1 Benzene can be converted to phenylamine, $C_6H_5NH_2$, in two steps.

$$C_6H_6 \xrightarrow{\text{Step 1}} C_6H_5NO_2 \xrightarrow{\text{Step 2}} C_6H_5NH_2$$

(a) (i) Name the **two** reagents needed in Step 1.

(1)

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(ii) Suggest why the temperature should not be allowed to go above 55 °C in Step 1.

(1)

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(iii) Identify the **two** reagents used to carry out the reduction in Step 2.

(1)

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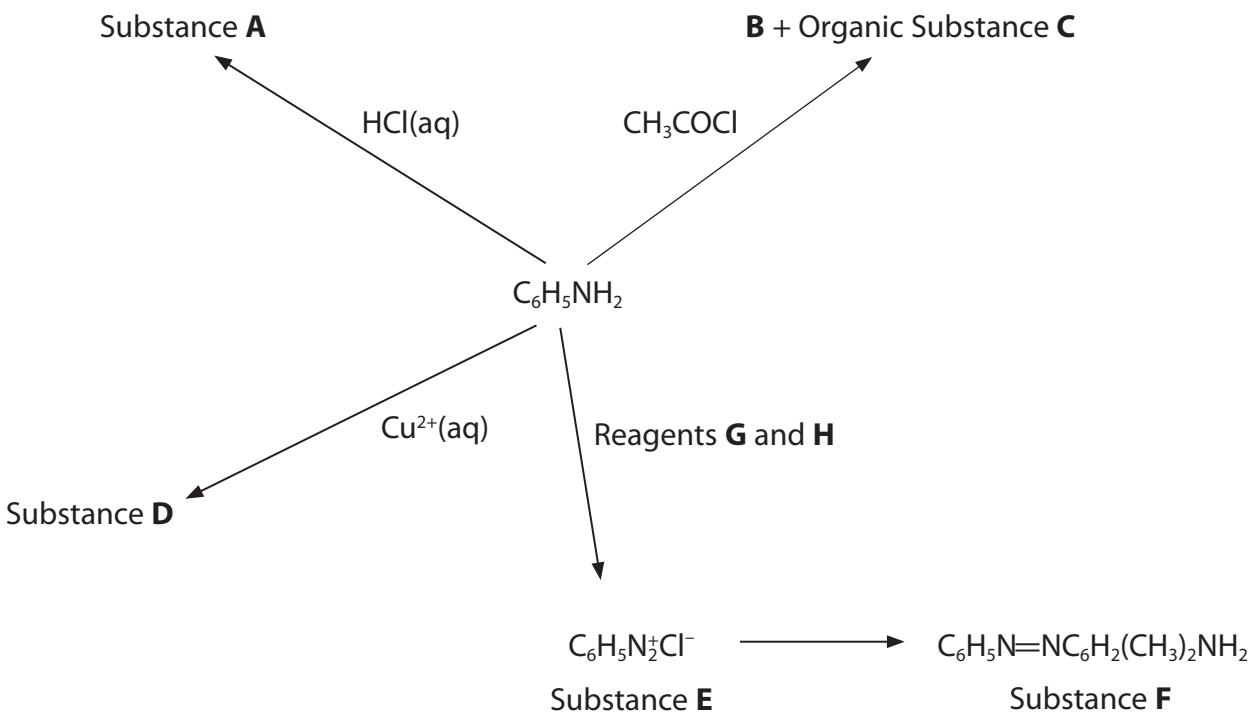
(b) Some reactions of phenylamine are shown below.



(i) Give the formula of Substance **A**.

(1)

.....

(ii) Draw the displayed formula of the organic Substance **C**.

You need not display the benzene ring.

(1)

(iii) Substances **D** and **F** are both brightly coloured but for different reasons. Classify Substances **D** and **F**.

(2)

Substance **D** .....

Substance **F** .....

(iv) Name Substance **E**.

(1)

.....

(v) What **two** Substances, **G** and **H**, are required in the conversion of phenylamine to Substance **E**?

(1)

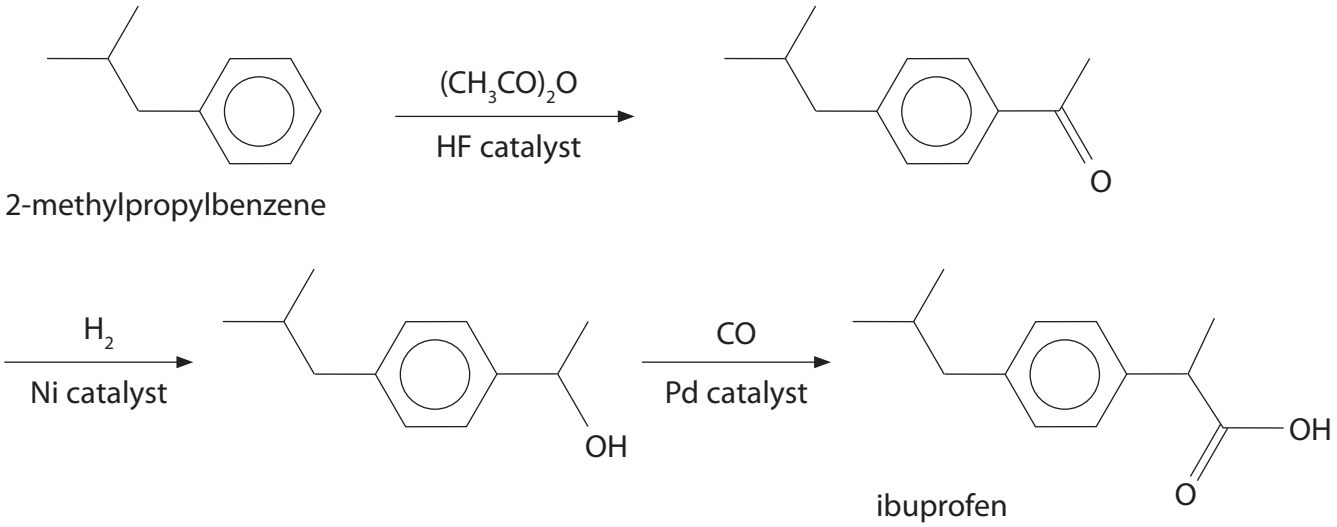
.....

(vi) Suggest the structural formula of the substance which reacts with Substance **E** to form Substance **F**.

(1)

(Total for Question = 10 marks)

2 Ibuprofen is a nonsteroidal anti-inflammatory drug (NSAID) widely used as an analgesic (pain reliever). It was discovered in the 1960s by the Boots Group which developed a six step synthesis from 2-methylpropylbenzene. The synthesis shown below was introduced in the 1990s by the BHC Company and received a Presidential Green Chemistry Challenge award in 1997. The citation noted that the synthesis has just three steps, all of which are catalytic, and an effective atom economy of 99%. Both syntheses are carried out in solution.



(a) (i) Suggest why a three step synthesis is likely to be 'greener' than a six step process.

(1)

.....

.....

(ii) Why does the use of catalysts make processes 'greener' (as well as faster)?

(1)

.....

.....

(b) The first step of the synthesis is an electrophilic substitution which is usually carried out in a school laboratory using ethanoyl chloride and an aluminium chloride catalyst.

(i) Write an equation showing the formation of the electrophile in the **school** experiment.

(1)

(ii) Give the mechanism for the electrophilic substitution of 2-methylpropylbenzene by ethanoyl chloride, using the electrophile you have given in (b)(i).

(3)

(iii) Suggest **one** environmental benefit of using $(CH_3CO)_2O$, rather than ethanoyl chloride, in the manufacture of ibuprofen.

(1)

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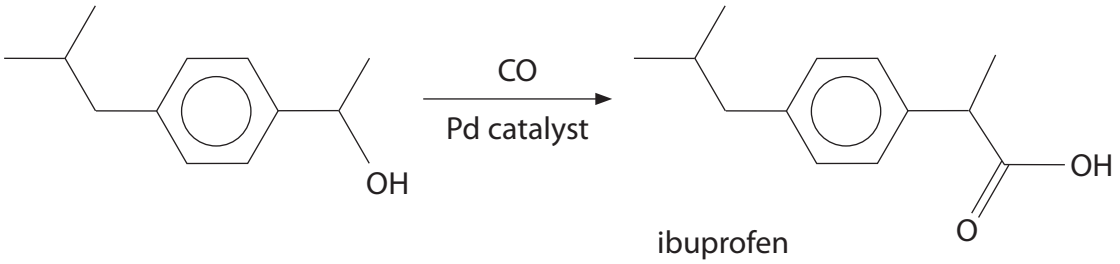
(c) The final stage of the modern synthesis for ibuprofen is shown below.



ibuprofen

(i) Suggest a benefit of using a **solid** catalyst in this reaction.

(1)

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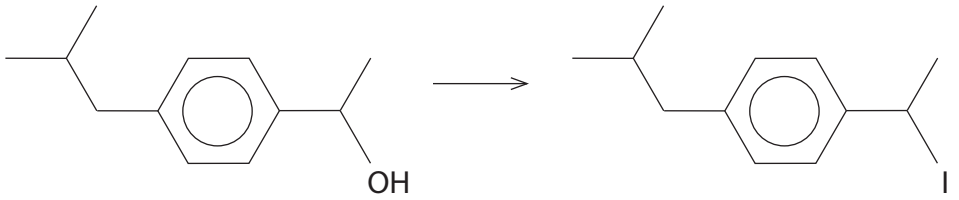
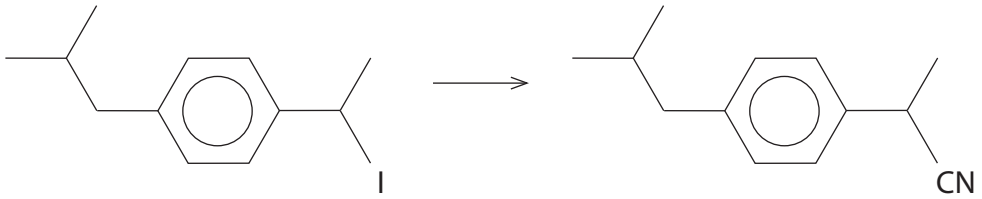
(ii) The preparation in part (c) can be carried out in a laboratory in three reactions.

(3)

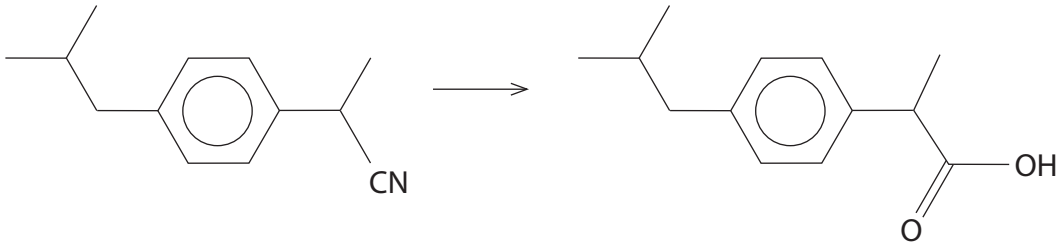
Reaction 1



Reaction 2



Reaction 3



Give:

The reagents for **Reaction 1**

.....

.....

The reagents and conditions for **Reaction 3**

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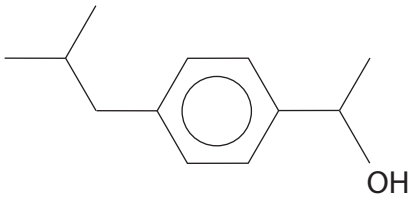
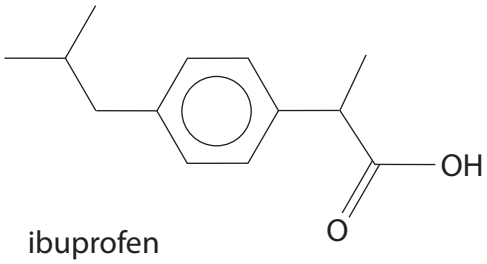
.....

(iii) Using your Data Booklet, explain how infrared spectroscopy can be used to distinguish between the two structures shown below.

(2)





ibuprofen

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(d) Ibuprofen is a chiral molecule and only one of its enantiomers is biologically active. However, although the synthesis produces a racemic mixture, an isomerase enzyme in the body converts the inactive enantiomer into the active enantiomer.

(i) Explain the term 'chiral molecule'.

(1)

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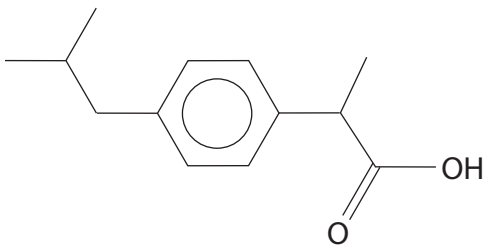
(ii) Mark with an asterisk (*) the chiral centre on the structure of ibuprofen below.

(1)



(iii) Explain the term 'racemic mixture'.

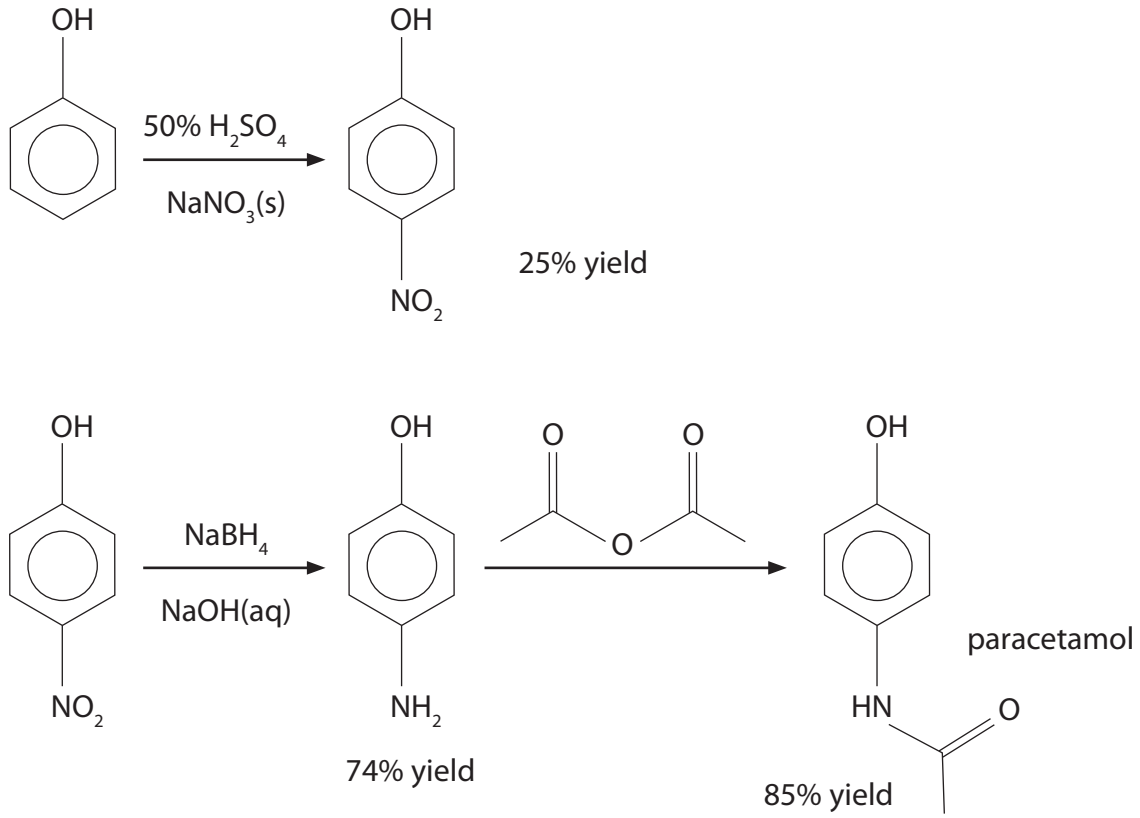
(1)

(iv) Suggest **two** benefits that arise from the isomerization of the inactive enantiomer of ibuprofen.

(2)

(Total for Question = 18 marks)

3 Paracetamol is a mild painkiller which also reduces the temperature of patients with fever, actions known as analgesic and antipyretic respectively. The reaction scheme below summarises a laboratory synthesis of paracetamol starting from phenol. The yields shown are for the particular product of each step in the synthesis.



(a) The nitration of benzene is an electrophilic substitution reaction that requires concentrated nitric and sulfuric acids.

(i) Write an equation for the formation of the electrophile by the reaction between concentrated nitric and concentrated sulfuric acids.

(2)

(ii) Give the mechanism for the formation of nitrobenzene from benzene.

(3)

(iii) Explain why phenol is nitrated in much milder conditions than benzene.

(2)

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(iv) Suggest why the yield for the nitration of phenol is so low.

(1)

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(v) Suggest an alternative to $NaBH_4$ that could be used in aqueous solution.

(1)

.....

(vi) Calculate the overall yield of the synthesis.

(1)

(b) The paracetamol, prepared by the synthesis shown at the start of the question, may be purified by recrystallization. In this process, the paracetamol is dissolved in a minimum volume of hot water, the hot mixture filtered, the filtrate cooled and the resulting crystals filtered and dried. The table below summarises the solubility of paracetamol in water at various temperatures.

Temperature / °C	5	10	20	95
Solubility / g / 100 g	0.82	0.94	1.3	5.2

(i) Explain the purpose of each of the filtrations in the recrystallization of paracetamol.

(2)

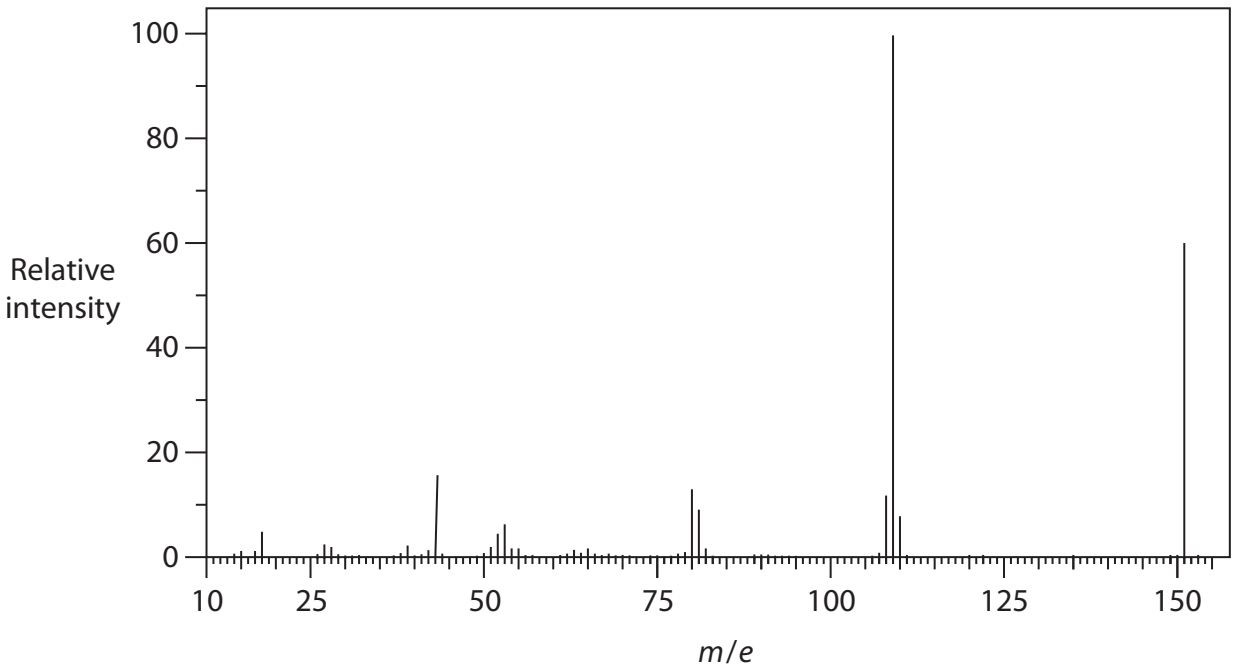
(ii) From the temperatures given in the table, choose the pair of temperatures that will give the highest yield of paracetamol from the recrystallization. Explain your choice.

(2)

(iii) Name the technique that could be used in a **school** laboratory to check the purity of the recrystallized paracetamol.

(1)

(c) The mass spectrum of paracetamol is shown below.



(i) Label the molecular ion peak, with an **M**, on the mass spectrum.

(1)

(ii) Suggest the formula of an ion that could cause the peak at $m/e = 43$.

(1)

(d) Paracetamol is highly toxic: overdosing causes irreversible liver damage. Despite this, paracetamol is readily available from pharmacies and even supermarkets. Suggest **one** control measure that sellers might employ to reduce the risk to paracetamol users.

(1)

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(Total for Question = 18 marks)