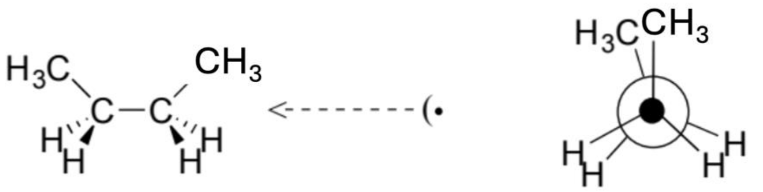
2.1 Newman projections

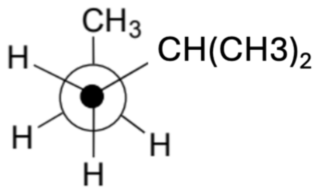
a) Draw the Newman projections of the lowest-energy and highest-energy conformations of butane when looking down the C2-C3 bond. Which conformation is more stable? Explain your answer.



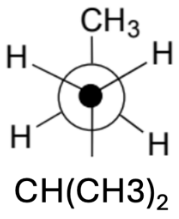
highest energy
(eclipsed)

The staggered conformation is more stable than eclipsed because it minimizes steric hindrance and torsional strain. In the eclipsed conformation, electron clouds of bonds overlap, causing repulsion, while in staggered, bonds are maximally separated, reducing energy.

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?



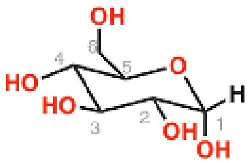
gauche

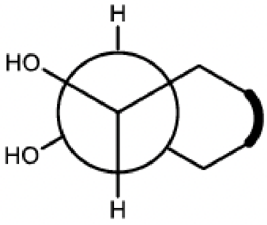


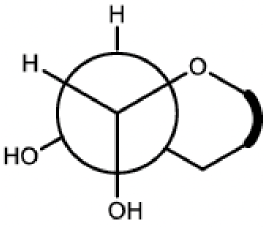
anti

The anti conformation is more stable than gauche because it minimizes steric hindrance and torsional strain. In gauche, bulky groups are closer (≈60°), causing repulsion, while in anti (180°), they are far apart, reducing energy and increasing stability.

c) Draw a Newman projection of α-D-glucose along the bond between C3 and C4 and along C1 and C2.

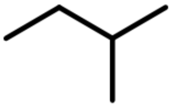






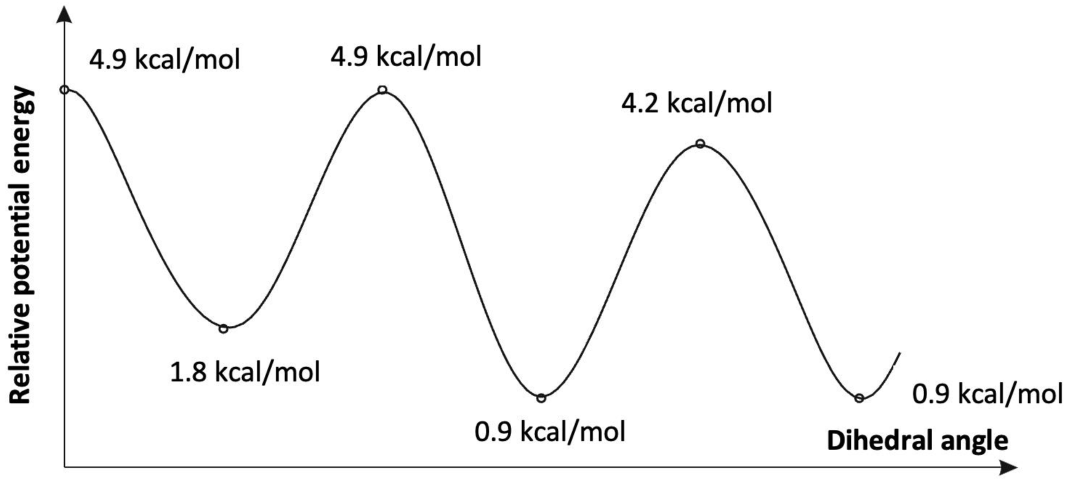
2.2 Conformational energies

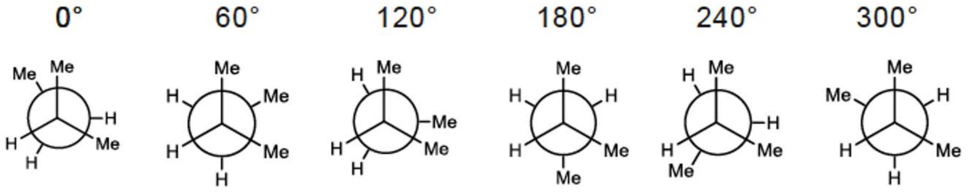
a) Draw the conformations for 2-methylbutane as Newman projections along the bond between C2 and C3 for the dihedral angles 0°, 60°, 120°, 180°, 240° and 300° in the energy diagram below. Estimate the relative energies of all conformations. To do this, create an energy diagram on which the relative potential energies of the respective conformations are plotted against the dihedral angle.



Keep in mind the following table of conformational energies:

Conformer	Energy / kcal mol-1
H ecliptic to H	1
H ecliptic to Me	1.4
Me ecliptic to Me	2.5
Me gauche to Me	0.9

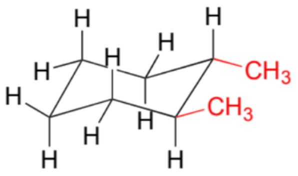




2.3 Chair conformations of cyclohexane

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

a) trans-1,2-dimethylcyclohexane



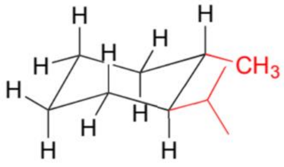
Draw the alternative chair conformation. Compare the energies of the two conformations.

An alternative chair conformation would imply two axial methyl groups, which is less favorable than two equatorial methyl groups because axial methyl groups experience 1,3-diaxial interactions, leading to steric hindrance. In contrast, equatorial methyl groups avoid these clashes, making the conformation more stable.

Which molecule, trans-1,2-dimethylcyclohexane or trans-1,3-dimethylcyclohexane, has a greater energy difference between its two chair conformations?

Trans-1,2-dimethylcyclohexane has a greater energy difference because one chair form has both methyl groups equatorial (stable), while the other has both axial (unstable due to 1,3-diaxial interactions). In trans-1,3-dimethylcyclohexane, each conformation has one axial and one equatorial methyl, keeping the energy difference smaller.

b) trans-1-isopropyl-2-methylcyclohexane



trans-1-isopropyl-2-methylcyclohexane

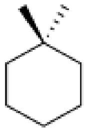
Draw the alternative chair conformation. Compare the energies of the two conformations.

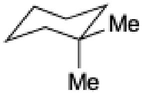
Which molecule, trans-1-isopropyl-2-methylcyclohexane or cis-1-isopropyl-2-methylcyclohexane, has a greater energy difference between its two chair conformations?

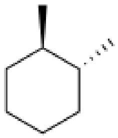
In trans-1-isopropyl-2-methylcyclohexane, the two substituents are either both axial (diaxial) or both equatorial (diequatorial). In cis-1-isopropyl-2-methylcyclohexane, one is axial, and the other is equatorial. The energy difference between the diaxial and diequatorial conformations is greater.

2.4 Energetically Favorable Chair Conformations

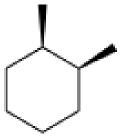
Draw the most energetically favorable conformations of the following molecules:



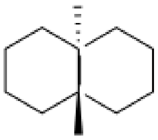


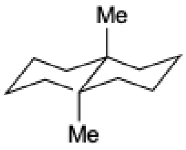


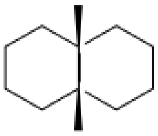
Both Me equatorial

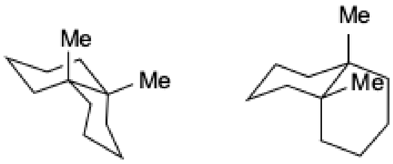


Both conformations are equally stable







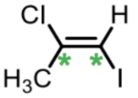


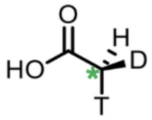
Both conformations are equally stable

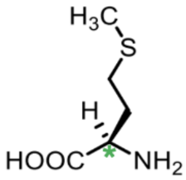
2.5 Stereochemistry

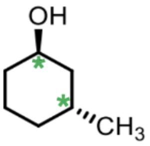
a) Which of the following compounds are chiral? Mark the stereogenic centers with an asterisk (*).

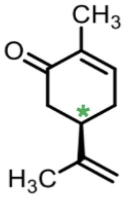
All but the first compound are chiral.

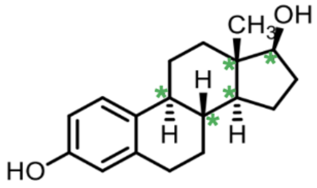




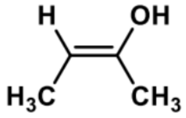




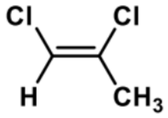




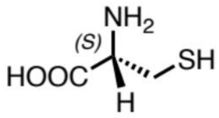
b) Indicate the absolute configuration of all stereogenic centers and double bonds in the compounds shown below according to the Cahn-Ingold-Prelog priority rules with R/S and E/Z, respectively.



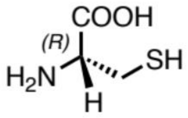
E



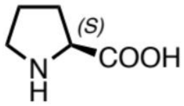
Z



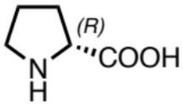
D-Cystein



L-Cystein



L-Prolin



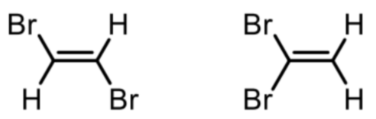
D-Prolin

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



Constitutional Isomers

Enantiomers

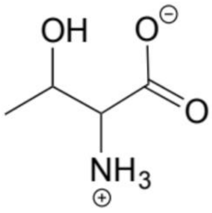
No Isomers

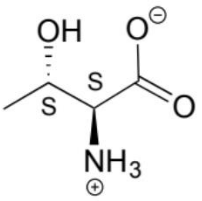
Enantiomers

Constitutional Isomers

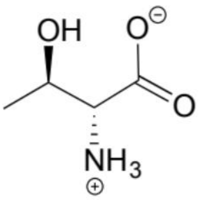
Diastereomers

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.

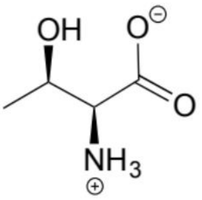




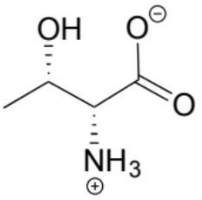
(D)-threonine



enantiomer of
(D)-threonine



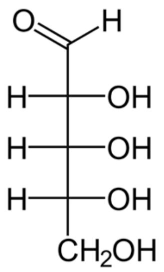
diasteromer of
(D)-threonine



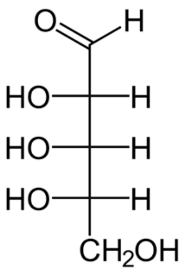
diasteromer of
(D)-threonine

2.8 Fischer and Haworth projections.

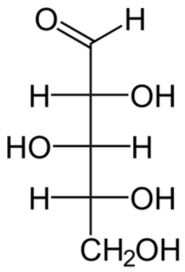
a) Draw 'zigzag' structures (using the solid/dash wedge convention to show stereochemistry) for the sugars below. Label all stereocenters R or S.To make it easy to check your answers, draw your structures using the framework below.



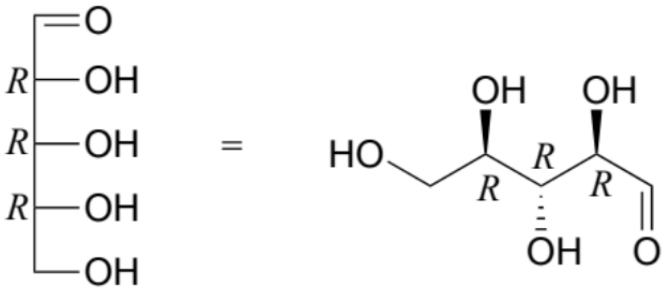
D-Ribose



L-Ribose



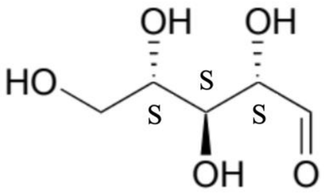
D-Xylose

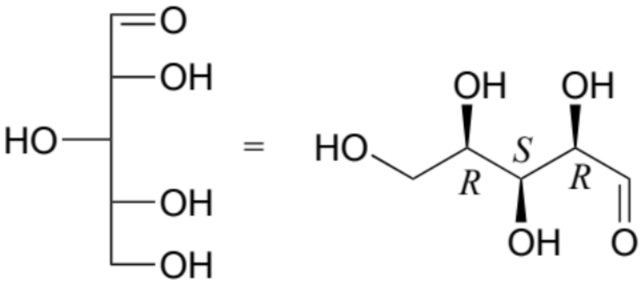


D-ribose

The alternation happens because, in a Fisher projection, all horizontal groups point toward the viewer, but when converting to a zig-zag form, each carbon adopts a tetrahedral shape, naturally flipping the orientation of its substituents. As a result, OH groups that were all on the right in Fisher end up alternating down-up-down in the zig-zag structure due to the spatial arrangement of carbon atoms.

D-Ribose and L-Ribose are enantiomers, so if D-ribose is RRR, then L-ribose must be SSS:

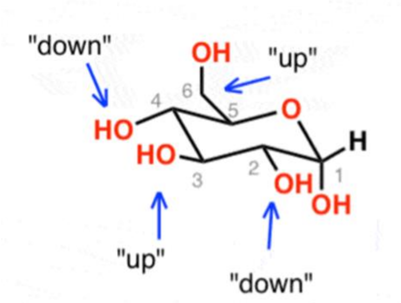




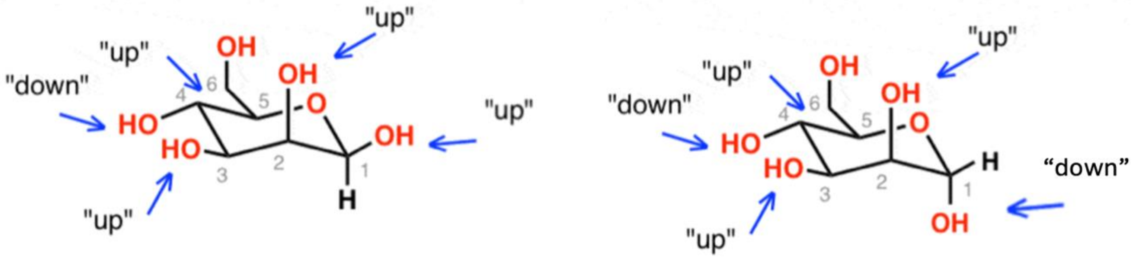
D-xylose

b) Convert the following Haworth projections into their chair conformations.

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