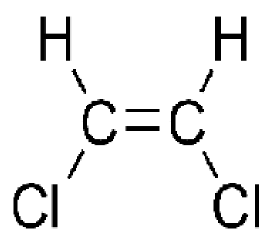
Stereoisomerism

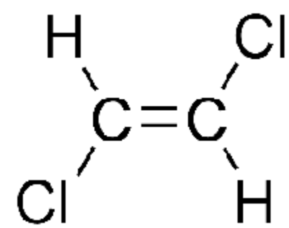
There are two types of stereoisomerism, E-Z Isomerism and Optical Isomerism.

E – Z Isomerism

This type tells us about the positions of substituent's either side of the carbon carbon double bond. The two substituent's can either be on the same side of the double bond (Z) OR on opposite sides (E).



Z-1,2 dichloroethene



E-1,2 dichloroethene

Why does this occur?

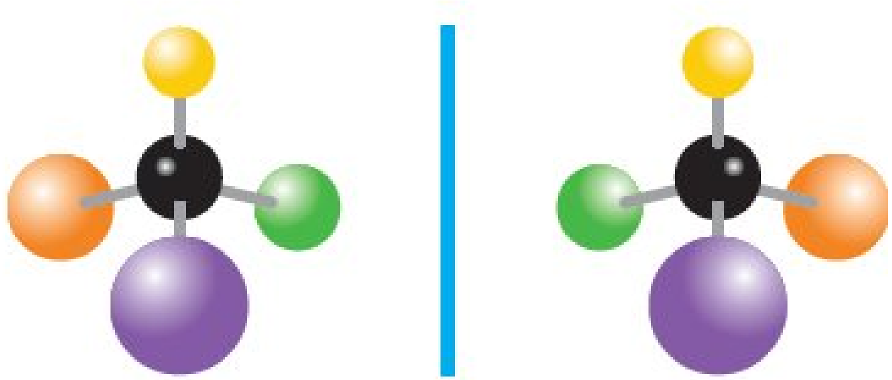
Single bonds are able to rotate freely but double bonds have restricted rotation and this gives rise to the E-Z isomerism. E is from the German word Entegen meaning Opposite whereas Z is from the word Zusammen meaning together.

Optical Isomerism

Optical isomers occur when a compound contains a carbon atom with four different atoms, or groups of atoms, joined to it. This is an asymmetric carbon atom. Its presence means that the compound can have two optical isomers, called enantiomers. These are mirror images of each other, and they are non-superimposable. No matter how you turn the two enantiomers around, you cannot get all the atoms and groups attached to the asymmetric carbon atom to match up.

Enantiomers

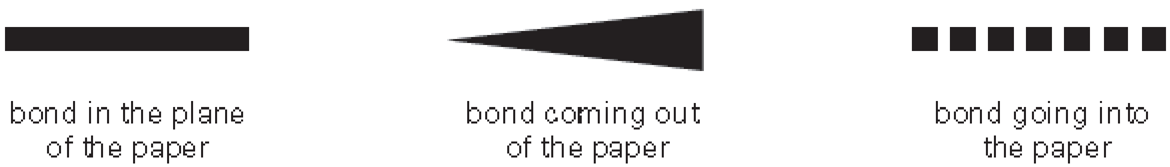
Picture a carbon atom with four different atoms joined to it. For example, this happens in bromo(chloro)fluoro(iodo)methane. The diagram shows its two enantiomers. Notice that they are non-superimposable mirror images. You can match up the carbon atom and two of the halogen atoms, but not the other two halogen atoms.



The enantiomers of bromo(chloro)fluoro(iodo)methane are mirror images.

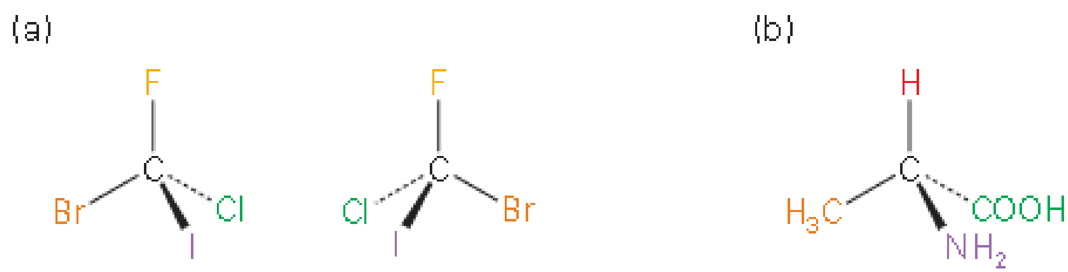
Representing enantiomers

Enantiomers extend in three dimensions, so their bonds are drawn to give a sense of depth.



Different bond styles show if a bond comes towards you or goes away from you.

The diagrams show the displayed formulae of the enantiomers of bromo (chloro)fluoro(iodo)methane and 2-aminopropanoic acid (alanine, an amino acid).



Enantiomers of (a) bromo(chloro)fluoro(iodo)methane and (b) alanine.

Chiral centres

Human hands are chiral objects. An asymmetric carbon atom is a **chiral centre**, pronounced 'ky-ral'. This name comes from the Greek word for *hand*.

A pair of gloves comprises two gloves that are non-superimposable mirror images of each other.

Showing optical activity

Enantiomers of a compound have identical chemical properties, unless they are reacting with another chiral compound. Optical activity is shown using a polarimeter.

Light waves can vibrate in an infinite number of directions or planes. Polaroid filters only let rays that vibrate in a particular plane to pass through. Sunglasses often have Polaroid filters to block the glare from bright sunlight. The light that emerges from a Polaroid filter is planepolarized light. Optical isomers can rotate the plane of this light.

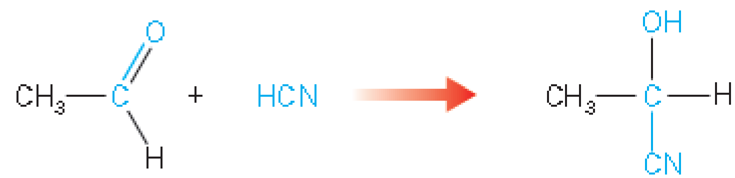
A simple polarimeter comprises a light source, two Polaroid filters, and a glass cylinder. Light passes upwards through the first filter, the cylinder, then through the second filter and into the observer's eye. The filter nearest the eye is rotated until the two filters are 'crossed' and no light emerges. A solution of one of the enantiomers is poured into the cylinder. Light emerges again because optical isomers can rotate the plane of plane-polarized light. The filter is then rotated again until light no longer emerges, and the angle needed is measured.

Naming enantiomers

Enantiomers can be named according to the direction in which they rotate plane-polarized light. One enantiomer rotates it in one direction, and the other enantiomer rotates it in the opposite direction. Looking through a polarimeter towards the light source, the enantiomer that rotates light anticlockwise, or to the left, is the laevorotatory or (-) enantiomer. The enantiomer that rotates light clockwise, or to the right, is the dextrorotatory or (+) enantiomer.

Racemates

A mixture containing equal amounts of the two enantiomers is called a racemic mixture or racemate. A racemate does not show optical activity, because the rotating effect of one enantiomer is cancelled by the opposite effect from the other enantiomer. Racemates typically occur when chemicals are synthesized in the laboratory. The reaction between ethanal and hydrogen cyanide provides a good example.



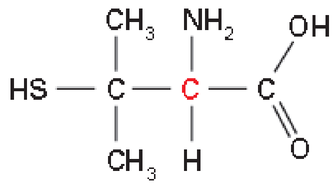
The carbonyl group >C=O in ethanal is planar. The cyanide ion CN^- can attack from above or below the molecule, so a racemate of 2-hydroxypropanenitrile is formed. If only the (-) or (+) enantiomer were formed, it would show that the cyanide ion could only attack in one direction.

Stereochemistry and Drugs

When a compound with a chiral centre is synthesized in the laboratory, the product is usually a racemate. But the same compound synthesized by living organisms consists of just one enantiomer. This is because only one enantiomer of a reactant can bind to an enzyme's active site, the place where an enzyme-catalysed reaction happens. And enzymes can only make one enantiomer of a product. For example, (+)glucose can be digested but (-)glucose cannot. Some enantiomers can be distinguished by their taste or smell:

- One enantiomer of asparagine tastes sweet and the other tastes bitter.
- One enantiomer of carvone tastes of spearmint and the other of caraway (like aniseed).
- One enantiomer of limonene smells of oranges and the other of lemons.

The enantiomers of medical drugs can be the difference between a toxic substance and one with beneficial effects on the body. For example, d-penicillamine is used to treat rheumatoid arthritis, but l-penicillamine is toxic. When penicillamine was first introduced in the US, the synthetic racemate was used. It caused optic nerve damage and the drug was initially withdrawn. The penicillamine introduced in the UK was derived from penicillin. Only the d enantiomer was present and so the toxic effects were not seen.

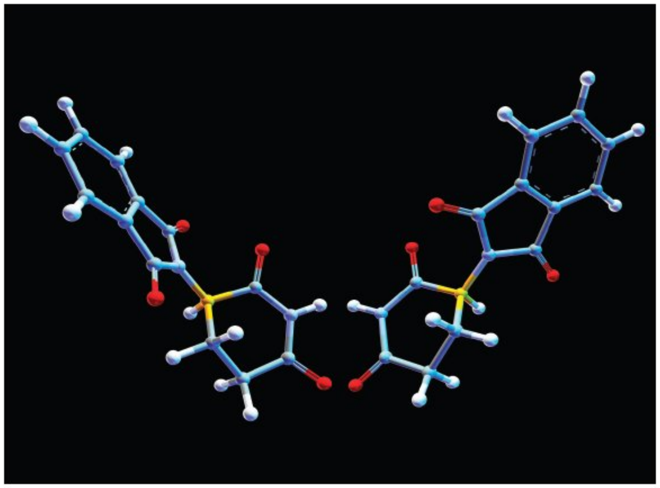


Penicillamine. The chiral centre is coloured red.

Thalidomide

In the late 1950s, thalidomide was introduced as a drug to treat morning sickness during pregnancy. But evidence emerged that it was teratogenic and so caused serious birth defects. Thousands of babies were born between 1956 and 1962 with deformities such as very short limbs.

Thalidomide is chiral and was available as the racemate. One enantiomer relieves morning sickness and is not teratogenic, but the other enantiomer is teratogenic. Unfortunately, even if the safe enantiomer had been synthesized, it would not have helped. This is because the body converts one enantiomer into the other. Thalidomide was withdrawn from general use in 1962 and the regulations regarding drug testing were made more stringent. The compound is available today, but this time to treat leprosy. And it is not prescribed to pregnant women.



The two enantiomers of thalidomide. The chiral centre is coloured yellow.

Praziquantel

Schistosomiasis is a tropical disease caused by a parasitic worm. The parasite lives in the blood vessels of the small intestine, where it feeds on red blood cells. Over 200 million people are infected around the world. Schistosomiasis is spread through contact with contaminated water such as irrigation channels, rivers, and lakes. Praziquantel kills the worms, with few side effects for the patient. It is available as the racemate but only one enantiomer actually kills the worms.

Research is being carried out to synthesize the active enantiomer at a cost that is competitive with the racemate. Many drugs have undergone this 'chiral switch'.
The use of single enantiomer drugs reduces the risk of side effects and lowers the dose needed. It may be easier for patients to take a drug if its tablets are smaller as a result.

A pair of Schistosoma mansoni *worms, about 1 cm long. The male is the larger of the two. The female can lay around 300 eggs a day.*