

Amino Acids

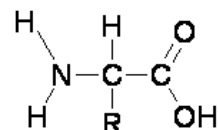
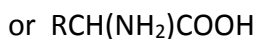
Amino acids are the building blocks for biological molecules called peptides, and for proteins (polypeptides). The body has 20 different amino acids from which to assemble proteins.

Structure

An amino acid contains the functional groups -NH_2 and -COOH (amine and carboxylic acid).

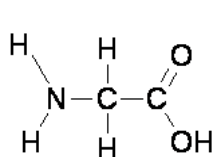
In an α -amino acid (such as the 20 the body uses to make proteins) the -NH_2 and -COOH groups are both bonded to the same carbon atom.

The general formula of an α -amino acid can therefore be written as:

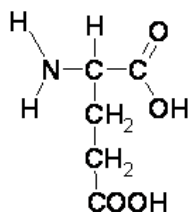


The R-group is usually an alkyl group but can contain -OH , -SH , -COOH or -NH_2 groups.

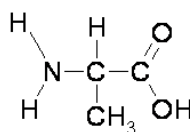
Example of α -amino acids:



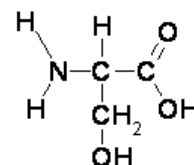
glycine
(aminoethanoic acid)



glutamic acid
(2-aminopentanedioic acid)



alanine
(2-aminopropanoic acid)



serine
(2-amino-3-hydroxypropanoic acid)

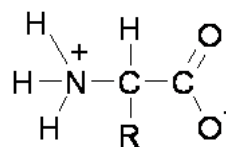
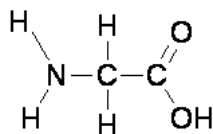
EXTENSION MATERIAL – NOT ON SPECIFICATION

Zwitterions

The acidic carboxylic acid group can donate a proton to the basic amine group. The result is an internal salt (a molecule having both a positive and a negative charge on different parts of the same molecule) known as a zwitterion.

A zwitterion has no overall charge.

e.g.

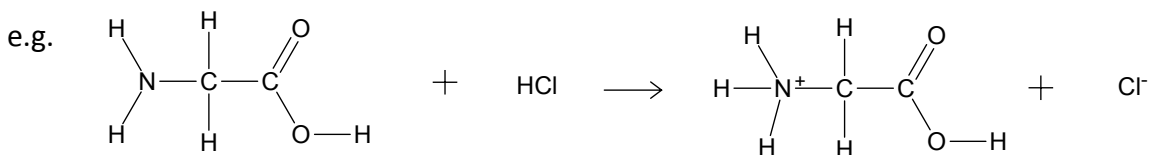


Each amino acid has a characteristic pH called the **ISOELECTRIC POINT** at which it exists as a zwitterion. The exact value of pH depends on the nature of the R- group. The presence of an acidic group such as $-\text{COOH}$ in the R-group shifts the isoelectric point to a lower (more acidic) pH, while the presence of a basic group such as $-\text{NH}_2$ in the R- group shifts the isoelectric point to higher (more alkaline) pH.

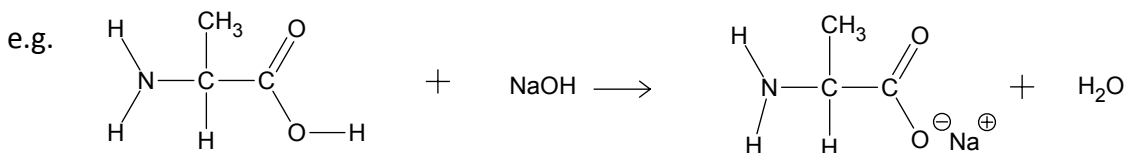
Amphoteric properties of amino acids

Amino acids are amphoteric – which means they can react with both acids and bases.

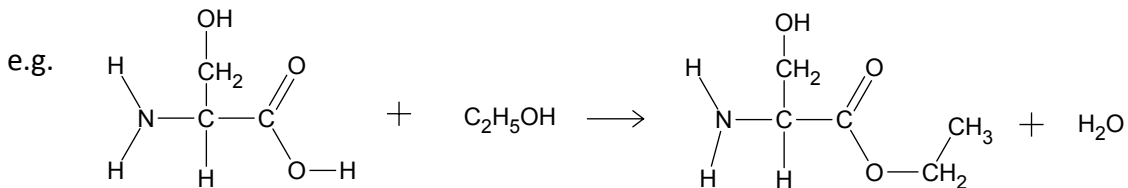
The $-\text{NH}_2$ group, like any amine, is able to act as a **base** by using the lone pair on the N atom to **accept a proton**. It can therefore neutralise acids, forming salts.



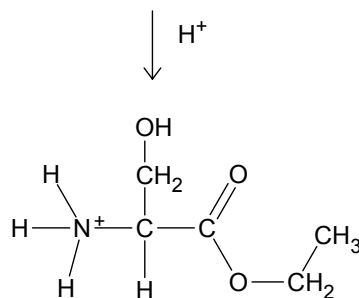
The $-\text{COOH}$ group, as in carboxylic acid, can act as a **proton donor**. The carboxylic acid group in an amino acid therefore can form salts when reacted with alkalis,



and form esters when heated with an alcohol in the presence of concentrated sulphuric acid as a catalyst.



Note that because this reaction is carried out under acidic conditions, the amine group in the amino acid (which is a base) will also react with the acid and become protonated.



Chirality and Optical Isomerism

We have already met stereoisomerism in the form of E/Z (and the more specific cis-trans) isomerism. Here the restricted rotation around double bond results in two isomers. These two isomers may have different chemical properties – why might this be?

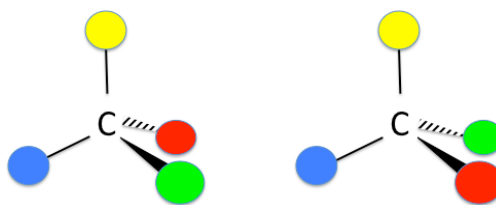
e.g. The acid $\text{HOOCCH}=\text{CHCOOH}$ can be extracted from unripe tomatoes and apples, and also from the wild flower *Fumaria officinalis*. When heated, the acid obtained from unripe tomatoes or apples reacts, forming a cyclic acid anhydride. The acid from the wild flower, however, does not react.

The explanation for this, that the acid from the tomatoes or apples has the acid functional groups on the same side of the double bond where they can react, while the acid from the wild flower has the acid groups on opposite sides of the double bond where restricted rotation around the bond prevents them from reacting, gained van't Hoff the first Nobel Prize in Chemistry for his contribution of the ideas of cis- and trans-isomers in stereochemistry.

With the exception of glycine, amino acids are examples of molecules that show a different type of stereoisomerism: **optical isomerism**.

This occurs when a carbon atom in a molecule has four different groups attached to it. For example, the C in an alanine molecule has $-\text{H}$, $-\text{CH}_3$, $-\text{NH}_2$ and $-\text{COOH}$ attached to it. We call such a carbon atom **chiral**.

Because of the tetrahedral arrangement of groups around a carbon with four single bonds, there are two possible arrangements for these groups. They are mirror images of one another. Rotations of the molecule about the carbon atom cannot make one optical isomer the same as the other.



Definition: optical isomerism occurs when a molecule has non-superimposable mirror images about a chiral centre. Optical isomers are also referred to as enantiomers.

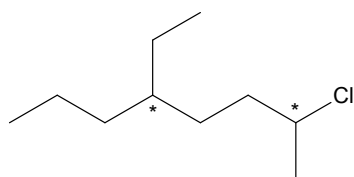
Optical isomers are chemically identical, although they have different physical properties, in that they rotate plane-polarised light in different directions.

A molecule can have more than one chiral centre. Each produces two optical isomers, so if a molecule has two chiral carbon atoms it will have two pairs of isomers (i.e. four optical isomers).

Identifying optical isomers

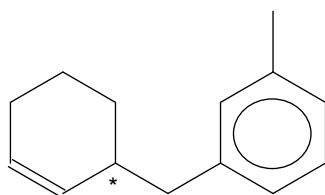
We find a chiral centre anywhere the four groups attached to a carbon atom are different. This sounds straight forward, but can be made difficult in two ways:

i) when the molecule is presented skeletally (and so hydrogen atoms are hidden)



e.g. in 2-chloro-5-ethyloctane there are two chiral carbons, indicated with *. Hint: it is easier to see chiral carbons if you re-draw the molecule displayed.

ii) when the molecule is large or contains rings - the points of difference can be quite a distance from the chiral carbon, and the whole of the molecule has to be considered.



e.g. this molecule only has one chiral centre, indicated with *. You need to be sure you understand both why this carbon is chiral, and why the others aren't – especially the carbon two to the right of the chiral one.

Practice:

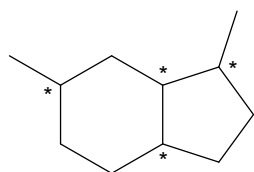
Which of the following molecules has chiral centers, and where are they:

$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OH}$ - no

$\text{CH}_3\text{CH}_2\text{CH}(\text{NH}_2)\text{CH}_3$ - yes 3rd C from the left is chiral

$\text{CH}_3\text{CHClCH}_3$ - no

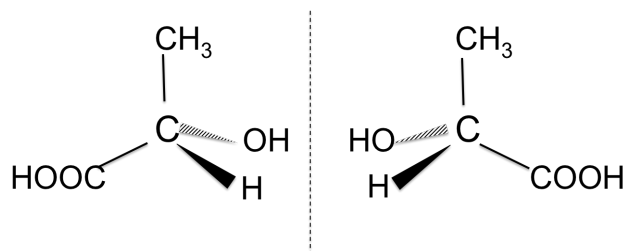
$\text{CH}_3\text{CH}(\text{OH})\text{Br}$ - yes 2nd C from left is chiral



- yes, four of them shown with *

Drawing the optical isomers

- Structures must be drawn around a correctly-drawn 3D tetrahedral carbon centre
- Each enantiomer is then drawn as the mirror image of the other one
- Structural formulae may be used for attached groups if convenient (and unless told otherwise in the question)
- Use a vertical dotted line to show the mirror plane between the two molecules
- Remember to draw the connecting bonds to the correct atoms on the four groups

**Significance of Optical Isomerism**

Optical activity is important in biological systems where frequently only one of the optical isomers is biologically active – only one of the optical isomers will interact with an enzyme due to the specific geometry of the receptor sites on enzymes – we call this being stereospecific. This can result in them having different sensory effects or medical effects.

e.g. leucine – an amino acid with $R = -CH_2CH(CH_3)_2$

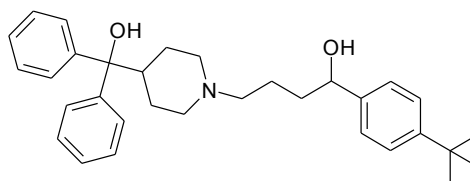
One optical isomer tastes sweet, the other tastes bitter and is used as a food additive.

e.g. Thalidomide (1954)

- prescribed to prevent morning-sickness in pregnant women
- drug was later found to be chiral – only one enantiomer had the required therapeutic effect
- the drug was not marketed in the US because the FDA demanded further testing before licensing, and during this process the activity of the other enantiomer was discovered
- the other optical isomer led to deformities in developing babies – some 10,000 were affected in Europe

e.g. Seldane – one of the first antihistamines

- used to relieve hayfever symptoms
- chiral with one enantiomer having the required therapeutic effect
- after testing and licensing, it was found that the “inactive” isomer caused a potentially fatal heart condition in some patients



e.g. Ibuprofen

- one active optical isomer controls pain effectively by blocking messages to the brain and reducing swelling and inflammation
- the other isomer is inactive, but is fortuitously converted into the active isomer in the body, so the whole dose is active

