Cambridge (CIE) A Level Chemistry

Your notes

Acyl Chlorides

Contents

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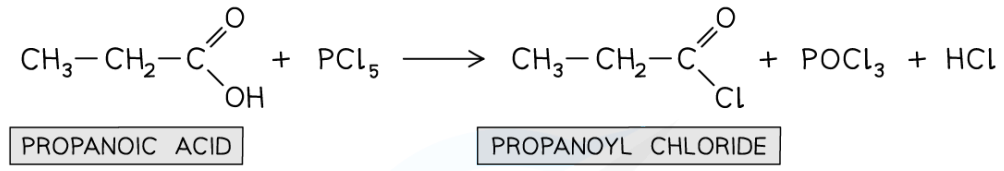
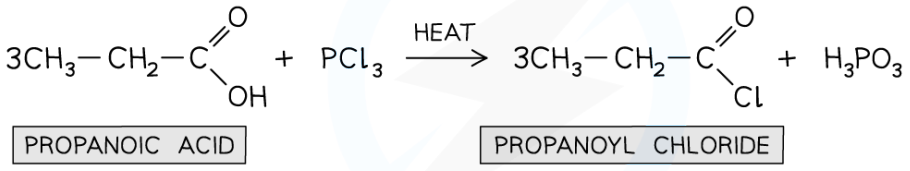
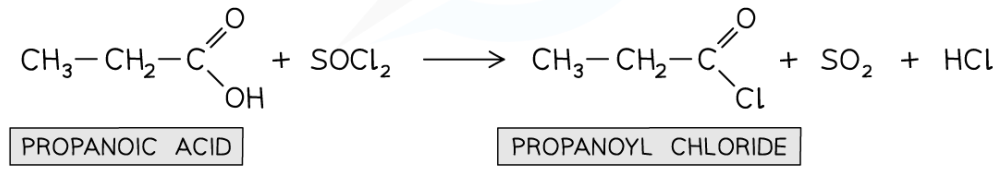
Production of Acyl Chlorides

- Due to the increased reactivity of acyl chlorides compared to carboxylic acids, they are often used as **starting compounds** in organic reactions
- Acyl chlorides are compounds that contain an -COCl functional group and can be prepared from the reaction of carboxylic acids with:
  - **Solid** phosphorus(V) chloride (PCl_5)
  - **Liquid** phosphorus(III) chloride (PCl_3) and heat
  - **Liquid** sulfur dichloride oxide ($SOCl_2$)
- Propanoyl chloride can this way be prepared from propanoic acid using the reactions above

Using propanoic acid to form propanoyl chloride







Propanoic acid can be used to produce propanoyl chloride with different by-products depending on the reagent used

Reactions of Acyl Chlorides

- **Acyl chlorides** are **reactive** organic compounds that undergo many reactions such as **addition-elimination reactions**
- In addition-elimination reactions, the **addition** of a small molecule across the C=O bond takes place followed by **elimination** of a small molecule

- Examples of these addition-elimination reactions include:
  - **Hydrolysis**
  - Reaction with alcohols and phenols to form **esters**
  - Reaction with ammonia and amines to form **amides**

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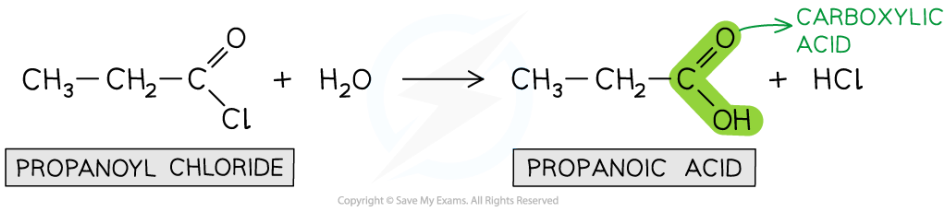
Hydrolysis

- The **hydrolysis** of acyl chlorides results in the formation of a **carboxylic acid** and **HCl** molecule
- This is an **addition-elimination** reaction
  - A **water molecule** adds across the C=O bond
  - A hydrochloric acid (HCl) molecule is **eliminated**
- An example is the hydrolysis of propanoyl chloride to form propanoic acid and HCl

Hydrolysis of acyl chlorides

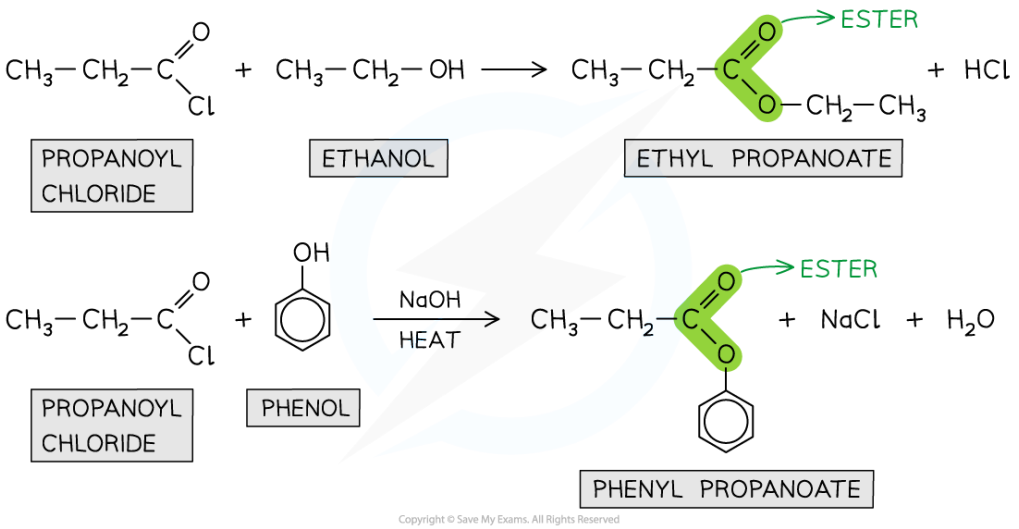


Acyl chlorides are hydrolysed to carboxylic acids

Formation of esters

- Acyl chlorides can react with **alcohols** and **phenols** to form esters
  - The reaction with phenols requires **heat** and a **base**
- Esters can also be formed from the reaction of **carboxylic acids** with phenol and alcohols however, this is a **slower** reaction as carboxylic acids are less reactive and the reaction does **not go to completion** (so less product is formed)
- Acyl chlorides are therefore more useful in the synthesis of esters
- The esterification of acyl chlorides is also an **addition-elimination** reaction
  - The alcohol or phenol adds across the C=O bond
  - A HCl molecule is eliminated

Esterification reactions using acyl chlorides



Acyl chlorides undergo esterification with alcohols and phenols to form esters

Formation of amides

- Acyl chlorides react with **ammonia** or **primary amines** to form **amides** in a **condensation reaction**.
- A **lone pair** on the nitrogen atom attacks the **carbonyl carbon** in the acyl chloride.
- The reaction proceeds via a nucleophilic **addition–elimination mechanism**:
  - The nucleophile adds to the C=O bond
  - A chloride ion (Cl^-) is eliminated
  - **Hydrogen chloride (HCl)** is formed

What happens to the HCl?

- The **HCl formed** does not remain unreacted.
- It is **immediately neutralised** by a **second molecule** of ammonia or amine present in excess.
- This forms an **ammonium salt** (e.g. NH_4Cl, CH_3NH_3Cl).

Why 2 molecules are needed

- The **1st molecule** of ammonia/amine forms the **amide**
- The **2nd molecule** of ammonia/amine neutralises the **HCl** and forms **ammonium salt**

Examples

- **Reaction with ammonia**
- **Product:** Primary amide (propanamide) and ammonium chloride

$$CH_3CH_2COCl + 2NH_3 \rightarrow CH_3CH_2CONH_2 + NH_4Cl$$

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- **Reaction with methylamine**
- **Product:** Secondary (substituted) amide and methylammonium chloride

$$CH_3COCl + 2CH_3NH_2 \rightarrow CH_3CONHCH_3 + CH_3NH_3Cl$$

- **Reaction with ethylamine**
- **Product:** Secondary (substituted) amide and ethylammonium chloride

$$CH_3COCl + 2CH_3CH_2NH_2 \rightarrow CH_3CONHCH_2CH_3 + CH_3CH_2NH_3Cl$$

Summary for formation of amides

- All reactions form **HCl**, which is **not observed** as a separate product
- The **HCl is neutralised** by excess ammonia or amine
- The final products are an **amide** and an **ammonium salt**

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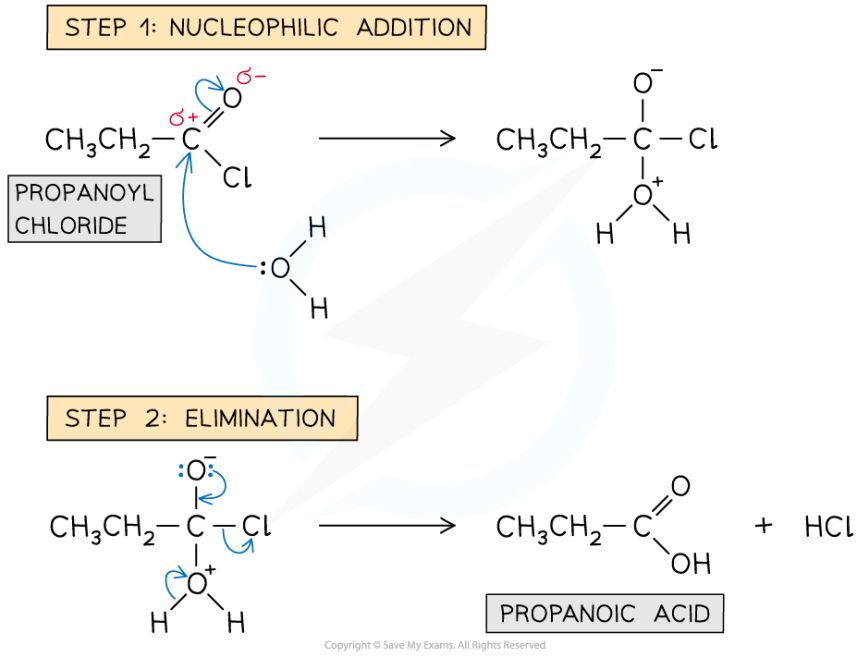
Mechanism of Addition – Elimination in Acyl Chloride Reactions

- Acyl chlorides undergo **addition-elimination** reactions such as **hydrolysis**, **esterification** reactions to form esters, and **condensation** reactions to form **amides**
- The general mechanism of these addition-elimination reactions involves two steps:
  - **Step 1 –** Addition of a **nucleophile** across the C=O bond
  - **Step 2 –** Elimination of a **small molecule** such as HCl or H_2O

Mechanism of hydrolysis of acyl chlorides

- In the **hydrolysis** of acyl chlorides, the water molecule acts as a **nucleophile**
  - The lone pair of the oxygen atom from water carries out an **initial attack** on the carbonyl carbon
  - This is followed by the elimination of a hydrochloric acid (HCl) molecule

Reaction mechanism of the hydrolysis of acyl chlorides



The two-step addition-elimination reaction mechanism of propanoyl chloride to form propanoic acid

Formation of esters: reaction mechanism

- In the **esterification** reaction of acyl chlorides, the alcohols or phenols act as a **nucleophile**
  - The lone pair of the alcohol / phenol oxygen atom carries out an **initial** attack on the carbonyl carbon
  - This is again followed by the elimination of an HCl molecule
- With phenols, the reaction requires **heat** to proceed and needs to be carried out in the presence of a **base**
- The base **deprotonates** the phenol to form a **phenoxide** ion which is a **better nucleophile** than the phenol molecule
  - The **phenoxide ion** carries out an **initial attack** on the carbonyl carbon
  - A small molecule of NaCl is eliminated

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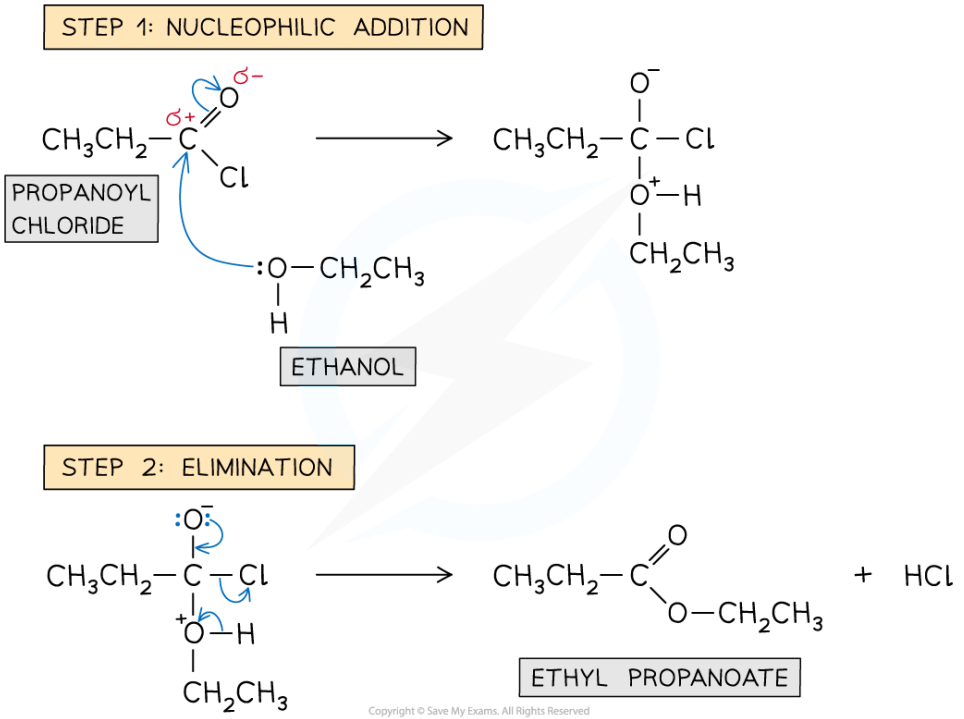
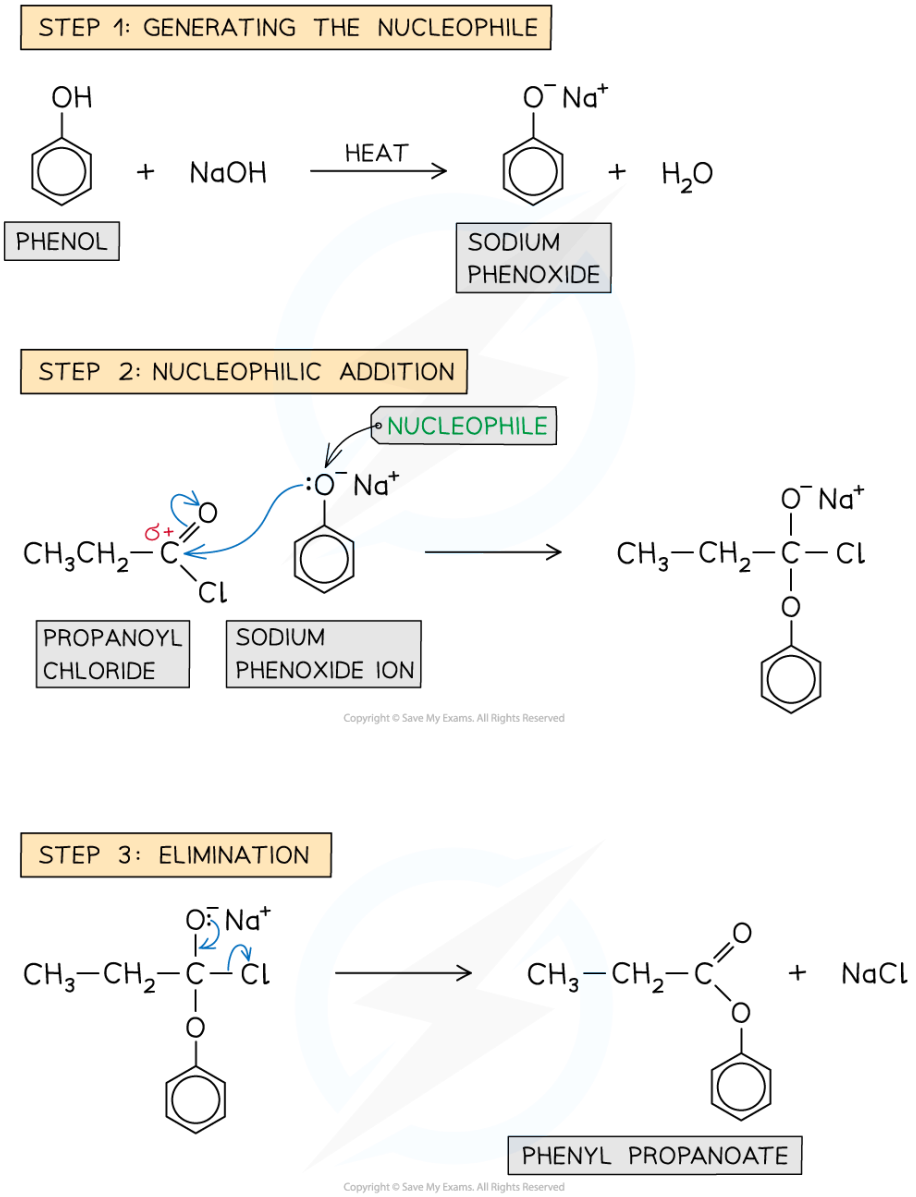
Reaction mechanism of the esterification of acyl chlorides with alcohols



The two-step addition-elimination reaction mechanism of propanoyl chloride and ethanol to form ethyl propanoate and water

Reaction mechanism of the esterification of acyl chlorides with phenols



The three-step addition-elimination reaction mechanism of propanoyl chloride with phenol to form phenyl propanoate

Formation of amides: reaction mechanism

- The nitrogen atom in **ammonia** and **primary/secondary amines** act as a **nucleophile**
  - The lone pair of the nitrogen atom carries out an **initial** attack on the carbonyl carbon
  - This is followed by the elimination of an HCl molecule
- Both reactions of acyl chlorides with ammonia and amines are **vigorous** however there are also differences
  - With **ammonia** - The product is a **non-substituted amide** and **white fumes** of HCl are formed

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- With **amines** – The product is a **substituted amide** and the HCl formed reacts with the **unreacted amine** to form a **white organic ammonium salt**

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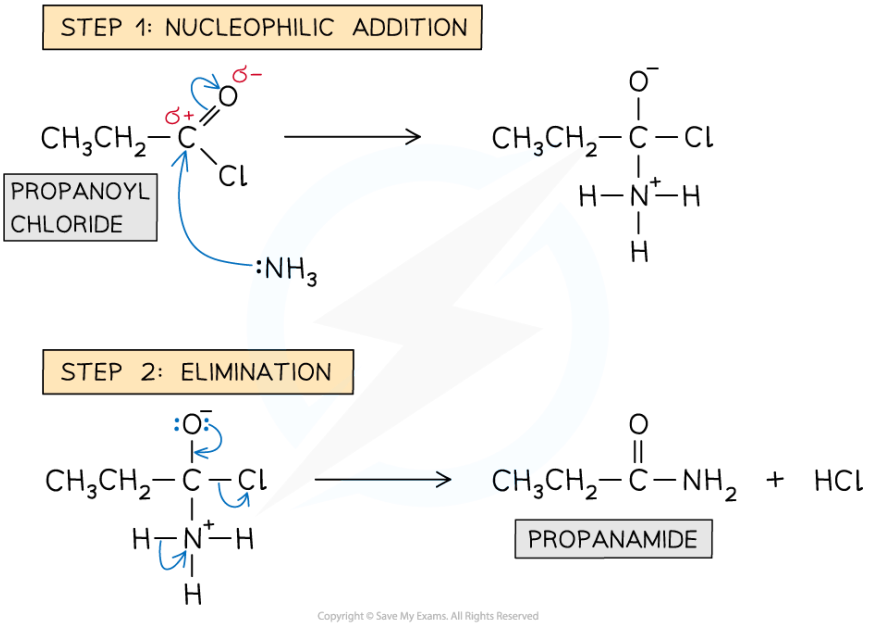
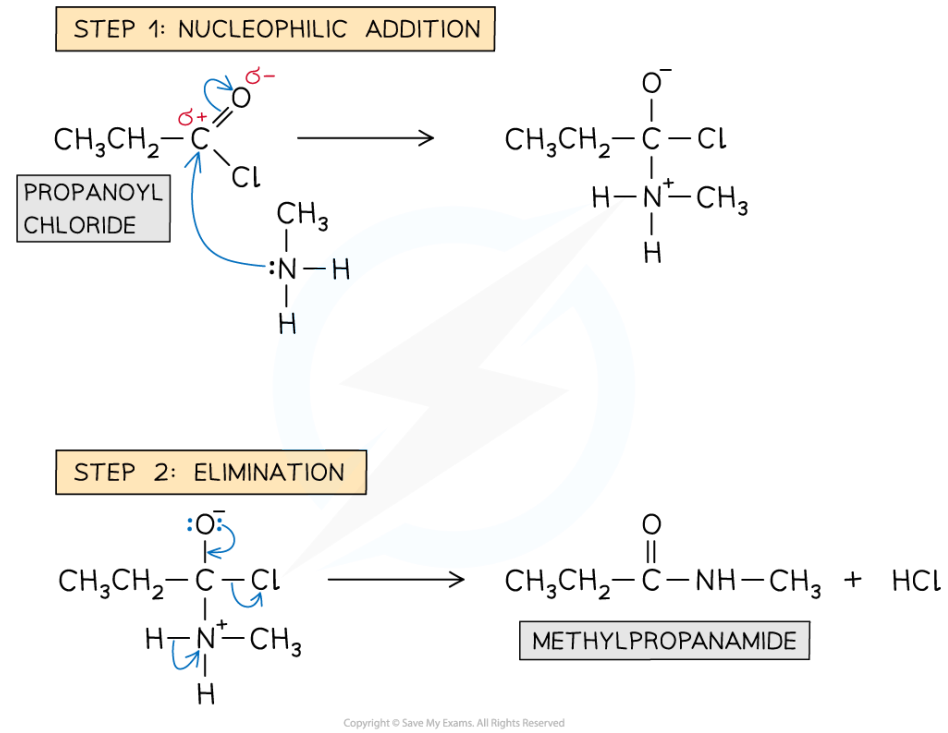
Reaction mechanism of the formation of amides from acyl chlorides with ammonia



The two-step addition-elimination reaction mechanism of propanoyl chloride and ammonia to form propanamide

Reaction mechanism of the formation of amides from acyl chlorides with primary amines



The addition-elimination reaction mechanism of propanoyl chloride and methylamine to form methylpropanamide

Reaction mechanism of the formation of amides from acyl chlorides with secondary amines

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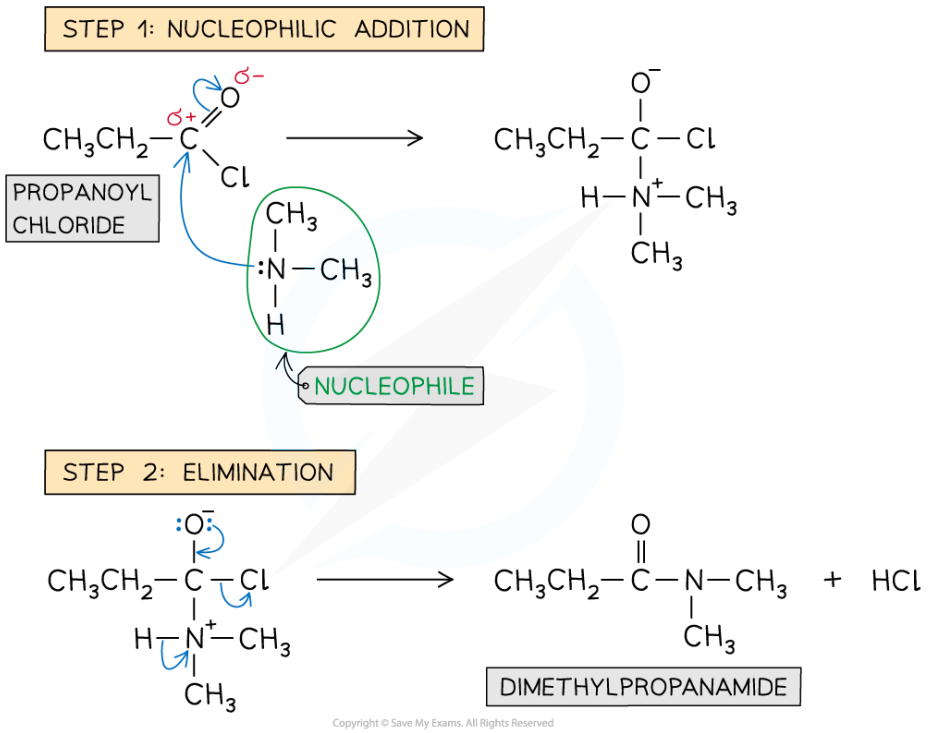

The addition-elimination reaction mechanism of propanoyl chloride and dimethylamine to form dimethylpropanamide

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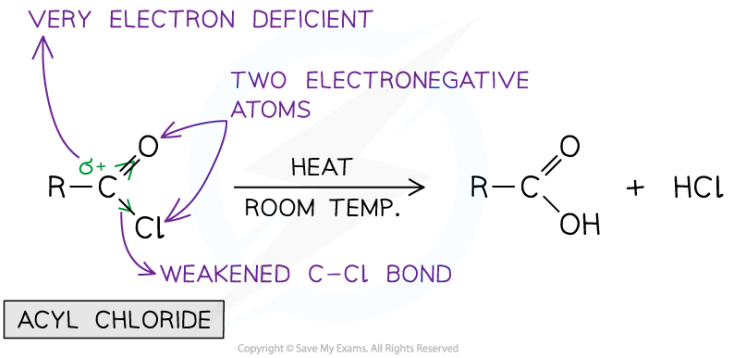
Hydrolysis of Acyl Chlorides, Alkyl Chlorides & Halogenoarenes

- **Hydrolysis** is the breakdown of a compound using **water**
- The ease of hydrolysis for different organic compounds may differ
- For example, the ease of hydrolysis, starting with the compounds most readily broken down, is: acyl chloride > alkyl chloride > aryl chloride
- This trend can be explained by looking at the **strength** of the C-Cl

Strength of C-Cl bond in acyl chlorides

- Acyl chlorides are hydrolysed most readily at **room temperature**
- This is because the carbon bonded to the chlorine atom is also attached to an oxygen atom
- There are two **strong electronegative** atoms pulling electrons away from the carbonyl carbon, leaving it very **δ^+**
- The C-Cl bond is therefore **weakened** and **nucleophilic attack** of the carbonyl carbon is much more **rapid**

Hydrolysis of acyl chlorides



The hydrolysis of acyl chlorides occurs most readily

Strength of C-Cl bond in alkyl chlorides

- The carbonyl carbon in alkyl chlorides is only attached to **one electronegative** atom which pulls electrons away from it
- This carbon atom is therefore not very **δ^+** and the C-Cl bond is stronger than the C-Cl bond in acyl chlorides

- The hydrolysis of alkyl chlorides, therefore, requires a **strong alkali** (such as OH^-) to be **refluxed** with it
- An OH^- ion will hydrolyse the alkyl chloride as it is a **stronger nucleophile** than H_2O

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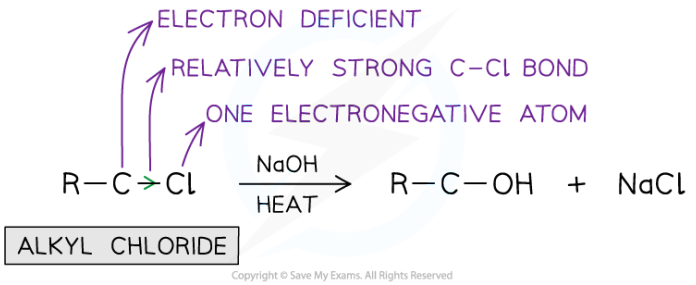
Hydrolysis of alkyl chlorides

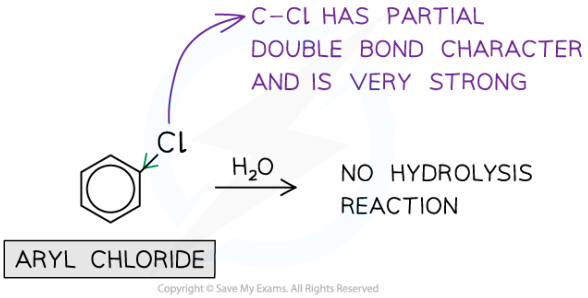


The hydrolysis of alkyl chlorides requires a strong nucleophile

Strength of C-Cl bond in aryl chlorides

- In aryl chlorides, the carbon atom bonded to the chlorine atom is part of the **delocalised π bonding system** of the benzene ring
- One of the lone pairs of electrons of the Cl atom **overlaps** with this **delocalised** system
- The C-Cl bond, therefore, has some **double-bond character** causing it to become **stronger**
- As a result, the C-Cl bond is difficult to break and **hydrolysis** will **not occur**

Hydrolysis of aryl chlorides



Due to the strong C-Cl bond in aryl chlorides, these compounds will not undergo hydrolysis