CHEM 109A
Organic Chemistry

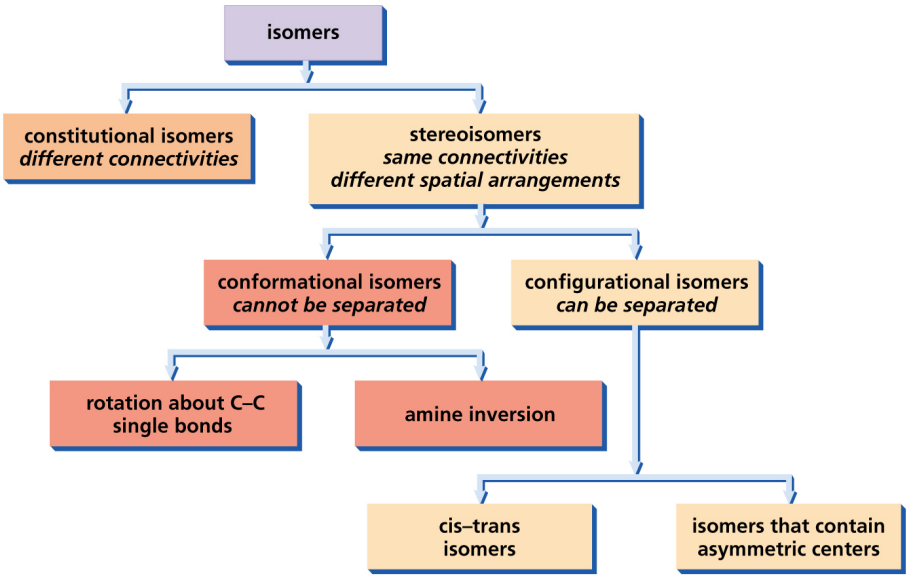
https://labs.chem.ucsb.edu/zakarian/armen/courses.html

Chapter 4
Isomers

The arrangement of atoms in space

Isomers

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



Constitutional Isomers

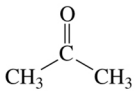
Constitutional isomers differ in the way the atoms are connected.

constitutional isomers

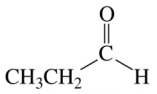
CH_3CH_2OH and CH_3OCH_3
ethanol dimethyl ether

$CH_3CH_2CH_2CH_2Cl$ and $CH_3CH_2CH(Cl)CH_3$
1-chlorobutane 2-chlorobutane

$CH_3CH_2CH_2CH_2CH_3$ and $CH_3CH(CH_3)CH_2CH_3$
pentane isopentane



and

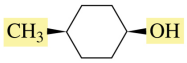


acetone propionaldehyde

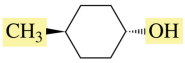
Cis–Trans Isomers

cis–trans isomers result from restricted rotation

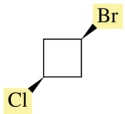
1. Cyclic structures restrict rotation.



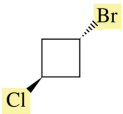
cis-4-methylcyclohexanol



trans-4-methylcyclohexanol



cis-1-bromo-3-chlorocyclobutane



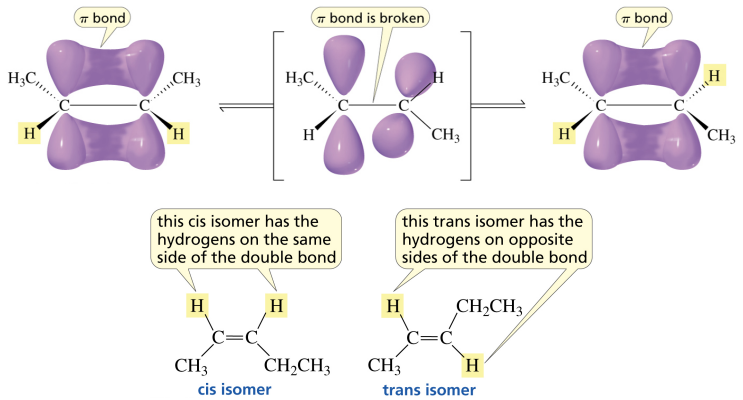
trans-1-bromo-3-chlorocyclobutane

Cis: The substituents are on the same side of the ring.

Trans: The substituents are on opposite sides of the ring.

Cis–Trans Isomers

2. Double bonds restrict rotation.

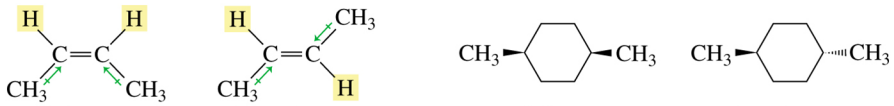


Cis: The hydrogens are on the same side of the double bond.

Trans: The hydrogens are on opposite sides of the double bond.

Cis–Trans Isomers

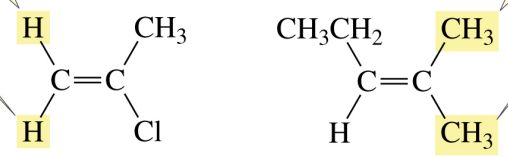
Cis–trans isomers have different physical properties.



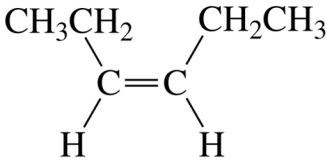
cis isomer	trans isomer	cis isomer	trans isomer
bp = 3.7 °C	bp = 0.9 °C	bp = 99.3 °C	bp = 91.8 °C
μ = 0.33 D	μ = 0 D		

Some Alkenes Do Not Have Cis–Trans Isomers

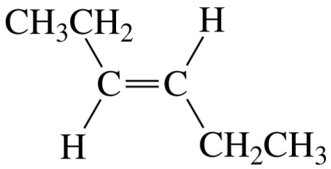
cis and trans isomers are not possible for these compounds because two substituents on an sp^2 carbon are the same



Cis-Trans Isomers



cis isomer

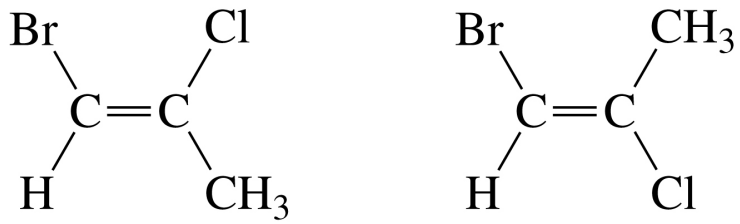


trans isomer

Cis hydrogens are on the same side of the double bond

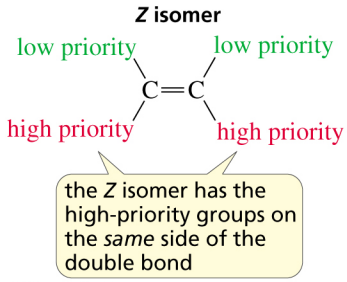
Trans hydrogens are on the opposite sides of the double bond

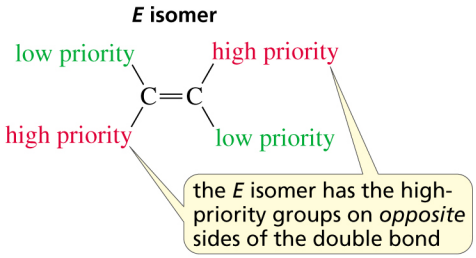
Which is Cis and Which is Trans?



Which isomer is cis and which is trans?

The *E*,*Z* System of Nomenclature

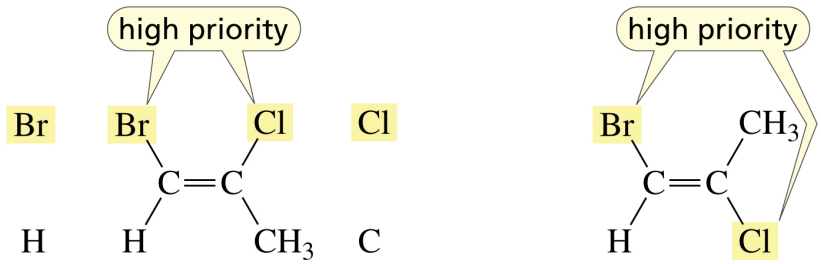




Z = Zusammen (together)

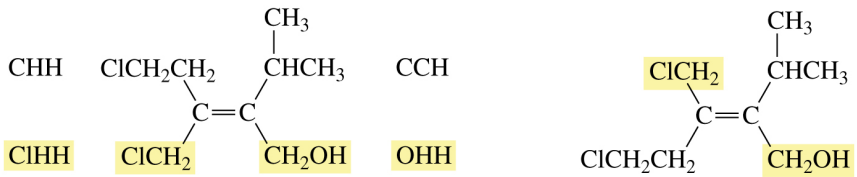
E = Entgegen (opposite)

E and *Z* Isomers



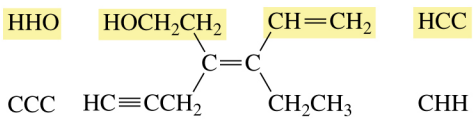
Z isomer *E* isomer

E and *Z* Isomers

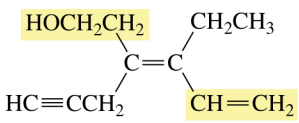


Z isomer *E* isomer

E and *Z* Isomers

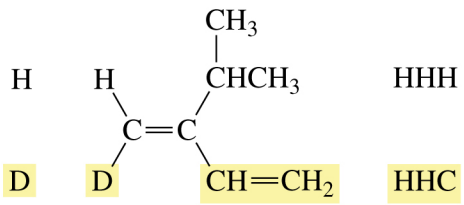


Z isomer

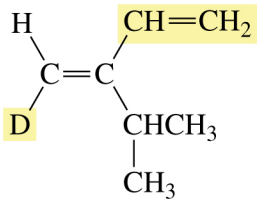


E isomer

E and *Z* Isomers



Z isomer

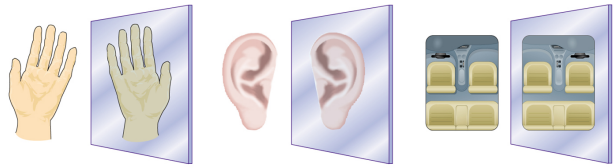


E isomer

Chiral and Achiral Objects

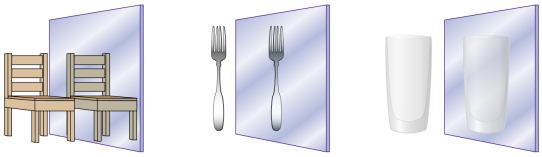
A chiral object has a nonsuperimposable mirror image.

chiral objects



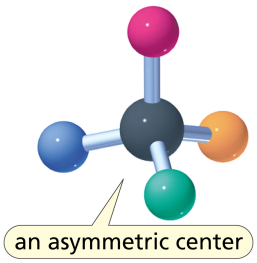
An achiral object has a superimposable mirror image.

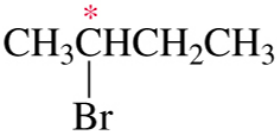
achiral objects



Chiral Molecules

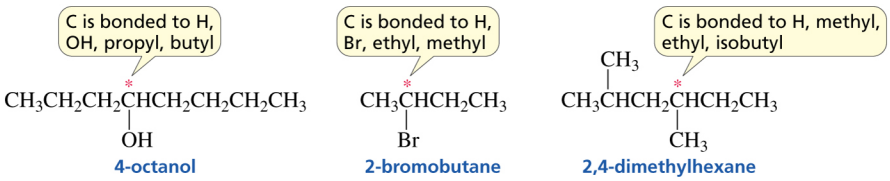
A chiral molecule has an asymmetric center.
An asymmetric center is an atom
that is attached to four different groups.



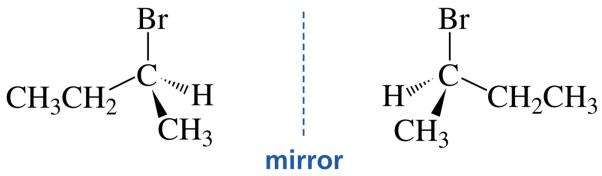


2-bromobutane

Compounds with an Asymmetric Center



Enantiomers



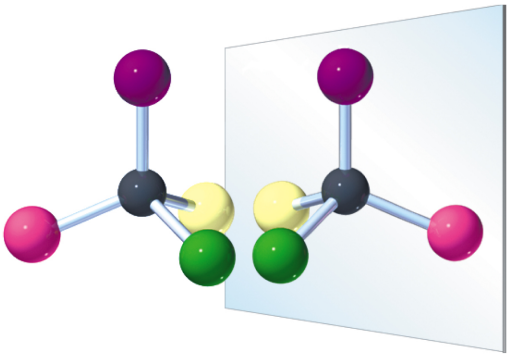
two stereoisomers of 2-bromobutane

The two stereoisomers are called enantiomers.

Enantiomers are different compounds: they can be separated.

Enantiomers have the same physical and chemical properties.

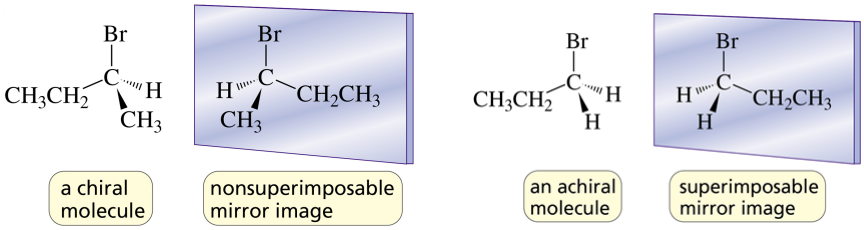
Enantiomers



nonsuperimposable mirror images

Enantiomers are nonsuperimposable mirror images.

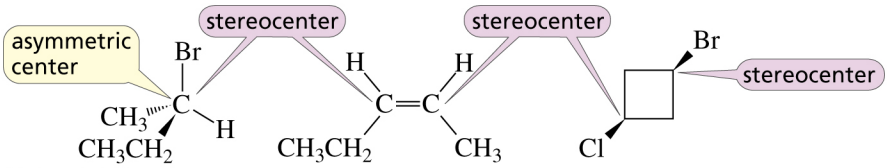
Chiral and Achiral Molecules



A chiral compound has a nonsuperimposable mirror image.

An achiral compound has a superimposable mirror image.
(it and its mirror image are identical molecules).

Asymmetric Center *versus* Stereocenter

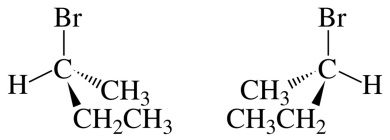


Asymmetric center: an atom attached to four different groups.

Stereocenter: an atom at which the interchange of two groups produces a stereoisomer.

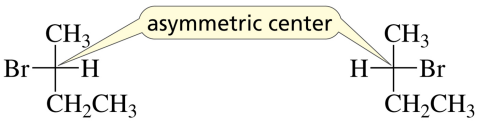
How to Draw Enantiomers

Perspective formulas



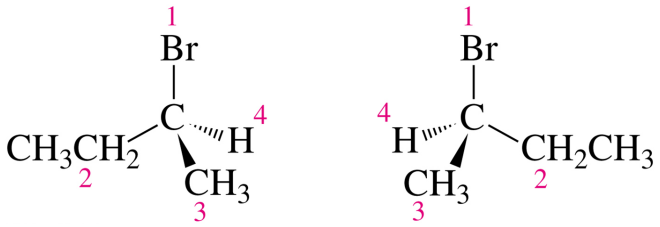
perspective formulas of the enantiomers of 2-bromobutane

Fischer projections



Fischer projections of the enantiomers of 2-bromobutane

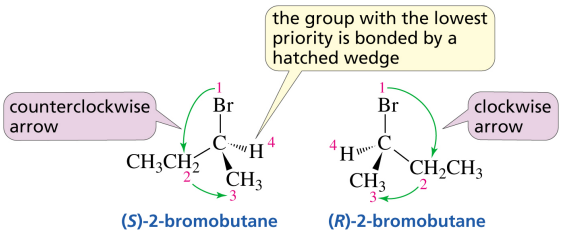
Naming Enantiomers



Assign relative priorities to the four groups.

Naming Enantiomers

Draw an arrow from 1 to 2 to 3.



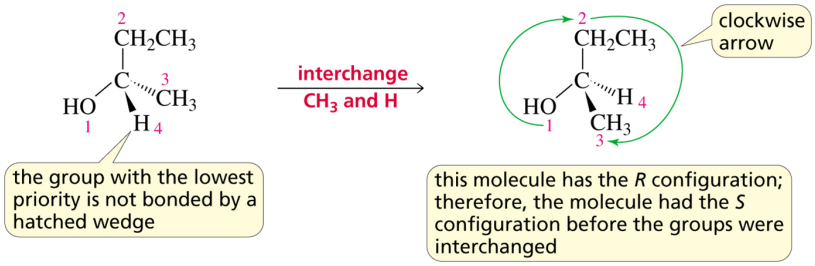
If the lowest priority group is on a hatched wedge, then

clockwise = *R*
and
counterclockwise = *S*

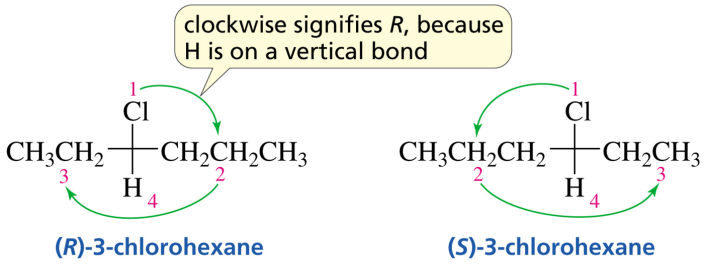
Naming Enantiomers

If the lowest priority group is not on a hatched wedge,
switch a pair so it is on a hatched wedge.

Then, name the new compound.



Naming Enantiomers

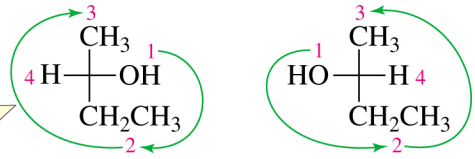


If the lowest priority group is on a vertical bond, then

clockwise = *R*
and
counterclockwise = *S*

Naming Enantiomers

clockwise signifies *S*,
because H is on a horizontal bond

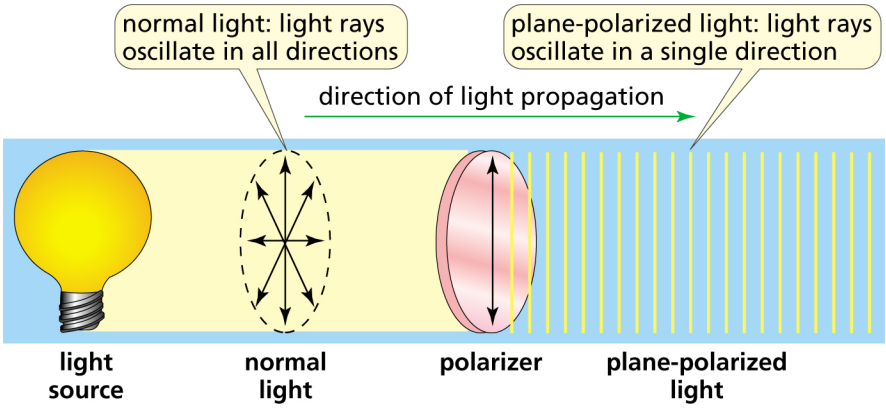


(*S*)-2-butanol (*R*)-2-butanol

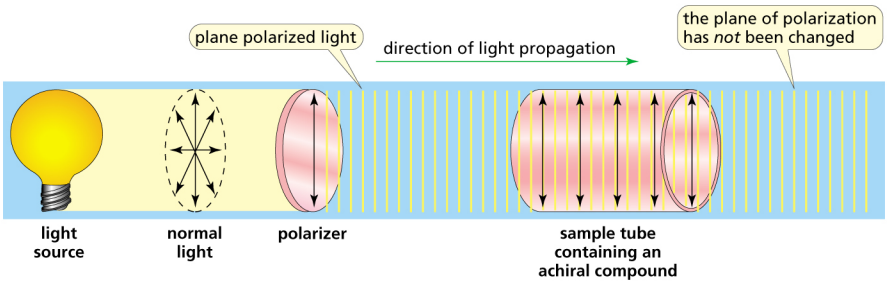
If the lowest priority group is on a horizontal bond, then

counterclockwise = *R*
and
clockwise = *S*

Plane-Polarized Light

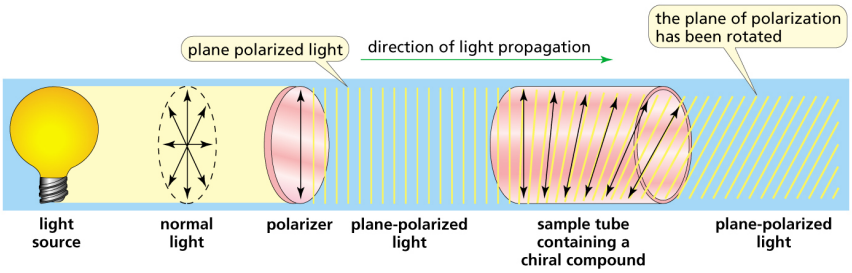


An Achiral Compound is Optically Inactive



An achiral compound does not rotate the plane of polarization of plane-polarized light.

A Chiral Compound is Optically Active



A chiral compound rotates the plane of polarization of plane-polarized light.

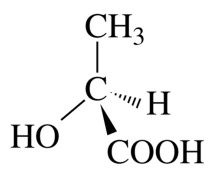
If it rotates the plane clockwise = (+)

If it rotates the place counterclockwise = (–)

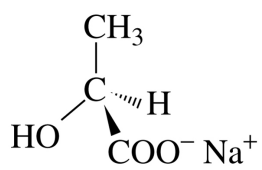
R and *S versus* (+) and (–)

Some *R* enantiomers are (+) and some are (–).

Some *S* enantiomers are (+) and some are (–).

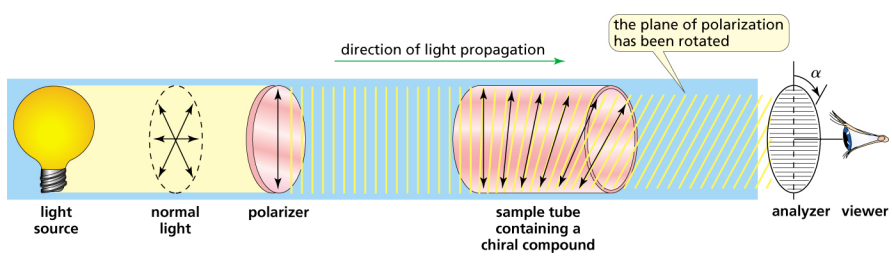


(*S*)-(+)-lactic acid



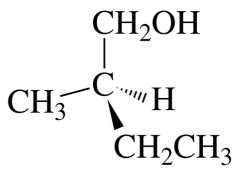
(*S*)-(–)-sodium lactate

A Polarimeter



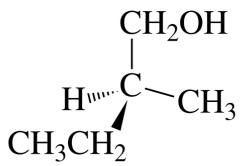
$$[\alpha]_{\lambda}^{T} = \frac{\alpha}{l \times c}$$

If One Enantiomer is (+), the Other is (–)



(*R*)-2-methyl-1-butanol

$[\alpha]_D^{20\,°C} = +5.75$



(*S*)-2-methyl-1-butanol

$[\alpha]_D^{20\,°C} = -5.75$

Enantiomeric Excess

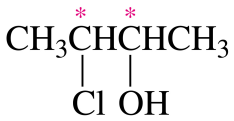
Enantiomeric excess tells us how much of an excess of one enantiomer is in a mixture.

$$\text{enantiomeric excess} = \frac{\text{observed specific rotation}}{\text{specific rotation of the pure enantiomer}} \times 100\%$$

For example, if the sample of 2-bromobutane has an observed specific rotation of +9.2, then the enantiomeric excess is 40%. In other words, the excess of one of the enantiomers comprises 40% of the mixture.

$$\text{enantiomeric excess} = \frac{+9.2}{+23.1} \times 100\% = 40\%$$

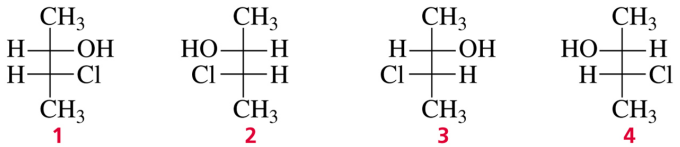
Compounds with Two Asymmetric Centers



3-chloro-2-butanol

maximum # of stereoisomers = 2^n

(n = # of asymmetric centers)



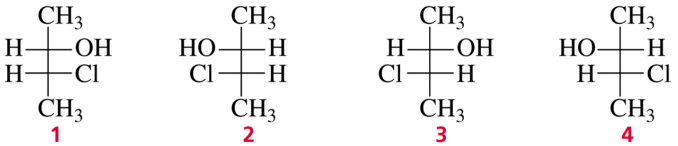
1 2 3 4

erythro enantiomers threo enantiomers

Fischer projections of the stereoisomers of 3-chloro-2-butanol (eclipsed)

1 and 2 are enantiomers. 3 and 4 are enantiomers.

Diastereomers



1 2 3 4

erythro enantiomers threo enantiomers

Fischer projections of the stereoisomers of 3-chloro-2-butanol (eclipsed)

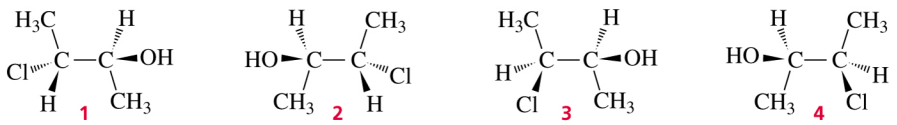
1 and 2 are enantiomers. 3 and 4 are enantiomers.

Diastereomers are stereoisomers that are not enantiomers.

1 and 3 are diastereomers. 2 and 3 are diastereomers.
1 and 4 are diastereomers. 2 and 4 are diastereomers.

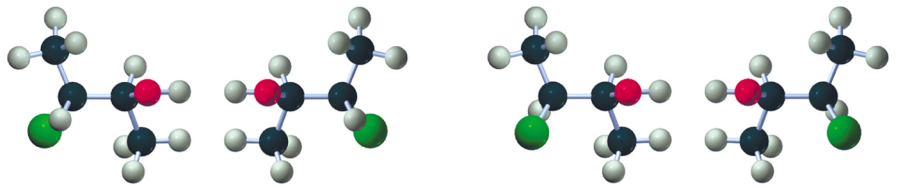
Diastereomers have different physical and chemical properties.

Perspective Formulas of the Four Stereoisomers



erythro enantiomers threo enantiomers

perspective formulas of the stereoisomers of 3-chloro-2-butanol (staggered)



stereoisomers of 3-chloro-2-butanol

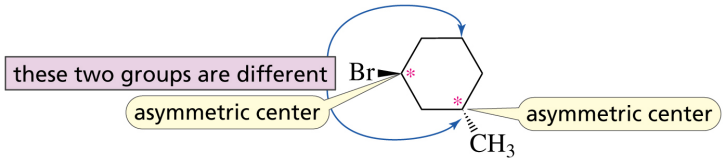
Two Asymmetric Centers, Four Stereoisomers

cis-1-bromo-2-methylcyclopentane enantiomers

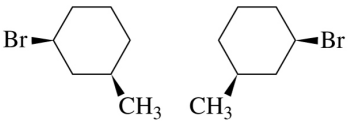
trans-1-bromo-2-methylcyclopentane enantiomers

The cis stereoisomers are a pair of enantiomers.
The trans stereoisomers are a pair of enantiomers.

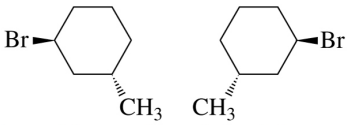
Identifying an Asymmetric Center



An asymmetric center is attached to four different groups.



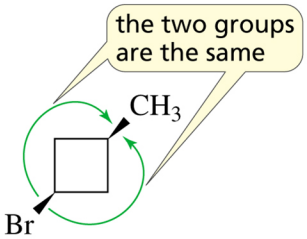
cis-1-bromo-3-methylcyclohexane
enantiomers



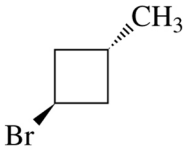
trans-1-bromo-3-methylcyclohexane
enantiomers

two asymmetric centers, four stereoisomers

No Asymmetric Centers



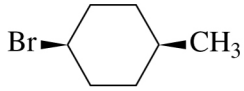
cis-1-bromo-3-methylcyclobutane



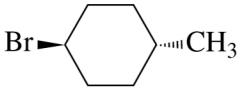
trans-1-bromo-3-methylcyclobutane

There are only two stereoisomers: cis and trans.

No Asymmetric Centers



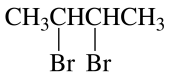
cis-1-bromo-4-methylcyclohexane



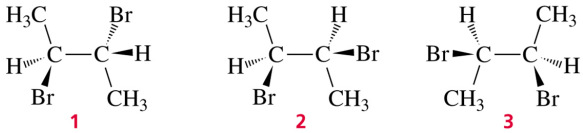
trans-1-bromo-4-methylcyclohexane

There are only two stereoisomers: cis and trans.

Two Asymmetric Centers: Three Stereoisomers (a Meso Compound and a Pair of Enantiomers)

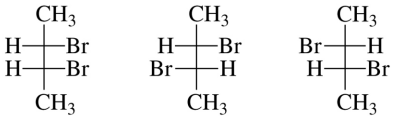


2,3-dibromobutane



1 2 3

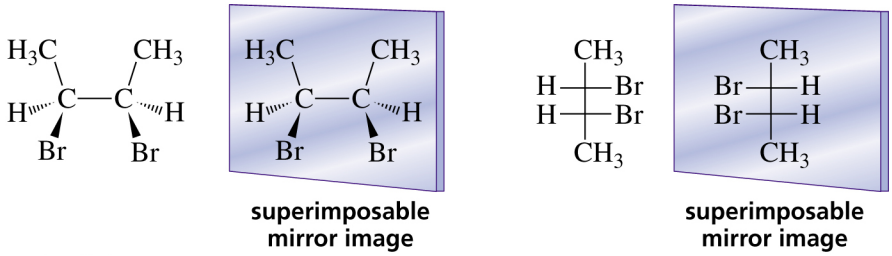
perspective formulas of the stereoisomers of 2,3-dibromobutane (staggered)



1 2 3

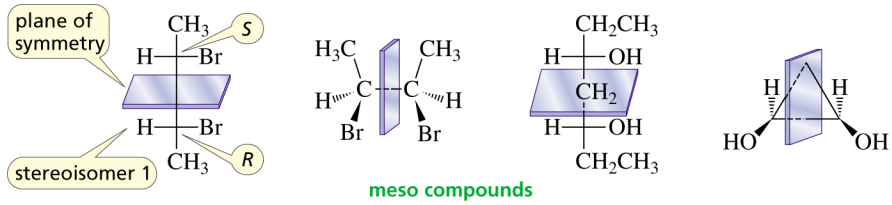
Fischer projections of the stereoisomers of 2,3-dibromobutane (eclipsed)

A Meso Compound Has a Superimposable Mirror Image

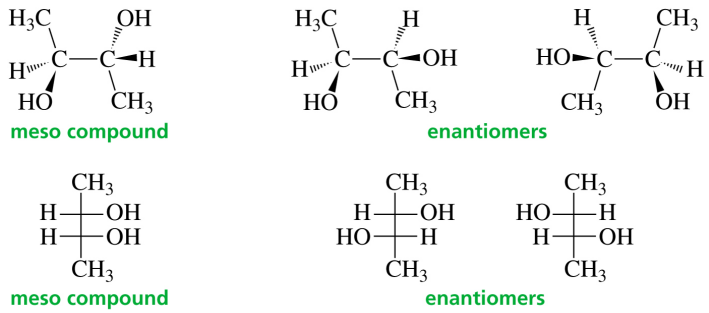


Meso compounds are optically inactive
even though they have asymmetric centers.

A Meso Compound Has a Plane of Symmetry



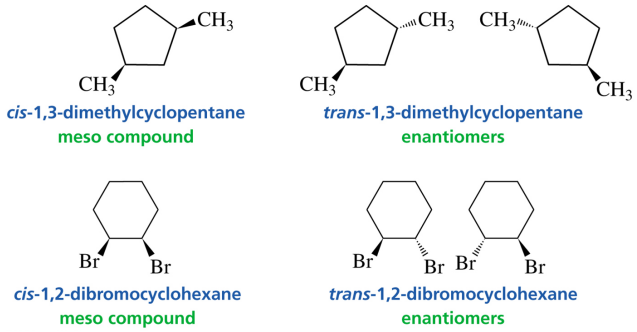
A Meso Compound



A compound with two asymmetric centers that has the same four groups bonded to each asymmetric center will have three stereoisomers:

a meso compound and a pair of enantiomers.

A Meso Compound



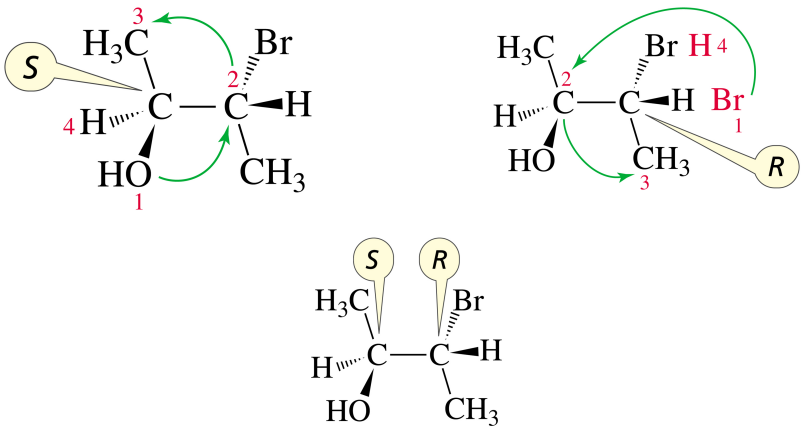
For cyclic compounds with the same substituents bonded to two asymmetric centers,

cis = a meso compound

and

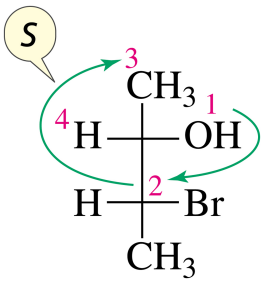
trans = a pair of enantiomers.

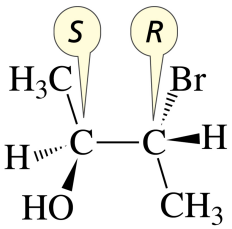
Naming Stereoisomers



(2*S*,3*R*)-3-bromo-2-butanol

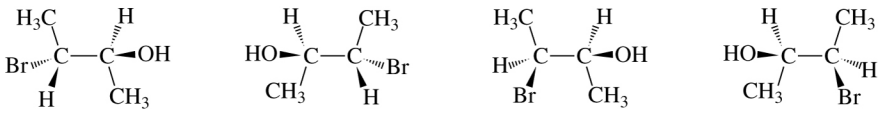
Naming Stereoisomers





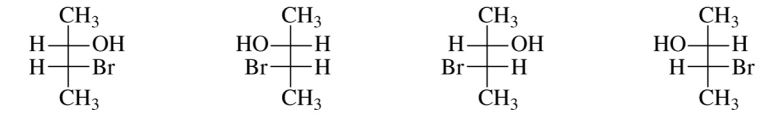
(2*S*,3*R*)-3-bromo-2-butanol

Naming Stereoisomers



(2*S*,3*R*)-3-bromo-2-butanol | (2*R*,3*S*)-3-bromo-2-butanol | (2*S*,3*S*)-3-bromo-2-butanol | (2*R*,3*R*)-3-bromo-2-butanol

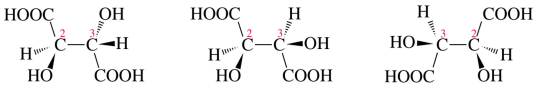
perspective formulas of the stereoisomers of 3-bromo-2-butanol



(2*S*,3*R*)-3-bromo-2-butanol | (2*R*,3*S*)-3-bromo-2-butanol | (2*S*,3*S*)-3-bromo-2-butanol | (2*R*,3*R*)-3-bromo-2-butanol

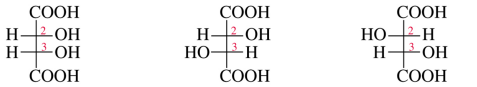
Fischer projections of the stereoisomers of 3-bromo-2-butanol

Physical Properties of Stereoisomers



(2*R*,3*S*)-tartaric acid (meso compound) | (2*R*,3*R*)-tartaric acid | (2*S*,3*S*)-tartaric acid (enantiomers)

perspective formulas of the stereoisomers of tartaric acid



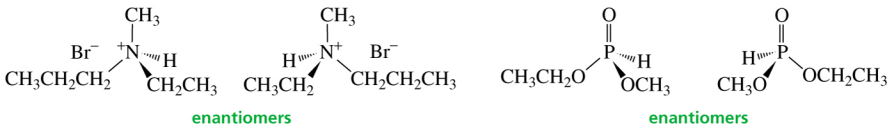
(2*R*,3*S*)-tartaric acid (meso compound) | (2*R*,3*R*)-tartaric acid | (2*S*,3*S*)-tartaric acid (enantiomers)

Fischer projections of the stereoisomers of tartaric acid

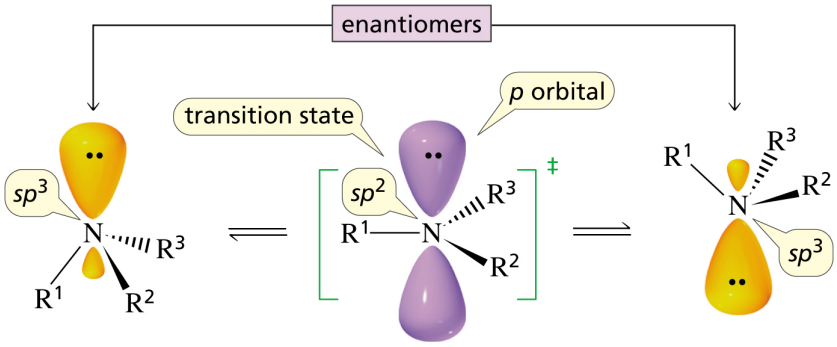
Table 4.2 Physical Properties of the Stereoisomers of Tartaric Acid

	Melting point, °C	Specific rotation	Solubility, g/100 g H_2O at 15 °C
(2*R*,3*R*)-(+)-Tartaric acid	171	+11.98	139
(2*S*,3*S*)-(−)-Tartaric acid	171	−11.98	139
(2*R*,3*S*)-Tartaric acid (meso)	146	0	125
(±)-Tartaric acid	206	0	139

Nitrogen and Phosphorus Can Be Asymmetric Centers



Amine Inversion

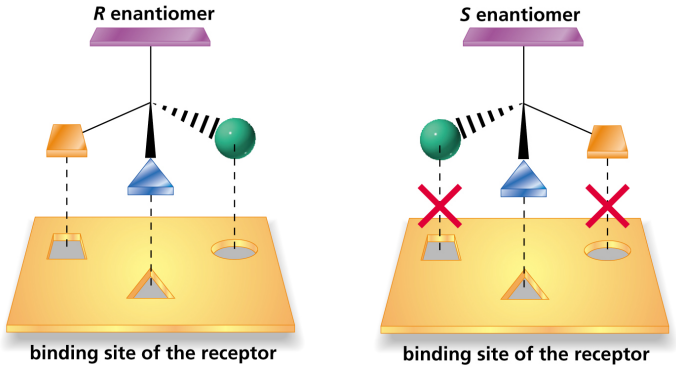


If one of the four groups attached to N is a lone pair,
the enantiomers cannot be separated,
because they interconvert as a result of amine inversion.

A Receptor is a Protein
Proteins are Chiral Molecules

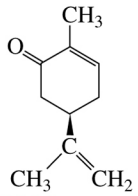
Because a receptor is chiral, it binds one enantiomer.

A right-handed glove fits only a right hand.



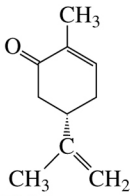
A Receptor Binds One Enantiomer

(*R*)-(–)-carvone
smells like
spearmint



(*R*)-(–)-carvone

$[\alpha]_D^{20\,°C} = -62.5$



(*S*)-(+)-carvone

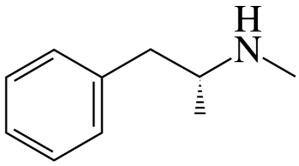
$[\alpha]_D^{20\,°C} = +62.5$

(*S*)-(+)-carvone
smells like
caraway seeds

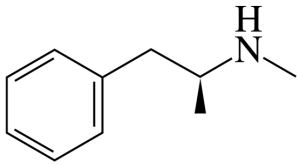
Each enantiomer binds to a different receptor in the nose.

Physiological Properties of Enantiomers

Enantiomers can have very different physiological properties.

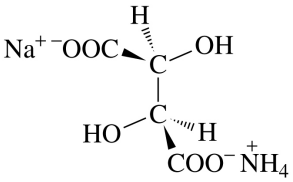


the active ingredient in Vicks Vapor Inhaler®

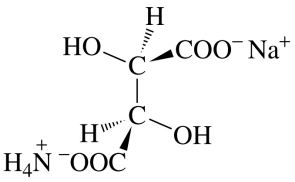


methamphetamine "meth"

Separating Enantiomers



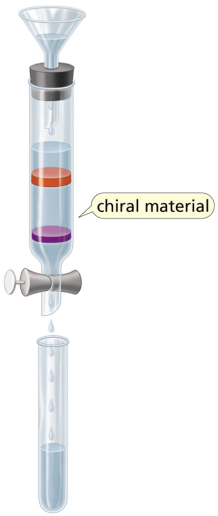
left-handed crystals



right-handed crystals

sodium ammonium tartrate

separating by hand



separating by chromatography