



CEM3B20: ADVANCED ORGANIC CHEMISTRY

2019 SUPPLEMENATRY EXAMINATION

ASSESSOR: PROF H KINFE

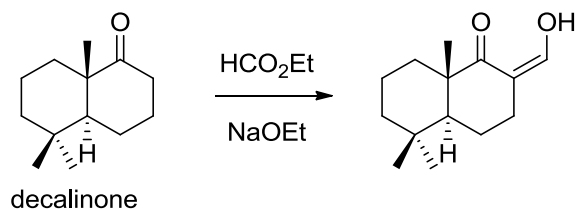
EXTERNAL MODERATOR: PROF ANWAR JARDINE

INSTRUCTIONS

- (1) The examination is out of 80 marks and you have 3 hours to complete it. No extra time will be given.
- (2) You can use a pen of any color **except** RED AND GREEN to write your answers.
- (3) Read the whole question paper carefully before you start answering. You are allowed to start with any question, just clearly number it in your answer sheet.

QUESTION 1

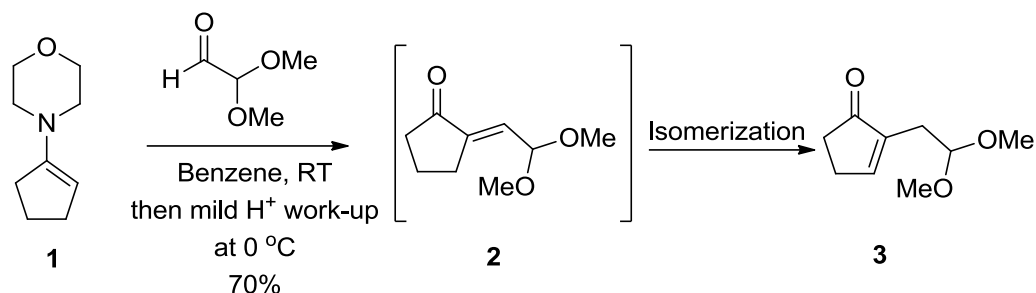
The 1st step of the reaction in the total synthesis of Warburganal and Isotadeonal (natural products isolated from Warburgia species which are native to Eastern and Southern Africa) involves functionalising the decalinone as shown below:



- Propose a plausible mechanism for the formation of the enol product. **[4]**
- What is the name of such a reaction? **[1]**

QUESTION 2

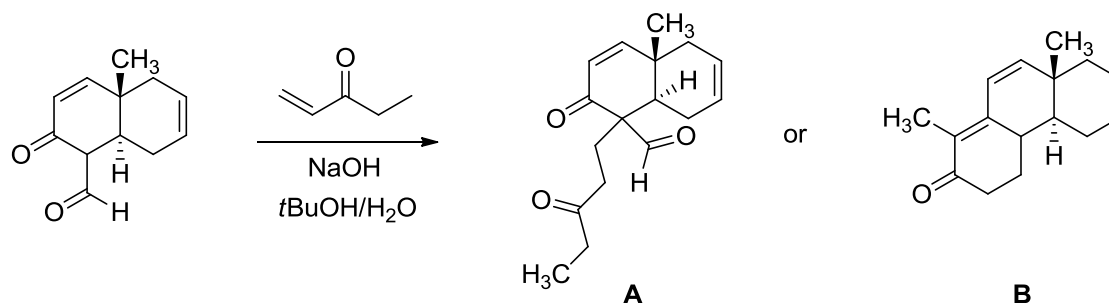
The Nobel laureate E.J. Corey reported the synthesis of a natural product called ginkgolide B. One of the key steps of this synthesis is shown below.



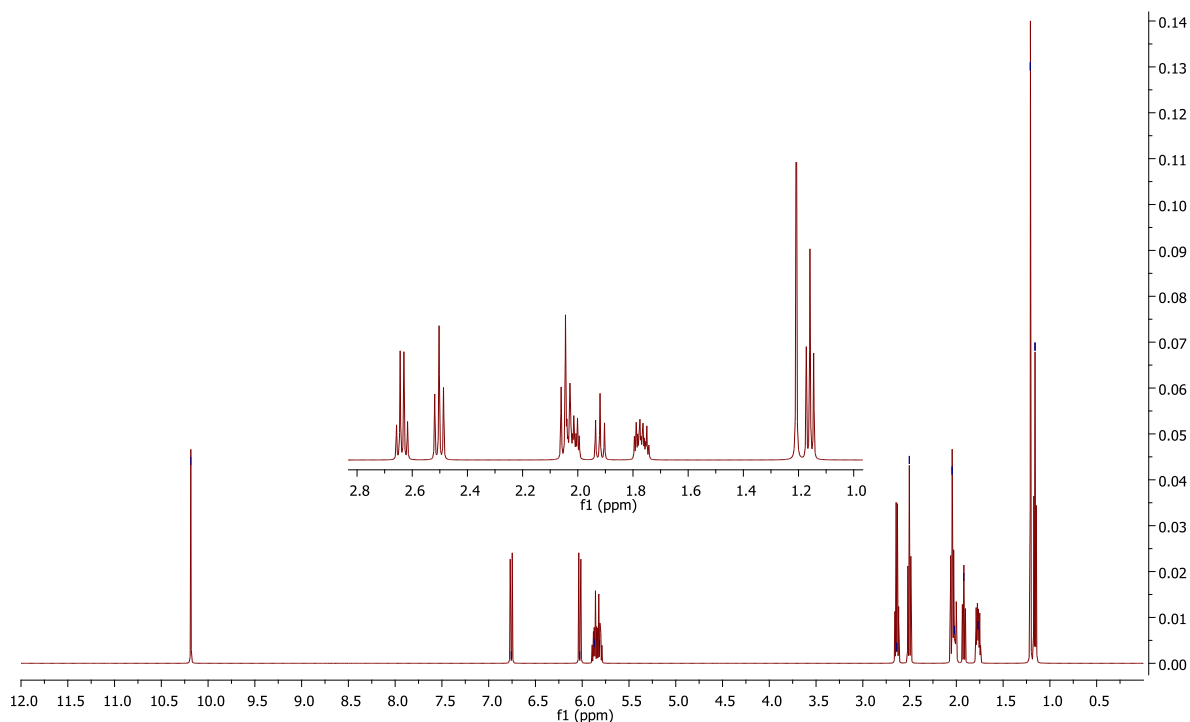
Give the full mechanism for the conversion of the enamine **1** to the α,β -unsaturated ketone **2** (no need to show the mechanism of the hydrolysis of the iminium ion intermediate). [6]

QUESTION 3

The following question comes from Woodward's classic 1951 synthesis of cholesterol. In the reaction below, two products are possible, with the team hoping for product **B**. Use this scheme and the ^1H NMR spectrum re-produced below to answer the questions.



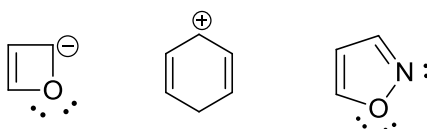
- (i) Use the ^1H NMR spectrum to decide whether the compound isolated was the desired compound **B** or the intermediate compound **A**. Give three good reasons to support your answer. [5]
- (ii) Give the mechanism for the formation of compound **A**. [4]
- (iii) Why is sodium hydroxide sufficient to catalyse this reaction? [2]
- (iv) Briefly explain the regioselectivity (the beta carbon Vs the carbonyl carbon) of the electrophile in the reaction to afford **A**. [2]



^1H NMR (500 MHz, Chloroform) δ 10.18 (s, 1H), 6.76 (d, 1H), 6.03 (d, 1H), 5.90 – 5.78 (m, 2H), 2.64 (q, 2H), 2.50 (t, 2H), 2.05 (t, 2H), 2.05 – 1.99 (m, 2H), 1.92 (t, 1H), 1.79 – 1.75 (m, 2H), 1.21 (s, 3H), 1.16 (t, 3H). (the question was reproduced with the permission of Prof van Otterlo and Dr Arnot)

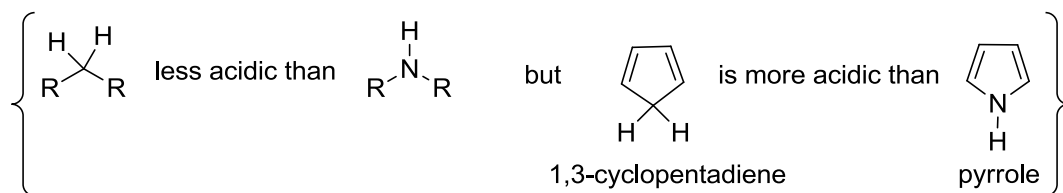
QUESTION 4

Using the Hückel $4n+2$ rule and the criteria of aromaticity, determine whether each of the following compound is likely to be aromatic. **[2 x 3 = 6]**



QUESTION 5

An amine R_2NH is typically more than 20 pK_a units more acidic than the hydrogens of the carbon analog, R_2CH_2 . However, the acidities of 1,3-cyclopentadiene and pyrrole are an exception.

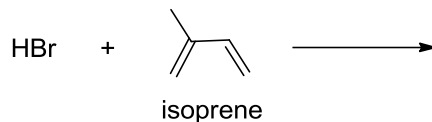


Use the theory of aromaticity to explain this exception.

[5]

QUESTION 6

The reaction of one equivalent of HBr with isoprene (shown below) provides a mixture of adducts.

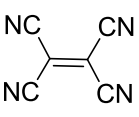


(i) Predict the products of the reaction and explain your reasoning with short sentences and reaction mechanisms. [5]

(ii) Which of the adducts are likely to be the kinetically controlled products and which are likely to be the thermodynamically controlled ones? Give your explanation of your choice with short sentences. [4]

QUESTION 7

A mixture of 0.1 mol of (2*E*,4*E*)-2,4-hexadiene and 0.1 mol of (2*E*,4*Z*)-2,4-hexadiene was

allowed to react with 0.1 mol of . After the reaction, the unreacted diene was found to consist of only one of the starting 2,4-hexadiene isomers.

(i) Which isomer did not react and why? [4]

(ii) What is the chemical structure of the product formed? [2]

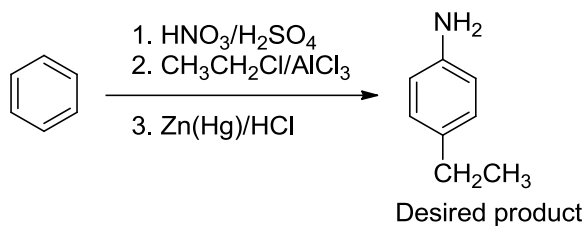
QUESTION 8

When benzene reacts with 1-chloro-2,2-dimethylpropane in the presence of AlCl_3 , the major product is 2-methyl-2-phenylbutane, not 2,2-dimethyl-1-phenylpropane. Explain this result.

[5]

QUESTION 9

The following reaction will fail to provide the desired product if carried out under the reaction conditions.

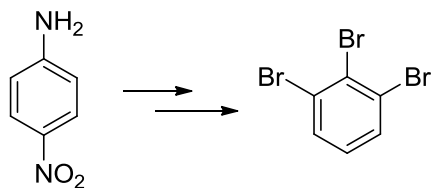


(i) Explain what is wrong with the reaction? [5]

(ii) Outline a likely synthetic pathway for the synthesis of the desired product. [5]

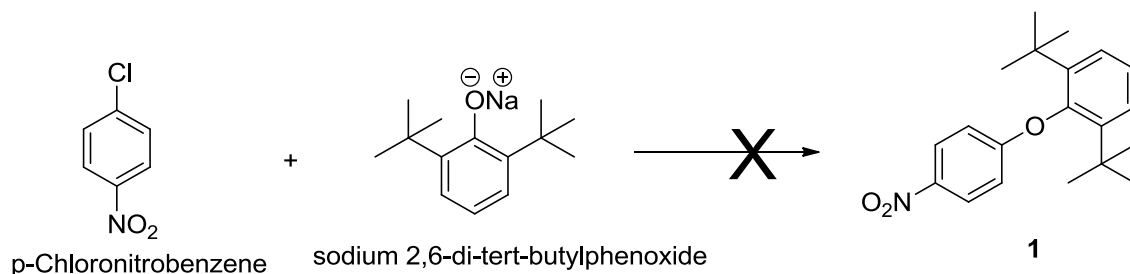
QUESTION 10

Starting with *p*-nitroaniline, show how you might synthesise 1,2,3-tribromobenzene. [10]



QUESTION 11

p-Chloronitrobenzene was allowed to react with sodium 2,6-di-*tert*-butylphenoxide with the intention of preparing the diphenyl ether **1**. The product was not the expected diphenyl ether **1**, but rather was an isomer of **1** that still possessed a phenolic hydroxyl group. [5]



What was this product, and how can one account for its formation?

The End