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Index no:.....

UNIVERSITY OF RUHUNA – FACULTY OF ALLIED HEALTH SCIENCES

DEPARTMENT OF PHARMACY

FIRST BPHARM PART II EXAMINATION - JANUARY 2018

PH 1213 PHARMACEUTICAL CHEMISTRY II (SEQ)

TIME: THREE HOURS

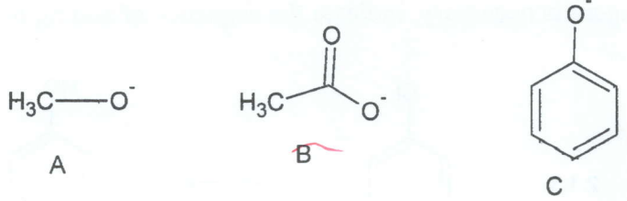
INSTRUCTIONS

- There are **six** (**06**) questions in Parts A, B, C, D and E of the SEQ paper.
- Answer **each** part in separate booklet provided.
- No paper should be removed from the examination hall.
- Do not use any correction fluid.
- Use illustrations where necessary.

PART A

1. Answer all parts

1.1 Giving appropriate structures and reasons, rank the following three organic anions **A**, **B** and **C**, in the order of **decreasing** stability. (***30 marks***)



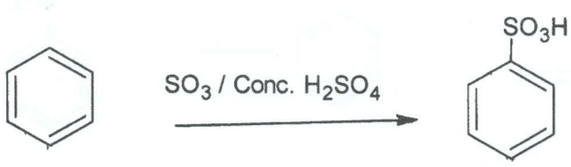
1.2 Compare the aromaticity of pyrrole and furan.

(***20 marks***)

1.3

1.3.1 Explain why substitution reactions are favored in benzene.

1.3.2 Consider the following electrophilic substitution reaction of benzene.



benzene sulphonic acid

1.3.2.1 What is the electrophile involved in the above reaction?

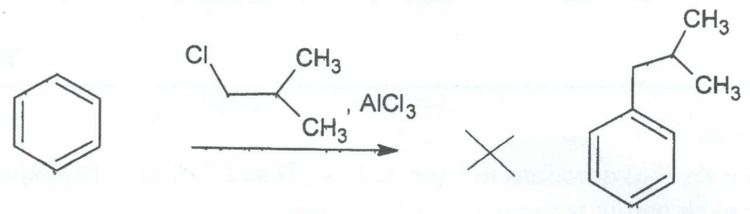
1.3.2.2 Outline the mechanism for the above reaction.

1.3.2.3 How is the above formed intermediate stabilized?

1.3.2.4 Draw the energy profile for the above reaction and assign the structures to the each main point of the diagram drawn.

(***30 marks***)

1.4 A student has tried to prepare isobutylbenzene starting from benzene using the reaction given below. The reaction failed to give the desired product but different product was formed.



isobutyl benzene

1.4.1 State the reasons not to form isobutylbenzene as expected.

1.4.2 What would be the structure of the product formed in the above reaction?

(*20 marks*)

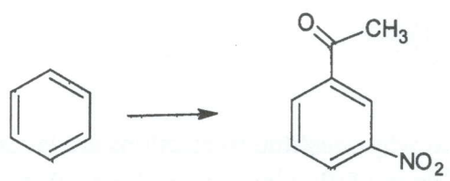
2. Answer **all** parts

2.1 Write down the reagent(s) which is(are) necessary for the conversions given below. If more than one reagent is necessary, indicate the sequence of adding of reagents when required.

2.1.1

2.1.2

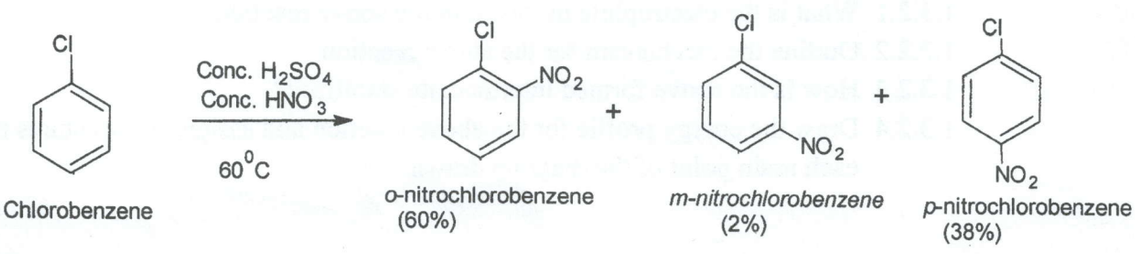
2.1.3



2.1.4

(*20 marks*)

2.2 Given below is the nitration reaction of chlorobenzene to produce nitrochlorobenzene.



Chlorobenzene

o-nitrochlorobenzene (60%)

m-nitrochlorobenzene (2%)

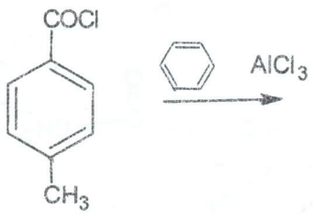
p-nitrochlorobenzene (38%)

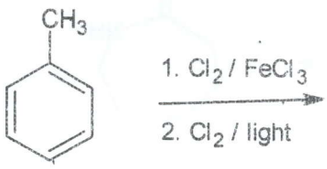
2.2.1 According to the products formed above, chlorobenzene has acted as an *ortho/para* director. Using electronic effects, explain the reasons to require strong conditions for the nitration of chlorobenzene. (***20 marks***)

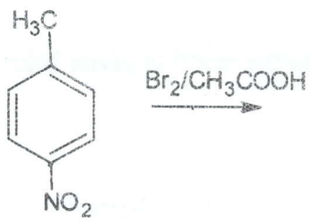
2.2.2 By considering the stability of the intermediates formed, justify the formation of the above **all three** products in the relative yields.

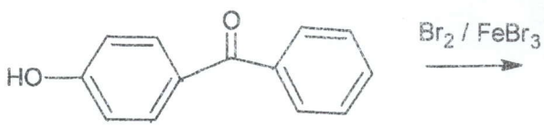
(***20 marks***)

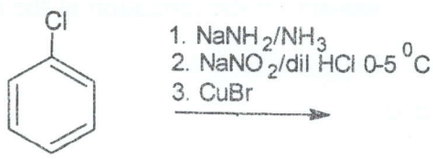
2.3 Draw the structures of the product(s) formed in the reactions given below.

2.3.1 

2.3.2 

2.3.3 

2.3.4 

2.3.5 

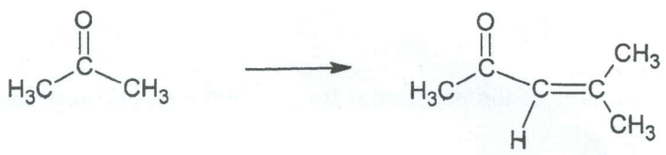
(***40 marks***)

3. Answer all parts.

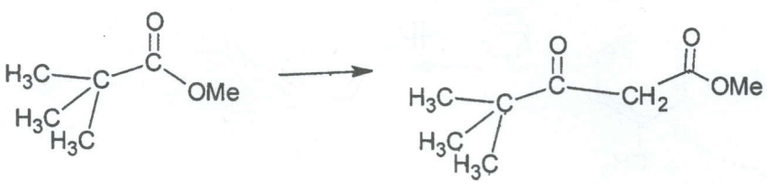
3.1 Give the reagent/ reagent mixture required for the following transformations. If more than one reagent/reagent mixture is/are added, indicate the sequence of adding where required.

3.1.1

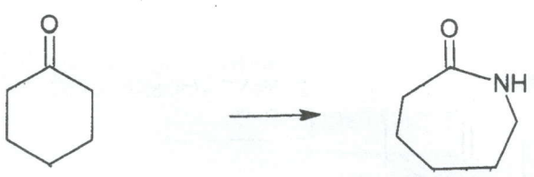
3.1.2



3.1.3

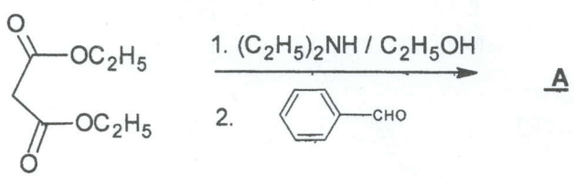


3.1.4



(32 marks)

3.2 Answer the following questions by considering the reaction given below.



3.2.1 Predict and draw the structure of the product (**A**) given in the reaction above.

(12 marks)

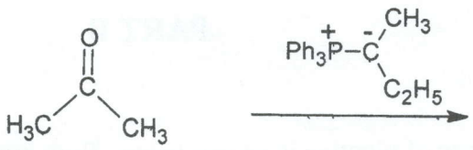
3.2.2 Draw an acceptable mechanism for the formation of the product suggested above.

(12 marks)

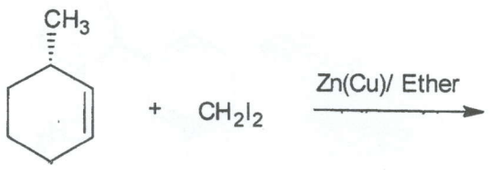
3.2.3 Name the above reaction. ***(12 marks)***

3.3 Giving emphasis to the stereochemistry where appropriate, draw the structure of the product(s) formed in the reactions given below.

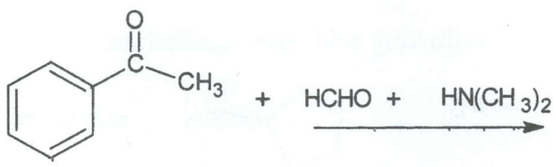
3.3.1



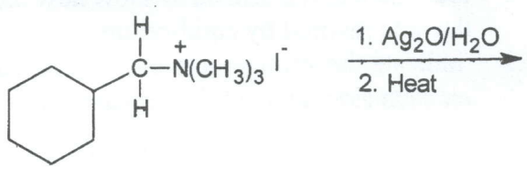
3.3.2



3.3.3



3.3.4



(*32 marks*)

4. Answer all parts

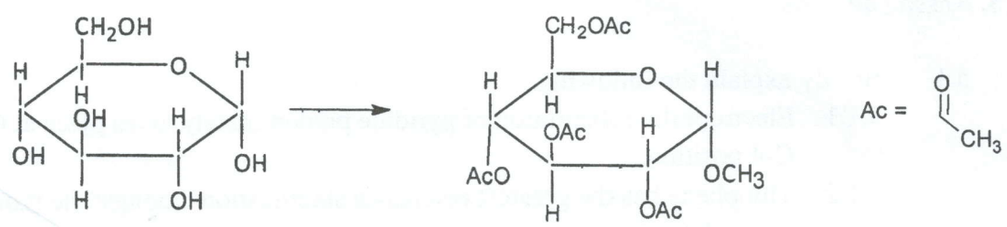
4.1.

4.1.1 Draw the Fischer projection formula of D-glucose and its Harworth projection of the six-member ring structure. Show the anomeric carbon. (*07 marks*)

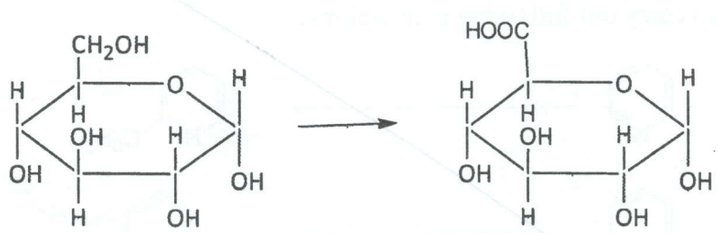
4.1.2 With the structures, explain briefly why aqueous solution of glucose can be oxidized by Tollens reagents whereas methyl glycoside (Methyl α-D-glucopyranoside) cannot be? (*08 marks*)

4.1.3 Giving necessary reagents and reaction conditions show how you would carry out the following transformations of sugars.

4.1.3.1



4.1.3.2



(*10 marks*)

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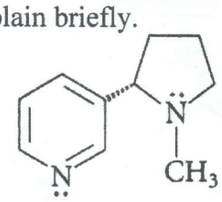
PART B

4.2

4.2.1 The structure of nicotine is shown below. Both nitrogens of nicotine are basic. Which nitrogen is more basic? Explain briefly.



(*10 marks*)

4.2.2 For the following acid/base equilibrium:

4.2.2.1 draw the curved arrows to show how the acid base reaction occurs and indicate the side favored by equilibrium. (*15 marks*)

4.2.2.2 indicate the stronger and the weaker acid/conjugate acid and base/conjugate base on each side, give a brief explanation for your choice of stronger/weaker base. (*15 marks*)

4.3 Draw the structures and give their trivial names of the following compounds.

4.3.1 2-amino-6-oxy purine 4.3.2 2,4-dioxy pyrimidine (*15 marks*)

4.4 5-Bromouracil (BrU) exists in three tautomeric forms that have different base pairing properties. It is a common mutagen used to treat certain types of skin cancer. The mutagenicity arises because of the bromine atom increases the population of the enol form of 5-bromouracil which mimics cytosine and hence forms hydrogen bonding to guanosine instead of adenosine.

4.4.1 Draw the structures of the 2 possible enol tautomers for 5-BrU. (*10 marks*)

4.4.2 Illustrate how the keto tautomer of 5-BrU forms a hydrogen bond pair with guanine. (*10 marks*)

PART C

5. Answer all parts

5.1 Briefly explain the following.

5.1.1 Electrophilic substitution of pyridine predominately takes place at C-3 position, not at C-4 position. (*15 marks*)

5.1.2 Thiophene has the greatest resonance stabilization amongst the mono-heterocyclic aromatics. (*15 marks*)

5.2 How would you carry out following conversions?

5.2.1

5.2.2

5.2.3

5.2.4

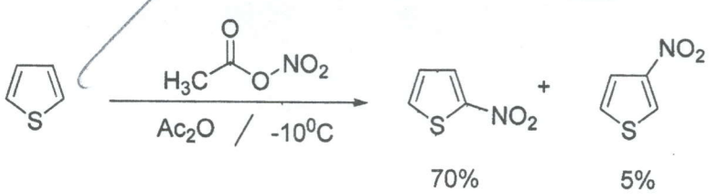
5.2.5

5.2.6

(*30 marks*)

5.3 Briefly explain the orbital structure of imidazole. (*20 marks*)

5.4 Comment on the percentages of yields of products of the following reaction. (*20 marks*)



PART D

6. Answer <u>all</u> parts.

6.1. There are only **<u>two</u>** amino acids which have sulphur in their structure out of 20 α-amino acids used in protein synthesis.

6.1.1. Give the names of these two amino acids and their three letter codes. (*05 marks*)

6.1.2. Draw the chemical structures of these two amino acids. (*05 marks*)

6.1.3. One of the above amino acids is very specific on protein folding. Name the amino acid and mention the specificity. (*05 marks*)

6.2. What are the four levels of protein structures? Describe briefly. (*12 marks*)

6.3. The hydrolysis of a peptide **K** gives the following amino acids, Ala_2, Arg, Lys, Met, Phe, and Ser. Determine the amino acid sequence of peptide **K** by using the results obtained from the following treatments (i-iii).

(i) with carboxypeptidases gives Ala.

(ii) with CNBr cleaves into a dipeptide (Ala, Ser) and a pentapeptide (Ala, Arg, Lys, Met, Phe).

(iii) with trypsin it cleaves into two dipeptides (Ala, Arg and Lys,Phe), and a tripeptide (Ala, Met, Ser).

(*23 marks*)

PART E

6.4

6.4.1 List **three** techniques which are used in the lipid analysis. (*15 marks*)

6.4.2 Define the term "antioxidant". Give **two** examples for natural antioxidants. (*15 marks*)

6.4.3 Give the necessary reagents and reaction conditions for the following conversion.

$$C_6H_5CCH_3{=}CCH_3\ C_6H_5 \longrightarrow 2C_6H_5COCH_3$$ (*10 marks*)

6.4.4 Write down the types of polymers classified according to the number of applied monomers. (*10 marks*)

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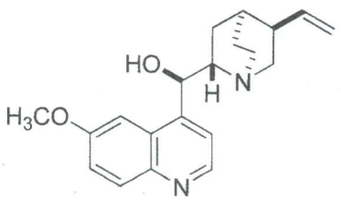
5.

5.1 The antimalarial drug quinine has the following structure.



5.1.1 Which class of heterocyclic compounds is quinine belongs to? (***05 marks***)

5.1.2 Draw and briefly explain the orbital structure of the heterocycle you mentioned in 5.1.1.

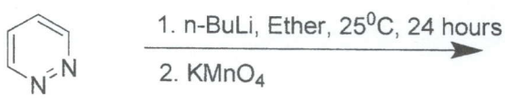
(***20 marks***)

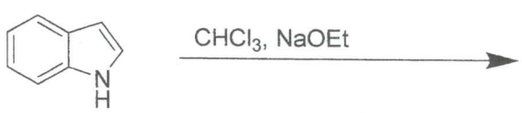
5.1.3 Does the molecule you mentioned in 5.1.1 obey Hückle rule? Justify your answer.

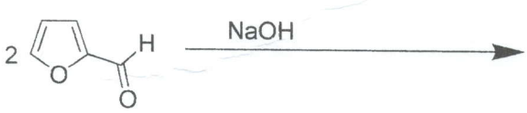
(***10 marks***)

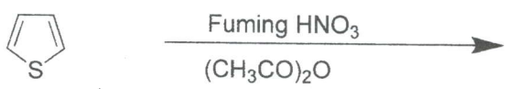
5.2 Draw the structures of the product(s) formed in the given reactions below. (***30 marks***)

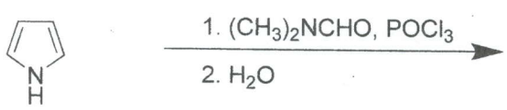
5.2.1 

5.2.2 

5.2.3 

5.2.4 

5.2.5 

5.2.6 

5.3 Following questions are based on pyridine.

5.3.1 Although pyridine is resistant towards oxidation, under proper conditions it can be oxidized to the N-oxide. Show how you would synthesize pyridine N-oxide from pyridine. (***10 marks***)

5.3.2 Pyridine–N–oxides are more reactive towards both nucleophilic and electrophilic reagents than pyridine itself. Justify this behavior of pyridine–N–oxides giving suitable resonance structures. (***10 marks***)

5.3.3 Show how you would carry out the following conversion. (***10 marks***)

Pyridine-N-oxide → 4-nitropyridine

5.3.4 What product(s) you would expect from pyridine when heated with KOH at 320^0C?

(***05 marks***)