Contemporary Organic Chemistry

22CMD213

Semester 1 2022/23 In-Person Exam paper

This examination is to take place in-person at a central University venue under exam conditions. The standard length of time for this paper is **2 hours**.

You will not be able to leave the exam hall for the first 30 or final 15 minutes of your exam. Your invigilator will collect your exam paper when you have finished.

Help during the exam

Invigilators are not able to answer queries about the content of your exam paper. Instead, please make a note of your query in your answer script to be considered during the marking process.

If you feel unwell, please raise your hand so that an invigilator can assist you.

You may use a calculator for this exam. It must comply with the University's Calculator Policy for In-Person exams, in particular that it must not be able to transmit or receive information (e.g. mobile devices and smart watches are **not** allowed).

Answer **ALL** questions

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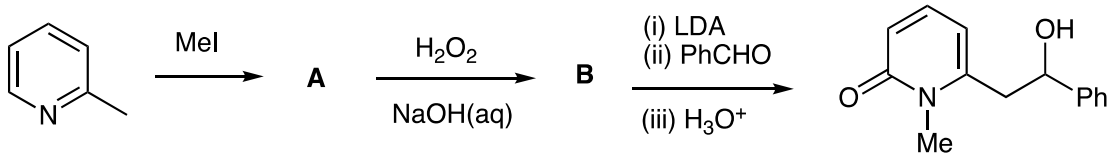
1. Answer **ALL** parts

Explain each of the following reaction sequences involving heterocyclic compounds. Give a detailed mechanism to account for the course of the reaction in each case, and identify the products and/or intermediates formed (**A, B**).

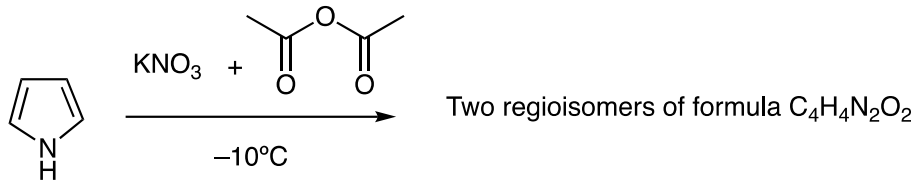
(a)



[9 marks]

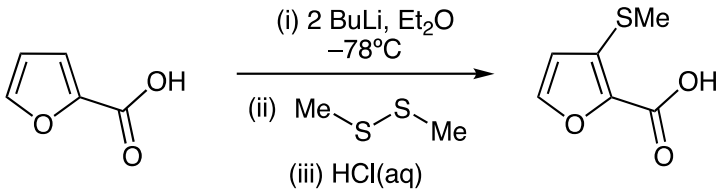
continued…

(b)



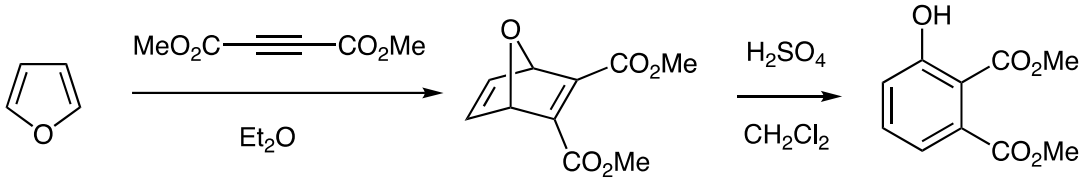
[6 marks]

(c)



[4 marks]

(d)

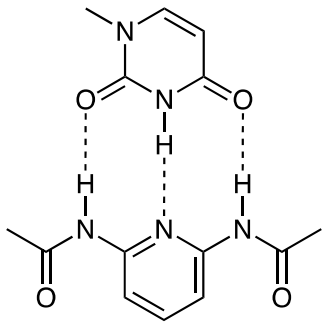


[6 marks]

2. Answer **ALL** parts

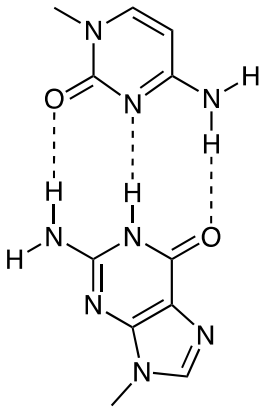
(a) The following drawings show the binding constants (K_a values determined in chloroform) of three different host-guest complexes. Explain the large variation in these binding constants.

C



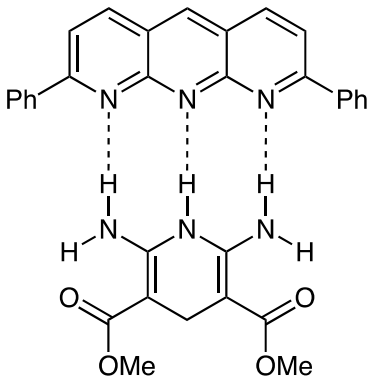
K_a near 10^2 M^{-1}

D



K_a near 10^4 M^{-1}

E



K_a near 10^5 M^{-1}

[4 marks]

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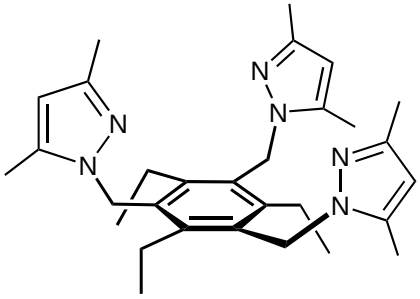
(b) The molecule below contains three pyrazole units attached to a benzene core. It was found to have approximately 400:1 selectivity for the ammonium ion compared with the K^+ ion in chloroform.



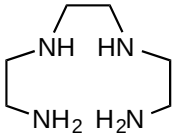
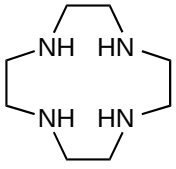
i) Sketch a plausible binding mode of an ammonium ion to the receptor and explain why the selectivity for the ammonium ion is so high.

[5 marks]

ii) Describe two spectroscopic methods that could be used to signal the binding interaction between host and guest. Explain how the spectroscopic data can be used to determine the binding constant (K_a value)

[6 marks]

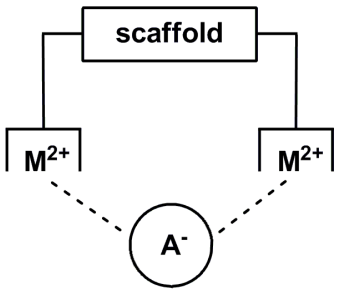
(c) Thermodynamic parameters for the binding of Zn^{2+} ions with two different ligands are given below (aqueous solution, 298 K). Use this data to calculate the binding constants (log K_a values) for the resulting 1:1 host-guest complexes. Explain the differences in stability observed.

Ligand	ΔH^o (kJ mol^{-1})	$T\Delta S^o$ (kJ mol^{-1})
	-90.4	24.3
	-76.6	64.0

[5 marks]

continued…

(d) Propose a structure of chemosensor that utilises the cyclen-Zn^{2+} binding motif to recognise the anion 1,4-benzenedicarboxylic acid. Describe the features of the chemosensor that provide anion selectivity and signalling.



[5 marks]

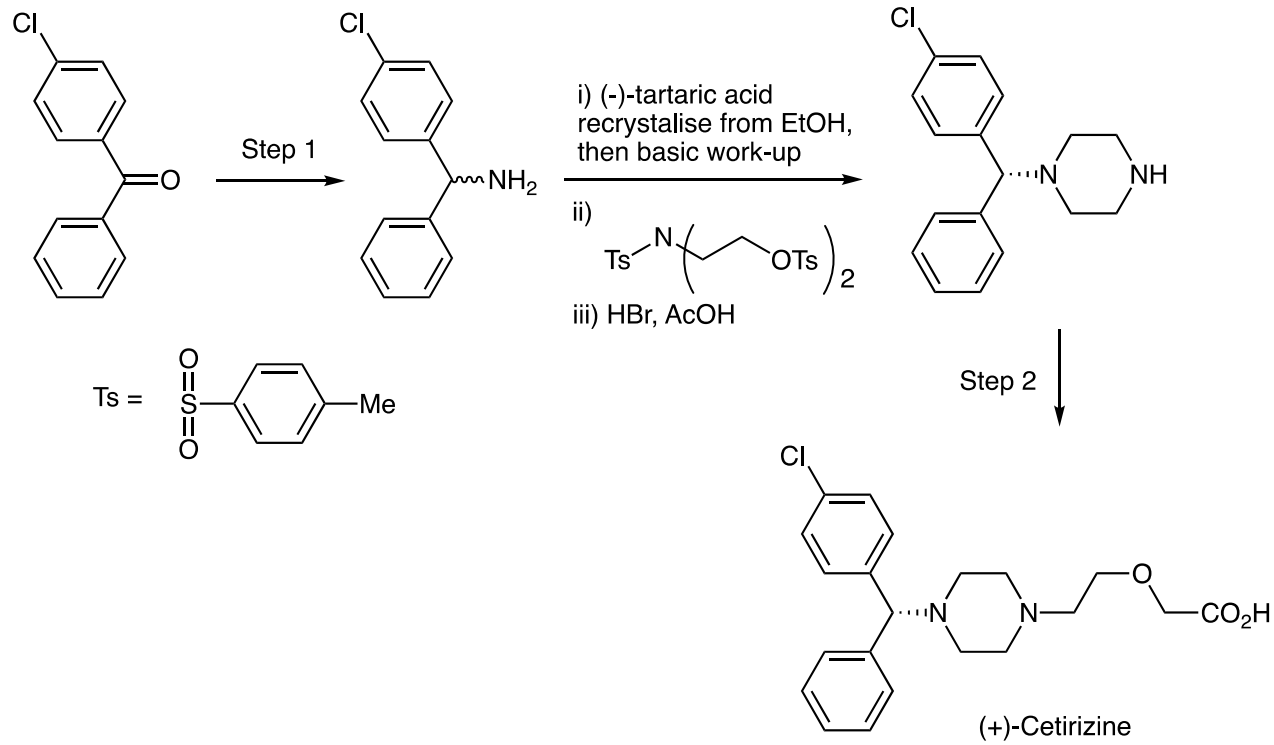
3. Answer **ALL** parts

(a) Cetirizine is an over-the-counter second-generation antihistamine and is used in the treatment of allergies and hay fever. A route to the compound is given below. Answer the following questions about the route:

(i) Suggest reagents for Step 1; more than one step may be involved. [3 marks]

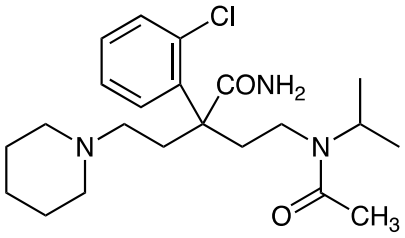
(ii) Explain the choice of reagents in steps (i), (ii) and (iii). [5 marks]

(iii) Suggest reagents for Step 2; more than one chemical step may be involved. [4 marks]



continued…

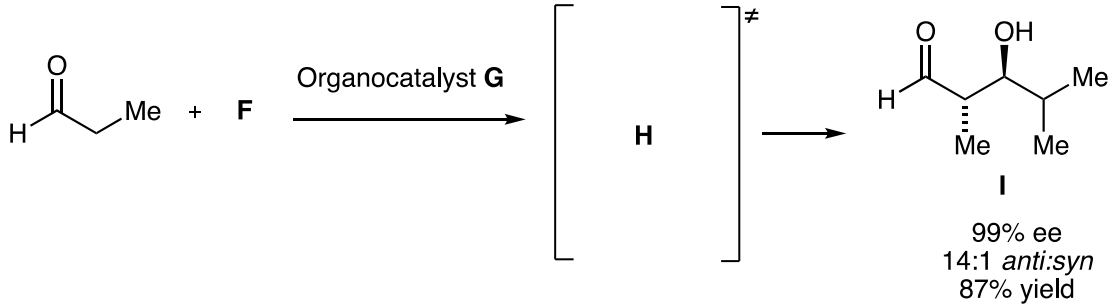
(b) The compound below is bidisomide has strong antiarrhythmic properties. Suggest a synthetic route to the compound below using any simple mono- or di-substituted benzene compounds as starting materials. Use retrosynthesis analysis to help with your answer. Explain the chemistry involved in each of the forward steps.



[13 marks]

4. Answer **ALL** parts

A highly enantioselective organocatalytic Cross-Aldol reaction is shown below:



a) Identify the Reagent **F**.

[2 marks]

b) Give a suitable Organocatalyst **G** for this reaction.

[2 marks]

c) Draw out a plausible mechanism for this transformation and include in your answer the transition state model **H** to rationalise the origin of enantioselectivity found in product **I** (see the Scheme).

[18 marks]

d) Explain how under the reaction conditions employed the Cross-Aldol reaction dominates over the Homo-Aldol reaction

[3 marks]

B. R. BUCKLEY, S. J. BUTLER, A. V. MALKOV, G. J. PRITCHARD