I MSc., CHEMISTRY
ORGANIC CHEMISTRY – I
SEMESTER – I
CODE: DCHII

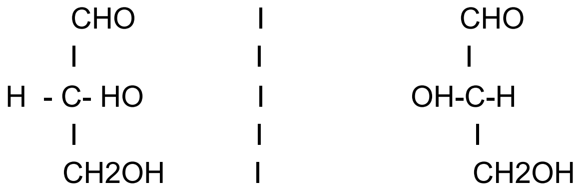
UNIT – 1
STEREOCHEMISTRY

By,
Dr.B. SHARMILA INDIRANI,
ASSOCIATE PROFESER OF CHEMISTRY,
PERIYAR ARTS COLLEGE,
CUDDALORE – 1.

ORGANIC CHEMISTRY - 1
STEREO CHEMISTRY-UNIT-1

OPTICAL ACTIVITY AND CHIRALITY

A Chiral molecule is one which rotates the plane polarised light and it shows optical activity .If a molecule is not superimposable on its mirror image , it is chiral. If its is superimposable on Its mirror image, it is achiral . Chiral molecules, that are non-superimposable mirror images (D&L-glyceraldehyde) are examples of optical isomers as they rotate the plane polarised light in opposite direction.



```
      CHO          I             CHO
       I           I              I
H  - C- HO         I          OH-C-H
       I           I               I
      CH2OH        I              CH2OH
```

D-glyceraldehyde   l-glyceraldehyde

since these two are mirror images of each other , these optical isomers are enantiomers.

CHIRALITY:

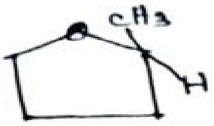
If a molecule has only one chiral carbon, that shows optical activity and its chiral and it possess chirality . It has more than one chiral carbon atoms the molecule as a whole should be Disymmetric . Then only it shows chirality

a).CLASSIFICATION OF CHIRAL COMPOUNDS

A molecule abcd is chiral when a# b# c# d and the groups around the carbon should not be equal the groups can be alkyl, aryl, hetero atomic or their combintion

(i)Among the following compounds, compound (1) achiral and compound (II) is chiral. in compound (1) , the ring residues are identical . In compound (II) the four groups (CH3,H,O,and CH2) being different .

(I)



(II)

(iii) All molecules with a single chiral atom belong to point group C1 and must display optical activity .

(iv) compound (III) is optically active, even two substituents show a very small difference .
(a hydrogen atom and its isotope deuterium)

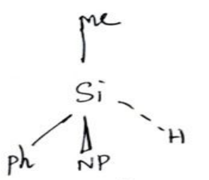
```
        H
        I
CH2-C-OH
 I      I
 CH2 D
 I
 CH3
```

(III)

1- BUTANOL

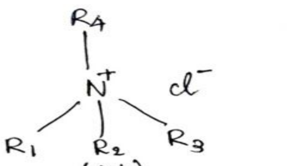
b) COMPOUNDS WITH OTHER QUADRIVALEND CHIRAL ATOMS ;-

A molecule with an atom , with its 4 bonds pointing to the corners of a tetrahedran will display chirality provided the four groups are different . The tetrahdral centres are si,Ge, N.(IV,V,and VI)



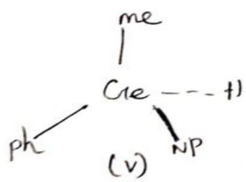
(iv)

Np - α-naphthyl



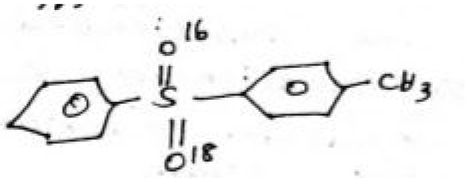
(vi)

Quaternary ammonium compound



(v)

In sulfones , sulphur atom bonds tetrahedrally . However , as two of the groups have to be oxygen , normally the sulphones do not display chirality . An optically active sulfone(vii) has been prepared in which both oxygen are different (16O AND 18O)

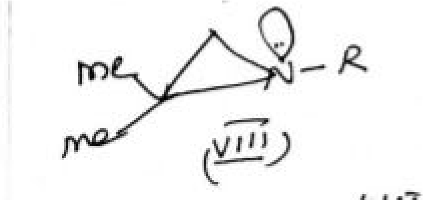


c) COMPOUNDS WITH TERVALENT CHIRAL ATOMS;-

(I) Chiral amines have pyramidal geometry . They cannot be resolved due to pyramidal inversion

(ii) If two of the nitrogen substituents form the part of cyclic system , the barrier to inversion is increased and the enantiomers have been isolated.

EXAMPLE;-2-disubstitued aziridines

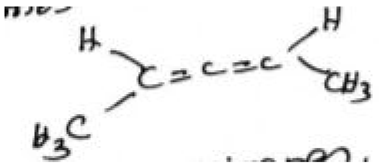


(VIII)

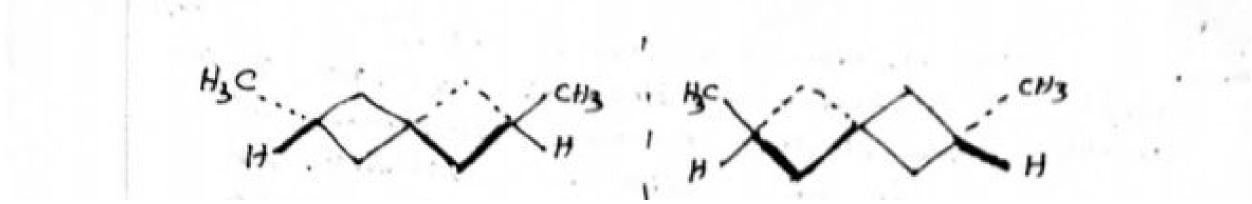
d) COMPOUNDS WITH CHIRAL AXIS ;-

(I) Several molecules do not have a chiral centre but have chiral axis example allenes and spiranes .

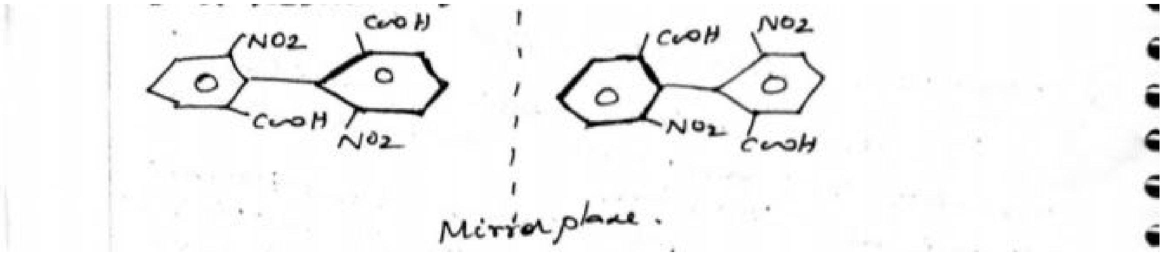
(ii) In allenes , if the terminal carbon atoms are substituted differently , they occupy in mutually perpendicular planes and the compound becomes chiral.



(iii) In spiranes, the two rings are mutually perpendicular to each other and they are not planar due to this , spiranes are chiral

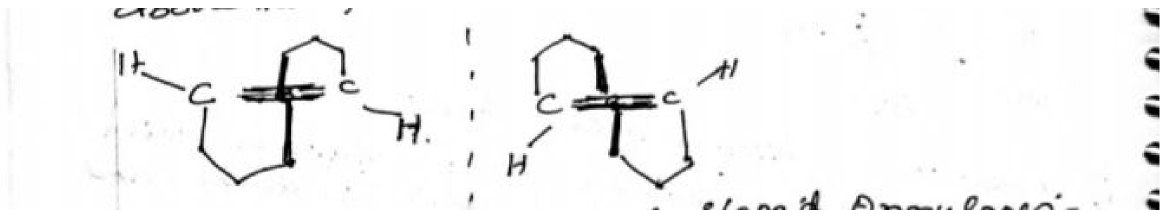


(iv) Substituted biphenyls also have a chiral axis. If biphenyls are substituted with larger sized ortho substitutuents; they are twisted from the coplanar conformation as a result of steric strain .



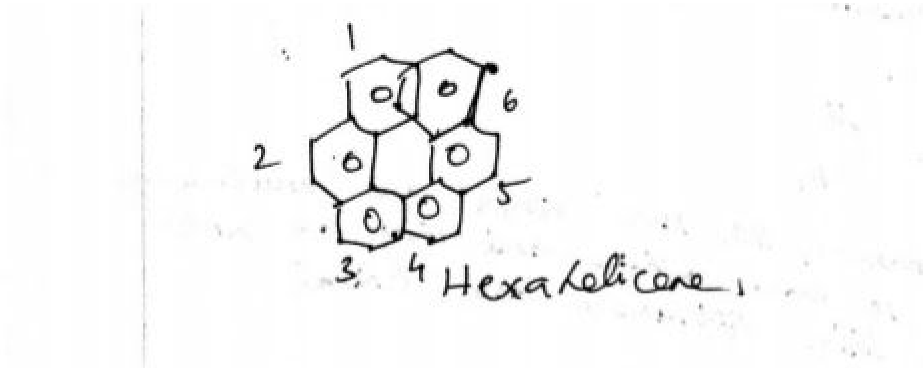
e) MOLECULES WITH CHIRAL PLANE ;-

Trans cyclooctene has chirality due to the presence of plane of chirality , since there are two asymmetric arrangements of the tetramethylene bridge either below or above of carbon - carbon double bond .

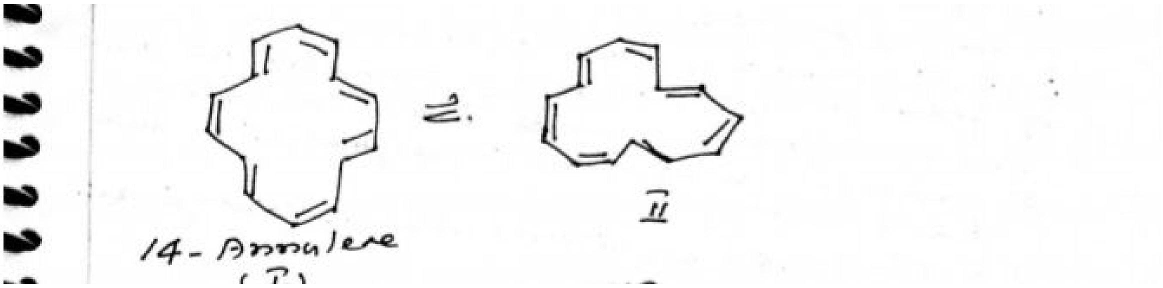


f)MOLECULES WITH HELICAL SHAPE ANNULENES;-

Several molecules display chirality due to helical shape (eg) hexahelicene



Annulenes are macrocyclic compounds with conjugated double bonds . Annulenes are also chiral due to its shape and chiral plane.



(i) and (II) are diastereoisomers.

OPTICAL ACTIVITY OF ALLENES , SPIRANES AND BIPHENYL COMPOUNDS ;-

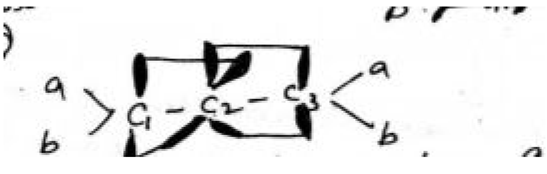
ALLENES;-

The presence of a chiral carbon atom in an organic molecule is a sufficient condition for showing optical activity . Disymmetry of molecule is the necessary condition for the same.

1. The general structural formula of allenes is

   $>c=c=c<$

2. Allenes exhibit optical isomerism , provided that the two groups attached to each terminal carbon atoms are different
3. The two terminal carbon atoms, (C1&C2)in allenes are is a state of trigonal SP2 hybridisation and the central carbon atom is SP-hybridised state .

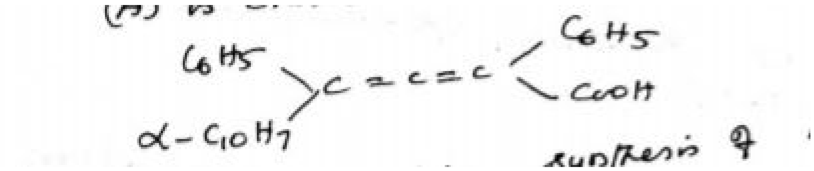


4. The central carbon atoms is attached to adjacent carbon atoms by two colinear sigma bonds and two bi-bonds . The two bi bonds are in planes at right angles to each other . one (bix) is in the plane of the paper and the other (biy) is at right angles to the paper

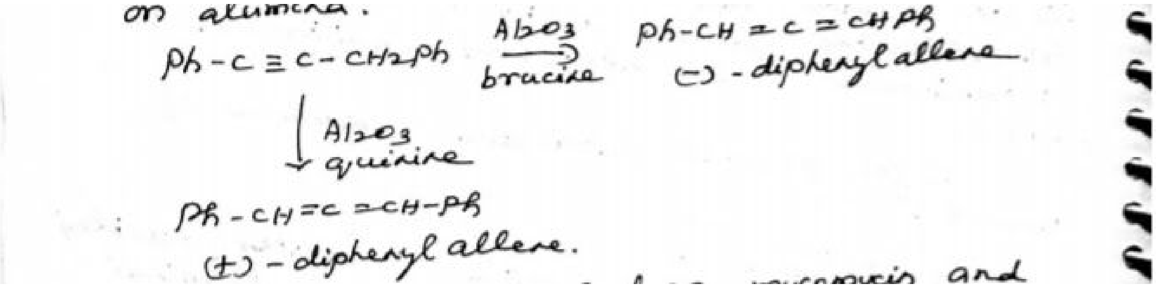
5. The pi bond is perpendicular to the plane containing three sigma bonds.

6. The groups a and b attached to carbon1 are lying in the plane of the paper and the groups a&b attached to carbon 2 lie in the plane perpendicular to the plane of the paper.
7. So the molecule possess neither plane of symmetry nor centre of symmetry and forms non -superimposable mirror images and hence the molecule on the whole is asymmetric and optically active.

8.3-alpha-naphthyl-1,3-diphenyl allene -1- carboxylic acid (A) is chiral.

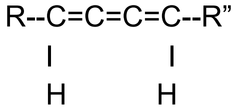


9. An asymmetric synthesis of 1,3 - diphenylallene was achieved by absorption of 1,3-diphenyl Propyne -1 on alumina



10. Various antibiotics such as mycomycin and nemotinic acid are found to contain allene Grouping.

11. The terminal substituent in cumulenes with an odd number of double bonds would be is the Same plane and optically inactive

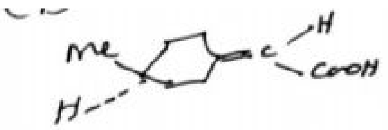


$$R\text{--}\underset{H}{\underset{|}{C}}=C=C=\underset{H}{\underset{|}{C}}\text{--}R''$$

12. Allene type of optical isomerism is formed in cumulens having an even number of double bonds .

13. General shape of allene molecule is retained if one of the double bonds in allene is replaced by a six membered ring

(eg)4-methyl cyclohexylidene- 1-acetic acid



SPIRANES;-

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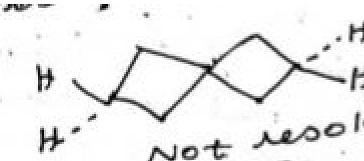
1)If both the double bonds in allenes are replaced by ring system in which two rings have one atom in common . such bicyclic system in spiranes .

2). The two rings are at right angles to each other.

3). The parent compound spiro-(3,3)- heptane (I) is not resoluble became it has two planes of symmetry .



Not resolvable
(I)

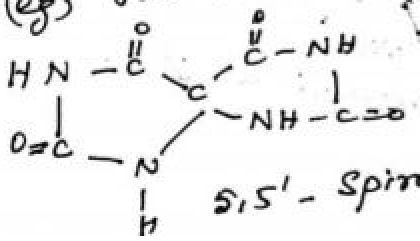
4) These planes may be removed not only by attaching two unequal groups at the sides of the rings but also by introducing suitable groups within the ring .

An example for first kind is

An (eg) for first

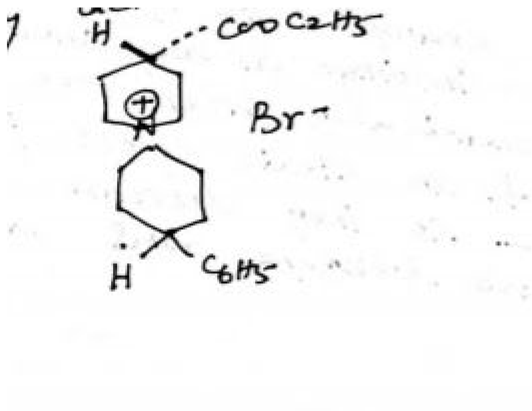
X = COOH / NH_2, any bigger group.

An (eg) for second kind is

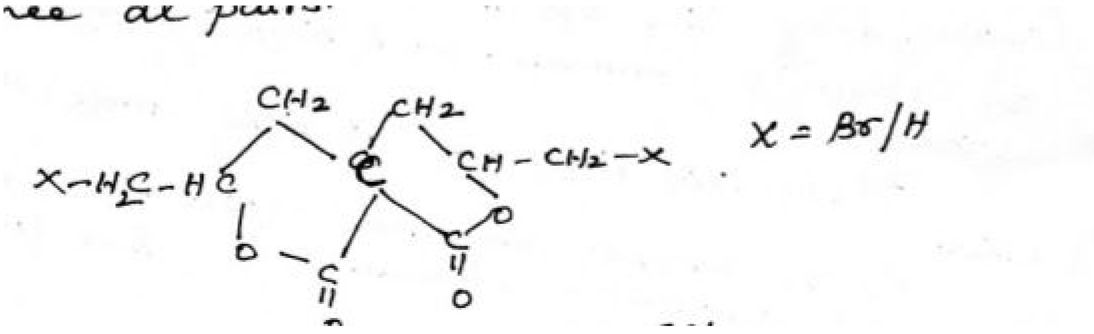


5,5'- Spirobihydantoin

5). The quaternary ammonium salt (II) spirobispiperidinium salt has been obtained is optically active. Form.



6). The molecule having asymmetric carbon atom as well as . spirane asymmetry exist as three dl pairs.

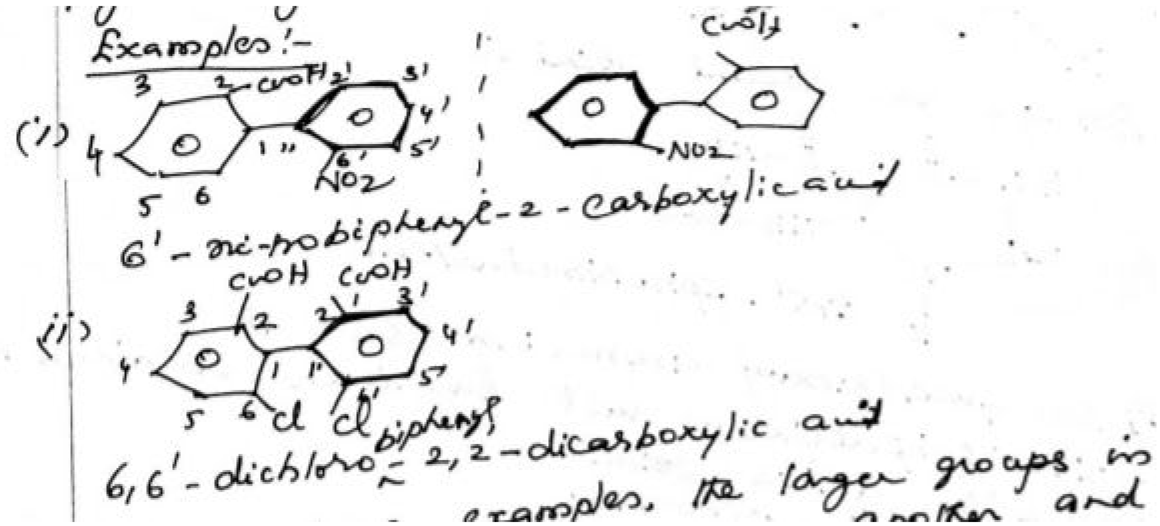


OPTICAL ACTIVITY IN BIPHENYL;-

1). The biphenyl molecule containing two benzene rings which are coaxial and the molecule is inactive and non-resolvable. It is superimposable on its mirror image.

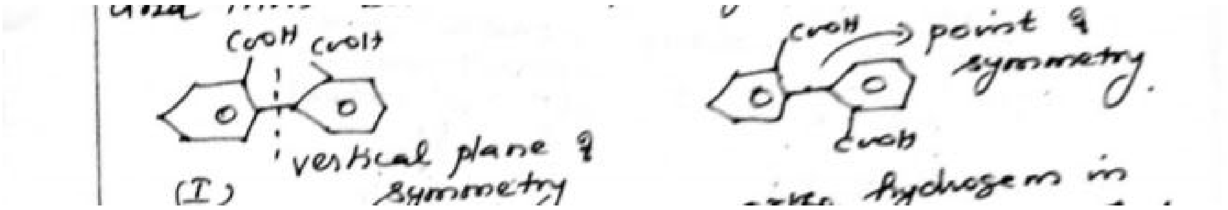
2) Biphenyl to exhibit optical activity , two conditions are to be satisfied .

- Ortho positions must be substituted by larger groups such as NO2 Cl, COOH etc.
- Neither rings must have a plane of symmetry .
- EXAMPLES.

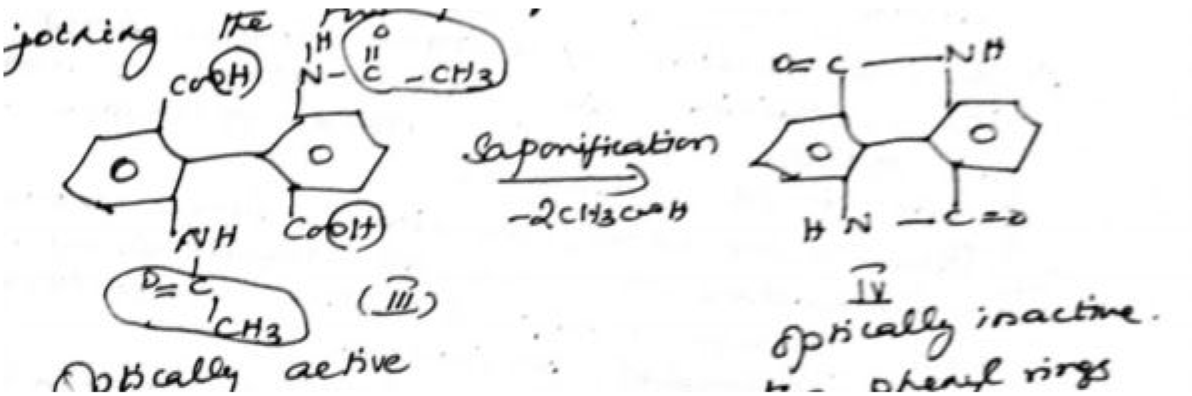


3) In the above examples the larger groups is ortho positions impinge on one another and interfere mechanically when free rotation was attempted . so steric effect prevented free rotation . so they become optically active . since the two benzene rings are not coplanar.

4) Compound (I) has vertical plane of symmetry and compound (II) has point of symmetry and thus both are optically inactive .

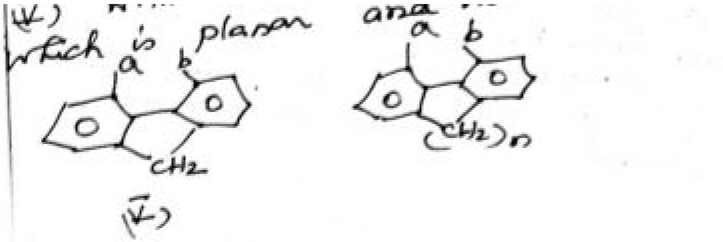


5). The distance between ortho hydrogen is adjacent in biphenyls is (0.29nm) which is greater than the vander waals radius of hydrogen (2.0x0.12) =.24nm. but is substituent biphenyls the distance between ortho hydrogens in adjacent rings in biphenyl is lesser than the vanserwaals radius and so rotation about the single bond and so rotation about the single joining the two phenyl rings is prevented.

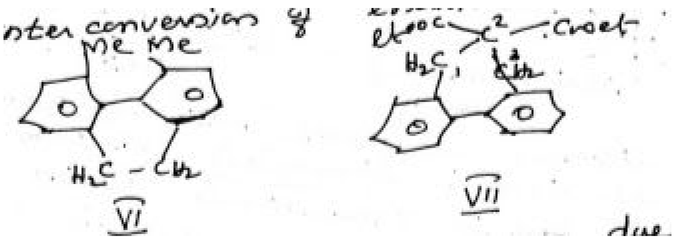


In compound (iii) the two phenyl rings are not coplanar, due to bulky subsitituents in ortho in ortho positions . But during lactum formation , in compound Iv , the phenyl rings become coplanar and compound IV , is optically inactive.

7). To generate optical activity via the effect of 2,2’-bridge of the shown is Iv with n=1 , we get disubsitued fluorene which is planar and not resolvable.



8). When n=2 compound vi is resoluble . And when n=3 ,as in (vii), the angular strain associated with twisting rotation about the central double bond prevents interconversion of enantiomers.



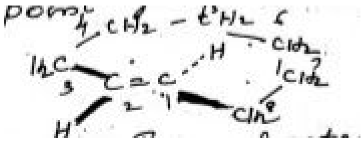
9). This type of isomerism , arises due to restricted rotation around a single bond is known as atropisomerism and the iosmers are called as atropisomers.

PLANAR CHIRALITY;-

1) The introduction of a trans double bond into a ring containing six carbon atoms or less is not possible since it would introduce larger strain in the molecule .

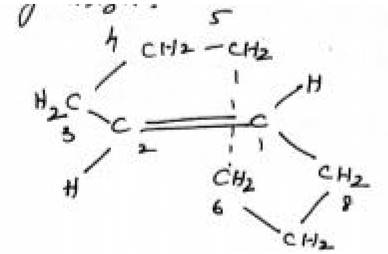
2). In trans cyclo octene , the ring is large enough to accomadate the geometry required by a trans double bond.

3). The molecule has a C2 axis of symmetry passing through the centre of the double bond and bisecting 5-6 bond and belongs to C2 point group .



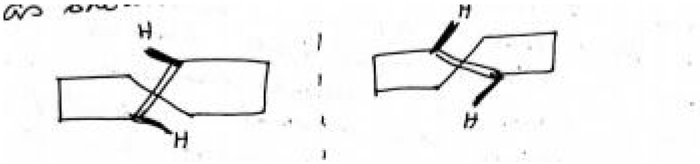
Trans cyclooctene (i)

4). The interconversion of cis & trans isomers is impossible is(i) . The interconversion of enantiomers requires a double bond rotation process. Rotation of the methylene groups as C5-C6 through the ring followed by a similar rotation of the trans disubstituted double bond portion of the molecule.The energy between barrier for this rotation is very high.



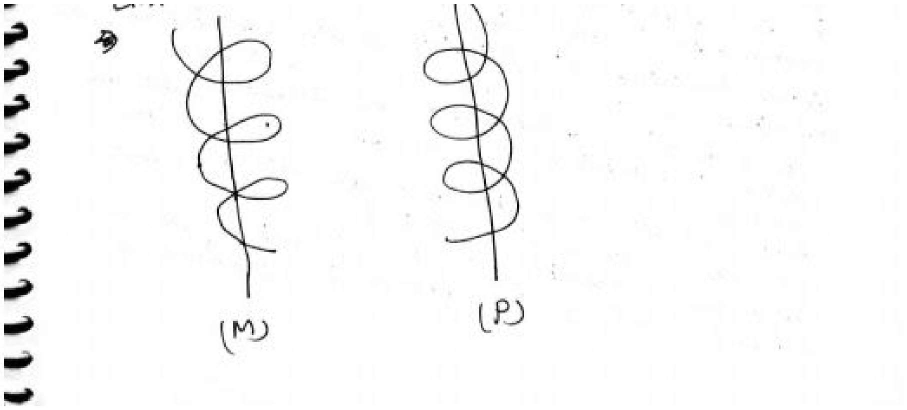
5). Trans cyclooctene is chiral , due to the presence of chiral plane containing two carbons (1+2) joined by double bond, two hydrogens and two carbons immediately (3&8) .

6). The conformation of trans cyclooctene have been separated and are optically active, which are mirror images, of each other as shown below.



OPTICAL ACTIVITY OF COMPOUNDS DUE TO HELICITY;-

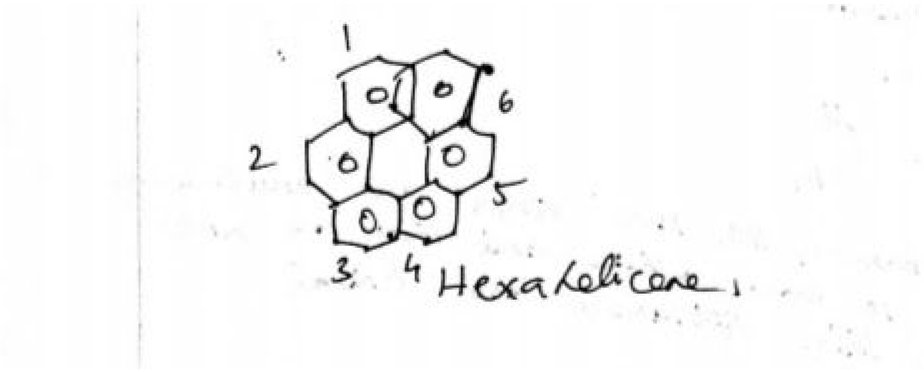
1). Due to helical shape , hexahelicene is chiral, which may be right handed or left handed helix . Right handed helix is designated as P (plus) . When viewed along the axis and moving from front to the rear, it (plus) undergoes clockwise rotation. When it undergoes anticlockwise rotation it is minus (M).



2). The terminal benzene rings is hexahelicene cannot occupy the same plane without coming in serious conflict with one another .

3. The molecule is forced to adopt a non-planar shape in which one side of the molecule

lie above the other because of crowding.



4.) Hexahelicene, the middle rings (2&5) in a plane , while the terminal rings (1 & 6) and (3&4) lie above and below the plane respectively.

5). Enantiomeric forms of hexahelicene is secondary structures of polypeptides and many protein . They have stable alpha - helix structure which can be either left/right handed.

6).Molecules such as benzo phenanthrene and phenanthrenes, which are normally expected to be planer, but due to molecular overcrowding they assume a helical shape.

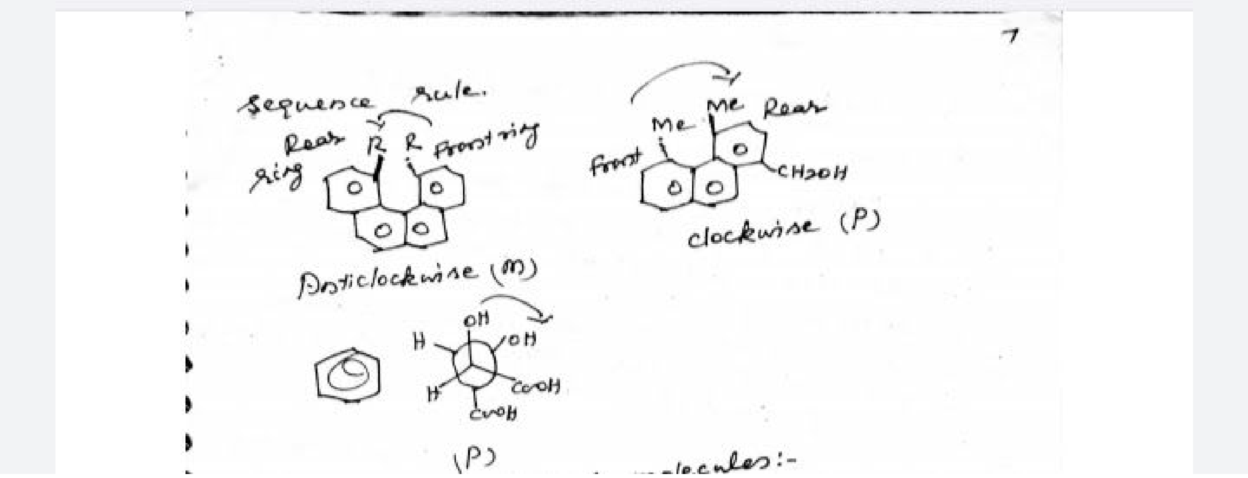
7) In helical molecules, the molecule is represented in Newmann projection and the highest priority group of the front is related to the highest priority group of the rear.

8). In this process, if it leads to clockwise turn, then the configuration is P(positive). On the other hand, if hand anticlockwise turn is described, the configuration is M(minus).

9). In deciding the priority of the substituents, the following sub rules must be considered .

a) If all the substituents are identical, the one which is providing the smallest torsion angle is chosen.
b) If all the substituents are different, the sequence rule is applied.

c) If two substituents are identical the one which is unique is choses independent of sequence rules.

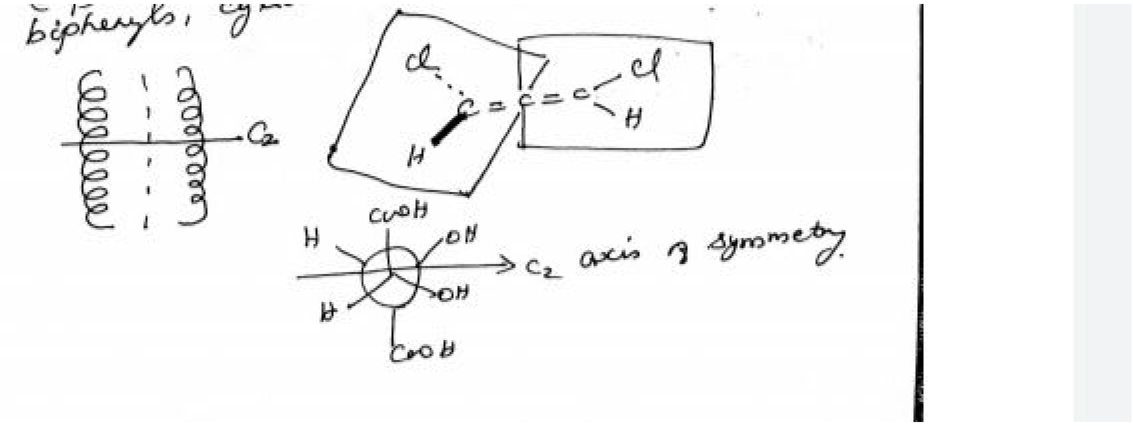


CLASSIFICATION OF CHIRAL MOLECULES:-

ASYMMETRY AND DISSYMMETRY:-

1. Chiral molecules belongs to c1 point group are referred to as asymmetric molecules. A molecule belongs to c1 point group, if it does not possess any symmetry element other than the rotation axis of order.
2. C1 axis of rotation is not considered as a symmetry element since it is present in all molecules and objects. Rotation of any object regular / irregular around an axis by 360 generates an identical structure.
3. A molecule is said to be disymmetric, if it belongs to the Cn point group (n>1) and it lacks mirror / reflection symmetry but possesses rotation symmetry.

Example: optically active tartaric acid, allenes, biphenyls, cylindrical helix.



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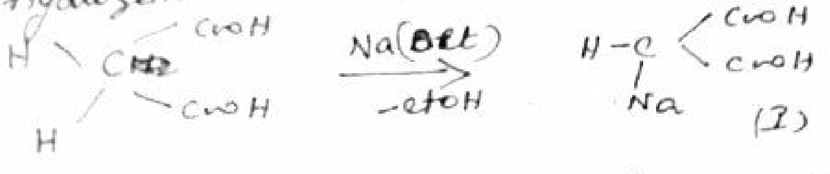
①

UNIT - I

Homotopic, enantiotopic and diastreotopic ligands & faces

I Homotopic ligands &faces:-

Any molecule of type CH_2Y_2 (example -$(CH_2)(COOH)_2$ - malonic acid) If we replace either of the CH_2 hydrogen by a group Z, the identical compound results. Thus the two hydrogens are equivalent.



(I)

II

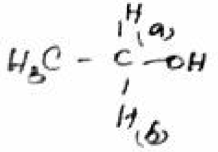
Compounds I & II are equivalent

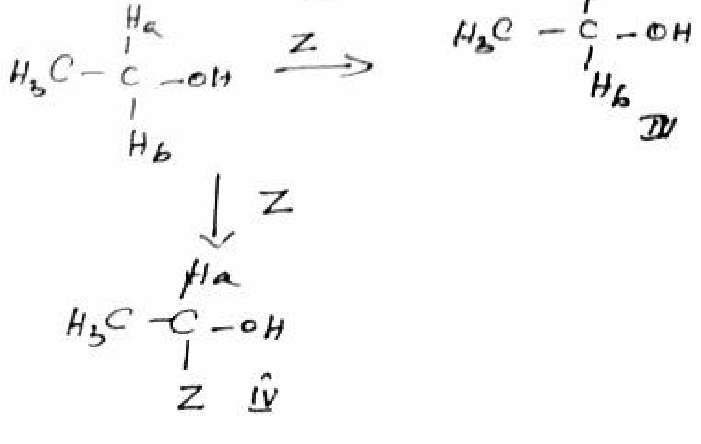
These two hydrogen atoms are homotopic ligands

II ENATIOTOPIC LIGANDS/ATOMS:-

Two same atoms/groups/ligands of a compound upon replacement with a third group give enantiomers. Those atoms are called as enantiotopic atom.

(Eg) Two hydrogen atoms of CH_2 group of ethanol.

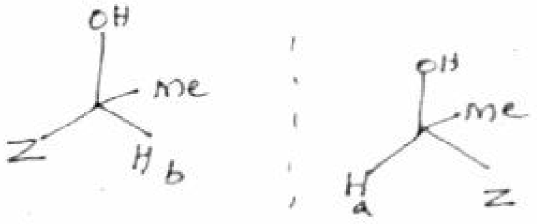




III

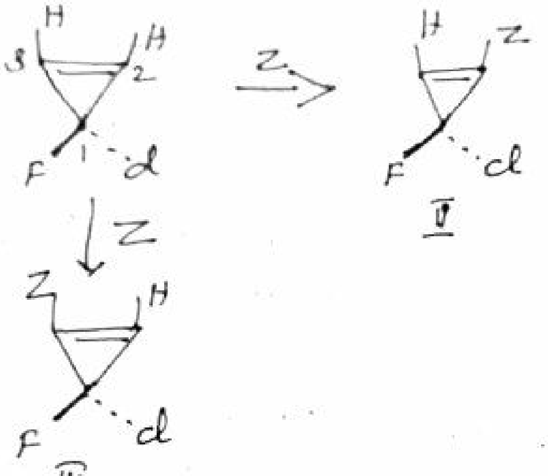
IV

Compounds III & IV are enantiomers.



In any symmetrical environment, two hydrogen atoms are behaving as equivalent. But in a disymmetrical environment they behave differently.

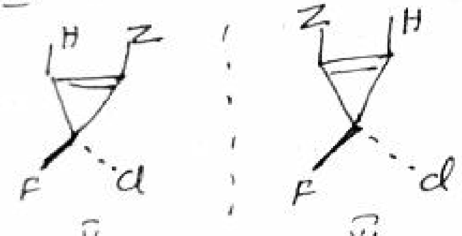
Eg 2 3-Fluoro-3-chloro-cyclopropene



V

VI

V & VI are enantiomers.



V

VI

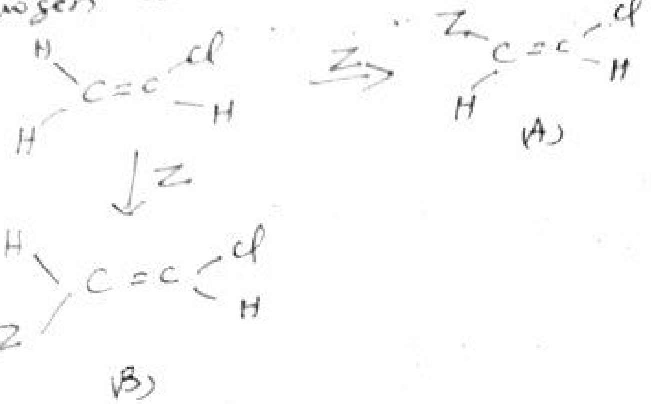
ET8232418711N

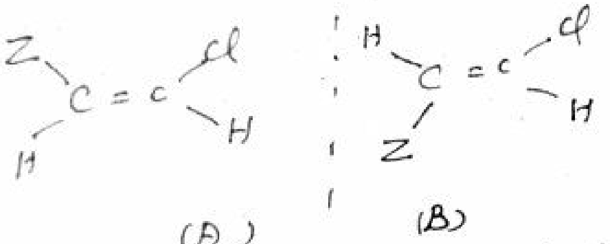
III Diastereotopic atoms/groups/ligands:-

When two atoms/groups/ligands in a molecule are in such positions that replacing each of them by a group Z, gives rise to diastereomers, the atoms/groups are called as diastereotopic

E.g

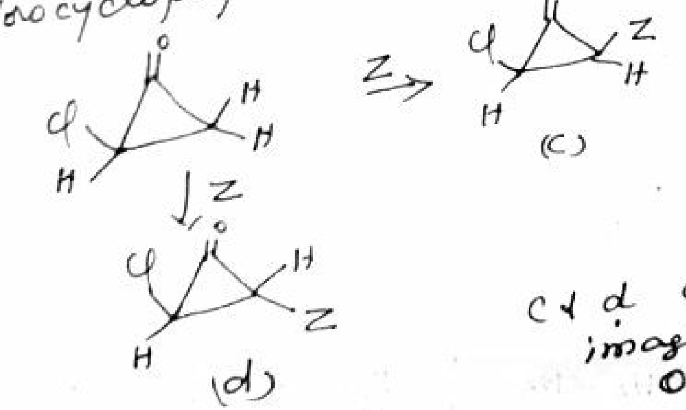
① Hydrogen atoms of vinyl chloride.



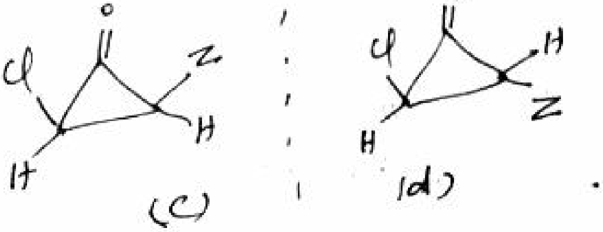


A + B are not mirror images of each other and they are called as diastereoisomers.

② Chlorocyclopropanone



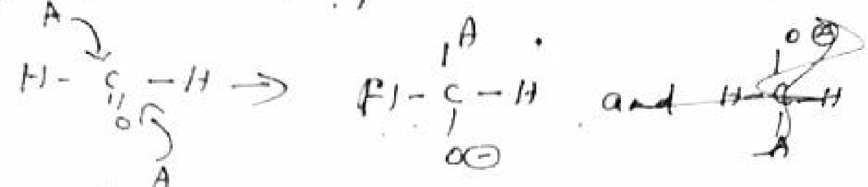
C & d are mirror images of each other.

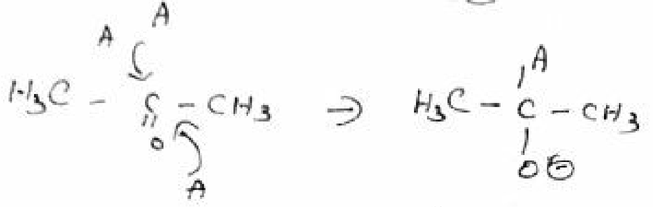


HOMOTOPIC
~~ENANTIOTOPIC~~ FACES:-

Attack by an achiral reagent (A) from either face of the molecule gives rise to the same transition state and product means, the two faces are equivalent and they are called as homotopic faces.

(E.g) formaldehyde / acetone

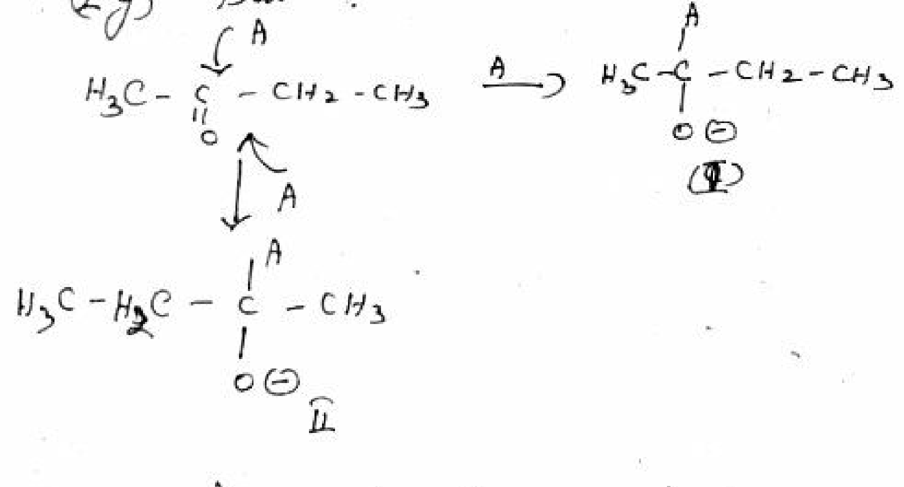


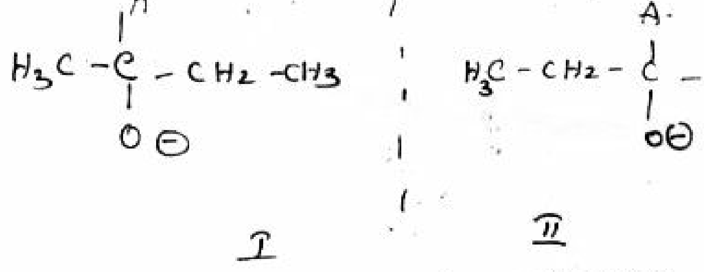


ENANTIOTOPIC FACES:-

Attack by an achiral reagent (A) at one face gives transition state and product (I) which is an enantiomer to the product II ~~when~~ during attack at another face.

(E.g) Butanone & acetaldehyde



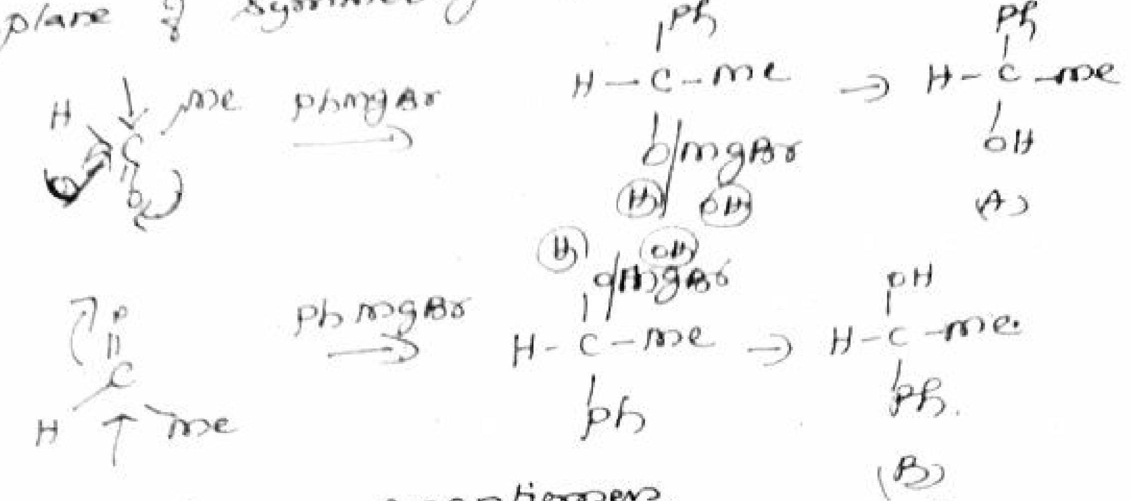


RBL
RBR

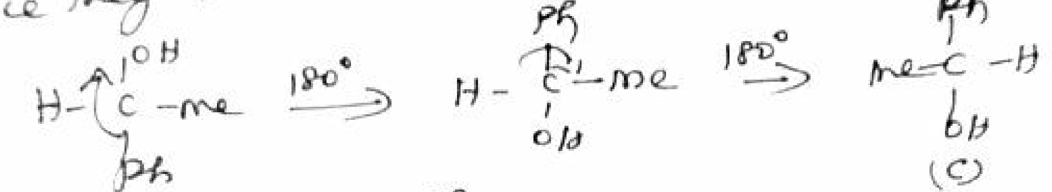
I & II are enantiomers.

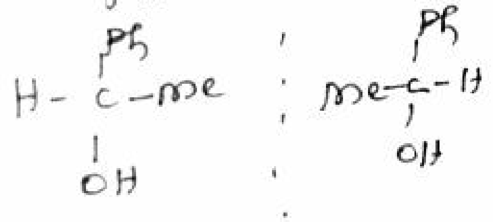
(5)

Enantiotopic faces are the opposite faces parallel to the nodel plane of a π orbital system by an alternating axis (Sn). Acetaldehyde has enantiotopic faces (ie) they are exchanged by a plane of symmetry equivalent to S1.



A & B are enantiomers, since they are mirror images of each other.





Stereospecific and stereoselective reactions:-

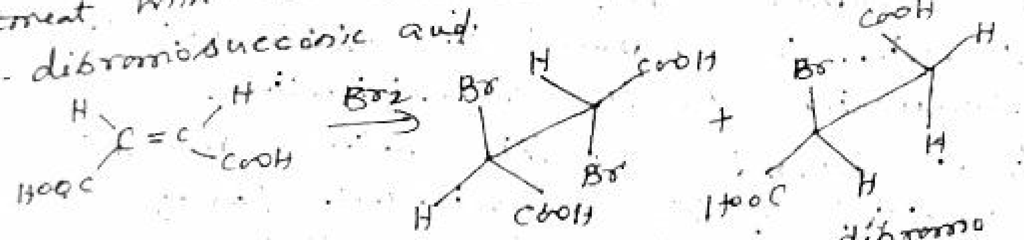
A reaction is stereospecific, when the substrate can exist in stereoisomeric forms and each gives a different stereoisomeric product. Given isomer gives one product, while another stereoisomer gives the opposite product.

Stereoselective reaction is one in which the reactant is not neccessarily chiral but in which the reaction produces predominantly or exclusively one stereoisomeric form of the product.

STEREOSPECIFIC REACTION:-

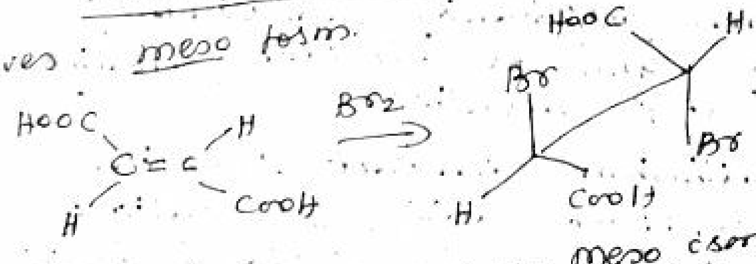
All stereospecific reactions are necessarily stereoselective, but the converse is not true.

The addition of bromine to an olefinic π bond is stereospecific. Maleic acid on treatment with bromine gives dl pair of 2,3-dibromosuccinic acid.



(±)-pair of 2,3-dibromo succinic acid

Fumaric acid on treatment with Br_2 gives meso form.



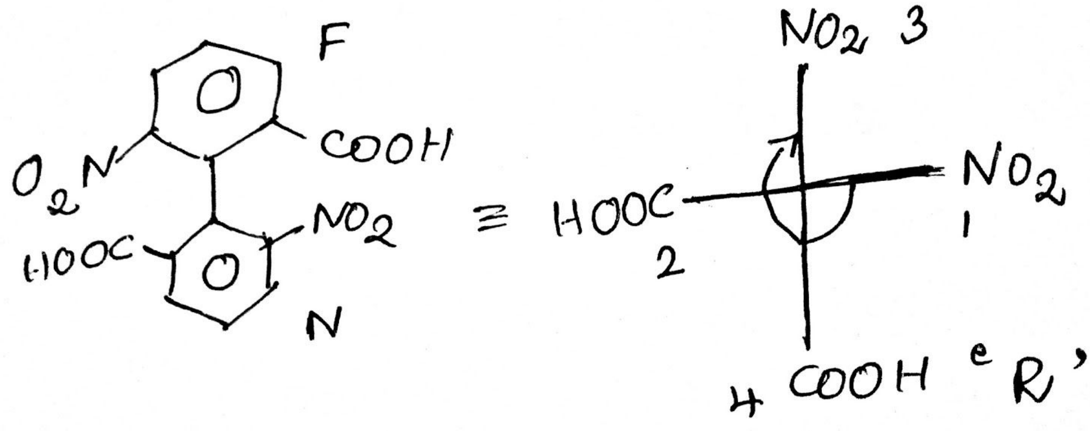
meso isomer

R/S Configuration of active biphenyls:

Proximity Rule:

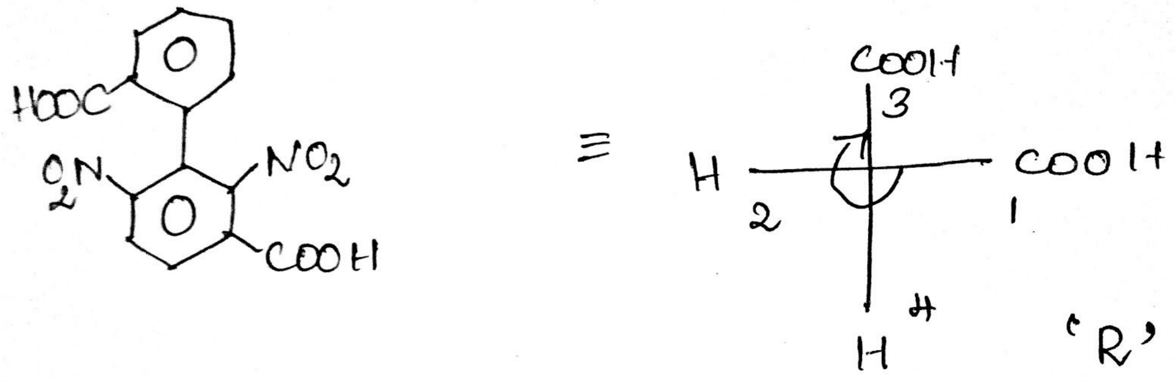
"Near groups precede far groups"

- The ortho groups present in the near ring(i.e)the ring closer to the observer are placed in horizontal lines.
- The ortho groups present in the far away ring (i.e)the ring far away from the observer are placed in a vertical line.
- In



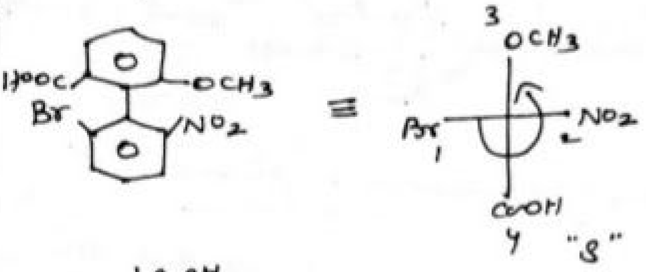
NO2 group gets precedence over COOH group. The rear group is the group of the lowest precedence and is placed at the bottom.

- When the ortho substituents are the same, and if a substituent is present in the 3rd position,the ring in which it occurs is placed in front and 3,5 substituents rather than 2,6 substituents determine the sequence.

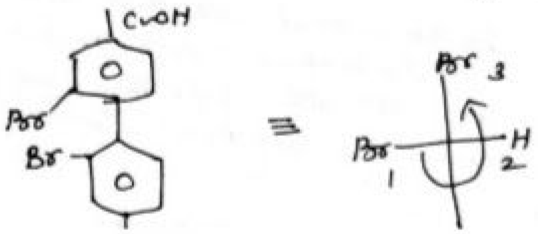


Some more examples:-

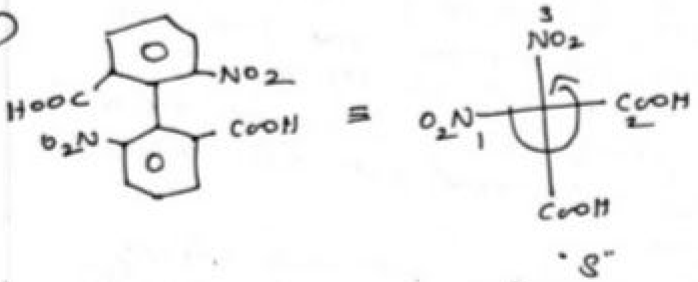
1)



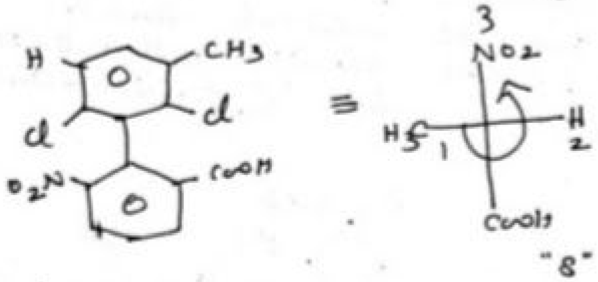
2)



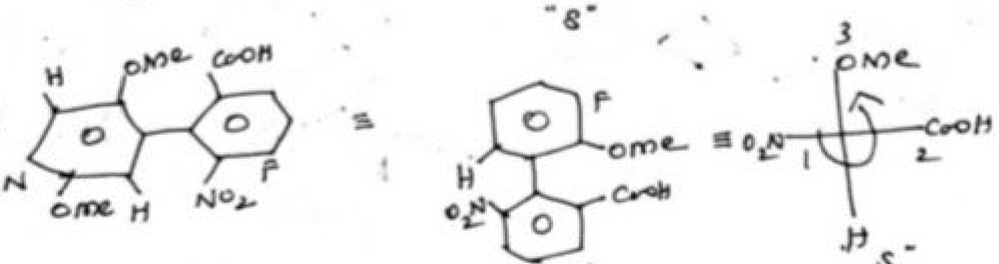
3)

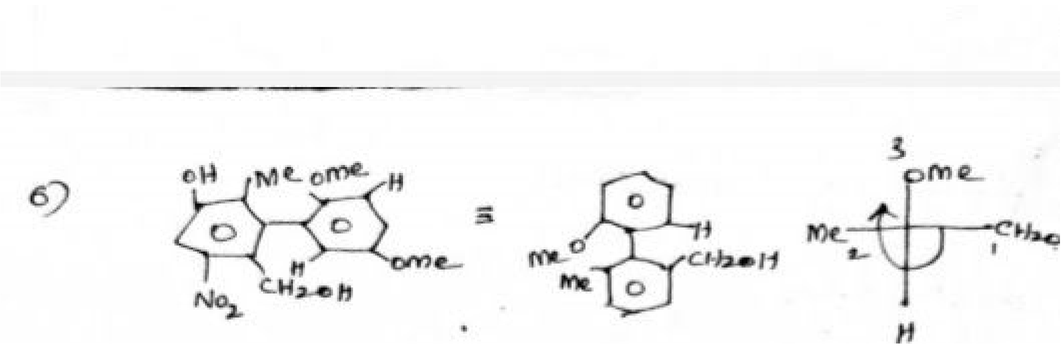


4)



5)





R/S Configuration of allenes and spiranes:

Step I :

The molecule is rotated so that the groups in the plane of the paper (shown by continuous lines)are at the top the groups perpendicular to this plane (shown by broken lines)are at the bottom.

Step II

Near groups precede far groups.

Step III

Near groups are present in vertical lines that too the group of lowest priority is present at the bottom and put 2 to the bottom group and 1 to the top one.

Step IV

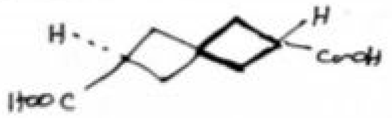
Far groups are present as such in the horizontal lines and put 3 to the highest priority group.

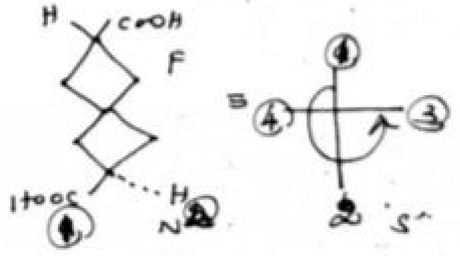
Step V

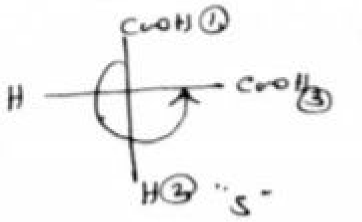
If the sequence 1 --->2---->3 shows <u>clockwise direction</u>, the molecule has ‘R’ configuration.If 1--->2--->3 shows <u>anticlockwise direction</u>,the molecule has ‘S’ configuration.

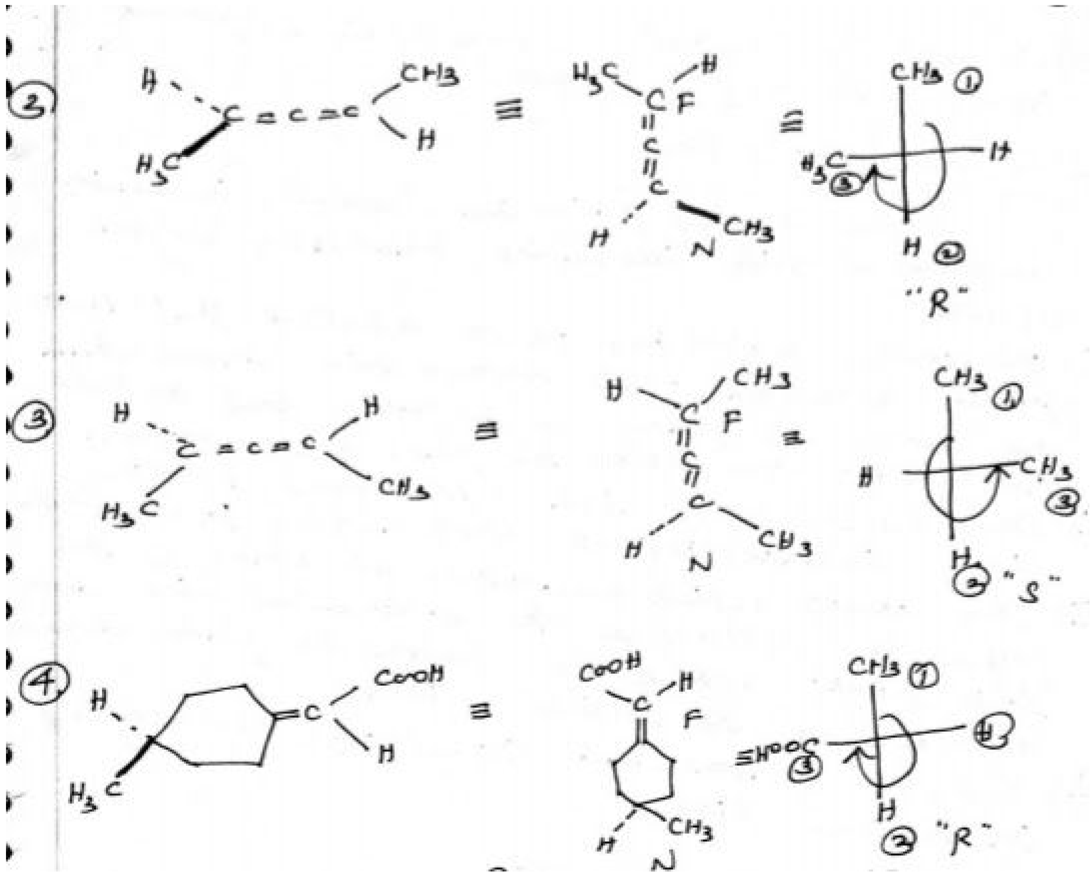
<u>Examples:-</u>

1.







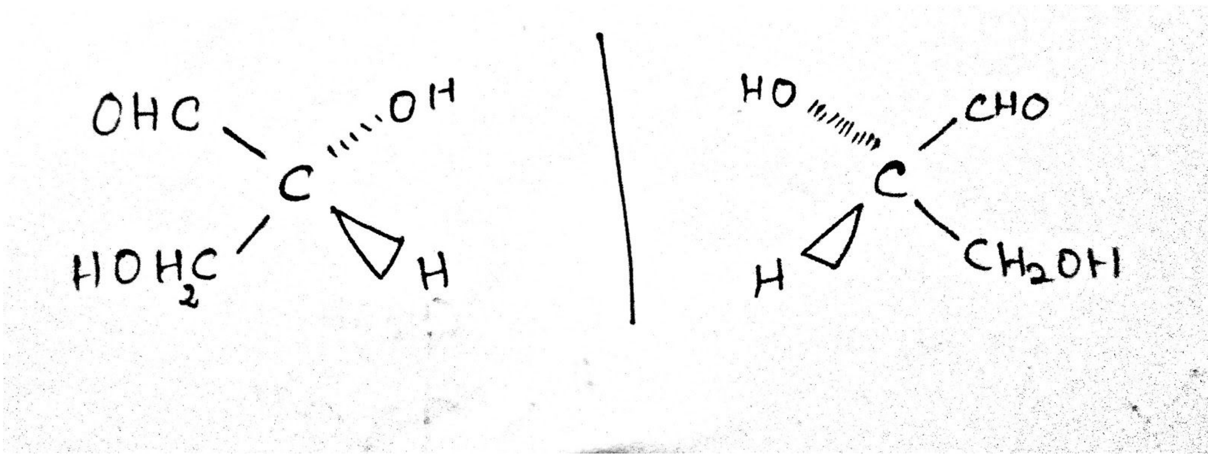


Two dimensional projection formulae:

1) Wedge Projection :

- This projection is convenient to represent the molecules with one and two symmetric carbon atoms.
- Of the four groups,attached to the tetrahedral carbon atom,two groups and the central carbon atom are placed in the plane of the paper such that of the two remaining groups,one lies above the plane and the other below the plane of the paper.

- The group which is above the plane of the paper is drawn as a bold/thick wedge and the one,which is below the plane of the paper is drawn with a dotted wedge.
- Thus enantiomers of glyceraldehyde are given below.



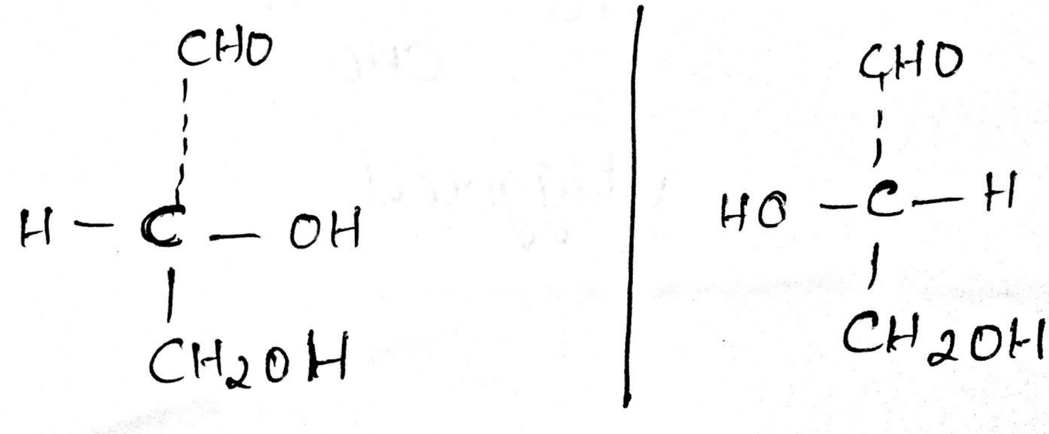
- Usually the longest carbon chain is placed in the plane of the paper.

2.Fischer Projection:

Since Wedge projection becomes increasingly complicated with an increasing number of carbon atoms.

- The wedge projection is so notated that two groups attached to the asymmetric carbon atom are above the plane of the paper and the other two groups are below the plane of the paper.

- The molecule is then represented by two lines intersecting at right angles to each other.
- The groups which are above the plane of the paper are attached to the horizontal line and those groups which are below the plane are attached to the vertical line.
- Longest carbon chain is always represented in vertical line.

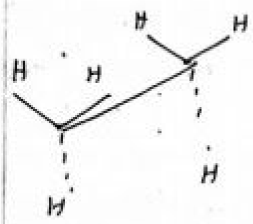


Enantiomers of glyceraldehyde.

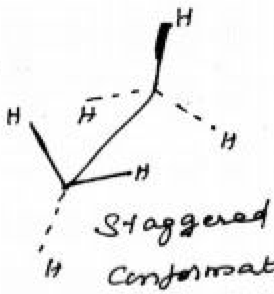
3)Sawhorse representation :

The bond between the chiral carbon atoms is drawn diagonally,implying that it runs downwards through the plane of the paper.

- The substituents on each of the carbon atoms are then projected on the plane of the paper and can be represented in staggered and the eclipsed conformation.
- The bonds projected above the plane are given in dark lines.
- The bonds projected below the plane are given in dotted lines.



Eclipsed Conformation of ethane.

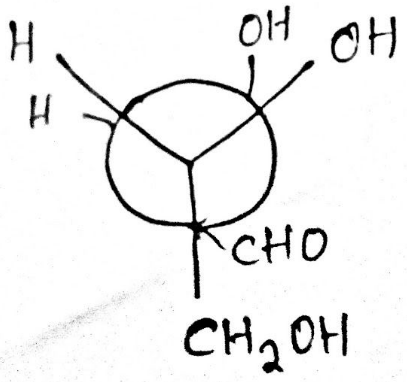


Staggered Conformation of ethane.

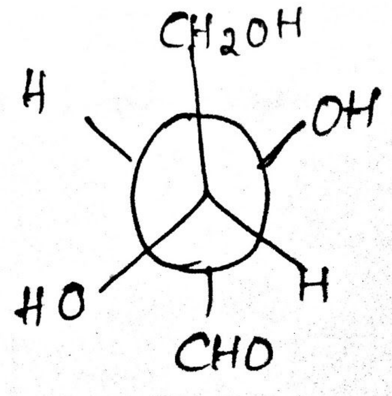
4)<u>Newmann projection:</u>

- The nearest carbon atoms is at the centre of the circle,represented by a dot.
- The molecule is viewed along the bond joining the chiral carbon atoms and those are represented as superimposed circles,only one circle being drawn.
- The remaining bonds and the substituents are then projected onto the plane of the paper.

- The substituents attached to the farther carbon atoms are attached to the perimeter as follows.



Eclipsed

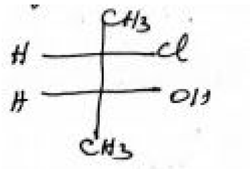


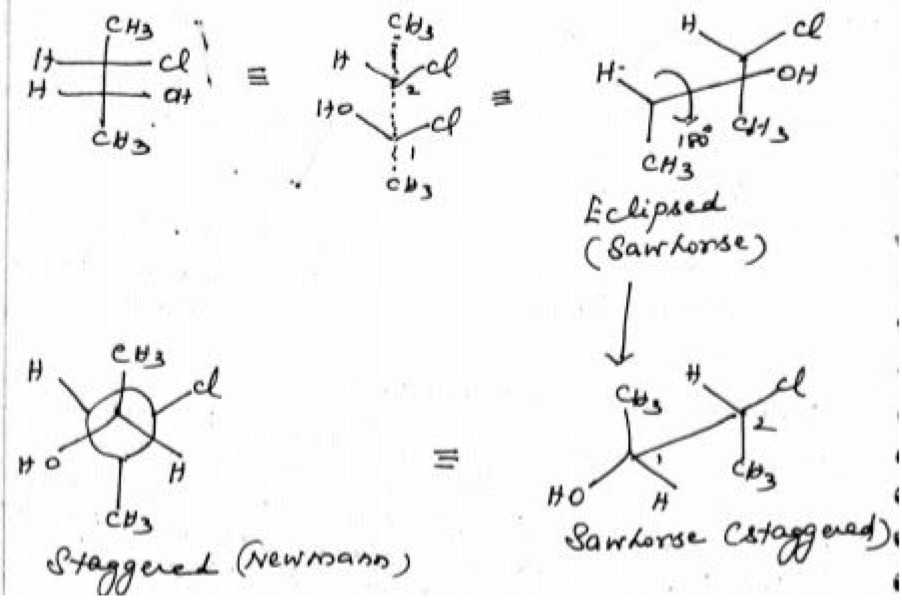
staggered.

Conversions Among Three Projection:

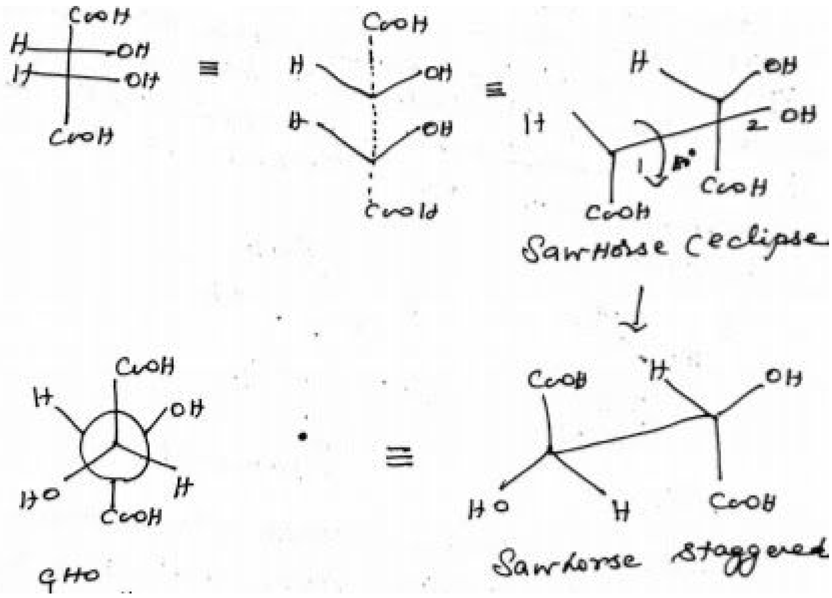
1)Convert the following Fischer projection into staggered forms of Sawhorse & Newman projection.

- Fischer projection is always in eclipsed form.



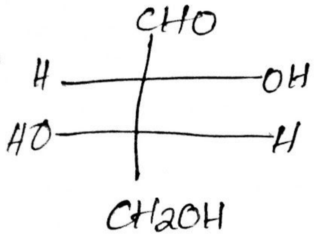

CH3
H
Cl
H
OH
CH3
≡
CH3
H
Cl
2
HO
Cl
1
CH3
≡
H
Cl
H
OH
180°
CH3
CH3
Eclipsed
(Sawhorse)
H
CH3
Cl
HO
H
CH3
Staggered (Newmann)
≡
CH3
H
Cl
2
1
CH3
HO
H
Sawhorse (staggered)

②


COOH
H
OH
H
OH
COOH
≡
COOH
H
OH
H
OH
COOH
≡
H
OH
H
2
OH
1
180°
COOH
COOH
Sawhorse (eclipse
COOH
H
OH
HO
H
COOH
≡
COOH
H
OH
HO
H
COOH
Sawhorse staggered

CHO

③



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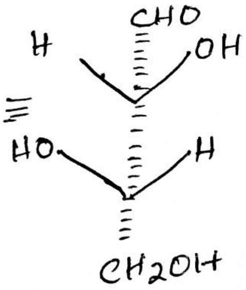

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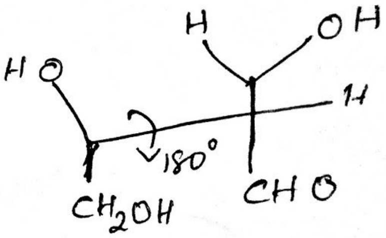
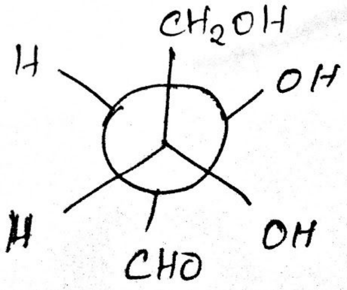


Sawhorse eclipsed

↓



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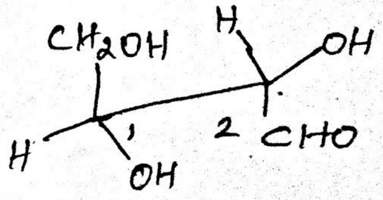
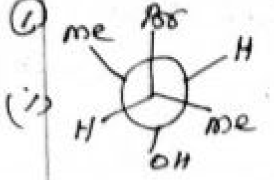


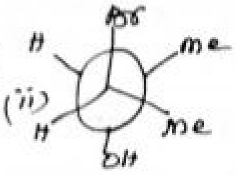
staggered

II Translate the following into equivalent Fischer projections and mention the relationship between them.

①



and



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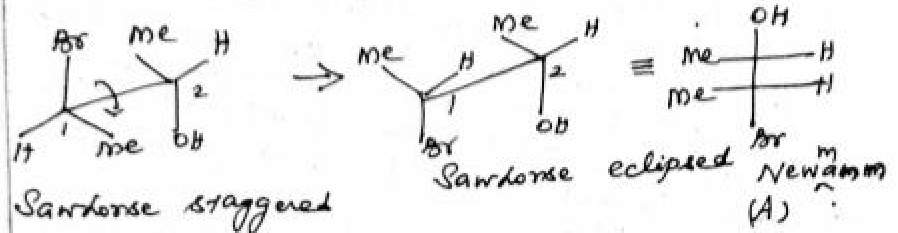
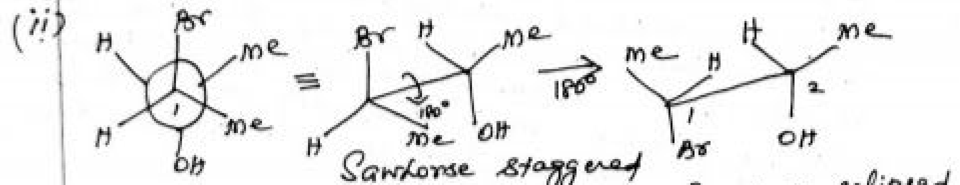


Sawhorse staggered

Sawhorse eclipsed

Newmann (A)

(ii)

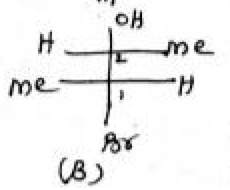


Sawhorse staggered

Sawhorse eclipsed

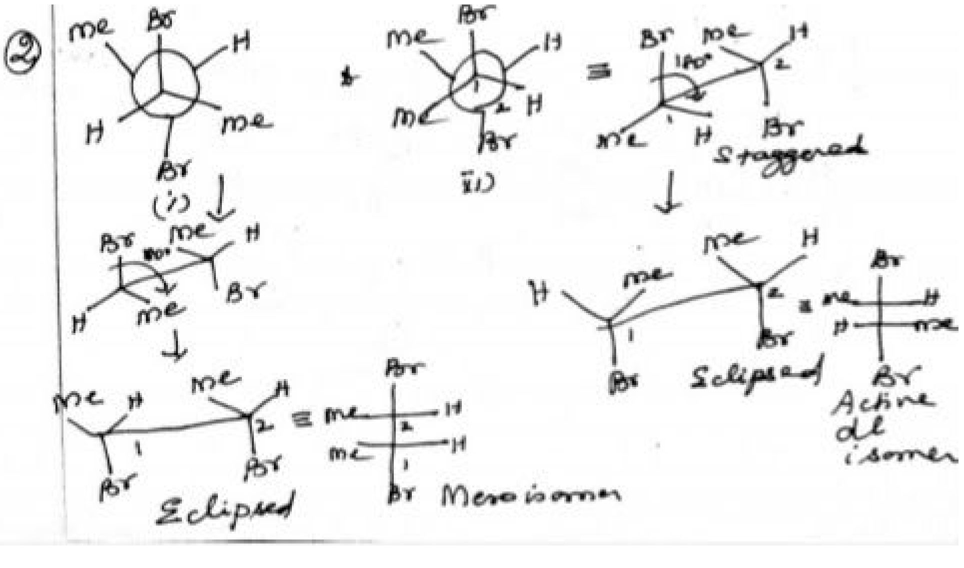
A & B are erythro & threo forms.

|||



(B)

②



Erythro & Threo Nomenclature :

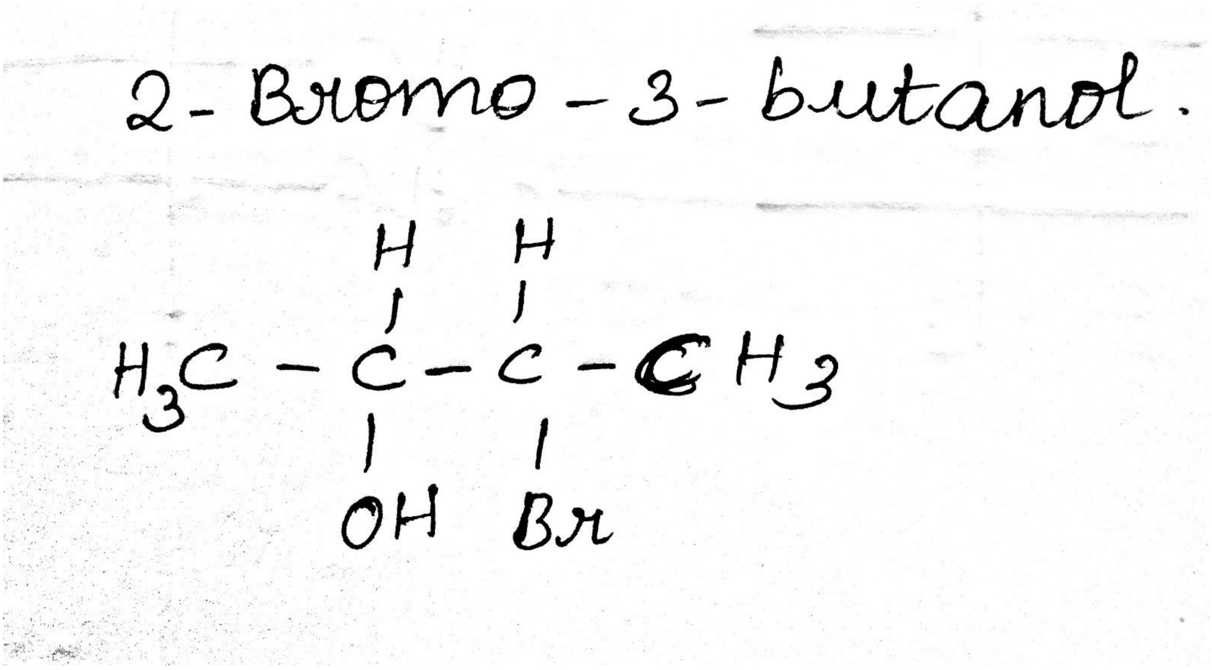
1. Erythro and threo nomenclature is used for diastereoisomers.
2. Diastereoisomers are a pair of optically active isomers which are not mirror images of each other.
3. Erythro diastereoisomer satisfies the following two conditions.

- In eclipsed Newmann & Sawhorse conformations, two sets of identical groups on adjacent carbon atoms can be eclipsed.
- In fischer projection ,two sets of identical groups lie one above the other and identical groups lie on the same side.

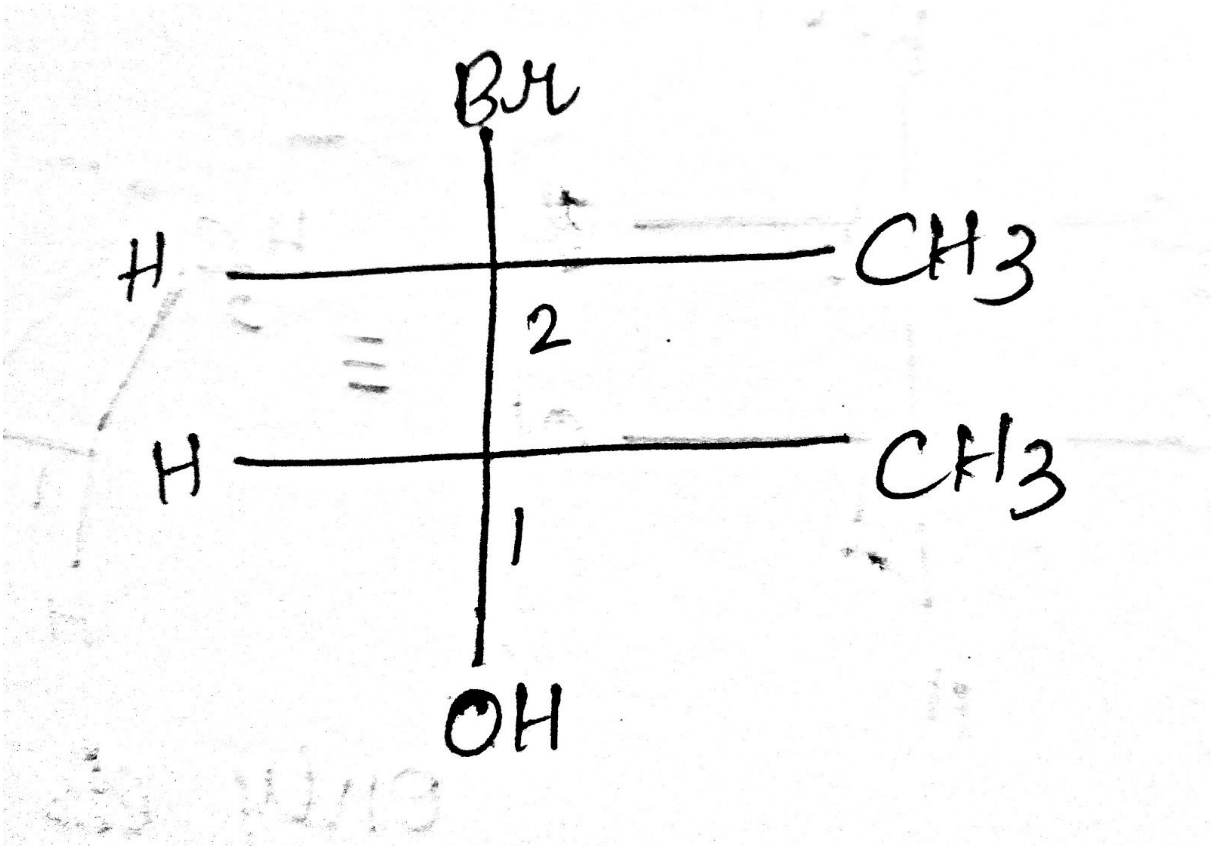
4. Threo isomer should satisfy the following two conditions.

  - In eclipsed Newmann and Sawhorse conformations , one only set of identical groups on adjacent carbon atoms can be eclipsed.
  - In Fischer projection,only one set of identical groups lie one above the other.

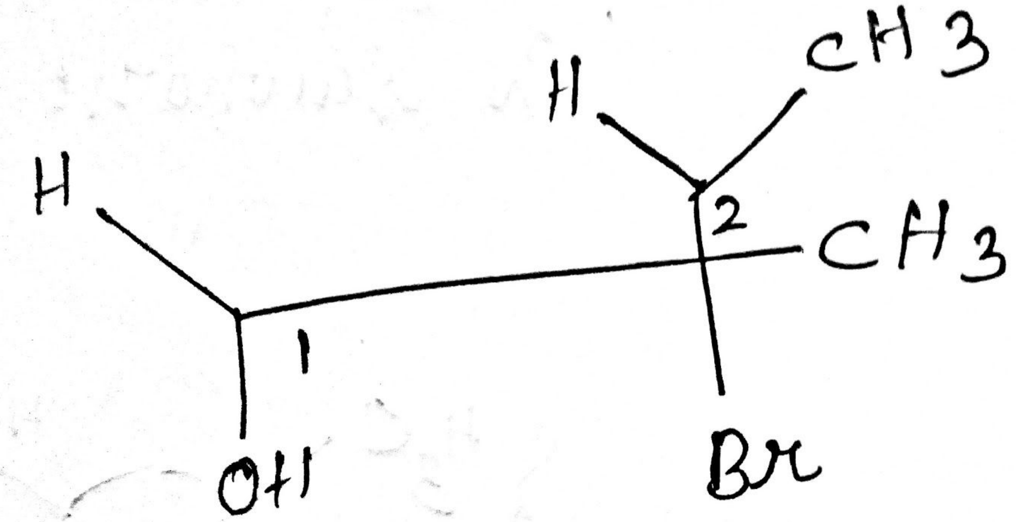
5)(E.g) 2-bromo-3-butanol.



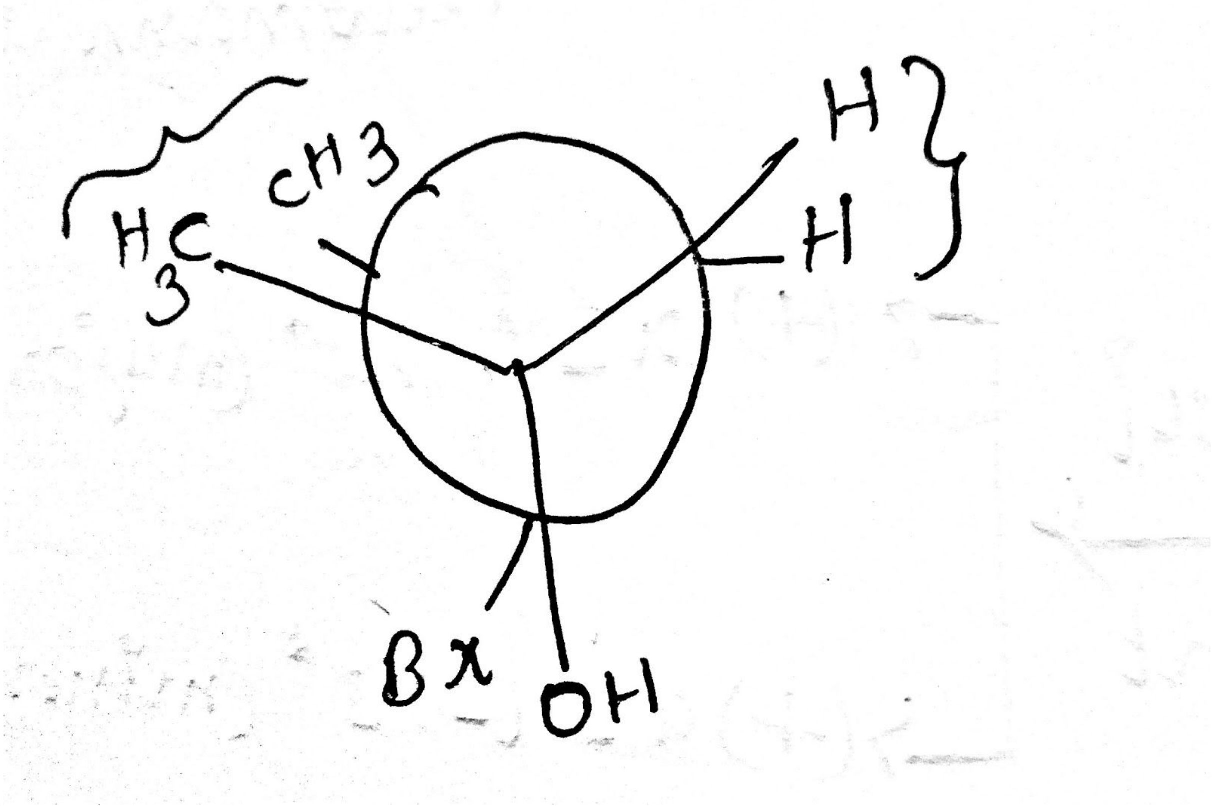
Erythro 2-bromo-3-butanol is represented as follows.



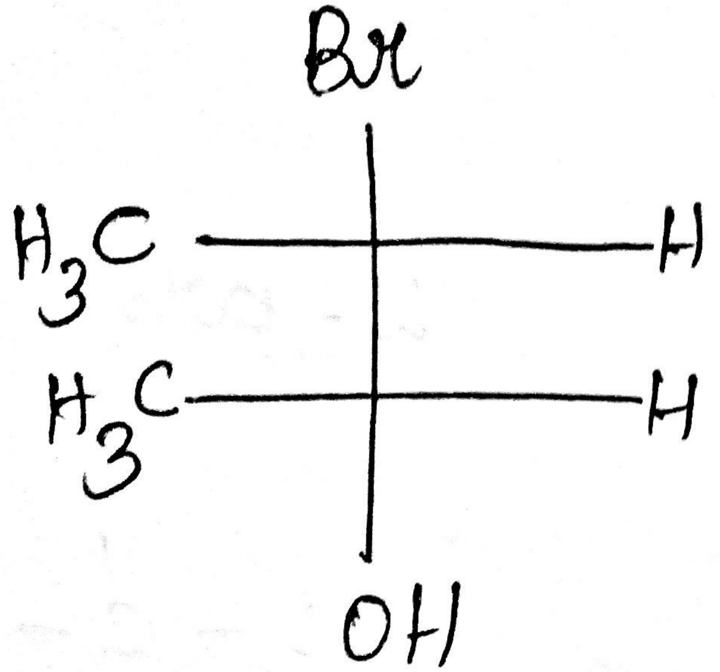
a)In Sawhorse eclipsed projection below,two sets of identical groups CH3/CH3 & H/H are eclipsed.



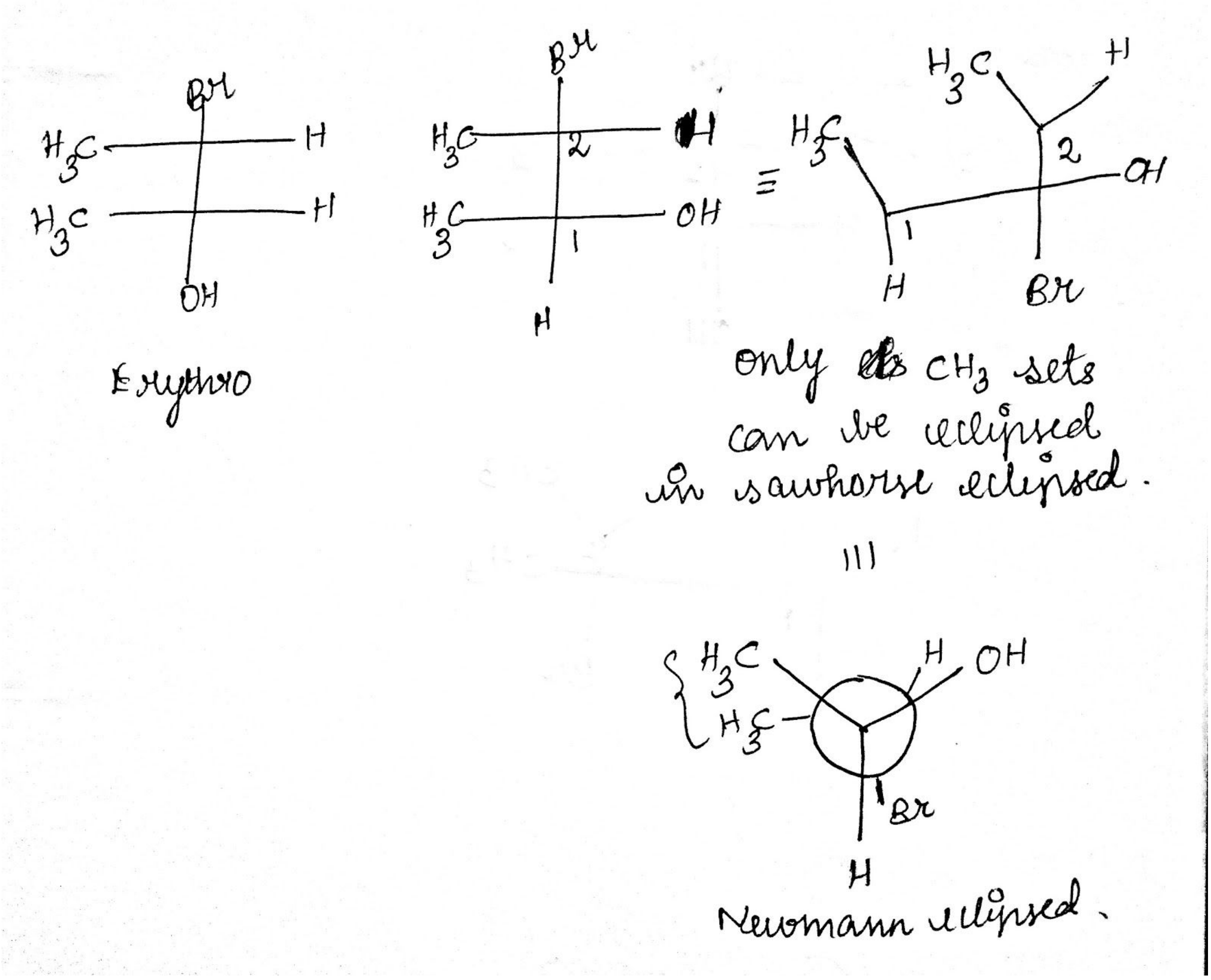
b)In Newmann eclipsed conformation also,two sets of identical groups (i.e) CH3/CH3 &H/H are eclipsed as below.



c)In Fischer projection two sets of identical groups lie one above the other.



6) a)In threo -2-bromo-3-butanol,only one set of identical groups is eclipsed in Sawhorse to Newmann projection as below,



only ~~cis~~ CH3 sets can be eclipsed in sawhorse eclipsed.

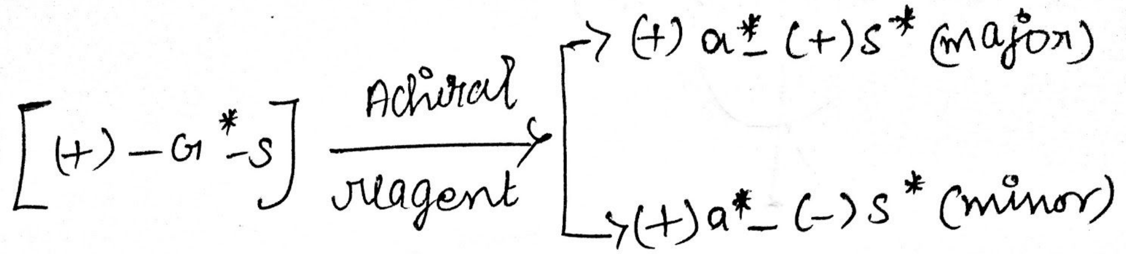
Newmann eclipsed.

Asymmetric synthesis:

Asymmetric synthesis involves the formation of new chiral unit in a substrate molecule under the influence of a chiral group.

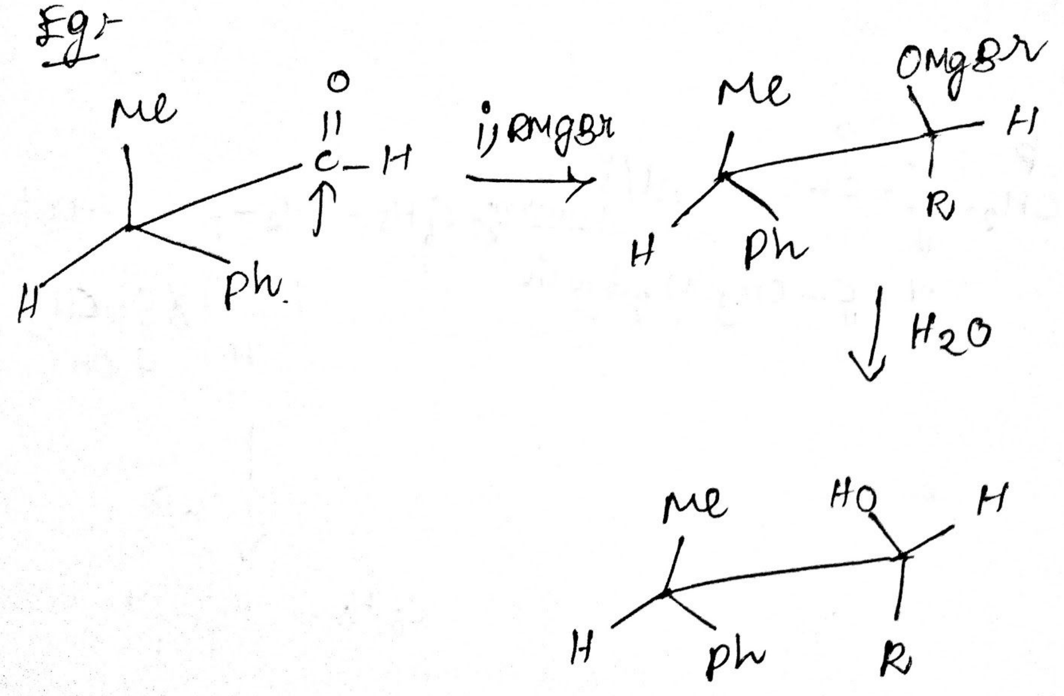
I. Substrate controlled methods :

The introduction of new chiral unit is achieved by an achiral reagent at a diastereotopic site of the substrate generating two diastereomeric transition states.As a result, the two diastereomeric products are formed in unequal amounts.



S → substrate
a* → chiral unit of the substrate
R → Achiral reagent

(E.g)



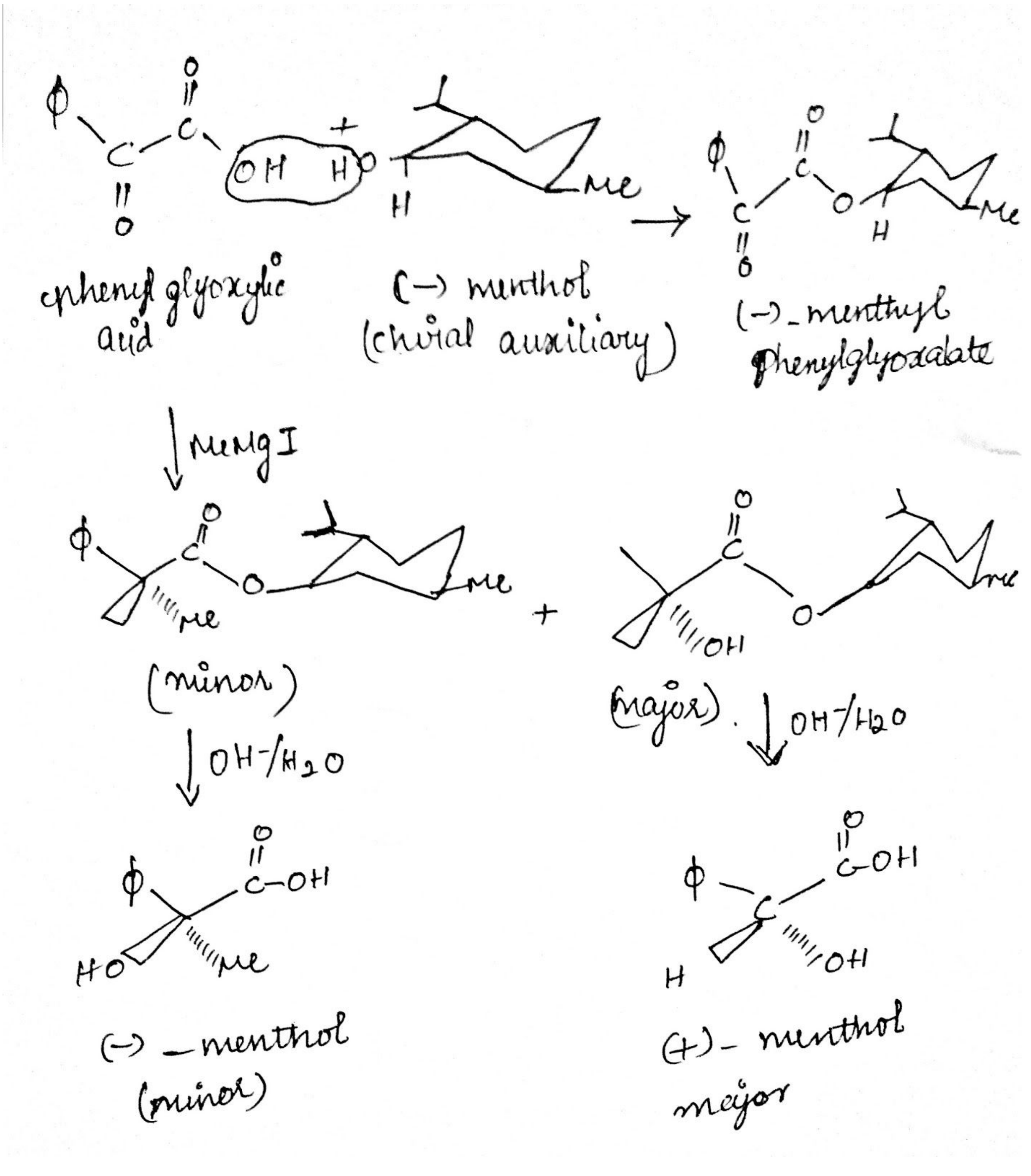
The steric course of addition to the carbonyl group is influenced by the adjacent chiral centre .Cram's rule accounts for the stereoselectivity of such relation.

II.Auxiliary controlled methods:

(Second generation)

a)The directing group,the chiral auxiliary is attached to the achiral substrate in order to direct the reaction and removed after the reaction.In the way ,a new chiral centre is generated in a molecule,already possessing chiral centre ,two diastereoisomers are formed in unequal amounts.

b)(E.g)asymmetric synthesis involving alpha-ketoester derived from chiral alcohols.



III.<u>Reagent controlled methods :</u>

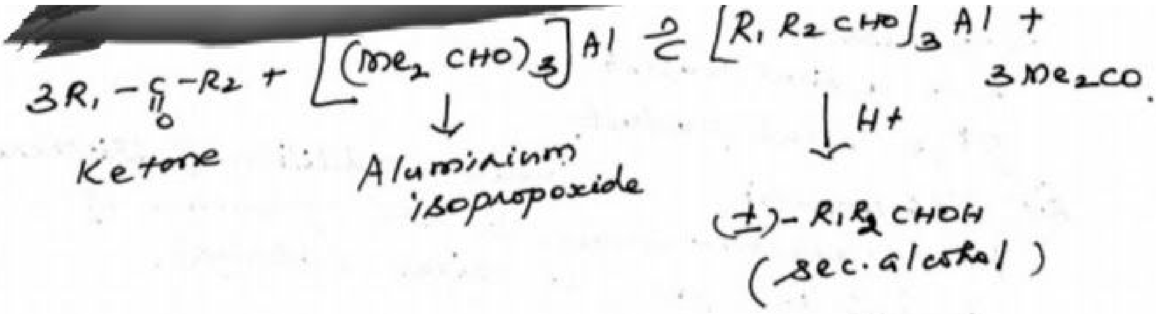
(Third generation methods)

In reagent controlled methods,an achiral substrate is directly converted into a chiral product by the use of a chiral reagent which exerts intermolecular control.

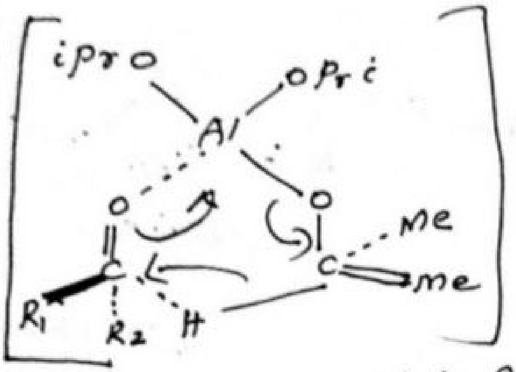
s------R*------>p*

(E.g)MPV reduction .By complexation with chiral ligand,hydride ion will be made chiral complex.

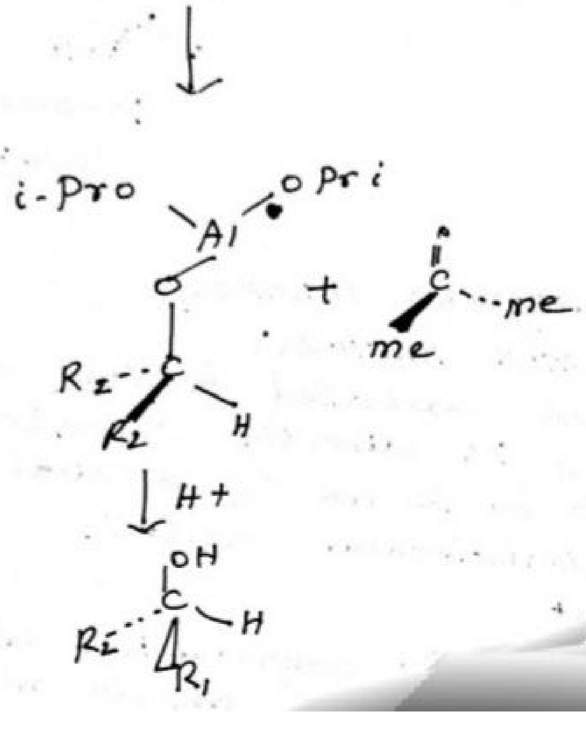
In this reduction ,the substrate aldehyde / ketone and the alkoxide one achiral,the reduction product is racemic (R&S),since the hydride ion can randomly be transferred to either face of the carbonyl group with equal facility.



$$3R_1-\underset{\underset{O}{\|}}{C}-R_2 + [(Me_2CHO)_3]Al \rightleftharpoons [R_1R_2CHO]_3Al + 3Me_2CO \xrightarrow{H^+} (\pm)\text{-}R_1R_2CHOH$$



Transition state of MPV



IV <u>Catalyst controlled methods:</u>

In this method,a chiral catalyst is used to convert an achiral substrate into a chiral product directly with an achiral reagent.

S------R------>P*

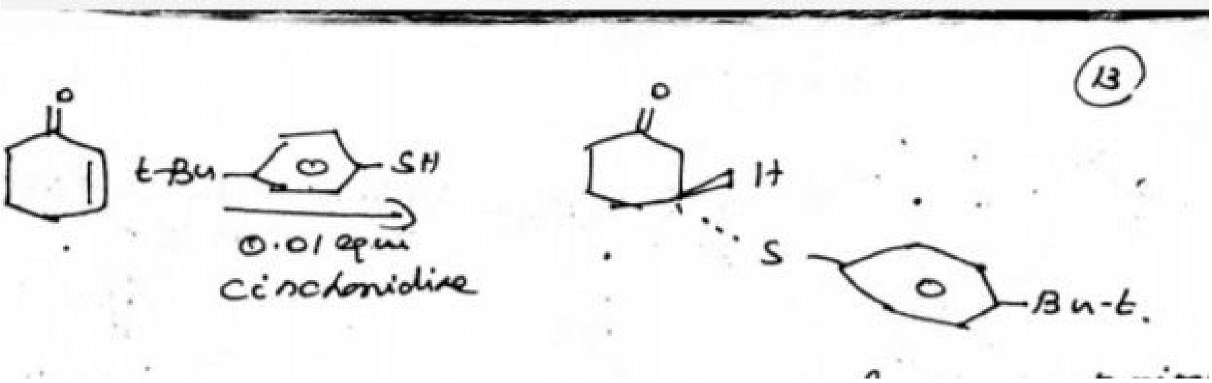
chiral catalyst

S------>Substrate,

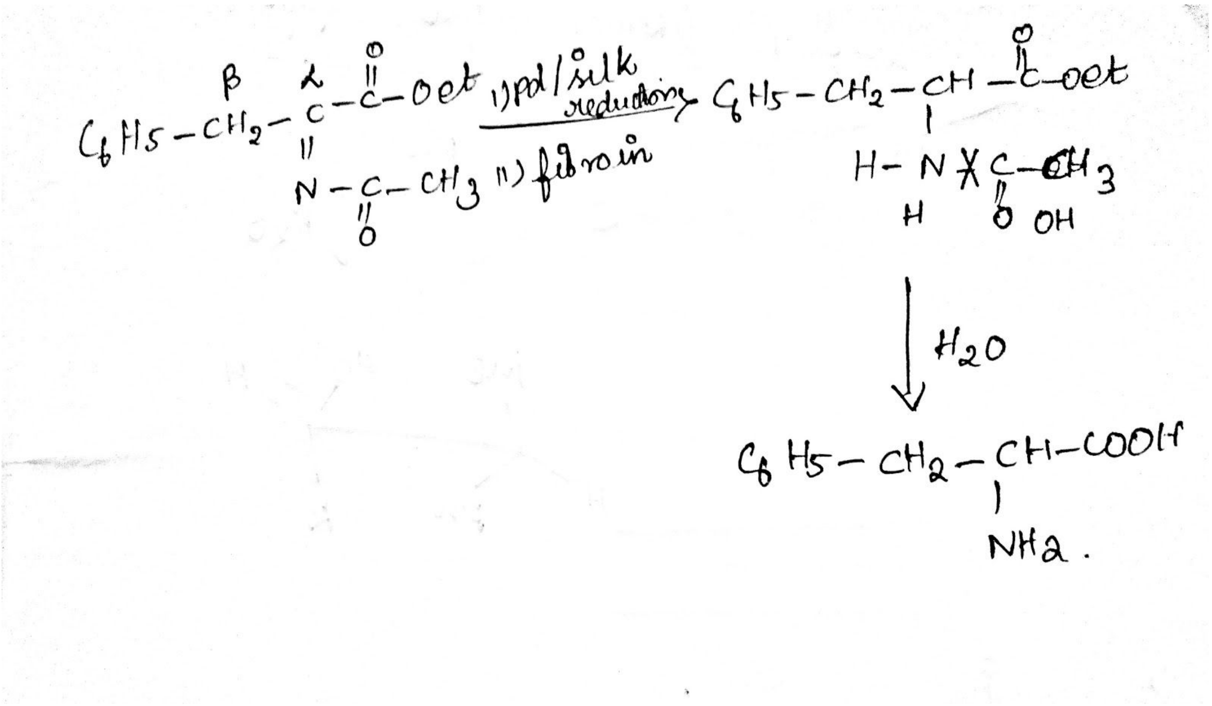
R------>achiral reagent,

P*---->chiral product.

(E.g)Asymmetric conjugate addition of thiophenol to cyclohexen-2-one in the presence of cinchmidine as a chiral catalyst.



The reaction of a ethyl-alpha-acteoximine-beta -phenyl pyruvate using pd catalyst supported by silk fibroin (optically active)followed by hydrolysis.



These methods include many enzyme catalysed transformations in which the catalyst can be recovered unchanged.

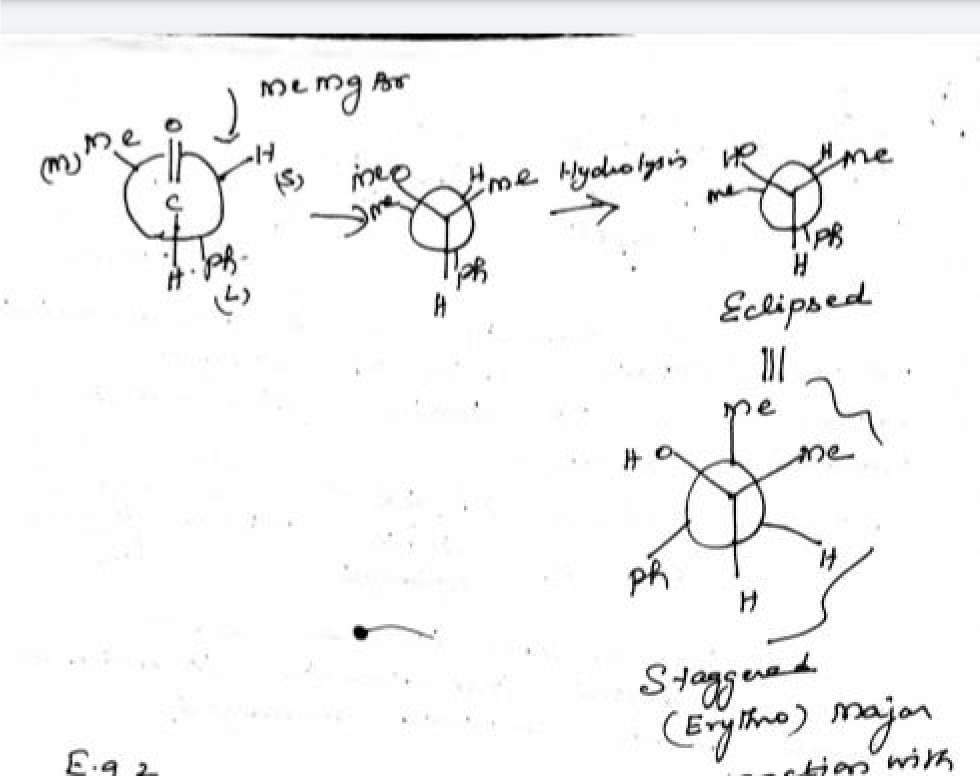
CRAM” S RULE

1). In a kinetically controlled addition to a carbonyl carbon atom , which has a chiral centre in the alpha- position , an anion attacks from the side containing the small group, when the chiral group is so oriented that the medium group is in the eclipsing position to the carbonyl.

2). Cram”s rule is useful to predict which diastereoisomer will predominate in certain additions to the carbon-oxygen double bond of aldehydes and ketones having a chiral carbon .

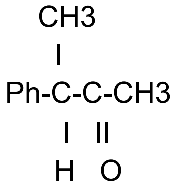
EXAMPLE; Optically active alpha - phenyl propionaldehyde (I) with grignards reagents yields the erythro compound as the major product compared to threo isomer.

Ph-CH-C-H
I II
CH3 O
alpha -phenyl propionaldehyde



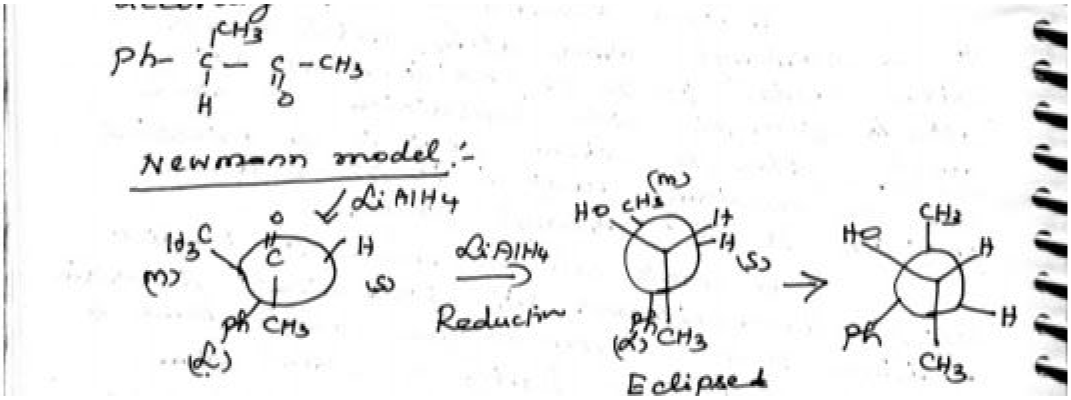
EXAMPLE-2

Alpha - phenyl- 2 butanone on reaction with LiAlH4 gives exclusively threo 70% according to CRAMS RULE.



$$Ph\text{-}\overset{\overset{CH_3}{|}}{\underset{\underset{H}{|}}{C}}\text{-}\underset{\underset{O}{||}}{C}\text{-}CH_3$$

NEWMANN MODEL;-



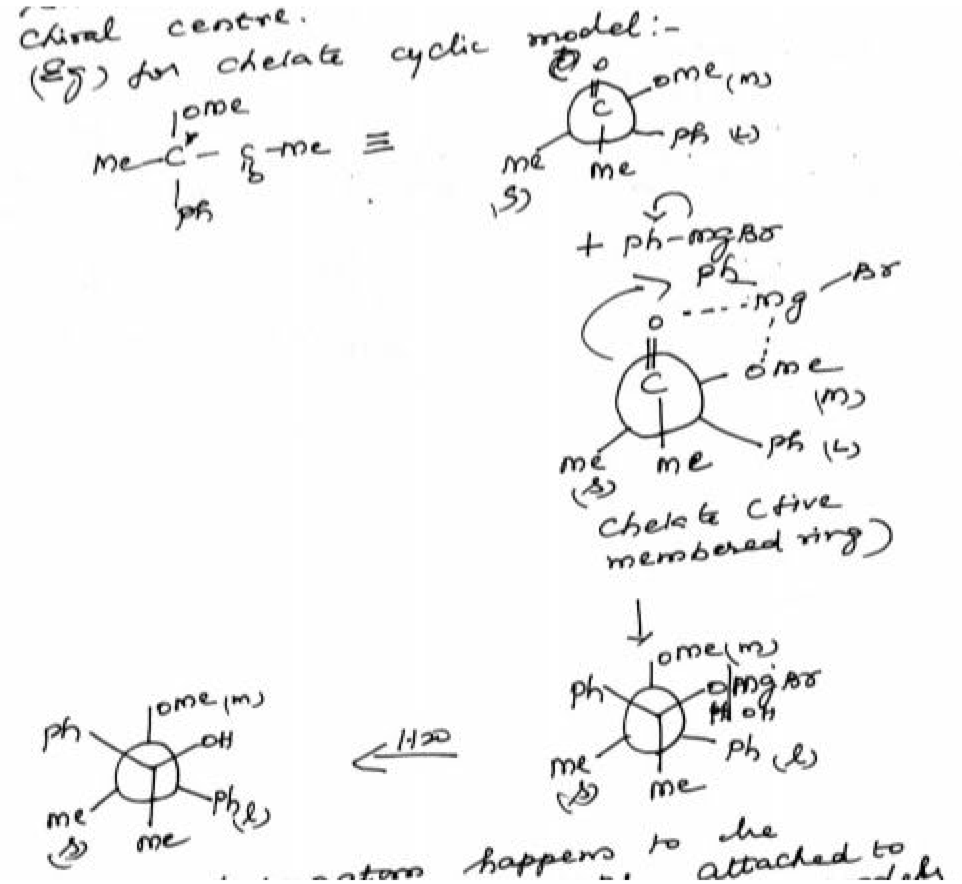
3). CHELATE CYCLIC MODEL;-

For substrate containing hetero atoms such as hydroxy amino and methoxy groups which can coordinate with organo metallic reagent , another model known as chelate model is proposed.

Organometallic reagent first coordinates with the hetero atom of the alpha- carbon atom and the carbonyl group to form five membered ring. As a result they occupy the eclipsed position or held syn-planar to each other.

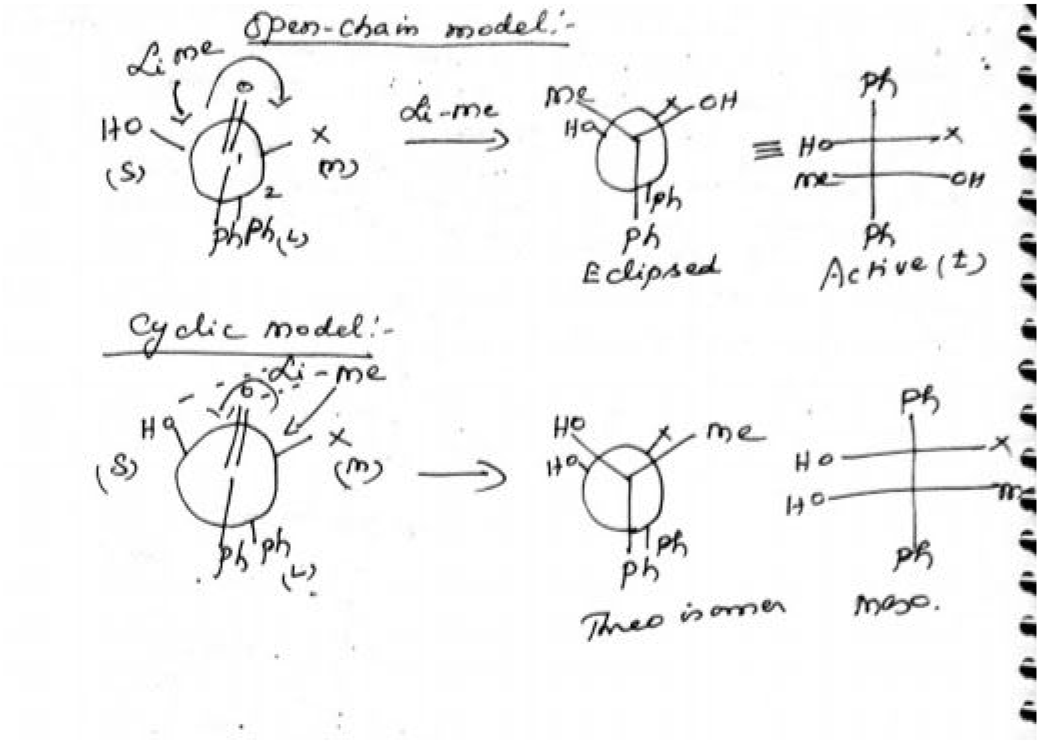
The organometallic reagent then approaches the carbonyl carbon from the side of the smaller of the groups attached to the chiral centre.

EXAMPLE;- for chelate cyclic model;-



- If the hetero atom happens to be medium sized of the groups attached to the asymmetric centre , then the two models give the same result , but if OH/NH2 group happens to be the smallest of the three groups attached to the alpha-chiral centre , the use of open chain model leads to errors . for example the major product of the following reaction is meso and not active +

OPEN CHAIN MODEL



ASYMMETRIC SYNTHESIS

3). BY USING CHIRAL REAGENT

REAGENT CONTROLLED PROCESS;-

Creation of a new chiral centre is an inactive (achiral) molecule can be accomplished with an active chiral reagent.

Achiral substrate + chiral reagent
(I) (II)
I

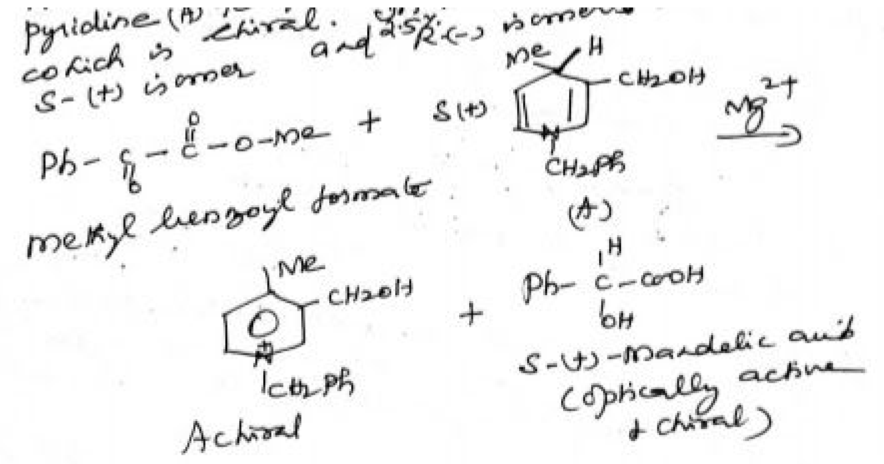
Chiral product + achiral reagent

(III) (IV)

Reactions like this, in which one reagent gives up its chirality to another are called as self immolative.

During this process , an inactive substrate is converted selectively to one of two enantiomers is called as enantioselective reaction and the process is known as asymmetric induction.

An example is the reduction of methyl benzoyl formate (achiral) with N-benzyl -3-(hydroxy methyl) -4- methyl-1,4-dihydro pyridine (A) to produce mandelic acid which is chiral . In this process 97.5% S-(+) isomer and 2.5 % R-(-) isomers are formed.



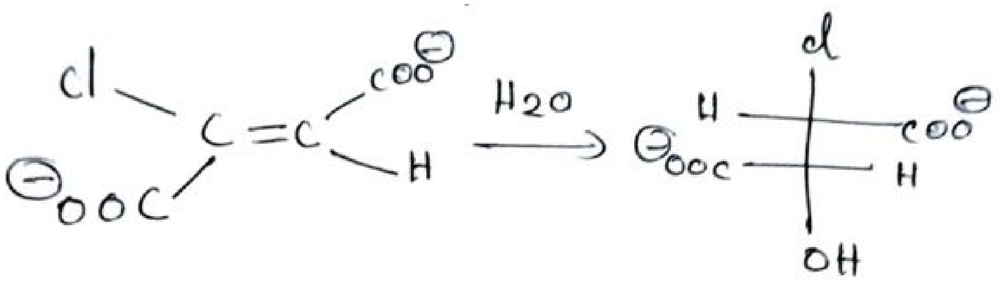
4). BY USING CHIRAL CATALYST.

Substrate (achiral) $\xrightarrow[\text{catalyst}]{\text{chiral}}$ chiral product

An inactive achiral substrate is converted substrate is converted into chiral product by the use of chiral catalyst .

EXAMPLE;-

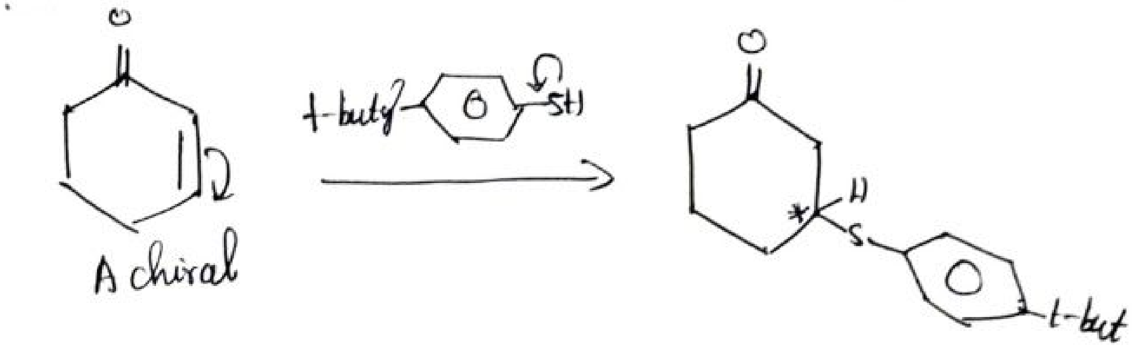
(i) conversion of chlorofumaric acid (is the form of its diion) to (-) -threo isomer of the diion of chloromalic acid by treatment with H2O and the enzyme fumarase



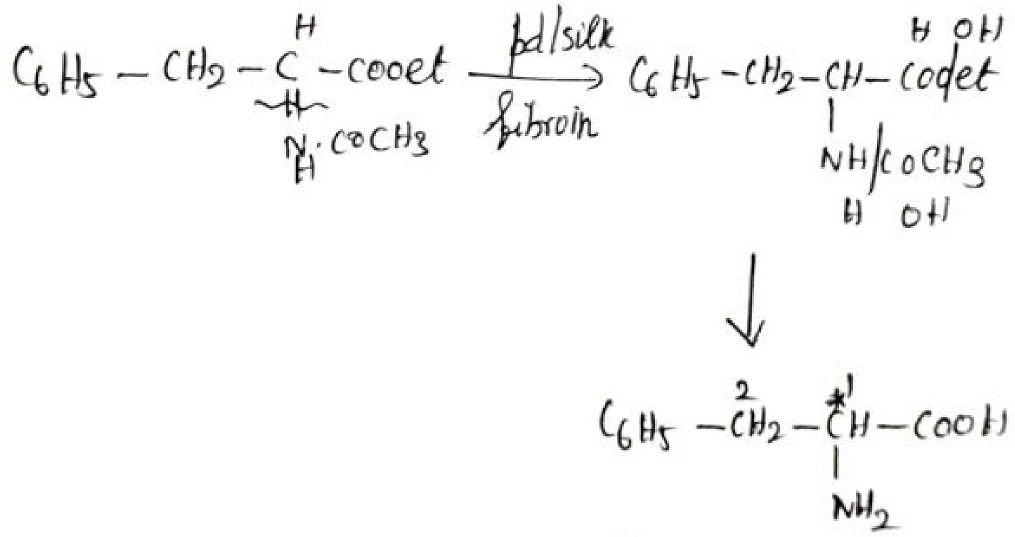
(-) -threo isomer

This is also an example of enantioselective reaction, since one of the enantiomers is formed in excess . And it is also an asymmetric induction reaction since achiral substrate is converted into chiral one.

(ii) Asymmetric conjugate addition of p-t-butyl thiophenol to cyclo hexene-2-one in the presence of cinchoxidine as a chiral catalyst .



(ii) The reaction of alpha- acetoximino- beta- phenyl ethyl pyruvate using Pd catalyst supported on silk fibroin (optically active) followed by hydrolysis.



$$C_6H_5-CH_2-\underset{\underset{\underset{H}{N}\cdot COCH_3}{\cancel{H}}}{\overset{H}{C}}-COOEt \xrightarrow[fibroin]{Pd/silk} C_6H_5-CH_2-\underset{\underset{H\ \ OH}{NH|COCH_3}}{CH}-\overset{H\ OH}{CO|Et}$$

$$\downarrow$$

$$C_6H_5-\overset{2}{C}H_2-\overset{*1}{C}H\underset{NH_2}{}-COOH$$

1-Amino-2-phenyl-propanoic acid

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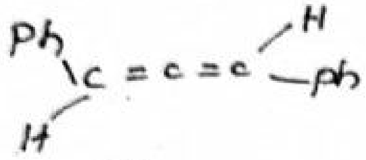
ORGANIC CHEMISTRY-I

ASSIGNMENT-I

Assign R/s configuration of the following compounds:-

1)



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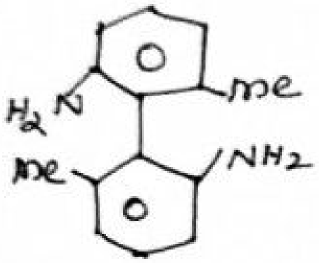
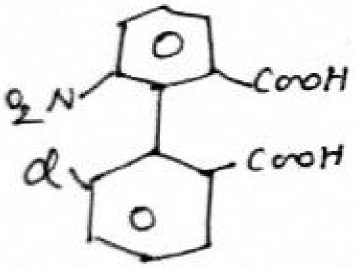


3.



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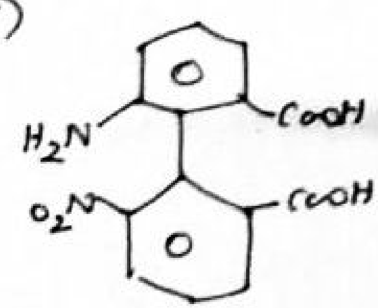
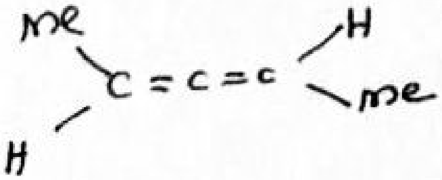
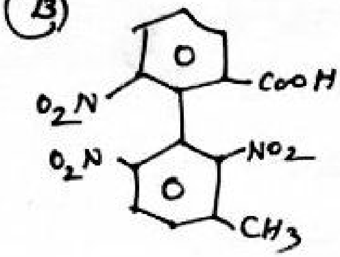


5)



⑧

⑬



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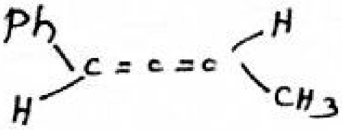

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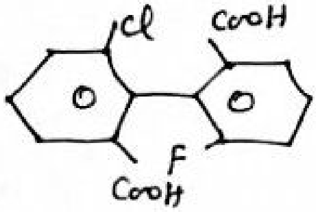
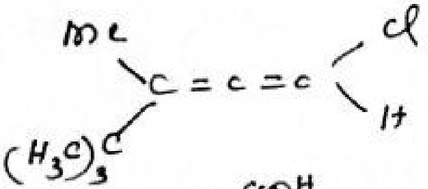


16)



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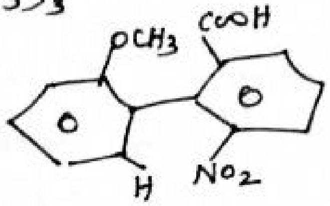

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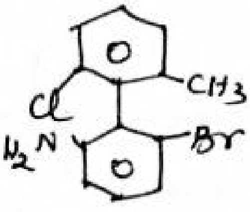

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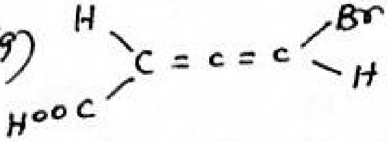

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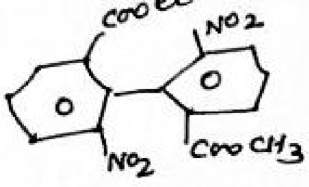
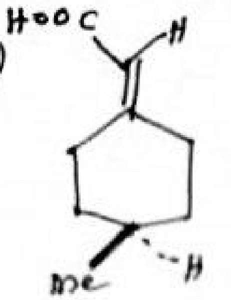
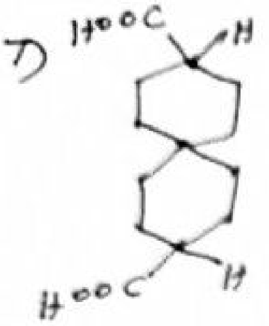


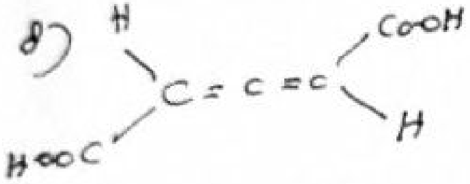
6)


HOOC
H
Me
H

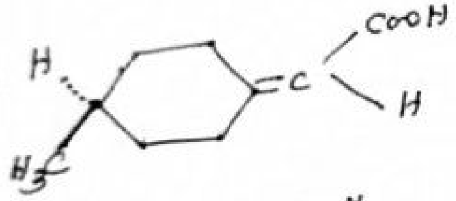
7)


HOOC
H
HOOC
H

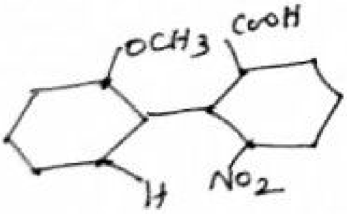
8)


H
COOH
C = C = C
HOOC
H

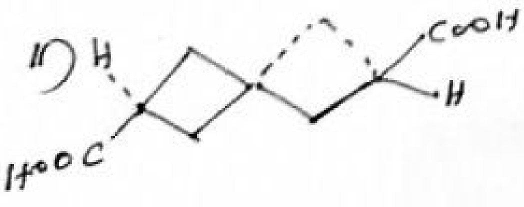
9)


COOH
H
C
H
H3C

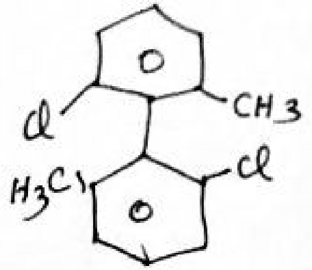
10)


OCH3
COOH
H
NO2

11)


H
COOH
H
HOOC

12)


Cl
CH3
H3C
Cl