CHEM 222
Organic Chemistry II

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Section I: Spectroscopy and Structure Determination

It is important for chemists to know what they have made in the laboratory. In order to determine the structure of a newly synthesized compound, they rely on techniques that will provide pieces of information regarding the structure of the molecule. There are a variety of methods, and each of them is a broad subject on its own. This part in organic chemistry II is a survey of the main methods. Note that none of the methods provides chemists with the whole molecular structure, solving for it is similar to playing puzzles, different pieces of information need to be combined.

***Exam Relevance:
- Extract information from the given spectra (MS, IR, $^{13}$C and $^1$H).
- Attempt to provide a reasonable structure.

Mass Spectrometry

Spectrometric method: does not involve interaction between light and matter.

Ion selection: ionized and possibly fragmented chemical species enter a magnetic field. Only the ions with the correct mass-to-charge ratio (m/z) are detected.

Ionization methods: Hard and Soft, depending on the energy of the ion source.

Hard ionization: high energy, favoring fragmentation of molecules, provides information on the structure, generally used for small molecules with mass lower than a few hundred units (e.g. common organic molecules). Electron Impact (E.I.) is an example of hard ionization method.

Soft ionization: low energy, does not favor fragmentation, provides information on the molecular mass, generally used for large molecules with mass in the range of a few thousand units (e.g. proteins). Electrospray Ionization (E. S. I.) is an example of soft ionization method.

Molecular Ion Peak:

On a mass spectrum, this peak, if it exists, is found on the far right of the spectrum. Note that it may not be the most intense peak. If the molecule is easily fragmented, then this may just be a little peak. Nonetheless, this peak allows for the determination of the molecular mass, which is useful in validating the proposed structure.

Note that if the value of m/z for this peak is odd, then there is an odd number of nitrogen atoms present in the structure. The reason is that nitrogen is trivalent, therefore the number of hydrogen atoms will be one less. It is obvious that for a molecular ion peak having an even value of m/z, the number of nitrogen atoms is even. However, it is rare that test or exam questions will include more than one nitrogen atom.

Base Peak:

The most intense peak on the spectrum. It is assigned a relative intensity of 100, the intensity of other peaks is relative to this peak. However, since it may not necessarily (and probably not going to be) the molecular ion peak, for Chem 222, it is not particular useful.
Mass Spectrum of Adamantane (M=136) https://sdbs.db.aist.go.jp/sdbs No.: 6768.

Isotopic Peak: \((m+1)\) for Carbon-13

Due to carbon-13 isotope, this peak is generally at **one unit to the right of the molecular ion peak**, hence it is called the \((m+1)\) peak. From the relative height of the two peaks, one can determine the number of carbon atoms in the molecule, but a more reliable method is \(^{13}\)C NMR.

Isotopic Peak: \((m+2)\) for Chlorine-37 and Bromine-81

Chlorine has two isotopes, chlorine-35 (75% abundance) and chlorine-37 (25% abundance). Hence, for molecules that contain chlorine, there will be a peak at \((m+2)\), two mass unit more than the molecular ion peak, with approximately \(1/3\) **the intensity** due to the 3:1 ratio from the relative natural abundance of chlorine.

Bromine, too, has two isotopes, bromine-79 and bromine-81. Since their natural abundance is approximately equal, the \((m+2)\) peak of a molecule containing bromine will have **similar intensity** as the \(m^+\) peak.

Note that if there are two carbon-13 atoms in a molecule, it will also contribute to the \((m+2)\) peak. However, the **likelihood of observing this is much smaller** compared to that of having chlorine-37 or bromine-81, therefore the contribution from two carbon-13 atoms is considered negligible.

***Exam Relevance & Important Points for Analyzing a Mass Spectrum:***

- Find the molecular ion peak at the far end to the right, that is the mass of the molecule.
  - Odd number \(\rightarrow\) odd number of nitrogen atoms.
  - Even number \(\rightarrow\) no nitrogen atom, or even number of them (rare).
- Evaluate the \((m+2)\) position.
  - \(1/3\) intensity \(\rightarrow\) presence of chlorine.
  - Same intensity \(\rightarrow\) presence of bromine.
- Move onto other methods for more information and come back at the end for verification.
Exercise: indicate the molecular ion peak, the base peak, and if chlorine or bromine exists.

https://sdb.db.aist.go.jp/sdb No.: 2109 and No.: 550.

**UV-VIS Spectroscopy**

It provides information on the presence of a conjugated system, i.e. presence of multiple $\pi$ bonds.

Not particularly useful because it is difficult to draw definitive conclusions from it.

Larger conjugated system $\rightarrow$ lower energy for electron promotion $\rightarrow$ longer excitation wavelength

Generally not given on an exam as it provides little to no useful information.

UV Spectra of Benzoic Acid (left) and Naphthalene (right). Pavia et al. *Introduction to Spectroscopy*, 5th ed. 2015.

***Exam Relevance & Important Points for Analyzing a UV-VIS Spectrum (if provided):***

- Find a peak in the region of 220 to 320 nm.
  - If a peak exists, then a conjugated system exists in the structure.
  - If not, then there is no conjugation.
Infrared Spectroscopy

Molecules, more specifically chemical bonds, can vibrate.

Vibrational energy, which is much lower compared to electronic transitional energy, is the key to IR.

Three major concepts to understand in IR: wavenumber, peak intensity, peak shape.

Wavenumber:

The frequency of vibration, $\nu$, of a chemical bond is not plotted on an IR spectrum, instead, it is the inverse of vibrational frequency, called the wavenumber, $\bar{\nu}$, that is plotted.

Range of wavenumbers: from $4000 \text{ cm}^{-1}$ to $400 \text{ cm}^{-1}$.

**Diagnostic** region: from 4000 to $1500 \text{ cm}^{-1}$.

**Fingerprint** region: from $1500$ to $400 \text{ cm}^{-1}$.

As the names suggest, the diagnostic region is where characteristic peaks appear, and that is the focus of Chem 222; while the fingerprint region is for detailed analysis and identification of the compound.

Peak Intensity:

It reflects the intensity in **change in dipole moment** during vibration of a chemical bond.

More intense (lower transmittance) $\rightarrow$ great change in dipole moment $\rightarrow$ very polar bond (e.g. $R_2C=O$).

Less intense (higher transmittance) $\rightarrow$ small change in dipole moment $\rightarrow$ not very polar bond (e.g. $RC\equiv CR$).

![Infrared Spectrum of Acetone](https://sdfs.db.aist.go.jp No.: 319)
Peak Shape:

A peak can be narrow or broad on an IR spectrum. Broad peaks result from **hydrogen bonding** of the functional group. Hence, the signals from OH, NH and COOH appear as broad peaks.

![Infrared Spectrum of Propionic Acid](https://sdb.db.aist.go.jp)

To analyze an IR spectrum, one must learn the following functional groups and wavenumbers:

<table>
<thead>
<tr>
<th>Functional Group (Bond being studied)</th>
<th>Wavenumber/ cm(^{-1})</th>
<th>Intensity</th>
<th>Shape</th>
</tr>
</thead>
<tbody>
<tr>
<td>O—H</td>
<td>3200~3500</td>
<td>Strong</td>
<td>Broad</td>
</tr>
<tr>
<td>R(CO)O—H</td>
<td>2400~3400</td>
<td>Strong</td>
<td>Very Broad</td>
</tr>
<tr>
<td>N—H</td>
<td>3300~3400</td>
<td>Medium</td>
<td>Broad</td>
</tr>
<tr>
<td>C(_{\text{sp}})H</td>
<td>3200</td>
<td>Strong</td>
<td>Narrow</td>
</tr>
<tr>
<td>C(_{\text{sp}^2})H</td>
<td>3000~3200</td>
<td>Medium</td>
<td>Narrow</td>
</tr>
<tr>
<td>C(_{\text{sp}^3})H</td>
<td>&lt;3000</td>
<td>Medium ~ Strong</td>
<td>Narrow</td>
</tr>
<tr>
<td>R(CO)—H</td>
<td>2800~3000</td>
<td>Medium</td>
<td>Narrow</td>
</tr>
<tr>
<td>C = C</td>
<td>~2300</td>
<td>Varies</td>
<td>Narrow</td>
</tr>
<tr>
<td>C = N</td>
<td>1650~1850</td>
<td>Very Strong</td>
<td>Narrow</td>
</tr>
</tbody>
</table>

There is no need to memorize this table on purpose, with practice, the numbers come naturally.

***Exam Relevance & Important Points for Analyzing an IR Spectrum:***

- Look for the presence of carbonyl, carboxylic acid, hydroxyl, amine, nitrile and alkyne.
- Evaluate the peaks near 3000 cm\(^{-1}\).
  - Does it only have saturate carbon atoms? i.e. no band above 3000 cm\(^{-1}\).
  - Does it have unsaturated carbon atoms? i.e. band above 3000 cm\(^{-1}\).
- Identify as many peaks as possible, but make sure to assign them correctly.
Exercise: identify the functional groups present in the structure based on its IR spectrum

Exercise: from the formula $C_8H_7N$, propose a reasonable structure consistent with each of the following IRs.

https://sdbs.db.aist.go.jp/sdbs/ No.: 1010, No.: 718 and No.: 16674.
Nuclear Magnetic Resonance Spectroscopy: Hydrogen-1

It detects the change in nuclear spinning state in the presence of an external magnetic field.

The nucleus of hydrogen, when placed in a magnetic field, can be either aligned with (α position, lower in energy) or against (β position, higher in energy) the field.

Stronger magnetic field strength → larger energy gap between the two states → clearer signals.

Three important concepts in ¹H NMR: chemical shift, integration, and multiplicity.

Chemical Shift:

Due to differences in local environment, there can be subtle differences in the resonance frequency.

This is a measure relative to the resonance frequency of the hydrogen atoms on (CH₃)₄Si, tetramethylsilane, or TMS. It provides information on how many different types of hydrogen atoms there are in the structure.

\[
\text{chemical shift} = \delta = \frac{v_i - v_0}{v_0} \times 10^6
\]

The chemical shift is independent of the frequency of the spectrometer used because it is a relative measure. A spectrum acquired using a 90-MHz spectrometer will show the same signals at the same locations as a spectrum acquired using a 600-MHz spectrometer, but the latter shows narrower peaks due to higher sensitivity.

Shielded vs. Deshielded: (they are relative terms!)

A hydrogen atom is shielded when it is “protected from” (or not exposed to) the external magnetic field. In practice, this occurs when the hydrogen atom in question is near alkyl groups which are electron density donors. In this case, the chemical shift will be lower.

On the other hand, a hydrogen atom near electronegative atoms or groups is said to be deshielded because electron density is pulled away and it is exposed to the external magnetic field. Deshielded protons will have higher values of chemical shift.

As a starting point, it is good to remember the following ranges of chemical shift values.

<table>
<thead>
<tr>
<th>Chemical Shift Range</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 ppm</td>
<td>TMS</td>
</tr>
<tr>
<td>0~1.5 ppm</td>
<td>Alkyl groups far from electronegative groups</td>
</tr>
<tr>
<td>1.5~2.5 ppm</td>
<td>Allylic hydrogen ( H - C - C = ) alpha-hydrogen of carbonyl ( O = C - CH )</td>
</tr>
<tr>
<td>2.5~4.5 ppm</td>
<td>Hydrogen geminal to an electronegative group ( H - C - X )</td>
</tr>
<tr>
<td>4.5~6.5 ppm</td>
<td>Vinylic hydrogen ( H - C = C )</td>
</tr>
<tr>
<td>6.5~8.5 ppm</td>
<td>Aromatic hydrogen ( Ar - H )</td>
</tr>
<tr>
<td>8.5~10 ppm</td>
<td>Aldehydic hydrogen ( O = C - H )</td>
</tr>
<tr>
<td>&gt;10 ppm</td>
<td>Carboxylic acid hydrogen ( COOH )</td>
</tr>
</tbody>
</table>

Alcohol and amine hydrogen atoms have variable positions and are difficult to give an approximate range. They can be really deshielded with chemical shift approaching 9.0 ppm, or quite shielded at near 2.0 ppm.
Integration:

It represents the number of equivalent hydrogen atoms from a signal.

Equivalent hydrogen atoms are ones that are in the same chemical environment, for example, the hydrogen atoms on a methyl group are considered equivalent. The six hydrogen atoms on acetone are also equivalent.

Exercise: identify the equivalent proton(s) in the following structures

Generally, integration is done by the computer. On a test, the height of the line is measured, and the relative ratio is calculated, as shown in the following example,

\[
\frac{3.2}{1.4} = 2.3 \quad \frac{1.4}{1.4} = 1 \quad \frac{2.1}{1.4} = 1.5
\]

Obviously, there cannot be half a hydrogen atom, therefore the values are multiplied by two to give,

\[
2.3 \times 2 = 4.6 \approx 5 \text{ } H \quad 1 \times 2 = 2 \text{ } H \quad 1.5 \times 2 = 3 \text{ } H
\]

Therefore, the signal at 7.4 ppm represents a group of 5 equivalent hydrogen atoms, very likely to be from an aromatic ring (they are equivalent at lower resolution, better spectrometers can distinguish them and more peaks will be observed). The signal at 5.1 ppm represents a group of 2 equivalent hydrogen atoms, and the one at 2.0 ppm represents 3 equivalent hydrogen atoms.

It is possible to “eyeball” the relative height to find approximate ratio, but this approach is not recommended on evaluations. Only do it if time is running out.
Multiplicity:

It represents the **number of equivalent neighboring hydrogen atoms**.

For \( n \) equivalent neighboring hydrogen atoms, the signal will be split into \( n + 1 \) parts.

The following theoretical spectrum illustrates the point of this rule.

The signals are, from right to left, a quartet, a singlet and a triplet.

Applying the \((n + 1)\) rule, the three groups of \( H \) atoms have: three, none and two neighbors, respectively.

Exercise: determine the number of hydrogen atoms represented by each signal, and the number of neighbors.

***Exam Relevance & Important Points for Analyzing a \(^1\text{H} \) NMR Spectrum:***

- Make a table listing: chemical shift, integration and multiplicity.
- With information from other spectra and the above table, propose possible fragments for each signal.
- Combine the fragment together to suggest a reasonable structure.

https://www.nmrdb.org/
Nuclear Magnetic Resonance Spectroscopy: Carbon-13

Same principle as $^1$H NMR, but provides less information (at the level of Chem 222).

Only carbon-13 responds to a magnetic field because it has the quantum mechanical spin property from an odd number of nucleons in the nucleus. Carbon-12 do not respond (even number of protons and neutrons).

Since the natural abundance of carbon-13 is approximately 1.1%, the acquisition time of a $^{13}$C NMR spectrum is much longer.

The number of peaks corresponds to the minimal number of carbon atoms in the structure.

Similar to $^1$H NMR, knowing the following ranges can be helpful.

<table>
<thead>
<tr>
<th>Chemical Shift (ppm)</th>
<th>Type of Carbon Atoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 80 ppm</td>
<td>$sp^3$ hybridized carbon</td>
</tr>
<tr>
<td>80~100 ppm</td>
<td>$sp$ hybridized carbon</td>
</tr>
<tr>
<td>100~160 ppm</td>
<td>$sp^2$ hybridized carbon</td>
</tr>
<tr>
<td>160~200 ppm</td>
<td>Carbon of a carboxylic acid derivative</td>
</tr>
<tr>
<td>&gt;200 ppm</td>
<td>Carbon of carbonyl</td>
</tr>
</tbody>
</table>

Exercise: list the signals and determine the type of carbon atoms from the following spectra.

***Exam Relevance & Important Points for Analyzing a $^{13}$C NMR Spectrum:
- Make a table listing: chemical shift and the type of carbon atoms.
- Move onto other spectra and gather more information from them.

https://www.nmrdb.org/
A Solved Problem on Structural Determination:

Given the following spectra, propose a reasonable structure of the compound.

Mass Spec Data:

\[ m^+ + 151 \rightarrow \text{odd number, presence of nitrogen} \]

Absence of \((m + 2)\) peak, no chlorine or bromine

1H NMR Data:

\[ \begin{align*}
\delta & \quad \int H \quad \text{multi} \quad \text{fragment} \\
9.7 & \quad 1 \quad \text{singlet} \quad \text{X-NH-X} \\
9.1 & \quad 1 \quad \text{singlet} \quad \text{H-X} \\
7.4 & \quad 2 \quad \text{doublet} \\
6.7 & \quad 2 \quad \text{doublet} \\
2.0 & \quad 3 \quad \text{singlet} \quad \text{R-(C=O)-CH}_3 \\
\end{align*} \]

\( \text{X = electronegative group or element} \)

IR Data:

\(3326 \text{ cm}^{-1} \) alkene or amine

\(3165 \text{ cm}^{-1} \) alcohol

\(3149 \text{ cm}^{-1} \) \(C_{sp^2}-H\) (same for 3114 and 3036 \(\text{cm}^{-1}\))

\(2930 \text{ cm}^{-1} \) \(C_{sp^3}-H\)

\(13C\) NMR Data:

6 peaks \(\rightarrow\) minimum of 6 carbon

1 peak representing a \(sp^3\) carbon

4 peaks from 100~160 ppm, likely aromatic

1 peak at around 168 ppm, carboxylic acid derivative

Proposed Structure: \[ \text{mass check: } 12\times8+16\times2+14\times1+1\times9=151 \rightarrow \text{consistent with MS} \]

https://sdb.s.db.aist.go.jp/sdbs/ No.: 3290.