20 Nitrogen compounds

Many biological molecules contain nitrogen. This topic introduces the chemistry of a variety of organic compounds that contain nitrogen.

20.1 Primary Amines ☐

20.2 Amides ☐

NITROGEN COMPOUNDS

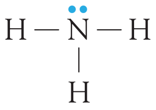
20 Nitrogen compounds

Many biological molecules contain nitrogen. This topic introduces the chemistry of a variety of organic compounds that contain nitrogen.

	Learning outcomes Candidates should be able to:
20.1 Primary amines	**a) describe the formation of alkyl amines such as ethylamine (by the reaction of ammonia with halogenoalkanes; the reduction of amides with $\mathrm{LiA}\ell\mathrm{H_4}$; the reduction of nitriles with $\mathrm{LiA}\ell\mathrm{H_4}$ or $\mathrm{H_2/Ni}$) and of phenylamine (by the reduction of nitrobenzene with tin/concentrated $\mathrm{HC}\ell$)** **b) describe and explain the basicity of amines** **c) explain the relative basicities of ammonia, ethylamine and phenylamine in terms of their structures** **d) describe the reaction of phenylamine with:** **(i) aqueous bromine** **(ii) nitrous acid to give the diazonium salt and phenol** **e) describe the coupling of benzenediazonium chloride and phenol and the use of similar reactions in the formation of dyestuff**
20.2 Amides	**a) describe the formation of amides from the reaction between $\mathrm{NH_3}$ or $\mathrm{RNH_2}$ and $\mathrm{R'COC}\ell$** **b) recognise that amides are neutral** **c) (i) describe amide hydrolysis on treatment with aqueous alkali or acid** **(ii) describe the reduction of amides with $\mathrm{LiA}\ell\mathrm{H_4}$**

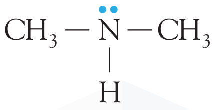
AMINES

Amines are nitrogen compounds in which one or more of the hydrogen atoms in ammonia, NH_3, is replaced by an alkyl or an aryl group.



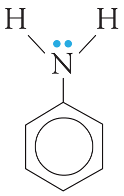
$$\mathrm{H-\underset{\underset{H}{|}}{\overset{\bullet\bullet}{N}}-H}$$

ammonia



$$\mathrm{CH_3-\underset{\underset{H}{|}}{\overset{\bullet\bullet}{N}}-CH_3}$$

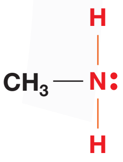
dimethylamine



phenylamine

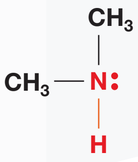
AMINES

The number of these groups determines whether the compound is a primary amine, a secondary amine or a tertiary amine.



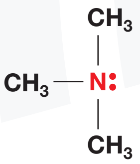
$$\mathrm{CH_3-\overset{\overset{H}{|}}{\underset{\underset{H}{|}}{N}}\colon}$$

methylamine
(a primary amine)



$$\mathrm{CH_3-\overset{\overset{CH_3}{|}}{\underset{\underset{H}{|}}{N}}\colon}$$

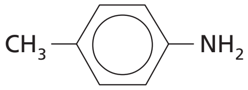
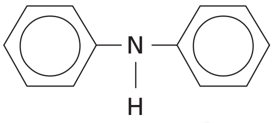
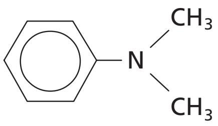
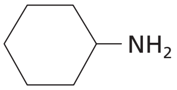
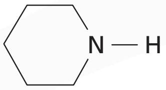
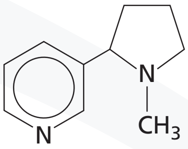
dimethylamine
(a secondary amine)



$$\mathrm{CH_3-\overset{\overset{CH_3}{|}}{\underset{\underset{CH_3}{|}}{N}}\colon}$$

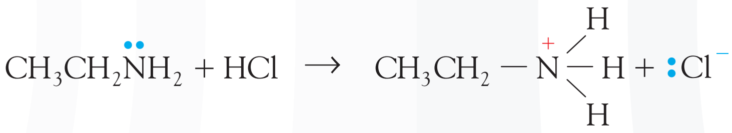
trimethylamine
(a tertiary amine)

AMINES

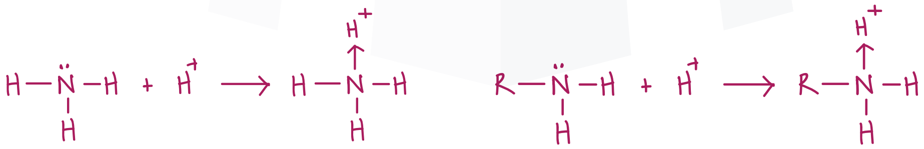
Primary amines	Secondary amines	Tertiary amine
$CH_3CH_2NH_2$ ethylamine	$(CH_3CH_2)_2NH$ diethylamine	$(CH_3CH_2)_3N$ triethylamine
 4-methylphenylamine	 diphenylamine	 *N*,*N*-dimethylphenylamine
 cyclohexylamine	 piperidine	 nicotine

BASICITY

Amines are basic. They react with acids to form salts (just like ammonia):



$$\mathrm{CH_3CH_2\ddot{N}H_2 + HCl \rightarrow CH_3CH_2-\overset{+}{N}H_3 + :Cl^-}$$



$$\mathrm{H-\ddot{N}(H)-H + H^+ \rightarrow H-N(\leftarrow H^+)(H)-H \qquad R-\ddot{N}(H)-H + H^+ \rightarrow R-N(\leftarrow H^+)(H)-H}$$

BASICITY

A base (Brønsted–Lowry) is a proton acceptor. Thus, when a base is put into water it accepts a proton from water:

$$B: \quad + \quad H_2O \quad \longrightarrow \quad HB^+ \quad + \quad OH^-$$

The more the position of equilibrium lies to the right, the stronger the base.

Methylamine reacts with water to form the methylammonium ion:

$$CH_3CH_2NH_2 \quad + \quad H_2O \quad \longrightarrow \quad CH_3CH_2NH_3^+ \quad + \quad OH^-$$

BASICITY

In amines, the N is the most electronegative atom and will have a small negative charge.

H^+ ions will thus be attracted to the N and the lone pair of electrons will be used to form a dative covalent bond to the H^+.

Basicity depends on the availability of the lone pair of electrons on nitrogen to form a dative bond with a proton, H^+.

In general, the greater the negative charge on the N the more it will attract H^+ ions and the stronger base it will be.

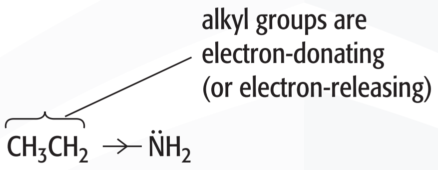
BASICITY OF ALKYL AMINES

Alkyl groups attached to the nitrogen atom increase the basicity of amines.

Electron donation from an alkyl group will encourage dative bond formation.

Alkyl groups are electron-releasing (positive inductive effect) and so will push electron density onto the N, making it more negative and therefore more likely to attract H^+ and form a dative bond.

E.g., Ethylamine, $CH_3CH_2NH_2$, is a stronger base than ammonia.

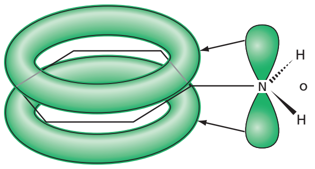


BASICITY OF PHENYL AMINE

Phenyl amine is a weaker base than ammonia.

This is because in phenylamine, the lone pair of electrons on the nitrogen atom is delocalised over the benzene ring.

The bonds around the nitrogen atom can take up a planar arrangement, with the nitrogen's lone pair in a p orbital, so that extra stability can be gained by overlapping this p orbital with the delocalised π bond of the benzene ring.



BASICITY OF PHENYL AMINE

This overlap causes the lone pair of the N atom in phenylamine to be delocalised into the benzene ring and results in the lone pair to be much less basic (and also much less nucleophilic).

The overlap of the lone pair on the N with the benzene delocalised system makes the lone pair less available for donation to H^+ (to form a co-ordinate bond).

REACTIVITY OF PHENYL AMINE

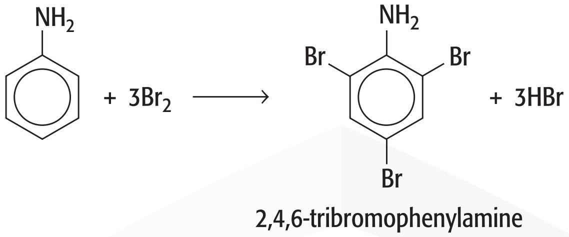
The overlap that causes the lone pair of the N atom in phenylamine to be delocalised into the benzene ring increases the electron density of the ring.

This results in the ring being more electron rich, and it undergoes electrophilic substitution reactions much more readily than benzene.

The enhanced reactivity of phenylamine in this regard is similar to that of phenol, an example being the ease with which phenylamine decolorises bromine water.

PHENYL AMINE WITH BROMINE WATER

Like phenol, phenylamine decolourises bromine water to give a white precipitate of 2,4,6-tribromophenylamine.

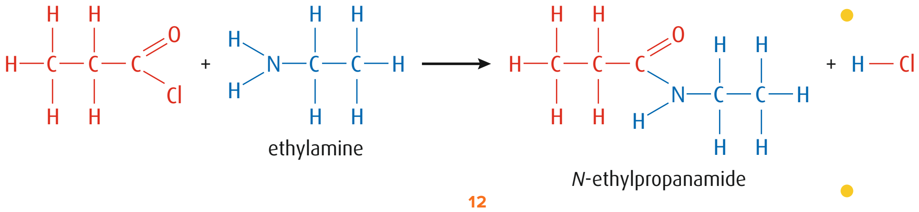


AMINES AS NUCLEOPHILES

Amines are strong nucleophiles as well as strong bases, just like ammonia.

As nucleophiles, their lone pair of electrons is attracted to any positive ion or positive centre in a molecule.

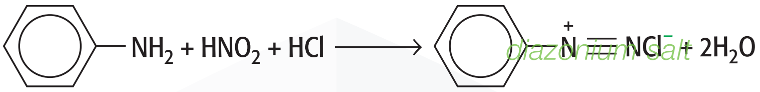
When amines are reacted with acyl chlorides (at low temperature) N-substituted amides are formed.



DIAZONIUM SALTS

Phenylamine is an important compound in the synthesis of dyes.

The first step is the reaction between phenylamine and nitrous acid, HNO_2, to give a diazonium salt. We can make the nitrous acid using sodium nitrite and dilute hydrochloric acid.



DIAZONIUM SALTS

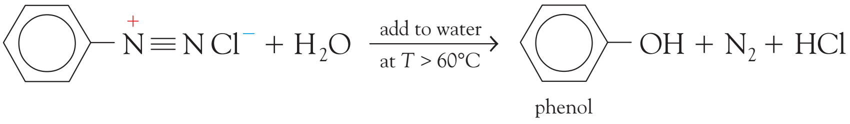
The reaction mixture must be kept below 10 °C by using ice. This is because the diazonium salt is unstable and will decompose easily, giving off nitrogen gas, N_2, and phenols at room temperature.

Nitrous acid, HNO_2, is unstable, and has to be made as required by reacting together sodium nitrite and hydrochloric acid:

$$NaNO_2 + HCl \rightarrow NaCl + HNO_2$$

REACTIONS OF DIAZONIUM SALTS

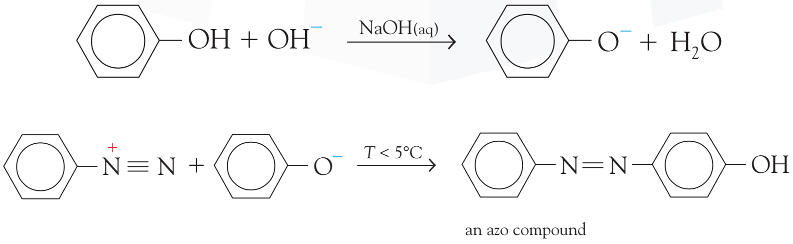
Adding a solution of a diazonium salt to hot water causes decomposition, and produces phenol:



AZO DYES

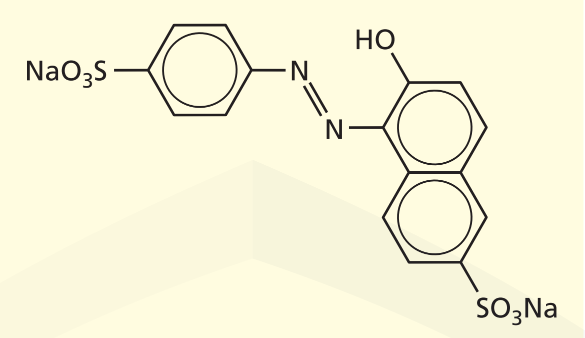
The most important reactions of diazonium salts are their use in the formation of azo dyes.

When a solution of a diazonium salt is added to an alkaline solution of a phenol, a coupling reaction takes place:



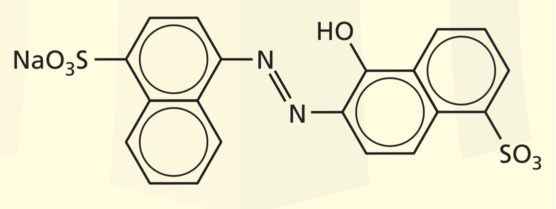
SKILL CHECK 1

Q. Draw the structures of the two compounds from which Sunset Yellow can be made by a coupling reaction.



SKILL CHECK 2

Q. What are the structures of the two compounds that couple to form Carmoisine?



PREPARING AMINES

Two of the three main methods of preparing alkyl amines both start with halogenoalkanes.

- By nucleophilic substitution of a halogenoalkane with ammonia
- By nucleophilic substitution of a halogenoalkane with sodium cyanide, followed by reduction using either $LiAlH_4$ (lithium aluminium hydride) or hydrogen over a nickel catalyst.
- By the the reduction of amides with $LiAlH_4$.
- Phenylamine can be prepared by the reduction of nitrobenzene with tin/ concentrated HCl.

HALOGENOALKANE WITH AMMONIA

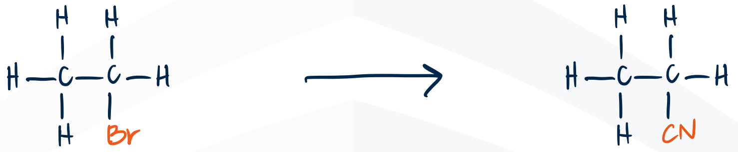
Reagent	Ammonia, NH_3 (conc. or dissolved in ethanol)
Condition	heat under reflux
Product	Amine
Type	nucleophilic substitution

$$CH_3CH_2Br + NH_3 \longrightarrow CH_3CH_2NH_2 + HBr$$

HALOGENOALKANE WITH CN⁻

Reagent	potassium cyanide, KCN, (or sodium cyanide, NaCN) dissolved in ethanol
Condition	heat under reflux in **ethanolic** solution
Product	Nitrile
Type	nucleophilic substitution

$$CH_3CH_2Br + CN^- \longrightarrow CH_3CH_2CN + Br^-$$



Importance of the reaction with CN⁻ is that it extends the carbon chain by one carbon atom.

REDUCTION OF NITRILES

Nitriles can be reduced to amines by using either $LiAlH_4$ (lithium aluminium hydride) or hydrogen over a nickel catalyst.

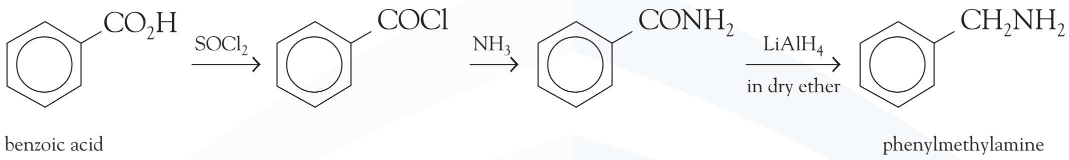
$$CH_3CH_2CN \longrightarrow CH_3CH_2CH_2NH_2$$

REDUCTION OF AMIDES

Amines are also produced when amides are reduced by $LiAlH_4$ (lithium aluminium hydride).

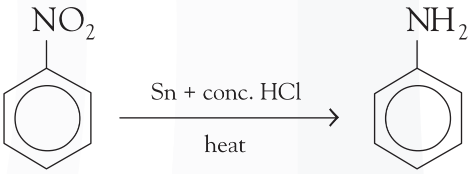
$CH_3CH_2CONH_2 \longrightarrow CH_3CH_2CH_2NH_2$

This allows amines to be synthesised from carboxylic acids:



REDUCTION OF NITROBENZENE

Aryl amines are most commonly prepared by the reduction of aromatic nitro compounds.



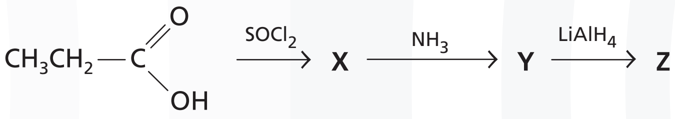
EXAMPLE

The ‘good feeling’ factor in chocolate has been identified as 2-phenylethylamine, $C_6H_5CH_2CH_2NH_2$.

Suggest a synthesis of this compound from chloromethylbenzene, $C_6H_5CH_2Cl$.

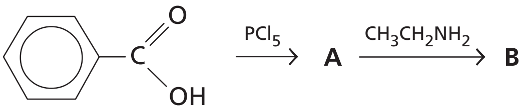
SKILL CHECK 3

Suggest products of the following reaction:



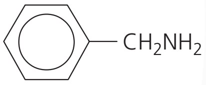
SKILL CHECK 4

Suggest products of the following reaction:

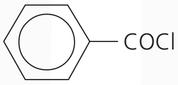


SKILL CHECK 5

Suggest two-stage syntheses of the following compounds, from the stated starting materials.



from



$(CH_3)_2CH—CH_2NH_2$ from $(CH_3)CH—Br$

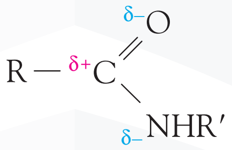
AMIDES

Amides have the following functional group, where R and R′ can be alkyl, aryl or hydrogen.

Most amides are solids at room temperature, and quite a number are soluble in water.

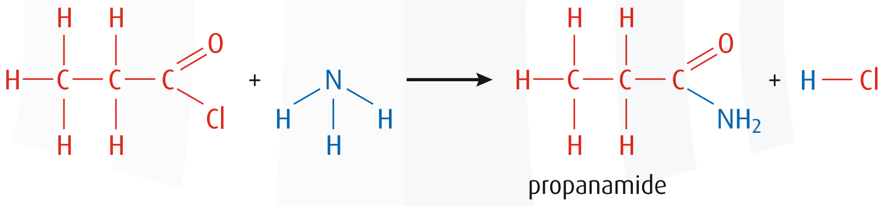
Unlike amines, amides form neutral solutions in water.

Amides are most readily prepared by reacting acyl chlorides with ammonia or amines.



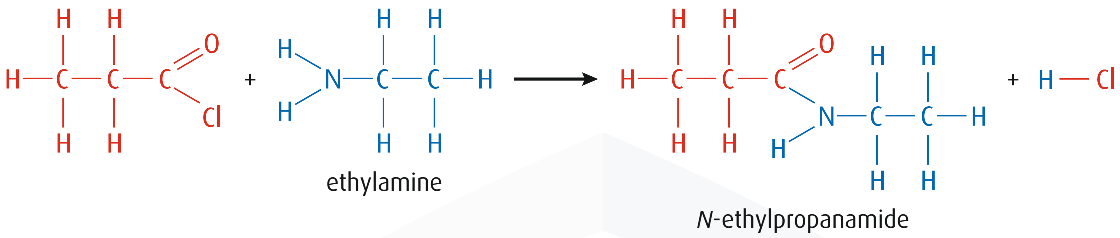
REACTION WITH AMMONIA

When concentrated ammonia solution is added to an acyl chloride at 0°C a primary amide is formed.



REACTION WITH AMINES

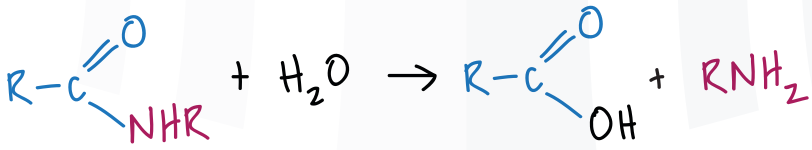
When acyl chlorides are reacted with amines (at low temperature) N-substituted amides are formed.



AMIDE HYDROLYSIS

Because of the high degree of positive charge on the carbon atom in amides, they are susceptible to nucleophilic attack.

Hydrolysis of amides produces a carboxylic acid and an amine.



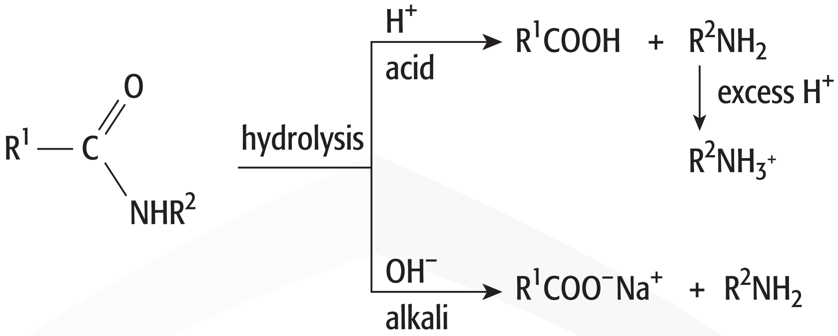
carboxylic acid ***amine***

$$RCONH_2 + H_2O \longrightarrow RCO_2H + NH_3$$

$$RCONHR' + H_2O \longrightarrow RCO_2H + R'NH_2$$

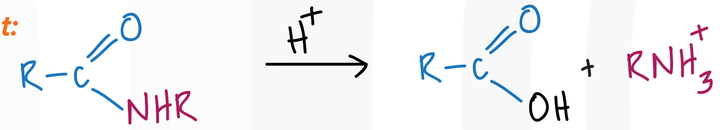
AMIDE HYDROLYSIS

Hydrolysis of amides is usually carried out in the presence of an acid or a base; reaction with water is very slow.

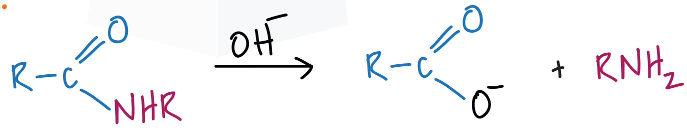


AMIDE HYDROLYSIS

with dil HCl and heat:



with NaOH and heat:



REDUCTION TO AMINES

Amines are also produced when amides are reduced by $LiAlH_4$ (lithium aluminium hydride).

$$CH_3CH_2CONH_2 \longrightarrow CH_3CH_2CH_2NH_2$$