UNIVERSITI SAINS MALAYSIA

Second Semester Examination
2011/2012 Academic Session

June 2012

KOT 323 – Organic Chemistry III
[Kimia Organik III]

Duration : 3 hours
[Masa : 3 jam]

Please check that this examination paper consists of TWENTY TWO pages of printed material before you begin the examination.

Instructions:

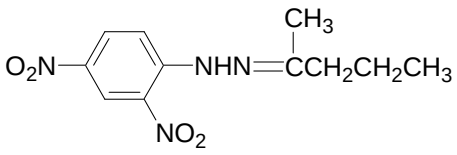
Answer any **FIVE** (5) questions.

You may answer the questions either in Bahasa Malaysia or in English.

If a candidate answers more than five questions, only the answers to the first five questions in the answer sheet will be graded.

In the event of any discrepancies, the English version shall be used.

1. (a) Compound **A** reacts with warm concentrated $KMnO_4$ to give compound **B**. Reaction of compound **B** with the acidic solution of 2,4-dinitrophenylhydrazine form a characteristic yellow to orange-red precipitate (**I**).



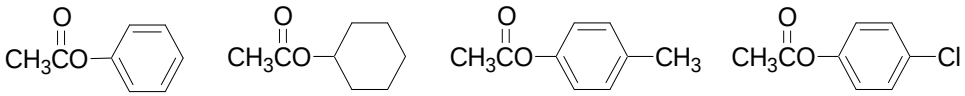
(**I**)

(i) What are compounds **A** and **B**?

(ii) Give the reaction mechanism between compound **B** and 2,4-dinitrophenylhydrazine.

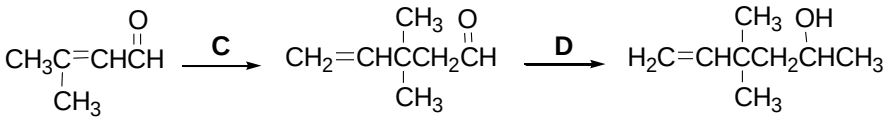
(8 marks)

(b) List the following esters in order of decreasing reactivity (most reactive to least reactive) in the nucleophilic acyl substitution reaction. Explain your answer.



(6 marks)

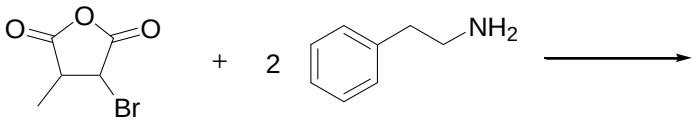
(c) Give the reagents (**C** – **G**) of each of the following reactions:

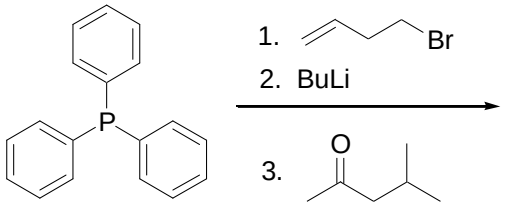
(i) 

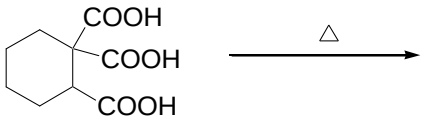
(ii)

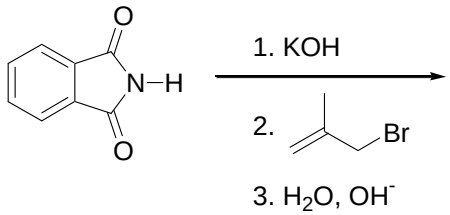
(6 marks)

2. (a) Give the product for each of the following reactions:

(i) 

(ii) 

(iii) 

(iv) 

(v) $CH_3CH_2-O-\overset{\overset{O}{\|}}{C}-O-CH_2CH_3$ $\xrightarrow[2.\ H_3O^+]{1.\ \text{excess PhMgBr}}$

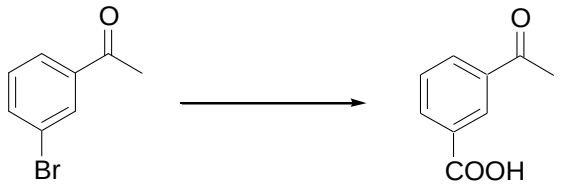
(10 marks)

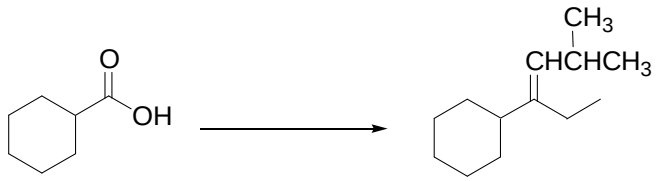
(b) An attempt to carry out the following esterification is failed. Explain.

$CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}-OH + CH_3CH_2OH \xrightarrow{NaOH} CH_3CH_2CH_2\overset{\overset{O}{\|}}{C}-O-CH_2CH_3$

(2 marks)

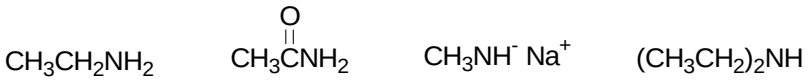
(c) Propose the synthetic method for each of the following conversions. No mechanism is needed.

(i) 

(ii) 

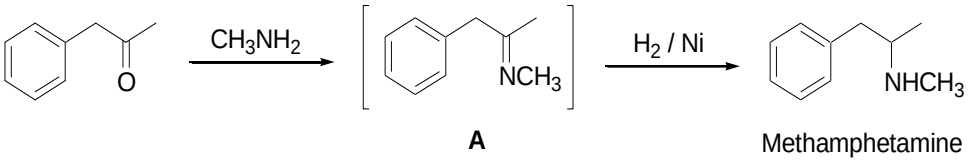
(8 marks)

3. (a) List the following compounds in order of decreasing basicity. Explain your answer.



(5 marks)

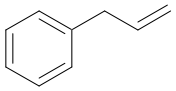
(b) Methamphetamine can be synthesized by reacting phenyl-2-propanone with methylamine in the presence of H_2/Ni.



A Methamphetamine

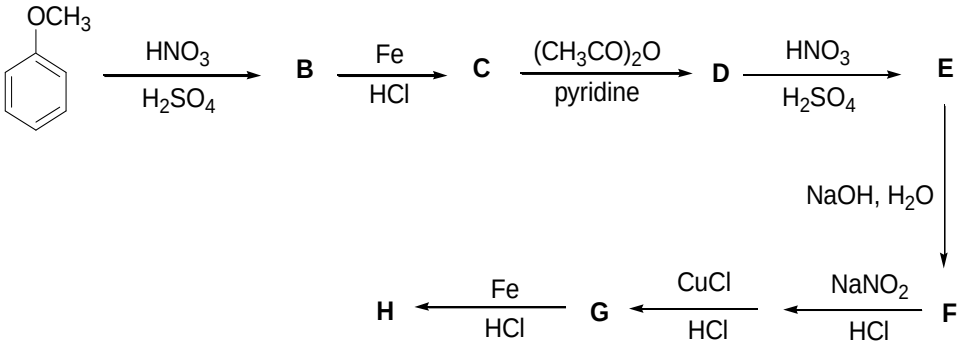
(i) Although the yield of methamphetamine is good, some unreacted phenyl-2-propanone remains after the reaction is completed. Describe how methamphetamine (in its free form) can be separated from phenyl-2-propanone using liquid-liquid extraction.

(ii) Propose a stepwise synthesis to convert methamphetamine to the following compound:



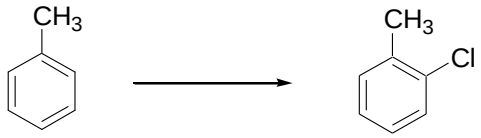
(8 marks)

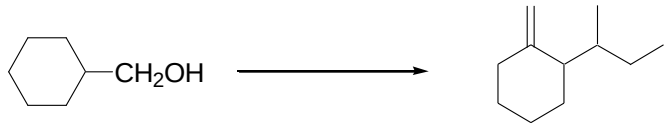
(c) Give the structures of **B** – **H** in the following reactions:

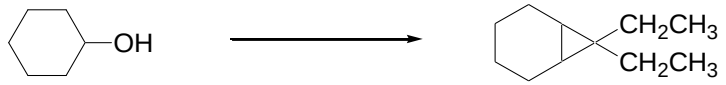


(7 marks)

4. (a) Give the stepwise synthesis for each of the following reactions:

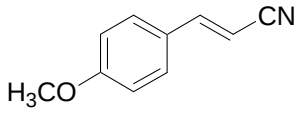
(i) 

(ii) 

(iii) 

(10 marks)

(b) Compound **A** as shown below can be prepared from a Heck reaction.



A

(i) What are the starting materials needed to prepare compound **A**?

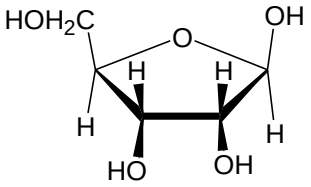
(ii) Give the reaction mechanism for the preparation of compound **A**.

(7 marks)

(c) What will happen if an alkyl halide such as bromoethane is used as the halide in a Heck reaction?

(3 marks)

5. (a) Convert the following Haworth projection of the aldopentose, **A** to the acyclic form, **X**.



A

(2 marks)

(b) The acyclic structure **X** from 5 (a), undergoes reactions below to form compounds **B – G**.

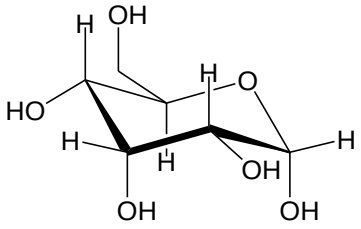
(i) Give the structures for these compounds.

(ii) Give the reagents (in sequence) for the Killiani-Fischer synthesis.

(iii) What are the common reagents used in Wohl degradation?

(8 marks)

(c) The structure of α-glucose in chair conformation is shown below:



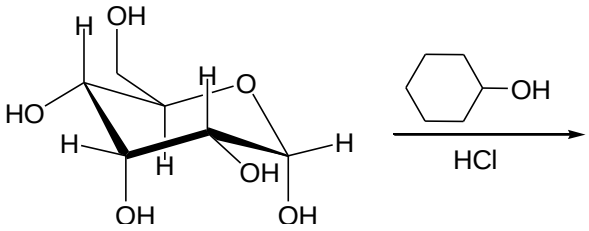
(i) Two molecules of α-glucose react to form a disaccharide. Draw this disaccharide structure with an α-glucosidic linkage.

(ii) Reaction of an α-glucose with methyl iodide and silver oxide gives product **H**. Draw the structure for **H**.

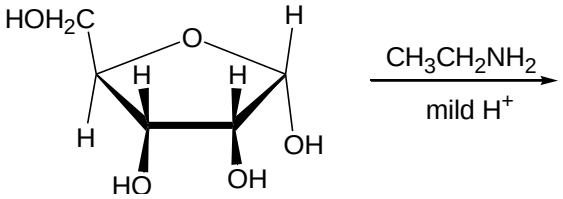
(3 marks)

(d) Draw the products of each reactions.

(i)



(ii)

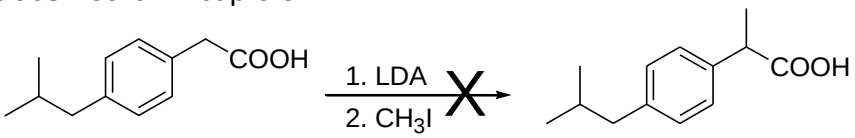


(4 marks)

(e) What are the differences between a reducing sugar and a non-reducing sugar? Draw one example for each of these sugars.

(3 marks)

6. (a) Direct alkylation of **A** by reaction with one equivalent of LDA and CH_3I **does not** form ibuprofen.

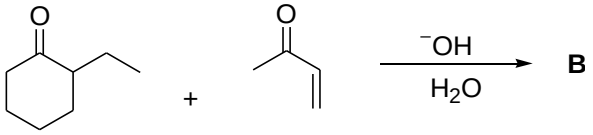


A ibuprofen

Identify the product of this reaction and explain how it is formed.

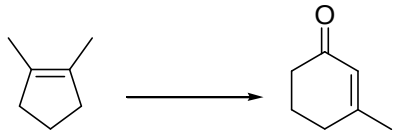
(3 marks)

(b) In the Robinson annulations mechanism, there are three C-C bond forming steps and several proton transfer steps (protonation and deprotonation). Draw this stepwise mechanism for the reaction below to form compound **B**.



(5 marks)

(c) Propose a synthesis of **D** from **C**. Show all necessary reagents and intermediates.



C **D**

(5 marks)

(d) Draw the products (**E - I**) formed in the reactions below.

(i)

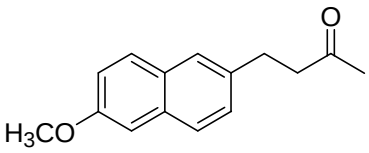
(ii)

(iii)

(iv)

(7 marks)

7. (a) Nabumetone is a pain reliever and anti-inflammatory agent.



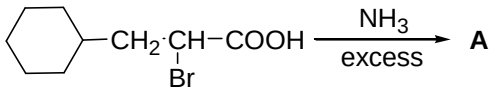
Nabumetone

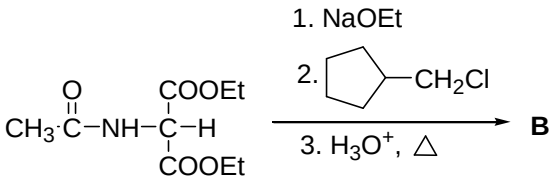
(i) Use the acetoacetic ester synthesis to produce Nabumetone.

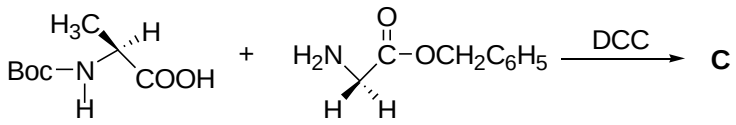
(ii) What starting materials (ketone and alkyl halide) are needed to synthesize Nabumetone by direct enolate alkylation.

(7 marks)

(b) Give the structures of **A – C** in the reactions below:

(i) 

(ii) 

(iii) 

(3 marks)

(c) Strecker amino acid synthesis converts an aldehyde into an amino acid, as shown in the reaction below. Show the stepwise mechanism for this transformation from aldehyde to α-amino nitrile.

α-amino nitrile amino acid

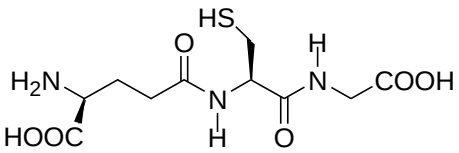
(5 marks)

(d) Give the amino acid sequence of a octapeptide that contains the amino acids Tyr, Ala, Leu (2 equiv), Cys, Gly, Glu and Val. Partial hydrolysis of the peptide gave the following fragments:

Val-Cys-Gly-Glu Ala-Leu-Tyr Tyr-Leu-Val-Cys.

(2 marks)

(e) Gluthathione, a powerful antioxidant that destroys harmful oxidizing agents in cells, is composed of glutamic acid, cysteine and glycine and has the following structure:



Gluthathione

(i) What product is formed when gluthathione reacts with an oxidizing agent?

(ii) What is unusual about the peptide bond between glutamic acid and cysteine?

(3 marks)

TERJEMAHAN

Sila pastikan bahawa kertas peperiksaan ini mengandungi DUA PULUH DUA muka surat bahan bercetak.

Arahan:

Jawab **LIMA** (5) soalan.

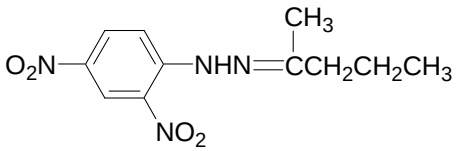
Anda dibenarkan menjawab soalan ini sama ada dalam Bahasa Malaysia atau Bahasa Inggeris.

Jika calon menjawab lebih daripada lima soalan, hanya lima soalan pertama mengikut susunan dalam skrip jawapan akan diberi markah.

Sekiranya terdapat sebarang percanggahan pada soalan peperiksaan, versi Bahasa Inggeris hendaklah diguna pakai.

Jawab hanya **LIMA** soalan.

1. (a) Sebatian **A** bertindak balas dengan $KMnO_4$ pekat yang panas untuk memberikan sebatian **B**. Tindak balas sebatian **B** dengan larutan berasid 2,4-dinitrofenilhidrazina menghasilkan suatu mendakan kuning hingga jingga kemerahan (**I**).



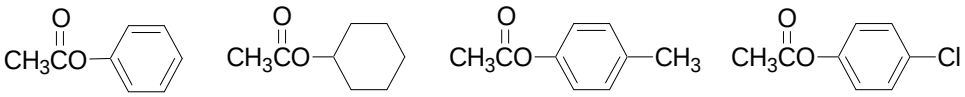
(**I**)

(i) Apakah sebatian **A** dan **B**?

(ii) Berikan mekanisme tindak balas antara sebatian **B** dengan 2,4-dinitrofenilhidrazina.

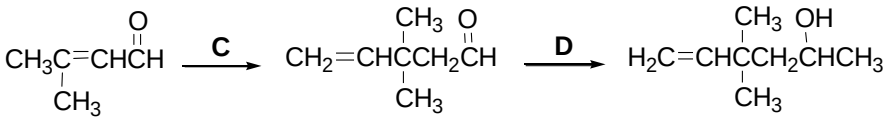
(8 markah)

(b) Senaraikan ester berikut dalam tertib kereaktifan menurun (paling reaktif kepada kurang reaktif) dalam tindak balas penukargantian nukleofilik asil. Terangkan jawapan anda.



(6 markah)

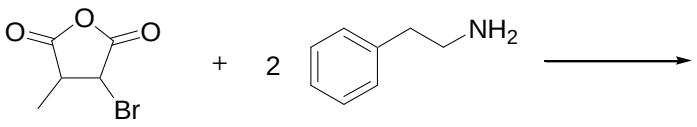
(c) Berikan reagen (**C** – **G**) bagi setiap tindak balas berikut:

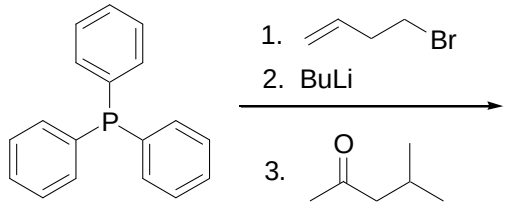
(i) 

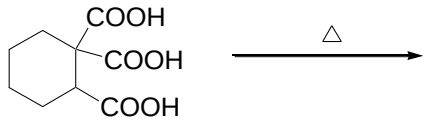
(ii)

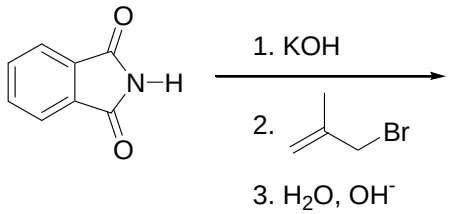
(6 markah)

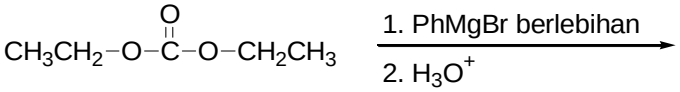
2. (a) Berikan hasil bagi setiap tindak balas berikut:

(i) 

(ii) 

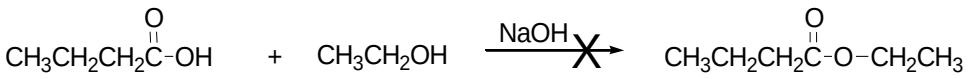
(iii) 

(iv) 

(v) 

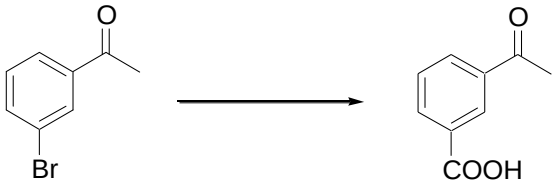
(10 markah)

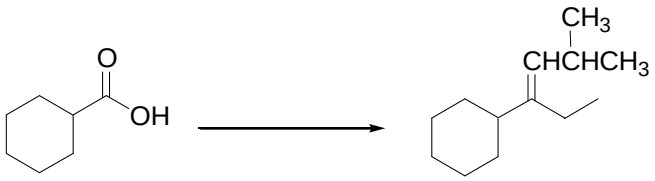
(b) Suatu percubaan bagi tindak balas pengesteran berikut gagal. Jelaskan.



(2 markah)

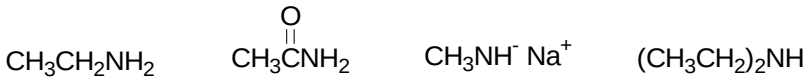
(c) Cadangkan suatu cara sintesis bagi setiap penukaran berikut. Mekanisme tidak diperlukan.

(i) 

(ii) 

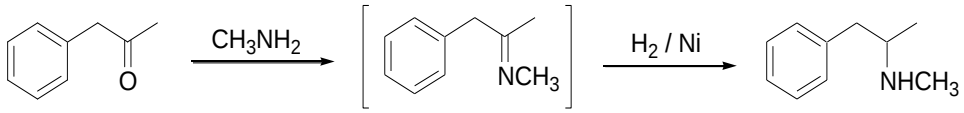
(8 markah)

3. (a) Senaraikan sebatian berikut dalam tertib kebesan menurun. Terangkan jawapan anda.



(5 markah)

(b) Metamfetamina dapat disintesiskan melalui tindak balas antara fenil-2-propanon dengan metilamina dalam kehadiran H_2/Ni.

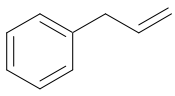


A

Metamfetamina

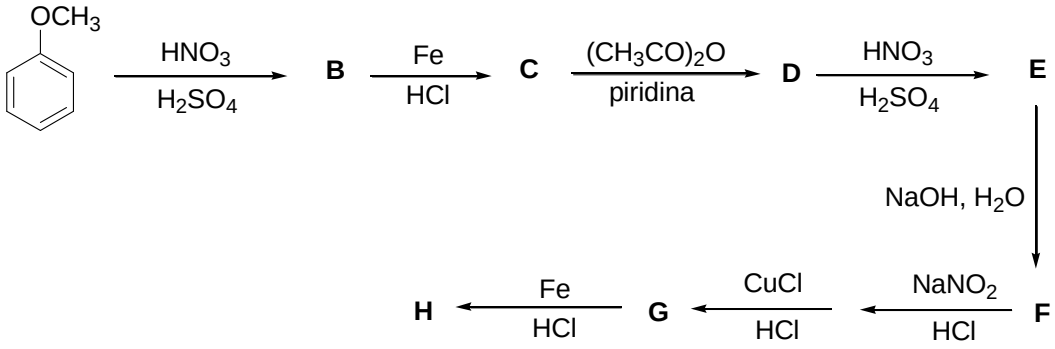
(i) Walaupun hasil metamfetamina adalah memuaskan, sesetengah fenil-2-propanon yang tidak bertindakbalas masih tertinggal selepas tindak balas sudah lengkap. Terangkan bagaimanakah metamfetamina (dalam bentuk bebas) dapat diasingkan daripada fenil-2-propanon menggunakan pengekstrakan cecair-cecair.

(ii) Cadangkan suatu sintesis berperingkat untuk menukarkan metamfetamina kepada sebatian berikut:



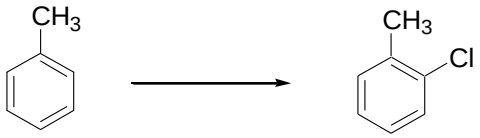
(8 markah)

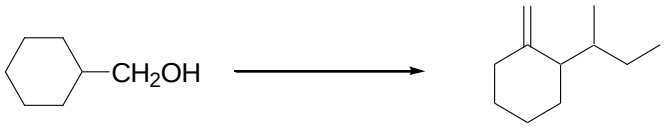
(c) Berikan struktur **B** – **H** dalam tindak balas berikut:

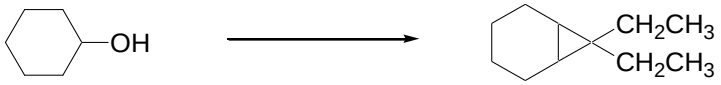


(7 markah)

4. (a) Berikan sintesis berperingkat bagi setiap tindak balas berikut:

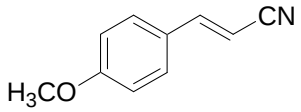
(i) 

(ii) 

(iii) 

(10 markah)

(b) Sebatian **A** seperti yang ditunjukkan di bawah dapat disediakan melalui tindak balas Heck.



A

(i) Apakah bahan pemula yang diperlukan untuk menyediakan sebatian **A**?

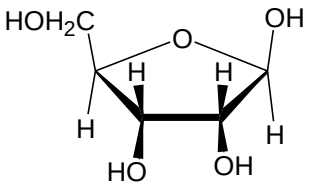
(ii) Berikan mekanisme tindak balas bagi penyediaan sebatian **A**.

(7 markah)

(c) Apakah yang akan berlaku sekiranya suatu alkil halida seperti bromoetana digunakan sebagai halida dalam suatu tindak balas Heck?

(3 markah)

5. (a) Tukarkan projeksi Haworth berikut bagi aldopentosa, **A** kepada bentuk asiklik, **X**.



A

(2 markah)

(b) Struktur asiklik **X** daripada 5(a), mengalami tindak balas di bawah bagi membentuk sebatian **B – G**.

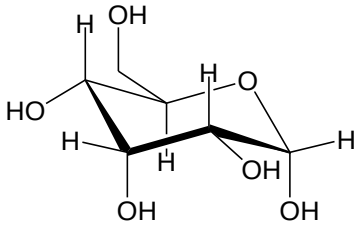
(i) Berikan struktur bagi kesemua sebatian ini.

(ii) Berikan reagen (mengikut tertib) bagi sintesis Killiani-Fischer.

(iii) Apakah reagen yang biasa digunakan dalam degradasi Wohl?

(8 markah)

(c) Struktur α-glukosa dalam konformasi kerusi ditunjukkan di bawah:



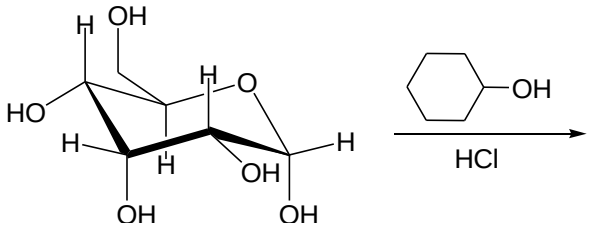
(i) Dua molekul α-glukosa bertindakbalas bagi membentuk suatu disakarida. Lukiskan struktur disakarida ini dengan ikatan α-glukosidik.

(ii) Tindak balas suatu α-glukosa dengan metil iodida dan argentum oksida memberikan hasil **H**. Lukiskan struktur bagi **H**.

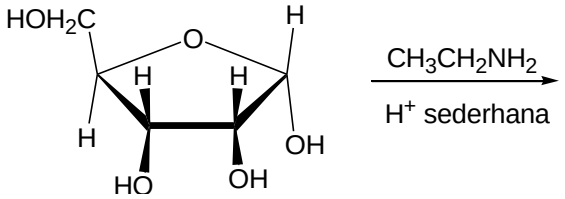
(3 markah)

(d) Lukiskan hasil bagi setiap tindak balas.

(i)



(ii)

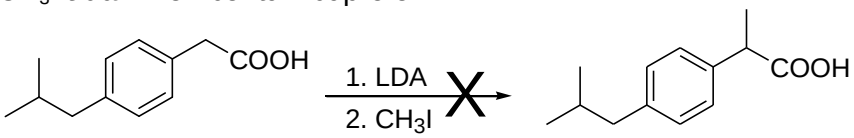


(4 markah)

(e) Apakah perbezaan antara gula penurun dengan gula bukan penurun? Lukiskan satu contoh bagi setiap gula ini.

(3 markah)

6. (a) Pengalkilan terus **A** secara tindak balas dengan satu ekuivalen LDA dan CH_3I **tidak** membentuk ibuprofen.

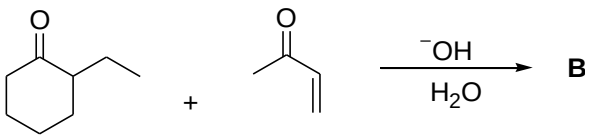


A ibuprofen

Kenalpastikan hasil bagi tindak balas ini dan terangkan bagaimana hasil ini terbentuk.

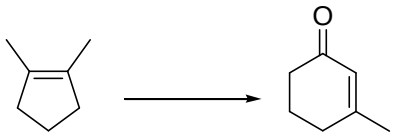
(3 markah)

(b) Dalam mekanisme anulasi Robinson, terdapat tiga langkah bagi pembentukan ikatan C-C dan beberapa langkah pemindahan proton (pemprotonan dan penyahprotonan). Lukiskan tertib mekanisme tindak balas di bawah bagi membentuk sebatian **B**.



(5 markah)

(c) Cadangkan satu sintesis bagi **D** daripada **C**. Tunjukkan kesemua reagen dan bahan perantara.



C **D**

(5 markah)

(d) Lukiskan hasil (**E - I**) yang terbentuk dalam tindak balas di bawah:

(i)

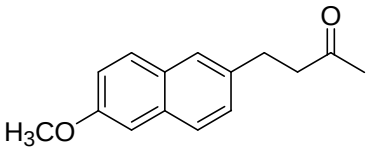
(ii)

(iii)

(iv)

(7 markah)

7. (a) Nabumetone ialah penahan sakit dan agen anti-radang.



Nabumetone

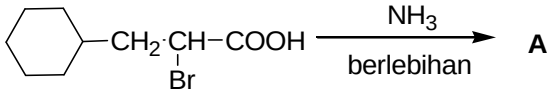
(i) Gunakan sintesis ester asetoasetik bagi menghasilkan Nabumetone.

(ii) Apakah bahan pemula (keton dan alkil halida) yang diperlukan dalam sintesis Nabumetone secara pengalkilan terus enolat.

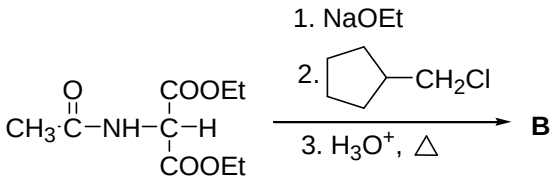
(7 markah)

(b) Berikan struktur bagi **A – C** dalam tindak balas di bawah:

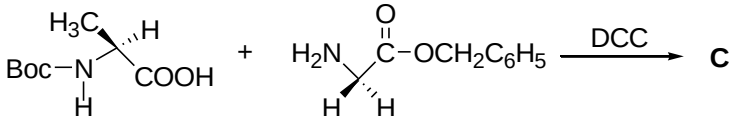
(i)



(ii)



(iii)



(3 markah)

(c) Sintesis Strecker asid amino menukarkan suatu aldehid kepada suatu asid amino, seperti yang ditunjukkan dalam tindak balas di bawah. Tunjukkan tertib mekanisme bagi transformasi ini daripada aldehid kepada α-amino nitril.

α-amino nitril asid amino

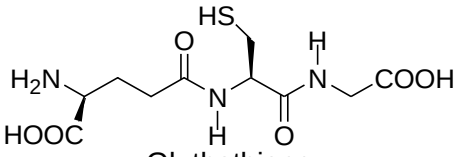
(5 markah)

(d) Berikan tertib asid amino bagi oktapeptida yang mengandungi asid amino Tyr, Ala, Leu (2 ekuivalen), Cys, Gly, Glu dan Val. Hidrolisis separa bagi peptida ini memberikan fragmen berikut:

Val-Cys-Gly-Glu Ala-Leu-Tyr Tyr-Leu-Val-Cys.

(2 markah)

(e) Gluthathione, suatu antioksida yang kuat dan boleh memusnahkan agen pengoksidaan yang bahaya dalam sel, terdiri daripada asid glutamik, sisteina dan glisina mempunyai struktur berikut:



Gluthathione

(i) Apakah hasil yang terbentuk apabila Gluthathione bertindak balas dengan suatu agen pengoksidaan?

(ii) Apakah yang luar biasa tentang ikatan peptida antara asid glutamik dan sisteina?

(3 markah)

-oooOooo-