Autumn Examinations 2012 / 2013

Exam Code(s) 3BS9; 3BPC
Exam(s) Third Year Science & Third Year Biopharamceutical 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 8 (including this front page)
School(s) Chemistry

Requirements None
Section A
Answer either question 1 or 2

1. Answer each of the following:

(i) Compare and contrast the influence of the heteroatom in pyrrole, furan and thiophene on (a) the electronic structure of these molecules (b) their reactivity. In your answer clearly indicate (with reasoning) the most favoured position for electrophilic aromatic substitution.

[12 marks]

(ii) Describe a concise synthesis for any two of molecules (A), (B) or (C) starting from 2-chloropyridine, thiophene and imidazole respectively. Provide a mechanism for the aromatic substitution reaction.

[13 marks]

2. Answer each of the following:

(i) Alkyne (D) was used to trap unstable thiophene sulfone as Diels-Alder adduct (E), as shown in Scheme 1. Cycloaddition adduct (E) readily lost SO₂ to give bicyclic product (F) in 68% yield. Give chemical structures for (D) and (E) and a mechanistic explanation (using curly arrows) for the formation of (E) and (F). Briefly explain why thiophene cannot undergo the Diels-Alder reaction.

[12.5 marks]

(ii) Draw all possible isomeric diazoles and triazoles. Name all molecules and draw their NH-tautomers (where possible). Rationalise the acidity of tetrazole using resonance structures, and briefly explain its use in drug discovery.

[12.5 marks]
Section B
Answer either question 3 or 4

3. Answer each of the following:

(i) Draw a tripeptide comprising one example of each of the following amino acid types:
   - Aliphatic
   - Positively charged
   - Sulfur containing
   Indicate the N- and C-termini and give the name of each of the chosen amino acids.
   [8 marks]

(ii) Discuss the statement: In protein structure, all combinations of the dihedral angles $\phi$ and $\psi$ are allowed. Illustrate your answer with a sketch of a Ramachandran plot.
   [8 marks]

(iii) Draw a detailed structural diagram of a salt bridge between side chains containing a carboxylate and an amino group.
   [4 marks]

(iv) Explain what is meant by isoelectric point ($pI$). Give representative $pI$ values for an acidic protein and a basic protein, respectively.
   [5 marks]

4. Answer each of the following:

(i) What does the term “amphipathic” mean? Name a representative amphipathic molecule and explain why it is essential for living systems.
   [5 marks]

(ii) Draw the general structure of cholesterol and list two of its biological functions.
   [5 marks]

(iii) Describe the contrasting solubility of glucose and cholesterol in the cell, naming a specific environment where each molecule is likely to be encountered.
   [5 marks]

(iv) Protein P is a glucose-binding protein. Name and draw the structure of two polar/neutral side chains that will likely contribute to the binding site. Name and draw a detailed structural diagram of a non-covalent interaction between glucose and one of these side chains.
   [10 marks]
Section C

Answer either question 5 or 6

5. Answer each of the following:

(i) Define $pK_a$ and explain why $pK_a$ values are measured. The $pK_a$ of methane is near 45, acetonitrile's $pK_a$ is 25.0 whereas that of dicyanomethane (malonitrile) is 11.2 and tricyanomethane is 5.1. Why does the addition of each cyano group lower the $pK_a$?  
[7 marks]

(ii) One reason used to explain why cyclohexanol is less acidic than phenol resides in a resonance analysis. Give another explanation as to why phenol is more acidic?  
[4 marks]

(iii) Explain how a Hammet plot study of the following reaction might be carried out. Would a negative or positive $\rho$ value be expected?

![Reaction Scheme]

[6 marks]

(iv) If $C_6D_6$ was used instead of benzene in the above reaction would a difference in the rate of reaction be observed? Explain your answer.  
[2 marks]

(v) Give mechanisms for the formation of products from the following reaction.

![Reaction Scheme]

[6 marks]
6. Answer each of the following:

(i) Draw an electron pushing mechanism (curly arrow mechanism) for the H$_3$O$^+$ catalysed tautomerisation of acetone (CH$_3$COCH$_3$) in water. [5 marks]

(ii) The structures of ‘keto’ compounds A-E are shown. The equilibrium constants for tautomerisation of A-E to enols are also included. Draw the enols and state if the ‘keto’ or ‘enol’ form is preferred in each case. Give reasons for the differences in $K$ between A and B and between D and E.

(iii) Draw an electron pushing mechanism for the conversion of F to G. [9 marks]

(iv) During the S$_N$1 solvolysis of allyl chloride some scrambling of the position of the chloride occurs as shown by $^{13}$C labelling. Give the mechanism for the reaction, and explain why the extent of scrambling is not dependent on the concentration of added chloride salts. [5 marks]
Section D
Answer either question 7 or 8

7. Answer each of the following:

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

(ii) Pure (R)-(−)-2-pentanol can be purchased from a particular chemical supplier at a price of €110 for 1 ml; the \([\alpha]_D^{20}\) (neat) is given as −13.5°.

(a) What information is provided by (i) the descriptor “(R)”, and (ii) the descriptor “(−)”?

**[3 marks]**

(b) What additional information is provided by the fact that “(R)” and “(−)” are used together in describing this 2-pentanol?

**[2 marks]**

(c) A sample of 2-pentanol is prepared in the laboratory and its \([\alpha]_D^{20}\) is found to be −6.5°. In view of the information provided above for the commercial sample, what does the \([\alpha]_D^{20}\) value indicate about the sample prepared in the laboratory.

**[2 marks]**

(iii) The resolution of a racemic mixture is an important process in the pharmaceutical industry. Explain in general terms what this process involves and outline any method by which a racemic mixture of the following amine could, at least in principle, be resolved

![Chemical Structure](image)

**[6 marks]**

(iv) Explain what is meant by the term “chiral pool” and explain why the “chiral pool” is important in terms of asymmetric synthesis.

**[6 marks]**

8. Answer each of the following:

(i) Outline the retrosynthetic analysis of a molecule of your choice and use it to explain what is meant by the following terms: (a) disconnection, (b) synthon, and (c) synthetic equivalent. **[9 marks]**

(ii) Explain why methods for the synthesis of six-membered carbocyclic rings are particularly important in the context of organic synthesis. Using examples, outline any two **methods** by which the synthesis of a six-membered carbocyclic ring can be achieved. **[8 marks]**
(iii) (a) Using an example, explain why, and how, a protecting group would be used in synthesizing a molecule.

(b) Explain why the following transformation could not be carried out as written, and suggest how it could be achieved.

\[
\text{O} \quad \text{O} \\
\text{OCH}_2\text{CH}_3 \\
\text{CO} \\
\text{OCH}_2\text{CH}_3 \\
\text{O} \\
\text{H}_3\text{C} \\
\text{H}_3\text{C-MgBr} \\
\text{O} \\
\text{H}_3\text{C} \\
\text{H}_3\text{C} \\
\text{OH}
\]

[8 marks]