(109)

UNIVERSITY OF RUHUNA – FACULTY OF MEDICINE

ALLIED HEALTH SCIENCES DEGREE PROGRAMME

FIRST BPHARM PART II EXAMINATION - MARCH 2012

PH 1213 - PHARMACEUTICAL CHEMISTRY II

DATE: 19/03/2012

THREE (03) HOURS

INDEX NO: .....

- *Answer* **only six (06)** *questions on this paper itself*
- *Write your answer in the space provided for each question, Please note that the space provided is sufficient for the answer and that extensive answers are not expected*

For Examiner's Use Only

Question No	Marks
01	
02	
03	
04	
05	
06	
07	
08	
09	
Total	
Percentage	

01. Answer **all** parts

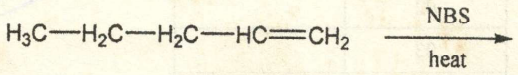
1.1.1 State the difference between a localized double bond and a conjugated double bond. Give their appropriate structures.

(08 marks)

1.1.2 Which one of the above two is more stable? Justify your answer giving necessary structures.

(08 marks)

1.1.3 What are the possible products of the following reaction?



(08 marks)

1.1.4 Draw the structure of the intermediates formed in the above reaction

(08 marks)

(110)

1.1.5 Discuss the stability of the proposed intermediates above.

(08 marks)

1.1.6 Consider the two reactions given below:

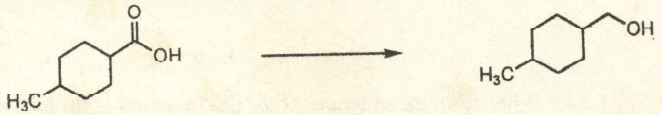
$H_2C{=}CHCH_2{-}Cl \xrightarrow{C_2H_5OH} H_2C{=}CHCH_2{-}OCH_2CH_3$

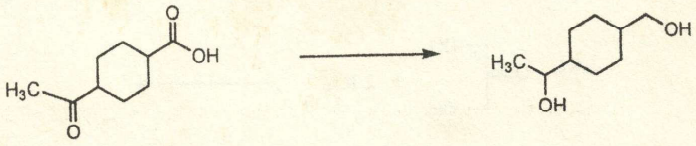
$CH_3CH_2{-}Cl \xrightarrow{C_2H_5OH}$ no reaction

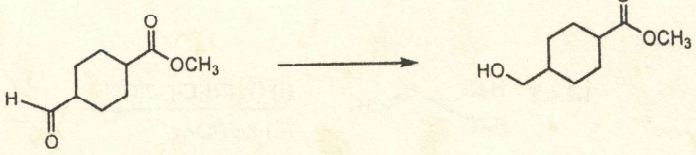
Justify the above observations.

(10 marks)

1.2.1 You are provided with the reducing agents, $LiAlH_4$ and $NaBH_4$. Select the most suitable one to carry out the following transformations:

1.2.1.1 

1.2.1.2 

1.2.1.3 

(05 x 3 marks)

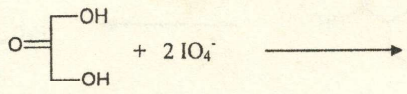
1.2.2 Write down the reaction scheme for the synthesis of alkynes via vicinal dihalides.

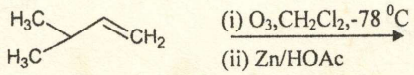
(15 marks)

1.2.3 Briefly explain the mechanism involved in the reduction of carbonyl compounds using sodium borohydride.

(10 marks)

1.2.4 Write down the structures of the final products of the following reactions:

1.2.4.1 

1.2.4.2 

(10 marks)

(111)

02. Answer **all** parts

2.1 Explain the stability of benzene using the theory of resonance

(10 marks)

2.2 The [10] annulene shown below is **not** aromatic.

2.2.1 Explain why the above compound is not planar

2.2.2 How does the planarity of a compound affect its aromaticity?

2.2.3 State a structural modification that you would propose to convert the above compound to an aromatic one.

(25 marks)

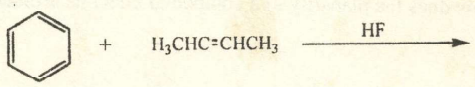
2.3 "Although cyclopentadiene is a hydrocarbon it shows acidity, and can be easily deprotonated using strong bases".

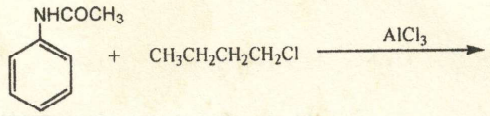
2.3.1 Discuss the above statement using appropriate structures.

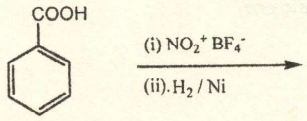
2.3.2 State the structural modification necessary to increase the acidity of cyclopentadiene.

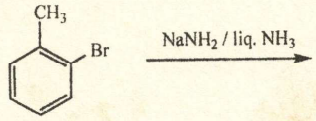
(25 marks)

2.4 Write down the products you expect from the following reactions?

2.4.1 

2.4.2 

2.4.3 

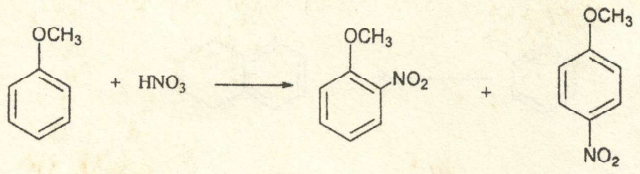
2.4.4 

(40 marks)

(1/2)

03. Answer **all** parts

3.1 The nitration of anisole takes place under mild nitration conditions with HNO_3.



anisole

44 %
o-nitroanisole

55%
p-nitroanisole

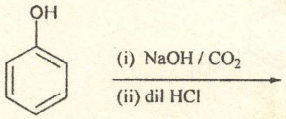
3.1.1 Explain the above observation.

(15 marks)

3.1.2 Above reaction is 10,000 times faster than that of benzene and gives only ortho and para products. Considering the stability of the intermediates formed, explain these observations briefly.

(20 marks)

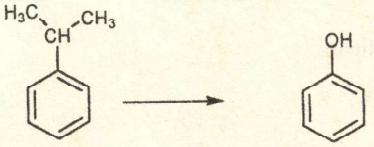
3.2 Giving plausible mechanism, predict the product(s) of the following reaction

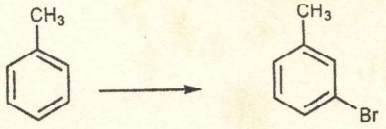


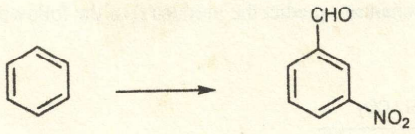
(25 marks)

3.3 Giving necessary reagents, reaction conditions and intermediates formed; show how you would carry out following conversions.

3.3.1 

3.3.2 

3.3.3 

3.3.4 

(10 x 4 marks)

113

04. Answer **all** parts

4.1. Identify the most acidic proton in each of the following compounds and suggest a reason for the trend in acidity.

PhH ($K_a = 10^{-45}$) Ph_2CH_2 ($K_a = 10^{-34}$) Ph_3CH($K_a = 10^{-32}$)

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(15 marks)

4.2. Rank the following compounds in order of increasing basicity. Justify your answer

$PhNH_2$, Ph_2NH, Ph_3N

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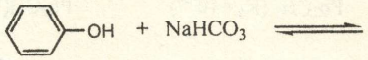
(15 marks)

4.3. Complete the following acid base reactions and predict the direction of equilibrium (to the **right** or **left)** for each. pK_q values of phenol, carbonic acid, and triethyl ammonium ion are 9.95, 6.36, and 10.75, respectively.

4.3.1  + $NaHCO_3$ ⇌

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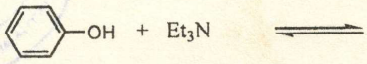
4.3.2  + Et_3N ⇌

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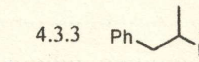
4.3.3  + $NaHCO_3$ ⇌

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(10 x 3 marks)

4.4 *pKa* values of some common drugs are given in the following table: Give the pH required to ionize approximately 99.9% of each drug

Drug	**pKa value**	**pH required for 99.9% ionization**
Acidic drugs		
Aspirin	3.5	
Paracetamol	9.5	
Basic drugs		
Diazepam	3.3	
Diphenhyramine	9.0	

(15 marks)

(114)

4.5 Name three polycyclic aromatic hydrocarbons.

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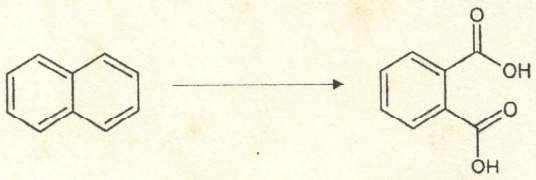
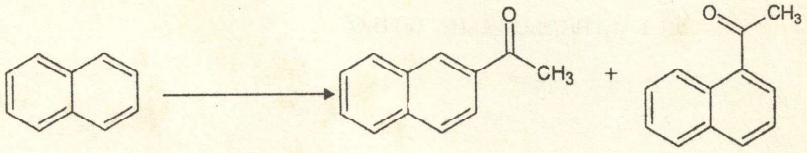
(05 marks)

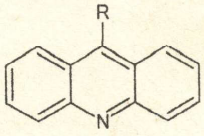
4.6 How you would do the following conversions.

4.6.1 

4.6.2 

(10 marks)

4.7 Show how you would synthesize the following compound.



(10 marks)

05. Answer **all** parts

5.1 Write the structural formulas for the products formed when **propanal** reacts with each of the following reagents.

5.1.1 $LiAlH_4$, then H_2O

5.1.2 $(C_6H_5)_3\ P^+ : {}^-CHCH_3$

5.1.3 (i) $BrCH_2CO_2C_2H_5$ (ii) H_3O^+

5.1.4 $Ph\ NHNH_2$

5.1.5 CH_3CH_2CHO/OH^-

(10 x 5 marks)

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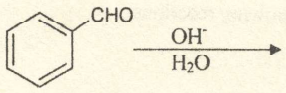
5.2.1 What products you would expect from the following reaction?



(10 marks)

5.2.2 When the reaction is carried out in $\mathbf{D_2O}$, only one product contains **D**. Explain this behavior.

(20 marks)

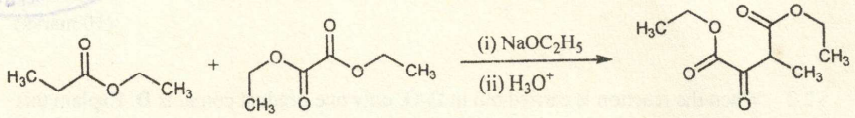
5.2.3 When $(CH_3)_2CHCHO$ and $Ba(OH)_2/H_2O$ are heated in a sealed tube, the reaction produces only $(CH_3)_2CHCH_2OH$ and $((CH_3)_2CHCO_2)_2Ba$. Provide an explanation for the formation of these products instead of those expected from an aldol reaction.

(20 marks)

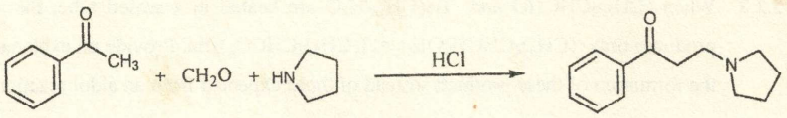
06. Answer **all** parts

6.1 Write the mechanisms for the following reactions.

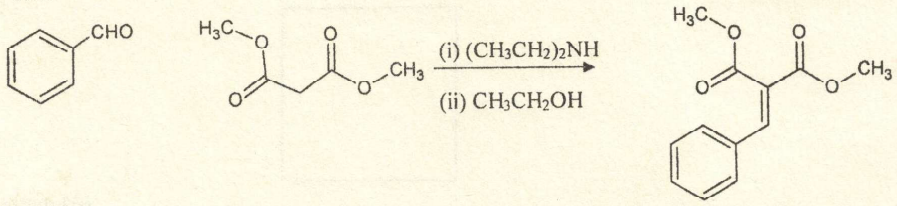
6.1.1



6.1.2



6.1.3

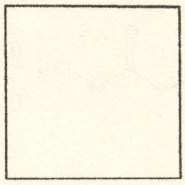


(10 x 3 marks)

6.2. Outline the **Perkin condensation** that takes place when benzaldehyde reacts with acetic anhydride in the presence of potassium acetate.

(20 marks)

6.3. Draw the general formula of an α-amino acid.



(04 marks)

6.4.1. Give the names of **two** basic and acidic amino acids each.

6.4.2. Write three-letter code and one-letter code of each of the above amino acids.

	Basic			Acidic			
6.4.1	.....	.....		.....	.....		
6.4.2	.....	.....	.....	.....	.....	.....	.....	.....

(08x2 marks)

6.5 List **three** properties of a peptide group (CONH).

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(06 marks)

6.6 Name **two** methods that are used to identify N-terminal of peptides.

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(06 marks)

6.7 Derive the product(s) of the octapeptide (Gly-Arg-Tyr-Met-Lys-Ala-Thr-Ala) by the treatment with

6.7.1. Trypsine 6.7.2. Chymotrypsine 6.7.3. CNBr

6.7.1.....

6.7.2.....

6.7.3 .....

(18 marks)

07. Answer **all** parts

7.1 Comment on the following statements.

7.1.1. "Pyrrole is aromatic, but resembles towards more reactive benzene derivatives (*e.g.* phenol) in its reactivity".

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7.1.2. Pyridine undergoes electrophilic substitution reactions slower than benzene.

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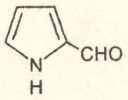
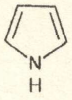
(10 x 2 marks)

7.2 How would you synthesize

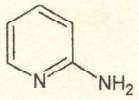
7.2.1



from



7.2.2



from

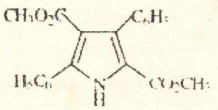
(10 x 2 marks)

7.3 Briefly explain the orbital structure of pyrrole.

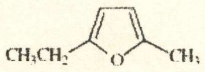
(20 marks)

7.4 Show how you would synthesize the following compounds.

7.4.1



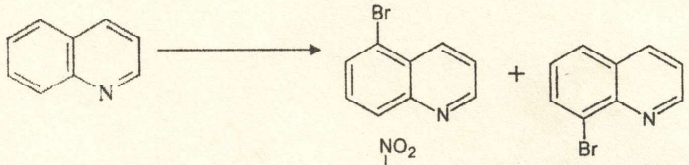
7.4.2

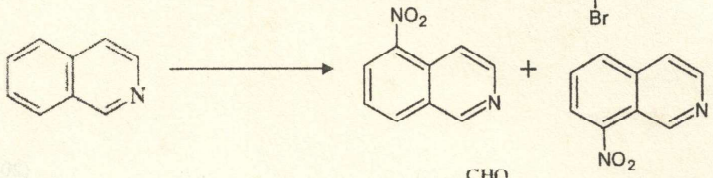


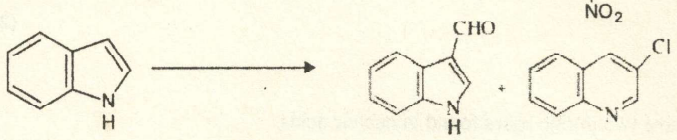
(20 x 2 marks)

08. Answer **all** parts

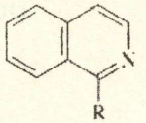
8.1 Write down the necessary reagents and conditions for the following conversion.

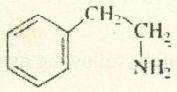
8.1.1 

8.1.2 

8.1.3 

(03 x 5 marks)

8.2 How would you synthesize 

from 

(30 marks)

8.3 Briefly explain the **tautomerism** in "imidazole".

Hint: 4(5)-methylimidazole

(20 marks)

8.4 Name two purine bases found in nucleic acids.

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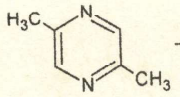
(10 marks)

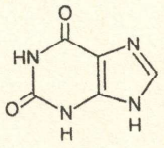
8.5 Write down the final products of the following reactions.

8.5.1 

H_2O_2, AcOH, 60 ^{0}C

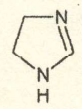
8.5.2 

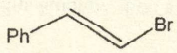
$Et_3O^+BF_4^-$,
$Cl(CH_2)_2Cl$, Reflux

8.5.3 

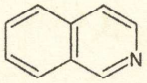
100% HNO_3,
AcOH, 120^{0}C

119

8.5.4 



Cu_2O, Cs_2CO_3,
MeCN, L, 130 ^{0}C
AcOH, 120 ^{0}C

8.5.5 

alk.$KMnO_4$

(05 x 5 marks)

09. Answer **all** parts

9.1 Give the structure for aldose and ketose.

(04 marks)

9.2 List two biological importance of glucose

(02 marks)

9.3 What is mutarotation

(03 marks)

9.4 Explain the chemistry behind mutarotaion

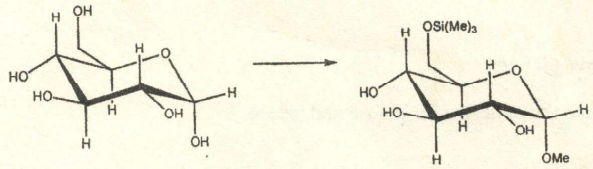
(06 marks)

9.5 Glucose is a reducing sugar whereas sucrose is a non-reducing sugar. Using appropriate structures, justify this difference.

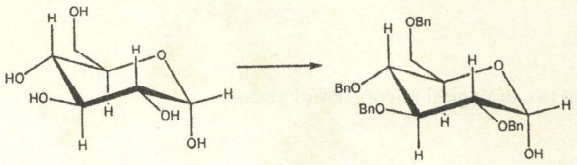
(06 marks)

9.6 How you would carry out following conversions of sugars

9.6.1

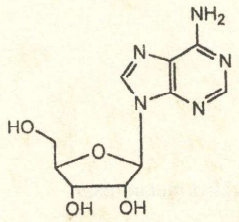


9.6.2



(04 marks)

9.7. The structure of *adenosine*, a principal nucleoside obtained for RNA is shown below:



9.7.1 number the purine ring

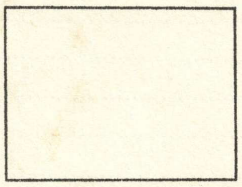
9.7.2 number the sugar unit

9.7.3 indicate the N-glycosidic bond

(10 marks)

120

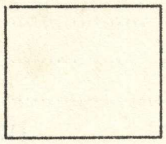
9.8 Adenosine 3'-5'-cyclic monophosphate (*cyclic AMP*) is an important regulator of a large number of biological processes. Draw its structure.



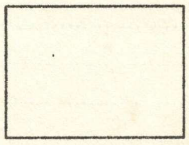
(06 marks)

9.9 Write a structural formula for each of the following drugs

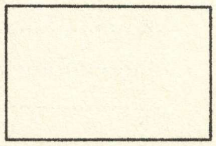
9.9.1. 5-Fluorouracil (used in cancer chemotherapy)
9.9.2. 6-mercaptopurine (used for the treatment of acute leukemia)
9.9.3. 6-thioguanine (used for the treatment of acute leukemia)



9.9.1



9.9.2



9.9.3

(03 x 3 marks)

9.10. "When oil is used for edible purpose (in frying) it should not be used for several times". Identify the scientific reason behind this statement.

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(10 marks)

9.11. What are the analytical tests carried out in quality control of fats and oil?

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(10 marks)

9.12 List the characteristics of an ideal polymer that can be used for drug delivery

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(10 marks)

9.13. Identify the areas of application of polymers in pharmaceutical field.

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(10 marks)

9.14. Synthetic biodegradable polymers are preferred over natural biodegradable polymers in drug delivery; justify.

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(10 marks)

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