Organic synthesis

Identifying functional groups from reactions, predicting reactions of molecules with several functional groups, and planning and analysing multi-step synthetic routes from the AS Level reactions.

21.1 Organic synthesis

Identifying functional groups

Use the characteristic tests and reactions:

Observation	Functional group
Decolourises aqueous bromine	C=C
Orange precipitate with 2,4-DNPH	C=O (aldehyde or ketone)
Silver mirror (Tollens') or red precipitate (Fehling's)	aldehyde
Orange to green with acidified $K_2Cr_2O_7$, warm	primary or secondary alcohol (or aldehyde)
Yellow precipitate with alkaline iodine	CH_3CO- or $CH_3CH(OH)-$
Effervescence with Na_2CO_3	–COOH
Hydrogen released with Na(s)	–OH (or –COOH)
Precipitate with warm $AgNO_3$ in ethanol	halogenoalkane
Hydrolysed by NaOH (aq) to an acid salt and an alcohol	ester

For a molecule with **several functional groups** (for example a hydroxy acid or an unsaturated aldehyde), each group reacts as it would on its own, so you can predict the reactions and properties by treating each group in turn. Choose reagents carefully: $LiAlH_4$ reduces C=O but not C=C, whereas H_2/Ni reduces both.

Reaction map (AS Level)

- Alkane → halogenoalkane: Cl_2 or Br_2, UV light.
- Alkene → halogenoalkane: HX, room temperature. Alkene → alcohol: steam, H_3PO_4. Alkene → diol: cold $KMnO_4$.
- Halogenoalkane → alcohol: NaOH(aq), heat. → nitrile: KCN, ethanol, heat. → amine: NH_3/ethanol, pressure. → alkene: NaOH in ethanol, heat.

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- Alcohol → alkene: heated Al_2O_3 or concentrated H_2SO_4. → halogenoalkane: PCl_5 or HX. → aldehyde: dichromate, distil. → ketone (secondary): dichromate. → acid: dichromate, reflux. → ester: carboxylic acid, H_2SO_4.
- Aldehyde/ketone → alcohol: $NaBH_4$ or $LiAlH_4$. → hydroxynitrile: HCN, KCN.
- Nitrile → carboxylic acid: dilute acid or alkali, heat. Ester → acid + alcohol: hydrolysis.

Planning a route

1. Compare the **starting material and the target**: what has changed (the carbon chain, the functional group, or both)?
2. Work **backwards** from the target (retrosynthesis).
3. Check each step for the correct **reagents and conditions**, possible **by-products** and **yield**.

> **TRY IT**
>
> Plan a synthesis of ethanoic acid from ethene, and a second route that makes propanoic acid from ethene.

Ethanoic acid: ethene + steam with H_3PO_4 catalyst gives ethanol; reflux the ethanol with excess acidified $K_2Cr_2O_7$ to give ethanoic acid. **Propanoic acid** needs one more carbon: ethene + HBr gives bromoethane; KCN in ethanol, heat gives propanenitrile; reflux with dilute HCl gives propanoic acid.

Analysing a route

For each step state the **type of reaction** (substitution, addition, elimination, oxidation, reduction, condensation, hydrolysis), the **reagents and conditions**, and likely **by-products** (for example, a mixture from free-radical substitution, or an elimination product alongside substitution of a halogenoalkane).

Start with the carbon skeleton

Write structures for the starting material and target, count their carbons and mark the functional groups. If the target has an extra carbon, an ordinary oxidation, reduction or hydroxide substitution will not create it. Cyanide substitution or carbonyl addition can supply a new carbon. If the carbon count is unchanged, first look for a direct functional-group conversion before proposing unnecessary chain-building steps.

Worked example: propan-1-ol to propanoic acid requires oxidation under reflux with excess suitable acidified oxidant. Propan-1-ol to butanoic acid needs chain extension: convert OH to a leaving group, substitute with cyanide to form butanenitrile, then hydrolyse. Merely “oxidise further” cannot add the fourth carbon.

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Work backwards through specific intermediates

A target alcohol could come from carbonyl reduction, alkene hydration or halogenoalkane hydrolysis, but these routes may differ in positional selectivity. A target carboxylic acid could come from a primary alcohol, aldehyde, nitrile or ester. Choose an intermediate whose structure matches the target rather than naming a broad class only.

Worked route: ethene to ethyl ethanoate requires an acid fragment and an alcohol fragment. Hydrate ethene to ethanol, retain part of the ethanol and oxidise another portion under reflux to ethanoic acid. Esterify the acid with retained ethanol using an acid catalyst and heat. If all ethanol were oxidised first, the proposed final mixture would lack the required alcohol unless a further supply were added.

> **TRY IT**
>
> Give two steps to convert bromoethane to ethene and then back to ethanol, stating solvent/conditions.

Answer: Heat bromoethane with ethanolic hydroxide to eliminate HBr and form ethene. Hydrate ethene with steam and a phosphoric-acid catalyst under suitable conditions. Aqueous hydroxide in the first step would instead favour direct substitution.

Reagents are incomplete without conditions

For primary alcohol oxidation, distillation favours aldehyde collection, whereas reflux with excess oxidant gives acid. For halogenoalkane reactions, aqueous versus ethanolic hydroxide distinguishes preferred substitution and elimination. For nitrile or ester hydrolysis, alkaline conditions initially give a salt; acidification must be stated if the target is a free acid.

Worked correction: “Bromoethane, NaOH, propanoic acid” cannot be completed as a one-step route. NaOH does not add carbon, and substitution would give ethanol. The correct chain-extension reagent is cyanide in a suitable solvent with heat, followed by nitrile hydrolysis. Check atom accounting before polishing reagent names.

> **TRY IT**
>
> A route heats an ester with NaOH and labels the isolated product directly as a carboxylic acid. What step is missing?

Answer: Acidification of the carboxylate salt after hydrolysis. The strongly alkaline mixture contains mainly carboxylate, not free acid.

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Multifunctional compounds require selectivity

Mark every reactive group before applying a reagent. A molecule containing an alkene and an aldehyde can undergo addition at C=C or nucleophilic addition/reduction at C=O. Sodium borohydride generally reduces the carbonyl while leaving an ordinary isolated C=C unchanged under standard syllabus conditions. Hydrogenation selectivity depends on catalyst and conditions; do not assume every functional group is inevitably reduced equally.

Worked example: $CH_2=CHCHO$ reduced with suitable $NaBH_4$ conditions gives $CH_2=CHCH_2OH$, retaining alkene. Strong oxidative treatment could affect both the aldehyde and the double bond, so it is a less selective option if preserving C=C is required. For a hydroxy acid, sodium metal can react with acidic hydrogens in both OH-containing groups; gas stoichiometry therefore needs attention to the complete structure.

> **TRY IT**
>
> A compound contains COOH and CHO. Which ordinary syllabus reagent could reduce the aldehyde without also reducing the acid group?

Answer: $NaBH_4$ under appropriate conditions. $LiAlH_4$ is a stronger reagent that can also reduce the carboxylic acid, so it is less suitable for that selectivity goal.

Identification is an evidence problem

Treat a test result as a constraint rather than an automatic complete structure. Bromine decolourisation is compatible with C=C but later aromatic groups can also react. Sodium releases hydrogen from both alcohols and acids. DNPH detects aldehyde/ketone functionality but does not distinguish them. Negative tests are valuable when the reagent and conditions are appropriate and a reliable positive control exists.

Worked identification: C_4H_8O gives DNPH precipitate, no Tollens' response and positive iodoform. DNPH supplies the carbonyl constraint, negative Tollens' supports a ketone, and iodoform requires a methyl-carbonyl group. Butanone fits all three and the molecular formula. Butanal fits the formula and DNPH but fails the other constraints.

Yield and route evaluation

For consecutive independent stages, multiply fractional yields. Two 80.0% steps give $0.800^2=64.0\%$ overall, not 160% or 80%. More steps often reduce material recovery and increase purification demands, even when each transformation is chemically plausible. A short route is useful only if it gives the required connectivity and manageable selectivity.

Worked calculation: starting with 0.100 mol, stage yields of 75.0%, 80.0% and 90.0% leave $0.100(0.750)(0.800)(0.900)=0.0540$ mol final product, or 54.0% overall. Use stoichiometric

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coefficients as well if any step is not 1 : 1.

> **TRY IT**
>
> A 60.0% first step and 50.0% second step start from 0.200 mol in a 1 : 1 sequence. Find the final amount.

Answer: $0.200(0.600)(0.500) = 0.0600$ mol, corresponding to 30.0% overall yield.

Chapter check: draw every intermediate, balance carbon count, state conditions, check competing functional groups and calculate cumulative yield. Use the reaction chapters as a reference rather than treating a reaction map as an unexplained list.

References and further reading

Scope follows section 21 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.

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