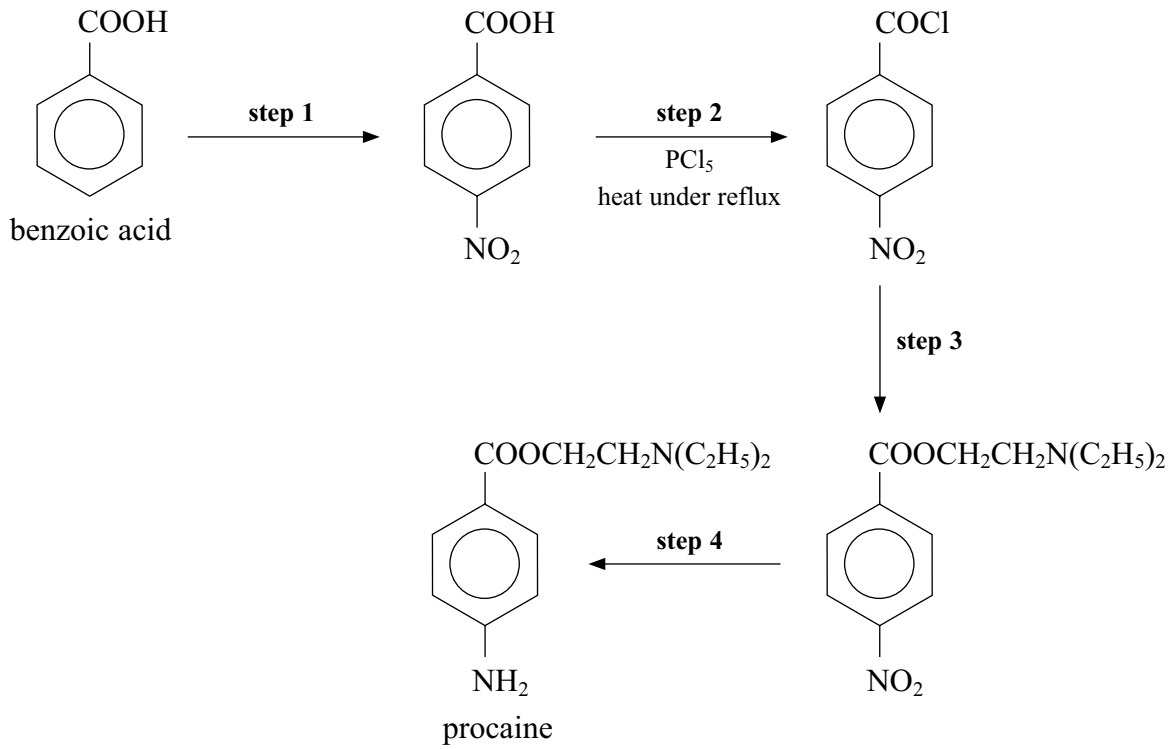
1 This question is about synthetically produced painkillers and anaesthetics.

(a) The local anaesthetic procaine can be synthesised from benzoic acid. The simplified route is shown below.



(i) Suggest the two reagents needed for **step 1**.

(2)

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(ii) Draw the apparatus needed to heat under reflux in **step 2**.

(3)

(iii) Suggest why the reagents for the reaction in **step 2** are

(2)

heated .....

.....

under reflux .....

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(iv) Give the structural formula for the organic reagent needed in **step 3**.

(1)

(v) What type of reaction is taking place in **step 4**? Suggest the reagents used.

(2)

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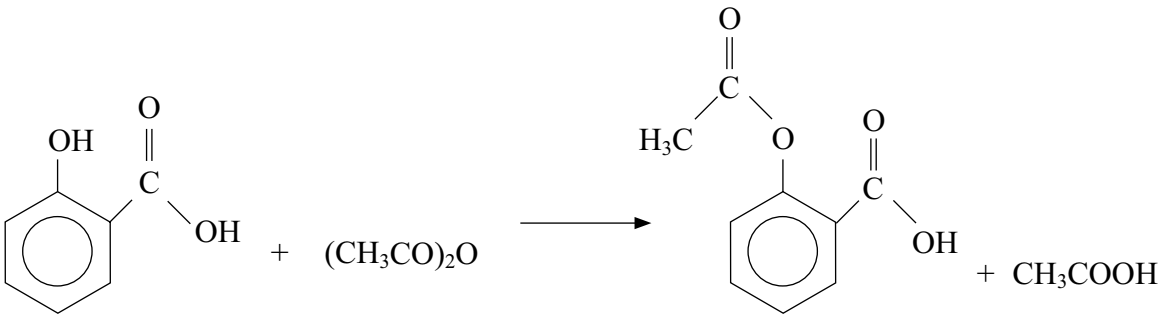
(b) A student produced a sample of aspirin by the esterification of 9.40 g of 2-hydroxybenzoic acid with excess ethanoic anhydride.



2-hydroxybenzoic acid ethanoic anhydride aspirin

After purification by recrystallization, 7.77 g of aspirin was obtained.

[M_r of 2-hydroxybenzoic acid 138, M_r of aspirin 180]

(i) Calculate the percentage yield obtained.

(3)

*(ii) Outline how to purify a solid, such as aspirin, by recrystallization, using water as the solvent.

(4)

(iii) Explain what effect recrystallization has on the final yield.

(1)

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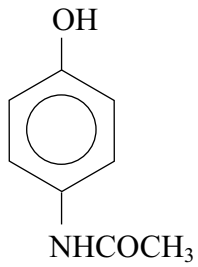
(c) Paracetamol is found in many non-prescription painkillers, often in conjunction with other compounds such as codeine.



paracetamol

(i) Suggest, by name or formula, a reagent that could be used to form paracetamol from 4-aminophenol.

(1)

(ii) Suggest why sales of non-prescription painkillers, often containing paracetamol and codeine, are limited to 32 tablets.

(1)

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(iii) Explain why paracetamol is only slightly soluble in water although it can form hydrogen bonds with water.

(1)

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(Total for Question 21 marks)

2 (a) Tiglic acid is a compound that is used as a defensive agent by some beetles.

(i) Tiglic acid contains, by mass, 60% carbon, 8% hydrogen, with the remainder being oxygen. Show that these data are consistent with the formula $C_5H_8O_2$.

(1)

(ii) Tiglic acid contains a carbon-carbon double bond and a carboxylic acid group.

Suggest **one** test for each of these groups in tiglic acid. State what you would do and what you would see as a positive result for the tests.

(4)

Test for C═C .....

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Test for —COOH .....

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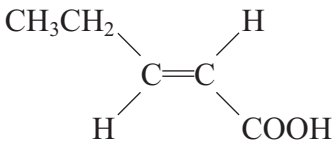
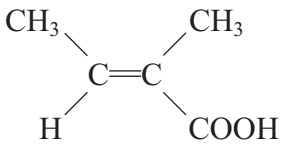
(b) It is suggested that the structure of tiglic acid is either that of **A** or **B**.



A



(i) State, with a reason, whether **B** is the *E*- or *Z*- isomer.

(2)

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(ii) The mass spectrum of tiglic acid shows two prominent peaks at mass/charge ratios 45 and 55. Write the formulae of the fragments giving rise to each of these peaks.

(2)

45 .....

55 .....

(iii) Does this data from the mass spectrum **alone** enable you to decide which of **A** or **B** is the structure of tiglic acid? Explain your answer.

(1)

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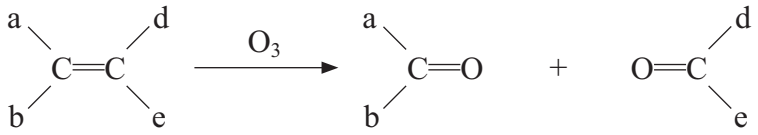
(c) The position of a C═C double bond in a molecule can be determined by ozonolysis. The compound is reacted with ozone and then dilute acid, two carbonyl compounds being produced as shown below.



Ozonolysis of tiglic acid gives two carbonyl compounds, **C** and **D**.

Compound **C** gives a silver mirror with Tollens' reagent and gives iodoform with iodine in alkali.

Compound **D** does **not** give a silver mirror with Tollens' reagent, but does give iodoform with iodine in alkali.

*(i) From the results of the experiments, deduce the functional groups present in **C** and **D**. By considering the two possible structures for tiglic acid, give the structural formulae of **C** and **D**.

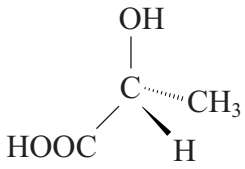
From the structures you have drawn, state which of the structures **A** or **B** could represent tiglic acid.

(6)

(ii) Explain whether or not these tests show definitely that your answer to (c)(i) represents tiglic acid.

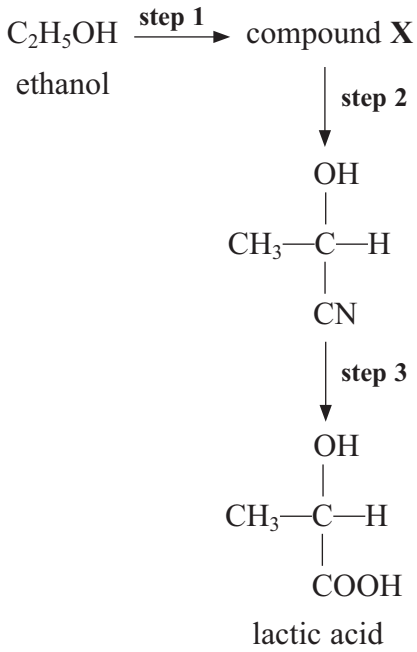
(1)

(d) Lactic acid is a chiral molecule that is found in sweat as the ( ) isomer only. Its structural formula is



( ) - lactic acid

(i) Lactic acid can be made from ethanol in three steps.



Give the structural formula of the intermediate **X** and the reagents and conditions required for **steps 1** and **2**.

(4)

Step 1 .....

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Step 2 .....

.....

(ii) Classify the type and mechanism of the reaction that occurs in **step 2**.

(1)

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*(iii) By considering the stereochemistry of the mechanism in **step 2**, explain why this synthesis would **not** give a single optical isomer of lactic acid.

(2)

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(iv) Suggest why synthetic pathways for the manufacture of pharmaceuticals may require reactions that are highly stereospecific.

(1)

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(Total for Question 25 marks)