

Nitrogen compounds

A2

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Read first: [Nitrogen compounds](#), [Halogen compounds](#), [Hydrocarbons](#), [Carboxylic acids and derivatives](#)

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What you need to know

At AS you made a primary amine from a halogenoalkane and met nitriles. At A Level this topic adds how amines behave as bases, phenylamine and the azo dyes made from it, amides, and amino acids. You should be able to:

Amines

- Recall four ways to make amines**, with reagents and conditions:
 - a halogenoalkane with ammonia dissolved in ethanol, heated under pressure, gives a primary amine;
 - a halogenoalkane with a primary amine in ethanol, heated in a sealed tube (under pressure), gives a secondary amine;
 - an amide reduced by LiAlH_4 gives an amine;
 - a nitrile reduced by LiAlH_4 , or by hydrogen with a nickel catalyst, gives a primary amine.
- Describe how ammonia or an amine reacts with an acyl chloride** at room temperature to give an amide (a condensation reaction: HCl is lost).
- Describe and explain why aqueous amines are basic.**

Phenylamine and azo compounds

- Describe how phenylamine is made from benzene**: nitrate benzene to nitrobenzene, reduce it with hot tin and concentrated hydrochloric acid, then add NaOH(aq) .
- Describe two reactions of phenylamine**: with bromine water at room temperature; and with nitrous acid, HNO_2 (or NaNO_2 and dilute acid), below 10°C to give a diazonium salt, which gives phenol when warmed with water.
- Describe and explain the order of basicity** of aqueous ammonia, ethylamine and phenylamine.
- Know about azo compounds**: benzenediazonium chloride couples with phenol in NaOH(aq) to make an azo compound; spot the azo group, $-\text{N}=\text{N}-$; know that azo compounds are often dyes; and know that other azo dyes are made the same way.

Amides

- Recall how amides are made**: an acyl chloride with ammonia, or with a primary amine, at room temperature.

9. **Describe the reactions of amides:** hydrolysis by aqueous acid or aqueous alkali, and reduction of the C=O group by LiAlH_4 to give an amine.
10. **State and explain why amides are much weaker bases than amines.**

Amino acids

11. **Describe the acid and base behaviour of amino acids:** how they form zwitterions, and what the isoelectric point is.
12. **Describe how amino acids join by amide (peptide) bonds** to make dipeptides and tripeptides.
13. **Interpret and predict electrophoresis results** for mixtures of amino acids and dipeptides at different pH values. You will not be asked how to set up the apparatus.

Understand it

Amines and amides: telling them apart

An **amine** has a nitrogen atom joined only to carbon and hydrogen atoms. Count the carbon atoms bonded to the N:

Class	Carbons on N	Example
Primary	1	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$, pentan-1-amine
Secondary	2	$\text{CH}_3\text{CH}_2\text{CH}_2\text{NHCH}_3$, N-methylpropan-1-amine
Tertiary	3	$(\text{CH}_3)_3\text{N}$, trimethylamine

A ring carbon counts like any other: phenylamine, $\text{C}_6\text{H}_5\text{NH}_2$, is a primary amine, and a nitrogen inside a ring bonded to two ring carbons (as in pyrrolidine, $(\text{CH}_2)_4\text{NH}$) is secondary.

An **amide** has the nitrogen joined to a C=O group: $-\text{CONH}_2$ (primary amide), $-\text{CONHR}$ or $-\text{CONR}_2$. The C=O changes everything about the nitrogen, so never call an amide an amine, or the other way round. In big drug molecules, check each N: if its neighbour carbon has a double-bonded O, it is an amide.

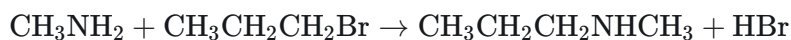
Making amines

From a halogenoalkane. Ammonia's lone pair attacks the $\delta+$ carbon of the C–halogen bond and the halide leaves (nucleophilic substitution). Heat the halogenoalkane with ammonia **dissolved in ethanol** in a **sealed tube** (under pressure), so the volatile ammonia can't escape:



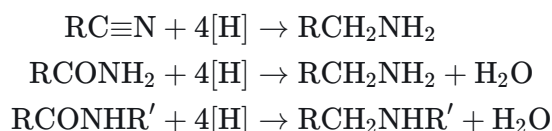
The amine made still has a lone pair on N, so it can attack another halogenoalkane molecule, giving a **secondary** amine, then a tertiary amine, then a quaternary ammonium salt. A **large excess of ammonia** makes it far more likely that each halogenoalkane meets ammonia rather than the amine, so the primary amine is the main product.

To make a **secondary** amine on purpose, use a primary amine in place of ammonia, again in ethanol in a sealed tube:

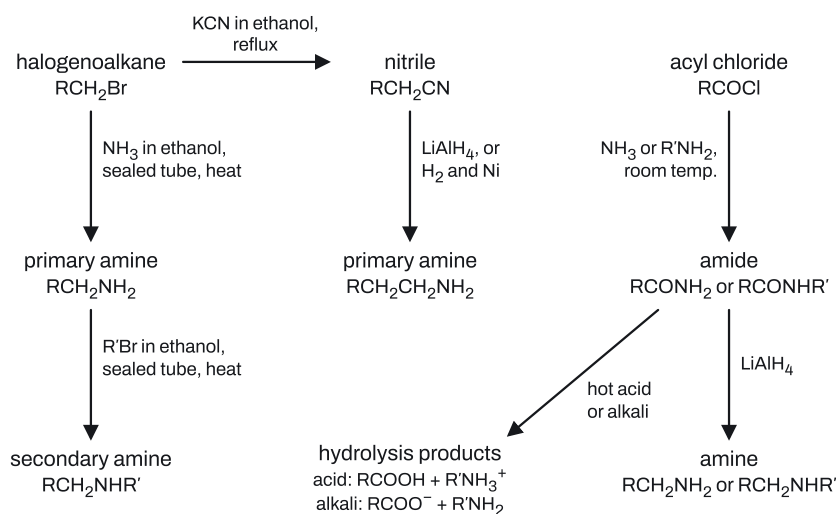


(the HBr then reacts with more amine to form a salt). An aryl amine such as phenylamine reacts the same way: with an excess of bromomethane, both H atoms on its N are replaced, giving $\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_2$.

By reduction. LiAlH_4 in dry ether is a strong reducing agent. It reduces a **nitrile** to a primary amine with one more carbon than the halogenoalkane the nitrile came from, and it reduces an **amide** by turning its $\text{C}=\text{O}$ into CH_2 . Hydrogen gas with a nickel catalyst also reduces nitriles. In equations, write $[\text{H}]$ for each hydrogen atom from the reducing agent:

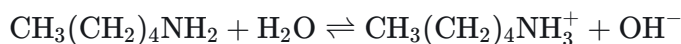


So an amide $-\text{CONH}-$ becomes a secondary amine $-\text{CH}_2\text{NH}-$. LiAlH_4 also reduces COOH to CH_2OH and an ester to two alcohols, but it leaves $\text{C}=\text{C}$ bonds and benzene rings alone.



Why amines are bases

A base accepts a proton, H^+ . The nitrogen of an amine has a **lone pair** that can form a dative bond to H^+ . In water a little of the amine takes a proton from water, leaving hydroxide ions, so the solution has pH above 7:

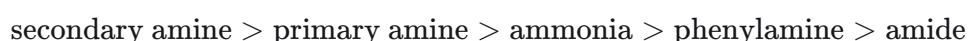


With an acid the reaction goes to completion, giving a salt: $\text{RNH}_2 + \text{HCl} \rightarrow \text{RNH}_3^+ \text{Cl}^-$, and with a carboxylic acid, $\text{RNH}_2 + \text{CH}_3\text{COOH} \rightarrow \text{RNH}_3^+ \text{CH}_3\text{COO}^-$. A salt is ionic and dissolves in water; adding a strong base such as $\text{NaOH}(\text{aq})$ takes the proton back and frees the amine.

The more available the lone pair, the stronger the base. Four things change its availability:

- **Alkyl groups push electrons towards N** (a positive inductive effect). This raises the electron density on N, so the lone pair accepts H^+ more readily. Ethylamine is a stronger base than ammonia, and a secondary amine, with two alkyl groups, is stronger again.
- **A benzene ring pulls the lone pair in.** In phenylamine the lone pair on N sits in a p orbital that overlaps with the ring's delocalised π system, so it is spread over the ring and less available. Phenylamine is a much weaker base than ammonia.
- **A $\text{C}=\text{O}$ group next to N pulls the lone pair in even more.** In an amide the lone pair is delocalised over N, C and the electronegative O. It is hardly available at all, so amides are **neutral**: they do not act as bases in water.
- **Electron-withdrawing groups on the ring**, such as NO_2 , make an aryl amine an even weaker base than phenylamine.

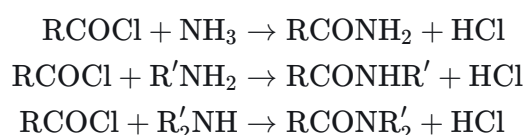
So, from strongest to weakest base:



For the syllabus trio: **ethylamine > ammonia > phenylamine**. A CH_2 between a ring and the NH_2 (as in $\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{NH}_2$) stops the lone pair reaching the ring, so that amine behaves like an alkyl amine.

Making amides from acyl chlorides

An acyl chloride reacts at once with ammonia or with a primary or secondary amine at room temperature. The N lone pair attacks the very δ^+ carbon of $-\text{COCl}$ and HCl is lost, so it is a **condensation** reaction, and its mechanism is **nucleophilic addition–elimination**:



The HCl reacts with a second molecule of the base, so two moles are used: $\text{RCOCl} + 2\text{R}'\text{NH}_2 \rightarrow \text{RCONHR}' + \text{R}'\text{NH}_3^+\text{Cl}^-$. A tertiary amine has no H on N and cannot form an amide.

The mechanism has four steps:

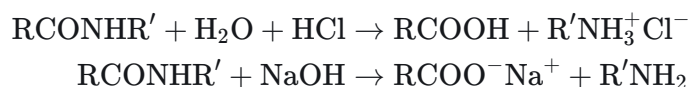
1. The lone pair on N attacks the carbon of $\text{C}^{\delta+}=\text{O}^{\delta-}$ (curly arrow from lone pair to C), and the $\text{C}=\text{O}$ π bond breaks onto O (curly arrow from the $\text{C}=\text{O}$ bond to O).
2. The intermediate has four groups on the carbon: O^- , Cl, R and the N, which now carries a + charge.
3. A lone pair on O^- reforms $\text{C}=\text{O}$, and the $\text{C}-\text{Cl}$ bond breaks with both electrons going to Cl, which leaves as Cl^- .
4. N^+ loses H^+ , which joins Cl^- as HCl .

The nitrogen of an **amide** is not a nucleophile (its lone pair is delocalised), so in a molecule with both an amine NH_2 and an amide CONH_2 , an acyl chloride reacts only at the amine.

Reactions of amides

Hydrolysis breaks the C(=O)–N bond, adding the parts of water. It needs heat under reflux with aqueous acid or alkali, and the conditions decide which form each product is in:

- **Hot aqueous acid** (HCl(aq)): the acid part becomes RCOOH; the nitrogen part is protonated, R'NH₃⁺ (or NH₄⁺ from –CONH₂).
- **Hot aqueous alkali** (NaOH(aq)): the acid part becomes RCOO[–] (a sodium salt); the nitrogen part is the free amine, R'NH₂ (or NH₃ gas). Any COOH or phenol OH already in the molecule is also deprotonated.



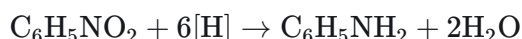
With alkali two things happen: **hydrolysis** and an **acid–base (neutralisation)** reaction. Products "isolated at pH 4" are in their acid-solution forms: every amine as –NH₃⁺, every acid as COOH.

Reduction with LiAlH₄ turns the C=O into CH₂: the amide becomes an amine with the same number of carbons.

Phenylamine

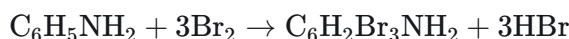
Phenylamine is made from benzene in two steps:

1. **Nitration**: concentrated nitric acid and concentrated sulfuric acid, at about 50 °C, give nitrobenzene (electrophilic substitution; see "Hydrocarbons").
2. **Reduction**: heat nitrobenzene under reflux with **tin and concentrated hydrochloric acid**. The tin is a reactant, not a catalyst. In the acid the amine is made as its salt, C₆H₅NH₃⁺, so finish by adding **NaOH(aq)** to release phenylamine.



Each NO₂ group needs 6[H] and gives 2H₂O, so a compound with two NO₂ groups needs 12[H]. Other nitroarenes are reduced to aryl amines in the same way.

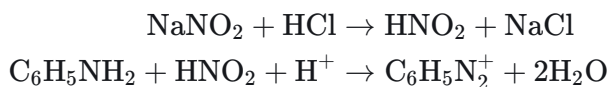
With bromine water. Phenylamine's lone pair feeds electron density into the ring, especially at positions 2, 4 and 6, so the ring is attacked far more easily than benzene's. It polarises bromine molecules without any catalyst. At room temperature bromine water is decolourised (orange to colourless) and a **white precipitate** of 2,4,6-tribromophenylamine forms:



Alkyl amines have no ring, so they give no precipitate; that makes bromine water a test to tell an aryl amine from an alkyl amine. If one of positions 2, 4 or 6 already has a group, only the free ones are brominated.

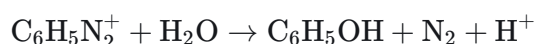
Diazonium salts and azo dyes

Diazotisation. Nitrous acid, HNO₂, is unstable, so it is made in the flask from sodium nitrite and dilute hydrochloric acid. Keep the mixture **below 10 °C** (in ice):

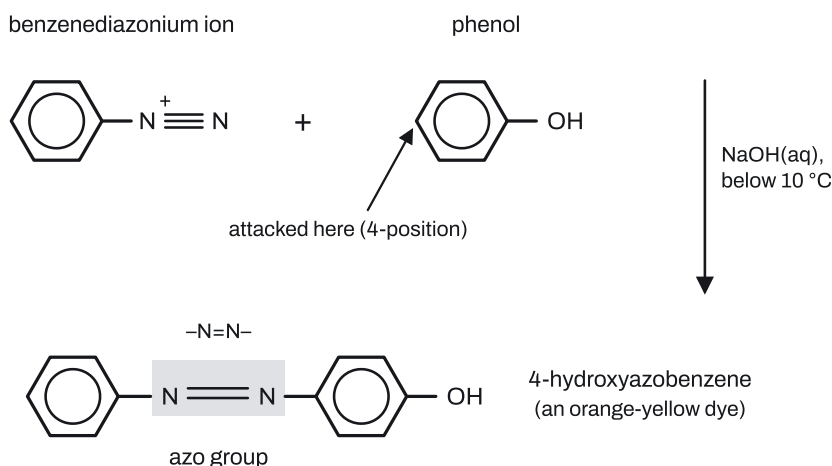
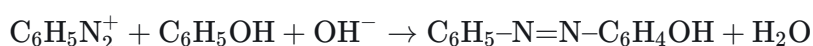


The product is benzenediazonium chloride, $\text{C}_6\text{H}_5\text{N}\equiv\text{N}^+ \text{Cl}^-$. The + charge is on the nitrogen joined to the ring.

Warming with water. Above 10 °C the diazonium ion breaks down: nitrogen gas bubbles off and a phenol forms. This is why diazotisation must be kept cold, and it is also a way to turn NH_2 into OH on a ring (two steps: HNO_2 below 10 °C, then warm with water):



Coupling. In cold alkaline solution, phenol is present as the phenoxide ion, whose ring is very electron-rich. The diazonium ion attacks it at the 4-position (opposite the O), keeping both N atoms, so the two rings are joined by an **azo group**, $-\text{N}=\text{N}-$:



The product is brightly coloured because the azo group links the two rings' delocalised electrons into one long system that absorbs visible light. Azo compounds are widely used as **dyes** (for fabrics and foods) and some as indicators. Other azo dyes are made the same way: change the aryl amine (any ArNH_2 , including rings carrying CH_3 , OCH_3 , SO_3^- or COOH groups) or change the coupling partner (another phenol, a naphthol, or an aryl amine such as $\text{C}_6\text{H}_5\text{N}(\text{CH}_3)_2$). A compound with **two** NH_2 groups on rings is diazotised at both, and each diazonium group then couples with one molecule of the partner.

To work back from an azo dye, cut the $-\text{N}=\text{N}-$: the side that becomes $-\text{N}_2^+$ came from an aryl amine (usually the side without OH or NR_2), and the other side is the coupling partner with an H where the azo group was.

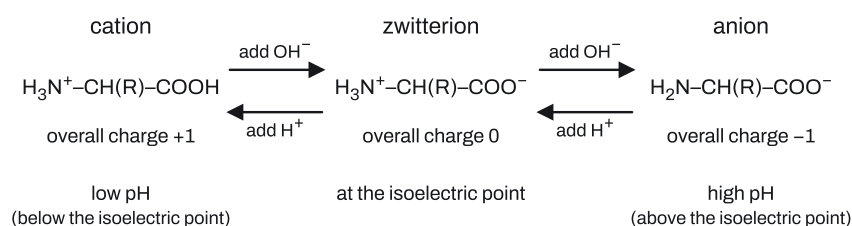
Amino acids and zwitterions

An amino acid has an amine group and a carboxylic acid group on the same carbon: $\text{H}_2\text{NCH(R)COOH}$. R is the side chain. Because the molecule has an acid and a base, a proton moves from COOH to NH_2 inside the molecule, giving a **zwitterion**, $\text{H}_3\text{N}^+\text{CH(R)COO}^-$: one ion carrying both a positive and a negative charge, with no charge overall. This is why amino acids are crystalline solids with high melting points and dissolve in water.

What you draw depends on the pH:

- **Low pH (acid added):** COO^- takes a proton back: $\text{H}_3\text{N}^+\text{CH(R)COOH}$, a **cation**.
- **High pH (alkali added):** NH_3^+ loses its proton: $\text{H}_2\text{NCH(R)COO}^-$, an **anion**.

The **isoelectric point** is the pH at which the amino acid is a zwitterion, with no overall charge. Below its isoelectric point an amino acid is positive; above it, negative. Because it can take up H^+ or OH^- , an amino acid solution also resists changes in pH.



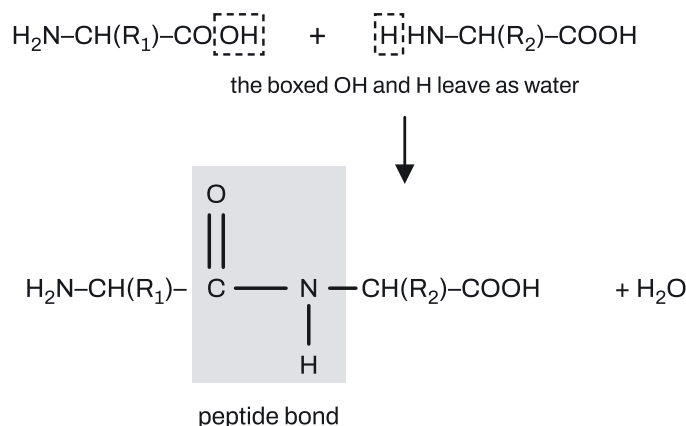
Side chains with an extra acid or base group have more forms. A side chain with a COOH (an acidic amino acid, isoelectric point around 3) is COOH at low pH and COO^- at high pH; a side chain with an NH_2 (a basic amino acid, isoelectric point around 10) is NH_3^+ at low pH and NH_2 at high pH. Work out each group separately:

- every NH_2 (main or side chain) is NH_3^+ when the pH is below about 9, and NH_2 at higher pH;
- every COOH is COOH at very low pH (about 1–2) and COO^- at higher pH;
- a side-chain **amide** (CONH_2) or alcohol OH is **never** protonated or deprotonated: amides are neutral.

For example, an amino acid with a side chain $\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2$ is $\text{H}_3\text{N}^+\text{CH}(\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_3^+)\text{COOH}$ (charge +2) at pH 1 and $\text{H}_2\text{NCH}(\text{CH}_2\text{CH}_2\text{CH}_2\text{NH}_2)\text{COO}^-$ (charge -1) at pH 13. At its isoelectric point, the form with charge 0 has one NH_3^+ , one COO^- and the other amine as NH_2 .

Peptides

The COOH of one amino acid and the NH_2 of another join, losing water (a **condensation** reaction), to form an amide link. In proteins it is called a **peptide bond**, $-\text{CO}-\text{NH}-$. Two amino acids make a **dipeptide**; three make a **tripeptide**; many make a polypeptide.



- A **named** dipeptide is written from the free NH_2 end: in Met–Trp, methionine's COOH has joined tryptophan's NH_2 , so methionine keeps its NH_2 and tryptophan keeps its COOH . Trp–Met is a different (isomeric) dipeptide.
- The peptide bond uses the NH_2 and COOH on the **central** carbon. Side-chain NH_2 , COOH or CONH_2 groups are left as they are.
- Two different amino acids can give **four** dipeptides (A–A, B–B, A–B, B–A); three different amino acids used once each give $3 \times 2 \times 1 = 6$ tripeptides.
- A dipeptide's formula is the two amino acids' formulae added together, minus H_2O ; a tripeptide loses $2\text{H}_2\text{O}$.
- A section of a polypeptide made from one amino acid repeats $-\text{NH}-\text{CH}(\text{R})-\text{CO}-$; draw continuation bonds at both ends and bracket one repeat unit.

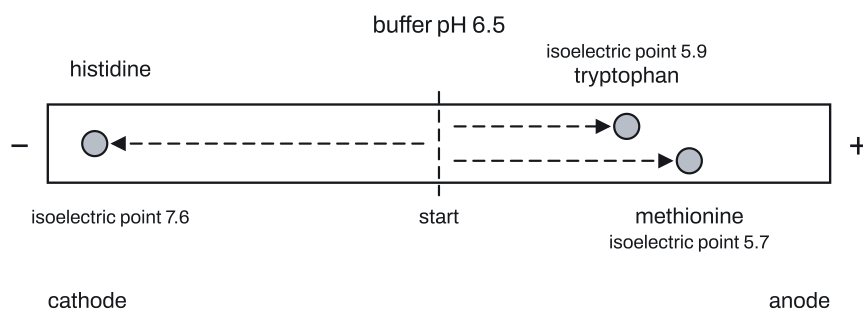
Hydrolysis of a peptide (hot $\text{HCl}(\text{aq})$, or hot $\text{NaOH}(\text{aq})$) breaks every peptide bond and gives back the amino acids, as cations in acid or as carboxylate anions in alkali.

Electrophoresis

In electrophoresis a mixture is placed on the middle of a gel or paper soaked in a **buffer** of fixed pH, and a voltage is applied. Each species moves according to its charge at that pH:

- **pH below its isoelectric point:** positive, so it moves to the **cathode** (negative electrode).
- **pH equal to its isoelectric point:** no overall charge, so it **stays** where it was put.
- **pH above its isoelectric point:** negative, so it moves to the **anode** (positive electrode).

How far a species moves depends on its **charge** (a bigger charge moves further) and its **size** (M_r): a smaller ion moves further than a larger one with the same charge. So an amino acid moves further than a dipeptide with the same charge. A dipeptide's charge comes from its free groups: the NH_2 end, the COOH end and any acidic or basic side chains.



In the figure, the buffer's pH is 1.1 units below histidine's isoelectric point, so histidine is positive; it is furthest from its isoelectric point, so it carries the largest charge and moves furthest. It is above the isoelectric points of tryptophan (by 0.6) and methionine (by 0.8), so both are negative. Methionine is further from its isoelectric point, so it carries a slightly larger charge, and it is also the smaller molecule, so it moves further than tryptophan.

Key facts and formulas

"Given" means it is printed on the Periodic Table or in the Data Booklet in the exam. "Learn it" means you must remember it; reagents, conditions and equations are never printed, and structures and isoelectric points of amino acids are given in the question when you need them.

Formula	Status
Relative atomic masses: H 1.0, C 12.0, N 14.0, O 16.0, Na 23.0, S 32.1, Br 79.9	Given
Molar volume of gas at room conditions = $24.0 \text{ dm}^3 \text{ mol}^{-1}$	Given
$\text{RX} + 2\text{NH}_3 \rightarrow \text{RNH}_2 + \text{NH}_4\text{X}$ (ethanol, sealed tube, heat; excess NH_3)	Learn it
$\text{RX} + \text{R}'\text{NH}_2 \rightarrow \text{RNHR}' + \text{HX}$ (ethanol, sealed tube, heat)	Learn it
$\text{RCN} + 4[\text{H}] \rightarrow \text{RCH}_2\text{NH}_2$ (LiAlH_4 in dry ether, or H_2/Ni)	Learn it
$\text{RCONH}_2 + 4[\text{H}] \rightarrow \text{RCH}_2\text{NH}_2 + \text{H}_2\text{O}$ (LiAlH_4 in dry ether)	Learn it
$\text{RCOCl} + \text{R}'\text{NH}_2 \rightarrow \text{RCONHR}' + \text{HCl}$ (room temperature)	Learn it
$\text{RNH}_2 + \text{H}_2\text{O} \rightleftharpoons \text{RNH}_3^+ + \text{OH}^-$	Learn it
Basicity: secondary amine > primary amine > NH_3 > phenylamine > amide	Learn it
$\text{ArNO}_2 + 6[\text{H}] \rightarrow \text{ArNH}_2 + 2\text{H}_2\text{O}$ (hot Sn and conc. HCl, then NaOH(aq))	Learn it

Formula	Status
$\text{C}_6\text{H}_5\text{NH}_2 + 3\text{Br}_2 \rightarrow \text{C}_6\text{H}_2\text{Br}_3\text{NH}_2 + 3\text{HBr}$ (room temperature, white precipitate)	Learn it
$\text{NaNO}_2 + \text{HCl} \rightarrow \text{HNO}_2 + \text{NaCl}$	Learn it
$\text{ArNH}_2 + \text{HNO}_2 + \text{H}^+ \rightarrow \text{ArN}_2^+ + 2\text{H}_2\text{O}$ (below 10 °C)	Learn it
$\text{ArN}_2^+ + \text{H}_2\text{O} \rightarrow \text{ArOH} + \text{N}_2 + \text{H}^+$ (warm)	Learn it
Coupling: $\text{ArN}_2^+ + \text{phenol in NaOH(aq)} \rightarrow \text{Ar-N=N-C}_6\text{H}_4\text{OH}$ (4-position)	Learn it
Amide hydrolysis: acid $\rightarrow \text{RCOOH} + \text{R}'\text{NH}_3^+$; alkali $\rightarrow \text{RCOO}^- + \text{R}'\text{NH}_2$	Learn it
Isoelectric point: the pH at which the amino acid is a zwitterion (no overall charge)	Learn it
Electrophoresis: pH < isoelectric point $\rightarrow$ cathode; pH = isoelectric point $\rightarrow$ stays; pH > isoelectric point $\rightarrow$ anode	Learn it

How to do it

In the Paper 4 questions we have tagged for this topic (65 questions, 2021–2025; 48 different questions, 17 of them repeated in another variant), the types came up this often. 48 of the 65 mix more than one type, so the counts add up to 166. The topic is usually several parts of one long organic question, often built around a drug, a dye or named amino acids.

Question type	Questions
Compare and explain relative basicities	19
Draw a dipeptide, tripeptide or polypeptide section	19
Diazotise an aryl amine and couple it to make an azo dye	18
Give reagents and conditions to make an aliphatic amine	17
Define the isoelectric point and draw an amino acid at a given pH	17
Make an amide from an acyl chloride	16
Draw the products of amide or peptide hydrolysis	14
Make an aryl amine by reducing a nitro compound	13
Identify amine and amide groups and classify the amine	10
Predict electrophoresis results	8

Question type	Questions
Phenylamine and bromine water	8
Draw the product of reducing an amide with LiAlH_4	7

1. Compare and explain relative basicities (19 questions)

- Write the order** in the boxes the right way round (check whether the question wants "most basic" or "least basic" first): secondary amine > primary alkyl amine (including ArCH_2NH_2 and cyclohexyl amines) > ammonia > phenylamine > nitro-substituted aryl amine > amide.
- Link basicity to the lone pair once:** "basicity depends on how available the lone pair on N is to accept a proton".
- Give one reason per compound:**
 - alkyl amine: the alkyl group is electron-donating (positive inductive effect), so the lone pair is more available; two alkyl groups donate more;
 - phenylamine: the lone pair (p orbital) on N overlaps with / is delocalised into the ring's π system;
 - amide: the lone pair on N is delocalised into the $\text{C}=\text{O}$ group (over N, C and O);
 - NO_2 on the ring: electron-withdrawing, so the lone pair is even less available.

Variations you will meet:

- "Explain why amides are much weaker bases than amines"** on its own: the lone pair link, then "delocalised into the $\text{C}=\text{O}$ group", so it is less available to accept a proton.
- "Explain why the aqueous solution has pH greater than 7"**: the N lone pair accepts a proton from water, with the equation $\text{RNH}_2 + \text{H}_2\text{O} \rightleftharpoons \text{RNH}_3^+ + \text{OH}^-$.
- "Why does a secondary amine solution have a higher pH than a primary amine solution of the same concentration?"**: two electron-donating alkyl groups on N raise its electron density more.
- An amine plus a carboxylic acid**: a salt forms, $\text{R}_2\text{NH} + \text{CH}_3\text{COOH} \rightarrow \text{R}_2\text{NH}_2^+ \text{CH}_3\text{COO}^-$.

2. Draw a dipeptide, tripeptide or polypeptide section (19 questions)

- Put the amino acids in the order named**: the first keeps its NH_2 , the last keeps its COOH .
- Join COOH of one to NH_2 of the next** on the central carbons, removing OH and H as water.
- Display the peptide bond** when asked: $\text{C}=\text{O}$ and $\text{N}-\text{H}$ drawn out, with the C, O, N and H all shown, and a saturated carbon on each side.
- Copy the side chains unchanged**, then check the molecular formula if one is given.

Variations you will meet:

- A polymer from one amino acid** (or two different ones): draw two or three residues joined in a chain with continuation bonds at each end and mark one repeat unit. Side-chain amides or acids do **not** join the chain.
- Both possible dipeptides** from two amino acids: A–B and B–A, which are structural isomers.

- **How many dipeptides or tripeptides** can form from a mixture: count the orders, allowing repeats if the question does.
- **Name the reaction:** condensation.

3. Diazotise an aryl amine and couple it to make an azo dye (18 questions)

1. **Diazotisation:** HNO_2 (or NaNO_2 and dilute HCl), **below 10 °C**. Draw $\text{Ar}-\text{N}^+\equiv\text{N}$ with the + on the nitrogen joined to the ring.
2. **Coupling:** the diazonium salt with a phenol (or naphthol or aryl amine) in **NaOH(aq)** , kept cold. Join the rings through $-\text{N}=\text{N}-$ at the position opposite the OH (or NR_2).
3. **Circle the azo group** if asked, and give the use: dye (or indicator, or food colouring).

Variations you will meet:

- **Work back from a dye:** split at the azo group; the amine side becomes ArNH_2 (and its diazonium ion ArN_2^+); the other side is the phenol or aryl amine. Use molecular formulae to check.
- **Two NH_2 groups** (a diamine) are both diazotised; each end then couples, so the dye has two azo groups and two partner molecules.
- **Warm the diazonium salt with water:** the product is a phenol and N_2 . Phenylamine $\rightarrow$ phenol takes two steps: HNO_2 below 10 °C, then warm with water above 10 °C.
- **Equations:** $\text{NaNO}_2 + \text{HCl} \rightarrow \text{HNO}_2 + \text{NaCl}$ and $\text{ArNH}_2 + \text{HNO}_2 + \text{H}^+ \rightarrow \text{ArN}_2^+ + 2\text{H}_2\text{O}$.
- **Groups such as SO_3^-** usually "do not react": carry them through unchanged.

4. Give reagents and conditions to make an aliphatic amine (17 questions)

From	Reagents and conditions	Product
Halogenoalkane	Excess NH_3 in ethanol, heat in a sealed tube (under pressure)	Primary amine
Halogenoalkane	A primary amine in ethanol, heat in a sealed tube	Secondary amine
Nitrile	LiAlH_4 in dry ether, or H_2 and Ni	Primary amine, one more C than the halogenoalkane
Amide	LiAlH_4 in dry ether	Amine, same carbons
Halogenoalkane $\rightarrow$ nitrile	KCN in ethanol, heat under reflux	Chain one carbon longer
Acyl chloride $\rightarrow$ amide	NH_3 or a primary amine, room temperature	Amide

1. **Work out the starting compound from the carbons:** the same number of C as the amine for a halogenoalkane or amide; one fewer for the halogenoalkane that is turned into a nitrile first.

2. **Give reagent and condition:** "sealed tube" or "under pressure" and "ethanol" for the ammonia route; "dry ether" with LiAlH_4 .

Variations you will meet:

- **Name the mechanism** of halogenoalkane + NH_3 : nucleophilic substitution. Give a by-product: a secondary or tertiary amine (for example $(\text{RCH}_2)_2\text{NH}$), and say an excess of ammonia reduces it.
- **Equation with [H]:** an amide takes $4[\text{H}]$ and gives H_2O ($\text{RCONH}_2 + 4[\text{H}] \rightarrow \text{RCH}_2\text{NH}_2 + \text{H}_2\text{O}$); a nitrile takes $4[\text{H}]$ and gives no water.
- **Three different one-step routes** to the same amine: a halogenoalkane with NH_3 , a nitrile one carbon shorter with H_2/Ni , an amide with LiAlH_4 .
- **A secondary amine by two routes:** a primary amine with a halogenoalkane (sealed tube), or reduction of an N-substituted amide (RCONHR') with LiAlH_4 .
- **Curly arrows** for the substitution: N lone pair to the δ^+ carbon, C–Br bond electrons to Br.

5. Define the isoelectric point and draw an amino acid at a given pH (17 questions)

1. **Definition:** the pH at which the amino acid exists as a zwitterion (has no overall charge).
2. **Compare the pH with the isoelectric point** given in the question.
3. **Treat every group separately:** at low pH every $\text{NH}_2 \rightarrow \text{NH}_3^+$ and every COOH stays COOH ; at high pH every $\text{COOH} \rightarrow \text{COO}^-$ and every NH_2 stays NH_2 ; at the isoelectric point draw the zwitterion.
4. **Leave side-chain amides and alcohols alone.**

Variations you will meet:

- **Acidic or basic side chains** at several pH values (for example pH 1, 3, 9 and 14): add or remove one proton at a time, the most acidic group first (the main-chain COOH), then the side-chain COOH , then the NH_3^+ groups.
- **The ions formed as acid is added** to a basic amino acid from its isoelectric point: protonate the remaining NH_2 , then the COO^- .
- **Buffer equations:** $\text{H}_3\text{N}^+\text{CH(R)COO}^- + \text{H}^+ \rightarrow \text{H}_3\text{N}^+\text{CH(R)COOH}$ and $\text{H}_3\text{N}^+\text{CH(R)COO}^- + \text{OH}^- \rightarrow \text{H}_2\text{NCH(R)COO}^- + \text{H}_2\text{O}$.
- **Amino acid with NaOH(aq) :** COOH becomes COO^-Na^+ and water forms.

6. Make an amide from an acyl chloride (16 questions)

1. **Draw the amide:** replace Cl of the acyl chloride with the NH part of the ammonia or amine (for NH_3 : $-\text{CONH}_2$; primary amine: $-\text{CONHR}$; secondary amine: $-\text{CONR}_2$).
2. **Write the equation** with HCl as the other product; conditions: room temperature.
3. **Name the reaction:** condensation, or (nucleophilic) addition–elimination as the mechanism.

Variations you will meet:

- **The mechanism** (4 marks): N lone pair; arrow to the C of C=O; dipole on C=O; arrow from C=O to O; the intermediate with O^- and N^+ ; then arrows reforming C=O and breaking C–Cl; products amide + HCl.
- **Molecules with two groups**: with an NH_2 and an OH, an acyl chloride can give an amide or an ester; with an excess it acylates both (use the molecular formula to decide). An amide $CONH_2$ never reacts.
- **A diacyl chloride with two molecules of an amine** (for example an amino acid): each $COCl$ makes one amide, so three molecules join; count the amide groups.
- **Work back**: identify the acyl chloride from the amide by cutting the $C(=O)–N$ bond.

7. Draw the products of amide or peptide hydrolysis (14 questions)

1. **Find every amide** (and ester, which hydrolyses too) and mark the $C(=O)–N$ bond that breaks.
2. **Hot acid**: each acid part is $COOH$; each amine part is $-NH_3^+$ (NH_4^+ from $-CONH_2$); alcohols from esters stay as OH.
3. **Hot alkali**: each acid part is COO^- (with Na^+); each amine part is $-NH_2$ (NH_3 from $-CONH_2$); a phenol OH becomes O^- .
4. **Count the products**: pieces = bonds broken + 1.

Variations you will meet:

- **"Name the two types of reaction"** with hot $NaOH(aq)$: hydrolysis and acid–base (neutralisation).
- **Products "at pH 4"** or after acid hydrolysis: all amines NH_3^+ , all acids $COOH$.
- **Reagent for a hydrolysis step**: dilute $HCl(aq)$ (or $H_2SO_4(aq)$) and heat under reflux.
- **Groups the question says don't react** (such as CH_3O- on a ring) are carried over unchanged.

8. Make an aryl amine by reducing a nitro compound (13 questions)

1. **Step 1, nitration** (if needed): concentrated HNO_3 and concentrated H_2SO_4 , about $50\text{ }^\circ\text{C}$.
2. **Step 2, reduction**: tin and concentrated HCl , heat under reflux; then $NaOH(aq)$. Type of reaction: reduction.
3. **Equation**: add $6[H]$ and $2H_2O$ for each NO_2 .

Variations you will meet:

- **Two nitro groups**: $12[H]$ and $4H_2O$.
- **Longer routes** from methylbenzene: the order of nitration, oxidation of CH_3 to $COOH$ (hot $KMnO_4$) and reduction matters, because of directing effects (see "Hydrocarbons"). An NH_2 then made can be alkylated with a halogenoalkane (nucleophilic substitution) or acylated with an acyl chloride.
- **Identify the compound reduced to give a given amine**: the same molecule with NO_2 in place of NH_2 .
- Iron and concentrated HCl also works in place of tin.

9. Identify amine and amide groups and classify the amine (10 questions)

1. **Go round the molecule group by group:** N next to C=O is an amide; N with only C and H is an amine; also look for ester, carboxylic acid, alcohol (primary, secondary or tertiary), phenol, alkene, ketone, arene.
2. **Classify each amine** by the number of carbons on N (primary, secondary, tertiary), and each alcohol by the number of carbons on the C–OH carbon.

Marks are usually "any two correct, 1 mark; all correct, 2 marks", so list every group. Don't give "amine" for an amide or "ketone" for the C=O of an amide or ester.

10. Predict electrophoresis results (8 questions)

1. **For each species compare the buffer's pH with its isoelectric point:** below → positive → towards the cathode; equal → stays at the start; above → negative → towards the anode.
2. **Distance:** larger charge further; for the same charge, smaller M_r , further (an amino acid beats a dipeptide).
3. **Draw and label** each spot on the correct side of the start line, and explain in words.

Variations you will meet:

- **Identify spots** from a given result: match each spot's direction and distance to charge and size.
- **Change the pH:** a species that stayed put at its isoelectric point moves to the anode at a higher pH and to the cathode at a lower pH.
- **A dipeptide's charge:** count its NH_3^+ and COO^- groups at that pH (a lysine-type side chain adds +1, a glutamic-acid-type side chain adds –1).
- **How the pH is kept constant:** a buffer solution.

11. Phenylamine and bromine water (8 questions)

1. **Conditions:** bromine water, room temperature, no catalyst.
2. **Observations:** orange (or yellow-brown) colour disappears; white precipitate.
3. **Product:** 2,4,6-tribromophenylamine (Br on both positions next to NH_2 and the one opposite), plus 3HBr .
4. **Explain:** the lone pair (p orbital) on N overlaps with the ring's π system, raising the ring's electron density, so the ring polarises Br_2 and is attacked easily; benzene's ring is not electron-rich enough to react without a catalyst.

Variation: telling an aryl amine from an alkyl amine: only the aryl amine gives a white precipitate; the alkyl amine gives no precipitate.

12. Draw the product of reducing an amide with LiAlH_4 (7 questions)

1. **Every amide C=O becomes CH_2 :** $-\text{CONH}_2 \rightarrow -\text{CH}_2\text{NH}_2$; $-\text{CONH}- \rightarrow -\text{CH}_2\text{NH}-$.
2. **Other groups in an excess of LiAlH_4 :** $\text{COOH} \rightarrow \text{CH}_2\text{OH}$; ketone or aldehyde → alcohol; ester → two alcohols; nitrile → CH_2NH_2 . C=C and benzene rings are **not** reduced.

3. **Give the type of reaction** (reduction) and, if asked, the reagent (LiAlH_4 in dry ether).

Worked examples

The bold codes show where marks are earned, as in Cambridge mark schemes. The number is how many marks.

- **M1** method mark: for a correct method, even if the numbers slip.
- **A1** accuracy mark: for a correct answer; it needs the M mark before it.
- **B1** mark for a correct result on its own, with no method needed.

Example 1

1-(4-aminophenyl)ethanone, $\text{CH}_3\text{COC}_6\text{H}_4\text{NH}_2$ ($\text{C}_8\text{H}_9\text{NO}$), is an aryl amine with a ketone group on the ring carbon opposite the NH_2 . It is used to make a yellow azo dye with 2-hydroxybenzoic acid, $\text{HOC}_6\text{H}_4\text{COOH}$ (OH on carbon 2, COOH on carbon 1). The ketone group does not react.

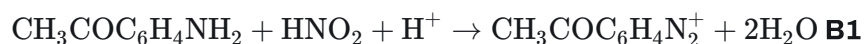
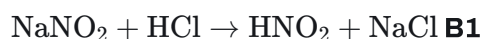
(a) Give the reagents and conditions for converting 1-(4-aminophenyl)ethanone into its diazonium salt, and write equations for the two reactions involved. **[3]**

(b) 2-hydroxybenzoic acid is dissolved in an excess of cold NaOH(aq) before the diazonium salt is added. Give the organic ion present in this solution, and explain why the alkaline solution helps the coupling. **[2]**

(c) Coupling happens at carbon 5 of 2-hydroxybenzoic acid, the carbon opposite the OH. The mixture is then acidified to give the dye. Describe the structure of the dye, identify the azo group, and give the dye's molecular formula. **[2]**

(d) 3.24 g of 1-(4-aminophenyl)ethanone gives 5.12 g of the dye. Calculate the minimum mass of sodium nitrite needed and the percentage yield of the dye. **[3]**

(a) Sodium nitrite and dilute hydrochloric acid, below 10°C . **B1**



(b) Both acidic groups lose a proton, giving the ion $^-\text{OC}_6\text{H}_4\text{COO}^-$. **B1** A lone pair on the O^- is delocalised into the ring even more strongly than the lone pair of an OH group, so the ring is very electron-rich and the weakly electrophilic diazonium ion can attack it. **B1** The diazonium salt solution is kept cold and used at once, because it breaks down, giving off nitrogen, if it warms up.

(c) $\text{CH}_3\text{CO}-\text{C}_6\text{H}_4-\text{N}=\text{N}-\text{C}_6\text{H}_3(\text{OH})\text{COOH}$: the $-\text{N}=\text{N}-$ azo group joins the ring carbon that carried the NH_2 to carbon 5 of the second ring, opposite its OH; the OH and COOH stay next to each other on carbons 2 and 1. **B1** Molecular formula $\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_4$. **B1**

(d) $M_r(\text{C}_8\text{H}_9\text{NO}) = 96.0 + 9.0 + 14.0 + 16.0 = 135.0$, so $3.24 \div 135.0 = 0.0240$ mol. One mole of NaNO_2 ($M_r = 69.0$) is needed per mole of amine: $0.0240 \times 69.0 = 1.66$ g. **B1**

$M_r(\text{C}_{15}\text{H}_{12}\text{N}_2\text{O}_4) = 180.0 + 12.0 + 28.0 + 64.0 = 284.0$, so the maximum mass of dye is $0.0240 \times 284.0 = 6.82$ g. **M1** Yield = $5.12 \div 6.82 \times 100 = 75.1\%$. **A1**

Example 2

1,5-dibromopentane, $\text{Br}(\text{CH}_2)_5\text{Br}$, is heated with ammonia in ethanol in a sealed tube. The main organic product, E, has molecular formula $\text{C}_5\text{H}_{11}\text{N}$. E contains no bromine, does not decolourise bromine water, and its aqueous solution has a pH above 7.

(a) Suggest the structure of E, classify it as a primary, secondary or tertiary amine, and explain how it forms. **[3]**

(b) E is heated with bromoethane in ethanol in a sealed tube to give F, $\text{C}_7\text{H}_{15}\text{N}$. Give the structure of F, classify it, and write an equation for its formation. **[2]**

(c) At room temperature E reacts with benzoyl chloride, $\text{C}_6\text{H}_5\text{COCl}$, to give G, $\text{C}_{12}\text{H}_{15}\text{NO}$, but F does not react. Give the structure of G, name the type of reaction, and explain why F does not react. **[3]**

(d) 4.60 g of 1,5-dibromopentane gives 1.19 g of E. Calculate the percentage yield. **[2]**

(a) E is piperidine, $(\text{CH}_2)_5\text{NH}$: a six-membered ring of five CH_2 groups and one NH. **B1** Its N is bonded to two carbons, so it is a secondary amine. **B1** Ammonia replaces one Br (nucleophilic substitution), giving $\text{Br}(\text{CH}_2)_5\text{NH}_2$; the lone pair on this N then attacks the carbon of the C–Br bond at the other end of the same chain, closing the ring, and HBr is lost. **B1** There is no C=C, so bromine water is not decolourised, and the N lone pair makes E basic.

(b) F is N-ethylpiperidine, $(\text{CH}_2)_5\text{NCH}_2\text{CH}_3$, a tertiary amine. **B1**

$(\text{CH}_2)_5\text{NH} + \text{CH}_3\text{CH}_2\text{Br} \rightarrow (\text{CH}_2)_5\text{NCH}_2\text{CH}_3 + \text{HBr}$ **B1**

(c) G is $(\text{CH}_2)_5\text{N}-\text{COC}_6\text{H}_5$: the benzoyl group is joined to the ring N, giving an amide with no N–H. **B1** Condensation (the mechanism is nucleophilic addition–elimination). **B1** F has no H on its N. Its lone pair can attack the acyl chloride, but the N^+ formed cannot lose H^+ to give a neutral amide. **B1**

(d) $M_r(\text{C}_5\text{H}_{10}\text{Br}_2) = 60.0 + 10.0 + 159.8 = 229.8$, so $4.60 \div 229.8 = 0.02002$ mol. **M1**

$M_r(\text{C}_5\text{H}_{11}\text{N}) = 85.0$, so the maximum mass is $0.02002 \times 85.0 = 1.702$ g, and the yield is $1.19 \div 1.702 \times 100 = 69.9\%$. **A1** Keep the unrounded moles: rounding to 0.0200 mol first gives 70.0%.

Example 3

Pentanoyl chloride, $\text{CH}_3(\text{CH}_2)_3\text{COCl}$, is added slowly at room temperature to a large excess of ethane-1,2-diamine, $\text{H}_2\text{NCH}_2\text{CH}_2\text{NH}_2$. The main organic product is L, $\text{C}_7\text{H}_{16}\text{N}_2\text{O}$.

(a) Give the structure of L, write an equation for its formation using two moles of the diamine, and name the type of reaction. [3]

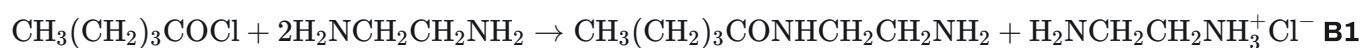
(b) When the diamine is added to an excess of pentanoyl chloride instead, the product is M, $C_{12}H_{24}N_2O_2$. Give the structure of M, and explain why a large excess of the diamine gives mainly L. [2]

(c) L reacts with one mole of $HCl(aq)$. Draw the ion formed and explain which nitrogen atom accepts the proton. [3]

(d) Give the products when L is heated with $NaOH(aq)$, and name the two types of reaction that happen. [2]

(e) L is reduced with $LiAlH_4$ in dry ether. Give the product and write an equation using $[H]$. [2]

(a) L is $CH_3(CH_2)_3CONHCH_2CH_2NH_2$: one end of the diamine has become an amide and the other is still an amine. **B1**



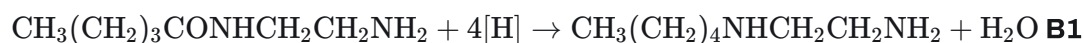
Condensation (nucleophilic addition–elimination). **B1**

(b) Both NH_2 groups have become amides: M is $C_4H_9CONHCH_2CH_2NHCOC_4H_9$. **B1** With a large excess of diamine, each acyl chloride molecule is far more likely to meet an unreacted diamine molecule than the free NH_2 of an L molecule. **B1**

(c) $CH_3(CH_2)_3CONHCH_2CH_2NH_3^+$ **B1**. The amine N's lone pair is available to accept a proton, helped by the electron-donating alkyl chain. **B1** The amide N's lone pair is delocalised into the $C=O$ group, so it is not available; the amide N is not protonated. **B1**

(d) Sodium pentanoate, $CH_3(CH_2)_3COO^-Na^+$, and ethane-1,2-diamine. **B1** Hydrolysis and acid–base (neutralisation). **B1**

(e) The $C=O$ becomes CH_2 : $CH_3(CH_2)_4NHCH_2CH_2NH_2$, which has one secondary and one primary amine group. **B1**



Example 4

Methionine (Met), $CH_3SCH_2CH_2CH(NH_2)COOH$, has isoelectric point 5.7. Tryptophan (Trp), $C_{11}H_{12}N_2O_2$, is $H_2NCH(CH_2Ar)COOH$, where Ar is a ring system, C_8H_6N , that does not react; its isoelectric point is 5.9. Histidine (His), $C_6H_9N_3O_2$, has isoelectric point 7.6.

(a) State what is meant by the isoelectric point of an amino acid. [1]

(b) Draw the zwitterion of methionine, and the ion formed when dilute $NaOH(aq)$ is added to it. [2]

(c) Draw the dipeptide Met–Trp, with the peptide bond displayed, and give its molecular formula and M_r . [3]

(d) How many different dipeptides could form from a mixture of methionine and tryptophan? [1]

(e) Methionine must be separated from histidine by electrophoresis. A buffer of pH 6.6 is chosen, close to halfway between their isoelectric points. Predict the direction in which each moves, and explain why this choice of pH gives a clear separation. [3]

(f) Give the organic products when Met–Trp is heated with an excess of NaOH(aq). [1]

(a) The pH at which the amino acid exists as a zwitterion, with no overall charge. **B1**

(b) Zwitterion: $\text{CH}_3\text{SCH}_2\text{CH}_2\text{CH}(\text{NH}_3^+)\text{COO}^-$. **B1** With NaOH(aq) the NH_3^+ loses its proton: $\text{CH}_3\text{SCH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{COO}^-$. **B1**

(c) $\text{CH}_3\text{SCH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{--CO--NH--CH}(\text{CH}_2\text{Ar})\text{COOH}$, with the peptide bond drawn as C=O and N–H, a CH on each side. **M1** (displayed peptide bond) **A1** (rest correct: methionine keeps the NH_2 , tryptophan keeps the COOH).

$\text{C}_5\text{H}_{11}\text{NO}_2\text{S} + \text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_2 - \text{H}_2\text{O} = \text{C}_{16}\text{H}_{21}\text{N}_3\text{O}_3\text{S}$, $M_r = 149.1 + 204.0 - 18.0 = 335.1$. **B1**

(d) Four: Met–Met, Trp–Trp, Met–Trp and Trp–Met. **B1**

(e) pH 6.6 is 0.9 above methionine's isoelectric point, so methionine is overall negative (an anion) and moves towards the anode. **B1** pH 6.6 is 1.0 below histidine's isoelectric point, so histidine is positive and moves towards the cathode. **B1** The two move in opposite directions, so their spots end up on opposite sides of the start line however far each travels. At a pH above both isoelectric points both would move to the anode, and only a difference in charge and M_r , would pull them apart. **B1**

(f) $\text{CH}_3\text{SCH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{COO}^-\text{Na}^+$ and $\text{ArCH}_2\text{CH}(\text{NH}_2)\text{COO}^-\text{Na}^+$. **B1**

Common mistakes

- **Not linking basicity to the lone pair accepting a proton.** Examiners report that many answers get the order and the inductive effect right but never say the lone pair on N is more or less available to accept H^+ , and lose that mark. Leaving the words "lone pair" out of the phenylamine or amide explanation loses marks too.
- **Saying phenylamine's lone pair is delocalised "into the nitrogen"** or forgetting the ring. Say "the lone pair on N is delocalised into the benzene ring".
- **Protonating an amide.** Amides are neutral: a side-chain CONH_2 stays CONH_2 at pH 1. Writing $-\text{CONH}_3^+$ is one of the commonest errors examiners see.
- **Making the peptide bond with a side chain.** Use the NH_2 and COOH on the central carbon; don't join through a side-chain amide, amine or acid. Draw a dipeptide when a dipeptide is asked for, not a tripeptide or a ring.
- **Writing the peptide link wrongly**, such as $-\text{COO--NH--}$ or with a carbon that has only three bonds. Check each carbon has four bonds.
- **Calling tin a catalyst.** In the reduction of nitrobenzene, tin and concentrated HCl are reactants. Remember NaOH(aq) afterwards.

- **Getting diazotisation conditions wrong:** missing "below 10 °C", or writing " HNO_3 " for HNO_2 . Put the + charge of ArN_2^+ on the nitrogen joined to the ring, and call it a diazonium ion, not a "diazo" or "azo" group.
- **Leaving the diazonium salt out of a reaction scheme:** coupling needs the diazonium salt and the phenol, not phenylamine and phenol.
- **Bromine positions.** Phenylamine gives 2,4,6-tribromophenylamine, not 3,5-dibromo; and the observation is a white precipitate, not just "decolourised".
- **Explaining electrophoresis distance by M_r alone.** Direction comes from the sign of the charge; distance comes from the size of the charge **and** the M_r .
- **Hydrolysis products in the wrong form:** in acid, amines must be NH_3^+ ; in alkali, acids must be COO^- . An acyl chloride is never a hydrolysis product.
- **Curly arrows from an atom instead of a lone pair,** or forgetting the lone pair on the amine's N in the addition–elimination mechanism. Draw the lone pair and start the arrow from it.

How to get the marks

- **"State the relative basicities ... explain":** the order (1), the lone pair-accepts-a-proton link (1), then one structural reason per compound (inductive effect, delocalised into the ring, delocalised into C=O). Mark schemes accept "lone pair" or "p orbital", and "delocalised into", "overlaps with" or "incorporated into" the ring.
- **Reagents and conditions** means both: "excess NH_3 in ethanol, heat in a sealed tube"; " LiAlH_4 in dry ether"; "Sn and conc. HCl, heat, then NaOH(aq) "; " NaNO_2 and HCl, below 10 °C"; "phenol in NaOH(aq) ".
- **Structures:** draw exactly what is asked (displayed peptide bond, skeletal, or structural formula), keep every other group unchanged, and check against a molecular formula if one is given. For ions, show the charges.
- **Equations:** balanced, with every product (H_2O , HCl, HBr, N_2 , NH_4Cl). Use $[\text{H}]$ for a reducing agent, with $4[\text{H}]$ per nitrile or amide C=O and $6[\text{H}]$ per NO_2 .
- **Definitions:** the isoelectric point is "the pH at which the amino acid is a zwitterion / has no overall charge"; it must say pH.
- **"Suggest"** means apply the rules to an unfamiliar molecule: a drug, a dye, an unusual amino acid. Marks go to using the rules consistently.
- **Electrophoresis:** draw each spot on the correct side of the start line, label every spot, and explain both direction (charge) and distance (charge and M_r).
- **"Describe" observations:** say what you see, such as "orange solution decolourised and a white precipitate", "effervescence" or "brightly coloured product". "No change" counts as an observation and must be written.
- **Calculations:** use the Data Booklet A_r values and $24.0 \text{ dm}^3 \text{ mol}^{-1}$, show the moles, and give 3 significant figures unless told otherwise.

Quick check

- 1-bromo-3-nitrobenzene is reduced to 3-bromophenylamine. Give the reagents and conditions, explain why NaOH(aq) is added at the end, and write an equation using [H].
- 1.72 g of 3-bromophenylamine, $\text{BrC}_6\text{H}_4\text{NH}_2$, reacts completely with an excess of bromine water at room temperature. Name the white precipitate, write an equation, and calculate the maximum mass of precipitate.
- Methionine, $\text{CH}_3\text{SCH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{COOH}$, has isoelectric point 5.7. Draw its structure at pH 1 and at pH 13. Towards which electrode does methionine move during electrophoresis at pH 3.0, and at pH 9.0?
- The tripeptide Met–Trp–His is made from methionine ($\text{C}_5\text{H}_{11}\text{NO}_2\text{S}$), tryptophan ($\text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_2$) and histidine ($\text{C}_6\text{H}_9\text{N}_3\text{O}_2$). How many peptide bonds does it have? Give its molecular formula and M_r . How many different tripeptides contain one residue of each of the three amino acids?
- 1.65 g of ethyl 4-aminobenzoate, $\text{H}_2\text{NC}_6\text{H}_4\text{COOCH}_2\text{CH}_3$ ($\text{C}_9\text{H}_{11}\text{NO}_2$), is converted into its diazonium salt, and the cold solution is then warmed to 50 °C until no more gas is given off. The ester group does not react. Name the organic product, identify the gas and calculate its volume at room conditions.

Answers

1. Tin and concentrated hydrochloric acid, heated under reflux. In the acid the amine is formed as its salt, $\text{BrC}_6\text{H}_4\text{NH}_3^+$; NaOH(aq) removes the proton to give the free amine. $\text{C}_6\text{H}_4\text{BrNO}_2 + 6[\text{H}] \rightarrow \text{C}_6\text{H}_6\text{BrN} + 2\text{H}_2\text{O}$ (the Br on the ring is not affected).
2. The precipitate is 2,3,4,6-tetrabromophenylamine: Br goes onto the free positions 2, 4 and 6 next to and opposite the NH_2 , joining the Br already at 3. $\text{C}_6\text{H}_6\text{BrN} + 3\text{Br}_2 \rightarrow \text{C}_6\text{H}_3\text{Br}_4\text{N} + 3\text{HBr}$.
 $M_r(\text{C}_6\text{H}_6\text{BrN}) = 171.9$, so $1.72 \div 171.9 = 0.0100$ mol; $M_r(\text{C}_6\text{H}_3\text{Br}_4\text{N}) = 408.6$, so the maximum mass is $0.0100 \times 408.6 = 4.09$ g.
3. pH 1: $\text{CH}_3\text{SCH}_2\text{CH}_2\text{CH}(\text{NH}_3^+)\text{COOH}$. pH 13: $\text{CH}_3\text{SCH}_2\text{CH}_2\text{CH}(\text{NH}_2)\text{COO}^-$. At pH 3.0 (below 5.7) methionine is positive and moves towards the cathode; at pH 9.0 (above 5.7) it is negative and moves towards the anode.
4. Two peptide bonds (three residues). Formula: $\text{C}_5\text{H}_{11}\text{NO}_2\text{S} + \text{C}_{11}\text{H}_{12}\text{N}_2\text{O}_2 + \text{C}_6\text{H}_9\text{N}_3\text{O}_2 - 2\text{H}_2\text{O} = \text{C}_{22}\text{H}_{28}\text{N}_6\text{O}_4\text{S}$. $M_r = 22(12.0) + 28(1.0) + 6(14.0) + 4(16.0) + 32.1 = 472.1$. There are $3 \times 2 \times 1 = 6$ orders, so 6 tripeptides.
5. Ethyl 4-hydroxybenzoate, $\text{HOC}_6\text{H}_4\text{COOCH}_2\text{CH}_3$; the gas is nitrogen: $\text{CH}_3\text{CH}_2\text{OOCN}_2^+ + \text{H}_2\text{O} \rightarrow \text{CH}_3\text{CH}_2\text{OOCN}_2 + \text{H}^+$. $M_r(\text{C}_9\text{H}_{11}\text{NO}_2) = 165.0$, so $1.65 \div 165.0 = 0.0100$ mol of amine gives 0.0100 mol of diazonium ion and so 0.0100 mol of N_2 : $0.0100 \times 24\,000 = 240$ cm³.

Past questions to try

- **9701/42/O/N/23 Q9**: two routes to a secondary amine, basicities, an azo dye from phenylamine and the amide-forming mechanism.
- **9701/43/O/N/21 Q10**: drawing amino acids at different pH values, including a basic amino acid, and a displayed dipeptide.
- **9701/42/M/J/24 Q8**: basicities, phenylamine with bromine water, the addition–elimination mechanism, an isoelectric point and a dipeptide.
- **9701/43/M/J/23 Q7**: basicities with an amide, a buffering amino acid, a dipeptide and an electrophoresis result.