★ Stereospecific & Stereoselective Reactions / Synthesis

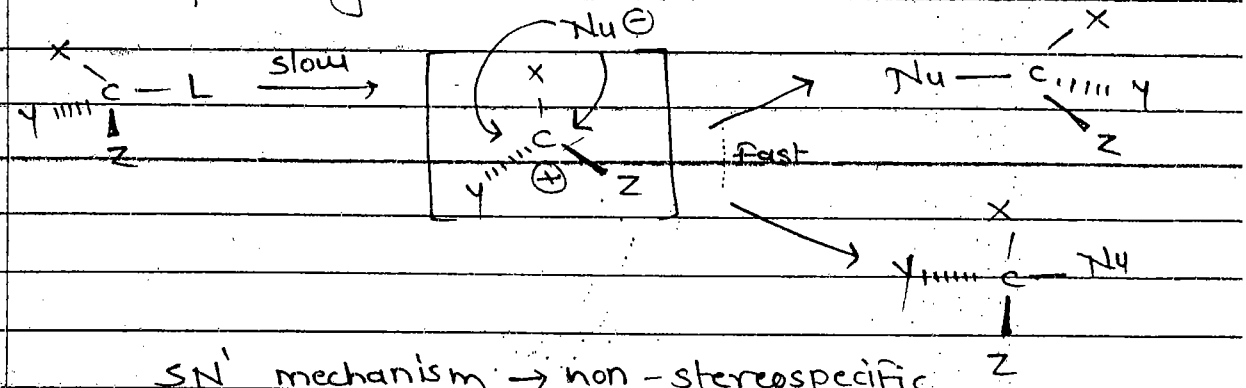
is Stereospecific :

— A reaction or Synthesis in which a particular stereo-isomer reacts to give one specific stereoisomer of the product is called as stereospecific reaction / synthesis

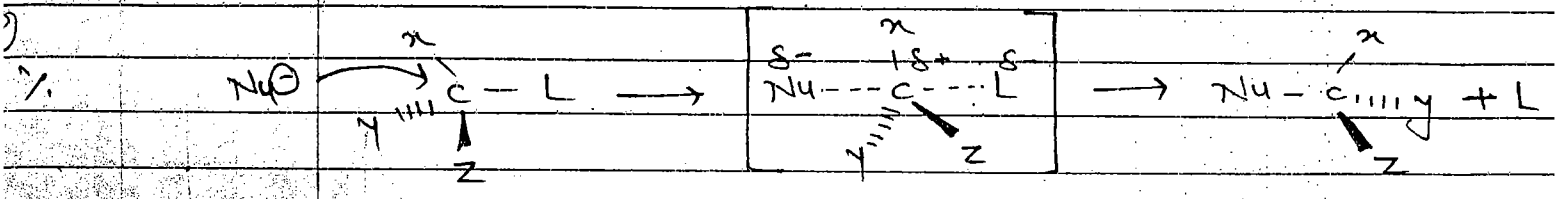
ng — In stereospecific reaction, the stereochemistry of the reactant Completely determines the stereochemistry of the product. Without any other option.

n — In case of Nucleophilic Substitution at sp^3 centres s can proceed by the stereospecific S_N2 mechanism, causing only one inversion, or by the non-specific ost S_N1 mechanism, the outcome of which can show a modest selectivity for inversion, depending on the reaction Conditions (in which the mechanism does not refer). The choice of mechanism adopted by a particular reactant Combination adopted by a particular reactant Combination depends on other factors.

one Stereospecificity in Substitution reactions.



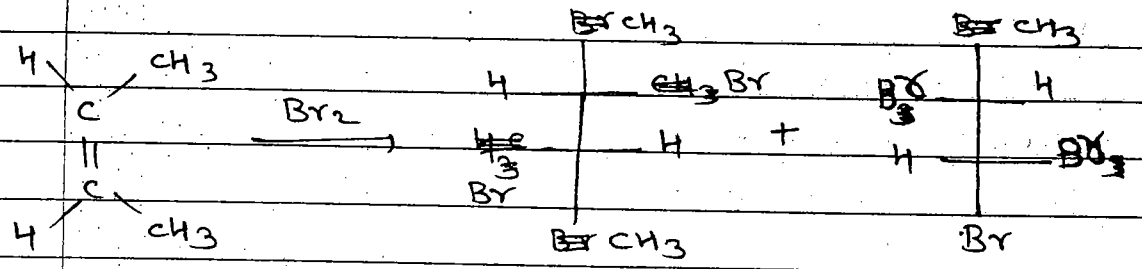
S_N1 mechanism → non-stereospecific



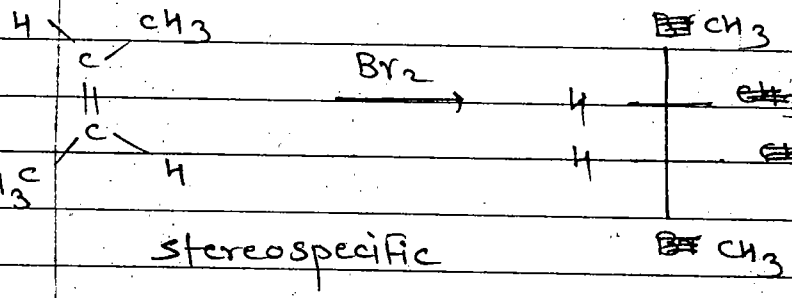
S_N2 mechanism ⇒ Stereospecific.

For example :

1) Addition of bromine to cis-butene gives racemic 2,3-dibromobutane, while the trans isomer gives meso 2,3-dibromo butane. This reaction is stereospecific because different diff. stereoisomers gives diff. stereoisomers. The reaⁿ involves anti addition of bromine.

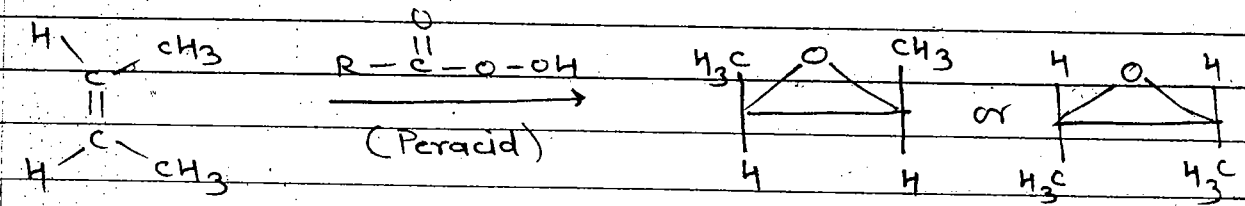


cis-2-butene Racemic mix.

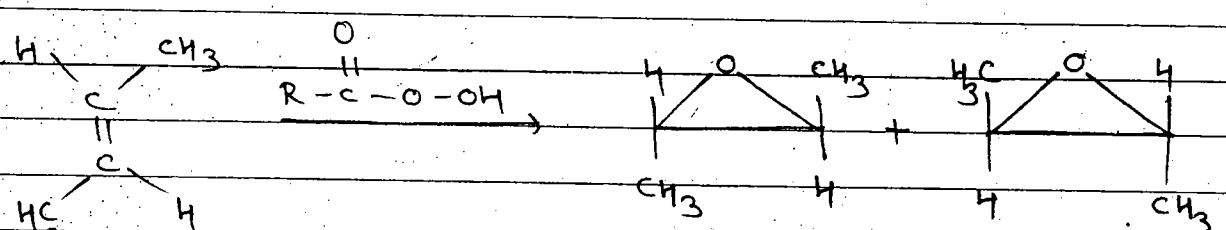


stereospecific meso-2,3-dibromo-butane.

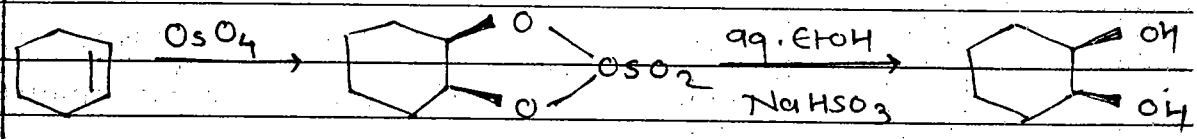
2) The formation of epoxides from alkene on treatment with peracids is a stereospecific reaction. cis-2-butene gives cis-2,3-dimethyloxirane, while trans-2-butene gives trans-2,3-dimethyloxiranes. The reaⁿ involves Syn addition of oxygen.



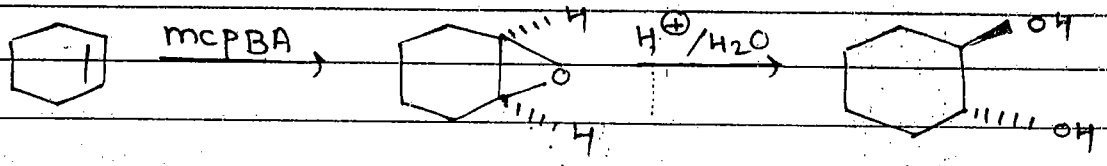
cis-2-butene cis-2,3-dimethyloxirane (meso)



3) 1,2-diols may be prepared from alkenes using stereospecific oxidative procedures. For example, reaction of cyclohexene with osmium tetroxide gives the osmate ester which may be cleaved to give the product with two hydroxyl groups on the same side of molecule i.e. cis diol.

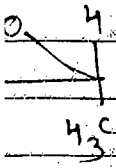


On the other hand, reaction of cyclohexene with a peracid gives an epoxide which on hydrolysis gives the product with two hydroxyl group on diff. sides of the molecule i.e. the anti or trans diol.

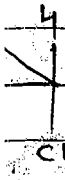


mCPBA → m-chloroperbenzoic acid.

The Concerted reactions have a precise spatial requirement of the orientations of the substrate & reagent eg. Diels-Alder reaction, S_N2 reactions, E_2 anti eliminations, Syn pyrolytic elimination, anti & syn additions to alkenes & several rearrangemer all are the examples of stereospecific reactions.

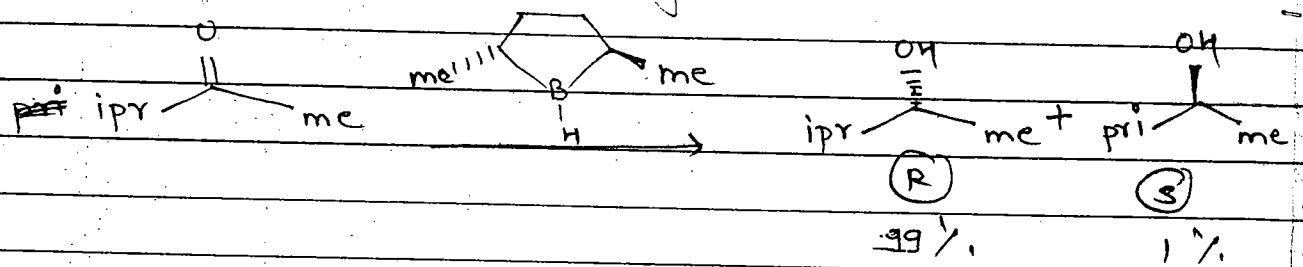


meso)



2) Stereoselective :

- The reaction (or Synthesis) in which one stereoisomer is formed predominantly or exclusively out of several stereoisomeric possibilites is called as stereoselective reaction.
- In a stereoselective reaction one stereoisomer is formed more rapidly than another, thus resulting in predominance of the favourred stereoisomer in the mixture of products.
- The stereoelectronic requirement of the mechanism of a stereoselective reaction offers alternative paths so that the reaction may proceed either via the most favourable path (Kinetic Control) or via the path which gives the most stable stereoisomer as the major product (Thermodynamic Control) and form one isomer predominant over other.
- stereoselectivity can be further subdivided into enantioselectivity & distereoselectivity.
- stereoselectivity can be further subdivided into
- Enantioselectivity is defined as the formation of one of the two enantiomers predominatly. In this reaction an optically active product is produced from achiral starting material, using either a chiral catalyst, an enzyme or a chiral reagent.
- examples of enantioselectivity



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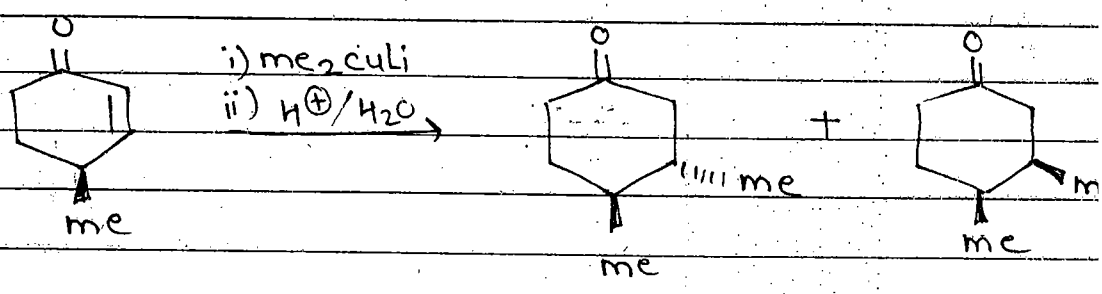
- Diastereoselectivity is defined as the formation of one of the two enantiomers or more diastereome predominantly.

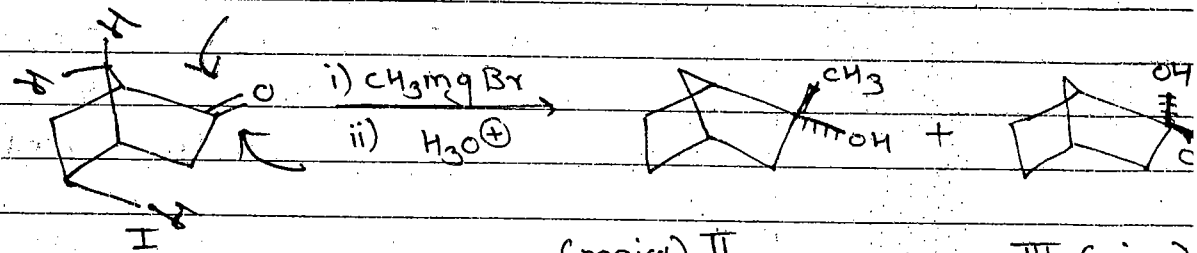
- Diastereoselectivity is most commonly achieved through the presence of steric hindrance.

1) For example, the conjugate addition of lithium dimethylcuprate to 4-methylcyclohexenone is highly diastereoselective. Because the approach of the bulky cuprate reagent occurs predominantly on the less sterically hindered face of the enone i-e. away from the 4-methyl group. Thus the trans isomer is the major product.



98% (trans) Dia (cis) 2%

2) The Conversion of 2-norboranone I into the diastereomeric alcohols II & III is stereoselective because the attack of Grignard reagent From the less hindered exo face is preferred to endo face.

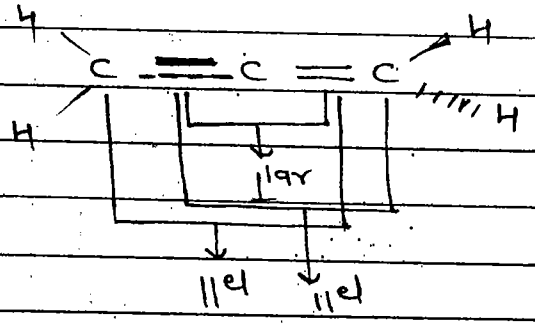


(major) II III (minor)

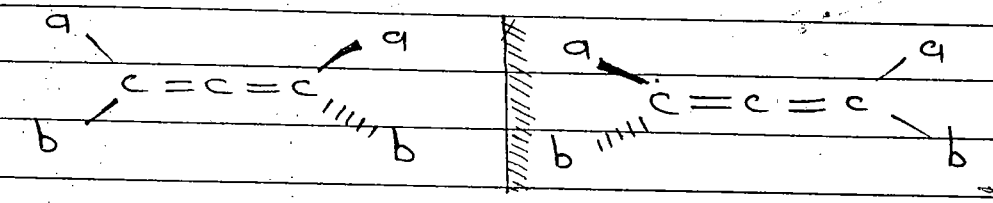
Diastereomers

★ Optical Activity of Allenes :

- When three or more adjacent Carbon atoms in a molecule are bonded by double bonds, the Comp. is called as Cumulene or is said to have Cumulative double bonds. Allene is a Simple Cumulene.
- The spatial arrangement of the cumulative double bond in allene is such that its terminal methylene groups are perpendicular to each other.
- The two terminal carbon in allene are in sp^2 & the central carbon is the sp hybrid state, thus the central carbon forms two π-bonds which are perpendicular to each other.



- Allene itself is achiral since it has two planes of Symmetry. In order to generate chirality, the two ~~sp~~ planes of symmetry must be eliminated.
- When unlike substituents are added at each ~~other~~ end of the C=C=C unit, the substituted allene becomes chiral.
- Allenes of type abC=C=Cab ($a \neq b$) are chiral i.e. not superimposable on mirror image & exist as enantiomers although they have no chiral centre.

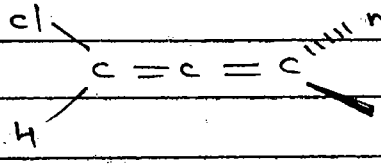


Enantiomers

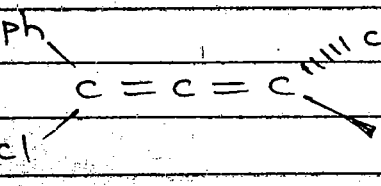
- Allenes have chiral axis as their element of chirality.

- Essential chirality Criteria For Allenes
  a) Proper substitution (diff. atoms at terminal carbons)
  b) No. of double bonds should be even.

eg.

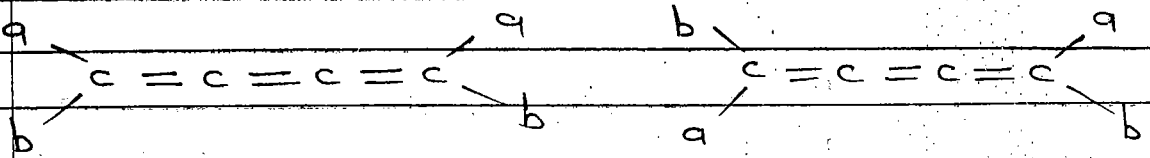


- Proper substitution
- Even no. of double bond
- No plane of symmetry
  Hence chiral



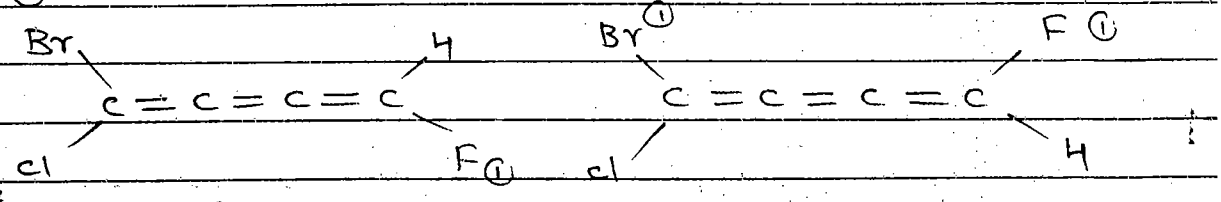
- Even no. of double bonds
- No proper substitution posses a plane of Symmetry &
  Hence achiral

- The Compounds with odd no. OF cummulated double bonds with proper substitution gives diastereomeric relationship. or Z-E (geometrical) isomerism.



cis ← Diastereomers → trans

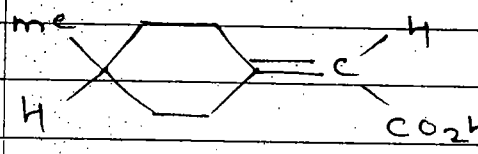
eg.



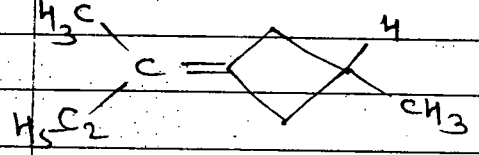
E Z

Diastereomers

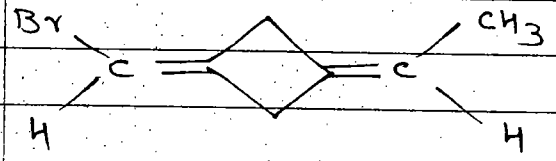
- The replacement of one double bond in an allene by a ring gives alkylidenecycloalkanes, does not alter the basic geometry of the system of allene and suitably substituted compounds, therefore exist in optically active form.
- Optical activity arieses if No. of db & ring are even & criteria is same as that of allene.



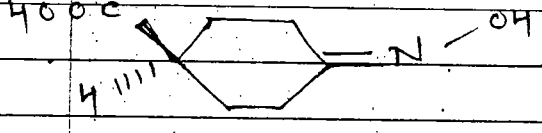
1 db + 1 ring = 2 even
Propeely substituted
chiral & optically active



1 db + 1 ring = 2 even
Propeely substituted
chiral



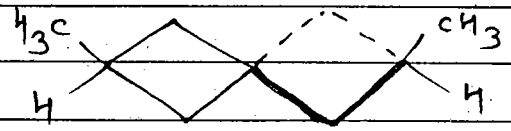
2 db + 1 ring = 3 odd
propeely substituted but
Passes POS
Hence, Achiral & optically active



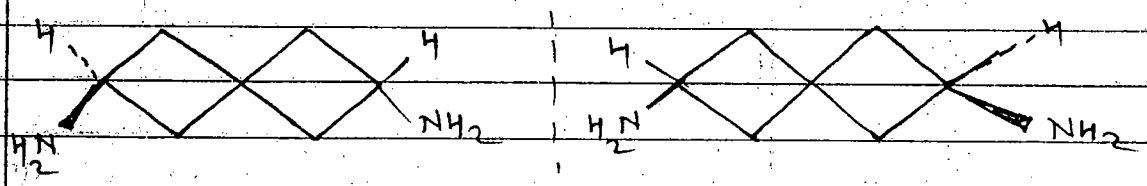
1 db + 1 ring = 2 even
Propeely substituted, No σ
Hence chiral & O.A

Optical Activity of Spiranes :

- If both double bonds in allene are replaced by ring system, the resulting molecules are known as spiranes or spiro compound.



- The condition for chirality in spirans are analogo or similar to those in allene.
- In spirans the two rings are perpendicular to each other, hence suitable substitution will make the molecule achiral i-e. it will exihibit enantiomerism.
- The element of chirality in spirans also is the presence of a chiral axis.



Enantiomers.

Optical Activity of Biphenyls :

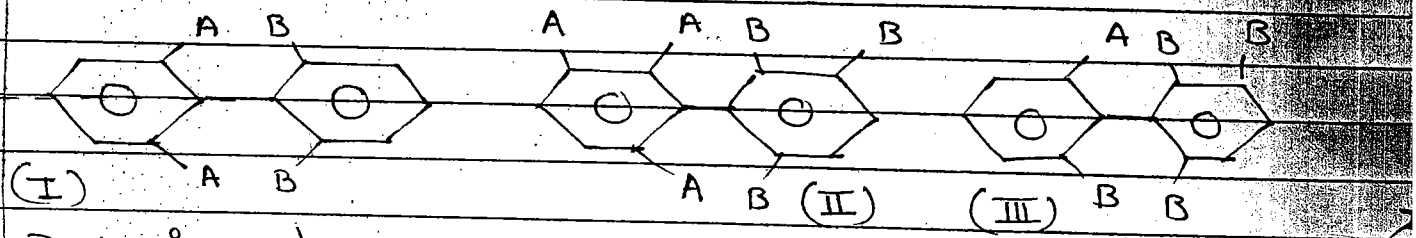
- Isolable stereoisomers resulting from restricted rotation about single bonds are called atropisomers.
- In their geometry atropisomer approach allene derivatives & have the axis of chirality but not the centre of chirality.
- For example, suitably substituted biphenyls exhibit enantiomerism due to the presence of a chiral axis, & these are atropisomers because they exhibit enantiomerism due to restricted

rotation about the single bond between the two phenyl rings.

- There is restricted rotation about the bond linking the two phenyl rings due to steric hindrance between the bulky ortho substituents. Because of this steric hindrance the two phenyl rings lie in different planes which are perpendicular, thus the molecule becomes chiral & exhibits enantiomerism.

- Biphenyls show enantiomerism when the following two conditions are satisfied :

1) Each ring must be unsymmetrically substituted. Thus I is not resolvable, but II & III are resolvable.

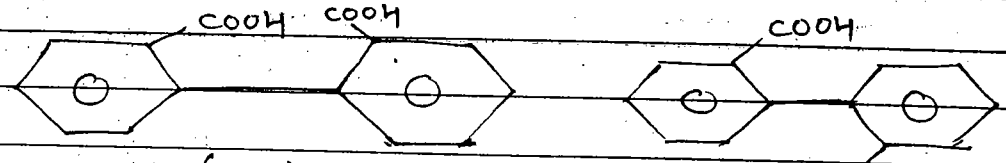


(I) (II) (III)

Both rings have POS hence achiral

No plane of POS hence chiral

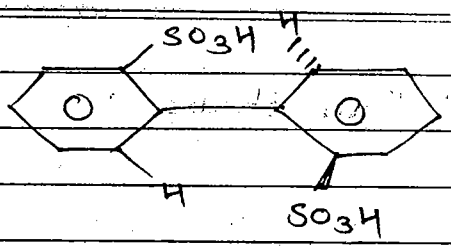
2) Both rings must be substituted in ortho positions and the substituents must have a large size (eg. Cl, Br, I, COOH, NO_2, SO_3H, CH_3 etc.)



(IV) (V)

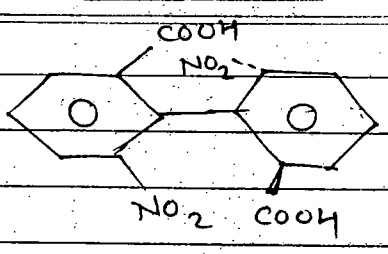
- If the substituents in ortho positions are in smaller in size, the two phenyl rings become planar i.e. free rotation occurs, & thus the compound cannot be optically active because it would possess a plane or centre of symmetry in Comp. IV & centre of symmetry V

eg.



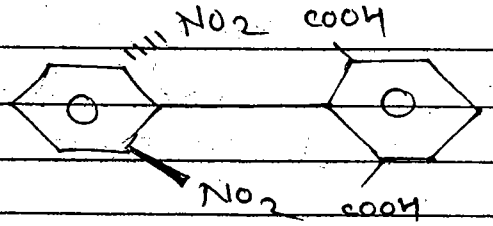
chiral

eg.



chiral

eg.

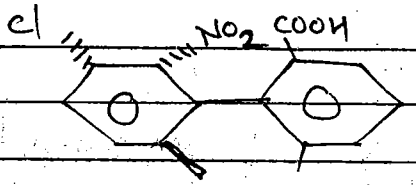


Achiral (POS)

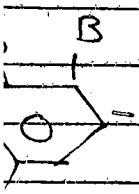
eg

Achiral (Plane of symme

eg.

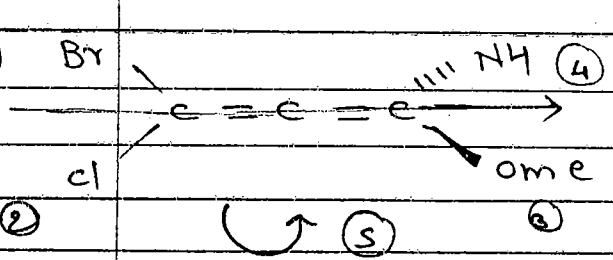


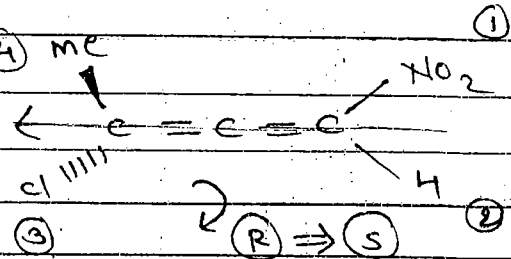
Achiral (POS)

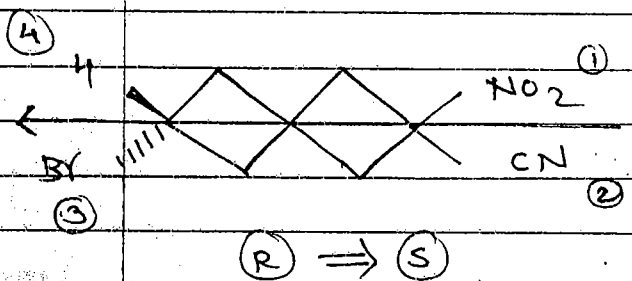


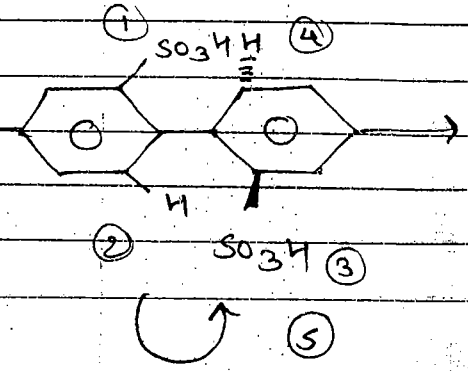
★ - Nomenclature of Allenes, Spiranes, Biphenyl

1) check chirality criteria of given molecule.
2) Pass chiral axis from substitutions which are inplane.
3) Give the priority to substitution of terminals which are inplane according to atomic No.







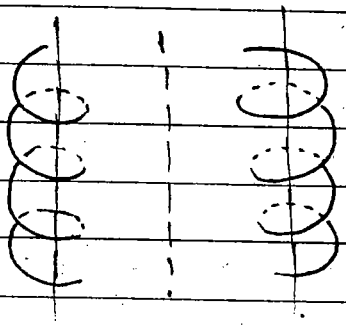


★ Chirality due to Helical shape :

- Helices are chiral objects, a right handed helix (a clockwise rotation when viewed along the axis of moving from the front to the rear) is designated as P/plus/+ while a left handed helix (anticlockwise rotation when viewed along the axis) designated by M/minus/-

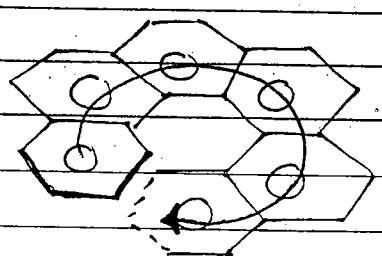
- The Concept of helicity provides a simple method for designating the chirality of Comp. with this feature.

Left handed
M/Minus/(-)



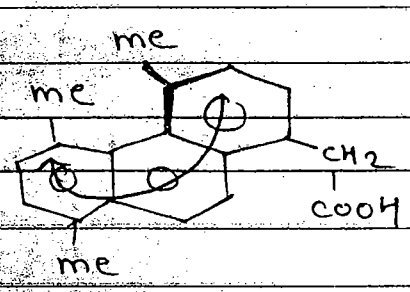
Right handed helix
P/plus/(+)

- The terminal benzene rings in hexahelicene, ~~for~~ cannot occupy the same plane without coming in serious conflict with one another.
- Therefore, the molecule is forced to adopt a non-planar shape in which one side of the molecule must lie above the other because of crowding

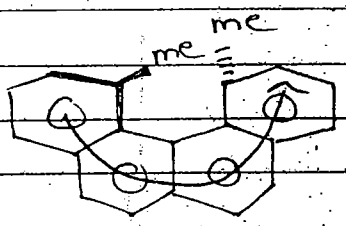


Hexahelicene (Plus (+))

- Hexahelicene is chiral by virtue of its helical shape which could be either left or right handed in orientation.
- The entire molecule is infact less than one full ~~form~~ turn of the helix, but this is enough to generate chirality in hexahelicene
- In hexahelicene the middle rings lie in a plane while terminal rings are above & below the plane.
- IF the orientation from above the plane to below the plane is clockwise it is termed as P/plus/+ & if vice versa termed as M/minus/-



Plus / P / +



Minus / M / -

Homotopic ligands :

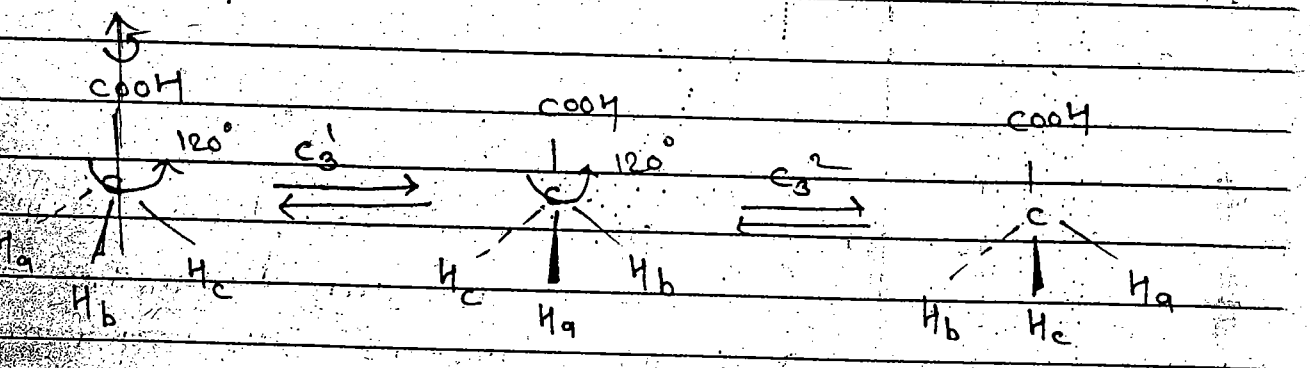
→ The ligands / atoms / groups in a molecule responsible to give homomers are known as homotopic ligands.

→ They are identified by two methods -

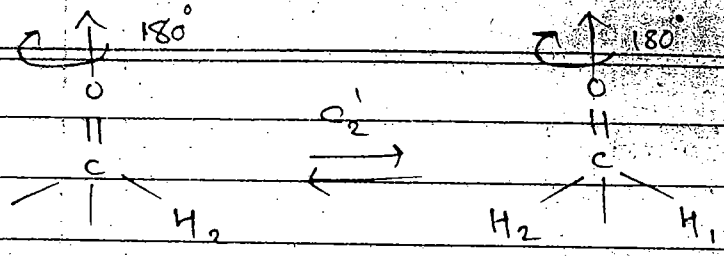
1) Symmetry Criteria
2) Substitution Criteria

1) Symmetry Criteria :

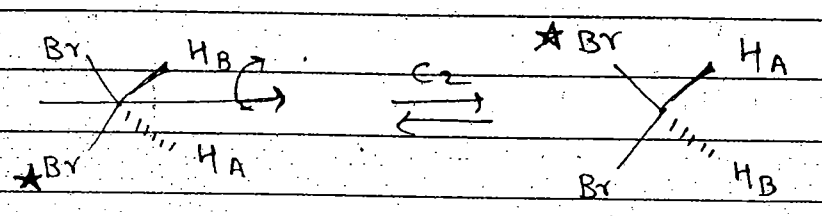
- Homomorphic ligands are interconvertible / interchangable with C_n Symmetry axis are known as homotopic ligands.
- Homotopic ligands are related to C_n axis of symmetry
- In a molecule eg. Acetic acid, two successive 120° rotations of a methyl group around the axis i.e. C_3 rotational axis, each allow each hydrogen to take the position of either of the other two.
- Thus in rapidly rotating methyl group of acetic acid all the hydrogens are equivalent and are thus called as homotopic.



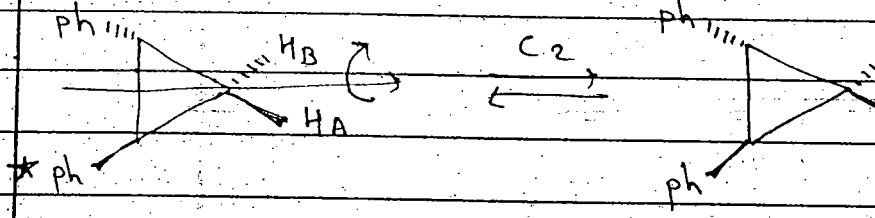
- All three hydrogens of acetic acid i-e. H_a, H_b & H_c are interconvertible with 'C_3' axis of symmetry and therefore Homotopic.

eg. 

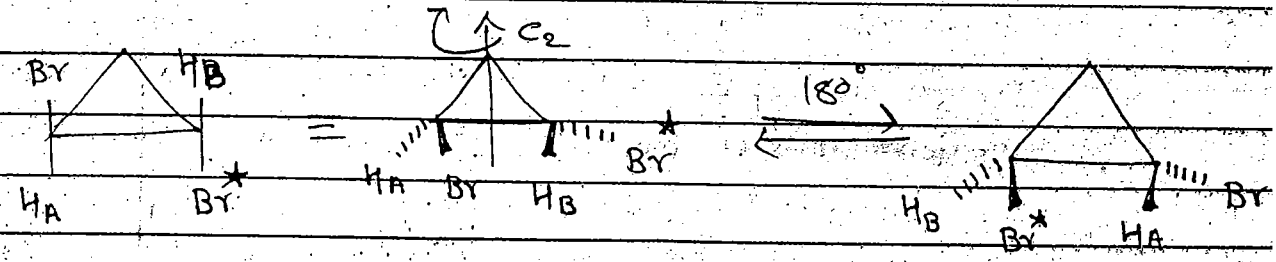
≡ H_1, H_2 are Homotopic with C_2 axis of sym

eg. 

≡ Br, Br* & H_A, H_B are homotopic with C_2 axis of symmet

eg. 

≡ ph, ph* & H_A, H are homotopic with C_2 axis of Sy

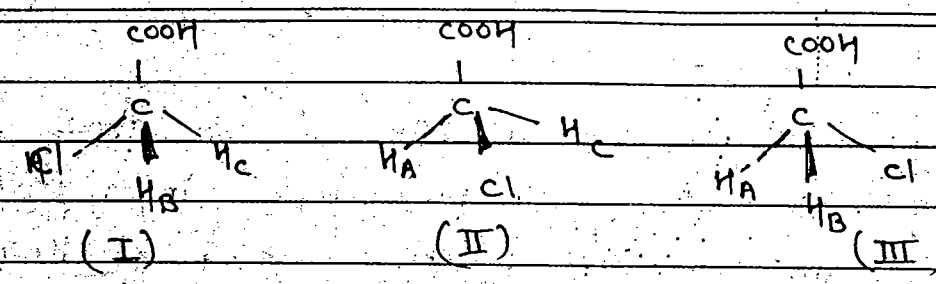
eg. 

Here Br, Br* & H_A, H_B are interconvertible with each other with C_2 axis of symmetry & therefore they are homotopic atom/groups.

2.) Substitution Criteria :

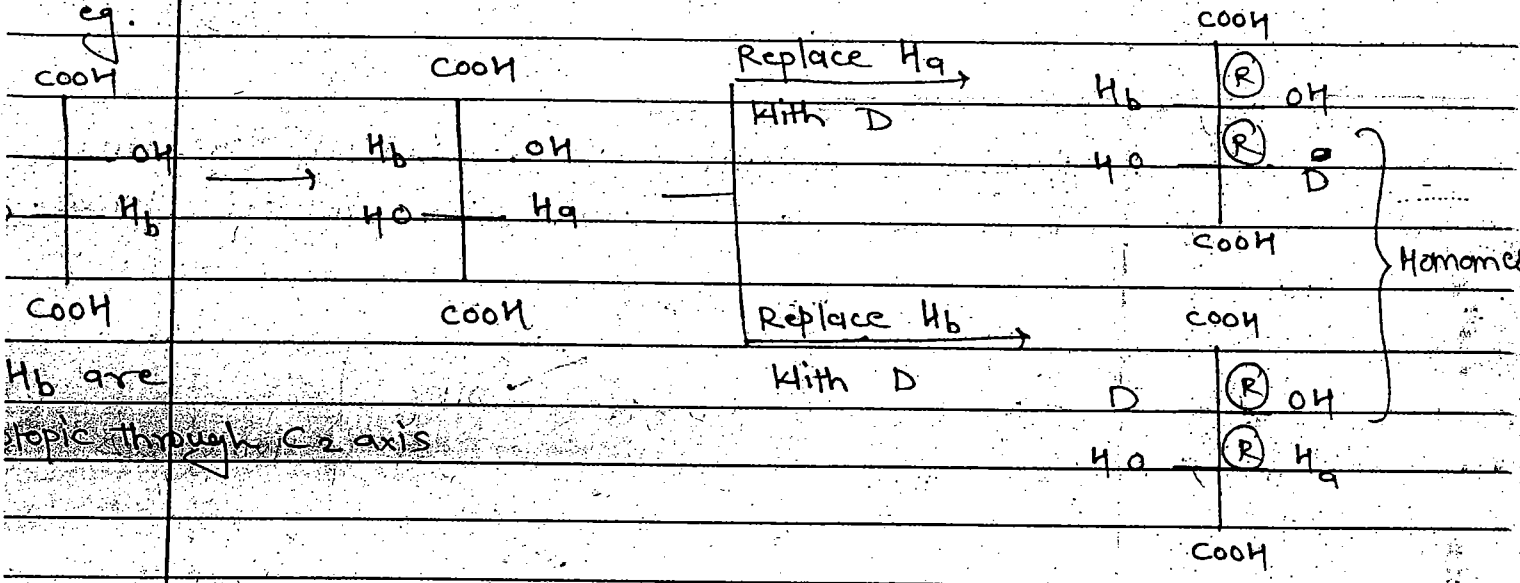
→ Two ligands / atoms / groups are homotopic if substitution of each one of them in turn by another atom or group leads to the same structure (the replacement ligand must be different not only from the original one, but also from all other ligands attached to the same carbon)

→ Thus the three methyl hydrogens in acetic acid are homotopic because replacing any one of these by eg. chlorine gives the same chloroacetic acid.



→ I, II & III are same/identical as they are formed by replacing and homotopic atoms with same atom i.e. Cl & gives same product chloroacetic acid.

eg.

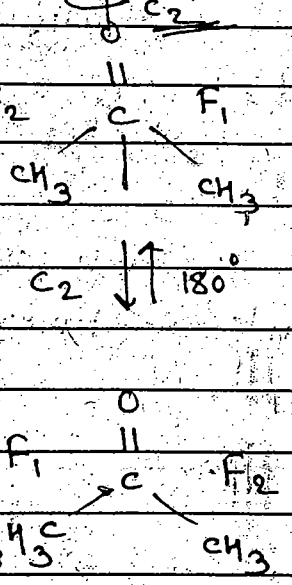


H_b are topic through C_2 axis

★ Homotopic faces :

1) Symmetry criteria :

If two faces of a reacting molecule exchangable / interconvertable with C_n axis of symmetry then faces are said to be Homotopic faces.

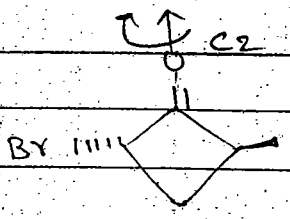


F_1 → Front side of molecule

F_2 → Back side of molecule.

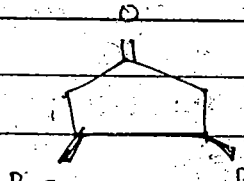
→ After rotation of molecule with C_2 axis gives an equivalent molecule. Means F_1 of molecule is interconvertible with F_2 of same molecule. Hence called as Homotopic Face

eg.



$F_1 = F_2$

Homotopic

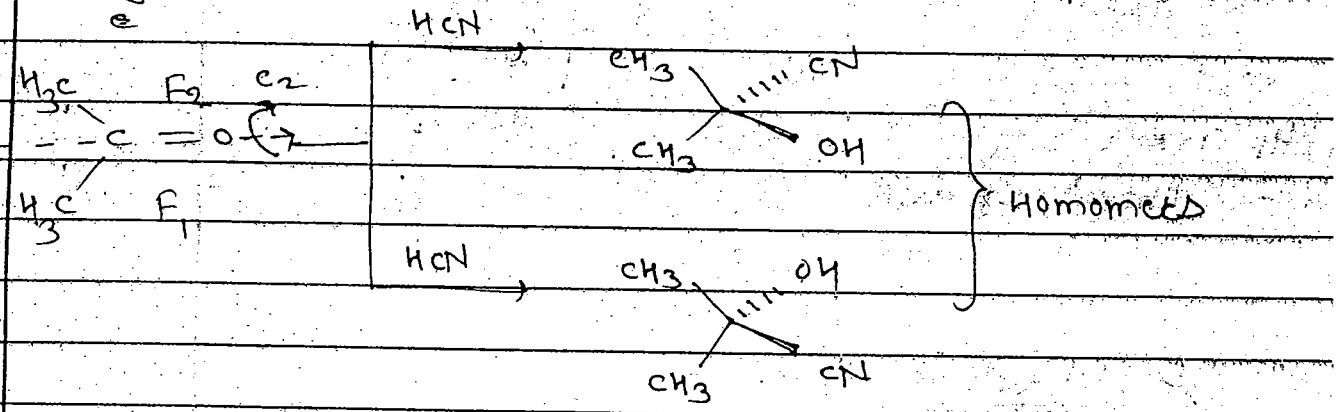


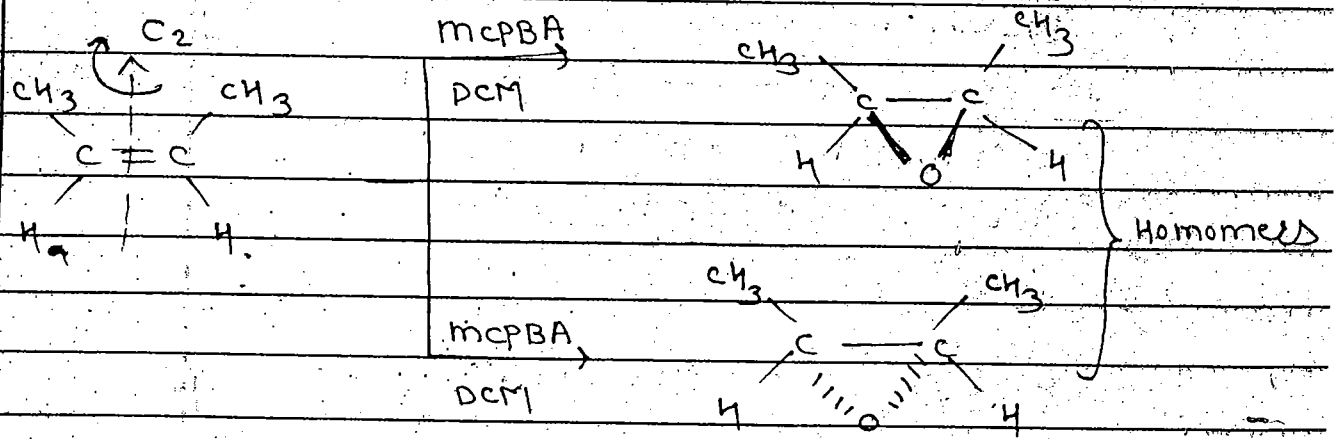
$F_1 \neq F_2$

No C_n axis of symmetry

2) Substitution Criteria :

Hypothetical substitution of reagent on two faces of give homomers are known as homotopic faces.





→ Above both the examples posses C_n axis of symmetry. ∴ Therefore have Homotopic ligands & faces which of substitution gives Homomers.

★ Heterotopic ligands :

The ligands which are responsible to give stereoisomers (enantiomers or diastereomers) are known as heterotopic ligands.

I) Enantiotopic ligands :

i) Symmetry criteria :

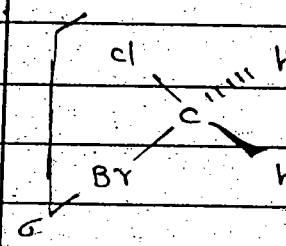
The ligands / atoms / molecule in a molecule are exchangable with second kind of symmetry elements (σ, C_i, S_n) are said to be enantiotopic ligand.

Rules :

i) Identify 'C_n' symmetry in molecule. IF C_n is present the exchangable ligands are homotopic

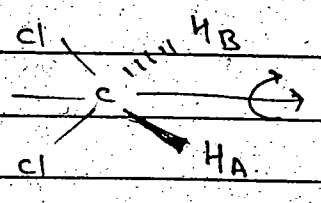
ii) IF C_n is absent, then directly suspend $\sigma / C_i / S_n$ exchangable ligands are known as enantiotopic ligands.

- eg.



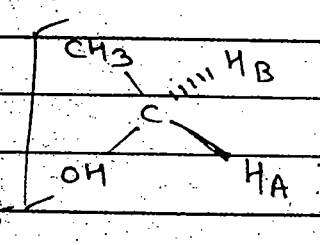
- In this example, C_n is absent but σ is present.
- Here H_A & H_B are exchangable with each other with plane of symmetry. (Reflected by plane).
- Therefore H_A & H_B are enantiotopic.

eg.



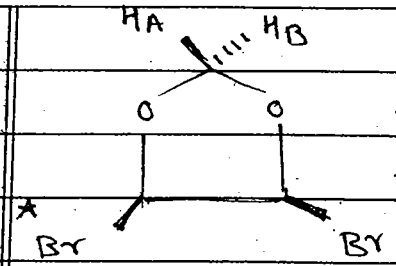
C_n present, H_A & H_B are homotopic.

eg. CH_3-CH_2-OH =



- σ is present
- H_A & H_B are enantiotopic

eg.

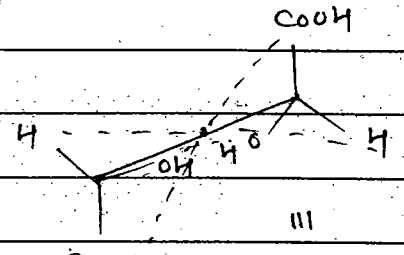


σ is present

→ Br, Br^* enantiotopic

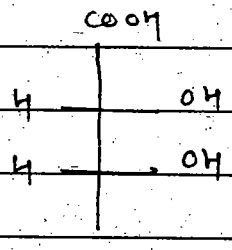
→ H_A, H_B diastereotopic

eg.

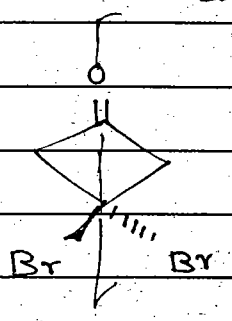


C_i is present

→ −OH, −OH
H, H
−COOH, −COOH
} enantiotopic



eg.



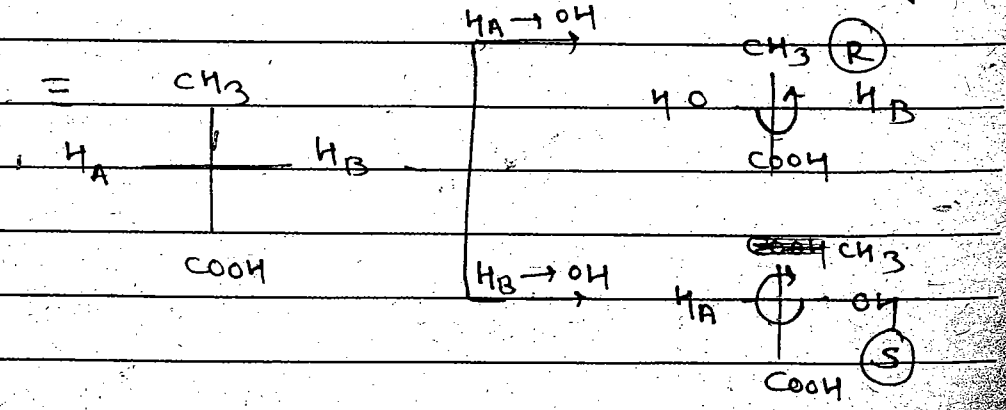
- σ is present
- Br, Br^* are enantiotopic.

2) Substitution Criteria :

Substitution on homomorphic ligands with new groups to give enantiomers are known as enantiotopic ligands.

eg.

CH_3-CH_2-COOH ≡



Sig. of Invigilator | Date | Roll No.

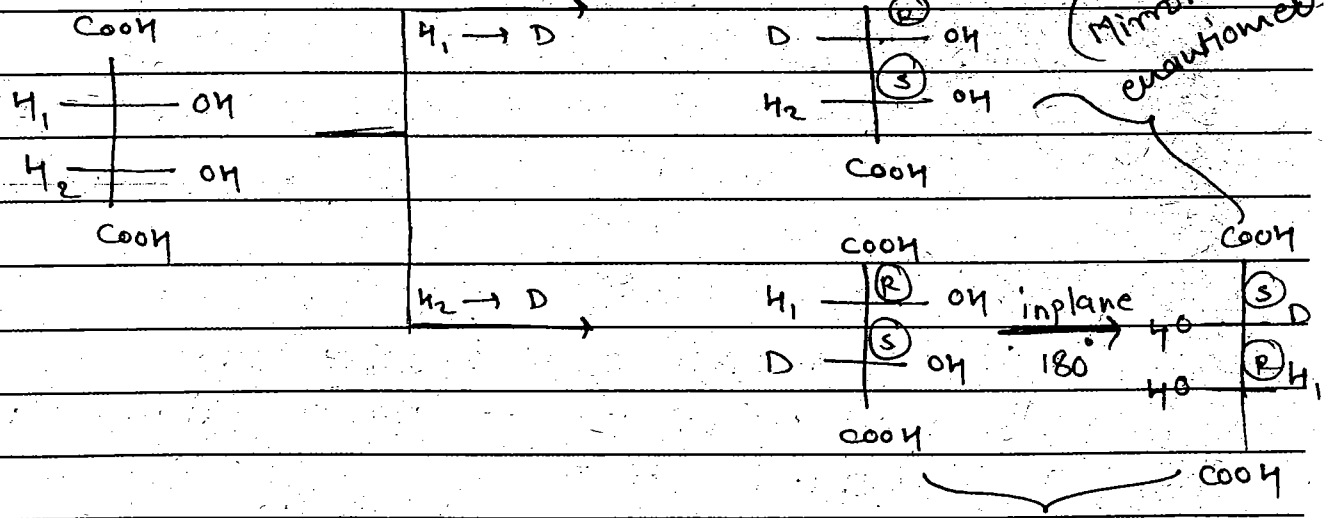
Dayanand Science College, Latur

Internal Assessment Examination 201 - 201

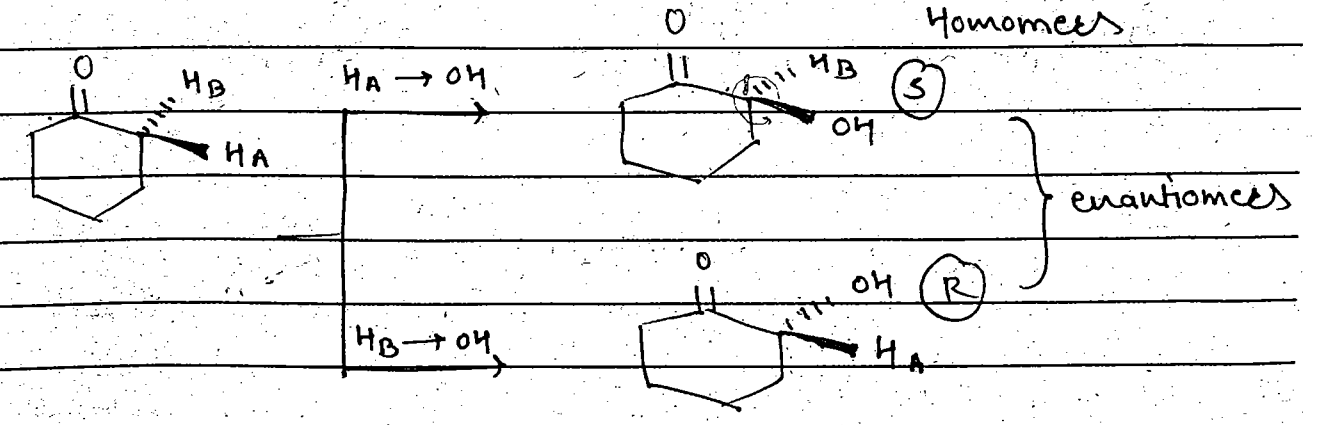
Q. 1	Q. 2	Q. 3	Q. 4	Q. 5	Q. 6	Grand Total	Sig. of Examiner

→ In case of propionic acid, two hydrogens of methylene are enantiotopic. firstly they posses plane of symmetry & secondly on substitution of each of them in turn gives enantiomers. (i.e. by replacing $H_A \rightarrow OH$ & in second by replacing $H_B \rightarrow OH$)

eg.



eg.

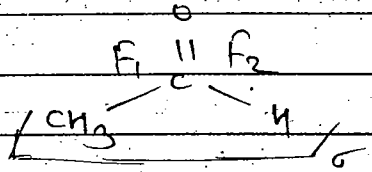


Enantiotopic faces :

1) Symmetry Criteria :

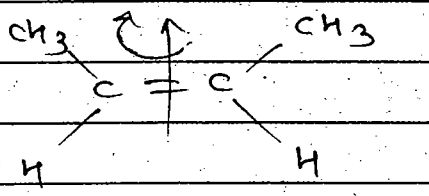
When the two faces of molecule are exchangab with second kind of Symmetry elements are known as enantiotopic faces.

- Always suspend σ in between two faces of molecule.

eg. 

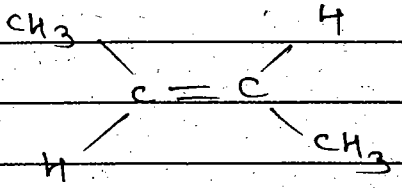
$F_1 = F_2$ (reflected by each other)

Posses ~~two~~ enantiotopic faces.

eg. 

C_n present

$F_1 = F_2$ Homotopic faces.

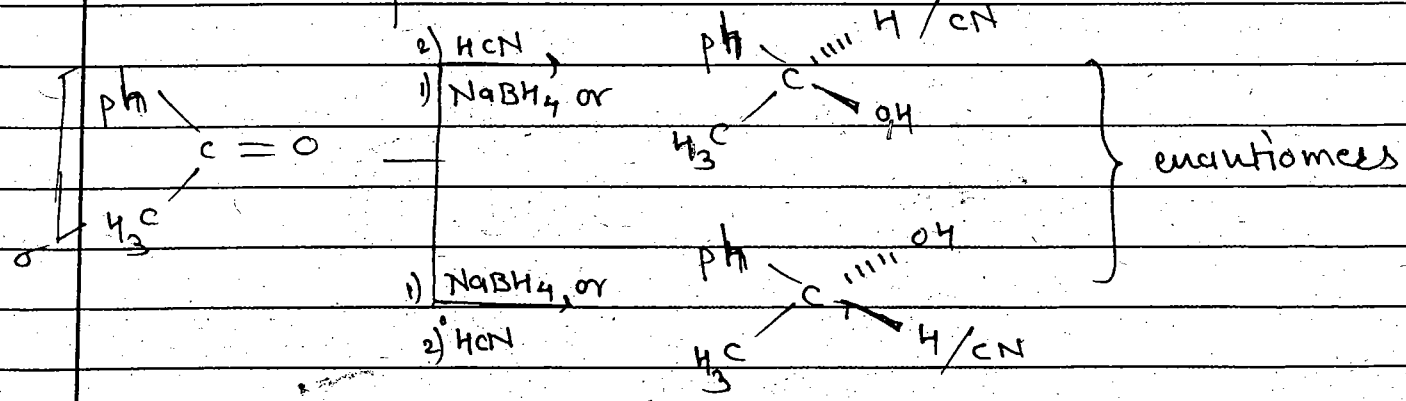
eg. 

C_i present

$F_1 = F_2$ enantiotopic faces.

2) Substitution Criteria :

Substitution on reacting faces of a molecule with new group / atom to give enantiomers are known as enantiotopic faces.



2) Diastereotopic ligands :

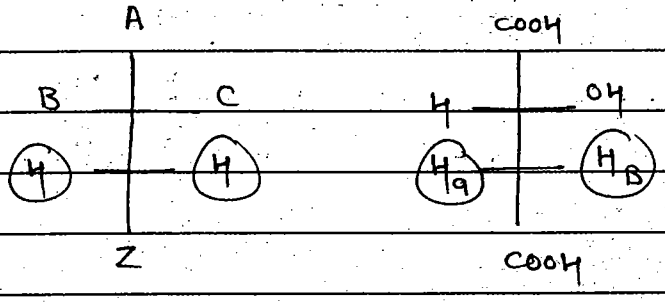
i) Symmetry Criteria :

→ Homomorphic ligands are not interchangable with $\sigma / C_n / S_n / C_i$ are known as diastereotopic ligands.

→ Diastereotopic ligands are free from symmetry elements.

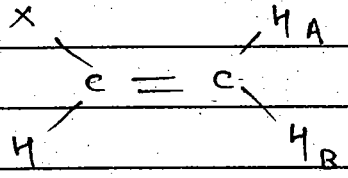
→ If chiral centre directly attached to atom having two identical subunits produce diastereomers / diastereotopic ligands.

eg.



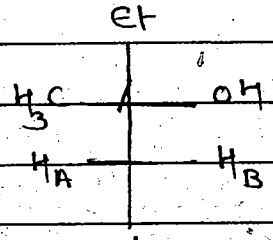
- * Diastereotopic ligands
- No symmetry
- adjacent to chiral centre

eg.



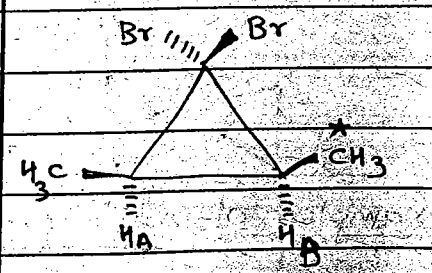
- Can not be interconvertable with any kind of symmetry (C_n, σ, S_n, C_i)
- H_A & H_B are diastereotopic

eg.



- H_A & H_B are diastereotopic

eg.

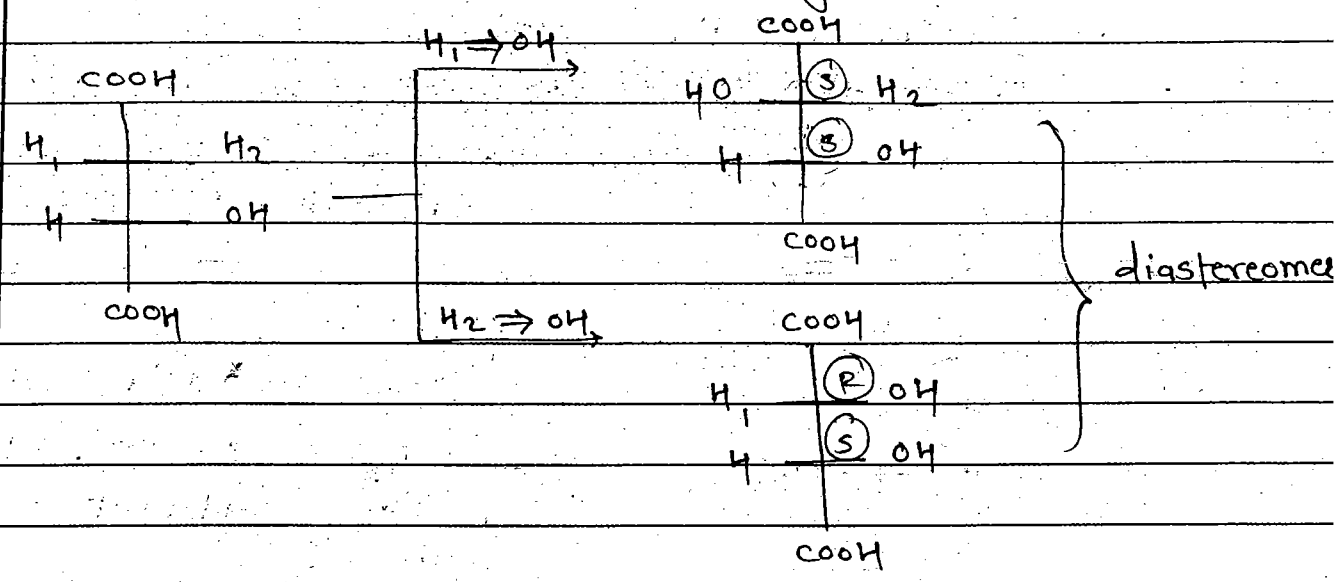


- Both Br are diastereotopic
- $-CH_3$, $-{}^{*}CH_3$ & $-H_A$, H_B are enantiotopic

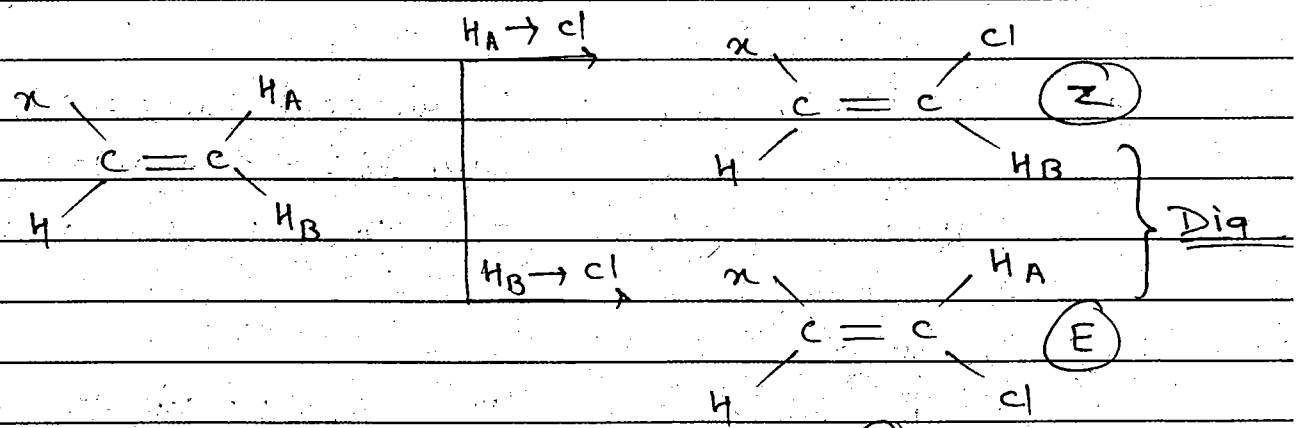
2) Substitution Criteria :

When the replacement of either of the two ligands by a different groups gives diastereomers, then such ligand are termed as diastereotopic ligands.

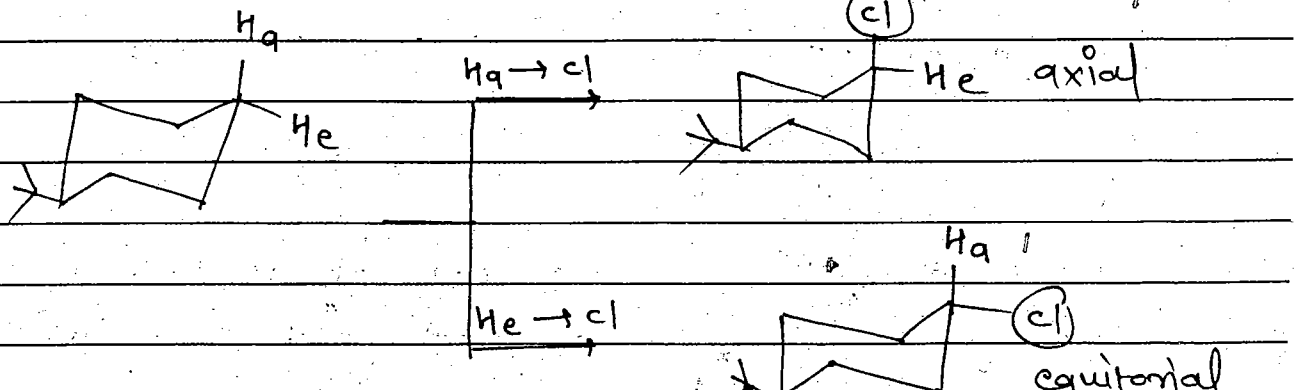
eg.



eg.

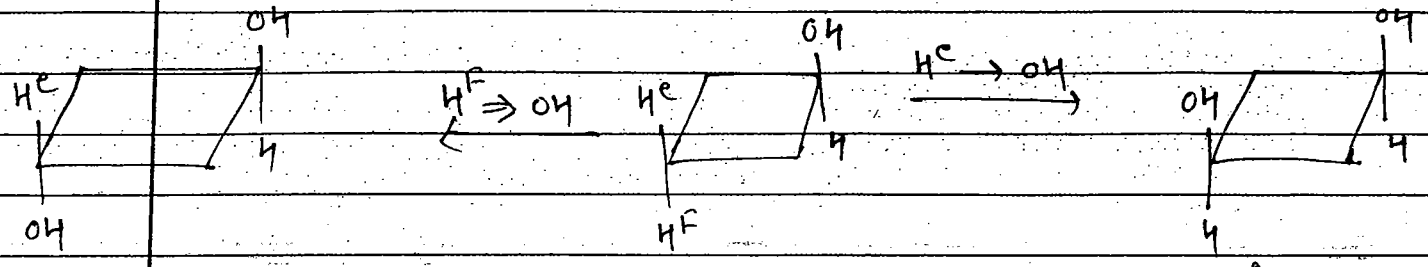


eg.

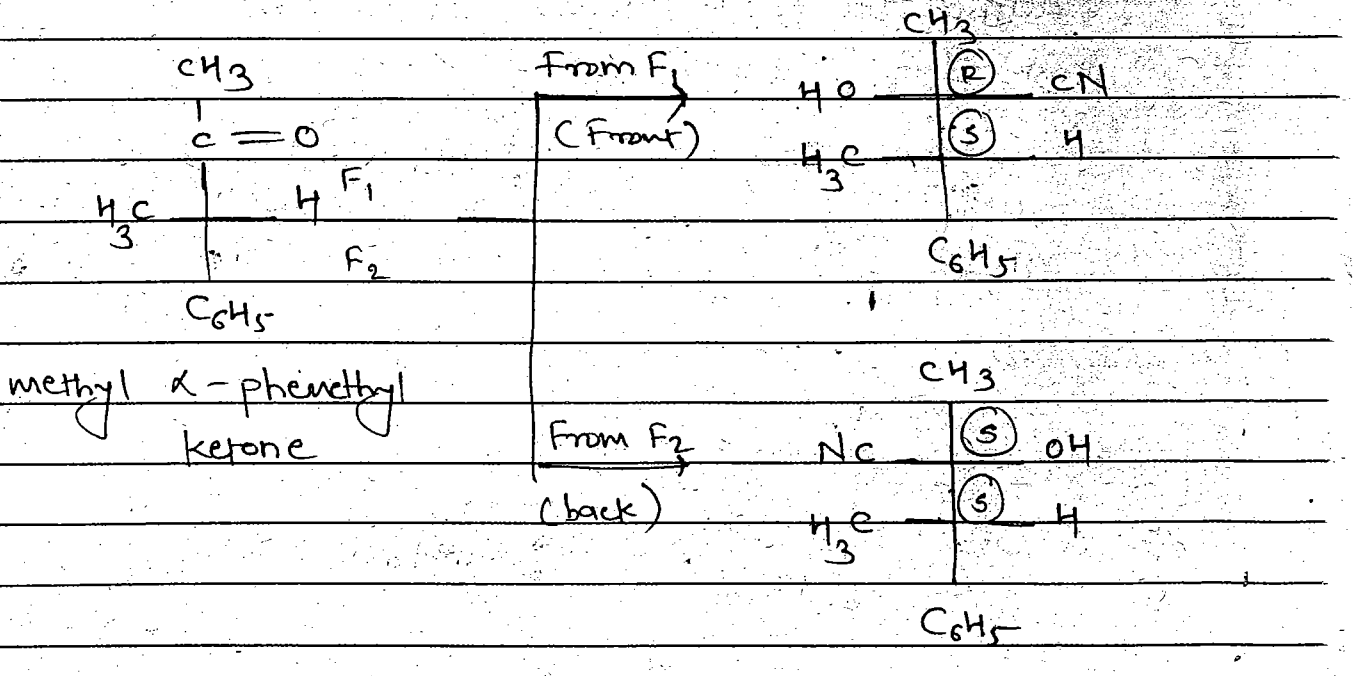


axial & equitorial are examples of diastereomers.

eg. In cyclobutanol, the ligands H^e & H^F are diastereotopic As H^e & H^F are not exchangable with any kind of symmetry elements. If they are substituted in turn by OH group give rise to diastereomeric products.



→ The two faces of Carbonyl group close to a stereo-Center / chiral Centre are diastereotopic. Thus addition of HCN to methyl α-phenethylketone gives diastereomers.



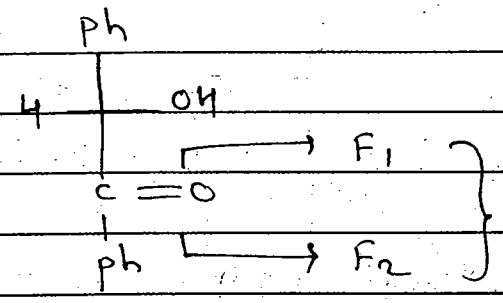
Both the obtained products are diastereomers of each other.

Diastereotopic face :

i) **Symmetry Criteria :**

Any face of a molecule are not related to symmetry elements ($C_n / \sigma / C_i / S_n$) are known as diastereotopic face.

- If chiral group directly attached to reacting face produce diastereomers.



ii) **Substitution Criteria :**

Addition of new group from reagent on reacting face to give diastereomers are known as diastereotopic faces.