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Mass Spectrometry I: Principles and Instrumentation

Mass spectrometry (MS) is a technique for creating gas phase ions from the molecules or atoms in a sample, separating the ions according to their mass-to-charge ratio, m/z , and measuring the abundance of the ions formed. MS is currently one of the most rapidly advancing fields of instrumental analysis. It has developed from an inorganic method used to prove that most elements exist as isotopes of differing masses to one of the corner-stone techniques used to elucidate the structure of biomolecules, especially high molecular weight proteins. MS provides the analyst with information as diverse as the structure of complex organic and biomolecules to the quantitative determination of ppb concentrations of elements and molecules in samples.

MS is an analytical technique that provides qualitative and quantitative information, including the mass of molecules and atoms in samples as well as the molecular structure of organic and inorganic compounds. MS can be used as a qualitative analytical tool to identify and characterize different materials of interest to the chemist or biochemist. MS is used routinely for the quantitative analysis of mixtures of gases, liquids, and solids. MS is used in many fields in addition to identifying and quantifying organic and biological molecules. These include atomic physics, physical chemistry, and geology.

This chapter will focus on MS principles and instrumentation for both organic and inorganic analysis. Chapter 10 will cover applications of MS for organic and inorganic analyses as well as interpretation of simple mass spectra for structural identification of organic compounds.

9.1. PRINCIPLES OF MS

The mass spectrometer is an instrument that separates gas phase ionized atoms, molecules, and fragments of molecules by the difference in their mass-to-charge ratios. The mass-to-charge ratio is symbolized by m/z , where the mass m is expressed in **unified atomic mass units** and z is the number of charges on the ion. The statement found in many texts that MS separates ions based on *mass* is only true when the charge on the ion is +1; in this case m/z is numerically equal to the mass of the ion. While some MS methods do generate mostly +1 charged ions, many new techniques generate ions with multiple charges.

The mass of an ion is given in **unified atomic mass units, u**. One unified atomic mass unit is equal to 1/12 of the mass of the most abundant, stable, naturally occurring isotope of carbon, ^{12}C . The mass of ^{12}C is defined as exactly 12 u. The abbreviation **amu**, for atomic mass unit, is now considered obsolete but may still be encountered in the literature.

A synonym for the unified atomic mass unit is the dalton (Da); $1 \text{ u} = 1 \text{ Da}$. In the SI unit of mass, $1 \text{ u} = 1.665402 \times 10^{-27} \text{ kg}$. Table 9.1 presents the exact masses for some common isotopes encountered in organic compounds.

The term z symbolizes the *number of charges* on the ion; this number may be positive or negative, such as +1, -1, +2, +10, and so on. The number of charges is not the same as the total charge of the ion in coulombs. The total charge $q = ze$, where e is the magnitude of the charge on the electron, $1.6 \times 10^{-19} \text{ C}$.

For simplicity, the following discussion will focus on what happens to an organic molecule in one type of MS experiment. One method of forming ions from sample molecules or atoms is to bombard the sample with electrons. This method is called **electron ionization (EI)**:



where M , is the analyte molecule; e^- , the electron; and M^{+} , the ionized analyte molecule; this species is called the **molecular ion**.

In many cases, only ions with a single positive charge are formed; that is, the number of charges on the ion, z , equals +1. The MS separates ions based on the mass-to-charge ratio, m/z ; for ions with a single positive charge, m/z equals the mass of the ion in unified atomic mass units. For a molecular ion, m/z is related to the molecular weight (also called the relative molecular mass) of the compound. The symbol M^{+} indicates that a molecular ion from an organic compound is a radical cation formed by the loss of one electron. In most cases, molecular ions have sufficient energy as a result of the ionization process to undergo *fragmentation* to form other ions of lower m/z . All these

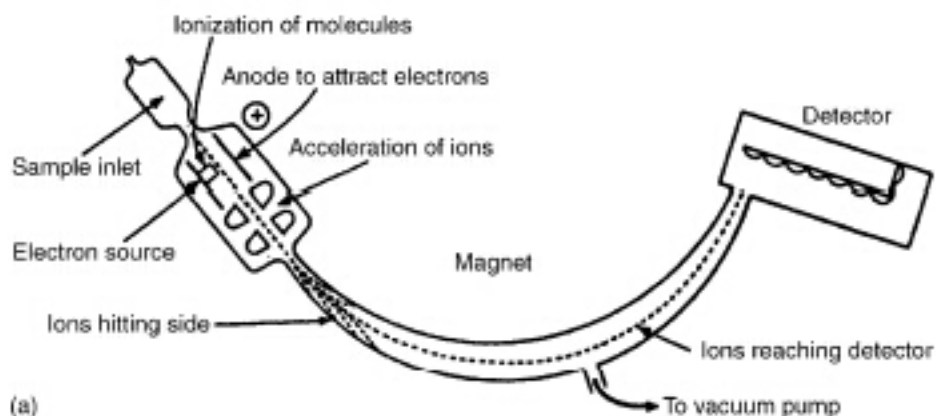
Table 9.1 Comparison of Atomic Weights and Measured Accurate Isotope Masses for Some Common Elements in Organic Compounds

Element	Atomic weight	Isotope	Mass ^a	% Abundance
Hydrogen	1.00794(7)	¹ H	1.007825	99.99
		² H(or D)	2.01410	0.01
Carbon	12.0107(8)	¹² C	12.000000 (defined)	98.91
		¹³ C	13.00336	1.1
Nitrogen	14.0067(2)	¹⁴ N	14.0031	99.6
		¹⁵ N	15.0001	0.4
Oxygen	15.9994(3)	¹⁶ O	15.9949	99.76
		¹⁷ O	16.9991	0.04
		¹⁸ O	17.9992	0.20
Fluorine	18.99840	F	18.99840	100
Phosphorus	30.97376	P	30.97376	100
Sulfur	32.065(5)	³² S	31.9721	95.02
		³³ S	32.9715	0.76
		³⁴ S	33.9679	4.22
Chlorine	35.453(2)	³⁵ Cl	34.9689	75.77
		³⁷ Cl	36.9659	24.23
Bromine	79.904(1)	⁷⁹ Br	78.9183	50.5
		⁸¹ Br	80.9163	49.5

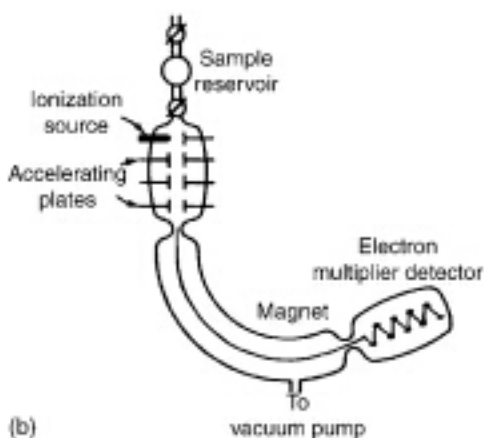
^aMany of the isotope masses have been determined by MS accurately to seven or more decimal places. Numbers in parentheses in the atomic weights represent the first uncertain figure. Atomic weights based on the values in *Pure Appl.Chem.* 2001, 73, 667–683 as tabulated at <http://www.chem.qmul.ac.uk/iupac/AtWt/>. Used with permission.

ions are separated in the mass spectrometer according to their m/z values and the abundance of each is measured.

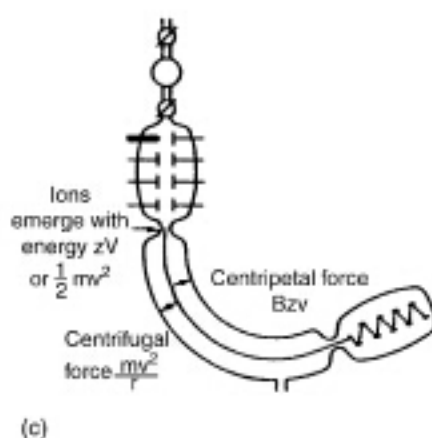
A magnetic sector mass spectrometer is shown schematically in Fig. 9.1. This instrument is a *single-focus* mass spectrometer. The gas phase molecules from the sample inlet are ionized by a beam of high energy (i.e., high velocity) electrons passing closely among them. The rapidly changing electric field can both eject electrons from the atom or molecule (ionization) and transfer sufficient energy to the molecule to cause its bonds to rupture (fragmentation). The ions are then accelerated in an electric field at a voltage V . If each ion has a single positive charge, the magnitude of the charge is equal to $+1$. The energy of each ion is equal to the charge z times the accelerating voltage, zV . The energy acquired by an ion on acceleration is kinetic energy. It is important to note that the kinetic energy of an ion accelerated through a voltage V depends only on the charge of the ion and the voltage, not on the mass of the ion. The translational component of the kinetic energy is equal to $1/2mv^2$. The kinetic energy of all singly charged ions is the same for a given accelerating voltage; therefore those ions with small masses must travel at higher velocity than ions with larger masses. That is, for



(a)



(b)



(c)

Figure 9.1 (a) Schematic magnetic sector mass spectrometer. (b) Schematic magnetic sector mass spectrometer showing a gas sample reservoir with fill and inlet valves and an EM detector. (c) Forces and energies associated with ions traveling through a magnetic sector mass spectrometer. For an ion to reach the detector, Bzv must equal mv^2/r .

ions with a single positive charge:

$$1/2mv^2 = zV \quad (9.2)$$

hence

$$v = \left(\frac{2zV}{m} \right)^{1/2} \quad (9.3)$$

where m is the mass of the ion; v , the velocity of the ion; z , the charge of the ion and V , the accelerating voltage.

As m varies, the velocity v changes such that $1/2mv^2$ remains a constant. This relation can be expressed for two different ions as follows:

$$\begin{aligned} zV &= 1/2m_1v_1^2 \text{ (ion 1)} \\ zV &= 1/2m_2v_2^2 \text{ (ion 2)} \end{aligned} \quad (9.4)$$

$$1/2m_1v_1^2 = 1/2m_2v_2^2$$

where m_1 is the mass of ion 1; v_1 , the velocity of ion 1; m_2 , the mass of ion 2 and v_2 , the velocity of ion 2.

The velocity of an ion depends on its mass; the velocity is inversely proportional to the square root of the mass of the ion.

After an applied voltage has accelerated the charged ions, they enter a curved section of a magnet of homogeneous magnetic field B and a fixed radius of curvature. This magnetic field acts on the ions, making them move in a circle. The attractive force of the magnet equals Bzv . The centrifugal force on the ion is equal to mv^2/r , where r is the radius of the circular path traveled by the ion. If the ion path is to follow the radius of curvature of the magnet, these two forces must be equal:

$$\frac{mv^2}{r} = Bzv \quad (9.5)$$

or

$$\frac{1}{r} = \frac{Bzv}{mv^2}$$

and

$$r = \frac{mv}{zB} \quad (9.6)$$

Substituting for v [Eq. (9.3)], we get

$$r = \frac{m}{zB} \left(\frac{2zV}{m} \right)^{1/2}$$

Squaring both sides, we have

$$r^2 = \frac{m^2}{z^2B^2} \frac{2zV}{m} = \frac{m2V}{zB^2} \quad (9.7)$$

which can be rearranged to give:

$$\frac{m}{z} = \frac{B^2 r^2}{2V} \quad (9.8)$$

That is, the radius of the circular path of an ion depends on the accelerating voltage V , the magnetic field B , and the ratio m/z . When V and B are kept constant, the radius of the circular path depends on the m/z value of the ionized molecule. Ions of different m/z travel in circles with different radii; this is the basis of the separation by m/z . Ions with different paths are shown as the dotted lines in Fig. 9.1(a); only one particular m/z has the right r to pass through the mass spectrometer under a given V and B . The others, as shown, follow paths that cause them to hit the sides of the instrument and be lost. By varying V or B , we can select which m/z will pass through the system. Voltage scanning is cheaper and was used in early instruments with permanent magnets. Scanning the magnetic field strength is more sensitive and is easily done with modern electromagnets. (In reality, a curved magnet with a path of significant width could accommodate a range of different m/z values, and it is the width and position of the exit slit that determine precisely which ions finally get through to the detector in a real scanning magnetic sector mass spectrometer.)

In all modern magnetic sector mass spectrometers, the applied magnetic field B of the electromagnet is varied while the accelerating voltage V is held constant. The radius of curvature of the magnetic sector of a given instrument is a constant, so only ions with a trajectory of radius r pass through. For a particular magnetic field strength, then, only ions with an m/z value that satisfies Eq. (9.8) will exit the chamber. Consequently, for different values of B , ions with different mass-to-charge ratios will pass through the instrument to the detector and by varying B , we can scan the range of mass-to-charge ratios of the sample ions and measure their abundance with a detector which either counts and sums individual ions or measures a current produced by their impact on the detector. A plot of m/z vs. abundance is called a **mass spectrum**. The mass spectral data can be shown as a plot or as a table. A digitized mass spectrum of benzene, C_6H_6 , is shown in Fig. 9.2(a); the plot is shown as a histogram. The most abundant peak in the spectrum, called the **base peak**, is scaled to 100, so the y-axis represents the **relative abundance** of the ions of each m/z value. The nominal mass of the benzene molecular ion is equal to the sum of the nominal masses of the C and H isotopes, so $6(12) + 6(1) = 78$; the most abundant peak in this benzene mass spectrum is the molecular ion peak at m/z 78. A number of fragment ions at lower values of m/z are also seen in this spectrum. Table 9.2 presents the same mass spectral data for benzene as shown in the plot. Figure 9.2(b) is a mass spectrum of cocaine, which exhibits many fragment ions. This example shows that the molecular ion is not always the most abundant ion. The base peak in the cocaine mass spectrum is the fragment ion at m/z 82. The m/z values and the fragmentation pattern enable the analyst to determine the molecular weight and structure of organic compounds by MS. Detailed interpretation of simple organic mass spectra will be covered in Chapter 10.

There is a difference between the mass of an atom (or ion) and what chemists are used to thinking of as the atomic weight or molecular weight of a species. Atomic weight is the average weight of all of the isotopes of an element and molecular weight is calculated from these average atomic weights. This is the value we would need to use if we wished to weigh out an exact number of moles of a substance whose component atoms have a distribution of different isotopes, which is usually the case. Each stable isotope (nuclide) of an element has an exact mass (more properly called a measured