IMPERIAL COLLEGE LONDON

BSc and MSci DEGREES – JUNE 2013, for Internal Students of the Imperial College of Science, Technology and Medicine

This paper is also taken for the relevant examination for the Associateship

ORGANIC CHEMISTRY IIB

Thursday 20th June 2013, 14:00-16:15

PLEASE NOTE THAT IT IS DEPARTMENTAL POLICY THAT THESE EXAM QUESTIONS MAY REQUIRE UNDERSTANDING OF ANY PRIOR CORE COURSE.

USE A SEPARATE ANSWER BOOK FOR EACH QUESTION. WRITE YOUR CANDIDATE NUMBER ON EACH ANSWER BOOK.

2.O2 – Heteroaromatics

Answer **ALL** parts of this question.

a) Explain **TWO** of the following, using curly arrow mechanisms to illustrate your answers.

i) Pyrrole undergoes relatively rapid nitration, selectively at the 2-position, whereas under the same conditions pyridine undergoes relatively slow nitration, selectively at the 3-position.

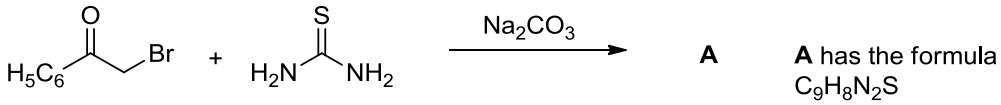
ii) On treatment with *n*BuLi, thiophene undergoes lithiation selectively at the 2-position.

iii) Indole undergoes electrophilic aromatic substitution selectively at the 3-position.

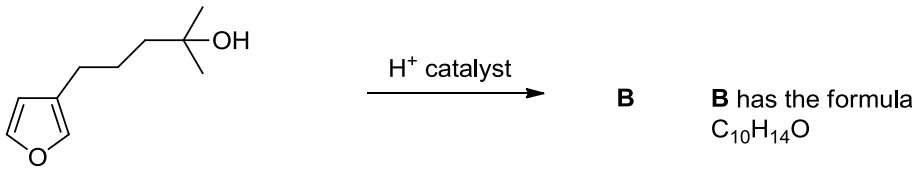
(5 marks each)

b) Identify the product of **ONE** of the following reactions, and write a mechanism for its formation.

i)



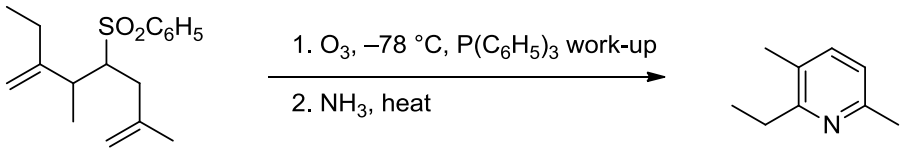
ii)



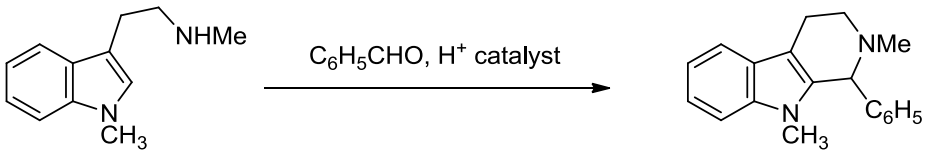
(5 marks)

c) For **EITHER** i) **OR** ii) below, give a detailed mechanism for the formation of the product shown.

i)

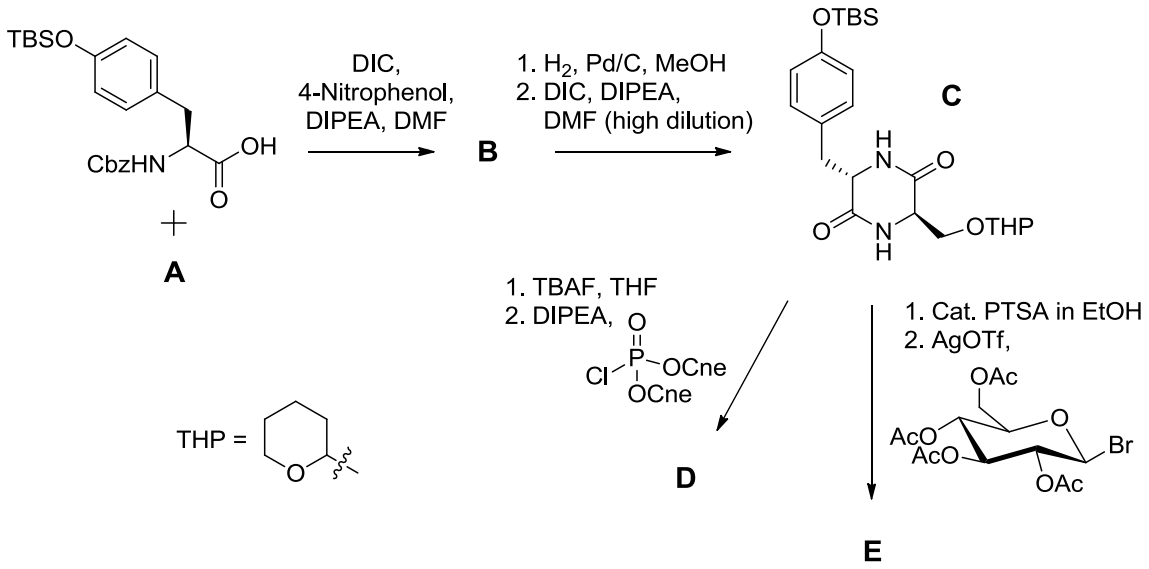


ii)



(10 marks)

2.O3 – Bio-organic Chemistry



Notes: Cbz = carboxybenzyl (-C(O)-OCH_2Ph); Cne = cyanoethyl (-CH_2CH_2CN); DIC = *N*,*N*'-diisopropylcarbodiimide; DIPEA = *N*,*N*-diisopropylethylamine; PTSA = p-toluenesulfonic acid; TBAF = $(^nBu)_4NF.(H_2O)_3$; TBS = *tert*-butyldimethylsilyl; THF = tetrahydrofuran; THP = tetrahydropyranyl.
Selected IR data for **A** (cm^{-1}): 3400, 3350, 1740, 1620.

Answer part a) and **EITHER** part b) **OR** part c) of this question.

a) Answer **ALL** parts of this question.

The scheme above shows a synthesis of compounds based on the diketopiperazine scaffold **C**; such compounds are readily synthesised from amino acids, and possess interesting biological activity as potential drugs.

i) Draw the molecules **A** and **B**.

(6 marks)

ii) Provide a mechanism for the formation of **B**.

(6 marks)

b) Answer **ALL** parts of this question.

i) Draw molecule **D**.

(4 marks)

ii) Provide mechanisms for each step in the formation of **D**.

(7 marks)

iii) Provide conditions for the removal of any protecting groups remaining on **D**.

(2 marks)

QUESTION CONTINUED OVERLEAF

c) Answer **BOTH** the following parts:

i) Draw molecule **E**.

(5 marks)

ii) Provide mechanisms for both steps in the formation of **E**.

(8 marks)

2.O4/2.O5 – Pericyclic reactions/Conformational Analysis

Answer part a) and **EITHER** part b) **OR** part c) of this question.

a) Answer **ALL** parts of this question.

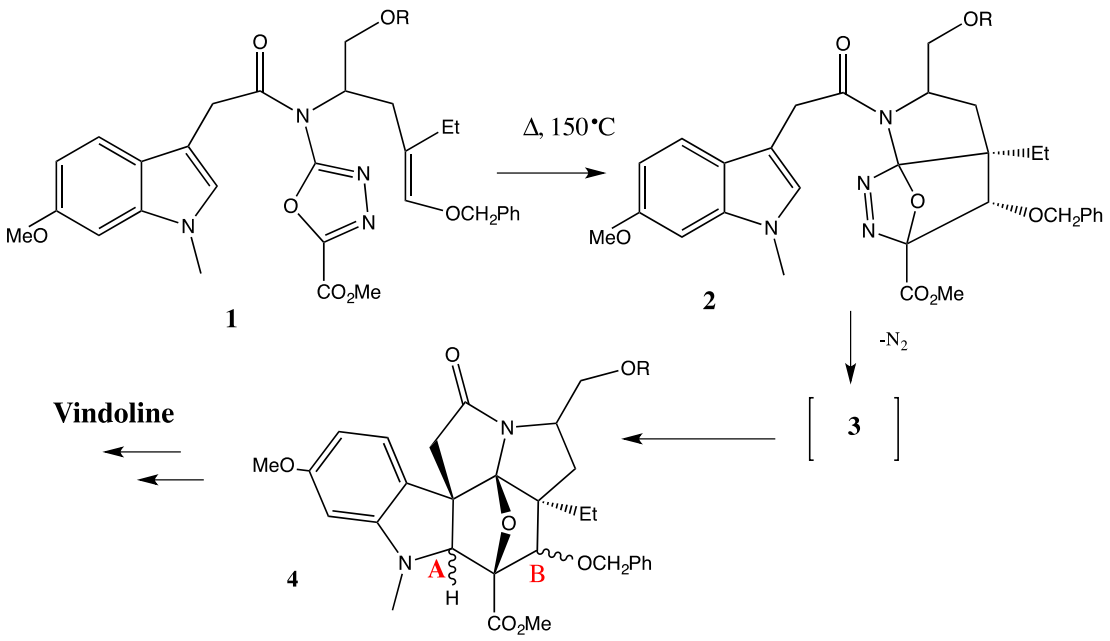
i) Discuss the difference between a conformational and configurational isomer, using the molecule 2-chloro-3-fluorobutane as an example. For any **one** configurational isomer show the possible conformational isomers, using a Newman projection for your answer.
(4 marks)

List the factors that will determine the relative energy of the isomers you have drawn.
(2 marks)

ii) Show one example of an electrocyclic reaction occurring with exactly one antarafacial component, and discuss the stereochemistry involved.
(4 marks)

b) Answer **ALL** parts of this question.

Part of the synthesis of the natural product vindoline[1] involves the following conversions of **1** to **2**, *via* intermediate **3**, to give **4**.



i) Identify the type of pericyclic reaction involved in the conversion of **1** to **2**, indicate using arrow pushing the number of electrons involved and classify these according to either the 4n or 4n+2 rule
(3 marks)

QUESTION CONTINUED OVERLEAF

[1] D. Kato, Y. Sasaki and D. L. Boger, *J. Am. Chem. Soc.*, **2010**, *132*, 3685–3687.

ii) Identify the type of pericyclic reaction that can account for the loss of nitrogen from **2** to give the intermediate **3** and suggest a structure for **3**.

(5 marks)

iii) Identify the type of pericyclic reaction involved in the conversion **3** to **4**, indicate the number of electrons involved and classify these according to either the 4n or 4n+2 rule.

(3 marks)

iv) Using the pericyclic selection rules, show the stereochemistry for the bonds marked **A** and **B** in structure **4**, giving reasons for your inference.

(2 marks each)

c) Using the principles of conformational analysis, suggest probable conformations for each of the four molecules shown below, indicating your reasons for each choice and illustrating the conformation using a Newman projection

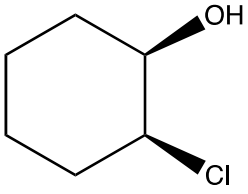
(3 marks each)

i) $Me_3Sn\text{-}CH_2\text{-}CH_2\text{-}CN$

ii) $MeO\text{-}CH_2\text{-}CH_2\text{-}^{+}NMe_3$

iii) $MeS\text{-}CH_2\text{-}CH_2\text{-}Br$

iv)



For the molecule iv), suggest **TWO** possible reactions that might occur if the molecule is treated with base, in your answer noting any conformational features that would promote either reaction.

(3 marks)