

## 20 Nitrogen compounds

### Primary Amines

#### Formation of amines

##### Forming a primary amine in a one step reaction of halogenoalkanes with ammonia

**Change in functional group:** halogenoalkane → amine

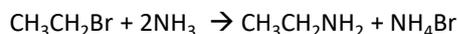
**Reagent:** NH<sub>3</sub> dissolved in ethanol

**Conditions:** Heating under pressure in a sealed tube

**Mechanism:** Nucleophilic Substitution

**Type of reagent:** Nucleophile, :NH<sub>3</sub>

Ammonia dissolved in ethanol is the initial nucleophile



Using an **excess of Ammonia** can limit the further subsequent reactions and will **maximise the amount of primary amine** formed

Primary amines can be formed by the **nucleophilic substitution** reaction between halogenoalkanes and ammonia in a **one step reaction**. However, as the lone pair of electrons is still available on the N in the amine formed, the primary amine can react in the same nucleophilic way in a successive series of reactions forming secondary, tertiary amines and quaternary ammonium salts.

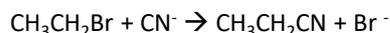
This is therefore not a good method for making a primary amine because of the further reactions. It would mean the desired product would have to be separated from the other products.

##### Preparing Amines from Nitriles

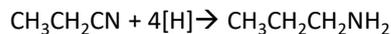
Using the method above of reacting halogenoalkanes and ammonia is not an efficient method for preparing a high yield of the primary amine because of the further substitution reactions that occur.

A better method is to use the following 2 step reaction scheme

Step 1. convert **halogenoalkane to nitrile** by using KCN in ethanol (heat under reflux)



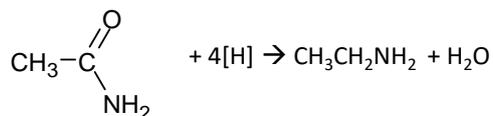
Step 2. reduce **nitrile to amine** by using **LiAlH<sub>4</sub> in ether** or by reducing with H<sub>2</sub> using a Ni catalyst



A disadvantage of this method is that it is a two step reaction that may therefore have a low yield. Also KCN is toxic.

##### Reduction of amides with LiAlH<sub>4</sub>

reduce an amide to amine by using **LiAlH<sub>4</sub> in ether**



This reaction is then followed by reaction with a dilute acid, such as dilute sulfuric or hydrochloric acid.

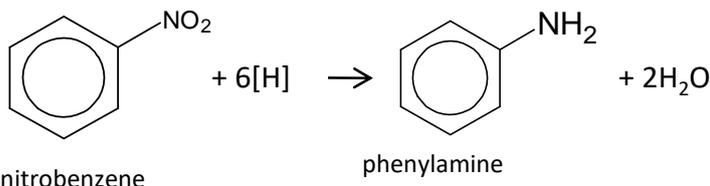
##### Reducing nitroarenes to aromatic amines

The nitro group on an arene can be reduced an amine group as follows

**Reagent:** Sn and HCl or Fe and HCl

**Conditions:** Heating

**Mechanism:** reduction



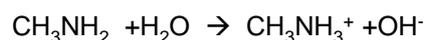
See the hydrocarbon chapter for how to form nitrobenzene from benzene.

As the reaction is carried out in HCl the salt C<sub>6</sub>H<sub>5</sub>NH<sub>3</sub><sup>+</sup>Cl<sup>-</sup> will be formed. Reacting this salt with NaOH will give phenylamine.

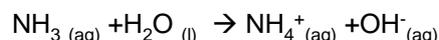


## Base Properties

Primary aliphatic amines act as Bronsted-Lowry Bases because the lone pair of electrons on the nitrogen is readily available for forming a dative covalent bond with a  $H^+$  and so accepting a proton.



Primary aliphatic amines are stronger bases than ammonia as the alkyl groups are electron releasing and push electrons towards the nitrogen atom and so make it a stronger base.

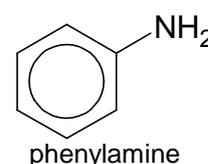


Secondary amines are stronger bases than primary amines because they have more alkyl groups that are substituted onto the N atom in place of H atoms. Therefore more electron density is pushed onto the N atom (as the inductive effect of alkyl groups is greater than that of H atoms).

One might expect using the same trend that tertiary amine would be the strongest amine base but the trend does not hold. The tertiary amines and corresponding ammonium salts are less soluble in water and this makes them less strong bases than the secondary amines. (This point will not be examined)

### Base strength of aromatic amines

Primary aromatic amines such as Phenylamine do not form basic solutions because the lone pair of electrons on the nitrogen delocalise with the ring of electrons in the benzene ring. This means the N is less able to accept protons.



### Overall order of base strength

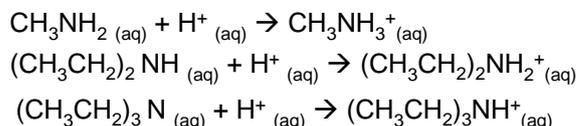
Aromatic amines < ammonia < primary amines < tertiary amines < secondary amines

**Weaker bases**

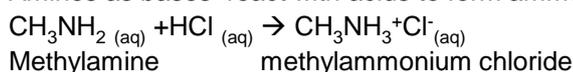
**Stronger bases**

### Reactions with acids

All amines will react with acids to become ammonium salts



Amines as bases react with acids to form ammonium salts.



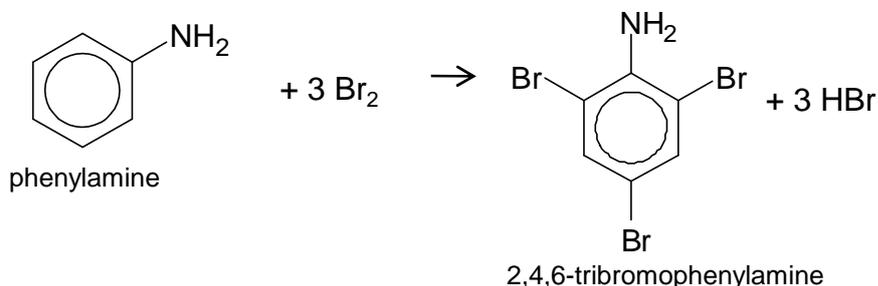
Addition of NaOH to an ammonium salt will convert it back to the amine

The ionic salts formed in this reaction means that the compounds are soluble in the acid.  
e.g. Phenylamine is not very soluble in water but phenylammonium chloride is soluble

These ionic salts will be solid crystals, if the water is evaporated, because of the strong ionic interactions.

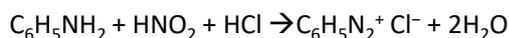
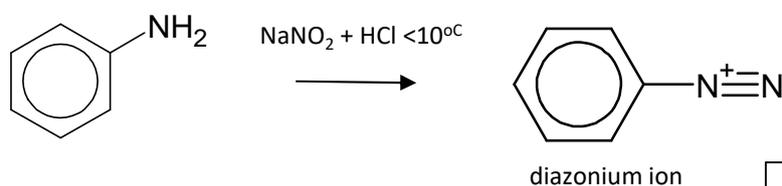
### Reaction of phenylamine with aqueous bromine

The lone pair of electrons on the nitrogen in the amine group delocalise with the ring of electrons in the benzene ring. This makes the benzene ring more reactive. Phenylamine reacts with aqueous bromine at room temperature. (Remember Benzene would not do this)



### Synthesis of azo dyes

Step 1: reaction of an aromatic amine with **nitrous acid, HNO<sub>2</sub>**, at **<10 °C**, forming a diazonium ion,

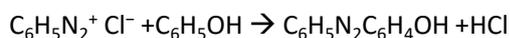
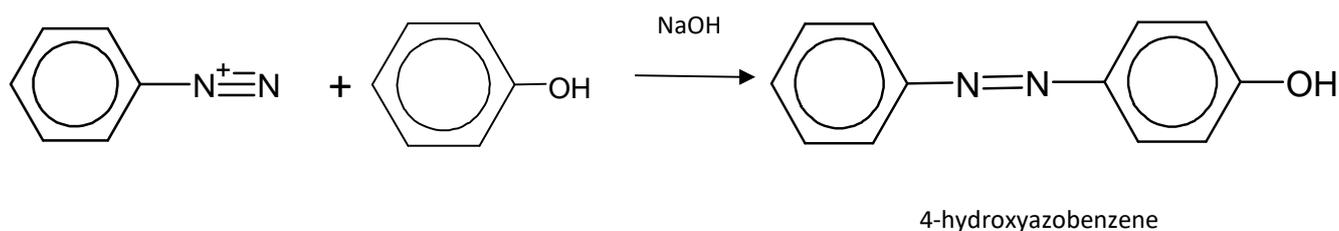


Nitrous acid is generated *in situ* from NaNO<sub>2</sub>/HCl.

Below 0°C the temperature is too low and the reaction would be too slow

If the diazonium ion is allowed to heat above 10°C it reacts with water to form phenol and N<sub>2</sub> gas  
 $\text{C}_6\text{H}_5\text{N}_2^+ + \text{H}_2\text{O} \rightarrow \text{C}_6\text{H}_5\text{OH} + \text{N}_2 + \text{H}^+$   
If this reaction is wanted then heat the diazonium ion

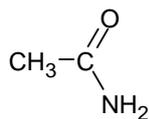
Step 2: coupling of diazonium ion with a **phenol under alkaline conditions**;



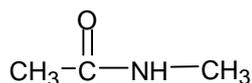
Azo dyes are used for dyes, pigments and colourings

## Amides

Amides are neutral



Primary amide  
ethanamide



Secondary amide  
N-methylethanamide

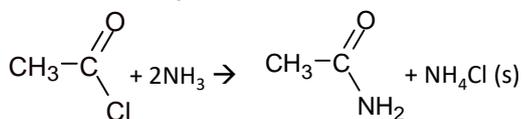
## Formation of amides

### Reaction of acyl chloride with ammonia

Change in functional group: **acyl chloride** → **primary amide**

Reagent: **ammonia**

Conditions: **room temp.**



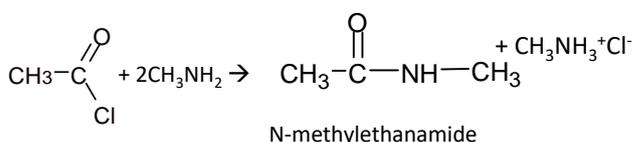
Observation: white smoke of  $\text{NH}_4\text{Cl}$  is given off

### Reaction of acyl chloride with primary amines

Change in functional group: **acyl chloride** → **secondary amide**

Reagent: **primary amine**

Conditions: **room temp.**

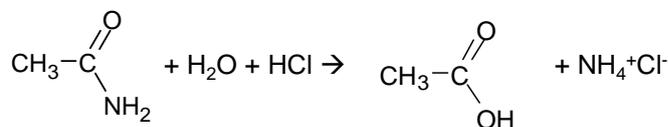


### Amide hydrolysis

primary amides can be hydrolysed by aqueous acids or alkalis.

With HCl an amide will be hydrolysed and split up into a carboxylic acid and an ammonium salt

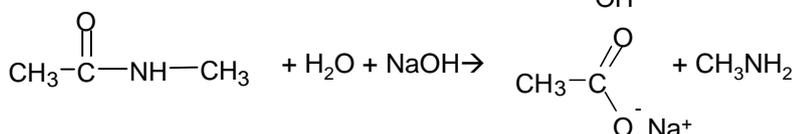
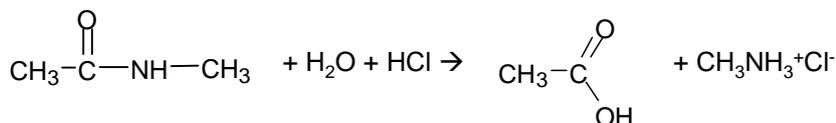
With NaOH an amide will be hydrolysed and split up into ammonia and the carboxylic acid salt



Secondary amides can be hydrolysed by aqueous acids or alkalis.

With HCl an amide will be hydrolysed and split up into a carboxylic acid and an amine salt

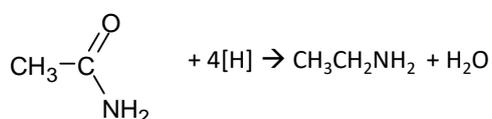
With NaOH an amide will be hydrolysed and split up into the amine and the carboxylic acid salt



### Reduction of amides with $\text{LiAlH}_4$

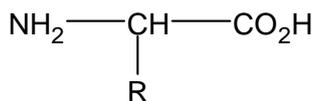
reduce an amide to amine by using  **$\text{LiAlH}_4$  in ether**

This reaction is then followed by reaction with a dilute acid, such as dilute sulfuric or hydrochloric acid.



## Amino Acids

### General structure of an amino acid



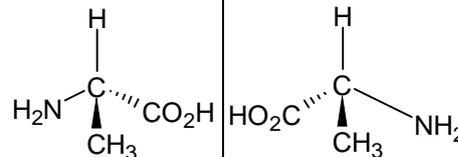
The R group can be a variety of different things depending on what amino acid it is.

The alpha in 'α' amino acid means both NH<sub>2</sub> and COOH groups are joined to the same C.

The simplest amino acid is glycine, where the R is an H  $\text{NH}_2 - \text{CH}_2 - \text{CO}_2\text{H}$

### Optical Activity

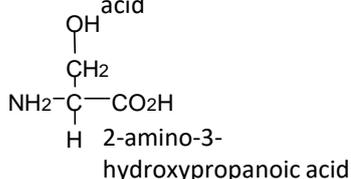
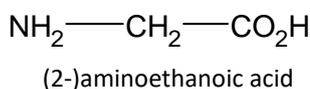
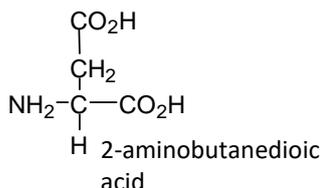
All amino acids, except glycine, are chiral because there are four different groups around the C



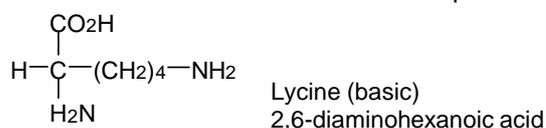
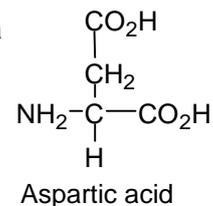
They rotate plane polarised light.

### Naming amino acids

You do not need to know any common names for the 20 essential amino acids. You should, however, be able to name given amino acids using IUPAC organic naming



Some amino acids have an extra carboxylic acid or an amine group on the R group. These are classed as acidic or basic (respectively) amino acids

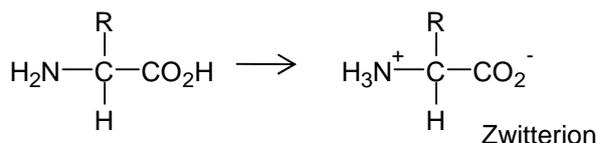


### Zwitterions

The no charge form of an amino acid never occurs. The amino acid exists as a dipolar zwitterion.

Amino acids are often **solids**

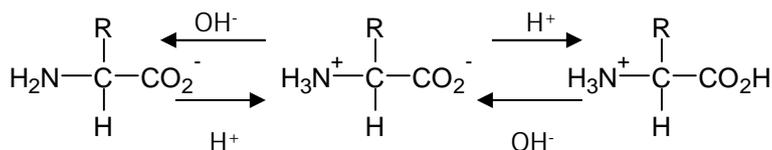
The **ionic interaction** between zwitterions explains the relatively high melting points of amino acids as opposed to the weaker hydrogen bonding that would occur in the no charge form.



### Acidity and Basicity

The amine group is basic and the carboxylic acid group is acidic.

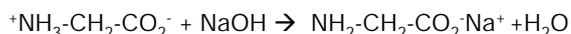
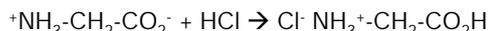
Amino acids act as weak buffers and will only gradually change pH if small amounts of acid or alkali are added to the amino acids.



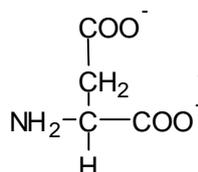
**Species in alkaline solution**  
High pH

**Species in neutral solution**

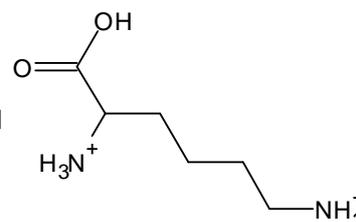
**Species in acidic solution**  
Low pH



The extra carboxylic acid or amine groups on the R group will also react and change form in alkaline and acid conditions



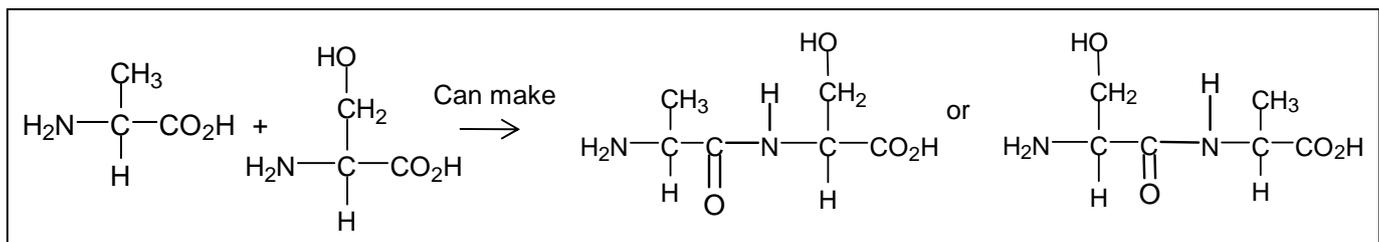
Skeletal formula of lycine in low pH



## Dipeptides

Dipeptides are simple combination molecules of two amino acids with one amide (peptide) link.

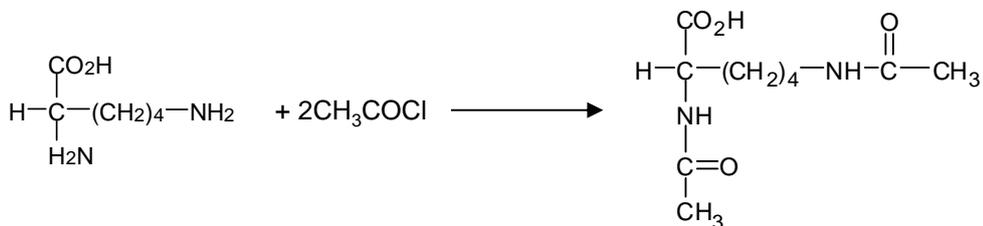
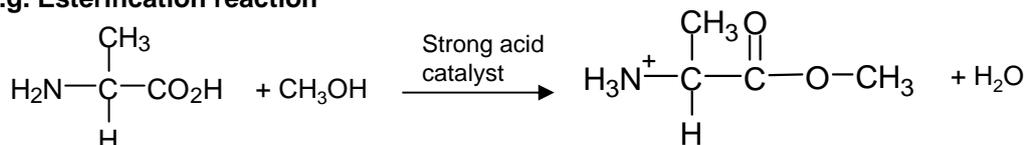
For any two different amino acids there are two possible combinations of the amino acids in the dipeptide.



### Other reactions of amino acids

The carboxylic acid group and amine group in amino acids can undergo the usual reactions of these functional groups met in earlier topics. Sometimes questions refer to these.

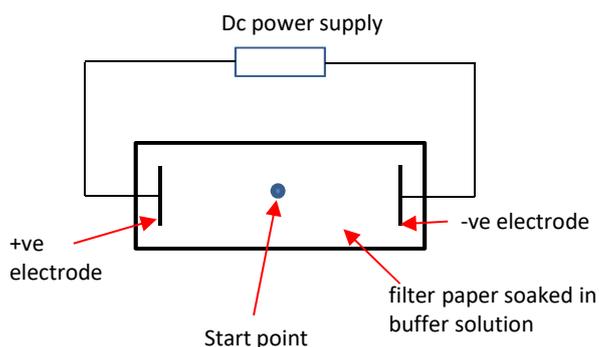
#### e.g. Esterification reaction



If the R group contains a amine or carboxylic acid then these will do the same reactions as the amine and carboxylic groups

## Electrophoresis of Amino Acids

A mixture of amino acids can be separated by electrophoresis



The mixture of amino acids is put at the start point.

A gel or filter paper soaked in a buffer solution is used.

The pH of the buffer solution makes a big difference to the results.

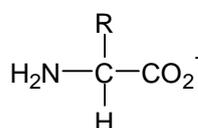
Amino acids are transparent and cannot be seen.

If ninhydrin is sprayed on an amino acid and then heated for 10 minutes then red to blue spots appear.

Different amino acids will move by different amounts depending on their size, charge and the pH of the buffer solution.

### If buffer is alkaline pH>7

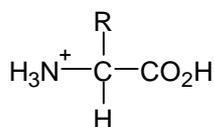
In alkaline conditions the amino acids will be negatively charged and therefore will move towards the positive plate



Amino acids with **smaller sized R** groups will move **further towards** the positive plate. If the R group contains a  $-\text{CO}_2\text{H}$  group (such as aspartic acid) then as it will have two  $\text{CO}_2^-$  groups. It will move further than if it was a similar sized neutral R group.

### If buffer is acidic pH<7

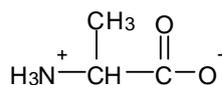
In acidic conditions the opposite will occur. The amino acids will be positively charged and therefore will move towards the negative plate



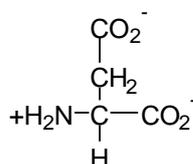
Amino acids with **smaller sized R** groups will move **further towards** the negative plate. If the R group contains a  $-\text{NH}_2$  group (such as lysine) then as it will have two  $\text{NH}_3^+$  groups. It will move further than if it was a similar sized neutral R group.

### If buffer is neutral pH=7

If an amino acid has a non-polar R group, it will exist in zwitterion form and it will not move.



If an amino acid has a R group that contains a  $-\text{CO}_2\text{H}$  group (such as aspartic acid) then as it will have two  $\text{CO}_2^-$  groups. It will move towards the positive plate



If an amino acid has a R group that contains a  $-\text{NH}_2$  group (such as lysine) then as it will have two  $\text{NH}_3^+$  groups. It will move towards the negative plate

