Unit 5.4 Organic chemistry – arenes, nitrogen compounds and synthesis

1 Arenes: benzene

5.4.1a use thermochemical, x-ray diffraction and infrared data as evidence for the structure and stability of the benzene ring

**Benzene structure**

Benzene can be represented as C₆H₆ or \( \text{\textcircled{C}} \). 

Evidence for the structure of benzene comes from x-ray diffraction. A pattern like the one above can be processed to indicate areas of high electron density in a molecule. See below for p-methoxybenzoic acid, which contains a benzene ring.
Task 5.4.1(a)(i).1 Draw fully displayed structural formulae for cyclohexane \( \text{C}_6\text{H}_{12} \), cyclohexene \( \text{C}_6\text{H}_{10} \), and benzene \( \text{C}_6\text{H}_6 \). Label sigma and pi bonds between carbon atoms.

IR spectra indicate that benzene is different from hexane and hexene.

![IR spectra graph]

Story 5.4.1(a)(i) A Dream about Benzene

Benzene is more thermodynamically stable than expected if it contained 3 C-C single bonds and 3 C-C double bonds. All C-C bonds are the same.
**Task 5.4.1(a)(i).2**
The enthalpy of hydrogenation of cyclohexene is given below:
\[ \text{C}_6\text{H}_{10} + \text{H}_2 \rightarrow \text{C}_6\text{H}_{12} \quad ; \quad \Delta H = \text{-120kJmol}^{-1} \]
What is the enthalpy of hydrogenation of benzene if it contains 3 C=C double bonds?

The experimental value for the enthalpy of hydrogenation of benzene is given below.
\[ \text{C}_6\text{H}_6 + 3\text{H}_2 \rightarrow \text{C}_6\text{H}_{12} \quad ; \quad \Delta H = \text{-208kJmol}^{-1} \]
Explain why the calculated value and the experimental values are not the same.

Each pair of carbon atoms form a normal covalent bond. This leaves 1 electron left over for each C atom. These 6 electrons are delocalised across all C atoms.

**5.4.1b describe the following reactions of benzene, limited to:**

**5.4.1b i describe combustion of benzene to form a smoky flame**
\[ \text{C}_6\text{H}_6 + 7.5\text{O}_2 \rightarrow 6\text{CO}_2 + 3\text{H}_2\text{O} \]
Incomplete combustion gives carbon (soot) as product.

**5.4.1b ii describe treatment of benzene with bromine**
Bromination: Conditions: (dry) Anhydrous \( \text{AlCl}_3 \)
\[ \text{C}_6\text{H}_6(l) + \text{Br}_2(l) \rightarrow \text{C}_6\text{H}_5\text{Br}(l) + \text{HBr}(g) \]
bromine bromobenzene
Conditions: UV light
\[ \text{C}_6\text{H}_6(l) + 6\text{Br}_2(l) \rightarrow \text{C}_6\text{Br}_6(l) + 6\text{HBr}(g) \]
bromine 1,2,3,4,5,6-hexabromozenzene

**Task 5.4.1b(ii).3** Classify each reaction as an addition or substitution reaction.
**Task 5.4.1b(ii).4** Draw fully displayed structural formulae for each of the products.
**Task 5.4.1b(ii).5** Suggest safety precautions for each reactions.
**Task 5.4.1b(ii).6** Draw suitable apparatus for these reactions.
5.4.1b iii describe benzene reaction with concentrated nitric and sulfuric acids
Benzene can be nitrated if it is boiled under reflux at 50°C with concentrated nitric and sulphuric acids (as a catalyst). This is called nitration.

\[ C_6H_6(l) + HNO_3(l) \rightarrow C_6H_5NO_2(l) + H_2O(l) \]

benzene nitrobenzene

5.4.1b iv describe benzene reaction with fuming sulfuric acid
Fuming sulfuric acid contains extra sulphur trioxide. This sulphonation reaction takes place at room temperature.

\[ C_6H_6 + SO_3 \rightarrow C_6H_5SO_3H \]

Benzene sulphonic acid

5.4.1b v halogenoalkanes and acyl chlorides with aluminium chloride as catalyst (Friedel-Crafts reaction)
Alkylation: Conditions: (dry) Anhydrous AlCl₃

\[ C_6H_6(l) + C_2H_5Cl(l) \rightarrow C_6H_5C_2H_4(l) + HCl(g) \]

chloroethane ethylbenzene

Acylation: Conditions: (dry) Anhydrous AlCl₃

\[ C_6H_6(l) + CH_3COCl(l) \rightarrow C_6H_5COCH_3(l) + HCl(g) \]

acid chloride phenylethanone

5.4.1b vi addition reactions with hydrogen
This reaction takes place at 150°C in the presence of finely divided nickel as catalyst.

\[ C_6H_6 + 3H_2 \rightarrow C_6H_{12} \]

cyclohexane

Task 5.4.1bvi Write equations for the reactions with hydrogen for phenol, chlorobenzene and methylbenzene.

5.4.1c describe the mechanism of the electrophilic substitution reactions of benzene in halogenation, nitration and Friedel-Crafts reactions including the formation of the electrophile

5.4.1c Heterolytic, electrophilic substitution (benzene)
Electrophilic substitution is possible in benzene rings. In this type of substitution two of the delocalised \([\pi]\) electrons on the benzene ring are
donated to the electrophile. An unstable $[\pi]$ complex containing both an electrophile and a leaving group is formed as an intermediate. Nitration is carried out under reflux at 50°C using a nitrating mixture. This contains equal amounts of concentrated nitric acid and sulphuric acid. The two acids react to generate the nitryl cation $\text{NO}_2^+$ or nitronium ion. This is the electrophile.

\[
\text{HNO}_3 + \text{H}_2\text{SO}_4 \rightarrow \text{H}_2\text{NO}_3^+ + \text{HSO}_4^-
\]

\[
\text{H}_2\text{NO}_3^+ \rightarrow \text{NO}_2^+ + \text{H}_2\text{O}
\]

\[
\text{HNO}_3 + \text{H}_2\text{SO}_4 \rightarrow \text{NO}_2^+ + \text{H}_2\text{O} + \text{HSO}_4^-
\]

\[\text{step 1}\]

\[\text{step 2}\]

*see animation of heterolytic, electrophilic substitution*
The reaction with bromine also follows this mechanism. Aluminium chloride is used as a catalyst which helps form the electrophile.

\[ \text{Br-Br + AlCl}_3 \rightarrow \text{Br}^{\Delta+} - \text{Br} - \text{AlCl}_3^{\Delta-} \]

Alkylation (Friedel-Crafts reaction) follows the same mechanism. Halogenoalkanes are weak electrophiles because their polar bond. e.g. \( \text{CH}_3^{\Delta+} - \text{Br}^{\Delta-} \). The catalyst AlCl\(_3\) makes the halogenoalkane a better electrophile.

\[ \text{CH}_3\text{-Br + AlCl}_3 \rightarrow \Delta^{+}\text{CH}_3\text{-Br} - \text{AlCl}_3^{\Delta-} \]

Acylation also follows the same mechanism. The electrophile is again improved by AlCl\(_3\).
Task 5.4.1c.1 Write balanced chemical equations for the mechanisms shown above.

Task 5.3.1c.2 Describe a mechanism for the formation of ethylbenzene.

Task 5.3.1c.3 Iron is sometimes added to bromine to catalyse the bromination of benzene. Explain how this works.

5.4.1d Practicals with electrophilic substitution

5.4.1d carry out the reactions in 5.4.1b where appropriate (using methylbenzene or methoxybenzene)

5.4.1e Reactions of phenol

carry out the reaction of phenol with bromine water and dilute nitric acid and use these results to illustrate the activation of the benzene ring.

5.4 (a) (iii) Reactions of phenol

Phenol with sodium hydroxide

Phenol dissolves in aqueous sodium hydroxide because phenol behaves as an acid and gives up its proton to the hydroxide ion which is a base. A soluble ionic product is formed.

\[ \text{C}_6\text{H}_5\text{OH(aq)} + \text{NaOH(aq)} \rightarrow \text{C}_6\text{H}_5\text{O}^-\text{Na}^+(aq) + \text{H}_2\text{O(l)} \]

Phenol with bromine

This is a substitution reaction in which an antiseptic smelling compound is formed. Note 2,4,6-trichlorophenol is called TCP. OH is electron releasing so activates the ring and speeds up the electrophilic substitution.
C₆H₅OH(aq) + 3Br₂(aq) ----> C₆H₂Br₃OH(aq) + 3HBr(aq)
2,4,6-tribromophenol

**Phenol with dilute nitric acid**
2,4,6-trinitrophenol is formed as a white precipitate (may appear yellow/brown) in this reaction. No conc is needed as the ring is activated by the electron releasing hydroxyl group.
C₆H₅OH + 3HNO₃ ---> C₆H₂(NO₂)₃OH + 3H₂O

**Phenol with ethanoyl chloride**
This reaction forms an ester. Conditions: dry
C₆H₅OH + CH₃COCl ---> CH₃COOC₆H₅ + HCl
phenol ethanoyl chloride phenylethanoate

**Task 5.3(a)(iii).1** Draw fully displayed structural formulae for the products above.
**Task 5.3(a)(iii).2** Describe how KOH reacts with phenol.
**Task 5.3(a)(iii).3** Describe how 2,4,6-trichlorophenol (TCP) can be prepared.

### 2 Organic nitrogen compounds: amines, amides, amino acids and proteins

**5.4.2a amines amides and amino acids**
give examples of:
- i molecules that contain amine and amide functional groups
- ii amino acids
All of these compounds contain an amino group but its properties are modified by its environment.

**amines**
Methyamine CH₃NH₂, ethylamine CH₃CH₂NH₂, phenylamine C₆H₅NH₂

**amides**
Ethanamide CH₃CONH₂, propanamide CH₃CH₂CONH₂

**aminoacids**
Aminoethanoic acid (glycine) NH₂CH₂COOH,
2-aminopropanoic acid (alanine) CH₃CH(NH₂)COOH

**Task 5.4.2a** Draw fully displayed structures for one example of each amino compound and name one more example of each.

**5.4.2b Reactions of amines**
describe and carry out, where appropriate (using butylamine and phenylamine), reactions to investigate the typical behaviour of primary amines. This will be limited to:
- i characteristic smell
- ii miscibility with water as a result of hydrogen bonding
and the alkaline nature of the resulting solution

iii formation of salts

iv complex ion formation with copper(II) ions

v treatment with ethanoyl chloride and halogenoalkanes, eg making paracetamol

smell
Amines all have characteristic fishy smells.

Solubility
The lower amines are quite soluble forming alkaline solutions. Each amine can form hydrogen bonds with water molecules with the lone pair on the nitrogen being responsible. Phenylamine has a low solubility. Its lone pair is delocalised around the ring so hydrogen bonding is less possible.

with hydrogen ions
Methylamine vapour reacts with conc HCl(aq) to form white crystalline solid (smoke), methylammonium chloride, \( CH_3NH_2 (g) + HCl(g) \rightarrow CH_3NH_3^+ Cl^- (s) \)

The solubility of aromatic primary amines in increased greatly by the addition of acid.

\[ C_6H_5NH_2(l) + H^+(aq) \rightarrow C_6H_5NH_3^+(aq) \]

with copper(II) ions
Solutions of amines are basic so copper ions can form hydroxide precipitates, \( Cu(OH)_2(s) \). This is better written \( Cu(H_2O)_4(OH)_2(s) \). In the presence of ammonia \( NH_3 \) molecules can replace hydroxide ions and some water molecules to give a soluble complex ion \( [Cu(NH_3)_6]^{2+}(aq) \). In the presence of an amine these molecules can surround copper in a complex ion e.g.

\[ [Cu(CH_3NH_2)_6]^{2+}(aq) \]

with ethanoyl chloride
\( CH_3COCl + 2RNH_2 \rightarrow CH_3CONHR_2 + RNH_2Cl \)

an amide

making paracetomol
This is a four step process:
1. Phenol is nitrated with dilute nitric acid which forms 2-nitrophenol and 4-nitrophenol.
2. Fractional distillation separates the 4-nitrophenol
3. 4-nitrophenol is reduced to 4-aminophenol with \( NaBH_4(aq) \)
4. A reaction with ethanoic anhydride gives paracetomol
Amines with halogenoalkanes

Halogenoalkanes react with concentrated ammonia under pressure in a sealed tube to form amines. These amines undergo further reaction with halogenoalkane to make a series of new amines.

\[
\begin{align*}
\text{CH}_3\text{Cl} + \text{NH}_3 & \rightarrow \text{CH}_3\text{NH}_2 + \text{HCl} \\
\text{CH}_3\text{Cl} + \text{CH}_3\text{NH}_2 & \rightarrow (\text{CH}_3)_2\text{NH} + \text{HCl} \\
\text{CH}_3\text{Cl} + (\text{CH}_3)_2\text{NH} & \rightarrow (\text{CH}_3)_3\text{N} + \text{HCl} \\
\text{CH}_3\text{Cl} + (\text{CH}_3)_3\text{N} & \rightarrow (\text{CH}_3)_4\text{N}^+\text{Cl}^- \\
\end{align*}
\]

**Task 5.4.2b** How does bromoethane form amines?

### 5.4.2c The reduction of nitrobenzene

5.4.2c describe the reduction of aromatic nitro-compounds using tin and concentrated hydrochloric acid to form amines.

The acid used forms hydrogen, itself a reducing agent.

\[
\begin{align*}
2\text{HCl} + \text{Sn} & \rightarrow \text{Sn}^{2+} + 2\text{Cl}^- + \text{H}_2 \\
\text{C}_6\text{H}_5\text{NO}_2 + 3\text{H}_2 & \rightarrow \text{C}_6\text{H}_5\text{NH}_2 + 2\text{H}_2\text{O} \\
\end{align*}
\]

Nitrobenzene \(\rightarrow\) aminobenzene (phenylamine)

Tin (II) ions are also a good reducing agent.

\[
\begin{align*}
\text{Sn}^{2+} & \rightarrow \text{Sn}^{4+} + 2\text{e}^- \\
\text{C}_6\text{H}_5\text{NO}_2 + 6\text{H}^+ + 6\text{e}^- & \rightarrow \text{C}_6\text{H}_5\text{NH}_2 + 2\text{H}_2\text{O} \\
\end{align*}
\]

1. Heat nitrobenzene, conc. HCl and tin under reflux.
2. Cool flask and add excess aqueous NaOH.
3. Steam distillation to give a cloudy water phenylamine distillate
4. Add saturated sodium chloride solution in separating funnel to salt out the phenylamine
5. Add ethoxyethane, shake and run off the aqueous layer
6. Add more ethoxyethane to the aqueous layer, shake and run off again
7. Repeat this solvent extraction and finally add all of the ethoxyethane fractions together.
8. Add solid potassium hydroxide as a drying agent. 
9. Distill the mixture and collect the distillate between 180 and 185°C.
5.4.2d Aromatic amines with nitrous acid
5.4.2d describe and carry out, where appropriate, the reaction of aromatic amines with nitrous acid to form benzenediazonium ions followed by a coupling reaction with phenol to form a dye.

HNO₂ is made in situ from HCl and NaNO₂

\[ C_6H_5NH_2 + HNO₂ + HCl \rightarrow 2H_2O + C_6H_5N⁺ \equiv N + Cl⁻ \]

diazonium ion

Much below 5°C and the mixture may freeze. Much above this temperature and the diazonium ion decomposes to liberate nitrogen.

Diazotized reaction

\[ C_6H_5N⁺ \equiv N + C_6H₅OH \rightarrow C_6H₅N = NC₆H₄-OH + H⁺ \]

a yellow azo dye

(4-hydroxyphenyl)azobenzene

\[ C_6H₅N⁺ \equiv N + C_6H₅NH₂ \rightarrow C_6H₅N = NC₆H₄-NH₂ + H⁺ \]

an orange azo dye

(4-aminophenyl)azobenzene

Task 5.4.2(d).1 Draw fully displayed structural formulae for the azo dyes above.

Task 5.4.2(d).2 Write an equation to show diazonium chloride reacting with C₆H₅N(CH₃)₂

5.4.2e Preparation of amides
5.4.2e recall the synthesis of amides using acyl chlorides

\[ CH₃COCl + 2CH₃NH₂ \rightarrow CH₃CONH CH₃ + CH₃NH₃Cl \]

N-methylethanamide

an amide

Acyl chlorides are very reactive and so room temperature is suitable. Amides are often solids so recrystallization is used in the purification process.
**Task 5.4.2e** Write equations for the preparation of N-phenylethanamide and N-ethylpropanamide.

### 5.4.2f Condensation and addition polymerization

5.4.2f describe:

i condensation polymerization for the formation of polyesters such as terylene and polyamides such as nylon and Kevlar

ii addition polymerization including poly(propenamide) and poly(ethenol)

#### The formation of polyesters

Molecules with two carboxyl groups can join to molecules with two hydroxyl groups to form polyesters. These polyesters are important for artificial fibres. A small molecule (water, in this case) is lost for each ester bond formed. This is called condensation polymerization.

\[
\text{monomer 1,6-hexanediioic acid} \quad \text{monomer hexan-1,6-diol} \\
- (\text{OCCH}_2(\text{CH}_2)_2\text{COOCH}_2(\text{CH}_2)_4\text{CH}_2\text{O})_n + n\text{H}_2\text{O} \\
\text{polyester polyhexylhexanoate}
\]

#### Task 5.4.2f.1 Redraw the full structures of the alcohols, acids and esters above showing all bonds.

#### The formation of polyamides

**Kevlar body armour - bullet proof vest**

Kevlar is a polyamide used in bullet proof vests.

\[-\{\text{COC}_6\text{H}_4\text{CONHC}_6\text{H}_4\text{NH}\}_n - \text{etc}\]
hexanedioic acid
HOOC-(CH₂)₄-COOH
1,6-diaminohexane
H₂N-(CH₂)₆-NH₂

<table>
<thead>
<tr>
<th></th>
<th>polyamide (nylon-6.6)</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>(-CO-(CH₂)₄-CO-</td>
</tr>
<tr>
<td></td>
<td>HN-(CH₂)₆-NH-)ₙ</td>
</tr>
</tbody>
</table>

In the laboratory the hexane-1,6-dioyl chloride can be used to make nylon as it reacts at a quicker more convenient rate.

Task 5.4.2f.2 Draw the full structural formulae for the reactants and products in the table above.

Addition polymers

**poly(propenamide)**

\[
\begin{array}{c}
\text{H}_2\text{C}=\text{CH} \\
\text{C}=\text{O} \\
n \text{NH}_2
\end{array} \rightarrow \left[ \begin{array}{c}
\text{H}_2\text{C}-\text{CH}- \\
\text{C}=\text{O} \\
\text{NH}_2
\end{array} \right]_n
\]

2-propenamide

polypropenamide

Cross linked chains can absorb water forming a soft substance.

Polyethenol

This needs a two step process.

**Step 1:** Ethenyl ethanoate polymerises to form polyethenyl ethanoate

\[ n\text{CH}_2=\text{CHO}_2\text{CH}_3 \rightarrow \left[ \text{-CH}_2-\text{CHO}_2\text{CH}_3-\text{CH}_2-\text{CHO}_2\text{CH}_3- \right]_n \]

**Step 2:** This polymer reacts with methanol in an ester exchange reaction to form polyethenol and methyl ethanoate.

\[ \left[ \text{-CH}_2-\text{CHO}_2\text{CH}_3-\text{CH}_2-\text{CHO}_2\text{CH}_3- \right]_n + n\text{CH}_3\text{OH} \rightarrow \left[ \text{-CH}_2-\text{CH(OH)}-\text{CH}_2-\text{CH(OH)}- \right]_n + n\text{CH}_3\text{COCH}_3 \]

5.4.2g Structural formulae of polymers

5.4.2g draw the structural formulae of the repeat units of the polymers in 5.4.2f

See 5.4.2f

5.4.2h Properties of polymers

5.4.2h comment on the physical properties of polyamides and the solubility in water of the addition polymer poly(ethenol) in terms of hydrogen bonding, eg soluble laundry bags or liquid detergent capsules (liquitabs)

**Nylon**

<table>
<thead>
<tr>
<th>property</th>
<th>use</th>
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<tbody>
<tr>
<td>high tensile strength</td>
<td>ropes, stockings, parachutes</td>
</tr>
<tr>
<td>Property</td>
<td>Image</td>
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<tr>
<td>--------------------------------</td>
<td>-------------</td>
</tr>
<tr>
<td>Low melting point</td>
<td><img src="image1.png" alt="Skirt Image" /></td>
</tr>
<tr>
<td>Permanent pleating</td>
<td><img src="image2.png" alt="Shirt Image" /></td>
</tr>
<tr>
<td>Low affinity for water</td>
<td><img src="image3.png" alt="Skirt Image" /></td>
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<tr>
<td>Easy drying garments</td>
<td><img src="image4.png" alt="Conveyor Belt Image" /></td>
</tr>
<tr>
<td>Resistance to abrasion</td>
<td><img src="image5.png" alt="Resistance Image" /></td>
</tr>
</tbody>
</table>

**Polyethenol**

**Hot and Cold Water Soluble Laundry Bags**

These soluble laundry bags are perfect for hospitals and nursing homes minimising the contact between staff and infected laundry. The formation of hydrogen bonds between polyethenol molecules and water enable solubility.
Persil colour care tablets contain detergent in a capsule which dissolves when water enters the washing machine. The capsules are made of polyethenol which dissolves due to hydrogen bonds formed between the polymer molecules and the water molecules.

5.4.2i Amino acids
5.4.2i describe and carry out, where appropriate, experiments to investigate the characteristic behaviour of amino acids.
This is limited to:
  i acidity and basicity and the formation of zwitterions
  ii separation and identification by chromatography
  iii effect of aqueous solutions on plane-polarised monochromatic light
  iv formation of peptide groups in proteins by condensation polymerization
  v reaction with ninhydrin.
See Core pract 29.

Acidity and basicity
An amino acid like aminoethanoic acid (glycine) NH$_2$CH$_2$COOH, can act as an acid or a base.

\[
\text{NH}_2\text{CH}_2\text{COOH}(aq) + \text{H}^+(aq) \rightarrow \text{NH}_3^+\text{CH}_2\text{COOH} \\
\text{NH}_2\text{CH}_2\text{COOH}(aq) + \text{OH}^-(aq) \rightarrow \text{NH}_2\text{CH}_2\text{COO}^-(aq) + \text{H}_2\text{O}(l)
\]

In solution the acidic hydrogen of the amino acid is lost and can attach itself to the nitrogen atom in the same molecule. The result is called a zwitterion.

\[
\text{CH}_3\text{CH}_2\text{CHCOO}^- \\
\text{NH}_3^+
\]

Both the zwitterion and the original amino acid structure can react with acids or bases so can act as buffers. A buffer maintains the pH of a solution when small amounts of acid or alkali are added.

Task 5.4.2i.1 Draw full displayed structural formulae for the substances and
ions shown above.
Write equations to show how 2-aminopropanoic acid and the resulting
zwitterion react with small amounts of acid and alkali.

**Separation and Identification**
Amino acids can be separated and identified by chromatography. The
process needs a stationary phase (e.g. paper) and a mobile phase (e.g.
suitable solvent). The sample is dissolved in the mobile phase. Different
components have different solubilities and different levels of adsorption
so end their journey over the stationary phase in different places.
Ninhydrin is sprayed onto the dry chromatogram to show up the locations
of the aminoacids. The acids take on a specific colour. Comparison with
the distance moved by a standard pure aminoacid can be used to identify
the acids in the sample.

**Effect on plane-polarised light**
Most aminoacids have chiral centres and so exist in two optical isomers
(enantiomers). An enantiomer rotates the plane of polarised light. If
equal amounts of both isomers form (a racemic mixture) rotation in
both directions is equal and cancels out the observed effect.

CH\(_3\)CH\(_2\) *CHCOOH has a chiral centre * as the C atom shown is

\[
\begin{array}{c}
| \\
\text{NH}_2
\end{array}
\]

surrounded by 4 different groups. (CH\(_3\)CH\(_2\), H, NH\(_2\), COOH)

**Task 5.4.2i.2** State which of the following would have optical isomers and
why. Glycine H\(_2\)NCH\(_2\)COOH, L-alanine H\(_2\)NCH(CH\(_3\))COOH, L-glutamic
acid H\(_2\)NCH(CH\(_2\)CH\(_2\)COOH)COOH

The amino acids below link to for proteins.
Task 5.4.2i.3 Draw connected sequences of amino acids showing the peptide links.

5.4.3 Organic synthesis

5.4.3a importance of organic synthesis
give examples to illustrate the importance of organic synthesis in research for the production of useful products
5.4.3b Sensitive chemical analysis
explain why sensitive methods of chemical analysis are important when planning and monitoring organic syntheses
For a new synthetic molecule identify each functional group and the exact carbon chain.
Choose reaction steps to build the carbon skeleton and the correct functional groups.
After each step analyse (titration, IR, mass spect, NMR etc) the products to check the correct substance has been made and the yield. Alternative steps may be needed when side products are made or the yield is too low. Any toxic compounds formed must be identified and safety measures put in place. Optically active products must be made in the form of the correct enantiomer. Polarimetry is needed in analyse enantiomers.

Task 5.4.3b Suppose you must make 3-phenyl-2-propenal C₆H₅CHCHCHO. Identify the carbon skeleton and the functional groups. If benzene and BrCHCHCOOH react in the presence of iron bromide to make an intermediate state how the mass spectrum and the NMR spectrum would change from reactants to intermediate. State how the IR spectrum of the product would change from the intermediate to the final product.

5.4.3c Empirical molecular and structural formulae
C deduce the empirical formulae, molecular formulae and structural formulae from data drawn from combustion analysis, elemental percentage composition, characteristic reactions of functional groups, infrared spectra, mass spectra and nuclear magnetic resonance

Starter 5.4.3c What can you say about these substances CH₂, C₄H₈, CH₃CH₂CH=CH₂, CH₃CH=CH CH₃
Empirical formula is the simplest ratio of the number of atoms of each element in a molecule of a substance. The molecular formula shows the actual number of atoms of each element in a molecule of a substance. If the empirical formula of a substance is CₓHᵧ then the molecular formula is nCₓHᵧ if
n=relative molecular mass of the substance/relative molecular mass of CₓHᵧ.

What is the empirical formula and the molecular formula of a compound which contains 1.2g of carbon and 0.2g of hydrogen if the relative molecular mass of the compound is 42?

\[
\begin{align*}
\text{mass} & = 1.2 \text{g} & \text{hydrogen} & = 0.2 \text{g} \\
\text{amount} = \text{mass/molar mass} & = 1.2/12 = 0.1 \text{mol} & 0.2/1 = 0.2 \text{mol} \\
\text{ratio(divide by smallest)} & = 1 : 2 \\
\text{empirical formula} & = \text{CH₂} \\
\text{molecular formula} & = n\text{CH₂} \\
\text{n} & = \text{relative molecular mass of substance/relative molecular mass of } \text{CH₂} \\
\text{n} & = 42/14 = 3
\end{align*}
\]
Molecular formula = \( n\text{CH}_2 = 3 * \text{CH}_2 = \text{C}_3\text{H}_6 \)

**Task 5.4.3c.1**

For a compound RMM = 46, 1.2g C is found with 0.3g H in 2.3g of compound. The third element is oxygen. What is the empirical and molecular formula of the compound?

**Combustion analysis**

A hydrocarbon is burnt and the gases passed through conc. sulphuric acid to absorb water and then through calcium hydroxide to absorb carbon dioxide. The acid increased in mass from 50.0g to 53.6g and the calcium hydroxide increased from 50.0g to 54.4g. What was the empirical formula of the hydrocarbon?

Mass of water = 53.6g - 50.0g = 3.60g
Amount of water = mass water/molar mass water = 3.60g/18.0gmol\(^{-1}\) = 0.200mol
Amount H in 0.20 mol H\(_2\)O = 0.40mol
Mass CO\(_2\) = 54.4g - 50.0g = 4.4g
Amount CO\(_2\) = mass CO\(_2\)/molar mass CO\(_2\) = 4.4g/44gmol\(^{-1}\) = 0.1mol
Amount C in 0.1mol CO\(_2\) = 0.1mol
Ratio amount C : amount H = 0.1:0.4 = 1:4
Empirical formula of hydrocarbon = CH\(_4\)

**Task 5.4.3c.2** 0.0234g of an organic compound produced 0.0792g of carbon dioxide and 0.0162g of water. Calculate the empirical formula for this compound. (CH)

**Task 5.4.3c.3** Complete combustion of 0.206g of an organic compound yields 0.5666g of carbon dioxide and 0.4635g of water. Work out its empirical formula. (CH\(_4\))

**HW 5.4.3c** From the internet collect IR, mass and NMR spectra for 2 carbon compounds e.g. ethanol and give one identifying chemical test for each.

5.4.3d use knowledge of organic chemistry contained in this specifications to solve problems such as:
5.4.3d(i) Unfamiliar compounds
i predicting the properties of unfamiliar compounds containing one or more of the functional groups included in the specification, and explain these predictions
(a) aspirin

(b) paracetamol

(c) DDT

(d) TNT

(e) LSD

(f) pethidine

(g) phenolphthalein

(h) 2,4,5-T (herbicide)

(i) dioxin

(j) valium

(k) monosodium glutamate

Na⁺ O⁻

O−CH₂−CH−CO₂H

NH₂

[Answers on page 79 ]
5.4.3d(ii) Planning reactions schemes

Planning reaction schemes of up to four steps, recalling familiar reactions and using unfamiliar reactions given sufficient information.

- ethane $\rightarrow$ bromoethane $\rightarrow$ ethanol $\rightarrow$ ethanol $\rightarrow$ 2-hydroxypropanonitrile

1. Br$_2$, inert solvent, UV light
2. reflux with OH-(aq)
3. dil sulfuric acid, K$_2$Cr$_2$O$_7$, distil
4. HCN in situ from KCN and HCl

**Task 5.4.3d(ii)** Construct a network of reaction pathways and use it to construct some 2, 3 and 4 step pathways. Include:
- carbonyls (oxidation, reduction, addition of HCN, 2,4-DNP, Iodine in alkali)
- carboxylic acids (prep by hydrolysis of nitriles, reduction, neutralization, PCl$_5$, alcohols)
- acyl chlorides (water, alcohols, ammonia, amines)
- esters (acid hydrolysis, base hydrolysis, polymerization, transesterification)
- benzene (combustion, bromine, conc HNO$_3$/H$_2$SO$_4$, fuming H$_2$SO$_4$
- halogenoalkanes, acyl chlorides, hydrogen)
- phenol (bromine water, nitric acid, formation of paracetamol)
- butylamine (HCl, copper (II) ions, ethanoyl chloride, halogenoalkanes)
- nitrobenzene with tin and HCl, aminobenzene

http://www.docbrown.info/page06/WMtestsNotes/OrgSyn01mix.htm
RSC synthesis explorer
http://synthesisexplorer.rsc.org/

5.4.3d(iii) Practical procedures

Selecting suitable practical procedures for carrying out reactions involving compounds with functional groups included in the specification.

An old text with diagrams
http://files.rushim.ru/books/praktikum/Mann.pdf
Modern site with photos animation and video of A2 apparatus and techniques.
http://orgchem.colorado.edu/hndbksupport/ochemlabtech.html

**HW 5.4.3d(iii)** Draw flow diagram of apparatus for a preparation of your choice.

5.4.3d(iv) Hazards

Identifying appropriate control measures to reduce risk during a synthesis based upon data of hazards.

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Control measure</th>
</tr>
</thead>
<tbody>
<tr>
<td>flammable</td>
<td>No naked flame, electric heating</td>
</tr>
<tr>
<td>Non-biodegradable</td>
<td>No discharge to drain, waste solvent bottle</td>
</tr>
<tr>
<td>Toxic-inhalation</td>
<td>Fume cupboard</td>
</tr>
<tr>
<td>Toxic-ingestion</td>
<td>Standard lab ban on food and drink</td>
</tr>
<tr>
<td>Toxic-skin absorption</td>
<td>Wear polymer gloves</td>
</tr>
<tr>
<td>Corrosive</td>
<td>Protect skin, safety glasses</td>
</tr>
</tbody>
</table>

5.4.3d(v) Understanding why, in the synthesis of stereo-specific drugs, it is important to understand the mechanism of the reaction and how this can help to plan the synthesis.
Aspartame below is sweet only in the L enantiomer as this fits the sweetness receptors on the tongue. The R enantiomer is not sweet.

Salbutamol in ventolin inhalers is a racemic mixture with only 50% of dose effective. The single enantiomer levalbuterol has 100% of dose effective.

*Methadone – the powerful* morphine-like analgesic
Results show *no stereospecificity* for *methadone although it is a chiral molecule*
Task 5.4.3d(v) Redraw methadone and Aspartame showing the two enantiomers.

5.4.3e Combinatorial chemistry
5.4.3e explain why the pharmaceutical industry has adopted combinatorial chemistry in drug research, including passing reactants over reagents on polymer supports.
Show video at H:\science\KS4\21stC\C6
HW 5.4.3e Research development of recent pharmaceutical product.

5.4.3f Compound preparation
5.4.3f describe and carry out, where appropriate, the preparation of a compound, eg cholesteryl benzoate (a liquid crystal) and of methyl-3-nitrobenzoate, requiring some of the following techniques:
i refluxing
ii purification by washing, eg with water and sodium carbonate solution
iii solvent extraction
iv recrystallization
v drying
vi distillation
vii steam distillation
viii melting temperature determination
ix boiling temperature determination.