



UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES

DEPARTMENT OF PHARMACY

FIRST BPHARM PART II EXAMINATION – JANUARY 2019

PH 1213 PHARMACEUTICAL CHEMISTRY II (SEO)

TIME: THREE HOURS

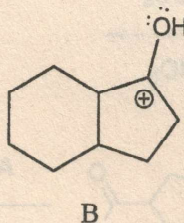
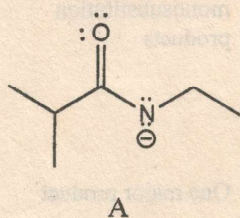
INSTRUCTIONS

- There are six questions (06) 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.
- Use illustrations where necessary.

Part A

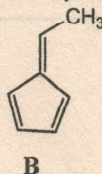
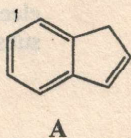
01. Answer all parts.

1.1 Draw a second resonance form for each of the following structures and indicate which resonance form is more stable in each case.



(30 marks)

1.2 Consider the following molecules: indene (A) and 5-ethylidenecyclopenta-1,3-diene (B).



1.2.1 Indicate which is (are) the most acidic proton(s) of each of the molecules A and B.

(10 marks)

1.2.2 Would there be any special stability associated with the anion (conjugate base) formed by the most acidic proton indicated in 1.2.1? Explain.

(20 marks)

1.3 Draw the structures and number the rings of the following polyaromatic hydrocarbons.

1.3.1 Naphthalene

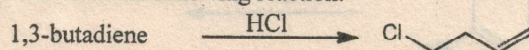
1.3.2 Anthracene

(10 marks)

1.4 Explain the reasons for the frequent electrophilic substitution at C-1 (alpha) position of naphthalene.

(10 marks)

1.5. The reaction of 1,3 butadiene and HCl gives no products resulting from addition of a proton to C-2 carbon as shown in the following reaction:



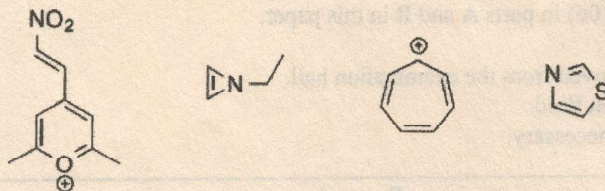
Account for this occurrence in terms of the stability of the expected intermediate carbonium ion and give the structures of the products formed.

(20 marks)

02. Answer all parts.

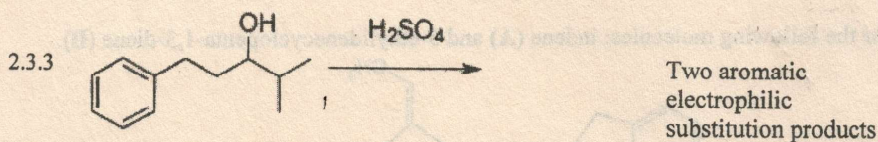
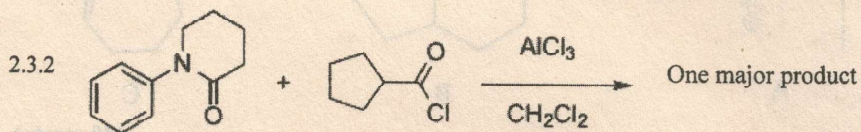
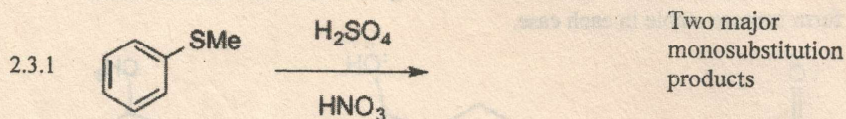
2.1 Draw the structure of the product of the FeBr_3 -catalyzed monobromination of benzene formed by electrophilic aromatic substitution and draw the structure that would be obtained if Br_2 were added to benzene (as with alkenes). Explain why substitution happens while addition does not. (20 marks)

2.2 Using the Hückel rules, briefly explain whether each of the following compounds is aromatic, antiaromatic, or non-aromatic.



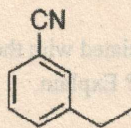
(25 marks)

2.3 Predict the major products of the following three reactions:



(25 marks)

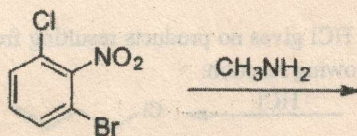
2.4 Propose a reasonable synthesis of 3-ethylbenzonitrile starting from benzene and any other inorganic or organic reagent with two or less carbon atoms.



3-ethylbenzonitrile

(15 marks)

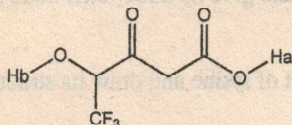
2.5 Identify the products of the following reaction. Draw a detailed mechanism that leads to the major product. Clearly indicate resonance structures, and charges in the intermediates.



(15 marks)

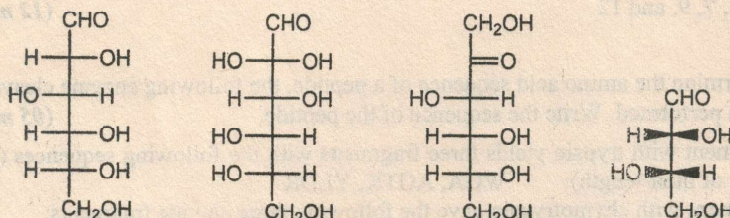
03. Answer all parts

3.1 Determine which proton (H_a or H_b) of the following molecule is more acidic and give reason(s) for your answer.



(10 marks)

3.2 Consider the following carbohydrates.



3.2.1 Give their common names.

(08 marks)

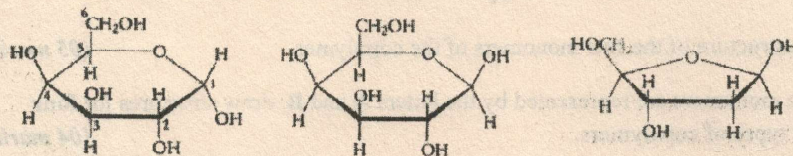
3.2.2 Identify them as D- or L- monosaccharides.

(08 marks)

3.2.3 Draw the Harworth projection formula (α -form) for the above three C-6 sugars.

(09 marks)

3.3. Identify the following as the α or β anomer:



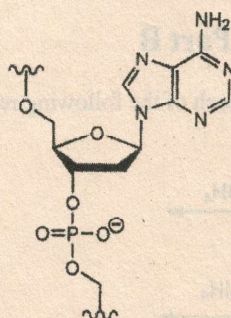
(A)

(B)

(C)

(25 marks)

3.4 A generic structure of an adenine nucleotide in a DNA strand is shown below:



3.4.1 Number the purine ring and the sugar unit.

(05 marks)

3.4.2 Name the two important bonds found in the sugar unit of this strand.

(10 marks)

3.4.3 Draw one change to that structure which is found in part of a RNA strand.

(10 marks)

3.4.4 This change makes RNA susceptible to undergo intramolecular cleavage more rapidly than DNA. Draw the cyclic phosphate generated by RNA strand cleavage at $pH = 7$.

(15 marks)

04. Answer all parts.

4.1 The amino acid lysine has three pKa values; pK₁ 2.18, pK₂ 8.95, pK₃ or pK_R 10.79.

4.1.1 Draw the structure of lysine and give its three-letter code and one-letter code.

(08 marks)

4.1.2 Calculate the isoelectric point of lysine and draw its structure at the isoelectric point.

(10 marks)

4.1.3 In what direction (toward the cathode, toward the anode or does not move) does the amino acid lysine move under an electric field at the following pH values?

pH 1, 3, 5, 7, 9, and 12

(12 marks)

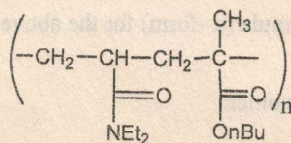
4.2 In order to determine the amino acid sequence of a peptide, the following enzyme cleavage steps have been performed. Write the sequence of the peptide.

(05 marks)

Step 1. Treatment with trypsin yields three fragments with the following sequences (in the order of their length): WGA, AGTK, YLDR

Step 2. Treatment with chymotrypsin gave the following three peptide fragments: GA, LDRW, AGTKY.

4.3 Repeating unit of a copolymer is shown below:



4.3.1 Draw the structure of the **two** monomers of the copolymer.

(05 marks)

4.3.2 If the two monomers are represented by the letters **A** and **B**, draw structures for **four** possible types of copolymers.

(04 marks)

4.3.3 What are the **three** primary mechanisms by which drugs can be released from a polymeric delivery system?

(06 marks)

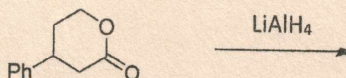
Part B

4.4. What products could be obtained from each of the following reactions?

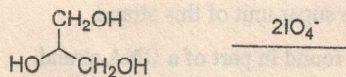
4.4.1.



4.4.2.



4.4.3.



(15 marks)

4.5. An alkene gave formaldehyde and 4, 4-dimethyl-2-pentanone on ozonolysis.

4.5.1. Identify the alkene.

(05 marks)

4.5.2. If regioisomer of this alkene gave acetone as one of the products on ozonolysis, identify the isomeric alkene and the other product.

(10 marks)

- 4.6. The two alkenes 2,3,3-trimethyl-1-butene and 1-octene were each subjected to allylic bromination with N-bromosuccinimide. One of these alkenes yielded a single allylic bromide, whereas the other gave a mixture of two constitutionally isomeric allylic bromides. Match the chemical behavior to the correct alkene and give the structure of the allylic bromide(s) formed from each. (20 marks)

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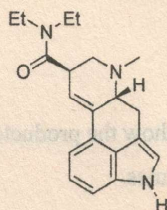
05. Answer all parts

- 5.1. Among the un-substituted five membered heterocyclic compounds, pyrrole shows relatively higher boiling point. Briefly explain the reason. (10 marks)

- 5.2. Arrange the following bases in the order of increasing basicity. (10 marks)

3-methylpyridine, trimethylamine, 3-nitropyridine, pyridine, ammonia

- 5.3. Structure of the hallucinogenic compound lysergic acid diethylamide is shown below.

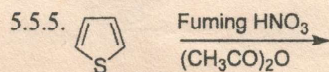
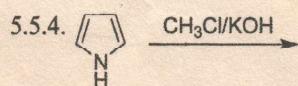
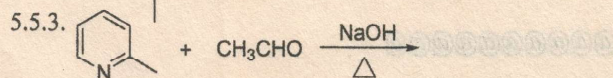
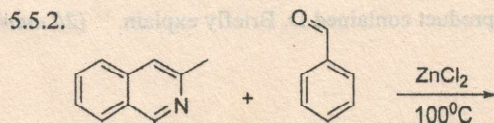
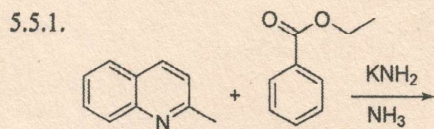


- 5.3.1. Identify the aromatic heterocyclic nucleus present in the molecule. (05 marks)

- 5.3.2. Briefly explain the orbital structure of the heterocycle that you identified above. (30 marks)

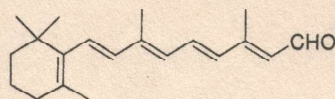
- 5.4. Histidine is one of the important amino acid residues found in the catalytic triad of enzyme chymotrypsin. Using a suitable diagram, briefly explain its mechanism in the cleavage of peptide bonds. (20 marks)

- 5.5. What product(s) would you expect from the following reactions? (25 marks)



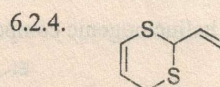
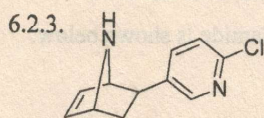
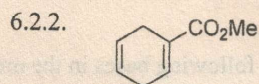
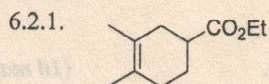
06. Answer all parts

6.1. β -Carotene is synthesized by the Wittig reaction using retinal (shown below) as one of the starting materials. Using a suitable reaction mechanism, show how you would synthesize β -carotene. (20 marks)

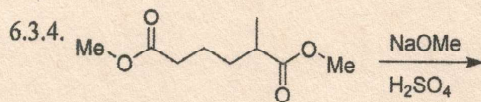
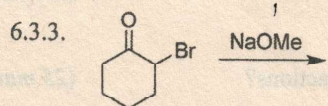
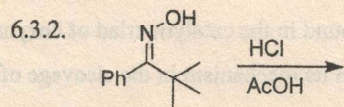
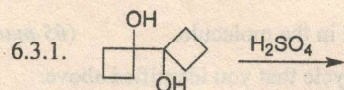


retinal

6.2. Draw the structures of dienes and dienophiles involved in the formation of the following products. (20 marks)



6.3. Using suitable reaction mechanisms, show the product(s) you would obtain from the rearrangement of the following molecules. (40 marks)



6.4. When benzaldehyde is treated with NaOH in H_2O , two products are formed. Similarly, when the reaction is carried out in D_2O only one product contained D. Briefly explain. (20 marks)

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