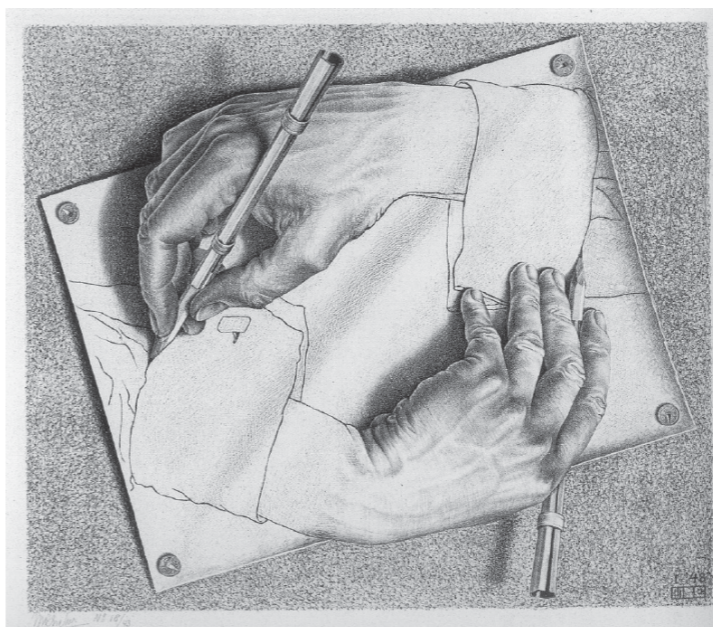


8

STEREOCHEMISTRY



M. C. ESCHER, DRAWING HANDS, 1948

8.2 MIRROR IMAGE OBJECTS, MIRROR IMAGE MOLECULES AND CHIRALITY

Figure 8.1 Objects and Their Mirror Images

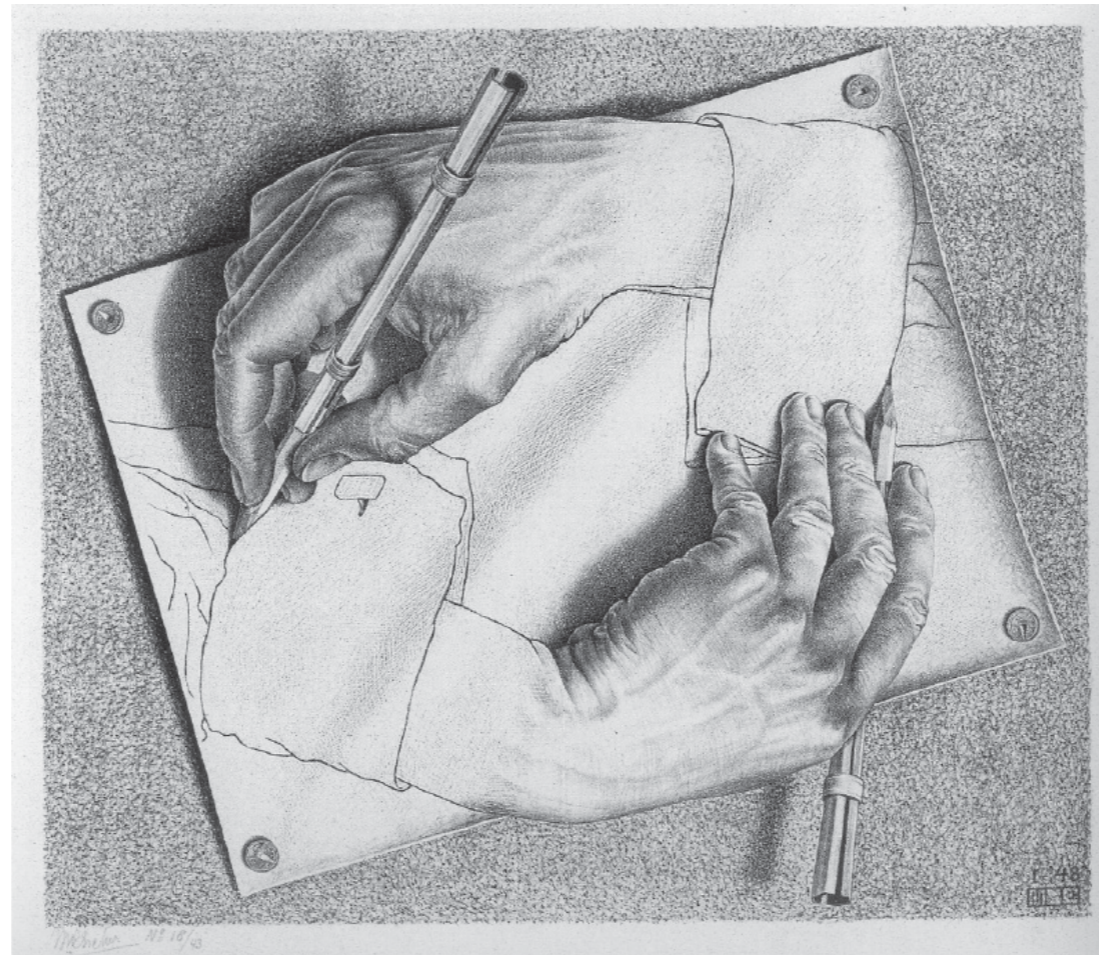
In (a), the chair and its mirror image are identical. They can be superimposed. In (b), the mirror image, side-arm chairs cannot be superimposed. One chair has a “right-handed” arm, the other has a “left-handed” arm. (These particular chairs were designed by the renowned woodworker George Nakashima.)



8.2 MIRROR IMAGE OBJECTS, MIRROR IMAGE MOLECULES AND CHIRALITY

Figure 8.2 Nonsuperimposable Mirror Images

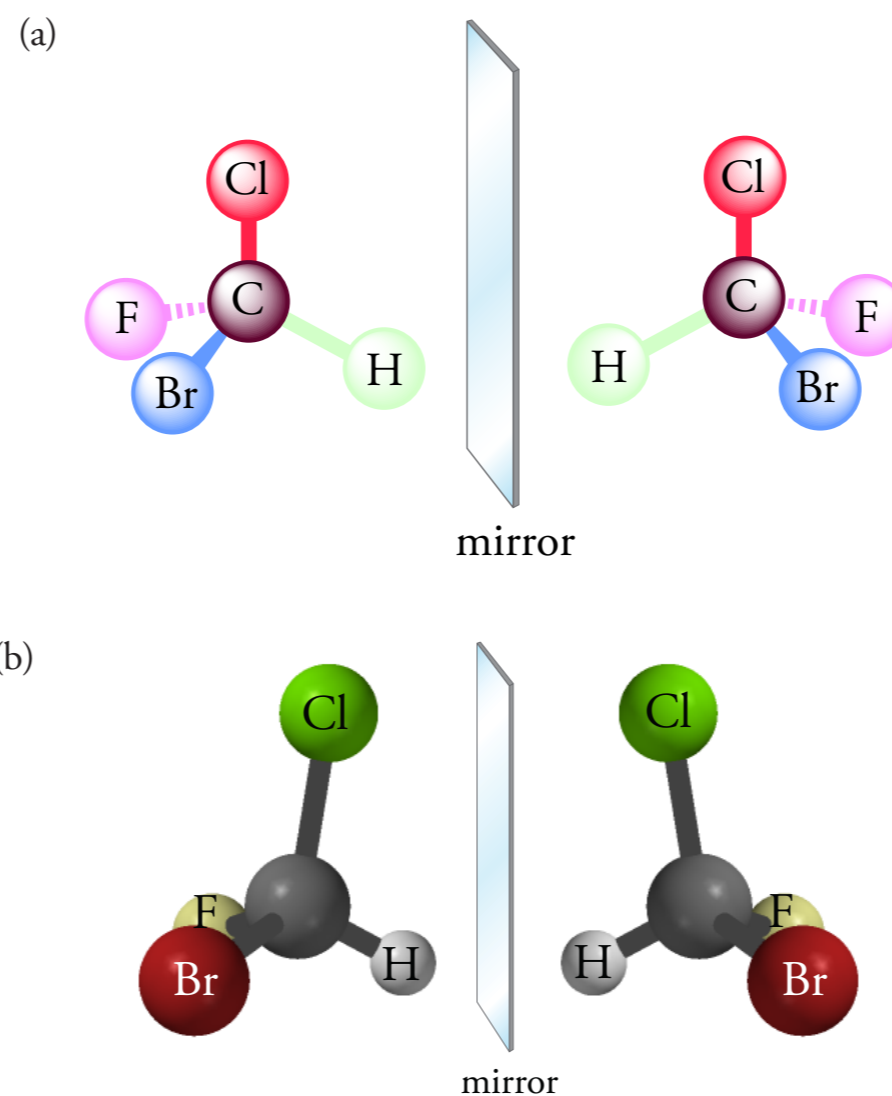
A left and a right hand are nonsuperimposable mirror images. (M. C. Escher, Drawing Hands)



8.2 MIRROR IMAGE OBJECTS, MIRROR IMAGE MOLECULES AND CHIRALITY

Figure 8.3 Nonsuperimposable Mirror Image Molecules

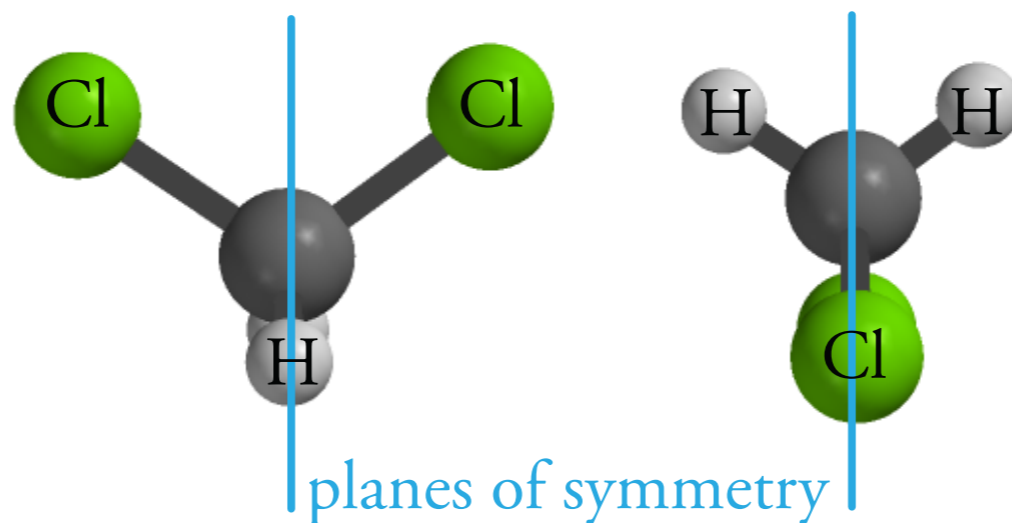
Bromochlorofluoromethane does not have a plane of symmetry. Therefore, it is chiral, and it exists as a pair of nonsuperimposable mirror image isomers. (a) Schematic diagram; (b) Ball-and-stick molecular models.



8.2 MIRROR IMAGE OBJECTS, MIRROR IMAGE MOLECULES AND CHIRALITY

Figure 8.4 Planes of Symmetry in Dichloromethane

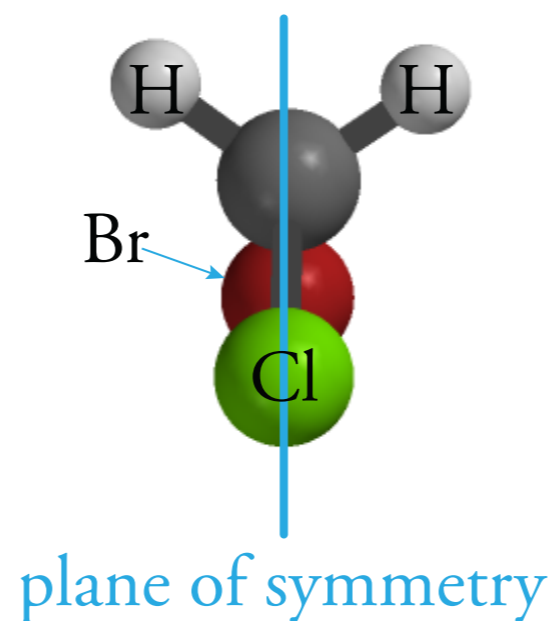
Dichloromethane, which has not one, but two planes of symmetry can be superimposed on its mirror image. It is achiral.



8.2 MIRROR IMAGE OBJECTS, MIRROR IMAGE MOLECULES AND CHIRALITY

Figure 8.4 Planes of Symmetry in Dichloromethane

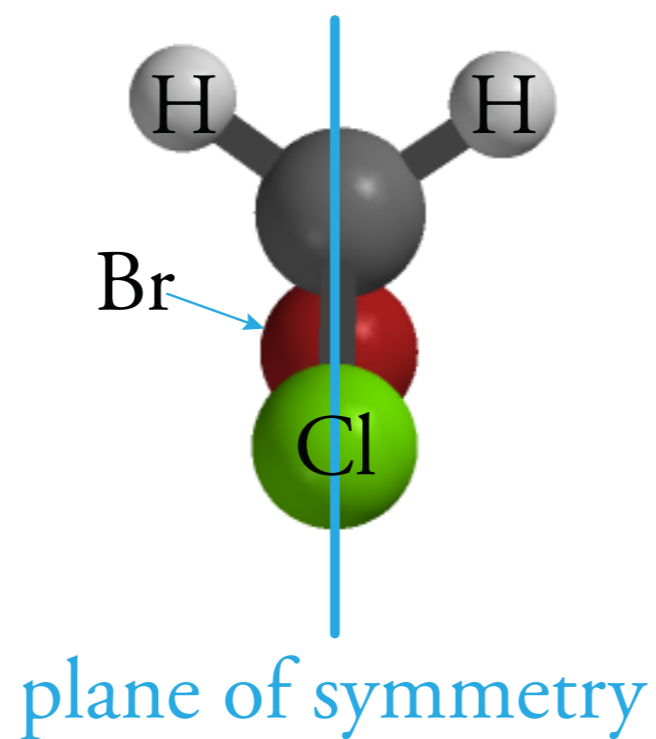
Dichloromethane, which has not one, but two planes of symmetry can be superimposed on its mirror image. It is achiral.



8.2 MIRROR IMAGE OBJECTS, MIRROR IMAGE MOLECULES AND CHIRALITY

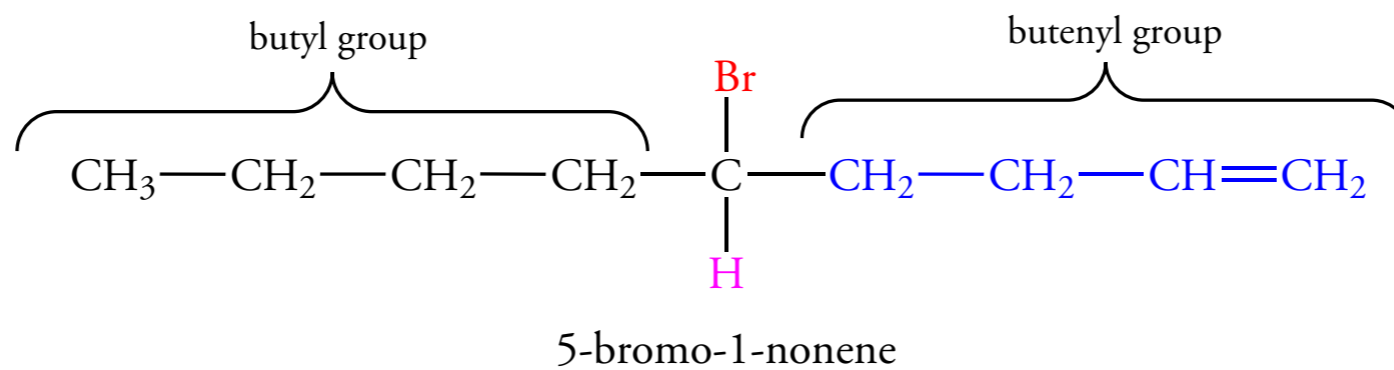
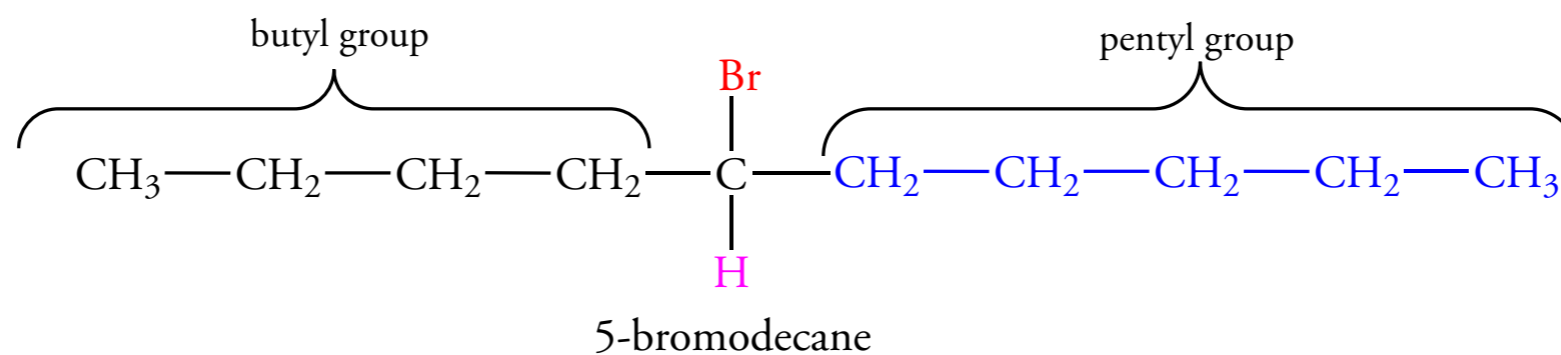
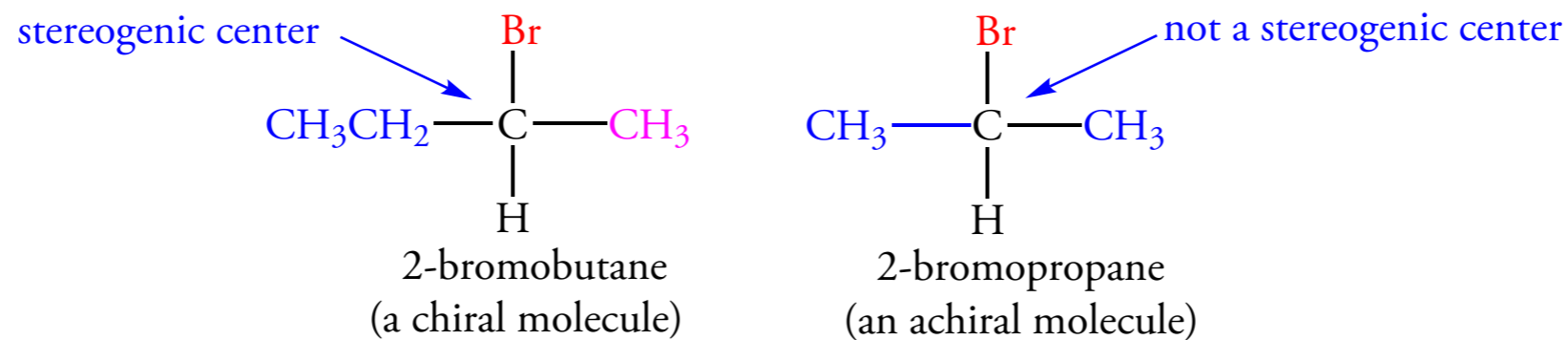
Figure 8.5 Plane of Symmetry in Bromochloromethane

Bromochloromethane has a plane of symmetry, and therefore it can be superimposed on its mirror image. It is achiral.



8.2 MIRROR IMAGE OBJECTS, MIRROR IMAGE MOLECULES AND CHIRALITY

Mirror Image Isomers

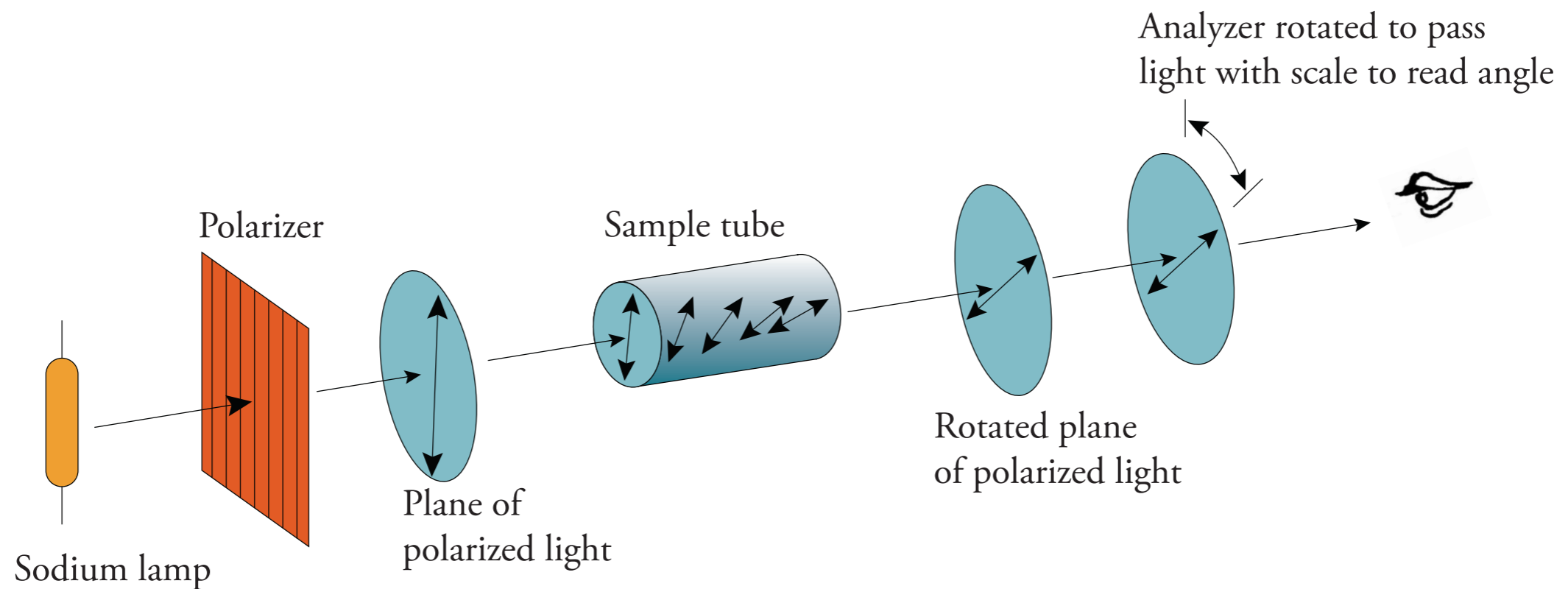


8.3 OPTICAL ACTIVITY

Plane Polarized Light

Figure 8.6 Schematic Diagram of a Polarimeter

Plane-polarized light is obtained by passing light through a polarizing filter. Any chiral compound in the sample tube rotates the plane-polarized light. The direction and magnitude of the rotation are determined by rotating the analyzer to allow the light to pass through with maximum brightness. In a modern instrument this is all done electronically, but the basic principle is the same.



8.3 OPTICAL ACTIVITY

Specific Rotation

$$[\alpha]_D = \frac{\alpha_{\text{obs}}}{l \times c}$$

Table 8.1
Specific Rotations of
Common Compounds

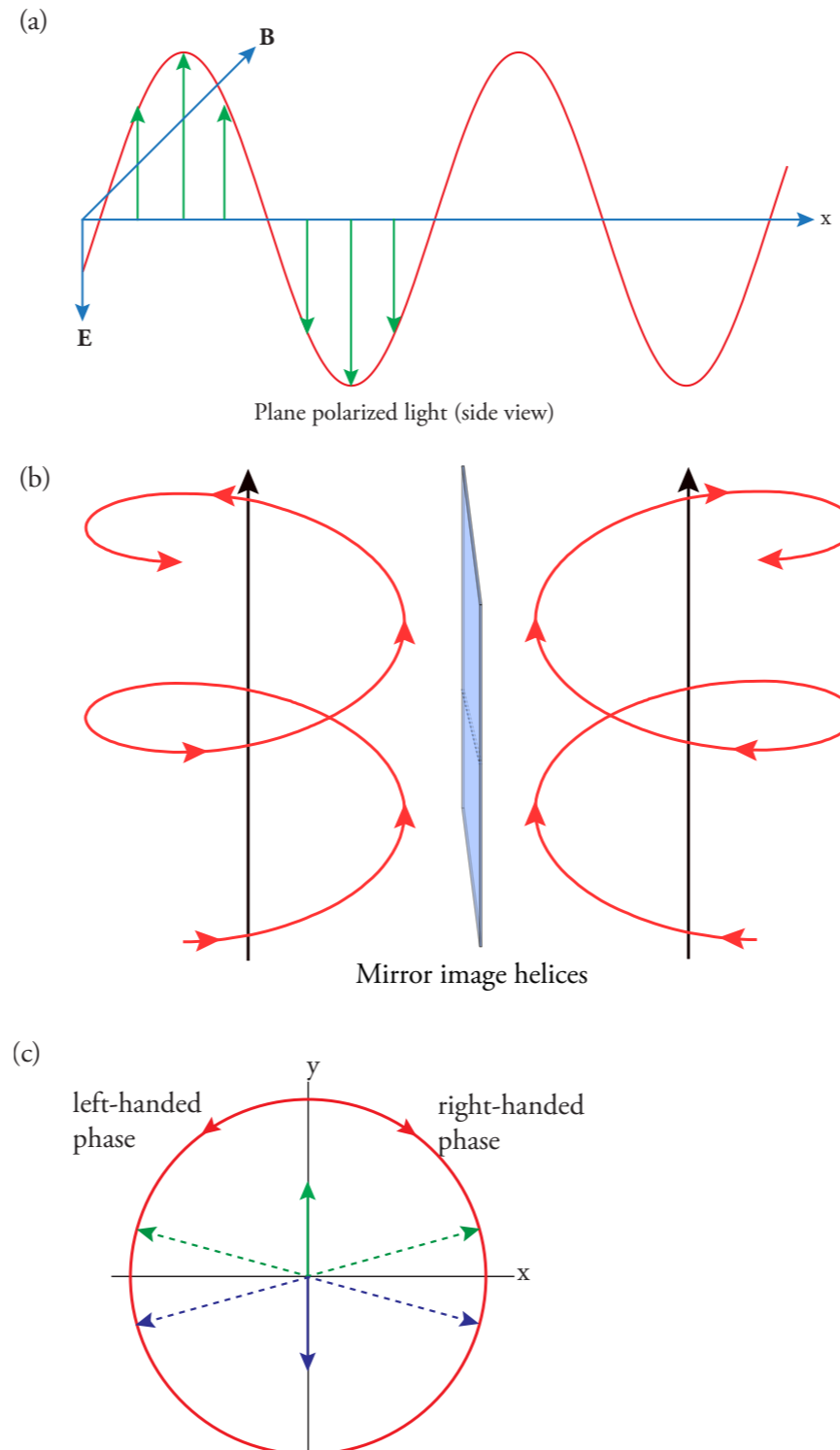
Compound	$[\alpha]_D$
azidothymidine (AZT)	+99°
cefotaxin (a cephalosporin)	+55°
cholesterol	-31.5°
cocaine	-16°
codeine	-136°
epinephrine (adrenaline)	-5.0°
levodopa	-13.1°
monosodium glutamate (MSG)	+25.5°
morphine	-132°
oxacillin (a penicillin)	+201°
progesterone	+172°
sucrose	+66°
testosterone	+109°

8.3 OPTICAL ACTIVITY

Circularly Polarized Light and Optical Rotation

Figure 8.6 Schematic Diagrams of Plane and Circularly Polarized Light

(a) In plane polarized light, the electric field vectors of the light all oscillate in a single plane. (b) In circularly polarized light, the electric field vector can rotate in a right-handed (clockwise) or left-handed (counterclockwise) direction. (c) If right-handed and left-handed phases of circularly polarized light are superimposed, the electric field vectors in the $+x$ - $-x$ directions cancel, and the y -components are additive, and directed along the y -axis. The net result is plane-polarized light.



8.3 OPTICAL ACTIVITY

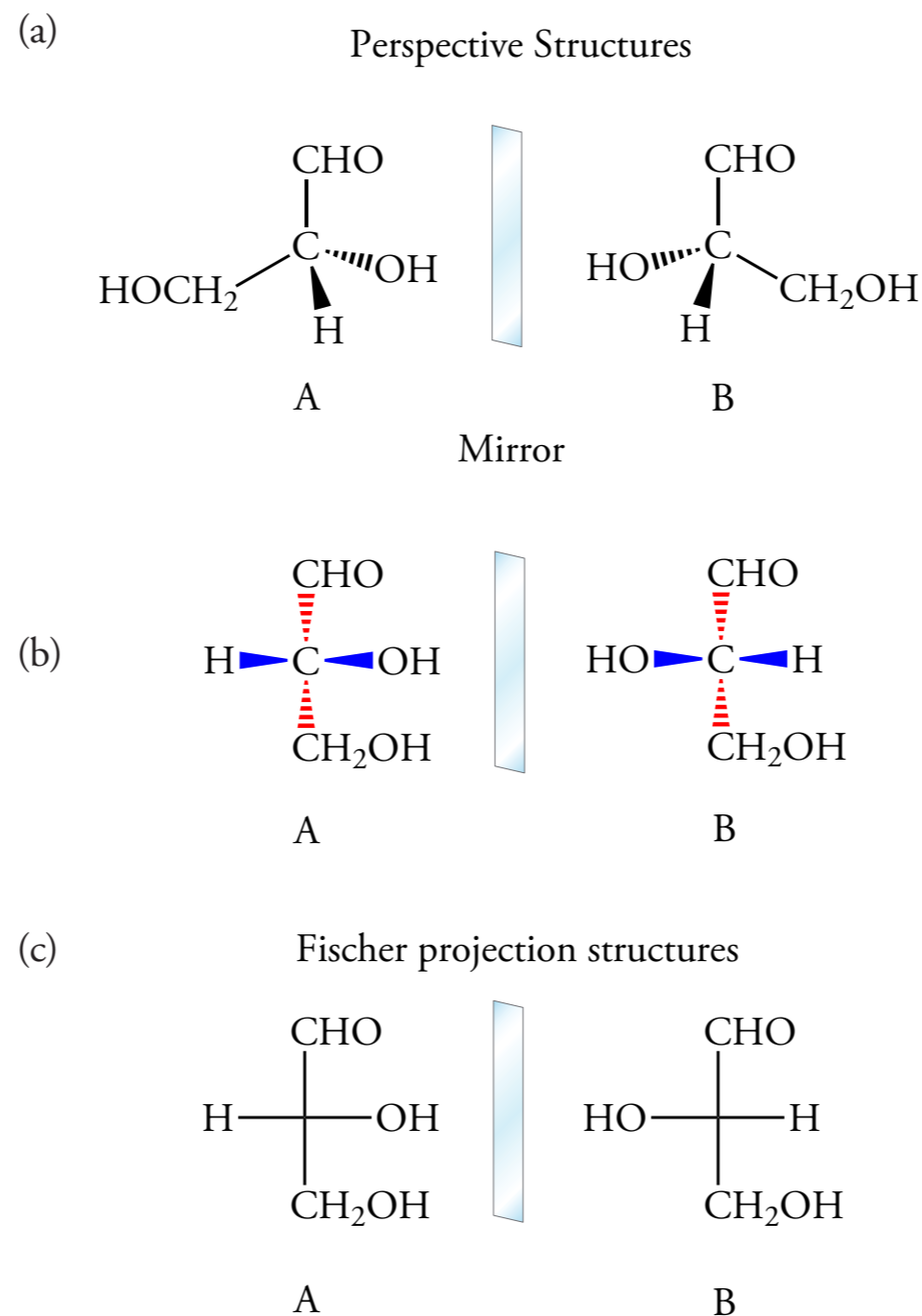
Optical Purity

$$\text{optical purity} = \frac{\text{observed rotation}}{\text{rotation of pure enantiomer}} \times 100\%$$

8.4 FISCHER PROJECTION FORMULAS

Figure 8.7 Fischer Projection Structures of Glyceraldehyde

(a) Perspective structures of glyceraldehyde. (b) Projection structures. (c) Fischer projection structures of the enantiomers glyceraldehyde. The chiral center is located at the point where the bond lines intersect. The carbon atom is not usually shown. The vertical lines extend away from the viewer, behind the plane of the page; horizontal lines extend toward the viewer, out of the plane of the page, as shown in part (b).

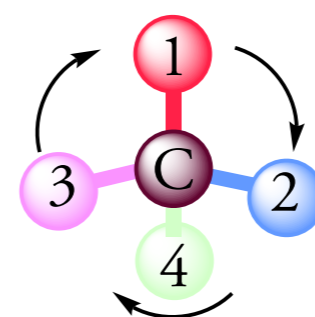
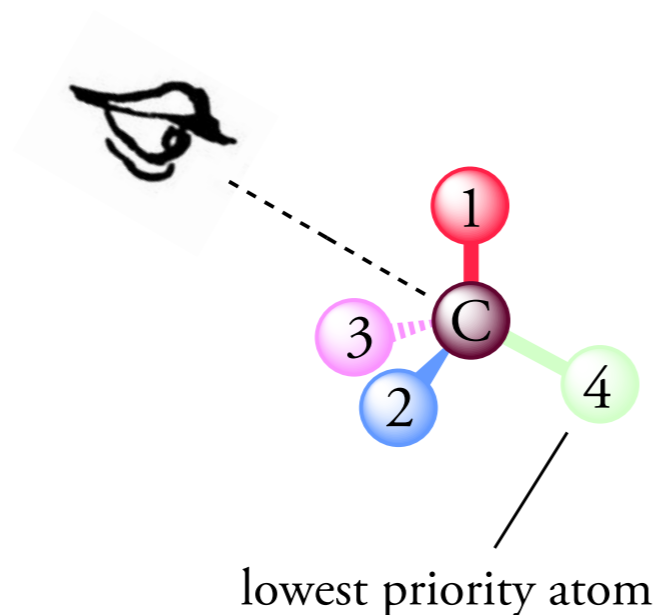


8.5 ABSOLUTE CONFIGURATION

R,S Configurations: The Kahn-Ingold-Prelog System of Configurational Nomenclature

Figure 8.8 Kahn-Ingold-Prelog System of Configurational Nomenclature

Place the lowest priority atom or group away from your eye, and view the chiral site along the axis of the carbon-bond to the lowest priority group. (The diagram of the eye in this figure is from a drawing in the notebooks of Leonardo da Vinci.)



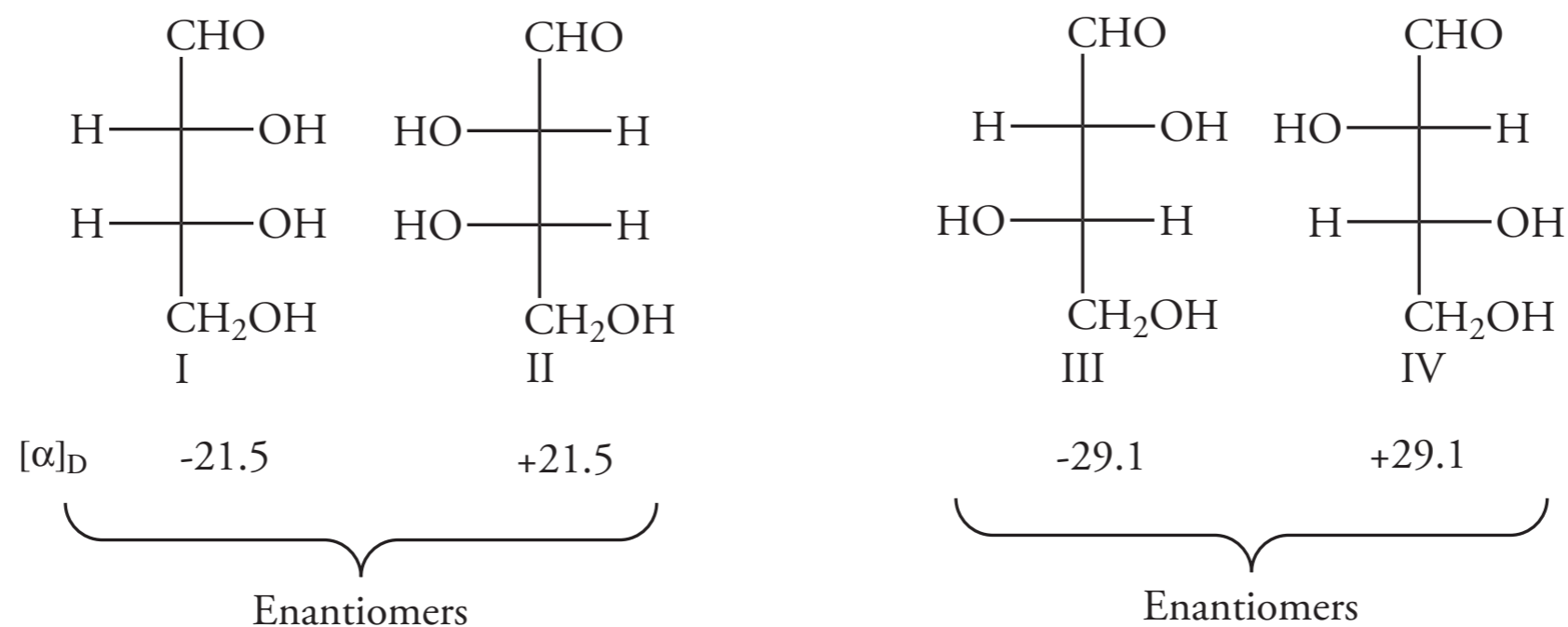
Clockwise rotation from 1, to 2, to 3 gives R configuration.

8.6 MOLECULES WITH TWO (OR MORE) STEREOGENIC CENTERS

Nonequivalent Stereogenic Centers

Figure 8.10 Enantiomers and Diastereomers

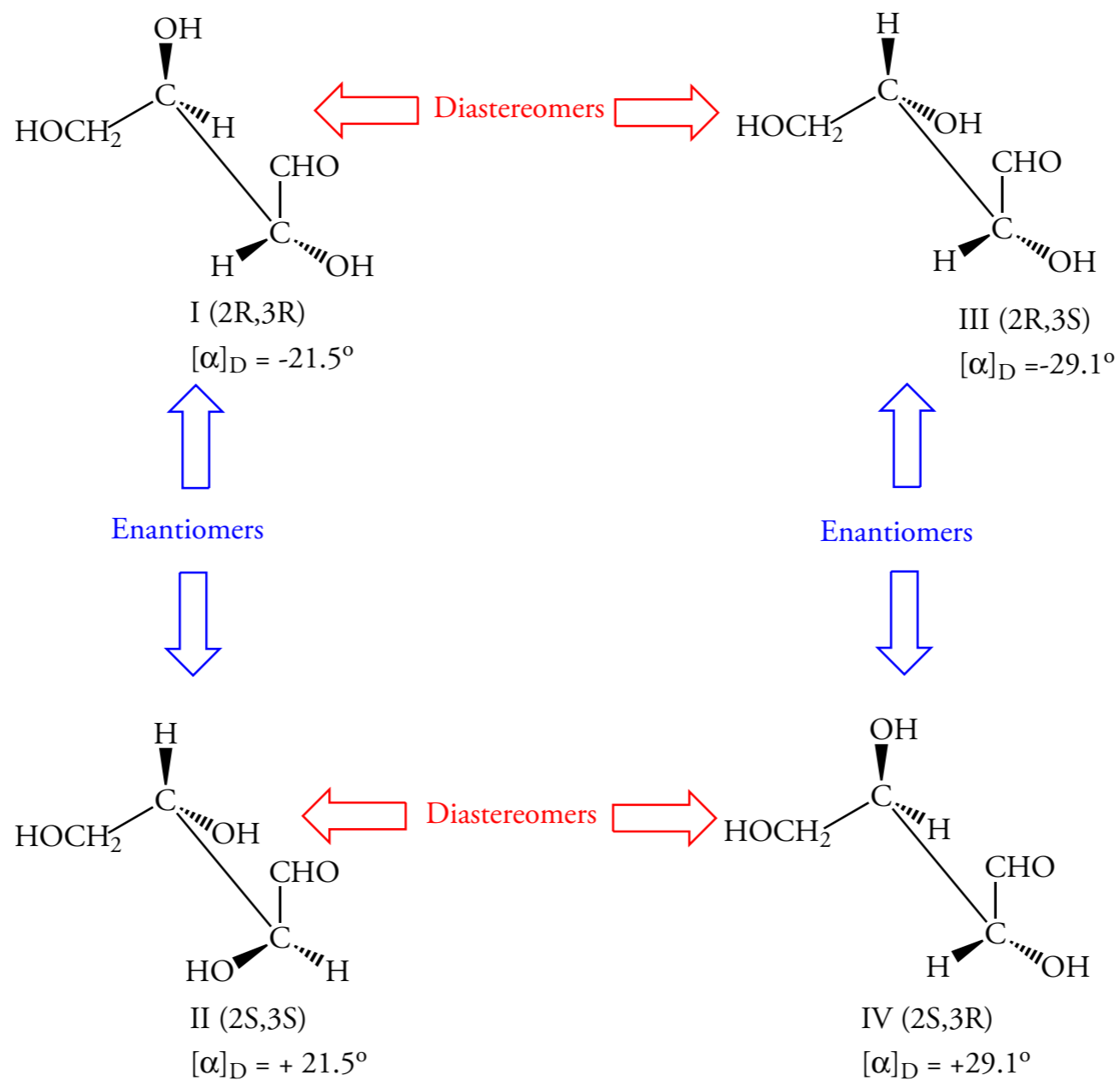
A molecule that contains two nonequivalent chiral centers, such as 2,3-4-trihydroxybutanal, can exist as four stereoisomers. They exist as two pairs of enantiomers. Stereoisomers that are not enantiomers are diastereomers.



8.6 MOLECULES WITH TWO (OR MORE) STEREOGENIC CENTERS

Nonequivalent Stereogenic Centers

Figure 8.11 Configurations of Enantiomers and Diastereomers

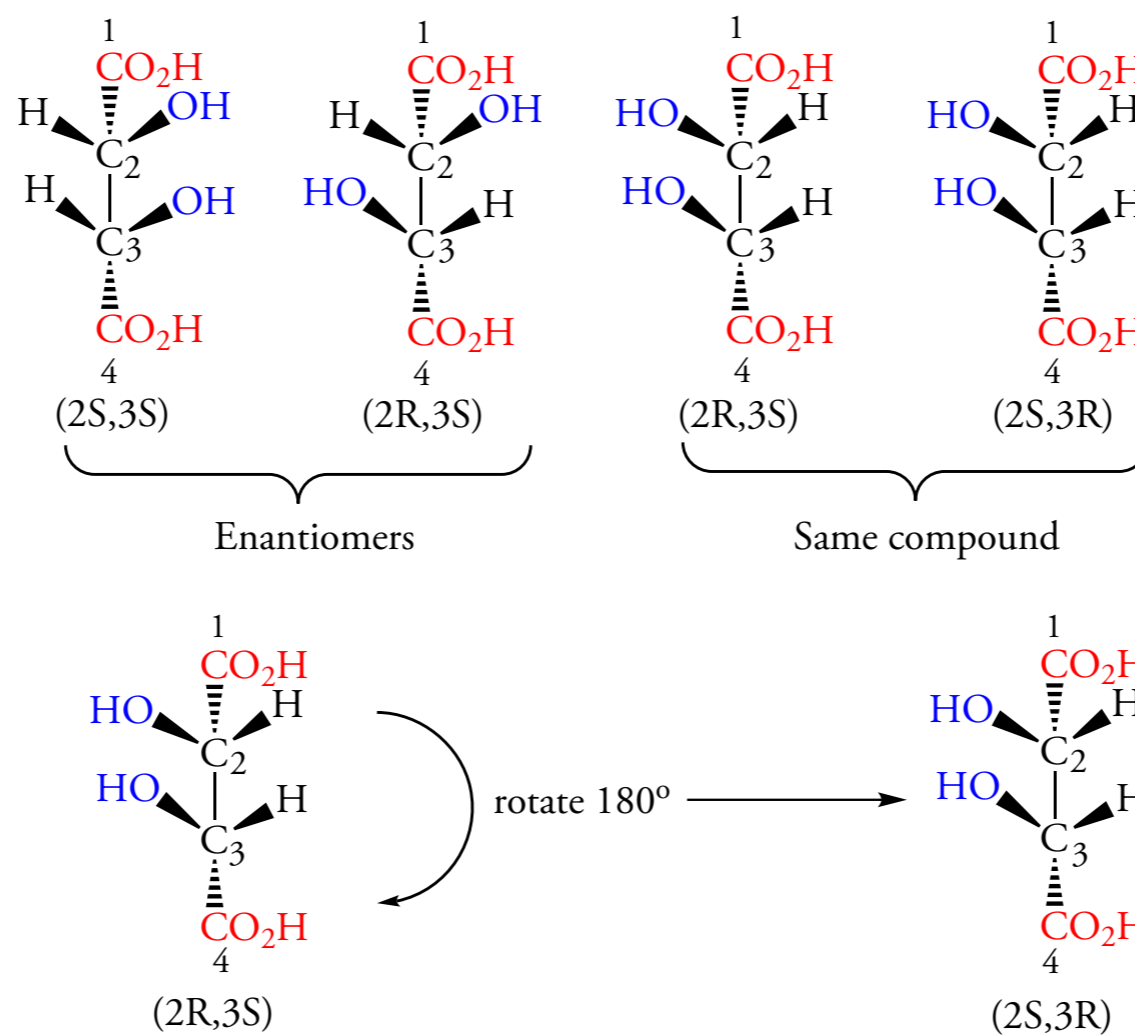


8.6 MOLECULES WITH TWO (OR MORE) STEREOGENIC CENTERS

Nonequivalent Stereogenic Centers

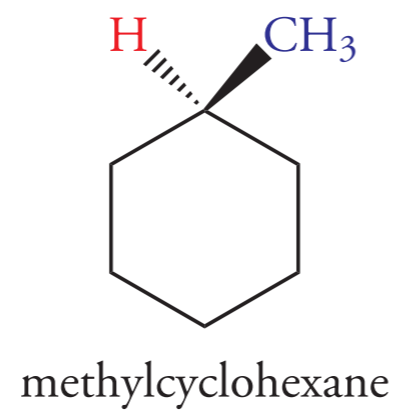
Figure 8.12 Configurations of Optically Active Tartaric Acids and Meso Compounds

Only three stereoisomers exist for tartaric acid because it has two equivalent chiral centers. Two of the stereoisomers are enantiomers. The third has a plane of symmetry, is optically inactive, and is called a *meso* compound; i.e. *meso*-tartaric acid.

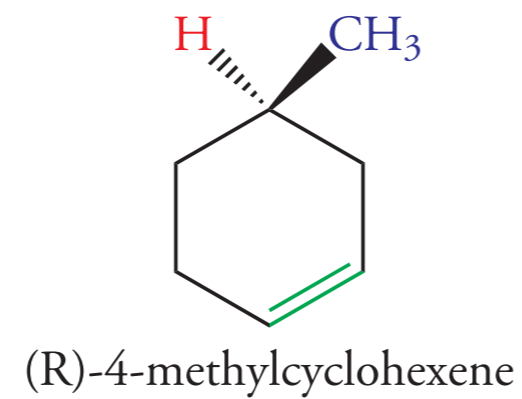
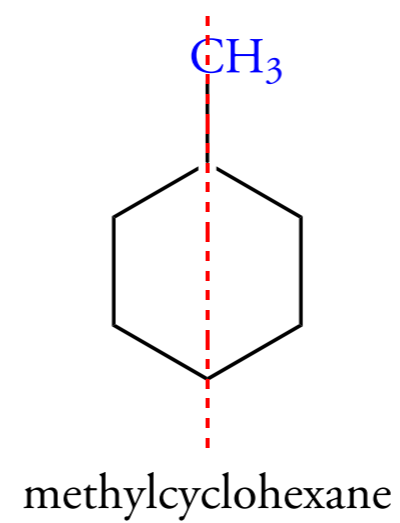


8.7 Cyclic Molecules with Stereogenic Centers

Cyclic Structures with One Stereogenic Center



plane of symmetry

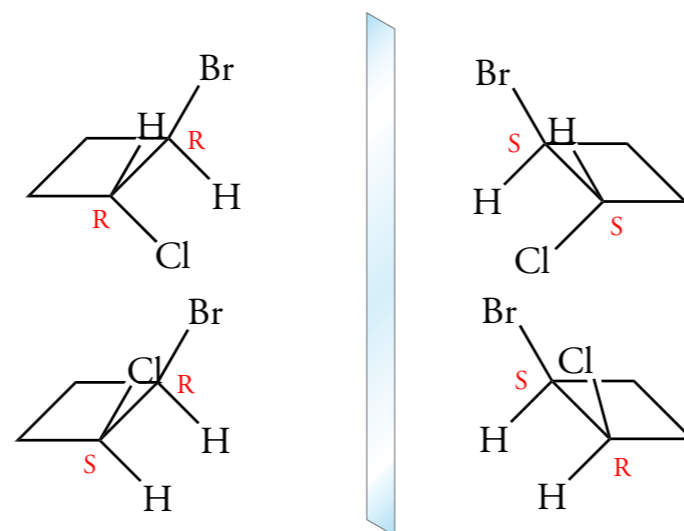


8.7 Cyclic Molecules with Stereogenic Centers

Cyclic Structures with Two Stereogenic Centers: Disubstituted Cyclobutanes

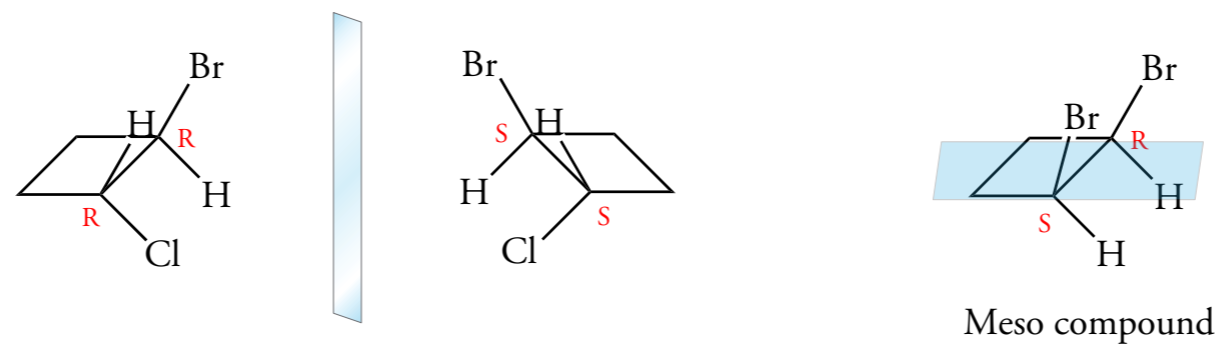
Figure 8.13 Diastereomers of 1,2-Disubstituted Cyclobutanes

(a) A 1,2-disubstituted cyclobutane with two nonequivalent chiral centers has four diastereomers. (b) However, a 1,2-disubstituted cyclobutane with two equivalent chiral centers has only three diastereomers, one of which is a *meso* compound.



Mirror

(a) Diastereomers of 1-bromo-2-chlorocyclobutane



Meso compound

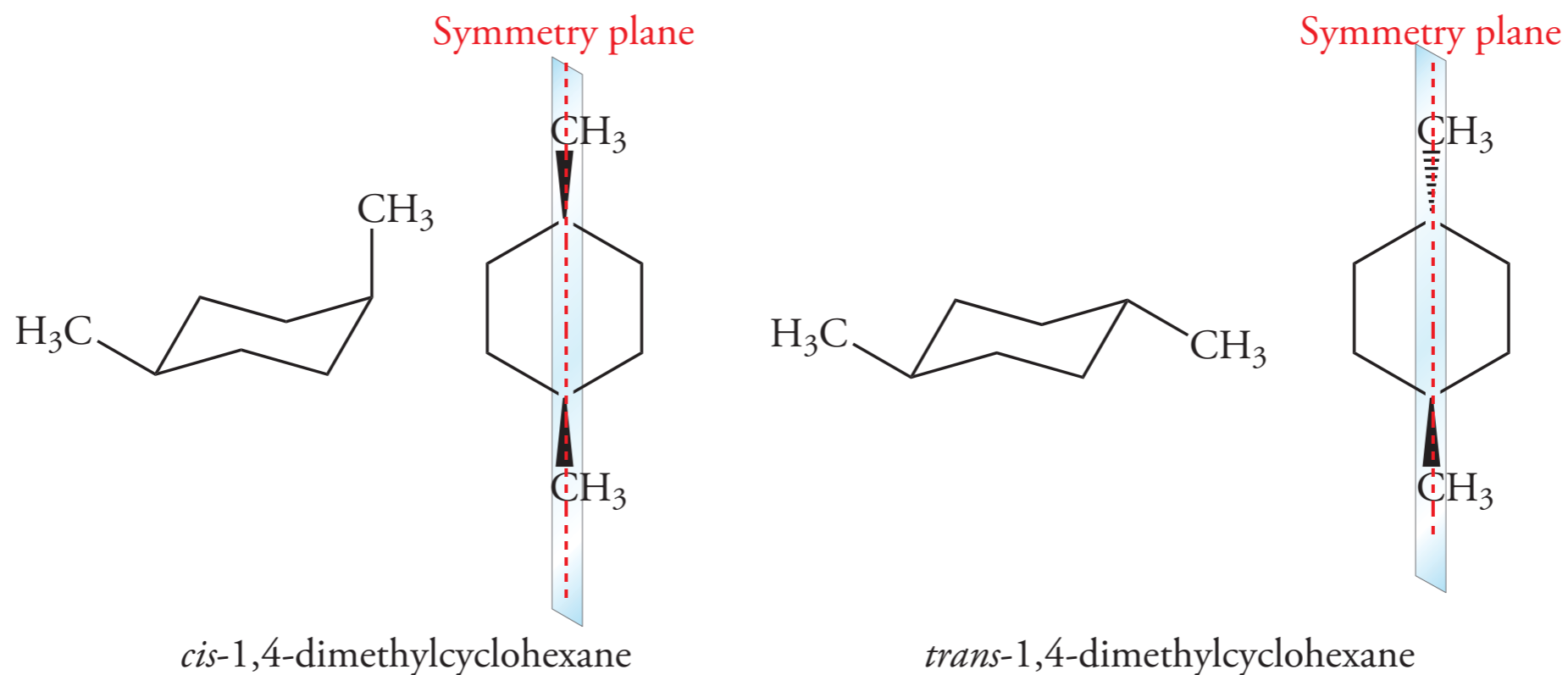
(b) Diastereomers of 1,2-dibromocyclobutane

8.7 Cyclic Molecules with Stereogenic Centers

Cyclic Structures with Two Stereogenic Centers: Dimethyl Cyclohexanes

Figure 8.14 Stereoisomers of 1,4-Dimethylcyclohexane

The *cis* and *trans* isomers of 1,4-dimethylcyclohexane are achiral because each has a plane of symmetry.

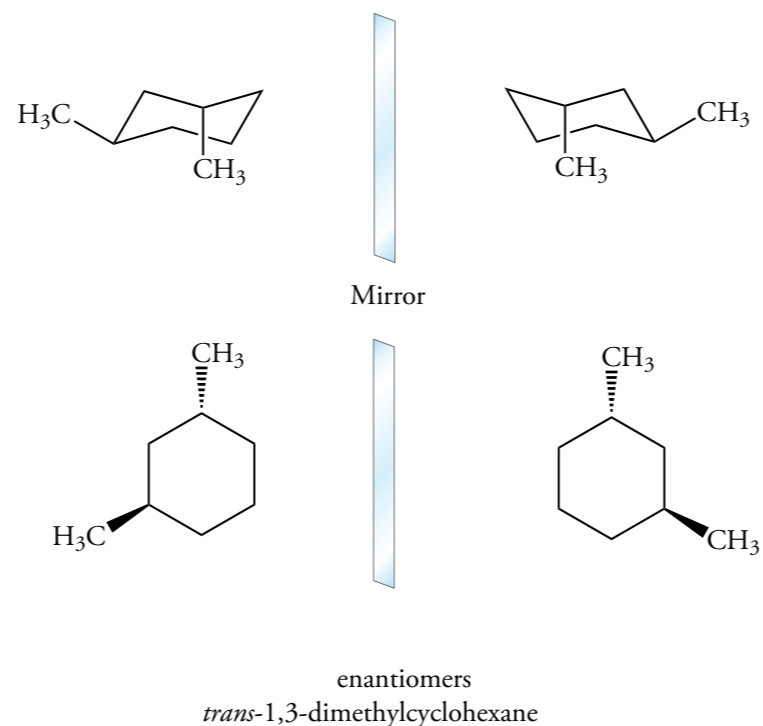
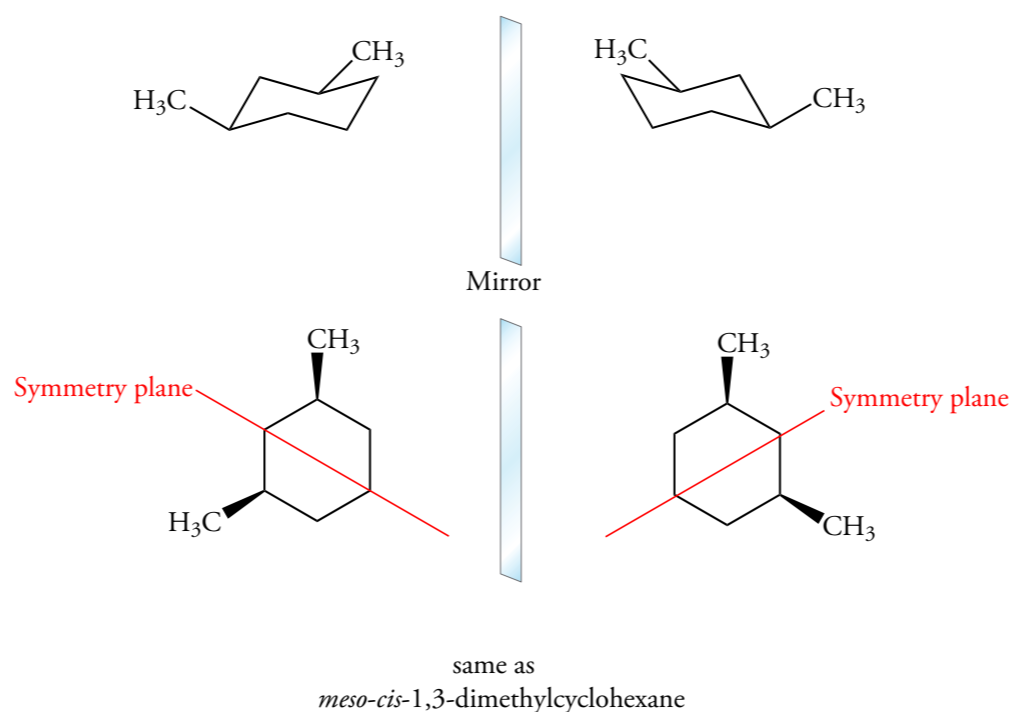


8.7 Cyclic Molecules with Stereogenic Centers

Cyclic Structures with Two Stereogenic Centers: Dimethyl Cyclohexanes

Figure 8.15 Diastereomers of 1,3-Dimethylcyclohexane

cis-1,3-Dimethylcyclohexane is a *meso* compound. It is achiral because it has a plane of symmetry. *trans*-1,3-Dimethylcyclohexane exists as a pair of enantiomers.

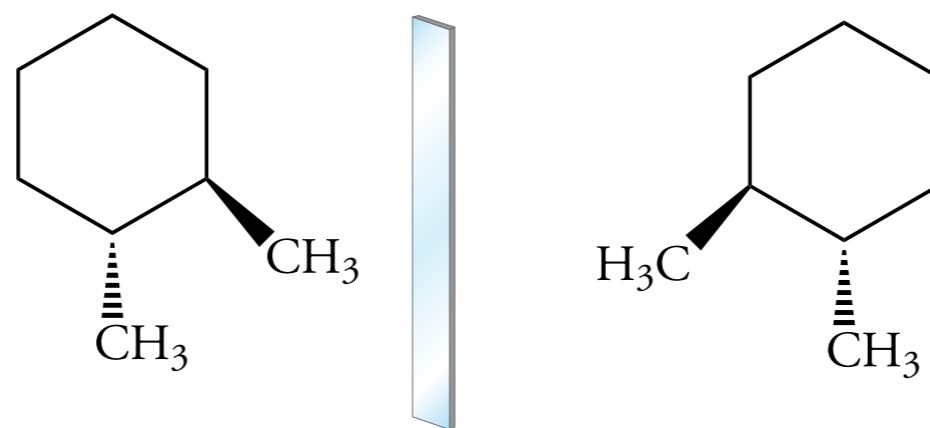
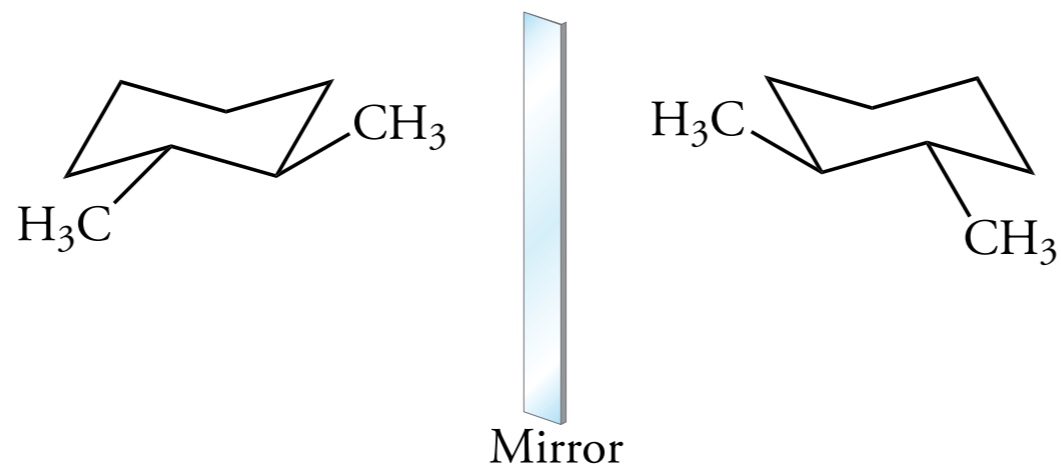


8.7 Cyclic Molecules with Stereogenic Centers

Cyclic Structures with Two Stereogenic Centers: Dimethyl Cyclohexanes

Figure 8.16 Enantiomers of *trans*-1,2-Dimethylcyclohexane

trans-1,2-Dimethylcyclohexane exists as a pair of enantiomers. There is no a plane of symmetry.



enantiomers

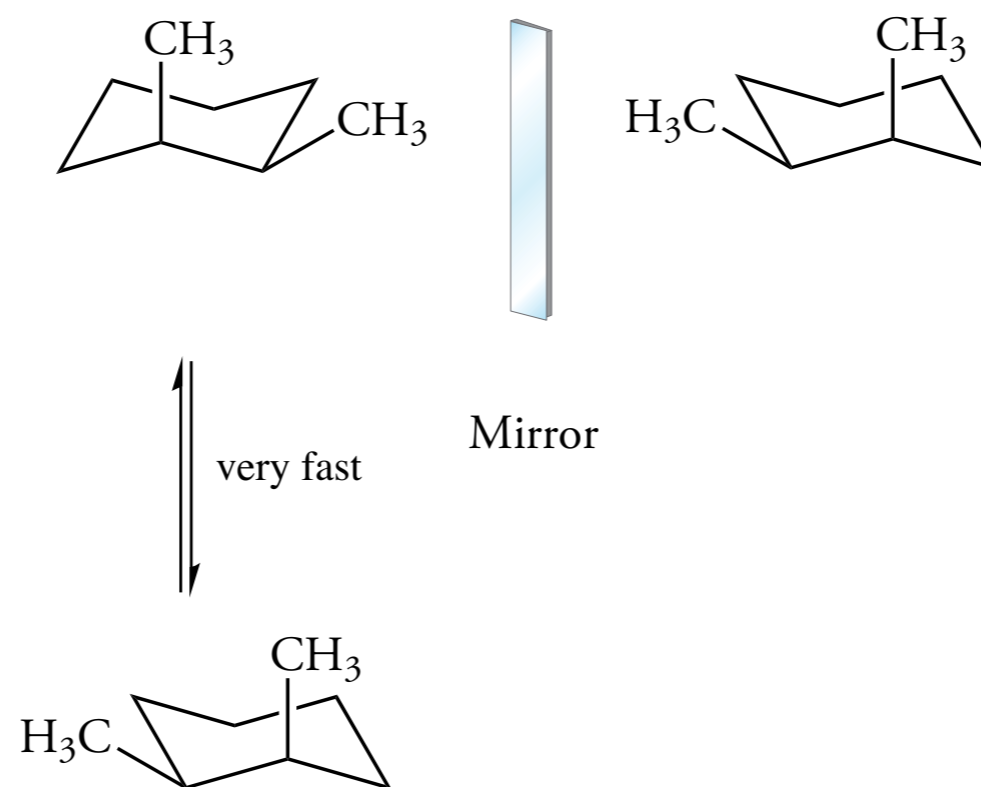
trans-1,2-dimethylcyclohexane

8.7 Cyclic Molecules with Stereogenic Centers

Cyclic Structures with Two Stereogenic Centers: Dimethyl Cyclohexanes

Figure 8.17 *cis*-1,2-Dimethylcyclohexane

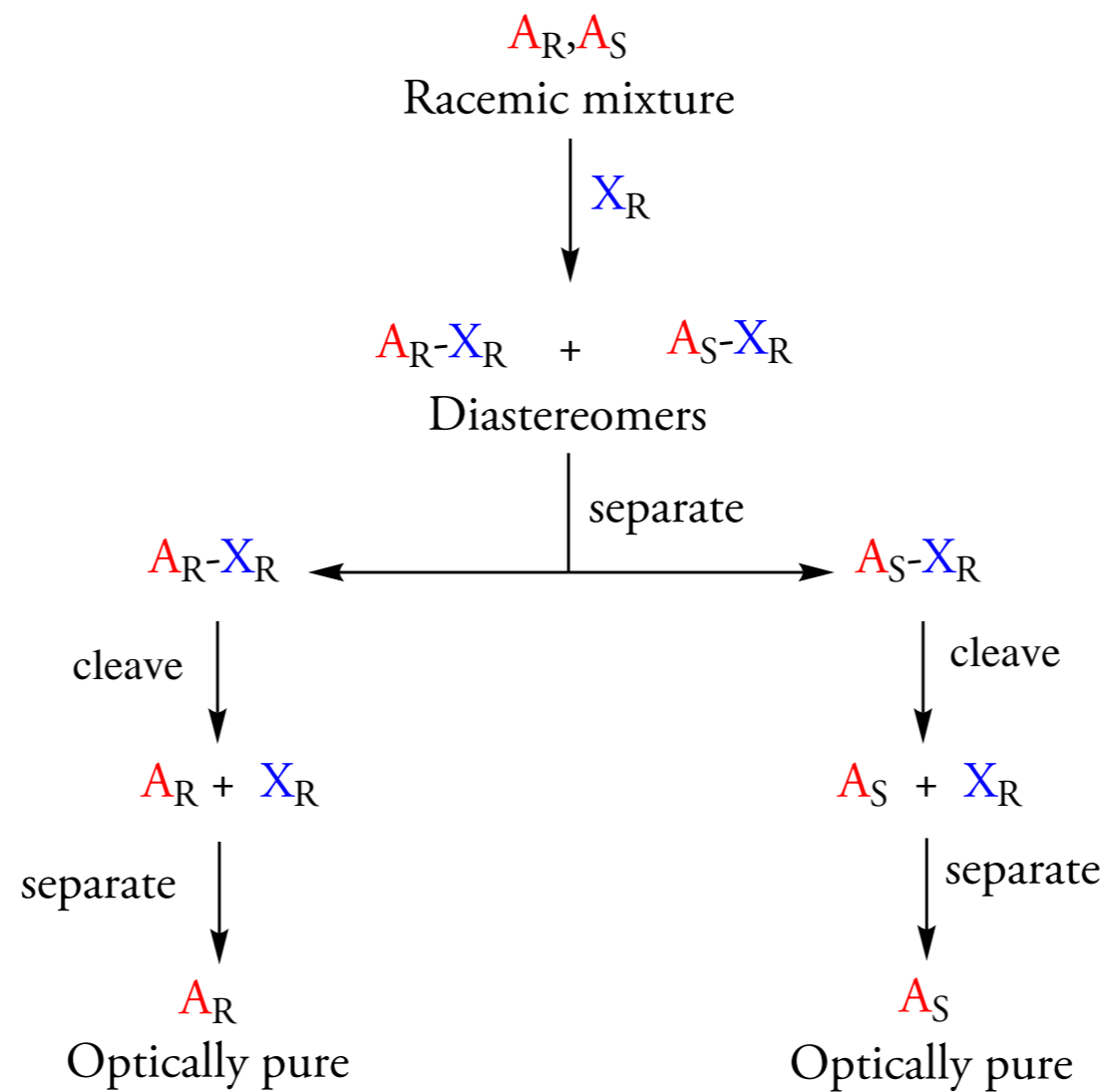
The mirror images of *cis*-1,2-dimethylcyclohexane are not superimposable. However, chair-chair interconversion is very fast, so the enantiomers cannot be separated.



8.8 SEPARATION OF ENANTIOMERS

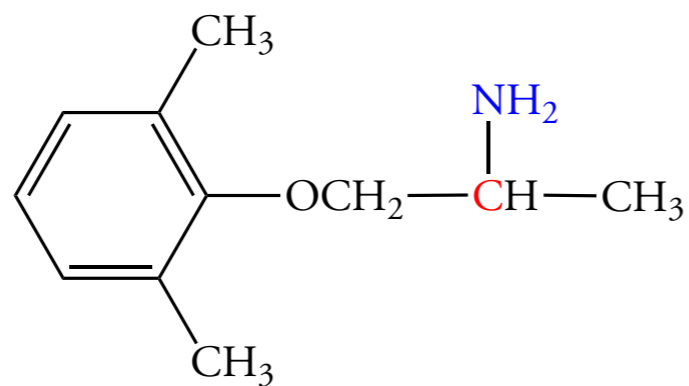
General Principles

Figure 8.18 General Method for Resolving Enantiomers

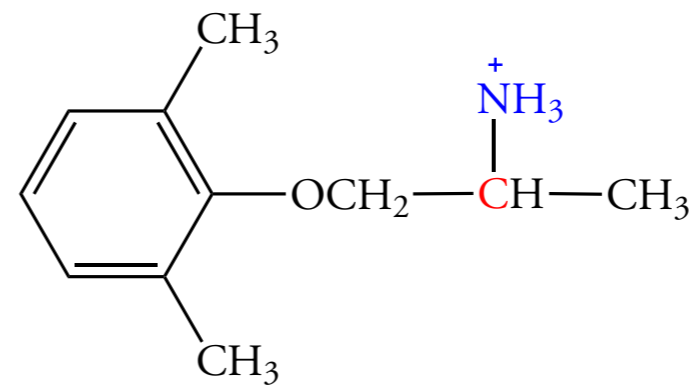


8.8 SEPARATION OF ENANTIOMERS

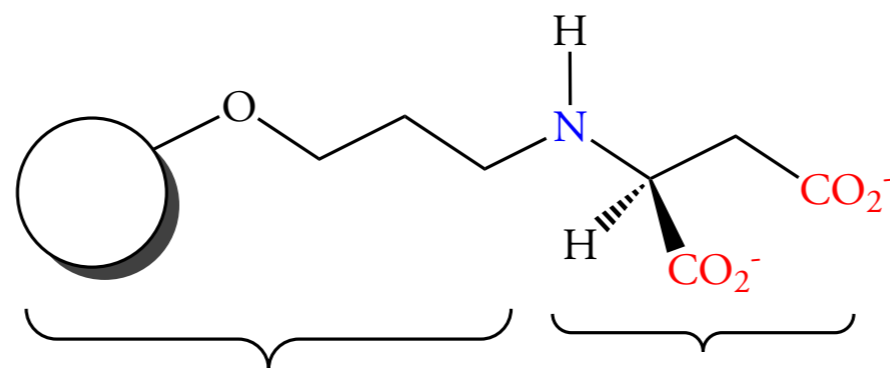
Chiral Chromatography



(±)-mexiletine (an antiarrhythmic drug)



conjugate acid of mexiletine (pH 7)

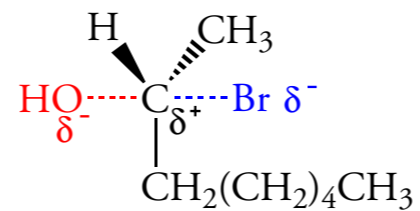
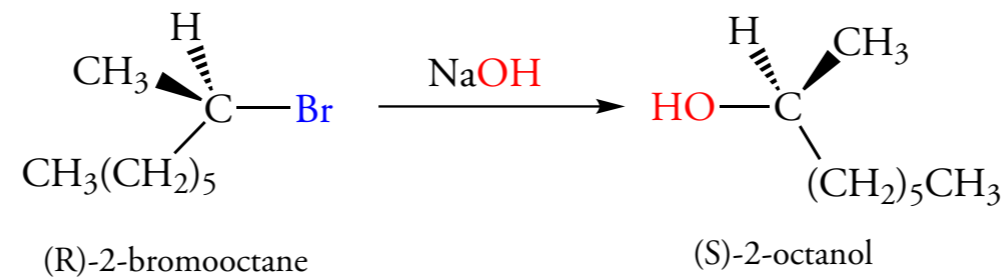


column support (matrix)

chiral ligand
(S)-aspartate

8.9 CHEMICAL REACTIONS AT STEREOGENIC CENTERS

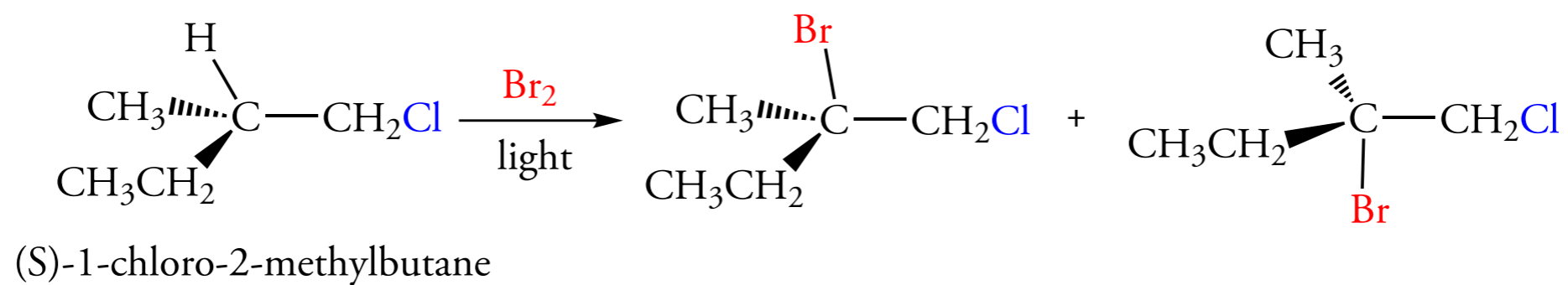
Preview: Stereochemistry of a Substitution Reaction at a Stereogenic Center



Transition state for inversion of configuration

8.9 CHEMICAL REACTIONS AT STEREOGENIC CENTERS

Stereochemistry of a Free Radical Reaction

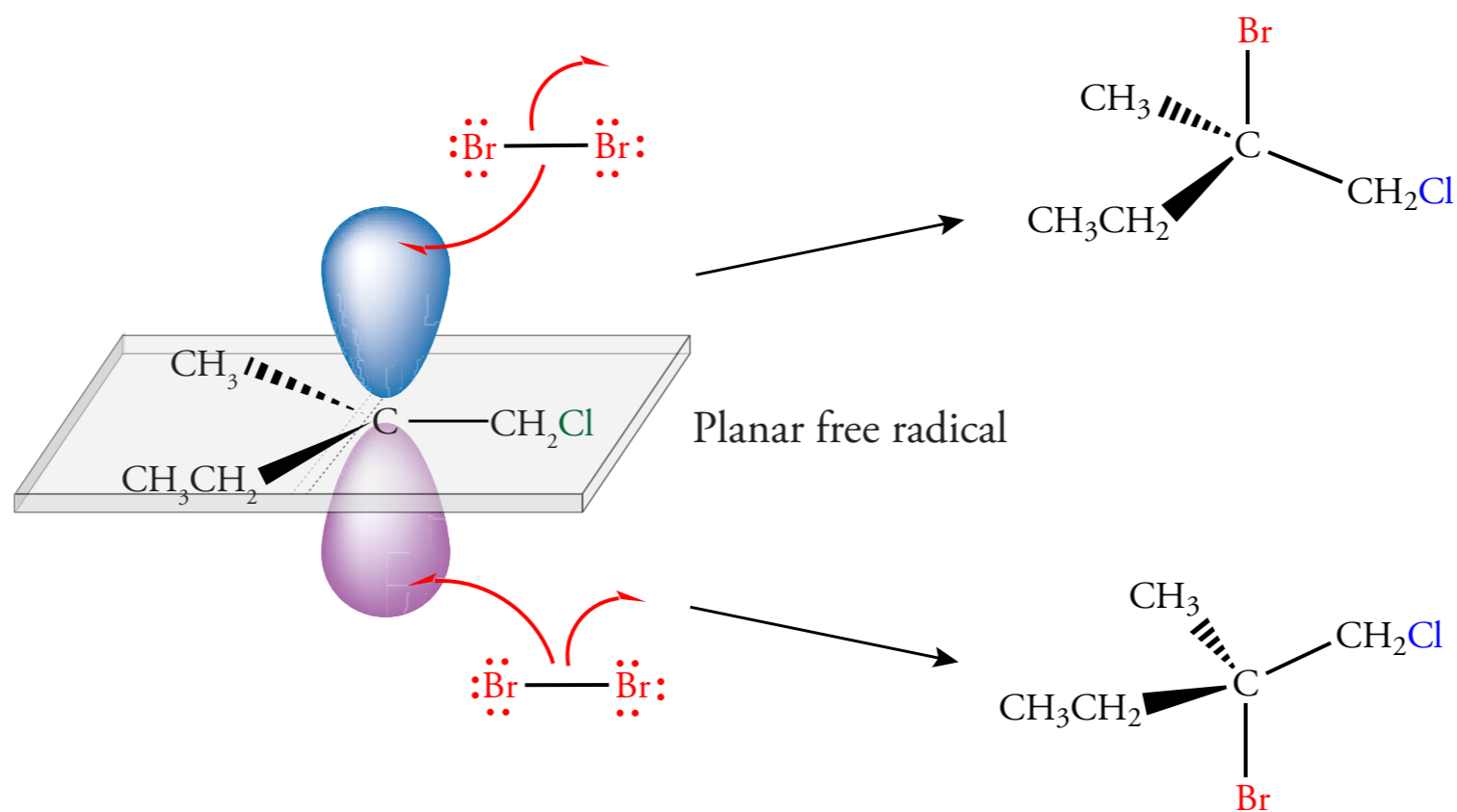


8.9 CHEMICAL REACTIONS AT STEREOGENIC CENTERS

Stereochemistry of a Free Radical Reaction

Figure 8.19 Free Radical Reaction at a Stereogenic Center

A free radical intermediate is achiral because it has a plane of symmetry. A bromine molecule can therefore attack with equal probability from above or below the plane to give a 50:50 mixture of enantiomers. The 2p orbital is half-occupied, and there is a 50% probability of finding an electron above or below the nodal plane of the orbital.

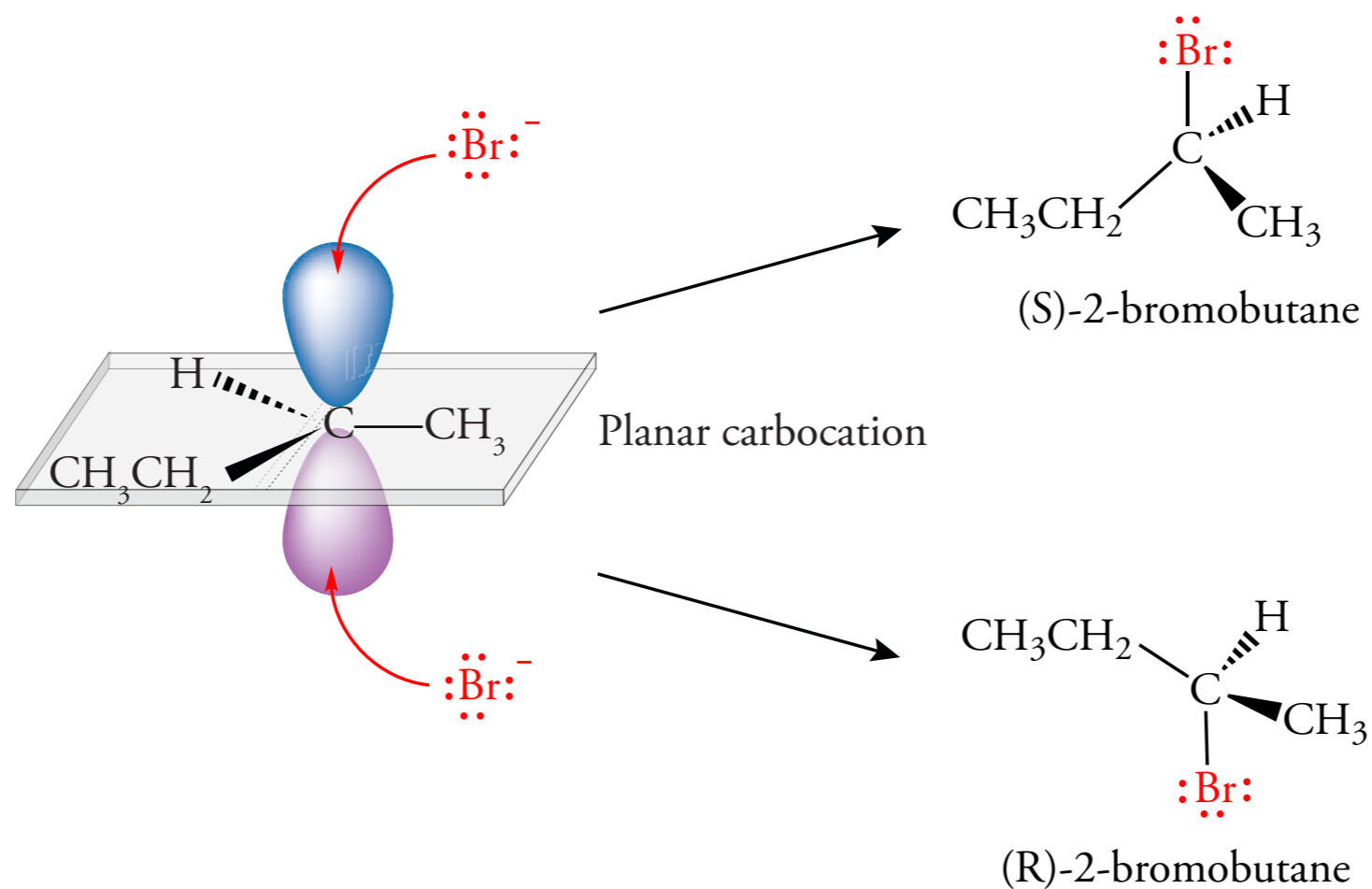


8.10 REACTIONS THAT PRODUCE STEREOGENIC CENTERS

Stereochemistry of Markovnikov Addition to Alkenes

Figure 8.20 Stereochemistry of Markovnikov Addition of HBr to 1-Butene

A proton adds to the double bond of 1-butene to give an intermediate secondary carbocation. It is achiral because it has a plane of symmetry. Bromide ion can attack with equal probability from the top or the bottom to give a racemic mixture.

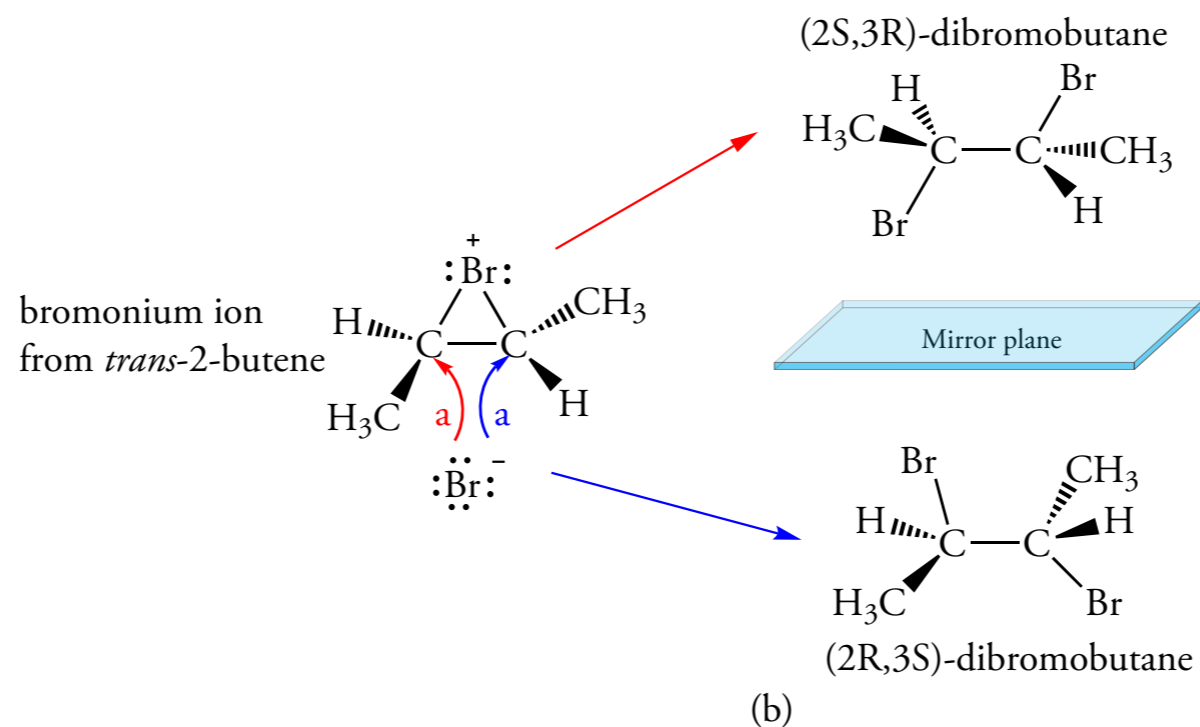
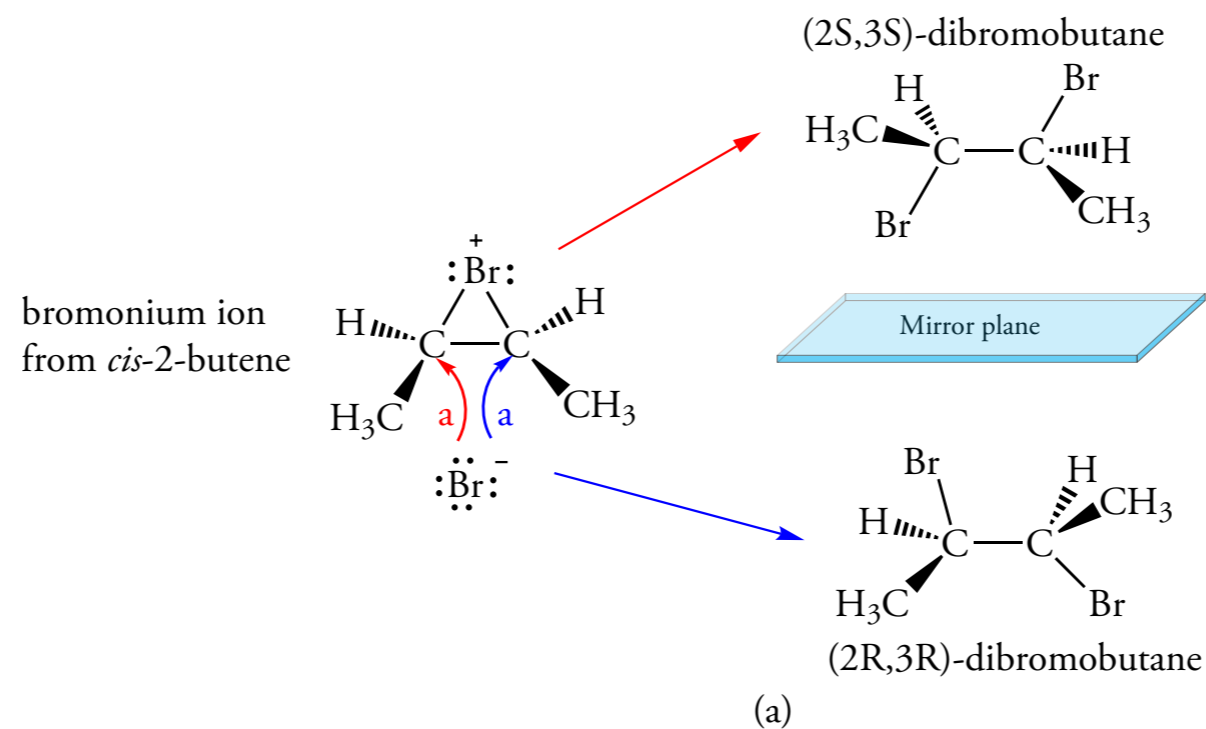


8.10 REACTIONS THAT PRODUCE STEREOGENIC CENTERS

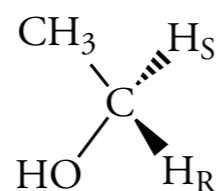
Stereochemistry of Alkene Bromination

Figure 8.21 Stereochemistry of Bromine Addition to Alkenes

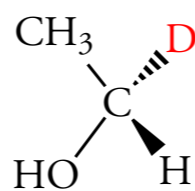
The reaction of bromine with an alkene produces a bromonium ion intermediate. This intermediate reacts with bromide ion in a process that results in net anti addition of bromine. The stereochemical consequences for adding bromine to *cis*-2-butene and *trans*-2-butene are different. *cis*-2-Butene yields a pair of enantiomers; *trans*-2-butene yields a *meso* compound.



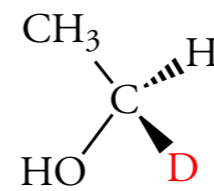
8.12 PROCHIRAL CENTERS



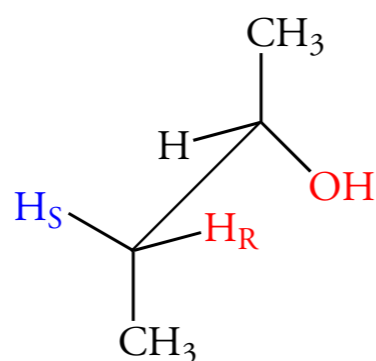
ethanol



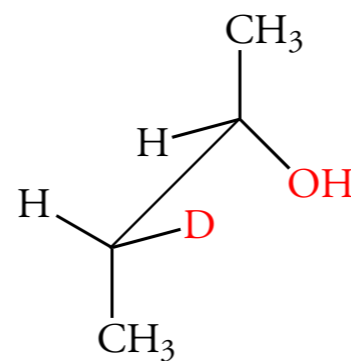
(S)-1-deuteroethanol



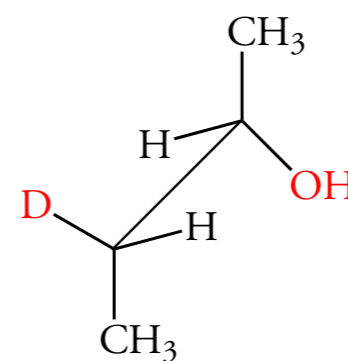
(R)-1-deuteroethanol



(R)-2-butanol



(2R,3R)



(2R,3S)

