Chem Factsheet

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# Organic Synthesis Routes

## This Chemistry Factsheet:

- Provides summary schematics detailing the reactions of aliphatic and aromatic compounds.
- Illustrates techniques for answering synthesis questions.
- Summarises chemical tests used in organic chemistry.

## Introduction

This Factsheet covers the organic reactions and chemical tests involving different organic functional groups. Different examination specifications may expect students to recall specific examples, reagents and conditions. For example: using acidified potassium dichromate(VI) or potassium manganate(VII) to oxidise alcohols; and sodium tetrahydroborate or lithium aluminium tetrahydride to reduce aldehydes and ketones. For this reason it is important to confirm with the specification and supporting textbooks the details expected in the examination.

This Factsheet includes a sequence of diagrams showing some of the important reactions of key functional groups. These are useful for determining means for devising synthetic routes. The reaction schematics are general to the family of compounds described, but do contain specific examples, such as using propene to describe the typical reactions of the alkenes (**Figure 2**).

When determining a simple organic reaction the following components must be identified:

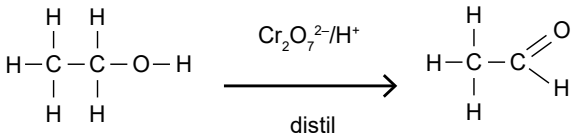
- What functional group(s) are present in the starting molecule?
- What functional group(s) are present in the product (target molecule)?
- What reagents and conditions are required?
- Are there any limitations (e.g. multiple substitutions, isomeric products)?

## One-Step Synthesis

For a simple one-step synthesis, the single-step reaction is identified using the appropriate functional group schematic.

## Example 1: The preparation of ethanal from ethanol.

Ethanol is a primary alcohol (**Figure 4a**) and can be oxidised to form the aldehyde (ethanal) using an appropriate oxidising agent, e.g. acidified sodium dichromate(VI). The conditions for this reaction are important as refluxing with excess oxidising agent leads to the formation of carboxylic acid. To ensure the aldehyde to formed, the reaction is gently heated, and the product distilled on formation.



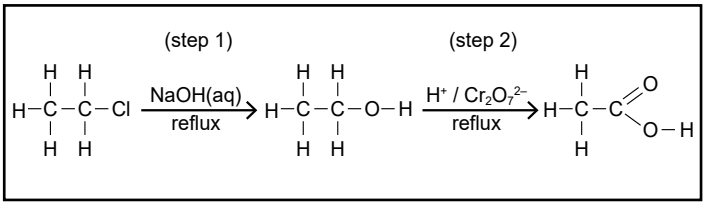

ethanol (primary alcohol) ethanal (aldehyde)

## Multi-Step Synthesis

Organic synthesis examination questions typically involve two or more separate reaction steps to form the desired product. This will require identifying the most appropriate synthesis route, possibly requiring combining functional group reaction schematics.

## Example 2: The preparation of ethanoic acid from chloroethane.

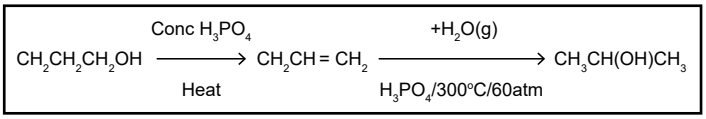
How can ethanoic acid be produced from chloroethane? One strategy is to identify a functional group that undergoes a simple reaction to produce the carboxylic acid product, e.g. a primary alcohol. Then identify a functional group that will react to provide the primary alcohol intermediate. Reviewing the reactions of the halogenoalkanes (**Figure 3**) and primary alcohols (**Figure 4a**) identifies a possible two-step synthesis.




This is actually a three-step reaction as the primary alcohol is initially oxidised to form the aldehyde. However, as there are strong oxidation conditions it is acceptable to describe the complete oxidation of the alcohol in the equation.

## Example 3: The preparation of propan-2-ol from propan-1-ol.

This appears relatively simple; to move the hydroxyl group along the chain. Completing an acid catalysed dehydration and then reacting the alkene intermediate with steam produces a mixture of propan-1-ol and propan-2-ol. The products can then be separated by fractional distillation, but the atom economy is low.

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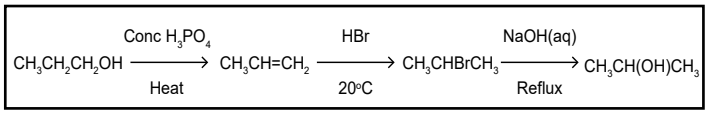
An alternative involving halogenoalkanes would preferentially select propan-2-ol due to the greater stability of the secondary carbocation intermediate. The major product is 2-bromopropane. Whilst the separation of the final product is required, this synthesis sequence has an improved atom economy.



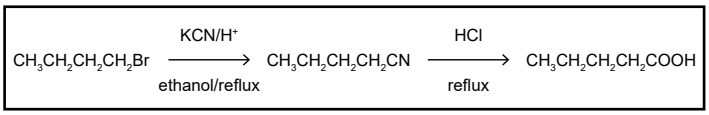

> ***Key Point:***
>
> *Markovnikov's rule states that the acid hydrogen bonds with carbon having the greater number of existing hydrogen substituents; the halide therefore bonds to carbon with more alkyl substituents.*

## Extending The Carbon-Chain

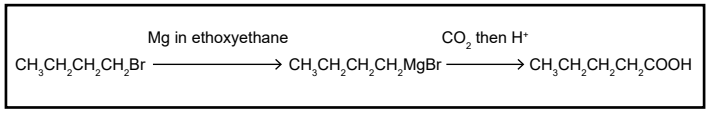
A synthesis may require extending the length of the carbon-chain. There are several possible reactions add a carbon to the original molecule. Selecting an appropriate method depends on the target product.

### Example 4: The preparation of pentanoic acid made from 1-bromobutane

The length of the carbon-chain needs to be increased from 4 to 5 carbons. One means for increasing the carbon-chain is to react the halogenoalkane with potassium cyanide, the cyanide ion provides the additional carbon. This forms the nitrile intermediate (**Figure 11a**). The nitrile is then hydrolysed with dilute hydrochloric acid to form the carboxyl group (**Figure 7**).




An alternative means for extending the carbon-chain is via a Grignard reagent. Grignard reagents are made in situ, typically by adding magnesium fillings to the required halogenoalkane in ether. The Grignard intermediate is then treated with carbon dioxide and the solution acidified (**Figure 11a**).




## Synthesis Of Aromatic Compounds

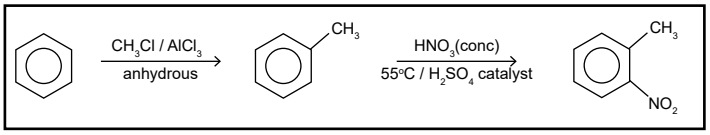
The synthesis of aromatic compounds plays an important role in the chemical industry and in the commercial production of a wide range of products, including pharmaceuticals, polymers, dyes and fragrances. The simplest aromatic molecule is benzene, which can undergo different reactions in order to present different side-groups (**Figure 8**). The coupling of aromatic molecules with aliphatic groups involves alkylation or acylation (via the Friedel-Craft reaction).

The initial substituted group will affect the relative positions of subsequent substitutions.

- Electron donating groups activate the π-electron ring system and direct substitution at the 2–, 4–, and 6– positions. Activating groups include –OH , $–NH_2$, $–CH_3$ and $–O–CH_3$ groups.
- Electron withdrawing groups deactivate the π-electron ring system and direct substitution at the 3– and 5– positions. Deactivating groups include $–NO_2$, –CO–R, $–SO_3H$ and $–CCl_3$.
- Halogens weakly deactivate the ring, but direct substitution at the 2–, 4–, and 6– positions.

### Example 5: The preparation of 2–nitromethylbenzene from benzene

This involves two substitution groups on benzene. The respective reactions are straightforward (**Figure 8**), but in order to obtained the correctly substituted product it is necessary to add the methyl group first, which will direct the subsequent nitro-group substitution at position 2– (and 6–). Substitution will also occur at 4–, requiring fractional distillation to separate the products.




$–NO_2$ is 3- and 5- directing, meaning if this is added first the methyl group will be substituted at position 3– (and 5–), forming 3–nitromethylbenzene.

## Testing For Functional Groups

The success of a synthesis may be determined by testing the product obtained. Simple chemical tests can be applied to identify functional groups present. This can be used to confirm if the reaction mixture contains unreacted reagents or unwanted products. For example testing for an aldehyde following an oxidation of an alcohol, or for an alcohol after hydrolysing a halogenoalkane. Examination questions will often present observed evidence of chemical tests to identify different functional groups (**Figures 12a, 12b and 12c**).

## Aliphatic Reaction Schematics

**Figure 1** Reactions of alkanes

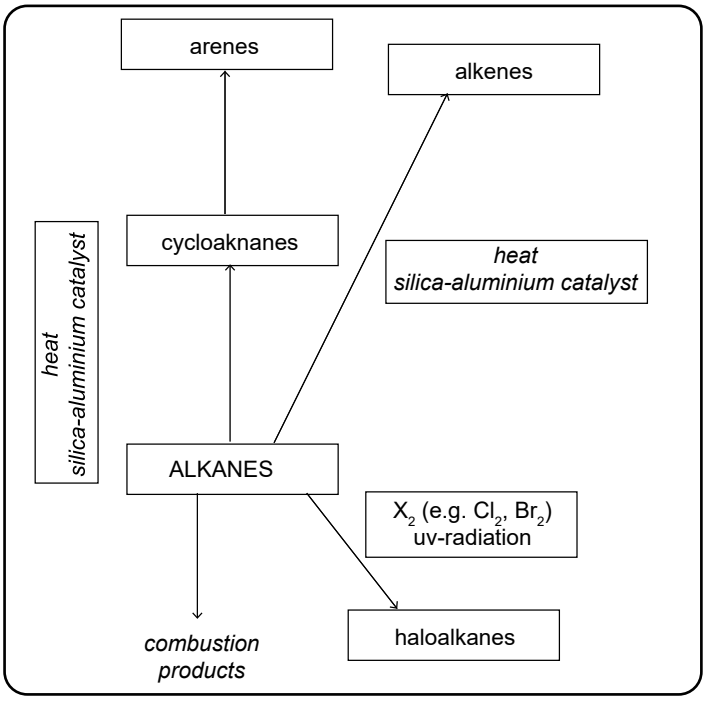


**Figure 2** Reactions of alkenes

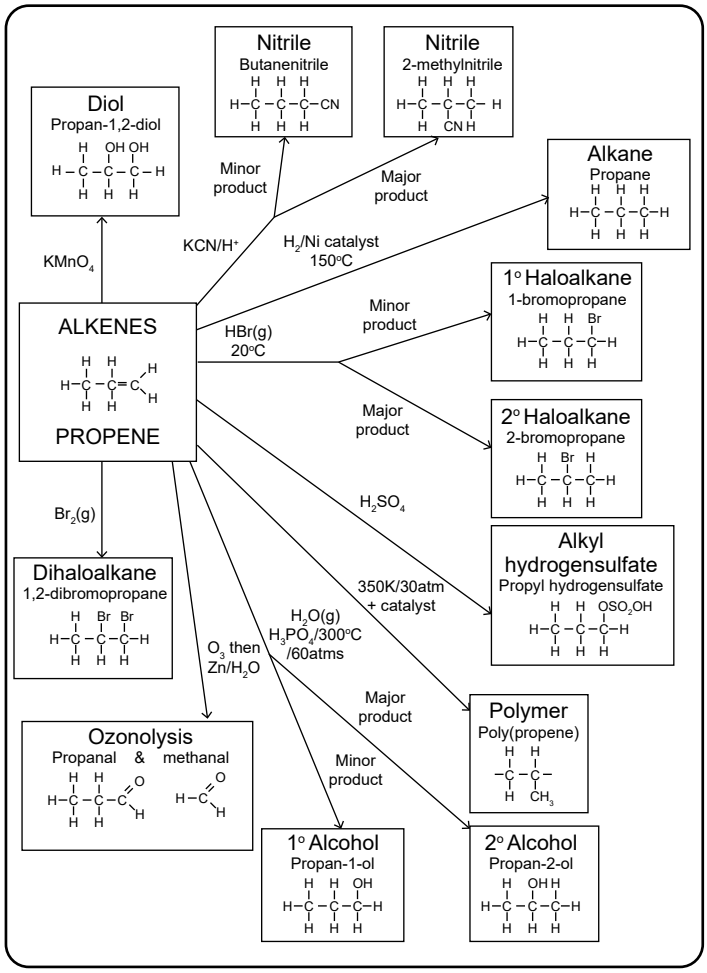



**Figure 3** Reactions of halogenoalkanes

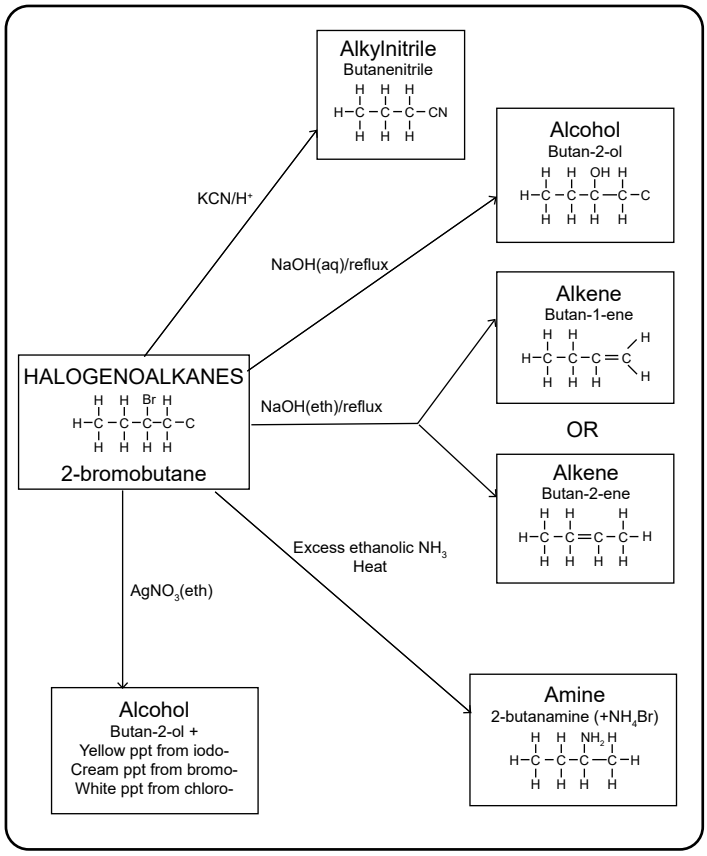



**Figure 4a** Reactions of primary alcohols

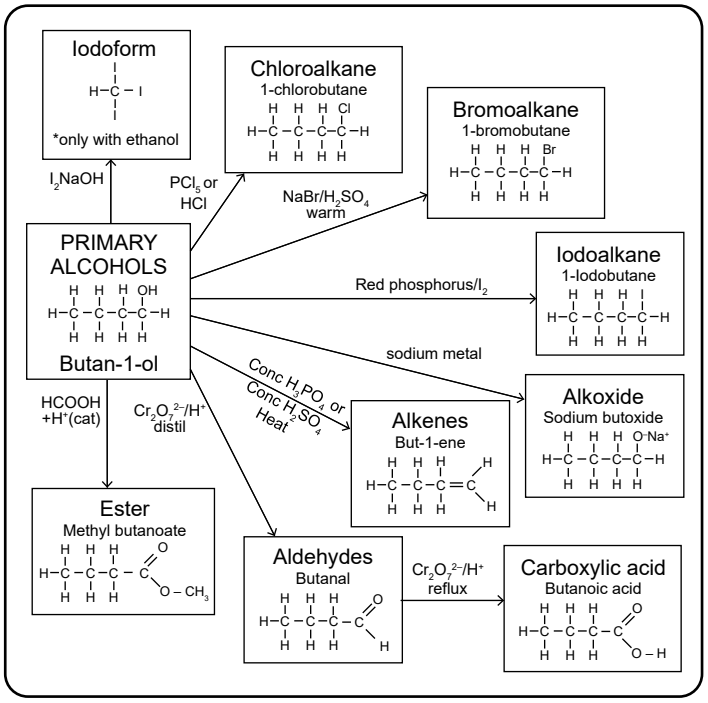



**Figure 4b** Reactions of secondary alcohols

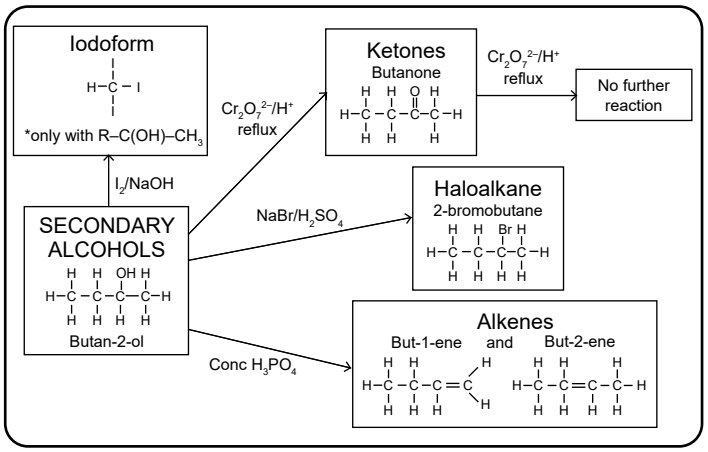



**Figure 5a** Reactions of aldehydes

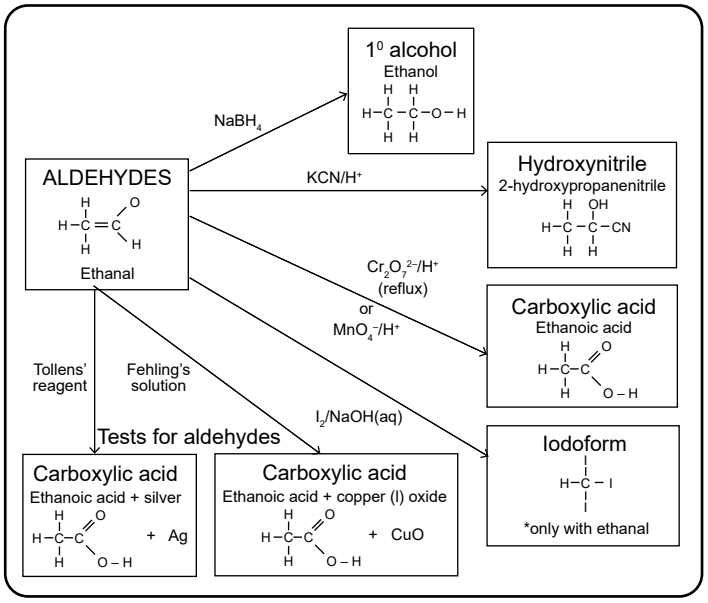


**Figure 5b** Reactions of ketones

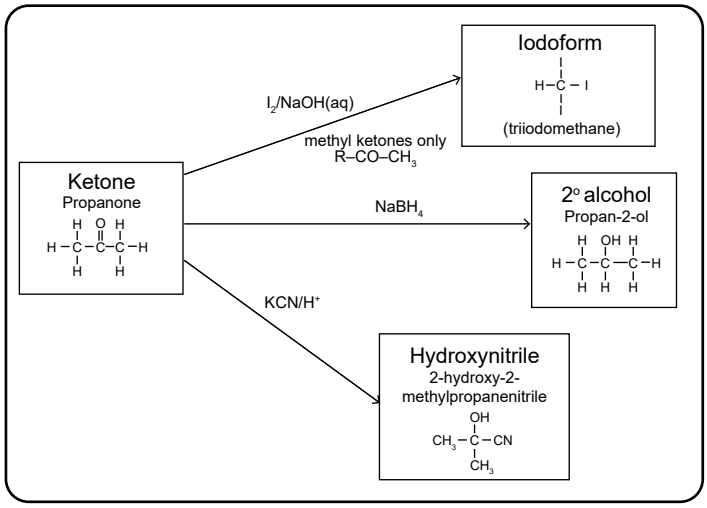



**Figure 6** Reactions of carboxylic acids

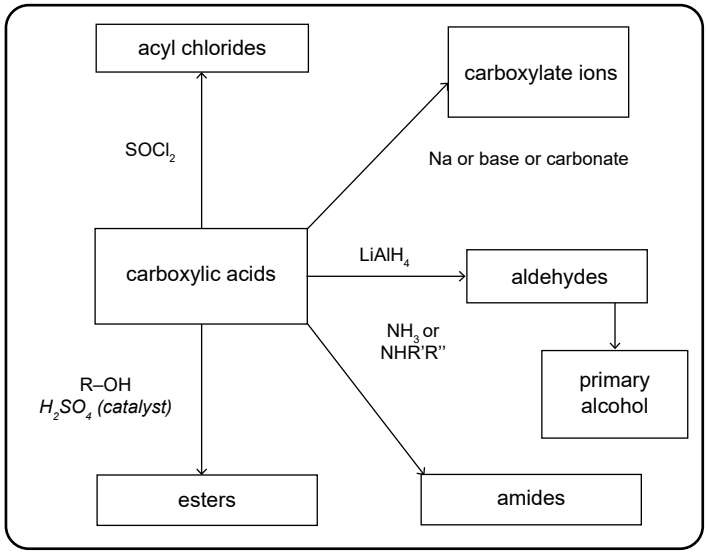
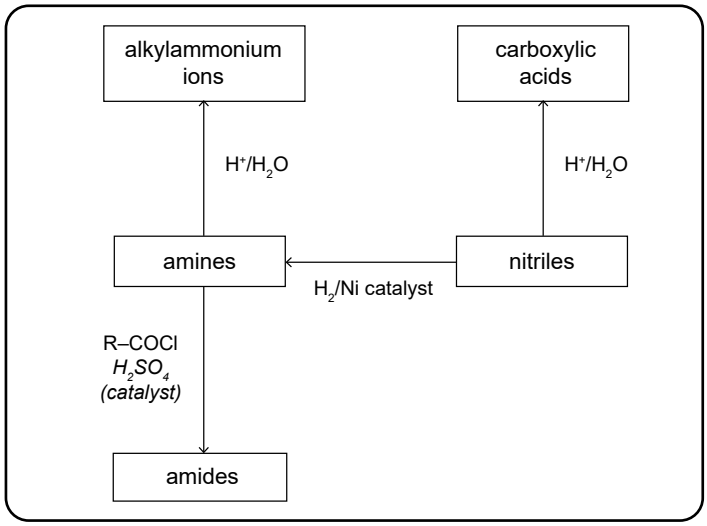



**Figure 7** Reactions of amines and nitriles




## Aromatic Reaction Schematics

**Figure 8** Reactions of benzene

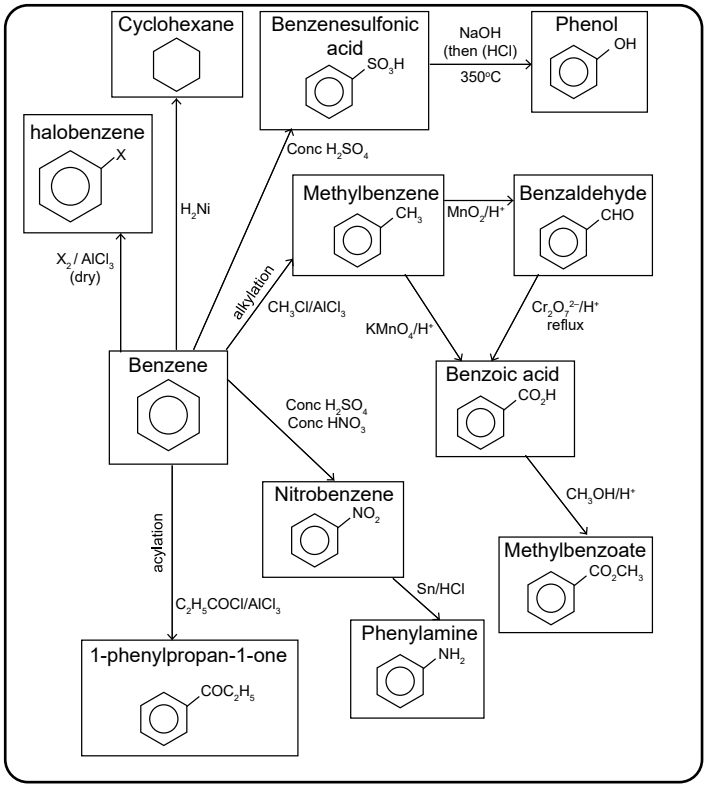



**Figure 9** Reactions of phenylamine (alanine)

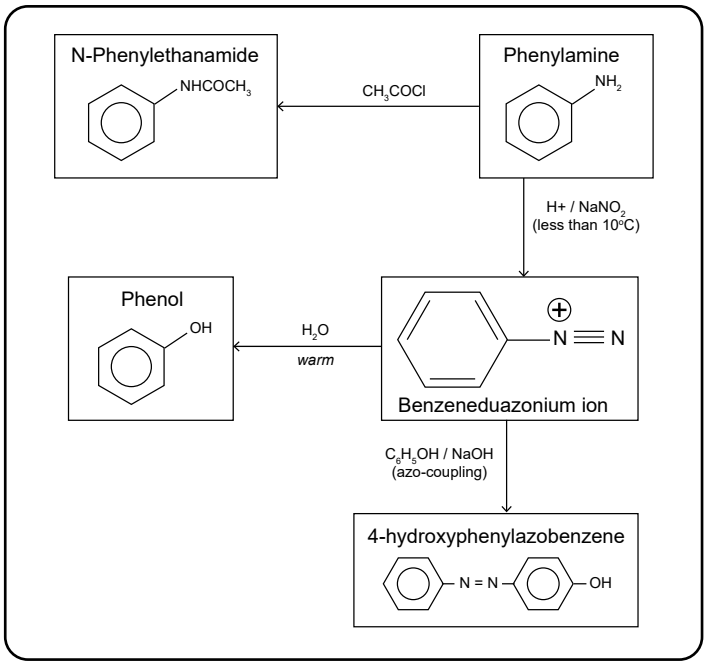
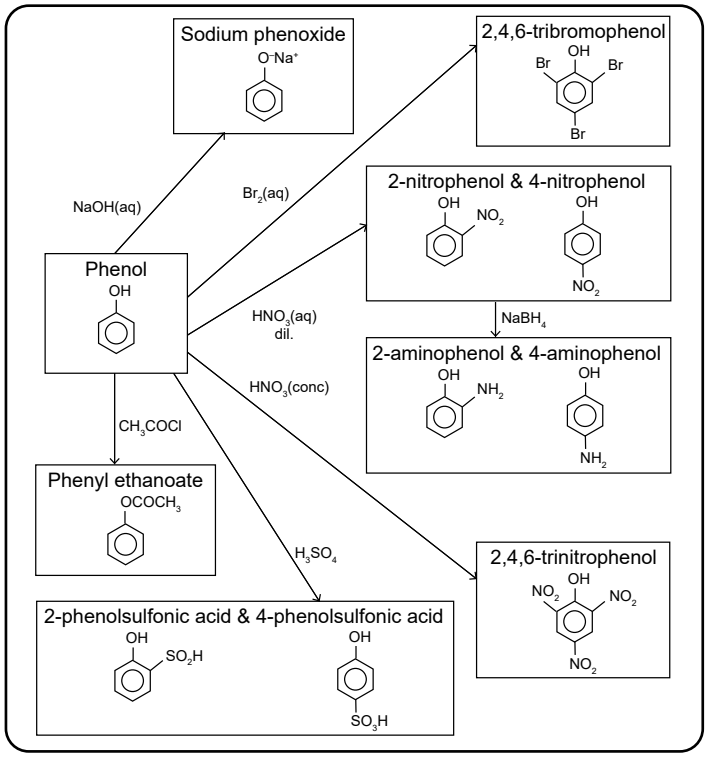


**Figure 10** Reactions of phenol




## Increasing the Carbon-chain

**Figure 11a** Increasing the carbon-chain (RX)

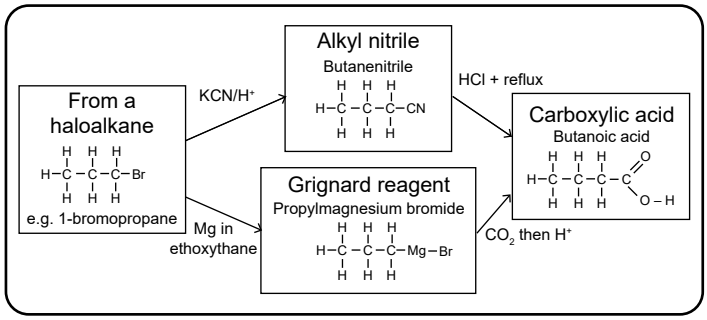
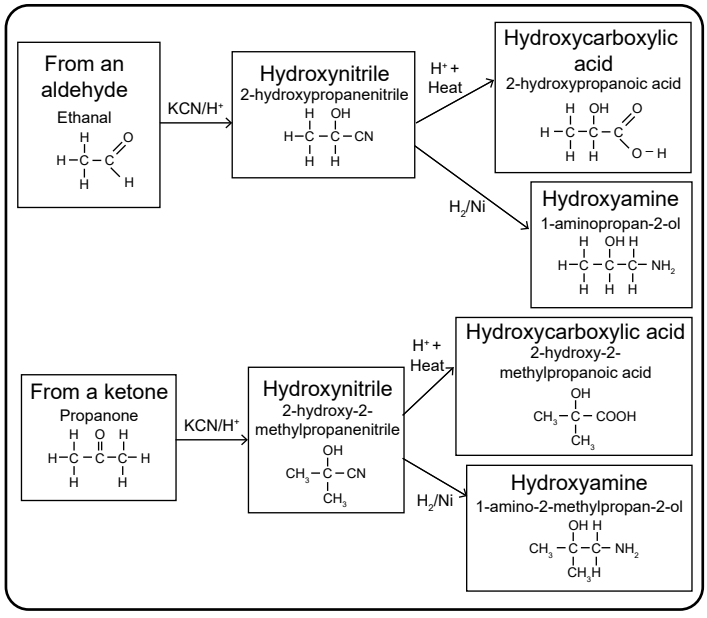



**Figure 11b** Increasing the carbon-chain (–CO–)




## Testing for Functional Groups

**Figure 12a** Testing for alkenes halogenoalkanes alcohols and carboxylic acids

| Functional Group | Test | Positive Outcome | |
|---|---|---|---|
| – C = C – (alkenes) | add to $Br_2$(aq) | orange/brown solution decolourises | |
| R–X (halogenoalkenes) | warm with NaOH(aq) and a water/ethanol solution containing $AgNO_3$ | white precipitate | chloroalkane |
| | | cream precipitate | bromoalkane |
| | | yellow precipitate | iodoalkane |
| R–OH (alcohols) | add acidified $Cr_2O_7^{2-}$(aq) and warm gently | orange solution turns green | (quickly) primary alcohol |
| | | | (slowly) secondary alcohol |
| | | orange solution unchanges | tertiary alcohol |
| –OH (hydroxyl– group) | add dry solid $PCl_5$ | white misty fumes formed (HCl) | |
| –COOH (carboxyl– group) | add drops $NaHCO_3$(aq) or $Na_2CO_3$(aq) | effervescences ($CO_2$ liberated) | |
| | add damp blue litmus paper | litmus paper turns red | |

**Figure 12b** Testing for carbonyls (aldehydes and ketones)

| Functional Group | Test | Positive Outcome | |
|---|---|---|---|
| – CO – (carboxyl– group) | add drops of Brady's reagent (2,4-dinitrophenylhydrazine) | yellow or orange precipitate | |
| | add acidified $Cr_2O^{2-}$ (aq) and warm gently | orange solution turns green | aldehyde |
| | | orange solution uncharged | ketone |
| R–CHO (aldehydes) | add Tollens' reagent (warm gently) | silver mirror (silver precipitate) | |
| | add Fehling's (blue) solution (warm gently) | (brick) red precipitate | |
| –CO–$CH_3$ (ethanal and methyl ketones) | add iodine (in KI(aq)) then NaOH dropwise to remove colour of iodine (warm gently) | yellow precipitate (iodoform) | |

**Figure 12c** Testing for amines amides phenols and nitro-group

| Functional Group | Test | Positive Outcome | |
|---|---|---|---|
| –NRR'' (amines) | add to $Cu^{2+}$(aq) solution | forms dark blue solution (complex ion) | |
| | add to $H^+$ / $NaNO_2$ (aq) | effervescences ($N_2$ liberated) | primary amine |
| | | yellow oil | secondary amine |
| | | colourless solution | tertiary amine |
| –CONR– (amides) | add to NaOH(aq) and boil acidify cooled solution | $NH_3$ liberated | aliphatic amine |
| | | white precipitate | aromatic amide |
| Ar–OH (phenols) | test pH and $Na_2CO_3$(aq) | pH 4-6 but does not react with $CO_3^{2-}$(aq) | |
| | add $Br_2$(aq) | bromine water decolourises White precipitate | |
| | add $Fe^{3+}$(aq) solution | solution turns purple | |
| $–NO_2$ (nitro group) | add $Fe(OH)_2$(aq) | red-brown precipitate | |

## Questions

1) Draw out the synthesis for the preparation of ethanoic acid from chloroethane.

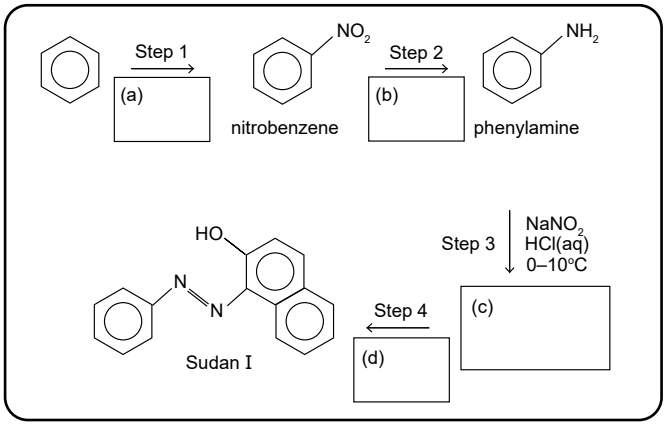
2) Complete the details on the multistep synthesis of the azo-dye **Sudan I** from benzene.

   a) Give reagents and conditions.

   b) Give reagents and conditions.

   c) Name intermediate (c).

   d) Draw the structure of the organic compound coupled to (c) in Step 4.




3) Identify compounds A, B and C given that all are organic compounds containing (i) **three** carbon atoms, and (ii) **one** functional group.

   (a) • Steamy fumes observed on adding $PCl_5$.
   • No observable change on adding $NaHCO_3(aq)$.
   • A pale-yellow precipitate forms on adding NaOH(aq) and then dropwise $I_2(aq)$.

   (b) • Steamy fumes observed on adding $PCl_5$.
   • Effervesces on adding $NaHCO_3(aq)$.

   (c) • Yellow-orange precipitate observed on adding Brady's reagent and warming.
   • A silver mirror is observed on adding Tollens' reagent and warming.

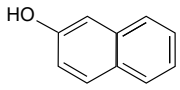
### Answers

1) $CH_3CH_2Cl \xrightarrow{NaOH/H_2O,\ reflux} CH_3CH_2OH \xrightarrow{Cr_2O_7^{2-}/H^+} CH_3COOH$

2) a) Concentrated $H_2SO_4$ and $HNO_3$ at 55 °C.

   b) Tin and concentrated HCl

   c) Benzenediazonium ion (chloride)

   d) 


3) (a) Propan-2-ol ($CH_3CH(OH)CH_3$)

   (b) Propanoic acid ($CH_3CH_2COOH$

   (c) Propanal ($CH_3CH_2CHO$)

***Acknowledgements:*** *This **Chemistry Factsheet** was researched and written by **David Willmot**, and published in **September 2020** by **Curriculum Press**.* 