Relation Between Substituents on Cyclohexane

1,2-trans

1,3-trans

1,4-trans

1,2-cis

1,3-cis

1,4-cis
Interaction Energies of Substituents on Cyclohexane

If substituents are very large, the instability of the axial conformer becomes high enough to not have a chair conformation at all.

This could also happen if substituents (even if they are not very bulky) are forced to have a 1,3-diaxial relation.

If the substituent is methyl, it amounts to $0.9 \times 2 = 1.8$ kcal/mol

1,2-diequatorial

Has a gauche butane relation. For dimethyl substitution this amounts to 0.9 kcal/mol

1,2-axial equatorial

Has a gauche butane relation. For dimethyl substitution this amounts to 0.9 kcal/mol
**Bicyclic Compounds - Decalin**

Compounds having two fused rings are called bicyclic compounds.

Decalins are compounds formed by fusing two six membered rings through one common bond.

*trans*-decalin

Two axial methyl groups are far away to be connected with just two more carbon bonds.

*trans*-Decalin cannot flip and is considered to be conformationally locked.
Bicyclic Compounds - Decalin

cis-decalin
Bicyclic Compounds - Decalin

cis-Decalin can flip as the new structure would also have one axial and one equatorial bond.
*cis Vs trans-Decalin*

*trans*-Decalin is more stable than *cis*-decalin by $3 \times 0.9 = 2.7$ kcal/mol
Anomeric Effect

An axial conformation becomes more favored for an electronegative substituent if the adjacent atom in the ring is bearing a lonepair of electrons.

Hyperconjugation: The lonepair of electrons on the oxygen atom interacts with the anti-bonding orbital of C-X bond in the axial anomer.
Isomerism in Organic Molecules

How are these molecules related?

- Constitutional isomers
- Stereoisomers
- Constitutional isomers

Isomers

- Constitutional Isomers
- Stereoisomers
  - Enantiomers
  - Diastereomers
**Stereochemistry**

Three-dimensional arrangement of atoms (groups) in space

**Stereoisomers:** molecules with the same connectivity but different arrangement of atoms (groups) in space

![cis-1,2-dimethylcyclopropane](image1.png)  
**cis-1,2-dimethylcyclopropane**

![trans-1,2-dimethylcyclopropane](image2.png)  
**trans-1,2-dimethylcyclopropane**

![trans-2-butene](image3.png)  
**trans-2-butene**

![cis-2-butene](image4.png)  
**cis-2-butene**

**Geometric isomers (Diastereomers)**
**Enantiomers and Diastereomers**

**Enantiomers:** These are mirror images of each other and are not superimposable. They have identical physical properties (m.p., b.p. etc). A tetrahedral carbon atom bonded to four different groups or atoms is called a chiral, asymmetric or a stereogenic center.

![Left hand](image1) ![Right hand](image2)

**Diastereomers:** Stereoisomers which are not mirror objects of each other. They have different physical properties.

A molecule with just one chiral center would exist as enantiomers. If a molecule has more than one chiral center it would have enantiomers and diastereomers.
**Symmetry and Chirality**

Molecules with a center of symmetry or a plane of symmetry would be achiral and cannot have enantiomers.

[Diagrams of molecules with and without symmetry planes]

**Optical Activity**

A substance is optically active if it rotates the plane of plane polarized light. Only chiral molecules exhibit optical activity. Enantiomers rotate the plane of plane polarized light to the same degree, but in opposite directions. If a sample has equal amounts of both the enantiomers of a compound, the optical activity is lost and the sample is said to be racemic.
Optical Activity

Specific Rotation: An inherent property of chiral molecules and is defined as,

\[ [\alpha] = \frac{\alpha_{\text{observed}}}{(c \times l)} \]

\( \alpha_{\text{observed}} \) is the angle by which plane of the plane polarized light is rotated by a sample of concentration, \( c \) (in g/mL) in a container of ‘path length’, \( l \) (in dm).

The [\( \alpha \)] may also depend upon solvent, therefore the solvent is usually specified. A monochromatic plane polarized light is used for detecting specific rotation. The most commonly used light is the sodium D line.

For alanine,

\[ [\alpha]_{D}^{20} = +14.5^\circ \text{ (c 10, 6 N HCl)} \]
Optical Purity

If a mixture contains unequal amounts of both enantiomers, it is possible to calculate the percentage of each of them, provided that the specific rotation of the enantiomers are known.

A sample of a chiral compound that contains only one of the enantiomers is said to be enantiomerically pure or that its enantiomeric excess is 100%.

\[
\% \text{ Enantiomeric excess} = \left( \frac{\text{observed specific rotation}}{\text{specific rotation of pure enantiomer}} \right) \times 100
\]

This can also be represented as

\[
\% \text{ Enantiomeric excess} = \left( \frac{\text{No. of moles of one enantiomer} - \text{No. of moles of the other}}{\text{Total no. of moles}} \right) \times 100
\]
Optical Purity

The specific rotation of \((S)\)-2-iodobutane is +15.90°. Determine the % composition of a mixture of \((R)\)- and \((S)\)-2-iodobutane if the specific rotation of the mixture is -3.18°.

\[
\text{ee} = \left(\frac{-3.18}{-15.90}\right) \times 100 = 20\%
\]

The solution contains 60% of \(R\) isomer and 40% of \(S\) isomer