# Cambridge (CIE) A Level Chemistry

Your notes

## Isomerism: Optical

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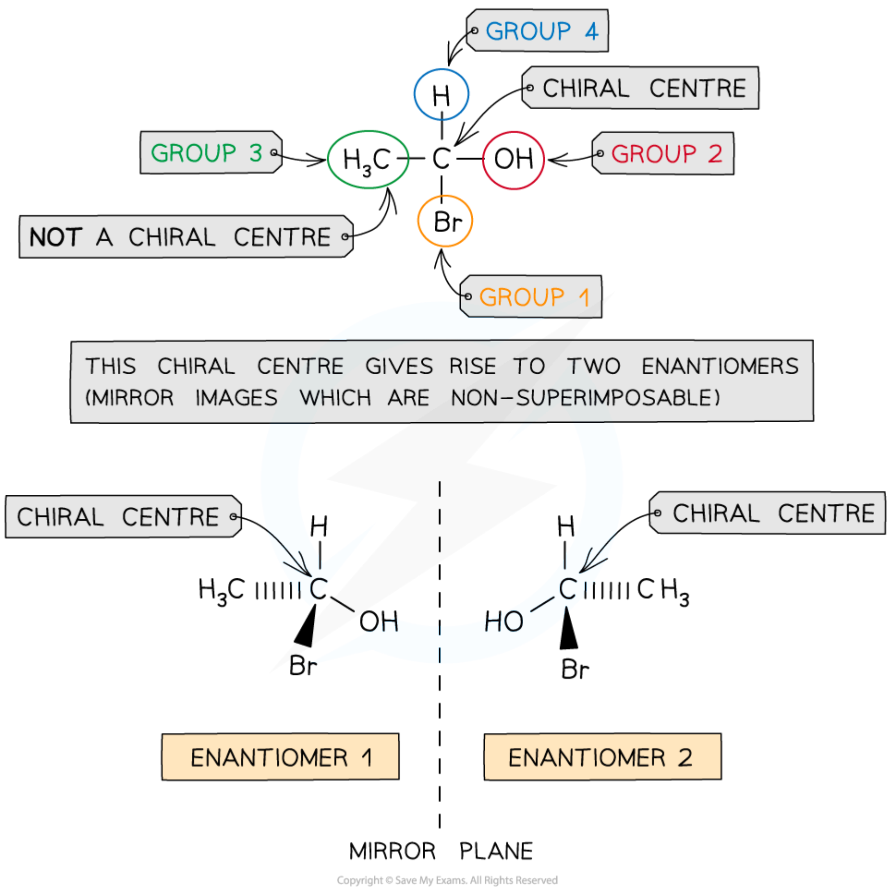
# Properties of Enantiomers

- **Stereoisomers** are molecules that have the same **structural formula** but have the atoms arranged differently in space
- There are two types of stereoisomerism
  - Geometrical (*cis / trans*)
  - Optical

## Optical isomerism

- A carbon atom that has **four different atoms** or **groups of atoms** attached to it is called a **chiral carbon** or **chiral centre**
- Compounds with a chiral centre (**chiral molecules**) exist as two **optical isomers** which are also known as **enantiomers**

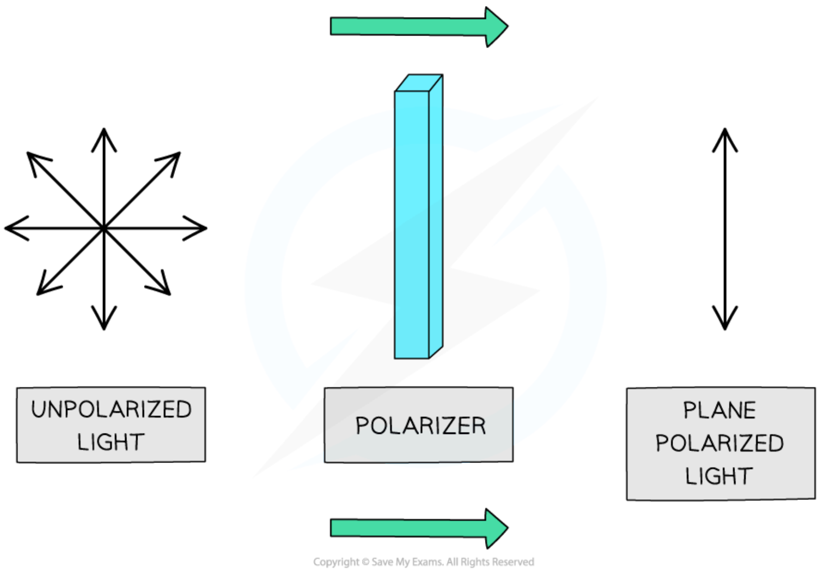
### How enantiomers occur



*A molecule has a chiral centre when the carbon atom is bonded to four different atoms or group of atoms; this gives rises to enantiomers*

- The enantiomers are **non-superimposable mirror images** of each other
- Their physical and chemical properties are **identical** but they differ in their ability to rotate **plane polarised light**
  - Hence, these isomers are called 'optical' isomers
  - One of the optical isomers will rotate the plane of polarised in the **clockwise** direction
  - Whereas the other isomer will rotate it in the **anti-clockwise** direction

## How a polarizer works

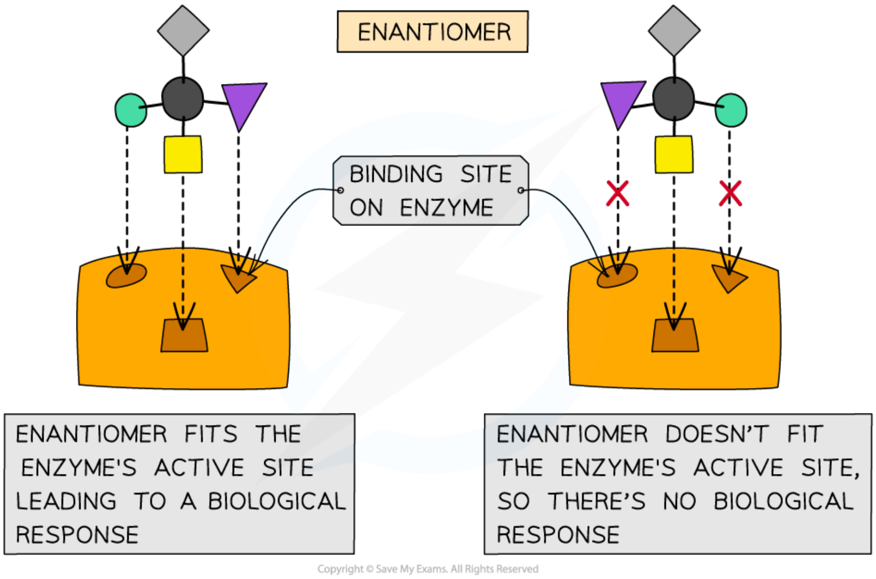



*When unpolarised light is passed through a polariser, the light becomes polarised as the waves will vibrate in one plane only*

# Biological activity of enantiomers

- Enantiomers also differ from each other in terms of their **biological activity**
- **Enzymes** are **chiral** proteins that speed up chemical reactions by binding **substrates**
- They are very target-specific as they have a specific **binding site** (also called active site) and will only bind molecules that have the **exact same shape**
- Therefore, if one enantiomer binds to a chiral enzyme, the mirror image of this enantiomer will not bind **nearly as well** if at all
  - It's like putting a right-hand glove on the left hand!

## Enzymes acting on different biological enantiomer substrates




*Enantiomers differ from each other in their biological activity*

# Optically Active Compounds & Racemic Mixtures

- **Enantiomers** are optical isomers that are mirror images of each other and are **non-superimposable**
- They have similar chemical properties but differ from each other in their ability to rotate **plane polarised light** and in their **biological activity**

## Optical activity

- Let's suppose that in a solution, there is 20% of the enantiomer which rotates the plane polarised light **clockwise** and 80% of the enantiomer which rotates the plane of polarised light **anticlockwise**
- There is an uneven mixture of each enantiomer, so the reaction mixture is said to be **optically active**
  - The net effect is that the plane of polarised light will be rotated **anticlockwise**
- Similarly, if the percentages of the enantiomers are reversed, the reaction mixture is still **optically active** but now the plane of polarised light will be rotated **clockwise**
  - In this case, there is 20% of the enantiomer, which rotates the plane **anticlockwise**
  - And 80% of the enantiomer, which rotates the plane **clockwise**
- A **racemic mixture** is a mixture in which there are **equal amounts** of enantiomers present in the solution
- A racemic mixture is **optically inactive** as the enantiomers will cancel out each other's effect and the plane of polarised light will **not change**

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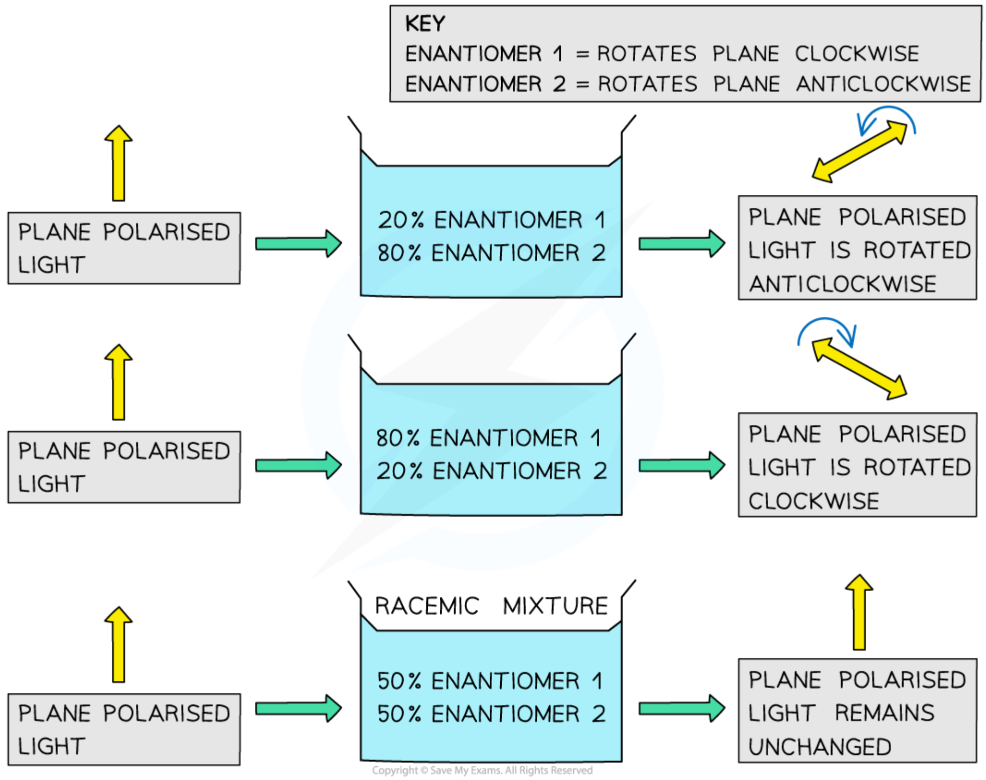
### How the percentage of enantiomers affects plane polarised light




***When one of the enantiomers is in excess, the mixture is optically active; when there are equal amounts of each enantiomer the mixture is optically inactive***

# Effect of Optical Isomers on Plane Polarised Light

- Molecules with a **chiral centre** exist as **optical isomers**
- These isomers are also called **enantiomers** and are non-superimposable mirror images of each other
- The major difference between the two enantiomers is that one of the enantiomers rotates plane polarised light in a **clockwise** manner and the other in an **anticlockwise** fashion
    - The enantiomer that rotates the plane **clockwise** is called the ***R*** enantiomer
    - The enantiomer that rotates the plane **anticlockwise** is called the ***S*** enantiomer
- These enantiomers are, therefore, said to be **optically active**
- Therefore, the rotation of plane polarised light can be used to determine the identity of an optical isomer of a single substance

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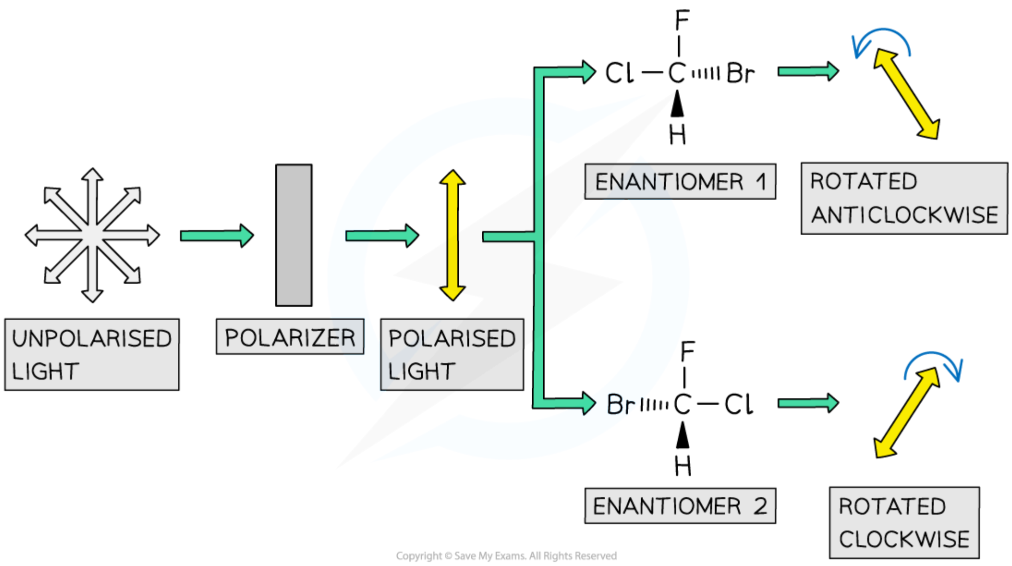
- For example, pass plane polarised light through a sample containing one of the two optical isomers of a single substance
    - Depending on which isomer the sample contains, the plane of polarised light will be rotated either clockwise or anti-clockwise
    - No effect will be observed when the sample is a **racemic mixture**

## Using polarized light to distinguish between R and S enantiomers




*Each enantiomer rotates the plane of polarised light in a different direction*

Your notes

# Chirality & Drug Production

- Most of the drugs that are used to treat diseases contain **one or more** chiral centres
- These drugs can therefore exist as **enantiomers** which differ from each other in their ability to rotate plane polarised light
- Another crucial difference between the enantiomers is in their potential **biological activity** and therefore their **effectiveness** as medicines
- Drug compounds should be prepared in such a way that only one of the optical isomers is produced, in order to increase the drugs' effectiveness
  - Some drug enantiomers can have very harmful side effects

## Potential biological activity of enantiomers

- If **conventional organic reactions** are used to make the desired drug, a **racemic mixture** will be obtained
  - In a racemic mixture, there are equal amounts of the two enantiomers
- The **physical** and **chemical** properties of the enantiomers are the same, however, they may have opposite biological activities
- For example, the drug **naproxen** is used to treat pain in patients who suffer from arthritis
  - One of the enantiomers of naproxen eases the pain, whereas another enantiomer causes liver damage
- One enantiomer of a drug used to treat tuberculosis is effective whereas another enantiomer of this drug can cause blindness
- Thalidomide is another example of a drug that used to be used to treat morning sickness, where one of the enantiomers caused very harmful side effects for the unborn baby

## Separating racemic mixtures

- Due to the different biological activities of enantiomers, it is very important to **separate** a racemic mixture into **pure single enantiomers** which are put in the drug product
- This results in **reduced side-effects** in patients
  - As a result, it protects pharmaceutical companies from legal actions if the side effects are too serious
- It also **decreases** the patient's **dosage** by half as the pure enantiomer is more **potent** and therefore reduces production costs
  - A more potent drug has better **therapeutic activity**

## Chiral catalysts

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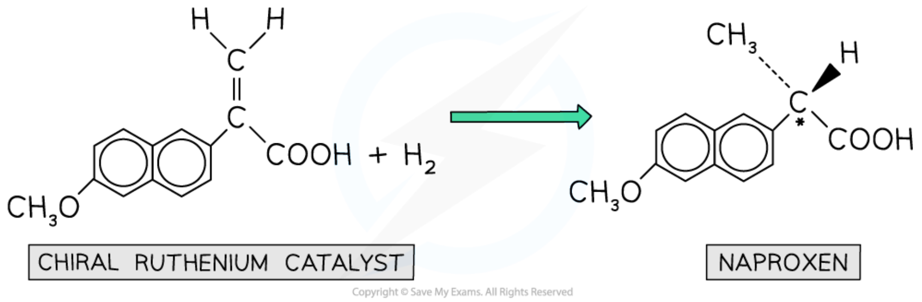
- In order to produce single, pure optical isomers, **chiral catalysts** can be used
- The benefits of using chiral catalysts are that only **small amounts** of them are needed and they can be **reused**
  - For example, an organometallic ruthenium catalyst is used in the production of **naproxen** which is used in the treatment of arthritis

## Using catalysts to direct the production on one enantiomer




***The organometallic ruthenium catalyst is a chiral catalyst which ensures that only one of the enantiomers is formed which can be used in treating arthritis***

- **Enzymes** are excellent biological chiral catalysts that promote **stereoselectivity** and produce single-enantiomer products only
  - **Stereoselectivity** refers to the preference of a reaction to form one enantiomer over the other
- Due to the **specific** binding site of enzymes, only one enantiomer is formed in the reaction
- The enzymes are fixed in place on **inert supports** so that the reactants can pass over them without having to later separate the product from the enzymes
- The **disadvantage** of using enzymes is that it can be **expensive** to isolate them from living organism
  - Therefore, more research has recently been carried out into designing **synthetic enzymes**
- Although using enzymes to produce pure enantiomers in drug synthesis takes longer than conventional synthetic routes, there are many advantages to it in the long run
  - For example, using enzymes to synthesise drugs is a **greener** process as fewer steps are involved compared to conventional synthetic routes