OCR (A) Chemistry A-level

Module 6: Organic Chemistry and Analysis

Organic Synthesis Notes

by Adam Robertson

DEFINITIONS

Heterolytic fission: The breaking of a covalent bond when one of the bonded atoms takes both of the electrons.

Homolytic fission: The breaking of a covalent bond when each of the bonded atoms takes one electron.

Addition reaction: Two reactants join together to form one product.

Substitution reaction: Two reactants where one atom or group of atoms replaces another set of atoms.

Elimination reaction: A reaction which involves the removal or a small molecule from a larger one

Electrophile: An atom or compound that are electron pair acceptors

Nucleophile: An atom or compound that are electron pair donors

REACTIONS

COMBUSTION

- Requires heat
- For complete combustion there must be adequate levels of oxygen

Complete: $C_6H_{14} + 9\frac{1}{2}O_2 \rightarrow 6CO_2 + 7H_2O$

Incomplete: $C_6H_{14} + 6\frac{1}{2}O_2 \rightarrow 6CO + 7H_2O$

$$C_6H_{14} + 3\frac{1}{2}O_2 \rightarrow 6C + 7H_2O$$

Radical substitution

- In presence of ultraviolet light
- Three steps : initiation, propagation and termination

1. Initiation reaction

$$Cl_2 \xrightarrow{h\nu} 2\,Cl\bullet$$

2. Chain propagation

$$Cl\bullet + CH_4 \longrightarrow HCl + CH_3\bullet$$

$$CH_3\bullet + Cl_2 \longrightarrow CH_3Cl + Cl\bullet$$

3. Chain termination reactions

$$Cl\bullet + Cl\bullet \longrightarrow Cl_2$$

$$CH_3\bullet + CH_3\bullet \longrightarrow CH_3{-}CH_3$$

$$Cl\bullet + CH_3\bullet \longrightarrow CH_3Cl$$

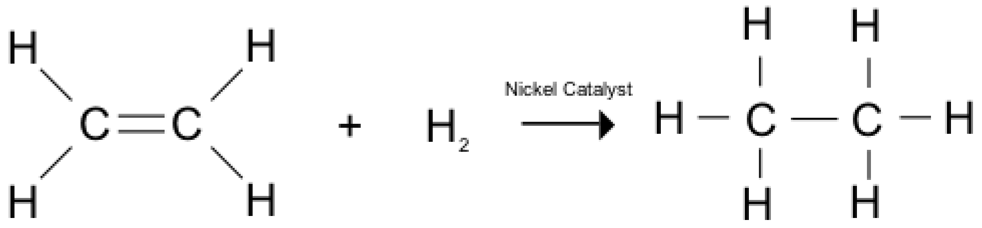
- Since the reaction is uncontrollable and can be very unstable, it is typically not used in synthesis.

- In addition several products are made rather than just desired products

- In this scenario CHLOROMETHANE can go on to react with another chlorine radical which will substitute another hydrogen atom creating DICHLOROMETHANE. Further substitution can occur to form TRICHLOROMETHANE and TETRACHLOROMETHANE
- substitution can also happen at any point on the carbon chain, leading to a low yield of a specific product

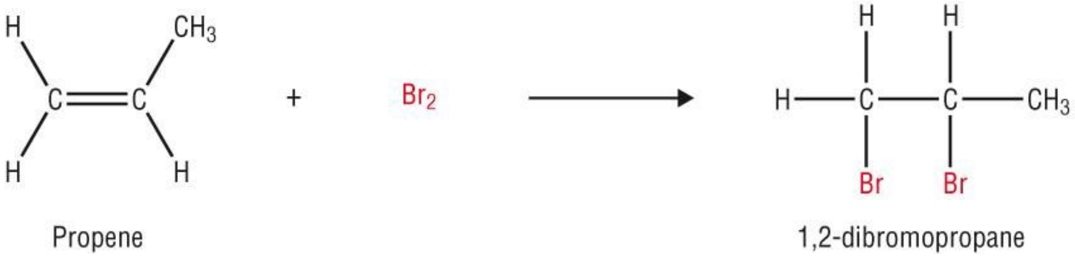
Hydrogenation

- At 423K
- Nickel catalyst



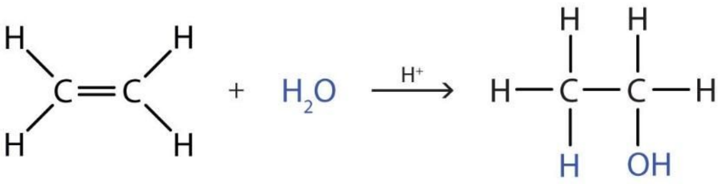
Halogenation

- How alkenes decolourise bromine water (orange-brown → colourless)
- Occurs at room temperature
- an electrophilic addition reaction



Hydration

- an alkene is reacted with steam
- phosphoric acid catalyst (H_3PO_4)
- if the alkene is unsymmetrical, a mixture of products is formed

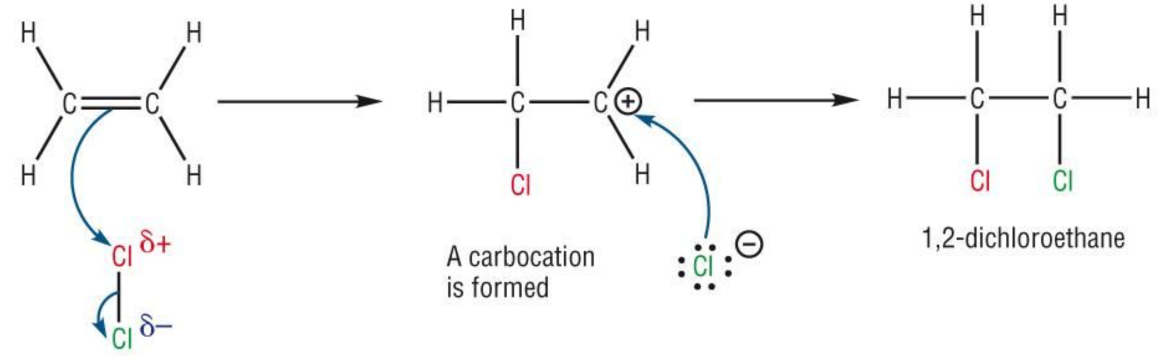


Addition reactions of alkenes with hydrogen halides

- conditions: room temperature
- reactant: hydrogen halide
- if the alkene is a gas, the two gases are mixed. If the alkene is a liquid, the hydrogen halide is bubbled through
- electrophilic substitution reaction
- if the alkene is unsymmetrical, a mixture of products will be formed

alkene + hydrogen halide → haloalkane

ELECTROPHILIC ADDITION

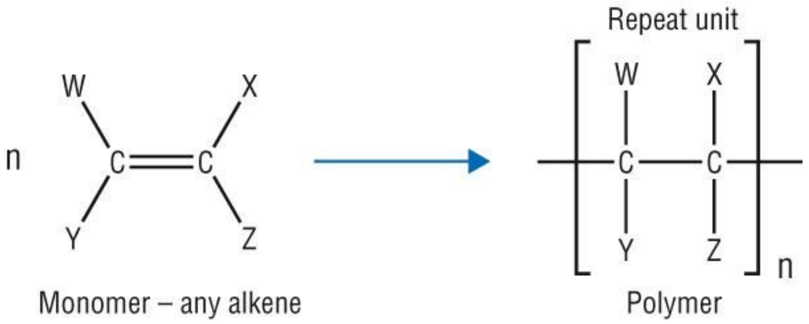


When Cl_2 approaches, the Cl–Cl bond becomes polar. A pair of electrons flows from the double bond to the slightly positive $Cl^{\delta+}$ and a bond formed.

- As with all of the reactions on this page, if the reactants allow it then two potential products can be formed. In order to find the major product we employ MARKOWNIKOFF'S RULE which states that the higher yield product is the more stable product with the larger amount of R groups, e.g. a primary product will be less stable than a secondary product therefore there will be less of that primary product

ADDITION POLYMERISATION (YR1)

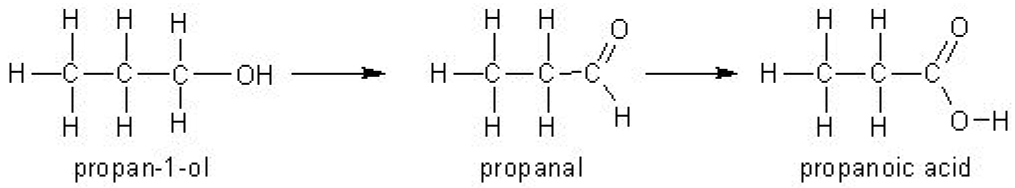
- Nickel catalyst
- Very high temperatures and pressure

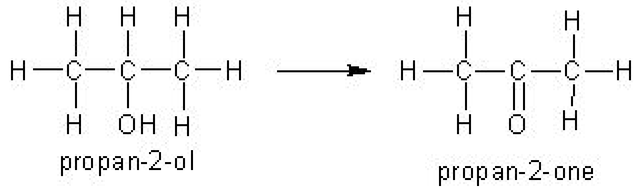


OXIDATION OF ALCOHOLS

- Both reactions require acidified potassium dichromate (works as an oxidising agent)
- Gentle heating
- Primary alcohols oxidise to form **aldehydes** and **carboxylic acids:**
    - under distillation + gentle heating: alcohol + [O] → aldehyde + H_2O

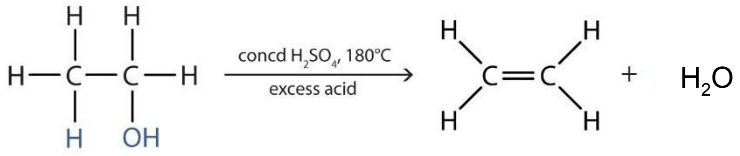
  - under reflux + strong heat, excess $K_2Cr_2O_7$: alcohol + 2[O] → carboxylic acid + H_2O
- Secondary alcohols oxidise to form **ketones:**
  - alcohol + [O] → ketone + H_2O





DEHYDRATION OF ALCOHOLS

- Heated under reflux
- Requires sulfuric or phosphoric acid



SUBSTITUTION OF ALCOHOLS

- Heat under reflux in the presence of sulfuric acid
- Reactants: sulfuric acid + sodium halide (forms hydrogen halide in situ e.g. NaBr + H_2SO_4 → $NaHSO_4$ + HBr)

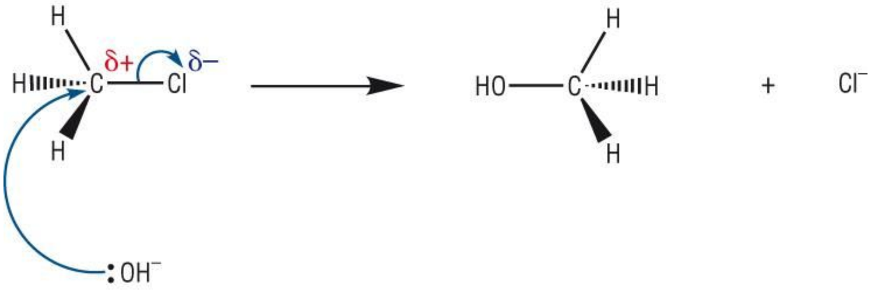
$$NaBr + H_2SO_4 \rightarrow NaHSO_4 + HBr$$

$$C_3H_7OH + HBr \rightarrow C_3H_7Br + H_2O$$

alcohol + HBr → bromoalkane + H_2O

Nucleophilic substitution of haloalkanes/hydrolysis

- Requires a source of OH ions (usually from NaOH)
- nucleophilic substitution reaction
- heated under reflux to get a good yield



The nucleophile attacks the back of the carbon atom donating an electron pair.
This causes a new bond to form and the carbon halogen bond to break.

- reaction:
  - bromoalkane + NaOH → alcohol + NaBr
  - bromoalkane + H_2O → alcohol + H^+ + Br^-
- Speed of hydrolysis is relevant to **bond strength** of C—X e.g: C—Cl reacts slower than C—I because C—Cl has the stronger bond (more bond enthalpy

Radical substitution of ozone layer

Initiation: $CF_2Cl_2 \rightarrow CF_2Cl\cdot + Cl\cdot$

Propagation: $Cl\cdot + O_3 \rightarrow ClO\cdot + O_2$

$ClO\cdot + O \rightarrow Cl\cdot + O_2$

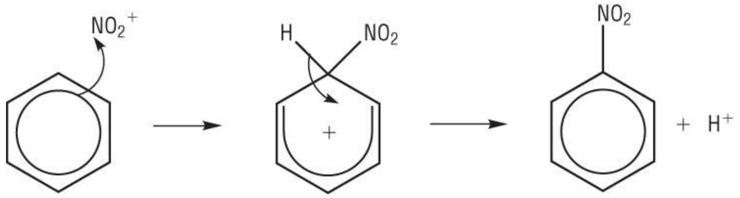
overall: $O_3 + O \rightarrow 2O_2$

Nitration of benzene

- Reaction happens at 50° with a concentrated sulfuric acid catalyst to form nitrobenzene
- Above 50° the product formed will be 1,3 dinitrobenzene
- electrophilic substitution reaction

- The reactant is concentrated nitric acid

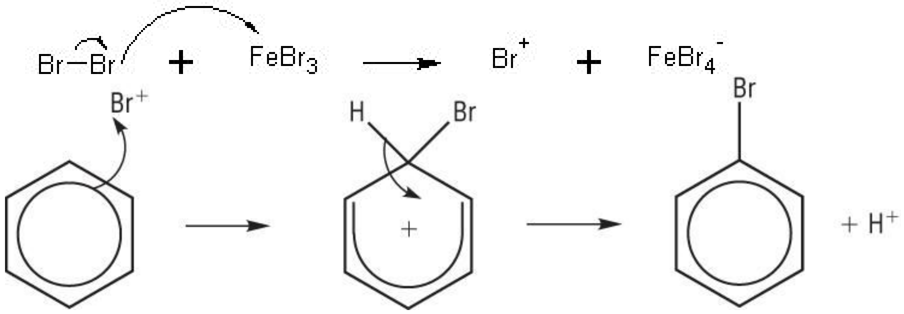
$$HNO_3 + H_2SO_4 \rightarrow NO_2^+ + HSO_4^- + H_2O$$



$$H^+ + HSO_4^- \rightarrow H_2SO_4$$

HALOGENATION OF BENZENE

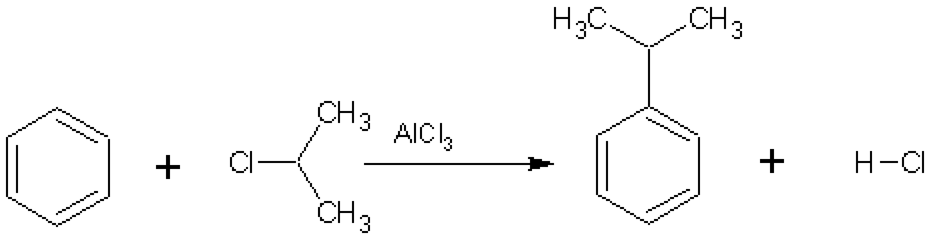
- conditions: room temperature + pressure
- Requires a halogen carrier since benzene is too stable
- Halogen carriers are either FeX or AlX
- electrophilic substitution reaction



$$H^+ + FeBr_4^- \rightarrow FeBr_3 + HBr$$

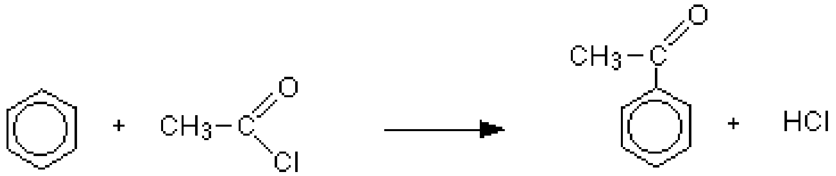
ALKYLATION OF BENZENE

- Benzene is reacted with a haloalkane
- Requires an aluminium chloride ($AlCl_3$) catalyst
- electrophilic substitution reaction



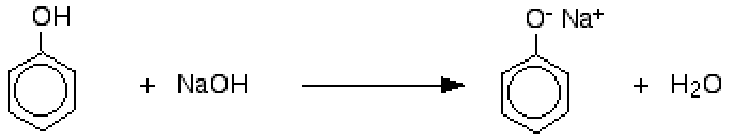
ACYLATION OF BENZENE

- benzene is reacted with an acyl chloride
- Requires an aluminium chloride ($AlCl_3$) catalyst
- Electrophilic substitution reaction



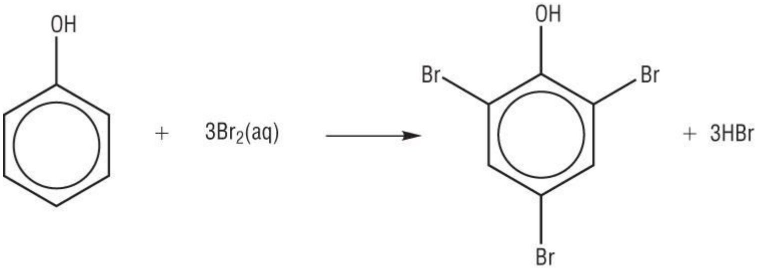
NEUTRALISATION OF PHENOL

- Phenol is more electronegative than benzene
- Phenol acts as a weak acid only reacting with the stronger bases



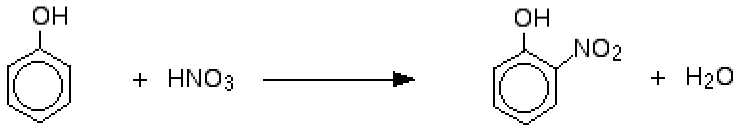
HALOGENATION OF PHENOL

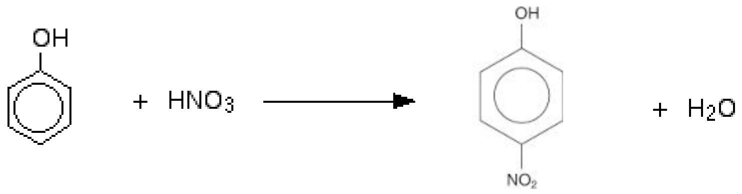
- Room temperature
- Electrophilic substitution reaction
- white ppt is formed and bromine is decolourised



NITRATION OF PHENOL

- At room temperature
- Reactant is dilute HNO_3
- electrophilic substitution reaction
- a mixture of 2 products is formed

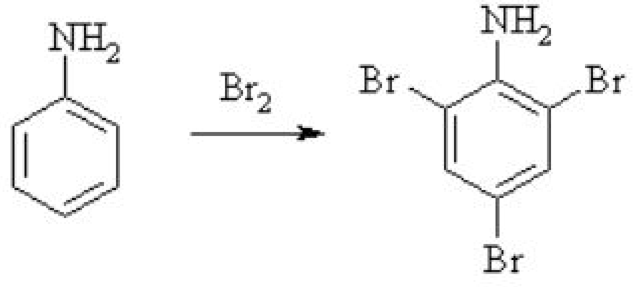




BROMINATION OF PHENYLAMINE

- rapid reaction speed, because NH_2 group activates the ring

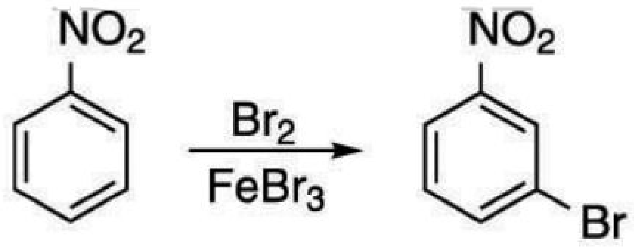
phenylamine + $3Br_2$ → 2,4,6-tribromophenylamine + 3HBr



BROMINATION OF NITROBENZENE

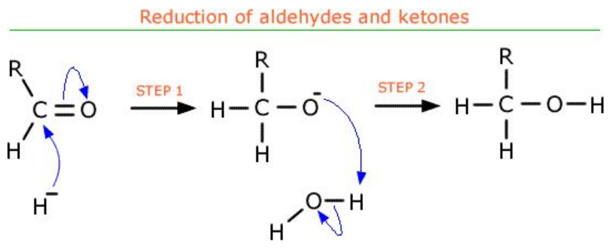
- a slow reaction because the NO_2 group deactivates the ring
- requires a halogen carrier and a high temperature

nitrobenzene + Br_2 → 3-bromo,1-nitrobenzene + HBr



REDUCTION OF THE CARBONYL WITH $NaBH_4$ (NUCLEOPHILIC ADDITION)

- $NaBH_4$ is used as the reducing agent
- The reducing agent and the carbonyl are warmed in aqueous solution
- aldehyde reaction: aldehyde + 2[H] → primary alcohol
- ketone reaction: ketone + 2[H] → secondary alcohol



Reduction of Carbonyl Compounds with HCN

- Hydrogen cyanide is very toxic, therefore sodium cyanide and sulfuric acid are used to provide the hydrogen cyanide safely for the reaction in the lab
- It is useful for increasing the length of the carbon chain to establish different properties of a material
- The mechanism is the same as above however the H(-) ion is replaced with a CN(-) ion
- In this reaction water can be protonated or the O(-) can bond with a H(+) ion
- aldehyde/ketone + HCN → hydroxynitrile (don't have to name these)

Oxidation of Aldehydes

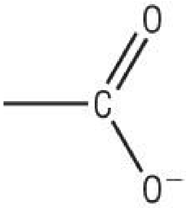
- ketones do not undergo oxidation
- aldehydes are heated under reflux with $Cr_2O_7^{2-}/H^+$ ions (usually from potassium dichromate and dilute sulfuric acid)

aldehyde + [O] → carboxylic acid

- this is the same as the reaction that takes place during the Tollen's Reagent test. The fact ketones don't undergo oxidation means that the Tollens test works.

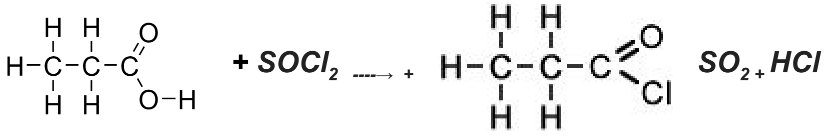
Redox/neutralisation of carboxylic acids

- React in the same manner as other acids however they form a carboxylate salt
- reaction with metals: observations: metal disappears, effervescence of H_2
- reaction with metal oxides or alkalis: H_2O produced
- reaction with carbonates: H_2O and CO_2 produced



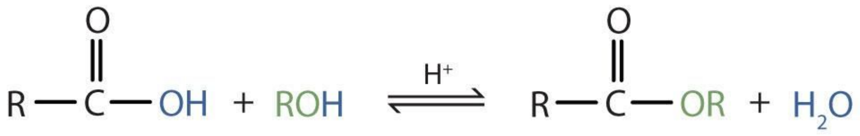
Preparation of acyl chlorides

- Because of the toxic nature of the gas by-products, this reaction takes place in a fume cupboard



Esterification of carboxylic acids

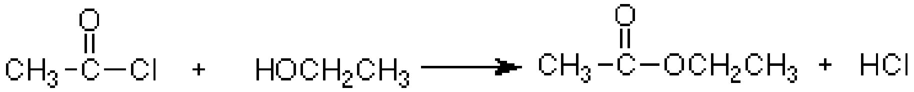
- The alcohol is warmed with a small amount of concentrated sulfuric acid



$$R-\overset{\overset{O}{\|}}{C}-OH + ROH \xrightleftharpoons{H^+} R-\overset{\overset{O}{\|}}{C}-OR + H_2O$$

Esterification of acyl chlorides

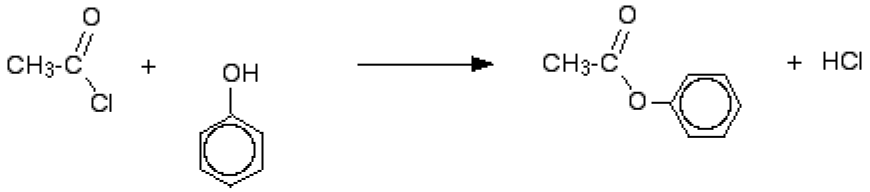
- The main difference here is that this form of esterification is irreversible and has the by-product of HCl instead of H_2O
- reaction: acyl chloride + alcohol → ester + HCl



$$CH_3-\overset{\overset{O}{\|}}{C}-Cl + HOCH_2CH_3 \longrightarrow CH_3-\overset{\overset{O}{\|}}{C}-OCH_2CH_3 + HCl$$

ACYL CHLORIDE AND PHENOL

- Unlike carboxylic acids, acyl chlorides and acid anhydrides are much more reactive which means they can form an ester with phenol

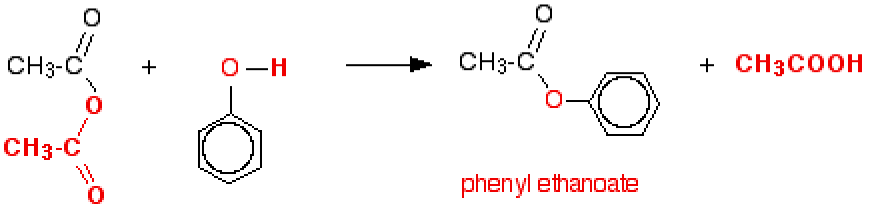


Acid anhydrides and phenol

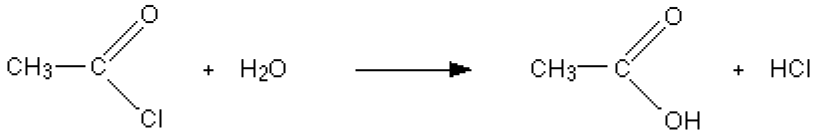
- Acid anhydrides react in the same way as acyl chlorides however do not produce as toxic products and the reactions are typically more controlled, hence why they are preferred in the lab.
- They are formed from two carboxylic acids

Acyl chloride to carboxylic acid

- acyl chlorides are reacted with water to produce a carboxylic acid

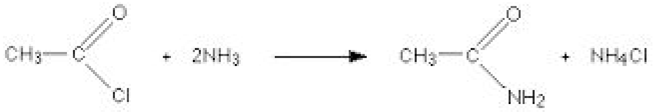


- A violentreaction that takes place in a fume cupboard due to the HCl gas



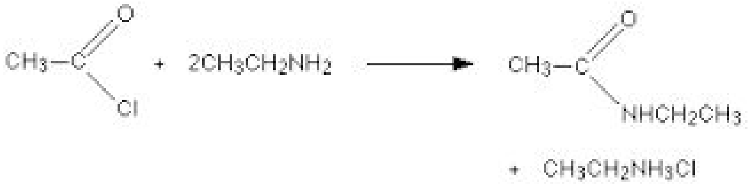
ACYL CHLORIDES TO FORM PRIMARY AMIDES

- Both ammonia and amines can act as nucleophiles by donating their lone pair of electrons from the nitrogen atom
- For a primary amide to be formed the reaction must take place with ammonia
- acyl chloride + 2NH_3 → primary amide + NH_4Cl



FORM SECONDARY AMIDES

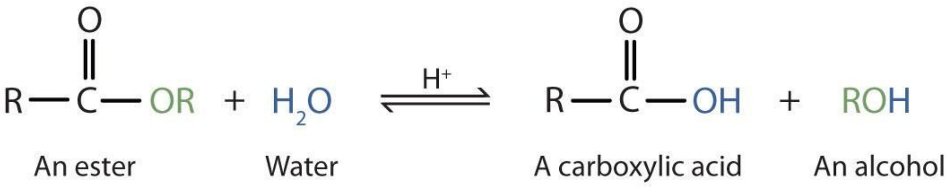
- In this reaction a primary amine replaces ammonia to form a secondary amide
- acyl chloride + primary amine → secondary amide + $CH_3NH_3^+Cl^-$



HYDROLYSIS OF ESTERS

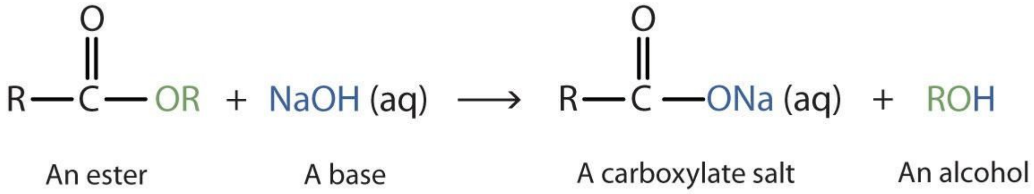
ACID

- Ester is heated under reflux with water and a dilute acid
- This reaction is reversible

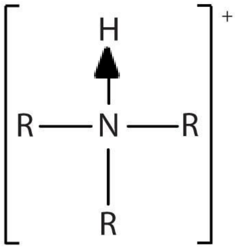


ALKALINE

- Ester is heated under reflux but with hydroxide ions instead
- This reaction is irreversible


$$R-\overset{\displaystyle O}{\overset{\|}{C}}-OR + NaOH\,(aq) \longrightarrow R-\overset{\displaystyle O}{\overset{\|}{C}}-ONa\,(aq) + ROH$$

AMINES AS BASES



- The lone pair of electrons on the nitrogen atom can accept a proton
- When a reaction takes place a dative covalent bond is formed
- e.g. $2CH_3CH_2NH_2 + H_2SO_4 \rightarrow (CH_3CH_2NH_3^+)_2SO_4^{2-}$

PREPARATION OF PRIMARY AMINES (NS)

- Reaction takes place with excess ammonia, which acts as the nucleophile due to its lone pair of electrons, and it also prevents further substitution into secondary and tertiary amines
- Ethanol is used as the solvent

$$\mathbf{CH_3CH_2CH_2Cl + NH_3 \rightarrow CH_3CH_2CH_2NH_3^+Cl^-}$$

haloalkane + NH_3 → alkylammonium chloride

$$\mathbf{CH_3CH_2CH_2NH_3^+Cl^- + NaOH \rightarrow CH_3CH_2CH_2NH_2 + NaCl + H_2O}$$

alkylammonium chloride + NaOH → amine + NaCl + H_2O

PREPARATION OF SECONDARY AMINES

$$\mathbf{CH_3CH_2CH_2Cl + CH_3CH_2CH_2NH_2 \rightarrow (CH_3CH_2CH_2)_2NH_2^+Cl^-}$$

haloalkane + primary amine → dialkylammonium chloride

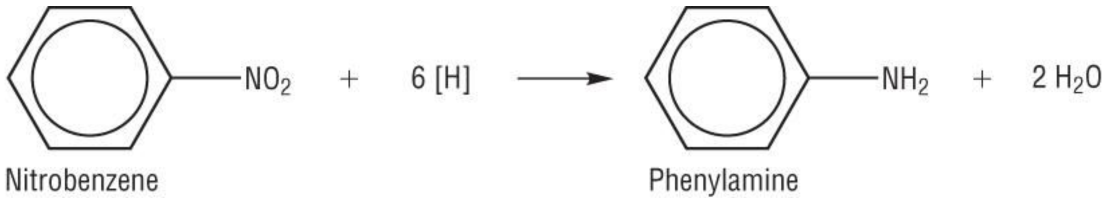
$$\mathbf{(CH_3CH_2CH_2)_2NH_2^+Cl^- + NaOH \rightarrow (CH_3CH_2CH_2)_2NH + NaCl + H_2O}$$

dialkylammonium chloride + NaOH → secondary amine + NaCl + H_2O

- Further substitutions can take place to create tertiary and quaternary amines by reacting the secondary and tertiary amines in the same manner respectively

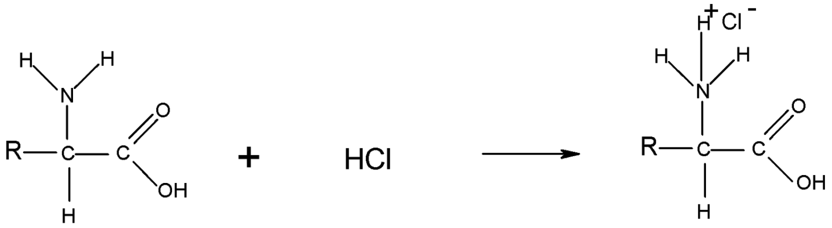
PREPARATION OF PHENYLAMINE

- Nitrobenzene is heated under reflux with tin and hydrochloric acid to form phenylammonium salt, which is then reacted with excess sodium hydroxide



AMINO ACID PLUS ACID

- Reacts to form a salt



AMINO ACID PLUS ALKALI

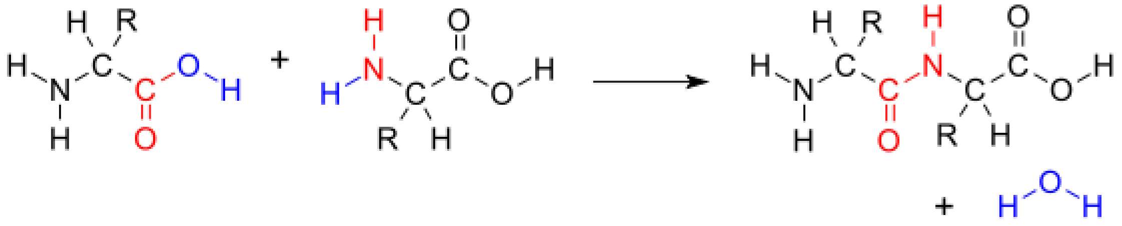
- Reacts to form a salt with the carboxylic acid group (e.g. COO-Na+) and water

ESTERIFICATION OF AMINO ACIDS

- conditions: heat and concentrated sulfuric acid catalyst
- amino acid + alcohol + H^+ → ester + H_2O

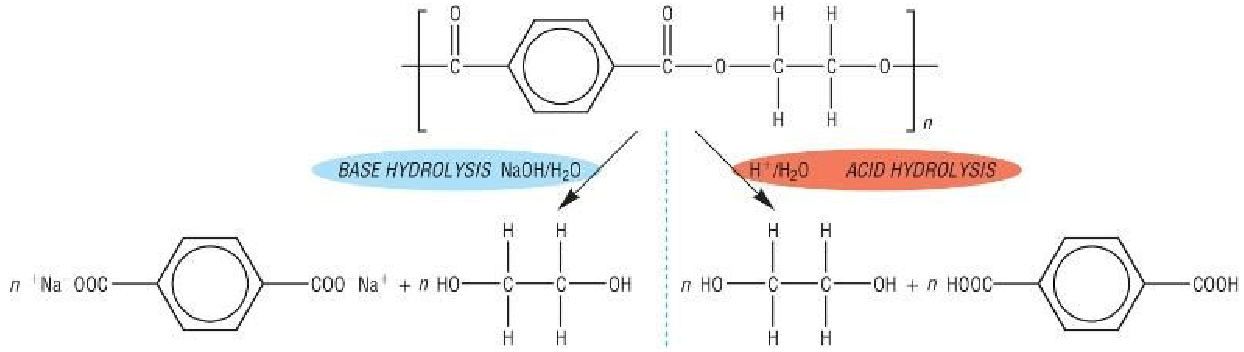
CONDENSATION POLYMERISATION

- Form a polyester or polyamide by removal of a water molecule or HCl
- Forms an ester or amide linkage respectively
- For polyesters either a monomer with a carboxylic acid group and an alcohol group is required or two different monomers, one a diol (2 hydroxyl groups) and the other a dicarboxylic acid (2 carboxylic acids)
- For polyamides either a monomer with a carboxylic acid/acyl chloride group and an amine group is required or two different monomers, a dicarboxylic acid/acyl chloride and the other a diamine



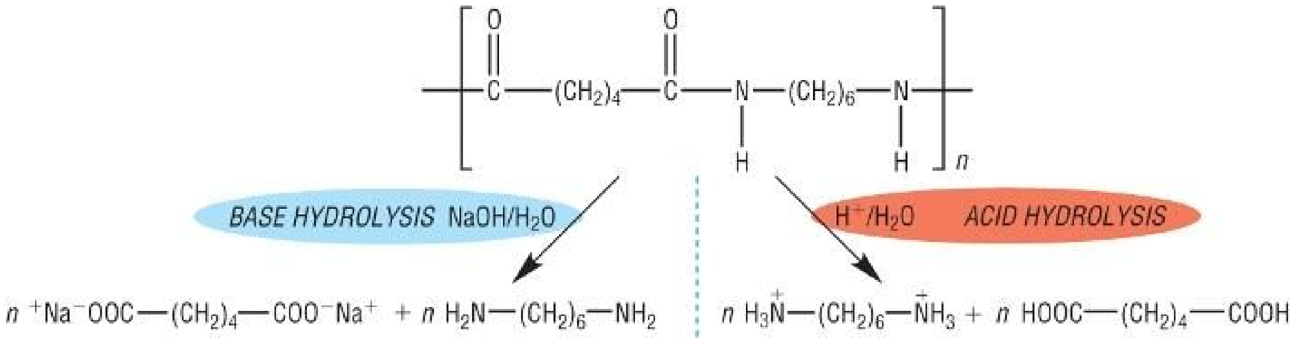
HYDROLYSIS OF POLYESTERS

- Hot acid



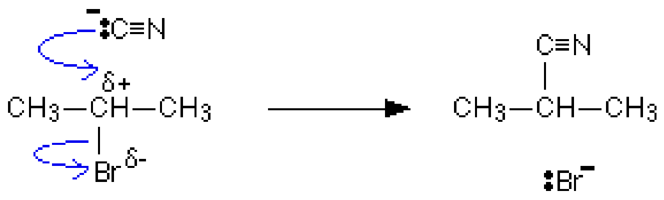
HYDROLYSIS OF POLYAMIDES

- Hot acid



HALOALKANE TO NITRILE

- Used to lengthen the carbon chain
- It's a nucleophilic substitution reaction with either sodium/potassium cyanide as hydrogen cyanide is very poisonous
- the reaction occurs in ethanol



Reduction of nitriles

- Reduced to an amine with a **nickel** catalyst and hydrogen

$$CH_3CN + 2H_2 \longrightarrow CH_3CH_2NH_2$$

Hydrolysis of nitriles

- Form carboxylic acids when heated with dilute acid and water

$$CH_3CN + 2H_2O + HCl \longrightarrow CH_3COOH + NH_4Cl$$