



NATIONAL UNIVERSITY OF SCIENCE AND TECHNOLOGY
FACULTY OF APPLIED SCIENCES
DEPARTMENT OF APPLIED CHEMISTRY

MASTERS IN ANALYTICAL CHEMISTRY – SCH 6140

PHARMACEUTICAL AND CLINICAL ANALYSIS

Second Semester Examination Paper 2024

This examination paper consists of 6 printed pages

Time Allowed:	3 hours
Total Marks:	100
Special Requirements:	Scientific Calculator
Internal Examiner:	Dr C. Changunda
External Examiner:	Prof. G. Mehlana

INSTRUCTIONS & INFORMATION

1. Answer **all** questions in Section A and any three questions in Section B. Section A carries 40 marks and each question in Section B carries 20 marks.
2. Start new question on a new page. (Not each part of a question).
3. Show mechanisms or synthesis by means of push and pull arrows.

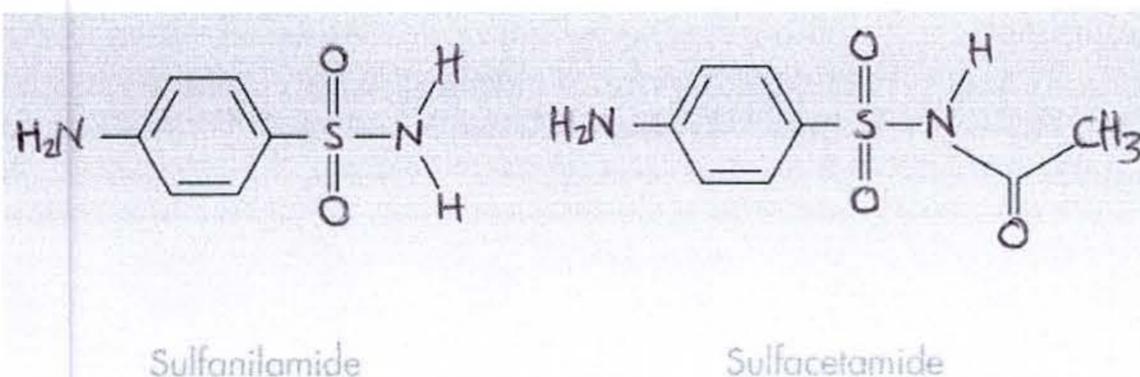
MARK ALLOCATION

QUESTION	MARKS
1.	40
2.	20
3.	20
4.	20
5.	20
6.	20
TOTAL POSSIBLE MARKS	100

Section A

QUESTION 1

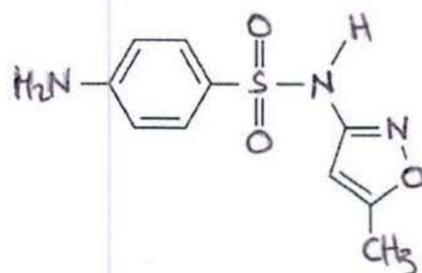
- a. Define the following terms as they relate to quantitative analysis:
- precision [2 marks]
 - standard deviation [2 marks]
 - confidence interval [2 marks]
 - confidence limit [2 marks]
 - limit of detection [2 marks]
- b. Ethanolamine ($\text{HOCH}_2\text{CH}_2\text{NH}_2$, relative molecular mass = 61.08) has a pK_a of 9.4.
- Explain what the term pK_a means. [2 marks]
 - Is ethanolamine freely soluble in water, and if so, demonstrate whether the resulting solution is acidic or basic. [2 marks]
 - Calculate the pH of 1%w/v solution of ethanolamine. [3 marks]
 - A solution of pH 9.0 is required that will resist changes in pH on the addition of small amounts of strong base. Indicate briefly a possible composition of such a solution, and show how pH changes are resisted. [3 marks]
- c. Using your knowledge of analytical chemistry, demonstrate how the following factors can be managed to enhance the quality of analytical measurements.
- Systematic errors [6 marks]
 - Non-systematic errors. [6 marks]
- d. If a weak acid is 91% neutralized at pH 5.7, what is the pK_a of the acid in question? [4 marks]
- e. The structures of sulphanilamide and sulfacetamide are shown below. Determine whether both drugs are basic or acidic and predict which one is strongly basic or acidic of the two. [4 marks]



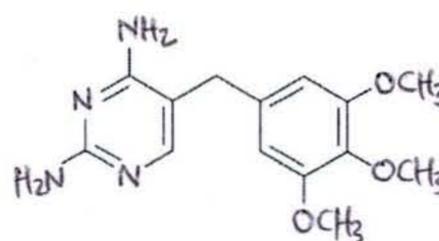
Section B

QUESTION 2

- a. Co-trimoxazole tablets contain sulfamoxazole and trimethoprim (below) and are used in the treatment of chest and urinary tract infections.



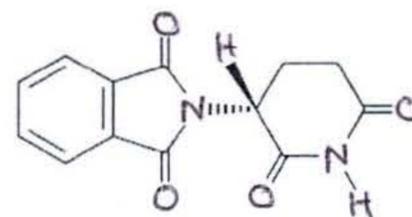
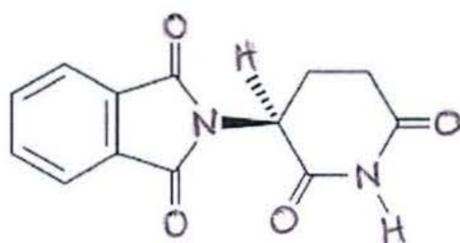
Sulfamethoxazole



Trimethoprim

- i. With reasoning, classify sulfamoxazole and trimethoprim as acidic, basic or neutral. [2 marks]
- ii. Describe clearly, how you would separate a mixture of the two drugs in a pharmaceutical laboratory using conventional glassware and reagents. [8 marks]
- b. The thalidomide disaster is one of the most disturbing drug-induced accident in the last 70 years. Marketed in Germany as a sedative, the drug was administered as a *racemic* mixture for the safe treatment of morning sickness associated with pregnancy.

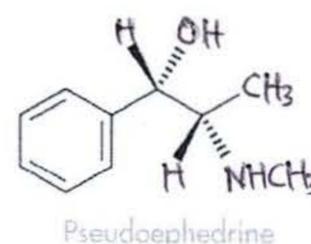
- i. What is a *racemic* mixture? [2 marks]
- ii. Assign the R/S configuration to the thalidomide isomers shown below. [2 marks]



- iii. In the late 1950s and mid-1960s, thousands of children with serious deformities were later born to mothers who had taken thalidomide during pregnancy. The *R* isomer was found to be effective whilst the *S* isomer was found to be *teratogenic*. Worse still, the *R* isomer was observed to undergo racemization to the *S* isomer – which led to the withdrawal and discontinuation of this medication. Briefly highlight the pharmaceutical significance of the thalidomide story. [6 marks]

QUESTION 3

- i. Ephedrine is a natural product isolated from the plant genus, *Ephedra*, and has been used for the treatment of asthma in the last century. However, pseudoephedrine is a decongestant and a constituent of several over-the-counter cold and flu remedies. Both ephedrine and pseudoephedrine (shown below) are *diastereomers*. What are *diastereomers*? [2 marks]



- ii. A technique called polarimetry is used in the laboratory to distinguish between enantiomers and to measure the extent to which each enantiomer rotates the plane of plane-polarised light. With the aid of a diagram, give a concise account of the principle of *polarimetry* and how it can be used to determine the optical activity of an analyte sample of your choice. [10 marks]
- iii. A 1.20 g sample of cocaine, $[\alpha]_D = -16$, was dissolved in 7.50 mL of chloroform and placed in a sample tube having a pathlength of 5.00 cm.
- a) What was the observed rotation? [6 marks]
- b) Is cocaine *dextrorotatory* or *levorotatory*? [2 marks]

QUESTION 4

Lithium carbonate (Li_2CO_3 , $M_r = 73.9$) is a drug widely used in the treatment of depression. The BP assay for lithium carbonate involves the addition of an excess of hydrochloric acid to a sample of the drug and back titration of the unreacted hydrochloric acid with sodium hydroxide.

- i. Explain why back titrations are sometimes used in volumetric analysis. [2 marks]
- ii. Write balanced chemical equations for the reactions expressed above, and hence calculate the weight of lithium carbonate equivalent to 1 mL of 1 M HCl (the equivalent relationship). [6 marks]
- iii. This assay was carried out and the following results were obtained
- Weight of bottle + sample = 11.7707 g
Weight of bottle + residual sample = 10.7142 g
Volume of 1 M ($f = 0.9989$) HCl added = 50.00 mL
Burette readings, titrant 1 M ($f = 1.012$) NaOH: Initial volume = 0.50 mL
Final volume = 21.55 mL
Calculate the percentage weight of lithium carbonate in the sample. [5 marks]

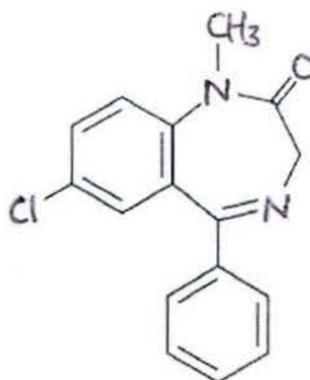
- iv. What is the significance of an answer greater than 100%? [2 marks]
- v. Suggest an indicator for this assay, and explain your reasoning. [5 marks]

QUESTION 5

The assay for Diazepam Tablets BP is as follows.

Weigh and powder 20 tablets. To a quantity of the powder containing 10 mg of diazepam, add 5 mL of water, mix and allow to stand for 15 minutes. Add 70 mL of a 0.5% w/v solution of sulfuric acid in methanol, shake for 15 minutes, add sufficient of the methanolic sulfuric acid to produce 100 mL and filter. Dilute 10 mL of the filtrate to 50 mL with the same solvent and measure the absorbance of the resulting solution at the maximum at 248 nm. Calculate the content of $C_{16}H_{13}ClN_2O$ taking 450 as the value of Absorbance at this wavelength.

- i. Draw the part of the molecule responsible for the absorption of light in this assay (see structure below). What is this part of the molecule called? [3 marks]



- ii. What assumptions are made in this assay? [4 marks]
- iii. When this assay was carried out on 5 mg diazepam tablets, the following results were obtained:

Weight of 20 tablets = 7.4878 g

Weight of sample taken = 0.7450 g

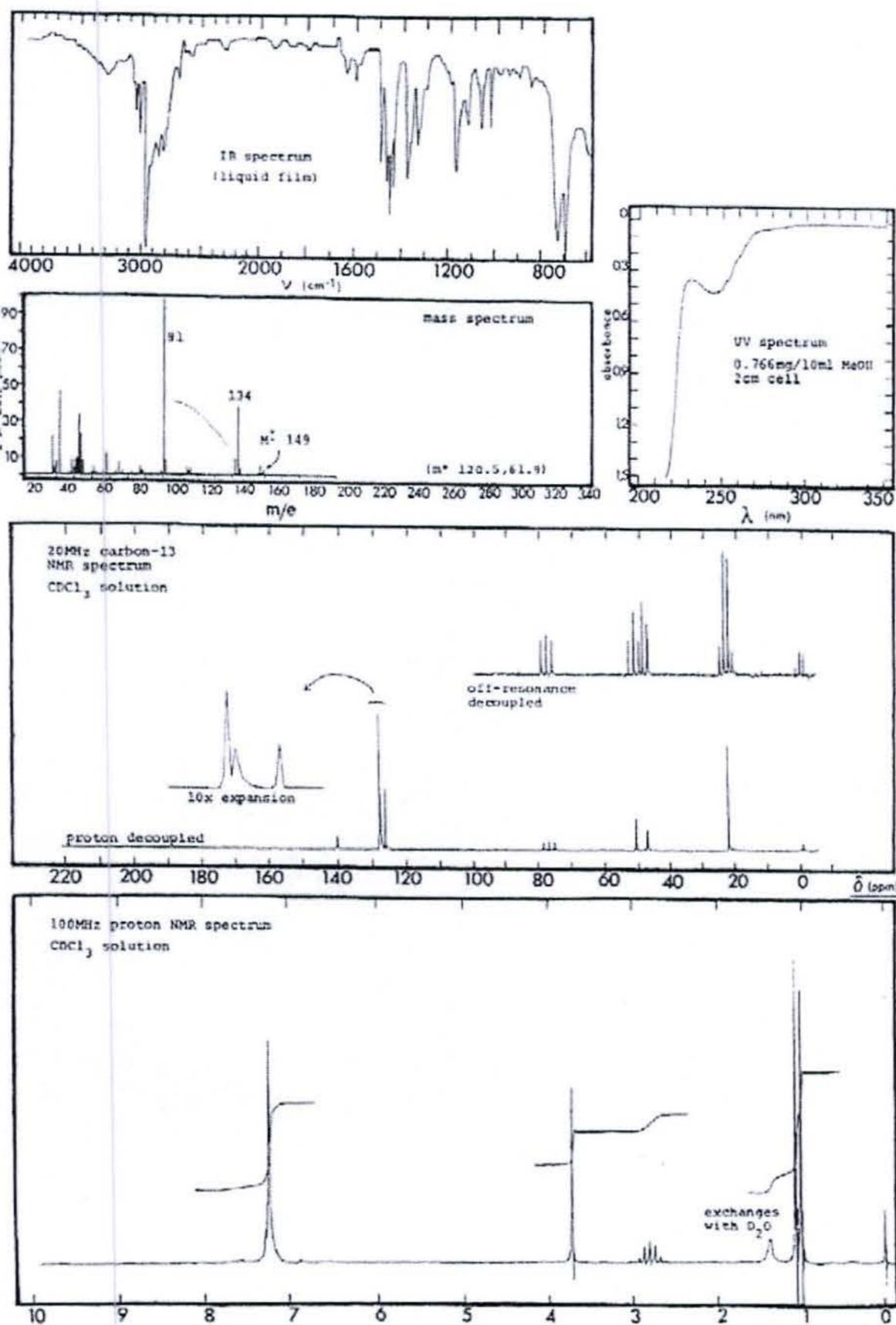
Absorbance of a 1 cm layer at 284 nm = 0.848

Calculate the content of diazepam in a tablet of average weight and hence calculate the percentage of the stated amount of diazepam in the tablets. [7 marks]

- iv. Suggest another assay method for the determination of diazepam in Diazepam Tablets. [6 marks]

QUESTION 6

Determine the structure of the unknown compound from the spectral data shown below. [20 marks]



End of Question Paper.