Isomerism

Recap Classification of isomers

Isomers
same molecular formula

Constitutional Isomers
Different nature/sequence of bonds

Stereoisomers
Different arrangement of groups in space

Conformational Isomers
Differ by rotation about a single bond

Configurational Isomers
Interconversion requires breaking bonds

Enantiomers
Non-superposable mirror images

Diastereoisomers
Not mirror images

Stereoisomers - enantiomers

Chiral molecules (optical isomers)

- A molecule is chiral if it is not superimposable upon its mirror image
- A pair of molecules which are not identical but are mirror images of each other are called enantiomers
- Almost all of the physical and chemical properties of a pair of enantiomers are identical (melting point, boiling point, solubility etc.)
- A chiral molecule contains a stereogenic centre (also known as a stereocentre or chiral centre)
- A stereogenic centre may be recognised as it is a carbon atom with four different groups attached to it
- In these molecules there is no plane of symmetry
**Chirality in nature**

We live in an asymmetric world!

- The enantiomers of a chiral molecule behave in an identical way when reacting with an achiral reagent (i.e., one that does not contain a stereogenic centre).
- But they may react quite differently to one another towards another chiral compound.

**Examples**

Our smell and taste receptors are chiral and so may differentiate between enantiomers.

Pharmaceuticals are often sold as a mixture of the two enantiomers.
There have been cases in which the two enantiomers have very different effects in the body.

Optical activity

How may we distinguish enantiomers in the lab?

- The physical properties of a pair of enantiomers are identical with the exception of their interaction with plane polarised light
- Plane polarised light consists of waves oscillating in only one plane

Polarimeter: when plane polarised light is passed through a solution of one pure enantiomer of a compound, the plane of polarisation is rotated

- The enantiomer is said to be optically active
- The amount of rotation (α) is a characteristic of the enantiomer
- Rotation in a clockwise direction is labelled (+) and rotation in a counterclockwise direction (-)
- One enantiomer rotates plane polarised light in a clockwise direction, the other enantiomer rotates the light by an equal amount in the opposite direction
- It is not (yet) possible to predict which enantiomer is (+) and which (-) without performing the experiment
- A mixture of equal amounts of the two enantiomers will give no net rotation and is called a racemic mixture
Nomenclature

The absolute configuration of a stereogenic centre refers to the exact three dimensional arrangement of the groups

- Identify the stereogenic centre
- Rank the atoms attached to the stereogenic carbon in order of atomic number; highest atomic number = highest priority

- If two atoms have the same atomic number, compare the atoms to which they are attached. Continue along carbon chains until a difference is reached.
- Multiple bonds are expanded to the same number of single bonds to that atom
- Orientate the molecule with the lowest priority group at the back
- Examine remaining three groups as if they are the spokes of a wheel and trace a curve from priority 1 to 2 to 3
- A clockwise curve indicates the R configuration; a counter-clockwise curve indicates the S configuration

Questions

The compound ‘fluoxetine’, shown below, is sold as a racemic mixture under the trade name prozac. It is a very effective anti-depressant but has no activity against migraine. The pure S-enantiomer however works well in preventing migraine. Identify the stereogenic centre in fluoxetine and draw the S-enantiomer.

Penicillin V has the absolute configuration shown. Assign the stereogenic centres as R or S.
Absolute configuration can not be correlated to direction of optical rotation

- Enantiomers rotate plane polarised light in opposite directions and have opposite absolute configurations
- But…the direction of rotation is not directly related to configuration

Questions
Lactic acid (CH\textsubscript{3}CH(OH)CO\textsubscript{2}H) can accumulate in muscle tissue where there is a deficiency of oxygen and cause cramp. Only the (\textit{S}) enantiomer is formed
- Draw the structure of (\textit{S})-lactic acid

- Identify the configuration (\textit{R} or \textit{S}) of the stereogenic centre in each of the following compounds:

- Give the structure of:
  - (\textit{S})-2-methyl-3-pentanol
  - (\textit{S})-1-phenylethylamine
  - (2\textit{R}, 3\textit{R})-2,3-dihydroxybutane

Summary
You should now be able to
- Recognise the structural features in a molecule that result in diastereoisomers and enantiomers
- Draw and correctly label (\textit{E}/\textit{Z}) the diasterisomers of an alkene
- Identify the stereogenic centre(s) in a molecule and use the priority rules to assign absolute configuration (\textit{R}/\textit{S})
- Draw a molecule indicating its stereochemistry from the systematic name of the compound
- Recognise the isomeric relationship between a series of stereoisomers