Properties of Enantiomers

Achiral Properties

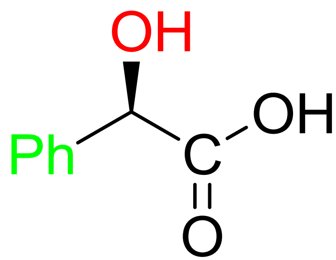
Any pair of enantiomers are physically and chemically indistinguishable by most techniques in achiral environments.

Enantiomers have identical achiral properties such as:

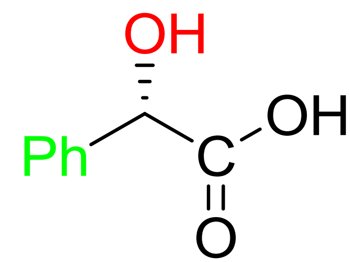
- melting point,
- boiling point,
- density,
- solubility in water,
- spectroscopic properties (NMR, IR, UV)
- same rate of reaction with achiral reagents

Properties of Enantiomers

Achiral Properties of Mandelic Acid



(R)



(S)

133^{o}C	Melting Point	133^{o}C
15 g per 100 mL	Solubility in water	15 g per 100 mL
1.3 g/cm^3	Density	1.3 g/cm^3

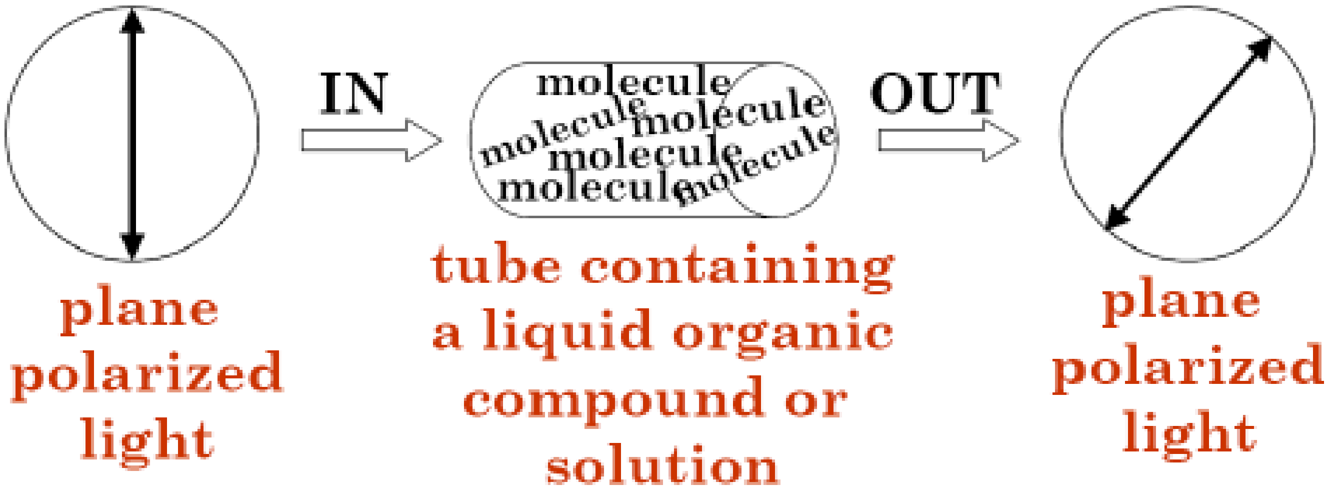
Mandelic acid is isolated from sweet and bitter almonds

Enantiomers

Chiral Properties: Optical Activity

Chiral molecules rotate plane-polarised monochromatic light either clockwise or counterclockwise. This phenomenon is called optical activity.

This property is inherent in the interaction between light and the individual molecules through which it passes.

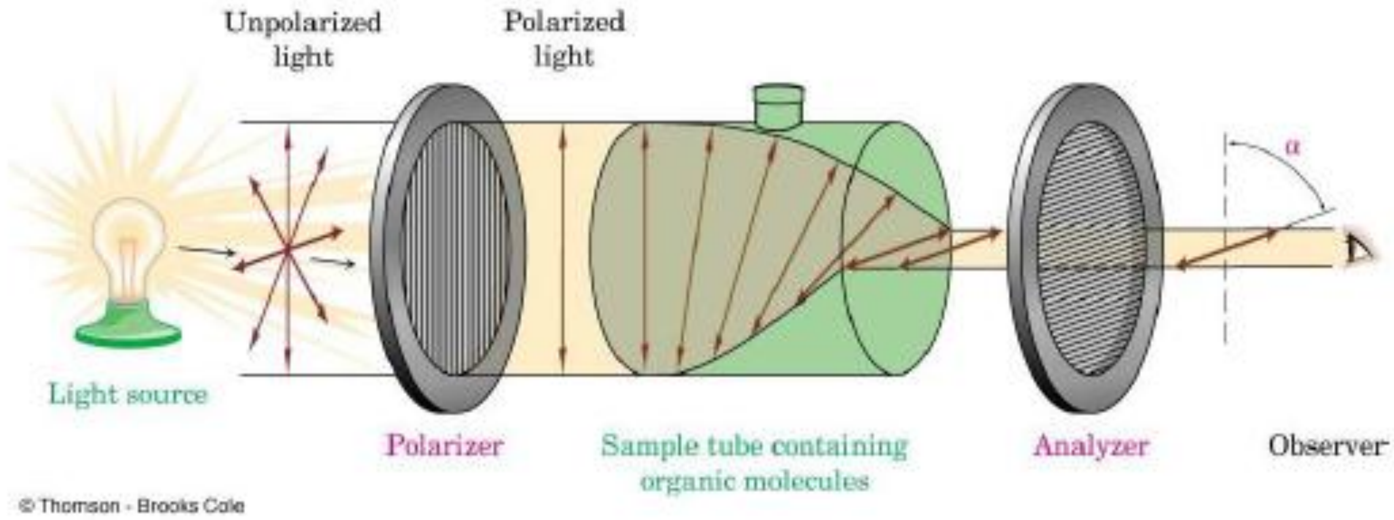


Chiral molecules are thus optically active.

Enantiomers

Measurement of Optical Rotation

The degree of rotation of plane-polarized light is measured using a *polarimeter.*



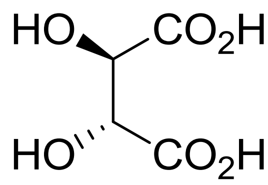
The source light passes through a *polarizer* and then is detected at an analyzer.

The angle between the entrance and exit planes is the optical rotation, α.

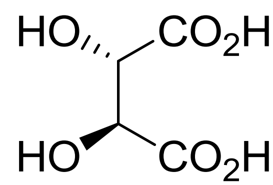
Enantiomers

Stereochemical Terminology vs Optical Activity

Enantiomerically pure or enantiopure: Comprises of exclusively one enantiomer.



or



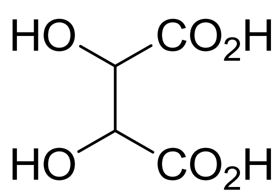
Dextrorotatory

$+12.7^{o}$

Levorotatory

-12.7^{o}

Racemic mixture: Comprises of an equal mixture of enantiomers.



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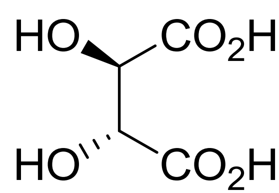

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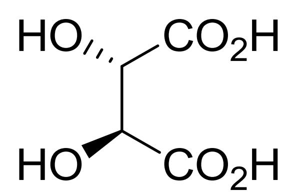


Racemic Tartaric Acid

Specific rotation = 0^{o}

Dextrorotatory

(50%)

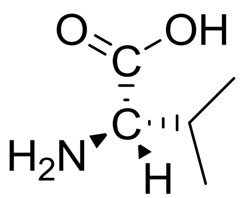
Levorotatory

(50%)

Enantiomers

Stereochemical Terminology vs Optical Activity

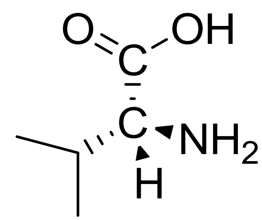
Dextrorotatory (+): an optically active compound that rotates plane polarized light in a clockwise direction. Usually represented with d (lower case).



S-(+)-Valine

$[\alpha] = +27.5^{o}$ (6M HCl)

L-(+)-Valine



R-(-)-Valine

$[\alpha] = -27.5^{o}$ (6M HCl)

D-(-)-Valine

Levorotatory (-): an optically active compound that rotates plane polarized light in a counterclockwise direction. Usually represented with l (lower case).

Enantiomers

Stereochemical Terminology vs Optical Activity

D/L vs d/l Notations

The D/L notation is unrelated to (+)/(−) or d/l; it does not indicate which enantiomer is dextrorotatory and which is levorotatory.

$[\alpha] = +27.5^{o}$ (6M HCl)

L-(+)-Valine

L-(d)-Valine

$[\alpha] = -27.5^{o}$ (6M HCl)

D-(-)-Valine

D-(l)-Valine

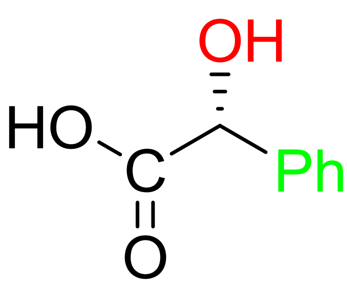
The D/L notations simply indicates that a compound's stereochemistry is related to the dextrorotatory or levorotatory enantiomer of glyceraldehyde. The dextrorotatory isomer of glyceraldehyde is, in fact, the D- isomer.

Enantiomers

Chiral Properties: Optical Activity

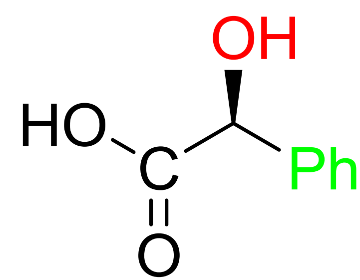
Enantiomers differ only in the properties that are chiral:

- direction of rotation of plane polarized light,
- their rate of reaction with chiral reagents,
- biological activity and taste.



(R)

Mandelic Acid



(S)

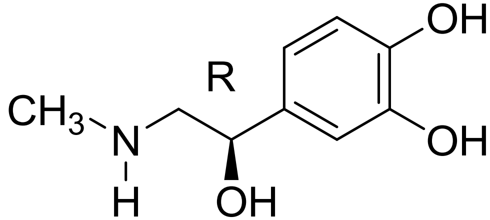
-154° Specific Rotation +154°

Isolated from Sweet and Bitter almonds

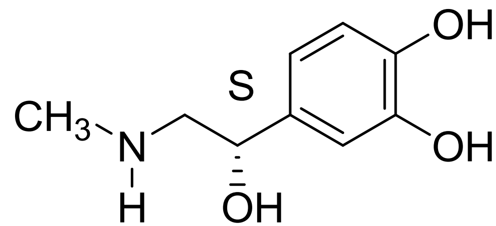
Enantiomers

Chiral Properties: Optical Activity and Aroma

Enantiomers of Adrenaline (Epinephrine)

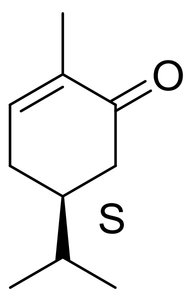


$[\alpha] = +53.3^{o}$



$[\alpha] = -53.3^{o}$

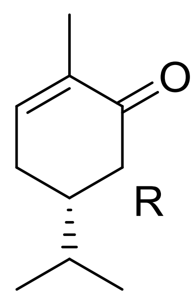
Enantiomers of Carvone



(+)-Carvone

Caraway aroma

$[\alpha] = +62.5^{o}$



(-)-Carvone

Spearmint aroma

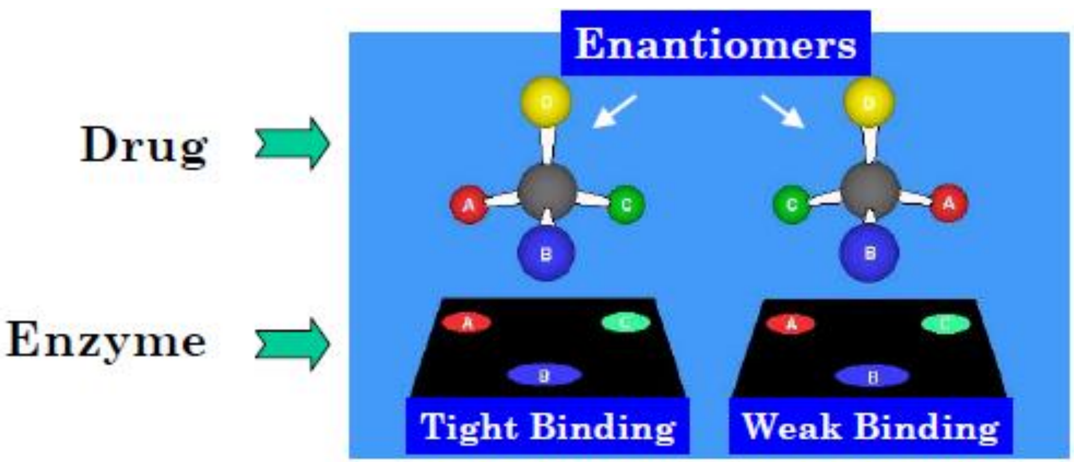
$[\alpha] = -62.5^{o}$

Enantiomers

Chiral Properties: Biological Activity

Stereochemistry is important in biological systems because most body reactions are **stereospecific**. Receptors on cells accept only molecules with specific spatial arrangements. Other configurations of the same chemical may not elicit a favorable response or be toxic.

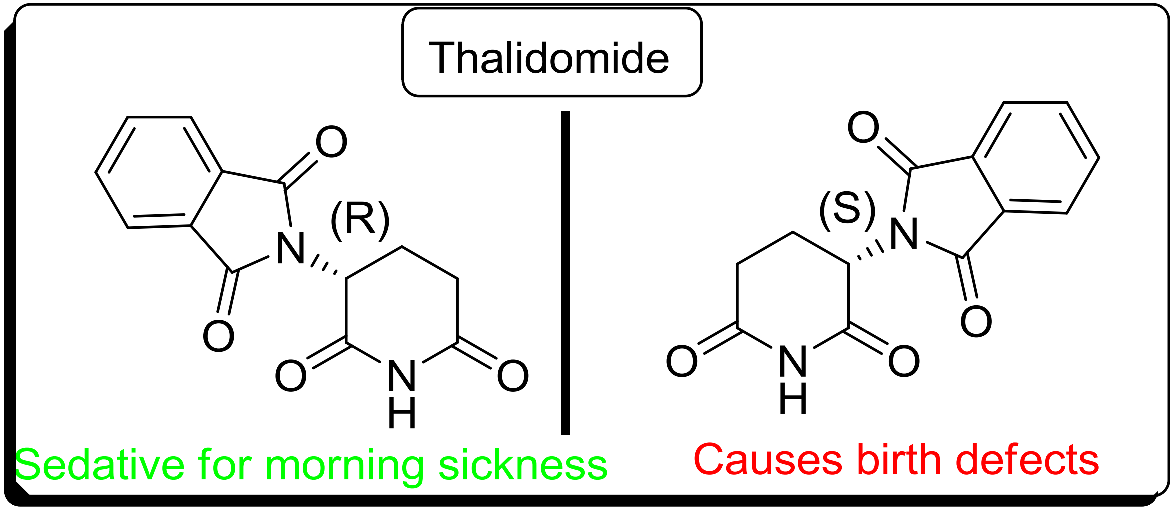
Enantiomers of a chiral drug interact with the biological environment as depicted below.



Enantiomers

Biological Activity: The Tragic Case of Thalidomide

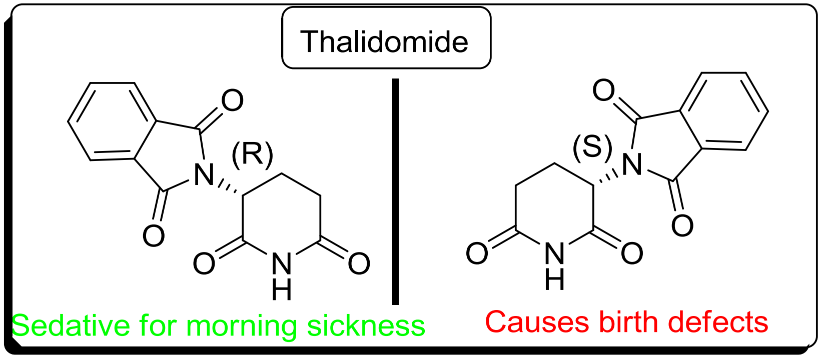
Thalidomide was once hailed as a "wonder drug" that provided a "safe, sound sleep". It was considered an effective sedative for pregnant women to combat many of the symptoms associated with morning sickness.



However, thalidomide later became notorious as the killer and disabler of thousands of babies.

Enantiomers

Biological Activity: The Tragic Case of Thalidomide



*T*he R enantiomer fits the active site of a specific enzyme (like a "key" for a specific "lock") producing the desired effect (sedative).

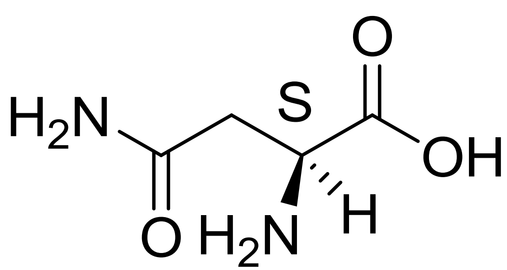
The S enantiomer cannot interact with the same site due to the different arrangement of atoms (3D shape). Instead, it fits a different enzyme active pocket triggering a different biological effect (toxic).

Enantiomers

Chiral Properties: Taste

Although there are individual variations between enantiomers, there are now well-recognized taste differences between enantiomers of many compounds.

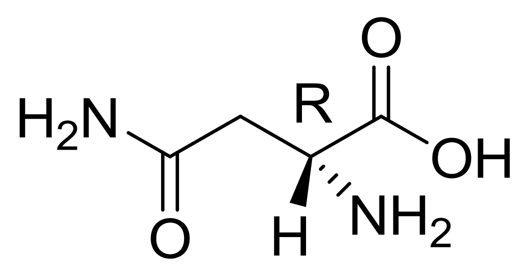
For example, D-asparagine has a sweet taste, while the natural L-asparagine is tasteless.



Natural

Tasteless

Asparagine



Unnatural

Sweet