

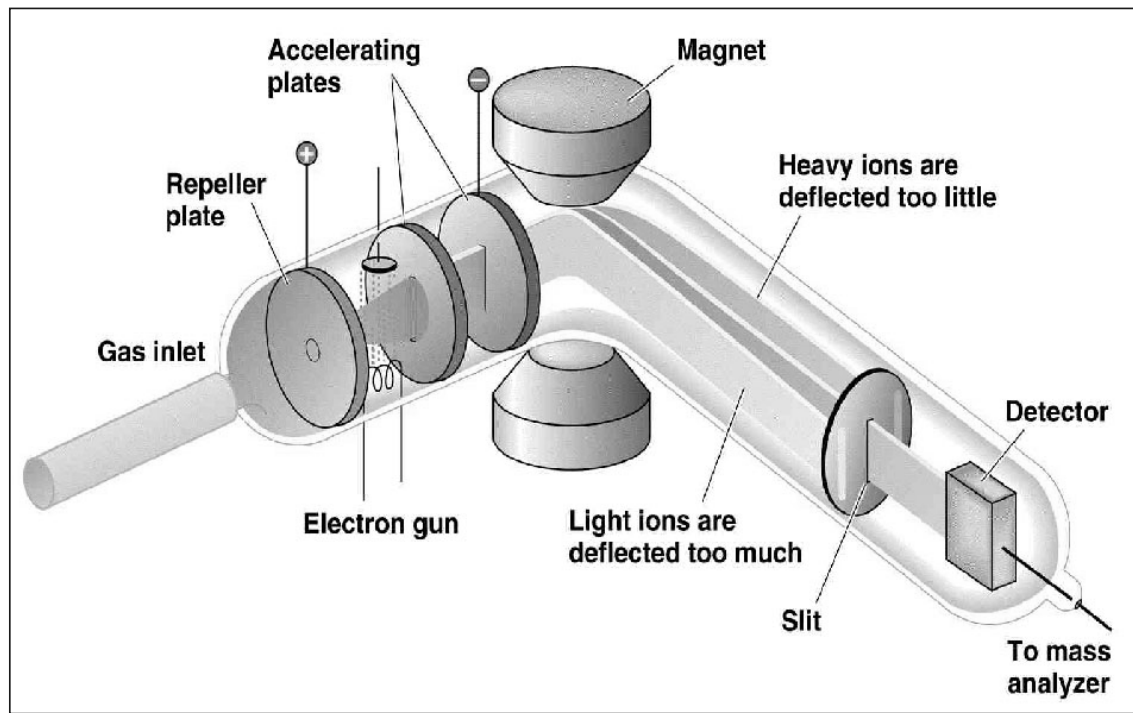
Mass Spectrometry

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Chap 14

Mass Spectrometry (MS)

- An analytical technique for measuring the mass-to-charge ratio (m/z) of ions in the gas phase
 - mass spectrometry is our most valuable analytical tool for determining accurate molecular masses
 - also can give information about structure
 - proteins can now be sequenced by MS

Mass Spectrometry (MS)

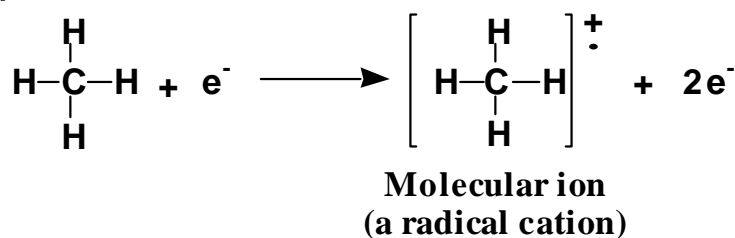


A Mass Spectrometer

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

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 in loss of electrons from sample molecules and formation of positive ions



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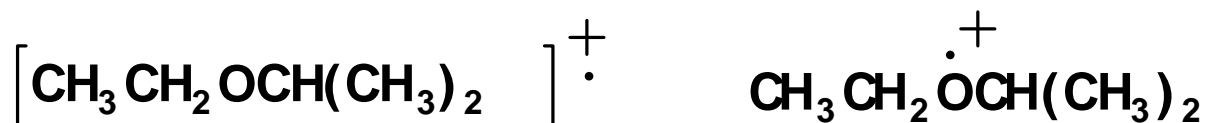
Molecular Ion

- Molecular ion (M): a radical cation formed by removal of a single electron from a parent molecule in a mass spectrometer
- For our purposes, it does not matter which electron is lost; radical cation character is delocalized throughout the molecule; therefore, we write the molecular formula of the parent molecule in brackets with
 - a plus sign to show that it is a cation
 - a dot to show that it has an odd number of electrons

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Molecular Ion

– at times, however, we find it useful to depict the radical cation at a certain position in order to better understand its reactions



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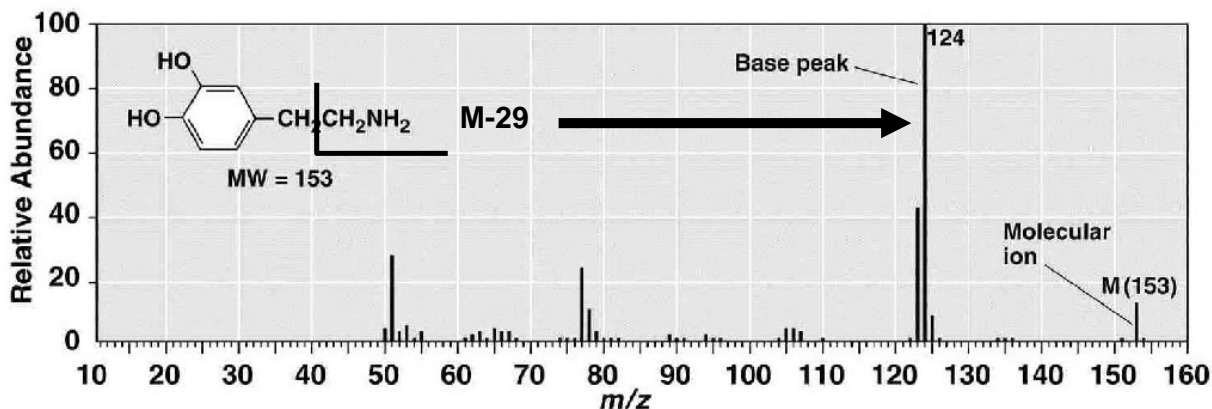
Mass Spectrum

- Mass spectrum: a plot of the relative abundance of ions versus their 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

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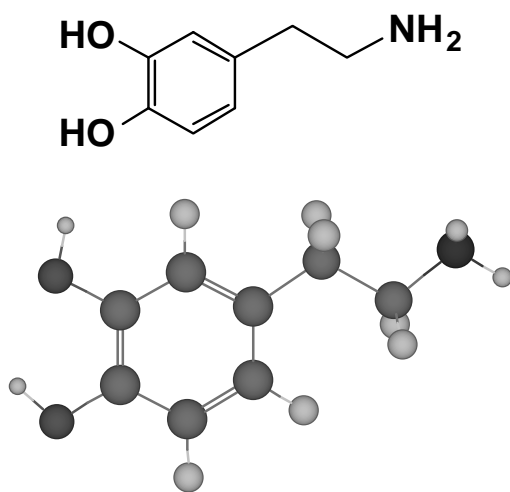
MS of dopamine

- a partial MS of dopamine showing all peaks with intensity equal to or greater than 0.5% of base peak



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- the number of peaks in the MS 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

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Other MS techniques

- What we have described is called electron ionization mass spectrometry (EI-MS)
- Other MS techniques include
 - fast atom bombardment (FAB)
 - matrix-assisted laser desorption ionization (MALDI)
 - chemical ionization (CI)
 - electrospray ionization (ESI)

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Resolution

- Resolution: a measure of how well a mass spectrometer separates ions of different mass
 - low resolution: refers to instruments capable of separating only ions that differ in nominal mass; that is ions that differ by at least 1 or more atomic mass units
 - high resolution: refers to instruments capable of separating ions that differ in mass by as little as 0.0001 atomic mass unit

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Resolution

- C_3H_6O and C_3H_8O have nominal masses of 58 and 60, and can be distinguished by low-resolution MS
- C_3H_8O and $C_2H_4O_2$ have nominal masses of 60
- distinguish between them by high-resolution MS

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

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Isotopes

–virtually all elements common to organic compounds are mixtures of isotopes

Element	Atomic weight	Isotope	Mass (amu)	Relative Abundance
hydrogen	1.0079	1H	1.00783	100
		2H	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
		^{18}O	17.9992	0.20
sulfur	32.066	^{32}S	31.9721	100
		^{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

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Isotopes

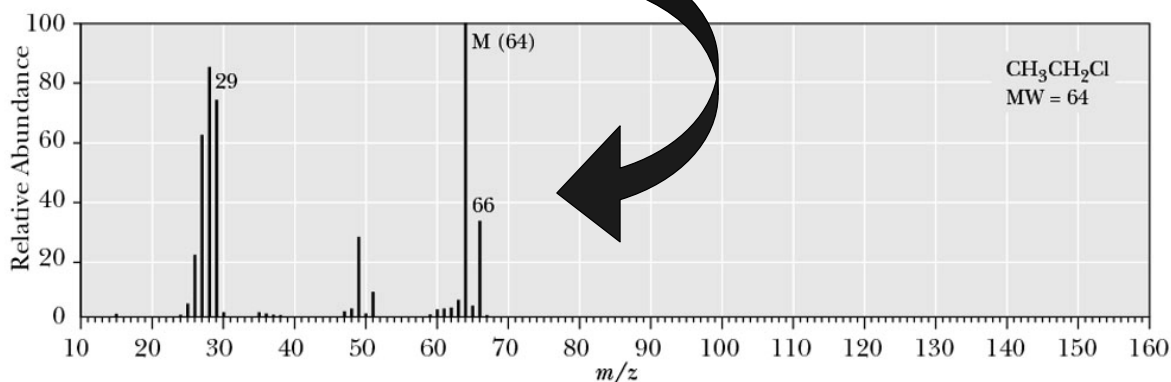
- carbon, for example, in nature is 98.90% ^{12}C and 1.10% ^{13}C
- there are 1.11 atoms of carbon-13 in nature for every 100 atoms of carbon-12

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

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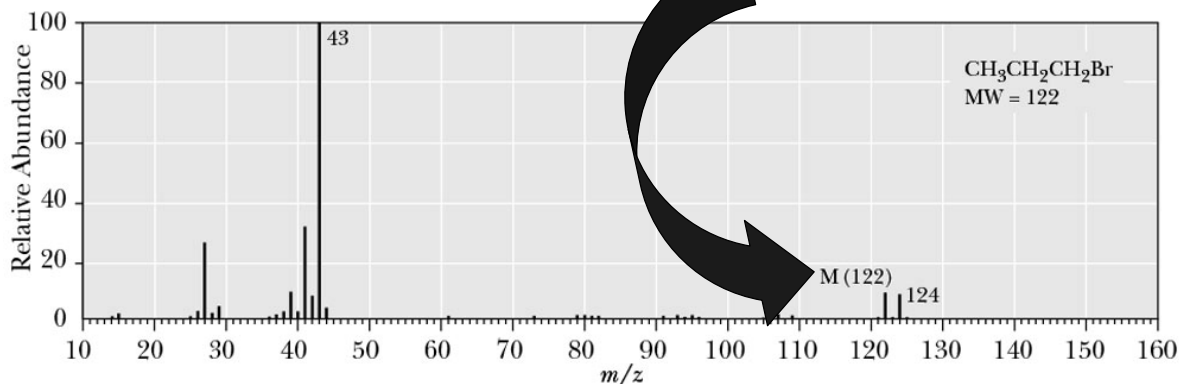
M+2 and M+1 Peaks

- The most common elements giving rise to significant 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



M+2 and M+1 Peaks

- 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



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M+2 and M+1 Peaks

- Sulfur is the only other element common to organic compounds that gives a significant M + 2 peak
 - $^{32}\text{S} = 95.02\%$ and $^{34}\text{S} = 4.21\%$
- Because M + 1 peaks are relatively low in intensity compared to the molecular ion and often difficult to measure with any precision, they are generally not useful for accurate determinations of molecular weight

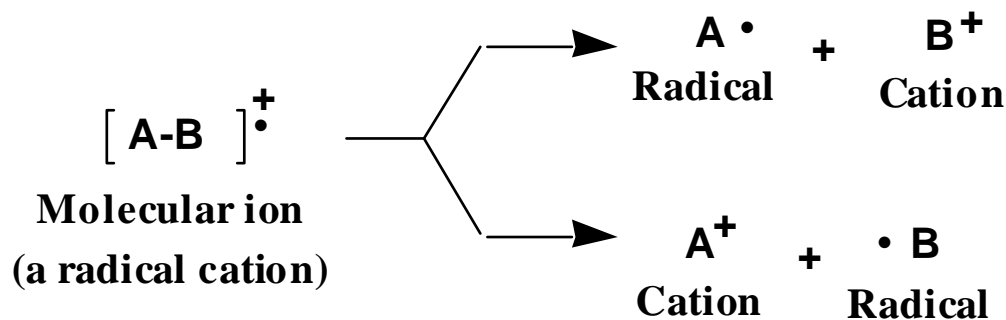
Fragmentation of M

- 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 [6750 kJ (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

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Fragmentation of M

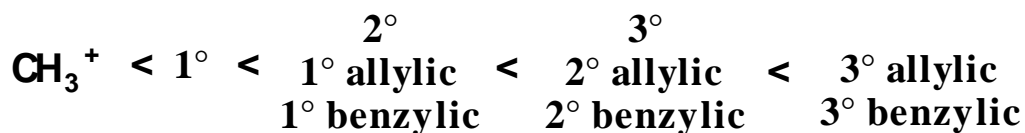
- Fragmentation of a molecular ion, M, produces a radical and a cation
 - only the cation is detected by MS



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



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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?
- Nitrogen Rule: if a compound has
 - zero or an even number of nitrogen atoms, its molecular ion will have an even m/z value
 - an odd number of nitrogen atoms, its molecular ion will have an odd m/z value

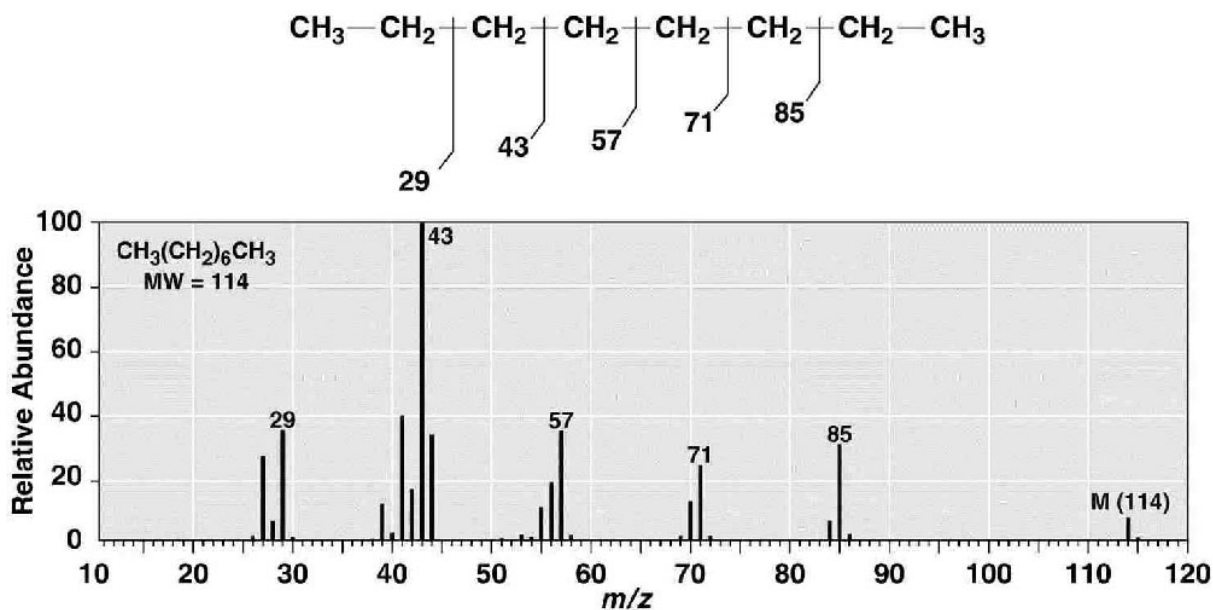
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Alkanes

- 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

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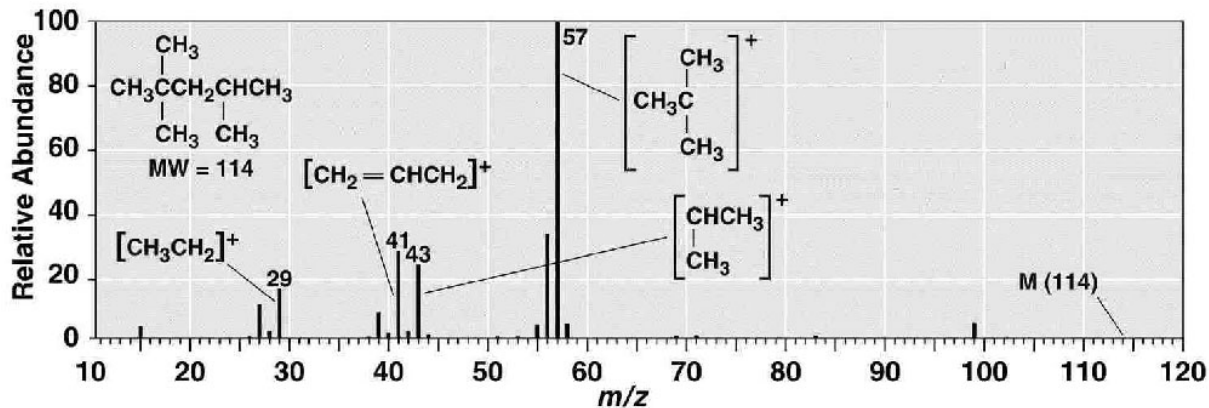
Alkanes



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Alkanes

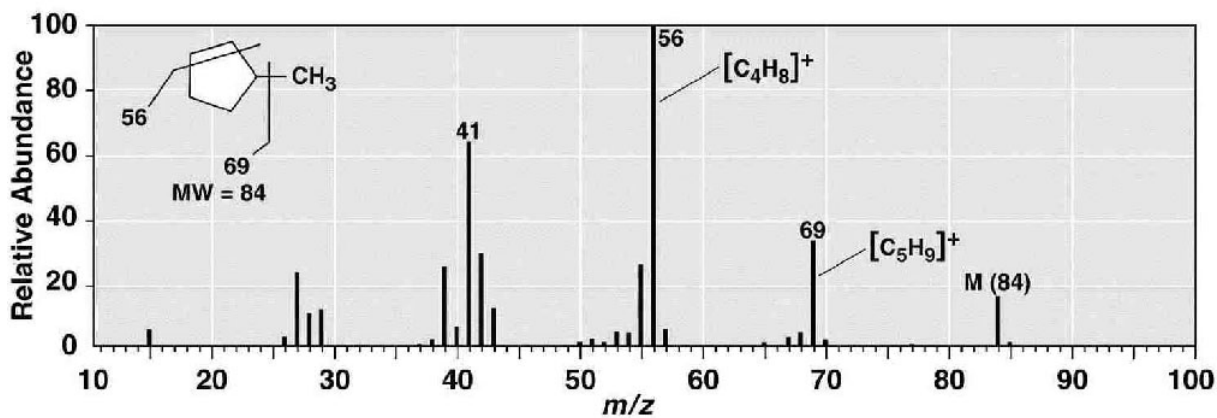
– MS of 2,2,4-trimethylpentane (Fig 14.6)



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Alkanes

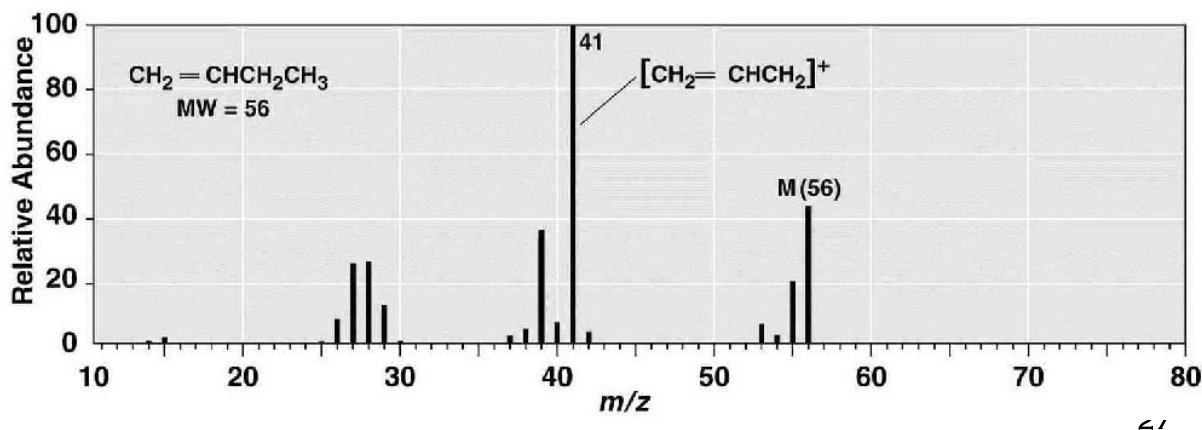
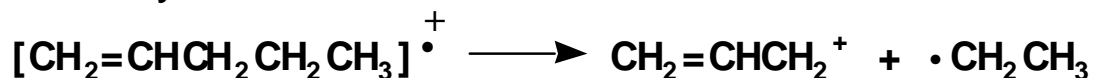
– MS of methylcyclopentane (Fig 14.7)



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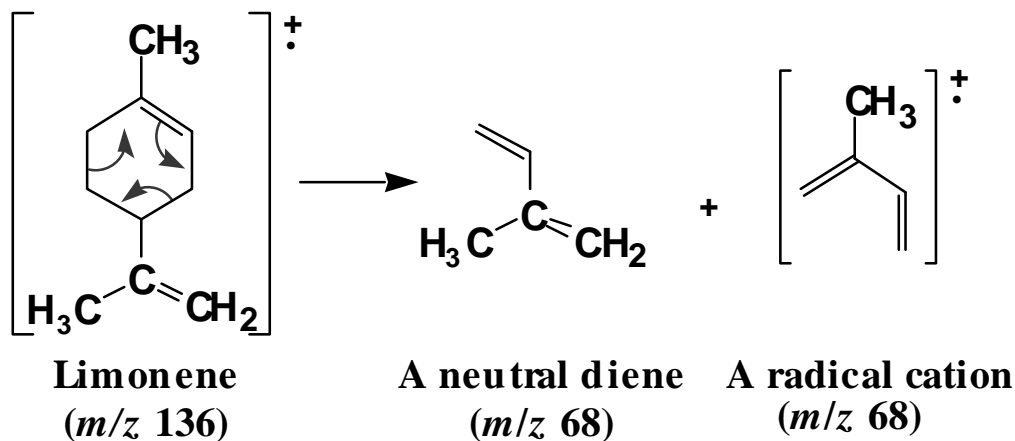
Alkenes

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



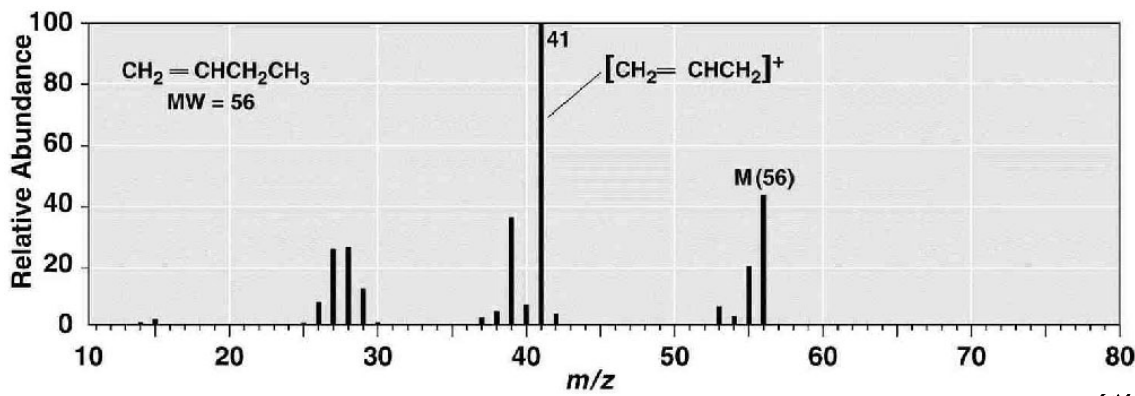
Cyclohexenes

- cyclohexenes give a 1,3-diene and an alkene, a process that is the reverse of a Diels-Alder reaction (Section 24.3)



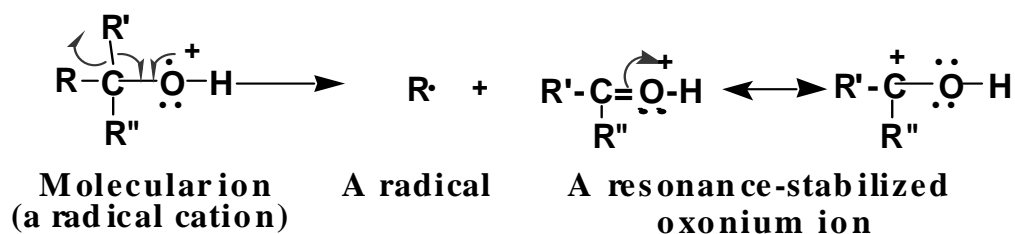
Alkynes

- Alkynes typically
 - show a strong molecular ion peak
 - cleave readily to form the resonance-stabilized propargyl cation or a substituted propargyl cation



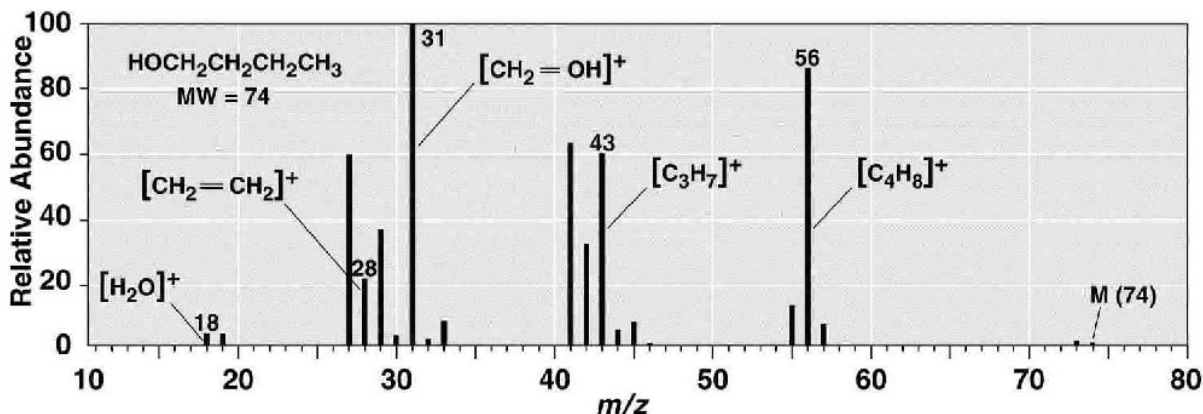
Alcohols

- One of the most common fragmentation patterns of alcohols is loss of H_2O to give a peak which corresponds to $M-18$
- 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

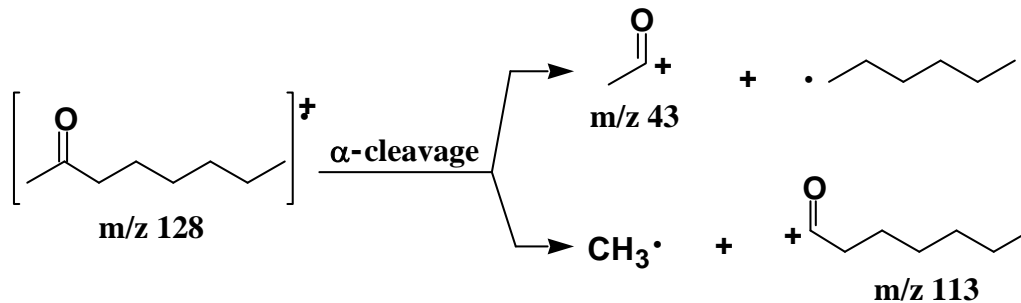
– MS of 1-butanol (Fig 14.8)



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Aldehydes and Ketones

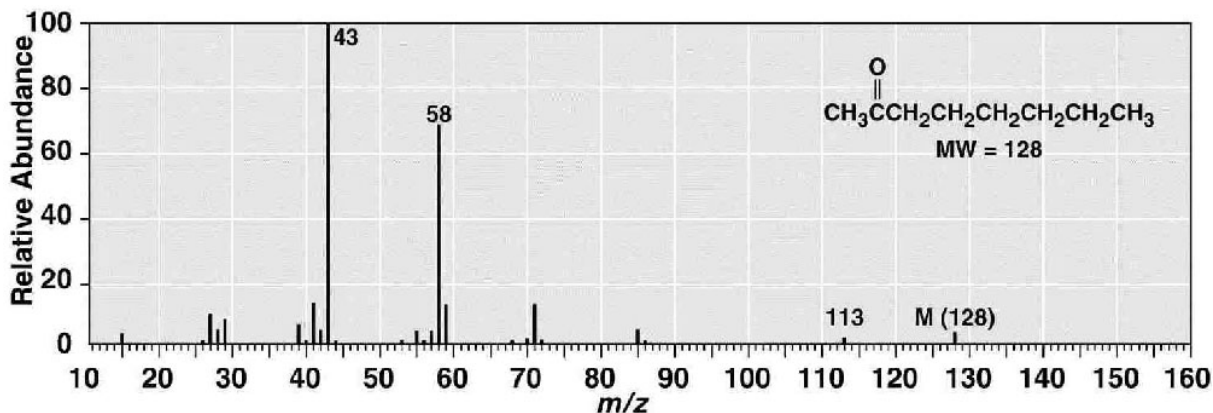
- Characteristic fragmentation patterns are
 - cleavage of a bond to the carbonyl group (α -cleavage)
 - McLafferty rearrangement



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Aldehydes and Ketones

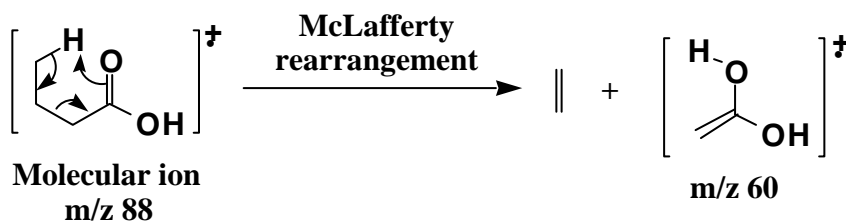
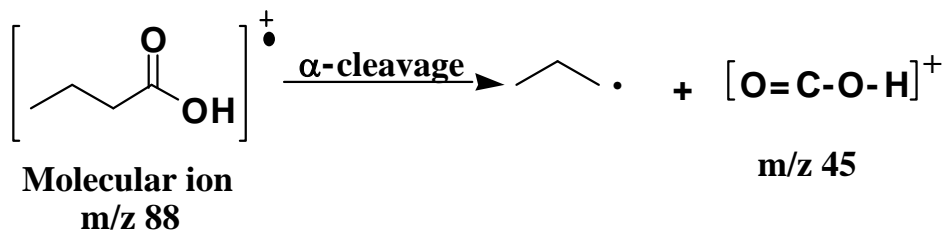
– MS of 2-octanone (Fig 14.9)



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Carboxylic Acids

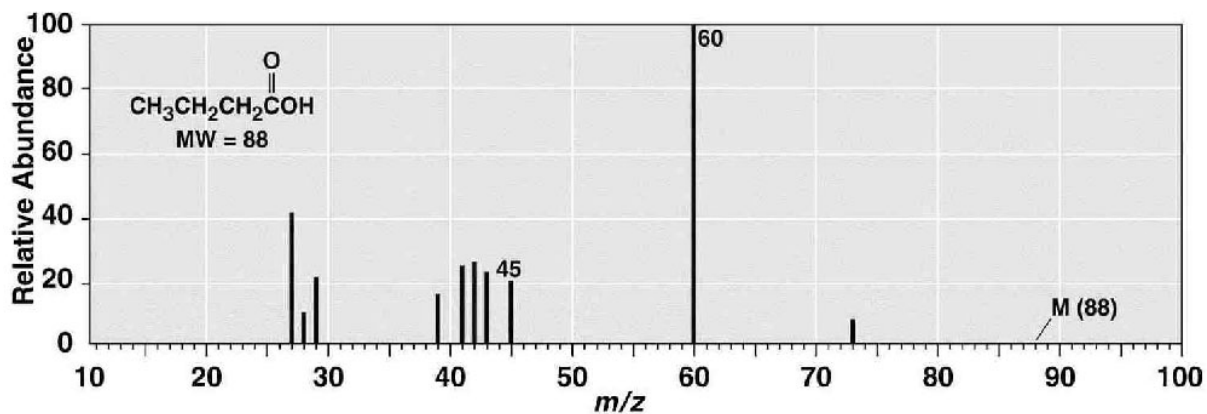
- Characteristic fragmentation patterns are
 - α -cleavage to give the ion $[\text{CO}_2\text{H}]^+$ of m/z 45
 - McLafferty rearrangement



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Carboxylic Acids

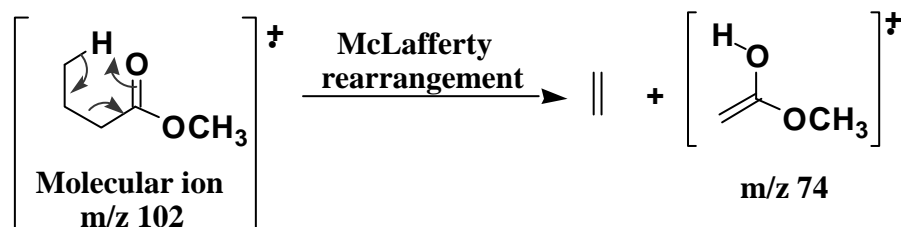
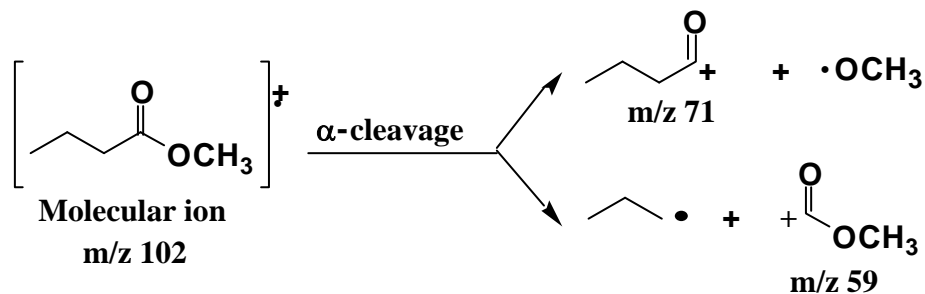
– MS of butanoic acid (Fig 14.12)



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Esters

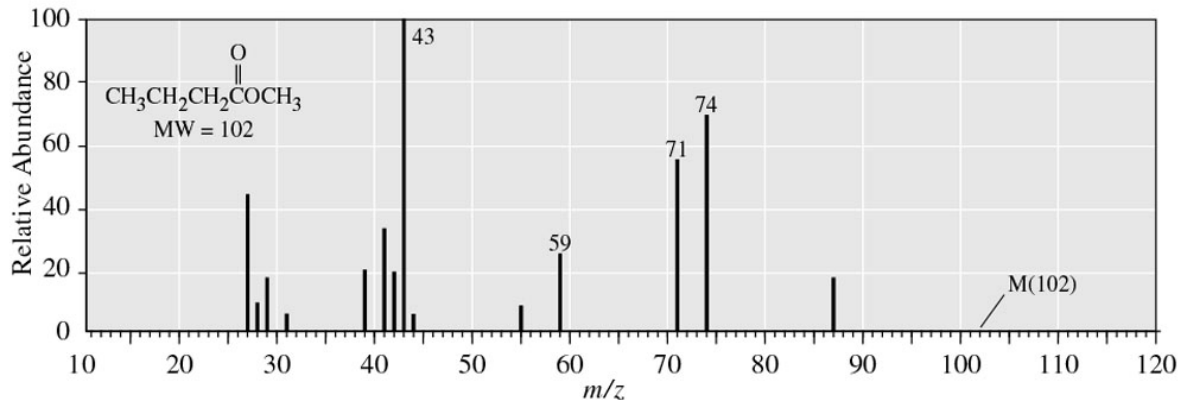
□ α -cleavage and McLafferty rearrangement



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Esters

– MS of methyl butanoate (Fig 14.13)

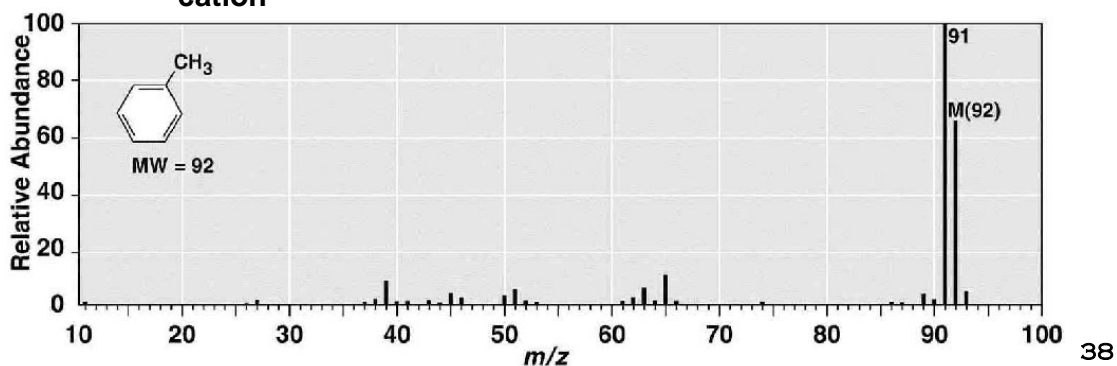
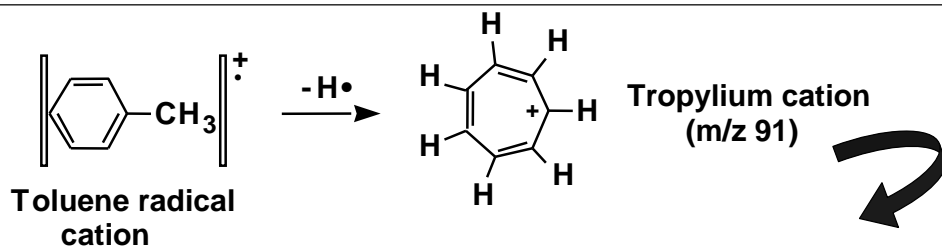


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Aromatic Hydrocarbons

- most show an intense molecular ion peak
- most alkylbenzenes show a fragment ion of m/z 91



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Amines

- The most characteristic fragmentation pattern of 1°, 2°, and 3° aliphatic amines is β -cleavage

