Nuclear Magnetic Resonance (NMR) Spectroscopy

Light and Energy

\[ E = hv = \frac{hc}{\lambda} \]

Where:
- \( E \) = energy
- \( v \) = frequency
- \( c = \) speed of light \( = 3 \times 10^8 \) meter/second
- \( h = \) Planck’s constant \( = 6.6 \times 10^{-34} \) Joule•second
- \( \lambda = \) wavelength

Electromagnetic Spectrum

- Short Wavelength, High Energy, High Frequency
- Long Wavelength, Low Energy, Low Frequency
Nuclear Magnetic Resonance (NMR)

If an atom has an odd number of protons and/or an odd number of neutrons, there is a nuclear magnetic moment (aka nuclear spin).

Examples:

- $^1$H has atomic number 1 (therefore 1 proton), no neutrons, and nuclear spin $\frac{1}{2}$; can be detected by NMR
- $^2$H (deuterium) has atomic number 1, number of neutrons 1, and nuclear spin 1
- $^3$H (tritium) has atomic number 1, number of neutrons 2, and nuclear spin $\frac{1}{2}$
- $^{12}$C has atomic number 6 (6 protons), number of neutrons 6, and no nuclear spin
- $^{13}$C (only 1% of all carbon) has atomic number 6, number of neutrons 7, and a nuclear spin of $\frac{1}{2}$ (and can be detected by NMR)
- $^{14}$C has atomic number 6, number of neutrons 8, no nuclear spin, radioactive and used for “carbon dating”

MRI (Magnetic Resonance Imaging): Based on the principles of NMR and developed by Paul Lauterbur

NMR Continued (focusing on $^1$H NMR)

An NMR experiment requires a magnet (e.g. 14 Tesla), and a radio frequency transmitter. A tube containing the sample is placed inside the magnet – Below is a crude drawing of the setup. (http://www.chemistry.ccsu.edu/glagovich/teaching/316/nmr/instrumentation.html)
When no magnetic field is present, there is no net orientation to the nuclei. If you apply a magnetic field ($B_0$) to an isolated $^1H$ nucleus, there are two possible energy states: one with the nuclear spin **aligned** with the field and the other with it **opposed**.

![Alignment of nuclear spin with and against magnetic field](http://www.chem.ucalgary.ca/courses/351/Carey5th/Ch13/ch13-nmr-1.html)

Note: $\Delta E = h\nu$ (\(\nu\) is in the radio frequency range)

\[ \Delta E = \frac{hc}{\lambda} \quad (c \text{ is } 3.0 \times 10^8 \text{ m/s}) \]

Absorption from the lower energy state to the higher one becomes possible, which allows a spectrum to be observed:

![Absorption spectrum](http://www.chem.ucalgary.ca/courses/351/Carey5th/Ch13/ch13-nmr-1.html)

**Chemical Shift**

Chemical shift measures the change in the frequency of absorption. The chemical shift is typically shown in units of parts per million (ppm), and is compared to a reference. For $^1H$ NMR, this reference is usually tetramethylsilane (TMS).

The hydrogen atoms in TMS are highly shielded, and the signal for TMS is set at 0 ppm.

**Deshielding** occurs when electrons are pulled away from a hydrogen atom, which can be caused by the presence of an electron-withdrawing group (e.g., a carbonyl). When the electrons are pulled away, the nucleus is more exposed to the magnetic field, resulting in a **downfield** chemical shift.
Downfield Deshielded

Upfield Shielded

Examples:

Intensity: 1 (2H’s) 3 (2 CH₃’s)

2-methyl-1-propene

The intensity (area under the peak) depends on the number of hydrogen atoms, in this case 2:6 which is the same as 1:3

1-chloroethene
chloroethylene
vinyl chloride

Hₐ is deshielded by the electron-withdrawing Cl.
Hₖ and Hₗ are different due to the distance from the Cl.
Hₖ is trans to the Cl, while Hₗ is cis.
Hₗ is more deshielded than Hₖ because it is closer to Cl.
### Diastereotopic Hydrogens

<table>
<thead>
<tr>
<th>What kinds of H does it have?</th>
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</thead>
<tbody>
<tr>
<td>O-H</td>
</tr>
<tr>
<td>H at C₂</td>
</tr>
<tr>
<td>CH₃ at C₁</td>
</tr>
<tr>
<td>CH₃ at C₄</td>
</tr>
<tr>
<td>Hₐ (Pro-R)</td>
</tr>
<tr>
<td>Hₜ (Pro-S)</td>
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</tbody>
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(S)-2-butanol  
butan-2-ol

The methyl group shows only one signal because the C-C bond can freely rotate and NMR cannot distinguish between the Hs on that carbon. The barrier to bond rotation is only a few kilocalories per mole (1-3 kcal/mole) and about 15 to 20 kilocalories per mole of energy are available at room temperature. Hence rotation is very rapid and the methyl hydrogens are all in the same chemical environment.

C-2 is a stereogenic centre, and there is no plane of symmetry in the molecule. Hₐ and Hₜ are in different chemical environments and have different chemical shifts, therefore they are **diastereotopic**.

If you substitute Hₐ or Hₜ with deuterium (labeled as D (²H; an isotope of hydrogen with one proton and one neutron)) you get diastereomers. These two hydrogens are called diastereotopic hydrogens.

**Note:** The chemical shifts of two diastereotopic protons **may not always be very different**.

Example:

(R)-2-dodecanol  
Every CH₂ group in this molecule has two diastereotopic protons.
Newman Projections

The round circle in the structure below is the back carbon (C-3 of 2-butanol) – carbon 2 is directly attached to it and is represented as the dot (point) where the bonds meet in front.

anti or staggered conformation  gauche conformation

Pro R - precursor to an R stereogenic center
(If you substitute it with deuterium, you will form an R stereogenic center)
Pro S - precursor to an S stereogenic center

When there is a stereogenic center present, the two hydrogens, H_A and H_B, of the methylene (CH₂) group cannot be brought into the same chemical environment. Bond rotation can bring H_B to the position where H_A was before, as represented by the above Newman projections of the two conformations, but the CH₃ groups are occupying different positions and therefore the two methylene H’s are not in the same chemical environment.

Spin-Spin Splitting (Coupling)

H_A is not a singlet due to the influence of H_B on its spin, and vice versa. This diagram below shows the energy for H_A, and the spins for H_B are shown (in red) only to show the effect on H_A.
$J_{AB} =$ **Coupling constant** between atoms A and B, measured in Hertz (Hz)

The $H_A$ coupling constant corresponds to the energy differences caused by the $H_B$ proton in alignment with and in opposition to the field. This energy difference is equal to the effect that the $H_A$ proton has on $H_B$, so both of these coupling constants are equal.

The coupled signal is centered around the same chemical shift value that the signal would have if there were no coupling.

**Limitations of Coupling**

1. 2 to 3 bonds separating nuclei (coupling is typically not seen between nuclei that are further apart than 3 bonds)
2. Usually no coupling across O, N, S, C=O

Example: In the following structure, $H_A$ and $H_B$ would not couple due to being 4 bonds apart (too far) and oxygen is in between

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A --- O --- B
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Note: There are exceptions to these rules