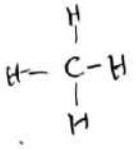
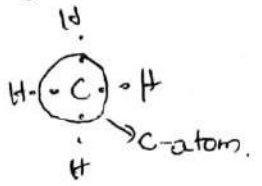
09/05/19

ORGANIC CHEMISTRY

* Study about hydrocarbons and their functional derivatives
* Organic compound posses covalent bond ⇒ cooperative to satisfy their valency sharing of electrons.





Valency of carbon is 4

* An orbital contain 2 electrons, H - contain 1 orbital & 1 electron

STEREO CHEMISTRY

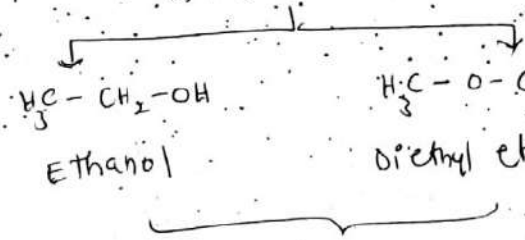
Isomerism in organic compounds.

Isomers are the compounds with same molecular formula but different functional arrangements of atoms (or) groups.

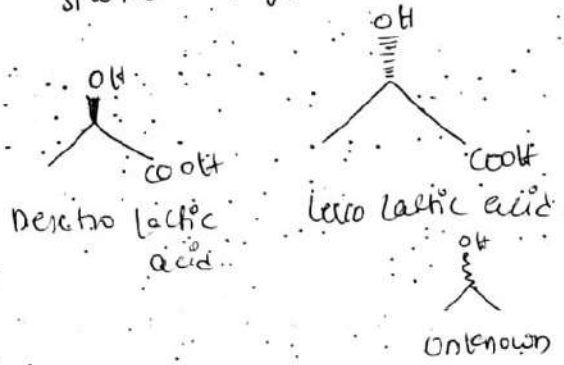
Basically Isomers are divided into 2 types.

Structural/Constitutional.	Stereoisomers. - 3D structure.
* They have different structure (or) constitution (or) composition.	* Same structure different in spatial arrangement.

Eg: C_2H_6O



Functional group Isomers



⑤ Types of Structural Isomerism:-

① Chain Isomers: These are the isomers with same molecular Formula but different alkyl chains.

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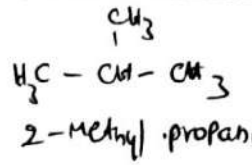
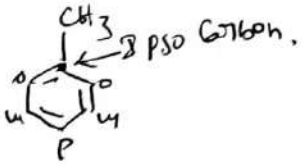


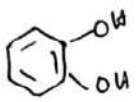
2-Methyl propane.

② ~~Metamers~~ / Positional group Isomers / Regio Isomers -

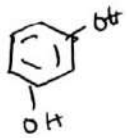
The 4 have Same Functional groups but different position of Functional groups.

→ Phenols Possess disinfectant / antimicrobial property.

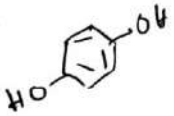




Cate chol
O-hydroxy phenol
1,2-dihydroxy phenol



Resoreinol
m-hydroxy phenol
1,3-dihydroxy phenol



Quinol.
p-hydroxy phenol.

* Quinol ~~posses~~ have more disinfectant property as the functional groups are differ in their distance and they are free & free from intermolecular hydrogen bond.

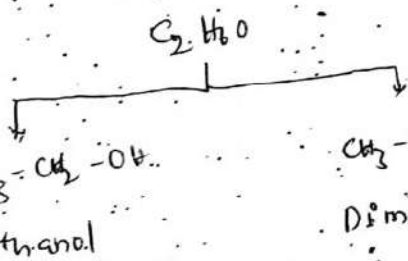
* * Phenol coefficient; Determination of disinfectant (or) Antiseptic property of new compound in comparision with phenol.

It contains - 2 methods

1) Riedel-walker coefficient
2) Chick-Martin coefficient.

③ Functional-Group Isomerism!

Same molecular formula but different functional group.



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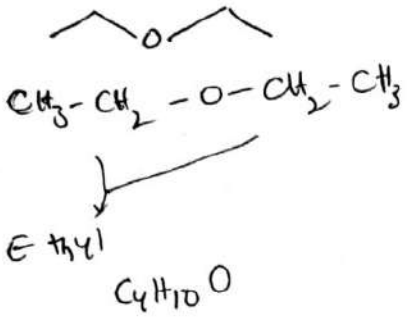
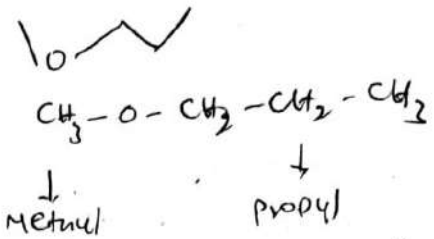
4) **Metamers**: Metamers possess same functional groups with different alkyl chains.

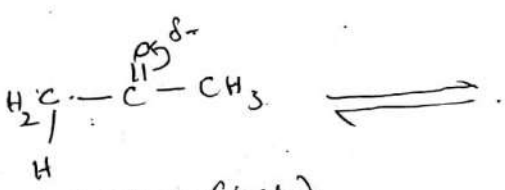


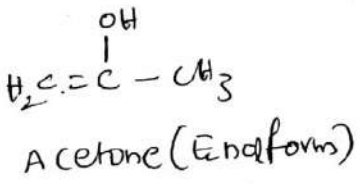
$C_4H_{10}O$



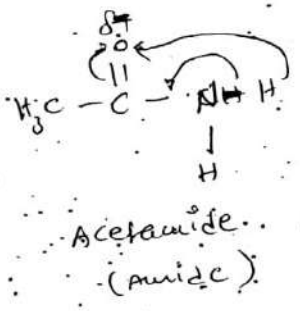
$C_4H_{10}O$.

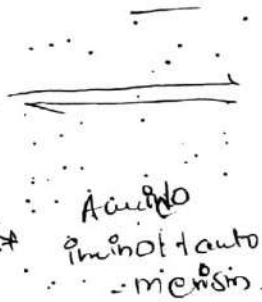
3) **Tautomers**: It is a type of Isomerism which arises due to migration of proton from one region of the molecule to other region.



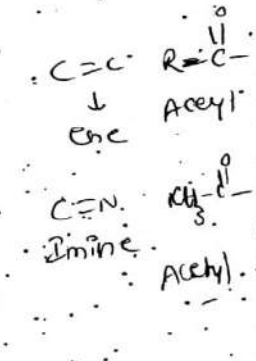


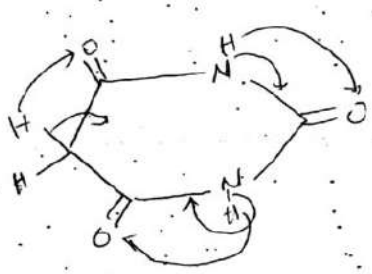
Keto-enol Tautomerism.

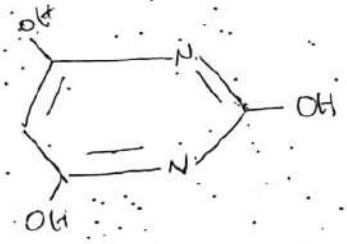




Amido iminol tautomerism.







⇒ Cyclic Imidol

Lactam

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Stereo Isomers / Spatial Isomers

Isomerism in space / in 3D

Conformational Isomers

* Formed due to bond rotation.

C–C

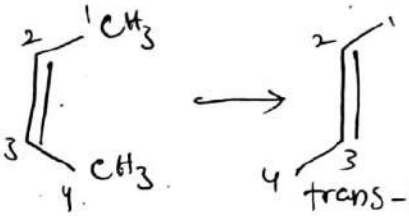
So they called rotational Isomers (or) Rotamers

* No bond breaking.

Configurational Isomers

Eg: Optical Isomerism.
Geometrical Isomerism.

* Bond breaking and Bond making



cis–2–butene → trans–2–butene

Double bond breaks & forms single bond & it rotates and forms Double bond again.

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Dt: 11/05/19

whether two molecules posses same molecular formula

→ NO → Not Isomers

If yes

Isomers

Is the Isomer is due to the constitution / structure

yes | NO

Structural / constitutional Isomers

Stereoisomers

Is the isomerism due to rotation about C-C single bond.

yes | NO

Conformational

Configurational

Is the isomerism is due to restricty rotation about a bond

yes | NO

Geometrical Isomerism

cis/Z trans/E

Optical Isomerism

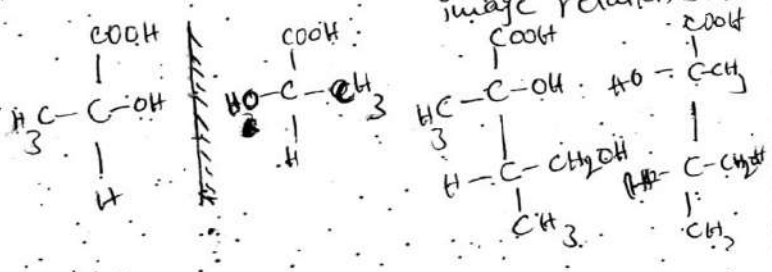
whether the optical isomers are non-superimposible Mirror images

yes | NO

ENANTIOMERS

DIASTEREOMERS

It has NO mirror image relation ship.



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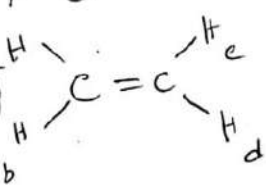
GEOMETRICAL ISOMERISM

For a molecule to exhibit Geometrical Isomerism, there should be restricted rotation.

* Generally presence of double bonded system restricts the rotation. Hence the compounds containing double bonded system usually exhibit Geometrical Isomerism however they are compounds which contain double bonded system but does not exhibit Geometrical Isomerism.

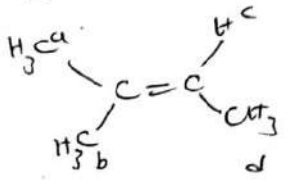
Eg: ①



These doesn't exhibit Geometrical Isomerism.

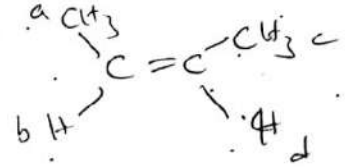
b=a c=c c=d

②



b=a c=c c≠d

③

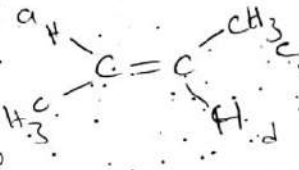


This is geometrical Isomer,

b≠a c=c c≠d

cis-2-butene

④



This is also geometrical Isomer.

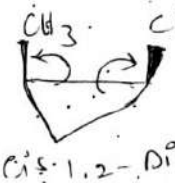
Trans-2-butene

b≠a c=c c≠d

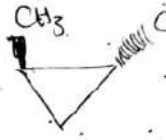
✓ Alkenes will exhibit Geometrical Isomerism

✓ 1,2 - disubstituted cyclo alkanes exhibit geometrical isomerism.

Cyclo Propane



cis-1,2-Dimethyl



Trans-1,2-Dimethyl

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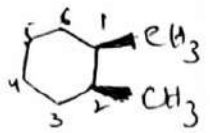
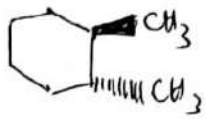
*

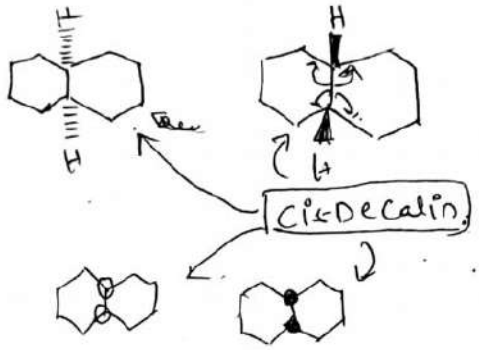


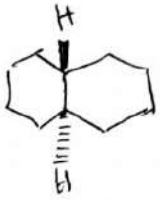
Cis - 1,2- Dimethyl cyclohexane



Trans - 1,2 - Dimethyl cyclohexane

* Fused Alicyclic rings



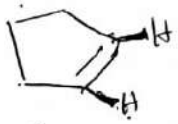


Trans - Decalin

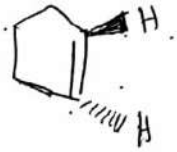
● → ABOVE the plane

○ → Below the Plane

* cyclo alkenes:



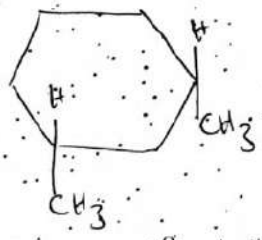
Cis - cyclopentene



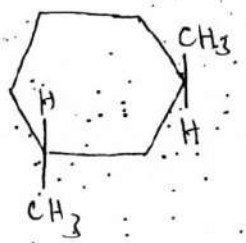
Trans - cyclopentene

(*) cyclo alkanes:

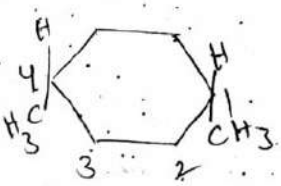
✓ 1,3- Disubstituted cyclo alkanes



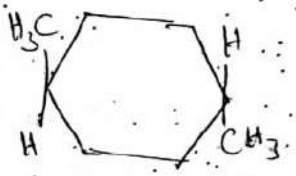
Cis -1,3- Dimethyl cyclo hexane



Trans - 1,3- Dimethyl cyclohexane



Cis 1,4- Dimethyl cyclohexane



Trans -1,4- Dimethyl cycloalkane

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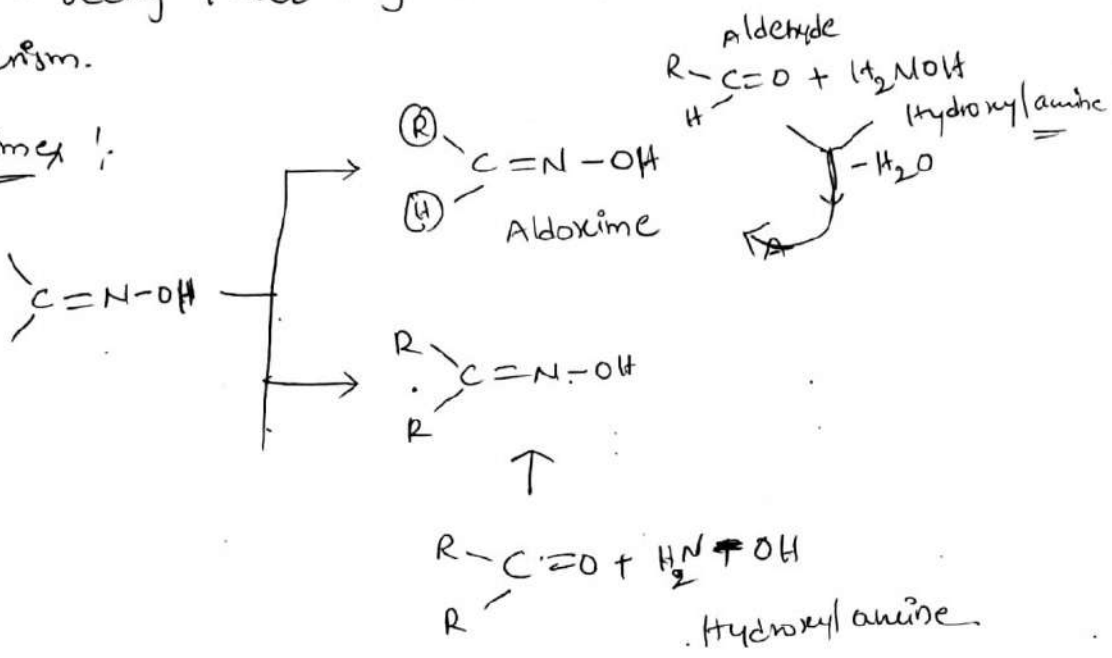
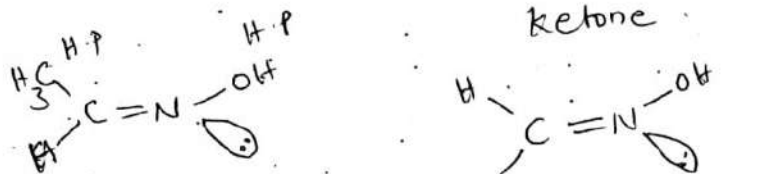
* Steroids will exhibits.

↳ Beeing Fused ring structures they exhibit Geometrical isomerism.

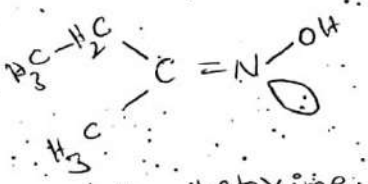
(*) Oximes :



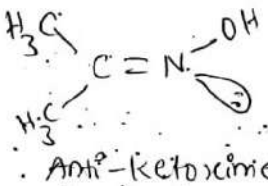


Cis / Syn Aldoxime.

Trans / anti - aldoxime



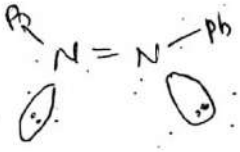
Syn-ketoxime.



Anti-ketoxime.

Azo compounds

(*) –N=N–



Syn / Z-Azabenzene

Anti / E-Aza benzene

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* Geometrical Isomers posses different physicochemical and Biological properties hence understanding geometrical Isomerism helps pharmaceutical chemist to understand their activities.

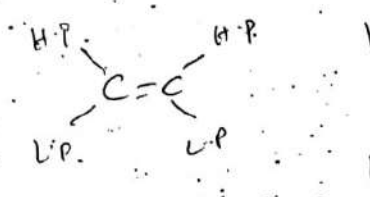
Z and E Nomenclature (priority rules)

- Z → cis
  - Z = Zussamen
  - ↓
  - on the same side.
- E → trans
  - E = Entagagen
  - ↓
  - opposite.

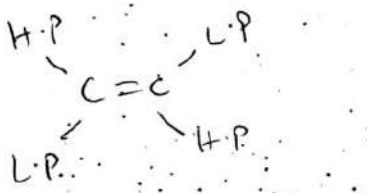
*1) Rank the atom directly attached to C-atom in the double bond in the order of decreasing atomic number so that atom of highest atomic number has highest atomic number, so that the atom of highest atomic number has highest priority.

Atom:- I > Br > Cl > F > O > N > C > H

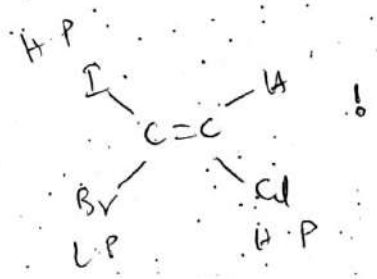
Atomic no:- 53 > 35 > 17 > 9 > 8 > 7 > 6 > 1



Z / cis Isomers

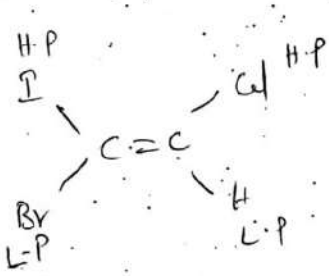


E / trans Isomers



Bromochloro Iodo Ethene

E / trans - isomer



Z / cis isomer.

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* When isotopes are present then the atom with highest atomic mass (mass number) should be given highest priority

mass number

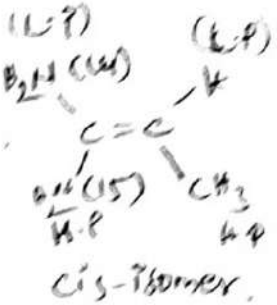
$^{1}_{1}H < {}^{2}_{1}H < {}^{3}_{1}H$

Atomic number: Hydrogen = Hydrogen < Tritium.

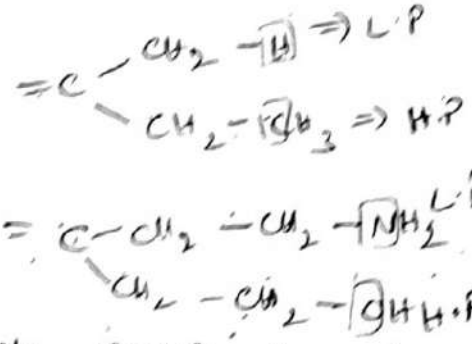
$^{14}_{6}C < {}^{15}_{7}N$

$^{35}Cl < {}^{37}Cl$

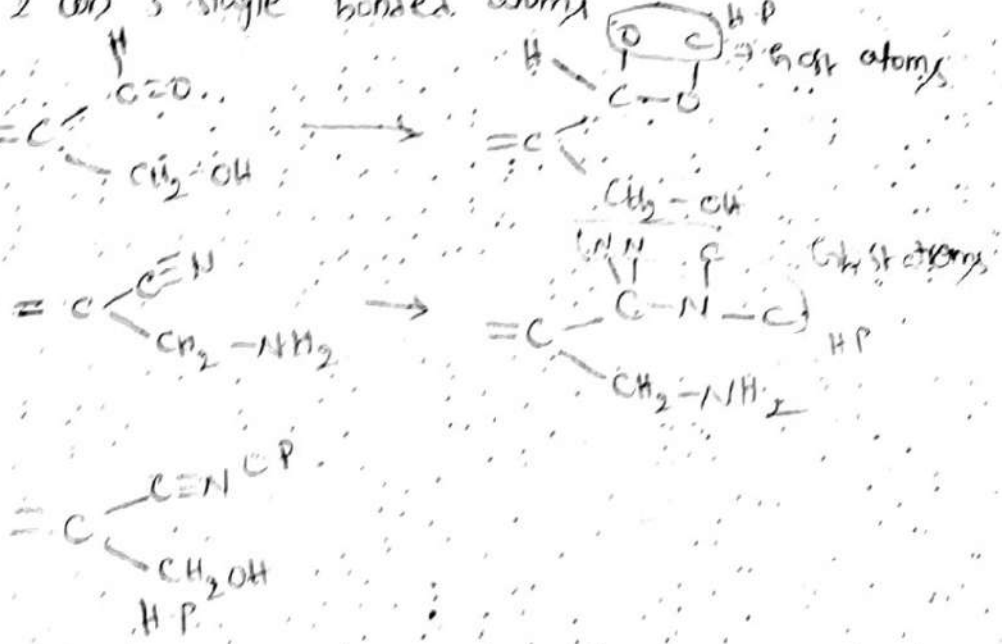
$^{79}Br < {}^{81}Br$



* If 2 atoms directly attached to alkene C atom are same then rank the 2nd, 3rd ... atoms (counting away from the C=C bond) one at a time until a difference is found this is called as first point of difference rule



* If the substituents contain double and triple bond treat the atoms joined by double (or) triple bonds as if they where linked to 2 (or) 3 single bonded atoms



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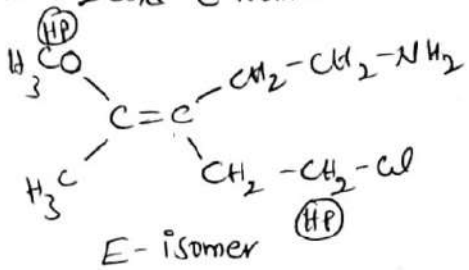
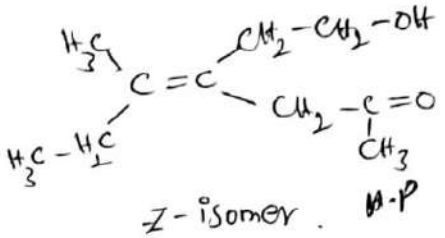
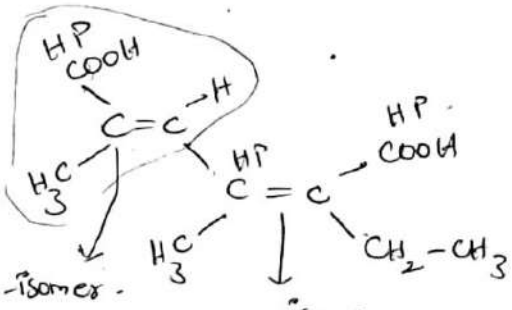
* Disubstituted alkenes are named either as cis (or) trans where as tri and tetrasubstituted alkenes will be named according to Z and E Nomenclature.



E-isomer



Z-isomer

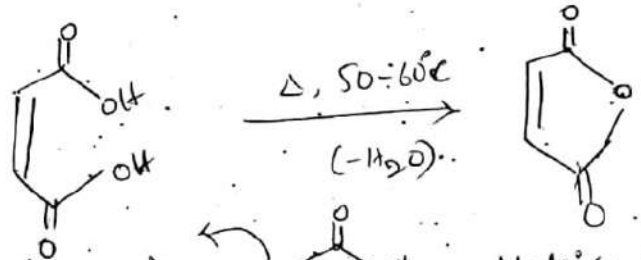


E-isomer

Z-isomer

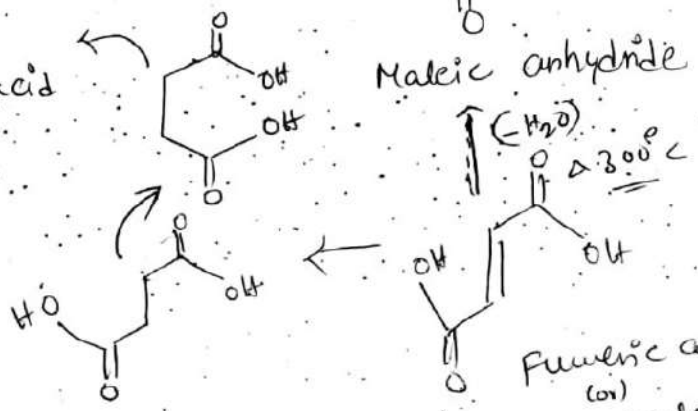
E-Z isomer

* Trans Isomers are more stable than cis isomers this is because cis isomers possess steanic clash.



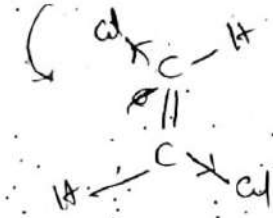
Maleic acid

Maleic anhydride



Trans 1,2-dichloro ethane

Fumeric acid (or) Trans-maleic acid



cis-1,2-Dichloro Ethane

$\mu = 1.86$ debyes

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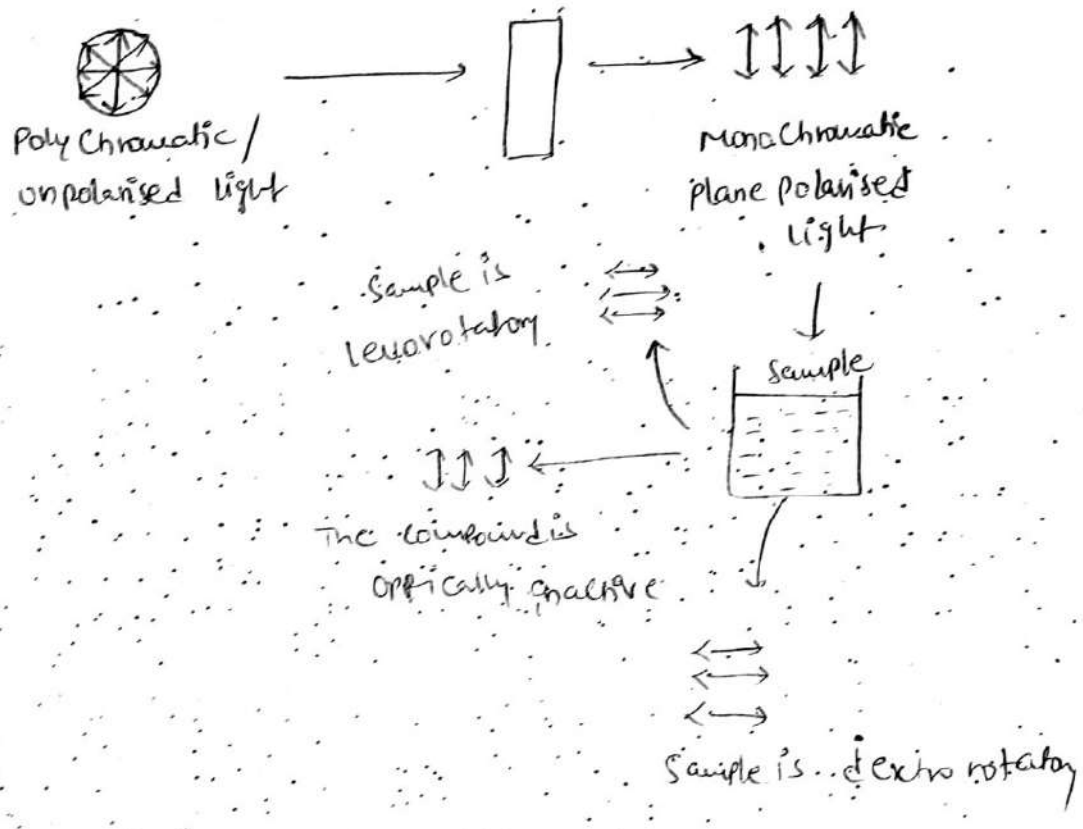
- Boiling point, molar refractivity and refractive index are High for cis Isomer where as thermal stability, M.P are higher for trans Isomer.

* Dipole moment as well as solubility are high for cis Isomers.
* Trans isomers are less reactive, more stable
  cis isomers are more reactive, less stable

OPTICAL ISOMERISM

Optical isomers are the isomers which show optical activity
Optical activity is the ability of a compound to rotate the plane Polarised light



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Never one can say whether the molecule is dextro (or) levo. The structures in the textbook already contain the terminology dextro (or) levo for a given compound. This was written based on the experiment already carried out using Polarimeter.

Both these are obtained by experimentally but not theoritically

(+)/d ⇒ dextro / clockwise / right hand side

(−)/l ⇒ levo / Anticlockwise / left hand side

D & L ⇒ Called as Relative (or) Comparitive Configuration.

↓ These are Theoretical but not experimental

→ It can be said by seeing structure

→ It is given by comparing with the standard.

The standard is glyceraldehyde

R & S ⇒ It is Absolute Configuration

⇒ No Standard is used.

⇒ Theoritically but not practical

For a molecule to exhibit optical activity it should possess asymmetry (that is when a molecule) is cut into two equal halfs one half of the molecule should not be the mirror image of other half of the molecule.

When a molecule is cut into two halfs and in one half of the molecule is mirror image of other than the molecule is called is called as Symmetrical molecule. Such molecule even though they contain Chiral centre they are optically inactive due to the element of Symmetry.

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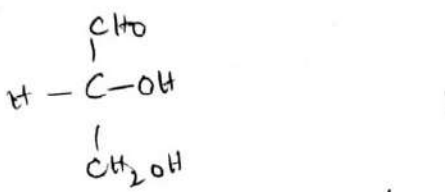
* Molecules which are optically active due to presence of chiral centre are called as as symetric molecules where as the molecules which are optically active with out chiral centre are called as dysmmetric molecules.

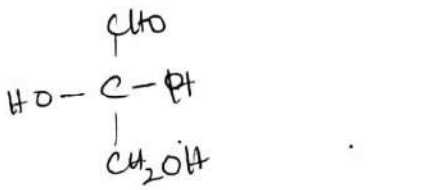
RELATIVE CONFIGURATION (D & L)

It is the determination of configuration (Spatial arrangement (or) orientation) of optical active compound by comparing it with a standard Glyceraldehyde.

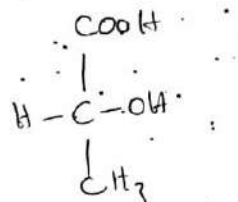
Eg.



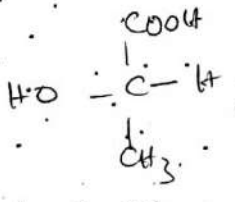
D - Glyceraldehyde



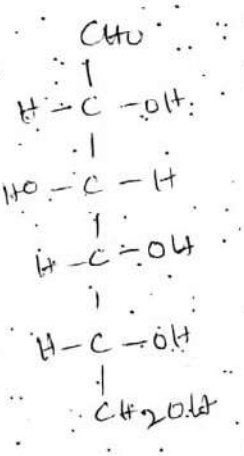
L - Glyceraldehyde



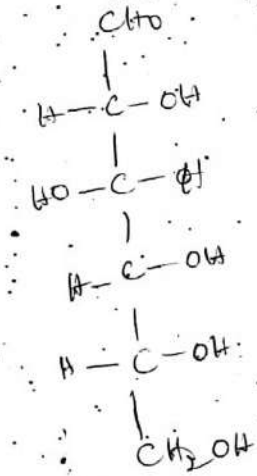
D - Lactic acid



L - Lactic acid



D - Glucose



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Absolute Configuration (R & S configuration)

CIP System

Cahn Ingold Prelog

Rules:

1) Rank the atoms on chiral centre with highest atomic number as 1 and atom with lowest atomic number as 4.

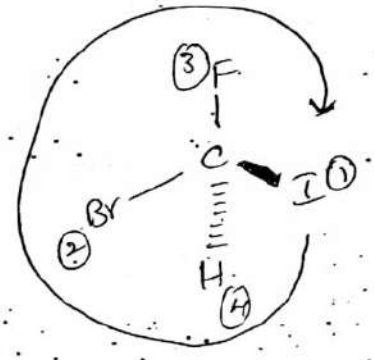
H C N O F ↑ lowest priority

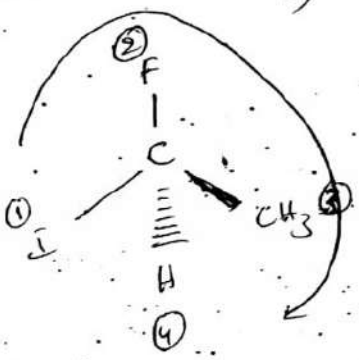
P S Cl

Br

I ↓ Top priority

2) Always see that atom or group with least priority is ranked 4 and is in the back (below the plane.)

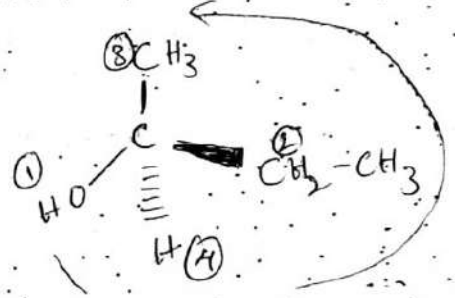




R → Rectus → clockwise

(R) Bromofluoroiodomethane (R)-Fluoroiodoethane

3) If two atoms attached to chiral centre are same then we have to move to the next atom till we get first point of difference.



Propane 2-ol

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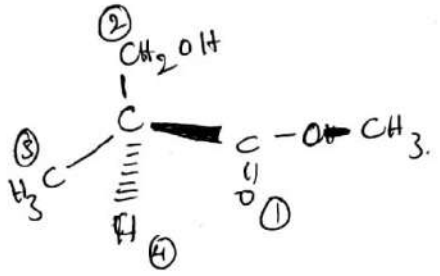
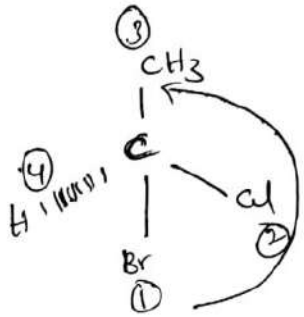
7) If the groups are having unsaturation we should consider double bonds as two single bonds ≡ bonds as three single bonds





Sinster (S) - isomer.

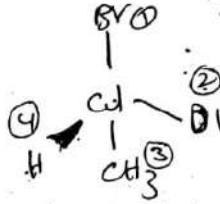
opposite

Anticlockwise

(S) configuration.

5) when ever the least priority atom of the group is above the plane then the actual configuration of the molecule will be the opposite configuration to which we will get the configuration. (or) property.

* If the least priority group is above the plane then write opposite configuration to which we get.



✓ Enantiomers are non-super impossible mirror images

✓ Diastereoisomers does not posses any mirror images

seemto be R but S is the actual configuration

Enantiomers	Diastereomers
✓ usually have 1 chiral centre	✓ usually have more than 1 chiral centre
✓ optically active	✓ optically active
✓ Have same physical property Hence hard to separate.	✓ Have different physical properties Hence easily separated
✓ Have identical chemical properties with an optically inactive reagent but doesn't have identical chemical	✓ Have similar chemical properties. but not identical that is rate of reaction is difficult

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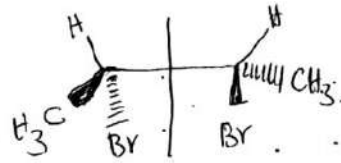
Elements of symmetry:

✓ A molecule even though it contain a chiral centre it will be optically inactive if it has elements of symmetry like planar symmetry, centre of symmetry (or) Alternating axcess of symmetry due to this symmetry one half of the molecule is mirror image of the other.

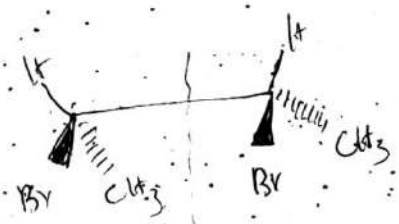
(1) Plane of symmetry (or) mirror plane:

It is an imaginary plane that bisects an object into a pair of mirror images.



2,3-Dibromo butane

→ Two molecules are not mirror image
They are optically active



→ Two molecules are mirror images
They are optically active

* If the number of possible stereoisomers for a compound with chiral centre is 2^n n = number of chiral centres

$2^2 = 4$

* If a molecule has 2 chiral centres and if the two chiral centres has same type of substituents then possible isomers is 2^{n-1}. This is due to the fact that the molecule will have elements of symmetry

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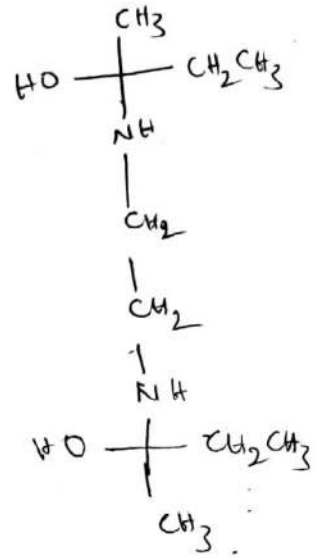
* For example

Ethambutol ⇒ an antitubercular agent has 2 Chiral centres but the possible no. of Stereo isomers is 3

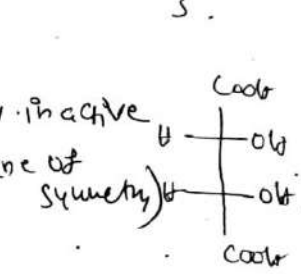


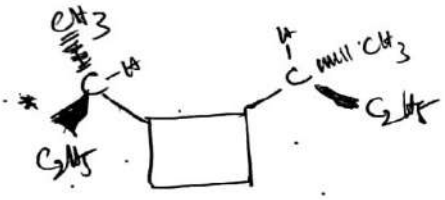
here $2^n - 1$.

$\Rightarrow 2^2 - 1 = 4 - 1$

$= 3$.

* 3 isomers are include. 1 dextro
1 levo
1 optically inactive
Meso Compound





1,2 - Di tertiary butyl Cyclobutane

optically inactive. (diastereomer image).

(Meso Compound).

Meso compounds are optically inactive due to internal compensation where as Racemic mixture is optically inactive due to external compensation.

(2) Centre of symmetry (or) point of symmetry (or) Centre of Inversion.

A centre of symmetry is an imaging point in an centre of a molecule from which the lines are drawn in any group on both sides to an equal distance and it divides the molecule into two halfs which are mirror images of each other.

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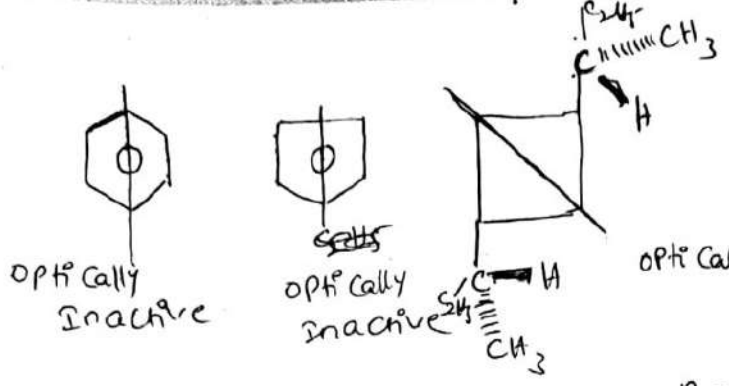
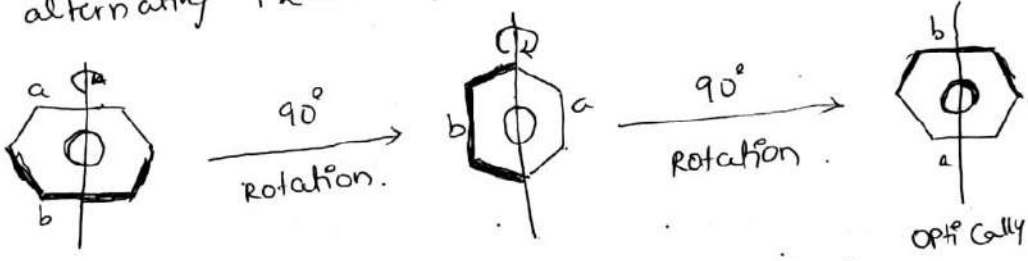


* Alternating axis of symmetry or Rotation axis.

This is an axis about which a rotation of 180° will arrive an alternating phase.



(3) Dissymmetry: Dissymetry molecule include optically active compounds without Chiral centre.

Eg: Allenes, ortho-ortho disubstituted biphenyl

o,o' - disubstituted binaphthynes

Spirans

* Stereochemistry of Allenes: Type of dienes particularly called as Cumulated diene of cumenes.

Dienes
- Conjugated dienes — C=C-C=C (1 Single bond & 2 double bonds)
- Isolated dienes — C=C-C-C=C (2 single bonds & 2 double bonds)
- Cumulated dienes (Allenes) — C=C=C (2 double bonds & NO Single bonds)

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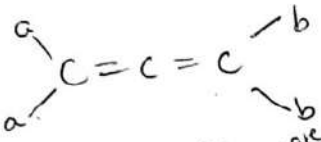
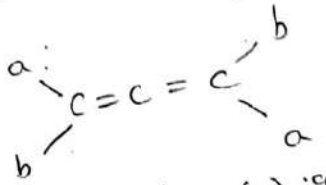
Alleneş have Planar sp^2 C- atoms. Alleues exhibit optical Isomerism. if the two groups attached to terminal C- atoms are different.

In alleneş the terminal C- atoms. Alleues exhibit optical isomerism ~~if the two gro~~ contain a - Substituents perpendicular to the plane, thus the whole moleeule is not in plane and exhibit assymetry.

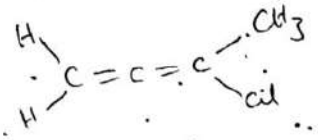


Terminal groups/atoms are same.
So optically inactive

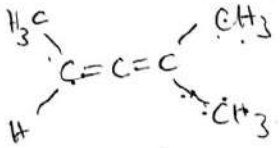


terminal atoms (or) groups are same different so optically active.

Achiral Alleues:

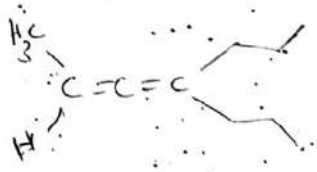


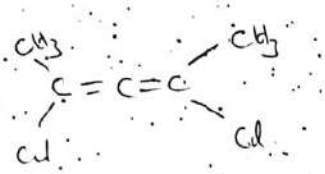
AChiral

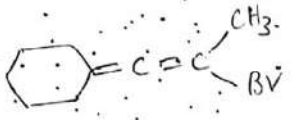


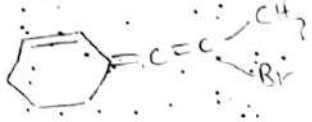
AChiral

here
Achiral = Assym.
Chiral =



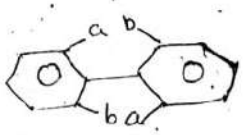




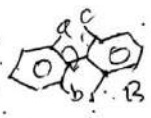


Atrope Isomerism:

Optical Isomerism due to restricted rotation



a & b are bulkier groups
Here rotation is locked / restricted so molecule has assymetry ⇒ optical active.



↳ It is due to

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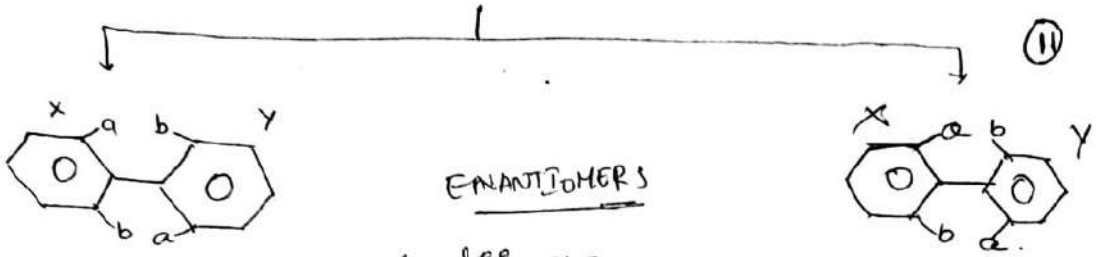
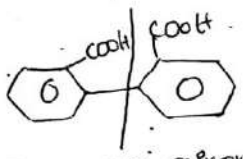


ENANTIOMERS

Both the molecules are non planar

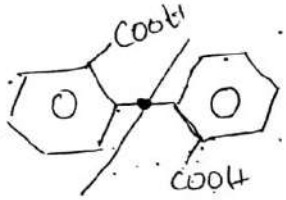
⊛ Criteria for Atrope Isomerism:

* presence of different ortho substituents on the ring
* Always their should be bulkier substituent in the ortho position
* Bulker groups like $-SO_3H$, $-NO_2$, $-CH_3$, $-COOH$ etc.
* Both the phenyl ring should be non co-planar.

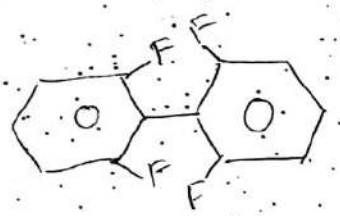
Eg: ① 

These are mirror images

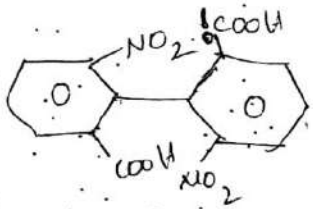
✓ Has plane of symmetry
✓ optically inactive

② 

✓ Has centre of symmetry optically inactive

③ 

Optically inactive due to:
* Same group on ortho position
* The groups are not Bulkier
does'nt exhibit atropisomerism

④ 

* Exhibits Atropisomerism.

* Vancomycin is anti-bacterial antibiotic exhibits Atropiso-merism

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* Gossypol is a 0,0'- disubstituted Binaphthyl isolated from Gossypium Herbaceum it exhibits Atropisomerism.

↳ Dextro: It has Antispermatogenesis property
Hence it is used as Male contraceptive

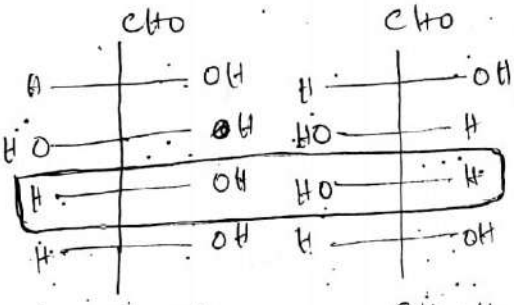
Leavo: Hemotoxic It decreases the oxygen carrying capacity of RBC

* Racemic mixture: Equal proportions of Dextro & leavoisomers

Separation of R-M into dextro & leavo mixture is called as Resolution.

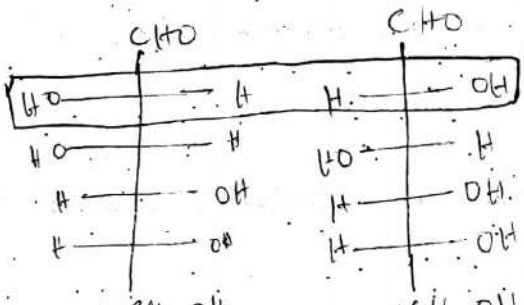
Epimers: These are the diastereoisomers differ in Stereo Chemistry at one stereogenic centre.

Eg: Glucose & Galactose are epimers bat Carbonphore
↳ C_4 position



D-Glucose D-Galactose

* D-Glucose and D-mannose are C_2 - epimers



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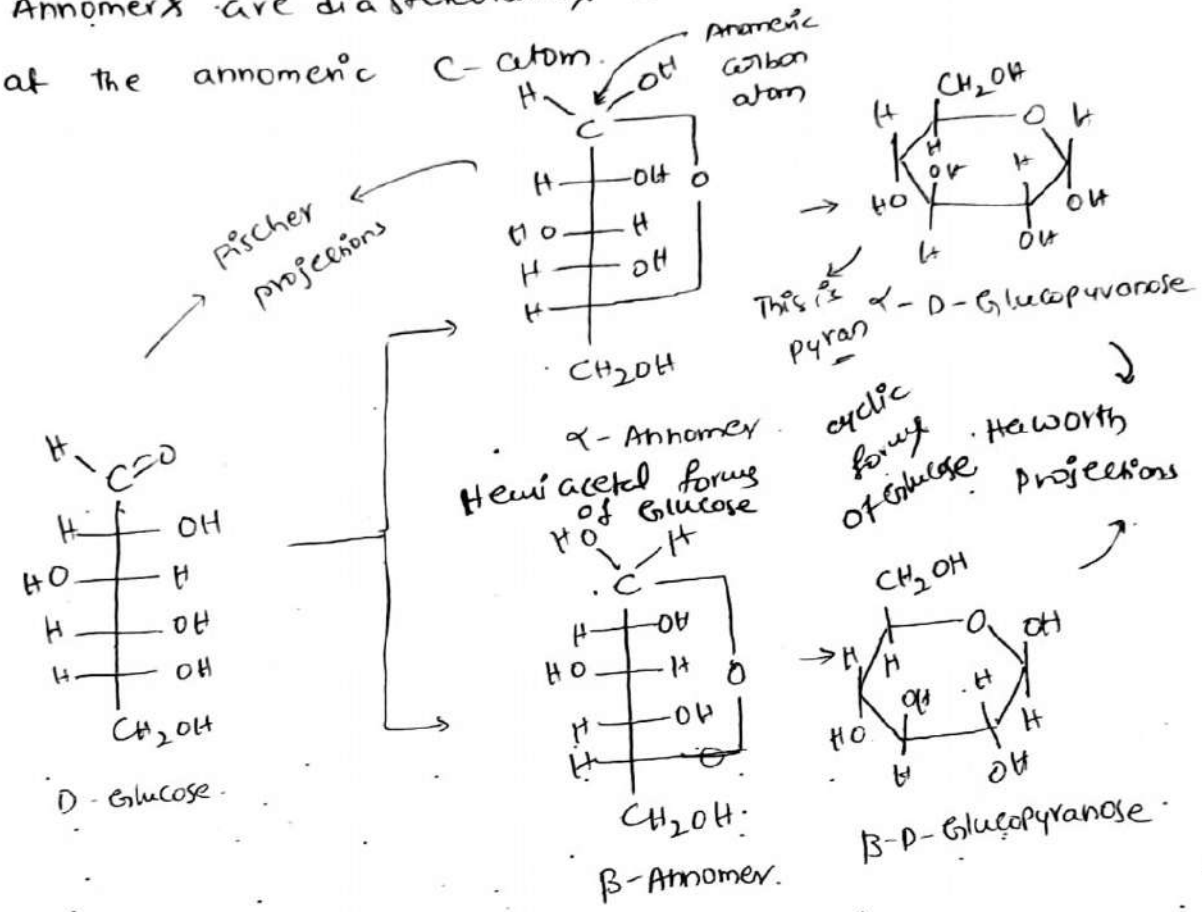
Annomers

* Annomers are diastereoisomers is differ in configuration at the annomeric C-atom.

*



Mutarotation

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

✓ Glucose molecule will exits in open chain forms & the cyclic and α & β-anomeric forms

✓ whenever either α-Annomer (or) β-annomer placed in usually they have a specific rotation of +113°; +19° after a while if we check the specific rotation valies in polarimeter. The specific rotation value of both these compounds it reaches the common value is ± 53°c This is called as mutarotain and it occur due to the fact that the α & β anomers will be in an equilibrium mixture where there is small amount of open chain form and nearly equal amounts of

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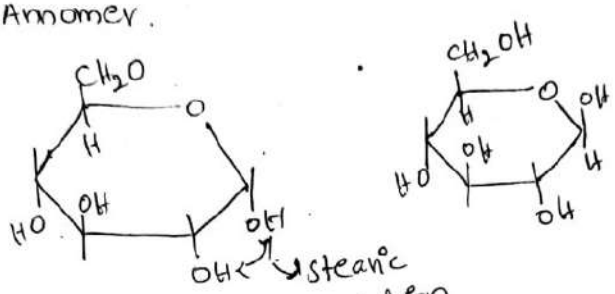
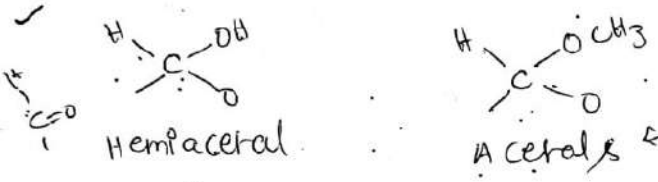
α and β- Anomers.

* This is occuring due to the presence of mobile Hydrogen.

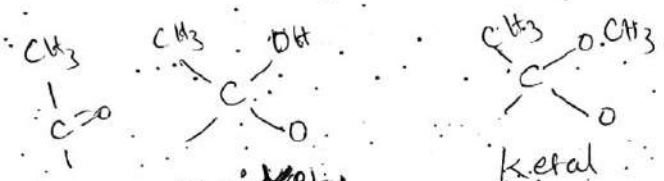
✓ Glucose can reduce Fheling's & Tollen's reagent as free aldehyde form group in the open chain form of glucose

✓ β-Anomer is more stable than α-anomer as there is steric repulsion between the Hydroxy groups at 1,2-positions of α-Anomer.



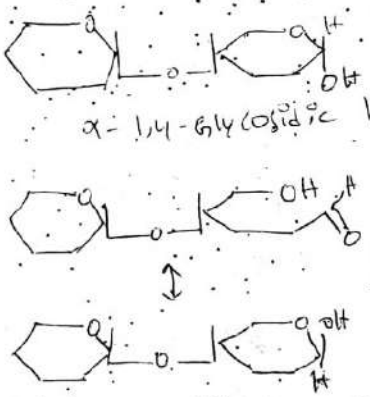


Glycosides (Glucose sugar + Non sugar) are Acetals



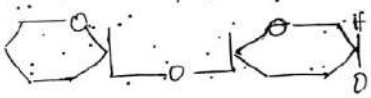
* Glycosides they lack mobile Hydrogen. Hence they don't reduce Fehling's & Tollen reagent They do not exhibit muterotation

Reducing disaccharides



✓ Reduces Tollen reagent & Fehling's
✓ Reduces Exhibit Mutarotation.

Non-Reducing disaccharides



Does not exhibit mutarotation.
does not Reduce Fehling's and Tollen reagent.

Sugars ⇒ Sucrose
↓ Hydrolysis
Glucose + Fructose.

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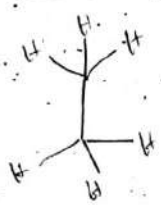
CONFORMATIONAL ISOMERISM

- 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 helps 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 k.cal and the ~~empty~~ energy associated with compounds containg C-C single bond is 5 to 10 k calories.
- Hence compounds with C-C single bond can rotate & exists in more than one conformational isomeric form.
- Studying about the energies & stabilities 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 Sawhorse formulas



Staggered

Eclipsed

Cannot draw skew conformers

② Newman's projections

Front Carbon

Back

* The order of Bond angles & Stability are:
Eclipsed < Skew < Staggered

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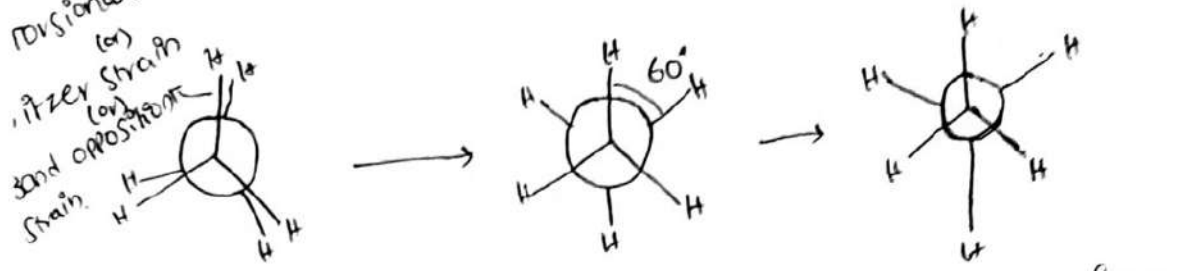
Here Torsional strain (or) Pitzer strain (or) Bond opposition strain.



Eclipsed conformer.

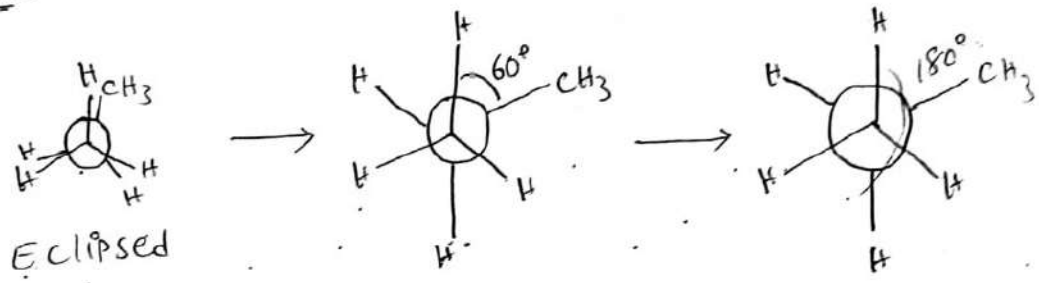
Skew / Gauche Conformer

Staggered conformer

↓

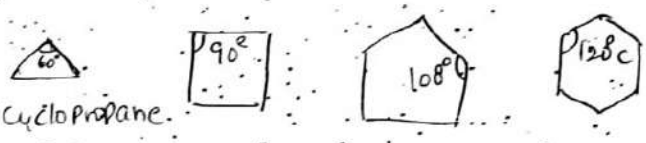
It has No Bond opposition (or) Pitzer strain / Torsional strain

Propane



Eclipsed ↓ Less Stable < Skew < Staggered ↓ More Stable

Cyclic Compounds:



Cyclopropane				
60°	90°	108°	120°	
109·28'	109·28'	109·28'	109°28'	The difference is Angle strain
49°28'	19·28'	1°28'	11°28'	

According to Bayer Strain theory:

1. All the Cycloalkanes are planar
2. More is the angle strain. Less will the stability of Cyclohexanealkane.

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i) Limitations of Bayer Strain theory:

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 cyclo hexane molecule will exists in strainless (or) puckered ring structures and these rings are not planar & the bond angle for these non planar compounds will be 109°.28'. So cyclohexane more stable than cyclopentane.

✓ Cyclopropane is unstable because of Angle Strain & Bond opposition Strain.

✓ Cyclopropane is used as Inhalational General anesthetic

Cyclo butane ⇒ open book conformer

↓ More stable due to 2° less Angle strain

Cyclopentane

Envelope ⇒ More stable

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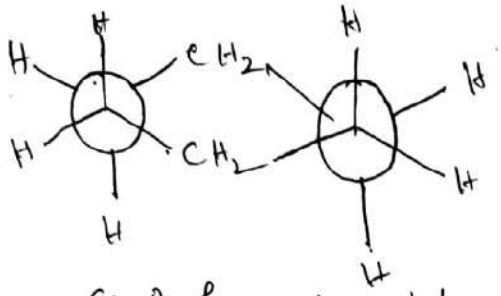
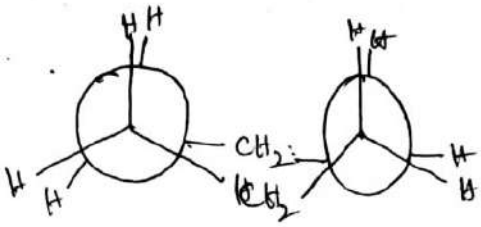


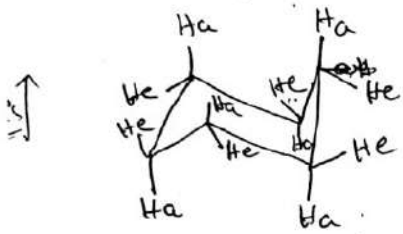
Chair form of cyclohexane
(in Newman's projection)



Boat form of cyclohexane

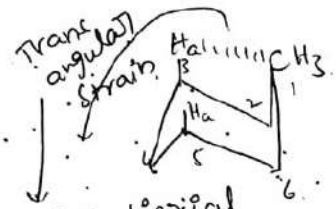
Flag. Polehydrogens
⇓
Flag Pole interactions
⇓
pitzer strain

⊛ Stereochemistry of Substituted Cyclohexane derivatives



Ha = Axial hydrogens
He = Equatorial Hydrogens

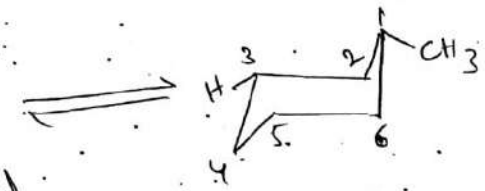
Mono Substituted Cyclohexane:-



Trans angular strain

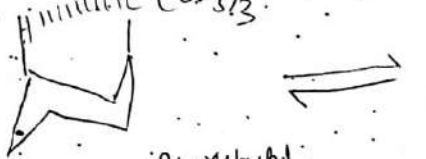
It has 1,3-diaxial interaction & 1,5-diaxial interactions

Equatorial methyl cyclo hexane
↓
Less Stable



There is no 1,3-diaxial interactions

Equatorial methyl cyclohexane
↓
More Stable



Axial tertiarybutyl cyclohexane

It is less Stable Compared to Axial methyl cyclohexane

Equatorial t-butyl cyclohexane

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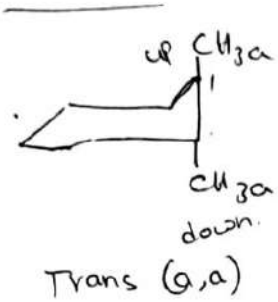
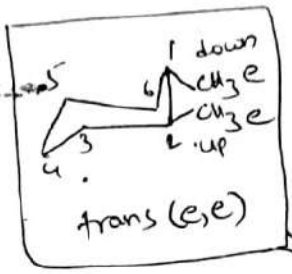
It is more Stable as the bulkier group is in equatorial position.

⊛ Disubstituted cyclohexane 1,2- Dimethyl cyclohexane:-



Trans (a,a)

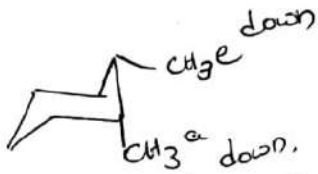


cis (a,e)

→ More Stable of all.

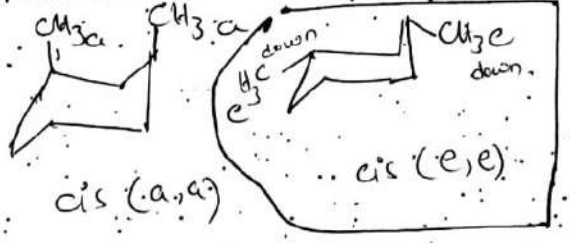
Trans (two are opposite side) up, down,

cis (two are same side) up, up. down, down



Commonly trans is more Stable than cis.

⊛ Disubstitued cyclohexane · 1,3-dimethyl · cyclohexane

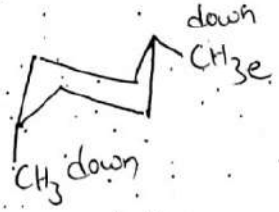


cis (a,a) cis (e,e)

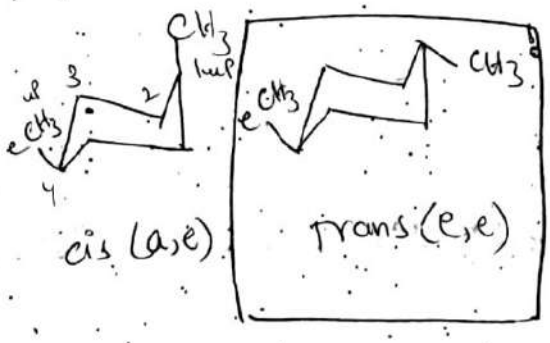
trans (e,a) Trans (a,e)

⊛ Disubstituted Cyclohexane 1,4-Dimethyl cyclohexane

Trans (a,a)



cis (a,a)



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* Enantiomeric excess:

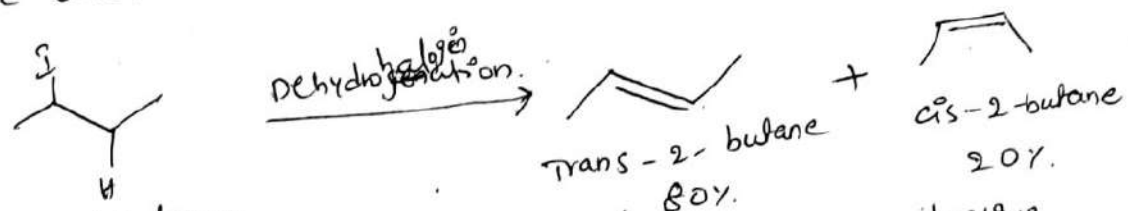
Is the quantity used to measure the enantiomeric purity

* 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.



Stereo selective reactions are may be either enantioselective (or) Diastereoselective.

✓ If the products are enantiomers and if one stereoisomered formed more and the reaction is Enantio-selective.

✓ 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.

* Stereo specific reaction:

The stereo specific reaction is the one which when carried in their stereo isomeric starting material, Gives a product with different stereochemistry, than the stereo-chemistry of reactant

R ⟶ S

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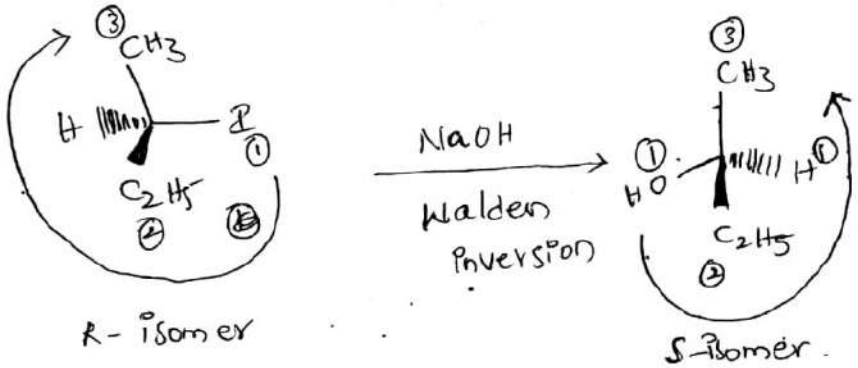
'S' isomer of Reactant form 'R' isomer of product and vice versa.

Eg: Walden inversion in S_N2 reaction is stereo specific



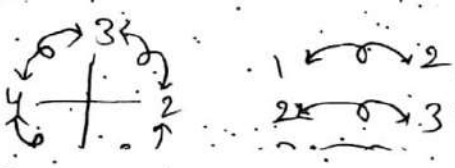
R - isomer

S - isomer

Asymmetric synthesis: It is the method of preparing of high yields of one enantiomer with minimum production of it mirror image.

Assinging R & S Configuration:

- To Assign R and S Configuration to the Chiral molecule the least priority group should be vertically down in fisher projection.
- If it is not so, then interchanges (swaps) in the positions are made (or) Carry out to bring it to that position but care need should be taken so that the interchanges dont chase the actual configuration of molecule
- This is done by following two rules
- 1: The interchange is to be carried out only b/w adjacent positions in Fischer projections.



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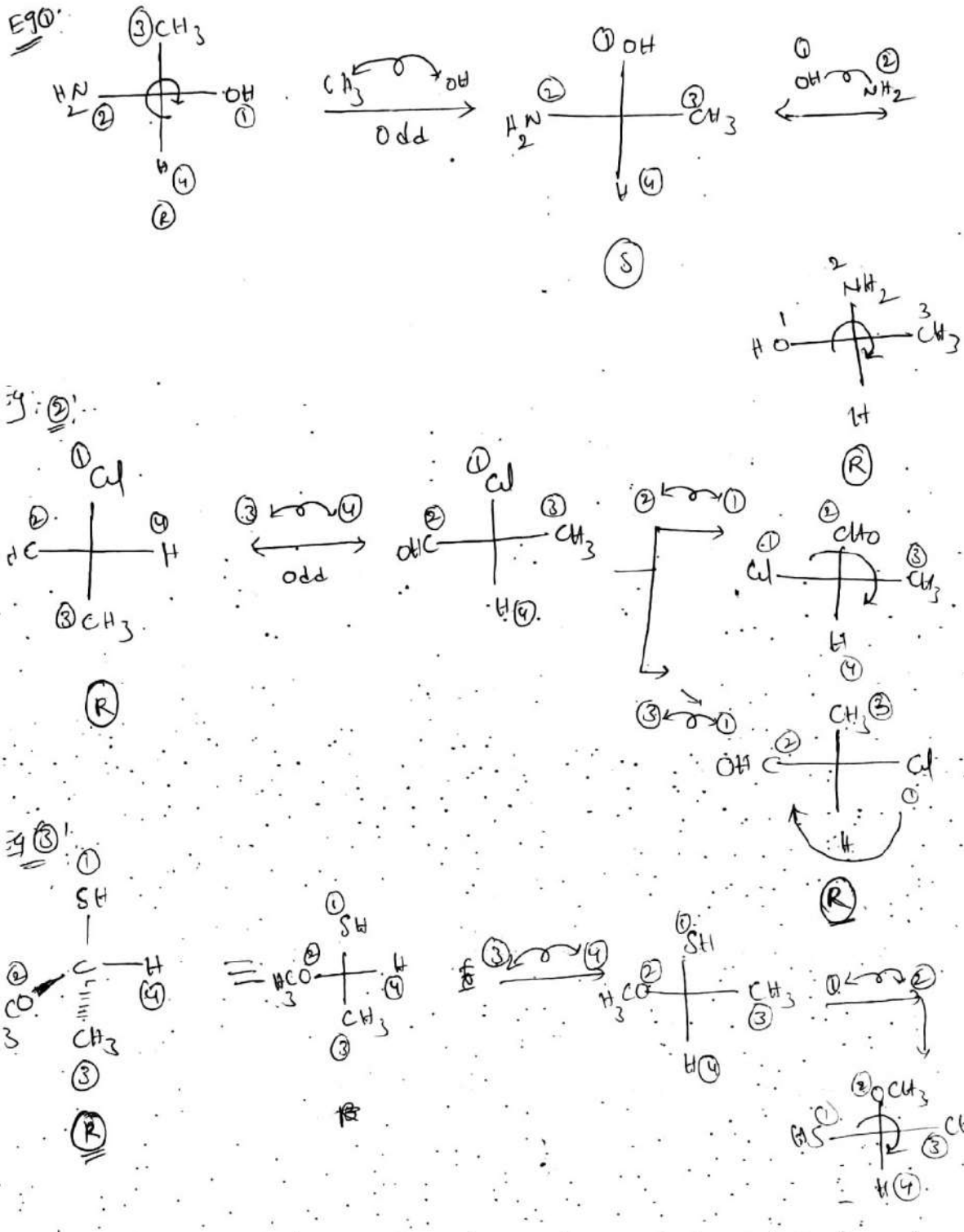
* An even number of inter changes must be carried out As they not chase actual configuration molecules It should be noted that odd no. of change in configuration of molecules & gives Enantiomer.

Eg①:



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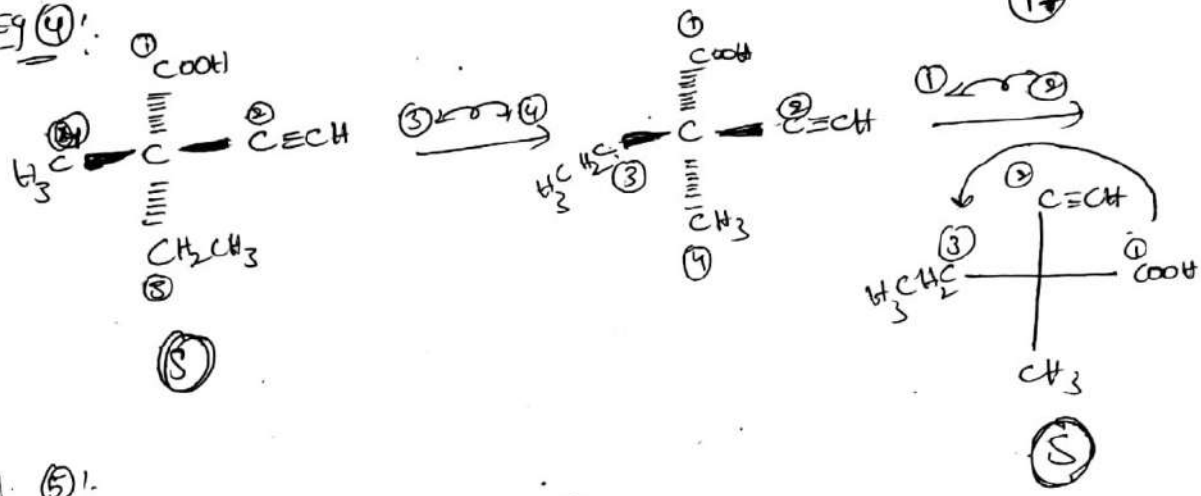
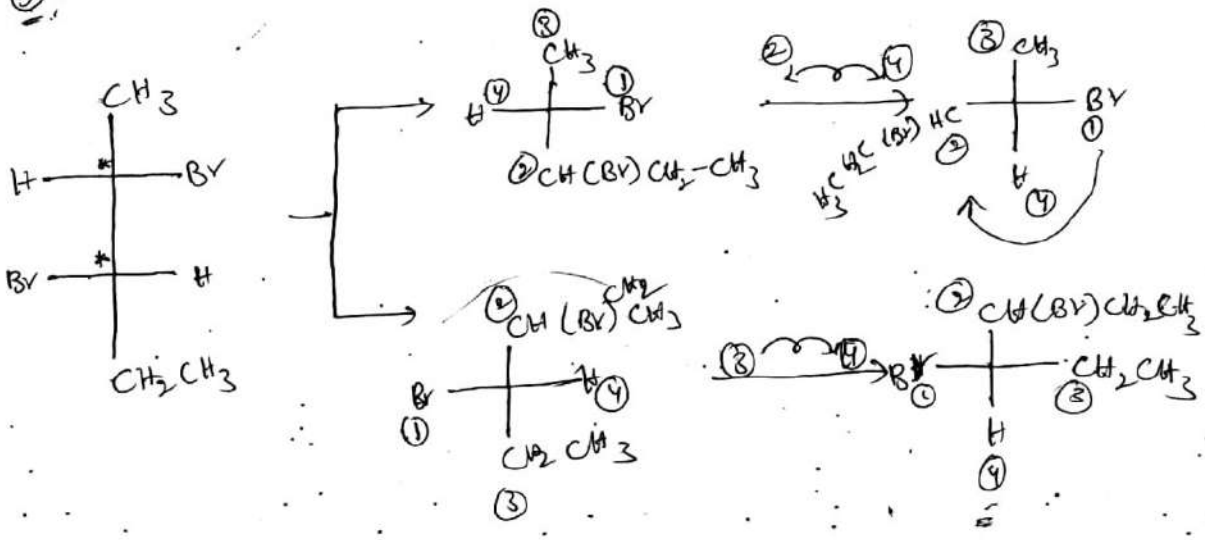
Eg (4):



(5):



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STEREOCHEMISTRY

Isomers → Same molecular formula but different arrangement of ~~structure~~ atom or group (i.e; different structural formula)

- They have different physical & chemical properties, biological properties

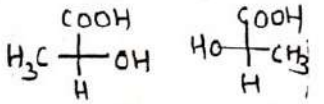
eg:-

C_2H_6O – molecular formula

- CH_3-O-CH_3 — dimethyl ether → anaesthetics
- CH_3-CH_2-OH — ethanol → antiseptic.

Isomers

- Structural isomers / constitutional isomer.
  - Have different structure / constitution
  - eg:- CH_3-O-CH_3 (2 methyl group) CH_3-CH_2-OH (one ethyl group)
- Stereoisomers / spatial isomers
  - Have same structure but differ in 3D arrangement



difference in 3D arrangement

Structural isomers →

1) Chain isomers →

Chain isomers have same molecular formula but differ in alkyl chains.

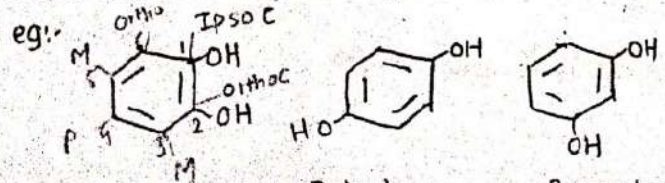
eg:- $CH_3-CH_2-CH_2-CH_3$ n-butane

$CH_3-CH(CH_3)-CH_3$ Isobutane / 2-methyl propane

2) Positional isomers / Regioisomers →

These are isomers with same functional groups & functional groups are in different regions or positions

eg:-



Catechol — o-hydroxy phenol

Quinol — p-hydroxy phenol

Resorcinol — m-hydroxy phenol.

* Phenol coefficient is used to determine the [illegible] compound in comparision to phenol

1) Chick-Martin coefficient
2) Riedel-Walker coefficient.

* All quinones are coloured compounds 

Schedule Q → standards for coal tar colours used in cosmetics & medicines → lactams → lactones

preparation.

3) Functional group isomers →

These are compounds with same molecular formula but different functional groups.

eg:- C_2H_6O

CH_3-O-CH_3
ether
dimethyl ether

CH_3-CH_2-OH
alcohol – Ethyl alcohol

4) Metamers →

These are isomers with same functional groups but different alkyl chains arranged around functional group.

eg:-

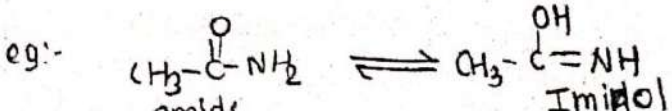
$CH_3-CH_2-O-CH_2-CH_3$
diethylether

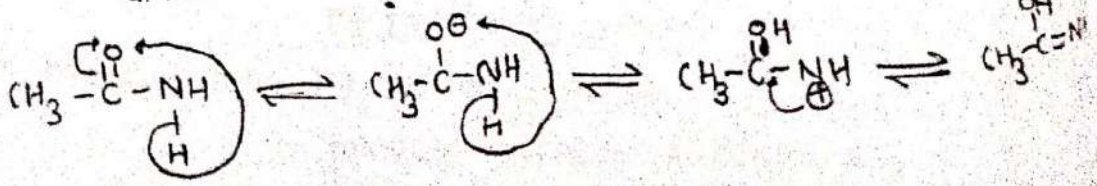
$CH_3-O-CH_2-CH_2-CH_3$
propyl methyl ether.

~~Metamerism is~~

5) Tautomers →

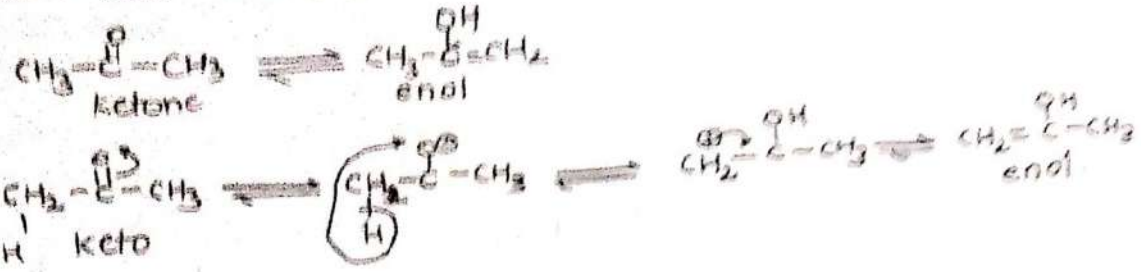
These are the isomers which are formed due to migration of a proton.

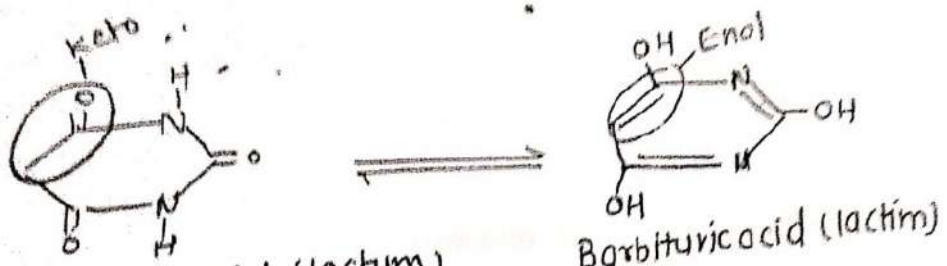
eg:- 



amido-iminol tautomerism.

Keto-enol tautomers →





Barbituric acid (lactum) Barbituric acid (lactim)

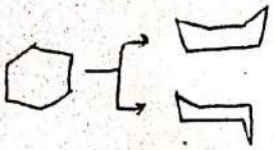
Barbituric acid exhibit both. keto-enol tautomerism
lactum-lactim tautomerism (more preference)

Stereoisomerism

↓

conformational isomers

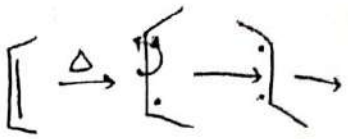
- Isomers formed due to rotation about C - C single bond.
- Rotational isomer



- no bond breaking / making.

constitutional isomers.

- Isomers are formed due bond breaking & making bond



constitutional isomers are types

1) Geometrical isomers
2) Optical isomers

Whether two molecules have same molecular formula?

No → Not isomers

Yes

Is the isomerism is due to it's structure / constitutio

yes → structural isomers / constitutional isomers

No → Stereoisomers

Is the isomerism is due to free rotatio about C-C single bond?

yes → conformational isomer

No → configurational isomers.

Is the isomerism is due to restricted rotation

yes → Geometrical isomerism.

cis trans

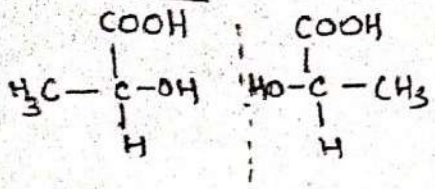
No → optical isomeri

whether the isomers are non-superimpos images?

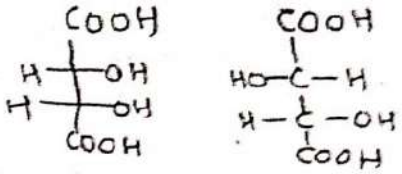
yes → Enantiomer

No → Diastereom

Enantiomer



Diastereomers



- non superimposible not mirro images of each other.

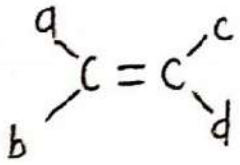
Geometrical isomerism→

- Geometrical isomerism is due to restricted rotation
- Generally the compounds that contain carbon-carbon double bond (C=C) bond has restricted rotation hence these compounds will exhibit geometrical isomerism

However there are compounds which contain C=C bond but do not exhibit geometrical isomerism

- There are compounds which contain C-C bond & exhibit geometrical isomerism because at that C-C bonded system there is restricted rotation.
- Generally ~~isomers~~ alkenes will exhibit geometrical isomerism.

for a geometrical isomerism

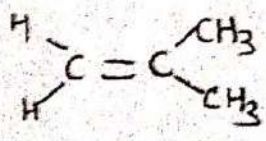


$a \neq b \quad c = c \quad \& \quad c \neq d$

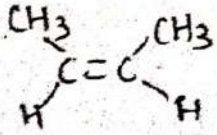
if $a = c$ & $b = d$ then it is cis isomers.

$a = d$ & $b = c$ then it is trans isomers

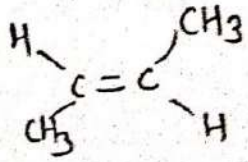
eg:-



Neither cis or trans



cis-2-butene



Trans-2-butene

1,2-disubstituted cyclo

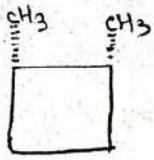
cyclobutane

→ free rotation of c-c bond
will exhibit conformational isomerism.

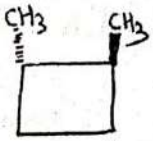
→ Restricted rotation due to two methyl groups

cis 1,2-Dimethyl cyclobutane.

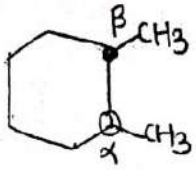
} configuration
(configuration
within the plane
unknown
configuration



cis 1,2-Dimethyl cyclobutane

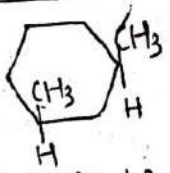


trans-1,2-Dimethylcyclobutane.

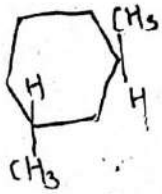


trans 1,2-Dimethylcyclohexane.

1,3-Disubstituted cycloalkanes →

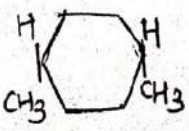


cis-1,3-Dimethyl cyclohexane

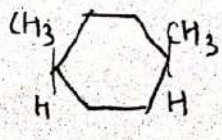


Trans-1,3-Dimethyl cyclohexane.

1,4-Disubstituted cyclohexane →



cis-1,4-Dimethyl cyclohexane



trans 1,4-Dimethyl cyclohexane

Cycloalkenes →

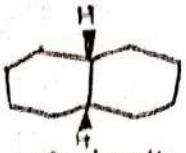
cis cyclohexene

trans-cyclohexene.

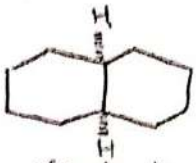
Fused rings →

(Perhydronaphthalene)

Decalin

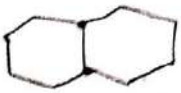


cis-decalin



cis-decalin

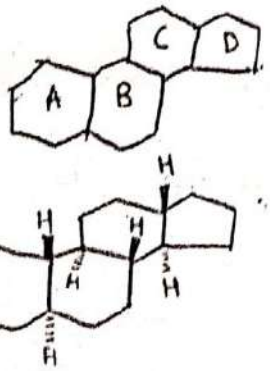
cis decalin



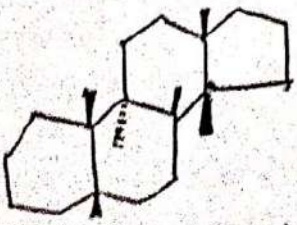
cis-decalin

Steroids →

contain cyclopentanoperhydrophenanthrene ring



A/B - trans
B/C - trans
C/D - trans
} sex hormones → testosterone, oestrogen, progesterone.
corticosteroids



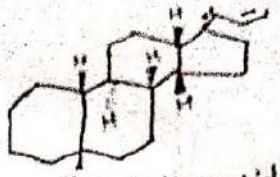
A/B - cis
B/C - trans
C/D - cis
} cardiac steroids → cardenolides - digitoxin, digoxin, strophanthin.
Bufadienolides → lactone

olide - lactone & cyclic ester

macrolides - large lactone ring

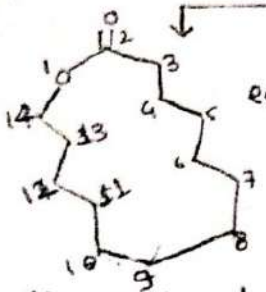
cardenolides

↳ used to treat CHF



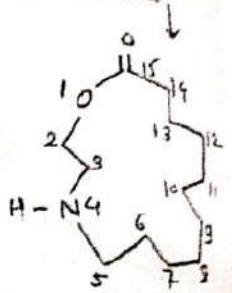
" Bufadienolides

- The patients who are allergic to penicillin are treated with macroli



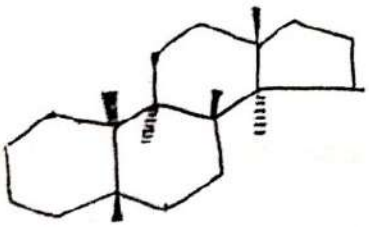
14-membered lactone ring

eg:- Erythromycin
Roxithromycin
Clarithromycin



15-membered lact

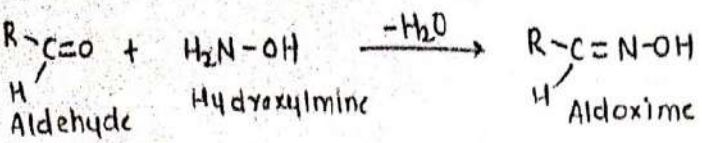
eg:- Azithromyci

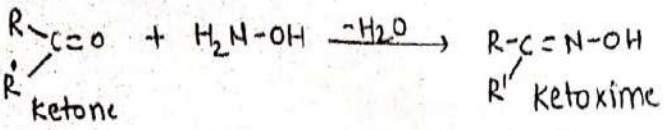


A/B-cis
B/c-trans
c/D-trans

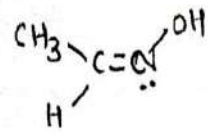
} bile acids — Glycholic acid
Taurocholic acid.

Oximes →

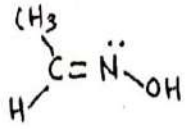




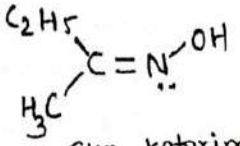
eg :-



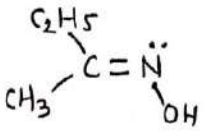
syn-aldoxime
cis-aldoxime



anti-aldoxime
trans-aldoxime.



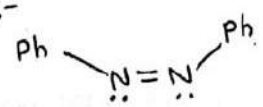
syn-ketoxime
cis-ketoxime



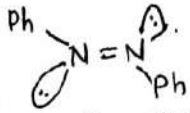
anti-ketoxime
trans ketoxime

Azo compounds →

eg :-



syn-azabenzene
Z-azabenzene



anti azabenzene
E-azabenzene.

Z & E nomenclature →

cis
Trans

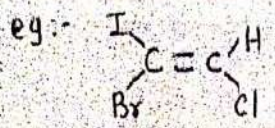
Z - Zussamen
E - Entagagen

(priority rules)

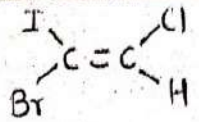
1) Rank the atom directly attached to the carbon atom in the double bond in the decreasing order of atomic number, so that atom of highest atomic number will get highest priority.

atoms -	I	>	Br	>	Cl	>	F	>	O	>	N	>	C	>	H
atomic number -	53		35		17		9		8		7		6		1

eg:-



~~Trans~~ E-isomer



Z - isomer

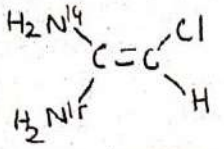
2) When isotopes are present, then isotope with highest atomic mass will have first priority.

eg:- T > D > H

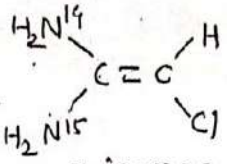
$^{3}_{1}H > ^{2}_{1}H > ^{1}_{1}H$

$^{37}_{17}Cl > ^{35}_{17}Cl$

$^{15}_{7}N > ^{14}_{7}N$



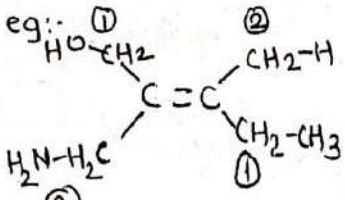
E - isomer
(trans)



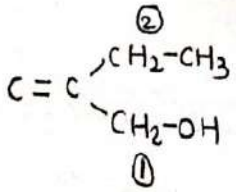
Z-isomer
(cis)

3) If the two atoms directly attached to alkene carbon atom are same, then rank the second, third, fourth & so on atoms (working from the C=C bond) one at a time until the difference is found. This is called as first point of difference rule.

eg:-

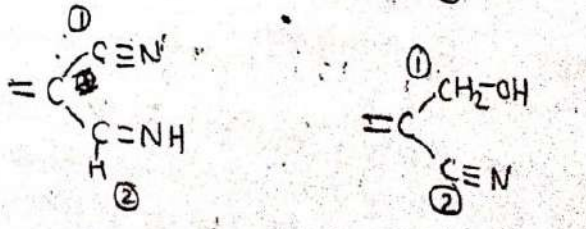


E-isomer.



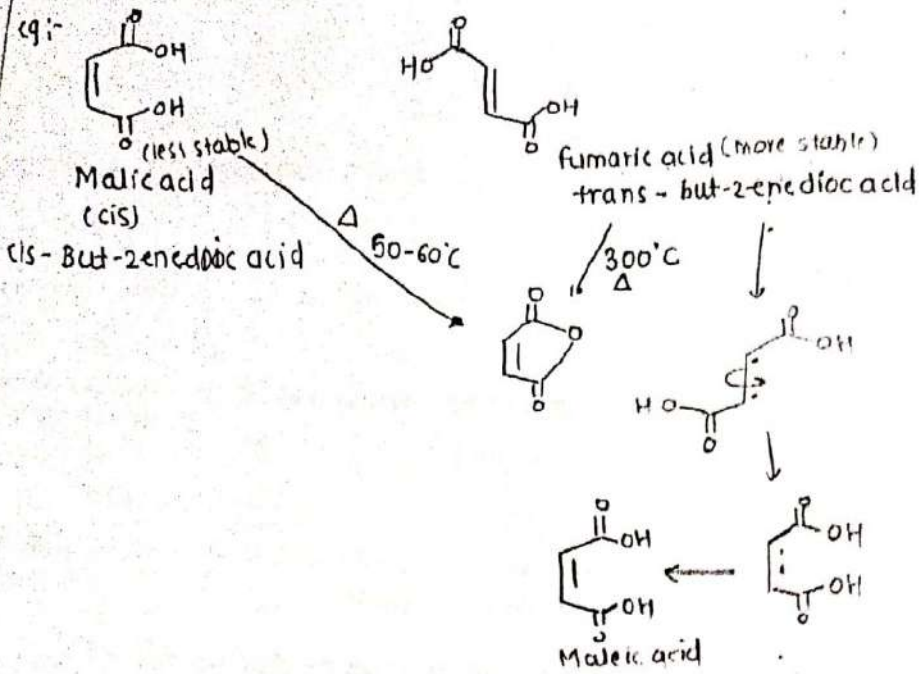
4) If the substituents contain double and triple bond then treat ato joined by double or triple bonds as a if they were linked to 2 c 3 single bonds

eg:-



5) Trans isomers are more stable than cis isomers

eg:-

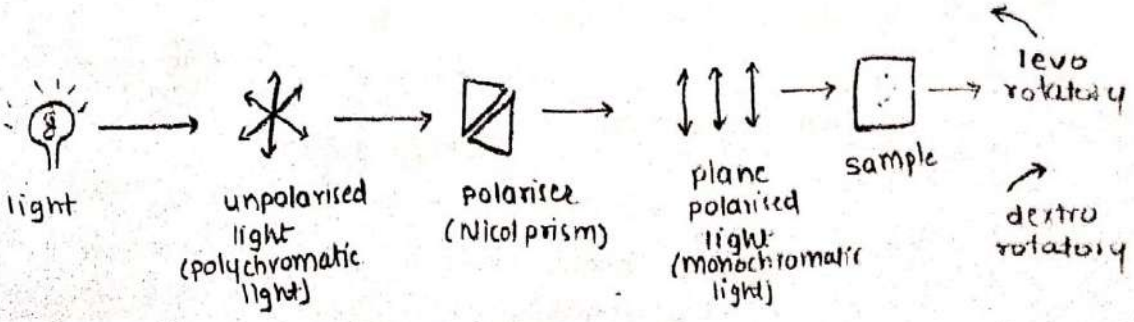


- B.P, molar refractivity, dipole moment, solubility & refractive index are high for cis isomer

whereas thermal stability, M.P are higher for trans isomer.

Optical isomers →

- Compounds which has the ability to rotate plane polarised light are called as optical isomers



Dextro → Right → d/(+)

Levo → Left → l/(-)

Racemic mixture is a mixture, which contain equal amounts of dextro & levo isomers, so net rotation is zero (external compensation)

Racemic mixture is optically inactive

The optical isomer with ... activity is called as Eutomer, whereas which has less biological activity is called as Distomer

Eudismic ratio = Eutomer / Distomer

used to determine how much one isomer is more active than other.

eg :- l-Hyoscamine (scopolamine) is 10-15 times more active than d-Hyoscamine

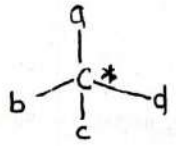
It is a drug of choice for treatment of motion sickness. (Travelling sickness)

-Never a one can say a compound is dextro or levo by seeing structure of molecule on a paper

- Whether the compound is levo or dextro can be known by performing polarimetry experiment.

- The structures in the text book already contain the terminology for a compound. this was written based on experiment already carried out using polarimeter.

-Chiral center or stereogenic center → Optically active



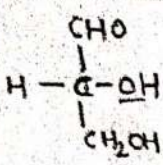
where $a \neq b \neq c \neq d$.

Assigning the configuration at stereogenic center :-

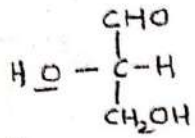
Spatial arrangement.

- Relative configuration
  - D & L system (not related to Dextro Levo at all).
    - Standard is used to assign configuration to chiral carbon
      - Glyceraldehyde
- Absolute configuration
  - R & S System.
    - There is no usage of standard to assign the configuration

Relative configuration →



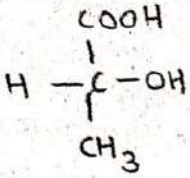
D-Glyceraldehyde



L-Glyceraldehyde

Standard used.

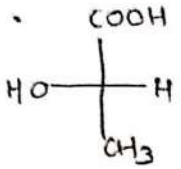
eg:-



D-(-)-lactic acid.

↓ → Levo (practically performed)

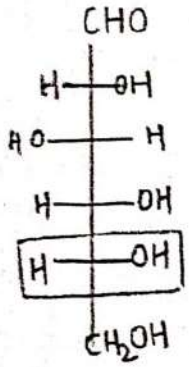
Relative configuration (bulky group is on right side)



L-(+) Lactic acid

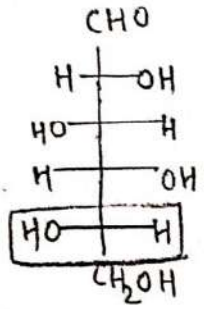
→ Dextro

↳ Relative configuration.



D-Glucose.

D-(+) Glucose.



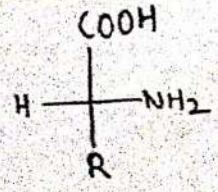
L-Glucose

* First group after CH_2OH is always selected to assign configuration

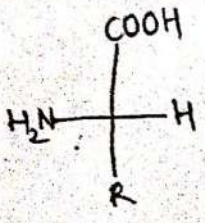
* D & L configuration is always used to assign the configuration of sugars & carbohydrates excellently

* In nature most of the naturally occuring sugars posses D configuration

Amino acids →

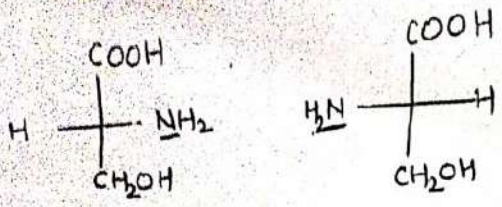


General structure D-amino acid



L-amino acid.

In amino acids standard used is serine.



D-serine L-serine

* Bacterial cell wall contain D-amino acid & plant & animals L-amin

Humans → L-amino acids.

* Penicillins act on D-amino acid only, they do n't act on L-amino a they are selectively bactericidal & doesn't harm host cell

* D-amino acid → R configuration
L-amino acid → S configuration

Absolute configuration →
(R & S configuration). R- Rectus (clockwise)
S - Sinister (anticlockwise).
CIP system
Cahn Ingold Prelog

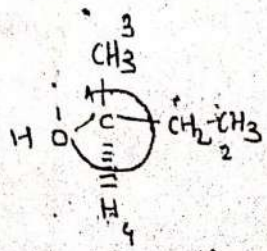
1) Rank the atoms on chiral center in order of ~~increasing~~ atomh atomic number as 1 & atom with lowest atomic number 4

2) H C N O F
P S Cl
Br
I

2) Always see that atom or group with least priority is ranked 4 & it should be on the back (below the plane)(.....)

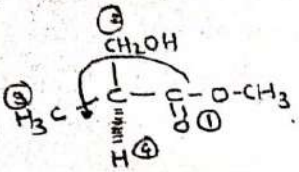
3) If 2 atoms attached to a chiral centers are same then we ~~to the~~ move to the next atom till we get first point of diff

eg:-



S-configuration

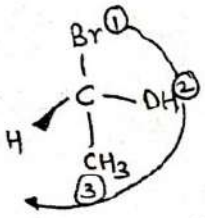
4) If there are unsaturation to group attached to chiral center then triple bonds are given preference over double bonds.



S-configuration.

5) Whenever the least ~~prio~~ priority atom or group is above the plane then you write opposite configuration to configuration you get

eg:-



R-configuration

but H-is ~~on~~ above the plane, configuration is reversed

S-configuration

6) Whenever the least priority group is within the plane then we have to use principles given by fischer to assign the R & S configuration.

a) To assign R & S configuration to chiral molecule, the least priority group ~~or~~ atom should be always vertically down in fischer projection

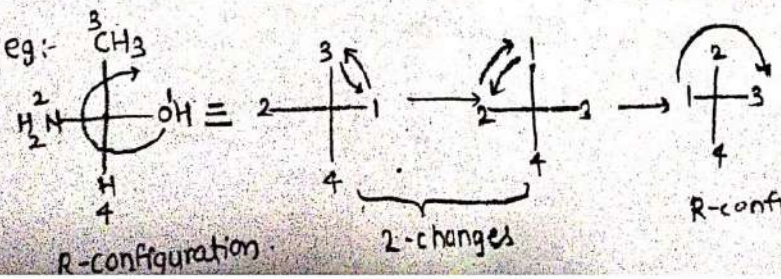
b) If it is not vertically downwards then interchanges in the positions are made to bring it to that position, but care need to be taken so that the interchanges do not change the actual configuration of molecule.

c) This done by following 2 rules

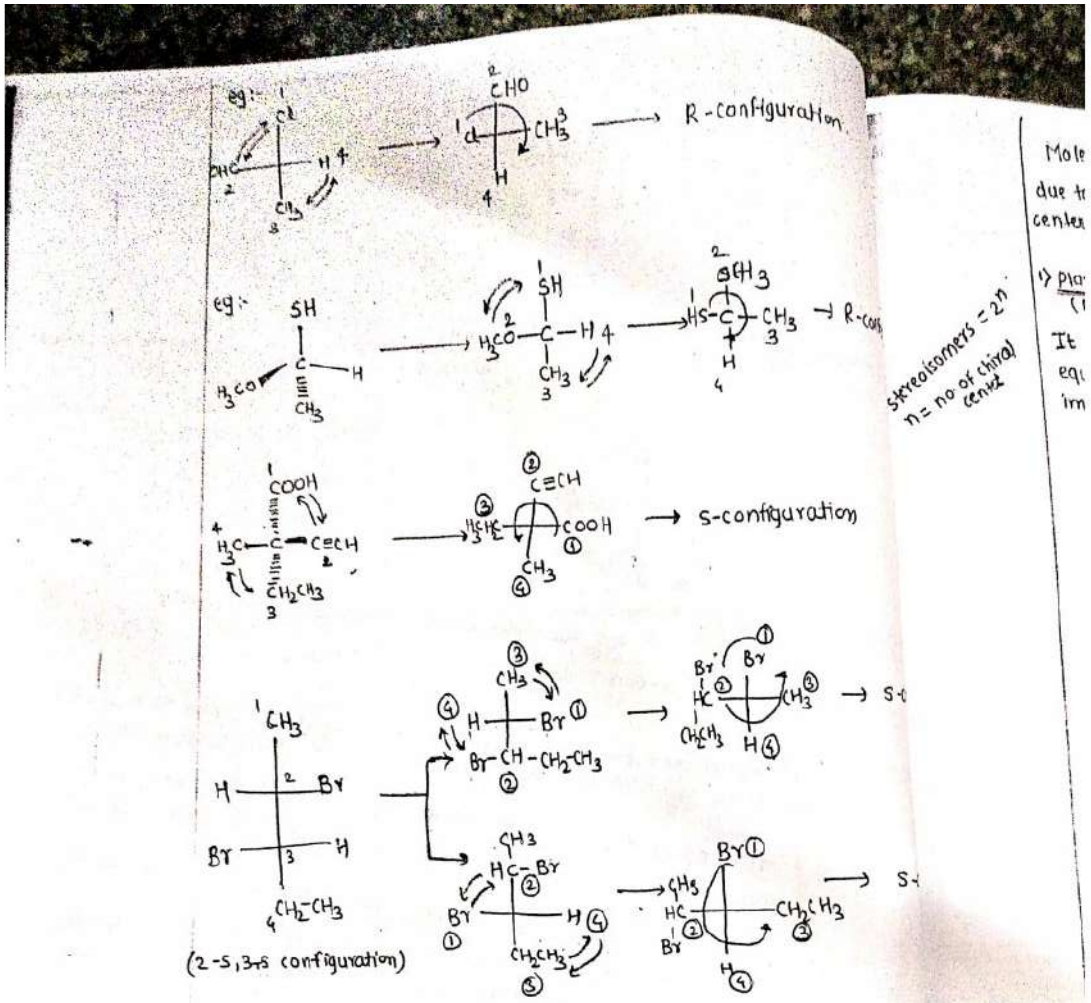
i) the interchange should be carried out only between adjecent position in fischer projection

ii) An even number of interchanges must be carried out as they will not change actual configuration of molecule.

eg:-

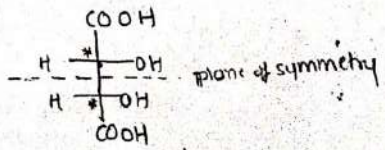


R-configuration. 2-changes R-configuration.



stereoisomers = 2^n
n = no of chiral centre

- Molecules which are optically active due to the presence of chiral center are called as asymmetric molecules
- Molecules which doesn't contain chiral center but exhibit optical acti are called as dissymmetric molecule
- Molecules which contain chiral center but they are optically inactive i.e. Meso compound (internal compensation)

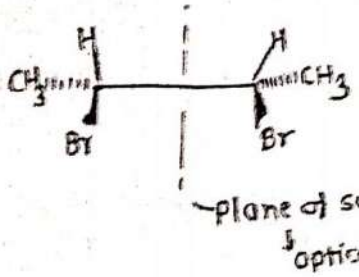


Meso compound

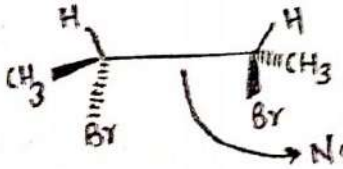
Molecules even though contain chiral center, they are optically inactive due to elements of symmetry like plane of symmetry, axis of symmetry, center of symmetry

1) plane of symmetry → (Mirror plane)

It is an imaginary plane that bisects an object into two equal halves, where in one half of the molecule is the mirror image of other half.



plane of symmetry.
↓
optically inactive



No plane of symmetry
optically active

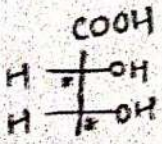
no. of stereoisomers possible for a chiral compound is given by 2^n where n is an no. of chiral center

eg :- 1 chiral center $2^n = 2^1 = 2$ stereoisomers

2 chiral center $2^2 = 4$ stereoisomer.

If a molecule has two chiral centers if the two chiral center possess same type of substituents then the possible number of stereoisomer is given by $2^n - 1$

eg:-



Tartaric acid

2 chiral center having same substituents

$2^n - 1$

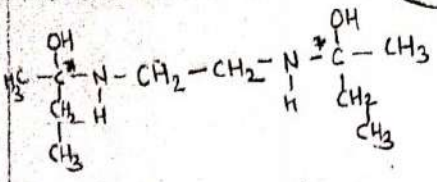
$2^2 - 1 = 4 - 1 = 3$ isomers
- Meso
- Dextro
- levo

These compounds which contain same substituent ... passes plane of symmetry so the molecule has optically active fu... i.e. Dextro & levo as well as optically inactive meso isomer

Meso compounds are optically inactive due to internal compensation.

Ethambutol → contain 2 chiral center, 3 stereoisomers

→ same substituents on both carbon



- Meso
- Dextro
- levo

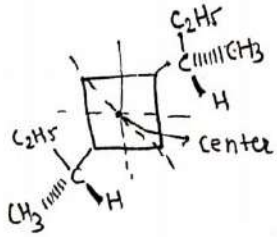
- Antitubercular agent

It will cause optic neuritis

-contraindicated in children as it severely affect optic nerve of ch... where children can't distinguish red & green colour

2) Center of symmetry →

A center of symmetry is an imaginary point in the center of molec... from which the lines are drawn in any group on both sides to an equal distance & it will divide molecules into two equal hal... which are mirror images of one another

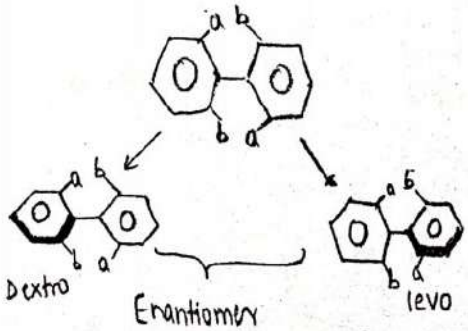


center of symmetry

↓ optically inactive

Atropisomerism → seen in disymmetric molecule

↓ optical activity due to restricted rotation



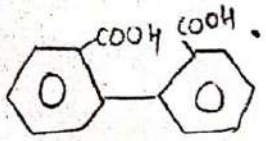
a & b - bulky groups

Conditions:

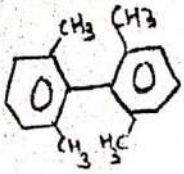
1) Presence of different ortho substituents

2) Always there should be bulkier substituents like $-CH_3$, $-NO_2$, $-COOH$, SO_3H at ortho position

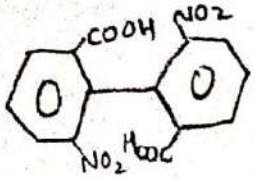
3) Both the phenyl ring should be non-coplanar .i.e. one ring should be within the plane & other ring should be outside the plane.



→ 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 Grossypium ~~debri~~ herbecium exhibit atropisomerism

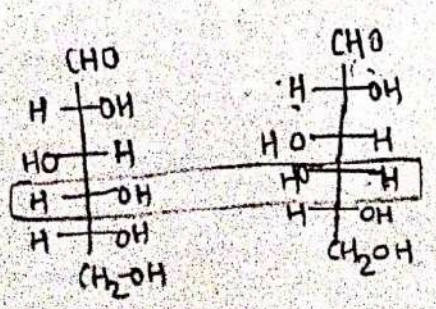
The dextro isomer → Male contraceptive → inhibit spermatocide

The levo isomer → Haemotoxic → ↓ the O_2 carrying capacity of blood.

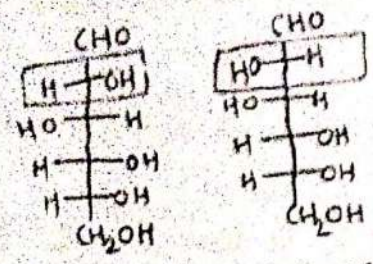
* Epimers →

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

eg:- Glucose & Galactose are epimers → C_4 epimers.



D-Glucose D-Galactose



D-Glucose D-mannose

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.

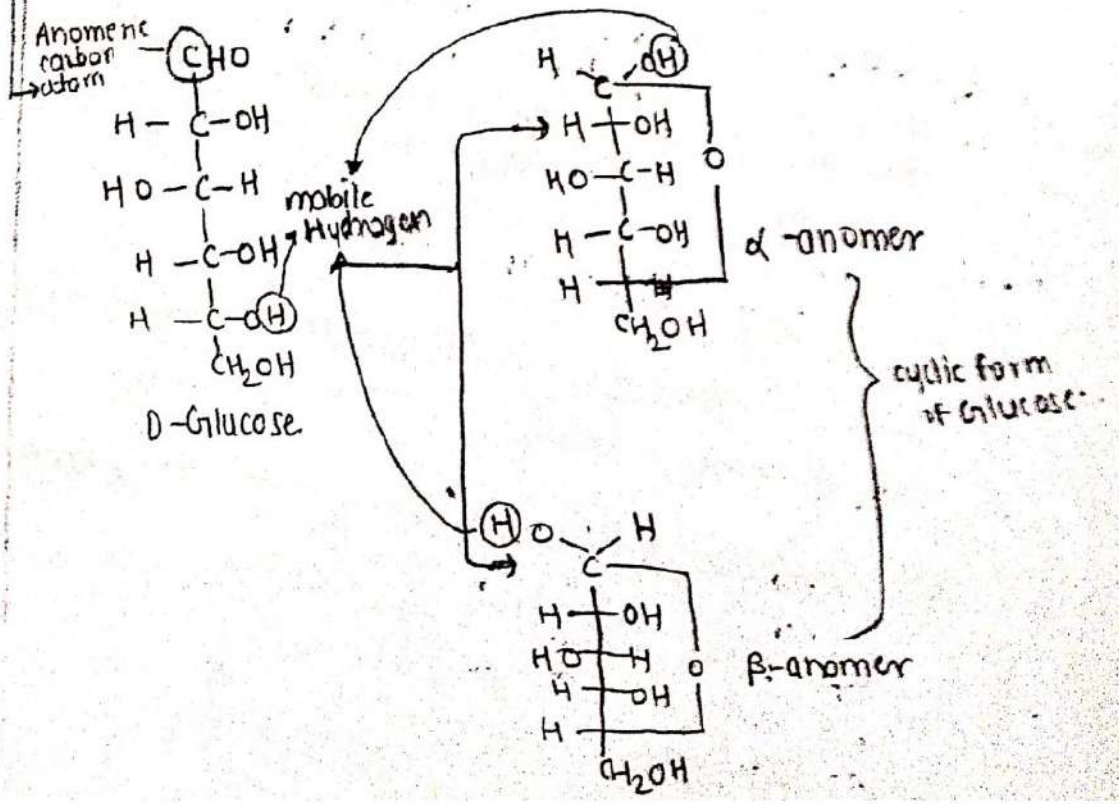
eg:-

dextro rotatory compound → specific rotation = +23°

(solvent)

initially +23° —30 min→ +56°C.

Mutarotation.



- Glucose molecule will exsists in open chain form & the cyclic α & β anomeric forms.

- Whenever α-anomer is placed in water, the initial specific rotation value is +113° & after a period of time the specific rotation value changes to +53°

Similarly whenever β anomer is placed in water it has a initial specific rotation value of +19° which gradually changes & reaches to a constant value of +53°.

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

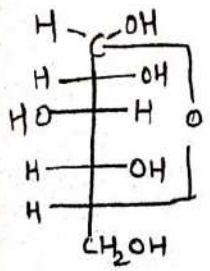
- The mutarotation occurs due to presence of mobile Hydrogen.

- 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.

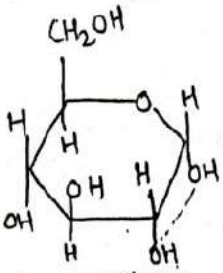
- Glucose molecule ~~with~~ doesn't respond +ve ly to <u>schiff's test</u> as the open chain (free aldehyde form) of glucose is very very less. which is unable to react to the less sensitive schiff's reagent.

<u>Fischer projection →</u>

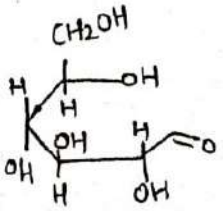


α-D-Glucose

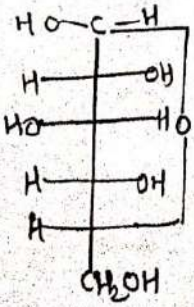
<u>Haworth projection →</u>



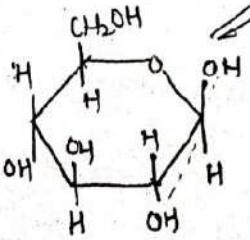
steric repulsion is more → less stable



open chain form.



β-D-Glucose.



steric repulsion is less → more stable

stability order - β anomer > α anomer > open chain

All aldose sugars

Acetal → Glycosidic (Aldose sugars)

Hemiketal → Fructose, All keto sugars

Ketal → Glycosidic (keto sugars)

Disaccharides →

Reducing disaccharides → eg:- Maltose - 2 Glucose
Cellobiose - 2 Glucose
Lactose - Glucose + Galactose

α-Glucose

Free aldehyde

β-Glucose

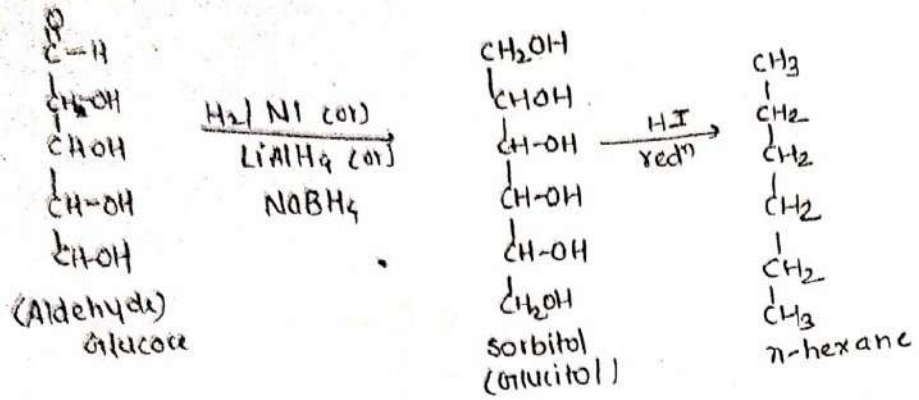
Non-reducing sugar → eg:- sucrose

Glucose + Fructose.

Both may or may not form anomeric sugar.

Reactions of Glucose →

1) Reduction of Glucose →



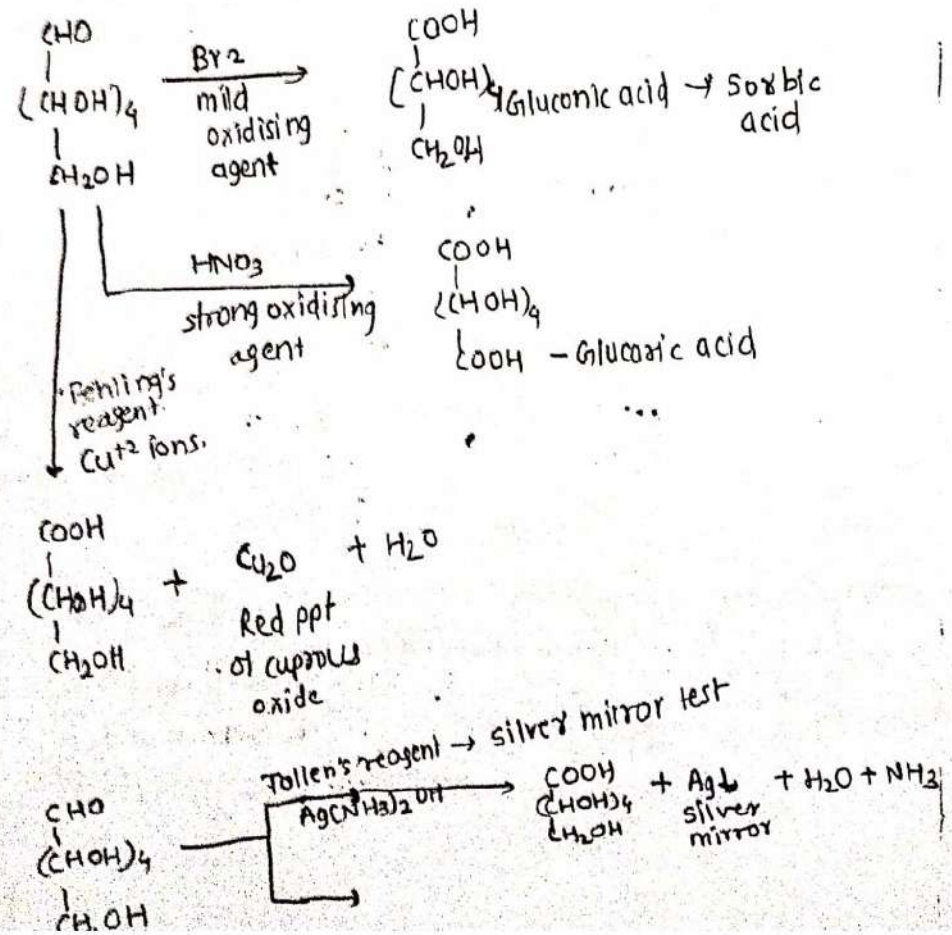
* Sorbitol & mannitol (osmitrol) are osmotic diurctics
osmotic diurectics are also used in treatment of Glaucoma.

The sweet taste of mannitol & sorbitol is due to negative heat of solution.

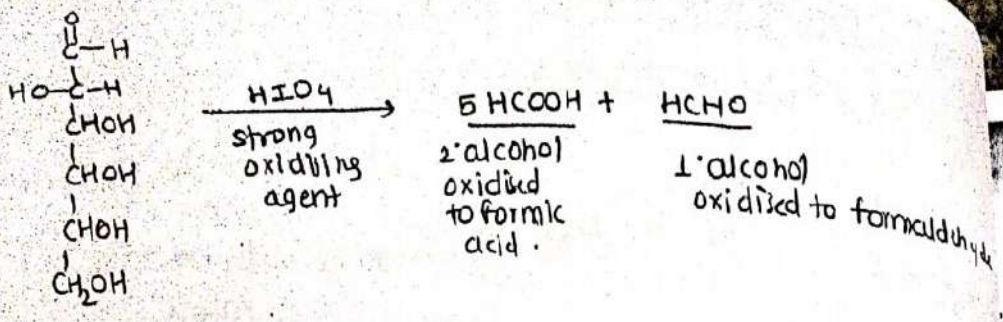
Mannitol is used in transdermal patches & osmotic pumps to create osmotic pressure & deliver the drug molecule.

* Sweet taste of cinnamon is due to mannitol

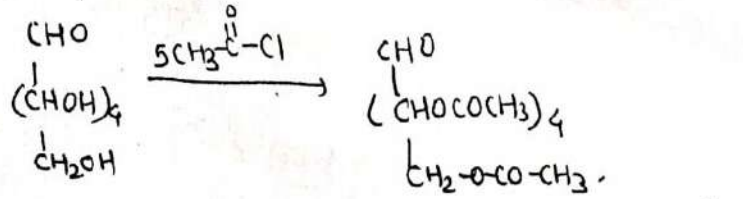
2) oxidation of glucose →



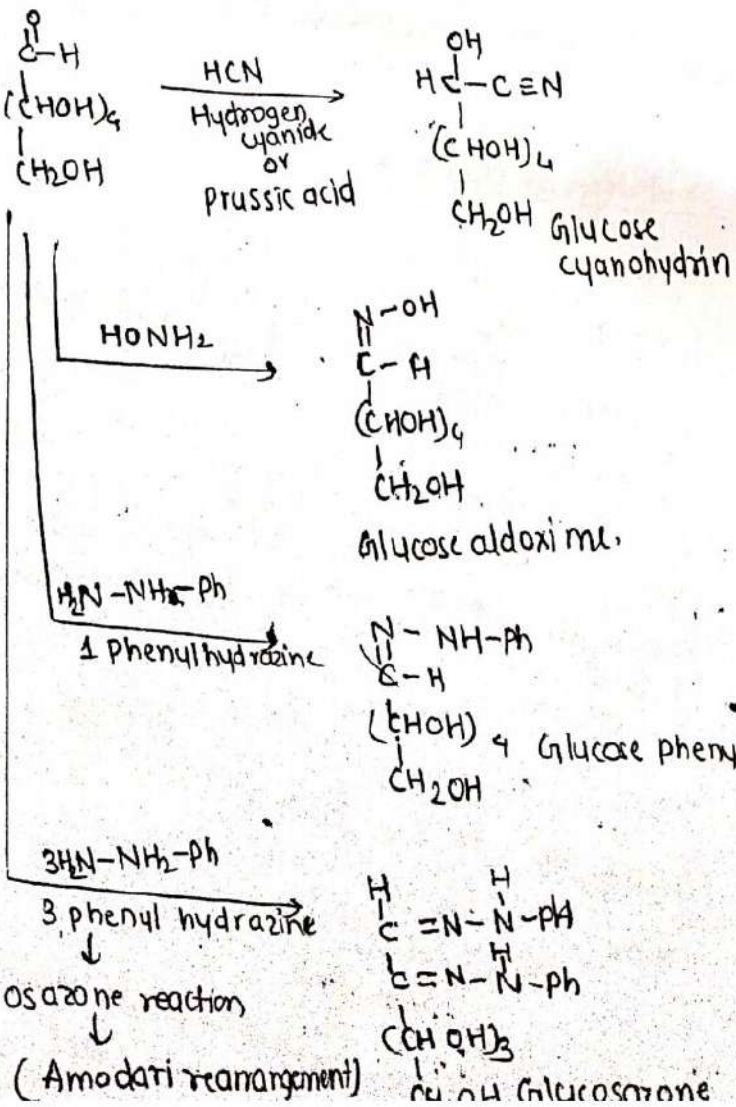
1° alcohols



3) Acetylation of Glucose →



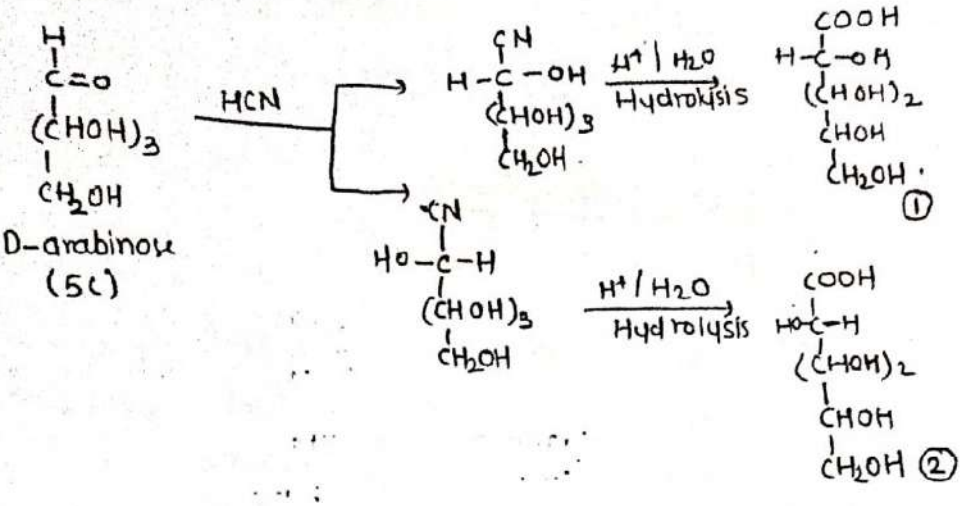
4) Reaction of aldehyde group →

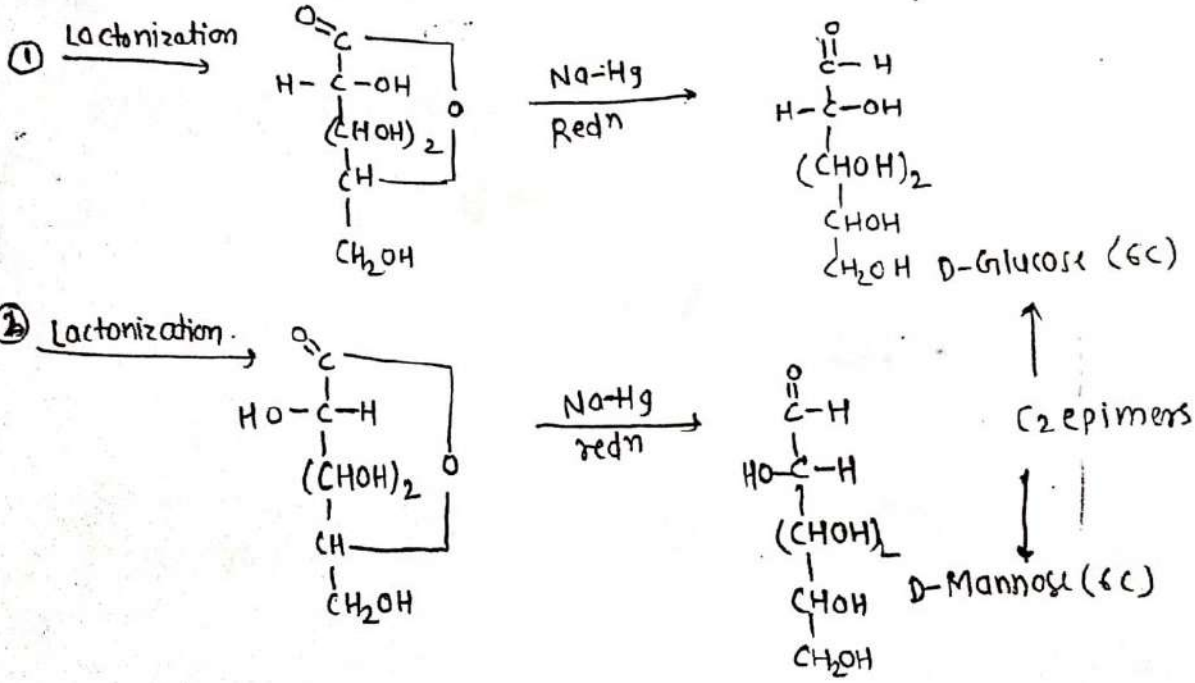


Chain extension of sugars → Kiliani Fischer synthesis →

- synthesis of sugar

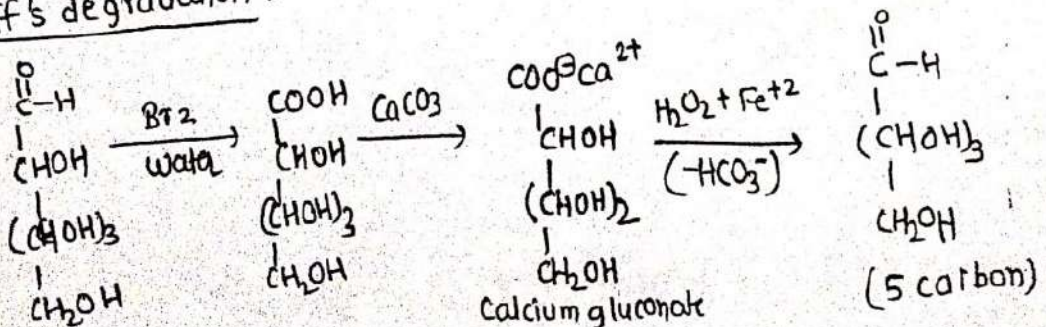
5 carbon sugar → 6 carbon sugar → 7 carbon sugars





Chain reduction of sugar → Ruff degradation
Wohl's degradation

1) Ruff's degradation →



Anthracycline antibiotics → Anticancer agent.

eg:- Doxorubicin
Daunorubicin
Epirubicin
Valrubicin
Idarubicin

These antibiotics have cardiotoxicity
- produce -OH radicals by Fenton's reactions in heart. these hydroxy radicals are responsible for cardiotoxicity.

2) Wohl's degradation →