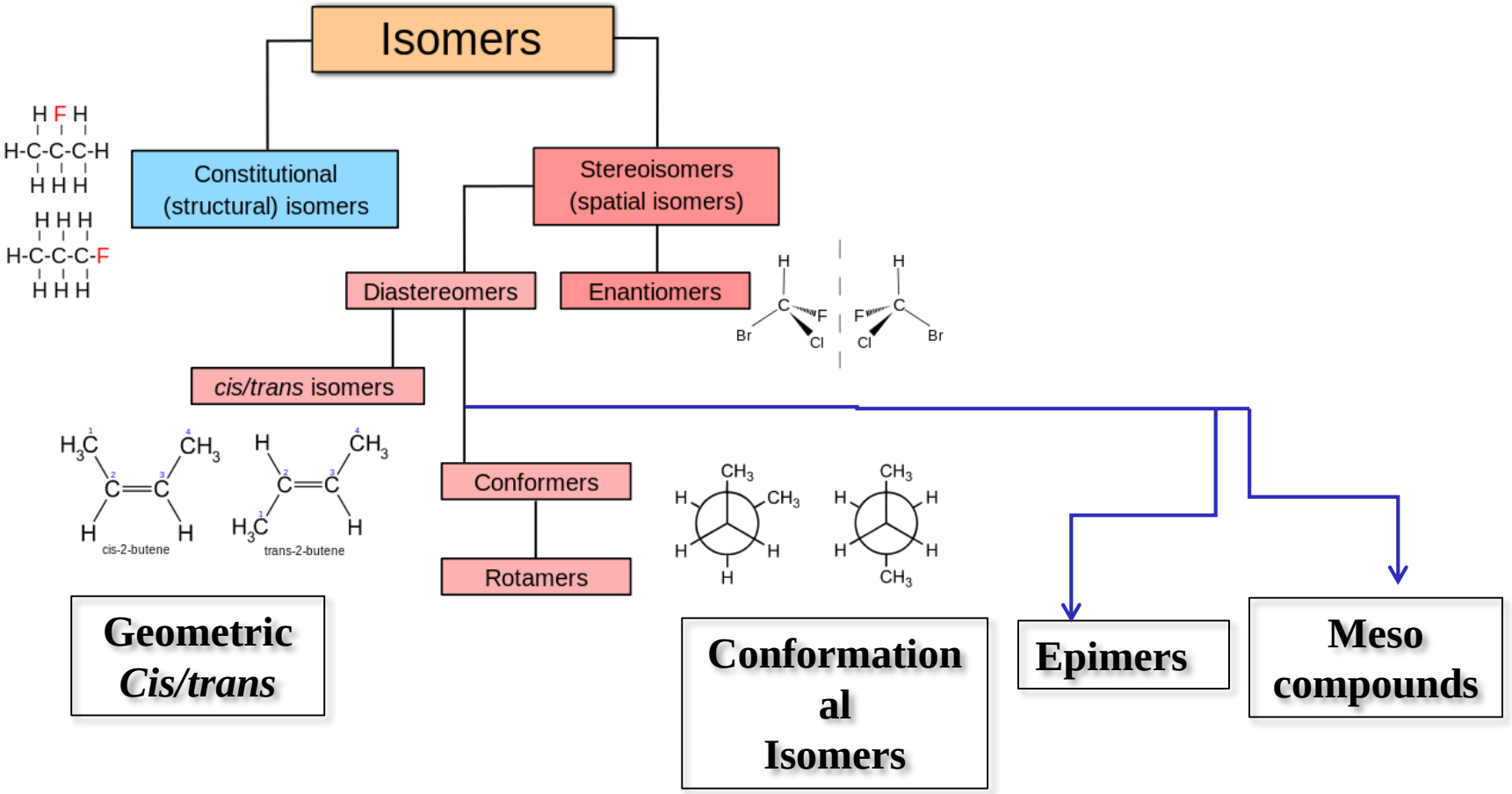
Stereochemistry

- Deals with:
  - Determination of the relative positions in space of atoms, groups of atoms
  - Effects of positions of atoms on the properties
- **Sterical structure:**
  - **Constitution**
  - **Configuration**
  - **Conformation**

Stereochemistry

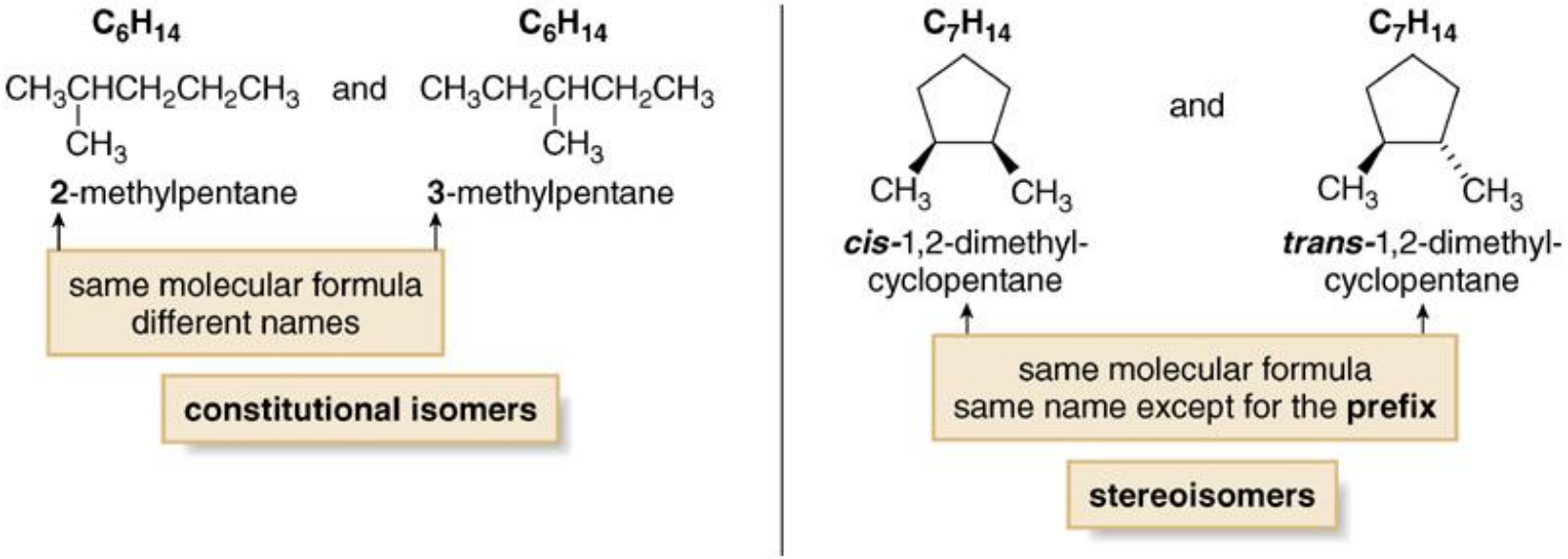


Stereochemistry

The Two Major Classes of Isomers

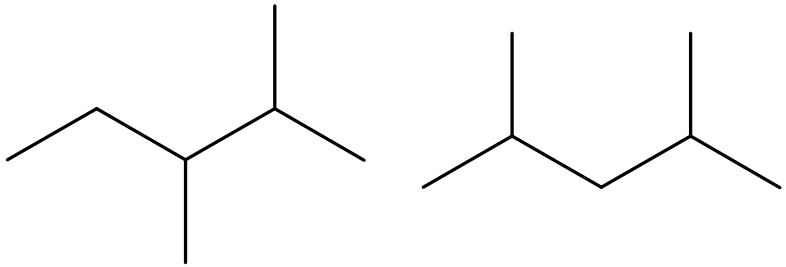
- **Recall that isomers are different compounds with the same molecular formula.**
- **The two major classes of isomers are constitutional isomers and stereoisomers.**
  - **Constitutional/structural isomers have different IUPAC names, the same or different functional groups, different physical properties and different chemical properties.**
  - **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.**

Figure 5.3
A comparison of consitutional isomers and stereoisomers



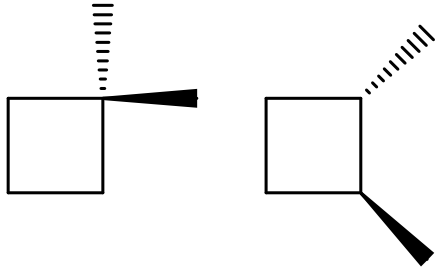
Are the following pairs of compounds consitutional isomers or stereoisomers?

a)



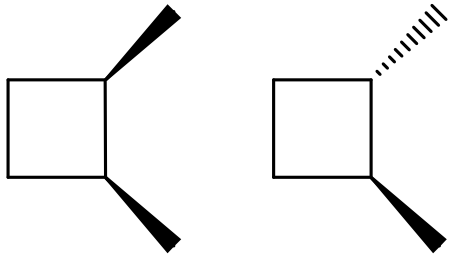
constitutional

b)



constitutional

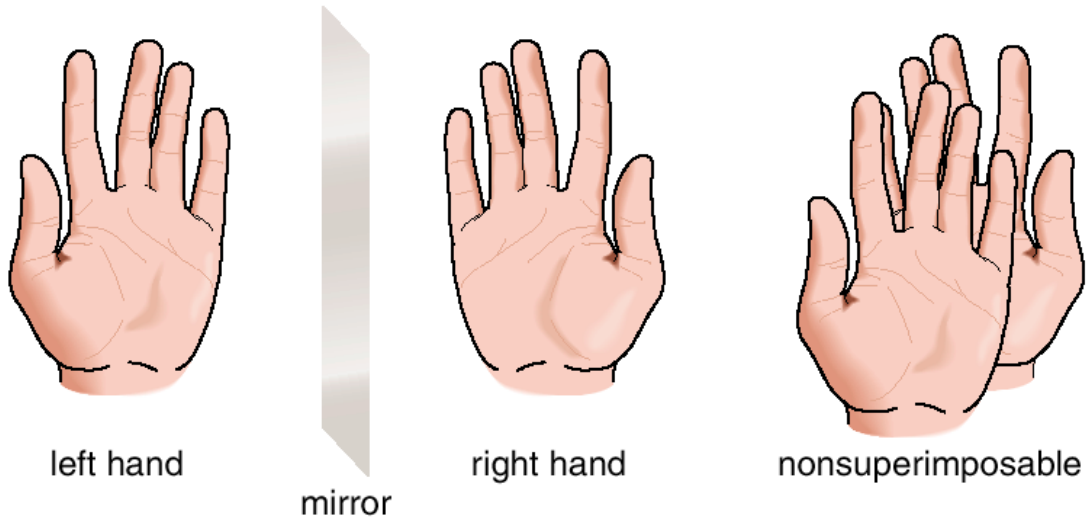
c)



stereoisomer

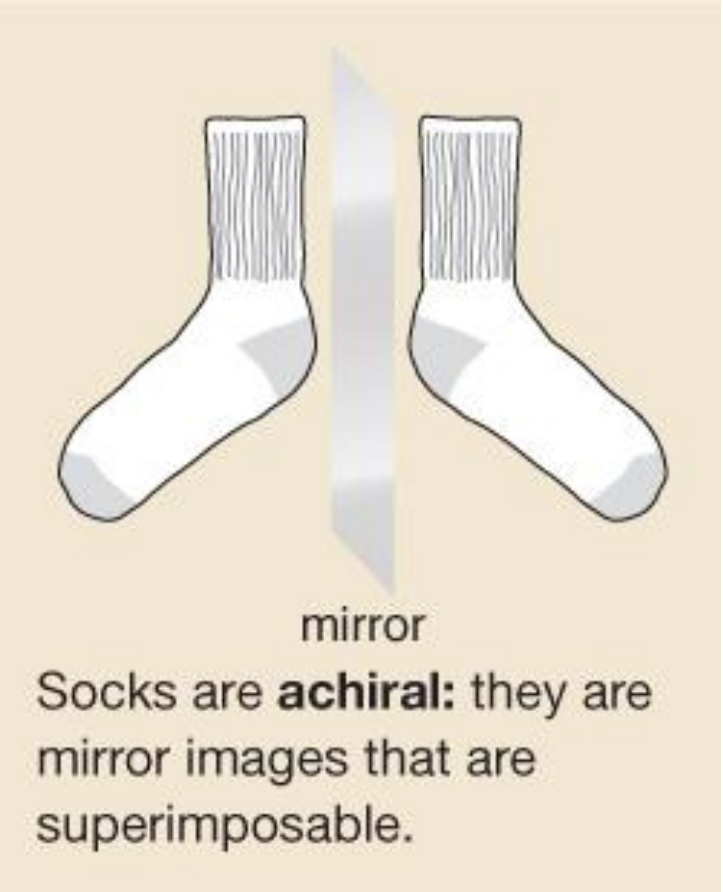
Chiral and Achiral Molecules

- **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.**

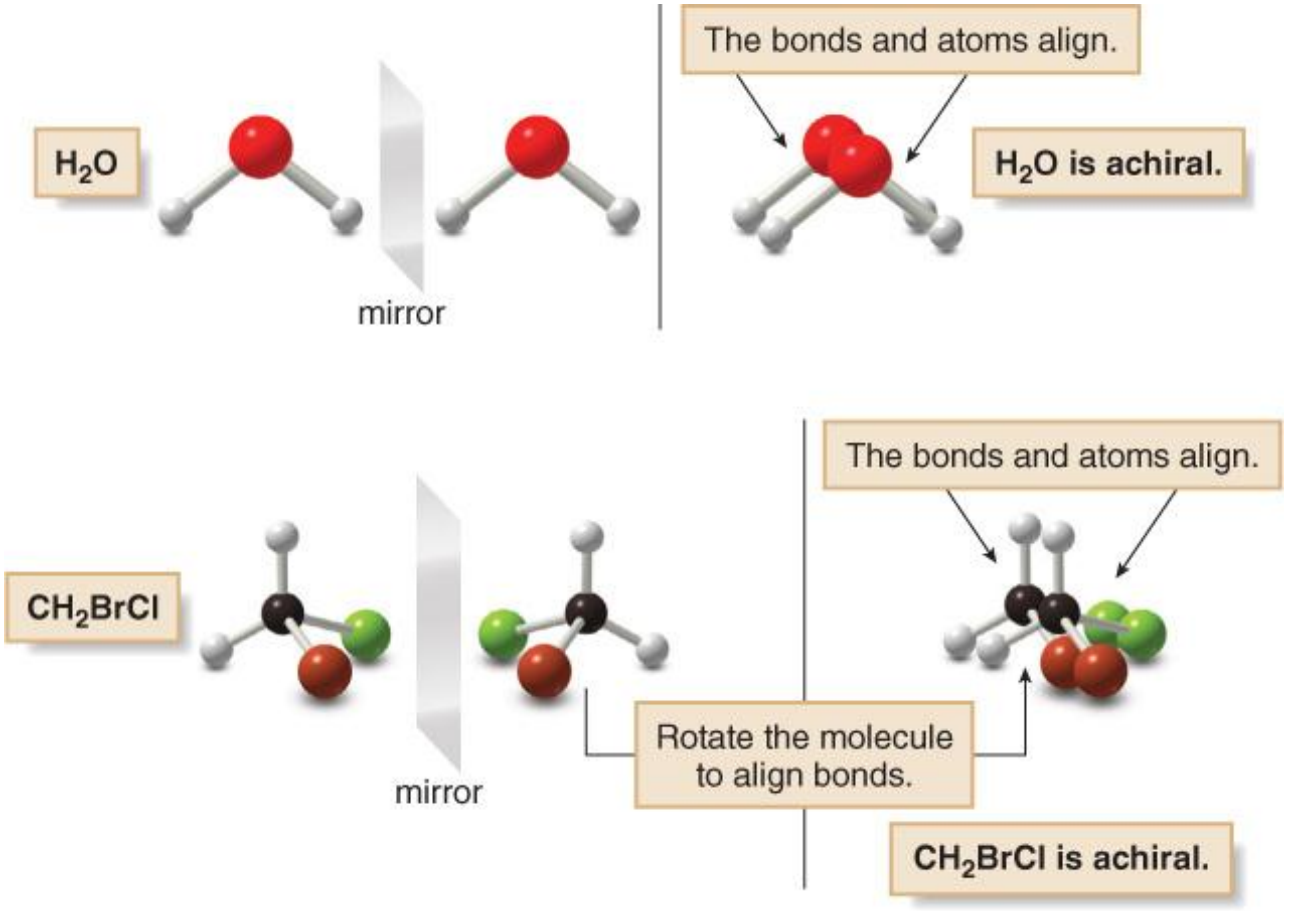


- A molecule (or object) that is *not* superimposable on its mirror image is said to be *chiral.*

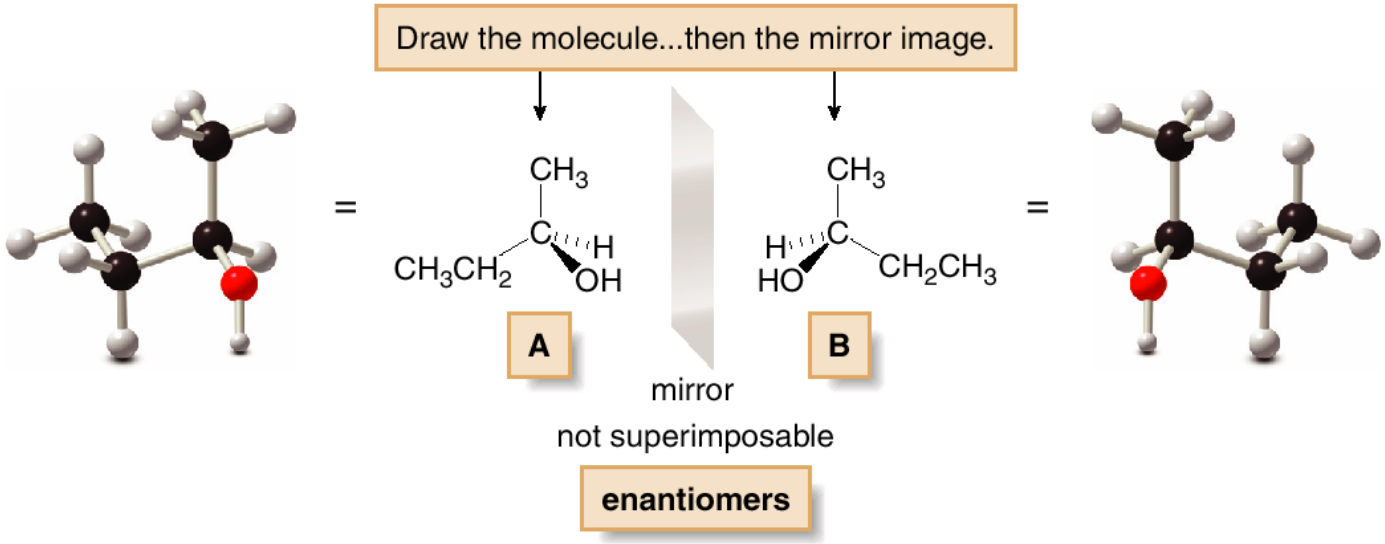
- **Other molecules are like socks. Two socks from a pair are mirror images that are superimposable. A sock and its mirror image are identical.**
- **A molecule or object that is superimposable on its mirror image is said to be achiral.**
- **A molecule or object that is not superimposable on its mirror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



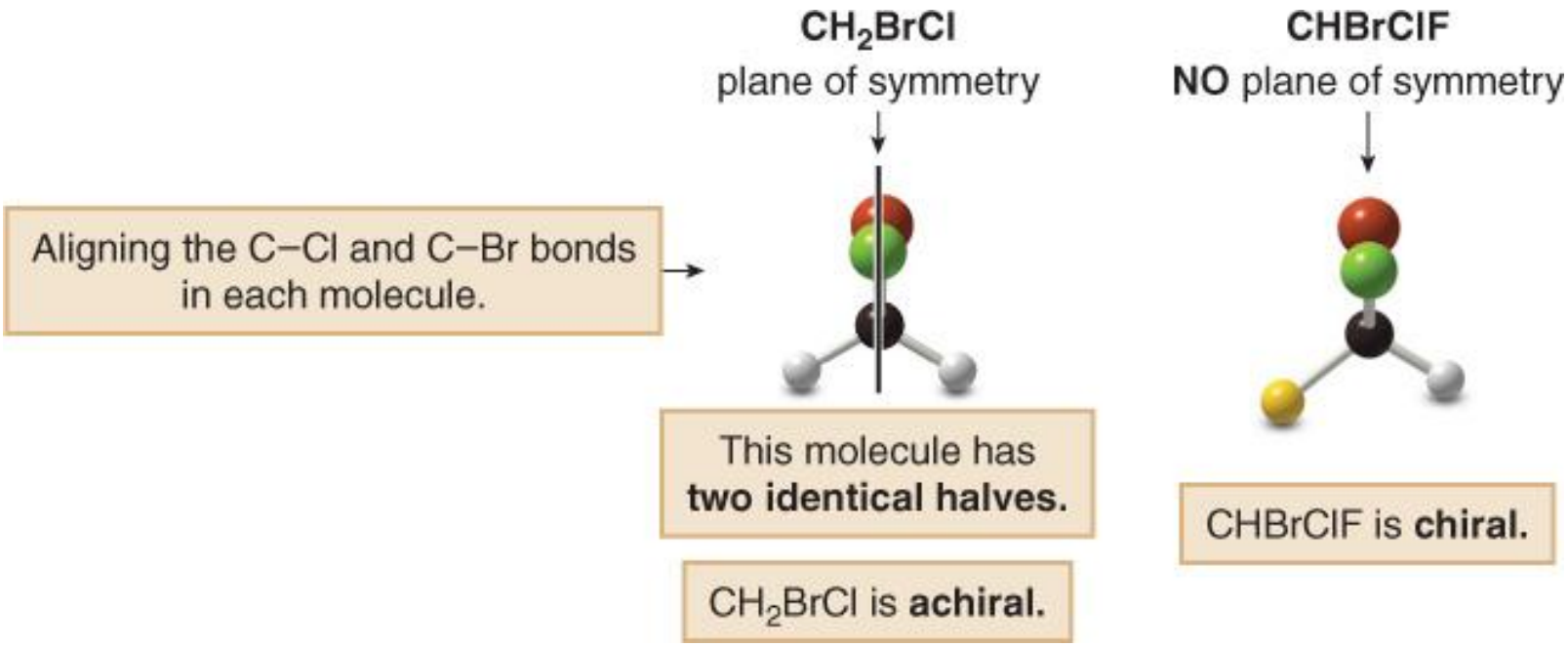
- **We can now consider several molecules to determine whether or not they are chiral.**



- **The molecule labeled A and its mirror image labeled B are not superimposable. No matter how you rotate A and B, all the atoms never align. Thus, CHBrClF is a chiral molecule, and A and B are different compounds.**
- **A and B are stereoisomers—specifically, they are enantiomers.**
- **A carbon atom with four different groups is a tetrahedral stereogenic center.**



- **In general, a molecule with no stereogenic centers will not be chiral.**
- **With one stereogenic center, a molecule will always be chiral.**
- **With two or more stereogenic centers, a molecule may or may not be 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.**

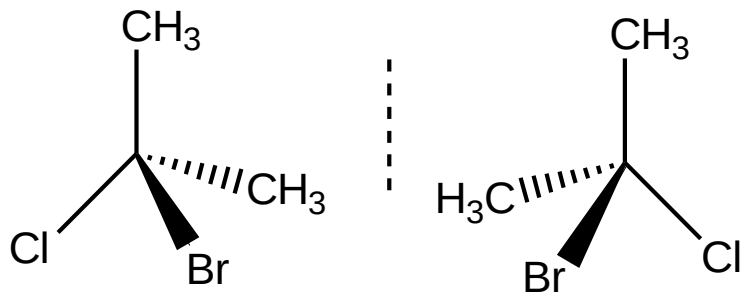

CH_2BrCl
plane of symmetry
Aligning the C–Cl and C–Br bonds in each molecule.
This molecule has **two identical halves.**
CH_2BrCl is **achiral.**
CHBrClF
NO plane of symmetry
CHBrClF is **chiral.**

Summary of the Basic Principles of Chirality:

- **Everything has a mirror image. The fundamental question is whether the molecule and its mirror image are superimposable.**
- **If a molecule and its mirror image are not superimposable, the molecule and its mirror image are chiral.**
- **The terms stereogenic center and chiral molecule are related but distinct. In general, a chiral molecule must have one or more stereogenic centers.**
- **The presence of a plane of symmetry makes a molecule achiral.**

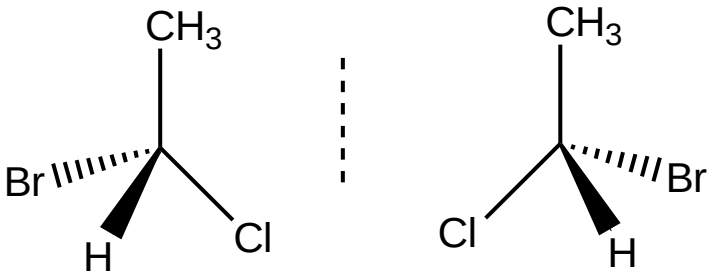
Clasiffy each of the following pairs as chiral or achiral.

a)



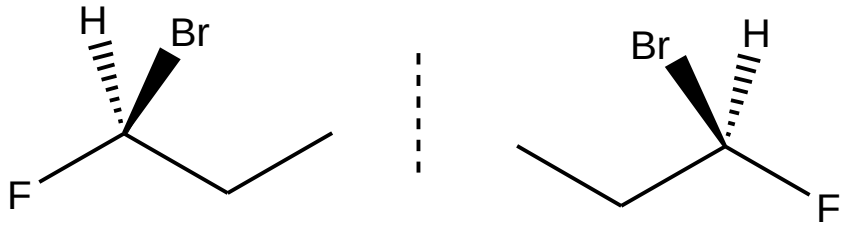
achiral

b)



chiral

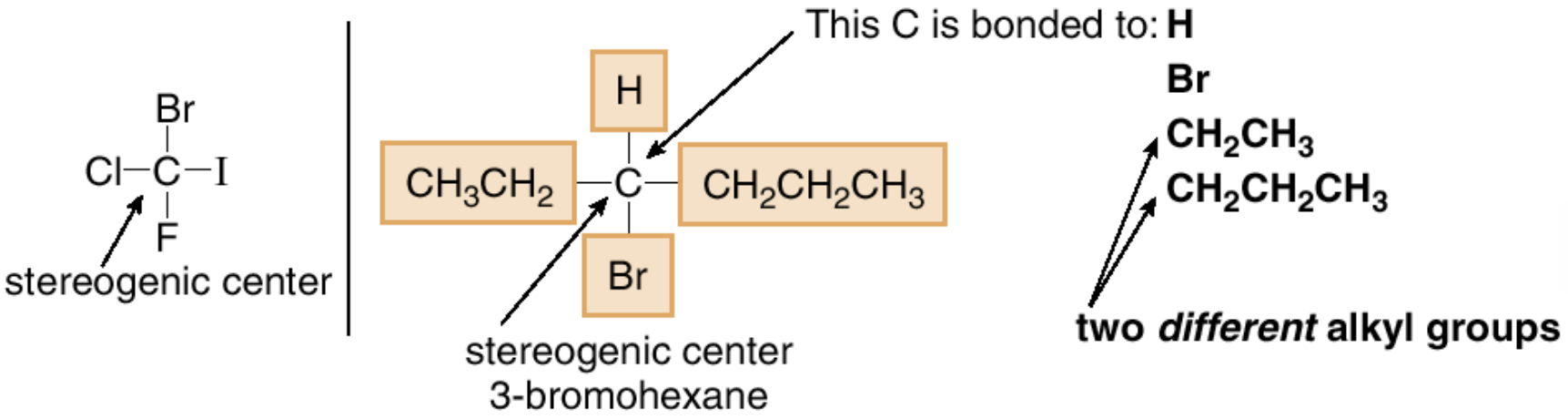
c)



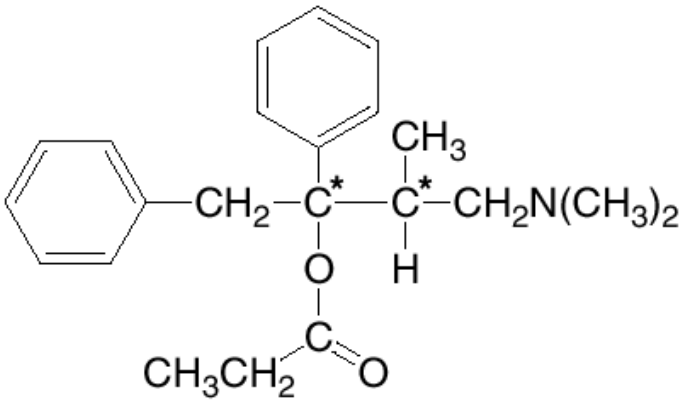
chiral

Stereogenic Centers

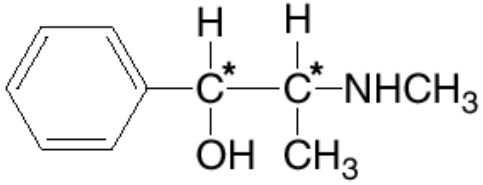
- **To locate a stereogenic center, examine each tetrahedral carbon atom in a molecule, and look at the four groups—not the four atoms—bonded to it.**
- **Always omit from consideration all C atoms that cannot be tetrahedral stereogenic centers. These include**
  - **CH_2 and CH_3 groups**
  - **Any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



- **Larger organic molecules can have two, three or even hundreds of stereogenic centers.**

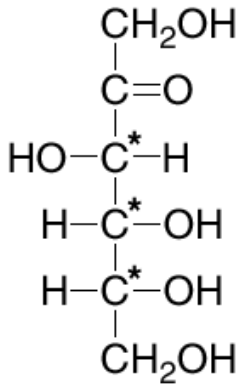


propoxyphene
Trade name: Darvon
(analgesic)



ephedrine
(bronchodilator, decongestant)

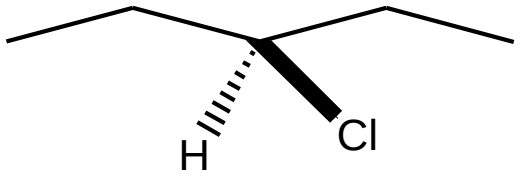
[* = stereogenic center]



fructose
(a simple sugar)

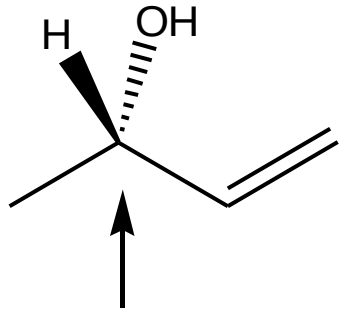
Label the stereogenic centers in each molecule and decide if it is chiral.

a) $CH_3CH_2CH(Cl)CH_2CH_3$



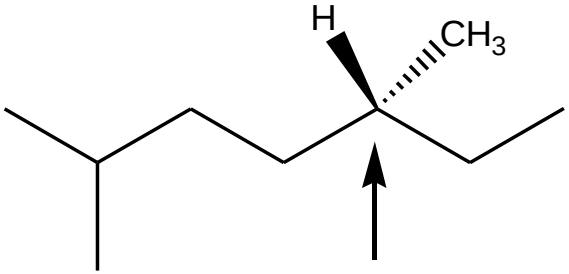
achiral

b) $CH_3CH(OH)CH{=}CH_2$



chiral

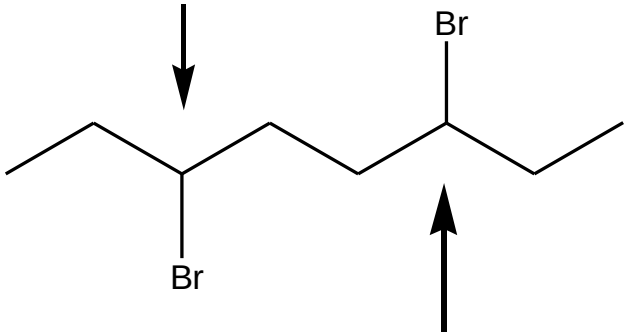
c) $(CH_3)_2CHCH_2CH_2CH(CH_3)CH_2CH_3$



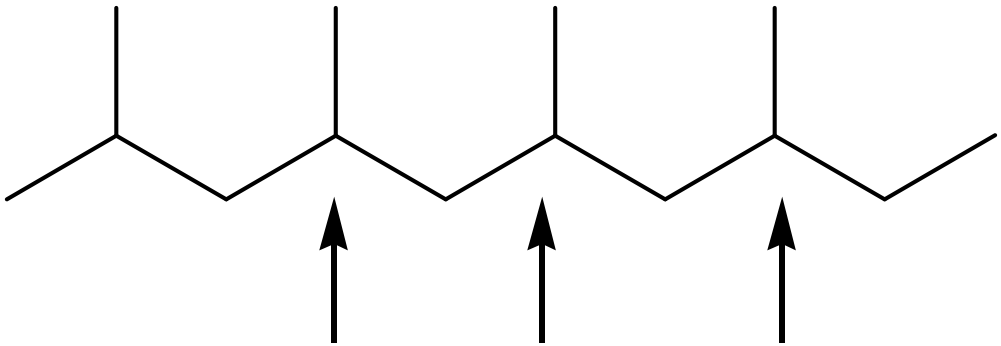
chiral

How many stereogenic centers does each molecule have?

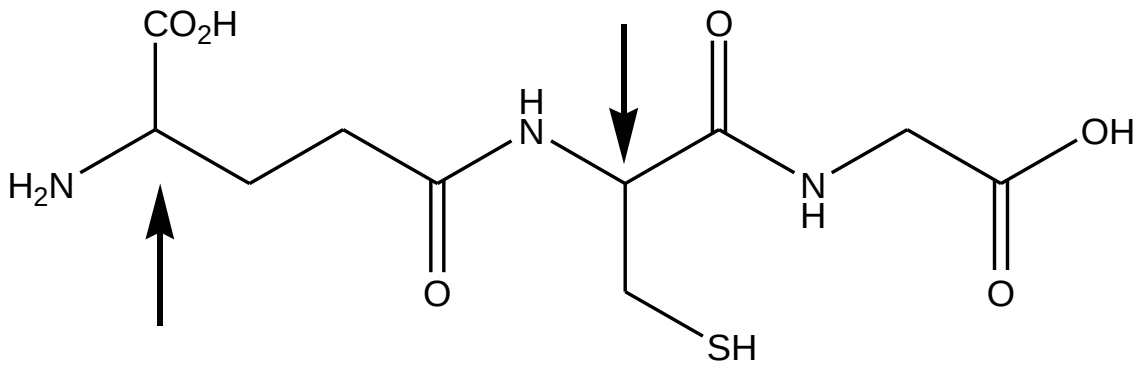
a)



b)



c)



Only carbons attached to four different groups.

- **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.**

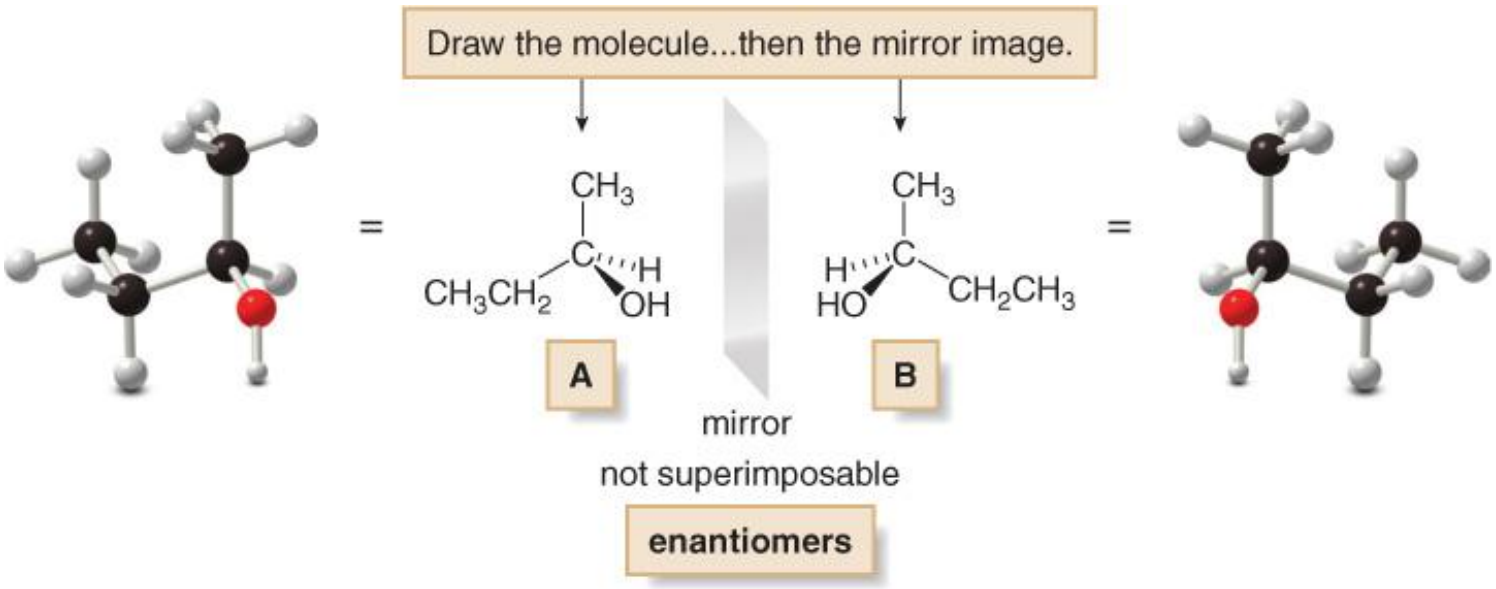
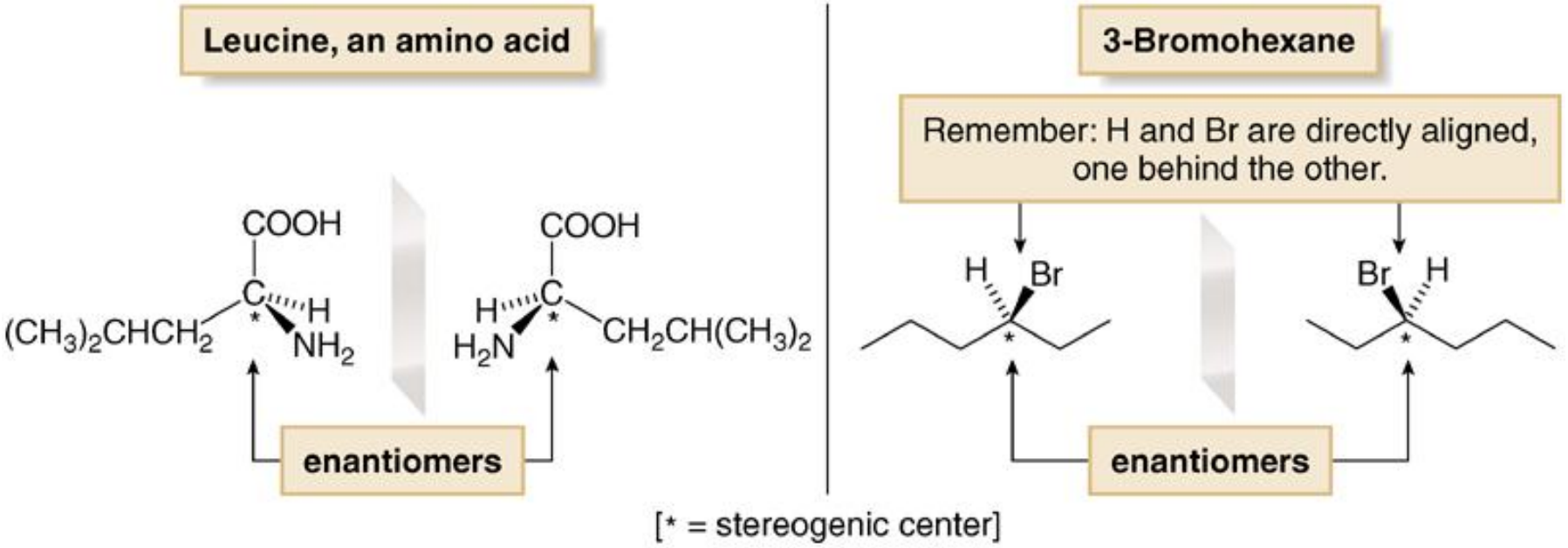
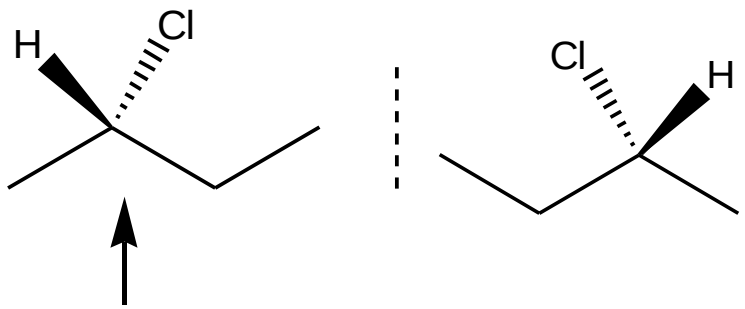


Figure 5.5
Three-dimensional representations for pairs of enantiomers

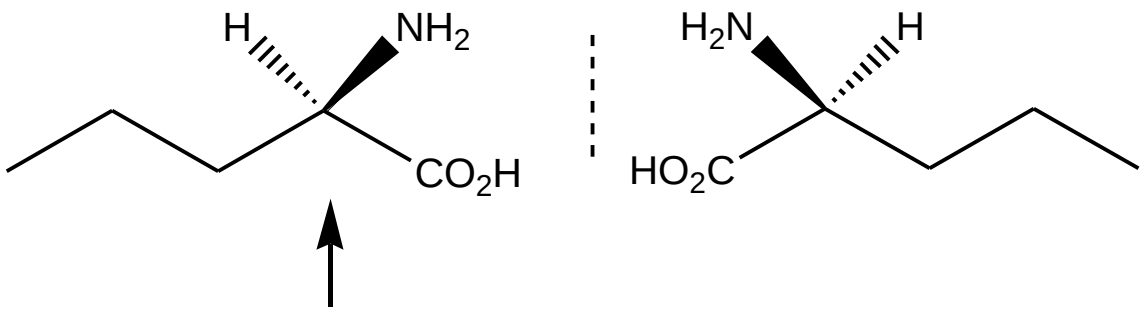


Locate each stereogenic center and draw both enantiomers.

a) $CH_3CH(Cl)CH_2CH_3$

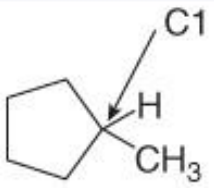


b)$CH_3CH_2CH_2CH(NH_2)COOH$

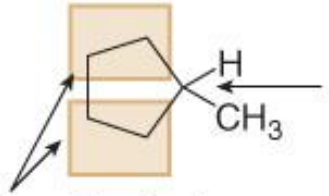


- **Stereogenic centers may also occur at carbon atoms that are part of a ring.**
- **To find stereogenic centers on ring carbons, always draw the rings as flat polygons, and look for tetrahedral carbons that are bonded to four different groups.**

Is C1 a stereogenic center?



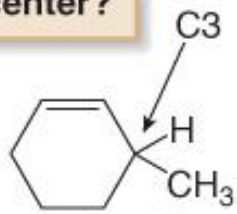
methylcyclopentane



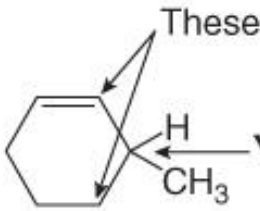
NO, C1 is **not** a stereogenic center.

two identical groups, equidistant from C1

Is C3 a stereogenic center?

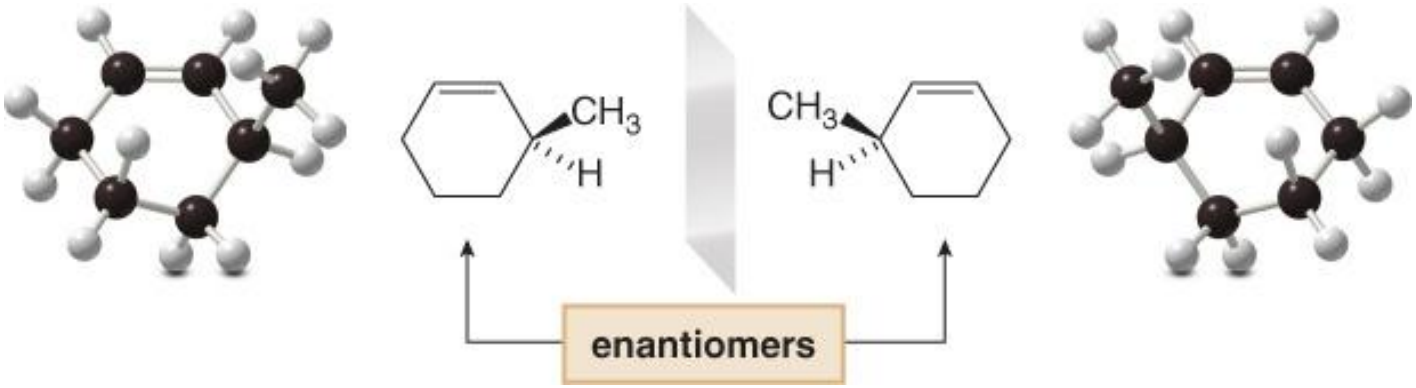


3-methylcyclohexene



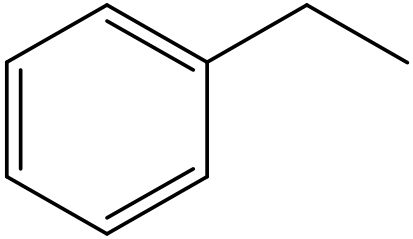
YES, C3 is a stereogenic center.

- **In 3-methylcyclohexene, the CH_3 and H substituents that are above and below the plane of the ring are drawn with wedges and dashes as usual.**



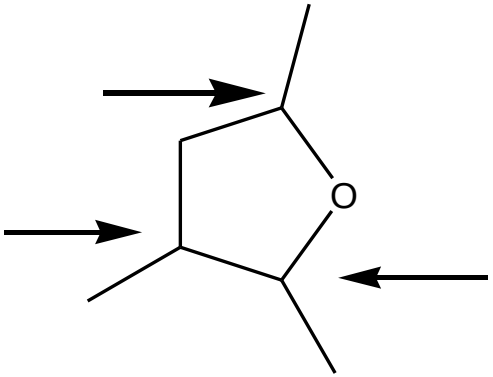
Locate the stereogenic center in the following:

a)



No stereogenic centers.

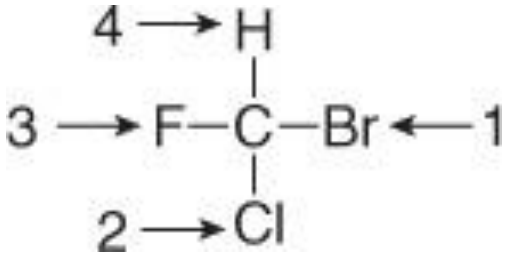
b)



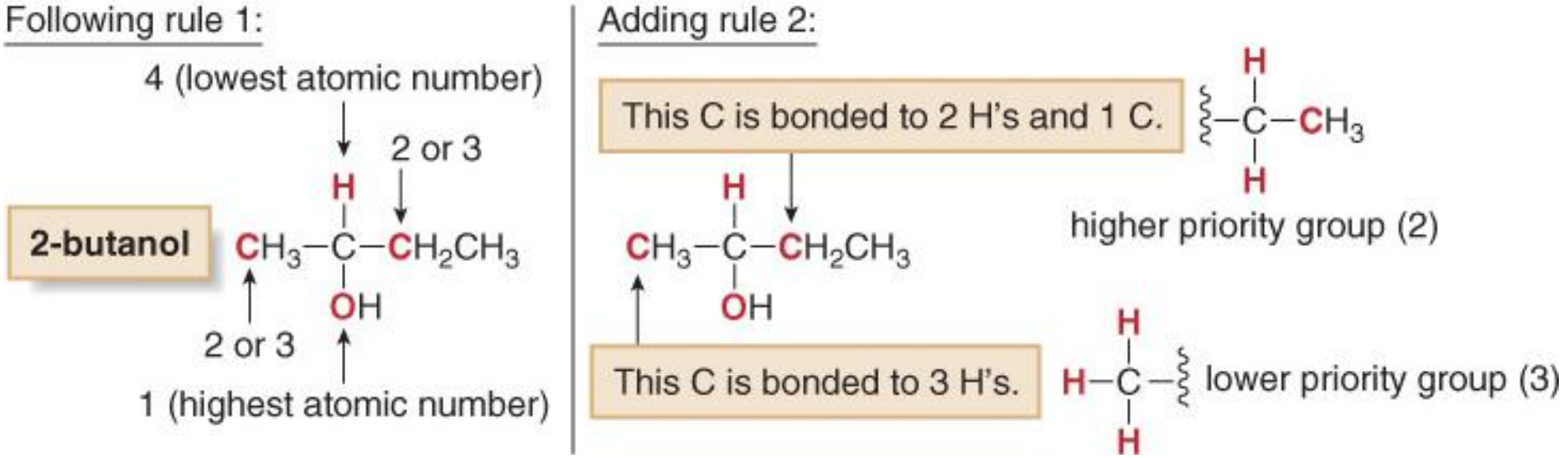
Labeling Stereogenic Centers with *R* or *S*

- **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.**

1- 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).



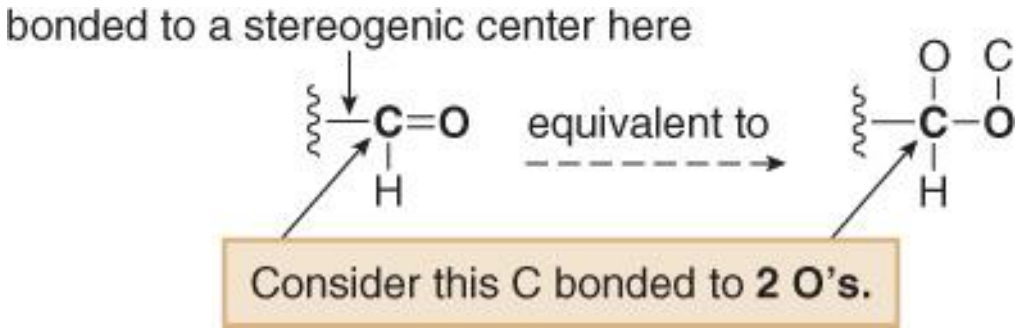
2- If two atoms on a stereogenic center are the same, assign priority based on the atomic number of the atoms bonded to these atoms. *One* atom of higher atomic number determines the higher priority.



3- 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

4- 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:**

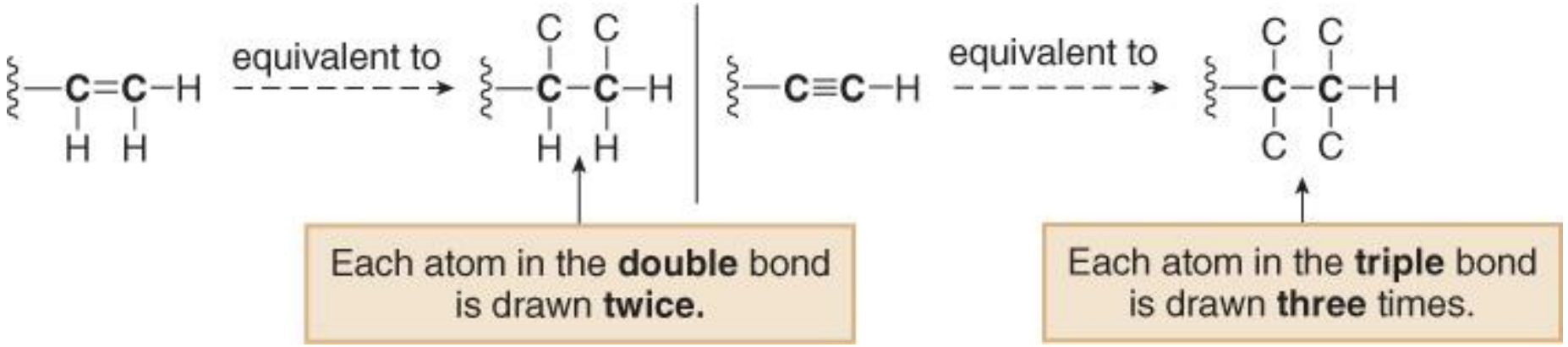
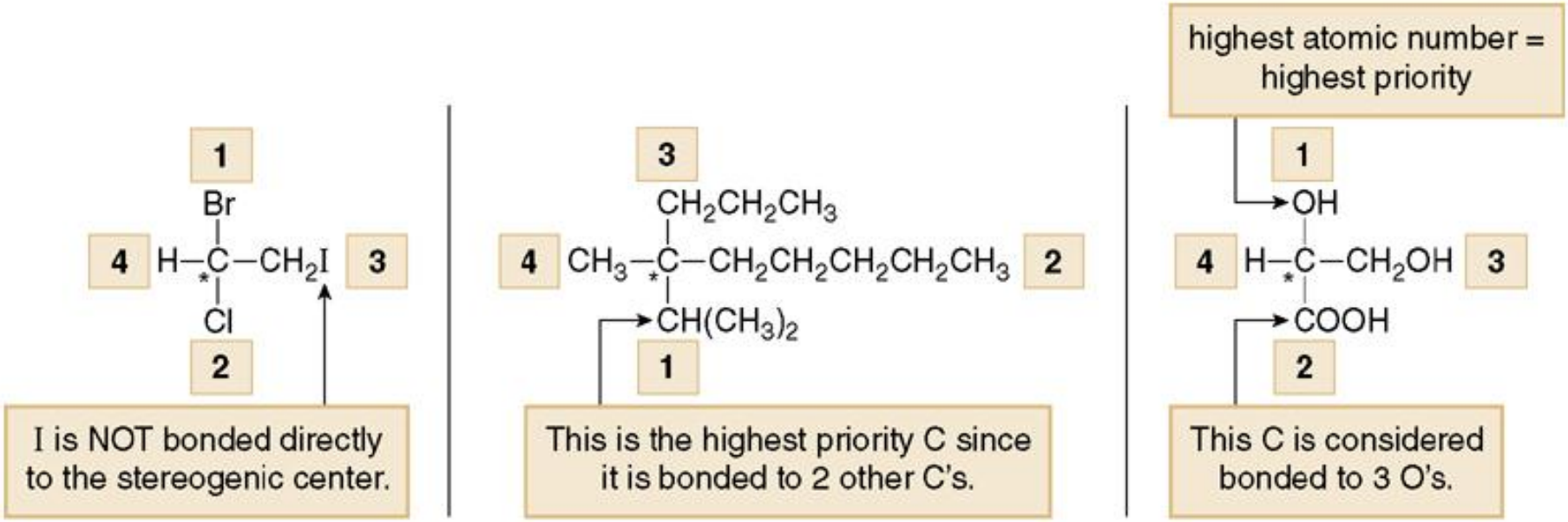
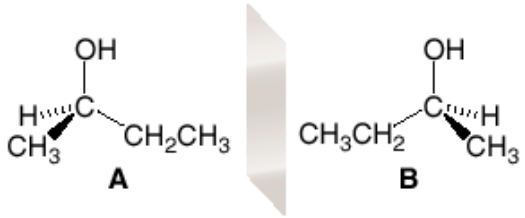


Figure 5.6
Examples of assigning priorities to stereogenic centers



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.

−OH	$-CH_2CH_3$	$-CH_3$	−H
1	2	3	4
highest			lowest

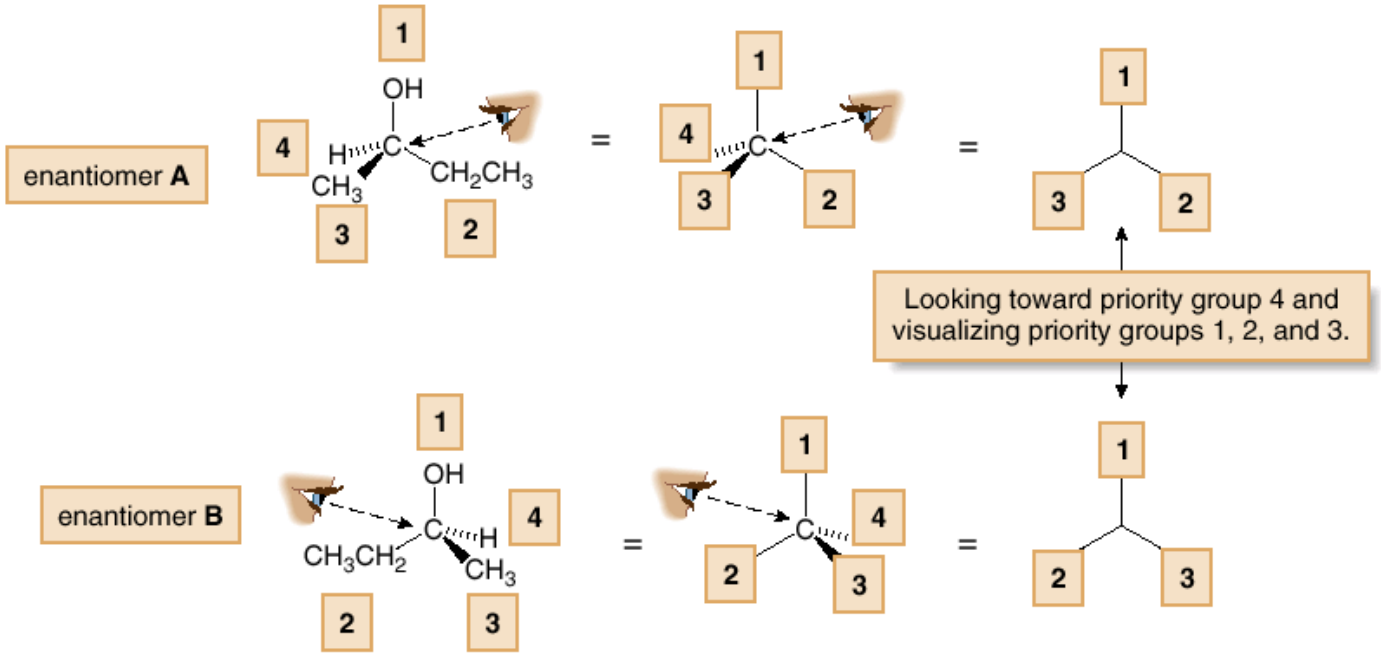
Decreasing priority

Labeling Stereogenic Centers with *R* or *S*

How To, continued . . .

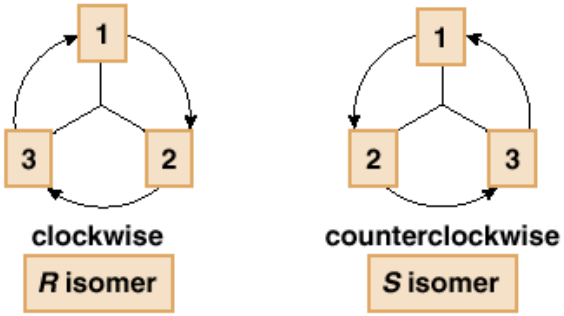
Step [2] Orient the molecule with the lowest priority group (4) *back* (on a *dash*), and visualize the relative positions of the remaining three groups (priorities 1, 2, and 3).

- 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 → 2 → 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***.



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

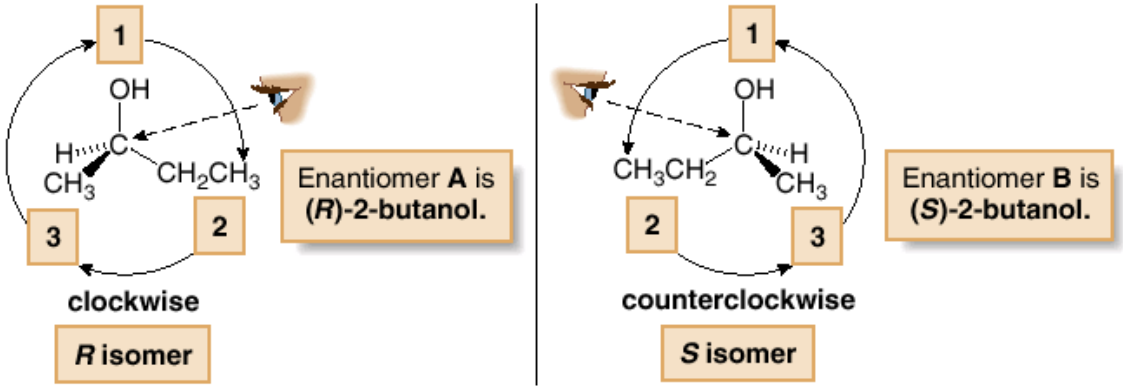
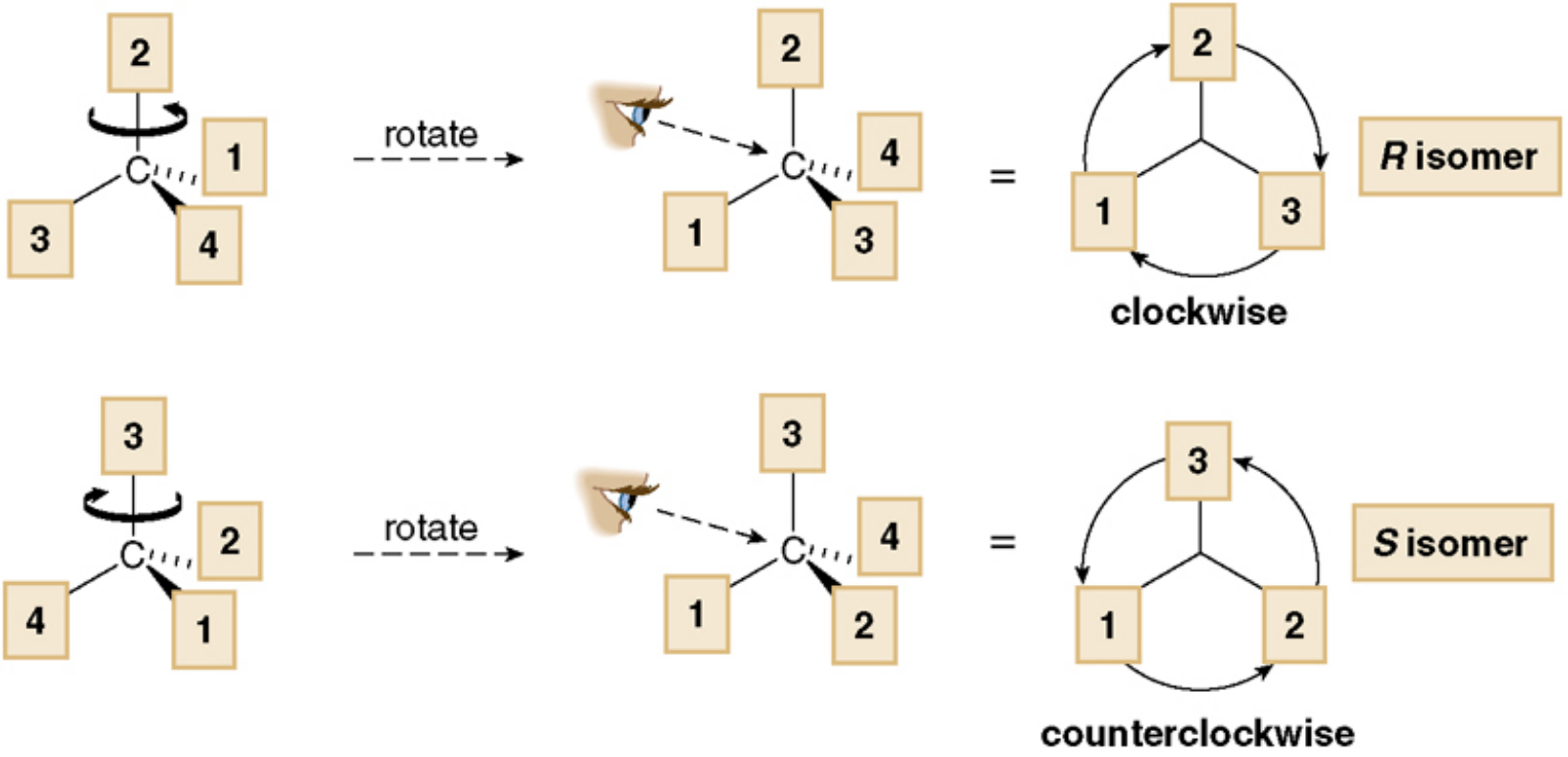


Figure 5.7

Examples: Orienting the lowest priority group in back



Which group in each pair has the highest priority?

a) $-CH_3$ or $-CH_2CH_3$

$-CH_2CH_3$

b) -I or -Br

-I

c) $-CH_3Br$ or $-CH_2CH_2Br$

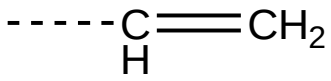
$-CH_3Br$

Rank in order of decreasing priority:

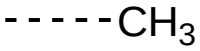
a) **-COOH** **-H** **-NH_2** **-OH**

3 **4** **2** **1**

b)



2



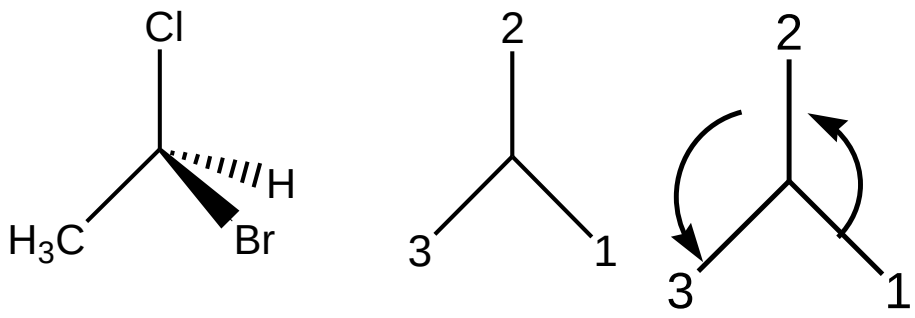
3

1

4

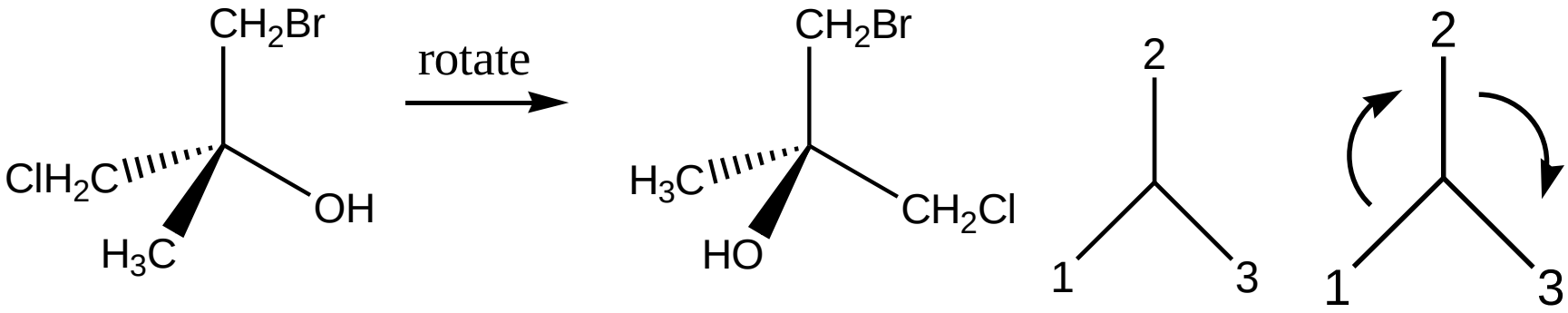
Label each compound as R or S.

a)



S

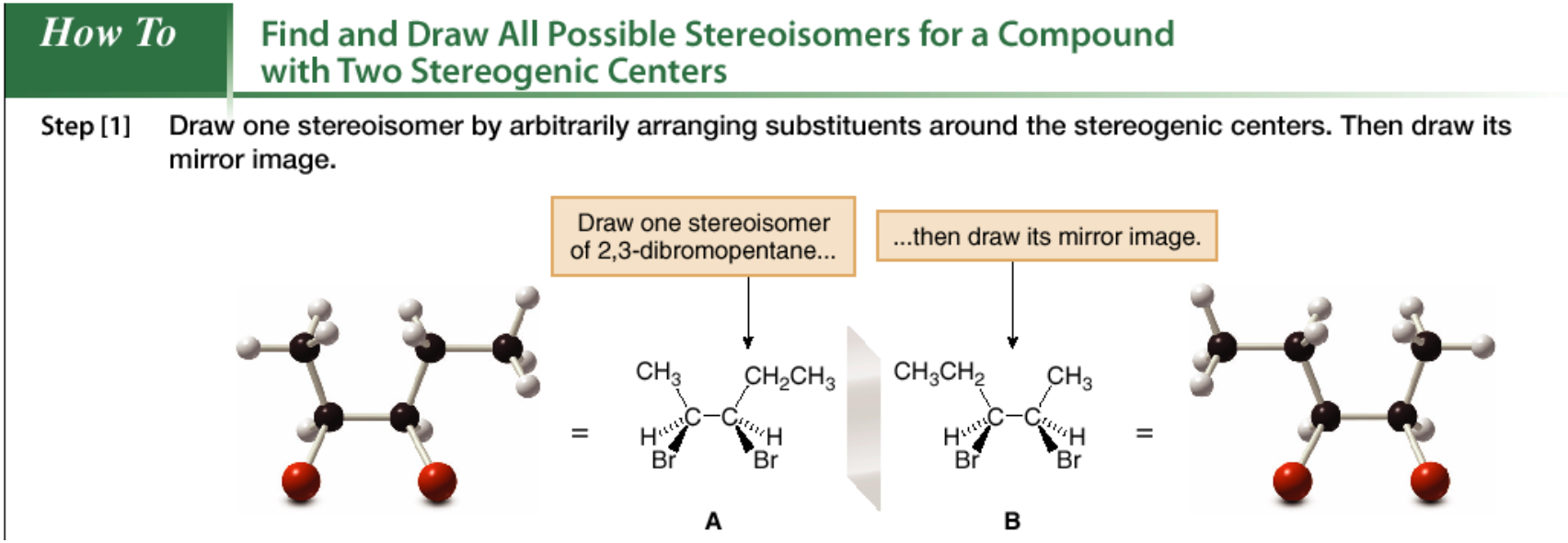
b)



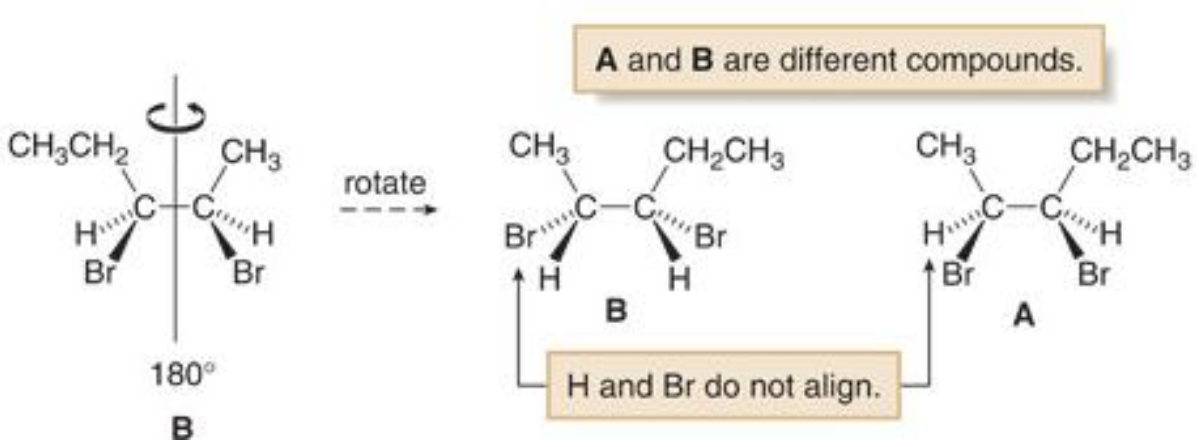
R

Diastereomers

- **For a molecule with *n* stereogenic centers, the maximum number of stereoisomers is 2^n. Let us consider the stepwise procedure for finding all the possible stereoisomers of 2,3-dibromopentane.**



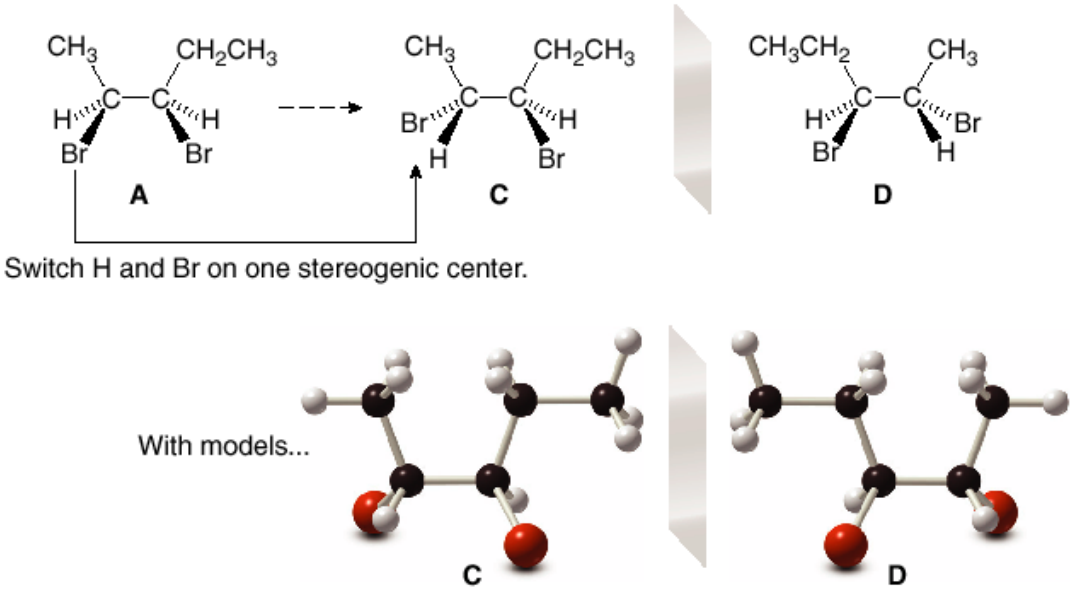
- **If you have drawn the compound and the mirror image in the described manner, you have only to do two operations to see if the atoms align. Place B directly on top of A; and rotate B 180° and place it on top of A to see if the atoms align.**



- **In this case, the atoms of A and B do not align, making A and B nonsuperimposable mirror images—i.e., enantiomers. Thus, A and B are two of the four possible stereoisomers of 2,3-dibromopentane.**

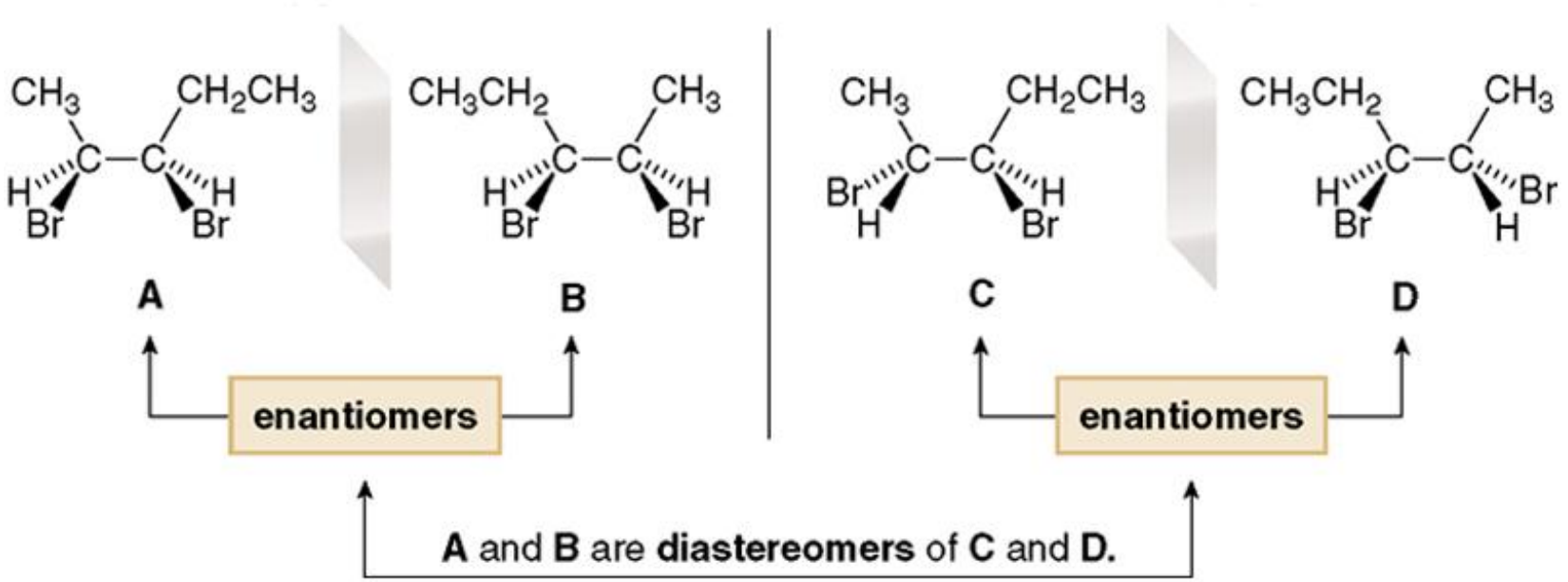
- **Switching the positions of H and Br (or any two groups) on one stereogenic center of either A or B forms a new stereoisomer (labeled C in this example), which is different from A and B. The mirror image of C is labeled D. C and D are enantiomers.**

How To, continued . . .



- **Stereoisomers that are not mirror images of one another are called diastereomers. For example, A and C are diastereomers.**

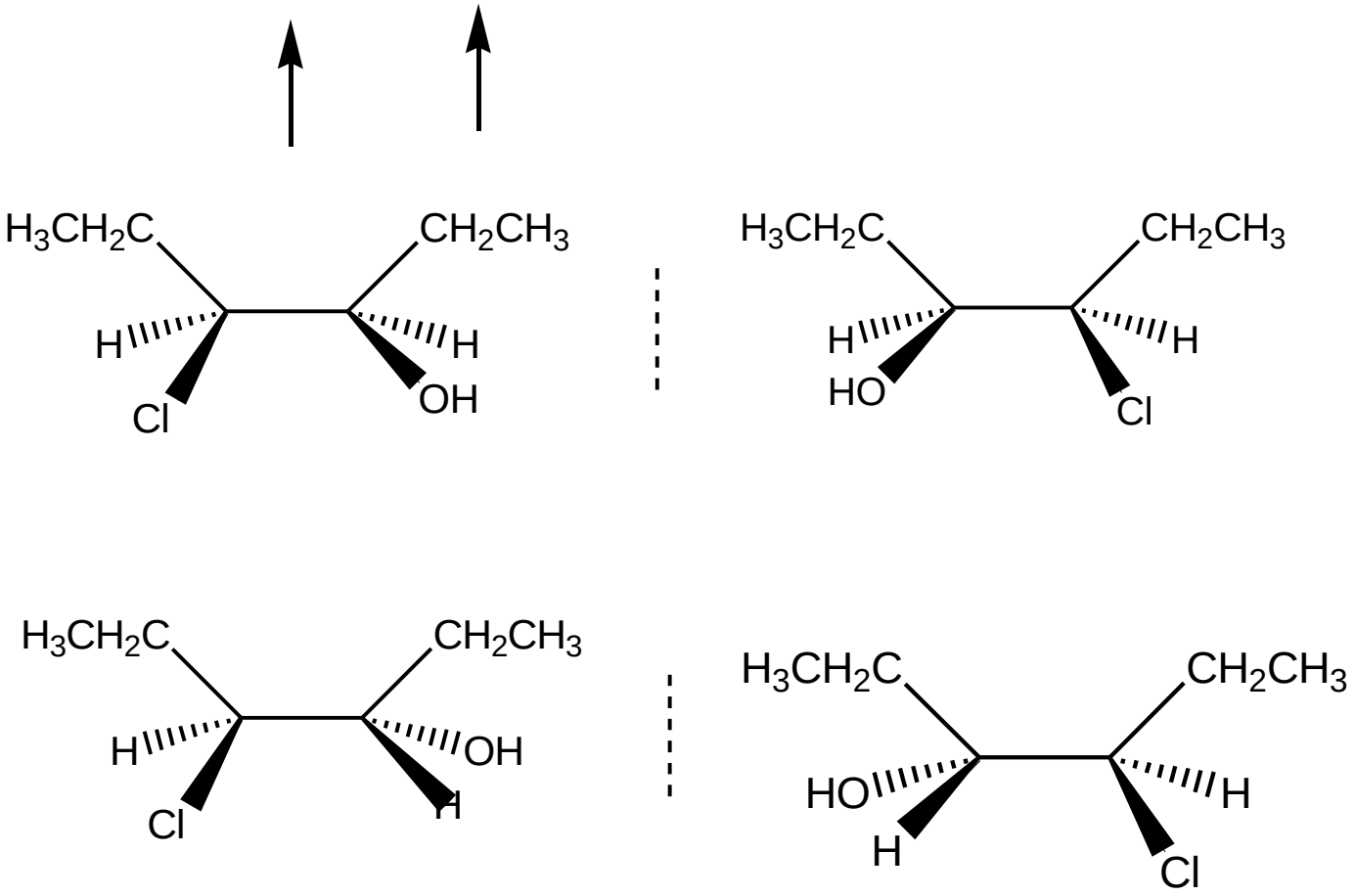
Figure 5.8
Summary: The four stereoisomers of 2,3-dibromopentane



- Pairs of enantiomers: **A** and **B; C** and **D.**
- Pairs of diastereomers: **A** and **C; A** and **D; B** and **C; B** and **D.**

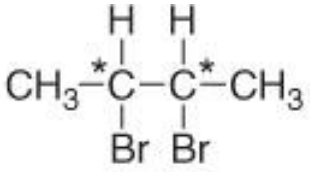
Label the stereogenic centers and draw all stereoisomers.

a) $CH_3CH_2CH(Cl)CH(OH)CH_2CH_3$



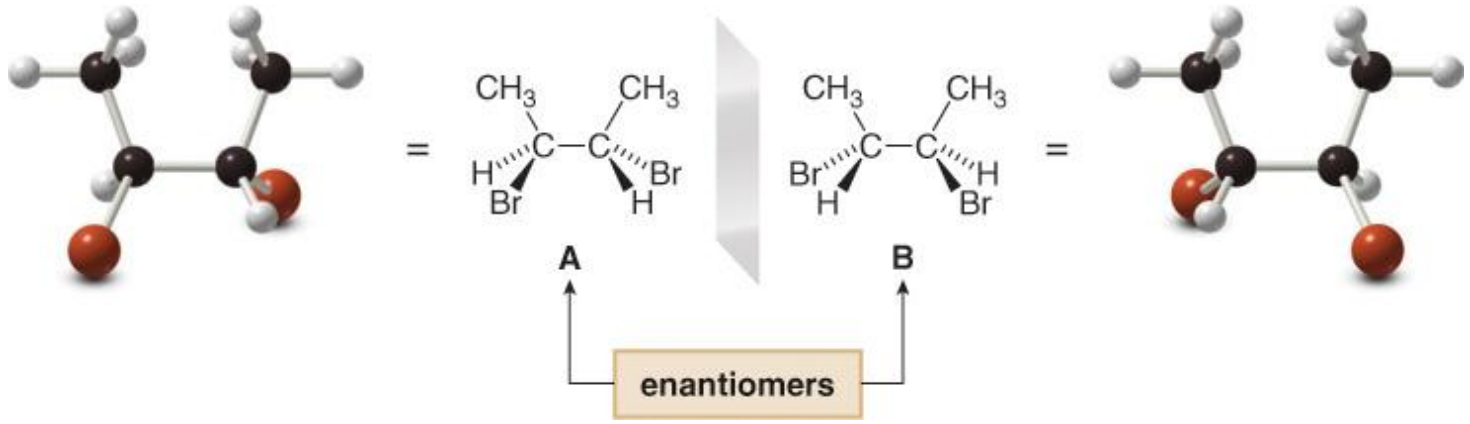
Meso Compounds

- **Let us now consider the stereoisomers of 2,3-dibromobutane. Since this molecule has two stereogenic centers, the maximum number of stereoisomers is 4.**

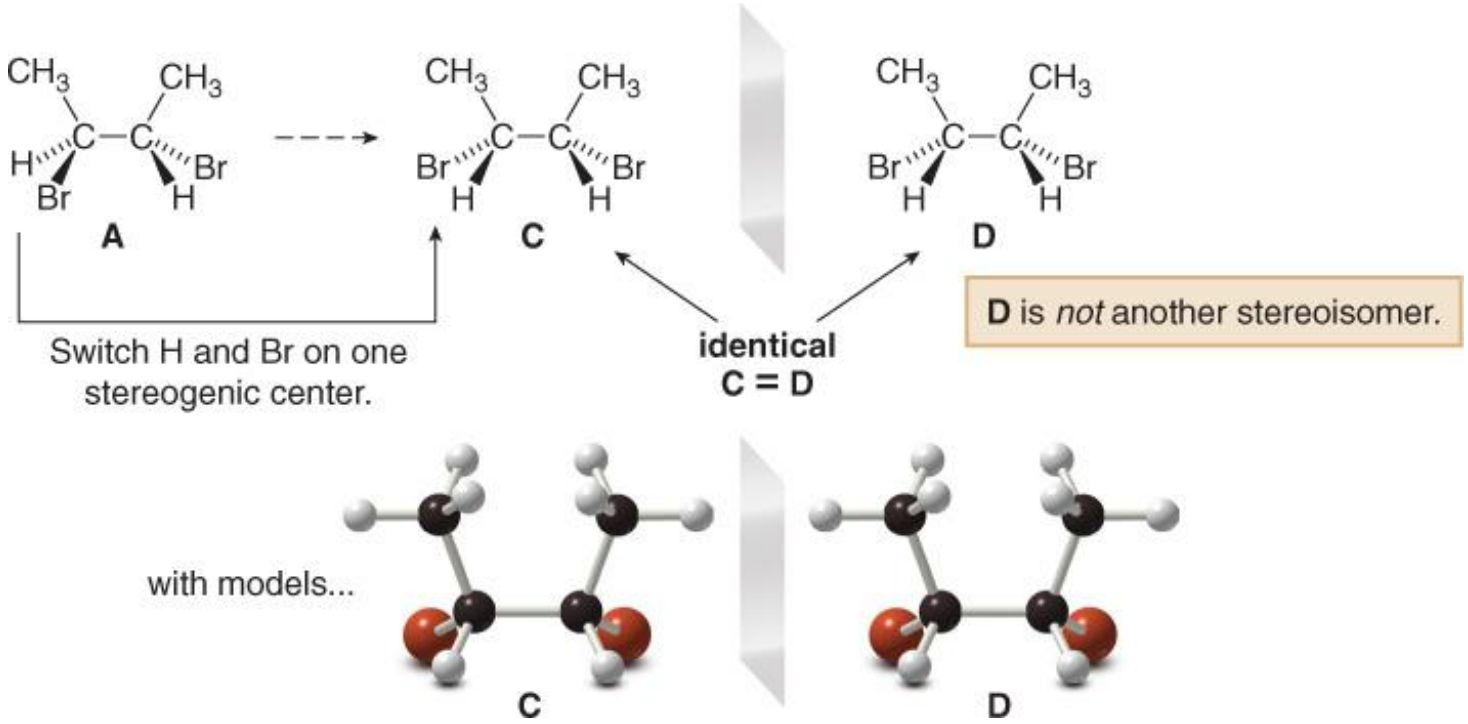


2,3-dibromobutane
[* = stereogenic center]

- **To find all the stereoisomers of 2,3-dibromobutane, arbitrarily add the H, Br, and CH_3 groups to the stereogenic centers, forming one stereoisomer A, and then draw its mirror image, B.**

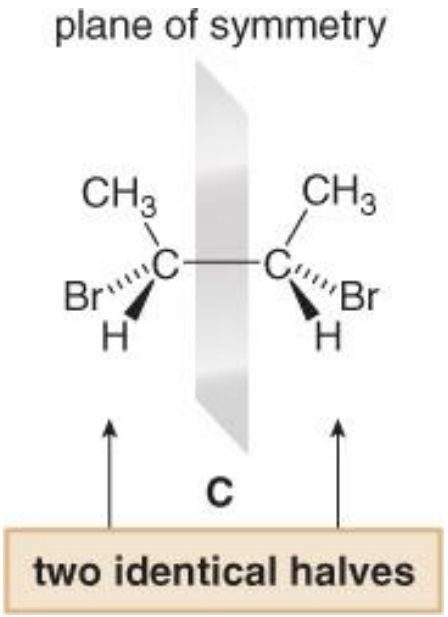


- **To find the other two stereoisomers if they exist, switch the position of two groups on one stereogenic center of one enantiomer only. In this case, switching the positions of H and Br on one stereogenic center of A forms C, which is different from both A and B.**



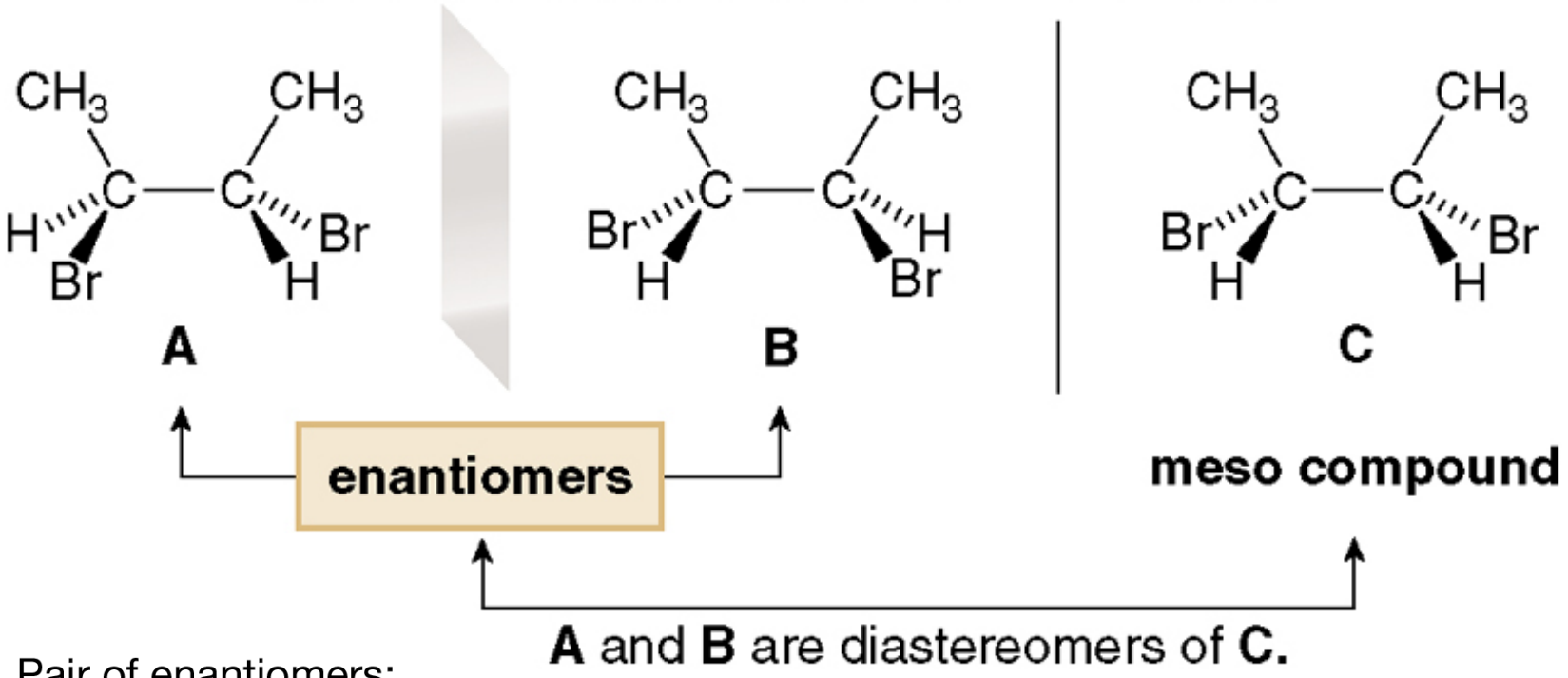
- **A meso compound is an achiral compound that contains tetrahedral stereogenic centers. C is a meso compound.**

- **Compound C contains a plane of symmetry, and is achiral.**
- **Meso compounds generally contain a plane of symmetry so that they possess two identical halves.**



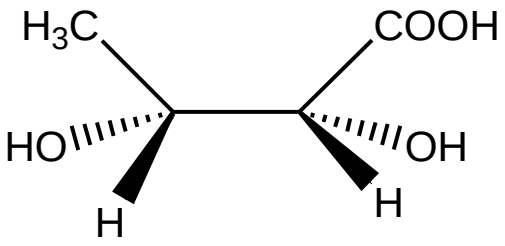
- **Because one stereoisomer of 2,3-dibromobutane is superimposable on its mirror image, there are only three stereoisomers, not four.**

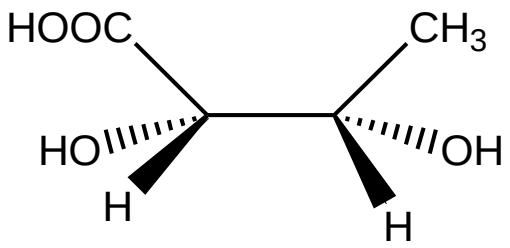
Figure 5.9
Summary: The three stereoisomers 2,3-dibromobutane

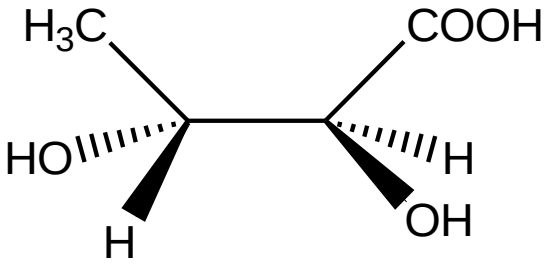


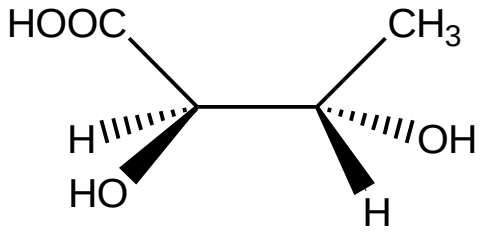
- Pair of enantiomers: **A** and **B.**
- Pairs of diastereomers: **A** and **C; B** and **C.**

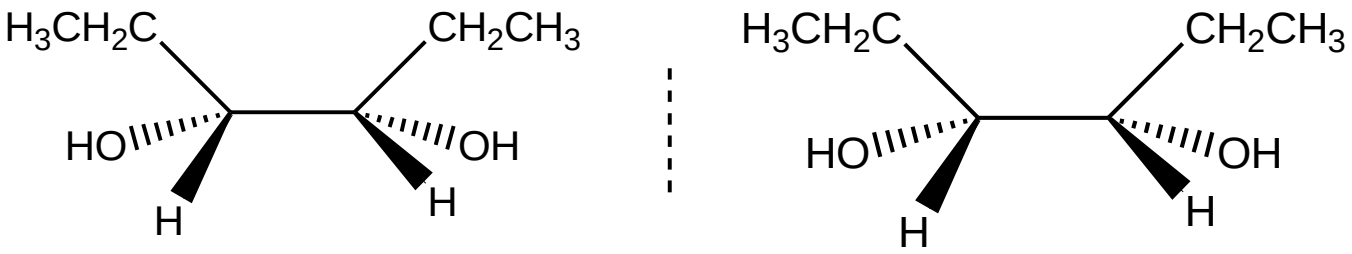
Draw the enantiomer and one diastereomer for the following compound.



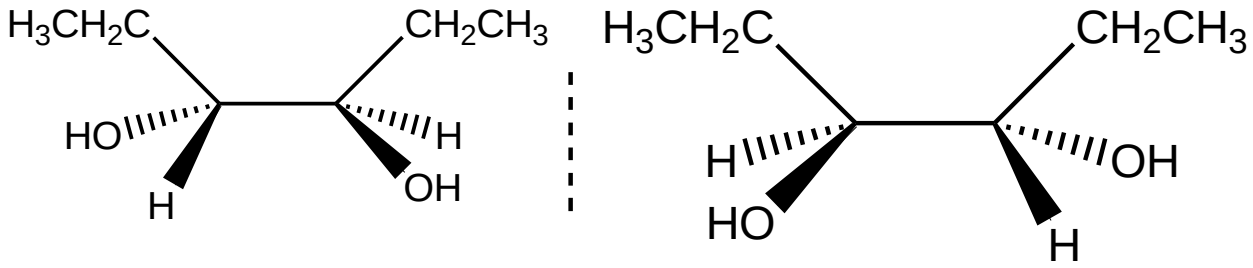








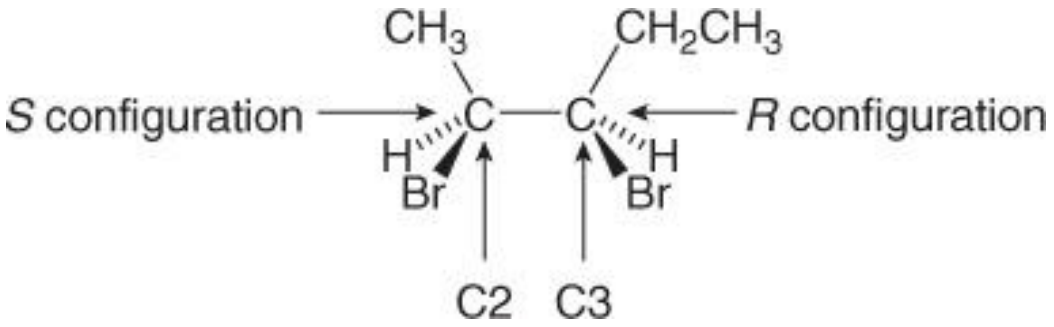
Superimposable mirror images, same compound



Meso compound due to presence of plane of symmetry.

R and *S* Assignments in Compounds with Two or More Stereogenic Centers.

- **When a compound has more than one stereogenic center, *R* and *S* configurations must be assigned to each of them.**



One stereoisomer of 2,3-dibromopentane

The complete name is (2*S*,3*R*)-2,3-dibromopentane

- Identical compounds have the *same R,S* designations at every tetrahedral stereogenic center.
- Enantiomers have exactly *opposite R,S* designations.
- Diastereomers have the *same R,S* designation for at least one stereogenic center and the *opposite* for at least one of the other stereogenic centers.

Figure 5.10
Summary—Types of isomers

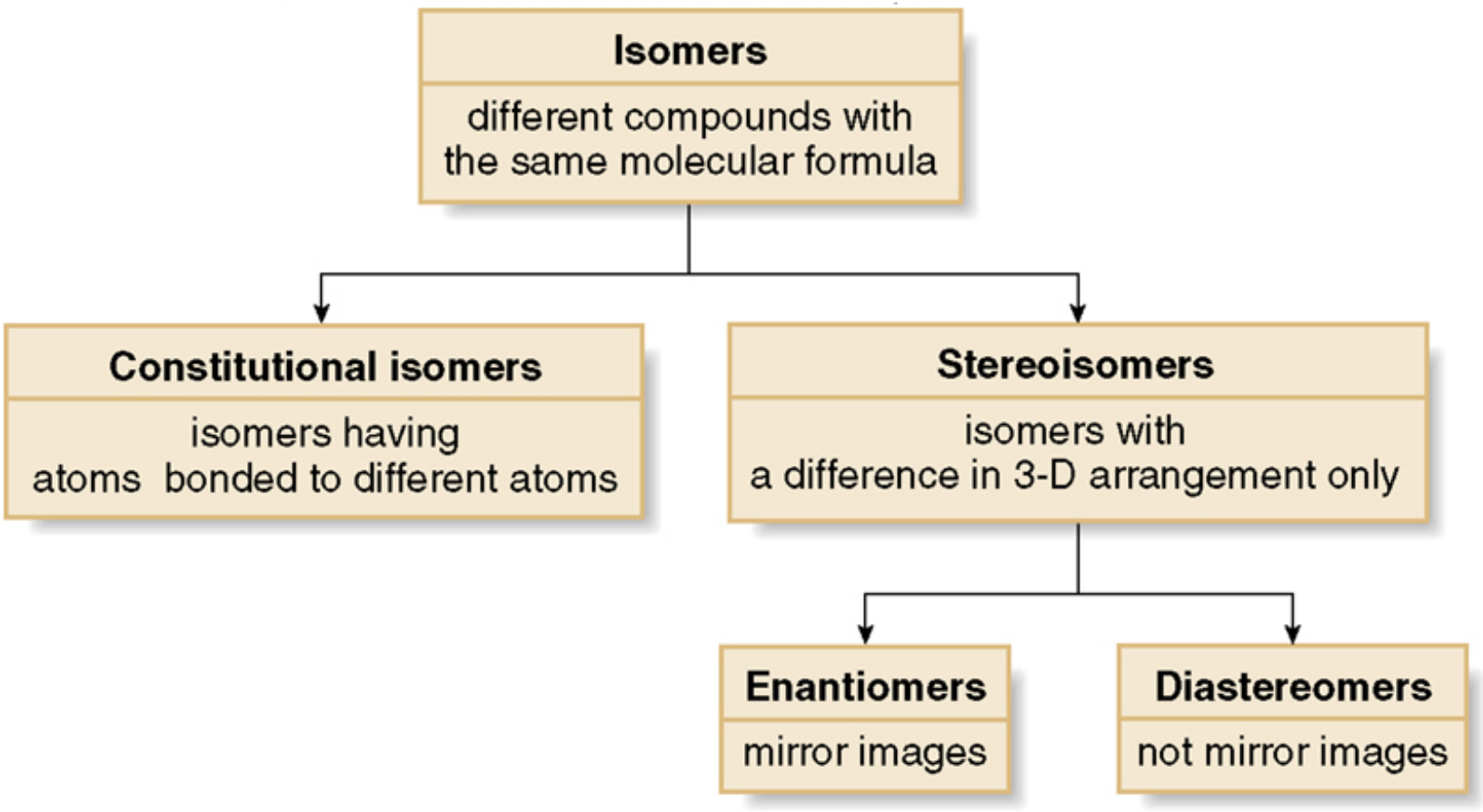
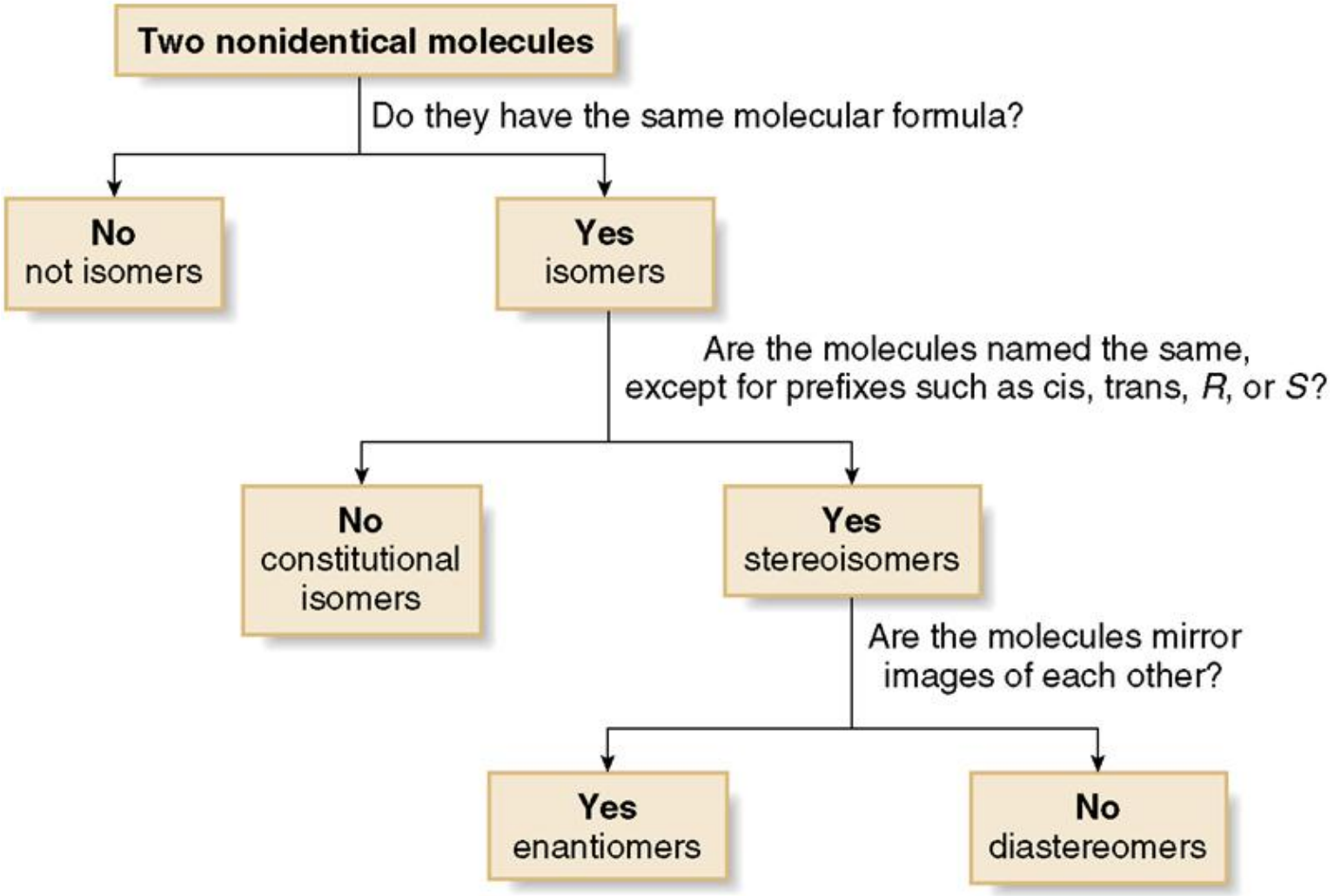


Figure 5.11
Determining the relationship between two nonidentical



Without looking at the structures, label each pair as either enantiomers or diastereomers.

a) (2R,3S)-2,3-hexanediol or (2R,3S)-2,3-hexanediol

One changes, one stays the same, diastereomers

b) (2R,3R)-2,3-hexanediol or (2S,3S)-2,3-hexanediol

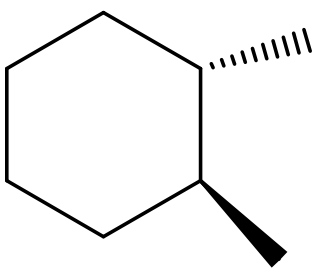
Both change, enantiomers

c) (2R,3S,4R)-2,3,4-hexanetriol or (2S,3R,4R)-2,3,4-hexanetriol

2 change, one stays the same, diastereomers

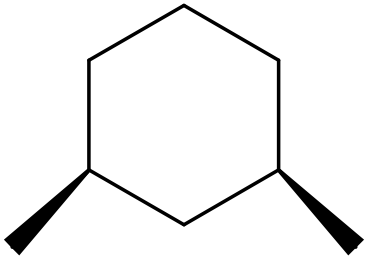
Which of the following are meso compounds?

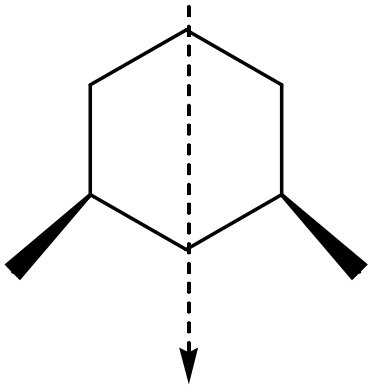
a)



Not meso, no plane of symmetry

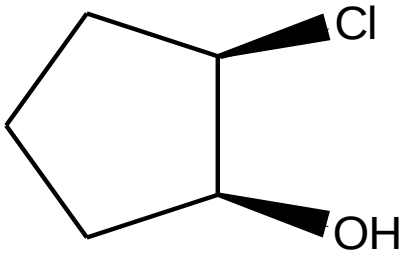
b)





meso

c)

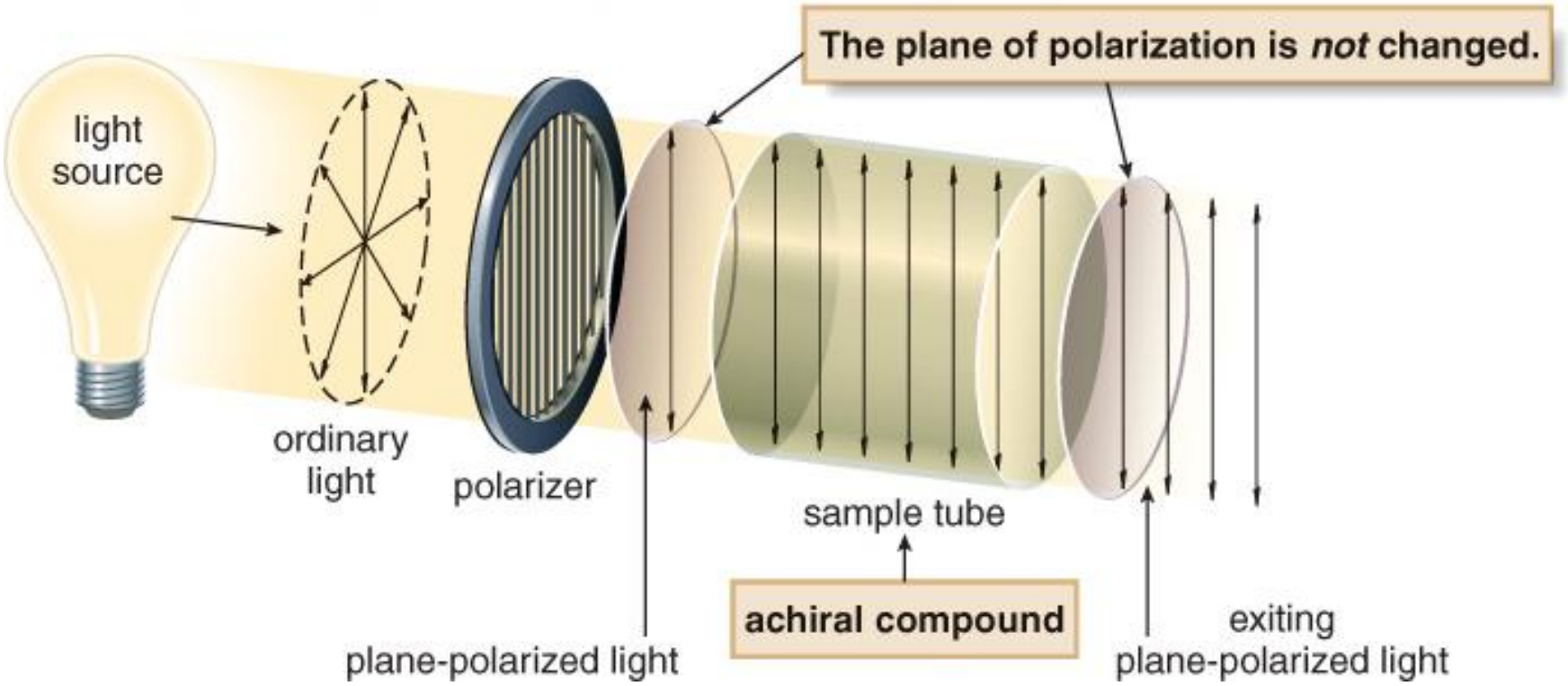


Not meso, no plane of symmetry

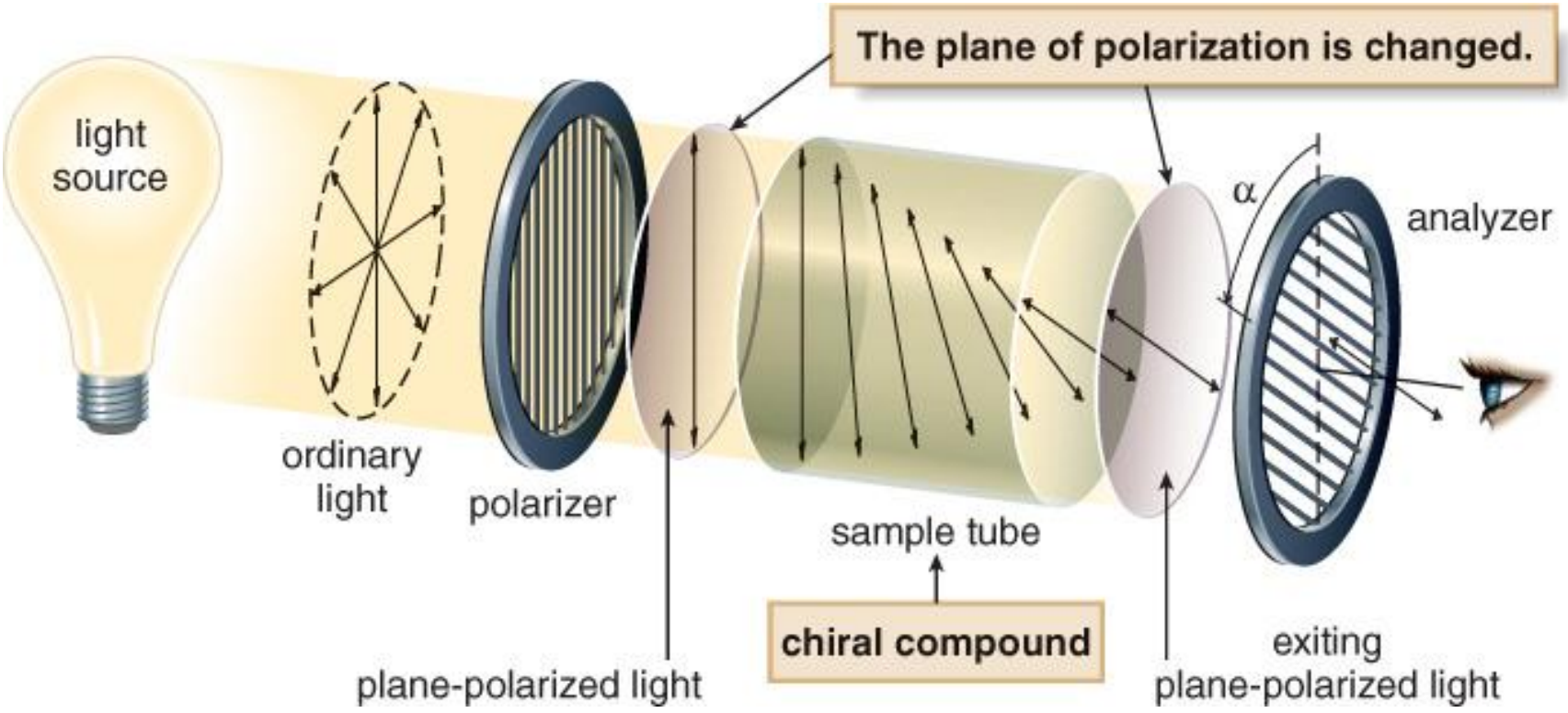
Physical Properties of Stereoisomers—Optical Activity

- **The chemical and physical properties of two enantiomers are identical except in their interaction with chiral substances. They have identical physical properties, except for how they interact with plane-polarized light.**
- **Plane-polarized (polarized) light is light that has an electric vector that oscillates in a single plane. Plane-polarized light arises from passing ordinary light through a polarizer.**
- **A 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.**

- **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.**



- **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.**



- **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°.**
- **No relationship exists between *R* and *S* prefixes and the (+) and (-) designations that indicate optical rotation.**

Physical Properties of Stereoisomers—Racemic Mixtures

- **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 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]

Physical Properties of Stereoisomers—Optical Purity

- **Enantiomeric excess (optical purity) is a measurement of how much one enantiomer is present in excess of the racemic mixture. It is denoted by the symbol *ee*.**

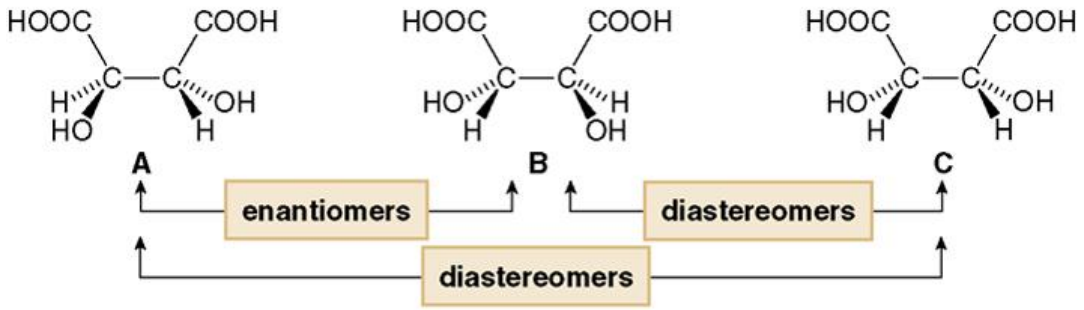
ee = % of one enantiomer - % of the other enantiomer.

- **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.**
- **The enantiomeric excess can also be calculated if the specific rotation [α] of a mixture and the specific rotation [α] of a pure enantiomer are known.**

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

- **Since enantiomers have identical physical properties, they cannot be separated by common physical techniques like distillation.**
- **Diastereomers and constitutional isomers have different physical properties, and therefore can be separated by common physical techniques.**

Figure 5.12
The physical properties of the three stereoisomers of tartaric acid



Property	A	B	C	A + B (1:1)
melting point (°C)	171	171	146	206
solubility (g/100 mL H_2O)	139	139	125	139
[α]	+13	−13	0	0
R,S designation	*R,R*	*S,S*	*R,S*	—
d,l designation	*d*	*l*	none	*d,l*

- The physical properties of **A** and **B** differ from their diastereomer **C.**
- The physical properties of a racemic mixture of **A** and **B** (last column) can also differ from either enantiomer and diastereomer **C.**
- **C** is an achiral meso compound, so it is optically inactive; [α] = 0.

A compound was isolated in the lab and the observed roation 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?

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

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

$$= +100$$

What is the ee of the following racemic mixture?

95% A and 5% B

ee = % of A - % of B

= 95 – 5 = 90 ee

Given the ee value, what percent is there of each isomer, 60% ee

60% excess A, then 40% racemic mixture(so 20% A and 20% B)

So, 60% + 20% = 80% A and leaves 20% B

A pure compound has a specific rotation of +24, a solution of this compound has a rotation of +10, what is the ee?

Ee = [α] of mixture / [α] of pure x 100

=+10/+24 x 100 = 42%