

Lec 3

5th stage

**Advanced Pharmaceutical Chemistry
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Boltzmann distribution in NMR-effect of field strength and temperature

In B_0 the nuclei divide themselves between two energy levels (spin 1/2 nuclei). The relative numbers of nuclei occupying each level (once thermal equilibrium has been achieved) can be calculated according to Boltzmann distribution law. It is clear that, for net absorption to occur there must be more particles in the lower energy state than in the higher energy state. So we can calculate from the Boltzmann law the relative number occupy each level. The Boltzmann law is

number of nuclei in the upper state (β -state)

$$\frac{N_{(\beta)\text{upper}}}{N_{(\alpha)\text{lower}}} = e^{-\Delta E/kT} = e^{-h\nu/kT}$$

1.380 $\times 10^{-23}$ JK⁻¹ (Boltzmann constant)

Absolute temperature (T)
($^{\circ}\text{C} + 273$)

number of nuclei in the lower state (α -state)

$$e^x = 1 + x$$

Example:- At 25 °C what fraction of ^1H nuclei in 5.87T field are in the upper and lower states?

$$\Delta E = h\nu = 250035828 \times 6.63 \times 10^{-34} = 1.66 \times 10^{-25} \text{ J}$$

$$\frac{N_{(\beta)\text{upper}}}{N_{(\alpha)\text{lower}}} = e^{-\Delta E/kT} = e^{-h\nu/kT}$$

$$\frac{N_{(\beta)\text{upper}}}{N_{(\alpha)\text{lower}}} = e^{-1.66 \times 10^{-25} \text{ J} / 1.380 \times 10^{-23} \text{ JK}^{-1} \times 298 \text{ K}} = 0.99996$$

since there are only two spin states,

$$N_{(\beta)\text{upper}} = 1 - N_{(\alpha)\text{lower}}$$

So

$$\frac{1 - N_{(\alpha)\text{lower}}}{N_{(\alpha)\text{lower}}} = 0.99996$$

$$N_{(\alpha)\text{lower}} = 0.50001$$

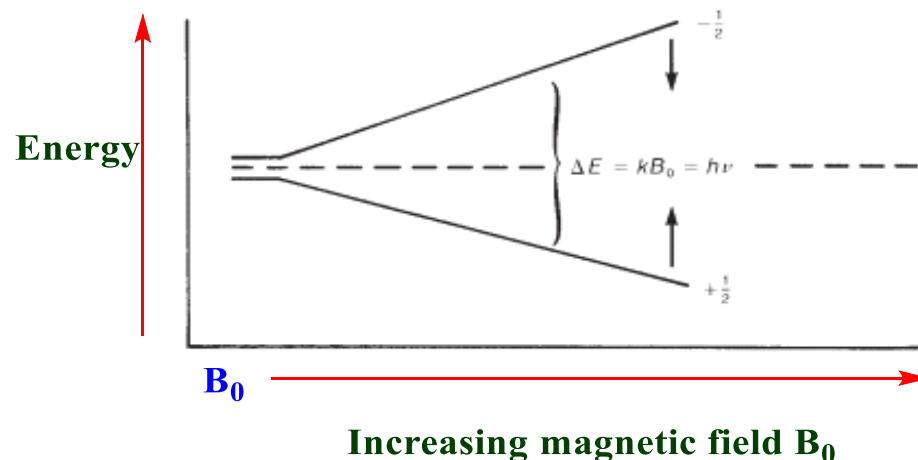
$$N_{(\beta)\text{upper}} = 1 - 0.50001 = 0.49999$$

$$\begin{aligned} \text{differences} &= 0.50001 - 0.49999 \\ &= 20\text{ppm} \end{aligned}$$

every million nuclei in the higher energy state (for protons at 25°C in a 5.87 T magnet) there is an excess of only 20 in the lower energy state (an excess of 20 ppm). And difference for other elements is even smaller because of their smaller γ value.

If the populations of the upper and lower states become exactly equal, we observe no net signal. This situation is called saturation. Therefore, the very small excess of nuclei in the lower spin state is quite important to NMR spectroscopy, and we can see that very sensitive NMR instrumentation is required to detect the signal. If we increase the operating frequency of the NMR instrument, the energy difference between the two states increases, which causes an increase in this excess.

Following table shows how the excess increases with operating frequency.



The spin-state energy separation as a function of the strength of the applied magnetic field B_0 4

Variation of ^1H Excess nuclei with operating frequency

Operating frequency (MHz)	^1H Excess nuclei
20	3
40	6
60	9
80	12
100	16
200	32
300	48
600	96

It also clearly shows why modern instrumentation has been designed with increasingly higher operating frequencies. The sensitivity of the instrument is increased, and the resonance signals are stronger, because more nuclei can undergo transition at higher frequency. Before the advent of higher-field instruments, it was very difficult to observe less-sensitive nuclei such as carbon-13, which is not very abundant (1.1%) and has a detection frequency much lower than that of hydrogen.

Number of signals

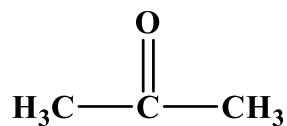
The number of signals in the NMR tells the number of different sets of equivalent protons in a molecule. Each signal corresponds to a set of equivalent protons. It may be noted that magnetically equivalent protons are chemically equivalent proton.

Chemically equivalent protons: - are protons in identical electronic environments, and have the same value of chemical shift in NMR spectroscopy.

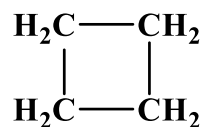
Chemical equivalent → chemical shift equivalent

Magnetically equivalent → coupling equivalent

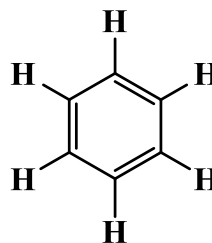
Compounds showing one signal



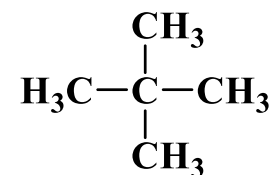
Acetone
one signal



Cyclobutane
one signal



Benzene
one signal



Tetramethyl methane
one signal

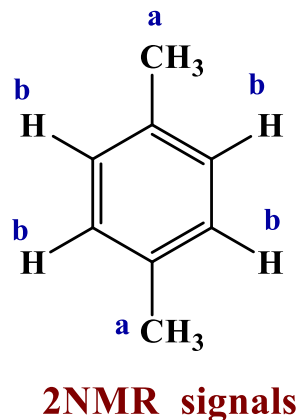
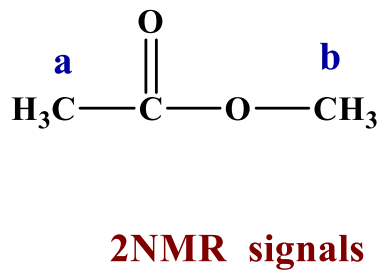
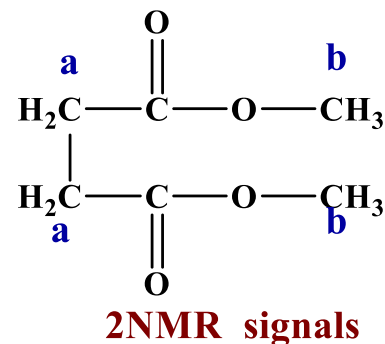
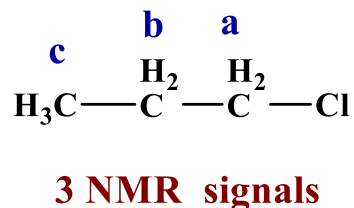
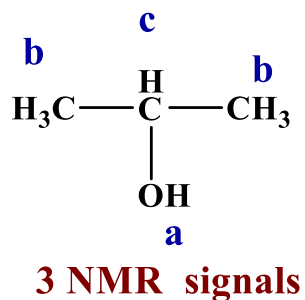
Molecule signal

TMS signal



Compounds showing more than one signal

Compounds showing more than one signal, a molecule that has sets of protons that are chemically distinct from one another may give rise to a different absorption peak from each set, in which case the sets of protons are chemically nonequivalent



Chemically equivalent protons must also be stereo chemically equivalent, particular set of protons are said to be chemically equivalent only if they remain in exactly similar environment when the stereo-chemical formula of the molecule under consideration is written



2-chloropropene

from this structure, one can expect two set of equivalent proton (two signals).

But stereochemical formula reveals three sets of protons in it.

H^b and H^c are not in exactly similar environment

3 NMR signals

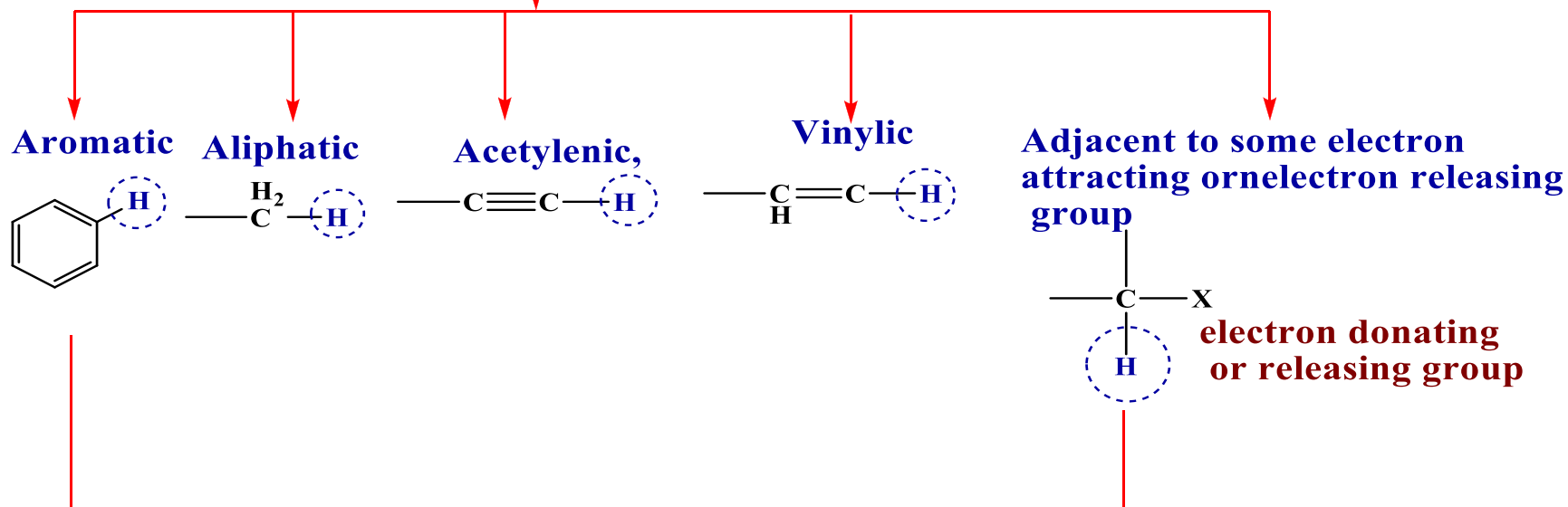
Positions of signals (Chemical shift)

The number of signals in the NMR → the number of sets of equivalent protons in a molecule

The positions of signal in the spectrum

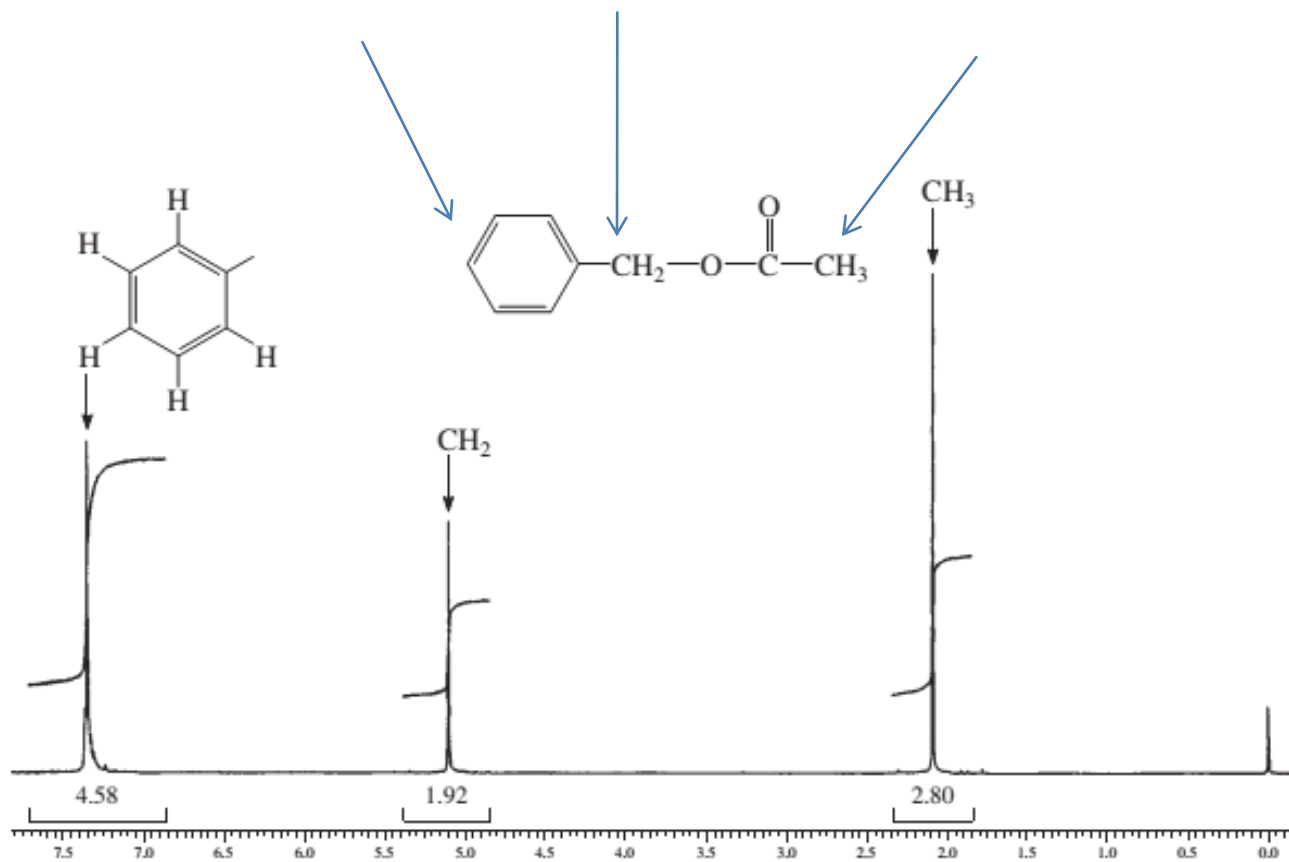
help us to know

Nature of proton



Each of these types of protons will have different electronic environments and thus, they absorb at different applied field strength

It is important to note that it is electronic environment which tells where a proton shows absorption in the spectrum.



The ^1H NMR spectrum of benzyl acetate (300 MHz)