STEREOCHEMISTRY

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ISOMERISM

Isomerism was first of all discovered by German chemist Leibig and Wohler in 1820. They found that silver cyanate (AgONC) and silver fulminate (AgCNO) have same atomic composition. Similarly Berzelius and Wohler found that thought ammonium cyanate (NH_4CNO) and urea (NH_2CONH_2) have same molecular formula CH_4N_2O, there is significant difference in properties. Gay – Lussae then suggested that mode of attachment of atoms in all these compounds is different.

C_2H_6O: CH_3-CH_2-OH & CH_3-O-CH_3 The dissimilarity in molecular structure of the compounds results into the dissimilarity in the properties.

Compounds which have same molecular formula but different molecular structure i.e. which have different physical and chemical properties are called isomers and this phenomenon is called the isomerism.

ISOMERISM

Structural Isomerism

Chain Isomerism

Positional Isomerism

Functional Group Isomerism

Mesomerism

Tautomerism

Stereoisomerism

Configurational Isomersim(High energy barrier):

Optical and Geometrical Isomerism

The Two Major Classes of Isomers:

The two major classes of isomers are constitutional isomers and stereoisomers:

- Constitutional/structural isomers have different IUPAC names, the same or different functional groups, different physical properties and different chemical properties.
- Stereoisomers differ only in the way the atoms are oriented in space. They have identical IUPAC names (except for a prefix like cis or trans). They always have the same functional group(s).

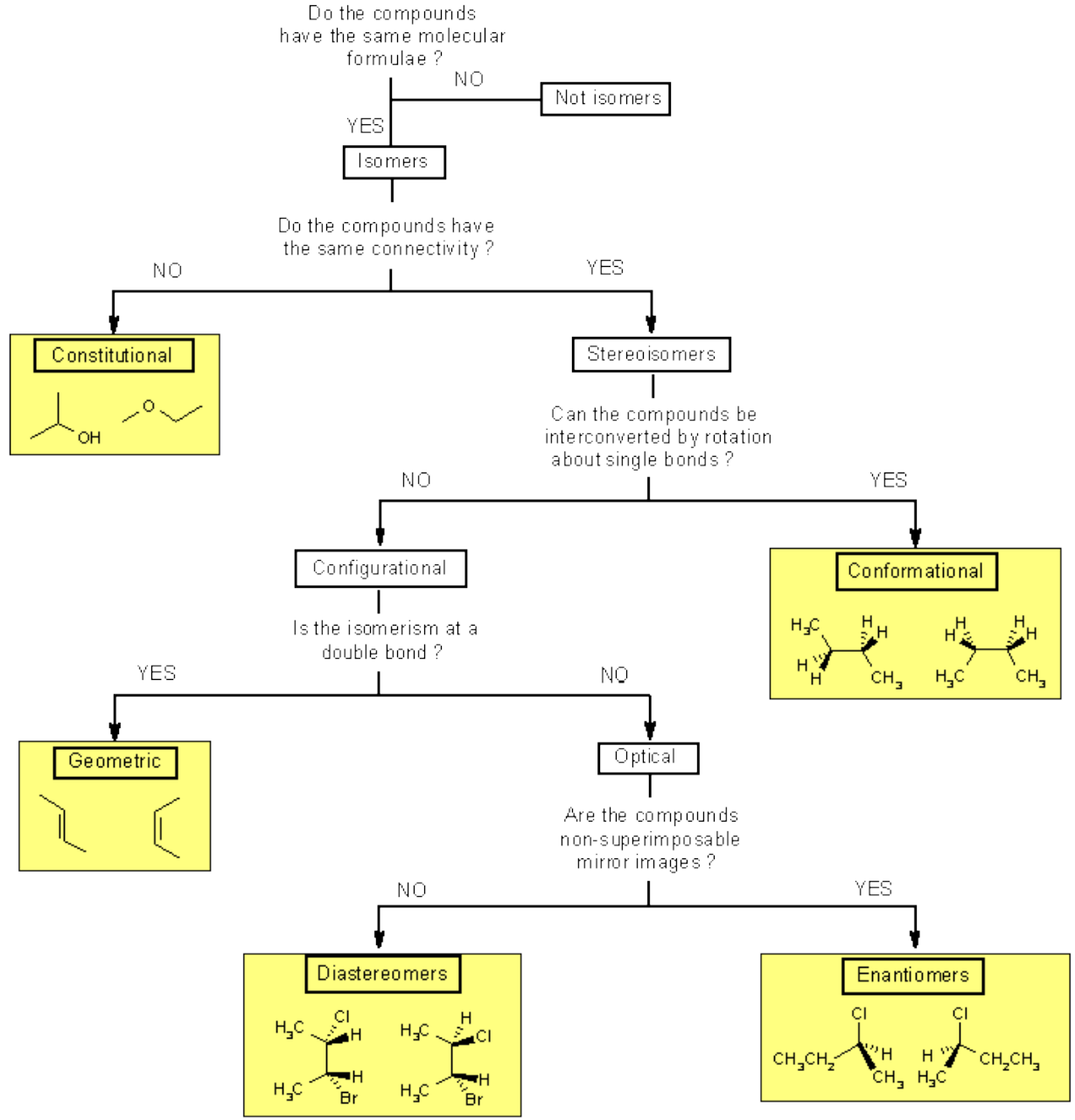
STEREOCHEMISTRY

Deals with:

- Determination of the relative positions in space of atoms, groups of atoms
- Effects of positions of atoms on the properties

Sterical Structure:

- Constitution
- Configuration
- Conformation


Do the compounds have the same molecular formulae ?
NO
Not isomers
YES
Isomers
Do the compounds have the same connectivity ?
NO
YES
Constitutional
OH
O
Stereoisomers
Can the compounds be interconverted by rotation about single bonds ?
NO
YES
Configurational
Conformational
Is the isomerism at a double bond ?
YES
NO
Geometric
Optical
Are the compounds non-superimposable mirror images ?
NO
YES
Diastereomers
Cl
H3C
H
Br
Enantiomers
CH3CH2
CH3
CH2CH3

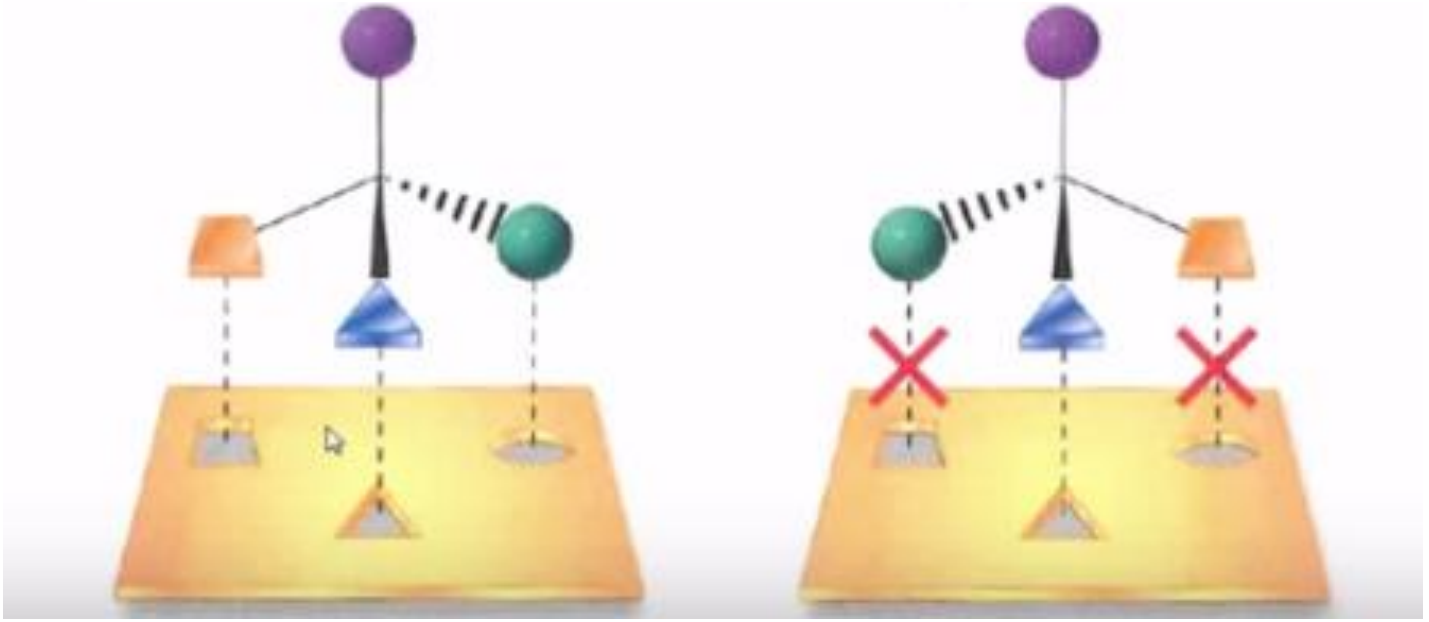
STEREOCHEMISTRY

Stereochemistry: The study of the three-dimensional structure of molecules

- **Structural (constitutional) isomers:** same molecular formula but different bonding sequence
- **Stereoisomers:** same molecular formula, same bonding sequence, different spatial orientation

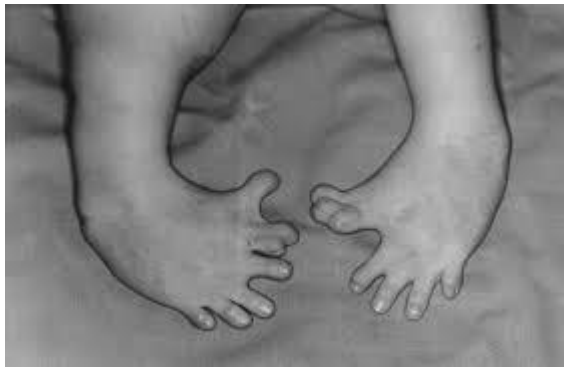
Why we need stereochemistry?

- Cis, butanoic acid "maleic acid" essential for plants and animals
- trans, butanoic acid "fumaric acid" toxic to tissue



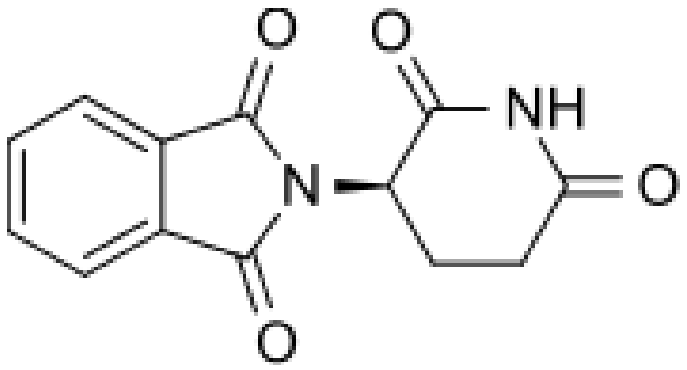
Thalidomide

Side effects- thousands of babies were born with missing or abnormal arms, hands, legs, or feet.

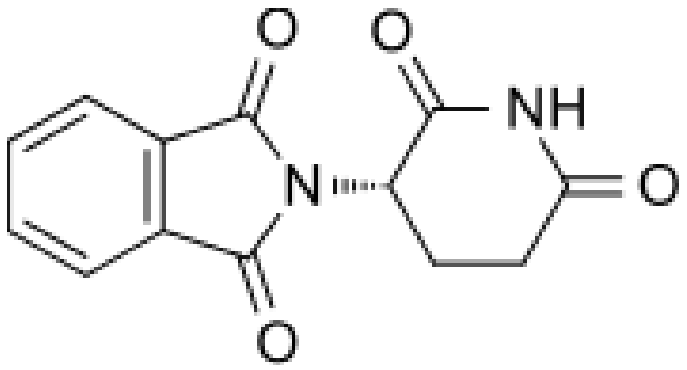


Thalidomide

Two stereoisomers of Thalidomide



(R)-thalidomide



(S)-thalidomide

(-)(*S*)-Thalidomide that caused the severe side-effects

Definitions

Stereoisomers – compounds with the same connectivity, different arrangement in space

Enantiomers – stereoisomers that are non-superimposable mirror images; only properties that differ are direction (+ or -) of optical rotation

Diastereomers – stereoisomers that are not mirror images; different compounds with different physical properties

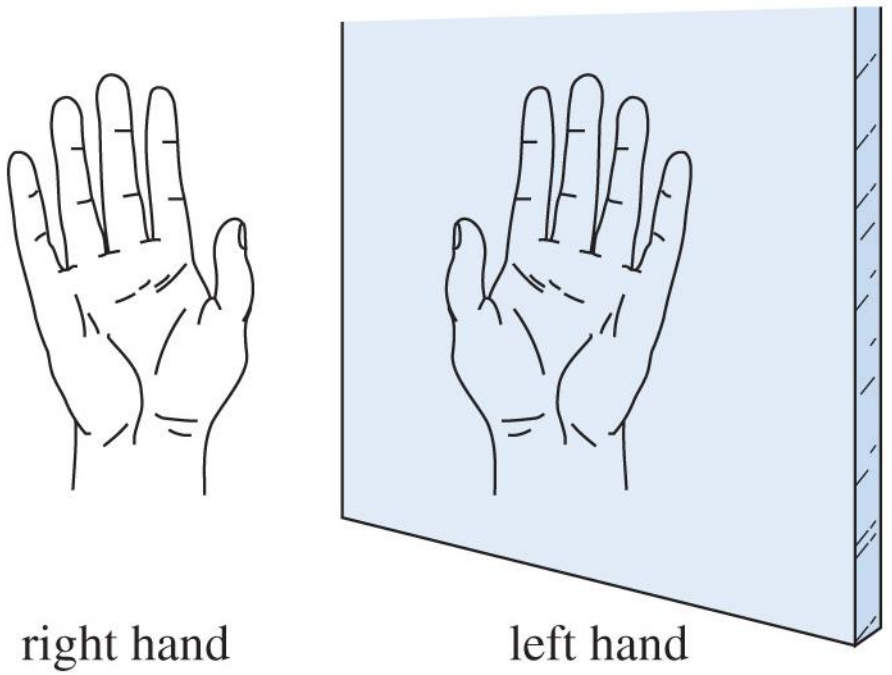
Asymmetric center – sp^3 carbon with 4 different groups attached

Optical activity – the ability to rotate the plane of plane –polarized light

Chiral compound – a compound that is optically active (achiral compound will not rotate light)

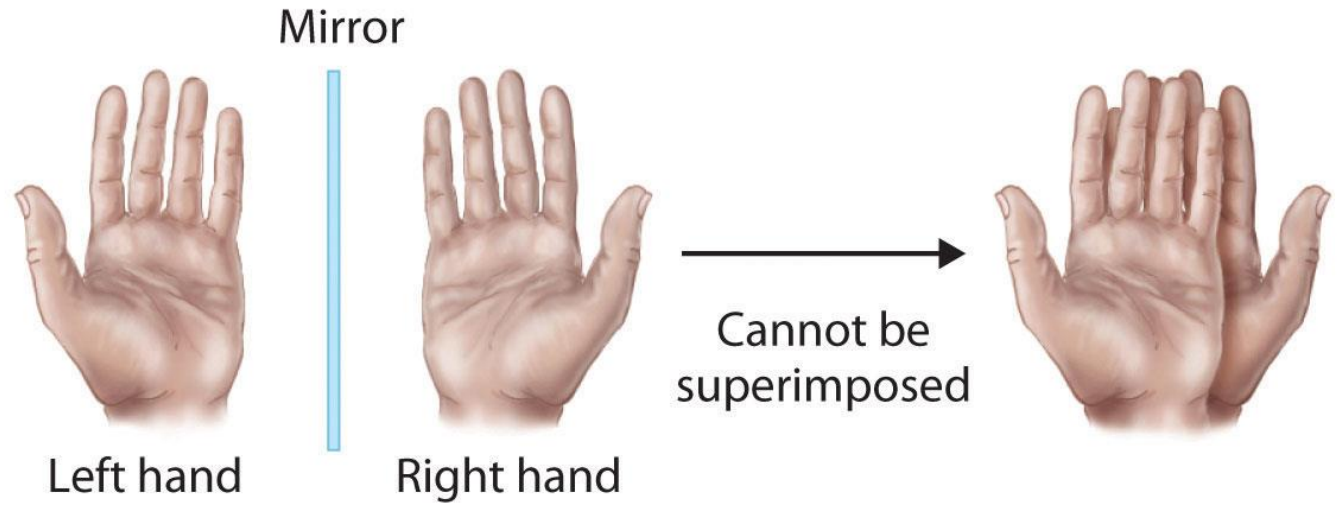
Polarimeter – device that measures the optical rotation of the chiral compound

Chirality

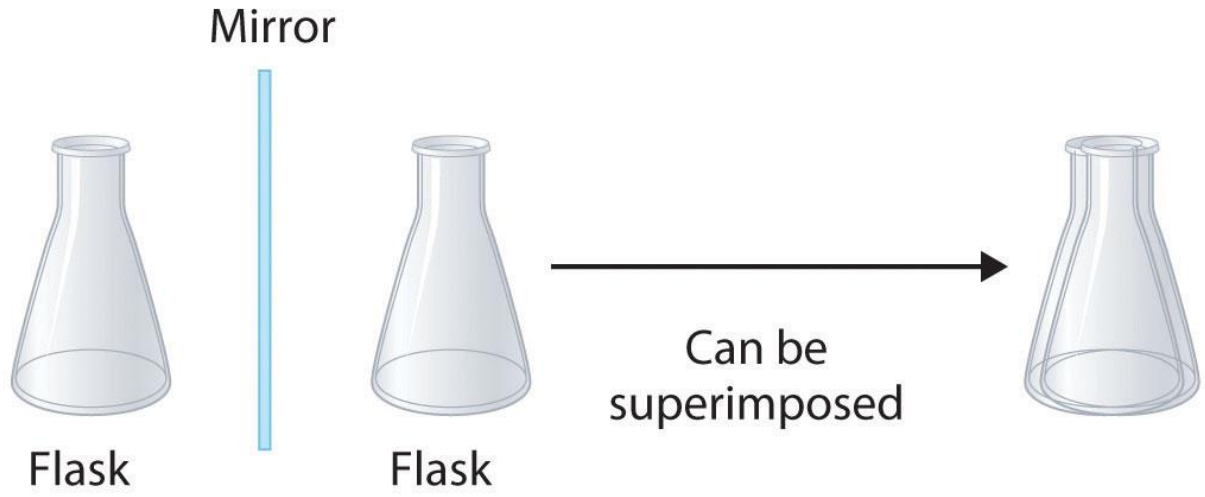


"Handedness": Right-hand glove does not fit the left hand.

An object is chiral if its mirror image is different from the original object.

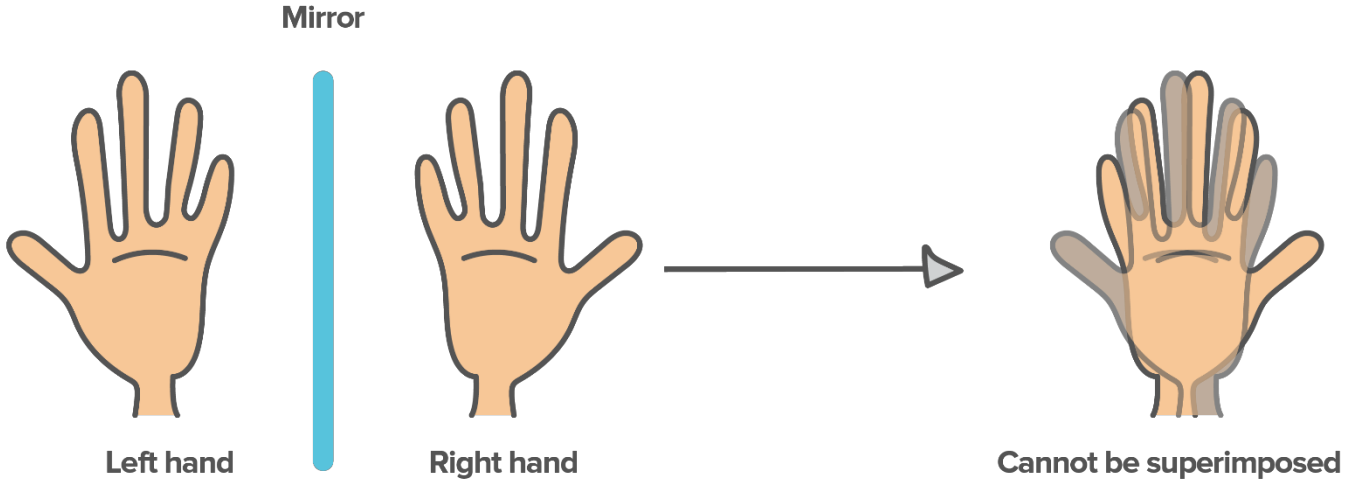


(a) Chiral objects

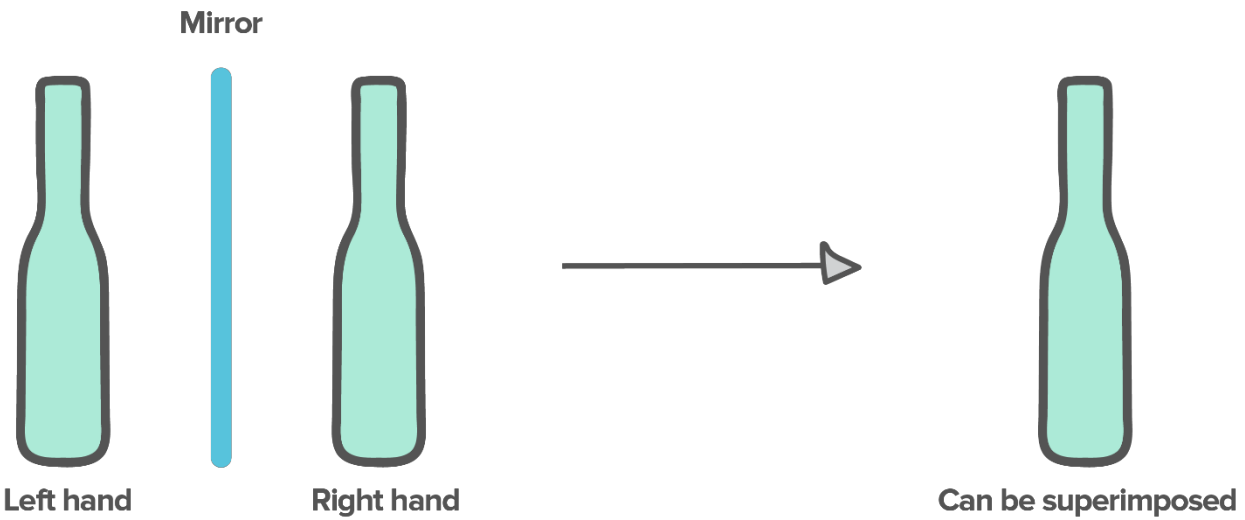


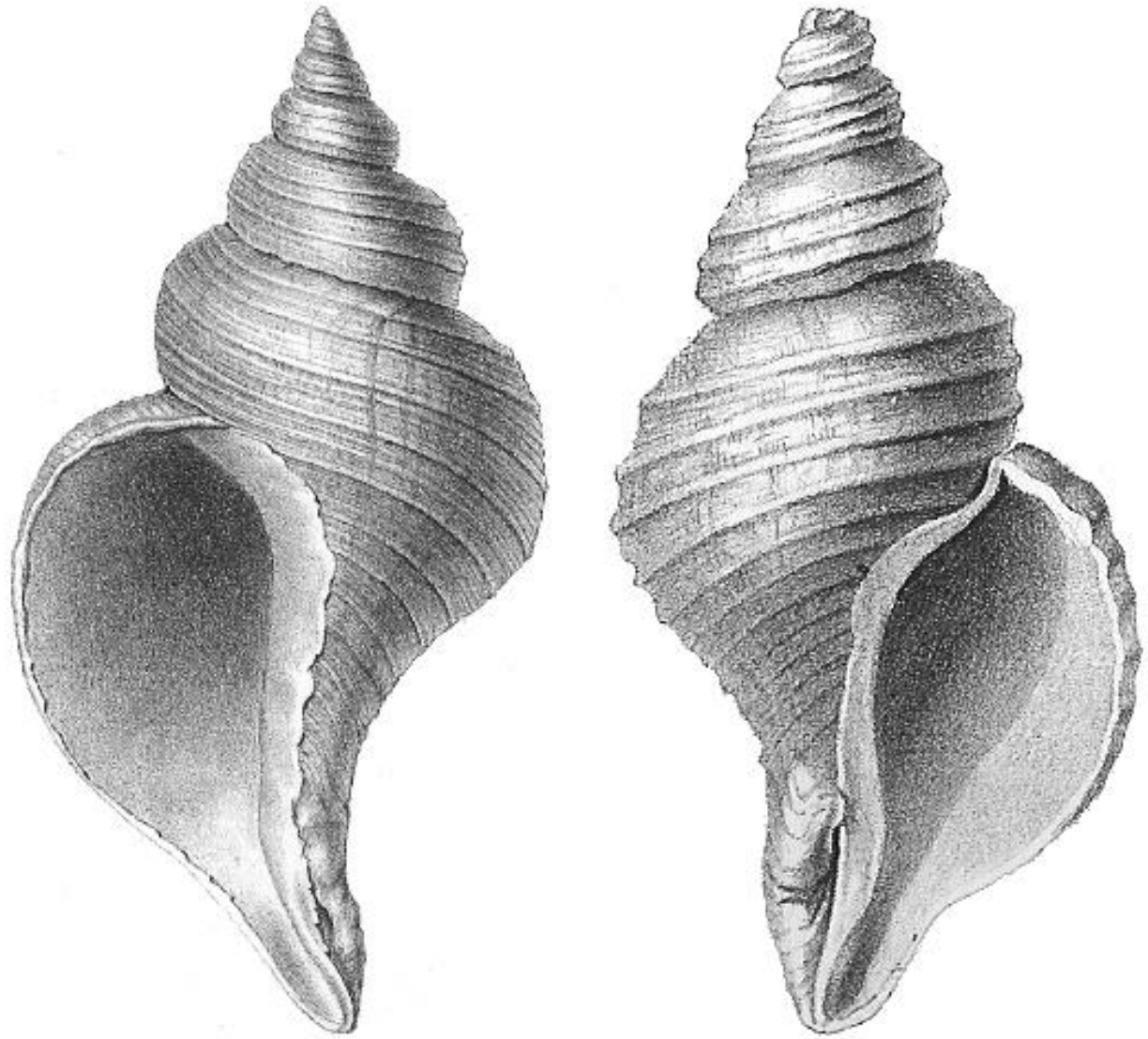
(b) Achiral objects

CHIRAL OBJECTS

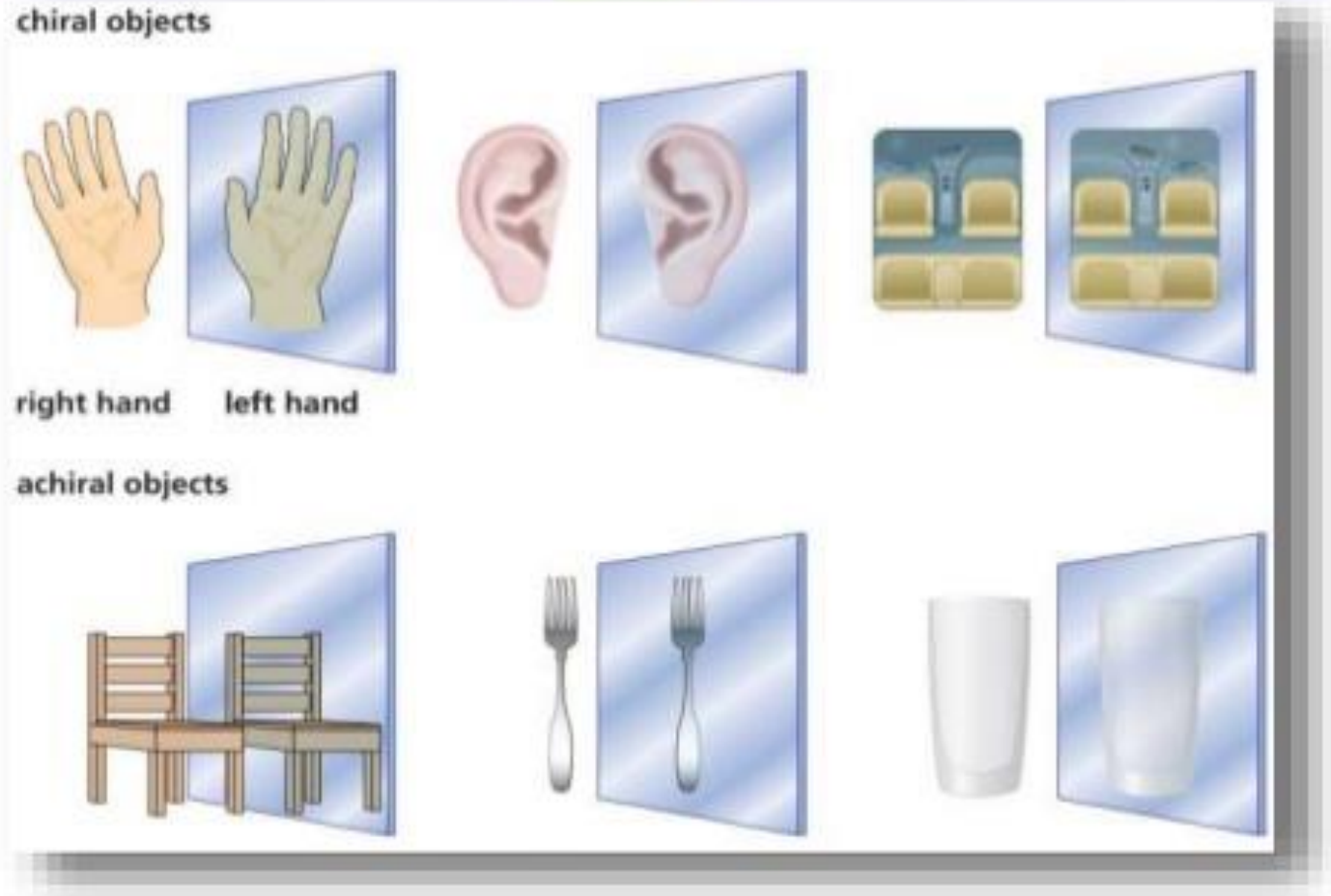


ACHIRAL OBJECTS





Chirality



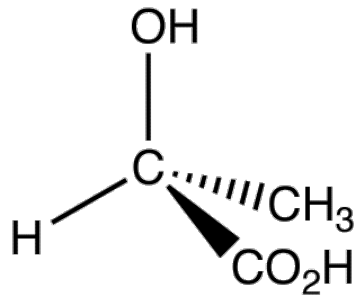
Chiral objects are objects with left-handed and right-handed forms

Achiral objects - objects that have superimposable mirror images

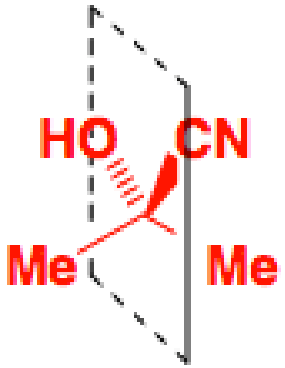
Nonsuperimposable mirror images - a mirror image that is not the same as the image itself - *chiral objects have nonsuperimposable mirror images*

Chiral Compounds

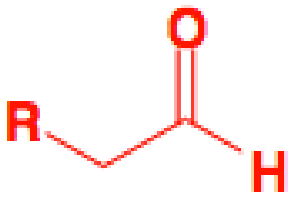
- All the four substituents of corbon are different
- Plane of symmetry should not be present in the molecule



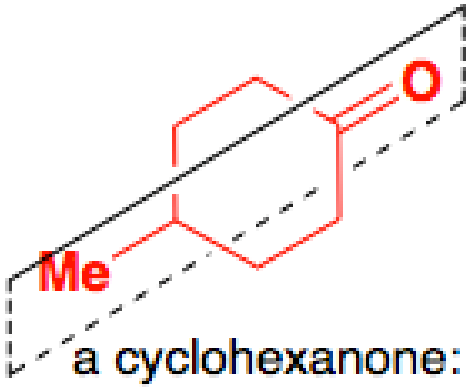
Plane of Symmetry



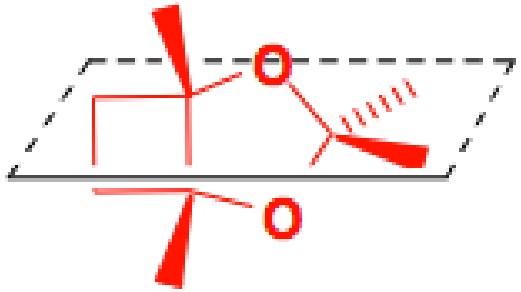
acetone
cyanohydrin



any planar
molecule:
the plane of
the screen is a
plane of symmetry

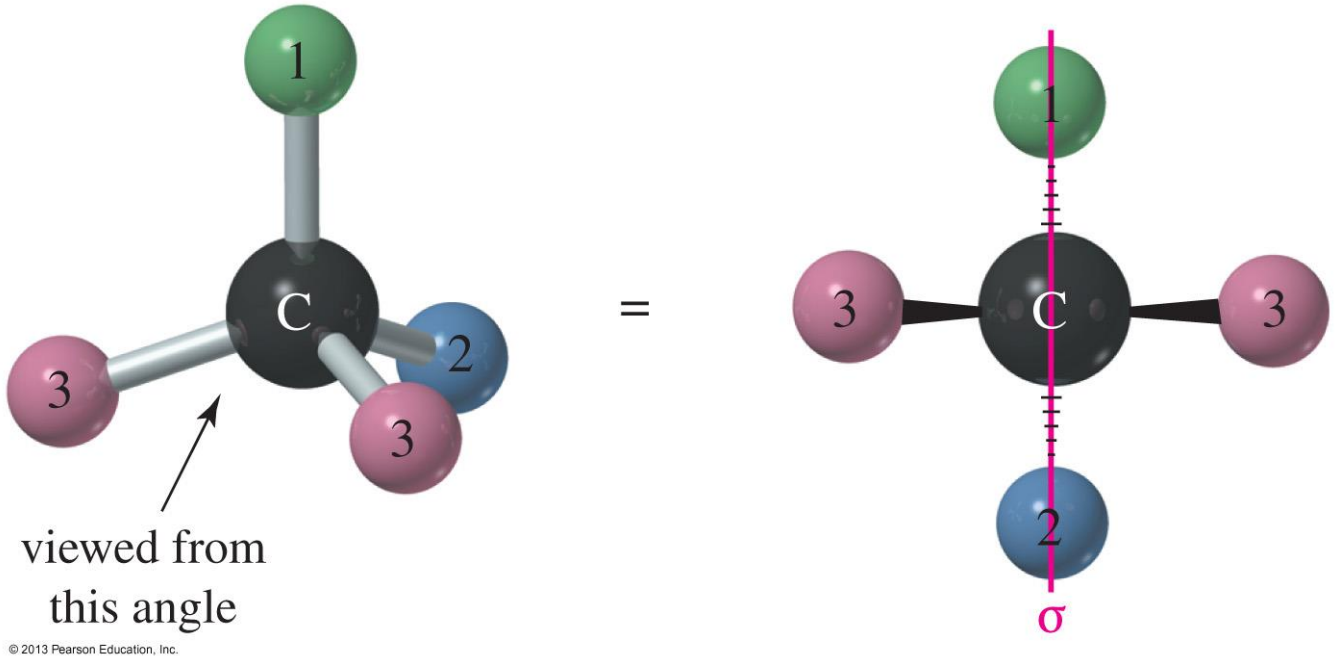


a cyclohexanone:
plane of symmetry
is orthogonal
to the screen



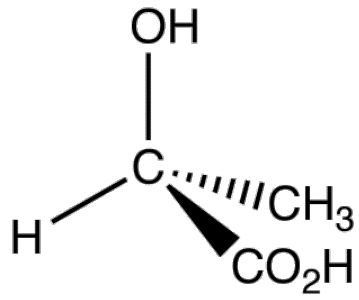
a bicyclic acetal:
plane of symmetry
is orthogonal
to the screen

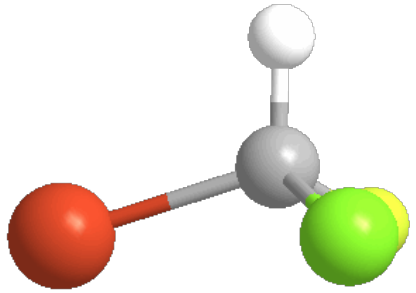
Planes of Symmetry



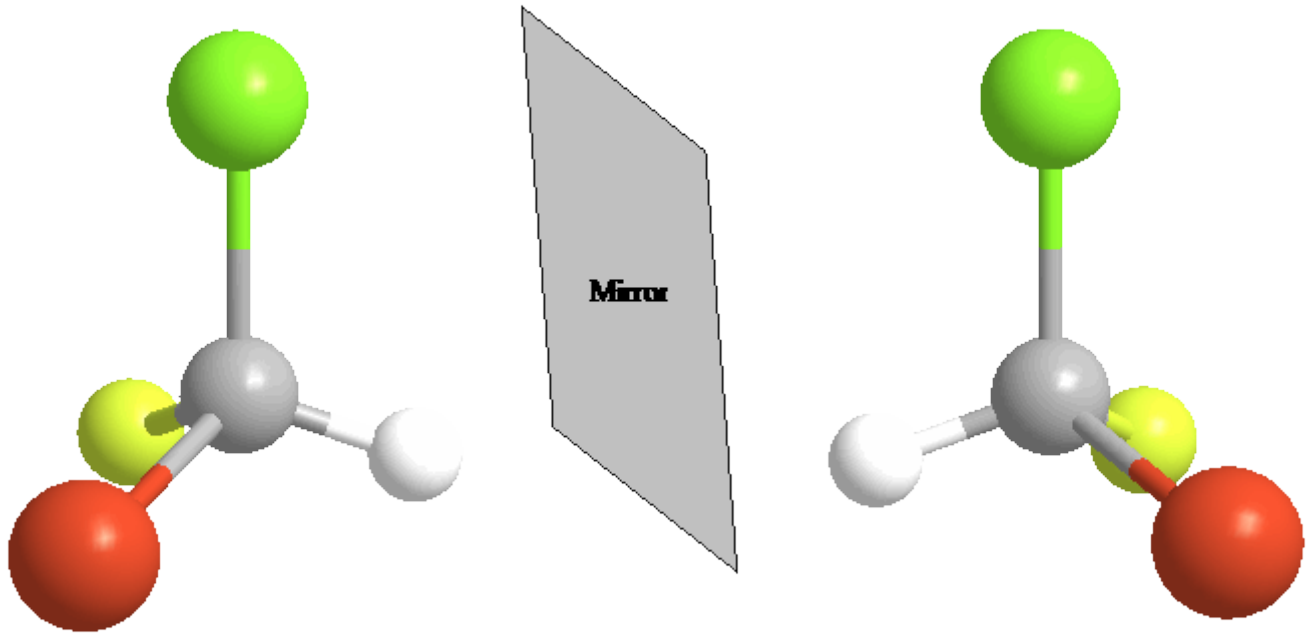
- A molecule that has a plane of symmetry is *achiral*.

Chiral Compounds

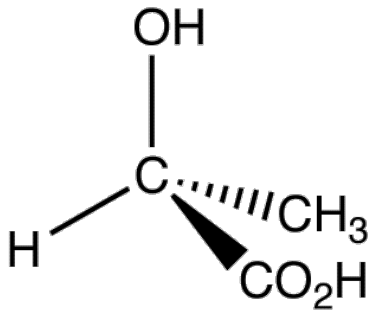




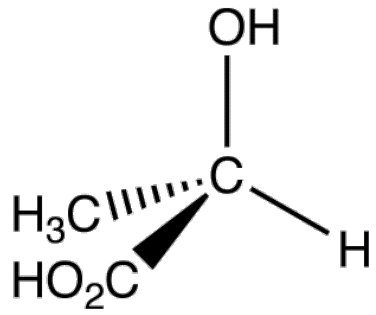
Mirror Image of Chiral Compound



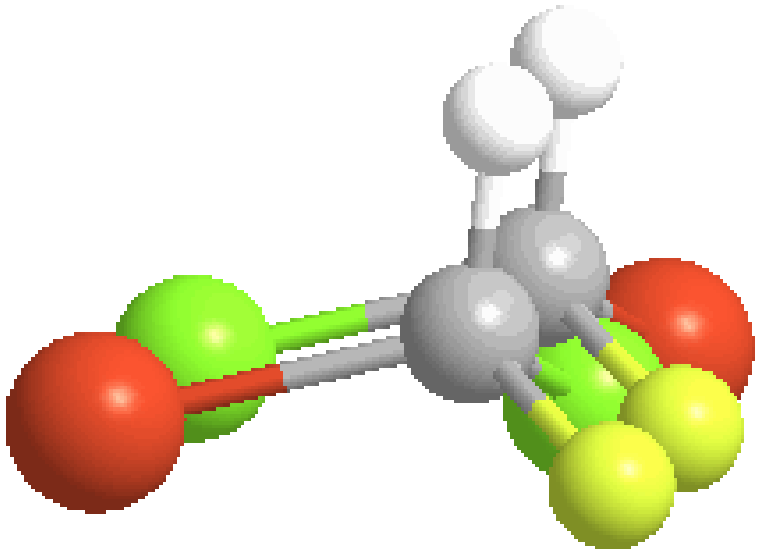
Chiral Compounds



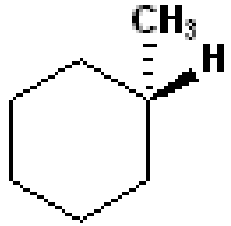
1

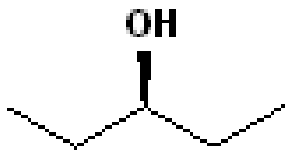


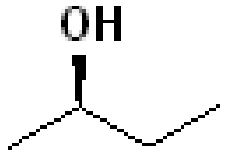
mirror image of **1**

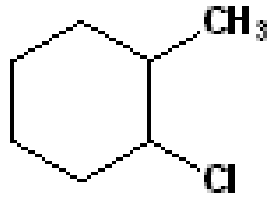


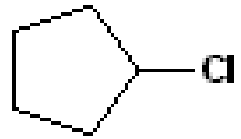
Indicate which Carbon atoms (if any) are chiral in the following structures

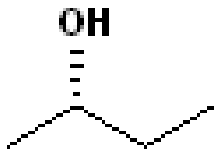


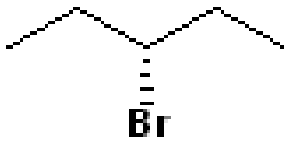


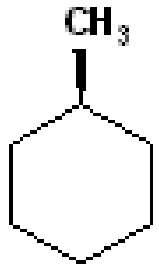


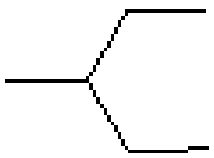


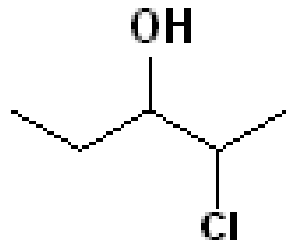


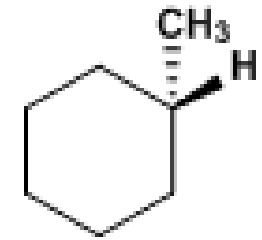






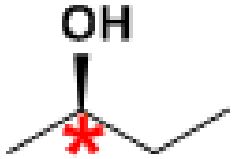


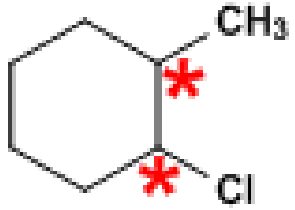




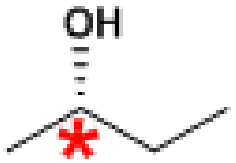
not chiral

not chiral

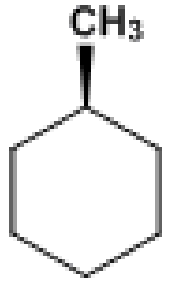




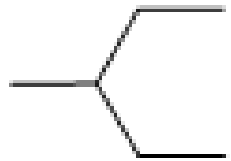
not chiral



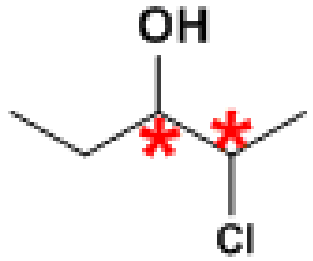
not chiral



not chiral

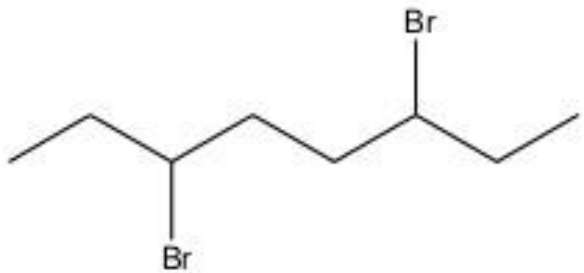


not chiral



How many stereogenic centers does each molecule have?

A)



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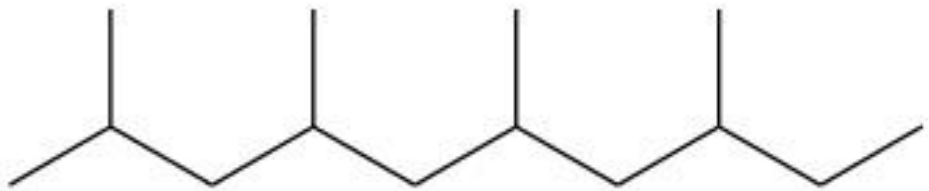

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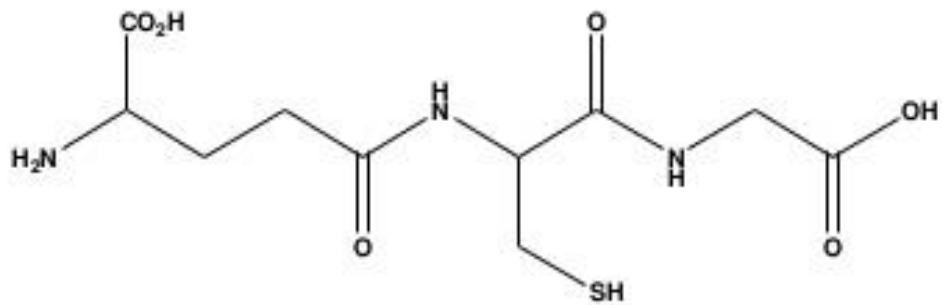


ASYMMETRIC CARBONS

The most common feature that leads to chirality in organic compounds is the presence of an asymmetric (or chiral) carbon atom. A carbon atom that is bonded to four different groups

In general:

no asymmetric C ----- usually achiral

1 asymmetric C ------ always chiral

≥2 asymmetric C ------ may or may not be chiral

CHIRAL VS. ACHIRAL

To determine if a compound is chiral:

0 asymmetric carbons: Usually achiral

1 asymmetric carbon: Always chiral

2 asymmetric carbons: Chiral or achiral

Does the compound have an internal plane of symmetry?

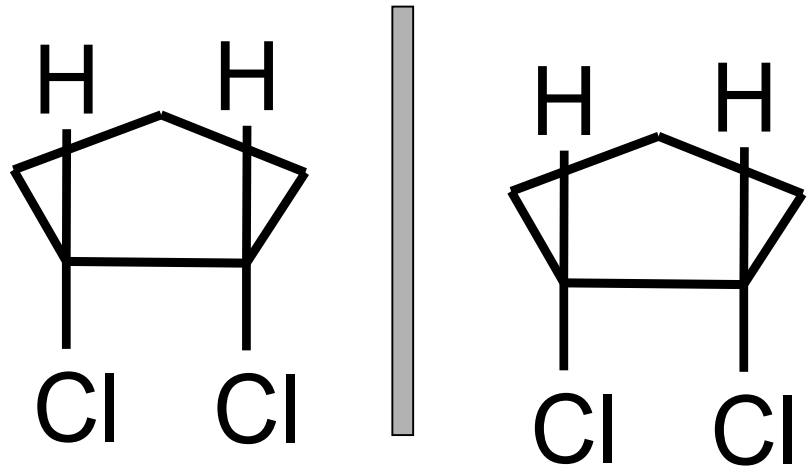
Yes: achiral

No: If mirror image is non-superimposable, then it's chiral.

If mirror image is superimposable, then it's achiral.

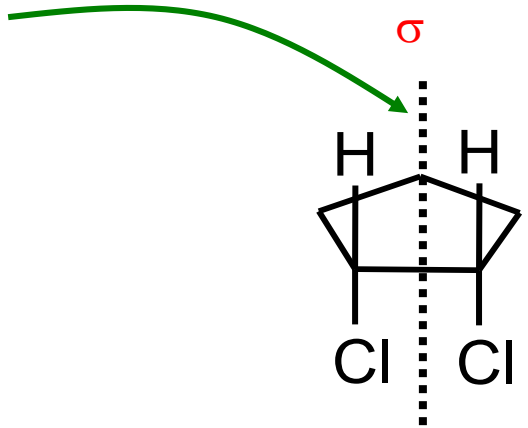
Achiral

- Many molecules and objects are achiral:
  - identical to its mirror image
  - not chiral



Internal Plane of Symmetry

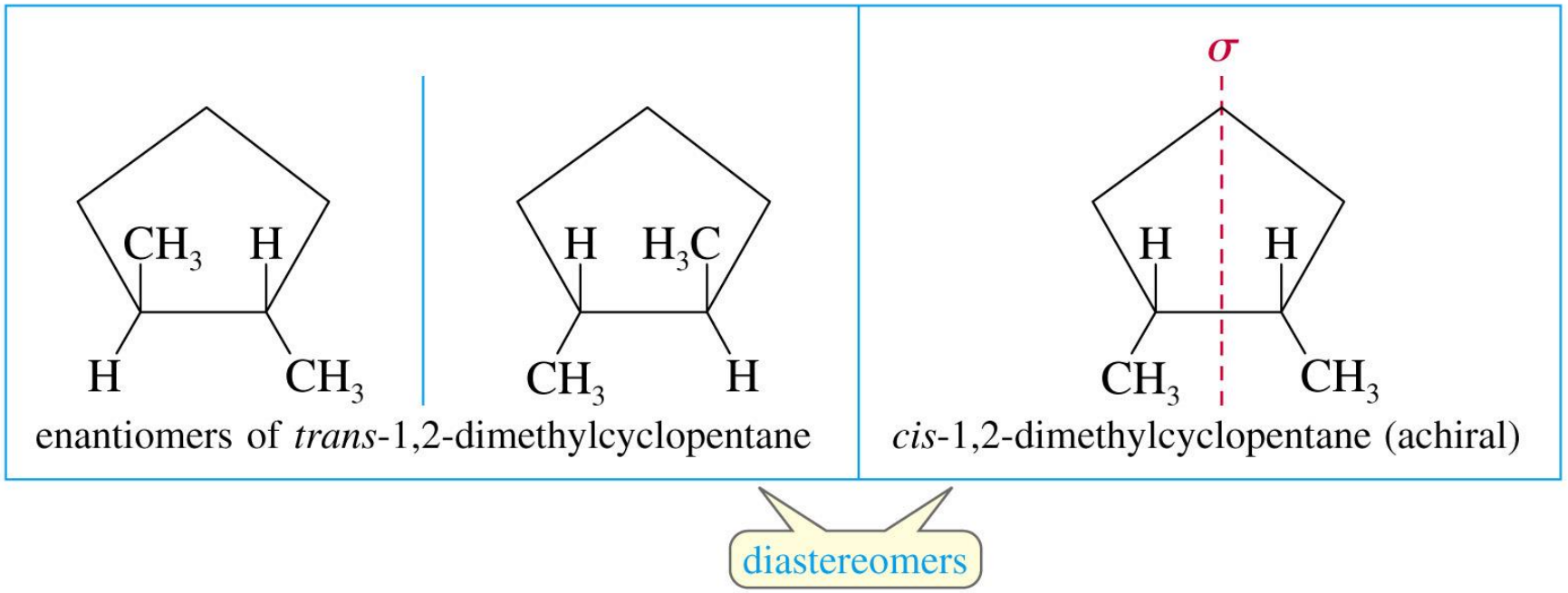
- Cis-1,2-dichlorocyclopentane contains two asymmetric carbons but is achiral.
  - contains an internal mirror plane of symmetry



- Any molecule that has an internal mirror plane of symmetry is achiral even if it contains asymmetric carbon atoms.

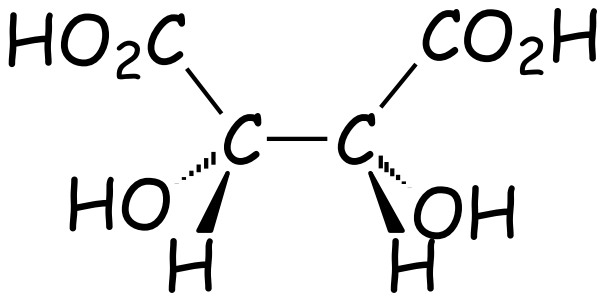
Internal Plane of Symmetry

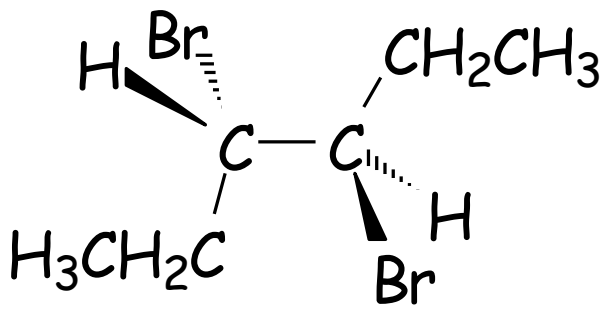
- **Cis-1,2-dichlorocyclopentane is a meso compound:**
  - an achiral compound that contains chiral centers
  - often contains an internal mirror plane of symmetry

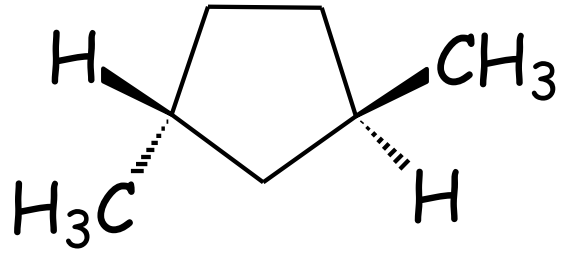


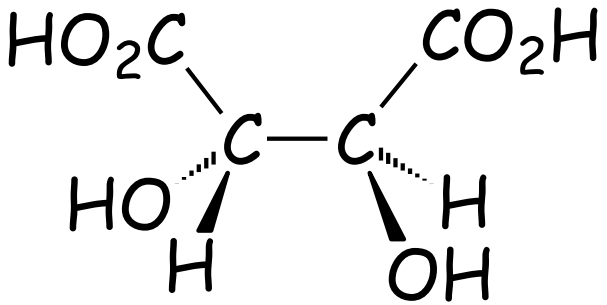
Internal Plane of Symmetry

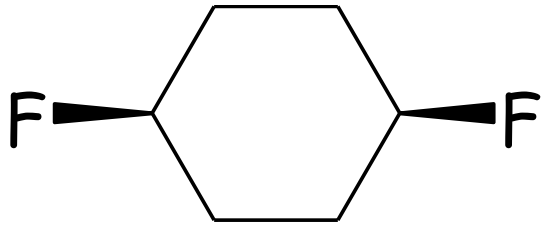
Example: **Which of the following compounds contain an internal mirror plane of symmetry?**

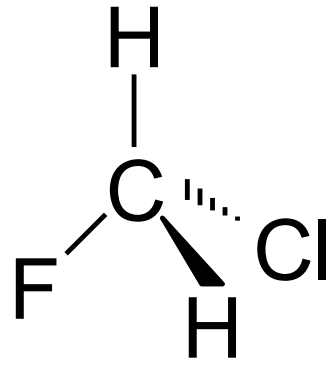






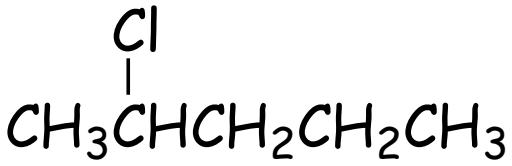


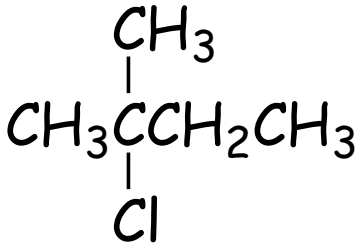


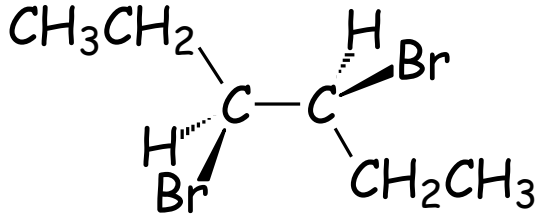


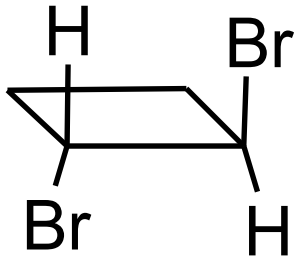
Chiral vs. Achiral

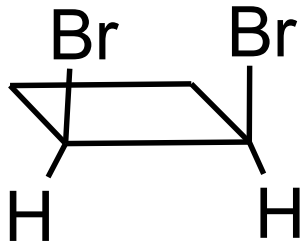
Example: Identify the following molecules as chiral or achiral.









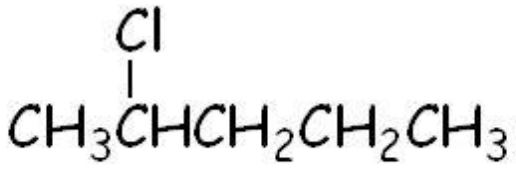


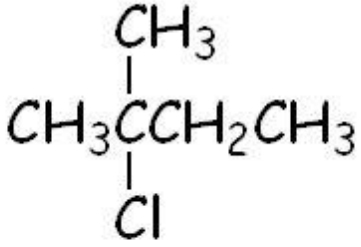
trans-1,3-dibromocyclohexane

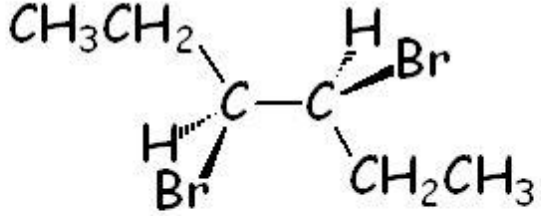
ethylcyclohexane

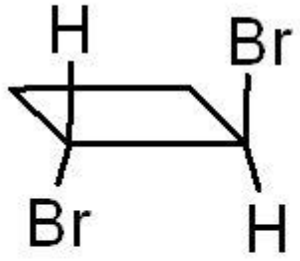
Chiral vs. Achiral

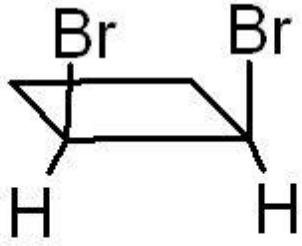
Example: Identify the following molecules as chiral or achiral.







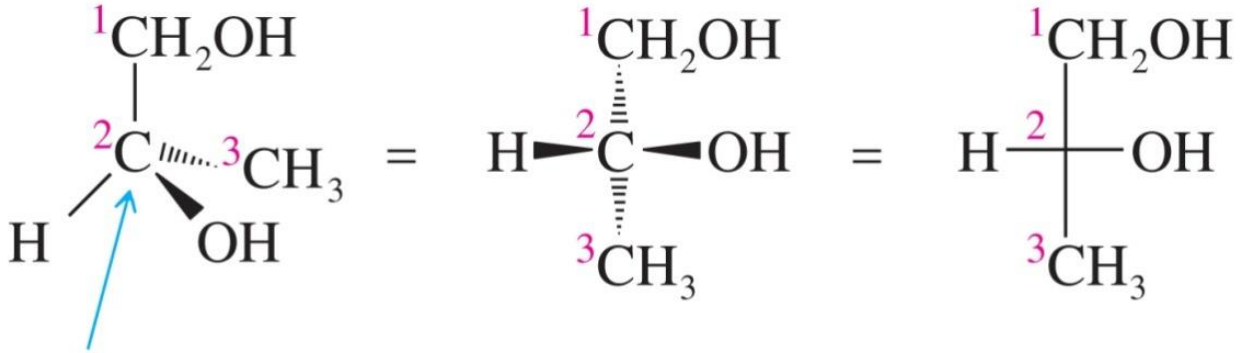




trans-1,3-dibromocyclohexane
ethylcyclohexane

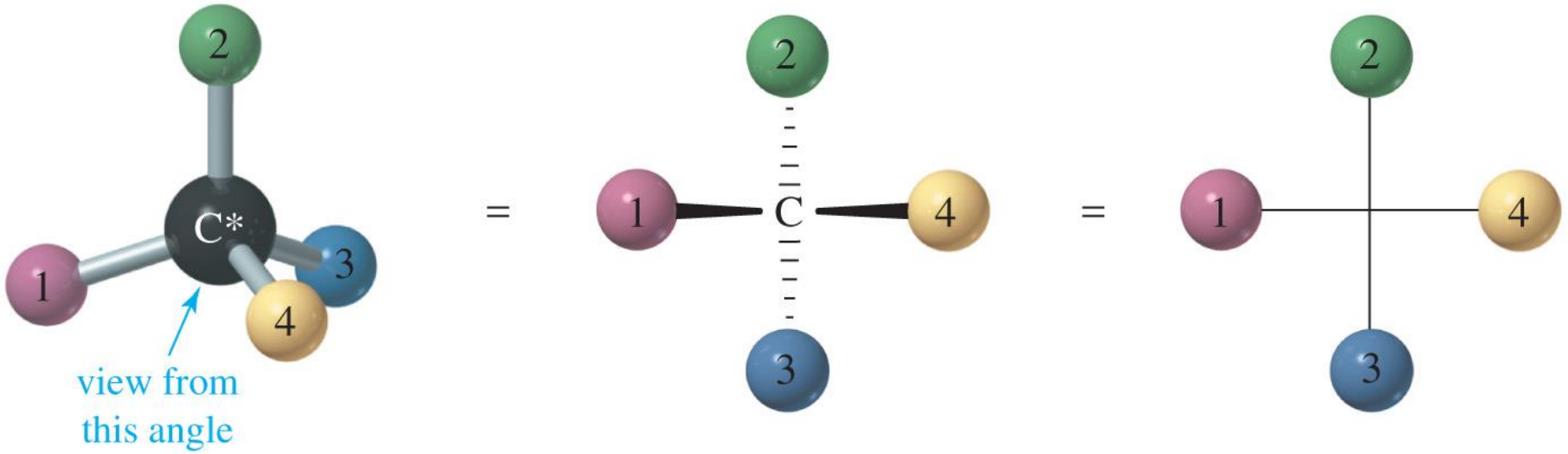
Fischer Projections

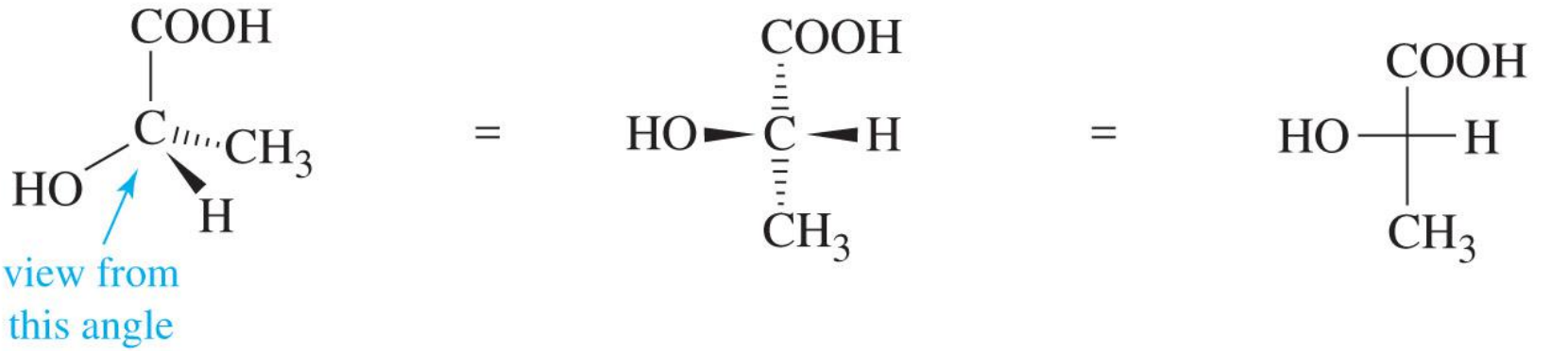
- Flat representation of a 3-D molecule.
- A chiral carbon is at the intersection of horizontal and vertical lines.
- Horizontal lines are forward, out of plane.
- Vertical lines are behind the plane.



(*R*)-propane-1,2-diol

Fischer Projections





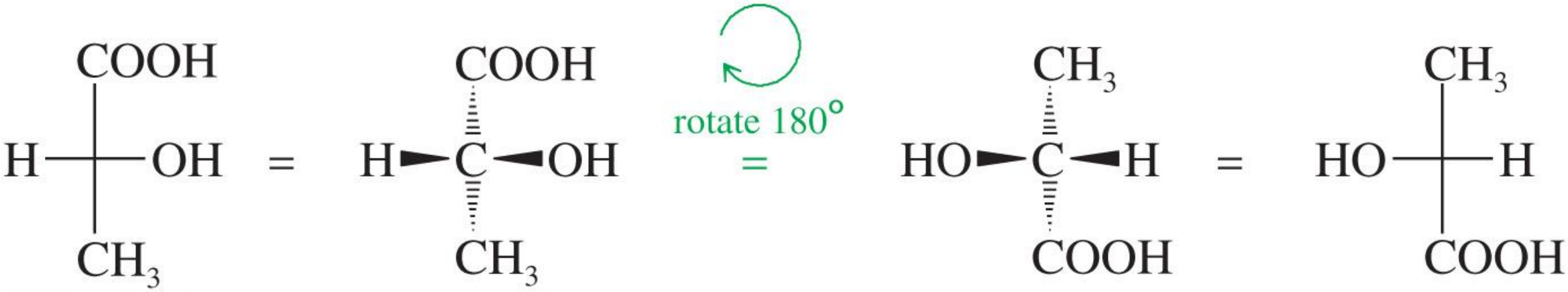
(*S*)-lactic acid
perspective drawing

(*S*)-lactic acid
Fischer projection

Fischer Rules

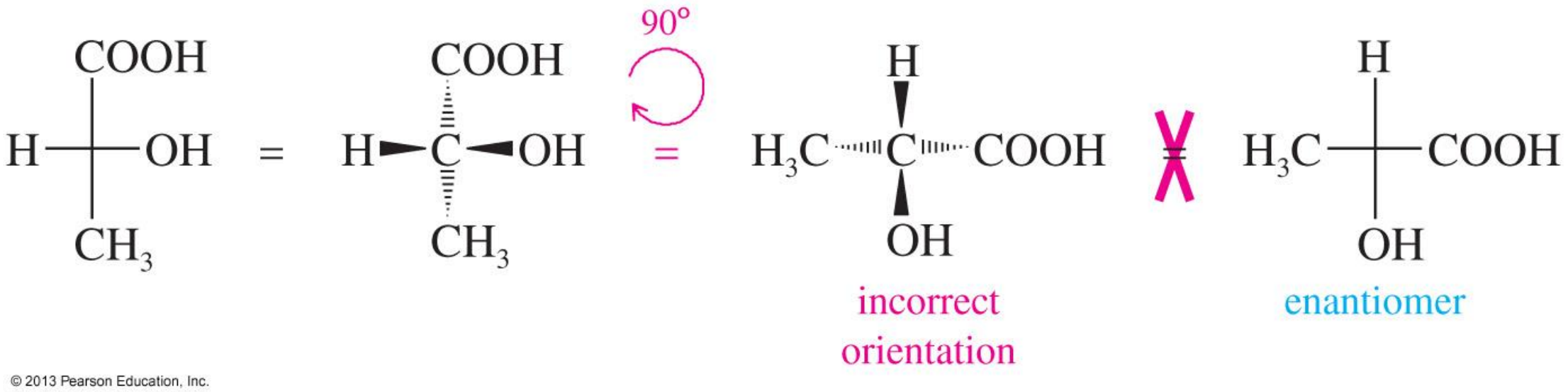
- Carbon chain is on the vertical line.
- Highest oxidized carbon is at top.
- Rotation of 180° in plane doesn't change molecule.
- Rotation of 90° is NOT allowed.

180° Rotation



A rotation of 180° is allowed because it will not change the configuration.

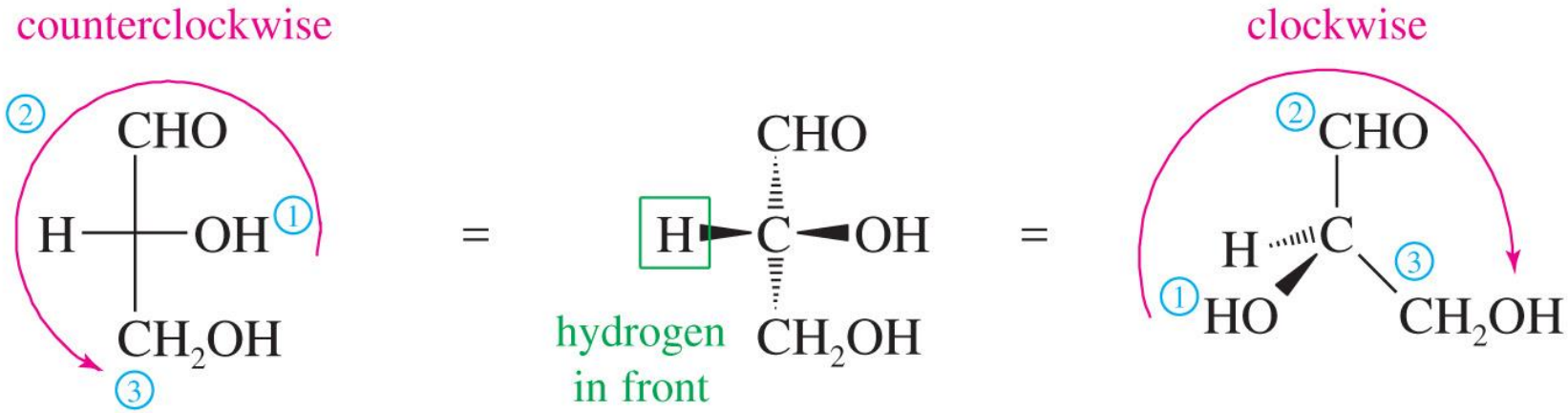
90° Rotation



- A 90° rotation will change the orientation of the horizontal and vertical groups.
- Do not rotate a Fischer projection 90°.

Glyceraldehyde

- The arrow from group 1 to group 2 to group 3 appears counterclockwise in the Fischer projection. If the molecule is turned over so the hydrogen is in back, the arrow is clockwise, so this is the *(R) enantiomer of glyceraldehyde.*



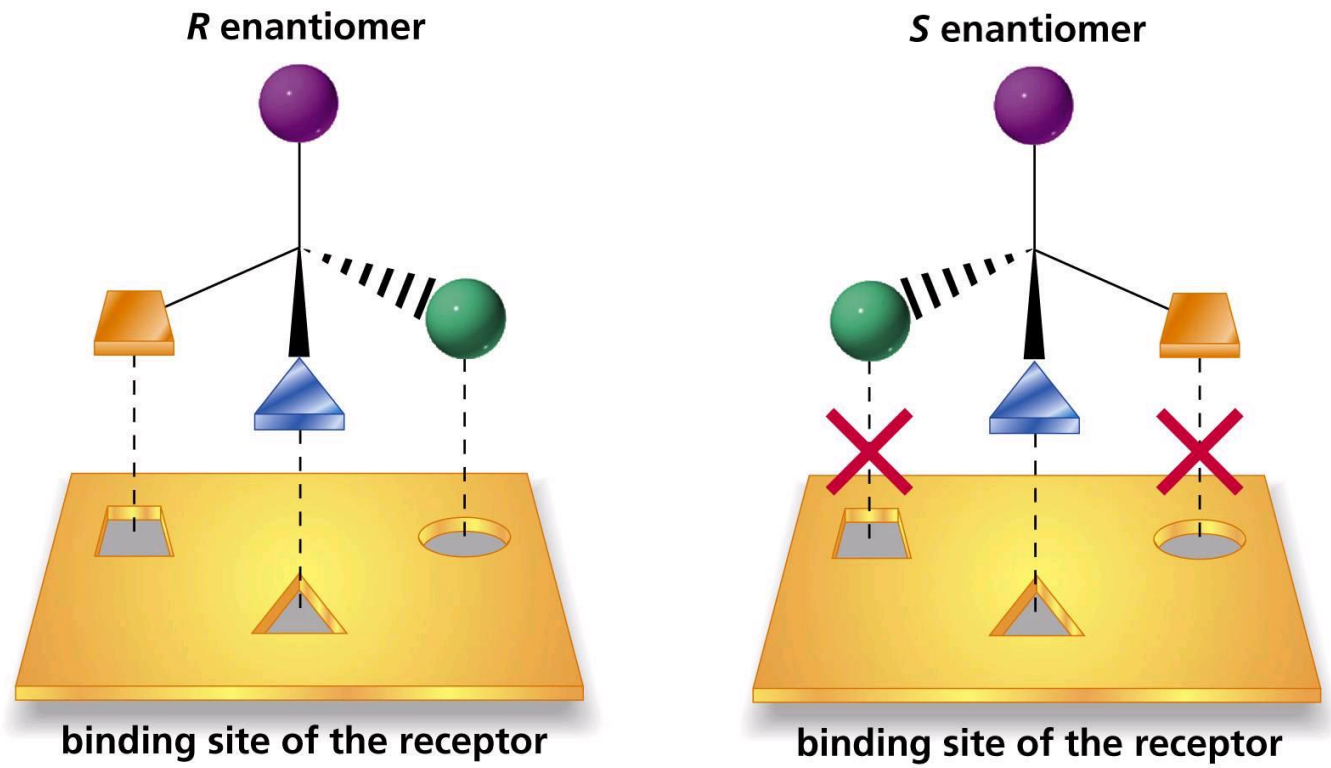
Fischer projection
(*R*)-(+)-glyceraldehyde

perspective drawing
(*R*)-(+)-glyceraldehyde

Cahn–Ingold–Prelog Priority System

- Enantiomers have different spatial arrangements of the four groups attached to the asymmetric carbon.
- The two possible spatial arrangements are called configurations.
- Each asymmetric carbon atom is assigned a letter (*R*) or (*S*) based on its three-dimensional configuration.
- Cahn–Ingold–Prelog convention is the most widely accepted system for naming the configurations of chirality centers.

- R-stereoisomer (Latin; *rectus* = right handed)
- S-stereoisomer (Latin; *sinister* = left handed)

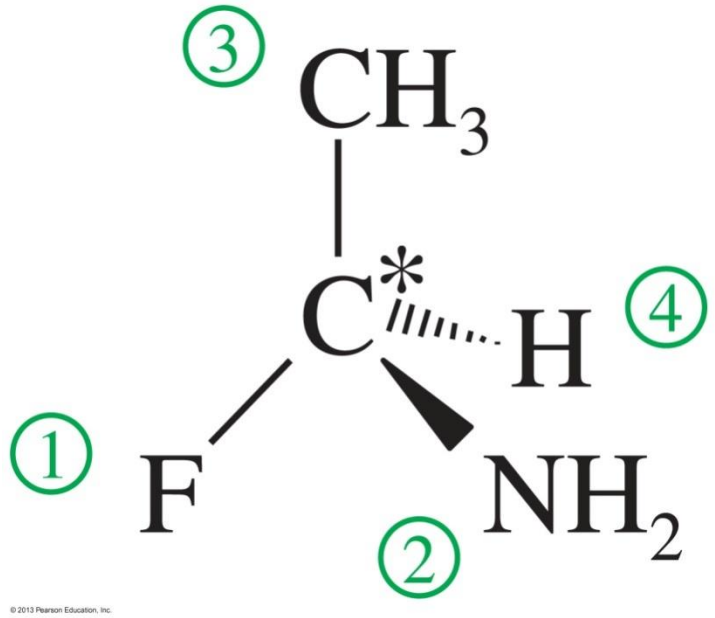


(R) and (S) Configuration: Step 1 Assign Priority

- Assign a relative "priority" to each group bonded to the asymmetric carbon. Group 1 would have the highest priority, group 2 second, etc.
- Atoms with higher atomic numbers receive higher priorities.

$I > Br > Cl > S > F > O > N > {}^{13}C > {}^{12}C > {}^{2}H > {}^{1}H$

Assign Priorities

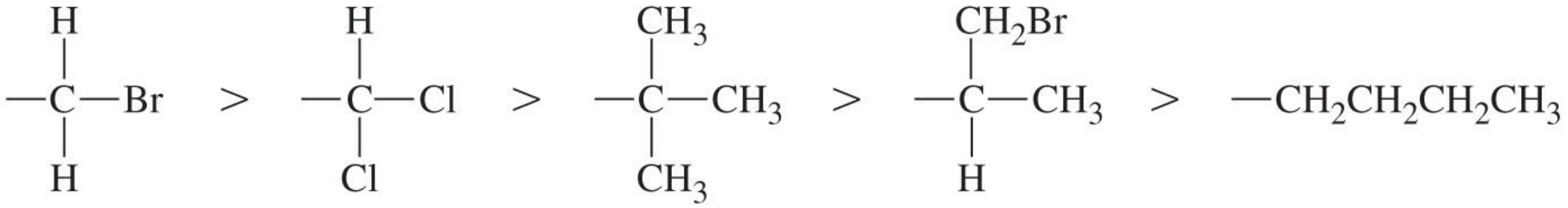


Atomic number: F > N > C > H

(R) and (S) Configuration: Breaking Ties

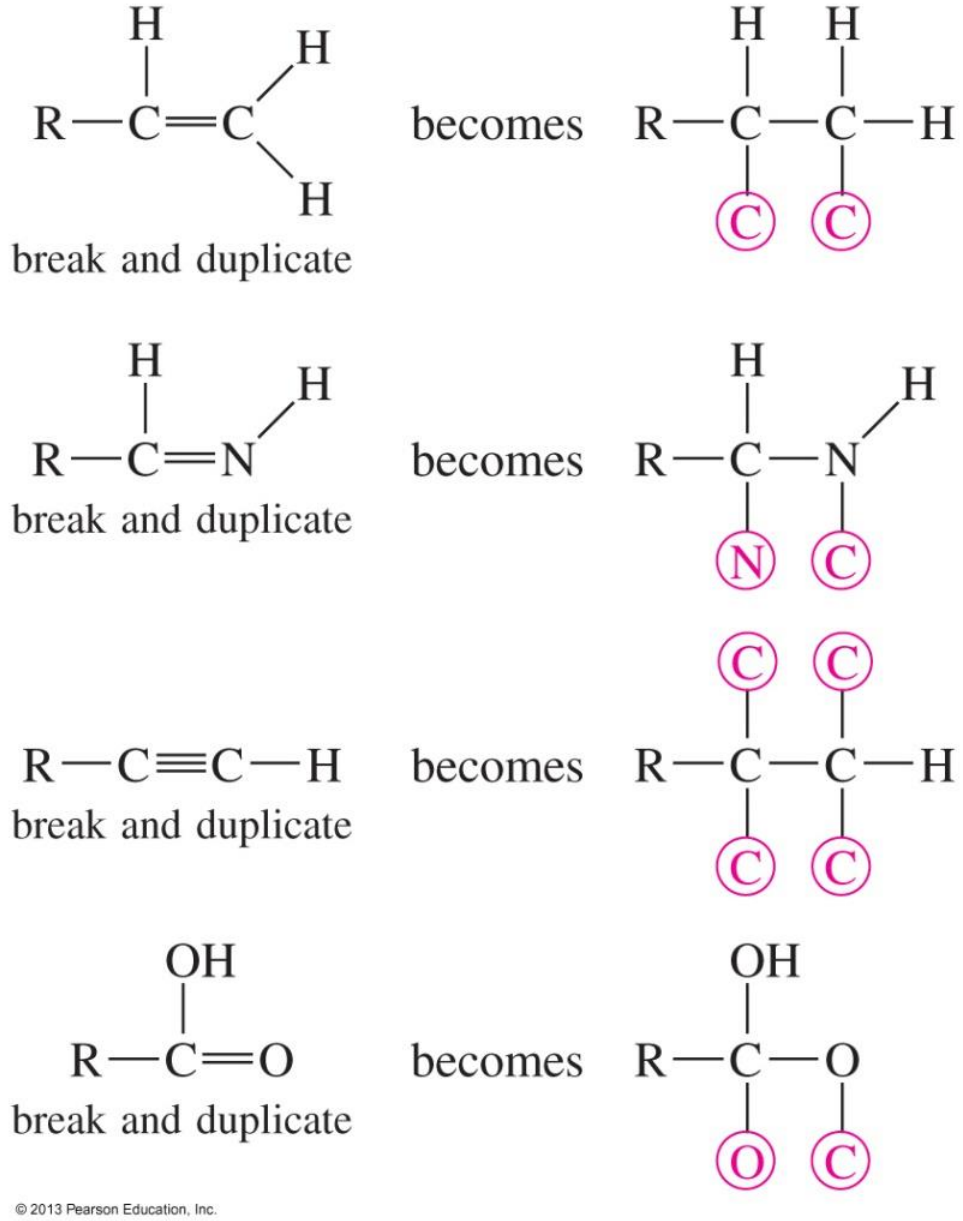
In case of ties, use the next atoms along the chain of each group as tiebreakers.

Examples



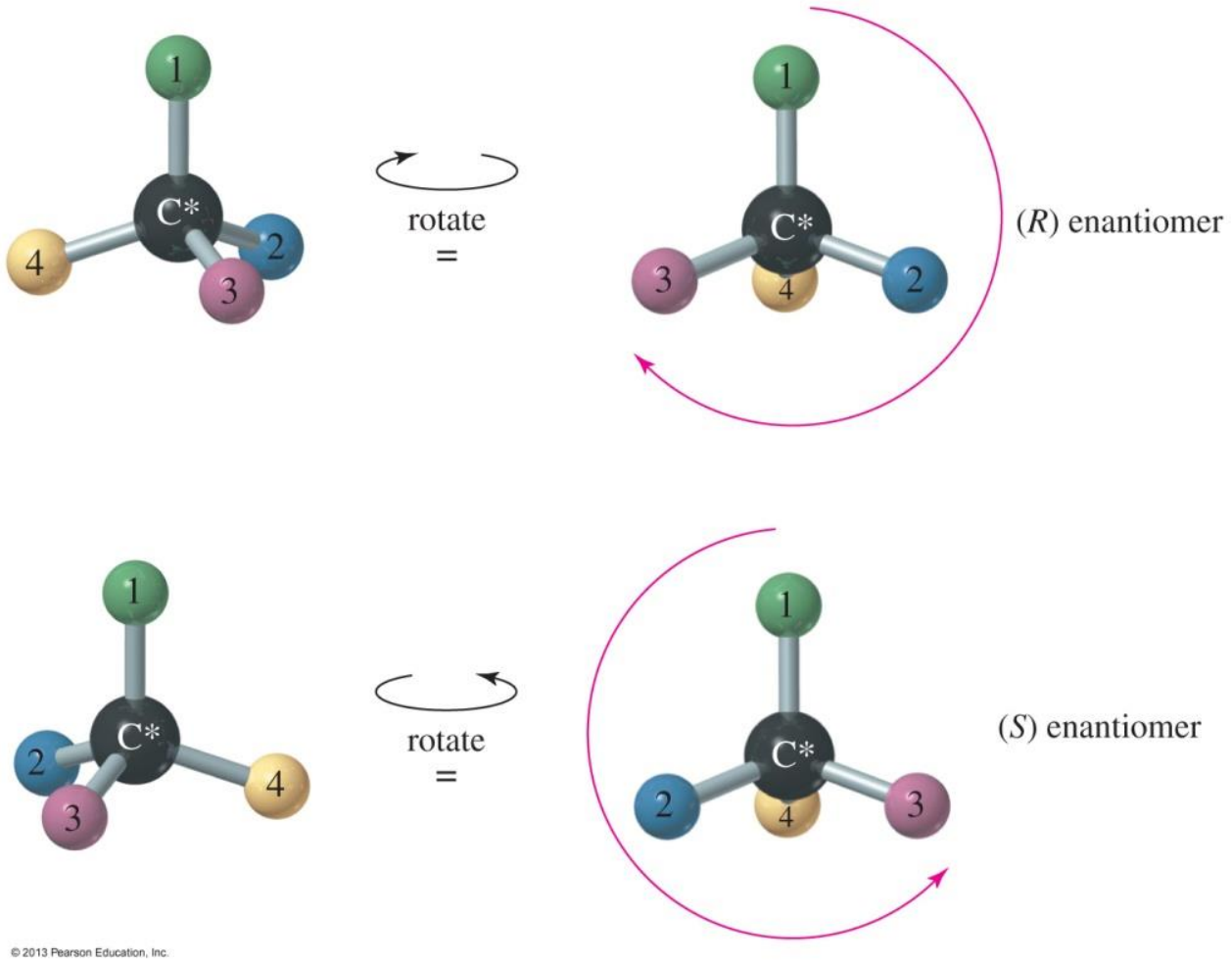
(R) and (S) Configuration: Multiple Bonds

Treat double and triple bonds as if each were a bond to a separate atom.

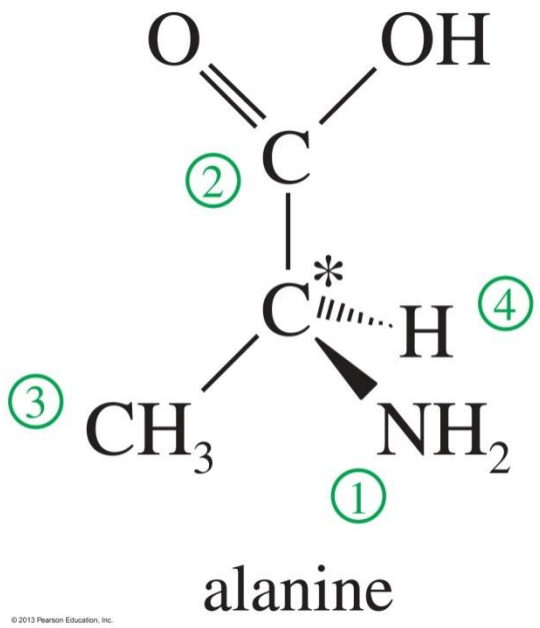


(R) and (S) Configuration: Step 2

- Working in 3-D, rotate the molecule so that the lowest priority group is in back.
- Draw an arrow from highest (1) to second highest (2) to lowest (3) priority group.
- Clockwise = (*R*), Counterclockwise = (*S*)



Assign Priorities



alanine

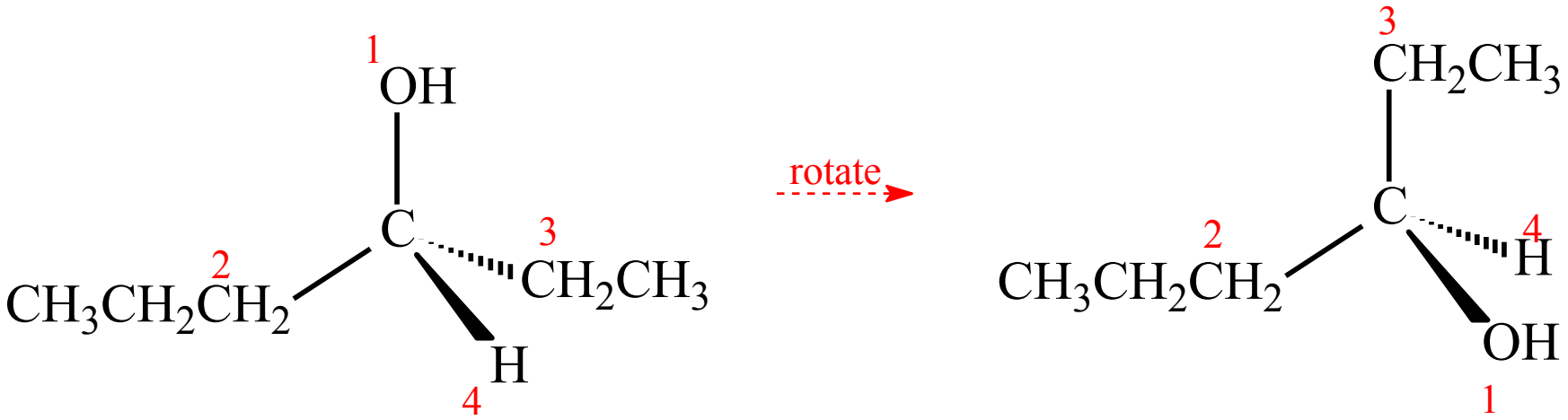
Counterclockwise

(*S*)

Draw an arrow from Group 1 to Group 2 to Group 3 and back to Group 1. Ignore Group 4.

Clockwise = (*R*) and Counterclockwise = (*S*)

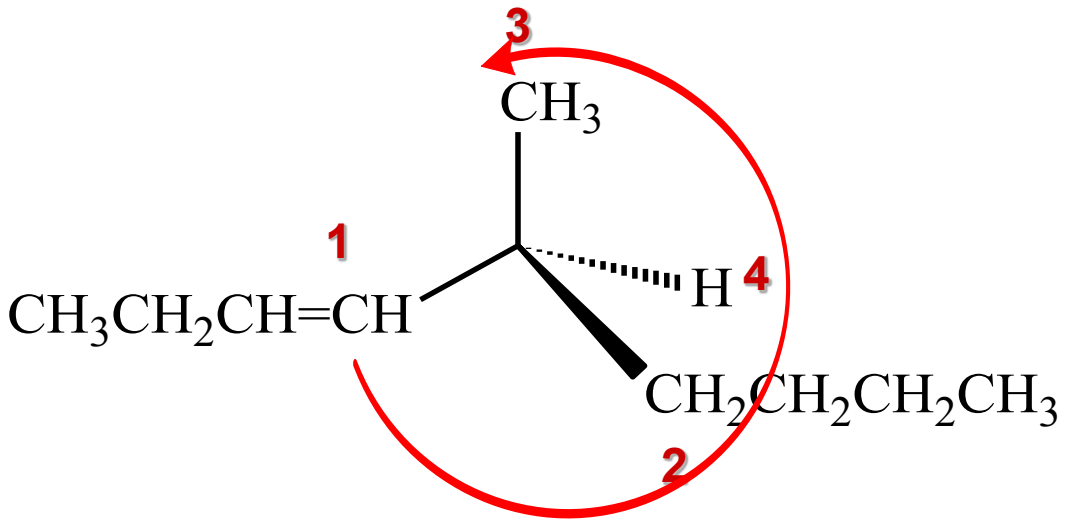
Example



Clockwise
(*R*)

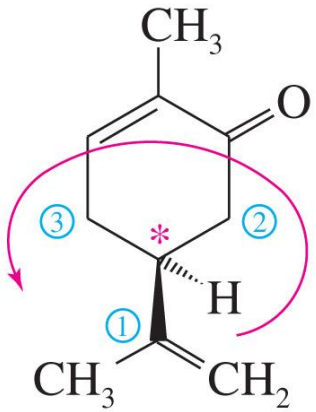
When rotating to put the lowest priority group in the back, keep one group in place and rotate the other three.

Example



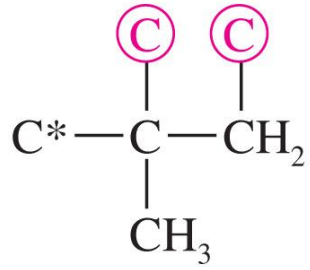
Counterclockwise
(*S*)

Configuration in Cyclic Compounds

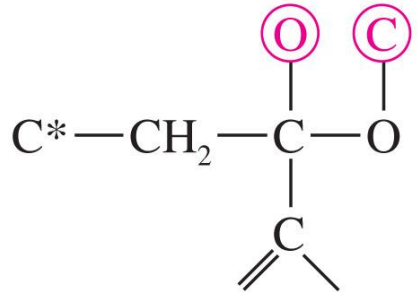


(*S*)-carvone

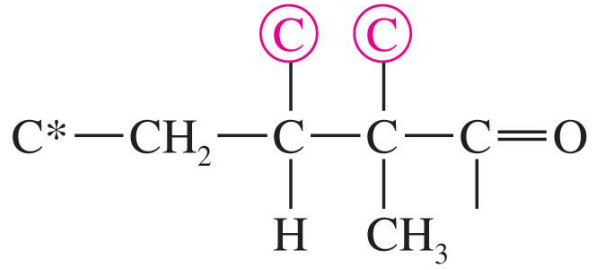
Group 1:



Group 2:



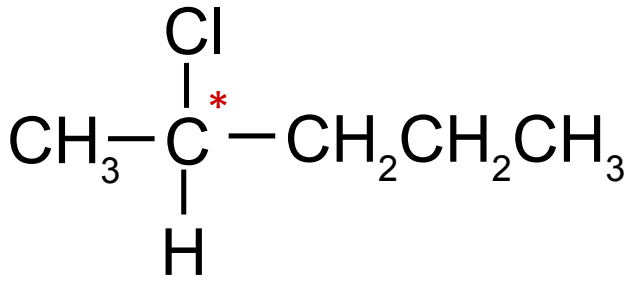
Group 3:



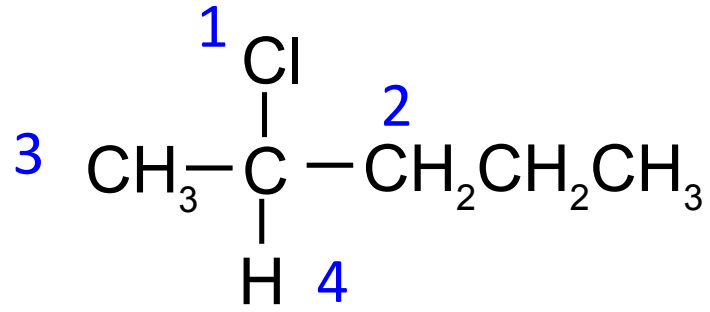
Depicting Structures with Asymmetric Carbons

Example: Draw a 3-dimensional formula for (R)-2-chloropentane.

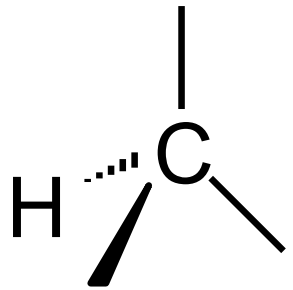
Step 1: Identify the asymmetric carbon.



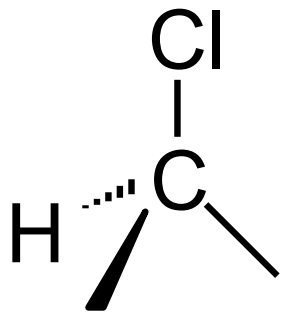
Step 2: Assign priorities to each group attached to the asymmetric carbon.



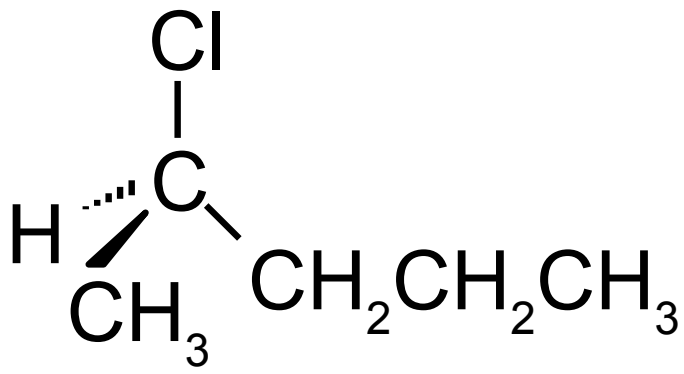
Step 3: Draw a "skeleton" with the asymmetric carbon in the center and the lowest priority group attached to the "dashed" wedge (i.e. pointing away from you).



Step 4: Place the highest priority group at the top.



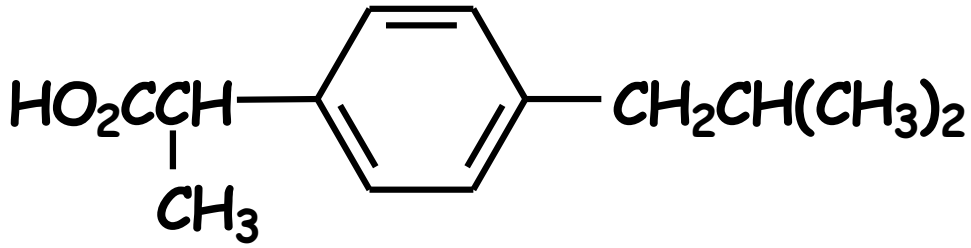
Step 5: For (R) configuration, place the 2nd and 3rd priority groups around the asymmetric carbon in a clockwise direction.



Step 6: Double-check your structure to make sure that it has the right groups and the right configuration.

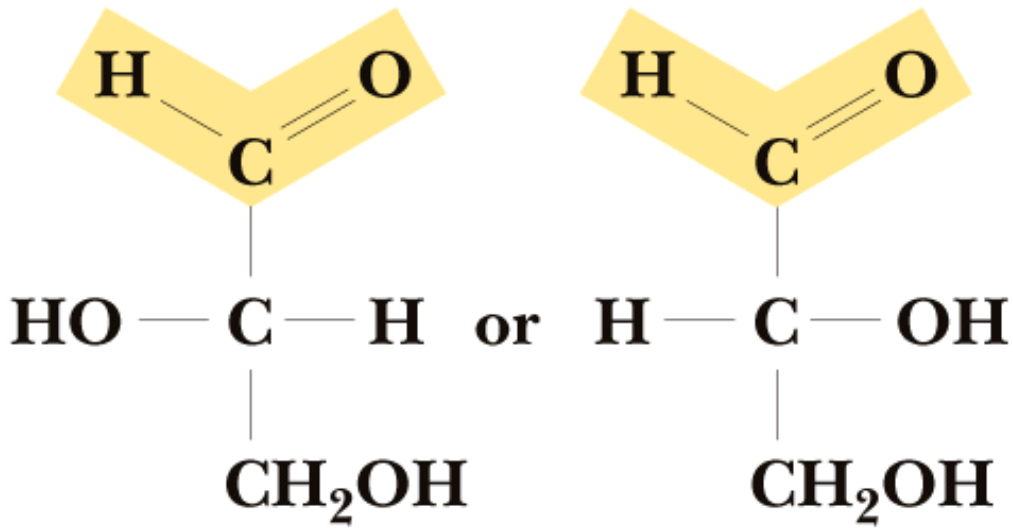
Depicting Structures with Asymmetric Carbons

Example: The R-enantiomer of ibuprofen is not biologically active but is rapidly converted to the active (S) enantiomer by the body. Draw the structure of the R-enantiomer.



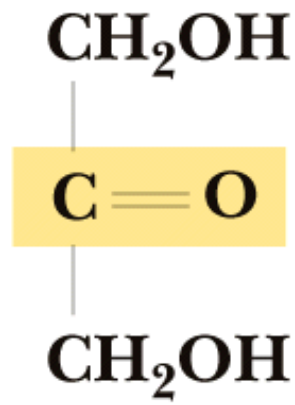
D-L Nomenclature

- D,L designation refers to the configuration of the highest-numbered asymmetric center
- D,L only refers the stereocenter of interest back to D- and L-glyceraldehyde!
- D,L do not specify the sign of rotation of plane-polarized light!
- All structures in Figures 7.2 and 7.3 are D
- D-sugars predominate in nature

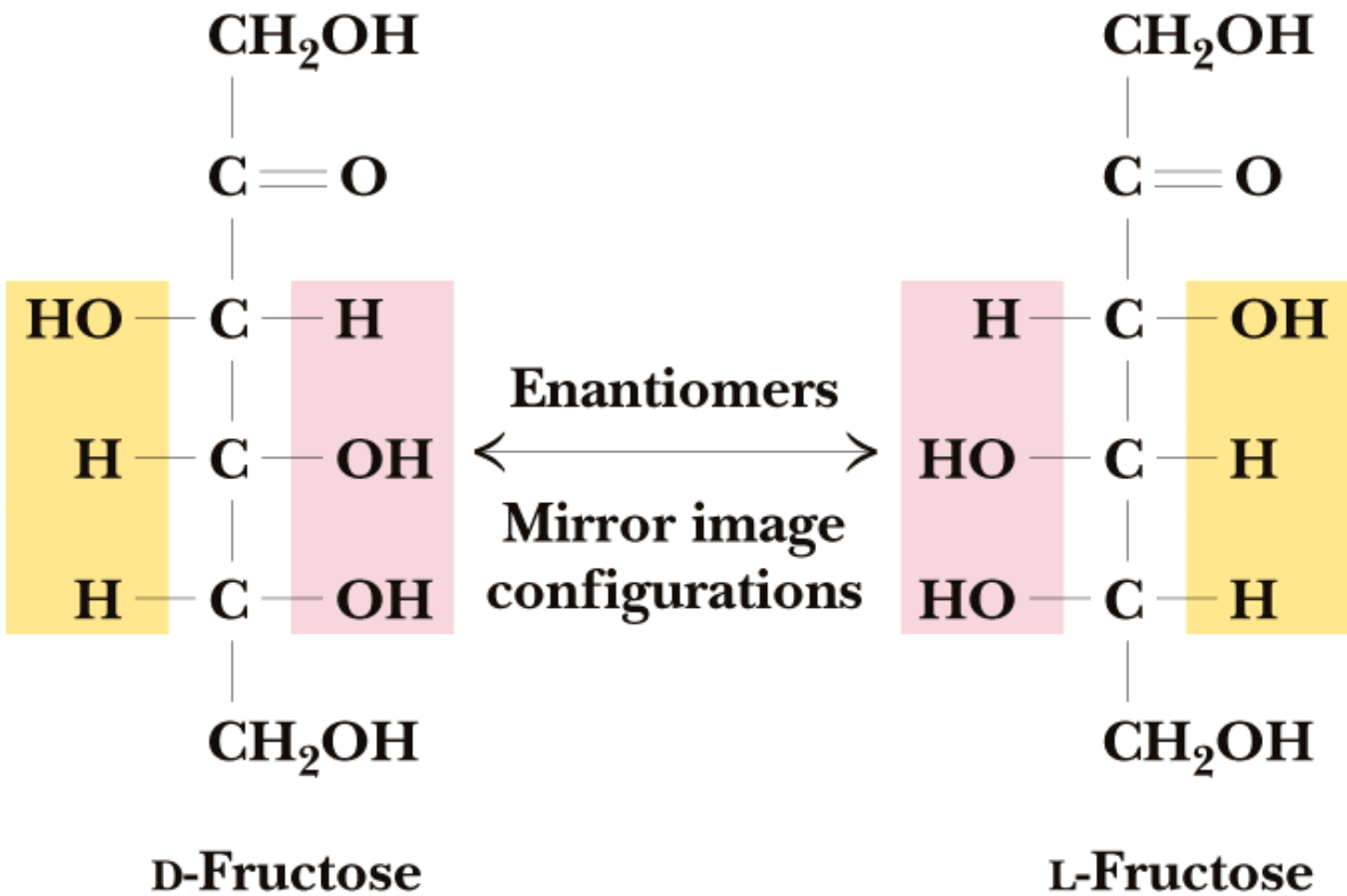


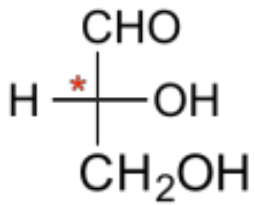
L-isomer D-isomer

Glyceraldehyde

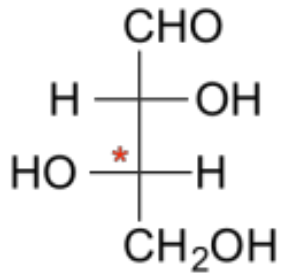


Dihydroxy-acetone

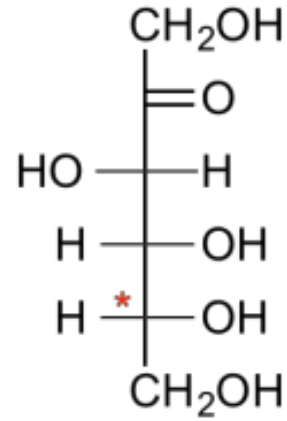

CH2OH
C=O
HO—C—H
H—C—OH
H—C—OH
CH2OH
Enantiomers
Mirror image configurations
CH2OH
C=O
H—C—OH
HO—C—H
HO—C—H
CH2OH
D-Fructose
L-Fructose



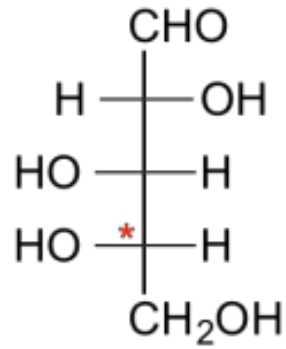
D-glyceraldehyde



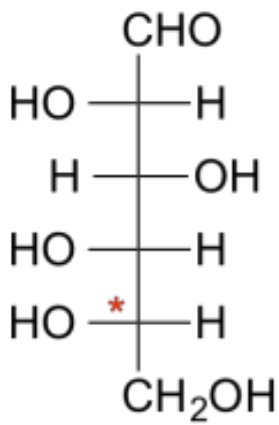
L-threose



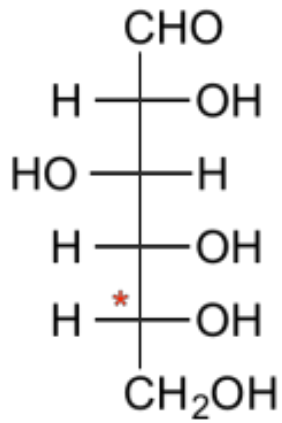
D-fructose



L-arabinose

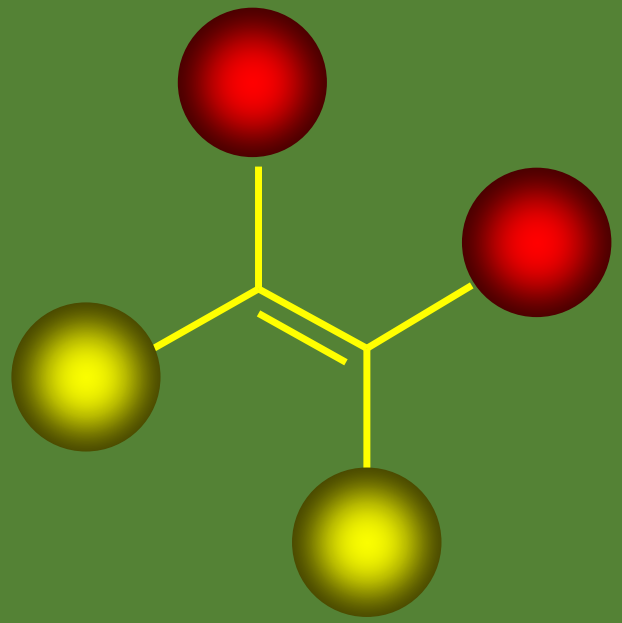


L-glucose

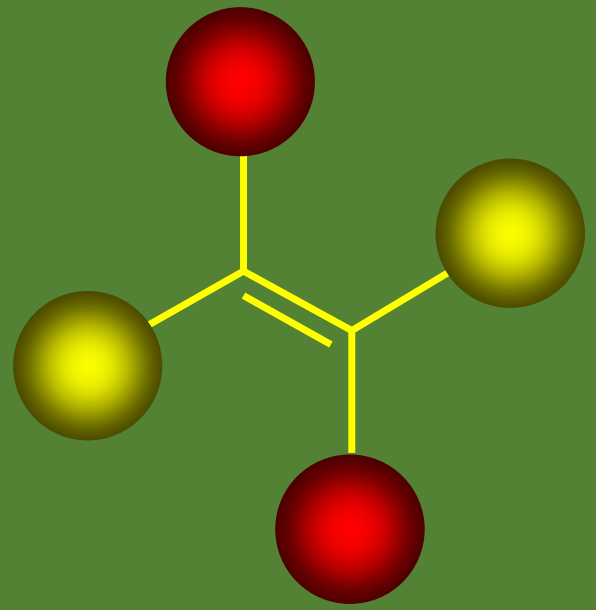


D-glucose

Stereochemical Notation

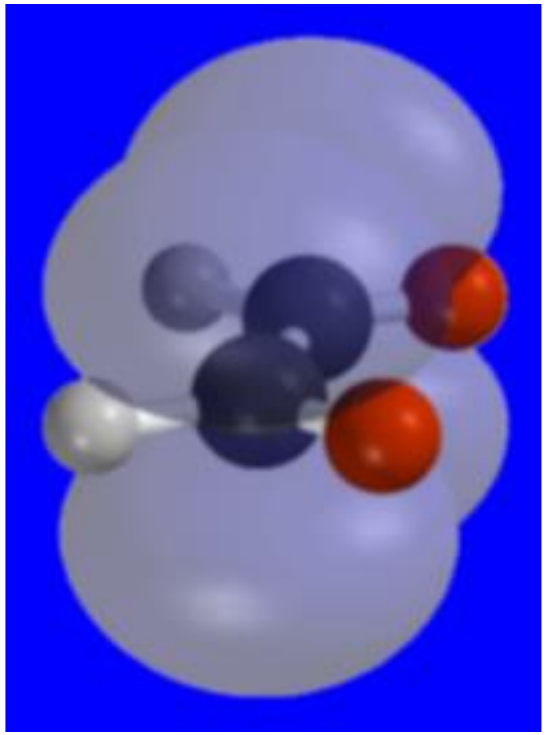


cis (identical or analogous substitutents on same side)

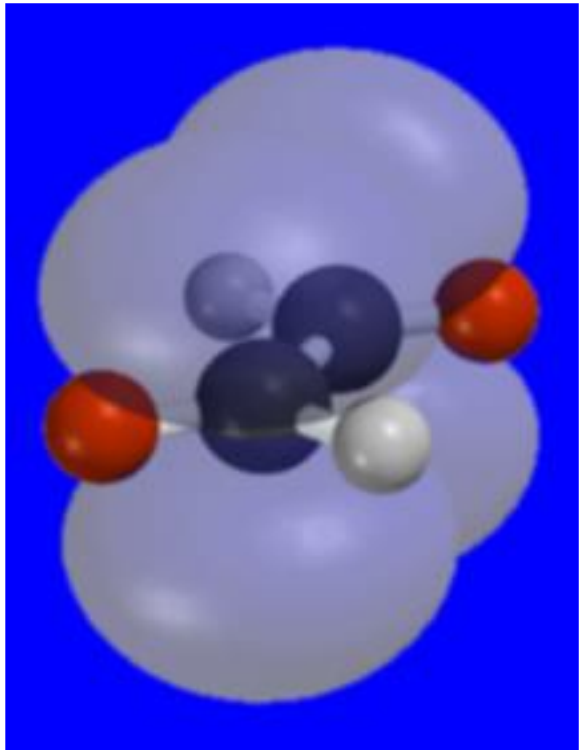


trans (identical or analogous substituents on opposite sides)

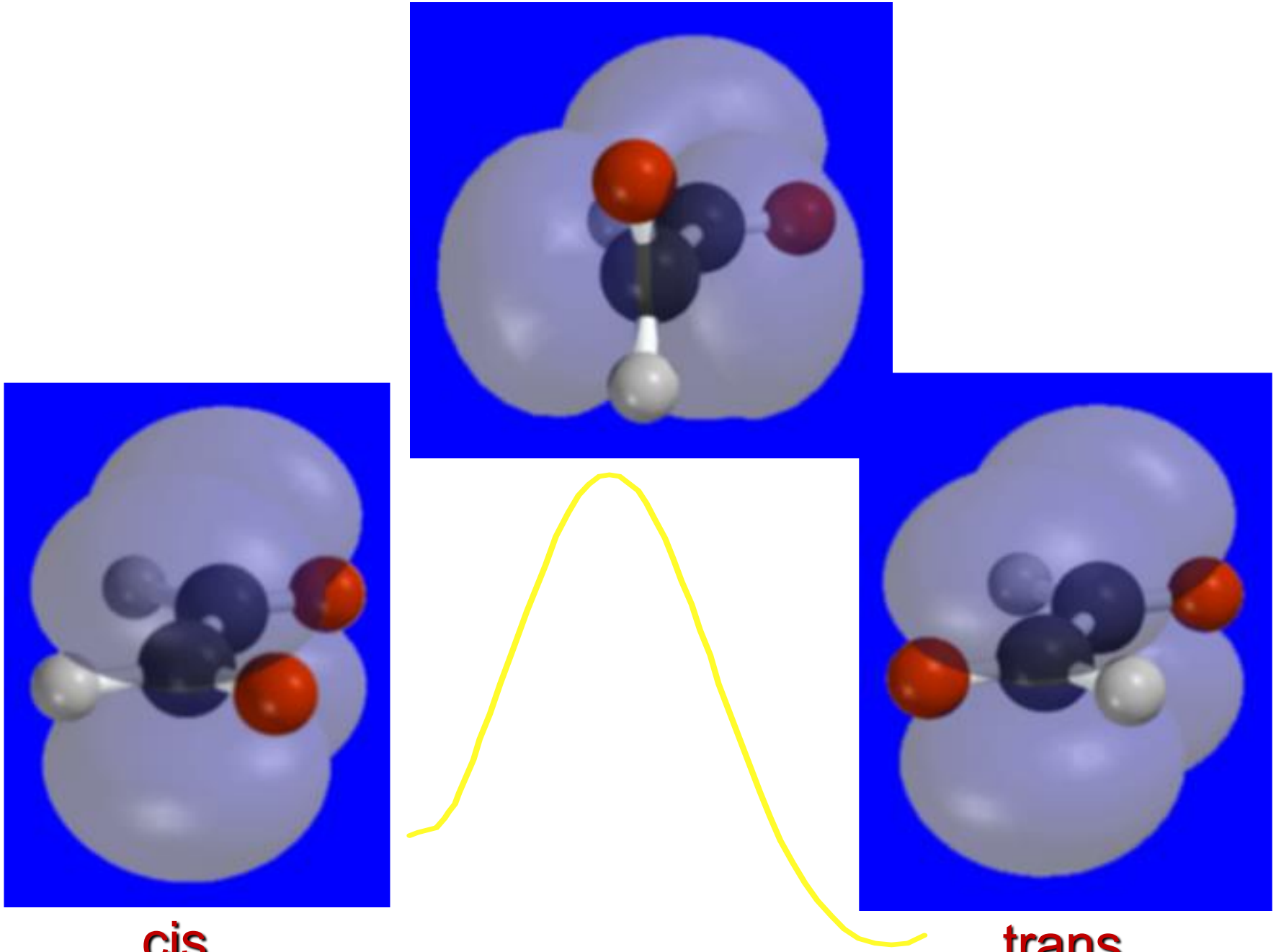
Interconversion of stereoisomeric alkenes does not normally occur. Requires that π component of double bond be broken.



cis

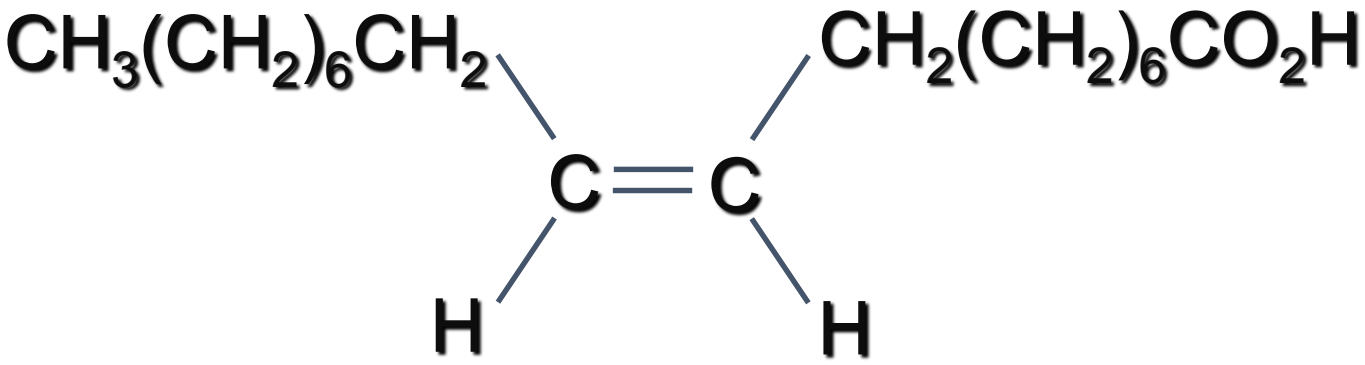


trans


cis
trans

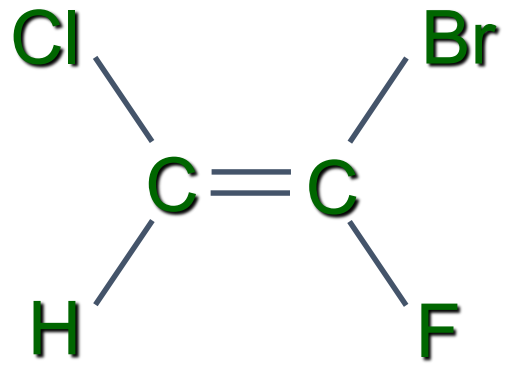
Naming Steroisomeric Alkenes by the E-Z Notational System

Stereochemical Notation



Oleic acid

- cis and trans are useful when substituents are identical or analogous (oleic acid has a cis double bond)
- cis and trans are ambiguous when analogies are not obvious



Cis or Trans

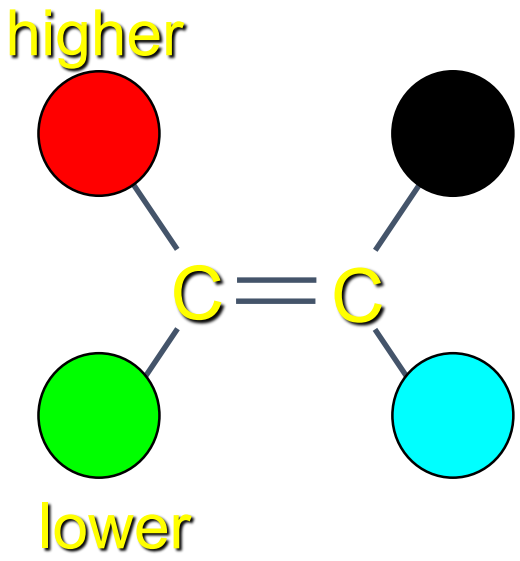
1) Systematic body of rules for ranking substituents

2) New set of stereochemical symbols other than cis and trans

The E-Z Notational System

E : higher ranked substituents on opposite sides

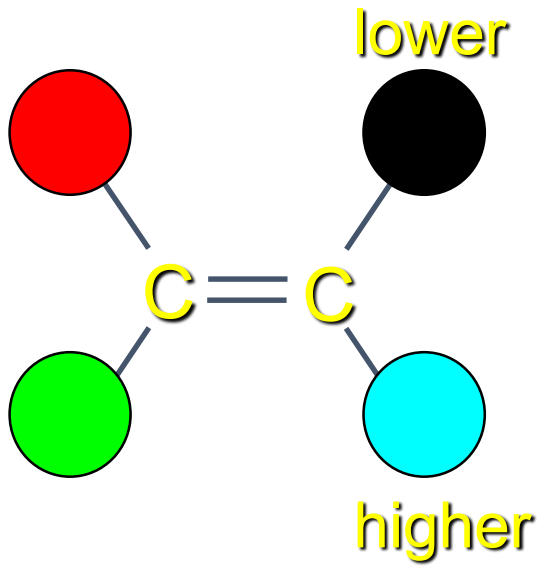
Z : higher ranked substituents on same side



The E-Z Notational System

E : higher ranked substituents on <u>opposite</u> sides

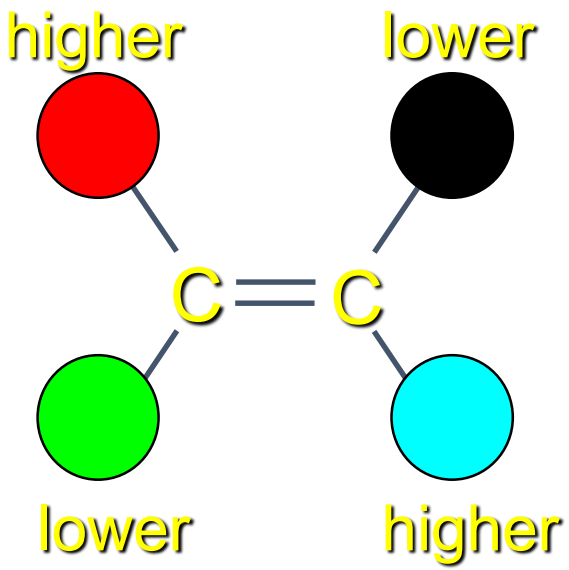
Z : higher ranked substituents on <u>same</u> side



The E-Z Notational System

E : higher ranked substituents on <u>opposite</u> sides

Z : higher ranked substituents on <u>same</u> side

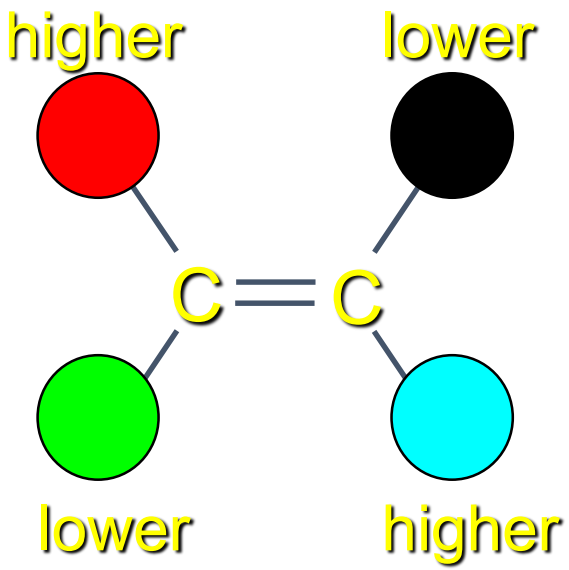


Entgegen

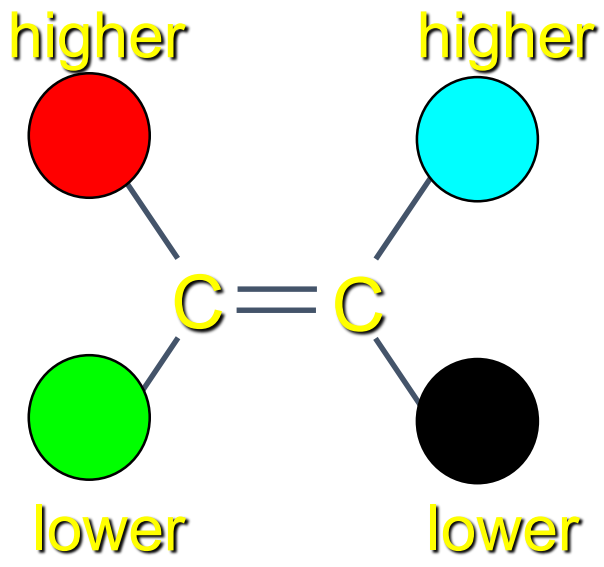
The E-Z Notational System

E : higher ranked substituents on <u>opposite</u> sides

Z : higher ranked substituents on <u>same</u> side



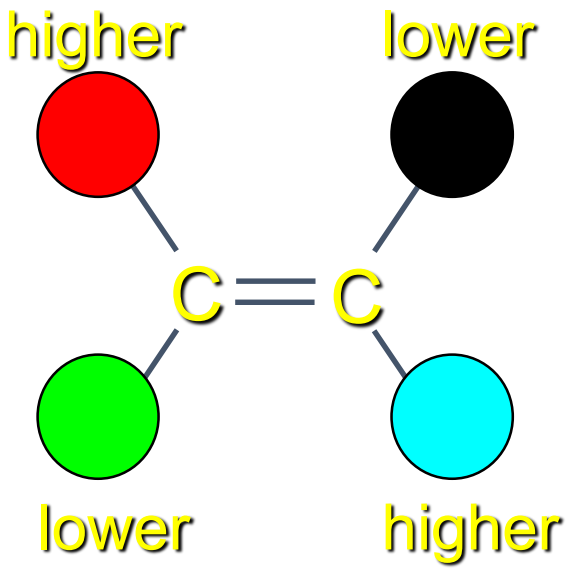
Entgegen



Zusammen

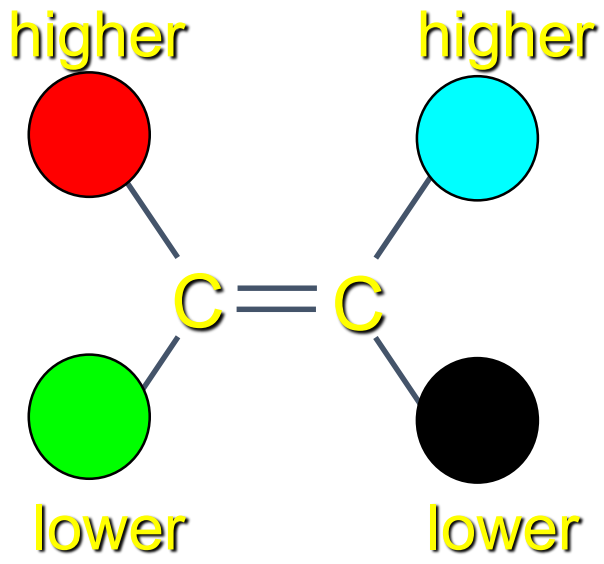
The E-Z Notational System

Question: How are substituents ranked?



E

Entgegen



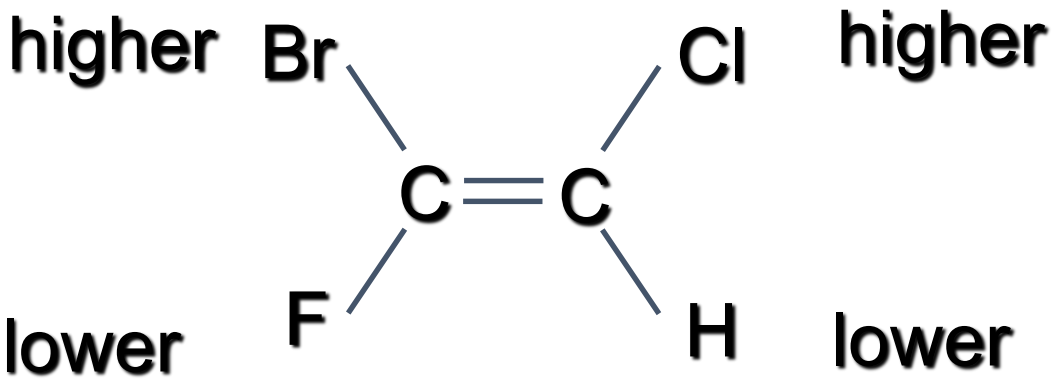
Z

Zusammen

Higher atomic number outranks lower atomic number

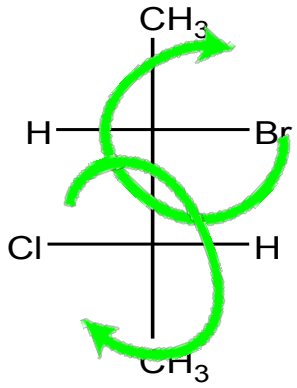
Br > F

Cl > H



(Z)-1-Bromo-2-chloro-1-fluoroethene

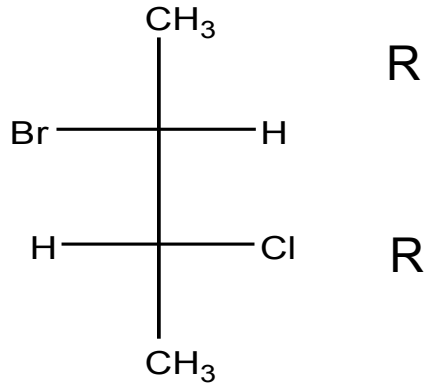
Multiple Chiral Centers



S

S

Do a single swap on each chiral center to get the enantiomeric molecule.



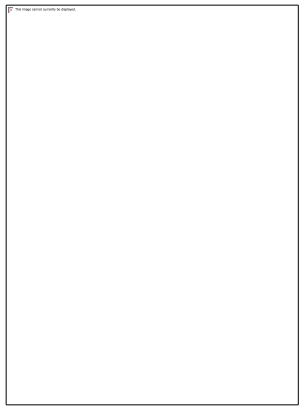
R

R

Each S configuration has changed to R.

(*2S,3S*) 2-bromo-3-chlorobutane

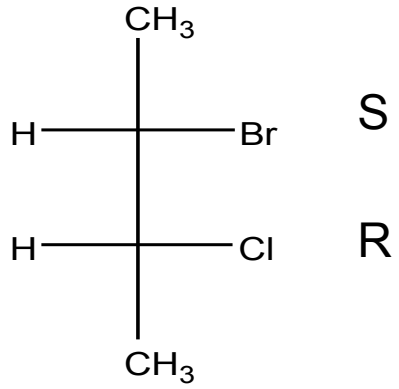
(*2R,3R*) 2-bromo-3-chlorobutane



R

S

Now do a single swap on only one chiral center to get a diastereomeric molecule (stereoisomers but not mirror objects).



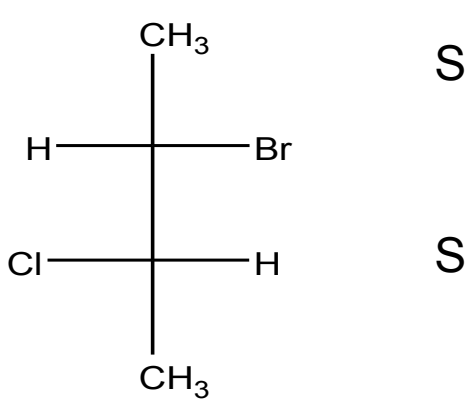
S

R

(*2R,3S*) 2-bromo-3-chlorobutane

(*2S,3R*) 2-bromo-3-chlorobutane

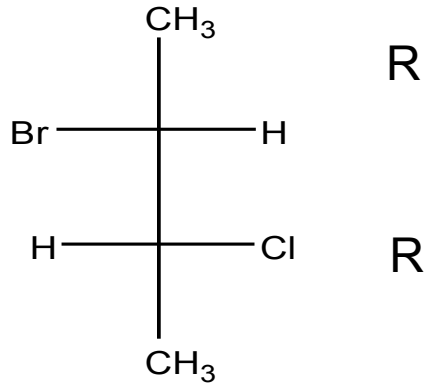
Multiple Chiral Centers



S

S

Enantiomers

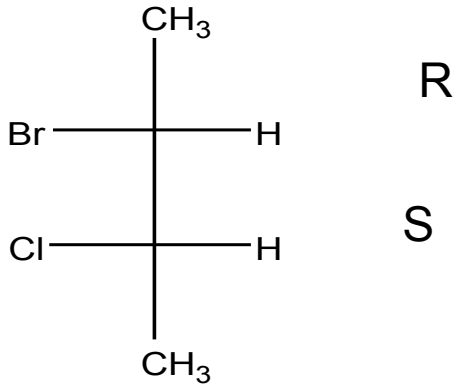


R

R

(*2S,3S*) 2-bromo-3-chlorobutane

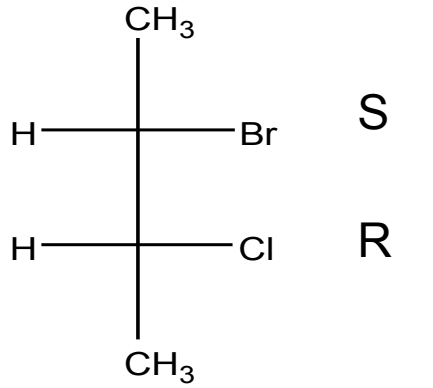
(*2R,3R*) 2-bromo-3-chlorobutane



R

S

Enantiomers



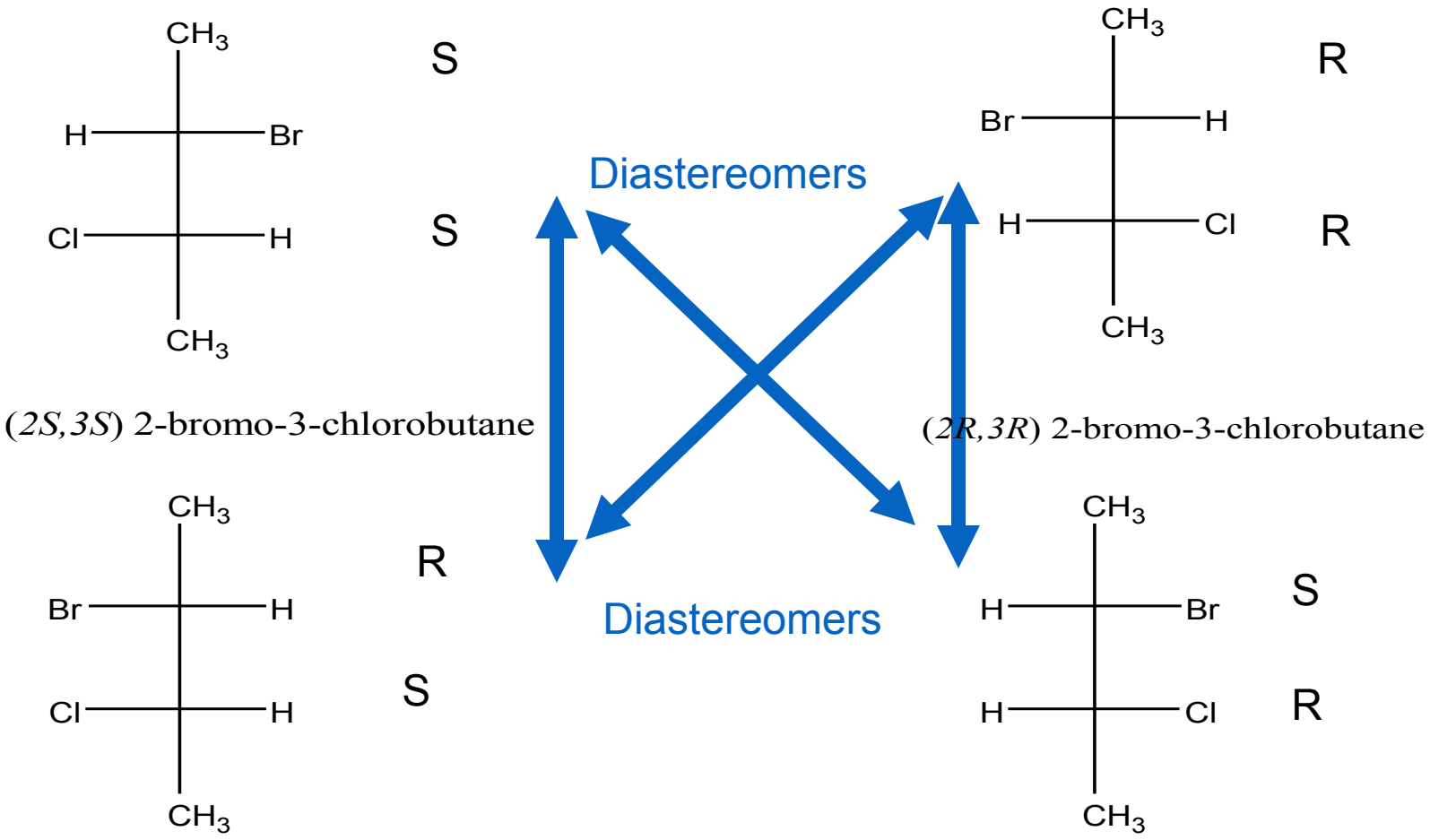
S

R

(*2R,3S*) 2-bromo-3-chlorobutane

(*2S,3R*) 2-bromo-3-chlorobutane

Multiple Chiral Centers

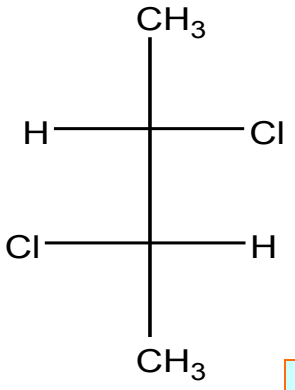


Diastereomers

- Require the presence of two or more chiral centers.
- Have different physical and chemical properties.
- May be separated by physical and chemical techniques.

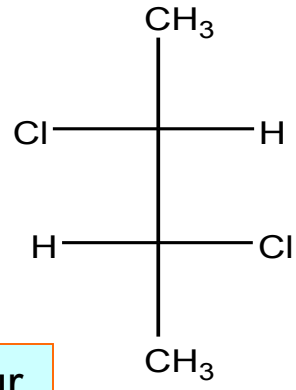
Meso Compounds

Must have same set of substituents on corresponding chiral carbons.



S

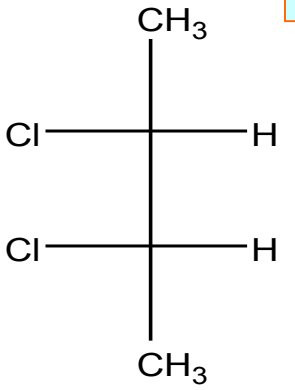
S



R

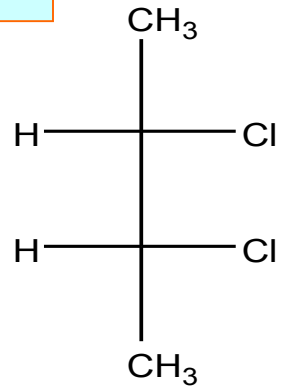
R

As we had before here are the four structures produced by systematically varying the configuration at each chiral carbon.



R

S

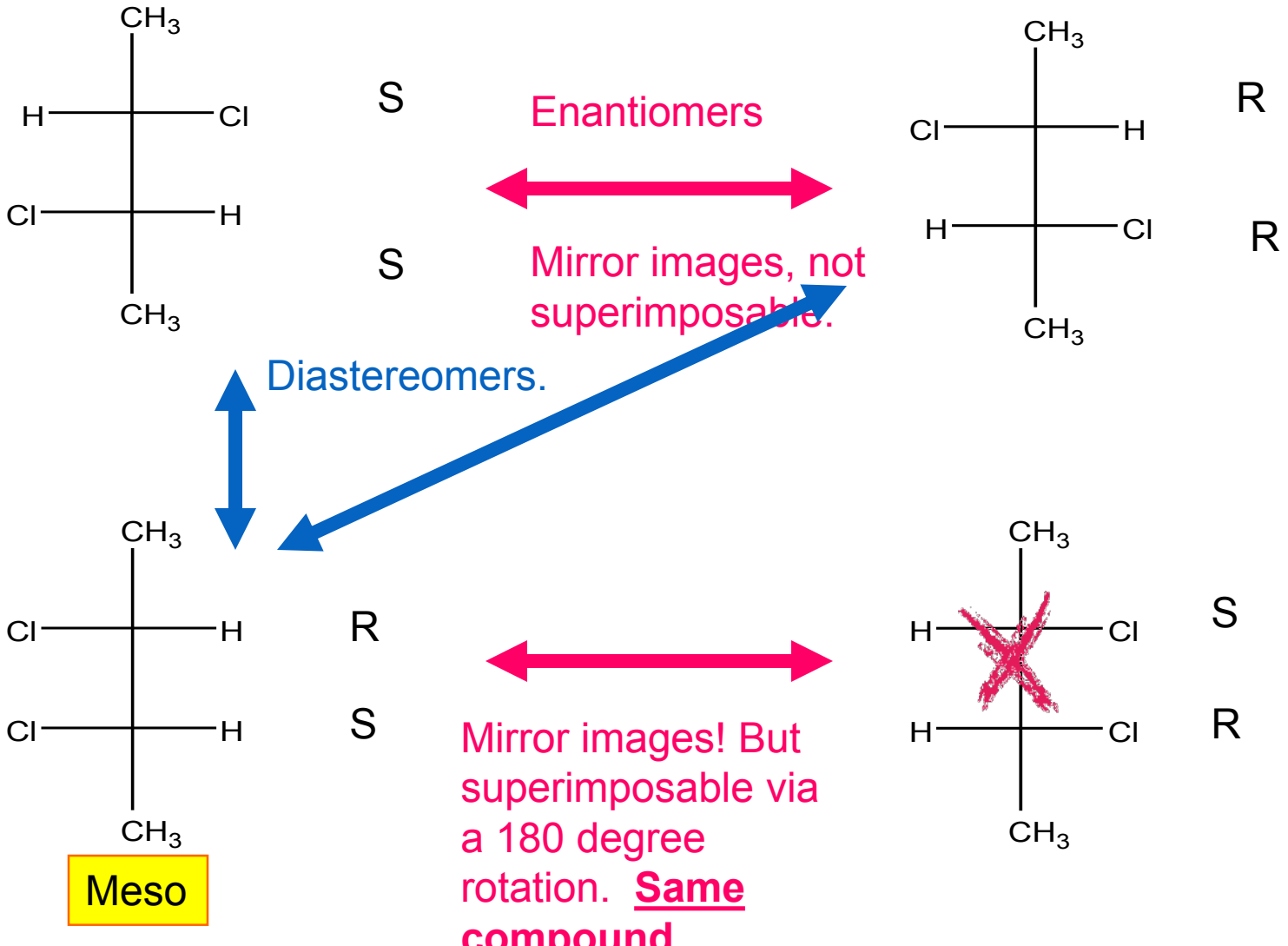


S

R

Meso Compounds

What are the stereochemical relationships?



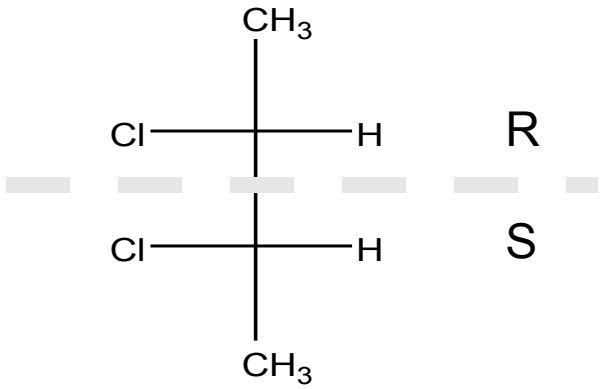
Meso Compounds

Has at least two chiral carbons.Corresponding carbons are of opposite configuration.

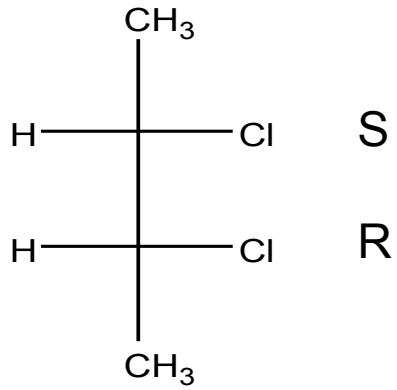
Can be superimposed on mirror object, optically inactive.

Can demonstrate mirror plane of symmetry

Molecule is achiral. Optically inactive. Specific rotation is zero.



Meso



Can be superimposed by 180 deg rotation.

Meso Compounds: Recognizing

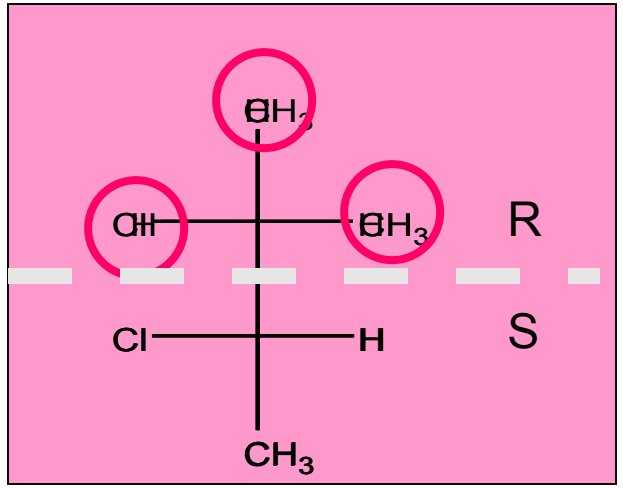
What of this structure? It has chiral carbons. Is it optically active? Is it meso instead?

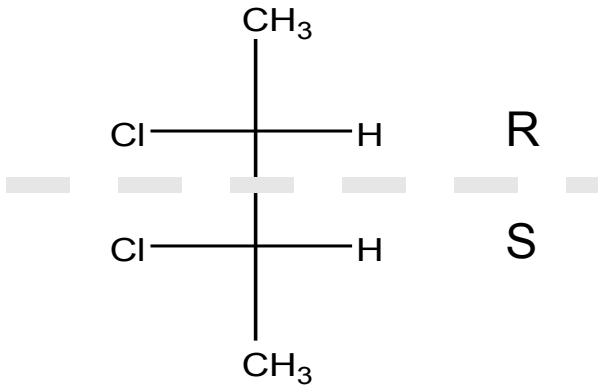
Assign configurations.

Looks meso. But no mirror plane.

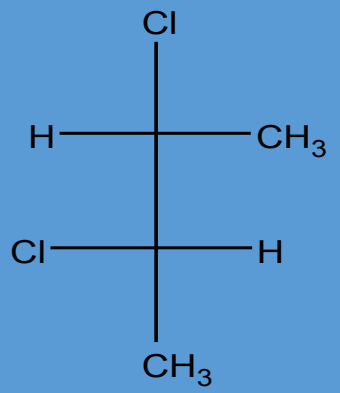
Rearrange by doing **even** number of swaps on upper carbon.

Now have mirror plane.



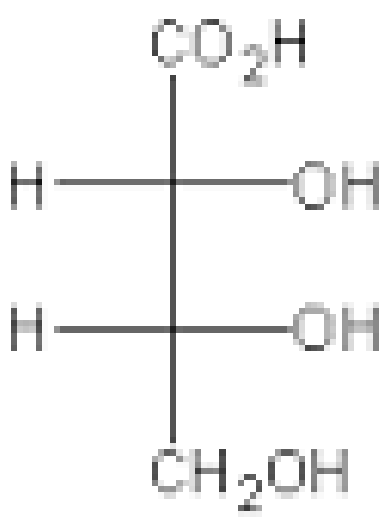


Meso

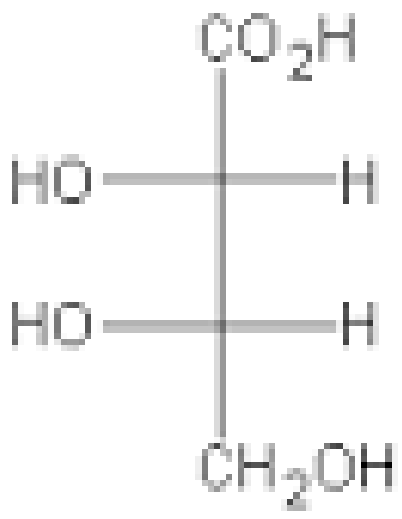


Original structure was meso compound. **In checking to see if meso you must attempt to establish the plane of symmetry.**

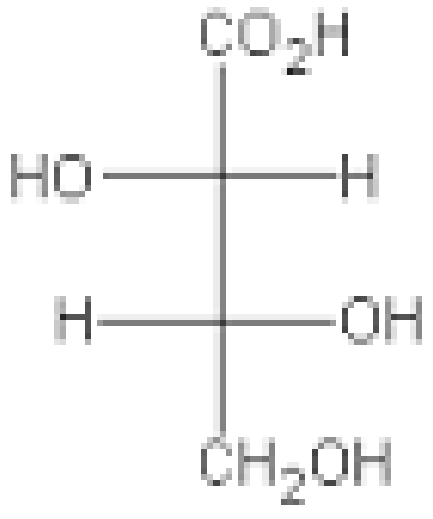
Identify Enantiomers, Diastereomers and Mesomers among following compounds?



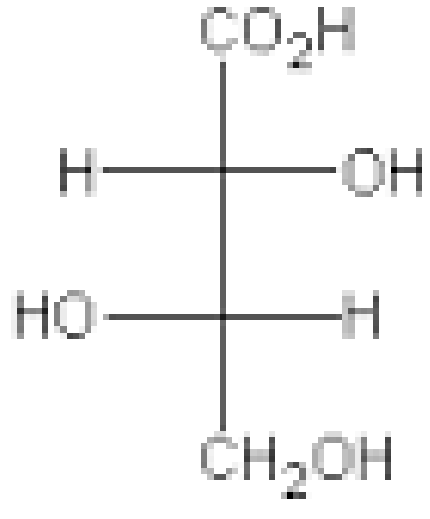
I



II



III



IV

Why are some substances optically active and others not? Can we predict which ones will be and which ones won't?

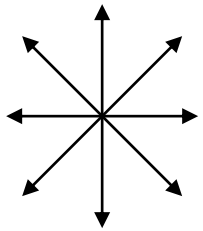
Louis Pasteur (1848) recrystallized sodium ammonium tartrate (optically inactive). He noticed that the crystals were of two types which he physically separated. The two types of crystals were optically active, but rotated the plane of polarized light in opposite directions. He proposed that the molecules came in two forms, "left handed" and "right handed". Together, the mixture of the two forms is optically inactive.

Properties of Enantiomers

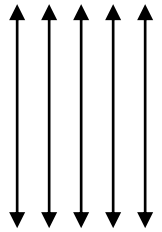
- Same boiling point, melting point, and density.
- Same refractive index.
- Rotate the plane of polarized light in the same magnitude, but in opposite directions.
- Different interaction with other chiral molecules:
  - Active site of enzymes is selective for a specific enantiomer.
  - Taste buds and scent receptors are also chiral. Enantiomers may have different smells.

Optical activity – when a substance rotates the plane of plane polarized light. (1815 by Biot)

Plane polarized light – light that has been passed through a nicol prism or other polarizing medium so that all of the vibrations are in the same plane.



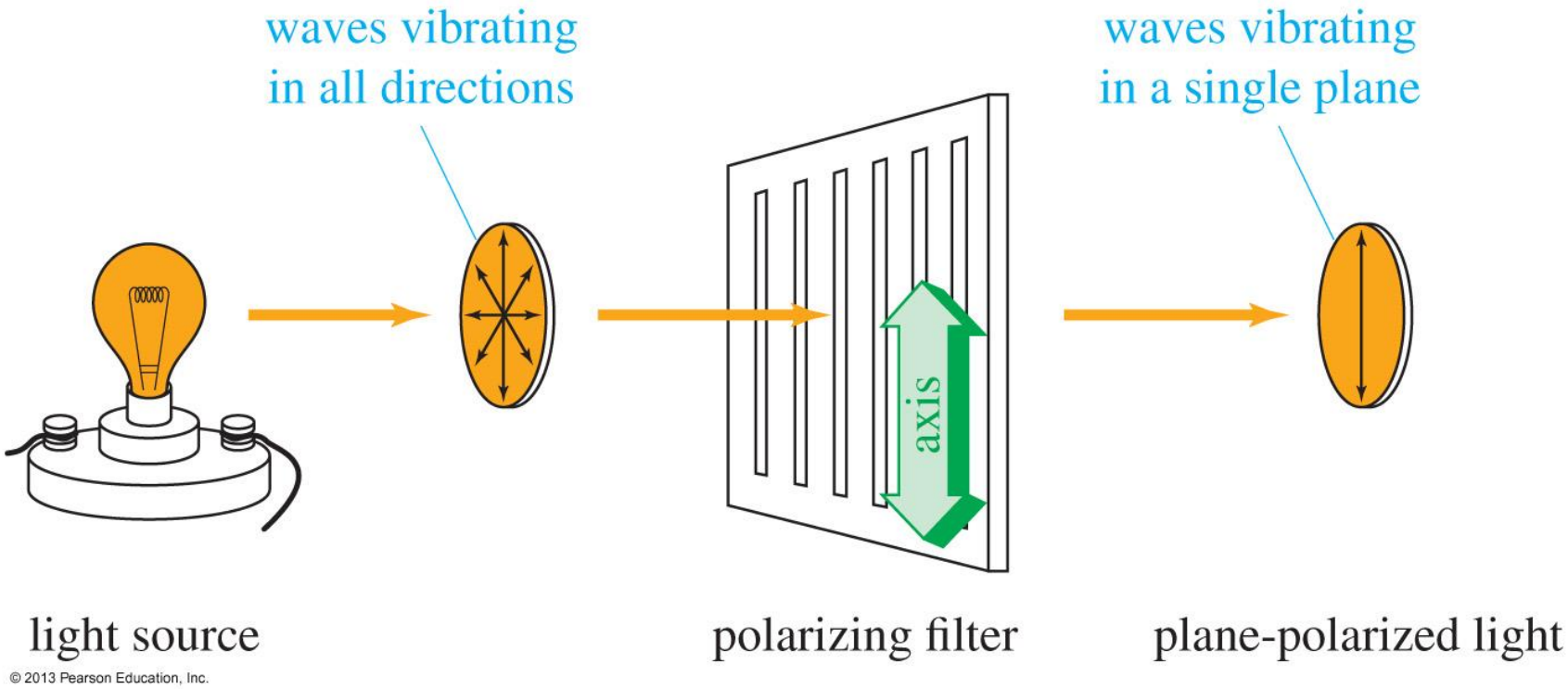
non-polarized



polarized

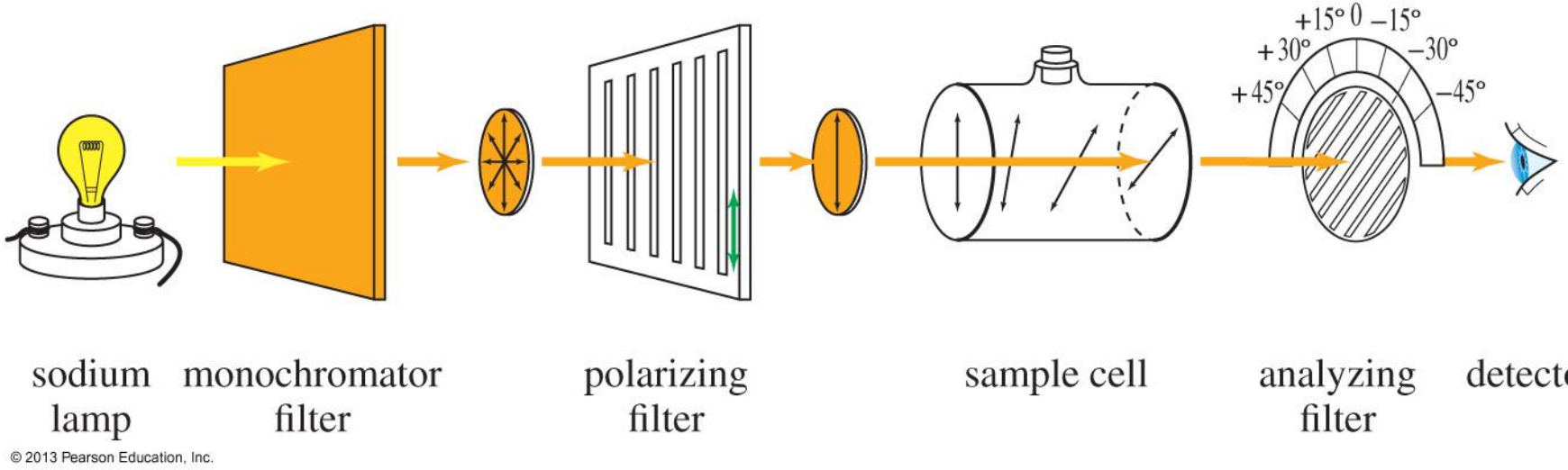
Polarized Light

Plane-polarized light is composed of waves that vibrate in only one plane.

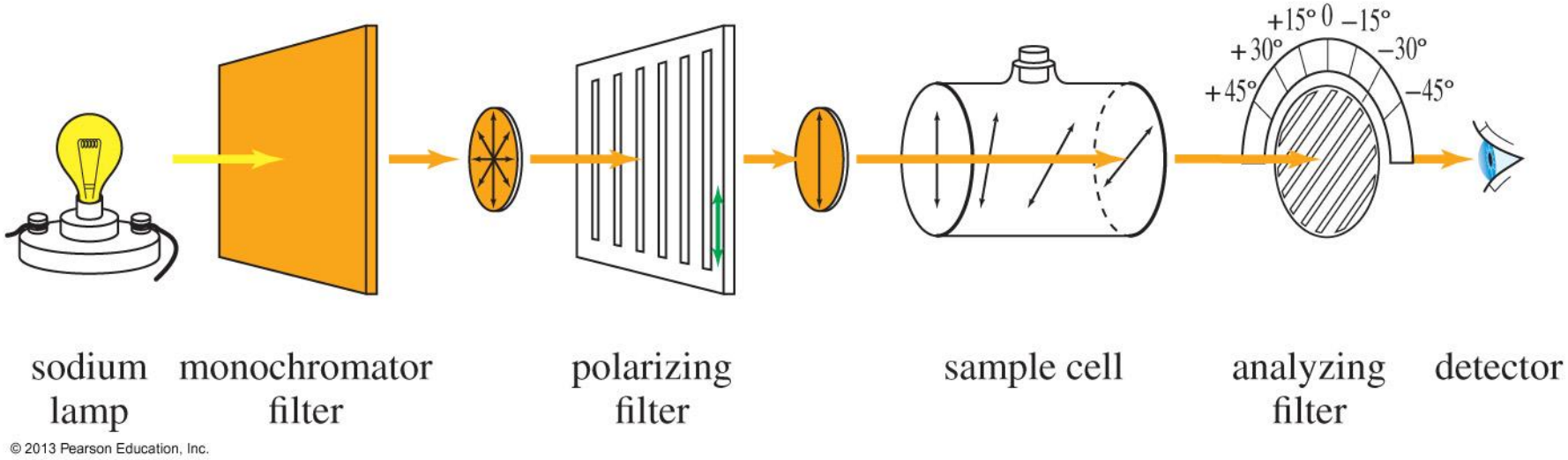


Optical Activity

- Enantiomers rotate the plane of polarized light in opposite directions, but same number of degrees.



Polarimeter



Clockwise

dextrorotatory (+) (*d*)

Counterclockwise

levorotatory (-) (*l*)

dextrorotatory – when the plane of polarized light is rotated in a clockwise direction when viewed through a polarimeter.

(+) or (*d*) do not confuse with D or R

levorotatory – when the plane of polarized light is rotated in a counter-clockwise direction when viewed through a polarimeter.

(-) or (*l*) do not confuse with L or S

The angle of rotation of plane polarized light by an optically active substance is proportional to the number of atoms in the path of the light.

Specific Rotation

Observed rotation depends on the length of the cell and concentration, as well as the strength of optical activity, temperature, and wavelength of light.

$$[\alpha] = \frac{\alpha \text{ (observed)}}{c \bullet l}$$

Where α (observed) is the rotation observed in the polarimeter, *c* is concentration in g/mL, and *l* is length of sample cell in <u>decimeters</u>.

Specific rotation – the angle of rotation of plane polarized light by a 1.00 gram per cm^{-3} sample in a 1 dm tube. $[\alpha]_D$ (D = sodium lamp, λ = 589 nm).

$$[\alpha]_D = \frac{\alpha}{l * d}$$

where α = observed rotation

l = length (dm)

d = concentration (g/cc)

(+)-alanine $[\alpha]_D = +8.5$

(-)-lactic acid $[\alpha]_D = -3.8$

Solved Problem

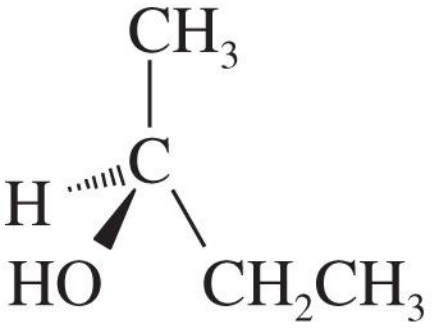
When one of the enantiomers of 2-butanol is placed in a polarimeter, the observed rotation is 4.05° counterclockwise. The solution was made by diluting 6 g of 2-butanol to a total of 40 mL, and the solution was placed into a 200-mm polarimeter tube for the measurement. Determine the specific rotation for this enantiomer of 2-butanol.

Solution

Since it is levorotatory, this must be (–)-2-butanol The concentration is 6 g per 40 mL = 0.15 g/mL, and the path length is 200 mm = 2 dm. The specific rotation is

$$[\alpha]_{D}^{25} = \frac{-4.05^{\circ}}{(0.15)(2)} = -13.5^{\circ}$$

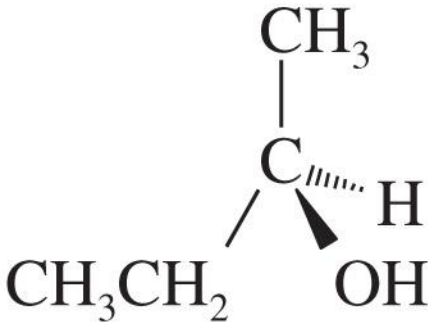
Racemic Mixtures



(*S*)-(+)-butan-2-ol

+13.5° rotation

and



(*R*)-(−)-butan-2-ol

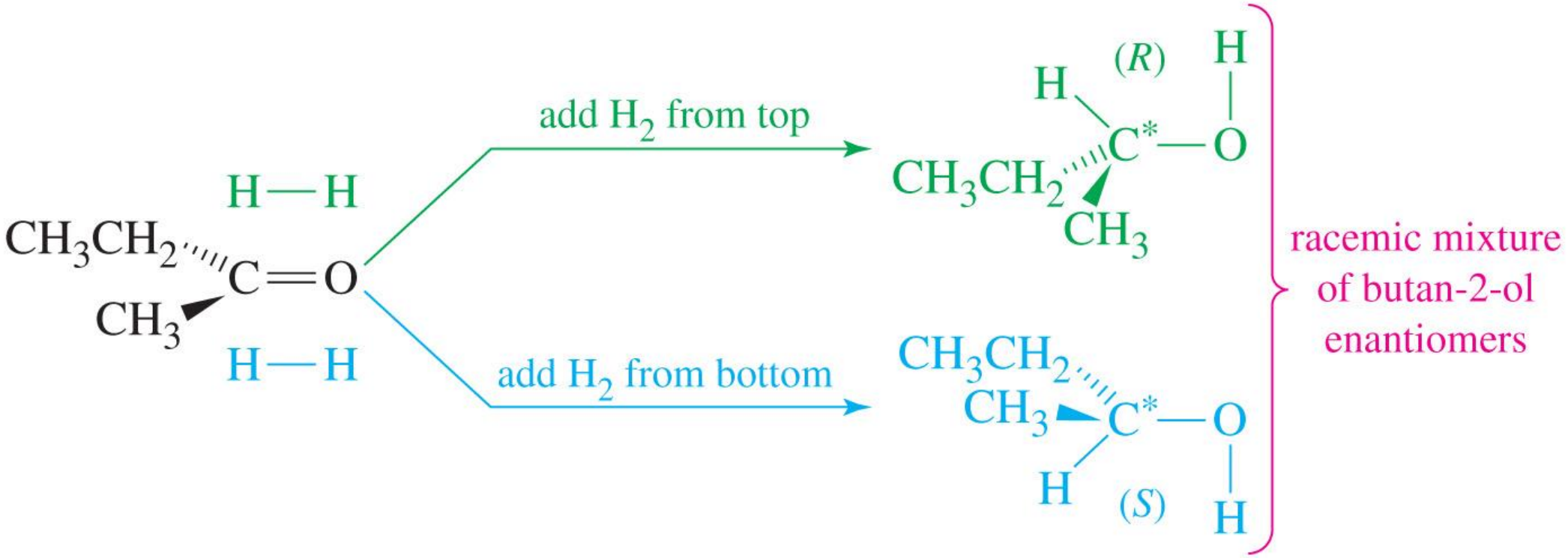
−13.5° rotation

A racemic mixture contains equal amounts of the two enantiomers.

- Equal quantities of *d*- and *l*-enantiomers.
- Notation: (*d*,*l*) or (±)
- No optical activity.
- The mixture may have different boiling point (b. p.) and melting point (m. p.) from the enantiomers!

Racemic Products

If optically inactive reagents combine to form a chiral molecule, a racemic mixture is formed.



Optical Purity

- Optical purity (o.p.) is sometimes called enantiomeric excess (ee).
- One enantiomer is present in greater amounts.

$$\text{o.p.} = \frac{\text{observed rotation}}{\text{rotation of pure enantiomer}} \times 100$$

Calculate % Composition

The specific rotation of (*S*)-2-iodobutane is +15.90°. Determine the % composition of a mixture of (*R*)- and (*S*)-2-iodobutane if the specific rotation of the mixture is -3.18°.

Sign is from the enantiomer in excess: levorotatory.

$$\text{o.p.} = \frac{3.18}{15.90} \times 100 = 20\%$$

$2l = 120\%$ $l = 60\%$ $d = 40\%$

1. What is the ee of the following racemic mixture?

95% A and 5% B

ee = % of A - % of B

= 95 - 5 = 90 ee

2. Given the ee value, what percent is there of each isomer,

60% ee

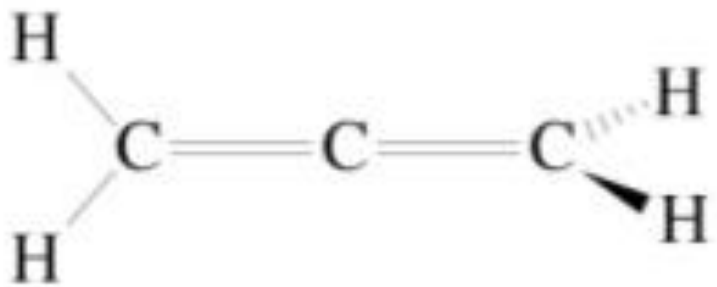
60% excess A, then 40% racemic mixture(so 20% A and 20% B)

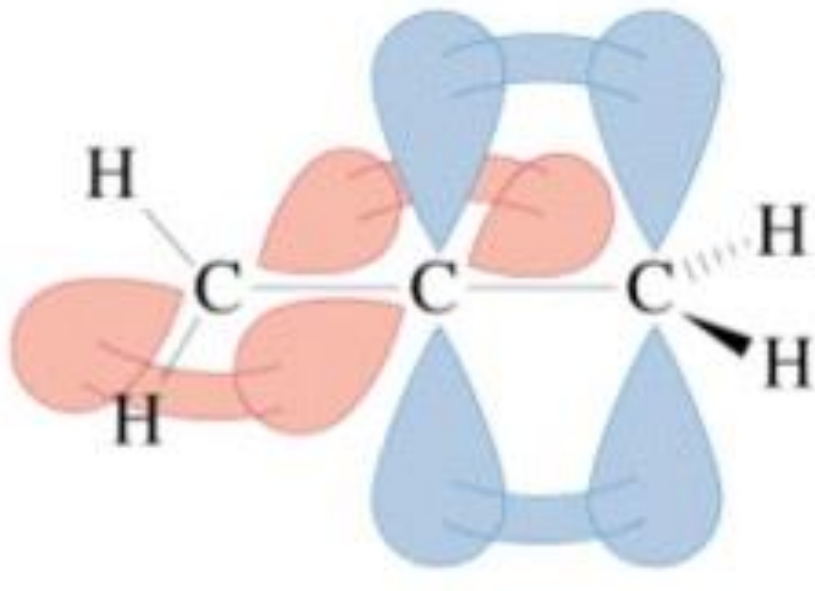
So, 60% + 20% = 80% A and leaves 20% B

Optical isomerism in Molecules without Chiral Centers

Allenes

- Chiral compounds with no chiral carbon
- Contains *sp* hybridized carbon with adjacent double bonds: -C=C=C-
- End carbons must have different groups.

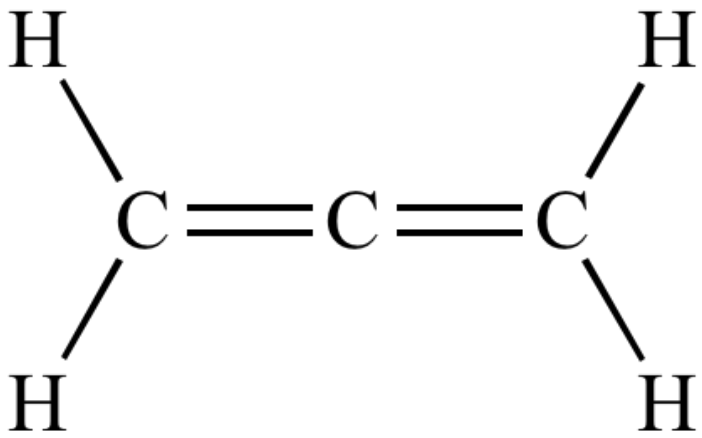


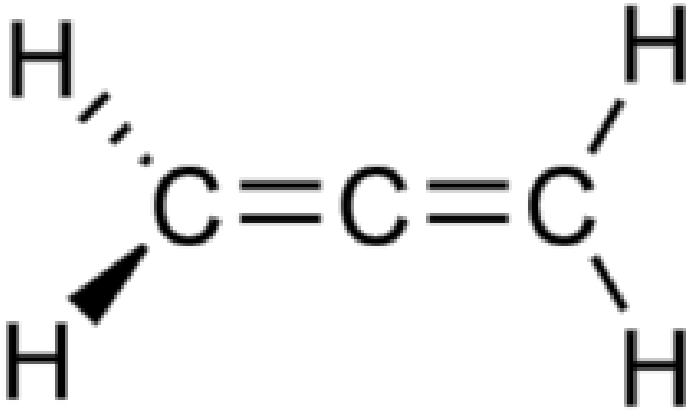


Allene is achiral.

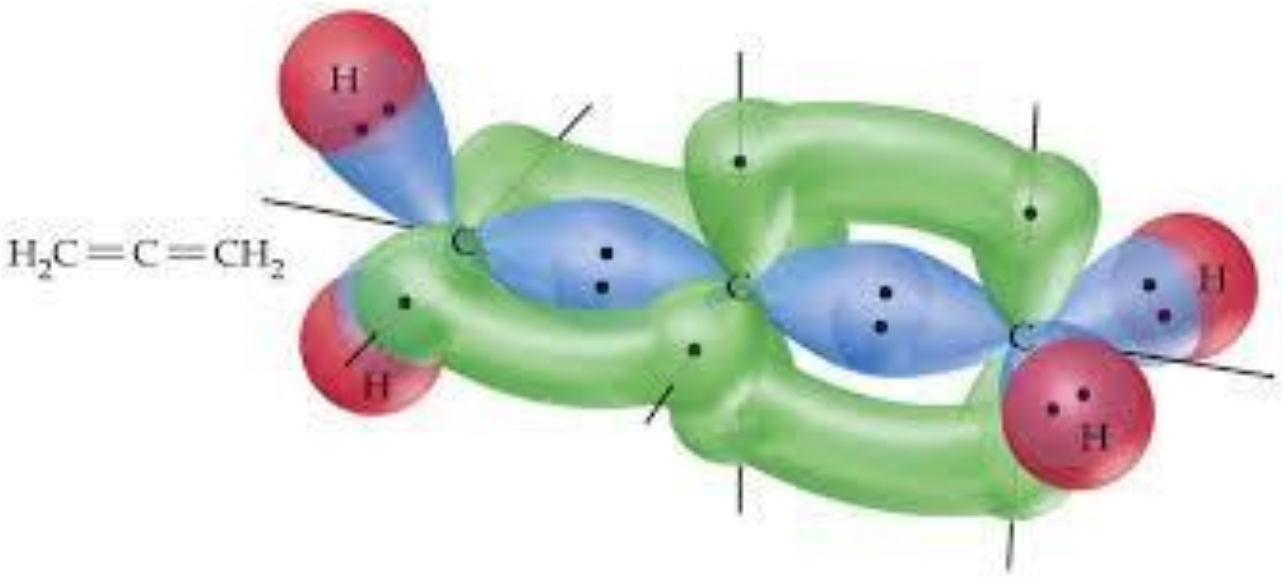
=>

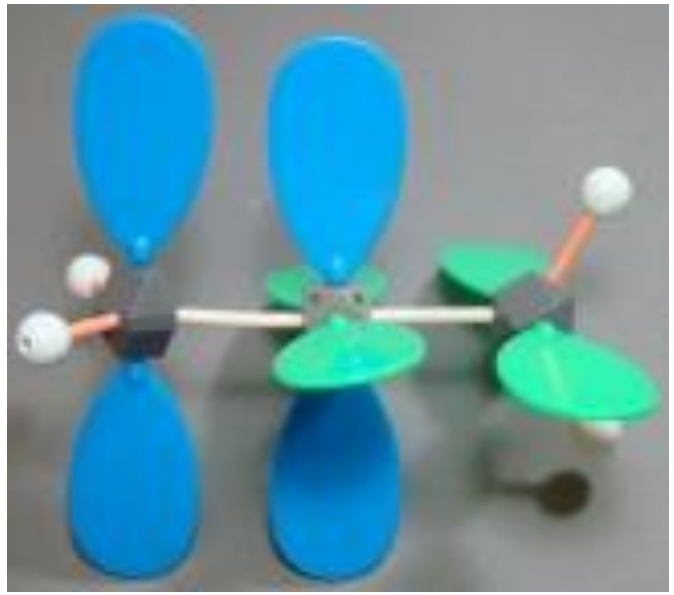
Allenes





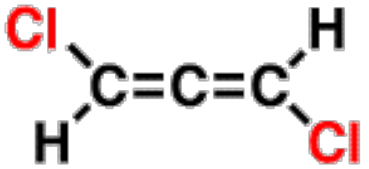
Achiral: Due to presence of same substituents at both ends

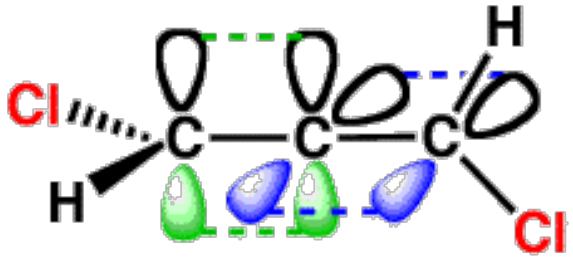




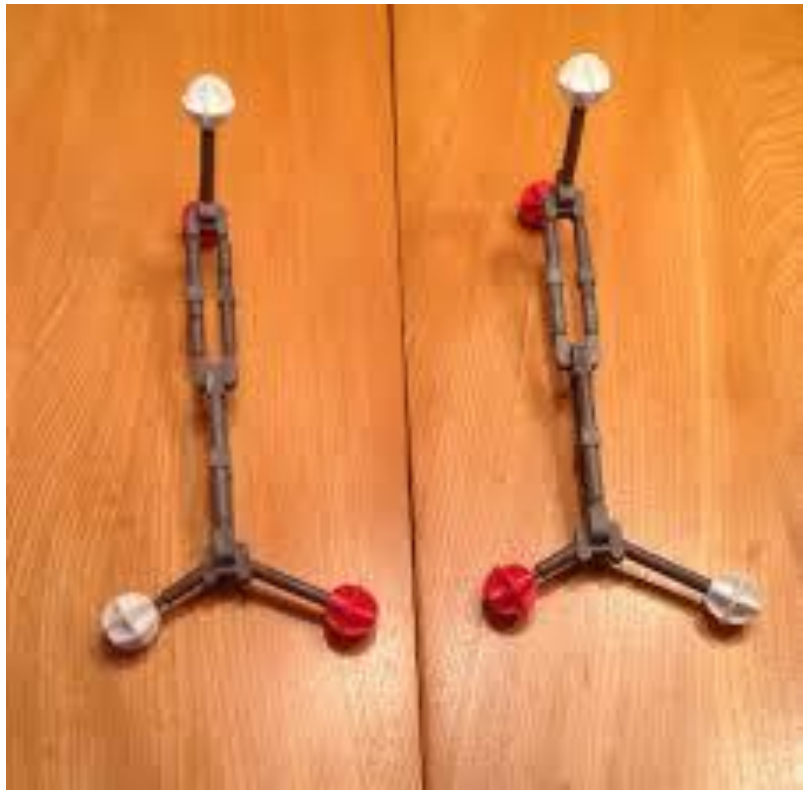
Allenes

Disubstituted allene





orbital drawing



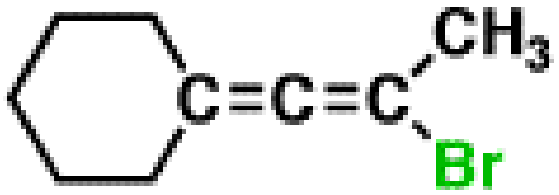
Chiral: Due to presence of DIFFERENT substituents at both ends

Allenes

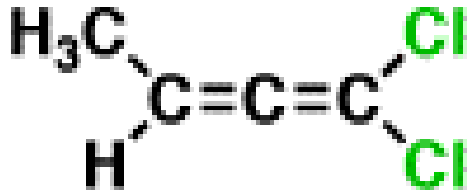
How to Recognize A Chiral Allene or Achiral Allene?

Examine both "ends" of the allene. If **either of those ends is attached to two identical substituents**, it is **achiral** – because it will have a mirror plane.

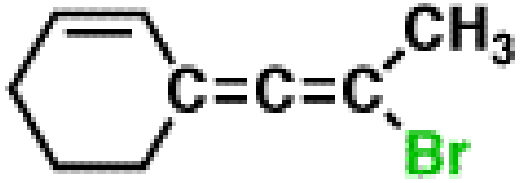
Allenes



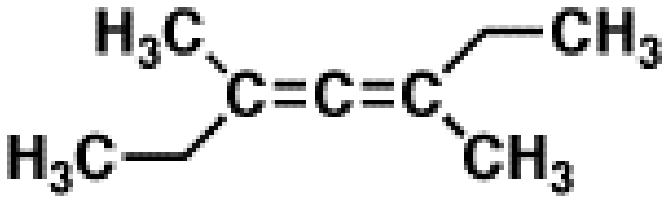
Achiral



Achiral

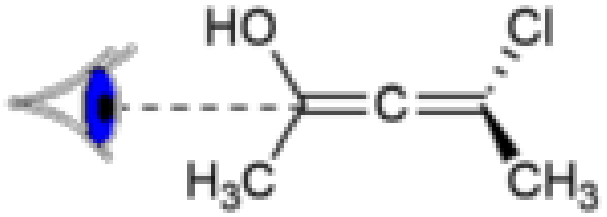


Chiral

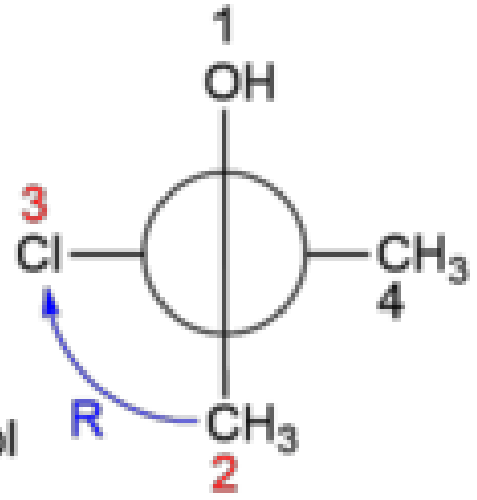


Chiral

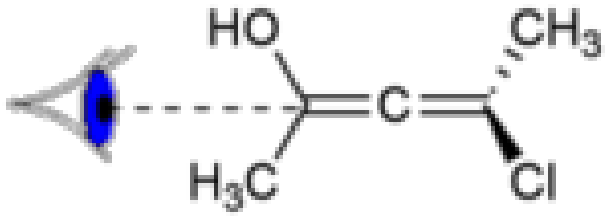
Nomenclature of Allenes



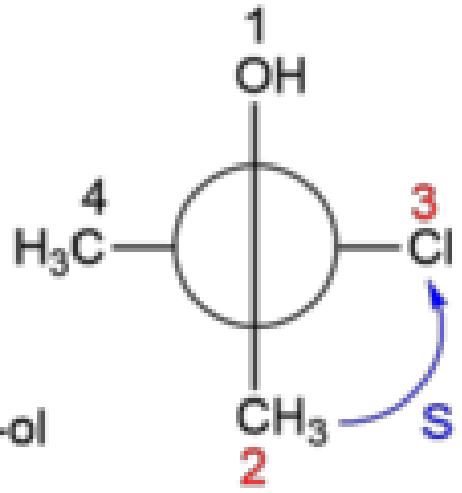
(*R*)-4-chloropenta-2,3-dien-2-ol



Clockwise = (*R*)



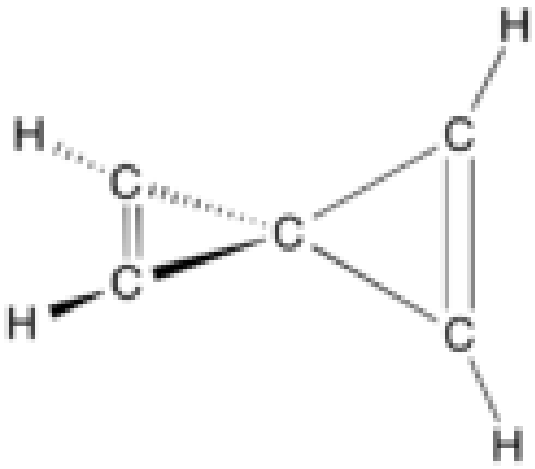
(*S*)-4-chloropenta-2,3-dien-2-ol



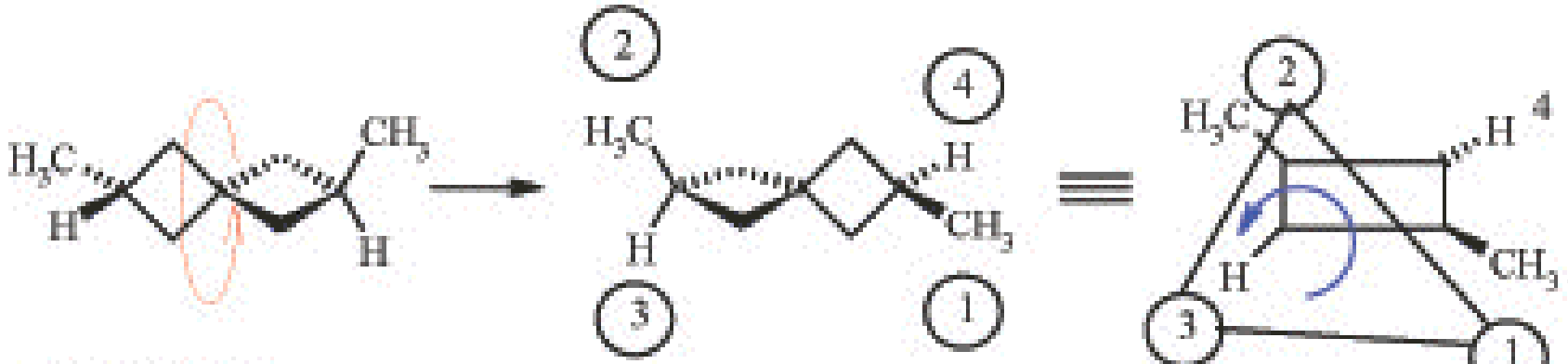
Anti-Clockwise = (*S*)

Spiranes

A spiro compound, or spirane, from the Latin *spīra*, meaning a twist or coil, is a chemical compound, typically an organic compound, that presents a twisted structure of two or more rings (a ring system), in which 2 or 3 rings are linked together by one common atom, examples of which are shown at right.

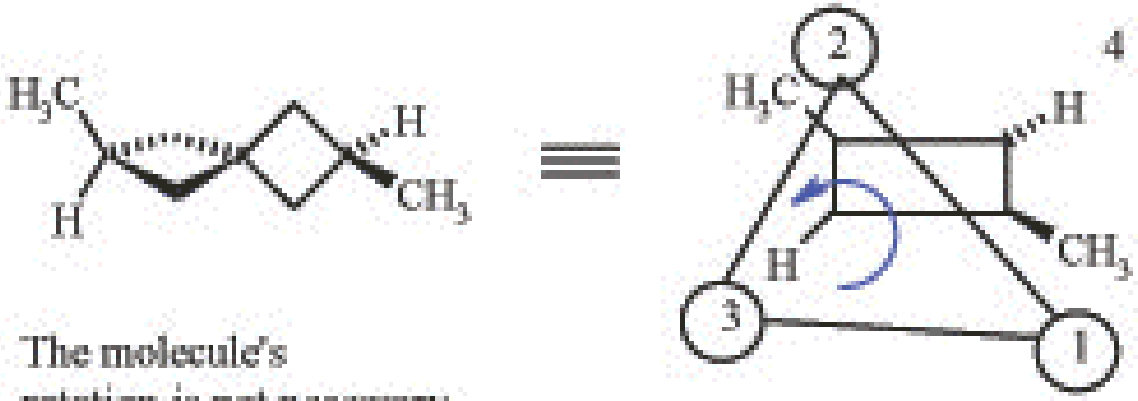


Nomenclature of Spiranes



The molecule's rotation is necessary

S

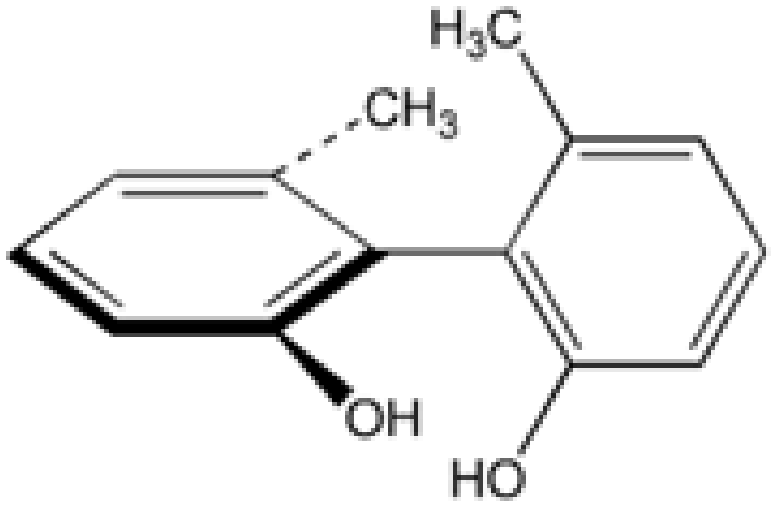


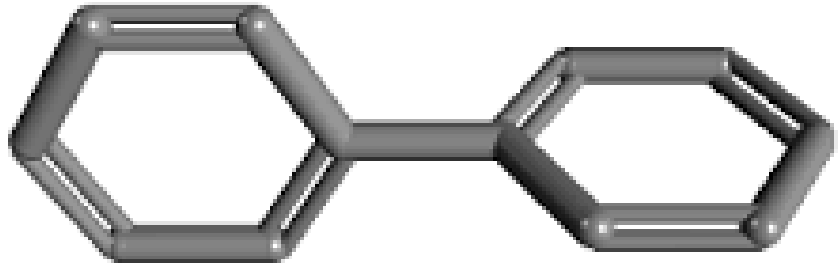
The molecule's rotation is not necessary

S

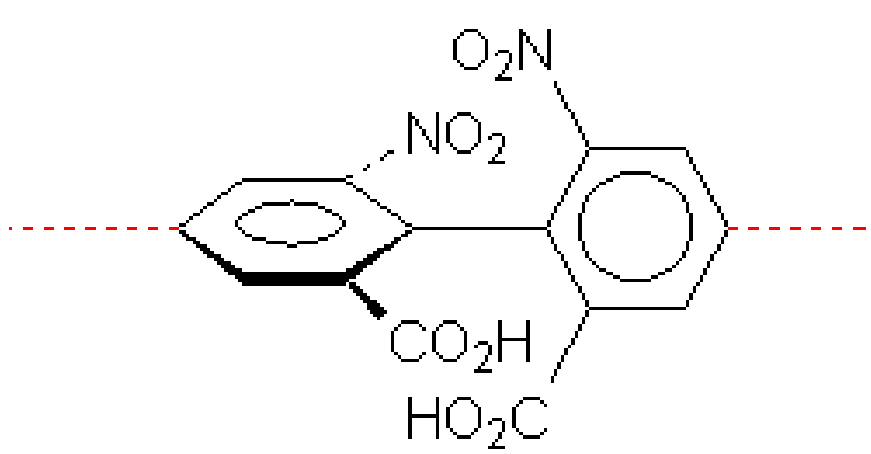
Biphenyls

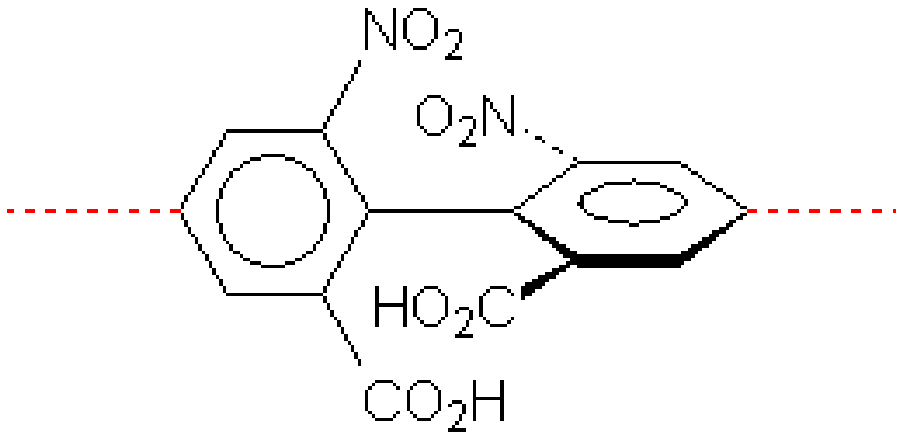
Those compounds in which two phenyl rings are attached to each other with single bond. Rotation about the single bond in biphenyl, and especially its ortho-substituted derivatives, is sterically hindered. For this reason, some substituted biphenyls show atropisomerism.





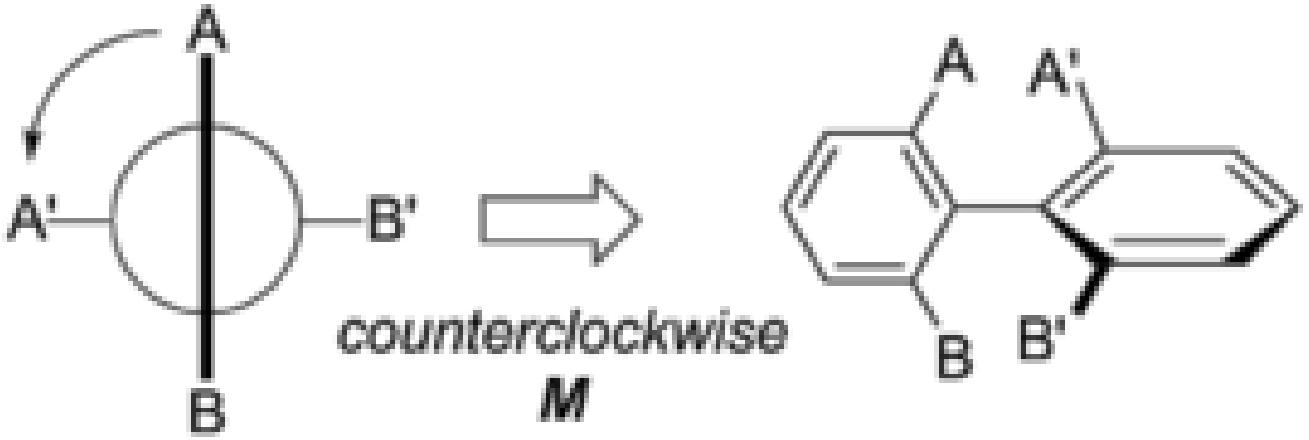
Biphenyls

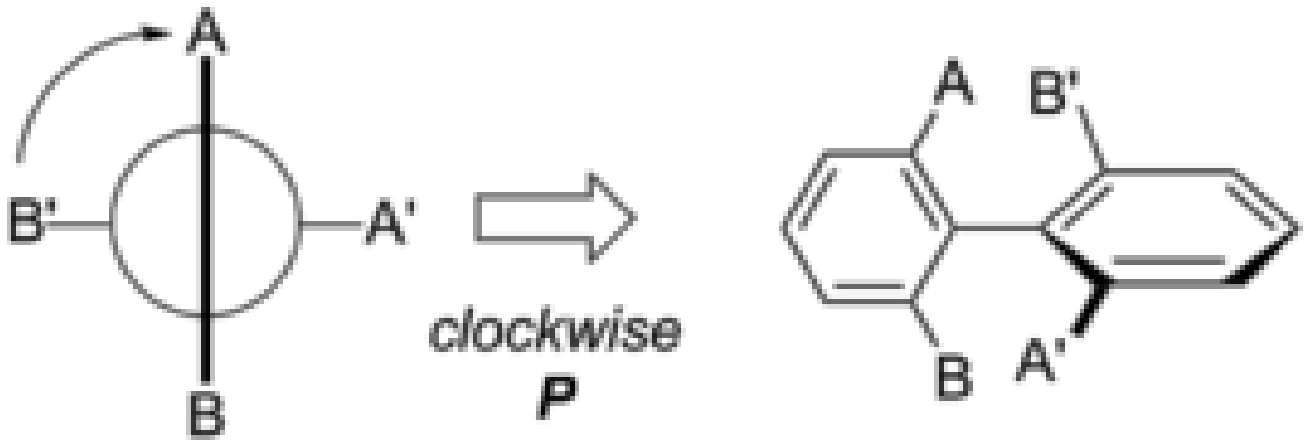




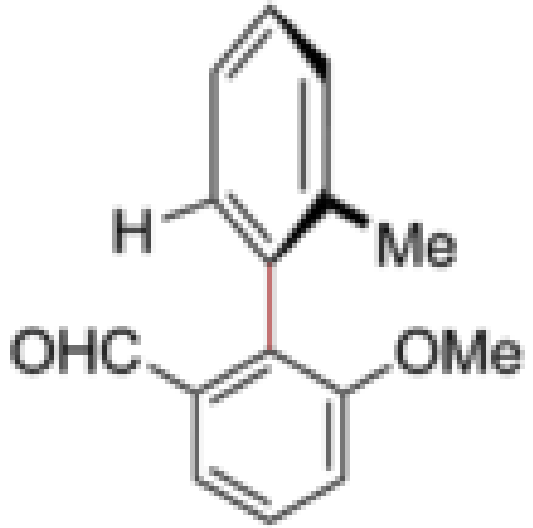
Chiral Axis

Nomenclature of Biphenyls



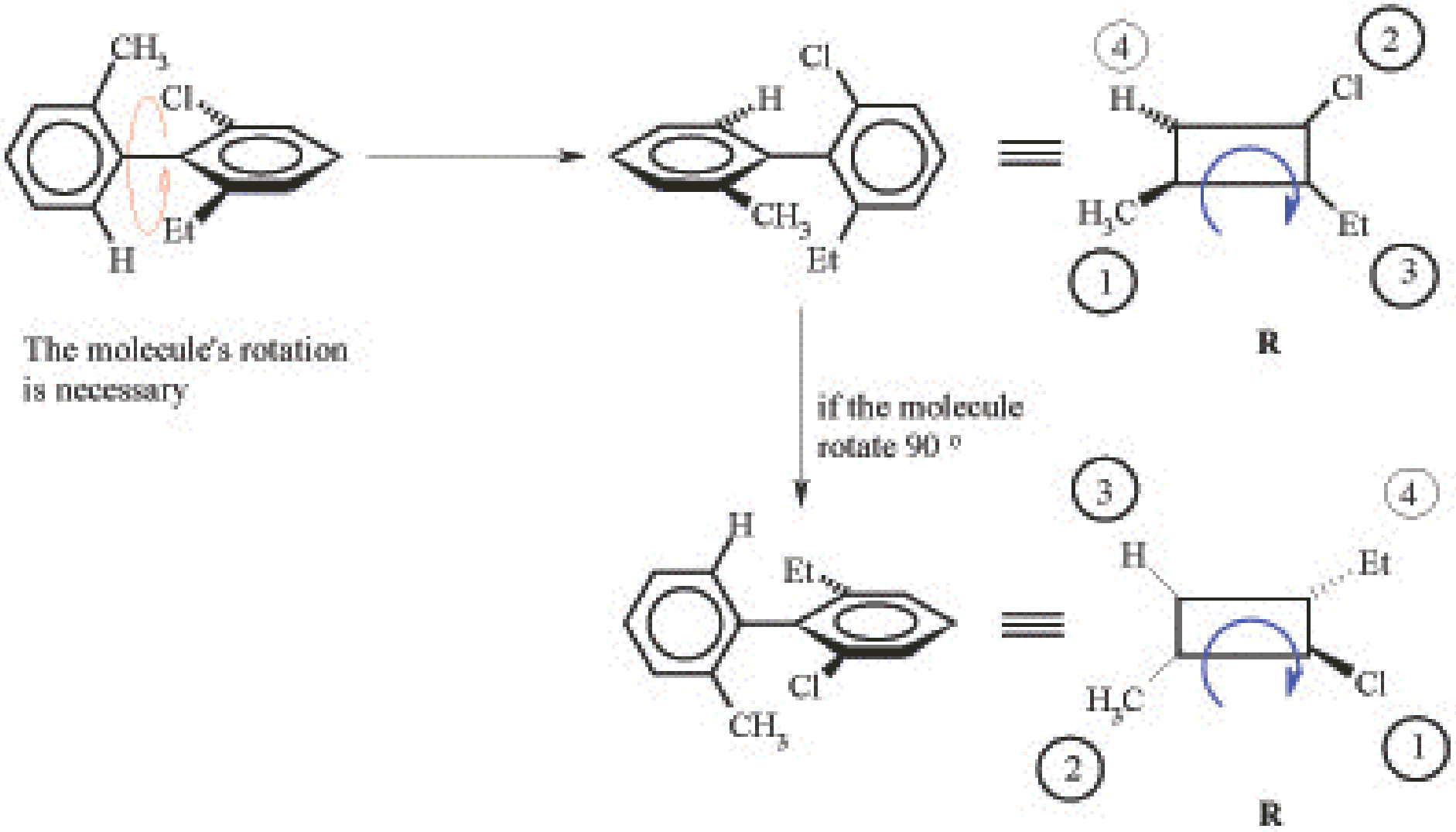


example:



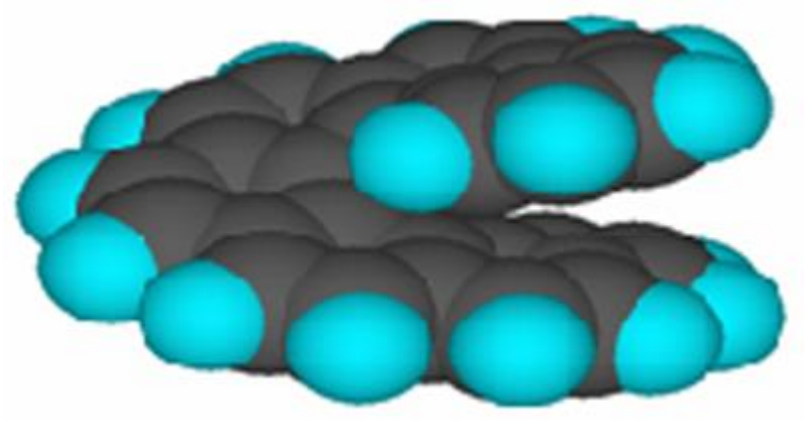
M *counterclockwise*

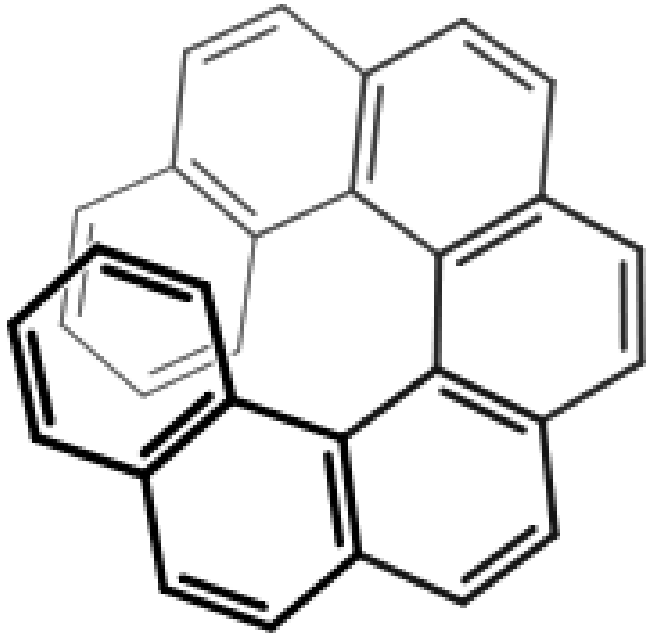
Biphenyls


CH3
Cl
Et
H
Cl
H
CH3
Et
4
2
H
Cl
H3C
Et
1
3
R
The molecule's rotation
is necessary
if the molecule
rotate 90 °
H
Et
Cl
CH3
3
4
H
Et
H3C
Cl
2
1
R

Helicene

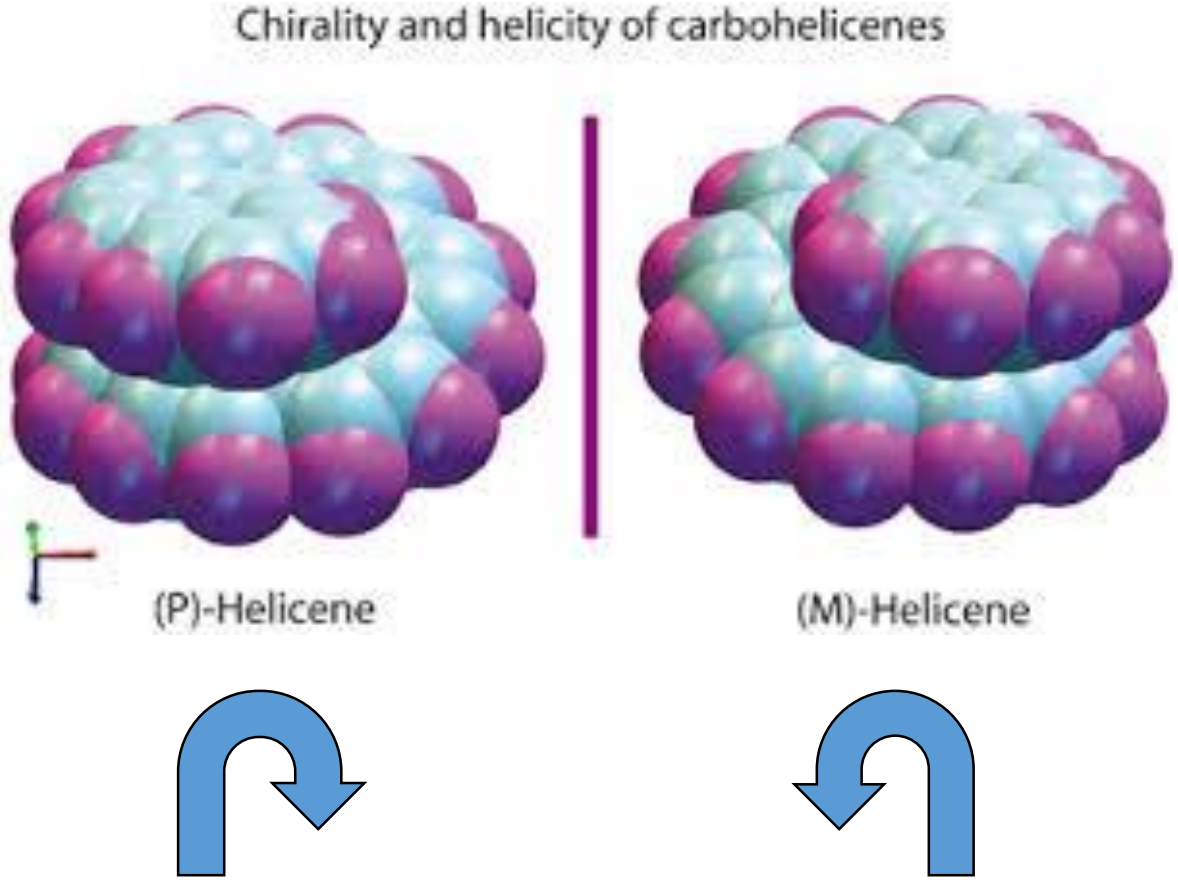
Helicenes are ortho-condensed polycyclic aromatic compounds in which benzene rings or other aromatics are angularly annulated to give helically-shaped molecules.



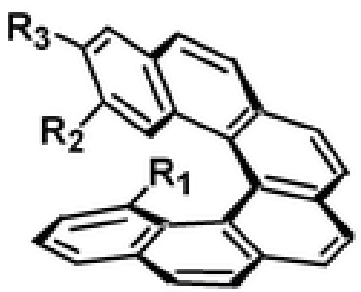


Helicene

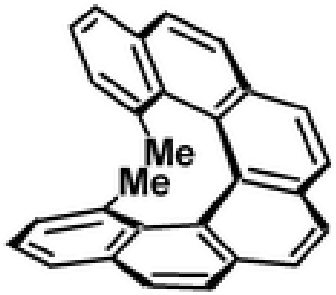
Helicenes are notable for having chirality despite lacking both asymmetric carbons and chiral centers. The chirality results from the handedness of the helicity itself. The clockwise and counterclockwise helices are non-superposable as a result of their axial chirality. By convention a left-handed helix is *minus* and labeled M, a right-handed helix is *plus* and labeled P.



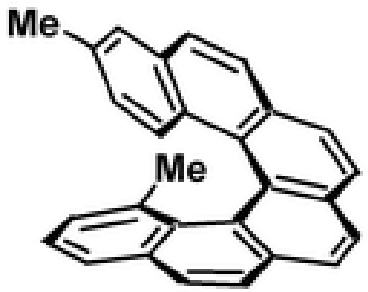
Helicene



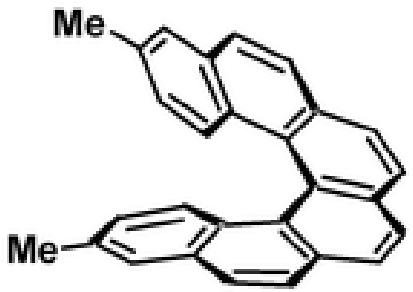
R_1=Me, R_2=H, R_3=H (P)-**12**
R_1=H, R_2=Me, R_3=H (P)-**13**
R_1=H, R_2=H, R_3=Me (P)-**14**



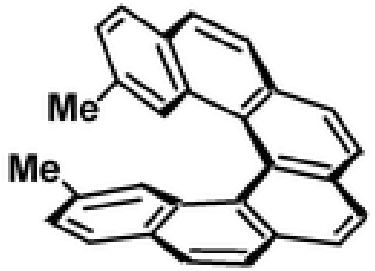
(P)-**15**



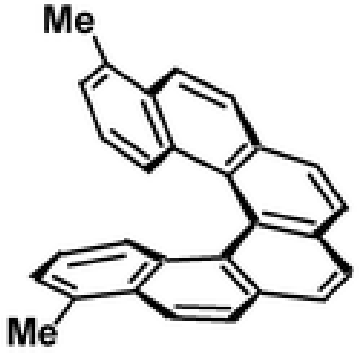
(P)-**16**



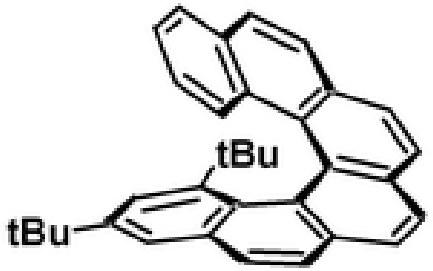
(P)-**17**



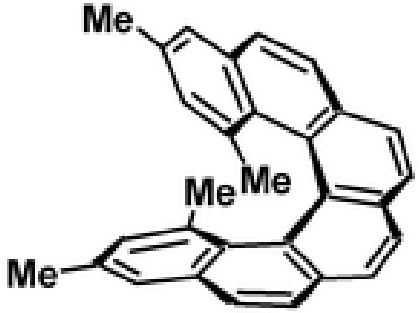
(P)-**18**



(P)-**19**

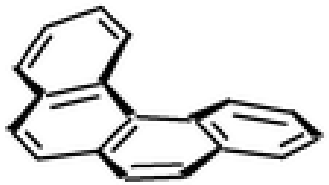


(P)-**20**

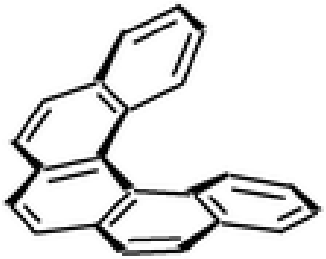


(P)-**21**

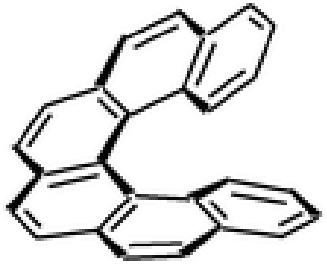
Helicene



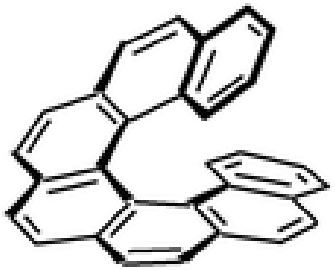
(M)-[4]helicene
(low barrier of racemization)



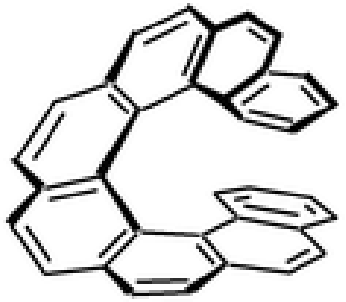
(M)-(-)-[5]helicene
$[\alpha]_{578}$ = -1670° (26°C, iso-octane)



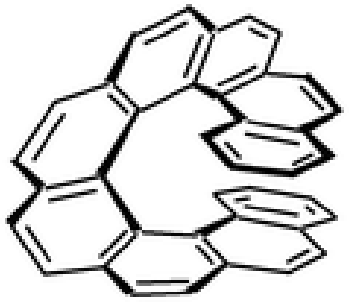
(M)-(-)-[6]helicene
$[\alpha]_{578}$ = -3570°
(22°C, c=0,24 $CHCl_3$)



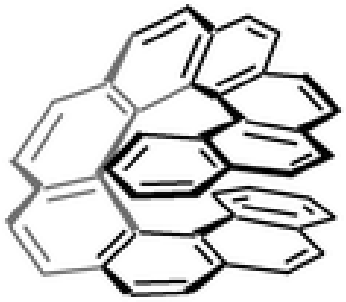
(M)-(-)-[7]helicene
$[\alpha]_{579}$ = -5900°
(25°C, c=0,06, $CHCl_3$)



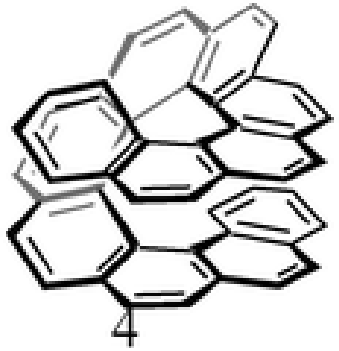
(M)-(-)-[8]helicene
$[\alpha]_{579}$ = -7170°



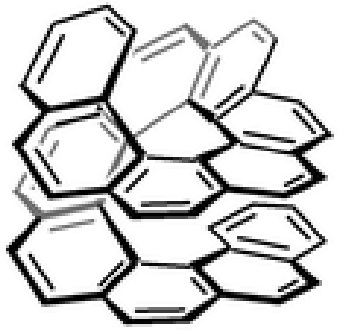
(M)-(-)-[9]helicene
$[\alpha]_{579}$ = -8150°



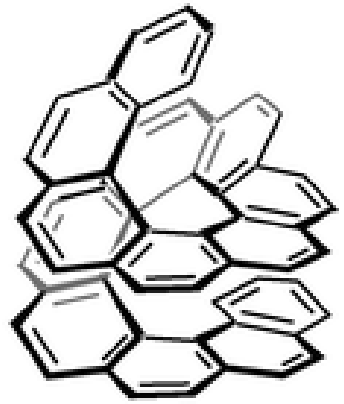
(M)-(-)-[10]helicene
$[\alpha]_{579}$ = -8940°



(M)-(-)-[11]helicene
$[\alpha]_{579}$ = -9310°



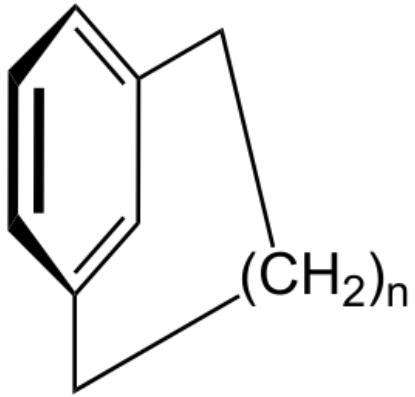
(M)-(-)-[12]helicene
$[\alpha]_{579}$ = not available



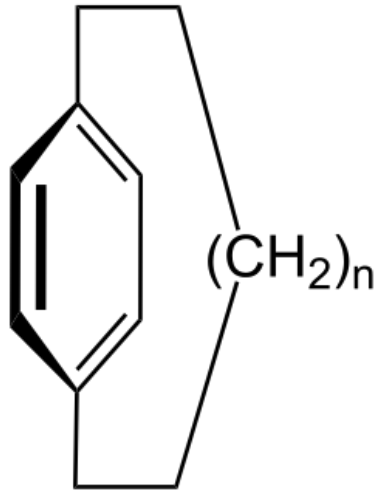
(M)-(-)-[13]helicene
$[\alpha]_{579}$= -9620°

Cyclophanes

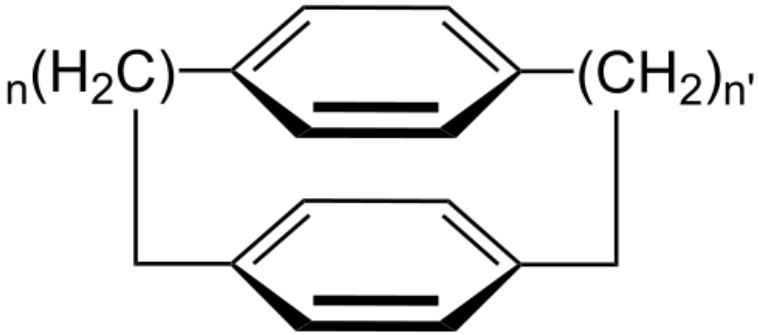
A cyclophane is a hydrocarbon consisting of an aromatic unit (typically a benzene ring) and an aliphatic chain that forms a bridge between two non-adjacent positions of the aromatic ring.



I

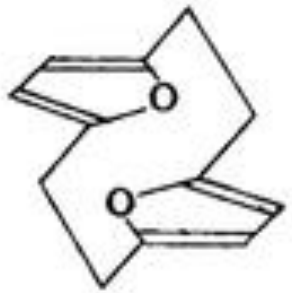


II

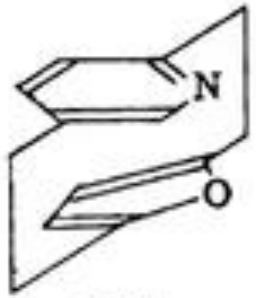


III

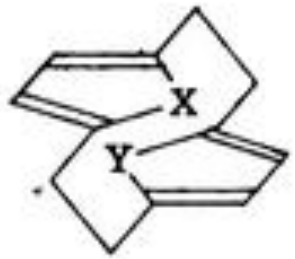
Nomenclature of Cyclophanes



2 Anti



245 Syn

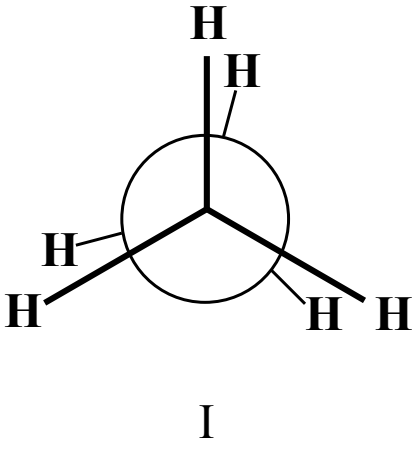


49 X = Y = S Anti

50 X = S; Y = O Anti

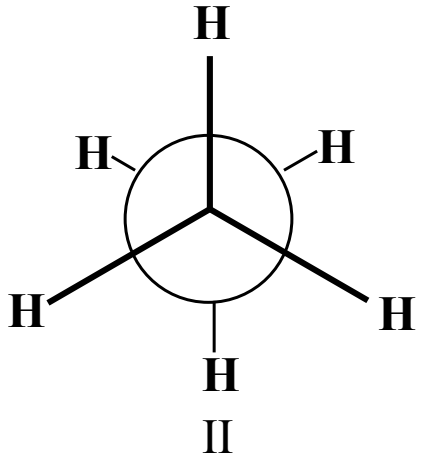
Conformations of Ethane

- Pitzer (1936) postulated that there exists a potential energy barrier which causes restriction in rotation.
- The extra energy of eclipsed conformation is called torsional strain. *The term torsional strain is used for the repulsion felt by bonding electrons on one substituent when it passes close to the bonding electrons of another substituent.*



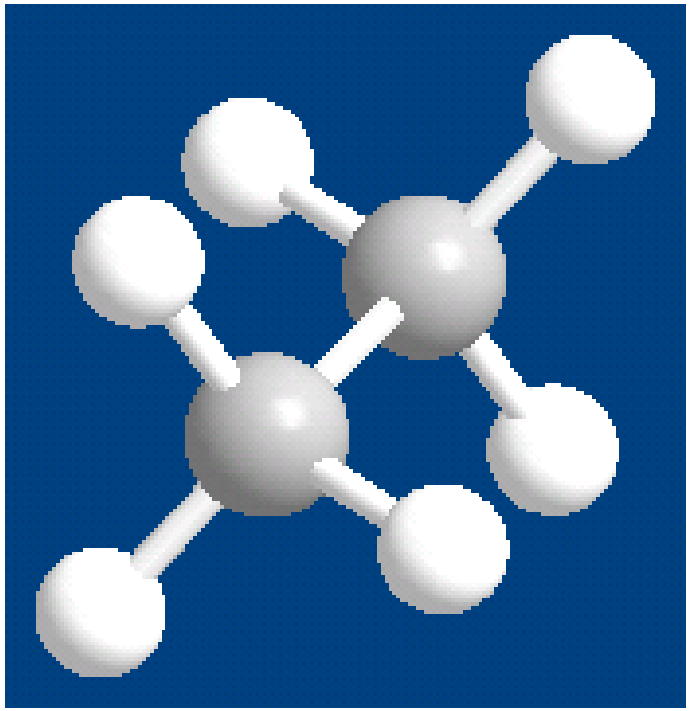
I

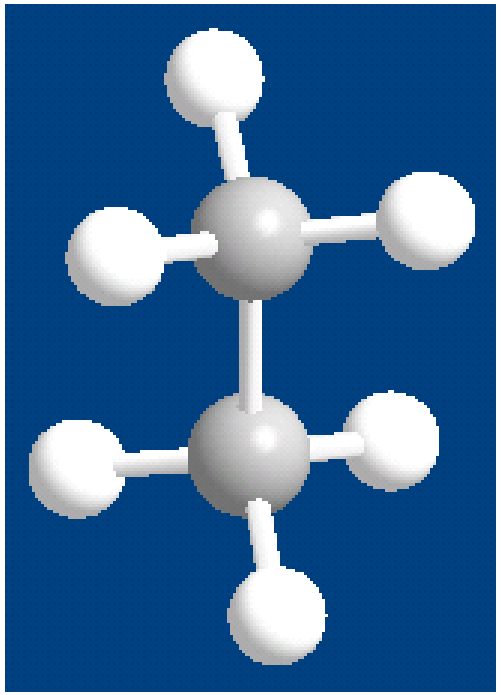
Eclipsed conformation

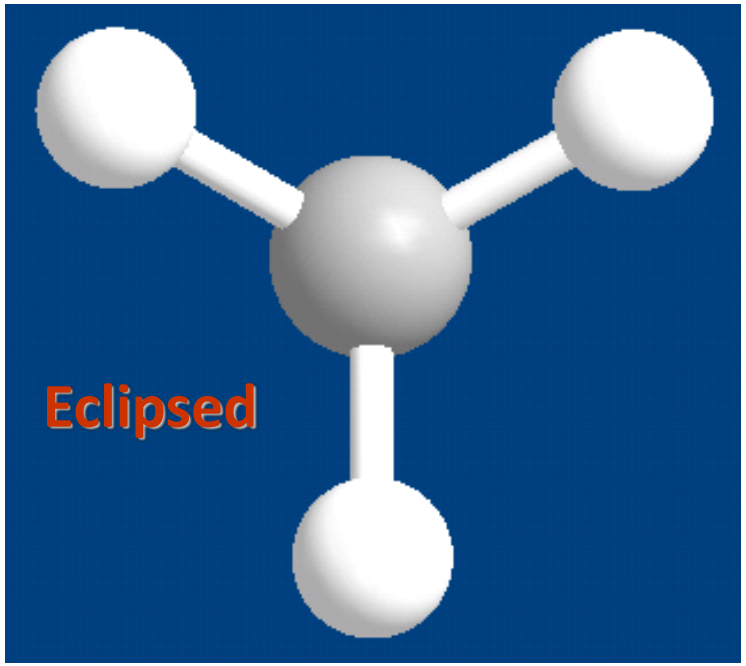


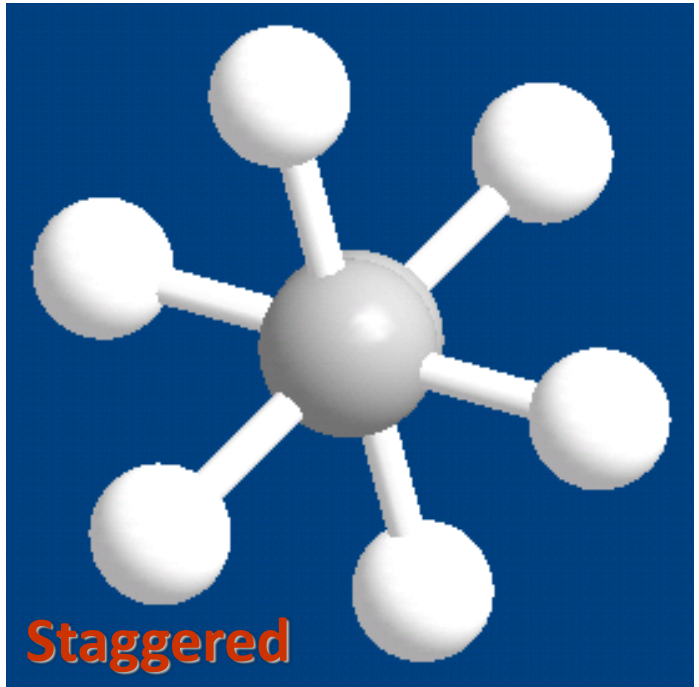
II

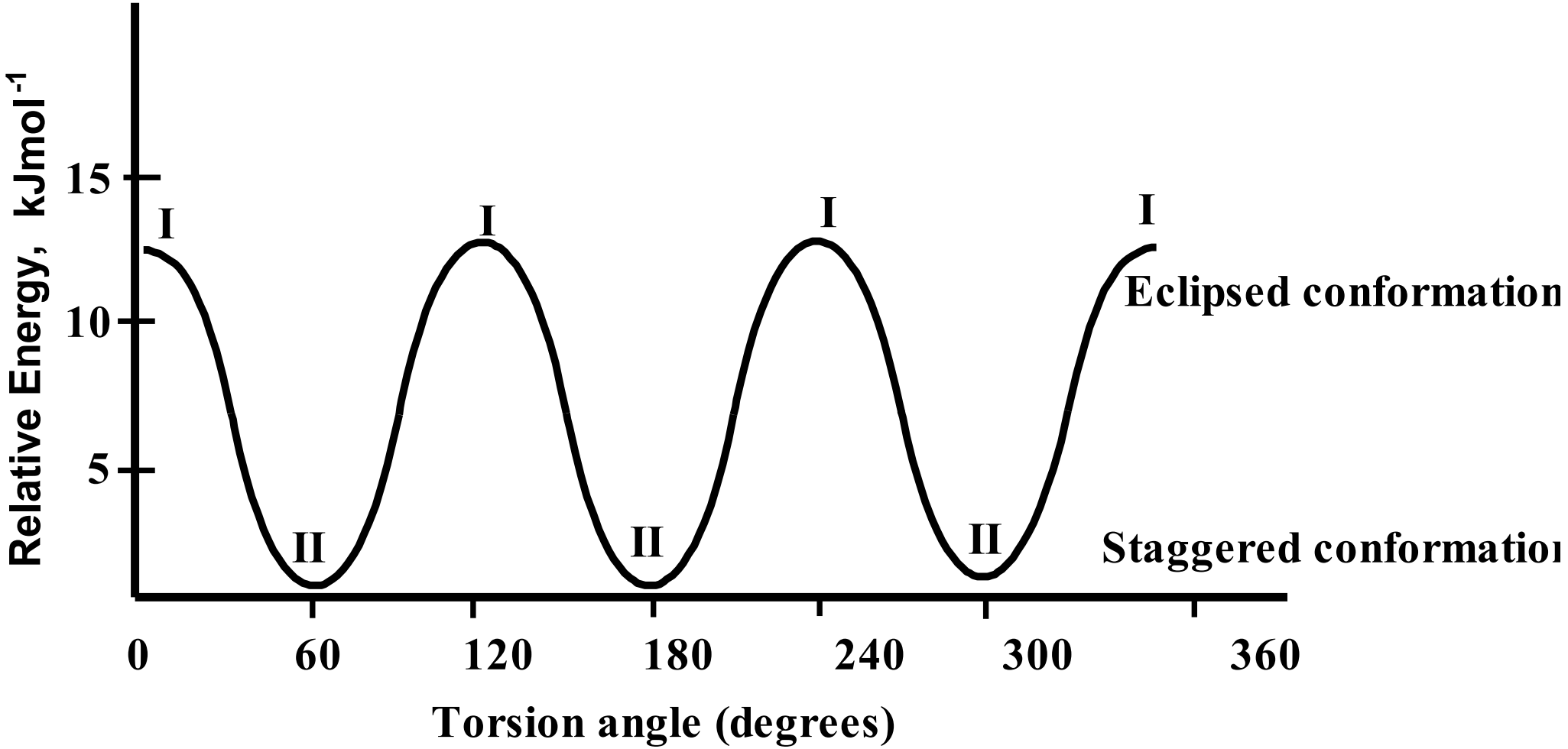
Staggered conformation






Eclipsed


Staggered

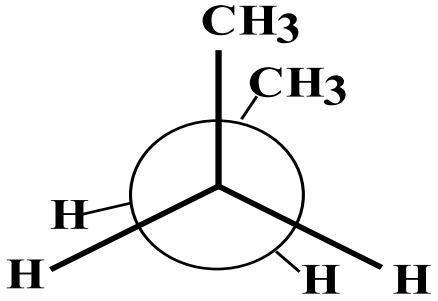


I at 0^{o}, 120^{o} and 240^{o}

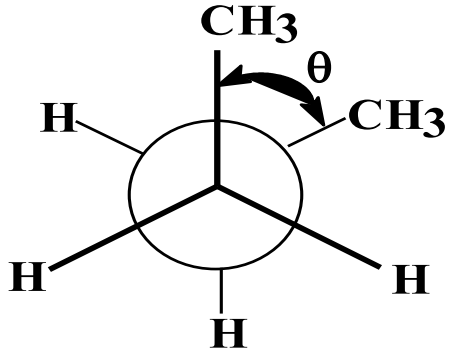
II at 60^{o}, 180^{o} and 300^{o}

Rotational and Torsional Energy in Ethane

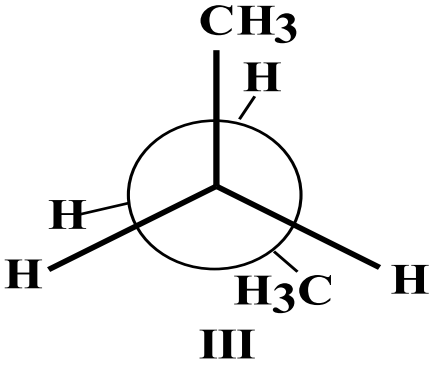
Conformations of *n*-Butane



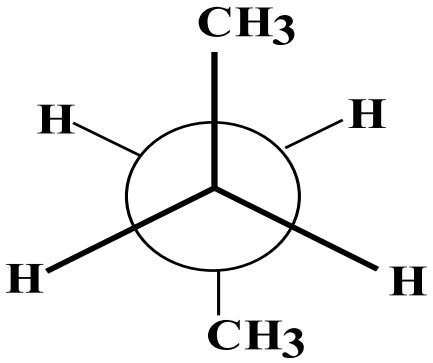
I
Fully Eclipsed
($\theta = 0^o$)



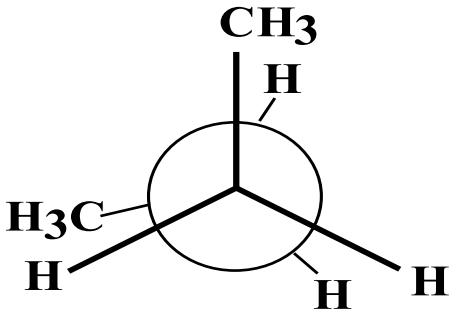
II
Gauche ($\theta = 0^o$)



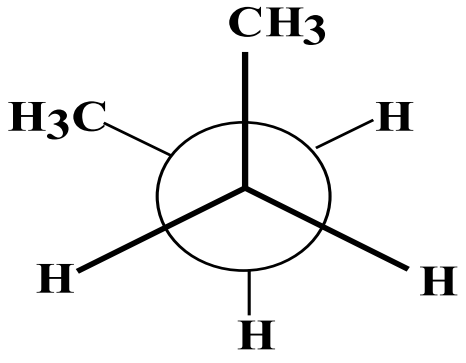
III
Partially Eclipsed
($\theta = 120^o$)



IV
Anti or *Trans* ($\theta = 180^o$)



V
Partially Eclipsed
($\theta = 240^o$)



VI
Gauche ($\theta = 300^o$)

Due to congestion in space a repulsive force acts between the methyl groups which is called van der Waals strain or steric hindrance. In butane, *gauche* conformation is less stable than *anti*-conformation due to vander Waals strains i.e. *n*-butane gauche (or skew) interaction.

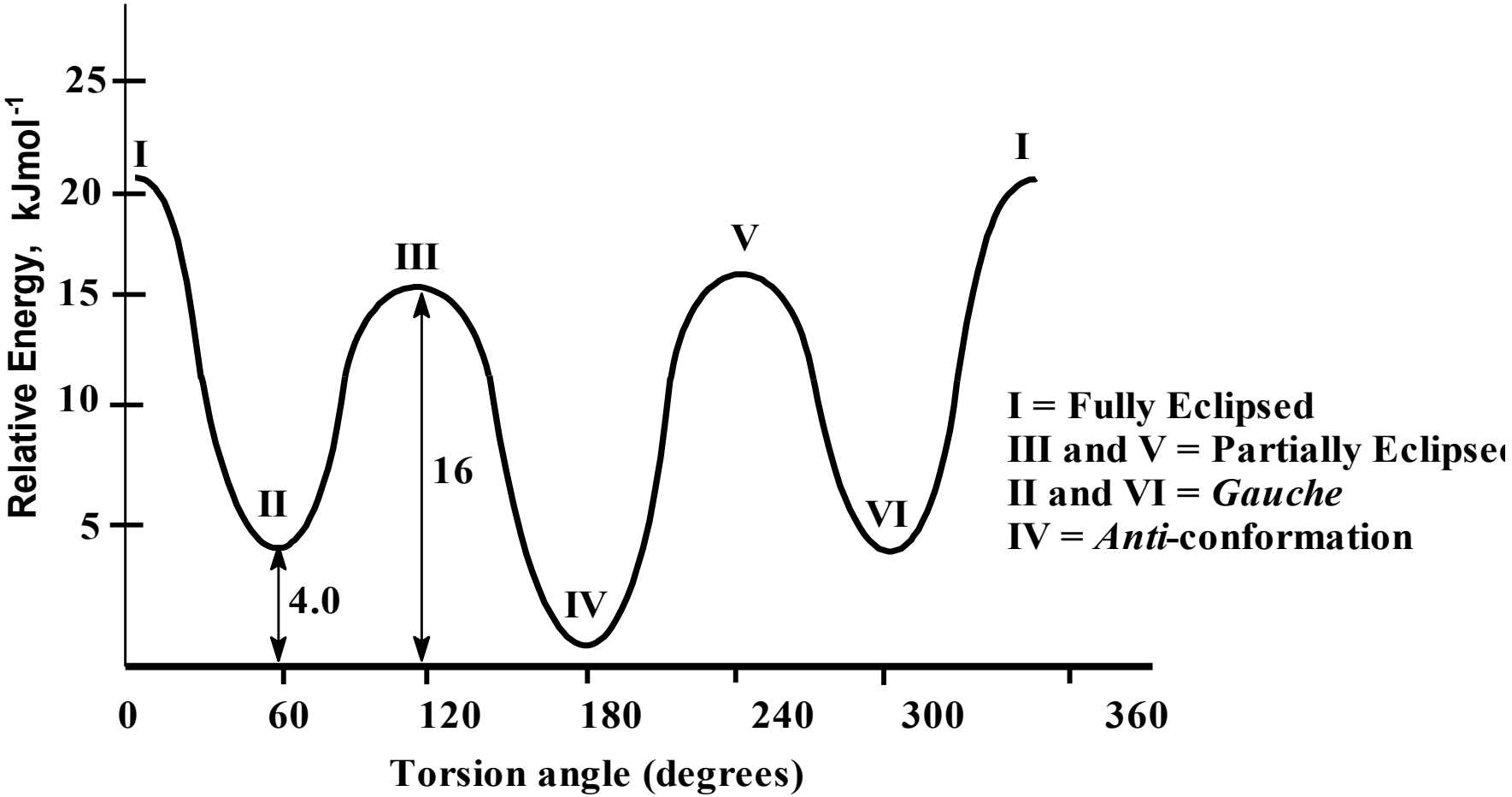
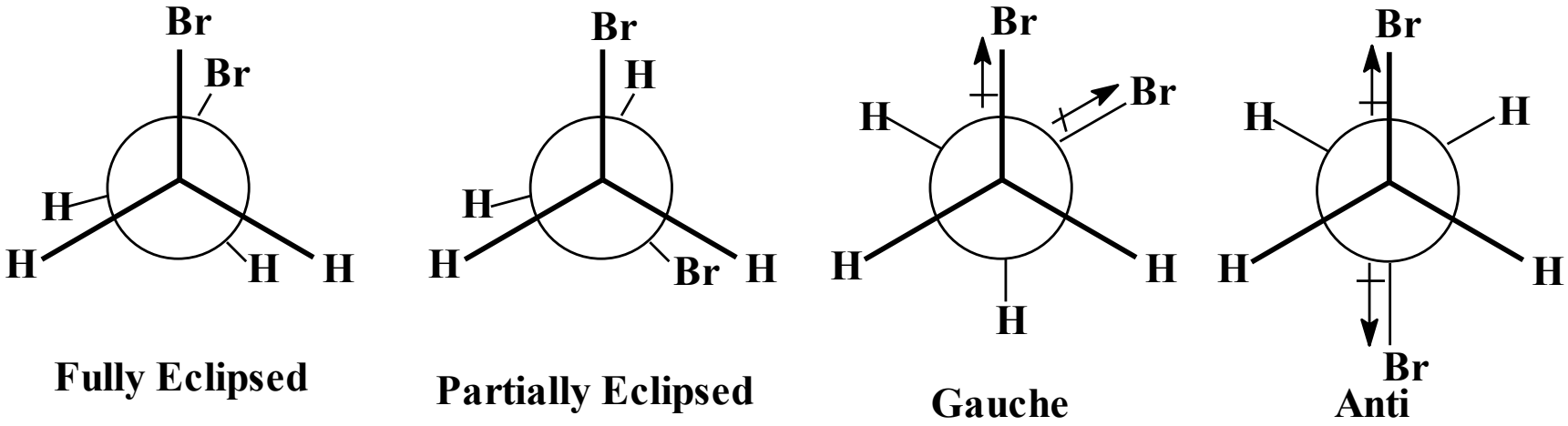


Fig. 3.8 Rotational or torsional energy in *n*-butane

At room temperature, almost all molecules exist in staggered conformation and amongst staggered conformations 78% exist in *anti* and 22% in *gauche* conformations.

Conformation of 1,2-Dibromoethane

- On the basis of *torsional strain* and *vander Waals steric hindrance*, staggered (*anti*) conformation of 1,2-dibromoethane is the most stable followed by *gauche*.

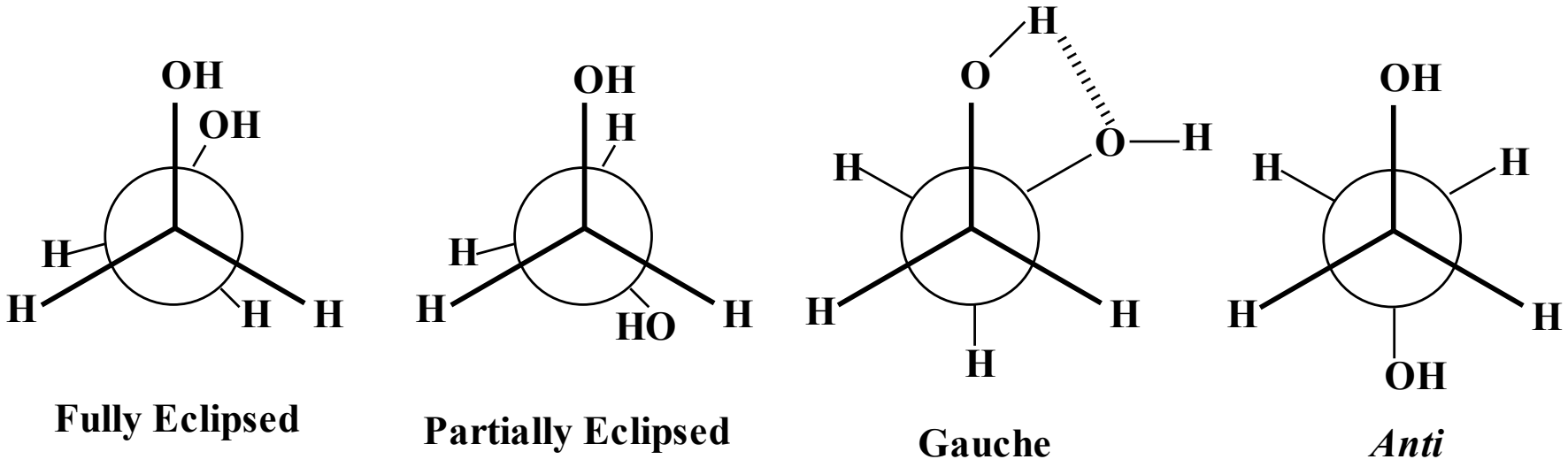


- Dipole moment of *anti*-conformation is zero while *gauche* conformation has some finite dipole moment since the two C—Br dipoles are at an angle of 60^0 to each other.
- Actual dipole moment of 1,2-dibromoethane is 1.0D, therefore, the molecule cannot exist entirely in the *anti* form. Hence

$$Anti \rightleftharpoons Gauche$$

Conformations of 1,2-Glycols : *Ethylene Glycol*

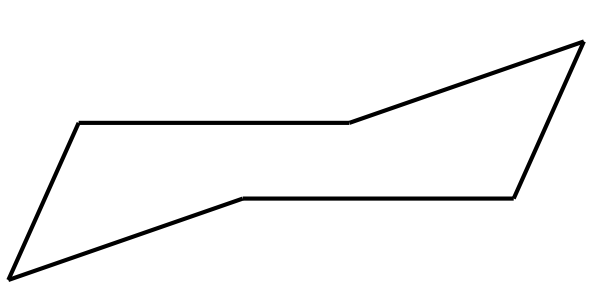
- In case of ethylene glycol due to intramolecular H-bonding the *gauche* form becomes more stable than *anti*-conformation because there will be no such H-bonding possible in anti-conformation. The formation of such H-bond stabilizes the molecule by approximately 20-30 kJ mol-1.



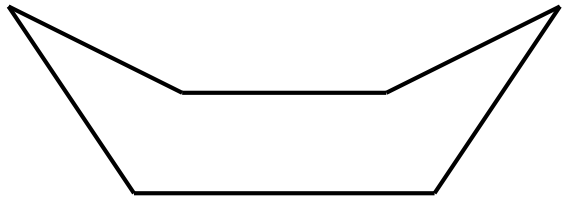
- Similarly due to intramolecular H- bonding ethylene chlorohydrin, ($CH_2Cl - CH_2OH$), exists in *gauche* conformation which is more stable than anti-form.

Alicyclic System: Cyclohexane

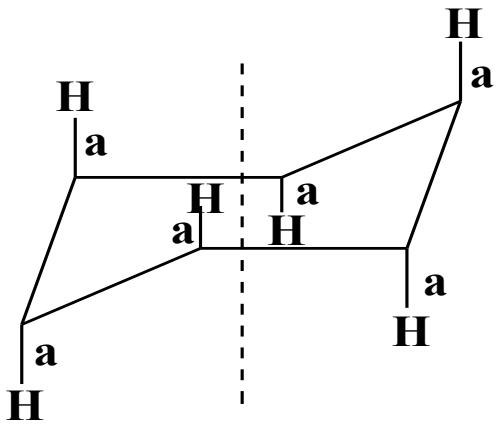
- Cyclohexane can have two conformations free from Baeyer or angle strain, called the *chair* form (I) and the *boat* form (II), respectively.

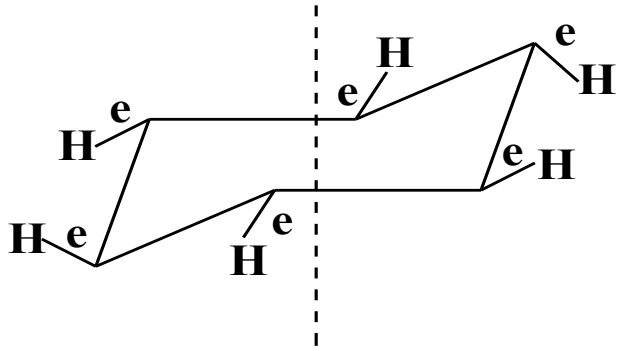


I

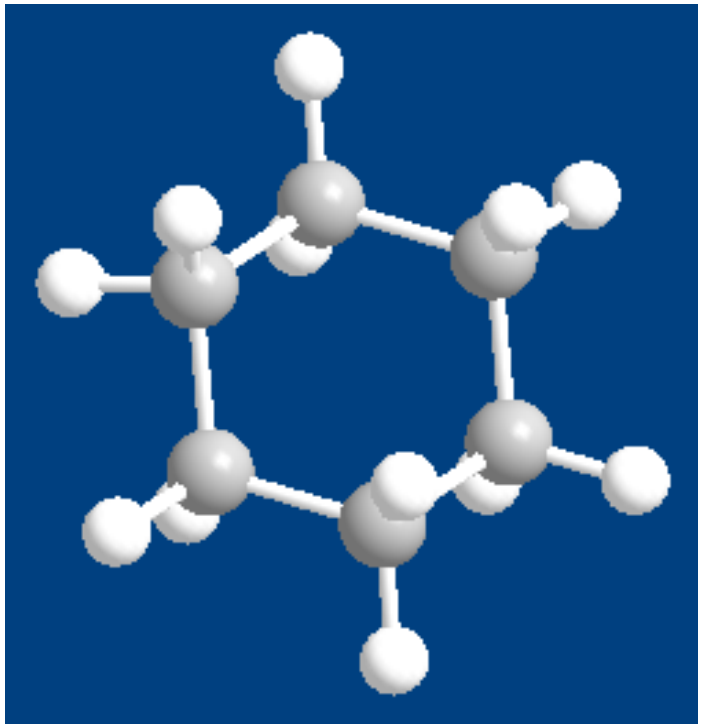


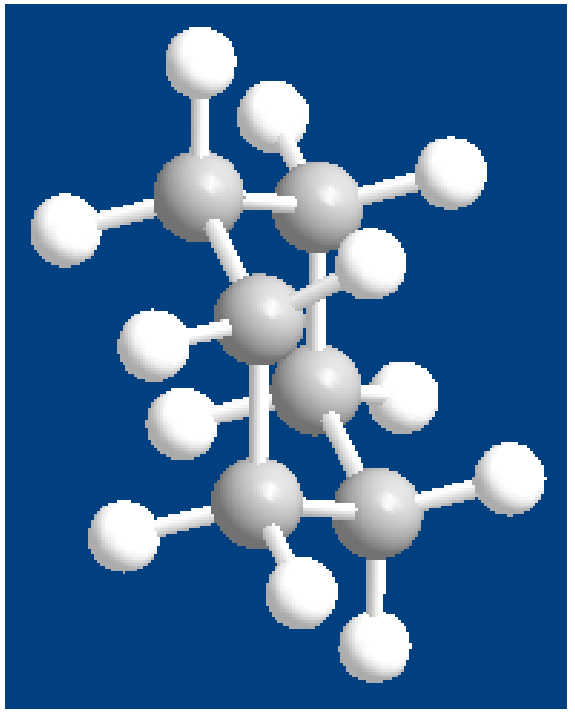
II

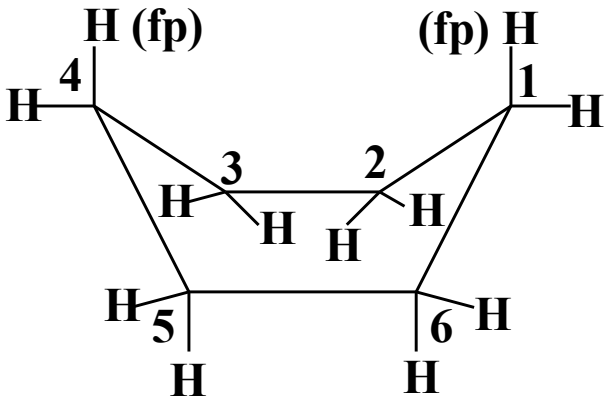




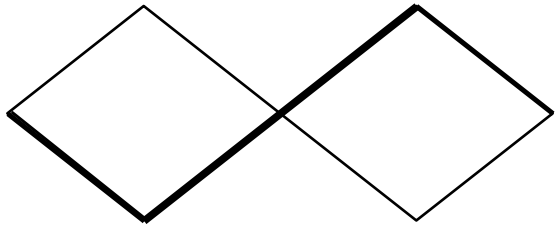
Chair conformations of cyclohexane with axial and equatorial bo



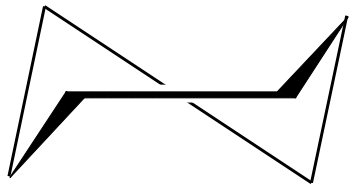




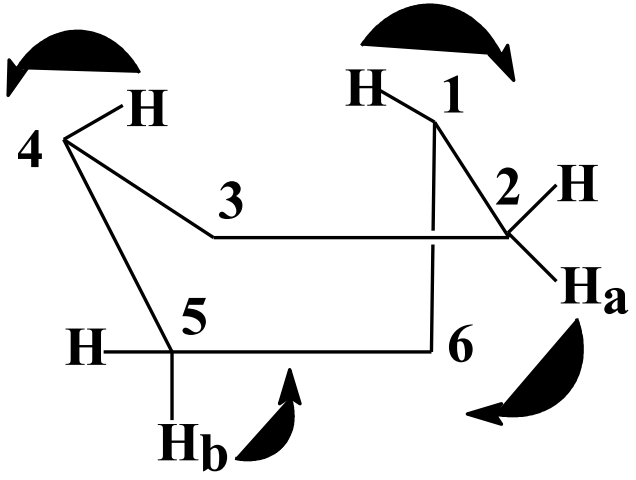
Boat



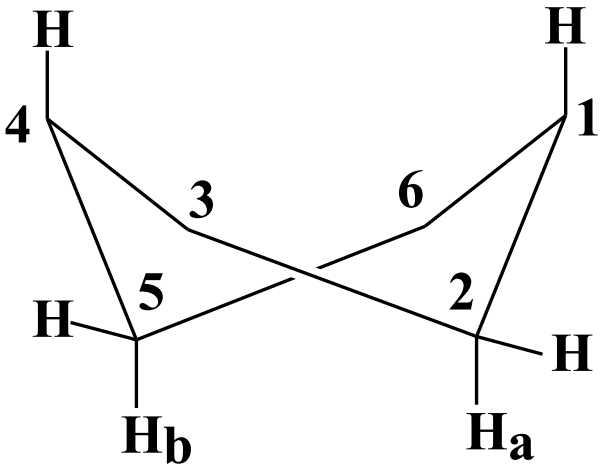
Twist Boat



Twist chair



Boat



Twist boat

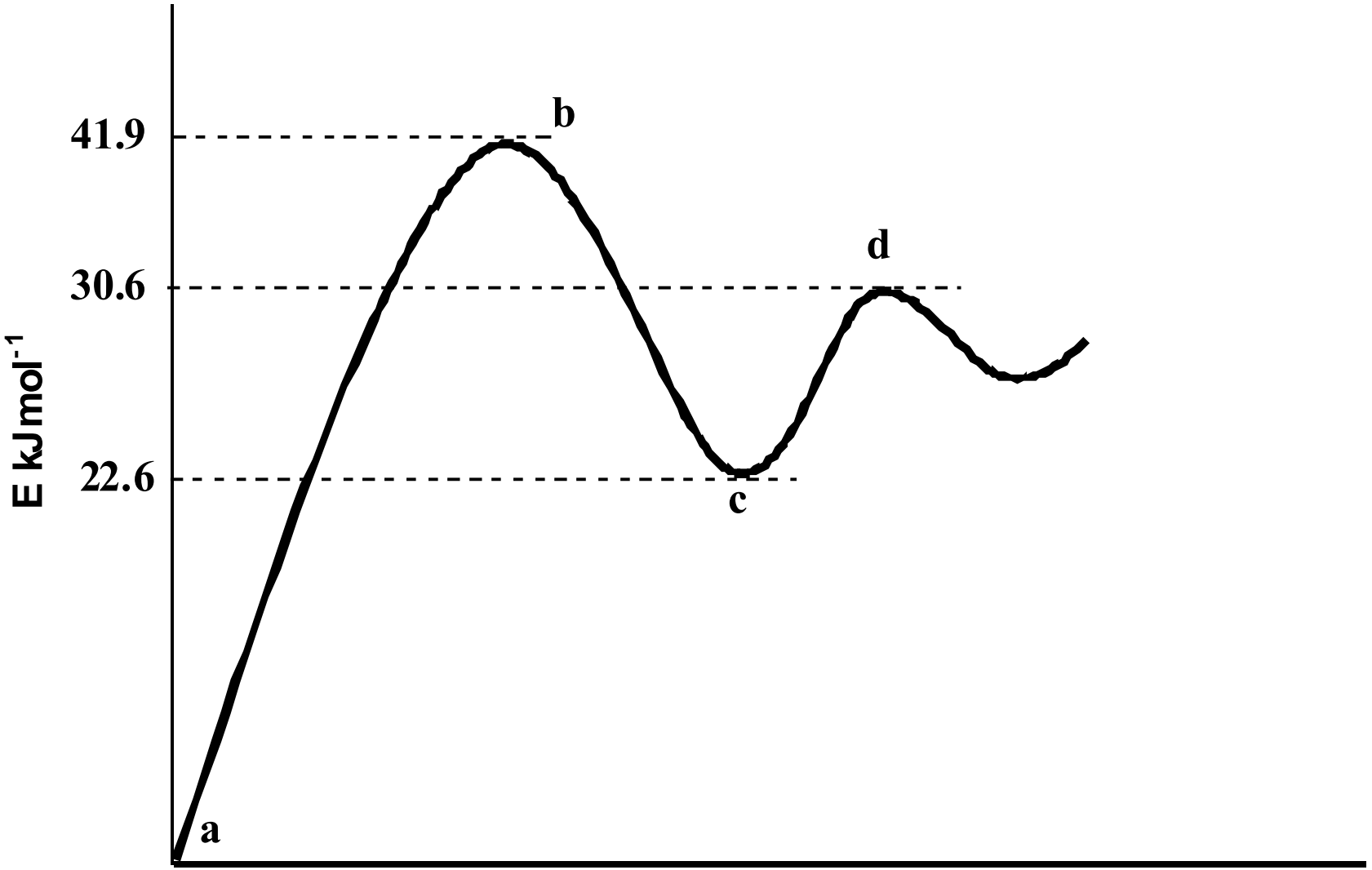
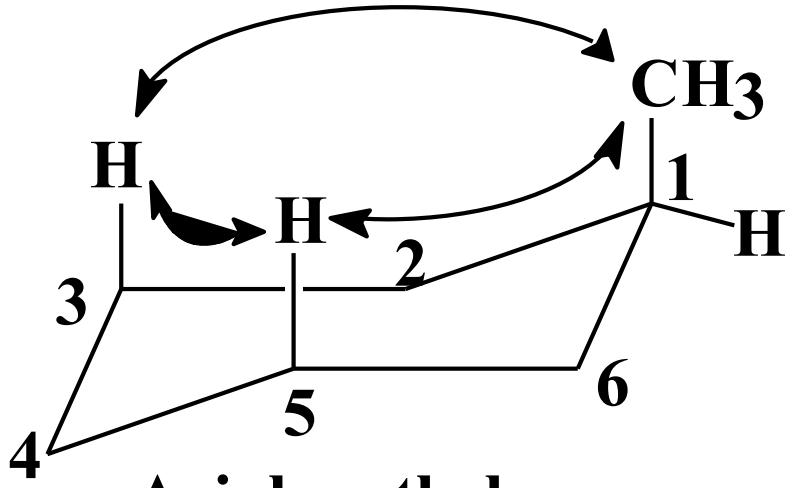


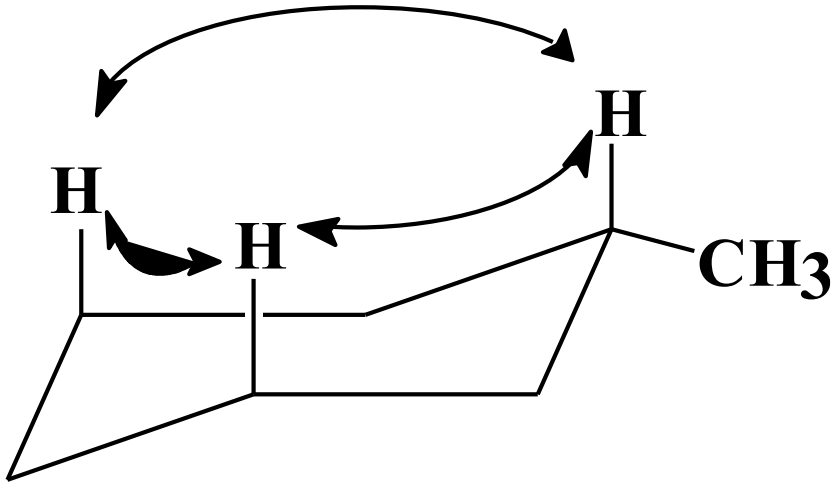
Fig. 3.10 Potential energy of cyclohexane, a, chair; b, twist chair; c twist boat; d, boat.

Cyclohexane Derivatives

If we consider that in the axial conformer the two axial hydrogens on C_3 and C_5 are closer to the axial than to the equatorial methyl group.



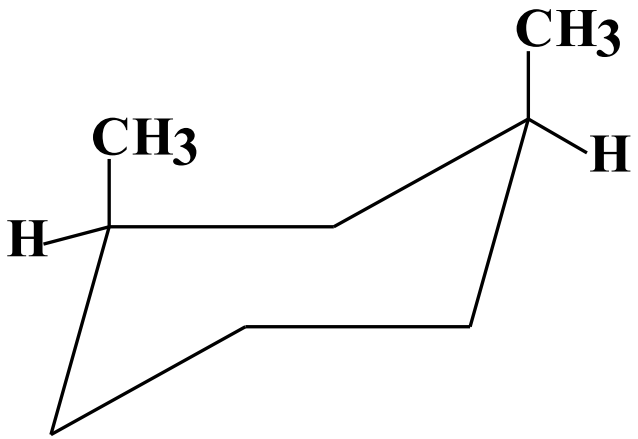
Axial methyl



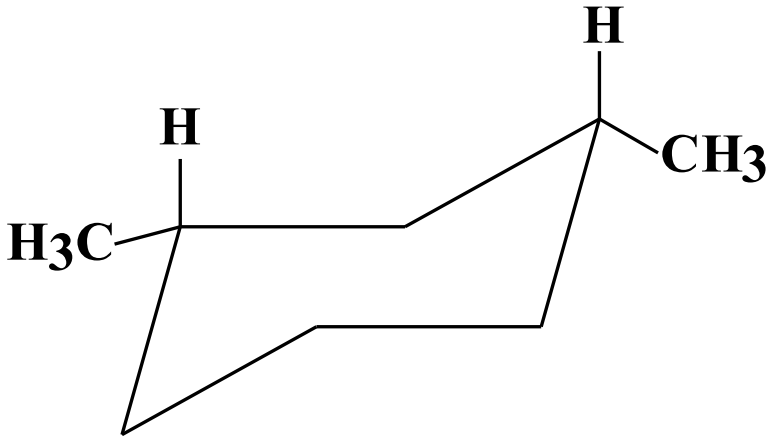
Equatorial methyl

Cis 1,3-dimethylcyclohexane

The interactions between the axial atoms or groups at 1- and 3- or 5-positions are called *1,3-diaxial interactions* and in the case of 1,3-dimethylcyclohexane, the 1,3-diaxial interaction has been assigned the value of 22.6kJmol^{-1}. Thus *cis* 1,3-dimethylcyclohexane exists at room temperatures almost wholly in the diequatorial conformation.

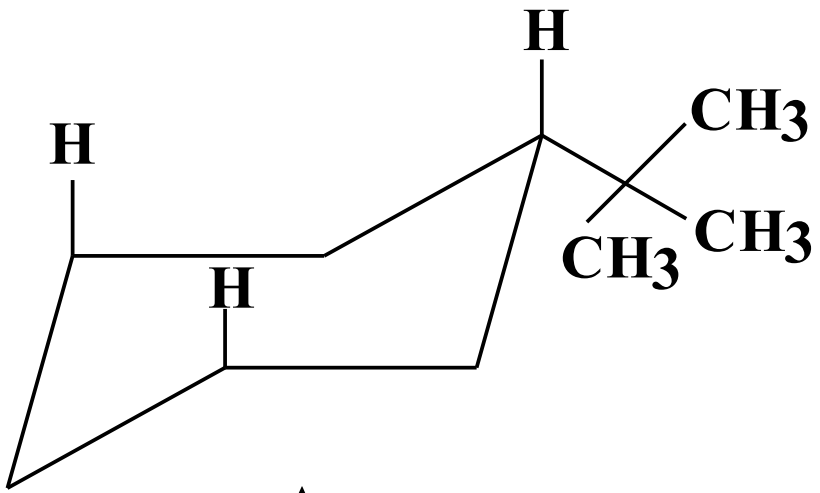


***cis* 1,3-Dimethylcyclohexane**
(diaxial conformer; much less stable)

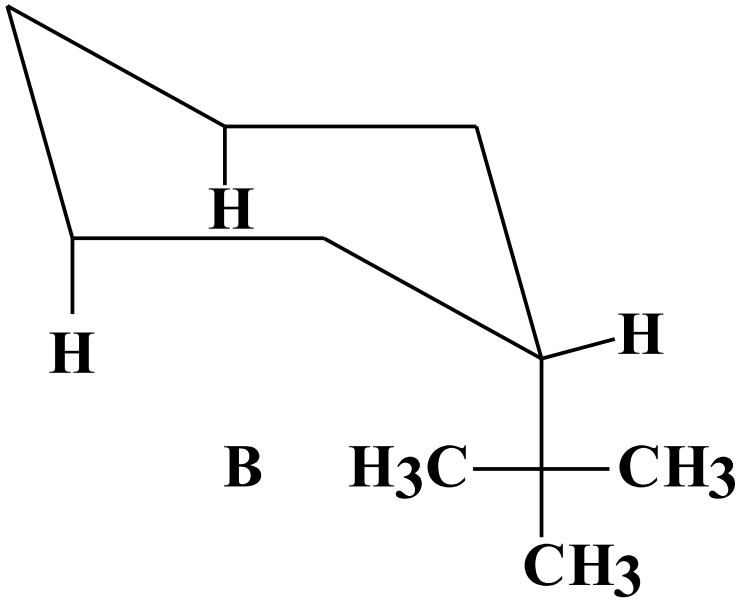


***cis* 1,3-Dimethylcyclohexane**
(diequatorial conformer; much more stable)

tert-Butylcyclohexane exists 100 per cent in the equatorial conformation (A), the ring being frozen due to the prevention of the flip to a conformation (B) in which the non-bonded 1,3-diaxial interactions between the axially bound *tert*-butyl group and the two axial hydrogens at the 3- and 5-positions will be forbiddingly large.



A



B

It is clear from the above considerations that the axial bonds experience non-bonded interactions with other axial bonds at 3-and 5-positions whereas the equatorial bonds are free from such steric interactions, i.e. axially bound groups will experience more steric crowding than the equatorially bound groups.

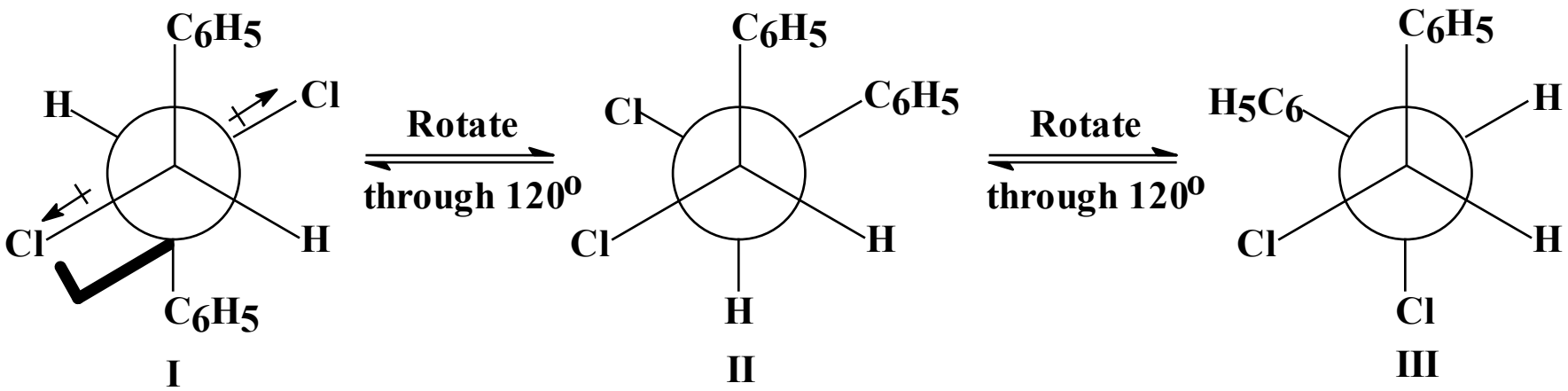
This explains why in most of the cases the equatorially bound groups in cyclohexane derivatives are more reactive than the axially bound ones. E.g. equatorially bound hydroxyl groups are more easily esterified than the axial ones. Similarly, the equatorial acetoxy group undergoes hydrolysis faster than the axial group.

Difference between conformation and configuration

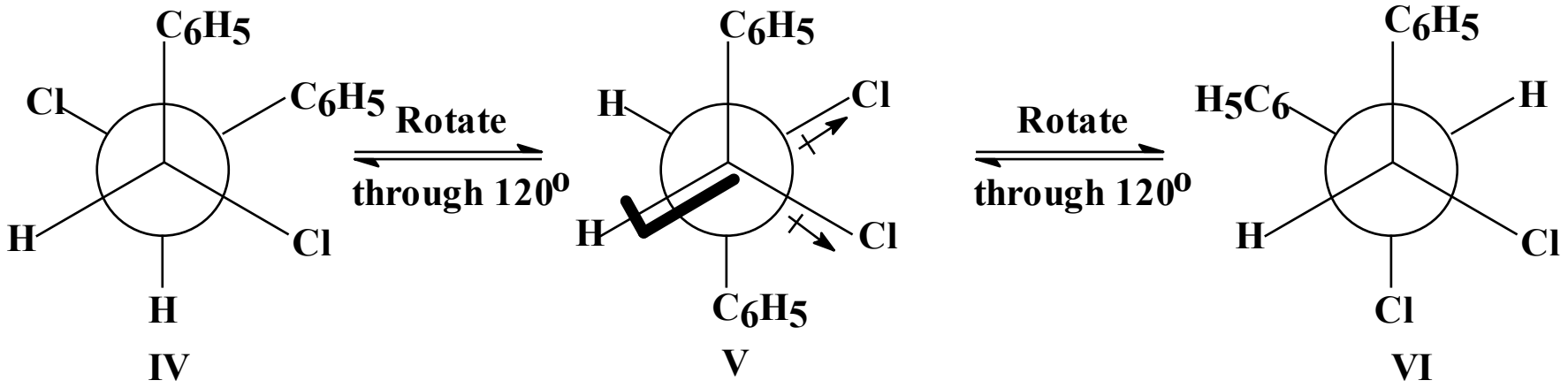
- Conformations is used for various spatial isomers which can be easily inter-converted.
- Configurations is used for various spatial isomers which can be interconverted only by breaking and making of covalent bonds.
- The energy difference between two conformers is very small due to which they can be interconverted by molecular collisions even at room temperature.
- Conformational isomers cannot be separated. But Configurational isomers can be separated easily.

Dipole moment of *meso* form is much lower (m =1.27 D) than optically active form (m = 2.75D) of stilbene dichloride. Why?

meso-form



(+ or -) form

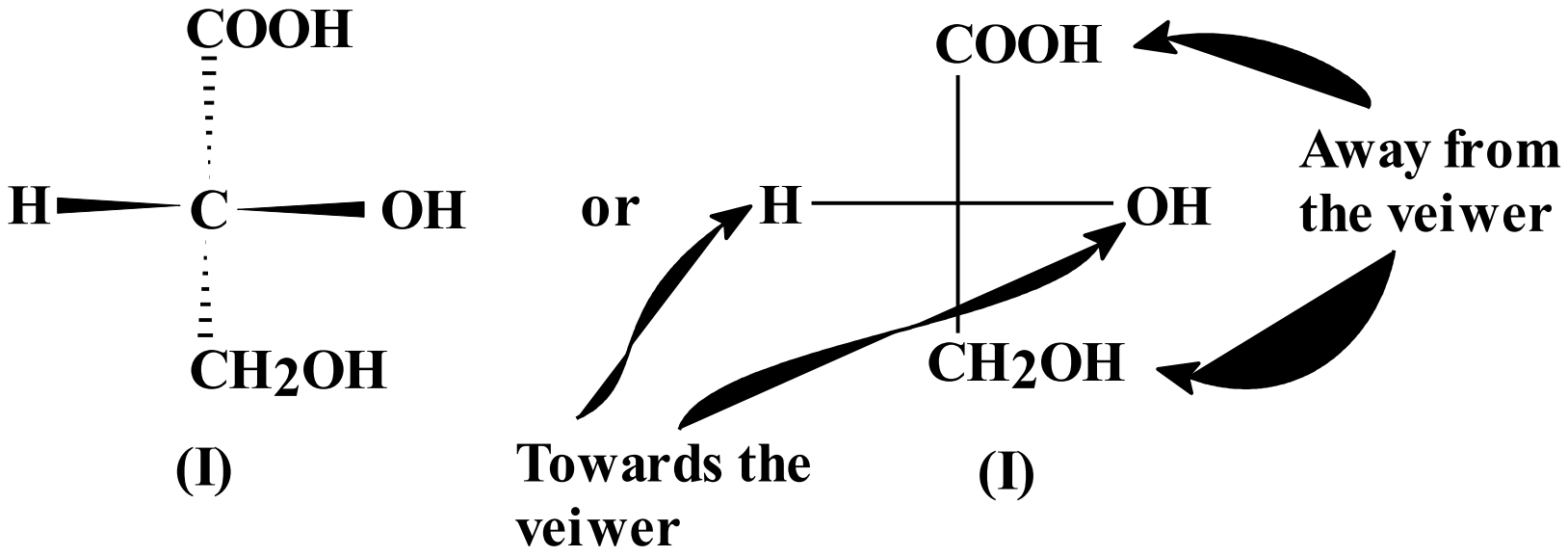


PROJECTION FORMULAS OF CHIRAL MOLECULES

Configuration of a chiral molecule is three dimensional structure and it is not very easy to depict it on a paper having only two dimensions. To overcome this problem the following four two dimensional structures known as projections have been evolved.

- 1. Fischer Projection
- 2. Newman Projection
- 3. Sawhorse Formula
- 4. Flying Wedge Formula

1. Fischer Projection



- **Characteristic features of Fischer projection:** Rotation of a Fischer projection by an angle of 180^0 about the axis which is perpendicular to the plane of the paper gives identical structure. However, similar rotation by an angle of 90^0 produces non - identical structure.

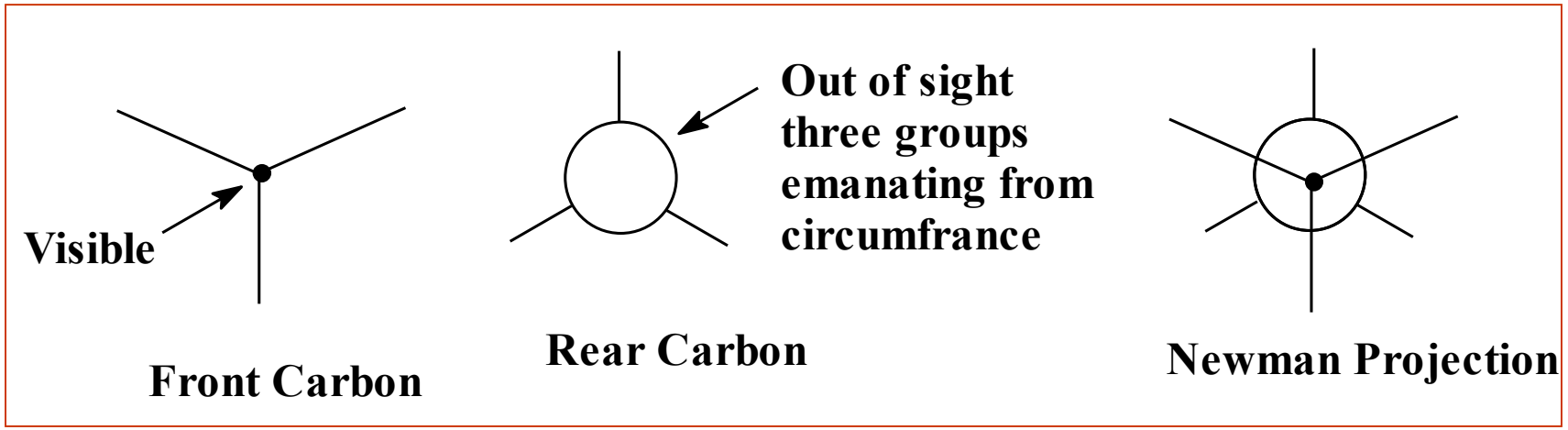
2. Newman Projection

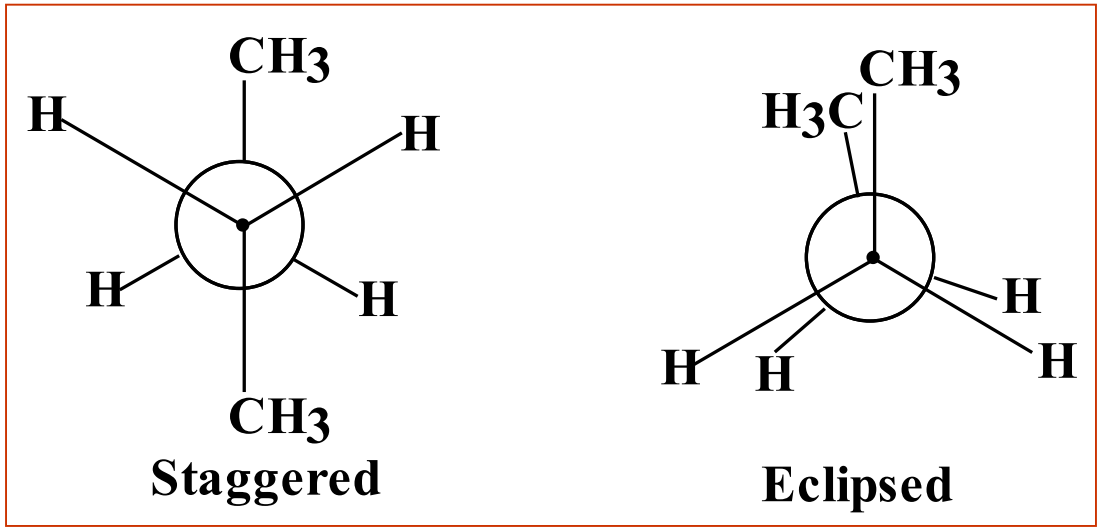
In Newman projection we look at the molecule down the length of a particular carbon - carbon bond. The carbon atom away from the viewer is called 'rear' carbon and is represented by a circle. The carbon atom facing the viewer is called 'front' carbon and is represented as the centre of the above circle which is shown by dot. The remaining bonds on each carbon are shown by small straight lines at angles of 120° as follows:

i) Bonds joined to 'front' carbon intersect at the central dot.

ii) Bonds joined to 'rear' carbon are shown as emanating from the circumference of the circle.

The concept of Newman projection for *n*-butane can be understood by the following drawings:

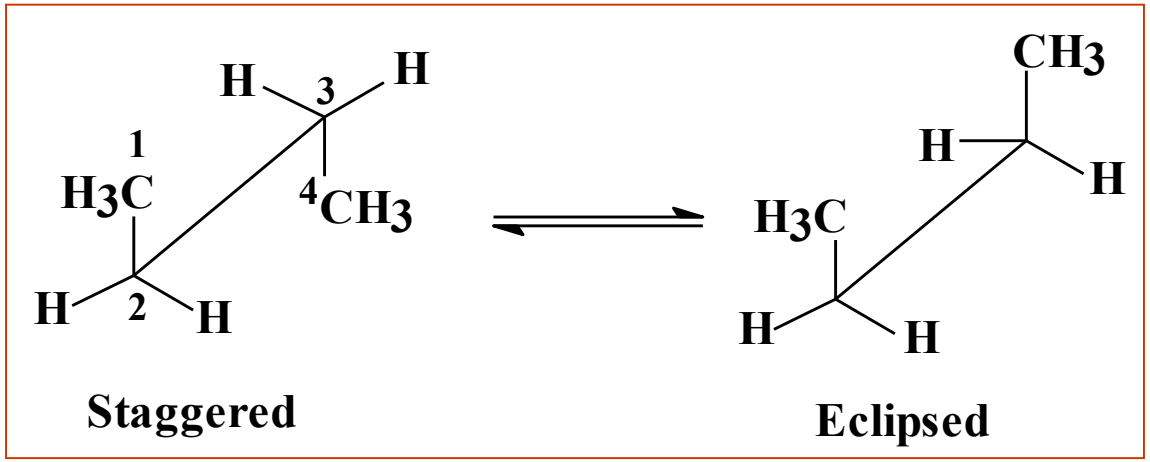




These conformations arise due to free rotation about the carbon - carbon single bond (front and rear carbon atoms).

3. Sawhorse projection

- The bond between two carbon atoms is shown by a longer diagonal line because we are looking at this bond from an oblique angle. The bonds linking other substituents to these carbons are shown projecting above or below this line.



- Due to free rotation along the central bond two extreme conformations are possible - the staggered and the eclipsed

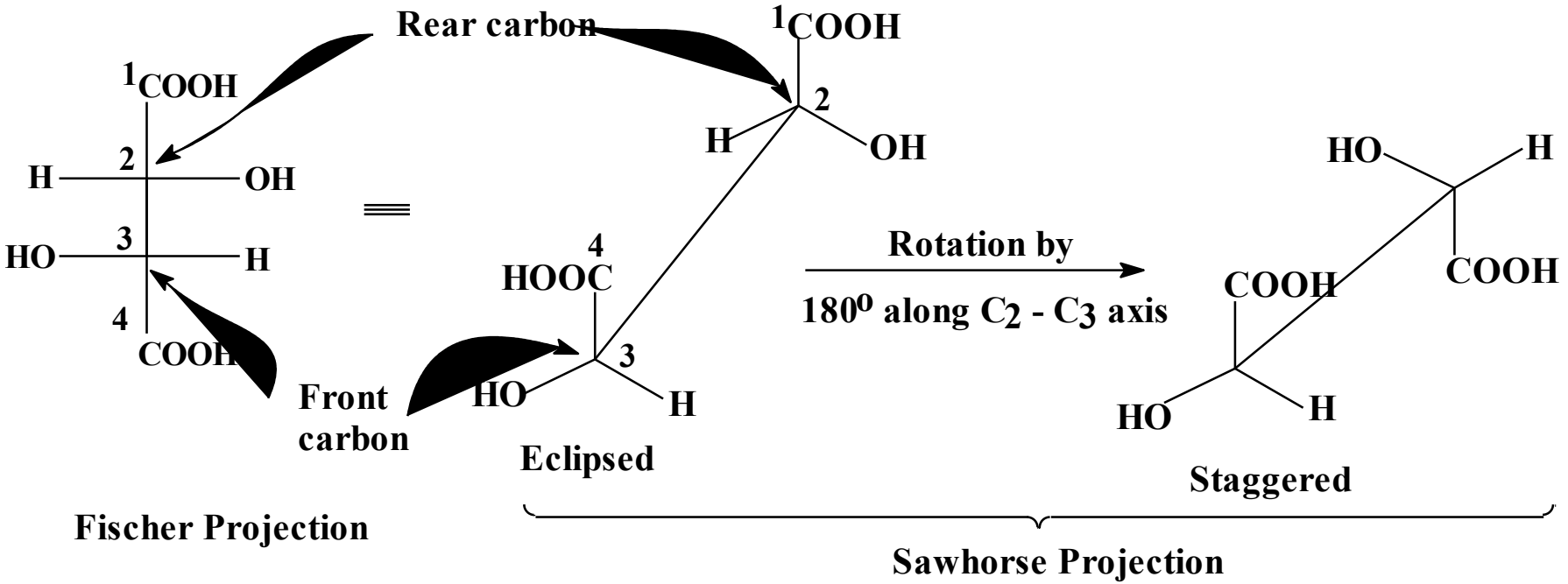
4. Flying Wedge Formula

- It is a three dimensional representation.
- The flying wedge formulas of two enantiomeric lactic acids are shown below:

- Both these structure are mirror image of each other.
- (Note: The main functional group is generally held on the upper side in the vertical plane.)

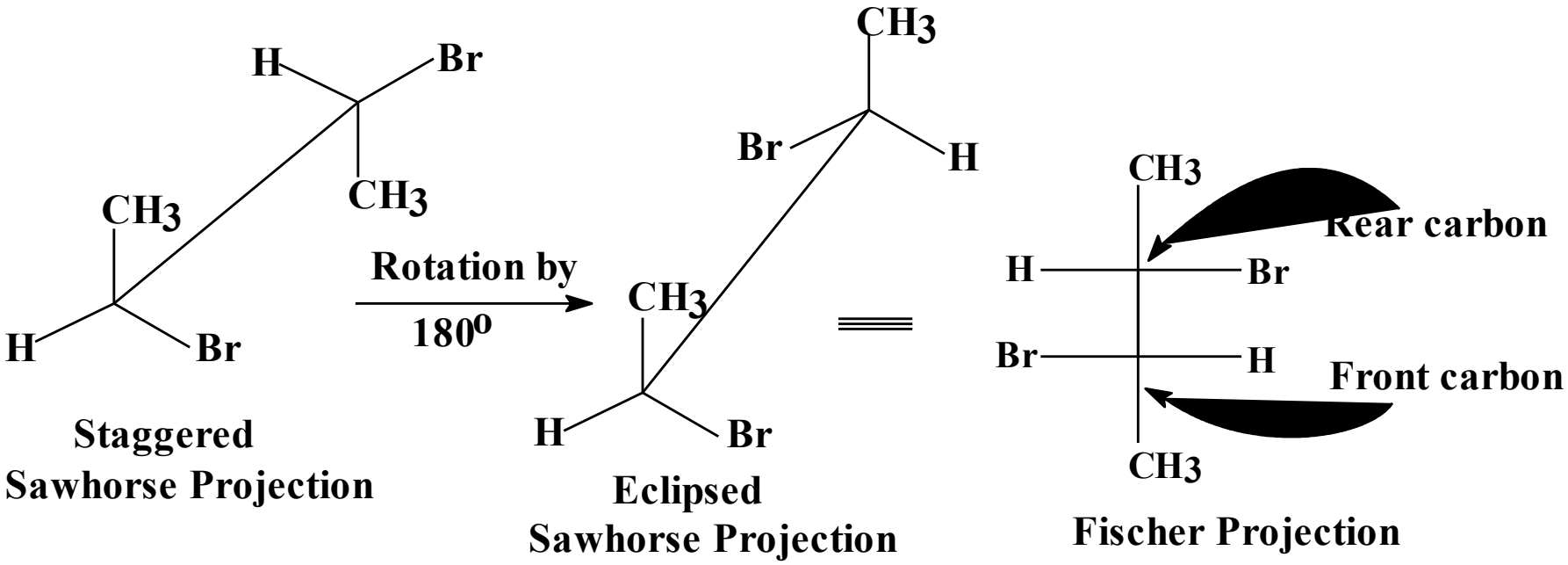
Conversion of Fischer Projection into Sawhorse Projection

- Fischer projection of a compound can be converted into sawhorse projection first in the eclipsed form by holding the model in horizontal plane in such a way that the groups on the vertical line point above and the last numbered chiral carbon faces the viewer. Then one of the two carbons is rotated by an angle of 180° to get staggered form (*more stable* or *relaxed form*).

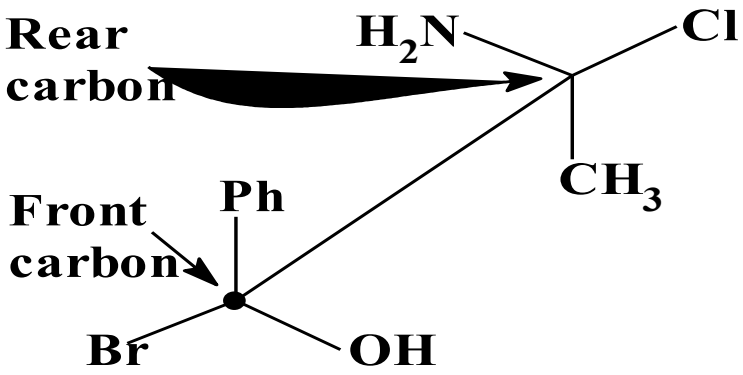


Conversion of Sawhorse projection into Fischer projection

- First the staggered sawhorse projection is converted in eclipsed projection. It is then held in the vertical plane in such a manner that the two groups pointing upwords are away from the viewer i.e. both these groups are shown on the vertical line. Thus, for 2,3-dibromobutane.

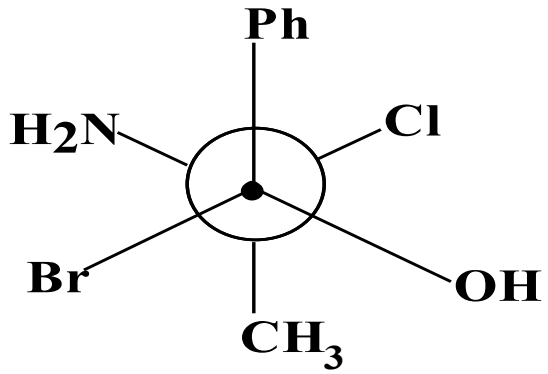


Conversion of Sawhorse to Newman to Fischer Projection



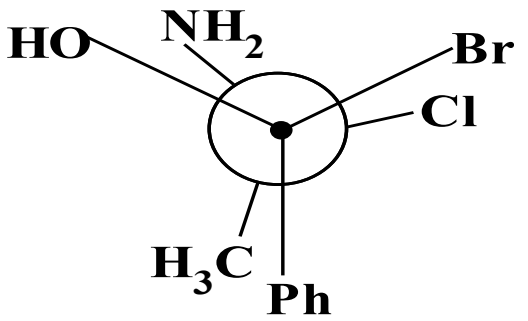
Staggered
Sawhorse Projection

View through
the front carbon



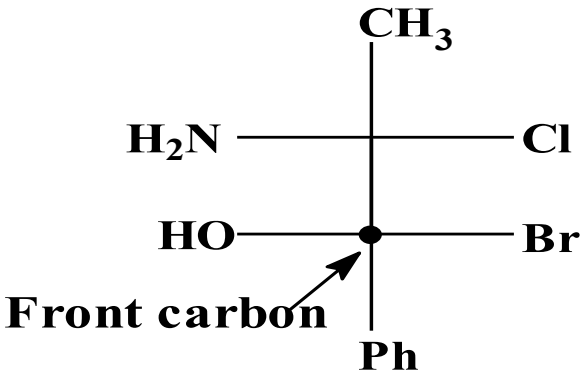
Staggered
Newman Projection

Rotate the front carbon
along the central
bond by 180^o



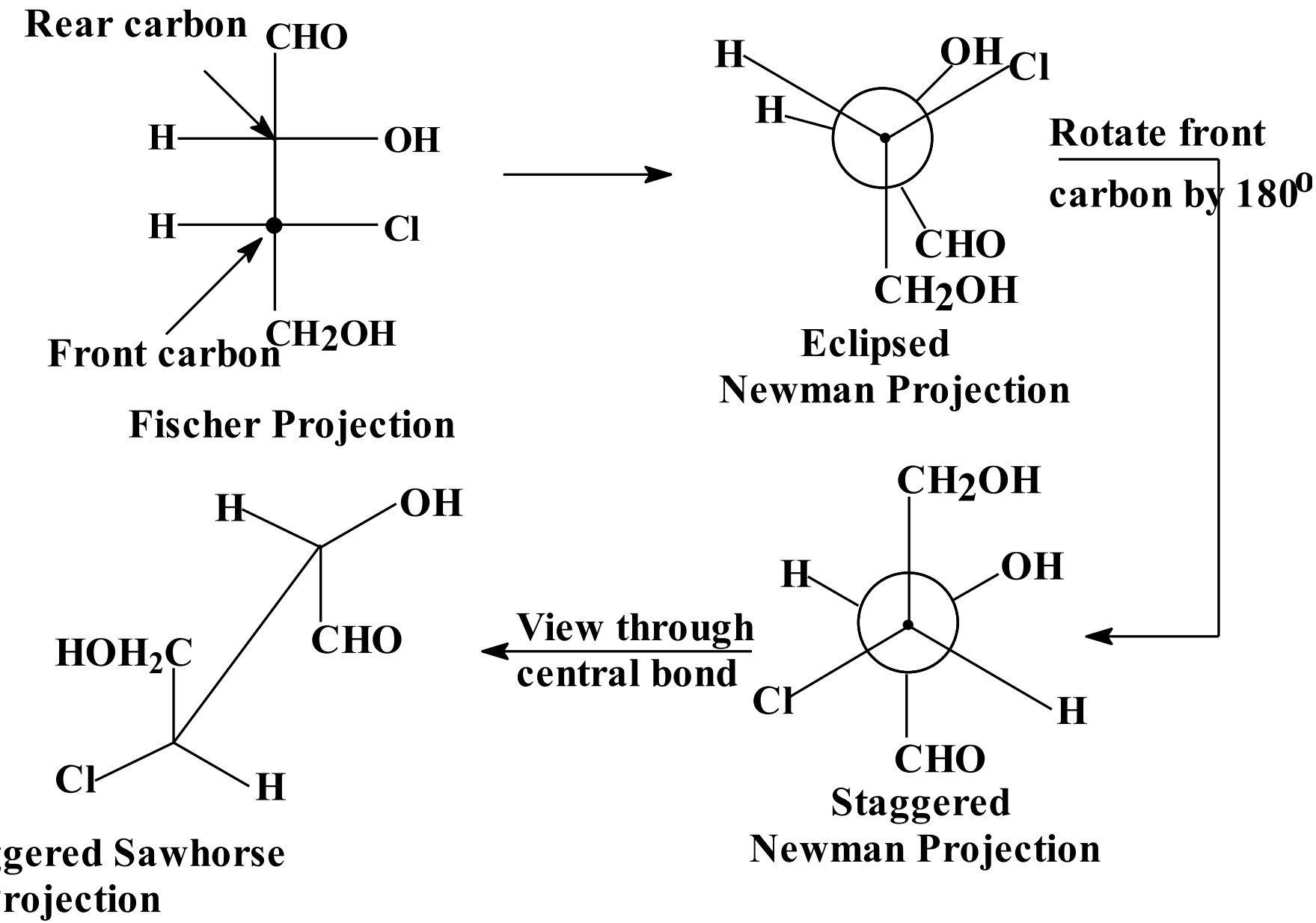
Eclipsed
Newman Projection

Hold in vertical plane
keeping front carbon as the
lowest



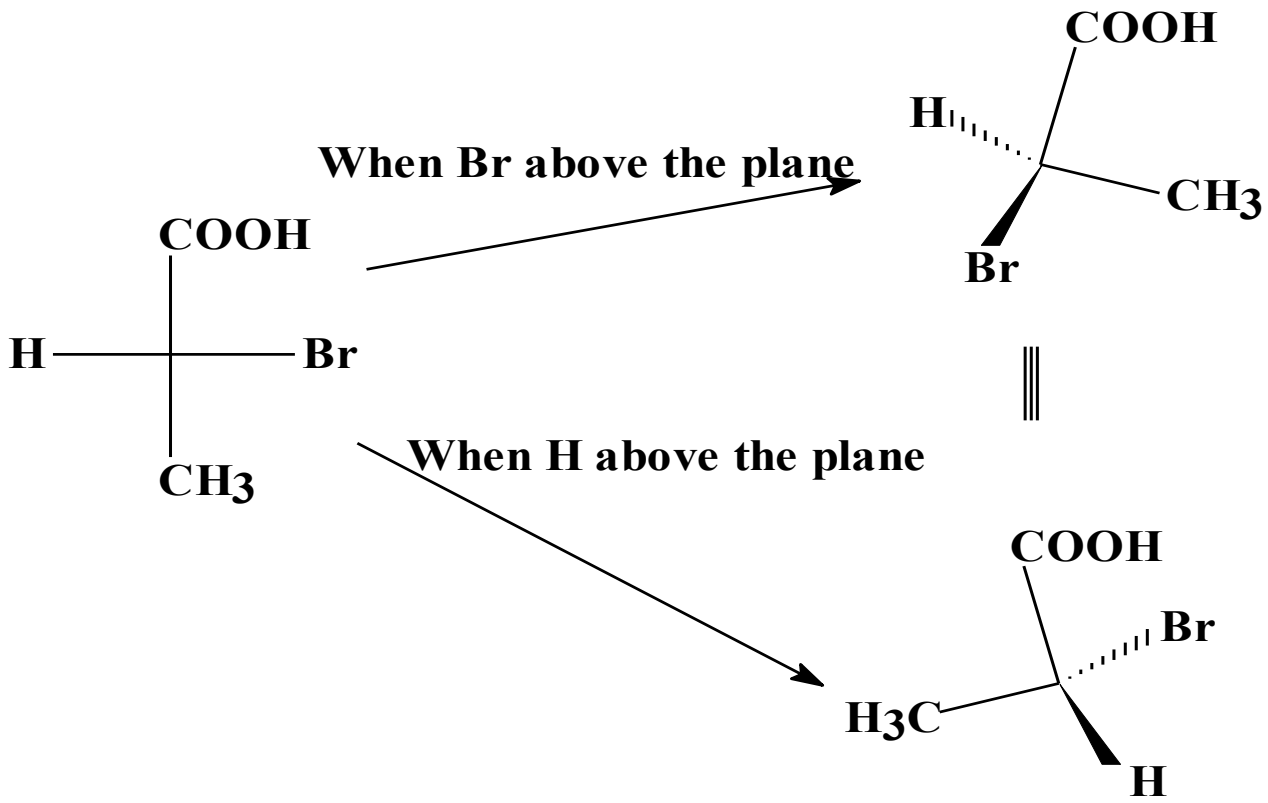
Fischer Projection

Conversion of Fischer to Newman to Sawhorse Projection



Conversion of Fischer Projection into Flying Wedge

- The vertical bonds in the Fischer projection are drawn in the plane of the paper using simple lines (—) consequently horizontal bonds will project above and below the plane.



Conversion of Flying Wedge into Fischer Projection

- The molecule is rotated (in the vertical plane) in such a way that the bonds shown in the plane of the paper go away from the viewer and are vertical.