Organic Chemistry I

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Organic Chemistry, (9th edition)

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5. Stereochemistry

Handedness is also important in organic and biological chemistry, where it arises primarily as a consequence of the tetrahedral stereochemistry of sp^3-hybridized carbon atoms.

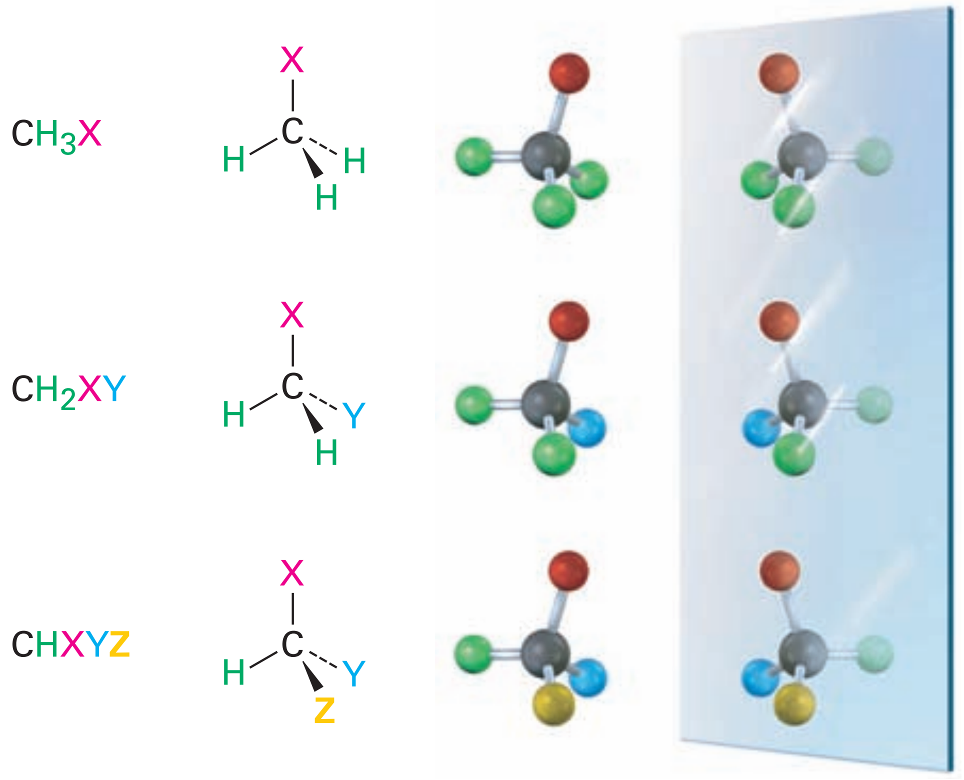
Many drugs and almost all the molecules in our bodies—amino acids, carbohydrates, nucleic acids, and many more—have a handedness.

Molecular handedness enables the precise interactions between enzymes and their substrates that are involved in the hundreds of thousands of chemical reactions on which life is based.

Enantiomers and the tetrahedral Carbon

On the left are three molecules, and on the right are their images reflected in a mirror. The CH_3X and CH_2XY molecules are identical to their mirror images and thus are not handed.

The CHXYZ molecule is *not* identical to its mirror image. You can't superimpose a model of this molecule on a model of its mirror image: they simply aren't the same.

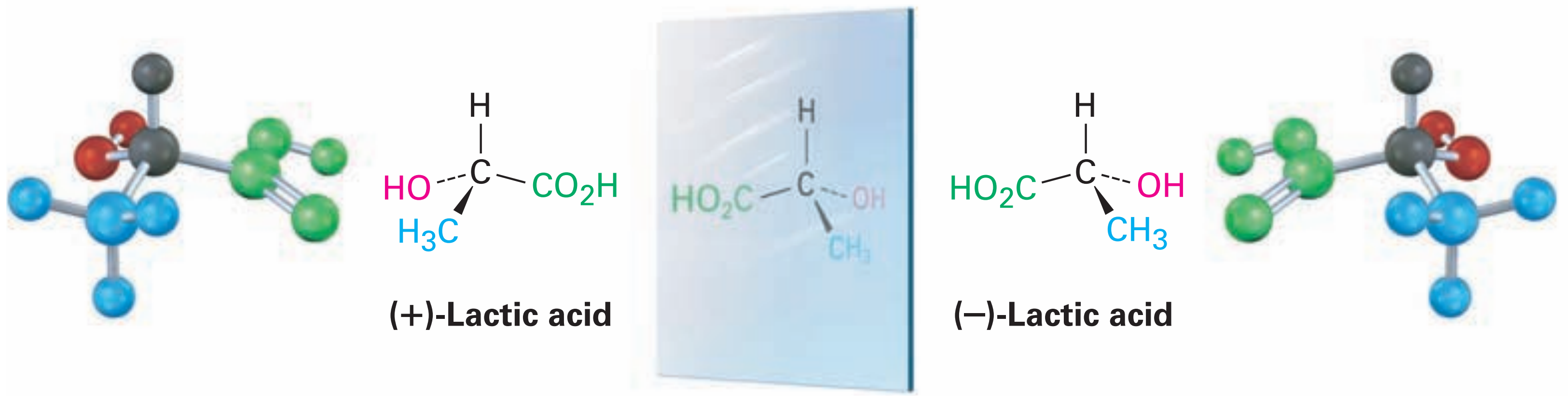


Molecules that are not identical to their mirror images are a kind of stereo-isomer called **enantiomers** (Greek *enantio,* meaning “opposite”). Enantiomers are related to each other as a tetrahedral carbon is bonded to four different substituents.

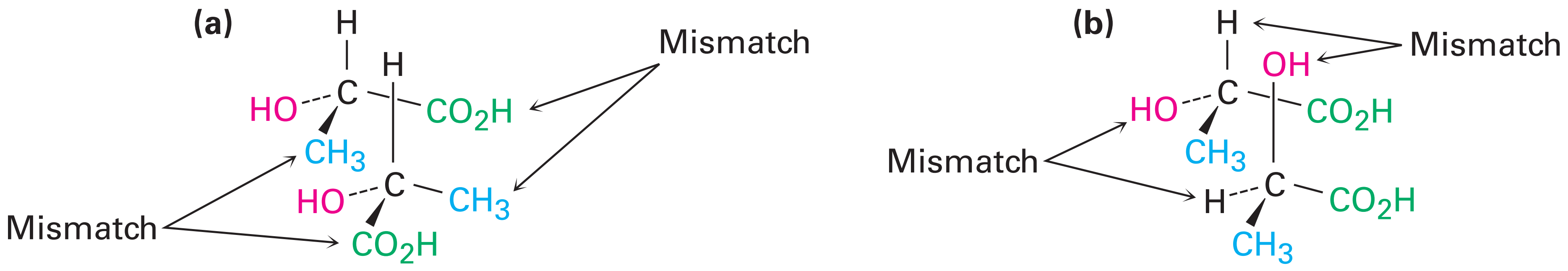
Lactic acid (2-hydroxypropanoic acid) exists as a pair of enantiomers. Its enantiomers are called (+)-lactic acid and (-)-lactic acid.

Both are found in sour milk, but only the (+) enantiomer occurs in muscle tissue.

Lactic acid: a molecule of the general formula CHXYZ



You can't superimpose a molecule of (+)-lactic acid on a molecule of (-)-lactic acid. If any two groups match up, say -H and -CO_2H, the remaining two groups don't match:



The reason for handedness in molecules: Chirality

A molecule that is not identical to its mirror image is said to be **chiral** (from the Greek *cheir,* meaning "hand").

How can you predict whether a given molecule is or is not chiral?

A molecule is not chiral if it has a plane of symmetry. A plane of symmetry is a plane that cuts through the middle of a molecule (or any object) in such a way that one half of the molecule or object is a mirror image of the other half.

A coffee mug has a plane of symmetry. If you were to cut the coffee mug in half, one half would be a mirror image of the other half.

A hand does not have a plane of symmetry. One “half” of a hand is not a mirror image of the other half.

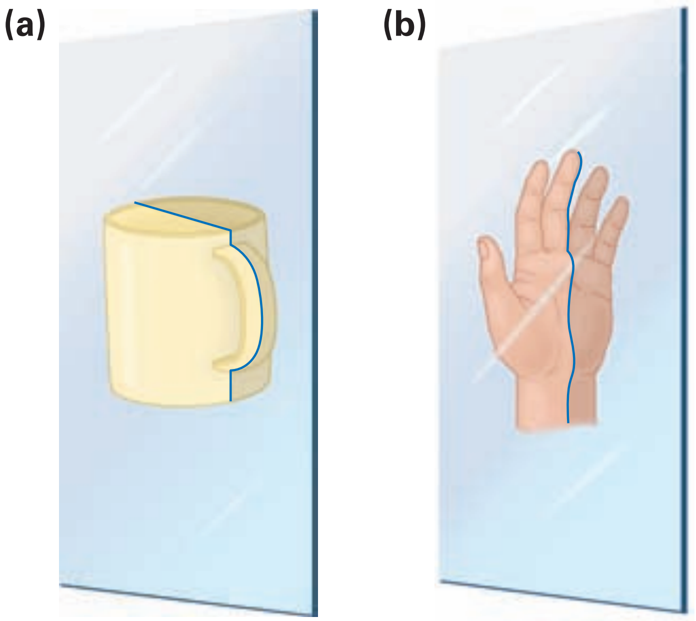
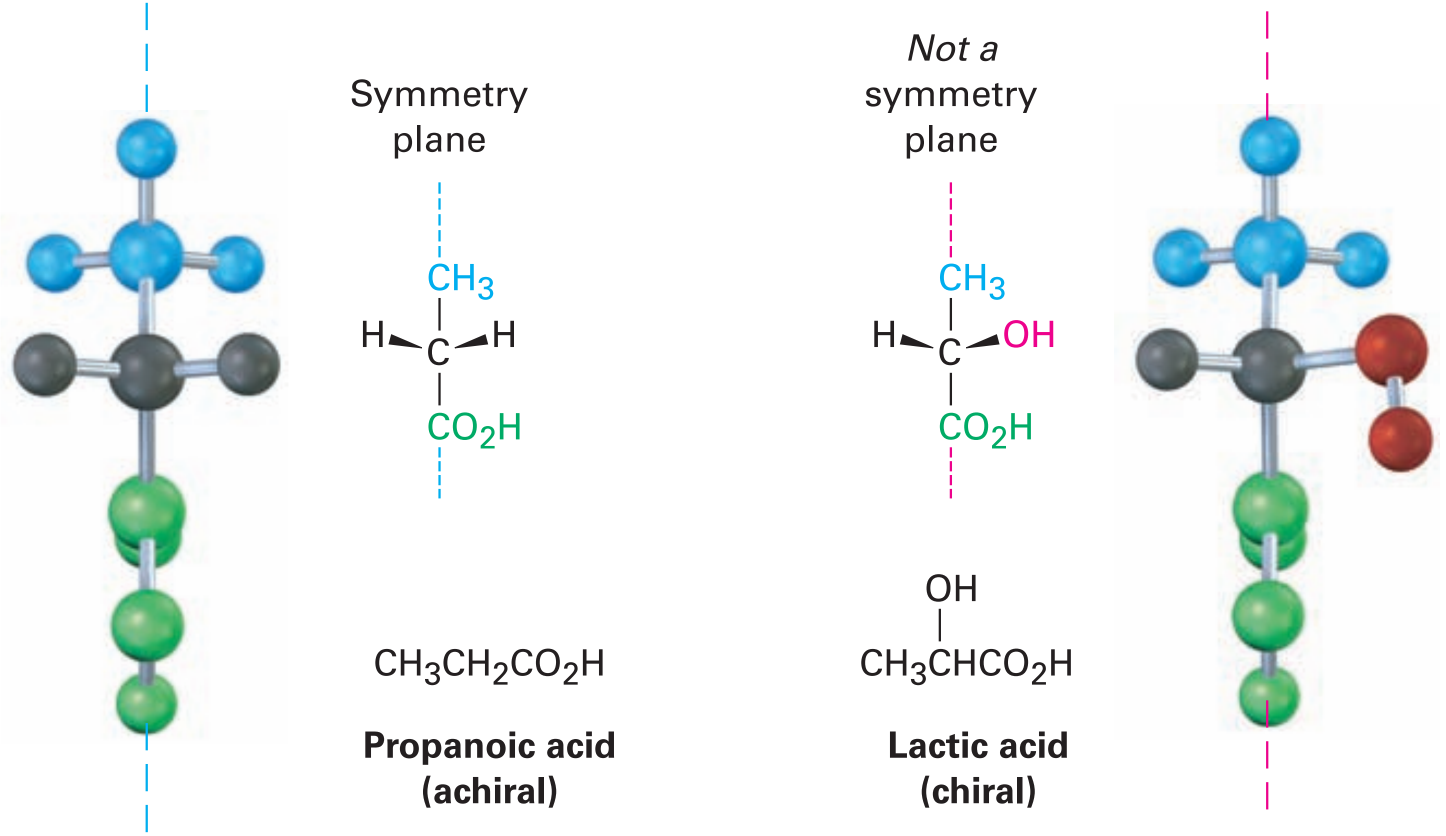


FIGURE 5-3 The meaning of *symmetry plane*. **(a)** An object like the coffee mug has a symmetry plane cutting through it so that right and left halves are mirror images. **(b)** An object like a hand has no symmetry plane; the right “half” of a hand is not a mirror image of the left half.

A molecule that has a plane of symmetry in any conformation must be identical to its mirror image and hence must be nonchiral, or **achiral**.

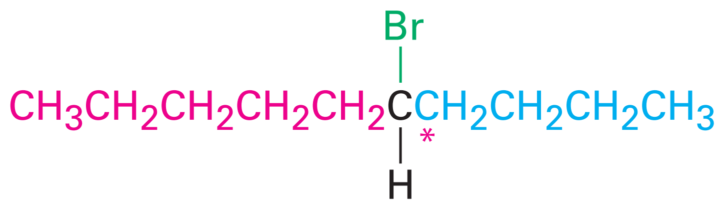
Propanoic acid, $CH_3CH_2CO_2H$, has a plane of symmetry when lined up and is achiral, while lactic acid, $CH_3CH(OH)CO_2H$, has no plane of symmetry in any conformation and is chiral.



The cause of chirality in organic molecules is the presence of a tetrahedral carbon atom bonded to four different groups.

Such carbons are referred to as **chirality centers**, although other terms such as *stereocenter, asymmetric center,* and *stereogenic center* have also been used.

Note that *chirality* is a property of the entire molecule, whereas a chirality *center* is the *cause* of chirality.



5-Bromodecane (chiral)

Substituents on carbon 5

—H

—Br

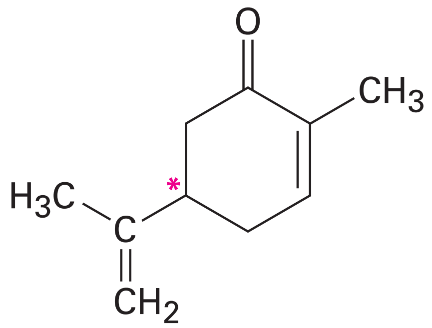
—$CH_2CH_2CH_2CH_3$ (butyl)

—$CH_2CH_2CH_2CH_2CH_3$ (pentyl)

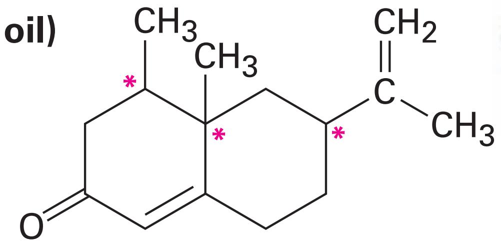
Methylcyclohexane is achiral because no carbon atom in the molecule is bonded to four different groups. The C6–C5–C4 “substituent” is equivalent to the C2–C3–C4 substituent, and methylcyclohexane is achiral.

Another way of reaching the same conclusion is to realize that methylcyclohexane has a symmetry plane, which passes through the methyl group and through C1 and C4 of the ring.

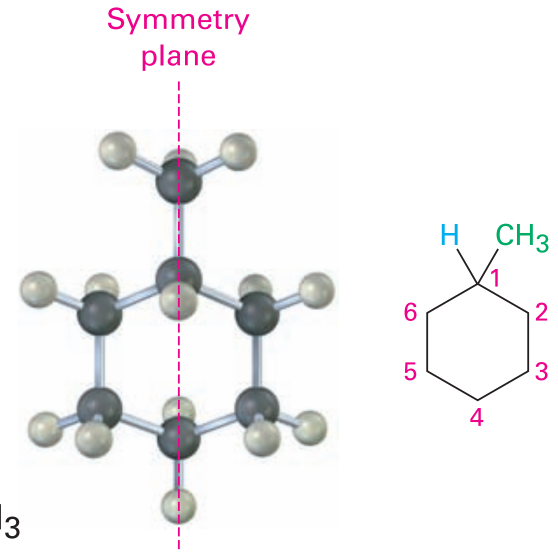
2-Methylcyclohexanone has no symmetry plane and is chiral because its C2 is bonded to four different groups.



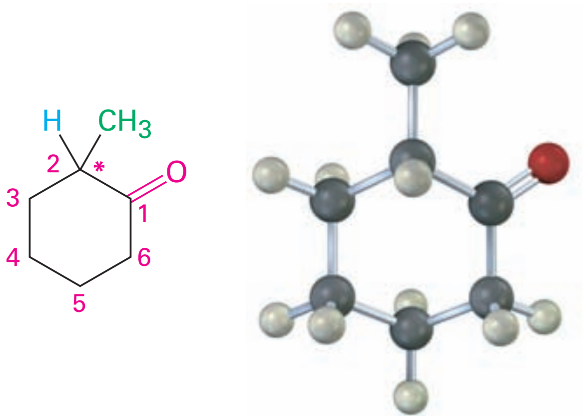
Carvone (spearmint oil)



Nootkatone (grapefruit oil)



Methylcyclohexane
(achiral)



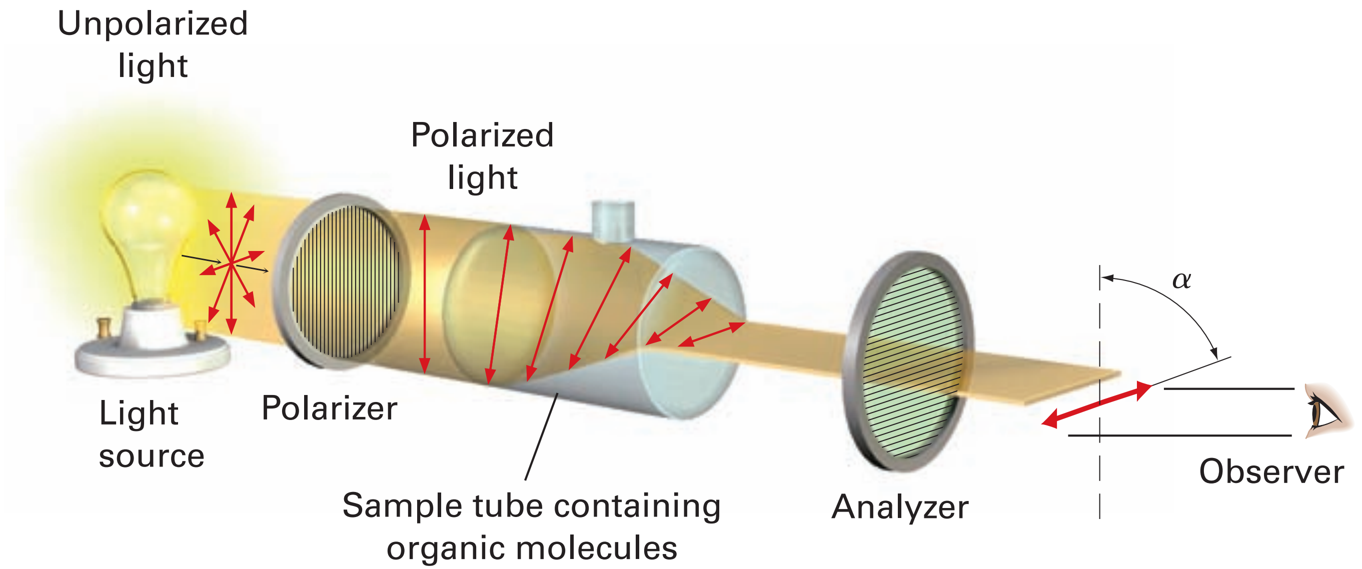
2-Methylcyclohexanone
(chiral)

Optical activity

When a beam of ordinary light passes through a device called a ***polarizer***, only the light waves oscillating in a single plane pass through and the light is said to be ***plane-polarized***.

When a beam of plane-polarized light passes through a solution of certain organic molecules (e.g. sugar, camphor), the plane of polarization is *rotated* through an angle, ***α***. Organic substances exhibit this property, are said to be **optically active**.

The angle of rotation can be measured with an instrument called a ***polarimeter***. A solution of optically active organic molecules is placed in a sample tube, plane-polarized light is passed through the tube, and rotation of the polarization plane occurs.



In addition to determining the **extent of rotation**, we can also find the **direction**: some optically active molecules rotate polarized light to the left (counter-clockwise) and are said to be **levorotatory**, whereas others rotate polarized light to the right (clockwise) and are said to be **dextrorotatory**.

Rotation to the left is given a (-) sign, while rotation to the right is given a (+) sign.

The extent of rotation observed, depends on the number of optically active molecules encountered by the light beam. This number depends on sample concentration and sample pathlength. The angle of rotation depends on the wavelength of the light used.

The **specific rotation, $[a]_D$**, is defined as the observed rotation when light of 589.6 nm (1 nm = 10^{-9} m) wavelength is used with a sample pathlength *l* of 1 dm (1 dm = 10 cm) and a sample concentration *c* of 1 g/cm^3 (Light of 589.6 nm, the so-called sodium D line, is the yellow light emitted from common sodium street lamps).

$$[\alpha]_D = \frac{\text{Observed rotation (degrees)}}{\text{Pathlength, } l \text{ (dm)} \times \text{Concentration, } c \text{ (g/cm}^3\text{)}} = \frac{\alpha}{l \times c}$$

When optical rotation data are expressed in this standard way, the specific rotation, $[a]_D$, is a physical constant characteristic of a given optically active compound.

For example, (+)-lactic acid has $[a]_D$ = +3.82, and (-)-lactic acid has $[a]_D$ = -3.82. The two enantiomers rotate plane-polarized light to exactly the same extent but in opposite directions. Note that the units of specific rotation are $[(\text{deg} \cdot \text{cm}^2)/\text{g}]$ but that these values are usually expressed without units.

TABLE 5-1 Specific Rotation of Some Organic Molecules

Compound	$[\alpha]_D$	Compound	$[\alpha]_D$
Penicillin V	+233	Cholesterol	−31.5
Sucrose	+66.47	Morphine	−132
Camphor	+44.26	Cocaine	−16
Chloroform	0	Acetic acid	0