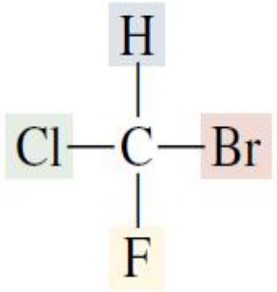
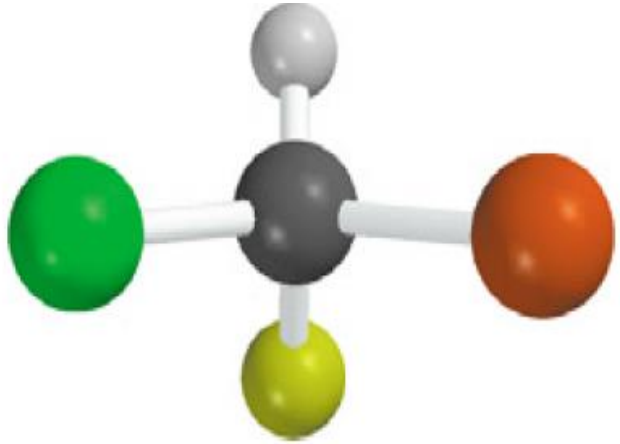
Stereochemistry

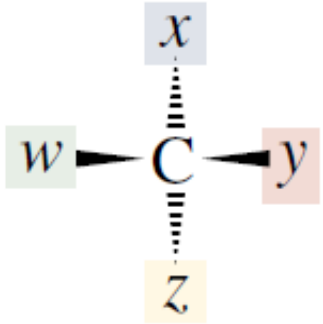
Chiral



Optical active



Bromochlorofluoromethane



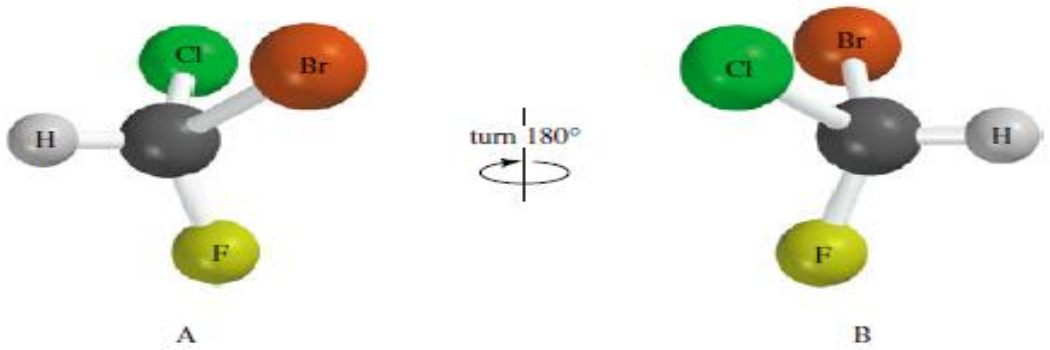
Stereogenic center

Stereoisomers:

1. Enantiomers; 2. Diastereoisomers

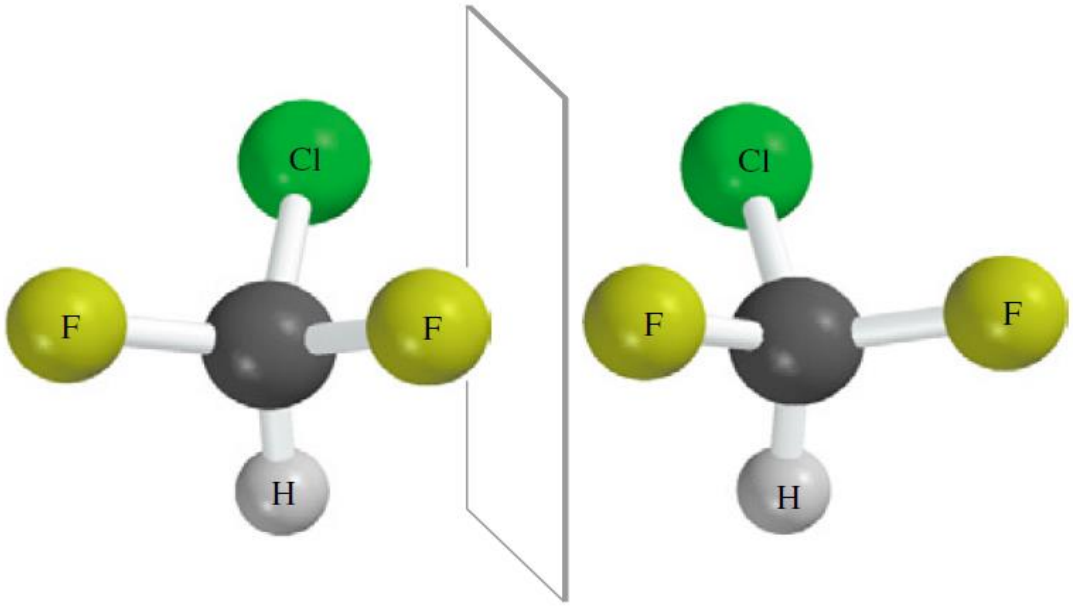
(*a*) Structures A and B are mirror-image representations of bromochlorofluoromethane (BrClFCH).

(*b*) To test for superposability, reorient B by turning it 180°.

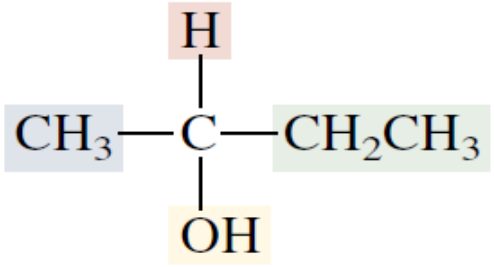


(*c*) Compare A and B. The two do not match. A and B cannot be superposed on each other. Bromochlorofluoromethane is therefore a chiral molecule. The two mirror-image forms are enantiomers of each other.

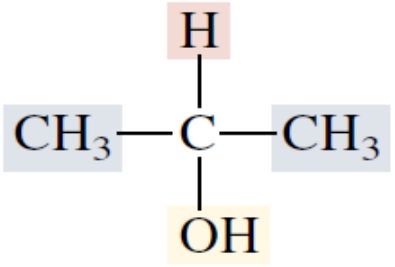
Optical inactive



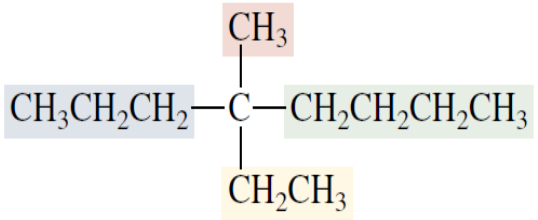
Optical active



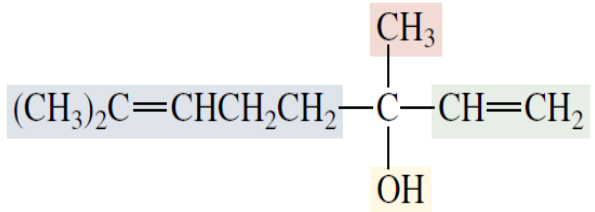
2-Butanol
Chiral; four different substituents at C-2



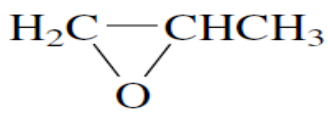
2-Propanol
Achiral; two of the substituents at C-2 are the same



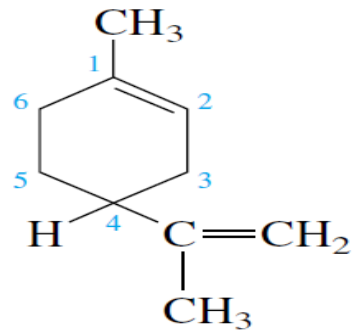
4-Ethyl-4-methyloctane
(a chiral alkane)



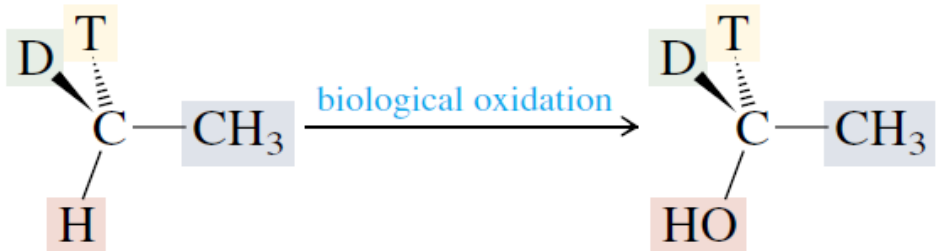
Linalool
(a pleasant-smelling oil
obtained from orange flowers)



1-2-Epoxypropane
(product of epoxidation of propene)

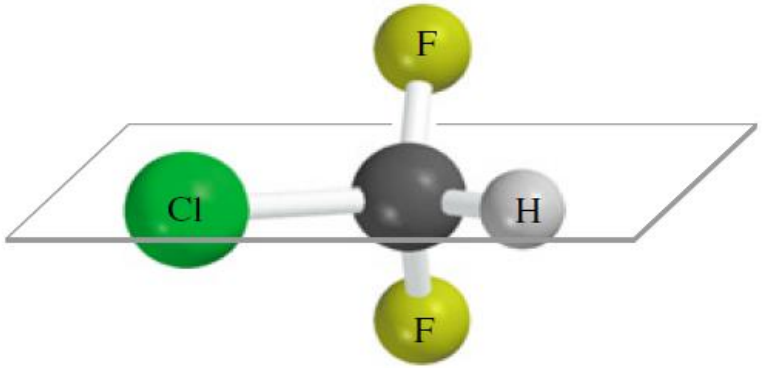


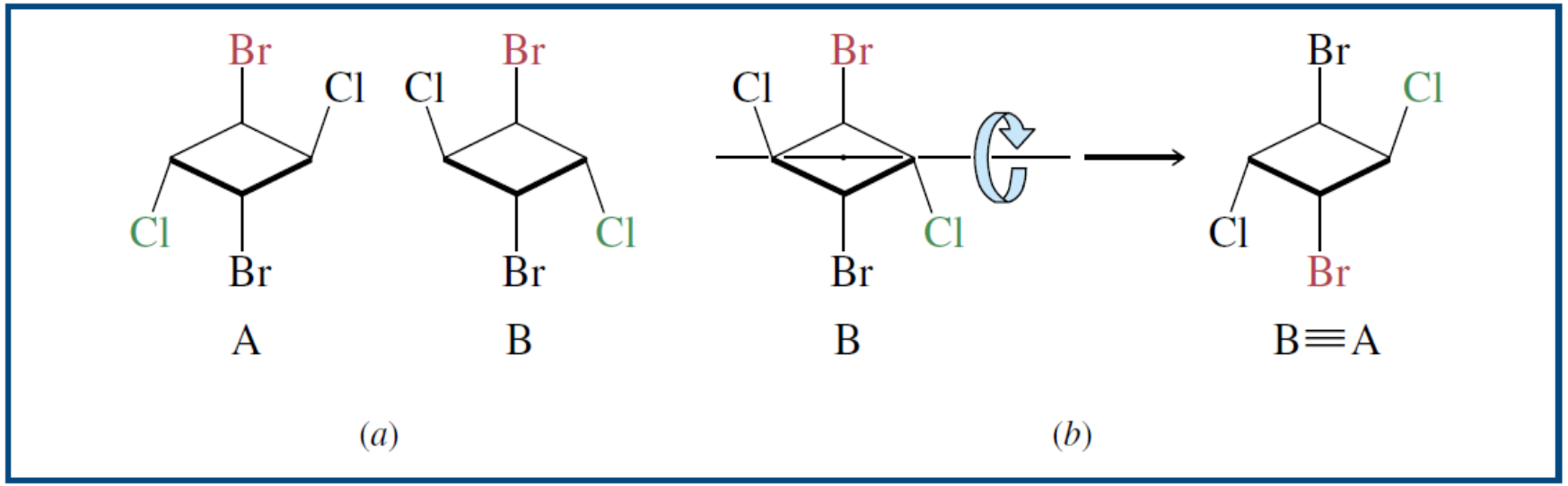
Limonene
(a constituent of lemon oil)



Symmetric in achiral structures

1. Plane of symmetry; 2. Centre of symmetry





Polarimeter

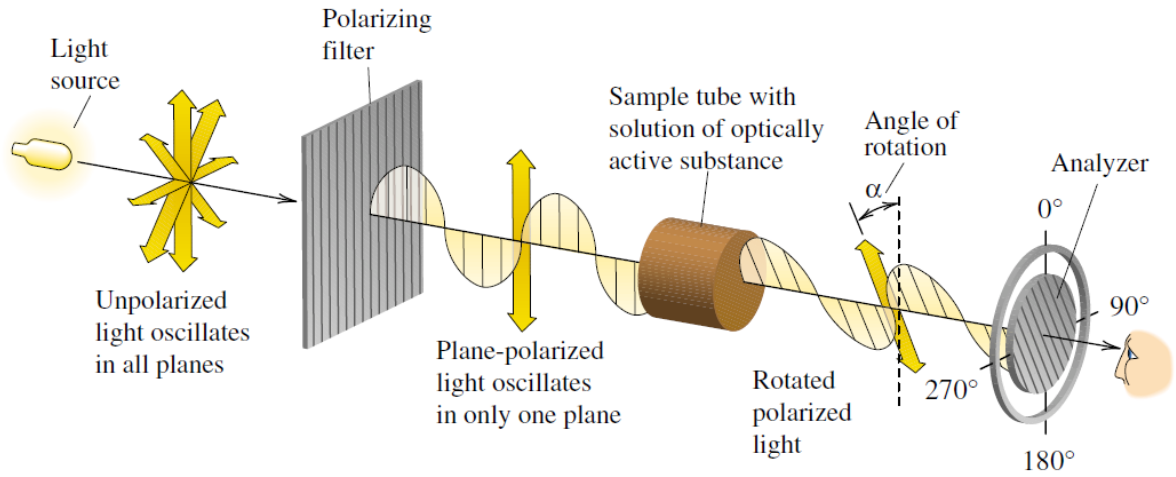


FIGURE 7.5 The sodium lamp emits light moving in all planes. When the light passes through the first polarizing filter, only one plane emerges. The plane-polarized beam enters the sample compartment, which contains a solution enriched in one of the enantiomers of a chiral substance. The plane rotates as it passes through the solution. A second polarizing filter (called the analyzer) is attached to a movable ring calibrated in degrees that is used to measure the angle of rotation α.

Optical activity

Mixtures containing equal quantities of enantiomers are called **racemic mixtures.** Racemic mixtures are optically inactive. Conversely, when one enantiomer is present in excess, a net rotation of the plane of polarization is observed. At the limit, where all the molecules are of the same handedness, we say the substance is **optically pure.** Optical purity, or *percent enantiomeric excess,* is defined as:

$$\begin{aligned}\text{Optical purity} &= \text{percent enantiomeric excess} \\ &= \text{percent of one enantiomer} - \text{percent of other enantiomer}\end{aligned}$$

Thus, a material that is 50% optically pure contains 75% of one enantiomer and 25% of the other.

Rotation of the plane of polarized light in the clockwise sense is taken as positive (+), and rotation in the anticlockwise sense is taken as a negative (−) rotation. The classical terms for positive and negative rotations are *dextrorotatory* and *levorotatory,* from the Latin prefixes *dextro-* ("to the right") and *levo-* ("to the left"), respectively. At one time, the symbols *d* and *l* were used to distinguish between enantiomeric forms of a substance. Thus the dextrorotatory enantiomer of 2-butanol was called *d*-2-butanol, and the levorotatory form *l*-2-butanol; a racemic mixture of the two was referred to as *dl*-2-butanol. Current custom favors using algebraic signs instead, as in (+)-2-butanol, (−)-2-butanol, and (±)-2-butanol, respectively.

The observed rotation α of an optically pure substance depends on how many molecules the light beam encounters. A filled polarimeter tube twice the length of another produces twice the observed rotation, as does a solution twice as concentrated. To account for the effects of path length and concentration, chemists have defined the term **specific rotation,** given the symbol [α]. Specific rotation is calculated from the observed rotation according to the expression

$$[\alpha] = \frac{100\alpha}{cl}$$

where c is the concentration of the sample in grams per 100 mL of solution, and l is the length of the polarimeter tube in decimeters. (One decimeter is 10 cm.)

Specific rotation is a physical property of a substance, just as melting point, boiling point, density, and solubility are. For example, the lactic acid obtained from milk is exclusively a single enantiomer. We cite its specific rotation in the form $[\alpha]_{D}^{25} = +3.8°$. The temperature in degrees Celsius and the wavelength of light at which the measurement was made are indicated as superscripts and subscripts, respectively.

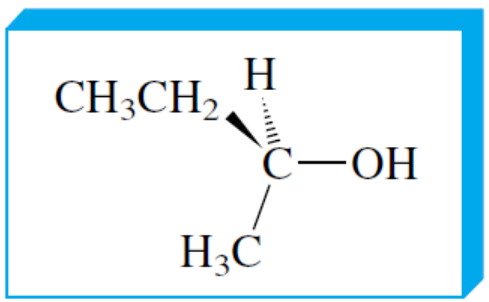
If concentration is expressed as grams per milliliter of solution instead of grams per 100 mL, an equivalent expression is

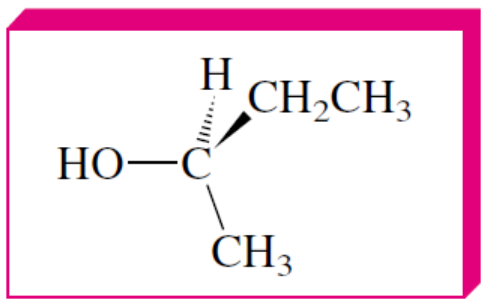
$$[\alpha] = \frac{\alpha}{cl}$$

It is convenient to distinguish between enantiomers by prefixing the sign of rotation to the name of the substance. For example, we refer to one of the enantiomers of 2-butanol as (+)-2-butanol and the other as (−)-2-butanol. Optically pure (+)-2-butanol has a specific rotation $[\alpha]_D^{27}$ of +13.5°; optically pure (−)-2-butanol has an exactly opposite specific rotation $[\alpha]_D^{27}$ of −13.5°.

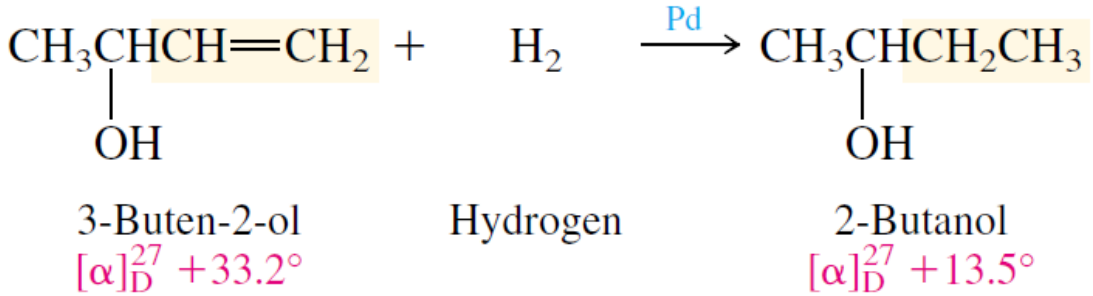
7.5 ABSOLUTE AND RELATIVE CONFIGURATION

The spatial arrangement of substituents at a stereogenic center is its **absolute configuration.** Neither the sign nor the magnitude of rotation by itself can tell us the absolute configuration of a substance. Thus, one of the following structures is (+)-2-butanol and the other is (−)-2-butanol, but without additional information we can't tell which is which.





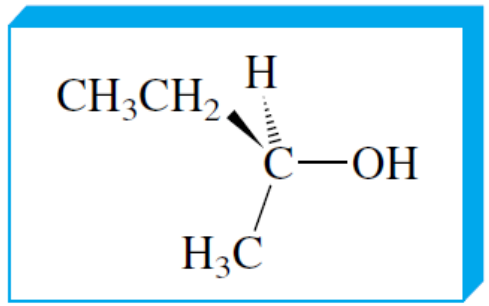
Although no absolute configuration was known for any substance before 1951, organic chemists had experimentally determined the configurations of thousands of compounds relative to one another (their **relative configurations**) through chemical interconversion. To illustrate, consider (+)-3-buten-2-ol. Hydrogenation of this compound yields (+)-2-butanol.



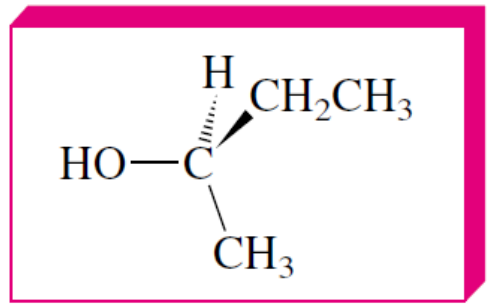
3-Buten-2-ol
$[\alpha]_D^{27}$ +33.2°

Hydrogen

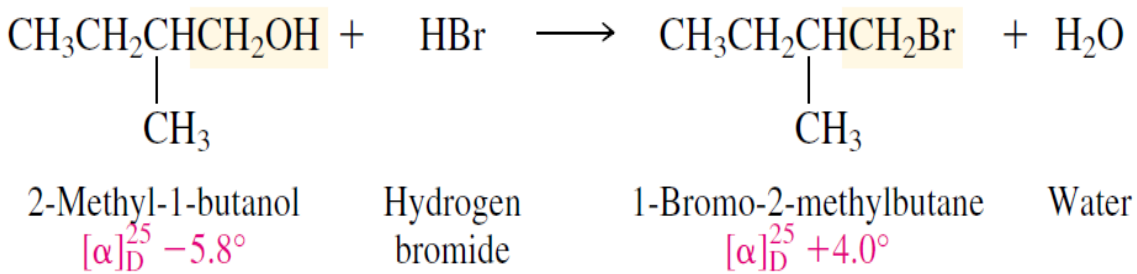
2-Butanol
$[\alpha]_D^{27}$ +13.5°



(+)-2-Butanol



(−)-2-Butanol

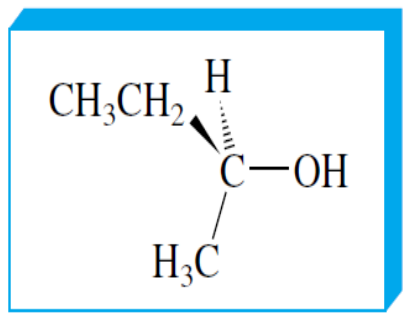


2-Methyl-1-butanol
$[\alpha]_D^{25}$ −5.8°

Hydrogen bromide

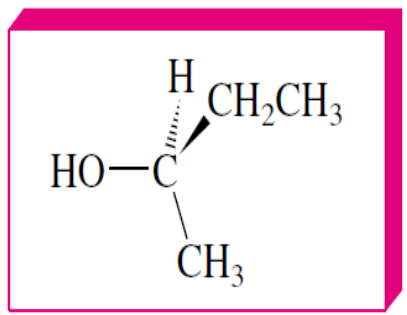
1-Bromo-2-methylbutane
$[\alpha]_D^{25}$ +4.0°

Water



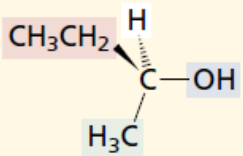
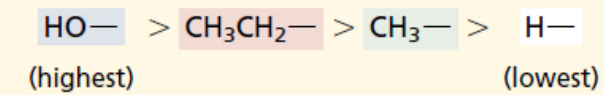
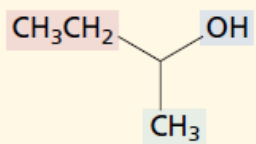
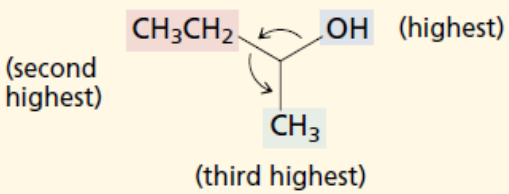
(*S*)-2-Butanol

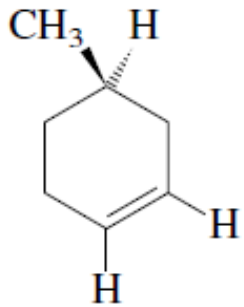
and



(*R*)-2-Butanol

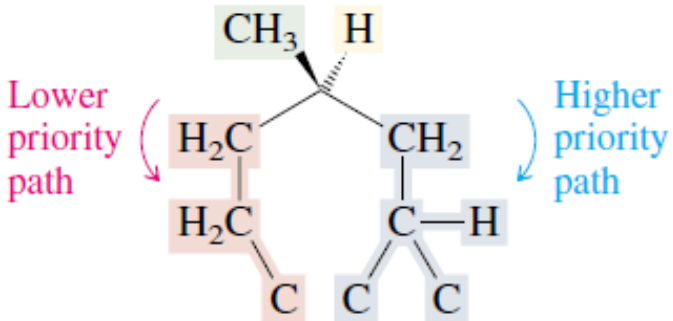
TABLE 7.1 Absolute Configuration According to the Cahn–Ingold–Prelog Notational System

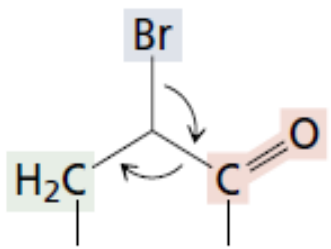
Step number	Example
Given that the absolute configuration of (+)-2-butanol is	 (+)-2-Butanol
1. Identify the substituents at the stereogenic center, and rank them in order of decreasing precedence according to the system described in Section 5.4. Precedence is determined by atomic number, working outward from the point of attachment at the stereogenic center.	In order of decreasing precedence, the four substituents attached to the stereogenic center of 2-butanol are  (highest) (lowest)
2. Orient the molecule so that the lowest ranked substituent points away from you.	As represented in the wedge-and-dash drawing at the top of this table, the molecule is already appropriately oriented. Hydrogen is the lowest ranked substituent attached to the stereogenic center and points away from us.
3. Draw the three highest ranked substituents as they appear to you when the molecule is oriented so that the lowest ranked group points away from you.	
4. If the order of decreasing precedence of the three highest ranked substituents appears in a clockwise sense, the absolute configuration is *R* (Latin *rectus,* "right," "correct"). If the order of decreasing precedence is anticlockwise, the absolute configuration is *S* (Latin *sinister,* "left").	The order of decreasing precedence is *anticlockwise.* The configuration at the stereogenic center is *S.*  (second highest) (highest) (third highest)



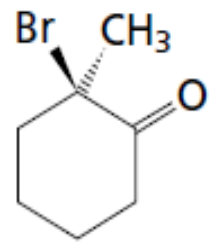
(+)-4-Methylcyclohexene

is treated as



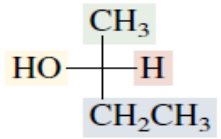


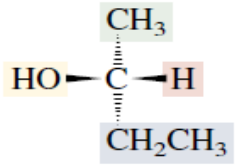
which leads to the structure



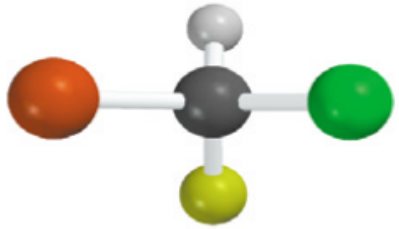
(*R*)-2-Bromo-2-methylcyclohexanone

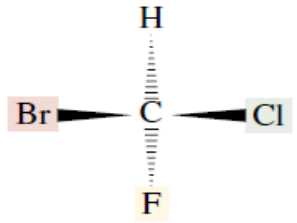
Fisher projection

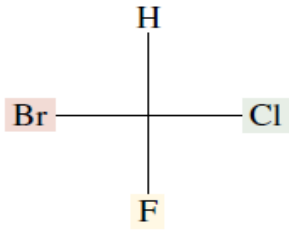
The Fischer projection 

corresponds to 

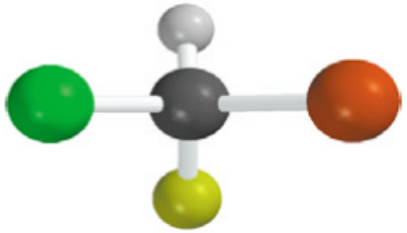
(*R*)-2-Butanol

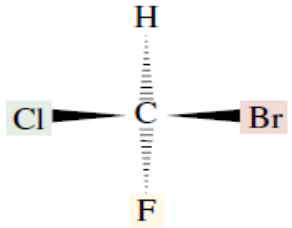


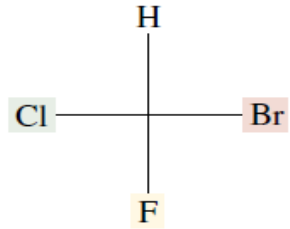




(*R*)-Bromochlorofluoromethane

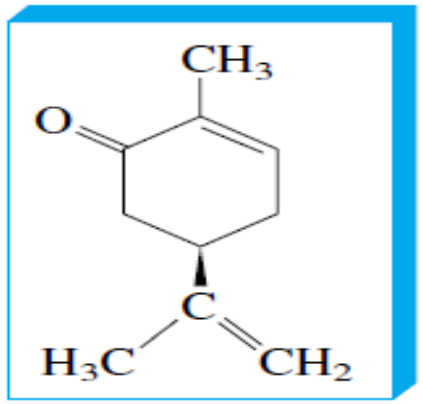






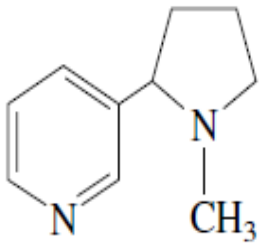
(*S*)-Bromochlorofluoromethane

Physical properties

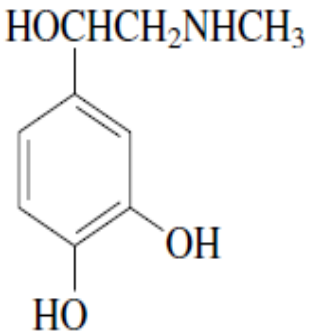


(*R*)-(−)-Carvone
(from spearmint oil)

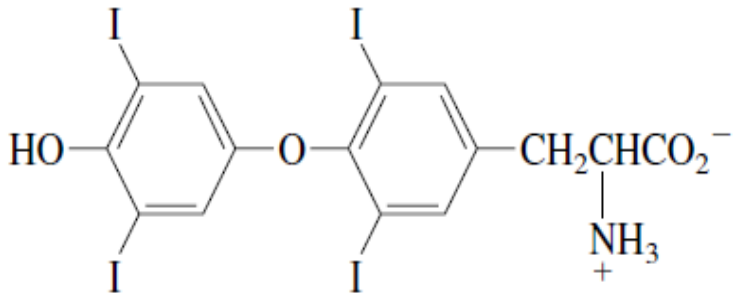
(*S*)-(+)-Carvone
(from caraway seed oil)



Nicotine



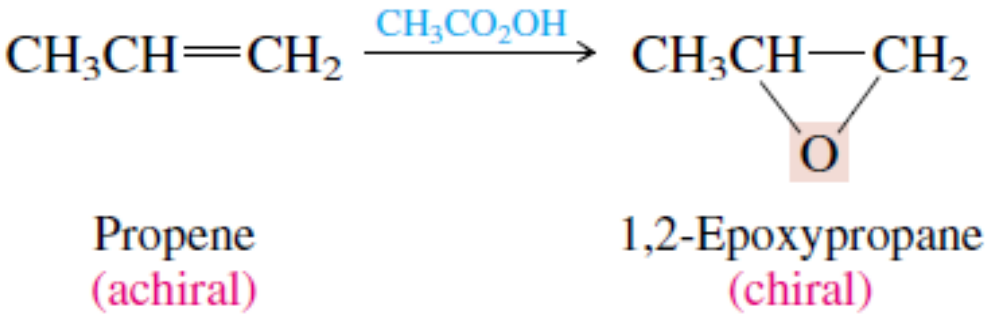
Adrenaline

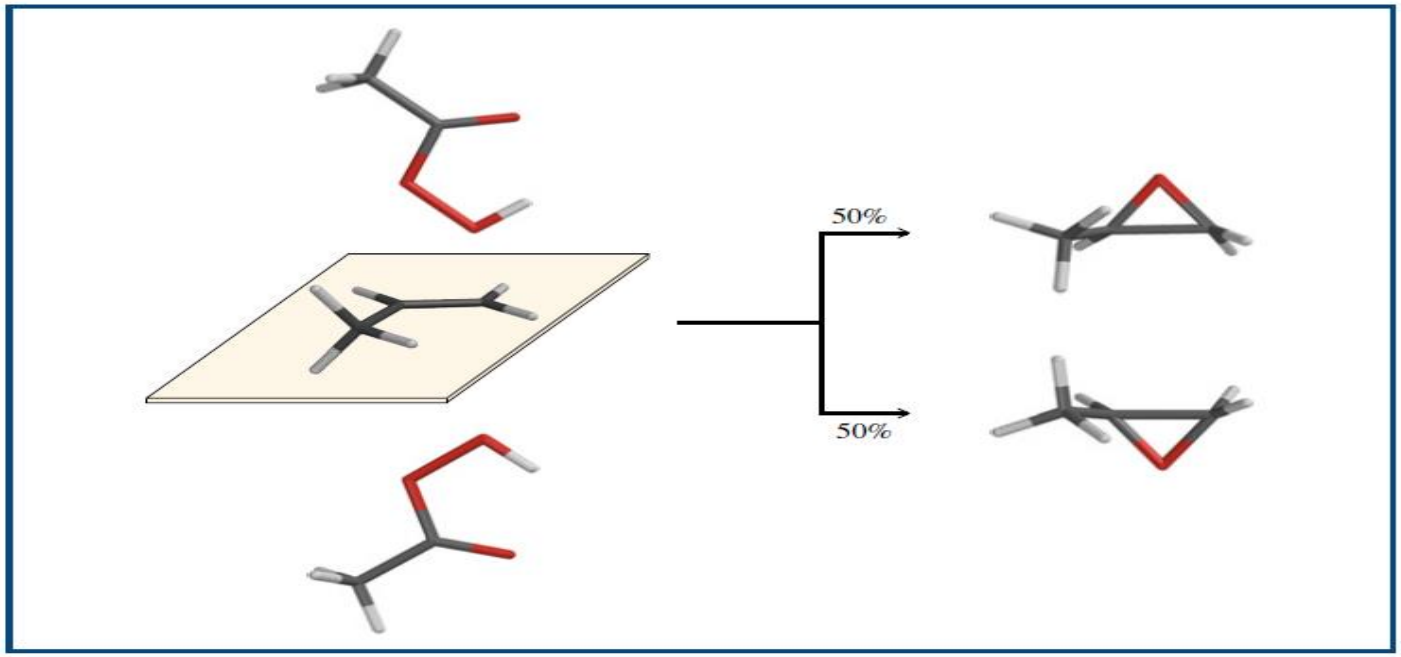


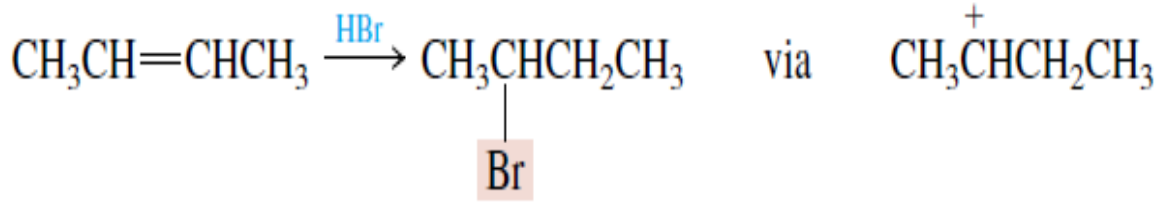
Thyroxine

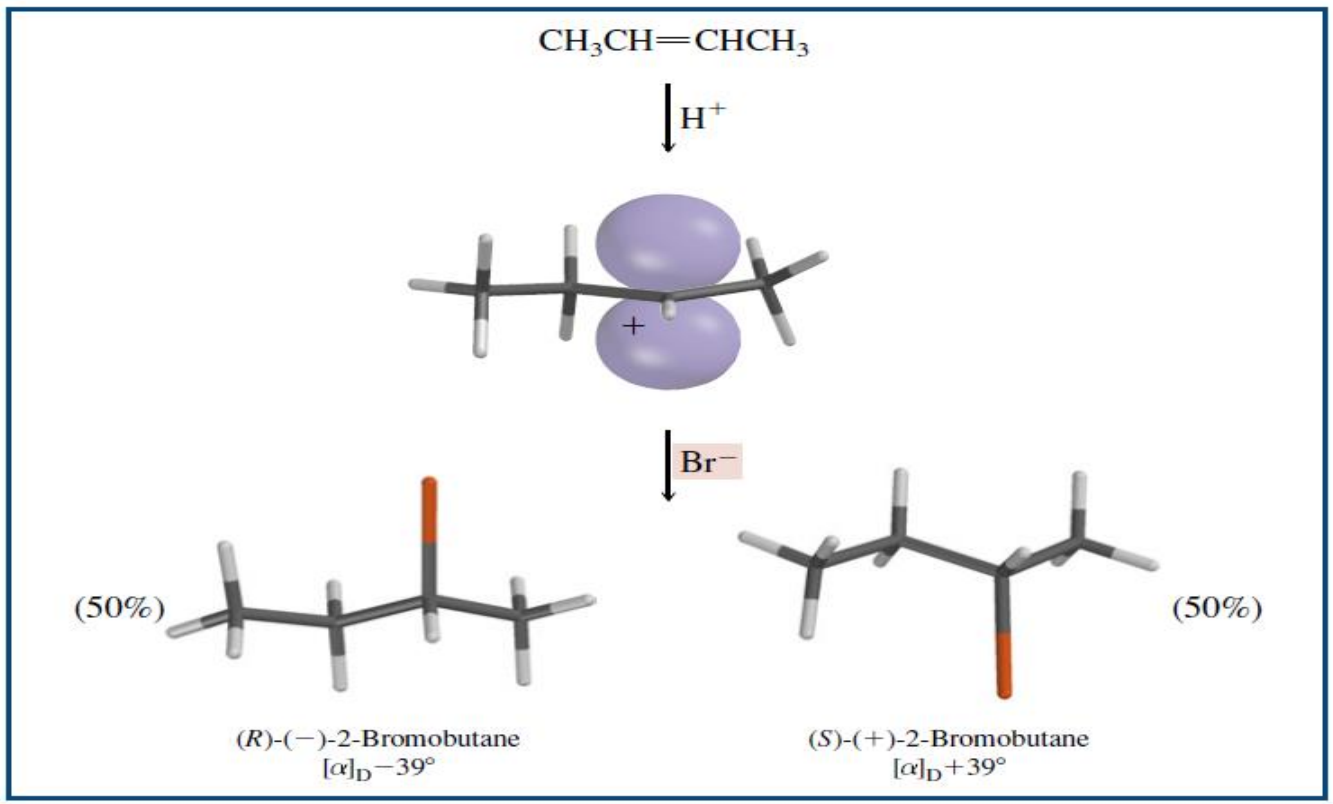
(Can you find the stereogenic center in each of these?)

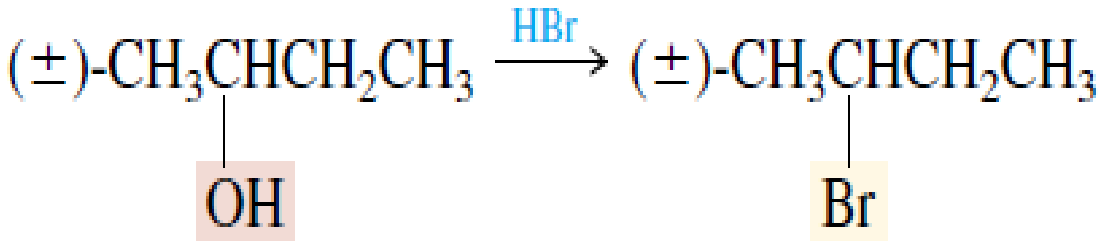
Creation of a stereogenic center





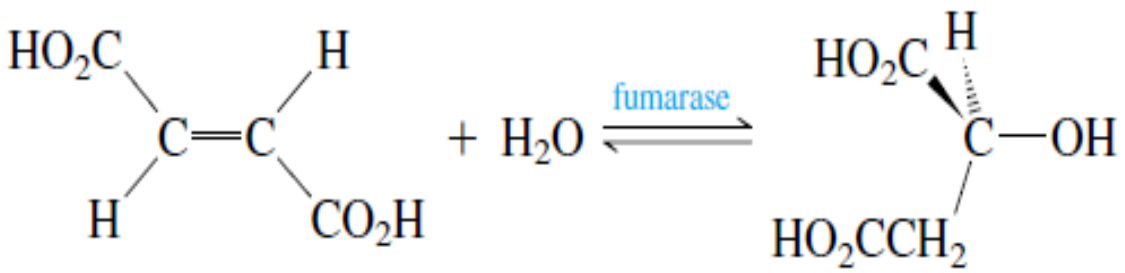

CH3CH=CHCH3
HBr
CH3CHCH2CH3
Br
via
+
CH3CHCH2CH3
(E)- or (Z)-2-butene
(achiral)
2-Bromobutane
(chiral)
sec-Butyl cation
(achiral)


CH3CH=CHCH3
H+
+
Br−
(50%)
(50%)
(R)-(−)-2-Bromobutane
[α]D −39°
(S)-(+)-2-Bromobutane
[α]D +39°



2-Butanol
(chiral but racemic)

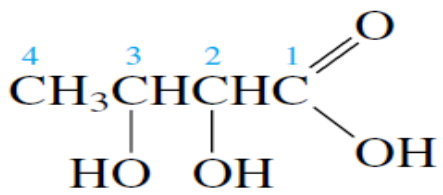
2-Bromobutane
(chiral but racemic)



Fumaric acid

(*S*)-(−)-Malic acid

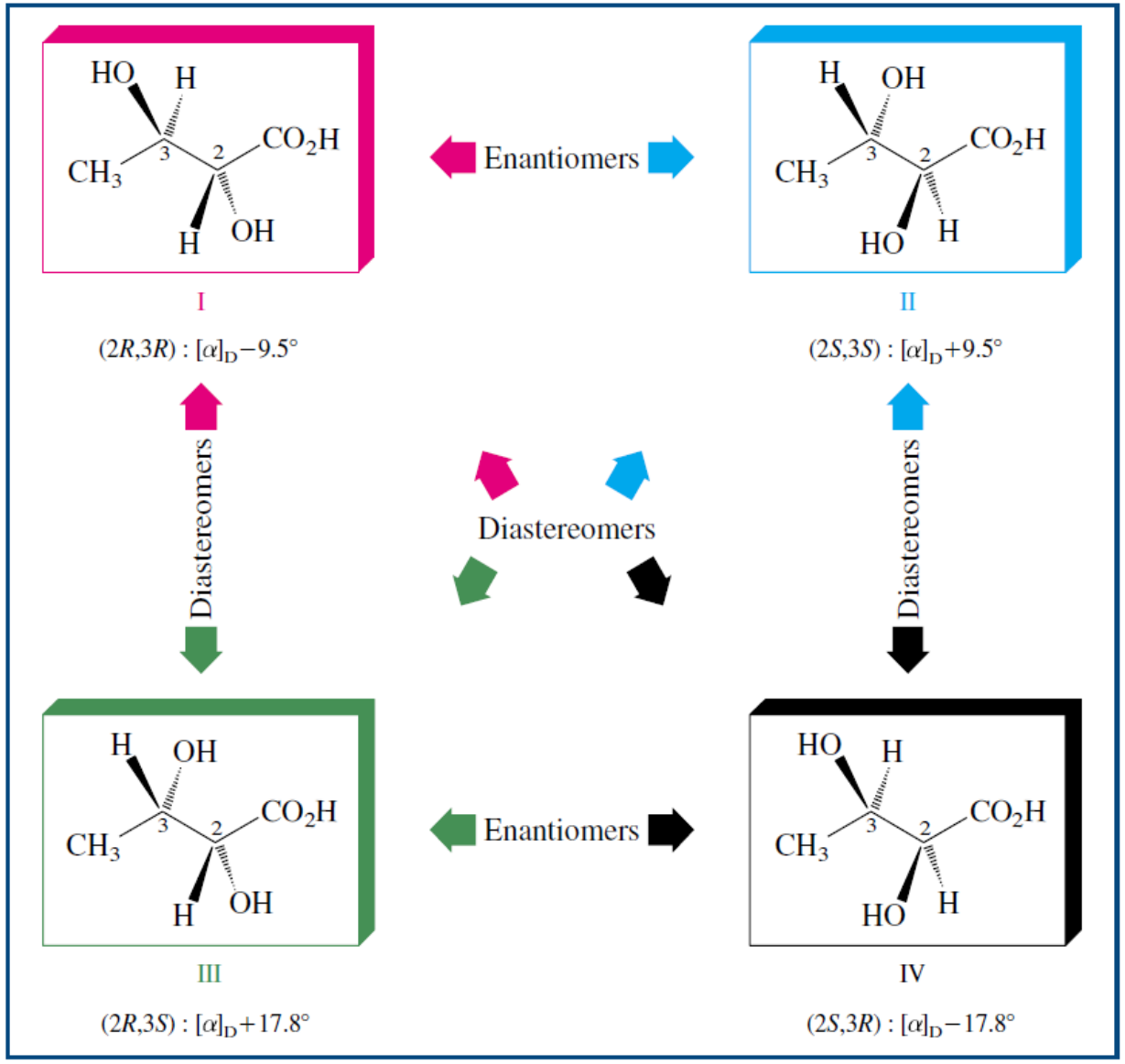
Molecules with two chiral centers

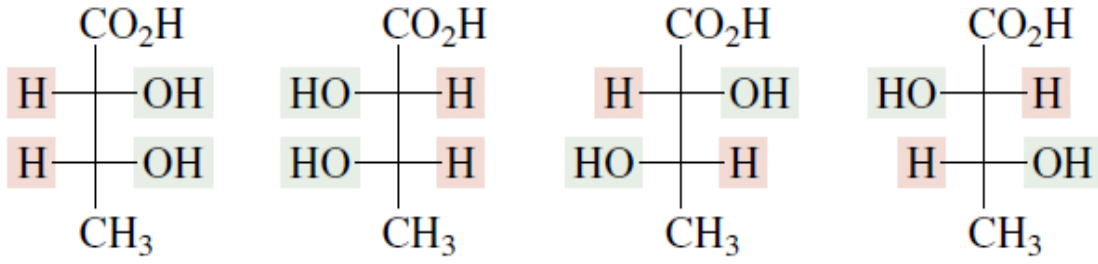


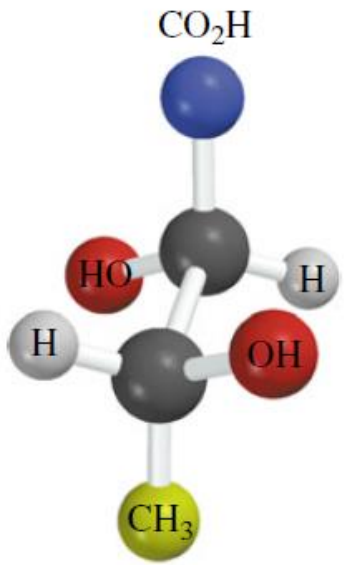
2,3-Dihydroxybutanoic acid

(2*R*,3*R*) (stereoisomer I) (2*S*,3*S*) (stereoisomer II)

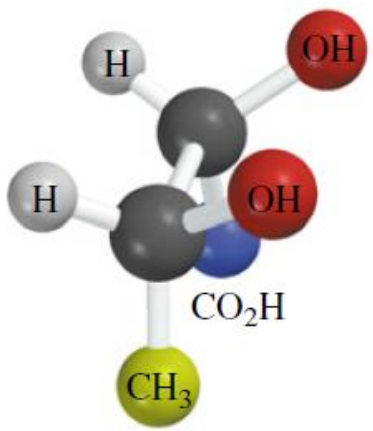
(2*R*,3*S*) (stereoisomer III) (2*S*,3*R*) (stereoisomer IV)



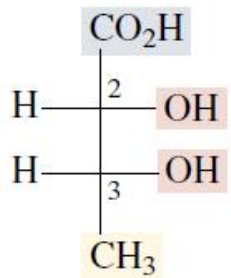

CO2H
H
OH
H
OH
CH3
I
erythro
CO2H
HO
H
HO
H
CH3
II
erythro
CO2H
H
OH
HO
H
CH3
III
threo
CO2H
HO
H
H
OH
CH3
IV
threo


CO2H
HO
H
H
OH
CH3

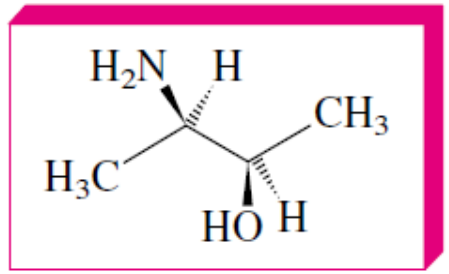
(*a*)


H
OH
H
OH
CO2H
CH3

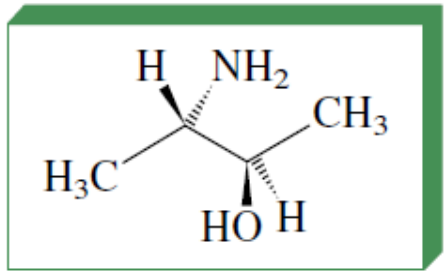
(*b*)


CO2H
2
H
OH
H
OH
3
CH3

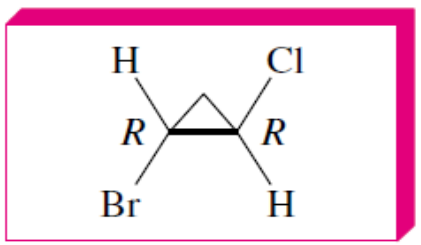
(*c*)



(2*R*,3*R*)-3-Amino-2-butanol
(liquid)

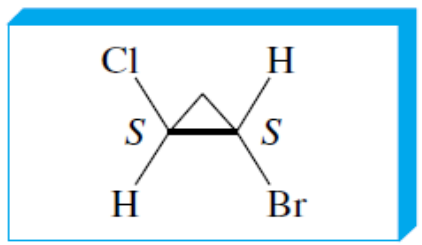


(2*R*,3*S*)-3-Amino-2-butanol
(solid, mp 49°C)

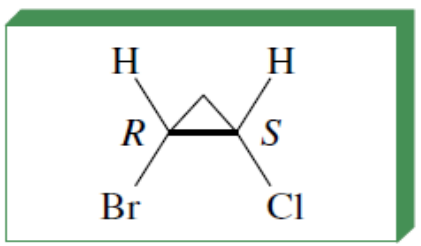


(1*R*,2*R*)-1-Bromo-2-chlorocyclopropane

Enantiomers

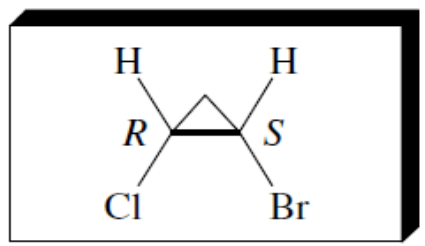


(1*S*,2*S*)-1-Bromo-2-chlorocyclopropane

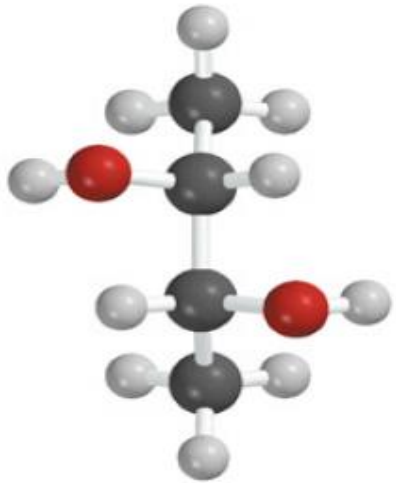


(1*R*,2*S*)-1-Bromo-2-chlorocyclopropane

Enantiomers

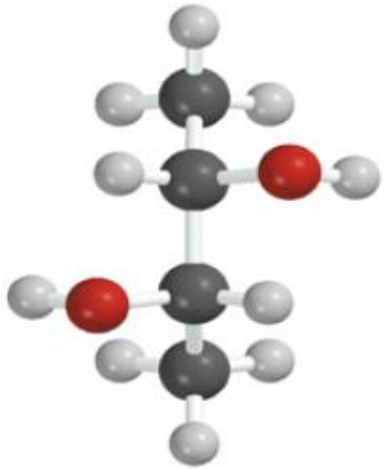


(1*S*,2*R*)-1-Bromo-2-chlorocyclopropane



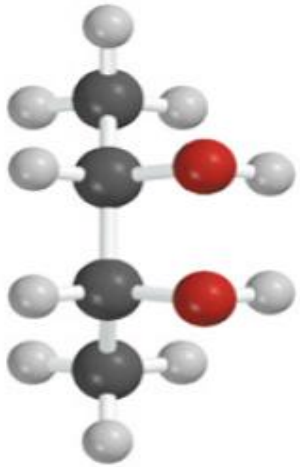
(2*R*,3*R*)-2,3-Butanediol

(*a*)



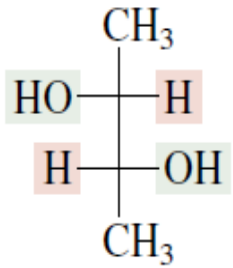
(2*S*,3*S*)-2,3-Butanediol

(*b*)

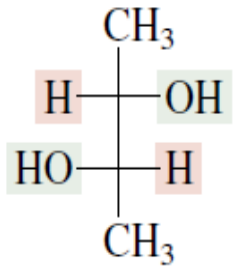


meso-2,3-Butanediol

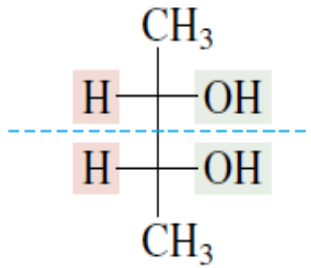
(*c*)



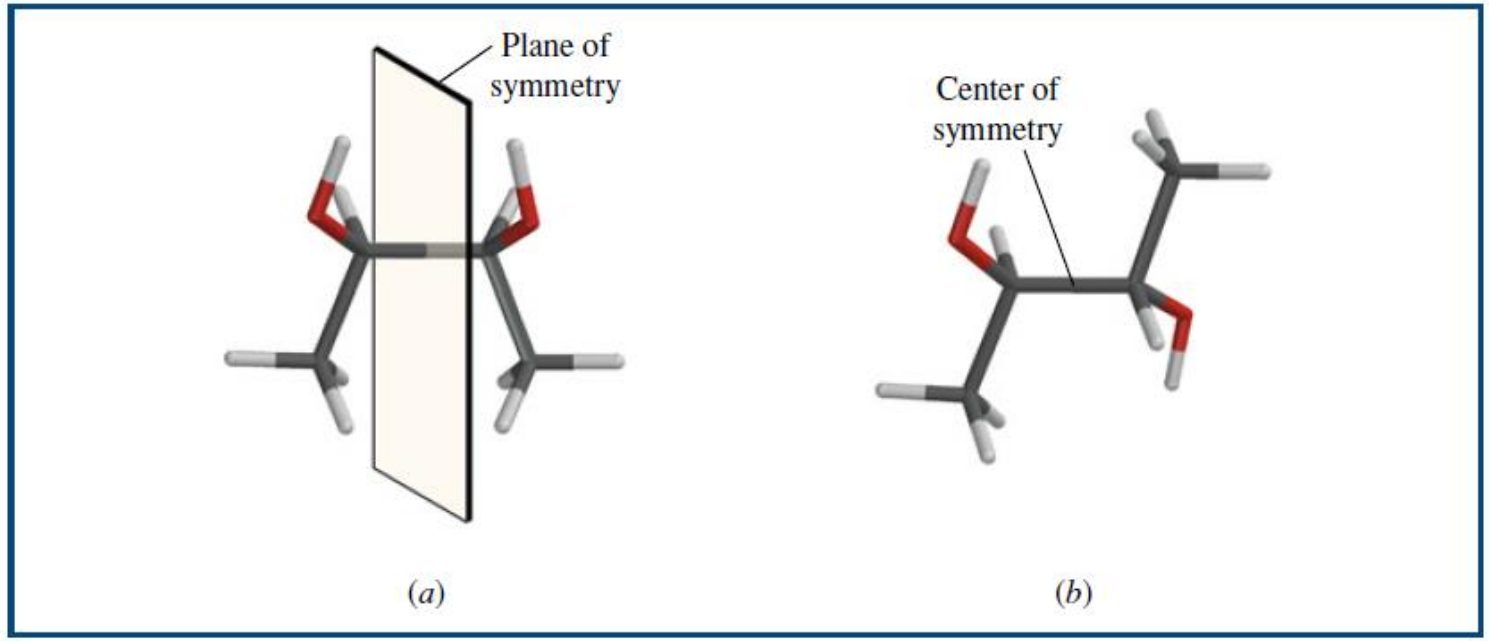
(2*R*,3*R*)-2,3-Butanediol

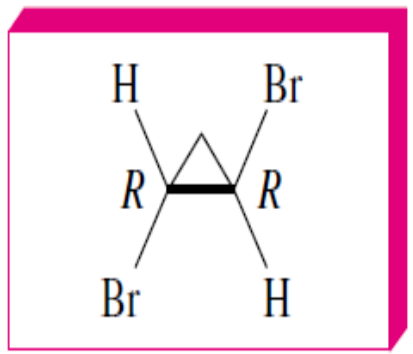


(2*S*,3*S*)-2,3-Butanediol

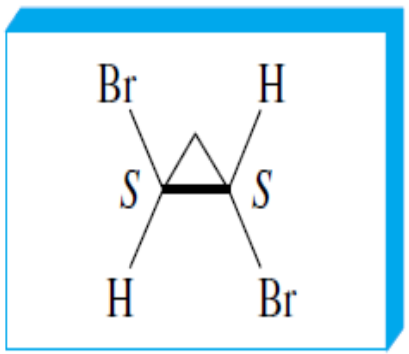


meso-2,3-Butanediol

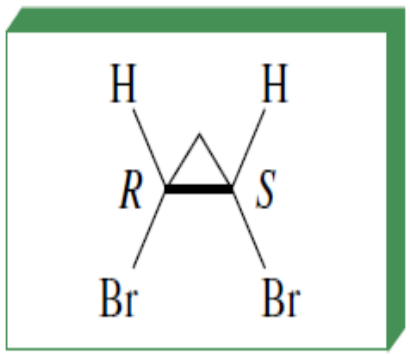




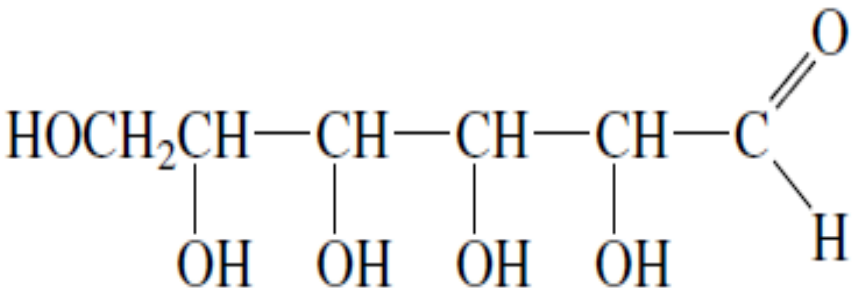
(1*R*,2*R*)-1,2-Dibromocyclopropane



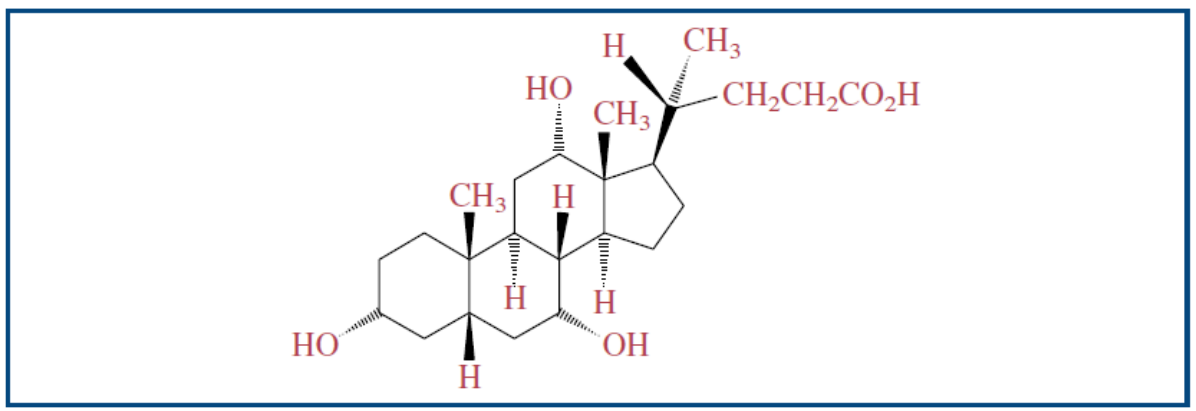
(1*S*,2*S*)-Dibromocyclopropane

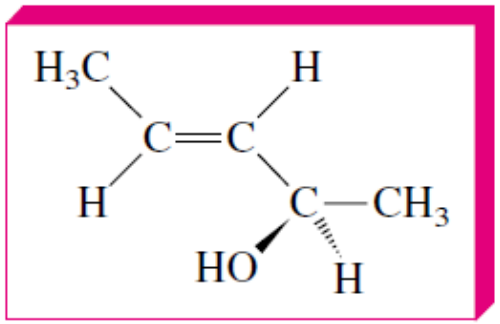


meso-1,2-Dibromocyclopropane

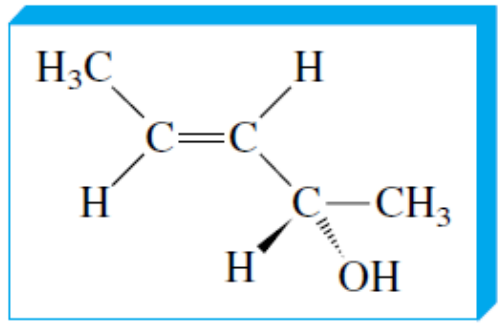


A hexose

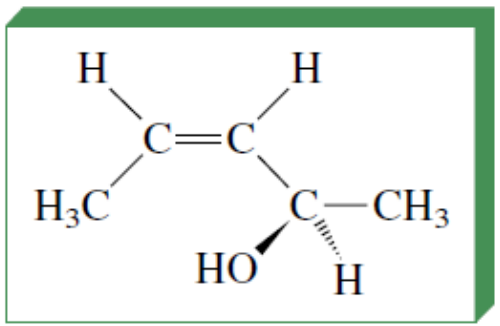




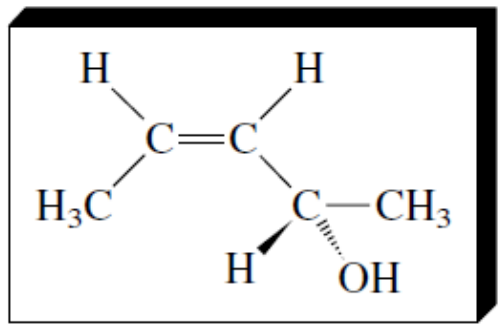
(2*R*,3*E*)-3-Penten-2-ol



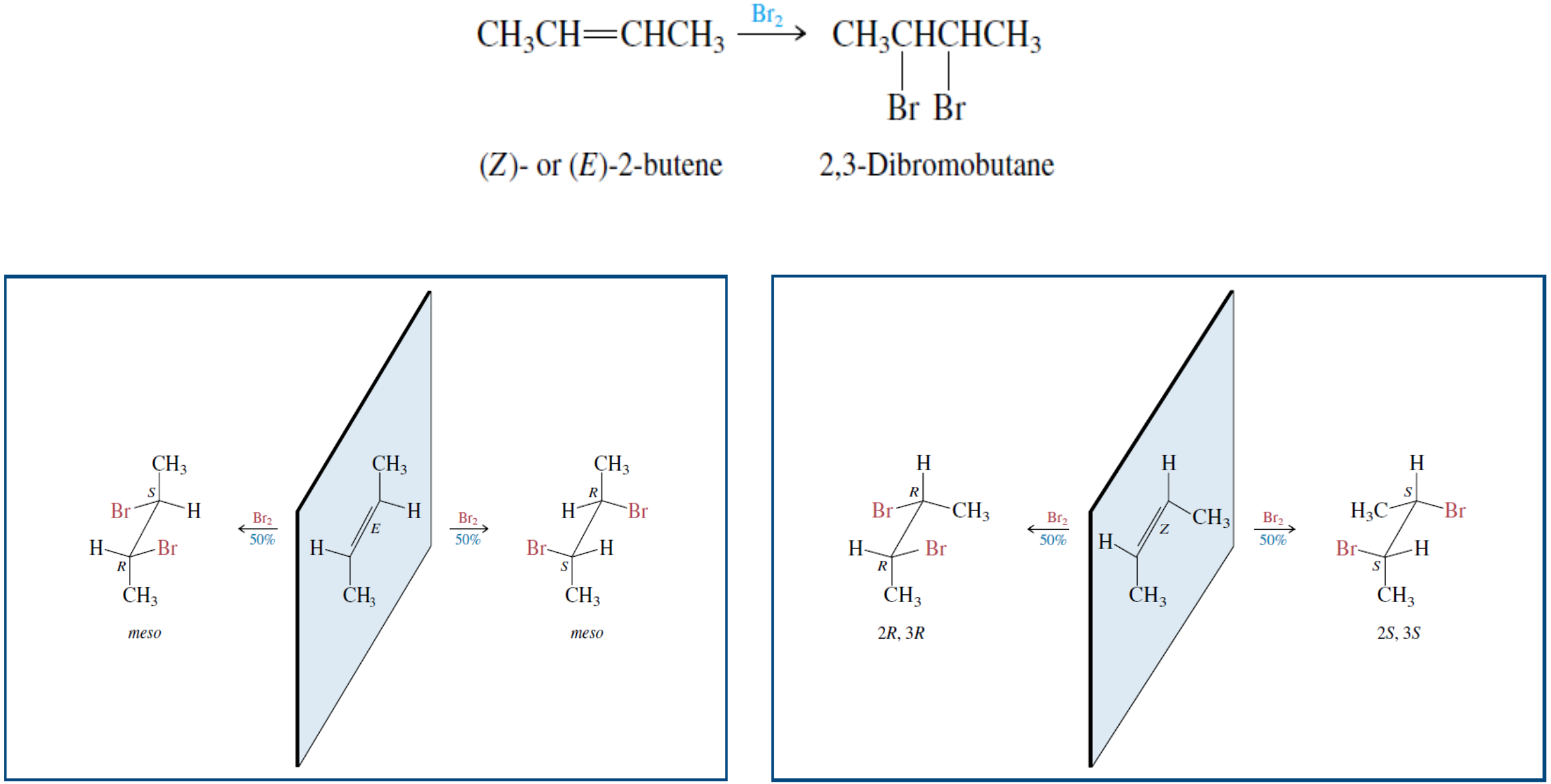
(2*S*,3*E*)-3-Penten-2-ol

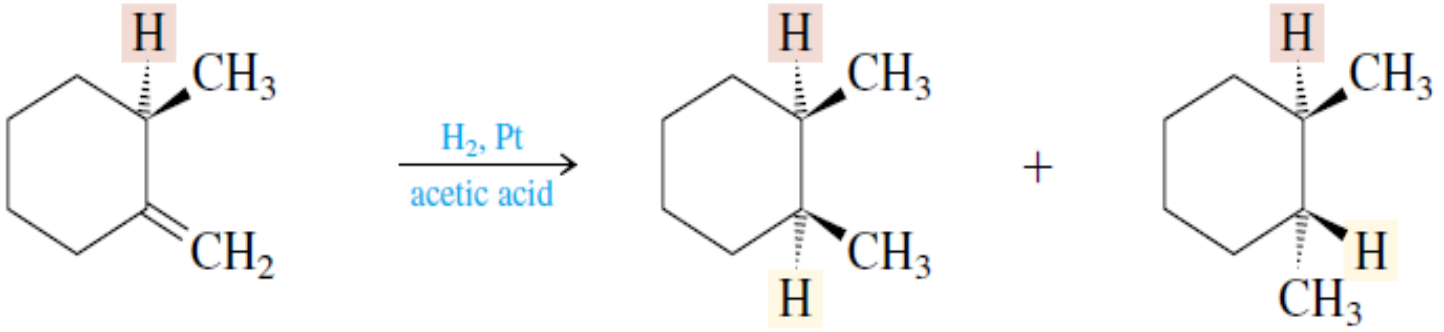


(2*R*,3*Z*)-3-Penten-2-ol



(2*S*,3*Z*)-3-Penten-2-ol

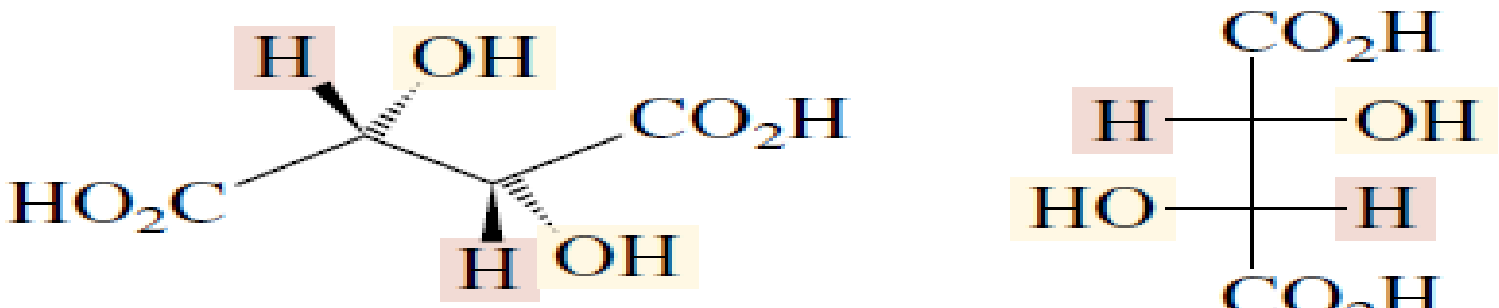

CH3CH=CHCH3
Br2
CH3CHCHCH3
Br Br
(Z)- or (E)-2-butene
2,3-Dibromobutane
CH3
S
Br
H
H
Br
R
CH3
meso
Br2
50%
CH3
H
E
H
CH3
Br2
50%
CH3
R
H
Br
Br
H
S
CH3
meso
H
R
Br
CH3
H
Br
R
CH3
2R, 3R
Br2
50%
H
Z
CH3
H
CH3
Br2
50%
H
S
H3C
Br
Br
H
S
CH3
2S, 3S



2-Methyl(methylene)cyclo-hexane

cis-1,2-Dimethylcyclo-hexane (68%)

trans-1,2-Dimethylcyclo-hexane (32%)



(2*R*,3*R*)-Tartaric acid (mp 170°C, $[\alpha]_D$ +12°)

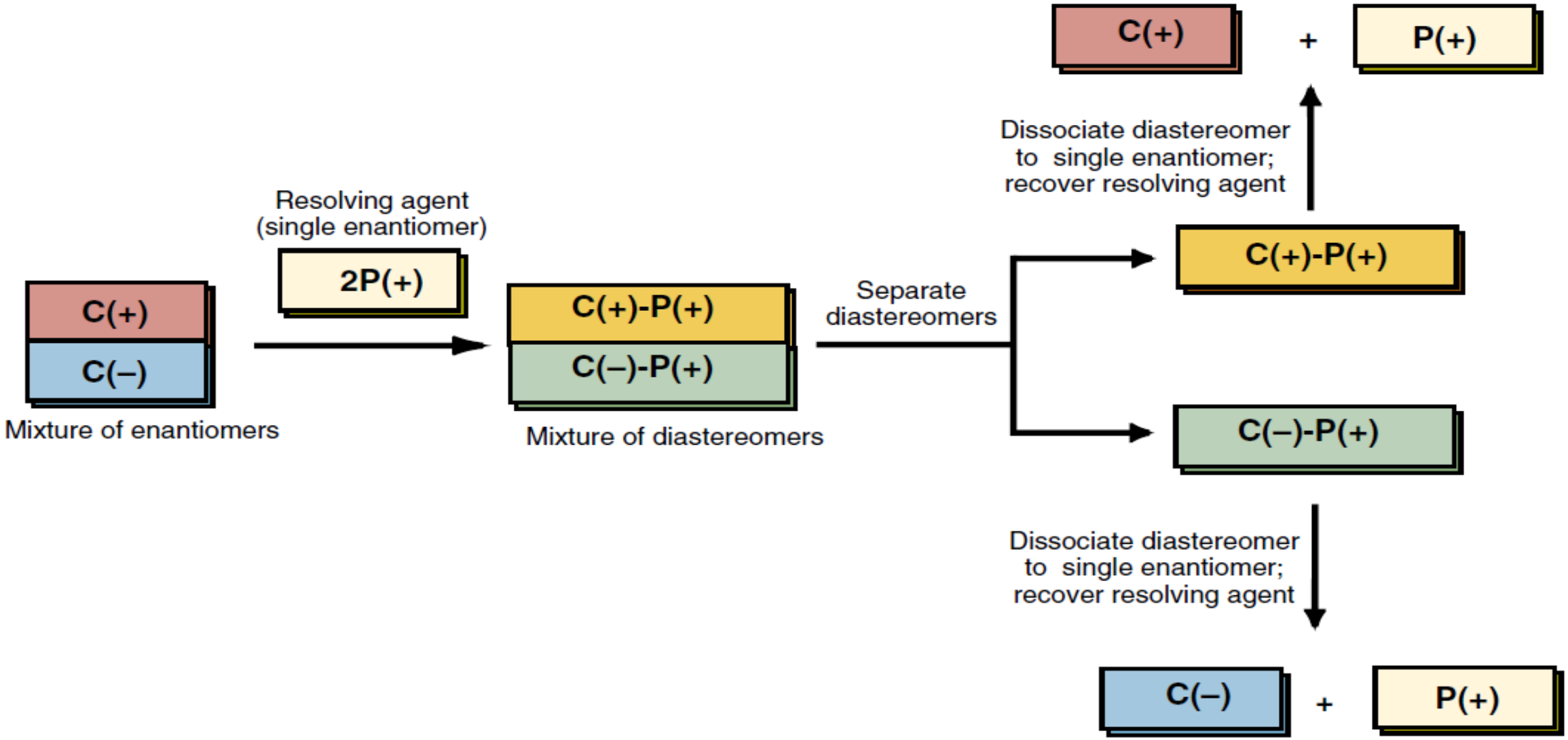
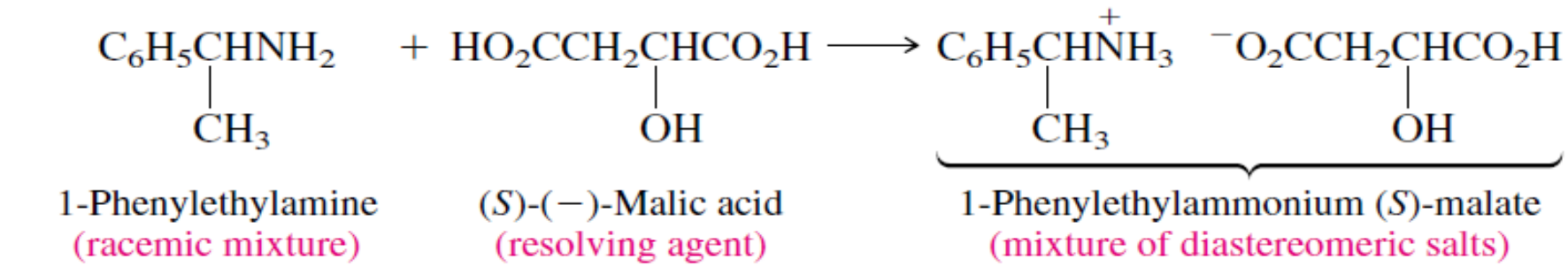
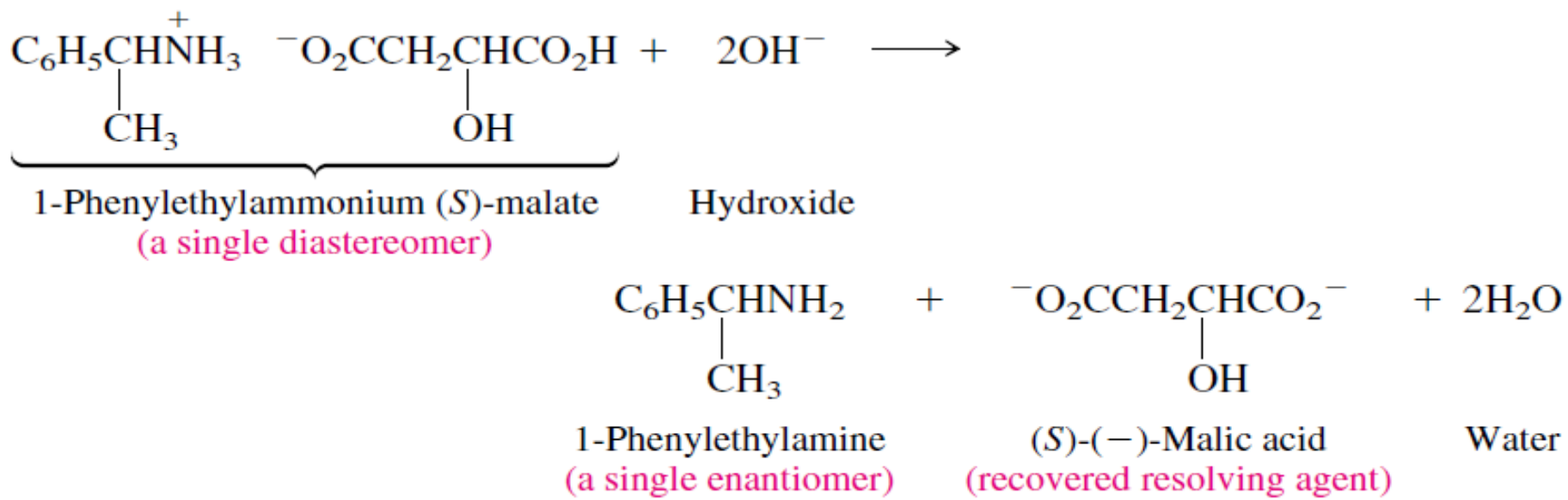

C(+)
C(–)
Mixture of enantiomers
Resolving agent
(single enantiomer)
2P(+)
C(+)-P(+)
C(–)-P(+)
Mixture of diastereomers
Separate
diastereomers
C(+)-P(+)
C(–)-P(+)
Dissociate diastereomer
to single enantiomer;
recover resolving agent
C(+)
+
P(+)
Dissociate diastereomer
to single enantiomer;
recover resolving agent
C(–)
+
P(+)

FIGURE 7.16 The general procedure followed in resolving a chiral substance into its enantiomers. Reaction with a single enantiomer of a chiral resolving agent P(+) converts the racemic mixture of enantiomers C(+) and C(−) to a mixture of diastereomers C(+)-P(+) and C(−)-P(+). The mixture of diastereomers is separated—by fractional crystallization, for example. A chemical reaction is then carried out to convert diastereomer C(+)-P(+) to C(+) and the resolving agent P(+). Likewise, diastereomer C(−)-P(+) is converted to C(−) and P(+). C(+) has been separated from C(−), and the resolving agent P(+) can be recovered for further use.



The diastereomeric salts are separated and the individual enantiomers of the amine liberated by treatment with a base: