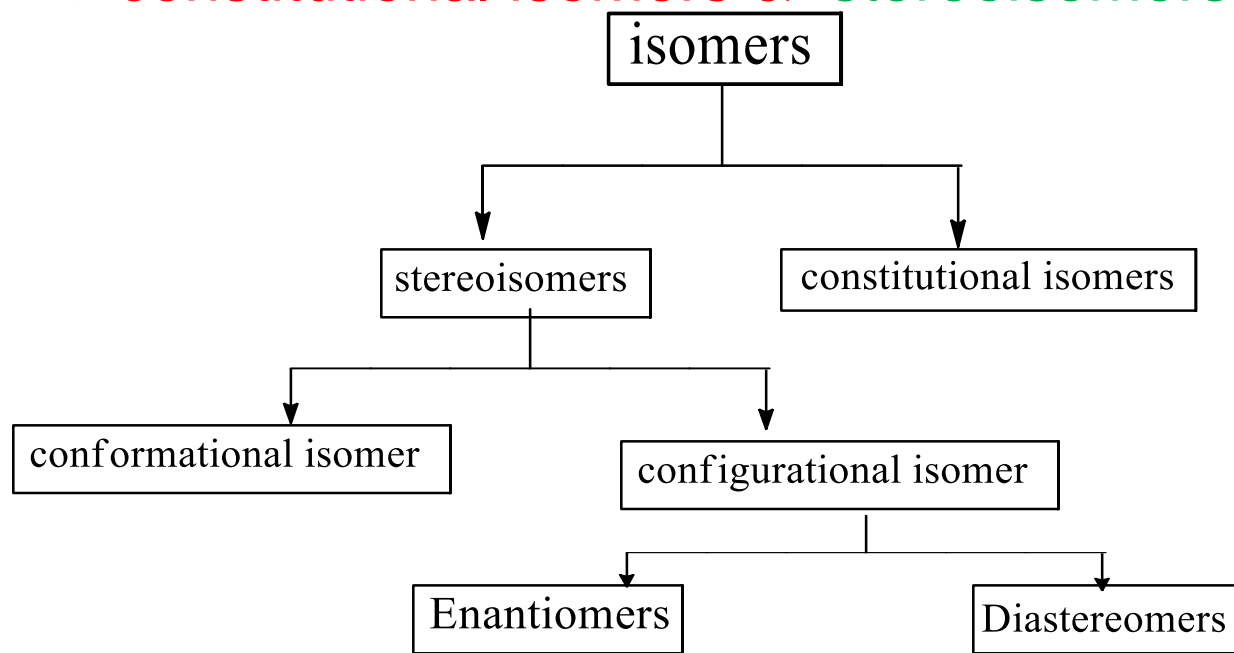


Chapter three

stereochemistry

Stereochemistry

- ❖ Stereochemistry is a chemistry that studies about three dimensional structure of organic compounds(arrangement in space).
- ❖ **Isomers**: different compounds with the same molecular formula of their atoms in space
- ❖ The two major classes of isomers are
 - constitutional isomers & stereoisomers

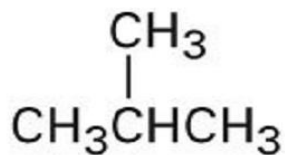


stereochemistry

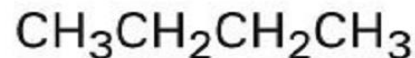
- **Stereoisomers** differ only in the way the atoms are oriented in space. They have identical IUPAC names (except for a prefix like *cis* or *trans*). They always have the same functional group(s). A particular three-dimensional arrangement is called a **configuration**. Stereoisomers differ in **configuration**.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

Examples of Constitutional/structural isomers

I. Constitutional isomers with different carbon skeletons



and



2-Methylpropane

n-Butane

II. Constitutional isomers with different functional groups



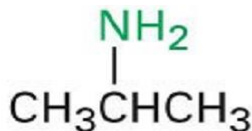
and



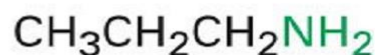
Ethanol

dimethylether

III. Constitutional isomers with different position of functional groups



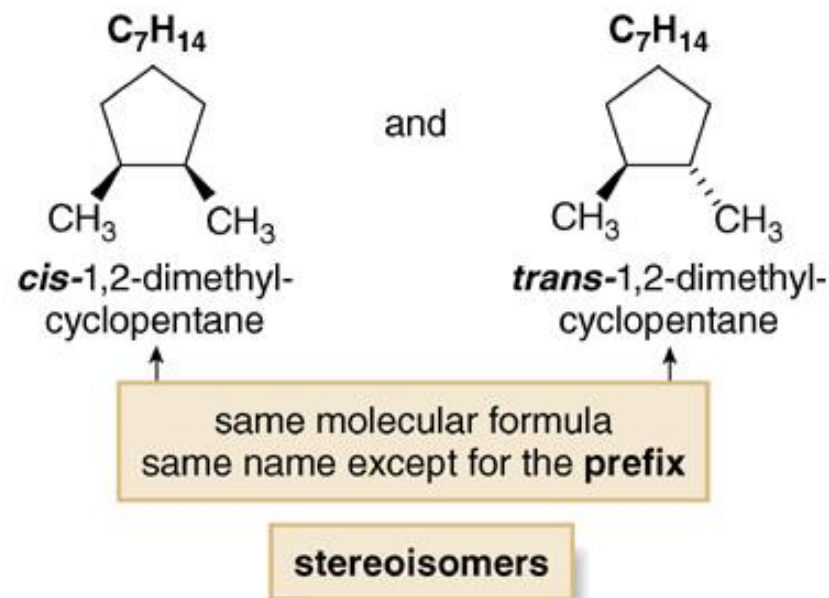
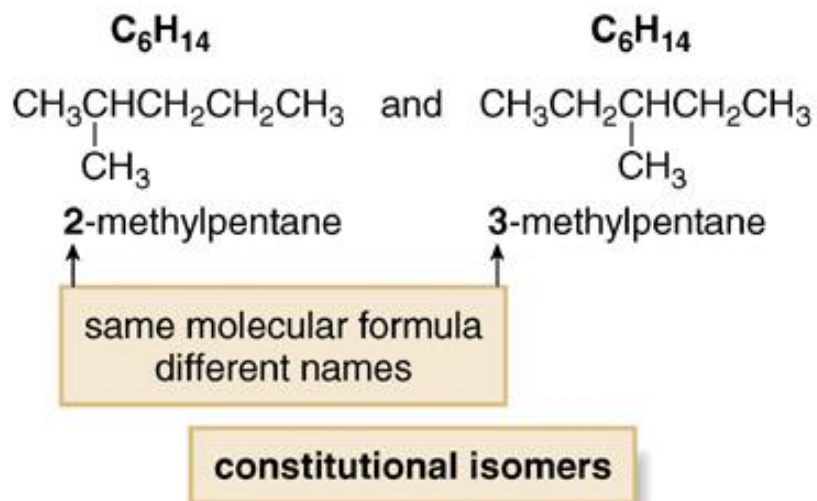
and



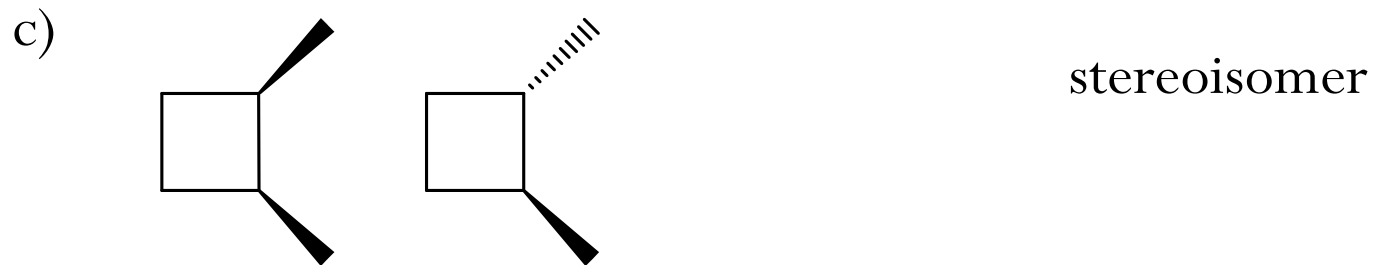
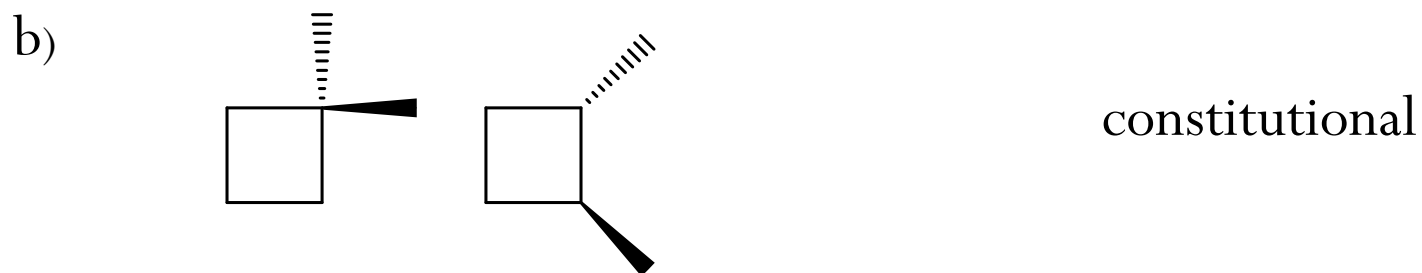
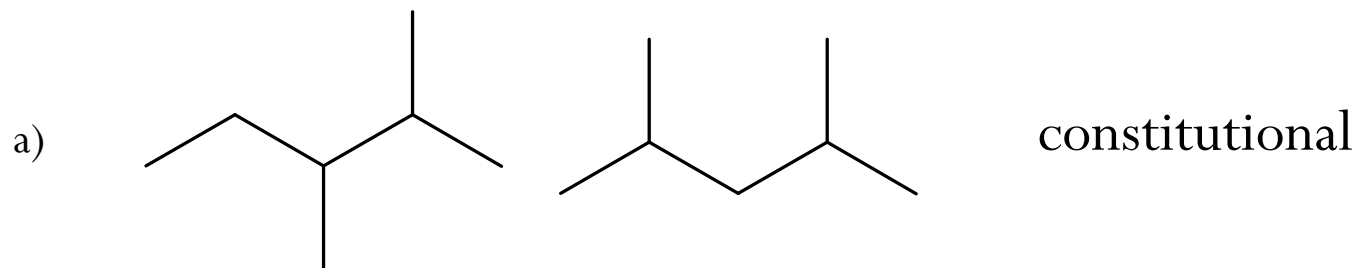
iso-propylamine

propylamine

- A comparison of constitutional isomers and geometric stereoisomers



➡ Are the following pairs of compounds constitutional isomers or stereoisomers?



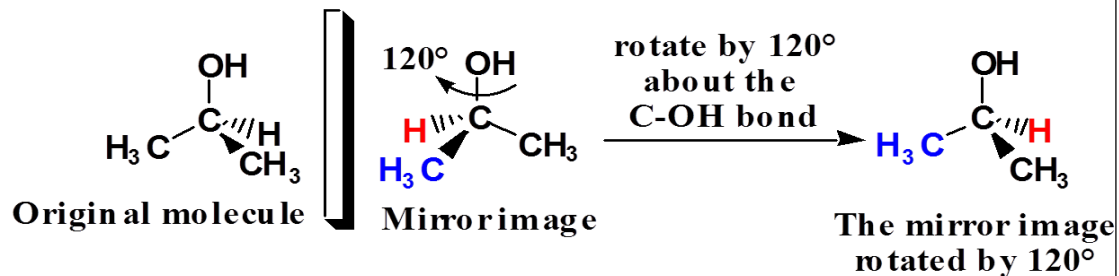
Chiral and Achiral objects

Achiral

- ❖ A molecule or object that is superimposable on its mirror image is said to be **achiral** (lacking-chirality).
- ❖ If carbon is attached at least with two same atom it is called symmetric carbon center.
- ❖ See the socks below



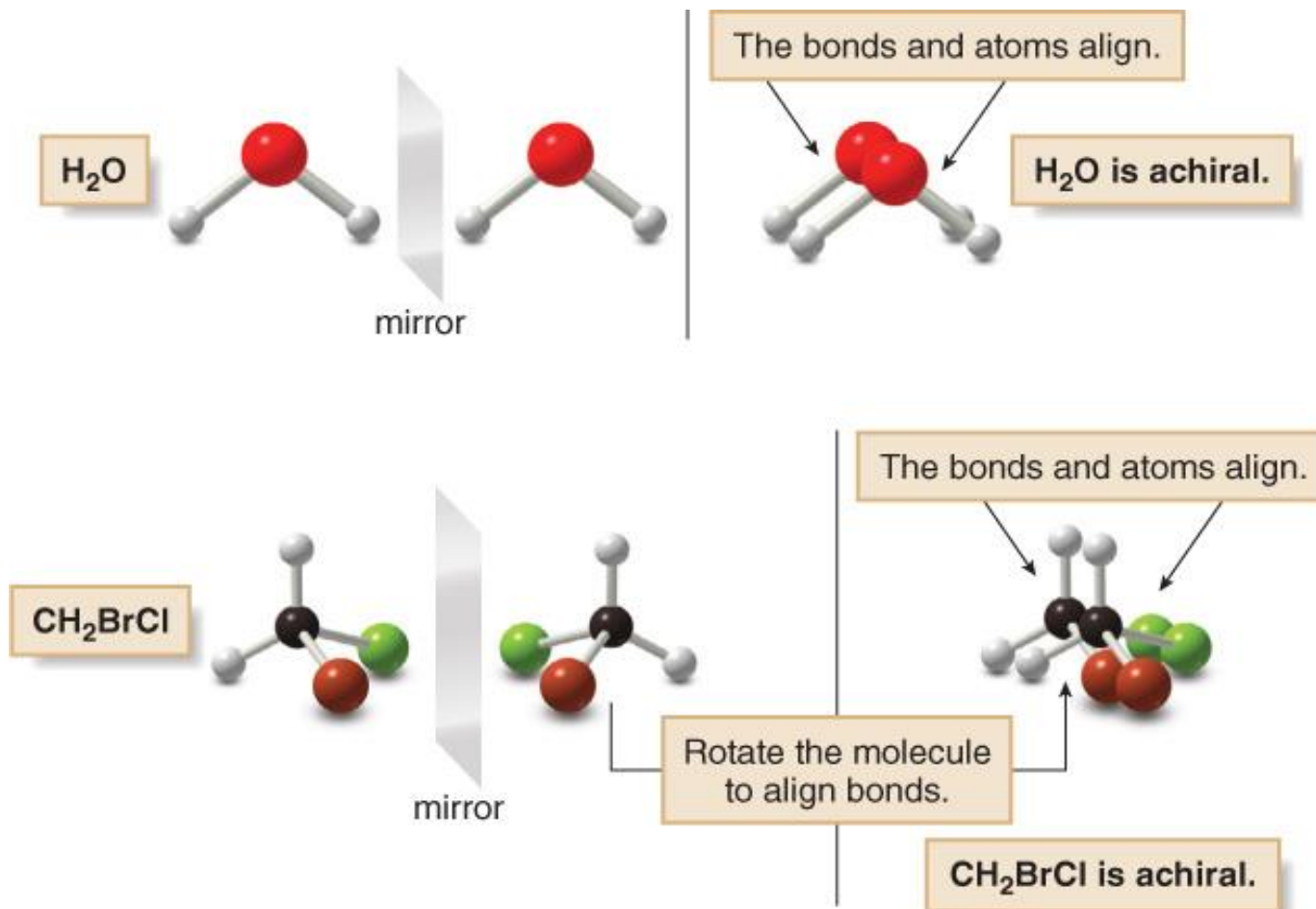
- To see the relationship between the original and its mirror image, rotate the mirror image by 120°



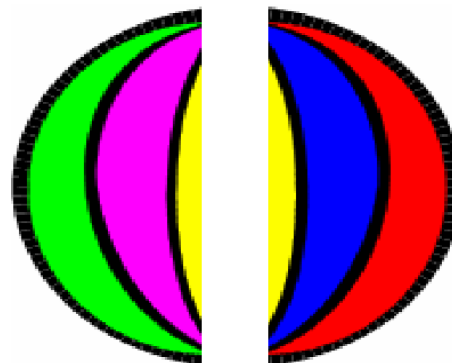
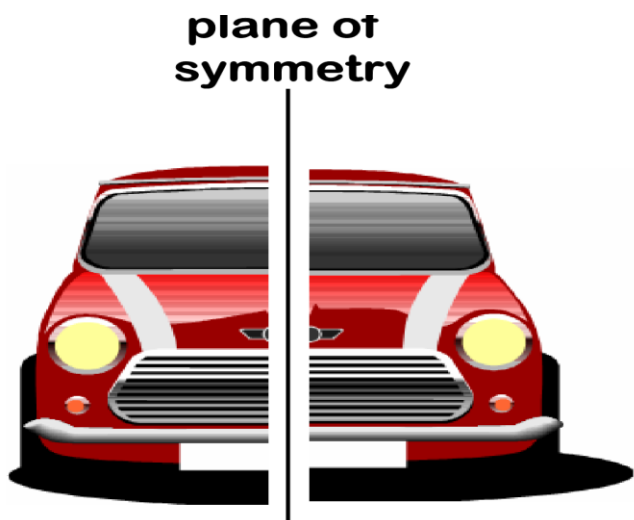
- Can see that all atoms and bonds of the mirror image fit exactly on the original when it is rotated
- Thus, original and its mirror image are the same molecule due to this they are achiral.

CONT'D

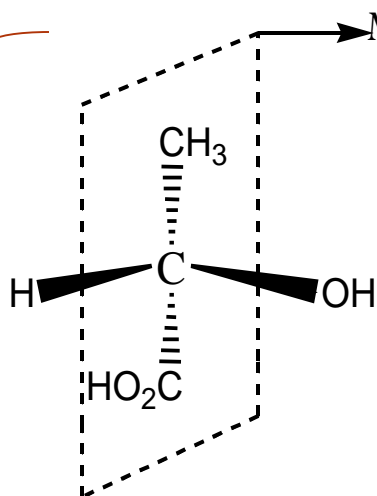
- We can now consider several molecules to determine whether or not they are **chiral**.



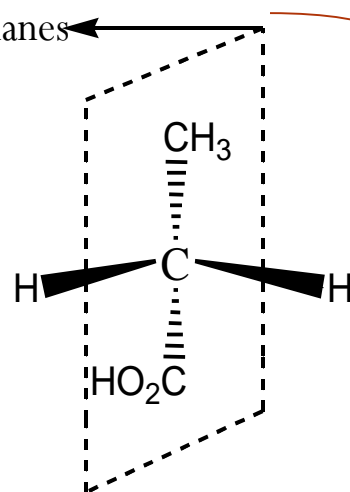
- Achiral molecules usually contain a **plane of symmetry** but chiral molecules do not.
- A **plane of symmetry** is a **mirror plane** that cuts the molecule in half, so that one half of the molecule is a reflection of the other half.
- if an object has a plane of symmetry, its mirror image will be identical.
identical mirror images will superimpose (match exactly when placed on top of each other)



✓ Has no plane of symmetry

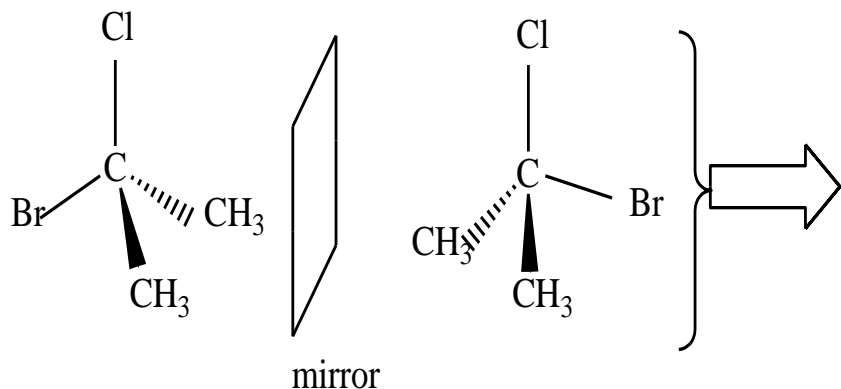


✓ half of the compound that found out of the plane are not the same due to this it is called **chiral**



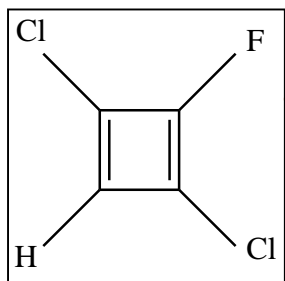
✓ Has plane of symmetry

✓ half of the compound that found out of the plane are the same due to this it is called **achiral**



- ✓ both are mirror image to each other and they superimpose on each other.
- ✓ Due to this they are called achiral.
- ✓ the carbon center is called symmetric carbon because all the surrounding atoms are not different (two CH₃ attached to carbon)

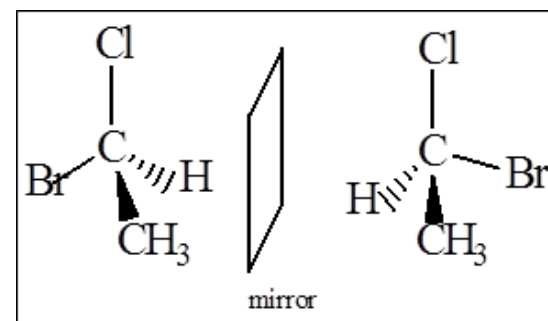
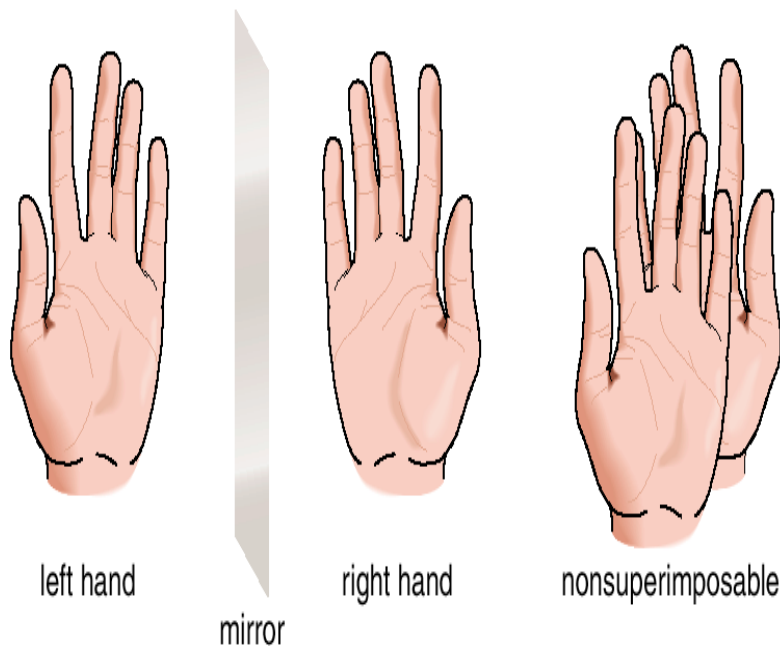
➤ A molecule that has a center of symmetry is **achiral**.



- ✓ This compound is achiral. Because when we draw line from the center of the compound toward H and F, half of the compound is the same as the half of the other side of the compound.

Chiral

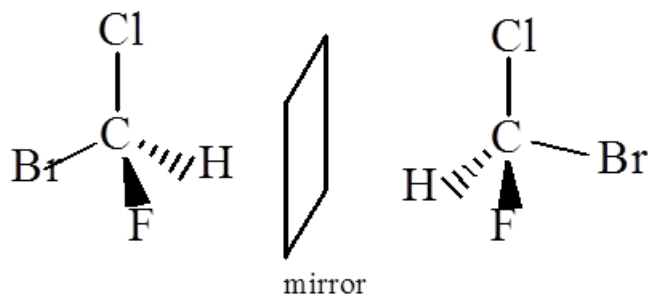
- ❖ A molecule or object that is not superimposable on its mirror image is said to be **chiral**.
- ❖ Generally, a chiral carbon atom is sp^3 with four different attachments and the carbon center is called **asymmetric carbon**.
- ❖ Some molecules are like hands. Left and right hands are mirror images, but they are not identical, or **superimposable**.



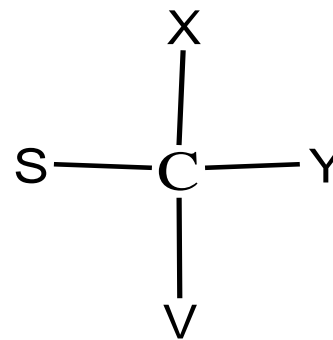
- ❖ both are mirror image to each other and the carbon center is called asymmetric carbon because all the surrounding atoms are different

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

- ❖ Bromochlorofluoromethane is chiral
- ❖ To show nonsuperposability, rotate this model 180° around a vertical axis.

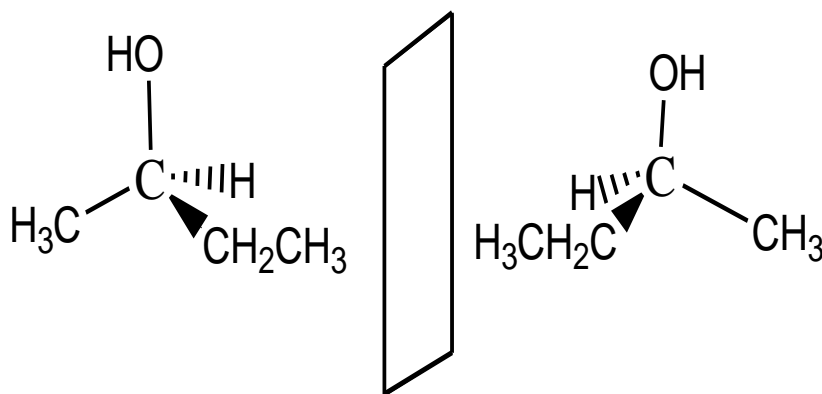


- ❖ Totally when carbon is attached with four different groups it is called
 - ✓ chiral center
 - ✓ asymmetric center
 - ✓ stereocenter
 - ✓ stereogenic center
- ❖ Example see the structure ($S \neq V \neq Y \neq X$)

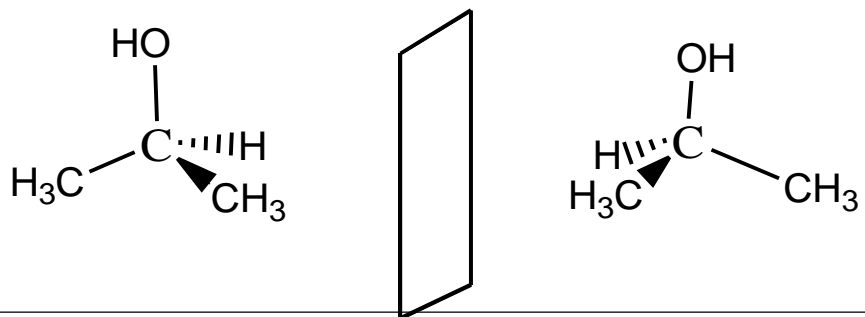


enantiomers

- Objects that are not superposable on their mirror images are **chiral**
- The most common cause of enantiomerism in organic molecules is a carbon with four different groups bonded to it.
 - a carbon with four different groups bonded to it is called a **stereocenter** also known as a **chiral carbon**.
- Example: 2-butanol



- If an object and its mirror image are superposable, they are identical and there is no possibility of enantiomerism
 - Identical molecules are **achiral** (without chirality)
- Example of achiral molecule: 2-propanol
 - Notice that it has no stereocenter



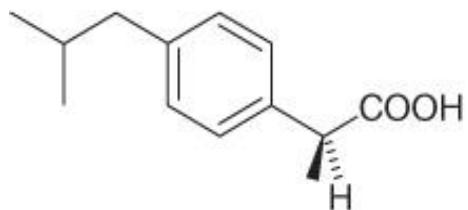
Properties of enantiomers

1. Physical properties of enantiomers

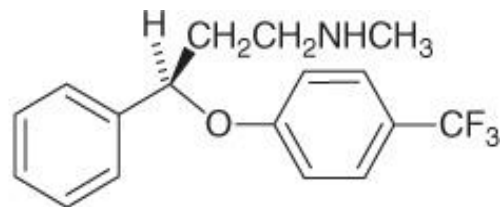
- ❖ Have same melting point, boiling point, density, etc totally they have the same physical properties and are difficult to separate mixtures of two enantiomers.

2. Chemical Properties of Enantiomers:

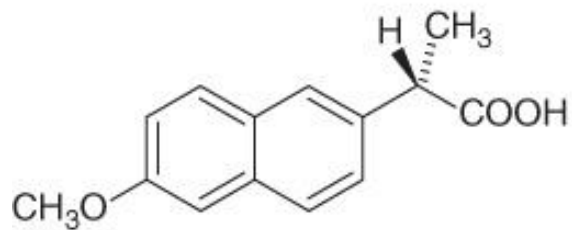
- Two enantiomers have exactly the same chemical properties except for their reaction with chiral non-racemic reagents.
- Many drugs are chiral and often must react with a chiral receptor or chiral enzyme to be effective. One enantiomer of a drug may effectively treat a disease whereas its mirror image may be ineffective or toxic.



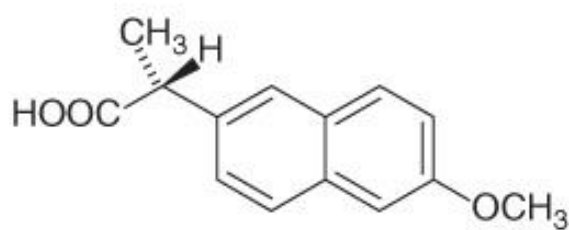
(S)-ibuprofen
anti-inflammatory agent



(R)-fluoxetine
antidepressant



(S)-naproxen
anti-inflammatory agent



(R)-naproxen
liver toxin

2. optical activity

- ❖ Is an activity shows whether a compound rotates the plane of plane-polarized light or not
- ❖ **Ordinary light:** light waves vibrating in all planes perpendicular to its direction of propagation
- ❖ **Plane-polarized light:** light waves vibrating only in parallel planes. Plane polarized light is the light that has an electric vector that oscillates in a single plane. Plane-polarized light arises from passing ordinary light through a polarizer.
- ❖ **Polarimeter:** is an instrument that allows polarized light to travel through a sample tube containing an organic compound. It permits the measurement of the degree to which an organic compound rotates plane-polarized light.

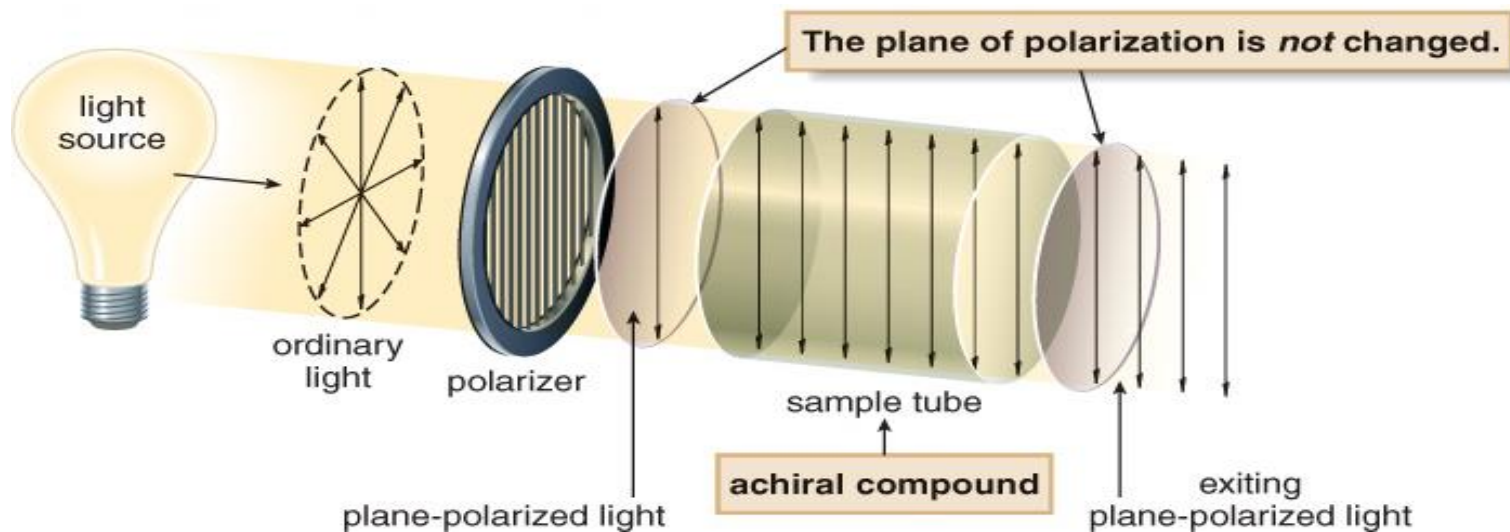
- ❖ Two enantiomers rotate plane-polarized light to an equal extent but in **opposite directions**. Thus, if enantiomer A rotates polarized light $+5^\circ$, the same concentration of enantiomer B rotates it -5° .
- ❖ With achiral compounds, the light that exits the sample tube remains unchanged. A compound that does not change the plane of polarized light is said to be **optically inactive**.
- ❖ Enantiomers (chirals) rotates plane polarized light toward clockwise or anticlockwise and said to be **optically active**.
- ❖ 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 (-).

- ❖ The rotation is finally calculated by specific rotation.
- ❖ **Specific rotation:** the observed rotation of an optically active substance at a concentration of 1 g/mL in a sample tube 10 cm long

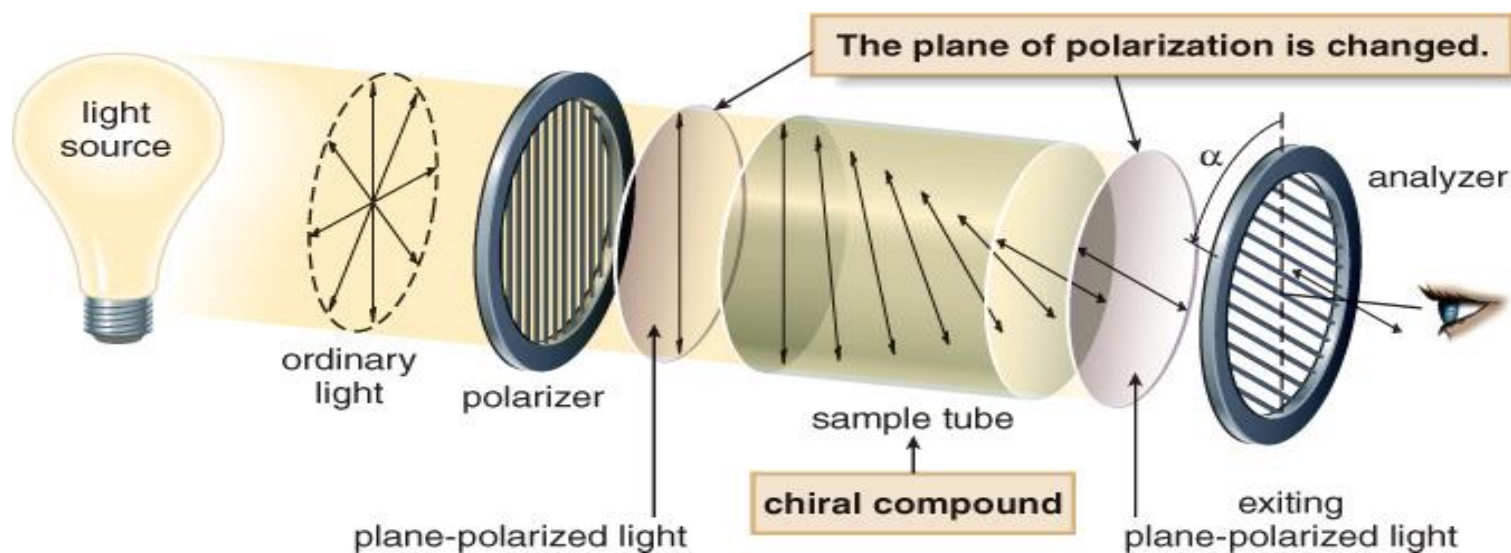
$$\text{specific rotation} = [\alpha] = \frac{\alpha}{l \times c}$$

α = observed rotation ($^{\circ}$)
 l = length of sample tube (dm)
 c = concentration (g/mL)

$\left[\begin{array}{l} \text{dm} = \text{decimeter} \\ 1 \text{ dm} = 10 \text{ cm} \end{array} \right]$



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



Racemic Mixtures

○An equimolar mixture of two enantiomers. is called a **racemic mixture** or a **racemate**. A racemic mixture is optically inactive. because a racemic mixture contains equal numbers of dextrorotatory and levorotatory molecules, its specific rotation is zero

The physical properties of Enantiomers A and B

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°

Enantiomeric excess and Optical purity (ee and op)

- **Enantiomeric excess (ee)** is a measurement of the excess of one enantiomer over the racemic mixture.

$$ee = \% \text{ of one enantiomer} - \% \text{ of the other enantiomer.}$$

- Consider the following example: If a mixture contains 75% of one enantiomer and 25% of the other, the enantiomeric excess is $75\% - 25\% = 50\%$. Thus, there is a 50% excess of one enantiomer over the **racemic mixture**.
- ee is numerically equal to **Optical Purity**.
- The optical purity can be calculated if the specific rotation $[\alpha]$ of a mixture and the specific rotation $[\alpha]$ of a pure enantiomer are known.

$$op = ([\alpha] \text{ mixture} / [\alpha] \text{ pure enantiomer}) \times 100.$$

Diastereomers

- ❖ Diastereomers are stereoisomers that are not mirror images.
- ❖ Because diastereomers are not mirror images of each other, they can have quite different physical and chemical properties.
- ❖ Diastereomers have different physical properties: m.p., b.p., etc
- ❖ They can be separated easily.
- ❖ Examples of diastereomers are

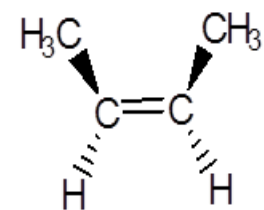
1. Geometric isomers (*cis* and *trans* isomers)

2. Conformational isomers

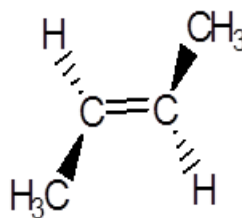
We will see conformational isomers later , let we discuss about geometric isomers

Geometric isomers

- ❖ Two isomers are not interchangeable



cis-2-butene



trans-2-butene

❖ **Cis:-** Substituent groups on the same side of double bond.

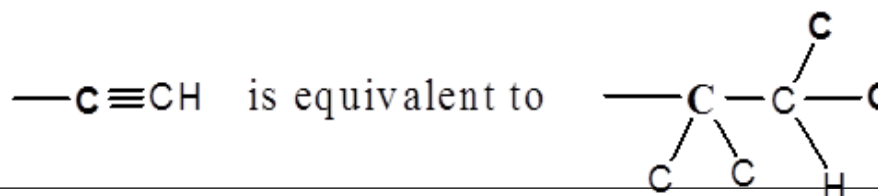
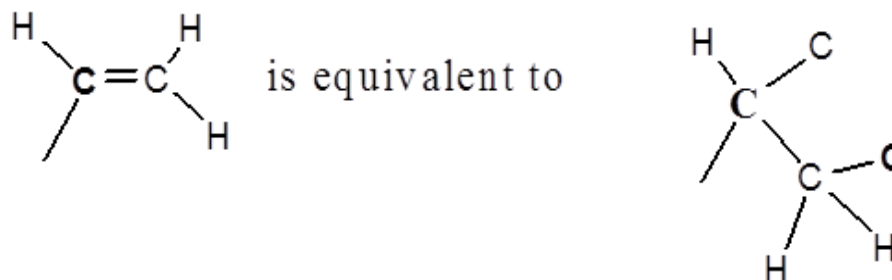
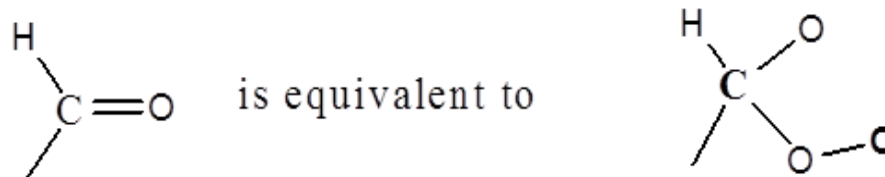
❖ **Trans:-**Substituents on opposite sides of double bond.

E, Z System

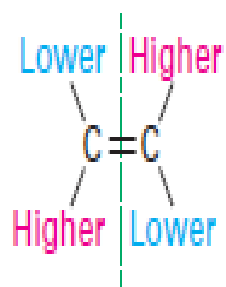
- ❖ The *Cis-trans* naming system use only with **di substituted** alkene (two substituents other than hydrogen on the double bond).
- ❖ but E,Z system works well with **tri** or **tetra substituted** alkene(3 or 4 substituents other than hydrogen on the double bond).

Rules to assign E or Z configuration

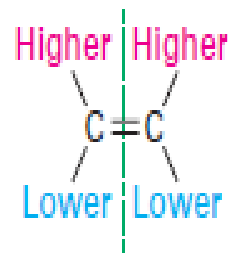
1. Leave alone the double bond and look only on the atoms directly attached to each and rank them according to atomic number. Eg. $\text{Br} > \text{F} > \text{C}$ in atomic #
2. If a decision can't be reached using rule-1, look at the 2nd, 3rd or 4th atoms away from the double bond carbons until the first difference is found. Eg. $-\text{CH}_2\text{CH}_3$ is found in higher priority than CH_3
3. Multiple bonded atoms are equivalent to the same number of single bonded atoms.



- ❖ **E- CONFIGURATION** : IF the two higher priority groups are on opposite sides.
- ❖ **Z- CONFIGURATION** : IF the two higher priority groups are on the same sides.
- ❖ Alkene is said to have Z geometry, for the German *zusammen*, meaning “together.”
- ❖ If the higher-ranked groups are on opposite sides, the alkene has *E* geometry, for the German *entgegen*, meaning “opposite.”

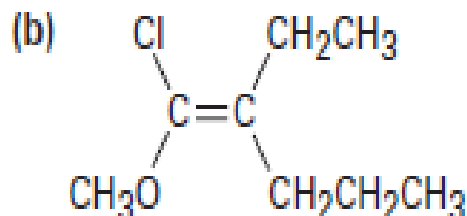
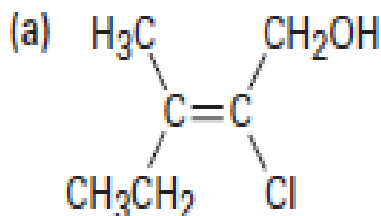


E double bond
(Higher-ranked groups
are on opposite sides.)



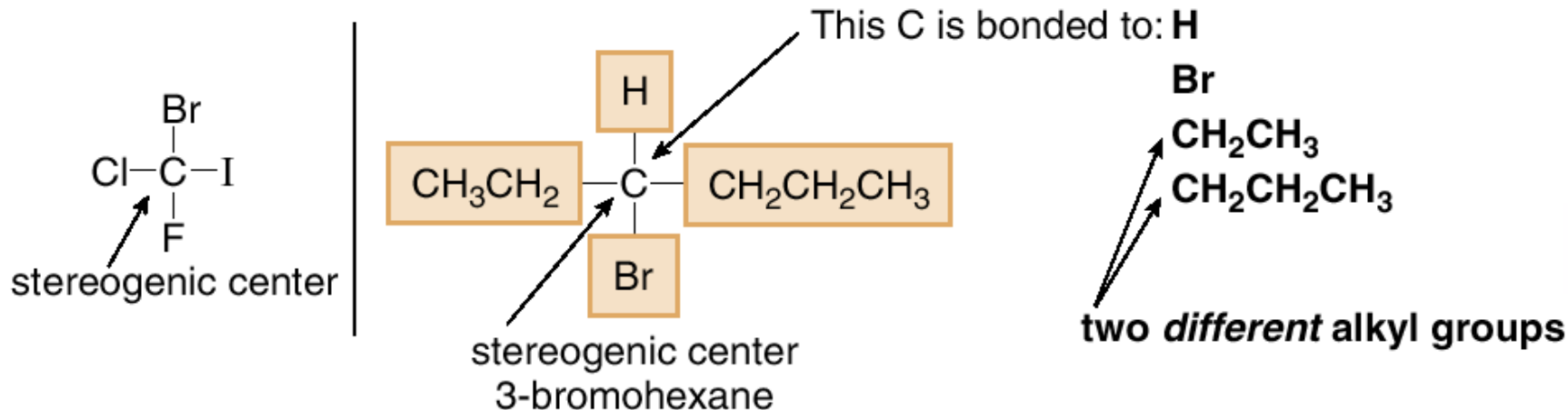
Z double bond
(Higher-ranked groups
are on the same side.)

Assign *E* or *Z* configuration to the following alkenes:



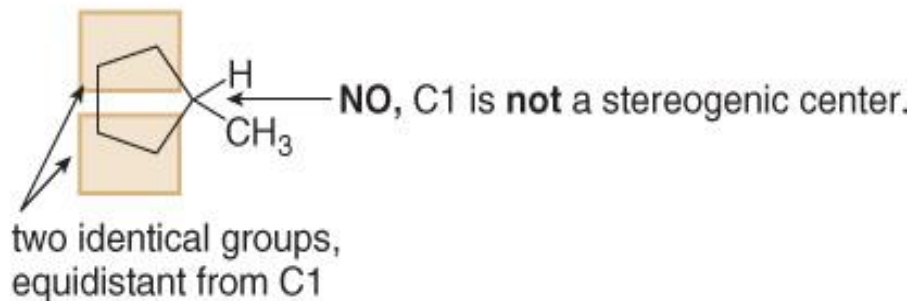
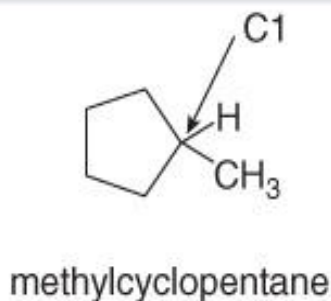
Stereogenic Centers:

- To locate a stereogenic center, examine each tetrahedral carbon atom in a molecule, and look at the four groups—not the four atoms—bonded to it.
- Always **omit from consideration** all C atoms that cannot be tetrahedral stereogenic centers. These include
 - ➡ CH_2 and CH_3 groups
 - ➡ Any sp or sp^2 hybridized C

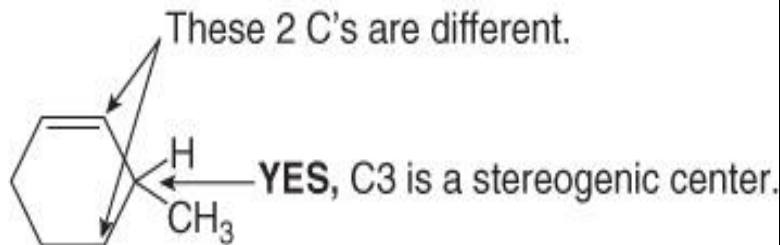
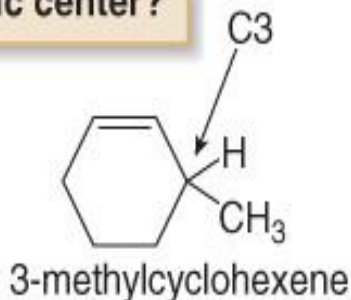


- ❖ Stereogenic centers may also occur at carbon atoms that are part of a ring.
- ❖ To find stereogenic centers on ring carbons, always draw the rings as flat polygons, and look for tetrahedral carbons that are bonded to four different groups.

Is C1 a stereogenic center?

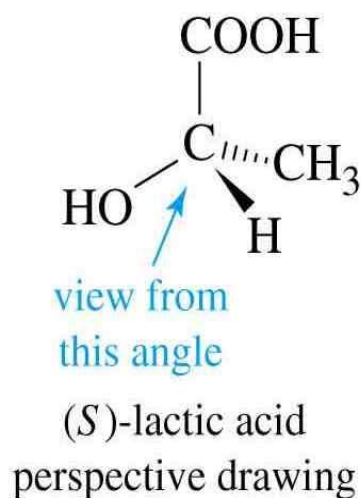


Is C3 a stereogenic center?

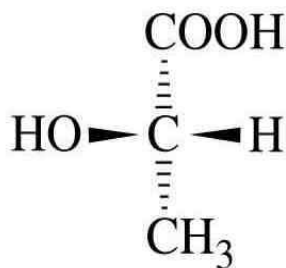


Fischer Projection:

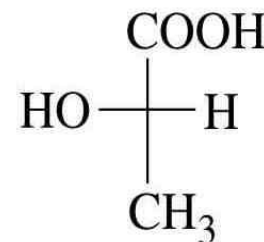
- ❖ In a Fischer projection of a chiral carbon and its mirror image:
 - horizontal bonds project toward the viewer and
 - vertical bonds project away from the viewer.
- ❖ The test for non-superimposability is to slide one on top of the other or rotate 180° and attempt the same.
- ❖ Fischer projections of the two enantiomers of 2-butanol:



=



=

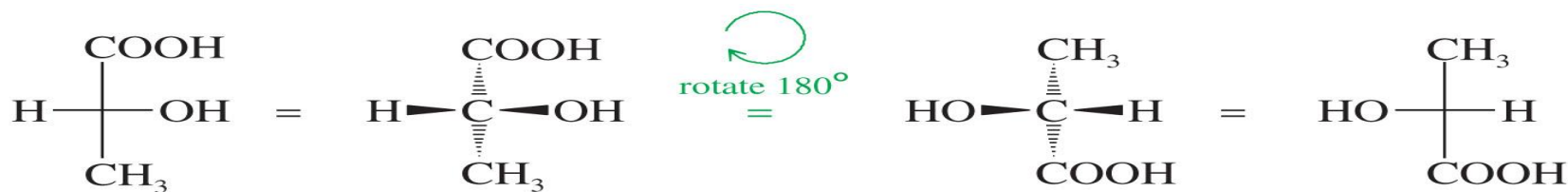


(S)-lactic acid
Fischer projection

Fischer Rules

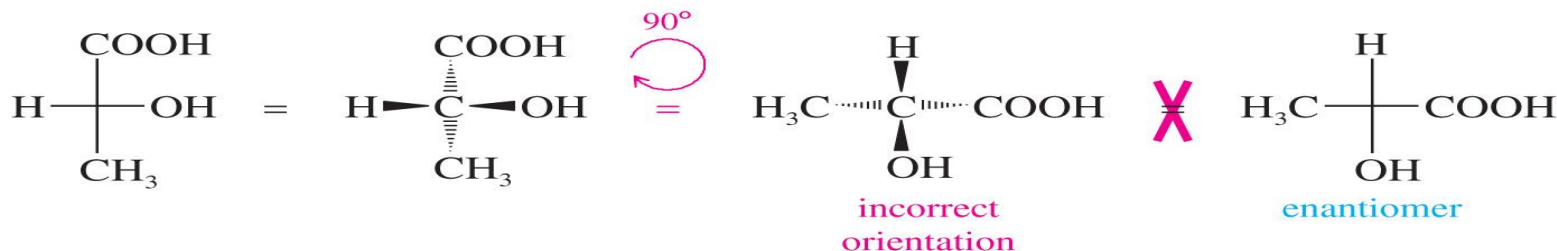
- Carbon chain is on the vertical line.
- Highest oxidized carbon is at top.
- Rotation of 180° in plane doesn't change molecule.
- Rotation of 90° is NOT allowed.

180° Rotation



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

90° Rotation



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

Labeling Stereogenic Centers with *R* or *S*

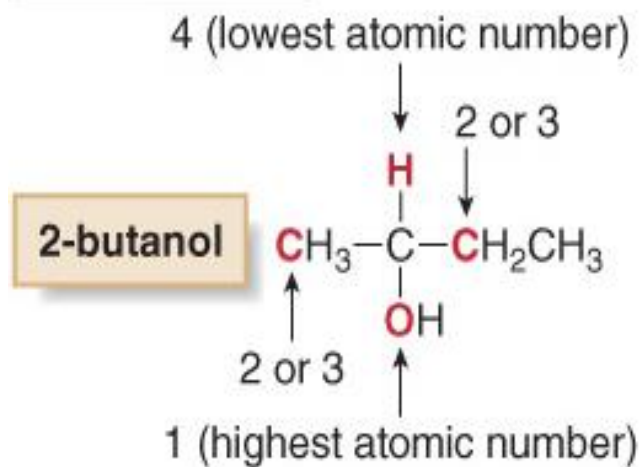
- ❖ Since enantiomers are two different compounds, they need to be distinguished by name. This is done by adding the prefix *R* or *S* to the IUPAC name of the enantiomer.
- ❖ Naming enantiomers with the prefixes *R* or *S* is called the **Cahn-Ingold-Prelog** system.
- ❖ To designate enantiomers as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

To assign an R or S configuration

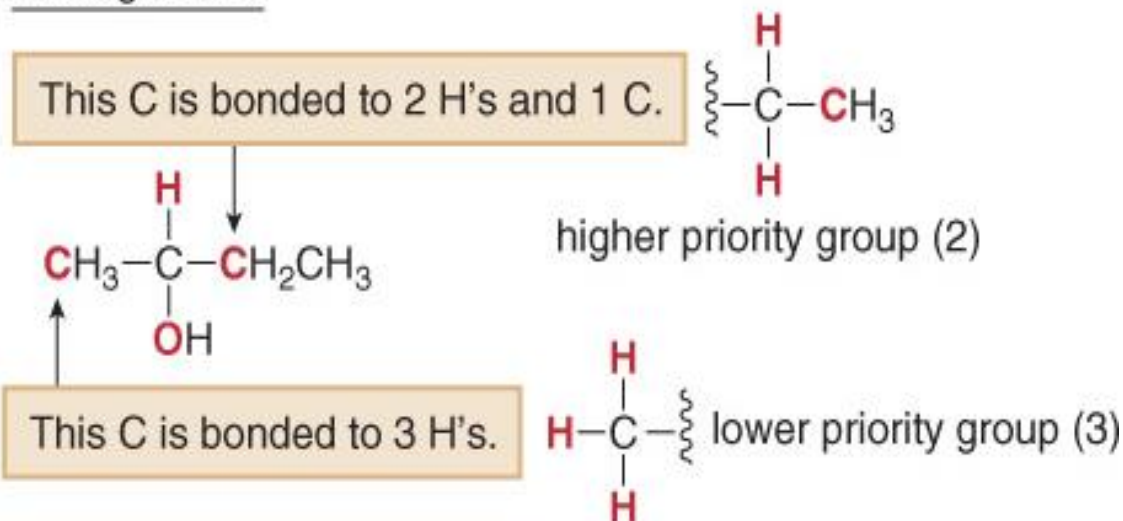
1. assign a priority from 1 (highest) to 4 (lowest) to each group bonded to the stereocenter
2. orient the molecule in space so that the group of lowest priority (4) is directed away from you; the three groups of higher priority (1-3) then project toward you
3. read the three groups projecting toward you in order from highest (1) to lowest (3) priority
4. if reading the groups 1-2-3 is **clockwise**, the configuration is **R**; if reading them is **counterclockwise**, the configuration is **S**

- ❖ 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.

Following rule 1:



Adding rule 2:

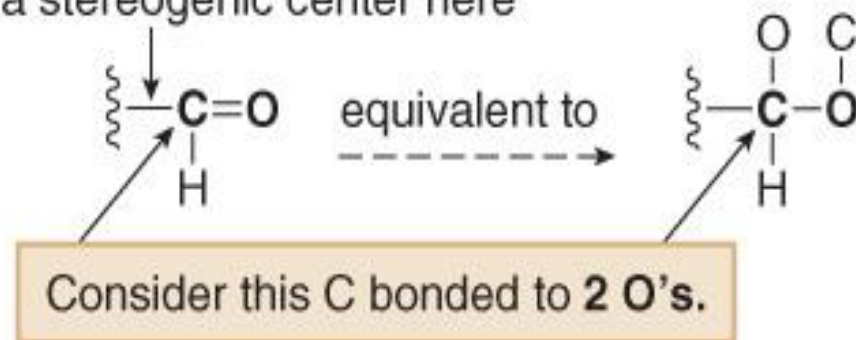


- ❖ If two isotopes are bonded to the stereogenic center, assign priorities in order of decreasing **mass number**. Thus, in comparing the three isotopes of hydrogen, the order of priorities is:

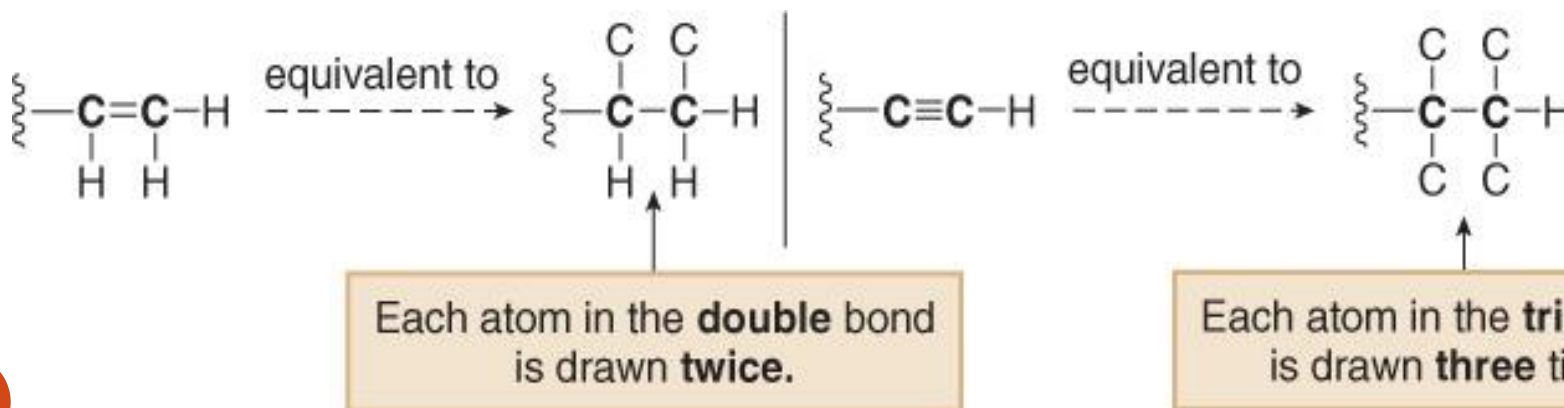
	Mass number	Priority
T (tritium)	3 (1 proton + 2 neutrons)	1
D (deuterium)	2 (1 proton + 1 neutron)	2
H (hydrogen)	1 (1 proton)	3

- ❖ 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.

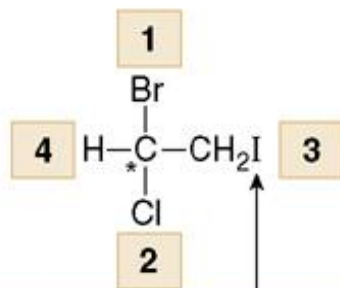
bonded to a stereogenic center here



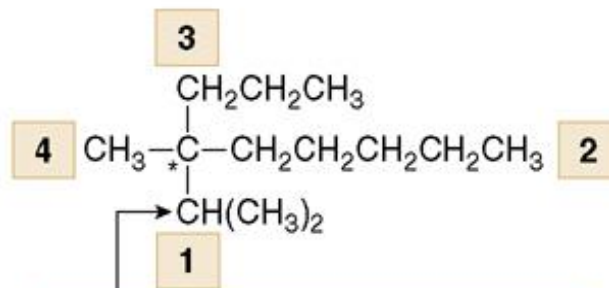
- ❖ Other common multiple bonds are drawn below:



Examples of assigning priorities to stereogenic centers



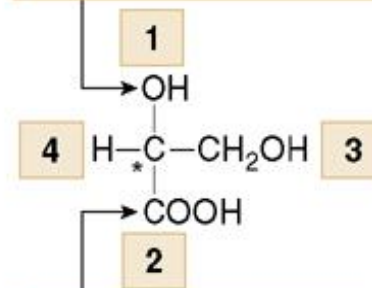
I is NOT bonded directly to the stereogenic center.



This is the highest priority C since it is bonded to 2 other C's.

[* = stereogenic center]

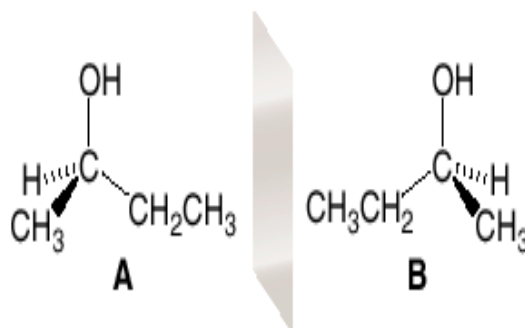
highest atomic number = highest priority



This C is considered bonded to 3 O's.

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

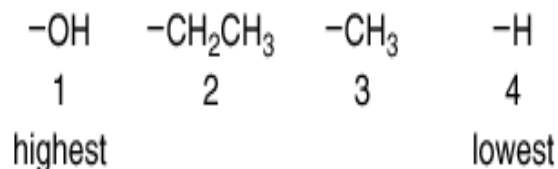
Example Label each enantiomer as *R* or *S*.



two enantiomers of 2-butanol

Step [1] Assign priorities from 1 to 4 to each group bonded to the stereogenic center.

- The priorities for the four groups around the stereogenic center in 2-butanol were given in Rule 2, on page 172.

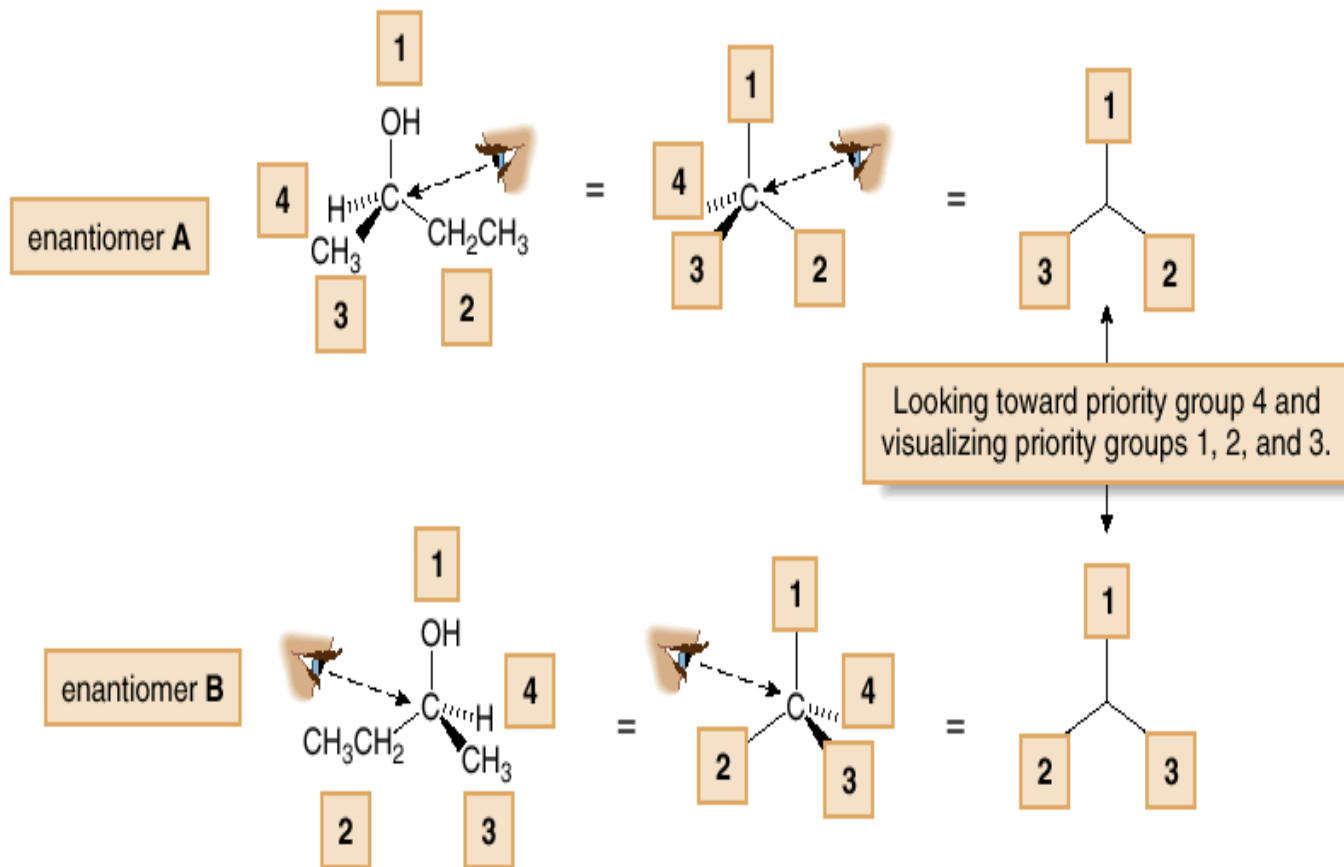


Decreasing priority

How To, continued . . .

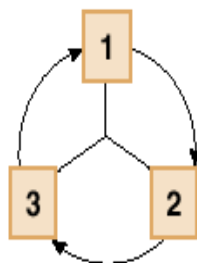
Step [2] Orient the molecule with the lowest priority group (4) *back* (on a *dash*), and visualize the relative positions of the remaining three groups (priorities 1, 2, and 3).

- For each enantiomer of 2-butanol, look toward the lowest priority group, drawn behind the plane, down the C–H bond.



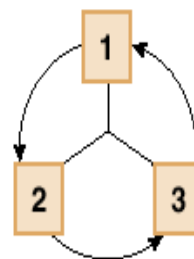
Step [3] Trace a circle from priority group 1 \rightarrow 2 \rightarrow 3.

- If tracing the circle goes in the **clockwise** direction—to the right from the noon position—the isomer is named **R**.
- If tracing the circle goes in the **counterclockwise** direction—to the left from the noon position—the isomer is named **S**.



clockwise

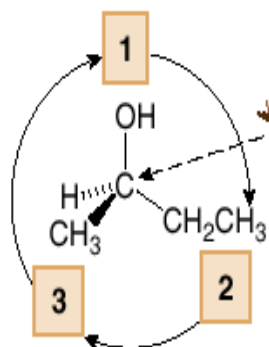
R isomer



counterclockwise

S isomer

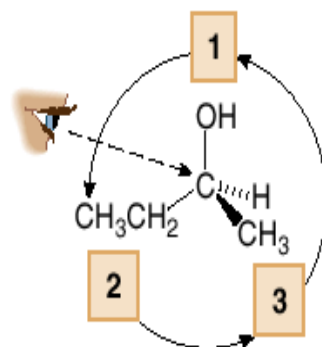
- The letters *R* or *S* precede the IUPAC name of the molecule. For the enantiomers of 2-butanol:



clockwise

R isomer

Enantiomer A is
(R)-2-butanol.

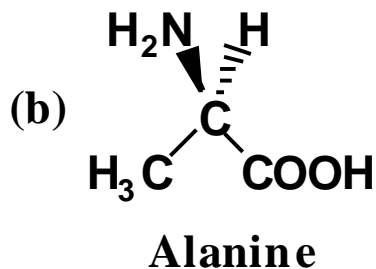
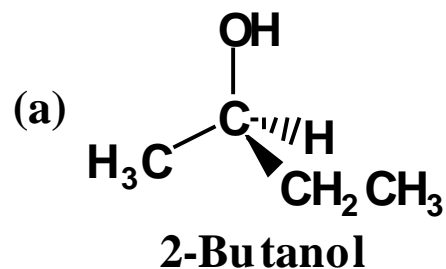


counterclockwise

S isomer

Enantiomer B is
(S)-2-butanol.

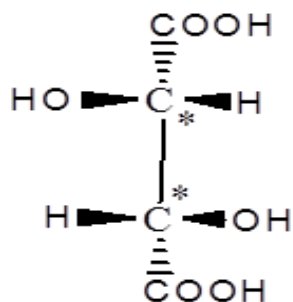
- **Example:** assign an R or S configuration to each stereocenter



More than Two Stereocenters (multi asymmetric centers)

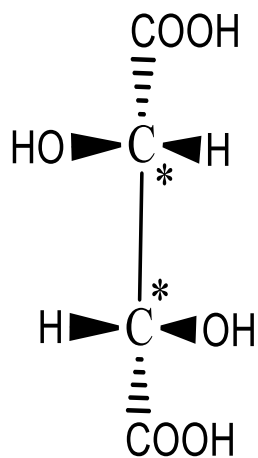
- ❖ For a molecule with n stereocenters, the maximum number of stereoisomers possible are 2^n
 - A molecule with one stereocenter has $2^1 = 2$ stereoisomers (one pair of enantiomers) possible
 - A molecule with two stereocenters has a maximum of $2^2 = 4$ possible stereoisomers (two pairs of enantiomers)
 - A molecule with three stereocenters has a maximum of $2^3 = 8$ possible stereoisomers (four pairs of enantiomers)
 - etc.

- Example

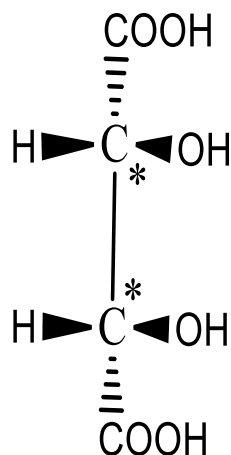


- ✓ in tartaric acid there are two stereogenic centers. This means $2^2 = 4$ isomers are present
- ✓ To obtain the 4 isomers interchange groups present on the horizontal line

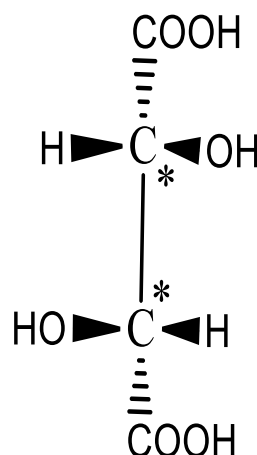
- There are four isomers



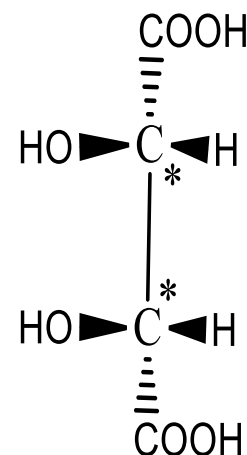
(A)



(B)



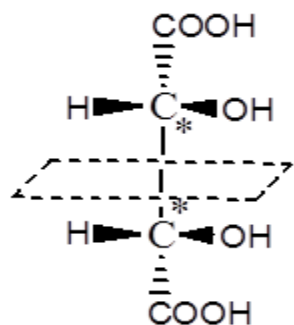
(C)



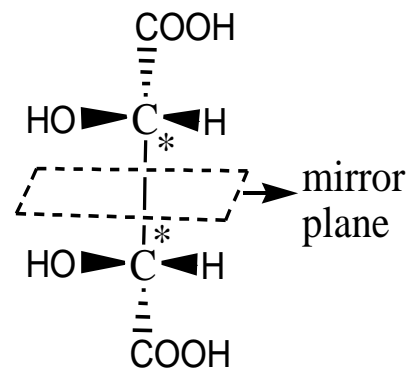
(D)

- Meso compounds

- Are isomers that superimpose on their mirror image when an internal mirror plane is place on half of the isomer
- Half of the compound is the same as the other half part of this isomer
- Are achiral
- B or D are the basic examples
- B & D are identical isomers .Totally the isomers will reduce to three from 4



isomer-2 (B)

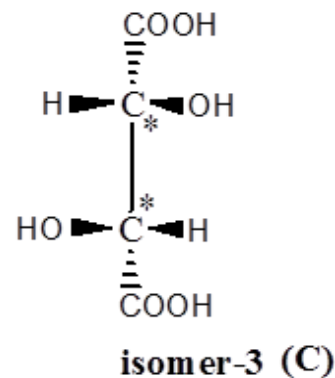
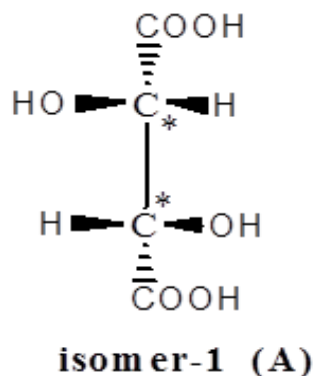


isomer-4 (D)

- Configuration: **2R,3S** **2S,3R**
- Half of the compound(top part) super impose on the other half this compound(bottom part)

- Enantiomers

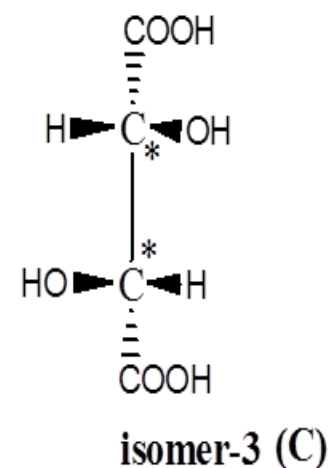
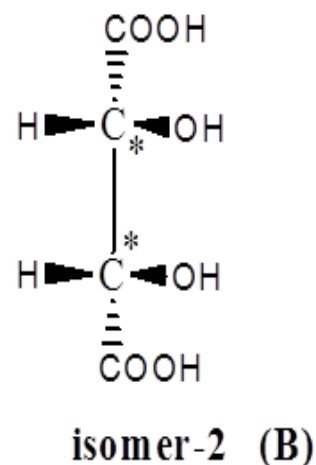
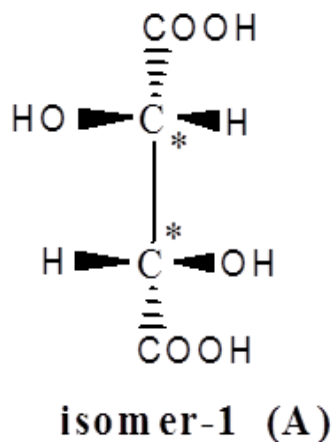
- are isomers that are non superposable on their mirror images
- Two enantiomers Have opposite absolute configuration (RR & SS)
- Are chiral
- (A) and (C) see the previous slide



- Configuration : 2S,3S 2R,3R
- Place mirror image between the two and you confirm that both are mirror image to each.
- Also they are not superimposable on each other

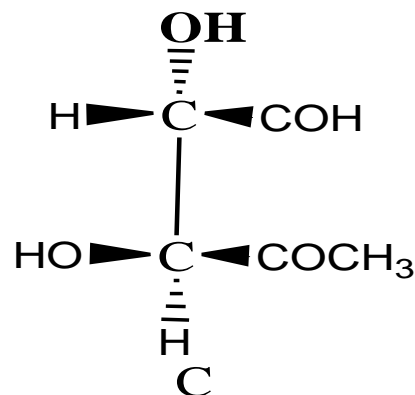
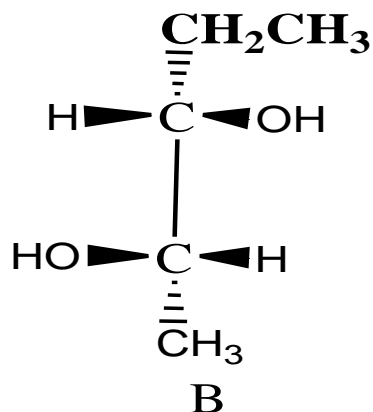
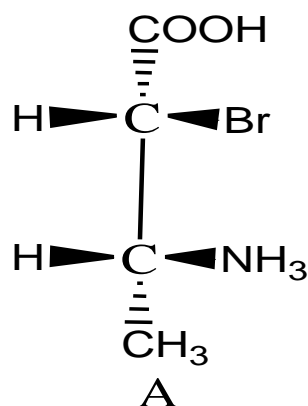
- Diastereomers

- Are isomers that are superimposable on their mirror images
- Two diastereomers have at least one opposite configuration (i.e RR & SR or RR & RS)
- Are achiral
- Since $B = D$ pairs of diastereomers are A & B , C & B



- Configuration: **2S,3S** **2R,3S** **2R,3R**

❖ For the following compounds

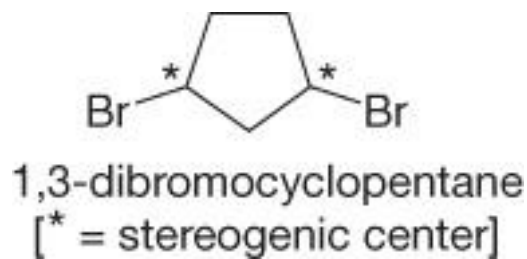


- Indicate the stereogenic carbon for each
- Draw the possible(reduced) isomers for each
- Write possible configuration
- Identify the pairs of
 - Enantiomers
 - Diastereomers
 - Meso compounds (if present)

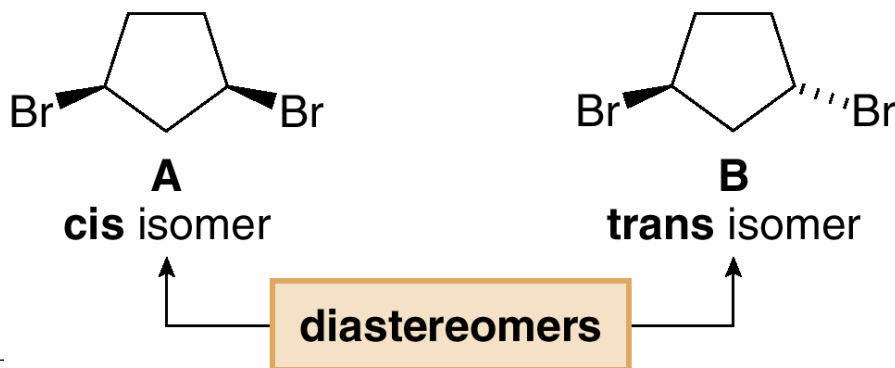
Stereochemistry

Disubstituted Cycloalkanes:

- Consider 1,3-dibromocyclopentane. Since it has two stereogenic centers, it has a maximum of four stereoisomers.



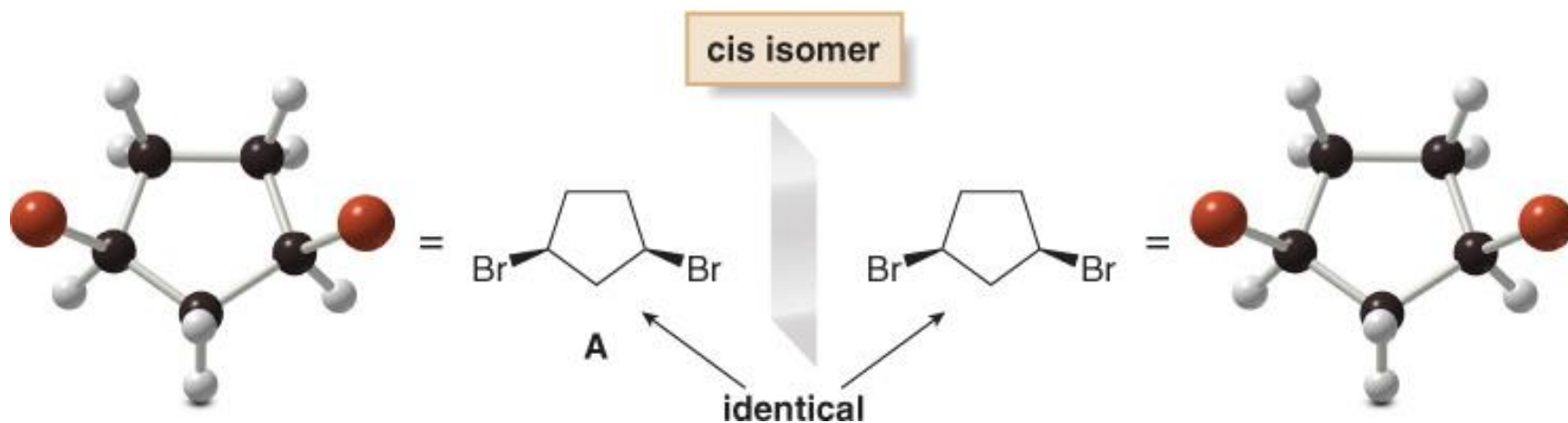
- Recall that a disubstituted cycloalkane can have two substituents on the same side of the ring (*cis* isomer, A) or on opposite sides of the ring (*trans* isomer, B). These compounds are stereoisomers but not mirror images.



Stereochemistry

Disubstituted Cycloalkanes:

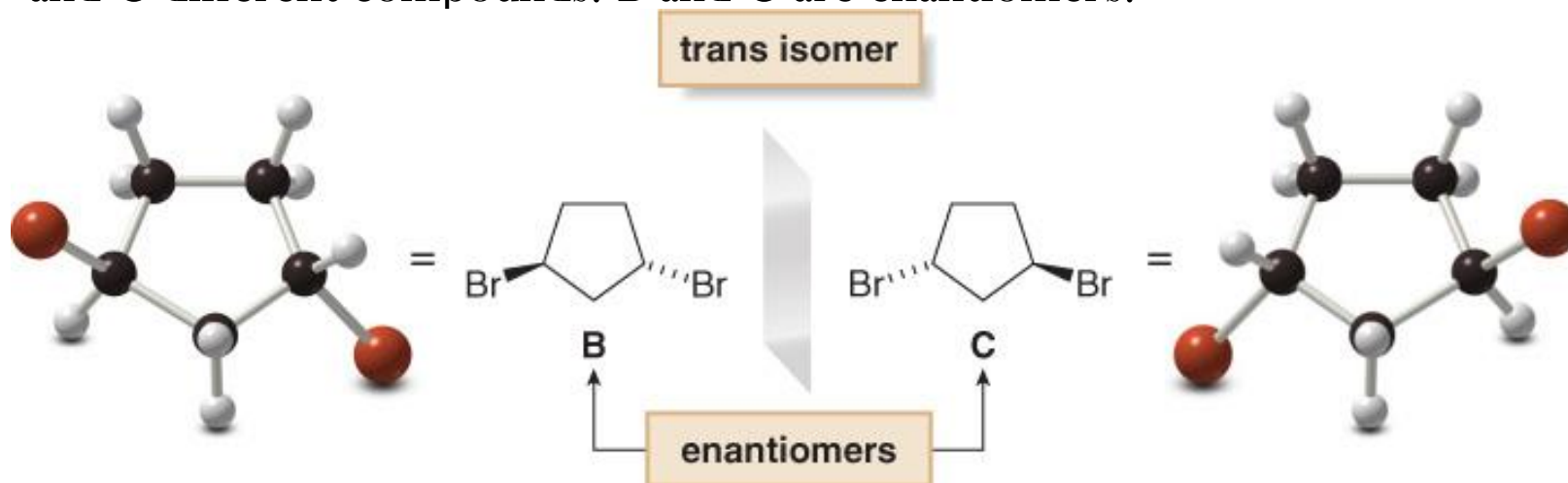
- To find the other two stereoisomers if they exist, draw the mirror images of each compound and determine whether the compound and its mirror image are superimposable.



- The *cis* isomer is superimposable on its mirror image, making the images identical. Thus, A is an achiral **meso compound**.

Disubstituted Cycloalkanes:

- The trans isomer is not superimposable on its mirror image, labeled C, making B and C different compounds. B and C are enantiomers.

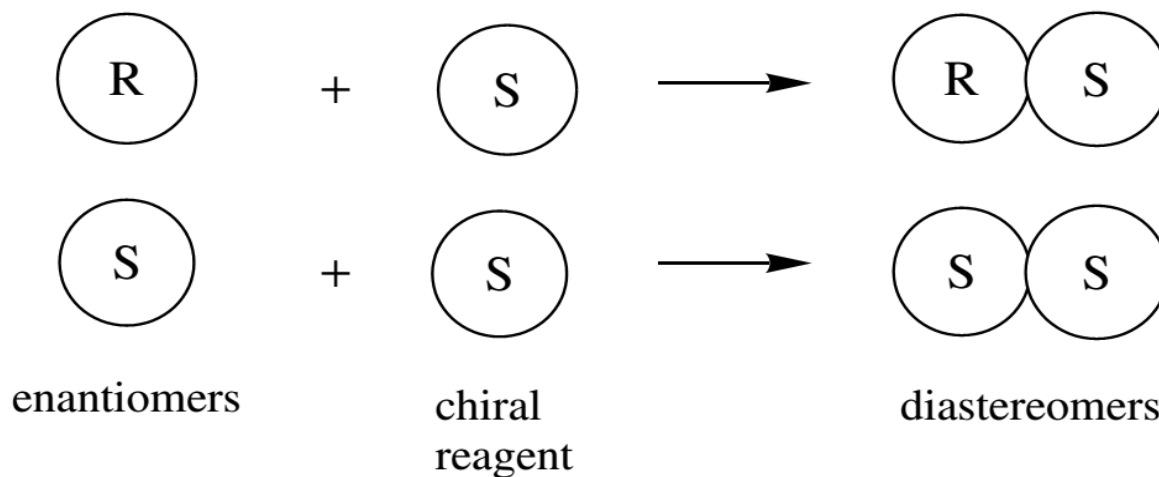


- Because one stereoisomer of 1,3-dibromocyclopentane is superimposable on its mirror image, there are only three stereoisomers, not four.

RESOLUTION OF ENANTIOMERS

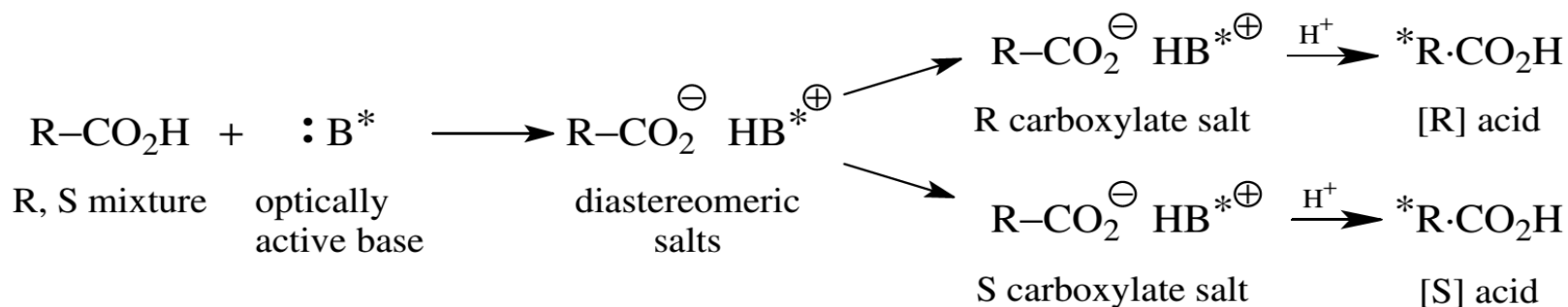
(RACEMIC MIXTURES)

- individual enantiomers have **identical physical properties** and only can be distinguished in a **chiral environment**. Plane-polarized light is such a chiral environment, and one enantiomer is dextrorotatory and one is levorotatory.
- Another way to distinguish **enantiomers** is to allow them to **react (or interact)** with other **chiral molecules**.
- The interaction of a **mixture** of **enantiomers** with a **single enantiomer** of a **chiral** molecule produces a **mixture of diastereomers** as following.

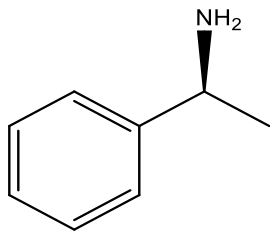


- Since **diastereomers** have **different physical properties**, they can be separated on the basis of those **physical properties**.

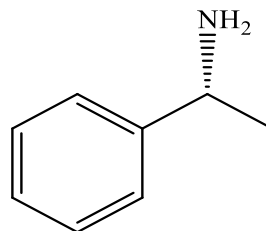
- **Crystallization** is the one the techniques that is usefull to sparate the diastereomers produced from a racemic mixture and a chiral resolving agent.
- **For example**, racemic carboxylic acids can be treated with an optically active base and the resulting diastereomeric salts are separated by crystallization.
- The individual enantiomeric acids are then regenerated from the salts.



- racemic acids can be resolved using commercially available chiral bases such as 1-phenylethanamine

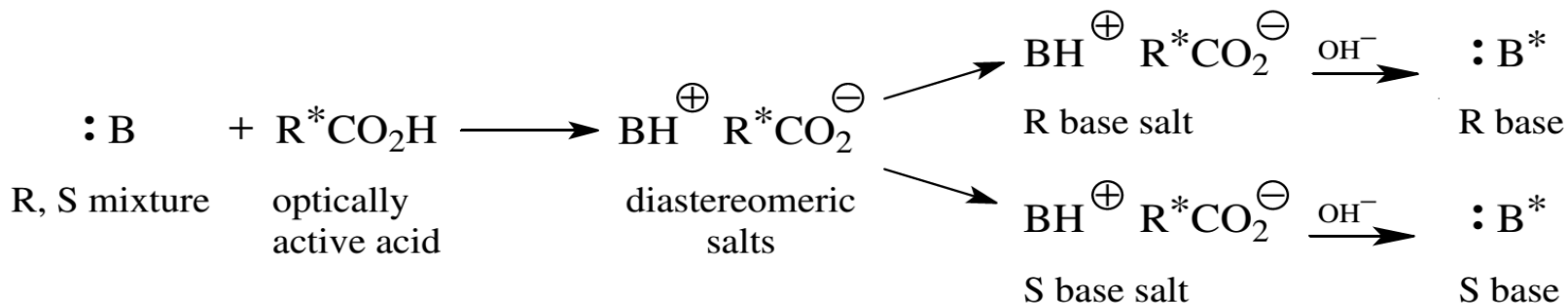


(S)-1-Phenylethanamine

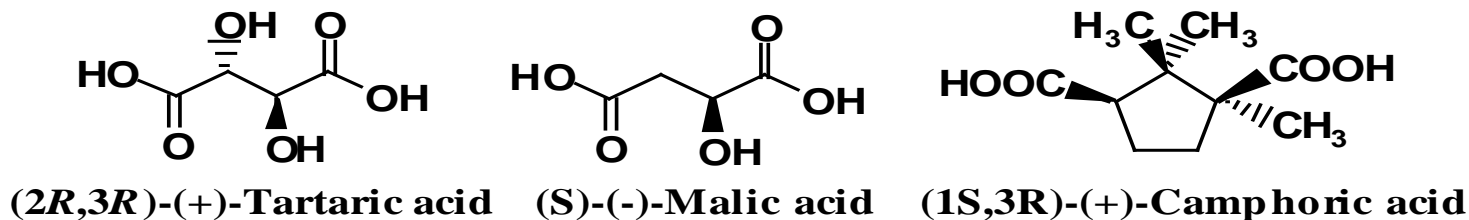


(R)-1-Phenylethanamine

- **Racemic bases** can be resolved by treating them with an **optically active acid** and separating the resulting **diastereomeric salts** by **fractional crystallization**.

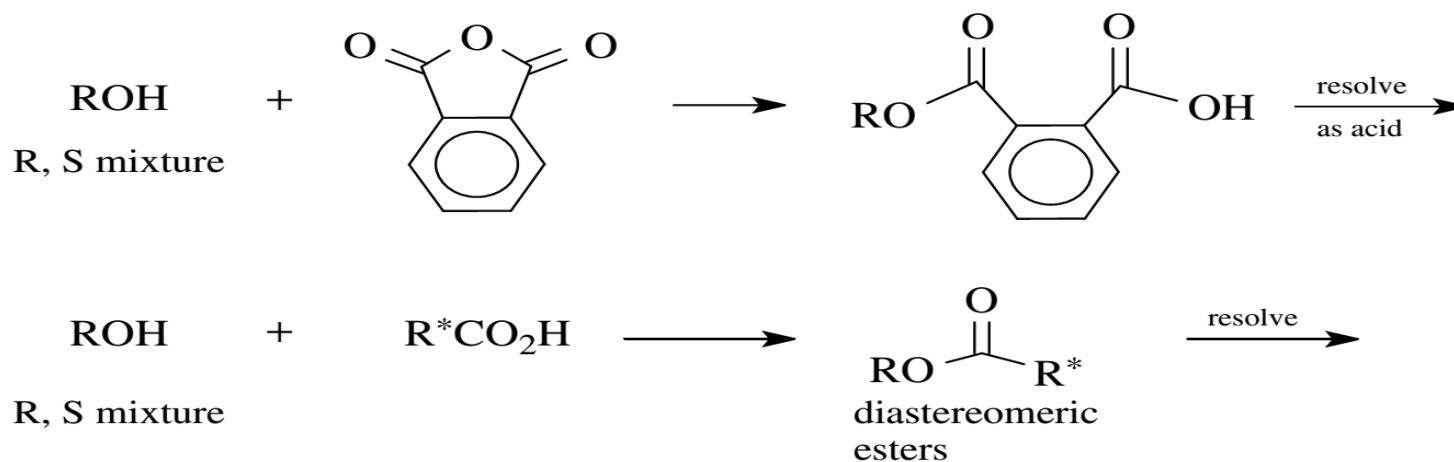


- The individual **enantiomeric bases** are regenerated from **the salts**.
- Common **acid-resolving agents** include **camphoric acid**, **tartaric acid**, **malic acid**, and **pyroglutamic acid**, among others.



- **Alcohols** are often resolved by conversion to **half esters** of **phthalic acid** or **succinic acid**, which are then resolved as typical **acids**.
- The **alcohol** is then regenerated from the resolved half ester by hydrolysis or reductive cleavage with LAH.

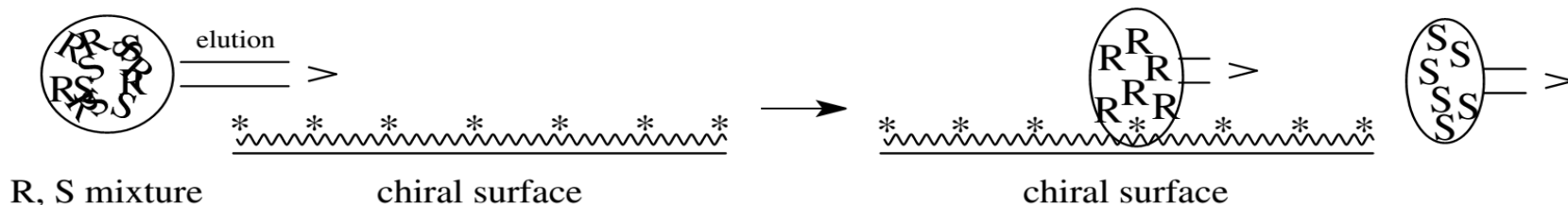
- **A second method** for resolving alcohols is to convert them to esters of optically active acids. This gives a mixture of diastereomeric esters which are separated by fractional crystallization and the alcohol is recovered by hydrolysis or reductive cleavage.



- **chromatography** is another major technique for separations

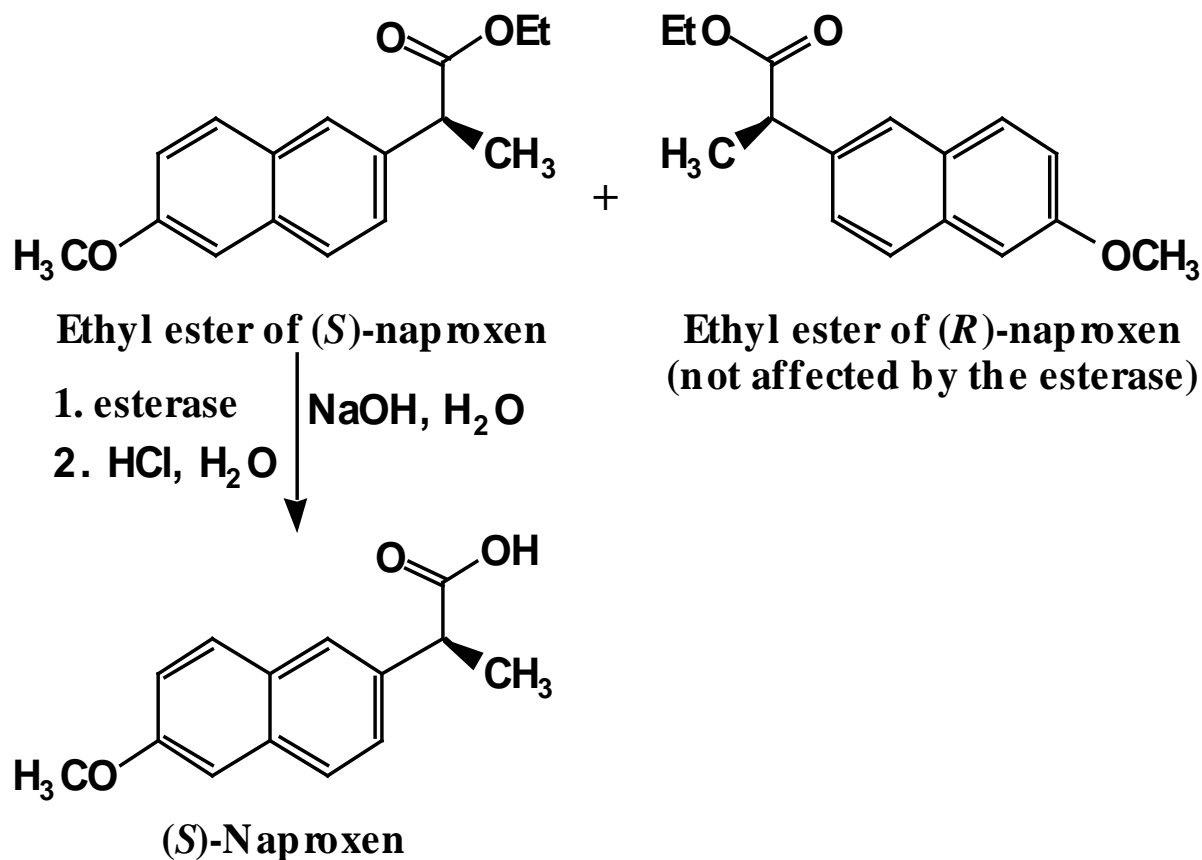
- has increasingly supplanted fractional crystallization as a way to separate diastereomeric compounds.
- Not only do **diastereomers** have different **solubilities**, they also interact with surfaces such as **silica gel** or **alumina differently**.
- The mixture of diastereomeric esters obtained by coupling a racemic alcohol to optically active acid can often be separated by
 - **high-performance liquid chromatography (HPLC),**
- Chromatography is often much **faster** and **more efficient** than crystallization. The individual alcohols can be regenerated in the usual fashion.

- **Chiral chromatography columns** are useful for the separation of a variety of compounds, including **amino acids**.
- A **chiral substance** is permanently attached to the column surface. If a mixture of enantiomers is passed over the surface, the individual enantiomers will interact with the chiral surface differently and thus will elute along the column at different rates.
- The **enantiomer** which interacts with the **surface more strongly** will elute **more slowly**.
- They can thus be **collected individually**. A variety of **chiral stationary phases** are available to separate an ever increasing number of examples.

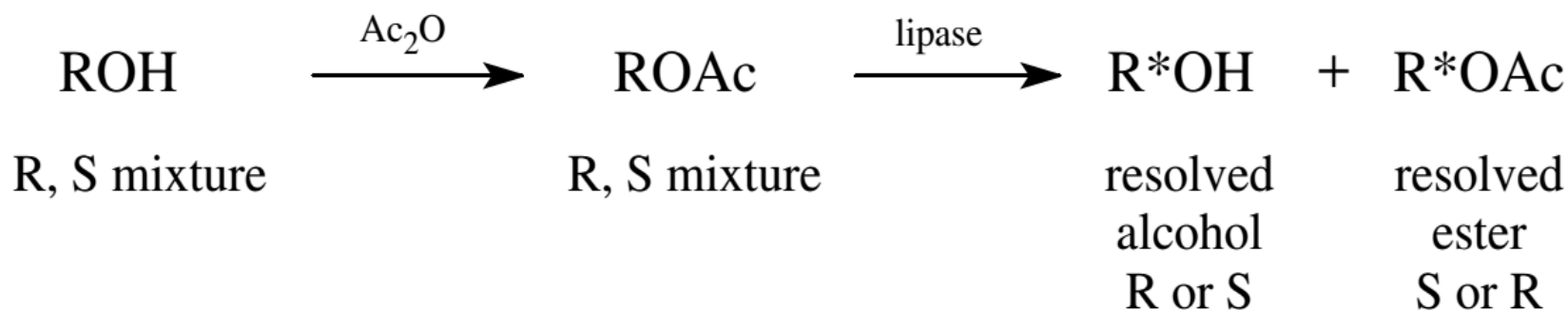


- Enzymes are the another popular method to resolve enantiomers.
- Enzymes are chiral catalysts** which often exhibit very high selectivity for one enantiomer of a racemic mixture.

Example



- Thus it is very easy to acetylate a racemic alcohol and treat the racemic mixture of acetates with a lipase.
- One enantiomer is hydrolyzed to the alcohol and the other remains as the ester. These are separated chromatographically and each component is obtained with high optical purity.



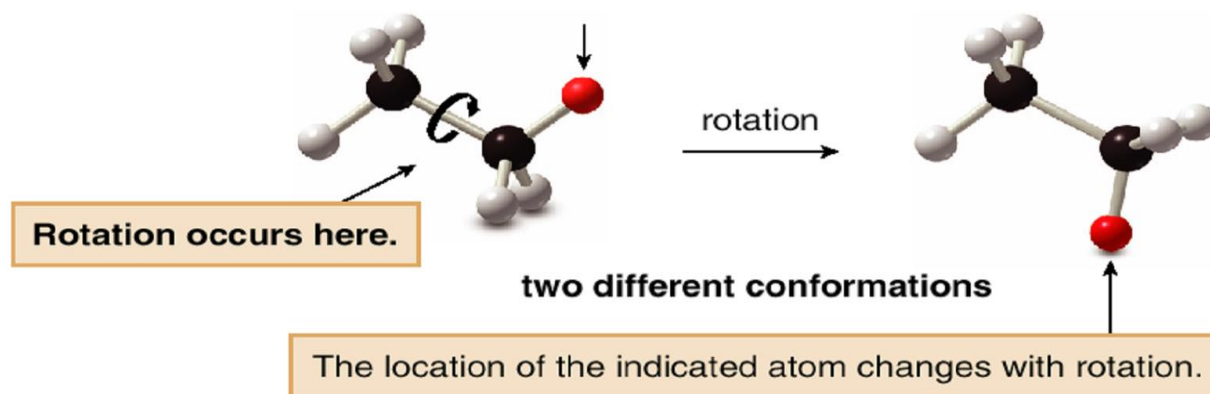
- The use of **kinetic resolution** to obtain a single enantiomer from a mixture of enantiomers is often useful for particular functional groups.
- Since individual enantiomers react at different rates with chiral reagents, treatment of a racemic mixture with a limited amount (0.5 equiv.) of a chiral reagent will convert one of the enantiomers to product in preference to the other.
- The efficiency of the kinetic resolution will depend on the relative rates of reaction of the two enantiomers.
- If rates of reaction (selectivity factor) vary by >100 , then the recovered enantiomer will be $>99\%$ optically pure. Lower selectivity factors will lead to less pure enantiomers.

- Optically active diisopinocampheylborane can be used to resolve racemic olefins. The reagent adds to one enantiomer, and the other is unchanged. Optical purities on the order of $\sim 37\text{--}65\%$ are possible.
- Chiral allylic alcohols can be resolved with chiral epoxidizing agents derived from tartrate complexes of titanium. One enantiomer is epoxidized and the other is not.
- Thus, the two alcohol enantiomers can be separated, one as the unsaturated alcohol and one as the epoxy alcohol.

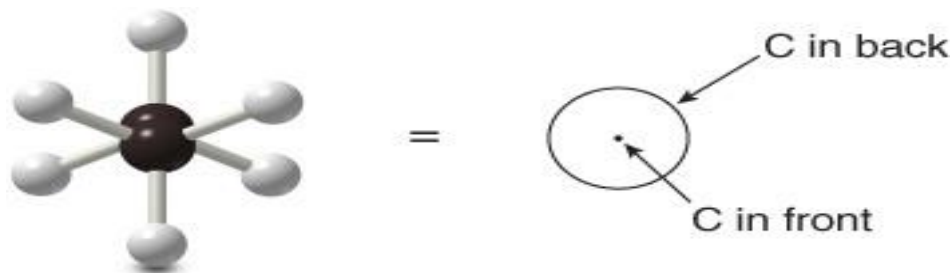
Conformational isomerism

Conformations of Acyclic Alkanes

- **Conformations** are different arrangements of atoms that are interconverted by rotation about single bonds.
- **Conformer**: a specific conformation of a molecule

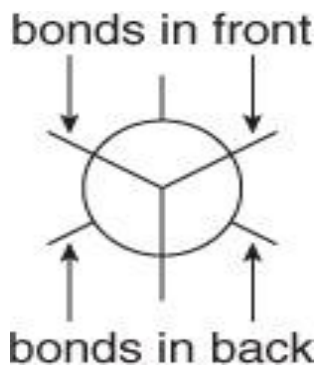


- End-on representations for conformations are commonly drawn using a convention called a **Newman projection**.
- **How to Draw a Newman Projection:**
- **Step 1.** Look directly down the C—C bond (end-on), and draw a circle with a dot in the center to represent the carbons of the C—C bond.



Step 2. Draw in the bonds.

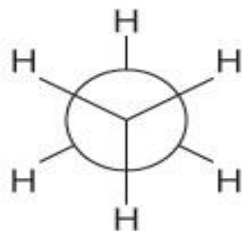
- Draw the bonds on the front C as three lines meeting at the center of the circle.
- Draw the bonds on the back C as three lines coming out of the edge of the circle.



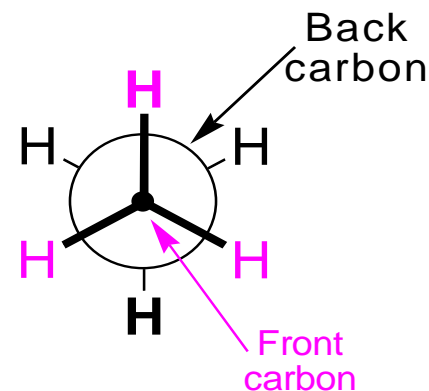
➤ Step 3. Add the atoms on each bond.



=



Each C has 3 H's in ethane.

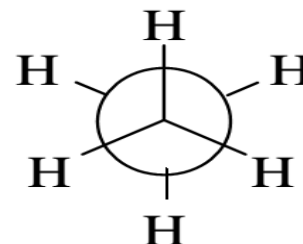
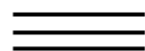
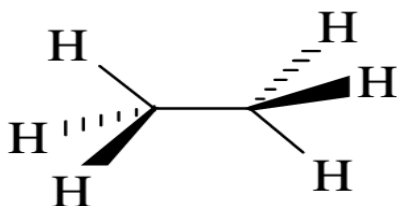
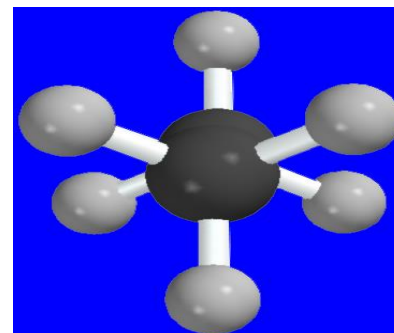
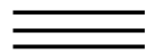
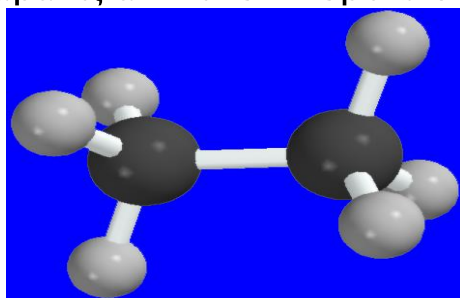


Conformation of ethane

- Ethane has two conformations
 - ☞ **Staggered conformation**
 - ☞ **Eclipsed conformation**

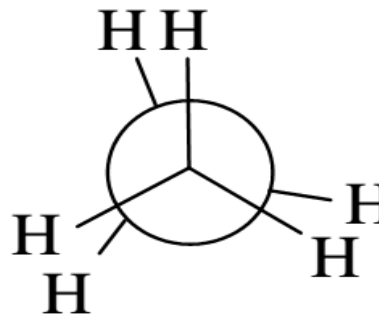
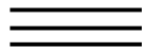
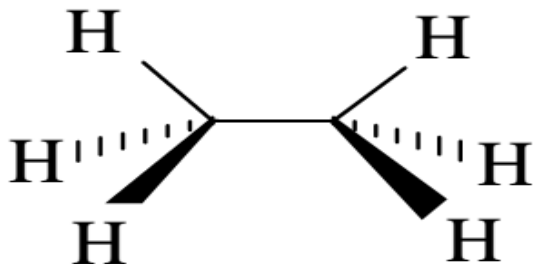
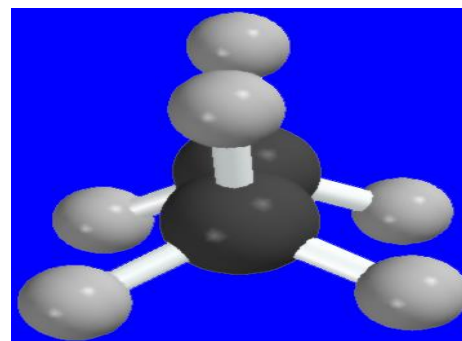
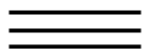
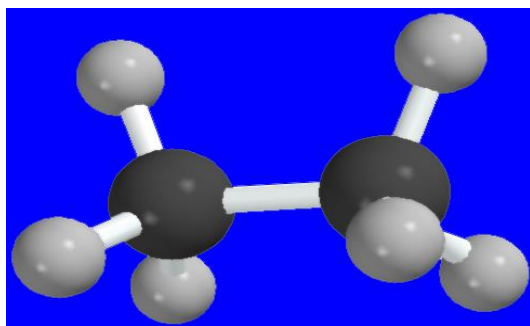
Staggered conformation

- The **lowest energy** conformation (synonymous with a conformational isomer) is the one in which the **C–H bonds** of each **methyl group** are staggered between the C–H bonds of the other **methyl group** across the σ bond.
- This is the lowest energy conformation because the electron clouds of the bonds are the farthest distance apart, and their repulsions are minimized.



Eclipsed conformation

- The highest energy conformation of ethane is the one in which the C–H bonds of each methyl group are eclipsed with the C–H bonds of the other methyl group across the σ bond.
- This is the highest energy because the electron clouds of the C–H bonds are as close as they can be, and their repulsions raise the energy of the molecule.



Eclipsed

- Dihedral (torsion) angle: angle between an atom (group) on the front atom of a Newman Projection and an atom (group) on the back atom
- Rotating the atoms on one carbon by 60° converts an eclipsed conformation into a staggered conformation, and vice versa.
- For ethane in the staggered conformation, the dihedral angle for the C—H bonds is 60° . For eclipsed ethane, it is 0° .
- Dihedral angles of ethanes:
 - ☞ Staggered conformation: 60° (gauche), 180° (anti), and 300° (-60° , gauche)
 - ☞ Eclipsed conformation: 0° , 120° , and 240° (-120°)

- The barrier (E_{act}) for a 120° rotation of ethane (from one staggered conformer to another) is 12 KJ/mol. The eclipsed conformer is the barrier to the rotation. An H-H eclipsing interaction = 4 KJ/mol
- Torsional Strain: strain (increase in energy) due to eclipsing interactions
- The eclipsed conformation of ethane is 12 kJ/mol less stable than the staggered.
- The eclipsed conformation is destabilized by torsional strain.
- Torsional strain is the destabilization that results from eclipsed bonds.

- An energy minimum and maximum occur every 60° as the conformation changes from staggered to eclipsed. Conformations that are neither staggered nor eclipsed are intermediate in energy.

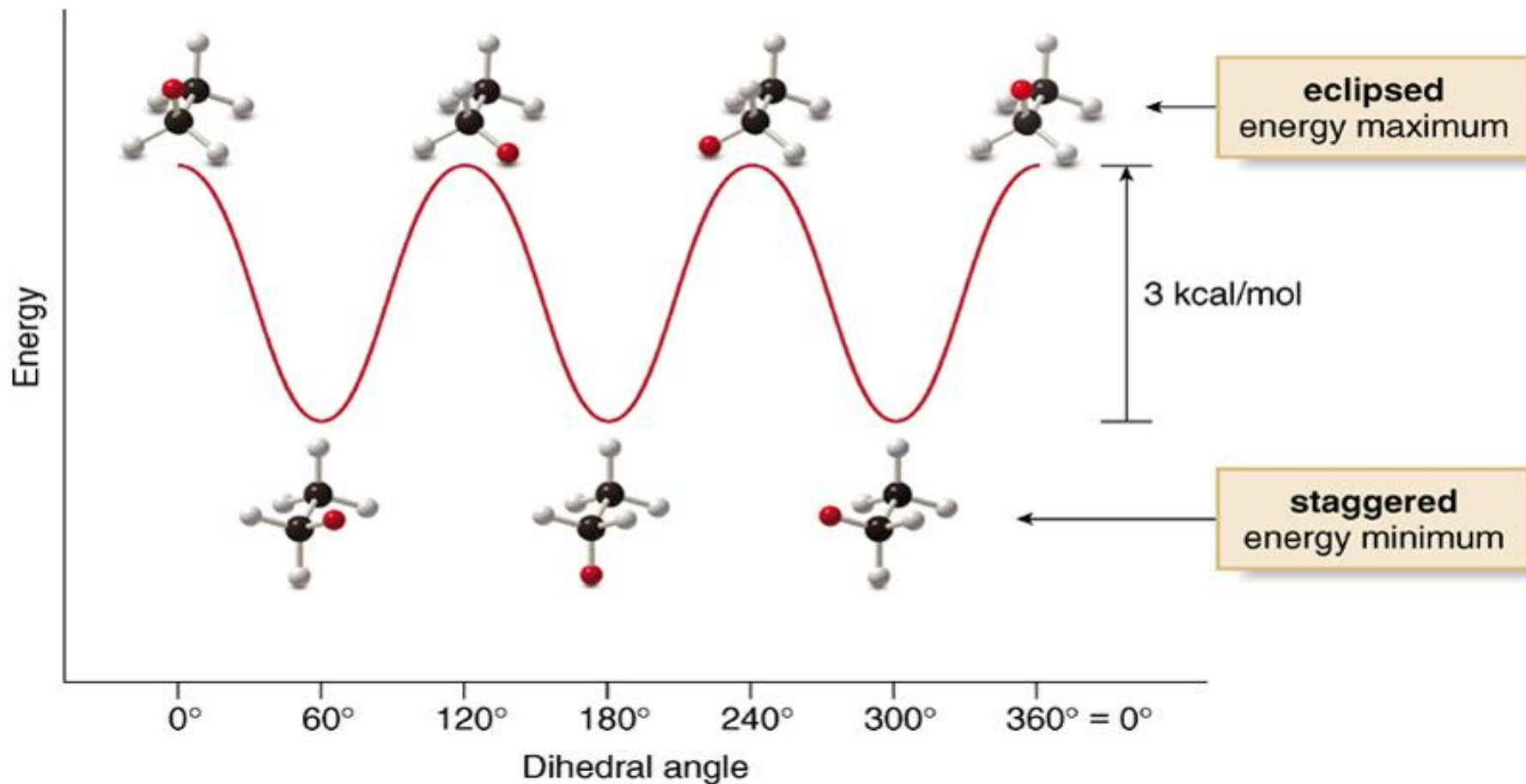
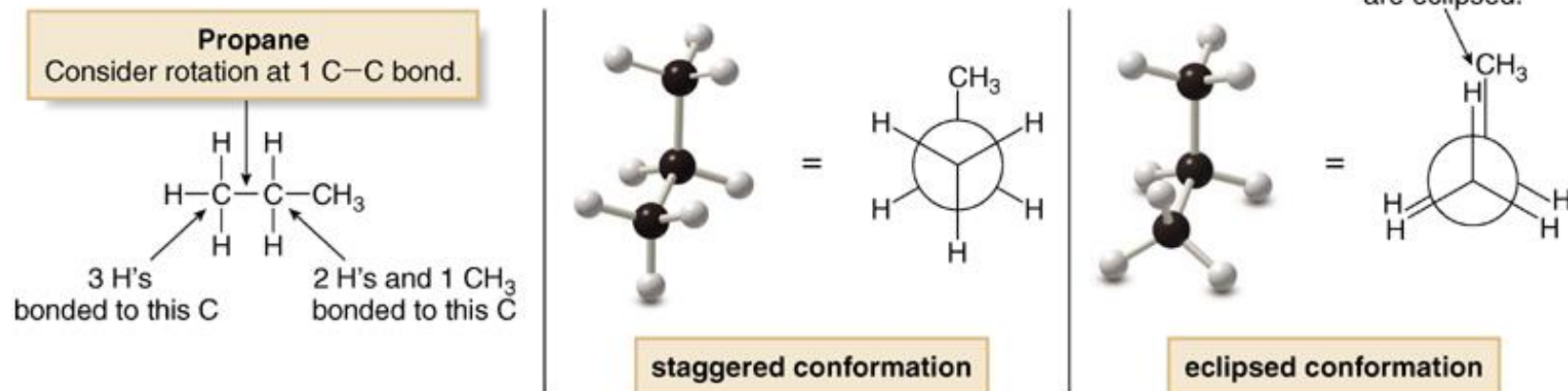


Figure : Energy vs. dihedral angle for ethane

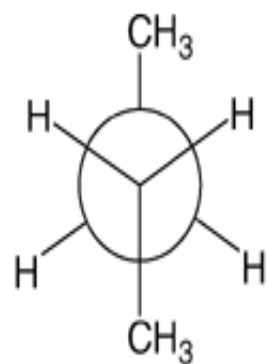
Conformation of propane



Conformation of butane

- Butane and higher molecular weight alkanes have several C—C bonds, all capable of rotation. It takes six 60° rotations to return to the original conformation.
 - Butane has three conformations
 - Anti
 - Guache
 - eclipsed
- staggered

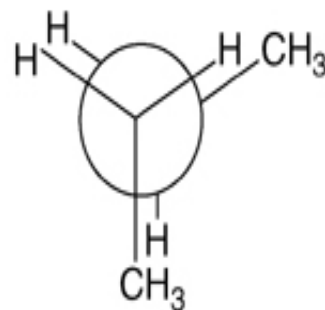
- A staggered conformation with two larger groups 180° from each other is called **anti**.
- A staggered conformation with two larger groups 60° from each other is called **gauche**.
- The staggered conformations are lower in energy than the eclipsed conformations.
- The relative energies of the individual staggered conformations depend on their steric strain.
- **Steric strain** is an increase in energy resulting when atoms are forced too close to one another.
- Gauche conformations are generally higher in energy than anti conformations because of steric strain.



1

staggered, anti

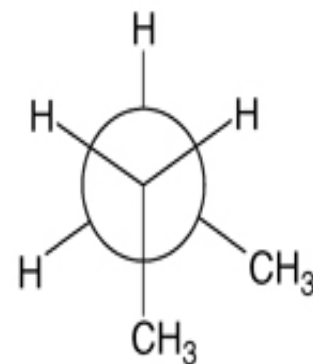
rotate
60°



2

eclipsed

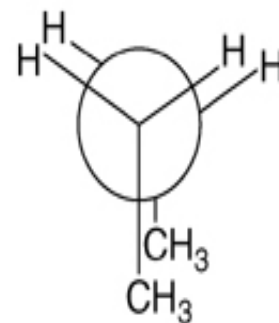
rotate
60°



3

staggered, gauche

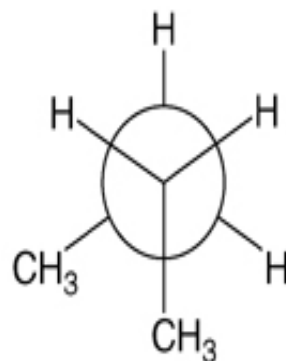
rotate
60°



4

eclipsed

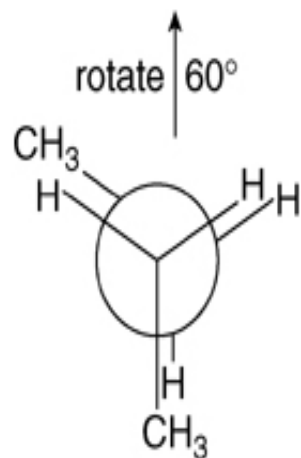
rotate
60°



5

staggered, gauche

rotate
60°



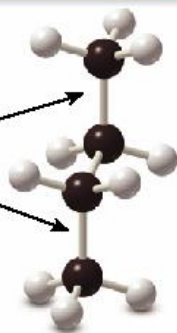
6

eclipsed

rotate
60°

Anti conformation

The 2 CH₃ groups are **180°** apart.

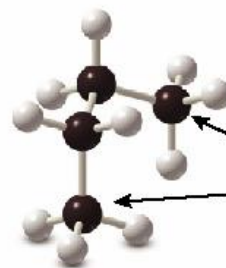


lower in energy
1

Gauche conformation

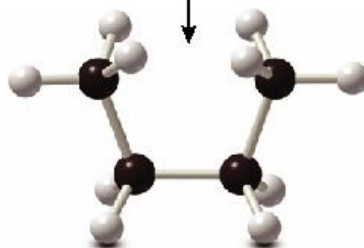
steric strain

The 2 CH₃ groups are only **60°** apart.



higher in energy
3

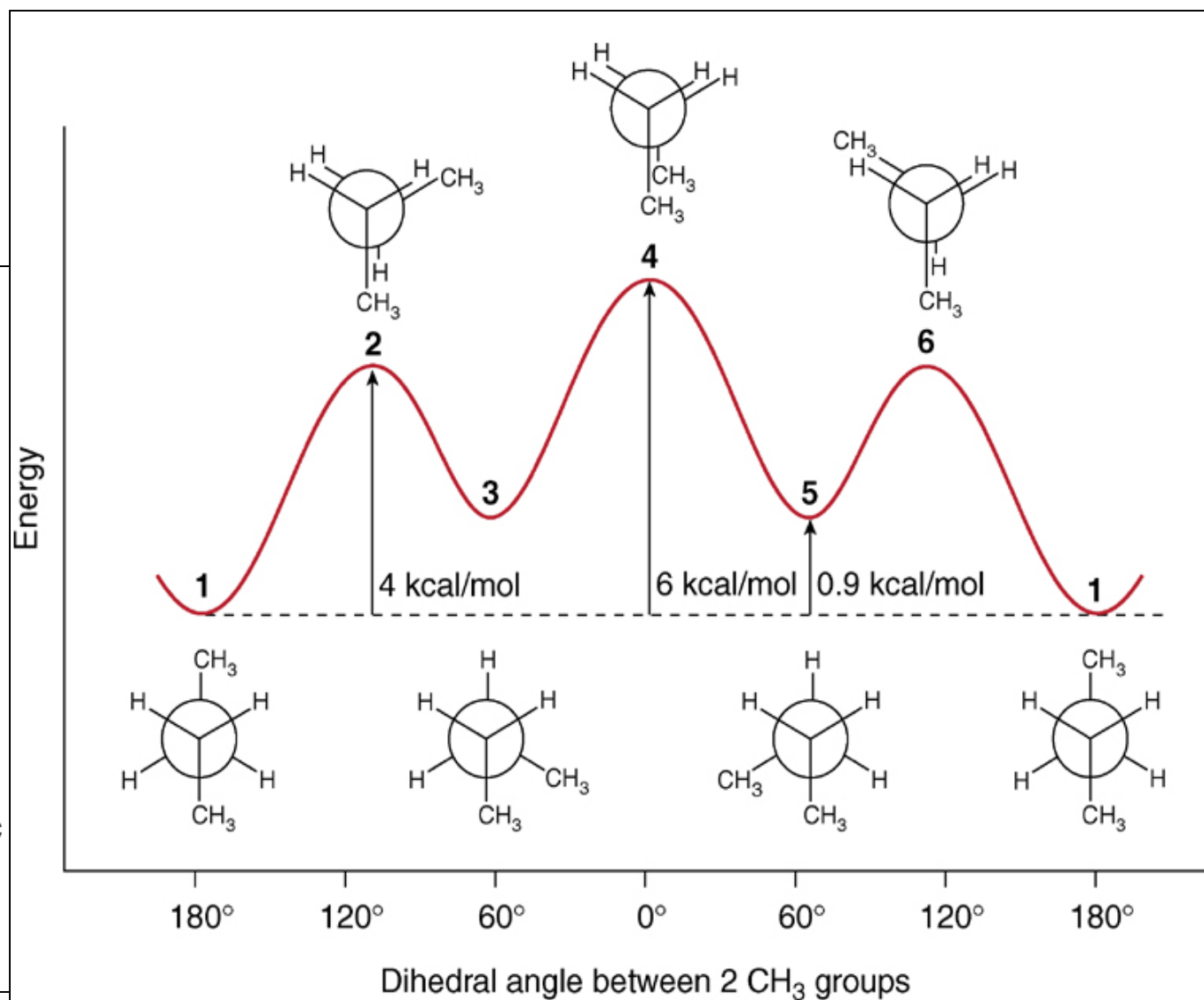
Steric strain caused by two eclipsed CH₃ groups



side view

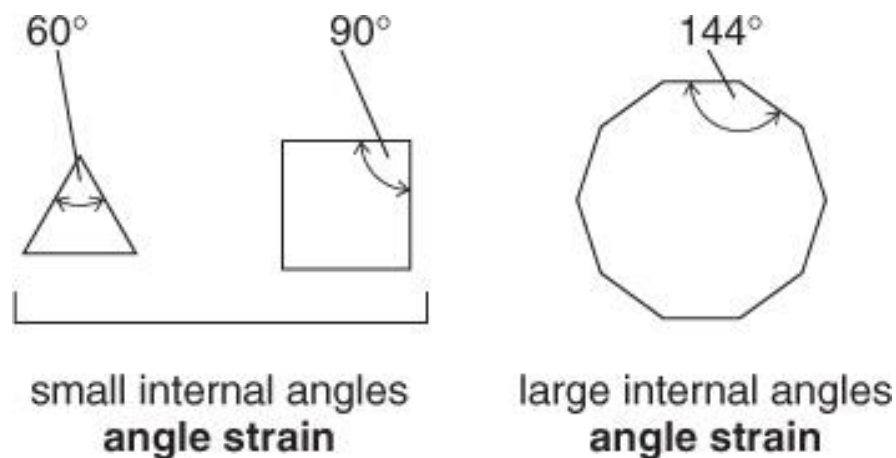
4

- Staggered conformations **1**, **3**, and **5** are at energy minima.
- Anti conformation **1** is lower in energy than gauche conformations **3** and **5**, which possess steric strain.
- Eclipsed conformations **2**, **4**, and **6** are at energy maxima.
- Eclipsed conformation **4**, which has additional steric strain due to two eclipsed CH_3 groups, is highest in energy.



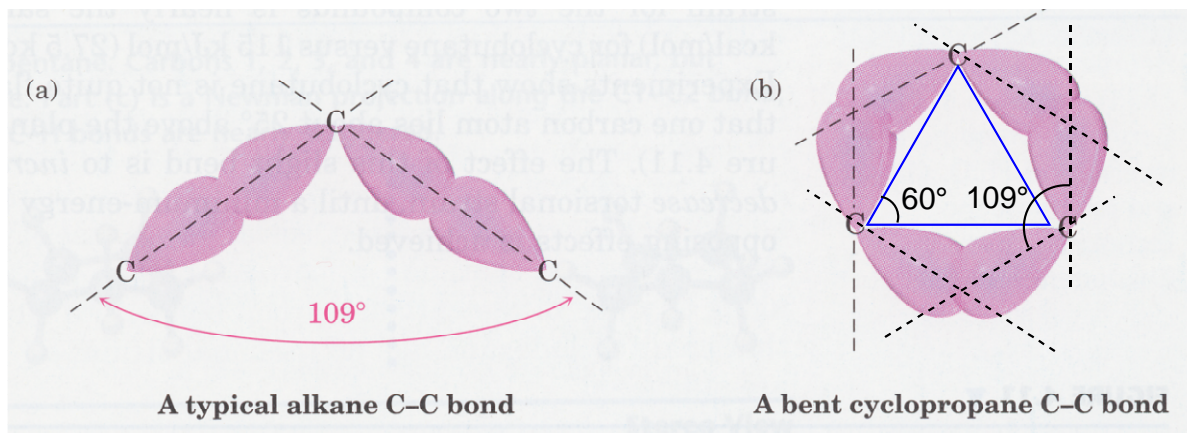
Conformation of cycloalkanes

- Besides torsional strain and steric strain, the conformations of cycloalkanes are also affected by **angle strain**.
- **Angle strain** is an increase in energy when bond angles deviate from the optimum tetrahedral angle of 109.5° .
- The **Baeyer strain theory** was formulated when it was thought that rings were flat. It states that larger rings would be very highly strained, as their bond angles would be very different from the optimum 109.5° .
- It turns out that cycloalkanes with more than three C atoms in the ring are not flat molecules. They are puckered to reduce strain.

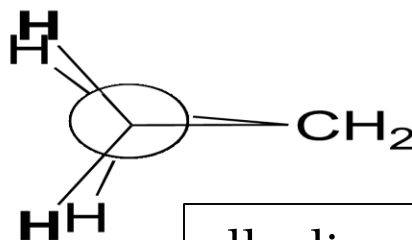


Conformation of Cyclopropane , Cyclobutane, cyclopentane and cyclobutane

- **Remember** :-Angle Strain is a strain that caused due to deforming a bond angle from its ideal value (Baeyer Strain Theory).
- Bonding in Cyclopropane: reduced overlap of the sp^3 -hybridized orbitals



- Total strain for cyclopropane = angle strain + torsional strain



all adjacent CH₂ groups are eclipsed

*END OF CHAPTER
THREE*