M.SC DEGREE END SEMESTER EXAMINATION OCTOBER 2016
SEMESTER – 3: PHARMACEUTICAL CHEMISTRY
COURSE: **P3CHET12/P3CPHT12– SPECTROSCOPIC METHODS IN CHEMISTRY**

Common for Regular (2015 Admission) & Supplementary / Improvement (2014 Admission)

Time: Three Hours   Max. Marks: 75

Section A
*(Answer **any Ten** questions. Each question carries **2** marks)*

1. In the ^{1}H NMR spectrum of 1-propoxybutane (butyl propyl ether), the two CH_2 groups (A and B) attached to oxygen appear as two triplets (2H each). How will you distinguish between the two CH_2 components (one from the butyl and the second from propyl components)?
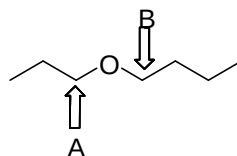
2. On the basis of noise-decoupled ^{13}C NMR spectrum, how will you differentiate between the two CH_2 components (A and B) in 1-propoxybutane?

3. In the EIMS spectrum of 1-propoxybutane, the base peak is observed at *m/z* 73. Show the fragmentation mode leading to this ion.

4. What are the prominent peaks observed in the UV-Vis and IR spectra of 1-ethoxypropane?

5. Give the name and molecular formula of a compound that will give identical numerical values for its mass as determined by High Resolution (resolution > 50,000) and typical mass spectrometers (resolution < 1000).

6. In the ^{1}H NMR spectrum of benzylsulfinylbenzene, two doublets (J = 14 Hz) are observed in the aliphatic region. Account for this observation.
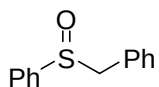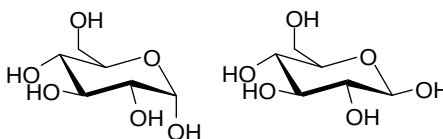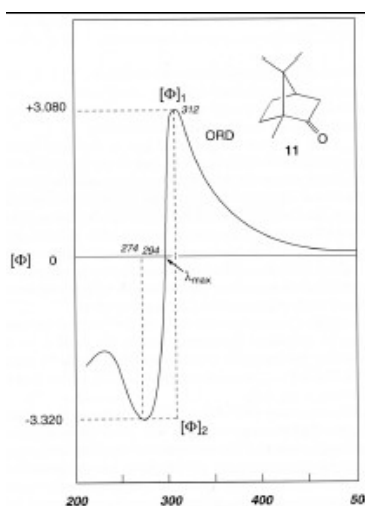
benzylsulfinylbenzene

7. On the basis of EIMS data, how will you differentiate between 3-methylcyclohexene and 4-methylcyclohexene?

(PTO)

8. On the basis of ^1H NMR spectral data, how will you differentiate between the α- and β-anomers of glucose?
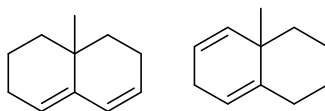

9. The ORD spectrum of camphor is given hereunder. Assign the sign of Cotton effect observed here. Justify your answer.

10. In the IR spectrum of acetone (recorded as thin film), a low intensity peak is observed around 3430 cm^{-1}. Account for the origin of this peak.

11. On the basis of λ_{max} data, how will you differentiate between the following isomers?

12. In the EIMS spectrum of an unknown compound peaks are observed at *m/z* 141 (M^+), 111, 95 (base peak), and 75 along with a metastable peak is observed at *m/z* 59.21. On the basis of these data, it was concluded that the compound contains nitrogen and fluorine. How?

13. In ^{13}C NMR spectrum of fluorobenzene (recorded at 15 MHz) the ipso carbon appears as doublet at δ 171.3 and 155.0. Calculate one-bond sp^2 carbon-fluorine coupling constant from this data.

(2 × 10 = 20)

Section B

(*Answer **any Five** questions. Each question carries **5** marks*)

14. On the basis of IR spectral data how will you differentiate between primary, secondary and tertiary amides?

15. Write briefly on any three factors affecting the magnitude of germinal coupling constants (of protons).

16. Pick the homotopic, enantiotopic, diastereotopic and heterotopic protons in (1*R*,2*R*)-cyclopropane-1,2-dicarbonitrile. Justify your answer. The four protons are labelled H^a, H^b, H^c, and H^d for your convenience.

(1*R*,2*S*)-cyclopropane-1,2-dicarbonitrile
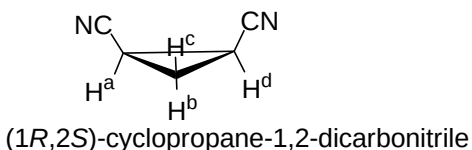
17. Assign the configuration (*R* or *S*) of the chiral carbon in of 3-*tert*-butyl)cyclohexanone exhibiting negative Cotton effect. Justify your answer.
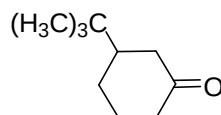
18. In the ^{1}H NMR spectrum of a compound exhibiting AMX spin system, three signals are observed: δ 6.20 (dd, J_{AM} = 17.9 Hz, J_{AX} = 0.9 Hz, 1H), 6.07 (dd, J_{MX} = 11.8 Hz, J_{AX} = 0.9 Hz, 1H), 5.70 (J_{AM} = 17.9 Hz, J_{MX} = 11.8 Hz). Determine the minimum field strength required to obtain a pure first order spectrum for this compound (on a 1T magnetic field, protons resonate at 42.6 MHz).
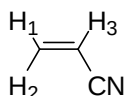
19. Give an example for chiral shift reagent (structure required) and explain how chiral shift reagents can be employed to determine *ee* in the asymmetric reduction of butan-2-one to butan-2-ol.

20. Under electron impact ionization, loss of small molecules is commonly observed. Draw fragmentation modes leading to loss of:

    a) ketene from benzyl acetate, and b) ethylene from pentan-2-one

21. In the absorption spectrum of ketones, λ_{max} (n-π* transition) depends on several variables. Consider the absorption spectrum of *trans*-2-decalone. Predict the change observed when a) solvent polarity is changed; b) a chlorine substituent is introduced at the α-position.
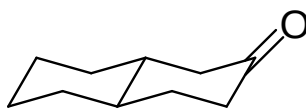
(5 × 5 = 25)

Section C
*(Answer **any Two** questions. Each question carries **15** marks)*

22. Draw the splitting pattern for an $A_2M_2X_2$ spin system exhibiting the following characteristics: δ_A = 1, δ_M = 3, δ_X = 5 ppm downfield of TMS, J_{AM} = 10 Hz, J_{AX} = 8 Hz, J_{MX} = 10 Hz. Predict the position (in Hz) and integrated intensity of individual lines when the spectrum is recorded on a 400 MHz instrument. Take integrated

intensity for one proton as 8. Predict the pattern observed and position and intensity of individual lines for signal M when the spectrum is recorded on a 100 MHz instrument.

23. Identify structure of compound **A** based on spectral data provided hereunder:

For compound **A**: UV (methanol) transparent above 249 (4300), 313 (30) nm; IR (CCl_4) 3011, 2929, 1714, 1611, 721 cm^{-1}; ^1H NMR (90 MHz in $CDCl_3$) δ 7.70-7.40 (m, 4H), 3.13 (t, J = 7 Hz, 2H), 2.68 (t, J = 6 Hz, 2H), ^{13}C NMR (15 MHz in $CDCl_3$) five signals at δ 206.6, 155.0 (disappears in DEPT-135), 137.1 (disappears in DEPT 135), 134. 5 (positive in DEPT-135), 127.2 (positive in DEPT-135), 126.7 (positive in DEPT-135), 36.3 (negative in DEPT-135), 25.8 (negative in DEPT-135); EIMS m/z (relative intensity) 132 (M^+, 95), 131 (23), 104 (100), 103 (42), 78 (30), and other peaks. Formula mass: 132.0575 corresponding to C_9H_8O. Fragmentation pattern leading to base peak and stereochemistry, if applicable, should be clearly indicated.

24. Identify structure of compound **B** based on spectral data provided hereunder:

For   compound   **B**:   UV   (methanol)   transparent above 285 (21000), 355 (shoulder, 450) nm; IR (CCl_4) 3065, 2814, 2716, 1677, 1125, 973, 748 cm^{-1}; ^1H NMR (90 MHz in $CDCl_3$) δ 9.63 (d, J = 8 Hz,1H), 7.72 (doublet of doublet, J_1 = 7 Hz, J_2 = 2 Hz, 2H), 7.43 (d, J = 16 Hz, 1H), 7.80-7.40 (m, 3H), 6.69 (doublet of doublet, J_1 = 16 Hz, J_2 = 8 Hz, 1H); ^{13}C NMR (15 MHz in $CDCl_3$) seven signals at δ 193.4 (positive in DEPT-135), 152.5 (positive in DEPT-135), 134.1 (disappears in DEPT-135), 131.2 (positive in DEPT-135), 129.1 (positive in DEPT-135), 128.6 (positive in DEPT-135), 128.5 (positive in DEPT-135); EIMS m/z (relative intensity) 132 (M^+, 74), 131 (100), 104 (27), 103 (55), 78 (30), 77 (35), and other peaks. Formula mass: 132.0575. Fragmentation pattern leading to base peak and stereochemistry, if applicable, should be clearly indicated.

25. Identify structure of optically active compound **C** based on spectral data provided hereunder:

For compound **C**: UV (methanol) λ_{max} (ε) transparent above210 nm; IR (CCl$_4$) 3400-2620 (intense, broad peak), 1700, 1460, 1314, 1198, 894 cm^{-1}; ^{1}H NMR (400 MHz in CDCl$_3$) five signals at δ 12.20 (broad singlet, D$_2$O-exchangeable, 2H), 2.67 (doublet of a doublet of a quartet appearing as a quintet, J_1 = 6 Hz, J_2 = 6Hz, J_3 = 6Hz, 1H), 2.50 (doublet of a doublet J_1 = 15 Hz, J_2 = 6Hz, 1H)), 2.31(doublet of a doublet, J_1 = 15 Hz, J_2 = 6Hz, 1H), 1.10 (d, J = 6 Hz, 3H); ^{13}C NMR (100 MHz in CDCl$_3$) five signals at δ 176.3 (disappears in DEPT-135), 172.9 (disappears in DEPT-135), 37.2 (positive in both DEPT-135 and DEPT-90), 35.2 (negative in DEPT-135), 16.8 (positive in DPT-135, disappears in DEPT-90); EIMS *m/z* (relative intensity) 132 (*M*$^+$, absent), 114 (35), 86 (51), 73 (30), 45 (50), 42 (100), 41 (49), and other peaks. Formula mass: 132.0423. Fragmentation pattern leading to base peak and stereochemistry, if applicable, should be clearly indicated.

Correlation data (COSY and HSQC)

^{1}H NMR signal (δ)	Correlates with	
	^{1}H NMR signal (δ)	^{13}C NMR signal (δ)
12.20	-	-
2.67	2.50, 2.31 and 1.10	37.2
2.50	2.67, 2.31	35.2
2.31	2.67, 2.50	35.2
1.10	2.67	16.8
-		176.3

(15 × 2 = 30)

****