2.3: Ionization Techniques

Learning Objectives

- Learn about different ionization techniques
- Explain common ionization methods

A small amount of sample is injected into the mass spectrometer, which is vaporized upon entering. It is then bombarded with a stream of high-energy electrons. When the molecule of interest is struck by this high-energy electron beam, a valence electron is knocked out and the molecule becomes a positive ion. It has become ionized. There are a variety of ways for the instrument to ionize the molecule, which will be discussed here.

Electron Impact (EI)

In electron impact ionization, a vaporized sample is passed through a beam of electrons. The high energy (typically 70 eV) beam strips electrons from the sample molecules leaving a positively charged radical species. The molecular ion is typically unstable and undergoes decomposition or rearrangement to produce fragment ions. Because of this, electron impact is classified as a “hard” ionization technique. One of the main limitations of EI is that the sample must be volatile and thermally stable.

Chemical Ionization (CI)

In chemical ionization, the sample is introduced to a chamber filled with excess reagent gas (such as methane). The reagent gas is ionized by electrons, forming a plasma with species such as CH_5^+, which react with the sample to form the pseudomolecular ion $[M+H]^+$. Because CI does not involve radical reactions, fragmentation of the sample is generally much lower than that of EI. CI can also be operated in negative mode (to generate anions) by using different reagent gases. For example, a mixture of CH_4 and NO_2 will generate hydroxide ions, which can abstract protons to yield the $[M-H]^-$ species. A related technique, atmospheric pressure chemical ionization (APCI) delivers the sample as a neutral spray, which is then ionized by corona discharge, producing ions in a similar manner as described above. APCI is particularly suited for low molecular weight, nonpolar species that cannot be easily analyzed by other common techniques such as ESI.

Field Ionization/Desorption

Field ionization and desorption are two closely related techniques which use quantum tunneling of electrons to generate ions. Typically, a highly positive potential is applied to an electrode with a sharp point, resulting in a high potential gradient at the tip (see figure below). As the sample reaches this field, electron tunneling occurs to generate the cation, which is repelled into the mass analyzer. Field ionization utilizes gaseous samples whereas in field desorption the sample is adsorbed directly onto the electrode. Both of these techniques are *soft*, resulting in low energy ions which do not easily fragment.

Schematic of field ionization.

Electrospray Ionization (ESI)

Electrospray ionization mass spectrometry is a desorption ionization method. Desorption ionization methods can be performed on solid or liquid samples, and allows for the sample to be nonvolatile or thermally unstable. Electrospray ionization is a soft ionization technique that is typically used to determine the molecular weights of proteins, peptides, and other biological macromolecules. Soft ionization is a useful technique when considering biological molecules of large molecular mass, such as the aformetioned, because this process does not fragment the macromolecules into smaller charged particles, rather it turns the macromolecule being ionized into small droplets. These droplets will then be further desolvated into even smaller droplets, which creates molecules with attached protons. These protonated and desolvated molecular ions will then be passed through the mass analyzer to the detector, and the mass of the sample can be determined. As the droplets shrink due to evaporation, the charge density increases until a *coulombic explosion* occurs, producing daughter droplets that repeat the process until individualized sample ions are generated (see figure below). One of the limitations of is the requirement that the sample be soluble. ESI is best applied to charged, polar, or basic compounds.

Schematic of electrospray ionization.

Matrix Assisted Laser Desorption Ionization (MALDI)

Laser desorption ionization generates ions by ablation from a surface using a pulsed laser. This technique is greatly improved by the addition of a matrix co-crystallized with the sample. As the sample is irradiated, a plume of desorbed molecules is generated. It is believed that ionization occurs in this plume due to a variety of chemical and physical interactions between the sample and the matrix (see figure below). One of the major advantages of MALDI is that it produces singly charged ions almost exclusively and can be used to volatilize extremely high molecular weight species such as polymers and proteins. A related technique, desorption ionization on silicon (DIOS) also uses laser desorption, but the sample is immobilized on a porous silicon surface with no matrix. This allows the study of low molecular weight compounds which may be obscured by matrix peaks in conventional MALDI.

Schematic of matrix assisted laser desorption ionization.

Inductively Coupled Plasma Mass Spectrometry (ICP-MS)

A plasma torch generated by electromagnetic induction is used to ionize samples. Because the effective temperature of the plasma is about 10,000 °C, samples are broken down to ions of their constituent elements. Thus, all chemical information is lost, and the technique is best suited for elemental analysis. ICP-MS is typically used for analysis of trace elements.

Fast Atom Bombardment (FAB) and Secondary Ion Mass Spectrometry (SIMS)

Both of these techniques involve sputtering a sample to generate individualized ions; FAB utilizes a stream of inert gas atoms (argon or xenon) whereas SIMS uses ions such as Cs^+. Ionization occurs by charge transfer between the ions and the sample or by protonation from the matrix material (Figure $2.3.4$). Both solid and liquid samples may be analyzed. A unique aspect of these techniques for analysis of solids is the ability to do depth profiling because of the destructive nature of the ionization technique.

Schematic of fast atom bombardment ionization.

Choosing an Ionization Technique

Depending on the information desired from mass spectrometry analysis, different ionization techniques may be desired. For example, a hard ionization method such as electron impact may be used for a complex molecule in order to determine the component parts by fragmentation. On the other hand, a high molecular weight sample of polymer or protein may require an ionization method such as MALDI in order to be volatilized. Often, samples may be easily analyzed using multiple ionization methods, and the choice is simplified to choosing the most convenient method. For example, electrospray ionization may be easily coupled to liquid chromatography systems, as no additional sample preparation is required. Table $2.3.1$ provides a quick guide to ionization techniques typically applied to various types of samples.

Table $2.3.1$ Strengths of various ionization techniques

Information Desired	**Ionization Technique**
Elemental analysis	Inductively coupled plasma
Depth profiling	Fast atom bombardment/secondary ion mass spectroscopy
Chemical speciation/component analysis (fragmentation desired)	Electron impact
Molecular species identification of compounds soluble in common solvents	Electrospray ionization
Molecular species identification of hydrocarbon compounds	Field ionization
Molecular species identification of high molecular weight compounds	Matrix assisted laser desorption ionization
Molecular species identification of halogen containing compounds	Chemical ionization (negative mode)