IMPERIAL COLLEGE LONDON

BSc and MSci DEGREES – JUNE 2010, 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 17th June 2010, 14:00-16:00

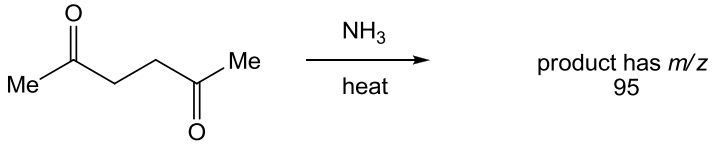
USE A SEPARATE ANSWER BOOK FOR EACH QUESTION. WRITE YOUR CANDIDATE NUMBER ON EACH ANSWER BOOK.

2.O2 – Heteroaromatics

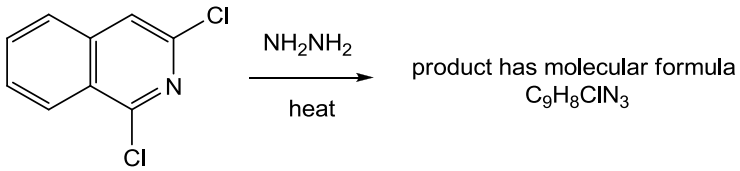
Answer **BOTH** part (a) **AND** part (b).

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

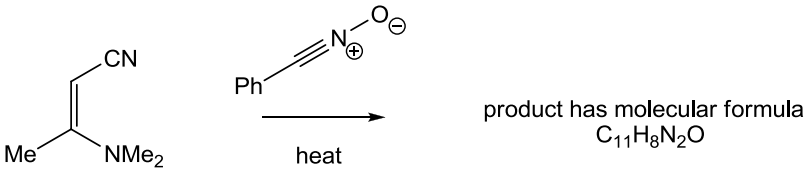
i)



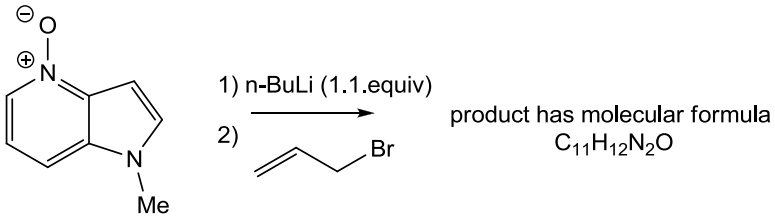
ii)



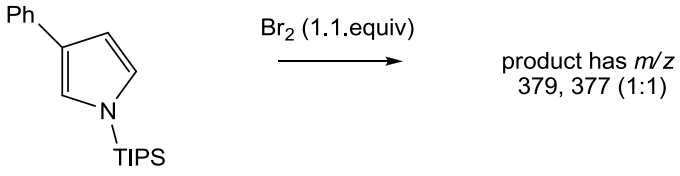
iii)



iv)



v)



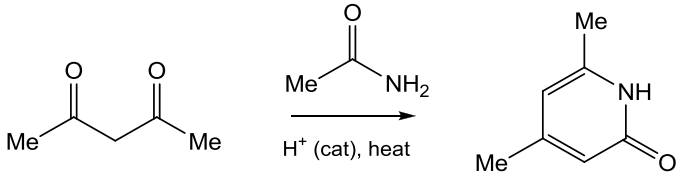
TIPS = Si(*i*-Pr)$_3$

(5 marks each)

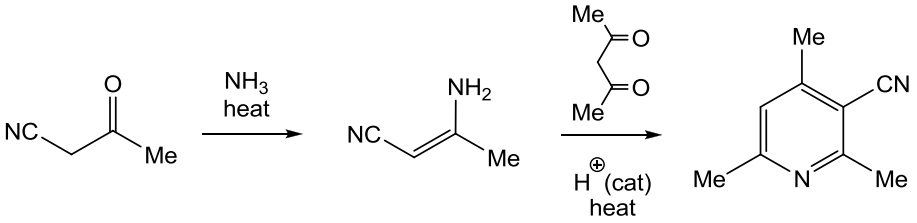
QUESTION CONTINUED OVERLEAF

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

i)



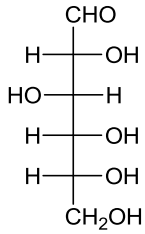
ii)



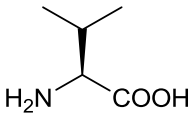
(10 marks)

2.O3 – Biological Chemistry

The following information is provided for reference:



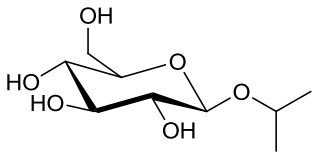
D-glucose (Glc)



L-Valine (Val)

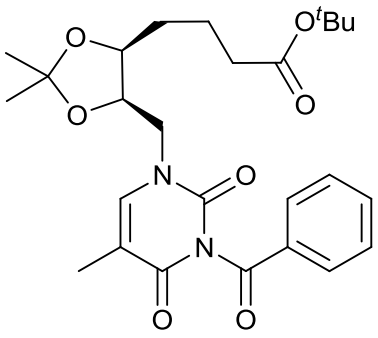
Answer any **TWO** of the three parts a), b) and c)

a) Draw a reaction scheme to describe a synthesis of molecule **A** (below) starting from D-glucose, providing suitable reagents for each step. Draw a mechanism for the glycosidation step.

A = 

(12.5 marks)

b) Consider the following polyfunctional molecule:

B = 

QUESTION CONTINUED OVERLEAF

i) Identify the orthogonal protecting groups in molecule **B**, and provide conditions for their removal.

(4 marks)

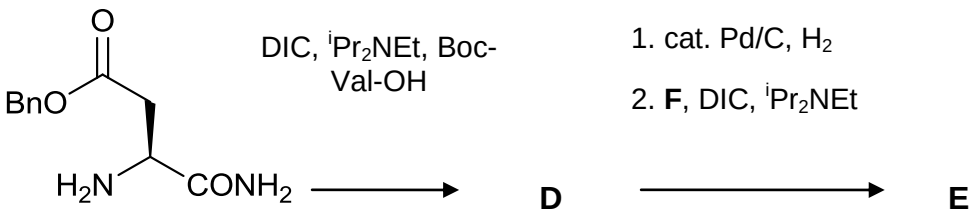
ii) Provide a mechanism for removal of any **ONE** of the protecting groups in **B**.

(4 marks)

iii) When **B** is treated with 95% trifluoroacetic acid in water it reacts to give a product **C** and two volatile by-products. The mass spectrum of **C** displays a MH^+ peak at 373. Draw the structure of **C** and the two by-products from the reaction.

(4.5 marks)

c) The scheme below illustrates the synthesis of a building block for the generation of glycopeptides, an important class of biomolecules. Provide a mechanism for the formation of intermediate **D** and draw out the full structures of **D** and **E**.



F = α-amino-D-glucoside 2,3,4,6-tetraacetate

Bn = benzyl; Boc = *tert*-butoxycarbonyl; DIC = *N*,*N'*-diisopropyl carbodiimide

(12.5 marks)

2.O4 – Pericyclic Reactions

Answer **BOTH** parts (a) **AND** (b)

a) Answer only **ONE** question from the two below

i) Give one example of a stereospecific electrocyclic reaction, showing clearly the arrow pushing for your selected example. Indicate whether your arrows correspond to a 4n+2 rule or a 4n electron rule for a pericyclic step and whether your reaction is promoted by heat or by light.

(6 marks)

Illustrate why your chosen example is stereospecific and how it conforms to the selection rule based on your 4n/4n+2 electron count and reaction conditions of heat or light.

(4 marks)

ii) Give one example of a sigmatropic reaction, showing clearly the arrow pushing for your selected example and indicating whether your arrows correspond to a 4n+2 rule or a 4n electron rule for a pericyclic step and whether your reaction is promoted by heat or by light.

(6 marks)

For your example, discuss whether the transition state for the reaction involves Huckel or Mobius aromaticity, including in your answer what the difference between them is.

(4 marks)

b) Answer **TWO** questions only from the parts i), ii), iii) and iv)

The following sequence of reactions is part of the total synthesis of the natural product Geneserine.[1] Compound **1** (shown as one enantiomer of a racemic mixture) is heated to produce intermediates **2** and **3**. Compound **2** is converted by further heating to **4**, and then **5** (which is formed as a racemate; again only one enantiomer is shown below). Compound **3** is a geometrical isomer of **2**, and it reacts differently to give **6**. Answer no more than **two** of the following questions about this sequence.

(7.5 marks per question)

i) Working forwards from compound **1**, propose a structure for compound **2**, showing a mechanism and nomenclature for this step.

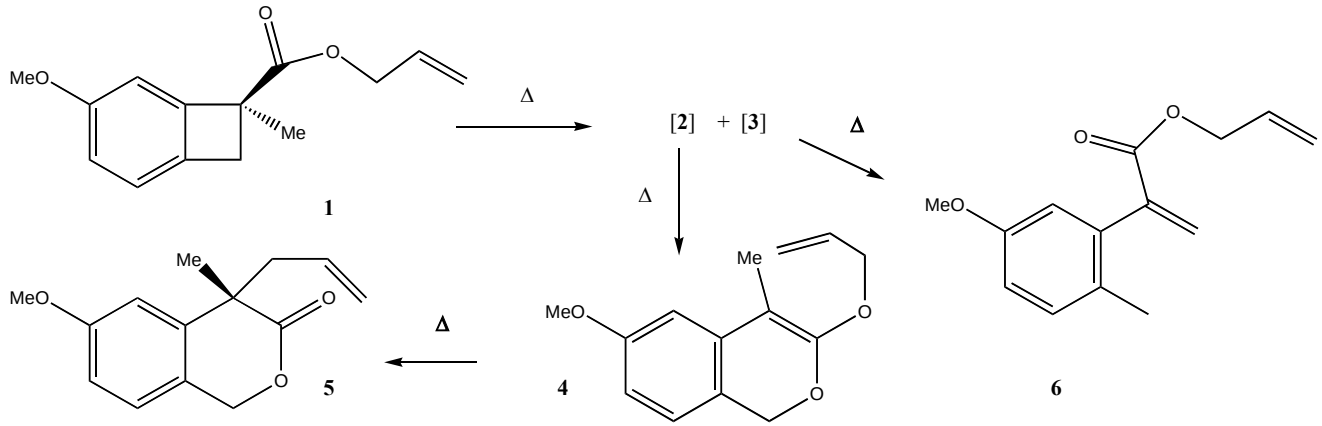
ii) Identify the mechanism for the transformation of compound **4** to compound **5**, including any nomenclature for all step(s), and identify whether these step(s) are 4n or 4n+2 electron thermal pericyclic reactions.

QUESTION CONTINUED OVERLEAF

[1] K. Shisido, K. Hiroya, H. Komatsu, K. Fumumoto and T. Kametani, *J. Chem. Soc., Perkin Trans* 1, **1987**, 2491-2495. DOI: 10.1039/P19870002491

iii) Working backwards from compound **4**, propose a structure for compound **2**, showing a mechanism and nomenclature for this step.

iv) Given that compound **3** is a geometrical isomer of **2,** propose a structure for it, and a mechanism and nomenclature for its transformation to **6**.



Spectroscopic information for [2]/[3]: Each shows complex multiplets in the region 5-6 ppm (8H in total), ~3.9 (3H s), ~4.2 (2H, m), ~1.5 (3H, s).

2.O5 – Conformational Analysis

Answer **BOTH** part a) **AND** part b)

a) Answer **ONE** of the following two questions.

i) Discuss the difference between the chemical meaning of the terms *molecular conformation* and *molecular configuration*, illustrating your answer with **one** simple example for each.

(10 marks)

ii) Explain the terms *Gauche effect* and *antiperiplanar*, illustrating your answer with one example which covers both effects, and include in your answer a simple orbital energy diagram with a brief explanation of its relevance.

(10 marks)

b) Answer any **TWO** of the following three questions about the compounds **1** and **2**.

i) Assuming that both the *trans*-decalins below adopt a chair-chair conformation, label the five ring substituents shown (*i.e.* two hydrogens, a OTs, a methyl and a nitrogen lone pair) as either axial or equatorial for both compounds.

(1.5 marks per pair, 7.5 marks in total)

ii) Compound **1**, when heated in the presence of $NaBH_4$ (both a mild reducing agent and a mild base), readily eliminates $^-$OTs to form a monocyclic compound, which by ^{1}H NMR is shown to contain just one disubstituted alkene, and in which the two remaining alkene hydrogens are shown by their ^{3}J coupling constant to have an *antiperiplanar* relationship. Using the principles of conformational analysis, provide a mechanistic explanation.

(5 marks)

and identify any other *antiperiplanar* relationships.

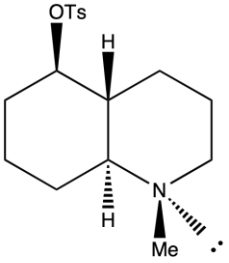
(2.5 marks)

iii) Compound **2**, when heated in the presence of $NaBH_4$ (both a mild reducing agent and a mild base), slowly eliminates $^-$OTs to form a bicyclic compound, which by ^{1}H NMR is shown to contain just one trisubstituted alkene. Using the principles of conformational analysis, provide a mechanistic explanation.

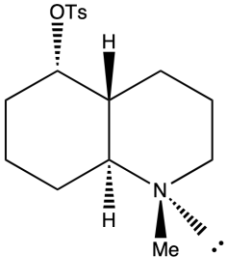
(5 marks)

and identify any *antiperiplanar* relationships.

(2.5 marks)



1



2