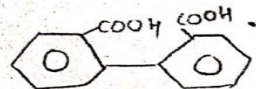
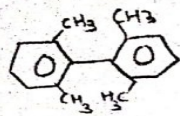


### Conditions

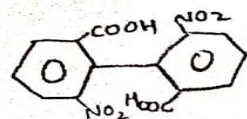
- 1) Presence of different ortho substituents
- 2) Always there should be bulkier substituents like  $-\text{CH}_3$ ,  $-\text{NO}_2$ ,  $-\text{COOH}$ ,  $\text{SO}_3\text{H}$  at ortho position
- 3) Both the phenyl ring should be non-coplanar i.e. one ring should be within the plane & other ring should be outside the plane.



→ It has free rotation as no bulky group on both sides, only one side have bulky group  
 - Plane of symmetry → optically inactive  
 - No atropisomerism.



→ No atropisomerism due to same ortho substituents



→ exhibit atropisomerism

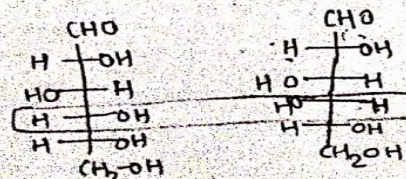
\* Vancomycin an antibacterial antibiotic → (aminoglycoside) glycopeptide  
 It will exhibit atropisomerism

\* Gossypol a compound isolated from Gossypium ~~det~~ herbecium exhibit atropisomerism  
 The dextro isomer → Male contraceptive → inhibit spermatocyte  
 The levo isomer → Haemotoxic → ↓ the  $\text{O}_2$  carrying capacity of blood.

### \* Epimers →

These are diastereoisomers that differ in stereochemistry at one stereogenic center.

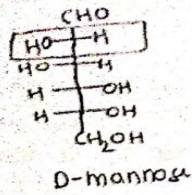
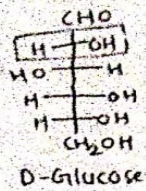
eg:- Glucose & Galactose are epimers →  $\text{C}_4$  epimers.



D-Glucose

D-Galactose

example: Fehling's reagent +ve for reducing sugar  
 Schiff's reagent - because of free aldehyde group on anomeric carbon



### Anomers →

Anomers are diastereoisomers that differ in configuration at anomeric carbon atom

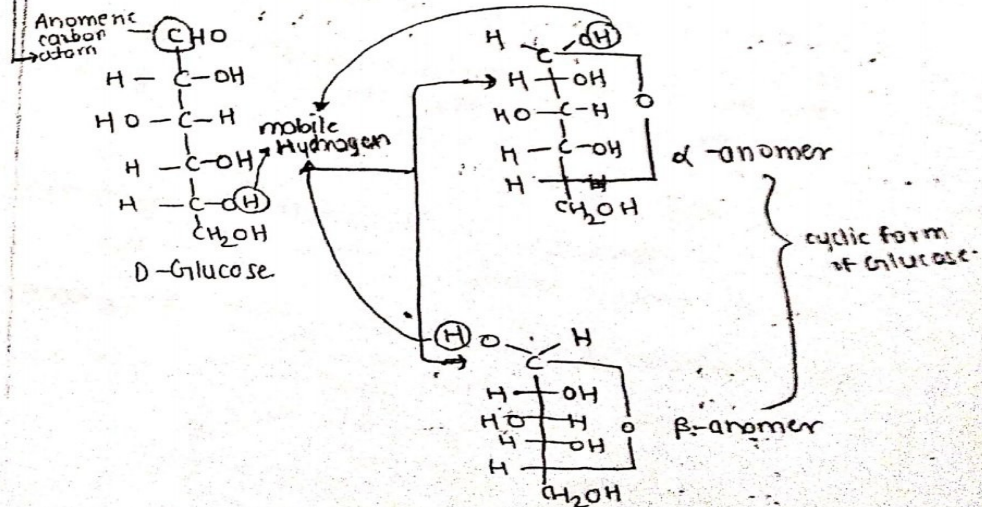
→ Anomeric carbon atom →

### Mutarotation →

It is the change in the specific rotation value of an optically active compound.

eg:-

dextro rotatory compound → specific rotation =  $+23^\circ$   
 (solvent)  
 initially  $+23^\circ$   $\xrightarrow{30 \text{ min}}$   $+56^\circ$   
 Mutarotation



- Glucose molecule will exist in open chain form & the cyclic  $\alpha$  &  $\beta$  anomeric forms.
- Whenever  $\alpha$ -anomer is placed in water, the initial specific rotation value is  $+113^\circ$  & after a period of time the specific rotation value changes to  $+53^\circ$ .

Similarly whenever  $\beta$  anomer is placed in water it has a initial specific rotation value of  $+19^\circ$  which gradually changes & reaches to a constant value of  $+53^\circ$ .

This ~~occurs~~ is called as mutarotation & it occurs due to the fact that the  $\alpha$  &  $\beta$  anomers will be in equilibrium mixture in addition to a small amount of open chain form.

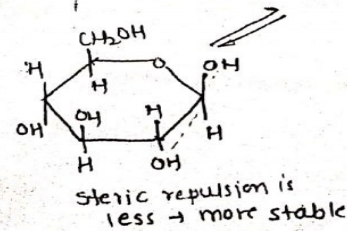
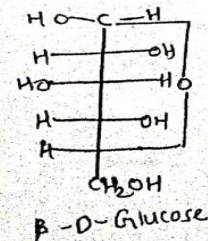
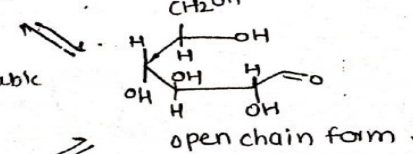
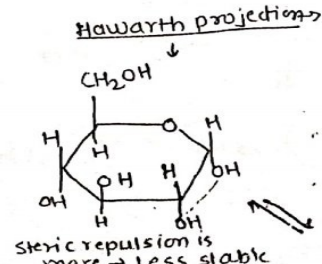
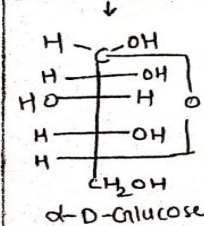
- The mutarotation occurs due to presence of mobile Hydrogen.

- Glucose can reduce Fehling's & Tollen's reagent as the glucose has free aldehyde group in open chain form (Glucose doesn't give +ve Schiff test).

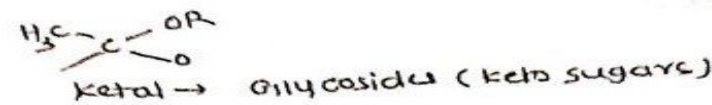
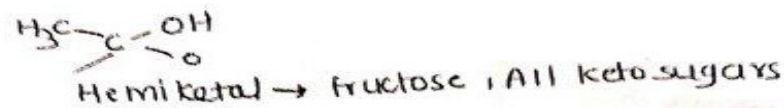
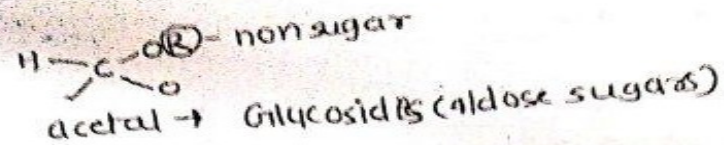
- Glycosides doesn't contain mobile hydrogens hence it can not exhibit mutarotation & can't reduce Fehling's & Tollen's reagent, Schiff's test.

- Glucose molecule ~~with~~ doesn't respond +ve ly to Schiff's test as the open chain (free aldehyde form) of glucose is very very less which is unable to react to the less sensitive Schiff's reagent.

Fischer projection  $\rightarrow$

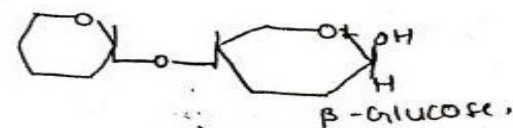
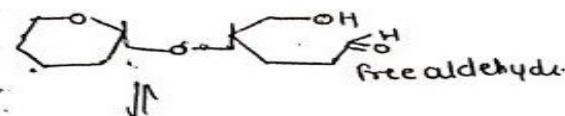
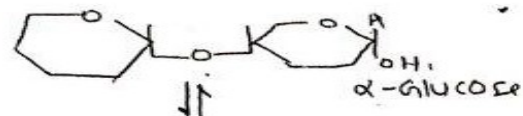


stability order -  $\beta$ anomer  $>$   $\alpha$ anomer  $>$  open chain

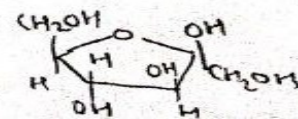


Disaccharides  $\rightarrow$

Reducing disaccharides  $\rightarrow$  eg: Maltose - 2 Glucose  
 cellobiose - 2 Glucose  
 lactose - 1 Glucose + 1 galactose

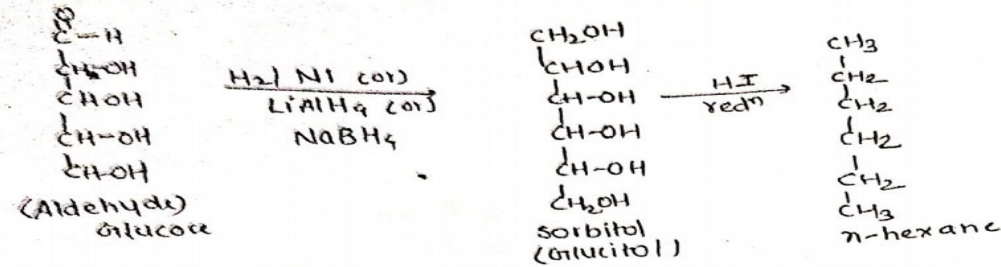


Non-reducing sugar  $\rightarrow$  eg: sucrose  
 Glucose + fructose



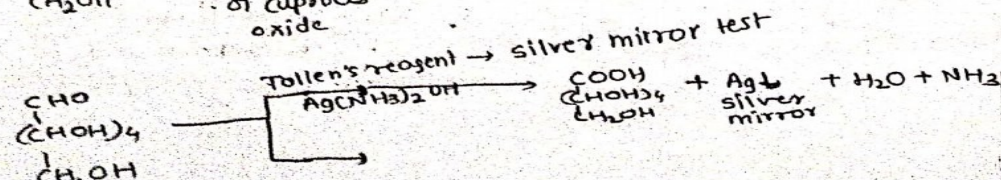
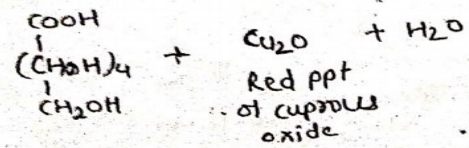
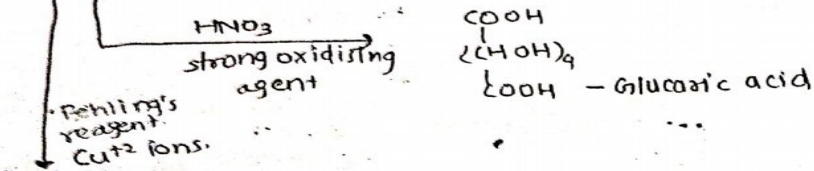
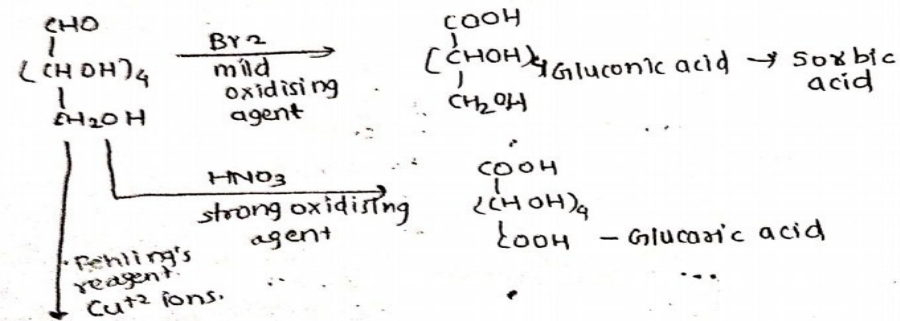
## Reactions of Glucose →

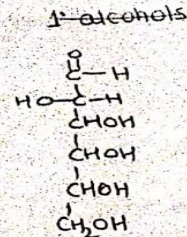
### 1) Reduction of Glucose →



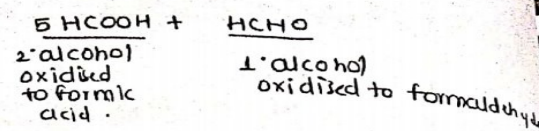
- \* Sorbitol & mannitol (osmitrol) are osmotic diuretics. Osmotic diuretics are also used in treatment of Glaucoma.
- The sweet taste of mannitol & sorbitol is due to negative heat of solution.
- Mannitol is used in transdermal patches & osmotic pumps to create osmotic pressure & deliver the drug molecule.
- \* Sweet taste of cinnamon is due to mannitol

### 2) Oxidation of glucose →

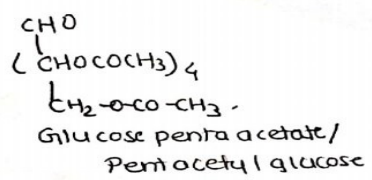
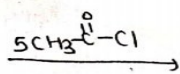
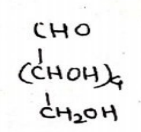




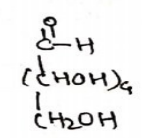
$\xrightarrow{\text{HIO}_4}$   
strong  
oxidizing  
agent



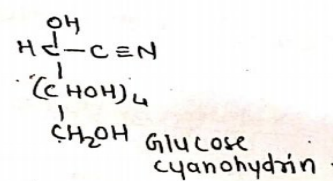
3) Acetylation of Glucose →



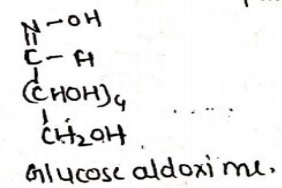
4) Reaction of aldehyde group →



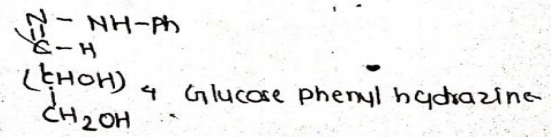
$\xrightarrow{\text{HCN}}$   
Hydrogen  
cyanide  
or  
prussic acid



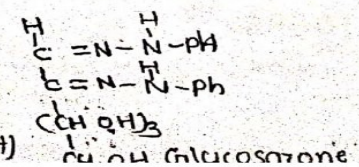
$\xrightarrow{\text{HONH}_2}$



$\xrightarrow{\text{H}_2\text{N}-\text{NH}_2-\text{Ph}}$   
1 Phenylhydrazine



$\xrightarrow{3 \text{H}_2\text{N}-\text{NH}_2-\text{Ph}}$   
3 phenyl hydrazine  
↓  
osazone reaction



or - Killiani test  
to identify  
ketose sugar  
(↓ deoxy sugar)

+ Fe<sup>+2</sup>  
↓  
Fehling's reagent

produces  
phic action  
oxy radical  
+ with e<sup>-</sup> re  
lar compone  
actia like  
elc acid + in  
eir growth  
↓  
inton's reac

Miller-Kiliani test  
used to identify  
aldohexose sugar  
(deoxy sugar)

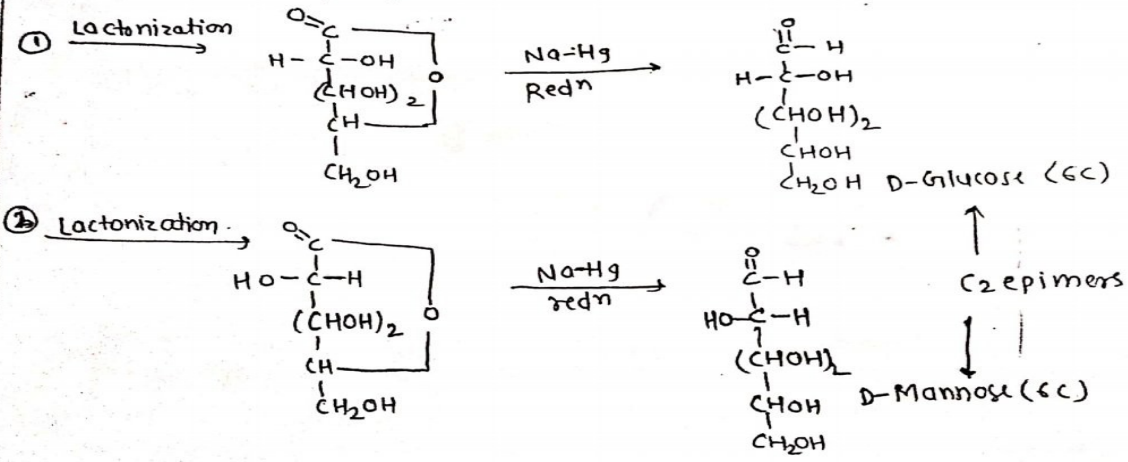
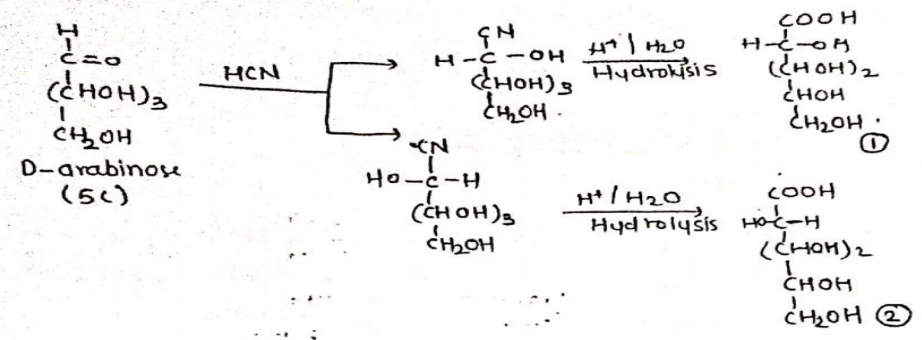
$\text{Fe}^{2+}$   
↓  
Fenton's reagent

2. produces  
septic action  
hydroxyl radical  
react with e<sup>-</sup> rich  
cellular components  
bacteria like proteins  
cell acid + inhibit  
their growth.  
↓  
Fenton's reaction

Chain extension of sugars → Kiliani Fischer synthesis →

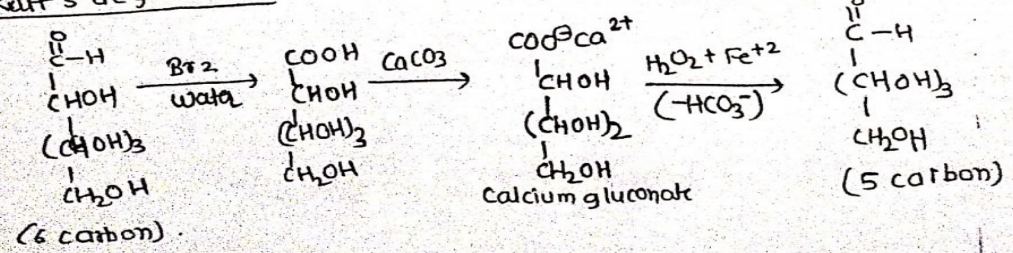
- synthesis of sugar

5 carbon sugar → 6 carbon sugar → 7 carbon sugars



Chain reduction of sugar →  $\left\{ \begin{array}{l} \text{Ruff degradation} \\ \text{Wohl's degradation} \end{array} \right.$

1) Ruff's degradation →

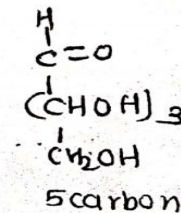
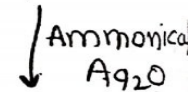
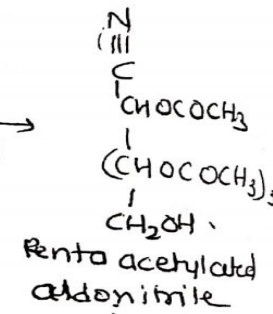
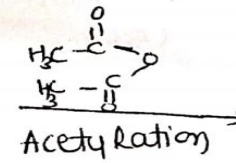
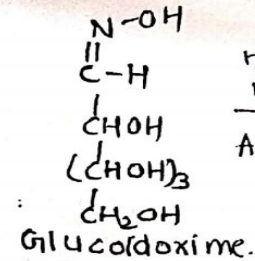
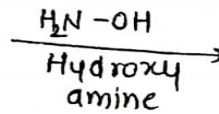
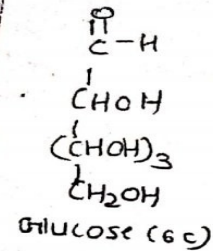


Anthracycline antibiotics → Anticancer agent.

eg:- Doxorubicin  
Daunorubicin  
Epirubicin  
Valrubicin  
Idarubicin

These antibiotics have cardiotoxicity  
- produce  $\cdot\text{OH}$  radicals by Fenton's reactions in heart. These hydroxy radicals are responsible for cardiotoxicity.

## 2) Wohl's degradation →



## CONFORMATIONAL ISOMERISM

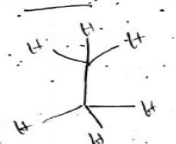
(13)

- ✓ It is due to free rotation about C-C single bond.
- ✓ Molecules containing C-C will rotate & exists in more than one isomeric form.
- ✓ The rotation about C-C single bond will help the molecule to convert into more stable conformer. By using its energy.
- ✓ The energy required for rotating a C-C single bond is 2 to 5 kcal and the energy associated with compounds containing C-C single bond is 5 to 10 kcal only.
- ✓ Hence compounds with C-C single bond can rotate & exists in more than one conformational isomeric form.
- ✓ Studying about the energy & stability of different conformational isomers is called as conformational analysis.
- ✓ NMR spectroscopy is used to study different conformations of molecule.
- ✓ Open Chain Compounds

Ethane → exists in 3 conformers

- Staggered (Faraway)
- Eclipsed (Crowding)
- Skew

### ① Andron Formulas



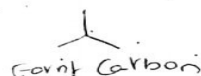
Staggered



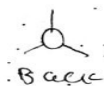
Eclipsed

Cannot draw skew conformers

### ② Newman's projections



Front Carbon

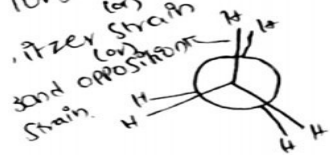


Back

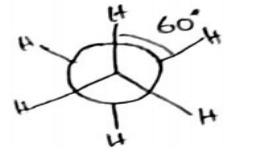
\* The order of Bond angle & Stability are

Eclipsed < Skew < Staggered

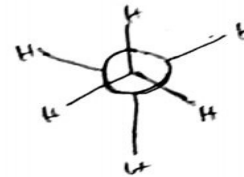
Here  
Torsional strain  
(or)  
Pitzer strain  
(or)  
Bond opposition  
strain



Eclipsed  
Conformer



Skew/ gauche  
Conformer



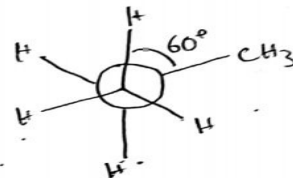
Staggered Conformer

It has NO Bond opposition  
(or)  
Pitzer strain/Torsional  
strain

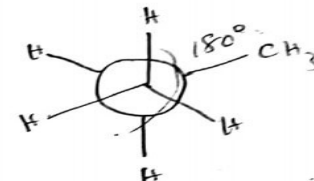
Propane



Eclipsed  
↓  
Less stable



Skew



Staggered  
↓  
More stable

Cyclic compounds

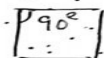


Cyclopropane

60°

109.28'

49.28'

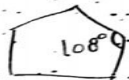


90°

90°

109.28'

19.28'

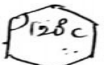


108°

108°

109.28'

1.28'



120°

120°

109.28'

11.28'

The difference  
is Angle strain

According to Bayer Strain theory

planar

non planar

1. All the cycloalkanes are planar

2. More is the angle strain. Less will the stability of cyclohexane alkane.

## Limitations of Bayer strain theory

(14)

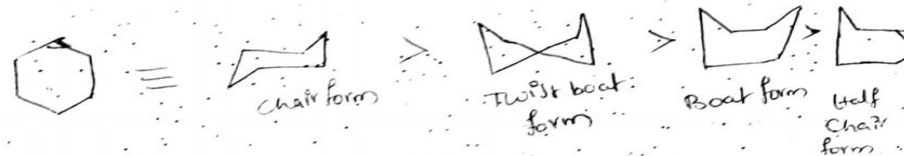
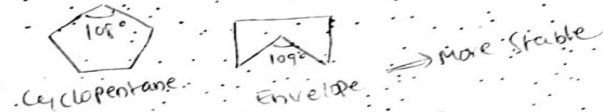
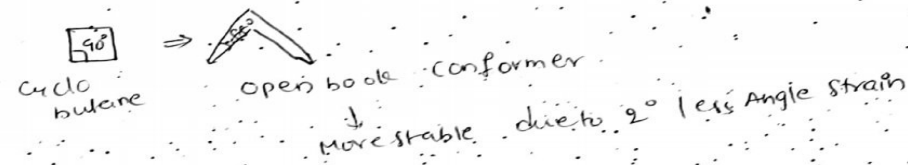
Bayer failed to explain the stability of cyclohexane. This is due to the fact that we thought all the cycloalkanes are planar.

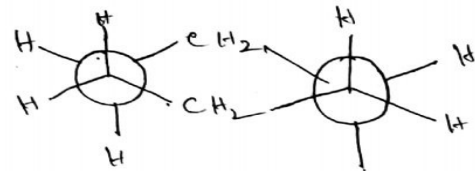
\* Stability of cyclohexane was explained by two scientists Sasche & Mohr's.

\* Who proposed that cyclohexane molecule will exist in strainless (or) puckered ring structures and these rings are not planar. & the bond angle for these non planar compounds will be  $109^{\circ}28'$ . So cyclohexane more stable than cyclopentane.

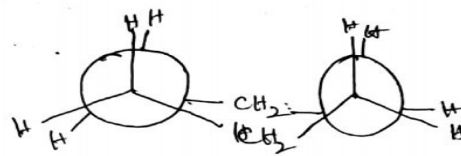
✓ Cyclopropane  $\Delta$  is unstable because of angle strain & bond opposition strain.

✓ Cyclopropane is used as Inhalational General anesthetic.





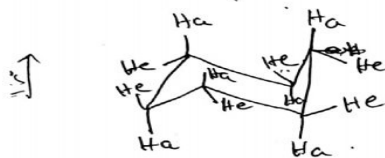
Chair form of cyclohexane  
(In Newman's projection)



Boat form of cyclohexane

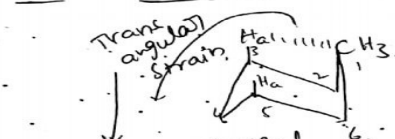
\*) Stereochemistry of substituted cyclohexane derivatives

Flag pole hydrogens  
 $\Downarrow$   
 Flag pole interaction  
 $\Downarrow$   
 Pitzer strain



Ha = Axial hydrogens  
 He = Equatorial hydrogens

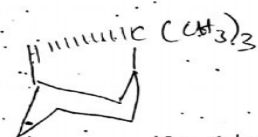
Mono substituted cyclohexane:



It has 1,3-diaxial interaction & 1,5-diaxial interactions

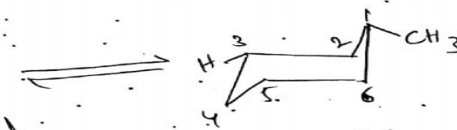
Equatorial methyl cyclohexane

↓  
less stable



Axial tert-butyl cyclohexane

It is less stable compared to Axial methyl cyclohexane



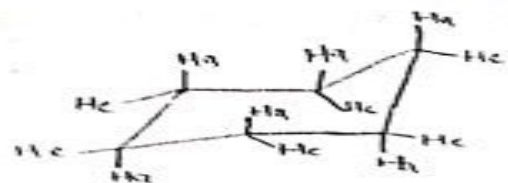
There is no 1,3-diaxial interactions

Equatorial methyl cyclohexane

↓  
more stable

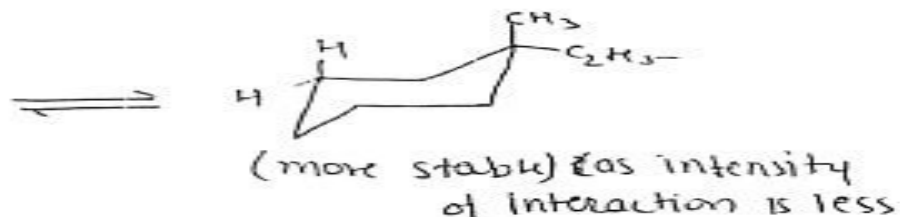
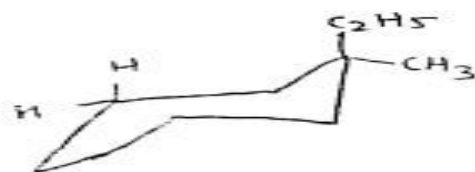
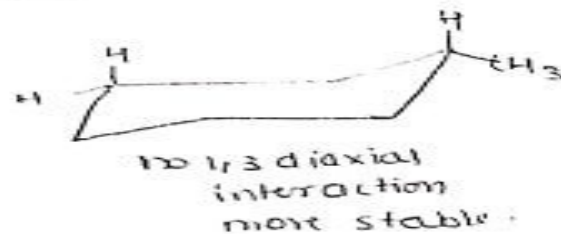
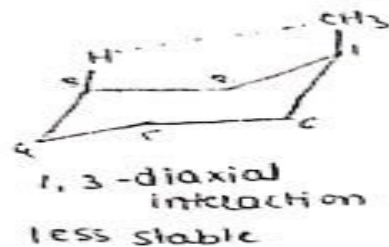


Equatorial t-butyl cyclohexane



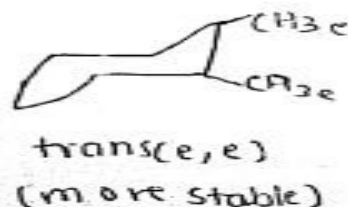
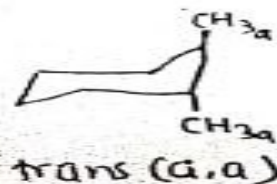
Ha - axial-H  
He - equatorial H

### monosubstituted cyclohexane

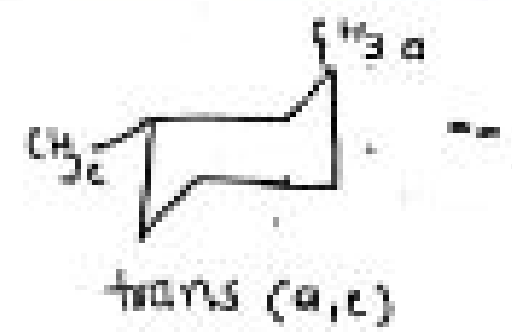


### Disubstituted cyclohexane

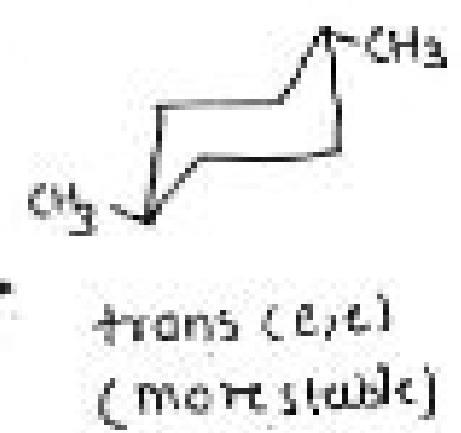
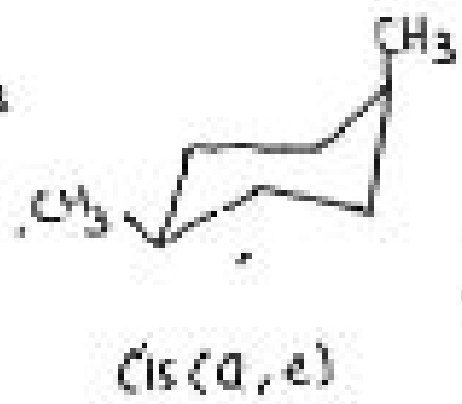
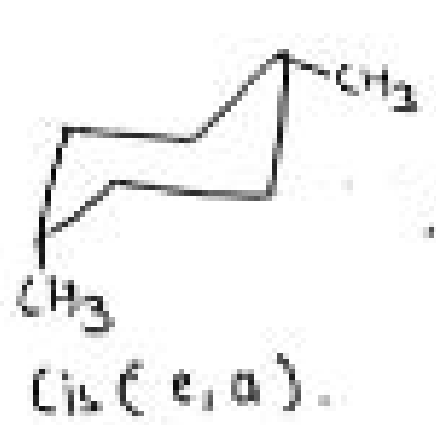
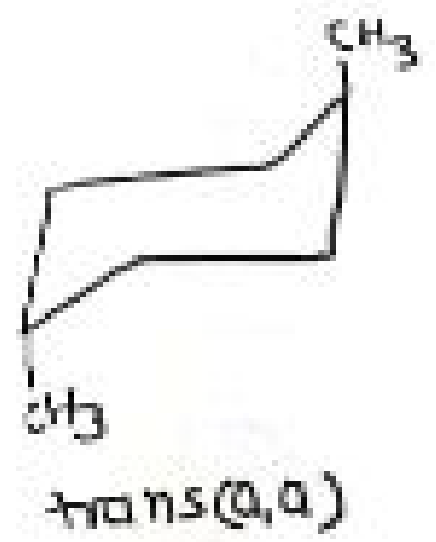
1. disubstituted - 1,2 dimethyl cyclohexane..



1,3-disubstituted - 1,3-dimethylcyclohexane.



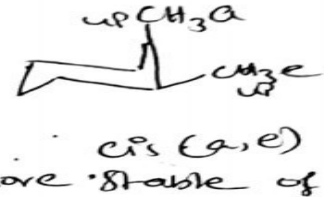
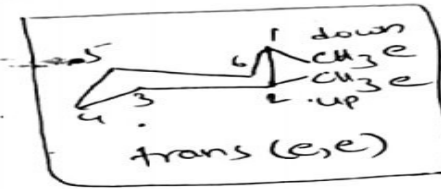
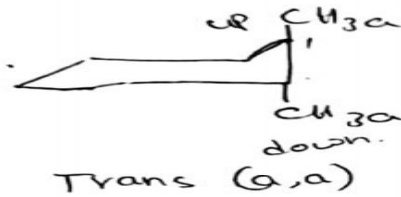
1,4-disubstituted - 1,4-dimethylcyclohexane.





It is more stable as the bulkier group is in equatorial position. (15)

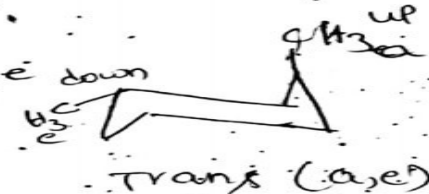
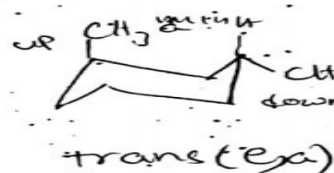
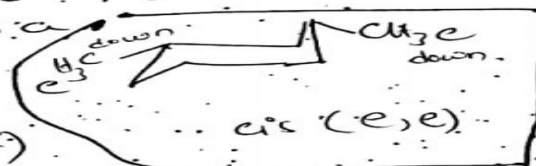
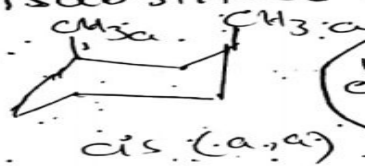
⊗ Disubstituted cyclohexane 1,2-Dimethylcyclohexane:-



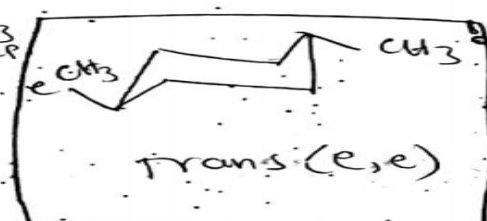
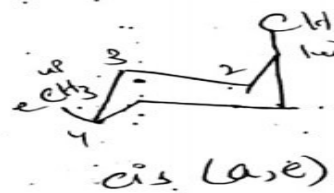
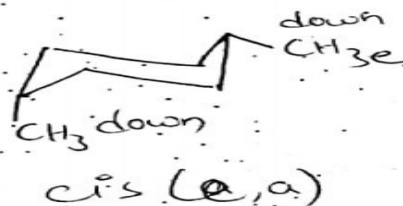
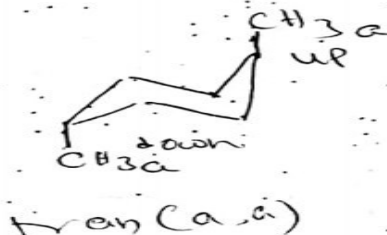
Trans (two are opposite side)  
up, down,  
cis (two are same side)  
up, up,  
down, down

Commonly trans is more stable than cis.

⊗ Disubstituted cyclohexane 1,3-dimethylcyclohexane



⊗ Disubstituted cyclohexane 1,4-dimethylcyclohexane



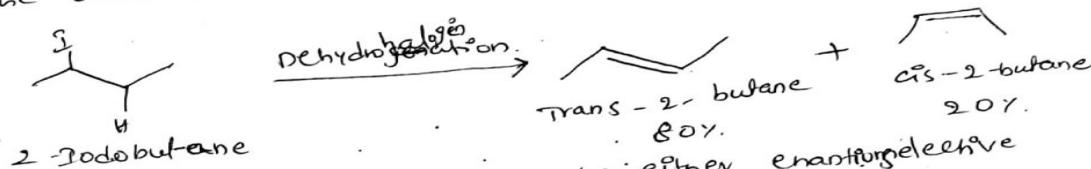
### \* Enantiomeric excess!

Is the quantity used to measure the enantiomeric purity

- \* For Racemate the enantiomeric excess is zero.
- \* A 40% Enantiomeric excess corresponds to a 70% of one enantiomer and 30% of another enantiomer.

### \* Stereoselective reactions!

Reactions that lead to the predominance of one Stereo isomer over the other is called as Stereoselective reaction.



Stereoselective reactions are may be either enantioselective (or) Diastereoselective.

✓ If the products are enantiomers and if one Stereoisomer formed more and the reaction is Enantioselective.

✓ If the products are Diastereomers and if one Stereoisomer formed more (or) Predominantly the reaction is Diastereoselective.

✓ Degree of selectivity is measured by enantiomeric excess and Diastereomeric excess.

### \* Stereospecific reaction!

The Stereospecific reaction is the one which when carried in their Stereoisomeric starting material, gives a product with different Stereochemistry, than the Stereochemistry of Reactant.

$R \rightarrow S$