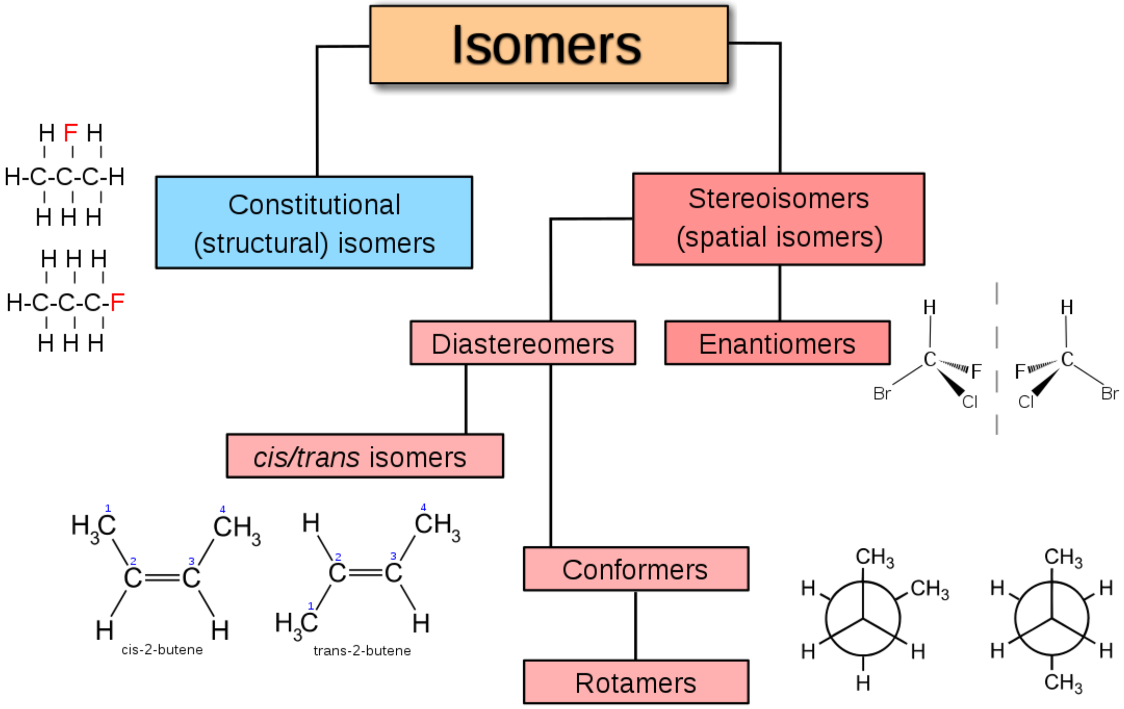
Isomers in organic compounds

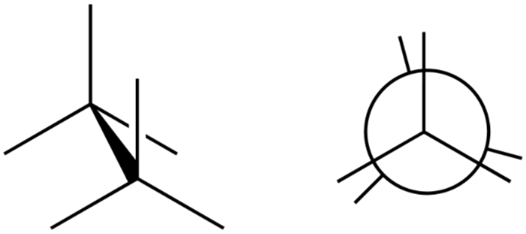
Link

Isomers are compounds that have the same molecular formula. Compounds with different molecular formulars NEVER be isomers. Isomers are of different types as shown in the diagram below:



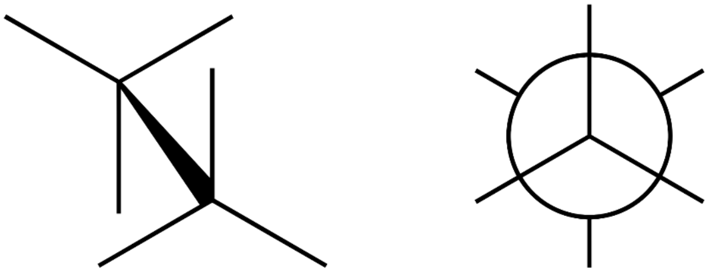
I- Conformers and Rotamers:

Rotamers are one type of conformers. They are related by rotation about one single bond (σ bond). Alkanes have large number of conformers and rotamers because all bonds are sigma bonds, where the rotation is likely. Of course, rotation about double bond is severely restricted. The three-dimensional structures produced upon rotation about sigma bonds are called conformational isomers (or conformers). Eclipsed and staggered forms are rotamors. They are conformers produced from rotation around the sigma bond. They represent two extremes. In the eclipsed conformation the C–H bonds on adjacent carbon atoms are parallel to each other and are in the same plane.



eclipsed conformer

The other is the staggered conformation where C–H bonds on adjacent carbon atoms are as far from one another as possible. Here, electrostatic repulsions are minimum which makes staggered conformations the most stable.

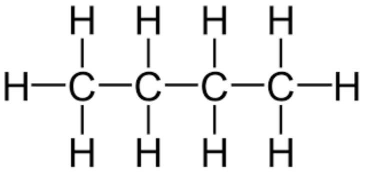
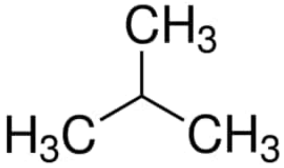


staggered conformer

[Staggered/Eclipsed conformers-youtube]

II- Structural isomers: (constitutional isomers)

Compounds that differ in the connectivity of the atoms. For example, both butane and 2-methylpropane are different compounds that have the same chemical formula, C_4H_{10}. So, structural isomers are different compounds of the same chemical formula.

	
butane	2-methylpropane

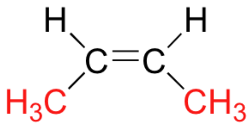
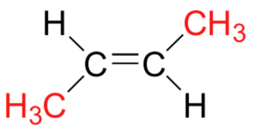
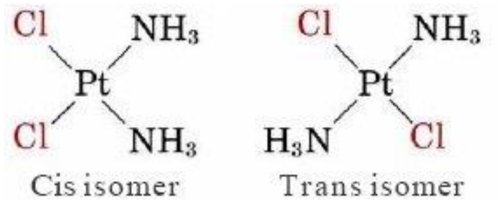
We saw some other examples earlier in the course material.

III- Stereoisomers.

They are compounds with identical molecular formulas and arrangements of atoms (same connectivity), but they differ only in the spatial orientation of the groups in the molecule. Actually, they are isomers of the same molecule. They are of two types:

A) Geometric isomers:

They differ in the spatial arrangement of substituents. The arrangement would be cis (or Z) or trans (or E). Geometric isomers are diastereomers. Diastereomers are compounds which have the same molecular formula and sequence of bonded elements but which are nonsuperimposable, and non-mirror images.

 *cis*-2-butene	 *trans*-2-butene	 Cis isomer Trans isomer	
$Z - Isomer$	$E - Isomer$	$Z - Isomer$	$E - Isomer$

In German language:

Zusammen means ‘together’ and **E**ntgegen means ‘opposite’.

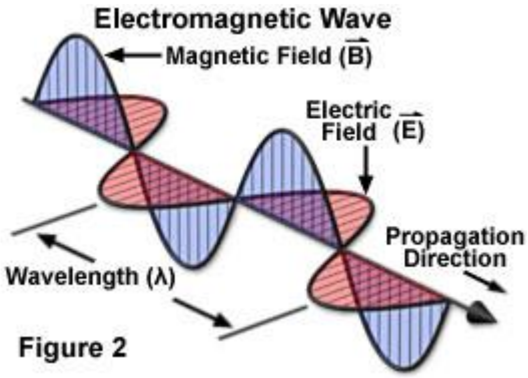
B) Optical isomers

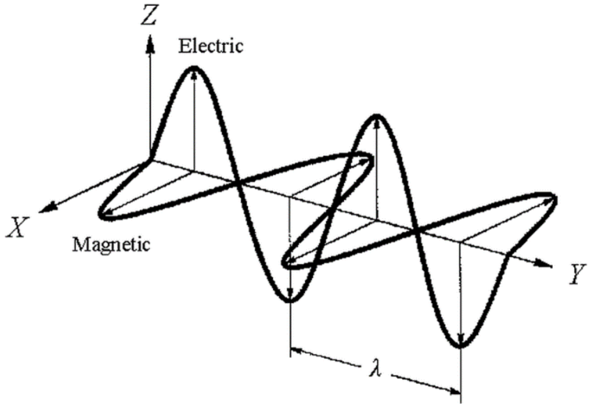
These isomers are called optical isomers because they affect the plane polarized light differently. They rotate the plane polarized light in two opposite directions.

Plane Polarized Light: Link to youtube Link Chirality Plane polarized light

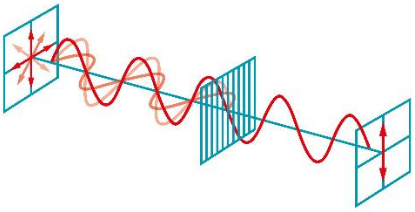
What is plane polarized light?

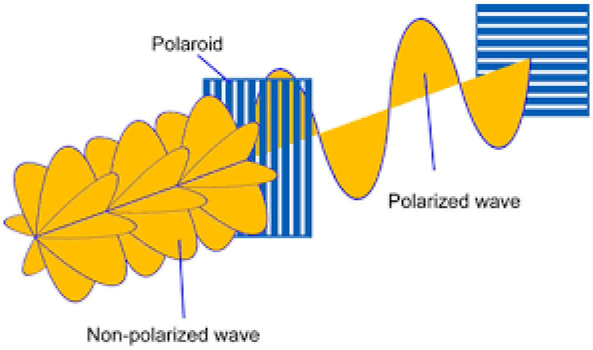
The electromagnetic Radiation has two components, electrical and magnetic. They produce electric and magnetic fields while the light is propagating. The propagation of light has a wave style. The electric and magnetic fields are perpendicular to each other, and are perpendicular to the direction of propagation.





While propagation, the light is rotating, keeping the electric and magnetic components perpendicular to each other at all instances. The electric component is the one of importance to us. When light is passed through a polarizer, it is allowed to pass in one direction only. As seen the figure below. This light is called plane polarized light.





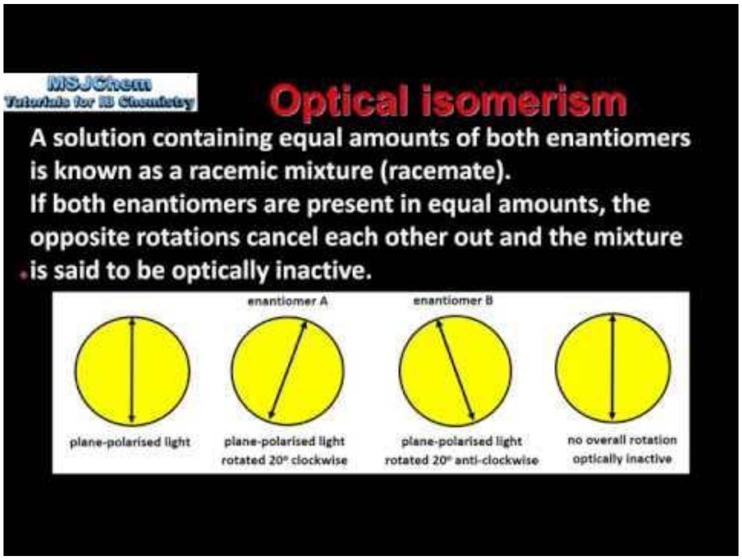
Obviously, the plane polarized light is vibrating in one direction only.

Optical activity is defined as the ability to rotate the plane polarized light.

Organic compounds that are optically active have the ability to rotate the plane polarized light in either of the directions, clockwise or counterclockwise.

Clockwise rotation is called dextrorotatory and is indicated in the compound's name by positive sign, (+), or (D-). Counterclockwise rotation is called levorotatory, designated by negative sign, (–) or (L-).

Optically inactive compound produces no net rotation. This happens when the concentrations of both enantiomers (the dextrorotatory and the levorotatory) of the compound are equal. A solution that contains equal concentrations of each enantiomer is called a racemic mixture.

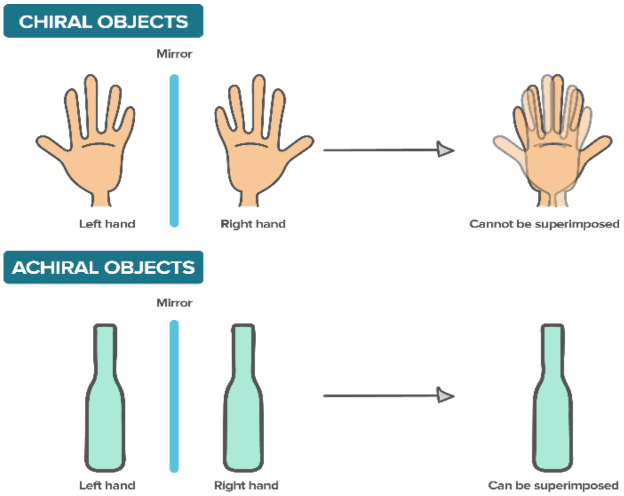


Optical isomerism

A solution containing equal amounts of both enantiomers is known as a racemic mixture (racemate).
If both enantiomers are present in equal amounts, the opposite rotations cancel each other out and the mixture is said to be optically inactive.

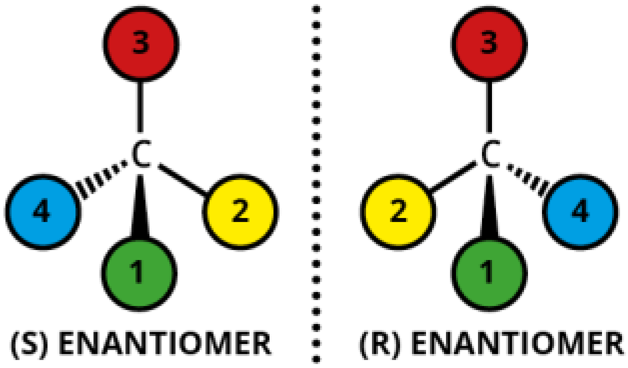
Enantiomers:

Enantiomers are compounds that have exactly the same connectivity, and are mirror images of each other. Enantiomers are not superimposable.

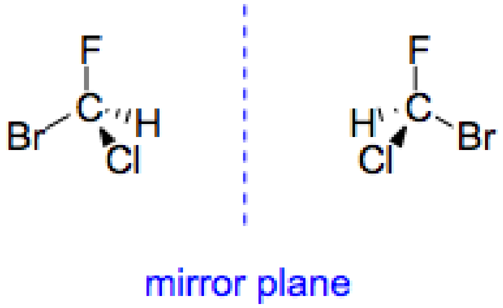


Compounds that are optically active have chiral centers. They are called chiral compounds.

Chiral compounds have chiral carbon. Chiral carbon is a carbon that is connected to four different groups (sp^3, tetrahedral arrangement). Optical isomers are only obtained in compounds that have chiral carbons. Carbons that are connected to four groups with two or more of them similar are not chiral carbons, consequently, the corresponding compound is not optically active. Carbons that have two hydrogens attached to it are never chiral centers. On the other hand, carbons that have four different atoms attached, say a carbon, hydrogen, oxygen, and nitrogen, are always chiral centers. The figure below shows a representation of two enantiomers.



They are mirror images, superimposable, have chiral centers, so, they are optical isomers.



A chiral carbon usually is <u>not</u> a branched group, or on the end of a chain, so you can eliminate these carbon atoms to be chiral carbons. Also, the hybridization of the chiral carbon is sp^3. Therefore, sp and sp^2 carbons in a chemical structure are eliminated from being chiral carbons.

(S) and (R) Enantiomers:

There are four steps to assign R or S to an optically active molecule:-

1. Assign priority to the groups attached to the chiral carbon. The priority based on their atomic/molar masses. The higher the atomic/molar mass, the higher priority, i.e, number (1) priority is given.

2. Point the lowest priority group away from you *(the dashed wedge in the example below, the hydrogen atom)*.

3. Number the remaining three groups according to priority: 1 = highest priority and 3 = lowest priority.

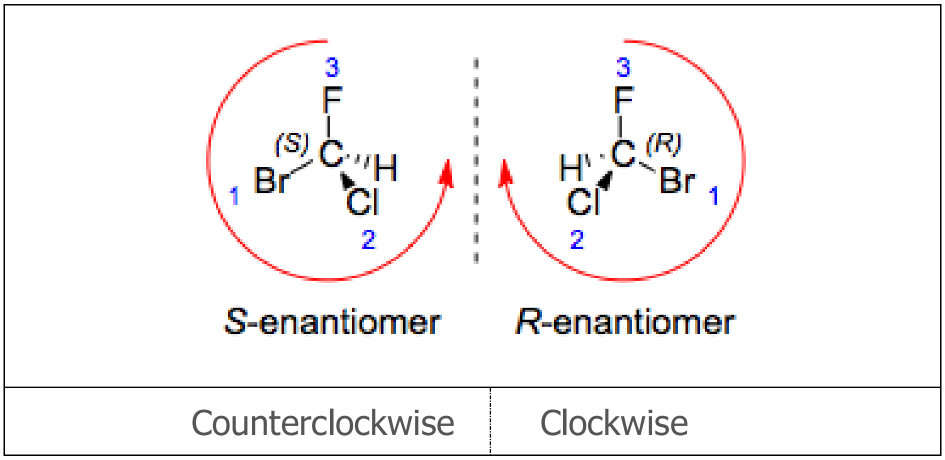
4. Draw an arrow circle beginning at the group numbered 1 and ends with at the group numbered 3.

If the arrow points clockwise, the compound is *R*. If the arrow points in a counter-clockwise the compound is *S*.

Example:

In the example below, there are four different groups (H, F, Cl, Br) attached to the carbon, so, this carbon is a chiral center. Hydrogen atom has the lowest atomic mass, so it has the lowest priority, so, pointed away. We left with Br, Cl and F. They are numbered as (1) for bromine, (2) for chlorine, and (3) for fluorine. (atomic mass order; highest to lowest).

When we draw the arrows, we can see that the compound on the left, the arrow is pointing counterclockwise, is *S* (from the Latin 'sinister', meaning 'left') and that on the right, the arrow is pointing clockwise, is *R* (from the Latin 'rectus', meaning 'right'). This letter is added in front of the isomer's name in order to indicate the priority of the substituents on the chiral carbon.



R and S, and D and L:

There is NO relationship between chiral compound's R/S designation and the direction of rotation of the plane polarized light, D/L designation. For example, S enantiomer would be L or D rotatory.

Compounds with more than one chiral carbon: *(Link 1 Examples)*

I) Optical Activity: A Link to optical isomers (more examples)

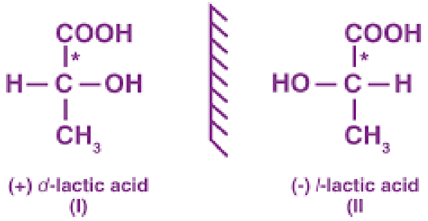
If all of the chiral centers are of opposite R/S configuration between two stereoisomers, they are enantiomers. If at least one, but not all of the chiral centers are opposite between two stereoisomers, they are diastereomers. Diastereomers are non-mirror images, and are non-superimposable. Also *remember, equal concentrations of the enentiomers make the mixture optically inactive.*

II) Number of optical isomers:

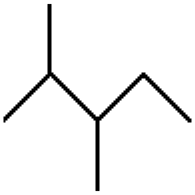
The maximum number of optical isomers of a compound is determined by calculating the number of chiral centers in it. The maximum number of optical isomers is given by the formula 2^n, where n is the number of chiral centers. Compounds with symmetry element (like plane of symmetry and inversion center) are optically inactive. Compounds that have symmetry elements are meso isomers. Meso isomers do not have enentiomers. (see meso isomers). A meso compound contains plane of symmetry that makes it superimposable on its mirror image. Meso compound is optically inactive. Meso compound is achiral compound that has chiral centers. Meso compouds are achiral diastereomers that contain chiral centers. presence of chiral centers in them does not make them optically active because of the presence of plane of symmetry.

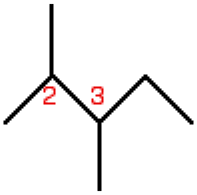
Structural relations between Enantiomers, diastereomers and meso forms are illustrated in this link.

Examples: Number of isomers in lactic acid: $(C_3H_6O_3)$

	One chiral center, n=1 Number of optical isomers = $2^n = 2$

Example: 2,3-dimethyl pentane



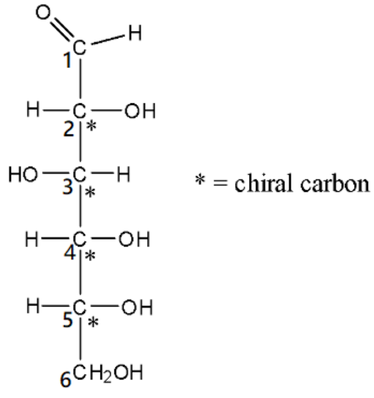


Carbon 2: Two methyl groups (similar) are attached, so, it is not chiral center.

Carbon 3: Four different groups are attached. Hydrogen, ethyl, methyl, isopropyl. All are different, so, this carbon is chiral carbon.

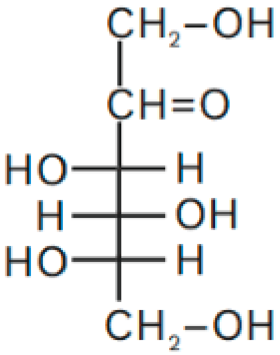
Maximum number of optical isomers = $2^1 = 2$.

Example: D-Glucose

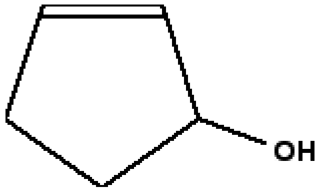
 D-Glucose	Maximum number of possible optical isomers = $2^4 = 16$

A compound that has 3 chiral atoms. The maximum number of possible optical isomers it can have is $2^3=8$.

Example: Fructose, the possible optical isomers are: $2^3=8$



Example: Cyclopent-2-ene-ol

	‣ The carbons of the double bond are attached to 3 groups ‣ The carbons that are singly bonded each has two hydrogens, so they are not chiral carbons. ‣ The carbon bonded to the (-OH) has 4 different groups around. So, it is a chiral carbon. ‣ Number of optical isomers=2^1=2.

Importance of Chirality and optical isomerism:

Chirality is very important in biological systems. Actually, 19 out of 20 of the amino acids that make up our bodies are chiral. Proteins are made of amino acids, so they are also chiral. The consequence of that these proteins specifically interact with molecules containing chiral carbons. So, protein may recognize one enantiomer of an organic molecule as a drug, and may have little or absolutely no effect on the other.

Utube: Chirality/optical isomerism (enentiomers) and drug action

A racemic mixture of a drug may have unwanted side effects due to the presence of both left and right handed enantiomers. The drug thalidomide was racemic and each enantiomer had different effects on pregnant women; the right handed drug alleviated morning sickness, the left handed drug caused birth defects.

Utube: shows models of two enantiomers.

Utube: Examples on chiral carbons/Arabic-very good, it explains optical isomers with examples.

importance of chirality in biochemistry

importance of chirality in drugs and drug action

importance of chirality in medicine

The **specific rotation** is the amount (in degrees) by which the plane of polarized light is rotated when light is passed through a solution containing 1.0 g of solute per 1.0 mL of solvent in a tube 10.0 cm long.