Anderson Serangoon Junior College
2025 H3 Chemistry
Nuclear Magnetic Resonance (NMR) Tutorial

1 (a) Outline in simple terms the principles of nuclear magnetic resonance.

[N2008/2b(i)]

In absence of magnetic field, the spin of the nucleus with odd proton number will oriented randomly. Once an **external magnetic field** is applied, they reorient their spin either **aligned with the field** or **against the field**. Orientation parallel to alignment of applied field is lower in energy that the one against the field.

When nuclei are irradiated with radiowave, the lower energy nuclei absorbed the photon and **flip to** the orientation with a **higher energy state**. These nuclei are said to be in resonance.

Nuclei in **different chemical environment** will have **different energy gap** between the two spin states and hence they will absorb the **radiowave** radiation at **different frequency**.

(b) Explain the use of each of the following in ^{1}H NMR spectroscopy:

- TMS
- Deuterated solvent
- D_2O

2015/2d(iii)

TMS is used as an internal reference as it is volatile and inert. The four carbon atoms attached to silicon in TMS are all equivalent. Silicon is more electropositive than carbon. Hence, the carbon are fairly electron-rich (or **shielded**), which means they resonate at frequency a little less than that of most organic compounds. Hence, it produces a strong singlet peak at a lower frequency than most ^{1}H absorptions in organic molecules, so its peak does not interfere with the other peaks. It will show a sharp singlet assigned δ = 0.The chemical shifts of protons are calculated using the difference between proton absorption frequency and that of TMS, divided by the irradiating frequency.

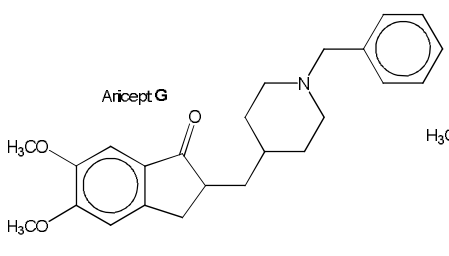
$$\delta_x = \frac{(frequency_x(Hz) - frequency_{TMS}(Hz))}{frequency_{TMS}(MHz)}$$

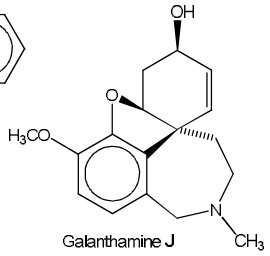
where δ_x
= chemical shift of proton x
$frequency_x$
= frequency of absorption of proton x
$frequency_{TMS}$
= frequency of absorption of the protons in TMS

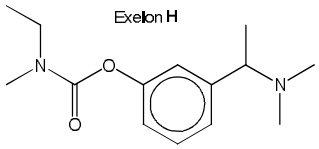
Deuterated solvent is used to dissolve the sample. Since the deuterium nuclei does not absorb in the same frequency range as ^{1}H nuclei, the solvent does not complicate the NMR spectra.

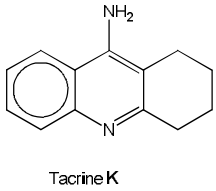
D_2O allows identification of labile protons. Rapid exchange with deuterium occurs, removing absorption peaks of labile protons from the NMR spectra.

2 The compounds below are competitive inhibitors of acetylcholinesterase. They can be used in treating people with Alzheimer's disease.







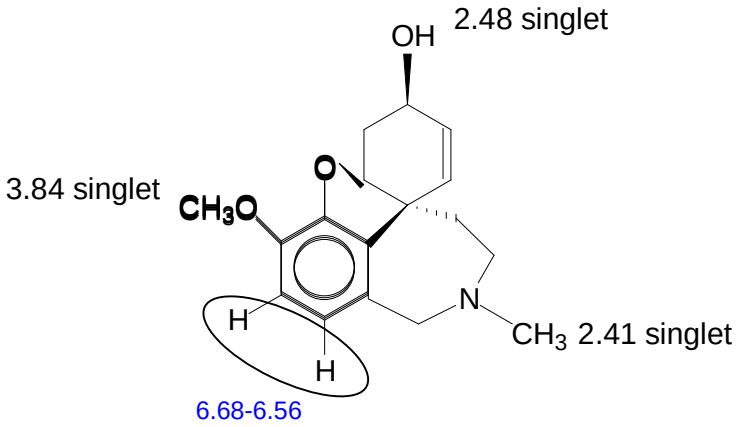


One of the four compounds above has the following NMR spectrum in CDCl_3 solution.

δ	6.68 – 6.56 (m 2H)	δ	3.30 (m 1H)
	6.07 (d 1H)		3.07 (m 1H)
	6.01 (m 1H)		2.69 (m 1H)
	4.62 (m 1H)		2.48 (s 1H)
	4.14 (m 1H)		2.41 (s 3H)
	4.11 (d 1H)		2.17 – 1.97 (m 2H)
	3.84 (s 3H)		1.59 (m 1H)
	3.70 (d 1H)		

(a) Identify the compound responsible for the above spectrum, and assign **four** of the signals to particular protons in the molecule. Give your reasoning.

Compound **J**



Chemical shift with integral number 3 suggests 2 non equivalent $-CH_3$ groups at 2.41 and 3.84. Chemical shift at 6.68-6.56 with integral number 2 suggest 2 aryl protons. Therefore, only compound J is valid.

Chemical shift at 3.84 suggest $-CH_3O$ since the C is bonded to the more electronegative O and chemical shift at 2.41 suggest $-N-CH_3$ where N is less electronegative

Only 1 H resonate at 2.48 as a singlet suggest it must be in the OH group where the labile proton undergoes rapid exchange with the water molecules, hence not able to couple with adjacent protons.

(b) Suggest why the addition of deuterium oxide (D_2O) to NMR samples allow the identification of labile protons. Identify the labile protons in compounds **G** to **K**.

[N2008/2b(ii)(iii)]

In the presence of D_2O, the D is able to exchange with the H in –OH in the following equilibrium system:

$ROH + D_2O \Leftrightarrow RO^- + HD_2O^+$

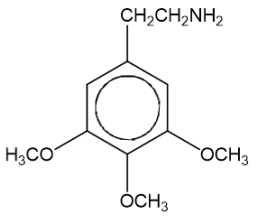
$RO^- + HD_2O^+ \Leftrightarrow ROD + HDO$

This leads the disappearance of the peak caused by labile H.

G and **H**: no labile H

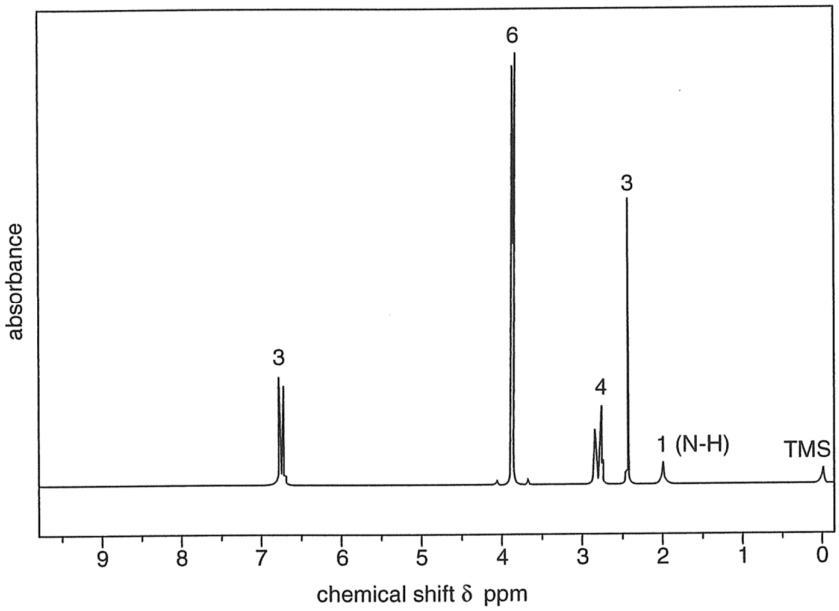
K: $-NH_2$ **J**: -OH

3 Mescaline is a hallucinogenic drug found in Mexican cacti.



Mescaline

Compound **A**, $C_{11}H_{17}NO_2$, is structurally related to mescaline. The NMR spectrum of compound **A** is given below. Deduce a structure for compound **A**, and explain your reasoning.



[N2007/3(e)]

The 1H NMR shows that there are 5 proton environments:

Chemical Shift ,δ ppm	multiplicity	No. of proton	Inference
2	Singlet	1	-N**H**
2.4	Singlet	3	-C**H**$_3$ adjacent to -NH
2.75	Doublet or 2 s	4	2x -C**H**$_2$ attached to benzene ring
3.8	Doublet Or 2 s	6	2 x -C**H**$_3$ adjacent to electronegative atom O
6.75	doublet	3	-C**H** in a benzene ring at 2,4 and 6 position

The structure is