

Organic Chemistry I

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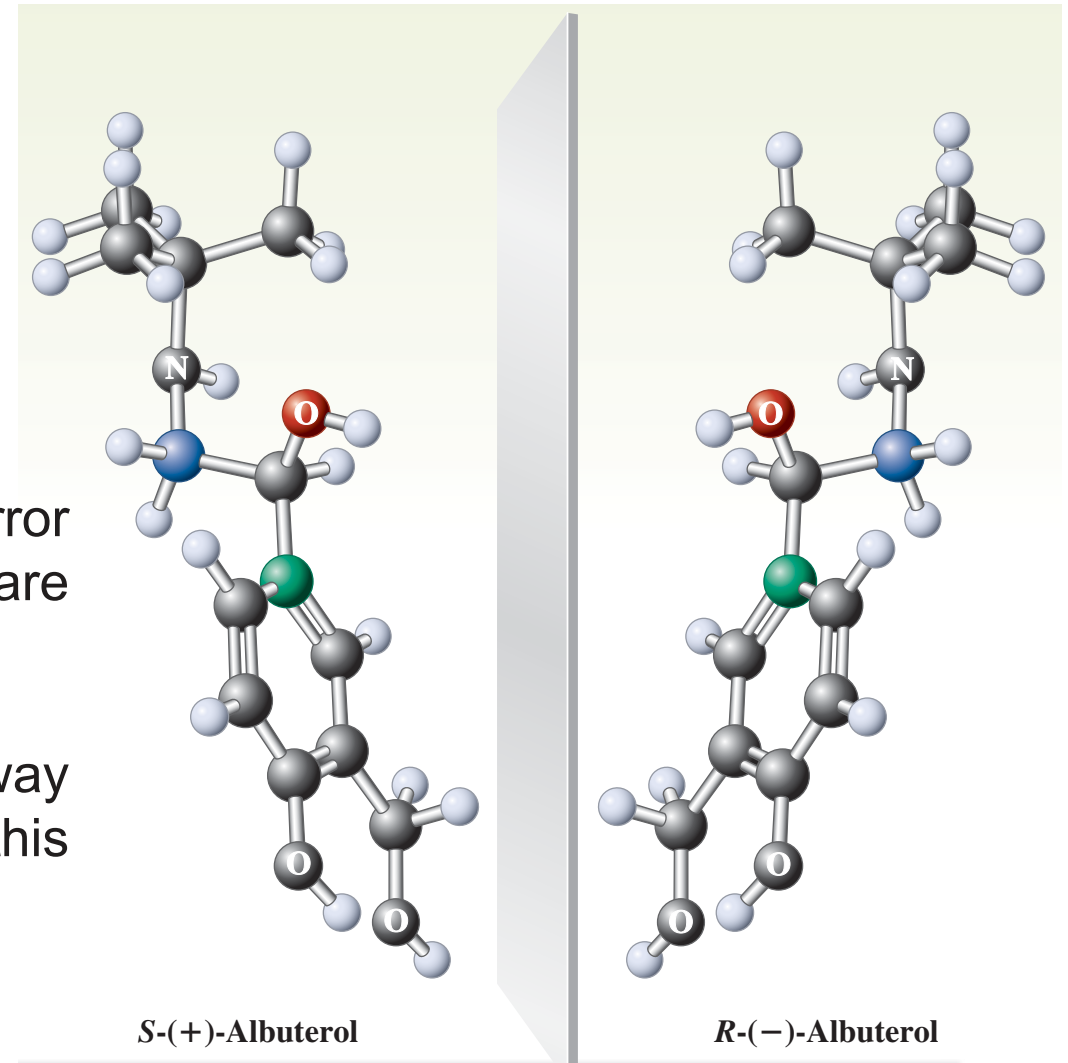
Organic Chemistry, *Structure and Function* (7th edition)

By *P. Vollhardt* and *N. Schore*, Elsevier, 2014

5. Stereoisomers

The physiological effects of the image and mirror image of the leading bronchodilator albuterol are dramatically different.

The ***R*** image increases the bronchial airway diameter, whereas the ***S*** mirror image cancels this effect and is a suspected inflammatory agent.

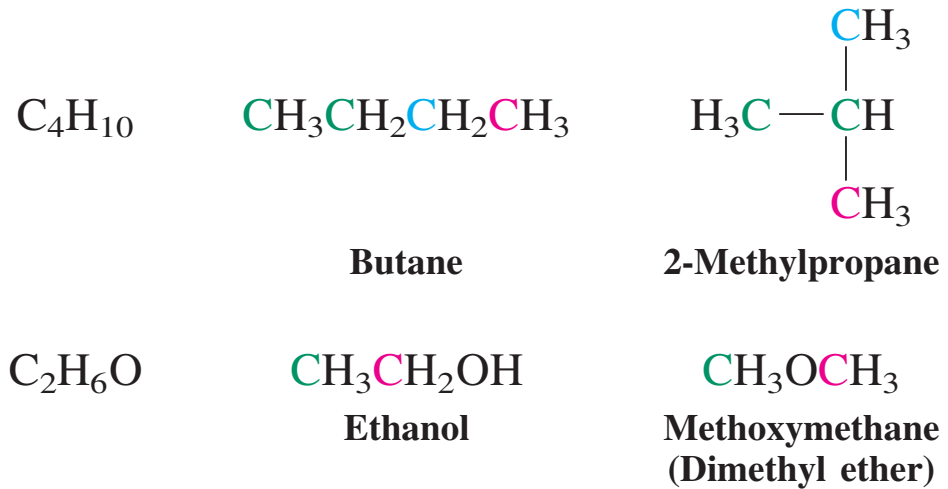


They have the same molecular formula, these molecules are isomers.

There are two kinds of isomerism: constitutional (also called structural) and stereo.

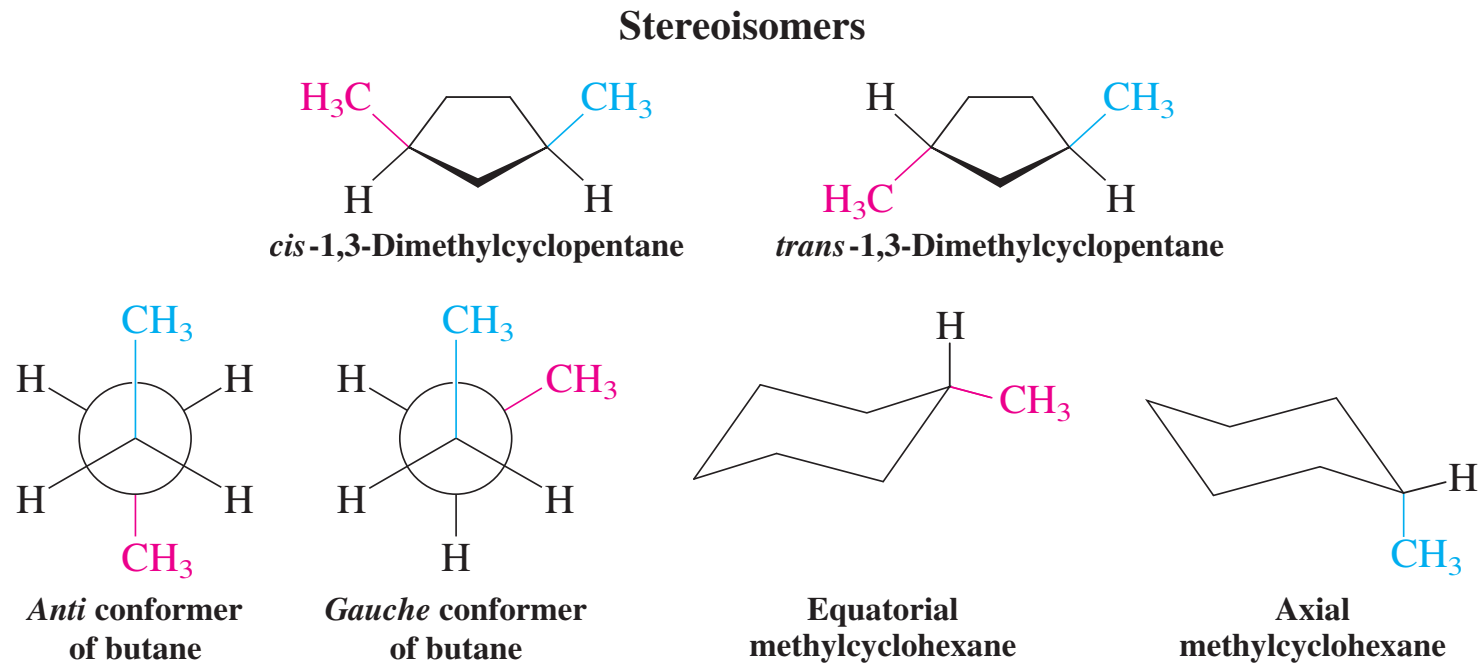
Constitutional isomerism describes compounds that have identical molecular formulas but differ in the order in which the individual atoms are connected

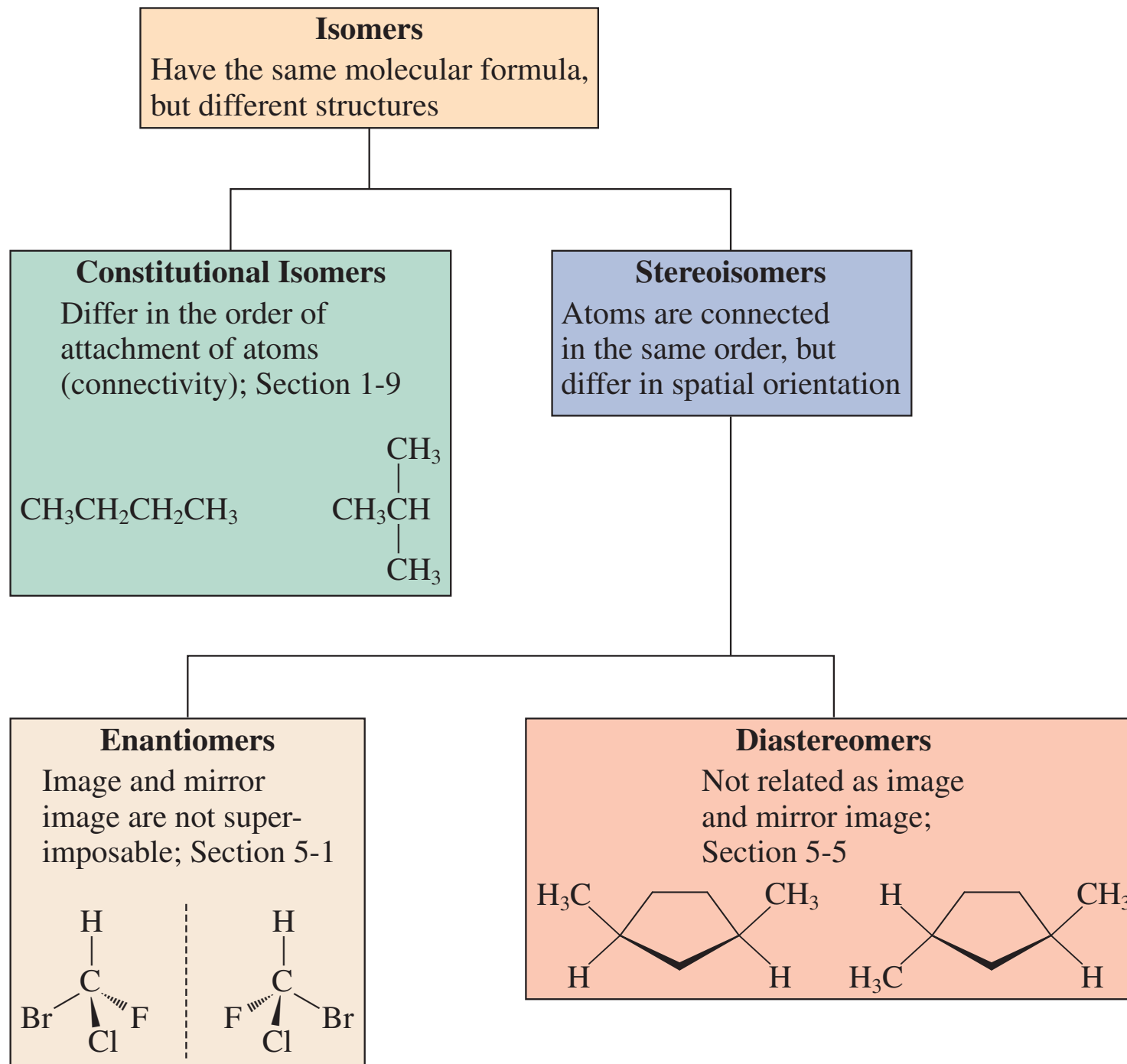
Constitutional Isomers



Stereoisomerism describes isomers whose atoms are connected in the same order but differ in their spatial arrangement.

Stereoisomers include the relatively stable and isolable cis-trans isomers and the rapidly equilibrating (and usually not isolable) conformational ones.

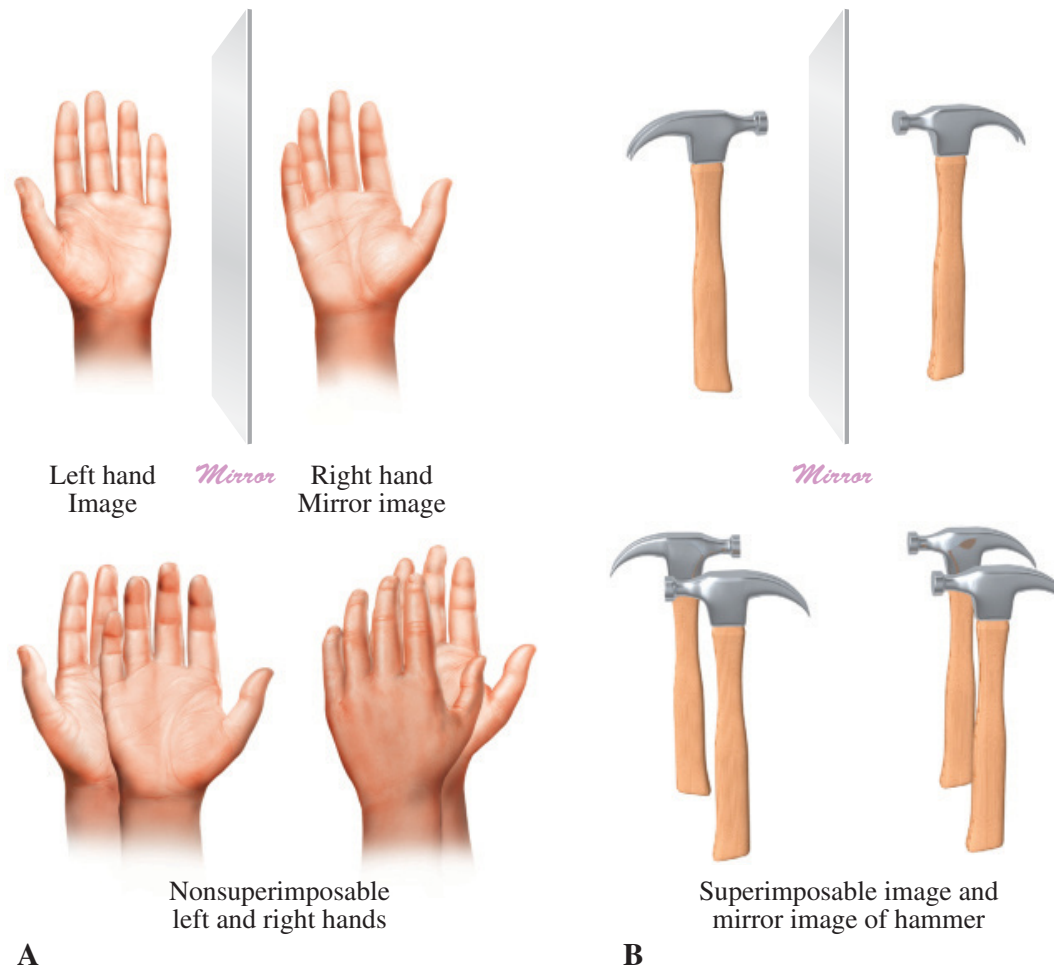




Mirror-image stereoisomerism. Molecules in this class are said to possess “handedness,” referring to the fact that your left hand is not superimposable on your right hand, yet one hand can be viewed as the mirror image of the other.

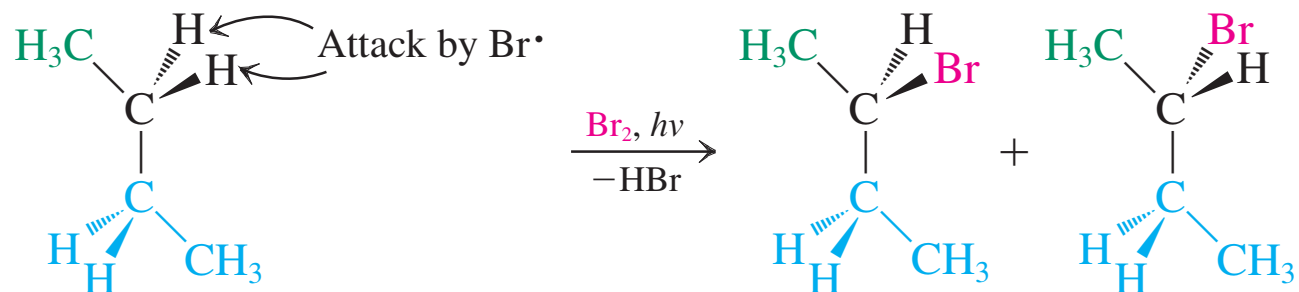
The property of handedness in molecules is very important in nature, because most biologically relevant compounds are either “left-” or “right-handed.”

They react differently with each other.



CHIRAL MOLECULES

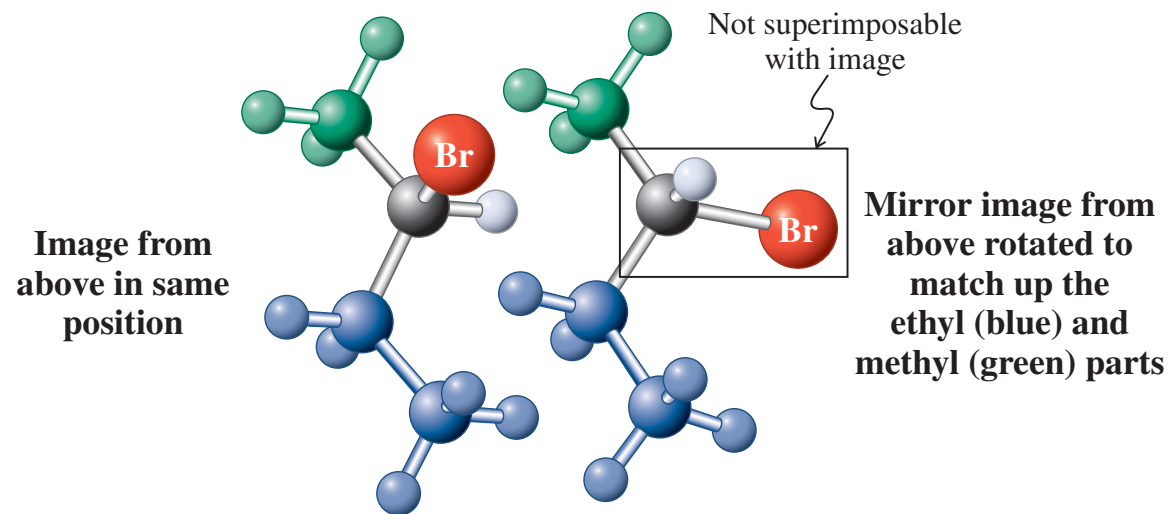
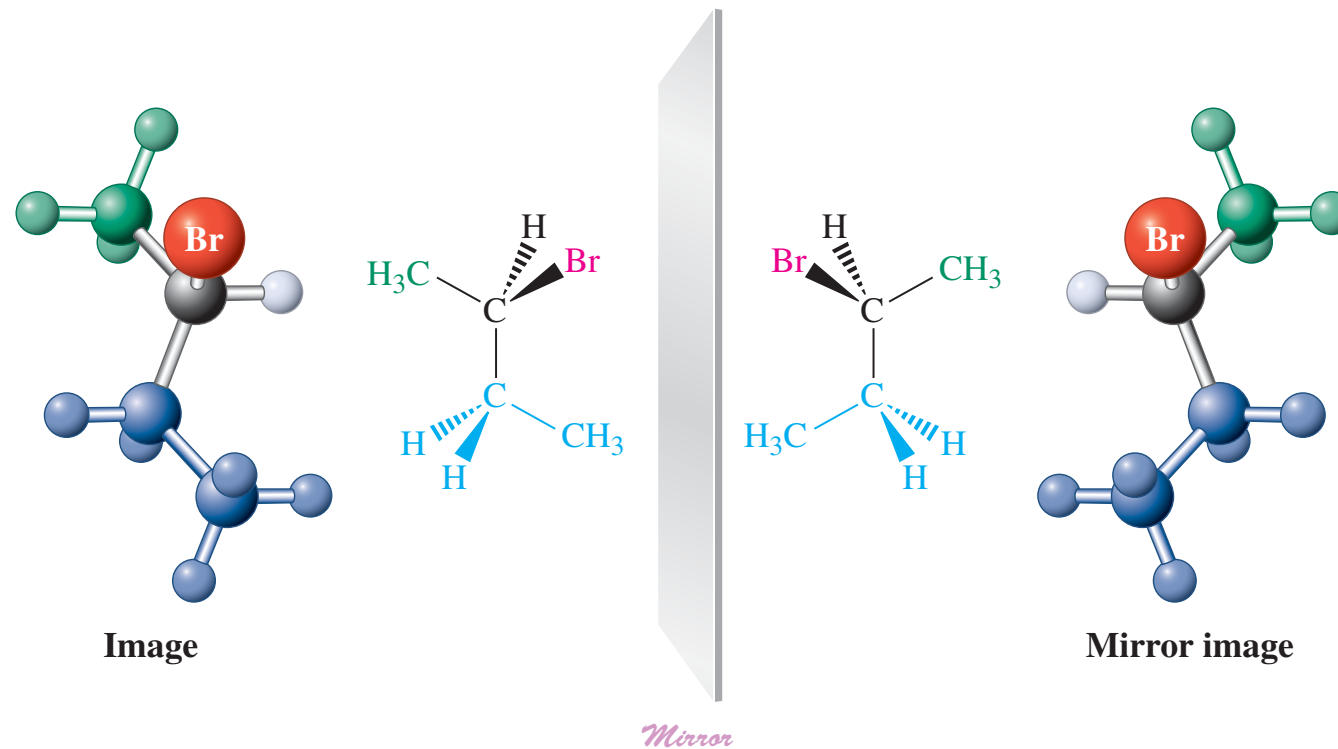
Consider the radical bromination of butane. The two hydrogens on that carbon may be replaced to give only one form of 2-bromobutane.



The two structures are nonsuperimposable and therefore *not identical*. The two molecules are related as object and mirror image, and to convert one into the other would require the breaking of bonds.

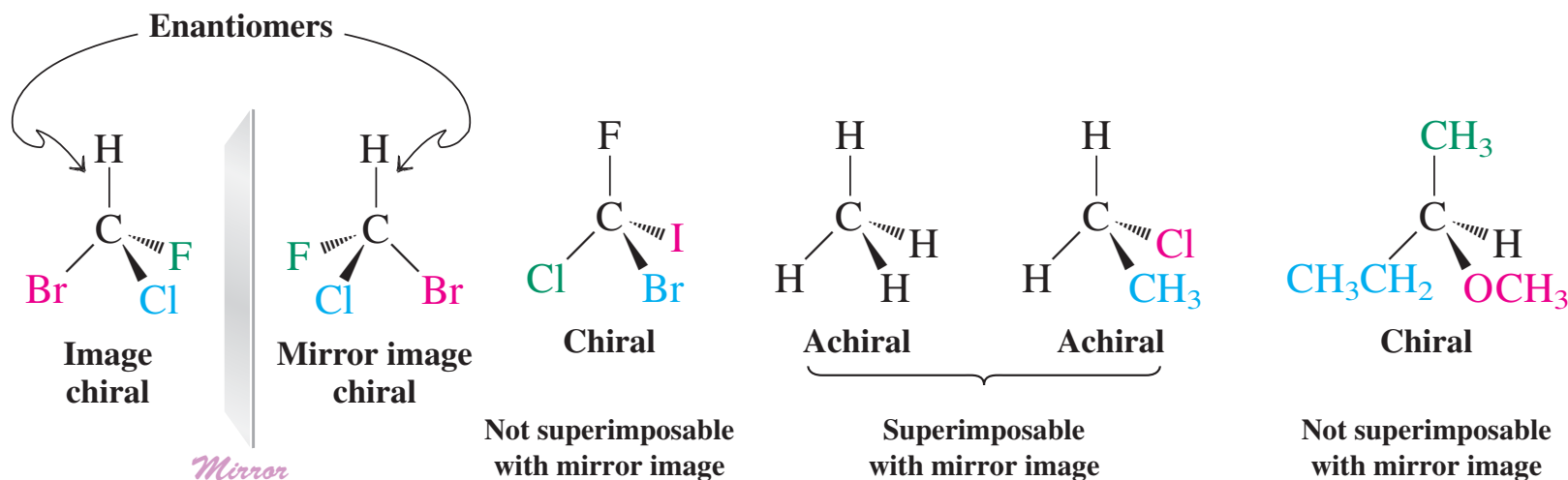
A molecule that is not superimposable on its mirror image is said to be **chiral**.

Each isomer of the image–mirror image pair is called an **enantiomer** (*enantios*, Greek, opposite).



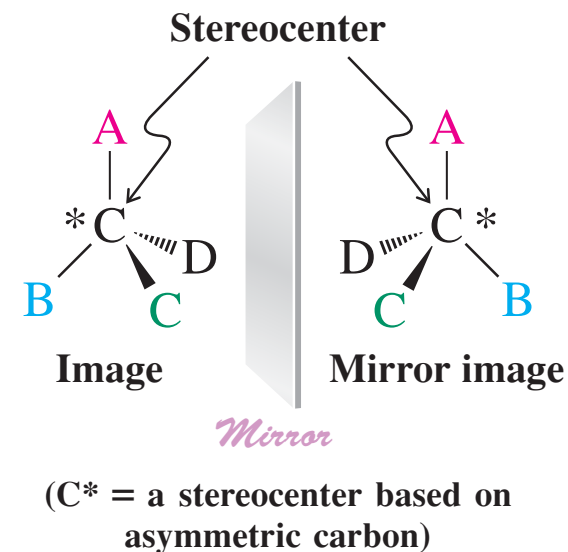
The two enantiomers of 2-bromobutane are nonsuperimposable

In contrast with chiral molecules, compounds having structures that *are* superimposable on their mirror images are **achiral**.



Chiral molecules contain an atom that is connected to four *different* substituent groups, called an **asymmetric atom** (e.g., asymmetric carbon) or a **stereocenter**.

Centers of this type are sometimes denoted by an asterisk. *Molecules with one stereocenter are always chiral.*



The symmetry in molecules helps to distinguish chiral structures from achiral ones

The word *chiral* is derived from the Greek *cheir*, meaning “hand” or “handedness.” Human hands have the mirror-image relation that is typical of enantiomers.

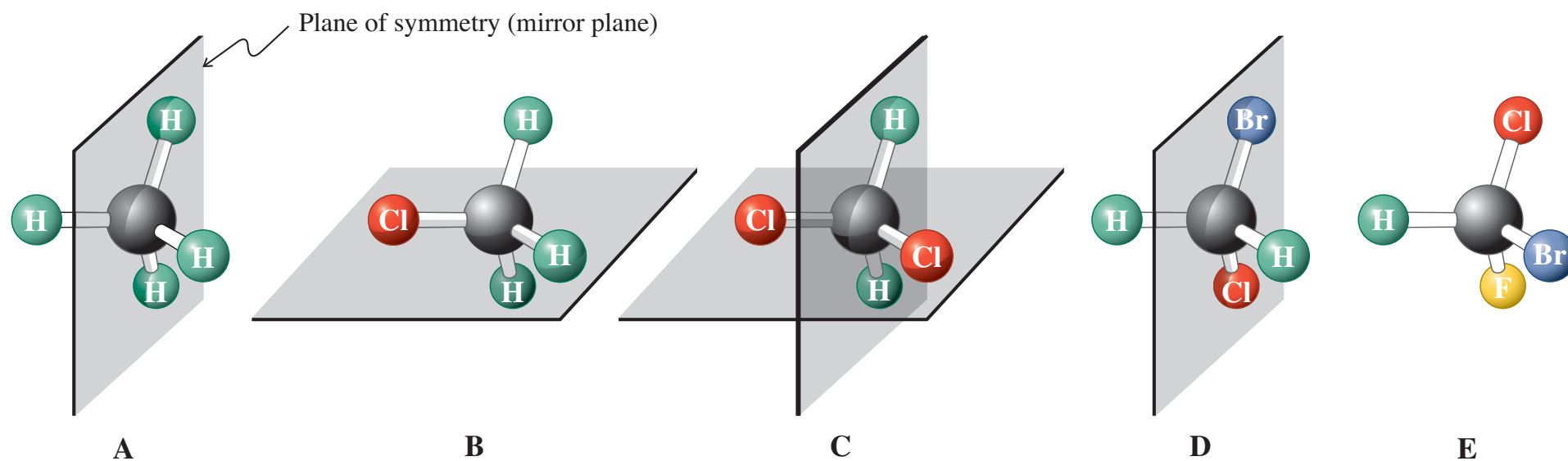
Many chiral objects, such as spiral staircases, do not have stereocenters. The same is true for many chiral molecules. *Remember that the only criterion for chirality is the nonsuperimposable nature of object and mirror image.*

How do we determine whether a molecule is chiral or not? A simpler method is to look for symmetry in the molecule under investigation: the presence or absence of a plane of symmetry.

A **plane of symmetry (mirror plane)** is one that bisects the molecule so that the part of the structure lying on one side of the plane mirrors the part on the other side.

For example, methane has six planes of symmetry, chloromethane has three, dichloromethane two, bromochloromethane one, and bromochlorofluoromethane none.

How do we use this idea to distinguish a chiral molecule from an achiral one? *Chiral molecules cannot have a plane of symmetry.*



OPTICAL ACTIVITY

If the two enantiomers of 2-bromobutane isolate in pure form, they would not distinguish on the basis of physical properties: boiling points, melting points, and densities.

Because their bonds are identical and so are their energy contents.

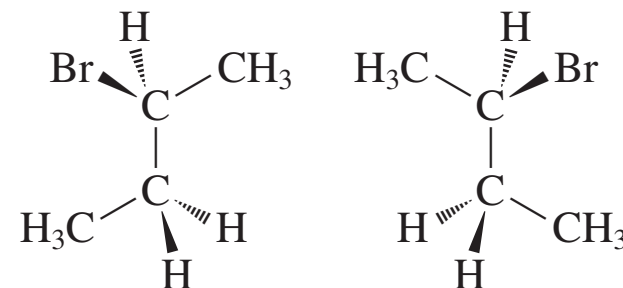
When a plane-polarized light is passed through a sample of one of the enantiomers, the plane of the incoming light is *rotated* in one direction (either clockwise or counter-clockwise).

When the same experiment is repeated with the other enantiomer, the plane of the polarized light is rotated by exactly the same amount *but in the opposite direction*.

An enantiomer rotates the plane of light in a clockwise: **dextrorotatory** (*dexter*, Latin, right), and the other enantiomer rotates the light in counter-clockwise: **levorotatory** (*laevus*, Latin, left).

Enantiomers of 2-Bromobutane

Identical physical properties, except:



(+) Enantiomer

(-) Enantiomer

Rotates plane
of light
clockwise:
dextrorotatory

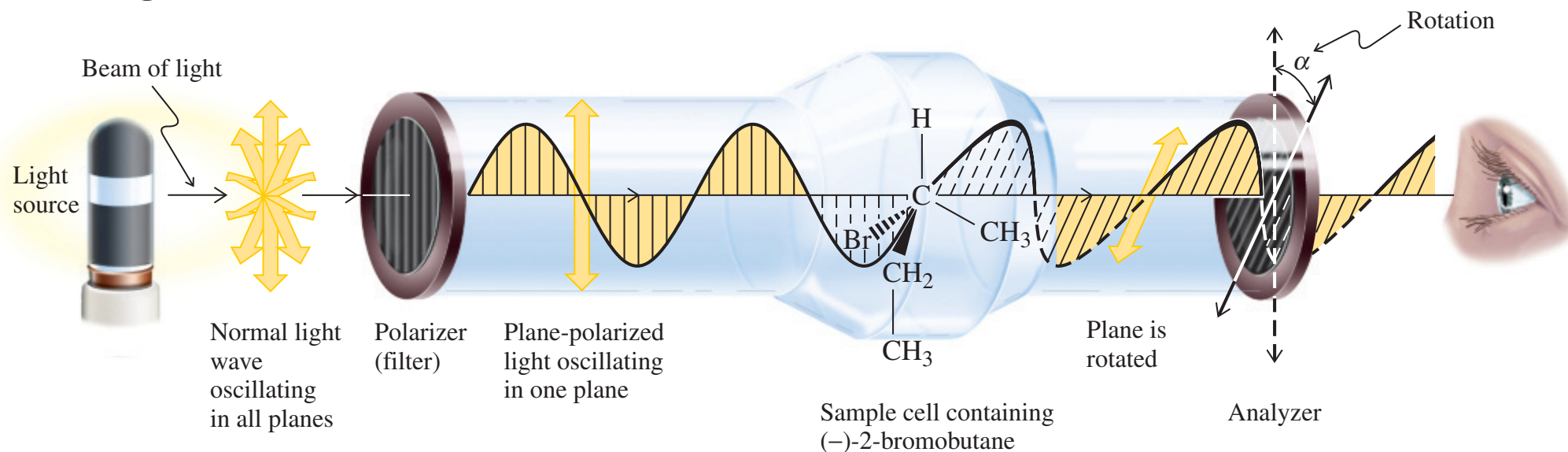
Rotates plane
of light
counterclockwise:
levorotatory

This special interaction with light is called **optical activity**, and enantiomers are frequently called **optical isomers**.

Optical rotation is measured with a polarimeter

Ordinary light can be thought of as bundles of electromagnetic waves that oscillate simultaneously in all planes perpendicular to the direction of the light beam.

When such light is passed through a material called a **polarizer**, all but one of these light waves are “filtered” away, and the resulting beam oscillates in only one plane: **plane-polarized light**.



When light travels through a molecule, the electrons around the nuclei and in the various bonds interact with the electric field of the light beam. If a beam of plane-polarized light is passed through a chiral substance, the electric field interacts differently with the “left” and “right” halves of the molecule.

This interaction results in a rotation of the plane of polarization, called **optical rotation**; the sample is referred to as **optically active**.

Optical rotations are measured by using a **polarimeter**. In this instrument, light is first plane polarized and subsequently traverses a cell containing the sample. The angle of rotation of the plane of polarization is measured by aligning another polarizer—called the **analyzer**—so as to maximize the transmittance of the light beam to the eye of the observer.

The measured rotation (in degrees) is the **observed optical rotation, α** , of the sample. Its value depends on the **concentration** and **structure** of the optically active molecule, the **length of the sample cell**, the **wavelength of the light**, the **solvent**, and the **temperature**.

Chemists have agreed on a standard value of the **specific rotation**, $[\alpha]$, for each compound. This quantity (which is solvent dependent) is defined as

Specific Rotation*

$$[\alpha]_{\lambda}^{t^{\circ}} = \frac{\alpha}{l \cdot c}$$

Measured rotation
Concentration of sample
Length of sample cell

where $[\alpha]$ = specific rotation

t = temperature in degrees Celsius

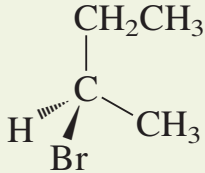
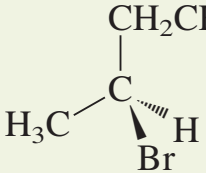
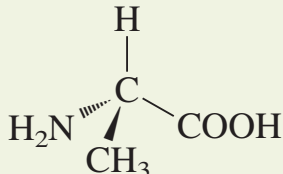
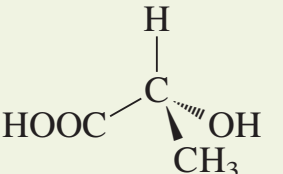
λ = wavelength of incident light; for a sodium vapor lamp, which is commonly used for this purpose, the yellow D emission line (usually indicated simply by D) has $\lambda = 589$ nm.

α = observed optical rotation in degrees

l = length of sample container in decimeters; its value is frequently 1 (i.e., 10 cm).

c = concentration (grams per milliliter of solution)

The specific rotation of an optically active molecule is a physical constant characteristic of that molecule, just like its melting point, boiling point, and density.

Table 5-1 Specific Rotations of Various Chiral Compounds $[\alpha]_D^{25^\circ\text{C}}$			
 (-)-2-Bromobutane	-23.1	 (+)-2-Bromobutane	+23.1
 (+)-2-Aminopropanoic acid [(+)-Alanine]	+8.5	 (-)-2-Hydroxypropanoic acid [(-)-Lactic acid]	-3.8
<i>Note:</i> Pure liquid for the haloalkane; in aqueous solution for the acids.			

Optical rotation indicates enantiomeric composition

A 1:1 mixture of (+) and (-) enantiomers shows no rotation and is therefore optically inactive, is called a **racemic mixture**.

If one enantiomer equilibrates with its mirror image, it is said to undergo **racemization**.

The optical activity of a sample of a chiral molecule is directly proportional to the ratio of the two enantiomers. When only one enantiomer is present, the sample is **optically pure**.

It is zero when the two enantiomers are present in equal amounts, and the sample is racemic and **optically inactive**.

When one enantiomer, in mixture, is in excess of the other, called **enantiomer excess (ee)**. The ee can be obtained from the % optical rotation of a mixture relative to that of the pure enantiomer (**optical purity**):

Enantiomer excess (*ee*) = % of major enantiomer – % of minor enantiomer

Optical Purity and Enantiomer Excess

$$\text{Enantiomer excess (ee) = optical purity} = \frac{[\alpha]_{\text{Mixture}}}{[\alpha]_{\text{Pure enantiomer}}} \times 100\%$$

ABSOLUTE CONFIGURATION: R,S SEQUENCE RULES

How do we establish the structure of one pure enantiomer of a chiral compound?

X-ray diffraction can establish the absolute configuration

Virtually all the physical characteristics of one enantiomer are identical with those of its mirror image, except for the sign of optical rotation.

There is no straightforward correlation between the sign of rotation and the structure of the particular enantiomer.

For example, conversion of lactic acid into its sodium salt changes the sign (and degree) of rotation, even though the absolute configuration at the stereocenter is unchanged.

