

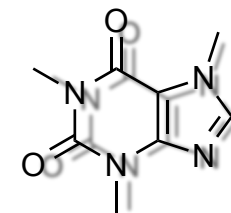
Chemistry 2500

Chapter 4

Stereochemistry

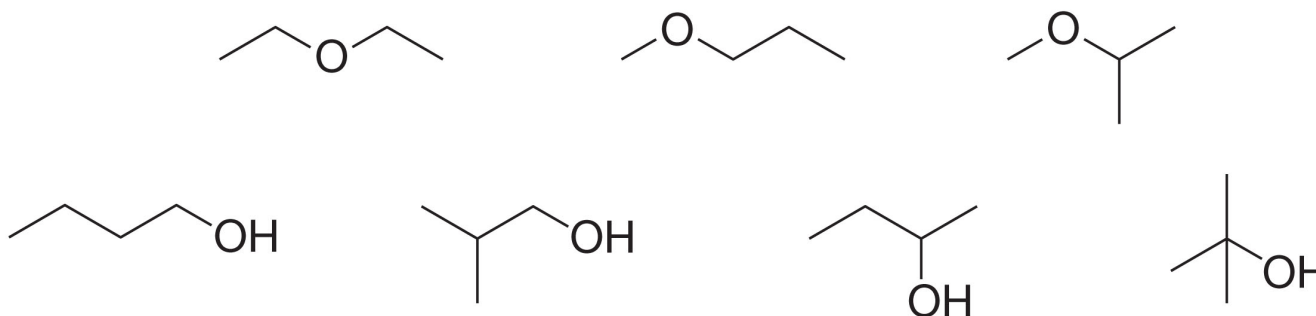
(sections 4.1-12 excluding 4.10 and 4.11)

Constitutional Isomers



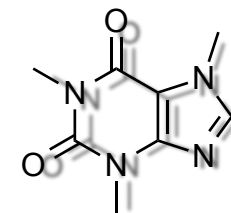
- The way that atoms are connected in a molecule determines the properties and chemical behavior of that molecule.
- A given set of atoms can usually be connected in more than one way giving rise to *isomers*.
- ***Constitutional isomers***: same molecular formula, different connectivity.

Seven constitutional isomers of $C_4H_{10}O$

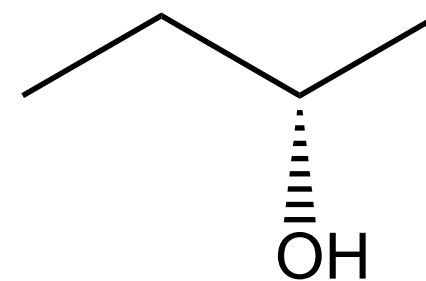
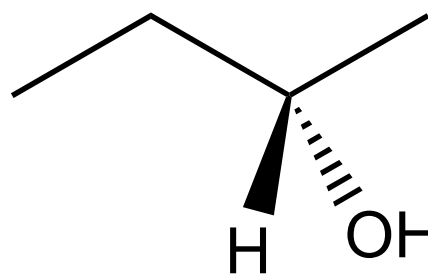
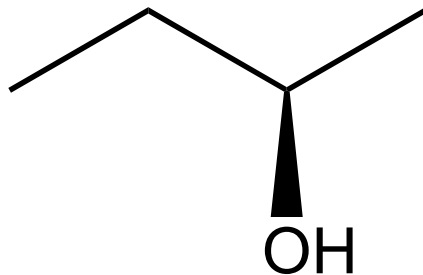
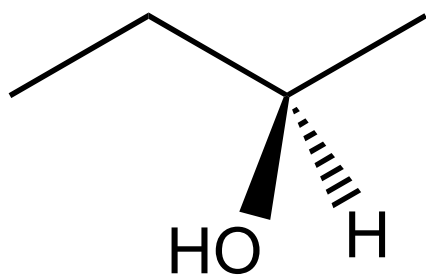


- Constitutional isomers are different molecules and have distinct physical and chemical properties.

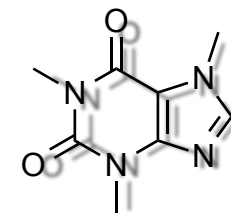
Stereoisomers



- ***Stereoisomers***: same molecular formula, same connectivity, different arrangement of atoms in space.
- The different 3-dimensional arrangement of stereoisomers are called ***Configurations***. The configuration of a molecule is permanent.
- The configuration of atoms in 3 dimensions is represented by on paper with solid wedge bonds (projecting out of the page) and dashed bonds (projecting into the page).

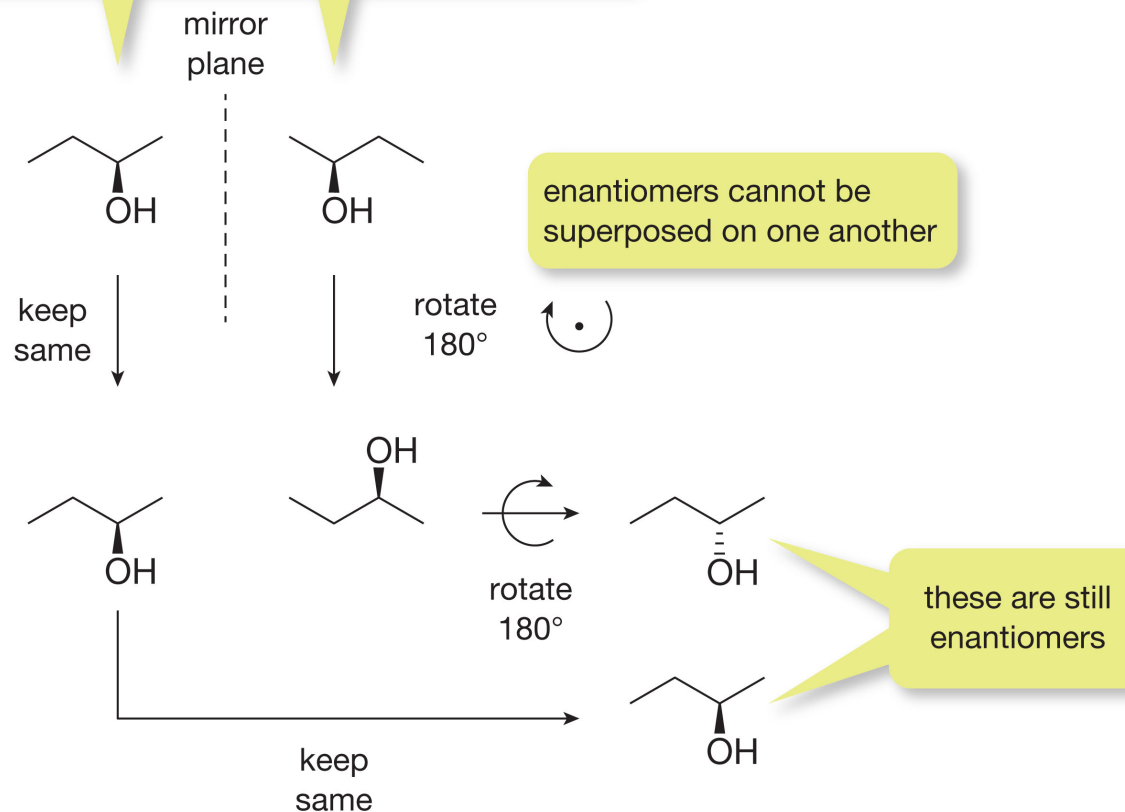


Stereoisomers

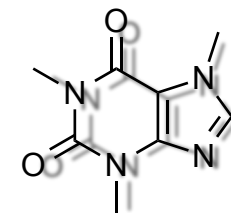


- ***Enantiomers*** are stereoisomers that are non-super(im)posable mirror images of one another.

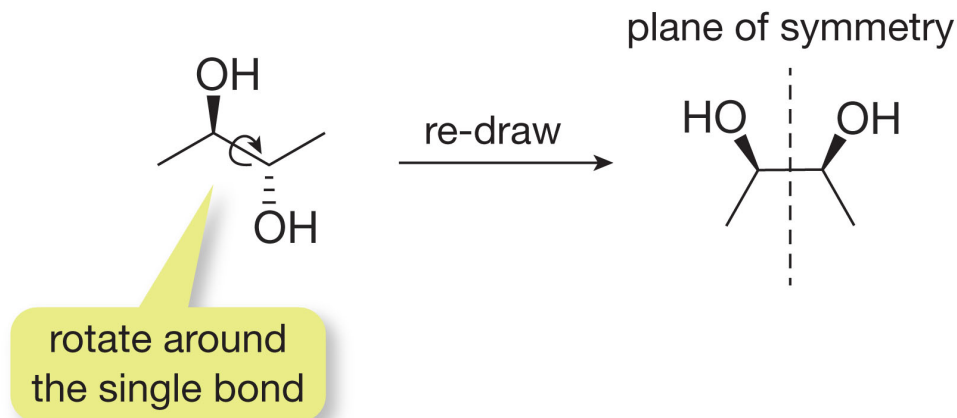
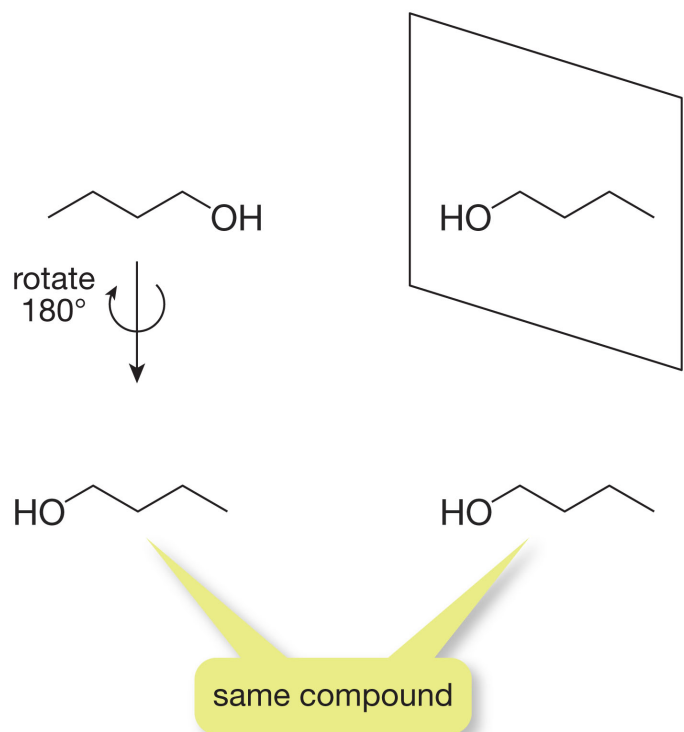
2-butanol can exist as non-superposable mirror images



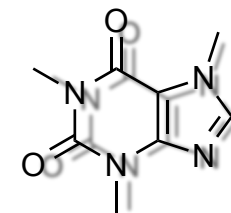
Stereoisomers



- Enantiomers are **chiral** molecules. **Chirality** is the property of objects such that they are non-super(im)posable on their mirror image.
- **Achiral** objects are super(im)posable on their mirror images. If an object has a plane of symmetry, it is achiral.

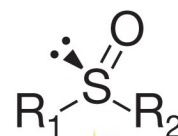
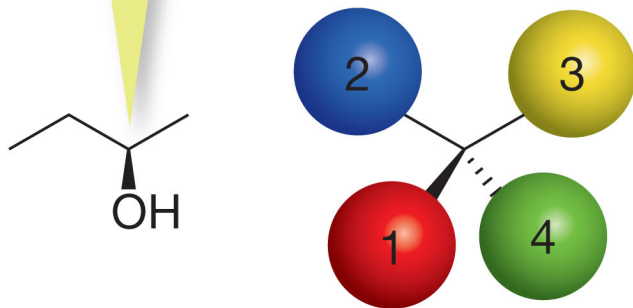


Chirality Centres

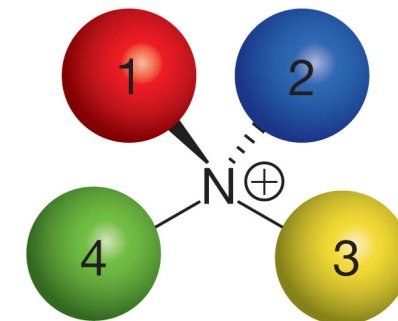
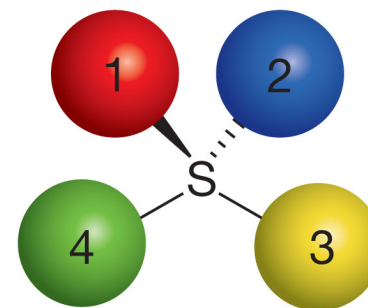


- Atoms (typically carbon) that are connected to 4 different groups can give rise to chiral molecules. These atoms are called ***stereocenters*** (asymmetric-, chiral-, or stereogenic centres).

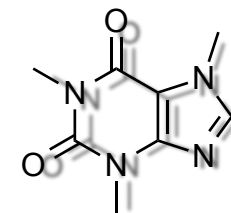
chirality centre (fourth group is H)



chirality centre (fourth group is lone pair of electrons)

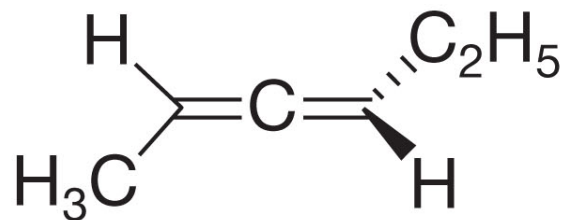


Chirality Centres



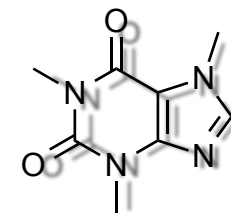
- Molecules can also be chiral even though they don't have any chiral centres.
- These molecules are chiral because they have features that prevent full rotation of some bonds.

chiral allene

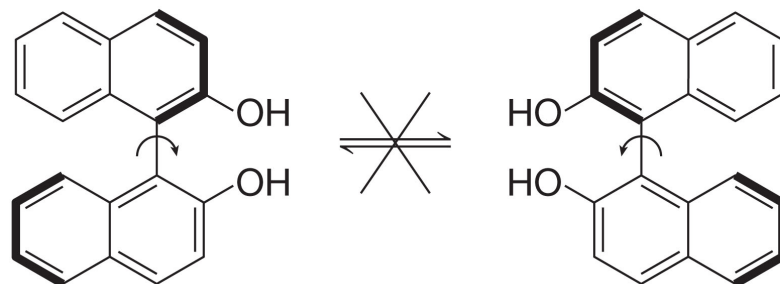


The π bonds in this molecule are 90° to each other. This locks a twist into the molecule and the two mirror images cannot superpose.

Chirality Centres



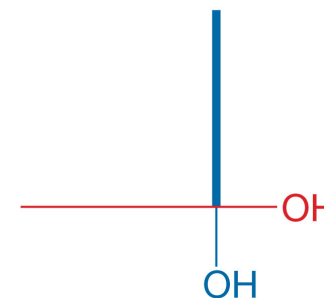
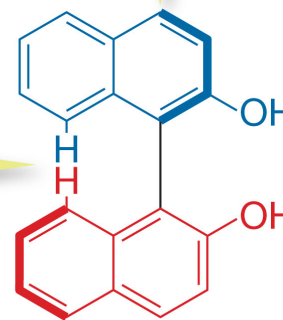
- These molecules are chiral because they have features that prevent full rotation of some bonds.



Binol exists as non-superposable mirror images because the single bond connecting the rings cannot rotate through 360° .

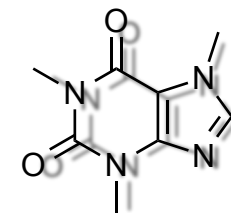
Viewing the molecule along the single bond from this direction (top view) shows the butterfly shape.

Ring hydrogens collide, preventing full rotation. The molecule exists in a chiral butterfly shape.

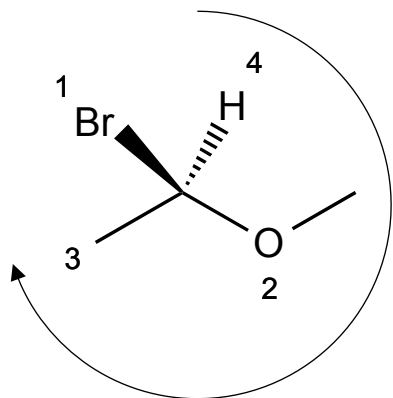


top view

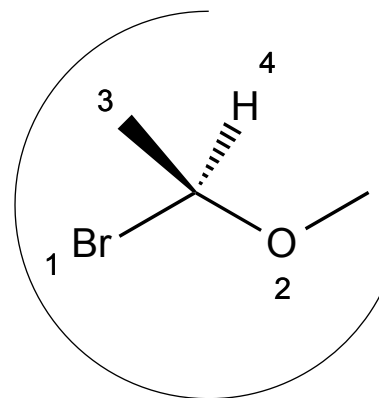
Cahn-Ingold-Prelog Nomenclature



- The Cahn-Ingold-Prelog system is used to describe the absolute configuration of a chirality centre.
 - Assign priorities (e.g. 1-4) to the substituents directly attached to the chiral centre
 - Orient the molecule such that the lowest priority group is pointing away from you.
 - If the remaining substituents are arrayed 1-2-3 in clockwise order, then the chiral centre is designated ***R***. If the substituents are arrayed in counterclockwise order, the chiral center is designated ***S***.

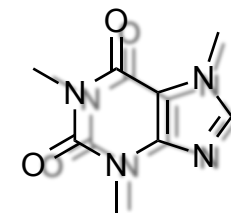


R



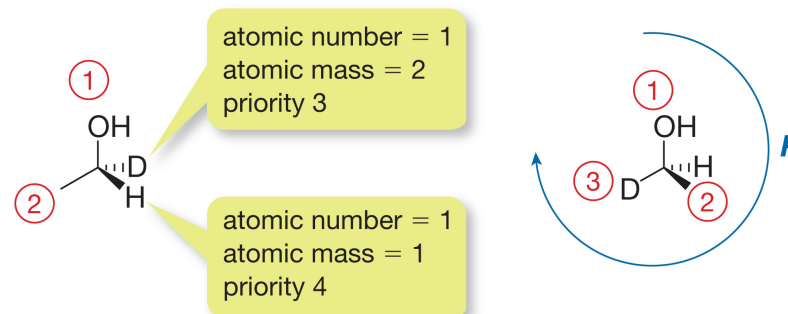
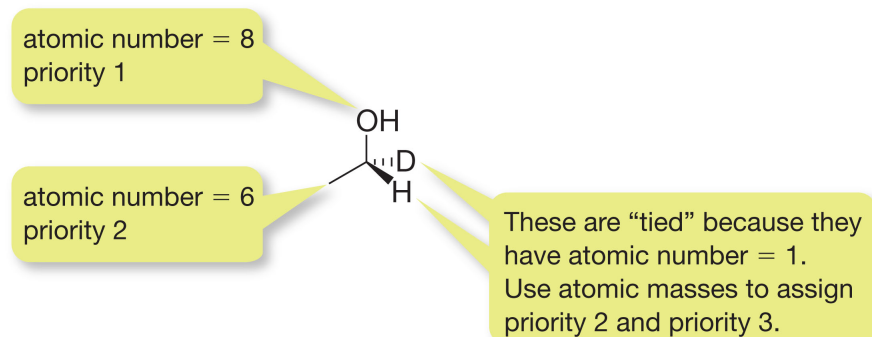
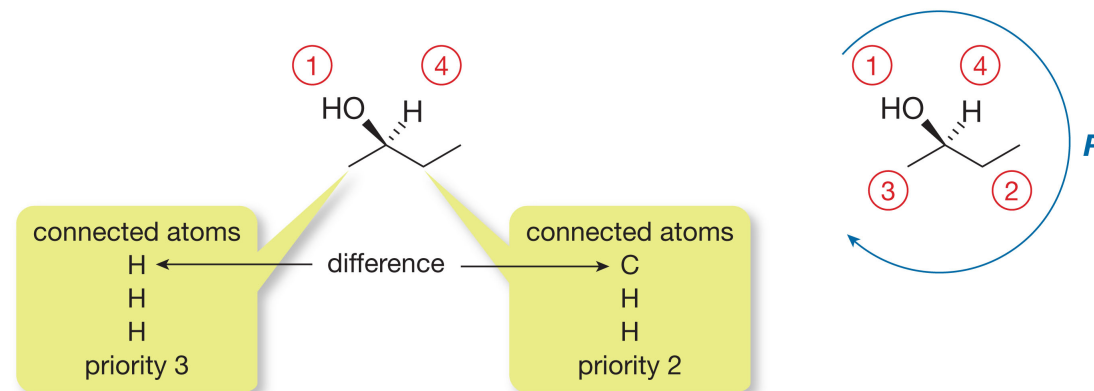
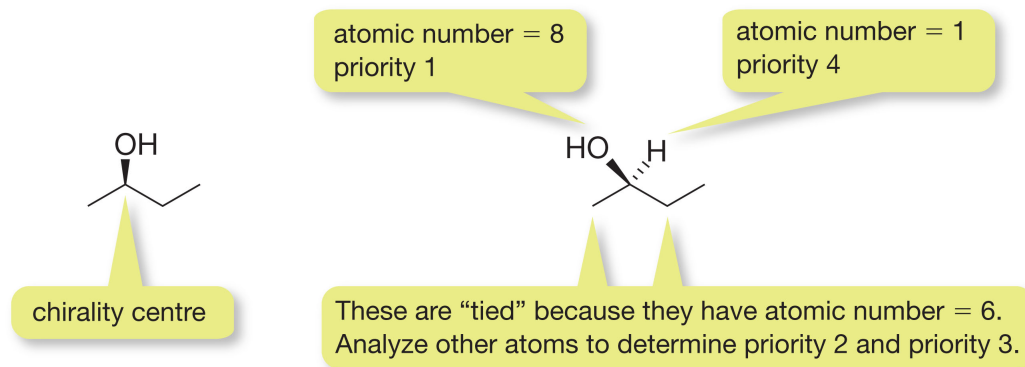
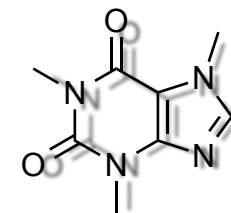
S

Cahn-Ingold-Prelog Substituent Priority

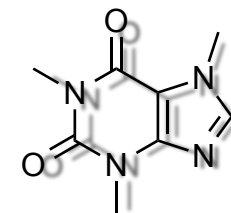


- The priority of the substituents attached to the chiral centre is based on the atomic numbers (Z) of the atoms directly attached to the centre.
 - The atom with the highest Z is assigned the highest priority; the atom with the second highest Z is assigned second priority, and so on.
 - For atoms with the same Z , the heavier isotope has higher priority (^{13}C vs ^{12}C).
 - If the atoms are tied in priority, then move out to the atoms immediately adjacent to the ones directly attached to the chiral centre, and list them in decreasing Z . The group with the highest Z at the *first point of difference* has the higher priority.
 - If a substituent contains π -bonds, interpret them as multiple σ -bonds between the same atoms (e.g. an aldehyde has a carbon which is bonded to 2 oxygen atoms and 1 hydrogen atom).
 - Electron pairs have an atomic number (Z) of 0.

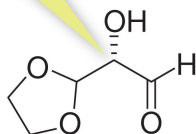
Cahn-Ingold-Prelog Nomenclature



Cahn-Ingold-Prelog Nomenclature

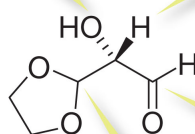


chirality centre



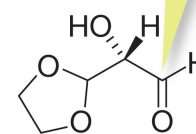
atomic number = 8
priority 1

atomic number = 1
priority 4

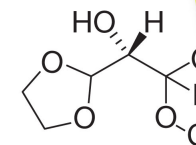


These are "tied" with
atomic number = 6.
Use next atoms to
assign priority 2 and
priority 3.

This atom is connected to an oxygen by the π bond;
duplicate a phantom oxygen atom.



becomes:



This atom is connected to a carbon by the π bond;
duplicate a phantom carbon atom.

connected atoms

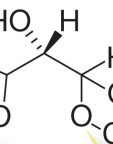
O
O
H

tie
tie
tie

connected atoms

O
O
H

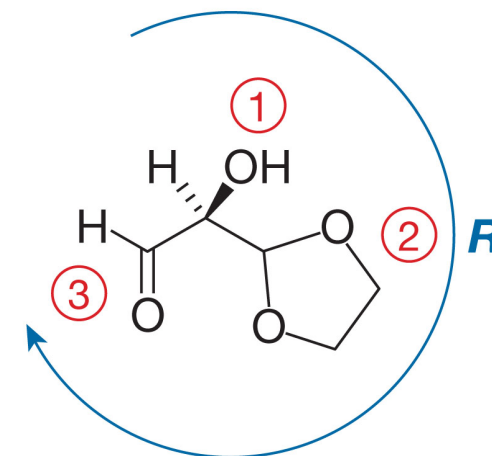
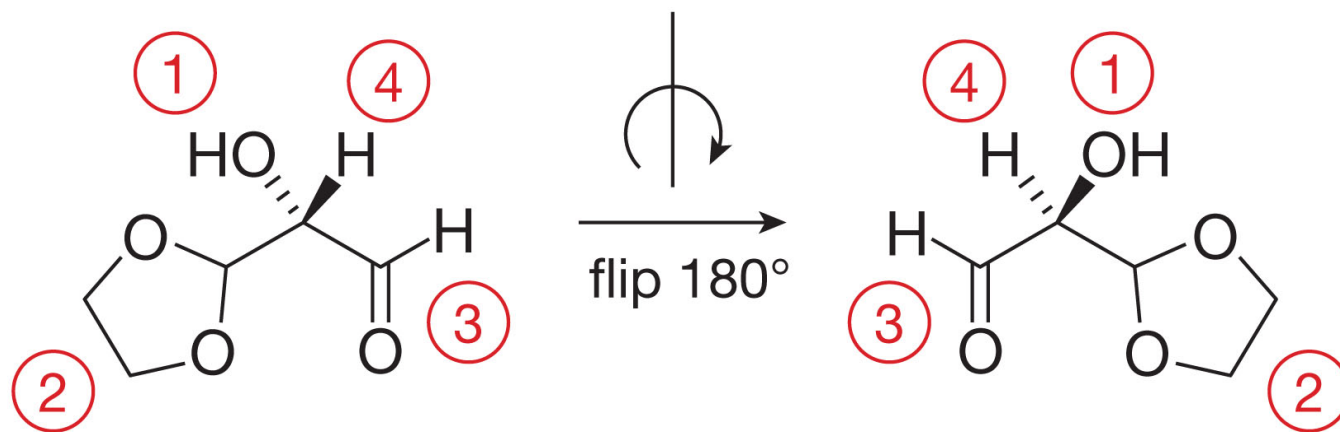
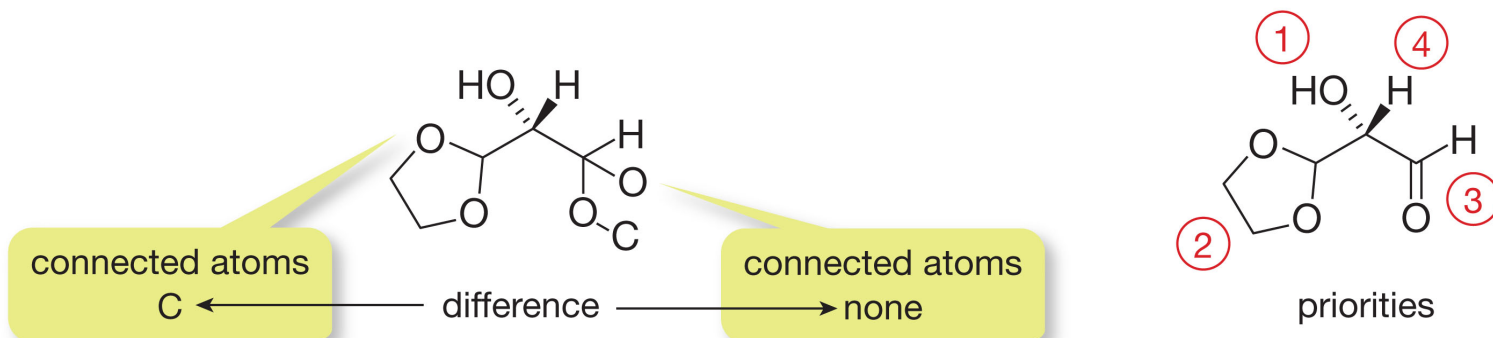
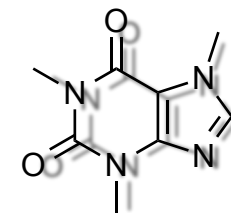
connected atoms
C



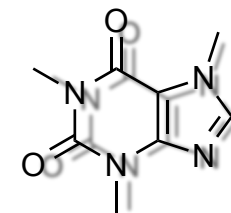
connected atoms
C

tie

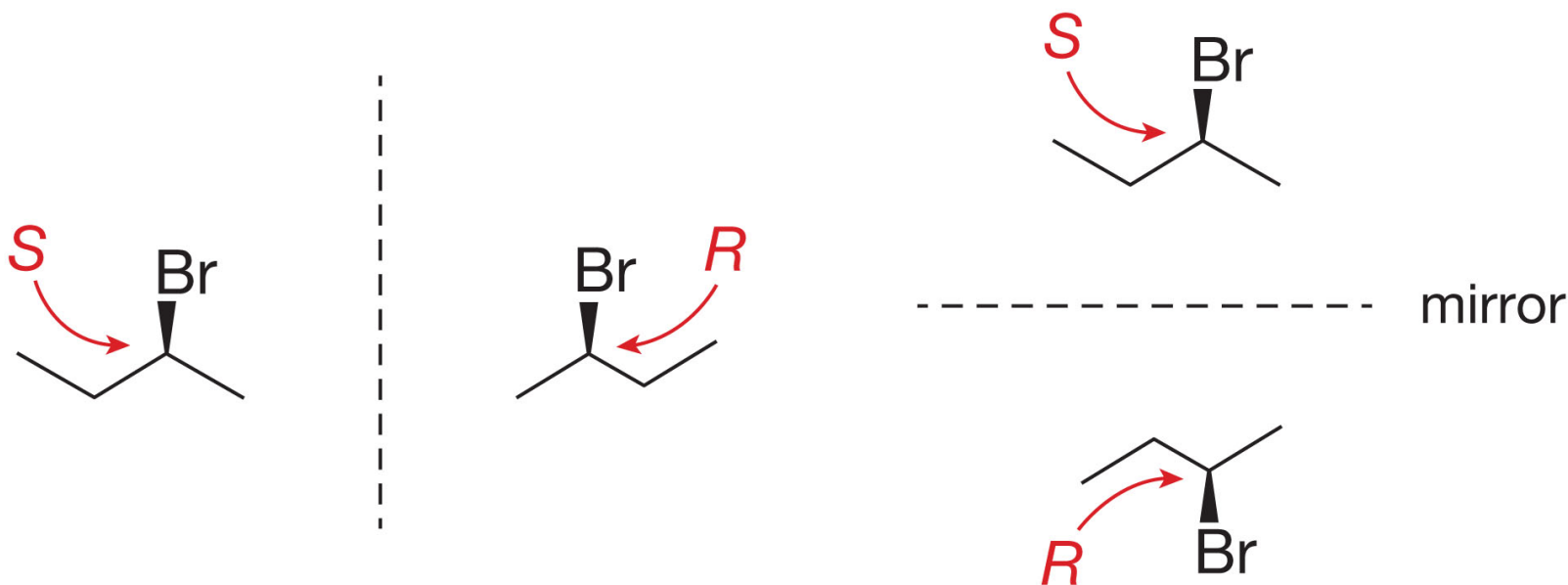
Cahn-Ingold-Prelog Nomenclature



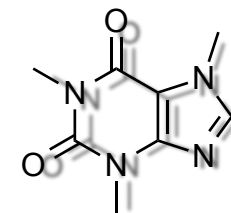
Drawing Enantiomers



- There are several techniques used to represent and compare enantiomers.
- 1. Use a mirror plane to reflect the molecule:



Drawing Enantiomers

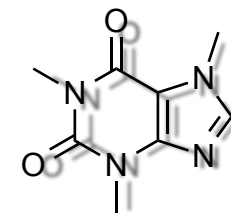


- There are several techniques used to represent and compare enantiomers.
- 2. Invert the configuration of the chiral centre by changing the dash/wedge bond:



backbone zig-zags remain the same

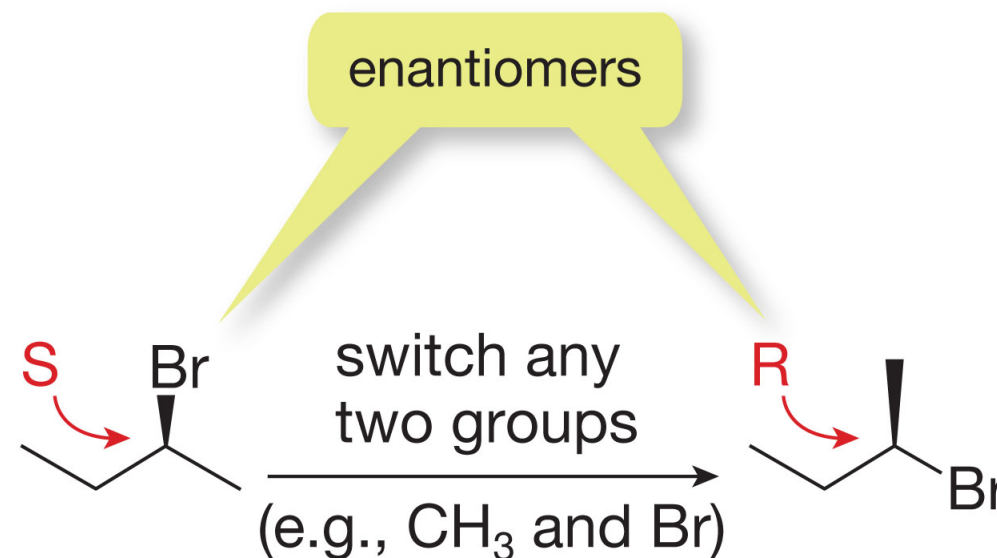
Drawing Enantiomers



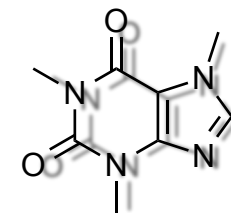
- Pay attention to the implications of switching 2 groups at a chiral centre; exchanging *any 2 groups* will invert the configuration.



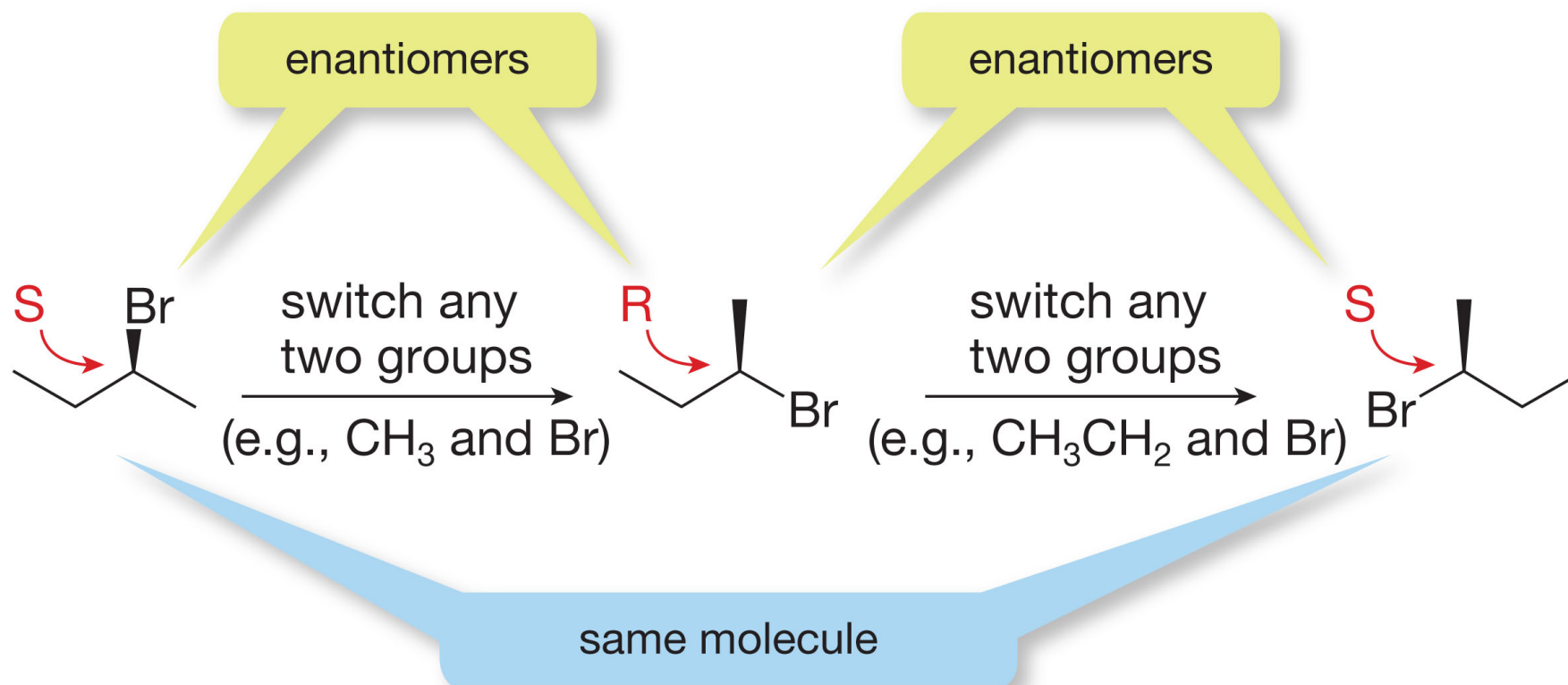
backbone zig-zags remain the same



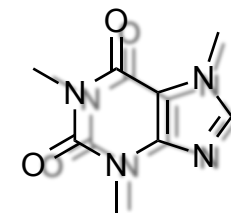
Drawing Enantiomers



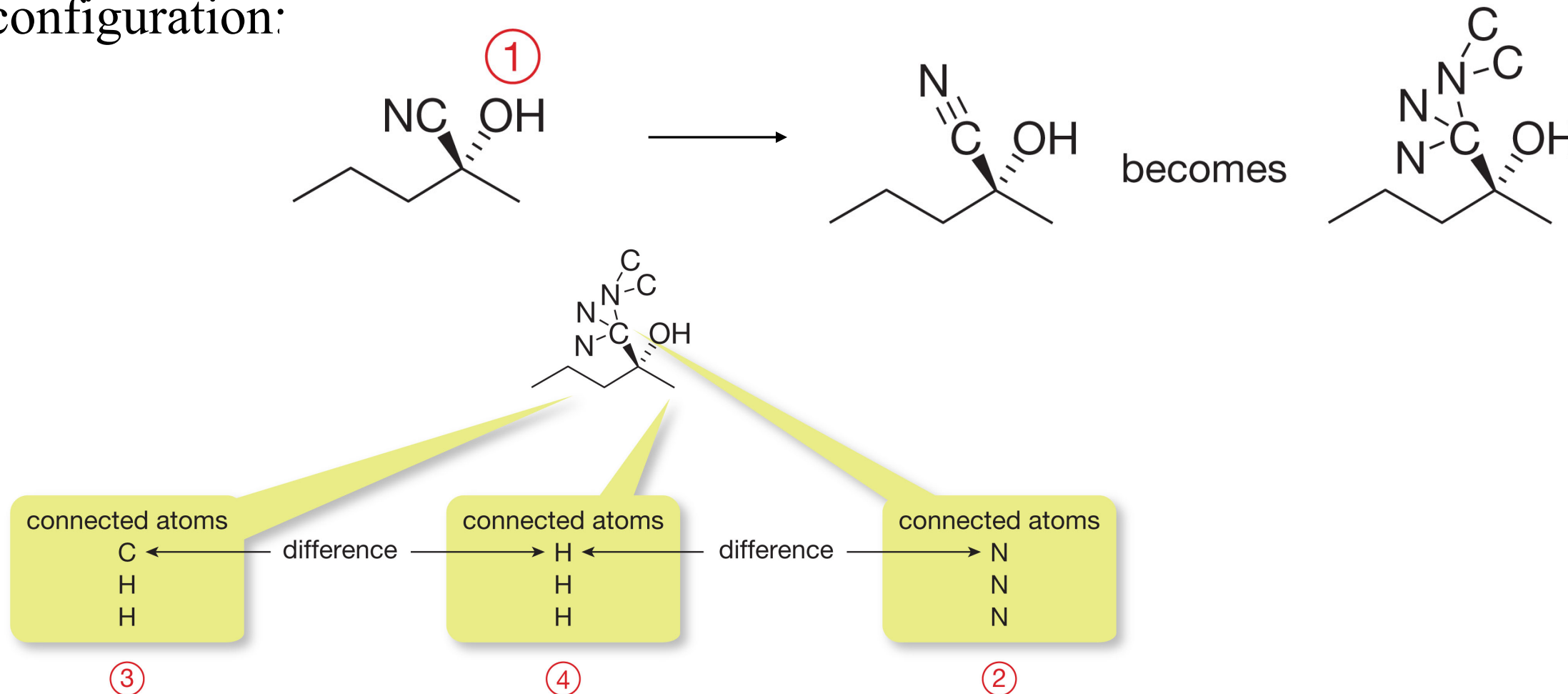
- *2 sequential* exchanges (double exchange) at a chiral centre will generate a new representation of that centre:



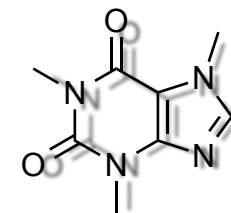
Drawing Enantiomers



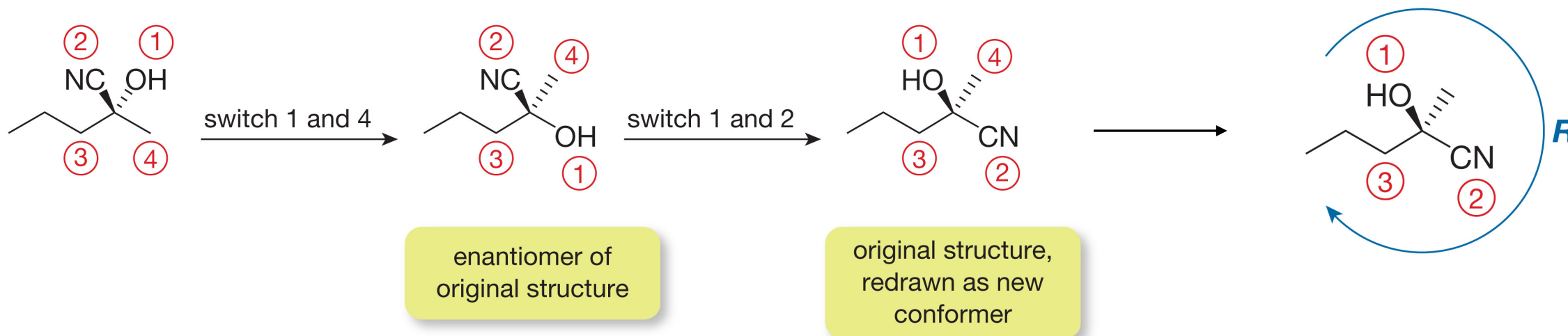
- Using double exchanges is a powerful method in assigning absolute configuration:



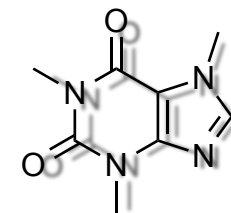
Drawing Enantiomers



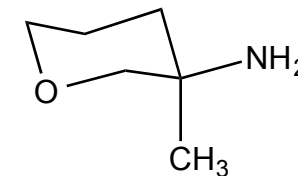
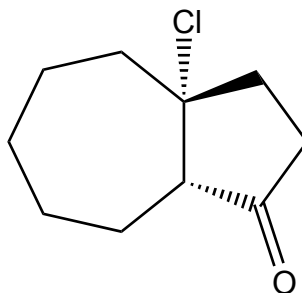
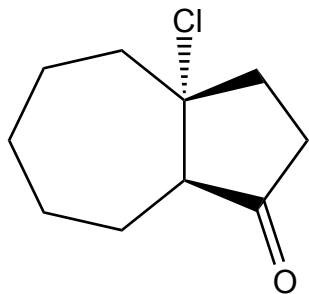
- Using double exchanges is a powerful method in assigning absolute configuration:



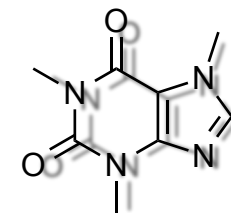
Assigning R/S



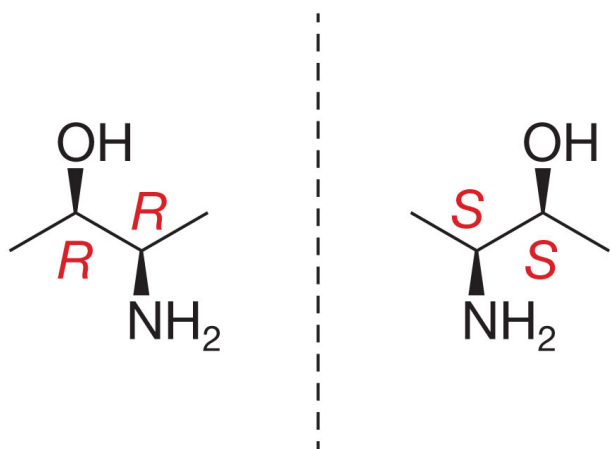
- For each of the following molecules, identify all the stereocentres and assign their absolute configuration (R/S).



Diastereomers

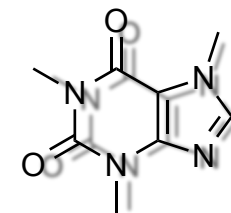


- Molecules often contain more than one chiral centre.
- Multiple chiral centres in a molecule can give rise to a new type of stereoisomer, *diastereomers*.
- ***Diastereomers*** are stereoisomers that are non-super(im)posable, non-mirror images of one another.
- Inverting all the stereocentres in a molecule creates the mirror image of the molecule; its *enantiomer*.

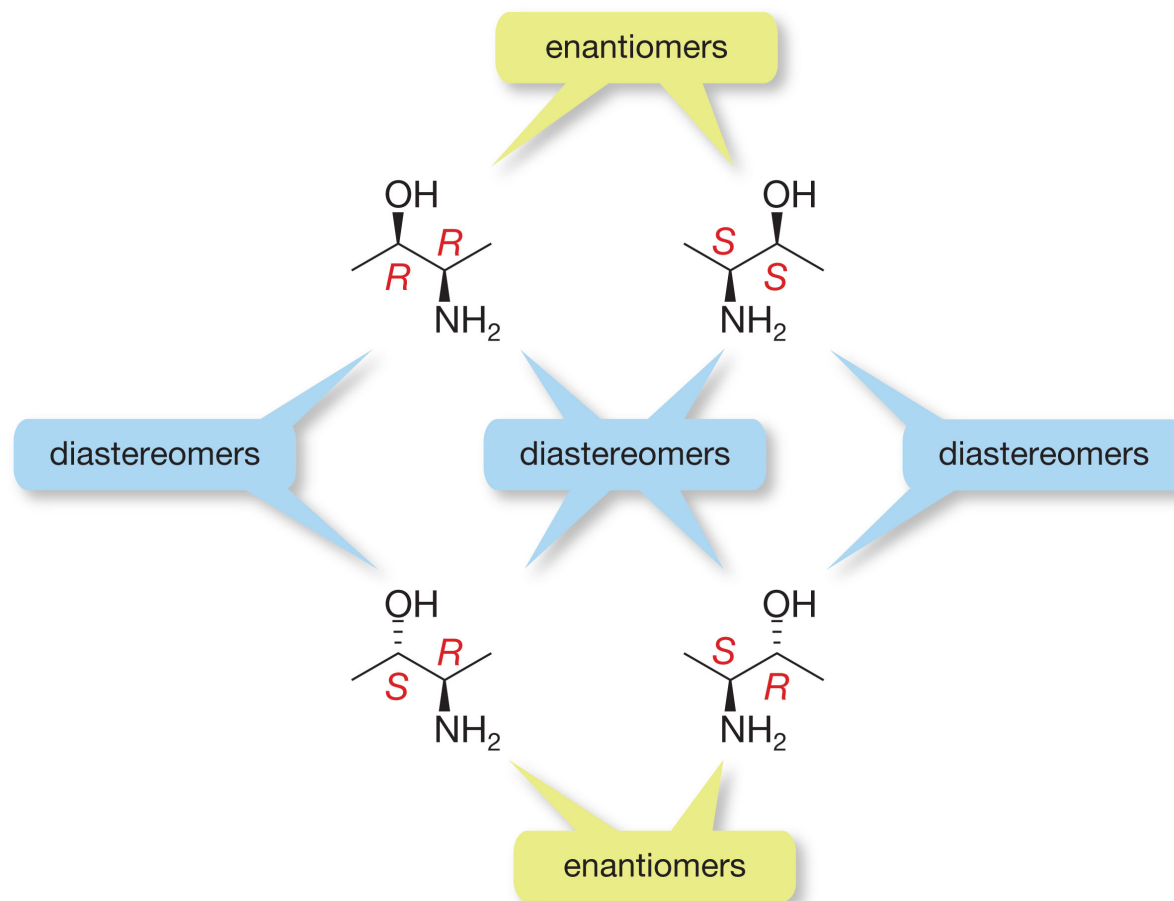


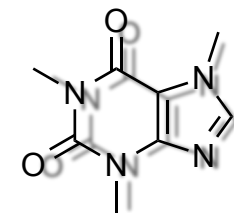
changing the configuration of all the stereocentres creates the mirror image (a pair of enantiomers)

Diastereomers



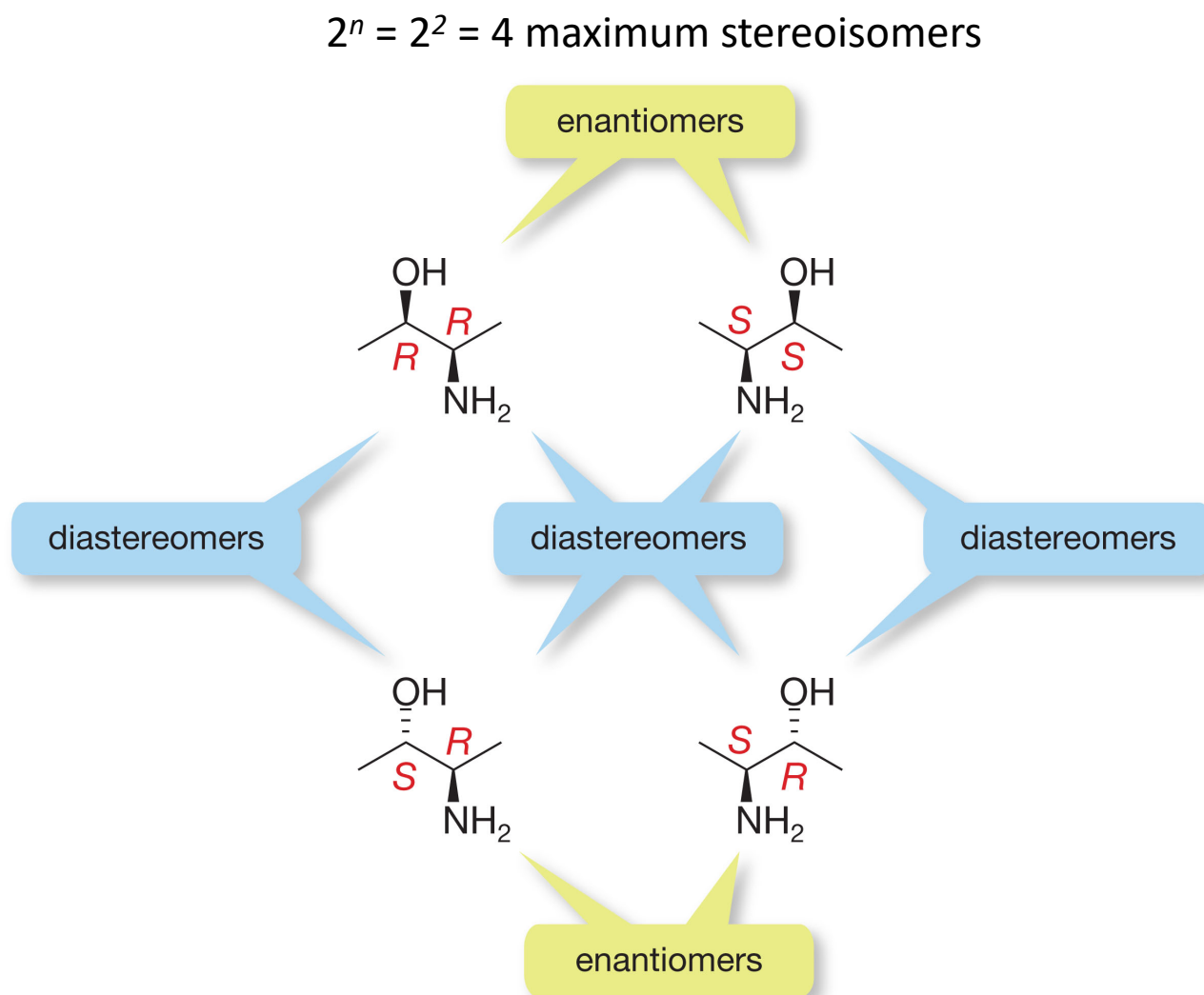
- Inverting some of the stereocentres in a molecule produces a *diastereomer*. Notice that the diastereomers are non-mirror images of each other.



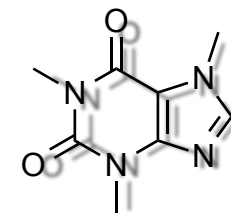


Estimating the Number of Stereoisomers

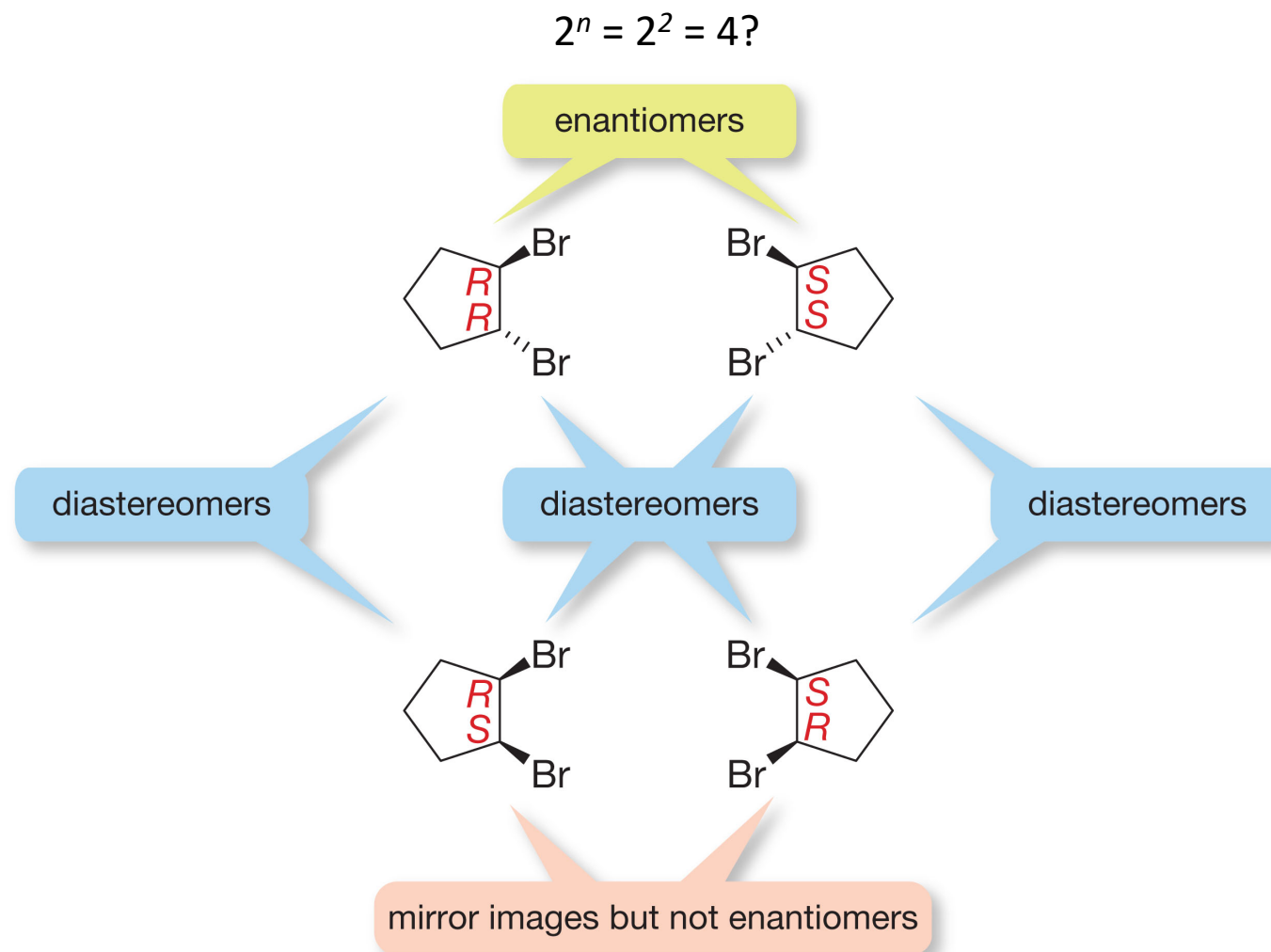
- The *maximum* number of stereoisomers can be estimated by 2^n , where n = the number of stereocentres.
- This formula predicts a maximum, because for some compounds, certain configurations produce identical molecules, reducing the actual number of stereoisomers.



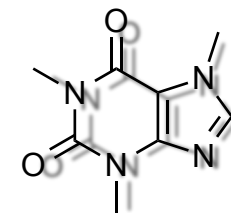
Meso Compounds



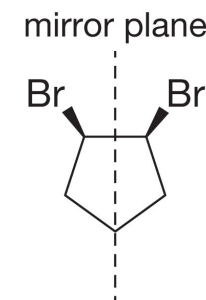
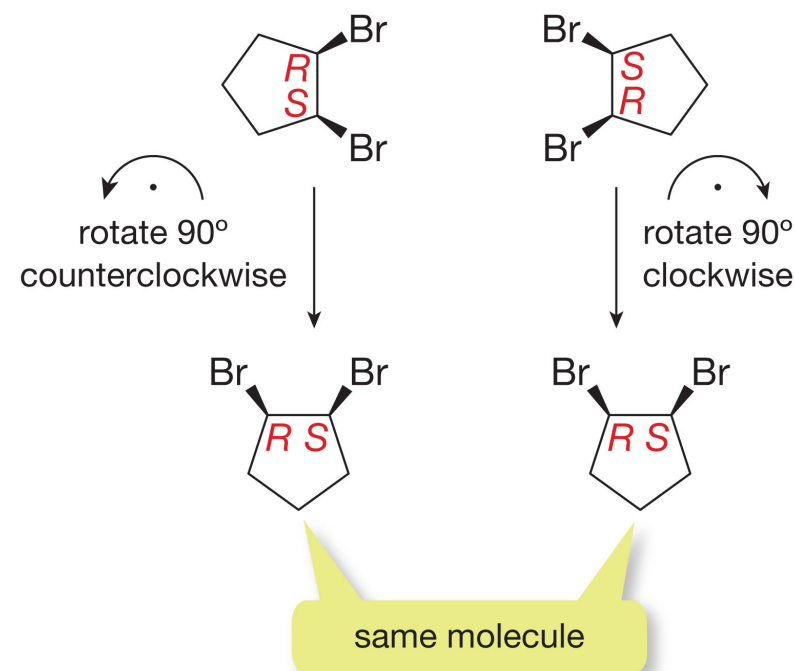
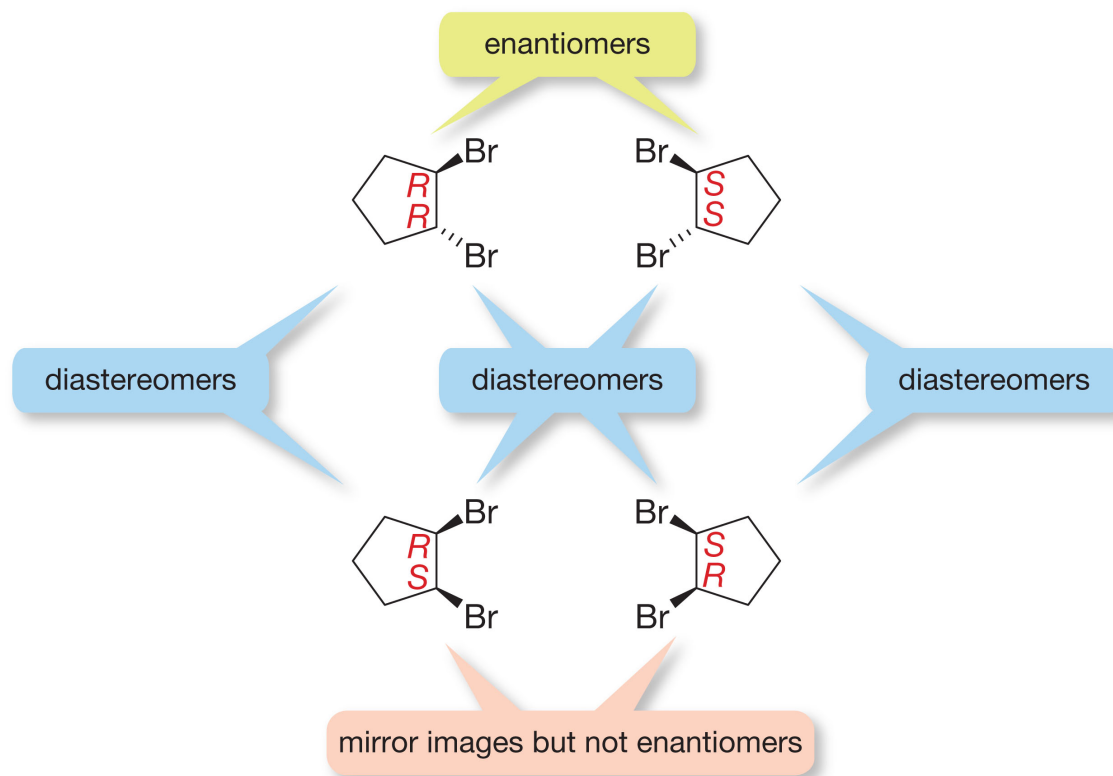
- Molecules that contain only 1 stereocenter are always chiral and have non-super(im)posable mirror images.
- However, molecules that contain more than 1 stereocenter are not always chiral.

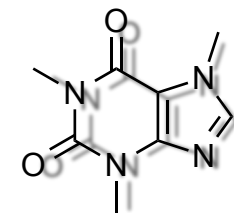


Meso Compounds



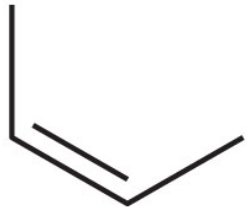
- Molecules that contain more than 1 stereocenter and have super(im)posable mirror images are called ***meso compounds***.
- Meso compounds also contain a plane of symmetry (mirror plane).





Double Bond Stereoisomers

- The arrangement of groups around a double bond can also produce stereoisomers.
- For each double bond, two geometries are possible.
- The *cis/trans* nomenclature is reserved for double bonds with only a single substituent on either side.

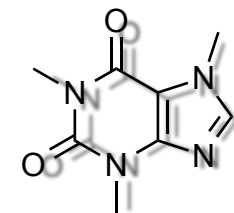


cis



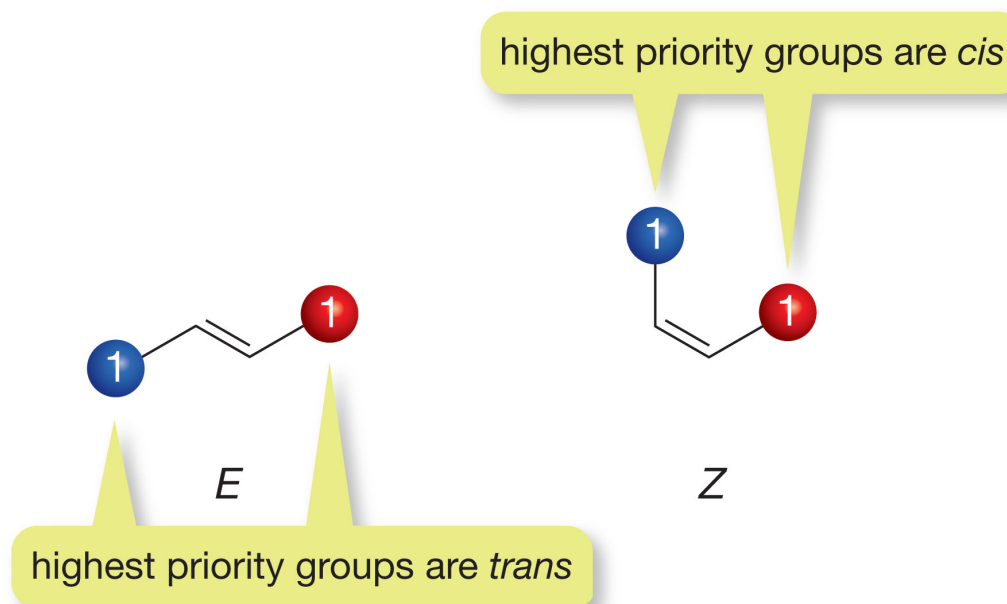
trans

- The *E/Z* nomenclature can be used for any double bonds with stereochemistry.

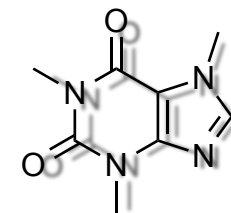


Double Bond Stereoisomers

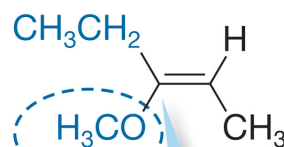
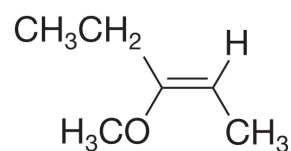
- The 2 substituents attached to each carbon of the double bond are assigned 1st or 2nd priority using the Cahn-Ingold-Prelog system.
- If the 2 highest priority groups are opposite to one another, the double bond is designated *E*.
- If the 2 highest priority groups are on the same side to one another, the bond is designated *Z*.



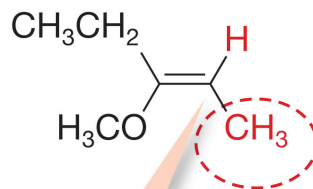
Double Bond Stereoisomers



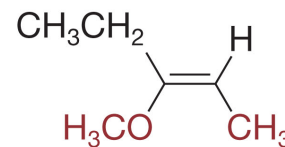
- The 2 substituents attached to each carbon of the double bond are assigned 1st or 2nd priority using the Cahn-Ingold-Prelog system.
- If the 2 highest priority groups are opposite to one another, the double bond is designated *E*.
- If the 2 highest priority groups are on the same side to one another, the bond is designated *Z*.



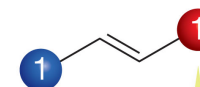
At this alkene carbon,
CH₃O is the first priority.
CH₃CH₂ is second priority.



At this alkene carbon,
CH₃ is the first priority.
H is second priority.



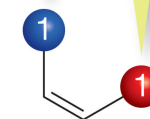
Do not assign priorities to
groups on different alkene
carbons.



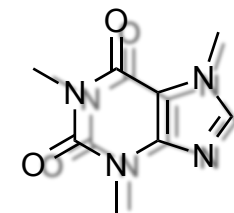
highest priority groups are *trans*

E

highest priority groups are *cis*

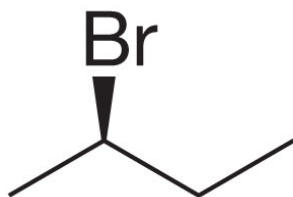


Z

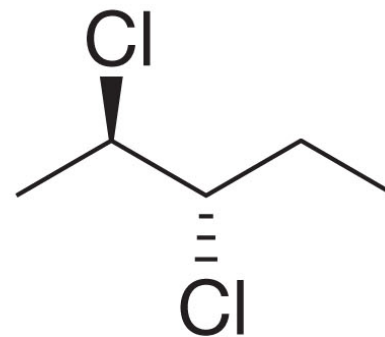


Double Bond Stereoisomers

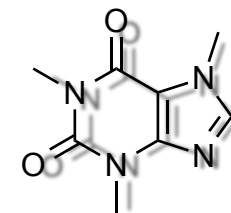
- Like the R/S designation, E/Z are written in italics and placed in parentheses at start of the name of the compound.
- If more than one designator is required, the atom number for location of each chiral centre/double bond is inserted before each R/S or E/Z designation.



(*R*)-2-bromobutane

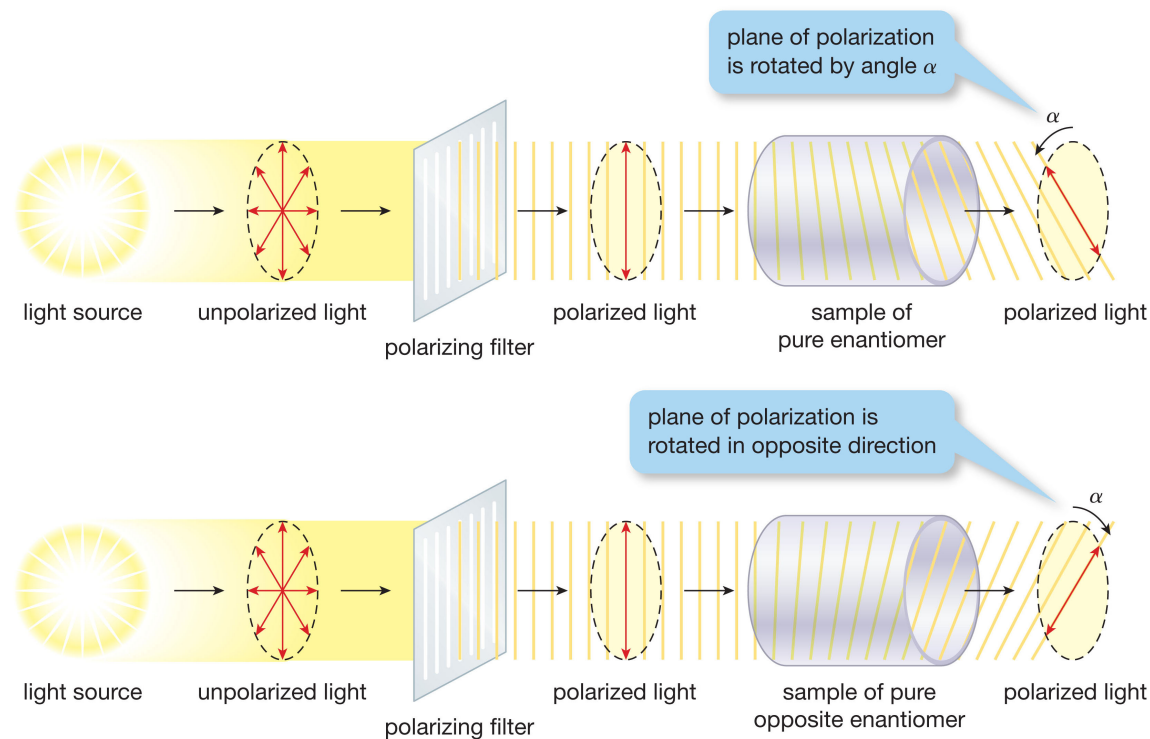


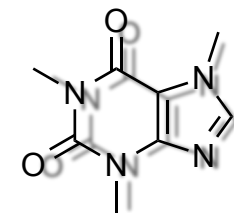
(2*R*, 3*S*)-2,3-dichlorobutane



Physical Properties of Enantiomers and Diastereomers.

- Diastereomers of a compound have distinct molecular structures, and so they have distinct physical and chemical properties.
- Pure enantiomers, however, have identical physical properties except for one; enantiomers rotate plane polarized light in opposite directions.

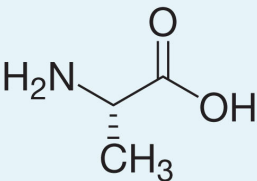
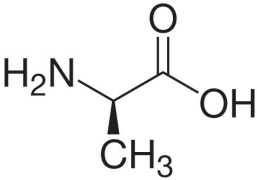




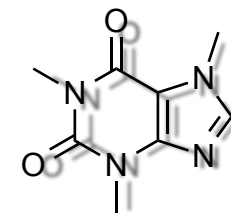
Physical Properties of Enantiomers and Diastereomers.

- Because enantiomers cannot interact with each other in the same way that identical molecules can, mixtures of enantiomers of a compound often have different physical properties than those of the pure *R* and *S* enantiomers.

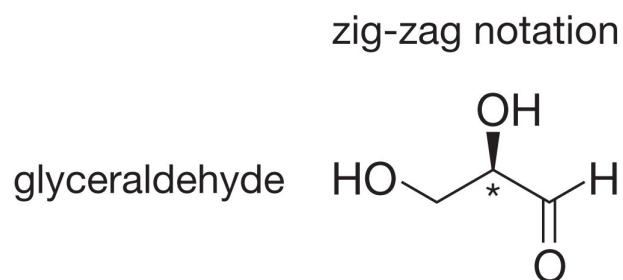
TABLE 4.1 Physical Properties of Enantiomers and Mixtures of Enantiomers

Compound	Melting point
<p>(<i>S</i>)-Alanine</p> 	314.5 °C
<p>(<i>R</i>)-Alanine</p> 	314.5 °C
(<i>RS</i>)-Alanine (50% <i>R</i> + 50% <i>S</i>)	289 °C

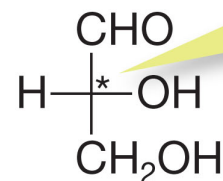
Fischer Projections



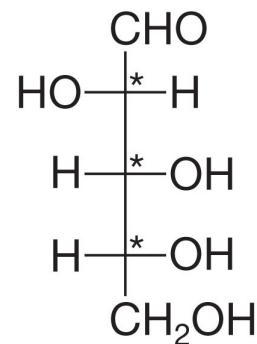
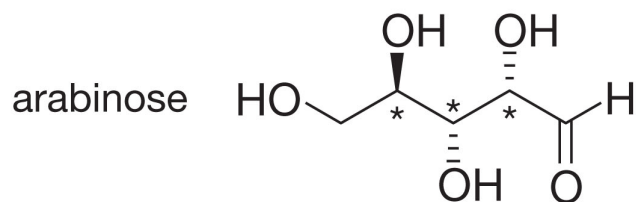
- ***Fischer projections*** are an efficient way to draw molecules (typically carbohydrates) that contain many stereoisomers.
- Vertical lines depict bonds angling ***into*** the page, and horizontal lines depict bonds projecting ***up and out*** of the plane of the page.



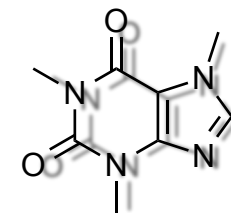
Fischer projection



chirality centre
(indicated
with an asterisk)

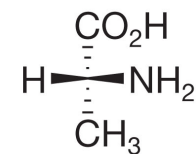
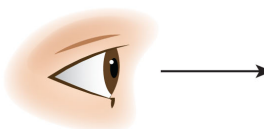
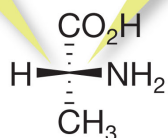
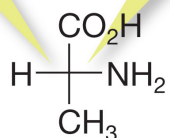


Fischer Projections

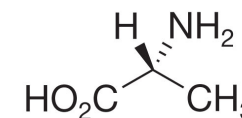


- When viewed from the side, the backbone of a Fischer projection forms an arch with the substituents pointing up above it.
- It is important to understand that Fischer projections are used for drawing purposes and do not represent real conformations.

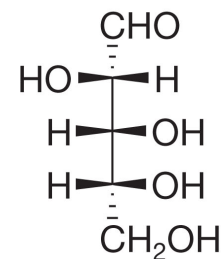
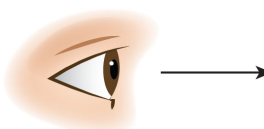
bonds drawn horizontally are assumed to project above the paper



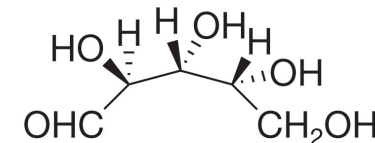
becomes



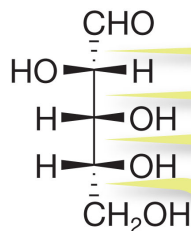
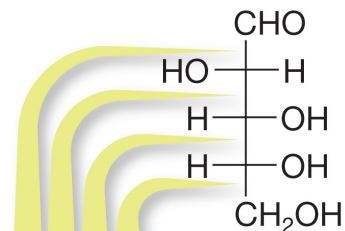
when viewed from the left side



becomes

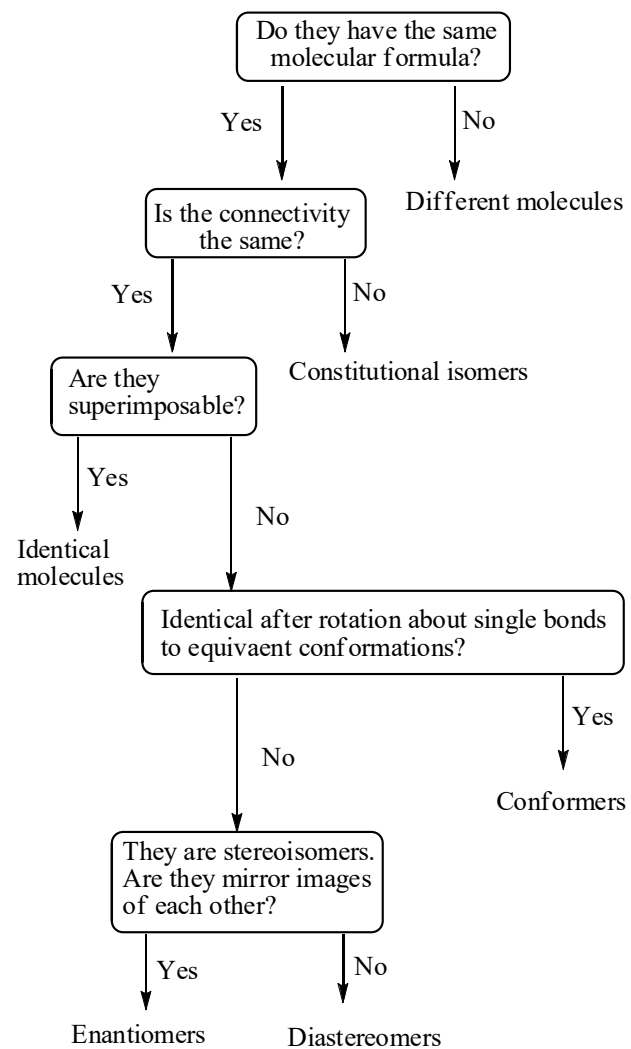
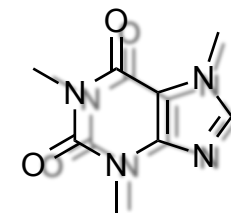


high energy conformation with many eclipsed atoms

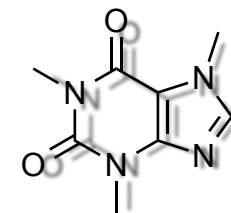


bonds drawn vertically are assumed to project into the paper

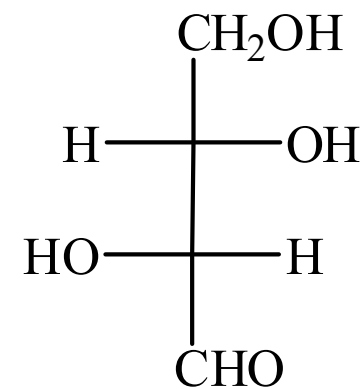
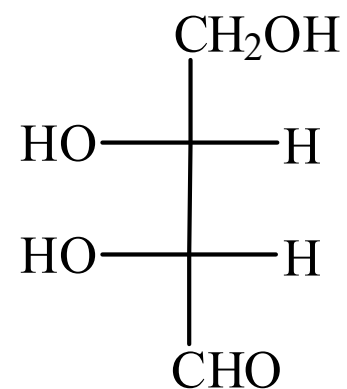
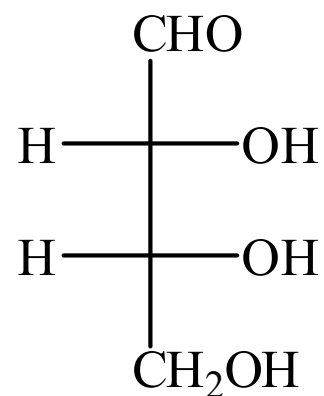
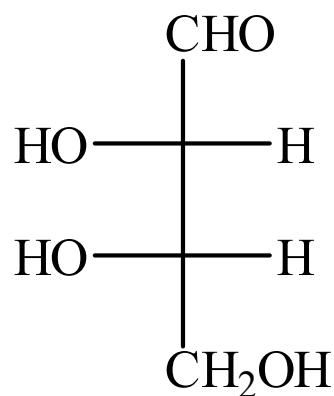
Strereochemistree



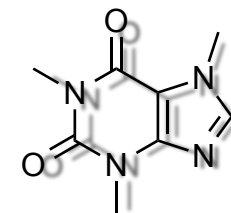
Fischer Projections – Relationships?



- What is the relationship between these 4 molecules?



Relationships



- Using the appropriate letter or letters, indicate the relationship(s) between the following pairs of molecules.

- A = stereoisomers
- B = constitutional isomers
- C = conformers
- D = diastereomers
- E = enantiomers
- F = identical molecules
- G = none of the above

