

# CIE A Level Chemistry



Your notes

## 7.6 Nitrogen Compounds (A Level Only)

### Contents

- \* 7.6.1 Production of Amines
- \* 7.6.2 Production of Amides
- \* 7.6.3 Basicity of Amines
- \* 7.6.4 Production & Reactions of Phenylamine
- \* 7.6.5 Relative Basicity of Ammonia, Ethylamine & Phenylamine
- \* 7.6.6 Azo Compounds
- \* 7.6.7 Reactions of Amides
- \* 7.6.8 Relative Basicity of Amides & Amines
- \* 7.6.9 Amino Acids
- \* 7.6.10 Peptide Bonds
- \* 7.6.11 Electrophoresis

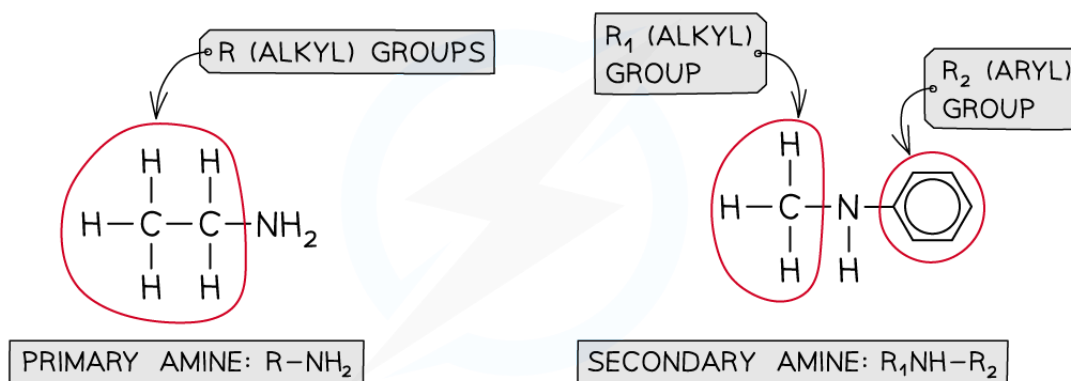


Your notes

## 7.6.1 Production of Amines

### Production of Primary & Secondary Amines

- **Primary amines** are organic compounds that have an  $\text{-NH}_2$  functional group attached to an alkyl or aryl group
- **Secondary amines** have two alkyl or aryl groups attached to an  $\text{-NH}$  group

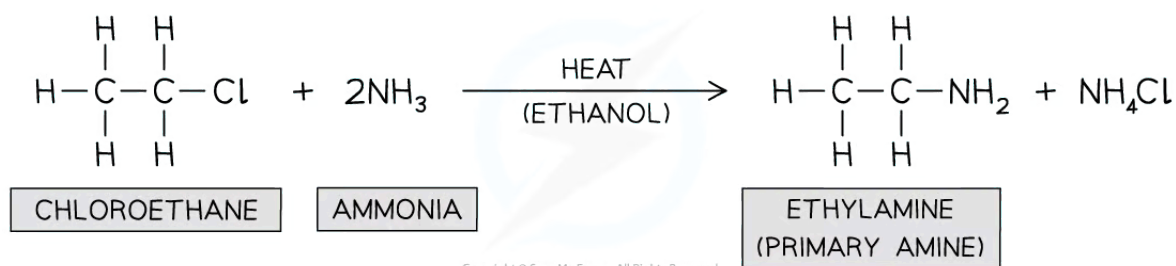


*Primary and secondary amines*

- Primary and secondary amines can be prepared from different reactions including:
  - The reaction of halogenoalkanes with ammonia
  - The reaction of halogenoalkanes with primary amines
  - The **reduction** of amides
  - The reduction of nitriles

#### Reaction of halogenoalkanes with ammonia

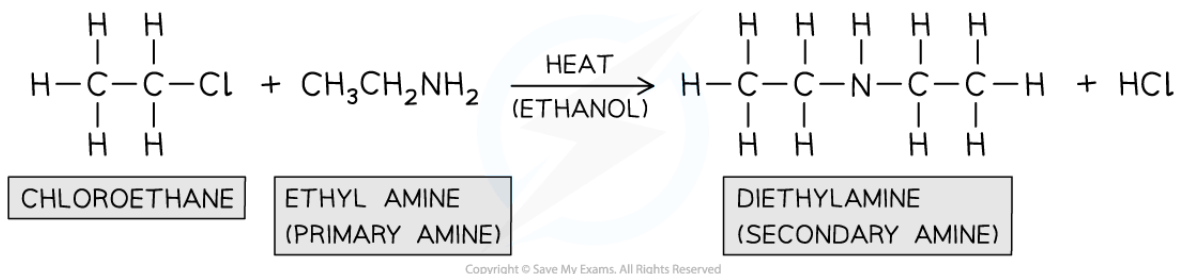
- This is a **nucleophilic substitution** reaction in which the nitrogen lone pair in ammonia acts as a **nucleophile** and **replaces** the halogen in the halogenoalkane
- When a halogenoalkane is reacted with **excess, hot ethanolic ammonia under pressure** a **primary amine** is formed



### Formation of primary amine

## Reaction of halogenoalkanes with primary amine

- This is also a **nucleophilic substitution** reaction in which the nitrogen in the primary amine acts as a **nucleophile** and **replaces** the halogen in the halogenoalkane
- When a halogenoalkane is reacted with a **primary amine** in **ethanol** and **heated in a sealed tube, under pressure** a **secondary amine** is formed



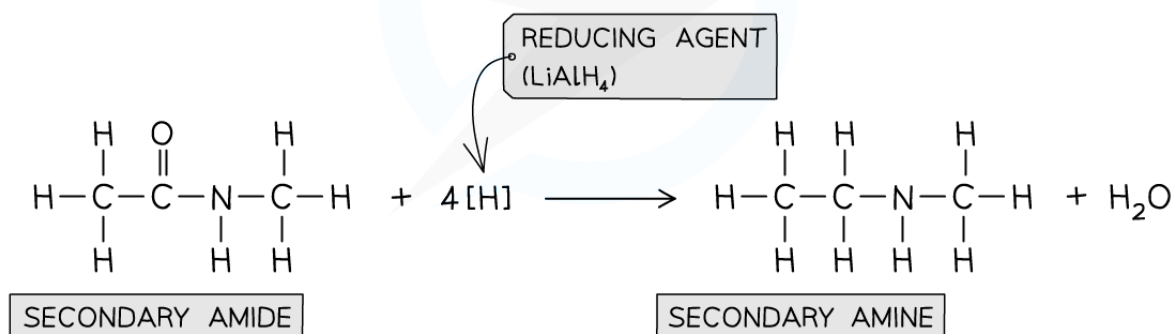
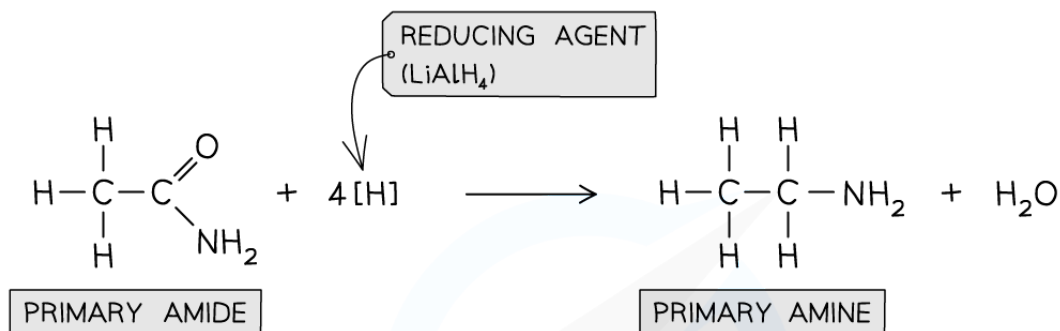
### Formation of secondary amine

## Reduction of amides

- Amines can also be formed from the **reduction** of **amides** by  $\text{LiAlH}_4$  in **dry ether**
- Whether a primary or secondary amine is formed depends on the nature of the amide



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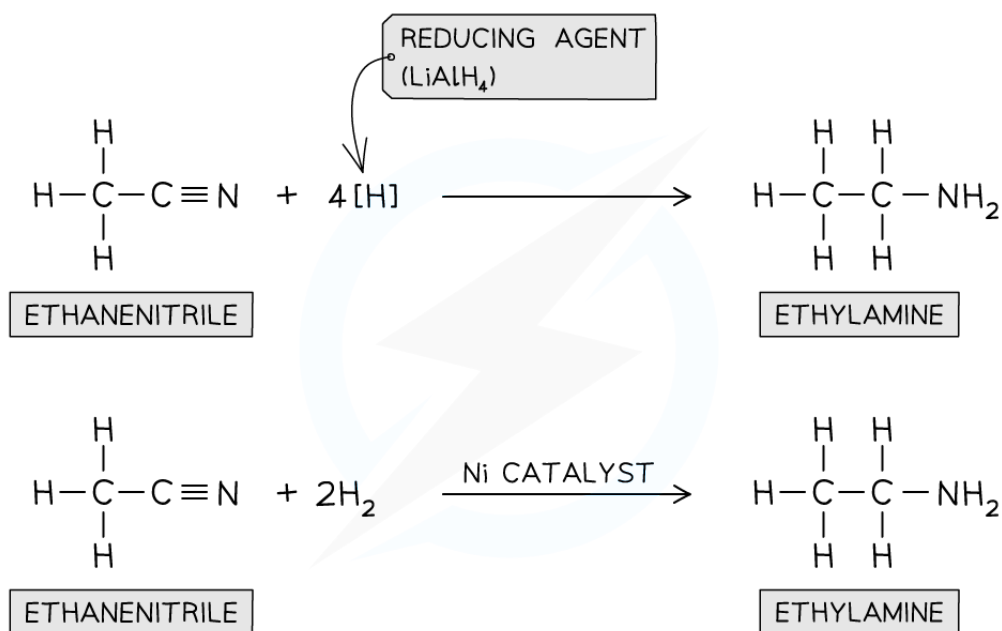
*Amides can be reduced by LiAlH<sub>4</sub> to form amines*

### Reduction of nitriles

- Nitriles contain a -CN functional group which can be **reduced** to an -NH<sub>2</sub> group
- The nitrile vapour and **hydrogen gas** are passed over a **nickel catalyst** or LiAlH<sub>4</sub> in **dry ether** can be used to form a **primary amine**



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***Nitriles can be reduced with LiAlH<sub>4</sub> or H<sub>2</sub> and Ni catalyst***



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## 7.6.2 Production of Amides

### Production of Amides

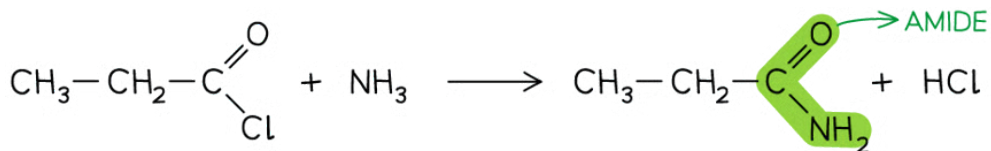
- **Amides** are organic compounds with an  $-\text{CONR}_2$  functional group
- They can be prepared from the **condensation reaction** between an **acyl chloride** and **ammonia** or **amine**
- In a **condensation** reaction, two organic molecules **join together** and in the process **eliminate** a small molecule
- In this case, the acyl chlorides and ammonia or amine **join together** to form an **amide** and **eliminate** an HCl molecule

### Condensation reaction

- The chlorine atom in acyl chlorides is **electronegative** and draws electron density from the carbonyl carbon
- The carbonyl carbon is therefore **electron-deficient** and can be attacked by **nucleophiles**
- The nitrogen atom in ammonia and amines has a lone pair of electrons which can act as a **nucleophile** and attack the carbonyl carbon
- As a result, the C-Cl bond is **broken** and an **amide** is formed
- Whether the product is a **substituted** amide or not, depends on the nature of the **nucleophile**
  - Primary and secondary amines will give a **substituted amide**
  - The reaction of acyl chlorides with ammonia will produce a **non-substituted amide**
- **Note** that amides can also be formed from the condensation reaction between **carboxylic acids** and ammonia or amines
- However, this reaction is **slower** as carboxylic acids are **less reactive** than **acyl chlorides** and the reaction doesn't go to completion

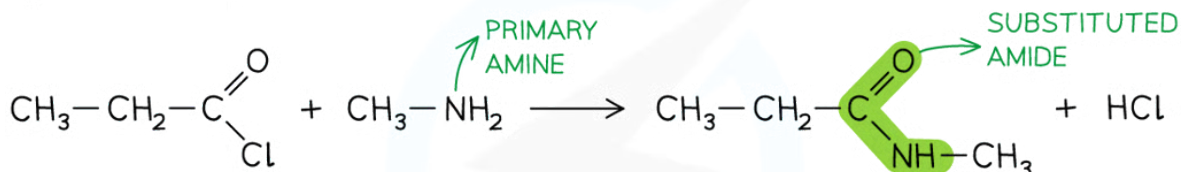


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 PROPANOYL  
CHLORIDE

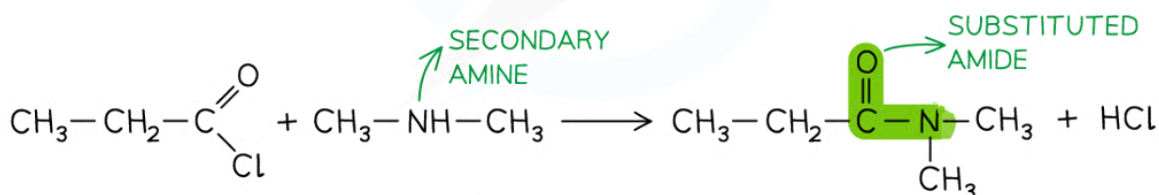
AMMONIA

PROPANAMIDE


 PROPANOYL  
CHLORIDE

METHYLAMINE

METHYL PROPANAMIDE


 PROPANOYL  
CHLORIDE

 DIMETHYL  
AMINE

DIMETHYL PROPANAMIDE

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**Acyl chlorides undergo condensation reactions with ammonia and amines to form amides**

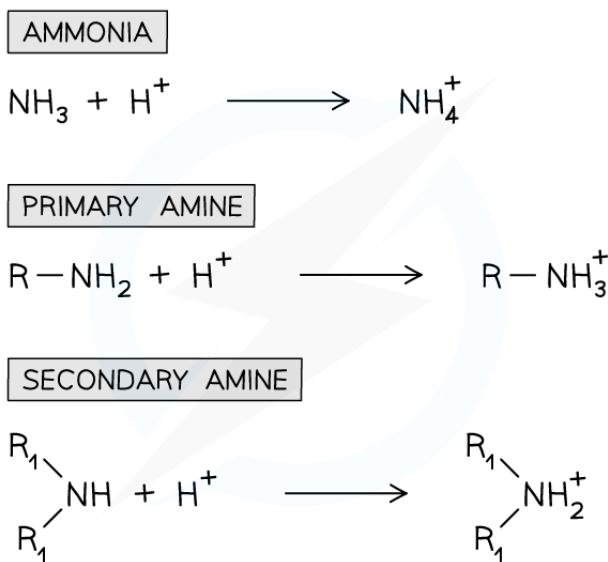
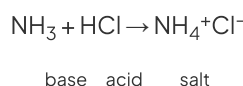


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## 7.6.3 Basicity of Amines

### Basicity of Aqueous Solutions of Amines

- The nitrogen atom in ammonia and amine molecules can **accept** a **proton** ( $\text{H}^+$  ion)
- They can therefore act as **bases** in aqueous solutions by **donating** its lone pair of electrons to a proton and form a **dative bond**
  - For example, ammonia undergoes an **acid-base** reaction with dilute hydrochloric acid (HCl) to form a salt



*The nitrogen atom in ammonia and amines can donate its lone pair of electrons to form a bond with a proton and therefore act as a base*

### Strength of ammonia and amines as bases

- The **strength** of amines depends on the **availability** of the lone pair of electrons on the nitrogen atom to form a dative covalent bond with a proton
- The **more readily** this lone pair of electrons is available, the **stronger the base** is
- Factors that may affect the **basicity** of amines include:
  - Positive inductive effect** - Some groups such as **alkyl groups** donate electron density to the nitrogen atom causing the lone pair of electrons to become more available and therefore

increasing the amine's **basicity**

- **Delocalisation** - The presence of aromatic rings such as the **benzene ring** causes the lone pair of electrons on the nitrogen atom to be **delocalised** into the benzene ring
- The lone pair becomes **less available** to form a dative covalent bond with ammonia and hence **decreases** the amine's **basicity**
- For example, ethylamine (which has an electron-donating ethyl group) is **more basic** than **phenylamine** (which has an electron-withdrawing benzene ring)



Your notes

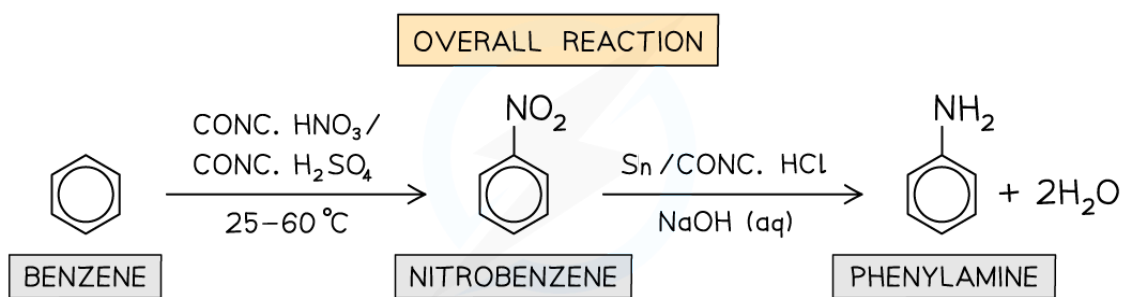


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## 7.6.4 Production & Reactions of Phenylamine

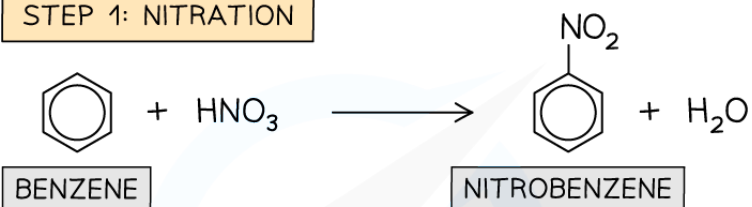
### Preparation of Phenylamine

- Phenylamine is an organic compound consisting of a benzene ring and an **amine** ( $\text{NH}_2$ ) functional group
- It can be produced in a **three-step synthesis** reaction followed by the separation of phenylamine from the reaction mixture
  - Step 1** – Benzene undergoes **nitration** with concentrated nitric acid ( $\text{HNO}_3$ ) and concentrated sulfuric acid ( $\text{H}_2\text{SO}_4$ ) at 25 to 60 °C to form **nitrobenzene**
  - Step 2** – Nitrobenzene is **reduced** with **hot tin** ( $\text{Sn}$ ) and **concentrated hydrochloric acid** ( $\text{HCl}$ ) **under reflux** to form an acidic mixture that contains the organic product  $\text{C}_6\text{H}_5\text{N}^+\text{H}_3$
  - Step 3** – Sodium hydroxide ( $\text{NaOH}$ ) is added to the acidic reaction mixture to form **phenylamine**
  - Step 4** – The phenylamine is separated from the reaction mixture by **steam distillation**



*The overall reaction of formation of phenylamine from benzene*

STEP 1: NITRATION

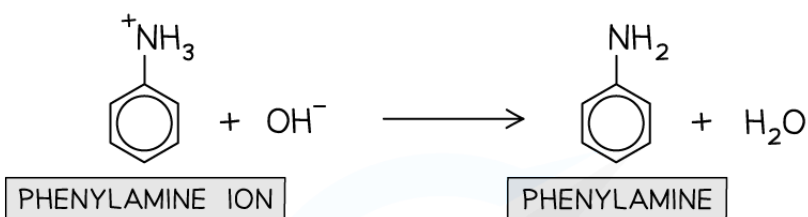


STEP 2: REDUCTION

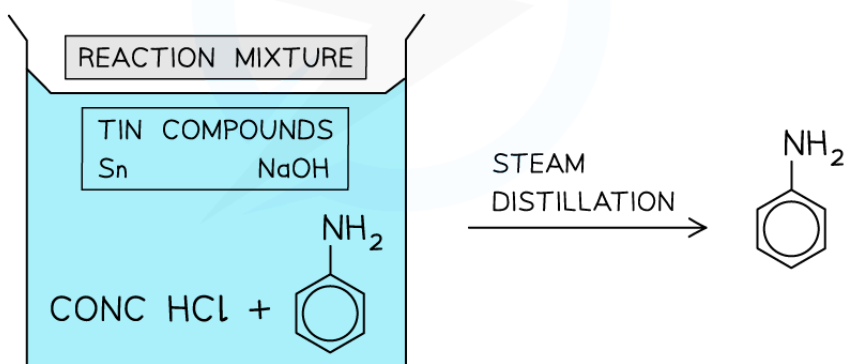


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STEP 3: DEPROTONATION



STEP 4: SEPARATION



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**Multi-step synthesis of phenylamine from benzene**



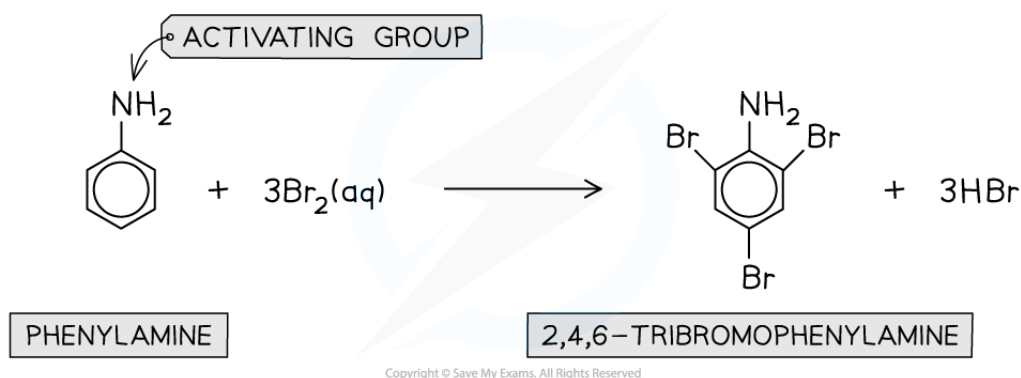
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## Reactions of Phenylamine

- Both the benzene ring as well as the  $\text{-NH}_2$  group in **phenylamine** can take part in chemical reactions
- These reactions include
  - The **bromination** of phenylamine
  - Formation of a **diazonium salt**

### Bromination of phenylamine

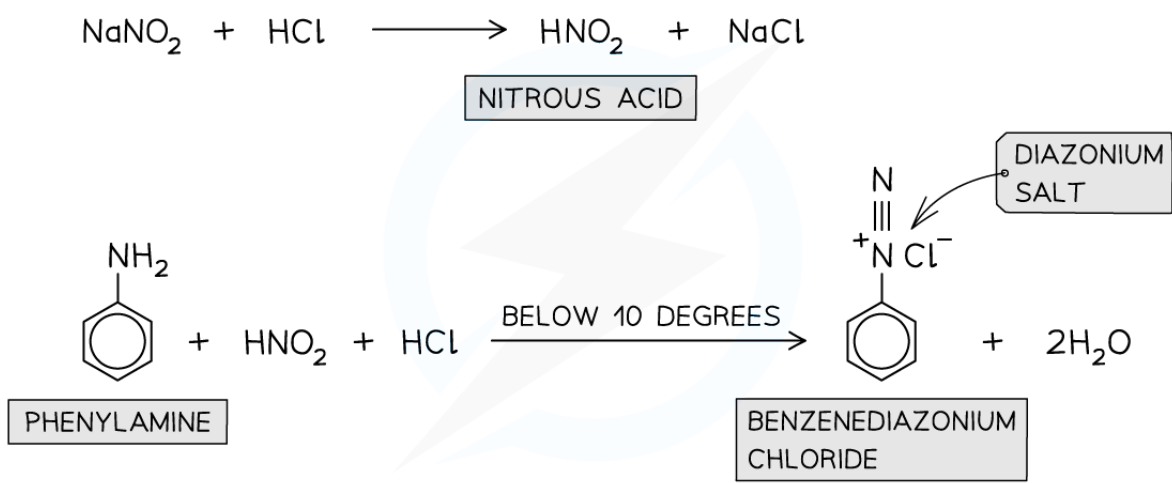
- Phenylamines react in **electrophilic substitution** reactions in a similar way as **phenols**
- The lone pair of electrons on the nitrogen atom in phenylamines donate electron density into the benzene ring
  - In phenols, the oxygen atom donates its lone pair of electrons instead
- The **delocalisation** of the electrons causes an **increased electron density** in the benzene ring
- The benzene ring, therefore, becomes **activated** and becomes more readily attacked by **electrophiles**
- The incoming electrophiles are directed to the 2,4 and 6 positions
- Phenylamines, therefore, react under milder conditions with **aqueous bromine** at **room temperature** to form 2,4,6-tribromophenylamine



***Bromination of phenylamines gives 2,4,6-tribromophenylamine***

### Formation of diazonium salt

- Diazonium** compounds are very reactive compounds containing an  $\text{-N}_2^+$  group
- The amine ( $\text{-NH}_2$ ) group of phenylamines will react with **nitrous acid** ( $\text{HNO}_2$ ) at a temperature below  $10^\circ\text{C}$  to form **diazonium salts**
  - Since nitric(III) acid is unstable, it has to be made in the **test-tube** by reacting sodium nitrite ( $\text{NaNO}_2$ ) and **dilute acid** (such as  $\text{HCl}$ )
- These **diazonium salts** are so unstable that they will upon further warming with water to form a **phenol**



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*Phenylamine can form an unreactive diazonium salt which thermally decomposes to a phenol*



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## 7.6.5 Relative Basicity of Ammonia, Ethylamine & Phenylamine

### Relative Basicity of Aqueous Ammonia, Ethylamine & Phenylamine

- Ammonia and amines act as **bases** as they can donate their lone pair of electrons to form a dative covalent bond with a proton
- The **basicity** of the amines depends on how readily available their lone pair of electrons is
- Electron-donating** groups (such as alkyl groups) increase the electron density on the nitrogen atom and cause the lone pair of electrons to become **more** available for dative covalent bonding
  - The amine becomes **more** basic
- Delocalisation** of the lone pair of electrons into an aromatic ring (such as a benzene ring) causes the lone pair of electrons to become **less** available for dative covalent bonding
  - The amine becomes **less** basic

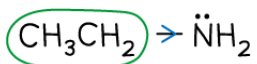
### Comparing basicity of ammonia, ethylamine & phenylamine

- The order of basicity of ammonia, ethylamine and phenylamine is as follows:



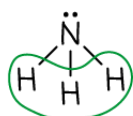
- This trend can be explained by looking at the groups attached to the amine ( $\text{-NH}_2$ ) group
- In ethylamine, the electron-donating alkyl group donates electron density to the nitrogen atom causing its lone pair to become more available to form a dative covalent bond with a proton
- Ammonia lacks an electron-donating group hence it is less basic than ethylamine however it is more basic than phenylamine as the lone pair on the nitrogen is **not delocalised**
- In phenylamine the lone pair of electrons overlap with the conjugated system on the benzene ring and become delocalised; As a result, the lone pair of electrons become less readily available to form a bond with a proton

ETHYLAMINE



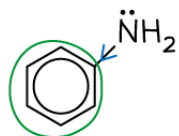
POSITIVE INDUCTIVE EFFECT ALKYL GROUP DONATES ELECTRON DENSITY TO THE N CAUSING ITS LONE PAIR OF ELECTRONS TO BECOME MORE AVAILABLE

AMMONIA



- NO ELECTRON DONATING GROUPS TO CAUSE POSITIVE INDUCTIVE EFFECT
- NO AROMATIC RINGS TO CAUSE DELOCALISATION OF NITROGEN'S LONE PAIR OF ELECTRONS

PHENYLAMINE



NITROGEN'S LONE PAIR OF ELECTRONS BECOMES DELOCALISED IN THE BENZENE RING AND IS THEREFORE LESS AVAILABLE TO FORM A DATIVE COVALENT BOND WITH  $\text{H}^+$

STRONGEST BASE



WEAKEST BASE

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*Trends in the basicity of ammonia, ethylamine, and phenylamine*

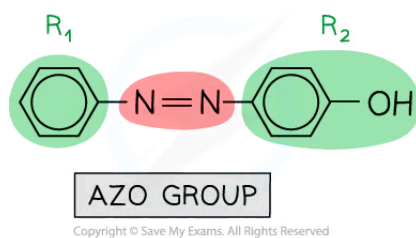
## 7.6.6 Azo Compounds



Your notes

### Azo Compounds

- **Azo (or diazonium) compounds** are organic compounds that have an  $R_1-N=N-R_2$  group
- They are often used as **dyes** and are formed in a **coupling reaction** between the **diazonium ion** and an **alkaline solution of phenol**



*Azo compounds are characterized by the presence of an  $R_1-N=N-R_2$  group*

### Coupling of benzenediazonium chloride with phenol in NaOH

- Azo compounds can be formed from the coupling reaction of a **benzenediazonium chloride salt** with **alkaline phenol**
- Making an azo dye is a **multi-step process**

Formation of azo compounds table

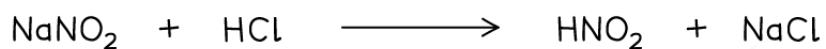


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Step	Description	Reaction Conditions
1 – Formation of nitrous acid	Nitrous acid is very unstable so has to be made in a test-tube using sodium nitrate ( $\text{NaNO}_2$ ) and hydrochloric acid ( $\text{HCl}$ )	N/A
2 – Diazotization	The reaction between nitrous acid and phenylamine to form the diazonium ion is called <b>diazotization</b>	The reaction mixture must be kept below $10^\circ\text{C}$ using ice as otherwise, the diazonium ion will <b>thermally decompose</b> to benzene and nitrogen ( $\text{N}_2$ ) Dilute acid (such as $\text{HCl}$ )
3 – Coupling reaction	The diazonium ion acts as an <b>electrophile</b> and substitutes into the benzene ring of the <b>phenol</b> at the 4 <sup>th</sup> position	Alkaline conditions are required to deprotonate the organic product and form the <b>azo compound</b>

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## STEP 1: FORMATION OF NITROUS ACID



NITROUS ACID

## STEP 2: DIAZOTIZATION

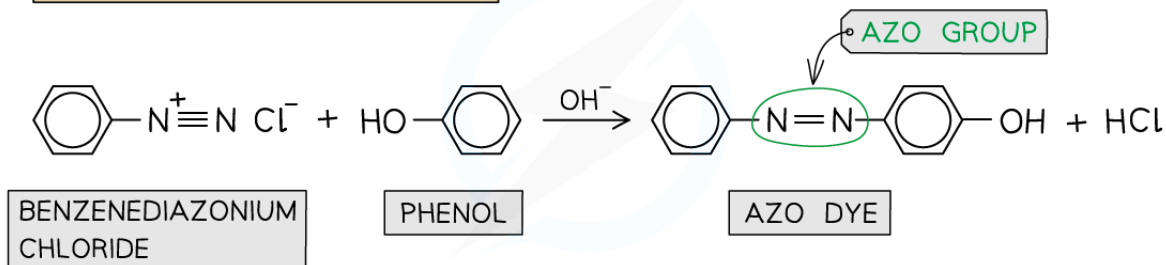


PHENYLAMINE

 BENZENEDIAZONIUM  
CHLORIDE

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## STEP 3: COUPLING REACTION



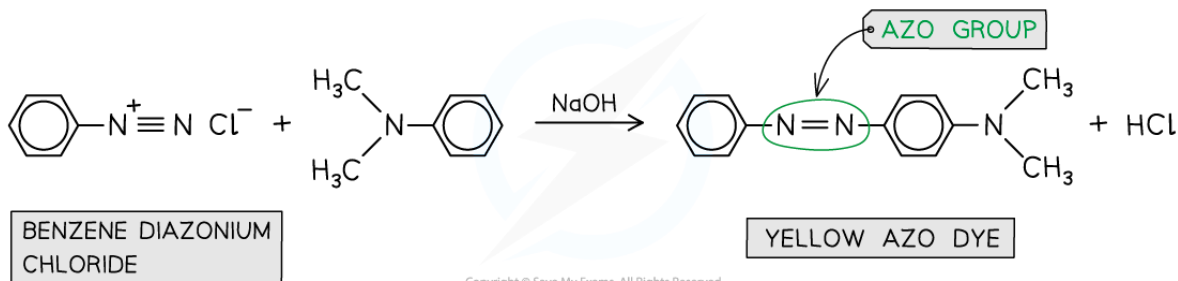
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**Reaction mechanism of the formation of azo compounds**

- The **delocalised** electrons in the  $\pi$  bonding systems of the two benzene rings are **extended** through the  $-N=N-$  which acts as a **bridge** between the two rings
- As a result of the delocalisation of electrons throughout the compound, azo compounds are **very stable**

**Making other azo dyes**

- Other dyes can be formed via a **similar route** as described above
- For example, the **yellow dye** can be formed from the **coupling reaction** between **benzenediazonium chloride** and  $C_6H_5N(CH_3)_2$  instead of phenol ( $C_6H_5OH$ )



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The yellow azo dye is formed via a coupling reaction between benzenediazonium chloride and  $C_6H_5N(CH_3)_2$



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## 7.6.7 Reactions of Amides

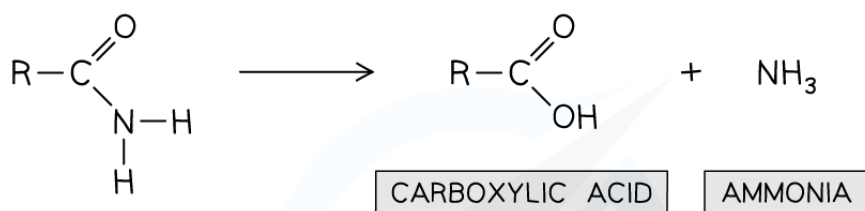
### Reactions of Amides

- Amides are formed from the **condensation reaction** of **carboxylic acids** or **acyl chlorides** with **ammonia** or **amines**
- The amide group ( $\text{CONR}_2$ ) in these compounds can undergo reactions including
  - Hydrolysis** with **aqueous alkali** or **aqueous acid**
  - Reduction** with  $\text{LiAlH}_4$

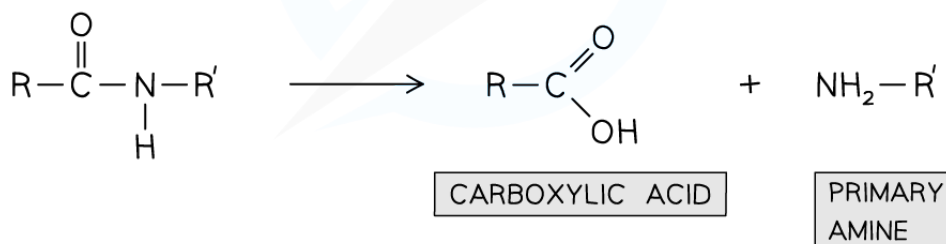
### Hydrolysis of amides

- The  $\text{-CON-}$  group in **substituted amides** links two hydrocarbon sections of their molecules together
- This amide link can be broken down by **hydrolysis** by **refluxing** it with an **acid** or **alkali**
- The products of a **non-substituted amide** are:
  - Carboxylic acid
  - Ammonia
- The products of a **substituted amide** are:
  - Carboxylic acid
  - Primary amine

#### NON-SUBSTITUTED AMIDE:

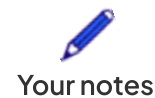


#### SUBSTITUTED AMIDE:

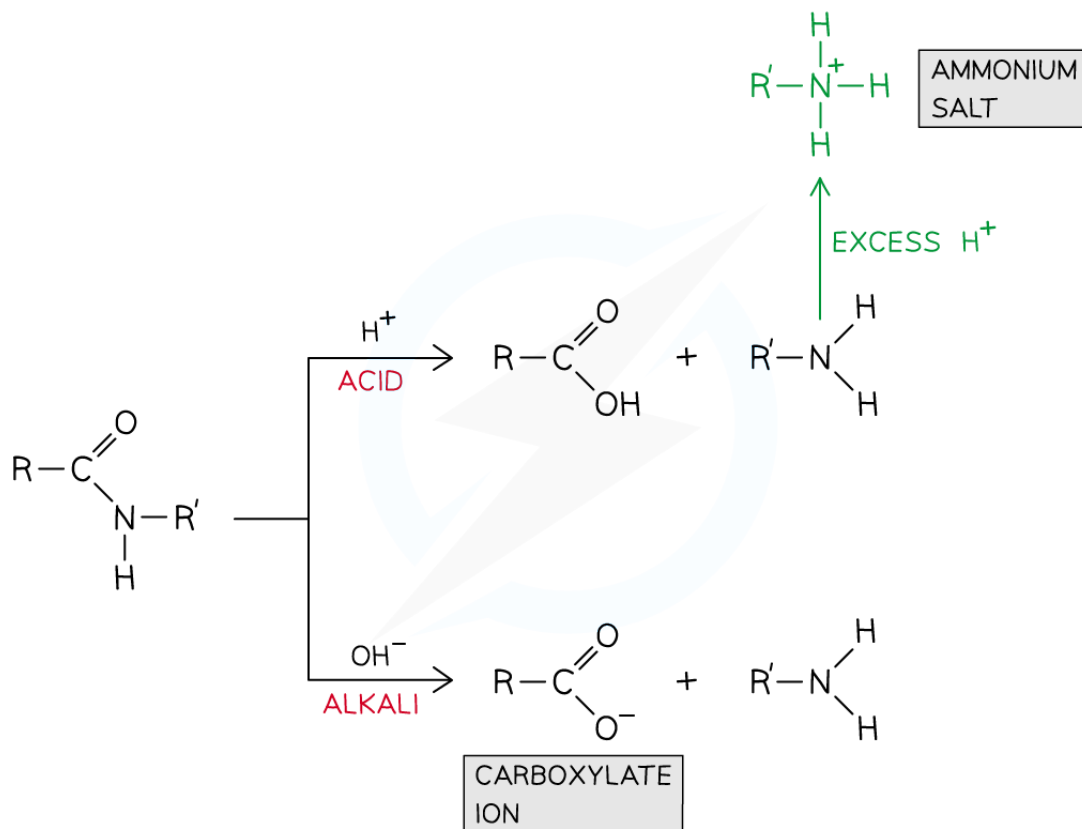


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### Hydrolysis of substituted and non-substituted amides



- Ammonia will react in **excess acid** to form an ammonium salt
- Carboxylic acid will get deprotonated in **excess base** to form a carboxylate ion



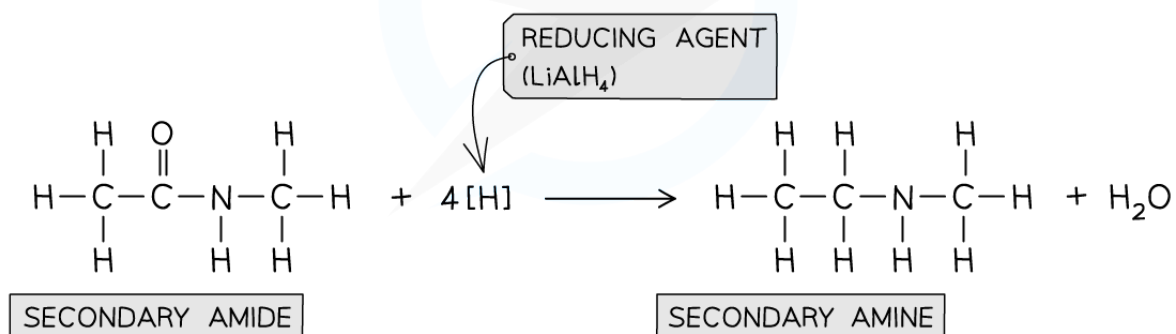
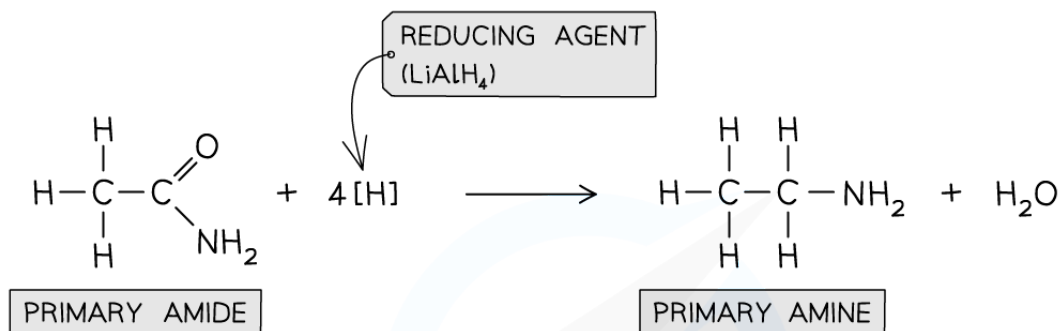
**Amides are hydrolysed to carboxylic acids and ammonia or primary amine when refluxed with acid or alkali**

### Reduction of amides

- The C=O group in amides can be **reduced** by the strong reducing agent  $\text{LiAlH}_4$  to form an amine
- The products of a **non-substituted amide** are:
  - A primary amine and water
- The products of a **substituted amide** are:
  - A secondary amine and water



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**Amides can be reduced to amines using LiAlH<sub>4</sub>**



Your notes

## 7.6.8 Relative Basicity of Amides & Amines

### Relative Basicity of Amides & Amines

- A **base** is a species that can **donate** its lone pair of electrons to form a **dative covalent bond** with another species
- **Amines** are basic as the **nitrogen** atom has a lone pair of electrons which can form a dative covalent bond with an electron-deficient species (such as an  $H^+$  ion)
- The **basicity** of the amine depends on the availability of this lone pair of electrons
  - The **more readily** available the lone pair of electrons is for dative covalent bonding, the **stronger the base**
  - The **less readily** available the lone pair of electrons is, the **weaker the base**
- **Electron-donating** groups such as alkyl groups **increase** the electron density on the nitrogen atom causing the lone pair to become more available
- **Electron-withdrawing** groups such as aromatic benzene rings, cause **delocalisation** of the lone pair of electrons which become less readily available
- This is why **phenylamine** (which contains an electron-withdrawing benzene ring) is a **weaker base** than **propylamine** (which contains an electron-donating alkyl group)

### Basicity of amides

- Amides also contain a nitrogen atom with a lone pair of electrons
- Again, the **basicity** of the amide depends on the availability of this lone pair for dative covalent bonding
- Due to the presence of the **electron-withdrawing** oxygen atom in the amide group, electron density is **removed** from the nitrogen atom
- The lone pair on the nitrogen atom, therefore, becomes **less readily** available and is not available to donate to an electron-deficient species
- Since this electron-withdrawing oxygen is characteristic of amides and is **not** present in amines, amides are **much weaker bases** than amines



Your notes

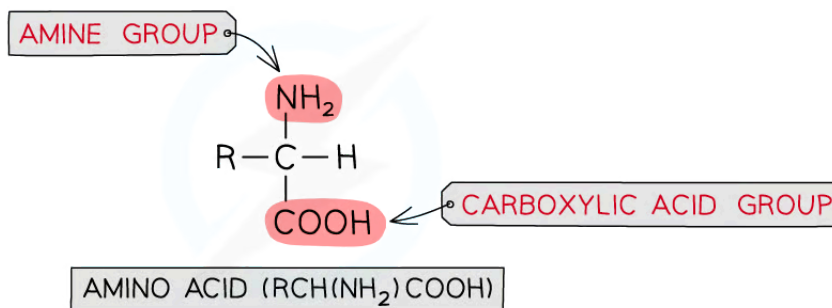
## 7.6.9 Amino Acids

### Acid / Base Properties of Amino Acids, Zwitterions & the Isoelectric Point

- **Amino acids** are **organic compounds** that contain two functional groups:
  - A basic **amino** ( $-\text{NH}_2$ ) group
  - An acidic **carboxylic acid** ( $-\text{COOH}$ ) group
- Due to the presence of both a **basic** and **acidic** group in amino acids, they are said to be **amphoteric**
  - They can act as both acids and bases

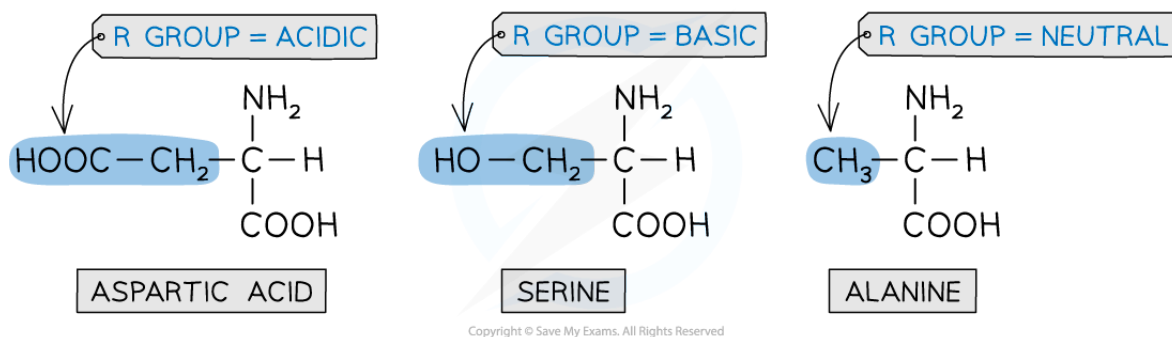
#### Naturally occurring amino acids

- **2-aminocarboxylic acids** are a type of amino acids in which the amine ( $-\text{NH}_2$ ) group is bonded to the carbon atom **next** to the  $-\text{COOH}$  group
- These type of amino acids form the 'building blocks' that make up **proteins**
- There are **20** naturally occurring amino acids with the general structural formula of  $\text{RCH}(\text{NH}_2)\text{COOH}$



#### General structural formula of amino acids

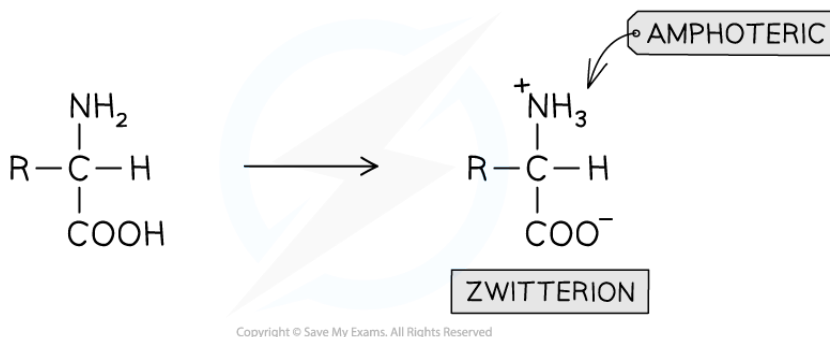
- The **R** group varies in different amino acids and can be:
  - Acidic
  - Basic
  - Neutral



*The R group varies in different amino acids*

### Acid / base properties of amino acids

- Amino acids will undergo most reactions of amines and carboxylic acids including acid-base reactions of:
  - Amines with acids
  - Carboxylic acids with bases
- However, they can also interact **intramolecularly** (within themselves) to form a **zwitterion**
- A zwitterion is an ion with both a **positive** ( $-\text{NH}_3^+$ ) and a **negative** ( $-\text{COO}^-$ ) charge
- Because of these charges in a zwitterion, there are **strong intermolecular forces of attraction** between amino acids
  - Amino acids are therefore **soluble crystalline solids**



*An amino acid molecule can interact within itself to form a zwitterion*

### Isoelectric point

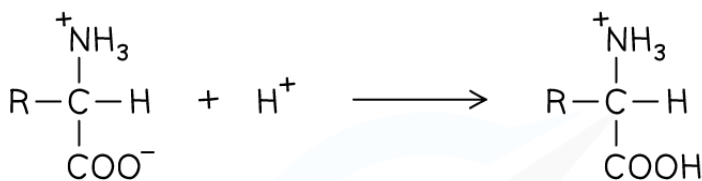
- A solution of amino acids in water will exist as **zwitterions** with both **acidic** and **basic** properties



Your notes

- They act as **buffer solutions** as they resist any changes in pH when **small** amounts of acids or alkali are added
- If an acid is added (and thus the pH is **lowered**):
  - The  $\text{-COO}^-$  part of the zwitterion will **accept** an  $\text{H}^+$  ion to reform the  $\text{-COOH}$  group
  - This causes the zwitterion to become a **positively charged ion**
- If a base is added (and thus the pH is **raised**):
  - The  $\text{-NH}_3^+$  part of the zwitterion will **donate** an  $\text{H}^+$  ion to reform the  $\text{-NH}_2$  group
  - This causes the zwitterion to become a **negatively charged ion**

INCREASE IN ACID (LOWERING pH)



ZWITTERION

POSITIVELY CHARGED ION

INCREASE IN BASE (RAISING pH)



ZWITTERION

NEGATIVELY CHARGED ION

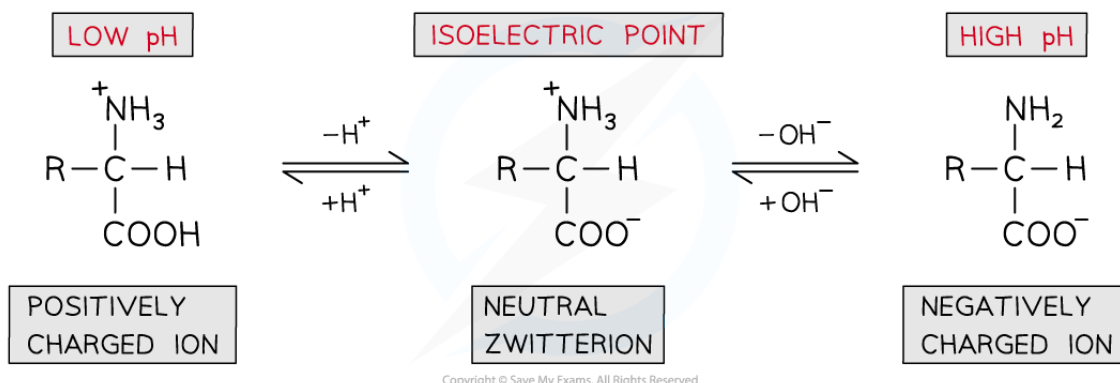
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**A solution of amino acids can act as a buffer solution by resisting any small changes in pH**

- The pH can be slightly adjusted to reach a point at which neither the **negatively charged** or **positively charged** ions dominate and the amino acid exists as a **neutral zwitterion**
  - This is called the **isoelectric point** of the amino acid



Your notes



**The isoelectric point of amino acids is the pH at which the amino acid exists as a neutral zwitterion**

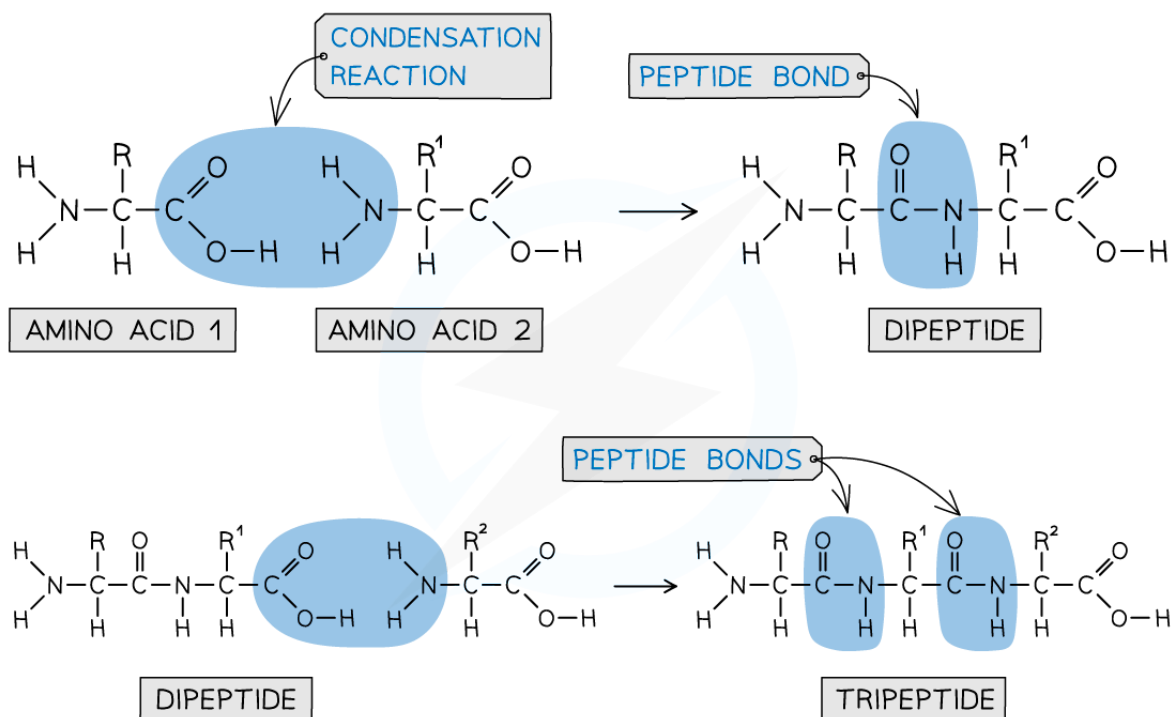


Your notes

## 7.6.10 Peptide Bonds

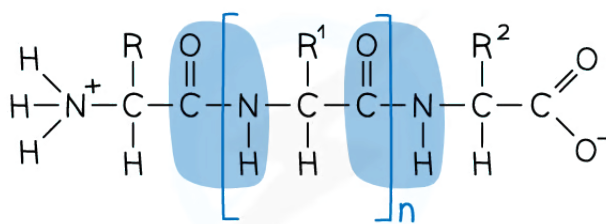
### Formation of Peptide Bonds

- Each amino acid contains an amine ( $\text{-NH}_2$ ) and carboxylic acid ( $\text{-COOH}$ ) group
- The  $\text{-NH}_2$  group of **one amino acid** can react with the  $\text{-COOH}$  group of **another amino acid** in a **condensation reaction** to form a **dipeptide**
  - The new **amide bond** between two amino acids is also called a **peptide link** or **peptide bond**
- Since this is a condensation reaction, a small molecule (in this case  $\text{H}_2\text{O}$ ) is **eliminated**
- The **dipeptide** still contains an  $\text{-NH}_2$  and  $\text{-COOH}$  group at each end of the molecule which can again participate in a condensation reaction to form a **tripeptide**



*A peptide bond is an amide bond between two amino acids*

- A **polypeptide** is formed when **many** amino acids join together to form a long chain of molecules



POLYPEPTIDE

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Your notes

*A polypeptide is a long chain of amino acid molecules joined together*



Your notes

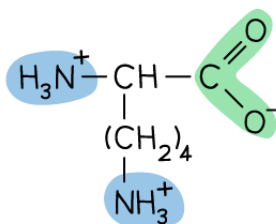
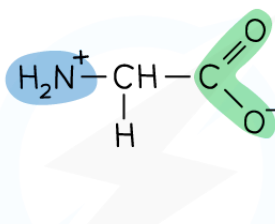
## 7.6.11 Electrophoresis

### Electrophoresis

- **Electrophoresis** is an **analytical technique** which separates ions by placing them in an electrical field
  - This method is often used in **biochemical analysis** to **identify** and **purify** proteins
- A sample of amino acids is placed between **two oppositely charged electrodes**
  - The positively charged ions will move towards the **negative electrode**
  - The negatively charged ions will move towards the **positive electrode**
- The **rate** (how fast) at which the ions move towards the electrodes depends on:
  - The **size** of the ions: larger ions move **more slowly**
  - The **charge** of the ions: highly charged ions move **more quickly**
- An **electropherogram** is the series of bands which are observed on the paper or gel after **electrophoresis** has occurred
  - Each band in the electropherogram corresponds to a particular species

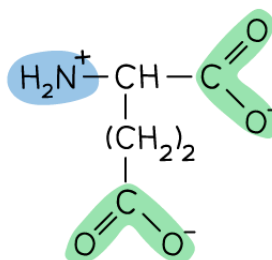
### Separating mixtures of amino acids by varying the pH

- The charge on the **amino acid ions** depends on the pH of the solution
- The movement of the ions to the electrodes during electrophoresis will therefore be affected by the pH
- Consider a sample which consists of a **mixture** of three amino acids at pH 7
  - Amino acid A: lysine, side-chain is **positively charged**
  - Amino acid B: glycine, side chain is **neutral**
  - Amino acid C: glutamic acid, side chain is **negatively charged**


 AMINO ACID A<sup>+</sup>


AMINO ACID B

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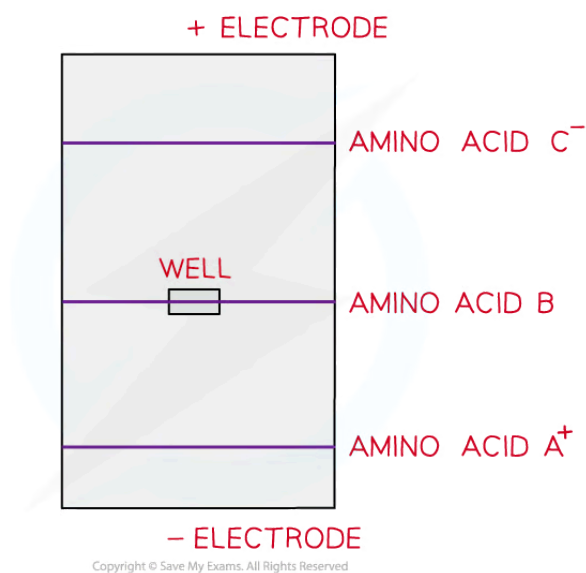

 AMINO ACID C<sup>-</sup>

The sample consists of a mixture of three amino acids which are separated using electrophoresis



Your notes

- The amino acids in this mixture can be separated by electrophoresis
  - Amino acid C will move towards the **positive** electrode
  - Amino acid B will remain in the **well** where the sample is applied to the gel
  - Amino acid A will move towards the **negative** electrode
- Since glutamic acid is **larger** than lysine, it will travel towards the positive electrode at a **slower rate** compared to lysine



**Separation of a mixture of amino acids by electrophoresis**