Mass Spectroscopy

CHEM 466
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History of Mass spectroscopy

- http://www.chemistry.ohio-state.edu/~allen/587%20W04/587%20W04%20130-136%20std.pdf
- http://www.cem.msu.edu/~cem333/Week18.pdf
- http://www.mhhe.com/physsci/chemistry/carey/student/olc/ch13ms.html

Introduction...

Mass spectroscopy is perhaps one of the most widely applicable of all the analytical tools available to the analytical chemist in the sense that this technique is capable of providing information about

(1) the qualitative and quantitative composition of both organic and inorganic analytes in complex mixtures

(2) the structures of a wide variety of complex molecular species

(3) isotopic ratios of atoms in samples and the structure and composition of solid surfaces.

Uses of Mass Spec

- **forms ions, usually positive, study charge/mass ratio**
- **very characteristic fragmentation pattern in charge/mass ratio**
- **data easier to interpret than IR and/or NMR**
- **provides accurate MW of sample**
- **used to determine isotopic abundances**

Where are Mass Spectrometers Used?

Mass spectrometers are used in industry and academia for both routine and research purposes. The following list is just a brief summary of the major mass spectrometric applications:

- Biotechnology: *the analysis of proteins, peptides, oligonucleotides*
- Pharmaceutical: *drug discovery, combinatorial chemistry, pharmacokinetics, drug metabolism*
- Clinical: *neonatal screening, haemoglobin analysis, drug testing*
- Environmental: *PAHs, PCBs, water quality, food contamination*
- Geological: *oil composition*
- http://www.varianinc.com/image/vimage/docs/products/chrom/gcms/shared/ms2200bro_r2.pdf

Mass Spectroscopy Units

In Mass Spectroscopy (MS), atomic and molecular weights are generally expessed in terms of *atomic mass units* (amu).

The atomic mass unit is based on upon a relative scale in which the reference is the carbon isotope $^{12}_{6}C$, which is assigned a mass of exactly 12 amu. Thus the amu is rdefined as 1/12 of the mass of one neutral carbon atom. Mass spectrometrists also call the amu the Dalton (Da).

Molecular Mass

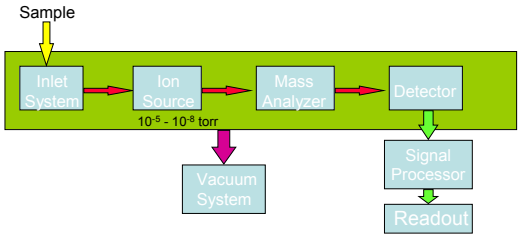
The chemical atomic weight or the average atomic weight (A) of an element in nature is given by the equation

$$A = A_1p_1 + A_2p_2 + ...+ A_np_n$$

where A_1, A_2, ... A_n are the atomic masses in Daltons of the *n* isotopes of the element and p_1, p_2 ..... p_n are the fractional abundance of these isotopes.

Components of Mass Spec

Fig. 20-10, pg. 512



Inlet System

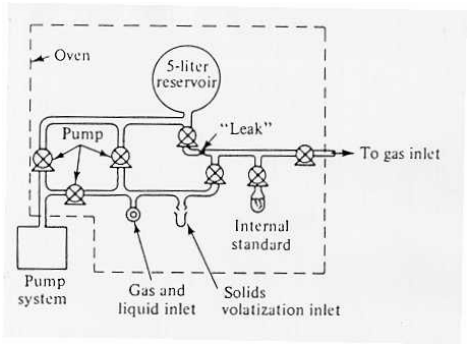


Table 20-3, pg. 505 Natural Abundances of Isotopes of Some Common Reagents

Element[a]	Most Abundant Isotope	Abundance of Other Isotopes Relative to 100 Parts of the Most Abundant[b]	
Hydrogen	^{1}H	^{2}H	0.015
Carbon	^{12}C	^{13}C	1.08
Nitrogen	^{14}N	^{15}N	0.37
Oxygen	^{16}O	^{17}O	0.04
		^{18}O	0.20
Sulfur	^{32}S	^{33}S	0.80
		^{34}S	4.40
Chlorine	^{35}Cl	^{37}Cl	32.5
Bromine	^{79}Br	^{81}Br	98.0
Silicon	^{28}Si	^{29}Si	5.1
		^{30}Si	3.4

[a] Fluorine (^{19}F), phosphorus (^{31}P), and iodine (^{127}I) have no additional naturally occurring isotopes.
[b] The numerical entries indicate the average number of isotopic atoms present for each 100 atoms of the most abundant isotope; thus, for every 100 ^{12}C atoms there will be an average of 1.08 ^{13}C atoms.

Components of Mass Spec

Fig. 20-11, pg. 513

"Schematic of (a) an external sample introduction system (note the that various parts are not to scale) and (b) a sample probe for inserting a sample directly into the ion source."

use book & ELMO

Sample Handling

- **batch inlet: 1-5 L surge tank**
- **gases and volatile liquids**
- **direct probe inlet: non-volatile liquids**
- **gas chromatographic inlet systems**
- **permeable porous material to release carrier gas**

Operation of Mass Spec

http://www.colby.edu/chemistry/OChem/DEMOS/MassSpec.html

Table 20-1, pg. 500 Ion Sources for Molecular Mass Spectroscopy

Name	Abbreviation	Type	Ionizing Agent	Date of Sustained Use
Electron ionization	EI	Gas phase	Energetic electrons	
Field ionization	FI	Gas phase	High-potential electrode	
Chemical ionization	CI	Gas phase	Reagent positive ions	1965
Field desorption	FD	Desorption*	High-potential electrode	1969
Fast atom bombardment	FAB	Desorption*	Energetic atoms	1981
Secondary ion mass spectrometry	SIMS	Desorption*	Low fluxes of energetic ions	1977
Plasma desorption	PD	Desorption*	High-energy fission fragments from ^{252}Cf	1974
Thermal desorption		Desorption*	Heat	1979
Laser desorption	LD	Desorption*	Laser beam	1978
Electrohydrodynamic ionization	EHMS	Desorption*	High field	1978

* Samples as solids, gases, or solutions.

Magnetic Sector Analyzers...

Magnetic sector analyzers employ a permanent magnet or electromagnet to cause the beam from the ion source to travel in a circular path of 180, 90, or 60 degrees. Here, ions are formed by electron impact.

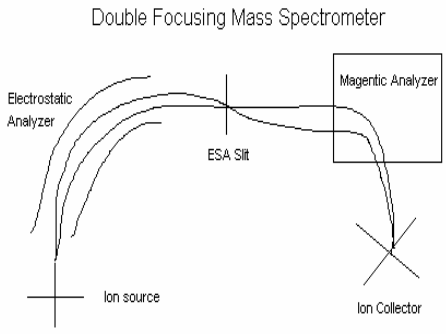
The translational energy of an ion of mass *m* and charge *z* upon exciting slit *B* is given by

$K = Zev = \frac{1}{2} mv^2$ Equation 1

where V is the voltage between A and B, v is the velocity of the ion after acceleration, and e is the charge of the ion.

Double Focusing Instruments...

These type of instruments, unlike *single-focusing* which simply minimize directional errors, are designed to limit both the errors introduced because ions are initially moving in different directions and also the errors introduced due to the fact that ions of the same mass-to-charge ratio may have different translational energies. A schematic of a double-focusing instrument is shown next.



Quadrupole Mass Filters...

- Quadrupole mass spectrometers are usually more compact, less expensive, more rugged than their magnetic sector counterparts. A quadrupole is analogous to a narrow-band filter in that it , set at any operating conditions, it transmits only ions within a small range of m/z values.

Time-of-Flight Analyzers...

In time-of-flight instruments, positive ions are produced periodically by bombardment of the sample with brief pulses of electrons, secondary ions or laser generated photons. The ions produced are then accelerated by an electric field and then made to pass into a field-free drift tube about a meter long.

Computerized Mass Spectrometers...

- Minicomputers and microprocessors are integral part of modern mass spectrometers. The figure below is a block diagram of the computerized control and data acquisition system of a triple quadrupole mass spectrometer.

Ion Sources...

The appearance of mass spectra for a given molecular species is highly dependant upon the method used for ion formation.

Gas-Phase Sources...

- Gas-phase sources require volatilization of the sample before ionization and thus are limited to thermally stable compounds that have boiling points less than about 500°C.

Mass Spectra

Fig. 20-2, pg. 501
"Mass spectra for 1-decanol:
(a) 70-ev electron impact
(b)chemical ionization with isobutane as reagent gas."

book & ELMO

Fig. 20-4, pg. 504

Electron impact mass spectra of:
(a) methylene chloride and
(b) 1 pentanol.

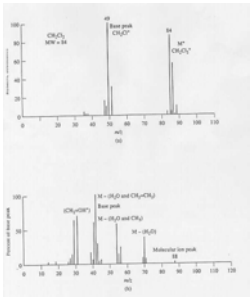
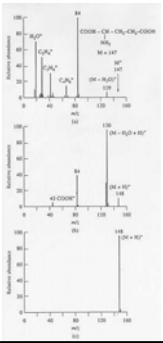


Fig. 20-6, pg. 507



Mass spectra for glutamic acid:
(a) electron impact ionization,
(b) field ionization, and
(c.) field desorption

Electron-impact ionization is not very efficient and only about one molecule in a million undergoes the primary reaction

$$M + e^- \rightarrow M.^+ + 2e^-$$

Electron Impact spectra are very complex due to the high energies possessed by the accelerated electrons which collide with the sample and lead to fragmentation. These complex spectra are very useful for compound identification.

Advantages of Electron Impact sources:

(1) They are convenient and produce high ion currents.
(2) Extensive fragmentation can lead to unambiguous identification of analytes.

Disadvantages of Electron Impact sources:

(1) The need to volatilize the sample limits this method since it excludes analysis of thermally unstable compounds.
(2) Excessive fragmentation can lead to the disappearance of the molecular ion peak therefore preventing the molecular mass of the analyte to be determined.

Chemical Ionization Sources...

- These sources employ the use of a reagent to impart energy to the sample. The reagent is bombarded with highly accelerated electrons and then made to collide with the sample in its gaseous phase.

Chemical Ionization Source

- **reagent gas 10^3 - 10^4 times concentrated as sample**
- **collisions with reagent gas ions causes ionization**
- **less fragmentation, simpler spectra**
- **special modifications to deal with higher pressures**

Spark Source

- **rf spark source, 30 kv**
- **sample part of electrodes, produces gaseous ionic plasma**

Field Ionization Source

- **metallic anode**
- **cathode acts as slit**
- **separation: 0.5 to 2 mm**
- **5 to 20 kv potential applied**
- **produces mainly M and M+1 peaks**

Desorption Sources...

- In desorption methods, energy is introduced in various forms to the liquid or solid sample in such a way as to cause direct formation of gaseous ions. As a consequence, spectra are greatly simplified and often consist of only the molecular ion or the protonated molecular ion.

Identification of Pure Compounds by Mass Spectroscopy...

Mass spectroscopy can be used to determine the molecular weight of a compound but this involves an identification of a molecular peak and a comprehensive study of a spectrum.

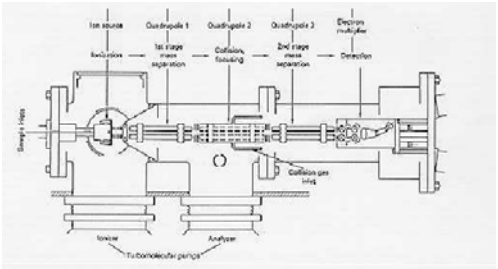
- TANDEM MASS SPECTROSCOPY: This type of spectroscopy simply involves the coupling of one mass spectrometer to another and this hyphenated technique has resulted in dramatic progress in the analysis of complex mixtures.

- SECONDARY ION MASS SPECTROSCOPY: This is one of the most highly developed of the mass spectrometric surface methods, with several manufacturers offering instruments for this technique. It involves the bombarding of a surface with a beam of ions formed in an ion gun. The ions generated from the surface layer are then drawn into a spectrometer for mass analysis.

MS/MS instrument

Fig. 20-24, pg. 530

"Schematic of a tandem quadrupole MS/MS instrument."

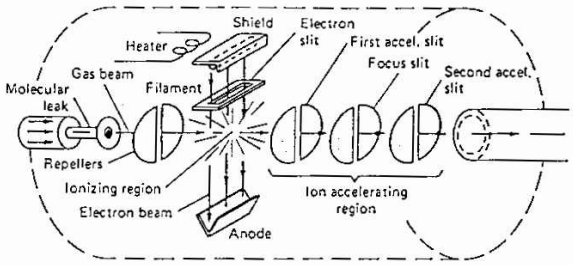


Electron Impact Source

- **bombardment of sample with beam of electrons**

Fig. 20-3, pg. 502

"An electron impact source."



Fragmentation Patterns

Table 20-2, pg. 503

"Some Typical Reactions in an Electron Impact Source."

Molecular ion formation	$ABCD + e \rightarrow ABCD^{\cdot +} + 2e$
Fragmentation	$ABCD^{\cdot +} \rightarrow A^{\cdot} + BCD^{+}$
	$\rightarrow A^{\cdot} + BCD^{+} \rightarrow BC^{+} + D^{\cdot}$
	$\rightarrow B + A^{+}$
	$\rightarrow CD^{\cdot} + AB^{+} \rightarrow A + B^{+}$
	$\rightarrow D + C^{+}$
	$\rightarrow AB^{\cdot} + CD^{+} \rightarrow C + D^{+}$
Rearrangement followed by fragmentation	$ABCD^{\cdot +} \rightarrow ADBC^{\cdot +} \rightarrow BC^{\cdot} + AD^{+}$
	$\rightarrow AD^{\cdot} + BC^{+}$
Collision followed by fragmentation	$ABCD^{\cdot +} + ABCD \rightarrow (ABCD)_2^{\cdot +} \rightarrow BCD^{\cdot} + ABCDA^{+}$

Electron Impact Ionization Process

$M + e^- \text{-----} > M^+ + 2e^-$

where M^+ => molecular ion

Electron Impact Ionization Process

Molecular Ions:

M^+

$(M+1)^+$

$(M+2)^+$

Electron Impact Ionization Process

Molecular Ions:

M^+

– **reults from removing an electron from a molecule**

Electron Impact Ionization Process

Molecular Ions:

$(M+1)^+$

– **results from one atom/molecular of C-13 or H-2**

Electron Impact Ionization Process

Molecular Ions:

$(M+2)^+$

– **small for most organics because it requires two heavy atoms/molecule**
  - **1 C-13 and 1 H-2**
  - **2 C-13s**
  - **2 H-2s**

– **sizeable for chlorinated or brominated compounds**

Electron Impact Ionization Process

Molecular Ions:

– peaks for collision products: function of concentration (pressure)

– stability of the molecular ion
  - **stabilized by π e^- systems, cyclic**

base peak

Electron Impact Ionization Process

base peak

– highest peak

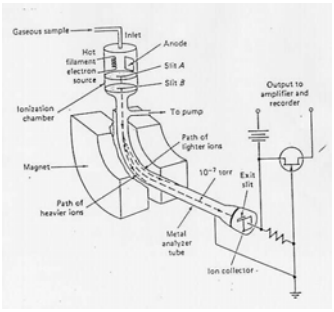
– peak height against which all others are measured for use in peak tables

Mass Analyzer

- **resolution vs price and application**

Single-Focusing Analyzers with Magnetic Deflection

Fig. 20-12
pg. 515
"Schematic of a magnetic sector spectrometer."



Magnetic Centripetal Force

$F_m = Bzev$

where F_m => magnetic centripetal force

B => magnetic field strength
v => velocity of particle
z => charge on particle
e => charge of electron

Centrifugal Force

$F_c = mv^2/r$

where F_c => balancing centrifugal force

r => radius of curvature of magnetic sector
m => mass of particle

Kinetic Energy

$KE = zeV = 1/2mv^2$

where KE => kinetic energy
V => accelerating potential

Mass to Charge Ratio, m/z

$F_m = F_c$
thus
$Bzev = mv^2/r$
where $v = Bzr/m$

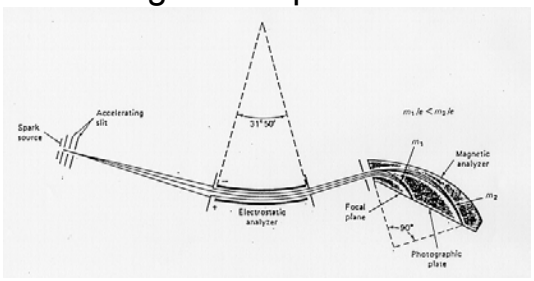
$m/z = (B^2r^2e)/2V$

Mass Analyzer

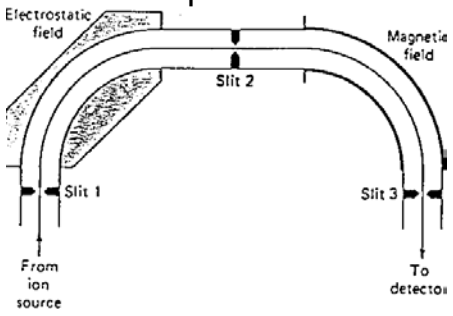
Double-Focusing Analyzers

– higher resolution, need higher amplification
– 2 magnets or 1 magnet & 1 electrostatic field

Fig. 20-13, pg. 517
Mattacuh-Herzog type double-focusing mass spectrometer.



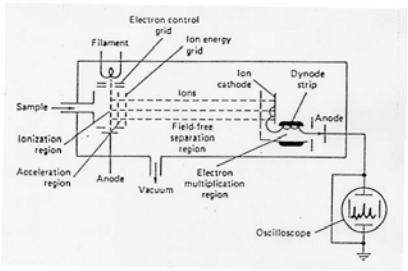
Double Focus Mass Spectrometer



Time of Flight Analyzers

– non magnetic separation
– detector- electron multiplier tube
– instantaneous display of results

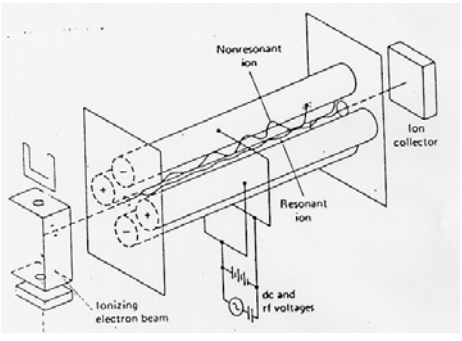
Fig. 20-14, pg. 518
Schematic of a time-of-flight mass spectrometer.



Quadrupole Analyzers

- **4 short parallel metal rods**
- **opposite rods same charge on dc source, AC rf applied ontop**

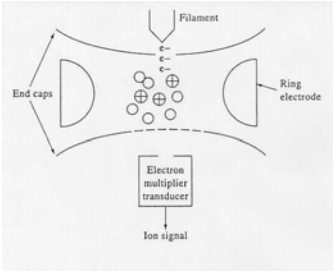
Quadrupole Mass Spectrometer



Ion Trap Analyzer

- Variable radio frequency voltage applied to the ring electrode
- ions of appropriate m/z circulate in stable orbit
- scan rf, heavier particles stable, lighter particles collide with ring electrode
- ejected ions detected by transducer as an ion current

Fig. 20-15, pg. 518
Ion Trap Mass Spectrometer



Detectors...

- Electron Multipliers: A discrete-dynode electron multiplier is designed for detection of positive ions. Each dynode is held at successively higher voltage and there is a burst of electrons that is emitted when struck by energetic electrons or ions. A continuous-dynode electrons electron multiplier is a trumpet-shaped device made of glass that is heavily doped with lead.

Detectors...

- The Faraday Cup detector: This detector functions as follows. When positive ions strike the surface of the cathode, electrons move flow from the ground through the resistor to neutralize the charge. The resulting potential drop across the resistor is amplified via a high-impedance amplifier.

Mass Analyzers...

There are several methods available for separating ions with different mass-to-charge ratios. Ideally, the mass analyzer should be capable of distinguishing between minute mass differences.

Resolution of Mass Spectrometers...

Resolution, in MS, refers to the ability of a mass spectrometer to differentiate between masses and is quantitatively defined as

$$R = m / \Delta m$$

where Δm is the mass difference between two adjacent peaks that are just resolved and m is the nominal mass of the first peak (the mean mass of the two peaks is sometimes used instead).

Measurement and Display of Results

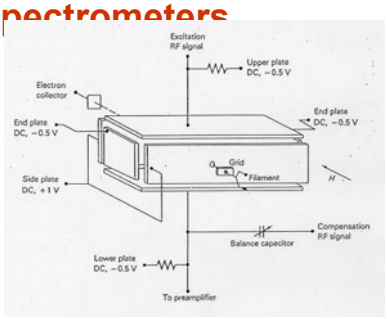
- **photographic results in double-focus**
- **electron current from well protected electrode**
- **galvanometers with sensitized paper**
- **strip chart recorder**
- **computer display**

Fourier Transform Mass Spectrometer

- Usually trapped ion analyzer
- ions created by brief electron beam burst
- short rf pulse that increase linearly in frequency with time

Computerized Mass Spectrometers

Fig. 20-17
pg. 520
"A trapped ion analyzer cell."



Computerized Mass Spectrometers

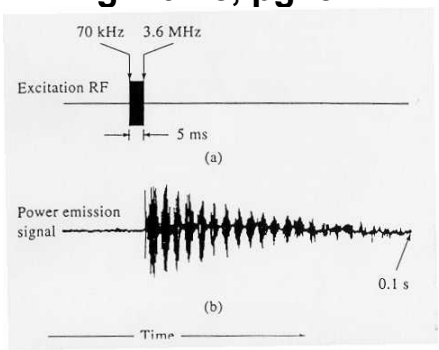
Fig. 20-18, pg. 521

"Schematic diagram showing the timing of

(a) the radio-frequency signal

(b) the transient image signal."

Fig. 20-18, pg. 521

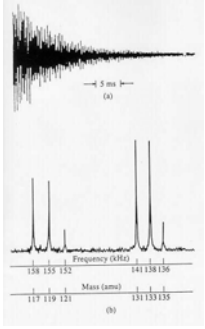


Computerized Mass Spectrometers

Fig. 20-19, pg. 521

"Time domain (a) and (b) frequency or mass domain spectrum for 1,1,1,2-tetrachloroethane."

Fig. 20-19, pg. 521



Computerized Mass Spectrometers

Fig. 20-21, pg. 523

"A computer display of mass-spectral data. The compound was isolated from a blood serum extract by chromatography. The spectrum showed it to be the barbiturate, pentobarbital."

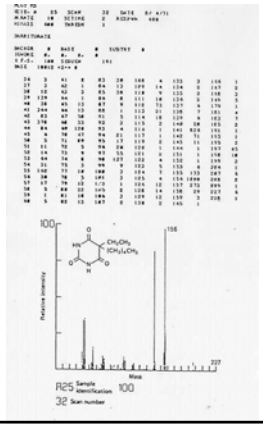


Fig. 20-21, pg. 523

Determination of Molecular Formula

distinguish between compounds of same MW

$C_5H_{10}O_4$ or $C_{10}H_{14}$

Determination of Molecular Formula

distinguish between compounds of same MW

	$C_5H_{10}O_4$
^{13}C	5 * 1.08% = 5.40%
^{2}H	10 * 0.016% = 0.16%
^{17}O	4 * 0.04% = 0.16%

$^{135}peak/^{134}peak$	5.72%

Determination of Molecular Formula

distinguish between compounds of same MW

	$C_{10}H_{14}$
^{13}C	10 * 1.08% = 10.8%
^{2}H	14 * 0.016% = 0.22%

$^{135}peak/^{134}peak$	11.0%

Determination of Molecular Formula

Table 20-6, pg. 526

"Isotopic Abundance Percentages and Molecular Weights for Various Combinations of Carbon, Hydrogen, Oxygen, and Nitrogen."

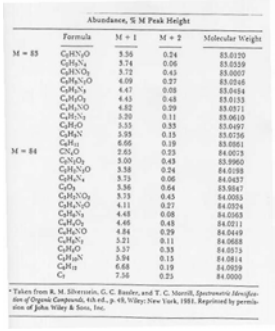
Example 20-5

Calculate the ratios of the $(M+1)^+$ to M^+ peak heights for the following compounds: dinitrogenbenzene and an olefin,

	$C_{12}H_{24}$	
^{13}C	12×1.08	$= 12.96\%$
^{2}H	24×0.015	$= 0.36\%$
	$(M+1)^+/M^+$	$= 13.32\%$

	$C_6H_4N_2O_4$	
^{13}C	6×1.08	$= 6.48\%$
^{2}H	4×0.015	$= 0.060\%$
^{15}N	2×0.37	$= 0.74\%$
^{17}O	4×0.04	$= 0.16\%$
	$(M+1)^+/M^+$	$= 7.44\%$

Table 20-6, pg. 526



Abundance, % M Peak Height

	Formula	M + 1	M + 2	Molecular Weight
M = 85	$C_6H_7N_2O$	5.56	0.24	83.0120
	$C_5H_9N_3$	5.74	0.06	83.0559
	$C_5H_7NO_2$	5.72	0.45	83.0007
	$C_6H_9N_2O$	4.09	0.27	83.0246
	$C_5H_9N_3$	4.47	0.08	83.0454
	$C_6H_7O_2$	4.43	0.48	83.0153
	C_5H_7NO	4.82	0.29	83.0371
	$C_4H_5N_3$	3.20	0.11	83.0610
	C_5H_7O	3.53	0.33	83.0497
	C_6H_9N	3.93	0.15	83.0736
	C_5H_{11}	6.66	0.19	83.0861
M = 84	CN_2O	2.83	0.23	84.0073
	$C_5N_2O_2$	3.00	0.43	83.9960
	$C_5H_8N_2O$	3.38	0.24	84.0198
	$C_5H_6N_2$	3.73	0.06	84.0437
	C_6O_2	3.36	0.64	83.9847
	$C_5H_8NO_2$	3.33	0.45	84.0085
	$C_5H_6N_2O$	4.11	0.27	84.0324
	$C_6H_8N_2$	4.48	0.08	84.0563
	$C_5H_8O_2$	4.46	0.48	84.0211
	C_6H_8NO	4.84	0.29	84.0449
	$C_5H_6N_2$	5.21	0.11	84.0688
	C_6H_8O	3.57	0.33	84.0573
	C_5H_8N	3.94	0.15	84.0814
	C_6H_{12}	6.68	0.19	84.0939
	C_7	7.56	0.25	84.0000

* Taken from R. M. Silverstein, G. C. Bassler, and T. C. Morrill, *Spectrometric Identification of Organic Compounds*, 4th ed., p. 48, Wiley: New York, 1981. Reprinted by permission of John Wiley & Sons, Inc.

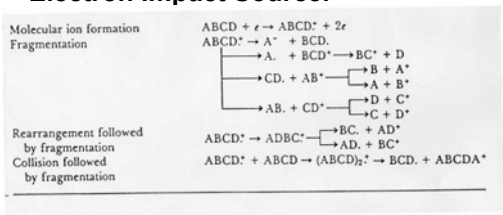
Nitrogen Rule

- **organic compounds with even MW, O or even number of N**
- **odd MW, odd number of nitrogen atoms**

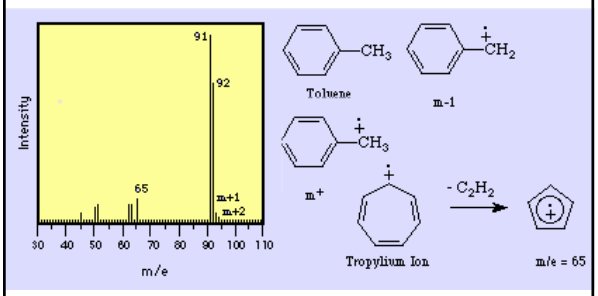
Fragmentation Patterns

Table 20-2, pg. 503

"Some Typical Reactions in an Electron Impact Source."

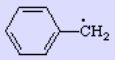


Mass Spectrum of Toluene

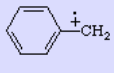


Common Fragments

Commonly Lost Fragments

m-15 $\cdot CH_3$
m-17 $\cdot OH$
m-26 $\cdot CN$
m-28 $H_2C{=}CH_2$
m-29 $\cdot CH_2CH_3$ $\cdot CHO$
m-31 $\cdot OCH_3$
m-35 $\cdot Cl$
m-43 $CH_3\dot{C}{=}O$
m-45 $\cdot OCH_2CH_3$
m-91 

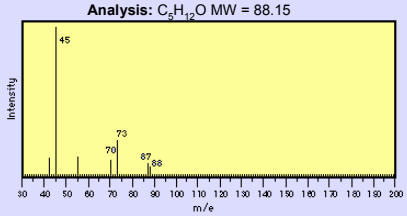
Common Stable Ions

m/e = 43 $CH_3{-}C{\equiv}O^+$
m/e = 91 

m/e = m-1 

Mass Spectrum

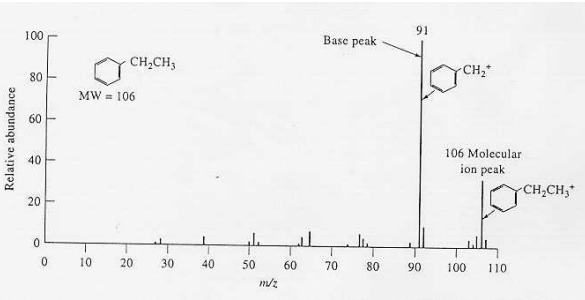
Analysis: $C_5H_{12}O$ MW = 88.15



http://chipo.chem.uic.edu/web1/ocol/spec/MSex3.htm

The spectrum shows a small molecular ion and a small m-1 peak, suggesting the presence of an alcohol (it cannot be an aldehyde since there are no degrees of unsaturation). The m-15 peak represents loss of a methyl group and the m-17 is consistent with loss of a hydroxy radical. For an alcohol, the base peak is often formed by expulsion of an alkyl chain to give the simple oxonium ion R'CR'' OH+; to generate the observed m/e = 45, R' must be

Fig. 20-1, pg. 500
Mass Spectrum of Ethyl Benzene

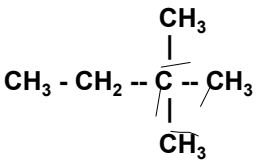


Identification of Compounds from Fragmentation Patterns

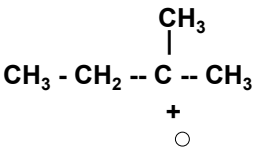
Fragmentation Patterns: Rules

- **C - C bonds weaker than C - H bonds**
- **fragmentation most likely at a branch**
- **positive charge remains with fragment with most branching**

Fragmentation Patterns



Fragmentation Patterns



m/e = 71

Fragmentation Patterns

$+CH_3$ m/e = 15

CH_3
$+C - CH_3$ m/e = 57
CH_3

$CH_3 - CH_2 +$ m/e = 29

Fragmentation Patterns

for alkenes: cleavage is favored at second bond away from double bond

$CH_3 - CH_2 - CH = CH - CH_3$
----->
$CH_2 = CH - CH - CH_3$
+
m/e = 55

Fragmentation Patterns

for aromatics: cleavage at beta bond from ring, m/e = 91

$\phi - CH_2 - R$ -----> $\phi - CH_2 +$

Fragmentation Patterns

terminal non-carbon group: cleaves non-carbon group

$R - X$ -----> $R +$

where R => Cl, Br, I OH, OR, SH, SR, NH_2, NHR, NR_2

Example: 2,2,4-trimethylpentane

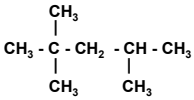
$CH_3 - C(CH_3)_2 - CH_2 - CH(CH_3) - CH_3$

Example: 2,2,4-trimethylpentane

$CH_3 - C(CH_3)_2 - CH_2 - CH(CH_3) - CH_3$

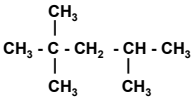
m/e	% of base peak	Fragment
57	100%	
56	33	
41	28	

Example: 2,2,4-trimethylpentane



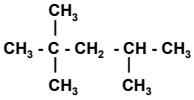
m/e	% of base peak	Fragment
43	25	
29	18	
27	11	

Example: 2,2,4-trimethylpentane



m/e	% of base peak	Fragment
99	5	
15	5	
55	4	

Example: 2,2,4-trimethylpentane



m/e	% of base peak	Fragment
42	2	
114	1	
71	1	
69	0.5	