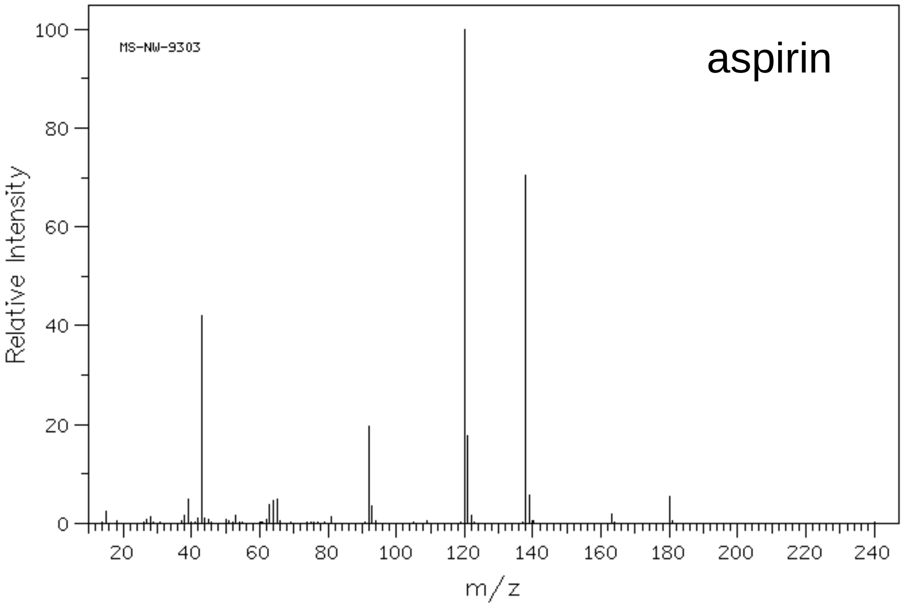
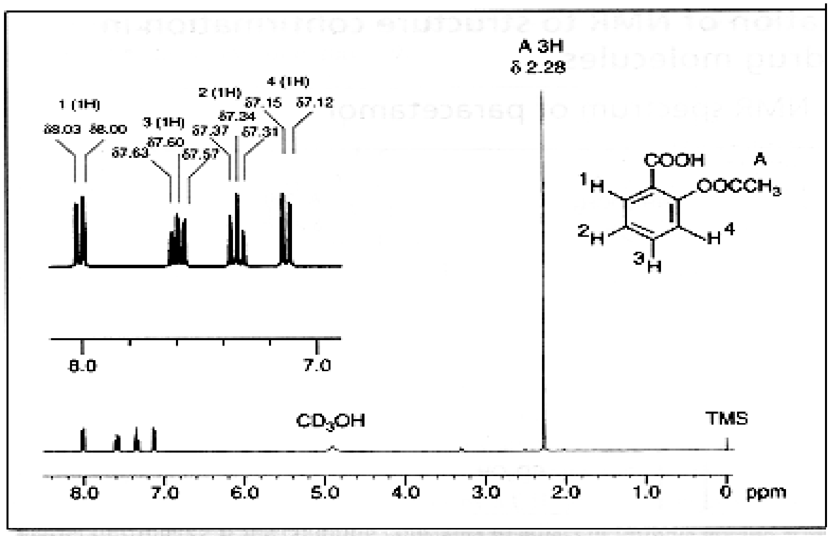
Mass Spectrometry Interpretation

MS vs NMR



EI-MS



NMR

MS vs. NMR

- MS peaks are narrower than NMR peaks
- MS is much more (10^4 x) more sensitive than NMR (among most sensitive tools)
- MS allows one to analyze much larger molecules (>50 kD) than NMR
- MS samples are more difficult to prepare
- MS is not particularly quantitative
- MS instruments cost a little less than NMR

Appearance of the Spectrum

- molecular ion
  - highest mass ion except for isotope peaks
  - molecular weight
- Nitrogen Rule (even-odd rule)
  - compounds with 0 or <u>even</u> numbers of N atoms have <u>even</u> molecular weights and fragments of <u>odd</u> mass
  - compounds with an <u>odd</u> number of N atoms have <u>odd</u> molecular weights

Interpretation of Mass Spectra

- Select a candidate peak for the molecular ion (M^+)
- Examine spectrum for peak clusters of characteristic isotopic patterns
- Test (M^+) peak candidate by searching for other peaks correspond to reasonable losses
- Look for characteristic low-mass fragment ions
- Compare spectrum to reference spectra

Exact Masses

Element	Symbol	Exact mass
hydrogen	$_{1}H^{1}$	1.00783
carbon	$_{6}C^{12}$	12.00000
nitrogen	$_{7}N^{14}$	14.0031
oxygen	$_{8}O^{16}$	15.9949

Molecular Weight Determination

Compounds with nominal mass 28.

Exact mass

	exact mass
CO	27.9949
N_2	28.0062
C_2H_4	28.0312

Natural Isotopic Abundance Ratios

Element		M+		M+1		M+2
hydrogen	${}_{1}H^{1}$	100	${}_{1}H^{2}$	0.016		
carbon	${}_{6}C^{12}$	100	${}_{6}C^{13}$	1.08		
nitrogen	${}_{7}N^{14}$	100	${}_{7}N^{14}$	0.38		
oxygen	${}_{8}O^{16}$	100	${}_{8}O^{17}$	0.04	${}_{8}O^{18}$	0.20
sulfur	${}_{16}S^{32}$	100	${}_{16}S^{32}$	0.78	${}_{16}S^{32}$	4.40
chlorine	${}_{17}Cl^{35}$	100			${}_{17}Cl^{37}$	32.5
bromine	${}_{35}Br^{79}$	100			${}_{35}Br^{81}$	98.0

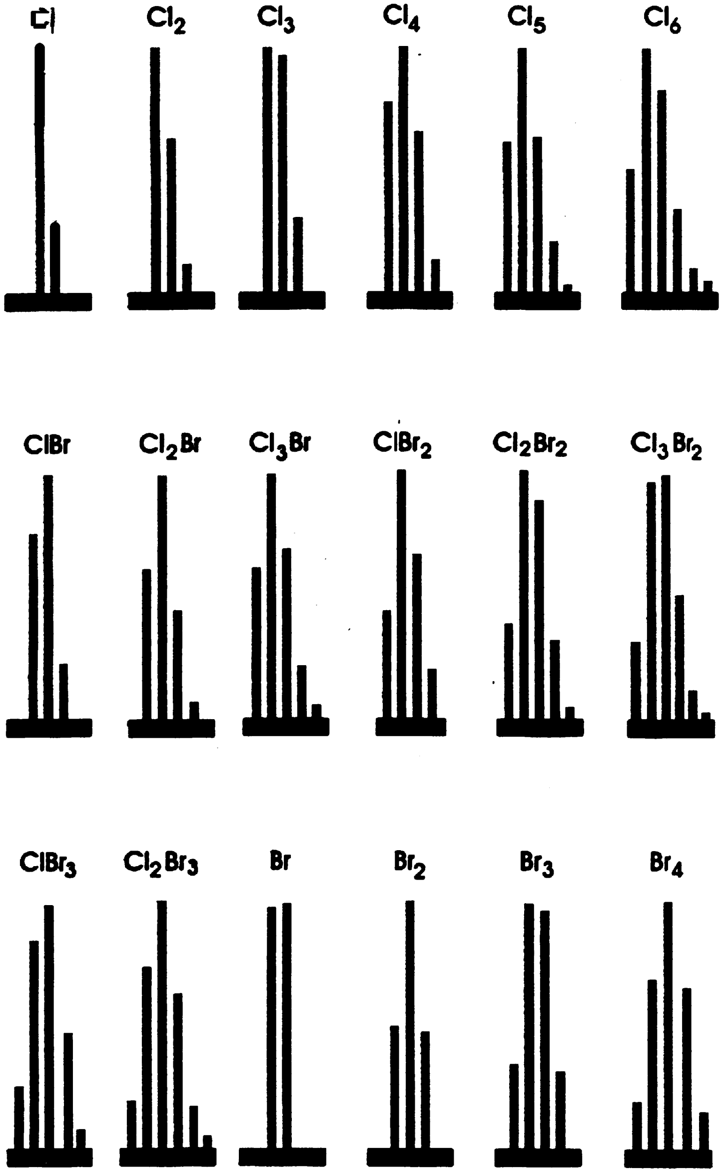
Molecular Weight Determination

Compounds with nominal mass 28.

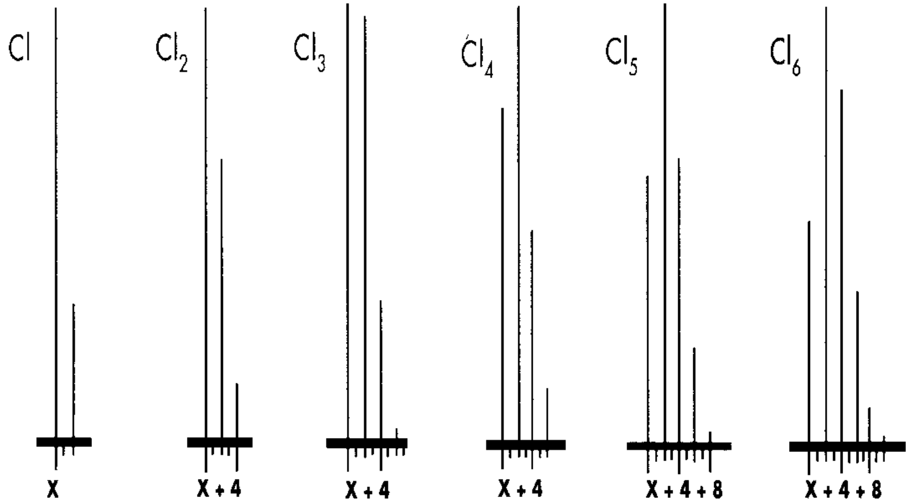
Isotope Clusters

	M	M+1	M+2
CO	100%	1.12	0.2
N_2	100%	0.76	0.00
C_2H_4	100%	2.23	0.01

Halogen Isotope Clusters

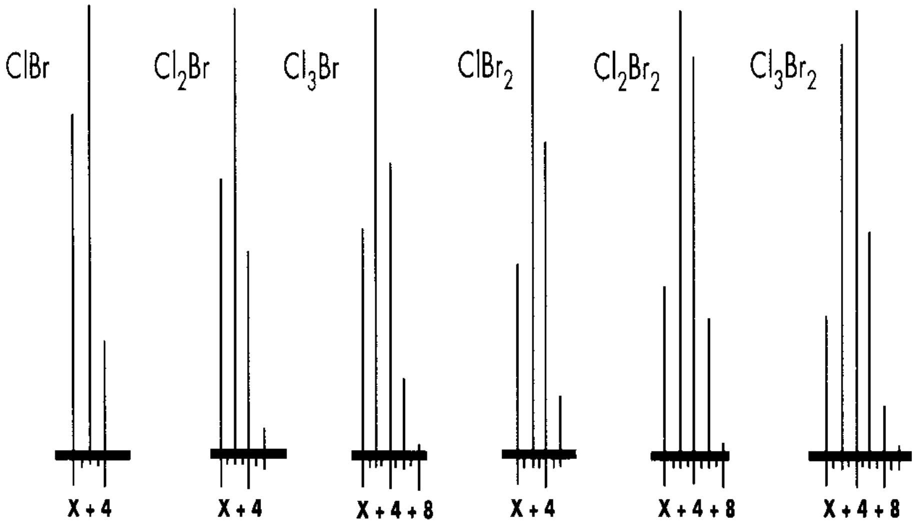


GRAPHICAL REPRESENTATION OF RELATIVE ISOTOPE PEAK INTENSITIES FOR ANY GIVEN ION CONTAINING THE INDICATED NUMBER OF CHLORINE AND/OR BROMINE ATOMS

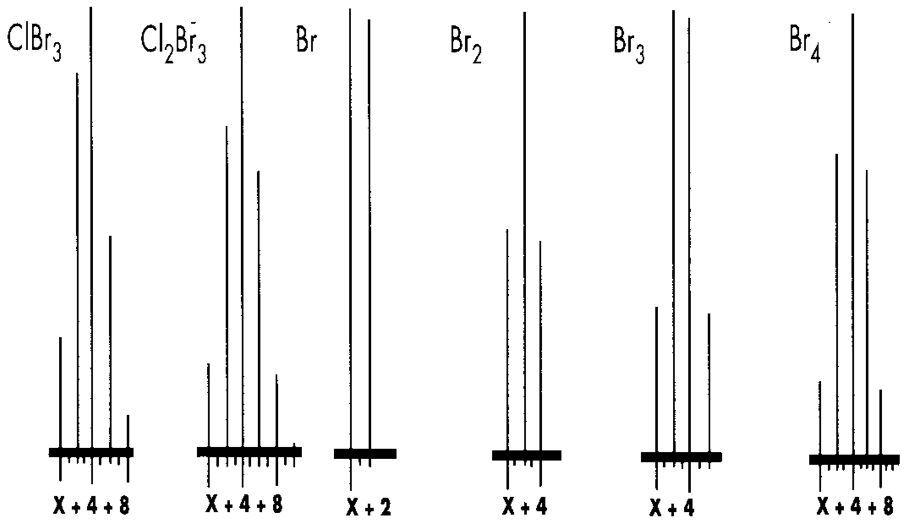


CHLORINE-BROMINE ISOTOPE ABUNDANCE RATIOS

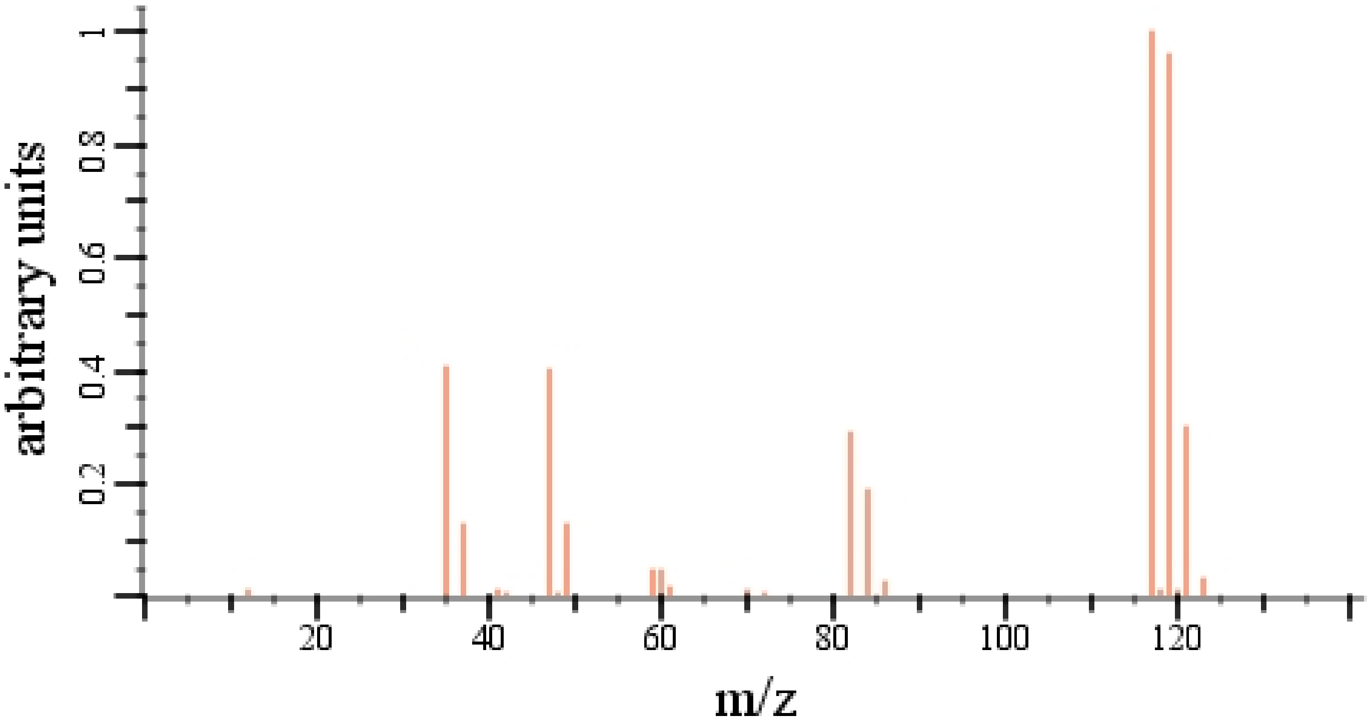
Cl-Br	X	X+2	X+4	X+6	X+8	X+10
Cl	100	32.5				
Cl_2	100	65.0	10.6			
Cl_3	100	97.5	31.7	3.4		
Cl_4	76.9	100	48.7	10.5	0.9	
Cl_5	61.5	100	65.0	21.1	3.4	0.2
Cl_6	51.2	100	81.2	35.2	8.5	1.1



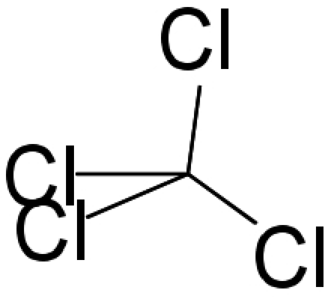
$ClBr$	76.6	100	24.4			
Cl_2Br	61.4	100	45.6	6.6		
Cl_3Br	51.2	100	65.0	17.6	1.7	
$ClBr_2$	43.8	100	69.9	13.7		
Cl_2Br_2	38.3	100	89.7	31.9	3.9	
Cl_3Br_2	31.3	92.0	100	49.9	11.6	1.0
$ClBr_3$	26.1	85.1	100	48.9	8.0	
Cl_2Br_3	20.4	73.3	100	63.8	18.7	2.0



Br	100	98.0			
Br_2	51.0	100	49.0		
Br_3	34.0	100	98.0	32.0	
Br_4	17.4	68.0	100	65.3	16.0



Position	Intensity
135	0%
133	0%
124	0%
123	3%
122	0%
121	30%
120	1%
119	96%
118	1%
117	100%
116	0%



SOME COMMON AND REASONABLE LOSSES FROM THE MOLECULAR ION

M - 1	loss of hydrogen radical	M- $^{\cdot}H$
M - 15	loss of methyl radical	M- $^{\cdot}CH_3$
M - 29	loss of ethyl radical	M- $^{\cdot}CH_2CH_3$
M - 31	loss of methoxyl radical	M- $^{\cdot}OCH_3$
M - 43	loss of propyl radical	M- $^{\cdot}CH_2CH_2CH_3$
M - 45	loss of ethoxyl radical	M- $^{\cdot}OCH_2CH_3$
M - 57	loss of butyl radical	M- $^{\cdot}CH_2CH_2CH_2CH_3$
M - 2	loss of hydrogen	M- H_2
M - 18	loss of water	M- H_2O
M - 28	loss of CO or ethylene	M- CO or M - CH_2H_4
M - 32	loss of methanol	M- CH_3OH
M - 44	loss of CO_2	M- CO_2
M - 60	loss of acetic acid	M- CH_3CO_2H
M - 90	loss of silanol: $HO\text{-}Si(CH_3)_3$	M- $HO - Si - (CH_3)_3$

Fragmentação

- Governada pela estabilidade do íon produzido
- consideração
  - regra do octeto
  - deslocalização por ressonância
  - polarizabilidade e hiperconjugação
  - eletronegatividade
- Regra de Stevenson:

  Para quebra de uma ligações simples, o fragmento com o potencial de ionização mais baixo fica com a carga

  (em outras palavras, forma-se o íon mais estável)

Regras Gerais de Fragmentação

Quebra de Uma Ligação (Quebras-α)

Quebra de Duas Ligações

- Eliminação de H-X
- retro Diels-Alder
- Rearranjo de McLafferty

FRAGMENTATION PATTERNS

ALKANES

The mass spectra of simple hydrocarbons have peaks at m/z values corresponding to the ions produced by breaking C-C bonds. Peaks can occur at ...

m/z	15	29	43	57	71	85	etc.
	CH_3^+	$C_2H_5^+$	$C_3H_7^+$	$C_4H_9^+$	$C_5H_{11}^+$	$C_6H_{13}^+$	

- **the stability of the carbocation formed affects its abundance**
- **the more stable the cation the higher the peak**
- **the more alkyl groups attached to the carbocation the more stable it is**

most stable tertiary 3° > secondary 2° > primary 1° least stable

alkyl groups are electron releasing and stabilise the cation

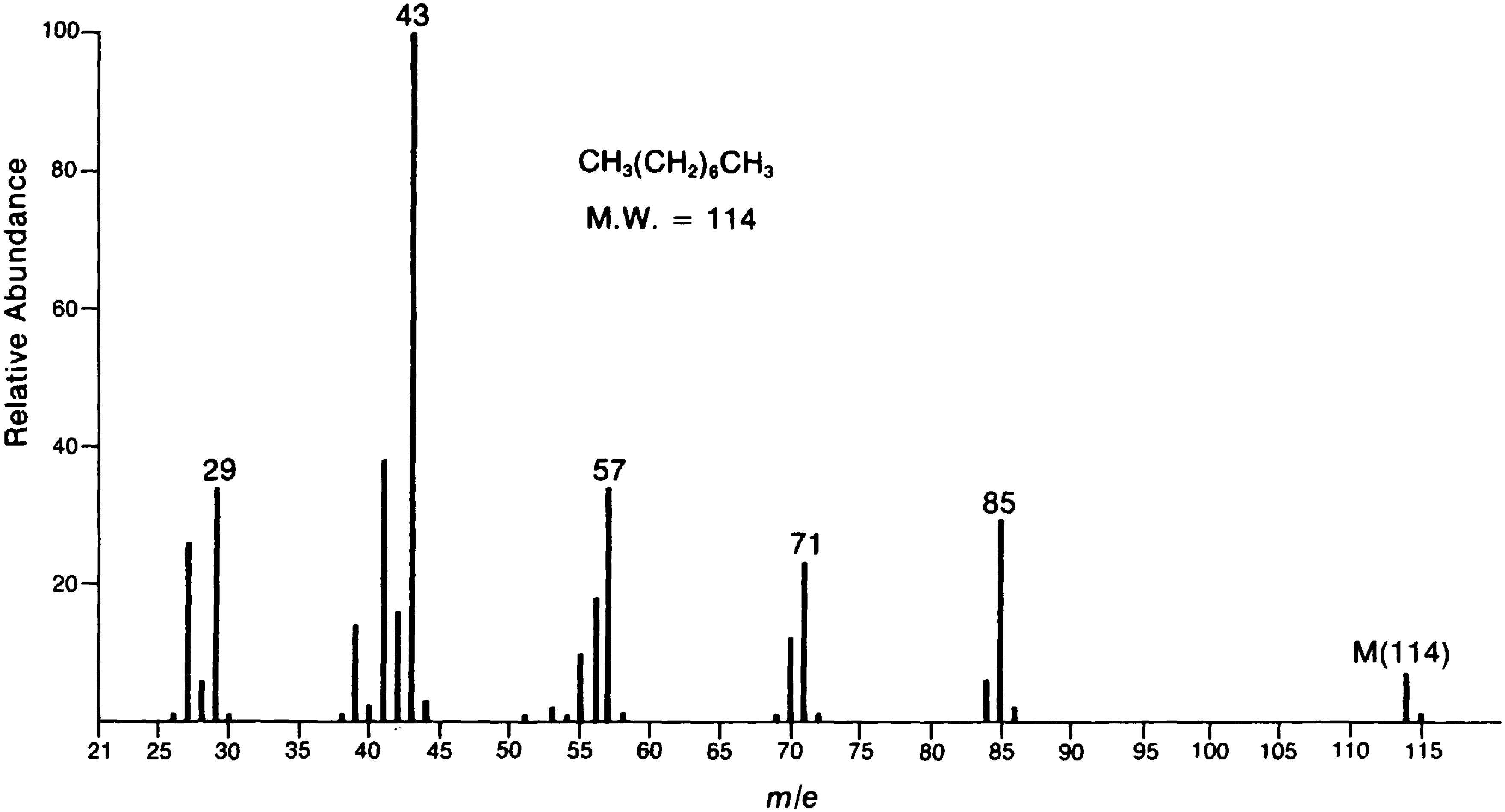
Alkane Fragmentation

- Long chains give homologous series of m/z = 14 units
- Long chains rarely lose methyl radical
- Straight chain alkanes give primary carbocation
- branched alkanes have small or absent M^+
- enhanced fragmentation at branch points

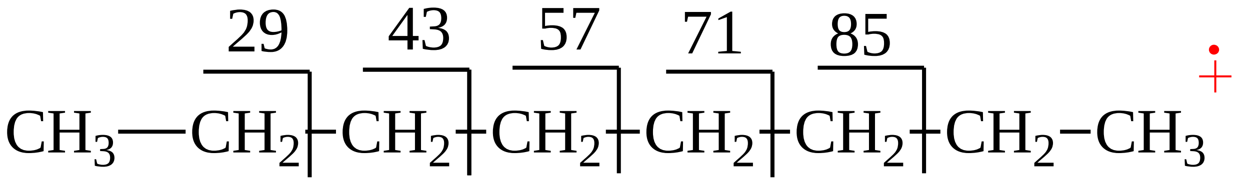
Cycloalkanes

- loss of side chain
- loss of ethylene fragments

octane



43
CH3(CH2)6CH3
M.W. = 114
29
57
85
71
M(114)
Relative Abundance
100
80
60
40
20
21
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
110
115
m/e



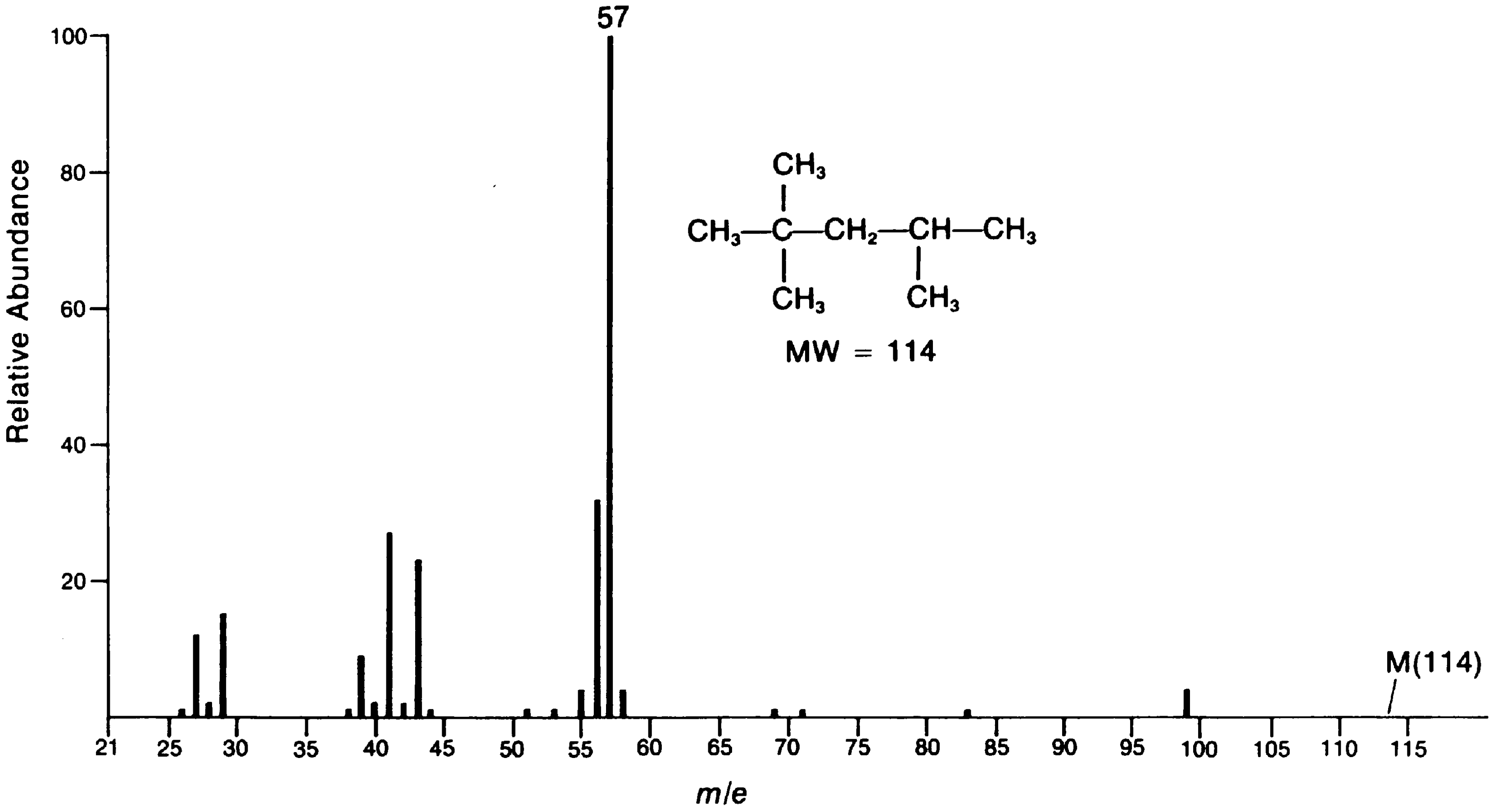
$$CH_3-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_3^{\bullet +}$$

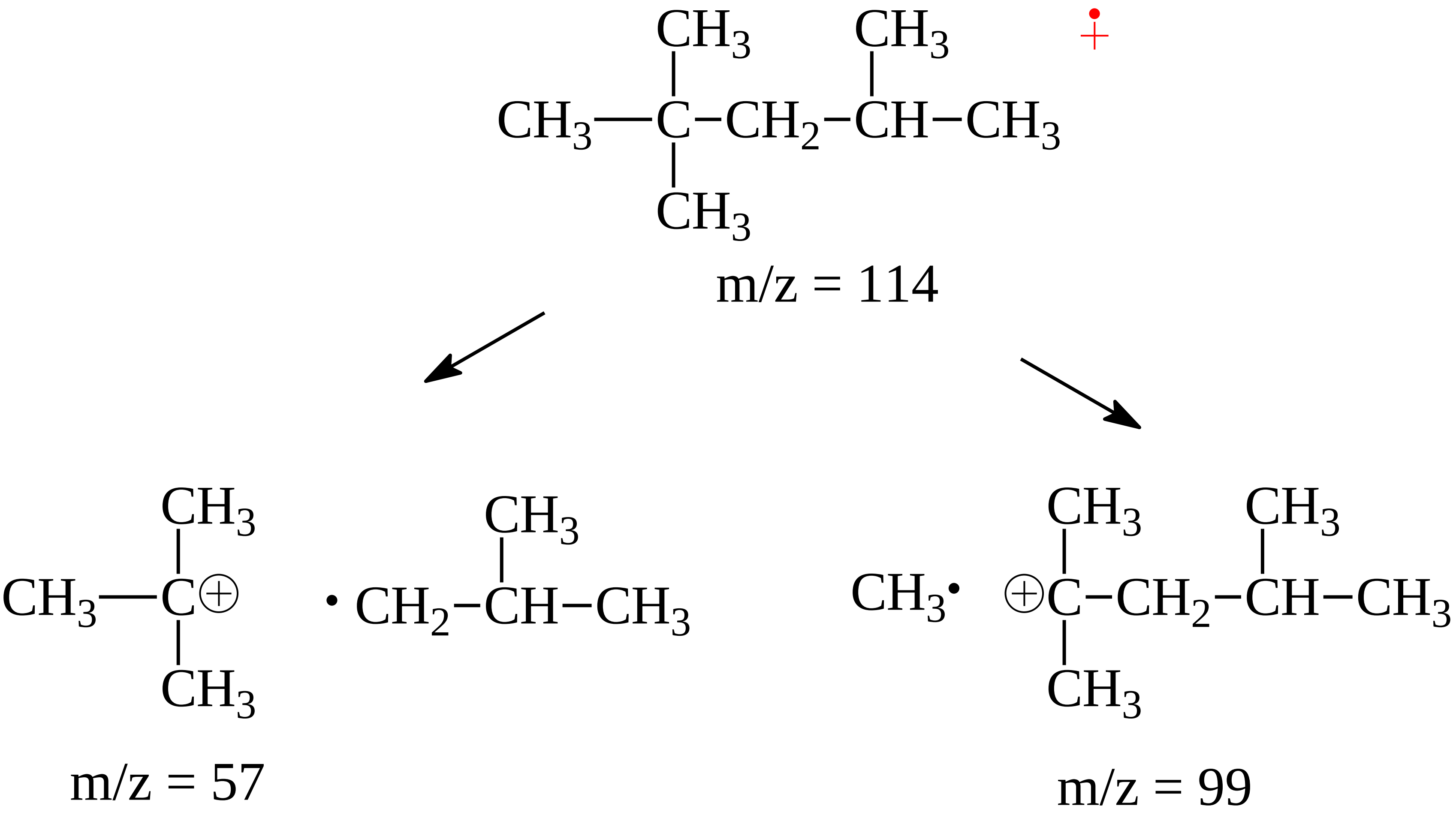
m/z = 114

linear alkane pattern

sequential peaks 14 mass units apart

isooctane


57
100
80
60
40
20
Relative Abundance
CH3
CH3—C—CH2—CH—CH3
CH3
CH3
MW = 114
M(114)
21
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
110
115
m/e



branched alkane - formation of most stable carbocation

Alkene Fragmentation

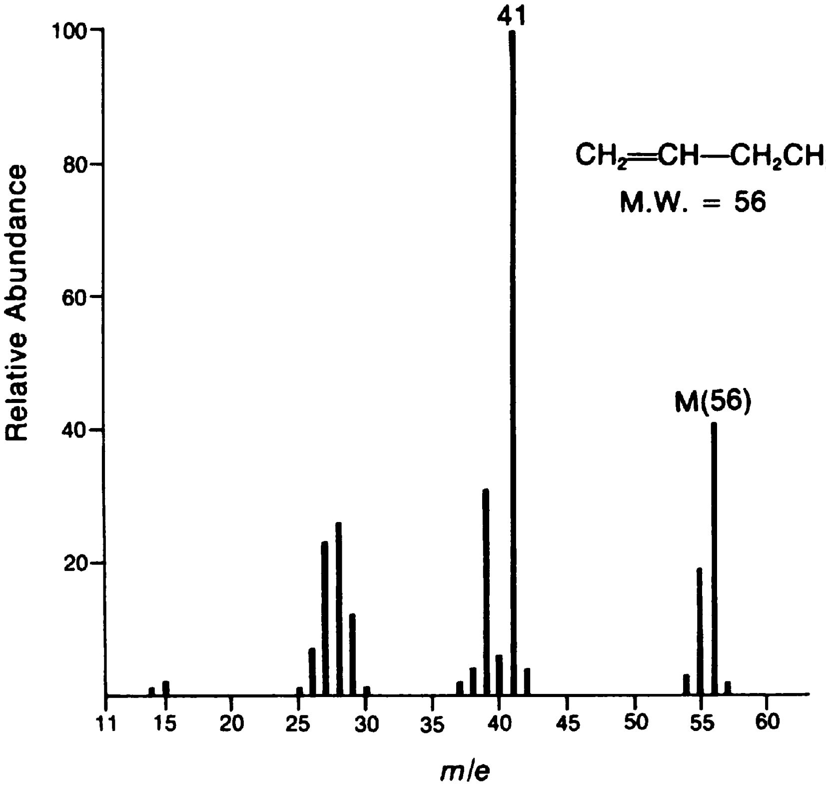
- Fairly prominent M^+
- fragment ions of $C_nH_{2n}^+$ and $C_nH_{2n-1}^+$
- terminal alkenes lose allyl cation if possible

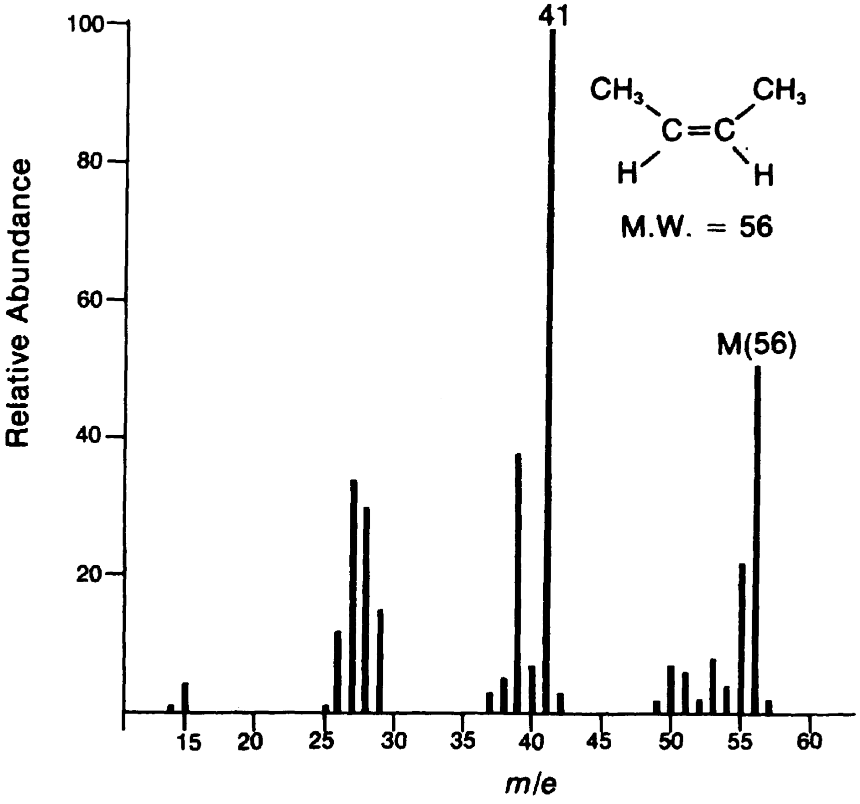
Cycloalkenes

- prominent molecular ion
- retro Diels-Alder cleavage

1-butene & 2-butene

mass spectra are identical - not a good method for alkene isomers





Alkyne Fragmentation

- Molecular ion readily visible
- terminal alkynes readily lose hydrogen atom
- terminal alkynes lose propargyl cation if possible

Aromatic Hydrocarbon Fragmentation

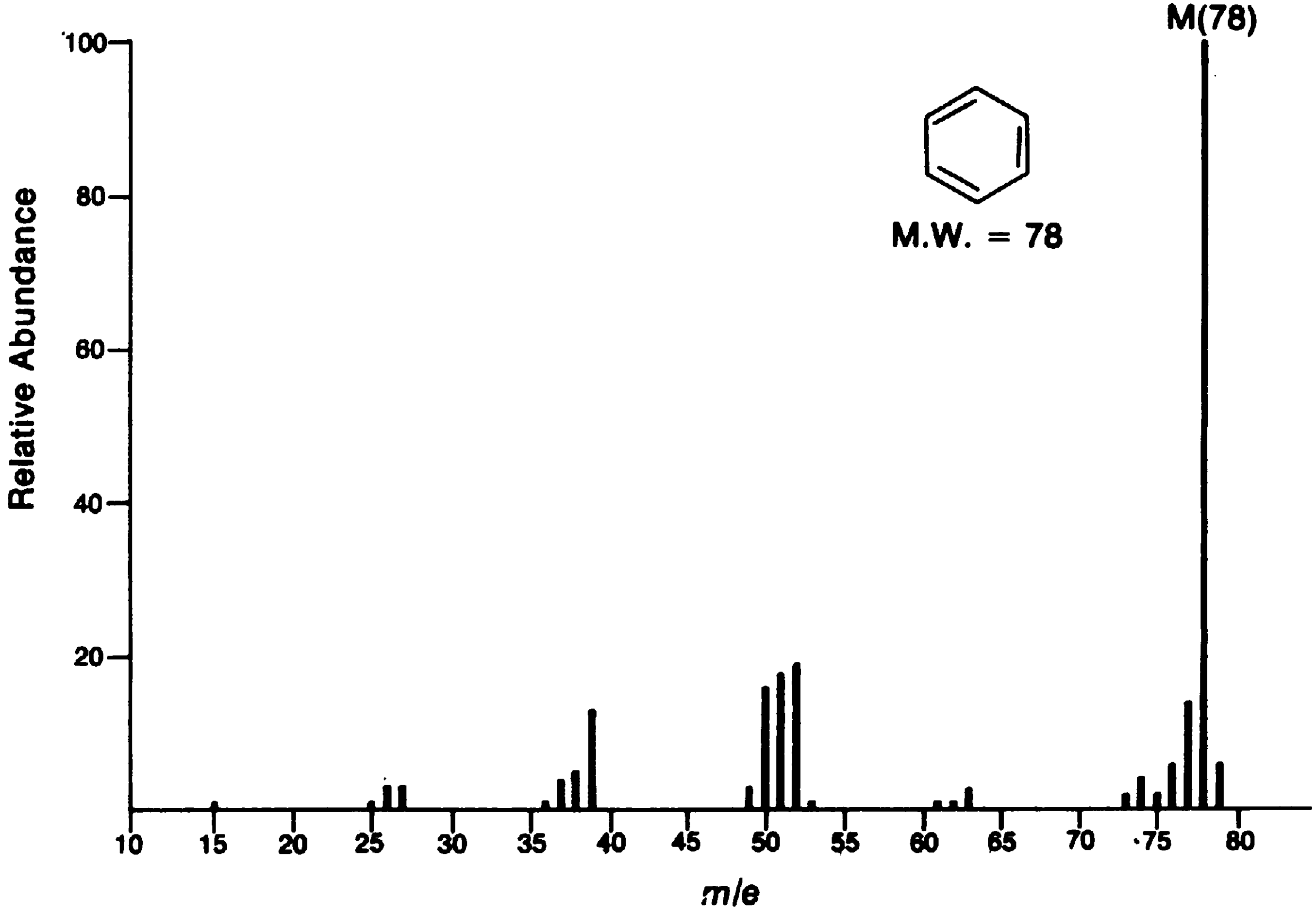
- Molecular ion usually strong
- alkylbenzenes cleave at benzylic carbon

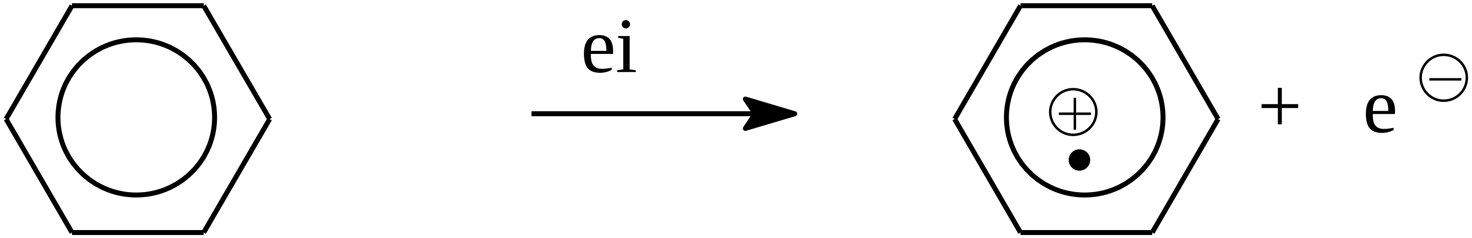
tropylium ion formation

- McLafferty rearrangement of aromatics

need γ-hydrogens

benzene


M(78)
M.W. = 78
Relative Abundance
100
80
60
40
20
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
m/e



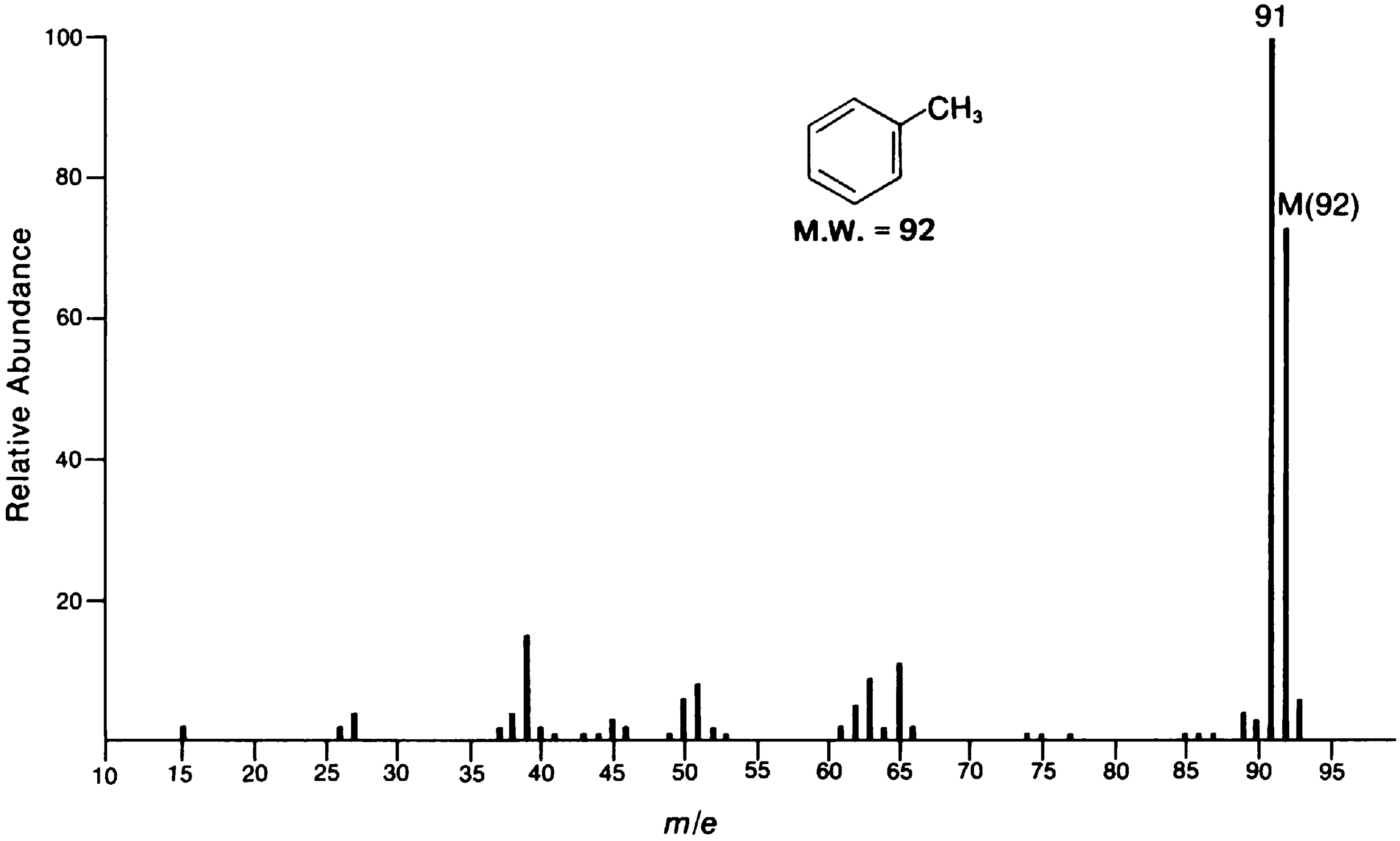
C_6H_6

m/z = 78

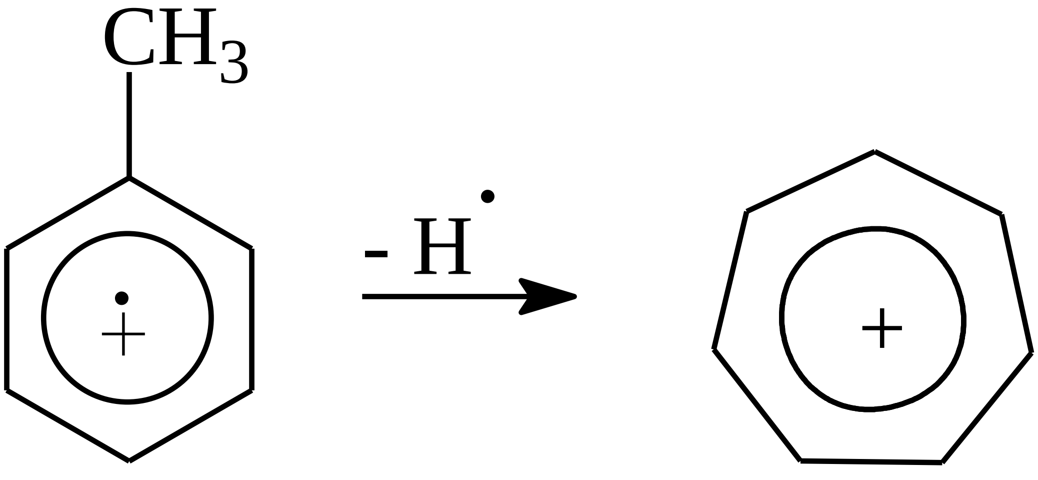
closed shell
(paired electrons)

open shell
(odd electron ion)

toluene



91
M(92)
CH₃
M.W. = 92
Relative Abundance
100
80
60
40
20
m/e
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95



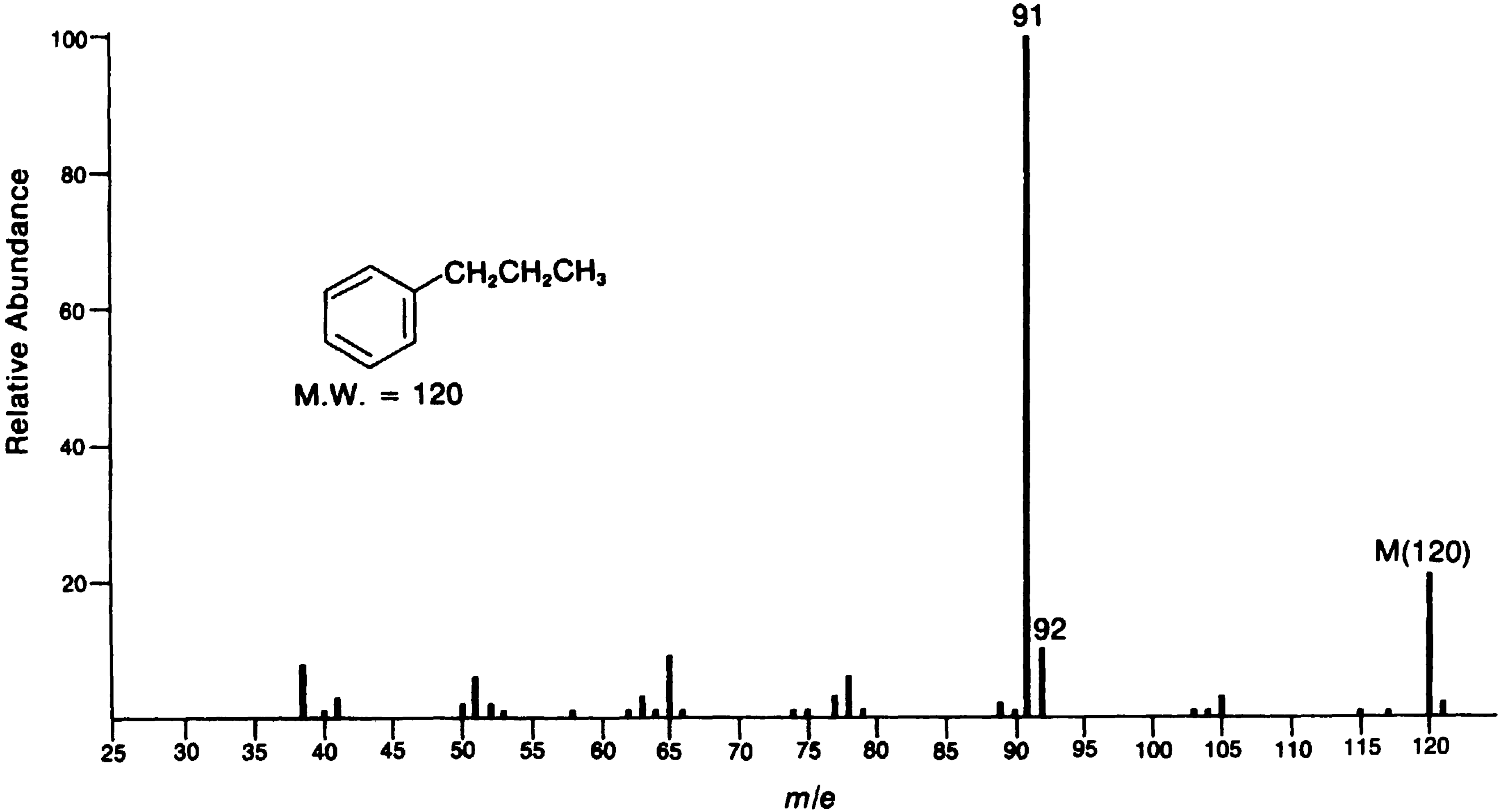
m/z = 92

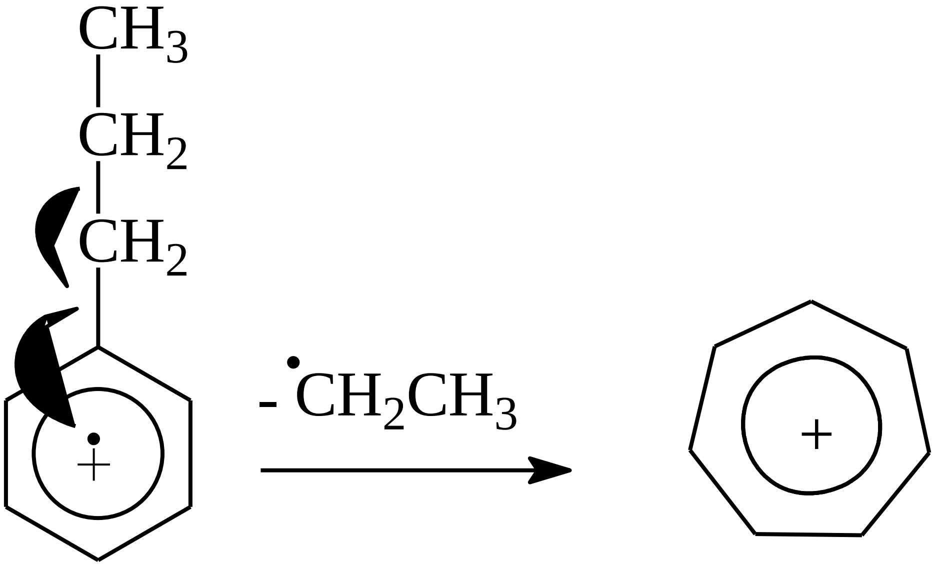
m/z = 91

C_7H_7

tropylium ion

n-propylbenzene

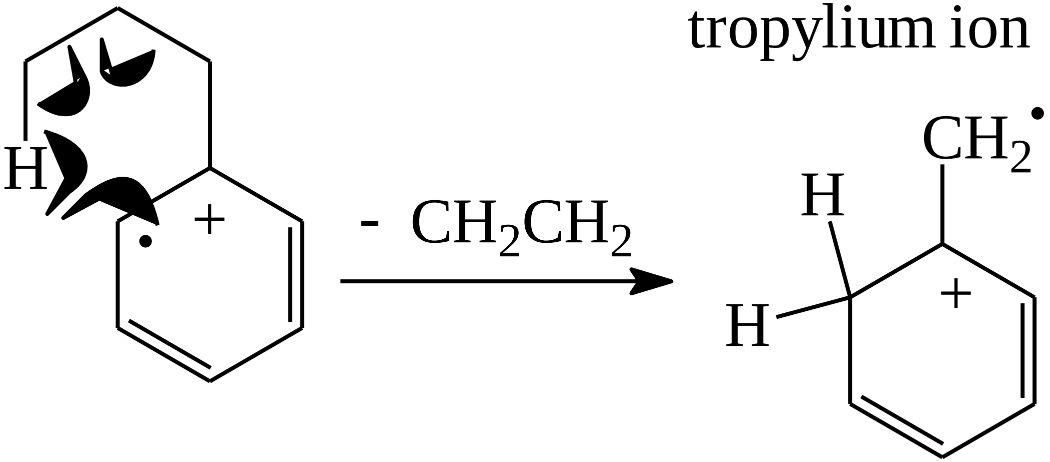




m/z = 120

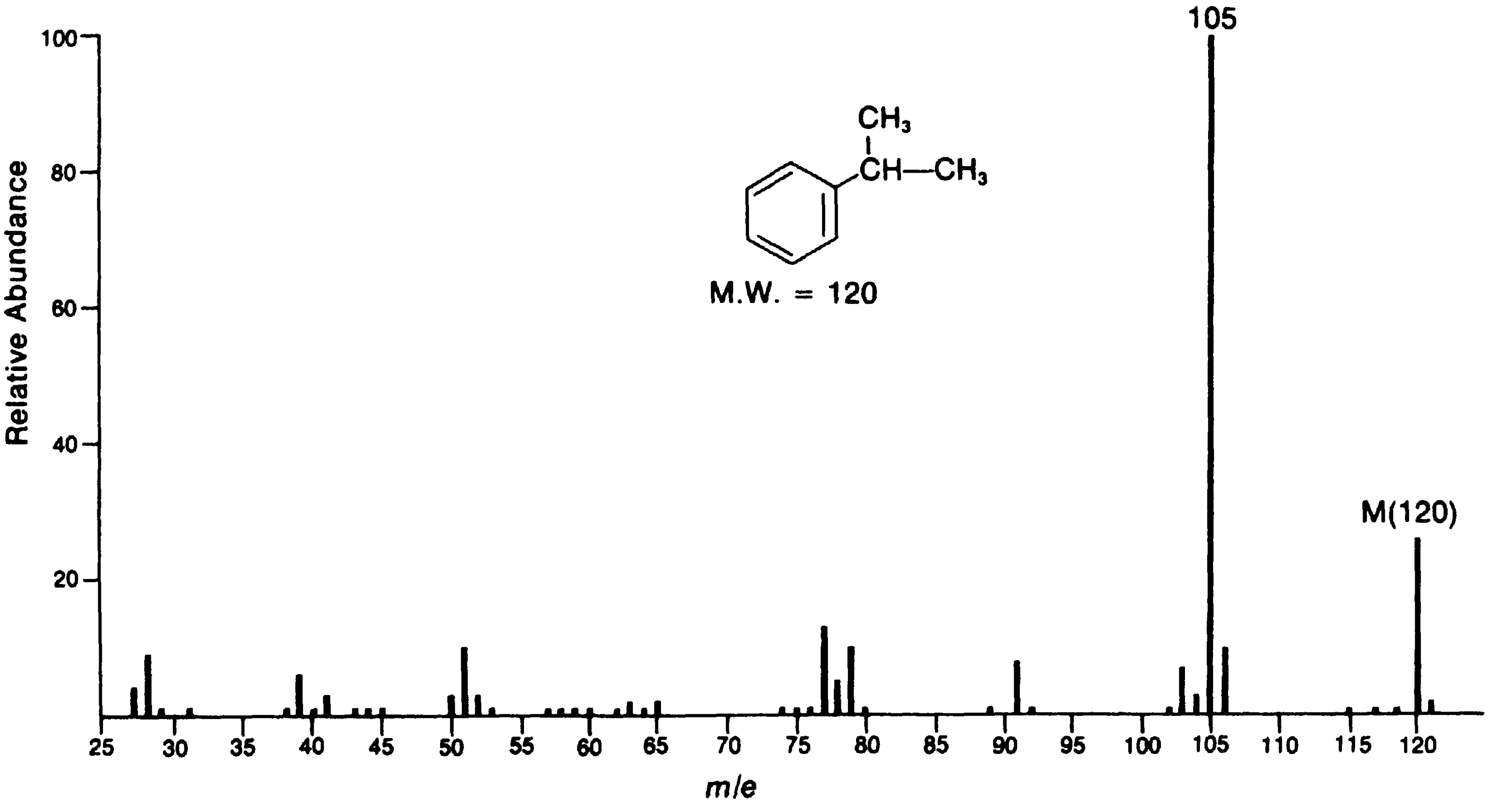
m/z = 91
C_7H_7

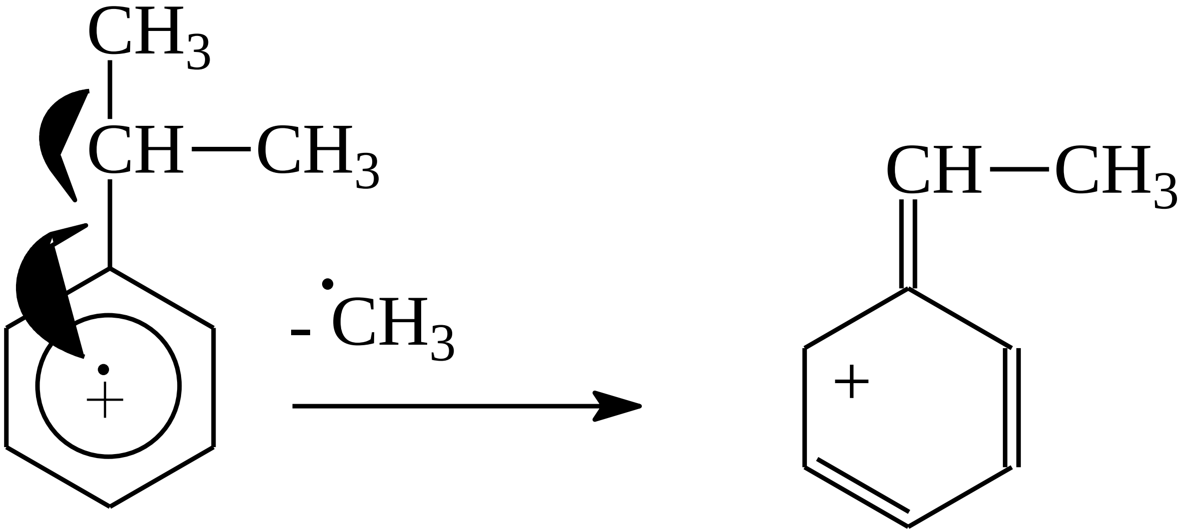
tropylium ion



m/z = 92

isopropylbenzene

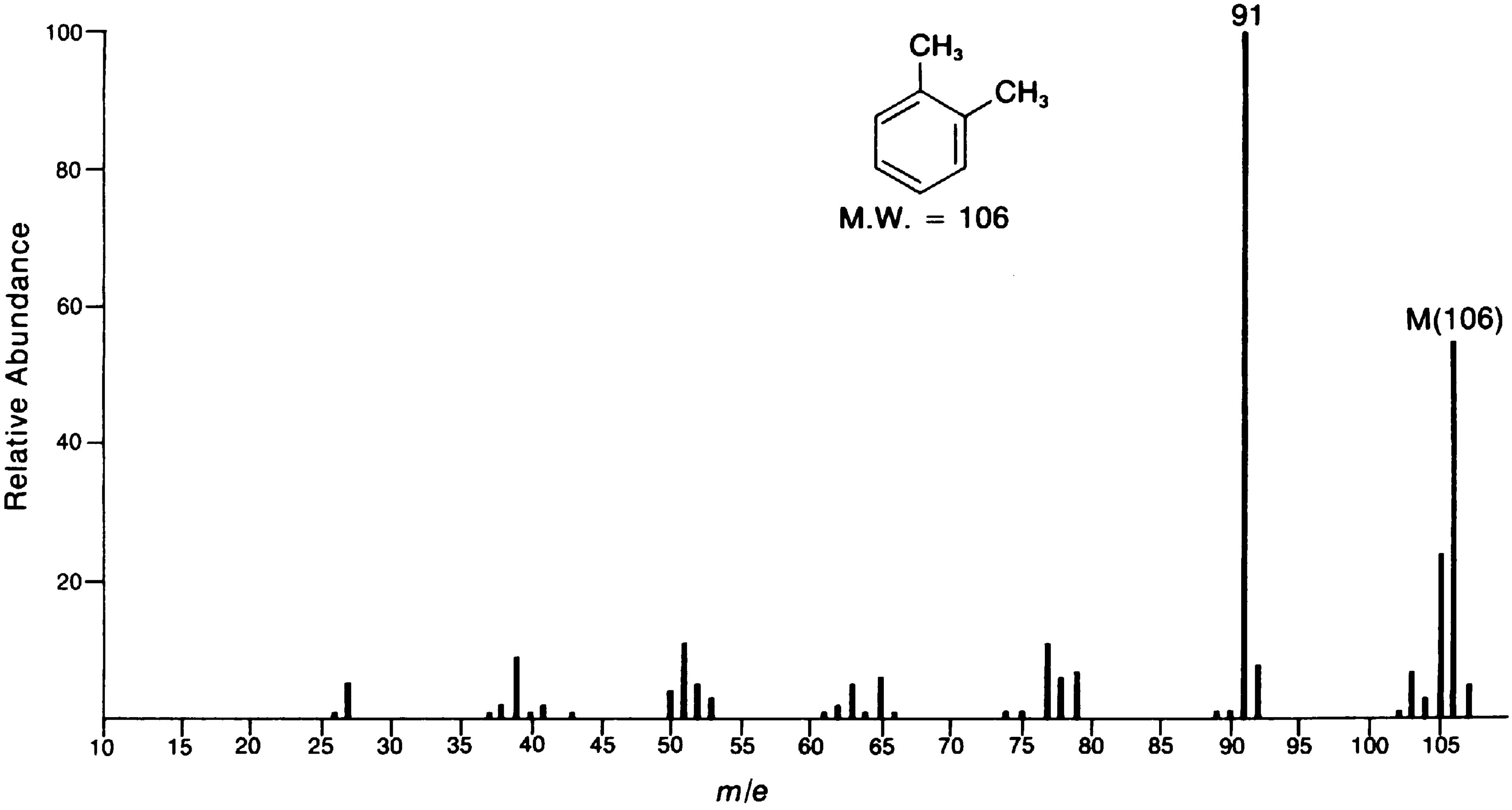




m/z = 120

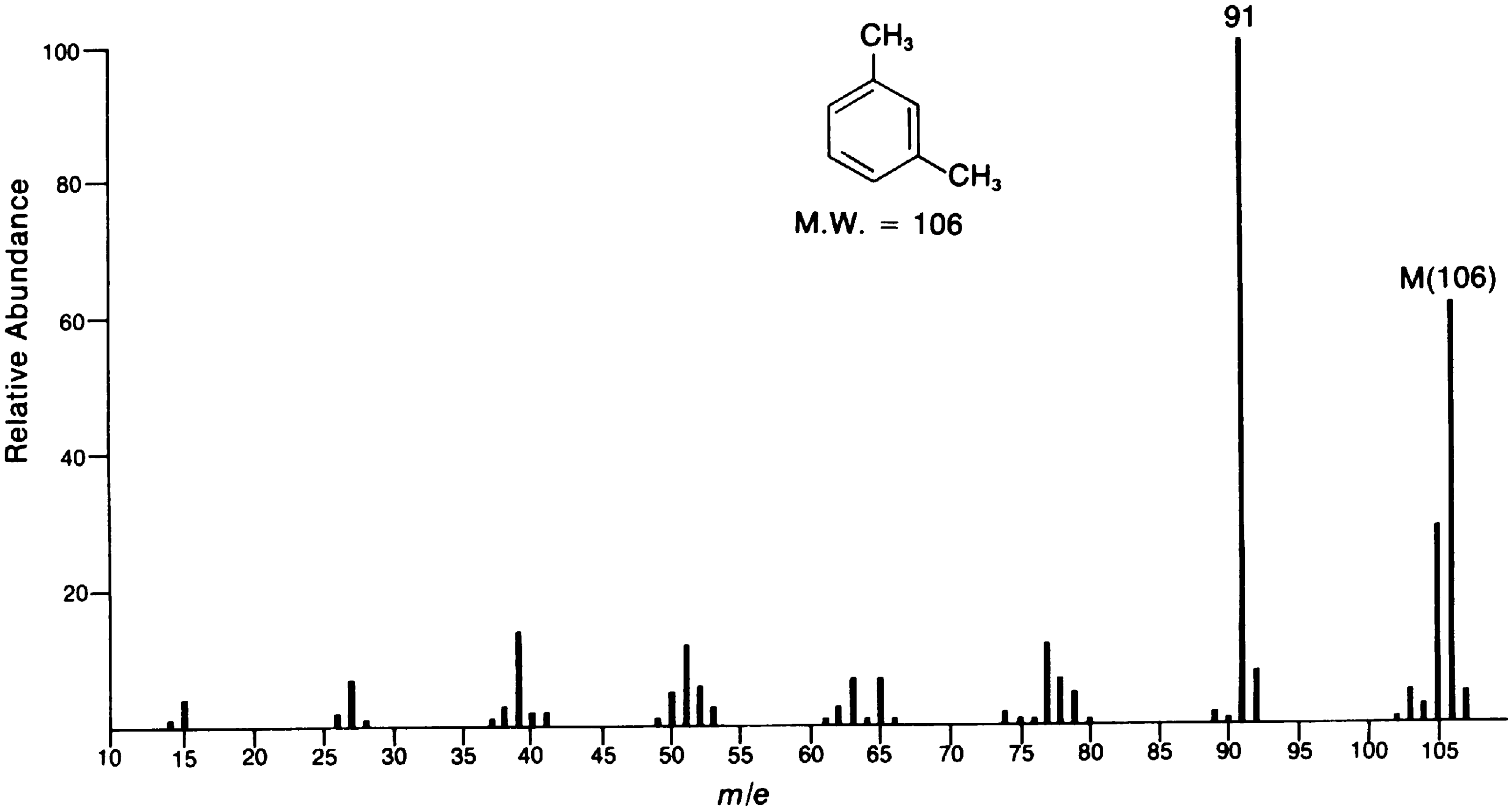
m/z = 105

o-xylene



91
M(106)
CH3
CH3
M.W. = 106
Relative Abundance
100
80
60
40
20
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
m/e

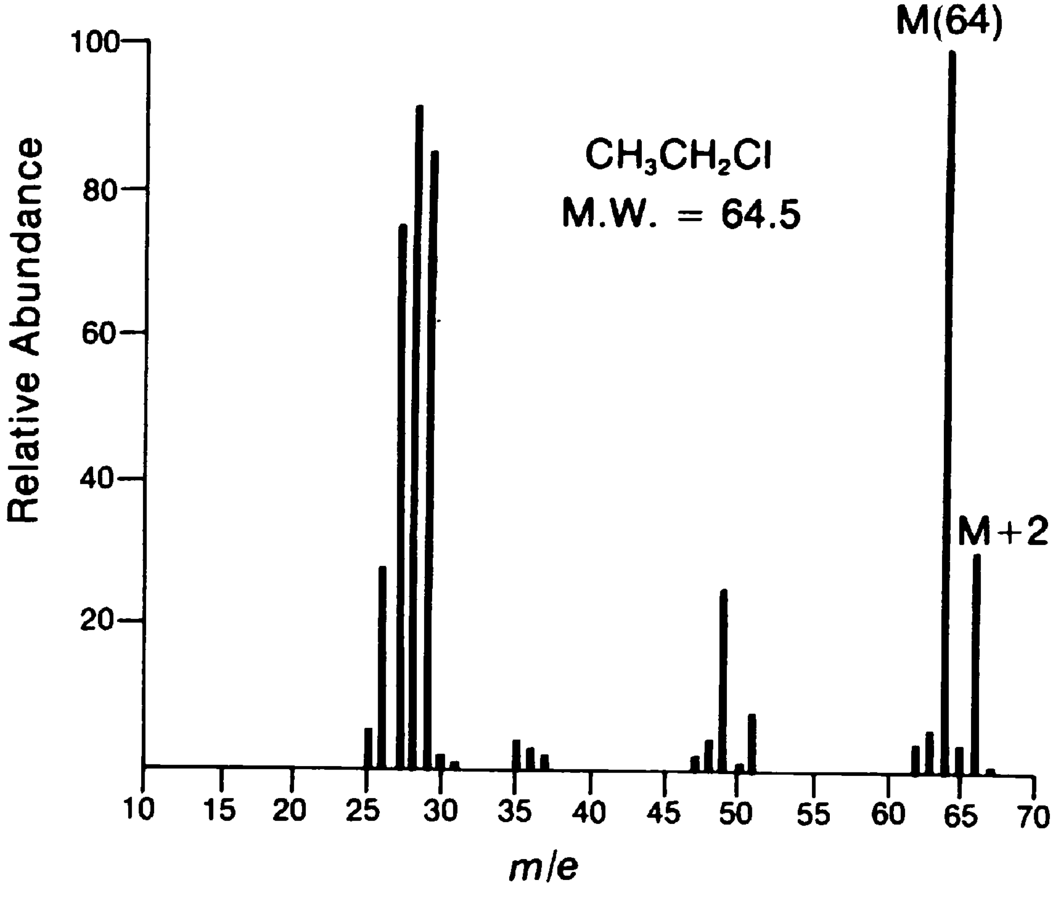
m-xylene

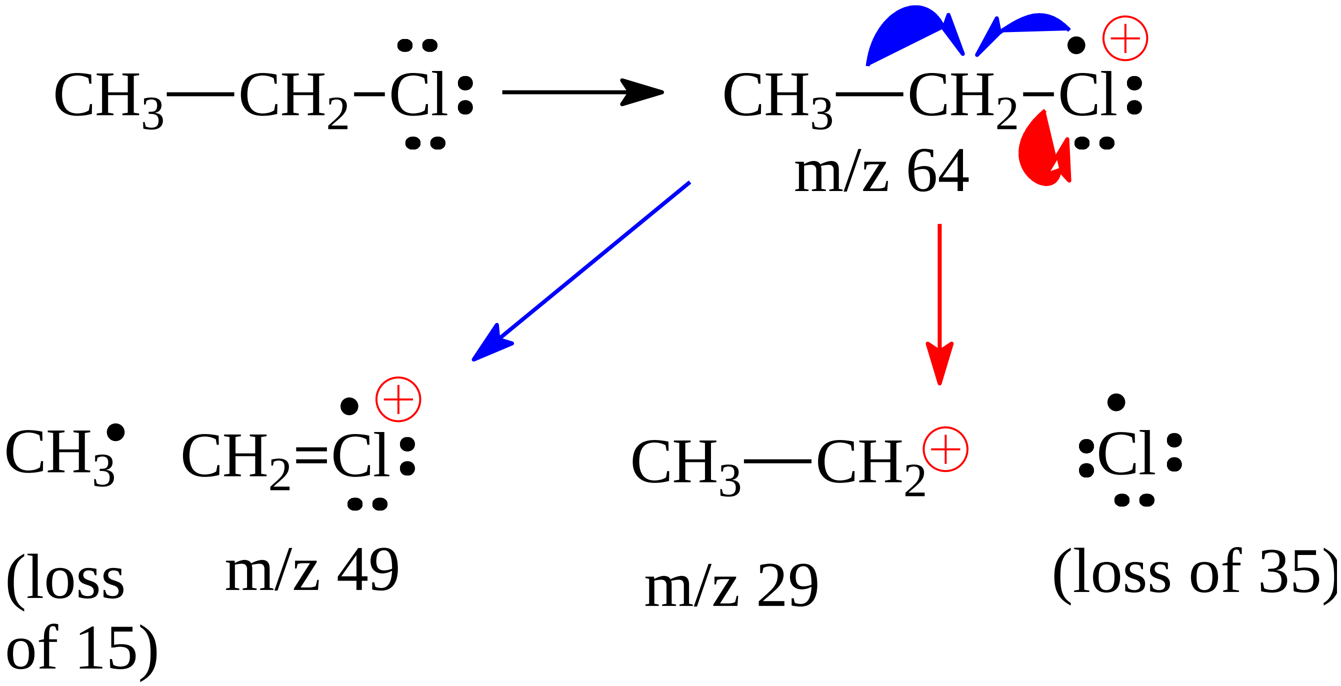

CH3
CH3
M.W. = 106
91
M(106)
Relative Abundance
100
80
60
40
20
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
m/e

Halide Fragmentation

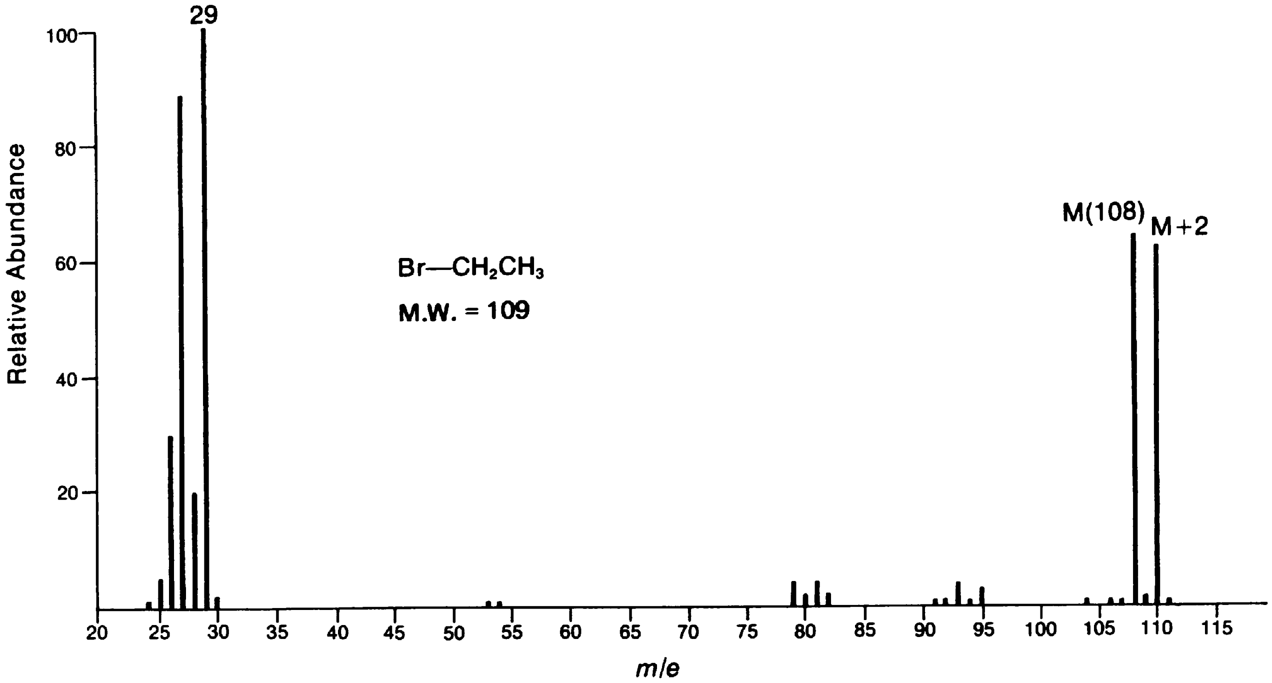
- Loss of halogen atom
- Elimination of HX
- alpha-cleavage
- 1,4-rearrangement

chloroethane

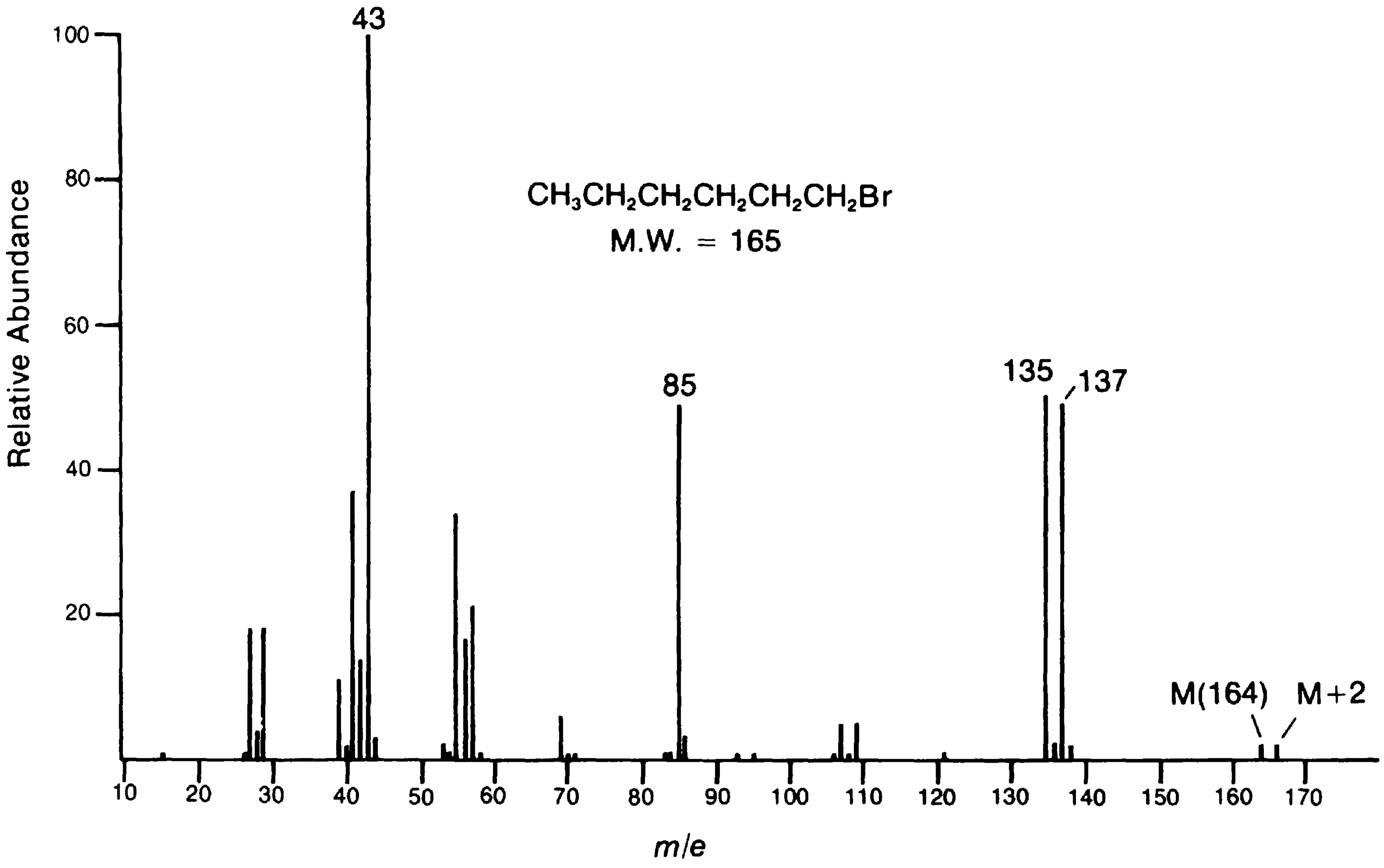


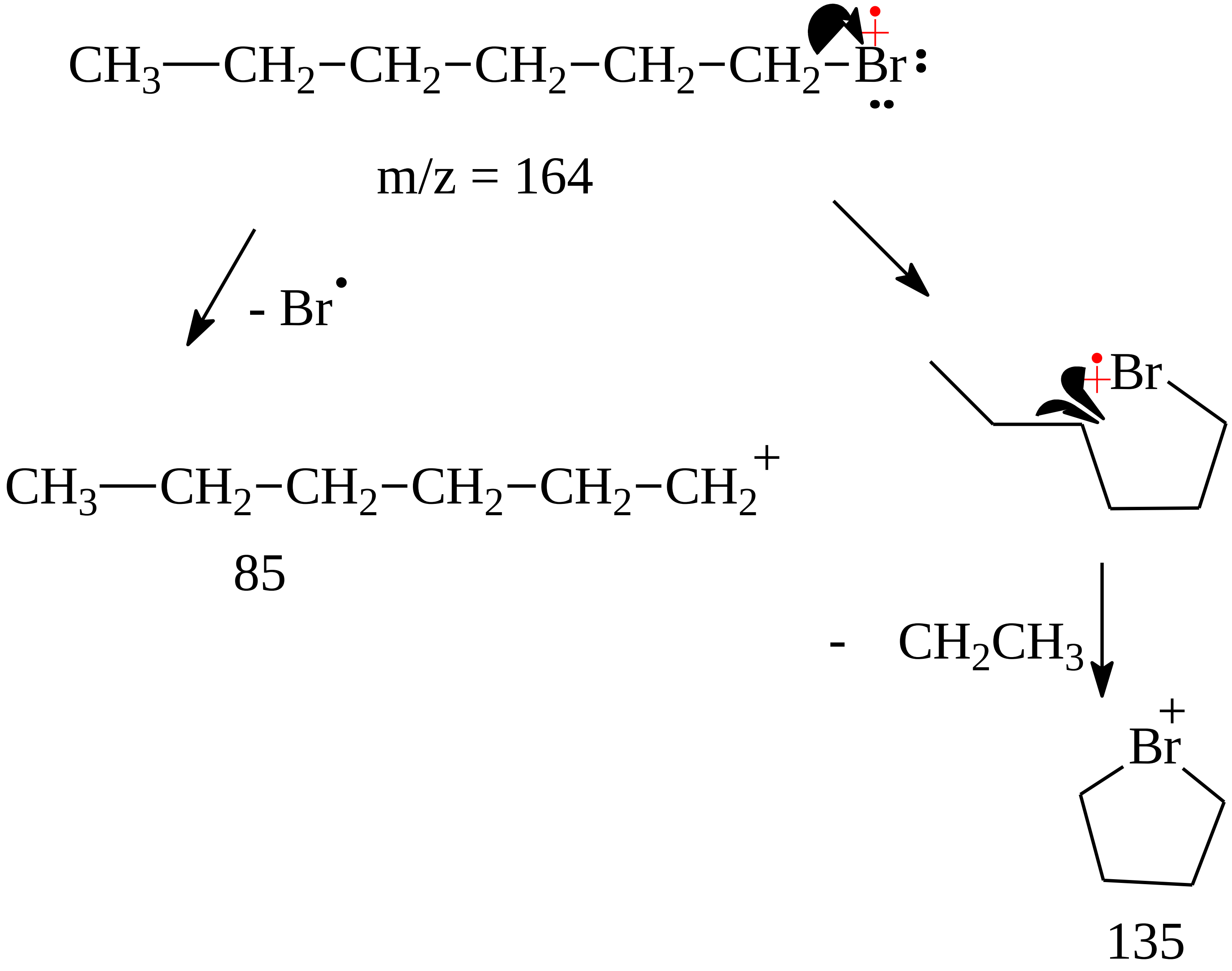

CH3—CH2−Cl
CH3—CH2−Cl
m/z 64
CH3
CH2=Cl
(loss of 15)
m/z 49
CH3—CH2
Cl
m/z 29
(loss of 35)

bromoethane



bromohexane





CH3—CH2−CH2−CH2−CH2−CH2−Br
m/z = 164
- Br
CH3—CH2−CH2−CH2−CH2−CH2+
85
Br
- CH2CH3
Br+
135

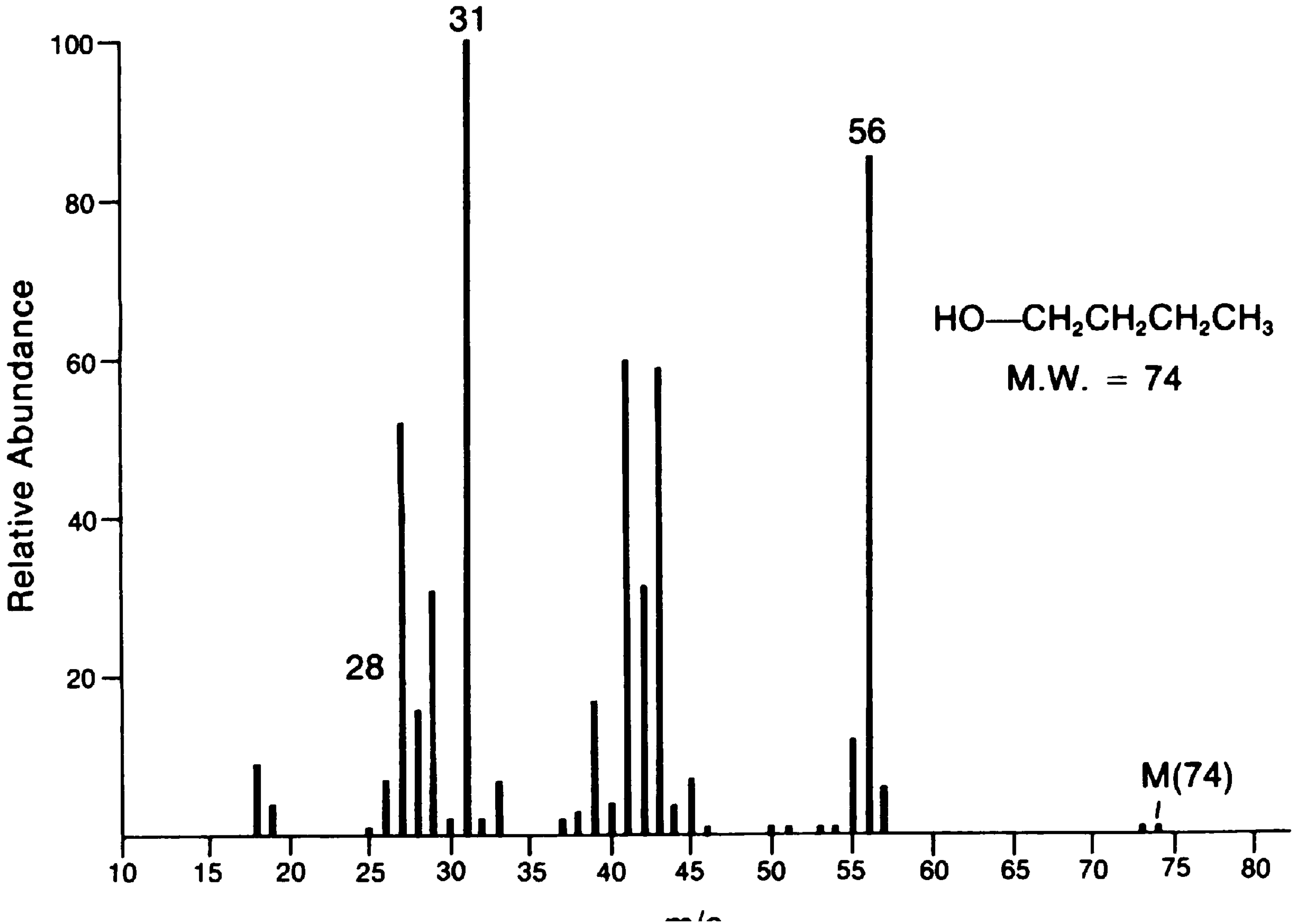
Alcohol Fragmentation

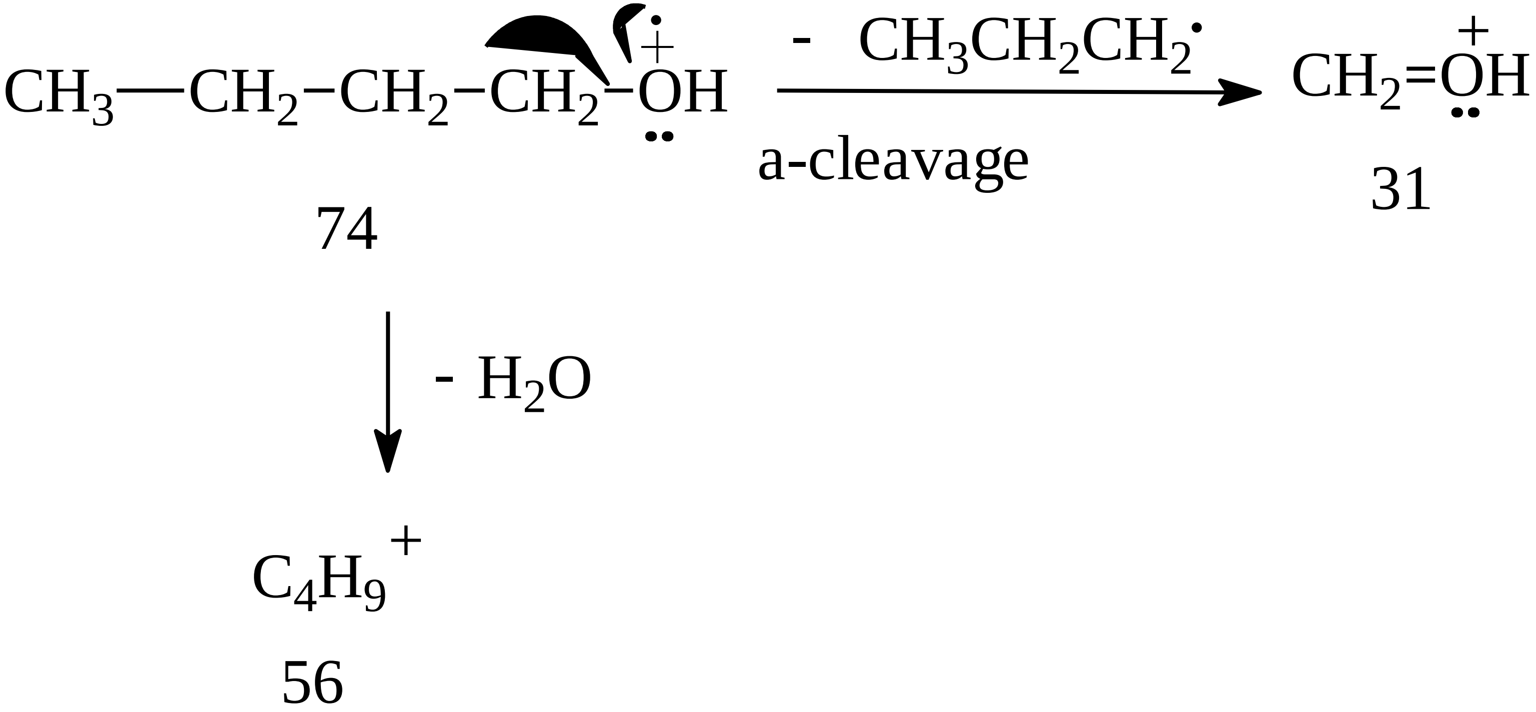
- Molecular ion strength depends on substitution

primary alcohol	weak M^+
secondary alcohol	VERY weak M^+
tertiary alcohol	M^+ usually absent

- Dehydration fragmentation
  - thermal vs. 1,4-dehydration of M^+
- Loss of alkyl group
  - largest R group lost as radical

1-butanol


31
56
28
M(74)
HO—CH₂CH₂CH₂CH₃
M.W. = 74
Relative Abundance
100
80
60
40
20
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80



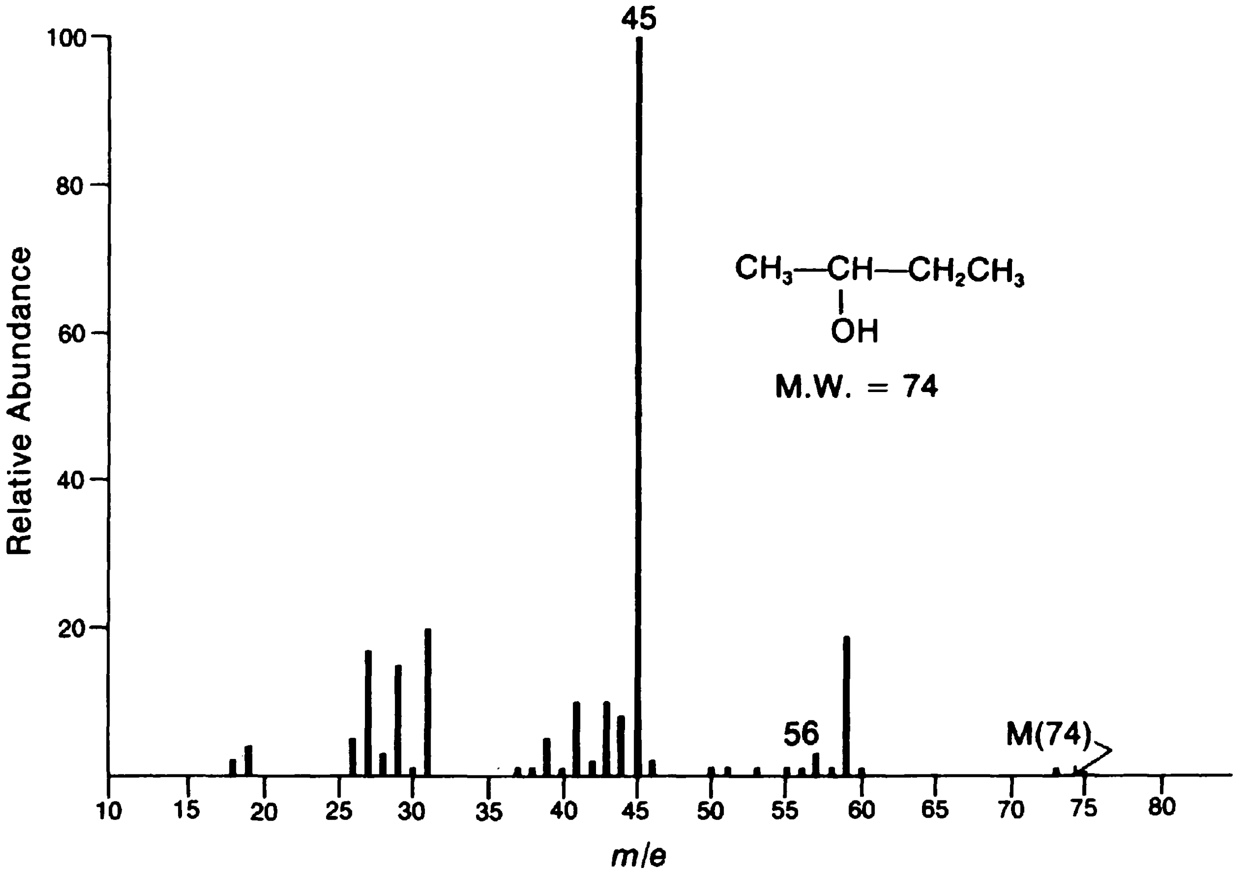
$$\begin{tikzcd} CH_3-CH_2-CH_2-CH_2-\overset{\cdot +}{\underset{\cdot\cdot}{O}}H \arrow[r, "- \; CH_3CH_2CH_2^{\cdot}", "a\text{-cleavage}"'] \arrow[d, "- \; H_2O"] & CH_2=\overset{+}{\underset{\cdot\cdot}{O}}H \\ C_4H_9^{+} & \end{tikzcd}$$

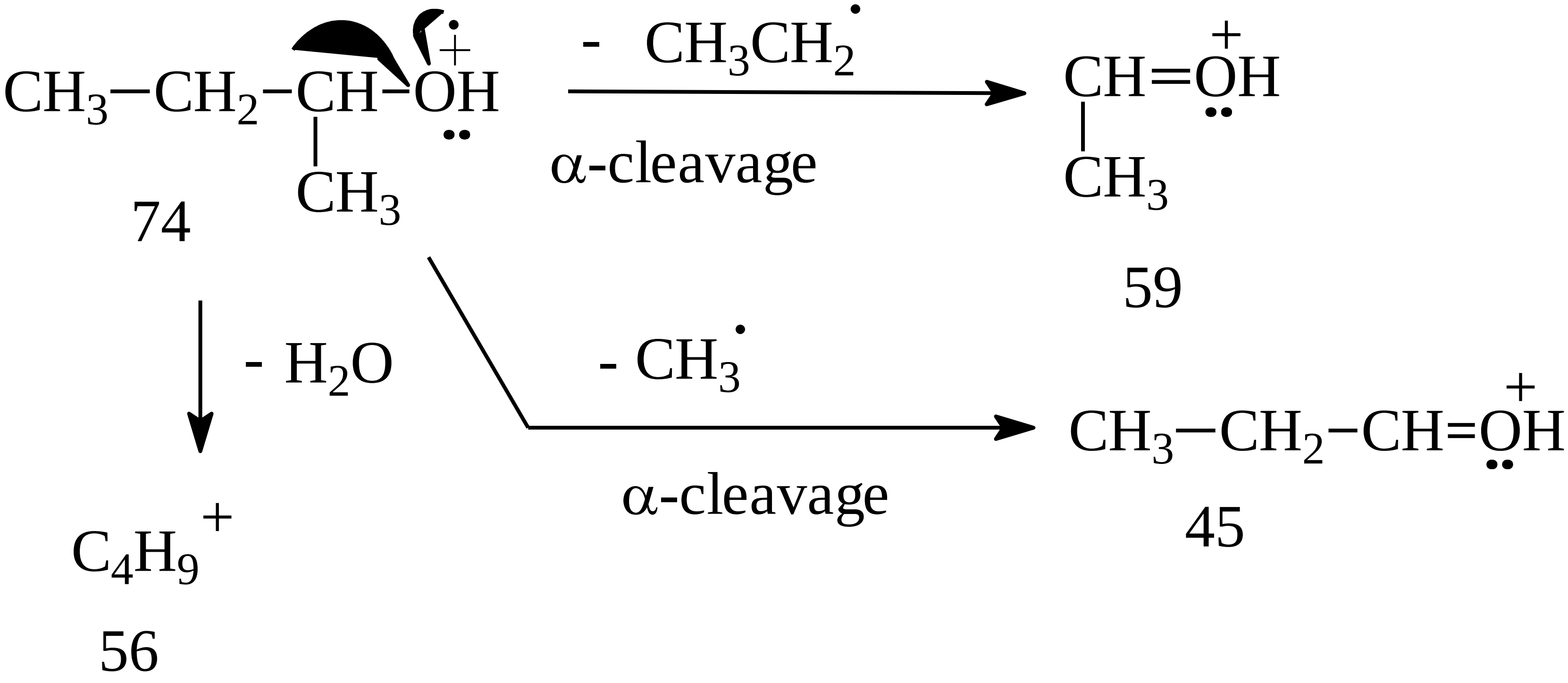
74

31

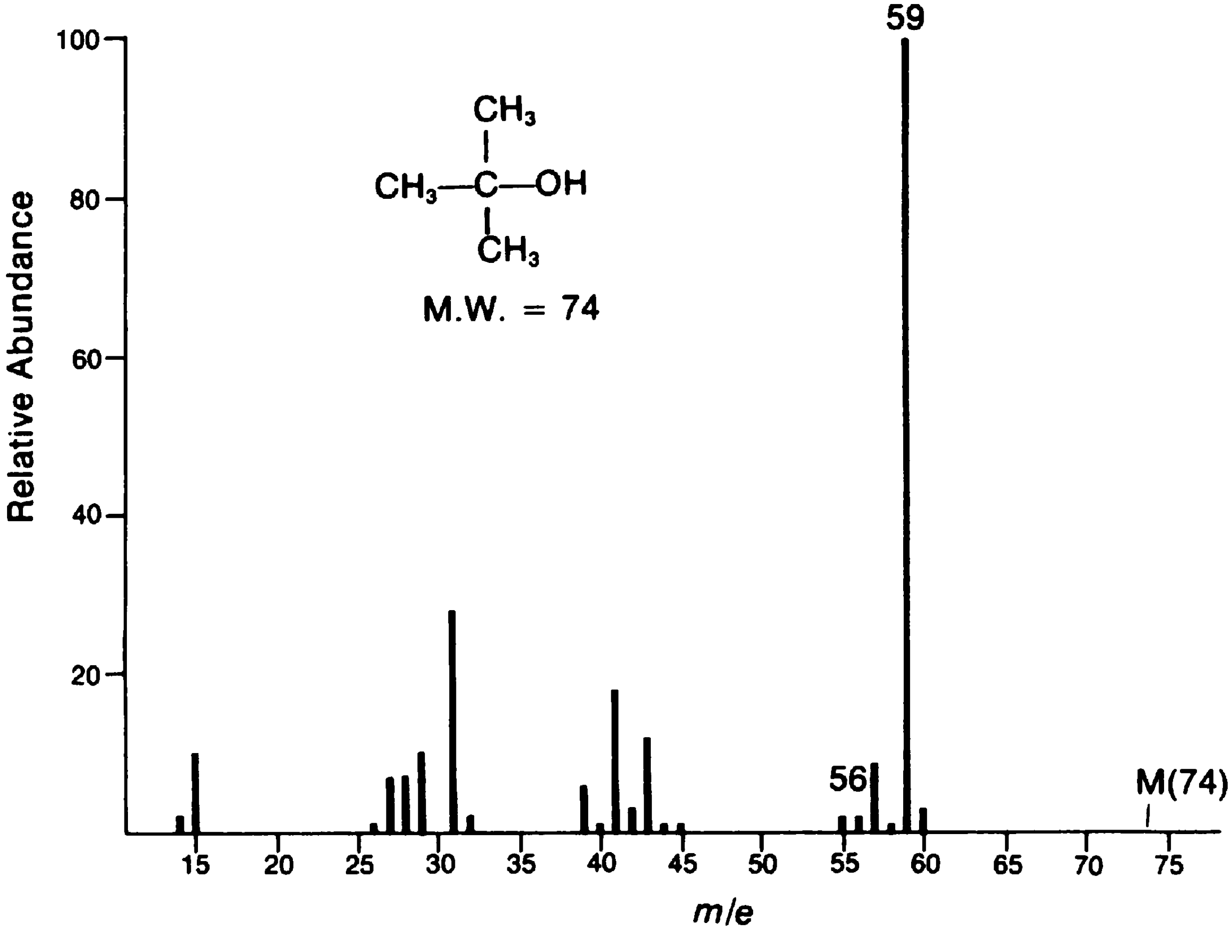
56

2-butanol

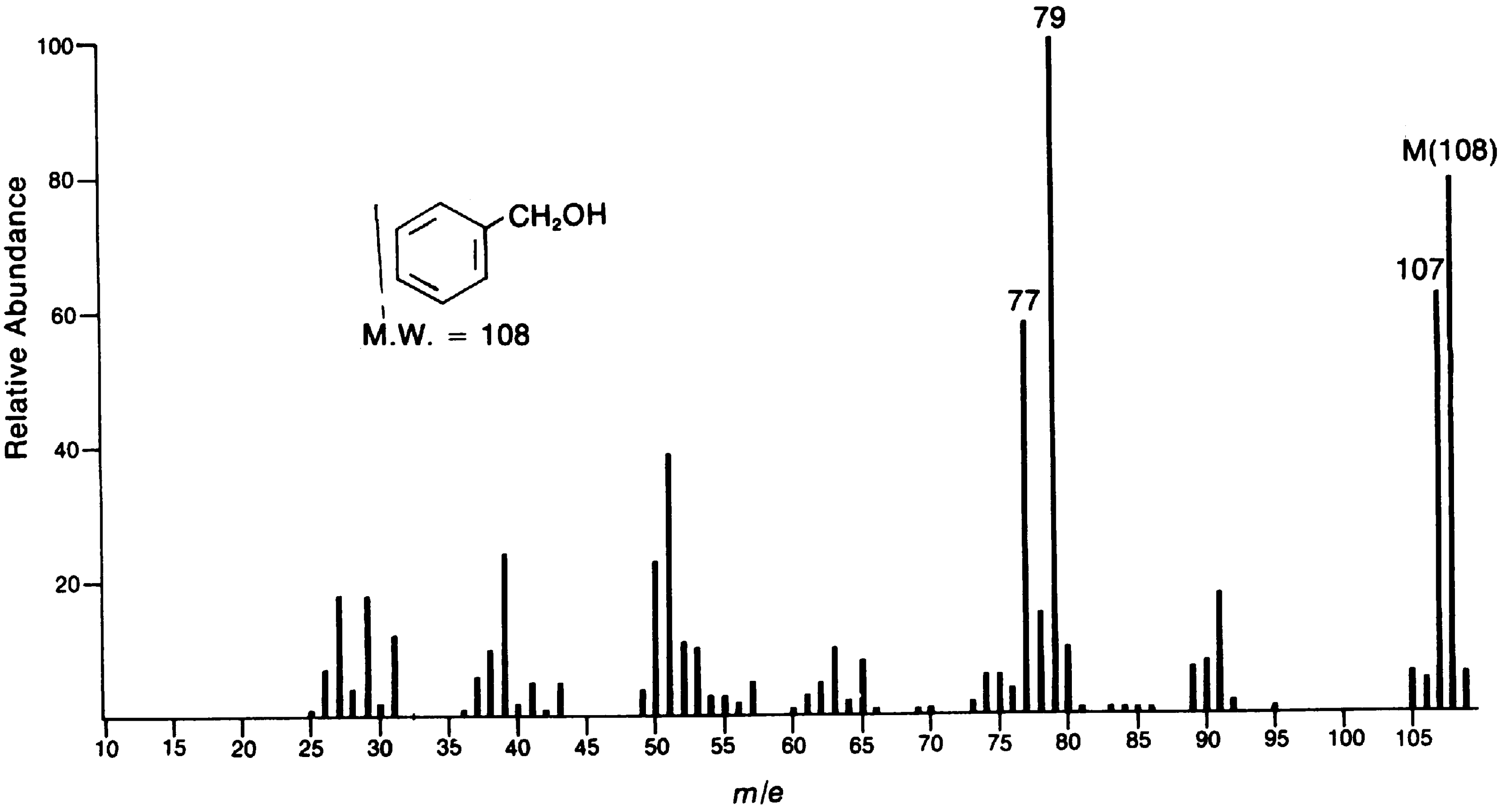

45
100
80
60
40
20
Relative Abundance
CH3—CH—CH2CH3
OH
M.W. = 74
56
M(74)
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
m/e

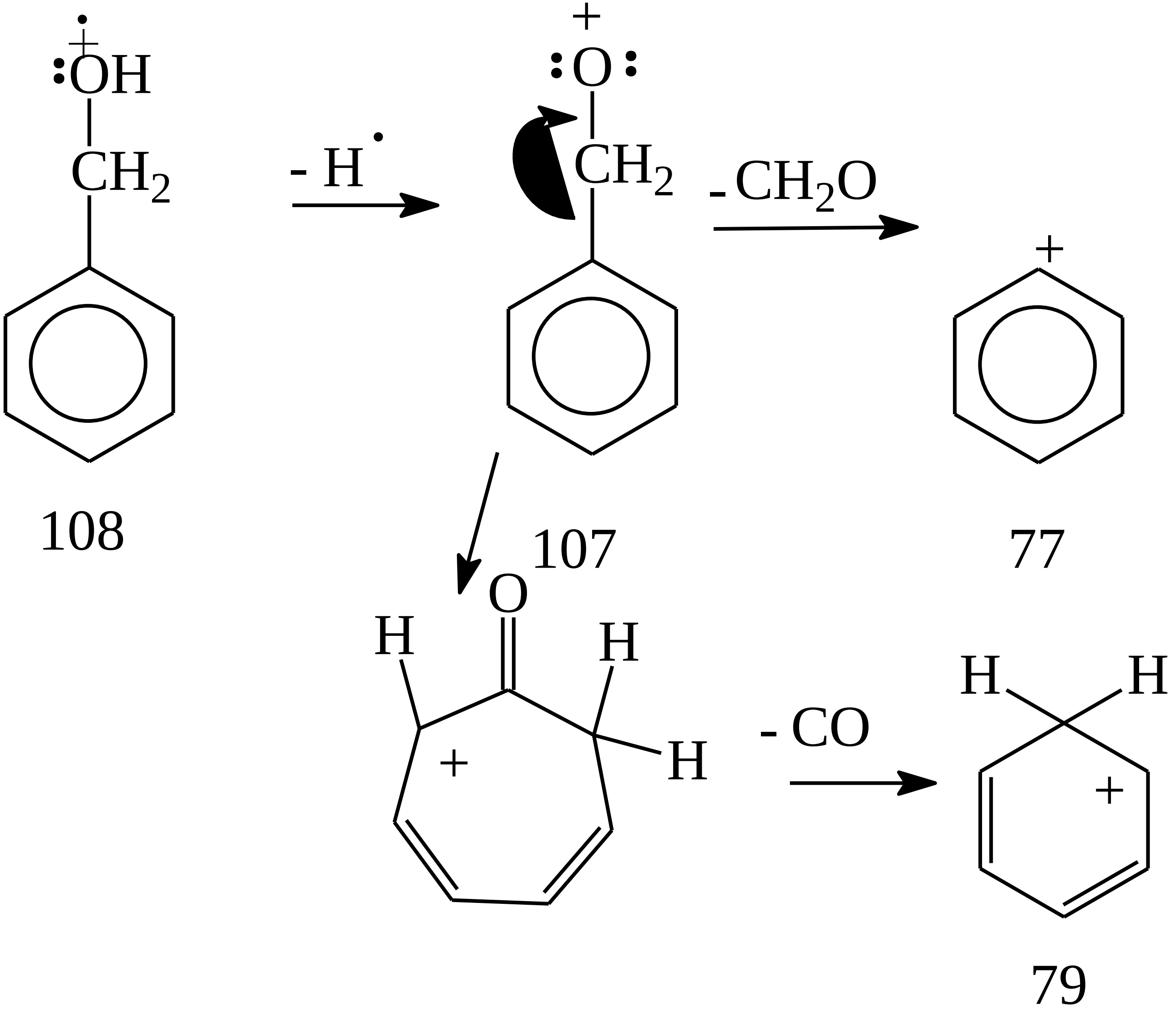

CH₃–CH₂–CH(CH₃)–OH⁺•
74
- CH₃CH₂•
α-cleavage
CH(CH₃)=OH⁺
59
- CH₃•
α-cleavage
CH₃–CH₂–CH=OH⁺
45
- H₂O
C₄H₉⁺
56

t-butanol


59
100
80
60
40
20
Relative Abundance
CH3
CH3—C—OH
CH3
M.W. = 74
56
M(74)
15
20
25
30
35
40
45
50
55
60
65
70
75
m/e

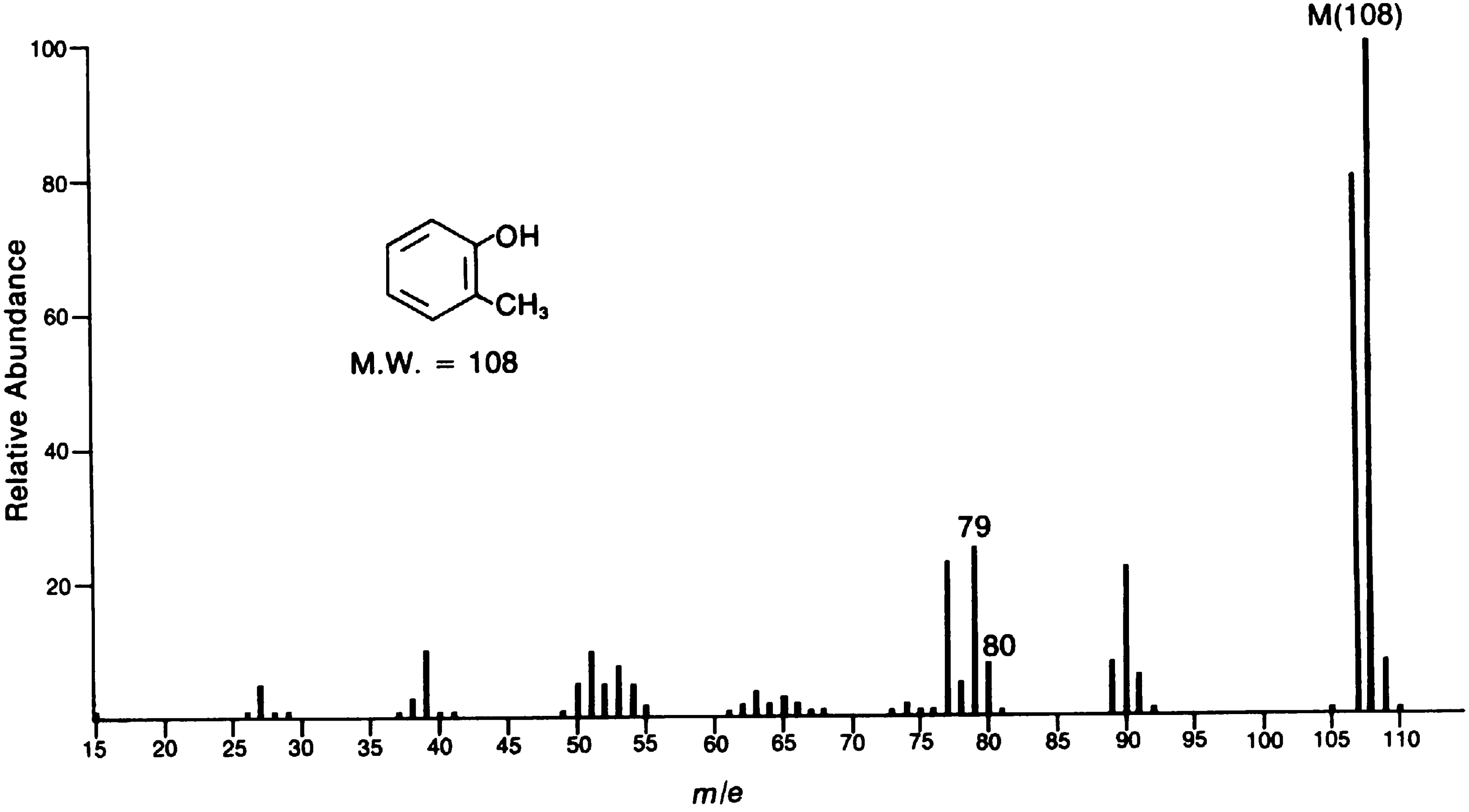
benzyl alcohol





OH
CH2
- H
O
CH2
- CH2O
108
107
77
O
H
H
H
- CO
H
H
79

o-cresol


M(108)
100
80
60
40
20
Relative Abundance
OH
CH3
M.W. = 108
79
80
15
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
110
m/e

Carbonyl Compounds

Dominant fragmentation pathways:

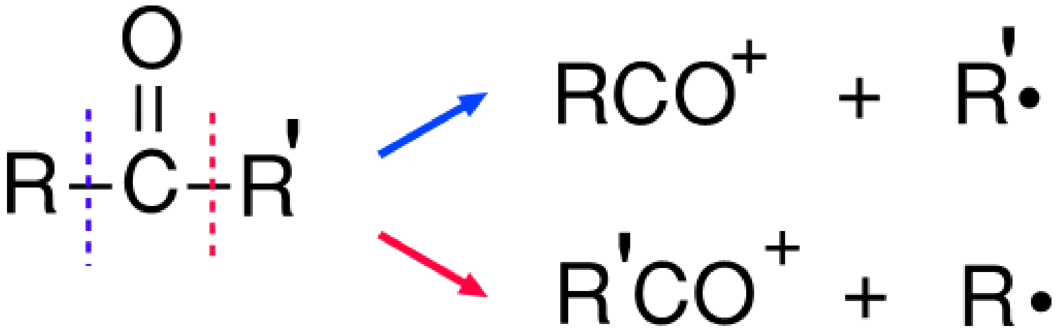
- α-cleavage
- β-cleavage
- McLafferty rearrangement

FRAGMENTATION PATTERNS

ALDEHYDES AND KETONES

Cleavage of bonds next to the carbonyl group (C=O) is a characteristic fragmentation of aldehydes and ketones. A common fragment is carbon monoxide (CO) but as it is a molecule and thus uncharged it will not produce a peak of its own. However, it will produce an m/z drop of 28 somewhere in the spectrum.

The position of the carbonyl group influences the fragmentation pattern because the molecular ion fragments either side of the carbonyl group

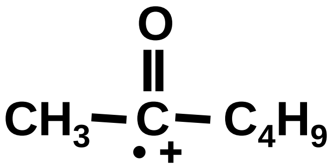


the more stable the acylium ion RCO^+, the more abundant it will be and the more abundant the species the taller its peak in the mass spectrum

FRAGMENTATION PATTERNS

Aldehydes and ketones

The position of the carbonyl group influences the fragmentation pattern because the molecular ion fragments either side of the carbonyl group.



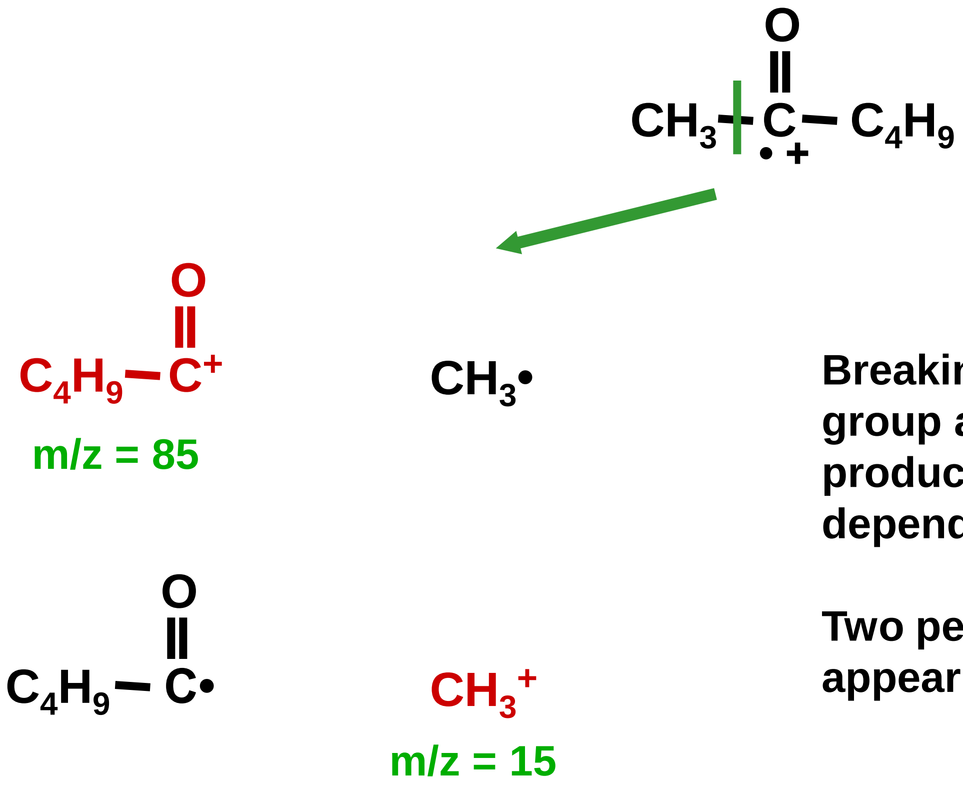
$$\mathrm{CH_3}-\underset{\bullet\ +}{\overset{\overset{\displaystyle \mathrm{O}}{\|}}{\mathrm{C}}}-\mathrm{C_4H_9}$$

MOLECULAR ION
has $m/z = 100$

FRAGMENTATION PATTERNS

Aldehydes and ketones

The position of the carbonyl group influences the fragmentation pattern because the molecular ion fragments either side of the carbonyl group.



$$CH_3-\overset{\overset{O}{\|}}{\underset{\bullet\,+}{C}}-C_4H_9$$

MOLECULAR ION
has m/z = 100

$$C_4H_9-\overset{\overset{O}{\|}}{C^+}$$

m/z = 85

$$CH_3\bullet$$

$$C_4H_9-\overset{\overset{O}{\|}}{C}\bullet$$

$$CH_3^+$$

m/z = 15

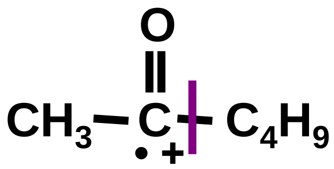
Breaking the bond between the methyl group and the carbonyl group produces two possible ions, depending on how the bond breaks.

Two peaks at m/z values 15 and 85 will appear in the mass spectrum.

FRAGMENTATION PATTERNS

Aldehydes and ketones

The position of the carbonyl group influences the fragmentation pattern because the molecular ion fragments either side of the carbonyl group.

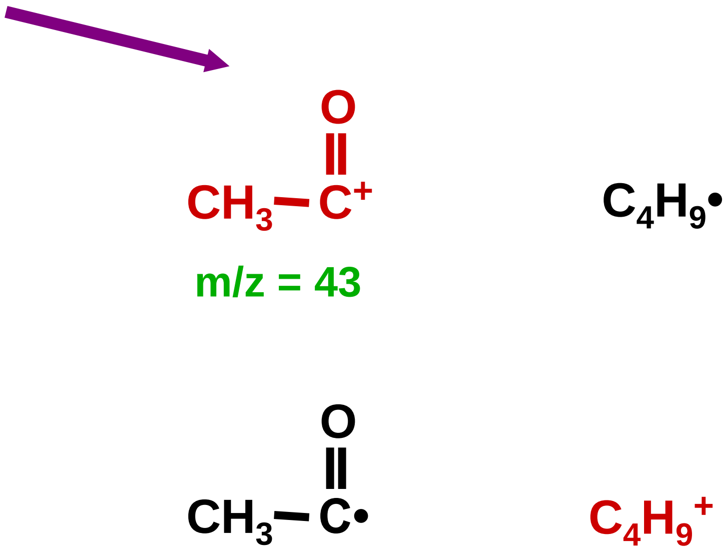


$CH_3-\overset{\overset{O}{||}}{C}-C_4H_9$ $\bullet +$

MOLECULAR ION
has m/z = 100

Breaking the bond between the butyl group and the carbonyl group produces two further ions, depending on how the bond breaks.

Two peaks at m/z values 43 and 57 will appear in the mass spectrum.



$CH_3-\overset{\overset{O}{||}}{C}^+$ $C_4H_9\bullet$

m/z = 43

$CH_3-\overset{\overset{O}{||}}{C}\bullet$ $C_4H_9^+$

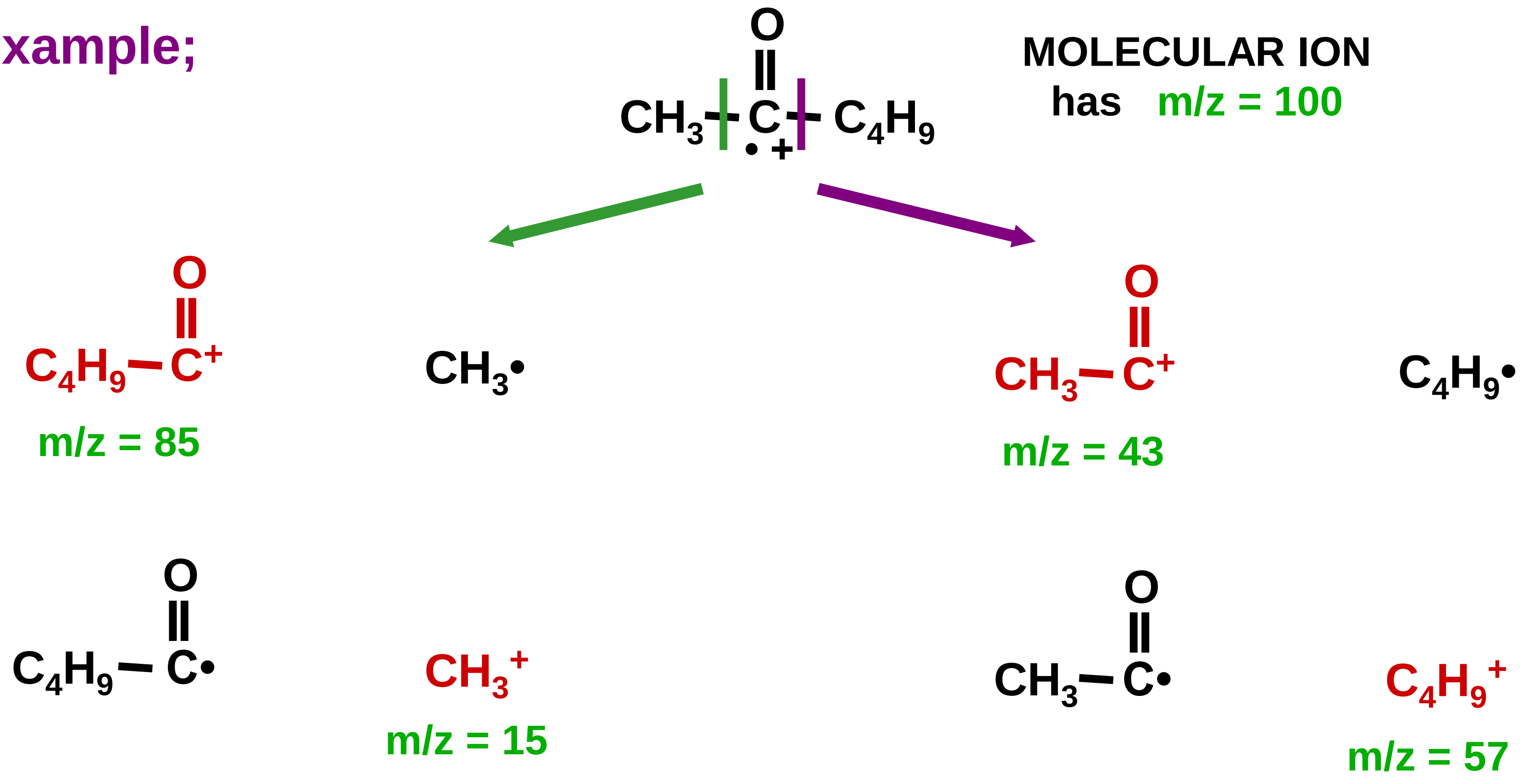
m/z = 57

FRAGMENTATION PATTERNS

Aldehydes and ketones

The position of the carbonyl group influences the fragmentation pattern because the molecular ion fragments either side of the carbonyl group.

Example;



$$CH_3-\underset{\bullet\,+}{\overset{\overset{O}{\|}}{C}}-C_4H_9$$

MOLECULAR ION
has m/z = 100

$$C_4H_9-\overset{\overset{O}{\|}}{C}{}^+ \qquad CH_3\bullet$$

m/z = 85

$$CH_3-\overset{\overset{O}{\|}}{C}{}^+ \qquad C_4H_9\bullet$$

m/z = 43

$$C_4H_9-\overset{\overset{O}{\|}}{C}\bullet \qquad CH_3^+$$

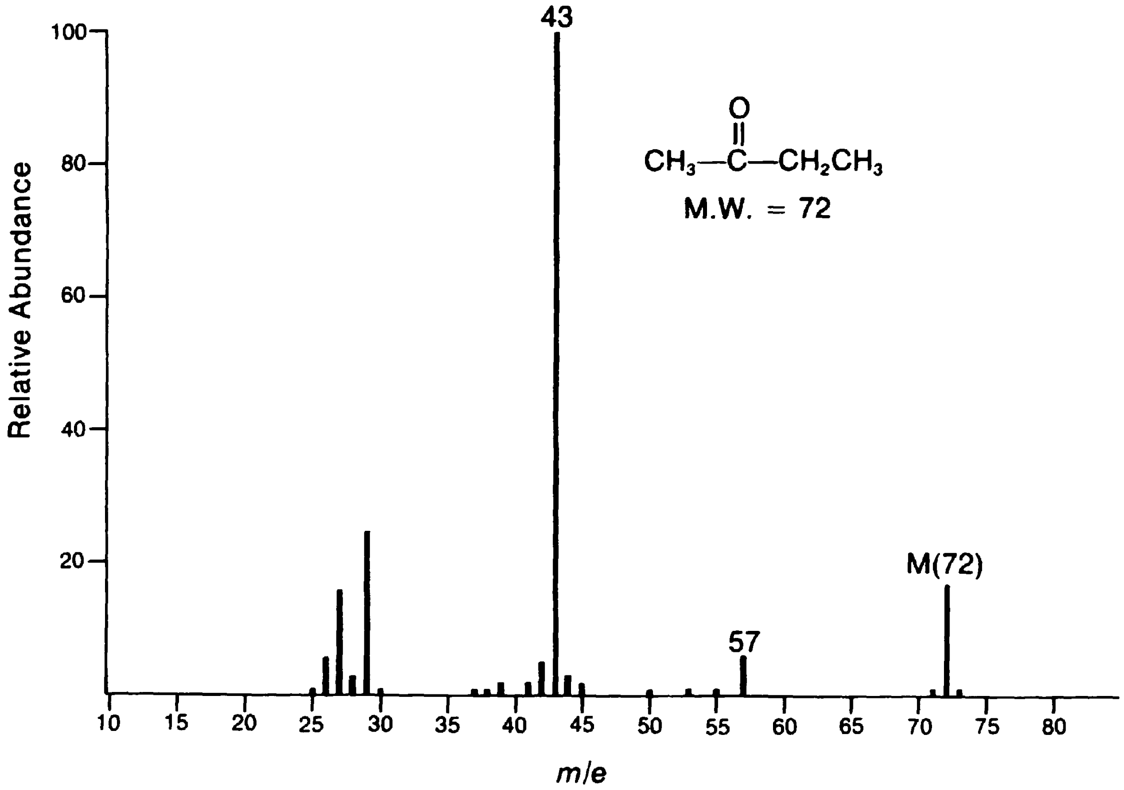
m/z = 15

$$CH_3-\overset{\overset{O}{\|}}{C}\bullet \qquad C_4H_9^+$$

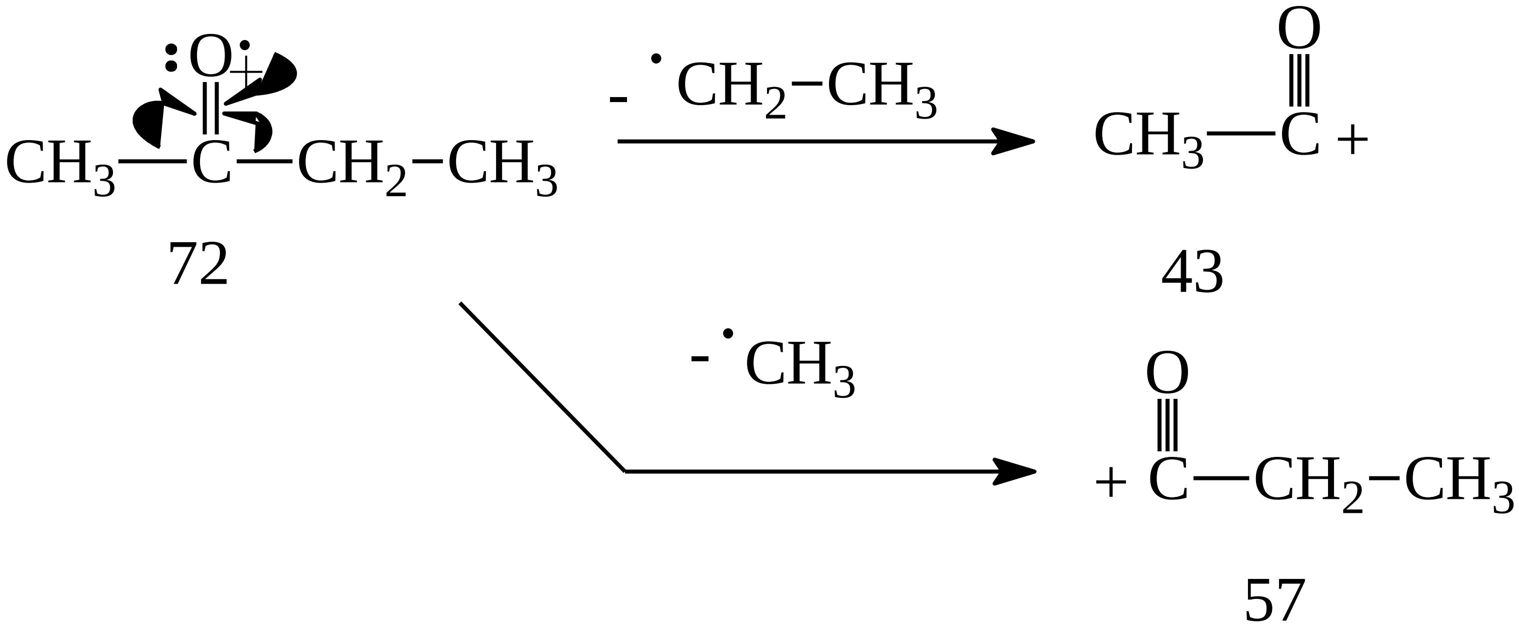
m/z = 57

A further peak occurs at m/z = 72 (100-28) due to loss of CO

2-butanone

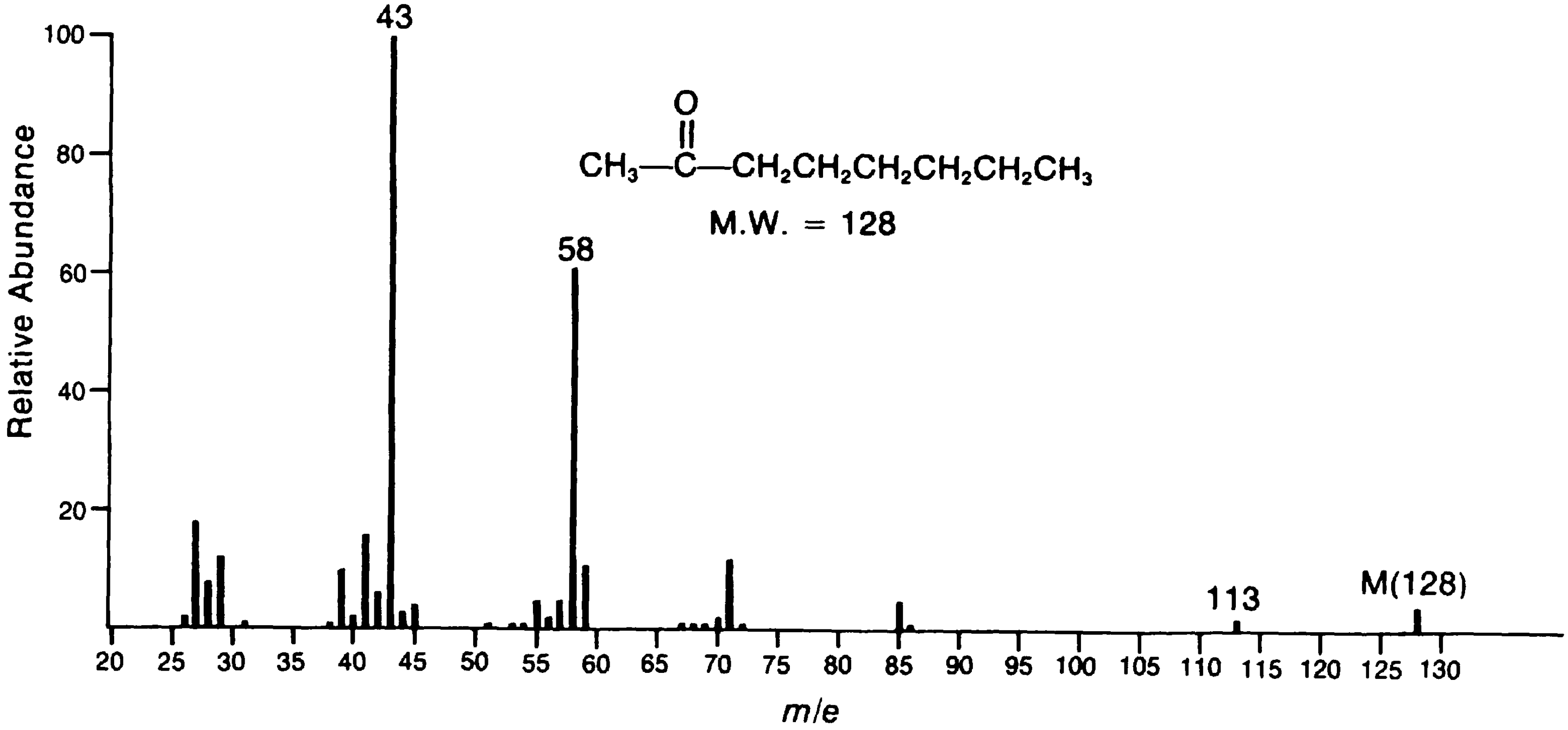

43
100
80
60
40
20
Relative Abundance
CH₃—C(=O)—CH₂CH₃
M.W. = 72
M(72)
57
10
15
20
25
30
35
40
45
50
55
60
65
70
75
80
m/e

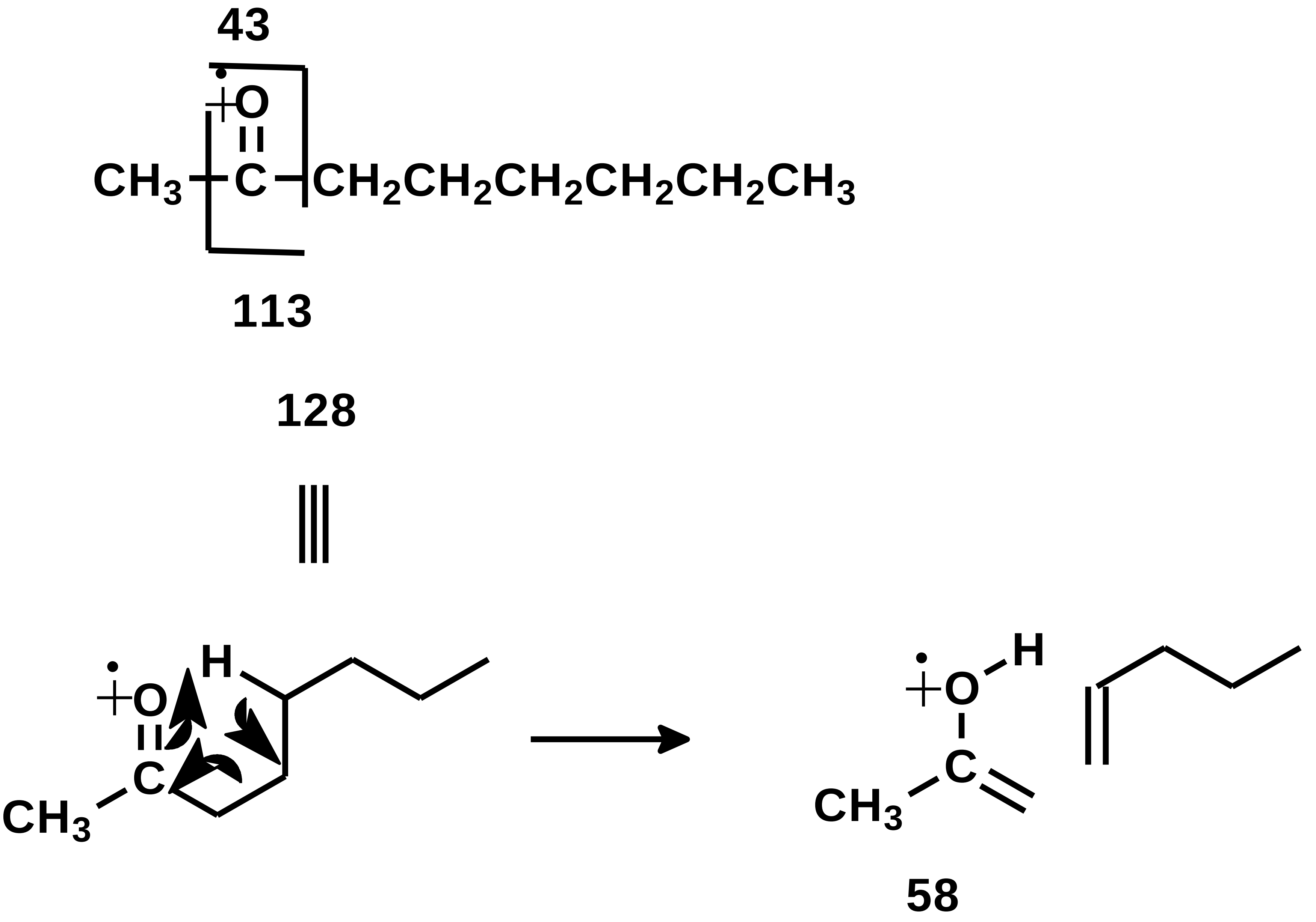
α-cleavage



favor loss of larger radical

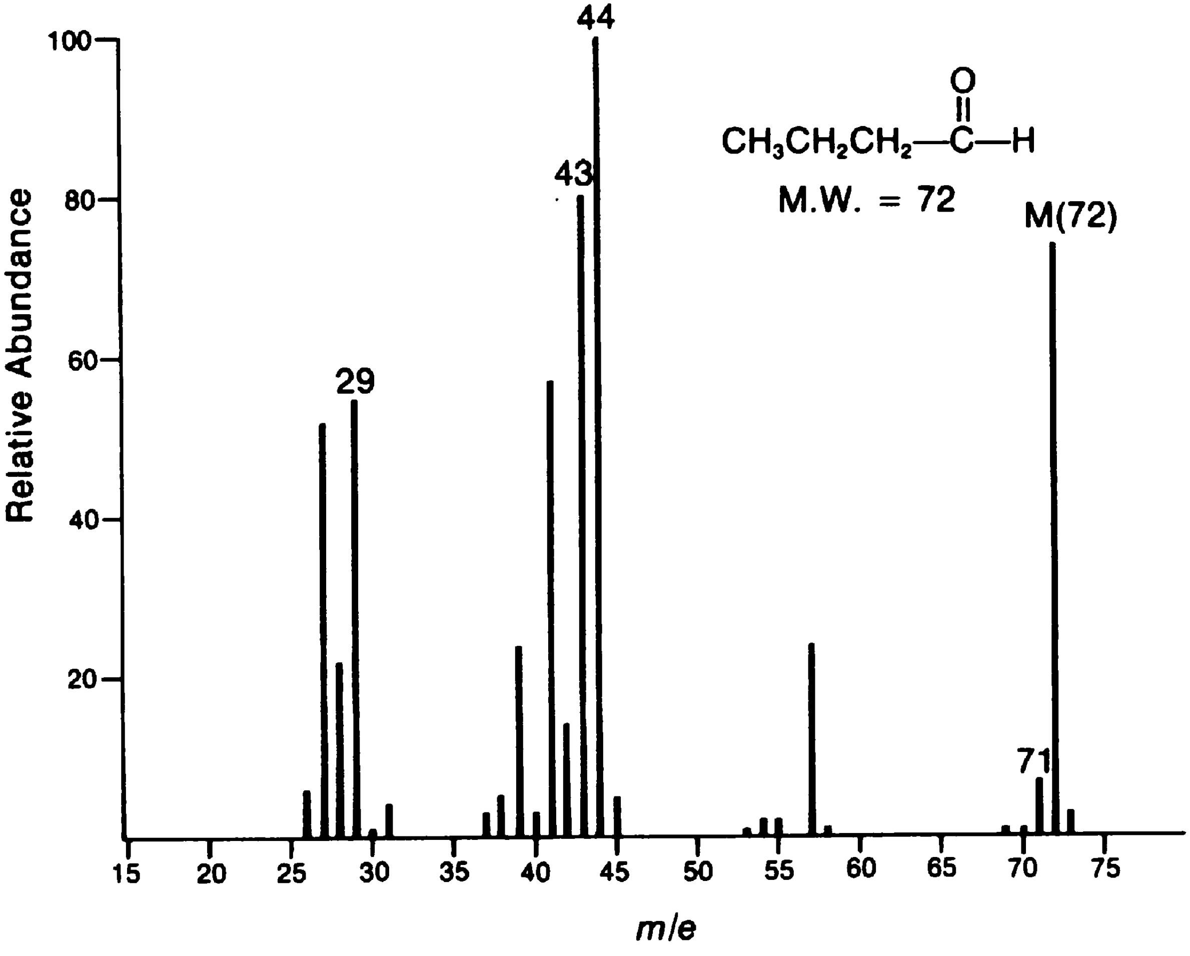
2-octanone


43
58
113
M(128)
O
CH3—C—CH2CH2CH2CH2CH2CH3
M.W. = 128
Relative Abundance
100
80
60
40
20
20
25
30
35
40
45
50
55
60
65
70
75
80
85
90
95
100
105
110
115
120
125
130
m/e

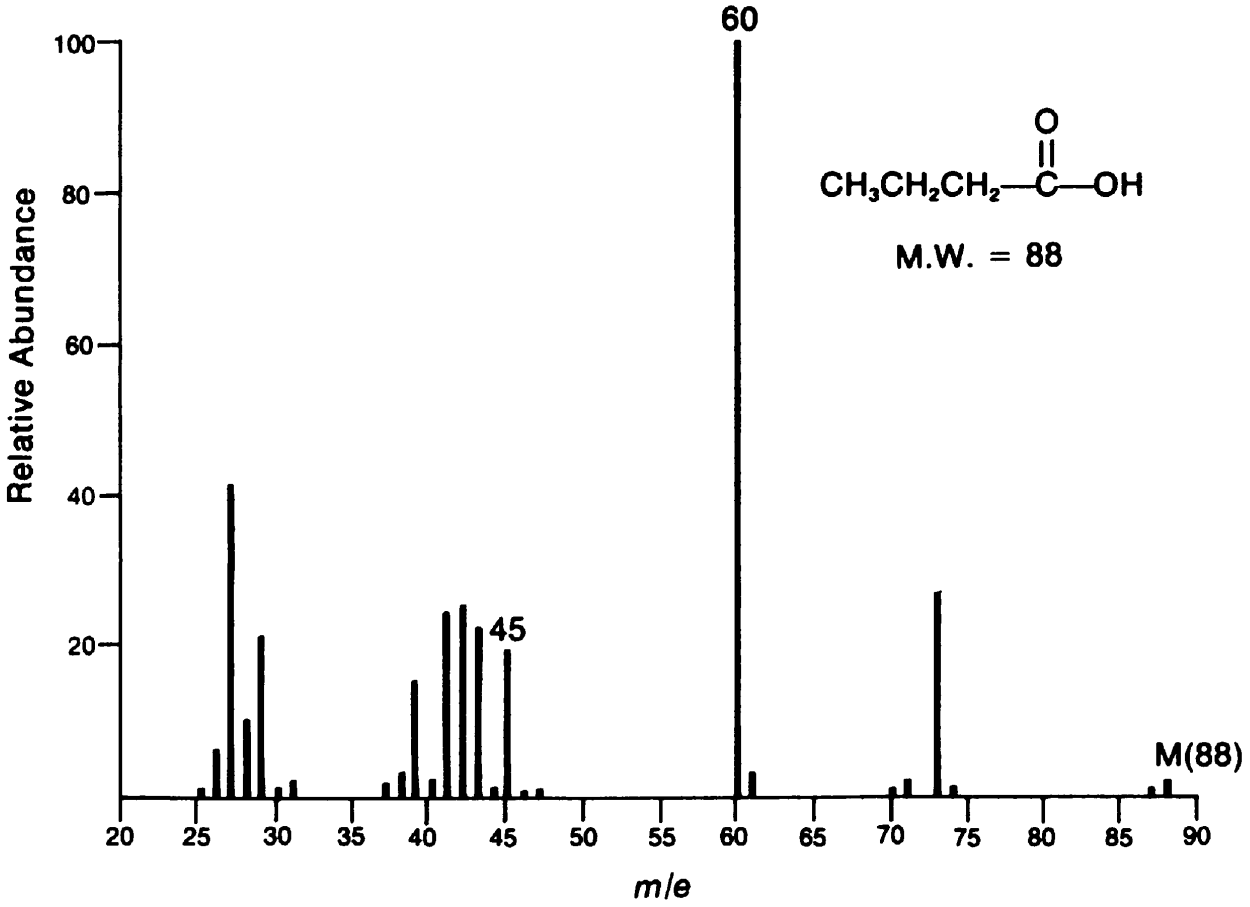


McLafferty Rearrangement

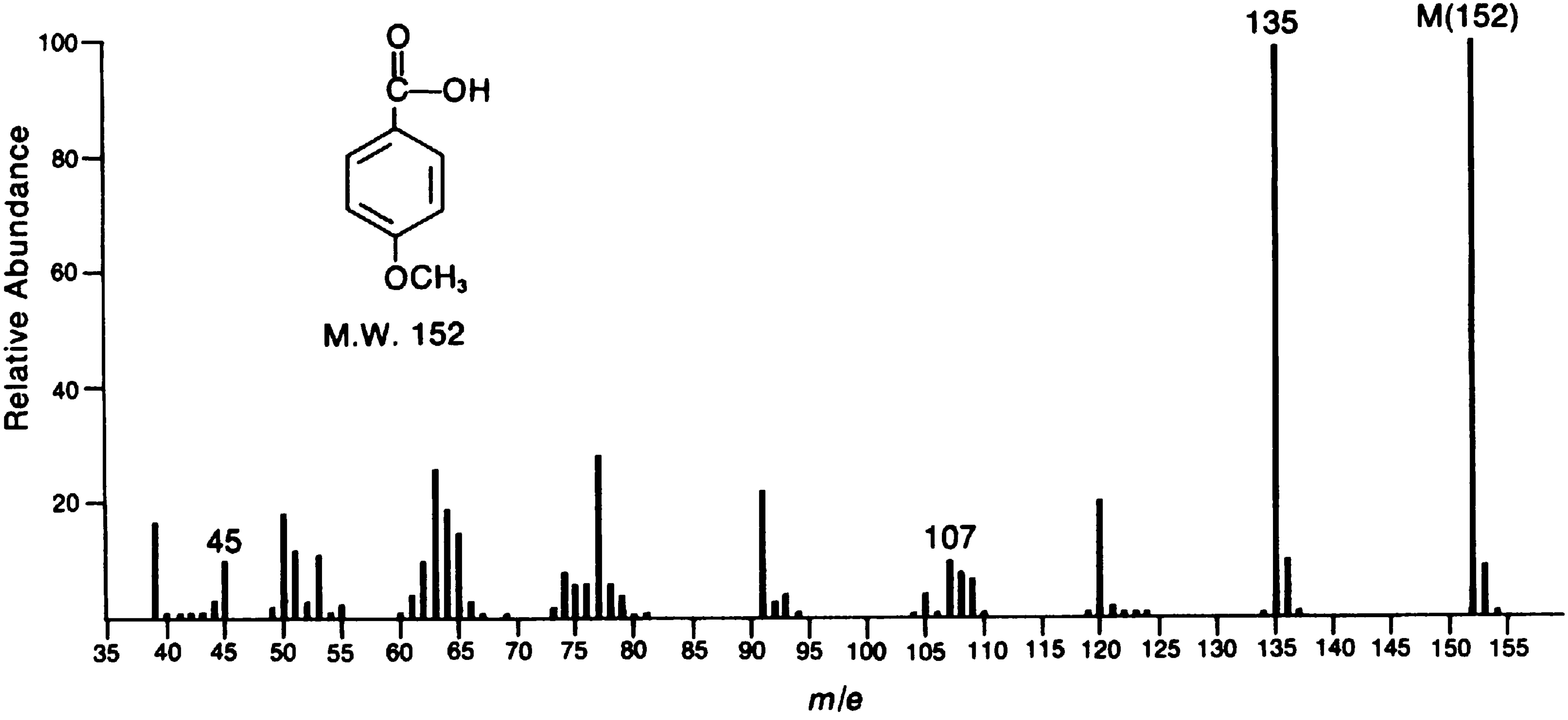
butyraldehyde



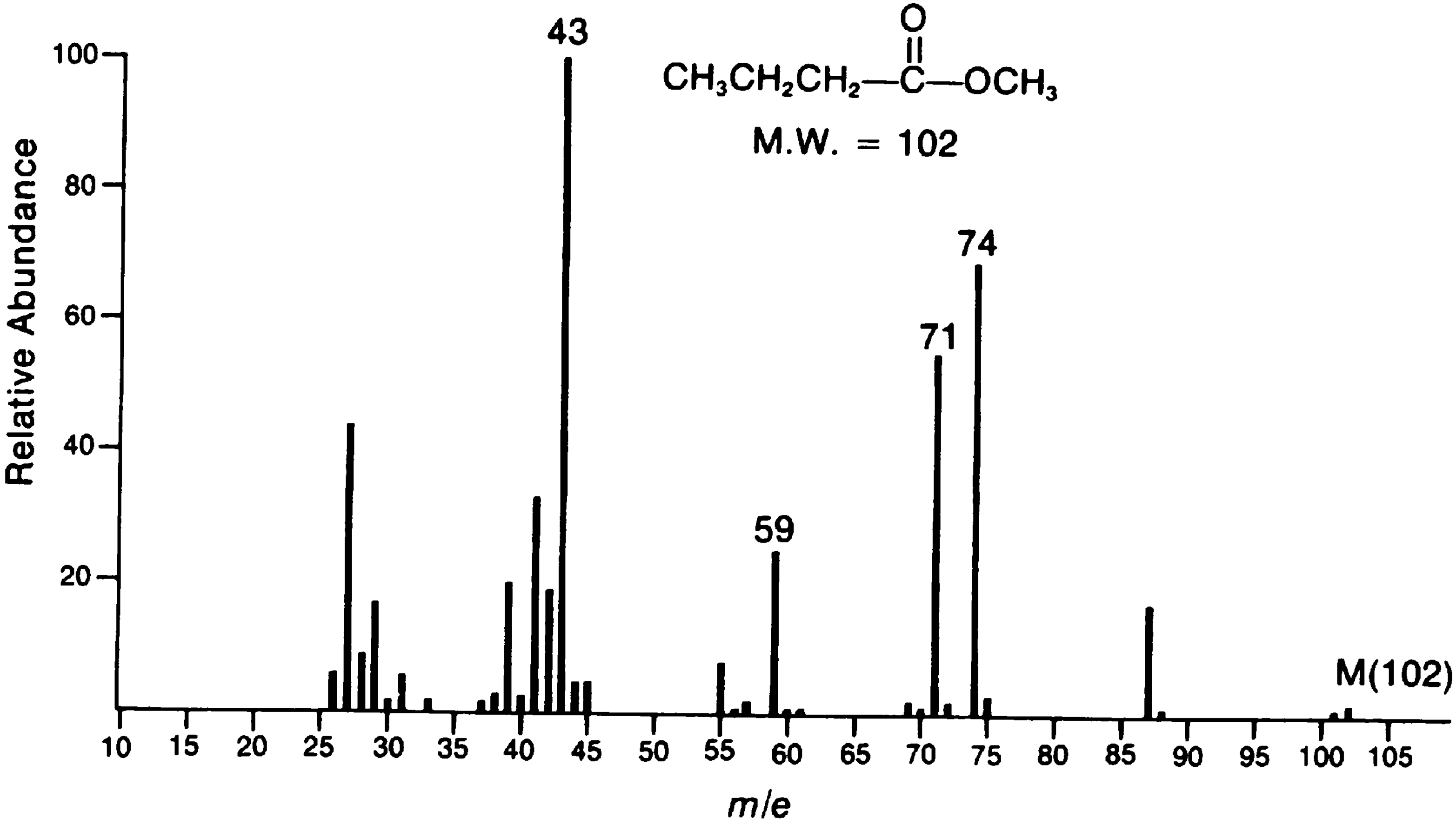
butyric acid

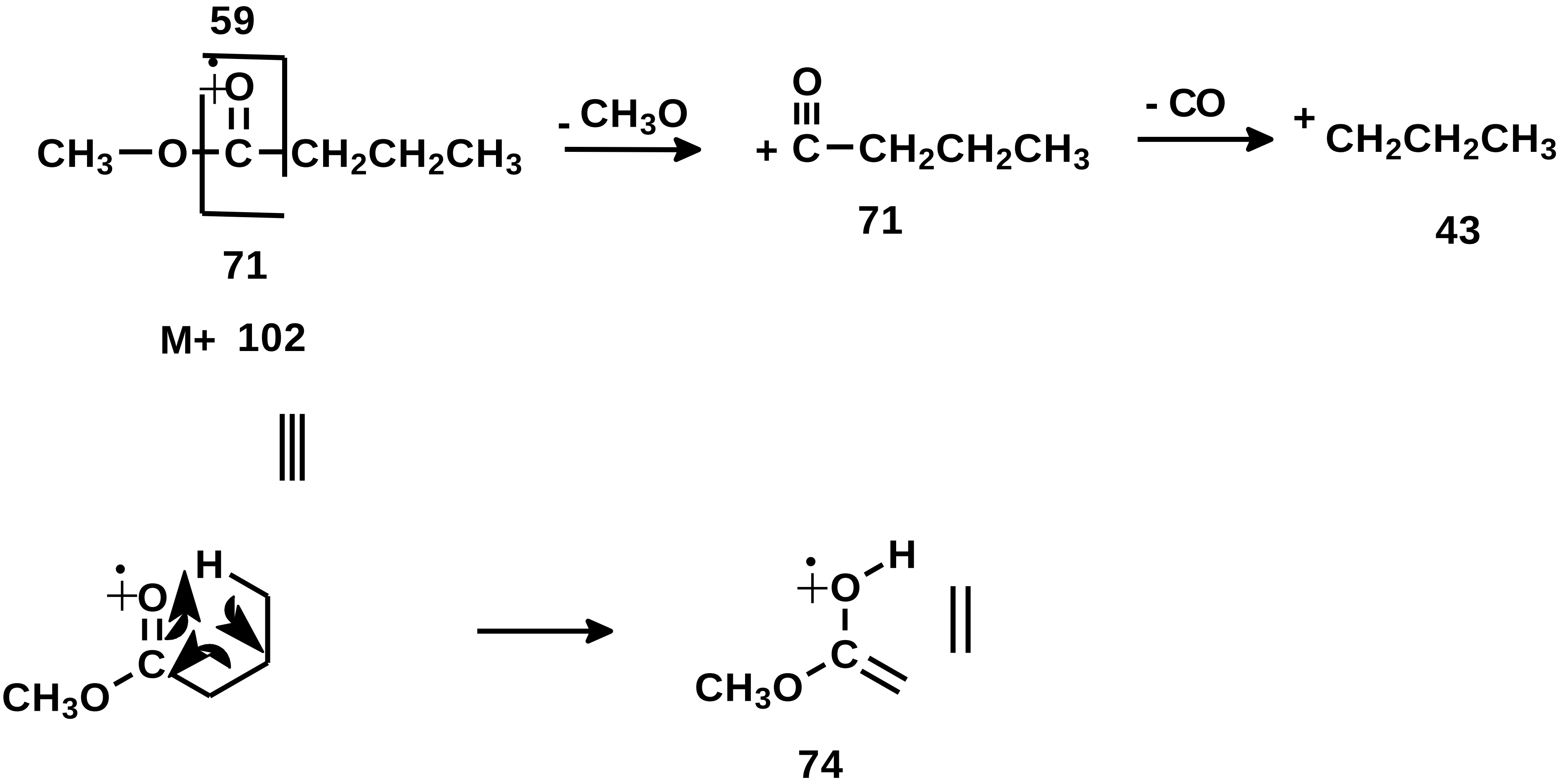


p-anisic acid



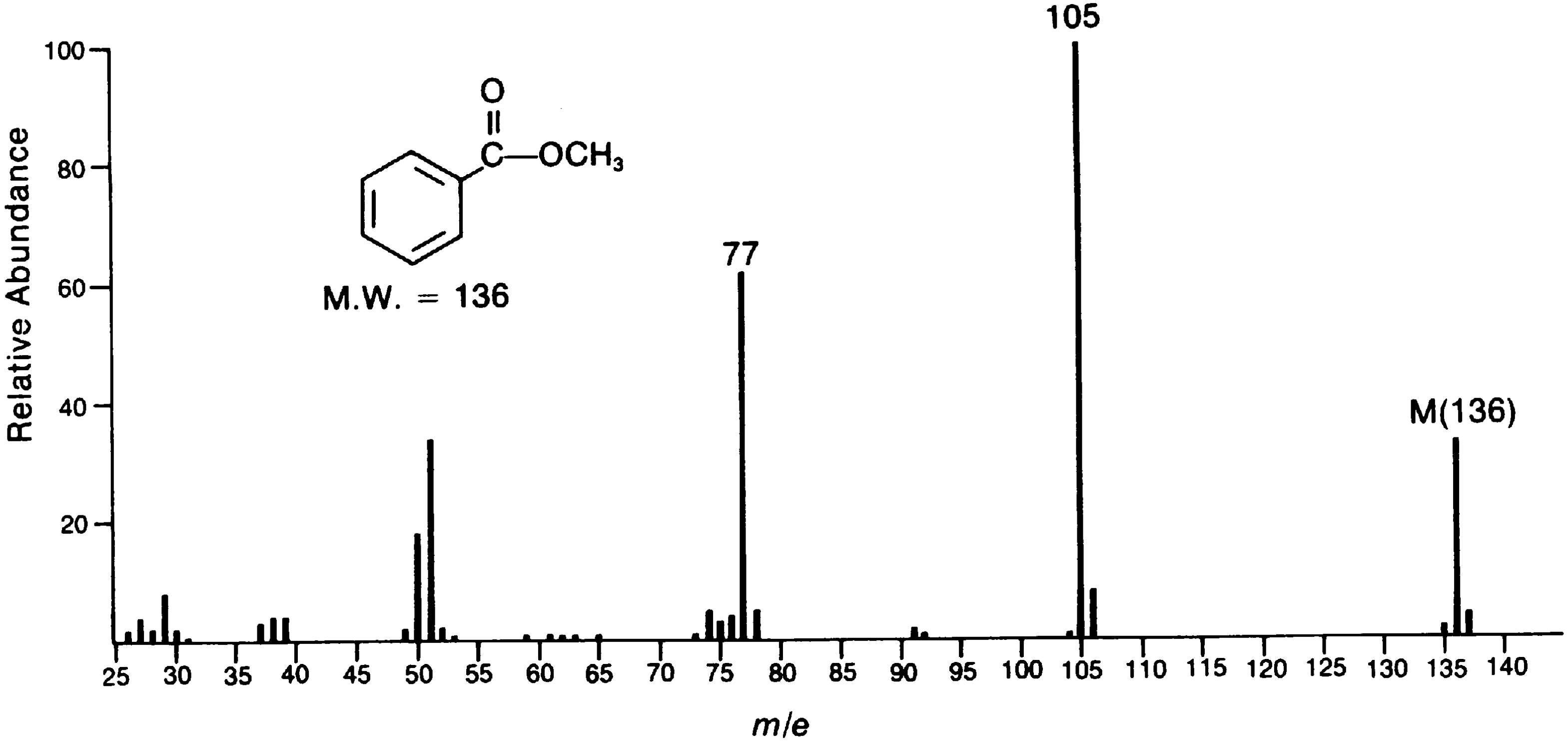
methyl butyrate





McLafferty Rearrangement

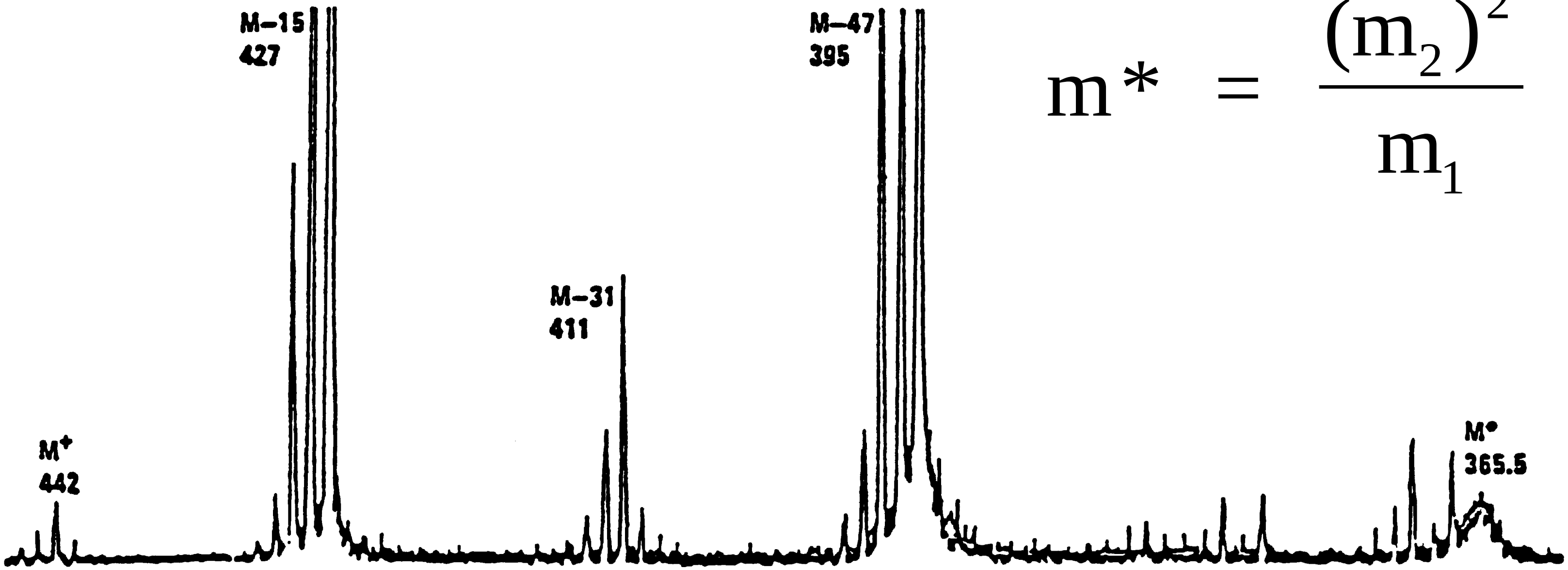
methyl benzoate



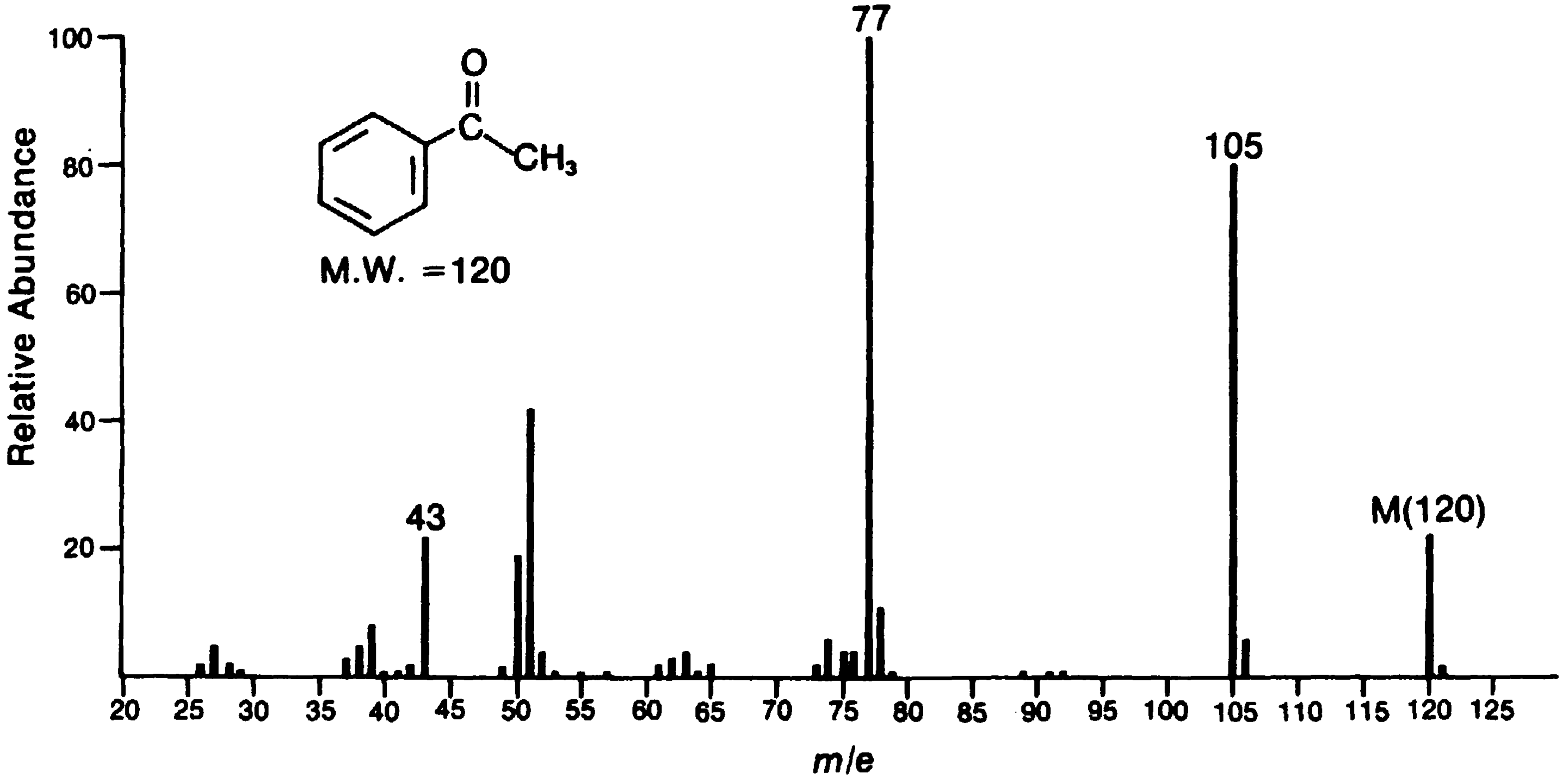
metastable

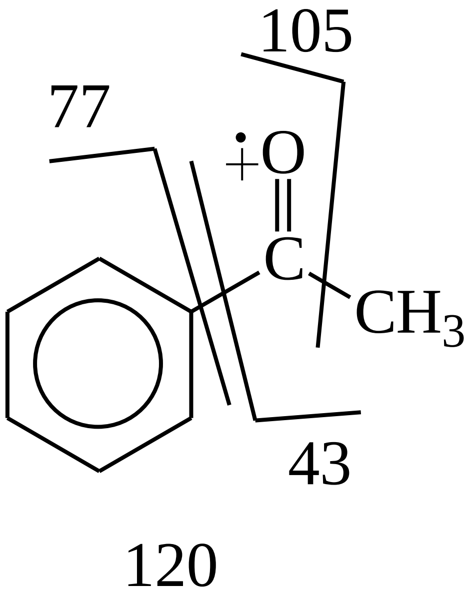
$$\mathbf{m_1^{+}} \longrightarrow \mathbf{m_2^{+}} + \textbf{neutral}$$

$$m^* = \frac{(m_2)^2}{m_1}$$



acetophenone





metastable peaks at 91.9, 56.4, 33.8

$$m^* = \frac{(m_2)^2}{m_1}$$

$$m^* = \frac{(105)^2}{120} = 91.875$$

$$m^* = \frac{(77)^2}{120} = 49.4$$

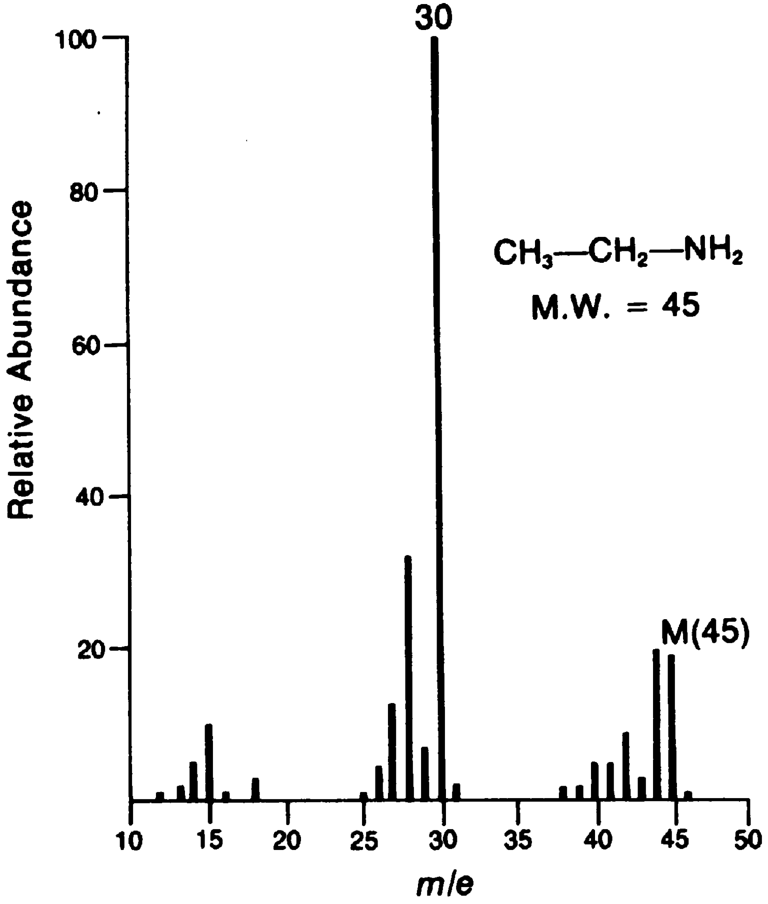
$$m^* = \frac{(77)^2}{105} = 56.47$$

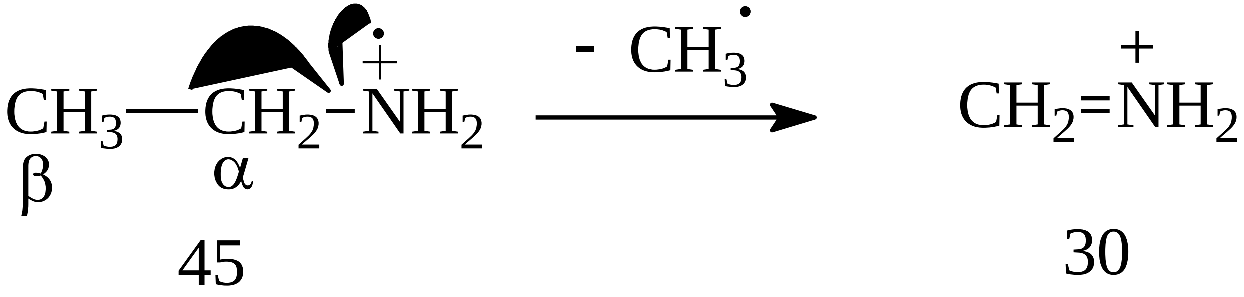
$$m^* = \frac{(51)^2}{77} = 33.8$$

timing of fragmentation

$$\boxed{120 \longrightarrow 105 \longrightarrow 77 \longrightarrow 51}$$

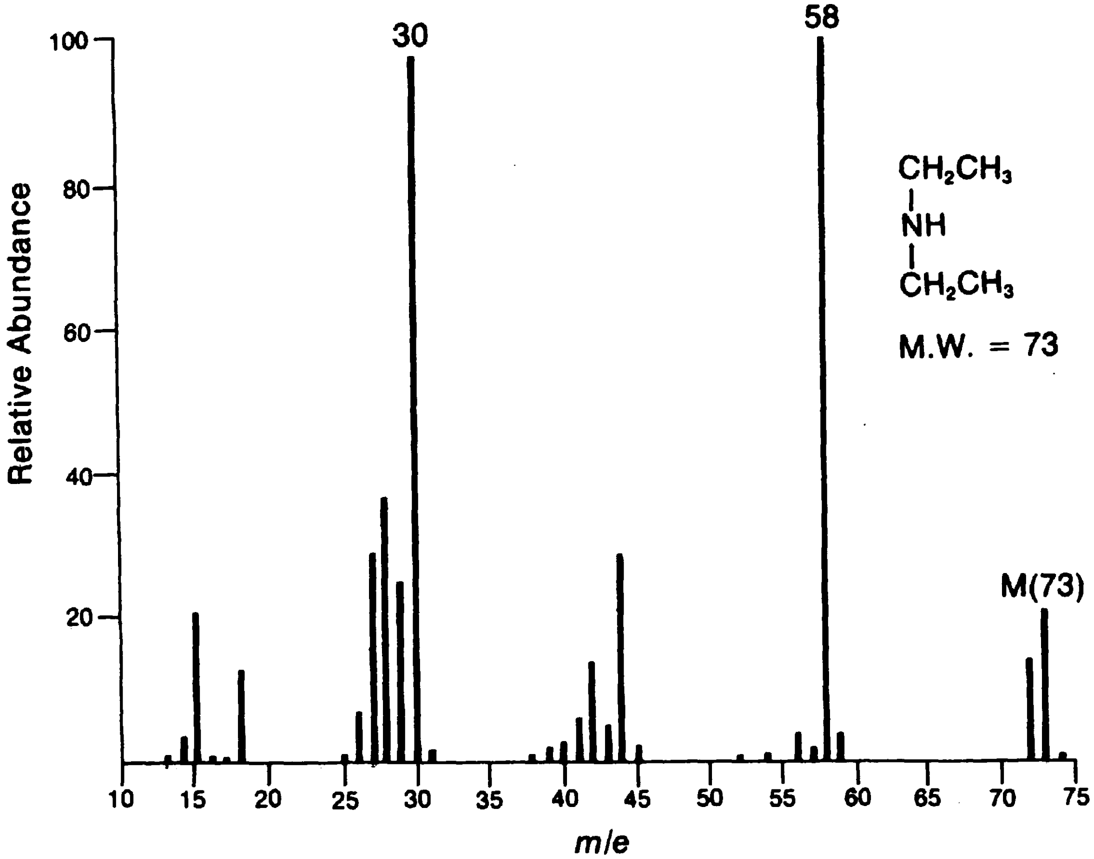
ethylamine

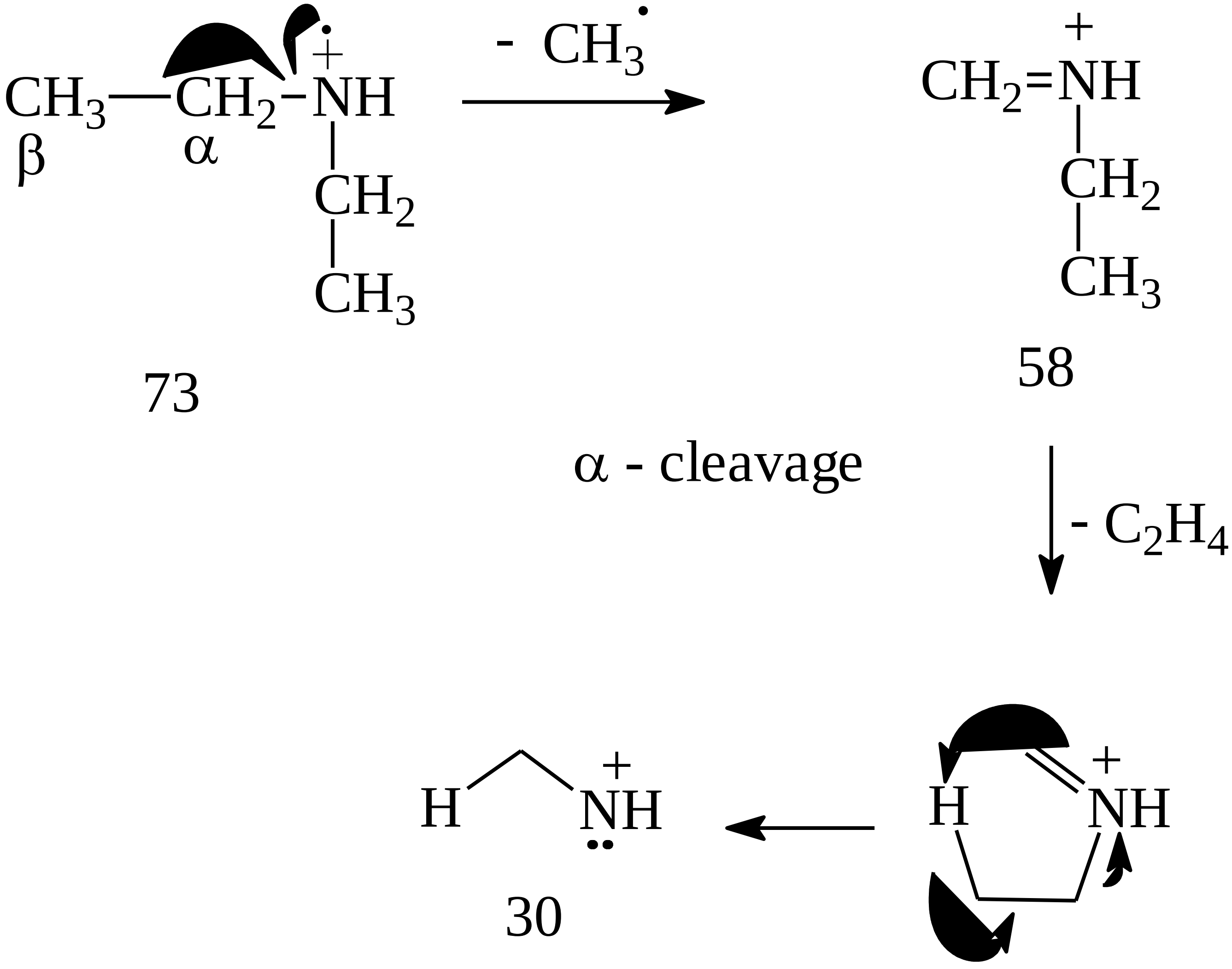

30
100
80
60
40
20
Relative Abundance
$CH_3—CH_2—NH_2$
M.W. = 45
M(45)
10
15
20
25
30
35
40
45
50
m/e



α - cleavage

diethylamine




CH3 β
CH2 α
NH
CH2
CH3
73
- CH3
α - cleavage
CH2=NH
CH2
CH3
58
- C2H4
H
NH
H
NH
30

triethylamine