GX341

Ollscoil na hÉireann, Gaillimh
National University of Ireland, Galway

SEMESTER II, 2002

THIRD UNIVERSITY B.Sc. EXAMINATION IN SCIENCE (INCLUDING DENOMINATED DEGREES)

Paper III: Organic Chemistry (CH311)

Professor I. Fleming, FRS
Professor R.N. Butler
and Internal Examiners

Time Allowed: Two Hours

Answer four questions –
Two from Section A and Two from Section B

All questions carry 25 marks distributed as shown.

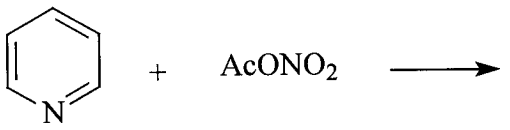
Leave the first page of the answer book blank and list on it clearly the numbers of the questions attempted.

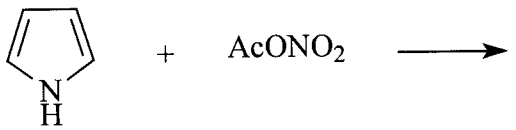
Section A

1. Answer each of the following:

(i) Explain the basicity of pyridine (basic pKa, 5.2) and show how it leads to ready D/H exchange at a site in the pyridine ring. **[8 marks]**

(ii) Compare and contrast the following reactions and explain the preferred sites of substitution



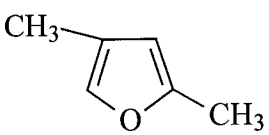


[10 marks]

(iii) Draw the structure of nicotine and show how its metabolism in the human body leads to cancer. **[7 marks]**

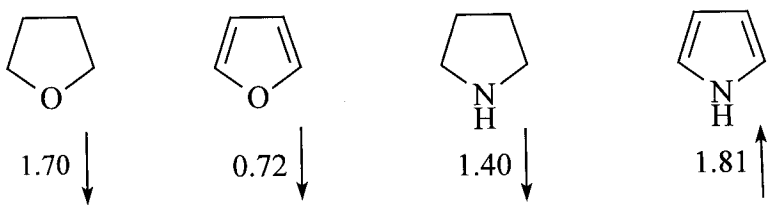
2. Answer each of the following:

(i) Explain the term "5-exo-trig" cyclisation and why it is a favoured process. Devise a synthetic route to the molecule (A) from any precursor(s) of your choice.



(A) **[8 marks]**

(ii) Comment on the significance of the following dipole moments (D units) measured in benzene at 25°C.



[8 marks]

(iii) Show the structure of thalidomide and briefly discuss chiral recognition in drug action. **[9 marks]**

3. Answer <u>each</u> of the following:

(i) Outline the principal stages of the Wittig reaction of triphenyl phosphine Ph_3P and alkyl halides RR'CHX leading to ylides and subsequent reaction with ketones $R_2C{=}O$. **[7 marks]**

(ii) Mention any evidence for the involvement of a four-centred cyclic intermediate (oxaphosphetane). **[6 marks]**

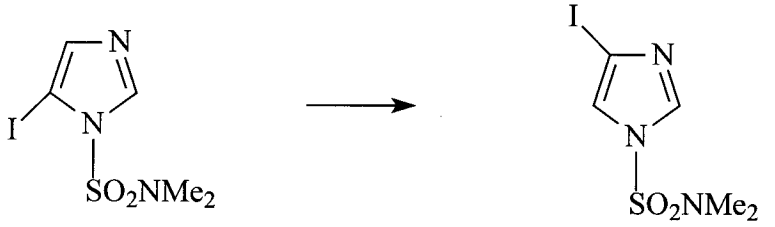
(iii) What are the advantages of the Wittig reaction for the synthesis of alkenes ? **[6 marks]**

(iv) How could you use the Wittig reaction to synthesize 2-methyl-1-phenyl-propene, PhCH=C(Me)Me? **[6 marks]**

4. Answer <u>each</u> of the following:

(i) Using **five** well chosen examples discuss briefly the use of isotopes to explore organic mechanisms. **[15 marks]**

(ii) Recently during the sulfamoylation of imidazole derivatives the interesting rearrangement of (**1**) to (**2**) took place. Using iodine-131 ($t_{½}$ ~ 8 days) and any other isotope(s) you wish to use show how you might probe the molecularity (inter- or intramolecular) of this rearrangement. **[10 marks]**



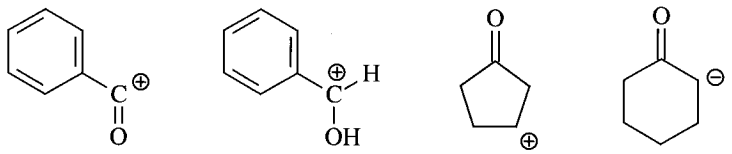
(**1**) (**2**)

Section B

5. Answer all parts

(i) Explain why a ketone group might need to be protected under certain reaction conditions and explain, using an example, how the overall procedure would be carried out in practice. **[9 marks]**

(ii) Draw the structure of a molecule which is synthetically equivalent to each of the following synthons and for any **two** give a reaction in which the molecule behaves like that synthon:

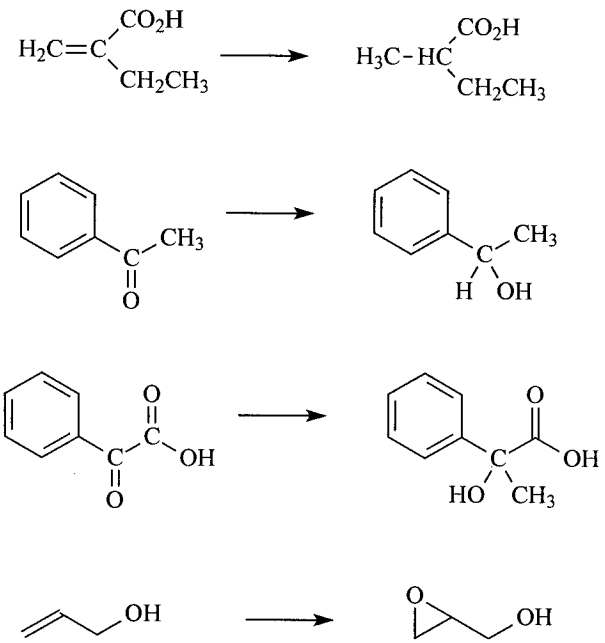


[8 marks]

(iii) Describe two different methods by which six-membered carbocyclic rings can be synthesized, providing a simple example of each type. **[8 marks]**

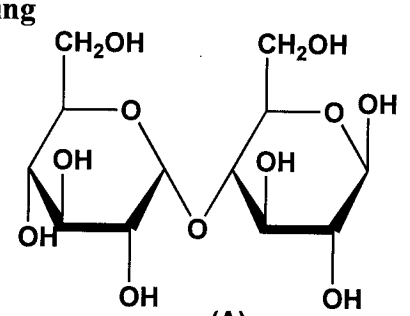
6. Outline the different approaches that can be adopted in attempting to synthesise a chiral molecule (asymmetric synthesis) and identify the problems/advantages associated with each. **[17 marks]**

Explain how the following transformations could be carried out enantioselectively:



[8 marks]

7. **Answer <u>each</u> of the following**



(A)

Structure **(A)** represents the Howarth formula of β-**(+)-maltose**, 4-*O*-(α-D-glucopyranosyl)-β-D-glucopyranose (hydrogen atoms have been omitted).

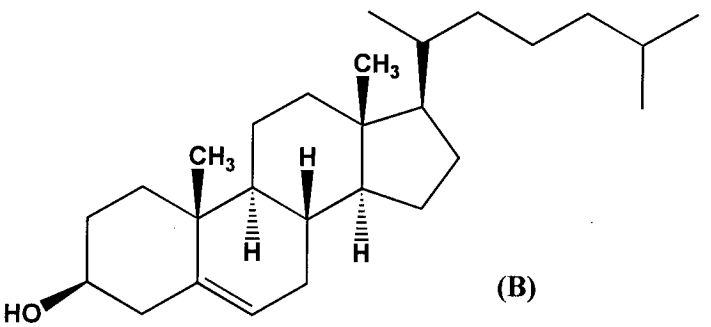
(i) Draw a three dimensional representation of the most stable conformation of **(A)**. **[5 marks]**

(ii) Draw the Howarth formula of α-**(+)-maltose**. **[2 marks]**

(iii) Draw the product of the bromine-water oxidation of maltose. Draw a Fischer projection of sucrose, and explain why it is not reactive towards bromine-water. **[12 marks]**

(iv) Give a mechanism for the hydrolysis of glycosidic linkages (bonds). **[6 marks]**

8. **Answer <u>each</u> of the following**



(B)

(i) Structure **(B)** represents cholesterol. When cholesterol was treated with peroxybenzoic acid (C_6H_5COOOH) it gave only one epoxide **C** in quantitative yield. The epoxide **C** was treated with hydrochloric acid solution to give cholestan-3β-ol derivative **D,** corresponding to the addition of HOCl to **B**, in quantitative yield. Draw structures accounting for the correct stereochemistry for epoxide **C** and product **D**. Outline a mechanism for the formation of product **D** from epoxide **C**, and draw the energy minimum conformation of product **D**. **[14 marks]**

(ii) The primary structure of a polypeptide is defined using two types of covalent bonds, a peptide and a disulfide bond. Draw the two resonance forms of the peptide bond. Draw two cysteine residues linked *via* a disulfide bond. Using a mechanism explain why the cleavage of disulfide bonds is referred to as *reversible denaturing*? **[11 marks]**