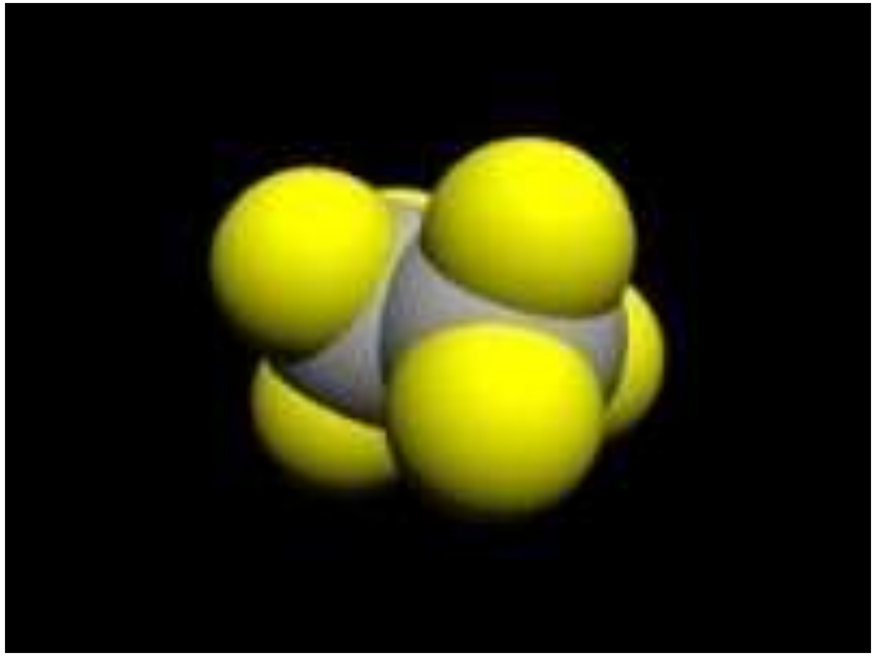
BIO-110: Exercise 02

Discussion

07.03.2025

2.1 Newman projections

Single-bonds (σ) can rotate! Conformation analysis is all about identifying the resulting most likely conformation.

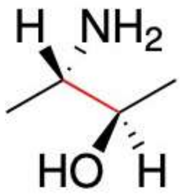


https://www.youtube.com/watch?v=V2pr7e9g3E4&ab_channel=DokeDJ

2.1 Newman projections. How to draw one? Step-by-step guide

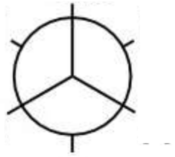
1. Choose the bond to analyze

- Look straight down the bond axis (e.g., C–C bond)



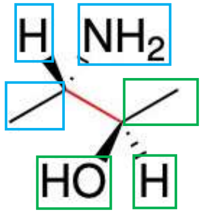
2. Draw the Newman Backbone

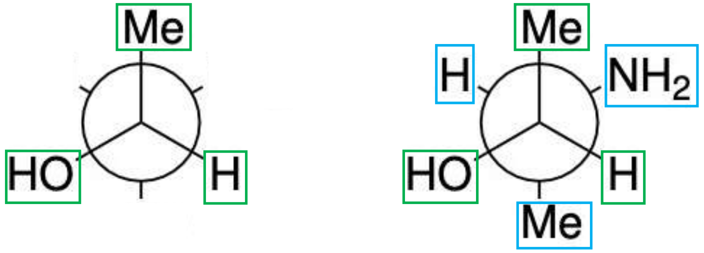
- **Front carbon** → Small **dot**
- **Rear carbon** → Larger **circle** behind it
- **Three bonds from each carbon** (front: from dot, rear: from circle edge). Keep in mind, that staggered conformation is more stable than eclipsed



3. Identify and Place Substituents

- Assign groups to each carbon (e.g., OH, H, CH3)
- Place substituents on the **front carbon first**, then the **rear carbon**, keeping geometry in mind



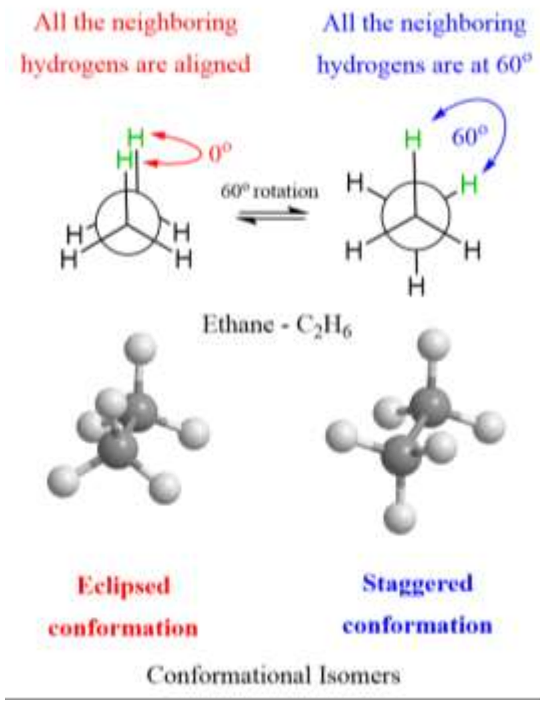


4. For Cyclic Systems

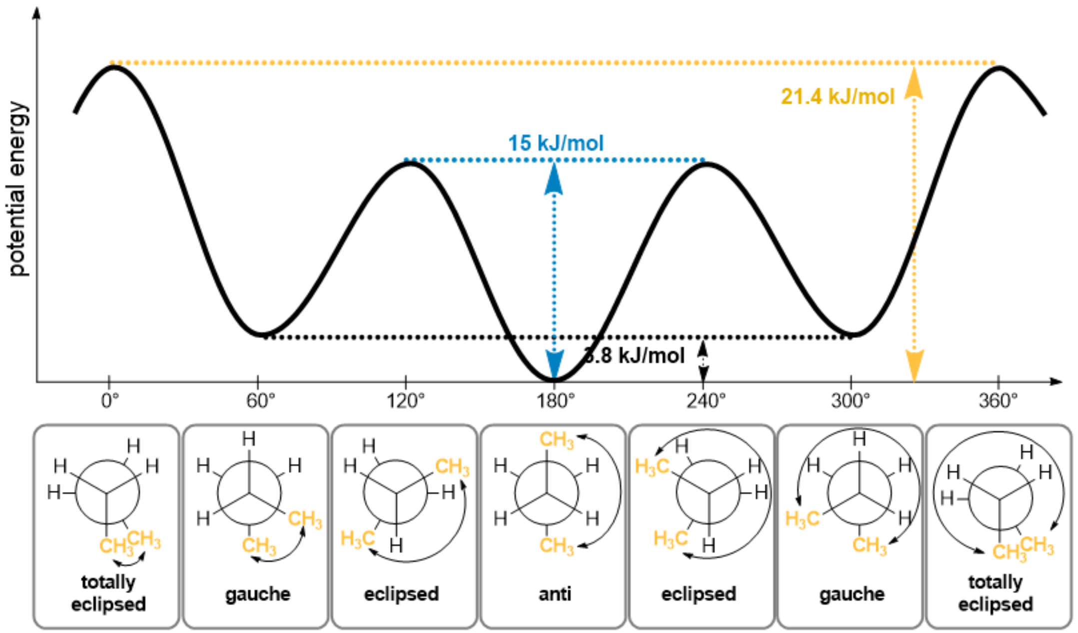
- Keep the ring backbone at **~60°** spacing
- Position other groups **above/below the plane** to reflect axial/equatorial

2.1-2.2 Newman projections and Conformational energies

Ethane: Conformational energies



Propane: Conformational energies



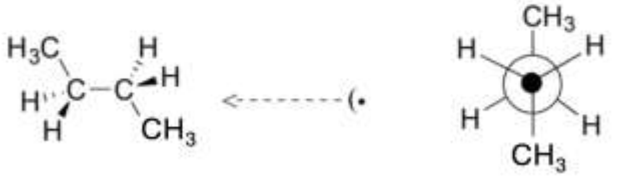
Steric hindrance: Repulsion between electron clouds of bulky groups.
Torsional strain: Electron repulsion in eclipsed bonds due to orbital overlap.
Both steric hindrance and torsional strain can be present in eclipsed conformations.

2.1 Newman projections

Ex. 2.1 (a) Draw the Newman projections of the lowest-energy and highest-energy conformations of butane when looking down the C2-C3 bond. Which conformation is more stable? Explain your answer.

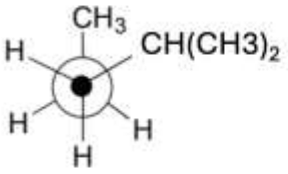
highest energy
(eclipsed)

Less stable because electron clouds overlap.

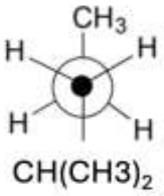


More stable because it minimizes steric hindrance and tortional strain.

Ex. 2.1 (b) Draw a Newman projection, looking down the C3-C4 bond of 2-methylpentane, in a gauche conformation. Now, draw the anti conformation. Which conformation is more stable and why?



gauche



anti

Anti is more stable because it minimizes steric hindrance and tortional strain.

Gauch and anti are both staggerred comformations.

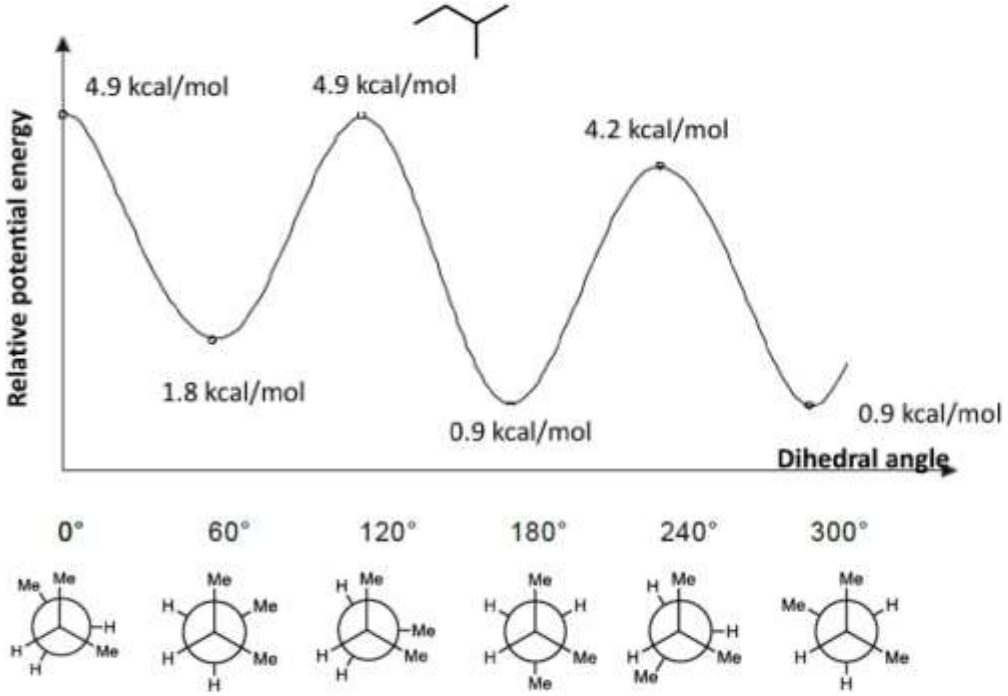
2.2 Conformational energies

Generally, two substituents experience mutual repulsion when they are in an ecliptic conformation. These torsional stresses and the gauche interactions, which result from the staggered arrangement of large substituents, have the following rough orders of magnitude and are **additive**:

Conformer	Energy / kcal mol^{-1}
H ecliptic to H	1.0
H ecliptic to Me	1.4
Me ecliptic to Me	2.5
Me gauche to Me	0.9

Me = Methyl = -CH_3
gauche = ‘staggered’

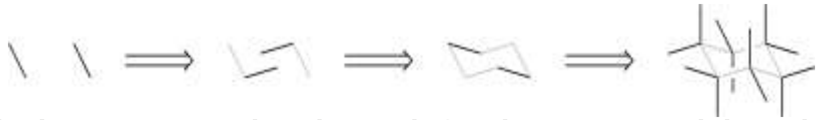
Ex. 2.2



Here, we keep the front fix while rotating the back (and therefore the bond)

2.3 Chair conformations of cyclohexane

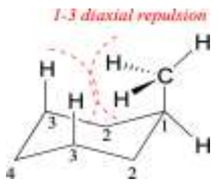
When drawing a chair, it is important that opposite ties are always drawn parallel.

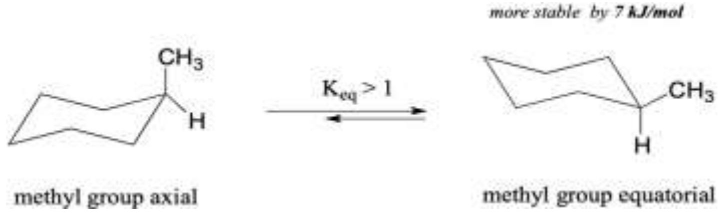


The upper corner of the chair has an axial bond facing up, while the lower corner has an axial bond facing down. Axial bonds alternate up and down along the carbon atoms. Once axial bonds are drawn, equatorial bonds can be added: if an axial bond is up, the equatorial bond is down (and *vice versa*).

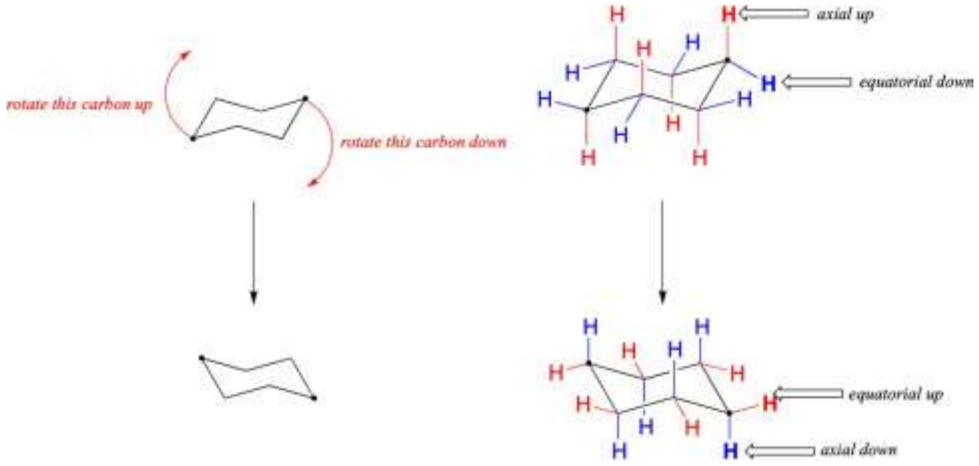
Two important concepts to understand chair conformations:

(a) 1,3 – diaxial replusion





(b) Ring flipping



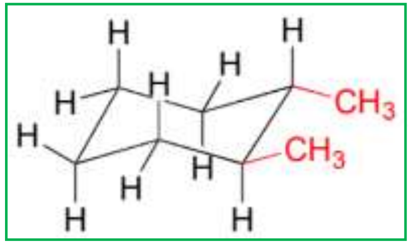
1,3-Diaxial repulsion is steric hindrance, where a bulky axial group on C1 clashes with axial hydrogens on C3 and C5. This makes the **equatorial position more stable**.

Ring flipping is the conformational interconversion of cyclohexane, where axial and equatorial bonds swap positions, altering steric interactions.

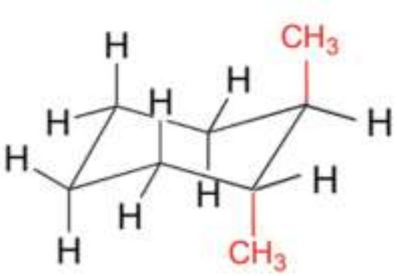
2.3 Chair conformations of cyclohexane

Draw the lower-energy chair conformations of the following molecules, indicating all axial and equatorial positions, including hydrogen atoms:

2.3 (a) trans-1,2-dimethylcyclohexane. Draw the alternative chair conformation. Compare the energies of the two conformations. Which molecule, trans-1,2-dimethylcyclohexane or trans-1,3-dimethylcyclohexane, has a greater energy difference between its two chair conformations?

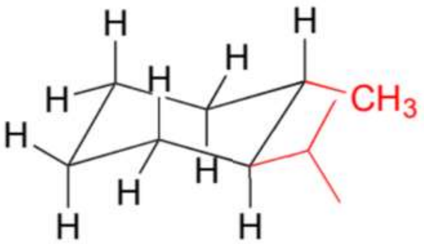


vs



Two axial methyl groups lead to steric hindrance, that is why two equatorial ones are preferred.

2.3 (b) trans-1-isopropyl-2-methylcyclohexane. Draw the alternative chair conformation. Compare the energies of the two conformations. Which molecule, trans-1-isopropyl-2-methylcyclohexane or cis-1-isopropyl-2-methylcyclohexane, has a greater energy difference between its two chair conformations?



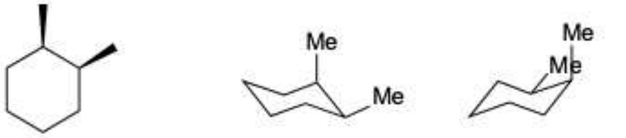
Diequatorial and diaxial have a higher energetical difference compared to one axial and one equatorial.

2.4 Energetically favorable chair conformations

One methyl must be equatorial, the other axial.

Both Me equatorial

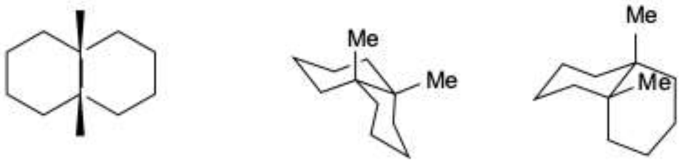
Diaxial is energetically unfavourable because of steric hindrance.



Both conformations are equally stable

One methyl must be equatorial, the other axial.

Methyls must be axial to allow proper fusion of the second ring.



One methyl must be equatorial, the other axial. The second ring can adopt two possible conformations (chair or twist-boat).

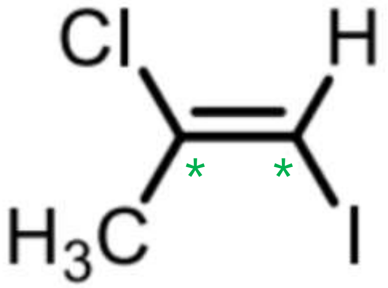
2.5 (a) Stereochemistry

Stereogenic Center

✓ An atom where swapping two groups results in a **stereoisomer**.
✓ Includes both **chiral centers (R/S)** and **E/Z double bond centers**.
✓ Can be **sp³ (tetrahedral)** or **sp² (trigonal planar, like C=C in E/Z isomers)**.
✓ **Example:** C=C in an alkene where each carbon has two different groups (E/Z isomerism).

Chiral Center

✓ A **special type of stereogenic center** that is **sp³-hybridized** and bonded to **four distinct groups**.
✓ Leads to **non-superimposable mirror images (enantiomers)** and follows **R/S nomenclature**.
✓ **Example:** The Cα in amino acids (except glycine).



Not chiral, two stereogenic centers

2.5 (a) Stereochemistry

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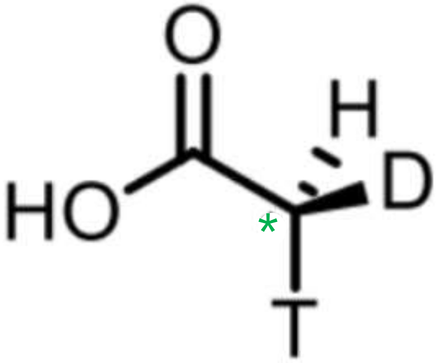
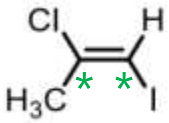


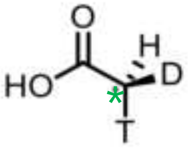
Chiral, one stereogenic center

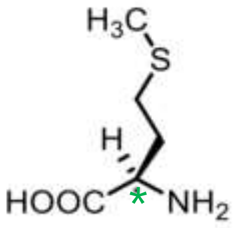
2.5 (a) Stereochemistry

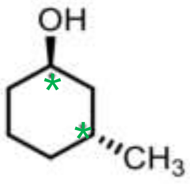
A) Which of the following compounds are chiral? Mark the stereogenic centers with an asterisk (*).

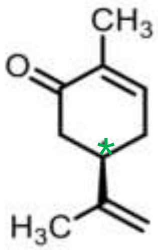
Repeat these steps for all molecules:

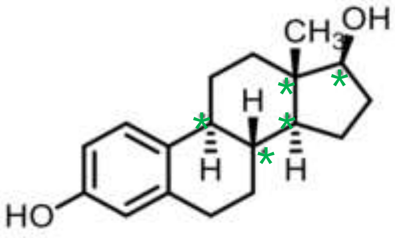












All chiral except the first molecule

2.5 Stereochemistry. Cahn-Ingold-Prelog (CIP) Priority Rules

1. Identify the Chiral Center

Find a **carbon bonded to four different groups**.

2. Assign Priorities by Atomic Number

Higher atomic number = higher priority (1 > 2 > 3 > 4). **Example:** Br (Z=35) > C (Z=6) > H (Z=1).

3. Resolve Ties by Comparing Directly Attached Atoms

If two groups have the **same first atom**, compare the next atoms in the chain. **Stop at the first difference**—do not evaluate the entire chain.

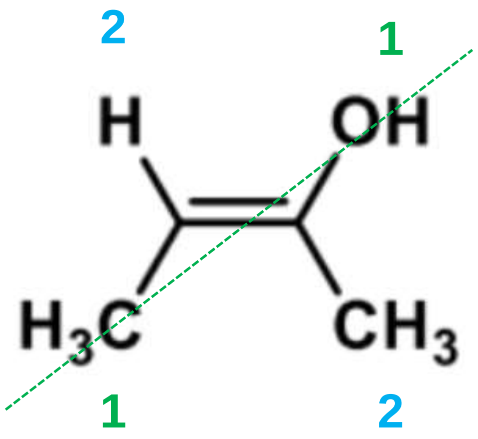
4. Determine R/S Configuration

Orient priority #4 (lowest) **away from view**.
Trace 1 → 2 → 3:

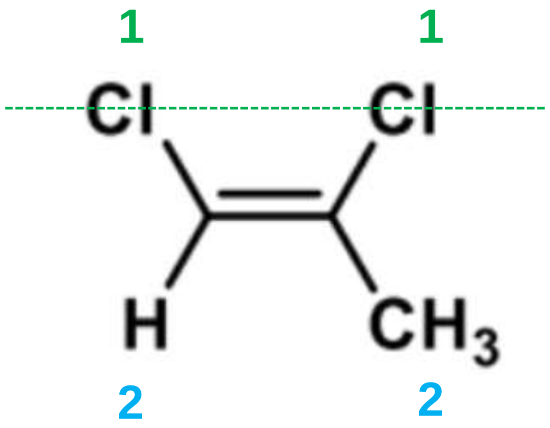
- **Clockwise = (R)**
- **Counterclockwise = (S)**

2.5 (b) Stereochemistry

Indicate the absolute configuration of all **stereogenic centers** and **double bonds** in the compounds shown below according to the **CIP convention** with R/S and E/Z, respectively.



Entgegen



Zusammen

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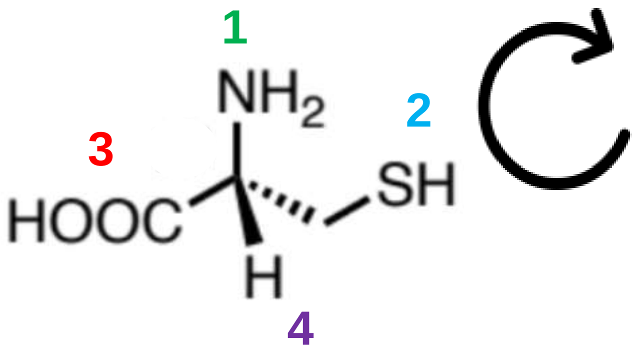
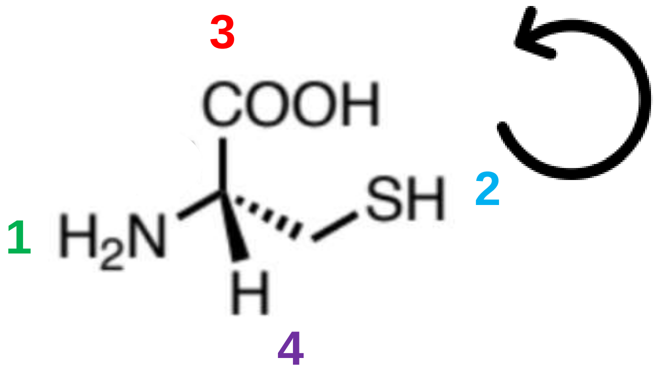


D-Cystein

Since H is pointing at us, this is an S-configuration



L-Cystein

Since H is pointing at us, this is an R-configuration

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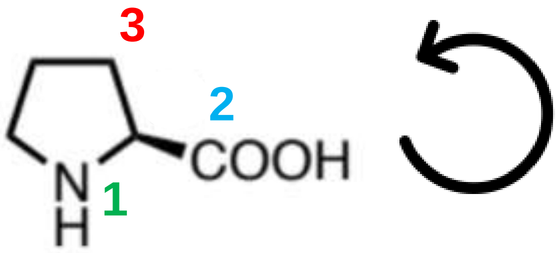
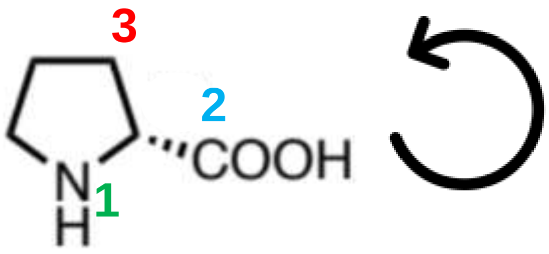


L-Prolin



D-Prolin

Since H is pointing away, this is an S-configuration

Since H is pointing at us, this is an R-configuration

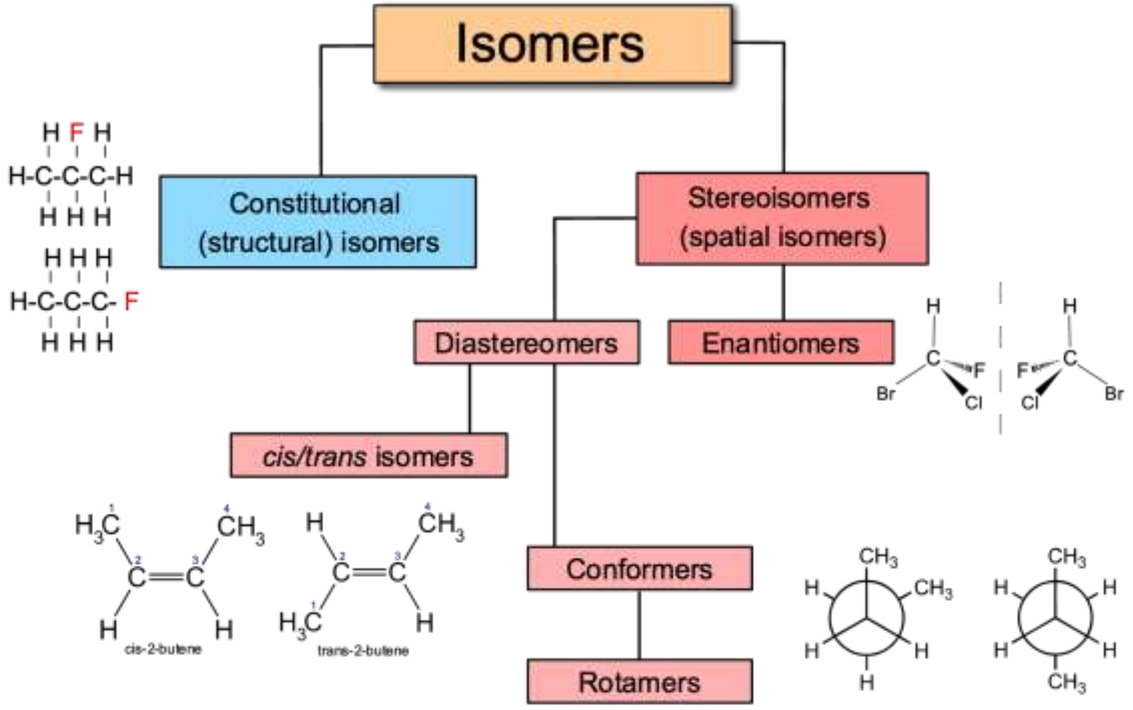
2.6 Stereochemistry – Types of Isomers

✓ **Isomers** → Same chemical formula, different arrangement

•**Constitutional (Structural) Isomers** → Different atom connectivity

•**Stereoisomers (Spatial Isomers)** → Same connectivity, different spatial arrangement

- **Enantiomers** → Mirror images, non-superimposable (stereocenters present)
- **Diastereomers** → Not mirror images



Isomers

Constitutional (structural) isomers

Stereoisomers (spatial isomers)

Diastereomers

Enantiomers

cis/trans isomers

Conformers

Rotamers

2.6 Stereochemistry - Isomers

Which of the following pairs of molecules are isomers? Indicate which kind of isomers (constitutional isomers, diastereomers or enantiomers) they are.

Diastereomers

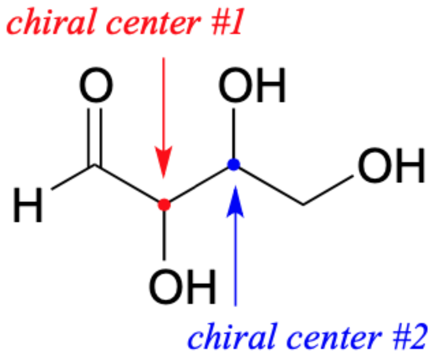
Constitutional Isomers

Enantiomers

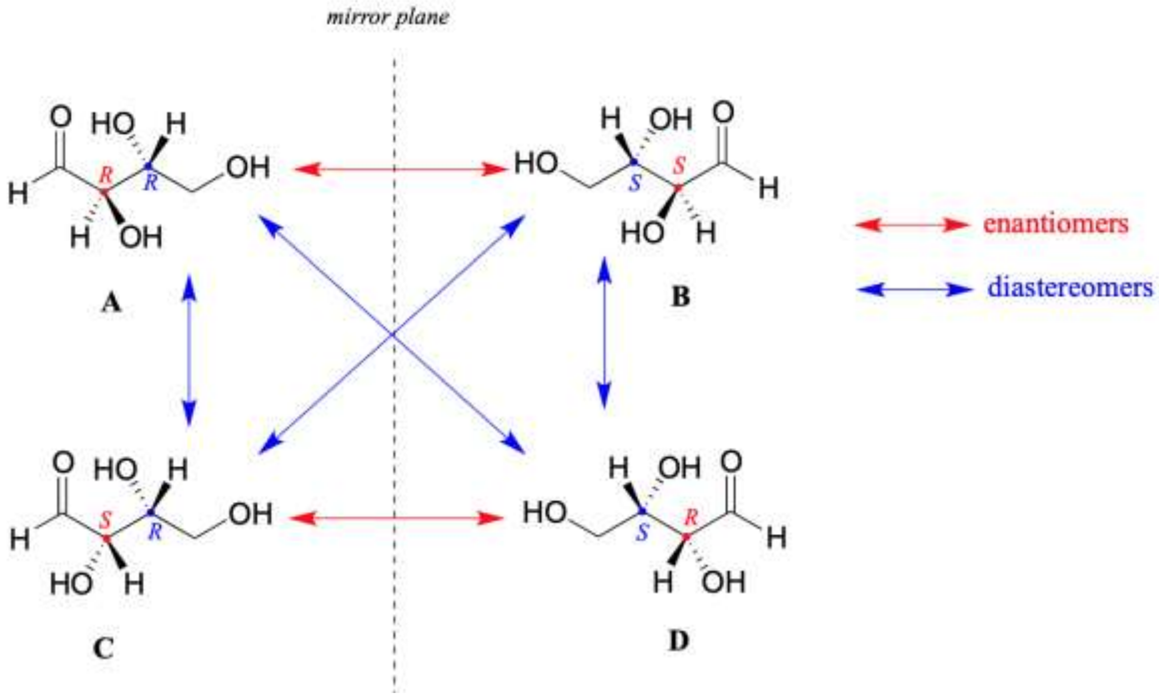
No Isomers

2.7 Compounds with multiple chiral centers

Example of a 4-carbon sugar



Different combinations of chiral centers

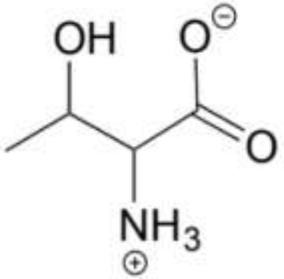


The four possible configurations:

RR
SS
RS
SR

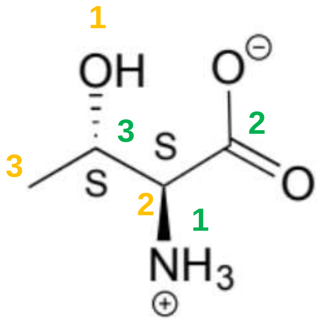
2.7 Compounds with multiple chiral centers

The structure of the amino acid D-threonine, drawn without stereochemistry, is shown below. D-threonine has the (S) configuration at both of its chiral centers. Draw D-threonine, it's enantiomer, and its two diastereomers.

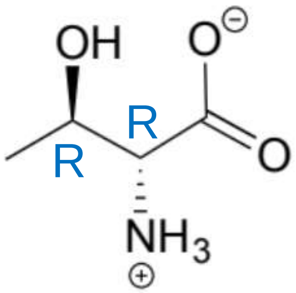


Step-by-Step Drawing Stereoisomers:

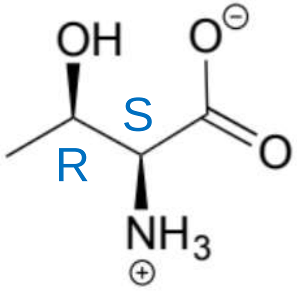
1. Identify stereogenic centers (chiral carbons, E/Z double bonds).
2. Draw the backbone in-plane, use wedges (out) and dashes (back) for 3D.
3. Assign priorities (CIP rules), swap wedge/dash for enantiomers.
4. For E/Z, place priority groups on the same (Z) or opposite (E) sides.
5. Check configurations, avoid symmetry mistakes, and label stereochemistry.



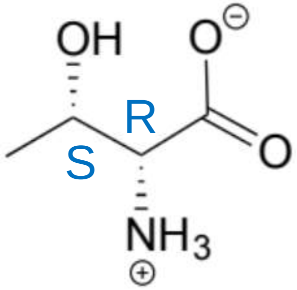
(D)-threonine



enantiomer of
(D)-threonine



diasteromer of
(D)-threonine

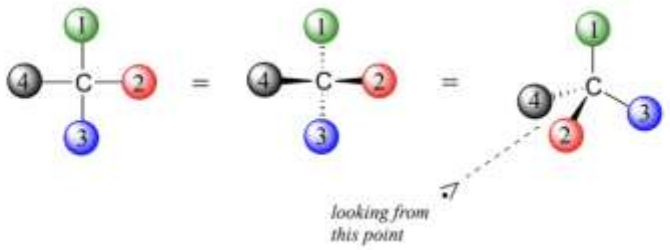


diasteromer of
(D)-threonine

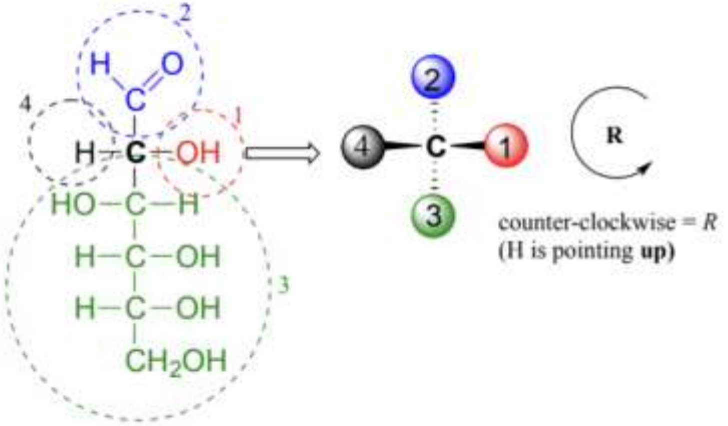
2.8 (a) Fischer and Haworth projections

Draw 'zigzag' structures (using the solid/dash wedge convention to show stereochemistry) for the sugars below. Label all stereocenters R or S.To make it easy to check your answers, draw your structures using the framework below.

Vertical bonds in Fischer point away (dashes), while horizontal bonds point toward us (wedges).

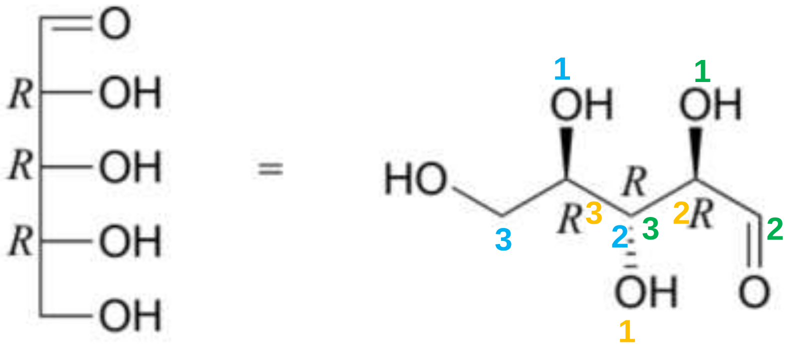


Hydrogen in Fischer projections is typically in front (horizontal bonds), meaning R/S rules are reversed.
Counterclockwise = R (since H is in front).
Clockwise = S (since H is in front).



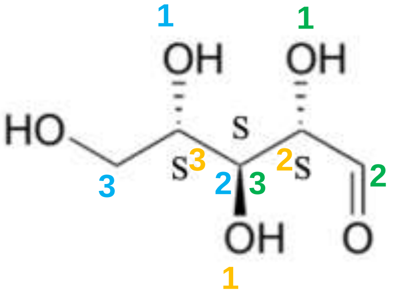
Shortcut for Fischer → R/S Assignment

✓ OH on the right → (R) (if H is on the horizontal).
✓ OH on the left → (S) (if H is on the horizontal).



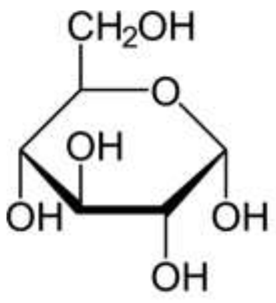
D-ribose

S-ribose =

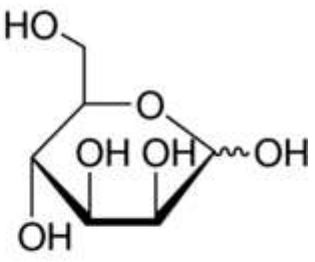


2.8 (b) Fischer and Haworth projections

Convert the following Haworth projections into their chair conformations.

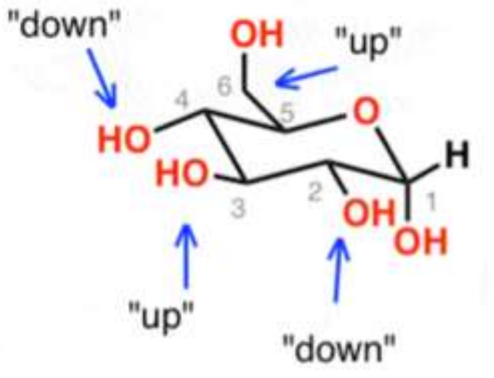


D-Glucose

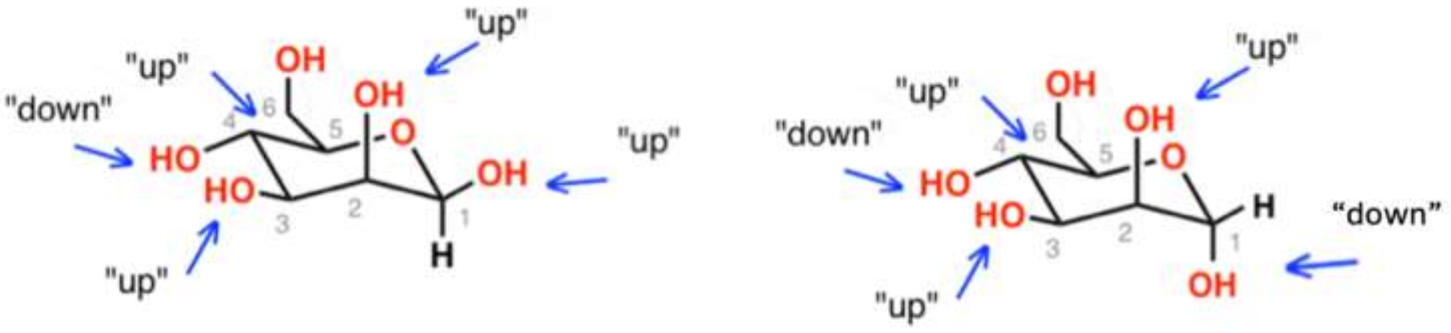


D-Mannose

The most stable chair form places C1 at the bottom right, ensuring that the maximum number of OH groups occupy equatorial positions, minimizing steric strain.



D-glucose



D-mannose