

Cambridge (CIE) A Level Chemistry



Your notes

Organic Synthesis

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- * Organic Synthesis
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- * Synthetic Routes



Elucidating Organic Molecules

- You are expected to be able to identify organic functional groups, their properties, how to test for their presence and how they are made

Functional groups

- The table below summarises the tests to identify the presence of certain functional groups and the reactions to make them

Functional groups, their reactions & identifying tests table

Functional Group	Test	Production
Alkane	No specific chemical test	Hydrogenation of alkenes using H_2 , Pt/Ni catalyst and heat Cracking of crude oil using heat and Al_2O_3 catalyst
Alkene	Decolourises bromine water	Elimination of halogenoalkanes by heating it with ethanolic NaOH Dehydration of alcohols using hot Al_2O_3 catalyst Cracking of crude oil using heat and Al_2O_3 catalyst
Halogenoalkane (primary, secondary and tertiary)	Form silver halide precipitate with dilute nitric acid, silver nitrate and dilute ammonia solution ($AgCl$ = white, $AgBr$ = cream and AgI = yellow)	Free-radical substitution of alkanes using UV and a halogen Electrophilic addition of hydrogen halides to alkenes Nucleophilic substitution of an alcohol, e.g. by reaction with HX (g) or with KCl and concentrated H_2SO_4 or concentrated H_3PO_4 or with PCl_3 and heat or with PCl_5 or with $SOCl_2$
Alcohol (primary, secondary and tertiary)	React with carboxylic acid and sulfuric acid to make esters which have fruity smells Primary alcohols get oxidised to aldehydes (give	Electrophilic addition of alkenes using hot steam, concentrated phosphoric(VI) acid as a catalyst Oxidation of alkenes using cold, dilute $KMnO_4$ to form a diol



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	<p>positive test with Fehling's and Tollens' solution and carboxylic acids</p> <p>Secondary alcohols are oxidised to ketones (positive test with 2,4-DNPH but not Fehling's and Tollens' solution)</p> <p>Tertiary alcohols cannot be oxidised</p>	<p>Nucleophilic substitution of halogenoalkanes using heat and NaOH (aq)</p> <p>Reduction of aldehydes and ketones using NaBH₄ and LiAlH₄ (aldehydes are reduced to primary alcohols and ketones are reduced to secondary alcohols)</p> <p>Reduction of carboxylic acid using LiAlH₄</p> <p>Hydrolysis of esters using dilute acid or dilute alkali</p>
Aldehyde	<p>Silver mirror in Tollens' reagent</p> <p>Red precipitate in Fehling's solution</p> <p>Orange precipitate with 2,4-DNPH</p>	<p>Primary alcohols can be oxidised to aldehydes using acidified K₂Cr₂O₇ or KMnO₄, with distillation to prevent further oxidation to carboxylic acids</p>
Ketone	<p>Orange precipitate with 2,4-DNPH</p>	<p>Oxidation of secondary alcohols in acidified K₂Cr₂O₇ or KMnO₄ and under distillation</p>
Carboxylic Acid	<p>React with carbonates to form CO₂ gas which will turn limewater cloudy</p>	<p>Oxidation of aldehydes and alcohols using acidified K₂Cr₂O₇ or KMnO₄ under reflux</p> <p>Hydrolysis of nitriles with dilute acid or dilute alkali followed by acidification</p> <p>Hydrolysis of ester with dilute acid or dilute alkali followed by acidification</p>
Ester	<p>Have sweet, fruity smells</p>	<p>Condensation reaction of alcohols and carboxylic acids with hot, concentrated H₂SO₄ as catalyst</p>
Amine	<p>Turns damp red litmus paper blue</p> <p>Turns universal indicator blue / purple</p>	<p>Nucleophilic substitution of halogenoalkanes when heated under pressure with NH₃ (ethanol)</p>
Nitrile	<p>No official test</p>	<p>Nucleophilic substitution of halogenoalkanes when heated under</p>



Types of reactions

- You should also be aware of the different type of reactions that functional groups can undergo

Reactions of functional groups table

Type of reaction	Definition	Reagents	Products
Hydrogenation	The addition of alkenes with hydrogen	H ₂ , Pt / Ni catalyst	Alkanes
Cracking	The process in which large, less useful hydrocarbon molecules are broken down into smaller, more useful molecules in an oil refinery	Al ₂ O ₃ catalyst and heat	Alkanes and alkenes
Free-radical substitution	The reaction in which halogen atoms substitute for hydrogen atoms in alkanes, The mechanism involves steps in which reactive free radicals are produced (initiation), regenerated (propagation) and consumed (termination)	Halogen and UV light	Halogenoalkane
Electrophilic Addition	The mechanism of the reaction in which an electrophile attacks the C=C bond and addition across the double bond occurs	Electrophile (eg. Br ₂ , HBr, H ₂ O and H ₂ SO ₄)	Halogenoalkane, alcohol or alkane
Nucleophilic Addition	The mechanism of the reaction in which a nucleophile attacks the carbon atom in a carbonyl group and addition across the C=O bond occurs	Nucleophile (e.g. HCN)	Halogenoalkane, alcohol, nitrile or amine



Your notes

Electrophilic Substitution	The replacement of an atom by another atom or group of atoms after initial attack by an electron—deficient species	Electrophile (eg. Br ₂ , NaOH, KCN, NH ₃ and HBr)	
Nucleophilic Substitution	The mechanism of the organic reaction in which a nucleophile attacks a carbon atom carrying a potential positive charge. This results in the replacement of an atom carrying a partial negative charge by the nucleophile	Nucleophile (eg. HCN)	
Oxidation	The loss of electrons or gain of oxygen of an atom, ion or molecule	Oxidising agent such as acidified K ₂ Cr ₂ O ₇ or KMnO ₄	Alcohol, aldehyde, ketone or carboxylic acid
Reduction	The gain of electrons or loss of oxygen of an atom, ion or molecules	Reducing agent such as NaBH ₄ or LiAlH ₄	Alkene, aldehyde, primary and secondary alcohol, carboxylic acid
Hydrolysis	The breakdown of a compound by water or by dilute acids or alkali		Water or dilute acid or alkali
Condensation	A reaction in which two organic molecules join together and in the process eliminate a small molecule such as water or hydrogen chloride	Two molecules that can react with each other	Small molecule and a larger molecule

Oxidising & reducing agents

- Certain functional groups only react with specific oxidising and reducing agents which you should be aware of

Oxidising & reducing agents table

Oxidising Agent			
	Oxidises	Oxidation Product	Colour Change



Your notes

Acidified potassium dichromate ($K_2Cr_2O_7 / H_2SO_4$)	Primary alcohols	Aldehydes then carboxylic acids	Orange to green
	Secondary alcohols	Ketones	Orange to green
	Tertiary alcohols	X	
	Aldehydes	Carboxylic acids	Orange to green
	Ketones	X	
Acidified potassium permanganate ($KMnO_4 / H_2SO_4$)	Primary alcohols	Aldehydes then carboxylic acids	Purple to colourless
	Secondary alcohols	Ketones	Purple to colourless
	Tertiary alcohols	X	
	Aldehydes	Carboxylic acids	Purple to colourless
	Ketones	X	
	Alkenes	Diol	Purple to colourless

Reducing Agent		
	Reduces	Reduction Product
Sodium borohydride ($NaBH_4$)	Carboxylic acids	X
	Aldehyde	Primary alcohol
	Ketone	Secondary alcohol
	Alkene	X



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Lithium aluminium hydride (LiAlH_4)	Carboxylic acids	Aldehyde then primary alcohol
	Aldehyde	Primary alcohol
	Ketone	Secondary alcohol
	Alkene	X
Hydrogen and Pt / Ni Catalyst (H_2 , Pt / Ni catalyst)	Carboxylic acids	X
	Aldehyde	Primary alcohol*
	Ketone	Secondary alcohol*
	Alkene	Alkane

*Catalytic hydrogenation **can** reduce aldehydes and ketones to alcohols. However, this reaction often requires different (sometimes harsher) conditions than the hydrogenation of an alkene.

Tests

- The test also requires you to distinguish between the different tests that identify functional groups in a compound

Tests identifying functional groups in a compound table

	Functional Group Tested	Colour Change
Fehling's Solution	Aldehydes	Clear blue solution turns opaque red/orange as a precipitate is formed
Tollens' Reagent	Aldehydes	Silver mirror
Bromine water	Alkenes	Bromine water changes from orange to colourless
2,4-dinitrophenylhydrazine (2,4-DNPH)	Carbonyl compounds (aldehydes and ketones)	Orange precipitate

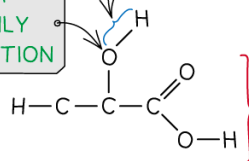


Your notes

1

REACTS WITH 2,4-DNPH ONLY AFTER OXIDATION

$\text{KMnO}_4 / \text{K}_2\text{Cr}_2\text{O}_7$
OXIDISES TO KETONE



LiAlH_4 REDUCES TO PRIMARY ALCOHOL

2

OXIDISED TO DIOL BY COLD DILUTE KMnO_4 OR ALDEHYDE AND THEN CARBOXYLIC ACID BY HOT, CONCENTRATED KMnO_4 OR $\text{K}_2\text{Cr}_2\text{O}_7$

REACTS WITH 2,4-DNPH TOLLENS' AND FEHLING'S SOLUTION

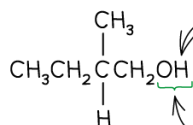
OXIDISED TO CARBOXYLIC ACID USING $\text{KMnO}_4 / \text{K}_2\text{Cr}_2\text{O}_7$

REDUCED TO PRIMARY ALCOHOL BY $\text{NaBH}_4 / \text{LiAlH}_4$

DECOLOURISES BROMINE WATER

REDUCED BY H_2 , Pt/Ni CATALYST AND HEAT TO AN ALKANE

3



OXIDISED TO ALDEHYDE AND CARBOXYLIC ACID BY $\text{KMnO}_4 / \text{K}_2\text{Cr}_2\text{O}_7$

REACTS WITH 2,4-DNPH, TOLLENS' AND FEHLING'S SOLUTION AFTER OXIDATION

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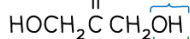
Your notes

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REDUCED BY NaBH_4 OR LiAlH_4 TO A SECONDARY ALCOHOL

REACTS WITH 2,4-DNPH ONLY

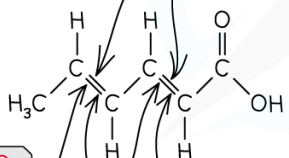
OXIDISED TO ALDEHYDE AND CARBOXYLIC ACID BY $\text{KMnO}_4/\text{K}_2\text{Cr}_2\text{O}_7$



REACTS WITH 2,4-DNPH, TOLLENS' AND FEHLING'S SOLUTION AFTER OXIDATION

5

DECOLOURISES BROMINE WATER



LiAlH_4 REDUCES TO PRIMARY ALCOHOL

REDUCED TO ALKANES BY H_2 , Pt/Ni AND HEAT

OXIDISED TO DIOL BY COLD, DILUTE KMnO_4 OR ALDEHYDE AND THEN CARBOXYLIC ACID BY HOT, CONCENTRATED KMnO_4 OR $\text{K}_2\text{Cr}_2\text{O}_7$

KEY

— TESTS

— OXIDISING AGENT

— REDUCING AGENT

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Multi-step Synthetic Routes

- Many organic molecules are made in multi-step synthetic routes
- You should be able to recall the different reactions each functional group undergoes and apply this knowledge when devising multi-step synthetic routes for preparing organic molecules



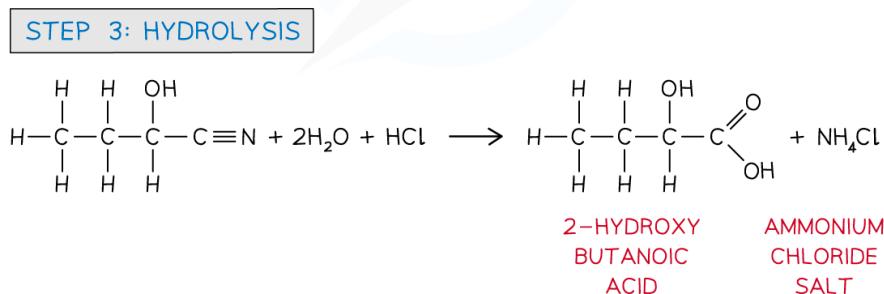
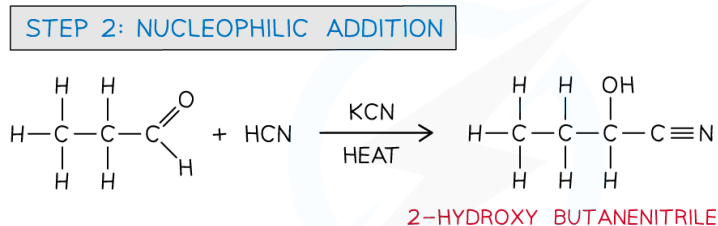
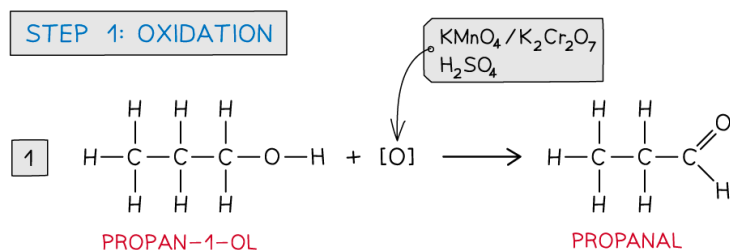
Worked Example

Devise multi-step synthetic routes for preparing the following organic molecules from propan-1-ol

- 2-hydroxybutanoic acid
- Ethyl propanoate
- Sodium propanoate salt

Answers:

1. 2-hydroxybutanoic acid



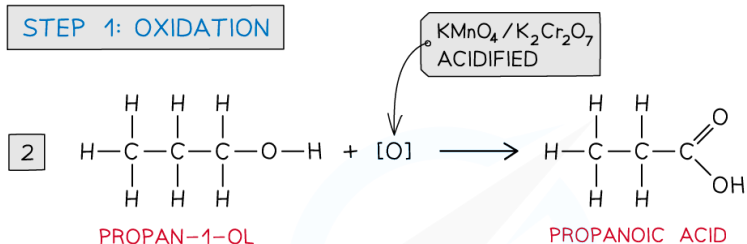
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2. Ethyl propanoate

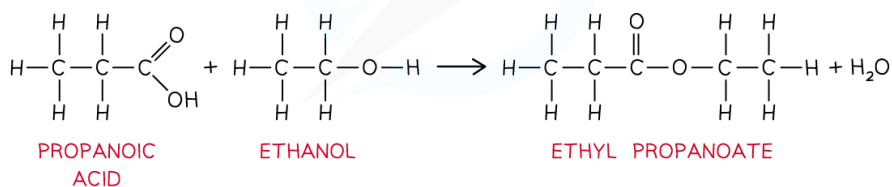


Your notes

STEP 1: OXIDATION



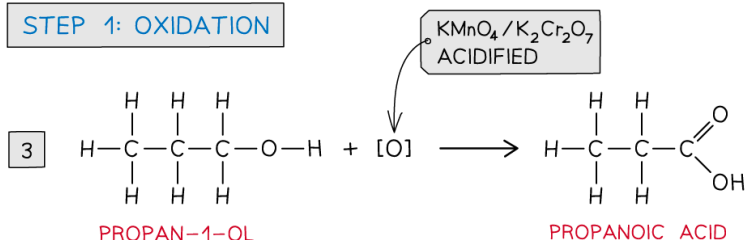
STEP 2: CONDENSATION/ESTERIFICATION



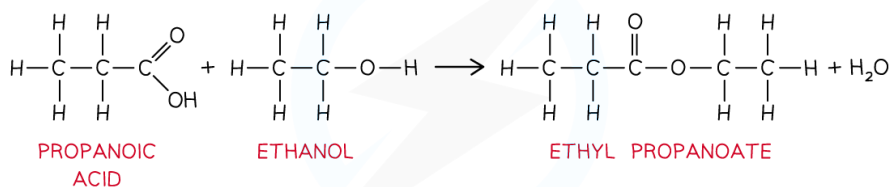
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3. Sodium propanoate salt

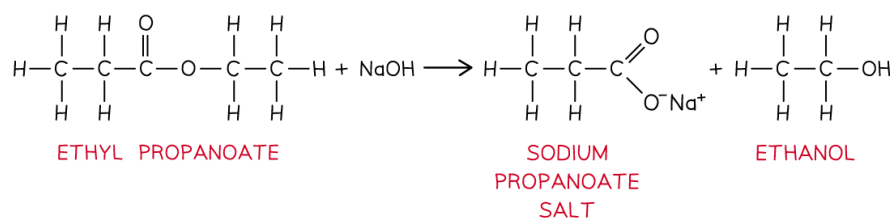
STEP 1: OXIDATION



STEP 2: CONDENSATION/ESTERIFICATION



STEP 3: HYDROLYSIS



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Analysis of Synthetic Routes



Worked Example

The synthesis of compound **X** takes place in 2 steps:

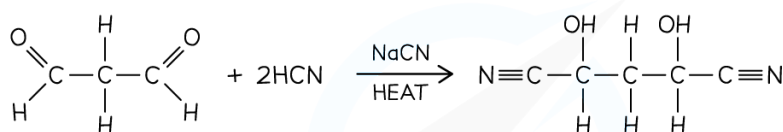
OHCCH ₂ CHO	step 1	intermediate	step 2	HO ₂ CCH(OH)CH ₂ CH(OH)C
				compound X

Which reagents could be used for this synthesis?

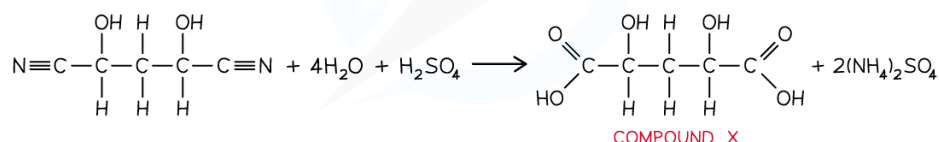
Answer:

- The first step involves a nucleophilic addition of CN⁻ using NaCN as catalyst and heat to form a hydroxynitrile
- In the second step, the nitrile is refluxed with dilute aqueous sulfuric acid causing hydrolysis of the nitrile forming a carboxylic acid and ammonium salt

STEP 1: NUCLEOPHILIC ADDITION



STEP 2: HYDROLYSIS



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Worked Example

The synthesis of hexanoic acid takes place in 2 steps

1-chloropentane	reagent X	compound Z	reagent Y	hexanoic acid
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Which reagents could be used for this synthesis?

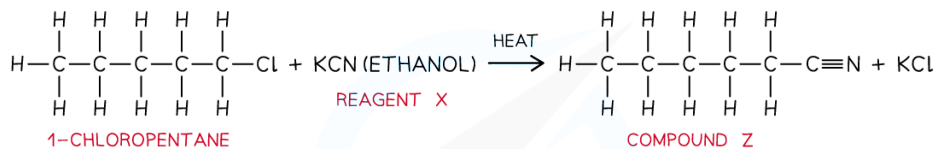
Answer:



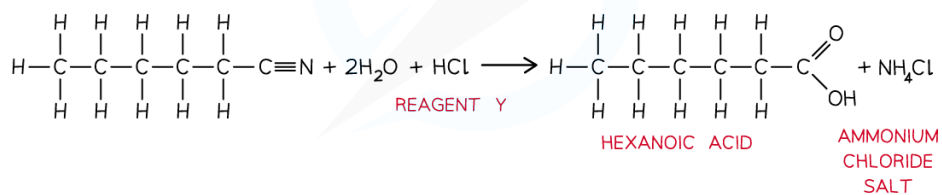
Your notes

- Halogenoalkanes can undergo **nucleophilic substitution** with ethanolic KCN in which the CN^- ion acts as a nucleophile and replaces the chlorine atom in 1-chloropentane to form a **nitrile**.
- The treatment of nitriles with concentrated hydrochloric acid will produce a carboxylic acid and an ammonium salt.
- In this case, hexanoic acid and ammonium chloride will be formed.

STEP 1: NUCLEOPHILIC SUBSTITUTION



STEP 2: HYDROLYSIS



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