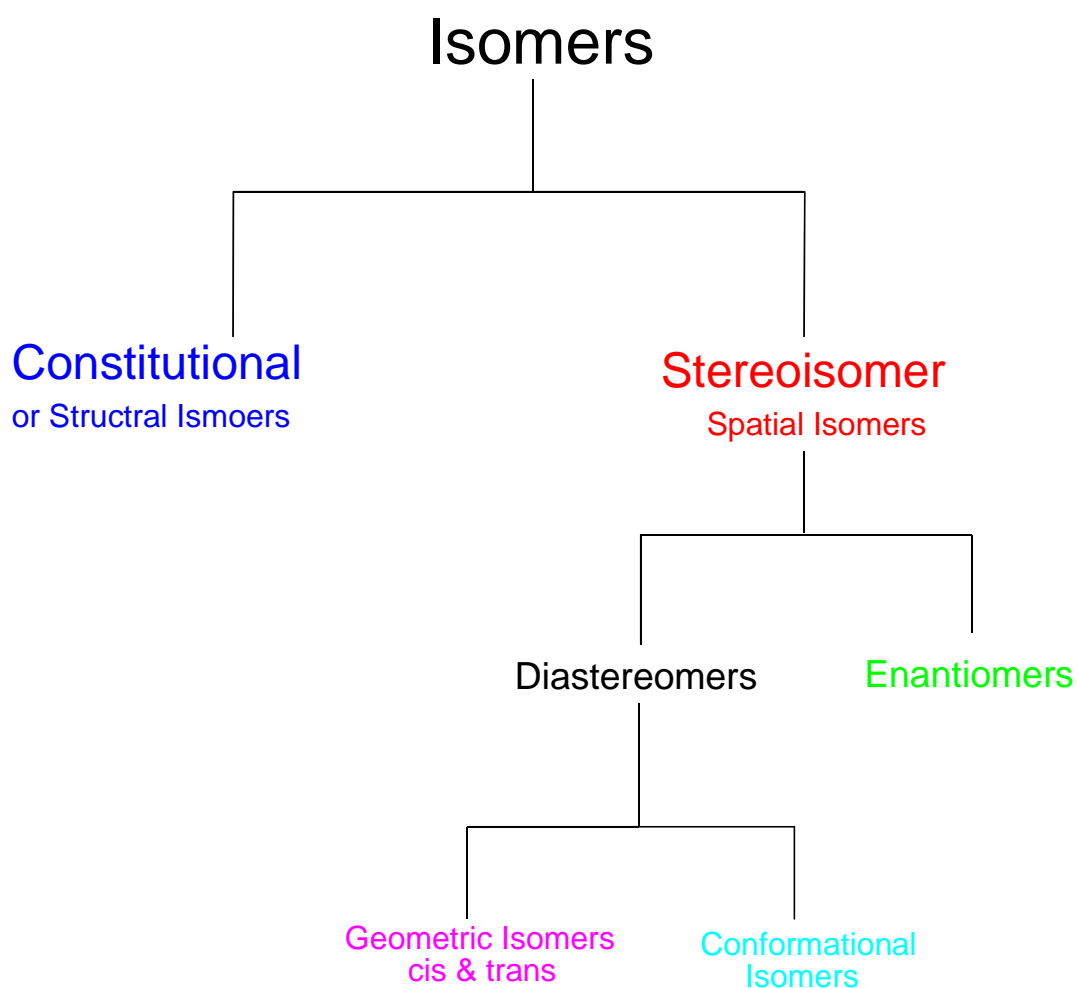


Stereochemistry

Definition of Isomers

If two or more different compounds have the same molecular formula we call them isomers. This is the general definition of isomer.

There are two major classes (types) of isomers, and under these major classes there are further classifications of isomers as in **Fig 1**.

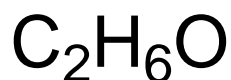


Now let us look individually at the different types of isomer and see some examples for each type.

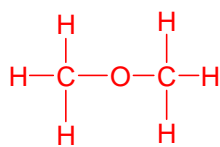
Constitutional Isomers (structural isomers)

Different compounds have the same molecular formula are called isomers and because they have different connectivity (which atom is bonded to which) we call them constitutional isomer or structural isomers.

Example 1

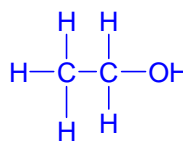


This compound has a molecular formula of $\text{C}_2\text{H}_6\text{O}$. Now we can draw two structures **1** & **2** for this molecular formula



1

Dimethylether



2

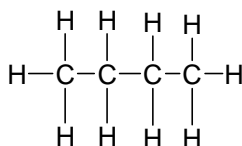
Methanol

Dimethyl ether **1** and Methanol **2** are constitutional isomers (or structural isomers) that because both of them have the same molecular formula $\text{C}_2\text{H}_6\text{O}$ but they have different structures due to the differing in the bond connectivity of atoms to each other. In **1** the bonds are **C-O-C** and each C atom has 3 H atoms. In structure **2** the bonds are **C-C-O** and each carbon has 2H and there is a one H bonded to O atom.

Example 2

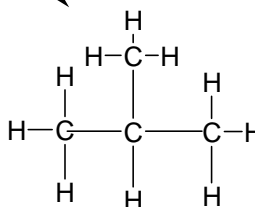
The molecular formula of butane is C_4H_{10} . How many structure we can draw for butane in order to obtain a saturated hydrocarbon with molecular formula C_4H_{10} ?

There are only two different structures you can draw for C_4H_{10} which are:



n-Butane

3



isoButane

4

Again

The two structures have the same molecular formula but they have different connectivity (which atom is bonded to which) so they are constitutional isomers.

Please note that **1** & **2** are completely two different compounds, they have different physical (b.p, mp, .etc.) and chemical properties. For example **2** is chemically active and it can react with carboxylic acid to form ester while **1** will not react.

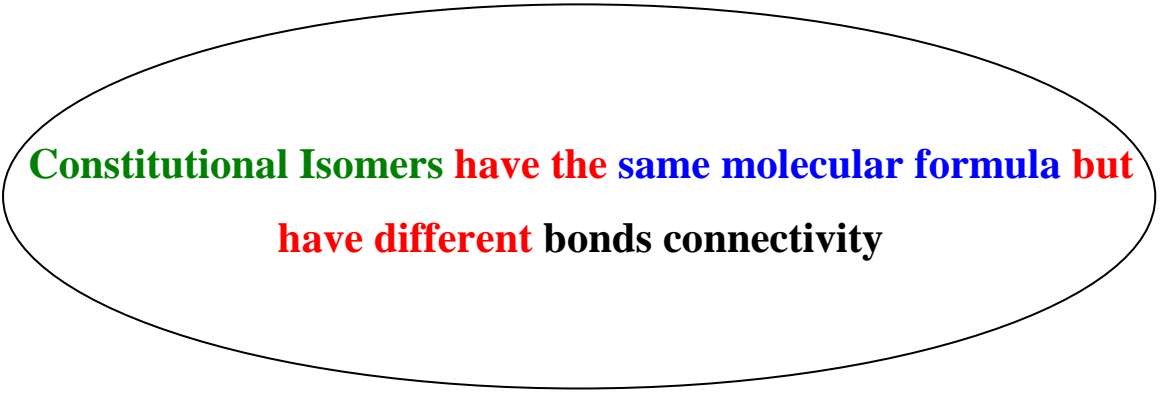
Now if I gave you models for both **1** & **2**, and ask you to convert **1** to **2** or *vies versa* You will never be able to do so without breaking the bonds and then re-build the molecules. The same thing is applicable in the case of structures **3** & **4**.

We will never be able to interconvert from one structural isomer to another by rotation about bonds. We only can do that *via* only breaking bonds.

Which type of isomers that can interconvert to another isomer *via* rotation about bonds?

If you do not know the answer, please go back to page 20 in the previous lecture notes and you will be able to answer this simple question.

In summary



Constitutional Isomers have the same molecular formula but have different bonds connectivity

*Is that clear? If yes go to the next section if not try to revise the subject again and
Please do not hesitate to ask me if you have any question*

2) Stereoisomers (spatial isomers)

Stereoisomers (spatial isomers) different compounds that have the same molecular formula and the same bonds connectivity **BUT** they have different arranging (orientation) in the space (in 3D).

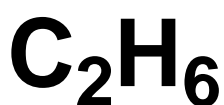
There are two types of stereoisomers which are:

- 1) **Conformational isomers**
- 2) **Configurational isomers**

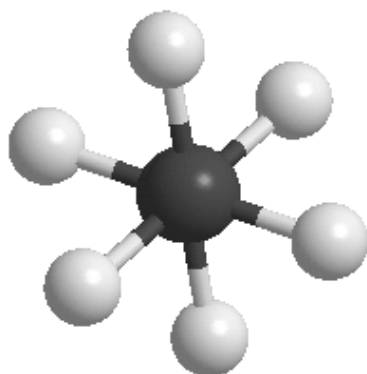
Both types are stereoisomers that mean both type have the same molecular formula and the same connectivity and both of them have different arrangement in the space!!!

So what is the difference between them?

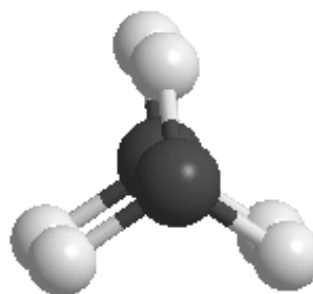
In the **Conformational isomers** we can convert from one isomer to other isomers by just rotation about C-C bonds. We have seen examples on this type of isomers on page 21 in the hand out you have been given before. Any way; Ethane is good and simple example on conformational isomers. Let us look at the most two important conformations of ethane **staggered** and **eclipsed** conformations.



Ethane



Staggered conformation

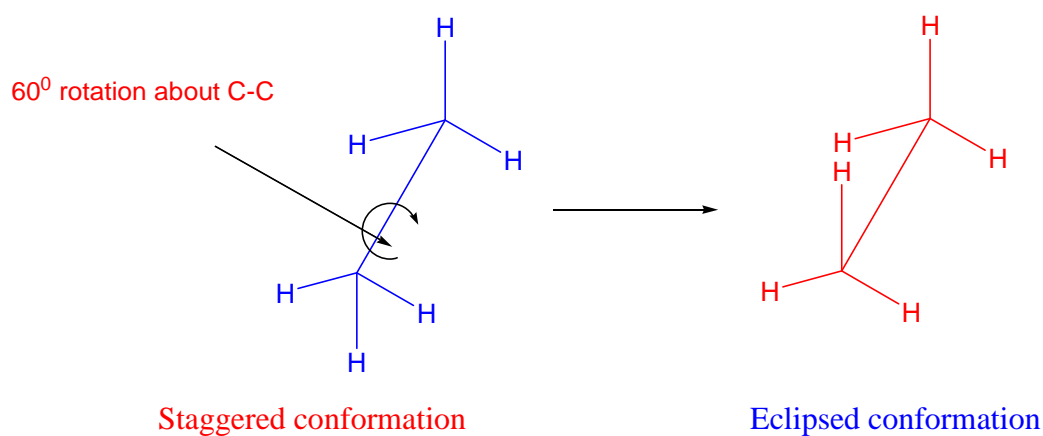


Eclipsed conformation

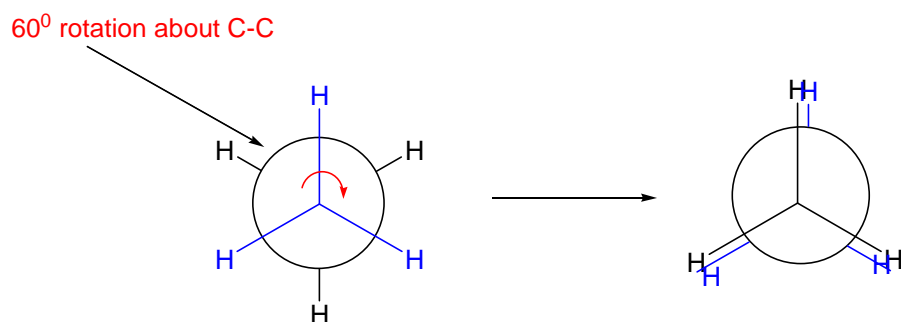
Now apply the definition of stereoisomers on the two isomers and see what you will find out?

The two structures have the same molecular formula that means they are **isomers**, they have the same bond connectivity that mean they are **stereoisomers**, they have different bonds arrangement in the space and so they may be either conformational isomers or configurational isomers. For sure now we can say they are conformational isomers

because we can convert from staggered conformation to the eclipsed one *via* rotation about the C-C bonds.



Another view



The conformations of propane, butane and all other conformations have the same property as the ethane so they all are conformational isomers.

[In summery](#)

Conformational isomers are **stereoisomers** that can be converted from one isomer to other isomers by rotation about C-C bond.

*Is that clear? If yes go to the next section if not try to revise the subject again and
Please do not hesitate to ask me if you have any question*

Now let us look at the second type of stereoisomers; **Configurational isomers**.

In the **Configurational isomers** we CAN NOT convert from one isomer to other isomers by rotation about bonds. We ONLY can convert from one isomer to other isomers *via* bond breaking.

There are two major types of **Configurational isomers** which are:

- 1) **Geometrical isomers**
- 2) **Optical isomers**

Geometrical isomers are isomers that have the same molecular formula, the same bond connectivity but the atoms are in different non-equivalent positions to one another. Geometrical isomers occur as a result of restricted rotation about a carbon-carbon bond. Restricted rotation about C-C bond can arise in two different situations:

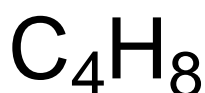
- (a) In a double bond
- (b) In a cyclic compound

That mean geometrical isomers can arise only if we have a double bonds and/or cyclic structures.

Why there is no rotation about C=C and in the C-C in cyclic compound?

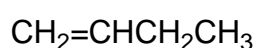
First let us answer the first part of the question.

Well to answer this question we need to know what is the type of hybridization in the C=C. Let us look at the following example to understand the full story.



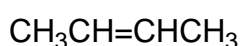
Butene

C₄H₈ is the molecular formula for the unsaturated hydrocarbon butene. We can draw butene in three different structures either as but-1-ene (**1**) or as but-2-ene (**2**) or as 2-methylpropene(**3**).



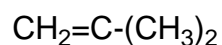
but-1-ene

1



but-2-ene

2



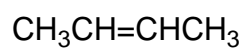
2-methylpropene

3

We will look only at the but-2-ene (**2**) as example of geometrical isomers.

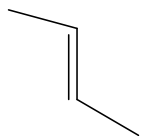
Can you tell what type of isomers is 1 & 2 & 3?

But-2-ene (**2**) can be drawn as the following two different structures **2-a** and **2-b**



but-2-ene

2



(*E*)-but-2-ene

trans-2-butene

2-a



(*Z*)-but-2-ene

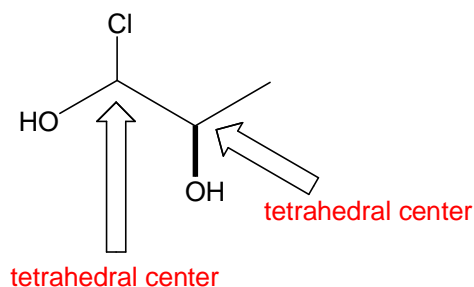
cis-2-butene

2-b

Optical Isomers

In the previous sections we have seen that there are two types of **configurational isomers**, and we have seen what **geometrical isomers** are. Now we will study the second type of configurational isomers which is the **optical isomers**.

Optical isomerism is one form of stereoisomerism. In optical isomerism; the isomerism present at a tetrahedral center. We mean by tetrahedral center that a C atom attached to four other atoms or group with single bonds (sp^3 hybridization).



Optical isomers are named like this because of their effect on plane polarised light (reacts with light) as we will see later.

There are two major types of optical isomers

1) **Enantiomers**

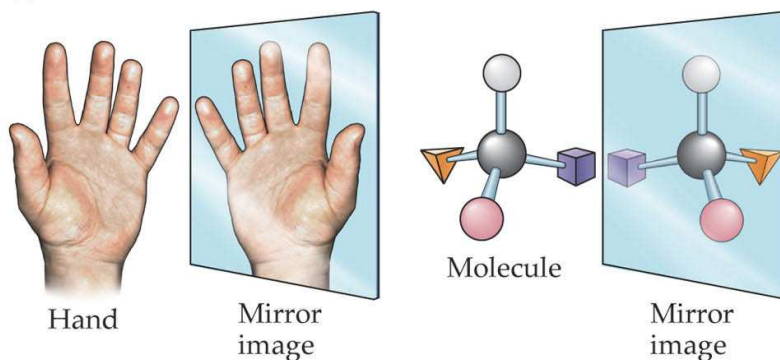
2) **Diastereomers**

However before we start studying the optical isomers in details we need to learn some new scientific definitions related to the stereochemistry.

CHIRALITY (any thing can be chiral or Achiral)

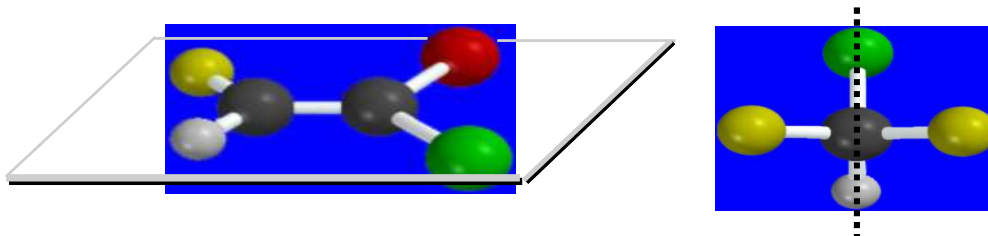
Chirality "handedness" (Greek cheir - the hand). **Chiral** objects (molecules) are these objects (molecules) which are not superimposable on (cannot be made to coincide with) their mirror image.

(a)



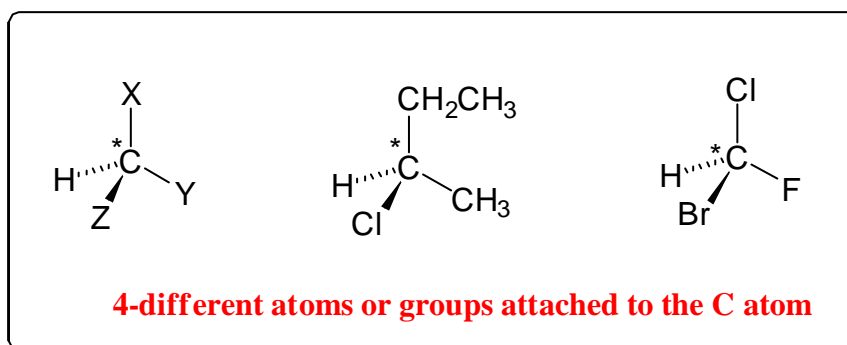
Superimposability The alignment of two images, one on top of the other.

An object will exhibit handedness if it has **no plane of symmetry**. **Plane of symmetry** is a position where an object can be cut in half and each half is identical. In other words **A plane of symmetry bisects a molecule into two mirror image halves**

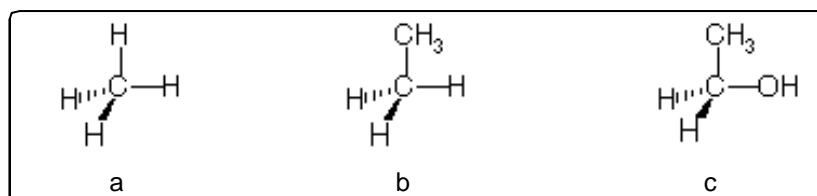


Chiral Carbon atom

The Chiral carbon is a carbon atom with 4 different atoms or groups attached directly to it. The hybridization on the chiral carbon must be sp^3 . **Examples:**



An sp^3 hybridized carbon with 1, 2, or 3 different atoms or groups attached can be superimposed on its mirror image and is, therefore *achiral*. None of the following three compounds (a, b, c) is chiral because they do not have 4 different atoms or groups on the sp^3 central C atom. Each of them are superimpose on its mirror image

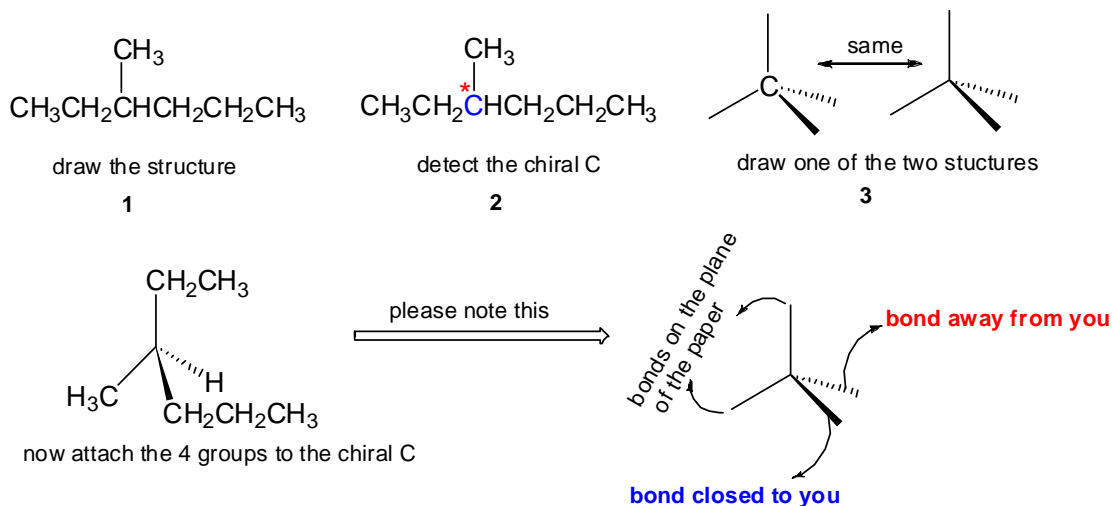


Prochiral molecule: Is any molecule that can be converted to chiral molecule in a single step (one step chemical reaction). We will see examples at the end of the chapter.

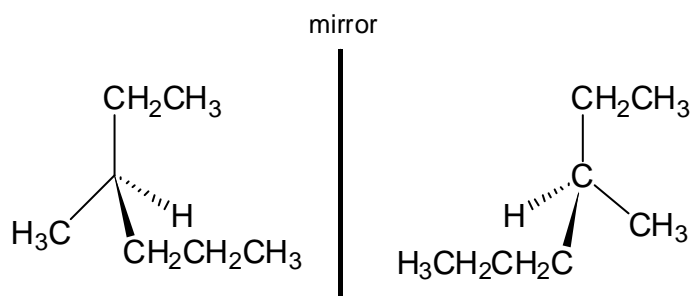
How you can draw chiral molecules?

Example:

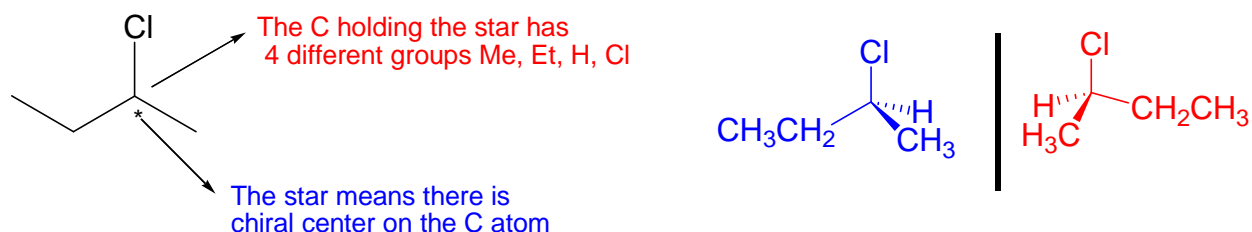
Draw the structure of 3-methylhexane.



Now it is important to learn how to draw the mirror image of the structure. All what you need to do is to imagine that you have a mirror and draw what you will see



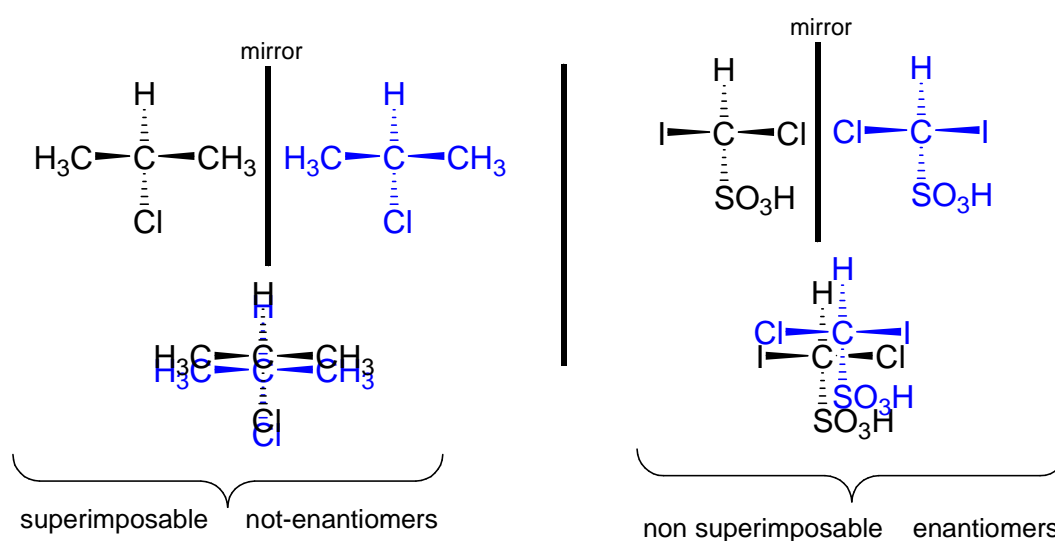
Example 2: 2-chlorobutane



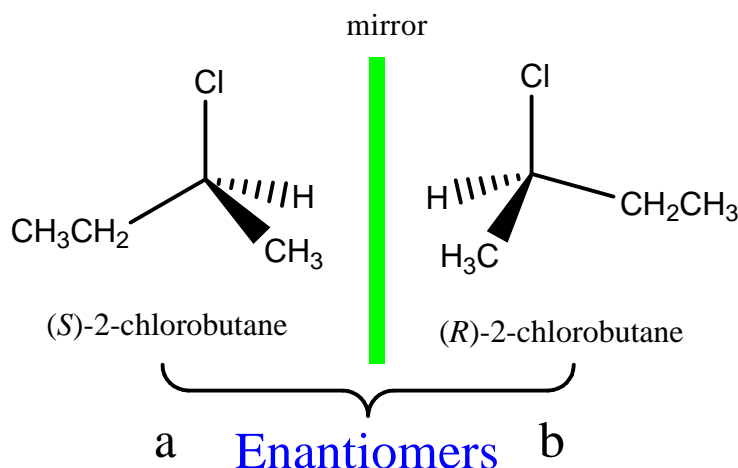
Enantiomers & Chirality

Molecules that are not superimposable on their mirror images are chiral. The existence of chirality is necessary and sufficient condition for the existence of enantiomers i.e. if a compound is chiral; it can exist as enantiomers and if it is Achiral it can not exist as enantiomers.

Enantiomers: Stereoisomers that are mirror image of each other and they are non-superimposable on their mirror images. In other words, if one isomer looked in a mirror, what it would see is the other one. The two isomers (the original one **a** and its mirror image **b**) have a different spatial arrangement, and so can't be superimposed on each other. All enantiomers are **chiral** (we will study them in more details soon)



Example:



In summary

Enantiomers: Stereoisomers that are mirror image of each other and they are non-superimposable on their mirror images.

Properties of Enantiomers

Physical properties: Physical properties including melting point, boiling point, color, hardness, density, etc. All physical properties of pair of enantiomers are the same except for one propriety which is **optical activity**. (we will study it soon)

Chemical properties:

Enantiomers have identical properties, except toward chiral substances where they will behave differently. That mean a pair of enantiomers react in different way with external chirl molecule (we will study it later in this chapter)

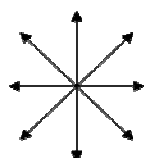
Optical Activity

As we just mentioned all of the properties of the compounds that constitute a pair of enantiomers are identical. Boiling points, Melting points, solubility in typical organic solvents are all the same for both compounds of a pair of enantiomers, however the major difference between two enantiomers is **how they interact with plane polarized light**.

Plane Polarized Light and Optical Activity

- 1) Light is composed of an oscillating electric and magnetic vector oriented at right angles to one another.
- 2) Under ordinary conditions, light rays emanating from a source have random orientations of their electromagnetic vectors.
- 3) If these vectors are forced into alignment in a single direction, the light is said to be plane polarized.

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.

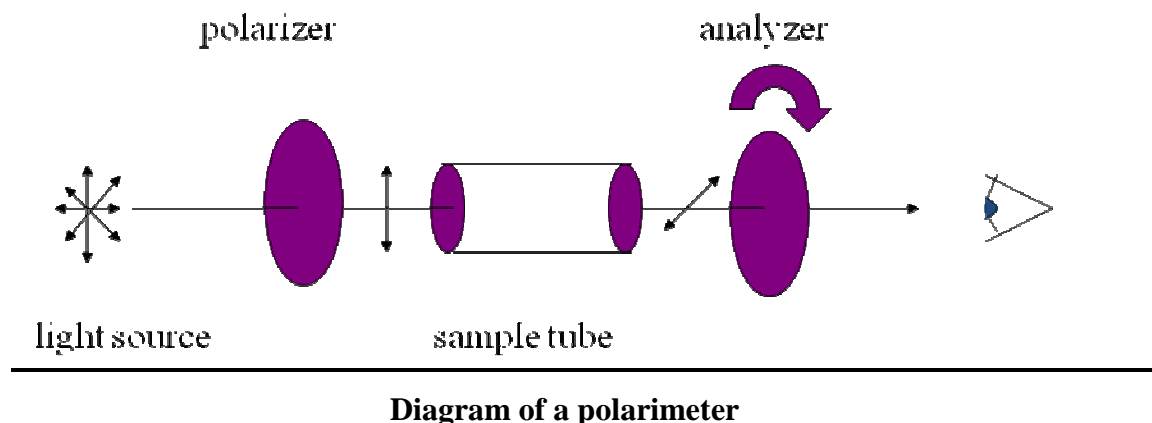


non-polarized



polarized

Polarimeter: an instrument used to measure optical activity (The amount of light rotation).



Optically active substance: A substance is optically active if it rotates the plane of polarized light.

Now when a polarized light pass through a sample in the polarimeter there are two possibility:

- 1) The polarized light will pass straight without any reflection, that means either the substance in the polarimeter is not chiral (we do not care about that).
OR

the substance in the polarimeter is an equal mixture of two enantiomers. In this cases we say the substance is optically inactive. Optically inactive substances are these substances which do not rotate the polarized light. An equal mixture of enantiomers is called *Racemic mixture*.

Racemic mixture (or modification): a mixture containing equal quantities of enantiomers (50:50) that mean (chiral molecule and its mirror image). The racemic mixture is optically inactive because one molecule will rotate the polarized light for example by 50° to the right, the other enantiomers will rotate the polarized light by 50° to the left so they cancel each other (the resultant is zero).

In summery

a sample that is optically inactive can be either an achiral substance or a racemic mixture

- 2) The second possibility when the polarized light of a polarimeter pass through a sample is the rotation of the polarized light either to the left or to the right depending on the nature of the substance. If such a rotation takes place we say the substance is optically active. For a substance to be optically active it must be chiral and it should be either single enantiomers or unequal mixture of enantiomers (one of them present in excess).

Dextrorotatory: when the plane of polarized light is rotated in a clockwise direction when viewed through a polarimeter (+)

Levorotatory: when the plane of polarized light is rotated in a counter-clockwise direction when viewed through a polarimeter (-)

The amount of rotation is called the **observed optical rotation, α** , this value is obtained directly from the polarimeter and it depends on:

1. **Concentration**
2. **length of the cell**
3. **the wavelength**
4. **solvent**
5. **temperature**

To compare samples a quantity called the **specific rotation, $[\alpha]$ is measured**

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, $\lambda = 589 \text{ m}\mu$).

The following formula is used to calculate the specific rotation.

$$[\alpha]_t^\lambda = \alpha / l \times c$$

$[\alpha]$ =specific rotation

t=temperature in $^{\circ}\text{C}$

λ =wavelength

α =observed rotation

l= length of sample container in decimeters

c=concentration in g/mL

Configuration and the R & S Convention

The arrangement of four different groups or atoms attached to C atom i.e. chiral molecule is called configuration of the molecule. Two enantiomers i.e. chiral molecule and its mirror image have different configuration that mean they have different arrangement in space or in three dimensional (3D). This difference is very important as one enantiomer can be used as medicine while the other enantiomer may be poisoning. It is important to learn how to determine the configuration of enantiomers and now we will see how to do so.

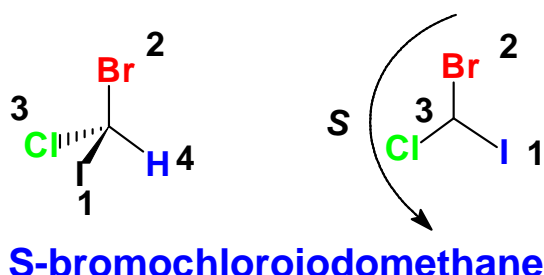
Look at the following example:

When you draw the strcture of 2-bromobutane you will find out that this is chiral molecule as it has a carbon attome with four different groups which are (H, Br, CH₃ and CH₃CH₂). This mean that we can draw two structures, simply the compound and its mirror image i.e. the enantiomers of 2-bromobutane. Ofcourse they have the same melting point , boiling point, solubility and even the same name but we have learend that they are different compounds. Becuase they are different compounds we need to determine the configuration of each single isomer.

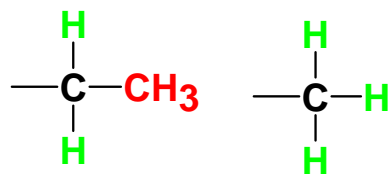
This part will be only described in the lectures and here I will only give the rules and example for practicing.

1. **Cahn – Ingold - Prelog sequence rules revisited**
 - a. **Rule 1:** Priority is established by the atomic numbers of the **attached** atoms. An atom of higher atomic number takes precedence over one of lower atomic number.

bromochloriodomethane

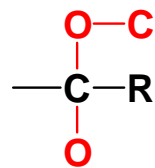
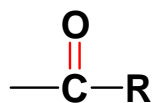
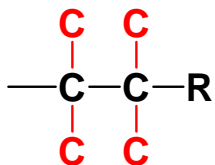
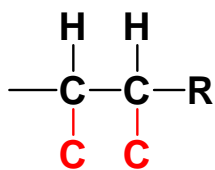
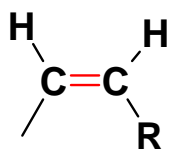


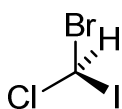
- b. **Rule 2:** if two directly attached atoms have the same rank,
rank the atoms along the substituent chain until a difference is found



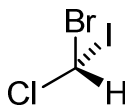
*higher
priority*

- c. **Rule 3:** Double and triple bonds are treated as if they were
saturated connections

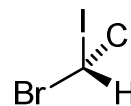




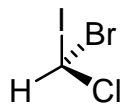
(S)-bromochloriodomethane



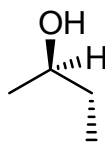
(R)-bromochloriodomethane



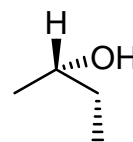
(R)-bromochloriodomethane



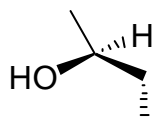
(R)-bromochloriodomethane



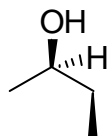
(R)-butan-2-ol



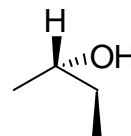
(S)-butan-2-ol



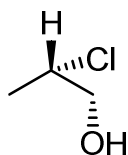
(S)-butan-2-ol



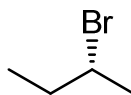
(R)-butan-2-ol



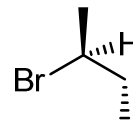
(S)-butan-2-ol



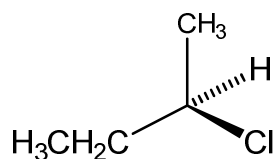
(S)-2-chloropropan-1-ol



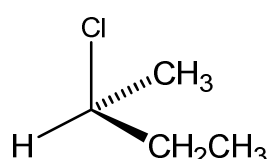
(R)-2-bromobutane



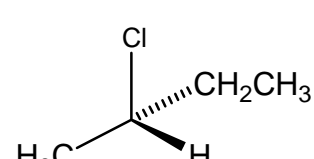
(S)-2-bromobutane



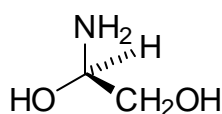
(R)-2-chlorobutane



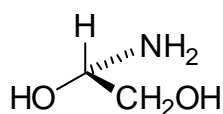
(S)-2-chlorobutane



(S)-2-chlorobutane



(R)-1-aminoethane-1,2-diol



(S)-1-aminoethane-1,2-diol