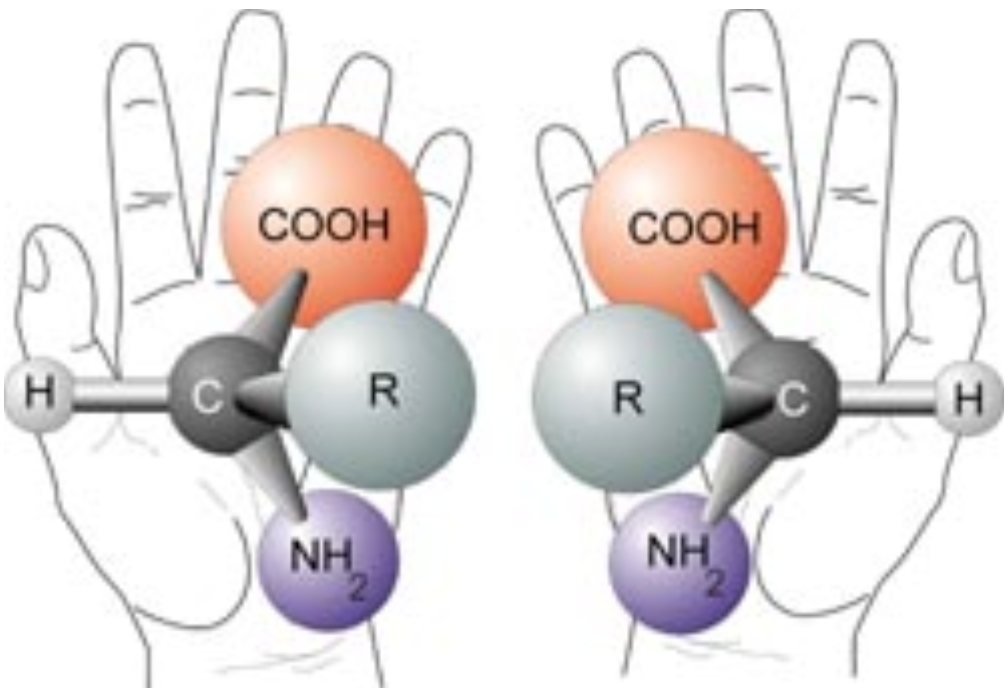
November Lectures 2015

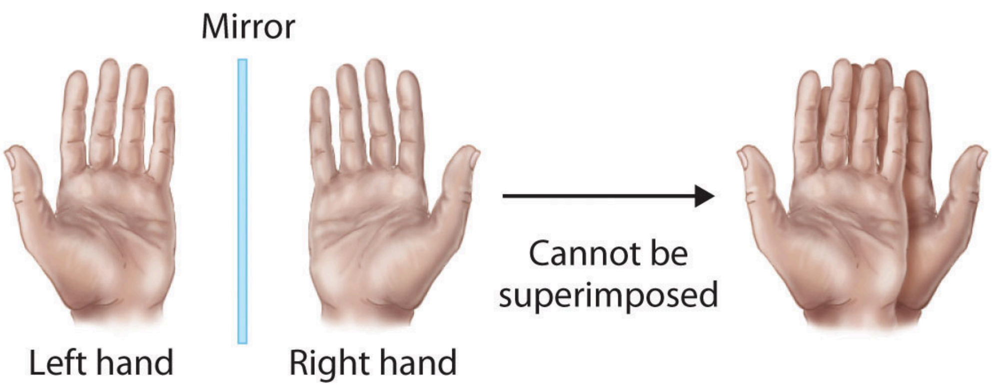
Stereochemistry and Chirality

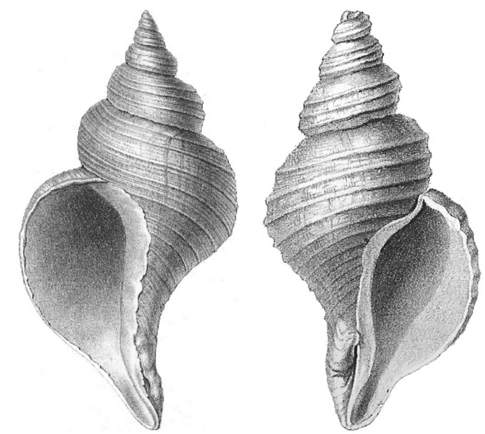


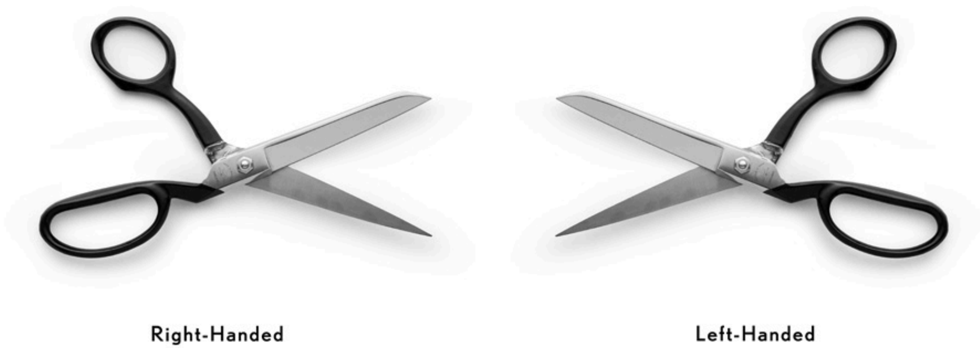
Sonia Horvat

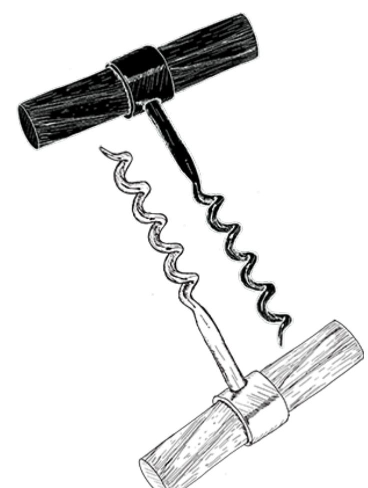
http://www.science.oregonstate.edu/~gablek/CH334/Chapter5/chirality.htm

Chirality – An object which is non-superimposable on its mirror image is said to be chiral (derived from the Greek term ‘cheir’ meaning hand).

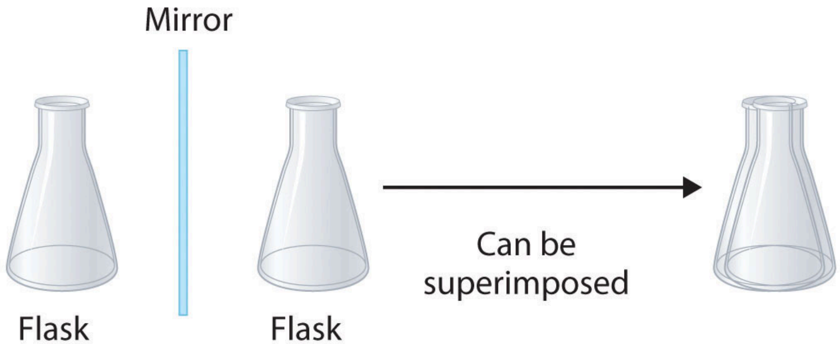








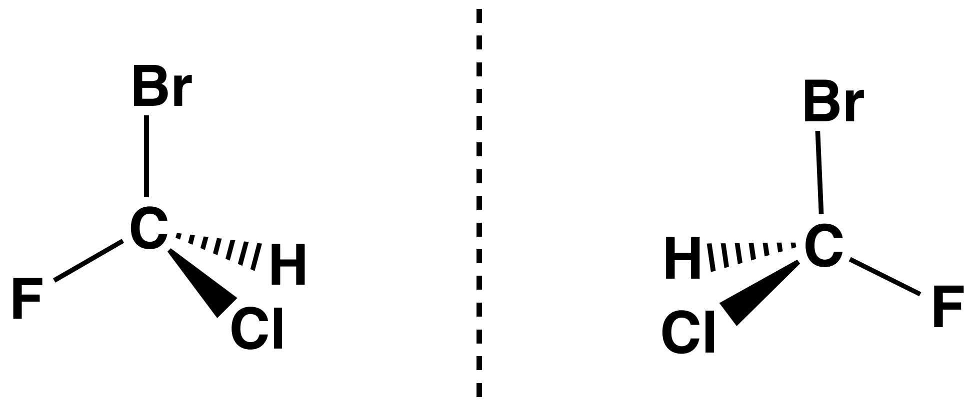
Achiral objects

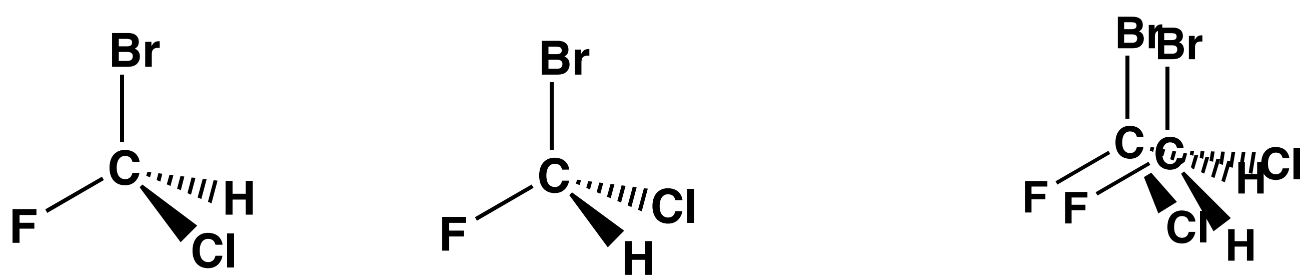


Object

Mirror image

Chiral Molecules: (1) Bromochlorofluoromethane
Contains a tetrahedral carbon with four different substituents (F, Cl, Br and H)





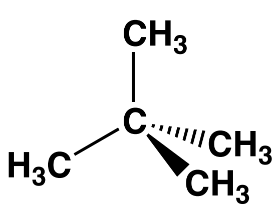
Molecules which are non-superimposable mirror images are called 'enantiomers' – Examples of stereoisomers

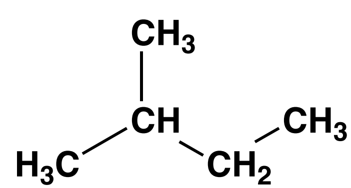
Isomers – Molecules with the same molecular formula but with different structure

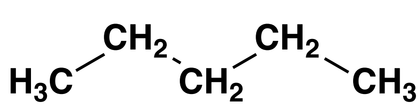
Isomers

Constitutional isomers

- different atom to atom connectivity







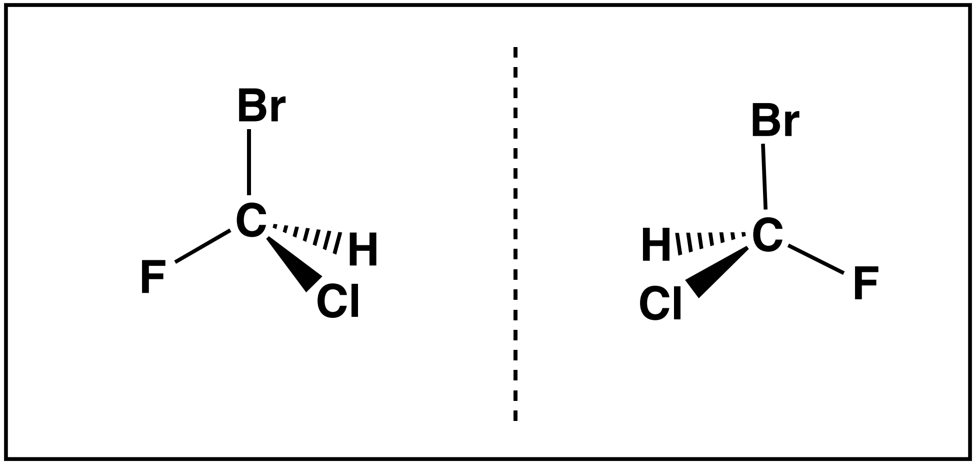
Stereoisomers

- same atom to atom connectivity but the arrangement in space is different

Stereoisomers

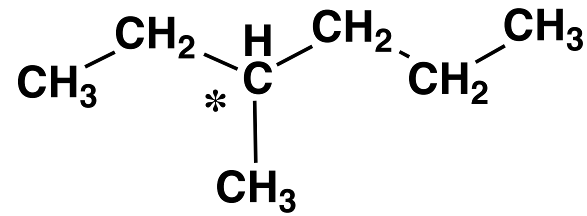
Same atom connectivity, but have a different 3-D arrangement of atoms

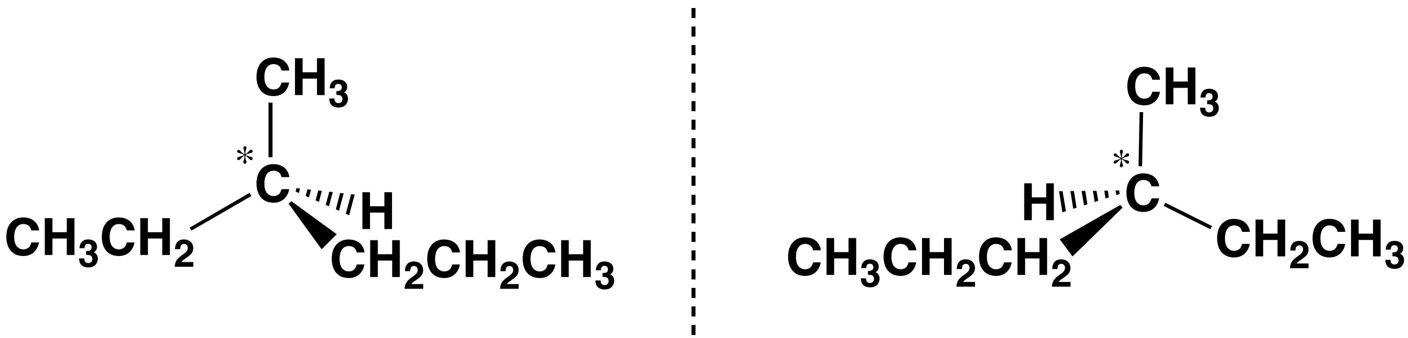
- Enantiomers are stereoisomers which are non superimposable mirror images

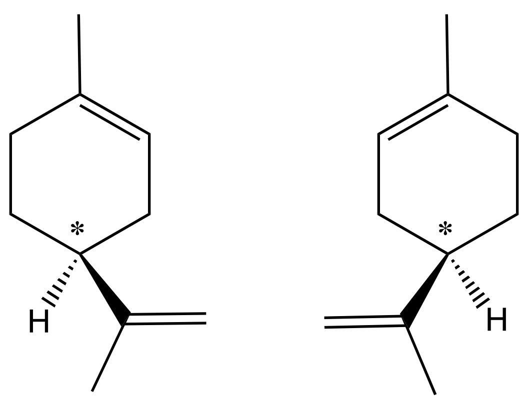


Examples of Chiral molecules

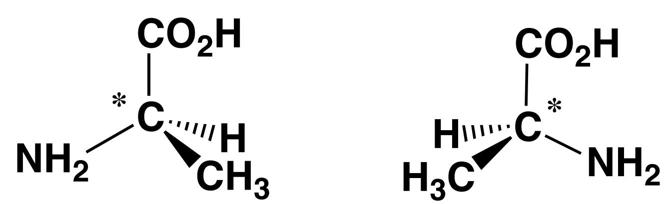
3-Methylhexane
* Denotes asymmetric carbon







Limonene enantiomers



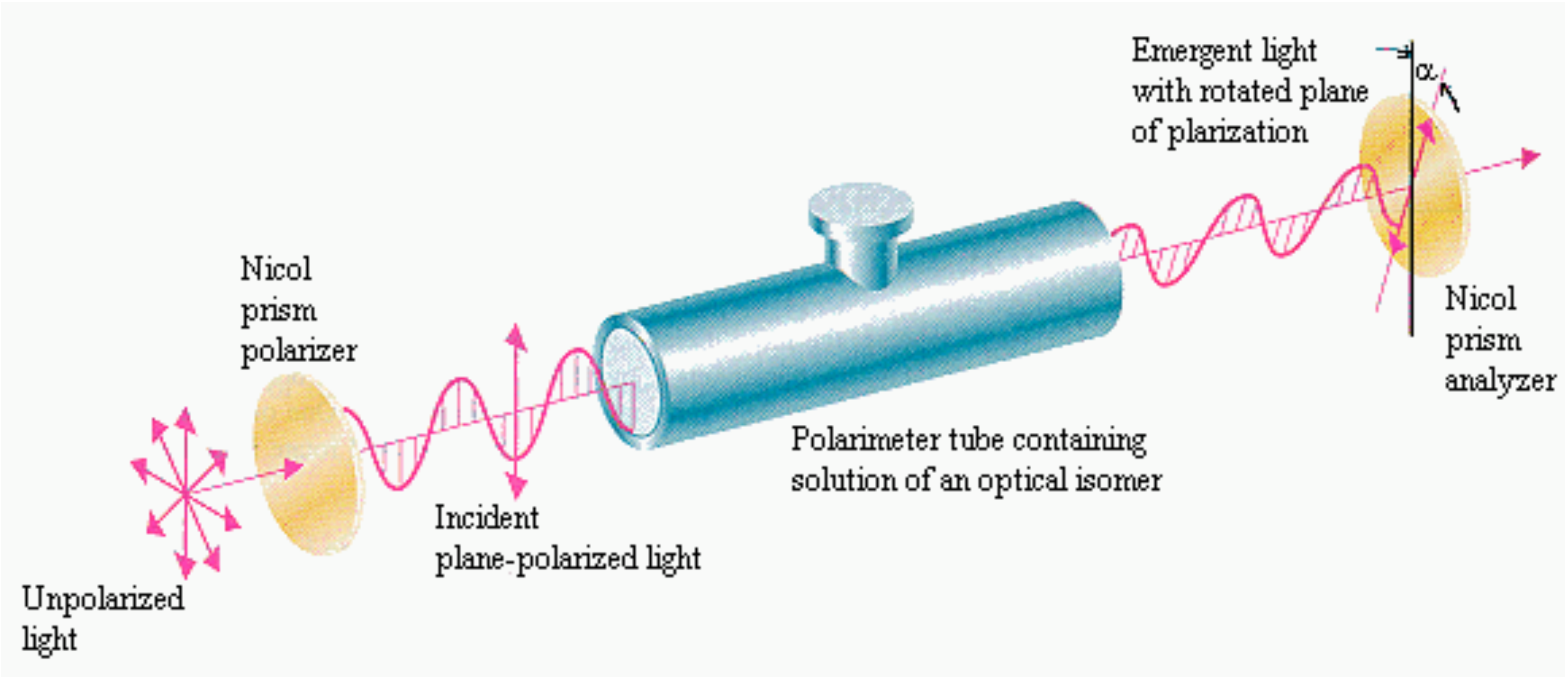
Enantiomers of the amino acid Alanine

How do the chemical and physical properties of enantiomers differ?

Enantiomers have identical physical properties except for the direction of rotation of plane-polarised light (PPL).

They will react in the same way with symmetric molecules but differently with asymmetric (often biological) molecules.

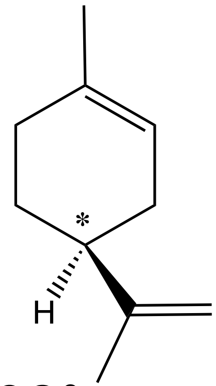
Polarimeter – An instrument for measuring the rotation of the plane of polarised light

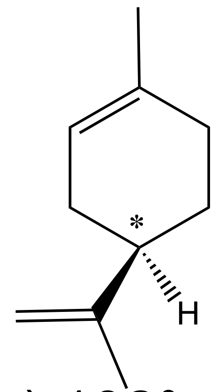


Demonstration of optical rotation using the enantiomers of Limonene

Some Terminology:

Molecules which rotate PPL are said to be *optically active*

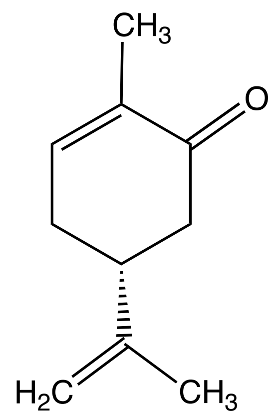




Specific rotation	(-) 102°	(+) 102°
	anticlockwise	clockwise
	levorotatory	dextrorotatory
	(*l*) Limonene	(*d*) Limonene
	or (-) Limonene	(+) Limonene

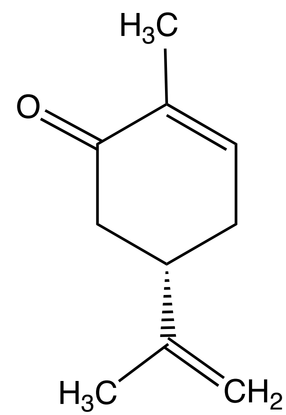
A 1:1 mixture of enantiomers is known as a racemic mixture or racemate. A racemate is optically inactive (rotations of each enantiomer cancel out).

Enantiomers differ in their interactions with other chiral molecules – particularly important in biological systems



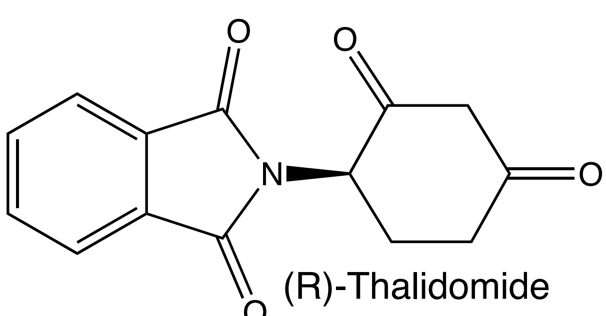
(-)-Carvone

(spearmint)

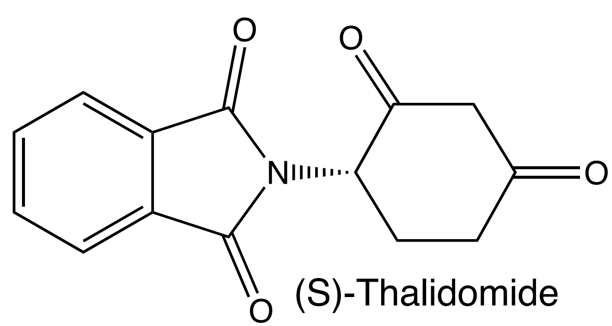


(+)-Carvone

(caraway)

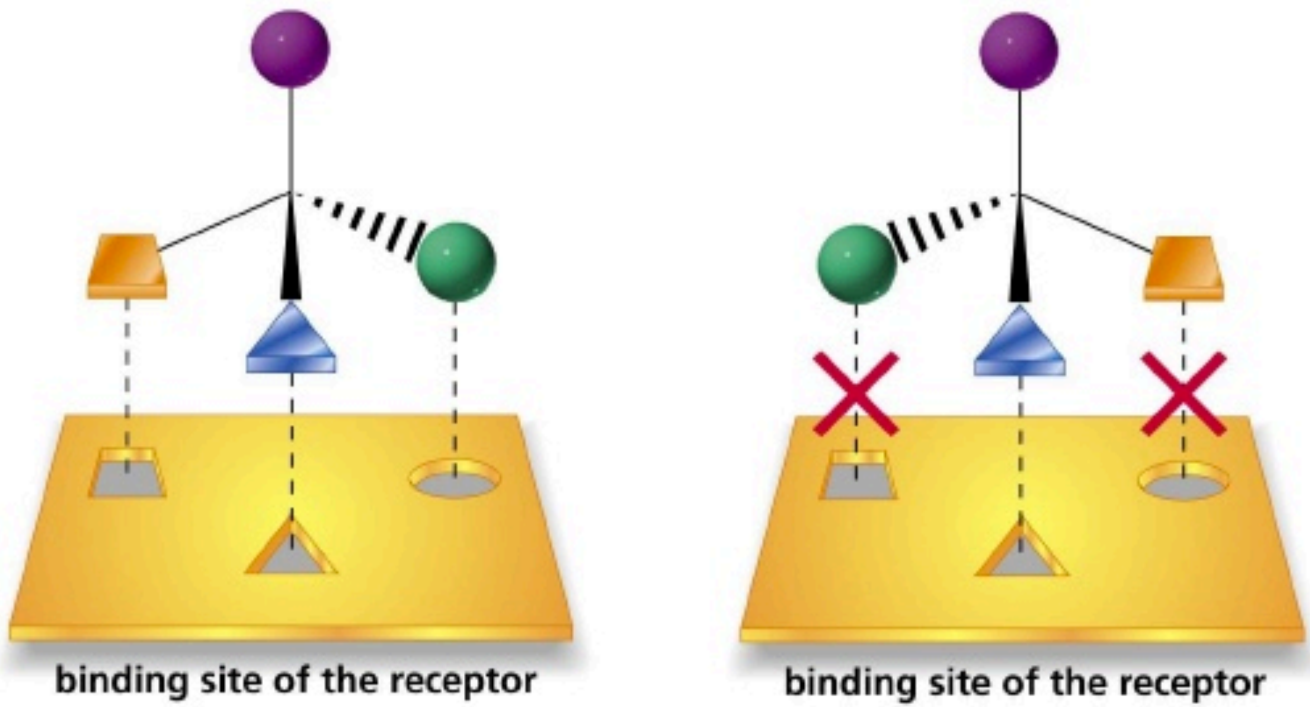


(R)-Thalidomide
(sedative)



(S)-Thalidomide
(teratogen)

Enzymes, which themselves are always chiral, often distinguish between the two enantiomers of a chiral substrate. Chiral objects (glove) have different interactions with the two enantiomers of other chiral objects (left and right hand).
Analogy: A left hand will not fit into a right-handed glove



Nomenclature: How can we differentiate between enantiomers?

Bromochlorofluoromethane – This name conveys information about the atom connectivity, but does not tell us the stereochemistry.

Assignment of configuration

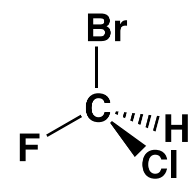
1. Assign priorities in order of decreasing atomic number of the immediately attached atom to the asymmetric carbon ie. highest atomic number is ranked first, lowest (often H) is fourth.

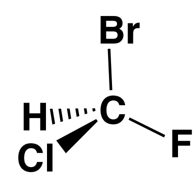
2. If a decision can't be reached by ranking the first atoms consider second, third and fourth atoms outwards until a difference is found.

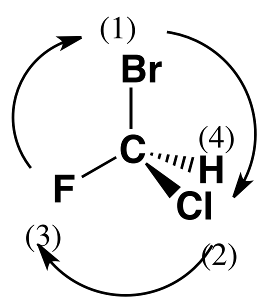
3. Orient the lowest ranked substituent away from you.

4. If the order of 1, 2 and 3 is clockwise then it is ***R***,
if the order is anticlockwise then it is ***S***.

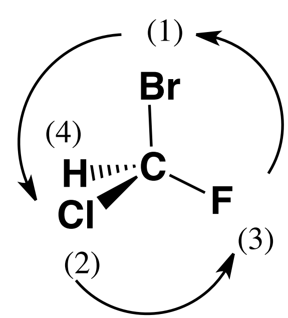
Assigning configuration to bromochlorofluoromethane





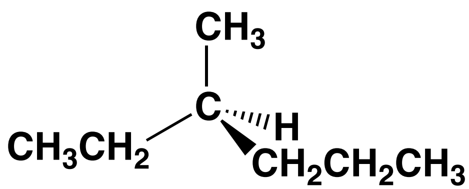


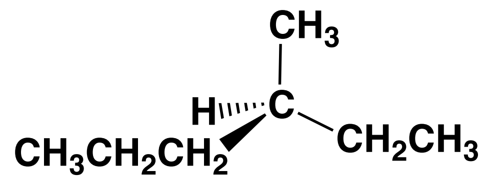
(*R*)-bromochlorofluoromethane

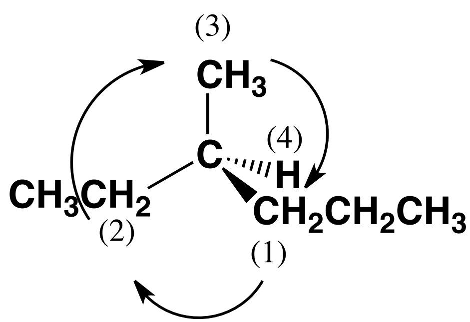


(*S*)-bromochlorofluoromethane

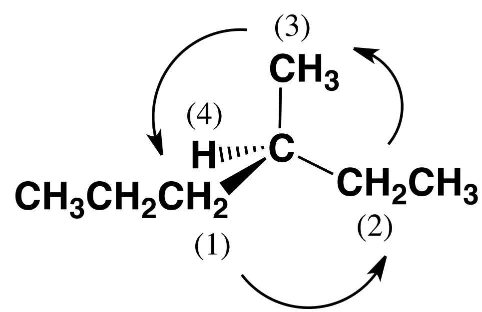
Assigning configuration to 3-methylhexane





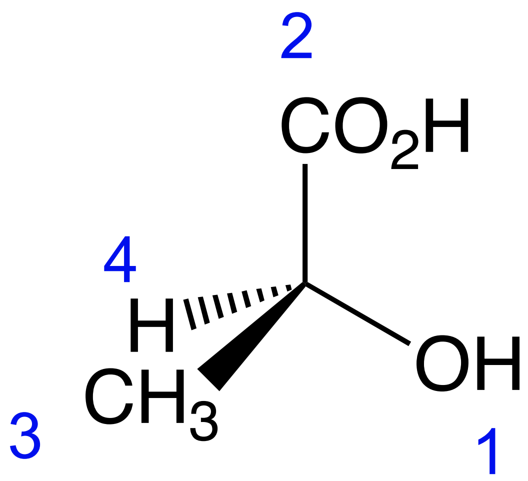


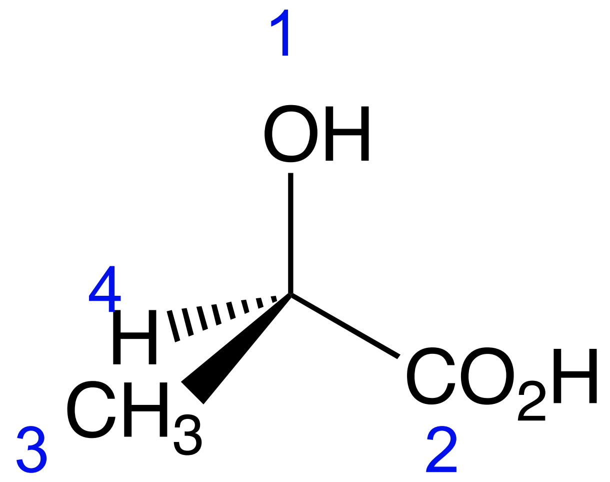
(*R*)-3-methylhexane



(*S*)-3-methylhexane

Lactic acid





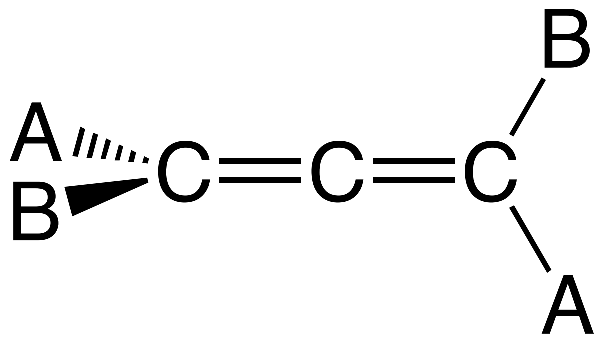
S-Lactic Acid
(L-(+)-lactic acid)

R-Lactic Acid
(D-(-)-lactic acid)

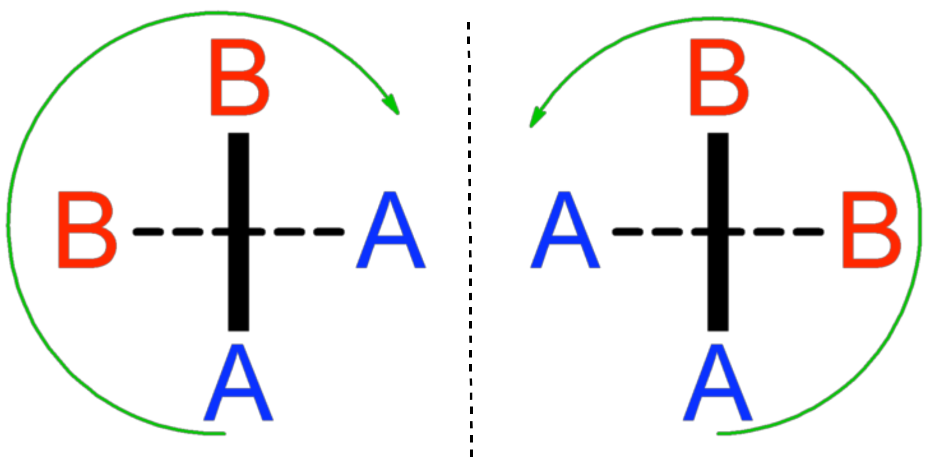
The *S* configuration is the one of biological importance.

Axial Chirality

Allenes

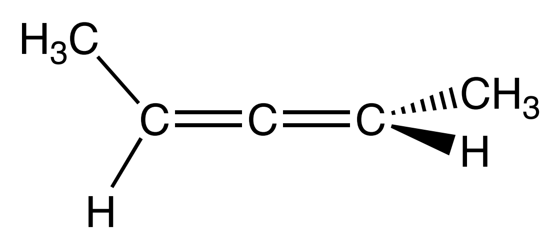


Where A has higher priority than B

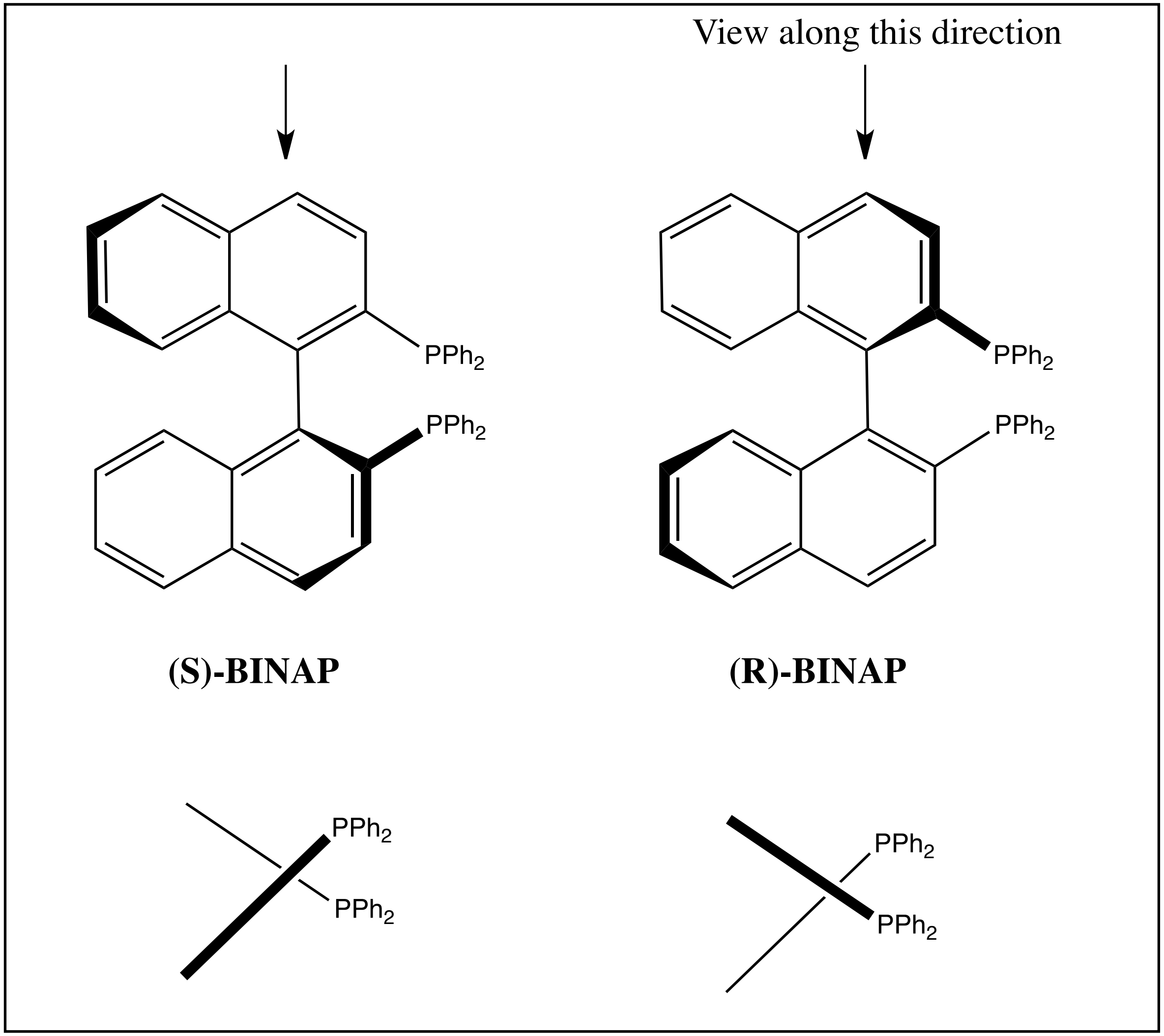


R *S*

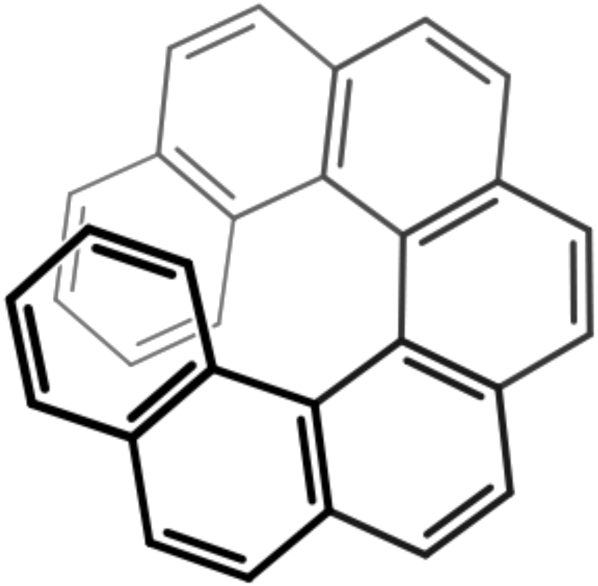
Name this structure



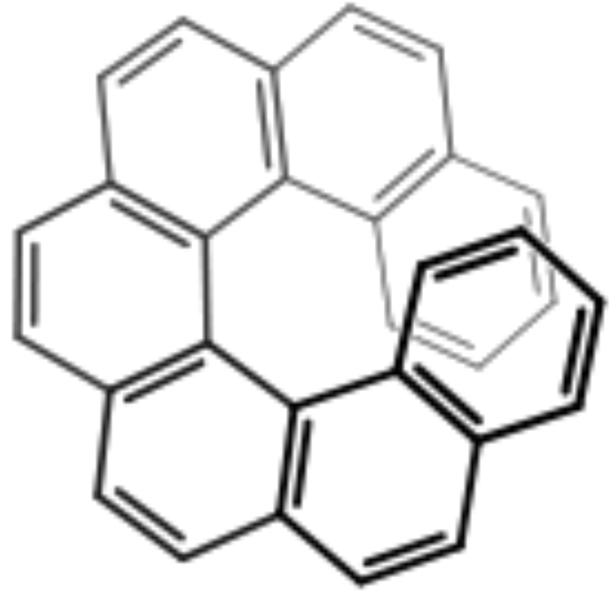
Axial Chirality



Axial Chirality

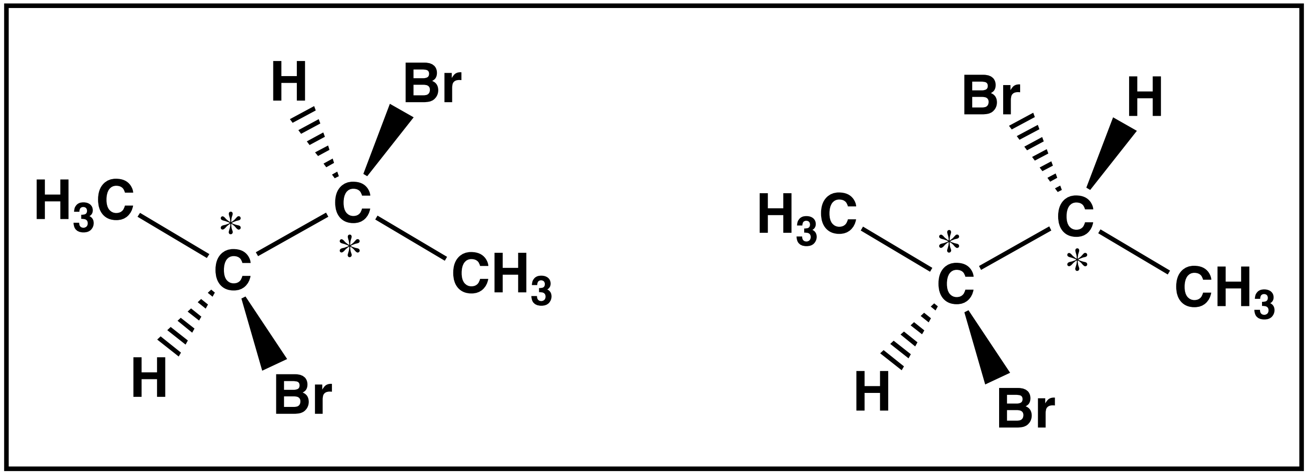


M Helicity



P Helicity

Diastereoisomers (stereoisomers which are not mirror images)

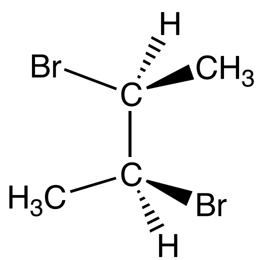


Diastereoisomers of 2,3-dibromobutane

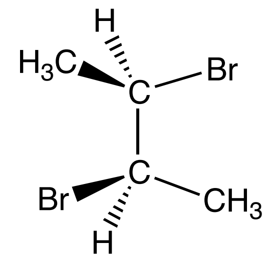
Configurational diastereoisomers

- arise when there is more than one asymmetric centre in the molecule.

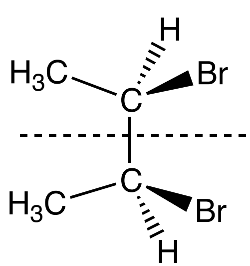
Diastereoisomers of 2,3-dibromobutane



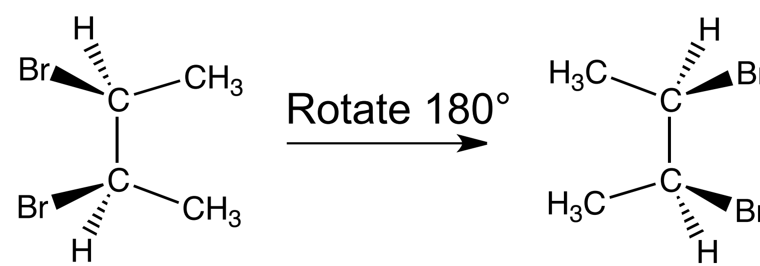
(2*S*,3*S*)-2,3-dibromobutane



(2*R*,3*R*)-2,3-dibromobutane



(2*R*,3*S*)-2,3-dibromobutane

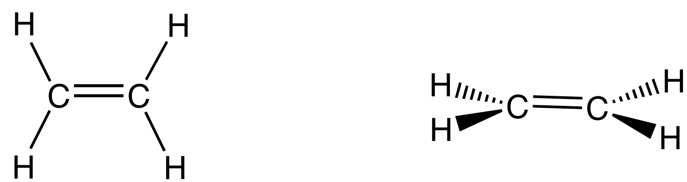


Meso-2,3-dibromobutane

Meso compound - A compound with more than one asymmetric centre, which is superimposable on its mirror image

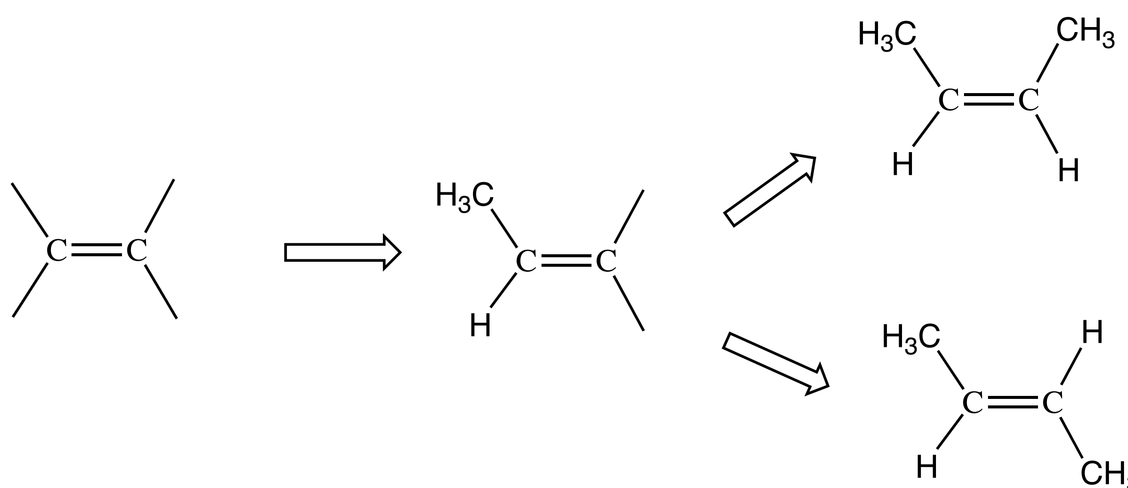
Stereoisomerism in Alkenes

Geometry of Ethene



Each carbon has a trigonal-planar geometry
The two carbons of the C=C and the four bonds to these are co-planar.
IMPT: C=C cannot rotate

Consider structure of 2-butene $CH_3CH=CHCH_3$



These cannot interconvert !

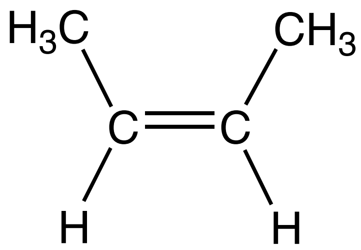
These two alkenes have the same connectivity of atoms, but have different 3-D arrangements of these atoms and are examples of stereoisomers. Stereoisomers which arise due to hindered rotation of bonds are known as *geometrical isomers*.

Alkenes which have two different groups at either end of a C=C double bond display geometrical isomerism.

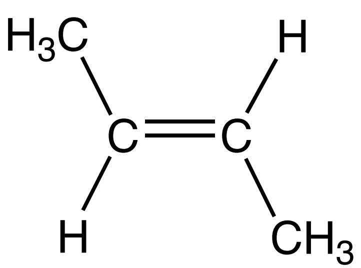
$A \neq B$ and $D \neq E$

Nomenclature for alkene geometrical isomers

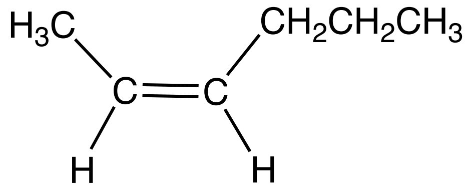
For simple, unsubstituted internal alkenes, e.g 2-butene, the *cis* – *trans* nomenclature was developed early on.



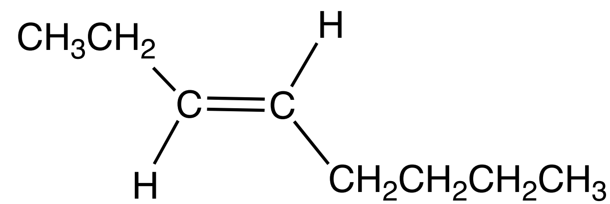
If the carbon substituents are on the same side of the C=C double bond, the geometry is designated as *cis.*
This compound is called *cis*-2-butene



If the carbon substituents are on the opposite side of the C=C double bond, the geometry is designated as *trans.*
This compound is called *trans*-2-butene

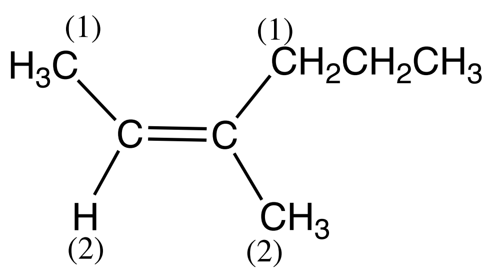


cis-hex-2-ene

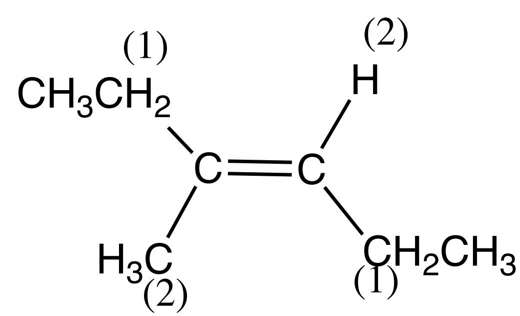


trans-oct-3-ene

The early *cis*-*trans* nomenclature does not work well for all alkenes, and has been replaced by the more general E / Z nomenclature:



Z-3-methyl-hex-2-ene



E-3-methyl-hex-3-ene

Youtube video:
http://www.youtube.com/watch?v=h_DROS_NNx4

Problems

What is chirality?

1. Identify five common objects that are <u>chiral</u>.

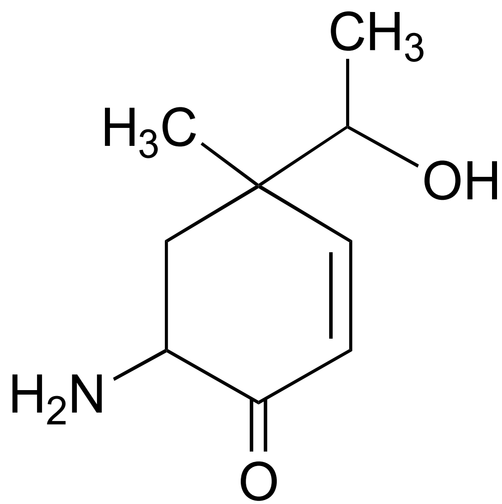
2. Identify five common objects that are <u>achiral</u>.

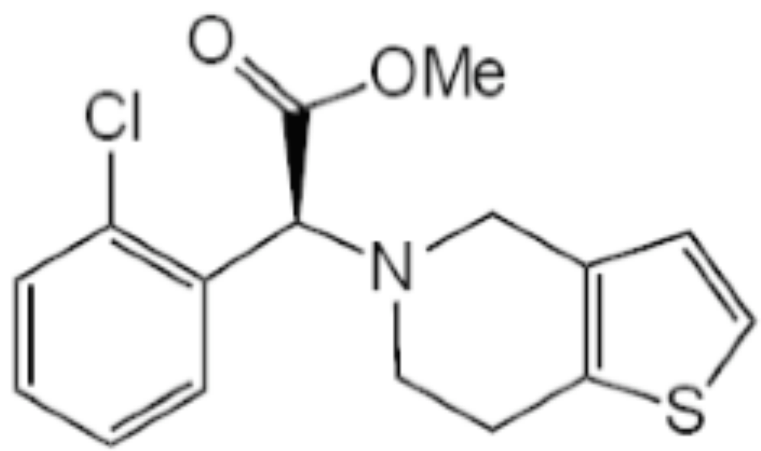
3. Are there simple ways to decide if an object is chiral?

1. Chiral molecules are said to be optically active. What does this mean?

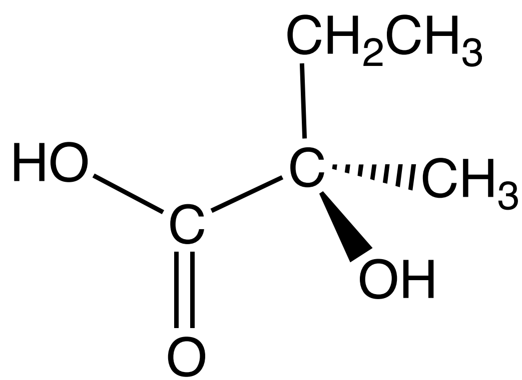
2. In organic chemistry what is a asymmetric (chiral) centre?

3. Place an asterisk (*) by each of the asymmetric (stereogenic) centres contained in the molecules shown below:





4. Indicate the absolute (*R*, *S*) configuration of the following molecule.



5 (a) Using the model-building kits provided, construct mirror images of 2-butanol ($CH_3CH(OH)CH_2CH_3$)

(b) Using the models determine whether these mirror images are superimposable on the original molecules.

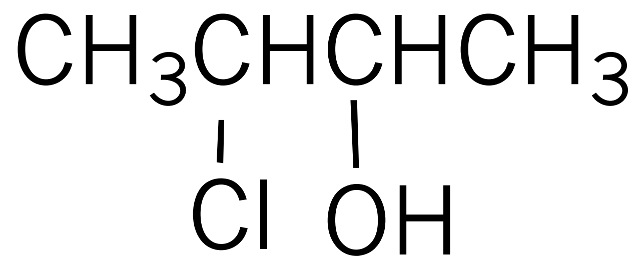
Are these molecules optically active?

(c) Reproduce these 3-D models on paper, labeling *R* or *S*.

[Draw tetrahedral 3-dimensional diagrams for all models, using wedges for 'out of the plane' and dotted (dashed) lines for ‘into the plane’.]

6 (a) What happens when we have more than one asymmetric centre in a molecule?

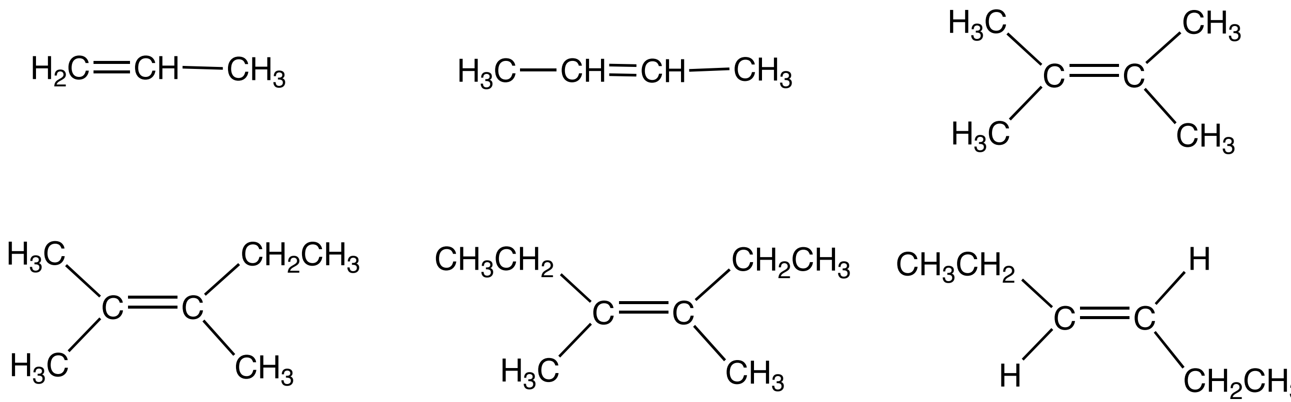
How many asymmetric atoms are in the following molecule?



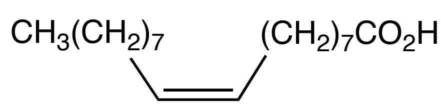
(b) How many stereoisomers do you expect for this compound?
(Hint: 2^n isomers are possible, where n is the number of asymmetric atoms).

Draw and label all the stereoisomers for the above compound.

8. Which of the following alkenes exhibits geometrical isomerism? Where relevant assign the geometry as *cis* or *trans*.



Oleic acid



Elaidic acid