Mechanisms of Ion Fragmentation

(McLafferty Chapter 4)

CU- Boulder
CHEM 5181
Mass Spectrometry & Chromatography

Prof. Jose-Luis Jimenez

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

This part of course

Advanced version, not covered in course

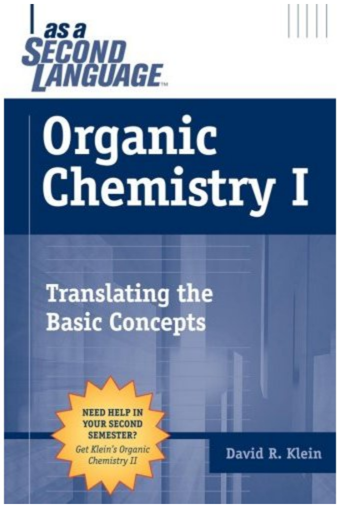
Useful read for databases, but somewhat out of date

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 pyrolitic, 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"

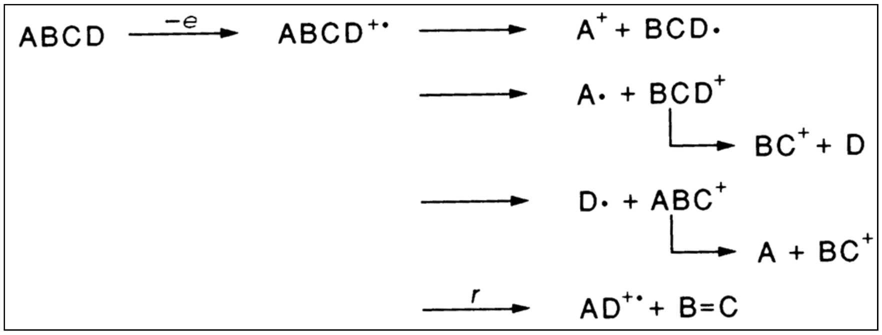


Unimolecular Decomposition Reactions I

- EI MS reactions are *unimolecular* (as opposed to other techniques, such as laser ablation ionization)
- $M^{+\cdot}$ are made with a wide range of internal energies
  - "Cool" $M^{+\cdot}$ will not decompose
  - $ABCD + e^- \rightarrow ABCD^{+\cdot}$

Unimolecular Decomposition Reactions II

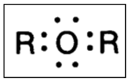
- “Excited” or “Hot” $M^{+\cdot}$ will decompose in a chain of energy-dependent reactions
  - Now things get interesting…
  - Each one with a neutral loss

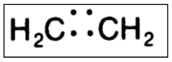


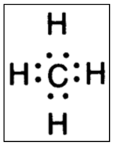
Site of Initial Ionization I

From Smith & Busch, sect. 3.2

- 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 heteroatmoms







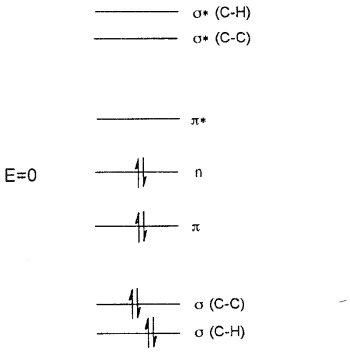


Figure 3.2. Relative energies of molecular orbitals in organic compounds

Site of Initial Ionization II

- n > π > σ

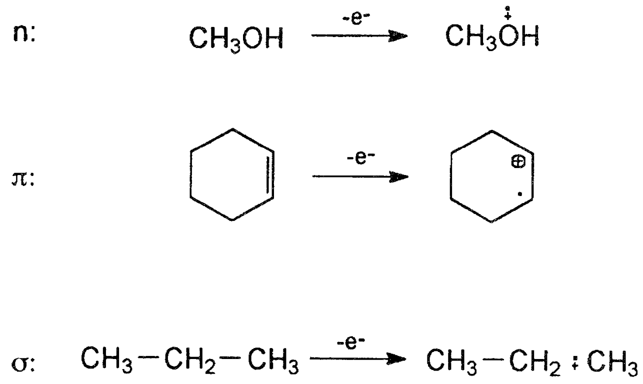


Figure 3.4. Examples showing notation for localization of initial ionization site.

From Smith & Busch, sect. 3.2

Factors that Influence Ion Abundance I

- Most important: <u>Stability</u> of the product ion
  - Electron sharing stabilization
    - From non-bonding orbital of heteroatom (n)

$CH_3\text{-}C^+\text{=}O \leftrightarrow CH_3\text{-}C\equiv O^+$ (*m/z* 43)

  - Resonance stabilization

$CH_2\text{=}CH\text{-}^+CH_2 \leftrightarrow {}^+CH_2\text{-}CH\text{=}CH_2$ (*m/z* 41)

Benzyl: $C_6H_5^+$ << phenyl $C_6H_5CH_2^+$

  - “Distonic radical ions”
    - Separation of charge and radical sites

$CH_3CH_2CH_2CH\text{=}O^{+\cdot} \rightarrow \cdot CH_2CH_2CH_2CH\text{=}O^+H$

$CH_3NH_2^{+\cdot} \rightarrow \cdot CH_2N^+H_3$

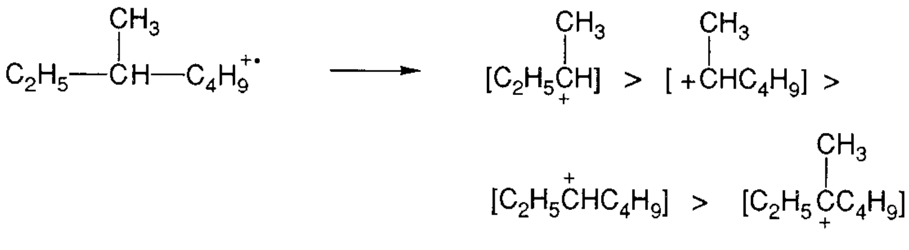
Factors that Influence Ion Abundance II

- Stevenson's Rule
  - In a cleavage of a single bond in an OE $^{+\cdot}$

    ABCD$^{+\cdot}$ can give A $^{+}$ + BCD $\cdot$ or A $\cdot$ + 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 (C_nH_{2n+1})
  - Exception to Stevenson's rule: abundance decreases with increasing ion stability



Alkanes & Branched Alkanes

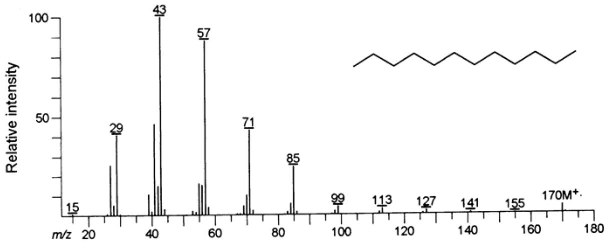


Figure 3.2. Mass spectrum of dodecane.

- Only important $OE^{+\cdot}$ is $M^{+\cdot}$
- C_3H_7 & C_4H_9 are most stable
- Loss of H_2 and H
- 27 < 29 ; 41 < 43 ; 55 < 57 ; 69 < 71

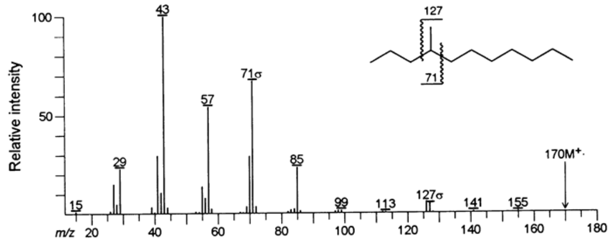


Figure 3.3. Mass spectrum of 4-methylundecane.

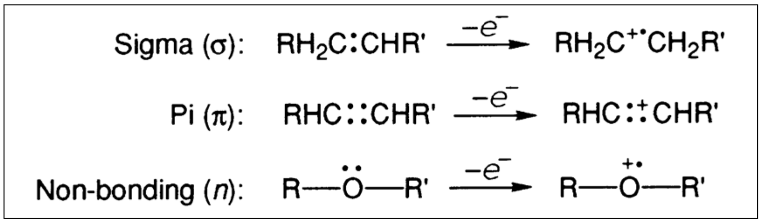
- Fragmentation at substituted C
- Loss of the larger alkyl

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_2O, C_2H_4, CO, NO, CH_3OH, H_2S, 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

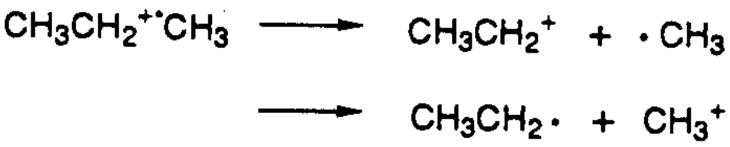
- Fragmentation reactions are often initiated at the favored sites for the unpaired electron or the charge
- The most favored radical and charge sites in the molecular ion are assumed to arise from loss of the molecule’s electron of lowest ionization energy
  - Favorability $\sigma < \pi < n$-electrons: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



Unlike $M^{+\cdot}$ charge localization is implied

Reaction Classifications I

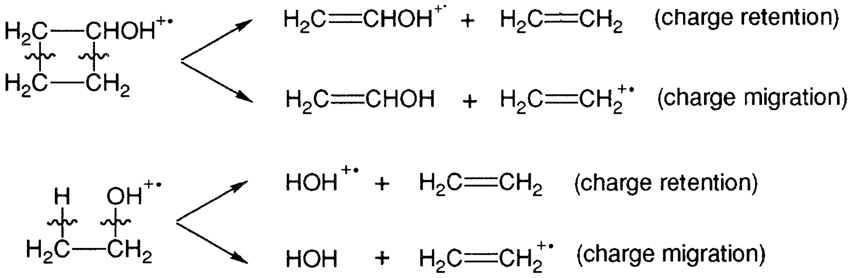
- Decompositions of odd electron ions involving single bond cleavage results in an even electron ion and a neutral radical



- 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 $\Rightarrow$ $OE^{+\cdot}$

Reaction Classifications II

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



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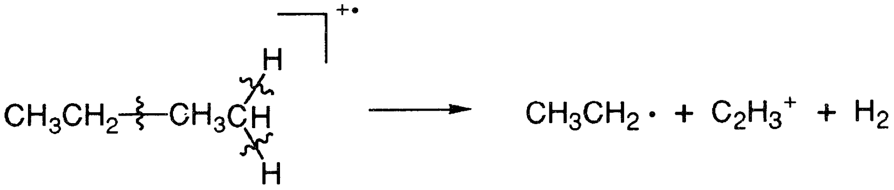
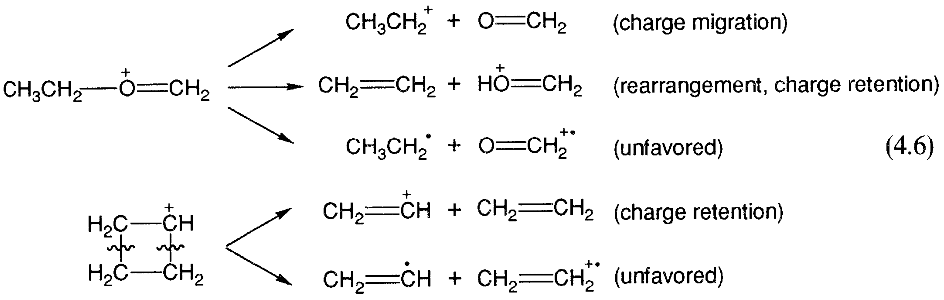
Reaction Classifications III

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



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



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Reaction Classifications V

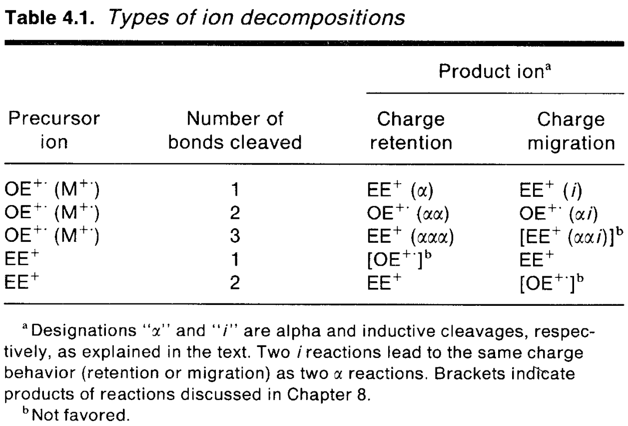


Table 4.1. *Types of ion decompositions*

Precursor ion	Number of bonds cleaved	Product ion[a] Charge retention	Charge migration
$OE^{+\cdot}$ ($M^{+\cdot}$)	1	EE^+ (α)	EE^+ (*i*)
$OE^{+\cdot}$ ($M^{+\cdot}$)	2	$OE^{+\cdot}$ (αα)	$OE^{+\cdot}$ (α*i*)
$OE^{+\cdot}$ ($M^{+\cdot}$)	3	EE^+ (ααα)	[EE^+ (αα*i*)][b]
EE^+	1	[$OE^{+\cdot}$][b]	EE^+
EE^+	2	EE^+	[$OE^{+\cdot}$][b]

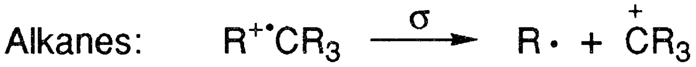
[a] Designations "α" and "*i*" are alpha and inductive cleavages, respectively, as explained in the text. Two *i* reactions lead to the same charge behavior (retention or migration) as two α reactions. Brackets indicate products of reactions discussed in Chapter 8.

[b] Not favored.

- $OE^{+\cdot}$ formation from fragmentation is only favored for cleavage of two bonds of precursor $OE^{+\cdot}$
  - This is why we mark important $OE^{+\cdot}$ ions in spectrum

Sigma-Bond Dissociation (σ)

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



Alkanes: $R^{+\bullet}CR_3 \xrightarrow{\sigma} R\cdot + \overset{+}{C}R_3$

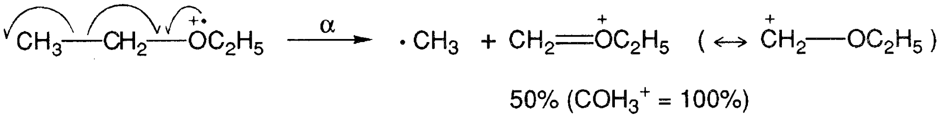
  - Ionization of C_2H_6 increases C-C bond length by 30%, halves its dissociation energy
- Fragmentation is favored at more substituted C

$(CH_3)C—CH_2CH_3 \xrightarrow{-e^-} (CH_3)_3C^{+\bullet}CH_2CH_3 \xrightarrow{\sigma} (CH_3)_3C^+ + \cdot CH_2CH_3$

100%

Radical-Site Initiation (α-cleavage) I

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



$CH_3—CH_2—\overset{+\bullet}{O}C_2H_5 \xrightarrow{\alpha} \cdot CH_3 + CH_2{=}\overset{+}{O}C_2H_5 \ (\leftrightarrow \overset{+}{C}H_2—OC_2H_5)$

50% (COH_3^+ = 100%)

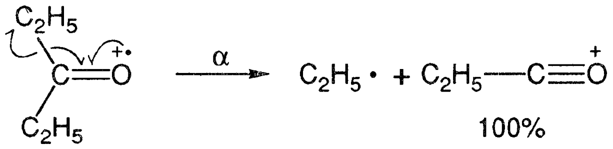
  - Fishook arrow is movement of single electron
  - Same as "homolytic cleavage" of organic chem
  - Only radical site moves, + stays

Radical-Site Initiation (α-cleavage) II

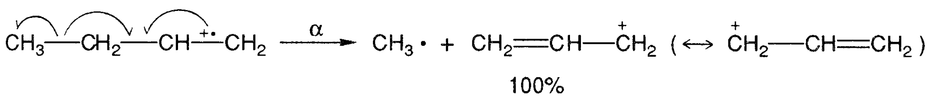
- Tendency of radical site to initiate reaction:
  - Parallels tendency of radical site to donate e^-
  - N > S, O, π, R· > Cl, Br > H
  - But it is affected by its environment in molecule
- Unknown 4.2: what will be the most abundant fragment of $HO\text{-}CH_2\text{-}CH_2\text{-}NH_2$?

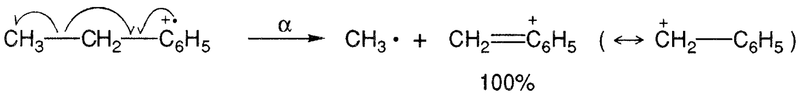
Radical-Site Initiation (α-cleavage) III

- Carbonyls:



- Double-bonds:





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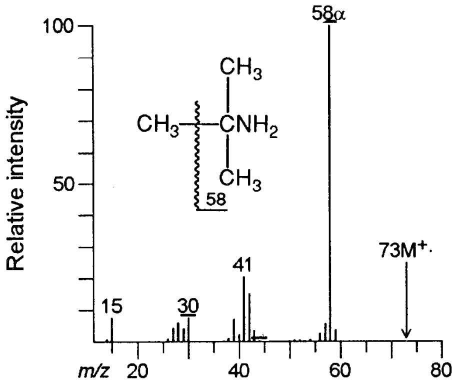
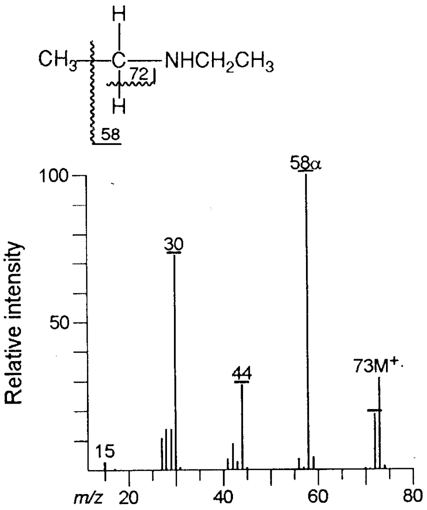
α-Cleavage of Aliphatic Amines

- Very dominant, due to e$^-$ donating ability of N





Spectra of Isomeric $C_4H_{11}N$

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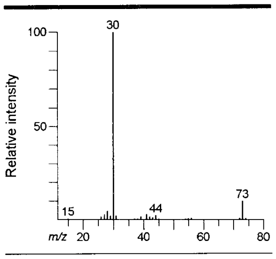

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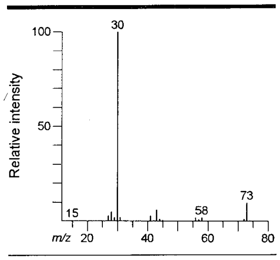

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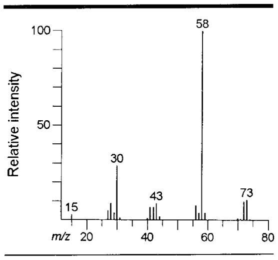
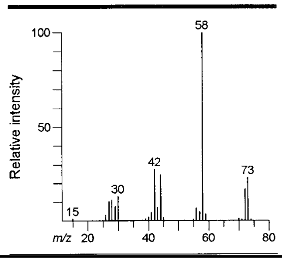
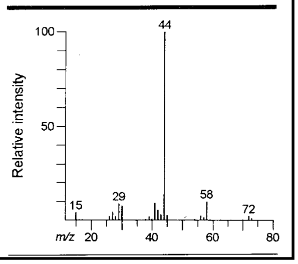


- Structure of each spectrum?

Unknown 4.7

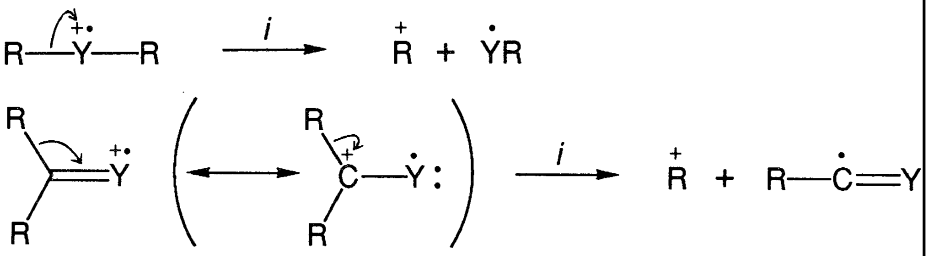


Unknown 4.8

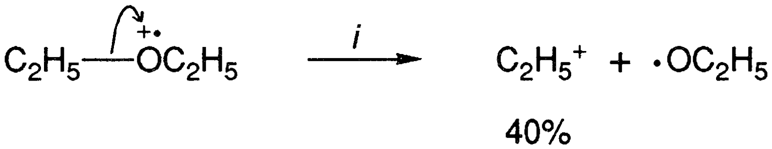


Charge-Site Initiation (*i*-cleavage)

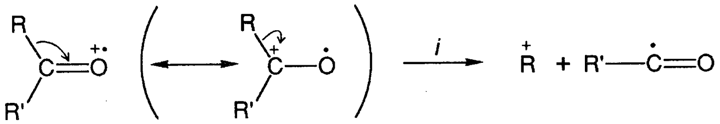
- Inductive cleavage (“heterolytic dissociations” of O-Chem)
- For OE$^{+\cdot}$



- Example:

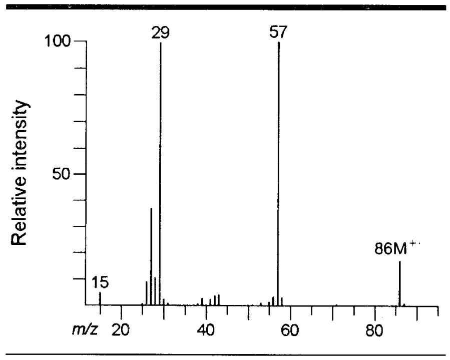


i-cleavage for Aliphatic Ketones



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

Unknown 4.9



Unknown 4.10