2. Optical Isomerism

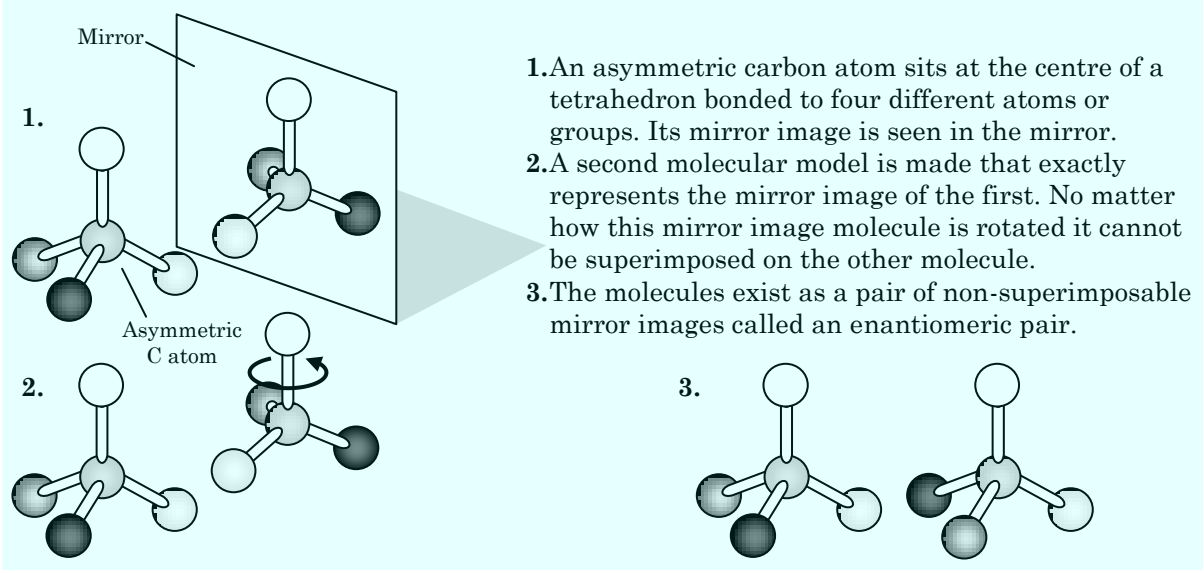
Optical isomerism occurs in molecules which have at least one **carbon atom which is bonded to four different atoms or groups**. A carbon bonded to four different atoms or groups is **asymmetric**. A molecule containing an asymmetric C atom is also usually (though not always) asymmetric. This means the molecule has neither a plane of symmetry nor a centre of symmetry.

At least in open-chain compounds, an sp^3 hybridised C atom is tetrahedrally coordinated. The four single bonds point towards to the corners of a tetrahedron. If we look more closely, we find there are two different ways to organise four different atoms or groups around an asymmetric carbon atom. These two arrangements are mirror images of one another. If we take these two mirror images and try and place them on top of one another – to superimpose them – we find they do not match. No matter how the two molecules are twisted or turned or rotated, they are not the same molecule; they are stereoisomers of each other. The two isomers are **non-superimposable mirror images**. These mirror-image stereoisomers are called **enantiomers**.

The simplest example of a pair of non-superimposable mirror images is our hands. Our left and right hand are mirror images of one another. Try and put a left-handed glove on your right hand and a right-handed glove on your left hand and you find that they don't fit. Imagine (but not too hard) that both of your hands were cut off at the wrists in a freak chemistry accident. The surgeon then makes the mistake of sewing your right hand on your left wrist. If you wanted your thumb to face forward, the palm on your "new" left hand would face outwards.

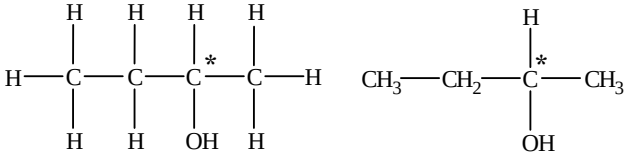
Figure 20.3 shows an asymmetric C atom at the centre of a "ball-and-stick" molecular model. A pair of model molecules is constructed that are non-superimposable mirror images of one another. You would need to take one of the models apart and reconstruct it so that it had exactly the same spatial arrangement as the other. The models represent a pair of mirror-image molecules called an **enantiomeric pair**. The molecules cannot be converted into one another without breaking single covalent bonds. It is recommended that you get a set of molecular models to really understand the spatial difference between these two molecules.

Figure 20.3 Molecular Models Representing an Enantiomeric Pair in a Chiral Molecule

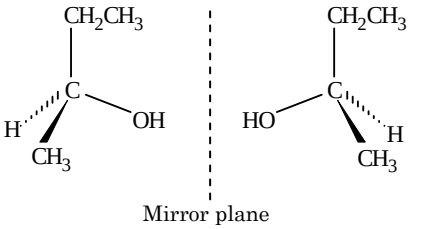


Objects like our hands that can exist as a pair of non-superimposable mirror images are said to be **chiral** (pronounced "*k*iral"). The same terminology is used for molecules that have this property (yes, there is a lot of terminology in this topic). The asymmetric carbon atom is called a **chiral centre**. Chiral C atoms are normally shown with an asterix * when the structure of a chiral molecule is drawn.

Chirality can occur in relatively simple molecules. Consider butan-2-ol, which is shown in two ways on the right. The chiral (asymmetric) carbon atom is asterixed. It is bonded to four different atoms or groups.



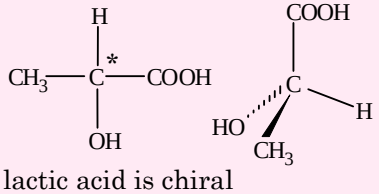
The best way of showing the difference in spatial arrangement between a pair of enantiomers is to draw the chiral C atom at the centre of a tetrahedron. The two enantiomers are separated by an imaginary mirror plane. Sometimes when you draw the enantiomers, it is necessary to reverse the order of some of the groups attached to the chiral C atom to make it clear which atom is bonded to which. This is done with the −OH group in the butan-2-ol isomer drawn to the right of the mirror plane.



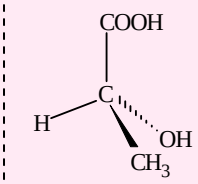
© 5. Work out whether the following molecules are chiral. Identify any chiral centres and draw the mirror images in the way shown for butan-2-ol above:
(a) 2-hydroxypropanoic acid (lactic acid) (b) 2-bromopropane (c) 2-bromobutane
(d) 1-bromobutane (e) 2-aminopropanoic acid (alanine) (f) aminoethanoic acid (glycine)

Solutions:

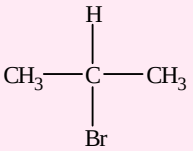
(a)



lactic acid is chiral

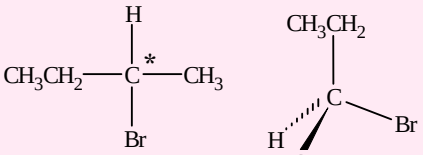


(b)

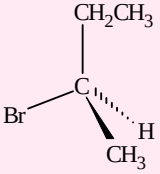


non-chiral

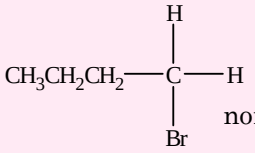
(c)



2-bromobutane is chiral

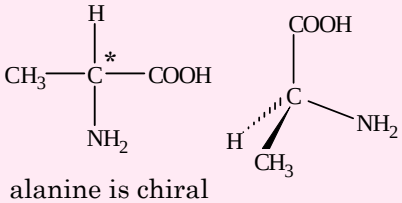


(d)

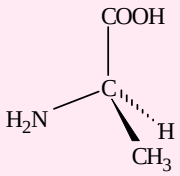


non-chiral

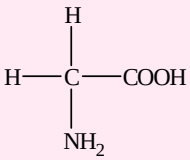
(e)



alanine is chiral



(f)



non-chiral

The spatial origin of chirality in molecules and some of its consequences are highlighted in the following video: http://www.youtube.com/watch?v=RBtgAz70_JY.

So why are these non-superimposable mirror image molecules called *optical* isomers? The answer lies in how pure samples of these isomers interact with plane-polarised light. We say that these isomers are **optically active**. Let's first explain what plane-polarised light is and, before that, the nature of light itself.

Light is a transverse wave. The wave's electrical field vibrates at right angles to the direction of travel. Not only does the electrical field vibrate up and down and from side to side, it vibrates in all directions perpendicular to the direction of travel. Light becomes polarised when it is passed through a polarising filter, like a Polaroid film, or though certain types of prism. This polarising filter is called the polariser. Polaroid film can be thought of having aligned rod-like molecules. The molecules allow only that portion of light with its electric field vibrating in one direction (one plane) to pass through; all the other light is absorbed (the Polaroid film makes things darker because less light is transmitted overall). This selectively transmitted light is called **plane-polarised light** (Figure 20.4). The electrical field of plane-polarised light vibrates in only one plane (in Figure 20.4 it vibrates along the *z*-axis).

Figure 20.4 Origin of Plane-Polarised Light

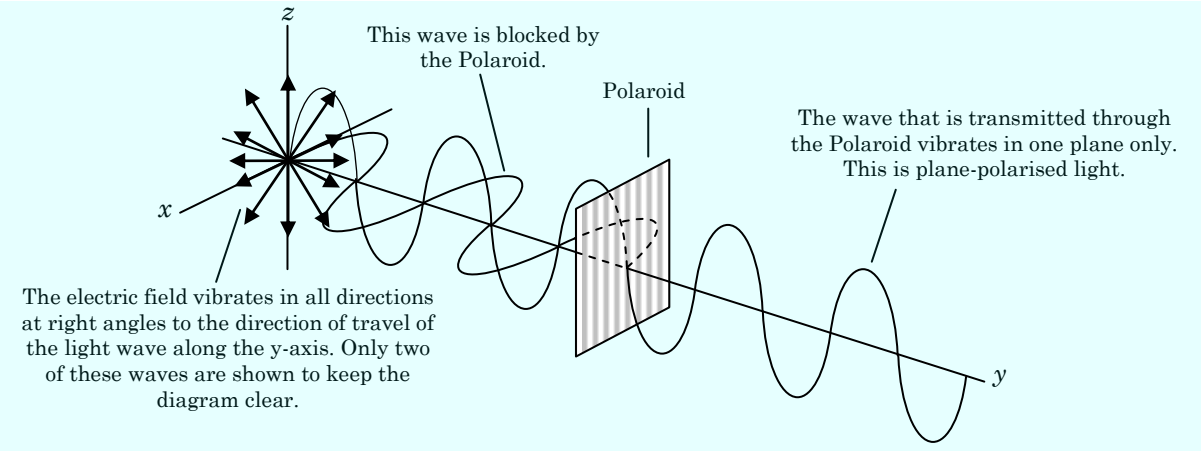
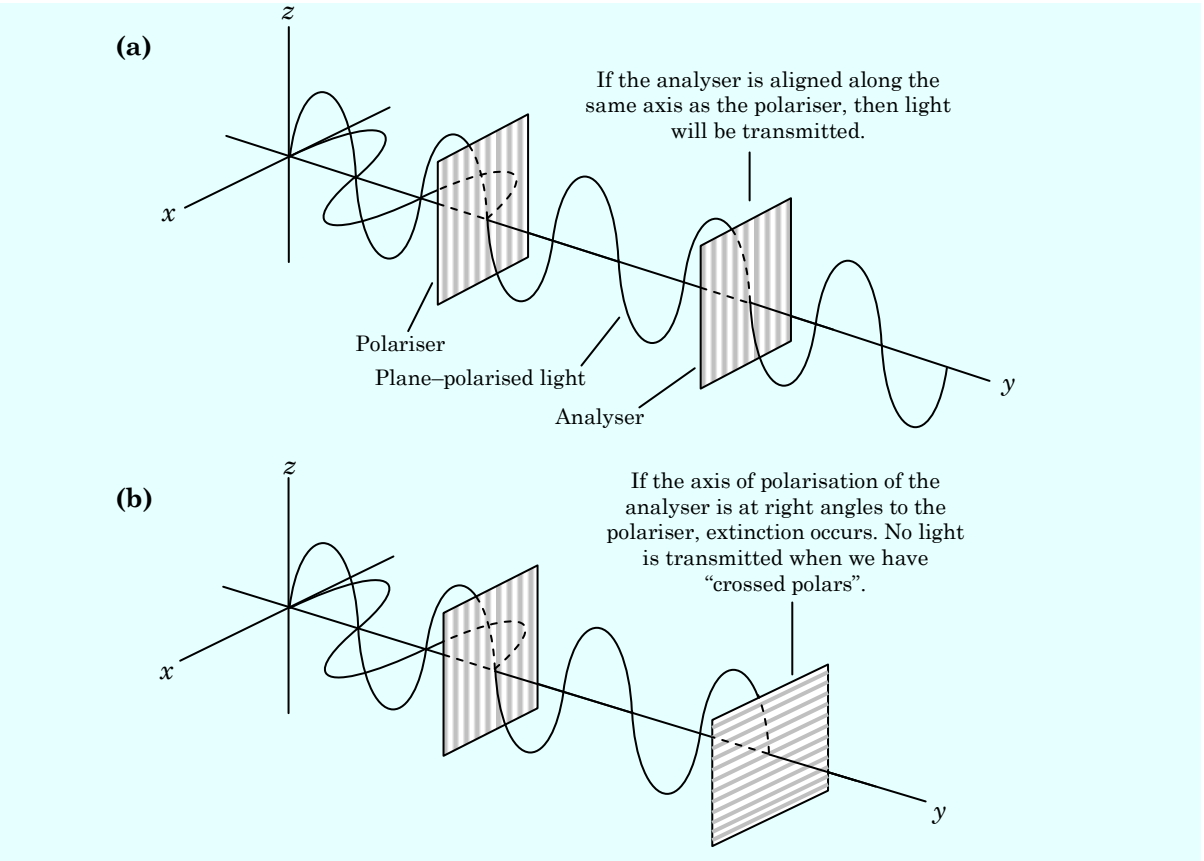


Figure 20.5 shows what happens if we shine the plane-polarised light onto a second Polaroid film. This second filter is called the analyser. If the two Polaroid films (polariser and analyser) have their polarising axis aligned, the maximum amount of plane-polarised light can pass through the analyser (Figure 20.5 (a)). If the analyser is now twisted through 90°, no light can pass through (Figure 20.5 (b)). This is called extinction.

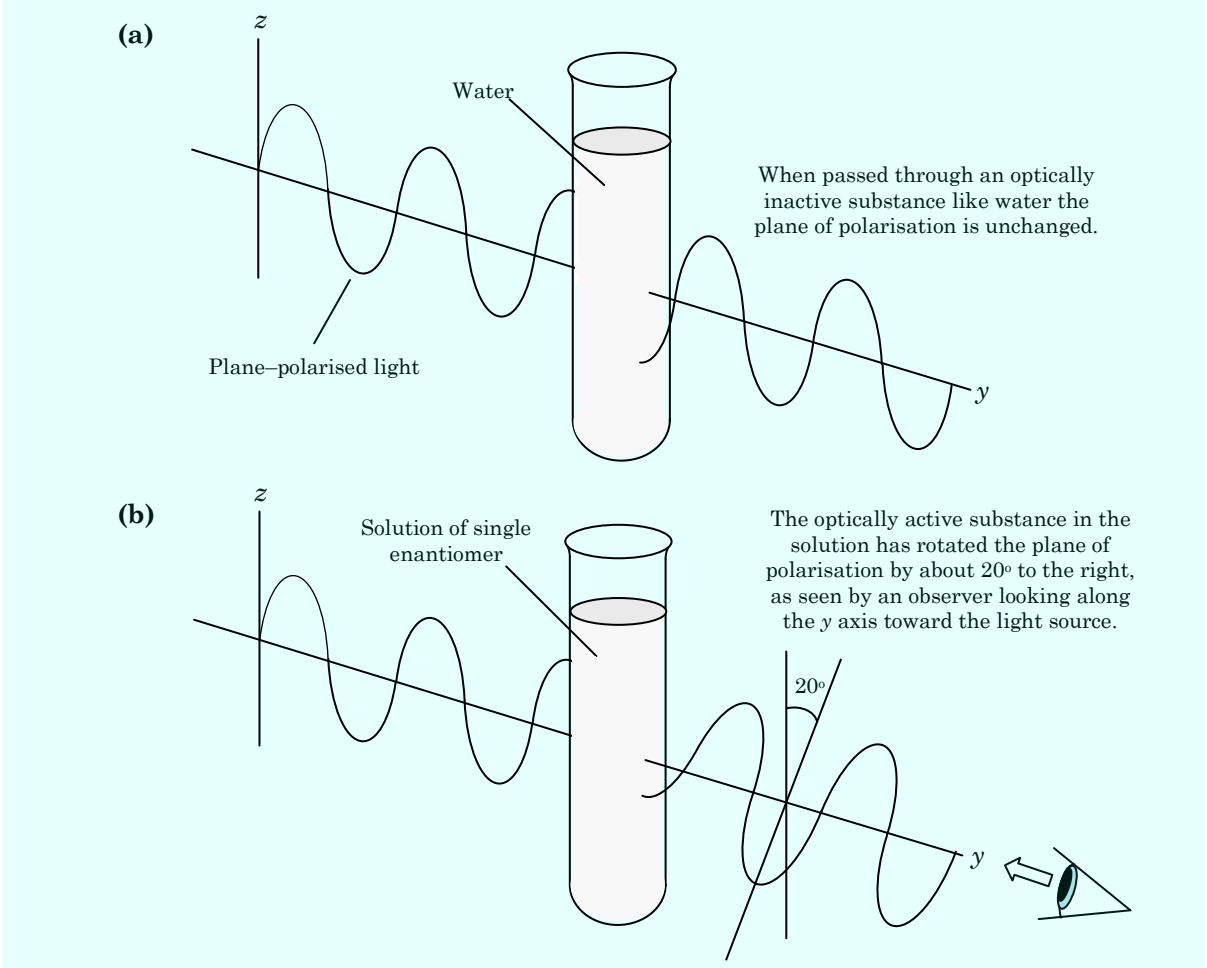
Figure 20.5 Light Passing Through Two Polarising Filters



You can see the same effect as that illustrated in Figure 20.5 if you have some high quality polarising sunglasses. The lenses in these sunglasses contain a thin polarising layer. Rotate your head when you have the sunglasses on and you will find that objects become lighter or darker. That's because a lot of the glare that you get when sun reflects off a surface like water is polarised. Alternatively, ask your teacher if they have some polarising lenses you can investigate. Rotate the two polarising lenses relative to each other and you will find they go light then dark as the polarising axes are aligned then crossed.

Now let's see what happens when an optically active substance is included in the arrangement illustrated in Figure 20.5. In Figure 20.6 (a), plane-polarised light is passed through water. The light that is transmitted is unchanged; it is still polarised in the same plane. Water is optically inactive. Figure 20.6 (b) shows what happens when plane-polarised light is passed through a pure solution of a **single enantiomer**. The plane in which the plane-polarised light is vibrating has been rotated. As we look back at the light source along the *y*-axis, we see that the plane has been rotated to the right through an angle of about 20°.

Figure 20.6 Rotation of Plane-Polarised Light



A **polarimeter** can be used to measure the direction and extent by which the plane of the polarised light has been rotated by an optically active substance. A polarimeter is essentially nothing more than a small tube with two polarising filters at either end. At one end of the tube there is the polariser and at the other there is the analyser. The sample is placed in the tube between the two filters. Monochromatic light (light of one wavelength) is shone along the tube through the polariser and analyser. When an optically inactive substance like water is placed in the polarimeter then the maximum amount of light will pass through the tube when the polarising axis of the polariser and analyser are aligned (as in Figure 20.5 (a)). But when an optically active solution is placed in the polarimeter, the analyser must be twisted in order to transmit the maximum amount of light through the polarimeter. In our example shown in Figure 20.6 (b), the analyser needs to be rotated clockwise, or to the right, through an angle of about 20°.

The angle through which the plane of the plane-polarised light is rotated depends on the molecule and also on other factors such as concentration, how far the light must pass through the sample, and the wavelength of the light. But the crucial thing to understand is that the plane of plane-polarised light is rotated by a pure sample of a *single* enantiomer, that is, a sample of one of the two mirror image molecules. Our example isomer in Figure 20.6 (b) rotates the plane of plane-polarised light to the right (or put another way, we must turn the analyser clockwise to have the maximum amount of light passing through the polarimeter). This isomer is called the

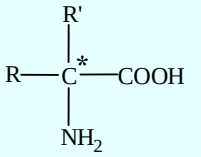
dextrororatory isomer (+ or "plus" isomer). Shine light through a pure sample of the other enantiomer and the plane of plane-polarised light will be rotated in the opposite direction (in this case anticlockwise). The other isomer is called the **laevorotatory isomer** (− or "minus" isomer).

The two optical isomers in a pair of enantiomers rotate the plane of plane-polarised light in opposite directions

The nature of plane-polarised light and the use of a polarimeter in detecting optical rotation is summarised in the following animation: http://www.youtube.com/watch?v=HuHphmJw-fA.

There are many optically active molecules with asymmetric carbon atoms. Many – but not all, as we will see – are found in nature or made in the laboratory as a **mixture of the two enantiomers**. This mixture is called a **racemic mixture** (or racemate). Shine plane-polarised light through a solution of a racemate and the plane of plane-polarised light is unaffected. This is because the rotatory effects of the two stereoisomers in the mixture cancel out. Trying to separate one isomer from the other in a racemic mixture (a process called resolving) is a tricky business. But why would we need to resolve a racemic mixture anyway? The physical properties of enantiomers are identical and, given that they have the same chemical groups, surely the chemical properties are identical too? Nature shows us that this is not always the case.

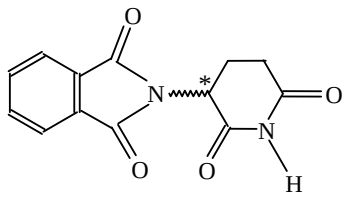
We might expect that in nature all things are symmetrical. After all there are an equal number of left and right hands in the world. But when we look more carefully, we find that nature often uses only one of the enantiomers of an asymmetric molecule. Take the 20 α-amino acids that are coded for by DNA in a human body. All except for the simplest one, glycine, are chiral. Amazingly, all the amino acids found in nature have the same spatial arrangement. In other words, only one of the isomers of the enantiomeric pair is found naturally. What this means that peptides, proteins and enzymes, all compounds made from linking amino acids together in a chain, have a fixed "handedness". Carbohydrates are also chiral molecules and so are nucleic acids (have you noticed that DNA twists one way and not the other?). In short, our own bodies are chiral environments. One consequence of this is that the receptors in our bodies often respond differently to the two enantiomers of an asymmetric molecule. Take, for example, the molecule aspartame. Aspartame is optically active. One of the enantiomers of aspartame tastes sweet and is used in artificial sweeteners like *Nutrasweet*; the other enantiomer tastes bitter. The analgesic morphine is also a chiral molecule. One of the enantiomers of morphine is a very powerful pain reliever and is non-addictive; the other enantiomer is highly addictive and not as effective as a pain-reliever.



α-amino acids are chiral when R≠R' (all except glycine when R=R'=H)

One of the most heartbreaking examples of the stereoselectivity of the human body is the story of thalidomide. The drug thalidomide was prescribed to thousands of pregnant women in the late 1950s and early 1960s. Thalidomide is an effective drug for relieving morning sickness. Tragically, many babies born to women who had taken thalidomide during the first trimester of pregnancy were born with terrible defects. Many so-called "thalidomide babies" were born with abnormally short legs and flipper-like arms.

Thalidomide



The drug thalidomide is chiral. The asymmetric carbon atom is asterisked in the structure. A ~~~line is used in this structure when we don't specify if the bond points up (▬), as in one enantiomer, or down (┈┈), as in the other enantiomer. One of the enantiomers is an effective antiemetic (it relieves sickness); the other enantiomer is a powerful foetus deformer. The drug was withdrawn from the market but not before over 10,000 babies had been affected. An emotive but informative history of Thalidomide can be seen at http://www.youtube.com/watch?v=o7U1xZjwu8c.

One of the greatest advances in organic chemistry in the past decade or so has been the development of **asymmetric synthesis**. Asymmetric synthesis is the selective preparation of one of the enantiomers of an asymmetric molecule. Three pioneers of catalytic asymmetric synthesis, William S. Knowles, K. Barry Sharpless and Ryoji Noyori, were jointly awarded the Nobel Prize for Chemistry in 2001. This new technology would not have prevented the thalidomide tragedy, even if it had been available at the time. This is because the two enantiomers of thalidomide