IMPERIAL COLLEGE LONDON

BSc and MSci DEGREES – JUNE 2017, for Internal Students of the Imperial College of Science, Technology and Medicine

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

CHEM50002 ORGANIC CHEMISTRY 2

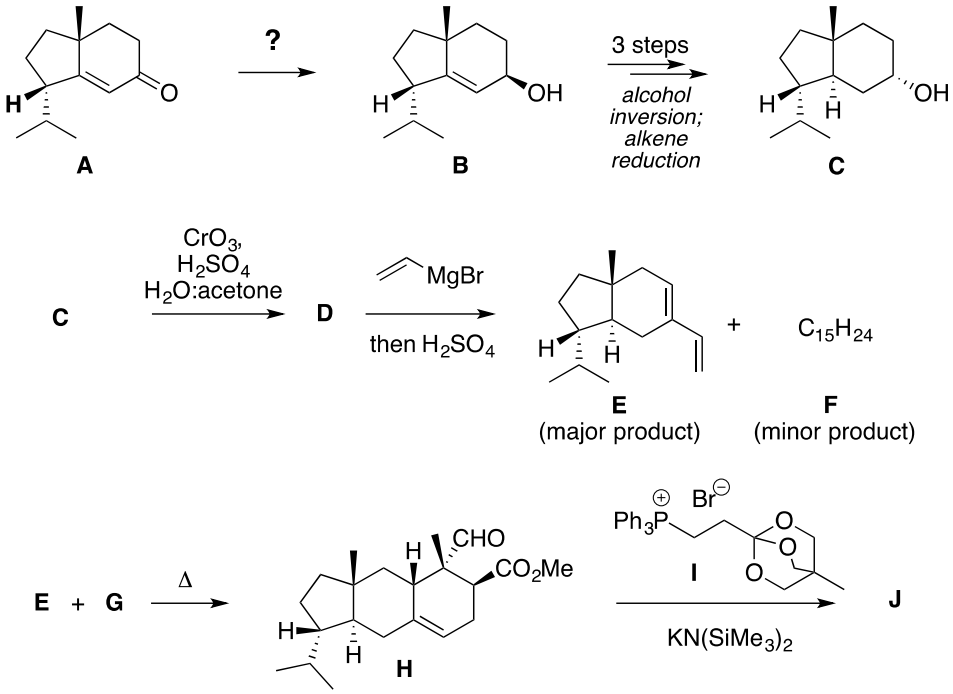
Monday 26th June 2017, 14:00-17:00

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.

Q1. Answer **ALL** parts, a) to d), **THEN** part e) **OR** part f) of this question.

The questions relate to the following reaction scheme.



a) Suggest a suitable reagent for the conversion of **A** into **B**. Identify the types of selectivity observed.

(2 marks)

b) Draw a 3D-conformational representation of compound **C** and describe the conformations of the two rings.

(2 marks)

c) Provide a structure for **D** and predict the IR stretching frequency of the newly created functional group.

(2 marks)

d) Draw a curly arrow mechanism for the conversion of **D** into **E**, and provide a structure of the minor product **F**.

(6 marks)

e) Provide a structure for **G** and draw a curly arrow mechanism for the formation of **H**. Comment on the type(s) of selectivity observed.

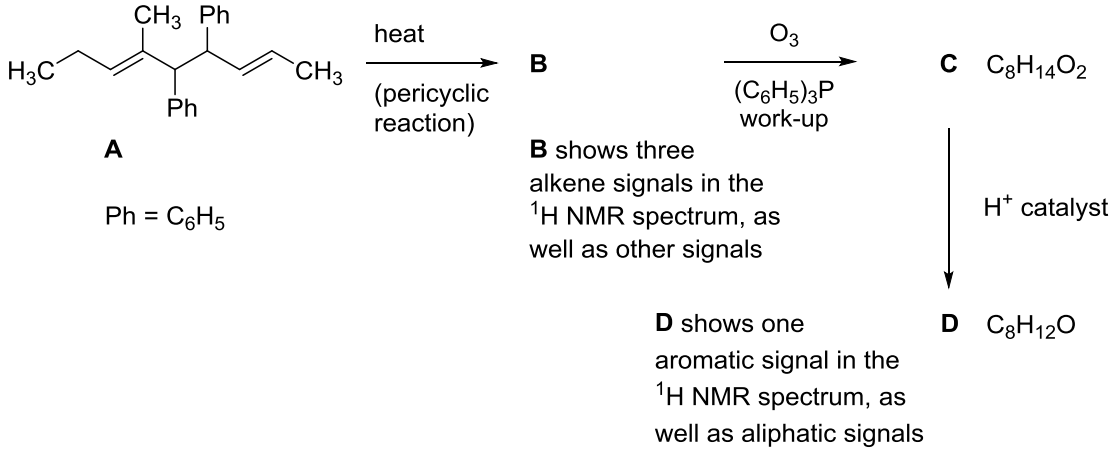
(8 marks)

f) Draw the structure of product **J** formed from reaction of **H** and **I** using the reagent shown. Provide a curly arrows mechanism, and comment on any selectivity. Suggest suitable starting materials for the preparation of compound **I**.

(8 marks)

Q2. Answer part a) **AND** either part b) **OR** part c) of this question.

a) Consider the reaction scheme below, and then answer the questions (i) – (iii) which follow the scheme.



i) Draw the structure of **B**. What kind of pericyclic reaction is taking place in the conversion of **A** into **B**? What is the driving-force of this reaction?

(4 marks)

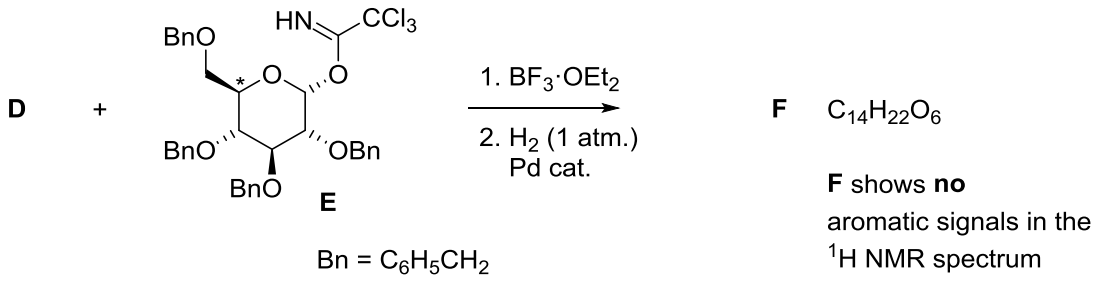
ii) Identify the product **C**, and write a mechanism for its formation from **B** under the reactions conditions shown.

(4 marks)

iii) Draw a structure for **D**, and write a mechanism for its formation from **C**.

(4 marks)

b) In the following scheme, the final product **D** in the scheme above was combined with compound **E** in the presence of $BF_3{\cdot}OEt_2$ followed by catalytic hydrogenolysis to give product **F**. Answer the questions (i) and (ii) which follow the scheme.



i) Draw a structure for product **F**. What is the mechanism of the reaction in step 1 of the conversion of **D** + **E** into **F**?

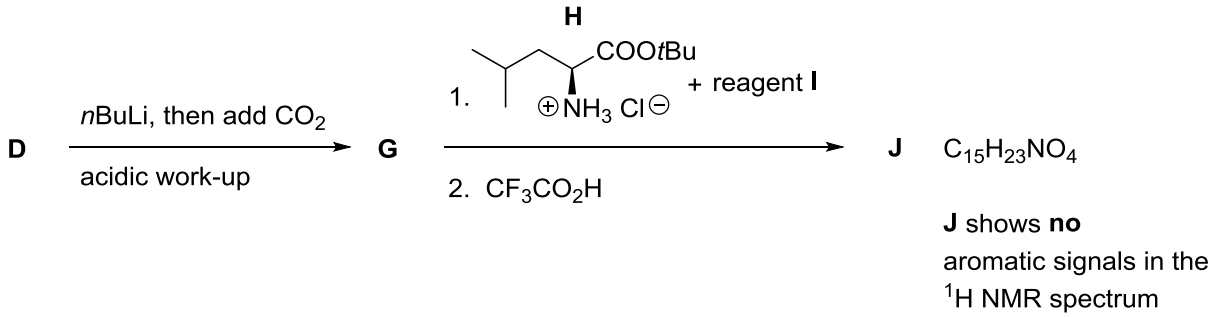
(6 marks)

ii) When the reaction in step 2 of the conversion of **D** + **E** into **F** is carried out under a much greater pressure of hydrogen, a <u>different</u> product to **F** is formed; this different compound has the formula $C_{14}H_{26}O_6$. Draw the structure of this product.

(2 marks)

QUESTION CONTINUED OVERLEAF

c) In an alternative sequence of reactions, the final product **D** from the first scheme above was first converted into **G** under the conditions shown in the scheme below. Product **G** was subsequently transformed into **J** as shown. Answer the questions (i) and (ii) which follow the scheme.



i) Draw the structure of **G**, and write a mechanism for its formation from **D**.

(4 marks)

ii) Draw the structure of product **J**. Write a mechanism for step 2 in the formation of product **J** from **G**.

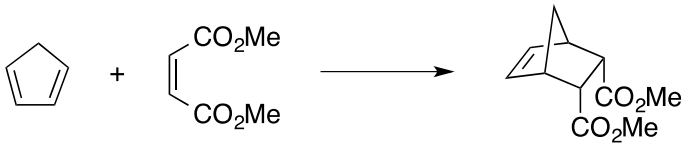
(4 marks)

Q3. Answer parts a) **AND** b) of this question.

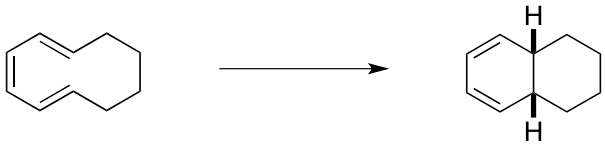
a) For **TWO** of the following **THREE** thermal reactions, draw a curly arrow mechanism and write down the class of pericyclic reaction to which it belongs.

i)

ii)

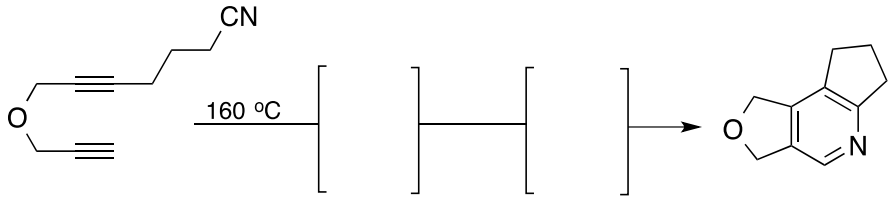


iii)



(10 marks)

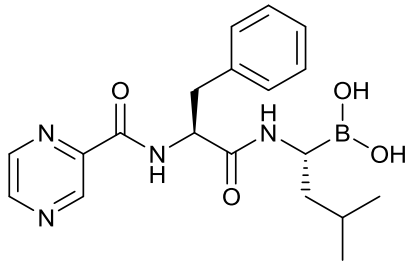
b) The reaction illustrated below takes place in three steps starting with a propargylic ene reaction. Write down the structures of the two intermediates.



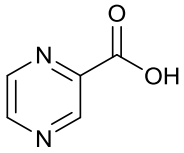
(10 marks)

Q4. Answer part a) **AND** part b) of this question.

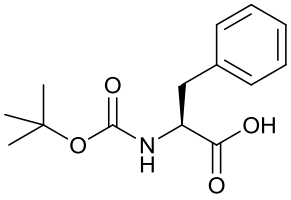
Bortezomib is a potent inhibitor of protein degradation in human cells, and is an important drug for the treatment of multiple myeloma. Bortezomib can be assembled in a multistep synthesis using compounds **A**, **B** and **C**.



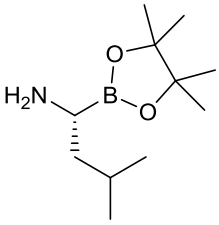
Bortezomib



A



B



C

a) Answer **TWO** of the following parts i)-iii) of this question.

i) Identify the protecting group present in compound **B**, and provide conditions and a plausible mechanism for its removal.

(4 marks)

ii) The protecting group present in compound **C** can be removed by transesterification with phenylboronic acid ($PhB(OH)_2$) under aqueous acidic conditions. Provide a plausible mechanism for this deprotection reaction.

(4 marks)

iii) Define the absolute configuration at each stereocentre in Bortezomib.

(4 marks)

b) Suggest a plausible synthetic route to Bortezomib, with reagents and conditions for each step. Provide mechanisms for any steps which do **not** involve deprotection.

(12 marks)

Q5. Answer part a) **AND** either part b) **OR** part c) of this question.

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

i) Consider the following distributions of poly(methyl acrylate) chains:

15 (wt) % chains of degree of polymerization 25
35 (wt) % chains of degree of polymerization 50
50 (wt) % chains of degree of polymerization 75

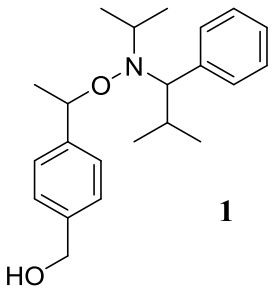
Calculate the number and weight average molecular weight of this collection of polymer chains.

(4 marks)

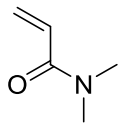
ii) Suggest two different polymerization methods that can be used to synthesise this polymer.

(2 marks)

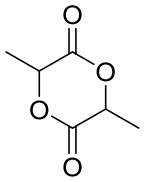
iii) Treatment of **1** with acrylamide monomer **2**, yields a macroinitiator **A**, which can be converted into a graft block copolymer **B** on the addition of **3** under appropriate conditions and in the presence of a catalyst. The resultant block copolymer **B** was then converted into a tri-block polymer **C** on treatment with styrene.



1



2



3

Draw the structures of **A**, **B** and **C**, including end-groups.

(6 marks)

Identify the two polymerisation mechanisms operating in the formation of **B** and **C**.

(2 marks)

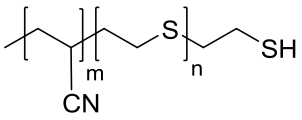
iv) Compare the reactivity of a styrene monomer with the reactivity of a vinyl chloride monomer in radical polymerisation, and account for the faster propagation rate of the vinyl chloride radical.

(2 marks)

QUESTION CONTINUED OVERLEAF

b) The copolymer **4** of precise block lengths n and m, shown below, can be easily synthesized by sequential addition of monomer using the same polymerization mechanism. Propose a mechanism, reagents and conditions. Why is a crown ether often required during the synthesis?

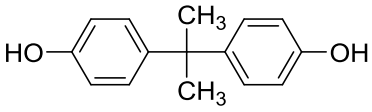
(4 marks)



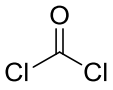
4

c) In the polymerisation of **5** with **6** the phosgene monomer **6** is in excess to the ratio 1:1.02 and the extent of reaction is 0.99. What is the number average molecular weight of the resulting polymer?

(4 marks)



5



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