Al-Azhar University
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Pharmaceutical Chem. Dept.

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Instrumental Analysis
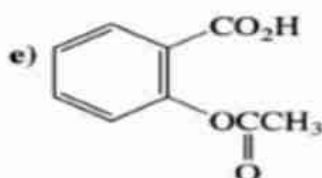
Introduction , H-NMR

1. Explain in brief the difference between classic and modern methods for analysis
2. What is the difference between Precision and accuracy?
3. What is Spectroscopy?
4. What is the difference between Spectrum and spectrometer?
5. What is EMR?
6. Which part does the UV radiation affect in chemical structure?
7. Which part does the IR radiation use to investigate?
8. What is the role of Mass spectroscopy in chemical analysis?
9. What is the role of NMR in chemical analysis?
10. What is the role of Helium and Nitrogen in NMR spectrometer system
11. Do all atoms have the feature to be run under NMR? Why
12. What are the most well-known atoms that are familiar to NMR analysis?
13. What is the role of NMR analysis?
14. What is the type of energy or EMR type used in NMR?
15. Talk in brief about NMR spectroscopy principles
16. What are the α-Spin and β-Spin States? What is difference between both states? Draw energy diagram that explain the case
17. What will happen if an external magnetic field is applied on hydrogen atoms?
18. What is the idea of signal formation in NMR?
19. Describe the NMR spectrometer "Machine"
20. Saturation and Relaxation are well-known NMR terms. What are they?
21. What is relaxation time?
22. How the energy gap ΔE is different among hydrogen atoms?
23. What does an external magnetic field cause for nuclei
24. What are the major parts of NMR machine?
25. Talk in brief about sample preparation in NMR analysis
26. What are the most important conditions for solvent choice?
27. What is the difference between $CDCl_3$ and $CHCl_3$?
28. The NMR solvent must be deuterated; why.
29. Using Instrumentation; how to distinguish between:-
    a. Paracetamol and aspirin?
    b. Aniline and methylamine?
    c. Fructose and Glucose?
    d. Benzophenone and dicyclohexylketone?

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30. Determine the DoU by both inspection and calculation for each of the following

a)
  benzene ring with C(=O)OCH₂CH₃

b) N≡ ... (structure)

c)
  cyclopentene with vinyl and Br

d)
  indole with CH₂—CH(NH₂)—C(=O)—OH
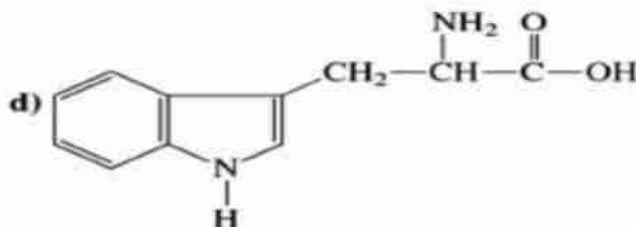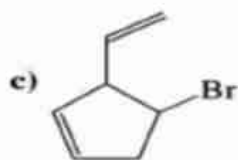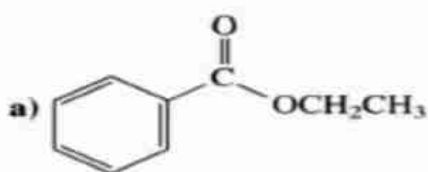
Tryptophan (an amino acid)

e)
  benzene with CO₂H and OCCH₃(=O)

31. What is the role of Pascal Triangle in NMR spectrum?

32. How does spin-spin splitting occur?

33. What does the following equation mean?

$$B_{\text{effective}} = B_{\text{applied}} - B_{\text{local}}$$

34. Deshielded protons are being detected at higher ppm. Why

35. Different chemical environment leads to different chemical shift. Why

36. What is chemical shift? What are the factors that cause a change in the value of chemical shift?

37. Draw the NMR spectrum template showing all terminology.

38. NMR would not be very valuable if all protons absorbed at the same frequency. Why

39. What are the two chemical shift references in NMR spectrum.

40. What would be the chemical shift of a peak that occurs 789.7 Hz downfield of TMS on a spectrum recorded using a 90 MHz spectrometer?

41. What is the anisotropic effect in NMR spectroscopy?

42. Why intramolecular Hydrogen bonding leads to more deshielding effect?

43. How would you use the H-NMR to distinguish between each of the following pairs of compounds? (Just tell how many peaks does each compound show)

a] &

b] & HO—⟨⟩—Cl

Y
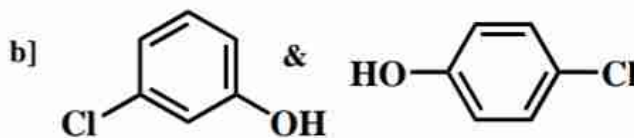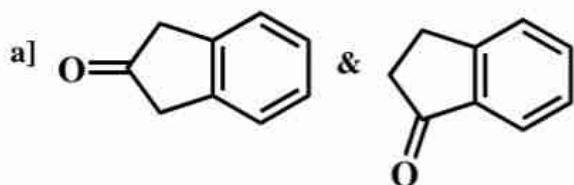
44. Propose the structure of a compound that exhibits the following H-NMR data.
   a. $C_4H_8O_2$ [1.21 δ (6H, doublet) 2.59 (1H, septet) 11.38 (1H, singlet)].
    b. $C_5H_{10}O$ [1.09 δ (6H, doublet) 2.12(3H, singlet) 2.58 (1H, septet)].
    c. C_8H_{10} [2.35 δ (6H, singlet) 7.09 (4H, singlet).

45. What are the characteristic features of N-H and OH protons?
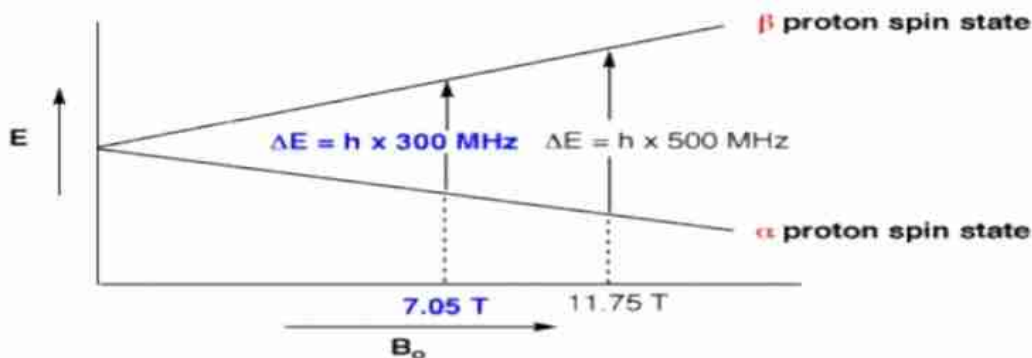46. Why O-H or N-H proton does appear broad or not seen in the NMR spectrum?
47. Why hydrogen bonding leads to increase the chemical shift for OH or NH proton?
48. How many H-NMR signal would you expect to find in each of the following three compounds

a]

b]

c]
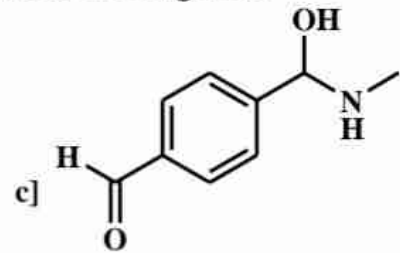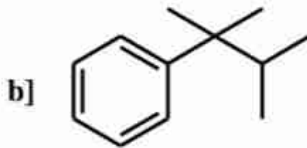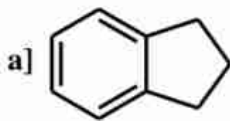
49. What does the following figure mean?

Figure 1. Graphical relationship between field B_o and frequency ν.

E

β proton spin state

ΔE = h x 300 MHz   ΔE = h x 500 MHz

α proton spin state

7.05 T   11.75 T

B_o

50. How to make sure that this is an O-H or N-H peak?
51. What is Hydrogen–deuterium exchange?
52. Regarding to Menthol; Provide your own comment.

Partial ¹H NMR Spectrum of Menthol in CDCl₃

+ 1 drop D₂O

3.6   3.4   3.2   3.0   2.8   2.6   2.4   2.2   2.0   1.8   1.6   1.4   ppm
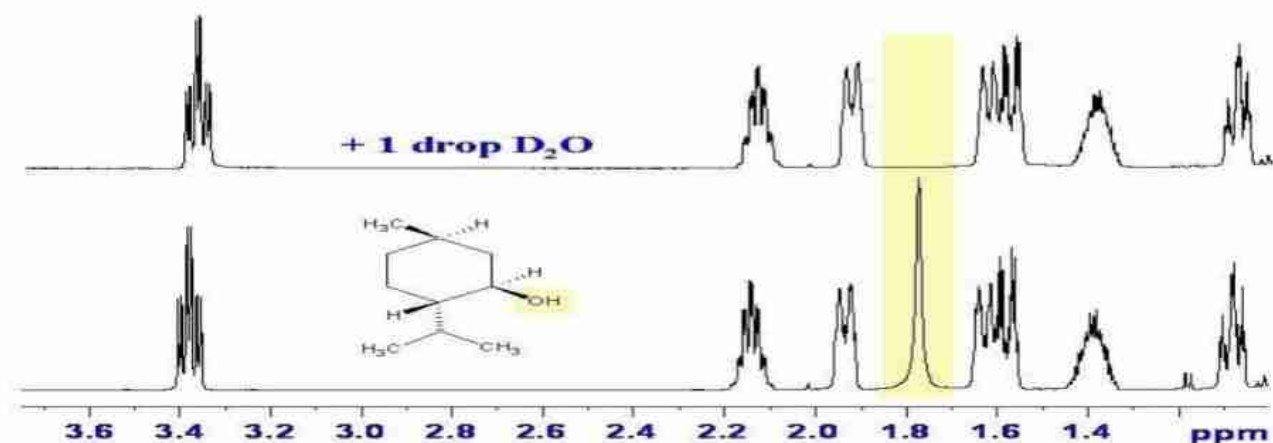
53. What impurities might be detected in NMR spectrum?
54. What is spin-spin coupling and what is the main reason that is responsible for signal splitting?
55. What is relationship between Pascal Triangle and NMR spectrum?
56. What is the difference between complex and simple splitting?
57. What is the most likely chemical shift for the CH 3OCH3 in 1H NMR?

   a) 1.0   b) 1.5   c) 4.0   d) 1.0   e) 5.1

58. Why

   a. C-H in hexane is less deshielded than C-H in benzene?
   b. C-H in ethene is less deshielded than C-H in benzene?
   c. C-H in benzene is less deshielded than C-H in CHO (aldehyde)?
   d. C-H in CHO (aldehyde) is less deshielded than C-H in acidic proton in carboxylic acid?
   e. Magnetically; equivalent hydrogens resonate at the same applied field.
   f.   Number of signal depends on the number of proton types.

59. What is the effect of external magnetic on the magnetic feature of the proton?
60. What is coupling constant J?
61. What is J-Coupling or "coupling constant"?
62. What is the difference between

       a. Simple and complex coupling?
   b. Triplet signal and doublet of doublet signal?

63. Draw the complex splitting tree for each of the following indicate the type of multiplicity.
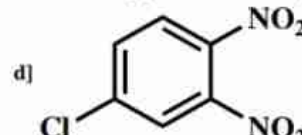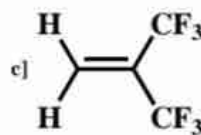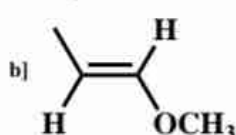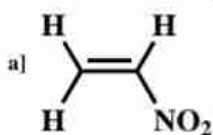
64. Draw the simple splitting tree for each of the following marked hydrogen. Indicate the type of   multiplicity
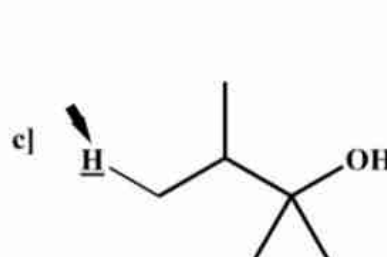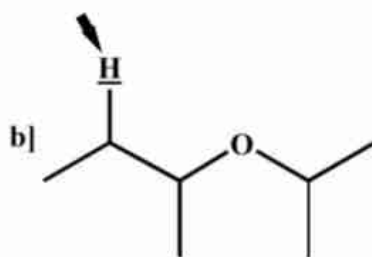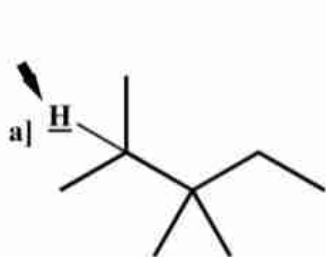
65. Sketch a 1H NMR spectrum for each of the following compounds, showing a simple line corresponding to the expected shift for each of the different hydrogens.
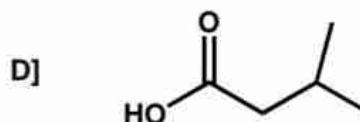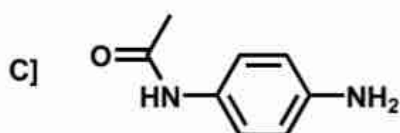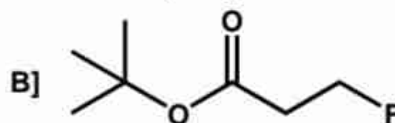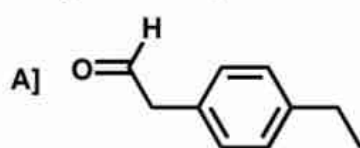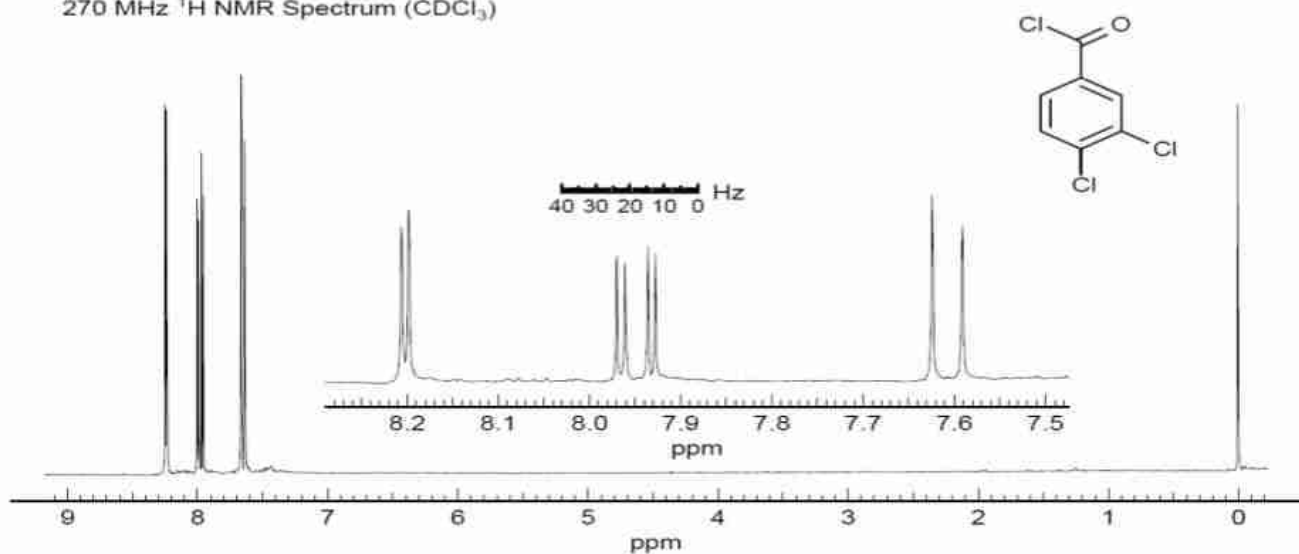
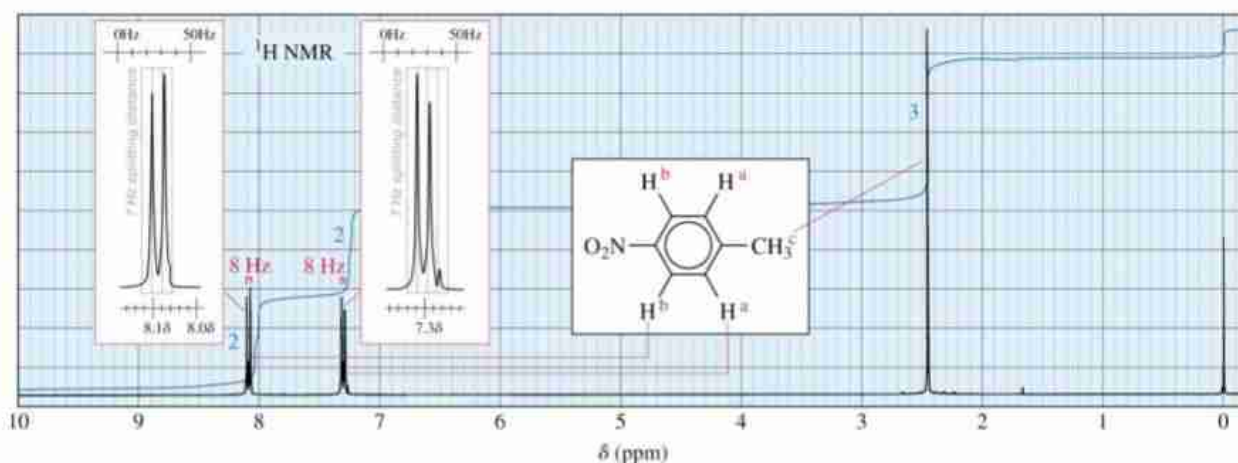**66. Which compound shows three signals (all singlets) in 1H NMR spectrum**

a)   b)   c)   d)   e)

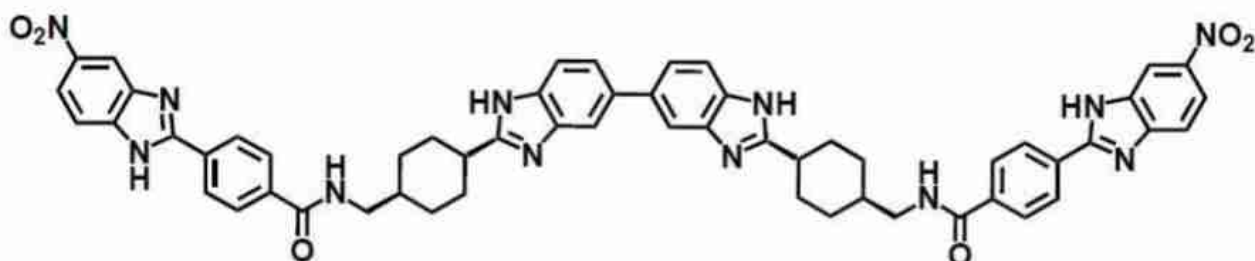**67.   Explain complex splitting in the following aromatic compound**

R-19M $C_7H_3Cl_3O$
270 MHz ^1H NMR Spectrum ($CDCl_3$)

40 30 20 10 0 Hz

8.2   8.1   8.0   7.9   7.8   7.7   7.6   7.5
ppm

9   8   7   6   5   4   3   2   1   0
ppm

68. Explain complex splitting in the following aromatic compounds.

^1H NMR

8 Hz   8 Hz

8.18 8.08

7.38

H^b H^a

O_2N—⬡—CH_3

H^b H^a

10   9   8   7   6   5   4   3   2   1   0
δ (ppm)

69. Using H-NMR; how many signal would expect this compound to show ?

O_2N NO_2

70. In the following spectra, explain all data you might know; chemical shift, splitting, integration and J-coupling.

300 MHz ^{1}H NMR in CDCl$_3$
Source: Aldrich Spectra Viewer/Reich
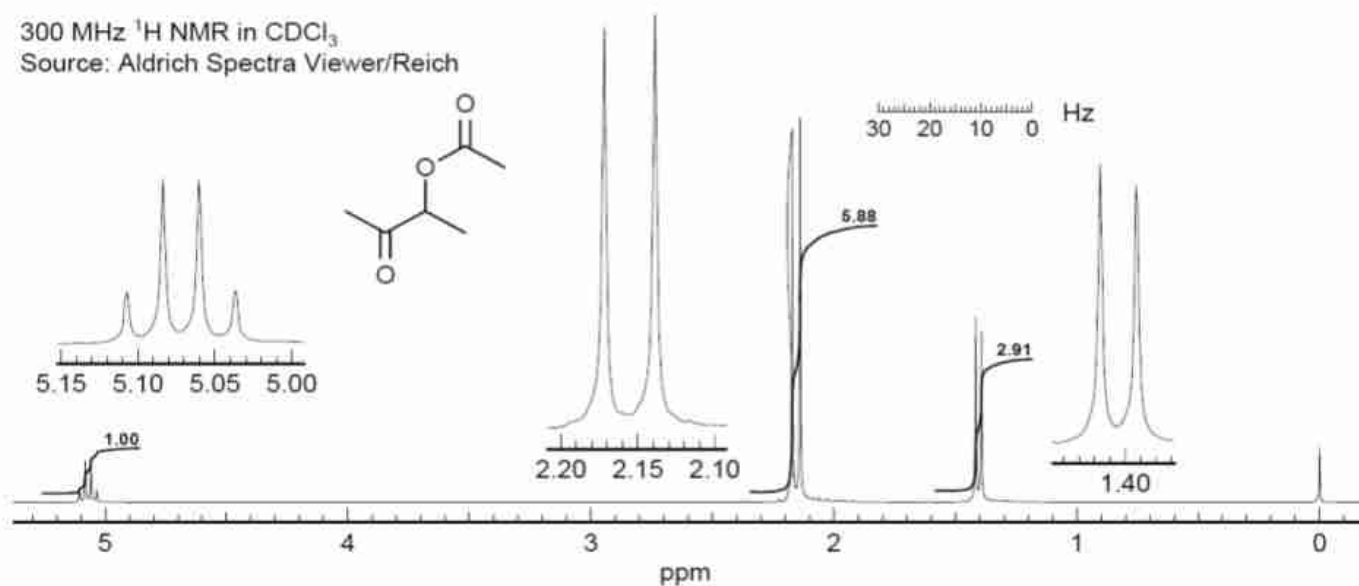
5.15 5.10 5.05 5.00

1.00

2.20 2.15 2.10

30 20 10 0   Hz

5.88

2.91

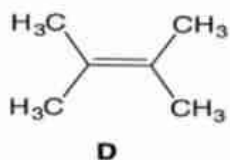1.40

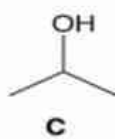5   4   3   2   1   0
ppm

71. Using both given spectrum and molecular formula to identify the unknown compound?

$C_3H_6O_2$

3H

2H

1H

12   11   10   9   8   7   6   5   4   3   2   1 PPM

72. Using both given spectrum and molecular formula to identify the unknown compound

9H

2H   2H

$C_{10}H_{14}O$

1H

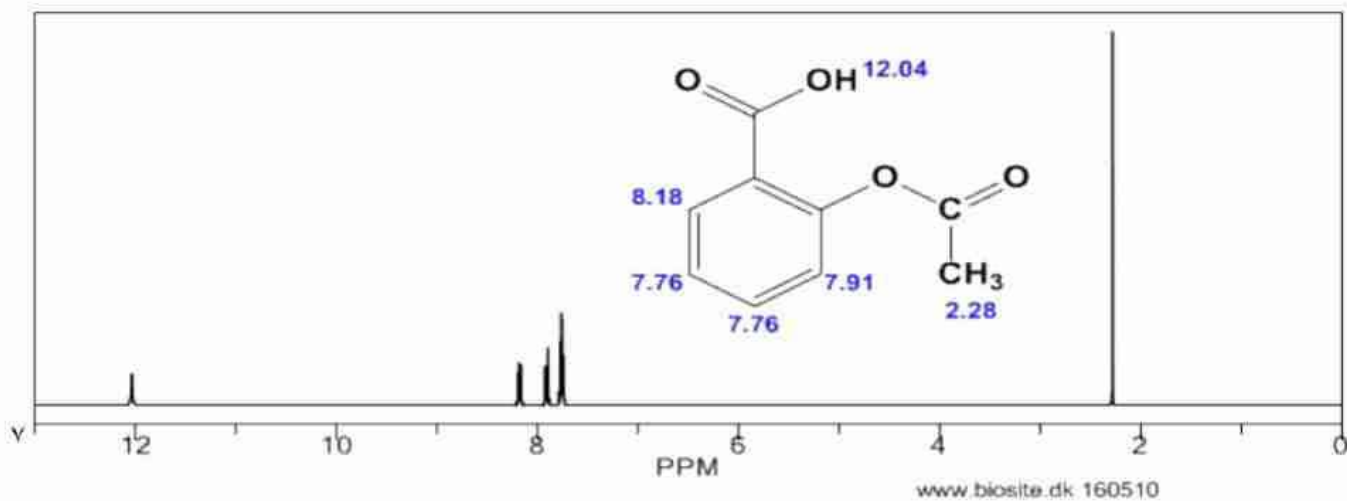8   7   6   5   4   3   2   1 PPM
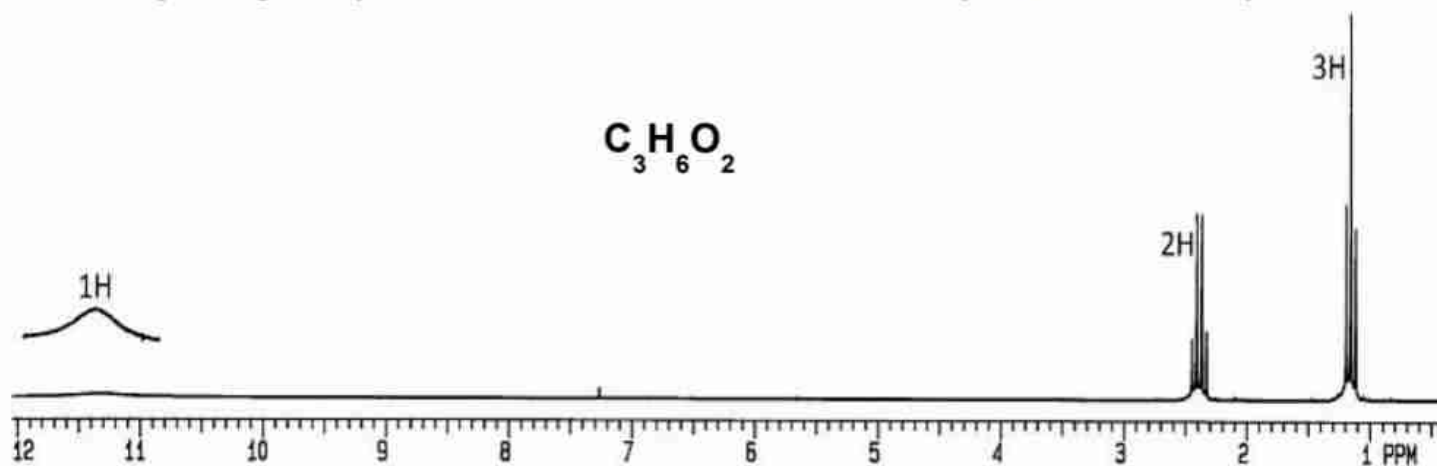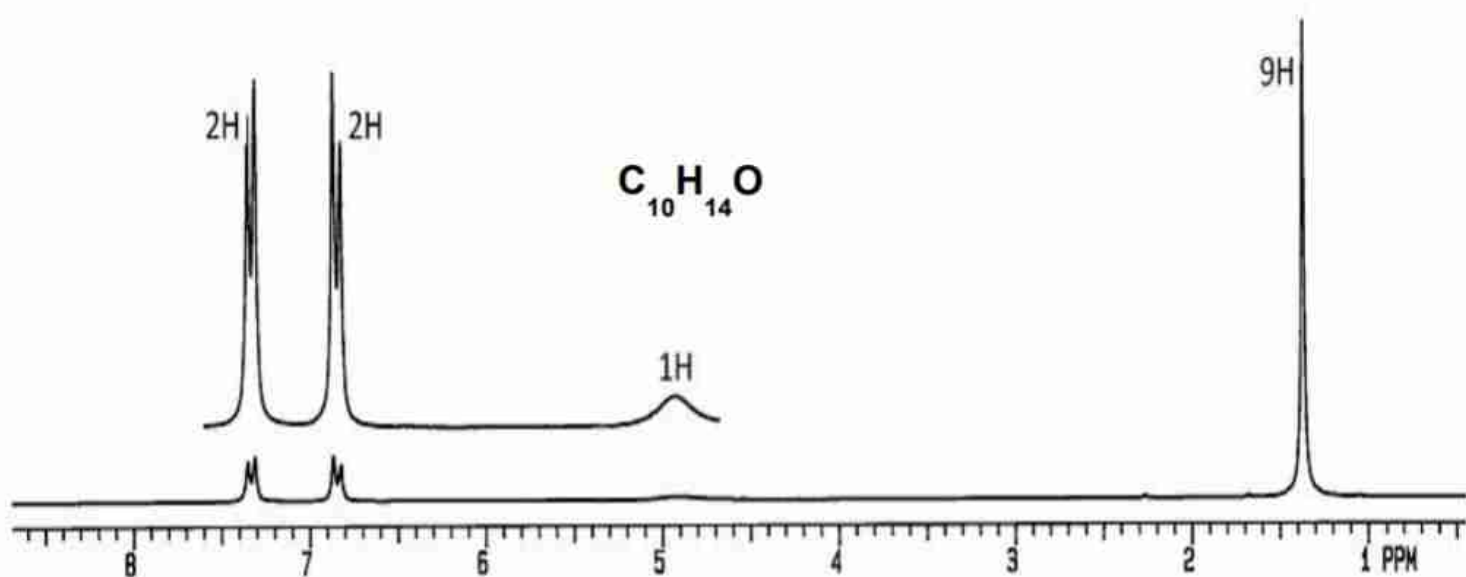
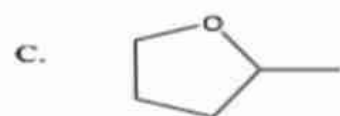**73.** Choose the letter corresponding to the appropriate molecule that matches the spectrum.
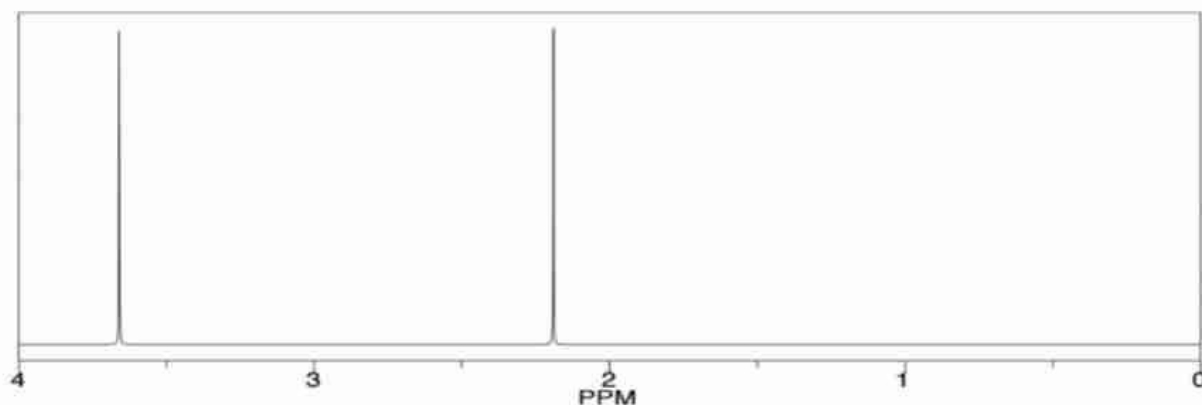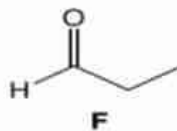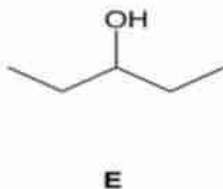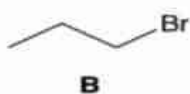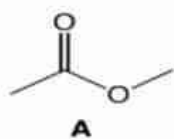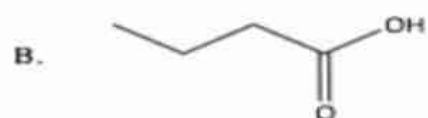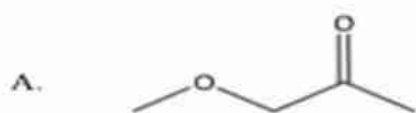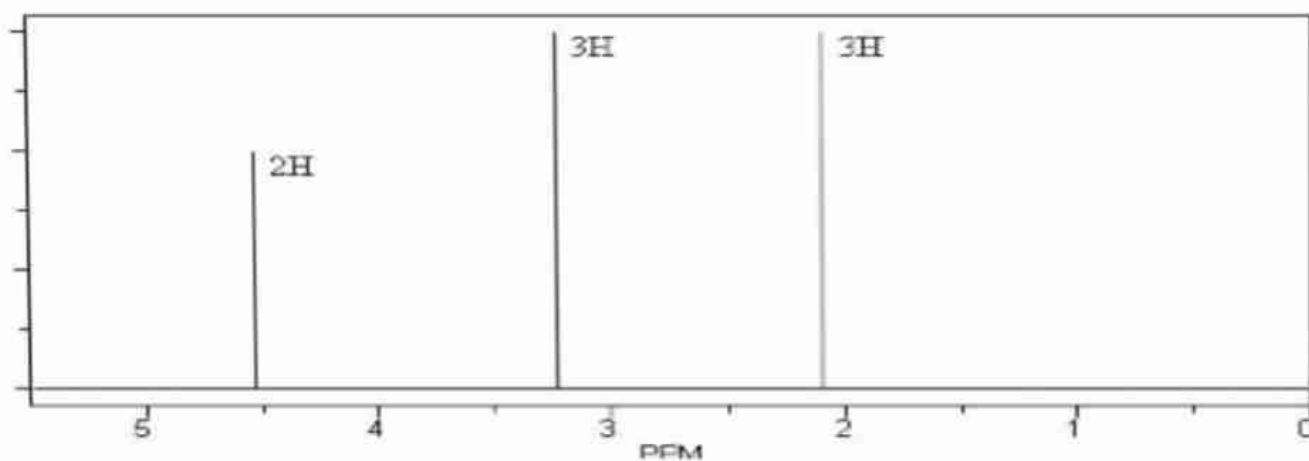

74. Discuss both simple splitting and chemical shift in the following ᵐ spectrum
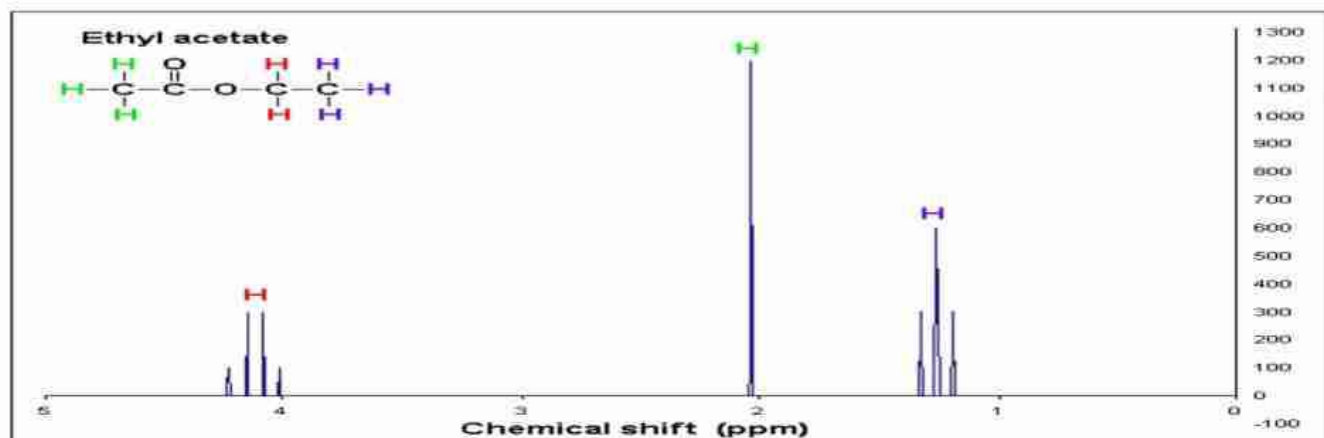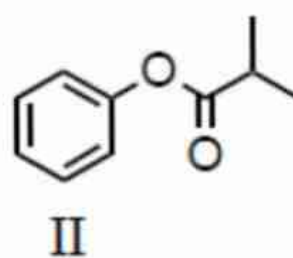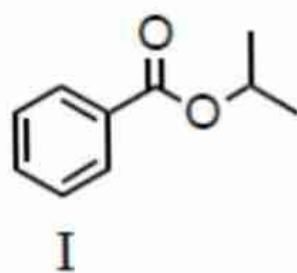

75. Discus in brief the aspirin NMR spectrum

www.biosite.dk 160510

76. Choose the structure that matches the given spectrum

3H   3H

2H

PPM

A.

B.   OH
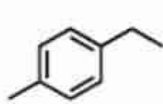
C.

D.

77. Using H-NMR; simply how can you distinguish between the following two isomers?
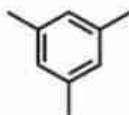

I   II

A

78. Determine the most likely structure of a compound, with the molecular formula C_9H_{12}, which gave a 1H NMR spectrum consisting of:
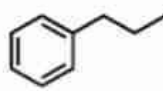   a) a doublet at 1.25 ppm
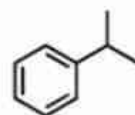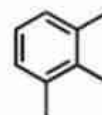   b) a septet at 2.90 ppm and
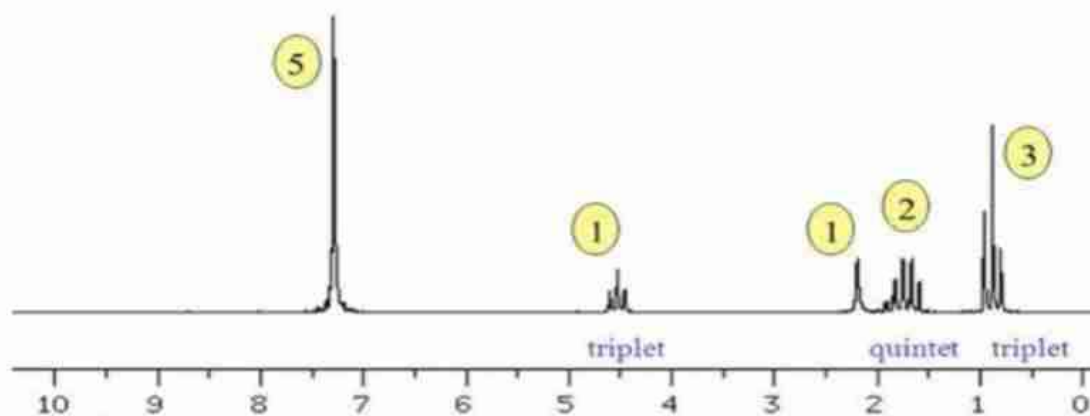   c) a multiplet at 7.25 ppm

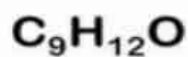I   II   III   IV   V

79. Using the below spectrum to propose a structure that has the given molecular formula;

$C_9H_{12}O$

triplet   quintet   triplet
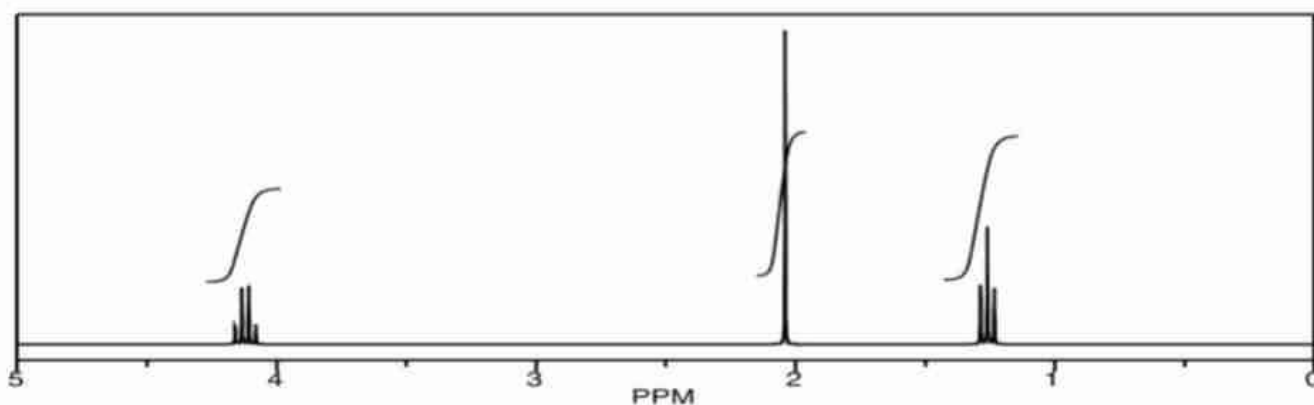
10 9 8 7 6 5 4 3 2 1 0

80. Looking at the 1H NMR spectra of the following compounds, indicate which peak belongs to which proton.

PPM

9

81. Discuss all related H-NMR terms

Phenacetin

picoSpin 80
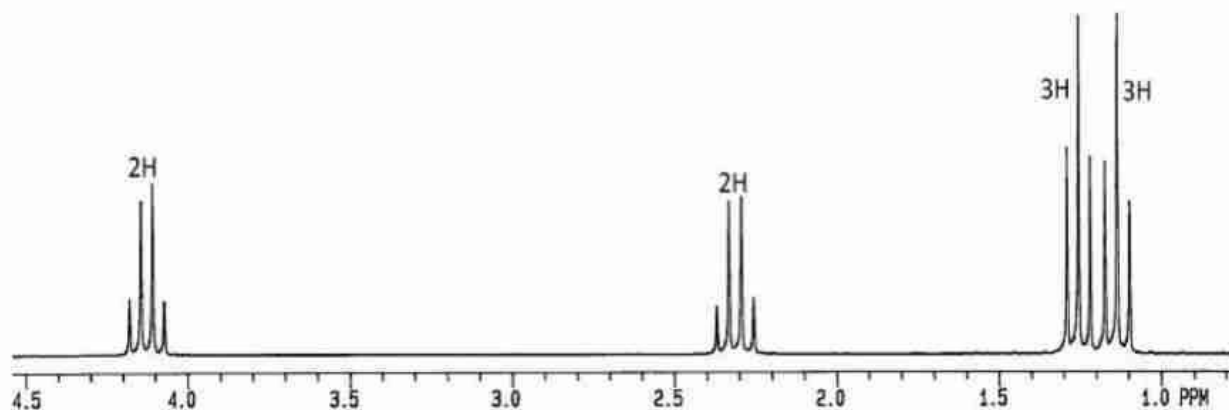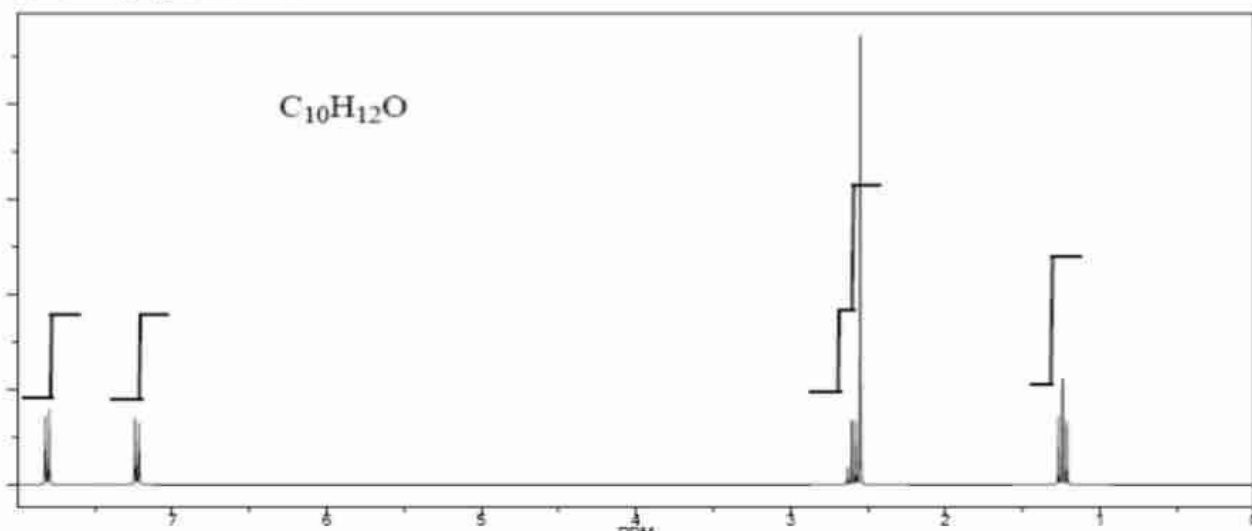1H NMR
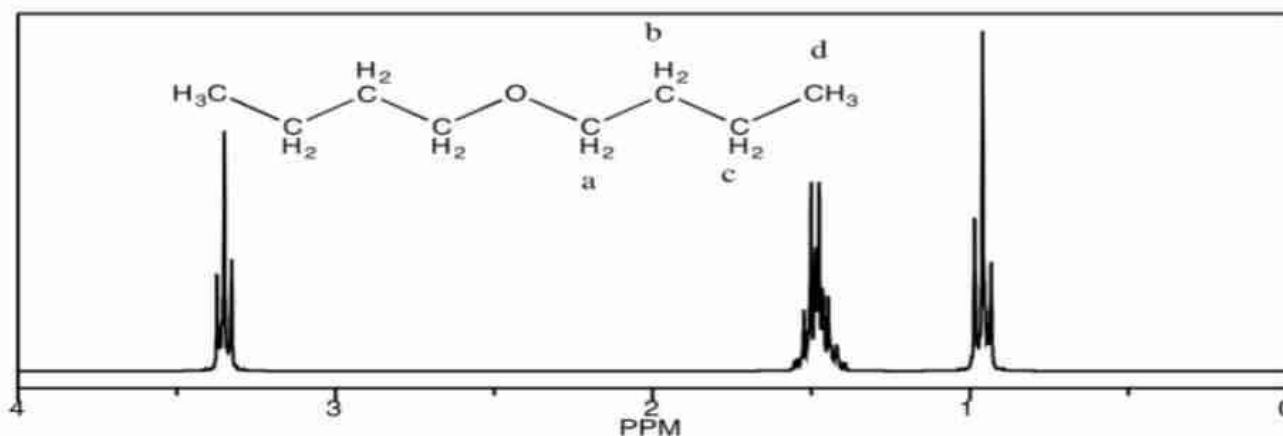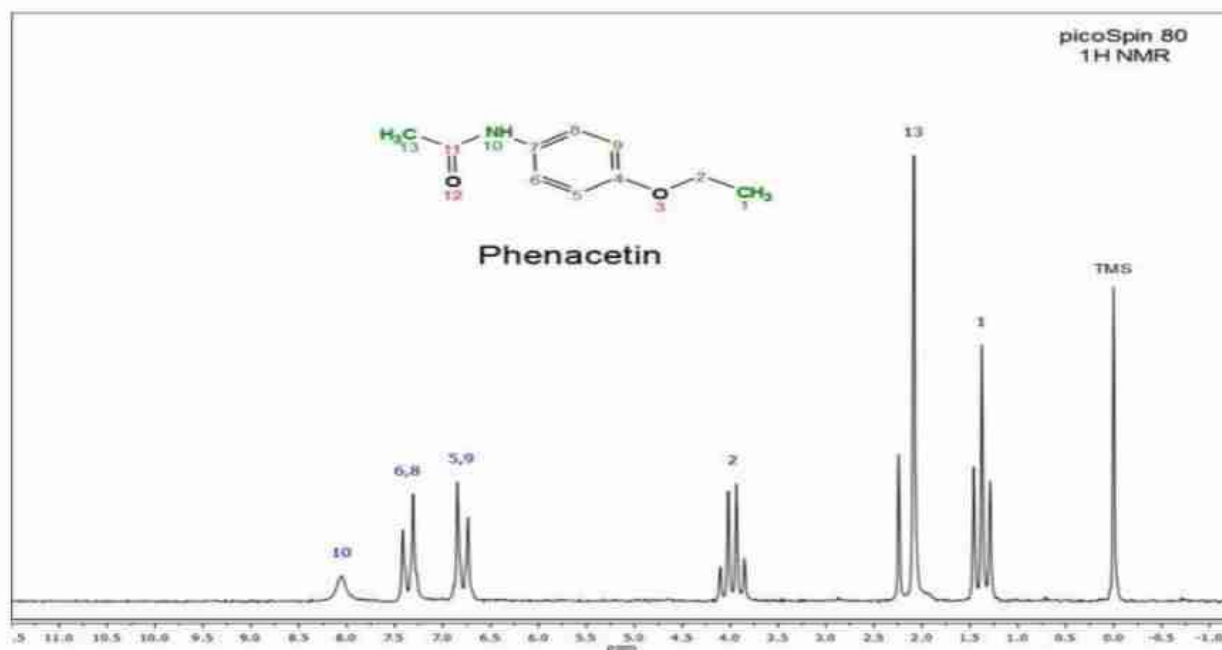
82. Predict the simple chemical structure of the molecular formula ($C_4H_8O_2$) that matches the following spectrum

PPM

83. Predict the simple chemical structure of the molecular formula ($C_5H_{10}O_2$) that matches the following spectrum ?

١.

84. Predict the simple chemical structure of the molecular formula $(C_{10}H_{12}O)$ that matches the following spectrum ?
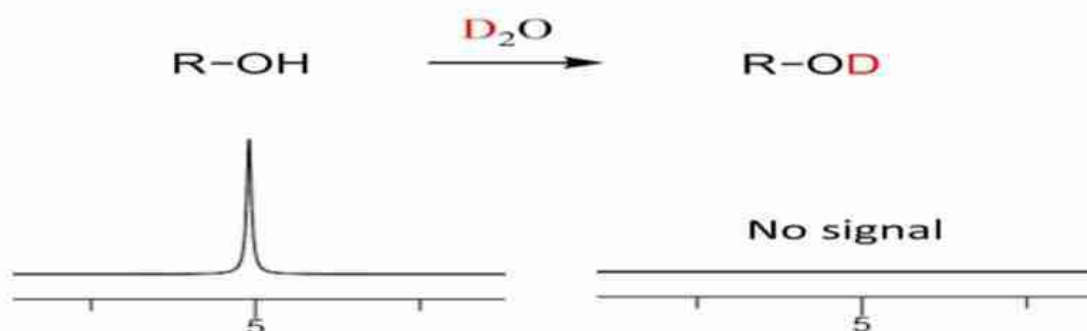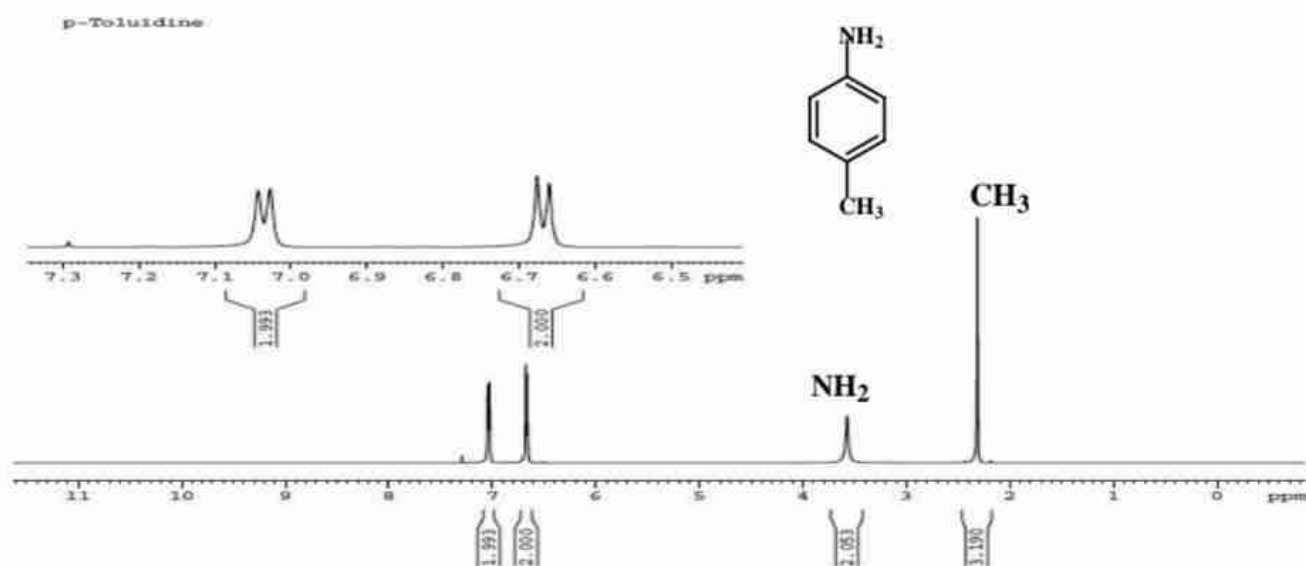
$C_{10}H_{12}O$

85. Correlate each signal to its hydrogen. Explain briefly

HSP-46-258

ppm

86. What does the following figure mean?

$$R-OH \xrightarrow{D_2O} R-OD$$

No signal

5

5

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87. Discuss all related H-NMR terms

p-Toluidine

7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6 6.5 ppm

NH₂

CH₃

NH₂

CH₃

11 10 9 8 7 6 5 4 3 2 1 0 ppm
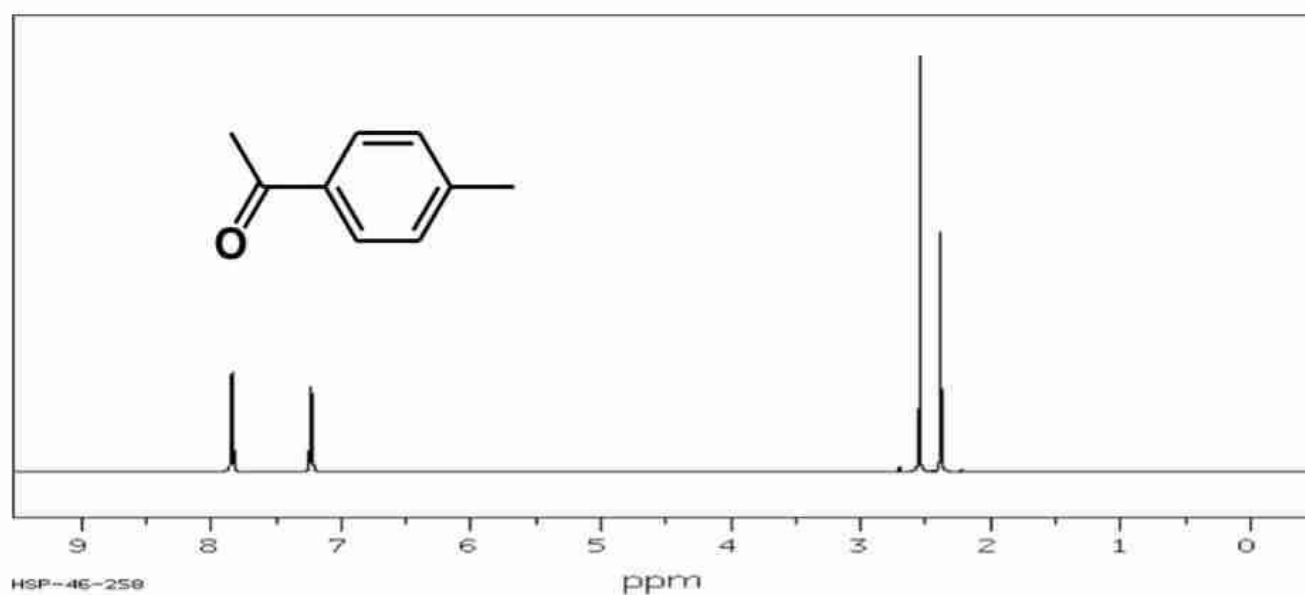
88. Analyze the following NMR spectrum for a molecule with the formula C₇H₇OBr. What is the structure of such compound?

+

9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
(ppm)
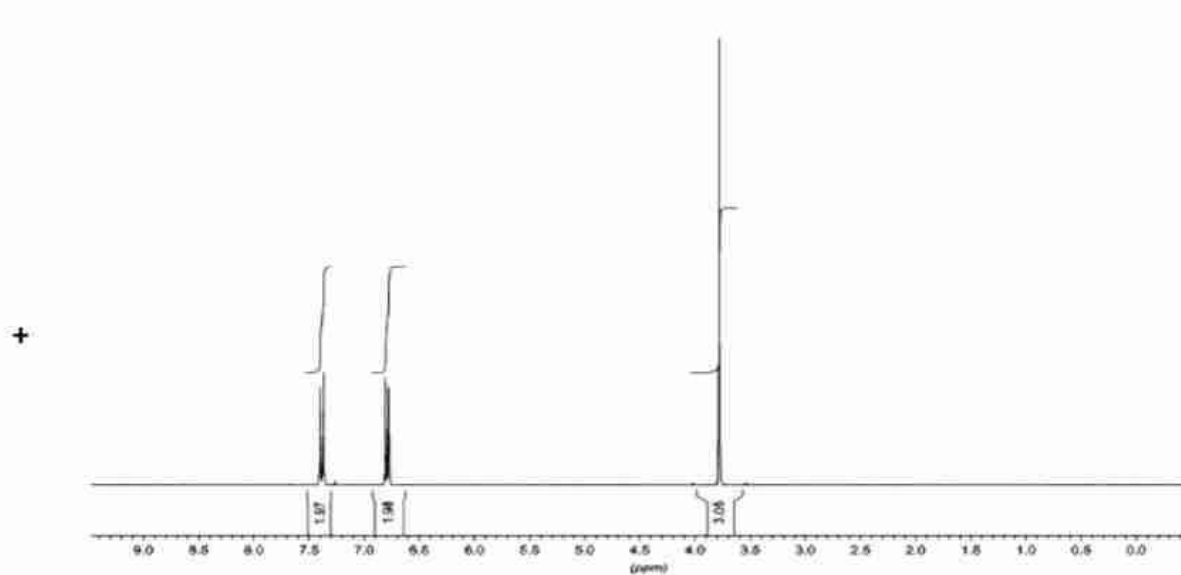
89. Given the following H-NMR spectrum for C₉H₁₀ formula; provide the structure for the compound that matches this spectrum (Note:- hydrogens in the spectrum as ratio)?

1H 1H

7.4 7.2 7.0 6.8 6.6 6.4 6.2 PPM

2H

1H

3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 PP

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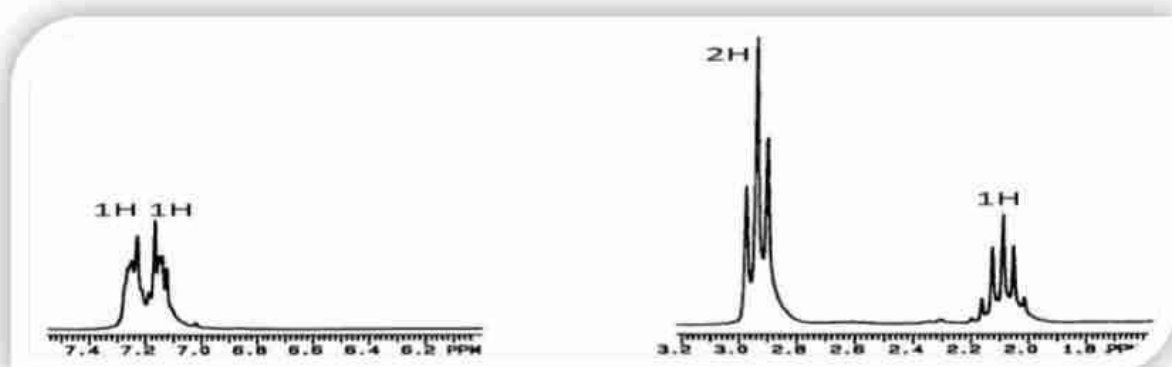
90. The 1H NMR spectrum of compound X (C$_2$H$_3$Cl$_3$) is shown below. Propose a structure for X.
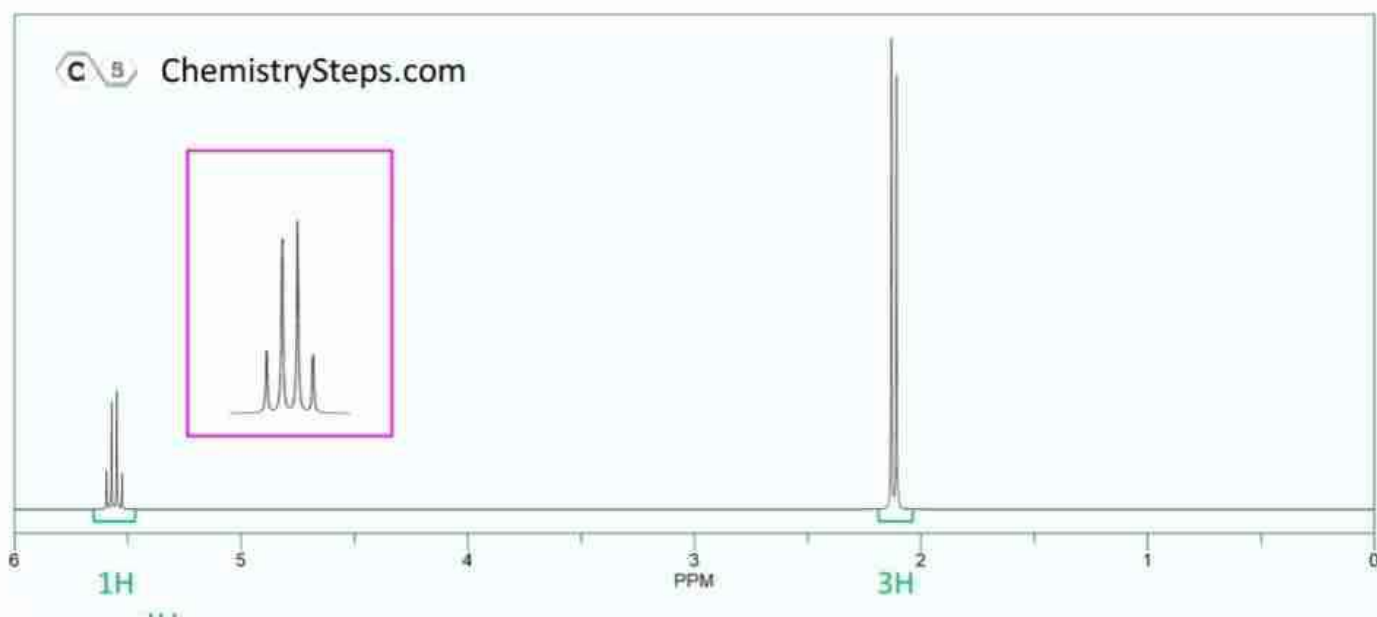
1H   2H   PPM
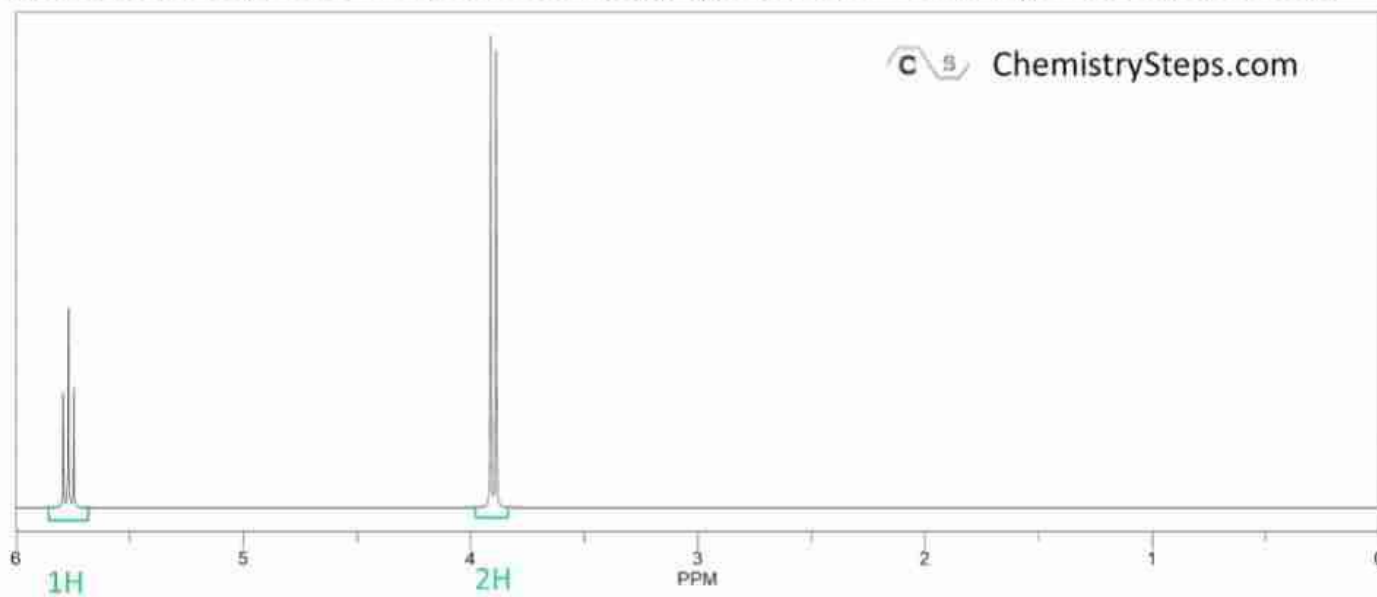
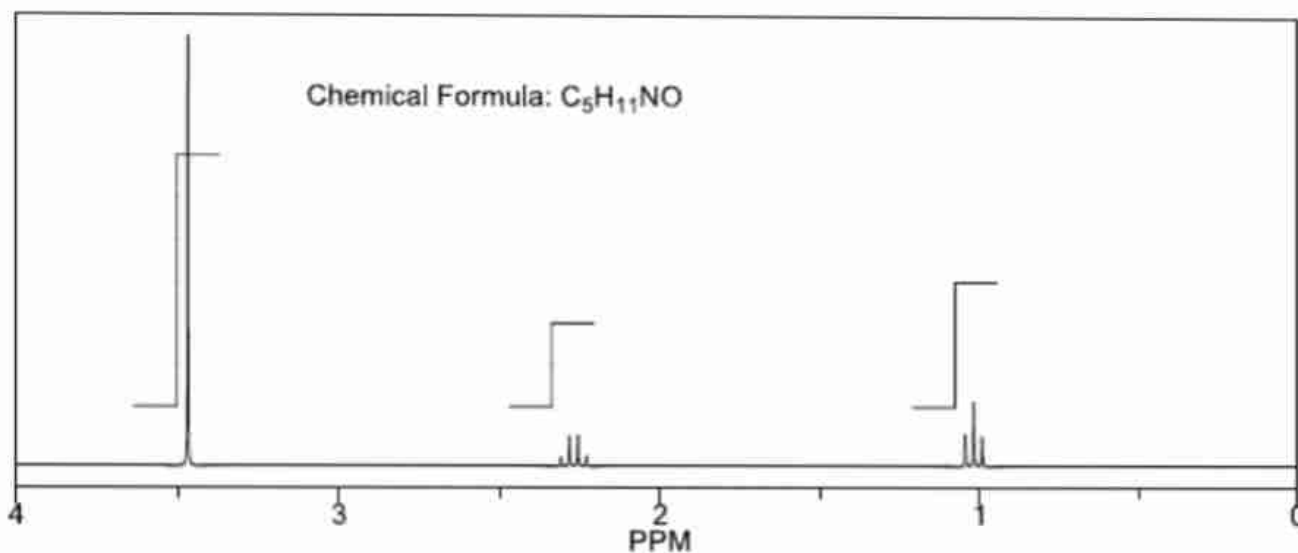**91.** The 1H NMR spectrum of compound X (C$_2$H$_4$Cl$_2$) is shown below. Propose a structure for X.

1H   PPM   3H

١٣

92. The 1H NMR of compound X ($C_9H_{10}O_2$) is shown below. Propose a structure for X.

ChemistrySteps.com

10   8   6   PPM   4   2   0

1H   2H   2H   2H   3H
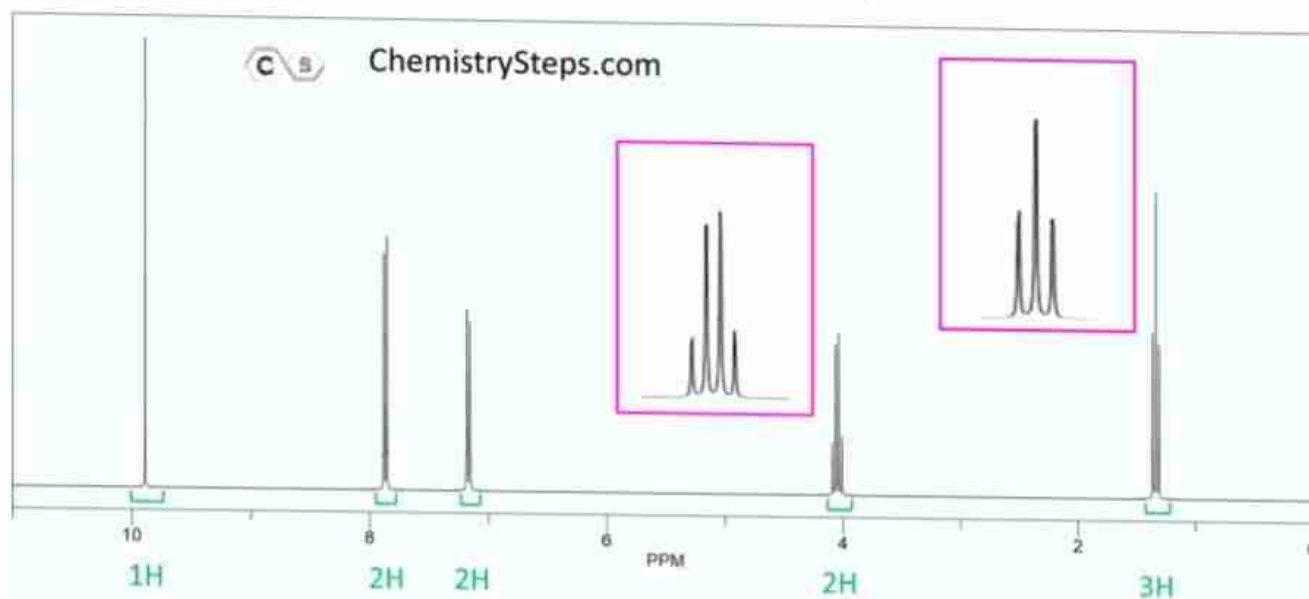
93. A compound with the molecular formula ($C_{10}H_{13}Cl$) gave the following 1H NMR spectrum:
singlet, 1.6 ppm , singlet, 3.1ppm   and   multiplet, 7.2 ppm (5H)
The most likely structure for the compound is:

I   II   III
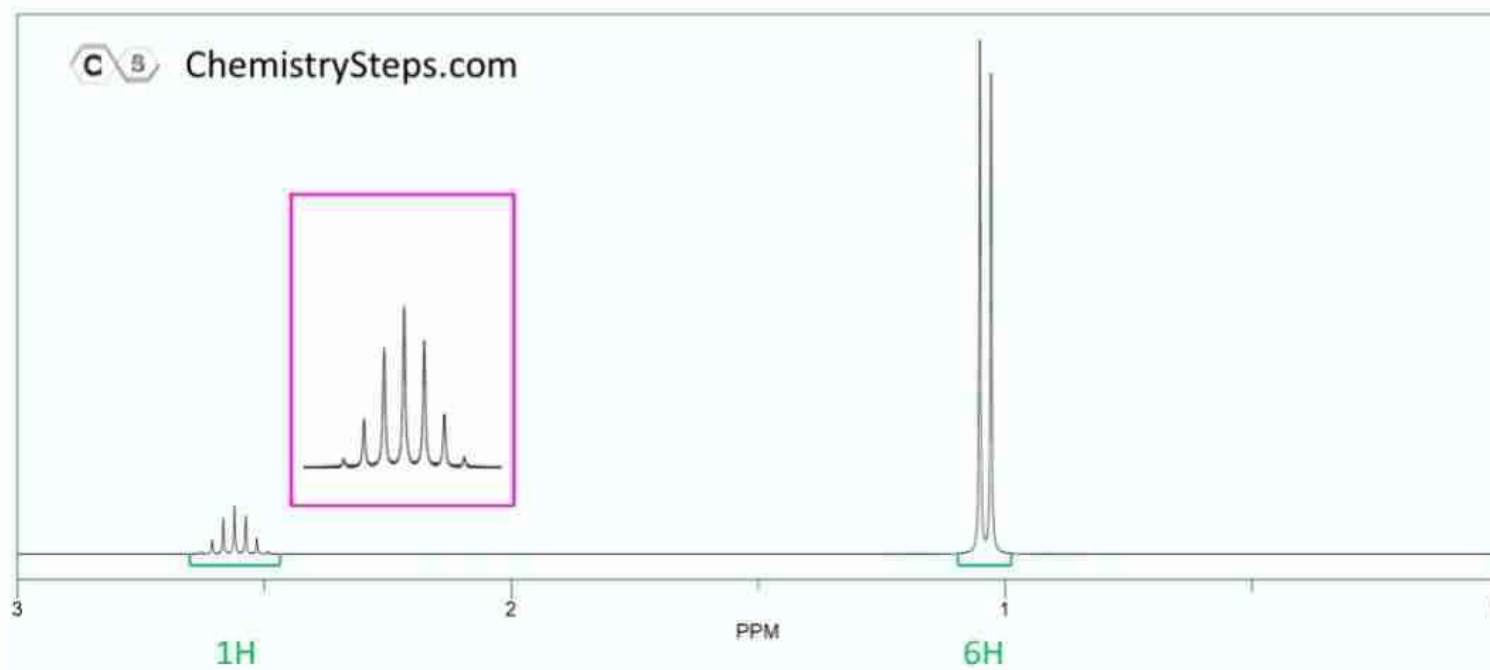
IV   V
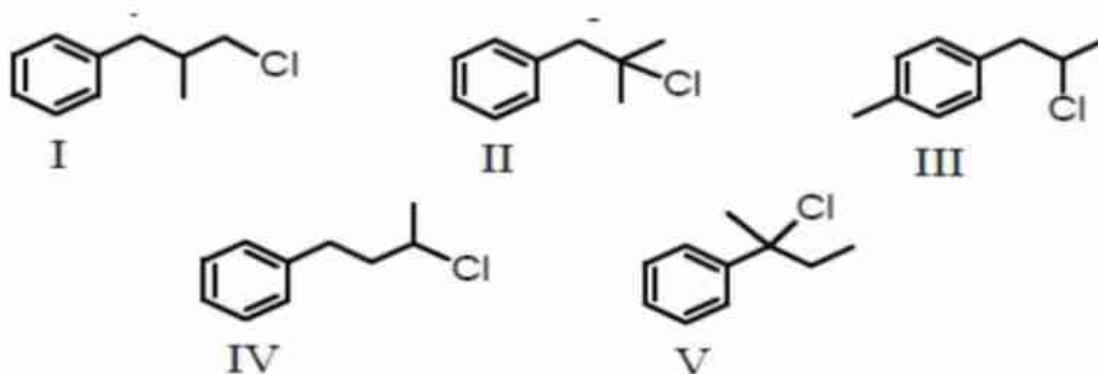
94. The 1H NMR spectrum of compound ($C_5H_{11}NO$) is shown below. Propose a structure for such formula.

Chemical Formula: $C_5H_{11}NO$

4   3   2   1   0
           PPM

95. The 1H NMR of compound X ($C_9H_{12}O$) are shown below. When the sample is mixed and shaken with an excess of deuterium oxide, the signal at 6 ppm disappears. Propose a structure for X.

ChemistrySteps.com

8   7   6   5   4   3   2   1
PPM

2H   2H   1H   1H   6H
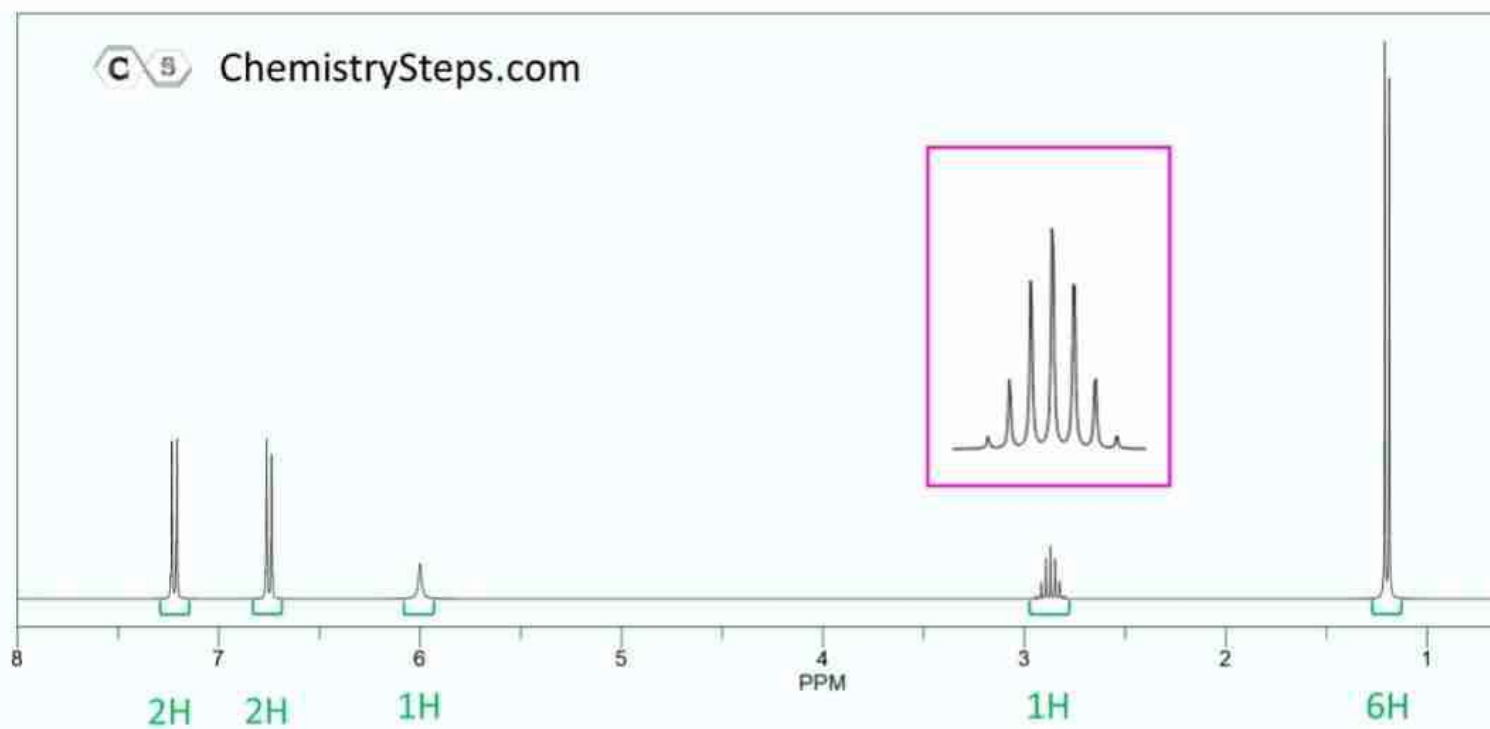
96. The 1H NMR of compound X ($C_7H_{14}O$) are shown below. Propose a structure for X.

ChemistrySteps.com

3   2   1
PPM

1H   6H

97. The 1H NMR spectrum of compound (C_4H_{11} N) is shown below. Propose a structure for such formula.

Chemical Formula: $C_4H_{11}N$

3H

2H

1H

2H

3H

PPM
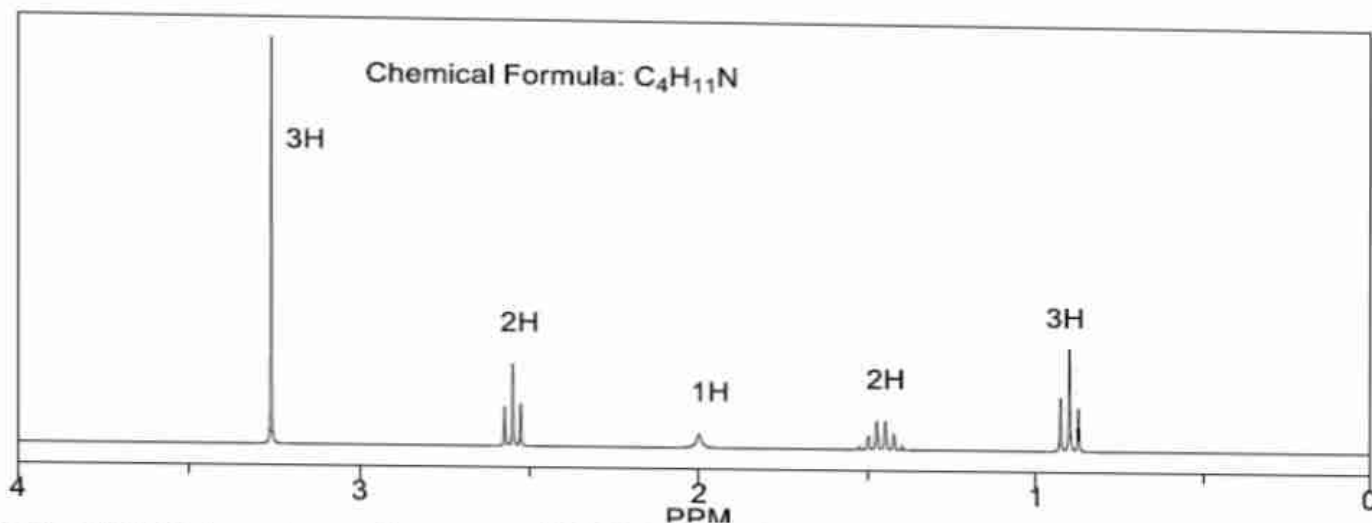
98. The 1H NMR spectrum of compound ($C_3H_7 NO_2$) is shown below. Propose a structure for such formula.

Chemical Formula: $C_3H_7NO_2$

3H (d)

2H (br s)   1H (q)

1H (br s)

PPM
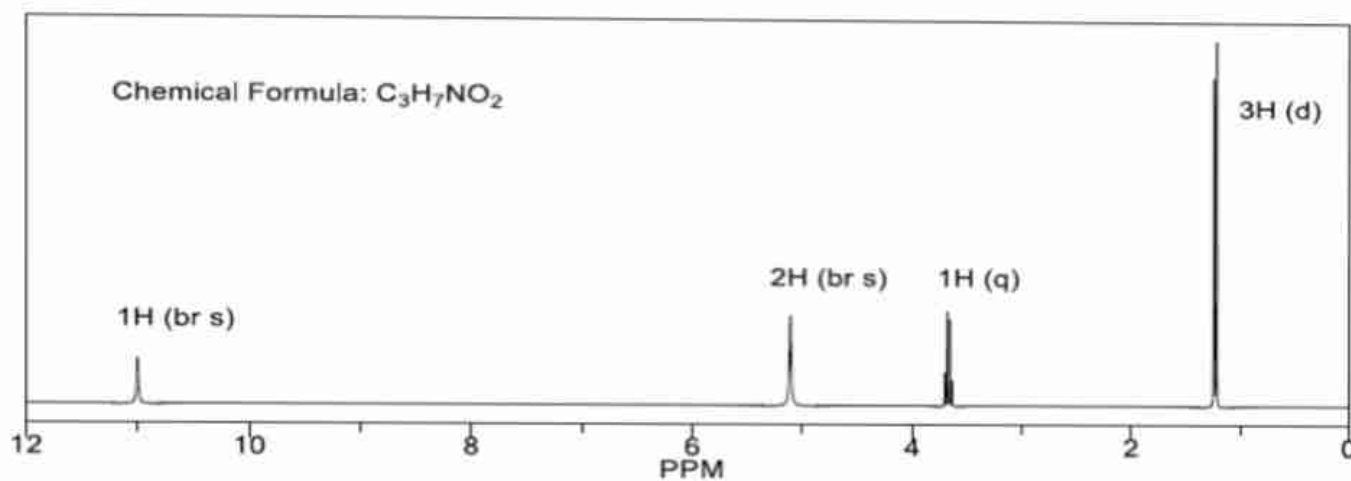
99. The 1H NMR spectrum of compound (C_3H_8 O) is shown below. Propose a structure for such

Chemical Formula: C_3H_8O

PPM
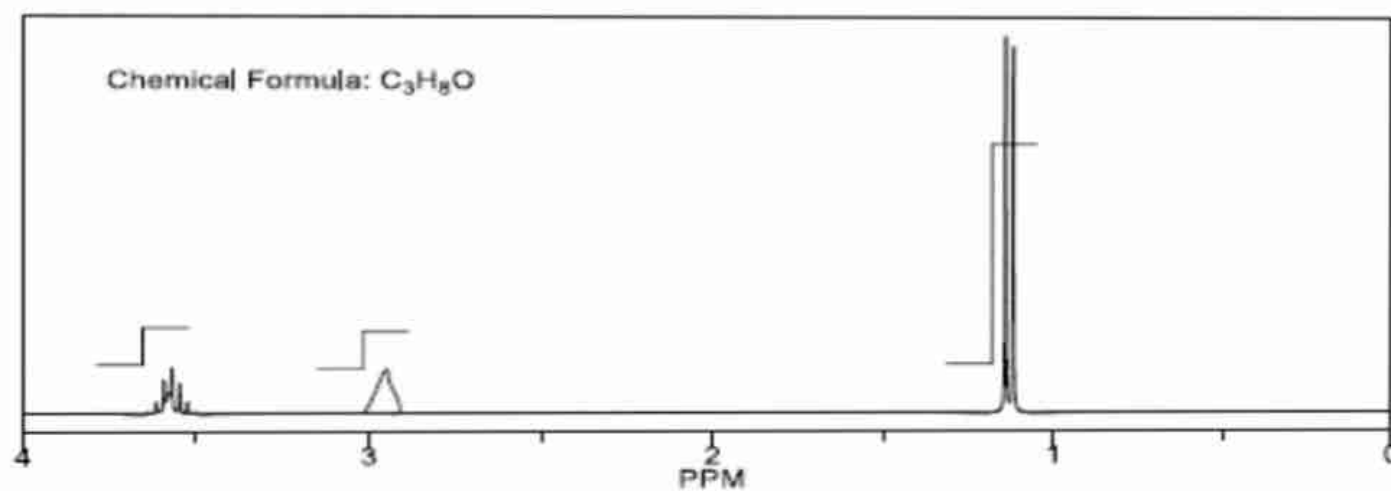
formula.

100. The 1H NMR spectra of two isomers of Butanol are shown below. Draw the structures of all the isomers for butanol and assign each spectrum to the correct isomer.