Mass Spectrometry: Fragmentation

Ethers & Sulfides

Ethers

- M^+ usually stronger than corresponding alcohol; may be weak/absent
- α-cleavage of an alkyl radical
- Inductive cleavage
- Rearrangement with loss of CHR=CHR’

Aryl Ethers

- M^+ strong
- C-O cleavage β to aromatic ring with subsequent loss of CO
- Cleavage adjacent to aryl ring also possible

Sulfides

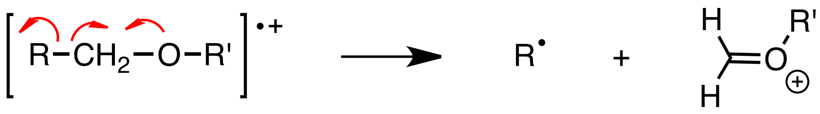
- M^+ usually stronger than corresponding ether
- cleavage pattern similar to ethers

Mass Spectrometry: Fragmentation

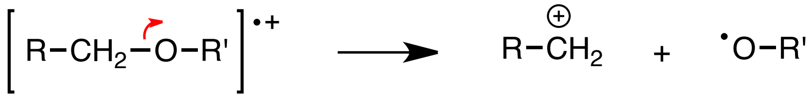
Ethers

fragmentation patterns

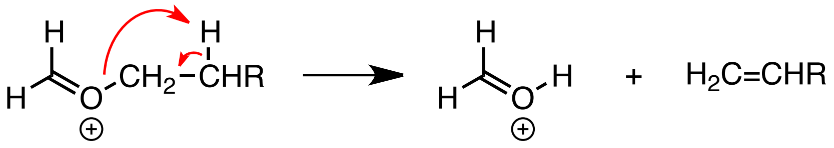
α-cleavage



inductive cleavage



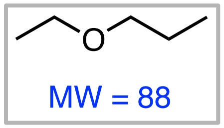
rearrangement

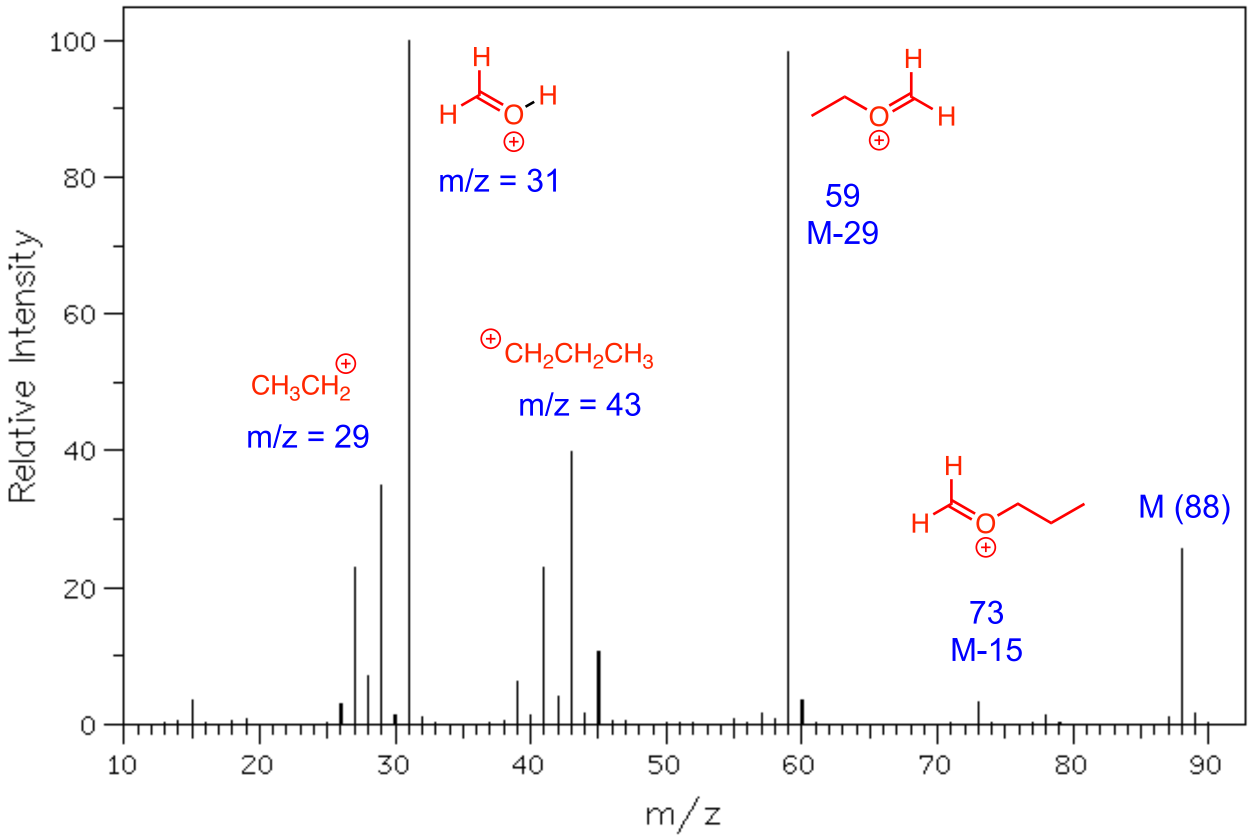


Mass Spectrometry: Fragmentation

Ethers

ethyl propyl ether

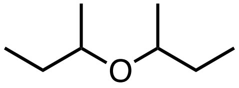




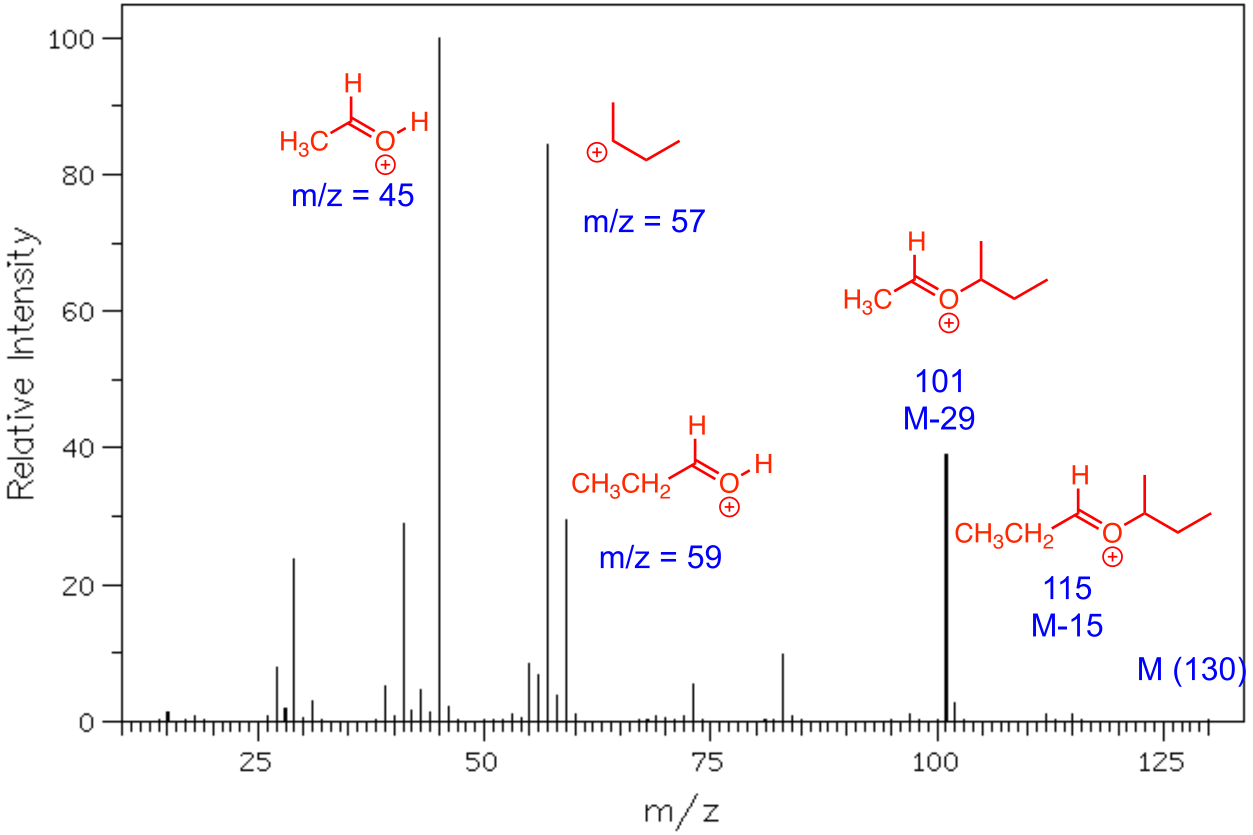
Mass Spectrometry: Fragmentation

Ethers

di-*sec*-butyl ether



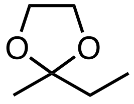
MW = 130



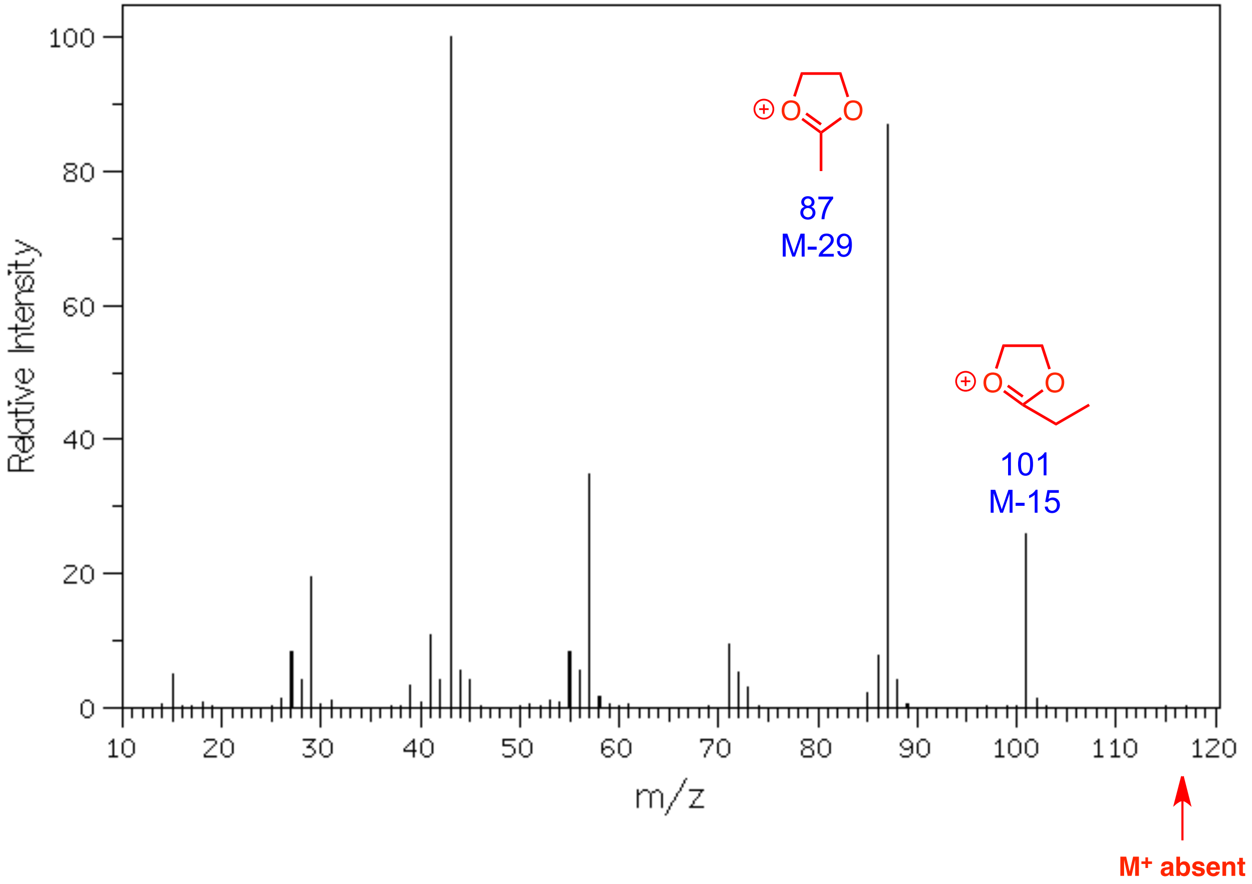
Mass Spectrometry: Fragmentation

Ethers

2-ethyl-2-methyl-1,3-dioxolane



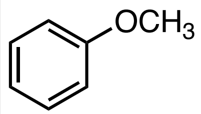
MW = 116



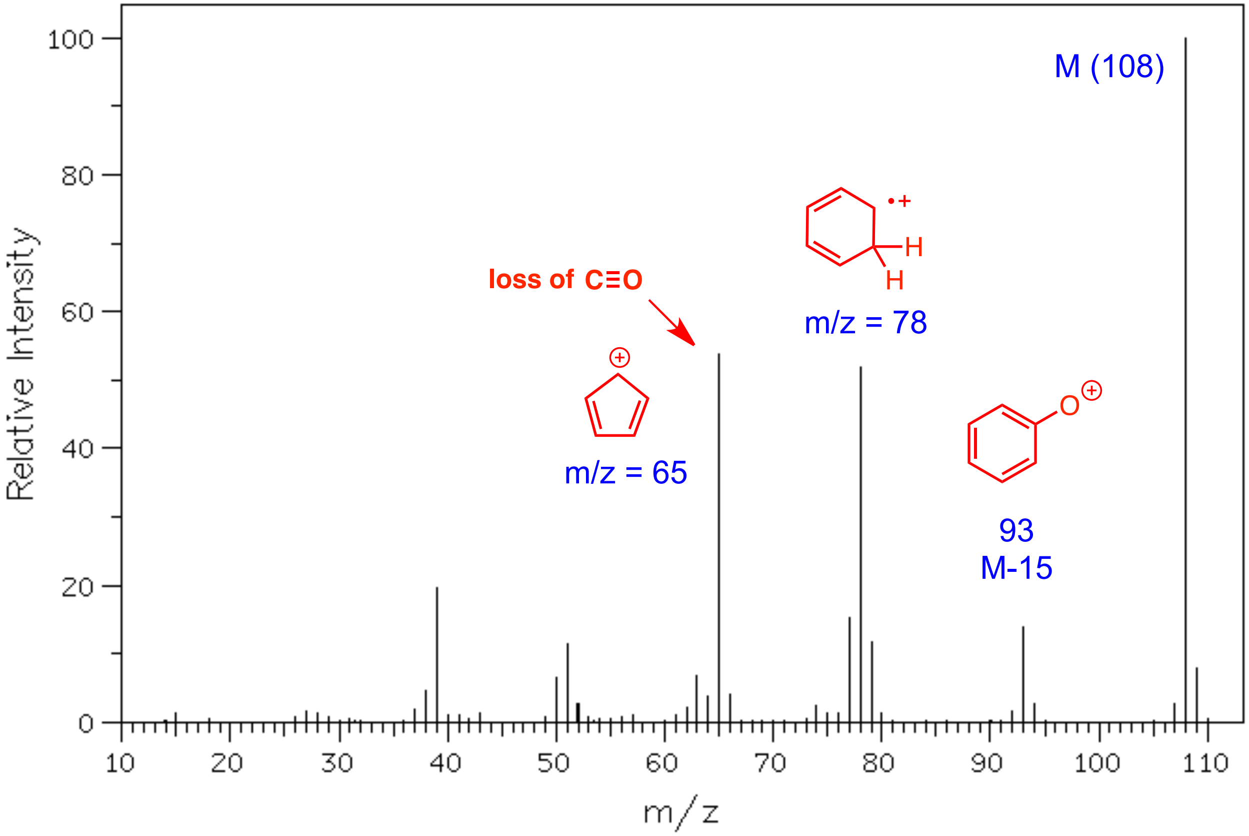
Mass Spectrometry: Fragmentation

Aryl Ethers

anisole



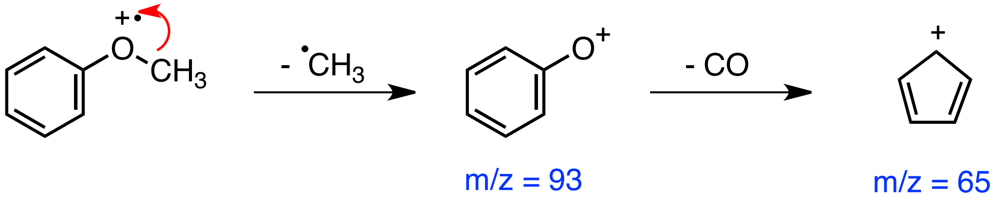
MW = 108

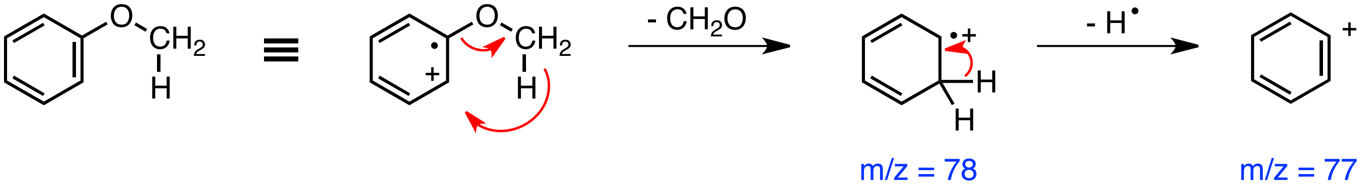


Mass Spectrometry: Fragmentation

Aryl Ethers

fragmentation of aryl ethers

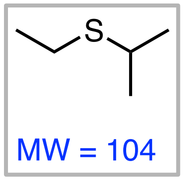


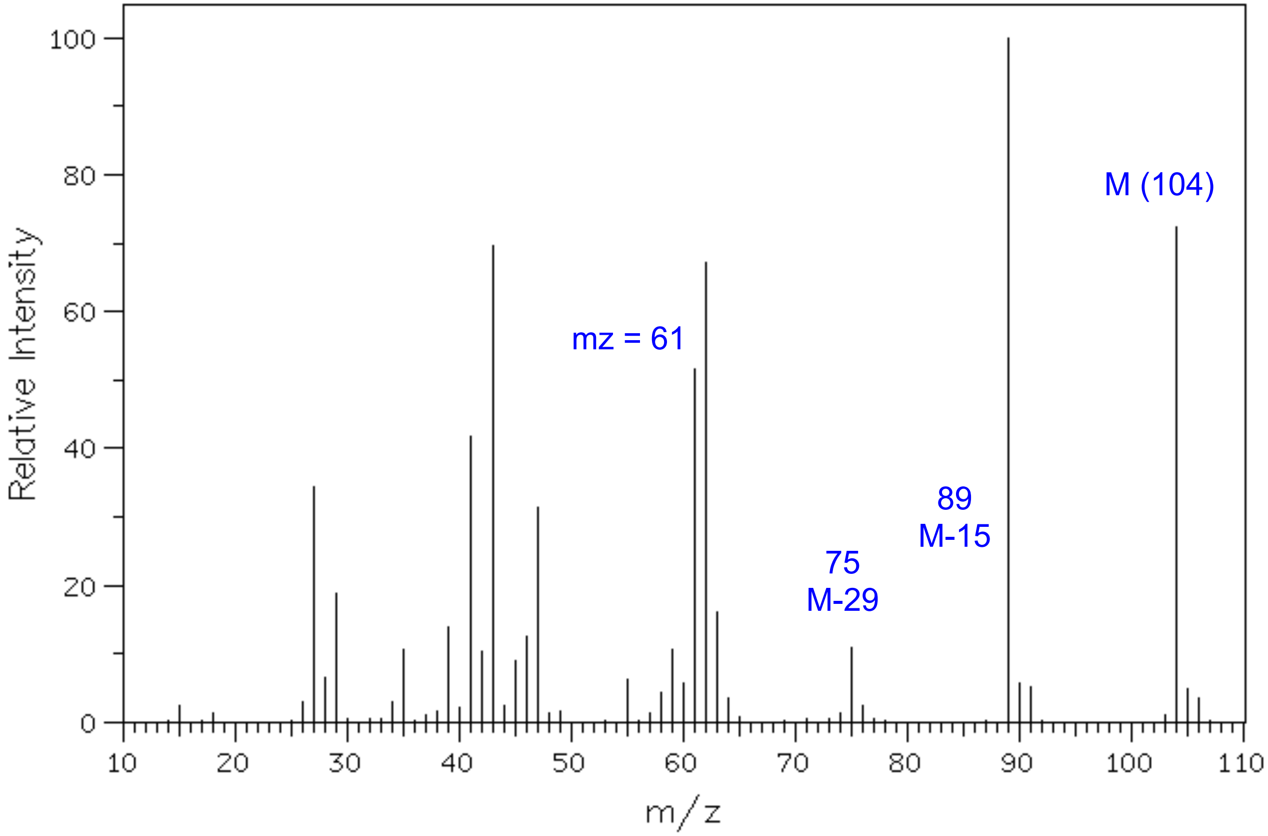


Mass Spectrometry: Fragmentation

Sulfides

ethyl isopropyl sulfide





Mass Spectrometry: Fragmentation

Amines

Aliphatic Amines

- M^+ will be an odd number for monoamine; may be weak/absent
- M-1 common
- α-cleavage of an alkyl radical is predominate fragmentation mode
  - largest group lost preferentially
- McLafferty rearrangement / loss of NH_3 (M-17) are not common

Cyclic Amines

- M^+ usually strong
- M-1 common
- fragmentation complex, varies with ring size

Aromatic Amines

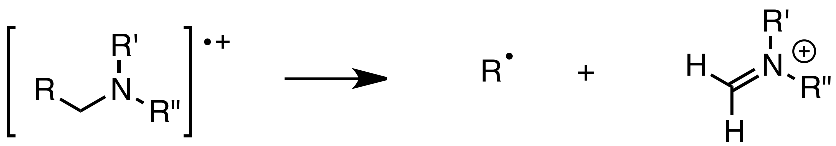
- M^+ usually strong
- M-1 common
- loss of HCN is common in anilines

Mass Spectrometry: Fragmentation

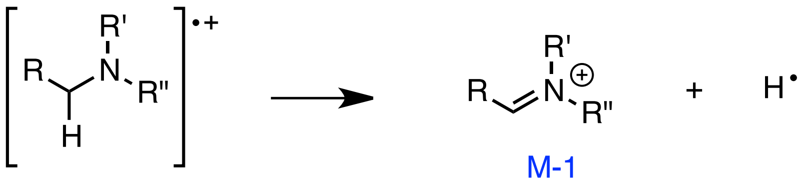
Amines

fragmentation patterns

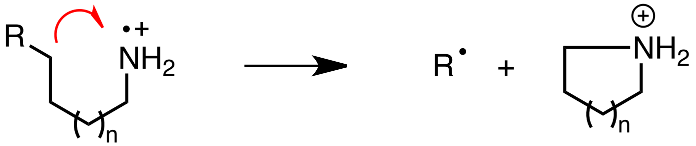
α-cleavage



loss of H radical



ring formation



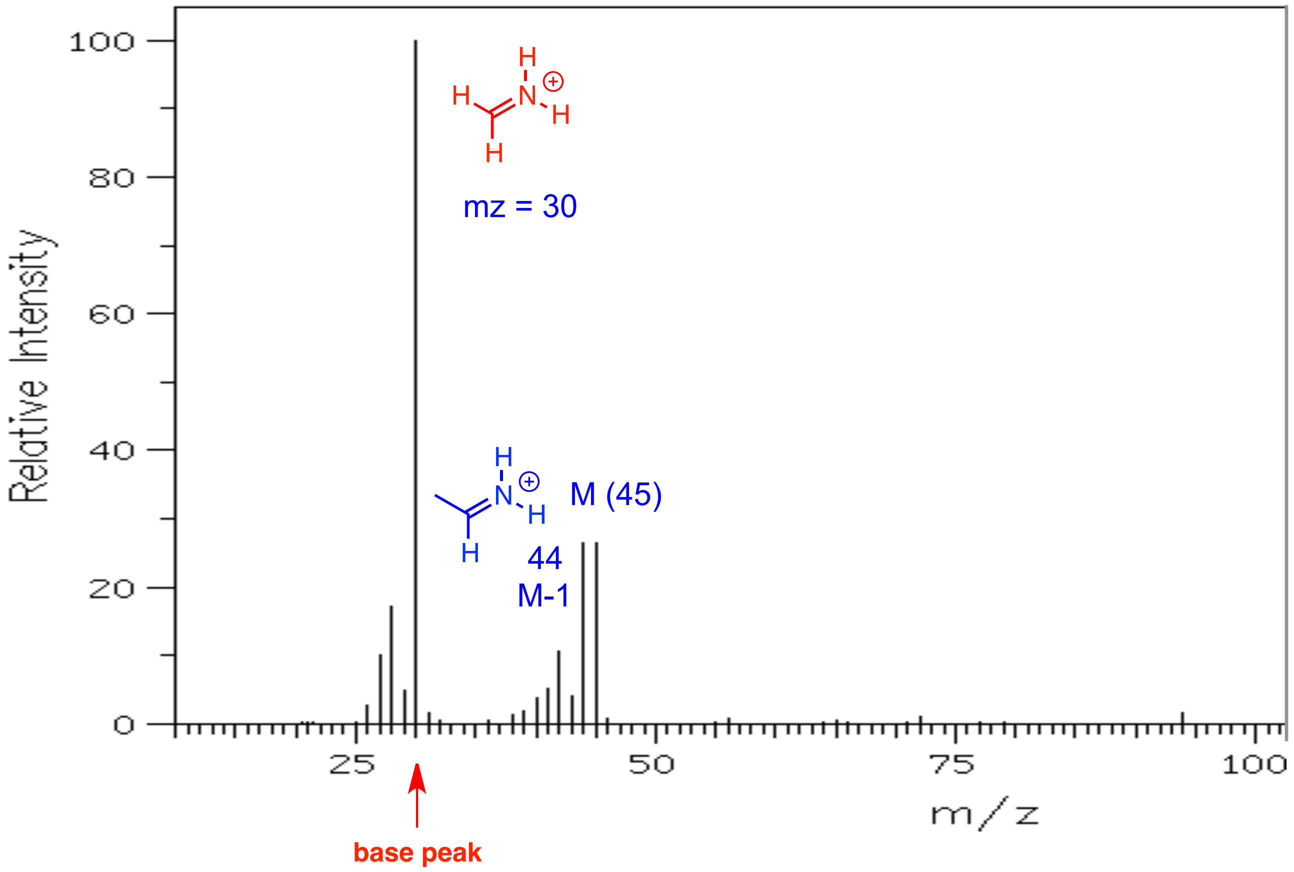
n = 1, m/z = 72
n = 2, m/z = 86

Mass Spectrometry: Fragmentation

Amines

ethylamine

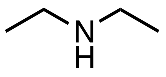
MW = 45

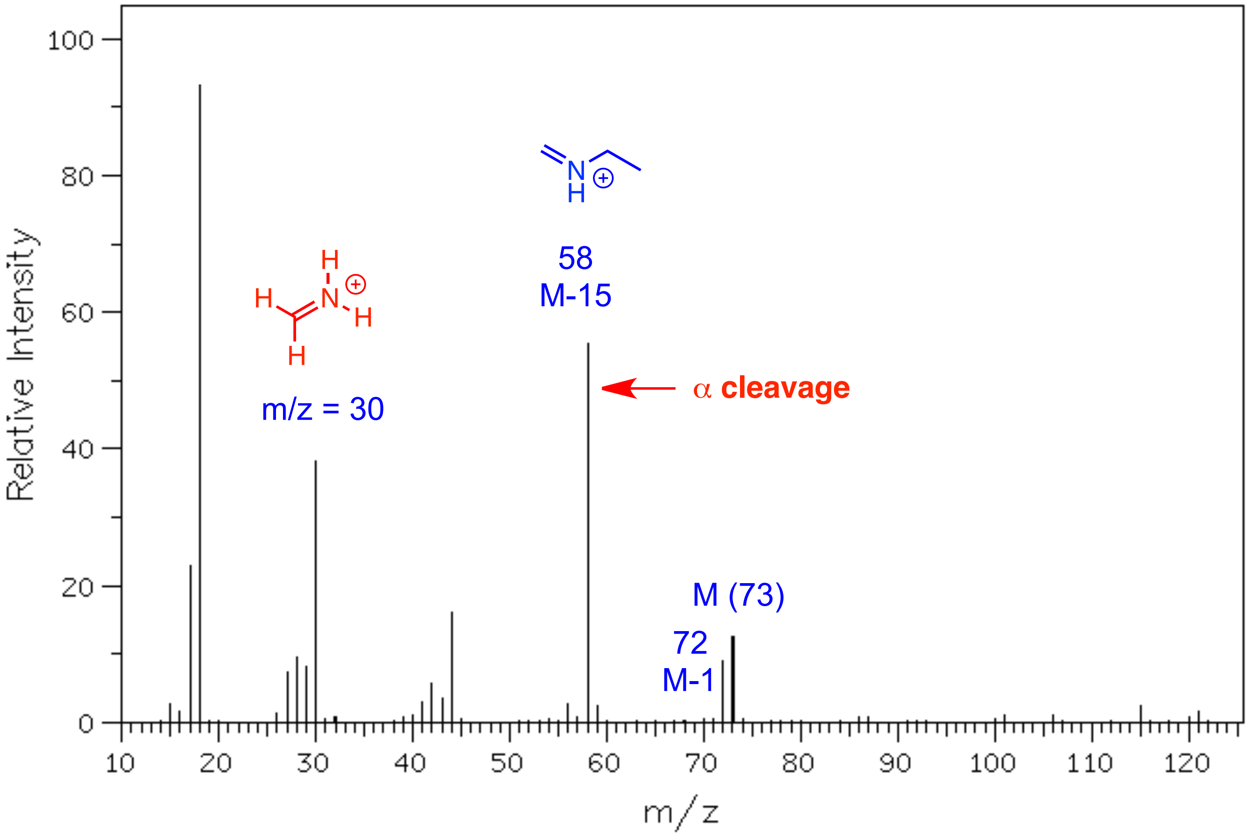


Mass Spectrometry: Fragmentation

Amines

diethylamine

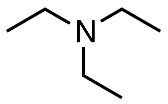

MW = 73



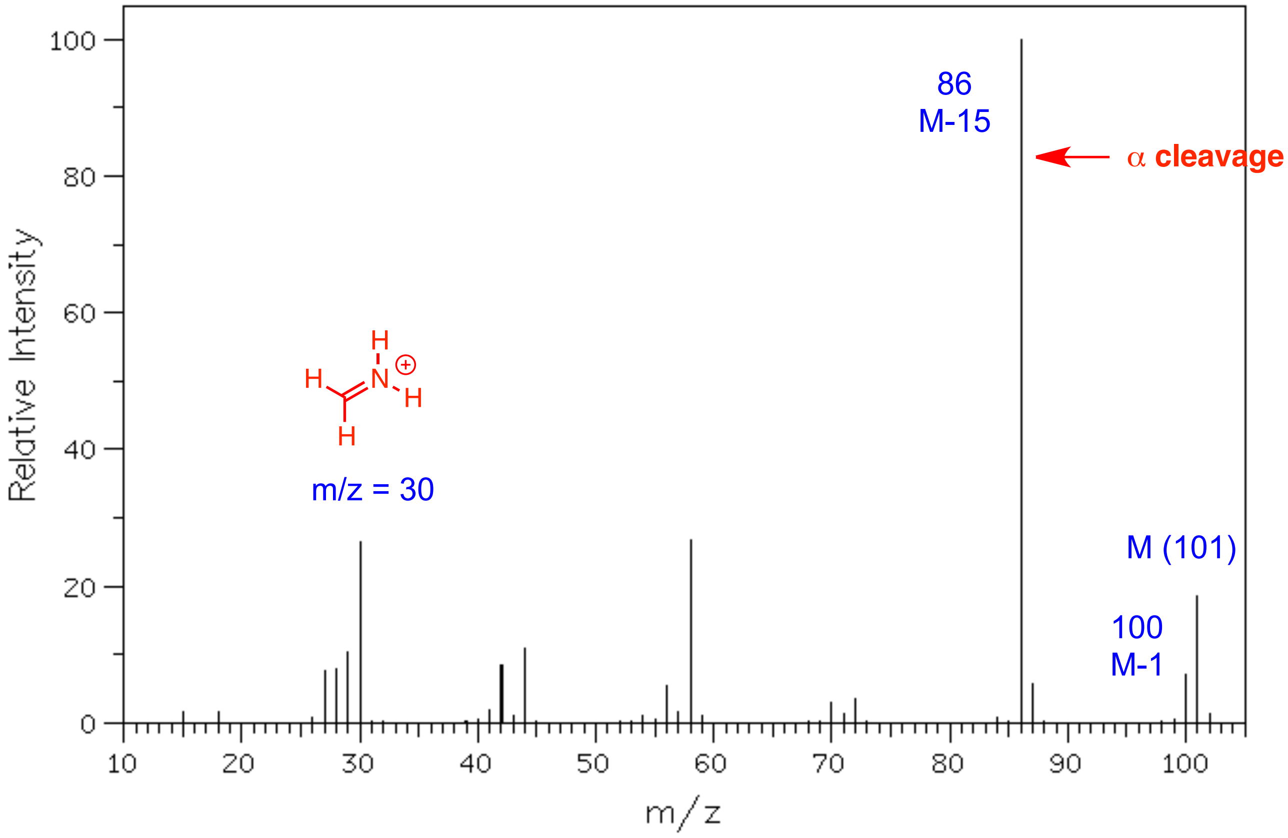
Mass Spectrometry: Fragmentation

Amines

triethylamine



MW = 101



86
M-15

α **cleavage**

m/z = 30

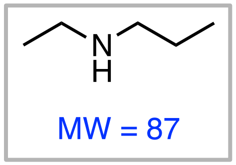
M (101)

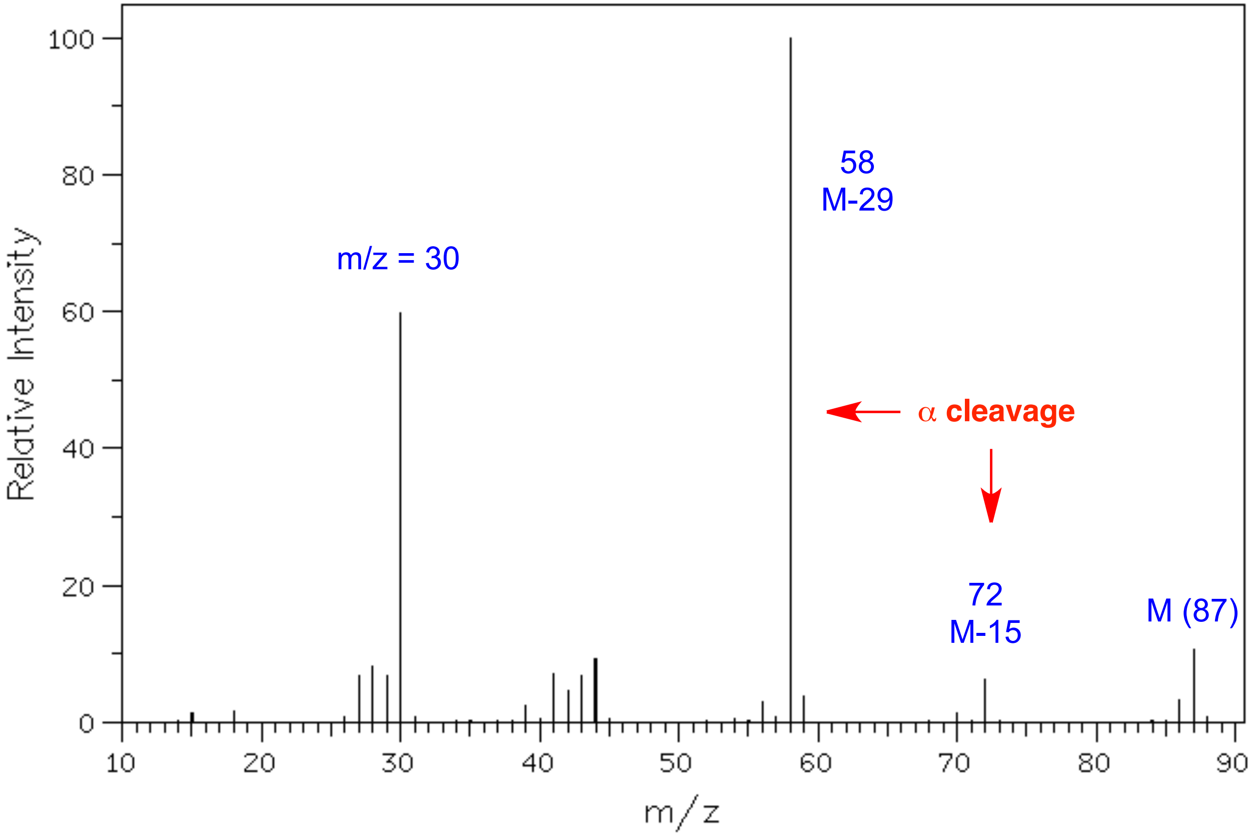
100
M-1

Mass Spectrometry: Fragmentation

Amines

N-ethylpropylamine

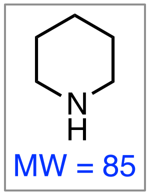




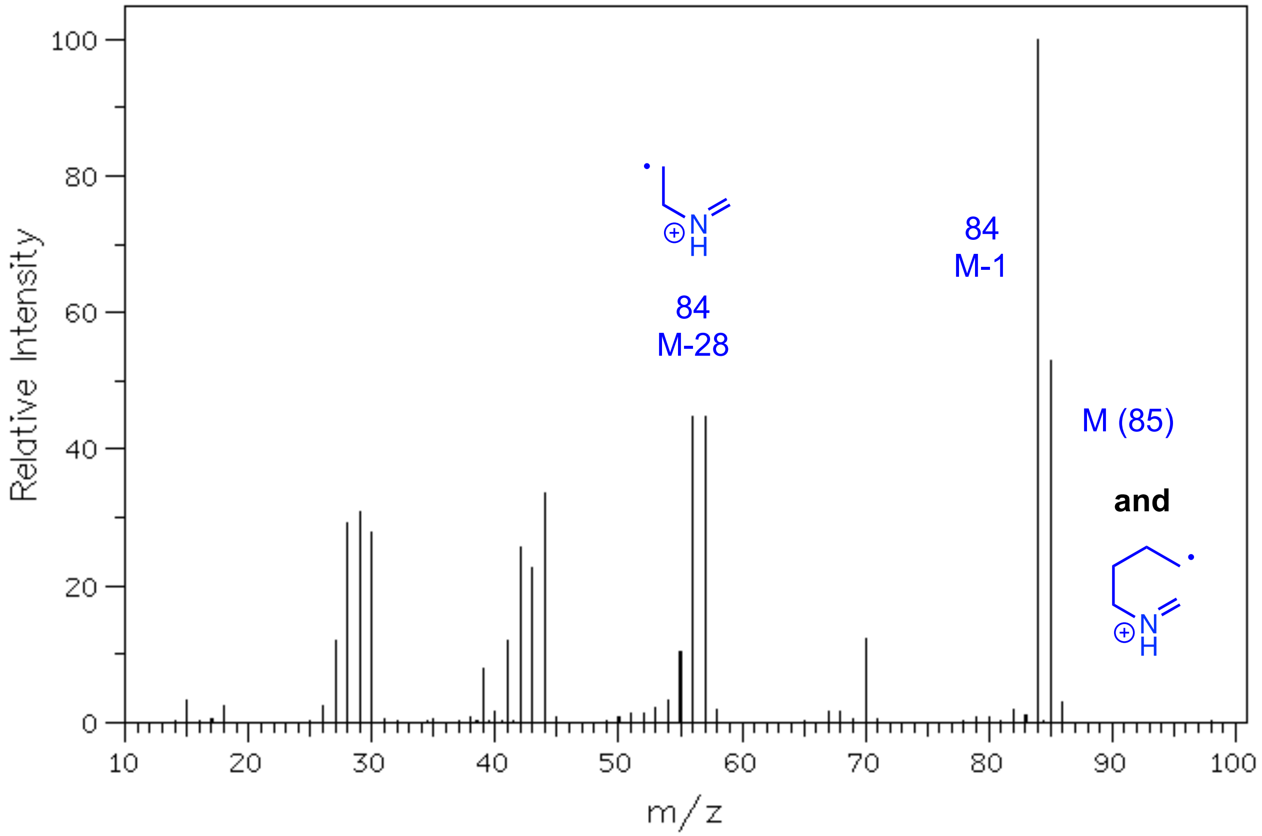
Mass Spectrometry: Fragmentation

Cyclic Amines

piperidine



MW = 85



84
M-28

84
M-1

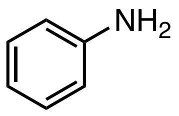
M (85)

and

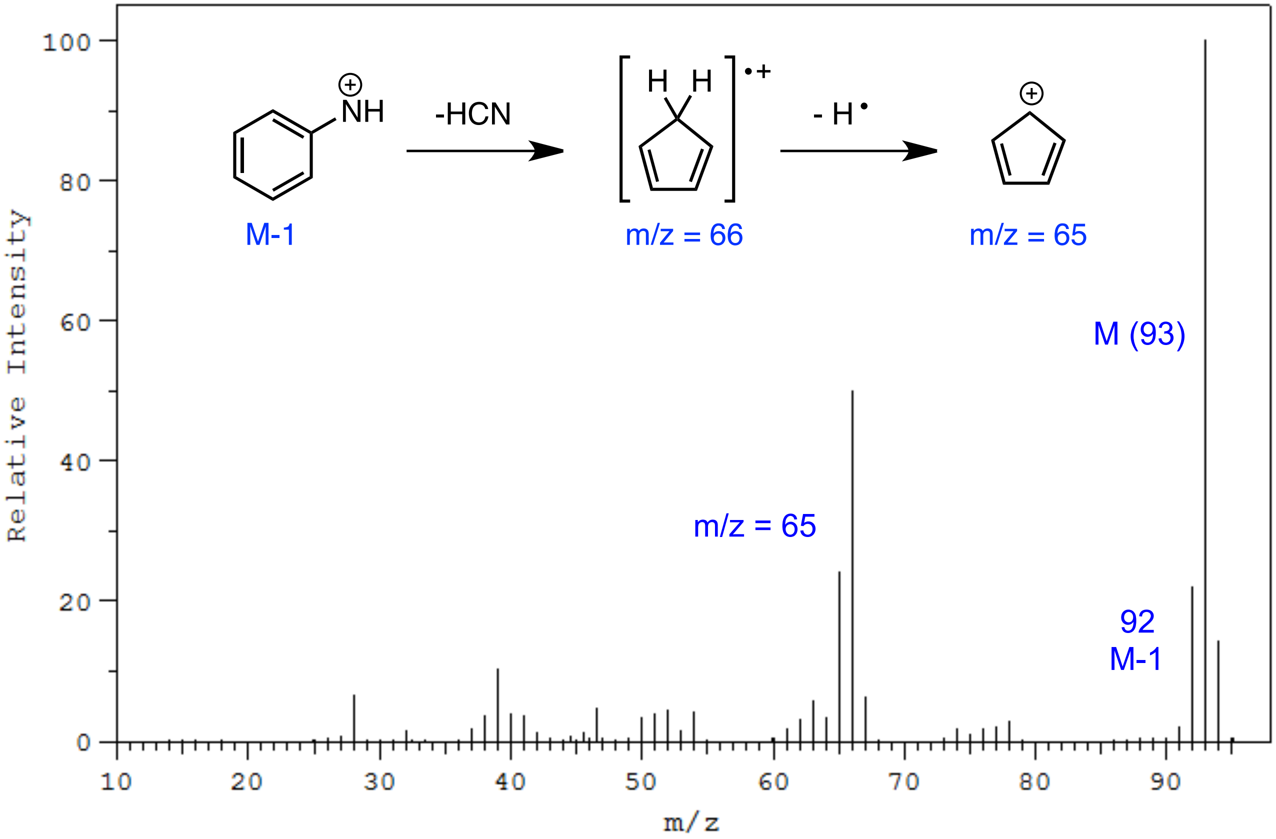
Mass Spectrometry: Fragmentation

Aromatic Amines

aniline



MW = 93



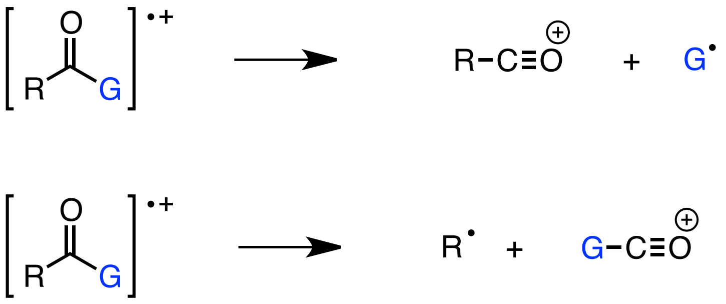
Mass Spectrometry: Fragmentation

Carbonyl Compounds

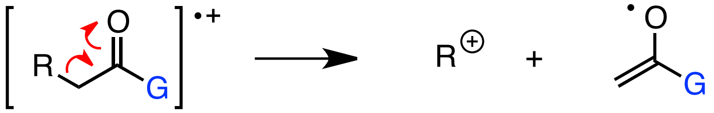
Common Fragmentation Modes

G = H, R', OH, OR', NR'_2

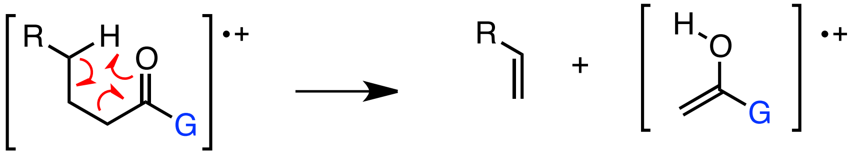
α-cleavage (two possibilities)



β-cleavage



McLafferty rearrangement



Mass Spectrometry: Fragmentation

Carbonyl Compounds

Aldehydes

- M^+ usually observed; may be weak in aliphatic aldehydes
- M-1 common (α-cleavage)
- α-cleavage is predominant fragmentation mode; often diagnostic (m/z = 29) especially in aromatic aldehydes (M-1; M-29)
- β-cleavage results in M-41 fragment; greater if α-substitution
- McLafferty rearrangement in appropriately substituted systems (m/z = 44 or higher)

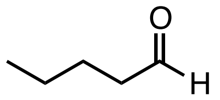
Ketones

- M^+ generally strong
- α-cleavage is the primary mode of fragmentation
- β-cleavage less common, but sometimes observed
- McLafferty rearrangement possible on both sides of carbonyl if chains sufficiently long
- Cyclic ketones show complex fragmentation patterns
- Aromatic ketones primarily lose $R^{\bullet}$ upon α-cleavage, followed by loss of CO

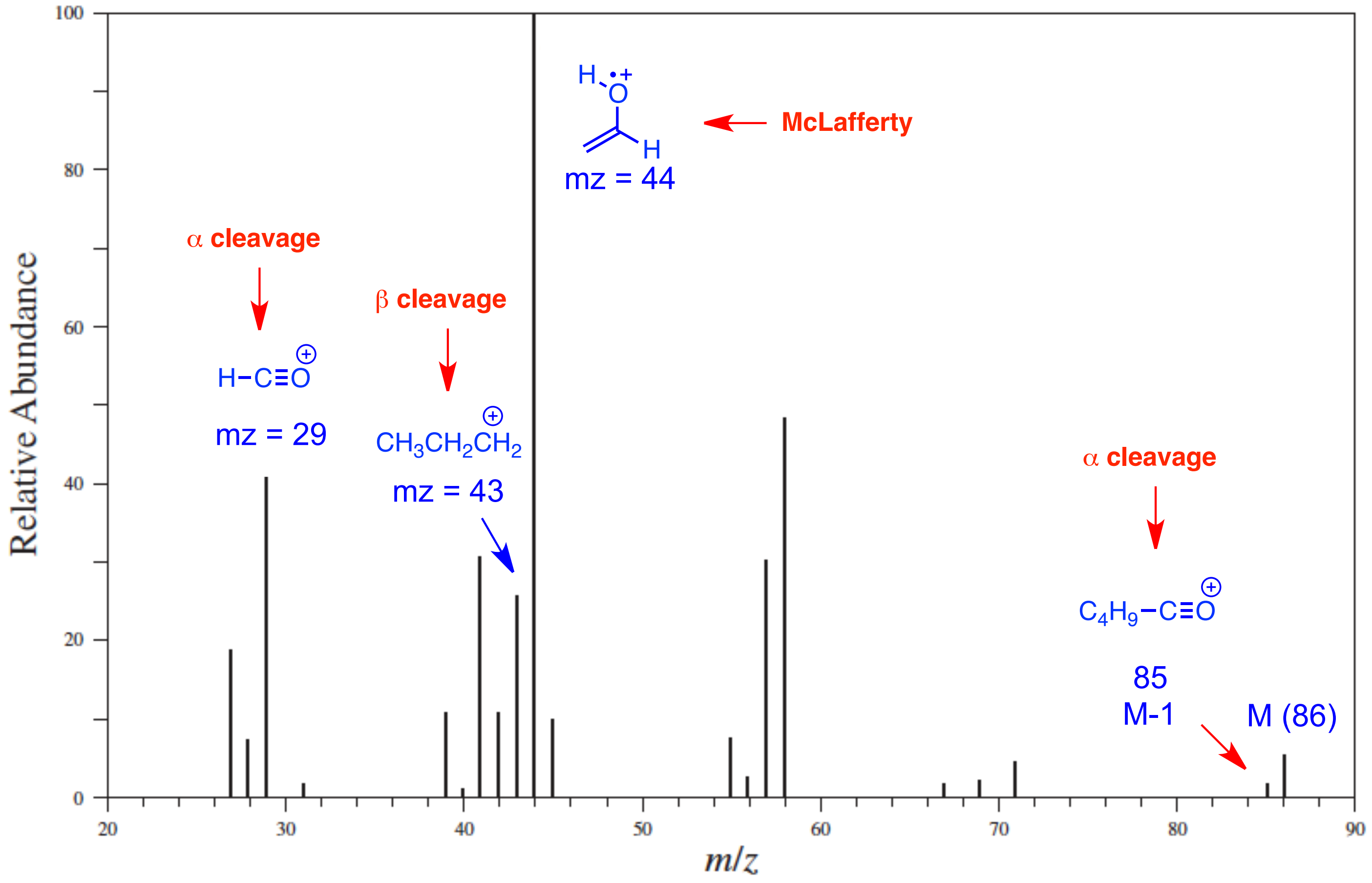
Mass Spectrometry: Fragmentation

Aliphatic Aldehydes

pentanal



MW = 86



$H\overset{\bullet +}{O}$

mz = 44

McLafferty

α cleavage

$H{-}C{\equiv}O^{\oplus}$

mz = 29

β cleavage

$CH_3CH_2CH_2^{\oplus}$

mz = 43

α cleavage

$C_4H_9{-}C{\equiv}O^{\oplus}$

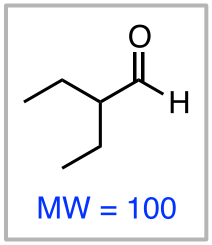
85
M-1

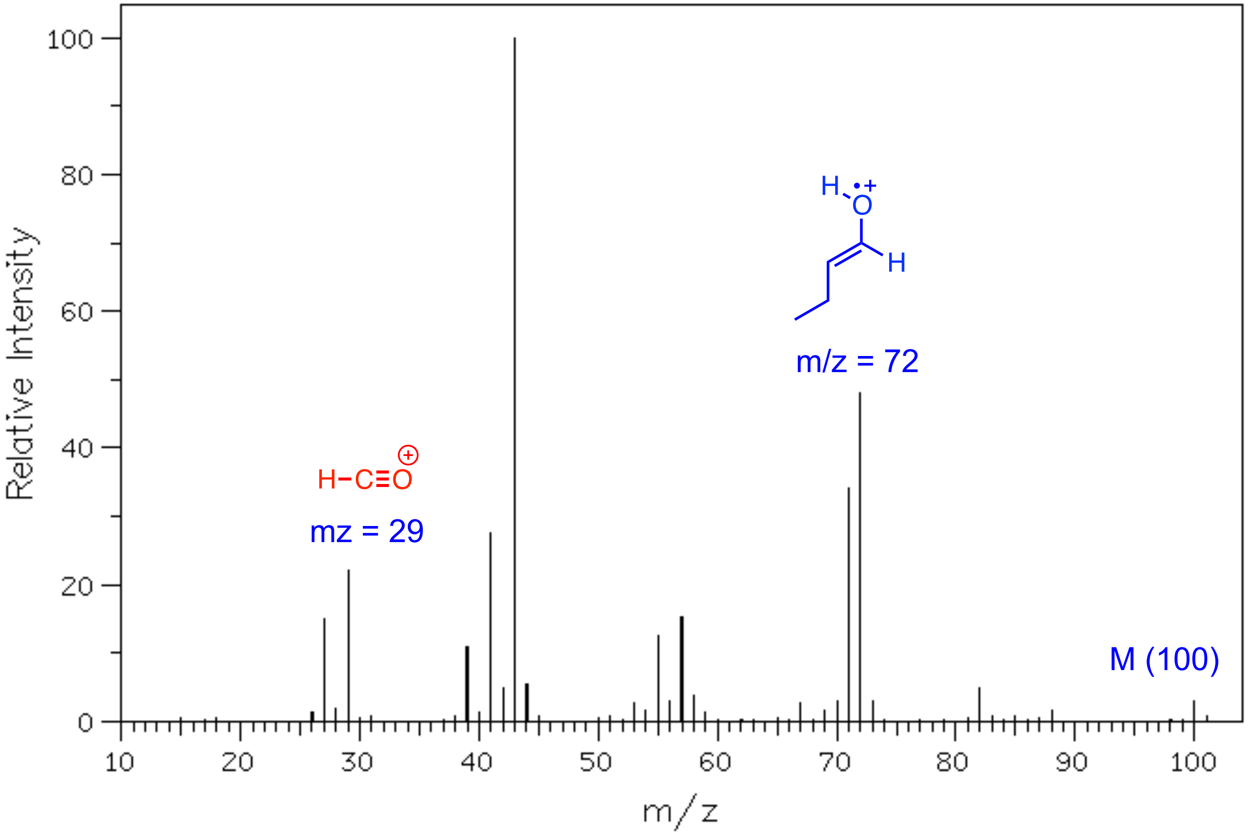
M (86)

Mass Spectrometry: Fragmentation

Aldehydes

2-ethylbutanal

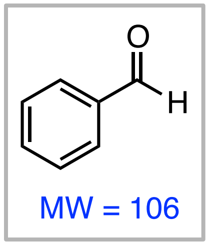


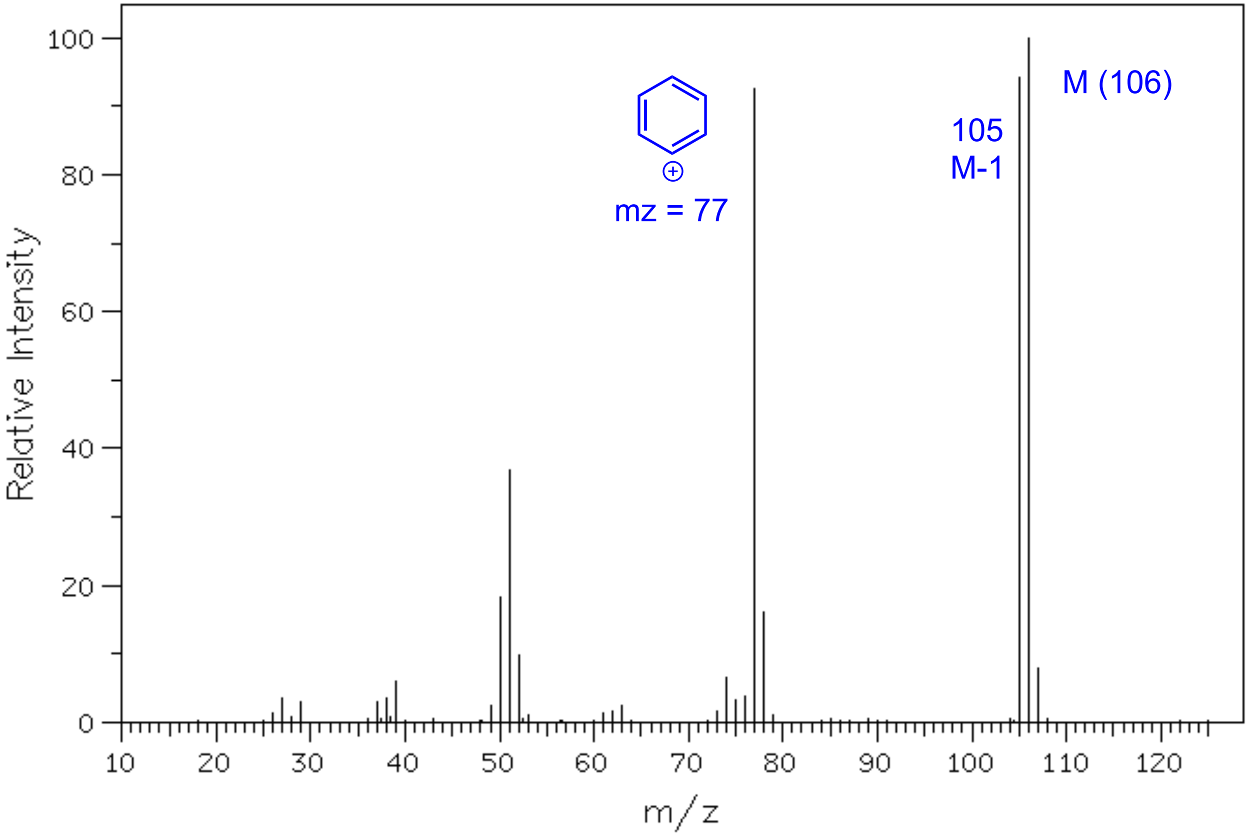


Mass Spectrometry: Fragmentation

Aromatic Aldehydes

benzaldehyde

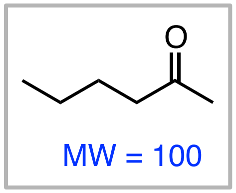


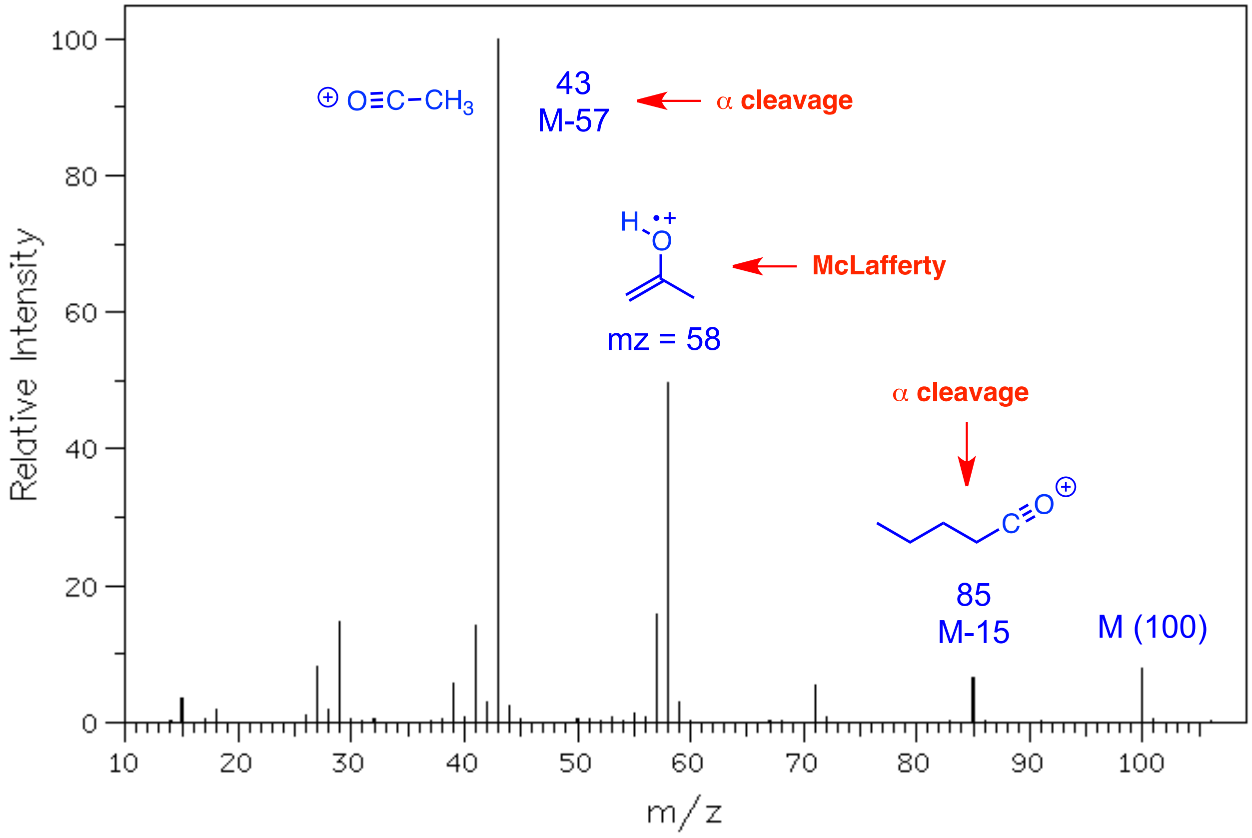


Mass Spectrometry: Fragmentation

Aliphatic Ketones

2-hexanone

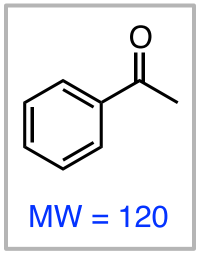

MW = 100

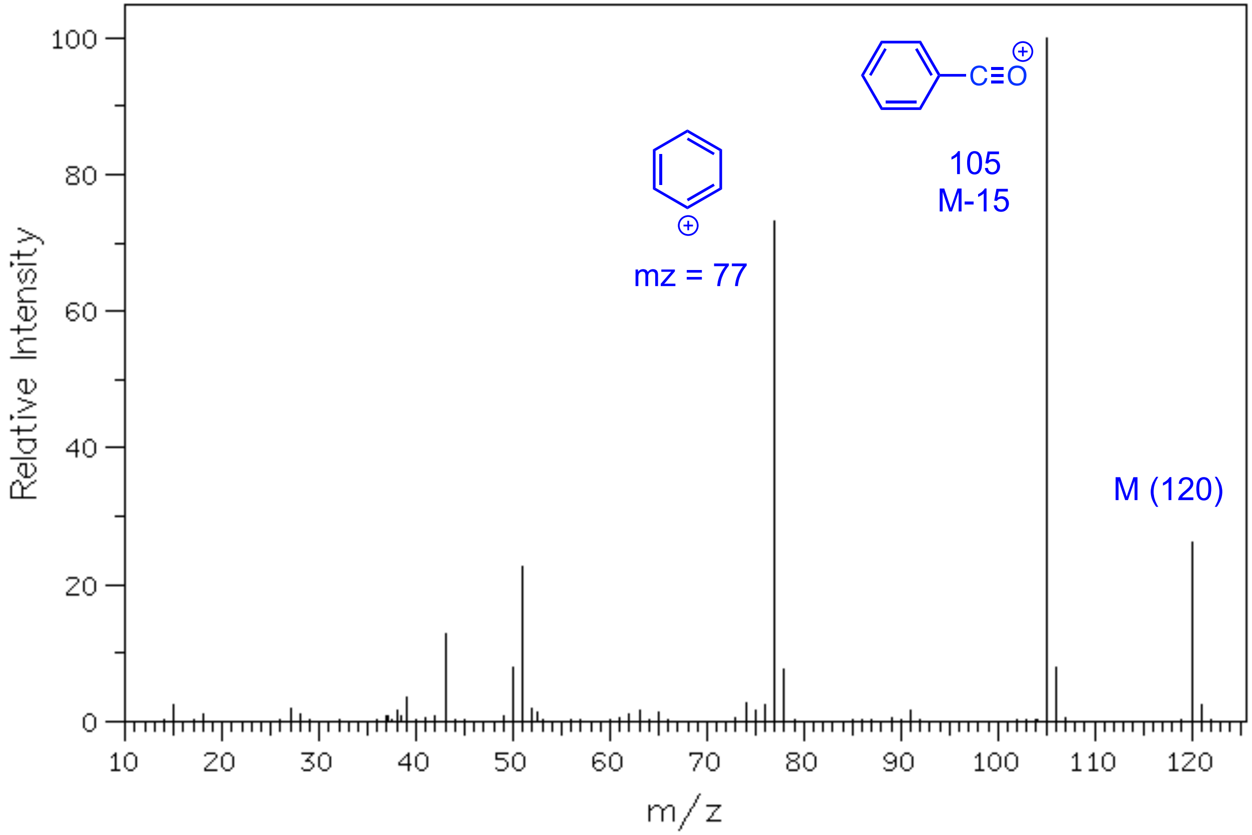


Mass Spectrometry: Fragmentation

Ketones

acetophenone

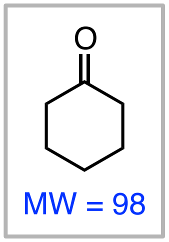


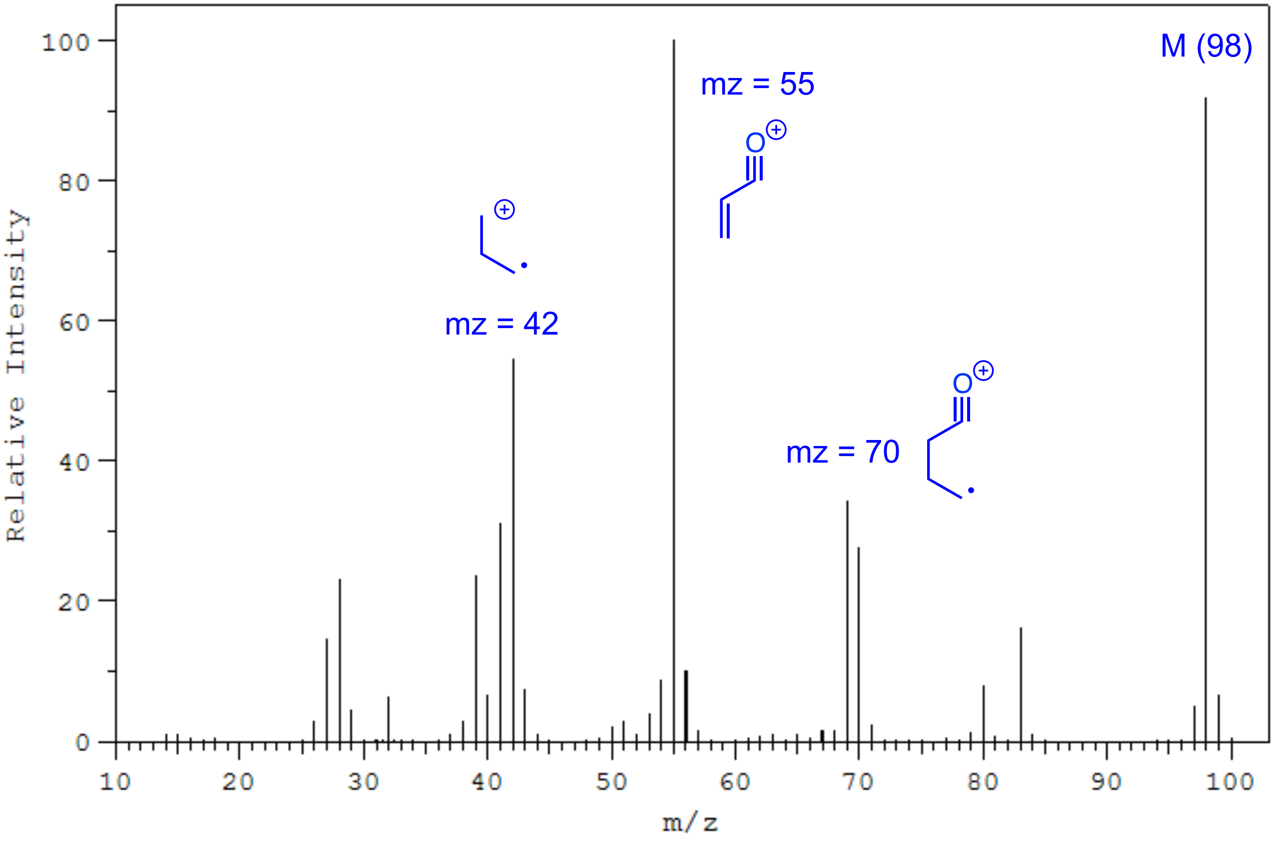


Mass Spectrometry: Fragmentation

Cyclic Ketones

cyclohexanone

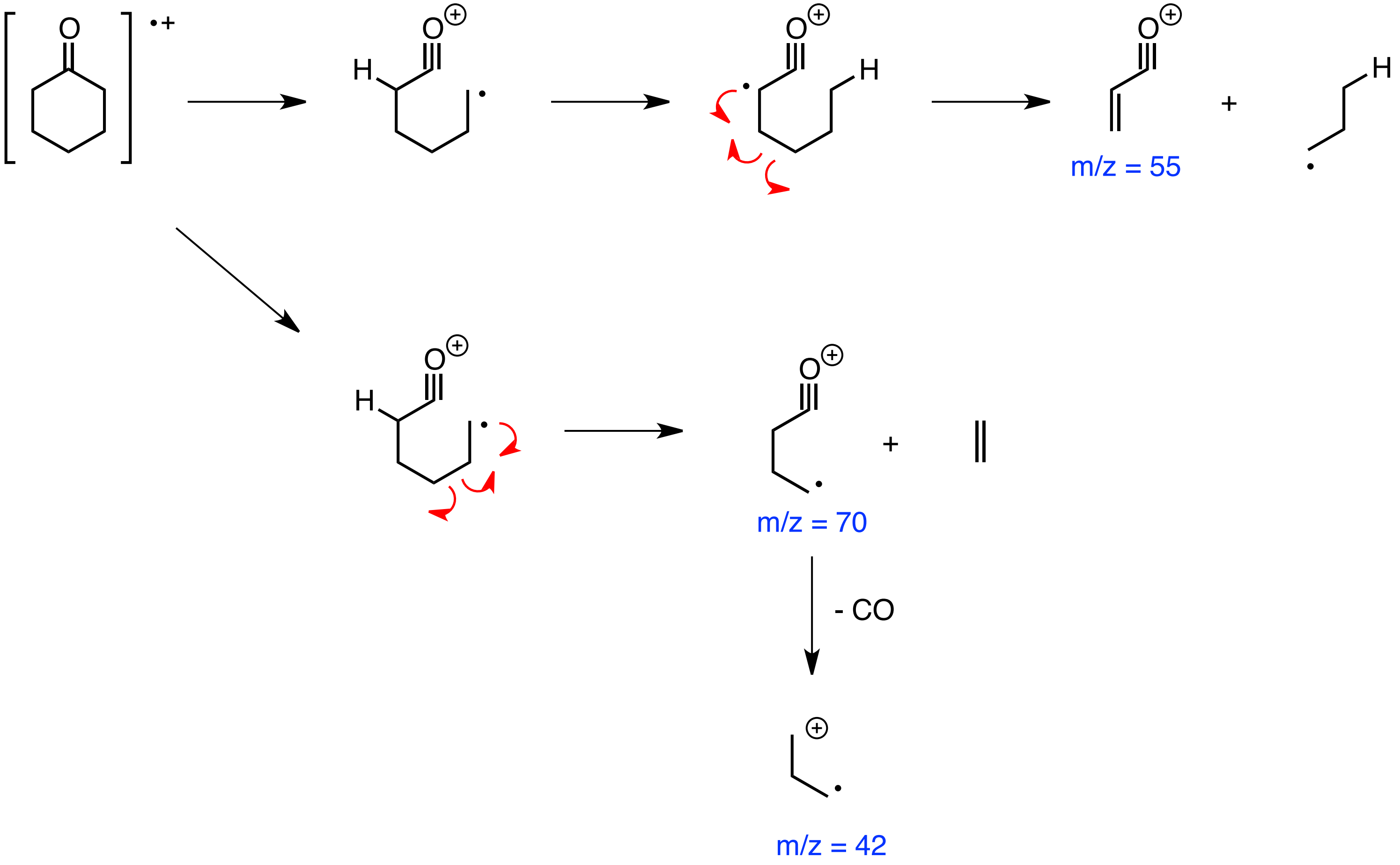




Mass Spectrometry: Fragmentation

Cyclic Ketones

cyclohexanone



Mass Spectrometry: Fragmentation

Carboxylic Acids, Esters & Amides

Carboxylic Acids

- M^+ weak in aliphatic acids; stronger in aromatic acids
- Most important α-cleavage involves loss of OH radical (M-17)
- α-cleavage with loss of alkyl radical less common; somewhat diagnostic (m/z = 45)
- McLafferty rearrangement in appropriately substituted systems (m/z = 60 or higher)
- Dehydration can occur in o-alkyl benzoic acids (M-18)

Esters

- M^+ weak in most cases; aromatic esters give a stronger parent ion
- Loss of alkoxy radical more important of the α-cleavage reactions
- Loss of an alkyl radical by α-cleavage occurs mostly in methyl esters (m/z = 59)
- McLafferty rearrangements are possible on both alkyl and alkoxy sides
- Benzyloxy esters and o-alkyl benzoates fragment to lose ketene and alcohol, respectively

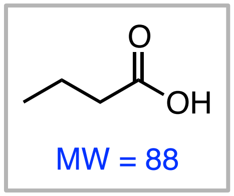
Amides

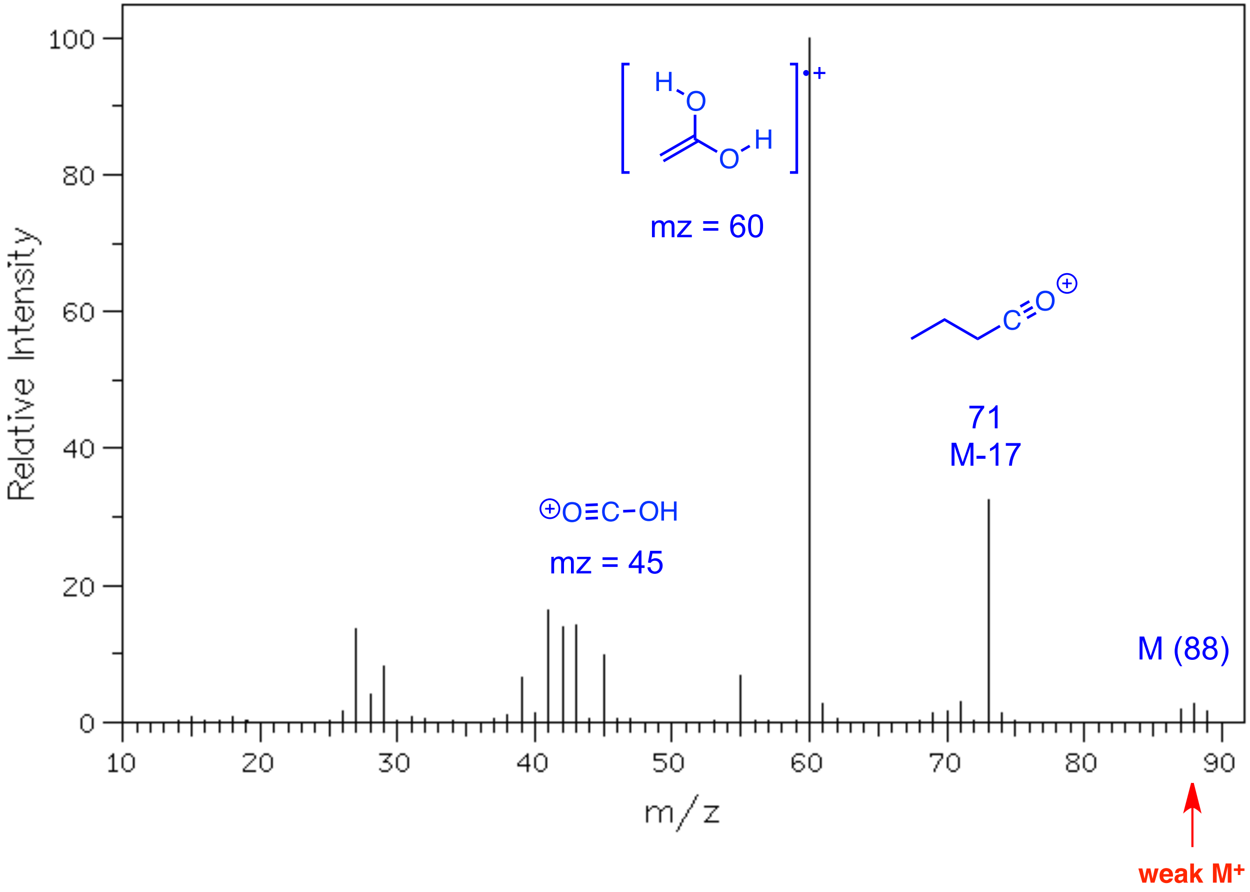
- M^+ usually observed; Follow the Nitrogen Rule (odd # of N, odd MW)
- α-cleavage affords a specific ion for primary amides (m/z = 44?
- McLafferty rearrangement observed when γ-hydrogens are present

Mass Spectrometry: Fragmentation

Aliphpatic Carboxylic Acids

butyric acid

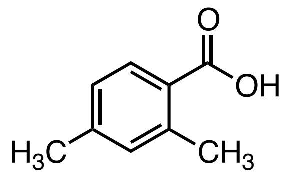




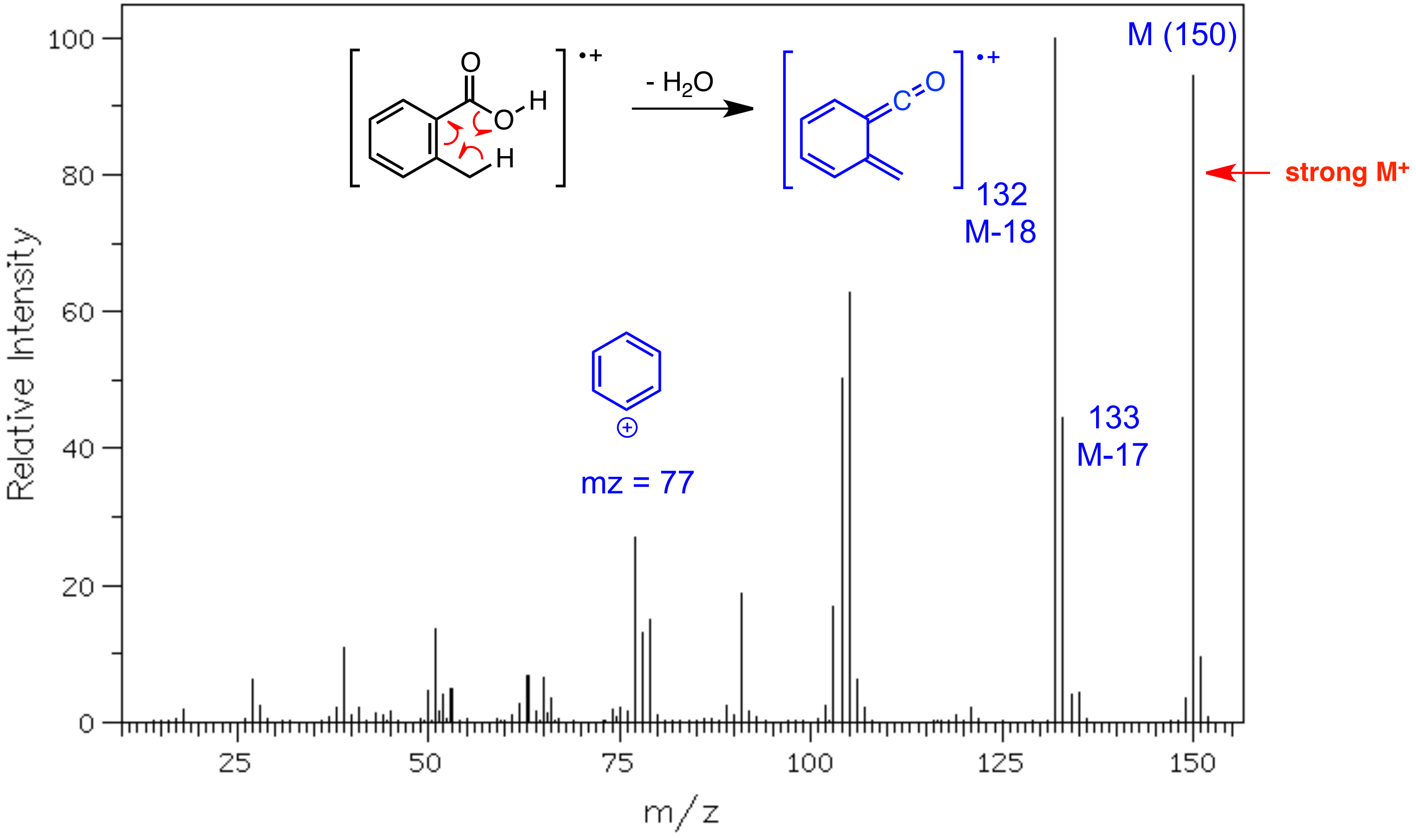
Mass Spectrometry: Fragmentation

Carboxylic Acids

2,4-dimethylbenzoic acid



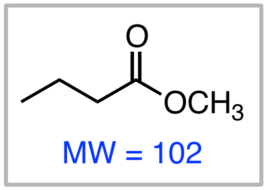
MW = 150



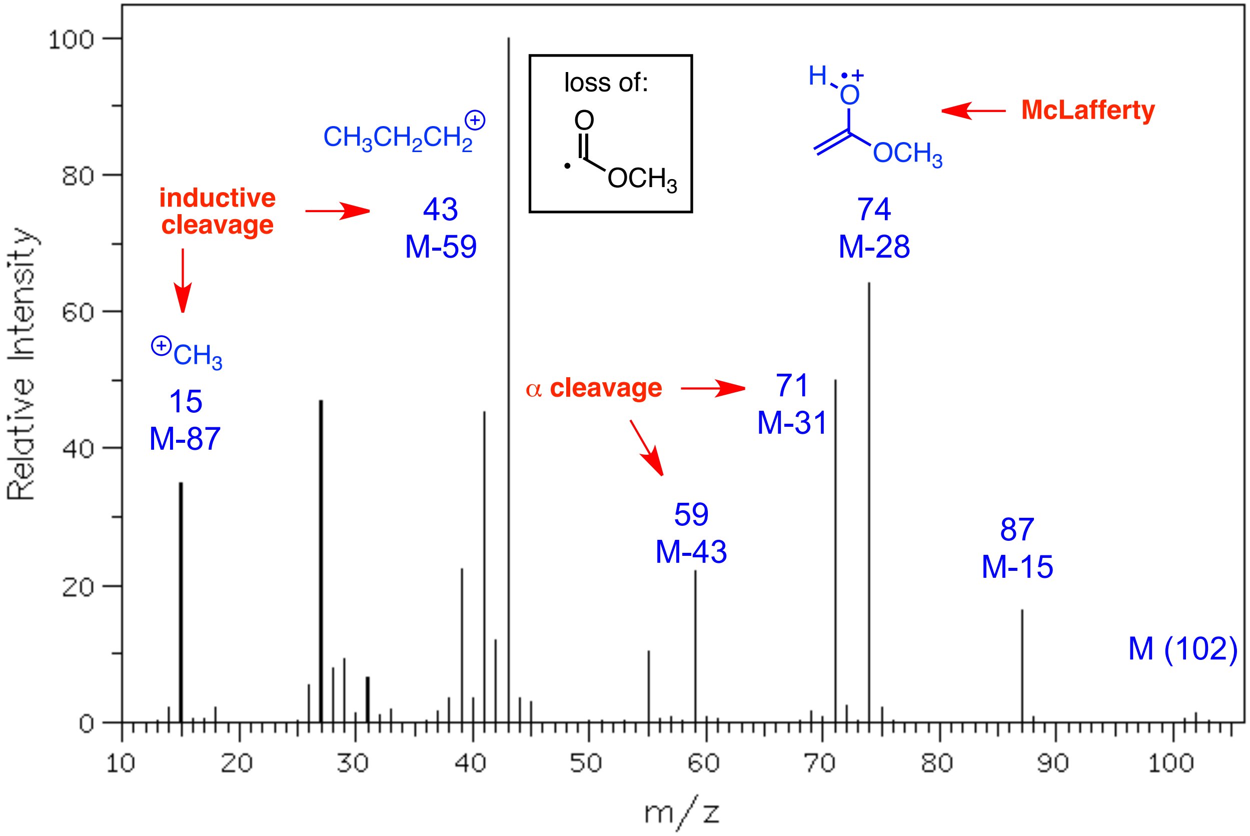
Mass Spectrometry: Fragmentation

Esters

methyl butyrate



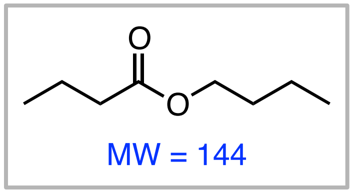
MW = 102

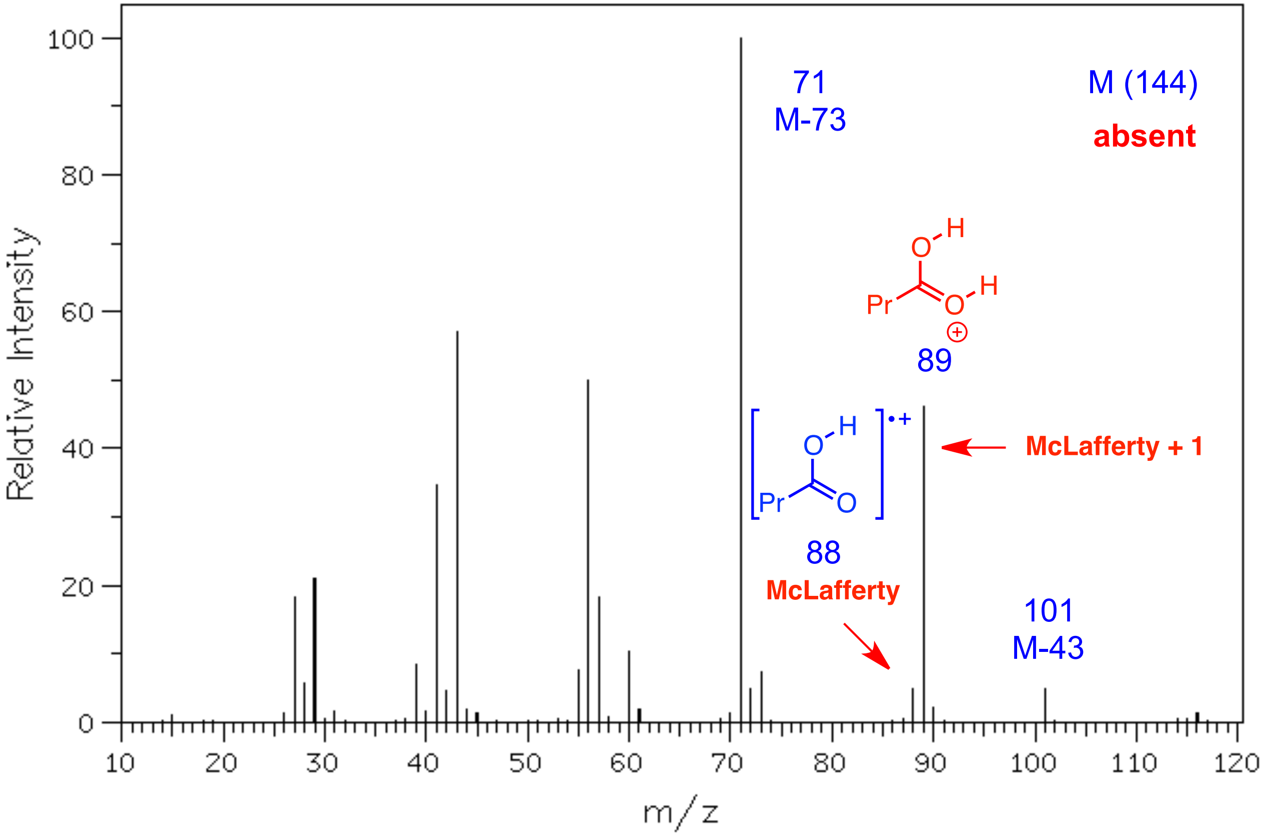


Mass Spectrometry: Fragmentation

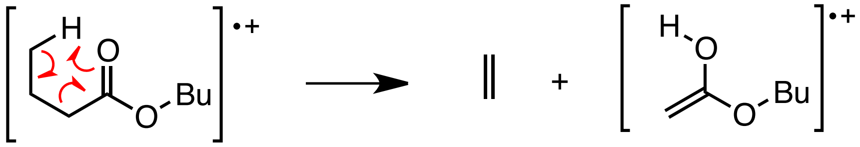
Esters

butyl butyrate





Mass Spectrometry: Fragmentation



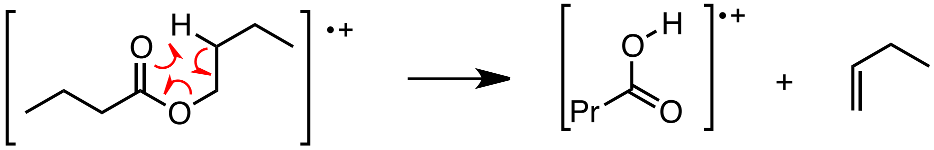
m/z = 116

(not observed)

Esters

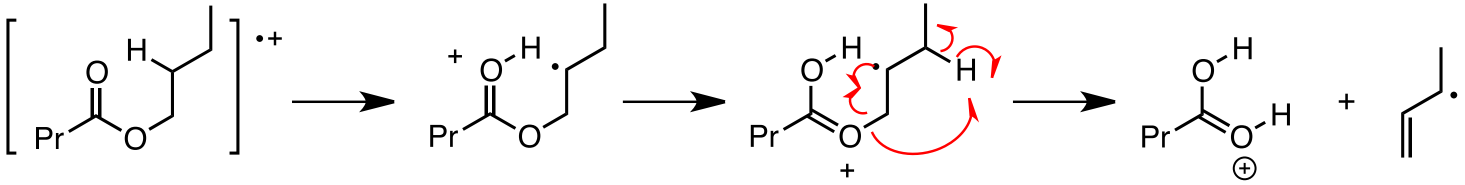
fragmentation patterns

McLafferty rearrangement



m/z = 88

McLafferty + 1

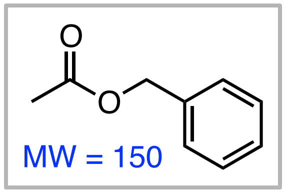


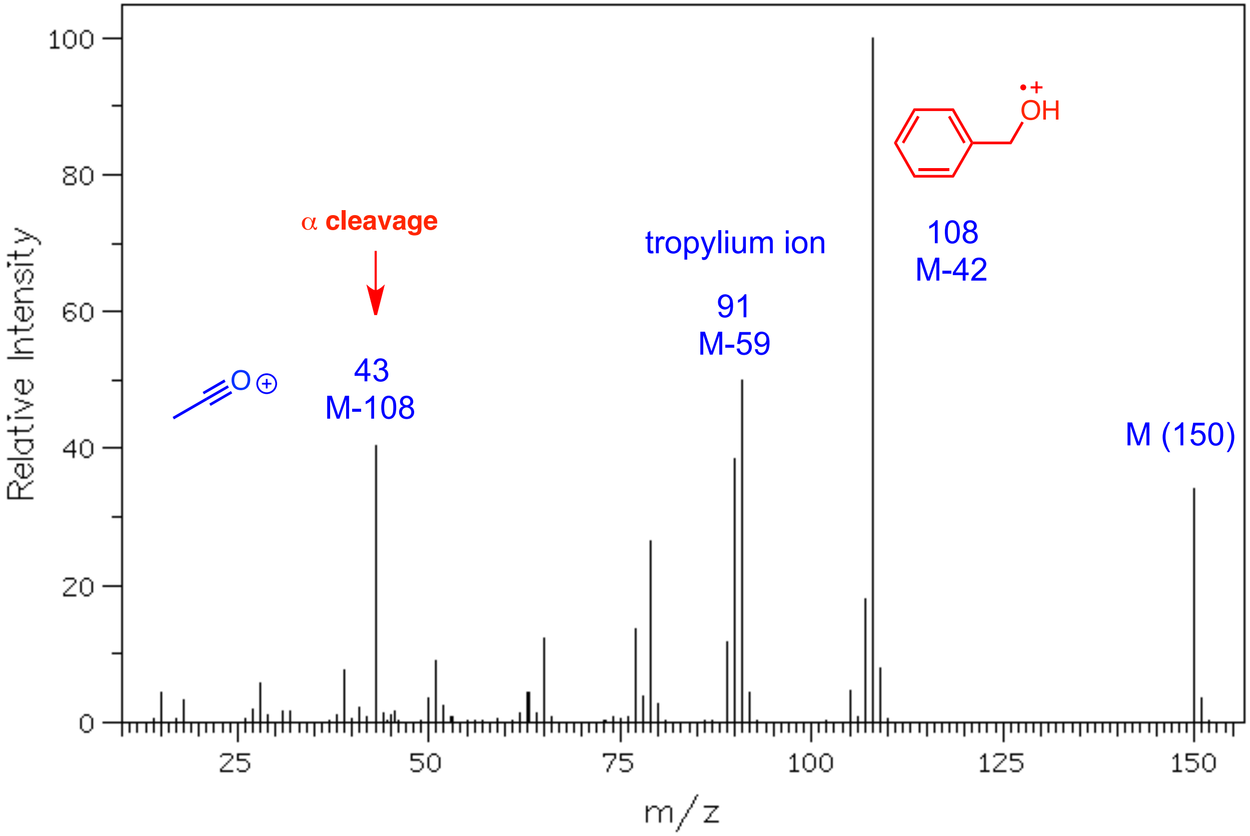
m/z = 89

Mass Spectrometry: Fragmentation

Esters

benzyl acetate



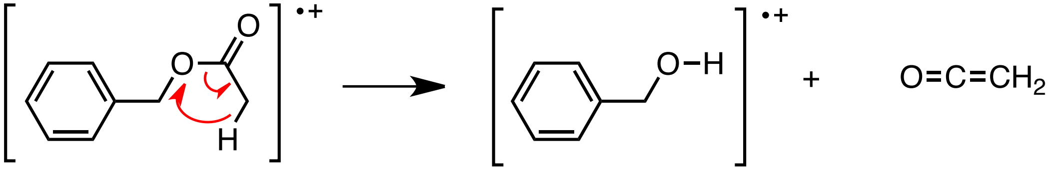


Mass Spectrometry: Fragmentation

Esters

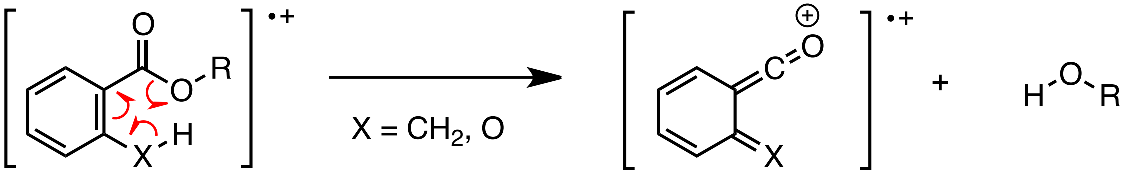
fragmentation patterns

Benzyl ester rearrangement



can fragment further

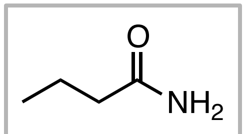
Loss of alcohol



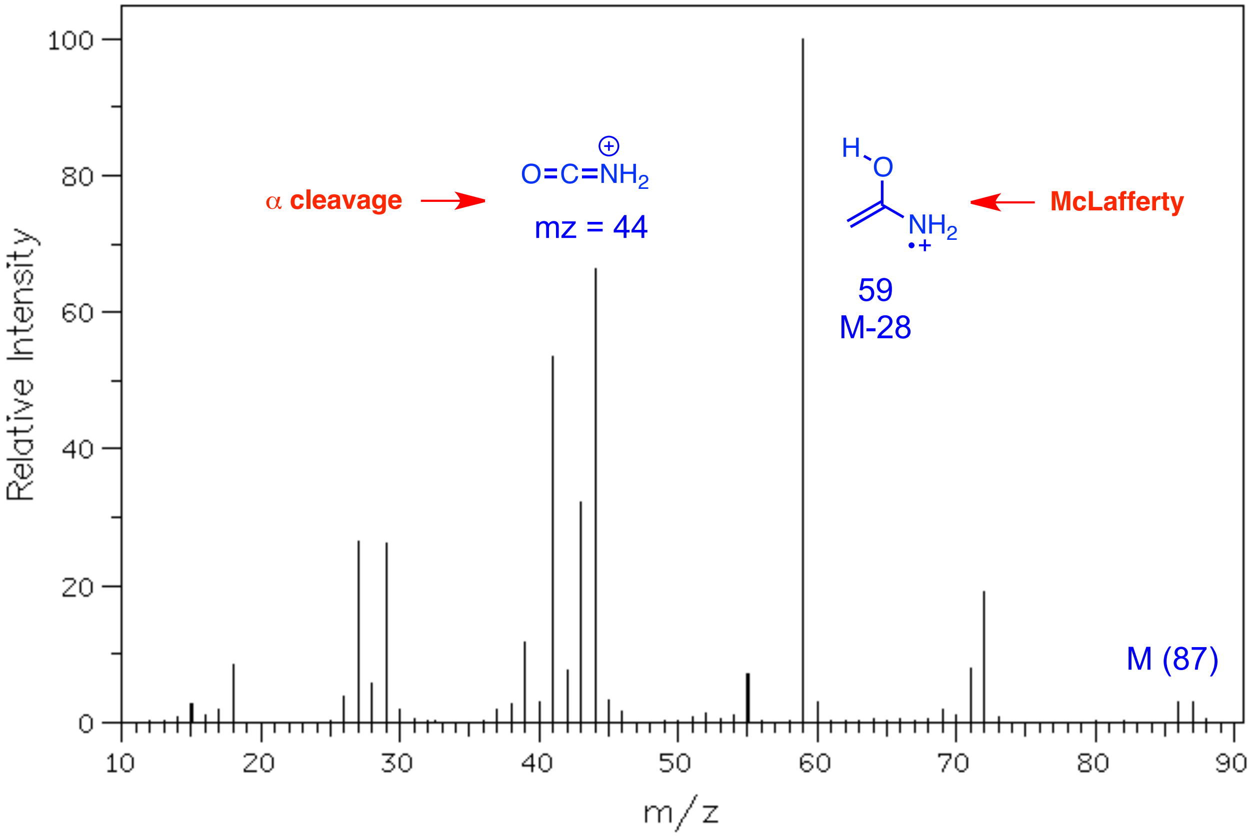
Mass Spectrometry: Fragmentation

Amides

butyramide



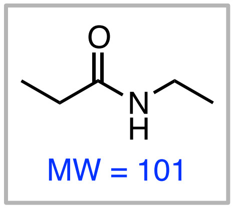
MW = 87

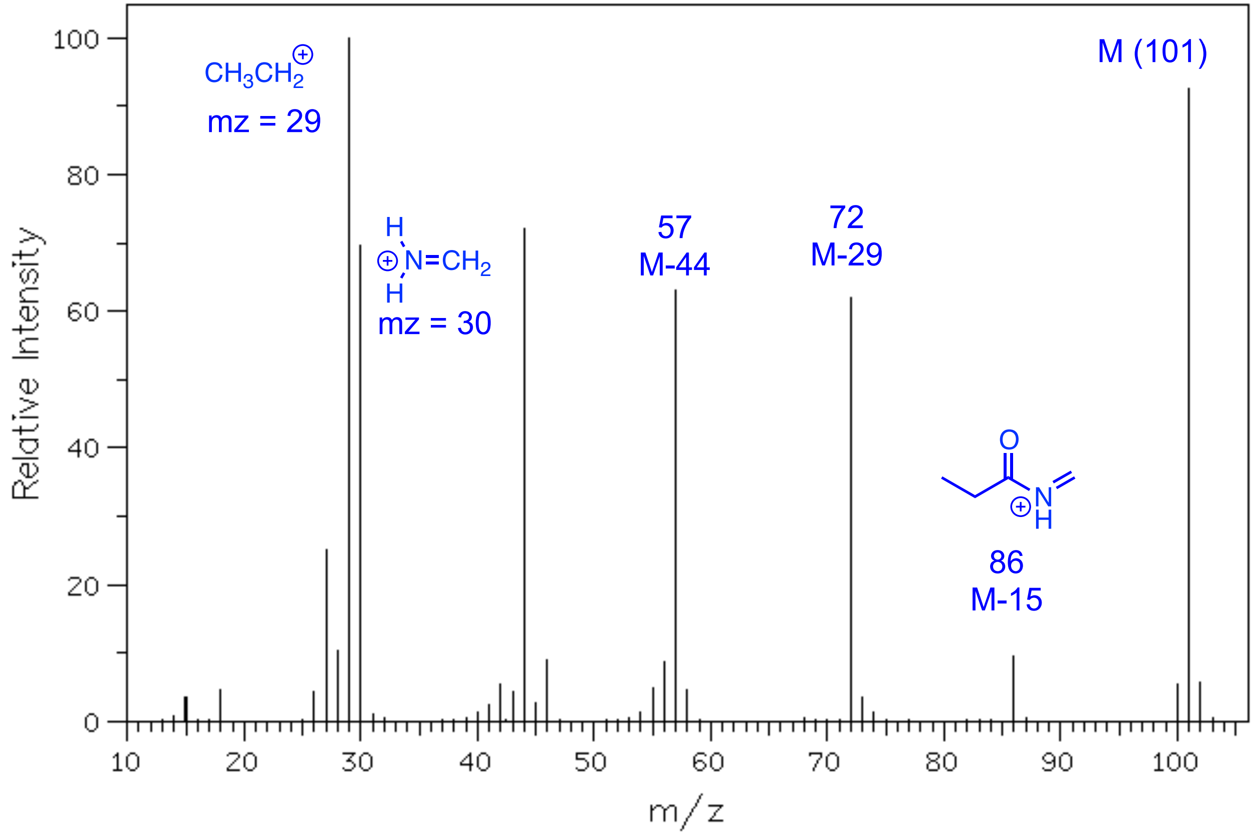


Mass Spectrometry: Fragmentation

Amides

N-ethylpropionamide

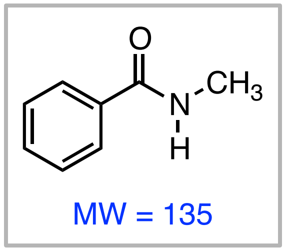




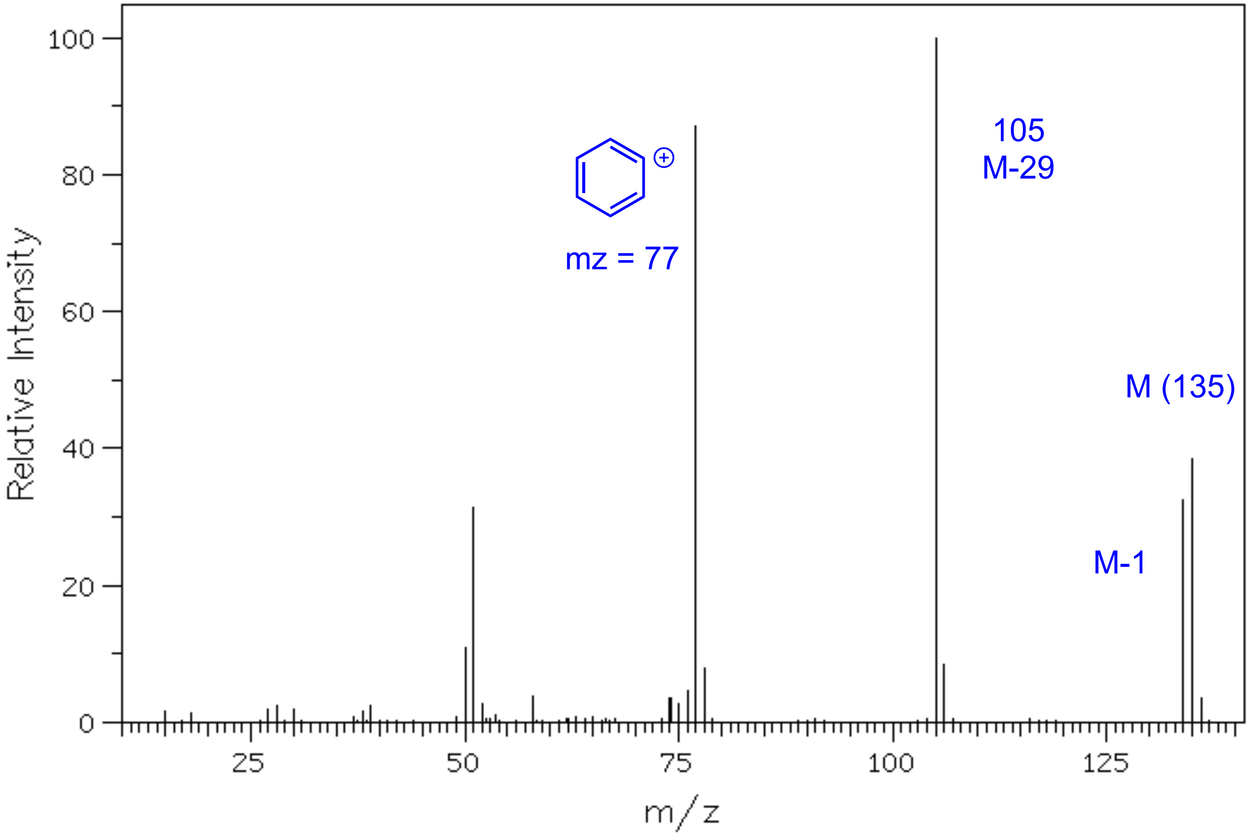
Mass Spectrometry: Fragmentation

Aryl Amides

N-methylbenzamimde



MW = 135



Mass Spectrometry: Fragmentation

Nitriles

Nitriles

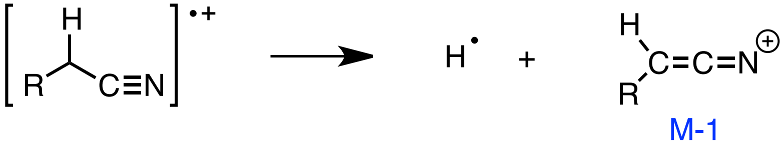
- M^+ may be weak/absent; strong M+ in aromatic nitriles; follow nitrogen rule
- Fragment readily to give M-1
- Loss of HC≡N fequently obsterved (M-27); aromatic nitriles also show loss of $^\bullet$CN (M-26)
- McLafferty rearrangement in nitriles of appropriate length (m/z = 41)

Mass Spectrometry: Fragmentation

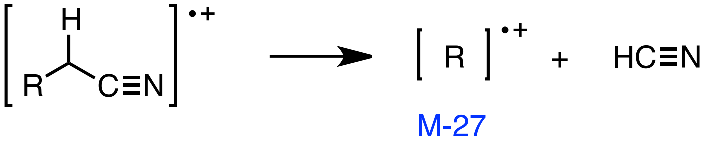
Nitriles

fragmentation patterns

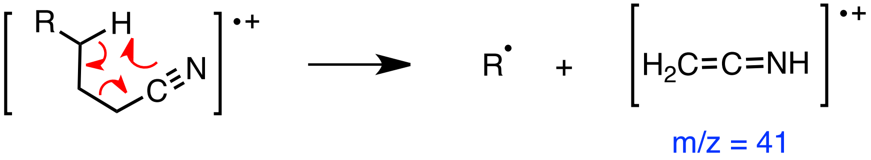
Loss of α-hydrogen



Loss of HCN



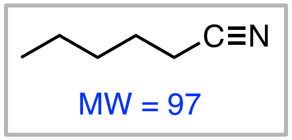
McLafferty rearrangement

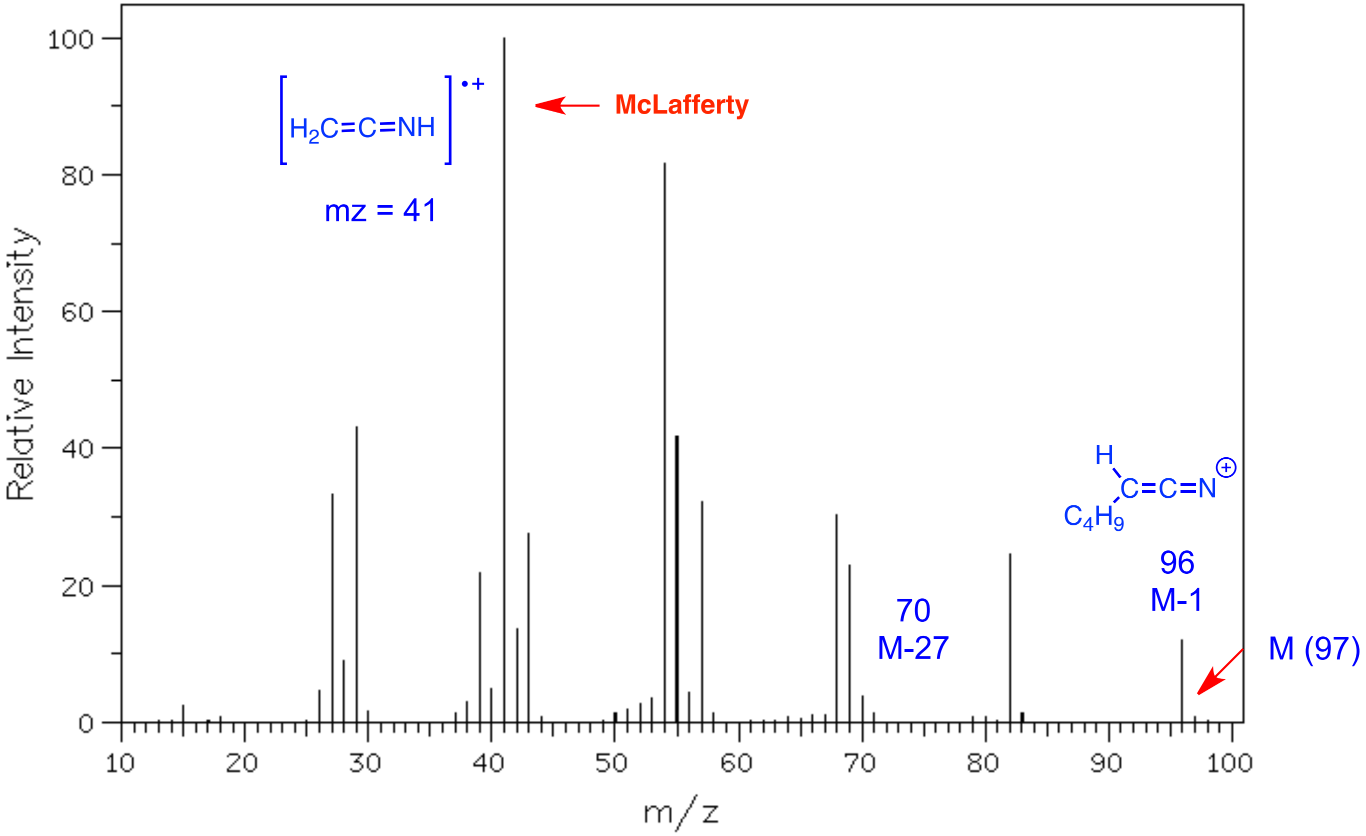


Mass Spectrometry: Fragmentation

Nitriles

hexanenitrile





Mass Spectrometry: Fragmentation

Nitro Compounds & Halides

Nitro Compounds

- M^+ almost never observed unless aromatic; follow nitrogen rule
- Principle degradation is loss of NO^+ ($m/z = 30$) and loss of NO_2^+ ($m/z = 46$)
- Aromatic nitro compounds show additional fragmentation patterns

Halides

- M^+ often weak; stronger in aromatic halides
- chloro and bromo compounds show strong M+2 peaks

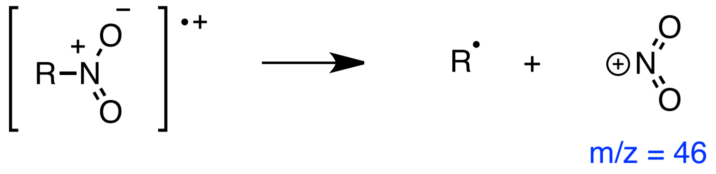
Cl – M : M+2	3 : 1
Br – M : M+2	1 : 1

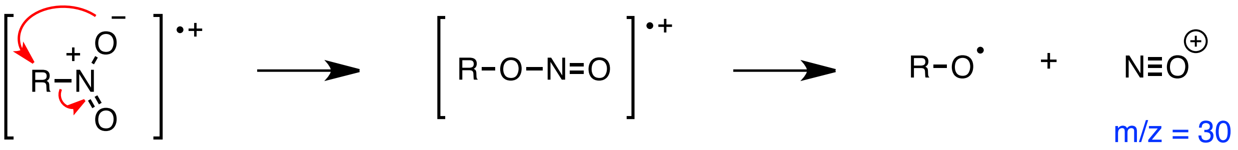
- principle fragmentation is loss of halogen
- Loss of HX also common
- α-cleavage sometimes observed

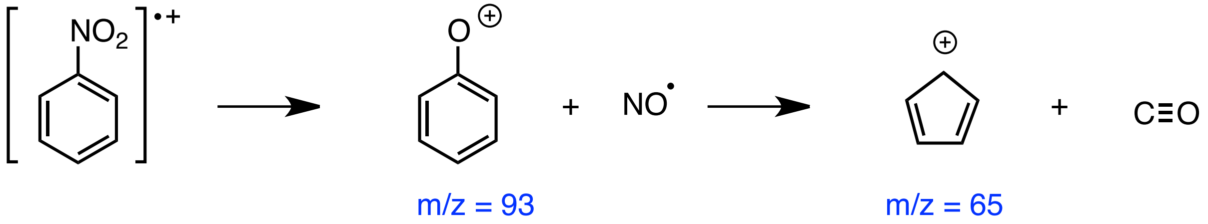
Mass Spectrometry: Fragmentation

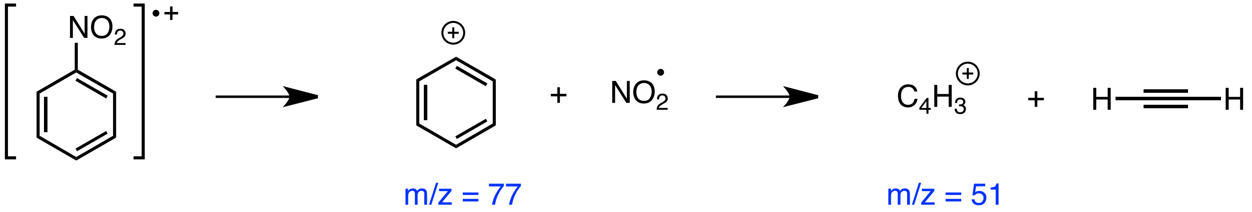
Nitro Compounds

<u>fragmentation patterns</u>





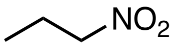




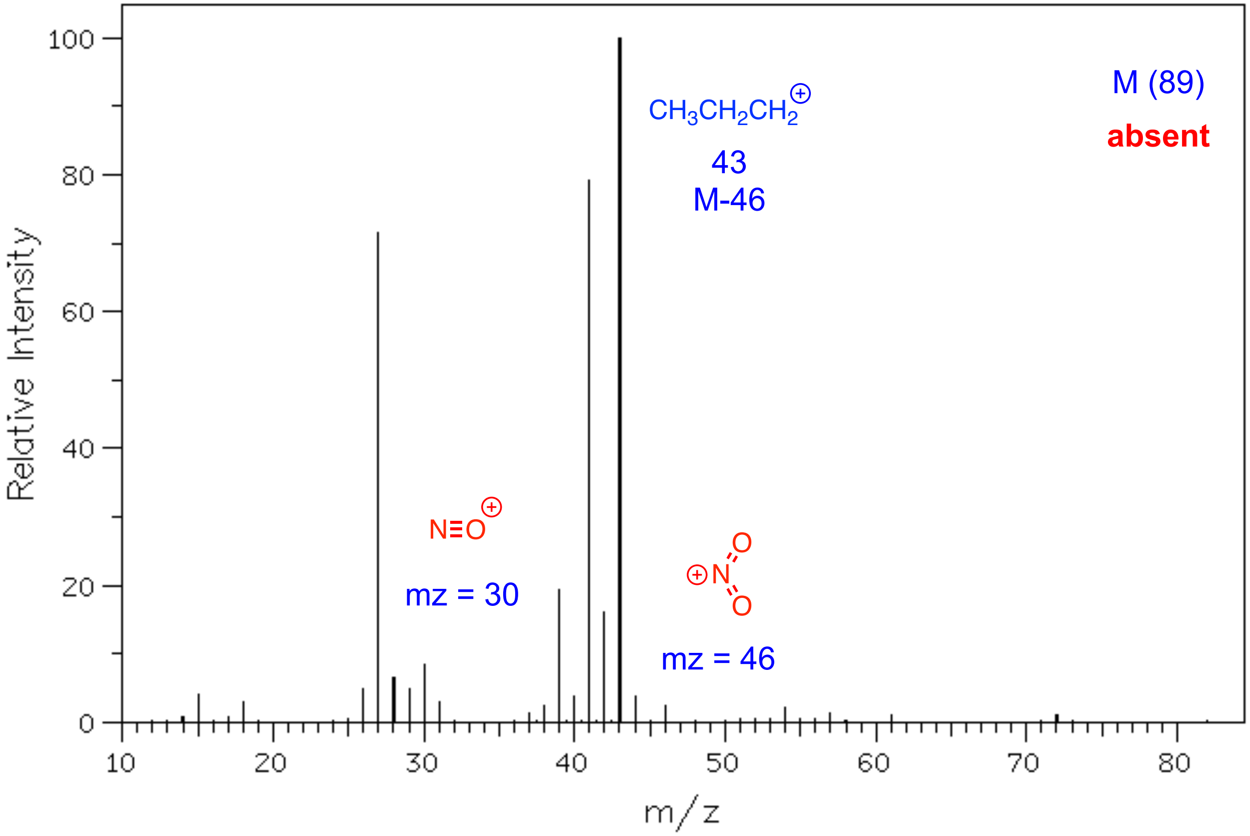
Mass Spectrometry: Fragmentation

Nitro Compounds

1-nitropropane



MW = 89



$CH_3CH_2CH_2^{\oplus}$

43

M-46

M (89)

absent

$N{\equiv}O^{\oplus}$

mz = 30

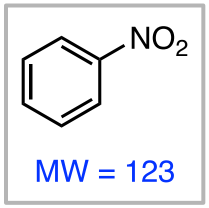
$^{\oplus}NO_2$

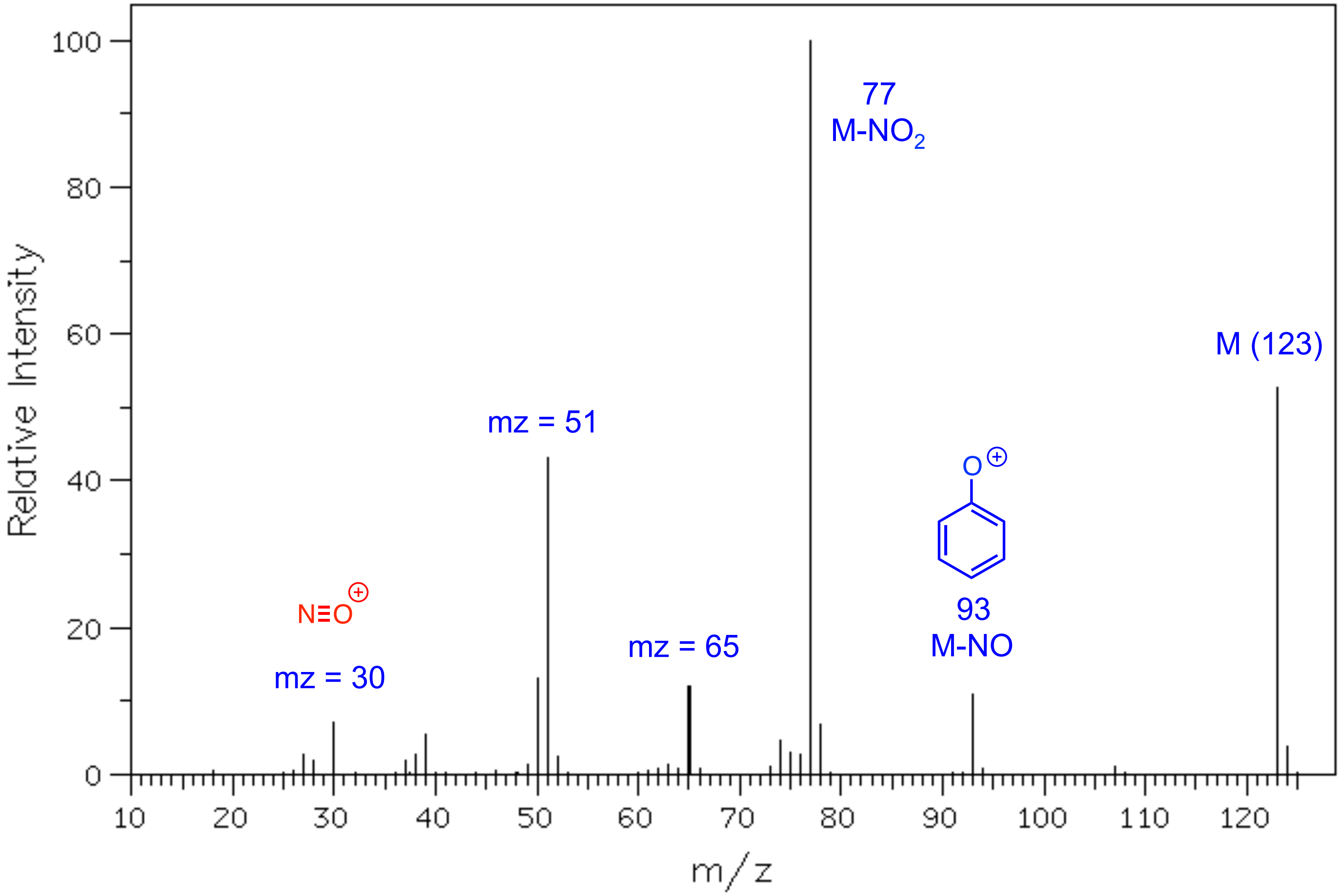
mz = 46

Mass Spectrometry: Fragmentation

Nitro Compounds

nitrobenzene



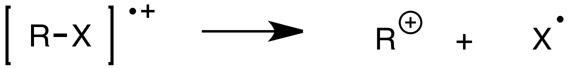


Mass Spectrometry: Fragmentation

Organic Halides

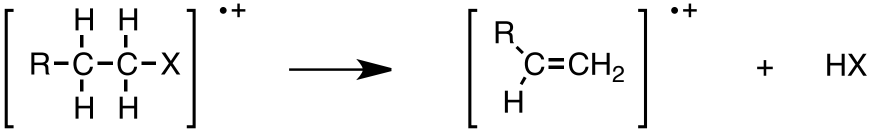
fragmentation patterns

Loss of Halide



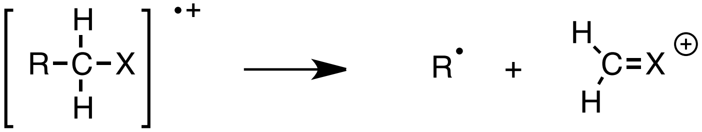
I > Br >> Cl > F

Loss of HX

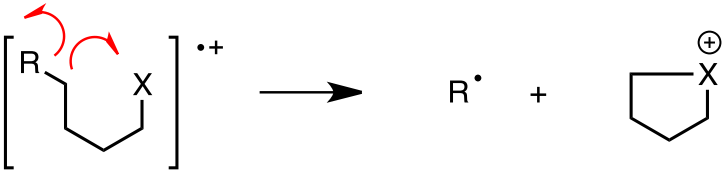


HF > HCl > HBr > HI

α-cleavage



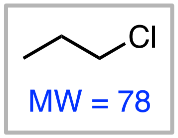
Loss of δ Chain

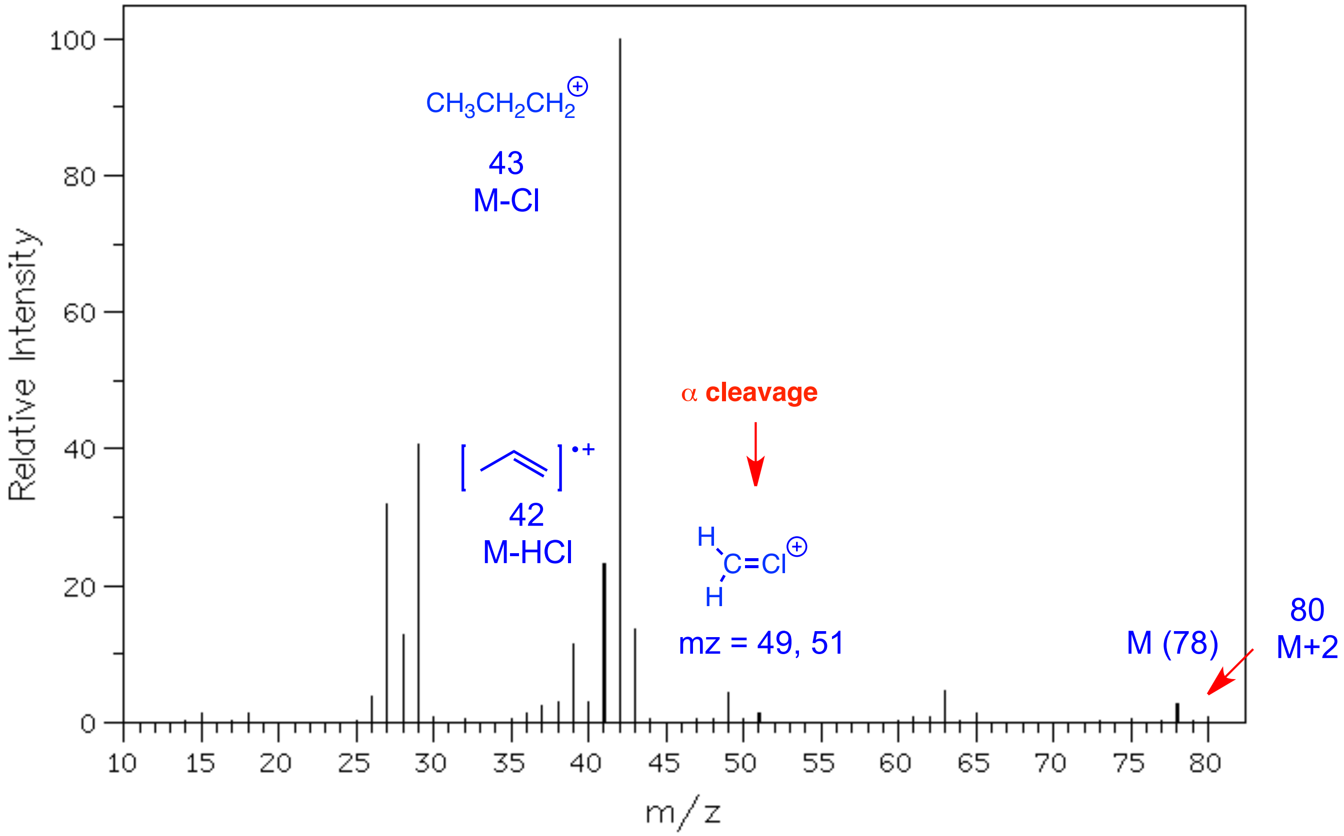


Mass Spectrometry: Fragmentation

Alkyl Halides

1-chloropropane

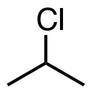




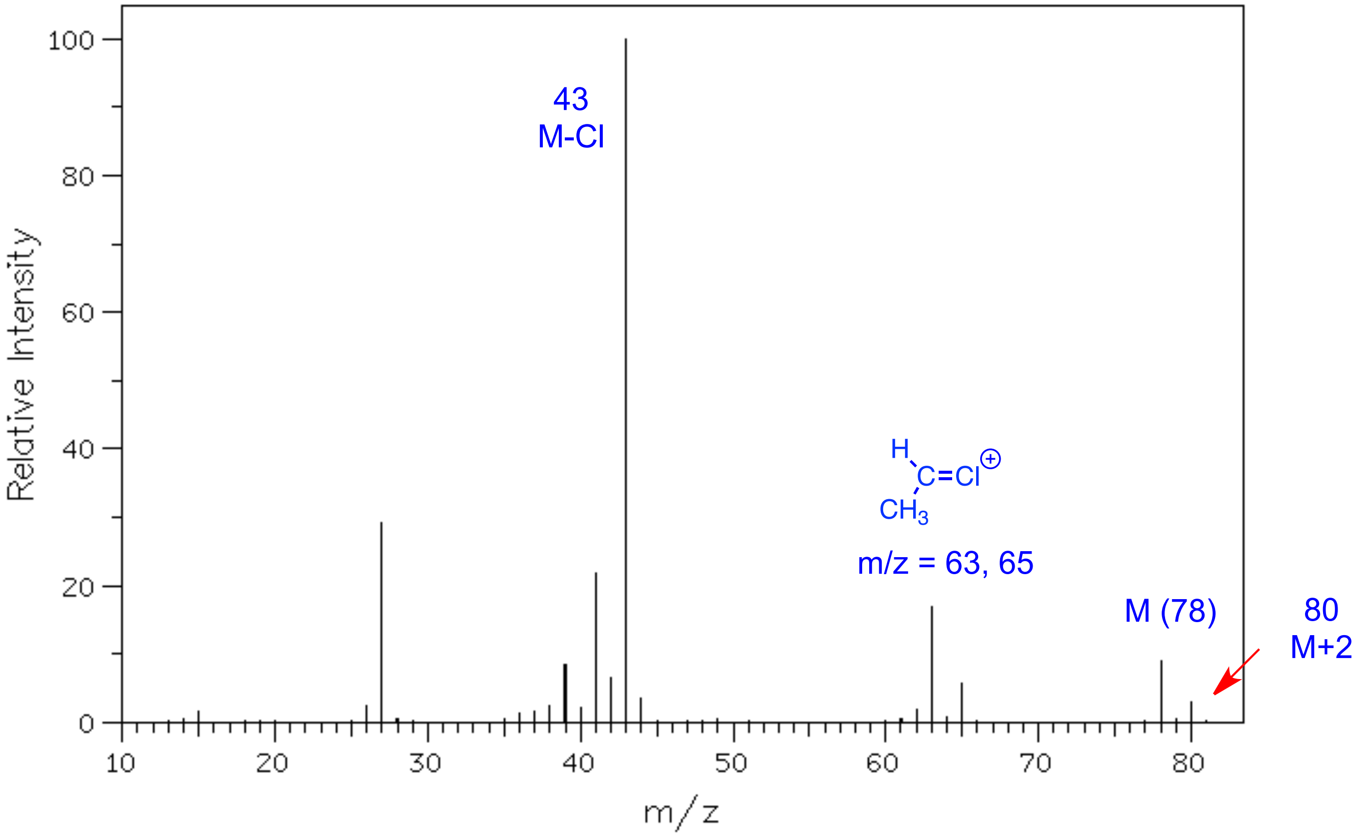
Mass Spectrometry: Fragmentation

Alkyl Halides

2-chloropropane



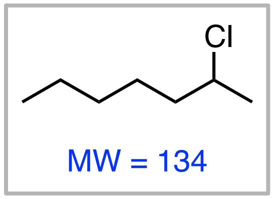
MW = 78

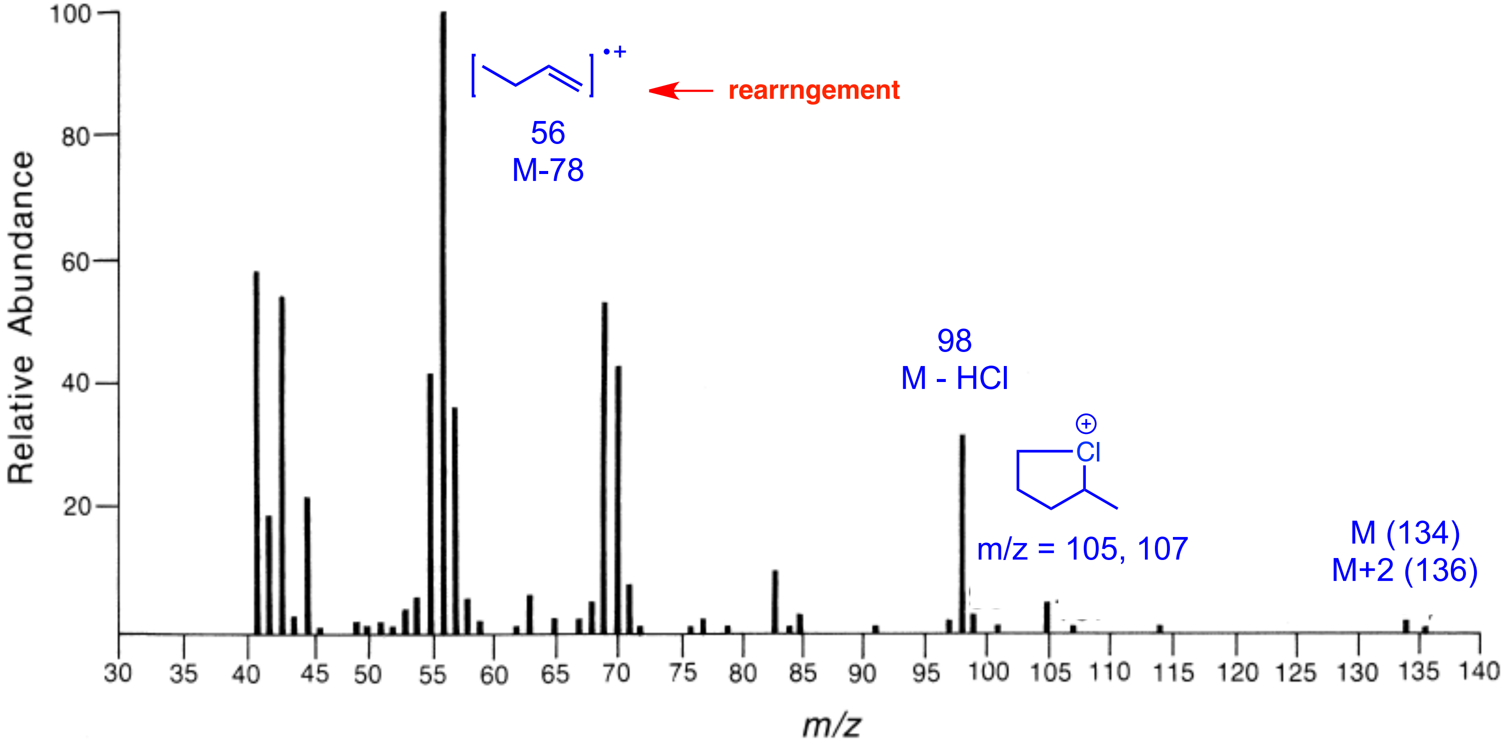


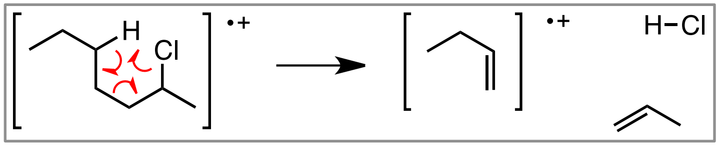
Mass Spectrometry: Fragmentation

Alkyl Halides

2-chloroheptane



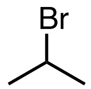




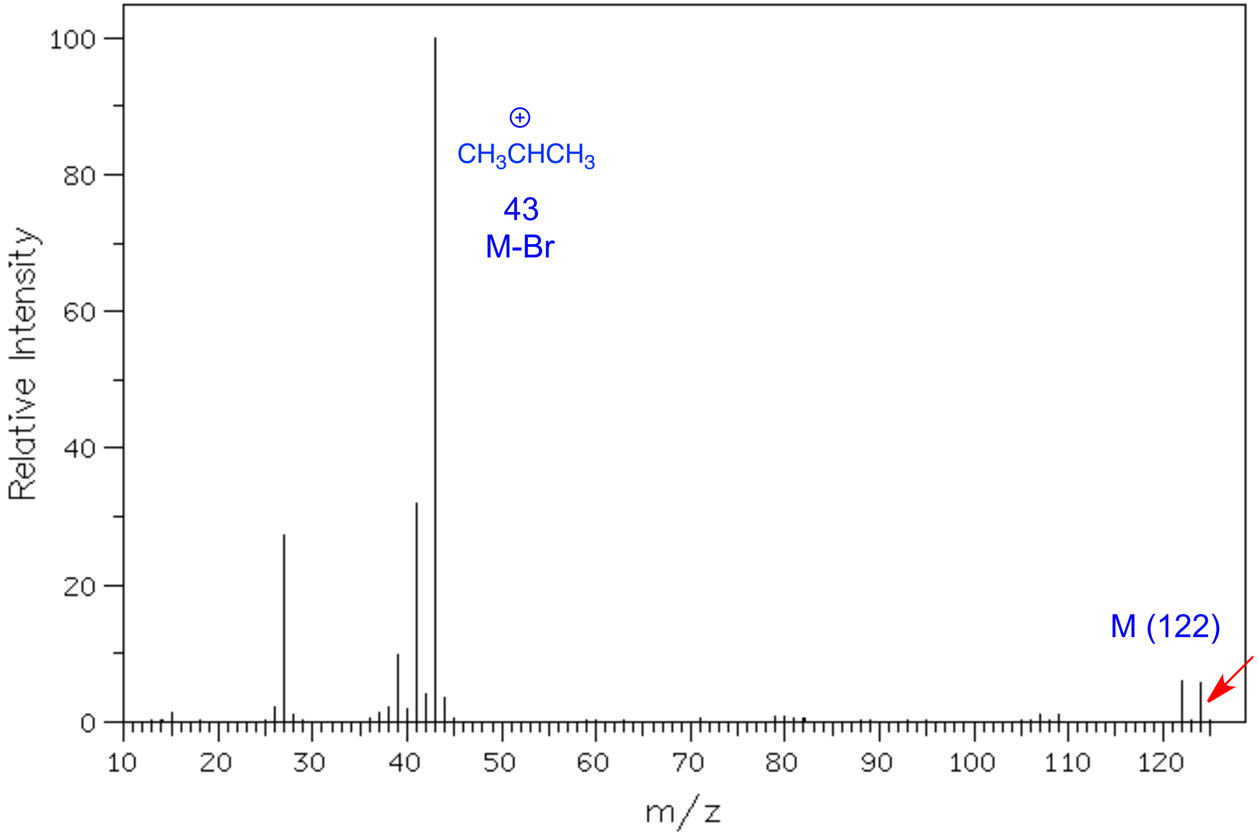
Mass Spectrometry: Fragmentation

Alkyl Halides

2-bromopropane



MW = 123



$CH_3\overset{\oplus}{C}HCH_3$

43
M-Br

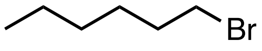
M (122)

124
M+2

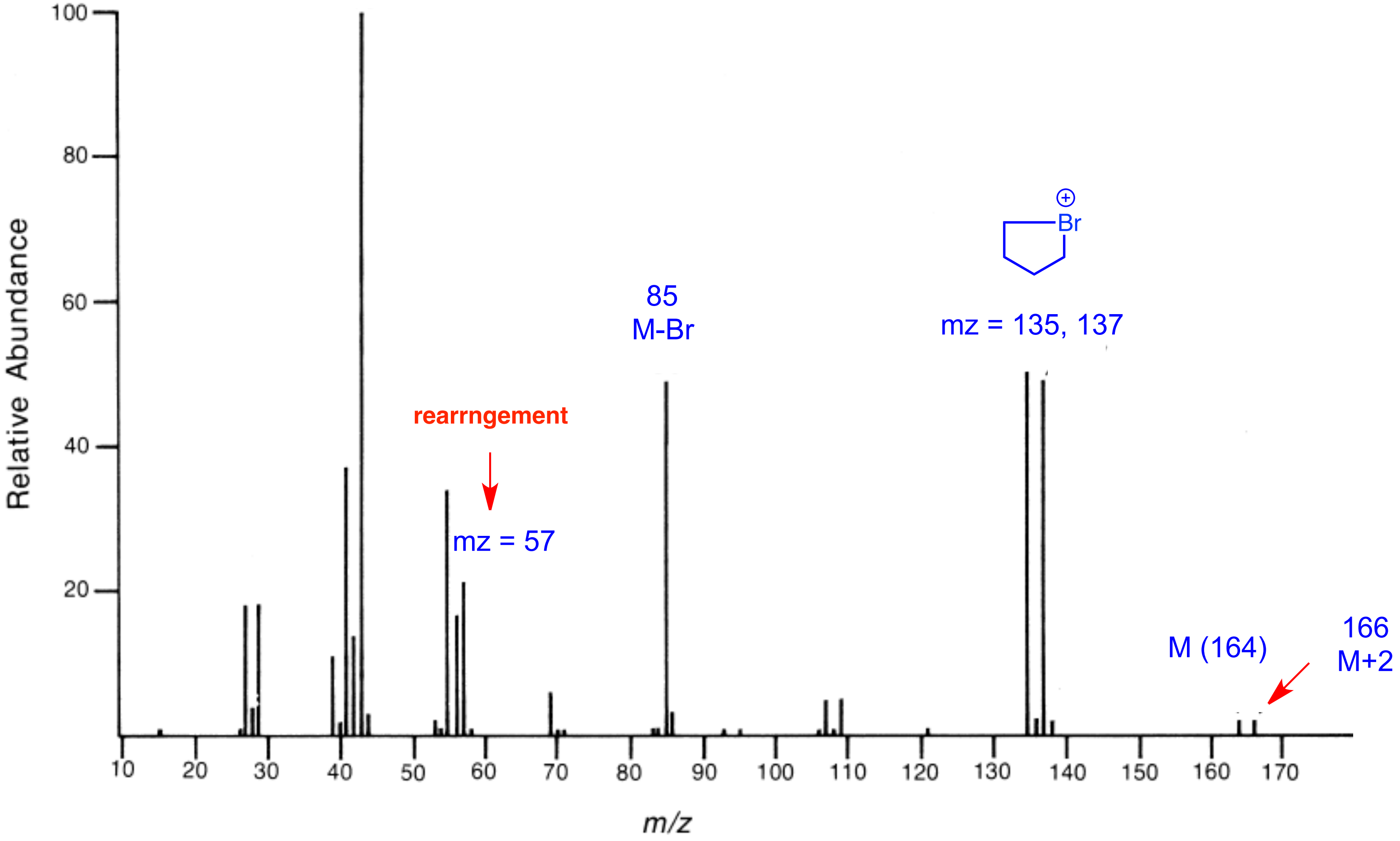
Mass Spectrometry: Fragmentation

Alkyl Halides

1-bromohexane



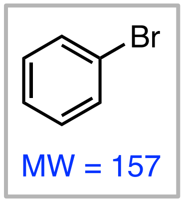
MW = 165

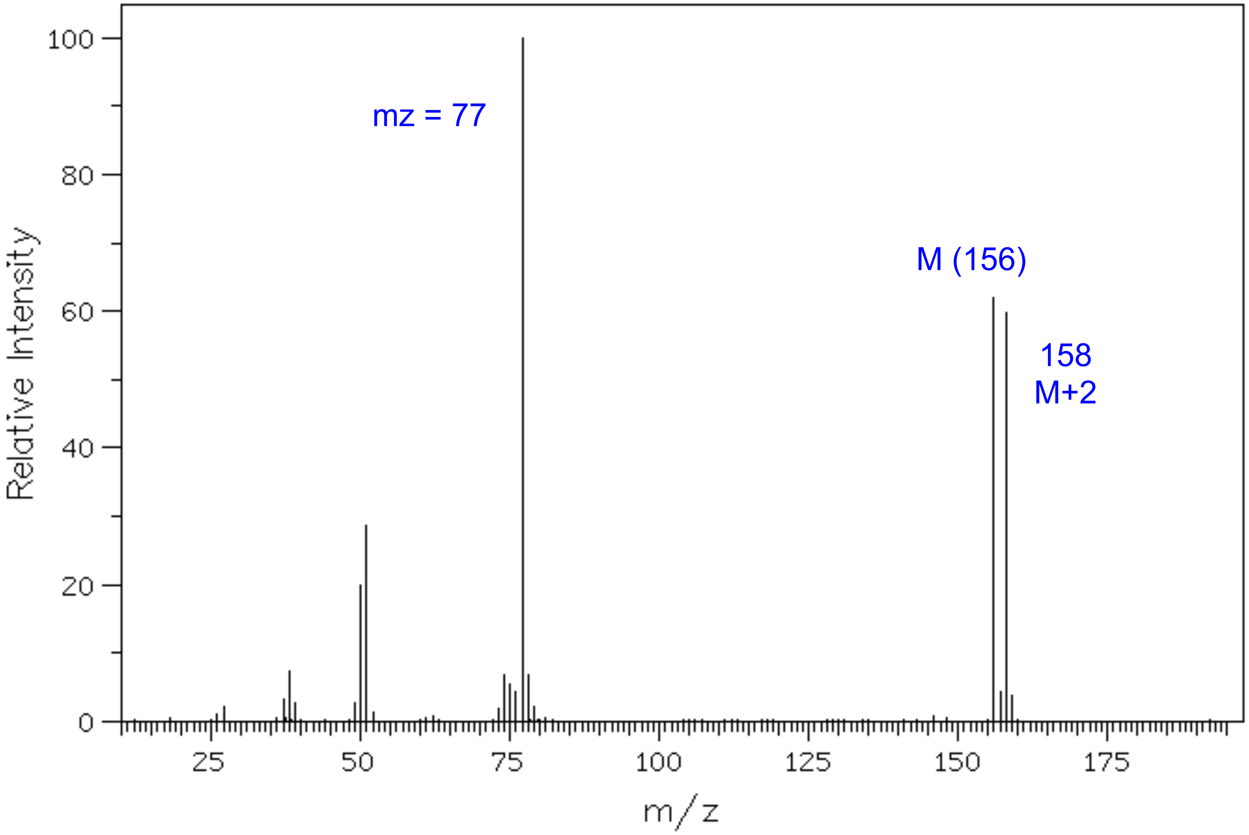


Mass Spectrometry: Fragmentation

Alkyl Halides

bromobenzene





Mass Spectrometry: Fragmentation

What Can the MS Tell You?

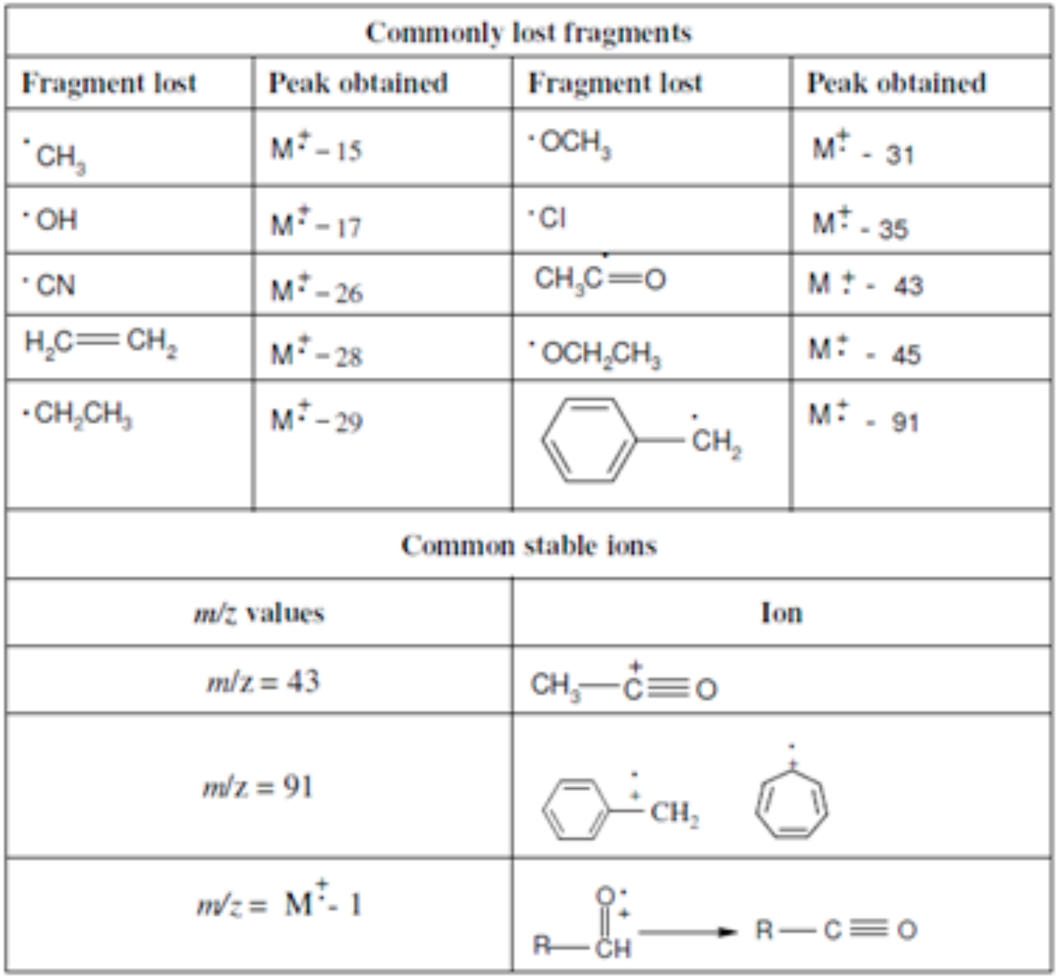
Evaluation of UnknownCompounds by Mass Spectr

1. Get an overview of the spectrum. Is it simple? Complex? Are there groups of peaks?
2. Identify and evaluate the molecular ion.
    - Is M+ strong or weak?
    - Are their significant peaks due to isotopes (e.g. M+1, M+2, etc.)?
    - Is the molecular ion an odd number (Apply the Nitrogen Rule)?
    - Is there an M-1 Peak?
    - If a molecular formular is not provided, check tables or on-line calculators to determine possible formulas
3. Evaluate the major fragments
    - What mass is lost from M+ to give these peaks?
    - What ions could give these peaks?
    - If available, use IR data to identify functionality, and consider known fragmentation patterns of these groups.
    - Consider the loss of small neutral molecules (e.g. H_2O, HOR, $H_2C{=}CH_2$, $HC{\equiv}CH$, HX, CO_2, etc.)
    - Consider possible diagnostic peaks (e.g. m/z = 29, 30, 31, 39, 41, 44, 91, 45, 59, etc.)
4. Use fragmentation information to piece together possible structure

Mass Spectrometry: Fragmentation

Commonly Lost Fragments

Pavia Appendix 11



Commonly lost fragments

Fragment lost	Peak obtained	Fragment lost	Peak obtained
$\cdot CH_3$	$M^{+\cdot} - 15$	$\cdot OCH_3$	$M^{+\cdot} - 31$
$\cdot OH$	$M^{+\cdot} - 17$	$\cdot Cl$	$M^{+\cdot} - 35$
$\cdot CN$	$M^{+\cdot} - 26$	$CH_3\dot{C}{=}O$	$M^{+\cdot} - 43$
$H_2C{=}CH_2$	$M^{+\cdot} - 28$	$\cdot OCH_2CH_3$	$M^{+\cdot} - 45$
$\cdot CH_2CH_3$	$M^{+\cdot} - 29$	$C_6H_5\dot{C}H_2$	$M^{+\cdot} - 91$

Common stable ions

m/z values	Ion
m/z = 43	$CH_3-\overset{+}{C}\equiv O$
m/z = 91	$C_6H_5\overset{+}{C}H_2$ $C_7H_7^{+}$
m/z = $M^{+\cdot} - 1$	$R-\overset{\overset{+\cdot}{O}}{\overset{\Vert}{C}}H \longrightarrow R-C\equiv O$

Mass Spectrometry: Fragmentation

Common Fragment Peaks

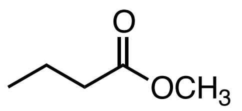
Pavia Appendix 12

Peak	*Fragment lost*	*Interpretation*
M–1	H·	aldehydes, 3° alcohols, cyclic amines
M–2	Multiple H·	2° alcohols
M–3	Multiple H·	1° alcohols
M–15	CH3·	methyl groups
M–17	HO·	alcohols, phenols, carboxylic acids
M–18	H_2O	alcohols
M–26	HC≡CH	
M–27	$\cdot HC=CH_2$	
M–28	$CH_2=CH_2$	cyclic alkanes, alkenes $CH_3CH_2CH_2C(=O)X$ [McLafferty rearr.]

Mass Spectrometry: Fragmentation

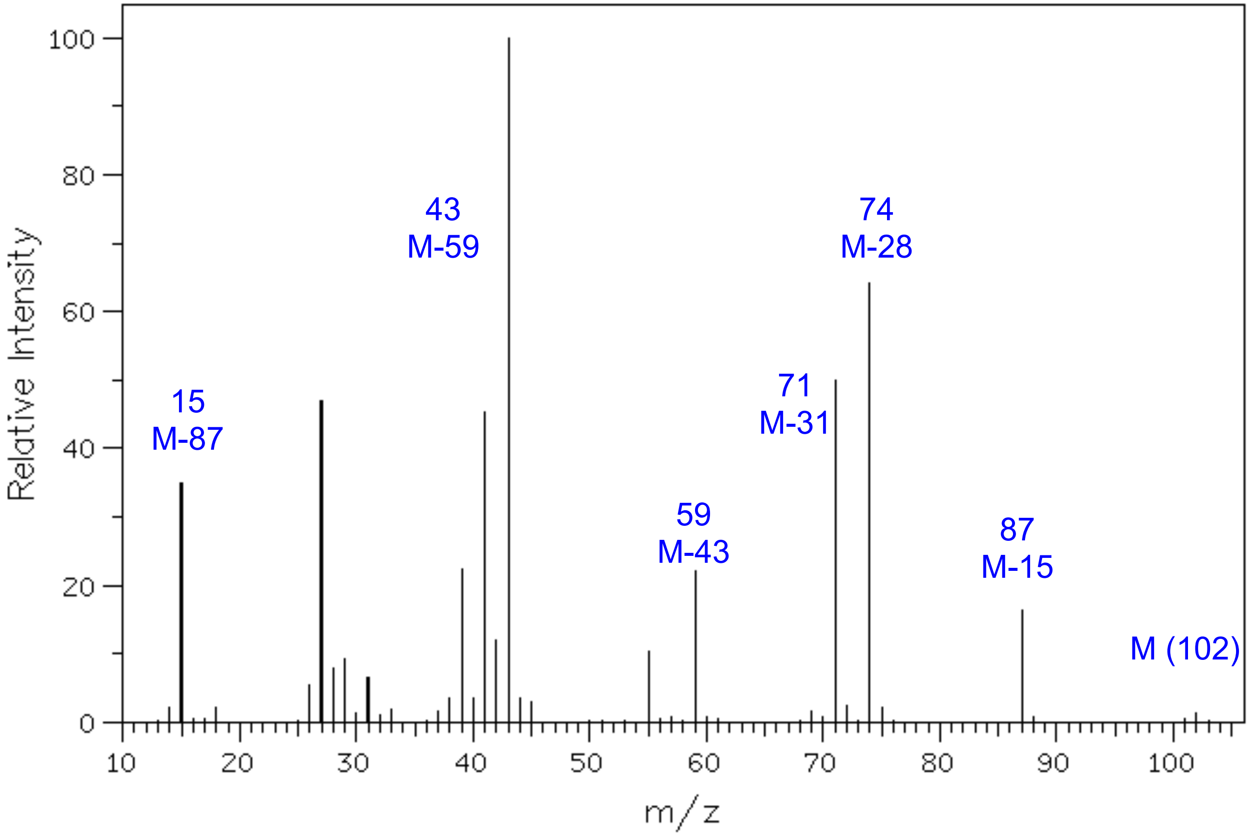
Reporting Mass Spec Data

Low Resolution Mass Spec



MW = 102

peak	intensity
14.0	2.1
15.0	35.0
18.0	2.1
26.0	5.4
27.0	47.0
28.0	7.9
29.0	9.2
30.0	1.2
31.0	6.5
32.0	1.1
33.0	1.9
37.0	1.6
38.0	3.5
39.0	22.5
40.0	3.5
41.0	45.3
42.0	12.1
43.0	100.0
44.0	3.6
45.0	3.1
55.0	10.4
59.0	22.2
69.0	1.5
71.0	49.9
72.0	2.3
74.0	64.2
75.0	2.2
87.0	16.4
102.0	1.4

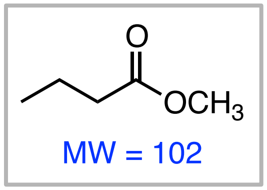


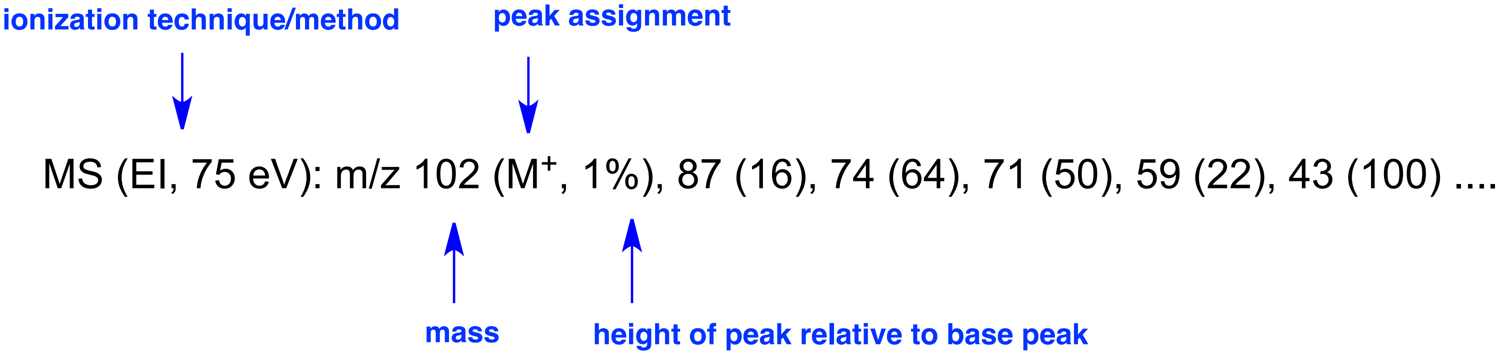
Source Temperature: 240 °C
Sample Temperature: 180 °C
RESERVOIR, 75 eV

Mass Spectrometry

Reporting Mass Spec Data

Low Resolution Mass Spec





ionization technique/method

peak assignment

MS (EI, 75 eV): m/z 102 (M^+, 1%), 87 (16), 74 (64), 71 (50), 59 (22), 43 (100) ....

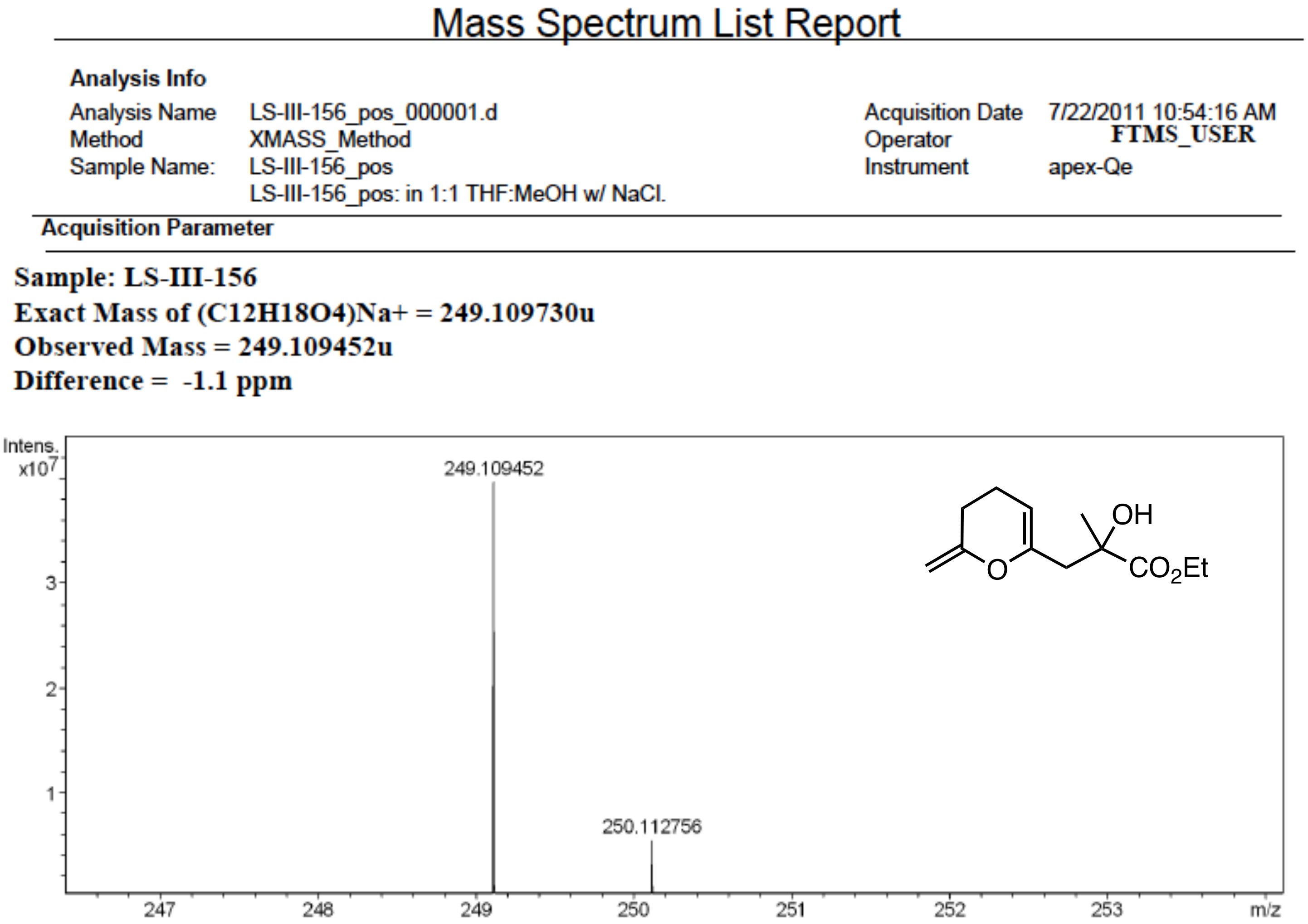
mass

height of peak relative to base peak

Mass Spectrometry

Reporting Mass Spec Data

High Resolution Mass Spec



Mass Spectrum List Report

Analysis Info

Analysis Name	LS-III-156_pos_000001.d	Acquisition Date	7/22/2011 10:54:16 AM
Method	XMASS_Method	Operator	**FTMS_USER**
Sample Name:	LS-III-156_pos	Instrument	apex-Qe
	LS-III-156_pos: in 1:1 THF:MeOH w/ NaCl.		

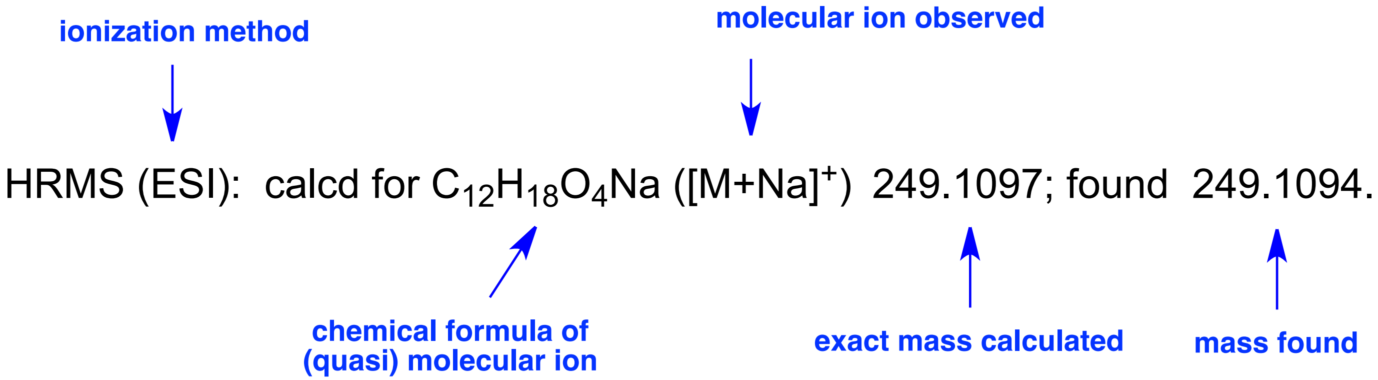
Acquisition Parameter

Sample: LS-III-156
Exact Mass of (C12H18O4)Na+ = 249.109730u
Observed Mass = 249.109452u
Difference = -1.1 ppm

Mass Spectrometry

Reporting Mass Spec Data

High Resolution Mass Spec



ionization method

molecular ion observed

HRMS (ESI): calcd for $C_{12}H_{18}O_4Na$ ([M+Na]$^+$) 249.1097; found 249.1094.

chemical formula of (quasi) molecular ion

exact mass calculated

mass found