**Autumn Examinations 2011 / 2012**

Exam Code(s) 3BS  
Exam(s) 3rd year Chemistry  
Module Code(s) CH311 – Organic Chemistry  
Module(s) Chemistry

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**INSTRUCTIONS:** Answer Four questions: one question must be attempted from each section (A, B, C and D)  
Use separate Answer Books for Section A, Section B, Section C and Section D.  
All questions carry 25 marks distributed as shown.  
Leave the front page of the Answer Book blank and clearly list on it the numbers of the questions attempted.

Duration 2hrs  
No. of Pages 7 (including this front page)  
School(s) Chemistry

Requirements None
Section A
Answer either question 1 or 2

1. Answer each of the following:

(i) Identify each of the products A-C from the reactions in Scheme 1. [6 Marks]

\[
\begin{align*}
\text{Me} & \quad \text{Me} & \quad \text{Me} \\
\text{OH} & \quad \text{Me} \\
\text{Me} \\
\end{align*} \\
\text{Ac}_2\text{O, DMAP, CH}_2\text{Cl}_2 \quad \text{product A}
\]

\[
\begin{align*}
\text{Cl} \\
\text{N} \\
\end{align*} \\
\text{PhSH, NEt}_3 \quad \text{product B}
\]

\[
\begin{align*}
\text{HNO}_3, \text{AcOH, Ac}_2\text{O} \\
\end{align*} \\
\text{product C}
\]

Scheme 1

(ii) Give a curly arrow mechanism for the formation of two of the products in Scheme 1. [12 Marks]

(iii) Write notes on the chemistry of indole, include a description of aromaticity, and a reaction scheme with mechanism in your answer. [7 Marks]

2. Answer each of the following:

(i) Write notes on the bonding, geometry and reactivity of imidazole. [6 marks]

(ii) Describe the synthesis of 2-nitroimidazole (azomycin) from imidazole, include reagents, and mechanisms in your answer. [12 marks]

(iii) Draw the \textit{exo} and \textit{endo} Diels-Alder cycloaddition adducts of the reaction between furan and maleic anhydride. Briefly explain why the \textit{exo}-adduct is the major reaction product at higher temperatures. [7 marks]
3. **Answer all parts:**

   (i) Draw a tetrapeptide comprising the four amino acids Thr-Trp-Ile-Thr. Clearly indicate the side chains and the N- and C-termini. **[10 marks]**

   (ii) Define what is meant by the tertiary structure of a protein and explain the contribution of the hydrophobic effect. **[10 marks]**

   (iii) The tetrapeptide Thr-Trp-Ile-Thr is part of an α-helix. Which side chain is most likely to be buried in the protein interior? Explain your answer. **[5 marks]**

4. **Answer all parts:**

   (i) Draw the general structure of a steroid. Name two members of this family and give a biological function for each. **[15 marks]**

   (ii) Protein P is a fatty acid-binding protein. Name and draw the structure of two side chains that will likely contribute to the binding site in protein P. Name and draw a detailed structural diagram of a non-covalent interaction between the polar end of the fatty acid and a polar side chain on the protein. **[10 marks]**
Section C
Answer either question 5 or 6

5. Answer all parts

(a) Explain in detail the relative acidities of A-C. The pK\textsubscript{a} values are provided.

\[
\begin{array}{ccc}
\text{CH}_3\text{NO}_2 & \text{NO}_2\text{CH}_2\text{NO}_2 & \text{CH(NO}_2)_3 \\
A & B & C \\
10.2 & 3.63 & 0.14
\end{array}
\]

[8 marks]

(b) A kinetic isotope effect (KIE) could be used to provide evidence as to whether the elimination reaction of 2-bromo-2-methylpropane proceeds by an E1 or E2 pathway. Explain what is the origin of a KIE. Design the KIE experiment to probe which reaction pathway is preferred. What substrates would be required for the experiment and discuss what the expected outcome of the experiment might be. The E1 and E2 mechanisms are provided to assist you develop your answer.

E1

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{Br} \\
\text{H}_3\text{C} & \quad \text{CH}_3 \\
\text{rate determining step} & \\
\text{H} & \quad \text{CH}_2 \\
\text{H}_3\text{C} & \quad \text{CH}_3
\end{align*}
\]

E2

\[
\begin{align*}
\text{H}_3\text{C} & \quad \text{Br} \\
\text{H}_3\text{C} & \quad \text{H} \\
\text{rate determining step} & \\
\text{H}_3\text{C} & \quad \text{CH}_2 \\
\text{H}_3\text{C} & \quad \text{CH}_3
\end{align*}
\]

[10 marks]
(c) The decomposition of \( \textbf{D} \) in water follows first order kinetics and the half time of the decomposition reaction is \( \sim 24 \) days at \( \text{pH} = 7 \). When the \( \text{pH} \) is increased to 8 the half time reduced to \( \sim 2.4 \) days. Suggest a mechanism for how penicillin decomposes in aqueous solution.

![Chemical structure of \( \textbf{D} \)](image)

6. Answer all parts

(a) Discuss various types of electrostatic interactions (ionic, ion-dipole, dipole-dipole, cation-π) and hydrogen bonding and their roles in formation and stabilisation of protein-ligand complexes. What is the origin of the hydrophobic effect. Use structural diagrams to illustrate your answer showing at least one example of each type of interaction. Why are multiple non covalent interactions needed for molecular recognition events to occur?

(b) Provided below is structural information for a retaining and inverting glucosidase. Show, using structural diagrams, a reaction that is catalysed by glucosidases? Explain why \( \textbf{A} \) is an inhibitor of glucosidases. In your answer discuss the types of interactions that could be important between \( \textbf{A} \) and its target receptor.

![Structural diagrams of retaining and inverting glucosidases](image)

(c) Write a detailed mechanism, using curly arrows, for the acid catalysed hydrolysis of any acetal of your choice. Show all intermediates and include curly arrows in your answer.
Section D
Answer either question 7 or 8

7. Answer all parts

(i) Using examples, explain the difference between an enantioselective and a diastereoselective reaction. [6 marks]

(ii) Using examples, explain the difference between conformational and configurational isomers. [6 marks]

(iii) Explain what is meant by enantiomeric excess and outline two methods by which it can be measured [5 marks]

(iv) Identify the relationship (identical, enantiomers, diastereomers or conformational isomers) between each of the pairs of structures, A - D. In each case the reason for your conclusion should be clearly given:

A

\[ \text{H} \quad \text{H} \quad \text{H} \quad \text{NH}_2 \quad \text{CH}_3 \quad \text{H} \quad \text{H} \quad \text{H}_3\text{C} \]

B

\[ \text{H} \quad \text{H} \quad \text{C} \quad \text{C} \quad \text{CH}_3 \quad \text{H} \quad \text{Br} \quad \text{CH}_3 \quad \text{H} \quad \text{H} \quad \text{H}_3\text{C} \]

C

\[ \text{O} \quad \text{S} \quad \text{Ph} \quad \text{CH}_2\text{CH}_3 \quad \text{O} \quad \text{S} \quad \text{Ph} \quad \text{CH}_2\text{CH}_3 \]

D

\[ \text{Br} \quad \text{Br} \quad \text{OH} \quad \text{H} \quad \text{H} \quad \text{H}_3\text{C} \quad \text{NH}_2 \quad \text{CH}_3 \quad \text{H} \quad \text{H} \quad \text{H}_3\text{C} \]

[4x2 marks]
8. Answer all parts

(i) List any three classes – for example total synthesis - into which organic syntheses can be divided and briefly explain what is involved in each of the classes you list.

[8 marks]

(ii) Using an example in each case, explain what is meant by the following terms: (a) disconnection, (b) synthon, and (c) synthetic equivalent.

[9 marks]

(iii) Draw the structures of molecules which are the synthetic equivalents of each of the following synthons, and for any two give a reaction in which the molecule behaves like that synthon:

[4x2 marks]