Mass Spectrometry: Fragmentation

Chem 8361/4361: Interpretation of Organic Spectra
Initial Charge

Where is it localized?

Where charge begins determines how all other fragments are formed

- In general HOMO-controlled → lost first
- Lost from heteroatoms in preference
Fragmentation

How to Represent Initial Radical Cation

Three ways to represent molecular ion of 1,3-cyclohexadiene

A. Delocalized structure with one less electron
   both electron and charge delocalized over $\pi$-system

B. & C. electron and charge localized on $\pi$-system
   both are possible and each could give different fragments
Fragmentation

General Considerations

1. Even-electron ions cannot cleave to a pair of odd-electron fragments
   • from thermodynamics

2. Mass loss of 14 from M$^+$ is extremely rare
   • will see separation of 14 in hydrocarbons
   • arise from 2 different fragmentations

3. Order of radical/carbocation loss
   • tertiary > secondary > primary > methyl > hydrogen
   • loss of longest is preferred

4. Fragment ion stability takes precedence over radical

5. Vinyl radical loss is not favorable, but possible
6. Several fragmentations can occur, especially if it leads to a highly stabilized cation/radical
7. If loss of stable neutral molecule is possible, will do so (simple alkenes, H₂O, CO, etc.)

Lastly...It is not possible to identify every peak in a mass spectrum. The key is to remember a few diagnostic fragment ions (e.g. $m/z = 77, 91$) and a few key mass losses in order to gain some insight into subunits.
Fragmentation

Fragmentation of Molecular I on

The initial radical cation can fragment in a number of ways

I. Homolytic (one electron at a time) cleavage
   - products are even-electron cation and a free radical

II. A less cluttered representation of reaction I

III. Heterolytic (two electrons at a time) cleavage
   - electrons move toward charged site
   - products are even-electron cation and a free radical

IV. Secondary fragmentation of even-electron cation by two electron process
Fragmentation

A Few General Mechanisms

A – one-bond $\sigma$-cleavage

(a) cleavage at C–C producing cation & radical

(b) cleavage at C–heteroatom producing cation & radical
- 2 electron process
- works well for $Z = O$, halogen

\[
\begin{align*}
R^1 + R^2 & \rightarrow R^1\cdot + R^2\oplus \\
\end{align*}
\]

in MS, loss of largest outweighs 3° cation

\[
\begin{align*}
\text{CH}_3\text{CH}_2\text{CH}_2\text{C}^\cdot \text{C}_7\text{H}_{15} & \rightarrow \text{CH}_3\text{H}_3\text{C}^\cdot \text{C}_7\text{H}_{15} + \cdot \text{C}_7\text{H}_{15} \quad 70\% \\
\text{CH}_3\text{CH}_2\text{CH}_2\text{C}^\cdot \text{C}_7\text{H}_{15} & \rightarrow \text{CH}_3\text{CH}_2\text{CH}_2\text{C}^\cdot \text{C}_7\text{H}_{15} + \cdot \text{C}_7\text{H}_{15} \quad 1\% \\
\end{align*}
\]
Fragmentation

A Few General Mechanisms

(c) α-cleavage

\[
\begin{align*}
\text{ Fragmentation } & \\
\text{ Charged species has heteroatom } & \\
\text{-isotope patterns in fragment ions } \\
\end{align*}
\]

\[
\begin{align*}
Z = N > O, \pi > \text{halogens} >> \sigma \\
\end{align*}
\]
Fragmentation

A Few General Mechanisms

(c) α-cleavage

\[
\begin{align*}
\text{H}_3\text{C} & \text{C}=\text{O} \rightarrow \text{H}_3\text{C} = \text{O} + \text{H}_2\text{C} \\
\text{H}_3\text{C} & \text{C}=\text{O} \rightarrow \text{H}_3\text{C} = \text{O} + \cdot \text{CH}_3
\end{align*}
\]

\( \cdot \text{CH}_3 \text{ lost in preference to } \cdot \text{H} \cdot \)

\( \Pi \) Systems

If loss of stable neutral molecule is possible, will do so
(simple alkenes, \( \text{H}_2\text{O} \), \( \text{CO} \), etc.)

\[
\begin{align*}
\text{H}_2\text{C} & \text{C}=\text{R} \rightarrow \text{H}_2\text{C} = \text{C} + \cdot \text{R} \\
\text{H}_2\text{C} & \text{C}=\text{R} \rightarrow \text{H}_2\text{C} = \text{C} + \cdot \text{R}
\end{align*}
\]

\[
\begin{align*}
\text{H}_3\text{C} & \text{C}=\text{N} \rightarrow \text{H}_3\text{C} = \text{N} + \cdot \text{CH}_2\text{H}_3 \\
\text{H}_3\text{C} & \text{C}=\text{N} \rightarrow \text{H}_3\text{C} = \text{N} + \cdot \text{CH}_2\text{H}_3
\end{align*}
\]

\( \text{m}/\text{z} = 72 \)

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\( \text{m}/\text{z} = 44 \)

\( \text{m}/\text{z} = 58 \)

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\( \text{m}/\text{z} = 30 \)

\( \text{m}/\text{z} = 30 \)
Fragmentation
A Few General Mechanisms

\[
\begin{align*}
H_3C-H\text{N-CH}_2\text{CH}_3 & \xrightarrow{-H^+} \text{H}_3\text{C}=\text{N-CH}_2\text{CH}_3 & \text{m/z} = 72 \\
\text{H}_2\text{C}=\text{N-CH}_2\text{CH}_3 & \xrightarrow{-\text{CH}_3^+} \text{H}_2\text{C}=\text{NH}_2 + \text{CH}_2\text{CH}_2 & \text{m/z} = 58 \\
\text{H}_3\text{C}=\text{N-CH}_2\text{CH}_3 & \xrightarrow{\text{two-electron process}} \text{H}_3\text{C}=\text{NH}_2 + \text{CH}_2\text{CH}_2 & \text{m/z} = 44
\end{align*}
\]
Fragmentation

A Few General Mechanisms

B – two-bond σ-cleavage or rearrangement

(d) elimination of vicinal H and heteroatom
- common with alcohols
- difficult to see $M^+$

(e) retro Diels-Alder cleavage
- mechanism involving single electrons also possible

Both can carry charge
Fragmentation

A Few General Mechanisms

(f) McLafferty rearrangement
- common with ketones, esters, carboxylic acids

Multiple McLafferty is possible
Ortho effect

also with esters, amides, OH, etc.

“McLafferty + 1”
- esters only

“McLafferty + 1”
- esters only
**Fragmentation**

*Odd-electron vs. Even-electron*  
*(Nitrogen rule revisited)*

For non-nitrogen-containing molecular ions, *odd-electron ions* occur as *even* mass.

- Molecular ions (OE) $\Rightarrow$ even mass
- $\downarrow$ fragment
- Most fragment ions (EE) $\Rightarrow$ odd mass

If ion has even mass then “unusual” fragmentation has occurred (e.g. retro Diels-Alder, McLafferty)
Fragmentation

Odd-electron vs. Even-electron
(Nitrogen rule revisited)

Example – 3-methyl-1-cyclohexene

$3\text{-methyl-1-cyclohexene}$

$m/z = 96$ (OE)

$\text{m/z = 81 (EE)}$

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$\text{m/z = 81 (EE)}$
Fragmentation

*Odd-electron vs. Even-electron*
(Nitrogen rule revisited)

Example – 3-methyl-1-cyclohexene
Fragmentation

Odd-electron vs. Even-electron
(Nitrogen rule revisited)

Example – 3-methyl-1-cyclohexene

![Mass spectrum of 3-methyl-1-cyclohexene](image)

- Odd-electron (OE) fragmentation at m/z = 96
- Even-electron (EE) fragmentation at m/z = 54

Double bond isomerization leads to:

- \(-\text{CH}_2=\text{CHCH}_3\)
- \(\text{m/z} = 54\) (EE)
Fragmentation

See Lambert Chapter 8 for common fragmentation pathways of various functional groups/compound classes