IMPERIAL COLLEGE LONDON

BSc and MSci DEGREES – JUNE 2012, 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

Tuesday 19th June 2012, 14:00-16:00

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) Using suitable diagrams, explain **TWO** of the following:

i) Pyridine is basic and pyrrole is not.

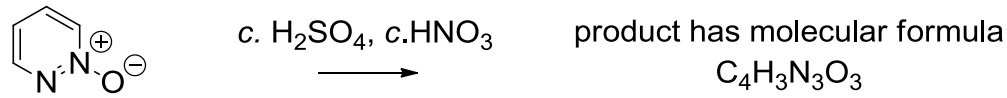
ii) Pyridine reacts with nucleophiles to give mixtures of 2- and 4-substituted products.

iii) Indole reacts with electrophiles to give 3-substituted products.

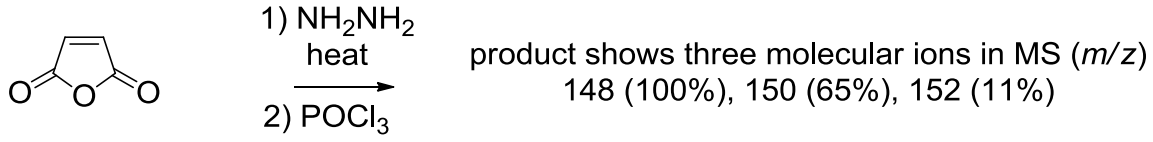
(5 marks each)

b) Predict the (major) products of **ONE** of the following reactions. Draw a mechanism for your selected transformation and explain any selectivity.

i)



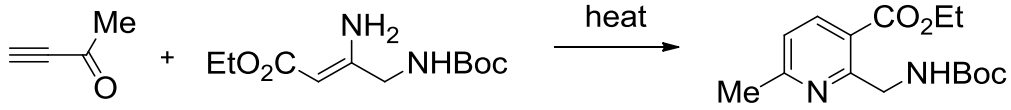
ii)



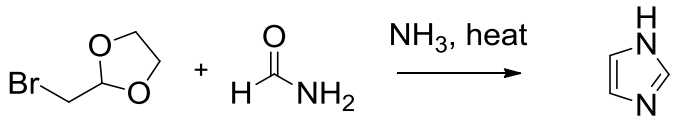
(5 marks each)

c) Give a mechanism for **ONE** of the following transformations:

i)

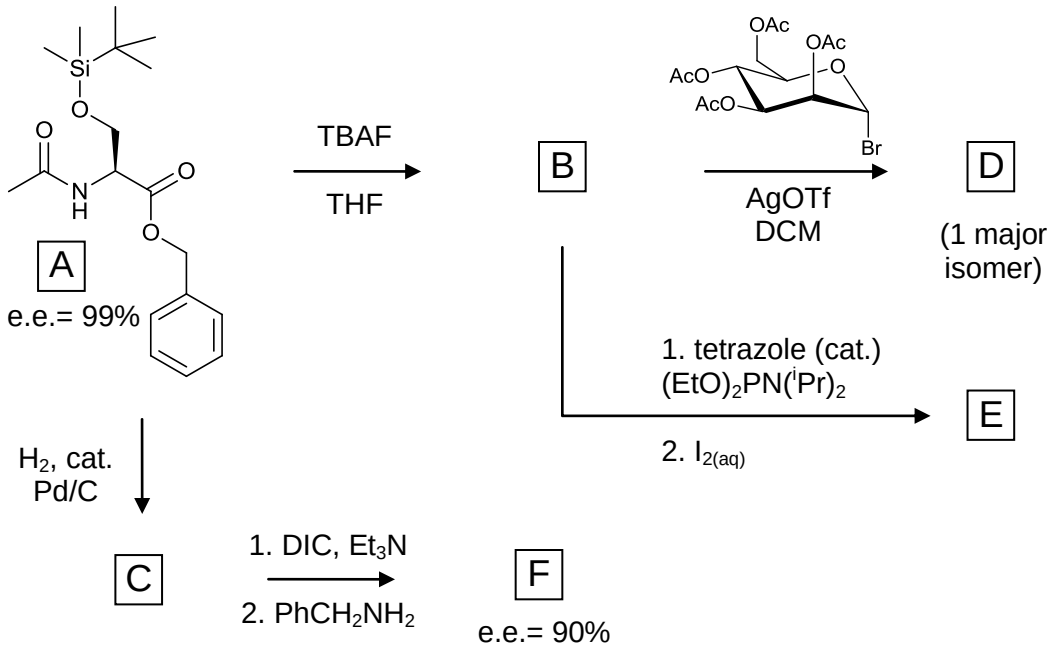


ii)



(10 marks each)

2.O3 – Biological Chemistry



Notes: TBAF = $(^{n}Bu)_4NF.(H_2O)_3$; THF = tetrahydrofuran; DCM = dichloromethane; DIC = *N*,*N*'-diisopropylcarbodiimide; e.e. = enantiomeric excess.
Selected IR data for **B** (cm^{-1}): 3400 (broad), 3050, 1740, 1650
Selected IR data for **C** (cm^{-1}): 3100 (broad), 1715, 1650
Chemical formula for **E**: $C_{16}H_{24}NO_7P$
Chemical formula for **F**: $C_{18}H_{30}N_2O_3Si$

Answer part a) and **ANY TWO** out of parts b), c) and d) of this question.

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

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

(4 marks)

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

(3 marks)

QUESTION CONTINUED OVERLEAF

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

i) Draw molecule **D**.

(4 marks)

ii) Provide a mechanism for the formation of **D** that accounts for the observed stereoselectivity of the reaction.

(5 marks)

c) Answer **BOTH** parts of this question.

i) Draw molecule **E**.

(3 marks)

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

(6 marks)

d) Answer **BOTH** parts of this question.

i) Draw molecule **F**.

(3 marks)

ii) Provide a mechanism that explains why **F** is formed in lower enantiomeric excess than is present in **A**.

(6 marks)

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

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

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

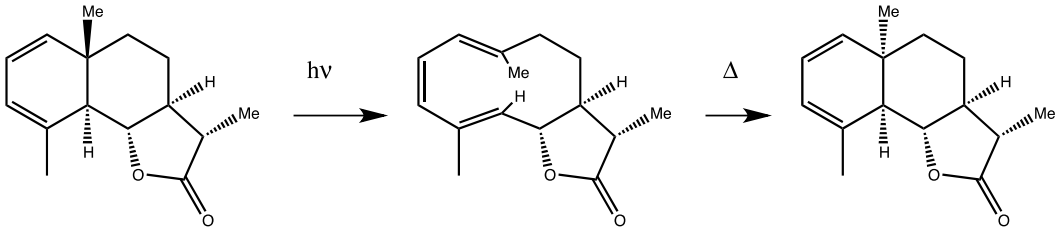
i) Cyclopentadiene (below) appears to have hydrogen atoms in three distinctly different environments. Its ^{1}H NMR spectrum shows just a single peak at room temperatures, but this gradually splits into three multiplets as the solution is cooled. Identify the pericyclic process that accounts for this observation, paying attention to its nomenclature and numbering, showing arrow pushing for the process and indicating whether the reaction proceeds *via* a transition state with Huckel or Möbius topology.

(5 marks)

ii) Give one example of the gauche effect, and briefly write down **one** electronic argument used to explain the conformational preference of your selected example.

(5 marks)

b) In 1965, Woodward and Hoffmann published their analysis of the stereochemistry of electrocyclic reactions. But two years earlier, Corey and Hortmann (10.1021/ja00907a030 and 10.1021/ja00952a037) had described the following reaction, in which compound **10** (their numbering) is converted by photolysis to **13**, a species that then slowly converts to **16** by the action of heat alone. Significantly they provided no analysis in either article of the origins of the observed stereochemistry. The Nobel prize was awarded in due course to Hoffmann (Woodward having died), and conspicuously not to Corey and Hortmann!



10 13 16

QUESTION CONTINUED OVERLEAF

Armed with 20/20 hindsight, your task is to provide that missing analysis by answering all of the following.

i) Identify the type of pericyclic reaction involved in the conversion **10** to **13**, indicate using arrow pushing the number of electrons involved and classify these according to either the 4n or 4n+2 rule.

(3 marks)

ii) Indicate whether the transition state involved in the reaction corresponds to Huckel or to Mobius topology, and clearly indicate any suprafacial or anatarafacial components involved in the reaction.

(3 marks)

iii) Identify the type of pericyclic reaction involved in the conversion **13** to **16**, indicate the number of electrons involved and classify these according to either the 4n or 4n+2 rule.

(3 marks)

iv) Indicate whether the transition state involved in the reaction corresponds to Huckel or to Mobius topology, and clearly indicate any suprafacial or anatarafacial components involved in the reaction.

(3 marks)

v) Indicate any other possible stereoisomers for the formation of either **13 OR** of **16** that would be *allowed* by the pericyclic selection rules (you do not have to explain why they are apparently not formed).

(3 marks)

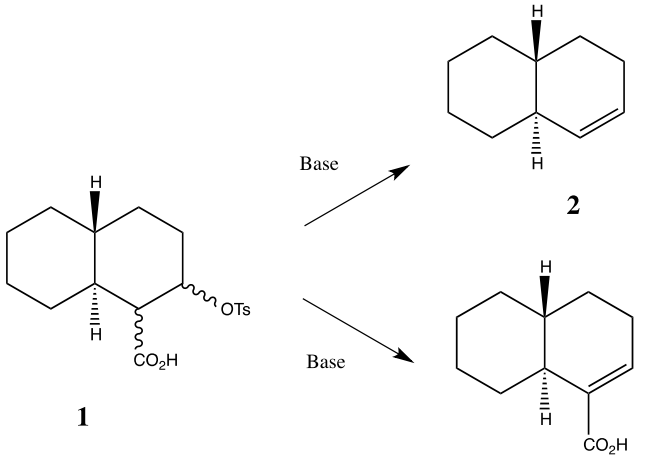
QUESTION CONTINUED OVERLEAF

c) **NB. Only ONE bonus mark will be awarded.**

Use the principles of conformational analysis to give an analysis of the following reactions.

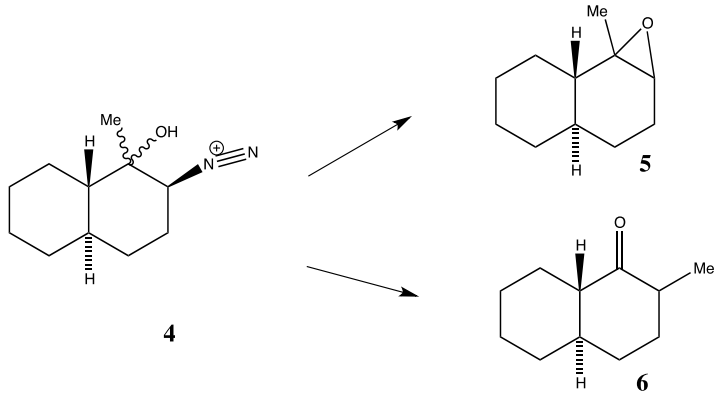
i) Species **1** is treated with base. Depending on the stereochemistry of the substituents (the glyph ∿∿∿ in the diagram below indicates either), either compound **2** or **3** is formed. Using the notations ◣ or ⋯⋯ indicate the stereochemical isomers of **1** that give both compound **2** and compound **3** (separate reactions), showing your reasoning for both.

(7 marks + 1 bonus)



1 **2** **3**

ii) Species **4** can undergo two different reactions depending on the absolute stereochemistry of the two substituents (Me or OH) attached to the ring to give either **5** or **6**.



4 **5** **6**

Using the notations ◣ and ⋯⋯ indicate the stereochemical isomers of **4** that give both compound **5** and compound **6** (separate reactions), showing your reasoning for both.

(7 marks + 1 bonus)