Isomers

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

- Isomers
  - Constitutional isomers
    - different connectivities
  - Stereoisomers
    - same connectivities
    - different spatial arrangements

- Conformational isomers
  - cannot be separated
- Configurational isomers
  - can be separated

- Rotation about C-C single bonds
- Amine inversion

Cis-trans isomers
- Isomers that contain asymmetric centers

Chapter 4
Isomers
The arrangement of atoms in space
Constitutional Isomers

Constitutional isomers differ in the way the atoms are connected.

<table>
<thead>
<tr>
<th>constitutional isomers</th>
</tr>
</thead>
<tbody>
<tr>
<td>CH₃CH₂OH and CH₃OCH₃</td>
</tr>
<tr>
<td>ethanol and dimethyl ether</td>
</tr>
<tr>
<td>CH₃CH₂CH₂CH₂CH₃ and CH₃CHCH₂CH₃</td>
</tr>
</tbody>
</table>

Cis–Trans Isomers

cis–trans isomers result from restricted rotation

1. Cyclic structures restrict rotation.

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.
Some Alkenes Do Not Have Cis–Trans Isomers

cis and trans isomers are not possible for these compounds because two substituents on an sp² carbon are the same

Cis-Trans Isomers

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)   \hspace{1cm}   E =$ Entgegen (opposite)

- **Z isomer**: low priority, high priority, high priority.
  - the $Z$ isomer has the high-priority groups on the same side of the double bond.

- **E isomer**: low priority, high priority, low priority.
  - the $E$ isomer has the high-priority groups on opposite sides of the double bond.
E and Z Isomers

Z isomer

E isomer

E and Z Isomers

Z isomer

E isomer
E and Z Isomers

\[ \text{HHO} \quad \text{HOCH}_2\text{CH}_2 \quad \text{CH}≡\text{CH} \quad \text{HCC} \quad \text{HOCH}_2\text{CH}_2 \quad \text{CH}_2\text{CH}_3 \]

\[ \text{CCC} \quad \text{HC}≡\text{CCH}_2 \quad \text{CH}_3\text{CH}_3 \quad \text{CHH} \quad \text{HC}≡\text{CCH}_2 \quad \text{CH}≡\text{CH}_2 \]

\text{Z isomer} \quad \text{E isomer}

E and Z Isomers

\[ \text{H} \quad \text{H} \quad \text{CH}_3 \quad \text{HHH} \quad \text{H} \quad \text{CH}≡\text{CH}_2 \]

\[ \text{D} \quad \text{D} \quad \text{CH}≡\text{CH}_2 \quad \text{HHC} \quad \text{D} \quad \text{CHCH}_3 \]

\text{Z isomer} \quad \text{E isomer}
Chiral and Achiral Objects

A chiral object has a nonsuperimposable mirror image.

An achiral object has a superimposable mirror image.

Chiral Molecules

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

\[
\text{CH}_3\text{CHCH}_2\text{CH}_3
\]

\[
\text{Br}
\]

\[
\text{2-bromobutane}
\]
Compounds with an Asymmetric Center

Enantiomers

The two stereoisomers are called enantiomers. Enantiomers are different compounds: they can be separated. Enantiomers have the same physical and chemical properties.
Enantiomers

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.

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How to Draw Enantiomers

**Perspective formulas**

**Fischer projections**

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* perspective formulas of the enantiomers of 2-bromobutane

* Fischer projections of the enantiomers of 2-bromobutane
Naming Enantiomers

Assign relative priorities to the four groups.

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

clockwise = R
and
clockwise = 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

\[
\text{clockwise} = R \\
\text{and} \\
\text{counterclockwise} = S
\]
Naming Enantiomers

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

- counterclockwise = $R$
- clockwise = $S$

Plane-Polarized Light

- Normal light: light rays oscillate in all directions
- Plane-polarized light: light rays oscillate in a single direction

Light source, normal light, polarizer, 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 (−).

![Chemical structures of (S)-(+) lactic acid and (S)-(−) sodium lactate](image)

**A Polarimeter**

\[
\left[ \alpha \right]_\lambda^T = \frac{\alpha}{l \times c}
\]
If One Enantiomer is (+), the Other is (−)

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.

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

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

$\text{maximum # of stereoisomers} = 2^n$

($n = \text{# of asymmetric centers}$)

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

Diastereomers

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

Two Asymmetric Centers, Four Stereoisomers

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.

two asymmetric centers, four stereoisomers

No Asymmetric Centers

There are only two stereoisomers: cis and trans.
There are only two stereoisomers: cis and trans.

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

meso compounds
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**, the

- **cis** = a *meso compound*
  and
- **trans** = a *pair of enantiomers*. 
Naming Stereoisomers

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

Naming Stereoisomers

(2S,3R)-3-bromo-2-butanol
Naming Stereoisomers

Physical Properties of Stereoisomers

<table>
<thead>
<tr>
<th>Table 4.2</th>
<th>Physical Properties of the Stereoisomers of Tartaric Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Melting point, °C</td>
</tr>
<tr>
<td>(2R,3S)(+)-Tartaric acid</td>
<td>171</td>
</tr>
<tr>
<td>(2S,3S)(−)-Tartaric acid</td>
<td>171</td>
</tr>
<tr>
<td>(2R,3S)-Tartaric acid (meso)</td>
<td>146</td>
</tr>
<tr>
<td>(+)-Tartaric acid</td>
<td>206</td>
</tr>
</tbody>
</table>
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 \textbf{one enantiomer}.

A right-handed glove fits only a right hand.

A Receptor Binds One Enantiomer

Each \textit{enantiomer} binds to a different \textit{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