

Stereochemistry II
SEM II
CBCS System



By

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Chirality arising out of stereoaxis:



Stereoisomerism of substituted cumulenes with even and odd number of double bonds; chiral axis in allenes, spiro compounds, alkylidenecycloalkanes and biphenyls; related configurational descriptors (*R_a/S_a*); atropisomerism; racemisation of chiral biphenyls.

Chirality of Organic Molecules without Chiral Centres:

There are organic molecules where stereoisomers originate due to other elements of chirality, namely chiral axis and chiral planes. Two most important classes of compounds with molecular chirality in the absence of chiral centres are –

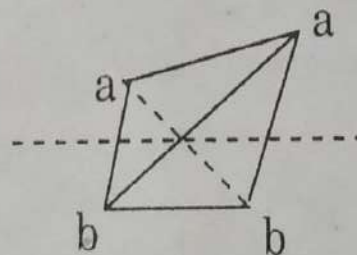
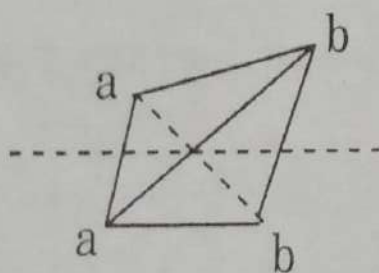
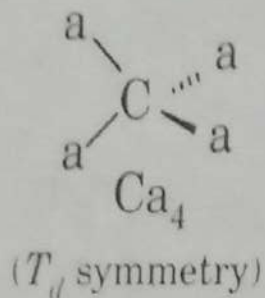
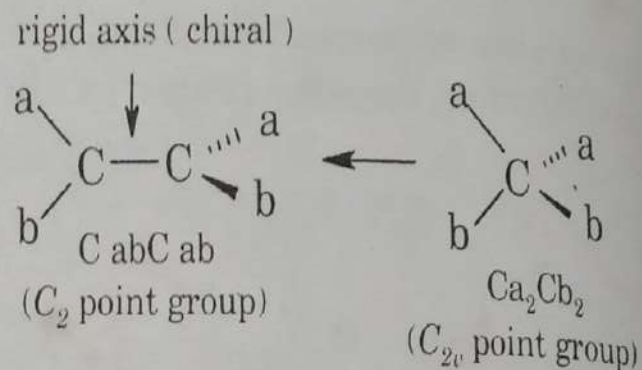
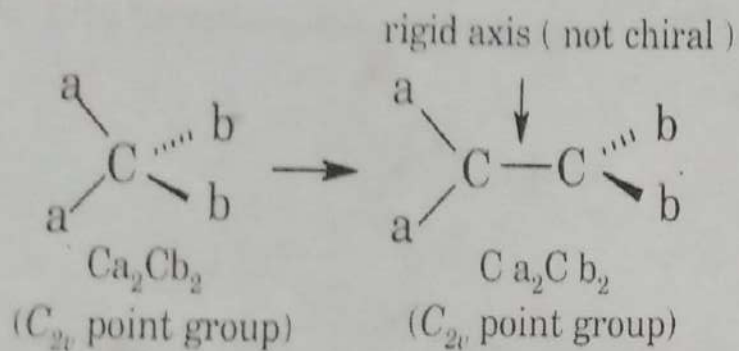
1. Appropriately substituted cumulenes with even number of double bonds.
2. Substituted biphenyls having restricted rotation about C-C σ bond joining the two rings.

* Certain alkylidenecycloalkanes and spiranes also exhibit molecular chirality.



Stereoisomerism of substituted cumulenes

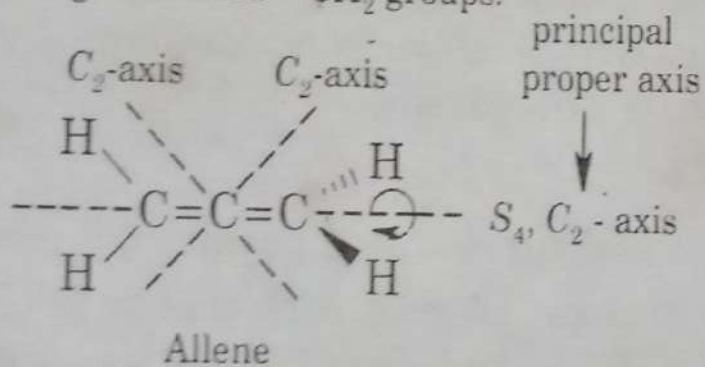
BASIC STEREOCHEMISTRY OF ORGANIC MOLECULES



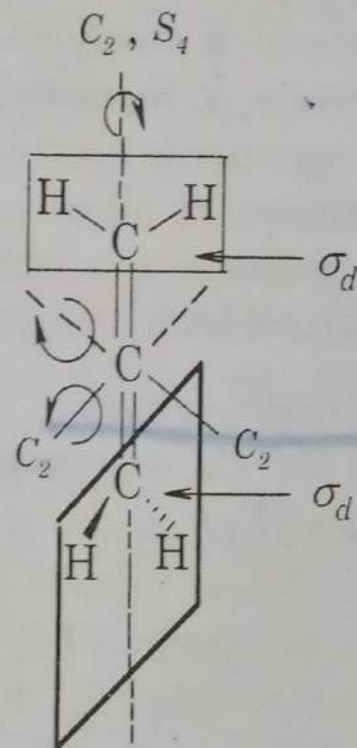
Stereochemistry of Allenes:

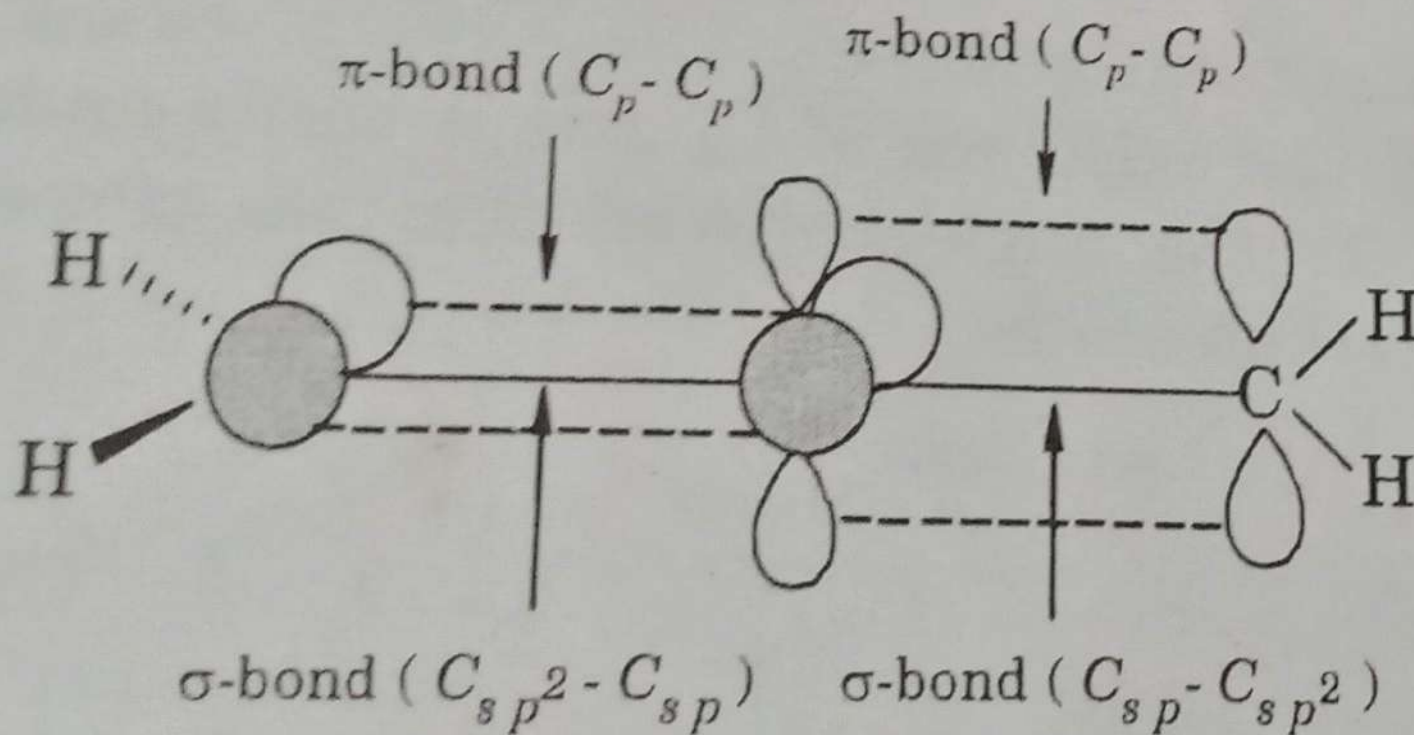


These C_2 axes pass through the plane bisecting the planes passing through terminal $=CH_2$ groups.



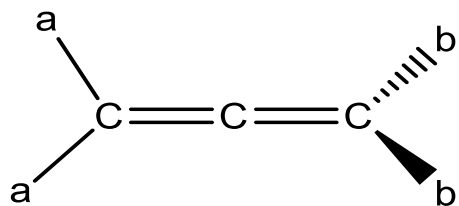
≡



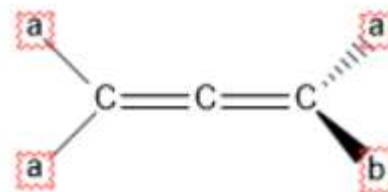


Orbital picture of allene

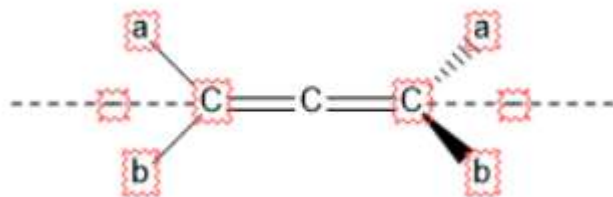
Chiral axis in allenes



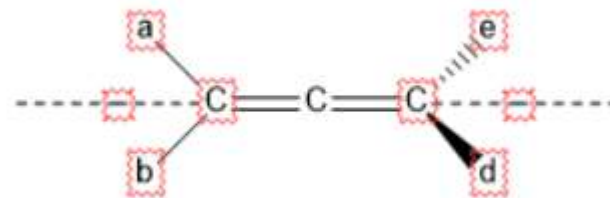
Has two σ planes perpendicular to each other



Has one σ plane



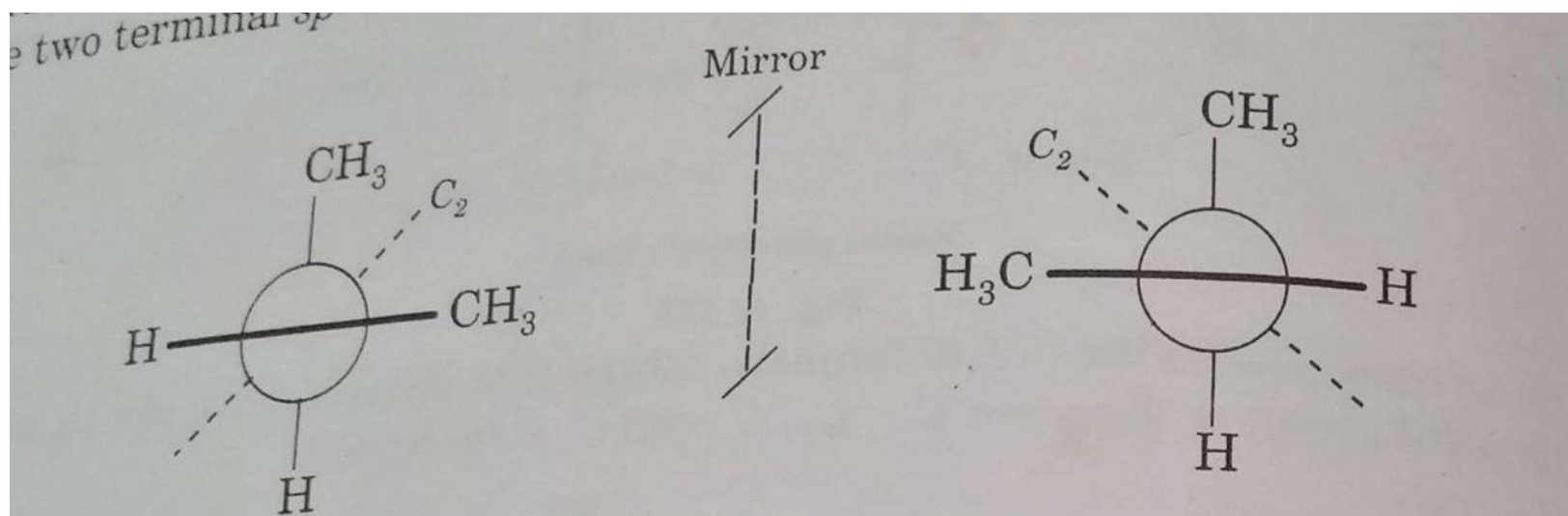
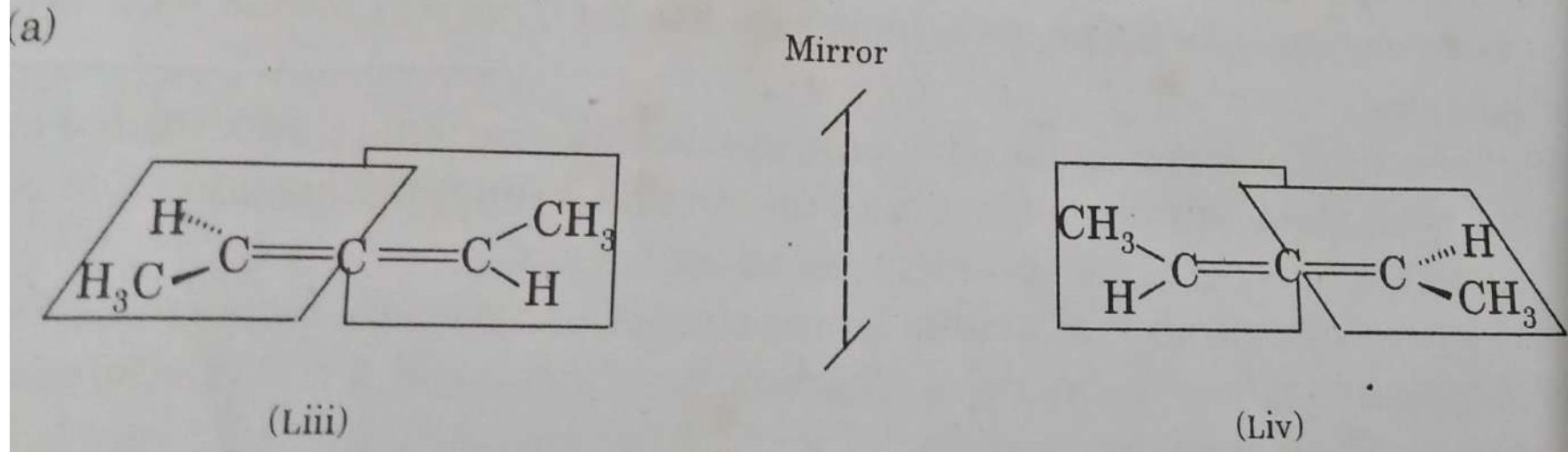
Only C_2 -axis



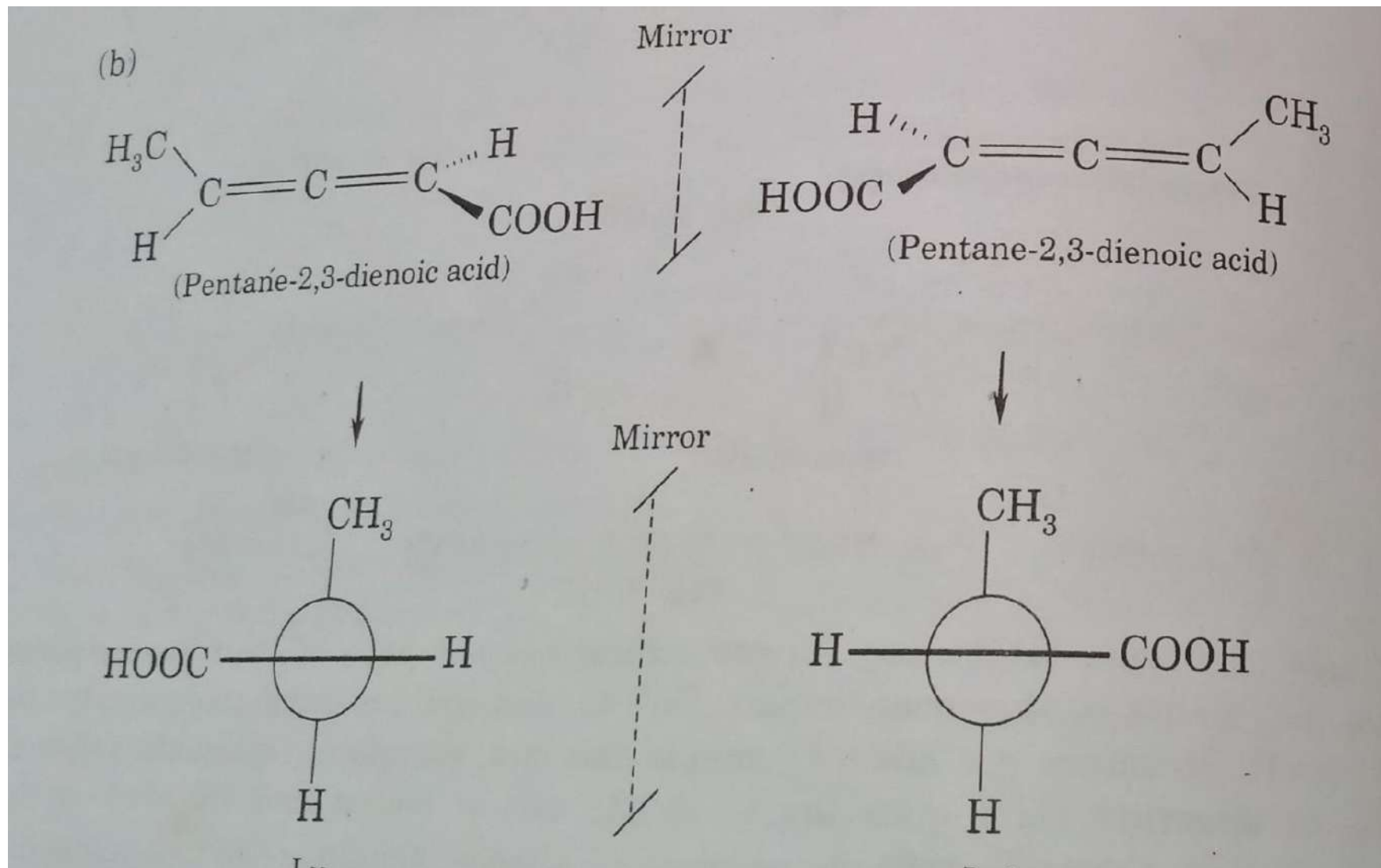
C_1 - axis only



Examples of dissymmetric allenes:



Example of asymmetric allene:



Key Points:

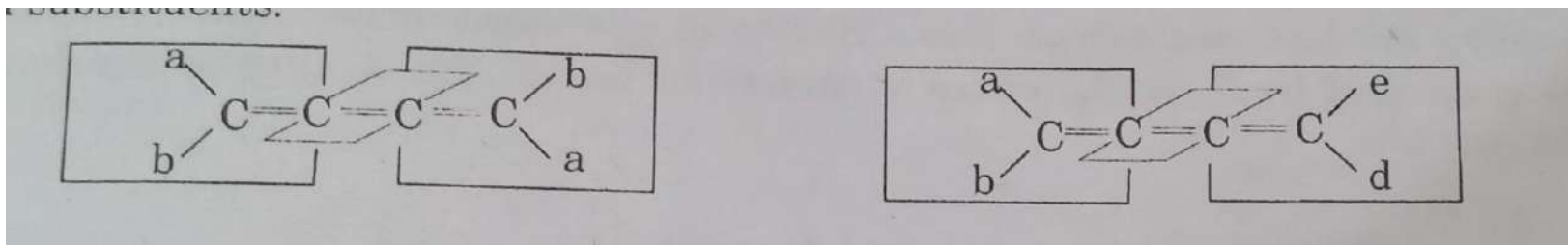
1. Cumulenes with even number of double bonds exhibit enantimorphism, if each of the terminal sp^2 carbon atoms contain non-identical substituents.
2. Cumulenes with even number of double bonds cannot exhibit cis-trans isomerism



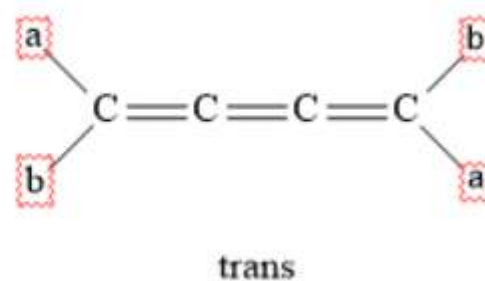
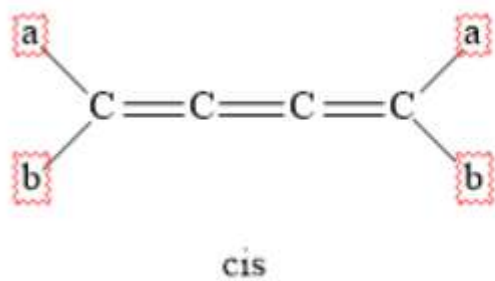
These allenes are not cis-trans diastereoisomers but enantiomers



3. Cumulenes with odd number of double bonds never exhibit enantiomorphism.

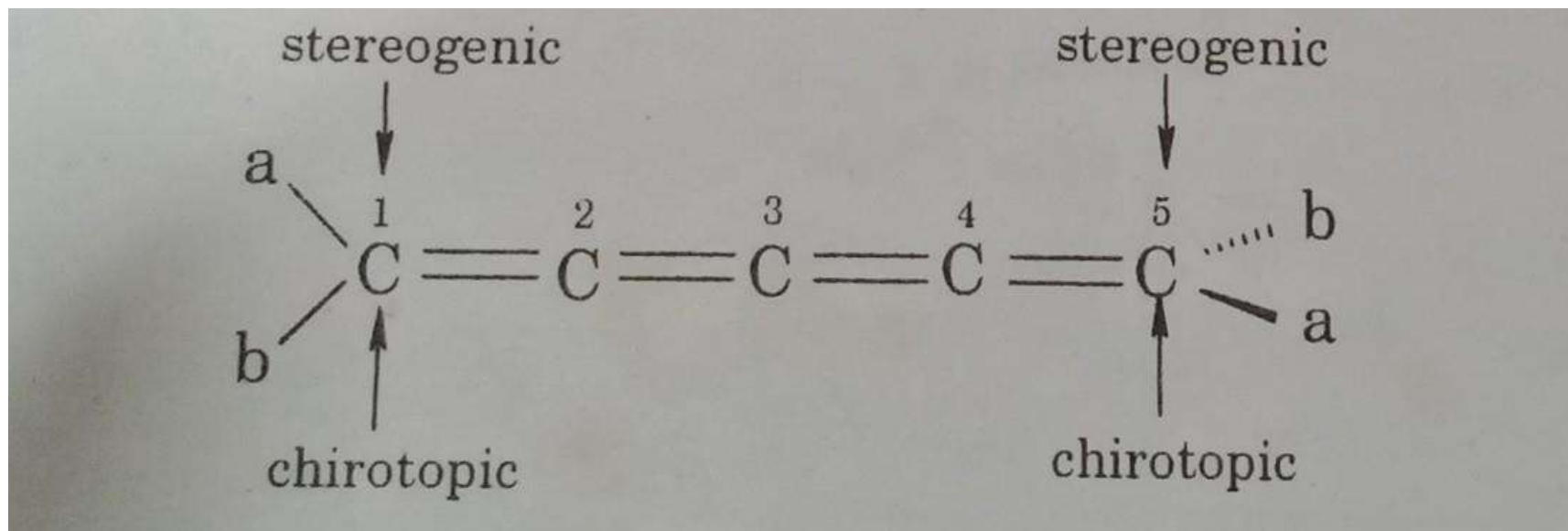


However, cumulenes with odd number of double bonds show cis-trans isomerism.

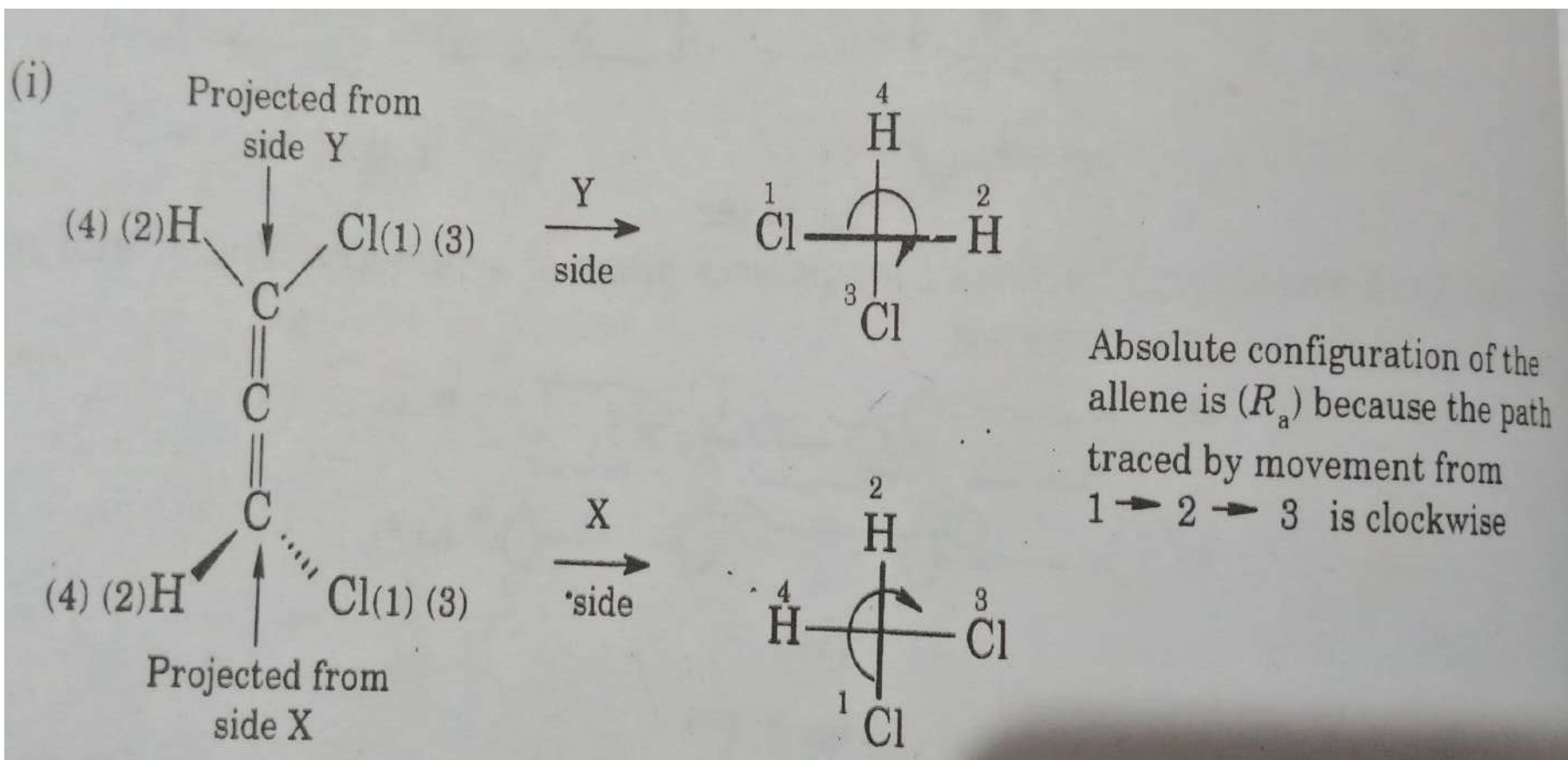


4. Terminal carbon atoms of cumulenes with even number of double bonds are chirotopic and stereogenic, provided each of these terminal carbons contain non-identical atoms.

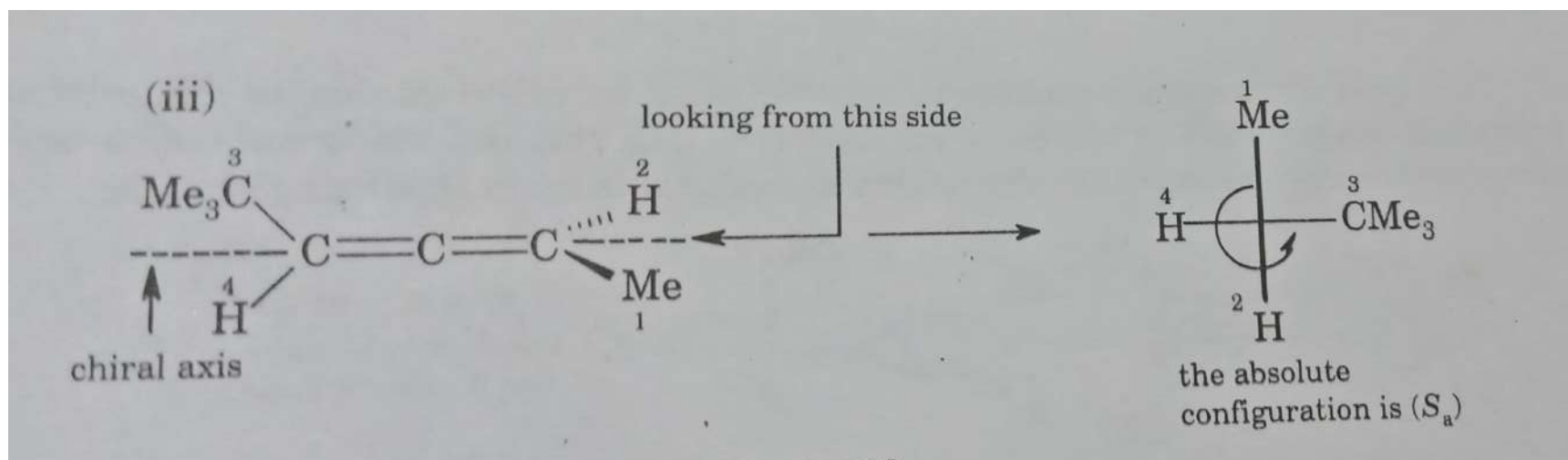
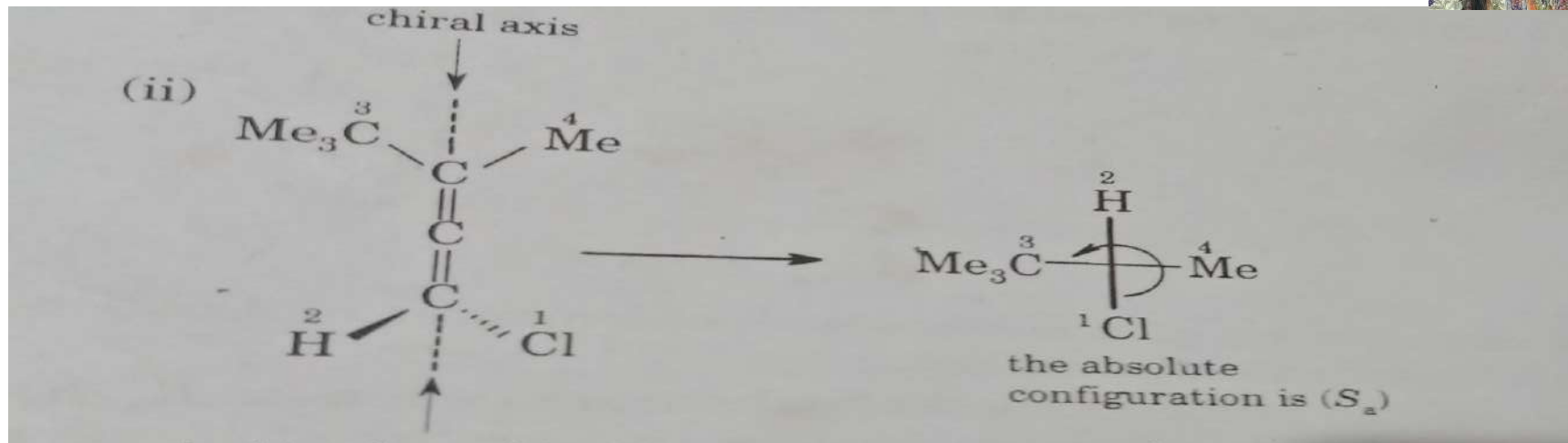
5. Terminal carbon atoms of cumulenes with odd number of double bonds are also stereogenic, but achirotopic.



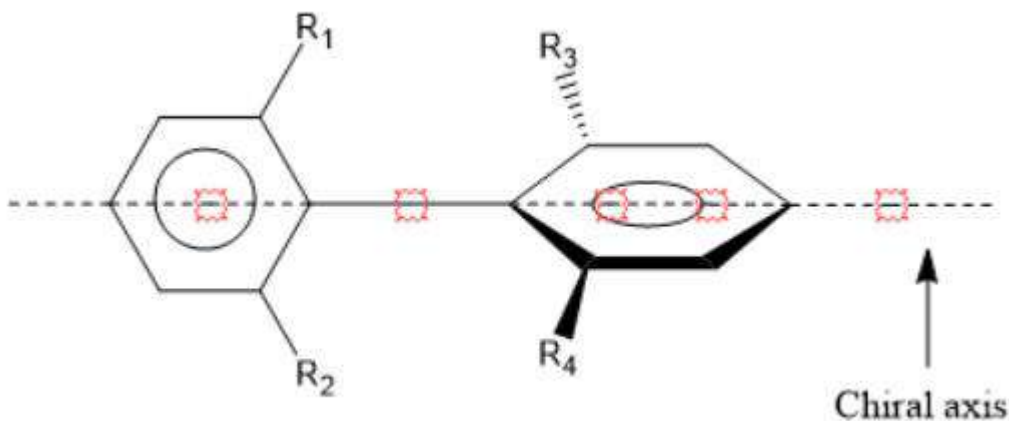
Configurational descriptors (R_a/S_a)



Examples:

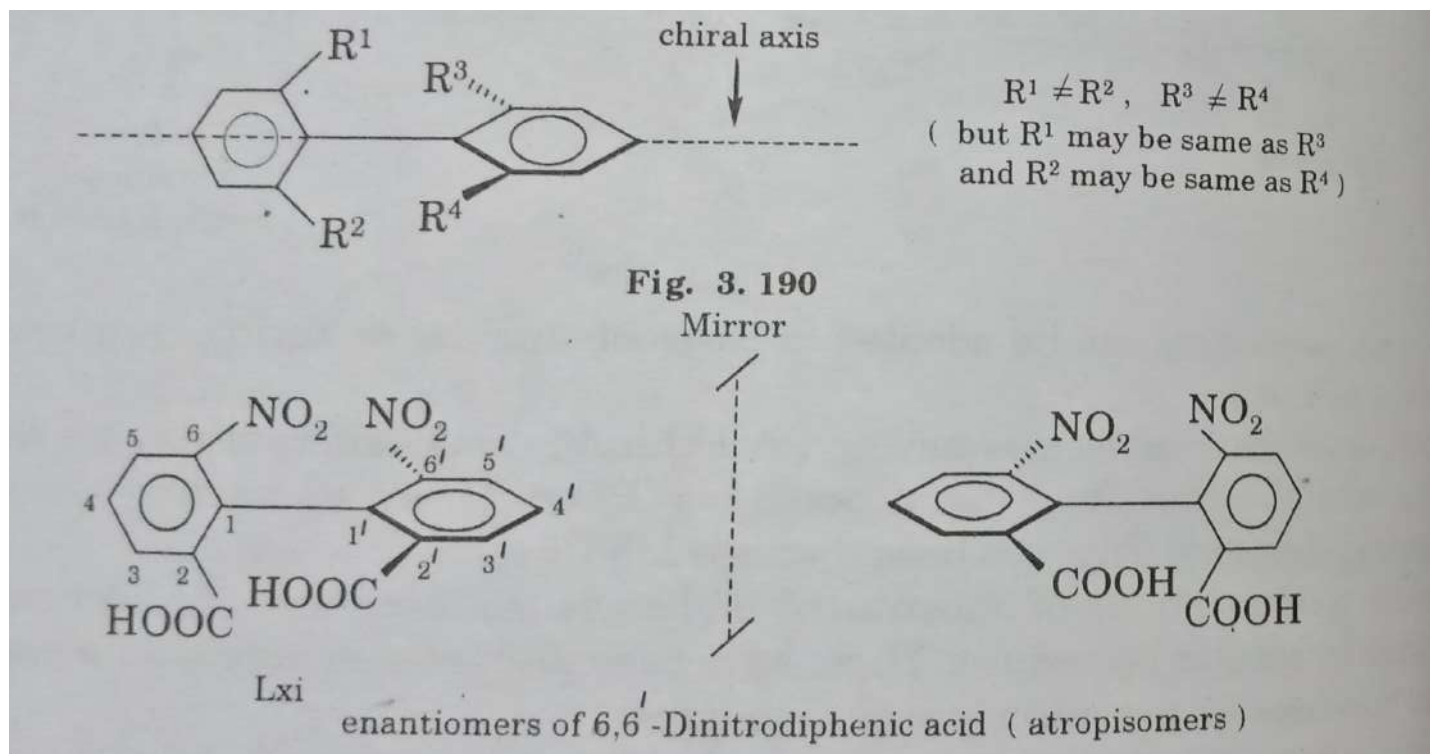


Atropisomerism: Conformational Chirality:



- Atropisomerism – a German word – meaning no rotation.
- It is a special type of stereoisomerism due to restricted rotation around C-C single bond.
- This type of isomerism was first detected in the compounds of biphenyl series.
- The steric interaction between the ortho substituents prevent rotation of the aromatic rings.
- In this situation, the preferred conformations are those in which the aromatic rings are perpendicular to each other.
- Then the minimum energy conformers are enantiomeric and the isomers can be isolated under usual experimental conditions.

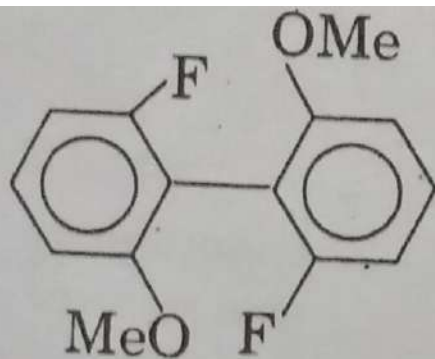
Biphenyl Isomerism



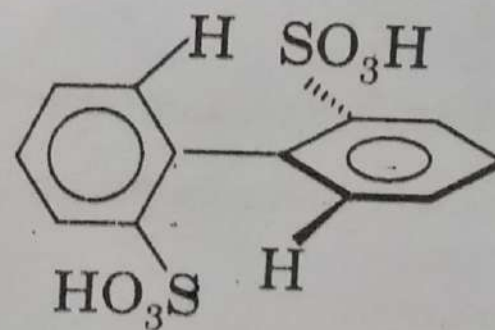
Definition:

The type of isomerism that owes its existence due to inhibited rotation around a single bond is called *atropisomerism* and the isolable enantiomers are called *atropisomers*.

Extent of Steric Interaction:

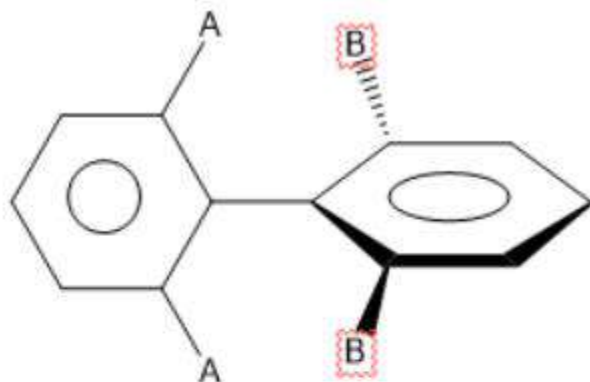


2,2'-Difluoro-6,6'-dimethoxybiphenyl
nonresolvable

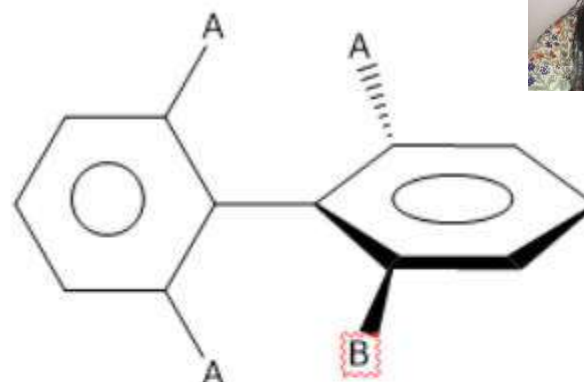


Biphenyl-2,2'-disulphonic
resolvable

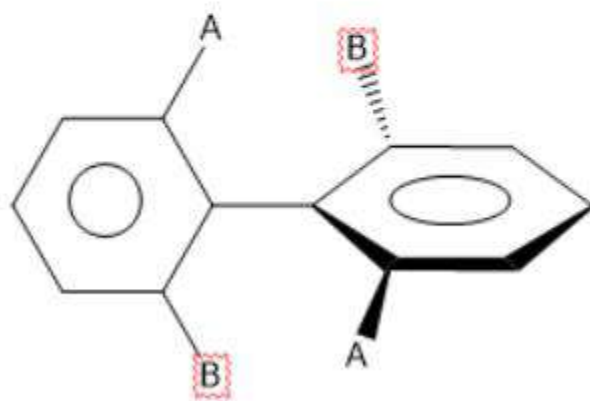
Different types of ortho-substituted biphenyls:



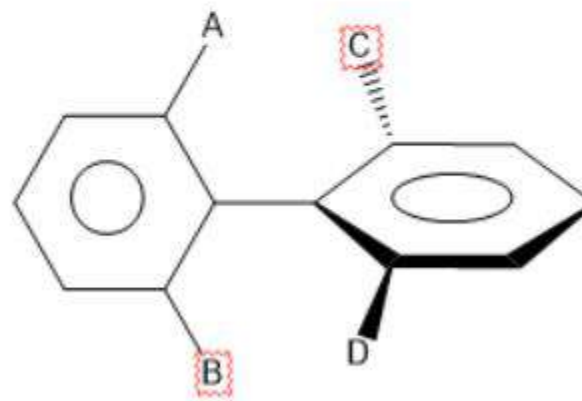
i (inactive) - C_{2v}



ii (inactive) - C_s

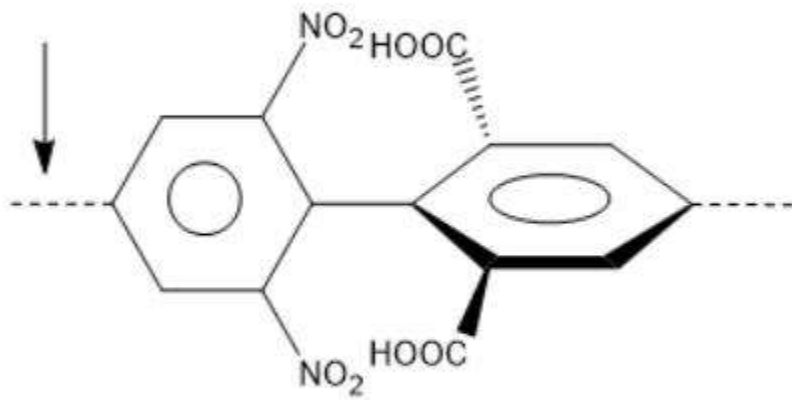


iii (active) - C_2



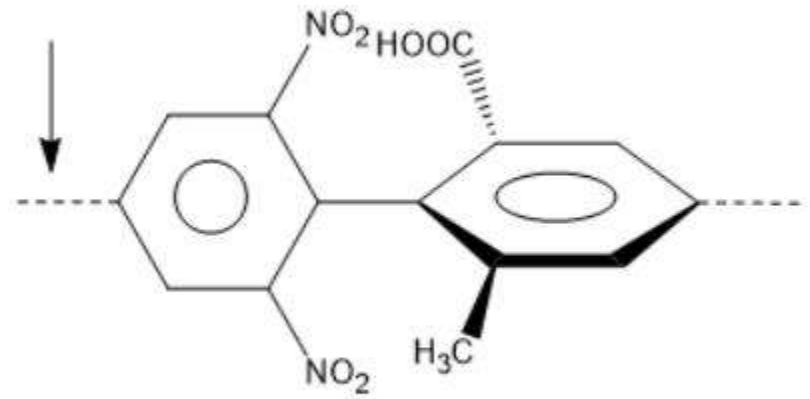
iv (active) - C_1

bisecting plane



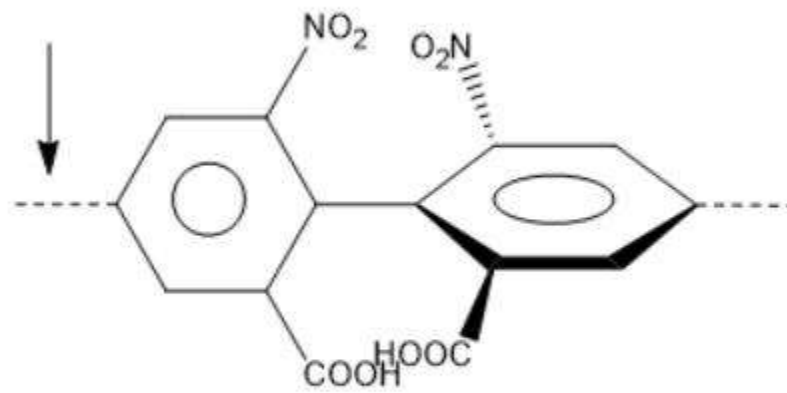
i (inactive)

bisecting plane



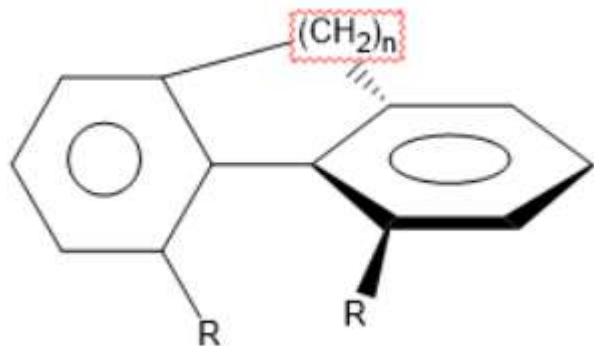
ii (inactive)

bisecting plane



iii (active)





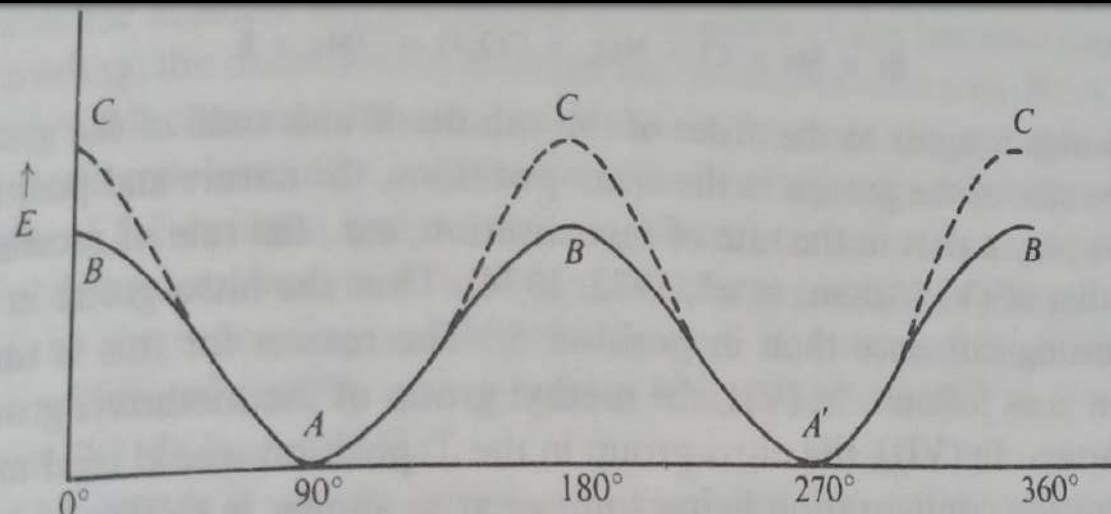
Biphenyls with 2 and 2' positions bridged with rings of various sizes can also exhibit atropisomerism. Biphenyls of this type, where $n > 2$ are always optically active.

Comparison between cumulenes and biphenyls:

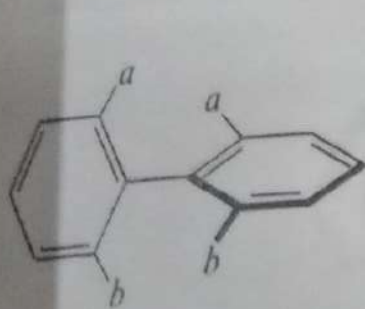
1. Both cumulenes and biphenyl derivatives exhibit enantiomerism due to presence of chiral axis.
2. Like substituted cumulenes with even number of double bonds, biphenyl derivatives having perpendicular rings do not exhibit cis-trans isomerism.
3. One fundamental difference between them is that enantiomorphism of biphenyl derivatives (atropisomers) may cease to exist with rise of temperature due to thermal racemisation.
4. Cumulenes are optically more stable than atropisomers.



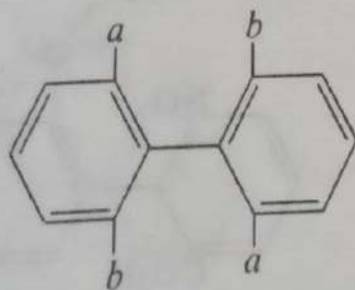
Racemisation of Biphenyl compounds: Energy Profile Diagram



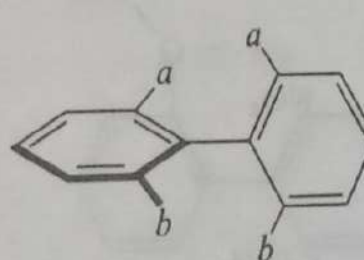
Dihedral angle



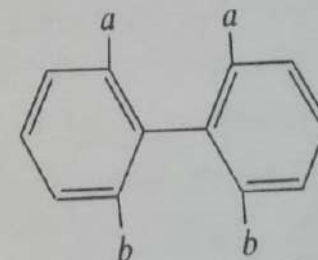
(A)



(B)

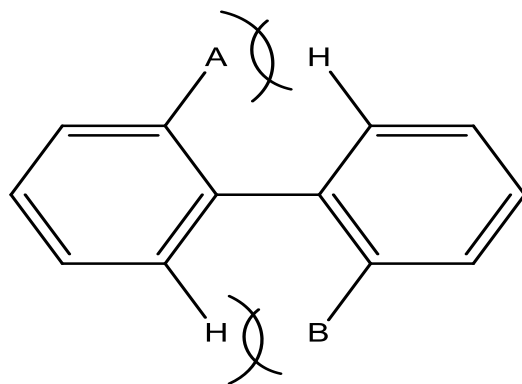


(A')



(C)

Recemisation of Chiral Biphenyls:



- In case of chiral biphenyls, chirality comes to exist due to the restricted rotation.
- If free rotation of the two rings is allowed then we get equimolecular amount of non-separable d- and l-isomers.
- The ortho-substituents interfere in the transition state for racemisation.

Interference for free rotation can be minimised by following manners –

- Bending the ortho substituents away from each other.
- compressing of ortho bonds.
- Stretching the inter-annular bonds.
- Deforming the angle between the benzene and the inter-annular bonds.
- Deforming the benzene rings themselves.

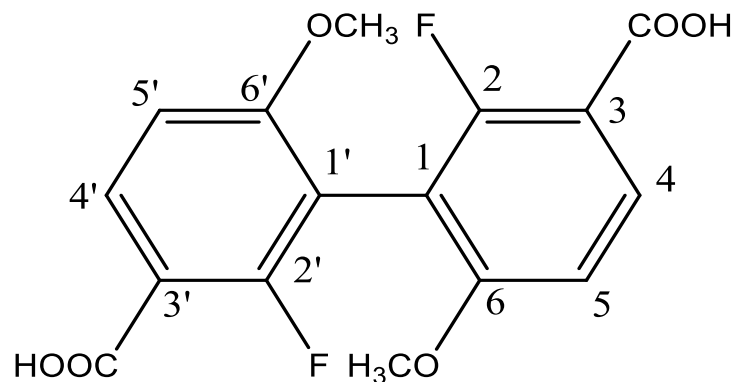
Classification:

2,2',6,6'-Tetrasubstituted biphenyl compounds may be classified under three headings according to the nature of the substituent groups:

(1) Non-resolvable:

These contain any of the following groups: H, -OMe or F.

The volumes of these groups are too small to prevent rotation about the single bond.



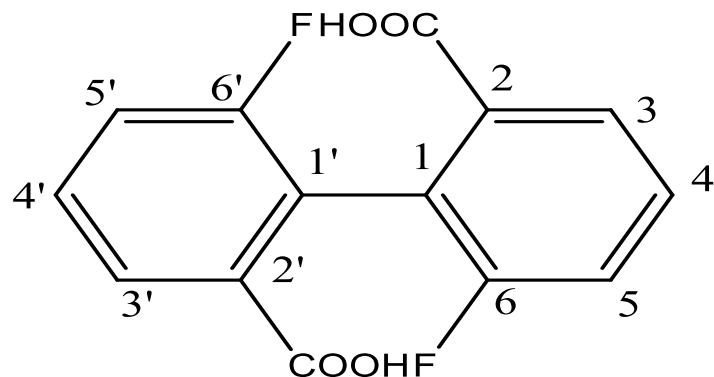
2,2'-difluoro-6,6'-dimethoxybiphenyl-3,3'-dicarboxylic acid

non-resolvable



2) Resolvable, but easily racemised:

These must contain at least two amino groups, or two carboxyl groups, or one amino and one carboxyl group; the remaining groups may be any of those given in (1), but not hydrogen.

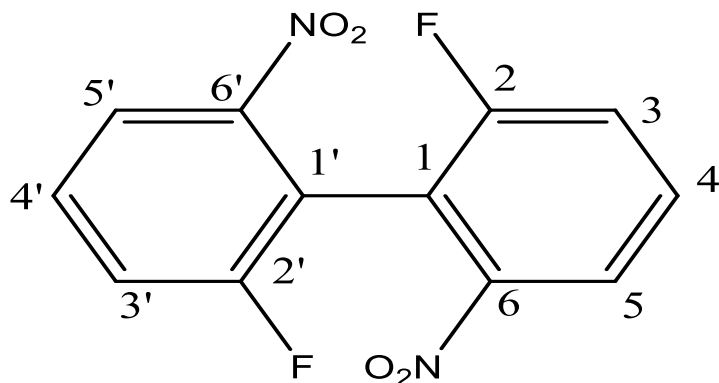


6,6'-difluorodiphenic acid
resolvable and easily racemised



3) Not racemisable at all:

These compounds contain at least two nitro groups; the remaining groups may be any of those given in (1), but not hydrogen and (2).

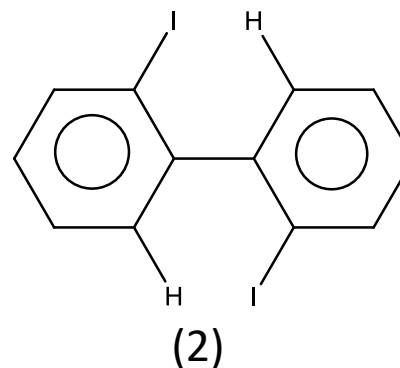
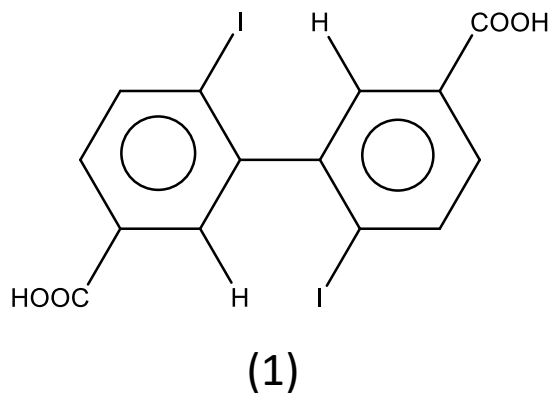


2,2'-difluoro-6,6'-dinitrobiphenyl
resolvable and cannot be racemised

The order of steric hindrance produced by various groups is –



Buttressing Effect:



Definition:

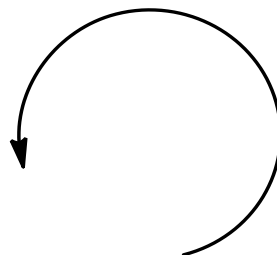
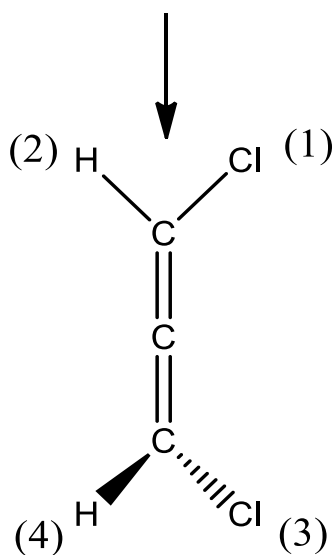
When a substituent is present at the meta position with respect to the σ bond joining the two rings, activation energy for racemisation of chiral biphenyls is enhanced. This is called buttressing effect.

- Buttressing effect occurs due to prevention of the outward bending of the ortho substituents,
- The magnitude of this effect depends on the size of the meta substituent.
- The compound (1) has higher activation energy of racemisation of about 21 kcal/mole than compound (2).

Configurational descriptors (R_a/S_a):



Looking from this side



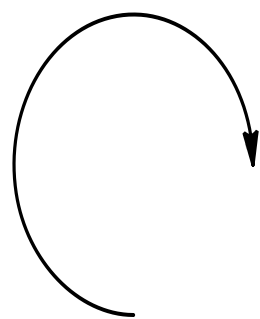
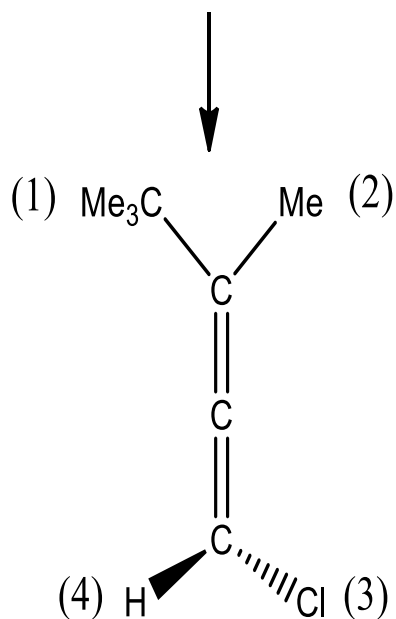
Anticlockwise

So it should be S_a

But as the lowest priority group is above the plane,

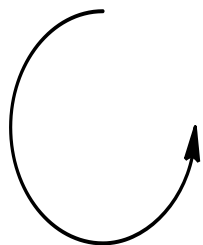
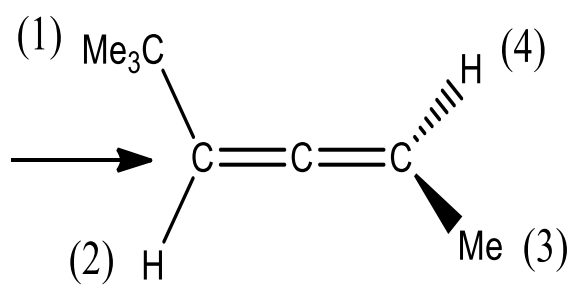
The configuration is R_a

Lowest priority group must be below the plane.



1 → 2 → 3
clockwise rotation

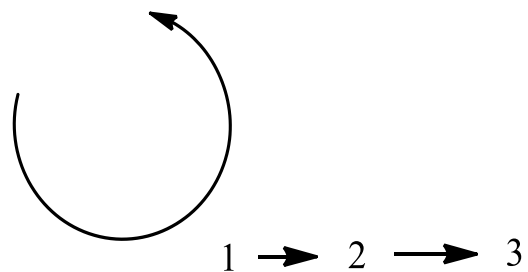
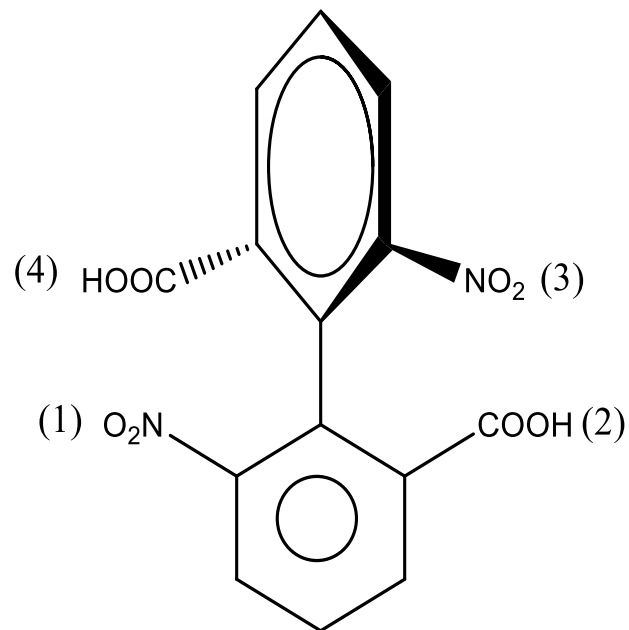
but as the lowest priority group is above the plane,
the configuration is S_a



1 → 2 → 3
Anti-clockwise rotation

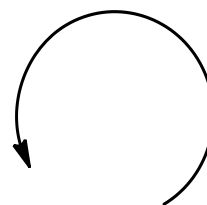
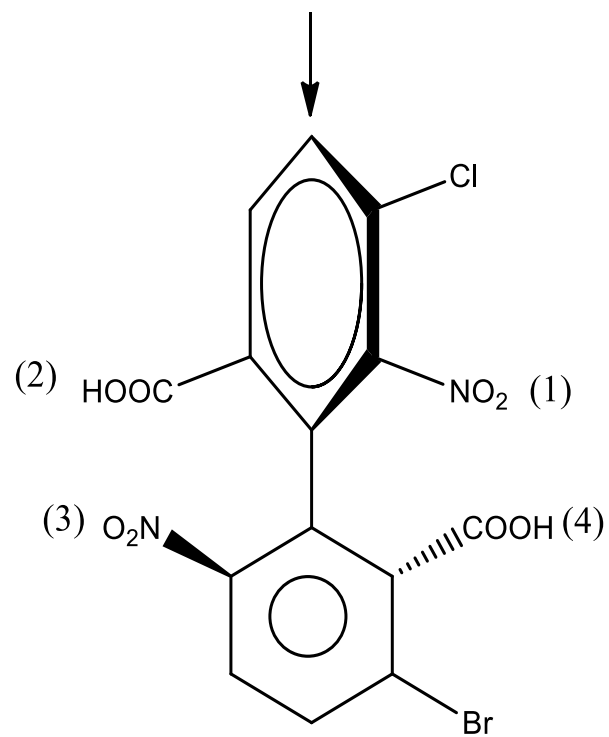
and as the lowest priority group is below the plane,
the configuration is S_a

Configurational Nomenclature of Active Biphenyl Derivatives



Anti-clockwise rotation

and as the lowest priority group is below the plane,
the configuration is S_a

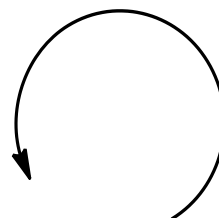
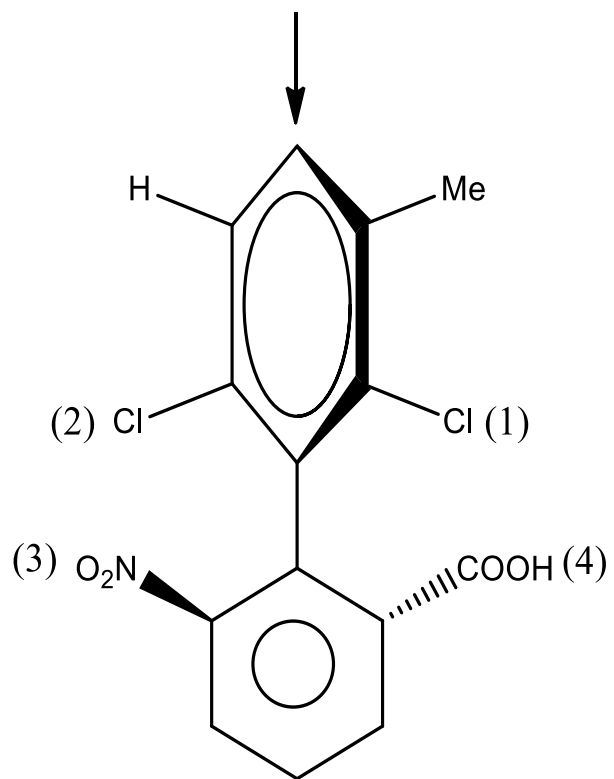


1 → 2 → 3

Anti-clockwise rotation

and as the lowest priority group is below the plane,
the configuration is S_a



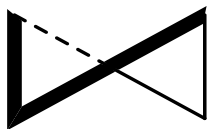


1 → 2 → 3

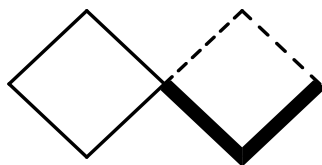
Anti-clockwise rotation

and as the lowest priority group is below the plane,
the configuration is S_a

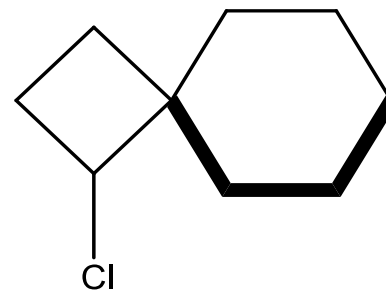
Stereoisomerism of spiro compounds:



spiro[2.2]pentane



spiro[3.3]heptane

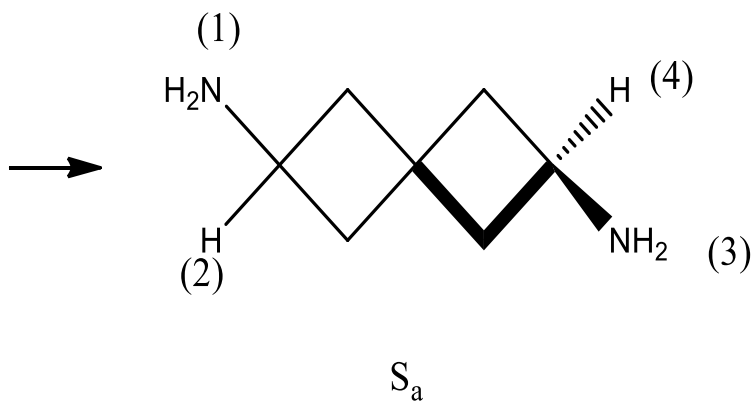
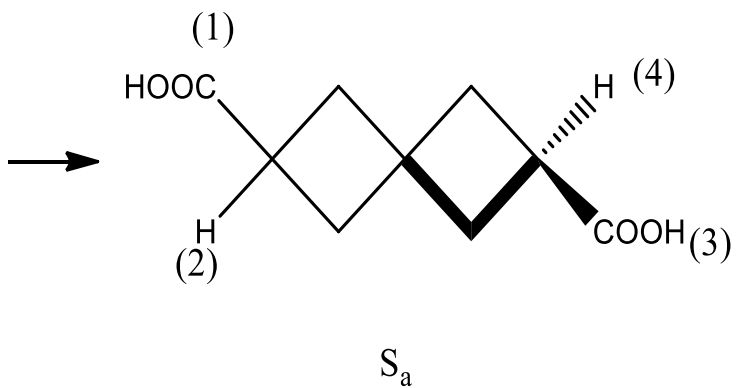


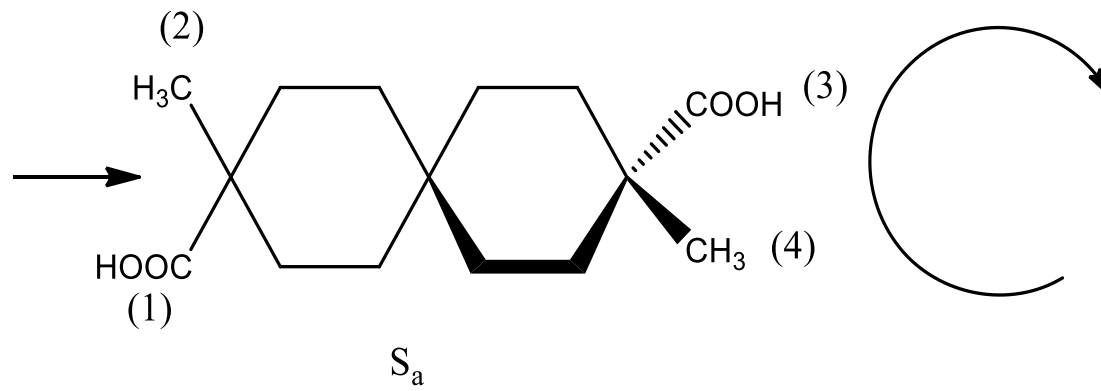
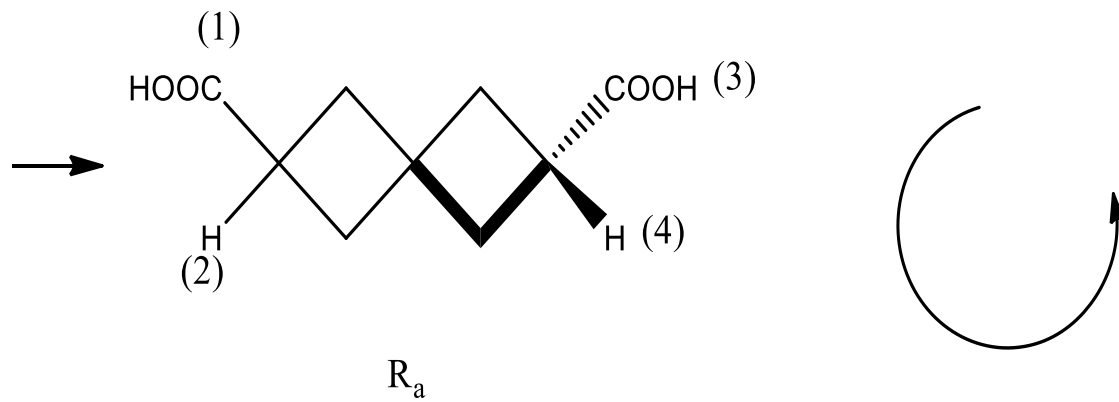
1-chlorospiro[3.5]nonane



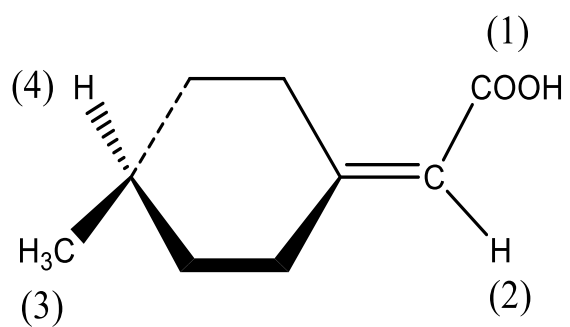
- two or more rings are joined by common tetrahedral carbon or other atoms
- 'spiro' has been taken from the Latin word *spira* meaning twist
- spiro-hydrocarbons are called 'spiranes'
- spiro compounds are nonplanar and their structural characteristic is primarily responsible for their chirality.

Specification of Absolute Configuration:





Alkylidenecycloalkanes :



R_a

4-methylcyclohexylideneacetic acid

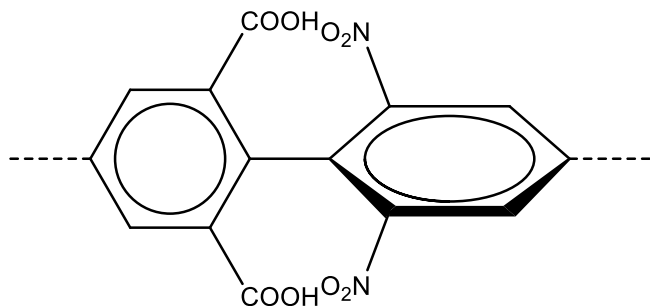
PROBLEMS



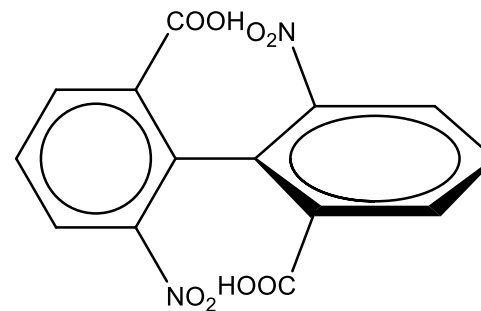
C.U. 2015

3.b) Comment on the chirality of the following compounds.

2

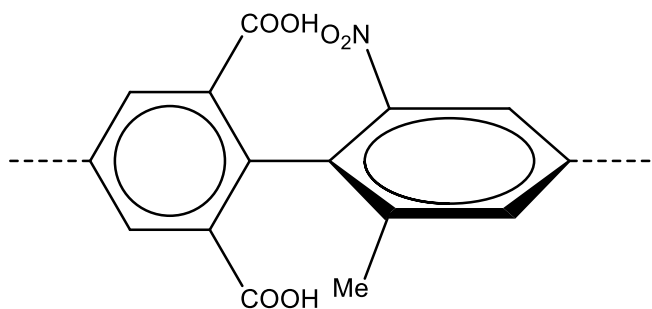


This molecule is optically inactive, as there are two σ planes present in the molecule containing the molecular planes of each ring. It has C_{2v} point group.

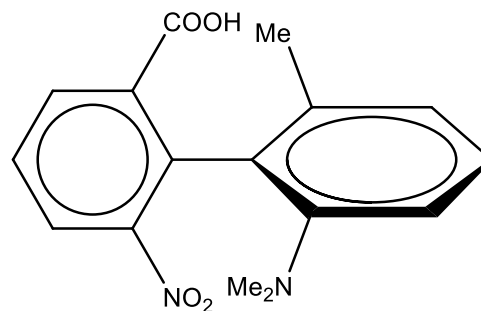


It is optically active, as it has only a C_2 axis, but no σ planes. It has C_2 point group. It is a dissymmetric molecule.





It is optically inactive, as it has a σ plane which bisects the first phenyl ring of the molecule into two equal halves and contains the molecular plane of the second ring. It has C_s point group.

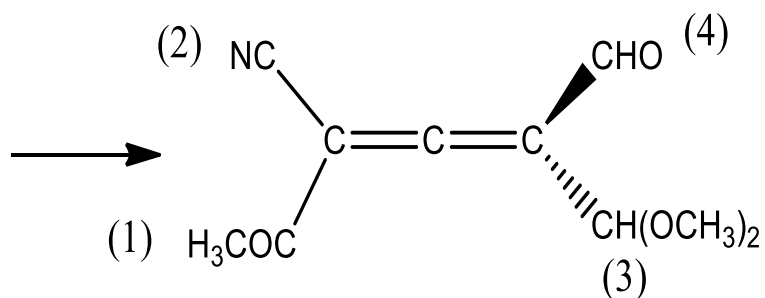
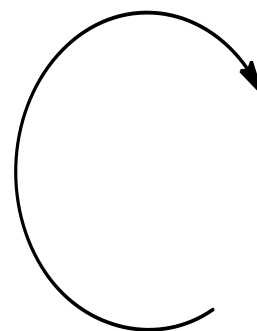


It is optically active, as it has no element of symmetry except a C_1 axis. It is an example of an asymmetric molecule with C_1 point group.



1.a.iii) Assign the following compound with R/S descriptor.

1

 S_a 

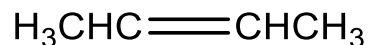
1-2-3 clockwise rotation. but as the lowest priority group is above the plane, so configuration will be S_a



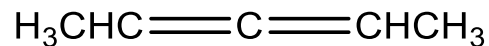
C.U.2013

4.b) Isomers of compound I differ widely in chemical properties, but those of compound II do not – why?

2

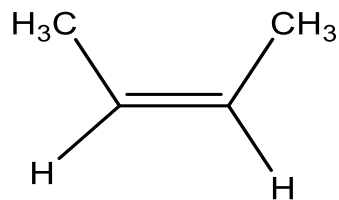


(I)

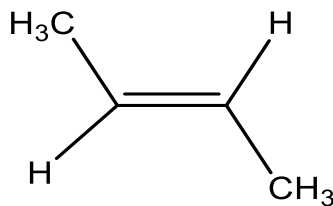


(II)

Compound (I) shows geometrical isomerism, i.e. it can exist as cis trans isomer. So isomers of compound (I) differ widely in chemical properties. But substituted allenes (II) with even number of double bonds never show geometrical isomerism. So their chemical properties are also very similar.

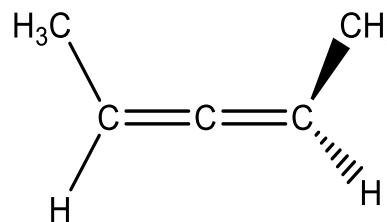


cis

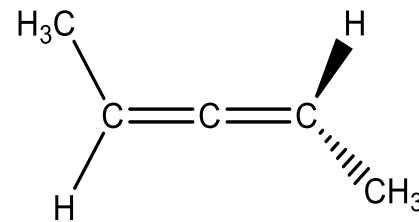


trans

(I)



S_a



R_a

II

C.U.2012

4.a) Explain the following with suitable example:

1.5

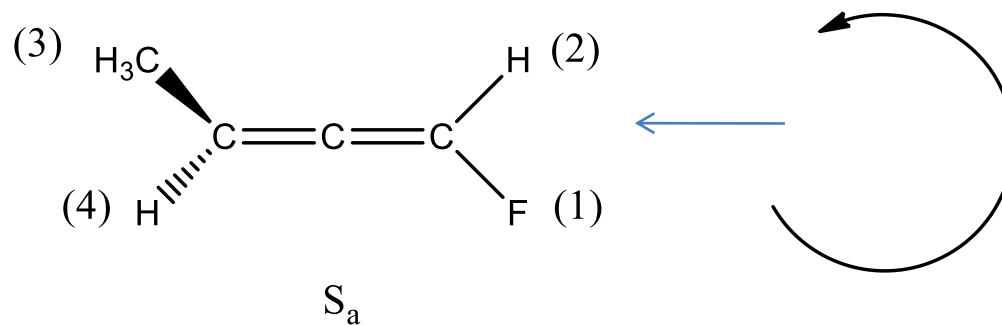
ii) Atropisomerism

Ans: Discussed before.

C.U. 2011

1.a) Assign R/S descriptor to the following compound:

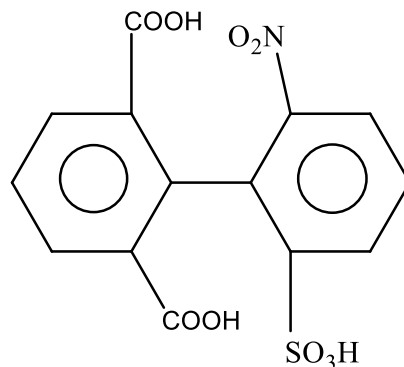
1



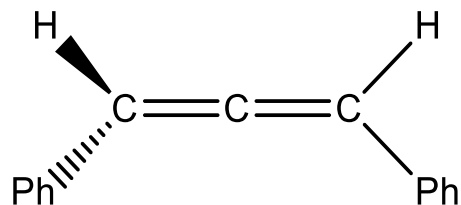
C.U.2011

2.a) Explain whether the following compounds are resolvable or not:

1



This compound is resolvable, as free rotation is restricted due to the presence of the four bulky substituents at the ortho position.

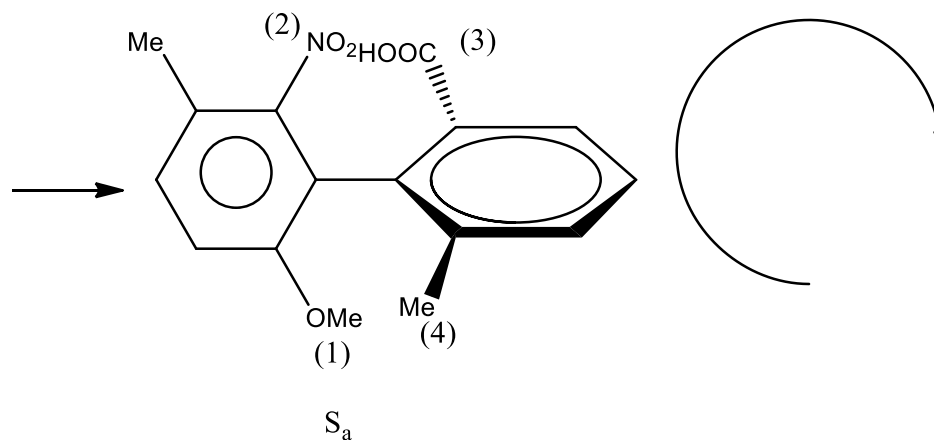
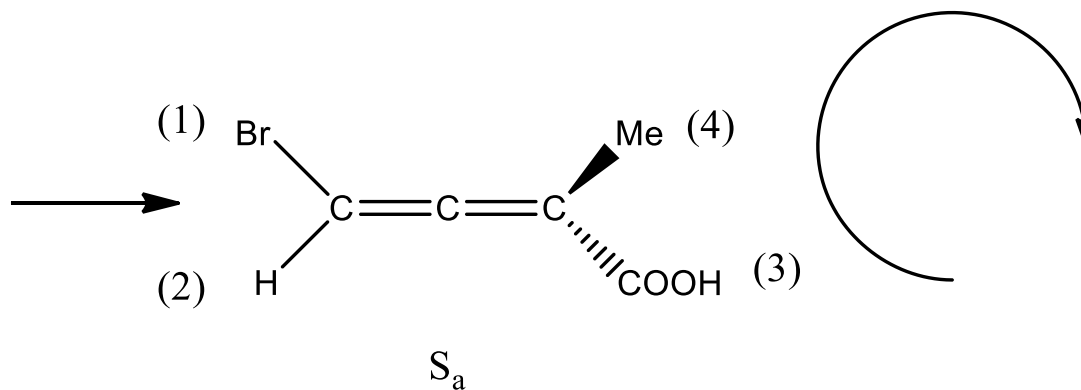


This compound is optically active with C_2 point group. So it is resolvable.

C.U. 2011, Third paper

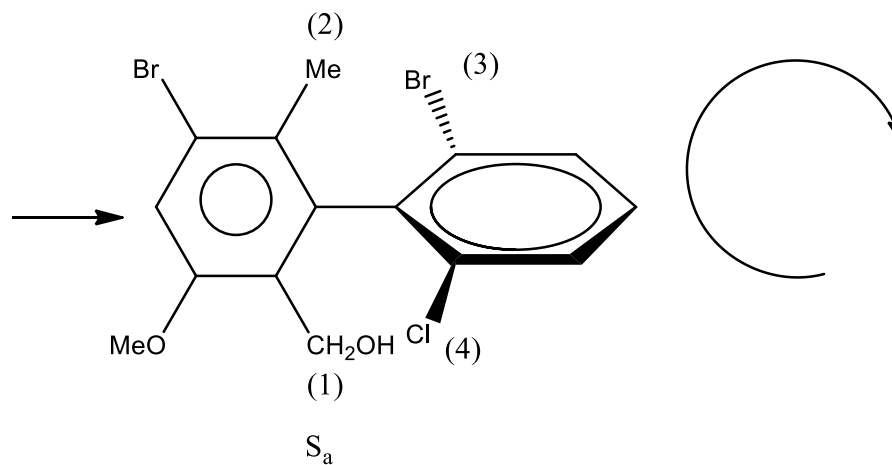
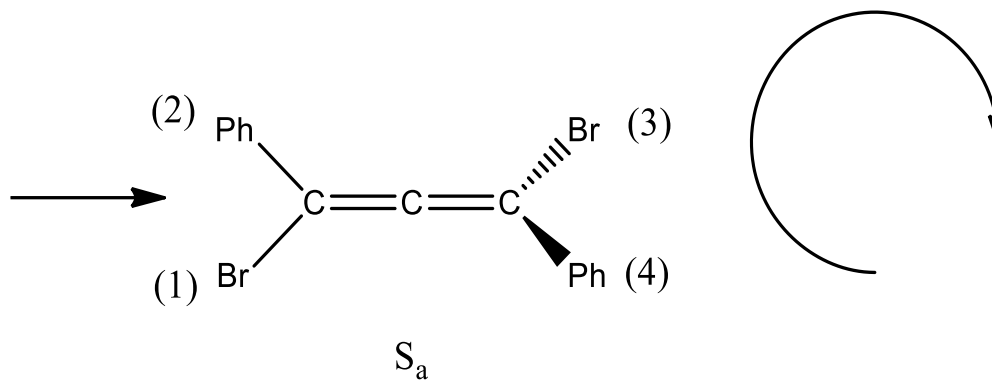
1.a) Find out the absolute (R/S) configuration of the following compounds:

1+1



C.U.2010

2.a) Assign R/S configuration to the following molecules:





BEST OF LUCK