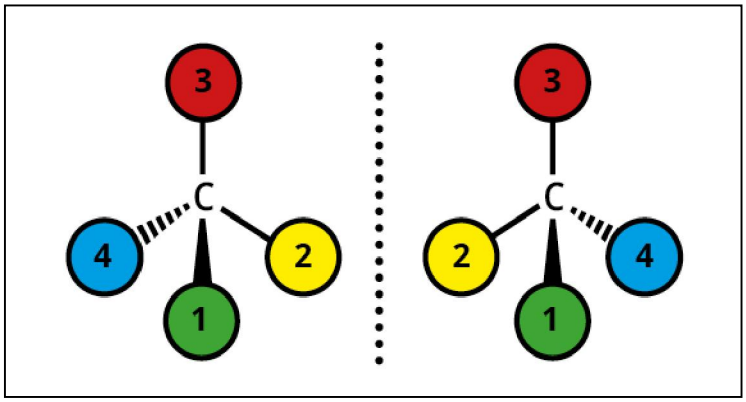
TC9 – Optical Isomerism

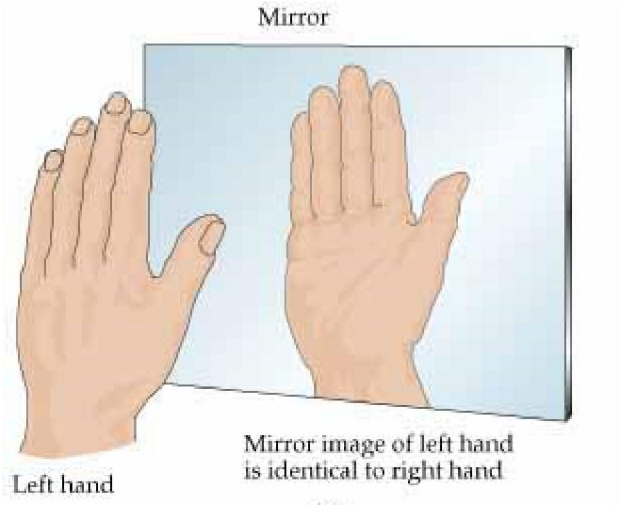
Stereoisomers have the same structural formula, but their atoms are arranged differently in space. **Optical isomerism** is a type of stereoisomerism where molecules have the same molecular and structural formula, but they cannot be superimposed.

Optical isomerism occurs in carbon compounds with 4 different groups of atoms attached to a carbon, and arranged in a **tetrahedral** structure. This is known as a **chiral** molecule as it contains a chiral carbon atom (an asymmetric carbon atom). A chiral molecule will have **no plane of symmetry** due to the chiral carbon. Only chiral molecules have optical isomers. We label a chiral carbon atom with an asterisk. (*)



Substances which display optical isomerism exist as two isomers which are the mirror image of each other, also known as **enantiomers** or **optical isomers**. No matter which way they are rotated, they cannot be **superimposed**. This means that you couldn't place one molecule exactly over the other as there will always be something facing in the wrong direction. If molecules can be superimposed then they are not optical isomers, they are known as achiral (not chiral).

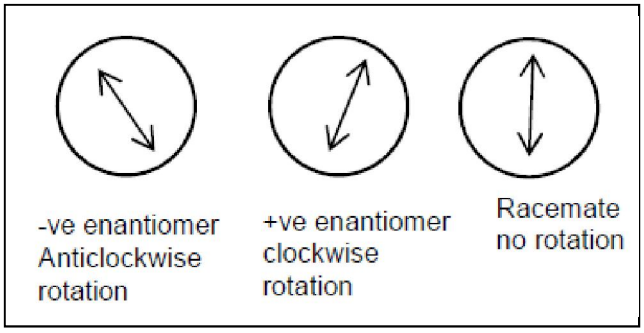
An example of this is your hands:



Your hands are mirror images of each other as shown in the image to the left. They are non-superimposable as no matter which way you rotate your left hand, it will never perfectly match up with your right hand. This is a good way to visualise and understand optical isomers.

Optical isomers are optically active – they **rotate plane polarise light**.

These isomers have the same physical and chemical properties, however they differ in only two characteristics. They rotate plane polarised light in **opposite directions** and they react differently with other chiral molecules. When you pass plane-polarised light through an optically active solution, the isomers will rotate the plane of the vibration of the light. One enantiomer will rotate it in a **clockwise** direction (this enantiomer will be positive) whilst the other rotates the light in an **anticlockwise** direction (this enantiomer will be negative), both at the same angle.

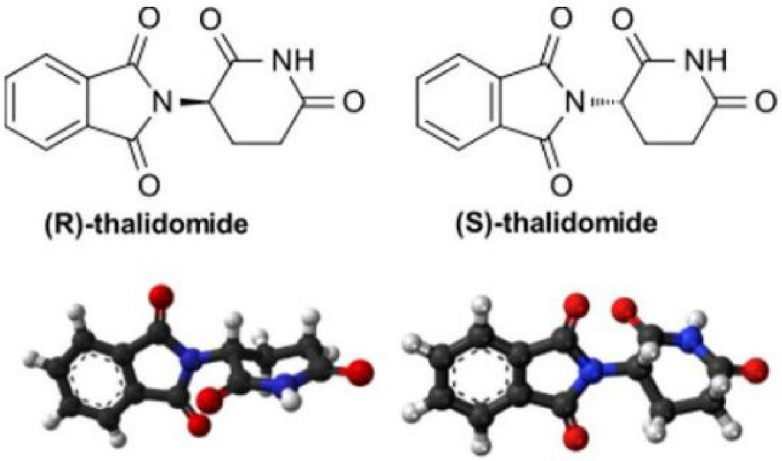


Racemic mixtures (also known as a racemate) contains a 50:50 mixture of each enantiomer of an optically active compound. A racemate will not rotate plane polarised light as it does not show any optical activity. This is because the two enantiomers rotate light in opposite directions, so they cancel the effect out.

Drug Action

The function of drugs can be determined by the stereochemistry of the molecule. If a drug is chiral then it will have two optical isomers which may have very different effects. An example of optical isomers in drugs is **thalidomide**.

Thalidomide is an **immunomodulatory drug** and it was primarily prescribed as a sedative or hypnotic. It was used to treat anxiety and insomnia. Thalidomide was also prescribed to pregnant women to alleviate morning sickness. However, the drug had not yet been tested on pregnant women and by 1960 it was found to damage the development of unborn babies. More than 10,000 babies around the world were affected by the drug as it led to them having very short limbs. Thalidomide was therefore banned around the world and drug testing became more attentive.

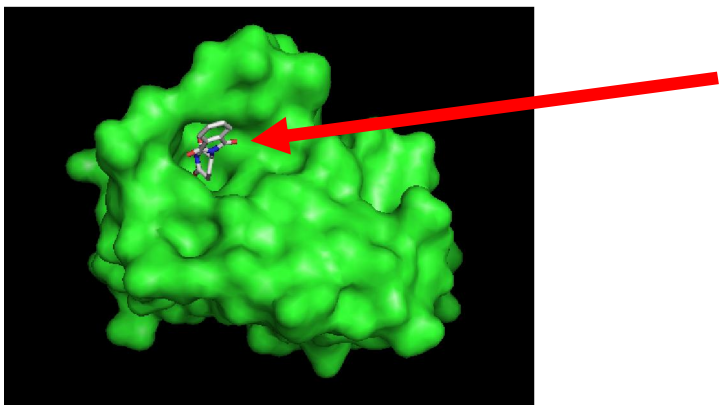


Thalidomide exists as **two enantiomers** (or optical isomers) as it has one chiral carbon atom. After the disaster, lab tests were constructed and it found that isomer 'R' was an effective sedative however the 'S' isomer was **teratogenic**. This meant that it was an agent which causes the **malformation of an embryo**, leading to the development of short limbs in unborn babies. Scientists have discovered that even if only one of the optical isomers was created and given to pregnant women, the same outcome would have occurred. This is because a racemic mixture is formed in the body, and so the disaster would not have been avoided.

PDBe:

To understand the structure of optical isomers and their enantiomers bind to other molecules, use the Protein Data Bank in Europe to research different proteins. Use the 4 character code given to you on the PDBe to put into PyMol. Using this you can manipulate the image of your chosen protein to view the structure.

An example would be to look at how thalidomide binds to molecules.



Thalidomide binding to Magnetospirillum gryphiswaldense to form a complex.

5amh

Recall Questions:

1. What is optical isomerism?
2. What does it mean if a molecule is ‘optically active’?
3. What is a chiral carbon?