Student Corner

Introduction to NMR Spectroscopy

K. Sarath D. Perera

Senior Professor in Chemistry, Department of Chemistry, The Open University of Sri Lanka

Nuclear Magnetic Resonance spectroscopy is probably the most powerful tool available for structure determination of organic, inorganic and organometallic compounds. It is also used by chemists to study mechanisms, molecular interactions, rates of chemical reactions and to identify intermediates formed during reactions.

Magnetic properties of nuclei

Over fifty isotopes of the elements in the Periodic Table are NMR-active. Elements with **nuclear spin (I)** greater than zero are called NMR active nuclei. The numerical value of **I** is related to the atomic number (Z) and the mass number (A) as follows.

A	Z	I	Examples
odd	even or odd	$\frac{1}{2}, \frac{3}{2}, \frac{5}{2}$	$^1H, ^{13}C, ^{19}F, ^{31}P, ^{11}B, ^{103}Rh, ^{195}Pt$
even	even	0	$^{12}C, ^{16}O, ^{32}S, ^{194}Pt$
even	odd	1, 2, 3	$^2H, ^{14}N, ^{10}B$

These NMR-active nuclei behave like *magnets* in an applied magnetic field (B_o) and will have (2I+1) orientation ranging from +I to –I. These are called *magnetic quantum numbers* ($\mathbf{m_I}$). For example, when a nucleus with a nuclear spin of ½ is placed in an applied magnetic field (B_o), it can have two orientations; the low-energy α-state ($m_I = +½$) and the high-energy β-state ($m_I = -½$) in which the nuclear magnetic moment is aligned anti-parallel to the external field.

The energy difference between α and β levels is related to the **operating frequency** (ν) of the spectrometer and $\mathbf{\gamma B_o = 2\pi v}$. ν is directly proportional to the applied magnetic field Bo. γ is the gyromagnetic ratio and it is a constant for a given isotope.

Quadrupolar nuclei

Nuclei with I ≥ 1 can possess an additional nuclear electric quadrupole moment because the positive charge distribution within the nucleus is not uniform. As a result, these nuclei relax very fast *via* spin-lattice relaxation, thus, spectral lines become very broad or non-observable.

Chemical shifts

NMR-active nuclei in a molecule experience different *local magnetic fields* due to varying electron densities around them. A nucleus in a particular chemical environment is characterized by a **chemical shift** (δ) with respect to a reference (or standard). The chemical shift of a sample is defined in terms of δ as given below.

$$\delta = \frac{v_{sample} - v_{reference}}{operating\ \ frequency} \times 10^6 \text{ ppm}$$

The chemical shift of the reference is taken as zero, δ = 0 ppm.

δ is a dimensionless quantity **independent** of the applied magnetic field. Chemically equivalent nuclei give rise to one NMR signal at a specific δ value. *i.e.* they are **isochronous**.

The reference compound used can either be an internal or an external compound depending on the way it is used during the analysis. The references used for some common NMR-active nuclei are given below.

Nuclei	Reference
$^1H, ^{13}C, ^{29}Si$	TMS
^{19}F	$CFCl_3$
^{31}P	85% aq. H_3PO_4
^{11}B	$Et_2O \cdot BF_3$
^{17}O	Water
$^{14}N, ^{15}N$	Liquid NH_3
^{195}Pt	$Na_2[Pt(CN)_6]$

Shielding and deshielding effect

The shielding and deshielding effects depend on the

electron density around a nucleus. The electron density around a nucleus depends on the electron donating / withdrawing ability of the other nuclei attached to it. A nucleus is said to be **shielded** when its electron density is increased, whereas **deshielding** is caused due to the reduction of electron density. The orientation of electrons around the nucleus generates a counter magnetic field, which opposes the applied magnetic field. Thus shielding (or screening) of a nucleus by surrounding electrons reduces the total influence of the applied magnetic field.
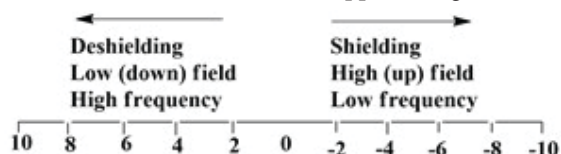
If the nucleus is shielded, it absorbs radio frequency radiation with a lower energy (low frequency), giving rise to a lower (more negative) chemical shift (δ) in ppm.

The trend in chemical shifts can be easily explained by considering the proton chemical shifts of methyl halides as given in Table 1.

The electronegativity (**EN**) decreases in the following order F > Cl > Br > I. Accordingly, substituents on carbon reduce the electron density around the methyl protons of halomethanes.

Table 1: Relationship between EN and δ_H of CH_3X

	X	EN	δ_H
	H	2.1	0.23
	I	2.5	2.16
CH_3X	Br	2.8	2.68
	Cl	3.1	3.05
	F	4.0	4.26
TMS	Si	1.8	0.00

The methyl protons in CH_3F are the **most deshielded** and give the highest chemical shift of 4.26 ppm.

Similarly, the proton chemical shifts of CH_3Cl, CH_2Cl_2 and $CHCl_3$ are 3.05, 5.30 and 7.27 ppm, respectively. The chemical shifts have been increased due to the higher deshielding effect imposed by the increase of electronegative substituents.

A proton attached to a transition metal centre is significantly shielded by the d-electrons present in the valence shell and metal **hydrides** show **negative** chemical shifts.

Intensity of peaks (Integration)

Generally, the peak intensity resembles the number of chemically equivalent nuclei present in a given compound and it is very helpful in structure elucidation. However, it is not always possible to determine the number of nuclei in a particular environment by calculating the intensities of peaks. Particularly, in a carbon-13 NMR spectrum, the intensities of different carbon atoms (e.g. primary, secondary, tertiary and quaternary) depend on the number of protons attached to a particular carbon due to the varying rates, at which these nuclei return to the ground state. The quaternary carbon atoms relax much slower resulting in weak signals.

Spin-spin coupling

The interaction between magnetically non-equivalent nuclei which are from the same compound will lead to spin-spin coupling. As a result of this phenomenon, single peaks turn into doublets, triplets, quartets *etc*.

Multiplicity is simply the splitting of single peaks due to spin-spin coupling. Apparently, it is determined by the relationship **2nI+1** where, n = number of isochronous nuclei coupled and I = nuclear spin of the coupled nuclei.

Pascal's triangle gives the relative intensities of the (n+1) lines of A in an AX_n spin-system where I of X is equal to ½.

Fig. 1 Pascal's triangle

Some spectra picturing the relative intensities of (**2nI+1**) line(s) in a **multiplet** of A, in an AX_n spin system are given below, I of X equals to ½, 1 or ³⁄₂.
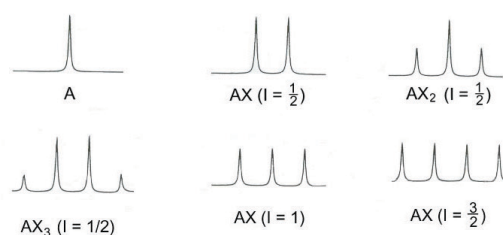
Fig. 2 Multiplicity in AX_n systems

When n dipolar nuclei (I = ½), are coupled to a magnetically active nucleus, the peak for this nucleus splits into (**n+1**) lines. This relationship is called the (**n+1) rule**.

Coupling constant

The spacing between the lines in each peak is a measure of the degree of interaction between the two nuclei. This interaction is completely independent of the value of the applied magnetic field and is always measured in Hertz (Hz). For example, (i) the **one bond** coupling constant between H and F in HF is ^{1}**J**(HF); (ii) the **two bond** coupling constant between H and F in CH_3F is ^{2}**J**(HF).

The superscript at the symbol J is to indicate the number of bonds through which the interaction occurs.

The magnitude of the coupling constant depends on the number of bonds between the two atoms. Various factors influence the strength of interaction between two nuclei, in general, one-bond couplings are larger than two-bond couplings.

The J value is directly proportional to the γ, therefore

$$\frac{J\left(HX\right)}{J\left(DX\right)} = \frac{\gamma_H}{\gamma_D}$$

J values can be positive or negative. Coupling through an odd number of bonds is expected to be positive, *i.e.*, ^{1}J, ^{3}J… are **positive**. ^{2}J, ^{4}J… are expected to be **negative**. By looking at a spectrum it is impossible to tell whether the J value is positive or negative. If two nuclear spins are coupled such that the spins are **anti-parallel**, then J is positive. Nuclear spin and electron spin in a bond prefer to be paired, making ^{1}J(CH) values always positive.

Some one-bond coupling constants (^{1}J) are given in Table 2. Note that the ^{1}J(^{13}CH) value increases with the increase of s-character in the bond.

Table 2: Some one-bond coupling constants

Coupling Constant (J)		Frequency/Hz
^{1}J(CH)	(sp^3 carbon)	115-125
^{1}J(CH)	(sp^2 carbon)	150-170
^{1}J(CH)	(sp carbon)	240-270
^{1}J(CD)		20-45
^{1}J(PH)		190-700
^{1}J(CF)		165-370
^{1}J(CP)		45-60

^{2}J(HH) is called geminal coupling (Latin, gemini = twin); ^{3}J(HH) is sometimes called vicinal coupling (Latin, vicinus = neighbour); some **absolute** values for ^{2}J and ^{3}J are given below.

^{2}J	Frequency/Hz	^{3}J	Frequency/Hz
^{2}J$_{HH}$	9-5	^{3}J$_{HH}$	6-8
^{2}J$_{FH}$	50	^{3}J$_{FH}$	5-20
^{2}J$_{PH}$	7-15	^{3}J$_{PH}$	ca.15

Magnetic equivalence

Identical nuclei in a symmetrical molecule are said to be chemically equivalent. Thus, those chemically equivalent nuclei are said to be magnetically equivalent only if they have the same chemical shift (isochronous) and are equally coupled to all other sets of nuclei in the molecule. The protons in ethene ($CH_2=CH_2$) are magnetically equivalent; and they do not split each other and only give rise to a single proton signal. In $CF_2=CH_2$, the two protons are **not** magnetically equivalent because they are not equally coupled to the fluorine atoms.

Spin decoupling

Spin decoupling or double resonance is a technique used to simplify NMR spectra and it can be used to identify the spin-spin interaction between two nuclei. In a spin decoupling experiment, a second radio frequency signal is applied while the spectrum is scanned in the usual manner. The ^{13}C NMR of CH_4 gives a quintet in the intensity ratio of 1:4:6:4:1 while the proton decoupled ^{13}C NMR gives a singlet. The proton decoupled ^{13}C NMR is symbolized as ^{13}C-{^{1}H} NMR.

Dynamic processes

The common dynamic processes observed with organic molecules are

a) conformational changes (*e.g.* cyclohexane)

b) exchange processes (*e.g.* proton exchange in alcohols) and

c) atom inversions in amines.

NMR spectroscopy can be used to study these inversions and exchange processes.

1D and 2D NMR spectroscopy

We are familiar with one dimensional (1D) NMR

spectroscopy of proton and carbon nuclei. The major drawback of it is that it is difficult to confirm the interactions between all the protons present in a complex organic molecule.

In the 1D ^{1}H NMR spectrum (Fig. 3) of n-propanol the four signals appeared for H^1 (triplet, 3H), H^2 (multiplet, 2H), H^3 (triplet, 2H) and H^4 (singlet, 1H, OH).
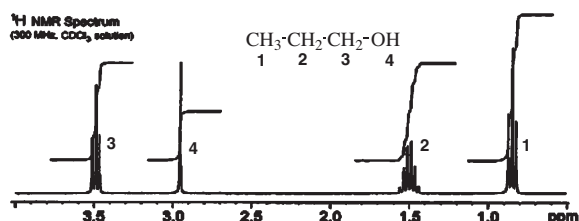

Fig. 3: ^{1}H NMR spectrum of n-propanol

2D NMR spectroscopy is very helpful in assigning all protons and carbons in almost all organic or organometallic compounds. 2D-spectra have two frequency axes and the signal intensity in the z-dimension.

2D NMR spectroscopy can be divided into two types: homonuclear and heteronuclear. Each type can provide either through bond or through space coupling information. There are **three main** 2D NMR experiments.

1. ^{1}H-^{1}H COSY (**CO**rrelation **S**pectroscop**Y**)
   It shows correlations between **protons** that are coupled to each other.

2. HSQC or HMQC - **H**eteronuclear **S**ingle/ **M**ultiple **Q**uantum Coherence which shows correlations between protons and carbons that are bonded **directly** to one another.

3. HMBC - **H**eteronuclear **M**ultiple **B**ond **C**orrelation which provides correlations between protons and carbons that are **two or three bonds apart**.

^{1}H-^{1}H COSY spectrum (Fig. 4) clearly indicates the three bond coupling/interaction between (i) H^1 and H^2 and (ii) H^2 and H^3. There is no coupling between H^1 and H^3. Due to rapid exchange among OH protons, H^4 is not coupled to H^3.
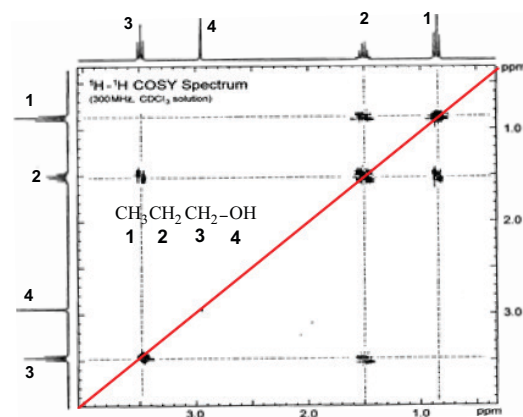

Fig. 4: ^{1}H-^{1}H COSY spectrum of n-propanol

HSQC spectrum is two-dimensional with one axis for protons and the other for a heteronucleus, which is usually ^{13}C or ^{15}N.

HSQC spectrum of γ-lactone (Fig. 5) clearly indicates the one bond coupling/interaction between (i) H^2 and C^2; (ii) H^3 and C^3; (iii) H^4 and C^4 and (iv) H^5 and C^5.
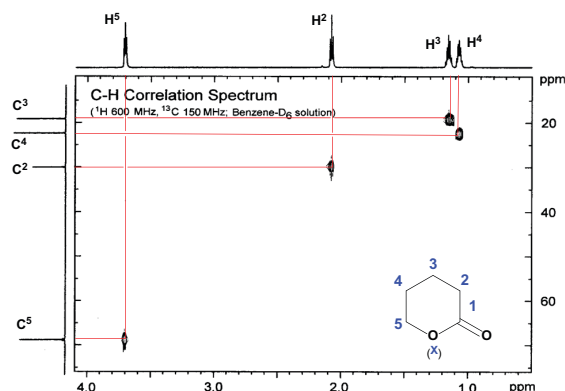
Fig. 5: HSQC spectrum of γ-lactone (**X**)

DEPT (**D**istortionless **E**nhancement by **P**olarisation **T**ransfer) experiments are used to distinguish **CH$_3$, CH$_2$, CH** and **quaternary** carbons. Diastereotopic **CH$_2$** groups can be easily identified by recording DEPT-ed-HSQC spectra.

Different types of correlation spectroscopy with differentiation are given below.

Name	F1 nucleus vertical axis	Mixing	F2 nucleus horizontal axis
COSY	^{1}H	J	^{1}H
TOCSY	^{1}H	J, J, J..	^{1}H
NOESY	^{1}H	NOE	^{1}H
HETCOR	^{1}H	^{1}JCH	^{13}C
HMQC	^{13}C	^{1}JCH	^{1}H
HMBC	^{13}C	^{2,3}JCH	^{1}H

TOCSY = Total Correlation Spectroscopy

NOE = Nuclear Overhauser Effect

HETCOR = Heteronuclear Correlation