Structural Determination of Organic Compounds

- How do you know your reaction worked?
- How do you know your final product is what you wanted?
  - Is the molecular formula of the product correct?
  - Are the atoms connected correctly to give you the desired structure?
  - Can you identify all the functional groups of your product?

How can you answer these questions?
Mass Spectrometry

- Provides the molecular mass of a compound
- The compounds are charged (positive or negative ion) and separated based on the m/z (mass/charge) ratio

Organic Spectroscopy:
Interaction of Light/Energy with matter

- UV-vis Spectroscopy
  - Presence or not of a chromophore (double bond containing compound)

- IR Spectroscopy
  - Presence or not of different functional groups

- NMR Spectroscopy
  - Presence or not of different functional groups
  - Information on C-C and C-H bonding
Mass Spectrometry
- The tallest peak in the mass spectrum is called the base peak.
- For methane the base peak is also the M peak (molecular ion), although this is usually not the case.
- Though most C atoms have an atomic mass of 12, 1.1% have a mass of 13.
- Thus, \(^{13}\text{CH}_4\) is responsible for the peak at \(m/z = 17\). This is called the M + 1 peak.
Mass Spectrometry

- Provides the molecular mass of a compound
- The compounds are charged (positive or negative ion) and separated based on the m/z (mass/charge) ratio

Organic Spectroscopy:
Interaction of Light/Energy with matter

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- NMR Spectroscopy
  
  - Presence or not of different functional groups
  
  - Information on C-C and C-H bonding
Electromagnetic Spectrum

- **UV-Vis**
  - UV: 200 – 400 nm
  - Visible: 400 – 800 nm

- **IR**
  - 800 – 1050 nm

- **NMR**
  - Radiowaves
  - 1 mm – 10,000 km

- **Radiowaves**
  - Penetrates Earth’s Atmosphere?

- **Radiowave Wavelength (m)**
  - Radio: $10^3$
  - Microwave: $10^{-2}$
  - Infrared: $10^{-5}$
  - Visible: $0.5 \times 10^{-6}$
  - Ultraviolet: $10^{-8}$
  - X-ray: $10^{-10}$
  - Gamma ray: $10^{-12}$

- **Approximate Scale of Wavelength**
  - Buildings
  - Humans
  - Butterflies
  - Needle Point Protozoans
  - Molecules
  - Atoms
  - Atomic Nuclei

- **Frequency (Hz)**
  - $10^4$
  - $10^8$
  - $10^{12}$
  - $10^{15}$
  - $10^{16}$
  - $10^{18}$
  - $10^{20}$

- **Temperature of objects at which this radiation is the most intense wavelength emitted**
  - 1 K: -272 °C
  - 100 K: -173 °C
  - 10,000 K: 9,727 °C
  - 10,000,000 K: ~10,000,000 °C
IR Spectroscopy
Absorption of IR Light

- Absorption of IR light causes changes in the vibrational motions of a molecule.
- The different vibrational modes available to a molecule include stretching and bending modes.

- The vibrational modes of a molecule are quantized, so they occur only at specific frequencies which correspond to the frequency of IR light.
Bond Stretching and Bending

- When the frequency of IR light matches the frequency of a particular vibrational mode, the IR light is absorbed, causing the amplitude of the particular bond stretch or bond bend to increase.

Different kinds of bonds vibrate at different frequencies, so they absorb different frequencies of IR light.

IR spectroscopy distinguishes between the different kinds of bonds in a molecule, so it is possible to determine the functional groups present.
Characteristics of an IR Spectrum

- In an IR spectrometer, light passes through a sample.
- Frequencies that match the vibrational frequencies are absorbed, and the remaining light is transmitted to a detector.
- An IR spectrum is a plot of the amount of transmitted light versus its wavenumber.
- Most bonds in organic molecules absorb in the region of 4000 cm$^{-1}$ to 400 cm$^{-1}$.
The IR spectrum is divided into two regions: the functional group region (at $\geq 1500$ cm$^{-1}$), and the fingerprint region (at $< 1500$ cm$^{-1}$).

Figure 13.9

- **A** and **B** show peaks in the same regions for their C=O group and $sp^3$ hybridized C–H bonds.
- **A** and **B** are different compounds, so their fingerprint regions are quite different.
Four Regions of an IR Spectrum

- Bonds absorb in four predictable regions of an IR spectrum.

Figure 13.11
<table>
<thead>
<tr>
<th>Bond type</th>
<th>Approximate $\tilde{\nu}$ (cm$^{-1}$)</th>
<th>Intensity</th>
</tr>
</thead>
<tbody>
<tr>
<td>O–H</td>
<td>3600–3200</td>
<td>strong, broad</td>
</tr>
<tr>
<td>N–H</td>
<td>3500–3200</td>
<td>medium</td>
</tr>
<tr>
<td>C–H</td>
<td>~3000</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• C$_{sp^3}$–H</td>
<td>3000–2850</td>
</tr>
<tr>
<td></td>
<td>• C$_{sp^2}$–H</td>
<td>3150–3000</td>
</tr>
<tr>
<td></td>
<td>• C$_{sp}$–H</td>
<td>3300</td>
</tr>
<tr>
<td>C≡C</td>
<td>2250</td>
<td>medium</td>
</tr>
<tr>
<td>C≡N</td>
<td>2250</td>
<td>medium</td>
</tr>
<tr>
<td>C=O</td>
<td>1800–1650 (often ~1700)</td>
<td>strong</td>
</tr>
<tr>
<td>C=C</td>
<td>1650</td>
<td>medium</td>
</tr>
<tr>
<td></td>
<td><img src="image" alt="Structure" /></td>
<td>1600, 1500</td>
</tr>
</tbody>
</table>
IR Spectrum of 2-Butanol

- The OH group of the alcohol shows a strong absorption at 3600-3200 cm\(^{-1}\).
- The peak at ~ 3000 cm\(^{-1}\) is due to \(sp^3\) hybridized C–H bonds.
• The C=O group in the ketone shows a strong absorption at ~1700 cm\(^{-1}\).
• The peak at ~3000 cm\(^{-1}\) is due to \(sp^3\) hybridized C–H bonds.
IR Spectrum of Octylamine

- The N–H bonds in the amine give rise to two weak absorptions at 3300 and 3400 cm$^{-1}$.
The amide exhibits absorptions above 1500 cm\(^{-1}\) for both its \(N-H\) and \(C=O\) groups: \(N-H\) (two peaks) at 3200 and 3400 cm\(^{-1}\); \(C=O\) at 1660 cm\(^{-1}\).
The C≡N of the nitrile absorbs in the triple bond region at \( \sim 2250 \text{ cm}^{-1} \).
NMR Spectroscopy
Nuclear Magnetic Resonance Spectroscopy

• Nuclear magnetic resonance spectroscopy is a powerful analytical technique used to characterize organic molecules by identifying carbon-hydrogen frameworks within molecules.

• Two common types of NMR spectroscopy are used to characterize organic structure:
  • $^1\text{H}$ NMR is used to determine the type and number of H atoms in a molecule; and
  • $^{13}\text{C}$ NMR is used to determine the type of carbon atoms in a molecule.

• The source of energy in NMR is radio waves which have long wavelengths, and thus low energy and frequency.

• When low-energy radio waves interact with a molecule, they can change the nuclear spins of some elements, including $^1\text{H}$ and $^{13}\text{C}$. 
NMR (Nuclear Magnetic Resonance) Spectroscopy

Spin Energy States

$+ \frac{1}{2}$ (or $\alpha$)  
$- \frac{1}{2}$ (or $\beta$)
NMR spectroscopy is applied to small and medium sized (proteins) organic molecules.

Most commonly used: $^1\text{H NMR}$
All different hydrogens in a compound have a unique interaction with the applied magnetic field resulting in different NMR signals.

What is the origin of the NMR signal?

**Same basic technique as:**

**MRI**
*(Magnetic Resonance Image)*

- An MRI is NMR-spectroscopy applied to whole body parts, not individual molecules (Biological NMR).

- Human body: 75% water
The $^1\text{H}$ atoms in each water molecule interact differently with the applied magnetic field based on their different environments, resulting in different signals...
Magnetic Fields in NMR

- When a charged particle such as a proton spins on its axis, it creates a magnetic field, causing the nucleus to act like a tiny bar magnet.
- Normally, these tiny bar magnets are randomly oriented in space.
- However, in the presence of a magnetic field \((B_0)\), they are oriented with or against this applied field.
- More nuclei are oriented with the applied field because this arrangement is lower in energy.
- The energy difference between these two states is very small (<0.1 cal).
Electron Environment

- The frequency at which a particular proton absorbs is determined by its electronic environment.
- Protons in different environments absorb at slightly different frequencies, so they are distinguishable by NMR.
- The size of the magnetic field generated by the electrons around a proton determines where it absorbs.
- Modern NMR spectrometers use a constant magnetic field strength $B_0$, and then a narrow range of frequencies is applied to achieve the resonance of all protons.
- Only nuclei that contain odd mass numbers (such as $^1$H, $^{13}$C, $^{19}$F, and $^{31}$P) or odd atomic numbers (such as $^2$H and $^{14}$N) give rise to NMR signals.
$^1$H NMR Spectra

- An NMR spectrum is a plot of the intensity of a peak against its chemical shift, measured in parts per million (ppm).

Sample $^1$H NMR spectrum
$\text{CH}_3\text{OC(CH}_3\text{)}_3$

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Interpreting NMR Spectra

• NMR absorptions generally appear as sharp peaks.
• Most protons absorb between 0-10 ppm.
• The terms “upfield” and “downfield” describe the relative location of peaks.
  • Upfield means to the right (higher magnetic field).
  • Downfield means to the left (lower magnetic field).
• An external standard, \((\text{CH}_3)_4\text{Si}\) (tetramethylsilane) is added to the sample tube prior to the NMR measurement.
• NMR absorptions are measured relative to the position of a reference peak at 0 ppm on the \(\delta\) scale due to tetramethylsilane (TMS).
• TMS is a volatile inert compound that gives a single peak upfield from typical NMR absorptions.
Structural Information from Features of a $^1$H NMR Spectrum

- Number of signals: indicates the number of different types of hydrogen in a molecule.
- Position of signals: indicates what types of hydrogen the molecule contains.
- Intensity of signals: indicates the relative amounts (how many) of each kind of hydrogen in the molecule.
- Spin-spin splitting of signals: gives further information of the neighboring environment for the various hydrogens in the molecule.
Number of Signals in $^1$H NMR

- The number of NMR signals equals the number of different types of protons in a compound.
- Protons in different environments give different NMR signals.
- Equivalent protons give the same NMR signal.
Number of $^1$H NMR Signals—Examples

Figure 14.2

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- To rigorously determine if two hydrogens in a molecule are the same:
  - replace each hydrogen by a different atom, Z (e.g., Cl) and
  - determine if the resulting compound is the same or different.
- For example, replacement of each methyl hydrogen at C$_1$ and C$_5$ in pentane produces 1-chloropentane, replacement of each methylene hydrogen at C$_2$ and C$_4$ leads to 2-chloropentane and at C$_3$ forms 3-chloropentane.
Shielding and Signal Position

- The \( H_b \) protons are **deshielded** because they are closer to the electronegative Cl atom, so they absorb **downfield** from \( H_a \).

- Because F is more electronegative than Br, the \( H_b \) protons are more **deshielded** than the \( H_a \) protons and absorb farther **downfield**.

- The larger number of electronegative Cl atoms (two versus one) **deshields** \( H_b \) more than \( H_a \), so it absorbs **downfield** from \( H_a \).
Characteristic Chemical Shifts

- Protons in a given environment absorb in a predictable region in an NMR spectrum.

<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>( \text{sp}^3 \text{C-H} )</td>
<td>0.9–2</td>
<td>( \text{sp}^2 \text{C} = \text{C} )</td>
<td>4.5–6</td>
</tr>
<tr>
<td>( \text{RCH}_3 )</td>
<td>~0.9</td>
<td>( \text{R}_2 \text{CH}_2 )</td>
<td>~1.3</td>
</tr>
<tr>
<td>( \text{R}_3 \text{CH} )</td>
<td>~1.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>( \text{Z} = \text{C, O, N} )</td>
<td>1.5–2.5</td>
<td>( \text{RCH} = \text{O} )</td>
<td>9–10</td>
</tr>
<tr>
<td>( \text{C} = \text{C-H} )</td>
<td>~2.5</td>
<td>( \text{RCHO} )</td>
<td>10–12</td>
</tr>
<tr>
<td>( \text{sp}^3 \text{C-H} )</td>
<td>2.5–4</td>
<td>( \text{RO-H} \text{ or } \text{R-N-H} )</td>
<td>1–5</td>
</tr>
</tbody>
</table>

Table 14.1 Characteristic Chemical Shifts of Common Types of Protons
Summary of $\pi$ Electron and Chemical Shift

<table>
<thead>
<tr>
<th>Proton type</th>
<th>Effect</th>
<th>Chemical shift (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image" alt="Benzene" /></td>
<td>highly deshielded</td>
<td>6.5–8</td>
</tr>
<tr>
<td><img src="image" alt="Alkene" /></td>
<td>deshielded</td>
<td>4.5–6</td>
</tr>
<tr>
<td><img src="image" alt="Alkyne" /></td>
<td>shielded</td>
<td>~2.5</td>
</tr>
</tbody>
</table>
Regions in the $^1$H NMR Spectrum

Figure 14.5

- Shielded protons absorb at lower chemical shift (to the right).
- Deshielded protons absorb at higher chemical shift (to the left).
\(^1\text{H} \text{ NMR Integration}\)

- Modern NMR spectrometers automatically calculate and plot the value of each integral in arbitrary units.
- The ratio of integrals to one another gives the ratio of absorbing protons in a spectrum.
- Note that this gives a ratio, and not the absolute number, of absorbing protons.
**$^1$H NMR—Spin-Spin Splitting**

- The spectra up to this point have been limited to single absorptions called singlets.
- Often signals for different protons are split into more than one peak.

![Diagram showing spin-spin splitting](image-url)
The frequency difference, measured in Hz between two peaks of the doublet is called the **coupling constant, \( J \).**

- One adjacent proton splits an NMR signal into a doublet.
Splitting Patterns

- Three general rules describe the splitting patterns commonly seen in the $^1$H NMR spectra of organic compounds.

  [1] Equivalent protons do not split each other’s signals.

  [2] A set of $n$ nonequivalent protons splits the signal of a nearby proton into $n + 1$ peaks.

  [3] Splitting is observed for nonequivalent protons on the same carbon or adjacent carbons.
Proximity and Splitting

Splitting is not generally observed between protons separated by more than three $\sigma$ bonds.

2-butanone

H$_a$ and H$_b$ are separated by four $\sigma$ bonds.

no splitting between H$_a$ and H$_b$

ethyl methyl ether

H$_a$ and H$_b$ are separated by four $\sigma$ bonds.

no splitting between H$_a$ and H$_b$
$^1$H NMR of 2-Bromopropane

- The 6 $H_a$ protons are split by the one $H_b$ proton to give a doublet.
- The $H_b$ proton is split by 6 equivalent $H_a$ protons to yield a septet.
Since $H_a$ and $H_c$ are not equivalent to each other, we cannot always add them together and use the $n + 1$ rule.

However, since the coupling constants, $J_{ab}$ and $J_{bc}$, are very similar, the signal for $H_b$ is a sextet (follows the $n + 1$ rule).
1H NMR of OH Protons

- Under usual conditions, an OH proton does not split the NMR signal of adjacent protons.
- The signal due to an OH proton is not split by adjacent protons.

Figure 14.12
Protons on Benzene Rings

- Benzene has six equivalent deshielded protons and exhibits a single peak in its $^1$H NMR spectrum at 7.27 ppm.
- Monosubstituted benzenes contain five deshielded protons that are no longer equivalent, and the appearance of these signals is highly variable, depending on the identity of $Z$.

Figure 14.13

- The appearance of the signals in the 6.5–8 ppm region of the $^1$H NMR spectrum depends on the identity of $Z$ in $C_6H_5Z$. 
HOW TO Use $^1$H NMR Data to Determine a Structure

Example Using its $^1$H NMR spectrum, determine the structure of an unknown compound X that has molecular formula $C_4H_8O_2$ and contains a C=O absorption in its IR spectrum.

<table>
<thead>
<tr>
<th>absorption</th>
<th>ppm</th>
<th>integration</th>
</tr>
</thead>
<tbody>
<tr>
<td>[A] triplet</td>
<td>1.1</td>
<td>15</td>
</tr>
<tr>
<td>[B] quartet</td>
<td>2.3</td>
<td>11</td>
</tr>
<tr>
<td>[C] singlet</td>
<td>3.7</td>
<td>14</td>
</tr>
</tbody>
</table>

Step [1] Determine the number of different kinds of protons.

- The number of NMR signals equals the number of different types of protons.
- This molecule has three NMR signals ([A], [B], and [C]) and therefore three types of protons ($H_a$, $H_b$, and $H_c$).
Step [2] Use the integration data to determine the number of H atoms giving rise to each signal (Section 14.5).

- Total number of integration units: $14 + 11 + 15 = 40$ units
- Total number of protons = 8
- Divide: $40$ units/8 protons = **5 units per proton**
- Then, divide each integration value by this answer (5 units per proton) and round to the nearest whole number.

$$
\frac{15}{5} = 3 \text{ H}_a \text{ protons} \quad \frac{11}{5} = 2.2 \approx 2 \text{ H}_b \text{ protons} \quad \frac{14}{5} = 2.8 \approx 3 \text{ H}_c \text{ protons}
$$

- signal [A] Three equivalent H's usually means a **CH$_3$** group.
- signal [B] Two equivalent H's usually means a **CH$_2$** group.
- signal [C] Three equivalent H's usually means a **CH$_3$** group.
1H NMR—Structure Determination, continued

**Step [3]** Use individual splitting patterns to determine what carbon atoms are bonded to each other.

- Start with the singlets. Signal [C] is due to a CH$_3$ group with no adjacent nonequivalent H atoms. Possible structures include:

  \[
  \text{CH}_3\text{O}^- \quad \text{or} \quad \text{C} = \text{O} \quad \text{or} \quad \text{CH}_3\text{C}^- \\
  \]

- Because signal [A] is a **triplet**, there must be 2 H's (CH$_2$ group) on the adjacent carbon.
- Because signal [B] is a **quartet**, there must be 3 H's (CH$_3$ group) on the adjacent carbon.
- This information suggests that X has an **ethyl** group $\text{CH}_3\text{CH}_2-$.

To summarize, X contains CH$_3-$, CH$_3$CH$_2-$, and C = O (from the IR). Comparing these atoms with the molecular formula shows that one O atom is missing. Because O atoms do not absorb in a $^1$H NMR spectrum, their presence can only be inferred by examining the chemical shift of protons near them. O atoms are more electronegative than C, thus deshielding nearby protons, and shifting their absorption downfield.
Step [4] Use chemical shift data to complete the structure.

- Put the structure together in a manner that preserves the splitting data and is consistent with the reported chemical shifts.
- In this example, two isomeric structures (A and B) are possible for X considering the splitting data only:

![Structural pieces and Possible structures](image)

- Chemical shift information distinguishes the two possibilities. The electronegative O atom deshields adjacent H’s, shifting them downfield between 3 and 4 ppm. If A is the correct structure, the singlet due to the CH₃ group (H_c) should occur downfield, whereas if B is the correct structure, the quartet due to the CH₂ group (H_b) should occur downfield.
- Because the NMR of X has a singlet (not a quartet) at 3.7, **A is the correct structure.**
\( ^{13}\text{C} \) NMR Spectrum Example

- \( ^{13}\text{C} \) Spectra are easier to analyze than \( ^{1}\text{H} \) spectra because the signals are not split.
- Each type of carbon atom appears as a single peak.