Universitat d'Alacant
Universidad de Alicante
Departament de Química Orgànica
Departamento de Química Orgánica

LESSON 3

CHIRALITY IN MOLECULES WITHOUT STEREOGENIC CENTRES

3.1. Molecules with an stereogenic axis

3.2. Helical structures

3.3. Molecules with an stereogenic plane

3.4. Problems

3.5. Molecular models

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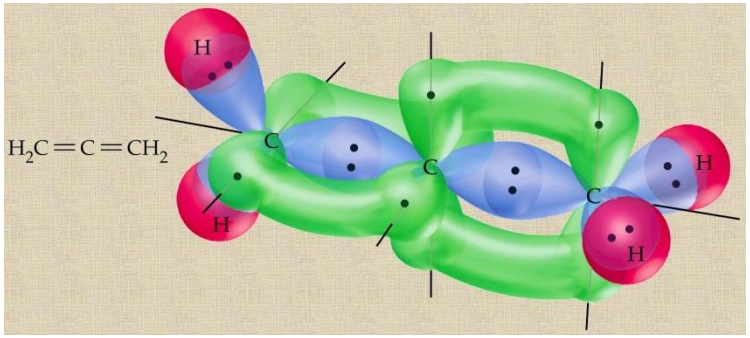
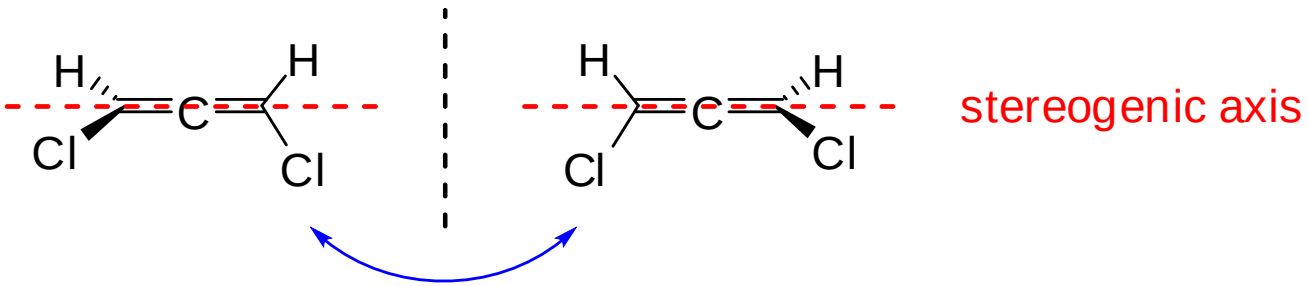
Allenes show an elongated tetrahedron structure. If there are different substituents at the two ends, then two enantiomeric forms appear.



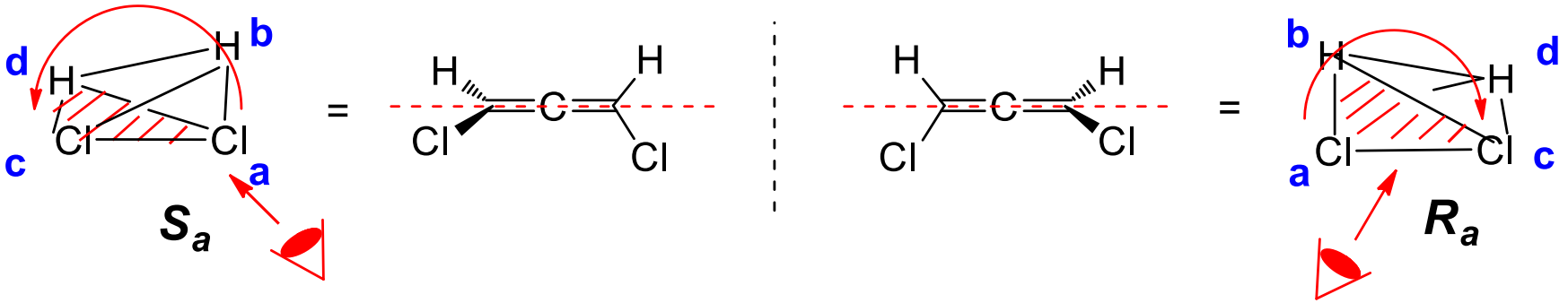
1,3-dichloroallene



non superimpossible

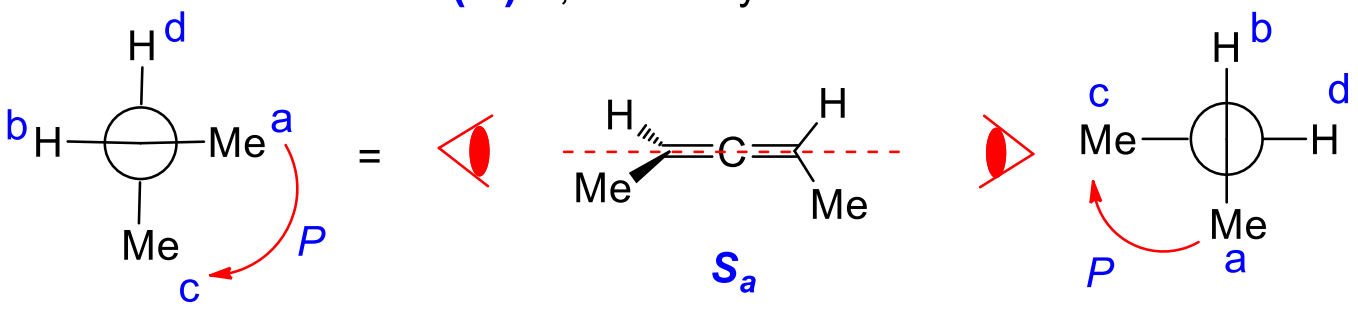
The stereochemistry can be given by the R_a or S_a descriptors. The allene is considered as an elongated tetrahedron where the double bonds are omitted for clarity. CIP rules are applied to each end of the allene. The molecule is observed from the opposite side to that in which the lowest priority substituent is located.

1,3-dichloroallene

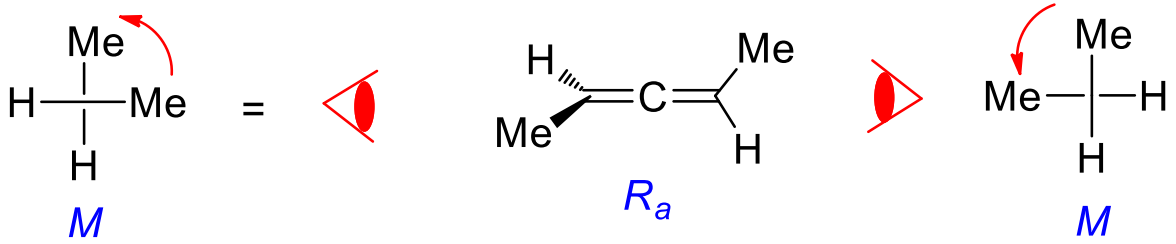


The substituents around the stereogenic axis allow considering these compounds as short helical segments. *P* stereodescriptor (plus: clockwise direction) or *M* (minus: anticlockwise direction). Direction from a to c in order to assign the stereodescriptor, S_a corresponds to *P* and R_a to *M*.

(*P*)-1,3-dimethylallene

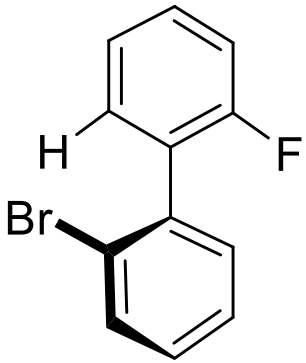


(*M*)-1,3-dimethylallene

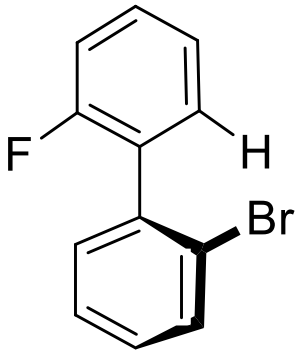


***ortho*-Substituted biaryls or biphenyls** are not co-planar. The restricted rotation around a single bond gives rise to *atropoisomers*.

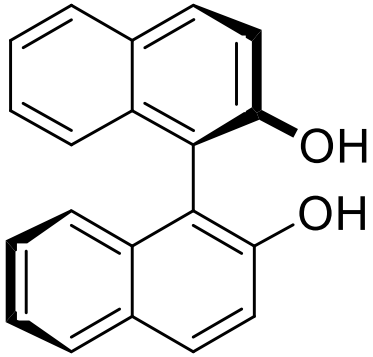
Contrary to conformers, these stereoisomers can be isolated.



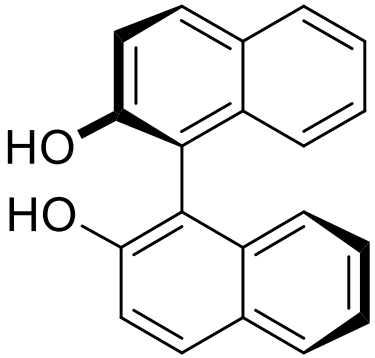
S_a *or P*



R_a *or M*



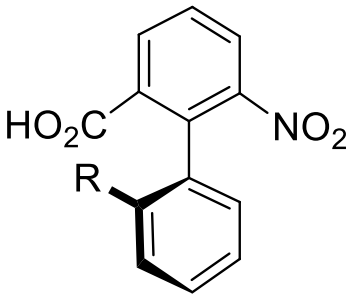
R_a or *M*



S_a or *P*

2,2'-binaphthol

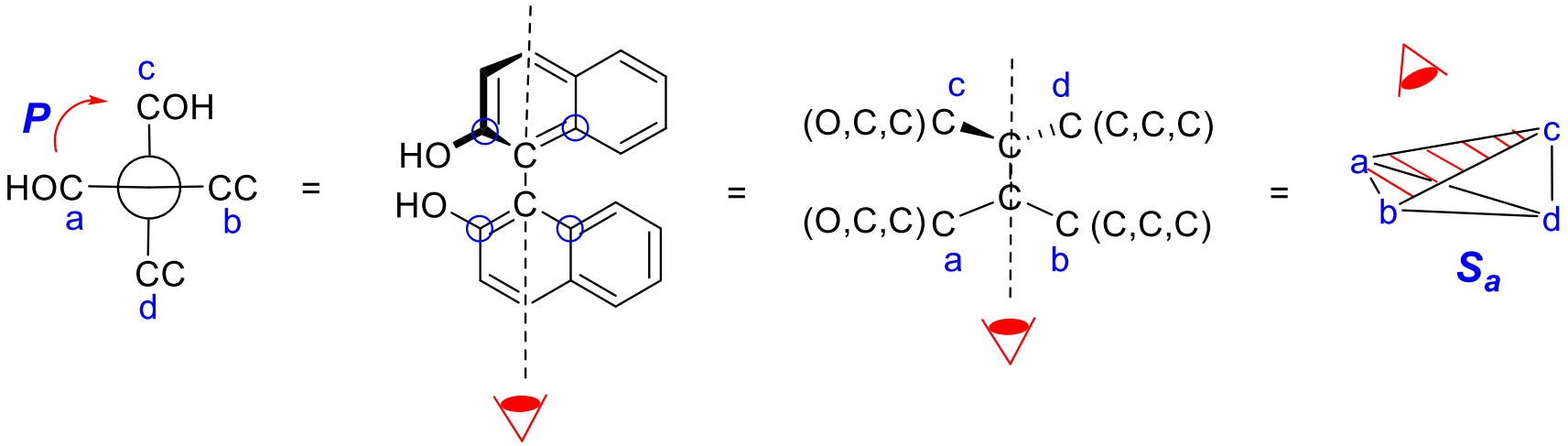
The rotation barrier of the atropoisomers depends on the temperature and size of the substituents. Racemisation occurs at low temperatures when small substituents are present.

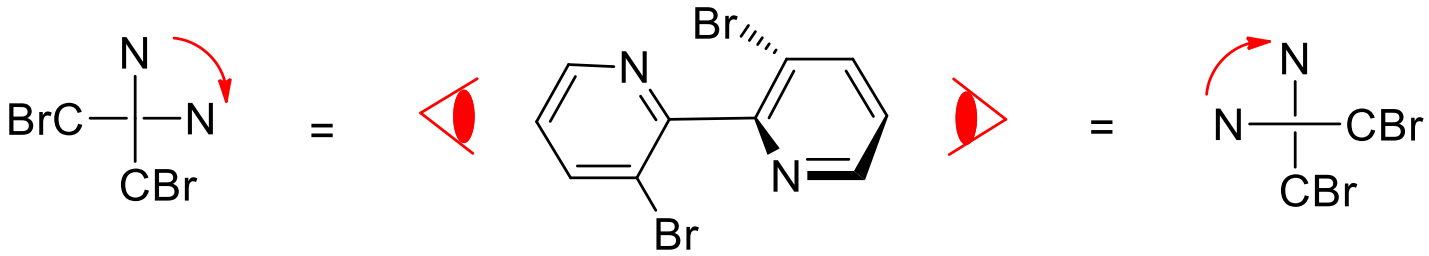


R	T (ºC)	t ½ (min)
Me	118	179
NO_2	118	125
CO_2H	118	91
OMe	25	9.4

Once the stereogenic axis is defined, the criteria and descriptors to assign the stereochemistry are the same as for allenes.

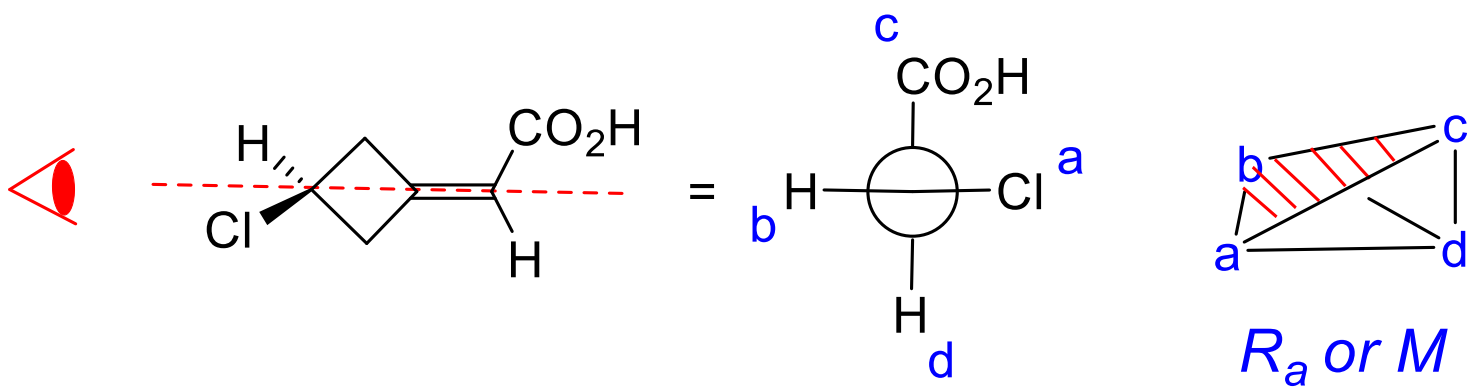
(***P*** *or* ***S_a***)-2,2'-binaphthol





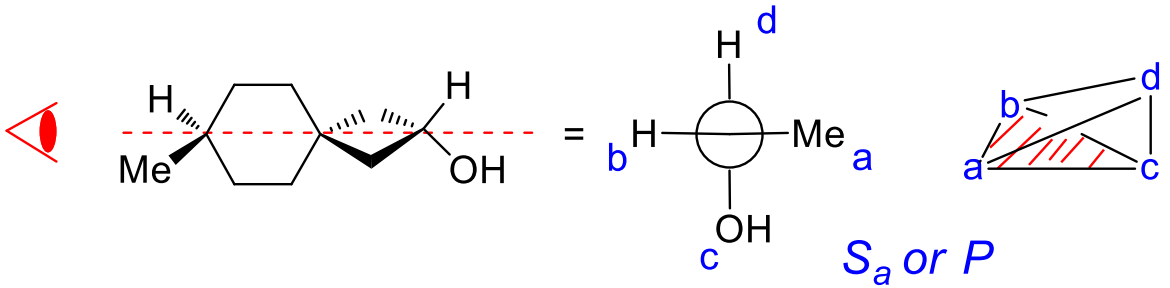
P (*P*)-3,3'-dibromo-2,2'-bipiridyl ***P***

Alkylidenecycloalkanes also have axial chirality.

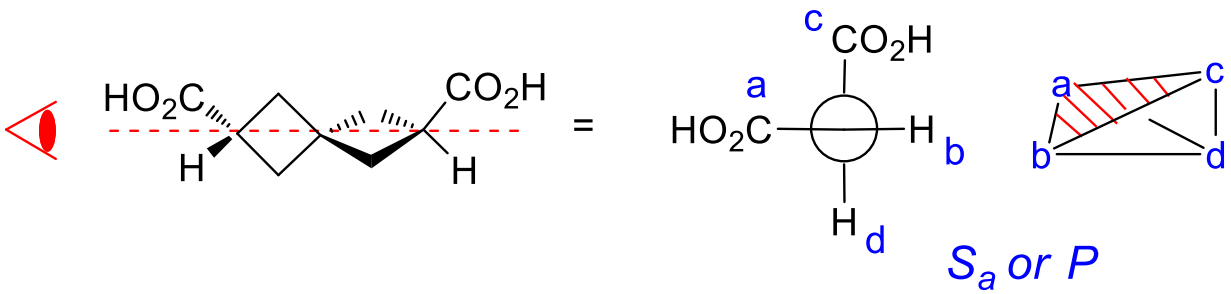


Spiro compounds are another examples of axial chirality.

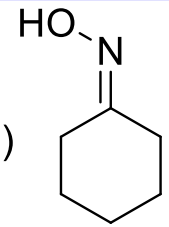
(*Sa*)-7-methylspiro[3.5]nonan-2-ol



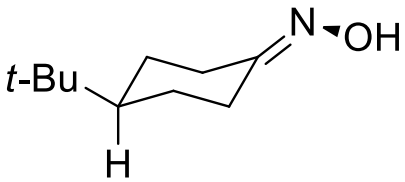
(*Sa*)-spiro[3.3]heptane-2,6-dicarboxylic acid



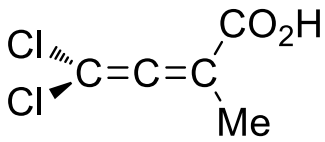
Which of the following compounds are chiral? Explain the answer and assign the right descriptor when applicable.

a) 

no

b) 

Sa

c) 

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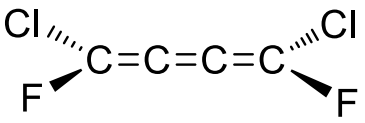
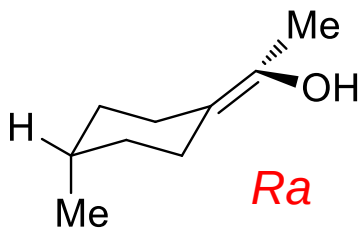
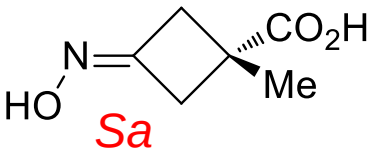
d) 

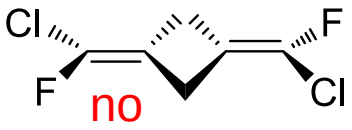
no

e) 

Ra

f) 

Sa

g) 

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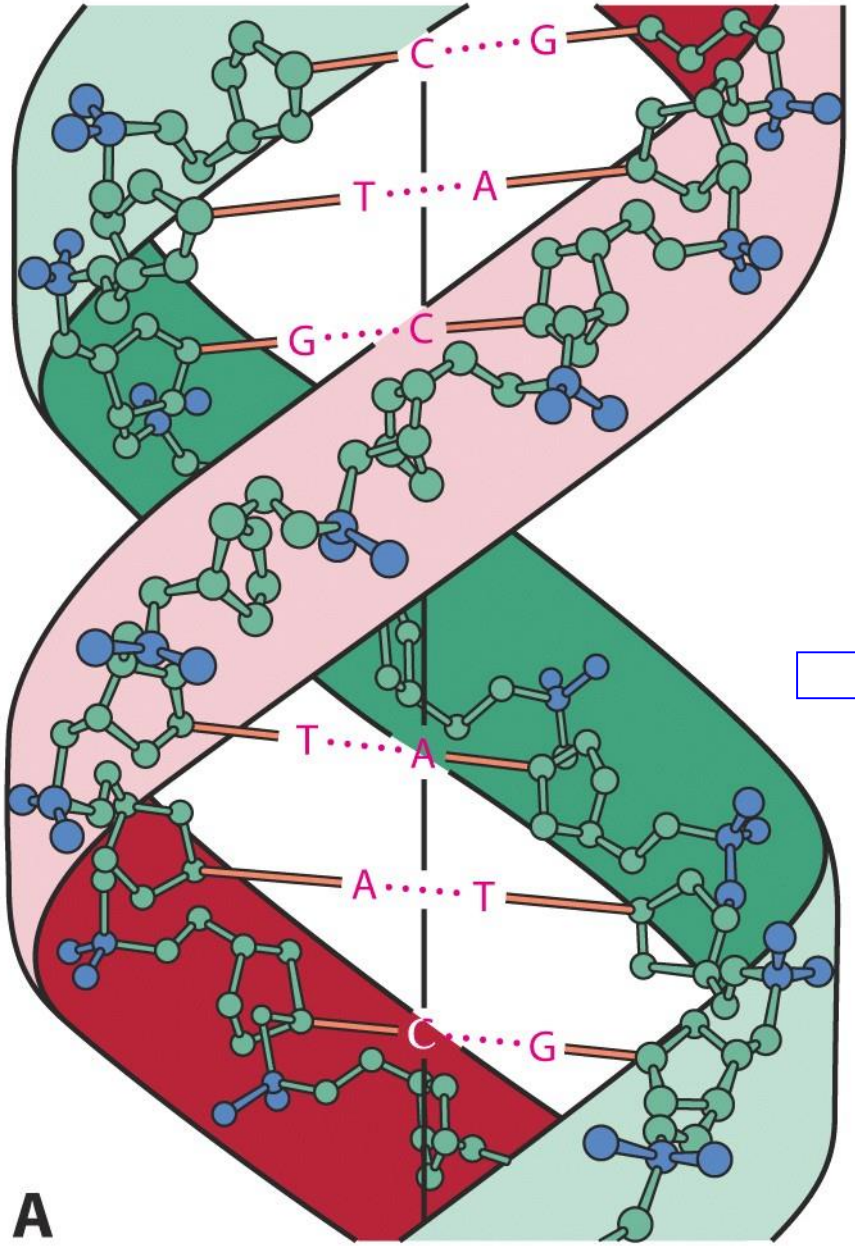
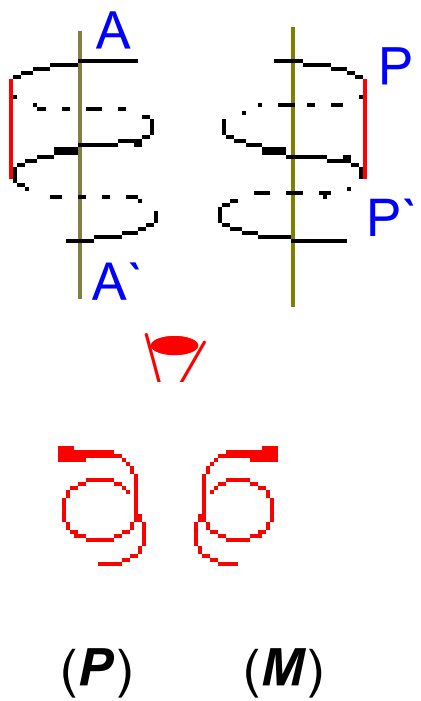


The compounds shown previously with axial chirality, as well as important biomolecules (DNA, RNA, proteins) and the helicenes show a helical structure and can be chiral.

DNA

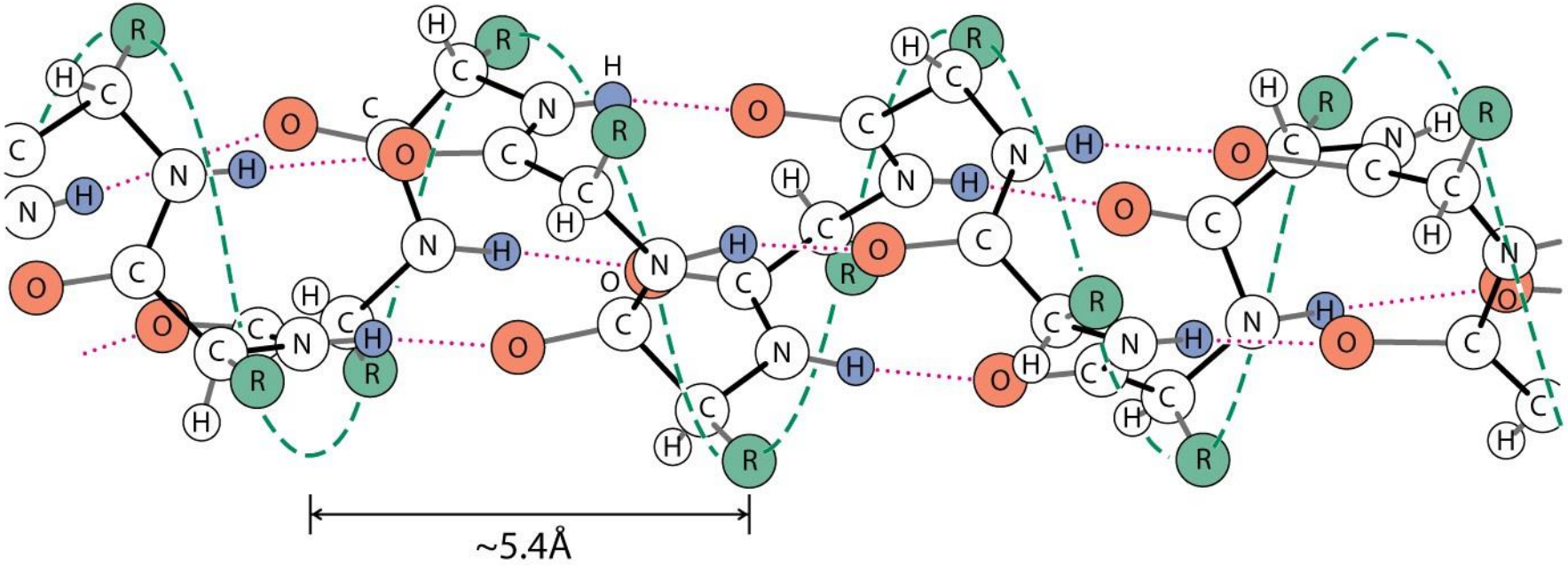


Helical structure

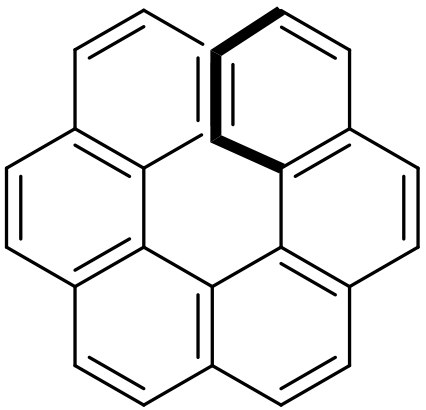
The distance PP' is the pitch of the helix, corresponding to a complete turn.

The helix is defined by its axis (AA'), pitch (PP') and direction.
If the helix moves away from the observer in the clockwise direction, the helix is right handed [*P* (plus) stereodescriptor]. In the case of anticlockwise direction, the helix is left handed [*M* (minus) stereodescriptor].

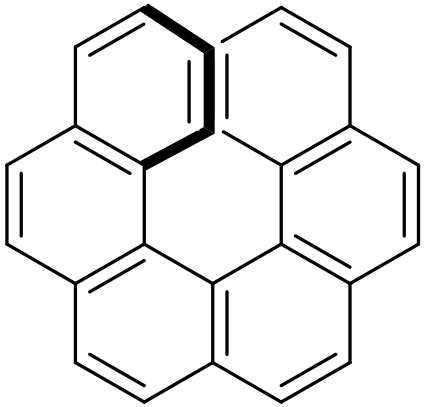
Some proteins show an α-helix structure, fixed by intramolecular hydrogen bonding. The example shown below is a right-handed helix (*P*) with 5.4 Å pitch of 3.6 amino acids.



The helical structure can be also easily seen in hexahelicene. The steric effect of the 6 aromatic rings forces them to stay out of the plane. One of the terminal rings lays above or below the other terminal ring.

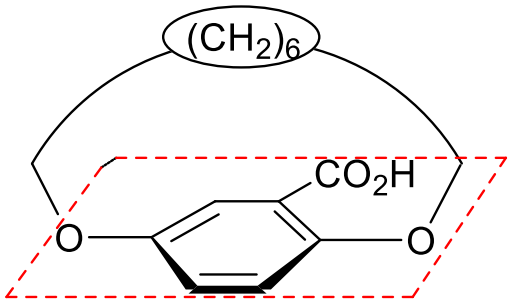


(*P*)-hexahelicene

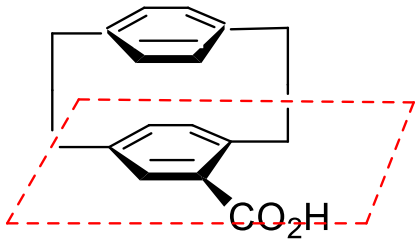


(*M*)-hexahelicene

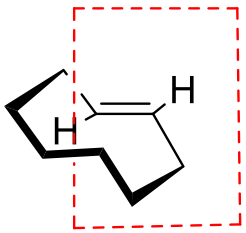
In some molecules the stereogenic element is a plane, which contains most of the substituents. Chirality is due to the fact that at least one substituent is not in that plane. Due to restricted rotation, there is no symmetry plane and stereoisomers are obtained when exchanging substituents (e.g., CO_2H / H_{ortho} in paracyclophane).



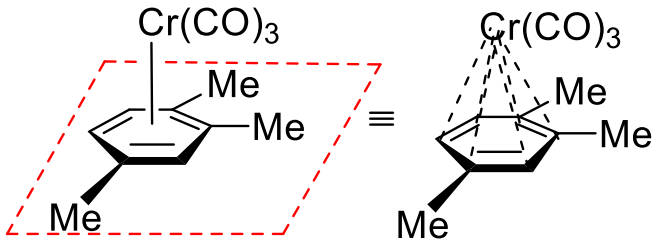
ansa compounds



paracyclophanes

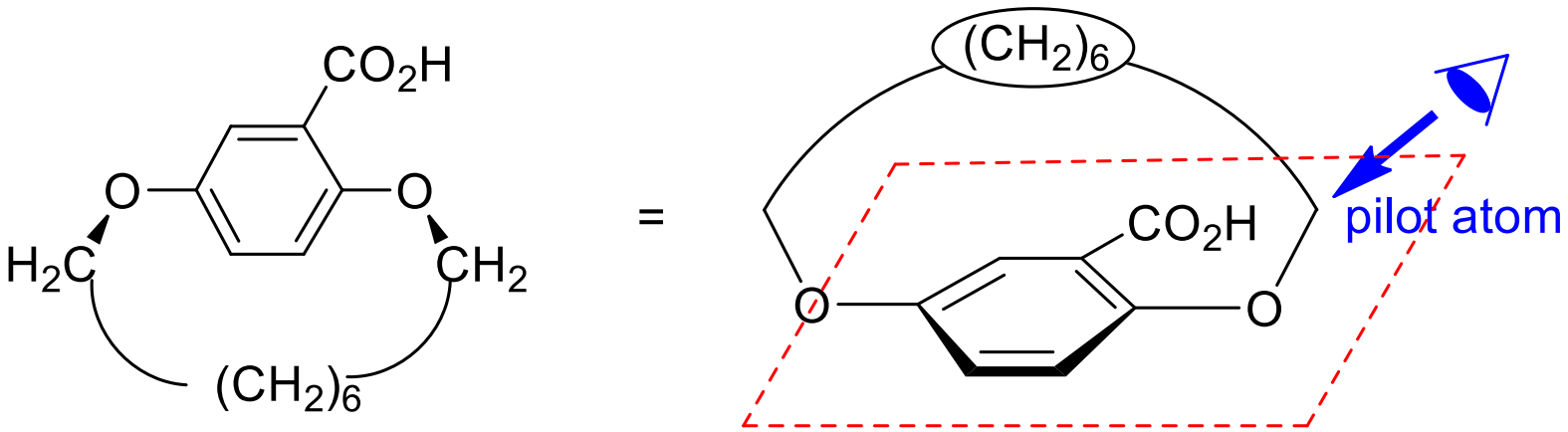


(E)-cycloalkenes



metalocenes

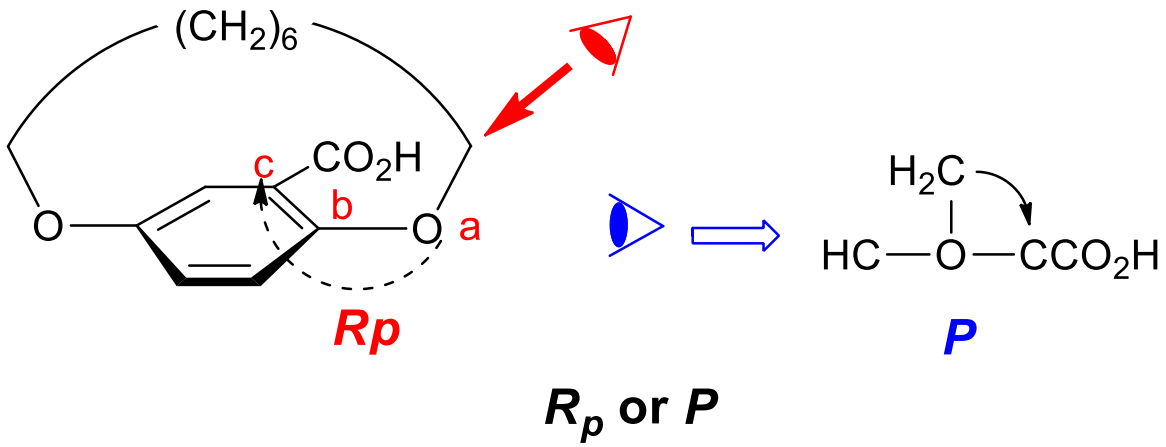
Ansa compounds



Stereodescriptors:

1) The **stereogenic plane** and the **pilot atom** (the nearest atom to the plane but out of the plane) must be identified.
2) If several possible options, the pilot atom is given by the CIP priority.

Ansa compounds

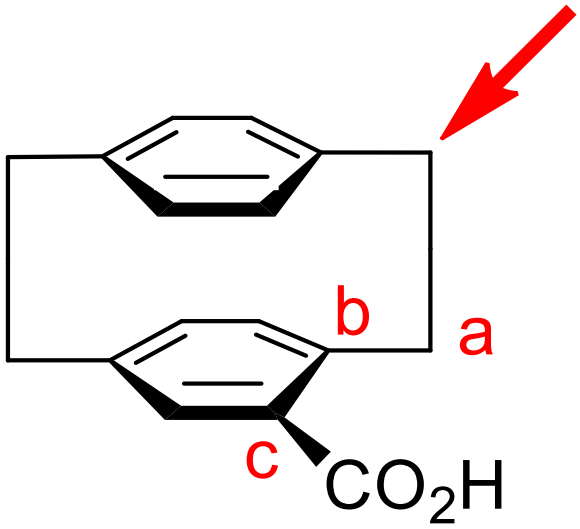


3) ***Rp*** or ***Sp*** (*p* means planar chirality) is assigned by following the direction of the three consecutive atoms in the stereogenic plane from the pilot atom. CIP rules must be also applied to priorize substituents.

4) ***P*** or ***M*** helical descriptors can be also applied, with the direction being given from the pilot atom to c.

Paracyclophanes

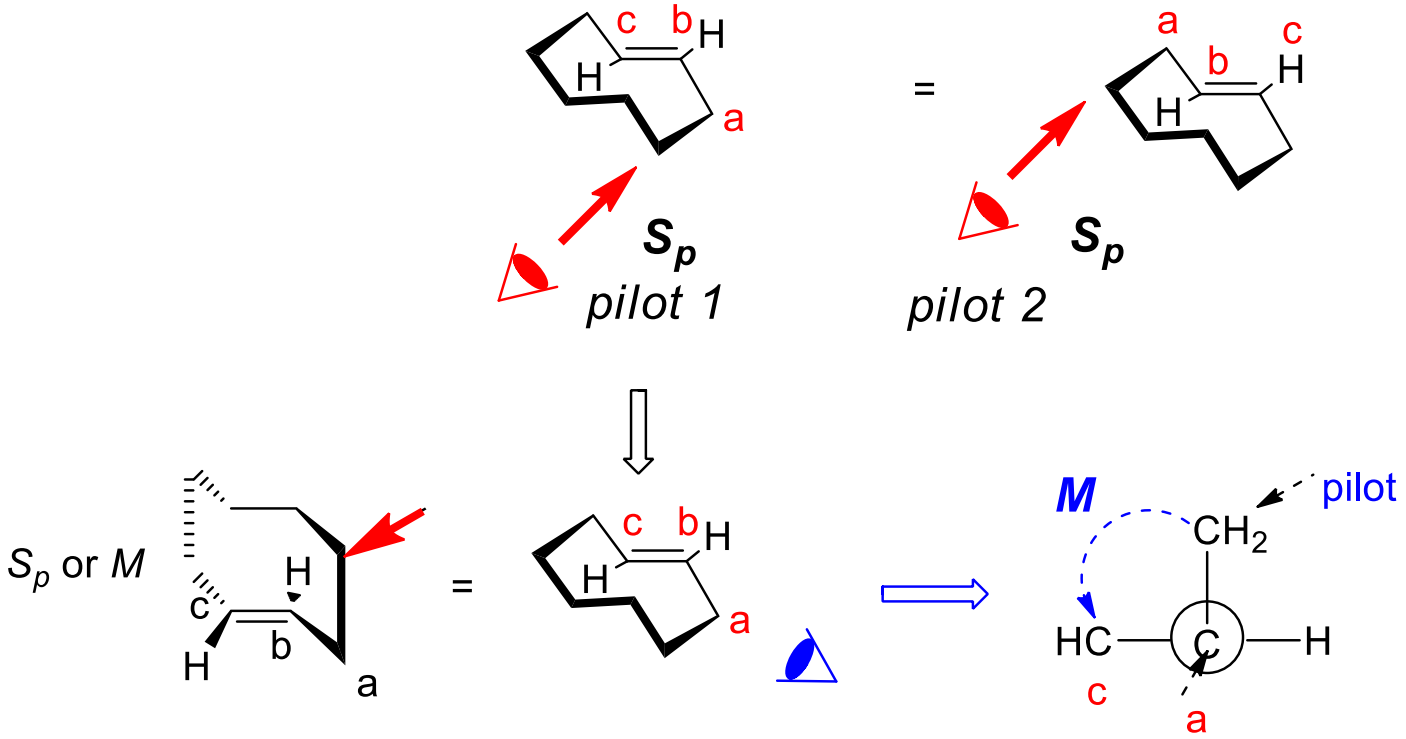
The stereogenic plane contains the most substituted ring. The configuration is assigned as for the ansa compounds.



S_p or M

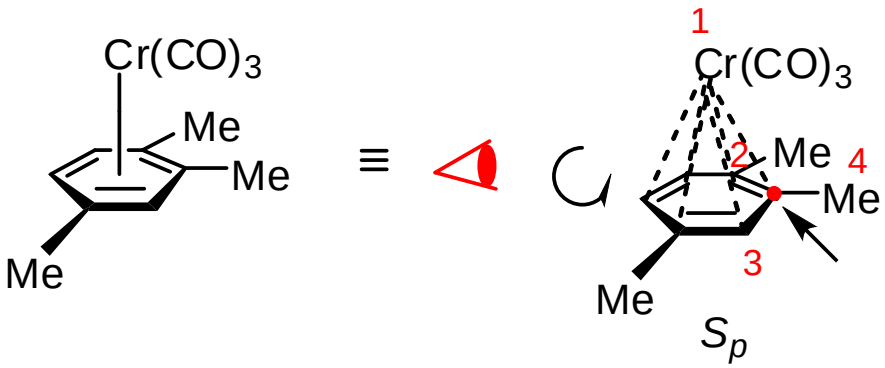
(E)-Cycloalkenes

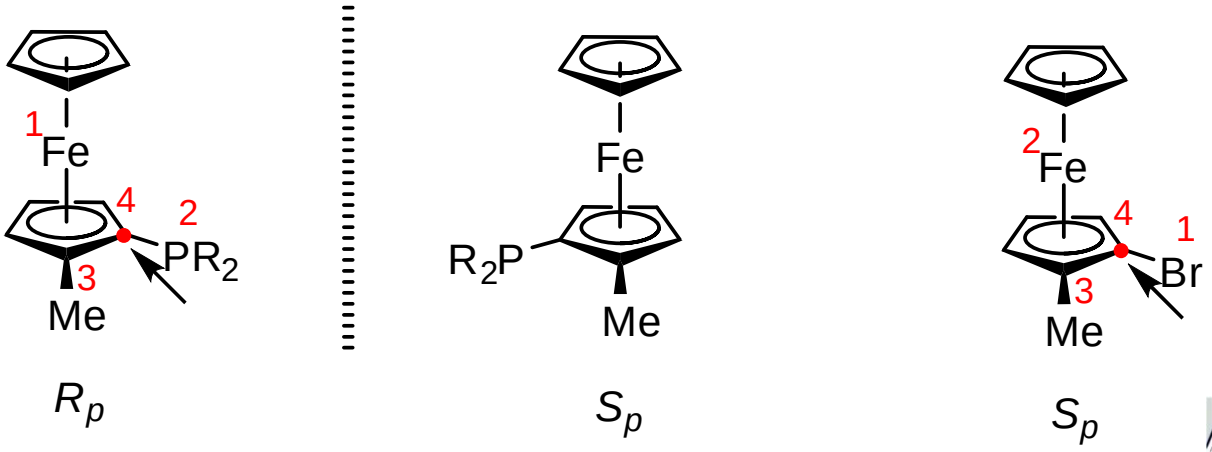
(E)-Cycloalkenes with short enough chains have an stereogenic plane because the chain is out of the plane. Descriptors and criteria are the same as for paracyclophanes and ansa compounds.



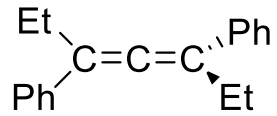
Metallocenes with an aromatic ligand properly substituted also exhibit planar chirality

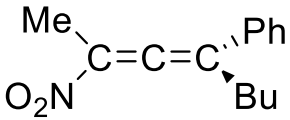
Such is the case of arene chromiumtricarbonyl complexes or sandwich complexes (e.g., ferrocene derivatives)

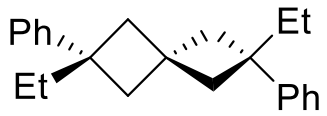


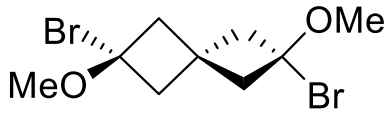


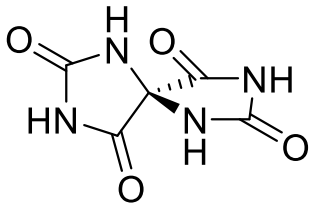
Indicate the absolute stereochemistry for the following molecules:

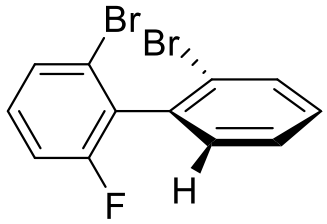
a) 

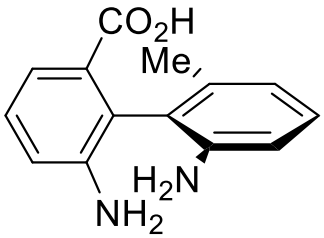
b) 

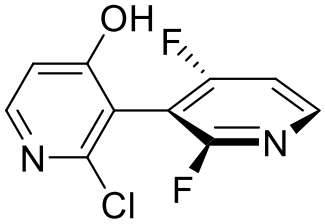
c) 

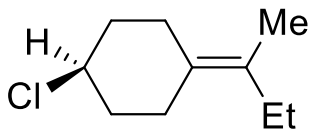
d) 

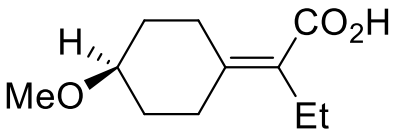
e) 

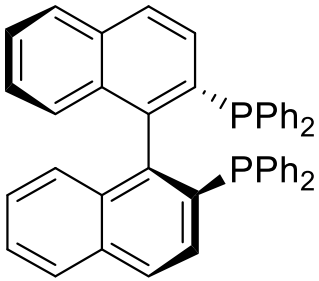
f) 

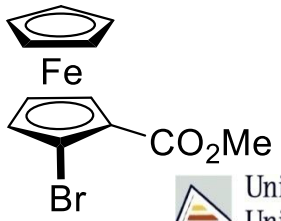
g) 

h) 

i) 

j) 

k) 

l) 

1. Build and draw the models of (R_a) y (S_a)-penta-2,3-diene.

2. Build and draw the two isomers of 2,2'-dimethylbiphenyl and 2,2'-dimethylbinaphthyl.

3. Build and draw the (*P*) and (*M*) hexahelicenes.

4. Build and draw the two enantiomers of [2.2]-paracyclophanecarboxylic acid, indicating the configuration.

5. Build and draw the models of *trans*-cyclooctene and *trans*-cyclononene. Determine the configuration in both cases.

6. Build and draw the model of (R_a)-4-methylethylidenecyclohexane.

7. Build and draw the model of (S_a)-2,7-dimethylspiro[3.5]nonane.