Nitrogen compounds (A Level)

Making and reacting primary and secondary amines, phenylamine and azo dyes, amides, the relative basicity of nitrogen compounds, and amino acids, zwitterions, peptides and electrophoresis.

34.1 Primary and secondary amines

Preparation of amines

- Halogenoalkane + **ammonia** (excess, in ethanol, heated under pressure) gives a **primary amine**.
- Halogenoalkane + a **primary amine** (ethanol, heated in a sealed tube or under pressure) gives a **secondary amine**: $C_2H_5Br + CH_3NH_2 \rightarrow C_2H_5NHCH_3 + HBr$.
- **Reduction of an amide** with $LiAlH_4$ in dry ether: $CH_3CONH_2 + 4[H] \rightarrow CH_3CH_2NH_2 + H_2O$.
- **Reduction of a nitrile** with $LiAlH_4$ or with H_2 and a Ni catalyst: $CH_3CN + 4[H] \rightarrow CH_3CH_2NH_2$.

Condensation with acyl chlorides

Ammonia or an amine reacts with an acyl chloride at room temperature to give an **amide** (see Acyl chlorides).

Basicity

An amine has a **lone pair on nitrogen** which accepts a proton, so it is a **weak base**: $RNH_2 + H_2O \rightleftharpoons RNH_3^+ + OH^-$. Amines react with acids to form salts: $C_2H_5NH_2 + HCl \rightarrow C_2H_5NH_3^+Cl^-$, and are displaced from the salts by NaOH.

Track nitrogen and carbon through reductions

Nitrile reduction converts $-C \equiv N$ into $-CH_2NH_2$ without adding carbon. Amide reduction converts the carbonyl carbon into CH_2 while retaining its bond to nitrogen. These transformations differ from hydrolysis, which separates the nitrogen-containing part from the acyl carbon skeleton.

Worked comparison: ethanenitrile, CH_3CN, gives ethylamine on reduction. Ethanamide, CH_3CONH_2, also gives ethylamine, but on hydrolysis gives ethanoic acid/carboxylate plus an ammonium/ammonia product. In both reductions the two starting carbons remain in the amine. Do not treat nitrile reduction as an additional carbon-extension step: the extra carbon was introduced earlier when cyanide was used.

Note Academy

With a primary amine and a halogenoalkane, nitrogen alkylation can give a secondary amine, while reaction with an acyl chloride gives an **amide**. These products must not be confused. $CH_3NH_2 + C_2H_5Br$ can form $CH_3NHC_2H_5$, whereas $CH_3NH_2 + CH_3COCl$ forms $CH_3CONHCH_3$ with an N–C=O connection.

> **TRY IT**
>
> What is formed by reducing propanamide with $LiAlH_4$, and how many carbons does it contain?

Answer: Propan-1-amine, $CH_3CH_2CH_2NH_2$, containing three carbons. The amide carbonyl becomes CH_2 rather than being lost.

34.2 Phenylamine and azo compounds

Preparation of phenylamine

1. **Nitrate** benzene with concentrated HNO_3/H_2SO_4 (25–60 °C) to give **nitrobenzene**.
2. **Reduce** with **hot tin and concentrated HCl** (Sn/conc. HCl), which gives the phenylammonium salt.
3. Add **NaOH(aq)** to liberate **phenylamine**, $C_6H_5NH_2$.

Reactions of phenylamine

- **With Br_2(aq)** at room temperature: a white precipitate of **2,4,6-tribromophenylamine** (the ring is activated by the lone pair on N).
- **With HNO_2** (from $NaNO_2$ and dilute HCl) **below 10 °C**: the **diazonium salt** $C_6H_5N_2^+Cl^-$. Warming this with water gives **phenol** and N_2.

Azo compounds

The benzenediazonium ion reacts with **phenol dissolved in NaOH(aq)** (below 10 °C), **coupling** to form an **azo compound**, with the **–N=N–** group linking two rings, in a bright **yellow-orange** colour. Azo compounds are strongly coloured because the –N=N– group extends the delocalised system across both rings, and they are used as **dyes** (other dyes are made by coupling with other aromatic compounds). The diazonium salt must be kept **cold**, since it decomposes to phenol and nitrogen at higher temperatures.

Relative basicity

Ethylamine > ammonia > phenylamine (in aqueous solution).

- **Ethylamine:** the alkyl group is electron-donating, which **increases** the electron density on N and makes the lone pair more available.

Note Academy

- **Ammonia:** the reference.
- **Phenylamine:** the lone pair on N is **delocalised into the benzene ring**, so it is **less available** to accept a proton.

Phenylamine preparation needs a work-up

Tin and concentrated acid reduce the nitro group, but the acidic mixture protonates the amine. Adding hydroxide liberates neutral phenylamine from its phenylammonium salt. A route ending at the acidic reduction mixture has not yet isolated the same free-base product. Keep the aromatic ring and carbon count unchanged through nitro-to-amino reduction.

The NH_2 lone pair both increases ring electron density and becomes less available for accepting a proton. These effects explain an apparent contrast: phenylamine is **more reactive towards ring electrophiles** than benzene but **less basic at nitrogen** than an alkylamine. Electron donation into the ring strengthens one type of reactivity while reducing another.

Worked example: phenylamine with bromine water gives ring substitution at 2,4,6 and a white precipitate. Phenylamine with HCl instead undergoes protonation at nitrogen. Identifying the reactive site explains why the same molecule behaves differently with the two reagents.

> **TRY IT**
>
> Explain the order ethylamine > ammonia > phenylamine for the stated aqueous basicity comparison.

Answer: Ethyl donation makes the nitrogen pair more available than in ammonia. In phenylamine the pair overlaps with the aromatic system and is less available for proton acceptance. In more elaborate comparisons, aqueous solvation also matters; this simple order should not be expanded into a universal ranking of every amine.

Diazotisation and azo coupling are separate stages

Generate nitrous acid in the cold using sodium nitrite and dilute acid. Keep the diazonium solution cold until the next reagent is ready. Coupling with alkaline phenol creates an N=N link to an electron-rich ring, commonly at an available para position. Warming with water instead produces phenol and nitrogen gas, so temperature choice controls a competing pathway.

The azo group extends conjugation across aromatic units. Absorption in the visible region gives colour, and different substituents alter that absorption. Azo compounds are not all exactly the same yellow-orange shade. Explain colour through the extended electronic system rather than assuming any nitrogen-containing compound is coloured.

Note Academy

34.3 Amides

Preparation of amides

An **acyl chloride** reacts at room temperature with **ammonia** (a primary amide) or a **primary amine** (an N-substituted amide).

Reactions

- **Hydrolysis** by heating with aqueous acid (gives a carboxylic acid and an ammonium salt) or with aqueous alkali (gives a carboxylate salt and ammonia): $CH_3CONH_2 + NaOH \rightarrow CH_3COONa + NH_3$.
- **Reduction** with $LiAlH_4$ gives an **amine**, since the C=O becomes CH_2.

Amides are very weak bases

The lone pair on N is **delocalised onto the carbonyl oxygen** (it overlaps with the C=O π bond), so it is not available to accept a proton. The nitrogen atom is also attached to an electron-withdrawing C=O group. Amides are therefore **much weaker bases than amines** and are almost neutral.

Amide structure, basicity and hydrolysis products

In an amide, nitrogen's lone pair overlaps with the carbonyl system, giving the C–N bond partial double-bond character and reducing the pair's availability for proton acceptance. Compare the complete conjugated group, not simply the electronegativity of nitrogen. Amides are substantially less basic than ordinary amines under the syllabus conditions.

Hydrolysis breaks the acyl C–N linkage. A primary amide gives ammonia in alkali or ammonium in acid; an N-substituted amide instead yields the corresponding amine or alkylammonium ion. The substituent originally attached to nitrogen is not transferred onto the acid carbon skeleton.

Worked example: $CH_3CONHCH_2CH_3$ heated with NaOH gives CH_3COO^- and ethylamine, not ammonia. Acidic hydrolysis gives ethanoic acid and ethylammonium. In both cases separate the two fragments at the C(O)–N bond and then assign protonation states for the medium.

> **TRY IT**
>
> How could you distinguish reducing ethanamide from hydrolysing it in the proposed product structures?

Note Academy

Answer: Reduction retains the C–N connection and gives ethylamine. Hydrolysis breaks that connection and gives ethanoic acid/carboxylate plus ammonia/ammonium. Products with the wrong retained bond reveal an incorrect transformation.

34.4 Amino acids

An **amino acid** has both an **amino group (–NH_2)** and a **carboxyl group (–COOH)**. In a 2-amino acid, both are on the same carbon: $H_2N{-}CHR{-}COOH$. They are **amphoteric**, behaving as both acid and base.

Zwitterions and the isoelectric point

In solution the amino acid exists mainly as a **zwitterion**: $H_3N^+{-}CHR{-}COO^-$ (overall neutral, with both charges).

- In **acid** (low pH) the carboxylate is protonated: $H_3N^+{-}CHR{-}COOH$ (a cation).
- In **alkali** (high pH) the ammonium loses a proton: $H_2N{-}CHR{-}COO^-$ (an anion).
- The **isoelectric point** is the pH at which the amino acid has **no net charge** (it exists as the zwitterion).

Peptides

Two amino acids join in a **condensation** reaction between the –COOH of one and the –NH_2 of the other, losing water and forming an **amide (peptide) bond** –CO–NH–. Two amino acids make a **dipeptide**, three a **tripeptide**, and so on.

Electrophoresis

A mixture is placed on a gel or paper at a given **pH** with an electric field. At a pH **below** its isoelectric point an amino acid is a **cation** and moves towards the **cathode** (negative); at a pH **above** it, it is an **anion** and moves to the **anode** (positive); at its isoelectric point it does not move. A larger charge and a smaller size mean faster movement. This lets you separate and identify amino acids and small peptides.

> **TRY IT**
>
> At pH 6, glycine (isoelectric point 6.0), lysine (9.7) and aspartic acid (2.8) are placed on the centre of a gel. In which directions do they move?

Glycine: no net charge, **stays**. Lysine: pH is below its isoelectric point so it is a **cation**, and moves to the **cathode**. Aspartic acid: pH is above its isoelectric point so it is an **anion**, and moves to the **anode**.

Note Academy

Protonation state is controlled by pH

For a simple amino acid without an ionisable side chain, strongly acidic solution favours $H_3N^+CHRCOOH$, intermediate conditions favour the zwitterion, and strongly alkaline solution favours $H_2NCHRCOO^-$. A zwitterion is not uncharged everywhere: it has opposite charges on different groups and zero **net** charge. These ionic interactions help explain amino acids' relatively high melting points and their behaviour in water.

The isoelectric point is a condition of zero average net charge, usually dominated by zwitterionic form; it does not mean every molecule must be one completely non-ionised structure. Side-chain acids or bases change the charge pattern, so compare pH with the supplied isoelectric point rather than forcing lysine or aspartic acid into glycine's simple diagram.

Worked electrophoresis: an amino acid with pI 5.0 at pH 8.0 has an average negative charge and migrates towards the positive anode. At pH 3.0 it is on average positive and migrates towards the negative cathode. Direction follows charge; speed additionally depends on size, charge magnitude and medium, so equal directions do not imply equal speeds.

> **TRY IT**
>
> Why can the same amino acid travel in opposite directions in two electrophoresis experiments?

Answer: Different buffer pH values can place it above or below its isoelectric point, changing the sign of its average net charge. The applied field need not have been reversed.

Peptides: bond direction and water count

Condensation joins the carboxyl carbon of one amino acid to nitrogen of another, forming $-CO-NH-$. The order of residues matters: glycine–alanine and alanine–glycine have different connectivity. For a simple linear peptide from n amino-acid molecules, there are $n-1$ peptide links and $n-1$ water molecules released, with one amino end and one carboxyl end remaining.

Worked example: three amino acids form a linear tripeptide with two peptide bonds and lose two waters, so its molar mass is the sum of the three amino-acid molar masses minus 36.0 g mol^{-1}. Hydrolysis adds water at each peptide link to recover residues, with protonation states set by acid/alkali conditions.

> **TRY IT**
>
> How many peptide links are in a linear pentapeptide, and why is the answer not five?

Answer: Four. Linking five initially separate molecules into one linear chain requires four connections; the two terminal groups remain unlinked at the ends.

Note Academy

Chapter check: distinguish amines from amides, explain the two consequences of lone-pair delocalisation, assign pH-dependent charge and count peptide bonds from chain connectivity.

References and further reading

Scope follows section 34 of the **Cambridge 9701 syllabus for 2025–2027**. **Chemguide's Cambridge topic index** links to alternative explanations. The worked exercises and added diagrams are original teaching examples; numerical examples are illustrative unless a specific source is identified.

Note Academy