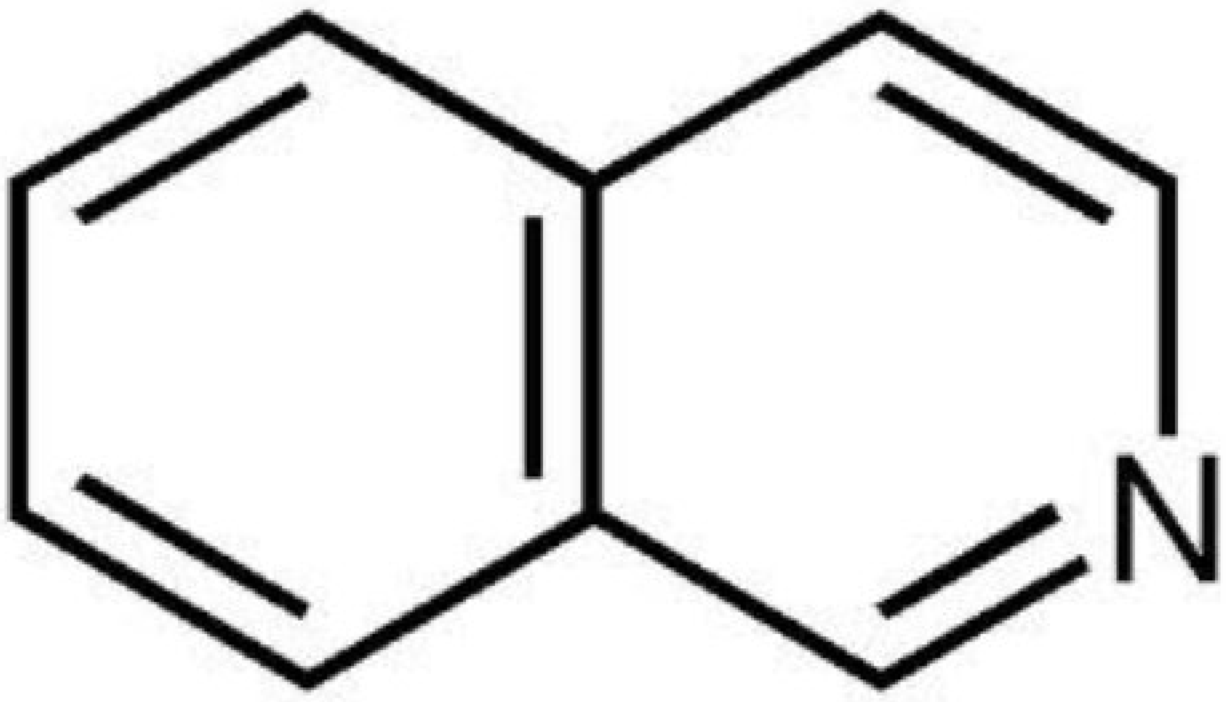


thiine

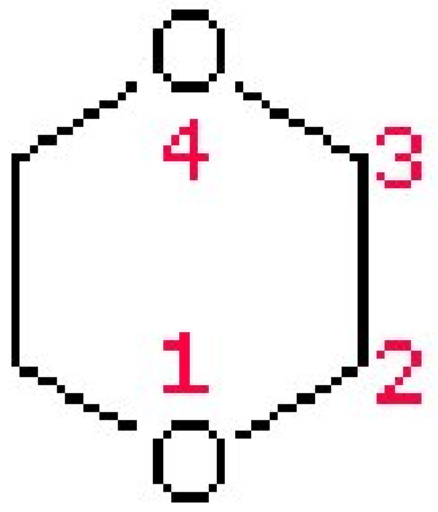
39.2.7 6-MEMBERED RINGS WITH TWO HETERO ATOM



pyrimidine



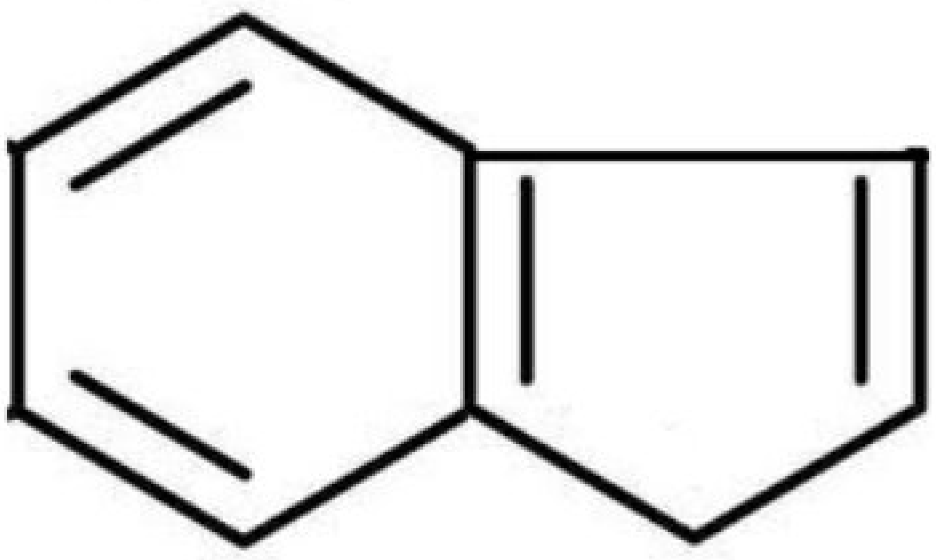
Quinoline
Benzoazine



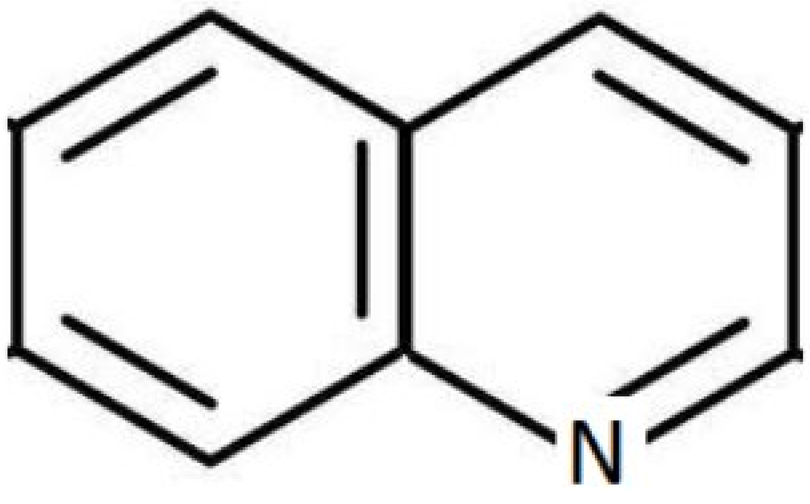
dioxane

1,4-dioxane

39.2.8 CONDENSED RING



Benzoazole

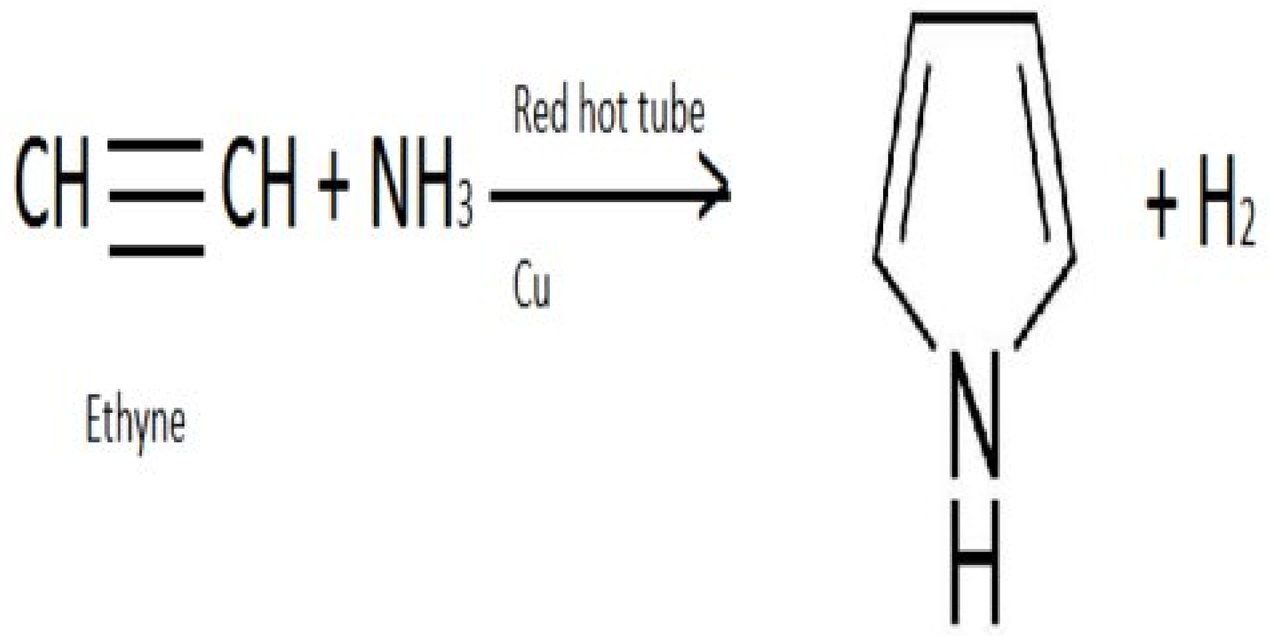


benzoazine

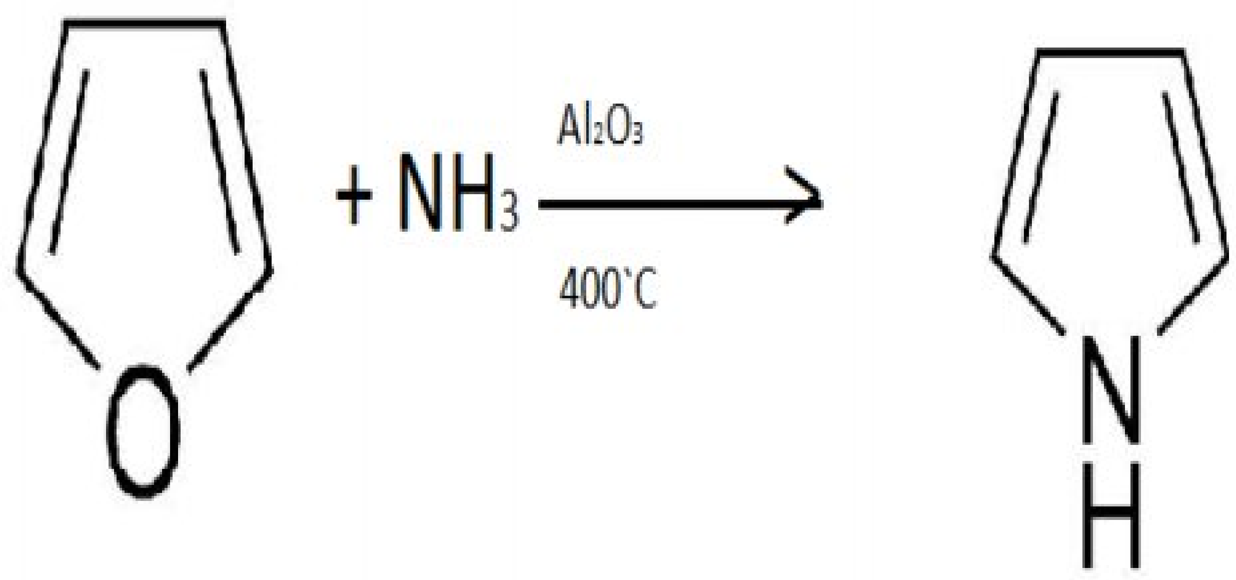
Chapter 40 AZOLE

MANUFACTURING:

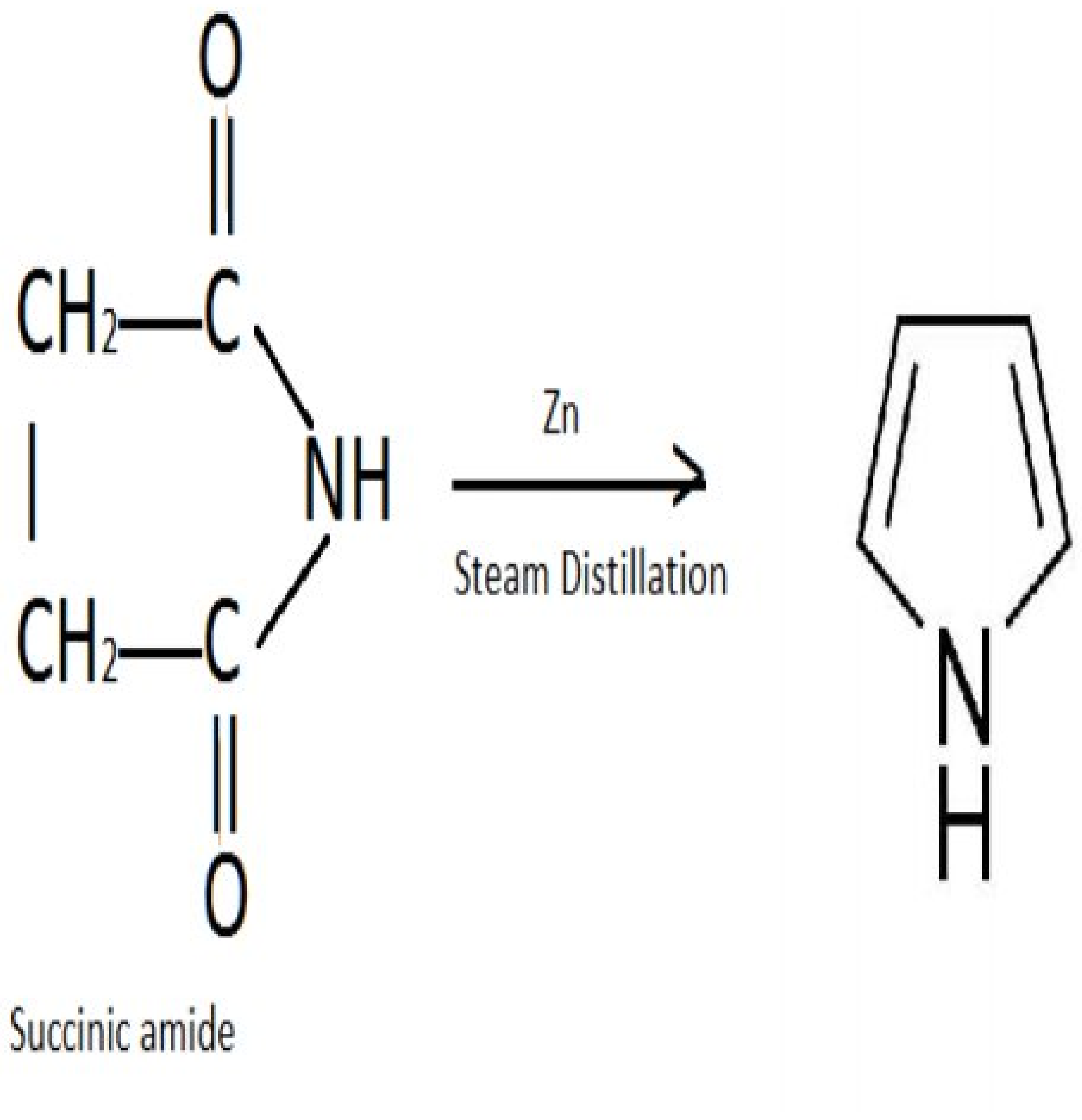
1) FROM ACETYLENE:



2) FROM FURAN



3) FROM DISTILLATION OF SUCCINE AMIDE:



PROPERTIES:

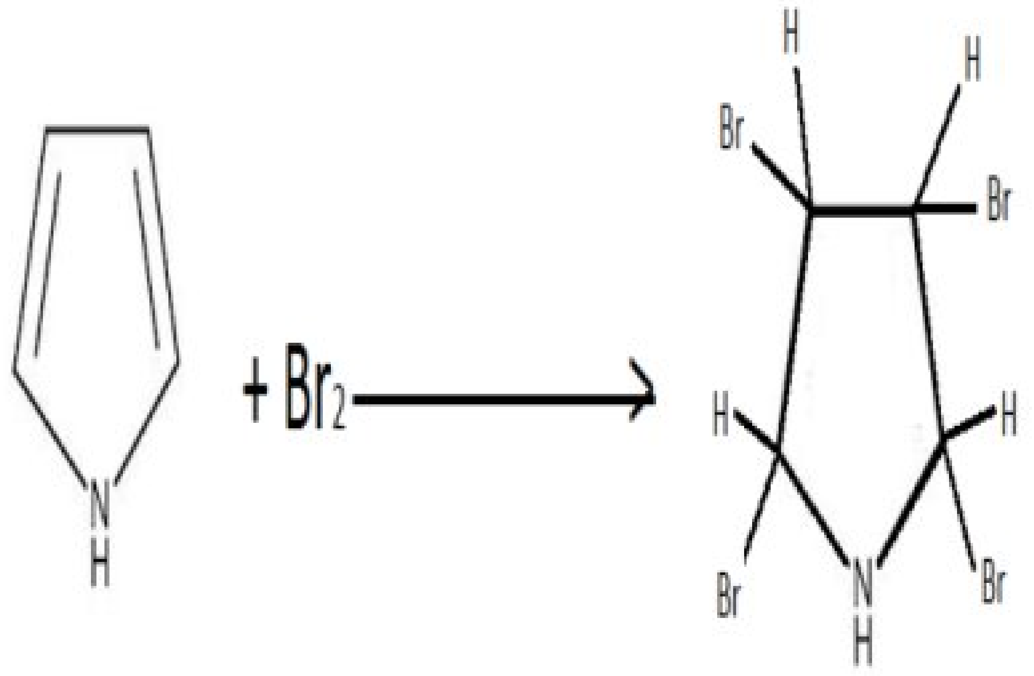
A) PHYSICAL:

- i. Colourless liquid with a boiling point of 131 degree centigrade.
- ii. Odour is similar to chloroform.
- iii. Slightly soluble in water while soluble in most of organic solvents and turns brown when exposed to air.

40.1.1 B) CHEMICAL PROPERTIES:

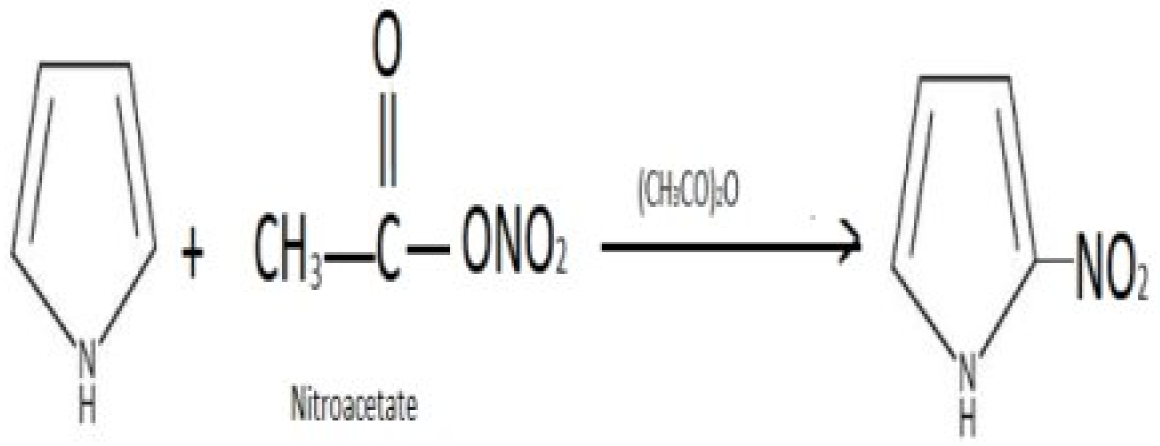
40.1.2 ELECTROPHILC SUBSTITUTION REACTION:

40.1.3 HALOGENATION:

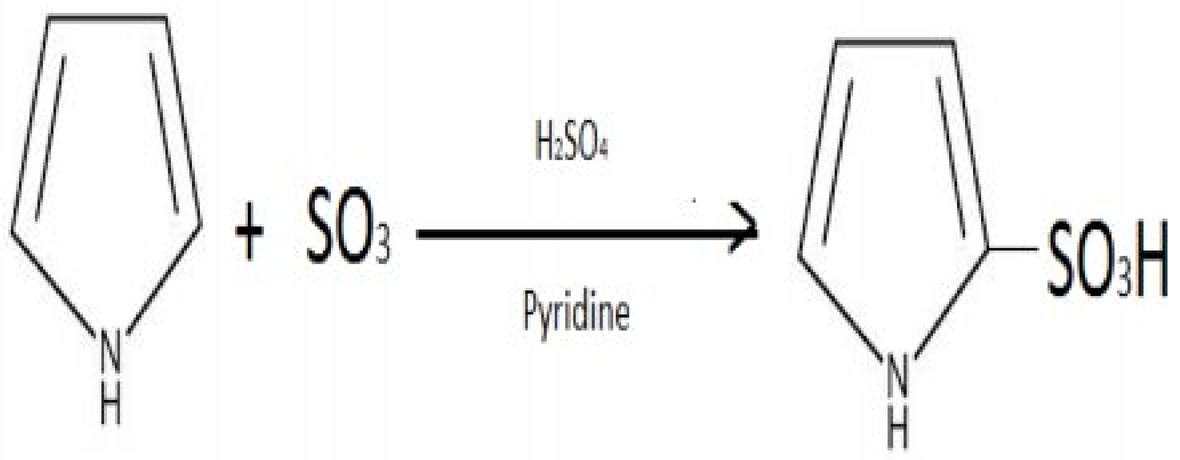


40.1.4

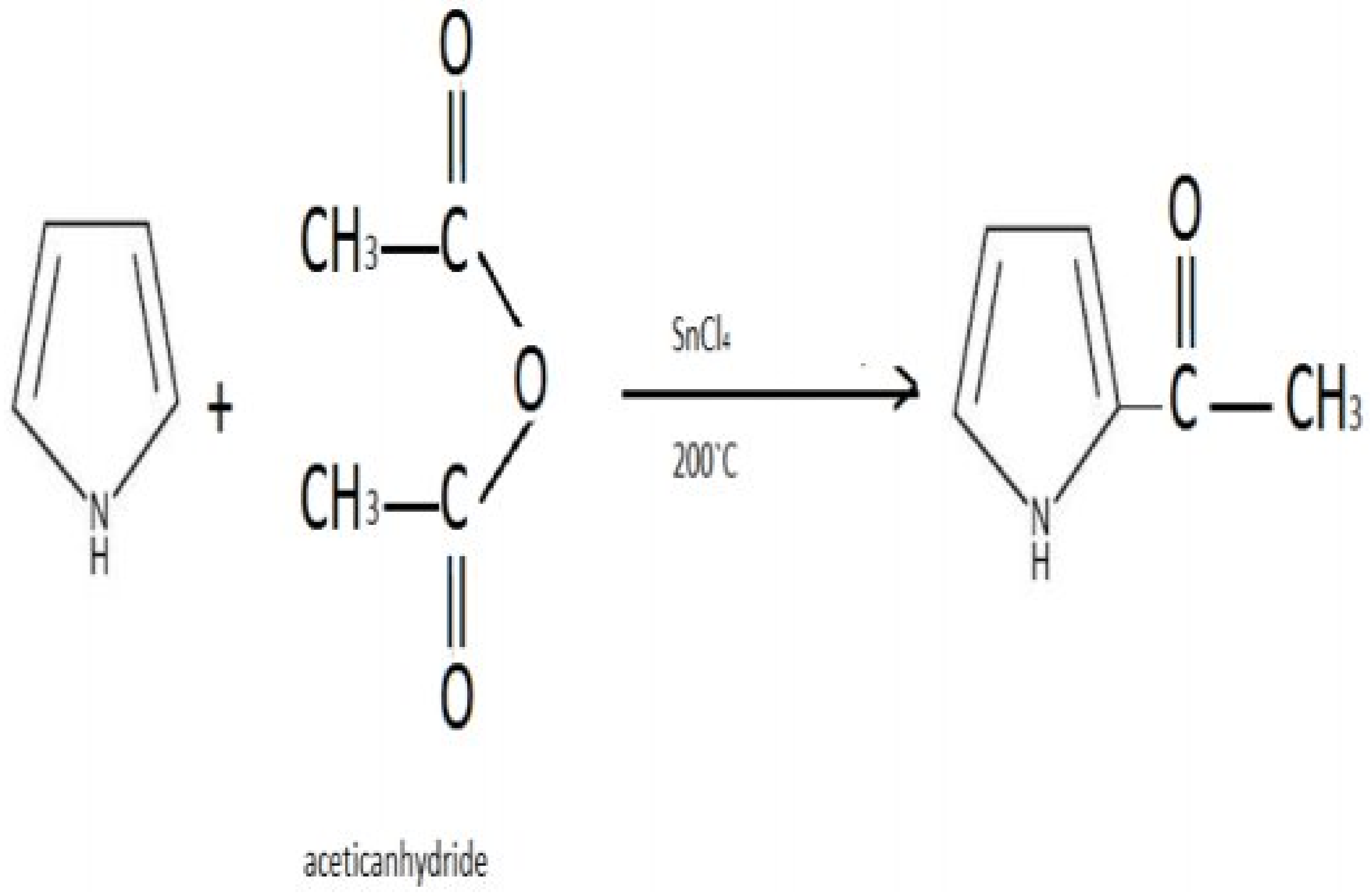
40.1.5 NITRATION:



40.1.6 SULPHONATION:

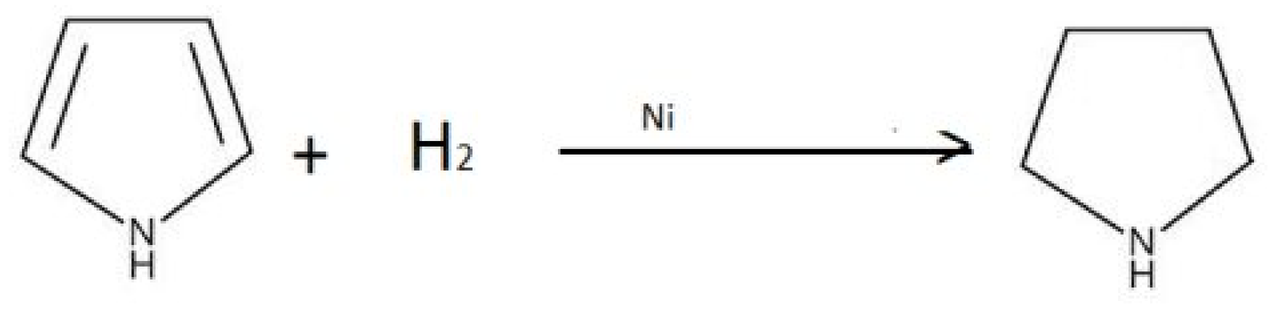


40.1.7 FRIEDEL CRAFT REACTION:



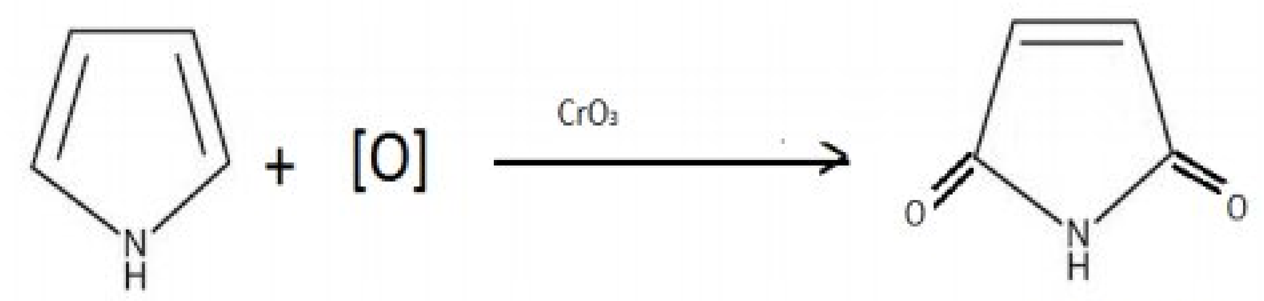
HYDROGENATION:

40.1.8



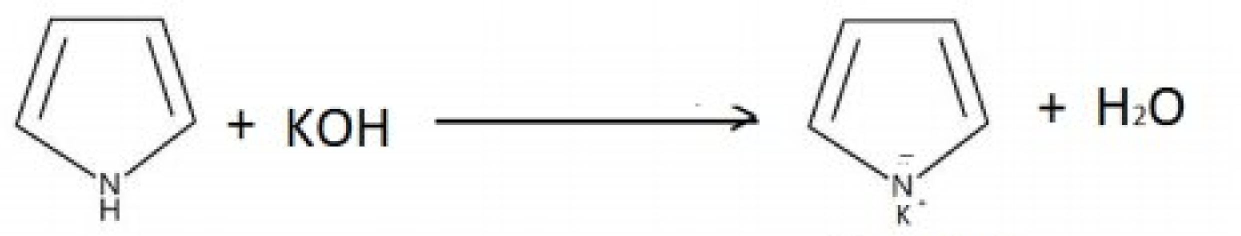
Tetrahydr

40.1.9 OXIDATION:



Malicamide

40.1.10 SALT FORMATION:

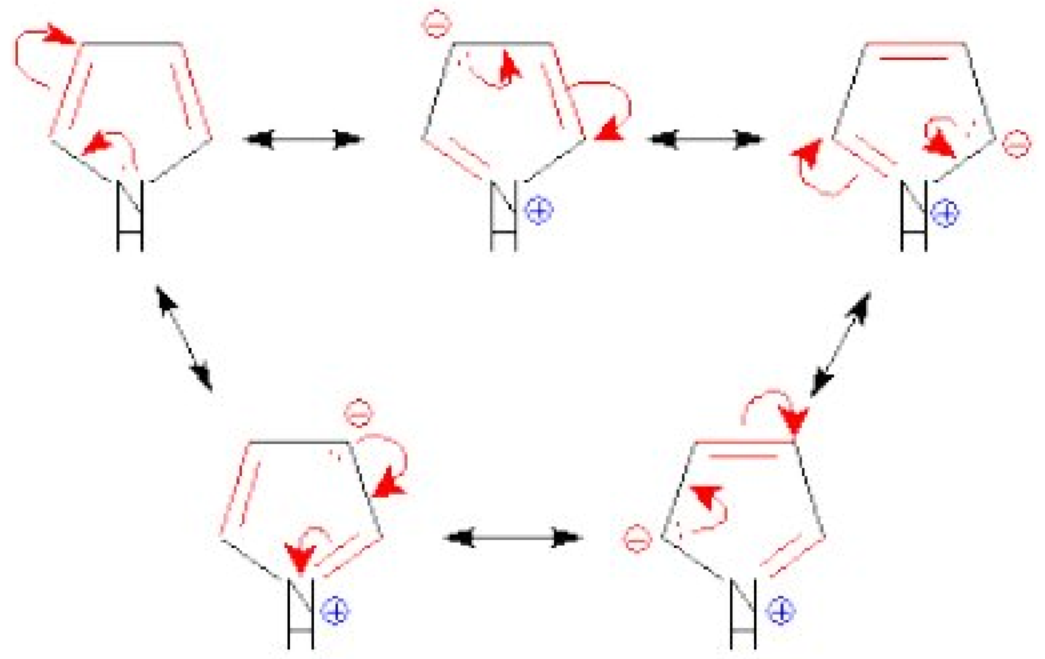


Potassium Azole

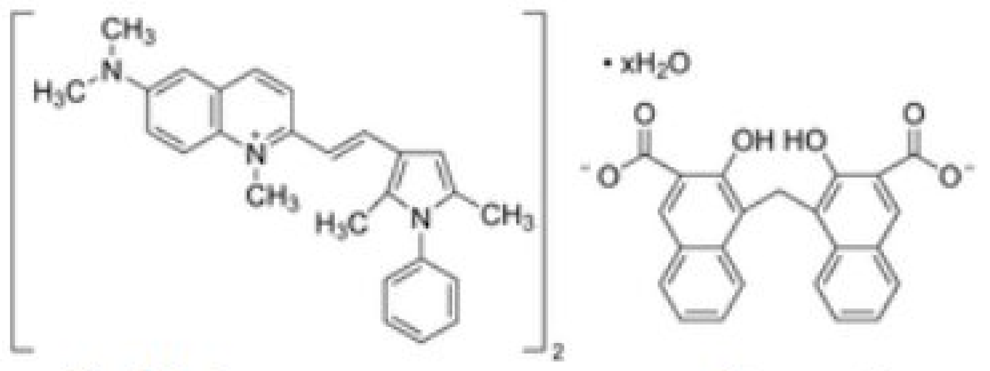
40.2 USES:

a. As a commercial solvent
b. In production of 6,6-nylon

40.3 RESONANCE STRUCTURE

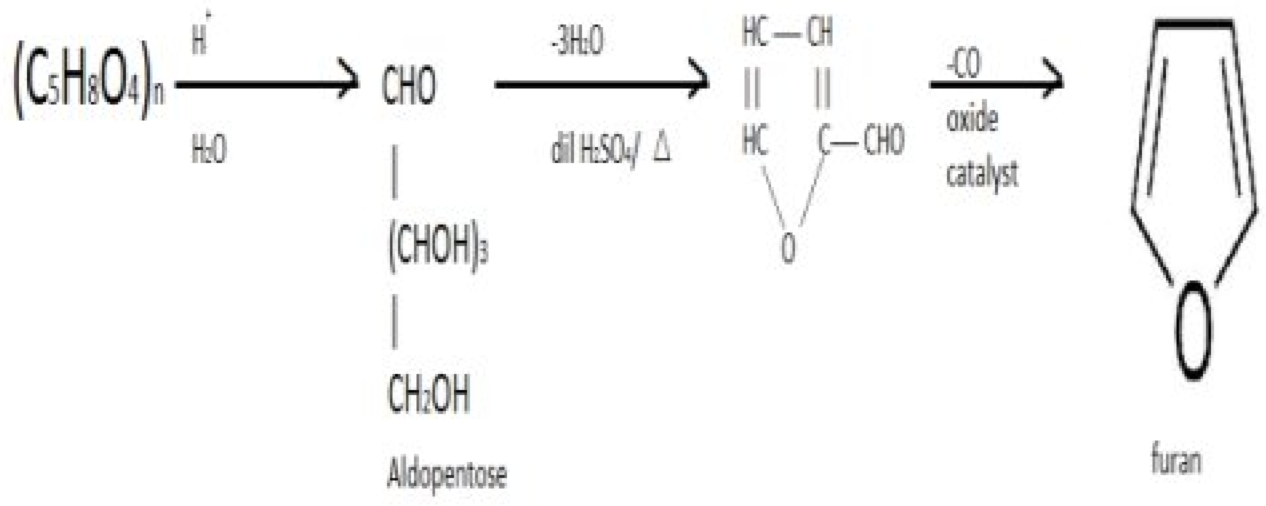


40.4 PHARMACEUTICAL COMPOUNDS HAVING AZOLE RING:


Pyrivinium Pamoate

Chapter 41 Furan (Oxole)

MANUFACTURING



PROPERTIES

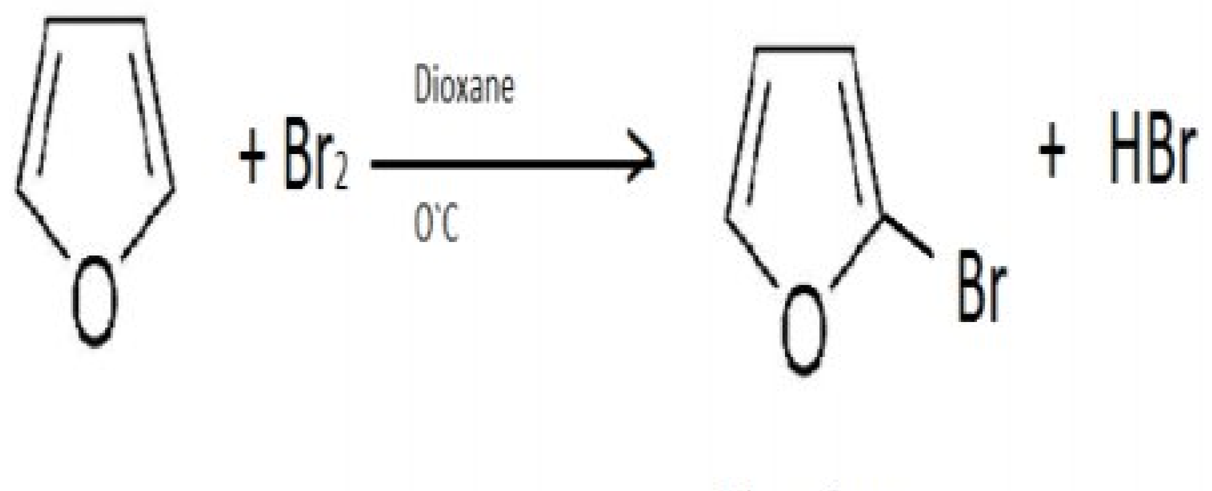
A) PHYSICAL:

- Colourless liquid with a boiling point of 31.4 degree centigrade
- Odour of chloroform
- Insoluble in ether
- Soluble in most of organic solvents

41.1.1 B) CHEMICAL:

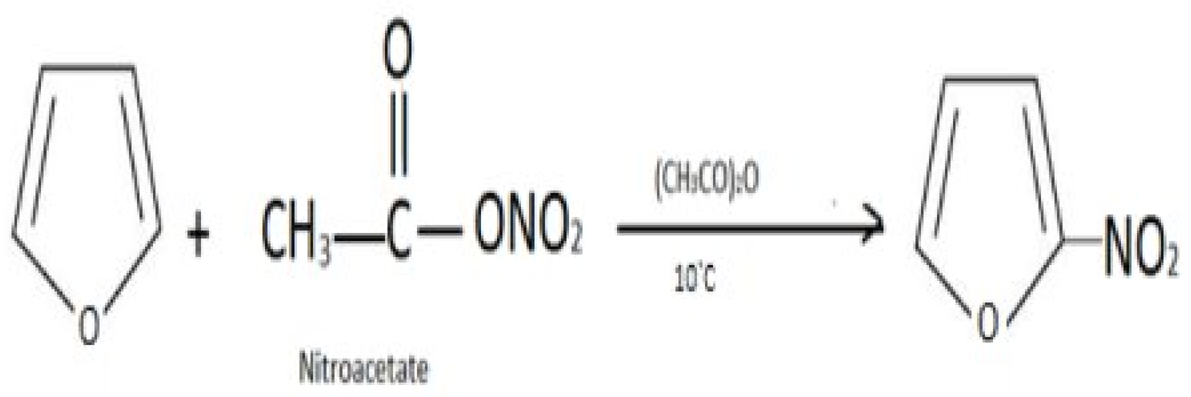
Electrophilic Substitution Reaction: most of the electrophilic substitution reaction occurs at position 2 and Furan is more reactive than benzene or any other organic compound (because of electron shifting)

HALOGENATION



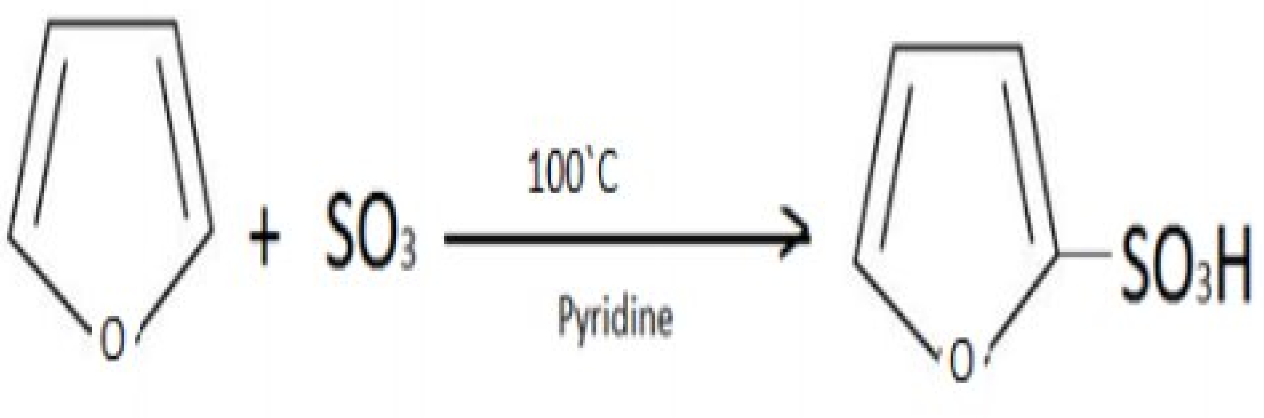
2- bromofuran

NITRATION



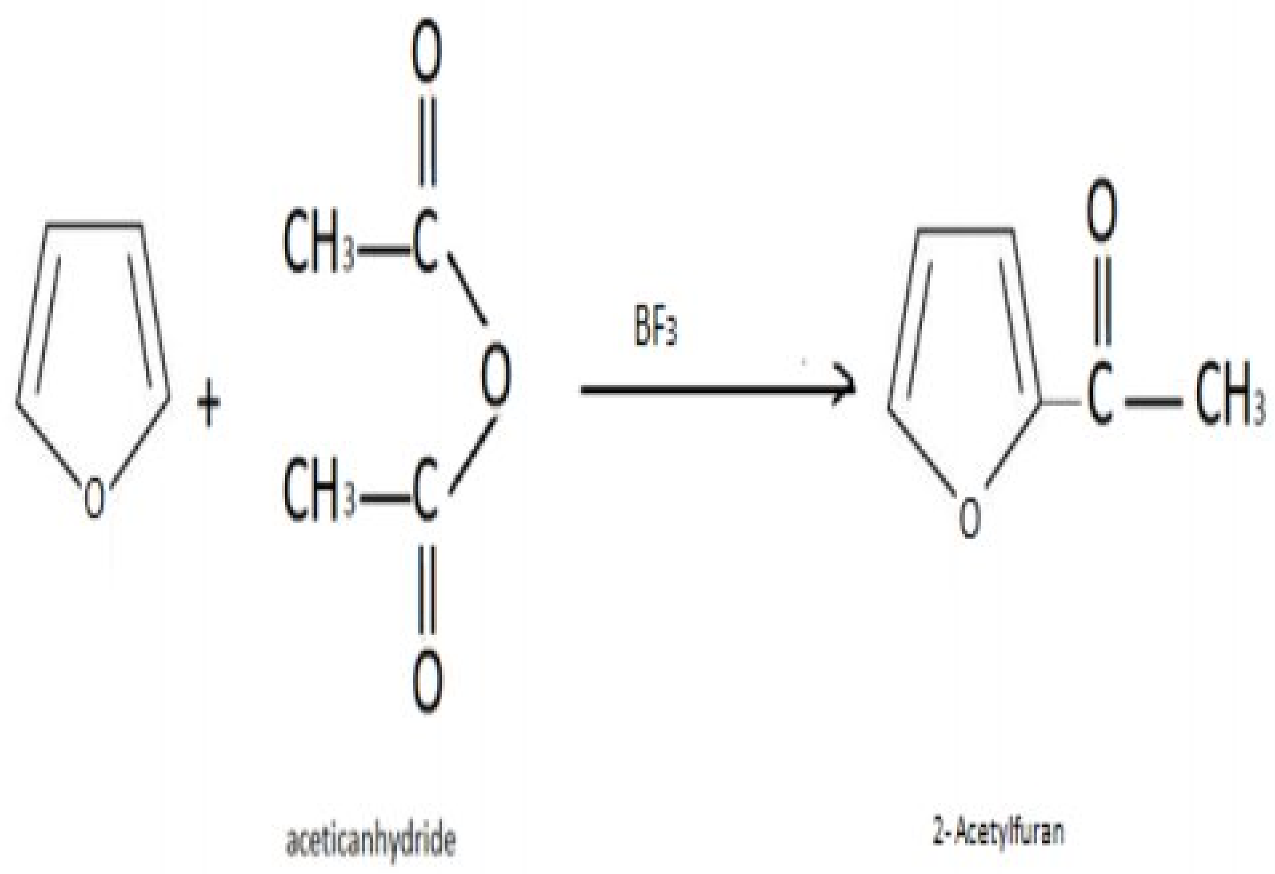
2-Nitrofuran

SULPHONATION

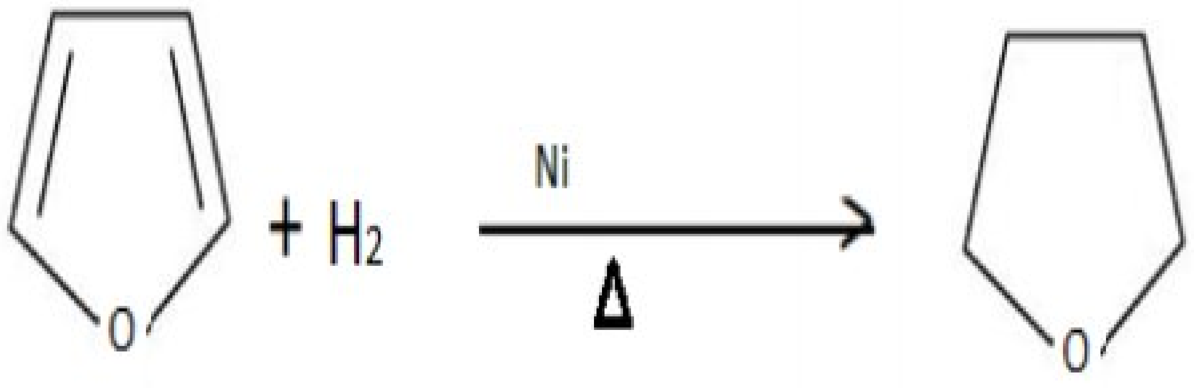


furansulphonic acid

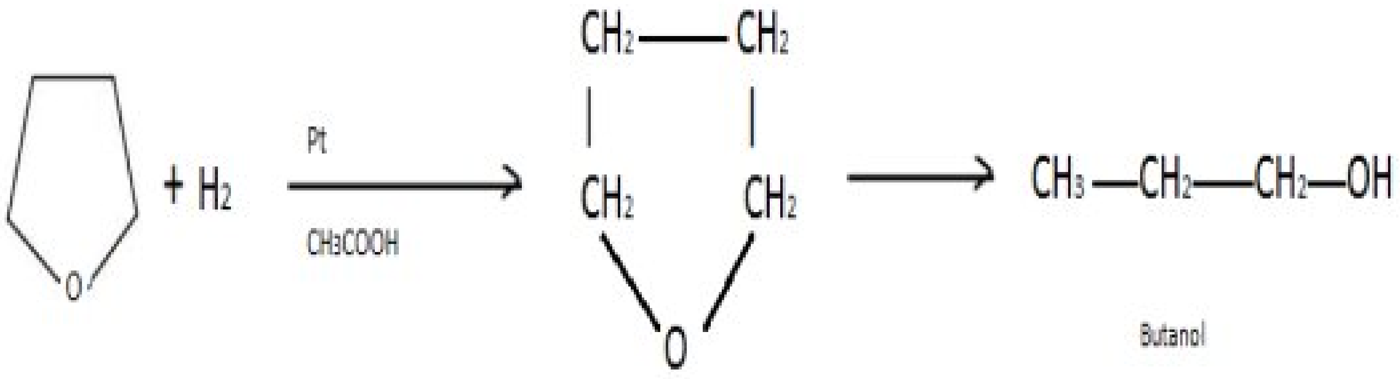
FRIEDEL CRAFT ACYLATION



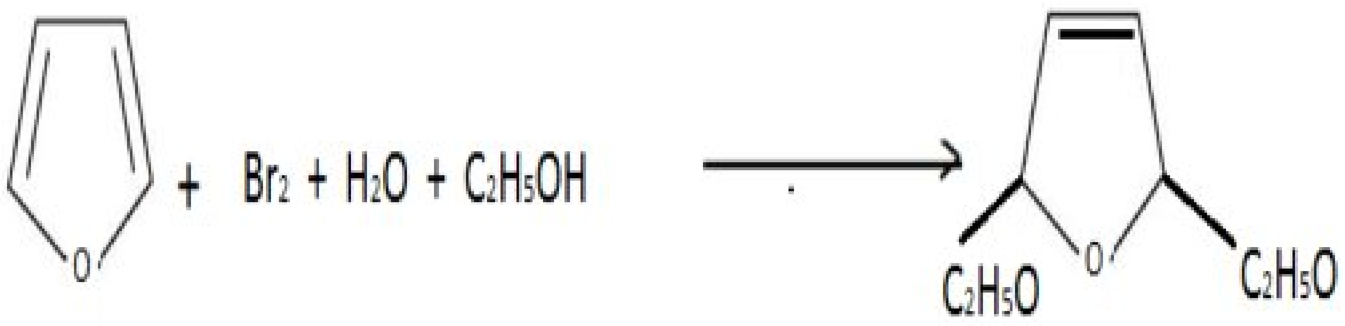
REDUCTION



Tetr hydrofuran

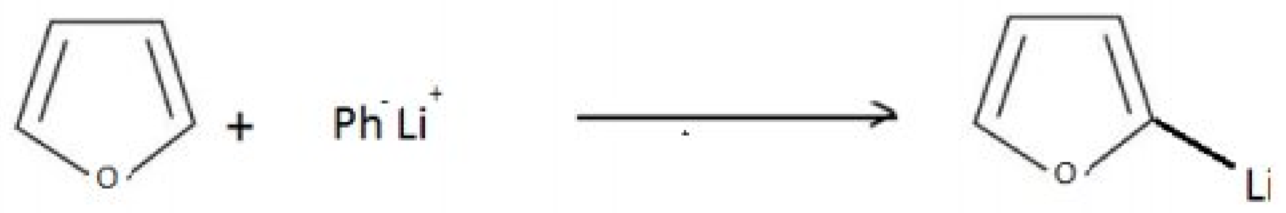


OXIDATION

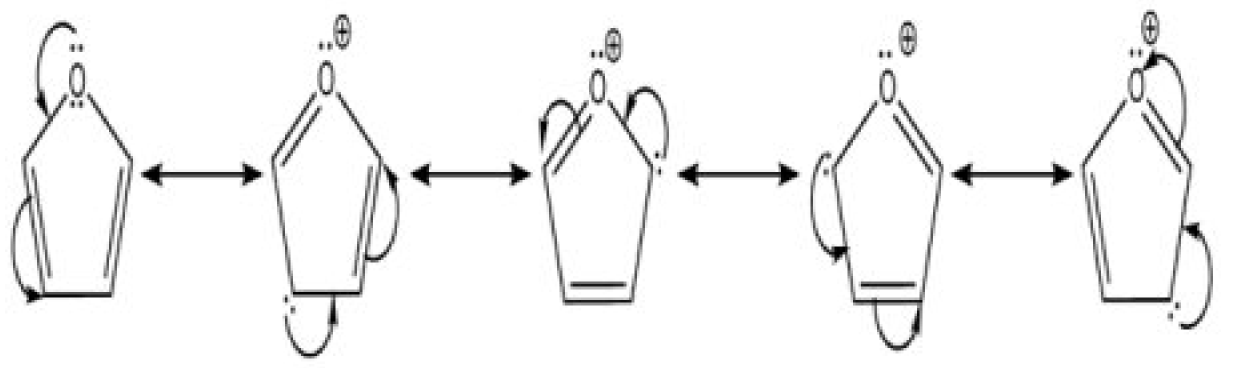


2,5- Diethoxyfuran

SALTFORMATION:

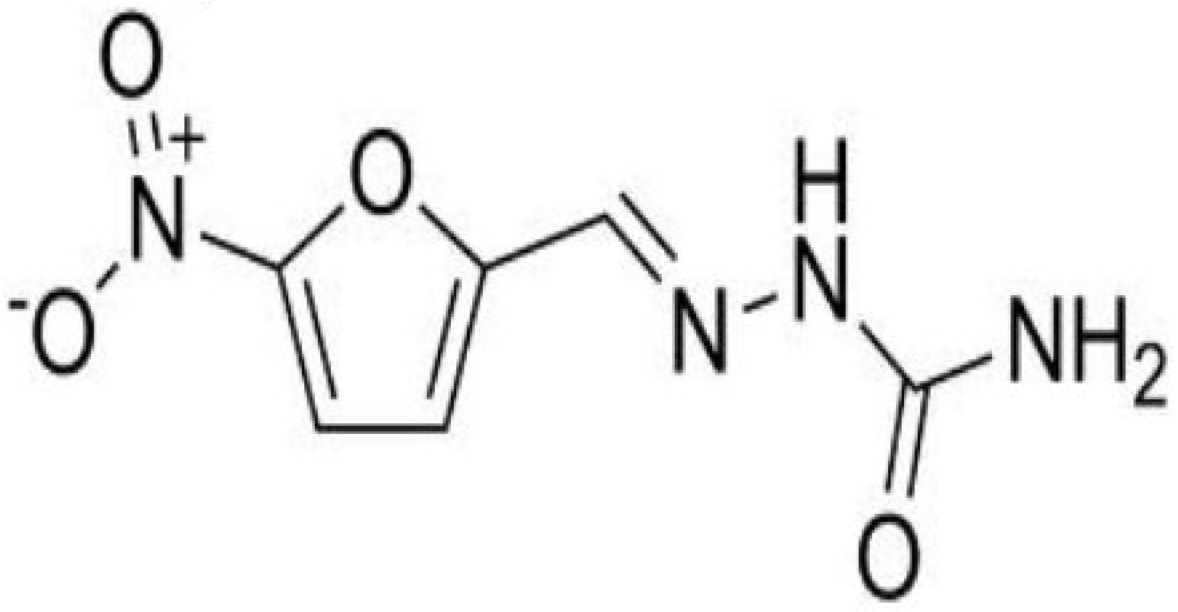


41.2 RESONANCE STRUCTURE



41.3 EXAMPLES OF PHARMACEUTICAL COMPOUNDS:

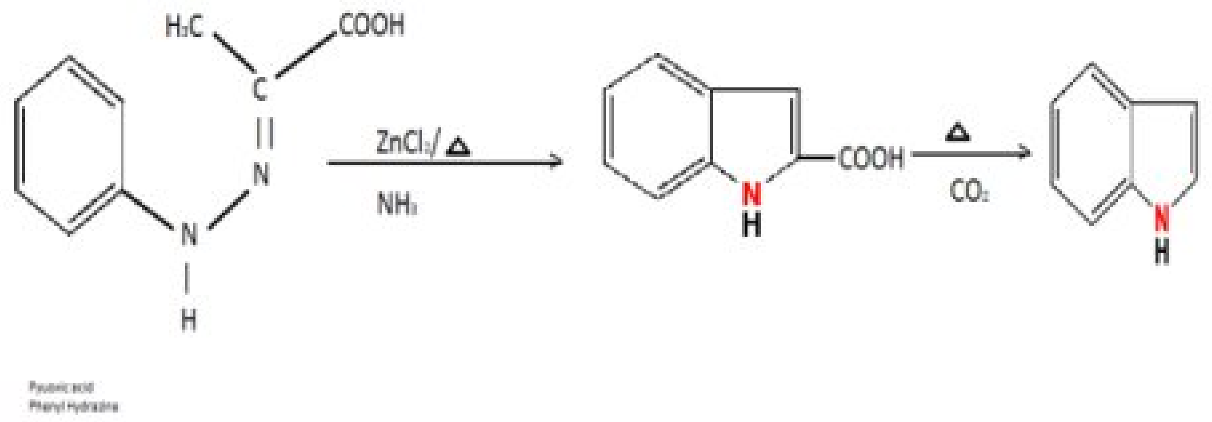
41.3.1 A)NITROFURAZONE:



Chapter 42 INDOLE

Indole occurs in coal tar, jasmine flower and orange blossom oil.

FISCHER-INDOLE SYNTHESIS:



PROPERTIES

42.1.1 PHYSICAL PROPERTIES

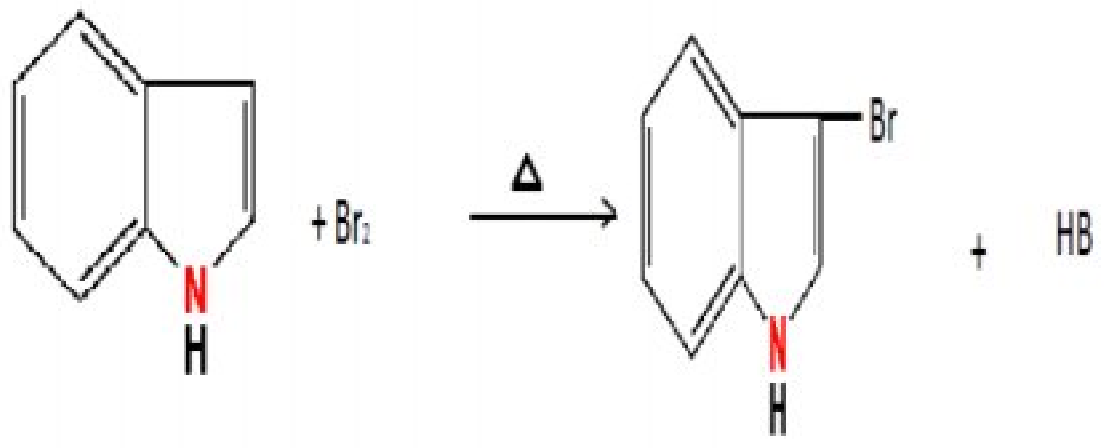
- Coloureless crystal with melting point 52.5 degree centigrade
- Soluble in hot water, alcohol and ether
- Strong fecal odour

42.1.2 CHEMICAL PROPERTIES

It gives most of the Azole's Reaction.

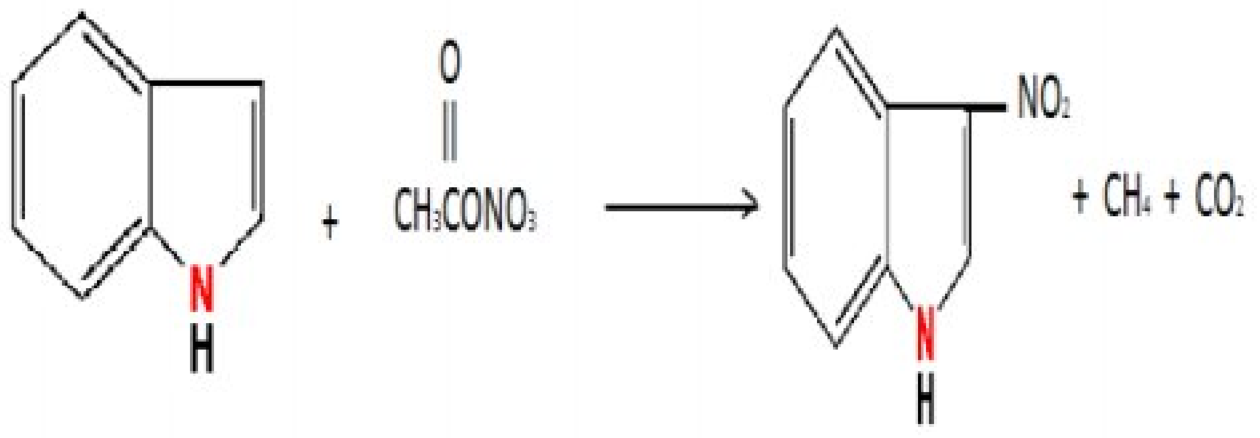
42.2 ELECTROPHILC SUBSTITUTION REACTION

HALOGENATION

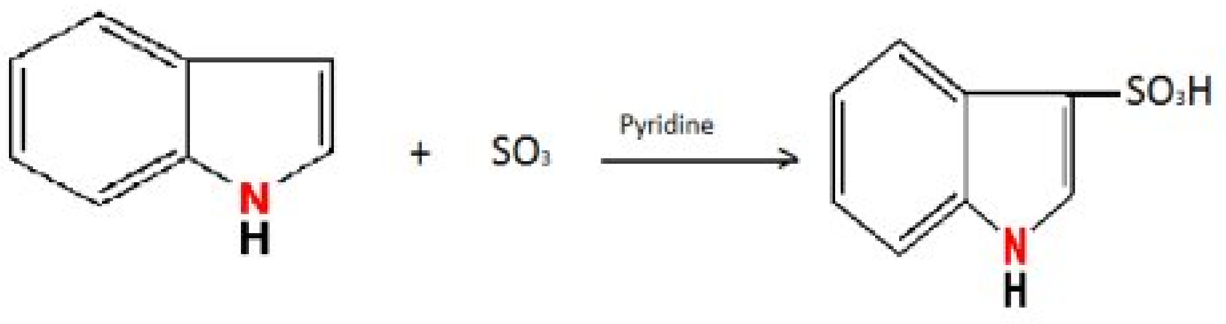


3-BromoIndole

NITRATION



SULPHONATION

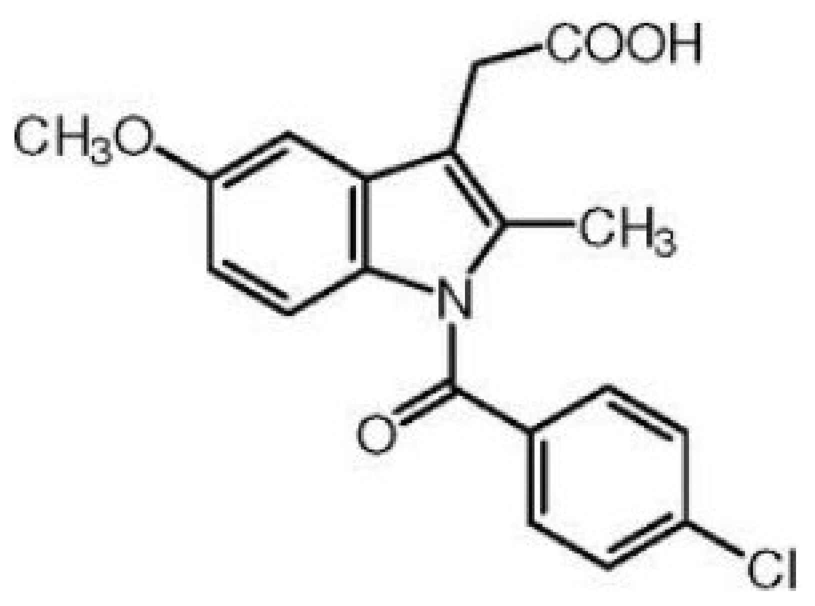


3- IndoleSulphonic acid

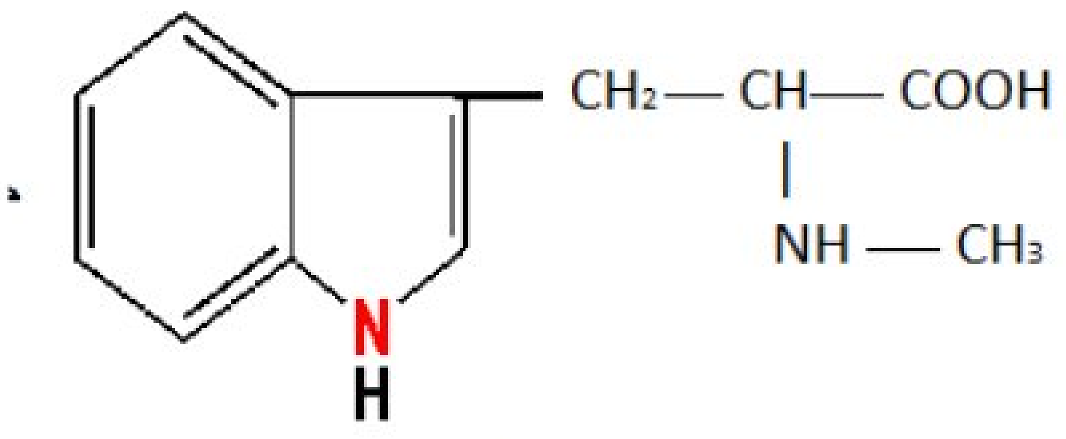
42.3 USES

It is used in perfuming industries for preparing jasmine and orange blends.

PHARMACEUTICAL EXAMPLES



Indomethacin



Abrin

Chapter 43 Pyridine (Azine)

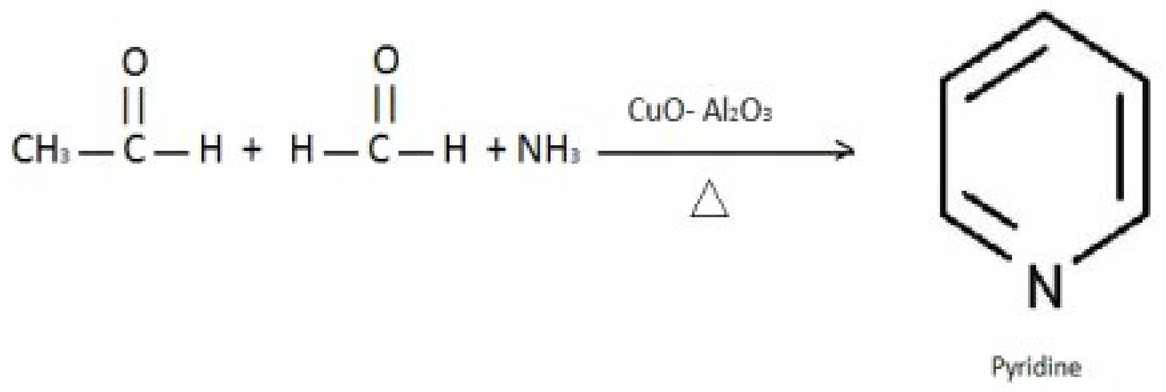
PREPARATION:

- FROM BY-PRODUCT OF COKE MANUFACTURING:

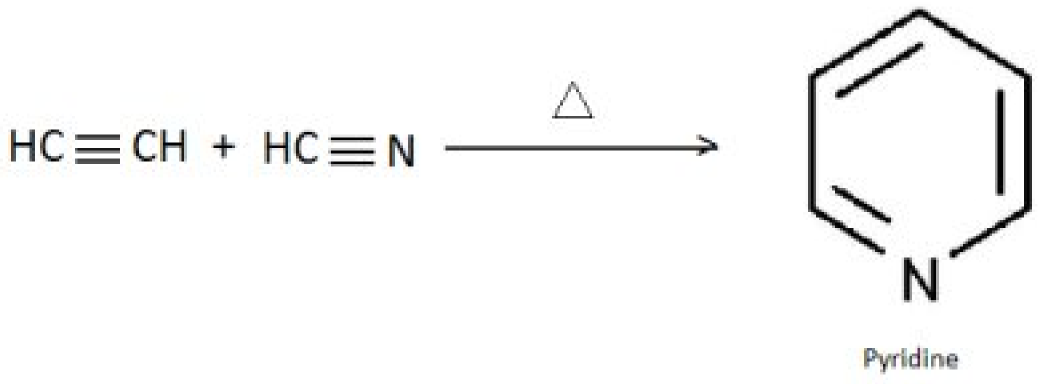
The light oil fractions of coal tar distillation are freed from phenol and washed with sulphuric acid. The acid extract containing pyridinium sulphate on treatment with NaOH restore pyridine which is separated with the help of fractional distillation.

Non condense gases coming from fractionating towers are washed with sulphuric acid. A fraction containing pyridinium sulphate and ammonium sulphate is obtained. Ammonium sulphate is removed by chilling and the mothor liquor is treated with the base to remove pyridine.

I. FROM ACETALDEHYDE, FORMALDEHYDE AND AMMONIA:



II. FROM ACETYLENE(ETHYNE) AND HYDROGEN CYANIDE:



43.1 PROPERTIES:

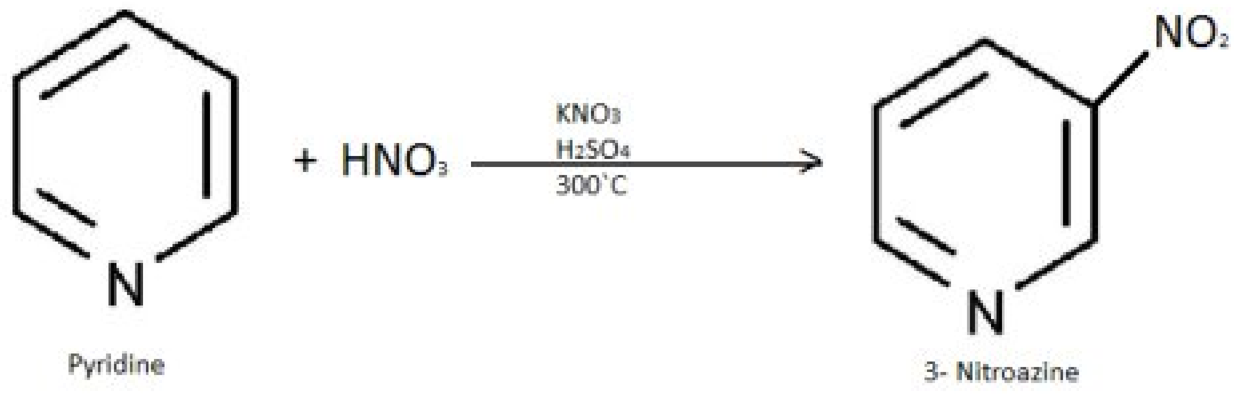
43.1.1 PHYSICAL:

i. Colourless liquid with boiling point of 115.5 degree centigrade
ii. Unpleasant odour
iii. Soluble in water and most of organic solvents

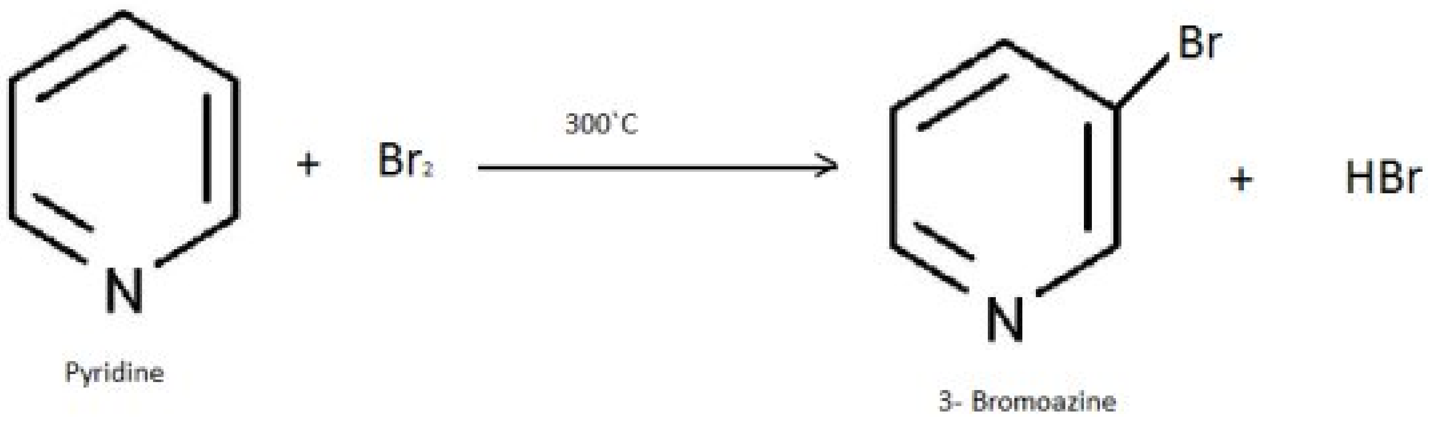
43.1.2 CHEMICAL:

ELECTROPHILIC SUBSTITUTION REACTION:

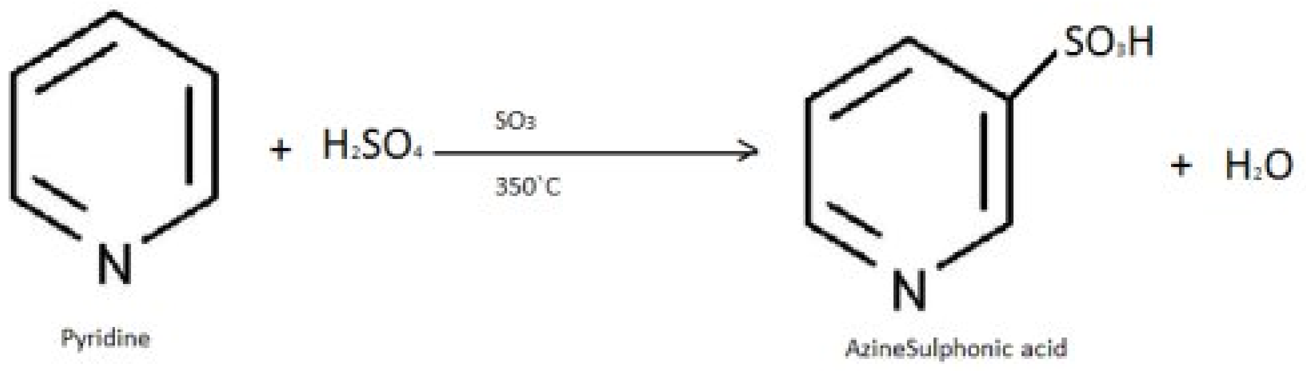
NITRATION:



HALOGENATION:

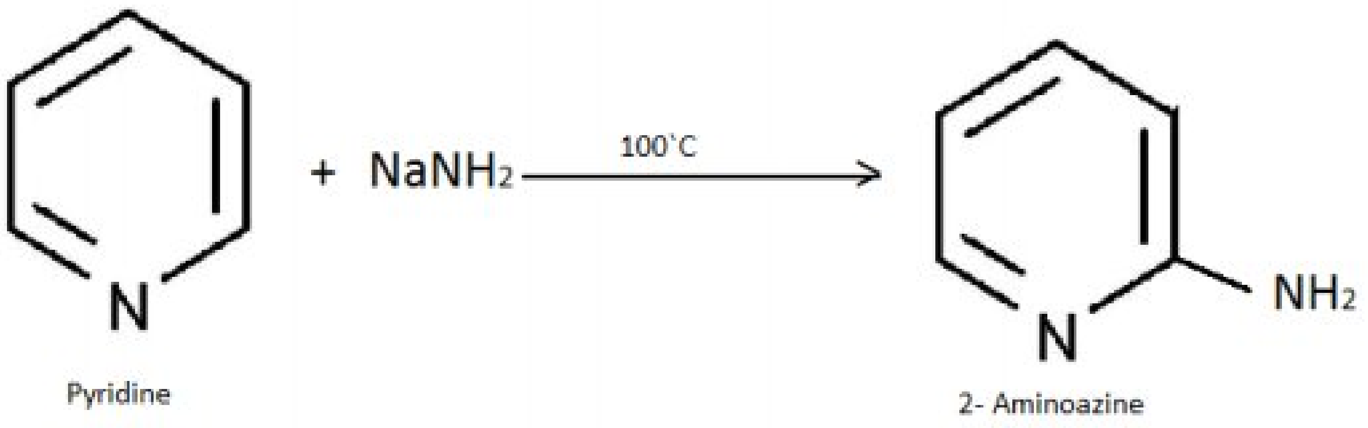


SULPHONATION:

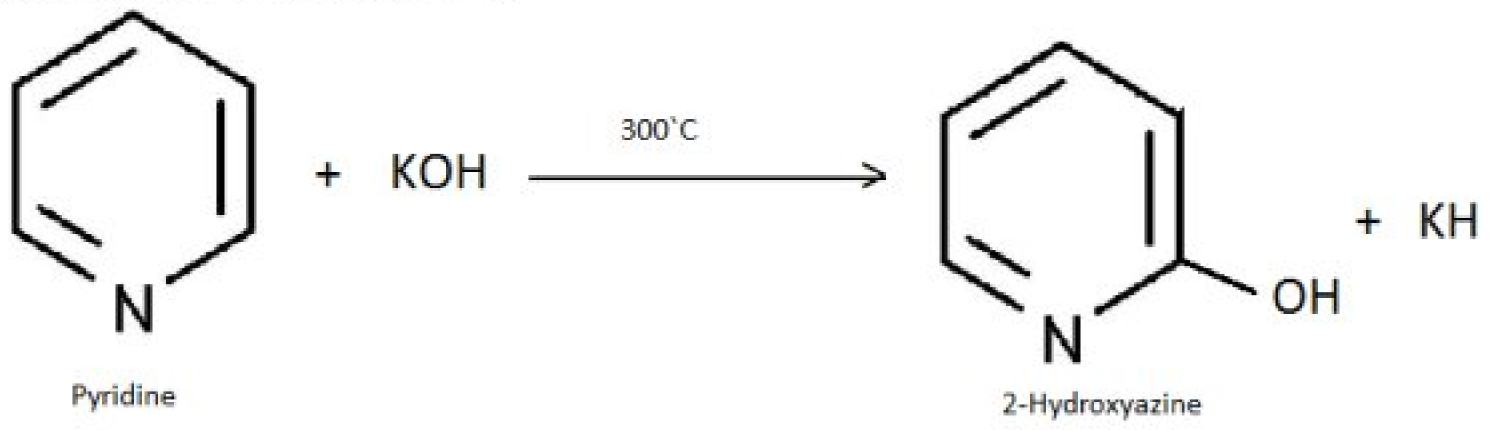


FRIEDEL CRAFT REACTION: Pyridine doesn't give this reaction.

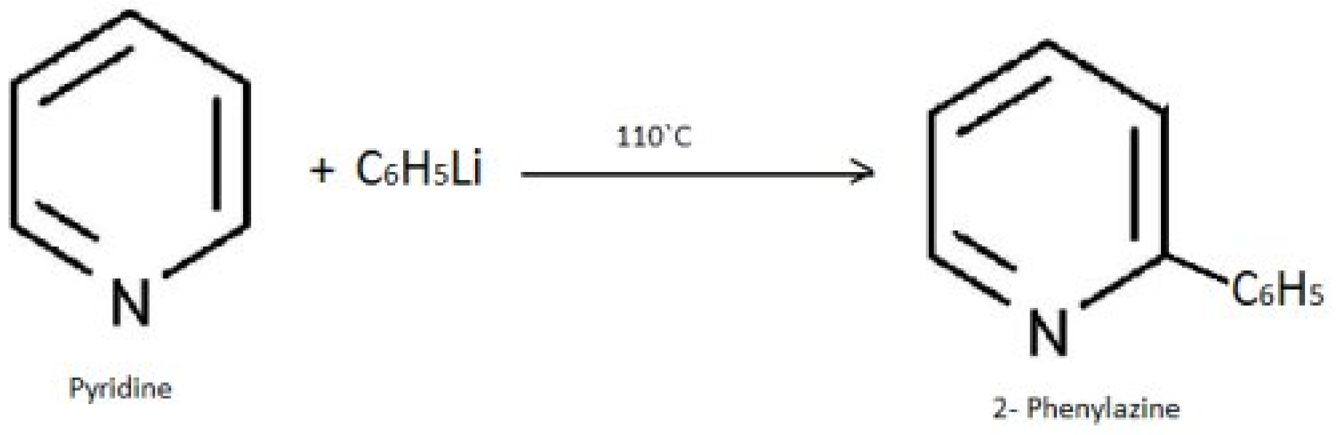
REACTION WITH AMIDE:



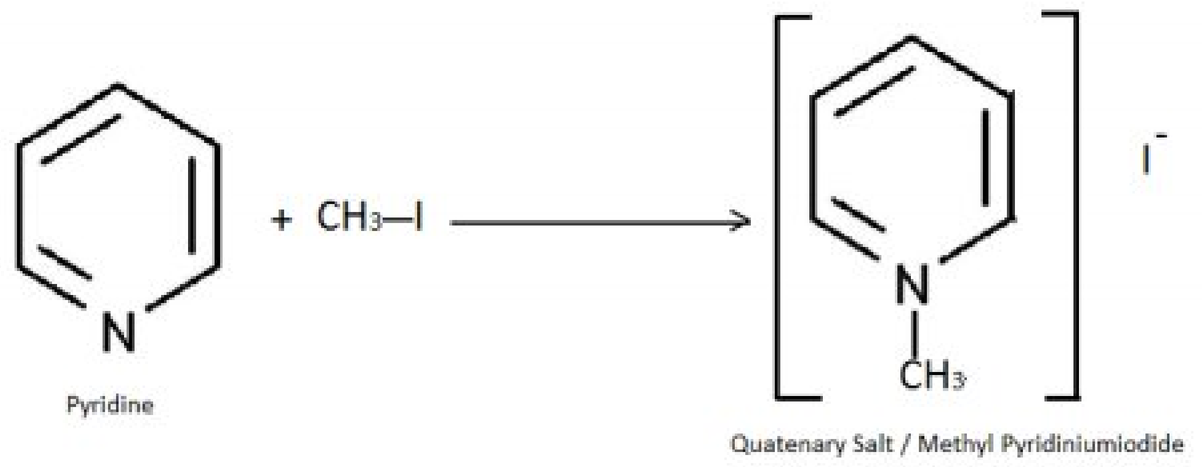
REACTION WITH KOH:



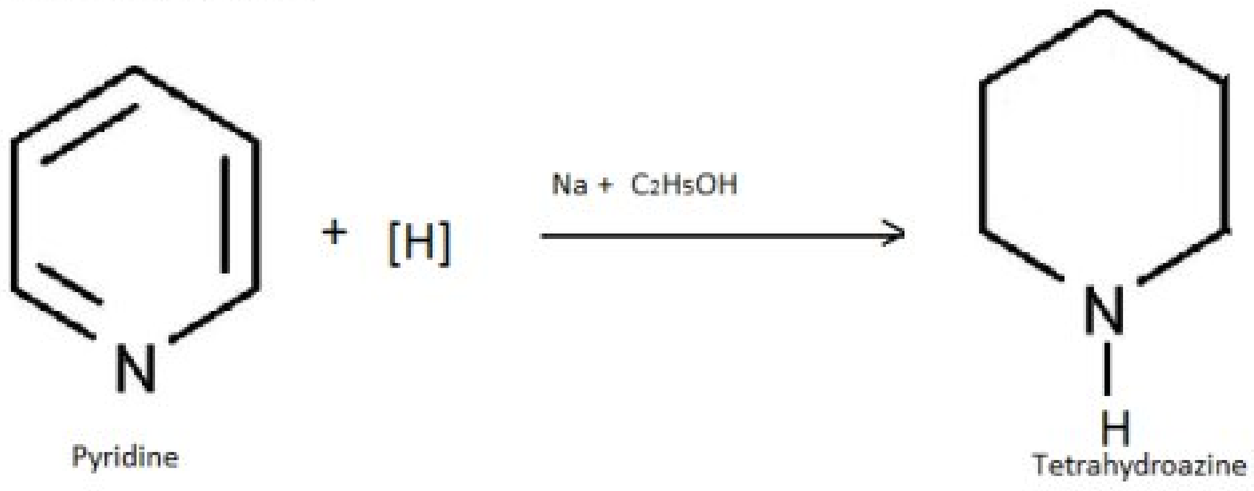
REACTION WITH PHENYL LITHIUM:



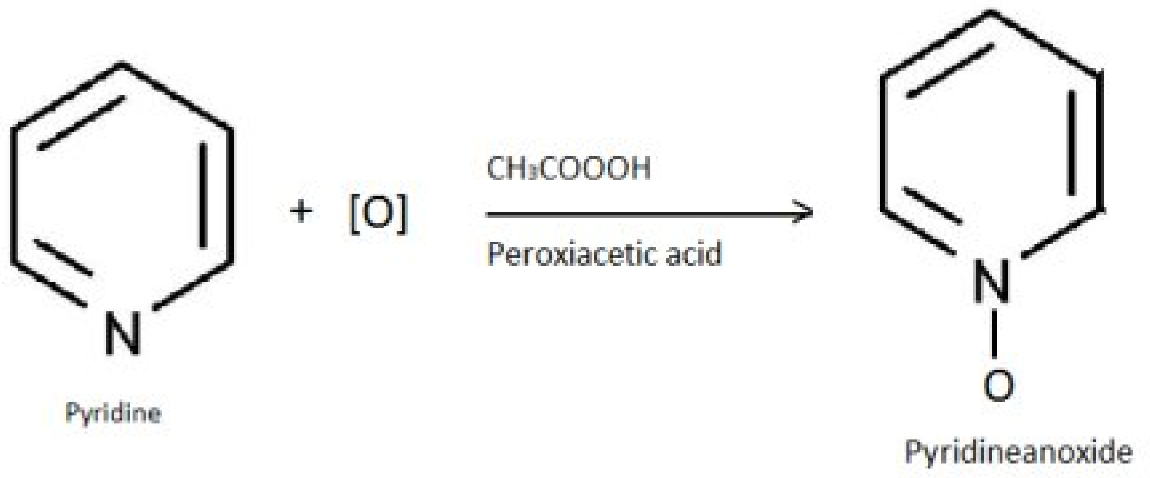
REACTION WITH ALKYL HALIDE:



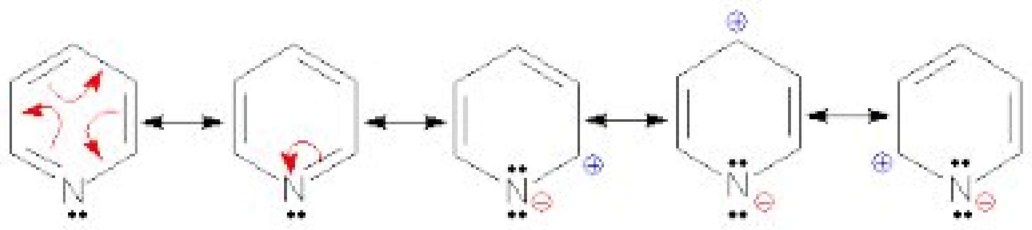
REDUCTION:



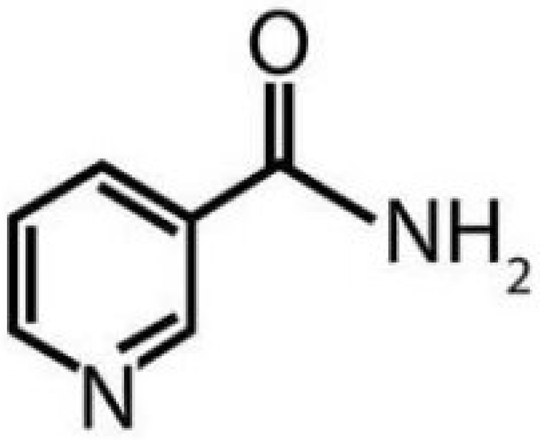
OXIDATION:



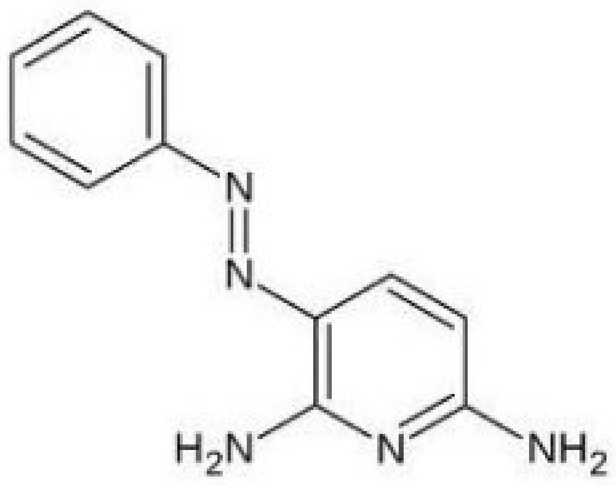
RESONANCE STRUCTURE



PHARMACEUTICAL COMPOUNDS:



Niacineamide



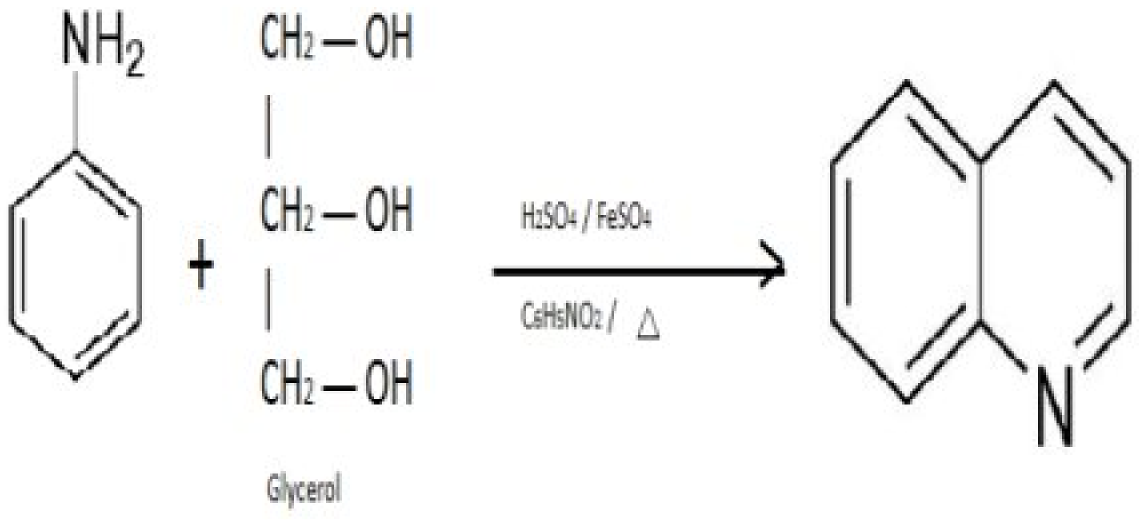
Phenazopyridine

Chapter 44 Quinoline

44.1 SYNTHESIS

FROM COAL TAR: Quinoline occurs in coal tar along with other bases and can be isolated with different technique

SKRAUPS SYNTHESIS: A mixture of aniline glycerol and sulphuric acid is heated in the presence of mild oxidizing agent such as nitrobenzene. The reaction is exothermic so as moderator is used such as $FeSO_4$.



44.2 PROPERTIES

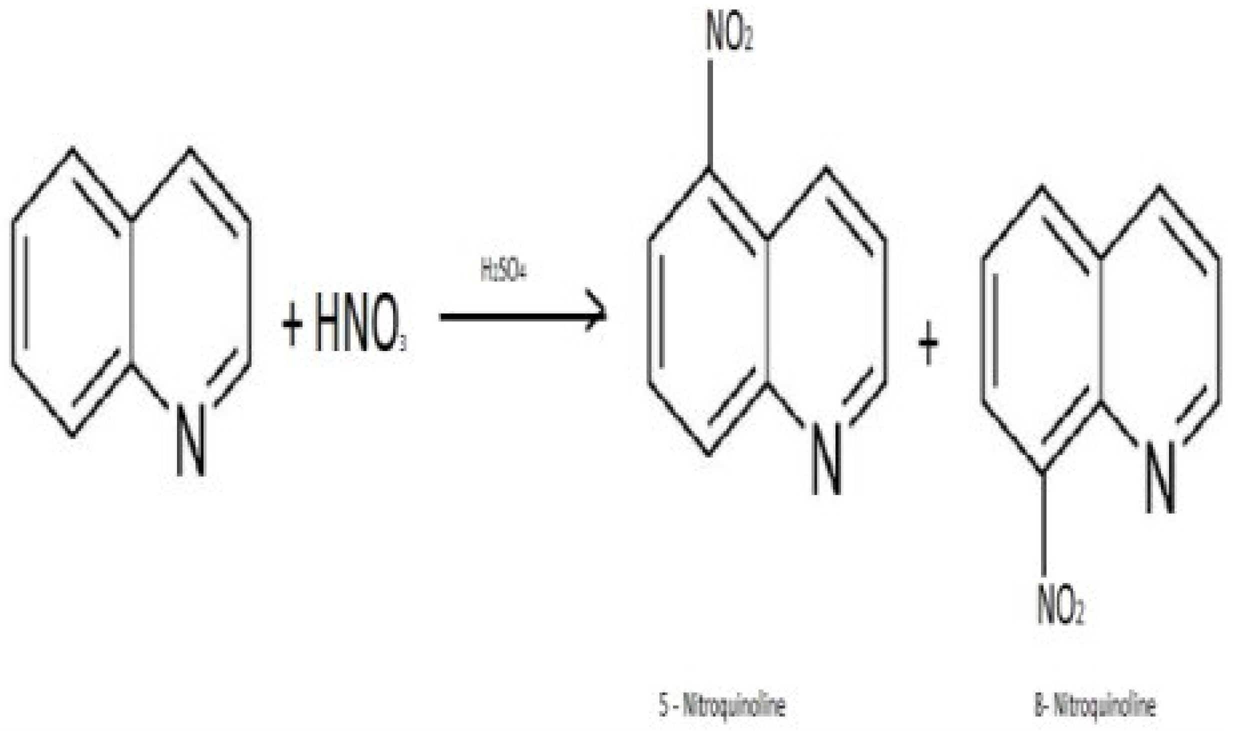
44.2.1 PHYSICAL PROPERTIES:

- Colourless liquid
- Boiling point of 238 °C
- Disagreeable pyridine like odour
- Soluble with water and miscible in alcohol

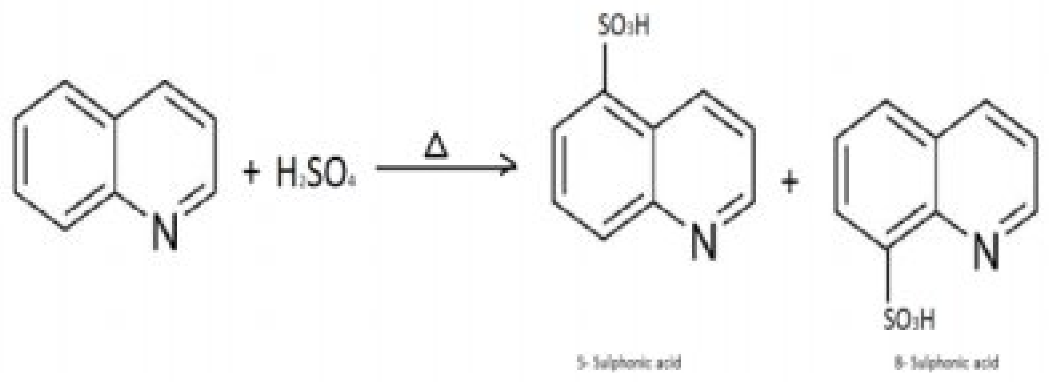
CHEMICAL PROPERTIES: Quinoline gives all reactions of pyridine Electrophilic substitution reactions of benzene.

44.2.2 ELECTROPHILIC SUBSTITUTION REACTIONS

44.2.3 NITRATION

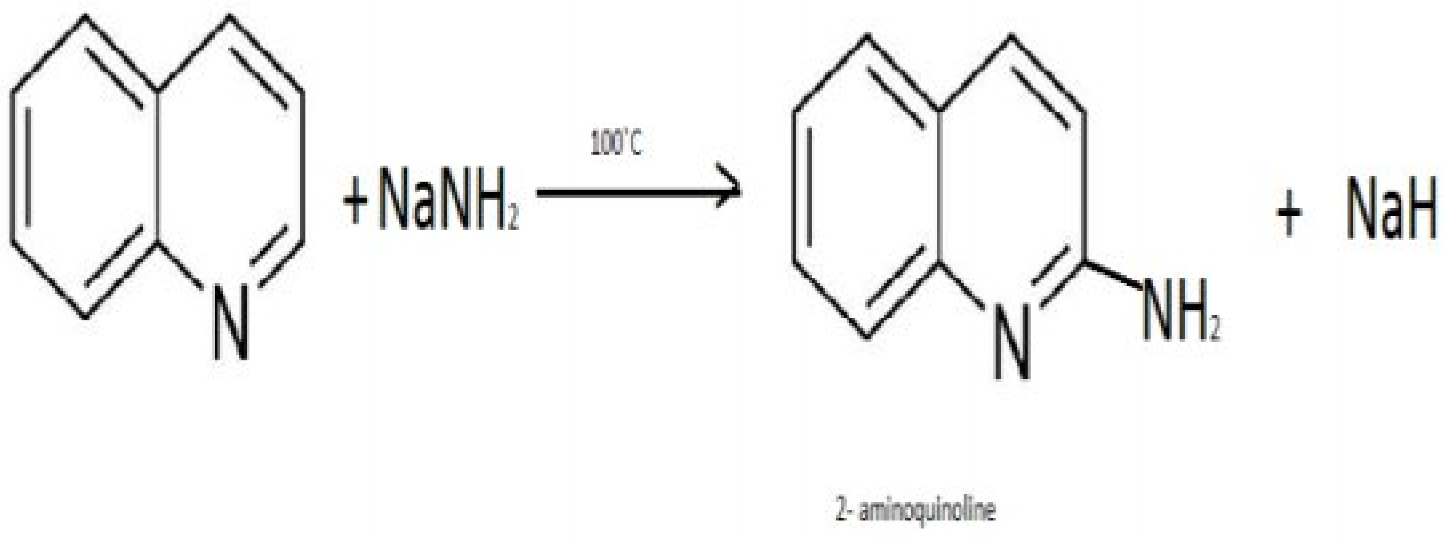


44.2.4 SULPHONATION

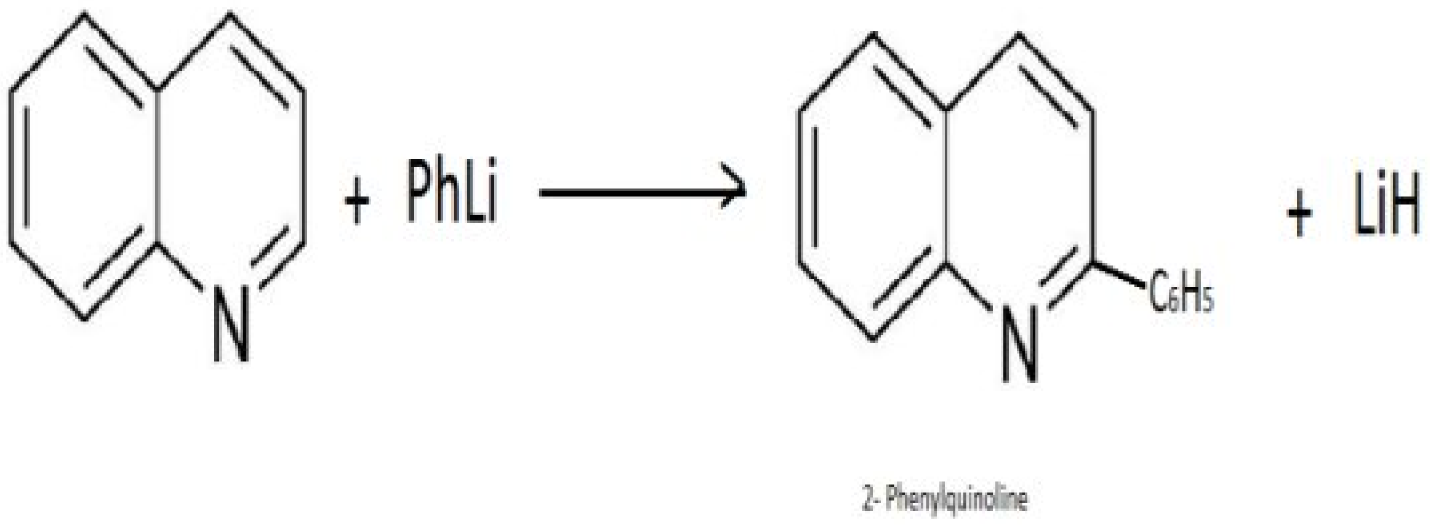


NUCLEOPHILIC SUBSTITUTION REACTION

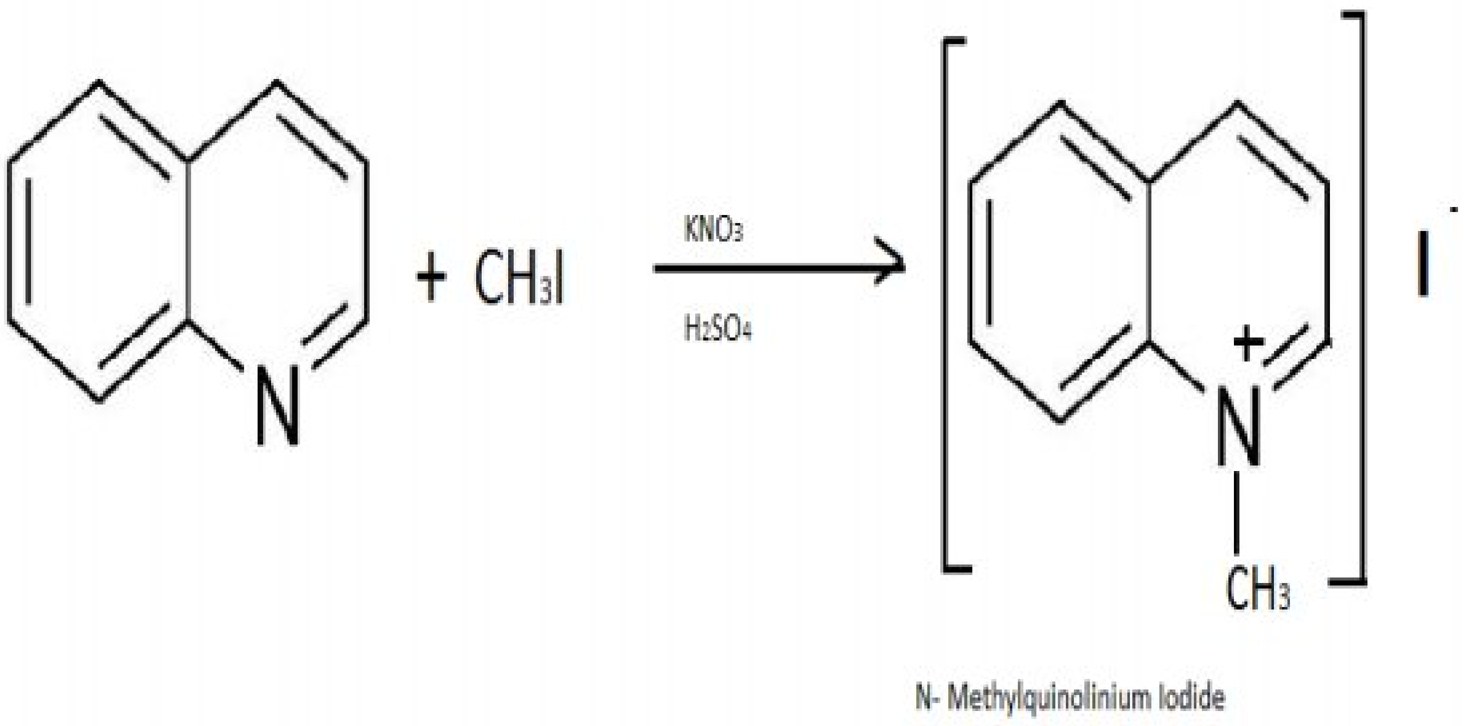
REACTION WITH SODIUM AMIDE



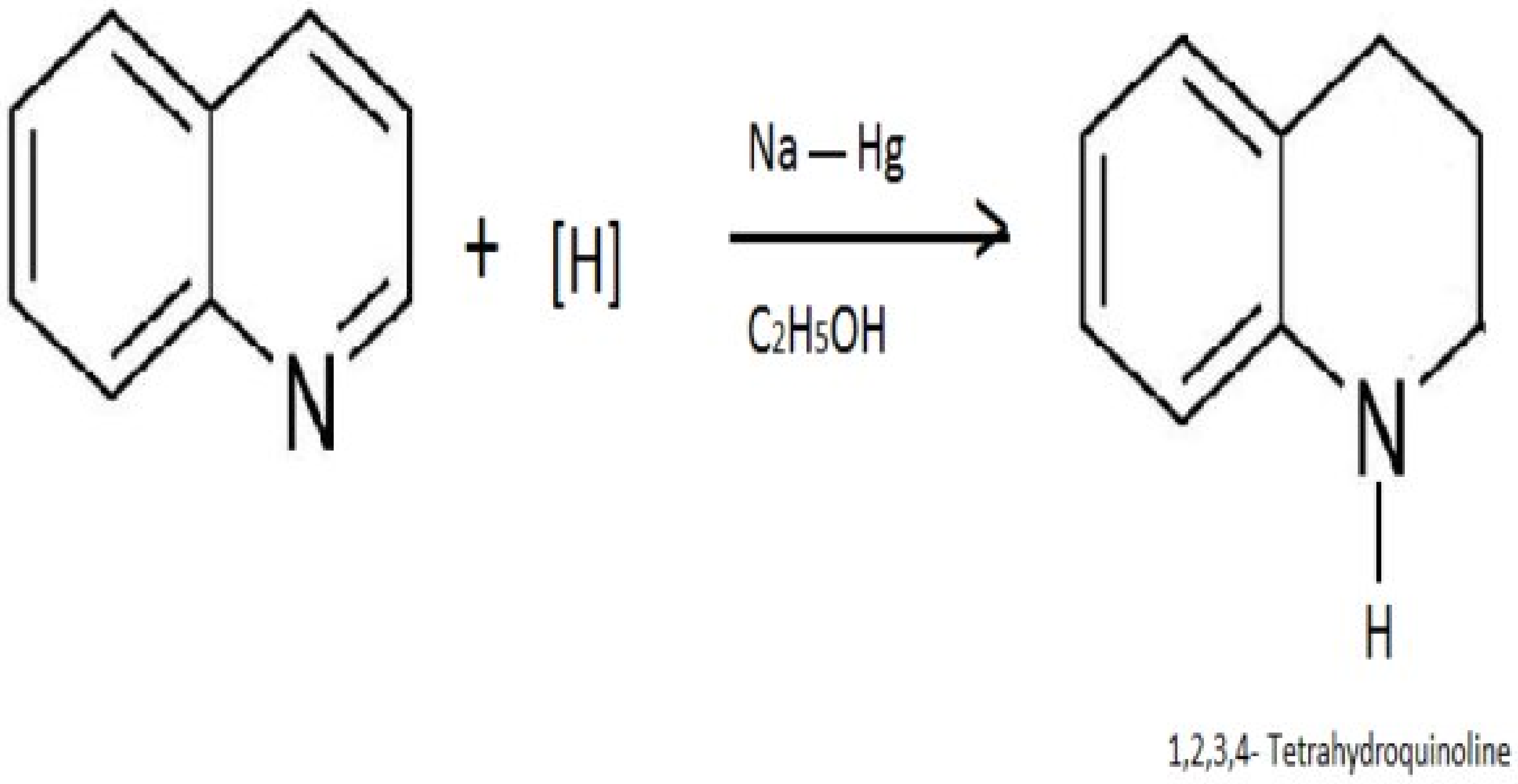
REACTION WITH PHENYL LITHIUM



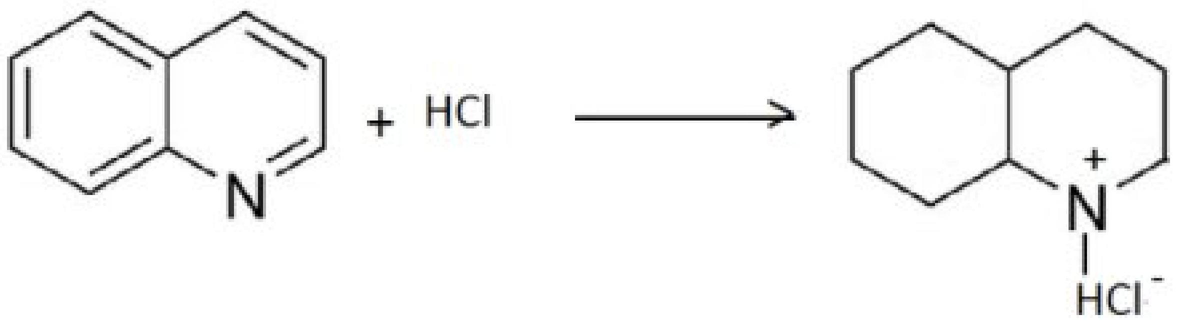
REACTION WITH ALKYL HALIDE



44.2.5 REDUCTION



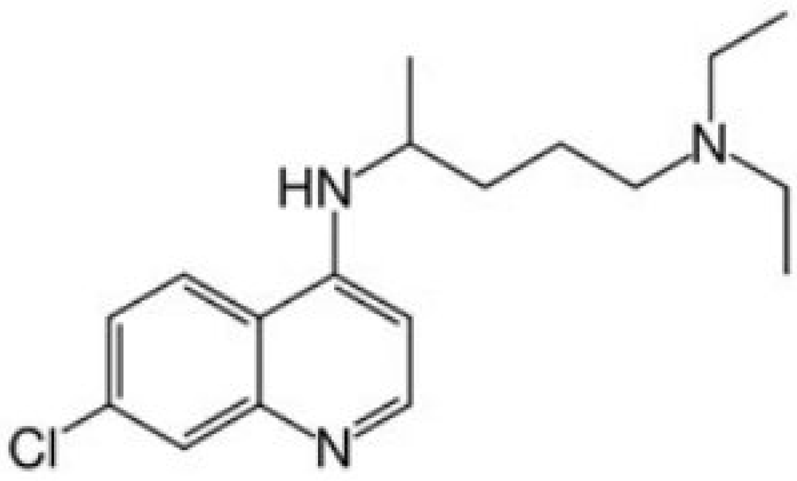
44.2.6 SALT FORMATION



USES

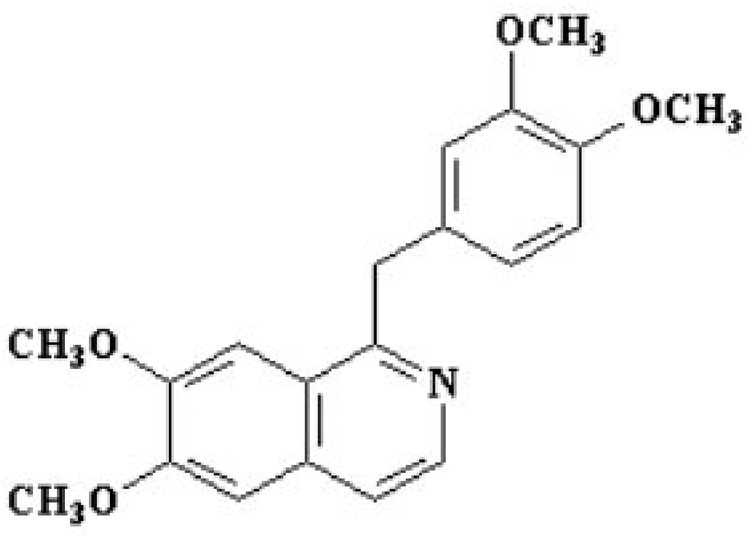
- As high boiling point organic solvent
- In the manufacture of pharmaceutical dyes and insecticides

44.3 COMPOUNDS CONTAINING QUINOLINE



Chloroquine

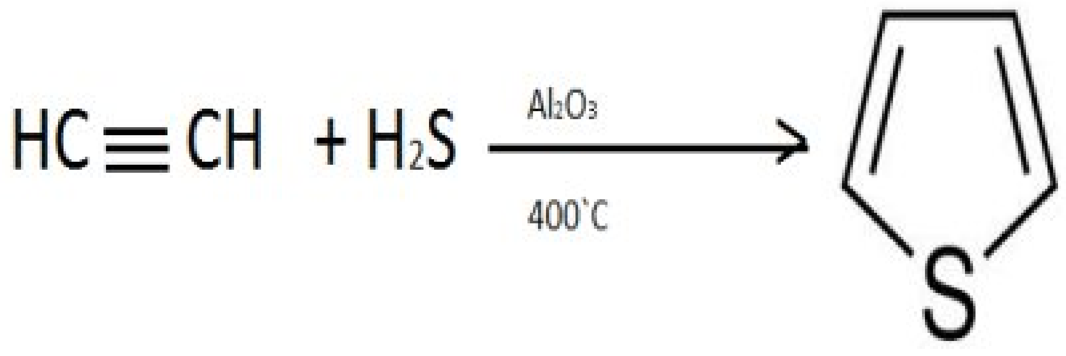
Papaverine
$C_{20}H_{21}NO_4$



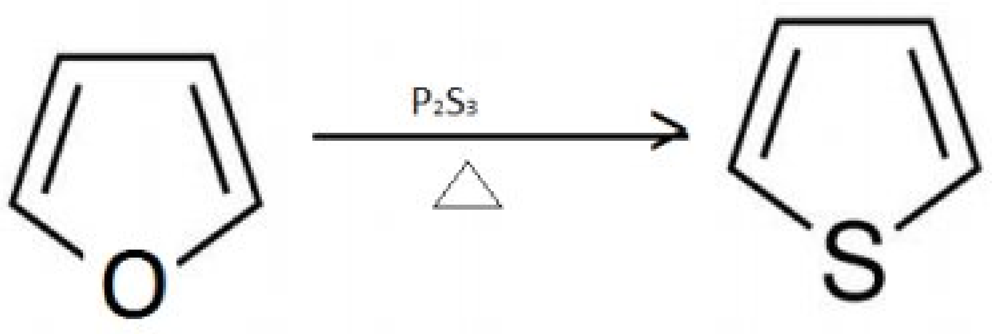
Chapter 45 THIOLE

MANUFACTURING:

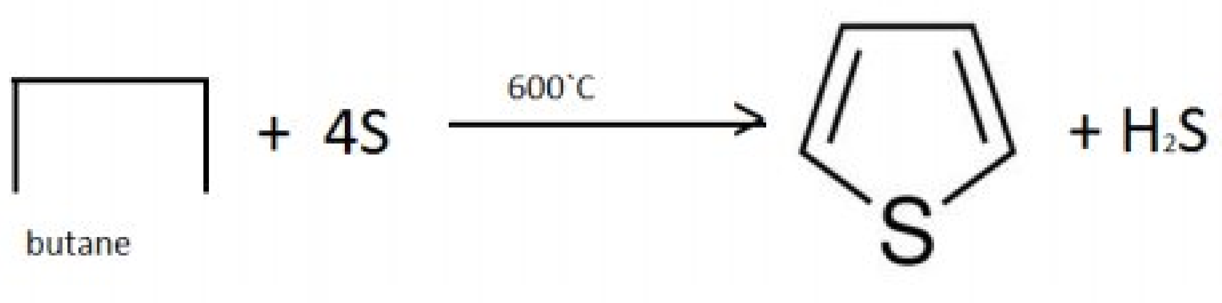
1) FROM ACETYLENE:



2) FROM FURAN:



3) FROM BUTANE:



PROPERTIES:

A) PHYSICAL:

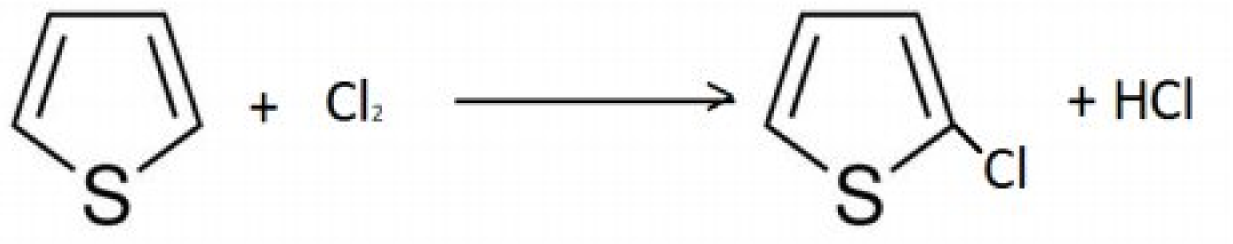
iv. Thiophene is a colourless liquid with a boiling point of 84 degree centigrade
v. Odour is similar to benzene
vi. Insoluble in water
vii. Freely soluble in alcohol, ether and acetone
viii. Flammable and moderately toxic

45.1.1 B) CHEMICAL PROPERTIES:

It is least reactive out of Furan and Pyyrol but three hundred times more reactive than benzene.

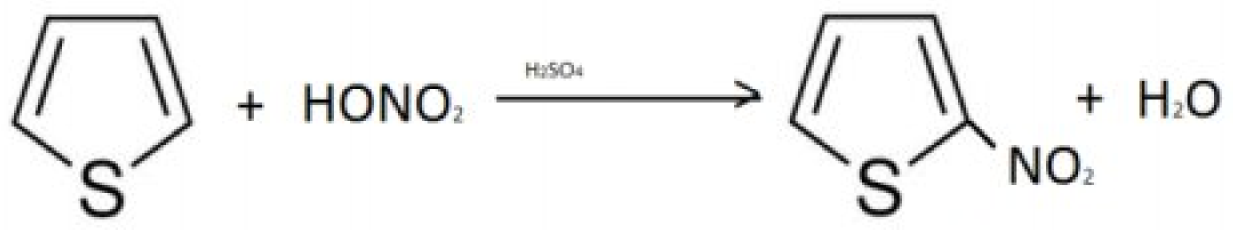
45.1.2 ELECTROPHILIC SUBSTITUTION REACTION:

45.1.3 HALOGENATION:



2- Chlorothiol

45.1.4 NITRATION:

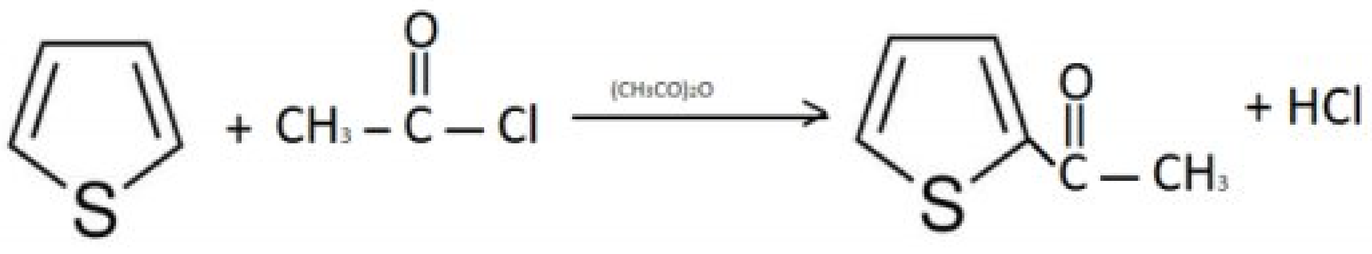


2- nitrothiol

45.1.5 SULPHONATION:

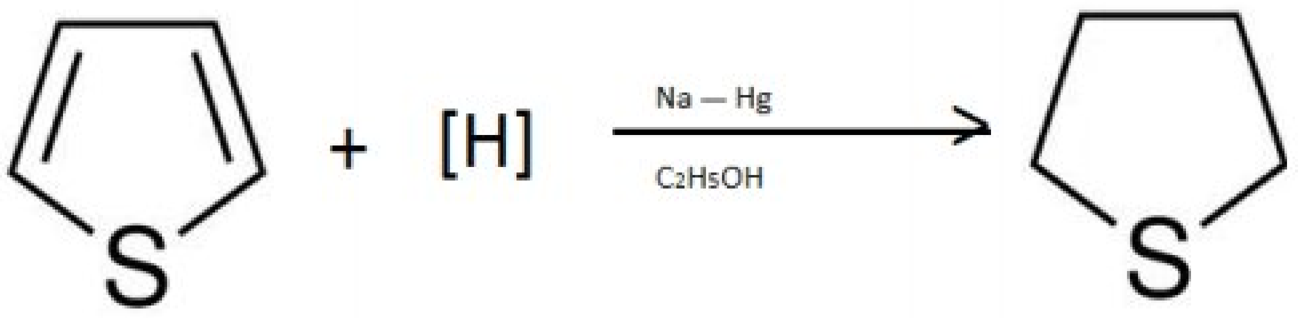
2- thiol sulphonic acid

45.1.6 FRIEDEL CRAFT REACTION:



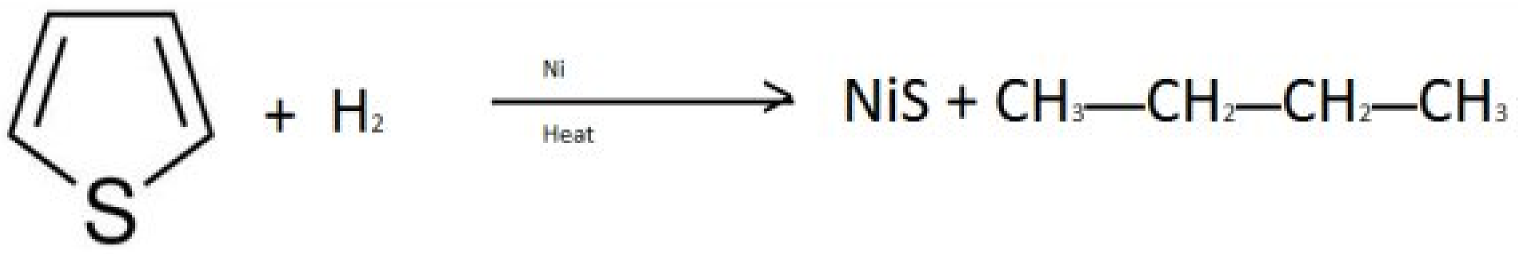
2- Acetylthiol

45.1.7 REDUCTION:



Tetrahydrothiophene

45.1.8 DESULPHURIZATION:



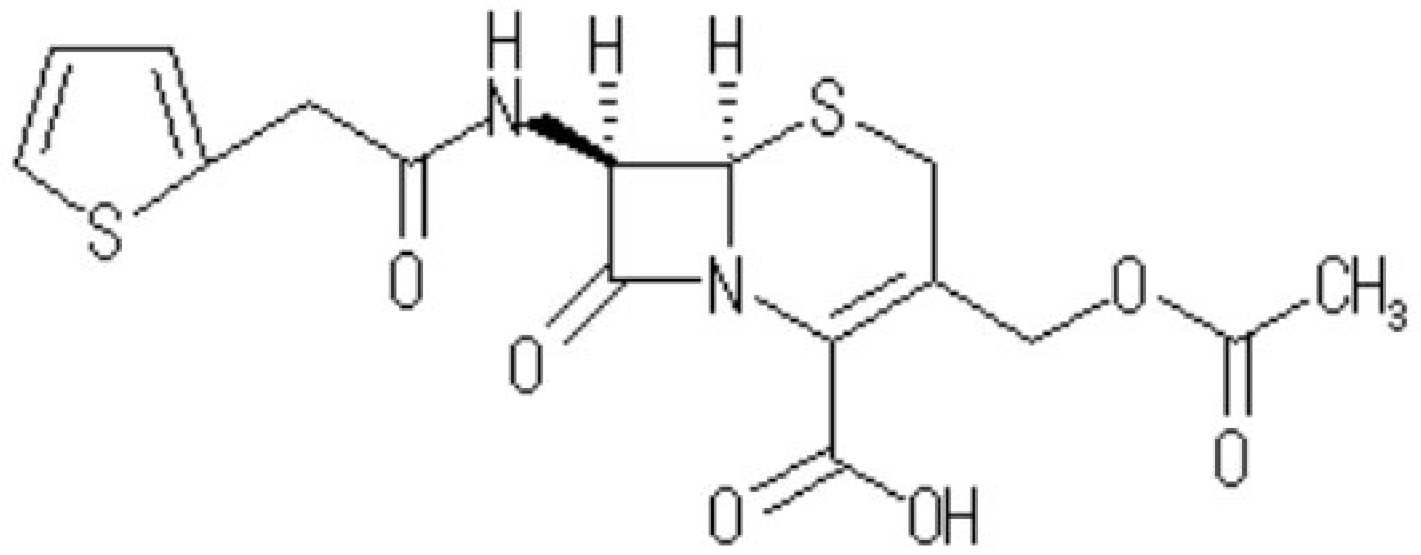
45.1.9 OXIDATION:

Does not give oxidation reaction

45.1.10 SALT FORMATION:

Does not form Salt

45.2 PHARMACEUTICAL COMPOUNDS HAVING THIOL RING:



Cephalothin

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