

MASS SPECTROMETRY

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Summary

In the technique of mass spectrometry, atoms or molecules from a sample are transformed into ions (the ionization phase), which are separated and identified by their mass to charge ratio (mass spectrometry), and counted (detection). The identification of the ions provides information on the elements or molecules present in the sample and also on the structure of molecules; the number of ions can be related to the elemental or molecular concentrations in the sample. Mass spectrometry is a very sensitive technique: for molecules, detection limits in the femtomole range (10^{-15}) are often cited, and only picomoles of sample are needed. The different means of ionization for gaseous, liquid and solid samples are described. The various techniques for ion separation are reported. Finally, the main commercial systems for mass spectrometry are reviewed, as are their main uses in research and for applications.

1. Introduction

Mass spectrometry is a technique in which neutral atoms or molecules present in solid, liquid or gaseous samples are transformed into negative or positive ions, which are subsequently separated according to their *mass to charge ratio* (m/z), counted, and sometimes studied structurally. These ions are like a fingerprint of the original samples, and the information provided by their number, their m/z , and their structure, can be used in many areas of research as well as in a large number of analytical applications. Because some mass spectrometers can store selected ions within small volumes and for relatively long periods of time, other areas of research like ion interaction with neutral molecules or with photons, are facilitated. Schematically, since the first mass spectra obtained by J.J. Thomson in 1912, mass spectrometry has first been used for the study of the isotopes of elements, and has later been used mainly for the study/analysis of inorganic samples. Nowadays, the most important field is that of the organic compounds, with a constant increase in the number of applications concerning molecules « of biological interest »; these are biological molecules or molecules of interest in the pharmaceutical industry. The rather recent development of versatile ionization methods/sources, has allowed the efficient coupling of separation techniques (gas and liquid chromatography, capillary electrophoresis, etc.) to powerful modern mass spectrometers; this has largely contributed to the increase of the applications in the field of organic chemistry, taken in a wide sense. The purpose of the present chapter is to briefly give an overview of mass spectrometry, including principles, instrumentation and applications; it is clear that only the important and perhaps more recent aspects can be covered, at the expense of complete and/or detailed information.

(see *Physical Methods, Instruments and Measurements*)

2. Mass Spectrometry, Principles and Instrumentation

Basically, a mass spectrometer is composed of an ion source, of a system to separate the ions according to their m/z , and of an ion detector. These elements operate under different pressures, from atmospheric pressure to ultra-high vacuum, depending on the nature of the samples and on the operating principles of the different elements of the mass spectrometer. Today, any type of ion source may be connected to any type of mass spectrometer. In fact, a single system may include different ion sources, a hybrid mass selector (quadrupole and time-of-flight for instance), and may also be directly coupled

to separation techniques, as mentioned above. Therefore, modern systems are very versatile, efficient and powerful.
 (see *Vacuum Technology*)

2.1. Ionization Methods

For gases and volatile samples, atoms or molecules are easily and directly obtained under vacuum and may then be ionized by different techniques. For not very volatile inorganic or not so volatile organic samples that are not appreciably decomposed by heat, gas phase atoms or molecules can be obtained by heating under vacuum. Finally, techniques that combine vaporization and ionization in a single step have been developed for non-volatile and/or heat sensitive samples. These are desorption-ionization techniques (for solids mostly) and desolvation-ionization techniques (for dissolved organic molecules).

2.1.1. Ionization of Atoms and Molecules in the Gas Phase

Five techniques may be mentioned: electron impact ionization (EI), chemical ionization (CI), electric discharge ionization, photon ionization (PI) and inductively coupled plasma (ICP). EI is a general technique; an energy of 70 *electron-volts* is often used because it has become a standard allowing comparison between different laboratories and instruments, and also because the ionization cross-sections are acceptably high at this energy which is well above the ionization thresholds of all atoms and molecules. EI is considered as a « hard » ionization technique, and it actually produces an important number of fragments, besides molecular ions. CI allows the formation of positive molecular ions by protonation (attachment of a H^+ ion) using acid species in the gas phase, and of negative molecular ions by deprotonation using basic species. CI is a softer ionization method than EI as fewer fragments are obtained. For PI, lamps or lasers may be used to obtain positive ions from atoms or molecules, by removing the least bound electron. Lasers are of special interest because a number of different processes may be used, not only for ionization, but also for many fundamental studies on electronic structure. A few examples of laser techniques: single photon ionization with high energy photons (vacuum ultraviolet, X-rays), non-resonant multiphoton ionization, resonant multiphoton ionization; all these processes can be implemented with lasers delivering pulses of different duration: nanoseconds, picoseconds or femtoseconds. Among all these possibilities resonant photoionization is to be noted, since it is the only one that allows the selective ionization of chosen atoms or molecules. The ICP method is in practice applied to atomic species; these are efficiently ionized at the very high temperatures reached in an argon plasma produced by a radiofrequency power.

(see *Optical Sources and Detectors*)

2.1.2. Ionization Methods for Solid Samples

Ions may be directly obtained from solid samples placed under vacuum, by using desorption-ionization processes, in which ions are obtained in a single step instead of vaporizing and then ionizing. Desorption-ionization is achieved by bombarding a sample with atoms or with photons; methods based on electric fields may also be

classified in that category. It should be noted that in all these techniques, neutral particles are produced simultaneously with the ions and in much larger quantity. Many different experimental conditions may be used when bombarding with atoms, always resulting in the ejection of ions from the solid by energy transfer. The projectiles may be monatomic ions, neutral atoms, or clusters. The energies of the projectiles may range from a few keV to more than a hundred MeV. The most used technique, however, is the bombardment with keV ions, resulting in sample sputtering. For laser beams, many different experimental conditions have been used, always resulting in the formation of microplasmas from which ions are extracted. Wavelengths from the ultraviolet to the infrared, and power regimes from 10^6 to 10^9 W/cm 2 , have been used. In the case of organic samples, these may be irradiated directly, or after mixing with an organic compound, which is called « matrix », and which possesses a strong absorption coefficient at the wavelength of the incident laser. This latter technique is known as the « matrix assisted laser desorption-ionization » (MALDI) technique. Finally, ions may be obtained from solids by creating sparks (spark source), stable currents (glow discharge), or high local fields (field emission), under application of suitable voltages.
(see electric discharge, field emission)

2.1.3. Ionization Methods for Liquid Samples

The bombardment with keV ions or keV neutral atoms (in the latter case called « fast atom bombardment », or « FAB ») under vacuum, is also applied to liquid samples. These samples are organic molecules dissolved in a « liquid matrix », which is a low vapour pressure compound (often glycerol) because of vacuum requirements. On the other hand, several methods of desolvation-ionization have been developed, which all go through a nebulization step. In the « electrospray » method (ESI), the solution is sprayed through a capillary under an electric field of several kV/cm; the analyte molecules are desolvated as they travel along the electric field. Under these conditions, multicharged positive or negative ions are obtained: the heavier the analyte molecules, the higher the number of charges that they may carry. To give an example, a DNA ion carrying 30000 charges has been detected. A great advantage of the electrospray ionization technique is that the mass spectrometry of very heavy molecules becomes accessible to mass spectrometers of limited m/z range; on another hand, the mass spectra are more complex, due to the presence of many charge states. Recently, a technique to reduce the number of charge states of ions from an electrospray source has been developed, and that may be of help to simplify mass spectra. This technique is called « charge reduced electrospray » ; it is based on the neutralization of the higher charge states by interaction with positive or negative ions generated in a CO₂+N₂ atmosphere by a Polonium 210 α -source ; this interaction predominantly yields singly charged ions and some doubly charged ions. In another method, called « atmospheric pressure chemical ionization » (APCI), the liquid sample flows through a heated capillary (~400°C) and is nebulized under an air flow at atmospheric pressure. The analyte molecules are ionized by reactive radical ions and also by electrons, created by an electric discharge (Corona discharge).

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Biographical Sketches

Debrun Jean-Luc: Director of research, Centre National de la Recherche Scientifique, PhD in chemistry. After a number of years in the field of nuclear analytical methods, is now involved in the study of mechanisms of laser ionization of organic molecules and related analytical applications.

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