

Edexcel

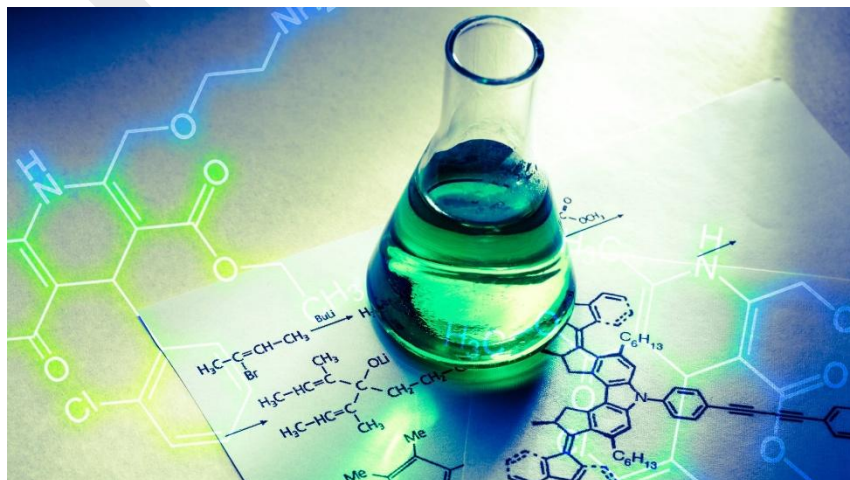
A - Level

Chemistry

CODE: (WCH11)

Topic 19

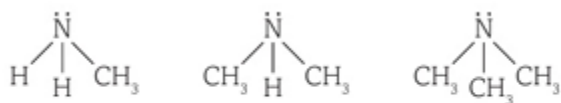
*Organic nitrogen compounds:
amines, amides,
amino acids and protein*



19A 1 Amines and their preparation

INTRODUCTION TO AMINES

These nitrogen-containing compounds have some similarities with ammonia. The three bonding pairs of electrons around nitrogen are distributed in a trigonal pyramidal shape. The nitrogen atom has a lone pair of electrons and three bonds to one or more alkyl groups. If there is one alkyl group, the amine is classed as primary. If there are two, then it is secondary. With three it is tertiary. Fig A shows the structures of the simplest amine in each of these classes.



▲ fig A These are the simplest examples of primary, secondary and tertiary amines.

NOMENCLATURE

We learned about amines in **Topic 10 (Book 1: IAS)**, but only as the product of reactions between halogenoalkanes and ammonia.

Table A shows the structural formulae and names of some examples of amines.

STRUCTURAL FORMULA	NAME
CH_3NH_2	methylamine
$\text{CH}_3\text{CH}_2\text{NH}_2$	ethylamine
$\text{CH}_3\text{CH}_2\text{CH}_2\text{NH}_2$	propylamine
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$	butylamine
$\text{C}_6\text{H}_5\text{NH}_2$	phenylamine

table A

DISPLAYED AND SKELETAL FORMULAE OF AMINES

Table B shows the displayed and skeletal formulae of the amines in **table A**.

NAME	DISPLAYED FORMULA	SKELETAL FORMULA
methylamine		
ethylamine		
propylamine		
butylamine		
phenylamine		

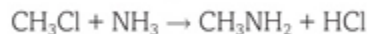
table B

PREPARATION OF ALIPHATIC AMINES

There are two main ways of making primary aliphatic amines, starting from halogenoalkanes or from nitriles.

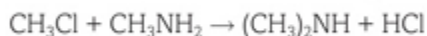
PREPARATION FROM HALOGENOALKANES

The method involves heating a halogenoalkane with ammonia. Because ammonia is a gas, this must be done under pressure and in a sealed container. Alternatively, the halogenoalkane can be mixed with concentrated aqueous ammonia. The equation for the preparation of methylamine is:



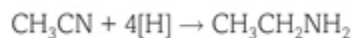
The reaction involves nucleophilic attack by the lone pair of electrons of ammonia on the electron-deficient carbon atom in the halogenoalkane. Notice that the amine formed also has a nitrogen atom containing a lone pair of electrons.

This means that it could also act as a nucleophile, competing with ammonia in the attack on the halogenoalkane. This would result in the reaction:



The product of this reaction is a secondary amine, in this case dimethylamine.

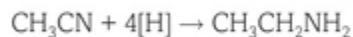
To prevent such unwanted side-reactions occurring, or at least reduce the chances of them happening, the ammonia is used in excess, so that it outnumbers the molecules of primary amine formed. Some of the excess ammonia reacts with the acidic hydrogen chloride formed, so a better equation to represent the preparation is:



PREPARATION FROM NITRILES

Nitriles can be reduced to primary amines by reduction, using the reducing agent lithium tetrahydridoaluminate, which you may remember from Topic 15 can also be used to reduce carbonyl compounds.

As before, the reactants are mixed in dry ether, to ensure that there is no water that could affect the reaction. The equation for the reduction of ethanenitrile is:

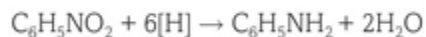


[H] represents hydrogen atoms produced by the reagent in a way that you do not need to know.

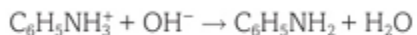
PREPARATION OF AROMATIC AMINES

A specific method is used to prepare aromatic amines, especially phenylamine, which is made by the reduction of nitrobenzene. In this method, the reducing agent is tin mixed with concentrated hydrochloric acid, and the reaction mixture is heated under reflux (fig C).

The reduction is achieved partly through the oxidation of tin to tin(II) ions and tin(IV) ions, and partly through the hydrogen produced in the reaction between tin and the acid. To make things simple we will represent the reducing agent by [H]. The equation for the reaction is:



As with other amines, phenylamine is basic and will react with the acid present to form the phenylammonium ion, but this can easily be converted into phenylamine by adding an alkali such as sodium hydroxide solution:



19A – Acid base reactions of amines

REACTIONS WITH WATER

Primary aliphatic amines are initially miscible with water, but their solubility decreases as the hydrocarbon part grows. They dissolve in water through hydrogen bonds and react slightly with water to form alkaline solutions.

Compare the equations using methylamine and ammonia:

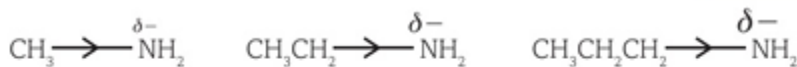


COMPARING BASICITIES

The **basicity** (basic strength) of a base can be quantified using the constant K, or the constant pK. The pK_b of water at 298 K is 7.00, and any value lower than 7.00 indicates a basicity greater than that of water. Water is equally good as a base and as an acid. Table A shows the pK_b values at 298 K for ammonia and some amines.

NAME	FORMULA	pK _b
ammonia	NH ₃	4.75
methylamine	CH ₃ NH ₂	3.36
ethylamine	CH ₃ CH ₂ NH ₂	3.27
propylamine	CH ₃ CH ₂ CH ₂ NH ₂	3.16
phenylamine	C ₆ H ₅ NH ₂	9.38

table A

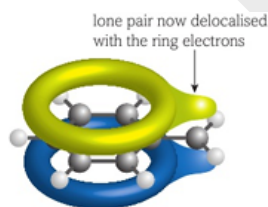


▲ **fig B** The diagram represents the slight increase in the electron-releasing effect of alkyl groups, causing a slight increase in electron density on the nitrogen atoms.

The equation for the reaction of butylamine with water is



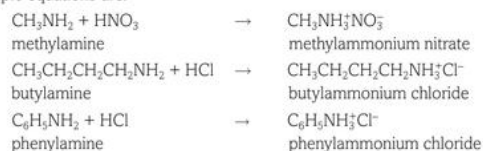
Phenylamine incorporates one of the lone pairs of electrons on oxygen into delocalised electrons in the benzene ring, making nitrogen less electron-rich and the lone pair less available for hydrogen bonding to water molecule hydrogen. This results in a delocalised system.



▲ **fig C** The electrons from the lone pair on the nitrogen have joined with the delocalised electrons on the benzene ring.

REACTIONS WITH ACIDS

Even though the amines vary in their basicity, they all react with strong acids to form ionic salts. Sample equations are:

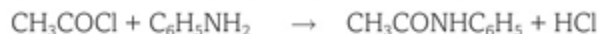


19A 3 Other reactions of amines

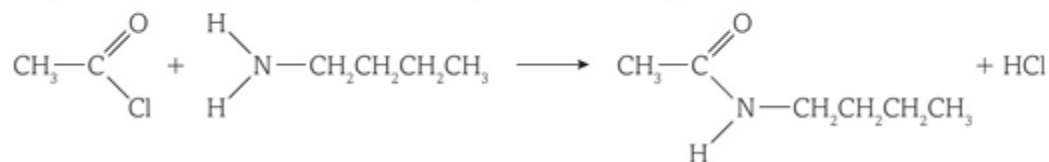
REACTIONS WITH ETHANOYL CHLORIDE

You do not need to know the mechanisms of these reactions. However, the name of the mechanism will help you understand how the reactions occur. The reaction type is **addition-elimination**, which means that the two molecules join together, and then a small molecule is eliminated - in these examples, hydrogen chloride. The organic product contains an new functional group - amide - in which a carbonyl group is next to an NH group. The equation for the reaction of phenylamine with ethanoyl chloride is:

The equation for the reaction of phenylamine with ethanoyl chloride is:

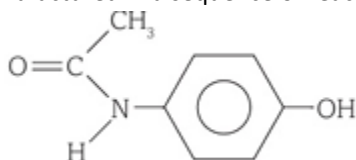


The equation for the reaction between ethanoyl chloride and butylamine is:



PARACETAMOL

This is one of the most common pharmaceuticals used to relieve the symptoms of fever and pain. It is manufactured in a sequence of reactions, one of which is an addition-elimination reaction. Its structure is:



REACTIONS WITH HALOGENOALKANES

You do not need to know the mechanisms of these reactions. However, you can see that the two would react together because a halogenoalkane contains an electron-deficient carbon atom and amines contains electro – rich nitrogen atom. Using general formula the reaction can be represented by :

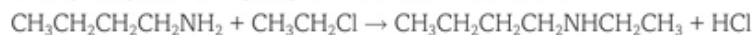


where R' is the alkyl group in the amine and R'' is the alkyl group in the halogenoalkane. The reaction is another example of substitution. The organic product is a secondary amine and the inorganic product is a hydrogen halide, often hydrogen chloride.

The equation for the reaction between phenylamine and chloroethane is:



An example equation using butylamine and chloroethane is:



Notice that the organic product also contains an electron-rich nitrogen atom, so it can also react with chloroethane. The equation for this further reaction is:



The organic product of this reaction is a tertiary amine.

Once again, the tertiary amine contains a nitrogen atom with a lone pair of electrons, which can also react with the halogenoalkanes. The equation for this further reaction is:



The equation for quaternary ammonium salt is different from HCl, as it doesn't require the loss of H from the organic reactant. This ionic compound, similar to ammonium chloride, has alkyl groups replacing hydrogens. Reactions with halogenoalkanes aren't ideal for preparation, but this sequence is common in industry, often used in fabric softeners.

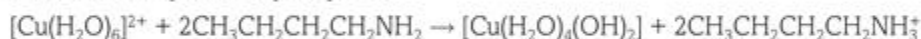
REACTIONS WITH COPPER(II) IONS

You will remember from Topic 17 that ammonia can act as a lone pair donor in its reactions with transition metal ions. This is the overall equation for its reaction with hexaaquacopper(II) ions:



Amines also have a lone pair of electrons on nitrogen, so can take part in similar reactions. The observations are the same as with ammonia – first of all a pale blue precipitate forms, then with excess butylamine the precipitate dissolves to give a deep blue solution. The equations for these reactions look complicated, but the only difference is the use of $\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$ in place of NH_3 .

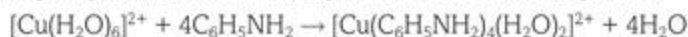
Formation of the pale blue precipitate:



Formation of the deep blue solution:



With phenylamine, the overall equation to form the complex is:



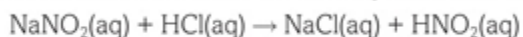
FORMATION OF AZO DYES

REACTION OF PHENYLAMINE WITH NITROUS ACID

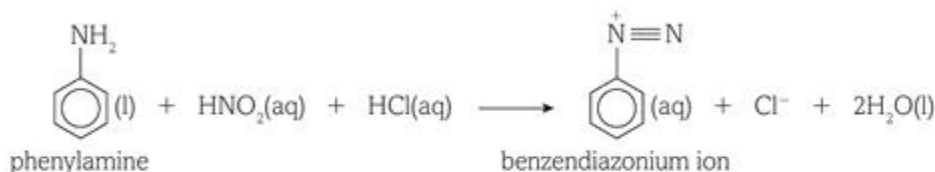
Nitrous acid is a very unstable compound. It exists only in aqueous solution and decomposes at room temperature.

The nitrous acid must be prepared in situ by mixing ice-cold solutions of sodium nitrite and dilute hydrochloric acid.

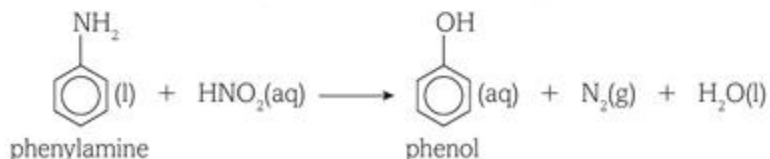
The equation for the reaction is:



If an aromatic amine, such as phenylamine, is then added to this reaction mixture, a diazonium ion is formed:

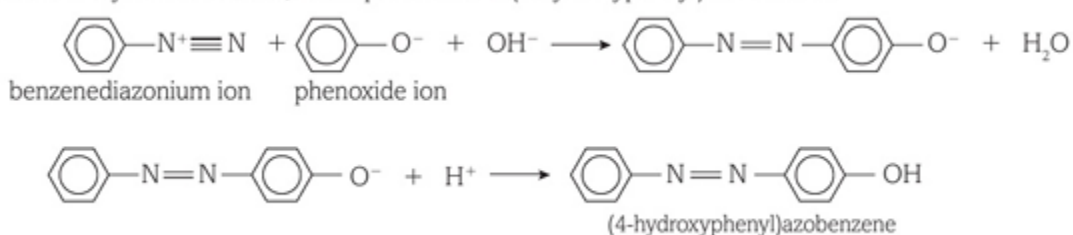


The reaction vessel must be kept in an ice-water mixture because the reaction must be carried out at 5 °C or lower. If the temperature rises above 5 °C, phenol is formed:

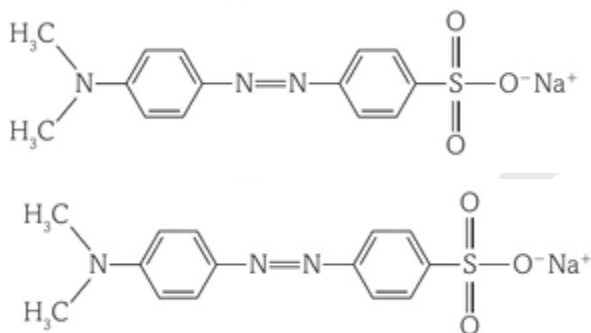


REACTION OF DIAZONIUM IONS WITH PHENOLS

Diazonium ions carry a positive charge and therefore can act as strong electrophiles. For example, the benzenediazonium ion reacts readily in cold, alkaline solution with both aromatic phenols and amines. The benzenediazonium ion reacts with an alkaline solution of phenol to produce, after acidification with dilute hydrochloric acid, a compound called (4-hydroxyphenyl)azobenzene:



A **coupling reaction** forms a yellow azo dye, characterized by extensive electron delocalization via nitrogen-to-nitrogen double bond, forming **conjugated systems** with alternating double and single bonds, resulting in light absorption.



SUBJECT VOCABULARY

addition-elimination reaction when two molecules join together, followed by the loss of a small molecule

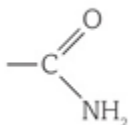
coupling reaction a reaction in which two organic molecules or ions join together to form one new molecule

conjugated system where single and double bonds alternate, allowing the electrons in the p-orbitals of the atoms to overlap and form a delocalised electron cloud

19A 4Amides and polyimides

AMIDES

We learned about amides in previous sections as the products of reactions. Amides have a functional group consisting of a carbonyl group joined to an amino group as shown.



NOMENCLATURE

Table A shows the structural formulae and names of some amides.

STRUCTURAL FORMULA	NAME
HCONH_2	methanamide
CH_3CONH_2	ethanamide
$\text{CH}_3\text{CH}_2\text{CONH}_2$	propanamide
$\text{CH}_3\text{CH}_2\text{CH}_2\text{CONH}_2$	butanamide

table A

DISPLAYED AND SKELETAL FORMULAE OF AMIDES

Table B shows the displayed and skeletal formulae of the amides in **table A**.

NAME	ABBREVIATION	STRUCTURE	ISOELECTRIC POINT
alanine	ala	$\begin{array}{c} \text{H}_2\text{N}-\text{CH}-\text{COOH} \\ \\ \text{CH}_3 \end{array}$	6.0
cysteine	cys	$\begin{array}{c} \text{H}_2\text{N}-\text{CH}-\text{COOH} \\ \\ \text{CH}_2-\text{SH} \end{array}$	5.1
glutamic acid	glu	$\begin{array}{c} \text{H}_2\text{N}-\text{CH}-\text{COOH} \\ \\ \text{CH}_2-\text{CH}_2-\text{COOH} \end{array}$	3.2
glycine	gly	$\text{H}_2\text{N}-\text{CH}_2-\text{COOH}$	6.0
lysine	lys	$\begin{array}{c} \text{H}_2\text{N}-\text{CH}-\text{COOH} \\ \\ \text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{NH}_2 \end{array}$	9.7

table A

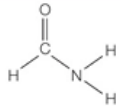

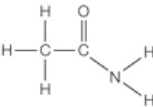

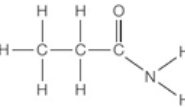

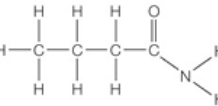

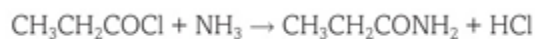
NAME	DISPLAYED FORMULA	SKELETAL FORMULA
methanamide		
ethanamide		
propanamide		
butanamide		

table B

PREPARATION OF AMIDES

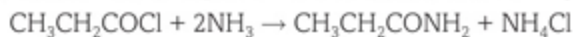
Amino acids can be prepared in the lab by mixing acyl chloride with concentrated aqueous ammonia. The reaction involves the electron-deficient carbon atom of acyl chloride attracting the nitrogen lone pair, forming hydrogen chloride as misty fumes. The equation for the reaction between propanoyl chloride and ammonia is:



Note that ammonia is basic and that the inorganic product is acidic, so there will be a reaction between the two molecules:



So, a better overall equation for the reaction, combining these equations, is:



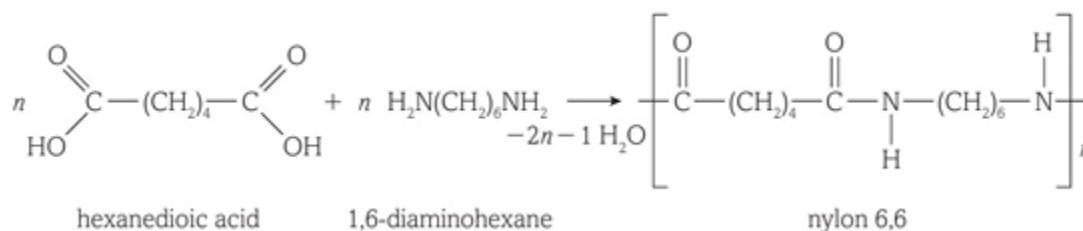
POLYAMIDES

Topic 15 discussed polyesters and polyamides, which are formed through condensation polymerisation reactions. Polymers require dicarboxylic acid and diol, while polyamides require dicarboxylic acid and diamine. Examples include HOOCCOOH and $\text{H}_2\text{NCH}_2\text{NH}_2$, which react to form a CONH group.

NYLON

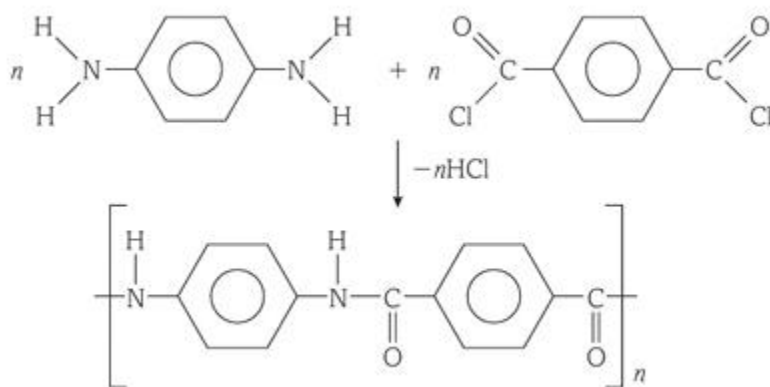
Nylon is a polyamide, with common monomers like hexanedioic acid and hexane-1,6-diamine containing six carbon atoms. Both have the same number of CH_2 groups and reactive groups.

The formation of this polymer is shown below:



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If benzene rings take the place of the CH_2 groups in the monomers used to make nylon 6,6, and a diol chloride is used in place of a dicarboxylic acid, then the monomers and the polymer structure can be shown like this:



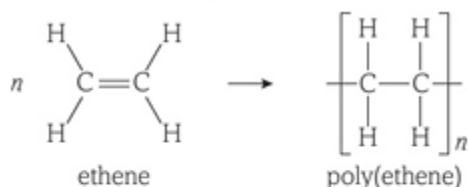
PROPERTIES OF POLYAMIDES

Polyamides, such as nylons, are semi-crystalline materials with excellent thermal and chemical resistance. They absorb moisture, increasing impact resistance and flexibility with moisture content. They are used in clothing, fishing lines, carpets, and Kevlar®. Polyamide film is used for food packaging and 'boil-in-the-bag' due to its toughness and high temperature resistance. However, they can be attacked by strong acids and alkalis.

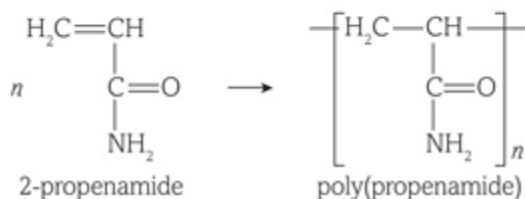
POLY(PROPENAMIDE)

In Topic 5 (Book 1: IAS) you learned about addition polymerisation. This is when many molecules (monomers) with double bonds join together to form a long-chain molecule (polymer). In this reaction, one of the bonds in the

double bond is broken and the monomers are linked together by single bonds. The most common example of this is the formation of poly(ethene) from ethene:

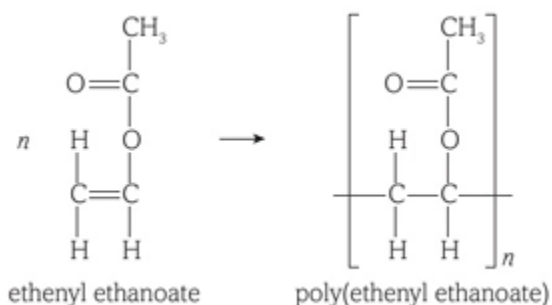


Poly(propenamide) is an addition polymer. It is formed by polymerising 2-propenamide (sometimes called acrylamide):

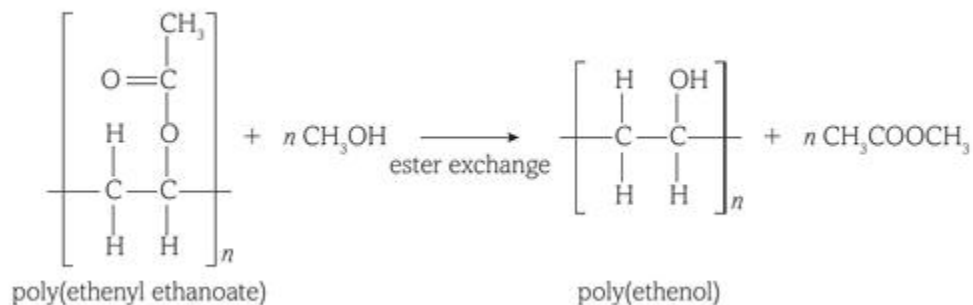


POLY(ETHENOL)

Poly(ethenol) is another addition polymer. It is sometimes called poly(vinyl alcohol). It is not manufactured in the usual way by directly polymerising a monomer. Instead it is made in two stages. The first stage is the polymerisation of ethenyl ethanoate:



In the second stage, poly(ethenyl ethanoate) is reacted with methanol to form poly(ethenol) and methyl ethanoate, in a process called ester exchange:

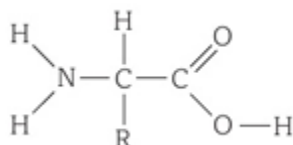


The amount of ester exchange can be controlled by altering the temperature.

19A 5 Amino acids

WHAT ARE AMINO ACIDS?

The name suggests the presence of an amino group and a carboxylic acid group. Unlike amides, these two groups are separated by a carbon atom and so retain most of their typical properties. Below is the general displayed formula of an amino acid.



NAME	ABBREVIATION	STRUCTURE	ISOELECTRIC POINT
alanine	ala	$ \begin{array}{c} \text{H}_2\text{N}-\text{CH}-\text{COOH} \\ \\ \text{CH}_3 \end{array} $	6.0
cysteine	cys	$ \begin{array}{c} \text{H}_2\text{N}-\text{CH}-\text{COOH} \\ \\ \text{CH}_2-\text{SH} \end{array} $	5.1
glutamic acid	glu	$ \begin{array}{c} \text{H}_2\text{N}-\text{CH}-\text{COOH} \\ \\ \text{CH}_2-\text{CH}_2-\text{COOH} \end{array} $	3.2
glycine	gly	$ \text{H}_2\text{N}-\text{CH}_2-\text{COOH} $	6.0
lysine	lys	$ \begin{array}{c} \text{H}_2\text{N}-\text{CH}-\text{COOH} \\ \\ \text{CH}_2-\text{CH}_2-\text{CH}_2-\text{CH}_2-\text{NH}_2 \end{array} $	9.7

table A

NOMENCLATURE

Although amino acids are usually referred to by their common names, such as glycine, $\text{H}_2\text{NCH}_2\text{COOH}$, and alanine, $\text{H}_2\text{NCH}(\text{CH}_3)\text{COOH}$, they also have systematic names using the rules defined by IUPAC. They are named as amine derivatives of carboxylic acids, using the prefix *amino* to indicate the presence of the amine group, NH_2 . A locant is used to indicate the position of the amine group in the carbon chain of the carboxylic acid.

Table B shows the structural formulae and names of some amino acids. The 3-amino acids are not naturally occurring.

STRUCTURAL FORMULA	NAME
$\text{H}_2\text{NCH}_2\text{COOH}$	2-aminoethanoic acid
$\text{CH}_3\text{CH}(\text{NH}_2)\text{COOH}$	2-aminopropanoic acid
$\text{H}_2\text{NCH}_2\text{CH}_2\text{COOH}$	3-aminopropanoic acid
$\text{CH}_3\text{CH}(\text{NH}_2)\text{CH}_2\text{COOH}$	3-aminobutanoic acid
$\text{C}_6\text{H}_5\text{CH}(\text{NH}_2)\text{COOH}$	2-aminophenylethanoic acid

table B

DISPLAYED AND SKELETAL FORMULAE OF AMINES

Table C shows the displayed and skeletal formulae of the amines in table B.

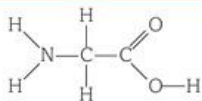
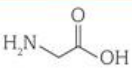
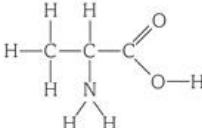
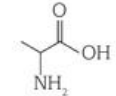
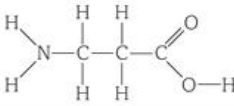
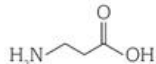
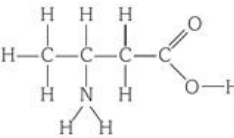
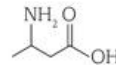
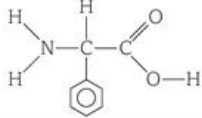
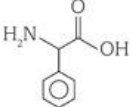
NAME	DISPLAYED FORMULA	SKELETAL FORMULA
2-aminoethanoic acid		
2-aminopropanoic acid		
3-aminopropanoic acid		
3-aminobutanoic acid		
2-aminophenylethanoic acid		

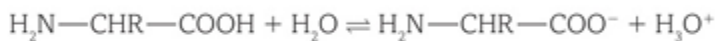
table C

ACIDIC AND BASIC PROPERTIES

The values of the **isoelectric points** of the amino acids have been included to help you understand their acid-base character. They are all soluble in water, and you can imagine that one of two reactions might occur. The molecule could act as a base and form an alkaline solution in a reaction like this:



Alternatively, it could act as an acid and form an acidic solution in a reaction like this:



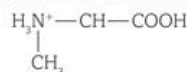
There is a third alternative – an H^+ ion could transfer from the COOH group to the NH_2 group in a reaction like this:



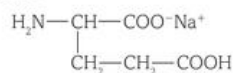
The product of this reaction is electrically neutral because it has a positive charge and a negative charge that balance each other. Such species are called **zwitterions**. Zwitter is the German word for hybrid, meaning a cross between two things and having the characteristics of both.

SALT FORMATION

All amino acids can form salts with acids and bases. For example, alanine can react with acids to form this protonated structure:



Glutamic acid can react with sodium hydroxide to form three possible salts. This is because there are two COOH groups, so either of them can react, or both can react. One salt has the structure:



You may have heard of this salt – its name is monosodium glutamate and is often used as a flavour enhancer in food.



fig A Monosodium glutamate can be used as a flavour enhancer in cooking.

OPTICAL ACTIVITY

Almost all 2-amino acids contain a chiral centre (the C of the CH group), and so are optically active. The exception is glycine, which has a CH₂ group instead. Aqueous solutions of the enantiomers rotate the plane of polarisation of plane-polarised light - some enantiomers are dextrorotatory (+) and others are laevorotatory (-). If an amino acid is synthesised in the laboratory, then a racemic mixture is formed.

SUBJECT VOCABULARY

isoelectric point (of an amino acid) the pH of an aqueous solution in which it is neutral

zwitterion a molecule containing positive and negative charges but which has no overall charge

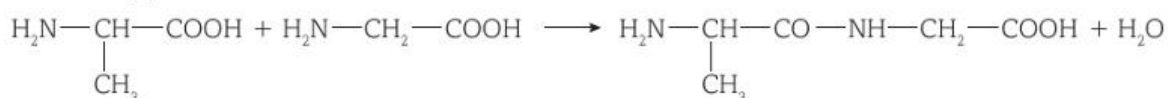
19A 6Peptisides and proteins**WHAT IS A PEPTIDE?**

When two amino acid molecules react together, an acid-base reaction occurs. The OH of the COOH group combines with one of the H atoms of the NH₂ group to form water. This is a condensation reaction, in which the two amino acids are joined together by an amide group (CO-NH). The bond that forms is known as a **peptide bond**, and the organic product is a dipeptide.

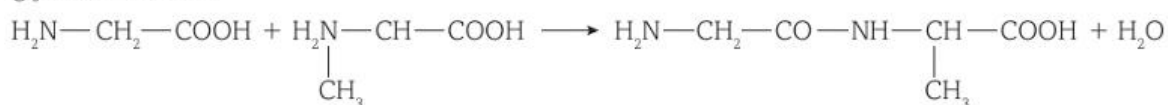
MORE THAN ONE DIPEPTIDE

When two amino acids combine together to form a dipeptide, there are always two possibilities - sometimes more. For example, when glycine reacts with alanine, the OH could be lost from either molecule, as shown below.

alanine + glycine:



glycine + alanine:



TRYPEPTIDES

When one molecule of each of three different amino acids reacts together to form a tripeptide, the six possibilities can be summarised using the three-letter abbreviations shown in the table in the previous section. They are:

ala-cys-glu ala-glu-cys cys-ala-glu cys-glu-ala glu-ala-cys glu-cys-ala

If you work out the possibilities in which two or more molecules of the same amino acid in these three react to form a tripeptide you will find that there are many more!

POLYPEPTIDES AND PROTEINS

Polypeptides and proteins are formed by condensation polymerisation of many amino acids. The main difference between a long-chain polypeptide and a protein is that proteins have further levels to their structures. These are to do with the way in which the polypeptide chains interact with each other in three dimensions, to give secondary, tertiary and quaternary structures, but these are beyond the aims of this book.

ANALYSING PROTEINS

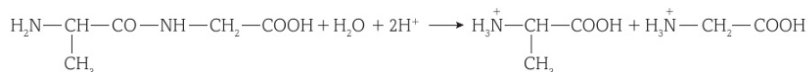
Many proteins have very large molar masses and complex structures. In recent decades, more and more proteins have been analysed. As several million different proteins are thought to exist, this work is still continuing but far from complete. Table A shows three examples of proteins, the first two of which have vital roles in the human body.

PROTEIN	WHERE FOUND	APPROXIMATE MOLAR MASS/g mol ⁻¹	APPROXIMATE NUMBER OF AMINO ACIDS
insulin	pancreas	5700	51
haemoglobin	blood	66 000	574
urease	soya beans	480 000	4500

table A

HYDROLYSING PROTEINS

Hydrolysis of proteins involves heating polypeptide chains with concentrated hydrochloric acid, breaking peptide bonds and protonating NH₂ groups. This process is more visible in dipeptides like alanine and glycine, with the hydrolysis equation being:



USING CHROMATOGRAPHY

Topic 15 covers various types of chromatography, including simple chromatography, which involves spotting amino acids on chromatography paper. These amino acids are colorless and can be sprayed with a developing agent like ninhydrin to see their positions. Once positions are established, R values can be calculated to identify individual amino acids. Insulin, a protein with 51 amino acids, is an example of a protein structure.

SUBJECT VOCABULARY

peptide bond the bond formed by a condensation reaction between the carbonyl group of one amino acid and the amino group of another amino acid

polypeptide a condensation polymer formed from many amino acids

protein a polypeptide that has folded into a specific shape in order to have a specific function



fig A This diagram shows the sequence of amino acids in insulin from a sheep. You can see that there are actually two separate sequences of amino acids in which cysteine molecules are joined by disulfide bonds.