CHEMISTRY

47th and 48th class, Date : 16-11-2021

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Last class….

- 3-D representation
- Conformational analysis

Last class….

- Chiral and achiral compounds
- Symmetry elements

In this class….

- Enantiomers
- CIP rules

Conformational analysis

- Conformational analysis is the study of the different energy levels associated with the different conformations of a molecule.
- Conformations are the different 3-dimensional arrangements that the molecule can acquire by freely rotating around σ-bonds.
- Conformations are simply different structural arrangements of the same molecule.
- Of particular interest and importance are the conformations produced by rotation about the central carbon-carbon bond.

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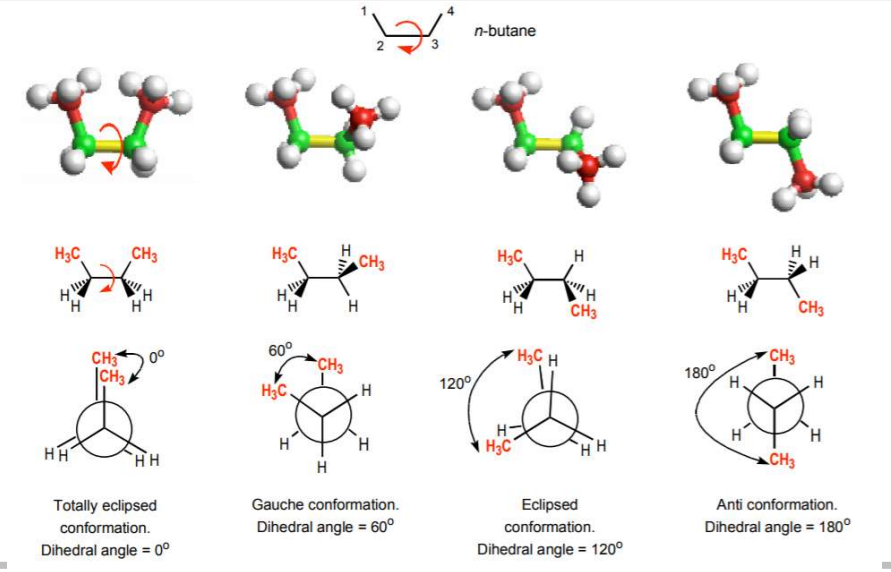
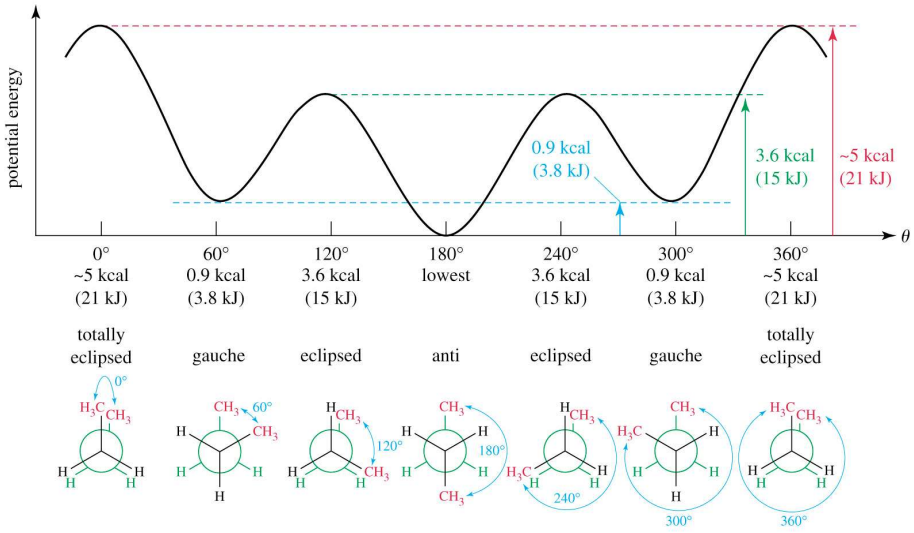
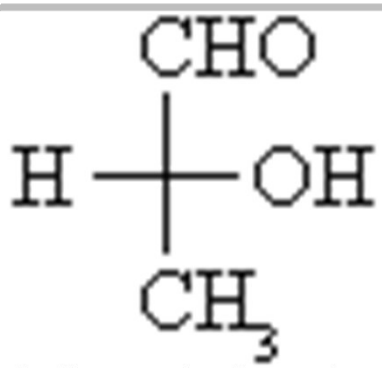
Conformational analysis, n-butane



PE Diagram for Butane

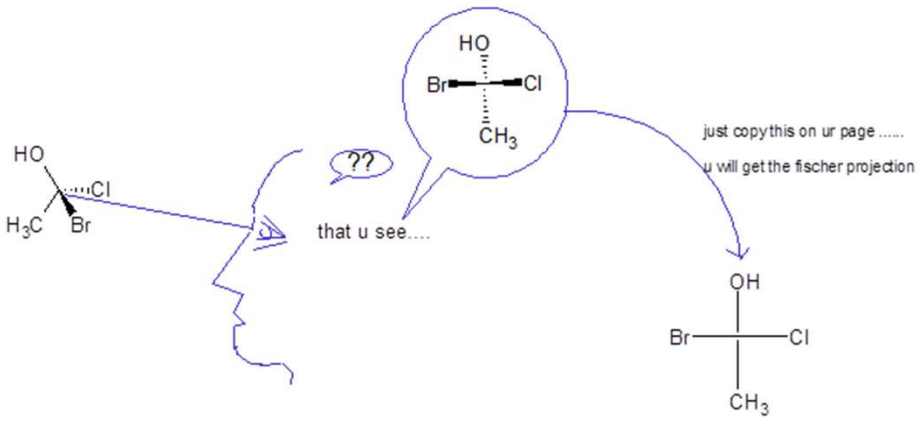


Fischer projection

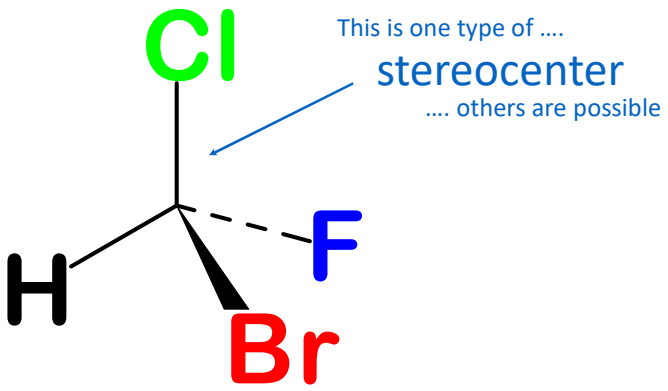


- In a **Fischer Projection**, each place where the horizontal and vertical lines cross represents a carbon.
- The **vertical lines are actually oriented away from you** (similar to *dashes* in the Wedge-Dash Notation) and the **horizontal lines are oriented toward you** (similar to *wedges* in the Wedge-Dash Notation).

Fischer projection

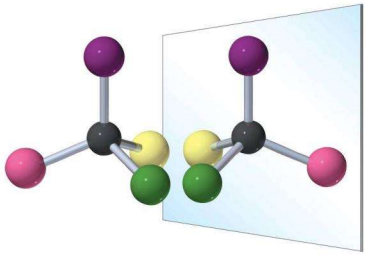


Stereogenic Carbon



A stereogenic carbon is tetrahedral and has four different groups attached.

Chirality



nonsuperimposable
mirror images

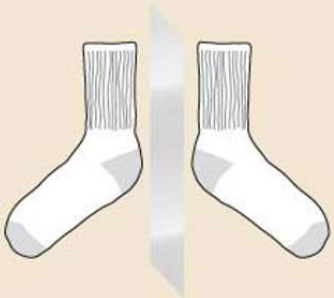
- Also called *asymmetric carbon* atom
- Carbon atom that is bonded to four different groups is chiral – non-superimposable on its mirror image
- Its mirror image will be a different compound (enantiomer)
- ***Achiral*** – Superimposable on its mirror image

Chirality

- **Although everything has a mirror image, mirror images may or may not be superimposable.**
- **Some molecules are like hands. Left and right hands are mirror images, but they are not identical, or superimposable.**

- A molecule (or object) that is *not* superimposable on its mirror image is said to be *chiral.*

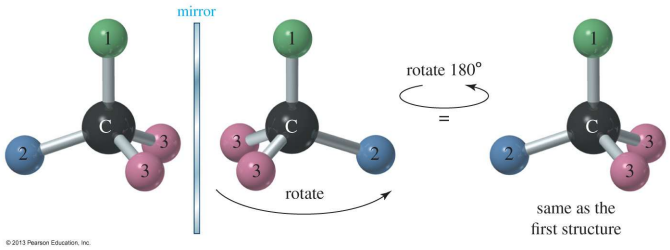
- Other molecules are like socks. Two socks from a pair are mirror images that are superimposable. A sock and its mirror image are identical.
- A molecule or object that is superimposable on its mirror image is said to be achiral.
- A molecule or object that is not superimposable on its mirror image is said to be chiral.



mirror

Socks are **achiral:** they are mirror images that are superimposable.

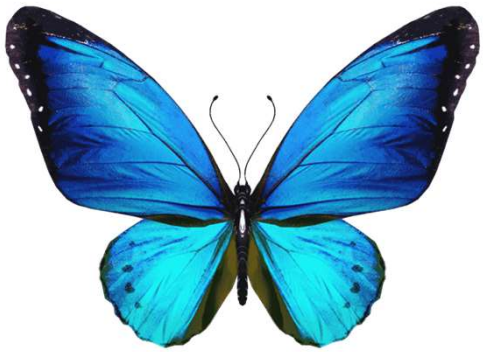
Achiral Compounds



Take this mirror image and try to superimpose it on the one to the left matching all the atoms. Everything will match.

When the images can be superposed, the compound is ***achiral***.

Chiral or not ? – Symmetry



reflect this butterfly, and it looks the same afterwards - it has reflectional symmetry

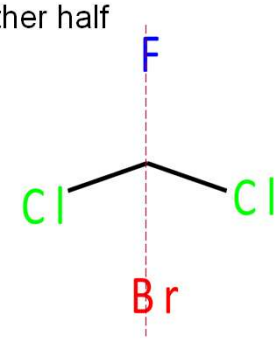
rotate this flower, and it looks the same afterwards - it has rotational symmetry.

Chiral or not ?

- If you want to find out whether a molecule is chiral or achiral we have to look at the symmetry elements
- A **symmetry operation** is a permutation of atoms such that the molecule or crystal is transformed into a **state indistinguishable** from the starting state, A **symmetry element** is a point of reference about which symmetry operations can take place.
- There are generally 4 symmetry elements and any of them may be present in a molecule
  - Plane of symmetry
  - Center of symmetry
  - Axis of symmetry
  - Alternative axis of symmetry

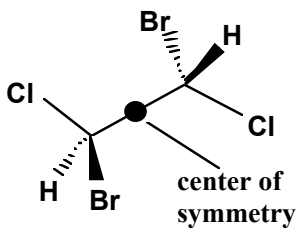
Plane of symmetry (σ)

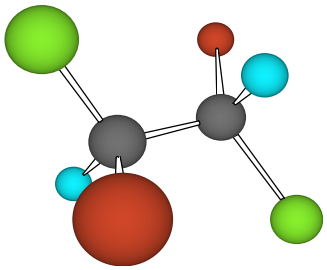
- Plane of symmetry: an imaginary plane passing through an object dividing it **such that one half is the mirror image of the other half**
- Molecules **are not chiral if they contain a plane of symmetry**: a plane that cuts a molecule in half so that one half is the mirror image of the other half



Centre of symmetry (inversion centre), i

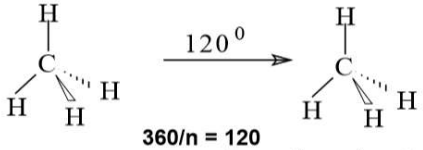
- Center of symmetry: a **point so situated that identical components of the object are located equidistant on opposite sides** and equidistant from the point along any axis passing through the point.
- Any **molecule with a plane of symmetry or a center of symmetry must be achiral**





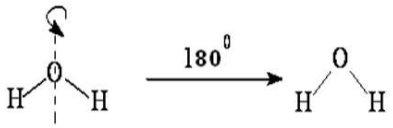
Axis of symmetry (C_n)

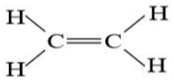
- A molecule has an axis of symmetry if **rotating the molecule about the axis by an angle of 360/n** produces a new structure indistinguishable from the original molecule



360/n = 120
n=3 So methane has C_3 axis

C_6 axis (principle rotation axis)





C_2 axis

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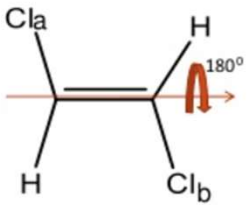
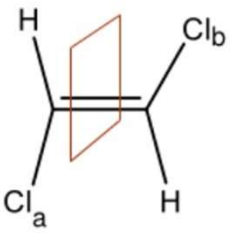
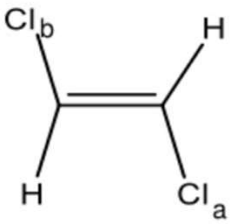
Alternating axis of symmetry (S_n)

- A molecule has an alternating axis of symmetry of order (n) if **rotation about the axis by 360/n degree following by reflection in a plane perpendicular to this axis** produces an equivalent structure. A molecule **which has no S_n axis for any value of n is a chiral molecule.**







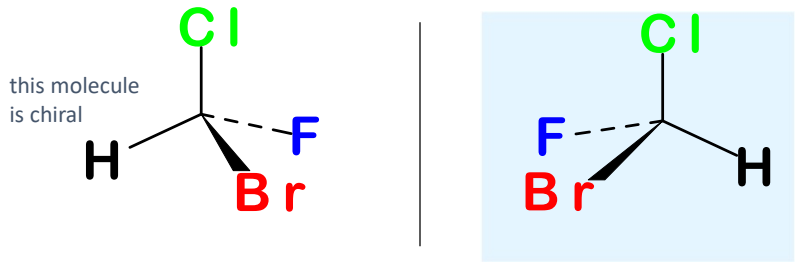
- The symmetry element is denoted as S_2.

Definitions

- **Stereoisomers** – compounds with the same connectivity, different arrangement in space
- **Enantiomers** – **stereoisomers that are non-superimposible mirror images;** only properties that differ are direction (+ or -) of optical rotation. ***Enantiomers have identical physical properties, i.e., b.p, m.p, etc***
- **Diastereomers** – **stereoisomers that are not mirror images**; different compounds with different physical properties

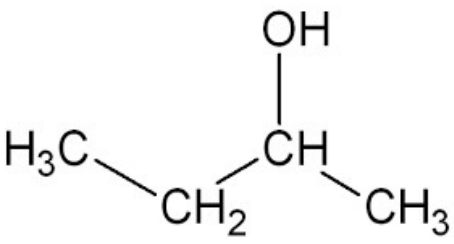
Stereoisomer, Enantiomers

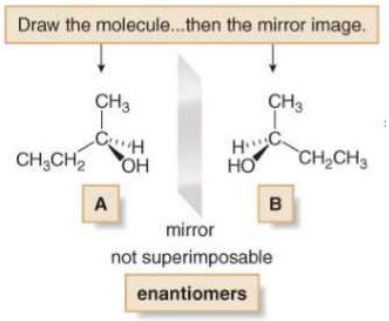
Enantiomers are **chiral molecules that are mirror images of one another**. Furthermore, the molecules are **non-superimposable on one another**. This means that the molecules cannot be placed on top of one another and give the same molecule



Typical convention for depicting a tetrahedron: place two bonds in the plane, one in front of the plane on a wedge, and one behind the plane on a dash. Then, to form the first enantiomer, arbitrarily place the four groups on any bond to the stereogenic center. Then draw the mirror image

Stereoisomer, Enantiomers

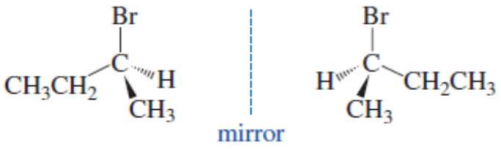




- **To draw both enantiomers of a chiral compound such as 2-butanol, use the typical convention for depicting a tetrahedron: place two bonds in the plane, one in front of the plane on a wedge, and one behind the plane on a dash. Then, to form the first enantiomer, arbitrarily place the four groups—H, OH, CH_3 and CH_2CH_3—on any bond to the stereogenic center. Then draw the mirror image.**

How enantiomers differ ?

nonsuperimposable mirror image



Two isomers are called Enantiomers

Need a way to name the individual stereoisomer

Experimentally : Plane polarised light

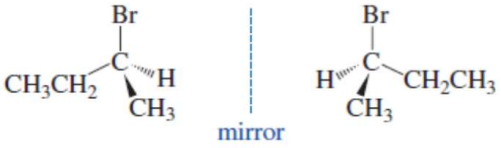
To indicate the absolute configuration : CIP Rules

How enantiomers differ ?

Isomerism of Organic Molecules: Enantiomer

As chiral or optically active molecule with only one chiral center will have two isomers
One isomer rotate the plane of a polarized light to right and other will rotate to left.

nonsuperimposable mirror image



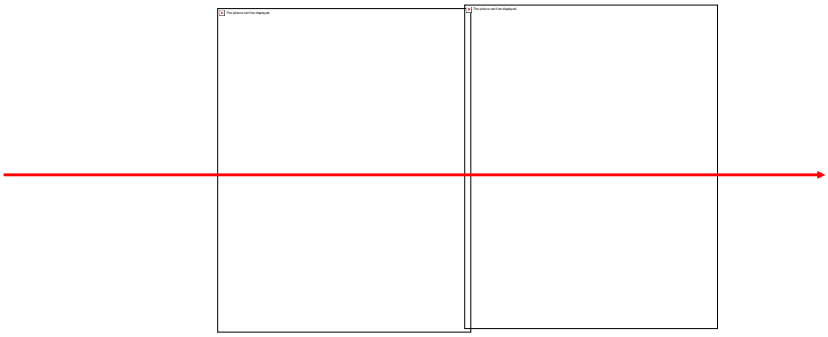
Two isomers are called Enantiomers

Need a way to name the individual stereoisomer

Cahn, Ingold, and Prelog devised ***R,S System of Nomenclature*** *to* indicate the **configuration (arrangement)** of the atoms or groups about the asymmetric carbon.

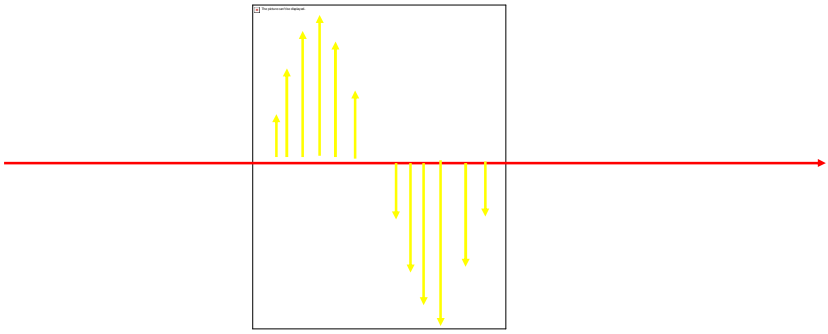
pair of enantiomers with one asymmetric carbon, one will have the ***R configuration*** *and the other will have the* ***S configuration.***

Light



has wave properties, periodic increase and decrease in amplitude of wave

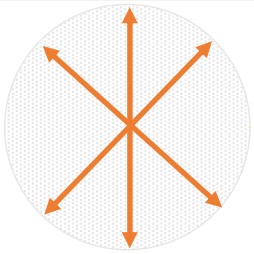
Light



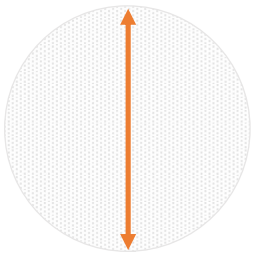
- Optical activity is usually measured using light having a wavelength of 589 nm
- This is the wavelength of the yellow light from a sodium lamp and is called the D line of sodium

Polarized light

Ordinary (nonpolarized) light consists of many beams vibrating in different planes

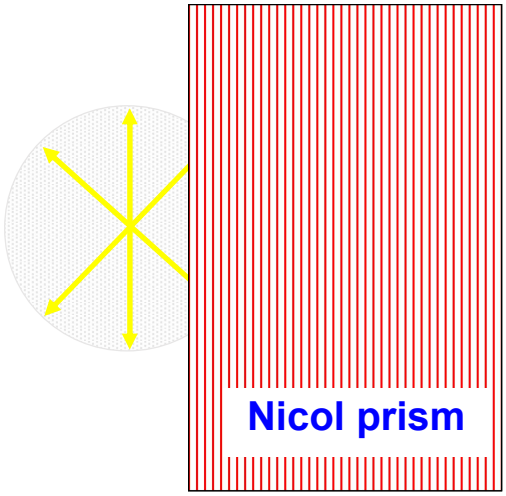


Plane-polarized light consists of only those beams that vibrate in the same plane

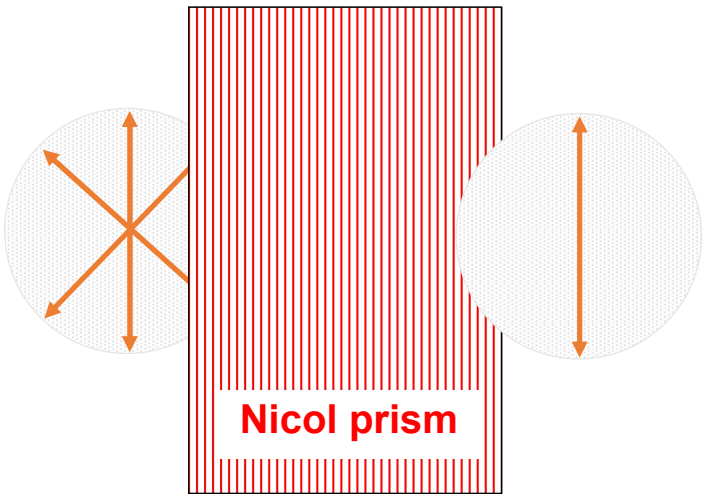


Polarization of light

Polarization of light

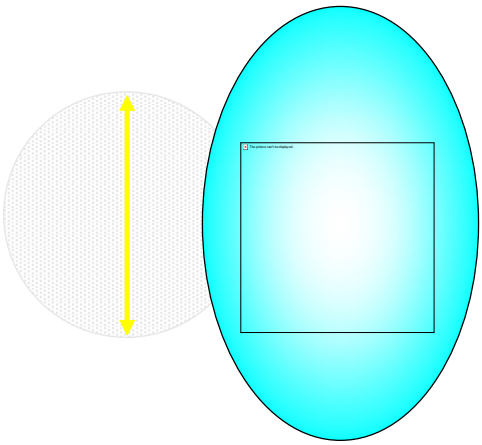


Polarization of light

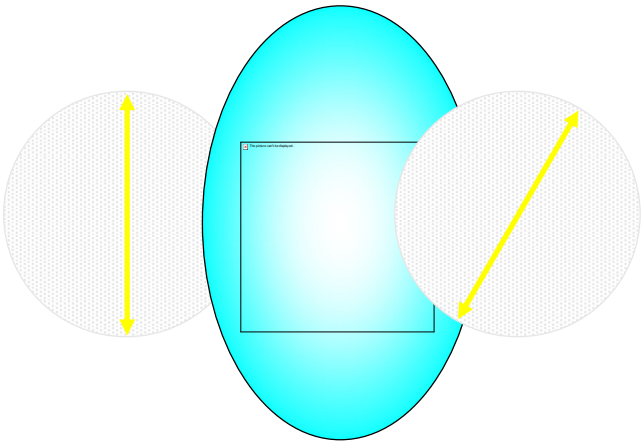


Rotation of plane polarized light

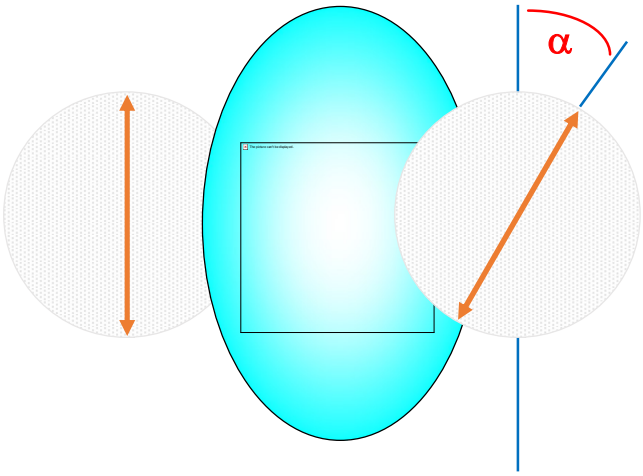
Rotation of plane polarized light



Rotation of plane polarized light



Rotation of polarized light

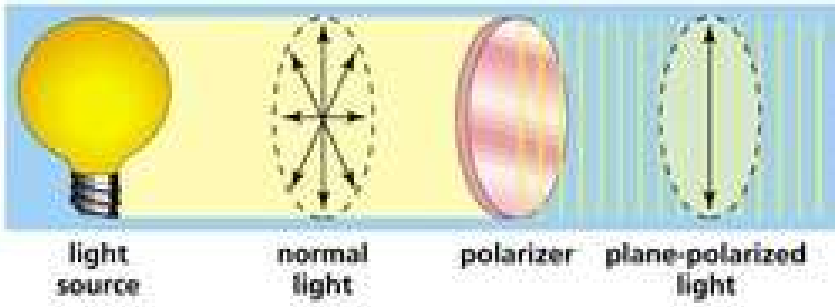


Observed rotation

observed rotation (α) depends on the number of molecules encountered and is proportional to:

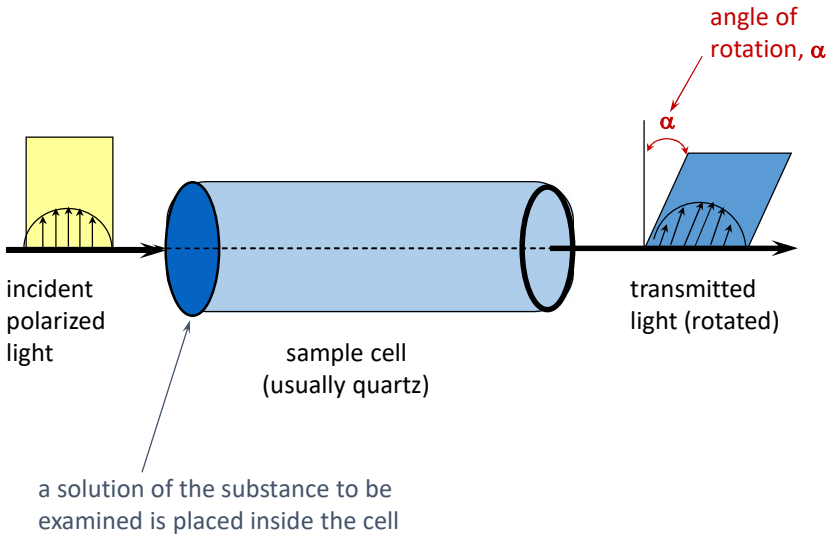
path length (l), and
concentration (c)

Plane polarised light

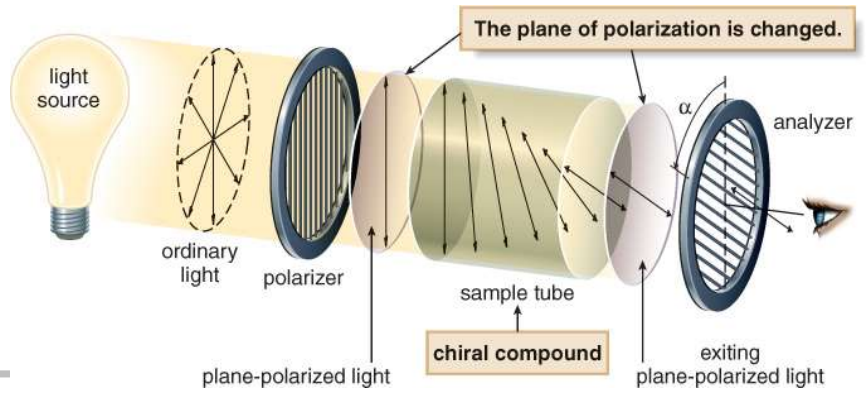


- Optical activity is usually measured using light having a wavelength of 589 nm
- This is the wavelength of the yellow light from a sodium lamp and is called the D line of sodium

Optical Activity

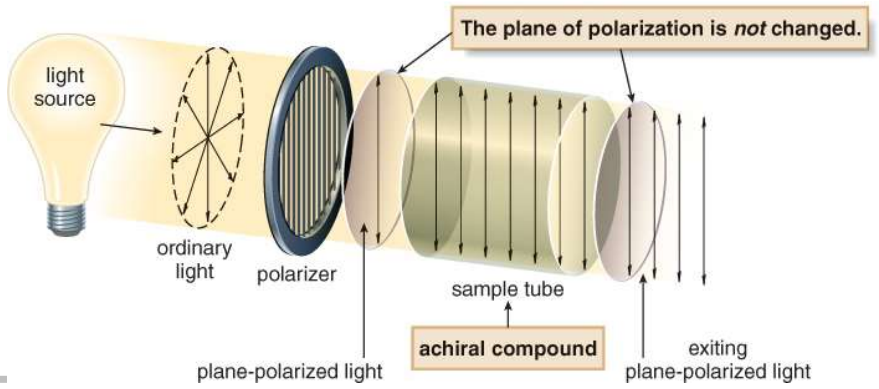


- With chiral compounds, the plane of the polarized light is rotated through an angle α. The **angle α** is measured in degrees (°), and is called the observed rotation. A compound that rotates polarized light is said to be **optically active**



Optical isomerism

- With **achiral compounds**, the light that exits the sample tube **remains unchanged**. A compound that does not change the plane of polarized light is said to be **optically inactive**



Polarimeter

- The rotation of polarized light can be **clockwise or anticlockwise**.
- If the rotation is **clockwise** (to the **right** of the noon position), the compound is called **dextrorotatory**. The rotation is labeled ***d*** or **(+)**
- If the rotation is **counterclockwise**, (to the left of noon), the compound is called **levorotatory**. The rotation is labeled ***l*** or **(-)**
- Two **enantiomers rotate plane-polarized light to an equal extent but in opposite directions.** Thus, if enantiomer A rotates polarized light +5°, the same concentration of enantiomer B rotates it –5°.
- **Observed rotation: the number of degrees, α** , through which a compound rotates the plane of polarized light

Racemic mixture or Racemate

- **An equal amount of two enantiomers is called a racemic mixture or a racemate. A racemic mixture is optically inactive. Because two enantiomers rotate plane-polarized light to an equal extent but in opposite directions, the rotations cancel, and no rotation is observed.**

Table 5.1 The Physical Properties of Enantiomers A and B Compared

Property	A alone	B alone	Racemic A + B
Melting point	identical to **B**	identical to **A**	may be different from **A** and **B**
Boiling point	identical to **B**	identical to **A**	may be different from **A** and **B**
Optical rotation	equal in magnitude but opposite in sign to **B**	equal in magnitude but opposite in sign to **A**	0°

Specific rotation

- **Specific rotation** is a standardized physical constant for the amount that a chiral compound rotates plane-polarized light
- Specific rotation is denoted by the symbol [α] and defined using a specific sample tube length (*l*, in dm), concentration (*c* in g/mL), temperature (25^0C) and wavelength (589 nm).

$$\text{specific rotation} = [\alpha] = \frac{\alpha}{l \times c}$$

α = observed rotation (°)
l = length of sample tube (dm)
c = concentration (g/mL)

[dm = decimeter
1 dm = 10 cm]

A compound was isolated in the lab. and the observed rotation was +10 when measured in a 1 dm. tube containing 1.0g of sample in 10ml of water. What is the specific rotation of this compound?

$[\alpha] = \alpha/(\text{length} \times (g/ml))$

$= 10/(1dm. \times (1.0g/10ml)) = +100$

Diastereomers

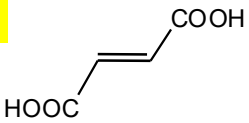
Diastereomers are stereoisomers that are not enantiomers

They are chemically (and physically) different

OR

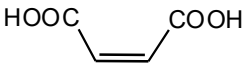
Stereoisomers that are not mirror images and non superimposable

E.g.,1



Fumaric Acid

MP: 299-300 ºC



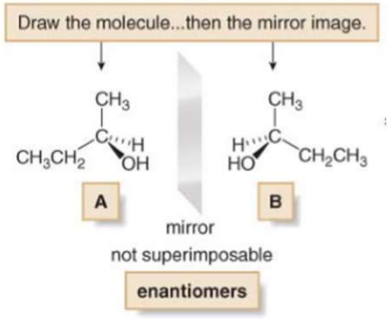
Maleic Acid

MP: 140-142 ºC

Forms anhydride upon heating

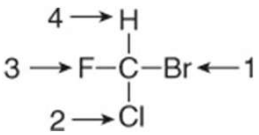
Labeling Stereogenic Centers with *R* or *S*

- Since enantiomers are **two different compounds**, they need to be distinguished by name. This is done by adding the **prefix *R* or *S*** to the IUPAC name of the enantiomer
- Naming enantiomers with the prefixes *R* or *S* is called the **Cahn-Ingold-Prelog** system

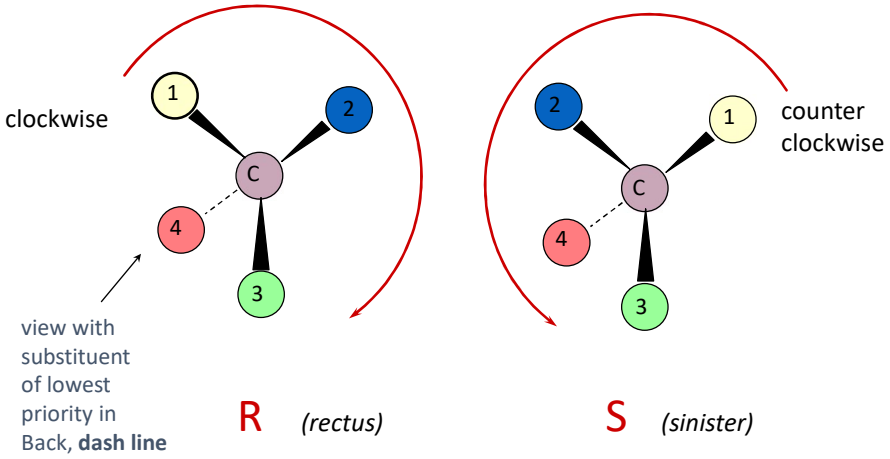


Naming Enantiomers, CIP rules

1. Locate the **stereocenter**
2. Assign a priority to each substituent **from 1 (highest) to 4 (lowest)**, priorities must be assigned to each group bonded to the stereogenic center, **in order of decreasing atomic number**. The atom of **highest atomic number gets the highest priority (1)**
3. Orient the molecule so that the group of **lowest priority (4) is directed away from you (wedge-dash)**
4. Read the three groups projecting toward you in order from **highest (1) to lowest priority (3)**
5. If reading is **clockwise, configuration is R (from the Latin rectus). If it is counterclockwise, configuration is S (from the Latin sinister).**

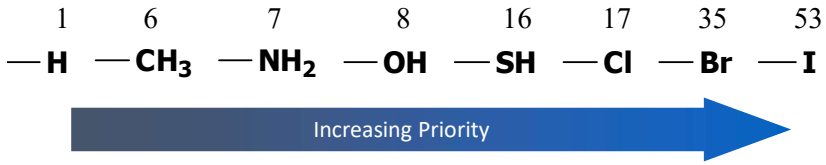


R, S Convention



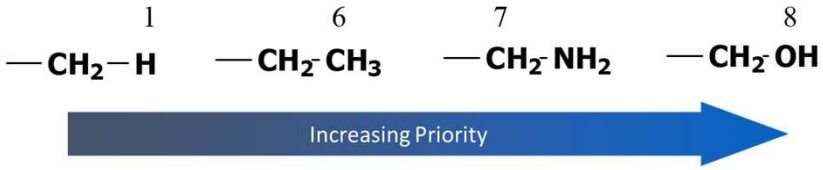
R,S Convention

- Priority rules (Cahn, Ingold, Prelog)
  - Each atom bonded to the stereocenter is assigned a priority, based on atomic number. The higher the atomic number, the higher the priority



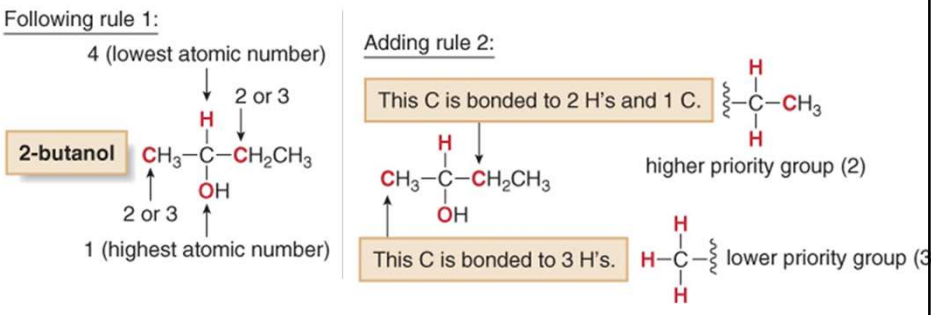
R,S Convention

- If **two atoms on a stereogenic center are the same**, assign **priority based on the atomic number of the atoms bonded to these atoms**. One atom of higher atomic number determines the higher priority.



R,S Convention

- If priority cannot be assigned on the basis of the atoms bonded to the stereocenter, look to the next set of atoms.
- Priority is assigned at the first point of difference.



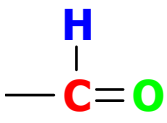
R,S Convention

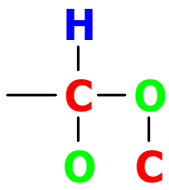
- If two isotopes are bonded to the stereogenic center, assign priorities in **order of decreasing mass number**. Thus, in comparing the three isotopes of hydrogen, the order of priorities is:

	Mass number	Priority
T (tritium)	3 (1 proton + 2 neutrons)	1
D (deuterium)	2 (1 proton + 1 neutron)	2
H (hydrogen)	1 (1 proton)	3

R,S Convention

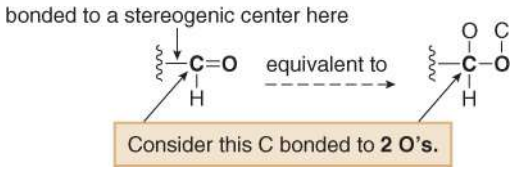
- Atoms participating in a double or triple bond are considered to be **bonded to an equivalent number of similar atoms by single bonds**



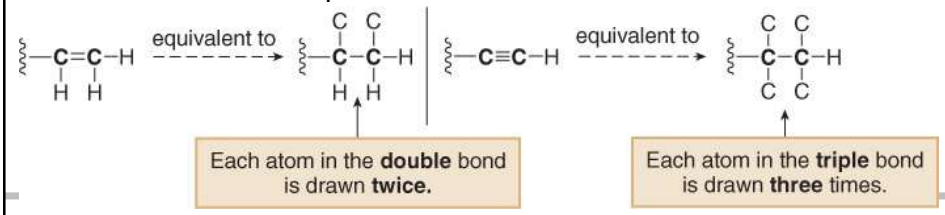


R,S Convention

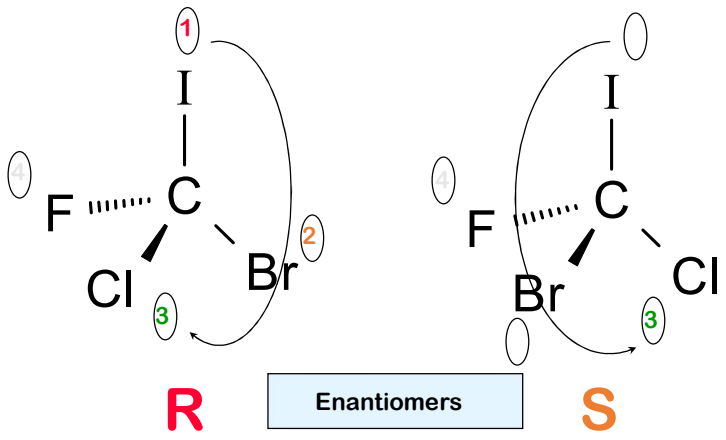
- To assign a priority to an atom that is part of a multiple bond, treat a multiply bonded atom as an equivalent number of singly bonded atoms. For example, the C of a C=O is considered to be bonded to two O atoms.



- Other common multiple bonds are drawn below:

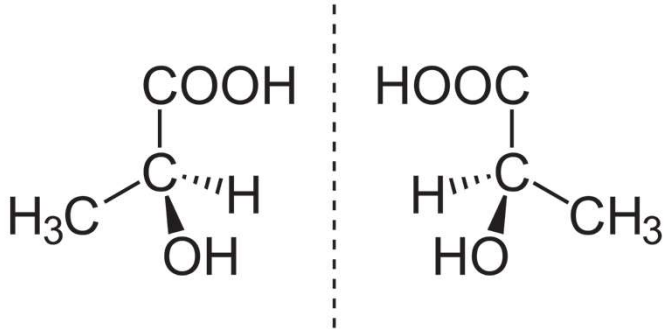


Bromochlorofluoroiodomethane

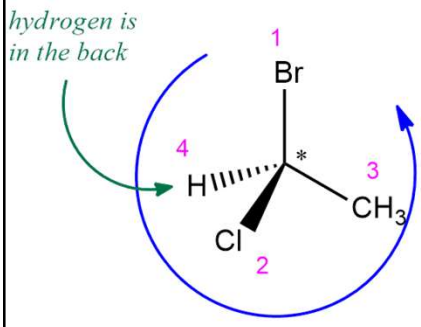


Example

1. -OH
2. -COOH
3. -CH_3
4. -H



(S)-(+)-lactic acid (left) and (R)-(–)-lactic acid (right) are nonsuperposable mirror images of each other.



Z (Br) = 35
Z (C) = 6
Z (Cl) = 17
Z (H) = 1

Z (Br) > Z (Cl) > Z (C) > Z (H)

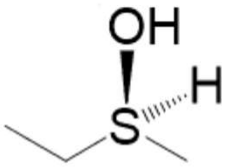
CCW → S

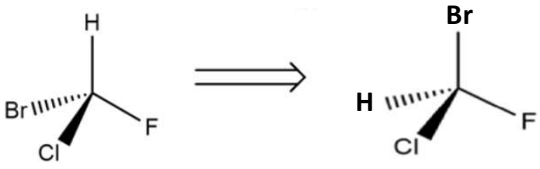
S-bromochlorofluoromethane

How To Assign *R* or *S* to a Stereogenic Center

Example Label each enantiomer as *R* or *S*.

- Carbon is not the only atom designated by R and S.
- In theory, any atom with four different groups is chiral and can be described by the R and S system.
- For example, phosphorous and sulfur chiral centers are often assigned as R or S.



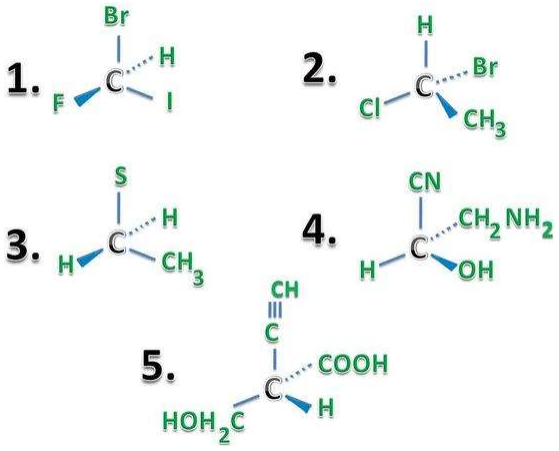


R-bromochlorofluoromethane

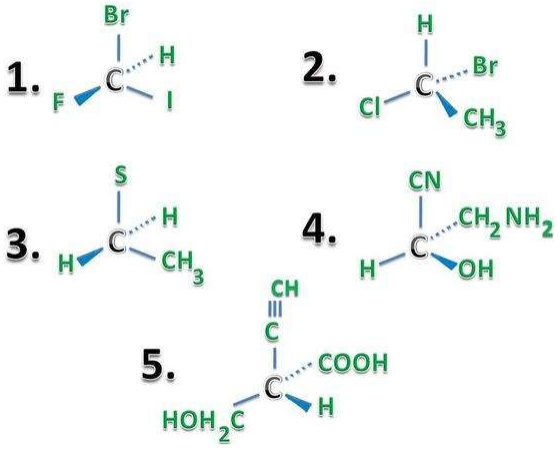
Single swap rule:

1) Interchange two atoms (the least priority atom has to be behind)
2) Once the least priority atom is behind, do the CIP rules as usual
3) Finally, by doing the above if you get 'S' then the original molecule given is 'R" and vice versa

Exercise, naming R, S



Exercise, naming R, S



1. **S**
2. **R**
3. **Neither R or S: This molecule is achiral.**
4. **R**
5. **S**

Thank you all for your attention

Information presented here were collected from various sources – textbooks, articles, manuscripts, internet and newsletters. All the researchers and authors of the above mentioned sources are greatly acknowledged.