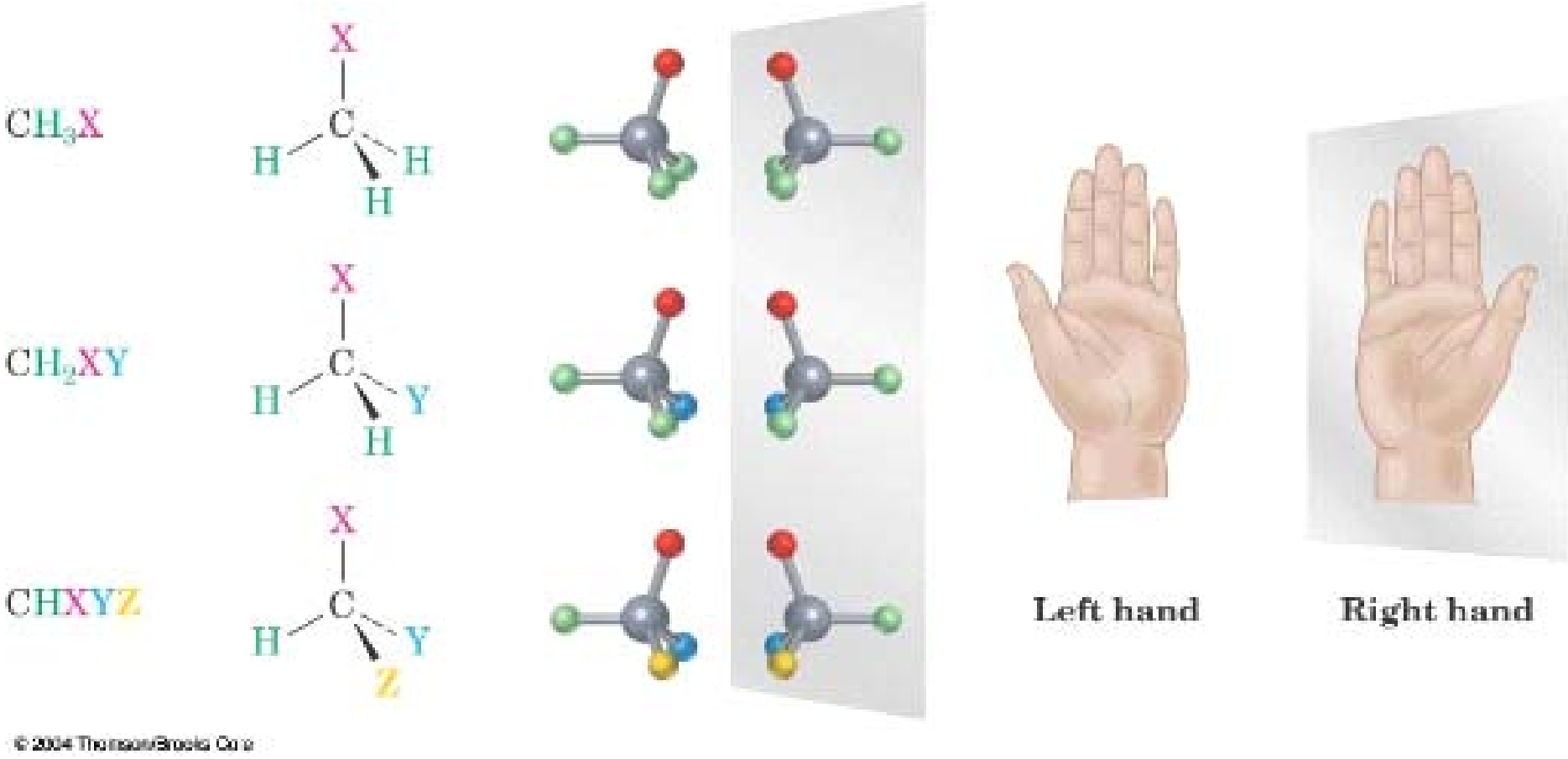
9. Stereochemistry

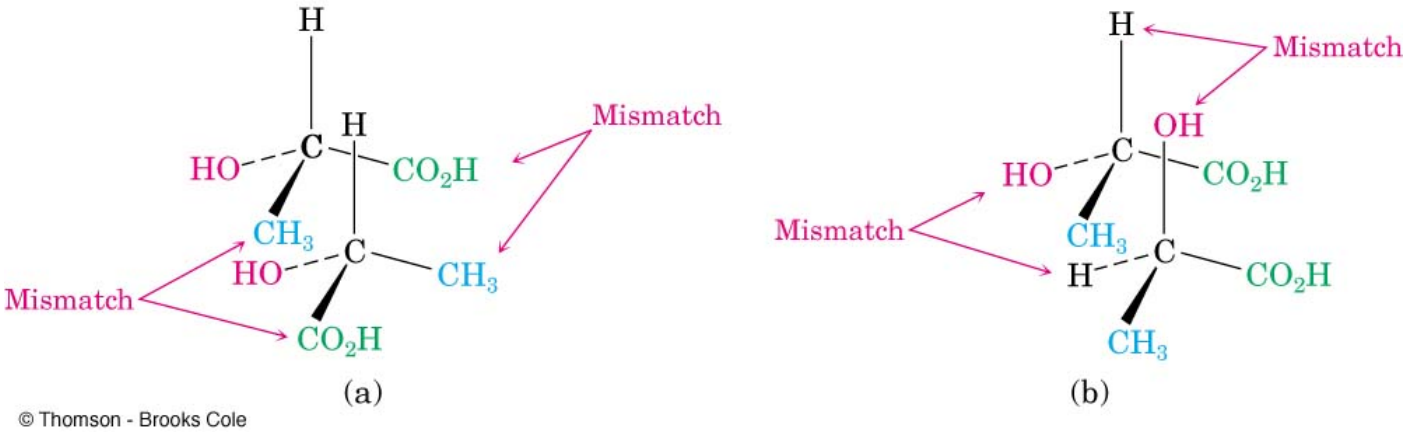
1 Some objects are not the same as their mirror images (technically, they have no plane of symmetry)
   - A right-hand glove is different than a left-hand glove (See Figure 9.1)
   - The property is commonly called “handedness”
2 Organic molecules (including many drugs) have handedness that results from substitution patterns on *sp3* hybridized carbon

1 Molecules exist as three-dimensional objects
2 Some molecules are the same as their mirror image
3 Some molecules are different than their mirror image
   - These are stereoisomers called enantiomers (mirror images)



9.1 Enantiomers and the Tetrahedral Carbon

1 **Enantiomers** are molecules that are not the same as their mirror image
2 They are the "same" if the positions of the atoms can coincide on a one-to-one basis (we test if they are *superimposable*)
3 This is illustrated by enantiomers of lactic acid



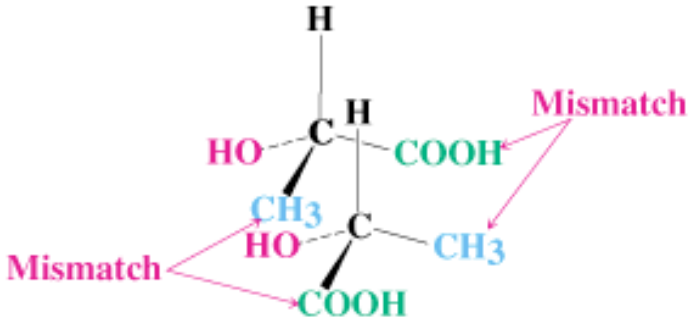
Examples of Enantiomers

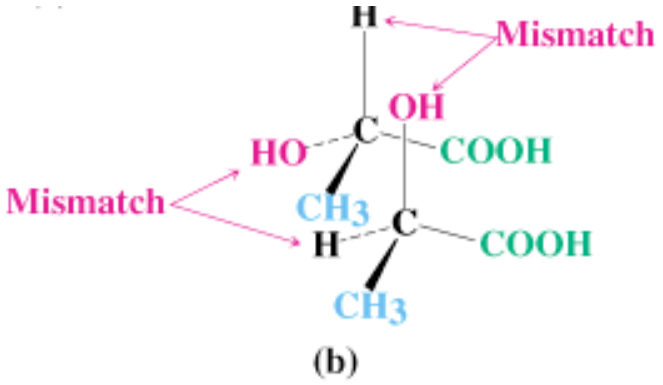
1 Molecules that have one carbon with 4 different substituents have a nonsuperimposable mirror image – enantiomer

2 Build molecular models to see this

Mirror-image Forms of Lactic Acid

1 When **H** and **OH** substituents match up, **COOH** and **CH3** don't
2 when **COOH** and **CH3** coincide, **H** and **OH** don't





(b)

9.2 The Reason for Handedness: Chirality

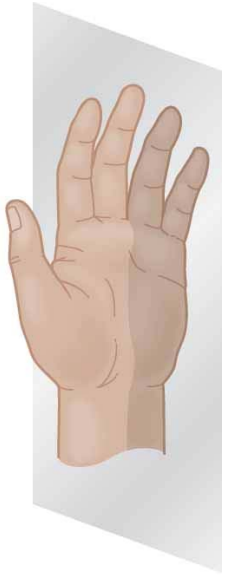
1 Molecules that are not superimposable with their mirror images are **chiral** (have handedness)

2 A **plane of symmetry** divides an entire molecule into two pieces that are exact mirror images

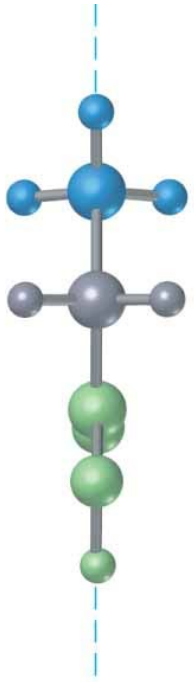
3 A molecule with a plane of symmetry is the same as its mirror image and is said to be **achiral or non chiral** (See Figure 9.4 for examples)

The plane has the same thing on both sides for the flask
There is no mirror plane for a hand

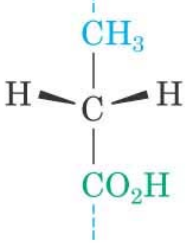
(a)



(b)



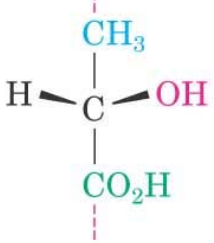
Symmetry plane



$CH_3CH_2CO_2H$

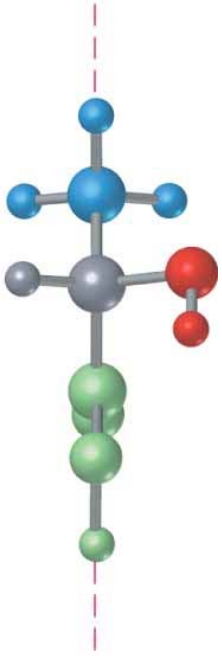
Propanoic acid (achiral)

NOT symmetry plane



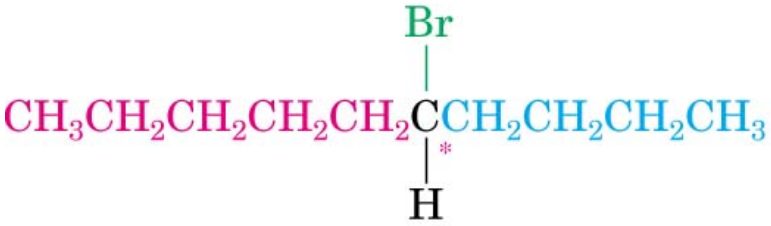
CH_3CHCO_2H

Lactic acid (chiral)



Chirality Centers

1. A point in a molecule where four different groups (or atoms) are attached to carbon is called a **chirality center (chiral center, or asymmetric center)**
2. There are two non superimposable ways that 4 different groups (or atoms) can be attached to one carbon atom
   - If two groups are the same, then there is only one way
3. A chiral molecule usually has at least one chirality center



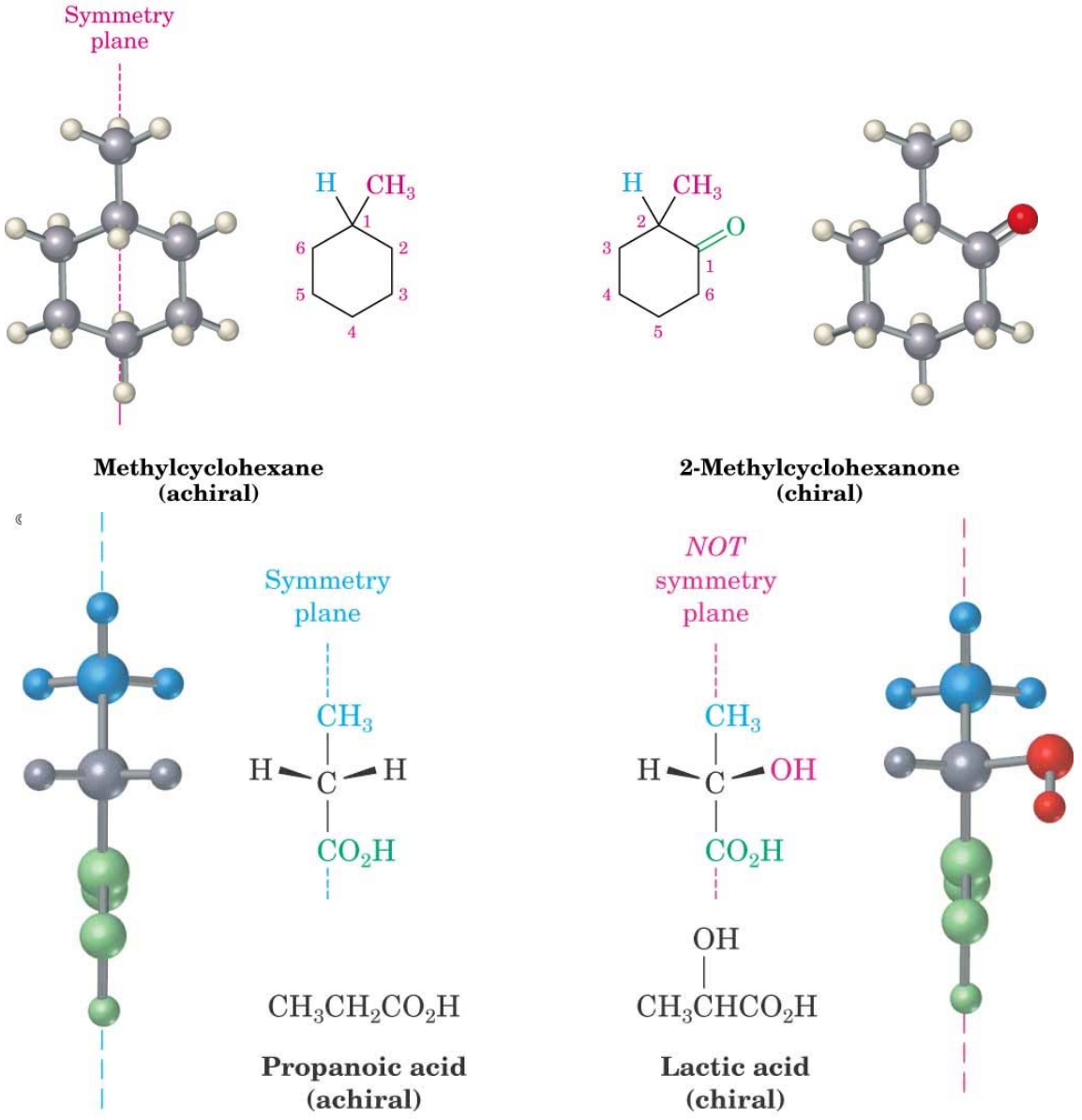
5-Bromodecane (chiral)

Substituents on carbon 5
—H
—Br
—$CH_2CH_2CH_2CH_3$ (butyl)
—$CH_2CH_2CH_2CH_2CH_3$ (pentyl)

Chirality Centers in Chiral Molecules

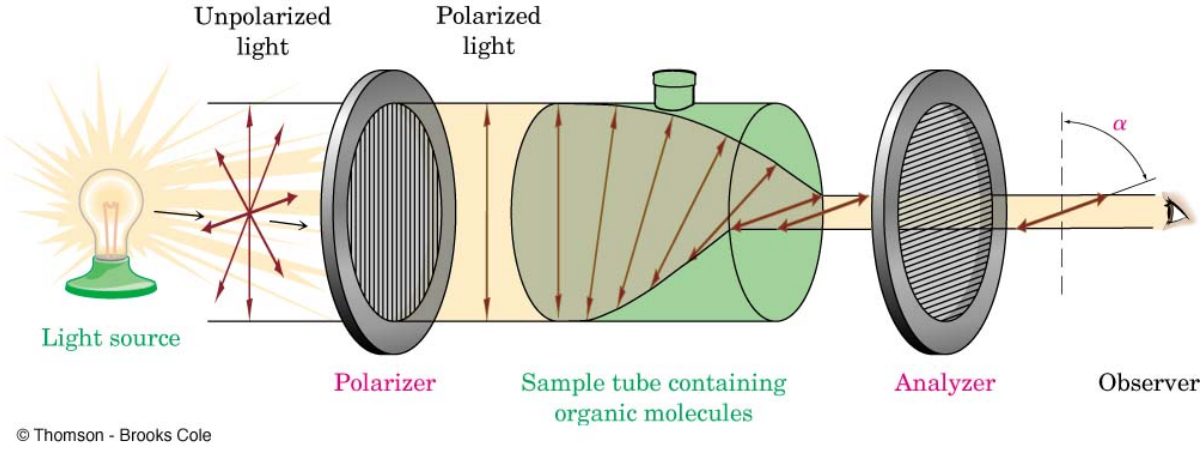
1 Groups are considered “different” if there is any structural variation (if the groups could not be superimposed if detached, they are different)

2 In cyclic molecules, we compare by following in each direction in a rin



9.3 Optical Activity

1 Light restricted to pass through a plane is *plane-polarized*
2 Plane-polarized light that passes through solutions of achiral compounds remains in that plane
3 Solutions of chiral compounds rotate plane-polarized light and the molecules are said to be *optically active*
4 Phenomenon discovered by Biot in the early 19th century



1 Light passes through a plane polarizer
2 Plane polarized light is rotated in solutions of optically active compounds
3 Measured with polarimeter, Rotation, in degrees, is [α]
4 Clockwise rotation is called **dextrorotatory**
5 Anti-clockwise is **levorotatory**

Measurement of Optical Rotation

1 A *polarimeter* measures the rotation of plane-polarized light that has passed through a solution
2 The source passes through a *polarizer* and then is detected at a second polarizer
3 The angle between the entrance and exit planes is the optical rotation.

9.4 Specific Rotation

1 To have a basis for comparison, define **specific rotation, $[\alpha]_D$** for an optically active compound
2 $[\alpha]_D$ = observed rotation/(pathlength x concentration)
$= \alpha/(l \times C) = degrees/(dm \times g/mL)$
3 Specific rotation is that observed for 1 g/mL in solution in cell with a 10 cm

path using light from sodium metal vapor (589 nanometers)

4 See Table 9.1 for examples

- Specific rotation is a characteristic property (physical property) of a compound that is optically active – the compound must be chiral
- The specific rotation of the enantiomer is equal in magnitude but opposite in sign

Specific Rotation of Some Organic Molecules

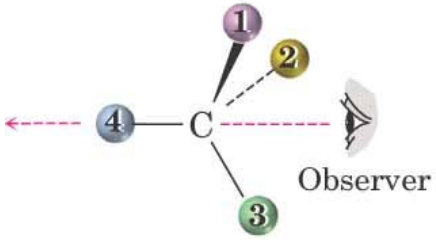
Compound	$[\alpha]_D$(degrees)	Compound	$[\alpha]_D$(degrees)
Penicillin V	-233	Cholesterol	-31.5
Sucrose	-66.47	Morphine	-132
Camphor	-44.26	Acetic acid	0
Monosodium glutamate	+25.5	Benzene	0

9.6 Sequence Rules for Specification of Configuration

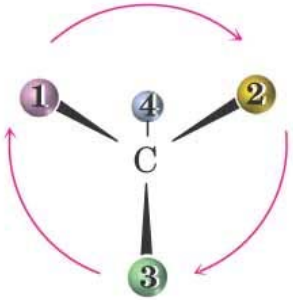
- A general method applies to the configuration at each chirality center (instead of to the the whole molecule)
- The configuration is specified by the relative positions of all the groups with respect to each other at the chirality center
- The groups are ranked in an established priority sequence and compared
- The relationship of the groups in priority order in space determines the label applied to the configuration, according to a rule

Sequence Rules (IUPAC)

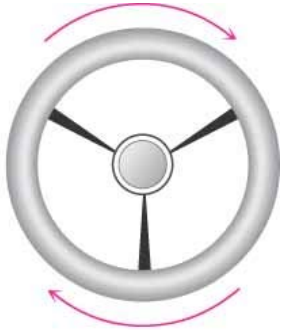
- Assign each group priority according to the Cahn-Ingold-Prelog scheme
  With the lowest priority group pointing away, look at remaining 3 groups in a plane
- Clockwise is designated R (from Latin Rectus for “right”)
- Counterclockwise is designated S (from Latin Sinister for “left”)



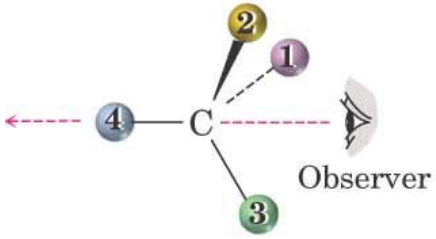
same as



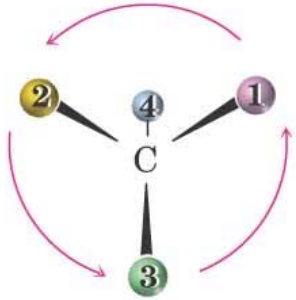
***R* configuration**



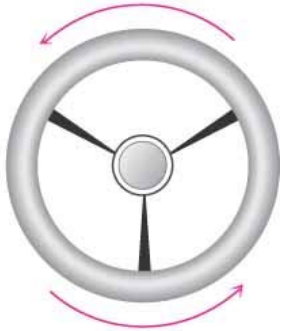
(Right turn of steering wheel)



same as

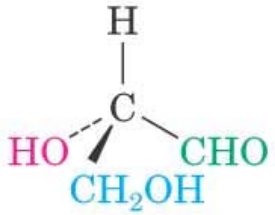


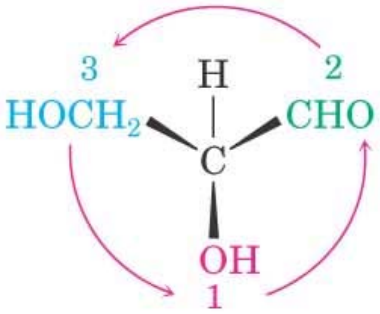
***S* configuration**

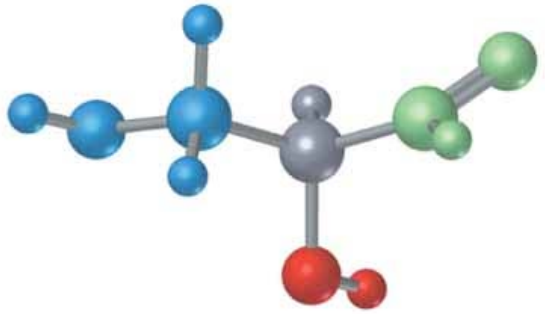


(Left turn of steering wheel)

(a)

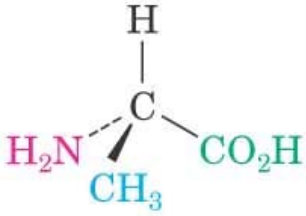


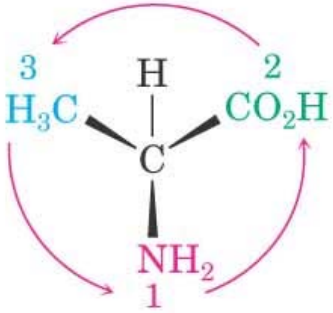


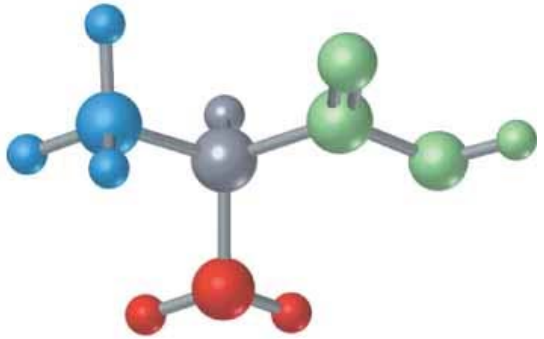


(*S*)-Glyceraldehyde
[(*S*)-(−)-2,3-Dihydroxypropanal]
$[\alpha]_D = -8.7°$

(b)





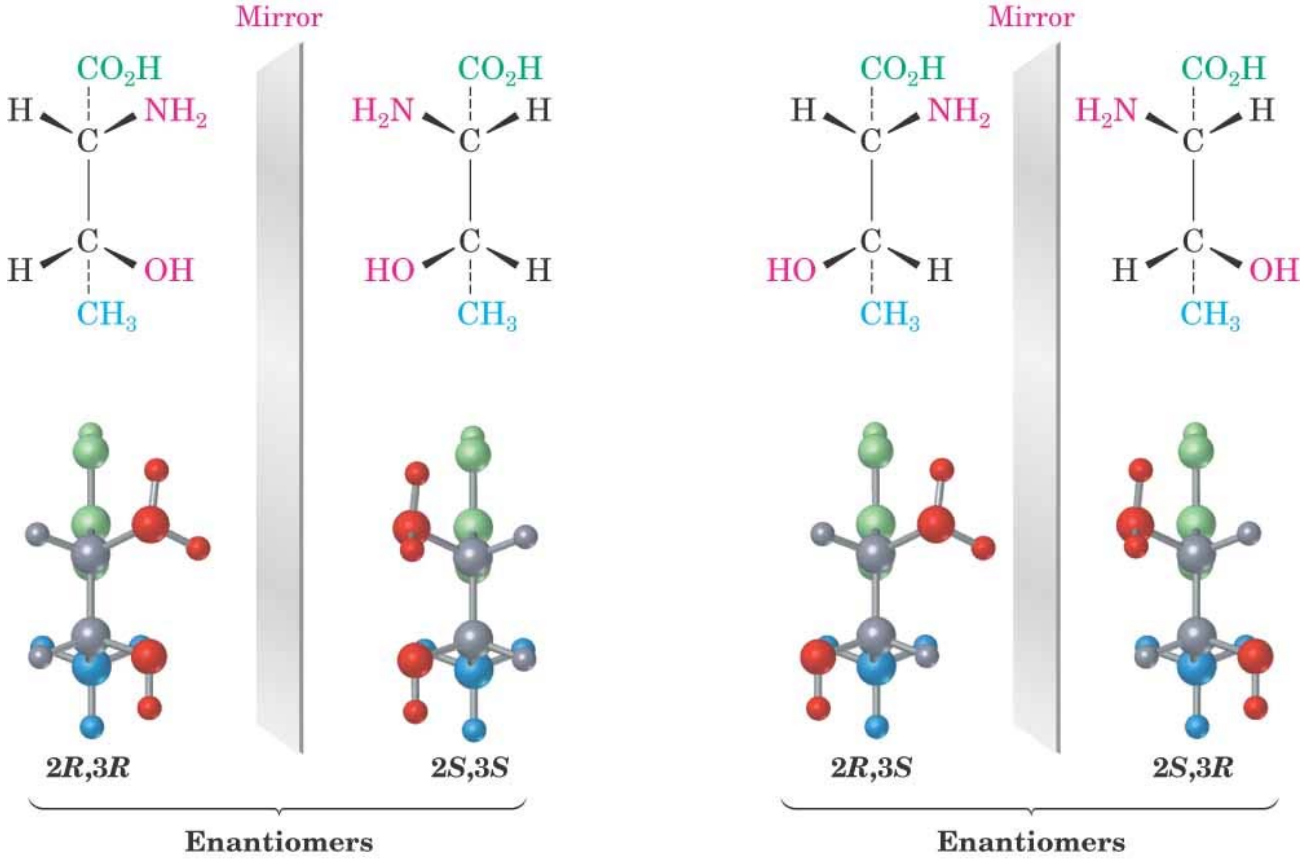


(*S*)-Alanine
[(*S*)-(+)-2-Aminopropanoic acid]
$[\alpha]_D = +8.5°$

9.7 Diastereomers

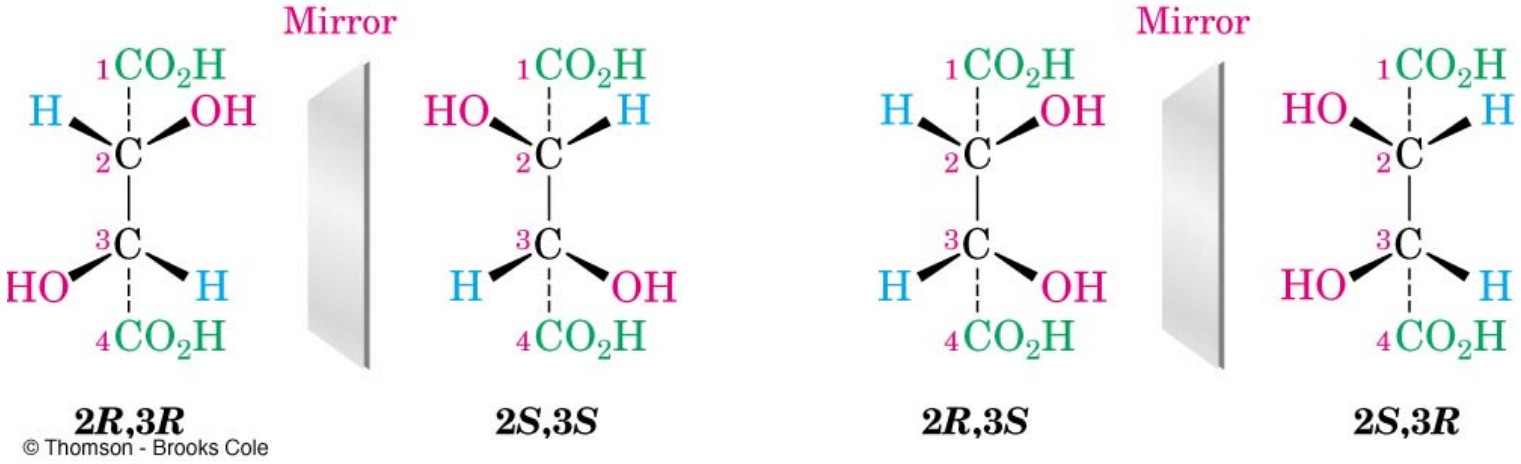
- Molecules with more than one chirality center have mirror image stereoisomers that are enantiomers. In addition they can have stereoisomeric forms that are not mirror images, called **diastereomers** (e.g. 2-amino-3-hydroxybutanoic acid)

The maximum number of stereoisomers a molecule can have is 2^n where n is the number of chiral centers.



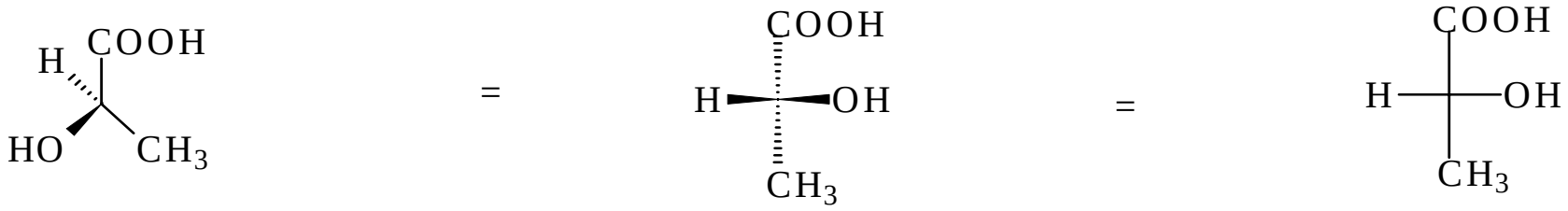
9.8 Meso Compounds

- Tartaric acid has two chirality centers and two diastereomeric forms
- One form is chiral and the other is achiral, but both have two chirality centers
- An achiral compound with chirality centers is called a *meso* compound – it has a plane of symmetry
- The two structures on the right in the figure are identical so the compound (***2R, 3S)*** is achiral (does not rotate PPL)



9.13 Fisher Projections

A tetrahedral carbon is represented in a Fisher projection by two crossed lines. Horizontal lines represent bonds coming out of the plane of the paper and vertical lines represent bonds going into (behind) the plane of the paper.

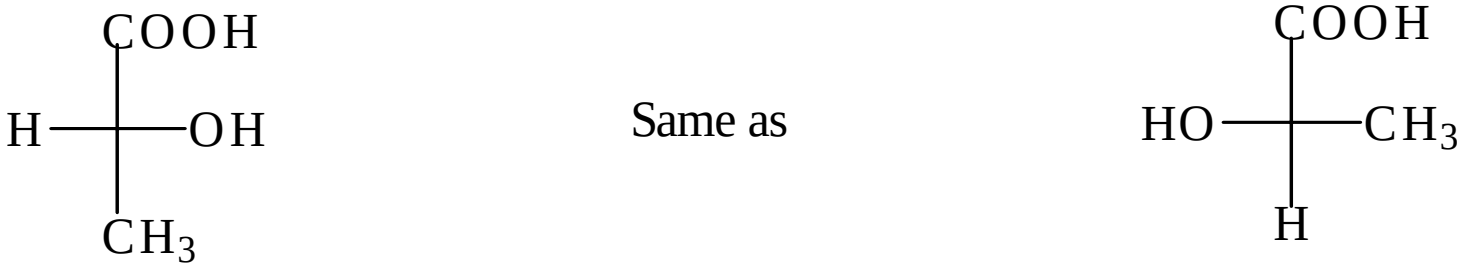


Since chiral molecules can be drawn in more than one way, it is necessary to compare two projections to see if they represent the same molecule or different ones. To do this comparison, two kinds of motions are allowed (motions that do not change the identity or the meaning of the projection).

1) A Fisher projection can be rotated by 180^{o} on the plane of the page (neither 90^{o} nor 270^{o}). e.g. the above projection of (R)-Lactic acid.

2) A Fisher projection can have one group held steady while the other three

rotate in either clockwise or counterclockwise direction.



9.14 Assigning R,S Configurations to Fisher Projections

Three steps must be followed to assign R,S configuration to Fisher projections:

1) Assign priorities to the four substituents as usual (Cahn-Ingold-Prelog)
2) Perform one of the two allowed motions to place the group of lowest priority at the top of the Fisher projection
3) Determine the direction of rotation of the three remaining groups 1,2,3 and assign R or S accordingly.