

# Chit - 4

## [ Stereo-chemistry ]

1ste \_\_\_\_\_  
1age \_\_\_\_\_

### Isomorphism -

Definition  
+  
Example

#### Isomers

##### Structural isomers

- i) Chain isomers.
- ii) Position isomers
- iii) Functional group isomers
- iv) Metamers
- v) Tautomers
- vi) Ring-chain isomers.

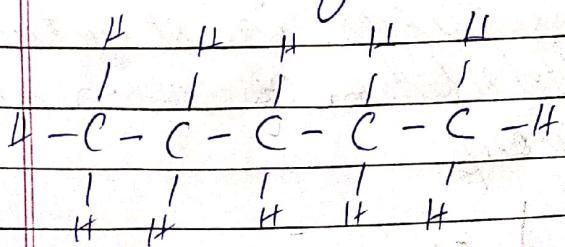
##### Stereo-isomers

- i) Geometrical isomers
- ii) Optical isomers.
- iii) Conformational isomers.

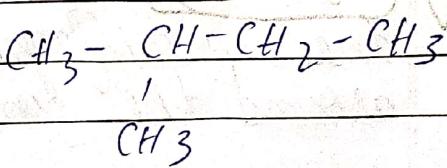
##### Structural isomers

Isomers having same molecular formula but different molecular structure due to different arrangement of atoms in their molecules.

- i) Chain isomers - These isomers have different skeleton of carbon atom in the chain

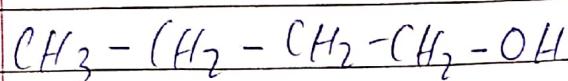


Pentane ( $C_5H_{12}$ )

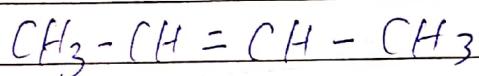


2-Methyl-butane ( $C_5H_{12}$ )

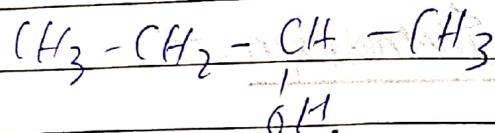
ii) Position iso-merism - These isomers have different position of functional group / multiple bond.



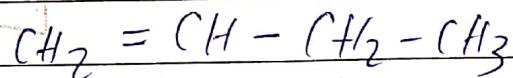
$\text{C}_4\text{H}_{10}\text{O} \rightarrow$  Butan - 1 - ol



But - 2 - ene



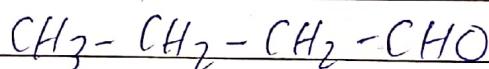
Butan - 2 - ol  $\text{C}_4\text{H}_{10}\text{O}$



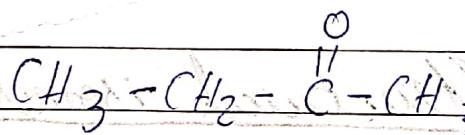
But - 1 - ene

iii) Functional isomerism - These isomers have different functional groups, so they belong to different families.

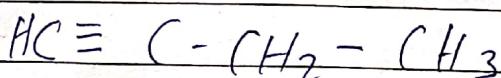
Eg:-



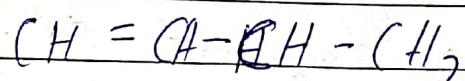
Butan - 1 - al



Butan - 1 - one

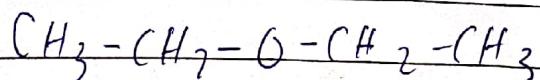


But - 1 - yne

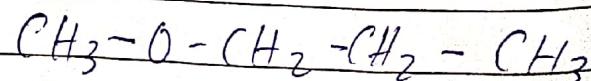


Buta 1, 3 - di - ene

iv) Metamerism - These isomers differ in structure due to difference in distribution of carbon atom around the functional group.

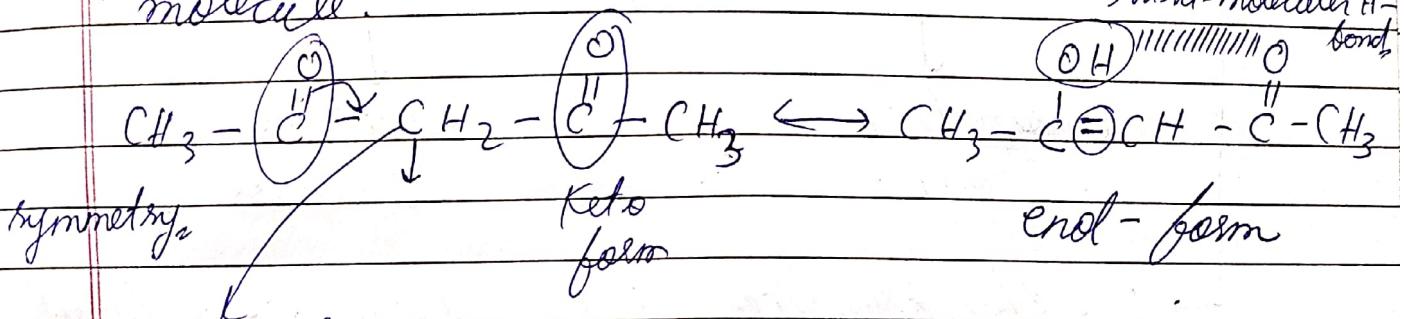


Ethoxy - ethane

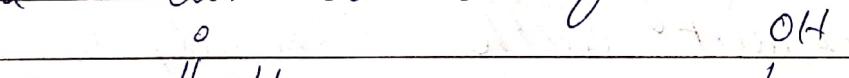


Methoxy propane

v) Tautomeress - It is type of functional group isomerism, where isomers exist simultaneously in dynamic equilibrium with each other.



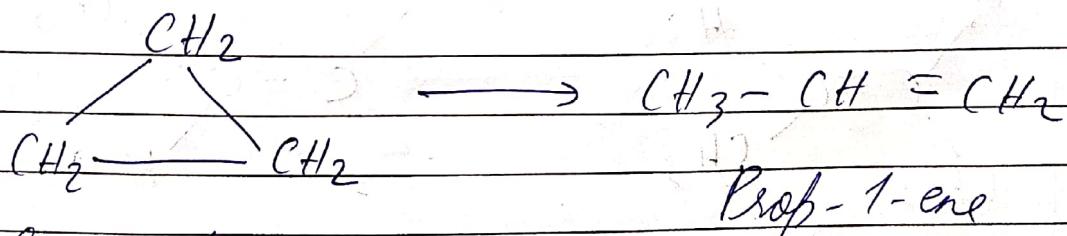
Here 2 carbo-cation is formed.



## Acetaldehyde

~~Ethenol~~  
Ethenol (vinyl alcohol)

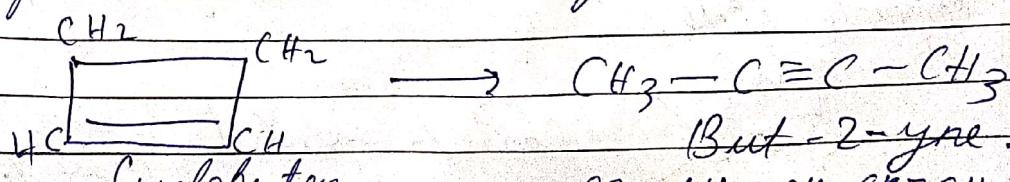
### vi) Ring-chain isomerism:-



Cyclo-propane  
 $C_3H_6$

Cyclo alkane  $\rightarrow$  alkene

cyclo alkene  $\rightarrow$  alkynes.



## Cyclobuten

But - 2 - you

or  $\text{CH}_3-\text{CH}_2-\text{C}\equiv\text{CH}$  But-1-yne

# Stereoisomerism -

Stereo-isomers have identical structures but differ in spatial arrangements of atoms

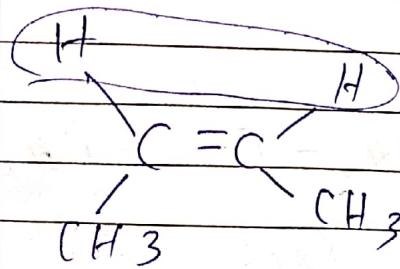
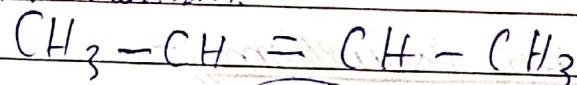
## Configuration Isomers

### Geometric Isomers

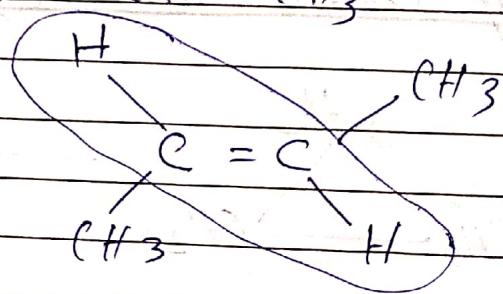
### Optical Isomers

In this isomerism inter-conversions involve bond-breaking process, so these isomers inter-convert with difficulty under normal conditions and they can be easily separated.

Geometric Isomerism :- a) It is also known as cis-trans isomerism.

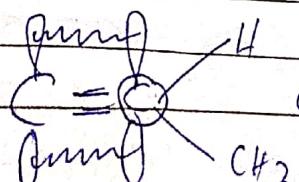


Cis- But-2-ene



Trans But-2-ene

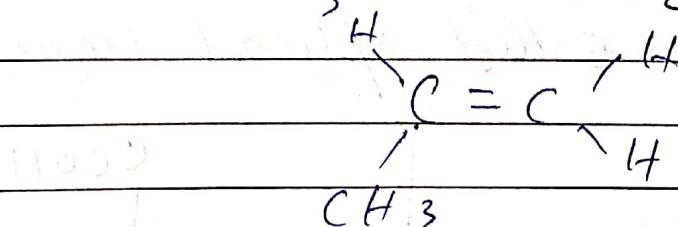
In cis-isomers, two bulky group or heavier group are on same side of double bond while in trans isomer, two bulky groups are on opposite side.



Can't be rotated & thus cis can't be converted to trans.

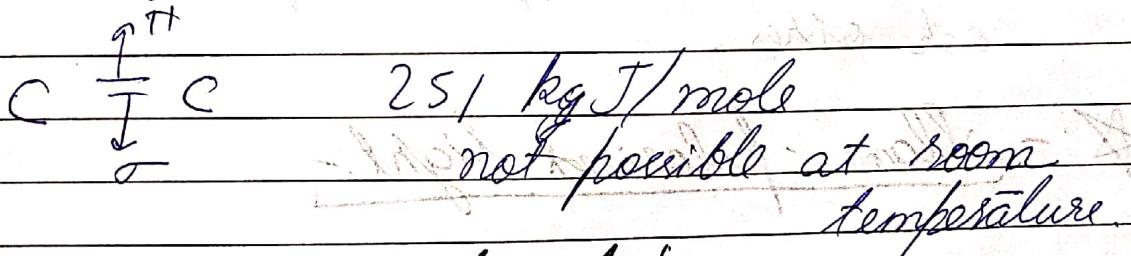
b) Geometric isomerism is due to spatial geometry associated with double bond which restrict rotation above it.

c) In case:-  $\text{CH}_3 - \text{CH} = \text{CH}_2$



Geometrical isomerism will not be possible if one of the unsaturated carbon atom is bonded to two identical group.

d) Restricted rotation around carbon atom about a double bond, is the main cause for geometrical isomerism.

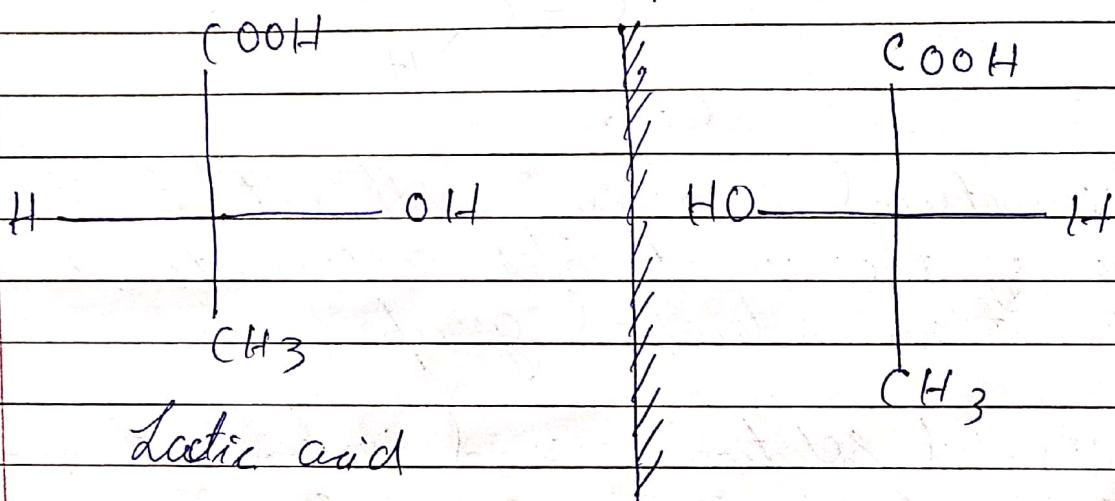


### Properties of geometrical isomers:-

- i) Different physical properties like M.P., B.P. etc.
- ii) Can be easily separated by fractional distillation or chromatography.
- iii) Almost similar chemical properties.
- iv) Trans is more stable, bulky group opposite side, steric hindrance is minimum.

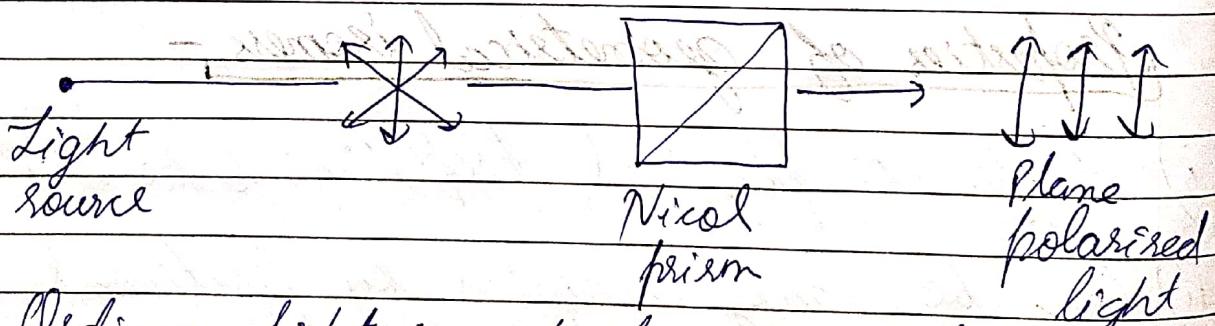
## \*:- Optical Isomers:-

Some compound can exist in two stereoisomeric forms whose molecular structure can't be super-imposed on one another. Such compounds are called optical isomers.



Don't super-impose, optical isomers of each other.

## \*:- Plane-polarized light:-



Ordinary light consist of waves vibrating in all the planes perpendicular to the line of propagation. When such light is allowed to pass through NICOL prism or crystalline  $\text{CaCO}_3$ , its vibrations in all the planes are cut off except one plane. Such a light whose vibrations occur only in single plane is known as PPL.

## \*:- Optically active substances:-

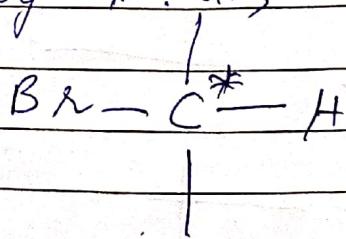
When plane polarised light is passed through the solution of certain substance, the plane of oscillation gets rotated. Substances which rotate the plane polarised light are called optically active substances.

## \* Dextrorotatory & Laevo rotatory substances:-

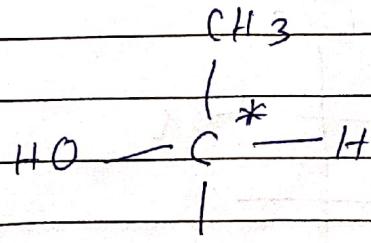
- i) Substances which rotate the plane-polarised light towards right are called dextro-rotatory substance. It is indicated by putting (+) or (d) sign before the name of the substance.
- ii) Substances which rotate plane-polarised light towards left are called laevo-rotatory substances. It is indicated by putting (-) or (l) sign before the name of the substance.

## \*:- Chirality center:-

A carbon bonded to four different atoms/groups in a molecule is called chirality centre. The carbon is called chiral carbon and represented by "\*".



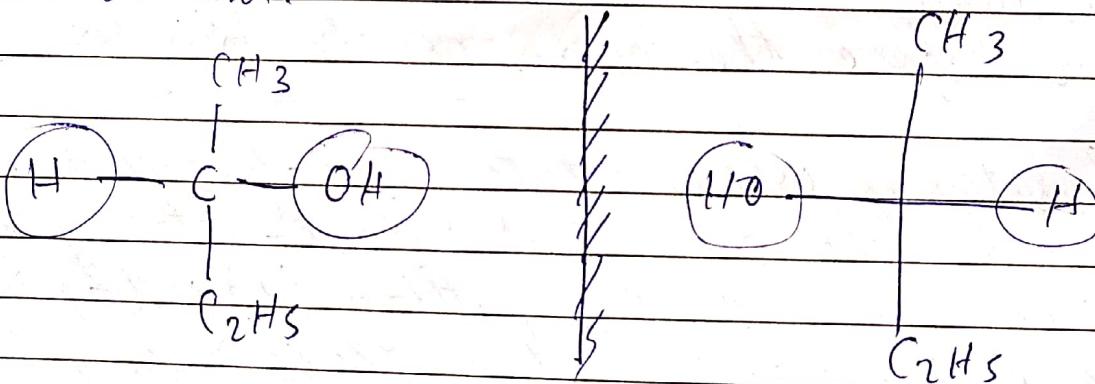
2 - Bromo - Butane



2 - Butanol.

## X:- Chiral object & Chiral molecules:-

- i) A molecule which does not have any plane of symmetry is said to be chiral
- ii) Chiral molecule have non-super-imposable mirror images
- iii) Chiral molecules are also called as dissymmetric molecules.
- iv) Common example of chiral object is our hand.



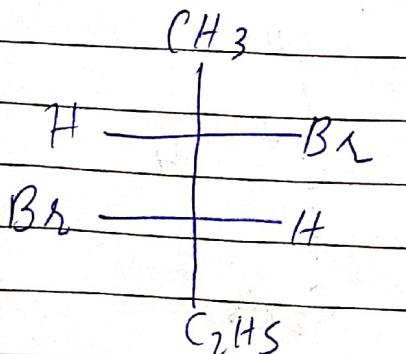
## X:- Enantiomers & Diastereomers [5-6 marks]

### a) Enantiomers,

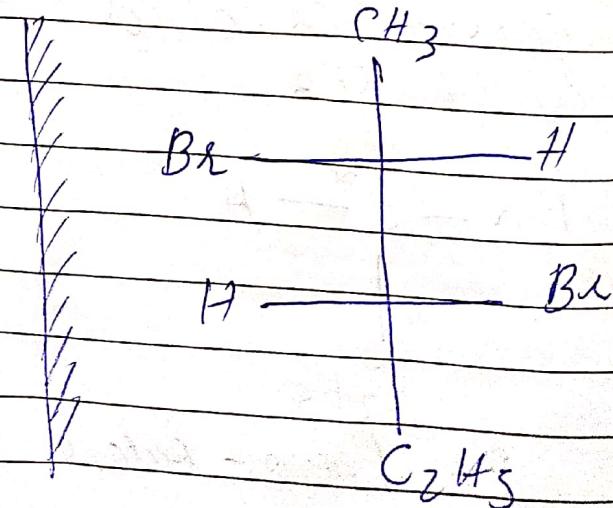
- i) The stereoisomers related to each other as non-superimposable mirror images are called Enantiomers.

not

super-imposing



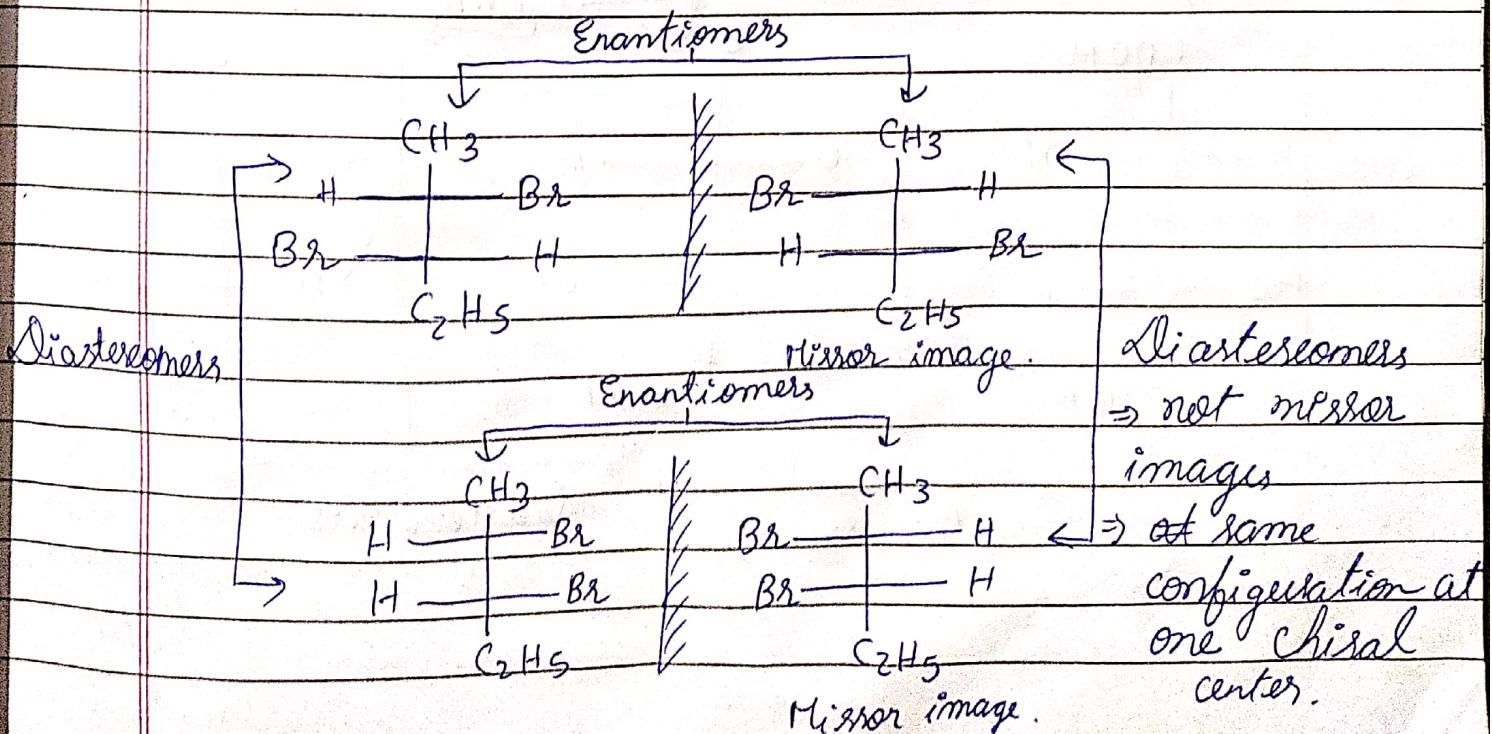
2,3 di-bromo  
pentane.



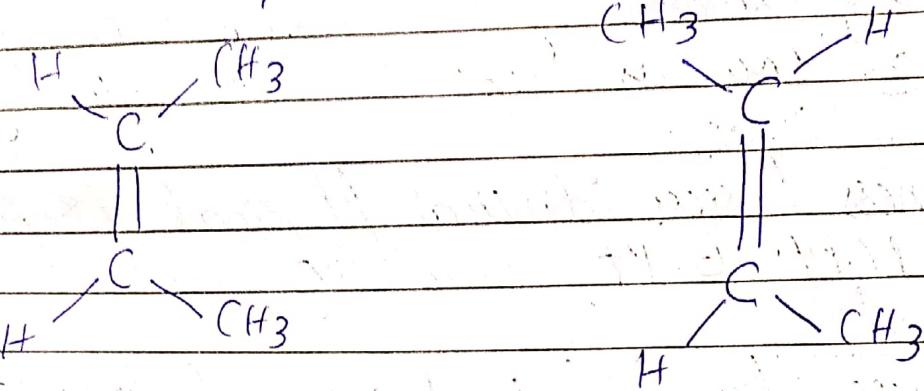
- ii) They rotate the plane polarized light through same angle but in opposite direction.
- (+) → towards right (dextro-rotatory)  
 (-) → towards left (leavo-rotatory)
- iii) Enantiomers possess identical physical properties namely M.Pt, B.Pt, solubility etc.
- iv) Enantiomers have identical chemical properties except their behaviour towards optically active compounds.
- v) They cannot be separated by methods such as fractional distillation, chromatography or crystallization.

## b) Diastereomers:-

- i) Diastereomers are isomers that are not enantiomers and have the same configuration at one chiral center but different configuration at other.



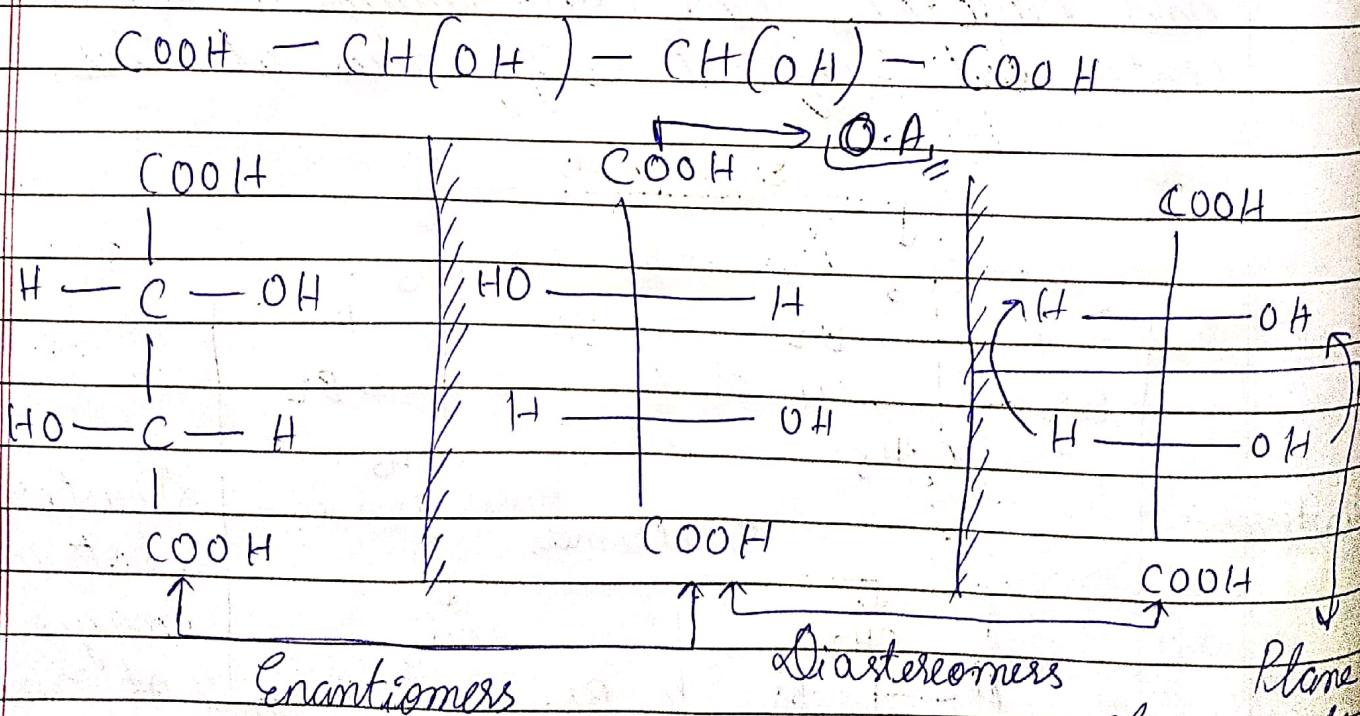
ii) Geometric isomers are also considered as diastereomers as they don't possess any mirror image relationship between them.



iii) Dia-stereomers are non-superimposable, non-mirror images of each other.

iv) They are only possible in compounds containing two or more chiral centers.

v) Diastereomers may or may not be optically active compounds.



Plane  
of symmetry  
Optically  
inactive

- vi) They have different physical properties like Melting Point, Boiling Point, Solubility.
- vii) They can be separated by fractional distillation, crystallisation, chromatography, etc.
- viii) They have similar chemical properties.

### A: Difference b/w Racemic mixture & Meso compound:

#### Racemic Mixture

#### Meso Compound

i) An equimolar mixture of two enantiomers both optically active, are mixed together, one is dextro-rotatory, another is levo-rotatory.	i) A compound which is optically inactive due to presence of symmetry.
ii) A racemic mixture is optically inactive due to external compensation.	ii) A meso-compound is optically inactive due to internal compensation.
iii) No element of symmetry in any of two enantiomers	iii) It possess plane of symmetry, center of symmetry, etc.
iv) Equimolar mixture of L & D tartaric acid	iv) Example $\rightarrow$ Meso-tartaric acid.
v) A racemate can be resolved to give optically active enantiomers.	v) Meso-Compound don't undergo resolution.

## A:- Configurational Notation for optical Isomers :-

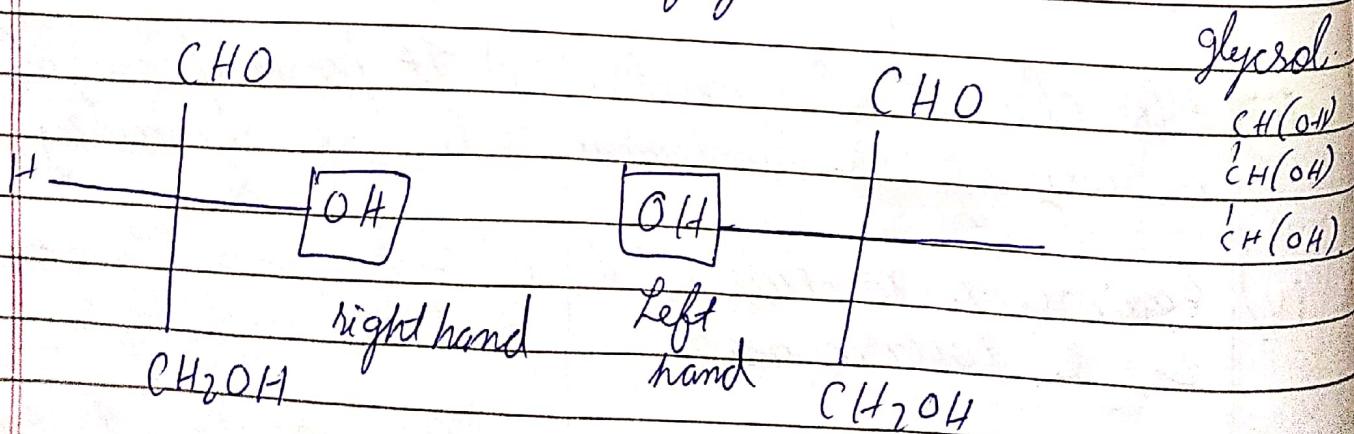
To define the structure of a compound completely, it is necessary to determine configuration at one chiral center at least.

Following are the different ways to assign configuration to stereoisomers :-

- Relative configuration (D, L notation).
- Absolute configuration (R, S notation).
- Erythro and threo configuration

### a) Relative configuration (D, L notation),-

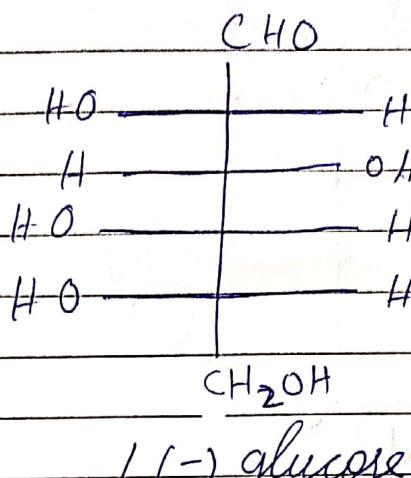
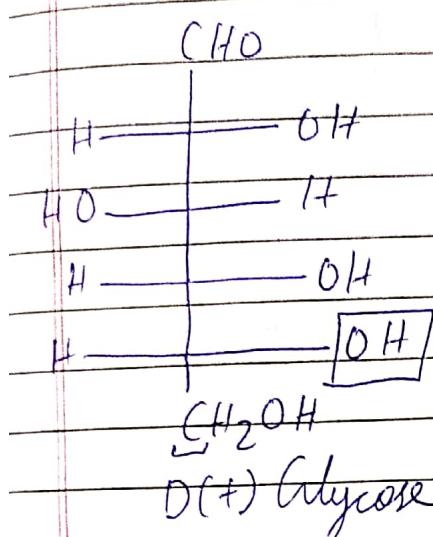
In this system, glyceraldehyde is chosen as standard and most of the sugar can be related to either D or L glyceraldehyde. The (+) enantiomer of glyceraldehyde which has -OH group on right hand side has D configuration, while (-) enantiomer of glyceraldehyde which has -OH group on left side has L - configuration.



D(+)Glyceraldehyde

L(-)Glyceraldehyde

In compounds containing several chiral carbon atoms, the bottom most chiral center is related to glyceraldehyde.

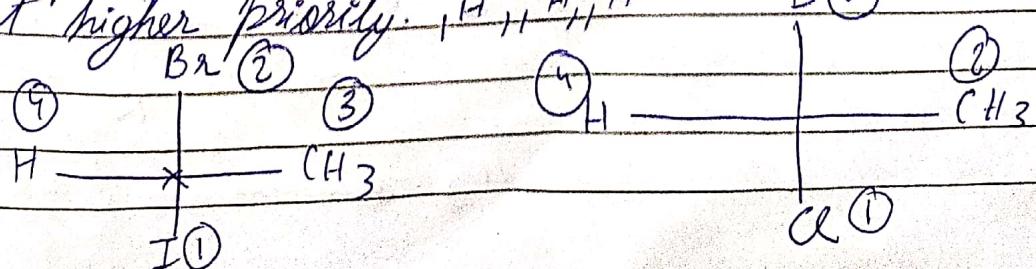


b) Absolute configuration (R,S notation) :- (Very Imp.)

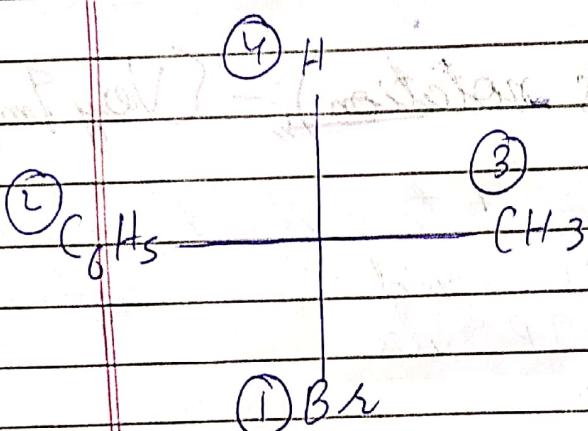
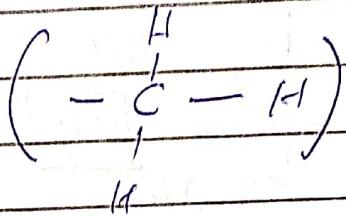
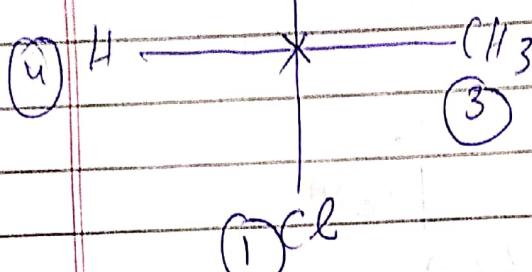
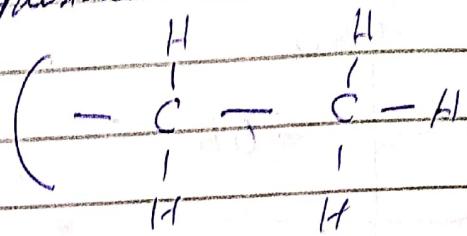
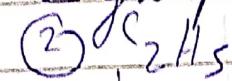
- Absolute configuration is assigned to different configurations by R.S Cahn, Siz Christopher Ingold & V. Prelog. So, they are also known as CIP rules.
- It involves two steps →

Step 0, → Using a set of sequence rules, a sequence of priority is assigned to the four ligands which remain attached to chiral center.

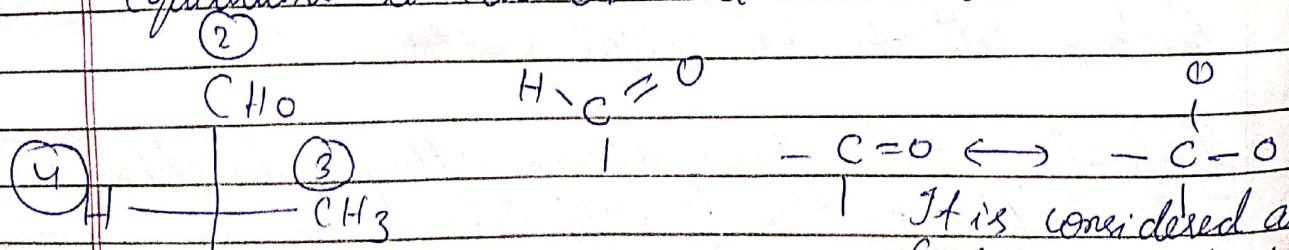
Rule - 0, :- If four atoms attached to chiral center are different, then priority depends on the atomic number, with the atom having higher atomic number getting higher priority. If two atoms are isotopes, then the one with higher mass numbers get higher priority.  $\text{H}, \text{H}^1, \text{H}^2, \text{H}^3$  D(3)



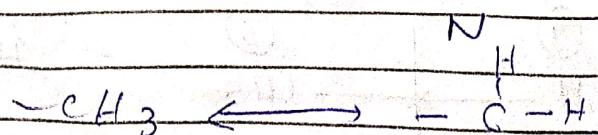
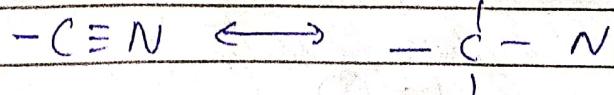
Rule (2) :- If two atoms directly attach to asymmetric center having same atomic number, then priority is assigned by similar comparison to the next atom in the group.



Rule (3) :- A doubly or triply bonded atom is equivalent to two or three such atoms

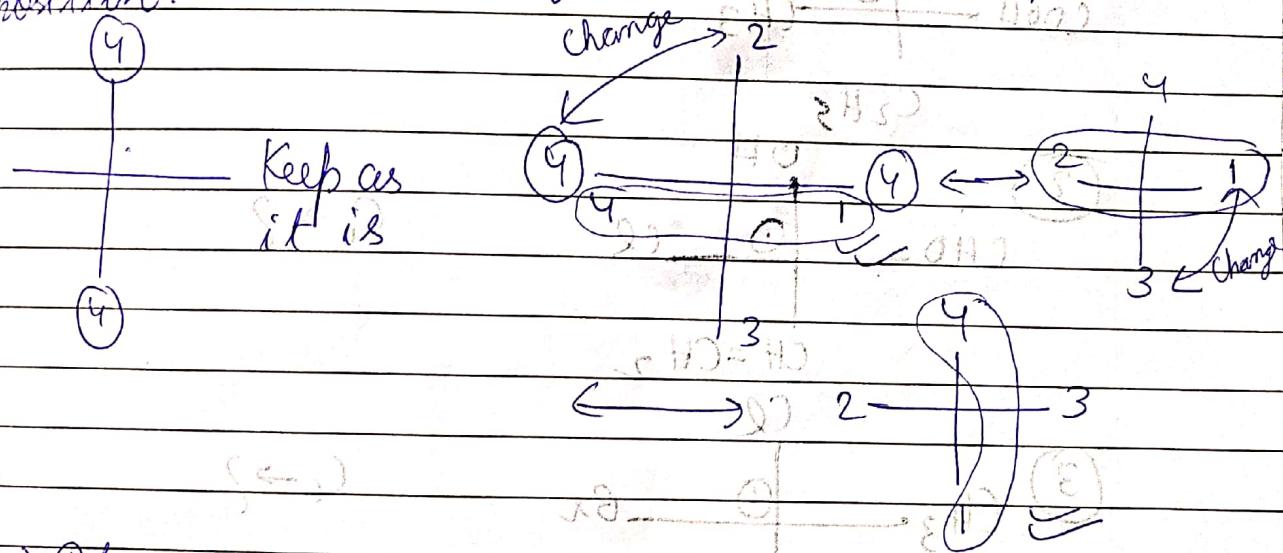


It is considered as  
Carbon is attached  
to 2 oxygen.

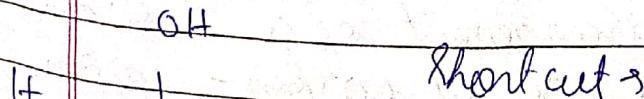
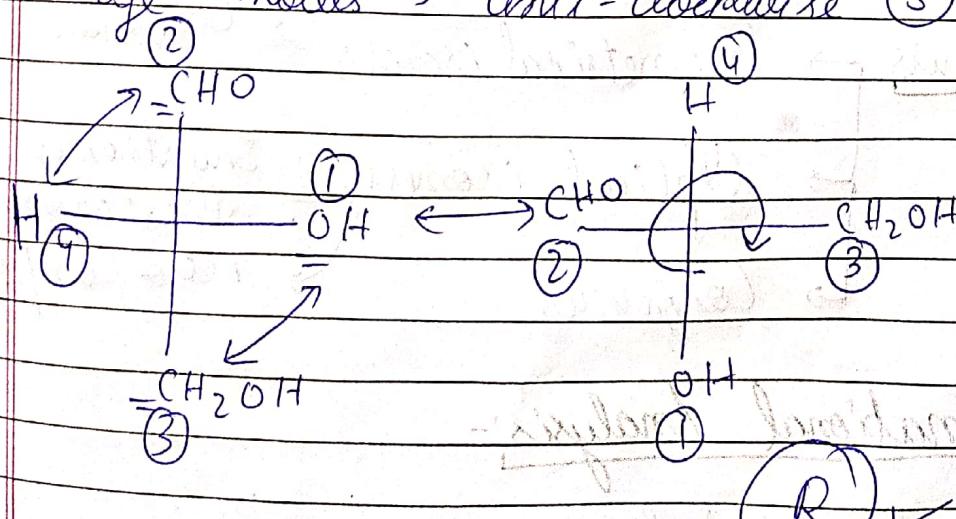


Step ② - i) Assign priority to all the four groups attached to chiral centers.

ii) If group or atom of least priority is present at vertical line, then there is no need to do any interchange of group, otherwise do any two interchanges of group so that group of lowest priority occupy vertically downward or upward position.



iii) Now move the eye  $\rightarrow ① \rightarrow ② \rightarrow ③$   
eye moves  $\rightarrow$  clockwise  $(R)$   
eye moves  $\rightarrow$  anti-clockwise  $(S)$



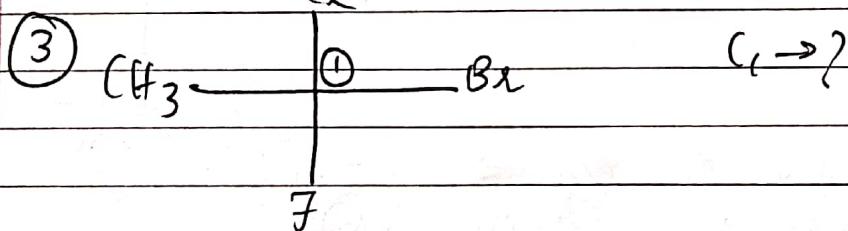
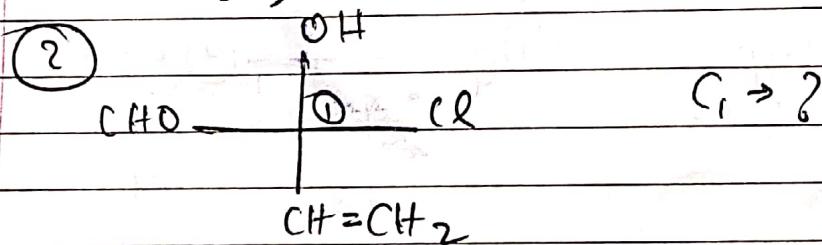
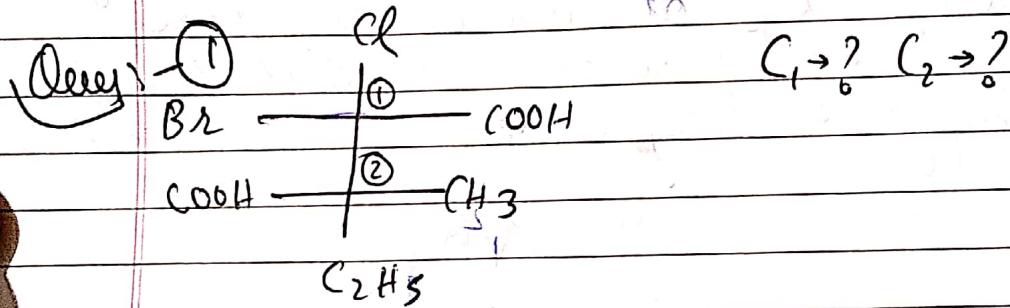
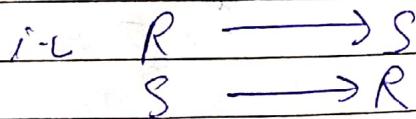
Shortcut  $\rightarrow$

If the group of least priority is at H-line, move eye on groups  $① \rightarrow ② \rightarrow ③$

The compound which rotates the plane polarized light is D & L is called optical activity

CLASSEmate  
Date \_\_\_\_\_  
Page \_\_\_\_\_

whatever configuration you get, just reverse it.



⇒ Stereoisomers → Geometrical isomers  $\rightarrow$  Cis, Trans

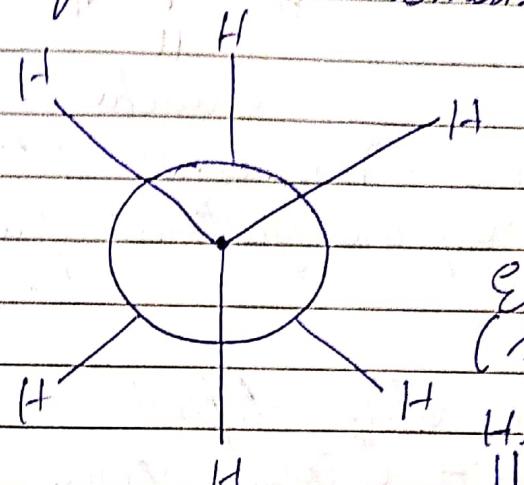
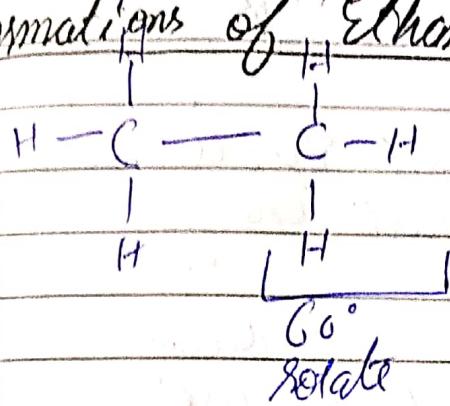
→ Optical isomers  $\rightarrow$  Enantiomers  
 $\rightarrow$  Diastereomers  
 $\rightarrow$  Conformers  $\rightarrow$  Meso Compound.

## Conformational analysis:-

The various spatial arrangement of a molecule due to free rotation around carbon-carbon single bond are called conformations.

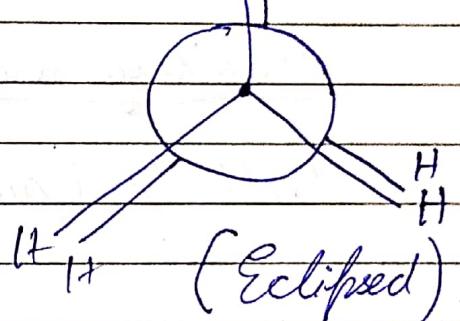
The isomers that differ in these conformations are termed as conformers or conformational isomers and the process is called conformational isomerism.

### Conformations of Ethane :-



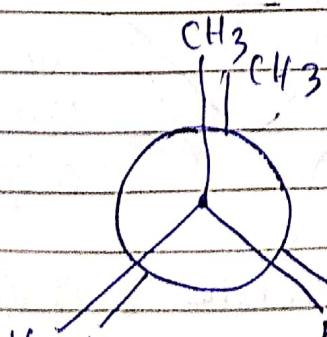
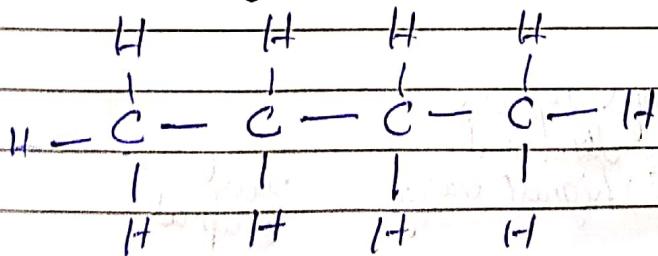
Ethane  
(Staggered)

after  
 $\xrightarrow{60^\circ \text{ rotate}}$



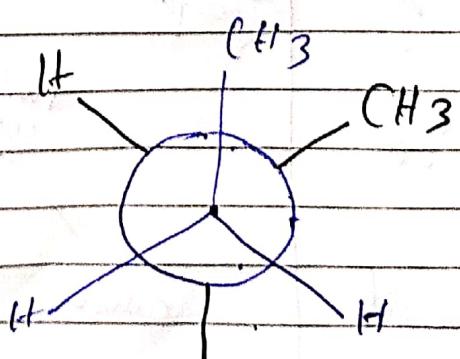
(Eclipsed).

### Conformations of Butane:-



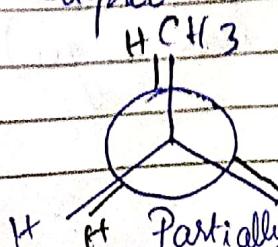
Fully eclipsed

$60^\circ$   
rotate



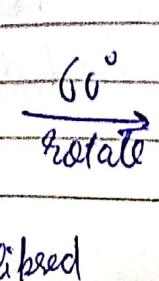
Gauche

$60^\circ$   
rotate



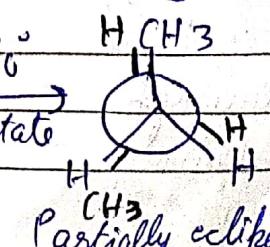
Partially Eclipsed

$60^\circ$   
rotate

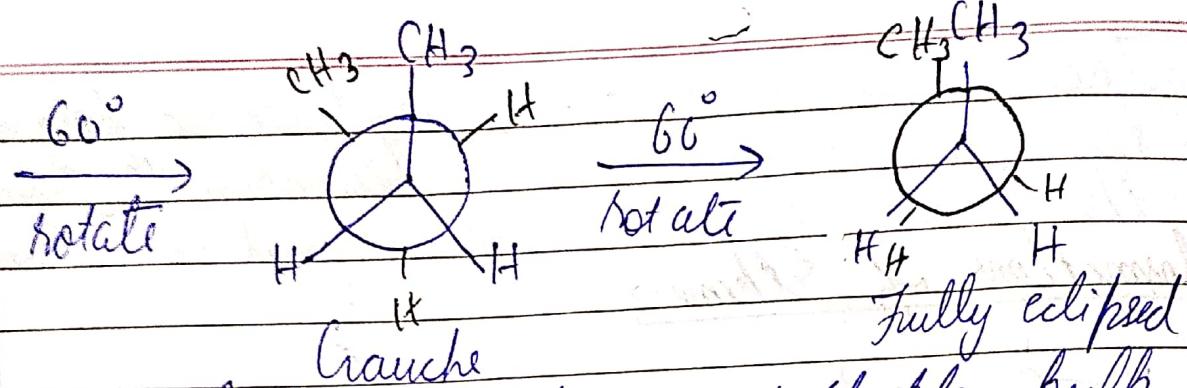


Anti form

$60^\circ$   
rotate



Partially Eclipsed



Here, in Anti form, it is most stable, bulky group are farthest apart (least energy).

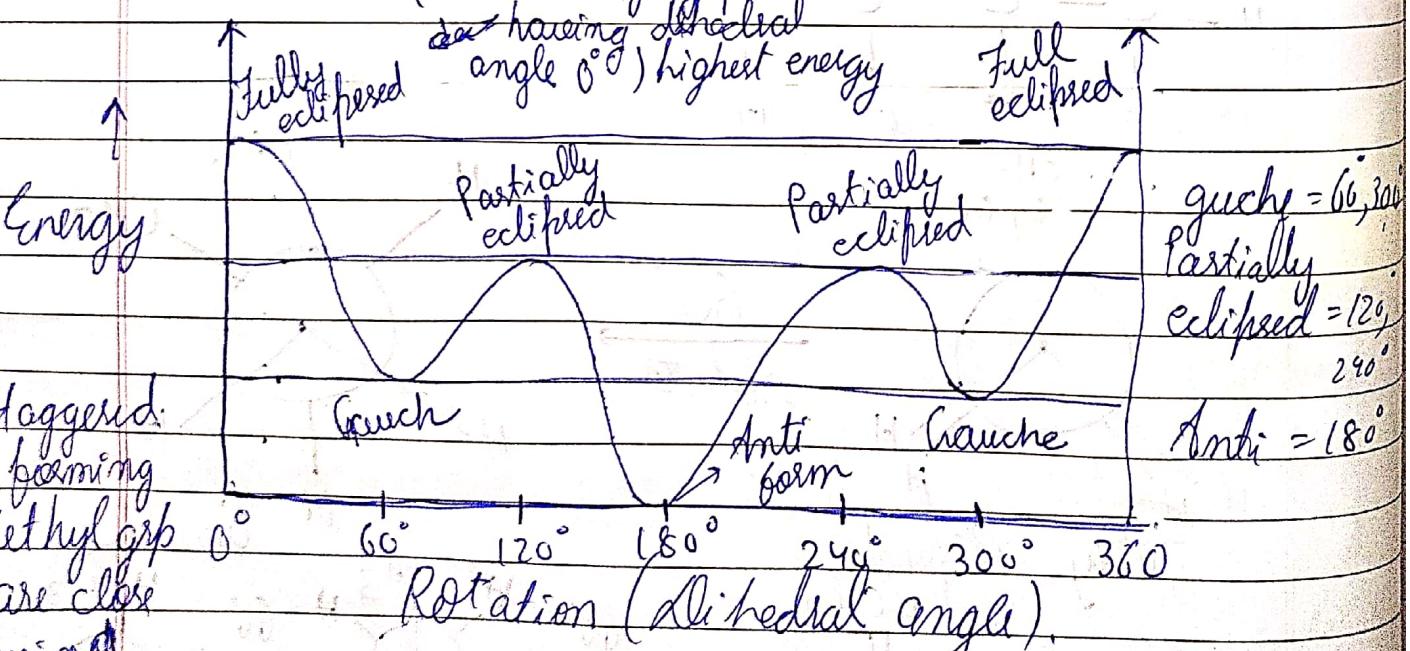
In bulky eclipsed, it is unstable, groups are quite close, steric hindrance.

### Stability order:-

Anti > Gauche > Partially eclipsed > Full eclipsed.

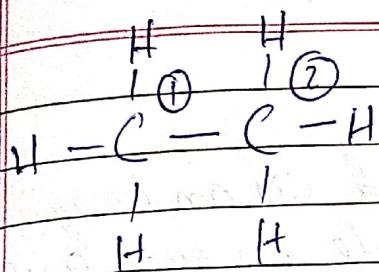
### Energy graph:-

(Both methyl grp are having dihedral angle 0°) highest energy

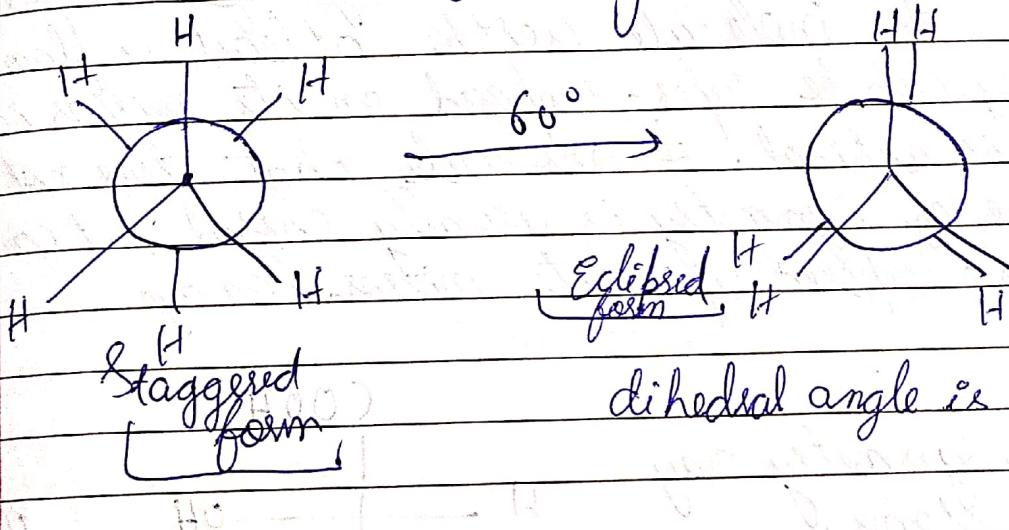


Staggered form is more stable than eclipsed form.

Methyl grp are close having dihedral angle > 60°



2 carbon C<sub>1</sub> & C<sub>2</sub> are denoted by 2 overlaid circles and one circle is drawn with its center denoting the front carbon C<sub>1</sub>, and circumference denoting the back carbon C<sub>2</sub>



### Element of Symmetry:-

Element of symmetry offer a simple device to decide whether a molecule or object is chiral or not i.e. whether it is super-imposable on its mirror image or not. When a molecule has element of symmetry, it is super-imposable on its mirror image and is achiral (optically inactive).

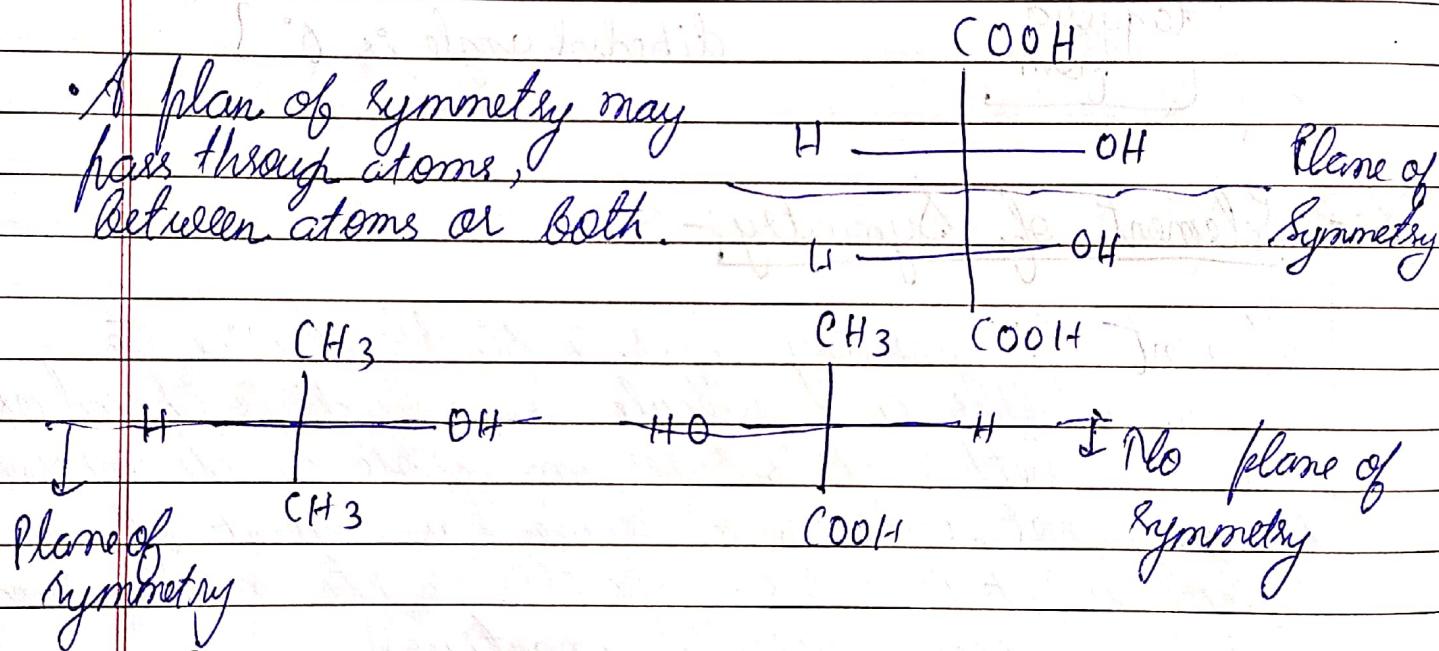
A molecule as a whole is non-symmetrical if it does not possess any element of symmetry, such as:-

- i) Plane of Symmetry.
- ii) Center of symmetry (not seen in Fisher projection).
- iii) Axis of Symmetry.

## 1. Plane of Symmetry (S) :-

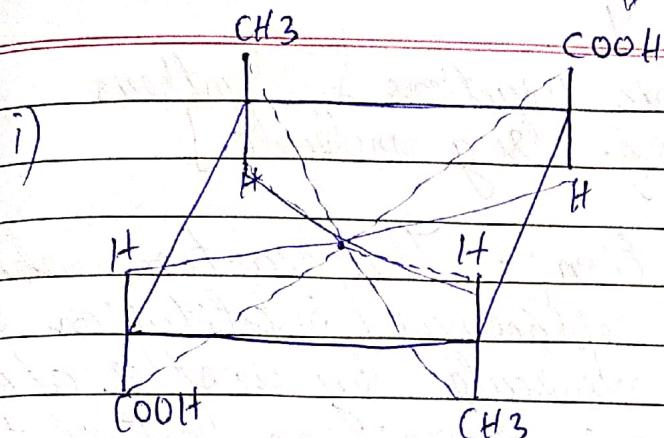
- A plane of symmetry is defined as an imaginary plane which divides a molecule in such a way that one half is mirror image of the other half. A molecule with at least a plane of symmetry can be super-imposed on its mirror image and is achiral. A molecule that does not have a plane of symmetry is usually chiral; it cannot be super-imposed upon its mirror image.

- A plane of symmetry may pass through atoms, between atoms or both.

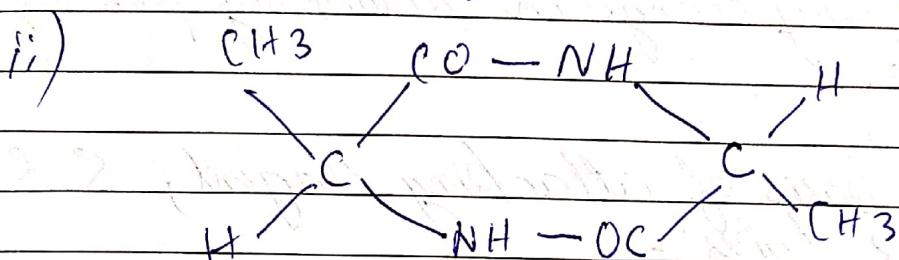


## 2. Center of symmetry or inversion ( $i$ ) or ( $E_i$ ) :-

- A center of symmetry (center of inversion) is defined as a point within the molecule such that if an atom is joined to it by a straight line which if extrapolated to an equal distance beyond it in opposite direction meets an equivalent atom. In other words it is a point at which all the straight lines joining identical points in the molecule cross each other.

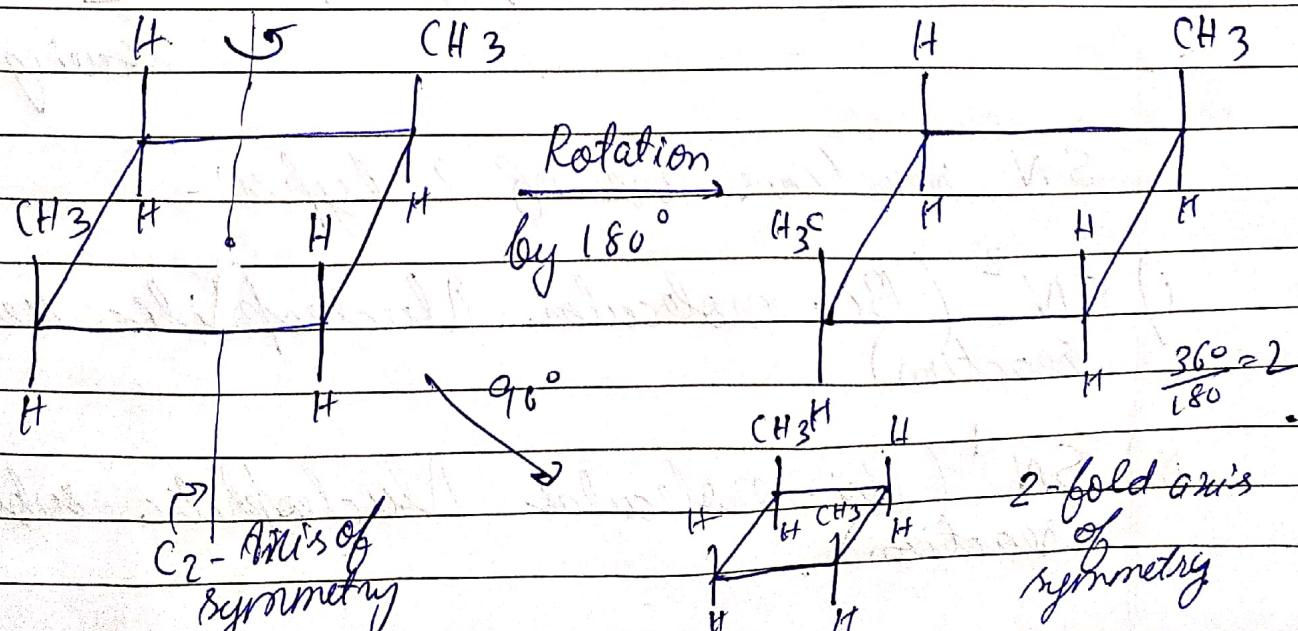


2,4-Dimethyl-cyclo  
butane - 1,3-Dicarboxylic  
acid has C<sub>2</sub>



### 3. Simple or proper axis of symmetry (C<sub>n</sub>):-

An imaginary line passing through the molecule in such a way that when the molecule is rotated about it by an angle of  $360^\circ/n$ , an arrangement indistinguishable from the original is obtained. Such an axis is called n-fold axis of symmetry. For e.g., C<sub>2</sub>-1,3-di-methyl-cyclo-butane has a two fold axis of symmetry (C<sub>2</sub>) i.e. rotation by  $180^\circ$  gives indistinguishable appearance.



## Unit-4

Part-2 [Organic Reactions & Synthesis  
of drug molecule]

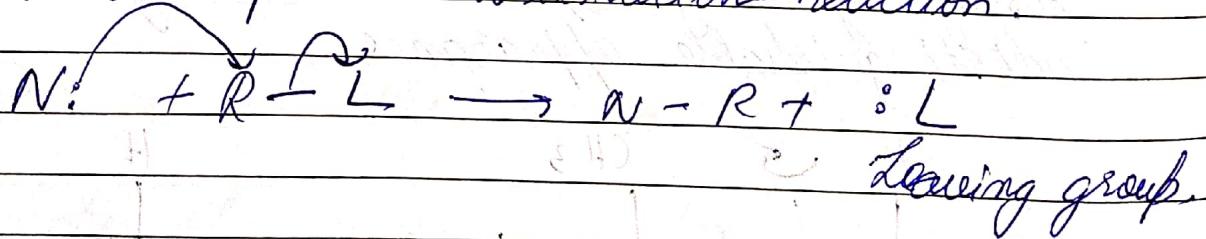
① Substitution Reaction :- The reaction which involves the direct replacement / substitution of an atom / group in a molecule by another atom / group without any change in remaining part of the molecule.

On the basis of attacking reagent, S.R are of three types:-

a) Nucleophilic Substitution Reac<sup>n</sup> (S<sub>N</sub>) →

Nucleophile  $\rightarrow$  leaving Nucleus      excess of electron pair (-ve charge ion).

When a substitution reaction involves an attack by a nucleophile, the reac<sup>n</sup> is termed as Nucleophilic Substitution reaction.

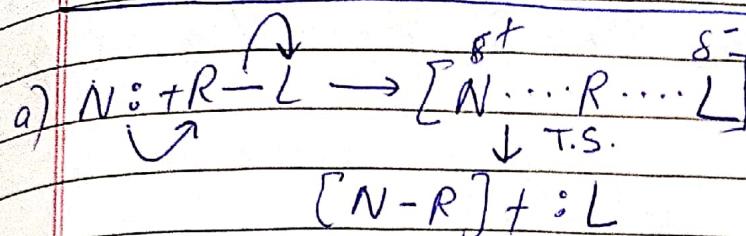


S<sub>N</sub> reactions are of 2 types:-

i) S<sub>N</sub><sup>2</sup> (Bi-molecular Nucleophilic Substitution reaction)

ii) S<sub>N</sub><sup>1</sup> (Uni-molecular Nucleophilic Substitution reaction)

## $S N^2$

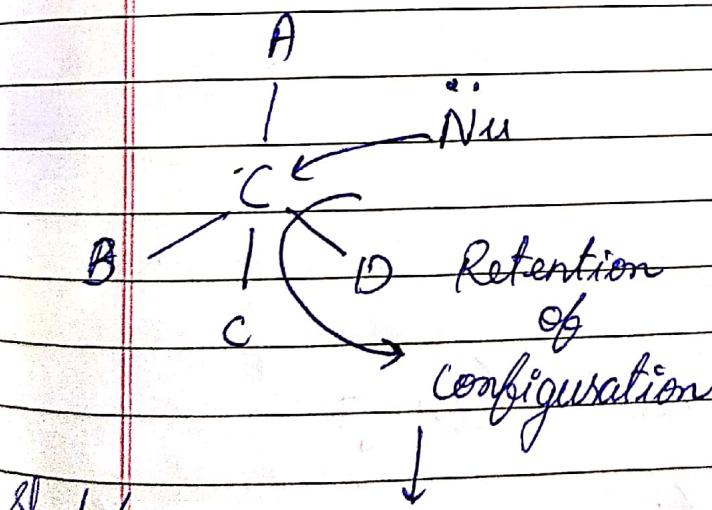


b) Rate of reaction depends upon both  $[:N][R-L]$

$$\text{rate} = K[R-L][:N]$$

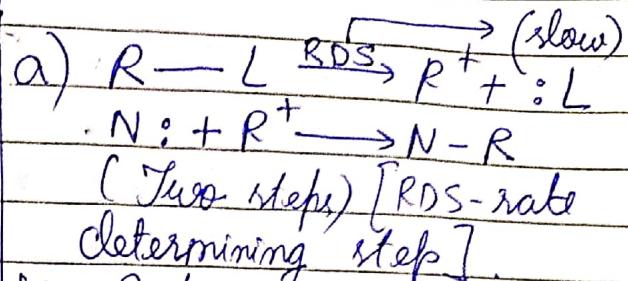
c) It follows second order kinetics.

d) In  $S N^2$ , inversion of the molecule occurs



$$\text{Speed of reaction} \rightarrow CH_3X > 1^\circ > 2^\circ > 3^\circ$$

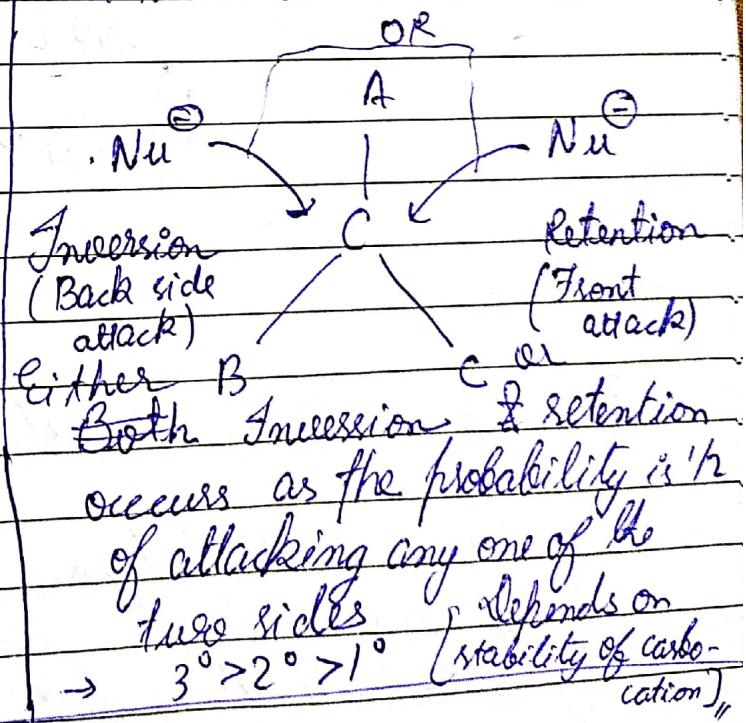
## $S N^1$



b) Rate of reaction depends only upon  $[R-L]$  so rate of reaction  $\rightarrow$  rate =  $K[R-L]$ .

c) It follows first order kinetics.

d) In  $S N^1$ , both inversion & retention occurs.



b) Electrophilic Substitution Reaction (SE):-

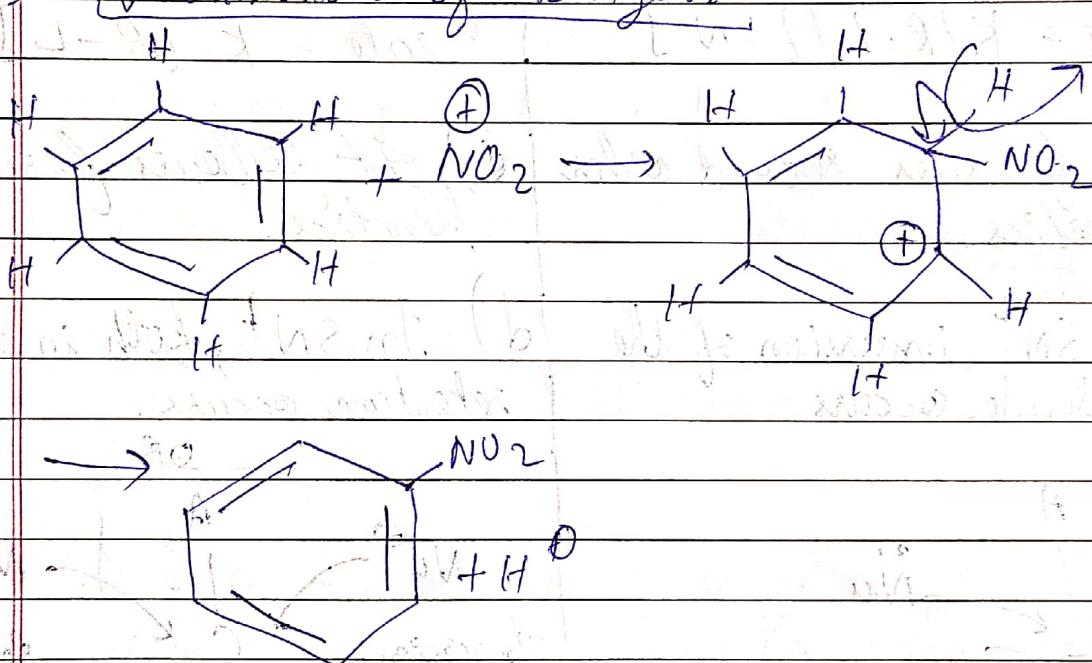
attacking reagent is Electrophile (+ve)  
Electron losing

These reactions are most found in aromatic systems where electron density are attracted by electrophiles.

Attacking species  $\rightarrow$  Electrophile

Leaving group  $\rightarrow$  that depart without the pair of bonding electrons.

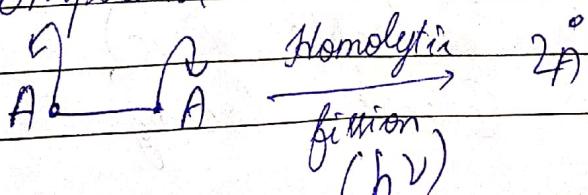
Eg:- Nitration of Benzene:-

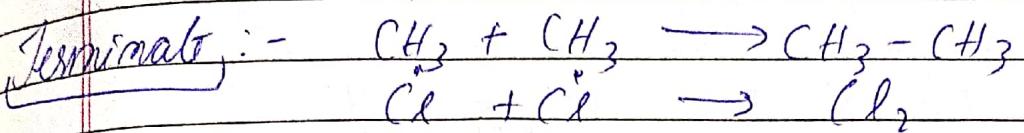
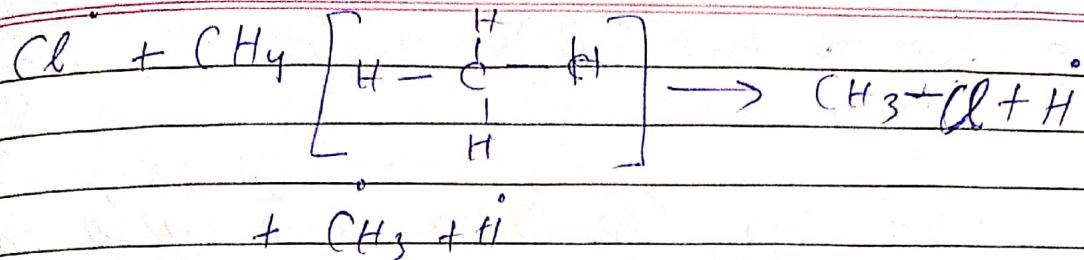
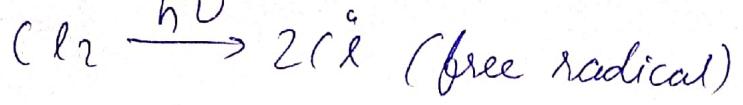


### Free Radical Substitution reaction:-

When substitution reaction involves any attack by free radical, then reaction is termed as free radical substitution reaction.

It takes place in alkanes and other saturated compound.





## (2) Elimination Reaction :-

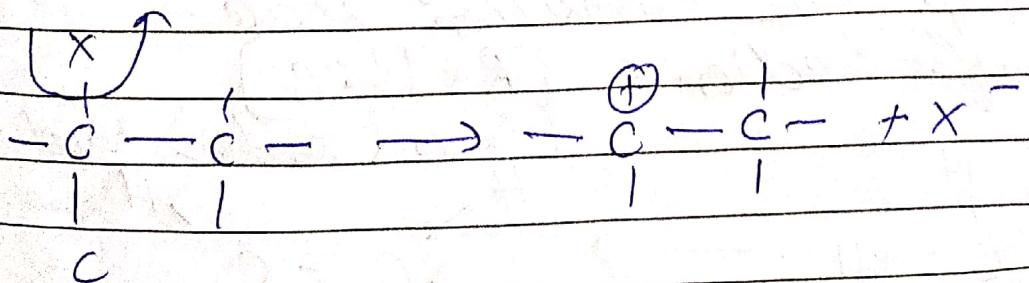
These reaction involve elimination or removal of two atoms / groups from the same or adjacent atom so that new multiple (double/ triple) bond is formed.

On the basis of rate determining, elimination reaction is divided into two types :-

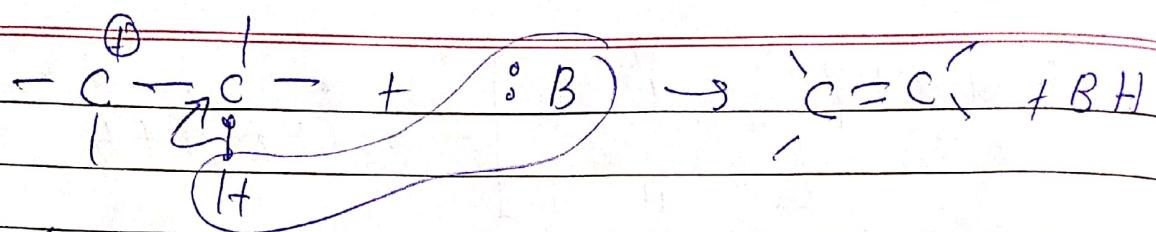
### a) E-1 (Uni-molecular elimination) :-

In this first step, the substrate undergo slow heterolysis to form carbo-cation (intermediate) and halide ion. It This is slow, rate determining step and as it involves only one substrate.

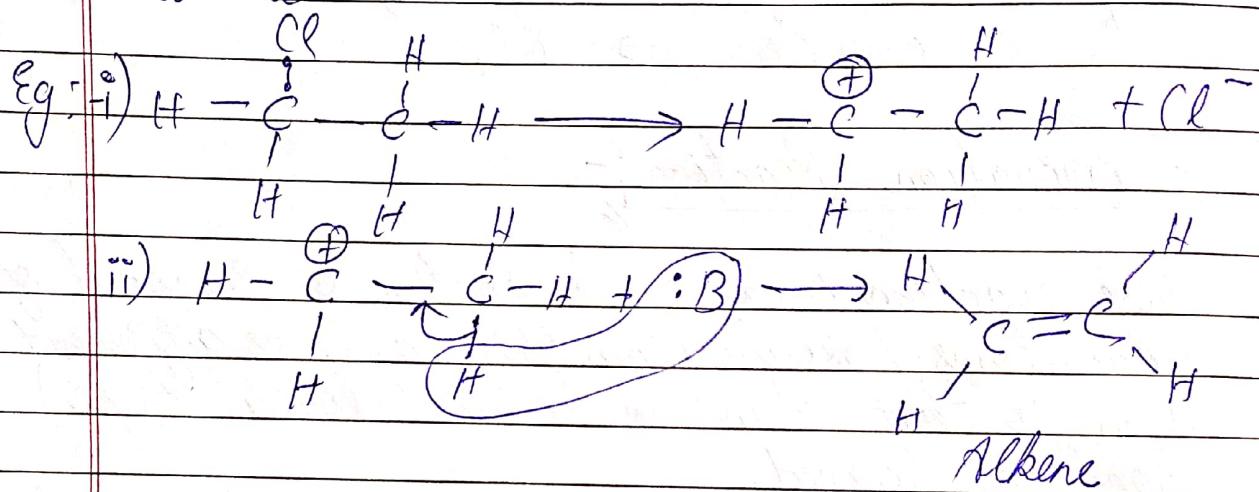
$$\text{So, rate} = k[R_X]$$



Rate depend upon  $P-X$



In second step, the intermediate carbocation rapidly loses a proton to base and form an alkene.

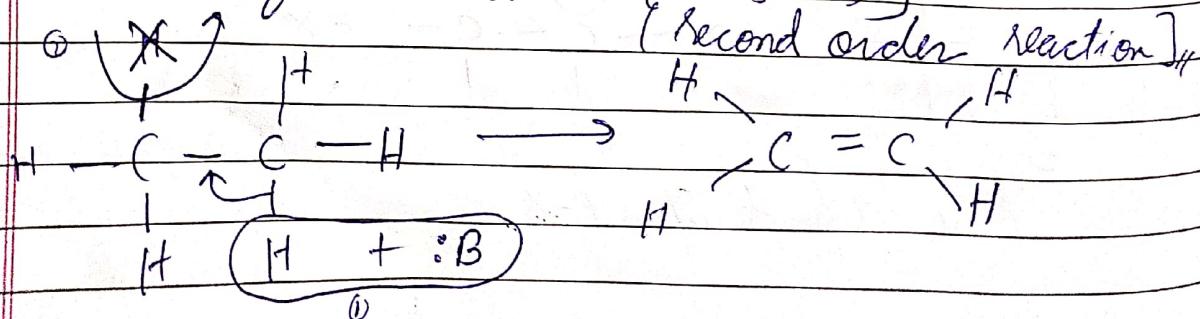


$$\text{Rate} = K [\text{C}_2\text{H}_5\text{Cl}]$$

### b) E-2 (Bi-molecular elimination):-

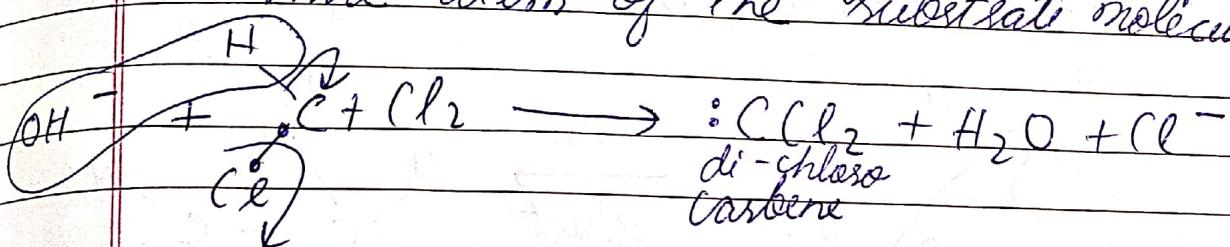
It involves single step, base pulls a proton from substrate, simultaneously leaving group deposits with its electron pair. But hydrogen leaves its electron behind, to form a double bond. Everything is happening simultaneously in single step via transition state.

$$\rightarrow \text{Rate of reaction} = [\text{RX}][\text{:B}]$$



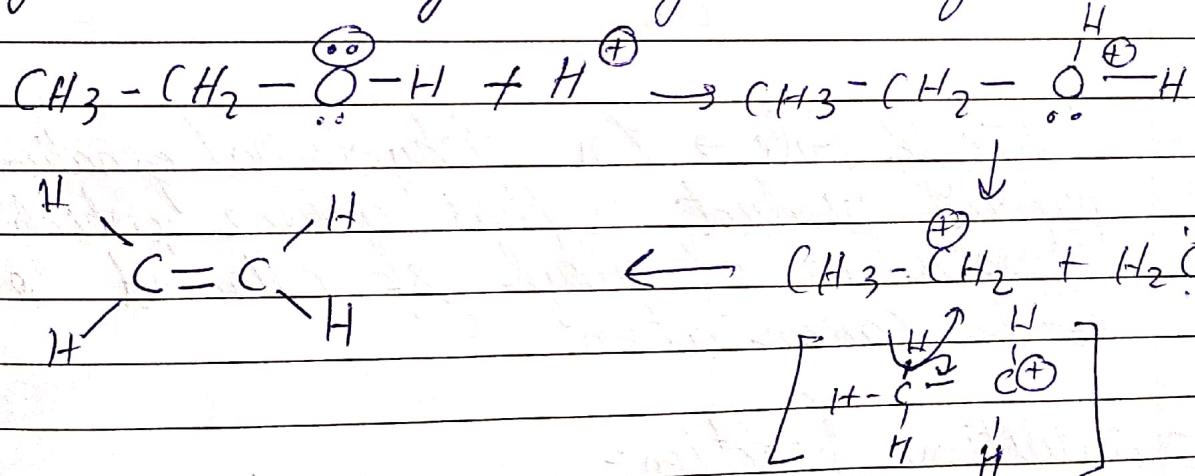
depending upon the relative position of the atom/group eliminated, these reaction are called  $\alpha$ ,  $\beta$ , & elimination reaction.

a)  $\alpha$ -elimination reac<sup>n</sup> - In these reactions, the loss of two atoms/groups takes place from the same atom of the substrate molecule [ $\text{CHCl}_3$ ].

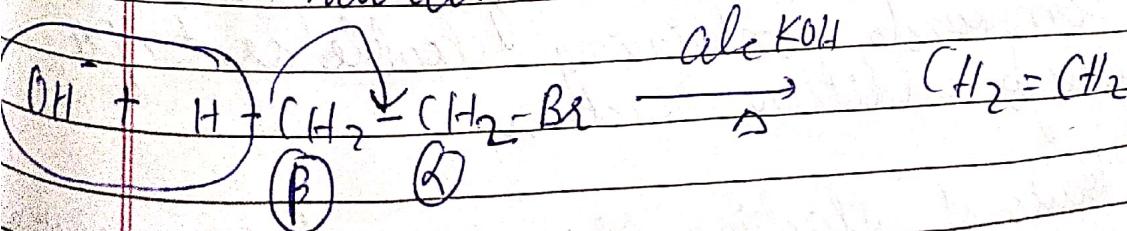


b)  $\beta$ -elimination reac<sup>n</sup> - In these reactions, the loss of two atoms/groups takes place from the adjacent atoms of substrate molecule.

Eg:- Acid catalysed dehydration of alcohol.

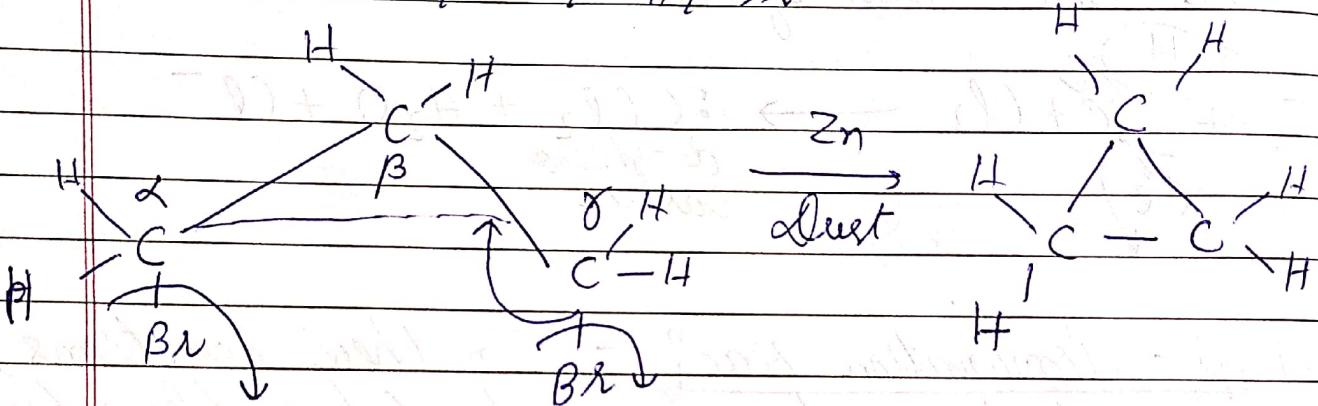
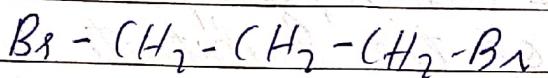


Eg:- Base catalysed dehydrohalogenation of alkyl halides:-

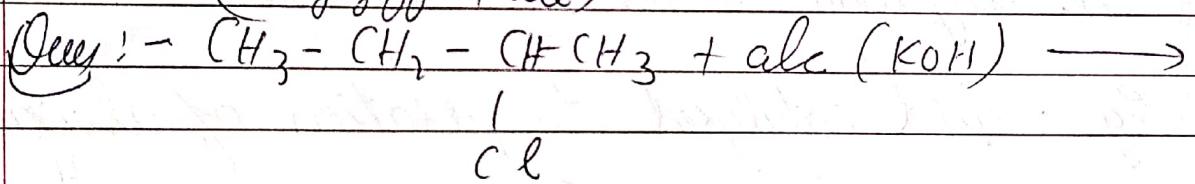


c)

$\beta$ -elimination reaction - In these type of reactions, loss of two atom/group takes place from  $\alpha$  and  $\beta$  position of substrate molecule leading to formation of three-membered ring.



(Saytzeff-Rule)  $\beta$ -elimination



Saytzeff Rule  $\rightarrow$  In dehydrohalogenation, the preferred product is that alkene which has greater no. of alkyl grp attached to double bonded carbon atom.

$\alpha$ -Addition Reaction:-

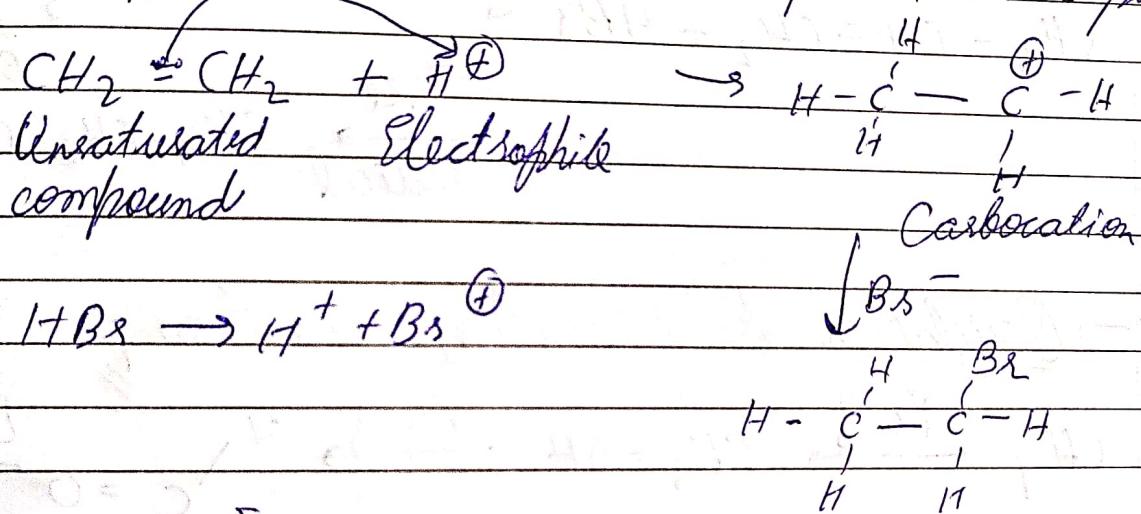
An addition reaction is one in which two substances combine to form a single compound. All organic compounds containing double or triple bonds undergo addition reaction.

On the basis of attacking reagent, addition reaction

are of following types:-

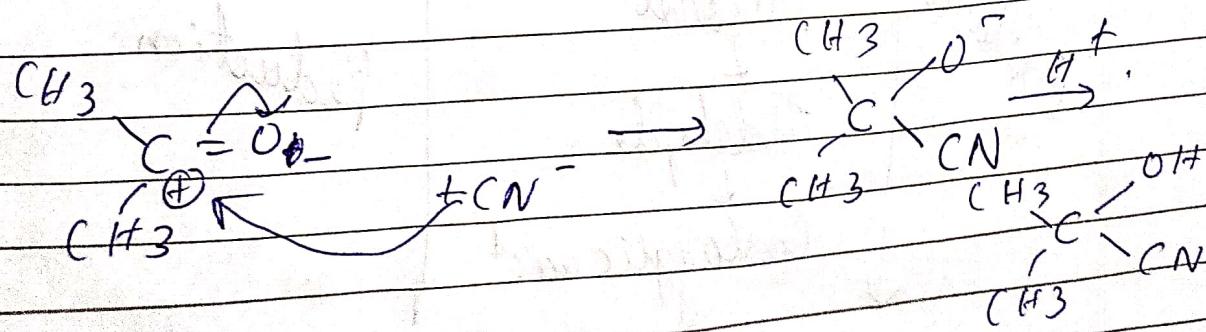
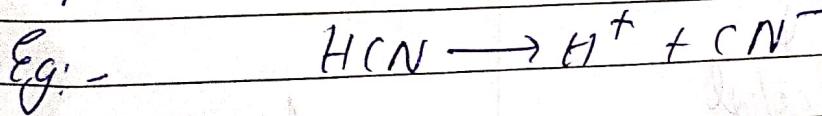
- ① Electrophilic addition reac<sup>n</sup> → Attacking reagent (electrophile).

For these reactions, carbocation is formed as an intermediate due to which reaction between electrophile & unsaturated compound takes place.



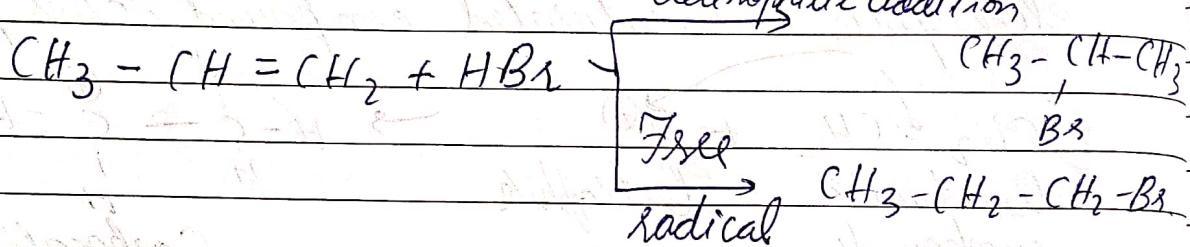
[Addition Reaction],

- ② Nucleophilic addition reac<sup>n</sup> - These reaction generally shown by carbonyl compounds (aldehydes & ketones), when nucleophile reagent approaches them:-

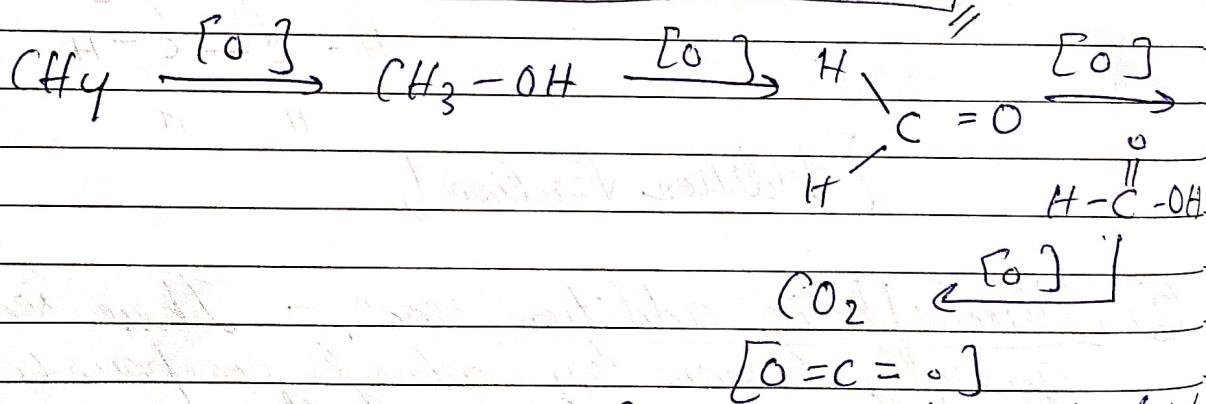


(3) Free radical addition reaction:- Addition of HBr to a double bond in the presence of peroxide proceed via free-radical mechanism.

Orientation of free-radical is anti-Markovnikov in comparison to electrophilic addition which is Markovnikov.

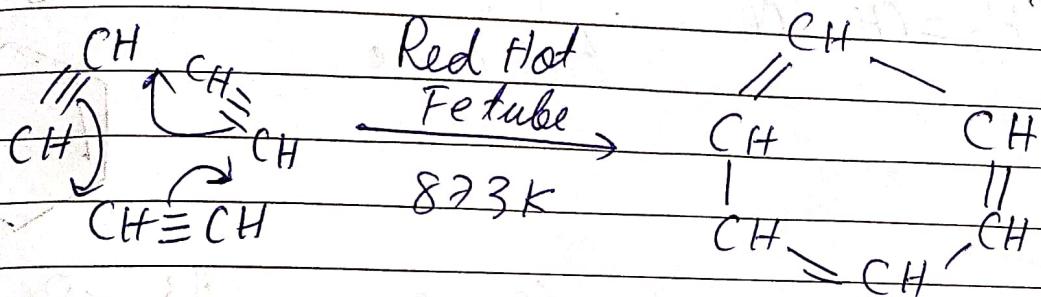


~~No~~- Oxidation & Reduction reaction:-

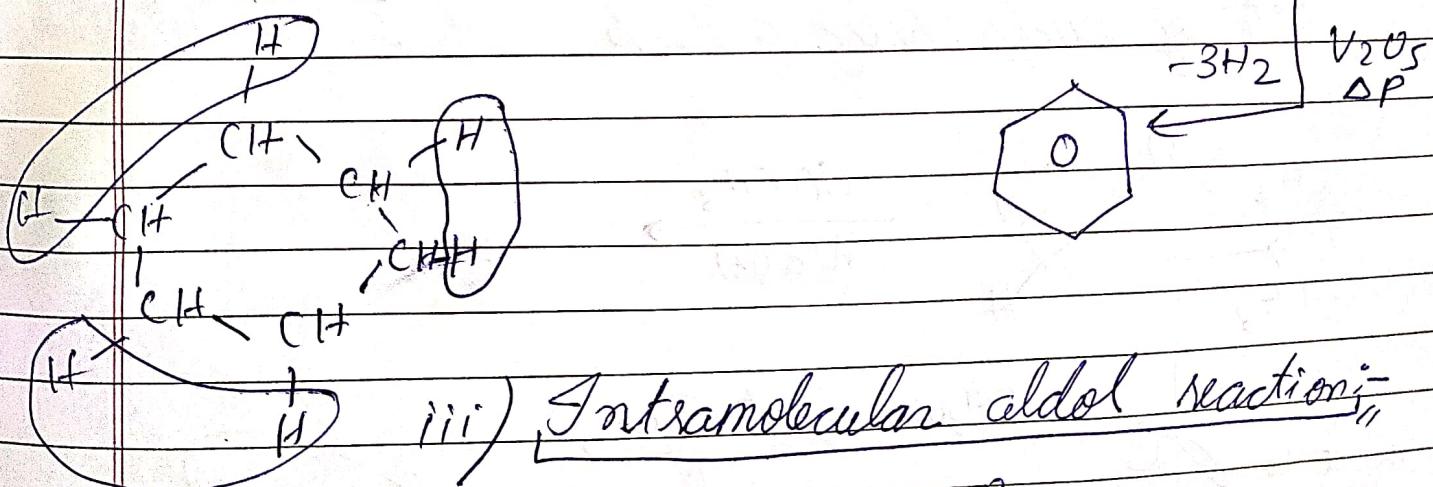
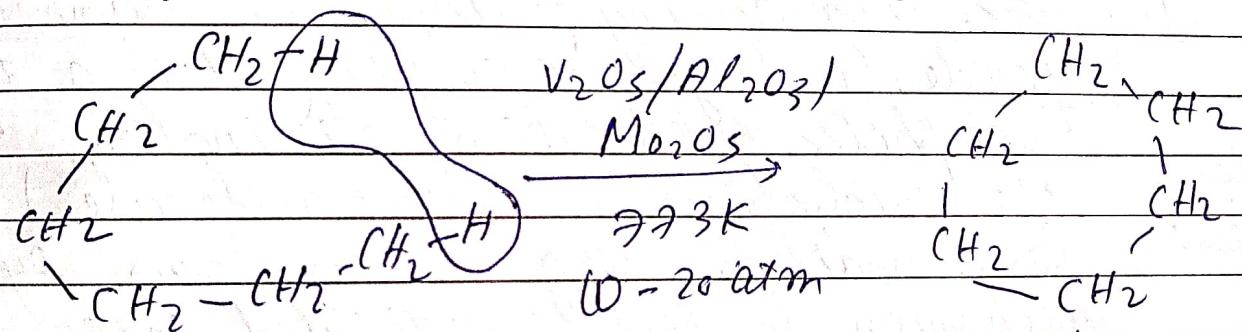


X:- Cyclisation :- In this 3 or more molecule of alkynes undergo cyclic polymerisation.

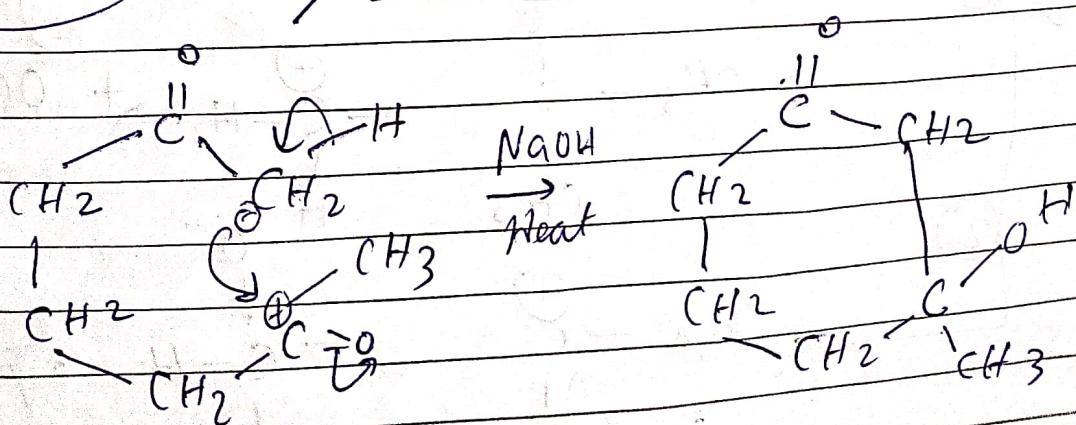
i) Ethyne to Benzene :-



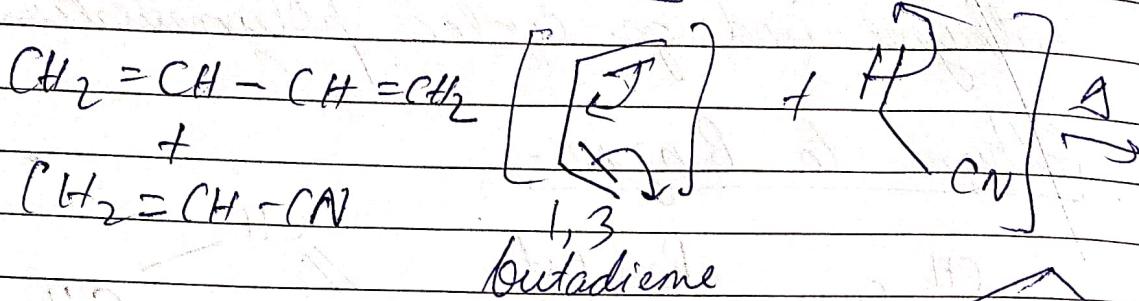
ii) Aromatization :- (Hexane  $\rightarrow$  Benzene).



iii) Intramolecular aldol reaction :-

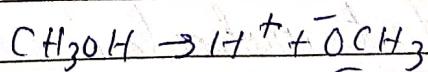
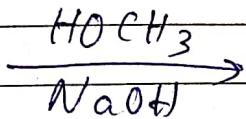
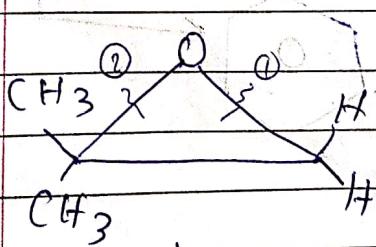


i) Diel-Alder reaction:-

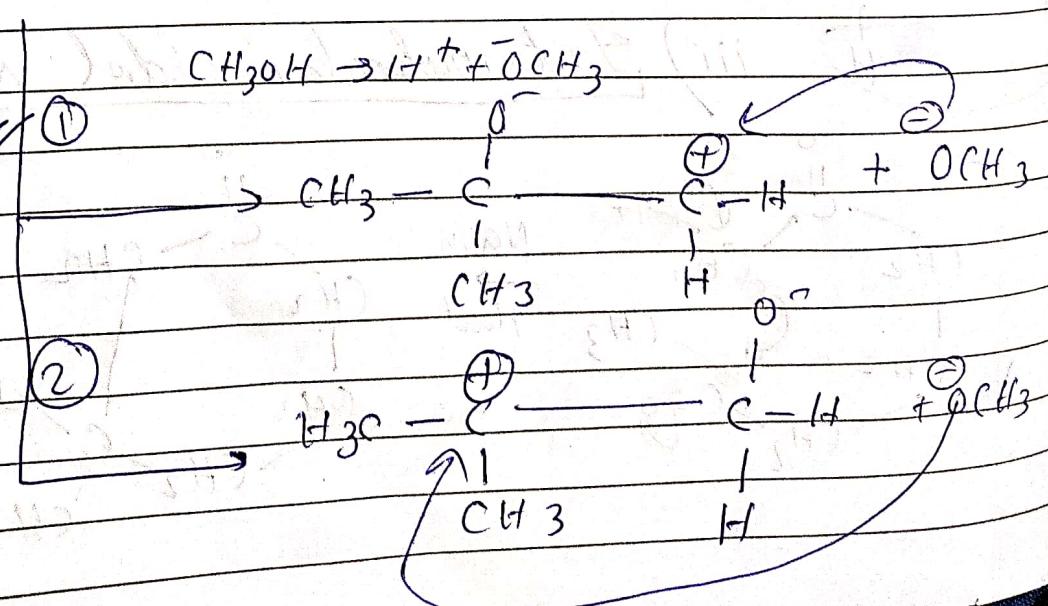


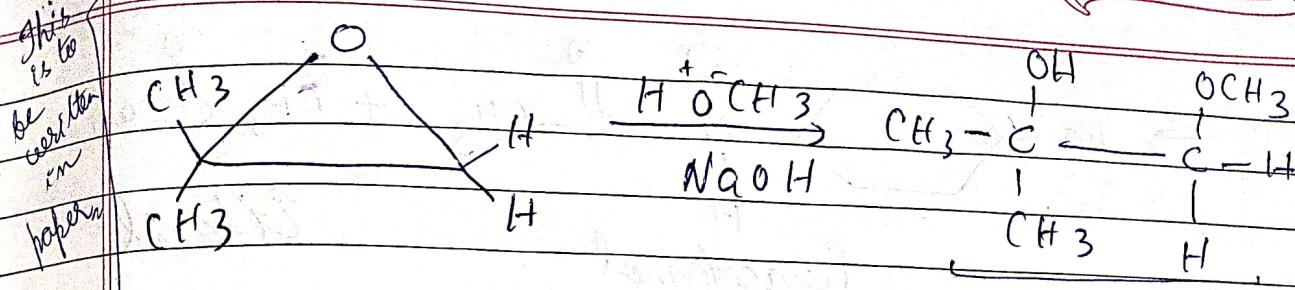
~~A:-~~ Ring opening reactions:-

① Basic ring opening - When an asymmetric epoxide undergoes solvolysis (it is a type of nucleophilic substitution/elimination, where the nucleophile is solvent molecule) in basic medium, ring opening occurs by  $\text{S}_{\text{N}}\text{2}$  mechanism & less substituted carbon is the site of nucleophilic attack.

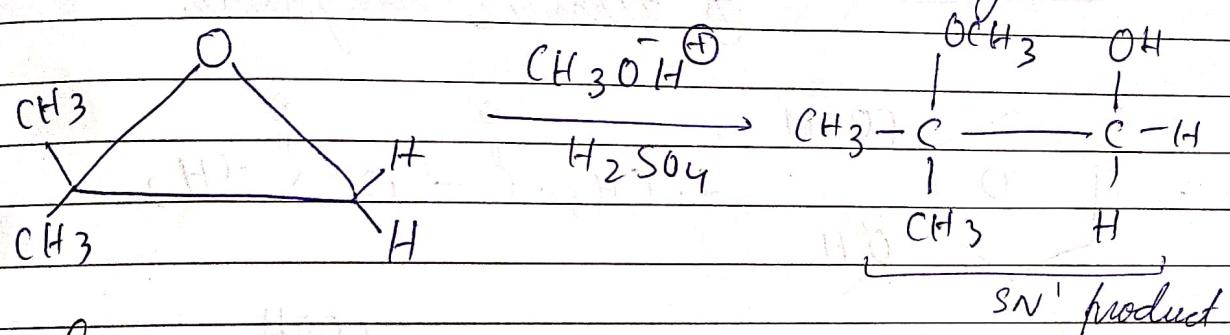


due to  
less  
hindrance  
at the site  
of attack





② Acidic Ring opening: When solvolysis occurs in acidic methanol, the reaction occurs by  $S_N^1$  mechanism.



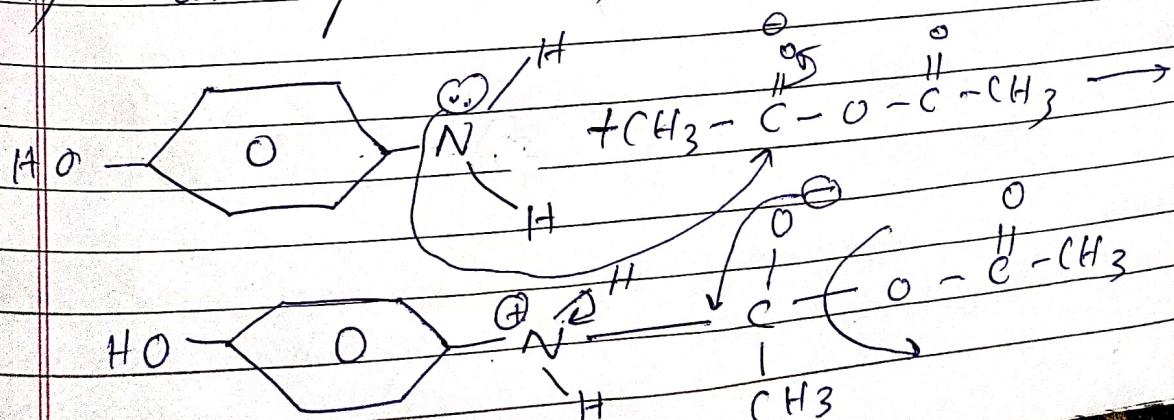
What is drug:-

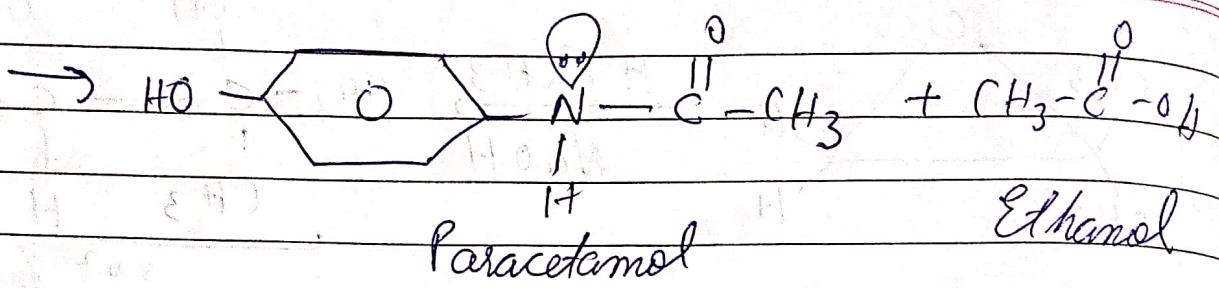
Any substance that inhaled, injection, smoked, consumed or dissolved under the tongue causes a physiological change in body.

Paracetamol :- (i) It is used as Analgesic (Reduce Pain)

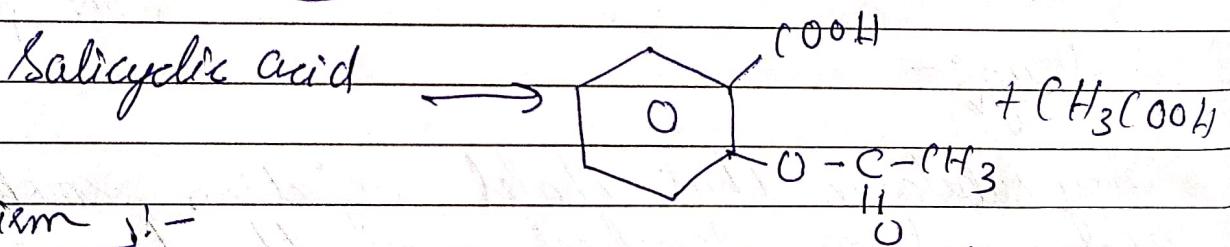
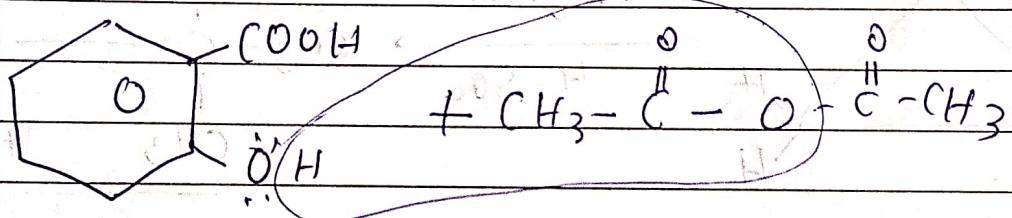
(ii) It is also used as Antipyretic (Reduce fever).

→ a) 4-Amino phenol + b) Ethanoic Anhydride

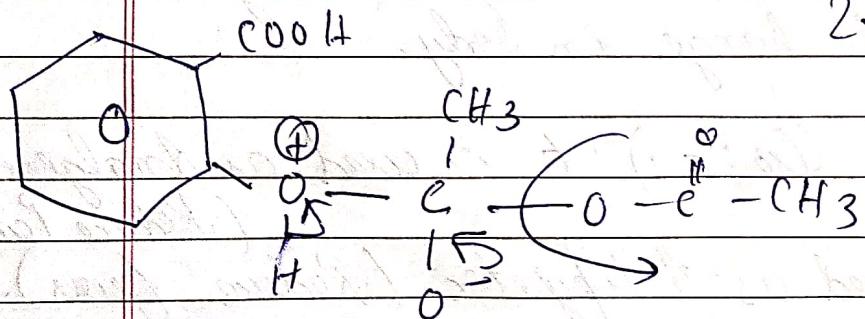




(Aspirin) :-    ① Salicylic acid  
                         ② Ethanoic anhydride.



Mechanism :-



*2-hydroxy benzoic acid.*

Use :- i) It reduces fevers.  
        ii) It reduces pain