Revision Guide

Chemistry - Unit 4
Physical and Inorganic Chemistry

These notes have been authored by experienced teachers and are provided as support to students revising for their GCE A level exams. Though the resources are comprehensive, they may not cover every aspect of the specification and do not represent the depth of knowledge required for each unit of work.

Content

4.1 - Stereoisomerism

We came across structural isomers at AS, where compounds have the same molecular formula, but different structures. We must now look at a different type of isomer that has the same arrangement of atoms, but different spatial arrangement (the way the bonds are arranged in space). There are two forms of stereoisomerism – E/Z isomerism and optical isomerism.

E/Z Isomerism

The C=C bond is central to E/Z isomerism. Compounds have different atoms or groups bonded to the carbon atoms of the double bond. These atoms can be the same or different, but you can't have two identical atoms or groups bonded to the same carbon atom. The simplest form of E/Z isomers are ones that have identical atoms attached to each carbon atom, eg 1, 2-dibromoethene: -
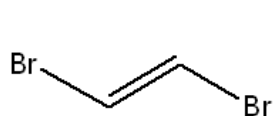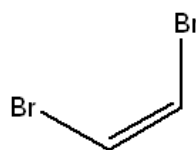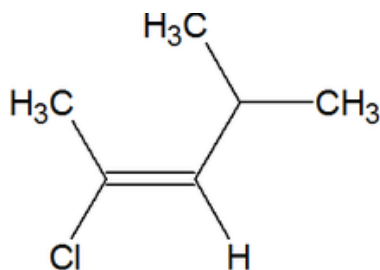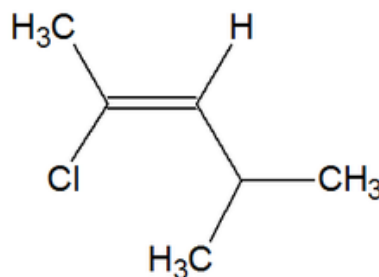

(E)-1,2-dibromoethene   (Z)-1,2-dibromoethene

- The E-isomer has atoms or groups opposite each other
- The Z-isomer has atoms or groups on the same side of the double bond.

The atoms or groups do not have to be the same as in the above example. Let's look at 2-chloro,4-methylpent-2-ene $CH_3CCl=CHCH(CH_3)CH_3$. There are two stereoisomers: -

(E)- 2-chloro,4-methylpent-2-ene

(Z) - 2-chloro,4-methylpent-2-ene

The reason why they are classed as E and Z depends on factors discussed at AS level, so you should look them up.

If you're asked to describe why E/Z isomers occur, then you should mention that the atoms or groups cannot rotate about the double bond.

Optical isomerism

As the name suggests, optical isomers influence light. They rotate the plane of plane polarised light in different directions, one to the left and one to the right.

Definitions
Chiral Centre – central carbon atom that is bonded to four *different* atoms or groups
Enantiomer – another name for an optical isomer. A molecule that is the *mirror image* of another molecule and one that rotates the plane of plane polarised light.
Racemic mixture - a solution that contains equal concentrations of each enantiomer, so it appears to have no effect on plane polarised light.
Optical activity – happens in molecules that rotate the plane of plane polarised light, ie enantiomers.

The diagram shows the optical isomers of 2-aminopropanoic acid, an amino acid found in living systems. Amino acids are often found in questions regarding optical isomerism as, not only can examiners ask questions about the structure, they can then go on to ask about the molecules as amino acids.
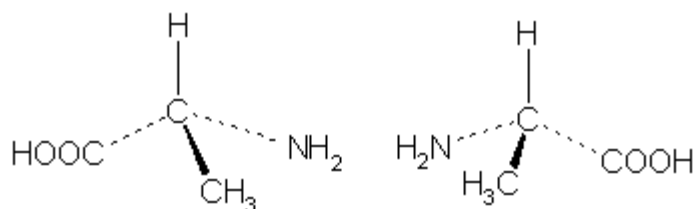

Enantiomers of 2-aminopropanoic acid

If you can imagine the blue line to be a mirror, then the two molecules are mirror images of each other. If you built two models of the isomers, then you would not be able to place one on top of the other as the atoms and groups attached to the chiral carbon are in a different order.
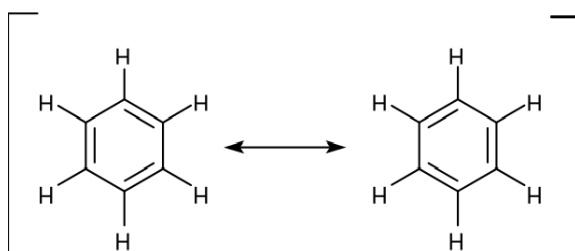
4.2 - Aromaticity

Benzene – structure

- Molecular formula C_6H_6

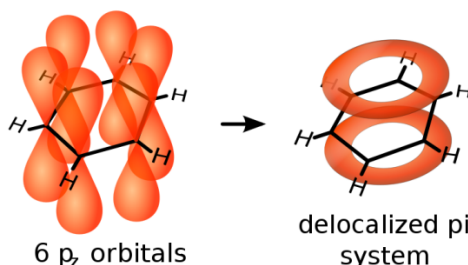- Structure from x-rays –
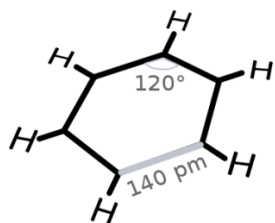
Planar Hexagon
Bond Length 140 pm

Internal C-C-C bond angle 120º
All C-C bond lengths equal, in between the lengths of single and double carbon – carbon bonds

- Suggested structure (Kekule, 1865): -

Ring of alternating single and double bonds, making it an alkene. However, it doesn't decolourise bromine water, so isn't an alkene. In fact, it is highly resistant to addition reactions.

- Actual structure (deduced by three pieces of evidence): -

Sigma Bonds
sp² Hybridized orbitals

6 p$_z$ orbitals

delocalized pi system

Benzene ring
Simplified depiction

There are the usual sigma bonds between the six carbon atoms and their hydrogens. The p-orbitals from each carbon atom overlap and form a delocalized ring system above and below the ring. Known as the delocalised π (pi)- system of electrons. The evidence for this structure is as follows: -

- All bond lengths are the same, they would be different with single and double bonds
- Benzene doesn't react by addition reactions, it reacts by substitution
- Enthalpy of hydrogenation of benzene is less than that calculated if it had alternate single and double bonds. The difference is around 150 kJ mol^{-1}, meaning that the actual structure is more stable than the Kekule structure. This energy is called the *resonance energy*.
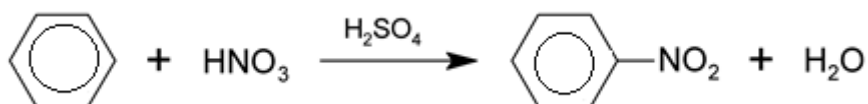
Benzene – reactions

Unlike alkenes, benzene does not carry out addition reactions. If it did, the stable delocalised electron ring would be disrupted, and the π-cloud lost. Benzene therefore reacts by electrophilic substitution of the hydrogen atoms. This keeps the electron ring intact.

Electrophilic substitution reactions

As the π-cloud has a negative charge it will attract electrophiles and undergo electrophilic substitution. The reactions below consist of attack by electrophiles made as part of the reaction.

Nitration of benzene

- **Reactants** - benzene, conc. nitric acid and conc. sulphuric acid.
- **Product** - nitrobenzene, $C_6H_5NO_2$ (above 50ºC, some 1, 3 – dinitrobenzene can be formed)
- **Temperature** - 50°C (above this temperature, dinitration can happen)
- **Overall reaction**: -

- Mechanism - 1st part of the reaction is the formation of a nitronium ion electrophile, NO_2^+ from the nitric and sulphuric acids. This then reacts with benzene to give nitrobenzene: -
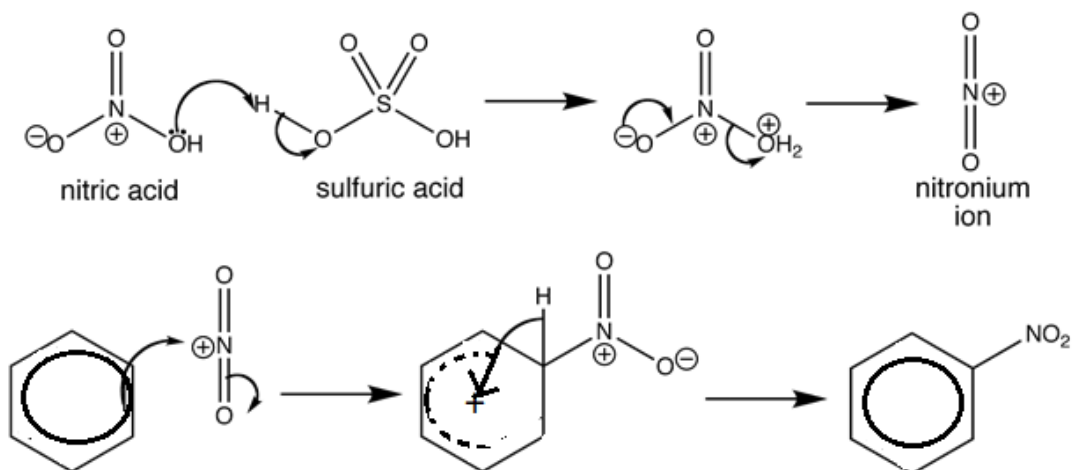
Halogenation of benzene

- **Reactants** – Benzene, bromine
- **Catalyst** – iron filings/iron(III) bromide/aluminium bromide
- **Product** – bromobenzene, C_6H_5Br
- **Temperature** – room temperature and out of direct sunlight
- **Overall reaction**: -
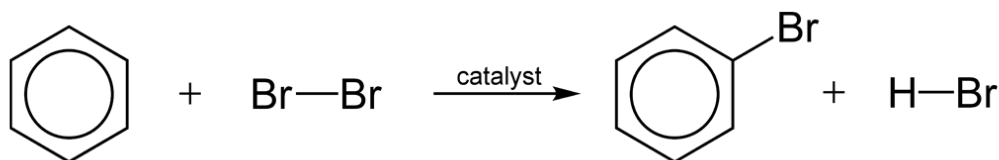
- **Mechanism** – The Br_2 molecule is polarised by the catalyst as the electron cloud is not nucleophilic enough to do so. The mechanism then follows this route: -
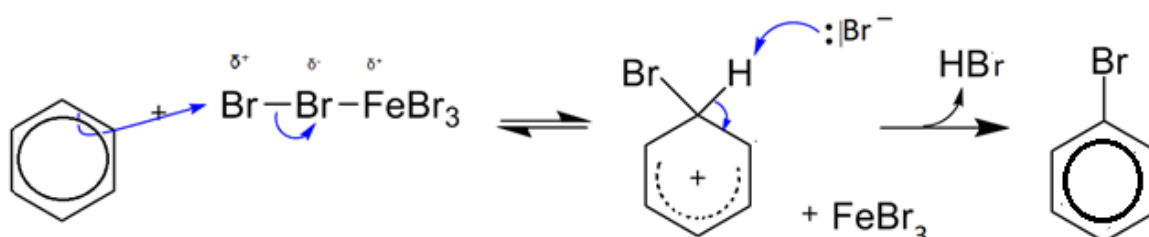
The end products are bromobenzene, hydrogen bromide (toxic, so use of a fume cupboard is required) and the regeneration of the iron(III) bromide catalyst.

Chlorobenzene is made in a similar way, but in the dark with an iron(III) chloride or aluminium chloride catalyst.

Alkylation of benzene (Friedel-Crafts reaction)
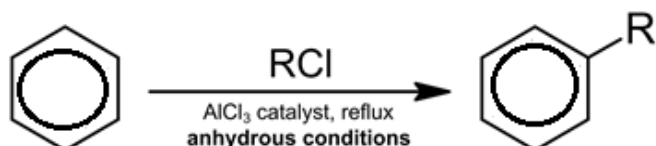
This is a way of adding an alkyl group to the benzene ring by substitution of a hydrogen atom by a methyl or ethyl group for example. The reaction is like the halogenation reaction, with a halogenoalkane used instead of the halogen and the commonest catalyst used being aluminium chloride.

The mechanism is similar to the ones we've already seen and is electrophilic substitution.
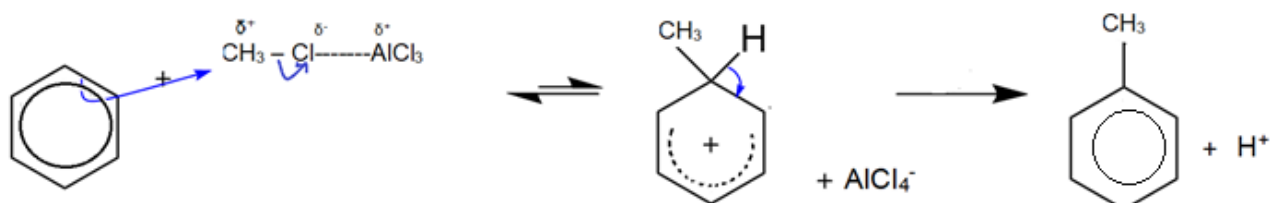
Comparing C-Cl bonds in chlorobenzene and chloroalkanes – hydrolysis reactions

Both chloroalkanes and chlorobenzene react with NaOH, but using different reaction mechanisms:-

eg, 1-chlorobutane

$$CH_3(CH_2)_2CH_2Cl + NaOH \rightarrow CH_3(CH_2)_2CH_2OH + NaCl$$
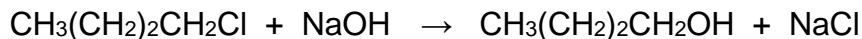
It's a **nucleophilic substitution** reaction: -
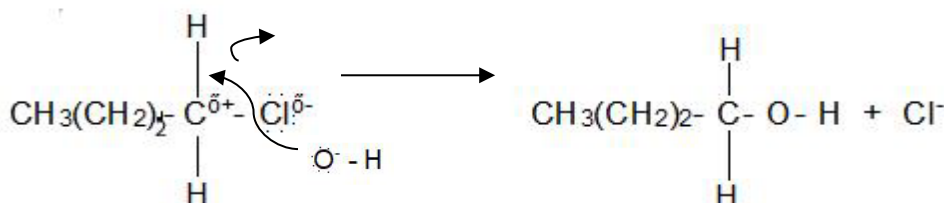
Chlorobenzene

- We know that benzene doesn't react with nucleophiles due to the disruption of the π-cloud.
- Also, the strength of the C-Cl bond in chlorobenzene (399 kJ mol^{-1}) is stronger than the C-Cl bond found in chloroalkanes (346 kJ mol^{-1}).
- The reason for this is that the lone pairs on the chlorine atom overlap with the π-electrons of the ring system and makes a stronger bond. This needs more energy for the bond to be broken.
- Making phenol from chlorobenzene needs high temperatures and pressures.
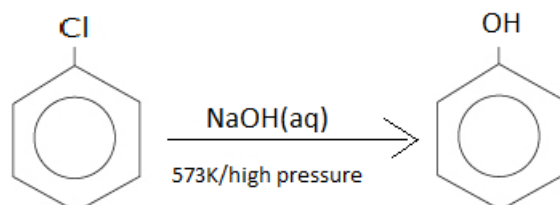
4.3 – Alcohols and phenols

Making primary and secondary alcohols

A reminder: -
- **Primary** alcohols have their -OH group joined to a carbon that is itself attached to no other or one other carbon.
- **Secondary** alcohols have their -OH group joined to a carbon that is itself attached to two other carbon atoms.
- **Tertiary** alcohols have their -OH group joined to a carbon that is itself joined to three other carbon atoms.

Two methods of formation: -

1. Substitution reaction from halogenoalkanes.
2. Reduction of aldehydes, ketones or carboxylic acids.

From Halogenoalkanes (see AS Unit 2)
- Reflux with **aqueous** solution of alkali (usually NaOH)
- Nucleophilic substitution reaction with OH^- ion as the nucleophile

    Eg: -
        1-chlorobutane will make butan-1-ol: -

        $CH_3CH_2CH_2CH_2Cl$ + OH^- $\longrightarrow$ $CH_3CH_2CH_2CH_2OH$ + Cl^-
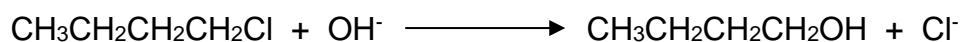
- Chlorobenzene cannot react in this way as described earlier

Reduction of carbonyl compounds and carboxylic acids
- Reverse reaction of oxidation of alcohols studied in Unit 2
- Carbonyl compounds reduced using $NaBH_4$, sodium tetrahydridoborate(III) dissolved in water, represented as [H] in an equation. Aldehydes produce 1° alcohols and ketones 2° alcohols: -
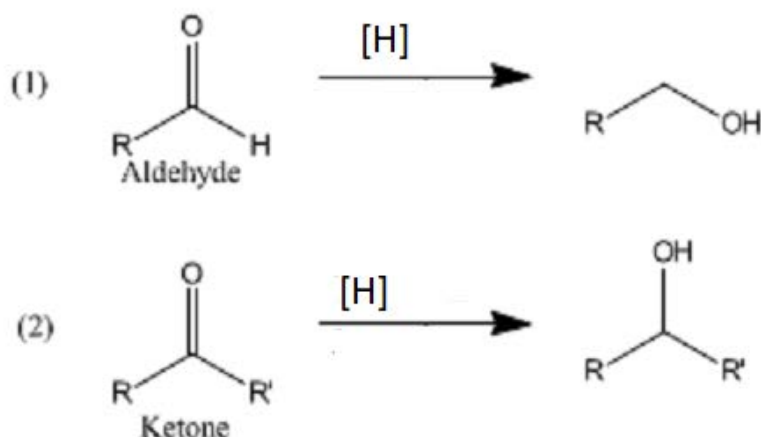
- Carboxylic acids need the stronger reducing agent of $LiAlH_4$, lithium tetrahydridoaluminate(III) dissolved in ethoxyethane.
- Reduction of carbonyl compounds is safer due to the nature of the reducing agent and its solvent.

Reaction of alcohols

a) Hydrogen halides

- Product is the halogenoalkane
- Slow and reversible reactions with poor yields
- Method depends on the halogen

Chlorine

- Pass HCl gas through alcohol with dry $ZnCl_2$ as a catalyst: -

$$CH_3(CH_2)_2CH_2OH \xrightarrow{ZnCl_2} CH_3(CH_2)_2CH_2Cl$$

- React alcohol with phosphorus(V) chloride, PCl_5. Phosphorus(v) oxide trichloride, $POCl_3$, and hydrogen chloride also form. Separation can be difficult if halogenoalkane produced has similar boiling temperature to $POCl_3$.
- React alcohol with sulfur(VI) oxide dichloride (thionyl chloride), $SOCl_2$. SO_2 and HCl are gaseous products of the reaction, so are easily lost.

Bromine

- Heat a mixture of the alcohol, KBr and 50% H_2SO_4: -

$$CH_3(CH_2)_2CH_2OH + KBr + H_2SO_4 \longrightarrow CH_3(CH_2)_2CH_2Br + KHSO_4 + H_2O$$

Iodine

- Warm damp red phosphorus and iodine which forms phosphorus(III) iodide, PI_3, and this reacts with the alcohol.

b) Ethanoyl chloride, CH_3COCl

- An **ester** is formed, giving off misty fumes of HCl.
- Better yield of ester than by using carboxylic acid as it's not a reversible reaction.
- Not cost effective in industry however, as acid chlorides are expensive.

propyl ethanoate

c) Carboxylic acids

- Commonest method of ester production
- Reactants refluxed together with concentrated H_2SO_4 (catalyst)
- Remaining acid neutralised by $NaHCO_3$ (aq)
- Ester *insoluble layer* is removed using a *separating funnel*
- Ester is distilled and collected at its boiling temperature.

ethyl ethanoate

Phenol's acidity and its reactions with bromine, ethanoyl chloride and iron(III) chloride

Acidity of phenol

- Phenol – aromatic alcohol where -OH group is bonded directly to the benzene ring.
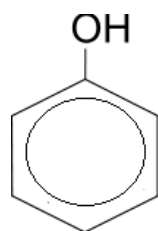
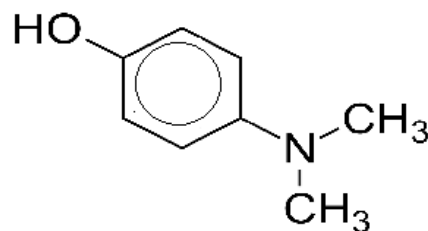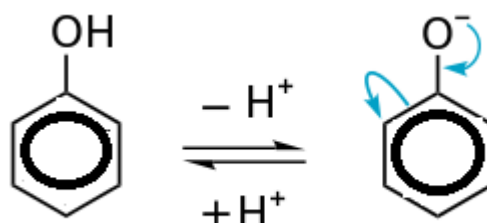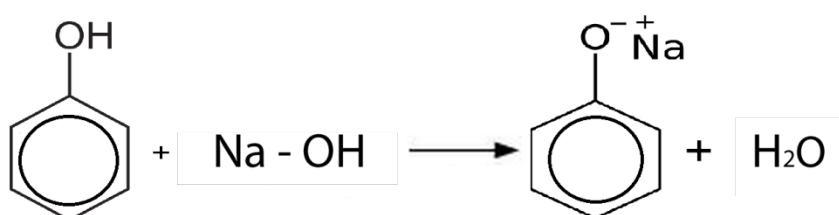

phenol
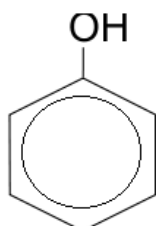
4-nitrophenol

4-dimethylaminophenol

- A lone pair from the oxygen atom overlaps with the π-electrons of the ring system, making the C-O bond stronger than in alcohol and also giving higher electron density to the ring. It is therefore more susceptible to electrophilic attack.
- H^+ ions are more easily lost in phenols than alcohols, making them stronger acids. The **phenoxide ion** is formed, which is more stable than expected due to the negative charge becoming delocalised around the ring system.


- Phenol will not dissolve readily in water because of the large hydrocarbon part to the molecule. It will dissolve readily in sodium hydroxide, however, showing its acidic properties as the H^+ ion reacts with the OH^- from the hydroxide to give water: -

- Substituents on the benzene ring affect the acidity of phenol. Any group on the ring that attracts electrons towards it, eg Cl^- will make the bond between the O and H weaker, making it easier for the compound to lose a proton.
- Phenols are more acidic than alcohols, but less acidic than carboxylic acids. A simple test to distinguish between a carboxylic acid and a phenol is to add sodium carbonate solution. **Carboxylic acids will react to produce CO_2 gas, but phenols won't** as they are not acidic enough.

Phenol and bromine

- Due to the electron delocalisation around the ring, phenol is more open to attack by electrophiles than benzene.
- The electron density polarises the bromine molecule. Bromine water reacts with phenol to give 2,4,6-tribromophenol: -
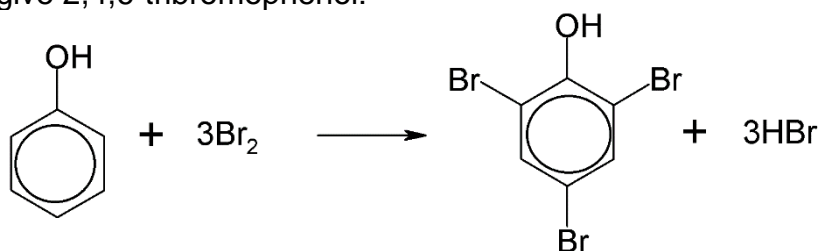

Add the bromine water to the phenol dropwise so you can see the colour change before the precipitate.

- The bromine water is decolourised and the 2,4,6-tribromophenol appears as a white precipitate. **This can be used as a test for phenol.** (Different to alkenes because of the white precipitate.)
- Mechanism is electrophilic substitution with $Br^{\delta+}$ being the electrophile.

Phenol with ethanoyl chloride

- Difficult to make esters using phenols as the delocalisation of the lone pair from the oxygen atom makes it difficult for the phenol to act as a nucleophile in the esterification reaction.
- Carboxylic acids are totally unsuitable to make esters with phenols, but the more reactive ethanoyl chloride will work. It is, however, a slow reaction at room temperature. A base can be added to speed up the reaction as it takes away the hydrogen chloride produced. An example of a base used is pyridine, C_5H_5N: -
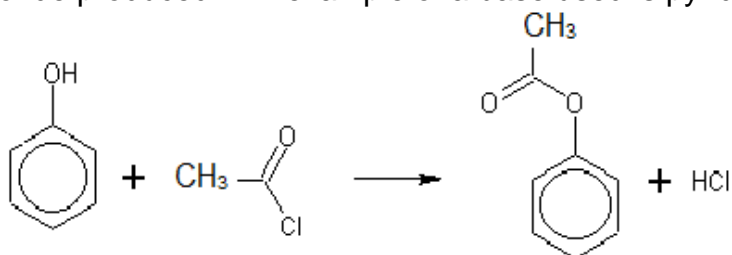
- As ethanoyl chloride is expensive, ethanoic anhydride $(CH_3COO)_2O$ is often used. The acidic product in this reaction is ethanoic acid.
- If ethanoic anhydride is reacted with a benzene ring with **two -OH** groups attached to it (dihydroxybenzene), then you will get a diester + HCl formed. *This is a good indicator for the number of hydroxyl groups on the benzene ring.*

Test for phenols with iron(III) chloride

- Aqueous iron(III) chloride (pale yellow) added to phenol will give a purple colour. This is the test for phenol: -

- In fact, any compound that has an -OH group bonded directly to a benzene ring will give a positive test with iron(III) chloride. They can be purple, blue or green in colour. (NB, iron(III) chloride also reacts with carboxylic acids to give a **red-brown** colour).

4.4 – Aldehydes and ketones

Structure and nomenclature

Both types of compound have the polar C=O group, with the oxygen being the more electronegative. The double bond mirrors the one found in alkenes with a σ-bond joining the carbons and a π-bond above and below the plane of the σ-bond.

Aldehydes

- The carbon atom of the carbonyl group bonds to *at least one hydrogen atom.*
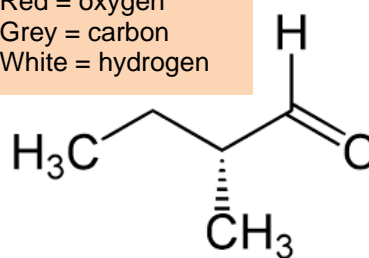- When naming aldehydes, the suffix -al is used at the end of the name of the compound.
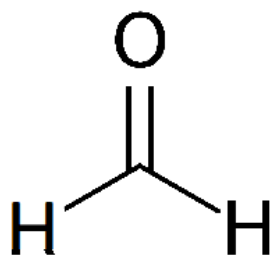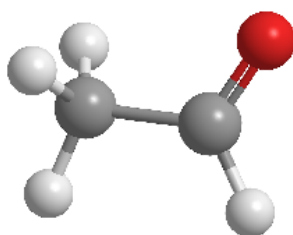
> Key to diagrams
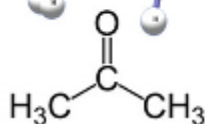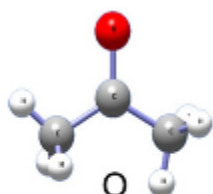> Red = oxygen
> Grey = carbon
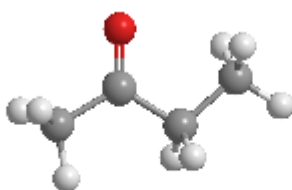> White = hydrogen

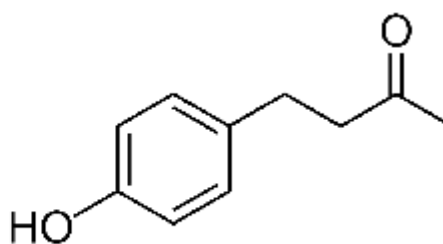methanal   ethanal   2-methylbutanal

Ketones

- Carbonyl carbon is bonded to *two other carbon atoms*
- When naming ketones, the suffix -one is used at the end of the name of the compound.

propanone   butanone   'Raspberry ketone' 4-(4-Hydroxyphenyl)-butan-2-one

Both aldehydes and ketones are found extensively in nature, with raspberry ketone being sold as an aid to weight loss.

Oxidation of alcohols

- 1° alcohols oxidised to aldehydes and carboxylic acids and 2° alcohols oxidised to ketones.
- Oxidising agent is **acidified potassium dichromate** or **acidified potassium manganate(VII)** (which you can show as [O] in an equation).
- Colour changes are **dichromate – orange $Cr_2O_7^{2-}$ to green Cr^{3+}, manganate(VII) – purple MnO_4^- to colourless Mn^{2+}**

propan-2-ol   propanone   primary alcohol   aldehyde   carboxylic acid
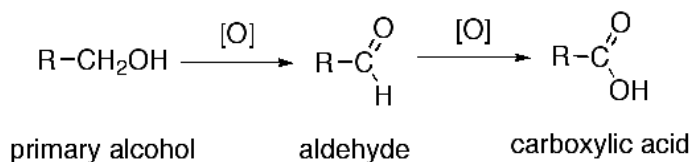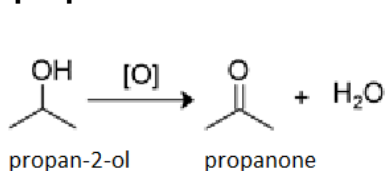
Identification of carbonyl compounds
i) Distinguishing between aldehydes and ketones
Tests are based on the following: -
- Aldehydes can be oxidised further to carboxylic acids, ketones can't be oxidised.
- Aldehydes are therefore reducing agents and will react with reagents that change colour on reduction.

Tollens' reagent (this used to be called the 'silver mirror test')
Contains silver nitrate. A small amount of unknown is added to the solution into a clean test tube and placed in a water bath. If an **aldehyde** is present, a **silver mirror** is seen on the inside of the test tube. Ketones do not react like this.

Fehling's reagent
(Used in Biology to test for reducing sugars like glucose). Blue Fehling's solution (containing copper(II) ions) is warmed with the unknown liquid. If it's an **aldehyde**, then the Cu^{2+} ions will become reduced to a **red-brown precipitate** of copper(I) oxide. Ketones will not react.

Acidified dichromate (orange to green) and **acidified manganate(VII)** (purple to colourless) can also be used to distinguish between aldehydes and ketones, with aldehydes being oxidised to a carboxylic acid.

ii) Identification of the carbonyl group (C=O)
2,4-dinitrophenylhydrazine (2,4-DNP) is used to identify whether an unknown compound has the C=O group. It is a **nucleophilic addition reaction**, followed by the **elimination** of water. (You don't need to know the equation for the reaction.) This type of reaction is often called a **nucleophilic addition-elimination reaction** (or condensation) reaction.

- Compound will react to give an orange-red precipitate.
- This is filtered, purified and dried.
- The melting point of the solid is determined and compared to book values.
- This will identify the aldehyde or ketone used at the start.
- Far better method than direct boiling points of flammable aldehydes and ketones.

iii) Triiodomethane (iodoform) reaction for identifying CH₃C=O group in ketones or CH₃CH(OH) group in alcohols
- Triiodomethane is the yellow solid that forms during the reaction.
- Reagents are iodine in aqueous NaOH (**I₂/NaOH**) or KI in aqueous sodium chlorate(I) (**KI/NaOCl**)
- Reagent used is oxidising, so will also convert alcohols with the CH₃CH(OH) group in it as well as ketones with the CH₃C=O group. The alcohol will first be oxidised to the ketone.
- Examples of ketones that will produce triiodomethane are propanone and butanone.
- Examples of alcohols that have a positive result are ethanol and propan-2-ol, but not propan-1-ol.
- If you're in doubt as to whether a compound will have a positive triiodomethane test, draw out the structure. You'll need to see this at one end: -
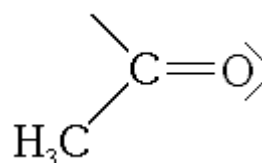
Reduction of aldehydes and ketones

This is covered in section 4.3 on Alcohols. Points to note: -

- Reducing agent is sodium tetrahydridoborate(III), $NaBH_4$, in aqueous solution.
- This is preferred over lithium tetrahydridoaluminate(III), $LiAlH_4$, as $NaBH_4$ is safer and can be used in aqueous conditions.
- When you write equations, it's alright to use [H] to represent the reducing agent.

Nucleophilic addition reactions

- Polar carbonyl group provides an electron deficient carbon atom for attack by nucleophiles:
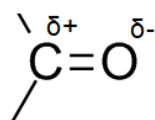
- Nucleophiles like CN⁻ can be added and this is a way of extending the length of the carbon chain.
- eg, addition of CN⁻ to propanone produces 2-hydroxy-2-methylpropanenitrile. Mechanism is that cyanide ions attack the propanone. H^+ ions from sulfuric acid are added.

2-hydroxy-2-methylpropanenitrile   2-hydroxy-2-methylpropanoic acid
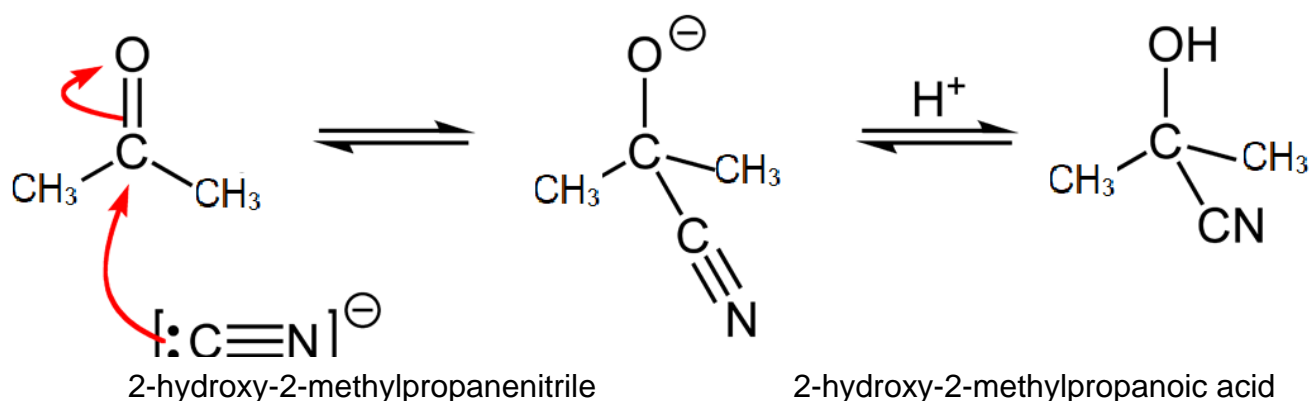
- The hydroxynitrile formed in this reaction can be refluxed with a dilute acid. Hydrolysis occurs and a hydroxyacid is formed: -
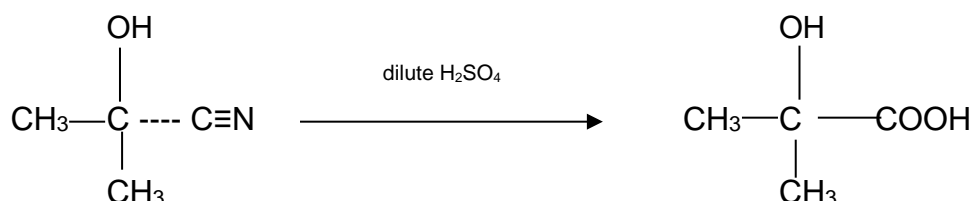
- **Hydroxynitriles** are also mentioned in the section on nitriles, so you need to know how these are formed. Page 19.

4.5 – Carboxylic acids

Structure and nomenclature

- Functional group -COOH
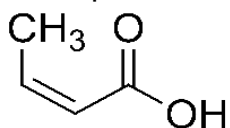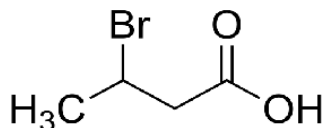- The carbon atom in this functional group contributes to the total number of atoms in the chain, so ethanoic acid is CH_3COOH and NOT CH_3CH_2COOH (propanoic acid)
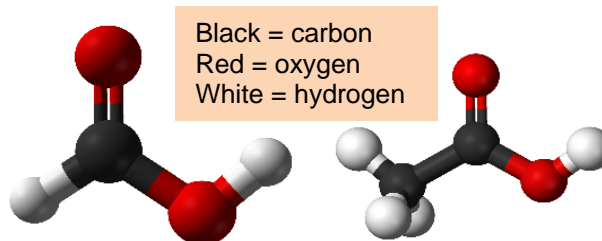- If you have other functional groups, then they are named as derivatives of the 'parent' acid.

Examples

(Z)-but-2-enoic acid

3-bromobutanoic acid

Black = carbon
Red = oxygen
White = hydrogen

methanoic acid

ethanoic acid

Comparing the acidity of carboxylic acids, phenols, alcohols and water

Here is the order of acidity, most acidic first: -

	carboxylic acids	>	phenols	>	water	>	ethanol
pH	2.9		5.5		7		~7.9

An acid is a compound that produces hydrogen ions when it dissolves in water. We know that carboxylic acids and phenols are weak acids because they don't dissociate fully into ions when they're in water. However, there are some H^+ ions produced, and it is the concentration of these that decides acid strength.

The number of hydrogen ions formed is partly dependant on the stability of the starting compound and the products formed.
The ions formed from **carboxylic acids** are more stable than those formed from ethanol and water because the negative charge is delocalised across the two oxygen atoms. Here is a model of an ethanoate ion (red = oxygen, white = hydrogen, grey = carbon):
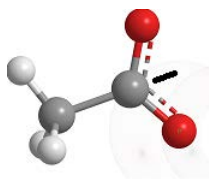
The negative charge can be spread across the two oxygen atoms, so this gives the ion more stability. It can exist on its own for a longer time.

The phenoxide ion from **phenol** is more stable than the ions formed from ethanol and water because the negative charge of the ion is delocalised around the π-electron ring system of benzene.

Ethanol molecules don't ionise as the ethoxide ion isn't stabilised by delocalisation of electrons.

- Only carboxylic acids can produce carbon dioxide when they react with a carbonate, phenol is not acidic enough. **This is a test that can distinguish between the two types of compound.**
- However, both types can be neutralised by sodium hydroxide, giving a salt.

Making carboxylic acids – oxidation
i) Primary alcohols and aldehydes

primary alcohol   aldehyde   carboxylic acid
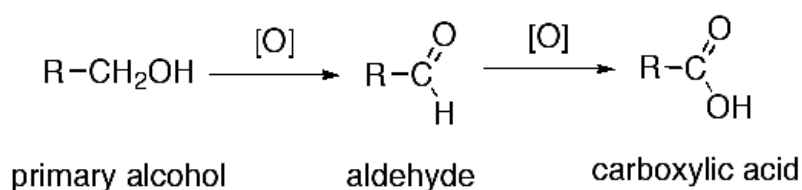
- Oxidising agent – acidified potassium dichromate solution $H^+/Cr_2O_7^{2-}$ (aq)
- Alcohol or aldehyde is refluxed with **excess** oxidising agent.
- Colour change – orange to green, but you do have excess orange oxidising agent present.
- Can also use the stronger acidified potassium manganate(VII) H^+/MnO_4^- (aq)
- Excess refluxed with the alcohol or aldehyde.
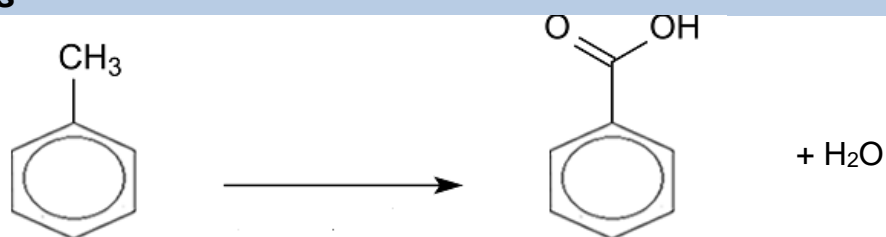- Colour change – purple to colourless. May be difficult to see due to excess oxidising agent.
- In either case, the acid is distilled from the mixture and then purified.

ii) Alkylbenzenes

$+ H_2O$

- Alkylbenzene – benzene with a hydrogen atom substituted with an alkyl group, eg methyl.
- Oxidising agent – alkaline potassium manganate(VII)
- Colour change – purple manganate(VII) to brown sludge of manganese(IV) oxide.
- Alkaline solution produces the salt of the carboxylic acid, eg $C_6H_5COO^-Na^+$.
- This is then acidified with a dilute acid and crystals of benzenecarboxylic acid are formed.

Reduction of carboxylic acids
- Very stable compounds, so need a strong reducing agent to convert them back to aldehydes and 1° alcohols.
- Reducing agent is lithium tetrahydridoaluminate(III), $LiAlH_4$. It reacts violently with water, so must be dissolved in a non-aqueous solvent (ethoxyethane).
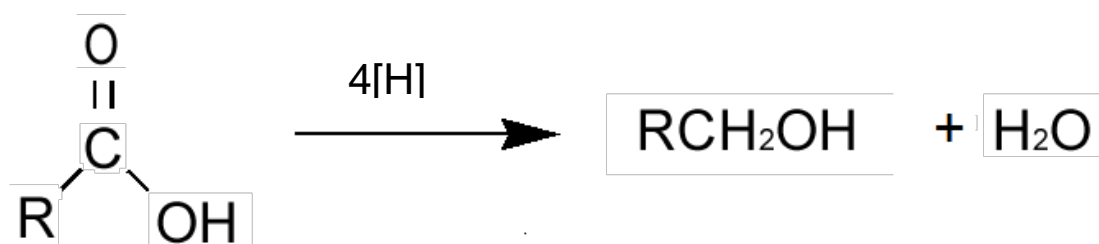
Decarboxylation of carboxylic acids

- This is removal of acidic carbon dioxide from a compound. Need to use a base for this reaction.
- **Soda lime** is usually used, a mixture of calcium hydroxide and sodium or potassium hydroxide. It absorbs carbon dioxide and water whilst remaining solid.
- Usually represented in equations as $NaOH$, $Ca(OH)_2$ or CaO for simplicity.
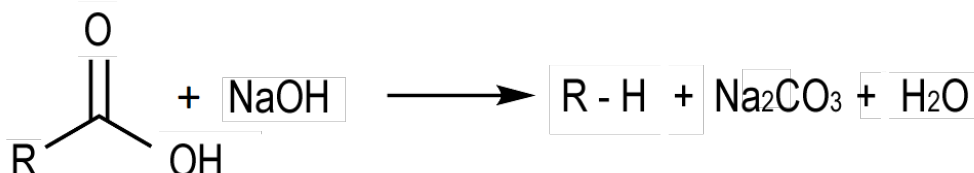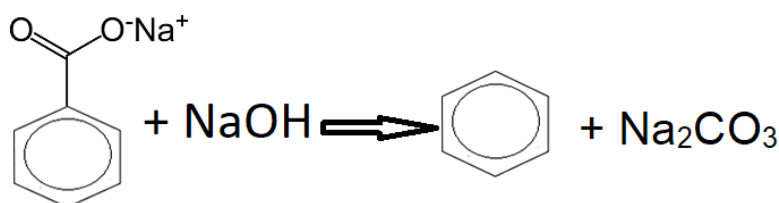- When carbon dioxide is removed from carboxylic acids, the carbon chain is reduced by one: -

$$+ \boxed{NaOH} \longrightarrow \boxed{R - H} + \boxed{Na_2CO_3} + \boxed{H_2O}$$

- Sodium salts of the carboxylic acids are often used in the decarboxylation reactions. If we use a salt of benzenecarboxylic acid, benzene is formed: -


$$+ NaOH \Longrightarrow + Na_2CO_3$$

sodium benzenecarboxylate

- Another way of removing carbon dioxide from a carboxylic acid is to strongly heat the calcium salt of the acid. The product of this reaction is an aldehyde or ketone. *Remember that a calcium salt of an acid will have **two** carboxylate groups.*

Esters and their hydrolysis

- Production of esters from carboxylic acids is covered in the alcohols section on page 9.

$$CH_3CH_2CH_2OH + H-C-C \xrightarrow{H_2SO_4} H-C-C + H_2O$$
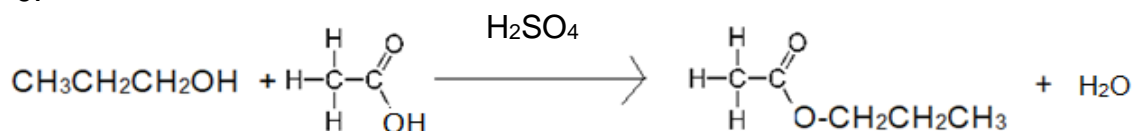
propyl ethanoate

Esters are usually named with the alcohol part first, followed by the acid name. When the structures are drawn, the acid part comes first and the alcohol part last.

One hydrogen is removed from the alcohol and the -OH group is taken from the acid.

- Esters can be solids or liquids at room temperature and have a characteristic smell, eg strawberries and pineapples owe their fragrance to esters.
- Esterification can be reversed in a reaction known as hydrolysis. This can be carried out in basic conditions, usually by heating with aqueous NaOH. Products are the alcohol and the salt of the carboxylic acid. The salt can then be acidified with HCl to form the acid.

$$R + NaOH \longrightarrow R + HO-R'$$

carboxylate ester   sodium hydroxide   sodium carboxylate   alcohol
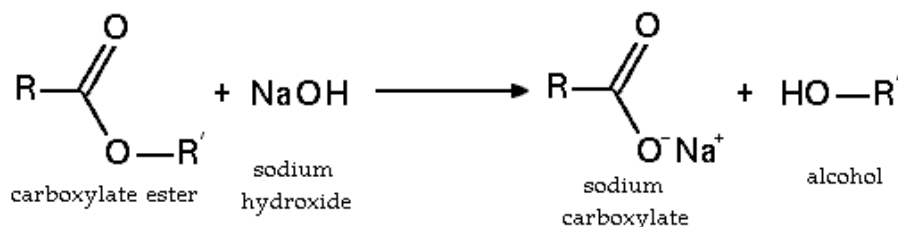
Hydrolysis can also be carried out using aqueous H_2SO_4, which produces the alcohol and acid.

Acid chlorides and their hydrolysis

- Acid chlorides are carboxylic acids where the -OH group has been substituted by a -Cl atom.
- Usual method is to react the acid with sulfur dichloride oxide, $SOCl_2$, although phosphorus(III) chloride, PCl_3, and phosphorus(V) chloride, PCl_5, can also be used.
- The $SOCl_2$ reaction is the best to use as the products that are not needed are gases and easily removed. If you use the phosphorus chlorides, then separation of the acid chloride is more difficult.
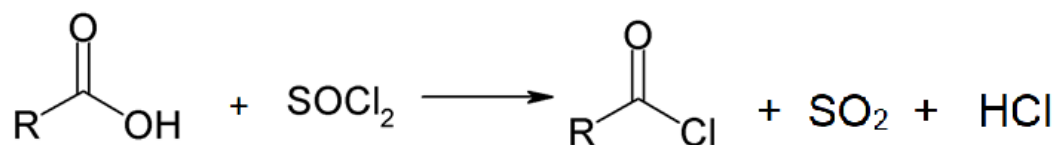
- Acid chlorides are reactive and easily hydrolysed by water, so must be made in a reaction where water isn't present.
- Hydrolysis is a reaction where decomposition occurs because of the addition of water. It happens much more readily in acid chlorides than carboxylic acids due to the carbonyl carbon in acid chlorides being deficient in electrons. This leaves it open to attack by the lone pairs on the oxygen in water. The carboxylic acid and hydrogen chloride are formed: -

$$CH_3COCl + H_2O \rightarrow CH_3COOH + HCl$$
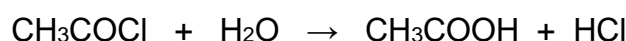
Amides and nitriles

- Amides are made from carboxylic acids by reacting with ammonia and then heating the ammonium salt that's formed.

| Ethanoic acid | Ammonia | Ammonium ethanoate | ethanamide |
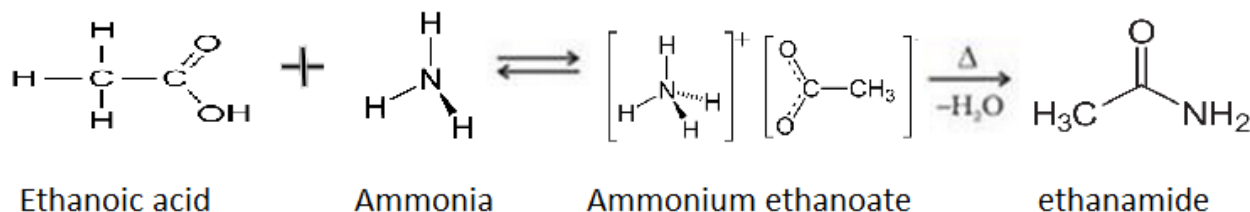
- You can also heat the acid or its ammonium salt with urea (120ºC)

- Dehydration of an amide produces a **nitrile**. Heat with phosphorus(V) oxide, P_4O_{10}.
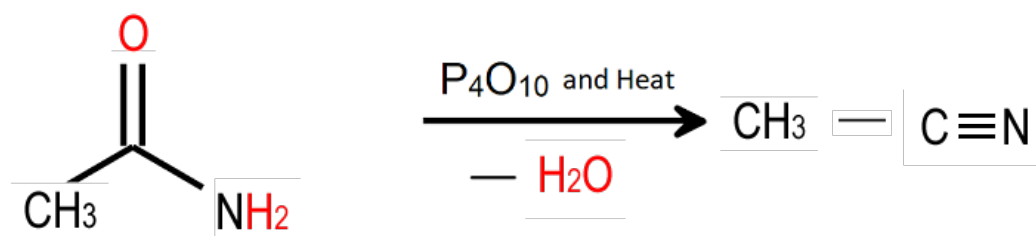
- When naming nitriles, you must include the carbon of the nitrile group as part of the carbon chain. The product of the above reaction is ethanenitrile, even though it only appears to have one methyl group.

Formation of nitriles from halogenoalkanes
- Made from halogenoalkanes with potassium cyanide dissolved in ethanol.

$$CH3CH2CH2Br + KCN \longrightarrow CH3CH2CH2-C \equiv N + KBr$$

1-bromopropane $\qquad\qquad$ butanenitrile

- This is a **nucleophilic** substitution reaction with the cyanide ion (carbon atom) acting as the nucleophile.
- The carbon chain is extended by one, in the above reaction propane becomes butane.

Formation of hydroxynitriles from aldehydes and ketones

- See page 14.

Hydrolysis of nitriles
- When warmed under reflux with dilute sulfuric acid, the nitrile is converted to the carboxylic acid – it's a hydrolysis reaction.

$$R - C \equiv N \xrightarrow[\text{reflux}]{H^+(aq) / H_2O} R - C \overset{O}{\underset{OH}{\big\backslash}}$$
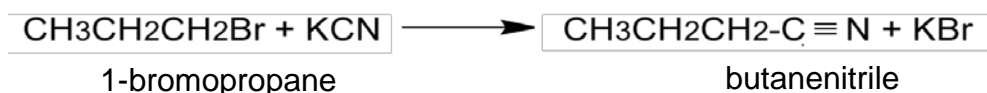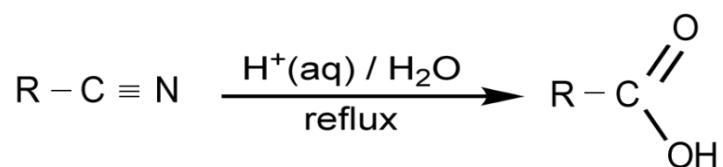
Hydrolysis of amides
- When heated under reflux with a base like sodium hydroxide, the amide is hydrolysed, producing **ammonia gas** and the sodium salt of the carboxylic acid: -

$$\underset{R}{\overset{O}{\|}}{NH_2} + NaOH \longrightarrow \underset{R}{\overset{O}{\|}}{ONa} + NH_3$$
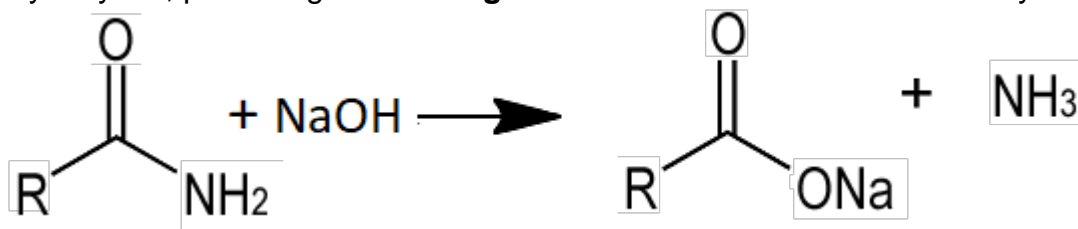
Reduction of nitriles
- Preferred reducing agent is lithium tetrahydridoaluminate(III) in ethoxyethane.
- This will reduce a nitrile to a primary amine.

$$R - C \equiv N \xrightarrow[\text{ethoxyethane}]{LiAlH_4} R - CH_2 - NH_2$$
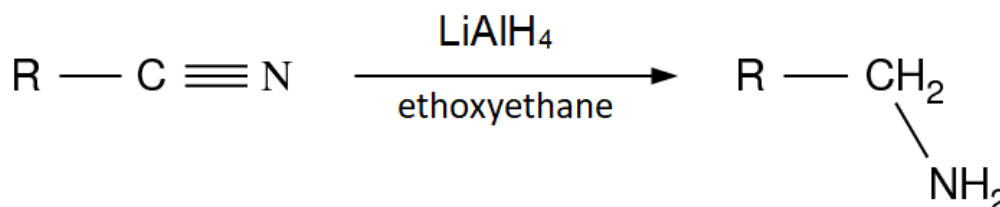
- Other reducing agents are hydrogen with a nickel catalyst and sodium with ethanol.
- These other agents produce the secondary amine as a by-product so LiAlH₄ is preferred – yields are higher.

Structure and Nomenclature

- All have a nitrogen atom bonded directly to a carbon atom of an alkyl or an aryl group.
- 1° amine is where nitrogen bonded to **only one carbon atom**
- 2° amine is where nitrogen bonded to **two carbon atoms**
- 3° amine is where nitrogen bonded to **three carbon atoms**

primary amine   secondary amine   tertiary amine

- in aromatic amines, the -N atom is bonded directly to the benzene ring.

Formation of aliphatic amines
i) from halogenoalkanes

- Reactants – halogenoalkane and ammonia dissolved in water/ethanol.
- Reaction carried out in sealed tube to avoid escape of ammonia, which is used in excess: -

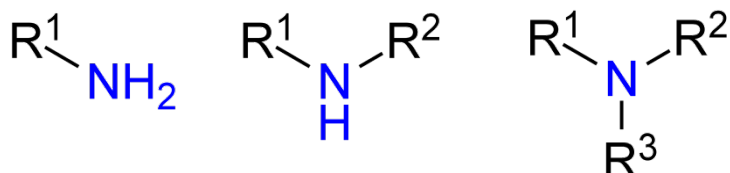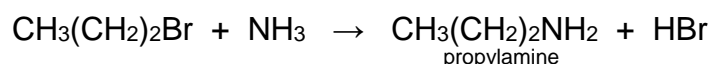$$CH_3(CH_2)_2Br + NH_3 \rightarrow CH_3(CH_2)_2NH_2 + HBr$$
propylamine

- Excess ammonia reacts with HBr formed to give ammonium bromide.
- If excess halogenoalkane is used, you will get further substitution to give a secondary amine and HBr: -

$$CH_3(CH_2)_2NH_2 + CH_3(CH_2)_2Br \rightarrow \{CH_3(CH_2)_2\}_2NH + HBr$$

- This happens because the amine acts as a nucleophile and attacks the δ+ carbon atom of the C-Br bond in a nucleophilic substitution reaction.
- Under certain conditions, amine will react with HBr to give the salt: -

$$CH_3(CH_2)_2NH_2 + HBr \rightarrow CH_3(CH_2)_2NH_3^+Br^-$$
propylammonium bromide
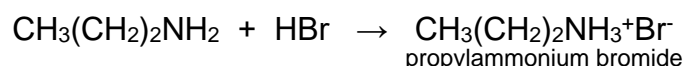
- If you compare amines with ammonia, you can think of an amine as being an ammonia atom with one of the hydrogens replaced with an alkyl group. Just like an ammonium salt, if the salt of an amine is heated with aqueous NaOH, then the amine is produced: -

$$CH_3(CH_2)_2NH_3^+Br^- + NaOH \rightarrow CH_3(CH_2)_2NH_2 + NaBr + H_2O$$
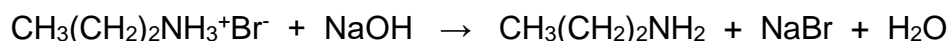
ii) from nitriles

- produced by reduction of nitriles using LiAlH$_4$. See bottom of page 20.

Formation of aromatic amines

- The ring electrons in benzene make it virtually impossible for it to undergo nucleophilic attack, so **phenylamine, $C_6H_5NH_2$ is made by the reduction of nitrobenzene.**

- Note that the reducing agent is tin with conc HCl. This is mainly used in the lab.
- Commercial reducing agents tend to be hydrogen with a nickel catalyst or iron with HCl.

Basic nature of amines

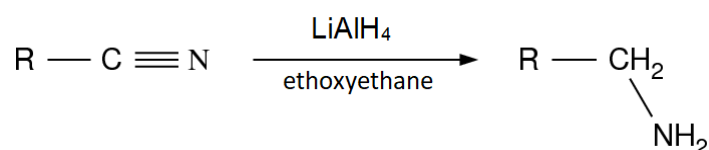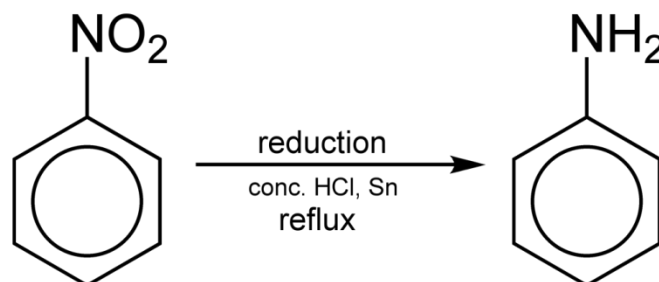- If we come back to comparing amines with ammonia, we see that amines, like ammonia, have a lone pair of electrons on the nitrogen atom. They can accept a proton using a co-ordinate bond. So methylamine will form the methylammonium ion, $[CH_3NH_3]^+$.
- The shorter chain amines will react with water, forming an equilibrium: -
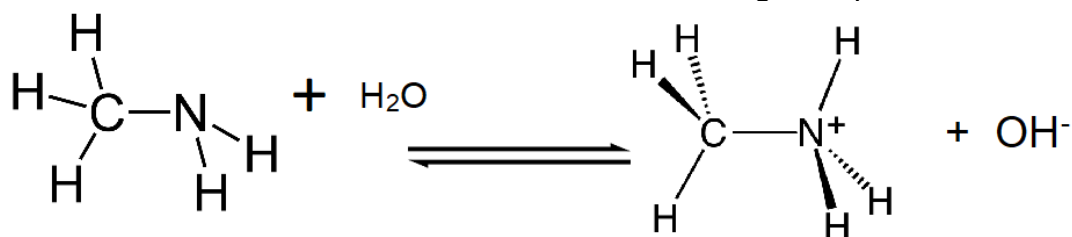
- The equilibrium lies well over to the left and the pH of a solution of methylamine of 0.1 mol dm^{-3} is around 11.8. This compares with 11.1 for ammonia.
- The reason for this difference in strength is that the alkyl groups on the amines 'push' electrons more onto the nitrogen atom, making it more δ- when you compare it with ammonia's nitrogen.
- Phenylamine is a weaker base than ammonia and alkylamines as the lone pair of electrons on the nitrogen becomes part of the delocalised π-electron system of the benzene ring. This makes it less δ-.
- Phenylamine is only slightly soluble in water because of the large benzene ring.
- All amines will react with acids, forming salts: -

$$CH_3(CH_2)_2NH_2 \; + \; HCl \; \rightarrow \; CH_3(CH_2)_2NH_3{}^+Cl^-$$

propylammonium chloride

phenylammonium chloride

22
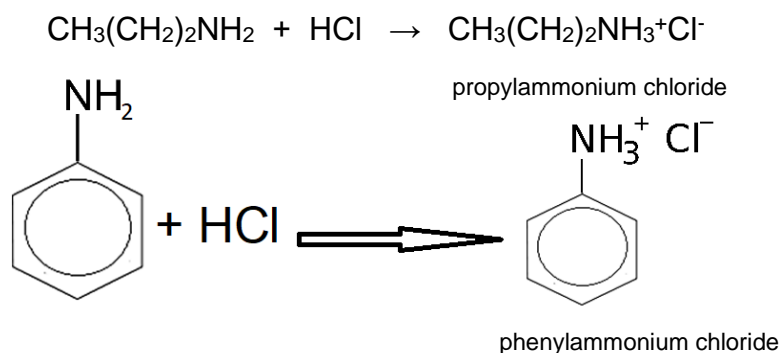
Ethanoylation of primary amines

- Amines can act as nucleophiles due to the nitrogen lone pair. They attack the δ+ carbon of the carbonyl group in an acid chloride: -

N-methylethanamide
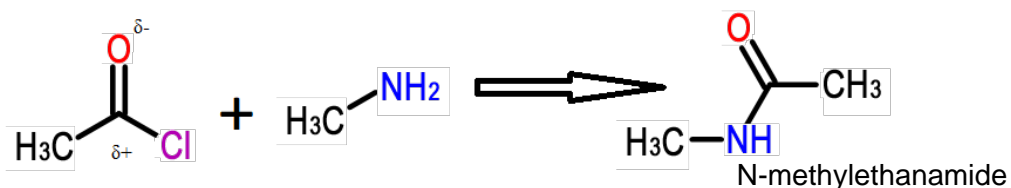
- **NB**, the letter N means that the methyl group is bonded to the nitrogen atom.
- Phenylamine can also react with ethanoyl chloride: -

N-phenylethanamide

Reaction of primary amines with cold nitric(III) acid (nitrous acid)

- Nitric(III) acid, HNO_2, has to be made in situ due to its instability.
- Made by reacting sodium nitrate(III) (sodium nitrite) with dilute HCl.

- Reactions of **aliphatic amines and aromatic amines** at **room temperature** form an alcohol, water and N_2 gas. The gas is seen as bubbles in the reaction mixture: -

$$CH_3(CH_2)_3NH_2 + HNO_2 \rightarrow CH_3(CH_2)_3OH + N_2 + H_2O$$
$$\text{butan-1-ol}$$
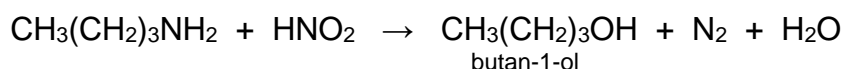
- Reactions of **primary aromatic amines below 10°C**, an intermediate **diazonium compound** is produced as part of the reaction: -

benzenediazonium chloride
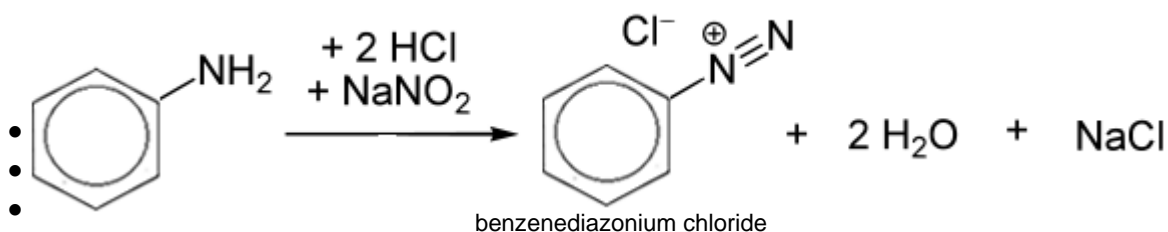
- If aqueous sulfuric acid is used instead of hydrochloric acid, then benzenediazonium sulfate is formed instead of the chloride.
- **Above 10°C**, decomposition of the benzenediazonium compound happens, giving phenol – see third bullet point above as it's similar to the aliphatic amine reaction.
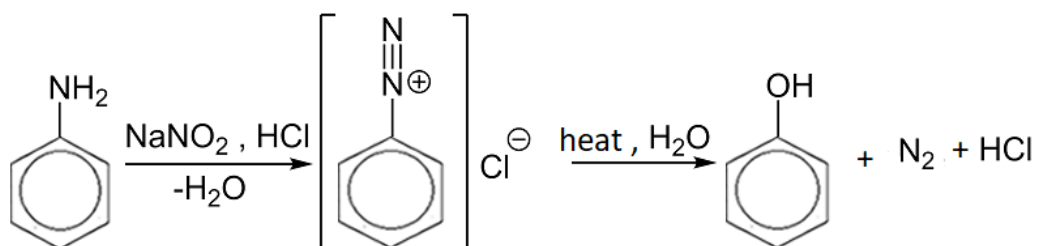
Coupling reactions of benzenediazonium salts – making azo dyes

- Benzenediazonium compounds are extremely reactive, below 10°C, they react with phenols and aromatic amines.
- Compounds formed contain the -N=N- azo group, which links the two benzene rings together: -

4-(phenylazo)phenylamine

- The ion in the above equation is a weak electrophile and needs high electron density to attack. The presence of an -OH or -NH$_2$ group bonded on the ring increases the electron density (called activation).
- The joining of two benzene rings together in this way is called **azo coupling** and usually ends up with the loss of a small molecule.

methyl orange

- Benzenediazonium chloride reacts with naphthalen-2-ol in alkaline solution to give 1-(phenylazo)naphthalen-2-ol, a red dye. It's known as Sudan 1 and is used in the food industry, but not in the UK, where it is now banned: -
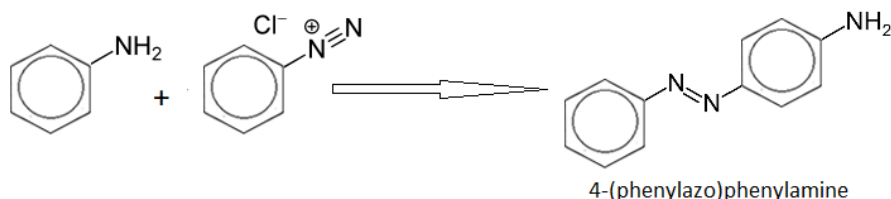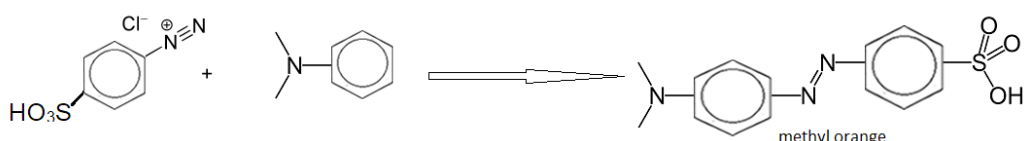

2-naphthanol   (7)   (8)   (9)

Sudan I
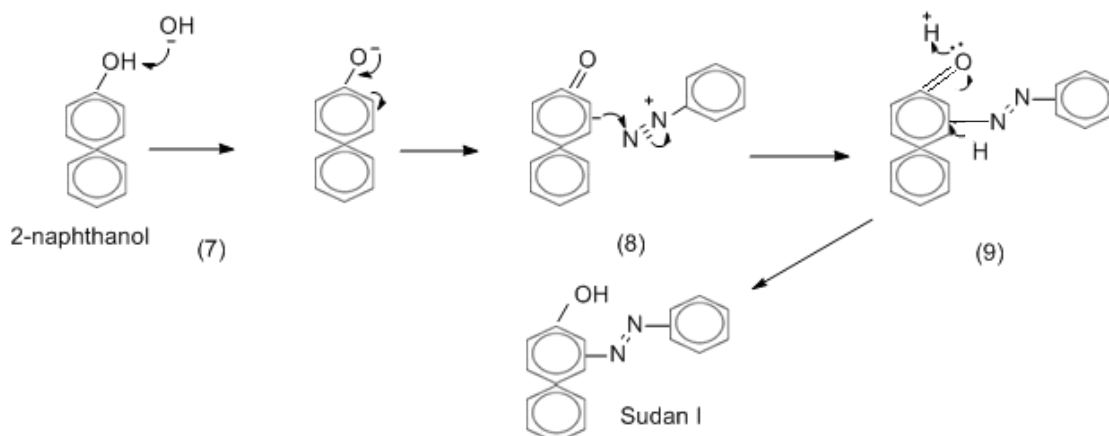
The role of the -N=N- chromophore in azo dyes and the origin of colour in terms of the wavelength absorbed

- Chromophore is the structural unit in a molecule that is responsible for the absorption of radiation of a certain wavelength.
- If this radiation is in the visible region, the colour seen is the colour that is not absorbed.
- Other parts of the molecule will also affect the wavelength of light absorbed, not just the chromophore.
- The **colour wheel on the next page** shows the wavelengths at which different colours are absorbed.
- As a rule of thumb, the colour absorbed by a compound is **opposite the colour that is seen**, eg if a compound shows a maximum absorption at the blue section of the spectrum (between 450nm and 490nm), then the colour seen will be orange. This is what is seen with methyl orange.
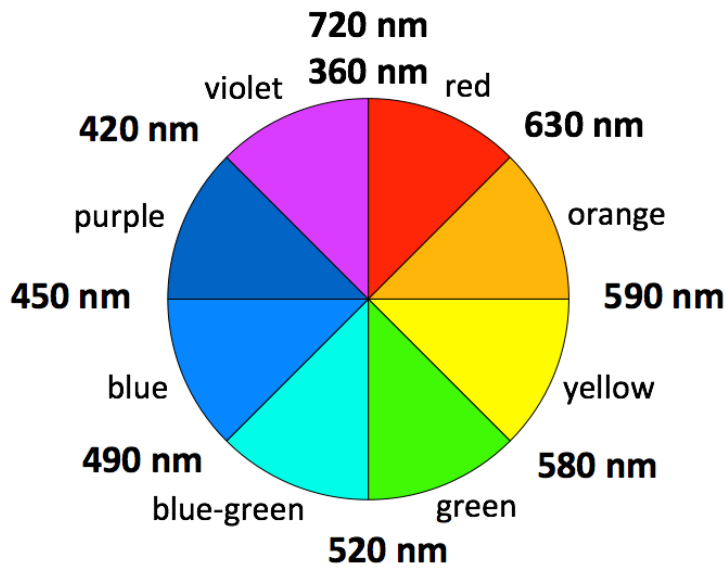
Colour wheel with absorption wavelengths

As a rule of thumb, the colour absorbed by a compound is **opposite the colour that is seen**, eg if a compound shows a maximum absorption at the blue section of the spectrum (between 450nm and 490nm), then the colour seen will be orange. This is what is seen with methyl orange.

- If we look at the graph of absorption for chlorophyll (a and b), we see that the only wavelength where there is no absorption is between 520 and 580, which is green. This is the colour normally associated with chlorophyll.
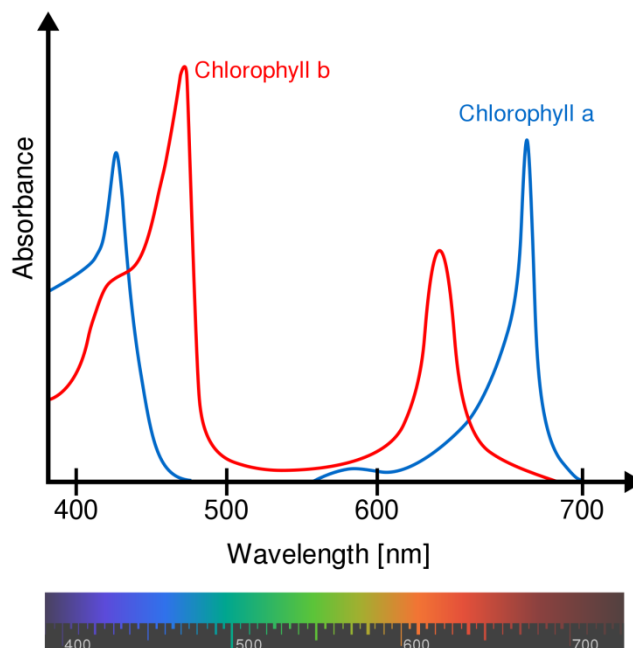
- Sudan 1, the red dye mentioned previously, has its maximum absorption in the blue-green region of the wheel. The colour opposite this is red, which is the colour of Sudan 1.

4.7 – Amino acids, peptides and proteins

Formula and classification of α-amino acids

- Amino acids are carboxylic acids that have a -NH_2 group as part of the molecule.
- α-amino acids have the -NH_2 group bonded to the same carbon atom that contains the -COOH group. This carbon is called the α-carbon (as seen in the diagram)
- Simplest one is aminoethanoic acid: -
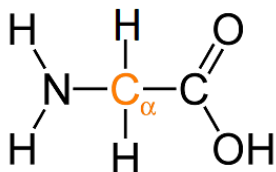
- Other α-amino acids have one of the H's on the central carbon replaced with an alkyl group, or a more complicated carbon group. Here are some other examples (the names in brackets are the traditional names that you may have come across in Biology): -
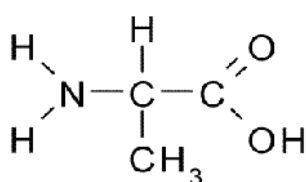
2-aminopropanoic acid (alanine)
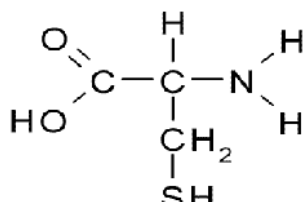
2-amino-3-sulfhydrylpropanoic acid (cysteine)

2-amino-3-phenylpropanoic acid (phenylalanine)

2-amino-3-hydroxypropanoic acid (serine)

- All α-amino acids have optical isomers apart from aminoethanoic acid. This means they have one or more chiral centres, of which one is centred on the α-carbon. Here are the optical isomers of aminopropanoic acid shown as mirror images: -
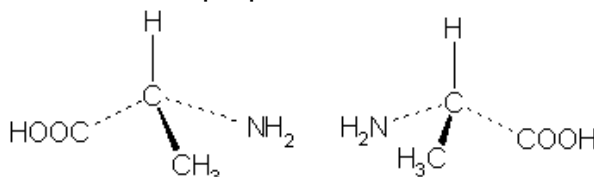
- α-amino acids exist as solids, whilst similar sized molecules are often liquids or low-melting point solids. The reason for this is that they occur as **zwitterions**.
- They come about because a H^+ ion is lost from the -COOH group and is gained by the nitrogen atom of the -NH_2 group.
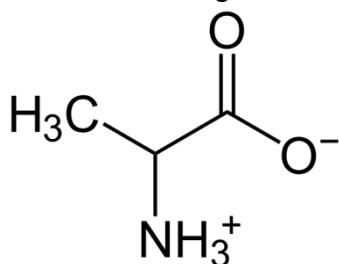
Zwitterion of aminoethanoic acid.
Because of the ionic nature of the molecules, there are strong interactions between the molecules, making the melting points high and mean that they can dissolve in water.

Amphoteric nature of α-amino acids

- When an α-amino acids are dissolved in a basic solution, they gain a proton.
- If dissolved in an acidic solution, they lose a proton: -
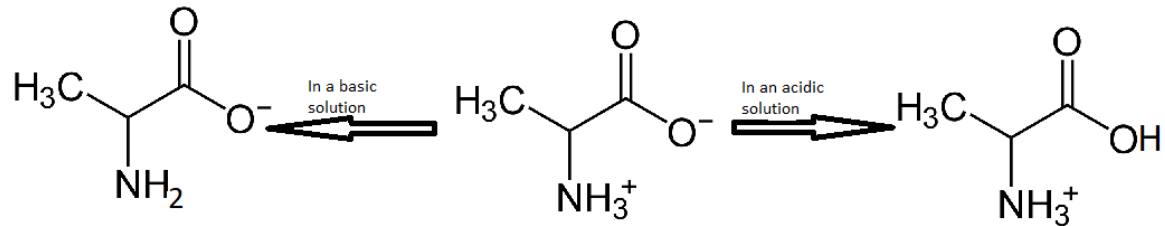
- When they react with a base, they are acting like an acid (losing a proton) and when they react with an acid, they are acting like a base (gaining a proton).

Formation of dipeptides

- Two amino acid molecules join in a condensation reaction to form a dipeptide. The amino acid molecules can either be the same or different.
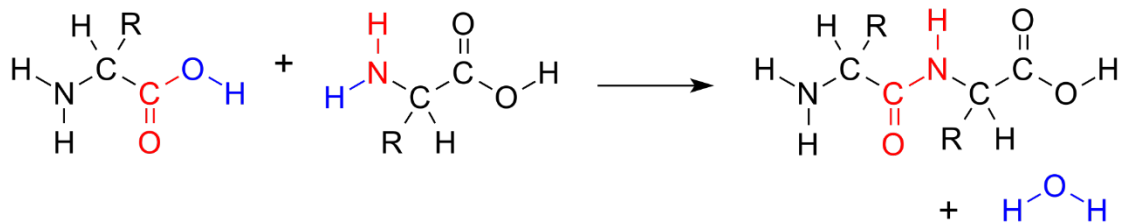
- -OH group from a carboxyl group on one is removed, along with a hydrogen atom from the amino group of the other. The atoms in red form a **peptide link** (or **peptide bond**).
- Here's an example: -

Homocysteine   Serine

-H₂O

Cystathionine
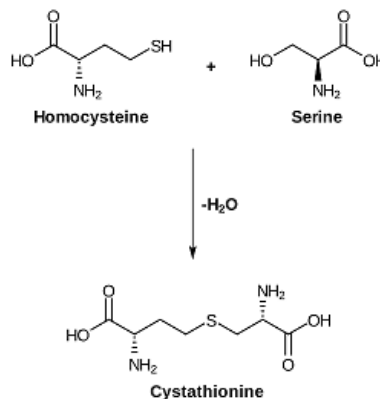
Formation of polypeptides and proteins

- Peptide formation can continue by condensation to form polypeptides: -

Val   Gly   Ser   Ala
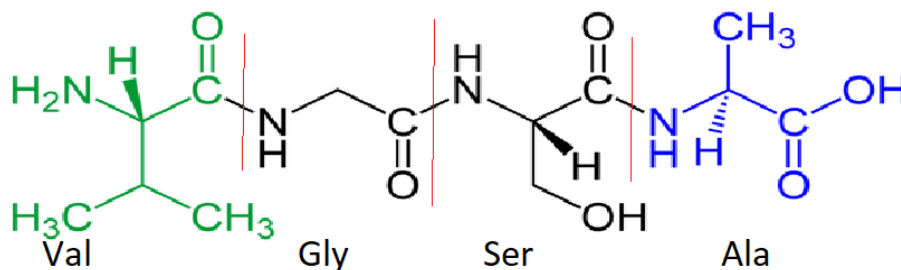
The three-lettered abbreviations are used when looking at the formula of a polypeptide.
Val = Valine
Gly = Glycine
Ser = Serine
Ala = Alanine
These are the traditional names, you can look up the systematic name!

Protein structure

There are three different types of structures in proteins: -

Primary structure

- This is the order of amino acids in the polypeptide chains.
- There are twenty amino acids that make up these chains. In the human body, we can make or obtain twelve. The other eight must come from the food we eat – the **essential amino acids**.
- These twenty acids can make a possible 400 dipeptides and 8000 tripeptides. This makes it possible to have a huge number of longer peptide chains.

Secondary structure

- This takes the primary chains and arranges them into two different types of structure.
- The first is the α-helix, where the chain is arranged in a spiral and held together by hydrogen bonds: -
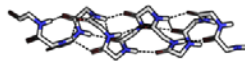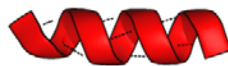
α-helix

- The second type of structure is a β-pleated sheet where the N-H and O-H groups are in separate sheets: -
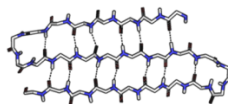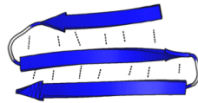
β-Sheet (3 strands)

Tertiary structure

- The tertiary structure is the whole protein and the way that the α-coil or the β-pleat of the protein fold and lie with respect to each other.

Amino acids

Primary Protein structure
sequence of a chain of
animo acids

Pleated sheet   Alpha helix

Secondary Protein structure
hydrogen bonding of the peptide
backbone causes the amino
acids to fold into a repeating
pattern

Pleated sheet

Tertiary protein structure
three-dimensional folding
pattern of a protein due to side
chain interactions

Alpha helix

The role of proteins in living systems

- Proteins are an essential part of the diet – they are required for growth and repair as they are present in all cells of the body, especially muscle cells. (Also present in nails, feathers, skin etc.)
- Enzymes are proteins and function as biological catalysts. Without them, biological processes would be too slow.

Enzyme name	Function
Amylase	Turns carbohydrates into glucose
Lipase	Breaks down fats into fatty acids and glycerol
Lactase	Breaks down lactose in milk
Alcohol dehydrogenase	Breaks down alcohols

- Some hormones are proteins, eg insulin. This 'regulates the way the body uses and stores glucose and fat' (https://www.diabetes.co.uk/body/insulin.html, accessed 14/02/18)

4.8 – Organic synthesis and analysis

Synthesis of organic compounds by a series of reactions

Questions based on this topic are often found to be difficult. You will need good problem-solving skills and it is in these questions that you will be able to show your knowledge on how different reactions are linked together. (See the end of this guide)

You will need to know the following: -
- how to make a given compound, perhaps using several stages. This might include a reduction or an increase in the length of the carbon chain.
- From this, the reactions needed to change the number of carbon atoms in the chain.
- Reaction conditions, eg pressure or catalyst needed for reaction to occur.

Increasing chain length
- KCN reacts with a halogenoalkane to produce a nitrile. Hydrolysis of this produces a carboxylic acid/Reduction of nitrile with $LiAlH_4$ gives the amine.
- Adding HCN to a carbonyl compound produces the hydroxynitrile. Hydrolysis of this gives a carboxylic acid with carbon chain lengthened by one.
- Aromatic only – Friedel-Crafts reaction can be used to introduce a side-chain to a benzene ring

Decreasing chain length
- Heating a carboxylic acid or its salt with soda lime gives the decarboxylation reaction.
- Triiodomethane (iodoform) reaction – methyl ketone is reacted with iodine in alkaline solution.

Worked example   (taken from a WJEC paper)

Ibuprofen is a common drug taken as an analgesic and anti-inflammatory treatment.

A possible route to the synthesis of ibuprofen is shown below.

(a) Step 1 is a Friedel-Crafts alkylation reaction. Give the reagent(s) and condition(s) required for this step. [3]

(b) Compounds **B** and **C** can be analysed using chemical tests.

   (i) Give a chemical test that would give a positive result for **both** compound **B** and compound **C**. Include reagent(s) and the observation(s) expected for a positive result. [2]

   (ii) Give a chemical test that would give a positive result for compound **C** but **not** for compound **B**. Include reagent(s) and the observation(s) for both compounds. [2]

(c) Compound **C** shows optical isomerism. Discuss this statement. Your answer should include: [4]
- What is meant by optical isomerism.
- What feature of compound **C** allows it to exhibit optical isomerism.
- Diagrams to show the two optical isomers of compound **C**.
- How the two optical isomers of compound **C** can be distinguished.

QWC [1]

(d) Give the reagent(s) and condition(s) required for step 5 and classify the reaction that occurs. [3]

(e) A student investigating alternative methods of producing ibuprofen suggests that it would be better to convert compound **C** into ibuprofen in a one-step process. Discuss whether this is correct. [4]

Your answer should include:

- The reagent(s) and condition(s) for a reaction expected to convert compound **C** directly into ibuprofen.

- Why it is generally better to use one step rather than two or more steps when producing a desired compound.

- A suggestion of why a two-step process is chosen for the synthesis of ibuprofen from compound **C** rather than a one-step process.

QWC [1]

[20]

This is a very long question and worth 20 marks, but it illustrates all of the points made above as to what you need to know.

   (a) Friedel-Crafts reaction is addition of a carbon chain to the benzene ring, so you will need to include the chain required and the reaction conditions: -

      Chain is – $CH_3CH(CH_3)_3CH_2Cl$, also require $AlCl_3$ or $FeCl_3$ as a halogen carrier (1 mark for each)

Conditions – At room temperature/In the dark.
Either one for a mark

(b) (i) C is an aldehyde and B is a ketone, so
(i) 2,4-DNP will give an **orange precipitate** with both
(ii) Tollen's reagent will give a silver mirror with C, but no reaction with B

(c) Optical isomerism is where a molecule has a mirror image - which means they cannot be superimposed on one another
Compound C has a chiral carbon atom – it has four different groups attached to one carbon atom
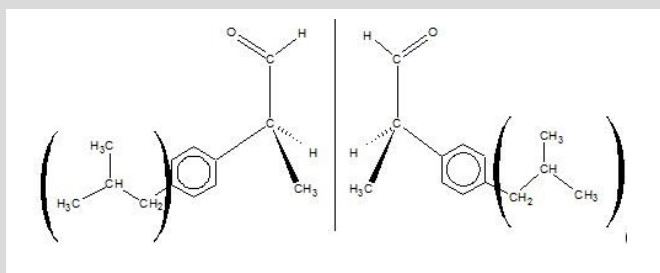
The two isomers of this compound can be distinguished by their ability to rotate the plane of polarised light in opposite directions.

(d) Step 5 is a hydrolysis reaction where the nitrile is heated with heated dilute acid.
(e) Compound C is an aldehyde and it can be converted into the carboxylic acid that is Ibuprofen using the oxidising agent acidified potassium dichromate(VI) (heated). One step reactions give a better yield as you usually have wastage at every stage. The two stage process might be used as it may be cheaper or produce a better yield in this case. Also, potassium dichromate could react with other parts of the molecule.

Main points of the principles of manipulation, separation and purification

Most organic compounds make other products than those required and reversible reactions will also have some unreacted products. The required products therefore require separation and purification. The method used depends on whether the products mix together or not.

- **Miscible** liquids will mix with each other.
- **Immiscible** liquids do not mix with each other. Some form definite layers, but some form as droplets within the other liquid.
- **Insoluble solids** are what they say – solids found in a liquid.
- **Soluble solids** will be dissolved in a liquid

Miscible liquids

- **Simple and fractional distillation** can be used if there is no danger of liquids decomposing at or near their boiling temperatures, with fractional distillation being used if the boiling points of the liquids are close to each other (20°C or less).
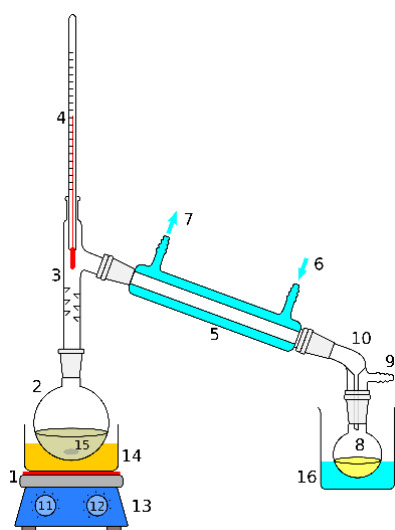
1: A source of heat 2: Round bottomed flask 3: Distillation column 4: Thermometer 5: Condenser 6: Cooling water in 7: Cooling water out 8: Distillate/receiving flask 9: Vacuum inlet 10: receiver 11: Heat control 12: Stirrer speed control 13: Stirrer/heat plate 14: Heating (Oil/sand) bath 15: Mechanical stirrer 16: Cooling bath
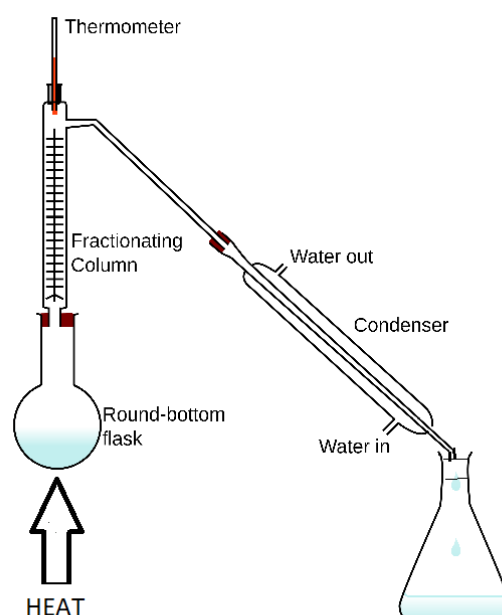
- If the liquids have high boiling temperatures, they can be distilled under reduced pressure, called vacuum distillation. This reduces the boiling temperature and can avoid decomposition at high temperatures.

Immiscible liquids

- **Steam distillation** is used in the perfume industry to get essential oils out of flowers. These oils are delicate and must not be heated directly to their very high boiling temperatures as they can decompose.
- Steam is passed through plant material and the oils distil over with the steam (even though it probably has a boiling point much higher than this).

Steam Distillation
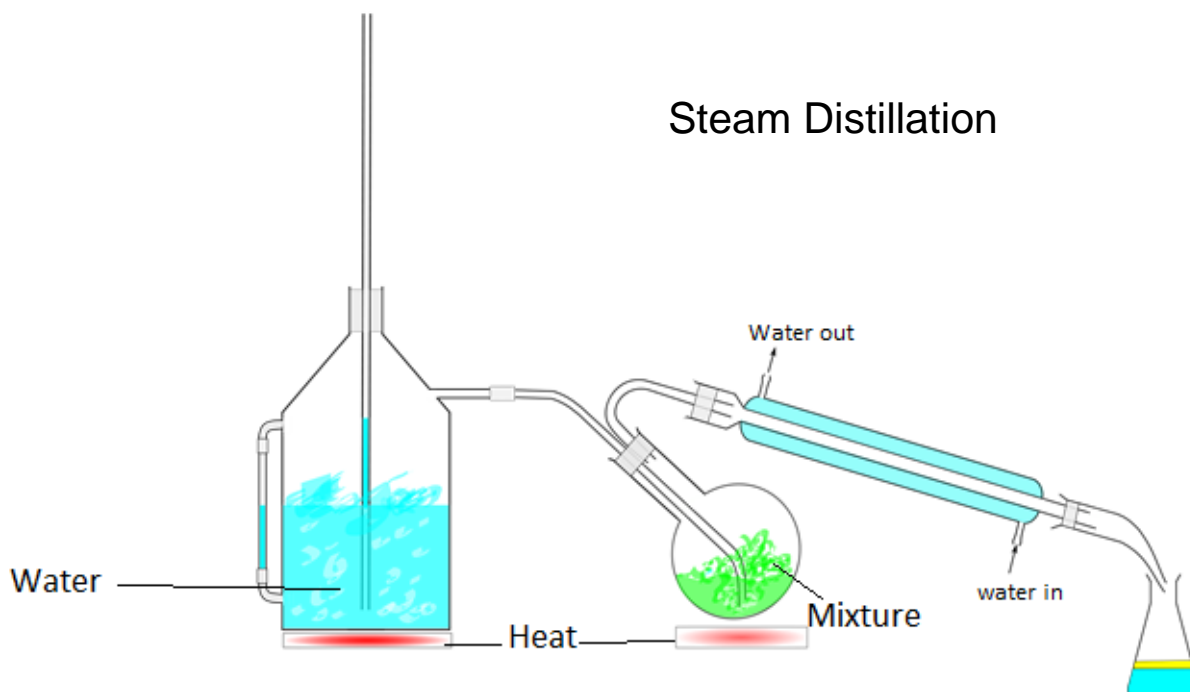
Solvent extraction

Compounds can have different solubilities in different solvents, eg caffeine has a solubility of 22 mg cm^{-3} in water and 140 mg cm^{-3} in dichloromethane. To extract caffeine from tea, it is firstly steeped in hot water and then shaken with dichloromethane. This means that the maximum amount of caffeine is extracted whilst leaving tannins behind in the water as they don't dissolve well in dichloromethane.
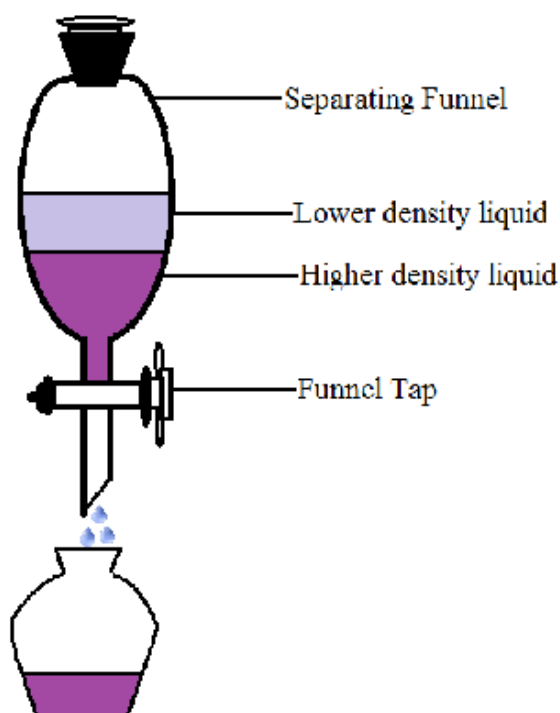
Dichloromethane and water don't mix, so they form two layers of liquids which can be separated using a **separating funnel.**

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Insoluble solids

There are two types of **filtration** that are routinely used to separate an insoluble solid from a liquid: -

- **Simple filtration** using a filter paper and funnel – fluted filter paper makes this quicker as there's only one layer of paper and there isn't as much paper touching the funnel.
- **Vacuum filtration** using a **Buchner funnel**
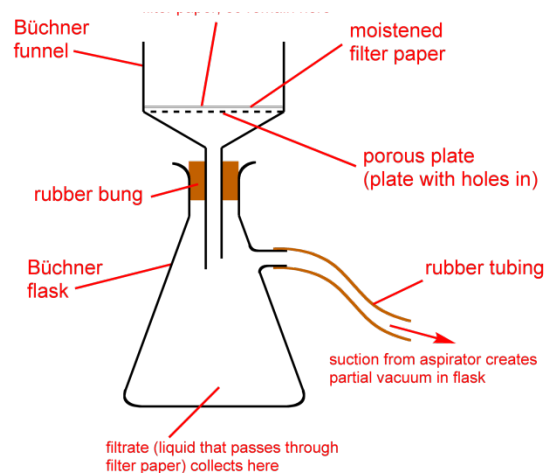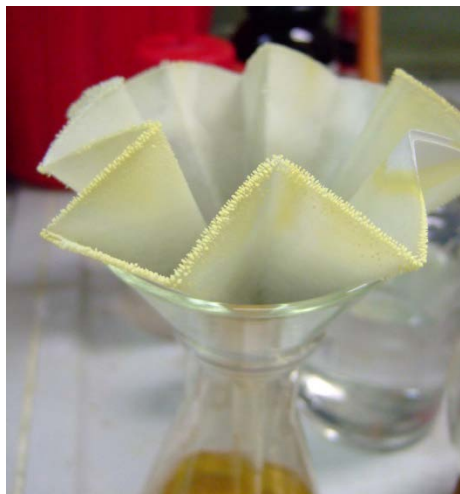
Soluble solids from a solution

Solute obtained from solution via **crystallisation**. Before this can happen, impurities can be removed using charcoal boiled with the solution. This must be filtered off whilst the solution is still hot. The solution is then **concentrated** by boiling. If the solution is concentrated enough, crystals will form on cooling. If this doesn't happen, then the solution needs to be boiled again to concentrate it more.

The crystals obtained in this manner need to be purified again. This can be done as follows: -
- Dissolve the crystals in the **minimum** amount of hot solvent.
- Filter to remove impurities (this can be done hot if necessary)
- Allow to cool
- Filter
- Wash the crystals with a small amount of solvent
- Dry between two pieces of filter paper at a temperature lower than the melting point

Using melting points to check the purity of a solid

If you've made a solid and want to test its purity, take its melting temperature. This is when it turns from a solid into a liquid and it can happen over one or two degrees. If a compound is impure, its melting temperature will be lower than expected, so this will be a good indication of the purity of a compound.

Condensation polymerisation and addition polymerisation – the difference between them

- **Addition polymerisation** was covered in unit 2 at AS. It involves the joining together of several **monomer** molecules, which contain the -C=C- double bond (alkenes). This is used to join the monomers together, giving a polymer that only contains single bonds between carbon atoms.

Chloroethene → Polychloroethene
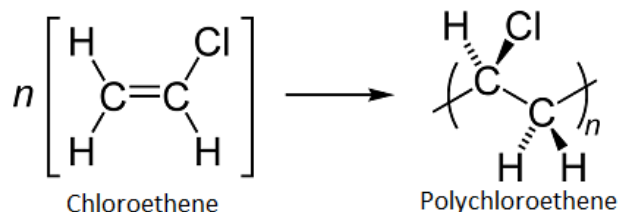
- **Condensation polymerisation** happens when many **monomer** molecules join together to form a long chain polymer, but with **the loss of small molecules** (usually water or HCl).
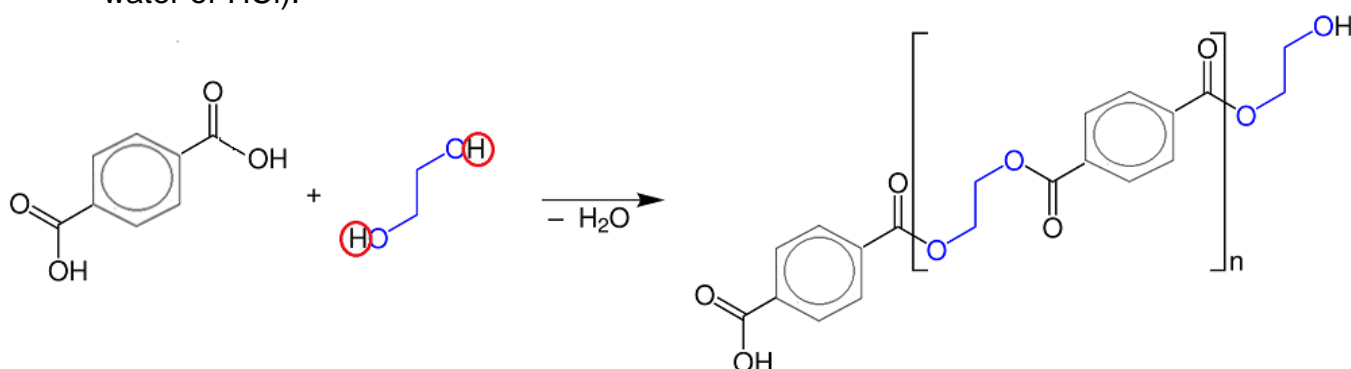
Addition polymeriasation	Condensation polymerisation
Contain double bond – alkenes	Contain functional groups: usually -OH, NH_2 or COOH
Double bond breaks and polymer only contains single bonds in an exclusively **carbon** chain	Two molecules join with the loss of a small molecule, removed from the functional groups on the end carbons of adjoining molecules. Chain isn't exclusively carbon, can contain **oxygen** for example
No other products formed	Small product formed as well as the polymer

Formation of polyesters and polyamides

- **Polyesters** are important materials – used to make clothes, plastic bottles and packaging. They are formed by condensation polymerisation.
- **PET (polyethylene terephthalate)** is one of the most common polyesters. It is made from the monomers ethane-1,2-diol and benzene-1,4-dicarboxylic acid (terephthalic acid)
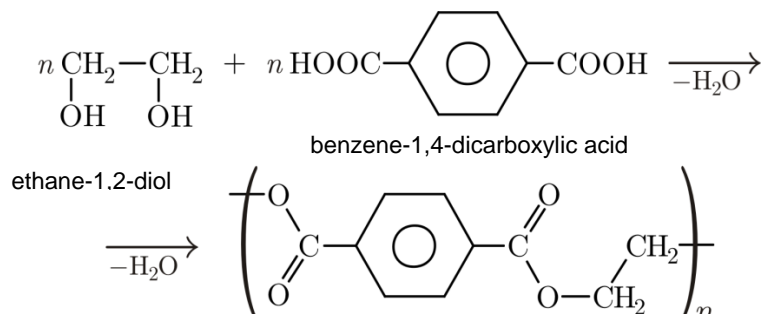
- **Polyamides** are also formed by condensation polymerisation - of a diamine and a carboxylic acid.
- 'Nylon' is an example of a polyamide. There are several different types, each with a number in the name. This number denotes the number of carbon atoms in each starting molecule of the starting monomers, eg **Nylon 6,6** is made from hexane-1,6-dioic acid and hexane-1,6-diamine: -
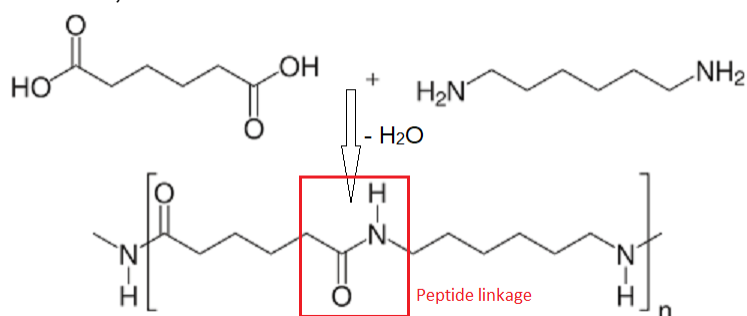
- **Nylon 6** only uses one starting compound – 6-aminohexanoic acid. This contains both the amino and carboxyl group on the same molecule.
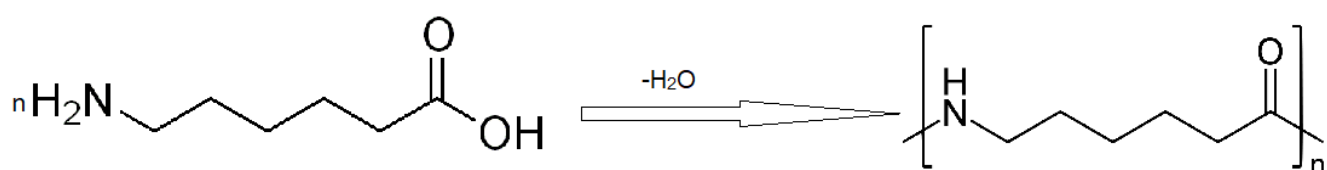
High resolution ^{1}H NMR – using it to find structures of organic molecules.

We encountered low resolution ^{1}H NMR spectroscopy at AS and this enables us to work out in how many different environments you can find protons and the ratio of number of protons in each environment.
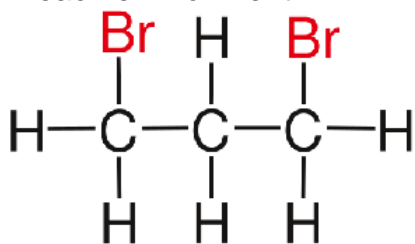
1,3-dibromopropane and its low resolution NMR spectrum. There are two peaks, each representing the different proton environments. One environment has two protons in it (from the central C atom) and the other environment has four protons from the two end carbon atoms.
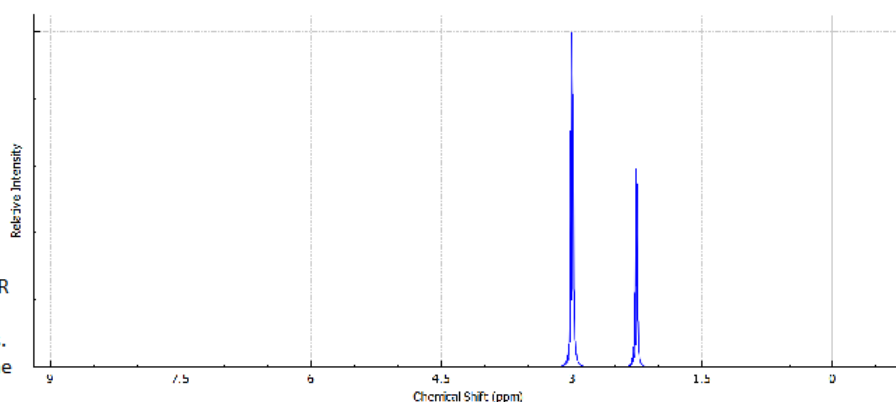
If we look at a high resolution ^{1}H NMR spectrum of ethyl ethanoate ($CH_3COOCH_2CH_3$), then we will see that the peaks showing the proton environments are split. This splitting happens because the environment of the protons in one group is affected by the environment of neighbouring groups of protons. Ethyl ethanoate has the following structure: -
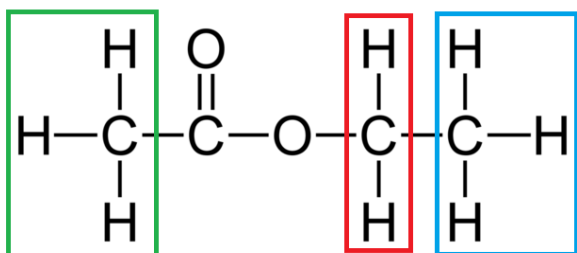
There are three different proton environments, highlighted by the different coloured boxes. The green protons will not be split in the spectrum as they don't have any neighbouring hydrogen atoms. The blue and red will be split as they have hydrogen atoms on the carbons next to them.

Here is the high resolution ^{1}H NMR spectrum for this molecule: -
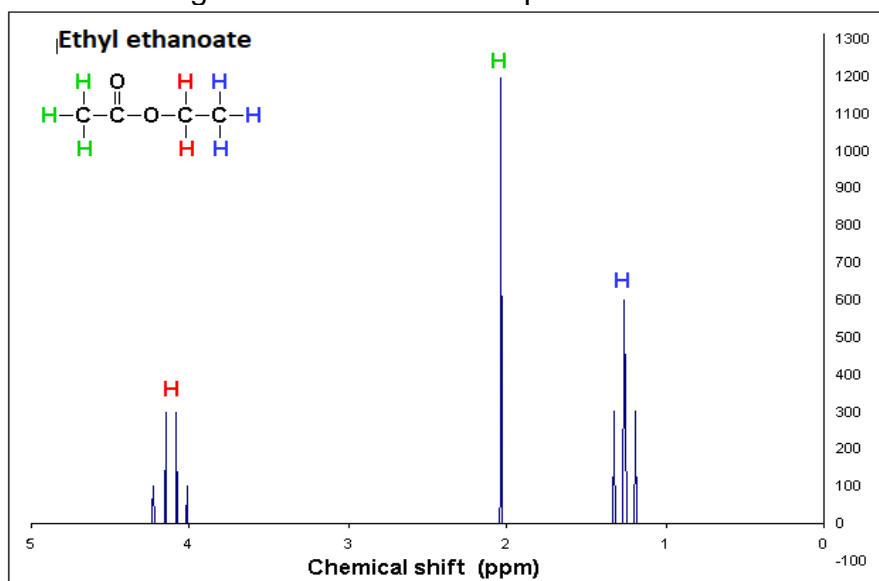
The green protons only have one peak, whilst the red protons have four peaks and the blue protons have three peaks. If you measured the height of the peaks and added them together you'd see them in the ratio of 3:2:3 for green:red:blue. This is to be expected if we look at the number of hydrogens involved.

We will look at the number of peaks that are obtained on splitting on the next page.

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Let's consider the ethyl ethanoate molecule in detail. The diagram explains what you see on the spectrum: -

These hydrogens aren't adjacent to a carbon carrying other hydrogens.

They have a single peak with no splitting and a relative height of 3
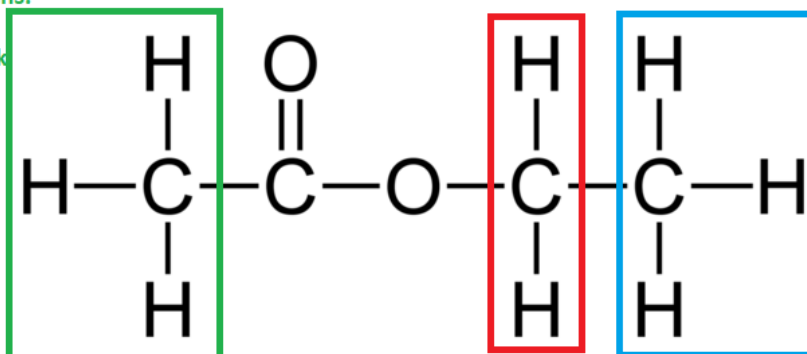
These two hydrogens are next to a carbon atom carrying three hydrogen atoms.

They have four peaks (called a quartet) and a relative height of 2

These three hydrogens are next to a carbon atom carrying two hydrogen atoms.

They have three peaks (called a triplet) and a relative height of 3

What can we learn from this? It would seem that: -

- The **relative height** of the peak(s) is connected to the **number** of hydrogen atoms in the environment
- The **number of peaks** is connected to the number of hydrogen atoms (bonded to C, N or O) that are found **adjacent** to those hydrogens, eg if hydrogens are adjacent to two others, then their peak is split into three. If they are adjacent to three others, then their peak is split into four. If they have no adjacent hydrogens, then there is no splitting, only one peak.
- If the hydrogen atoms from a particular peak are adjacent to n hydrogen atoms (bonded to C, N or O), then its peak will be split into (n+1) smaller peaks.

Worked example
This question is from a WJEC question paper and was accessed using the Question Bank: -

This question concerns isomers with structure $C_5H_{10}O_2$.
(a) Isomers P, Q, R and S all react with dilute sodium carbonate to produce carbon dioxide.
- Isomer P is a straight chain compound
- Isomer Q has a chiral centre
- Isomer R has only two peaks in its NMR spectrum, both of which are singlets

Draw the displayed formula for all **four** isomers.

(P) will be pentanoic acid as it is the straight chain compound, which means it has all five carbon atoms in a straight chain: -

$H_3C\text{-}CH_2\text{-}CH_2\text{-}CH_2C{\overset{\displaystyle O}{\underset{\displaystyle OH}{\diagup\diagdown}}}$

(Q) has a chiral centre, so will have four different atoms or groups on one of the carbons: -

$$\underset{\substack{| \\ H}}{\overset{\substack{CH_3 \\ |}}{H_3C\text{-}CH_2\text{-}C\text{-}C}} \overset{O}{\underset{OH}{\diagdown}}$$

(R) only has two peaks in its NMR spectrum, meaning there are only two hydrogen environments. Both peaks are singlets, which means that neither atom which has hydrogens bonded to it is bonded to another atom containing hydrogens: -

$$\underset{\substack{| \\ CH_3}}{\overset{\substack{CH_3 \\ |}}{H_3C - C - C}} \overset{O}{\underset{OH}{\diagup}}$$

There are nine 'yellow' hydrogens, all in the same environment and the carbon adjacent to the carbon atoms they are attached to have no hydrogens attached to it.

There is one 'green' hydrogen and the carbon adjacent to the oxygen atom it is attached to has no hydrogens attached to it.

(S) will be an isomer you haven't already drawn, it can be like Q, but with the methyl group on the third carbon atom instead of the second.

$$\underset{\substack{| \\ }}{\overset{\substack{CH_3 \\ |}}{H_3C\text{-}CH\text{-}CH_2\text{-}C}} \overset{O}{\diagup} \\ \underset{OH}{\diagdown}$$

(b) Isomer T has the structural formula shown below: -

$$H_3C - CH_2 - O - CH_2 - \overset{\overset{\textstyle O}{\|}}{C} - CH_3$$

List the peaks that you would find in the NMR spectrum of isomer T. Identify which protons are responsible for each peak, giving the approximate chemical shift (ppm) and splitting of the peak. (You will have a data sheet that gives the chemical shift for each type of environment)

Firstly identify the number of environments – there are four, each highlighted in a different colour.

*Yellow (CH₃-CO) has three hydrogens, attached to a carbon not containing hydrogens, so there will be **no splitting** - it will be a singlet. (chemical shift is 2.0 to 2.5 ppm)*
Green (CH₂-CO) – will again be a singlet as the oxygen and carbon it's attached to have no hydrogens attached to them. (chemical shift is 2.5 to 3.0 ppm)
Blue (CH₃CH₂-O) will have four peaks (a quadruplet) as their carbon is attached to a carbon that has three hydrogens attached to it (so 3+1 = 4). (chemical shift is 3.5 to 4.0 ppm)
Pink (CH₃CH₂) will have three peaks (a triplet) as their carbon is attached to a carbon that has two hydrogens attached to it (so 2+1 = 3). (chemical shift is 0.1 to 2.0 ppm)

## Chromatography – Paper/Thin layer, Gas and High performance liquid

You will have come across paper chromatography several times during your studies and will know it as a technique that's used to separate substances by their slow movement at different rates through a stationary phase (paper in this case). The substances are carried by the solvent, which is the mobile phase.

You will be required to use data from chromatographic techniques to find the composition of mixtures, so you won't need to know the theory and principles of the techniques covered.

Thin layer/Paper chromatography

These are covered together as the principles are the same. Thin layer chromatography uses a layer of silica or aluminium oxide coated onto a glass plate as the stationary phase.

- Spots of the starting substances dissolved into a suitable solvent are placed at the bottom of the paper or plate.
- This is placed into the mobile phase solvent, which must be below the line of the spots.
- The solvent rises up the paper or plate, separating the mixture into different spots.
- When the solvent front has reached a suitable place, the paper or plate is taken out and dried.
- Measurements are made of the distance each spot is from the starting line as well as the distance of the solvent front.
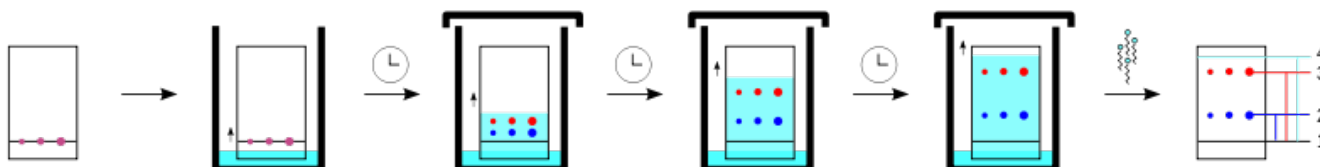
In this example, point 1 is the starting line, 2 is the distance the blue spot has moved and 3 is the distance the red spot has moved. Point 4 is where the solvent front travelled to.

- You can calculate the **R_f (retardation factor) value** for each colour using the following equation:

$$R_f = \frac{\text{distance travelled by spot}}{\text{distance travelled by solvent front}}$$

 NB R_f must always be less than 1 as the solvent front always travels further than the spots.

- If you have a R_f value of 1, then the compound is moving at the same rate as the solvent, so you should try a different solvent.
- Known R_f values can be used to compare with your experimental value in order to discover what an unknown substance may be.
- Some spots are colourless and can be made visible using UV light or spraying it with a developing agent.
- Each compound that has been separated can be obtained from the paper or plate by removing each spot, dissolving it in a suitable solvent and then evaporating.

Gas chromatography

The commonest type is gas-liquid chromatography, where the mobile phase is a gas and the stationary phase is a high boiling point liquid that is adsorbed onto a solid. The sample gases are carried through the column by an inert gas. The time taken for the compound to come out of the column is called the retention time. The relative area of each peak gives the percentage of each compound present in the mixture.

The diagram below shows the presence of octane and nonane in different mixtures.
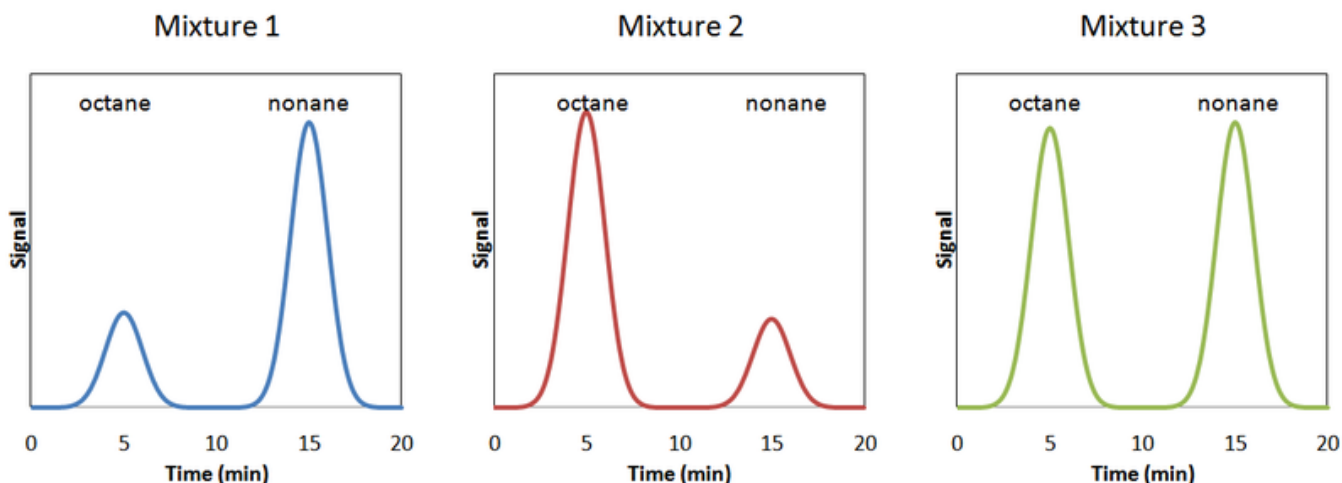
High performance liquid chromatography (HPLC)

If a compound needs high temperatures to turn it into a gas, then it might start to decompose. This is when it is useful to use HPLC. Here, the column is packed with uniform solid particles and the sample is dissolved in a solvent. The solution is then forced at high pressure through the column. This is the method that's used for testing athletes' urine during drug testing. It's also used extensively in the food and pharmaceutical industries.

The trace is similar to the ones you will see with gas chromatograpy.
Here is a trace for an antibiotic medicine Metronidazole benzoate: -
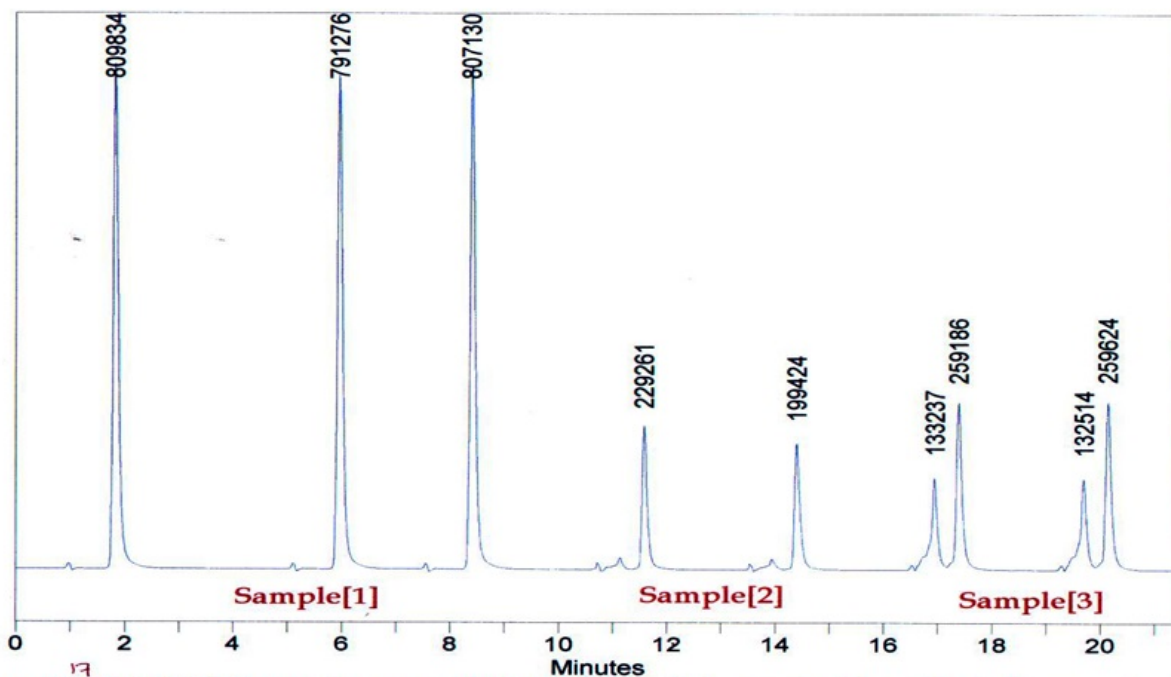
Acknowledgments

Section	Image	Acknowledgment
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