7.9
Reactions That Create A Stereogenic Center
Many reactions convert achiral reactants to chiral products.

It is important to recognize, however, that if all of the components of the starting state (reactants, catalysts, solvents, etc.) are achiral, any chiral product will be formed as a racemic mixture.

This generalization can be more simply stated as "Optically inactive starting materials can't give optically active products." (Remember: In order for a substance to be optically active, it must be chiral and one enantiomer must be present in greater amounts than the other.)
Example

\[
\text{CH}_2\text{CH} = \text{CH}_2 \xrightarrow{\text{CH}_3\text{COOH}} \text{H}_3\text{C} - \text{C} - \text{CH}_2
\]

Achiral  Chiral, but racemic
epoxidation from this direction gives $R$ epoxide
Epoxidation from this direction gives $R$ epoxide. Epoxidation from this direction gives $S$ epoxide.
epoxidation from this direction gives \( R \) epoxide

epoxidation from this direction gives \( S \) epoxide
Example

\[ \text{CH}_3\text{CH} \equiv \text{CH}_2 \xrightarrow{\text{Br}_2, \text{H}_2\text{O}} \text{CH}_3\text{CHCH}_2\text{Br} \]

Achiral

Chiral, but racemic
Example

\[ \text{CH}_3\text{CH} = \text{CHCH}_3 \xrightarrow{\text{HBr}} \text{CH}_3\text{CHCHCH}_2\text{CH}_3 \]

Achiral \quad \text{Chiral, but racemic}
Many reactions convert chiral reactants to chiral products.

However, if the reactant is racemic, the product will be racemic also.

Remember: "Optically inactive starting materials can't give optically active products."
**Example**

CH$_3$CHCH$_2$CH$_3$ \[\text{OH}\] \(\rightarrow\) CH$_3$CHCH$_2$CH$_3$ \[\text{Br}\]

Chiral, but racemic \(\rightarrow\) Chiral, but racemic
Many biochemical reactions convert an achiral reactant to a single enantiomer of a chiral product.

Reactions in living systems are catalyzed by enzymes, which are enantiomerically homogeneous.

The enzyme (catalyst) is part of the reacting system, so such reactions don't violate the generalization that "Optically inactive starting materials can't give optically active products."
Example

Fumaric acid

Achiral

(S)-(−)-Malic acid

Single enantiomer
7.10
Chiral Molecules
with
Two Stereogenic Centers

How many stereoisomers when a particular molecule contains two stereogenic centers?
2,3-Dihydroxybutanoic acid

What are all the possible $R$ and $S$ combinations of the two stereogenic centers in this molecule?
What are all the possible $R$ and $S$ combinations of the two stereogenic centers in this molecule?

Carbon-2  $R$  $R$  $S$  $S$

Carbon-3  $R$  $S$  $R$  $S$
2,3-Dihydroxybutanoic acid

\[
\text{CH}_3\text{CHCHCHCOH}
\]

4 Combinations = 4 Stereoisomers

<table>
<thead>
<tr>
<th>Carbon-2</th>
<th>R</th>
<th>R</th>
<th>S</th>
<th>S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon-3</td>
<td>R</td>
<td>S</td>
<td>R</td>
<td>S</td>
</tr>
</tbody>
</table>
2,3-Dihydroxybutanoic acid

\[
\begin{align*}
\text{CH}_3\text{CHCHCHCOH} \\
\text{HO} & \quad \text{OH}
\end{align*}
\]

4 Combinations = 4 Stereoisomers

What is the relationship between these stereoisomers?

Carbon-2: \( R \quad R \quad S \quad S \)

Carbon-3: \( R \quad S \quad R \quad S \)
2,3-Dihydroxybutanoic acid

\[
\begin{array}{c}
\text{CH}_3\text{CHCHCHCOH} \\
\text{HO OH}
\end{array}
\]

enantiomers: \(2R,3R\) and \(2S,3S\)  
\(2R,3S\) and \(2S,3R\)
enantiomers

$\alpha = -9.5^\circ$

$\alpha = +9.5^\circ$

$\alpha = +17.8^\circ$

$\alpha = -17.8^\circ$
2,3-Dihydroxybutanoic acid

but not all relationships are enantiomeric

stereoisomers that are not enantiomers are diastereomers

<table>
<thead>
<tr>
<th>Carbon-2</th>
<th>R</th>
<th>R</th>
<th>S</th>
<th>S</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbon-3</td>
<td>R</td>
<td>S</td>
<td>R</td>
<td>S</td>
</tr>
</tbody>
</table>
Isomers

- constitutional isomers
- stereoisomers
  - enantiomers
  - diastereomers
enantiomers

\[ [\alpha] = -9.5^\circ \]

\[ [\alpha] = +9.5^\circ \]

diastereomers

\[ [\alpha] = +17.8^\circ \]

\[ [\alpha] = -17.8^\circ \]
Fischer Projections

recall for Fischer projection:
horizontal bonds point toward you;
vertical bonds point away

staggered conformation does not have correct orientation of bonds for Fischer projection
Fischer projections

(transform molecule to eclipsed conformation in order to construct Fischer projection)
Fischer projections
Stereochemical prefixes used to specify relative configuration in molecules with two stereogenic centers are easiest to apply using Fischer projections. Orientation: vertical carbon chain.
when carbon chain is vertical, same (or analogous) substituents on same side of Fischer projection

\[ \text{Erythro} \]

\[
\begin{align*}
\text{CO}_2\text{H} & \quad \text{CO}_2\text{H} \\
\text{H} & \quad \text{OH} \\
\text{H} & \quad \text{OH} \\
\text{H} & \quad \text{CH}_3 \\
\text{H} & \quad \text{CH}_3
\end{align*}
\]

\(-9.5^\circ\)  \quad \(+9.5^\circ\)
when carbon chain is vertical, same (or analogous) substituents on opposite sides of Fischer projection

Threo

+17.8°  \( \text{CH}_3 \)

-17.8°  \( \text{CH}_3 \)
Two stereogenic centers in a ring

*trans*-1-Bromo-1-chlorocyclopropane

nonsuperposable mirror images; enantiomers
Two stereogenic centers in a ring

cis-1-Bromo-1-chlorocyclopropane

nonsuperposable mirror images; enantiomers
Two stereogenic centers in a ring

cis-1-Bromo-1-chloro-cyclopropane

trans-1-Bromo-1-chloro-cyclopropane

stereoisomers that are not enantiomers; diastereomers
It is possible for a molecule to have stereogenic centers yet be achiral.
Consider a molecule with two equivalently substituted stereogenic centers such as 2,3-butane diol.
Three stereoisomers of 2,3-butanediol

- $2R,3R$ chiral
- $2S,3S$ chiral
- $2R,3S$ achiral
Three stereoisomers of 2,3-butanediol:

1. $2R,3R$: Chiral
2. $2S,3S$: Chiral
3. $2R,3S$: Achiral
Three stereoisomers of 2,3-butanediol

2R,3R chiral

2S,3S chiral

these two are enantiomers
Three stereoisomers of 2,3-butanediol

2R,3R, chiral

2S,3S, chiral

these two are enantiomers
Three stereoisomers of 2,3-butanediol

The third structure is superposable on its mirror image.

$2R,3S$

achiral
Three stereoisomers of 2,3-butanediol

therefore, this structure and its mirror image are the same

it is called a meso form

a meso form is an achiral molecule that has stereogenic centers

2R,3S achiral
Three stereoisomers of 2,3-butanediol

CH₃

3-CH₃

HO H

HO H

therefore, this structure and its mirror image are the same

it is called a meso form

a meso form is an achiral molecule that has stereogenic centers

2R,3S

achiral

dihedral
Three stereoisomers of 2,3-butanediol

meso forms have a plane of symmetry and/or a center of symmetry

plane of symmetry is most common case

top half of molecule is mirror image of bottom half

2R,3S

achiral
Three stereoisomers of 2,3-butanediol

A line drawn the center of the Fischer projection of a meso form bisects it into two mirror-image halves.

2R,3S achiral
There are three stereoisomers of 1,2-dichloro-cyclopropane; the achiral (meso) cis isomer and two enantiomers of the trans isomer.
7.12 Molecules with Multiple Stereogenic Centers
How many stereoisomers?

\[ \text{maximum number of stereoisomers} = 2^n \]

where \( n \) = number of structural units capable of stereochemical variation

structural units include stereogenic centers and cis and/or trans double bonds

number is reduced to less than \( 2^n \) if meso forms are possible
Example

4 stereogenic centers
16 stereoisomers
Cholic acid (Figure 7.13)

Cholic acid

- 11 stereogenic centers
- $2^{11} = 2048$ stereoisomers
- One is "natural" cholic acid
- A second is the enantiomer of natural cholic acid
- 2046 are diastereomers of cholic acid
How many stereoisomers?

maximum number of stereoisomers = $2^n$

where $n =$ number of structural units capable of stereochemical variation

structural units include stereogenic centers and cis and/or trans double bonds

number is reduced to less than $2^n$ if meso forms are possible
How many stereoisomers?

3-Penten-2-ol

![Structures of 3-Penten-2-ol with stereochemistry](image-url)