Organic Qualitative Analysis

Using spectroscopic information
to deduce or confirm
the structure of a compound

Types of spectroscopic information

- **Mass Spectrometry**
  Molecular mass and formula
- **Infrared Spectroscopy**
  Functional groups
- **NMR Spectroscopy**
  Map of carbon-hydrogen framework

Index of Hydrogen Deficiency

- **Index of hydrogen deficiency (IHD): the sum of the number of rings and pi bonds in a molecule**
- **To determine IHD, compare the number of hydrogens in an unknown compound's equivalent hydrocarbon with the number in a reference hydrocarbon of the same number of carbons and with no rings or pi bonds**
  - **the molecular formula of the reference hydrocarbon is C_nH_{2n+2}**

$$IHD = \frac{H_{reference} - H_{molecule}}{2}$$

Molecular Formulas from Molecular Weights

- Find the highest possible number of carbon atoms by dividing by 12; the remainder is the number of hydrogen atoms.
- If the MW is odd, you know there is at least one nitrogen. For even molecular weights, substitute nitrogens in pairs (remember, N = CH_2).
- Try oxygens one at a time (O = CH_4).
- Halogens will appear in the MS data!

Molecular Formulas from Molecular Weights

- Decide which possible formula fits the other data. Discard any formulæ which have too many or too few hydrogens. "Convert" the formula to that of the equivalent hydrocarbon.

  C_nH_{2n+2} is the maximum!

  Each N takes one fewer H. $C_2H_5N \rightarrow$ "C_3H_6"

  O does not change the C/H ratio. $C_2H_6O \rightarrow$ "C_2H_6"

  Halogens substitute for hydrogens.
- Find the Index of Hydrogen Deficiency

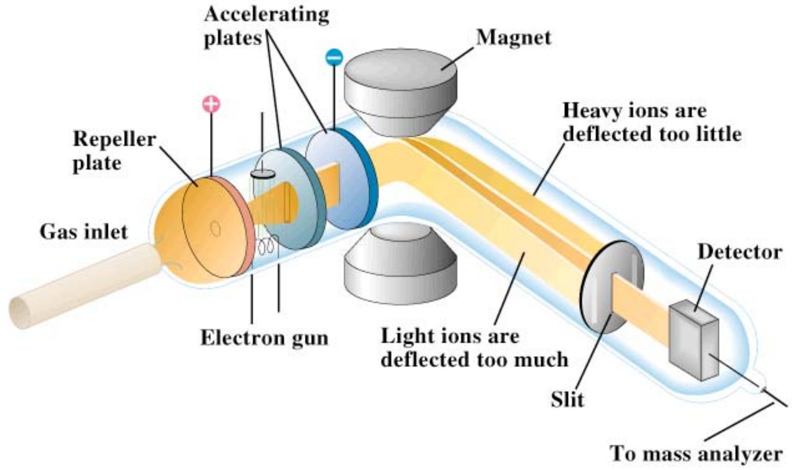
Mass Spectrometry (MS)

- An analytical technique for measuring the mass-to-charge ratio (m/z) of ions, most commonly positive ions, in the gas phase
- Today, mass spectrometry is our most valuable analytical tool for the determination of precise molecular weights

A Mass Spectrometer

- A mass spectrometer is designed to do three things
  1. convert neutral atoms or molecules into a beam of positive (or negative) ions
  2. separate the ions on the basis of their mass-to-charge ratio (m/z)
  3. measure the relative abundance of each ion

Electron impact (E1) mass spectrometer



A Mass Spectrometer

- **Electron Ionization MS**

  in the ionization chamber, the sample is bombarded with a beam of high-energy electrons

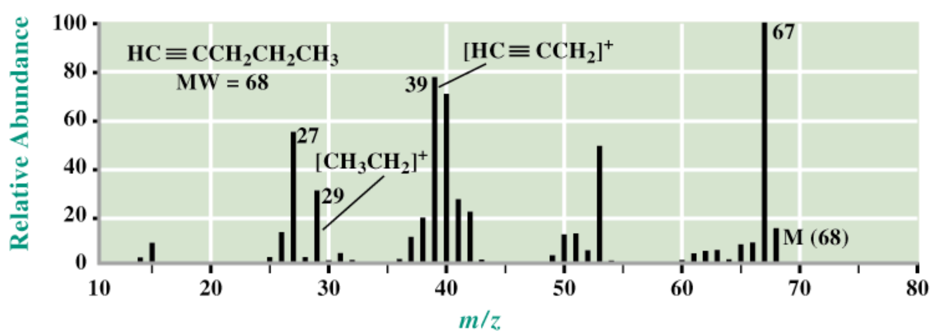
  collisions between these electrons and the sample result loss of electrons from sample molecules and formation of positive ions

$$CH_4 + e^- \longrightarrow [CH_4]^{\bullet +} + 2e^-$$

Molecular ion
(A radical cation)

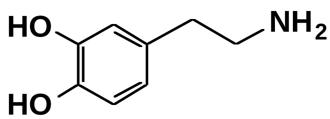
Mass Spectrum

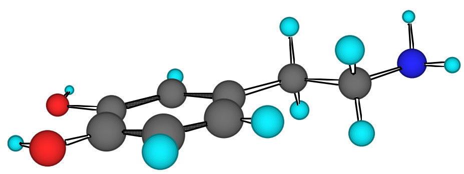
- **Mass spectrum: a plot of the relative abundance of each ion versus mass-to-charge ratio**
- **Base peak: the most abundant peak; assigned an arbitrary intensity of 100**
- **The relative abundance of all other ions is reported as a % of abundance of the base peak**



MS of Dopamine

- The number of peaks in the mass spectrum of dopamine is given here as a function of detector sensitivity





Peak Intensity Relative to Base Peak	Number of Peaks Recorded
> 5%	8
> 1%	31
> 0.5%	45
> 0.05%	120

Other MS techniques

- What we have described is called electron ionization mass spectrometry (EI MS)

- Other techniques include
  - fast atom bombardment (FAB)
  - matrix-assisted laser beam desorption ionization (MALDI)
  - chemical ionization (CI)

Resolution

- **Resolution:** a measure of how well a mass spectrometer separates ions of different mass

low resolution - capable of distinguishing among ions of different nominal mass, that is ions that differ by at least one or more mass units

high resolution - capable of distinguishing among ions that differ in mass by as little as 0.0001 mass unit

Resolution

C_3H_6O and C_3H_8O have nominal masses of 58 and 60, and can be distinguished by low-res MS

These two compounds each have a nominal mass of 60. They may be distinguished by high-res MS

Molecular Formula	Nominal Mass	Precise Mass
C_3H_8O	60	60.05754
$C_2H_4O_2$	60	60.02112

Isotopes

- Virtually all elements common to organic compounds are mixtures of isotopes
- Carbon, for example, in nature is 98.90% ^{12}C and 1.10% ^{13}C. Thus, there are 1.11 atoms of carbon-13 in nature for every 100 atoms of carbon-12

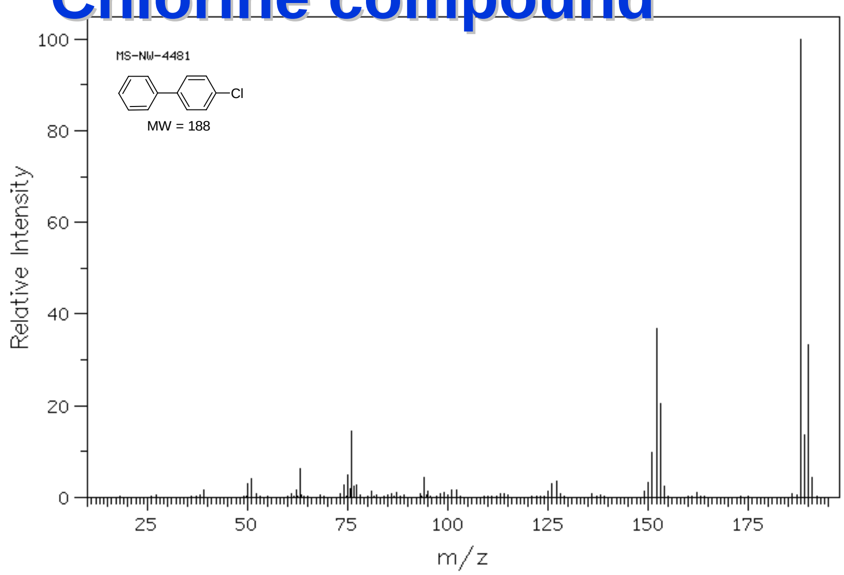
$$1.10 \times \frac{100}{98.90} = 1.11 \text{ atoms } ^{13}\text{C per 100 atoms } ^{12}\text{C}$$

Element	Atomic Weight	Isotope	Precise Mass (amu)	Relative Abundance
hydrogen	1.0079	^{1}H	1.00783	100
		^{2}H	2.01410	0.016
carbon	12.011	^{12}C	12.0000	100
		^{13}C	13.0034	1.11
nitrogen	14.007	^{14}N	14.0031	100
		^{15}N	15.0001	0.38
oxygen	15.999	^{16}O	15.9949	100
		^{17}O	16.9991	0.04
		^{18}O	17.9992	0.20
sulfur	32.066	^{32}S	31.9721	100
		^{33}S	32.9715	0.78
		^{34}S	33.9679	4.40
chlorine	35.453	^{35}Cl	34.9689	100
		^{37}Cl	36.9659	32.5
bromine	79.904	^{79}Br	78.9183	100
		^{81}Br	80.9163	98.0

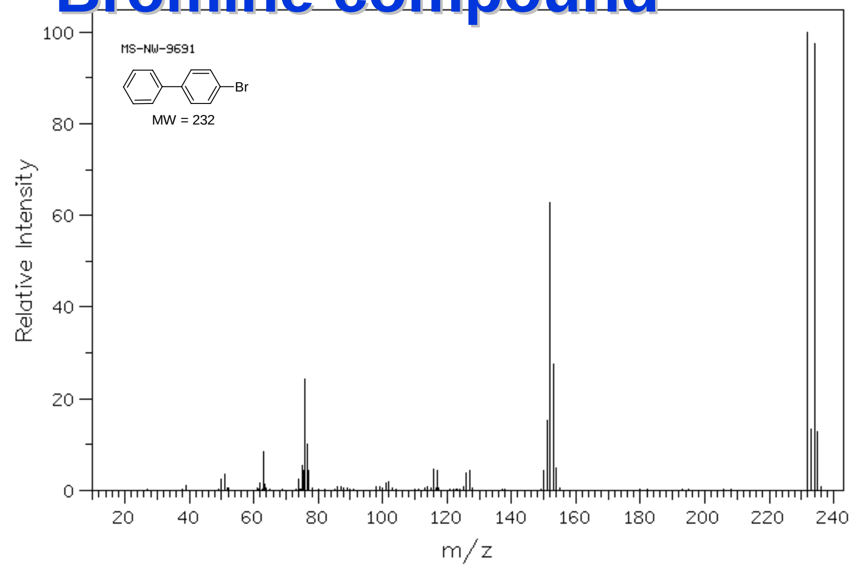
M+2 Peaks

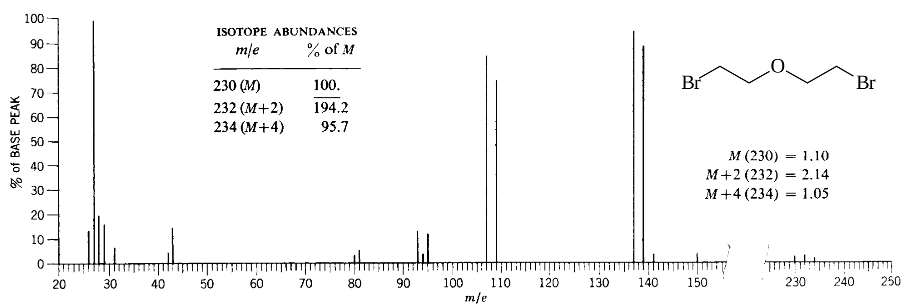
- The most common elements giving rise to M + 2 peaks are chlorine and bromine
- Chlorine in nature is 75.77% ^{35}Cl and 24.23% ^{37}Cl
  - a ratio of M to M + 2 of approximately 3:1 indicates the presence of a single chlorine in a compound
- Bromine in nature is 50.7% ^{79}Br and 49.3% ^{81}Br
  - a ratio of M to M + 2 of approximately 1:1 indicates the presence of a single bromine in a compound

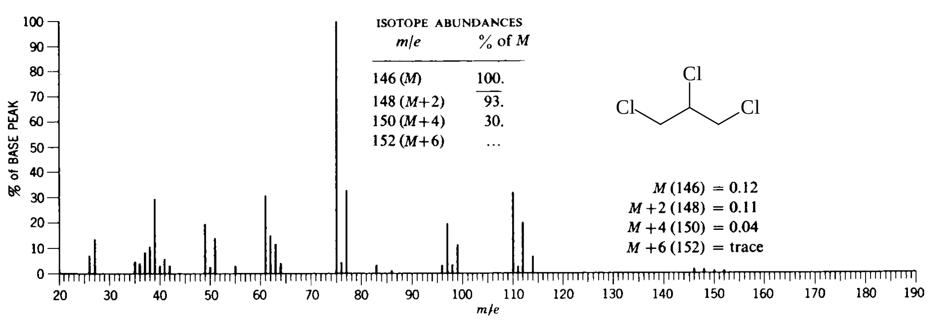
Chlorine compound



Bromine compound





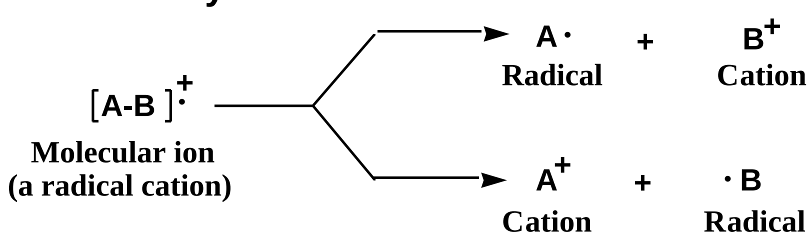


Fragmentation of M

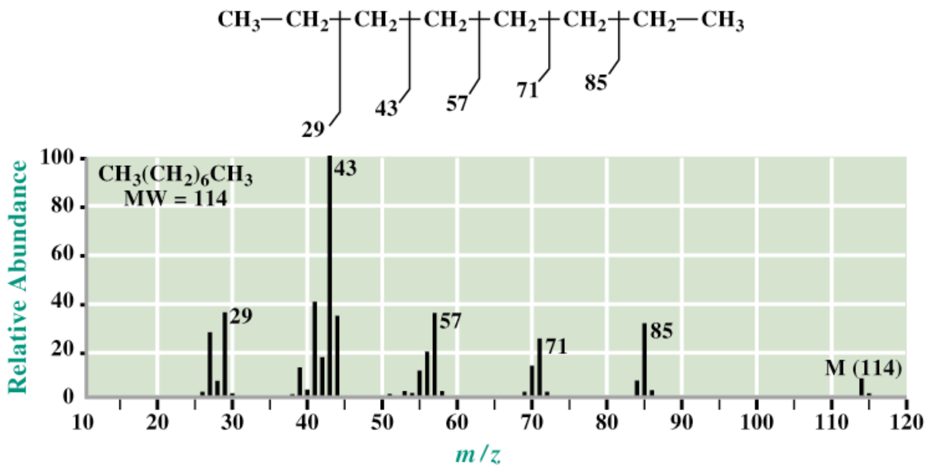
- To attain high efficiency of molecular ion formation and give reproducible mass spectra, it is common to use electrons with energies of approximately 70 eV (1600 kcal/mol)
- This energy is sufficient not only to dislodge one or more electrons from a molecule, but also to cause extensive fragmentation
- These fragments may be unstable as well and, in turn, break apart to even smaller fragments

Fragmentation of M

- Fragmentation of a molecular ion, M, produces a radical and a cation. Only the cation is detected by MS



Mass spectrum of octane



Fragmentation of M

- A great deal of the chemistry of ion fragmentation can be understood in terms of the formation and relative stabilities of carbocations in solution
- Where fragmentation occurs to form new cations, the mode that gives the most stable cation is favored

Fragmentation of M

- The probability of fragmentation to form new carbocations increases in the order

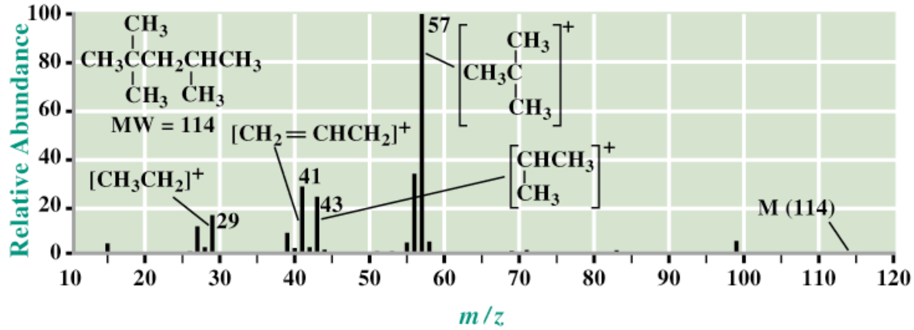
CH_3^+ < 1° < 2°, 1° allylic, 1° benzylic < 3°, 2° allylic, 2° benzylic < 3° allylic, 3° benzylic

Increasing carbocation stability →

Interpreting MS

- The only elements to give significant M + 2 peaks are Cl and Br. If no large M + 2 peak is present, these elements are absent
- Is the mass of the molecular ion odd or even?
- Caution: Some compounds will not show a molecular ion; the largest ion is often M-15, from loss of a methyl group!

Mass spectrum of 2,2,4-trimethylpentane



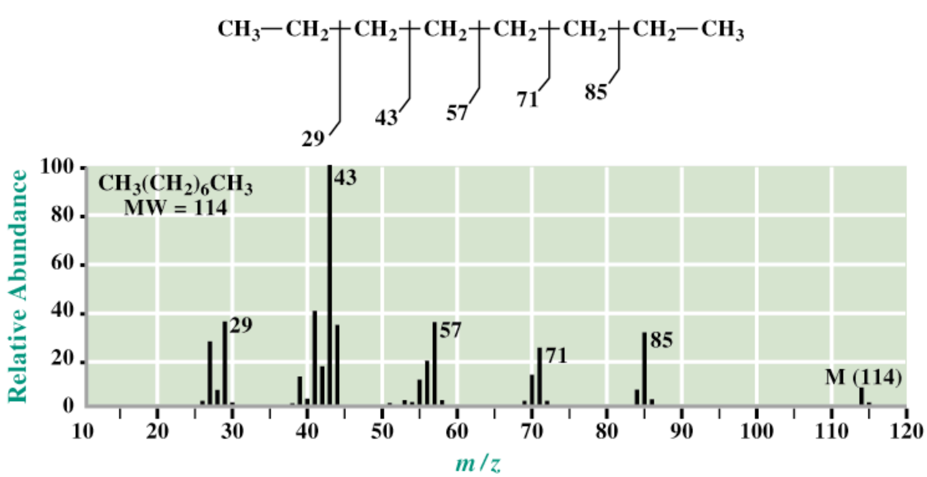
Interpreting MS

- Is the mass of the molecular ion odd or even?
- **Nitrogen Rule**: if a compound has
  - zero or an even number of nitrogen atoms, its molecular ion will appear as a even m/z value
  - an odd number of nitrogen atoms, its molecular ion will appear as an odd m/z value
  - Examples:
    - Aniline (C_6H_7N): MW = 93
    - Ethanediamine ($C_2H_8N_2$): MW = 60

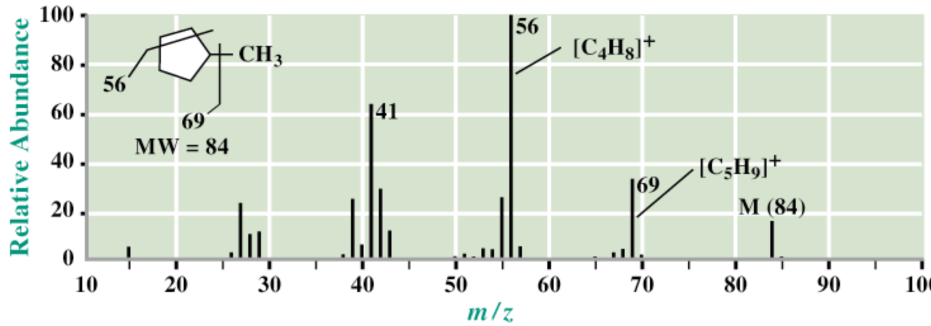
Alkanes

- Fragmentation tends to occur in the middle of unbranched chains rather than at the ends
- The difference in energy among allylic, benzylic, 3°, 2°, 1°, and methyl cations is much greater than the difference among comparable radicals
    - where alternative modes of fragmentation are possible, the more stable carbocation tends to form in preference to the more stable radical

Mass spectrum of octane



Mass spectrum of methylcyclopentane

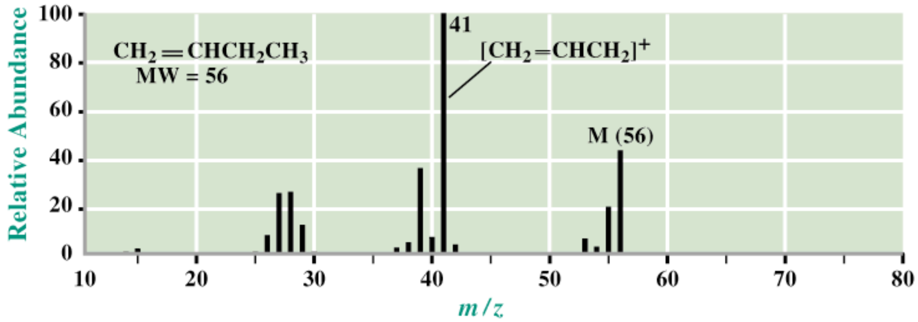


Alkenes

- Alkenes characteristically show a strong molecular ion peak
- They cleave readily to form resonance-stabilized allylic cations

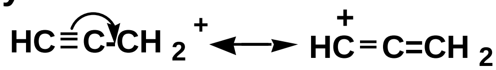
$$[CH_2{=}CHCH_2CH_2CH_3]^{+\bullet} \longrightarrow CH_2{=}CHCH_2^{+} + \cdot CH_2CH_3$$

Mass spectrum of 1-butene



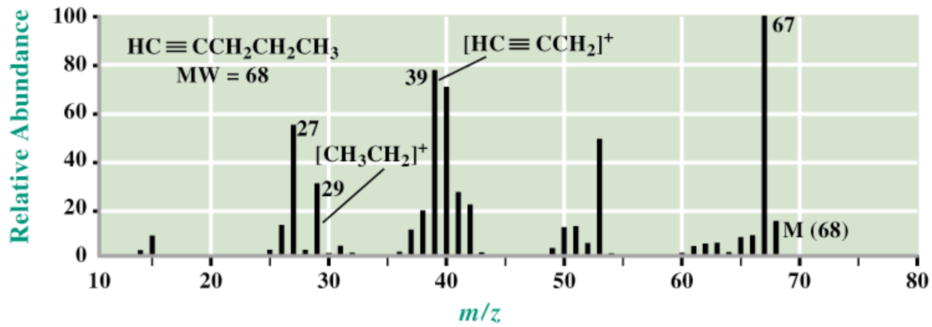
Alkynes

- Alkynes typically show a strong molecular ion peak; terminal alkynes show a strong M-1 peak.
- Alkynes cleave readily to form the resonance-stabilized propargyl cation or a substituted propargyl cation.



resonance-stabilized
propargyl cation

Mass spectrum of 1-pentyne

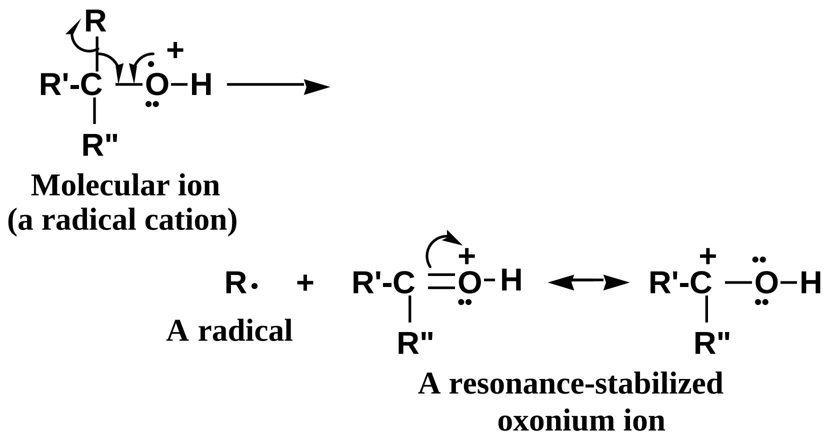


Alcohols

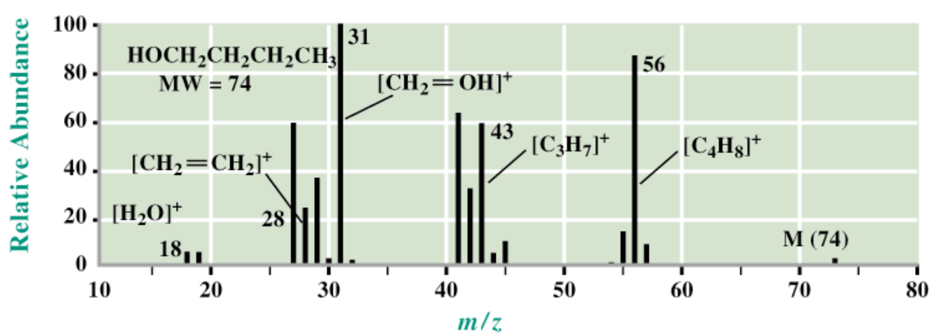
- One of the most common fragmentation patterns of alcohols is loss of H_2O to give a peak which corresponds to M - 18
  - This loss product has an even-number mass, so be careful not to mistake it for the molecular ion!

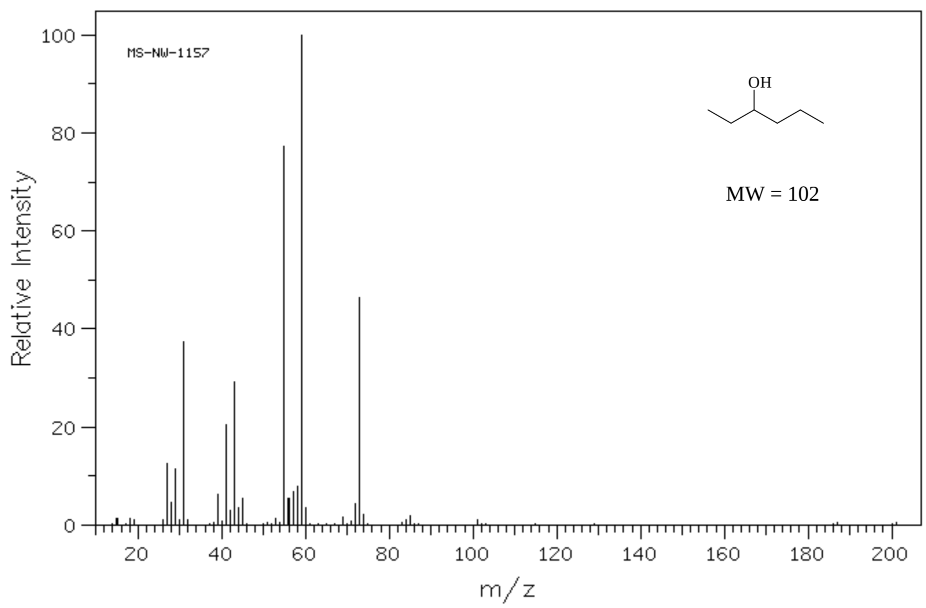
- Another common pattern is loss of an alkyl group from the carbon bearing the OH to give a resonance-stabilized oxonium ion and an alkyl radical

Alcohols

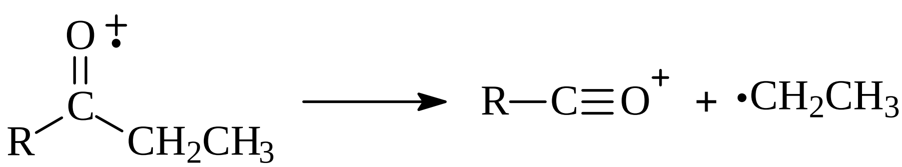


Mass spectrum of 1-butanol

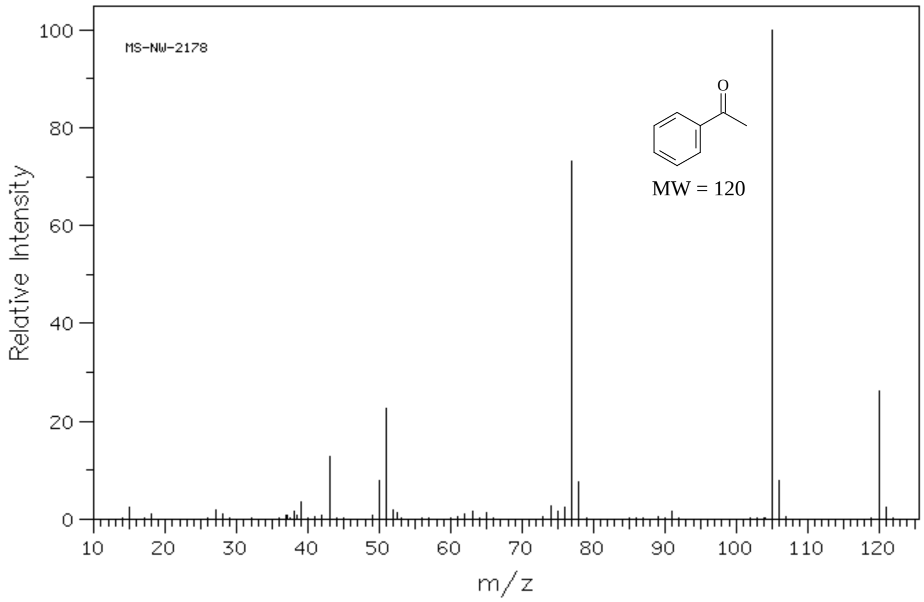




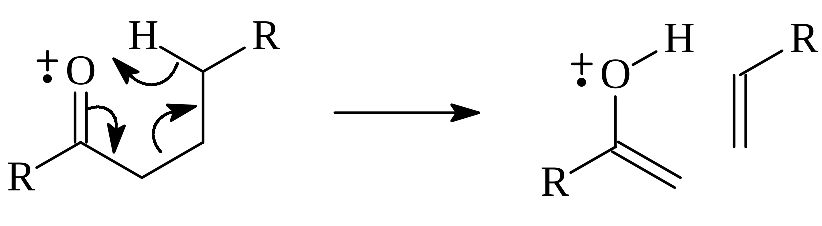
Carbonyls: the acylium ion

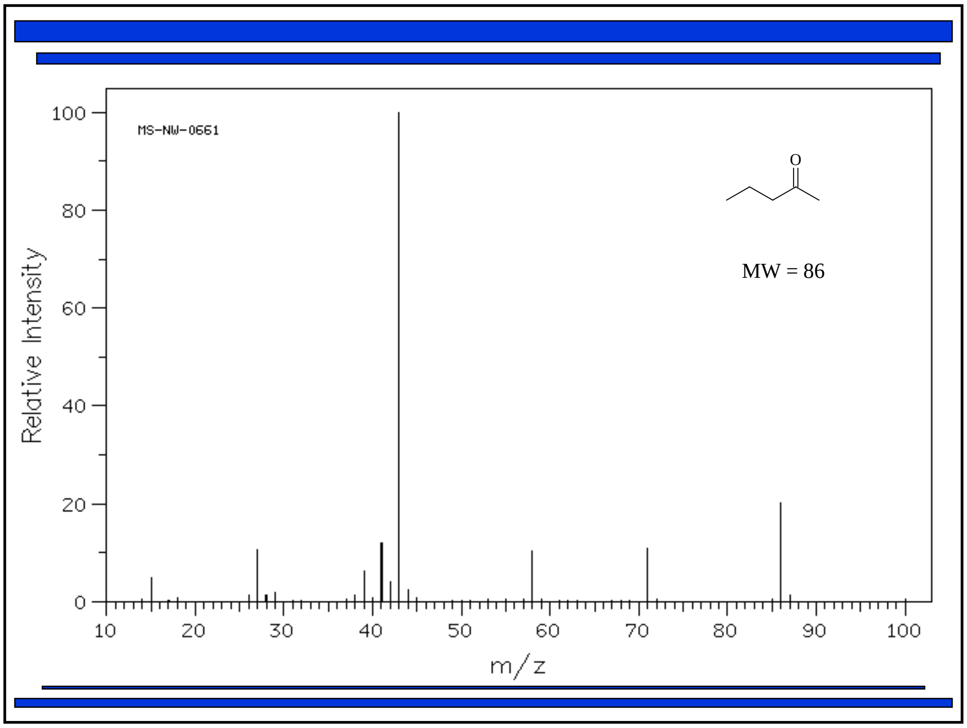


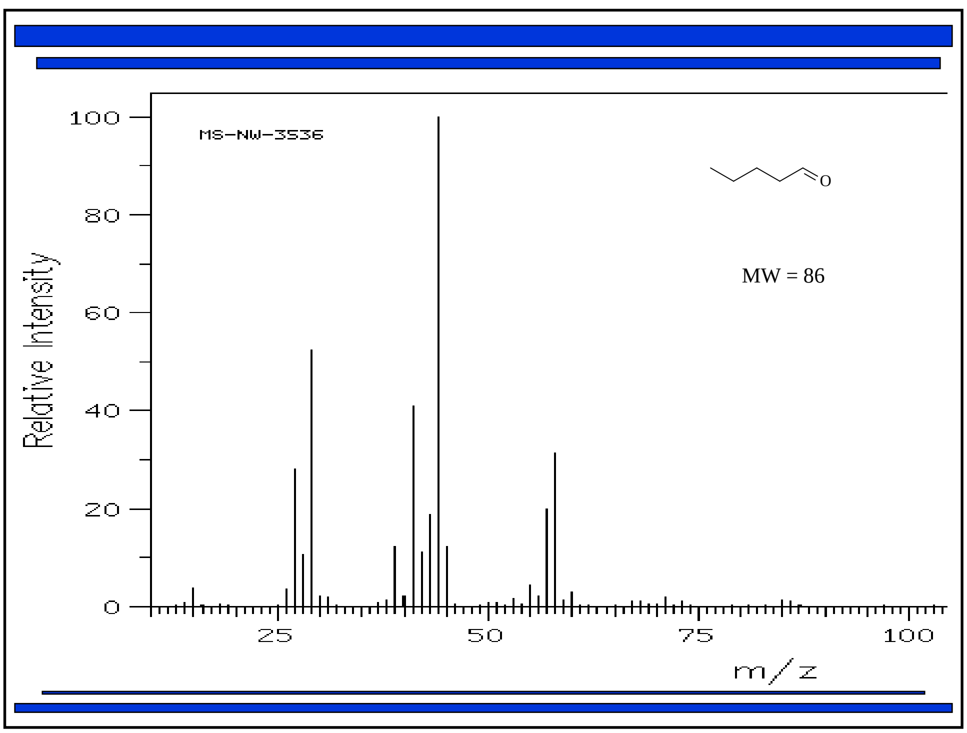
- This process is called α-cleavage
- Highly stabilized cation gives a strong peak



Carbonyls:
The McLafferty Rearrangement




MS-NW-0661
100
80
60
40
20
0
Relative Intensity
10
20
30
40
50
60
70
80
90
100
m/z
O
MW = 86


MS-NW-3536
100
80
60
40
20
0
Relative Intensity
25
50
75
100
m/z
O
MW = 86