Organic Chemistry I

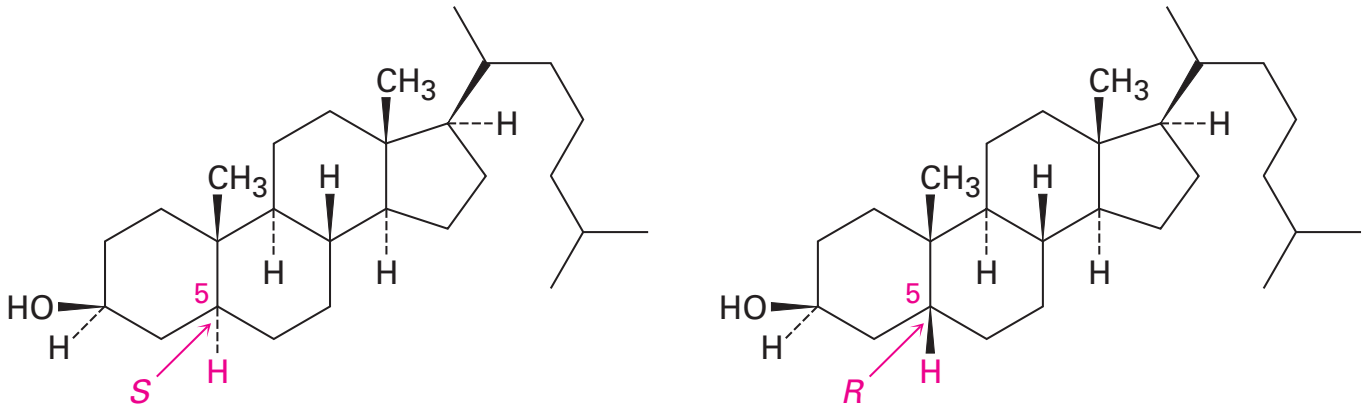
Mohammad Jafarzadeh

Faculty of Chemistry, Razi University

Organic Chemistry, (9th edition)

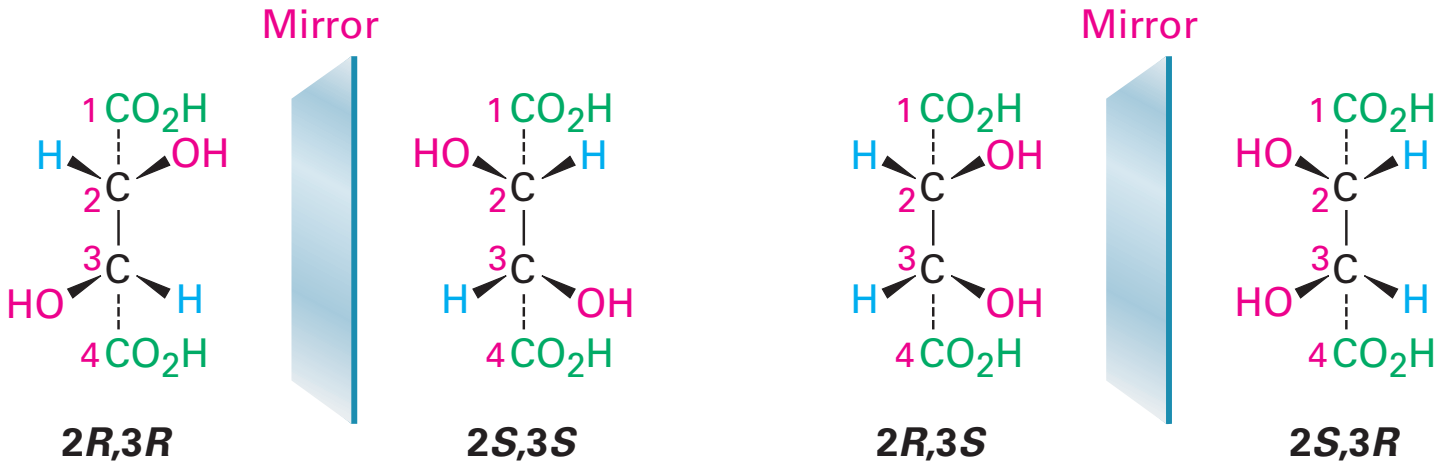
By *John McMurry*, Cengage Learning, 2016

In the special case where two diastereomers differ at only one chirality center but are the same at all others, we say that the compounds are **epimers**.

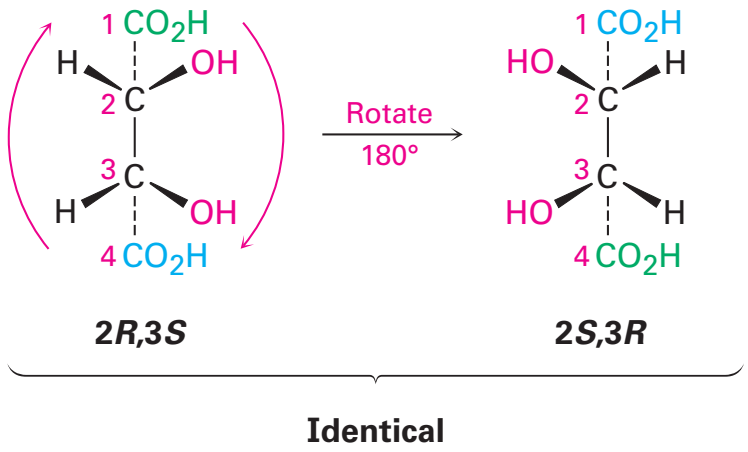


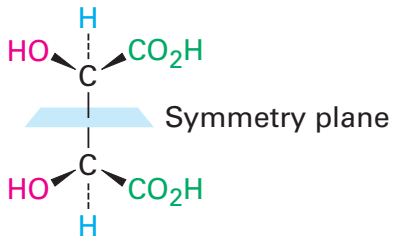
Meso Compounds

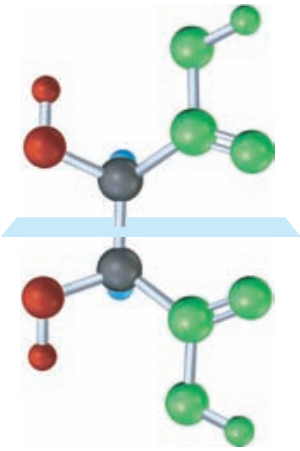
A compound with more than one chirality center: the tartaric acid used by Pasteur.



2*R*,3*S* and 2*S*,3*R* structures *are* superimposable and identical, by rotating one structure 180°. They are also identical because the molecule has a plane of symmetry and is therefore achiral.







Some physical properties of the three stereoisomers are listed in **Table 5-3**. The (+)- and (-)-tartaric acids have identical melting points, solubilities, and densities, but they differ in the sign of their rotation of plane-polarized light.

The meso isomer, by contrast, is diastereomeric with the (+) and (-) forms. It has no mirror-image relationship to (+)- and (-)-tartaric acids, is a different compound altogether, and has different physical properties.

TABLE 5-3 Some Properties of the Stereoisomers of Tartaric Acid

Stereoisomer	Melting point (°C)	$[\alpha]_D$	Density (g/cm^3)	Solubility at 20 °C (g/100 mL H_2O)
(+)	168–170	+12	1.7598	139.0
(−)	168–170	−12	1.7598	139.0
Meso	146–148	0	1.6660	125.0

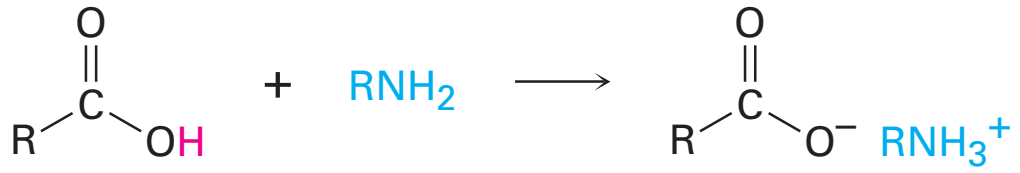
Racemic mixtures and the resolution of enantiomers

Racemate is a 50:50 *mixture* of the two enantiomers. Racemate, or ***racemic mixture***, is denoted by either the symbol (±) or the prefix *d,l* to indicate an equal mixture of dextrorotatory and levorotatory forms.

Racemates show **no optical rotation** because the (+) rotation from one enantiomer exactly cancels the (-) rotation from the other.

Resolution: separation of enantiomers

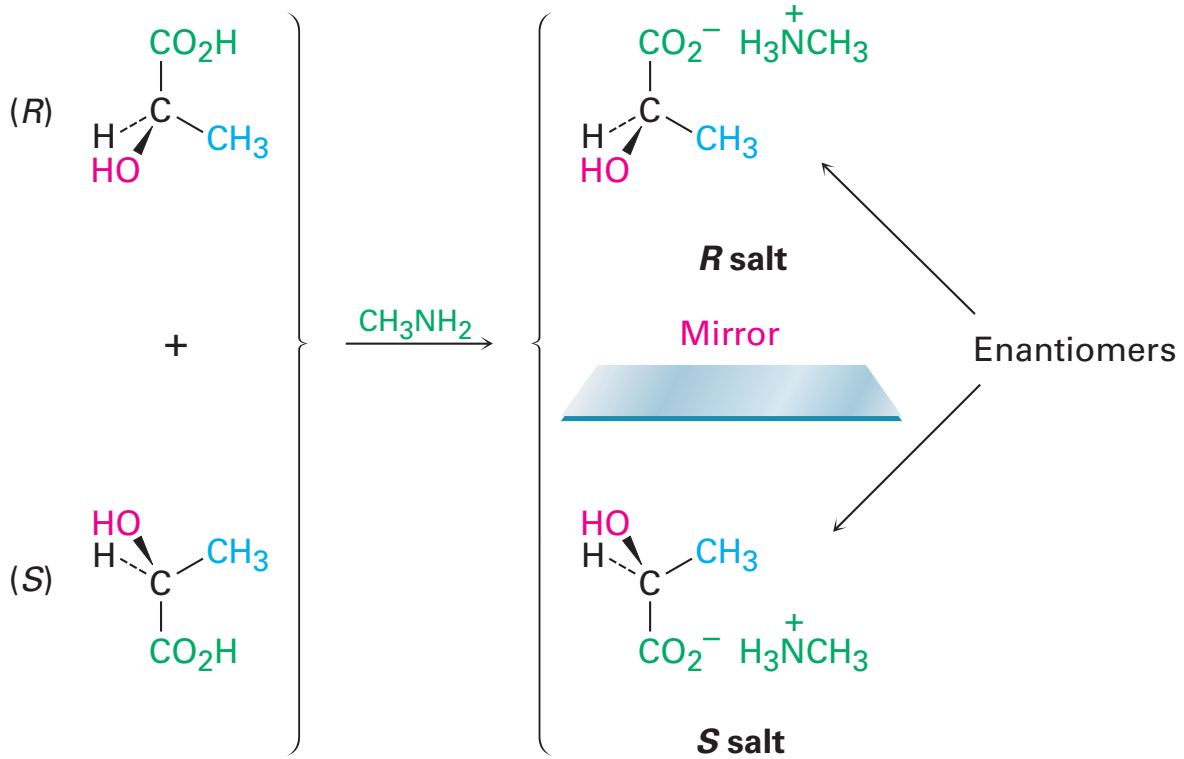
The most common method of resolution uses an acid–base reaction between the racemate of a chiral carboxylic acid (RCO_2H) and an amine base (RNH_2) to yield an ammonium salt:



Carboxylic acid **Amine base** **Ammonium salt**

A racemic mixture of chiral acids, such as (+)- and (-)-lactic acids, reacts with an achiral amine base, such as methylamine, CH_3NH_2.

Both (+)- and (-)-lactic acid react with methylamine equally well, and the product is a racemic mixture of the two enantiomers methylammonium (+)-lactate and methylammonium (-)-lactate.



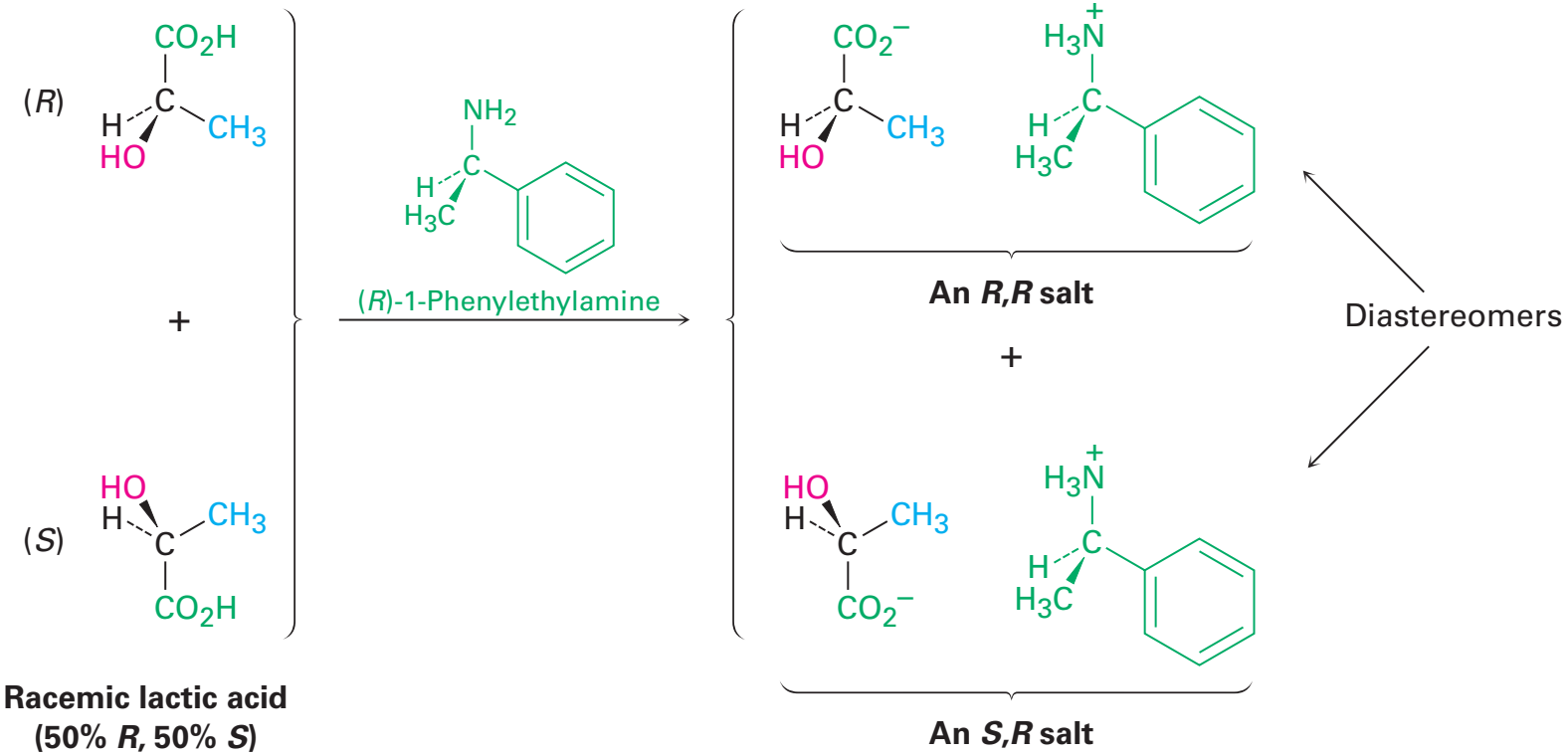
Racemic lactic acid (50% *R*, 50% *S*)

Racemic ammonium salt (50% *R*, 50% *S*)

When the racemic mixture of (+)- and (-)-lactic acids reacts with a single enantiomer of a chiral amine base, such as (*R*)-1-phenylethylamine, which give two different products.

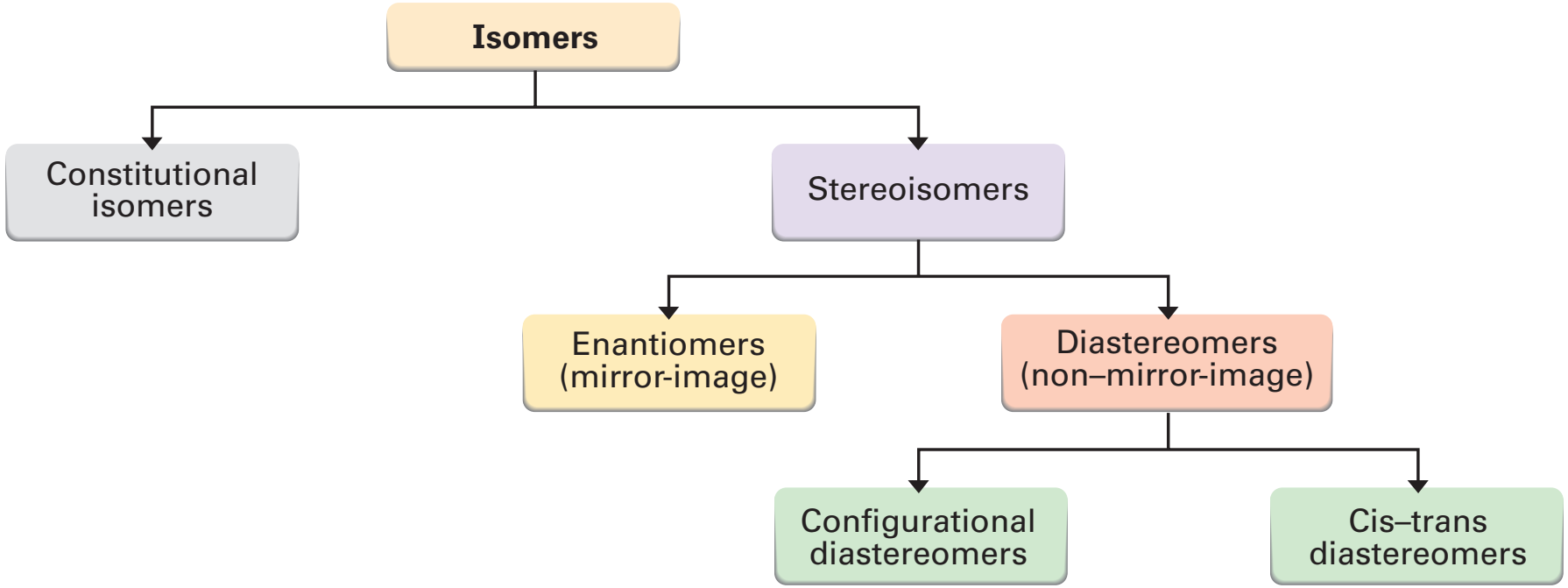
(*R*)-Lactic acid reacts with (*R*)-1-phenylethylamine to give the *R,R* salt, and (*S*)-lactic acid reacts with the *R* amine to give the *S,R* salt. *The two salts are diastereomers*.

They have different chemical and physical properties, and it may be possible to separate them by crystallization or some other means.



A review of isomerism

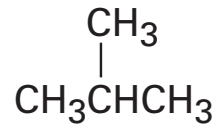
Isomers are compounds with the same chemical formula but different structures.



There are two fundamental types of isomers: constitutional isomers and stereoisomers.

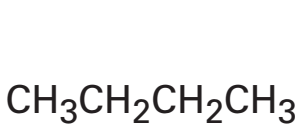
Constitutional isomers are compounds whose atoms are connected differently. Among the kinds of constitutional isomers we've seen are skeletal, functional, and positional isomers.

Different carbon skeletons



2-Methylpropane

and



Butane

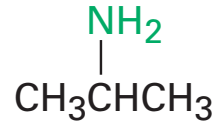
Different functional groups

Ethyl alcohol

and

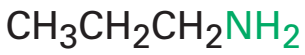
Dimethyl ether

Different position of functional groups



Isopropylamine

and

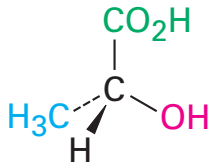


Propylamine

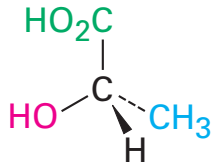
Stereoisomers are compounds whose atoms are connected in the same order but with a different spatial arrangement: enantiomers, diastereomers, and cis–trans.

Actually, cis–trans isomers are a subclass of diastereomers because they are non–mirror-image stereoisomers.

Enantiomers
(nonsuperimposable mirror-image stereoisomers)



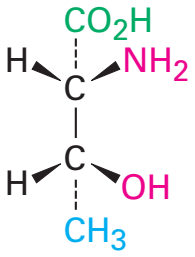
(*R*)-Lactic acid



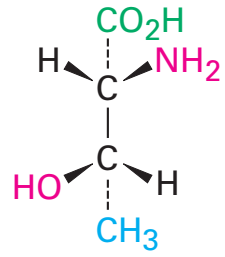
(*S*)-Lactic acid

Diastereomers
(nonsuperimposable non–mirror-image stereoisomers)

Configurational diastereomers

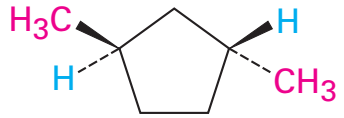


(2*R*,3*R*)-2-Amino-3-hydroxybutanoic acid



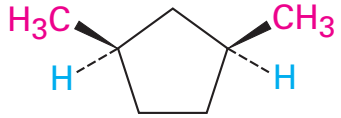
(2*R*,3*S*)-2-Amino-3-hydroxybutanoic acid

Cis–trans diastereomers
(substituents on same side or opposite side of double bond or ring)



***trans*-1,3-Dimethylcyclopentane**

and

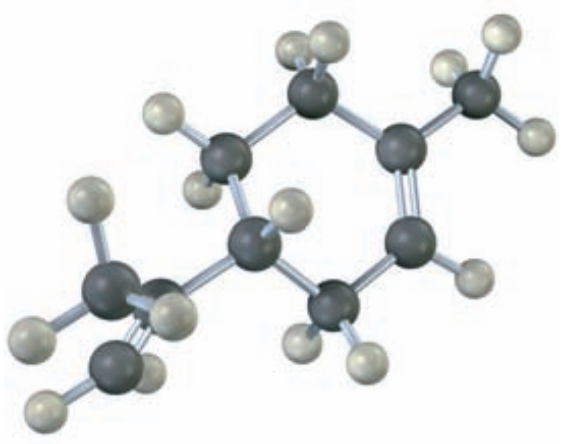


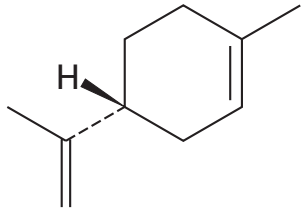
***cis*-1,3-Dimethylcyclopentane**

Chirality in nature and Chiral environments

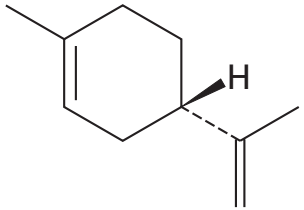
Although the different enantiomers of a chiral molecule have the same physical properties, they usually have different biological properties.

For example, the (+) enantiomer of limonene has the odor of oranges and lemons, but the (-) enantiomer has the odor of pine trees.

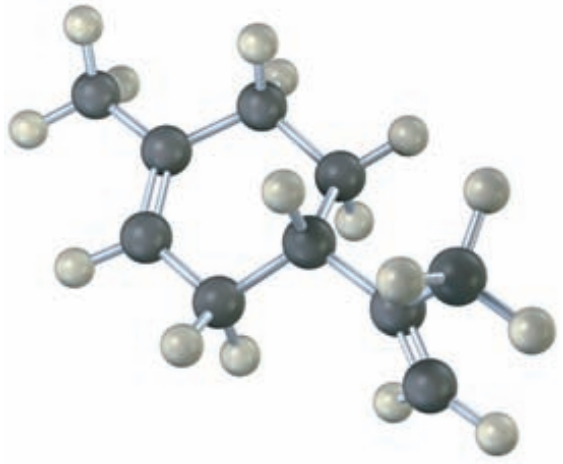




(+)-Limonene
(in citrus fruits)

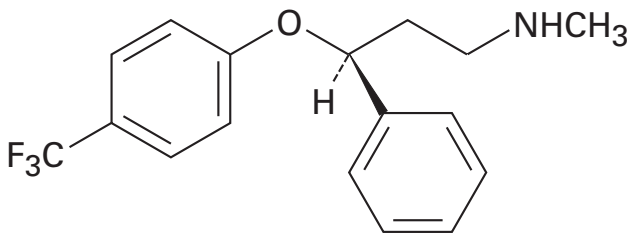


(–)-Limonene
(in pine trees)

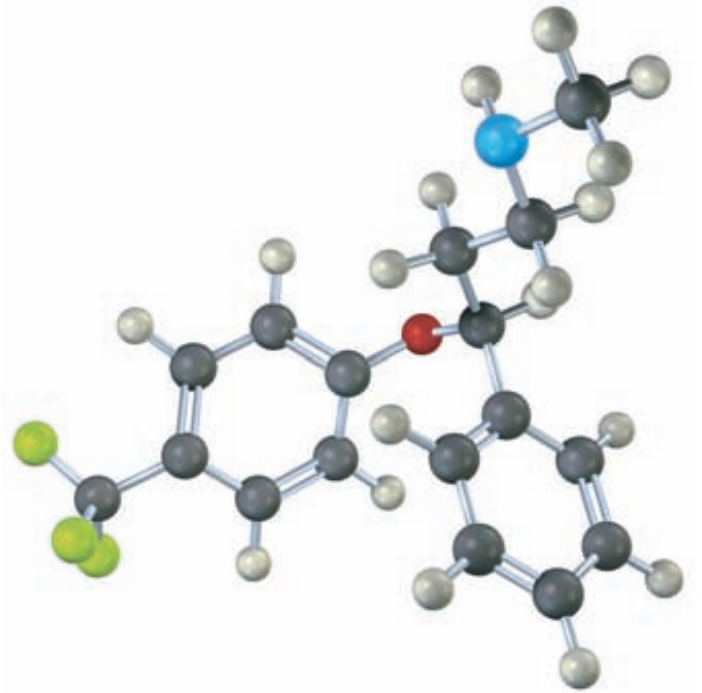


More dramatic examples of how a change in chirality can affect the biological properties of a molecule can be found in many drugs, such as fluoxetine, a heavily prescribed medication sold under the trade name Prozac.

Racemic fluoxetine is an extraordinarily effective **antidepressant** but has no activity against migraine. The pure ***S* enantiomer**, works remarkably well in **preventing migraine**.



(*S*)-Fluoxetine
(prevents migraine)



Why do different enantiomers have different biological properties?

To have a biological effect, a substance typically must fit into an appropriate receptor that has an exactly complementary shape.

Because biological receptors are chiral, only one enantiomer of a chiral substrate can fit.

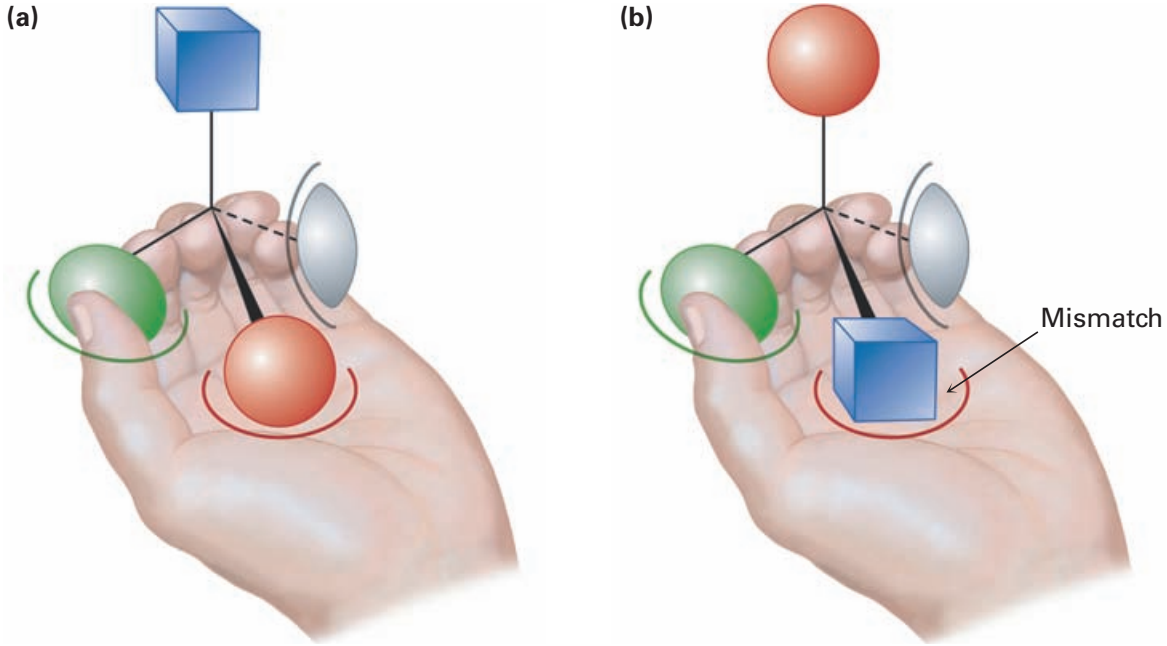


FIGURE 5-15 Imagine that a left hand interacts with a chiral object, much as a biological receptor interacts with a chiral molecule. **(a)** One enantiomer fits into the hand perfectly: **green thumb**, **red palm**, and **gray pinkie finger**, with the **blue substituent exposed**. **(b)** The other enantiomer, however, can't fit into the hand. When the green thumb and gray pinkie finger interact appropriately, the palm holds a blue substituent rather than a red one, with the **red substituent exposed**.