Edexcel International A Level (IAL) Chemistry

Your notes

Organic Synthesis

Contents

Your notes

Combined Techniques

- You will be expected to deduce the empirical, molecular and structural formulae of compounds from data such as:
  - Combustion analysis
  - Elemental percentage composition - also known as calculating empirical formulae
  - Characteristic reactions of functional groups - this can include test-tube reactions as well as interconversions
  - Infrared (IR) spectra
  - Mass spectra (MS)
  - Nuclear magnetic resonance (NMR) spectra
- The normal progression for the analysis of a compound is:
  1. Find the empirical formula
  2. Determine the molecular formula
  3. Identify the functional groups / structural components present
  4. Deduce the overall structure

Combustion analysis

- Sometimes combustion analysis is performed on an unknown compound to determine the elemental percentage composition
- The elemental percentage composition is then used to calculate the empirical formula
- In combustion analysis, a known mass of the compound is burned in an excess of dry oxygen
- The mass of carbon dioxide and water are then used to determine the percentage content of carbon, hydrogen and oxygen in the compound
  - This can also be applied to include sulfur and nitrogen, although you are not expected to do this, at this level
- To convert combustion analysis data to elemental percentage composition:
  1. Calculate the mass of carbon in the sample from the combustion analysis results
  2. Calculate the percentage of carbon in the sample
  3. Calculate the mass of hydrogen in the sample from the combustion analysis results
  4. Calculate the percentage of hydrogen in the sample

5. Use the percentage of carbon and hydrogen to deduce the percentage of oxygen in the sample

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Worked Example

Combustion analysis was performed on 2.90 g of an unknown carbohydrate, A.

6.60 g of carbon dioxide and 2.70 g of water were produced.

Calculate the carbohydrates percentage composition.

Answer

Step 1: Calculate the mass of carbon in the sample

- Mass of carbon = $\frac{\text{mass of carbon}}{\text{molecular mass of carbon dioxide}} \times \text{mass of carbon dioxide produced}$
  - Mass of carbon = $= \frac{12.0}{44.0} \times 6.60 = 1.80\ \text{g}$

Step 2: Calculate the percentage of carbon in the sample

- Percentage carbon = $\frac{\text{mass of carbon in sample}}{\text{mass of sample}} \times 100$
  - Percentage carbon $= \frac{1.80}{2.90} \times 100 = 62.1\%$

Step 3: Calculate the mass of hydrogen in the sample

- Mass of hydrogen = $\frac{\text{TOTAL mass of hydrogen}}{\text{molecular mass of water}} \times \text{mass of water produced}$
  - Mass of hydrogen = $= \frac{2.0}{18.0} \times 2.70 = 0.30\ \text{g}$

Step 4: Calculate the percentage of hydrogen in the sample

- Percentage hydrogen = $\frac{\text{mass of hydrogen in sample}}{\text{mass of sample}} \times 100$
  - Percentage hydrogen $= \frac{0.30}{2.90} \times 100 = 10.3\%$

Step 5: Calculate the percentage of oxygen in the sample

- Percentage oxygen = 100 - percentage of carbon - percentage of hydrogen
  - Percentage oxygen = 100 - 62.1 - 10.3 = 27.6%
  - Therefore, the percentage composition of the carbohydrate is 62.1% carbon, 10.3% hydrogen and 27.6% oxygen

Examiner Tips and Tricks

Don't forget to use 2.0 g for the mass of hydrogen as there are two hydrogen atoms in a water molecule

Your notes

Worked Example

Calculate the empirical formula for the unknown carbohydrate, A

Answer

- The percentage composition of the unknown carbohydrate, A, is 62.1% carbon, 10.3% hydrogen and 27.6% oxygen

Elements	C	H	O
Values	62.1%	10.3%	27.6%
Atomic mass, A_r	12.0	1.0	16.0
Divide $\left(\frac{\text{value}}{A_r}\right)$	$\frac{62.1}{12.0} = 5.175$	$\frac{10.3}{1.0} = 10.3$	$\frac{27.6}{16.0} = 1.725$
Ratio (divide by smallest)	$\frac{5.175}{1.725} = 3$	$\frac{10.3}{1.725} = 5.97 \approx 6$	$\frac{1.725}{1.725} = 1$

- Empirical formula = C_3H_6O

Characteristic reactions of functional groups

- For deducing structures, these will typically be the test-tube reactions, including (but not limited to):
  - Bromine: C=C bond
  - Acidified potassium dichromate(VI) solution: primary and secondary alcohols
  - Fehling's or Tollens': aldehydes and ketones
  - 2,4-dinitrophenylhydrazine (2,4-DNPH): C=O bond
  - Sodium carbonate: carboxylic acids
  - Iodoform: Methyl groups next to C=O

Spectral analysis

- These will include:
  - Infrared spectroscopy: to identify functional groups and certain bond types
  - Mass spectrometry: to identify molecular formula and fragments

- Carbon-13 (^{13}C) nuclear magnetic resonance: to identify compound structure
- Proton (^{1}H) nuclear magnetic resonance: to identify compound structure

Your notes

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Reaction Schemes

- A large number of organic products are made from a few starting compounds using appropriate reagents and conditions
- Knowing how organic functional groups are related to each other is key to the synthesis of a given molecule
- The main functional groups you need to know are
  - Alkanes
  - Alkenes
  - Haloalkanes
  - Nitriles
  - Amines
  - Alcohols
  - Carbonyls (aldehydes & ketones)
  - Hydroxynitriles
  - Carboxylic acids
  - Esters
  - Acyl chlorides
  - Primary and secondary amides

Aliphatic Reaction Pathways

- The key interconversions between functional groups are summarised here:

Aliphatic Reactions Table

Reactant	Product	Reagents	Reaction
Alkene	Haloalkane	X_2 / HX	Electrophilic addition
Alkene	Alcohol	Steam + H_2SO_4 / heat	Hydration
Alkene	Alkane	Hydrogen + Ni catalyst / 150 °C	Electrophilic addition / hydrogenation

Alcohol	Alkene	Al_2O_3 or conc. H_2SO_4 / heat	Elimination / dehydration
Alcohol	Haloalkane	NaX + H_2SO_4 / reflux	Nucleophilic substitution
Haloalkane	Alcohol	NaOH (aq) / reflux	Nucleophilic substitution
Alkane	Haloalkane	Halogen / UV light	Free radical substitution
Primary alcohol	Aldehyde	$K_2Cr_2O_7$ / H_2SO_4 / distil	Oxidation
Secondary alcohol	Ketone	$K_2Cr_2O_7$ / H_2SO_4 / Heat	Oxidation
Primary alcohol	Carboxylic acid	$K_2Cr_2O_7$ / H_2SO_4 / reflux	Oxidation
Aldehyde	Primary alcohol	$NaBH_4$ / H_2O	Reduction / nucleophilic addition
Ketone	Secondary alcohol	$NaBH_4$ / H_2O	Reduction / nucleophilic addition
Haloalkane	Nitrile	Aqueous ethanolic KCN / Heat	Nucleophilic substitution
Halogenoalkane	Amine	NH_3 / ethanol	Nucleophilic substitution
Nitrile	Carboxylic acid	H_2O / HCl	Hydrolysis
Aldehyde	Hydroxynitrile	NaCN / H^+	Nuclophilic addition
Alcohol	Ester	Carboxylic acid / H_2SO_4	Esterification
Carboxylic acid	Ester	Alcohol / H_2SO_4	Esterification
Ester	Carboxylate salt and alcohol	NaOH (aq)	Alkaline hydrolysis
Ester	Carboxylic acid	Dilute acid	Acid hydrolysis

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Carboxylic acid	Acyl chloride	$SOCl_2$	Chlorination
Acyl chloride	Carboxylic acid	H_2O	Hydrolysis
Acyl chloride	Primary amide	NH_3	Nucleophilic addition elimination
Acyl chloride	Secondary amide	Primary amine	Nucleophilic addition elimination

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Aromatic Reaction Pathways

- The key aromatic reactions are summarised here:

Aromatic Reactions Table

Reactant	Product	Reagents	Reaction
Benzene	Methylbenzene / toluene	CH_3Cl / $AlCl_3$	Alkylation / Electrophilic substitution
Benzene	Bromobenzene	Br_2 / $FeBr_3$	Bromination / Electrophilic substitution
Benzene	Chlorobenzene	Cl_2 / $AlCl_3$	Chlorination / Electrophilic substitution
Benzene	Nitrobenzene	HNO_3 / H_2SO_4	Nitration / Electrophilic substitution
Nitrobenzene	Aminobenzene / phenylamine / aniline	Sn / HCl	Reduction
Aminobenzene	2,4,6-tribromoaminobenzene / 2,4,6-tribromoaniline	Bromine	Electrophilic substitution
Benzene	Phenylethanone	CH_3COCl / $AlCl_3$	Acylation / Electrophilic substitution
Phenylethanone	1-phenylethanol	$NaBH_4$	Reduction

Designing a Reaction Pathway

Your notes

- The given molecule is usually called the **target molecule** and chemists try to design a synthesis as efficiently as possible
- Designing a reaction pathway starts by drawing the structures of the **target molecule** and the **starting molecule**
- Determine if they have the **same number** of carbon atoms
  - If you need to lengthen the carbon chain you will need to put on a **nitrile group** by nucleophilic substitution
- Work out all the compounds that can be made from the starting molecule and all the molecules that can be made into the target molecule
  - Match the groups they have in common and work out the reagents and conditions needed

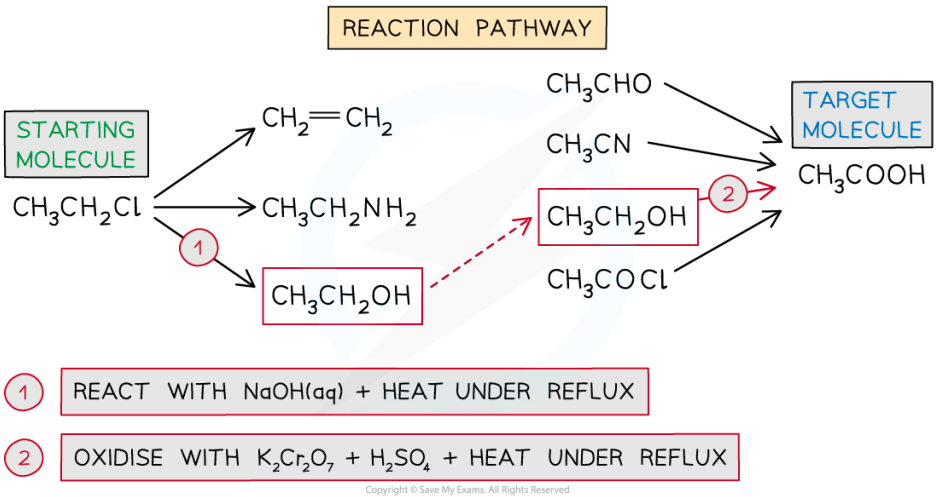
Worked Example

Suggest how the following syntheses could be carried out:

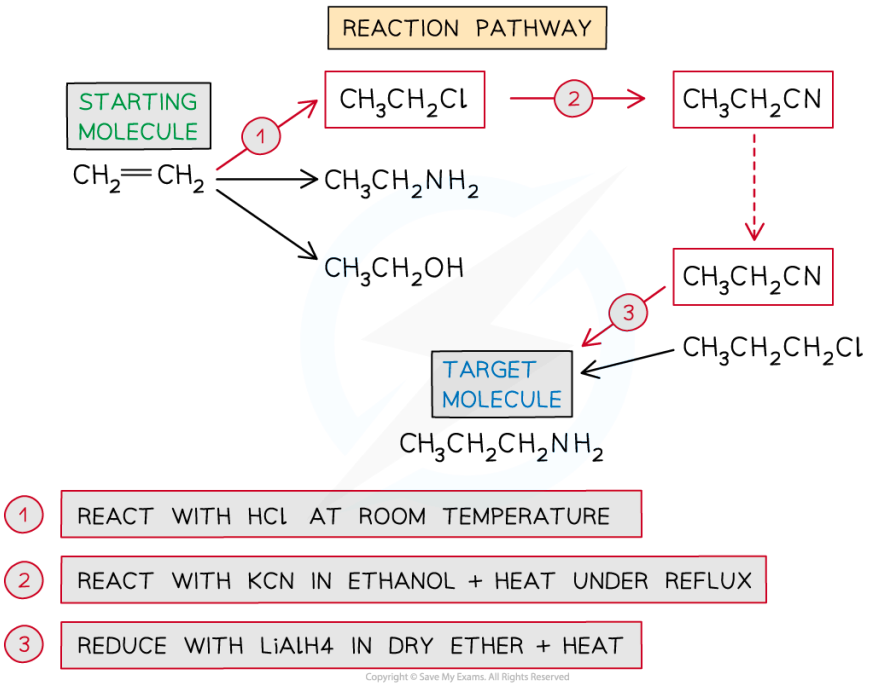
a) Chloroethane to ethanoic acid

b) Ethene to 1–aminopropane

Answer 1



Answer 2



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Examiner Tips and Tricks

You could be required to design a synthesis with up to four steps

Part of this process can include identifying appropriate control measures to reduce risk, based on data about hazards

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Increasing the Carbon Chain Length

- If we need to increase the chain length we can use **Grignard reagents**

Preparing Grignard reagents

- A halogenoalkane is dissolved in dry ether and reacted with magnesium to produce the reactive Grignard reagent
- If 1-iodoethane is reacted with magnesium, **ethyl magnesium iodide** is produced
- This is an example of a Grignard reagent

$$CH_3CH_2I + Mg \rightarrow CH_3CH_2MgI$$

- These compounds are highly reactive and the alkyl group (R group) can be considered to have a negative charge, therefore it can behave as a nucleophile
  - $R^-[^+MgI]$
- Carbonyl compounds and carbon dioxide will react with Grignard reagents to give different products as part of a two-step reaction (specific reaction details and mechanisms are not required at this level)
  - An initial product is formed during an addition reaction
  - Dilute acid is then added to hydrolyse this initial product

Reactions of Grignard with carbonyl compounds

- Grignard reagents react with **methanal** to produce a **primary alcohol**

$$RMgI + HCHO \xrightarrow{H_2O} RCH_2OH + Mg(OH)I$$

- For example, methanal can react with ethyl magnesium iodide to produce **propanol**

$$CH_3CH_2MgI + HCHO \xrightarrow{H_2O} CH_3CH_2CH_2OH + Mg(OH)I$$

- They also can react with **longer chain aldehydes** to produce **secondary alcohols**
- For example, ethanal can react with ethyl magnesium iodide to produce butan-2-ol

$$CH_3CH_2MgI + CH_3CHO \xrightarrow{H_2O} CH_3CH_2CH(OH)CH_3 + Mg(OH)I$$

- **Ketones** are also able to react with Grignard reagents producing a tertiary alcohol
- For example, propanone can react with ethyl magnesium iodide to produce **2-methylbutan-2-ol**

$$CH_3CH_2MgI + CH_3COCH_3 \xrightarrow{H_2O} CH_3CH_2C(CH_3)(OH)CH_3 + Mg(OH)I$$

Reactions of Grignard reagents with carbon dioxide

- This reaction will produce a carboxylic acid

$$CH_3CH_2MgI + CO_2 \xrightarrow{H_2O} CH_3CH_2COOH + Mg(OH)I$$

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Reflux & Types of Distillation

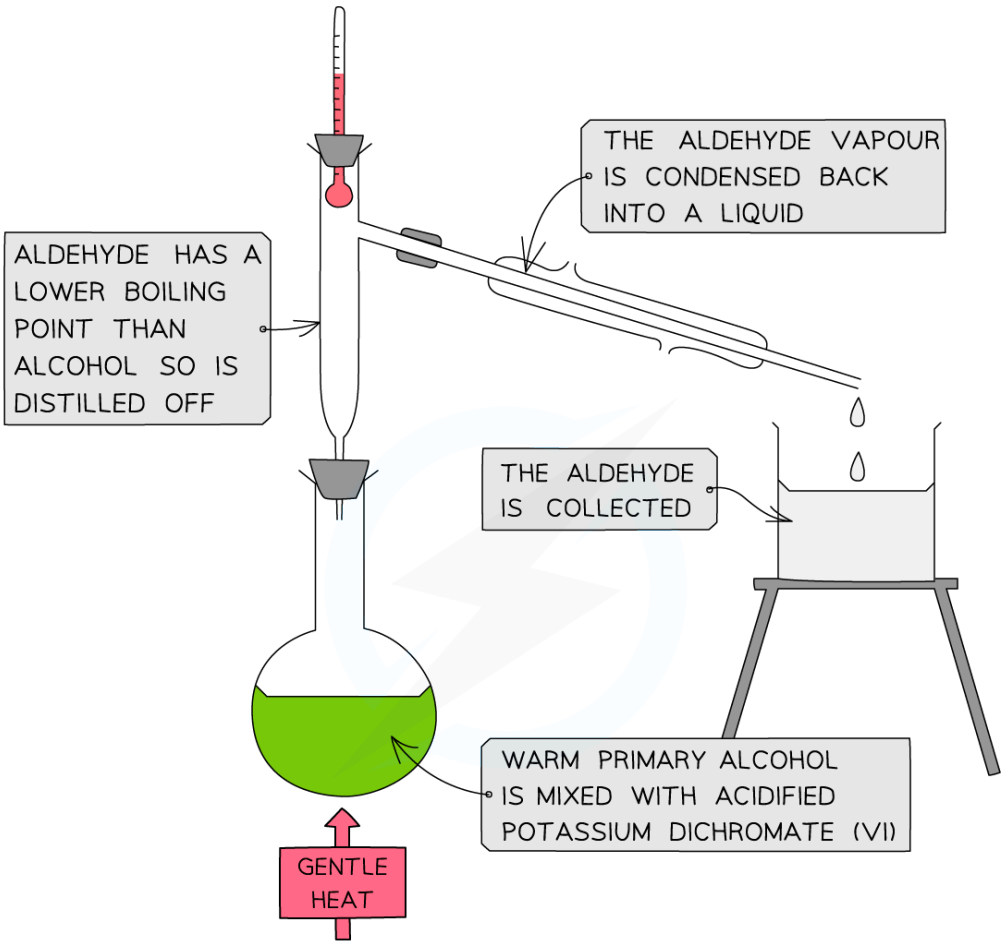
Simple distillation

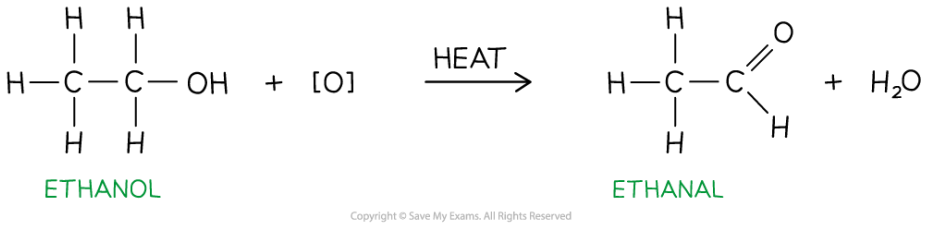
- Simple distillation is a common practical completed in organic chemistry
- It is used as there are times that a reaction does not go to completion or there are other chemicals produced as well as the desired product
- Simple distillation allows you to separate compounds by their boiling point
  - Chemicals with the lowest boiling point will distill first
- One of the most common simple distillation practicals is the oxidation of primary and secondary alcohol to aldehydes and ketones

The simple distillation process

- To produce an aldehyde from a primary alcohol, a reaction mixture containing the primary alcohol and acidified potassium dichromate solution is placed into a pear-shaped or round bottomed flask
- Anti-bumping granules are added to promote smooth boiling
- Quickfit apparatus is then set up, including a still head and condenser connected to the side
  - The joints of the Quickfit apparatus are often have a thin layer of silicon grease smeared over them to give a better seal as well as to make it easier to disassemble the equipment afterwards
- A Quickfit thermometer can be used, with the thermometer bulb sitting where the vapours will pass into the condenser
- A steady and constant stream of water passes through the condenser in a 'water jacket' - it enters at the bottom of the condenser and the drainage pipe removes the water from the top of the condenser

Your notes





Heating under Distillation Apparatus

- The reaction mixture is heated until it boils using a heating mantle
  - Electric heating mantles are used for this because the temperature can be controlled, and because you are using chemicals which are flammable
- The distillate which forms in the condenser drips directly into a receiving vessel
  - The distillate which should be collected, is that which is given off at +/- 2 °C of the boiling point of the desired product
  - Some distillate may be given off below this temperature - this needs to be discarded and a clean vessel used to collect the desired product
  - Stop collecting the distillate if the temperature rises above +/- 2°C of the boiling point of the desired product

- The **aldehyde** product has a lower boiling point than the **alcohol** (since it has lost the **H-bonding**) so it can be **distilled off** as soon as it forms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Steam distillation

- Steam distillation is used to separate an insoluble liquid from an aqueous solution
  - Steam is bubbled through a reaction mixture containing the aqueous solution and the insoluble liquid that forms a separate layer
  - As the steam bubbles through the reaction mixture it mixes the layers so they form part of the evaporating liquid
  - The resulting distillate can be cloudy if the desired compound is not miscible in water
- Advantages of steam distillation are:
  - The insoluble liquid distils at a temperature below its usual boiling point
  - It reduces the chances of thermal decomposition of the insoluble liquid

Heating under reflux

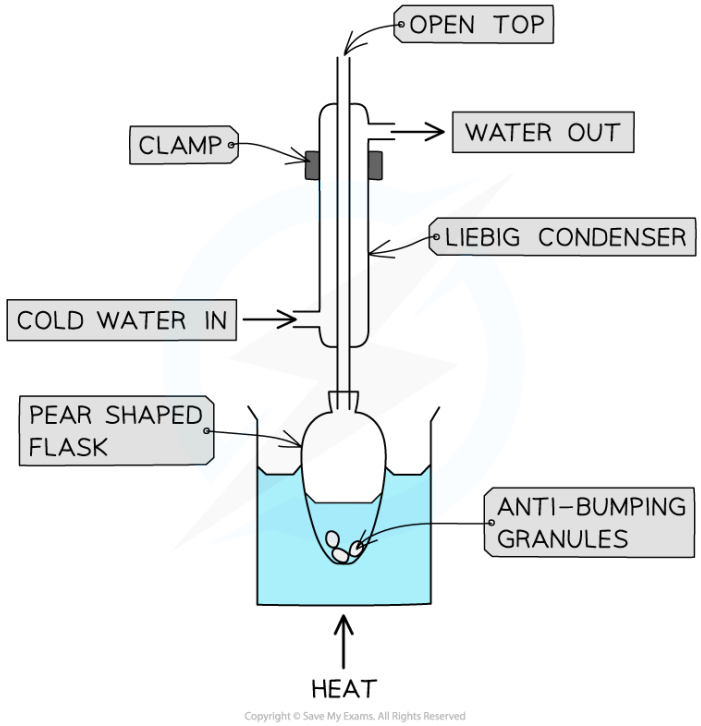
- Organic reactions often occur slowly at room temperature
- Therefore, organic reactions can be completed by heating under reflux to produce an **organic liquid**
- This allows the mixture to react as fully as possible without the loss of any reactants, products or solvent
  - In distillation, you are trying to separate a chemical or product from a mixture
  - When heating under reflux, you aim to keep all the chemicals inside the reaction vessel

The Heating under Reflux Process:

- Example reactions where heating under reflux could be used include:
  - The production of a carboxylic acid from a primary alcohol using acidified potassium dichromate
  - The production of an ester from an alcohol and acid in the presence of an acid catalyst
- The reaction mixture is placed into a pear-shaped or round bottomed flask
- Anti-bumping granules are, again, added to promote smooth boiling
- The flask is placed in a heating mantle or it can be immersed in a water bath for heating
- Quickfit apparatus is then set up with the condenser clamped vertically in place
  - The joints of the Quickfit apparatus are commonly greased as with distillation
- A steady and constant stream of water passes through the condenser in a 'water jacket' - it enters at the bottom of the condenser and the drainage pipe removes the water from

the top of the condenser

- The water is heated and the reaction mixture allowed to boil
- The heated is stopped and the mixture allowed to cool back to room temperature



The preparation of ethyl ethanoate involves heating under reflux for about 15 minutes

Examiner Tips and Tricks

- These practicals give you the opportunity to discuss:
  - The use of an electric heating mantles and water baths rather than a Bunsen burner
  - The choice and setup of laboratory apparatus
  - Health and safety considerations including the careful handling of different liquids, including those which are corrosive, irritant, flammable and toxic

Your notes

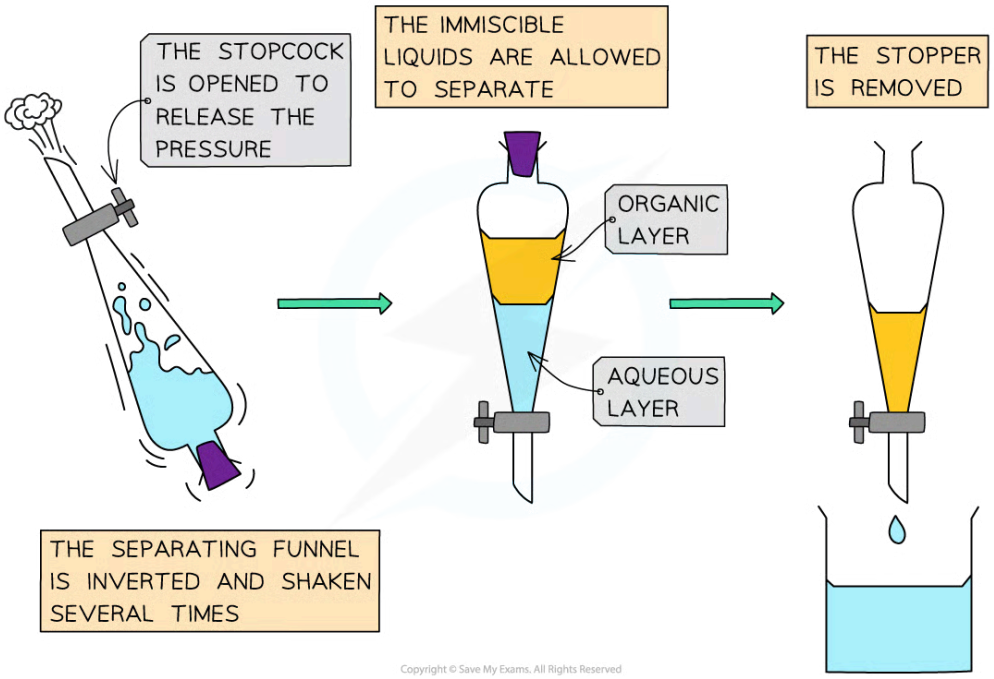
Your notes

Purification of Organic Compounds

- There are different methods to purify organic compounds, including:
  - Solvent extraction / use of a separating funnel
  - Use of drying agents
  - Recrystallisation

Solvent extraction / use of a Separating Funnel

- When organic liquids are being prepared, water can often be obtained along with the organic product
- The water will usually form an aqueous layer with the product in the organic layer
  - It can sometimes be hard to identify which layer is the organic layer - this can be achieved by simply adding water and seeing which layer increases in volume
- Other organic reactions may need to be neutralised before being purified, this can be achieved by adding sodium carbonate solution to the reaction vessel or separating funnel
  - This can also be used to remove other impurities by washing
- The contents of the reaction vessel are transferred to a separating funnel and a stopper added
- The separating funnel is inverted and the stopcock opened to release the pressure - this is repeated 15–20 times
  - If neutralisation has occurred then the stopcock is opened slowly to avoid losing any product
- The two layers are allowed to separate
  - In the following example, the aqueous layer is the bottom layer inside the separating funnel
- The stop cock is opened so that the aqueous layer drains away and the organic layer can be drained into a clean beaker



A separating funnel allows the product to be cleaned and isolated

Use of drying agents

- Drying agents can be used to remove traces of water from an organic product
- Drying agents are usually anhydrous inorganic salts that readily hydrate in the presence of water
  - Anhydrous calcium chloride is commonly used to dry hydrocarbons
  - Anhydrous calcium or magnesium sulfate are used more general purpose drying agents
  - Potassium hydroxide is a less common but relatively inexpensive drying agent
- A spatula of drying agent is added into the organic product and swirled
  - If the organic product has a low boiling point, a lid / stopped can be added to reduce the potential evaporation of any product
- If the drying agent clumps together, then there is still water in the organic liquid
- More drying agent is added until some remains dispersed in the organic liquid as a fine powder
- The dry organic liquid can then be decanted or filtered
  - If the organic liquid is dry then it should appear clear

Recrystallisation

- Recrystallisation is used to purify impure solids

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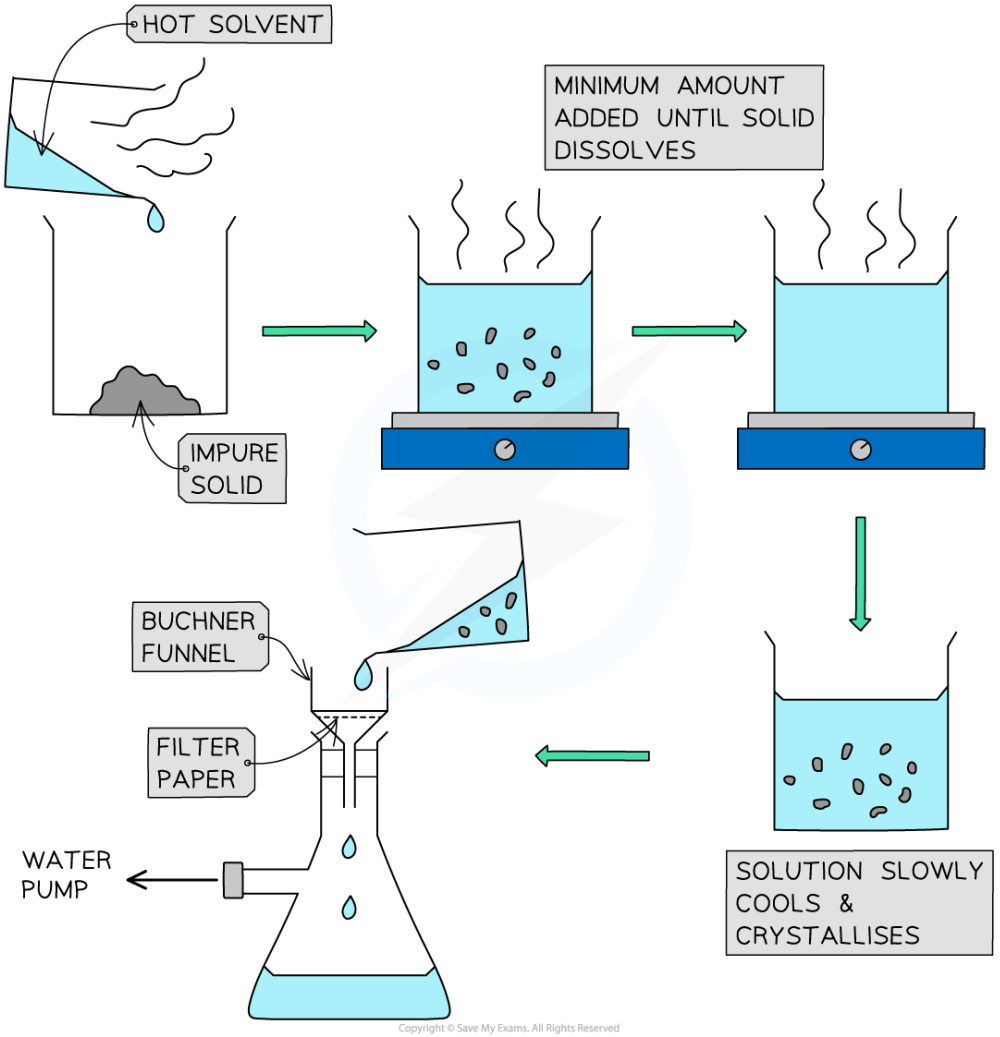
- The principle is that a hot solvent is used to dissolve both the organic solid and the impurities and then as the solution cools the solid crystallises out and leaves behind the impurities in the solution
- The key is using the minimum amount of solvent to dissolve the solid and avoid loss of the product
- If any solid impurities remain in the solution, a hot filtration can be carried out
- Once the solution has cooled down to room temperature and crystallised then the product crystals can be recovered by filtration
- This is faster using Buchner apparatus in which filtration occurs under reduced pressure



Recrystallisation and Buchner filtration

- After filtration the product is washed with fresh cold solvent and then allowed to dry on filter paper

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Examiner Tips and Tricks

Recrystallisation can be repeated more than once to ensure a very pure product, but each time the yield of product will decrease. Slow cooling results in bigger well defined crystals which are easier to filter and dry.

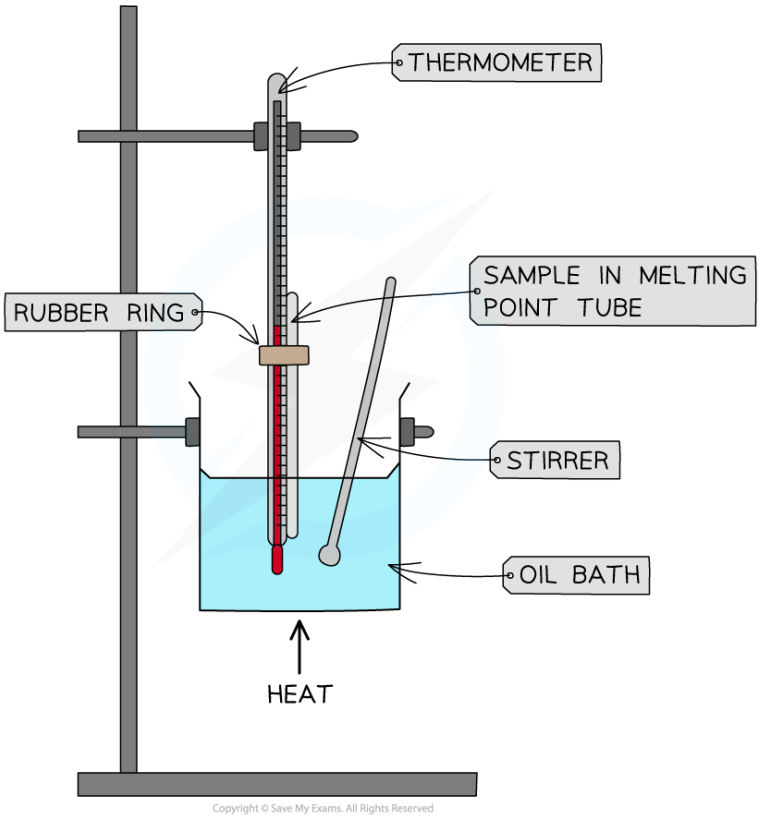
Your notes

Your notes

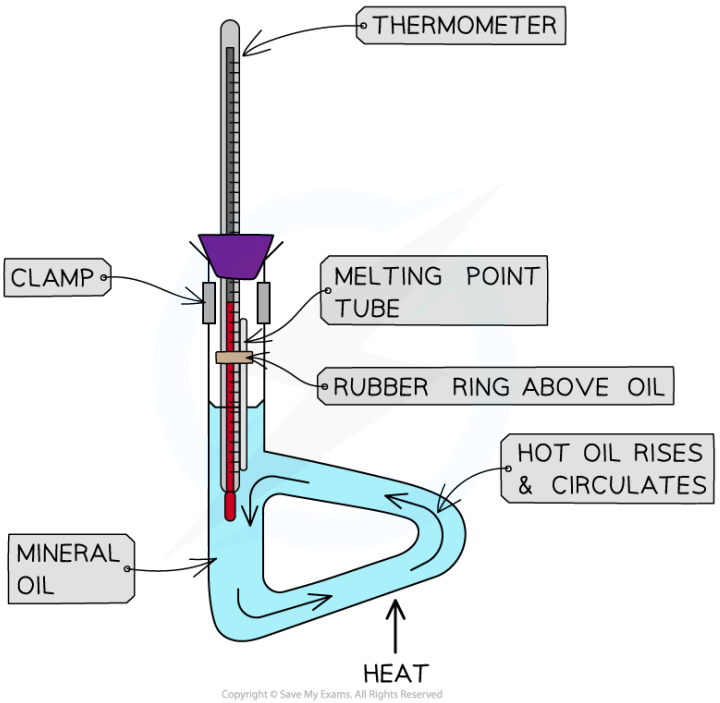
Melting & Boiling Temperature Determination

Melting point determination

- The melting point of a solid is indicative of its purity and identity
- A melting point can be matched to a known substance as a means of identification or confirmation of a desired product
- The proximity of a melting point to the actual data book value can express purity
  - Impurities tend to lower the melting point of a solid
- The melting point range also reveals the degree of purity
  - Pure substances have sharp well defined melting points
  - Impure substances have a broad melting point range, i.e. a large difference between when the substance first melts until it completely melts
- The skills needed in performing a melting point test are largely dependent on the specific melting point apparatus you are using
- However, there are some common key skills:
  - Correctly preparing the melting point tubes
  - Heating the tubes very slowly
  - Repeating to get a range of measurements (three would be normal)
- The sample solid must be totally dry and finely powdered - this can be achieved by crushing it with the back of a spatula onto some filter paper or the back of a white tile (this absorbs any moisture)
- Use the first tube to find the approximate melting point range and then repeat using a much slower heating rate



Melting point test using an oil bath



Melting point test using a Thiele tube

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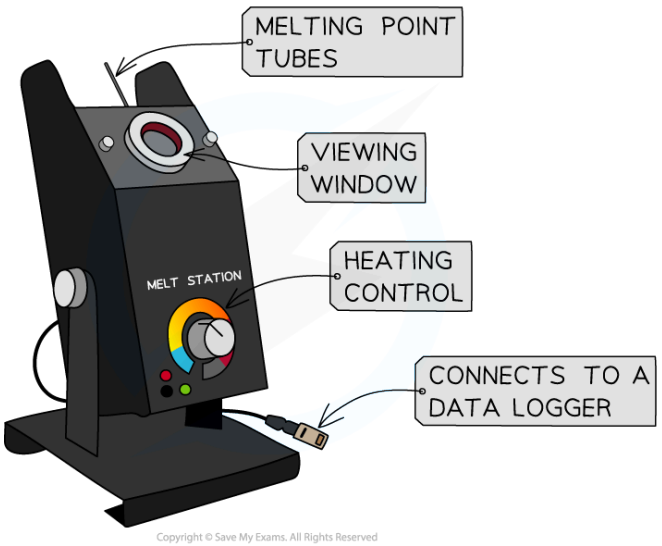

Melting point test using a melt station

Examiner Tips and Tricks

Always quote a melting point as a range + or - and reference a data book value if you have one.

Boiling point determination

- The boiling point of a liquid is indicative of its purity and identity
- Boiling point is determined by **distillation**
- The sample is gently heated until it boils and this temperature is recorded
  - This boiling point can then be compared against literature / database values
- If the sample contains impurities:
  - The boiling point may appear higher than the literature / database values
  - The sample may boil over a range of temperatures instead of at a single temperature