Mechanisms of Ion Fragmentation

(McLafferty Chapter 4)

CU- Boulder
CHEM 5181
Mass Spectrometry & Chromatography

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Business Items

- Last real lecture is today
  - Material from today, ART-MS, protein MS lectures included in exam. (At least one question from each)
  - Exam on Tue 6-Nov during class period
    - Proctored by Ingrid Ulbrich, Jose won’t be there (@ AGU meeting)
- Hand out final exam from 2010, recent CHEM cumulative exam
  - Work on them, we will discuss on Thu
- Please complete FCQs (remember bonus pt): only 2 out of 6 as of this morning
- Also will send Zoomerang survey later today (also bonus pt)
### Interpretation Lectures vs. McLafferty Chapters

- Ch. 1: Introduction
- Ch. 2: Elemental Composition
- Ch. 3: The Molecular Ion
- Ch. 4: Basic Fragmentation Mechanisms (*Today*)
- Ch. 5: Postulation of Molecular Structures
- Ch. 6: Auxiliary Techniques
- Ch. 7: Theory of Unimolecular Ion Decomp.
- Ch. 8: Detailed Fragmentation Mechanisms
- Ch. 9: Fragmentation of Compound Classes
- Ch. 10: Computer Methods

Covered in instrum. part

Advanced version, not covered in course

Useful read for databases, but somewhat out of date

### Introduction to Fragmentation Reactions

- Earlier: the mass spectrum shows the mass of the molecule & the masses of pieces from it
- Additional information: ion abundance
  - Relative abundance of an ion can be an indication the *structure* of the fragment and its *environment* in the molecule
- Source: Unimolecular ion-decomposition reactions
  - Another branch of chemistry
  - Not completely understood or predictable
    - Study spectra of closely related molecules
  - MS not sensitive to all structural features
  - Many close similarities to pyrolytic, photolytic, radiolytic reactions, as well to condensed-phase organic reactions
  - But here each reaction involves ions & often radicals under vacuum
  - Rearrangement reactions are possible
Catch-up on Organic Chemistry

- You’ll probably find this part easy if you have a strong org. chem. background
- If you don’t, you may need some catch-up reading before you understand McLafferty
- E.g. book by Klein “Org. Chem. as a second language”

Unimolecular Decomposition Reactions I

- EI MS reactions are unimolecular (as opposed to other techniques, such as laser ablation ionization)
- M⁺ are made with a wide range of internal energies
  - “Cool” M⁺ will not decompose
  - ABCD + e⁻ -> ABCD +
Unimolecular Decomposition Reactions II

- “Excited” or “Hot” M⁺ will decompose in a chain of energy-dependent reactions
  - Now things get interesting…
  - Each one with a neutral loss

Site of Initial Ionization I

- e⁻ most vulnerable to ionization are those of highest energy
  - HOMO: highest occupied molecular orbital
    - Also form the weakest bonds
  - IP is defined as the energy to remove the weakest bound electron (n > π > σ)
    - n: lone pairs from heteroatoms

Figure 3.2. Relative energies of molecular orbitals in organic compounds
Site of Initial Ionization II

• $n > \pi > \sigma$

\[
\begin{align*}
\text{n:} & \quad \text{CH}_3\text{OH} & \quad \overset{-e^{-}}{\rightarrow} & \quad \text{CH}_3\overset{+}{\text{OH}} \\
\text{\pi:} & \quad \text{CH}_3\text{C} & \quad \overset{-e^{-}}{\rightarrow} & \quad \text{CH}_3\overset{.}{\text{C}} \\
\text{\sigma:} & \quad \text{CH}_3-\text{CH}_2-\text{CH}_3 & \quad \overset{-e^{-}}{\rightarrow} & \quad \text{CH}_3-\overset{+}{\text{CH}}_2 : \text{CH}_3
\end{align*}
\]

Figure 3.4. Examples showing notation for localization of initial ionization site.

Factors that Influence Ion Abundance I

• Most important: Stability of the product ion
  – Electron sharing stabilization
    • From non-bonding orbital of heteroatom (n)
      \[\text{CH}_3\text{C}^+=\text{O} \leftrightarrow \text{CH}_3\text{C}ён^+ \quad (m/z \ 43)\]
  – Resonance stabilization
    \[\text{CH}_2=\text{CH}^+\text{CH}_2 \leftrightarrow ^+\text{CH}_2\text{-CH}=\text{CH}_2 \quad (m/z \ 41)\]
    Benzyl: C$_6$H$_5^+ <<$ phenyl C$_6$H$_5$CH$_2^+$
  – “Distonic radical ions”
    • Separation of charge and radical sites
      \[
      \begin{align*}
      \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}=&\overset{+}{\text{O}}^- \quad \rightarrow \quad \text{CH}_2\text{CH}_2\text{CH}_2\text{CH}=\overset{+}{\text{O}}^-\text{H} \\
      \text{CH}_3\text{NH}_2^+ & \quad \rightarrow \quad \text{CH}_2\text{N}^+\text{H}_3
      \end{align*}
      \]
Factors that Influence Ion Abundance II

• Stevenson’s Rule
  – In a cleavage of a single bond in an \( \text{OE}^+ \):
    \( \text{ABCD}^+ \) can give \( \text{A}^+ + \text{BCD} \cdot \) or \( \text{A} \cdot + \text{BCD}^+ \)
  – The fragment with the higher tendency to retain the unpaired electron should have the higher ionization energy (converse true)
    • It will be the less abundant ion in the spectrum

Factors that Influence Ion Abundance III

• Loss of the largest alkyl \( (\text{C}_n\text{H}_{2n+1}) \)
  – Exception to Stevenson’s rule: abundance decreases with increasing ion stability

\[
\begin{align*}
\text{CH}_3 & \quad \text{CH}_3 \\
\text{C}_2\text{H}_5 & \rightarrow \quad \text{CH}_3 \\
\text{C}_2\text{H}_5\text{CH} & \quad [\text{C}_2\text{H}_5\text{CH}] > [\text{CHC}_4\text{H}_6] > \\
\text{C}_2\text{H}_5\text{CH}_4\text{H}_9^+ & \quad [\text{C}_2\text{H}_5\text{CHC}_4\text{H}_9] > [\text{C}_2\text{H}_5\text{CC}_4\text{H}_9]
\end{align*}
\]
Alkanes & Branched Alkanes

- Only important OE\(^+\) is M\(^+\).
- C\(_3\)H\(_7\) & C\(_4\)H\(_9\) are most stable
- Loss of H\(_2\) and H
- 27 < 29 ; 41 < 43 ; 55 < 57 ; 69 < 71

- Fragmentation at substituted C
- Loss of the larger alkyl

Factors that Influence Ion Abundance IV

- Stability of the neutral product
  - (Stability of ion is much more important)
  - A favorable product site for the unpaired electron can provide additional influence
    - Electronegative sites such as oxygen (OR)
  - The neutral product can be a molecule
    - Small stable molecules of high ionization energy are favored
      - H\(_2\), CH\(_4\), H\(_2\)O, C\(_2\)H\(_4\), CO, NO, CH\(_3\)OH, H\(_2\)S, HCl, CH\(_2\)=C=O, and CO\(_2\)
      - Losses of 2, 16, 18, 28, 30, 32, 34, 36, 42, 44
Reaction Initiation at Radical or Charge Sites

- Fragmentation reactions are often initiated at the favored sites for the unpaired electron or the charge.
- The most favored radical and charge sites in the molecular ion are assumed to arise from loss of the molecule’s electron of lowest ionization energy.
  - Favorability \( \sigma < \pi < n \)-electrons: see example spectra

\[
\begin{align*}
\text{Sigma (}\sigma\text{):} & \quad \text{RH}_2\text{C:CHR'} - e^- \rightarrow \text{RH}_2\text{C''CH}_2\text{R'} \\
\text{Pi (}\pi\text{):} & \quad \text{RHC:CHR'} - e^- \rightarrow \text{RHC::CHR'} \\
\text{Non-bonding (}\eta\text{):} & \quad \text{R}\text{--O--R'} - e^- \rightarrow \text{R'O--R'}
\end{align*}
\]

Unlike \( M^+ \) charge localization is implied.

Reaction Classifications I

- Decompositions of odd electron ions involving single bond cleavage results in an even electron ion and a neutral radical.

\[
\begin{align*}
\text{CH}_3\text{CH}_2^{\bullet\bullet}\text{CH}_3 & \quad \rightarrow \quad \text{CH}_3\text{CH}_2^+ + \bullet\text{CH}_3 \\
\text{CH}_3\text{CH}_2^+ & \rightarrow \quad \text{CH}_3\text{CH}_2^\bullet + \text{CH}_3^+
\end{align*}
\]

- Stevenson’s rule applies.
- Reminder: in \( C_xH_yN_zO_n \)
  - RPDB = \( x+1/2y-1/2z+1 \)
  - \( y+z \) is odd \( \Rightarrow \) RPDB ends in 1/2 \( \Rightarrow \) EE^+
  - \( y+z \) is even \( \Rightarrow \) RPDB whole \( \Rightarrow \) OE^+. 
Reaction Classifications II

- Decompositions of odd electron ions involving two bond cleavages can result in an odd electron ion and a neutral
  - Rearrangements
  - Decomposition of rings.

\[
\begin{align*}
\text{H}_2\text{C} & \longrightarrow \text{CHOH}^{++} \\
\text{H}_2\text{C} & \longrightarrow \text{CH}_2
\end{align*}
\]

\[
\text{H}_2\text{C} = \text{CHOH}^{+} + \text{H}_2\text{C} = \text{CH}_2 \quad \text{(charge retention)}
\]

\[
\text{H}_2\text{C} = \text{CHOH} + \text{H}_2\text{C} = \text{CH}_2^{++} \quad \text{(charge migration)}
\]

\[
\begin{align*}
\text{H} & \longrightarrow \text{OH}^{++} \\
\text{H}_2\text{C} & \longrightarrow \text{CH}_2
\end{align*}
\]

\[
\text{HOH}^{++} + \text{H}_2\text{C} = \text{CH}_2 \quad \text{(charge retention)}
\]

\[
\text{HOH} + \text{H}_2\text{C} = \text{CH}_2^{++} \quad \text{(charge migration)}
\]

Reaction Classifications III

- Cleavage of three bonds in M\(^{+}\) (or any OE\(^{+}\)) produces an EE\(^{+}\)

\[
\begin{align*}
\text{CH}_3\text{CH}_2 & \longrightarrow \text{CH}_3\text{CH}_2 \cdot + \text{C}_2\text{H}_3^{+} + \text{H}_2
\end{align*}
\]
Reaction Classifications IV

• "Even-electron rule"
  – decompositions of even electron ions typically result in another even electron ion and a neutral
  – Odd electron formation is not energetically favorable

\[
\begin{align*}
\text{CH}_3\text{CH}_2^+ + \text{O} \equiv \text{CH}_2 & \quad \text{(charge migration)} \\
\text{CH}_2 \equiv \text{CH}_2 + \text{HO} \equiv \text{CH}_2 & \quad \text{(rearrangement, charge retention)} \\
\text{CH}_3\text{CH}_2^+ + \text{O} \equiv \text{CH}_2^{**} & \quad \text{(unfavored)} \quad (4.6) \\
\text{CH}_2 \equiv \text{CH} + \text{CH}_2 \equiv \text{CH}_2 & \quad \text{(charge retention)} \\
\text{CH}_2 \equiv \text{CH} + \text{CH}_2 \equiv \text{CH}_2^{**} & \quad \text{(unfavored)}
\end{align*}
\]

Reaction Classifications V

<table>
<thead>
<tr>
<th>Precursor ion</th>
<th>Number of bonds cleaved</th>
<th>Charge retention</th>
<th>Charge migration</th>
</tr>
</thead>
<tbody>
<tr>
<td>OE⁺ (M⁺)</td>
<td>1</td>
<td>EE⁺ (s)</td>
<td>EE⁺ (l)</td>
</tr>
<tr>
<td>OE⁺⁺ (M⁺⁺)</td>
<td>2</td>
<td>OE⁺⁺ (s₁)</td>
<td>OE⁺⁺ (s₁)</td>
</tr>
<tr>
<td>OE⁺⁺⁺ (M⁺⁺⁺)</td>
<td>3</td>
<td>EE⁺⁺⁺ (s₁₁)</td>
<td>EE⁺⁺⁺ (s₁₁)</td>
</tr>
<tr>
<td>EE⁺⁺ (M⁺⁺)</td>
<td>1</td>
<td>[OE⁺⁺⁺]**</td>
<td>EE⁺⁺ (l)</td>
</tr>
<tr>
<td>EE⁺⁺⁺ (M⁺⁺⁺)</td>
<td>2</td>
<td>EE⁺⁺⁺ (l)</td>
<td>[OE⁺⁺⁺]**</td>
</tr>
</tbody>
</table>

*Designations "s" and "l" are alpha and inductive cleavages, respectively, as explained in the text. Two / reactions lead to the same charge behavior (retention or migration) as two x reactions. Brackets indicate products of reactions discussed in Chapter 8.

*Not favored.

• OE⁺⁺ formation from fragmentation is only favored for cleavage of two bonds of precursor OE⁺⁺.
  – This is why we mark important OE⁺⁺ ions in spectrum
Sigma-Bond Dissociation ($\sigma$)

- E.g. alkanes
  - Every valence electron is shared in a bond
  - A bond finds itself with 1-electron, breaks

\[
\text{Alkanes: } \quad R^{\ddagger}\text{CR}_3 \xrightarrow{\sigma} R\cdot + \cdot\text{CR}_3
\]

- Ionization of C\textsubscript{2}H\textsubscript{6} increases C-C bond length by 30%, halves its dissociation energy

- Fragmentation is favored at more substituted C

\[
\left(\text{CH}_3\right)_2\text{C} = \text{CH}_2\text{CH}_3 \xrightarrow{-e^{-}} \left(\text{CH}_3\right)_3\text{C}^{\ddagger}\text{C} = \text{CH}_2\text{CH}_3 \xrightarrow{\sigma} (\text{CH}_3)_3\text{C}^{\ddagger} + \cdot\text{CH}_2\text{CH}_3
\]

Radical-Site Initiation ($\alpha$-cleavage) I

- Unpaired electron at radical site has strong tendency to be paired
  - Donate unpaired electron to form new bond
  - Need a 2\textsuperscript{nd} electron, take it from bond of adjacent C atom ("$\alpha$ carbon")

\[
\left(\text{CH}_3\right)_2\text{C} = \text{CH}_2\text{O}_2\text{H}_5 \xrightarrow{\alpha} \cdot\text{CH}_3 + \text{CH}_2 = \cdot\text{O}_2\text{H}_5 \quad (\leftrightarrow \cdot\text{CH}_2\text{O}_2\text{H}_5)
\]

- Fishhook arrow is movement of single electron
- Same as "homolytic cleavage" of organic chem
- Only radical site moves, + stays
Radical-Site Initiation (α-cleavage) II

- Tendency of radical site to initiate reaction:
  - Parallels tendency of radical site to donate e⁻
  - N > S, O, π, R⁻ > Cl, Br > H
  - But it is affected by its environment in molecule
- Unknown 4.2: what will be the most abundant fragment of HO-CH₂-CH₂-NH₂?

Radical-Site Initiation (α-cleavage) III

- Carbonyls:
  \[
  \begin{align*}
  \text{CH₃} & \xrightleftharpoons{\alpha} \text{CH₃} \cdot + \text{CH₂CHCH} & \quad (\leftrightarrow \text{CH₂CHCH₂}) \\
  \text{CH₃} & \xrightleftharpoons{\alpha} \text{CH₃} \cdot + \text{CH₂C₆H₅} & \quad (\leftrightarrow \text{CH₂C₆H₅})
  \end{align*}
  \]
  \[
  \begin{align*}
  & \quad \text{100%} \\
  & \quad \text{100%}
  \end{align*}
  \]

- Double-bonds:
\textbf{\(\alpha\)-Cleavage of Aliphatic Amines}

- Very dominant, due to e\(^{-}\) donating ability of N

\textbf{Spectra of Isomeric C\(_4\)H\(_{11}\)N}

- Structure of each spectrum?
Charge-Site Initiation (i-cleavage)

- Inductive cleavage ("heterolytic dissociations" of O-Chem)
- For OE⁺.

\[ R \quad Y \quad R \quad \xrightarrow{i} \quad \overset{\ddagger}{R} \quad + \quad \overset{\cdot}{Y} \quad R \]

\[ \overset{\ddagger}{C} \quad \overset{\cdot}{Y} \quad : \quad \overset{\ddagger}{R} \quad + \quad R \quad \overset{\cdot}{C} \quad \overset{\cdot}{Y} \quad \]

- Example:

\[ C_2H_5 \quad \overset{\ddagger}{OC_2H_5} \quad \xrightarrow{i} \quad C_2H_5^+ \quad + \quad \cdot OC_2H_5 \quad 40\% \]

i-cleavage for Aliphatic Ketones

3-pentanone and 3-methyl 2-butanone. Which is which?