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OpenCourseWare (2023)

## CHEMISTRY II

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## STEREOCHEMISTRY



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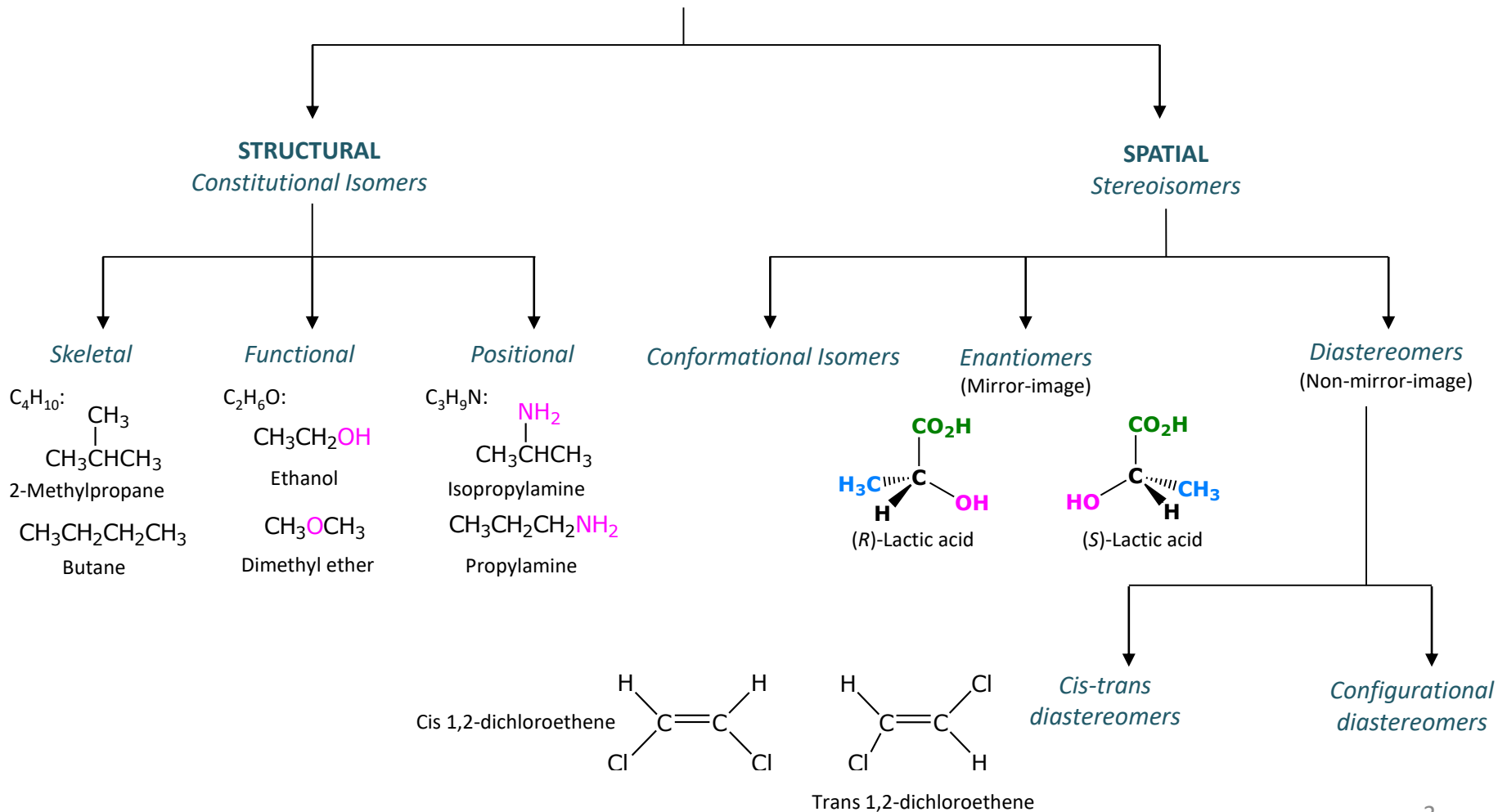
Fischer Projections

#### Diastereomers

## ISOMERISM

*Isomers*

They have the same molecular formula, but different structures



## Stereoisomerism

Describes isomers whose atoms are connected in the same order but differ in their spatial arrangement

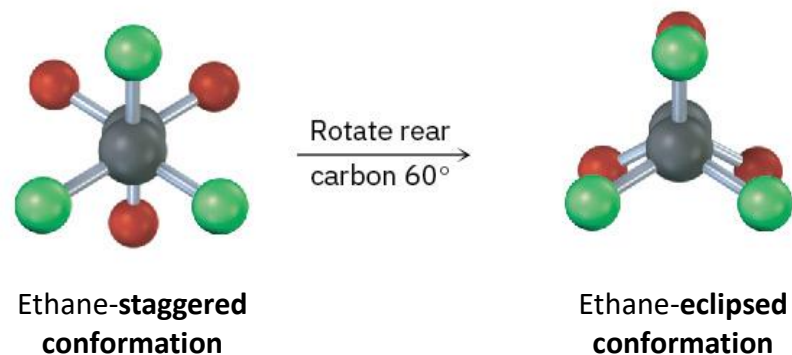
### Conformational Isomerism

Isomers can be interconverted exclusively by rotations about formally single bonds.

Rotation interconverts the conformations of *ethane*

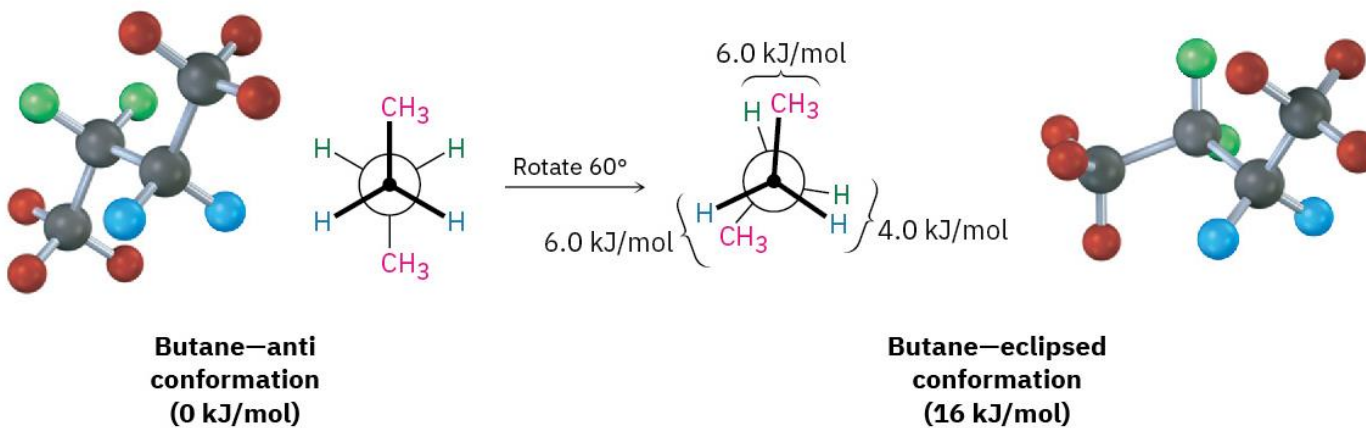
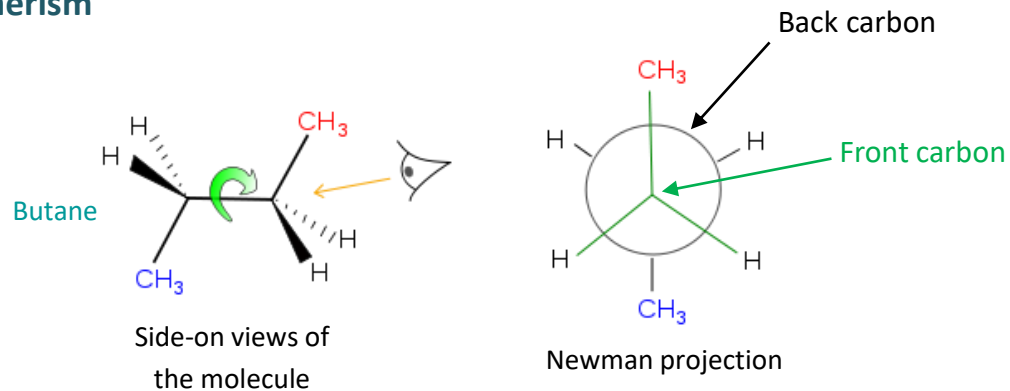


Conformations or Conformers:



## Conformational Isomerism

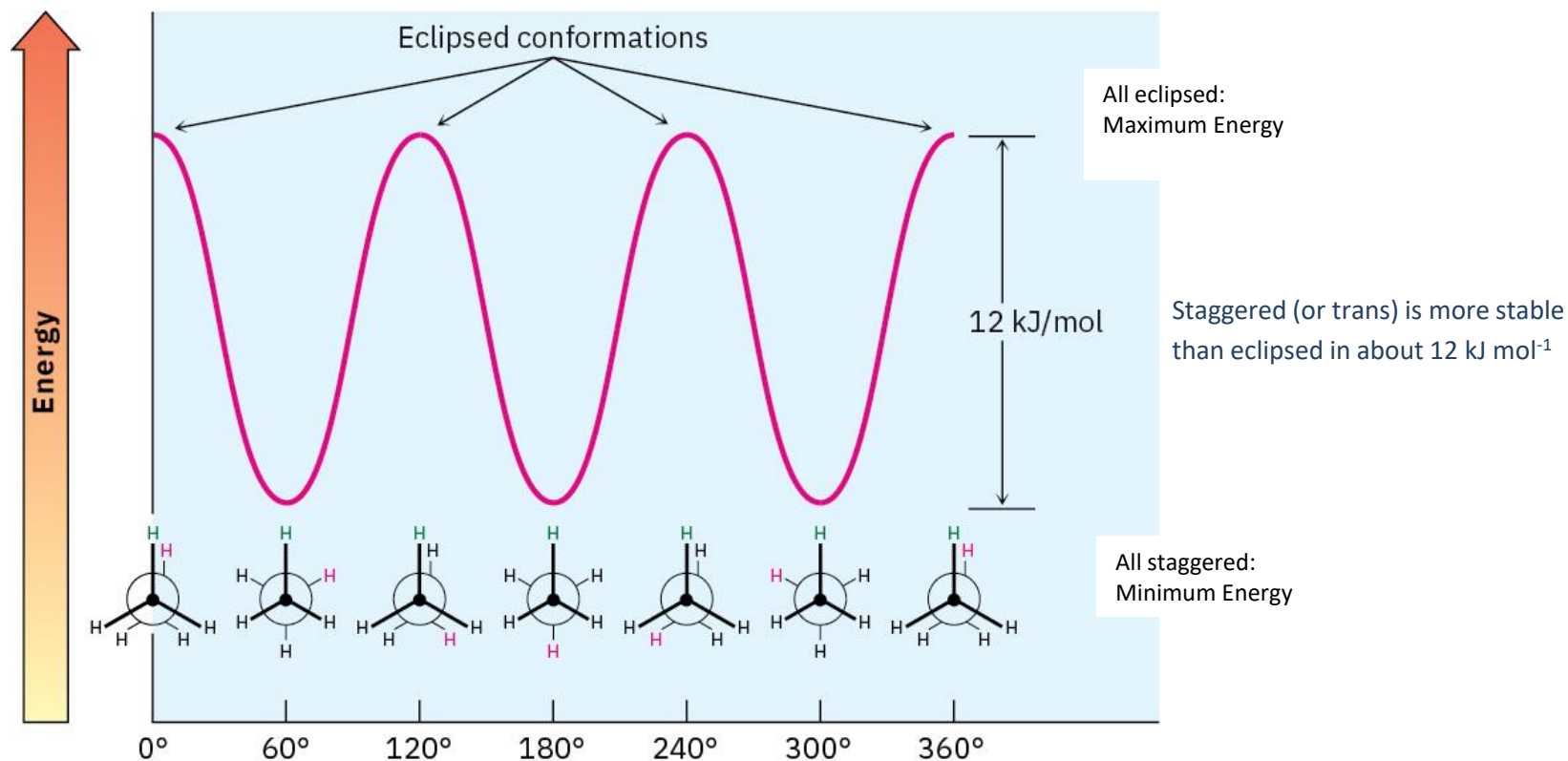
### NEWMAN PROJECTIONS



## Conformational Isomerism

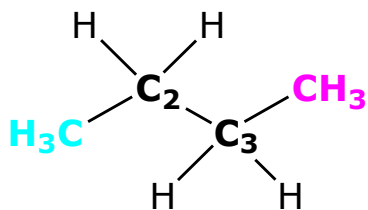
Potential energies of the conformers of *ethane*

*Torsional energy (rotational or torsional strain).*- The change in energy resulting from bond rotation from the staggered to the eclipsed conformation.



## Conformational Isomerism

Conformational analysis of *butane*

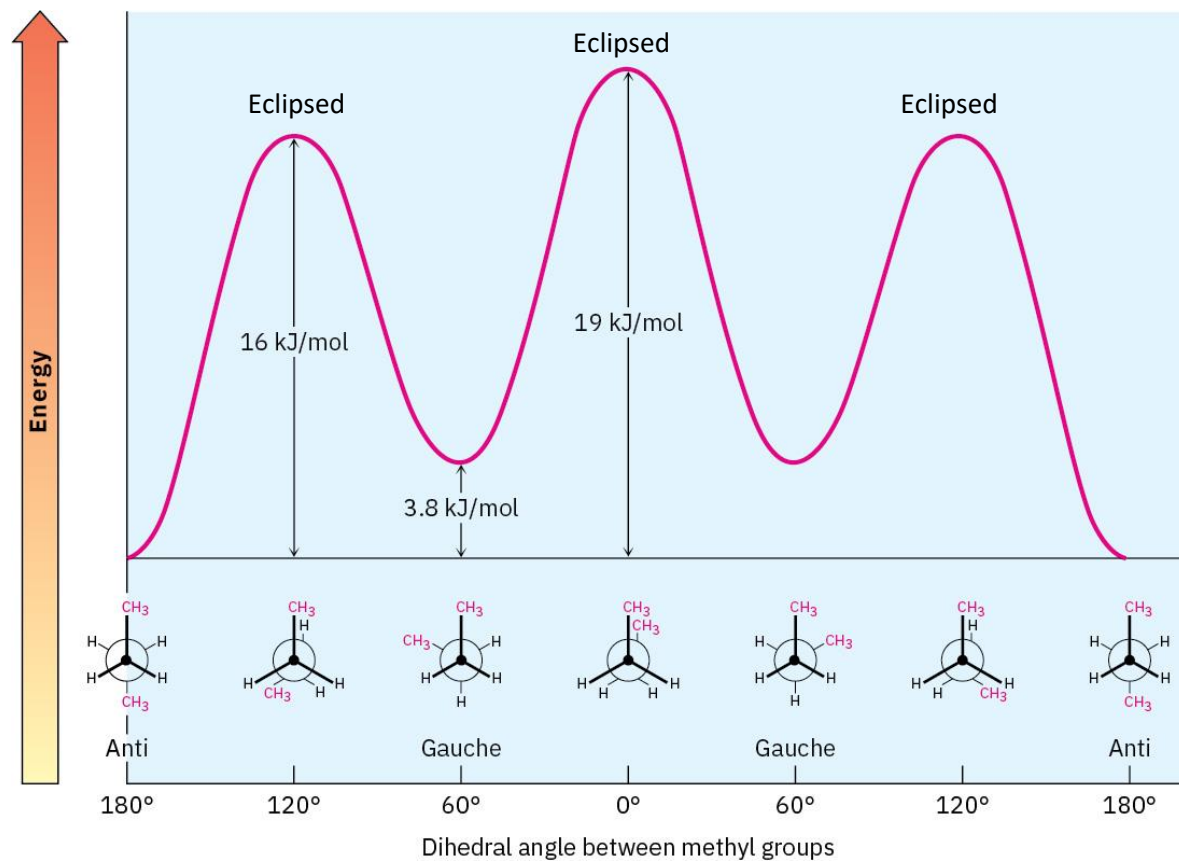


Steric hindrance raises the energy barrier to rotation

Newman projections about the C2-C3 bond

Approximate energy values for conformer interactions:

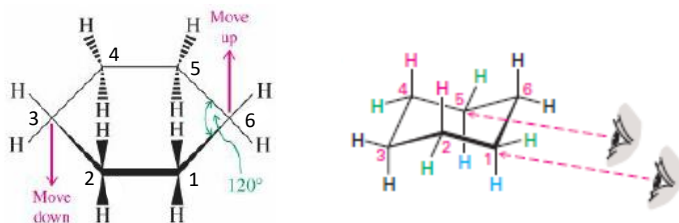
H ↔ H eclips.	4 kJ/mol
H ↔ CH <sub>3</sub> eclips.	6 kJ/mol
CH <sub>3</sub> ↔ CH <sub>3</sub> eclips.	11 kJ/mol
CH <sub>3</sub> ↔ CH <sub>3</sub> gauche	3.8 kJ/mol



## Conformational Isomerism

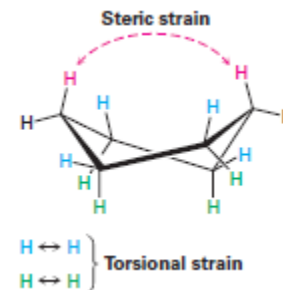
### Conformations of cyclohexane

#### Chair conformation

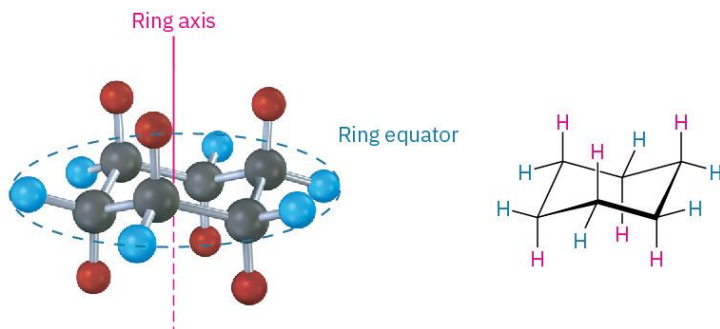


#### Twist-boat conformation

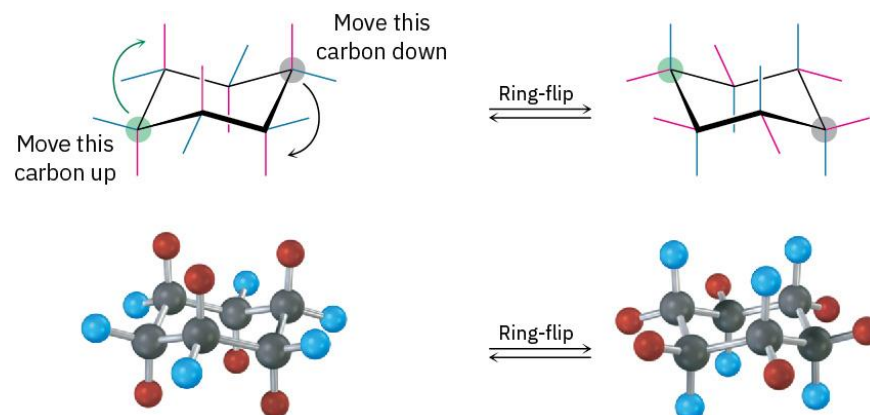
Steric strain and torsional strain, 23 kJ/mol higher in energy than the chair conformation.



Axial and equatorial positions in chair cyclohexane.



A ring-flip in chair cyclohexane interconverts axial and equatorial positions.



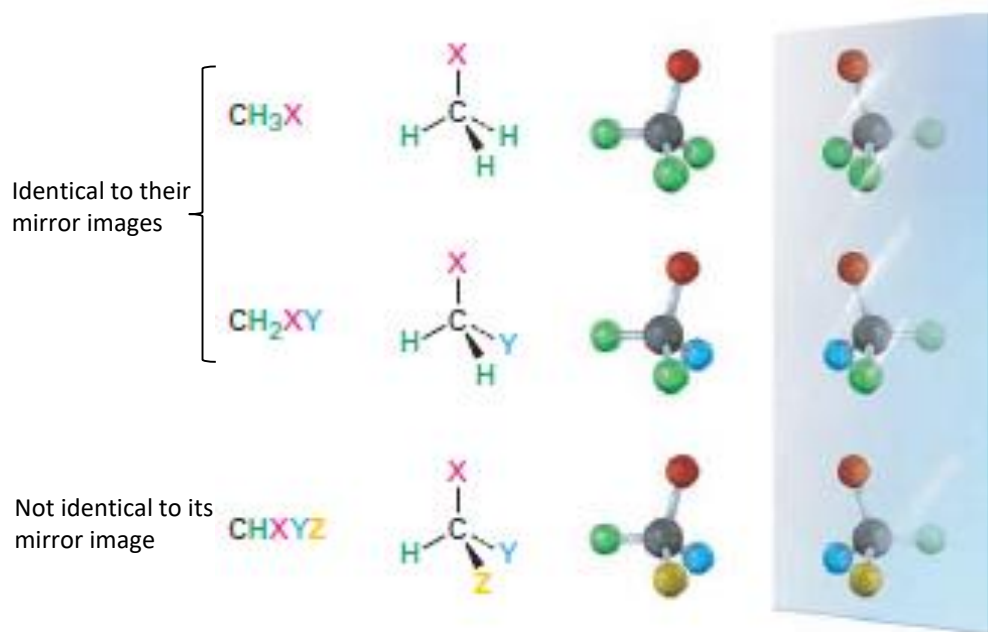


## Stereoisomerism

Describes isomers whose atoms are connected in the same order but differ in their spatial arrangement

**Enantiomers** are two stereoisomers that are related to each other by a reflection: they are mirror images of each other, which are **non-superimposed**.

Human hands are perhaps the most universally recognized example of chirality: The left hand is a non-superimposed mirror image of the right hand.

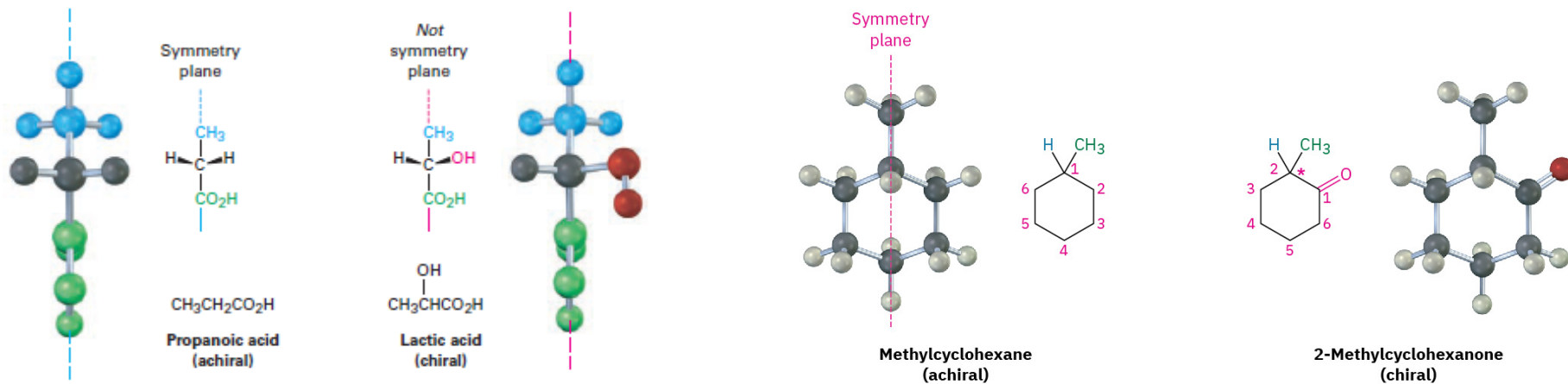


## Chirality

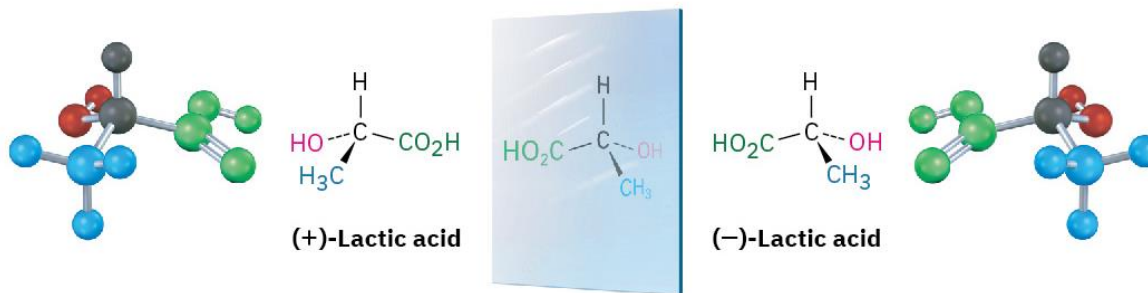
It appears when the four substituents of a C atom are different.

That C atom is called **CHIRAL CENTER**

Chirality. The symmetry in molecules



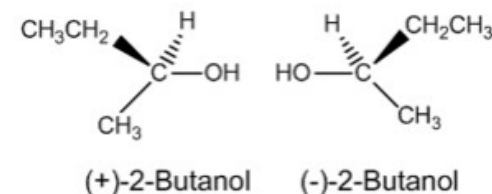
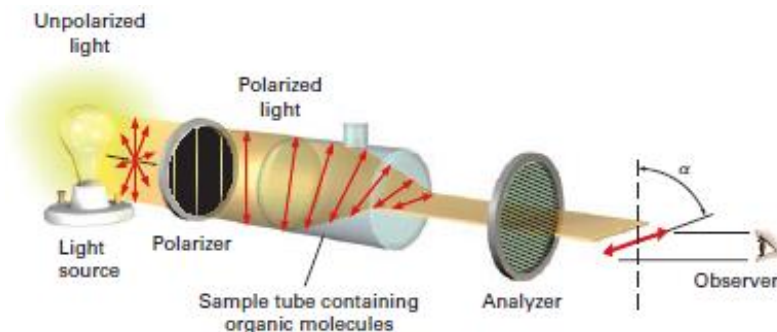
**ENANTIOMERS**



## Optical Activity

Enantiomers have the property of *polarizing light*: to change the polarization angle of light when it passes through a solution containing them. Substances which exhibit this property are said to be **optically active**.

*Polarimeter:*



An enantiomer can be named by the direction in which it rotates the plane of polarized light:

- ✓ If rotates the plane of light in a *clockwise* sense: dextrorotatory  $\Rightarrow$  (+) enantiomer.
- ✓ If rotates the plane of light in a *counterclockwise* sense: levorotatory  $\Rightarrow$  (-) enantiomer.

An equimolecular mixture of both is called **racemic mixture** and has no optical activity.

## Specific rotation $[\alpha]$

$[\alpha]$  is defined as the observed angle of optical rotation  $\alpha$  when plane-polarized light is passed through a sample with a path length of 1 decimeter and a sample concentration of 1 gram per 1 milliliter.

$\lambda$ : wavelength of incident light = 598 nm

t: temperature in  $^{\circ}\text{C}$

$$[\alpha]_{\lambda}^{t^{\circ}} = \frac{\alpha}{l \times c}$$

Observed optical rotation  $[\alpha]$   $^{\circ}$

Length of sample cell  $l$  [dm]

Concentration of sample  $c$  [g/mL]

## Absolute Configuration: *R*, *S* Sequence Rules

Cahn-Ingold-Prelog rules:

Sign of Rotation ~~↔~~ Structure of Enantiomer

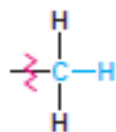
- Rank the four atoms, directly attached to the chirality center, according to atomic number.

Atomic Number      35   17   16   15   8   7   6   2   1

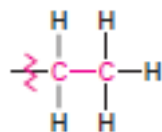
Higher Ranking      Br > Cl > S > P > O > N > C > <sup>2</sup>H > <sup>1</sup>H

Lower Ranking

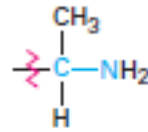
- If two substituents have the same rank, look at the the second, third, or fourth atoms away from the chirality center until the first difference is found.



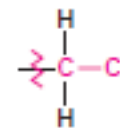
Lower



Higher

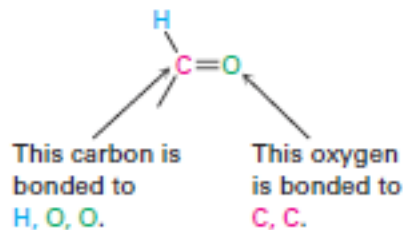


Lower

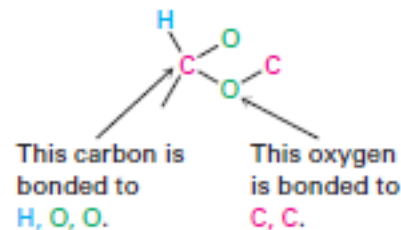


Higher

- Multiple-bonded atoms are equivalent to the same number of single-bonded atoms.



is equivalent to

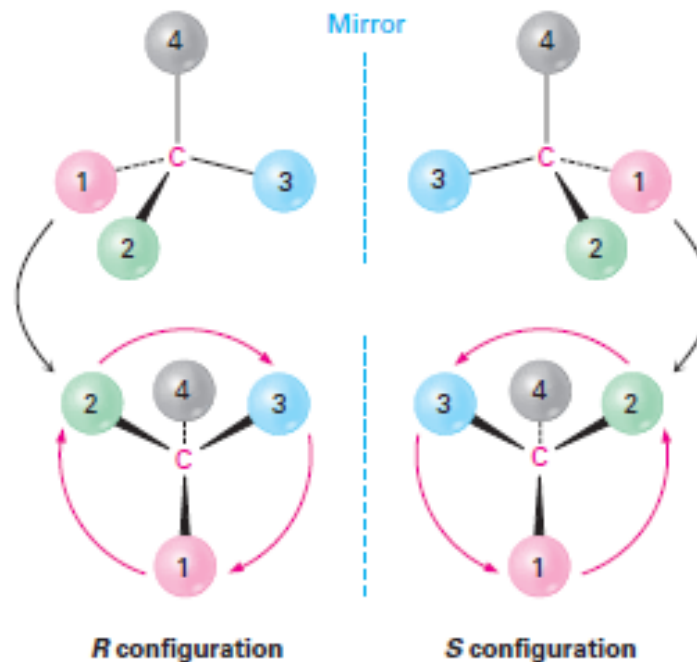


## Absolute Configuration: R, S Sequence Rules

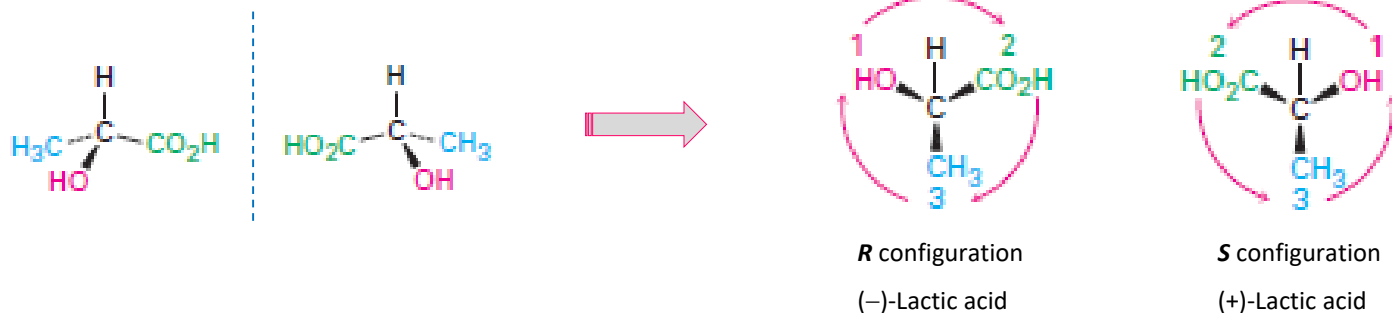
Cahn-Ingold-Prelog rules:

If the priority of the remaining three substituents decreases in **clockwise** direction, it is labeled **R** (from the Latin *Rectus*, meaning "right"), if it decreases in **counterclockwise** direction, it is **S** (from the Latin *Sinistra*, meaning "left").

**Note:** the sign of optical rotation, (+) or (–), is not related to the R, S designation.



Assignment configuration to Lactic acid:

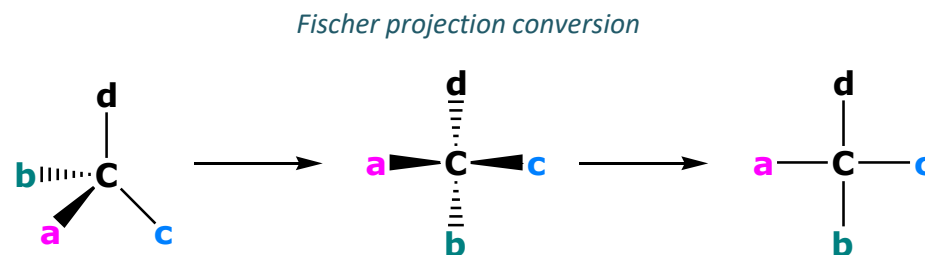


## Fischer Projections

They are 2D representations of stereochemistry at chirality centers, particularly in carbohydrate chemistry.

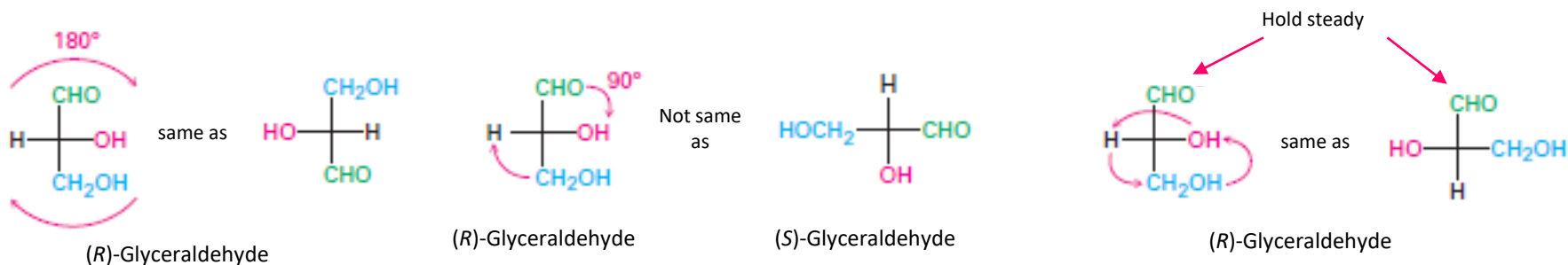
➤ Molecule is drawn in the form of a cross with the central C at the point of intersection:

- ✓ Horizontal lines signify bonds directed toward the viewer.
- ✓ Vertical lines are pointing away.



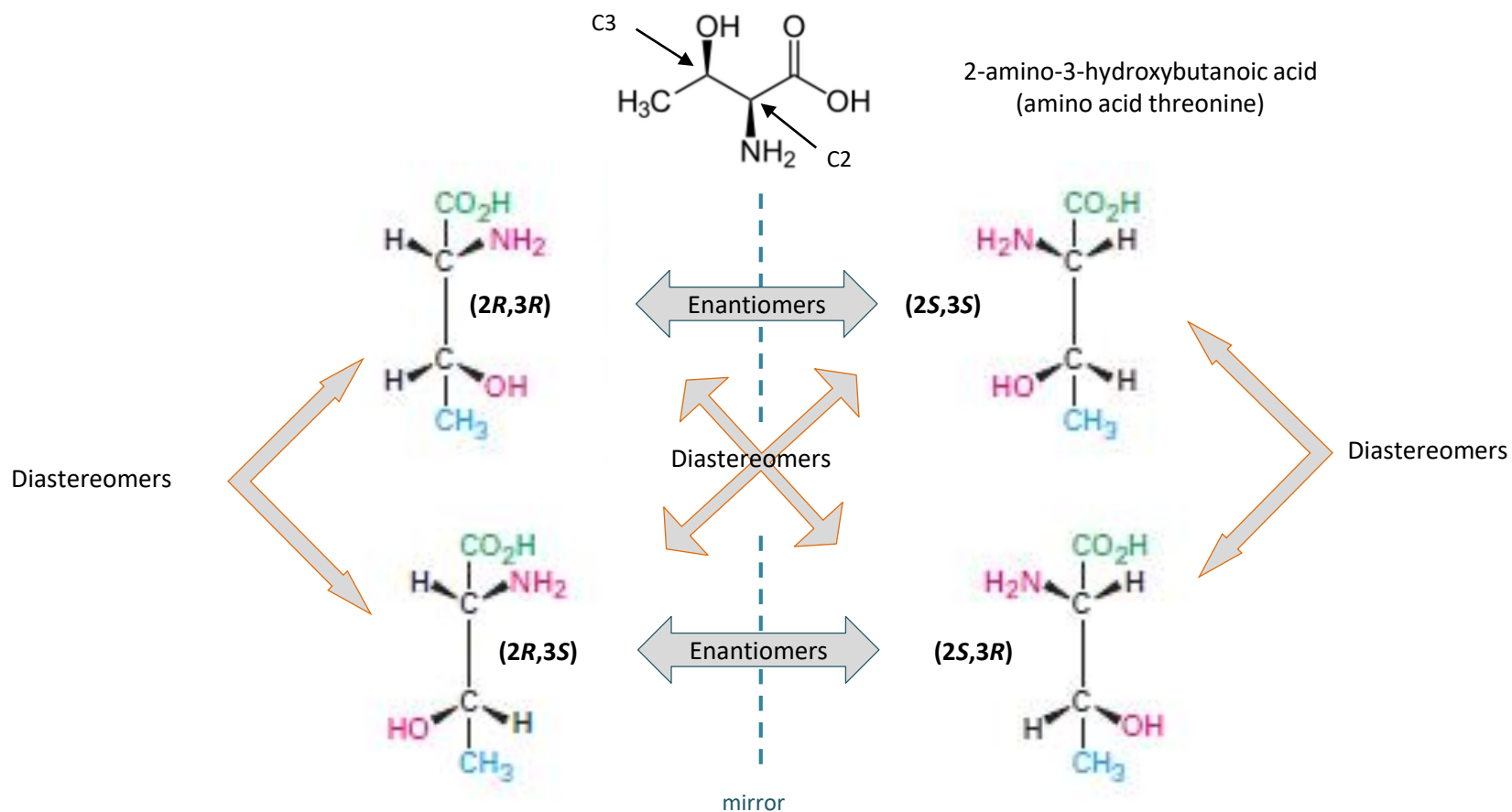
➤ It is only allowed to rotate 180°, NOT 90° NOR 270°.

➤ You can fix ONE group and rotate the other three in clockwise or anticlockwise without changing the configuration.



**Diastereomers.** Molecules incorporating several stereocenters.

When molecules contain more than one chiral center ( $n$  centers), the number of stereoisomers roughly grows as  $2^n$ . Some of these isomers are not enantiomers because they are not mirror images. These isomers are called *Diastereomers*.



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- Images made by the authors.

*Slides 4-10, 11 (polarimeter), 12-14, 15 (modified by authors):*

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*Slide 5:*

- Newman projection: Amelliug, CC BY-SA 3.0, <https://commons.wikimedia.org/wiki/File:Newman.svg>.

*Slide 11:*

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