



MASENO UNIVERSITY
UNIVERSITY EXAMINATIONS 2016/2017

**FOURTH YEAR FIRST SEMESTER EXAMINATIONS FOR THE
DEGREE OF BACHELOR OF SCIENCE IN INDUSTRIAL
CHEMISTRY WITH INFORMATION TECHNOLOGY**

MAIN CAMPUS

**SCS 450: MOLECULAR MODELLING AND DENSITY
FUNCTIONAL THEORY**

Date: 13th December, 2016

Time: 3.30 - 6.30 pm

INSTRUCTIONS:

- Answer question ONE and any other TWO questions.

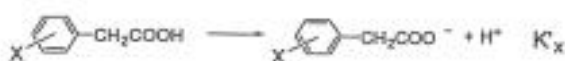


QUESTION ONE

- (a) The table below shows loadings for selected variables on the first two PCs from a total of 90 parameters describing 85 substituents

No	Parameter	PC ₁	PC ₂
1	PIAR	-0.72	0.90
2	PIAL	-0.96	0.11
3	FARR	-0.87	0.11
5	FALR	-0.25	0.16
6	FARHL	0.45	0.17
7	K	0.55	0.23
38	SX	0.91	-0.70
43	RE	0.04	0.01
44	I	0.14	0.07
50	HD	0.12	0.07
85	PABA	0.99	0.39

- Which PC explains much of the variations in the data? [2marks]
 - Identify the parameter that is explained in PC₁ [2marks]
 - Explain the trend that exists between PABA and parameters number 1 to 3 in PC₁ and draw a representative curve for the three [3marks]
 - Identify the outstanding parameter in PC₂ and state the trend that exists between parameter PIAR and 38 draw a representative curve for the relationship [2marks]
- (b) The following expression relates to the Hammett's equation.



$$\log_{10} \frac{K'_x}{K'_0} = \sigma_p$$

- Define both σ_p [2marks]
 - If X= electron withdrawing group (e.g. NO₂), what is the overall value of σ_p ?
 - If X= electron donating group (e.g. CH₃), what is the overall value of σ_p ? [4marks]
- (c) Calculate the substituent hydrophobicity and hydrophilicity Log P for the following aromatic compounds phenol, toluene and *p*-aminobenzoic Acid [3marks]

Refer to the table of π values below.

Hydrophobic		Hydrophilic	
Substituent	$\pi > 0$	Substituent	$\pi < 0$
-CH ₃	0.56	-NO ₂	-0.28
-CF ₃	0.88	-CHO	-0.65
-C ₆ H ₅	1.96	-CO ₂ H	-0.32
-C ₆ H ₁₁	2.51	-NH ₂	-1.23
-C(CH ₃) ₃	1.98	-OH	-0.67

- (d) Name two statistical models used in QSAR and QSPR and cite an example for each.

[2marks]

(e) Briefly describe the following statistical terms Correlation and Dependence?

[2marks]

(f) Give three QSAR/QSPR-Regression Types

[3marks]

(g) List five QSAR/QSPR Post-Qualifications

[5marks]

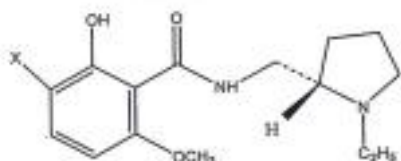
QUESTION TWO

(a) Correlation Coefficient Matrix below represents the variables considered in the study of a pyrethrin moiety

Const.	F	E_s	π	MR	P	V	MV	σ_1	σ_{π}
F	1.000								
E_s	-0.214	1.000							
π	-0.058	0.020	1.000						
MR	0.179	-0.193	-0.247	1.000					
P	0.220	-0.309	-0.206	0.949	1.000				
V	0.172	-0.375	-0.257	0.908	0.988	1.000			
MV	-0.049	-0.136	-0.215	0.843	0.905	0.921	1.000		
σ_1	0.954	-0.146	0.058	0.186	0.215	0.149	-0.102	1.000	
σ_{π}	0.939	-0.340	-0.067	0.116	0.168	0.123	-0.171	0.923	1.000

i. Identify the combination of variables that show significant relationships and describe the trends (use curves to display each of the trends) [5 marks]

(b) Study the tabulated results of the influence of X on properties of the compound whose structure is shown below and answer the questions that follow.



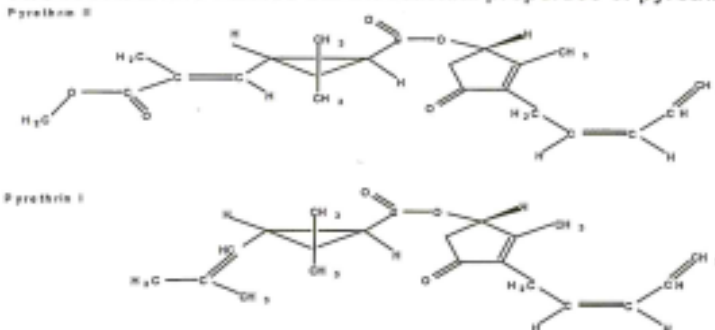
$$\text{Log}_{10}\text{IC}_{50} = 1.28\pi - 0.52\pi^2 - 0.69\sigma_m + 1.50$$

$n = 12, r^2 = 0.94, s = 0.40, F = 19.9$

X	CONH ₂	NH ₂	OH	CN	NHCH ₃	NO ₂	NHC ₂ H ₅	NMe ₂	NHC ₃ H ₇	NHC ₄ H ₉
σ_m	0.28	-0.16	0.12	0.56	-0.30	0.71	-0.24	-0.15	-0.24	-0.34
π	-1.49	-1.23	-0.67	-0.57	-0.47	-0.28	0.08	0.18	0.62	1.16

- How valid is the equation? [2marks]
- What are the best values for the substituent parameters, π and corresponding σ_m ? [2marks]
- From the table of substituents, what is the best substituent for X? [2marks]
- What is the IC₅₀ for the salicylamide with the substituent you have chosen? state whether it is hydrophobic or otherwise [1mark]

(c) Two researchers studied the insecticidal properties of pyrethrin esters I and II.



The statistics for each curve-fitting are given in the table below.

Curve A statistics			Curve B statistics		
n = 6; r = 0.98; s = 0.32; F = 32.39			n = 6; r = 1.00; s = 0.04; F = 1,389.47		

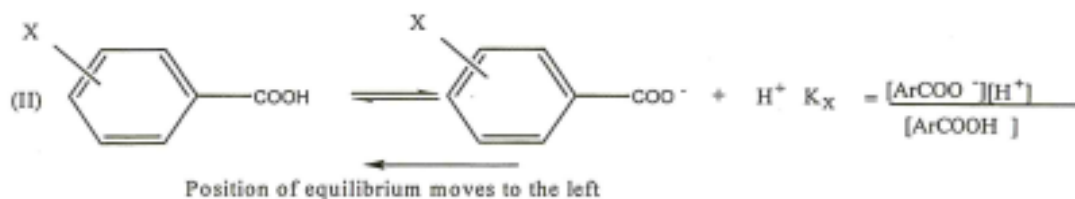
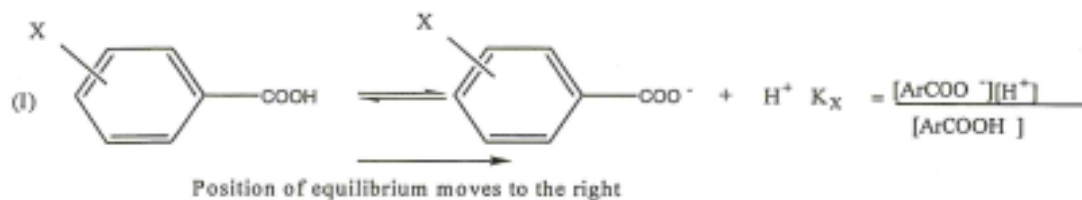
Curve A						
Log P	4	6	8	10	12	14
Log 1/C	10.1	10.4	10.8	11	9.5	7.8

Curve B						
Log P	4	6	8	10	12	14
Log 1/C	11	10.5	10.8	10.9	9.5	7.8

- Use the values given in the table above to plot the two curves A and B. [8marks]
- From the two curves which one gives the best optimal value for log P and for 1/C? [2marks]

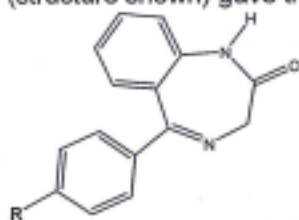
QUESTION THREE

(a) For equations (I) and (II) give the expressions for K_x and K_{Benzolic} and state the effect of electrons on the equilibrium



[4marks]

- (b) A study of the effect on anticonvulsant activity of substituent's, R, in 1,4-benzodiazepinones (structure shown) gave the following regression equation:



$$\text{Log } 1/C = -0.31 x^2 + 0.14 x + 1.29 y^2 + 0.12 y + 4.56$$

$$n = 10 \quad r = 0.87 \quad s = 0.47$$

- Define x and y . In the equation above [2marks]
- Determine the best values for x that give maximum anticonvulsant activity using the equation above. [2marks]
- If $\log P$ is 2.11 for the unsubstituted 1,4-benzodiazepinone, what is the $\log P$ for your substituted 1,4-benzodiazepinone? Write down the structure showing the best substituent R that you have established and tabulated as:

Substituents	NH ₂	OH	CN	NO ₂	H	F	SO ₂ Ph	OEt	CH ₃	Cl	CF ₃	N(Et) ₂
x	-1.23	-0.67	-0.57	-0.28	0.0	0.14	0.270	0.38	0.56	0.71	0.88	1.18
y	-0.66	-0.37	0.66	0.78	0.0	0.06	0.70	-0.24	-0.17	0.23	0.54	-0.90

[2marks]

- (c) List and explain the factors used to evaluate the validity of QSAR equations in multiple linear regression (MLR) analysis [10marks]

QUESTION FOUR

- (a) The hydrophilic or hydrophobic properties of molecules, for which the partition coefficient, P, of a molecule is used. P is defined by

$$P = \frac{[\text{drug}]_{\text{octanol}}}{[\text{drug}]_{\text{water}}}$$

Derive the logarithmic relationship [4marks]

[4marks]

- (b) Study the data presented in the table below generated from the reaction shown to answer questions that follow



R	H	CH ₃	OCH ₃	F	Cl	NO ₂
<i>ortho</i>	6.27	12.3	8.06	54.1	11.4	671
<i>meta</i>	6.27	5.35	8.17	13.6	14.8	32.1
<i>para</i>	6.27	4.24	3.38	7.22	10.5	37.0

- What is the effect of R on the acidity of the acids? [4marks]
 - Derive the expression for quantifying electronic properties in terms of K_a [4marks]
- (c) Give advantages and disadvantages of the Free-Wilson Approach [4marks]

(d) Define the terms $\log P$ and α , and briefly describe how they are obtained.

[4marks]