Chapter 14: NMR Spectroscopy

A. Introduction

• MS and IR can provide MW and a few other details, but we generally need way more info to fully determine a structure.

• Nuclear magnetic resonance (NMR) spectroscopy is a very powerful technique for structure determination.

• $^1$H NMR ("proton NMR") provides details about the number, types, and relationships of H atoms in a molecule.

• $^{13}$C NMR provides details about the number and types of C atoms in a molecule.

• NMR involves an effect on nuclei that occurs when molecules are exposed to radiofrequency energy while in a magnetic field...

B. The NMR Effect

All nuclei are charged, and have a spin quantum number ("I") that can be 0, $\frac{1}{2}$, 1, etc. depending on the type of nucleus.

If $I \neq 0$, the nucleus has a net spin. For $^1$H, the value is $\frac{1}{2}$.

When a charged particle (like a $^1$H nucleus, i.e., a proton) spins, it creates a tiny magnetic field, making it like a tiny bar magnet.

Normally, these are randomly oriented in space.

However, in an external magnetic field (B₀), they become aligned "with" or "against" this applied field.
This creates two possible energy states for each $^1$H: 

- alignment with $B_0$ is lower in energy, but only by a bit (< 0.1 cal), so the populations of the states are similar.

- If energy that matches the $\Delta E$ between these two states is applied, it is absorbed by lower energy nuclei, causing them to excite or “flip” to the higher $E$ orientation.

![Energy States Diagram]

- The value of $\Delta E$ needed lies in the radiofrequency (RF) range.

- At the appropriate $\Delta E$ for a given $B_0$, such excitation occurs, placing the nuclei in energetic “resonance” (not our usual definition of resonance...)

**C. Resonance Frequency**

- The stronger the $B_0$ (in tesla; T), the larger the $\Delta E$, and the higher the RF energy needed for resonance (in megahertz; MHz).

- Very powerful (superconducting!) magnets are needed to create large enough $B_0$ (and $\Delta E$) to make the experiment most useful.

![Resonance Frequency Diagram]

- NMR spectrometers are classified according to the RF energy value needed for $^1$H resonance (e.g., 300 MHz, 500 MHz, etc.)

- The magnet strength ($B_0$) is chosen to give these round numbers, e.g., if $B_0 = 7.04$ T, $^1$H frequency = 300 MHz
D. Chemical Shift

• A key element of the usefulness of NMR lies in the fact that environmental differences cause slight differences in the exact frequencies at which individual nuclei resonate.

• This phenomenon is called “chemical shift” (δ).

• These differences are on the order of parts-per-million (ppm); most ¹H NMR absorptions appear within a 10 ppm window.

Q: Why does the environment of a nucleus affect its resonating frequency?

A: The e⁻ nearby are also charged and affected by B₀.

• Their circulation leads to a contribution opposed to B₀ (in the vicinity of the nucleus)

• The H experiences a lower effective B, thereby increasing the external B needed for resonance (to compensate) and increasing the frequency (ΔE) needed, as well.

• Key, net result: The signal for the ¹H is “shifted” to higher field.

• Magnitude of effect depends on e⁻ density around the nucleus...

• As e⁻ density increases, nuclei are said to become more shielded. (Resonance frequency at higher magnetic field; more “upfield”).

• As e⁻ density decreases, nuclei are increasingly deshielded. (Resonance at lower field; further “downfield”).
• e⁻ density, in turn, depends on chemical environment (e.g., nearby functional groups, electronegativity of attached atoms, π e⁻ density in the area, resonance effects, etc.)

Consider these 3 examples (showing electronegativity effects):

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{Cl} & \quad \text{H}_b\text{'s have less e⁻ density than H}_a\text{'s due to Cl →} \\
& \quad \text{more deshielded → more downfield than H}_a\text{'s}
\end{align*}
\]

\[
\begin{align*}
\text{BrCH}_2\text{CH}_2\text{F} & \quad \text{H}_b\text{'s have less e⁻ density than H}_a\text{'s (F vs. Br) →} \\
& \quad \text{more deshielded → more downfield than H}_a\text{'s}
\end{align*}
\]

\[
\begin{align*}
\text{ClCH}_2\text{CHCl}_2 & \quad \text{H}_b\text{'s have less e⁻ density than H}_a\text{'s (2 Cl vs. 1 Cl) →} \\
& \quad \text{more deshielded → more downfield than H}_a\text{'s}
\end{align*}
\]

We’ve seen halide substituents reduce e⁻ density before, e.g., recall the effects of replacing H's with halides on pKₐ of CH₃COOH...

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E. A Modern NMR Spectrometer

• A pulse of energy is applied to a solution of a compound to achieve simultaneous resonance of all its \(^1\text{H}'s\).

• After this energy “pulse”, nuclei return to their equilibrium distribution—the instrument detects the emitted energy to generate a spectrum that shows the individual “resonances”.
F. ¹H NMR Spectra

• An NMR spectrum is a plot of peak intensity vs. chemical shift (δ) in ppm “downfield” relative to a standard reference (tetramethylsilane; TMS) set by convention as 0 ppm.

• TMS was chosen for many reasons, but because it is upfield of most organics, shift numbers increase from right to left.

\[
\text{CH}_3OC(CH_3)_3
\]

• The chemical shift of an NMR resonance (or “signal”), in ppm, is measured according to the following equation:

\[
\text{chemical shift (in ppm on the } \delta \text{ scale)} = \frac{\text{observed chemical shift (in Hz) downfield from TMS}}{v \text{ of the NMR spectrometer (in MHz)}}
\]

• Because shift of a signal is reported as a fraction (i.e., in ppm) of whatever NMR operating frequency is being used, it is a constant for a given sample.

• However, in a 300-MHz (i.e., 300 million Hz) spectrum, 1 ppm = 300 Hz. In a 600-MHz spectrum, 1 ppm = 600 Hz.

• Thus, signals will be more spread out at 600-MHz, making fortuitous, confusing overlap of different signals less likely.
Superconducting magnets are really expensive, but this begins to explain why we care about going to higher frequencies...

It improves both resolution of the signals and sensitivity.

This is most important for real-world samples that are limited in quantity and/or have complex structures showing many signals.

A 600-MHz $^1$H NMR spectrum of a more complex molecule:

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G. Types of Structural Info Provided by $^1$H NMR Spectra

- **Number** of signals: indicates the number of “different types of H” (i.e., different environments of H’s) in a molecule.

- **Position** of signals: helps sort out what types of H the molecule contains.

- **Intensity** (peak area) of signals: indicates the relative amounts (how many) of each kind of H.

- **Shape** (spin-spin coupling/splitting/multiplicity) of a signal: gives info about neighboring H’s in the molecule.
1. **Number of Signals**

- $^1$H’s in different environments give different NMR signals.
- $^1$H’s in equivalent environments collectively give one NMR signal.
- The number of signals equals the number of different types of $^1$H in a compound (unless signals fortuitously overlap…).

\[
\begin{align*}
\text{CH}_3\text{O-CH}_2 & \quad \text{CH}_3\text{CH}_2\text{Cl} & \quad \text{CH}_2\text{O-CH}_2\text{CH}_3 \\
\text{H}_a & \quad \text{H}_a & \quad \text{H}_a \\
\text{H}_b & \quad \text{H}_b & \quad \text{H}_c \\
\text{All equivalent H’s} & \quad 2 \text{ types of H’s} & \quad 3 \text{ types of H’s} \\
1 \text{ NMR signal} & \quad 2 \text{ NMR signals} & \quad 3 \text{ NMR signals}
\end{align*}
\]

\[
\begin{align*}
\text{Cl}\text{ICH}_2\text{CH}_3\text{Cl} & \quad \text{Cl}\text{ICH}_2\text{CH}_2\text{Br} & \quad \text{CH}_3\text{COOCH}_2 \\
\text{H}_a & \quad \text{H}_a & \quad \text{H}_a \\
\text{H}_b & \quad \text{H}_b & \quad \text{H}_b \\
\text{H}_c & \quad \text{H}_c & \quad \text{H}_c \\
1 \text{ type of H} & \quad 3 \text{ types of H’s} & \quad 2 \text{ types of H’s} \\
1 \text{ NMR signal} & \quad 3 \text{ NMR signals} & \quad 2 \text{ NMR signals} \\
\end{align*}
\]

a. Alkenes—issues introduced by C=C geometry…

- In comparing two H atoms on a C=C (or a ring…), two H’s are equivalent only if they are *cis* (or *trans*) to the same groups.

\[
\begin{align*}
\text{Cl} & \quad & \text{Cl} & \quad & \text{Cl} & \quad & \text{Cl} \\
\text{C=C} & \quad & \text{C=C} & \quad & \text{C=C} & \quad & \text{C=C} \\
\text{H} & \quad & \text{H}_a & \quad & \text{H}_b & \quad & \text{H}_a \\
\text{Cl} & \quad & \text{Br} & \quad & \text{H}_b & \quad & \text{H}_a \\
1,1\text{-dichloroethylene} & \quad & 1\text{-bromo-1-chloroethylene} & \quad & \text{chloroethylene} \\
1 \text{ type of H} & \quad & 2 \text{ types of H’s} & \quad & 3 \text{ types of H’s} \\
1 \text{ NMR signal} & \quad & 2 \text{ NMR signals} & \quad & 3 \text{ NMR signals}
\end{align*}
\]

- This shows that it is possible for two H’s *on the same C* to be different....
b. Substituted Cycloalkanes

• To determine whether two H’s in a cycloalkane (or an alkene) are equivalent, consider whether or not the H’s in question are cis (or trans) to the same groups.

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• To determine whether two H’s in a cycloalkane (or an alkene) are equivalent, consider whether or not the H’s in question are cis (or trans) to the same groups.

\[
\begin{align*}
\text{cyclopropane} & : \quad \text{All H’s are equivalent.} \\
\text{chlorocyclopropane} & : \quad \text{3 types of H’s} \\
\end{align*}
\]

All H’s are equivalent. 1 NMR signal

3 types of H’s 3 NMR signals

... (diagram)

\[
\begin{align*}
\text{c. Enantiotopic Protons} & : \quad \text{If} \ H_a \text{ below were replaced by “Z”, we’d get a different enantiomer than we would if} \ H_b \text{ were replaced by Z.} \\
\text{These two H’s are considered enantiotopic, and are chemical-shift equivalent (i.e., they will give one } \text{1H NMR signal).} \\
\end{align*}
\]

... (diagram)

\[
\begin{align*}
\text{H}_a \text{ and } \text{H}_b \text{ are enantiotopic.} \\
\end{align*}
\]

(Note that this molecule is achiral)

• It may seem obvious that two H’s on the same sp\(^3\) C would be equivalent, but look at the next case...
d. Diastereotopic Protons

• If \( H_a \) below were replaced by “Z”, we’d get a different diastereomer than we would if \( H_b \) were replaced by Z.

• *Thus, these* two H’s are diastereotopic, and are chemical-shift inequivalent (i.e., they will each give different \(^1\text{H} \) NMR signals!).

![Diagram of diastereomers](image)

(Note that this molecule is chiral)

Why? \( H_a \) & \( H_b \) will always be in different environments; this can be seen if you look at any Newman projection along the C2-C3 bond.

This may be easier to see in a cyclic case:

• If \( H_a \) below were replaced by “Z”, we’d get a trans isomer; if \( H_b \) were replaced by Z, we’d get a cis isomer—different diastereomers, so \( H_a \) and \( H_b \) are diastereotopic.

![Cyclic diastereomers](image)

• Note how \( H_a \) will always be trans to the CH\(_3\), while \( H_b \) will always be cis to it—different environments \(\rightarrow\) different shifts

• The other CH\(_2\)’s in this thing are all diastereotopic pairs, too!
Q: What is it about a molecule that make its CH₂'s diastereotopic?

A: Generally, this occurs for any molecule with one or more **stereocenters**, but monosubstituted cycloalkanes and unsymmetrical 1,1-disubstituted alkenes also qualify.

![Molecular structures](image)

Hₐ and H₋ are considered diastereotopic.

This can complicate ¹H NMR spectra significantly. We will see an example on slide 42; the ¹H NMR spectrum of

```
H₃C─CH─CH₂Cl
Cl
```

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2. **Position of Signals--Characteristic Chemical Shifts**

¹H's of a given type will absorb in a somewhat predictable region:

<table>
<thead>
<tr>
<th>Type of proton</th>
<th>Chemical shift (ppm)</th>
<th>Type of proton</th>
<th>Chemical shift (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>sp²</td>
<td>0.6-2</td>
<td>sp²</td>
<td>4.5-6</td>
</tr>
<tr>
<td>RCHO₂</td>
<td>0.6</td>
<td>R₂CO₂</td>
<td>0.2-5</td>
</tr>
<tr>
<td>R₂CH₂</td>
<td>-1.3</td>
<td>R₂CH₂</td>
<td>0.2-5</td>
</tr>
<tr>
<td>R₂COH</td>
<td>-1.1</td>
<td>Z = C, O, N</td>
<td>9-10</td>
</tr>
<tr>
<td>Z = C, O, N</td>
<td>1.6, 2.6</td>
<td>R₂OH</td>
<td>10-12</td>
</tr>
<tr>
<td>Z = N, O, N</td>
<td>-2.5</td>
<td>R₂O⁻H or R⁻N⁻H</td>
<td>1-6</td>
</tr>
<tr>
<td>Z = N, O, X</td>
<td>2.5-4</td>
<td>R₂O⁻H or R⁻N⁻H</td>
<td>1-6</td>
</tr>
</tbody>
</table>

Some differences can be explained by electronegativity, but not all....
a. Alkenes: why are C=C-H’s relatively downfield?

• $sp^2$ = “more electronegative” than $sp^3$, but that’s only part of it.

• In a magnetic field, the loosely held $\pi$ e$^-$ of the C=C circulate to create their own small, induced magnetic field, which reinforces $B_0$ in the vicinity of the H’s.

![Diagram of alkene with magnetic fields](14-21) This moves the $^1$H signals somewhat **downfield** (to $\sim$4.5-6.5 ppm).

• This is an “anisotropic” effect—the degree and direction of the shift depend on the location of the H’s within the induced field.

• The alkene H’s are in the “deshielding region” of the C=C.

b. Aromatics? A similar story…

• In a magnetic field, the $\pi$ e$^-$ in benzene circulate around the ring creating a “ring current”—a particularly strong effect.

• The induced field again reinforces $B_0$ in the vicinity of the H’s.

• Thus, the $^1$H’s again experience a **downfield** anisotropic effect—often even more so than alkene CH’s (to $\sim$ 6-8 ppm).

![Diagram of aromatic with magnetic fields](14-22) The circulating $\pi$ electrons create a ring current.

**Note:** CH’s where the C is connected to the ring (or C=C) will be affected by this, too, but not nearly as much.
c. Alkynes?

• The $\pi$ e$^-$ of a C≡C also circulate in a magnetic field, but in this case, the induced field opposes $B_0$ in the vicinity of the C≡C-H.

• Alkyne $^1$H’s thus absorb relatively upfield (∼ 2.5 ppm).

• Note, however, that hybridization is also a factor—sp orbitals are more electronegative than sp$^2$ or sp$^3$, so there is a downfield effect mixed in there, too…

\begin{center}
\includegraphics[width=0.5\textwidth]{alkyne_diagram.png}
\end{center}

\[ B_0 \quad B_{\text{Induced}} \quad B_{\text{Induced}} \]

\[ R \]

\[ C \]

\[ H \]

d. Other “Anisotropic” Effects

• The chemical shift of almost any kind of C−H usually increases with increasing alkyl substitution.

\begin{align*}
\text{RCH}_2\text{−H} & \sim 0.9 \text{ ppm} \\
\text{R}_2\text{CH}\text{−H} & \sim 1.3 \text{ ppm} \\
\text{R}_3\text{C}\text{−H} & \sim 1.7 \text{ ppm}
\end{align*}

Increasing alkyl substitution
Increasing chemical shift

Q: Hmm—this seems counterintuitive? R-groups are e$^-$-donating, right? Shouldn’t that increase shielding as we go to the right here? What’s the deal?

A: $\sigma$ e$^-$ circulate, too! The associated fields are weaker, but there are a lot of them. Their effects, together with typical geometric relationships among them, cause this general trend.
Overview of General $^1$H NMR Spectral Regions

Effects are additive, so these are just approximate ranges.

E.g., the CH$_2$O in CH$_2$=CHCH$_2$OH would be a bit further downfield than the one in CH$_3$CH$_2$CH$_2$OH.

And, generally, $\delta$ for CH > CH$_2$ > CH$_3$, given identical substituents.

3. Intensity of $^1$H NMR Signals

- The area of an $^1$H NMR signal/peak is proportional to the number of $^1$H’s associated with it.

- “Integration” of the peak areas is often plotted as a stepped curve (an integral) above the spectrum.

- The height of each “step” is proportional to the area under the peak, which is proportional to the number of $^1$H’s for that signal.
- NMR data systems calculate the value of each integral for you in arbitrary units (or you could just measure with a ruler...).

- The ratio of these values gives info about how many $^1$H’s of each type are represented by the various signals.

- This is a ratio—not the absolute number—of $^1$H’s—but if you know the molecular formula, you can figure out the numbers.

  > Ratio of signals is 3:1, but knowing formula (C₅H₁₂O), this must translate to 9H:3H

  > If you didn’t know the formula, this’d be tricky to figure out...

  > 3 equivalent CH₃’s—one signal for all 9H!

The text gives another example (C₉H₁₀O₂; below), but makes things look more complicated than they need to be...

- Their integrals are messed up (e.g., size of integral for A is clearly not more than twice that for B...??), but...

- Just eyeballing the numbers shown, with an available total of 10H, makes it pretty clear that the ratio must be 5:2:3...
4. Signal **Shape**: Spin-Spin Coupling/Splitting in $^1$H NMR

- The simple sample spectra that we have seen up to now have included only single-peak absorptions called **singlets**.

- However, signals for individual $^1$H types often show more complex shapes, i.e., they are split into more than one peak.

The reason? **Spin-spin coupling** (= splitting) generally occurs between non-equivalent $^1$H’s on the same C or adjacent C’s.

Q: **Why** does the CH$_2$ in BrCH$_2$CHBr$_2$ occur as a **doublet**?

- When exposed to $B_0$, the adjacent $^1$H (CHBr$_2$) can be aligned with ($\uparrow$) or against ($\downarrow$) $B_0$.

- Thus, the CH$_2$ can experience two slightly different net magnetic fields caused by this $^1$H’s own little field—one slightly larger than $B_0$, and one slightly smaller than $B_0$ (~50:50 chance)

- The corresponding CH$_2$’s absorb at two different frequencies, so the absorption gets **split** into a 1:1 doublet.

- As we will soon see, the CH$_2$ will also split the CH signal...
a. Coupling Constants

When two $^1\text{H}$’s split each other, they are said to be coupled.

The frequency difference, in Hz, between the two peaks of the doublet is called the coupling constant, $J$. This “$J$-value” is a constant and is independent of the $B_0$ being used.

---

Ok, fine. But why is the CHBr$_2$ signal a 3-line thing (a triplet)?

• When in $B_0$, the adjacent CH$_2$ protons $H_a$ and $H_b$ can each be aligned with (↑) or against (↓) $B_0$.

  ![Diagram of CHBr$_2$ molecule]

• Thus, a CHBr$_2$ proton could experience one of three slightly different net magnetic fields:
  - one slightly larger than $B_0$ (when the CH$_2$ spins are ↑↑)
  - one slightly smaller than $B_0$ (the ↓↓ case)
  - one the same strength as $B_0$ (the ↓↑ and ↑↓ cases)

• Because the CHBr$_2$ $^1\text{H}$’s can experience 3 different net magnetic effects, subsets of the population appear at 3 slightly different frequencies, resulting in a triplet.
• Because there are two ways to align one $^1$H with $B_0$, and one against $B_0$ (i.e., $\uparrow_a \downarrow_b$ and $\downarrow_a \uparrow_b$), the middle peak of the triplet is twice as intense as the two outer peaks.

• This makes the ratio of the areas under the three peaks 1:2:1.

• The distance in Hz between each peak in a simple “multiplet” like this (i.e., the $J$-value) will be the same.

b. Splitting Patterns

• Some general rules describe splitting patterns commonly seen in $^1$H NMR spectra of organic compounds.

[1] Equivalent protons do not split each other.

[2] A set of $n$ equivalent neighboring $^1$H’s will split the signal for a nearby $^1$H type into $n + 1$ peaks.

[3] Splitting is usually observed between non-equivalent $^1$H’s on the same C (geminal H’s) or adjacent C’s (vicinal H’s).
[4] Splitting is not generally observed between $^1$H’s separated by more than three $\sigma$ bonds.

![2-butane and ethyl methyl ether structures](image)

- $H_a$ and $H_b$ are separated by four $\sigma$ bonds.
- No splitting between $H_a$ and $H_b$.

Four-bond couplings can sometimes be seen through $\pi$-systems, but even these are usually relatively small.

Another example:

$\text{CH}_3$: 3 identical $^1$H split by 1 adjacent $^1$H; $n + 1 = 2$ peaks $\Rightarrow$ doublet

$\text{CH}$: 1 $^1$H split by 3 identical adjacent $^1$H; $n + 1 = 4$ peaks $\Rightarrow$ "quartet"

Quartet is $1:3:3:1$ because each $^1$H of the $\text{CH}_3$ $^1$H’s could have $\uparrow$ or $\downarrow$ spin.

All possible combinations will occur, in statistically expected $1:3:3:1$ ratio.

Often not perfect (as above), but this is the expected ratio.
This is a characteristic pattern for an isopropyl group.

The 6 $H_a$ protons are split by the one $H_b$ to give a doublet.

$H_b$ is split by 6 equivalent $H_a$ protons to yield a septet ($n + 1 = 7$).


Some other common $^1H$ NMR splitting patterns...

Keep in mind the difference between multiplicity and integration...
c. More Complex Splitting Patterns

• When two different sets of adjacent $^1$H’s are coupled to a given $^1$H (n $^1$H’s on one adjacent C and m $^1$H’s on another), things can get more complicated...

• If the $J$ with $n =$ the $J$ with $m$; the number of peaks in an NMR multiplet will = $(m + n) + 1$, as you might have expected.

• However, if the $J$ with $n \neq$ the $J$ with $m$, you could see a much messier multiplet; it could have $(m + 1) \times (n + 1)$ lines!

• Let’s consider these possible scenarios using an n-propyl group as an example

Consider the signal for the $H_2$ labelled below as “b”:

If $J_{ab} = J_{bc}$ (or if $J_{ab} \approx J_{bc}$), we’d expect $5 + 1 = 6$ peaks/lines for this $H_2$ signal. (We will see this on the next slide…)

But…what if $J_{ab}$ is different from $J_{bc}$? Just for kicks, let’s say $J_{ab} >> J_{bc}$…in that case, we could get 12 lines for that $H_2$ signal!
The Hc’s and Hα’s are not equivalent, so we can’t necessarily just add them together and use the \( n + 1 \) rule, but...

- \( J_{ab} \) and \( J_{bc} \) tend to be very similar in an open-chain system like this, so the \( n + 1 \) “rule” does work here--the Hb signal is a sextet.

The Actual \(^1\)H NMR Spectrum of 1-Bromopropane:

But here’s one where we do see some different vicinal \( J \)-values:

The CH\(_2\) \(^1\)H’s are diastereotopic (see slides 17-19), so they are inequivalent, and appear as two one-H signals (\( \delta 3.46 \) and \( 3.58 \)).

This also makes the CH and CH\(_2\) multiplets more complicated!

This is a very common phenomenon among compounds that have one or more stereocenters...
d. Alkene $J$-values

- $^1\text{H}$'s on C=C's often give characteristic splitting patterns. Consider the three possible disubstituted C=C's...

- When the $^1\text{H}$'s on the C=C are different (usually the case unless the thing is symmetrical), each $^1\text{H}$ splits the signal of the other so that each appears as a doublet (a “$d$”).

- The magnitude of the $J$ depends on the arrangement of the H's:

  \[ \nu_{\text{geminal}} < \nu_{\text{cis}} < \nu_{\text{trans}} \]

  0–3 Hz  5–10 Hz  11–18 Hz

This gives us an easy way to tell which kind of system we have!

---

*Cis vs. trans* isomers can easily be distinguished!

\[ (E)-3\text{-chloropropenoic acid} \]

\[ (Z)-3\text{-chloropropenoic acid} \]
Consider a vinyl group (-CH=CH₂). All three H's are different, and all three possible couplings show up:

\[ \begin{align*}
&\text{vinyl acetate} \\
&\delta_a = 1.2 \text{ Hz (geminal)} \\
&\delta_{ab} = 6.5 \text{ Hz (cis)} \\
&\delta_{bc} = 14 \text{ Hz (trans)} \\
\end{align*} \]

And the shifts are surprisingly different →

\[ \text{\textsuperscript{1}H NMR Spectrum of Vinyl Acetate} \]
e. NMR Solvents

- NMR spectra are usually collected using dilute solutions.
- Regular solvents pose a problem—so much more abundant than the analyte that they would give giant masking signals...
- Solution: deuterated solvents—classic example = CDCl₃ (as opposed to CHCl₃). D (= ²H) does not show a ¹H NMR signal!
- Could still see a small CHCl₃ signal (~7.26 ppm), but it is due to trace residual CHCl₃, not the CDCl₃.

![NMR spectrum diagram]

f. ¹H NMR Signals for OH Protons

- OH (and amine NH) protons behave differently from CH’s, mainly because they undergo H-bonding and/or exchange.
- An OH might not show coupling with adjacent CH’s (as below), but for another sample of the same compound, it might!
- Consider the spectrum of ethanol (CH₃CH₂OH) below:

![NMR spectrum diagram]
• The three-proton CH₃ signal is split by the CH₂ into a triplet.
• The two-proton CH₂ signal is split by the CH₃ into a quartet.
• But…the adjacent OH shows no coupling with the CH₂???
• OH’s often undergo intermolecular exchange so rapidly that a given OH proton is not around long enough to exert mutual spin effects with the CH₂ → no coupling!

• If rate is slowed somehow (e.g., in very dilute solution), coupling can sometimes be seen, but this is hard to predict.
• Intermediate situations can occur where coupling is not observed, but the OH shows up as a broad lump…can even be so broad that you don’t notice it!

g. Cyclohexane Conformers

• Cyclohexane conformers interconvert rapidly at room temperature. An NMR spectrum shows an average of these.

• Each C has two different types of H—one axial, one equatorial—but their rapid interconversion results in a single NMR signal due to the average environment that each H experiences.

• Otoh, if a system has a strongly preferred conformer, e.g., due to a t-butyl substituent, then the ax and eq H’s would be different.
h. Protons on Benzene Rings

- Benzene’s $^1\text{H}$’s are equivalent, and give one peak at 7.27 ppm.

- **Monosubstituted benzenes contain five $^1\text{H}$’s that are not all equivalent; the appearance of the signals varies, depending on what is attached.**

Think about why this might be—we’ll revisit it when we talk more about benzenes...

Patterns for more highly substituted benzenes will be diagnostic because their vicinal $J$-values are larger (ca. 7.5 Hz) than others.

i. Overlapping signals

- Efforts (even counting signals) can be hampered by overlap of signals that have very similar chemical shifts.

- For example, technically, 1-chlorooctane (below) has eight different kinds of $\text{H}$. (This is what the book would say...)

- However, the environments of some of the $\text{CH}_2$’s are so similar that they resonate at about the same place, giving a nearly uninterpretable blob with confusing integration...

Still get some useful info out of it, but this does complicate things...
H. Use of $^1$H NMR in Structure Determination

Some steps to consider are listed below. They do not have to be followed in this order. With practice, some will become intuitive.

1. Figure the number of unsaturations: $\#C - \frac{1}{2} \#(H + X) + \frac{1}{2} \#N + 1$

2. Count the signals: try to determine the # of different types of H

3. Look at integration to tell how many of each type you have. This can tell you whether a signal = a CH$_3$ or a CH or CH$_2$. Think about possible symmetry issues.

4. Look at splitting to tell what's next to what. Look for diagnostic patterns (e.g., see slide 38).

5. Consider chemical shifts (and any other available information, such as IR) to decide what kind of functional groups you might have, and which H's they are near.

Example: C$_4$H$_8$O$_2$; IR says there's a C=O

1. Number of unsaturations = 4 - 4 + 1 = 1 (the C=O must be the only one!)

2. Number of different types of H? There are three (three signals).
3. How many of each type (based on integration)? Ratio of 3:2:3
(and 3H + 2H + 3H = 8H; matches formula).

(Only 4 C → this must correspond to two CH₃’s and a CH₂).

So…we have a C=O, two different CH₃’s, a CH₂, and one more O. Not all that many possibilities….but let’s keep going…

4. Splitting? CH₃ at 1.1 ppm and CH₂ split each other → an ethyl pattern, just like in ethanol. The other CH₃ is a singlet—it must have no vicinal H neighbors!

5. Shift—at this point, there are only two chemically reasonable structures, and shift distinguishes them:

The only way the CH₃ singlet can be downfield of the CH₂ is to place it on the electronegative O

G. ¹³C NMR Spectra

• ¹²C is not NMR-active because its I value = 0.

• However, 1.1% of the carbon nuclei in nature are not ¹²C—they are ¹³C (remember that from the MS chapter?), and the I value for ¹³C = ½, just like ¹H, so we can see ¹³C’s by NMR!

• “Standard” ¹³C NMR spectra are easier to analyze because the signals are not split; each type of C appears as a single peak.

  • Huh? Why should that be??
  • Two reasons…
The $^{13}$C’s out there are randomly distributed among all possible positions within a molecule.

Due to its low natural abundance (1.1%), the chance of two $^{13}$C’s being bonded to each other is very small ($0.011 \times 0.011 = 0.0001\%$).

Thus, nearly all $^{13}$C’s will be attached to NMR-inactive $^{12}$C, which does not cause splitting.

Q: But couldn’t $^{13}$C NMR signals be split by nearby $^1$H’s?

A: Yes, but standard $^{13}$C NMR experiments employ a technique that “decouples” the $^1$Hs from the $^{13}$C’s, so that every $^{13}$C peak is simplified to a singlet.

This throws away coupling information, and prevents accurate integration, but makes the thing easier to interpret AND improves s/n (remember, we can only see 1% of the carbons in the sample...)

H. Types of Structural Info Provided by $^{13}$C NMR Spectra

Since we don’t see the coupling and can’t integrate, there are only two features of a standard $^{13}$C NMR spectrum that provide structural info:

- **Number** of signals: indicates the number of “different types of C” (i.e., different environments of C’s) in a molecule.

- **Position** of signals: shifts help sort out what types of C the molecule contains.

Re intensities: we can’t accurately integrate $^{13}$C NMR spectra, but signals that correspond to more than one identical C (e.g., the CH$_3$ in (CH$_3$)$_2$CHOH) do tend to be somewhat larger.

Also, C’s with no H on them tend to give somewhat smaller signals than others.
1. **Number of signals**

Recognizing the # of different types of C has analogy to the spotting the # of different types of H.

- 1 \(^{13}\)C NMR signal
- 2 \(^{13}\)C NMR signals
- 3 \(^{13}\)C NMR signals

Both C's are equivalent.

However, must be wary of symmetry issues…e.g., the compound below would have only four \(^{13}\)C NMR signals in the sp\(^2\) region (plus the OCH\(_3\) carbon in the sp\(^3\) region):

![Compound Image]

2. **Position—chemical shift range**

- \(^{13}\)C NMR signals occur over a much broader chemical shift range than \(^1\)H signals (ca. 0-220 ppm downfield from TMS).

- Why? C's can be hybridized differently—H cannot—and each C is bonded to more things than an H. There’s just more variety....

- **Chemical shift trends** in \(^{13}\)C NMR parallel those in \(^1\)H NMR, because the same basic kinds of factors influence them.

<table>
<thead>
<tr>
<th>Table 14.5 Common (^{13})C Chemical Shift Values</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of carbon</strong></td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>(\text{sp}^2) H</td>
</tr>
<tr>
<td>(\text{sp}^2) Z</td>
</tr>
<tr>
<td>Z = N, O, X</td>
</tr>
</tbody>
</table>
An advantage of the wide shift range and sharp signals is that $^{13}$C NMR spectra tend to have less of an issue with overlap.

Remember that blobby $^1$H NMR spectrum of 1-chlorooctane on slide 52?

The $^{13}$C NMR spectrum clearly resolves all eight $^{13}$C signals!
• Thus, $^{13}$C NMR is a useful compliment to $^1$H NMR in structure determination.

• Allows C-types to be counted, and shows signals for C’s that do not have $^1$H on them.

• e.g., $^1$H NMR alone would not explicitly show you that you have a C=O, but $^{13}$C NMR would...

• There are *many* other, more sophisticated NMR techniques available to help deal with more complicated structures, but they are beyond the scope of this course.

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**A Final NMR Note—Magnetic Resonance Imaging (MRI)**

MRI—a valuable technique used in medicine for visualizing soft tissues not well resolved by x-rays—employs NMR technology, but note how they avoided using the term “nuclear”...

an MRI instrument

an image showing an area of compression (box A) in a spinal column