Organic Synthesis

Organic synthesis is about making organic compounds.
The synthesis of new materials is important in the production of new dyes, pharmaceuticals, polymers, catalysts and antiseptics.
Some of the medicines that have been developed include aspirin, paracetamol (analgesics), salbutamol (asthma treatment) and chloramphenicol (typhoid treatment).

Organic chemists design synthetic pathways to convert an available starting material into a desired target molecule (product). The pathways may involve several steps.

If the number of carbon atoms in the chain is:

- **increased** by one, consider:
  - a) halogenoalkane with KCN → substitutes with halogen.
  - b) carbonyl with HCN → forms hydroxynitrile.

- **increased** by **more** than one, consider: Friedel-Crafts reaction for aromatic substances.

- **decreased** by one, consider the iodoform reaction. **R-CO- CH_3 → R-$CO_2^-Na^+$**

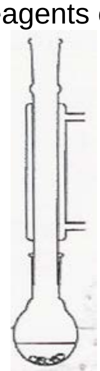
Safety in organic synthesis.

Organic compounds may be hazardous because of:

- Flammability - Use in small amounts avoids the undue risk of fire. Avoid naked flames. Use electrical heaters and water baths.
- Toxicity - The use of small amounts, fume cupboards, gloves and normal laboratory safety procedures reduces the risk of harmful amounts of a chemical entering the body by inhalation, ingestion or by skin absorption.
- Non-biodegradability - Some substances do not decay naturally in the environment. The hazard is reduced by using small quantities, and pouring waste solvents in a suitable container rather than pouring it down the sink.

Organic Practical techniques

Heating under reflux: is necessary when either the reactant has a low boiling temperature or the reaction is slow at room temperature. Enables reactions to be heated at their maximum temperature without the loss of any volatile reagents or products.



Key points – Condenser is vertical.
Do not put a bung in the condenser. (Pressure will build up!)
Water enters the condenser at the bottom.
Heat electrically – to avoid naked flames.

Purification Techniques

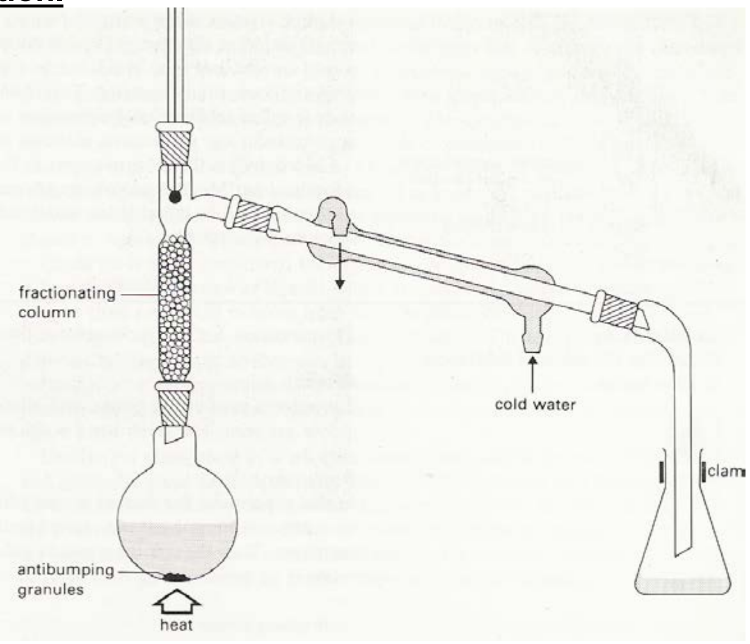
a) Recrystallisation.

This is used to purify an impure organic solid.

- Choose a suitable solvent. The solvent is suitable if the product is insoluble in the cold solvent but soluble in the hot solvent.
- Dissolve the impure sample in the minimum volume of hot solvent.
- Filter the solution hot under reduced pressure and collect the filtrate. This removes solid impurities which were insoluble in the solvent.
- Allow the filtrate to cool so that crystals of the product form.
- Again filter the mixture under reduced pressure. Soluble impurities are now removed.
- Wash the residue with a little cold solvent.

Dry the residue which should then be the pure product.

b) Fractional distillation.



This technique has a number of important applications:

- used to separate the components of liquid air; The air is compressed and cooled to liquefy it. Fractions are oxygen -183^oC, argon -186^oC, and nitrogen -196^oC.
- used to separate fractions from petroleum; The fractions are bitumen >350^oC, fuel oil 300 ^oC, diesel 240 ^oC, kerosene 200 ^oC, naptha 120 ^oC, petrol 40 ^oC, LPG <25 ^oC.
- used to produce whisky and other alcoholic drinks. Fractions are ethanol 78 ^oC and water 100 ^oC.

Determination of melting temperature.

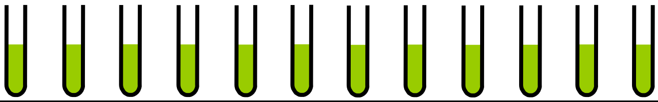
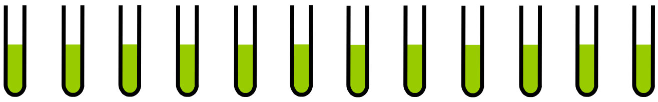
- A pure solid has a sharp melting point which can be found in a data book.
- If a solid product has been purified it can be identified from its melting point or if we know what it is we can tell if it is pure.
- Impurities lower the melting point.
  - The melting point apparatus is heated slowly until the solid is seen to melt.
  - The temperature is recorded.
  - After the sample is melted it is allowed to cool.
  - When the first crystals of solid appear in the sample the temperature is recorded again.

Modern Organic synthesis processes

One approach is to consider the purpose of the molecule, determine the structure required and then find a way of producing that molecule. Bacteria become resistant to antibiotics, the development of new antibiotics is important. The basic structure for the active component of an antibiotic molecule for blocking certain receptor sites in the vital enzymes of bacteria are known, and so it is possible to find a way of introducing this component into a new molecule to which the bacteria will not have resistance.

Often natural molecules perform a perfect function, yet cannot be produced on sufficient scale. A synthetic chemist can carry out analysis to determine the structure of such a molecule and determine a way of producing the substance on a larger scale.

Vast numbers of new molecules are produced by **combinatorial chemistry.**
By this process, large numbers of reactions are carried out on an almost haphazard way.
For example it is known that amines react with acyl chlorides. Mixing of various amines and acyl chlorides can then be carried out controlled by computer

Amine 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 are mixed with acyl chloride A	
Amine 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12 are mixed with acyl chloride B	

This process would be carried out for 8 acyl chlorides. This process would yield 96 new compounds all made automatically. These would then be tested to see if they are of medical or other use. By this procedure, many thousands of new compounds can be produced in a day.

Another way of carrying out combinatorial chemistry is the use of polymers.
When a given substance is treated in a number of steps, traditionally after each step the product would need to be separated and purified. Bearing in mind that each step will involve loss of material, the final product will probably have a low yield. In a new technique, the molecules of the starting material are attached to insoluble polymer beads. They can then be treated with the various chemicals, after each stage impurities can just be washed away while the molecules stay fixed to the polymer. When all the processing has been carried out, the new substance can be detached from the polymer again giving a high yield.

Organic Analysis

Analysis is a key tool for organic synthesis. On a basic level this analysis has included:

- Formula mass determination
- Quantitative analysis
- Combustion analysis
- Chemical tests to identify functional groups present

More sophisticated methods, using sensitive instrumentation are vital to modern organic synthesis. Such methods include:

- Various types of chromatography
- Mass spectrometry
- Infra red spectrometry
- Nuclear magnetic resonance spectrometry

It is important that analytical methods are very sensitive in order to

- Successfully analyse products that may be in low concentration
- Provide information on the purity of the synthetic product
- Identification of impurities, especially those that may be toxic at low concentration

Information about the presence of impurities is particularly important as any process can be customised in terms of temperature, pressure, catalyst or solvent in order to maximise the yield of desired product and minimise the production of by-products and impurities.

Synthesis problems

In a synthesis problem it will be necessary to describe how a particular compound can be made from a given starting material.

Reagents and reactions conditions will need to be given, based on reactions looked at in the specification.

Purification procedures will need to be described, these include the following:

- Washing with appropriate solvents.
- Solvent extraction (in a separating funnel).
- Recrystallisation (from a suitable solvent).
- Drying (with a suitable drying agent e.g. anhydrous magnesium sulphate)
- Distillation.
- Steam distillation (if the product is temperature sensitive and water soluble).
- Determination of melting point.
- Determination of boiling point.