

UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES DEPARTMENT OF PHARMACY

FIRST BPHARM PART II EXAMINATION – AUGUST 2022 PH 1213 PHARMACEUTICAL CHEMISTRY II (SEQ) – REVISED SYLLABUS

TIME: THREE HOURS

INSTRUCTIONS

- There are six questions in parts A and B in this paper.
- Answer all questions.
- No paper should be removed from the examination hall.
- Do not use any correction fluid.

PART A

01.

1.1 Consider the reaction of 2-bromo-2-methylpropane with water:

$$\rightarrow$$
Br H_2O \rightarrow OH + HBr

- 1.1.1 Write down the mechanism of the reaction and explain what would happen to the rate of the reaction under the following conditions. (30 marks)
 - a. Increasing the concentration of the water
 - b. Decreasing the concentration of alkyl halide
 - c. Changing the leaving group to either Cl or I
- 1.1.2 What difference(s) would you expect if the starting compound is 2-bromopropane? (10 marks)
- 1.2 Predict the major product(s) of the following reactions. Specify whether the reactions are SN_1 , SN_2 , E_1 or E_2 and explain your answer briefly. (40 marks)

1.2.4
$$\begin{array}{c} \text{SH} \\ \hline \text{(i) NaH} \\ \hline \text{(ii) CH}_{3}\text{I} \\ \end{array}$$
 1.2.5
$$\begin{array}{c} \text{Conc HBr (2.1 equiv)} \\ \hline \Delta \\ \end{array}$$

1.3 Giving a mechanism, complete the following reaction by drawing the intermediate charged substitution product, X and the neutral/charged final organic products P. The mechanisms for both steps are required. (20 marks)

$$\begin{array}{c|c}
 & & \\
 & & \\
\hline
 & &$$

02.

2.1 The following reaction produced **only one** product **A**. Draw the intermediates that would yield each product and explain why **B** is not observed. (15 marks)

2.2 Pyridine N-oxide is more activated for electrophilic and nucleophilic attack at both positions C-2 and C-4 than pyridine itself. Draw all the resonance forms for pyridine N-oxide to show this observation. (15 marks)

2.3 Using the Hückel rule, determine whether the following molecules are aromatic or not.

(20 marks)

$$H_{Si}$$
 H_{P} O_{-N} O_{N} $O_$

2.4 Draw the structure(s) of the major product(s) of following substitution reactions.

Give a brief explanation for your answers.

(50 marks)

$$\begin{array}{c|c}
\hline
\text{Cl}_2 \\
\hline
\text{AlCl}_3
\end{array}$$

2.4.2
$$\frac{\text{HNO}_3}{\text{OCH}_3}$$

03.3.1 Draw the structure(s) of the major product(s) of following substitution reactions.

(40 marks)

3.1.3 COOH
$$H_2SO_4$$

3.1.4
$$CH_3COCI$$
AlCl₃, < 0 ^{0}C

3.2 Starting from benzene, show a reaction sequence that could be used to prepare the following compound, 1-Fluoro-2,4-dinitrobenzene (commonly called Sanger's reagent) which is used for sequencing proteins.

(30 marks)

3.3 Write down the appropriate chemical reagents (A, B, C, and D) for the transformations given below and draw the structure of NBS. (30 marks)

04.

- 4.1 Explain the following.
 - 4.1.1 Furan (32 °C) has lower boiling point than pyrrole (126 °C). (10 marks)
 - 4.1.2 Pyridine reacts with methyl iodide to provide a salt but pyrrole does not react. Provide two possible reasons for this reactivity. (15 marks)

$$\begin{array}{c|c} & CH_3I \\ \hline \\ N \\ \hline \\ N \\ H \\ \end{array}$$

$$\begin{array}{c|c} CH_3I \\ \hline \\ N \\ I \\ \end{array}$$

$$\begin{array}{c|c} (\text{not formed}) \\ \hline \end{array}$$

4.2 In the presence of a base/Lewis acid, 4-methylpyridine reacts with benzaldehyde in the condensation reaction shown below:

(i) NaOH (ii) PhCHO,
$$\Delta$$

- 4.2.1 Propose a reasonable mechanism for the formation of the product above. (15 marks)
- 4.2.2 Under the same condition, 3-methylpyridine does not react with benzaldehyde in the condensation reaction. Explain this difference in reactivity. (05 marks)
- 4.2.3 Would you expect 2-methylpyridine to react with benzaldehyde under these conditions? Explain. (05 marks)
- 4.3 Predict the product expected from each of the following reactions. (50 marks)

4.3.2 (i) HCN, HCI (ii)
$$H_2O$$

$$4.3.3 \qquad \begin{array}{c} & \begin{array}{c} & \text{CH}_3\text{CO}_2\text{NO}_2\\ \hline & \text{(CH}_3\text{CO)}_2\text{O} \end{array}$$

4.3.4
$$N_{\text{Ph}}$$
 $nBuLi, CH_3I$

4.3.5
$$\frac{\text{Br}_2}{\text{Dioxane, } 0^{\circ}\text{C}}$$

05.

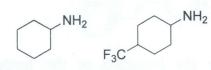
5.1

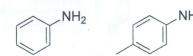
5.1.1 Show the structures of species **X** and **Y** in the following acid-base reactions and predict which side of the equilibrium is favored. (10 marks)

5.1.2 Arrange the following compounds in order of increasing acidity. (15 marks)

5.1.3 Arrange the following compounds in order of increasing basicity.

(15 marks)



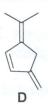


5.2 Methyl protons of one of the compounds (A-D) is more acidic than others. Indicate that one and explain its high acidity. (10 marks)









PART B

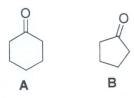
5.3 Draw the major products of following reactions.

(50 marks)

06.

6.1

6.1.1 Draw the structures of possible aldol condensation products from a mixture of cyclohexanone (A) and cyclopentanone (B). (20 marks)



- 6.1.2 Draw the mechanism showing correct arrow pushing for the formation of one of the products that you have drawn under part 6.1.1. (20 marks)
- 6.2 Identify the major and minor products expected from the following reaction. Briefly explain your answer using the mechanism for formation of the electrophile.

 (30 marks)

6.3 Benzaldehyde undergoes disproportionation reaction when heated with a base. Draw the structures of the products and the mechanism. (30 marks)