Nuclear Magnetic Resonance Spectroscopy:

Purpose: Connectivity, Map of C-H framework

Four Factors of Proton NMR (PMR OR $^1$H NMR):
1. **Symmetry**: Number of chemically different protons (symmetry) as shown by number of signals
2. **Chemical Shift** Value (X-axis): provides information regarding what kind of chemical environment the proton is in (electron-rich or electron-poor).
3. **Integration**: Electronic measurement of peak areas: provides you with the number of chemically equivalent protons producing each signal on the spectrum.
4. **Splitting Patterns**: Complexity of peak patterns - information is gained regarding the connectivity of neighboring protons.

General Notes:
1. We usually study one type of nucleus at a time. In Organic Chemistry, we focus on the hydrogen-1 isotope ($^1$H) and the Carbon-13 ($^{13}$C) isotope as they are the most widely used nuclei in the spectroscopy of organic compounds.
2. The position on the chart at which a nucleus absorbs is called its “chemical shift”. The X-axis of a proton NMR spectrum ranges from 0-10 (or as high as 14) ppm. The unit “ppm” stands for “parts per million” and is a standardized unit for the signal frequency.
3. The area under the peaks is calculated by the instrument and the ratio of protons per peak is determined based on the peak area. **Integration**.
4. On most spectra, a calibration peak will be visible. There are two possibilities:
   a. Tetramethylsilane (TMS) may be added to the solution. The 12 hydrogens of TMS are assigned a value of 0.0000 ppm.
   b. Deuterated solvents (Deuterium = H$^2$ isotope and has no magnetic field generation) must be used to prevent interference of a molecule’s spectrum with that of the solvent. Nevertheless, an internal standard can be found in most solvent used. Deuterated chloroform, CDCl$_3$, contains a trace amount of CHCl$_3$ - and that proton has a chemical shift value of 7.2600 ppm.

**Symmetry**: How many different types of protons?

isobutyl chloride: (CH$_3$)$_2$-CH-CH$_2$-Cl
3,3-dimethyl-1-butanol: HO-CH$_2$-CH$_2$-C(CH$_3$)$_3$

How many types of protons? (Number of Signals?)

Symmetry in Aromatic rings: How many types of aromatic protons?
Monosubstituted:

Disubstituted – Para

Disubstituted – Meta

Disubstituted – Ortho

New in 332: Trisubstituted aromatic rings
Trisubstituted – 1,2,3-

Trisubstituted – 1,2,4-
Trisubstituted - 1,3,5-

Chemical Shift – Electronic Environments

Protons on sp$^3$C (no EWG near by) 0-2 ppm

Protons next to unsaturations 1.8-3 ppm
   Benzylic Alpha to carbonyls

Protons on sp$^3$C with O, N or X attached 3-5 ppm

Protons on sp$^2$C (C=C): 6.5-8.5 ppm
   Aromatic

Protons of CHO (aldehydes) 8.5-10 ppm

Protons of CO$_2$H (carboxylic acids) 10-14 ppm

Protons of Hydroxyl groups:
Aliphatic (alcohols)  2-5 ppm  
Aromatic (phenols)  6-10 ppm

Protons of Amine groups:
Aliphatic (amines)  0.5-3 ppm  
Aromatic (anilines)  1-5 ppm

Protons on Amides  5.5-8 ppm

Chemical Shift Values? Types of protons?

Reminder about alcohols (amine and carboxylic acid protons): “exchangeable protons”
Under normal, slightly acidic conditions of CDCl₃, these protons "hop on and off" on a regular basis. This distorts the peak of the proton, broadening it so it is not as sharp in appearance as the other protons.

In the lab, an easy way to distinguish an alcohol proton from one that is not exchangeable is to add deuterated water (D₂O) to the sample. Deuterium does not have
a nucleus that can generate a magnetic field so it will not show up on the NMR spectrum. If deuterium substitutes for a proton, the signal will disappear!

\[
\text{R-O-H} \quad \overset{D^+}{\longrightarrow} \quad \text{R-\text{D}-H} \quad - \quad H^+ \quad \Longrightarrow \quad \text{R-\text{D}O} \\
\]

Example: Consider the proton NMR of isobutyl alcohol:

Now view deuterated isobutyl alcohol: What’s missing?

**Integration** - Ratio of Protons on a $^1$H NMR

- Peak areas are electronically measured by instrument
- To determine the ratio of protons producing signals, divide each peak area by smallest area to determine whole number ratio of peaks

Total of Protons should equal number of protons in molecular formula

$\text{C}_5\text{H}_{10}\text{O} - \text{Calculate the integration ratio}$
Splitting Patterns - Spin-Spin Coupling

Splitting Patterns are caused by the interaction of the magnetic fields of neighboring nuclei. In Proton NMR, only the magnetic fields of adjacent protons can interact.

- Tells you how many protons are on adjacent carbon atoms
- Always remember that splitting can only occur between NON-Equivalent Protons (consider \(CH_3CH_2CH_2CH_3\))
- **N+1 Rule** - The signal of a proton (or set of equivalent protons), with \(N\) number of protons on an adjacent carbon atom, will be split into \(N+1\) peaks

Let’s analyze what we’d see for some molecules:

Predict the NMR spectrum for bromoethane:

\[CH_3-CH_2-Br\]

Spectrum:
Predict the NMR spectrum for sec-butyl chloride (2-chlorobutane):

\[
\text{H}_3\text{C} - \text{CH}_2 - \text{C} = \text{CH}_3
\]

Spectrum:

Normally, you will be viewing proton NMR spectra. You need to analyze the splitting patterns of peaks to determine the molecular fragments of a molecule you are attempting to solve.

Splitting Patterns:
Singlet (symbolized as "s"): N+1 = 1 therefore N = 0, or no neighboring protons.

Doublet (symbolized as "d"): N+1 = 2 therefore N = 1, where a CH or OH may be in the adjacent position

Triplet (symbolized as "t"): N+1 = 3 therefore N = 2. A CH\text{\_2} may be adjacent or two symmetrical CH groups
Quartet (symbolized as "q"): N+1 = 4
therefore N = 3. A CH₃ is adjacent.

Quintet (no symbol): N+1 = 5
therefore N = 4. Two CH₂ groups
are adjacent

Sextet (no symbol): N+1 = 6
therefore N = 5. There is a CH₃
on one side and a CH₂ on the other side.

Septet (no symbol): N+1 = 7
therefore N = 6. Two CH₃ are
adjacent, one on either side.
May be hard to see side peaks.

Octet (no symbol): N=1 = 8
therefore N = 7. Two CH₃s and a
CH are attached on three sides
of a CH. Harder to see!

Nonet (no symbol): N=1 = 9
therefore N = 8. Two CH₃s and a
CH₂ are attached on three sides
of a CH. Hardest to see!

Multiplet (symbolized as "m"): Unable to count peaks and not recognizable
as any shown above. Unable to determine adjacent number of protons.
Should still be able to identify chemical shift for a multiplet and
calculate integration ratio.
Other signals:
Doublet-Doublet (symbolized as “dd”): There are two CH’s on either side that are chemically different or one CH and one OH. WARNING: May resemble a triplet.

Doublet-Triplet (symbolized as “dt“): On one side there is a CH (or OH) and on the other side there is a CH₂. WARNING: May resemble a quartet.

Doublet-Quartet (symbolized as “dq“): On one side there is a CH (or OH) and on the other side there is a CH₃. WARNING: May resemble a quintet.
Now, combine splitting patterns with the integration (shown in brackets below). What molecular fragment does each of the following represent?

a. \([3H]\, t\)

b. \([1H]\, q\)

c. \([2H]\, dt\)

d. \([3H]\, s\)

e. \([1H]\, septet\)

**Aromatic Systems: Splitting Patterns**

**Monosubstituted:** Total of five aromatic protons

No need to evaluate splitting patterns - if the aromatic region integrates to 5, the ONLY possible structure is the monosubstituted aromatic ring.
Disubstituted: total of **four aromatic protons**

Para: 1,4 disubstituted:

If disubstituted “para” with the same group, all four protons are exactly the same and no splitting would occur. You would see a singlet, integrating to four.

1,4-dibromobenzene:

If disubstituted “para” with two different groups, the plane of symmetry would result in two TYPES of aromatic protons (integration of two for each signal) and splitting patterns of doublets for each.

1-bromo-4-chlorobenzene:
Meta: 1,3-disubstituted

If disubstituted “meta” with the same group, the system is symmetrical, with three types of protons, with one being isolated and appearing as a singlet.

1,3-dibromobenzene

If disubstituted “meta” with two different groups, no plane of symmetry exists. All four protons are different. Four signals result. One will still be isolated from the rest and appear as a singlet. The others will be split.

1-chloro-3-hydroxybenzene
Enlarged Aromatic region:

Ortho: 1,2-disubstituted

If disubstituted "ortho" with the same group, a plane of symmetry would produce two types of protons and each will appear as a doublet.

1,2-dibromobenzene:
If disubstituted “ortho” with two different groups, no plane of symmetry exists so all four aromatic protons are different and would causing all signals to be split.

1-bromo-2-hydroxybenzene:

Now: Trisubstituted Aromatic Rings: Total of **three aromatic protons**

1, 2, 3-Systems:
With symmetry, there are only two types of protons.
Ex: 1,3-dibromo-2-chlorobenzene

 Without symmetry: all protons are different.
Ex: 1-bromo-2,3-dichlorobenzene

1, 2, 4-Systems: No symmetry. Ever.
Ex: 4-bromo-1,2-dichlorobenzene

1, 3, 5-Systems: Always singlets (Amount of symmetry changes number of signals)
The goal for proton NMR is to be able to interpret and reconstruct the molecule's structure.

Solve: $C_5H_{12}O$
Things to remember:
1. Begin by first identifying the number of signals and where on the X-axis they exist. Be flexible! Sometimes multiple functional groups are present and protons aren't always where you expect them to be.

2. Calculate the integration ratio. Identify how many of each type you have. Recognize the number of CH$_3$ versus CH$_2$ etc that you have in your molecule and STICK with that allotted number. Keep in mind that signals in the aromatic region are NEVER CH$_3$ or CH$_2$'s.

3. Splitting patterns are the toughest to interpret. Singlets, doublets and triplets are usually straightforward although triplets are often doublet-doublets in disguise. Quartets (telling you CH$_3$ is next door) are often Doublet-Triplets in disguise (telling you there is a CH and a CH$_2$ next door). Check back with your integration values to see if options are possible. Assign something as a multiplet if you don't really know what it is. Seek help if necessary! Don't flounder lost until the last moment...

Once the pieces are built, cross off the extra's that appear multiple times (CH$_3$-CH$_2$ and CH$_2$-CH$_3$, for instance). Narrow down to the correct number of carbons in your molecular formula. And for heaven's sake, don't violate the octet rule!