Specific Rotation and $R,S$ – Configuration

No necessary correlation exists between the (R) and (S) designation and the direction of rotation of plane-polarized light.

Relative vs. Absolute Configuration (5.15A)

(\(R\))-(+)-2-Methyl-1-butanol
\[ [\alpha]^{25}_D = +5.756^\circ \]

(\(S\))-(-)-2-Methyl-1-butanol
\[ [\alpha]^{25}_D = -5.756^\circ \]

\[ \text{Same configuration} \]

(\(R\))-(+)-2-Methyl-1-butanol

(\(R\))-(+)-1-Chloro-2-methylbutane
\[ [\alpha]^{25}_D = -1.64^\circ \]

(\(S\))-(-)-1-Chloro-2-methylbutane
\[ [\alpha]^{25}_D = +1.64^\circ \]
Racemic Forms (Racemate)

\[
\text{Butanone (achiral molecules)} + \text{Hydrogen (achiral molecules)} \xrightarrow{\text{Ni}} \text{(±)-2-Butanol}
\]

50:50 mixture \((R)\) and \((S)\)

\[
\begin{align*}
\text{Butanone} &: \quad \text{CH}_3\text{CH}_2\text{CCH}_3 \\
\text{Hydrogen} &: \quad \text{H} - \text{H}
\end{align*}
\]

\[
\begin{align*}
\text{(±)-2-Butanol} &: \quad \text{HO} \quad \text{CH}_3 \quad \text{CH}_2\text{CH}_3 \\
\text{(R)-(-)-(2)-Butanol} &: \quad \text{HO} \quad \text{CH}_3 \quad \text{CH}_2\text{CH}_3 \\
\text{(S)-(+)-(2)-Butanol} &: \quad \text{OH} \quad \text{CH}_3 \quad \text{CH}_2\text{CH}_3
\end{align*}
\]
Racemic Forms (Racemate)

(R)-2-butanol + (S)-2-butanol

Racemate = Equimolar mixture of (R) and (S) enantiomer

Optically inactive

0 rotation

(a) (R)-2-butanol (b) (S)-2-butanol (if present) Equal and opposite rotation by the enantiomer
Enantiomeric Excess (ee)

Non-equimolar mixture of \((R)\) and \((S)\) enantiomer

Enantiomerically enriched – Optically active

\[
\% \text{ Enantiomeric excess} = \frac{\text{moles of one enantiomer} - \text{moles of other enantiomer}}{\text{total moles of both enantiomers}} \times 100
\]

The enantiomeric excess can be calculated from optical rotations:

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

E.g. a mixture of the 2-butanol enantiomers showed a specific rotation of +6.76°

\[
\text{Enantiomeric excess} = \frac{+6.76^\circ}{+13.52^\circ} \times 100 = 50\%
\]

\((R)\)-2-butanol

\((S)\)  \((R)\)

\((-6.72^\circ)\)  \((+6.72^\circ)\)

Pure  Racemate (50:50)  50% ee (75:25)
Stereoselective Synthesis (Kinetic Resolution)

Racemate (50:50)

\[ \text{lipase} \quad \text{H-OH} \]

\[ \text{at time } t \]

\( >99\% \text{ ee} \)

\( (R) \)

\( (S) \)

\( \text{lipase} \quad \text{H-OH} \)

\( >99\% \text{ ee} \)

\( (S) \)

\( \text{O} \)

\( \text{OEt} \)

\( \text{F} \)

\( \text{H-OEt} \)

\( \text{H-OEt} \)
Stereoselective Synthesis (Kinetic Resolution)

>99% ee

\( \text{lipase} \quad \text{H-OH} \)

\[ \text{OEt} \]

**at time \( t' \)**

>99% ee

\[ \text{H-OEt} \]

\( \text{O} \)

\( \text{OH} \)

\( \text{F} \)

\( \text{S} \)

69% ee of (S)

>99% ee of (R)

\( \text{OEt} \quad \text{F} \quad \text{S} \)

\( \text{O} \quad \text{OH} \quad \text{F} \)

\( \text{R} \quad \text{O} \quad \text{OH} \quad \text{F} \)

15.5% (R)

15.5% (S)

\( \text{OEt} \quad \text{F} \quad \text{S} \)

\( \text{O} \quad \text{OH} \quad \text{F} \)

\( \text{R} \quad \text{O} \quad \text{OH} \quad \text{F} \)

\( \text{OEt} \quad \text{F} \quad \text{S} \)

\( \text{O} \quad \text{OH} \quad \text{F} \)

\( \text{R} \quad \text{O} \quad \text{OH} \quad \text{F} \)
**Chiral Drugs** (for Chiral Receptor)

**Ibuprofen** (Isobutyl phenyl pripionic acid)
(Advil, Motrin, Nuprin)

![Ibuprofen](image)

*Active anti-inflammatory agent*

![Ibuprofen](image)

*No anti-inflammatory activity*

---

**Methyldopa** (Aldomet)

![Methyldopa](image)

*Anti-hypertensivedrug*

![Methyldopa](image)

*No activity*

---

**Penicillamine**

![Penicillamine](image)

*Therapeutic agent for primary chronic arthritis*

![Penicillamine](image)

*Highly toxic*

---

**Acetaminophen** (Tylenol)

![Acetaminophen](image)

**Penicillin G**

![Penicillin G](image)
Molecules with Multi-Stereogenic Centers

Diastereomers have different physical properties: different m.p. and b.p., different solubilities, and so forth.

Total number of stereoisomers will not exceed $2^n$, where $n$ is equal to the number of tetrahedral stereogenic centers.
Diastereomers have different physical properties: different m.p. and b.p., different solubilities, and so forth.

Total number of stereoisomers will not exceed \(2^n\), where \(n\) is equal to the number of tetrahedral stereogenic centers.
Molecules with Multi-Stereogenic Centers

Meso Compounds

Enantiomers

(superimposable)

2,3-Dibromobutane
Molecules with Multi-Stereogenic Centers

**Meso Compounds**

Total number of stereoisomers will not exceed \(2^n\), where \(n\) is equal to the number of tetrahedral stereogenic centers.
Molecules with Multi-Stereogenic Centers
Fisher Projection Formula

Vertical lines represent bonds that project behind the plane of the paper (or that lie in it). Horizontal lines represent bonds that project out of the plane of the paper.
Molecules with Multi-Stereogenic Centers

Fisher Projection Formula

Vertical lines represent bonds that project behind the plane of the paper (or that lie in it). Horizontal lines represent bonds that project out of the plane of the paper.

2,3-Dibromobutane
Stereoisomerism of Cyclic Compounds

- Enantiomers
- Meso compound
- Plane of symmetry

Mirror plane

- trans-1,3-dimethylcyclohexane
- cis-1,4-Dimethylcyclohexane
- trans-1,4-Dimethylcyclohexane
- cis-1,3-dimethylcyclohexane
1,2-Dimethylcyclohexane

*trans*-1,2-dimethylcyclohexane

*Enantiomers*

*Me*  
*Me*  
*Me*  
*Me*

*cis*-1,2-dimethylcyclohexane

*Enantiomers*

*Me*  
*Me*  
*Me*  
*Me*
1,2-Dimethylcyclohexane

trans-1,2-dimethylcyclohexane

Enantiomers

1,2-dimethylcyclohexane
diastereomers

Enantiomers

cis-1,2-dimethylcyclohexane
1,2-Dimethylcyclohexane

trans-1,2-dimethylcyclohexane

diastereomers

Enantiomers

Identical

Enantiomers

cis-1,2-dimethylcyclohexane

1,2-dimethylcyclohexane
1,2-Dimethylcyclohexane

Enantiomers

Diastereomers

Identical

trans-1,2-dimethylcyclohexane

cis-1,2-dimethylcyclohexane

1,2-dimethylcyclohexane
Compounds with Stereogenic Centers Other than Carbon or No Stereogenic Centers

(S)-BINAP

(R)-BINAP

(S)-Naproxene

(S)-BINAP-Ru(Ac)₂

Mirror