Organic Chemistry

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Mass Spectrometry (MS)

- An analytical technique for measuring the mass-to-charge ratio (m/z) of ions, most commonly positive ions, in the gas phase.

- Today, mass spectrometry is our most valuable analytical tool for the determination of precise molecular weights.
A Mass Spectrometer

A mass spectrometer is designed to do three things:

1. convert neutral atoms or molecules into a beam of positive (or negative) ions

2. separate the ions on the basis of their mass-to-charge ratio (m/z)

3. measure the relative abundance of each ion
Electron Ionization MS

- in the ionization chamber, the sample is bombarded with a beam of high-energy electrons
- collisions between these electrons and the sample result in loss of electrons from sample molecules and formation of positive ions

\[
\text{Molecular ion (A radical cation)}
\]

\[
\begin{align*}
\text{H} - \text{C} - \text{H} + \text{e}^- & \rightarrow \left[ \begin{array}{c} \text{H} \mid \text{H} \\ \text{H} \end{array} \right] + 2 \text{e}^- \\
\text{Molecular ion} & \end{align*}
\]
Molecular Ion

Molecular ion (M): the species formed by removal of a single electron from a molecule.

For our purposes, it does not matter which electron is lost; radical cation character is delocalized throughout the molecule.
Therefore, we write the molecular formula of the parent molecule in brackets with:
• a plus sign to show that it is a cation
• a dot to show that it has an odd number of electrons
At times, however, we find it useful to depict the radical cation at a certain position in order to better understand its reactions:

\[
\left[\text{CH}_3\text{CH}_2\text{OCH(CH}_3)_2\right]^+ \quad \text{CH}_3\text{CH}_2\text{OCH(CH}_3)_2
\]
Mass Spectrum

Mass spectrum: a plot of the relative abundance of each ion versus mass-to-charge ratio

Base peak: the most abundant peak; assigned an arbitrary intensity of 100

The relative abundance of all other ions is reported as a % of abundance of the base peak
The number of peaks in the MS spectrum of dopamine is given here as a function of detector sensitivity.

<table>
<thead>
<tr>
<th>Peak Intensity Relative to Base Peak</th>
<th>Number of Peaks Recorded</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 5%</td>
<td>8</td>
</tr>
<tr>
<td>&gt; 1%</td>
<td>31</td>
</tr>
<tr>
<td>&gt; 0.5%</td>
<td>45</td>
</tr>
<tr>
<td>&gt; 0.05%</td>
<td>120</td>
</tr>
</tbody>
</table>
Other MS techniques

What we have described is called electron ionization mass spectrometry (EI MS)

Other techniques include
- fast atom bombardment (FAB)
- matrix-assisted laser beam desorption ionization (MALDI)
- chemical ionization (CI)
Resolution: a measure of how well a mass spectrometer separates ions of different mass

- low resolution - capable of distinguishing among ions of different nominal mass, that is ions that differ by at least one or more mass units
- high resolution - capable of distinguishing among ions that differ in mass by as little as 0.0001 mass unit
Resolution

- $\text{C}_3\text{H}_6\text{O}$ and $\text{C}_3\text{H}_8\text{O}$ have nominal masses of 58 and 60, and can be distinguished by low-resolution MS.

- these two compounds each have nominal mass of 60. Distinguish between them by high-resolution MS.

<table>
<thead>
<tr>
<th>Molecular Formula</th>
<th>Nominal Mass</th>
<th>Precise Mass</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\text{C}_3\text{H}_8\text{O}$</td>
<td>60</td>
<td>60.05754</td>
</tr>
<tr>
<td>$\text{C}_2\text{H}_4\text{O}_2$</td>
<td>60</td>
<td>60.02112</td>
</tr>
</tbody>
</table>
Virtually all elements common to organic compounds are mixtures of isotopes

<table>
<thead>
<tr>
<th>Element</th>
<th>Atomic weight</th>
<th>Isotope</th>
<th>Mass (amu)</th>
<th>Relative Abundance</th>
</tr>
</thead>
<tbody>
<tr>
<td>hydrogen</td>
<td>1.0079</td>
<td>$^1$H</td>
<td>1.00783</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$^2$H</td>
<td>2.01410</td>
<td>0.016</td>
</tr>
<tr>
<td>carbon</td>
<td>12.011</td>
<td>$^{12}$C</td>
<td>12.0000</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$^{13}$C</td>
<td>13.0034</td>
<td>1.11</td>
</tr>
<tr>
<td>nitrogen</td>
<td>14.007</td>
<td>$^{14}$N</td>
<td>14.0031</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$^{15}$N</td>
<td>15.0001</td>
<td>0.38</td>
</tr>
<tr>
<td>Element</td>
<td>Mass</td>
<td>Isotope</td>
<td>Abundance</td>
<td></td>
</tr>
<tr>
<td>------------</td>
<td>--------</td>
<td>---------</td>
<td>-----------</td>
<td></td>
</tr>
<tr>
<td>Oxygen</td>
<td>15.999</td>
<td>$^{16}\text{O}$</td>
<td>15.9949</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$^{17}\text{O}$</td>
<td>16.9991</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$^{18}\text{O}$</td>
<td>17.9992</td>
<td></td>
</tr>
<tr>
<td>Sulfur</td>
<td>32.066</td>
<td>$^{32}\text{S}$</td>
<td>31.9721</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$^{33}\text{S}$</td>
<td>32.9715</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$^{34}\text{S}$</td>
<td>33.9679</td>
<td></td>
</tr>
<tr>
<td>Chlorine</td>
<td>35.453</td>
<td>$^{35}\text{Cl}$</td>
<td>34.9689</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$^{37}\text{Cl}$</td>
<td>36.9659</td>
<td></td>
</tr>
<tr>
<td>Bromine</td>
<td>79.904</td>
<td>$^{79}\text{Br}$</td>
<td>78.9183</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>$^{81}\text{Br}$</td>
<td>80.9163</td>
<td></td>
</tr>
</tbody>
</table>
Carbon, for example, in nature is 98.90% $^{12}$C and 1.10% $^{13}$C. Thus, there are 1.11 atoms of carbon-13 in nature for every 100 atoms of carbon-12.

$$1.10 \times \frac{100}{98.90} = 1.11 \text{ atoms } ^{13}\text{C per 100 atoms } ^{12}\text{C}$$
M+2 and M+1 Peaks

The most common elements giving rise to M + 2 peaks are chlorine and bromine.

Chlorine in nature is 75.77% $^{35}$Cl and 24.23% $^{37}$Cl.
- A ratio of M to M + 2 of approximately 3:1 indicates the presence of a single chlorine in a compound.

Bromine in nature is 50.7% $^{79}$Br and 49.3% $^{81}$Br.
- A ratio of M to M + 2 of approximately 1:1 indicates the presence of a single bromine in a compound.
M+2 and M+1 Peaks

- Sulfur is the only other element common to organic compounds that gives a significant $M+2$ peak
  - $^{32}S = 95.02\%$ and $^{34}S = 4.21\%$

- Because $M+1$ peaks are relatively low in intensity compared to the molecular ion and often difficult to measure with any precision, they are generally not useful for accurate determinations of molecular weight
To attain high efficiency of molecular ion formation and give reproducible mass spectra, it is common to use electrons with energies of approximately 70 eV (1600 kcal/mol). This energy is sufficient not only to dislodge one or more electrons from a molecule, but also to cause extensive fragmentation. These fragments may be unstable as well and, in turn, break apart to even smaller fragments.
Fragmentation of a molecular ion, M, produces a radical and a cation. Only the cation is detected by MS.

\[ [A-B]^+ \rightarrow A^+ + \cdot B \]

\[ \text{Molecular ion} \quad \text{(a radical cation)} \]

\[ \rightarrow A^+ + \cdot B + B^+ \]

\[ \text{Radical} \quad \text{Cation} \]
Fragmentation of M

A great deal of the chemistry of ion fragmentation can be understood in terms of the formation and relative stabilities of carbocations in solution.

Where fragmentation occurs to form new cations, the mode that gives the most stable cation is favored.
The probability of fragmentation to form new carbocations increases in the order

\[
\text{CH}_3^+ < 1^\circ < 1^\circ \text{ allylic} < 2^\circ \text{ allylic} < 3^\circ \text{ allylic} < 3^\circ \text{ benzylic}
\]

Increasing carbocation stability
Interpreting MS

- The only elements to give significant $M + 2$ peaks are Cl and Br. If no large $M + 2$ peak is present, these elements are absent.

- Is the mass of the molecular ion odd or even?

- **Nitrogen Rule**: if a compound has
  - zero or an even number of nitrogen atoms, its molecular ion will appear as a even m/z value.
  - an odd number of nitrogen atoms, its molecular ion will appear as an odd m/z value.
Alkanes

- Fragmentation tends to occur in the middle of unbranched chains rather than at the ends.

- The difference in energy among allylic, benzylic, 3°, 2°, 1°, and methyl cations is much greater than the difference among comparable radicals.
  - Where alternative modes of fragmentation are possible, the more stable carbocation tends to form in preference to the more stable radical.
Alkenes characteristically show a strong molecular ion peak.

They cleave readily to form resonance-stabilized allylic cations.

\[
[\text{CH}_2=\text{CHCH}_2\text{CH}_2\text{CH}_3]^+ \quad \rightarrow \\
\text{CH}_2=\text{CHCH}_2^+ + \cdot \text{CH}_2\text{CH}_3
\]
Cyclohexenes

- cyclohexenes give a 1,3-diene and an alkene, a process that is the reverse of a Diels-Alder reaction (Section 22.2)

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{H}_3\text{C} & \quad \text{CH}_2 \\
\text{C} & \quad \text{C} \\
\text{C} & \quad \text{C} \\
\text{C} & \quad \text{C} \\
\text{H}_3\text{C} & \quad \text{C} \\
\text{C} & \quad \text{CH}_2
\end{align*}
\]

Limonene (m/z 136)

A neutral diene (m/z 68)

A radical cation (m/z 68)
Alkynes typically show a strong molecular ion peak.

They cleave readily to form the resonance-stabilized propargyl cation or a substituted propargyl cation:

\[ HC≡C\text{CH}_2^+ \quad \leftrightarrow \quad HC=C=CH_2^+ \]

resonance-stabilized propargyl cation
Alcohols

- One of the most common fragmentation patterns of alcohols is loss of H$_2$O to give a peak which corresponds to M - 18.

- Another common pattern is loss of an alkyl group from the carbon bearing the OH to give a resonance-stabilized oxonium ion and an alkyl radical.
Alcohols

Molecular ion (a radical cation)

\[ \begin{align*}
R' \text{-} & \quad \text{R} \quad \text{O}^{+} \quad \text{H} \\
R'' &
\end{align*} \]

A radical

\[ \begin{align*}
R' \text{-} & \quad \text{R} \quad \text{O}^{+} \quad \text{H} \\
R'' &
\end{align*} \]

A resonance-stabilized oxonium ion
Mass Spectrometry

End Chapter 12