Lecture Interp-3:
The Molecular Ion

(McLafferty & Turecek 1993, Chapter 3)

CU- Boulder

CHEM-5181

Mass Spectrometry & Chromatography

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Last Updated: Oct. 2013

Business Items

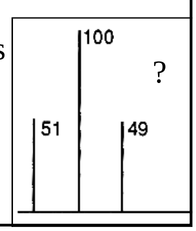
- Delinquent HW questions:
  - 10.1: LV install status: missing Abby, Lucas, Randall, Suichi
    - https://piazza.com/class/hiy250ehses10l?cid=106
  - 10.3: Asana install and test: missing Lucas, Randall, Ted, Scott
  - Please complete by the end of the week to save ½ of the HW points.
  - May assign tasks via Asana in the future, you need to monitor it
- Office hrs tomorrow Wed 4:30-6 per usual
- Questions or comments?

Standard Interpretation Procedure

2. Using isotopic abundances (where possible) deduce the elemental composition of each peak in the spectrum; calculate rings plus double bonds (last day).
3. Test molecular ion identity; must be the highest mass peak in spectrum, odd-electron ion, and give logical neutral losses. Check with CI or other soft ionization (TODAY).
4. Mark ‘important’ ions: odd-electron and those of highest abundance, highest mass, and/or highest in a group of peaks (TODAY).

The Molecular Ion

- Most valuable info of the mass spectrum
  - Molecular mass
  - Elemental composition
  - Fragments must be consistent with it
- Not always stable with EI
  - Careful about overinterpreting peak of highest *m/z*!
  - Use soft-ionization such as CI in parallel
    - But careful with e.g. Na^+ adducts
- MS Definition:
  - m/z of the molecular ion is the peak that contains the most abundant isotope of all the elements involved (by convention)
    - Won’t always be most abundant peak

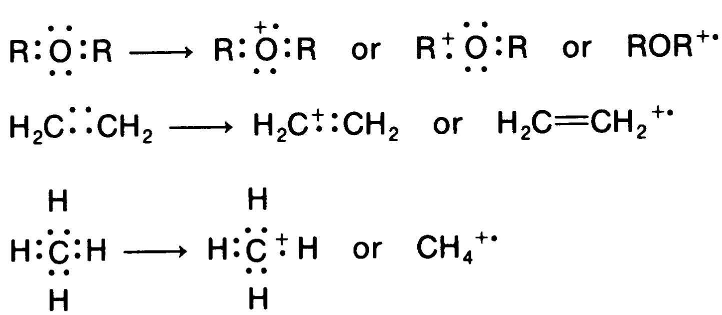


Requirements for the Molecular Ion (EI)

- Necessary *but not sufficient* conditions
  - It must be the ion of highest mass (isotope caveat)
  - It must be an odd-electron ion (for EI)
  - It must be capable of yielding the most important ions in the high-mass region by loss of *logical* neutral species
- If candidate fails either test, cannot be MI
- If candidate passes all tests, may or may not be MI

Odd-Electron Ions

- For EI, molecule becomes ionized by loosing one electron
  - Must have an unpaired electron (so it's a radical)



From McLafferty, Fig. 3.1-3.3

Even Electron Ions

- Even-electron ions:
  - All electrons on the outer shell are fully paired
  - Generally more stable
  - Often the more abundant fragment ions

$$CH_4^{+\cdot} \rightarrow CH_3^{+} + H^{\cdot}$$

  - Most ESI, CI (e.g. H^+ transfer) give even electron ions such as MH^+, resulting in lower fragmentation

More on Odd- & Even-Electron Ions

- If you can establish the elemental composition of the molecular ion (or *any* ion), the rings-plus-double-bonds rule will show whether ion is odd or even-electron:
  - Even: integer + 1/2 RPDB
  - Odd: integer RPDB
  - $C_xH_yN_zO_n$:

$$\boxed{RPDB = x - 1/2\,y + 1/2\,z + 1}$$

- Even or Odd?
  - $C_5H_5N^+$
  - $C_7H_5O^+$
  - H_3O^+

Clicker answer:
A. All odd
B. 2 odd and 1 even
C. 1 odd and 2 even
D. Some more even than others
E. I don’t know
F. Even Schmeven

The Nitrogen Rule I

- For most elements in organic compounds, there is a relationship between mass of the most abundant isotope and the valence
  - Both odd or both even
  - N is the exception

Element	Mass	Valence
H	1	1
C	12	4
O	16	2
F	19	1
Si	28 (30)	4
P	31	3
S	32 (34)	2
Cl	35 (37)	1
Br	79 (81)	1
I	127	1

The Nitrogen Rule II

- 'Nitrogen Rule': If a compound contains no (or even number of) N atoms, its molecular ion will be at an even mass number

Compound	Formula	Nominal mass
Ethane	C_2H_6	30
Octane	C_8H_{18}	114
Ethanol	C_2H_6O	46
Propanoic acid	$C_3H_6O_2$	74
Dichloromethane	CH_2Cl_2	84, 86, 88 (isotopes)
Hexafluoroethane	C_2F_6	138
Carbon disulfide	CS_2	76
Iodomethane	CH_3I	142
Ammonia	NH_3	17
Pyridine	C_5H_5N	79

The Nitrogen Rule III

- N-Rule applies to all ions
  - An odd-electron ion will be at an even mass number if it contains an even number of nitrogen atoms
  - An even-electron ion containing an even number of nitrogen atoms will appear at an odd mass number

Table 3.1. *Nitrogen rule.*

Mass values:	Odd	Even
N_0, N_2, N_4, . . .	EE^+	$OE^{+\cdot}$
N_1, N_3, N_5, . . .	$OE^{+\cdot}$	EE^+

Which ions are odd vs. even?

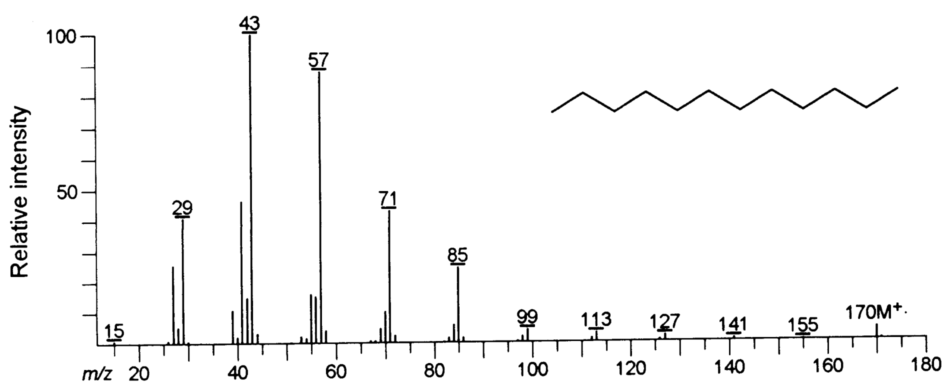


Figure 3.2. Mass spectrum of dodecane.

Nitrogen Rule Practice

- Which of the following are $OE^{+\cdot}$ and EE^{+}?
- Which have odd and even mass? Does it agree with N-Rule?
  - $C_2H_4^{+}$
  - $C_3H_7O^{+}$
  - $C_4H_9N^{+}$
  - $C_3H_9^{+}$
  - $C_4H_8NO^{+}$
  - $C_7H_{15}ClBr^{+}$
  - $C_3F_{10}^{+}$
  - $C_{29}F_{29}^{+}$
  - $C_3H_9SiO^{+}$

Clicker Q: how many are odd vs even electron ions?

A. 6 odd and 3 even
B. 5 odd and 4 even
C. 4 odd and 5 even
D. 3 odd and 6 even
E. I don't know
F. I am not paying attention

Clicker Question: N-Rule

- Choose one answer below

A. An odd-electron ion will be at an even mass number if it contains an even number of nitrogen atoms
B. An odd-electron ion will be at an odd mass number if it contains an even number of nitrogen atoms
C. An even-electron ion containing an even number of nitrogen atoms will appear at an odd mass number
D. A and C
E. A, B, and C

Relative Importance of Peaks

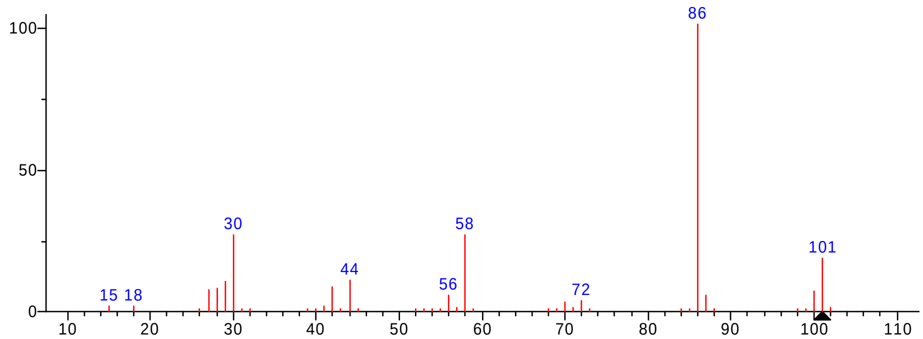
- OE $^{+\cdot}$ have special mechanistic significance
  - Mark all *important* OE $^{+\cdot}$ ions directly on the spectrum
- Importance increases with
  - Intensity
  - *m/z*
  - Mass in the peak group
  - What about isotopic peaks (e.g. ^{13}C)?

Clicker Question

A. CH_4^{++} is an odd electron ion
B. H_2O^- is an odd electron ion
C. $^{13}CH_4^+$ is an odd electron ion
D. A, B, and C
E. I don't know

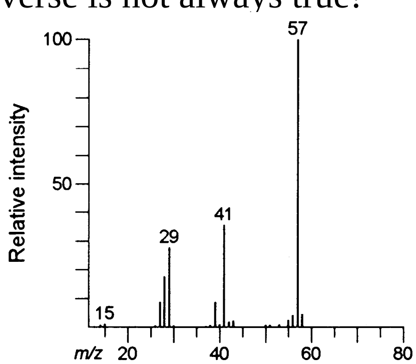
Imp. OE $^{+\cdot}$ ions at low *m/z: unlikely!*

- Important OE $^{+\cdot}$ ions are even less likely at low *m/z*
  - Intense even mass peaks in that region usually have an odd-number of N



Corollary to the Nitrogen Rule

- A scarcity of important even-mass ions, especially at lower *m/z*, indicates an even mass-molecular weight
  - The reverse is not always true!



From McLafferty, Fig. 3.1

Logical Neutral Losses I

- Only a certain number of low mass neutral fragments are commonly lost in decompositions of molecular ions
- Small neutral fragments lost from the molecular ion are commonly those attached by a single bond
  - Mass losses of 4 to 14 and 21 to 25 that give important peaks are highly unlikely - WHY?

Logical Neutral Losses II

- The presence of an 'important' ion separated from the highest mass ion by an anomalous mass or elemental formula will indicate that the latter ion is not the molecular ion!
  - E.g., if there is an abundant ion 5 mass units below the ion of highest *m/z*, can that be the molecular ion?
- Clicker Q: Can the ion of highest mass (first) be the molecular ion if the following are the major ions of high mass?

A. $C_{10}H_{15}O$, $C_{10}H_{14}O$, $C_9H_{12}O$, $C_{10}H_{13}$, $C_8H_{10}O$

B. $C_{10}H_{14}$, $C_{10}H_{13}$, C_9H_{11}, C_8H_9, C_7H_8, C_7H_7

C. Both can be

D. Neither can be

E. I don't know

Table A.5: Common Neutral Losses

Table A.5. *Common neutral fragments.*

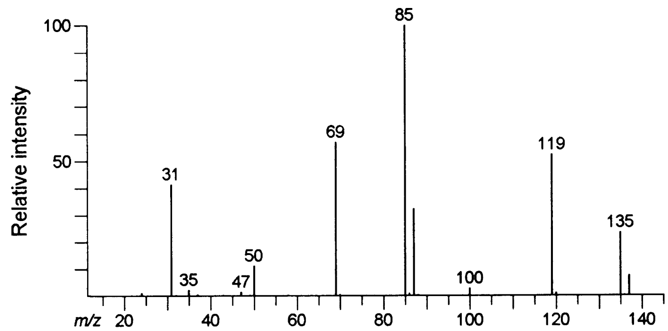
Δ^a	Mass	Formula	Example[b,c]
-4	79	Br	R⌇Br
	121	$C_7H_5O_2$	Benzoates
	51 65	C_3HN, C_4H_3N	Some nitrogen heterocyclic compounds
-3	38	H_6O_2	Some polycarboxylic acids
-2	39 53 67	C_nH_{2n-3}	Allyl esters and some cyclic carbonates—specific rearrangement loss of (C_nH_{2n-1} − 2H); some propargyl and allenic derivatives
-1	26 40 54	C_nH_{2n-2}	Aromatics; alkenyl aryl ethers
	54 68 82	C_nH_{2n-2}	4-Y-cycloalkenyls; $M^{+\cdot} - 69 - (68)_n$ in polyisoprenes[c]
	54	C_3H_2O	Cyclic—CO—CH═CH—
	26 40	$C_nH_{2n}CN$	R⌇CN, R⌇CH_2CN (stable R^+ only)
0	27 41 55 69, etc.	C_nH_{2n-1}	RCOOR′-specific rearrangement loss of (R − 2H) or (R′ − 2H) + (R − H), also from carbonates, amides, larger ketones, etc.; loss of activated C_nH_{2n-1} groups
	27	HCN	Nitrogen heterocyclic compounds, cyanides, aryl-NH_2, enamines, imines
$+1$	(±14: Homologous impurity)		
	28 42 56	C_nH_{2n}	RCH_2COCH_2R-specific rearrangement loss of (R − H) or $(R - H)_2$, also from many unsaturated functional groups; retro-Diels-Alder[c]
	14	N	Aryl—NO
	28	N_2	Aryl—N═N—Aryl, >C═N_2, cyclic—N═N—
	28	CO	Aromatic oxygen compounds (carbonyls, phenols), cyclic ketones, R⌇C═O^{+c}
	42 56 70	$C_nH_{2n}CO$	Unsaturated acetamides, alkanoates; di-, cyclic, and complex ketones; specific H rearrangement loss of —CR_2—CO—
$+2$	29	CH_3N	Some unsaturated-, aryl—$N(CH_3)_2$
	43 57 71	HNCO, $C_nH_{2n-1}NO$	Loss of—NR—CO—from carbamates, cyclic amides, uracils
	1	H	Labile H; aryl—CH_2—H, RC≡CH, alkyl cyanides, lower fluorides and aldehydes (stable RCO^+), cyclopropyl compounds
	15 29 43 57 71, etc.	C_nH_{2n+1}	Alkyl loss: α-cleavage or branched site favored (loss of largest R); elimination from cycloalkyl group with H rearrangement[b]
	29 43 57	$C_nH_{2n+1}CO$	$C_nH_{2n+1}CO$⌇R (stable R^+ only)

Molecular Ion Abundance I

- Abundance of molecular ion depends on:
  - Its stability (often not in spectrum)
  - The amount of energy needed to ionize the molecule
- There is a correlation between those properties and the structure of the molecule
  - The magnitude of $M^{+\cdot}$ provides an indication about the structure of the molecule

Unknown 3.5

m/z	Int.
31	42.
32	0.5
35	2.5
37	0.7
42.5	0.5
47	1.7
49	0.6
50	11.
69	57.
70	0.7
85	100.
86	1.1
87	33.
88	0.4
100	2.8
119	52.
120	1.2
135	24.
136	0.5
137	7.7



- Elemental composition
  - A+2, A+1, O, H, A
- Molecule?
- RPDB?
- Even/Odd e- ions?
  - Molec. ion?
- N-Rule?
- Neutral losses?

Molecular Ion Abundance II

- In general the chemical stability of $M^{+\cdot}$ parallels the stability of the molecule
  - $M^{+\cdot}$ increases with 'un-saturation' and rings
  - $M^{+\cdot}$ decreases with chain branching
  - Effect of MW is not as clear

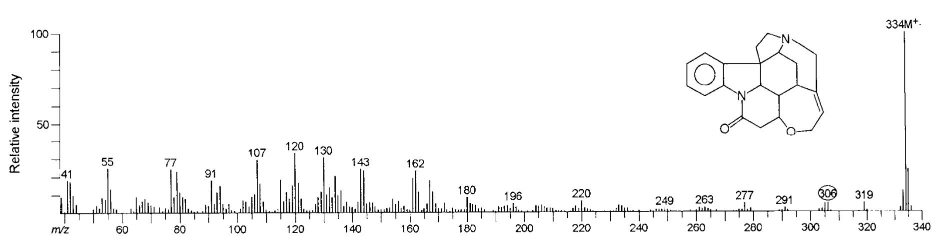


Figure 3.28. Mass spectrum of strychnine.

Molecular Ion Abundance III

- If less energy is needed to ionize the molecule, more molecular ions of lower internal energy ('cool' ions) will be formed
  - $M^{+\cdot}$ will be higher
- Ease of ionization increases down on a column in the periodic table or to the left in a row
  - E.g alcohols vs. mercaptans (3.8 vs. 3.21)
  - E.g. alcohols vs. amines (3.8 vs. 3.16)

Appendix: Very useful tables from McLafferty

Table A.4: $M^{+\cdot}$ Abundance vs. compound type

Table A.4. *Molecular ion abundances vs. compound type* (C_n indicates an unbranched alkyl chain of *n* carbon atoms).

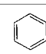
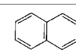
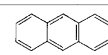
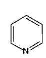
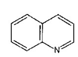
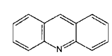
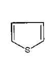
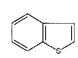
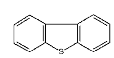
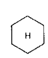
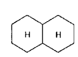
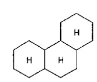
	Intensity of $M^{+\cdot}$ peak relative to most intense peak					
Compound type	M.W. ~ 75		M.W. ~ 130		M.W. ~ 185	
Aromatic		100		100		100
Heterocyclic		100		100		100
		100		100		100
Cycloalkane		70		90		90
Thiol	C_3SH	100	C_7SH	40	$C_{10}SH$	46
Sulfide	$C.SC_2$	65	C_1SC_6	45	C_5SC_5	13
Conjugated olefin	Hexatriene	55	*allo*-Ocimene	40	—	
Olefin	$C_2C{=}CC_2$	35	$C_3C{-}CC_4$	20	$C_{11}C{-}C$	3
			$C_6C{=}CC$	7		
Amide	C_2CONH_2	55	C_6CONH_2	1	$C_{11}CONH_2$	1
	$HCON(C_1)_2$	100	$C_1CON(C_2)_2$	4	$C_1CON(C_4)_2$	5
Acid	C_2COOH	80	C_6COOH	0.5	C_9COOH	9
Ketone[a]	C_1COC_2	25	C_2COC_5	8	C_6COC_5	8
			C_1COC_6	3	$C.COC_9$	10
Aldehyde[a]	C_3CHO	45	C_7CHO	2	$C_{12}CHO$	5
Alkane	C_5	9	C_9	6	C_{13}	5
Amine[a]	C_4NH_2	10	C_8NH_2	0.5	$C_{12}NH_2$	2
	$(C_2)_2NH$	30	$(C_4)_2NH$	11	$(C_7)_2NH$	4
			$(C_2)_3N$	20	$(C_4)_3N$	7
Ether[a]	C_2OC_2	30	C_4OC_4	2	C_6OC_6	0.05
Ester[a]	C_1COOC	20	C_1COOC_5	0.1	C_1COOC_8	0.1

Table A.6 Common Fragment Ions

Table A.6. *Common fragment ions (*, most important source for this mass per McLafferty and Venkataraghavan 1982).*

Δ[a]	m/z	Formula	Compound type[b]
X	31, 50, 69, 100, 119, 131, 169, 181, 193	C_nF_m	Perfluoroalkanes
X	38, 39, 50*, 51*, 63*, 64*, 65*, 74, 75*, 76*	Aromatic series—low	More abundant for aromatic compounds with electronega substituents
X	39, 40, 51, 52*, 65, 66*, 67, 77*, 78*, 79	Aromatic series—high	More abundant with electron-donating substituents, N an heterocycles
X	87–89*, 99–101, 112, 113, 125–127*, 138, 139, 150–152	Polycyclic aromatics	Plus ions of low aromatic series
X	45, 57, 58, 59, 69, 71, 83–85, 97, 98, 109–112	Endo-sulfur aromatic series	Thiophenes
X	69, 81–84, 95–97, 107–110	Exo-sulfur aromatic series	Sulfur attached to an aromatic ring
X	73, 147, 207, 221, 281, 295, 355		Dimethylsiloxanes
−7	76* 90* 104* 118* 132*	C_nH_{2n-8}	R-phenyl═HY*, R-phenyl═YY′, R-phenyl—C_nH_{2n-1}═HY
−6	77* 91* 105 119* 133*	$C_6H_5C_nH_{2n}$	Phenylalkyl (specific cleavage, also rearrangement)
	105* 119 133	$C_nH_{2n+1}C_6H_4CO$	Benzoyl (specific); 119 and above, unsaturated or cyclic phenoxy
	63 77 91	$C_nH_{2n+1}O_3$	ROCOOR-specific rearrangement loss of (R − 2H) or (R − 2H) + (R − H)
	49 63 77 91 105	$C_nH_{2n}Cl$	Chloroalkyl; *m/z* 91 largest for $R(CH_2)_5Cl$
−5	77 91 105 119 133	$C_nH_{2n-7}N$	R-pyridyl═HY*, R-phenyl—N(R′)═YY′, etc. (see 76, 90, .
	92* 106* 120* 134*	C_nH_{2n-6}	R-phenyl—CR′R″—Z—H
	92 106 120 134	$C_nH_{2n-8}O$	(—O—phenyl—R)═HY*, (—O—phenyl—R)—YY′, R-phenyl—COCHR′—Z—H
	78 92 106 120 134	$C_5H_4NC_nH_{2n}$	Pyridyl, aminoaromatic (specific cleavage, also rearrangement)

- Table A.7: Common elemental compositions of molecular ions

Table A.7. *Common elemental compositions of molecular ions.*[a]

m/z	Composition
16	CH_4
17	H_3N
18	H_2O
26	C_2H_2
27	CHN
28	C_2H_4, CO, N_2
30	C_2H_6, CH_2O, NO
31	CH_5N
32	CH_4O, H_4N_2, H_4Si, O_2
34	CH_3F, H_3P, H_2S
36	HCl
40	C_3H_4
41	C_2H_3N
42	C_3H_6, C_2H_3O, CH_2N_2
43	C_2H_5N, HN_3
44	C_2H_4O, C_3H_8, C_2HF, CO_2, N_2O
45	C_2H_7N, CH_3NO
46	C_2H_6O, C_2H_3F, CH_6Si, CH_2O_2, NO_2
48	C_2H_5F, CH_4S, CH_5P
50	C_4H_2, CH_3Cl
52	C_4H_4, CH_2F_2
53	C_3H_3N, HF_2N
54	C_4H_6, F_2O
55	C_3H_5N
56	C_4H_8, C_3H_4O, $C_2H_4N_2$
57	C_3H_7N, C_2H_3NO
58	C_3H_6O, C_4H_{10}, $C_2H_2O_2$, $C_2H_6N_2$
59	C_3H_9N, C_2H_5NO, CH_5N_3
60	C_3H_8O, C_3H_5F, $C_2H_8N_2$, $C_2H_4O_2$, C_2H_8Si, C_2H_4S, C_2HCl, CH_4N_2O, COS
61	C_2H_7NO, CH_3NO_2, CClN
62	C_3H_7F, C_2H_7P, $C_2H_6O_2$, C_2H_6S, C_2H_3Cl
64	$C_2H_2F_2$, C_2H_5FO, C_2H_5Cl, SO_2
66	C_5H_6, $C_2H_4F_2$, CF_2O, F_2N_2
67	C_4H_5N, CH_3F_2N, ClO_2
68	C_5H_8, C_4H_4O, $C_3H_4N_2$, C_3O_2, CH_2ClF
69	C_4H_7N, C_3H_3NO, $C_2H_3N_3$
70	C_5H_{10}, C_4H_6O, $C_3H_6N_2$, CH_2N_4, CHF_3
71	C_4H_9N, C_3H_5NO, F_3N
72	C_4H_8O, C_5H_{12}, $C_3H_4O_2$, C_4H_5F
73	$C_4H_{11}N$, C_3H_7NO, C_2H_3NS, $C_2H_7N_3$

Example Mass Spectra

- Show trends
  - Look for similarities to unknowns
- Refer back as we discuss fragmentation mechanisms
- Key to the symbols:

58	Important odd-electron ion
$\boxed{61}$	Important peak formed by 2H rearrangement
	Important odd-electron ion series
⊤	Important even-electron ion series
σ	Peak formed by sigma electron ionization
α	Peak formed by alpha cleavage
i	Peak formed by inductive cleavage

Alkanes & Branched Alkanes

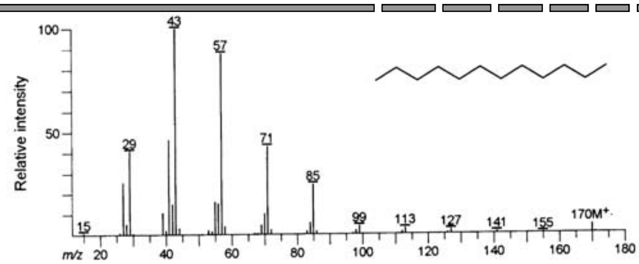


Figure 3.2. Mass spectrum of dodecane.

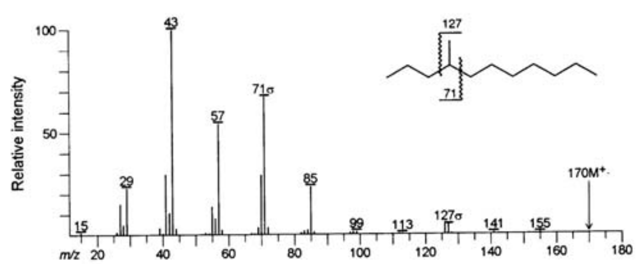


Figure 3.3. Mass spectrum of 4-methylundecane.

McLafferty Examples (not printed)

Highly Branched Alkanes & Alkenes

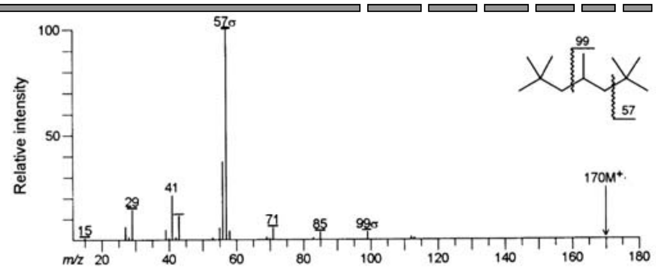


Figure 3.4. Mass spectrum of 2,2,4,6,6-pentamethylheptane.

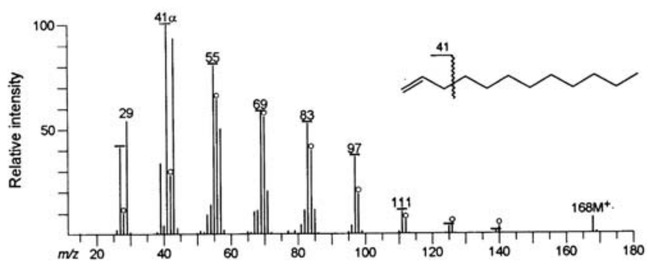


Figure 3.5. Mass spectrum of 1-dodecene.

Cycloalkanes & Aromatics

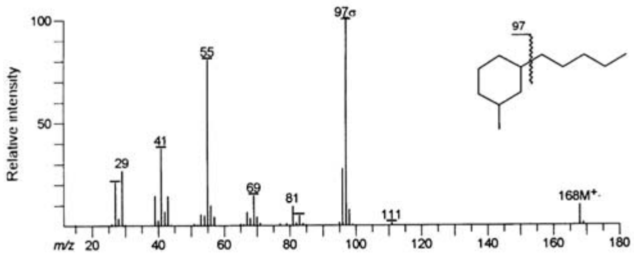


Figure 3.6. Mass spectrum of 1-methyl-3-pentylcyclohexane.

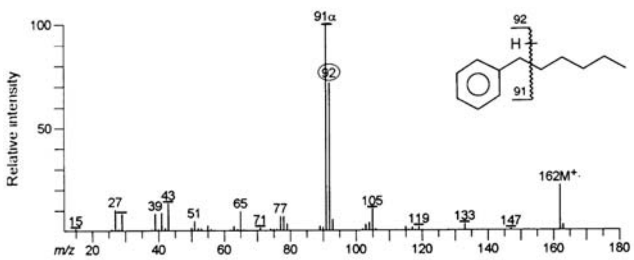


Figure 3.7. Mass spectrum of 1-phenylhexane.

Alcohols & Ethers

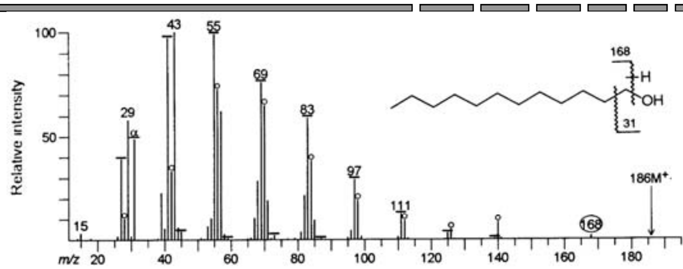


Figure 3.8. Mass spectrum of 1-dodecanol.

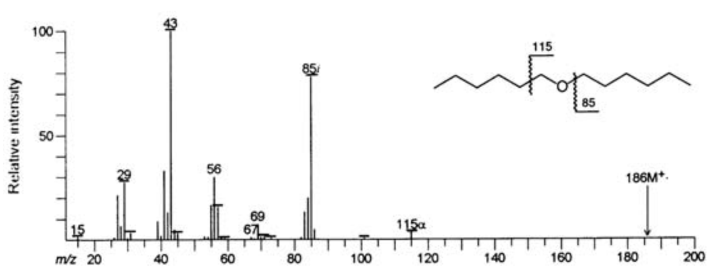


Figure 3.9. Mass spectrum of hexyl ether.

Ketones

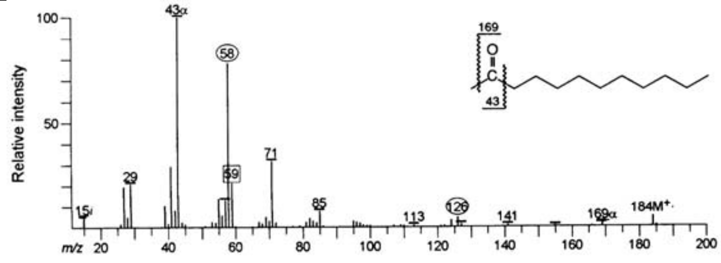


Figure 3.10. Mass spectrum of 2-dodecanone.

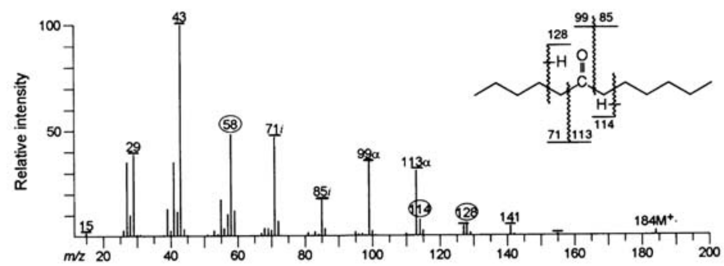


Figure 3.11. Mass spectrum of 6-dodecanone.

Acids & Esters

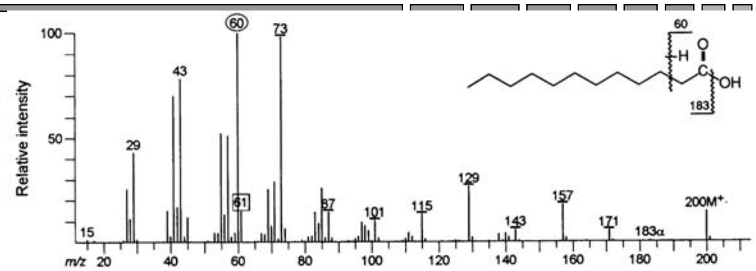


Figure 3.12. Mass spectrum of dodecanoic acid.

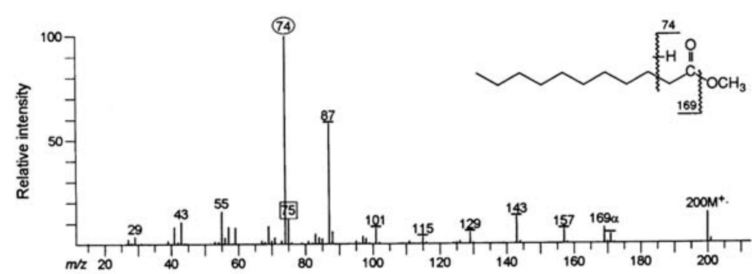


Figure 3.13. Mass spectrum of methyl undecanoate.

Esters

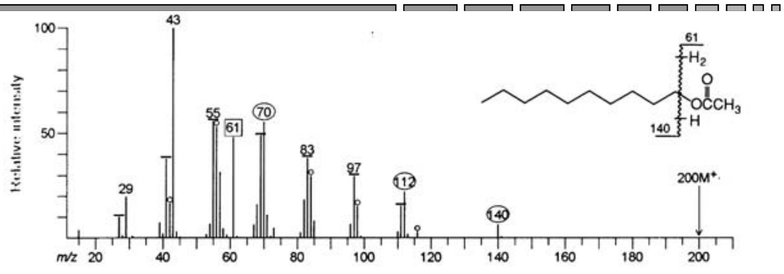


Figure 3.14. Mass spectrum of decyl acetate.

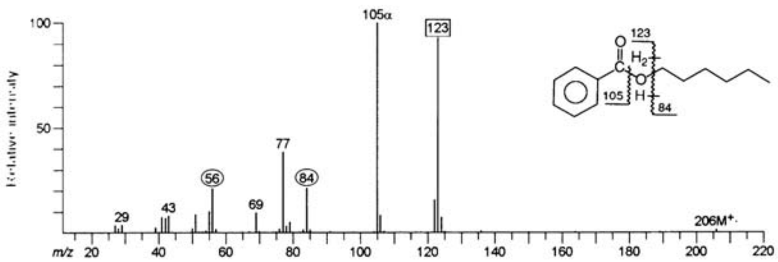


Figure 3.15. Mass spectrum of hexyl benzoate.

Amines

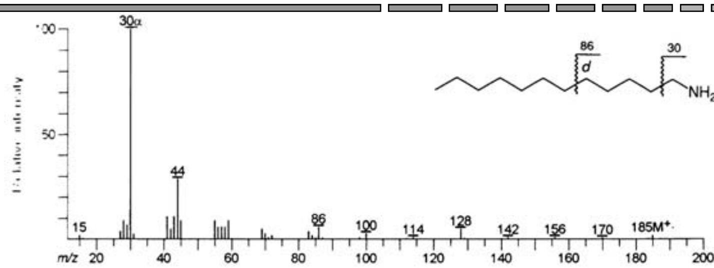


Figure 3.16. Mass spectrum of dodecylamine.

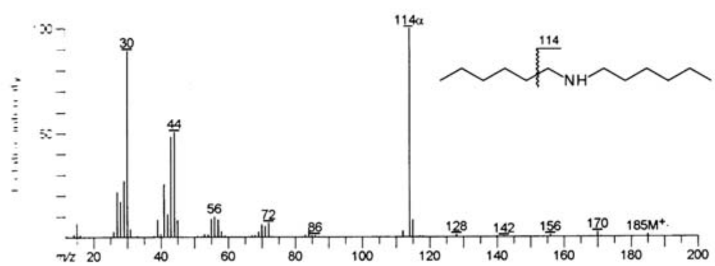


Figure 3.17. Mass spectrum of dihexylamine.

Amines & Amides

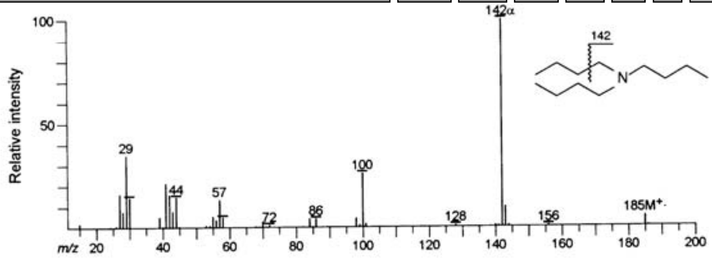


Figure 3.18. Mass spectrum of tributylamine.

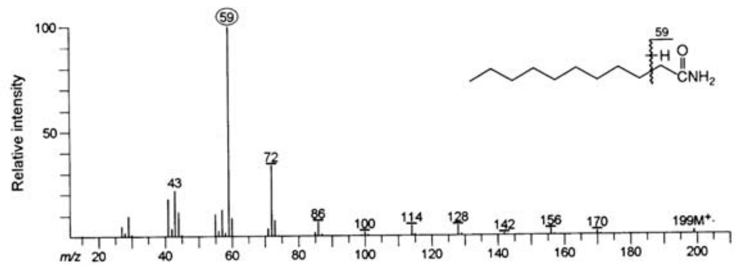


Figure 3.19. Mass spectrum of dodecanamide.

Amides & Mercaptans

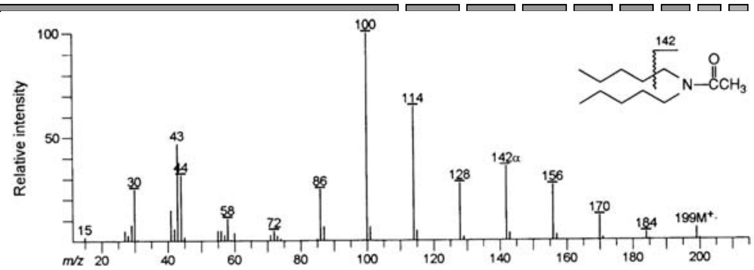


Figure 3.20. Mass spectrum of N,N-dipentylacetamide.

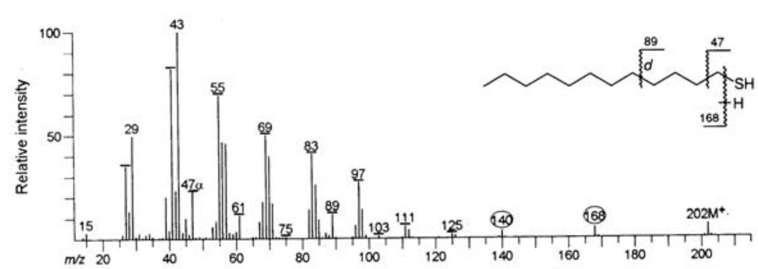


Figure 3.21. Mass spectrum of dodecanethiol.

Sulfites & Halogenated Alkanes

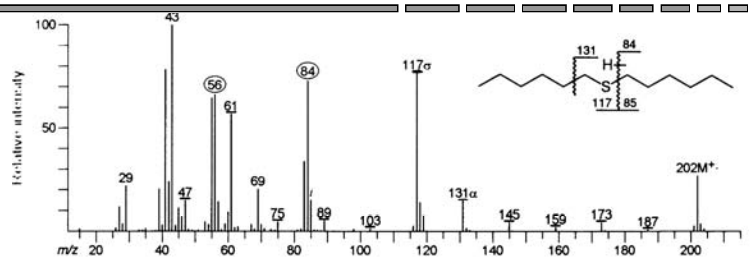


Figure 3.22. Mass spectrum of dihexylsulfide.

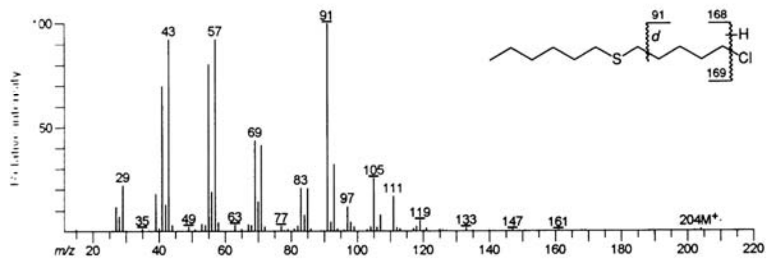


Figure 3.23. Mass spectrum of 1-chlorododecane.

Brominated Alkanes & Cyanides

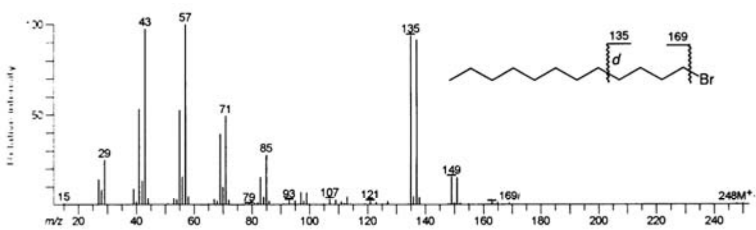


Figure 3.24. Mass spectrum of 1-bromododecane.

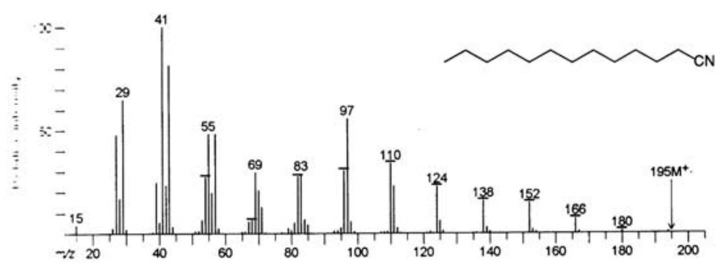


Figure 3.25. Mass spectrum of dodecyl cyanide.

Si and P containing compounds

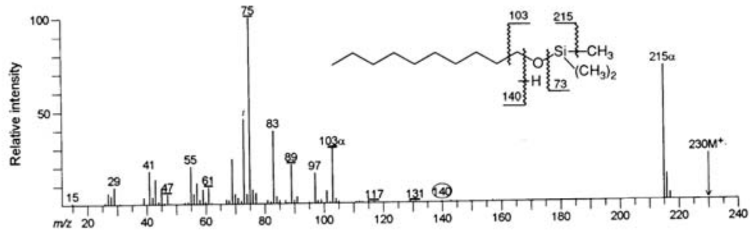


Figure 3.26. Mass spectrum of the trimethylsilyl derivative of decanol.

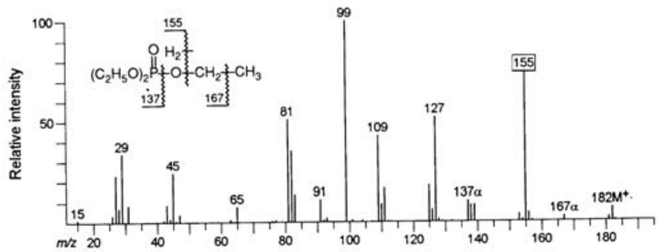


Figure 3.27. Mass spectrum of triethyl phosphate.