Practical Aspects of Electron Ionization

5

Learning Objectives

- Electron ionization ion sources – construction and operation
- Generating primary electrons for electron ionization
- Sample introduction into EI ion sources – methods and devices
- Databases of EI mass spectra

The use of *electron ionization* (EI) [1] dates back to the infancy of mass spectrometry in the early twentieth century. Before, only *spark source* (SS), *glow discharge* (GD), and *thermal ionization* (TI) had been in use [2]. In electron ionization, energetic electrons are shot onto gaseous neutrals to effect their ionization. EI definitely represents the classical approach to ionization in organic mass spectrometry. EI still remains an important technique for analyzing low- to medium-polarity, non-ionic organic compounds of molecular weights in the range of up to $M_r \approx$ 800 u. EI formerly has been referred to as *electron impact ionization* or simply *electron impact* (EI).

The physicochemical aspects of the ionization process in general, ion internal energy, and the principles determining the reaction pathways of excited ions have already been addressed (Chap. 2). Here, we will discuss practical aspects concerning the construction of EI ion sources and sample introduction systems. Finally, by considering EI mass spectral databases, this chapter directly leads over to the interpretation of EI mass spectra (Chap. 6).

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5.1 Electron Ionization Ion Sources

5.1.1 Layout of an Electron Ionization Ion Source

The basic layout of any ion source has already been introduced (Sect. 4.1). The design is arranged so that an ion generated within an electric field as realized between two oppositely charged plates, will be accelerated towards the plate oppositely charged to itself. If the attracting plate has a hole or a slit, a beam of approximately monoenergetic ions is produced. For practical reasons, the attracting electrode is usually grounded and the location of ion generation is set to high potential. Doing so allows to keep the mass analyzer grounded, thereby contributing substantially to safety of operation (Fig. 5.1).

The beam of neutral gaseous analyte molecules enters the *ionization chamber* or *ion volume*, i.e., the actual region of ionization within the *ion source block*, in a line vertical to the paper plane and crosses the electron beam in the center. In order to reduce loss of ions by neutralizing collisions with the walls, the ions are pushed out immediately after generation by action of a low voltage applied to the *repeller* electrode [3, 4]. They are then accelerated and focused towards the mass analyzer. Efficient ionization and ion extraction are of key importance for the construction of ion sources producing focusable ion currents in the nanoampere range [5].

Modern ion sources are of compact design to simplify the handling during exchange and cleaning (Figs. 5.2 and 5.5). Magnetic sector instruments either come with *combination ion sources* switchable from EI to *chemical ionization* (CI), *fast atom bombardment* (FAB), or *field ionization/field desorption* (FI/FD). Particularly EI/CI/FAB and EI/FI/FD [7, 8] ion sources have been widespread in use.

Some instruments are equipped with ion sources having exchangeable ion volumes that can be accessed via a (separate) vacuum lock to allow for their exchange without breaking the high vacuum.

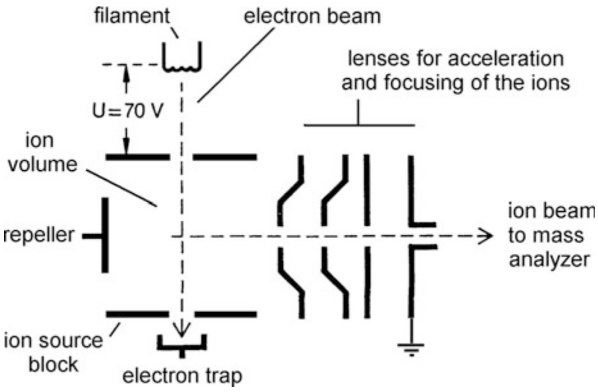


Fig. 5.1 Principle layout of an EI ion source (Adapted from Ref. [6] with permission. © Springer-Verlag Heidelberg, 1991)

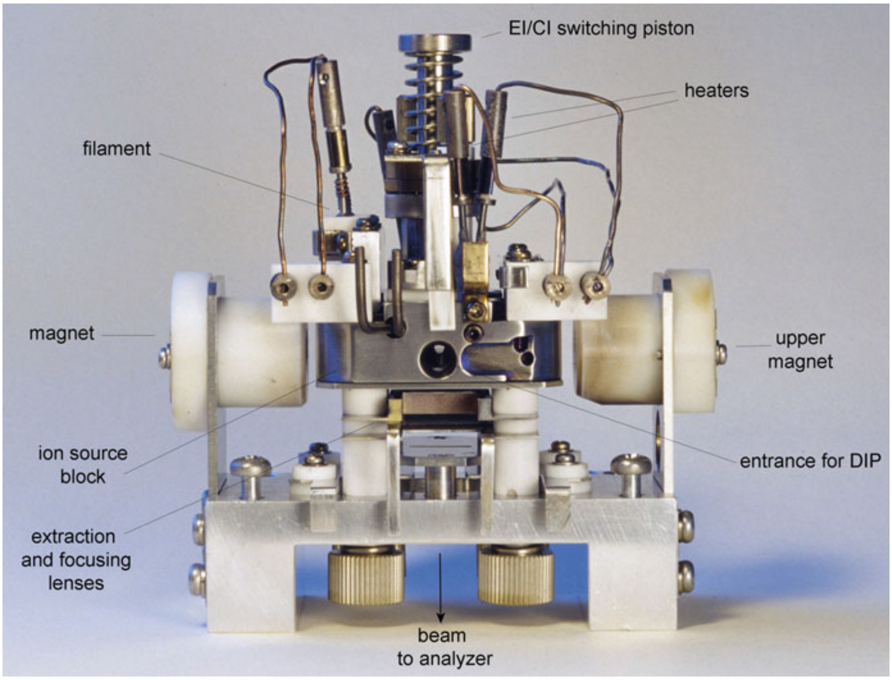


Fig. 5.2 EI/CI/FAB combination ion source of a JEOL JMS-700 sector instrument

More recently, there is a reverse trend to dedicated EI ion sources in order to achieve the utmost sensitivity. Dedicated sources – some even restricted to be used with *either* direct insertion probe *or* gas chromatograph – are optimized for trace level analyses. For covering a wide variety of samples, combination sources are hard to beat in versatility.

System contamination

High vacuum systems and ion sources, the more so, are almost inevitably prone to *contamination* in the process of *sample introduction*. Even though ion sources are operated at 150–250°C, decomposition products of low volatility cannot be removed by pumping. Instead, they form semiconducting layers on the surfaces which in turn cause defocusing due to badly defined potentials. Therefore, cleaning of an ion source is necessary on a regular basis. This includes disassembling, use of fine abrasives to polish the lenses, baking of the insulating ceramics, and thorough washing of the parts.

5.1.2 Generation of Primary Electrons

The beam of ionizing electrons is produced by *thermionic emission* from a resistively heated metal wire or *filament* typically made of rhenium or tungsten. The filament reaches up to 2000 °C during operation. Some reduction of the working temperature without loss of electron emission (1–10 mA mm^{-2}) can be achieved by use of thoriated iridium or thoriated rhenium filaments [9]. There is a wide variety of filaments available from different manufacturers working almost equally well, e.g., the filament can be a straight wire, a ribbon, or a small coil (Fig. 5.3).

The potential for acceleration of the primary electrons has to be carefully shielded from the acceleration voltage for the ions. Otherwise, badly defined ion kinetic energies cause substantial loss of resolution and mass accuracy. In addition, a pair of permanent magnets with their field aligned in parallel to the electron beam is attached above the filament and below the electron trap, thus preventing the electrons from spreading all over the ion volume (Fig. 5.2). This is achieved by action of the Lorentz force on divergent electrons which are forced to travel on helical paths; the resulting electron beam is about 1 mm in diameter. These features developed by Bleakney [10], and refined by Nier [11] were destined to direct the design of EI ion sources ever since [2, 4, 12] (the basic EI ion source is sometimes referred to as “Nier-type” ion source). Further improvements can be obtained by (*i*) more efficient shielding of the ion volume from the filament, a measure also reducing thermal decomposition of the analyte, and (*ii*) by use of stronger ion source magnets [3].

To achieve a more stable mode of operation, in modern instruments the heating current for the filament is *emission-controlled*, i.e., the current of the electron trap is used to keep emission comparatively independent from actual ion source conditions. Typical emission currents are in the range of 50–400 μA.

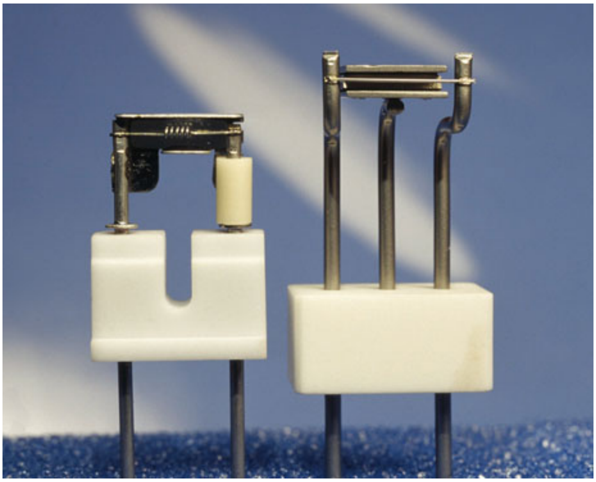


Fig. 5.3 Filaments for EI/CI ion sources. A coiled filament of the VG ZAB-2F (*left*) and a straight wire filament of the JEOL JMS-700 (*right*). The shields behind the filament are at the same potential as the wire itself and the white parts are made of ceramics for insulation

Filament lifetime

The lifetime of a filament is several weeks under proper operating conditions. However, this may become drastically shortened by the harsh conditions of aggressive analytes or reagent gases in chemical ionization, too high emission current, and in particular sudden breakdown of the high vacuum.

5.1.3 Overall Efficiency and Sensitivity of an EI Ion Source

The overall efficiency of an EI ion source depends on the intrinsic properties of the ionization process, the ion source design, and the actual operation parameters. The most astonishing fact is the extremely low ionization probability for a neutral entering the ion source. Only a minor fraction of the sample introduced becomes ionized, whereas the vast majority gets lost via the vacuum pumps. This is due to the disadvantageous combination of long mean free paths for ions and electrons and the low collision cross section of the electron itself. Remember, the path through the effective ionization volume is merely about 1 mm long. Nonetheless, EI provides high sensitivity as compared to other ionization methods.

In 70 eV EI mode, modern magnetic sector instruments are specified to have a sensitivity of about 4×10^{-7} C μg^{-1} for the molecular ion of methylstearate, *m/z* 298, at $R = 1000$. The charge of 4×10^{-7} C corresponds to 2.5×10^{12} electron charges. One microgram of methylstearate is equivalent to 3.4×10^{-9} mol or 2.0×10^{15} molecules. For a molecule entering the ionization volume one therefore calculates a chance of 1:800 to become ionized and to reach the detector as a molecular ion. The fraction of the neutrals that become ionized is definitely larger, maybe 1:100, because a significant fraction of them will dissociate to form fragment ions of other *m/z* values. Even then, a ratio of about 1:100 indicates an almost perfect ion source design as compared to $1{:}10^4$–10^5 in the 1970s. (For a comparison of EI to other ionization methods refer to Sect. 8.8.1.)

5.1.4 Optimization of Ion Beam Geometry

The extraction of ions and the shape of the ion beam can largely be improved if the acceleration voltage is applied in two or more successive stages instead of a single stage. In addition, by dividing the plates into an upper and a lower half or a left and a right one, the ion beam can be directed up and down or adjusted from right to left, respectively, by applying slightly different voltages to the corresponding halves (Figs. 5.1 and 5.2). This also allows for focusing of the ion beam.

In practice, the ion optical properties of an ion source are optimized by means of ion trajectory calculations. [13]. The standard tool for this task is the SIMION

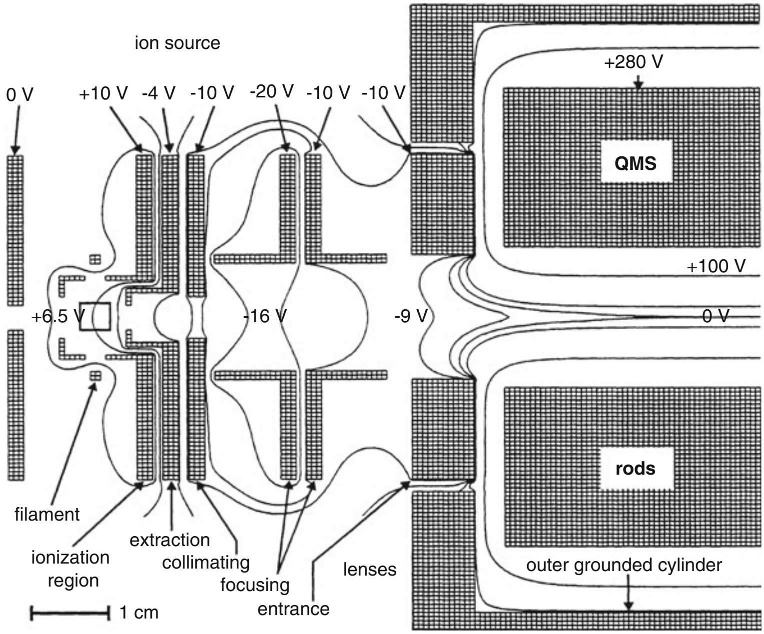


Fig. 5.4 The EI ion source of a quadrupole mass spectrometer with equipotentials as calculated by the computer simulation program SIMION three-dimensional version 6.0 (Reproduced from Ref. [15] with permission. © Elsevier Science, 1998)

software suite [14–17], while there are others, too [18]. Thus one can determine the optimum number, positions, voltages, and eventually shapes of the plates (Fig. 5.4). In order to compensate for slight mechanical deviations from theory and for effects exerted by contamination of the plates during elongated use, the voltages can be adjusted to yield optimum conditions.

Tuning the ion source

Usually, some *tuning* of the instrument is performed before actually starting measurements. Such a tuning procedure mainly means adjusting the voltages applied to the ion acceleration lenses of the ion source and eventually of some additional components of the ion optical system. Modern instruments may offer automatic tuning routines that are often faster and even more thorough than routine manual tuning would be. In any case, a reasonable mass spectrometer data system will also allow for manual corrections.

5.1.5 Mounting the Ion Source

While ion sources were rather fragile units in the past, modern ion sources are generally of compact design. Many manufacturers have understood that quick and reliable exchange of ion sources is as important in daily routine operations as the performance characteristics of the source. Thus, sources tend to be mounted via some sort of plugging mechanism that allows to insert or remove the ion source without touching any of the connection leads. Sometimes, a special probe-like tool is provided for exchange of the ion source. Some instruments require venting before and evacuation after exchanging ion sources (Fig. 5.5), others may even offer a vacuum lock that not only serves for the direct insertion probe but also allows for exchanging ion sources or at least ion volumes. Exchange of an ion source may thus require 15–60 min depending on whether the vacuum needs to be broken or not.

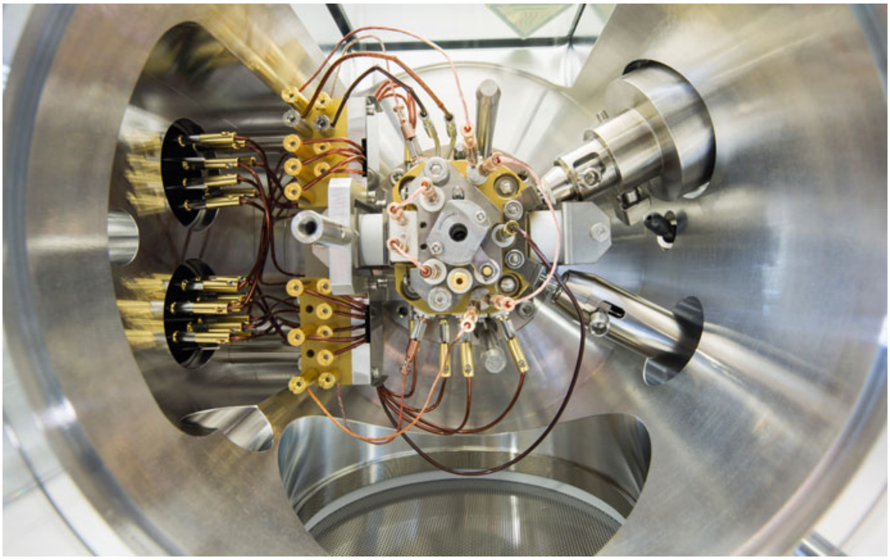


Fig. 5.5 An EI source mounted in the ion source housing of a JEOL AccuTOF GCx instrument. All voltages for operation are supplied via vacuum lead throughs from the left side. A connector to a gas chromatograph reaches down from the *upper right* while a connector to the reservoir inlet enters from the *lower right* side. Once the front cover plate bearing the vacuum lock has been mounted, a direct insertion probe can be introduced axially into the central notch of the ion source. The turbomolecular pump of the ion source housing is located directly below the protective wire mesh on the bottom

Nice to have
A window pane on top of the ion source housing allows to observe the probe during insertion, to locate an eventually lost sample vial, to roughly judge ion source contamination, and to check filament emission simply by observing whether it still shines brightly or remains dark.

5.2 Sample Introduction

For the purpose of sample introduction, any *sample introduction system* (also *sample inlet system* or *inlet*) can be employed that is suitable for the respective compound. Hence, *direct probes*, *reservoir inlets*, *gas chromatographs*, and even *liquid chromatographs* can be attached to an EI ion source. Which type of an inlet system is to be preferred depends on the type of sample to be analyzed. Whatever type the inlet system may be, it has to manage the same basic task, i.e., the transfer of the analyte from atmospheric conditions into the high vacuum of the EI ion source; Table 5.1 provides an overview.

Not for EI only
The below-mentioned sample introduction systems (reservoir inlets, various direct insertion probes, and chromatographs) are of equal importance to other ionization methods.

Table 5.1 Sample introduction systems for EI-MS

Inlet system	Principle	Analytes
Reservoir/reference inlet	Heated reservoir with sample vapor	Low to medium boiling liquids
Direct insertion probe, DIP	Sample in heated/cooled glass/metal vial as particles or film of analyte	Solids, waxes or high-boiling liquids
Direct exposure probe, DEP	Sample particles or film of analyte on resistively heated metal filament	Solids of extremely low volatility, especially if thermally labile
Gas chromatograph, GC	Elutes directly into ion source	Volatile components of mixtures
Liquid chromatograph, LC	Connected via particle beam interface	Analytes suitable for EI that cannot be separated by GC due to high polarity

5.2.1 Reservoir or Reference Inlet System

Highly volatile samples cannot be introduced into the ion source by means of a direct insertion probe even when cooling is applied. A *reference inlet system* or *reservoir inlet system* is better suited for that purpose [19]. The name of this type of inlet has been coined by the fact that reference inlets have been intended – and often are used for – the introduction of a mass calibrant (or *reference*) independent of the analyte in order to achieve internal mass calibration in accurate mass measurements (Sect. 3.6). Fluorocarbons such as *perfluorotributylamine* (PFTBA, aka FC43) or *perfluorokerosene* (PFK) can be admitted to the ion source via the reservoir inlet.

Reference/reservoir inlets serve equally well for the analysis of gases, solvents, and similar volatile samples. They are especially convenient when a continuous signal is desired for instrument tuning or long-lasting MS/MS experiments in ion chemistry. In addition, the components of a mixture are admitted to the ion source without fractionation, i.e., without affecting their partial pressures. Due to this property, reservoir inlets have extensively been used in the petroleum industry.

Typically, reference inlets are filled with a few microliters of liquid sample by means of a microliter syringe. Heating is applied to suppress adsorption of the analytes to the walls, and thus, to speed up the final removal of sample. As the analyte is exposed to prolonged heating, the application of reference inlet systems should be restricted to thermally stable analytes.

Basic components and features of a reference inlet system comprise (Fig. 5.6):

- Vessel of 30–100 ml that can be constantly heated to 80–200 °C.
- Access via a septum port or similar kind of injector.
- Connection to the ion source via a toggle valve (on/off) and a needle valve to adjust the partial pressure in the ion source housing.
- Roughing port to remove the sample after completion of the measurement by evacuation into a rotary or membrane pump.

Special reservoir types

To reduce the risks of catalytic degradation and selective adsorption of components of mixtures on the walls of the reservoir, an *all-glass heated inlet system* (AGHIS) [20, 21] and a teflon-coated reservoir inlet system have been commercially available as an alternative to stainless steel systems. To this end, *dynamic batch inlet systems* (DBIS) have been developed, where the analyte is transferred from the reservoir into the ion source by means of a capillary and where a carrier gas (H_2, He) can be used to reduce fractionation of mixtures having an extremely wide range of boiling points [21]. The *liquid introduction system* represents another variation of reservoir inlets where a few microliters of liquid are introduced by means of a kind of “micro DIP” [22].

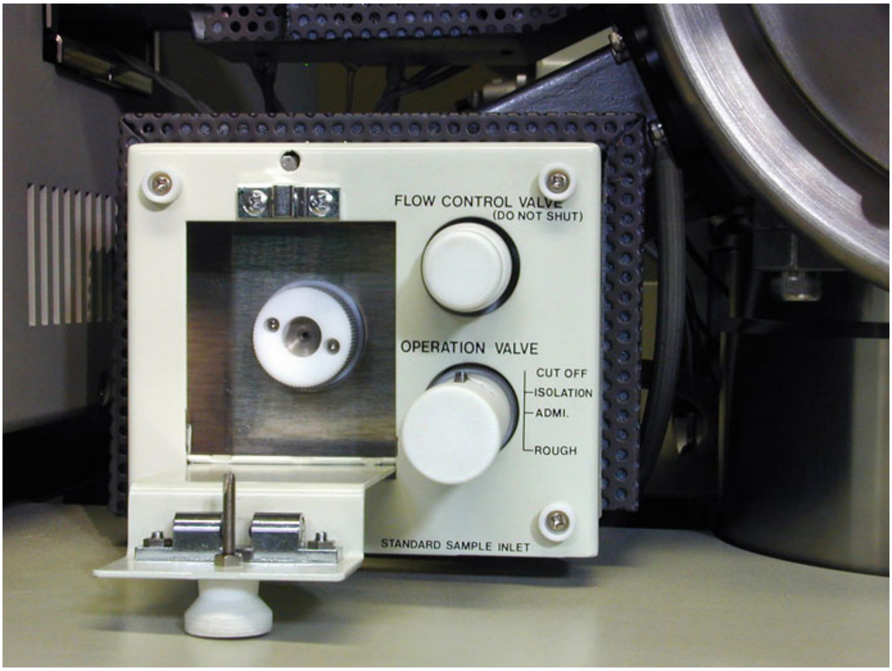


Fig. 5.6 Reservoir inlet of a JEOL JMS-700 sector instrument with the septum injection port opened. The "operation valve" switches between evacuation, isolation, and admission of the sample; a needle valve allows regulation of the sample flow. The GC transfer line crosses in the upper background from the GC (*left*) to the ion source housing (*upper right*)

5.2.2 Direct Insertion Probe

In early-day instrumentation, the introduction of solid samples into a mass spectrometer was performed by directly placing them inside the ion source, which was then mounted into the ion source housing, pumped down, and heated [23]. Obviously, exchanging the ion source for each run is laborious and too slow for routine work. A more convenient procedure is to use a micro *sample vial* or *crucible* containing some 0.1–2 μg of the analyte that can be directly applied close to the ion source by means of a *direct insertion probe* (DIP) or *direct inlet probe* (also DIP, Fig. 5.7). DIPs have been devised from the late 1950s and were in common use by the mid-1960s [24–26].

A DIP consists of a stainless steel shaft with a tip suitable to insert the sample vial. The shaft is polished to allow installation an effective vacuum seal against the O-rings of a vacuum lock. Being transferred into the high vacuum of the ion source housing through the *vacuum lock* [26], the probe is pushed in, eventually until it contacts the ion source block (Figs. 5.8 and 5.9). Spectra are then acquired while the analyte evaporates or sublimes from the vial directly into the ionization volume of

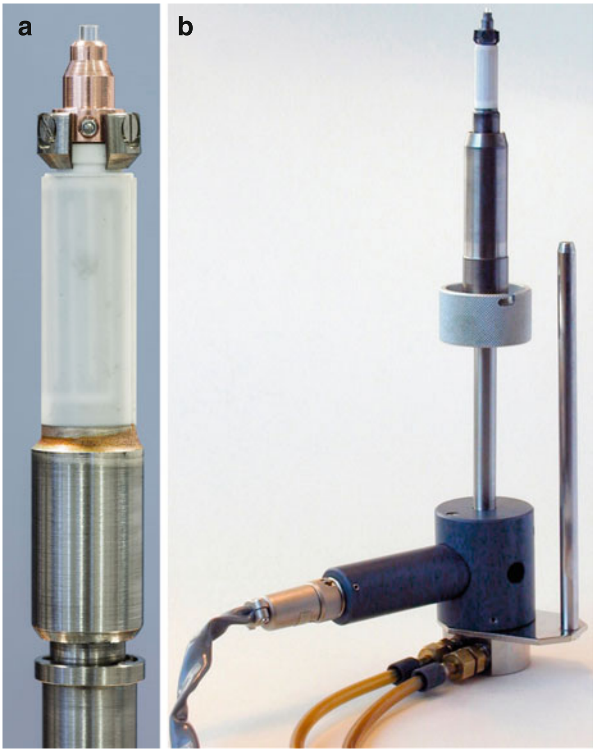


Fig. 5.7 Direct insertion probe (DIP) for use with EI, chemical ionization (CI), and field ionization (FI). (**a**) The copper probe tip holds the glass sample vial and is fitted to a temperature-controlled heater. The heater, a thermocouple, and cooling are provided inside. The (*white*) ceramics insulator protects the operator from the high voltage of the ion source. (**b**) Entire DIP of a JEOL JMS-700 equipped with water cooling

the ion source. Typically, the sample holder can be heated up to about 500 °C can be applied to enforce evaporation of the sample, which sometimes is accompanied by decomposition prior to evaporation. Special high-temperature probes reaching up to 1000 °C are also available. Modern direct probes have *temperature programed heaters* [27] allowing to set rates of 5–150 °C min^{-1} or are equipped with *ion current-controlled heaters* [28].

To prevent more volatile samples from suddenly evaporating a circulation watercooling is often incorporated in the DIP, and refrigerated probes for more volatile samples have also been developed [29]. Sometimes, glass wool is placed into the sample vial to increase the surface for adsorption, and thus to slow down evaporation of the sample; aluminum oxide and silica are also being used for this purpose [30]. Sudden evaporation causes distorted spectra and may even result in a temporary breakdown of the high vacuum.

5.2.3 Sample Vials for Use with Direct Insertion Probes

Sample vials for use with DIPs usually are about 2 mm in outer diameter and 10–20 mm in length. They are made from borosilicate glass or aluminum (Fig. 5.10). In general, the vials are disposed after use. However, although bearing

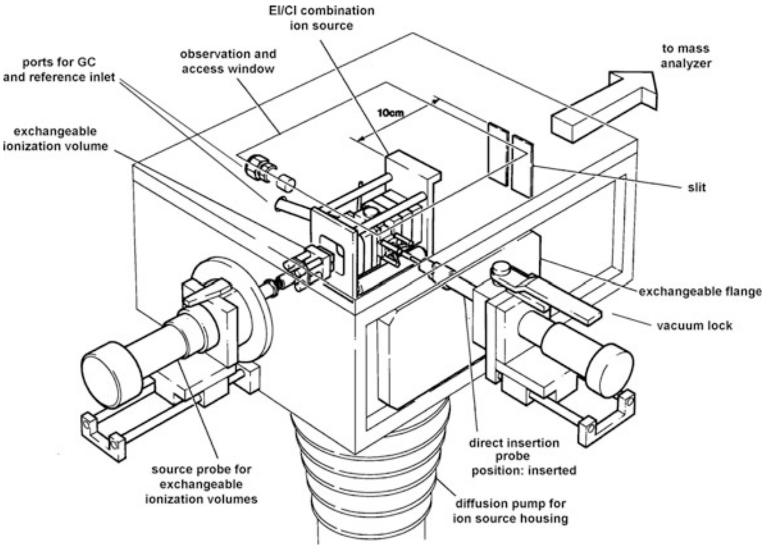


Fig. 5.8 Ion source housing of a Waters Micromass Autospec™ magnetic sector instrument. The ion source can be accessed from several directions to allow for simultaneous connection to DIP/DEP, GC and reference inlet system (By courtesy of Waters Corporation, MS Technologies, Manchester, UK)

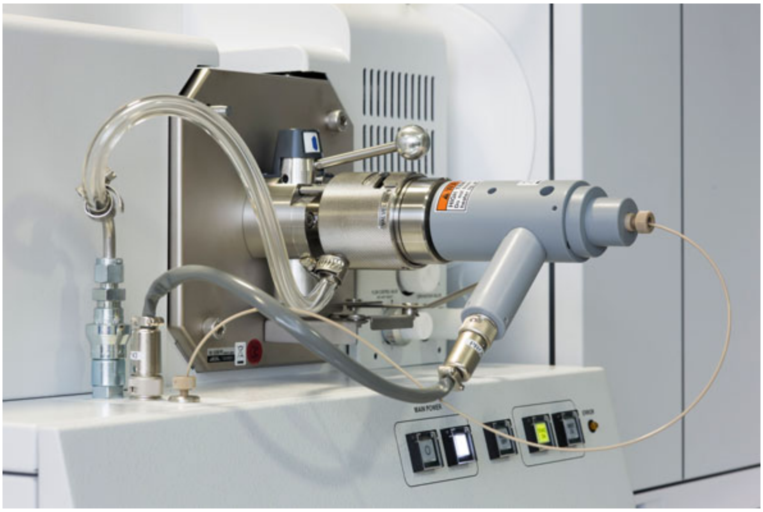


Fig. 5.9 A direct insertion probe on a JEOL AccuTOF GCx instrument. The probe is shown in its fully inserted position. The transparent hose (*left*) provides rough vacuum to the lock before insertion of the probe, the *gray* cable connection serves for heater power supply and temperature control, and the *light brown* capillary delivers pressurized gas for cooling the probe tip if required

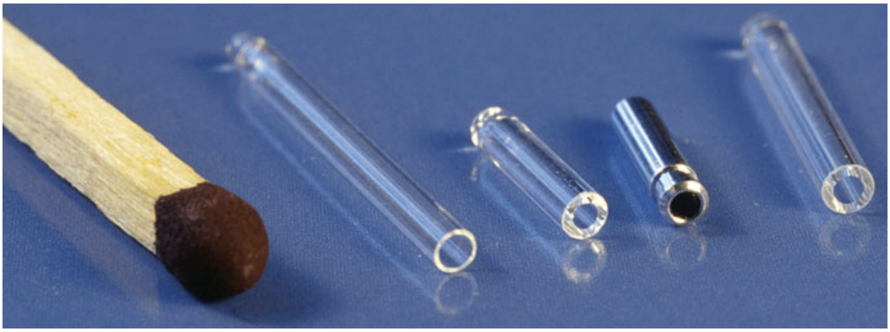


Fig. 5.10 Sample vials for different DIPs. From *left*: VG ZAB-2F, Finnigan TSQ700 glass and aluminum version, and JEOL JMS-700. The match illustrates the scale

the risk of memory effects or adsorption of analyte to residual pyrolysis products from previous samples, reusable quartz vials have also been employed in the past. The analyte may either be loaded in solution into the vial or as a tiny piece if solid or waxy (Fig. 5.11). Using solutions of known concentration allows for more reproducible loading of the vials which in other cases is not a prerequisite. The solvent should then be evaporated before insertion of the probe into the vacuum lock.

Disposable vials preferred
Disposable vials are devoid of memory effects. Glass vials bear the additional advantage of revealing the amount and position of sample within the vial. Afterwards, it is also possible that the analyte decomposes during the measurement yielding a black residue.

5.2.4 How to Run a Measurement with a Direct Insertion Probe

Direct insertion probes are suitable for use with electron ionization (EI), chemical ionization (CI, Chap. 7) and field ionization (FI, Sect. 8.5) as these methods require the introduction of gaseous sample into the ionization chamber of the respective ionization source.

The sample may either be loaded into the sample vial as a solid or from dilute solution. When a solid sample is provided, it is normally best to gently dip a fine needle or pin into the sample or to scratch some tiny crystals off the wall of the sample tube. An amount just visible with the bare eye is usually more than enough. The sample is then transferred into the sample vial, which is preferably fixed in a suitable holder. In case of a sample solution, one may either dip a pin into the solution to transfer a very small drop or one could use the smallest size of a microliter pipette, e.g., 0.5–10 μl tips. It is important to allow for the majority of

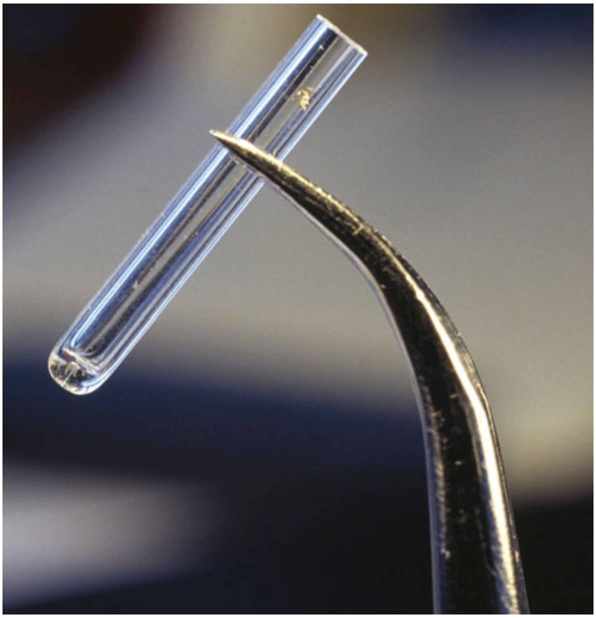


Fig. 5.11 Sample vial loaded with some analyte. The bright *yellow* speck halfway between the tip of the tweezers and upper rim of the vial is the solid material to be analyzed. Actually, this amount of sample is already in excess of what is ideally needed. The use of an additional amount of sample does not bear any advantage; rather, it may cause long-lasting ion source contamination

the solvent to evaporate leaving a film of the sample before inserting the probe. Otherwise, the drop will boil suddenly upon roughing, and thus, will spill the sample solution into the vacuum lock.

To start the measurement, the sample vial is mounted to the probe tip. Make sure that the tip has cooled down close to room temperature before placing the sample vial into the probe tip. The probe tip is generally equipped with some clipping or screwing mechanism to secure the vial in position. Losing the sample vial during transfer inside the vacuum lock can block the lock valve, result in air leaks from scratches or cause other damages. Dropping the vial inside the source housing may require venting and its removal prior to further operation or at least result in waiting time until the sample has evaporated to avoid superimposition of spectra. As any operator might use a vial once in a while, the rotor of the turbomolecular pump is protected from particle impact by a fine wire mesh cover (Fig. 5.5).

Preferably, the probe tip is cooled during insertion to prevent untimely evaporation of the analyte. Heating of the probe tip is only started when data acquisition is running. Typically, the probe tip is heated at a rate of 20–100 °C min^{-1} depending on sample volatility, and of course, on the scan speed of the mass spectrometer. Volatile sample will quickly evaporate during the first few seconds of a run, while "die-hards" can require heating to > 400 °C. After completion of the data acquisition, it is generally recommended to cool down the probe tip to < 100 °C before retracting it into the vacuum lock in order to avoid heat damages of the O-rings.

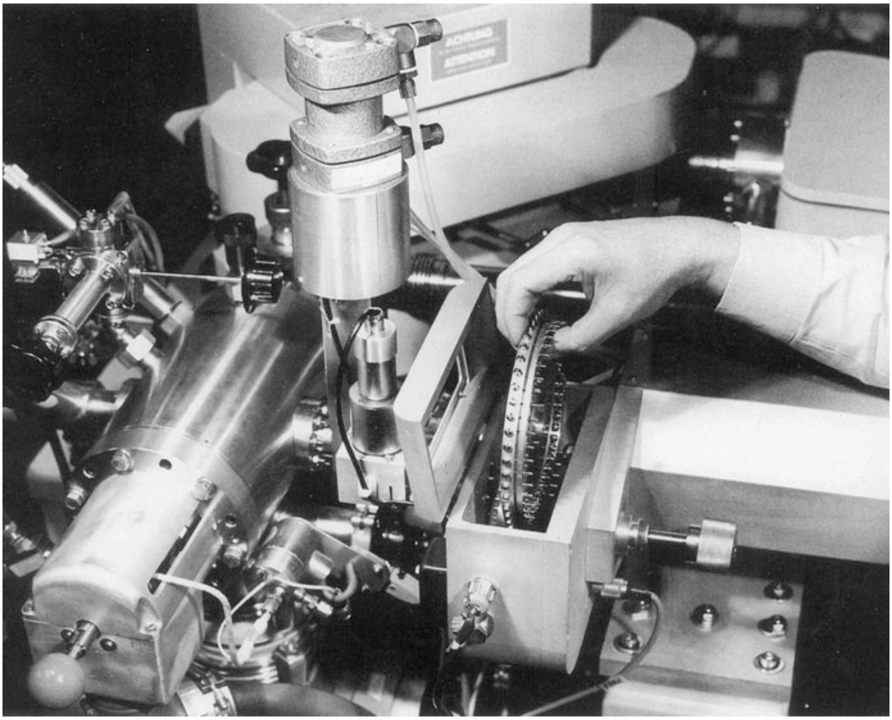


Fig. 5.12 Finnigan MAT AUDEVAP system where the turret wheel with 46 crucibles is being inserted into its housing. The probe mechanism is to the *right*, the vacuum lock and the ion source housing to the *left*. The mass spectrometer may either be a Finnigan MAT 212 or MAT 311 double-focusing sector instrument of BE geometry (Reproduced from Finnigan MAT technical documentation by courtesy of Thermo Fisher Scientific)

5.2.5 Automated Direct Insertion Probes

The first DIP for automated operation was presented in 1979 [31]. In 1982, with the Finnigan MAT AUDEVAP, a commercially available system appeared. It made use of a sample turret that could accommodate up to 46 aluminum crucibles. The probe would then pick up a crucible from the turret and move on through a vacuum lock (Fig. 5.12). Alternatively, the device could pick up DCI sample holders (Sect. 5.2.7) or even target tips for fast atom bombardment (FAB, Sect. 10.3). The AUDEVAP was designed to complete sample runs including data acquisition. Later, it was even possible to set up a system that performed internal mass calibration and formula assignment under data system control [32]. Worldwide, a few AUDEVAP systems are still in operation.

A modern and much more compact automated direct inlet probe is provided by Scientific Instruments Manufacturer (SIM). The SIM probe has a small diameter and is inserted into the ion source housing via a lock mechanism of very low dead

Fig. 5.13 Automated DIP in operation as visualized by multiple exposures. After having received the sample vial in vertical orientation, the rod is driven to the left and tilted downward for insertion through the lock. The photograph shows the SIM DIP mounted to a LECO Pegasus GC-HRT instrument

volume, thus permitting to quickly insert the probe even without prior evacuation of the vacuum lock (Fig. 5.13). The probes can either be loaded manually or be run in combination with an autosampler. The autosampler may either be employed to exchange filled sample vials on the DIP or pipette microliter volumes of liquid samples or solutions, respectively, into a vial at the probe tip. DIPs by SIM are custom-built for several instrument suppliers such as Agilent and LECO.

5.2.6 Fractionation When Using Direct Insertion Probes

The evaporation process out of the sample vial causes a certain degree of sample fractionation that can often be recognized from the *total ion chromatogram* (TIC) alone. Employing *reconstructed ion chromatograms* (RICs) in addition presents a valuable tool in identifying components of a simple mixture and in assigning their corresponding mass spectra. Generally, residual solvent is observed during the first few scans, while all other components appear more or less in order of increasing molecular weight as evaporation progresses.

Observing evaporation from a DIP The TIC of an EI measurement using a DIP already revealed ion formation during the first scans. After some period of relatively low TIC, heating of the DIP to about 200 °C finally led to evaporation of the

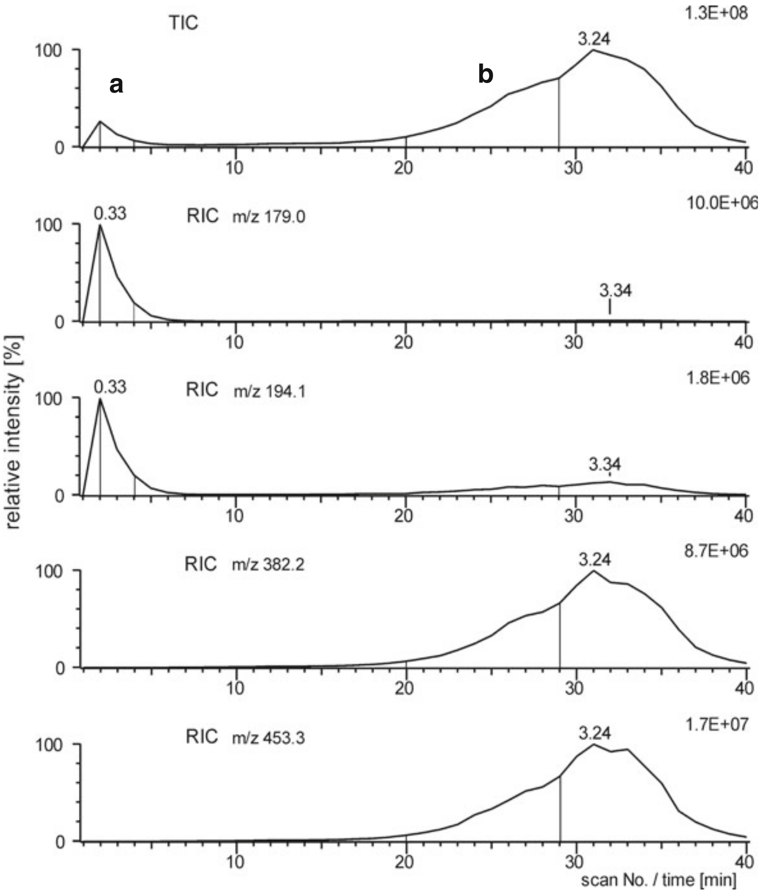


Fig. 5.14 Ion chromatograms from a DIP measurement. The TIC (*upper trace*) shows a bump during early scans that is also reflected in the RICs of *m*/*z* 179.0 and 194.1. Spectrum (**a**) corresponds to volatile impurities, whereas the RICs of *m*/*z* 382.2 and 453.3 are related to the target compound (**b**) that evaporates upon heating (cf. Fig. 5.15) (By courtesy of R. Gleiter, Organisch-Chemisches Institut, Universität Heidelberg)

major fraction of the sample, and thus produced a steeply rising TIC (Fig. 5.14). The TIC decreased again as all sample had evaporated. Thus, two different spectra were extracted from the data. The first was obtained by averaging scans 2–4, the second by averaging scans 20–29 (Fig. 5.15). Spectrum (**a**) corresponds to some impurities, whereas spectrum (**b**) represents the target compound, $C_{28}H_{47}NSi_2$.

Using RICs, the ions belonging to the same component can readily be identified from their parallel dependence in time (Fig. 5.14). The increase of the signal at *m*/*z* 194 in the chromatogram during late scans results from the presence of a minor signal at *m*/*z* 194 in the mass spectrum of the target compound. (More examples for the use of RICs are presented in Chap. 14.)

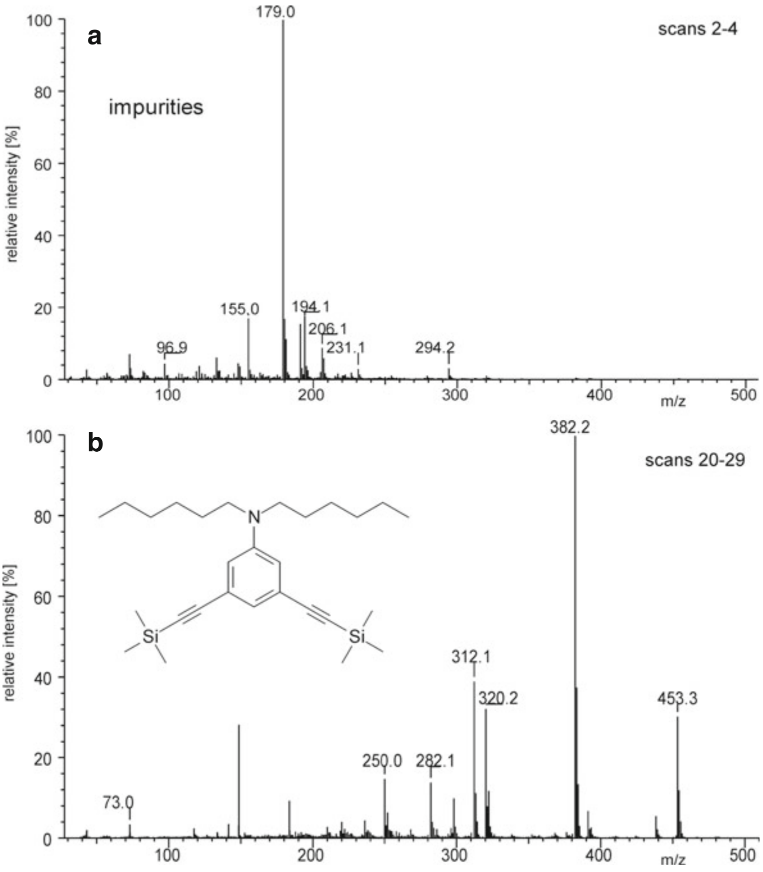


Fig. 5.15 Two EI mass spectra from the same sample. The spectrum obtained from scans 2–4 corresponds to some volatile impurities (**a**), the spectrum from scans 20–29 (**b**) represents the target compound (cf. TIC and RICs in Fig. 5.14) (By courtesy of R. Gleiter, Organisch-Chemisches Institut, Universität Heidelberg)

5.2.7 Direct Exposure Probe

Employing a *direct exposure probe* (DEP) may be helpful in case of analytes that cannot be evaporated from a sample vial without complete decomposition [33]. Here, the analyte is applied from solution or suspension to the outside of a thin wire loop or pin which is then directly exposed to the ionizing electron beam. This method has also been termed *in-beam* electron ionization. Early work describing the direct exposure of a sample to the electron beam came from Ohashi [34, 35], Constantin, [36] and Traldi [37, 38]. The idea behind the rapid heating of a DEP is to achieve evaporation faster than thermal degradation of the sample [39, 40]. This principle is realized in perfection with *energy-sudden* methods (Chaps. 10 and 11).

If the analyte is exposed to energetic electrons the method is called *direct electron ionization* (DEI) or *desorption electron ionization* (DEI), and accordingly it is termed *direct* or *desorption chemical ionization* (DCI) if the analyte is immersed in the reagent gas under conditions of chemical ionization (Chap. 7).

There are different types of DEPs in that some of them rely on the heated tip of a modified DIP [38], and others – widespread in use – that are capable of rapid resistive heating of a small loop made of chemically inert metal wire (rhenium). Resistively heated probes allow rates of several hundred °C s^{-1} and temperatures up to about 1500 °C (Fig. 5.16). As a consequence of rapid heating, fast scanning, e.g., 1 s per scan over the *m*/*z* range of interest, is required to follow the evaporation of the analyte. In either case, the use of a DEP allows to extend the temperature range for evaporation. In addition, it reduces thermal degradation as a result of heating the analyte faster than its thermal decomposition usually proceeds, and therefore expands the range of applications for EI and CI to some extent. In any case, employing direct exposure probes is by far no alternative to real desorption ionization methods [41, 42].

Application of DEI

The DEI technique has been applied to obtain mass spectra of four nonderivatized amino acids [38]. The method allowed for the observation of molecular ions and some primary fragment ions in contrast to conventional EI conditions which do not yield molecular ions. However, these additional signals are comparatively weak (Fig. 5.17).

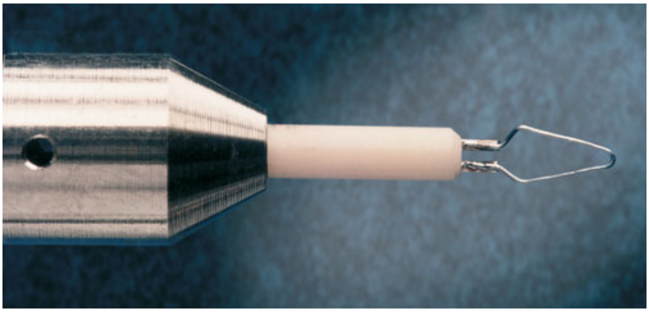


Fig. 5.16 Tip of a direct exposure probe of a GC-oaTOF mass spectrometer for EI and CI (By courtesy of Waters Corporation, MS Technologies, Manchester, UK)

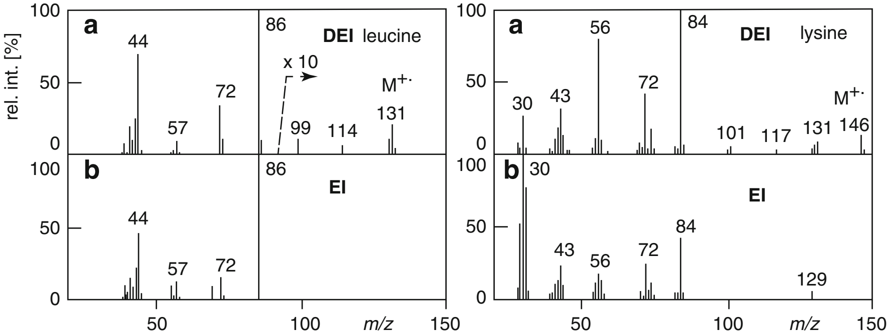


Fig. 5.17 Comparison of DEI (*upper*) and EI spectra (*lower*) of the amino acids leucine and lysine. In the leucine DEI spectrum the intensities above *m/z* 90 are shown in tenfold expansion (Adapted from Ref. [38] with permission. © John Wiley & Sons, 1982)

5.3 Pyrolysis Mass Spectrometry

The enormous temperatures attained on resistively heated sample holders can also be used to intentionally enforce the decomposition of nonvolatile samples, thereby yielding characteristic pyrolysis products. *Pyrolysis mass spectrometry* (Py-MS) can be applied to synthetic polymers [43], fossil biomaterial [44], food [45], and soil [46] analysis and even to characterize whole bacteria [47]. In polymer analysis, for example, Py-MS does of course not yield molecular weight distributions, though the type of polymer and the monomer units it is based on can usually be identified by Py-MS [43, 48]. Often, pyrolysis products are not directly introduced into the ion source but separated by GC beforehand. A detailed treatment of this branch of mass spectrometry is beyond the scope of the present book.

5.4 Gas Chromatograph

Gas chromatography (GC) provides the means for separation of volatile analytes in complex mixtures. GC eluting directly into the ion source of a mass spectrometer is called *GC-MS coupling* [49–51]. Capillary GC columns provide gas flow rates in the order of a few milliliters per minute, and therefore, their back end can be directly fitted into the entrance of the ion volume. In fact, the nano-LC-EI interface described in the next section is inspired by the standard direct coupling of capillary columns into EI ion sources.

EI is ideally suited as an ionization method for GC-MS applications. The specific properties of GC-MS are discussed later in more depth (Sect. 14.4). For the moment, it is sufficient to notice that proper coupling of a GC to an EI ion source neither exerts substantial effects on the EI process nor does it alter the fragmentation pathways of the ions.

5.5 Liquid Chromatograph

Chromatographic separation of polar analytes of low volatility can be performed by *liquid chromatography* (LC) prior to mass spectrometric analysis; such a setup is termed *LC-MS coupling*. Usually, atmospheric pressure ionization methods are employed when direct coupling of a liquid chromatograph to a mass spectrometer is required. However, it can be desirable to obtain EI spectra of LC-separated analytes or of dissolved analytes in general, e.g., when the analyte is only accessible by EI or when EI spectra are required for mass spectral database searches.

To this end, a simple and elegant solution makes use of very low flow rates as provided by nano-LC instrumentation [52, 53]. The flow from a fused silica column of 30 μm inner diameter is passed through a micro-nebulizer of just 5 μm inner diameter. The exit orifice of this nebulizer is slightly bent sideways into the ion source as to spray the droplets towards the opposite ion source wall (Fig. 5.18). A high ion source temperature of 200–300 °C serves to provide heat for solvent and analyte evaporation. An open source construction allows to keep the partial pressure of the solvent low inside the ionization volume, and thus, suppresses $[M+H]^+$ ion formation that would otherwise deteriorate the EI character of the spectra. As gas flow rates due to solvent vaporization are similar to flow rates of capillary GC,

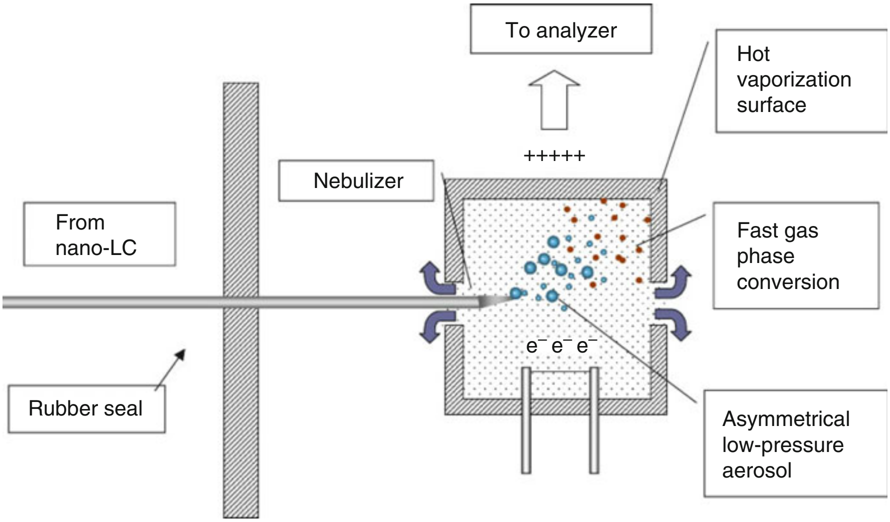


Fig. 5.18 Nano-LC-EI interface with direct connection of the LC capillary to a slightly modified EI ion source (Reproduced from Ref. [53] with permission. © Wiley Periodicals, Inc., 2005)

the nano-LC liquid flow of less than 1 μl min^{-1} can easily be accommodated by most ion source vacuum systems.

5.6 Low-Energy Electron Ionization Mass Spectra

Low-energy primary electrons limit the excess energy deposited onto a molecular ion. Using 12–15 eV instead of 70 eV electrons still ionizes most compounds while disadvantageous fragmentations are reduced. Superior EI mass spectra of large hydrocarbons can be obtained [54], even more so if the ion source is operated at 70 °C instead of 200 °C (Fig. 5.19). The concept of recording *low-energy, low-temperature EI mass spectra* has been postulated long ago [55] and has been extensively investigated since then [56–58]. Low-energy, low-temperature mass spectra are much easier to interpret than their conventional 70 eV counterparts for several reasons:

- The relative intensity of the molecular ion peak is enhanced, thus permitting this important peak to be identified more easily.
- Less fragmentation also means a simpler overall appearance of the spectrum.
- The fragmentation pattern is dominated by a few characteristic primary fragmentations carrying the largest portion of structural information.

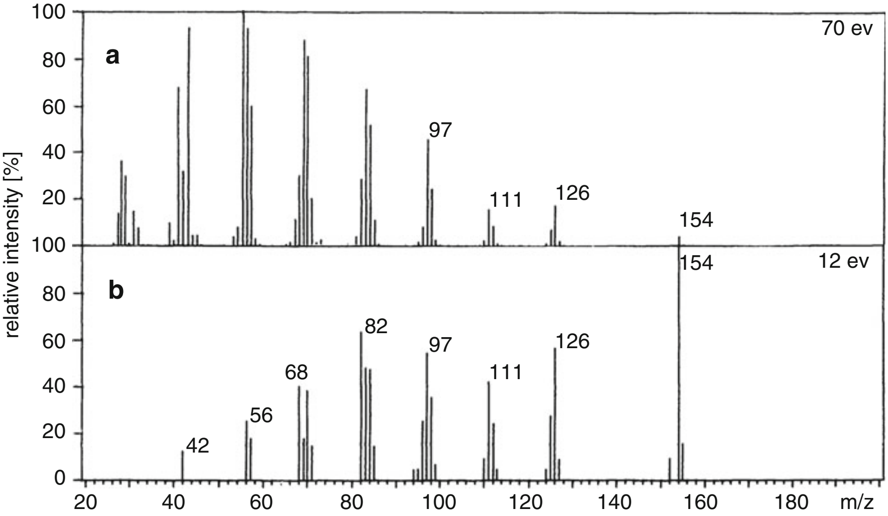


Fig. 5.19 Undecan-1-ol, $C_{11}H_{24}O$, M_r = 172 u: Comparison of 70 eV (**a**) and 12 eV EI mass spectra (**b**). The molecular ion peak is absent in both spectra, but the $[M–H_2O]^{+\bullet}$ peak and the primary fragments become more prominent at 12 eV. (The detailed fragmentation pathways of aliphatic alcohols are discussed in Sects. 6.2.8 and 6.11.3) (Reproduced from Ref. [57] with permission. © John Wiley & Sons, 1988)

Unfortunately, there are also some disadvantages:

- The decreased ionization efficiency at 12–15 eV goes along with a significant loss of sensitivity (Sect. 2.3).
- Low ion source temperatures cause long-lasting "memory" of previous samples due to slow desorption from the surfaces that have been in contact with the sample vapor.
- A weak molecular ion peak may well be enhanced. However, a spectrum showing no molecular ion peak at 70 eV will not turn into a spectrum exhibiting a strong molecular ion peak at 12 eV.

Nonetheless, during the first decades of analytical mass spectrometry, low-energy EI spectra were the only way to minimize fragmentation, and thereby to increase the relative intensity of a weak molecular ion peak. Nowadays, EI mass spectra are preferably complemented with spectra obtained from so-called *soft ionization methods* (Chaps. 7, 8, 10, 11, 12, and 13).

Bad memories

Signals from previous samples in the mass spectrum of the actual analyte are usually termed *memory*. Memory is caused by contamination of ion source or sample introduction system. To reduce memory one should use the lowest amount of sample necessary to produce good spectra, keep the ion source around 200 °C, and allow some pumping between measurements.

5.7 Analytes for EI

Classical organic chemistry provides a wide variety of potential analytes for electron ionization, the only limitation being that the analyte should be able to evaporate or sublime without significant thermal decomposition. These requirements are usually met by saturated and unsaturated aliphatic and aromatic hydrocarbons and their derivatives such as halides, ethers, acids, esters, amines, amides etc. Heterocycles generally yield useful EI spectra, and flavones, steroids, terpenes and comparable compounds can successfully be analyzed by EI, too. Therefore, EI represents *the standard method* for such kinds of samples.

GC-EI-MS can be used for the direct analysis of mixtures, e.g., to analyze synthetic by-products; an advantage that made GC-EI-MS benchtop instruments become widespread in modern synthetic laboratories. The GC-EI-MS combination is especially successful in monitoring environmental pollutants such as polycyclic aromatic hydrocarbons (PAHs), polychlorinated biphenyls (PCBs), polychlorinated dibenzodioxins (PCDDs), polychlorinated dibenzofuranes (PCDFs), or other volatile organic compounds (VOCs).

While low- and medium-polarity analytes are usually well suited for EI, highly polar or even ionic compounds, e.g., diols or polyalcohols, amino acids, nucleosides, peptides, sugars, and organic salts should not be subjected to EI unless properly derivatized prior to EI-MS [59–64].

There is – as with any other ionization method – no strict upper limit for molecular mass, a range of up to 800 u being a realistic estimate. There are exceptions of up to 1300 u if the analyte is extremely nonpolar, like molecules having several fluoroalkyl or trialkylsilyl groups that significantly reduce polarity while increasing their mass.

5.8 Mass Analyzers for EI

In case of EI, there is no restriction as to the type of mass analyzer (Chap. 4). Magnetic sector instruments used to dominate EI applications in the early days of mass spectrometry. With the growing number of GC-MS applications, single quadrupole instruments became more popular because of significantly higher scan speeds and reduced cost. The demand for improved analytical selectivity via MS/MS approaches favored the use of triple quadrupole instruments and (linear) quadrupole ion traps. In recent years, accurate mass measurements have gained new interest thereby increasing the demand for magnetic sector analyzers and even more so for high-resolving oaTOF instruments. In principle, FT-ICR analyzers can be used in conjunction with EI, but rarely are because of their high cost. Recently, an Orbitrap-GC combination has also become commercially available.

5.9 Mass Spectral Databases for EI

EI mass spectra are excellently reproducible when measured under standard conditions (70 eV, ion source at 150–250 °C, pressure in the order of 10^{-4} Pa). This is not only the case for repeated measurements on the same instrument, but also between different types and brands of mass spectrometers. Large EI mass spectral libraries exist in either printed [65–67] or digitized form [68]. The most comprehensive EI mass spectral databases are the NIST/EPA/NIH Mass Spectral Database and the Wiley/NBS Mass Spectral Database [69–72].

Searching for a mass spectrum of an unknown substance in a mass spectral database often very quickly identifies the unknown, provided the corresponding spectrum is already available in the database. However, even if this is not case, the search might deliver similar spectra of closely related compounds, thus facilitating structure elucidation [73].

The obvious approach of comparing a mass spectrum of an unknown with a library spectrum is termed *forward library search* [74]. Normally, only a subset of the measured spectrum, i.e., a set of signals having intensities above a threshold value or a set of signals as defined by user input, is used to search the database. Database spectra closely matching that of the unknown are then displayed with a points score to judge the probability of the respective hit. In a so-called *reverse library search*, a library spectrum is compared to the mass spectra of unknowns in a way disregarding all peaks of the unknown's spectrum that are absent in the library spectrum. This prevents a misled search by background signals that might derive from column bleed, impurities, residual solvent, or memory.

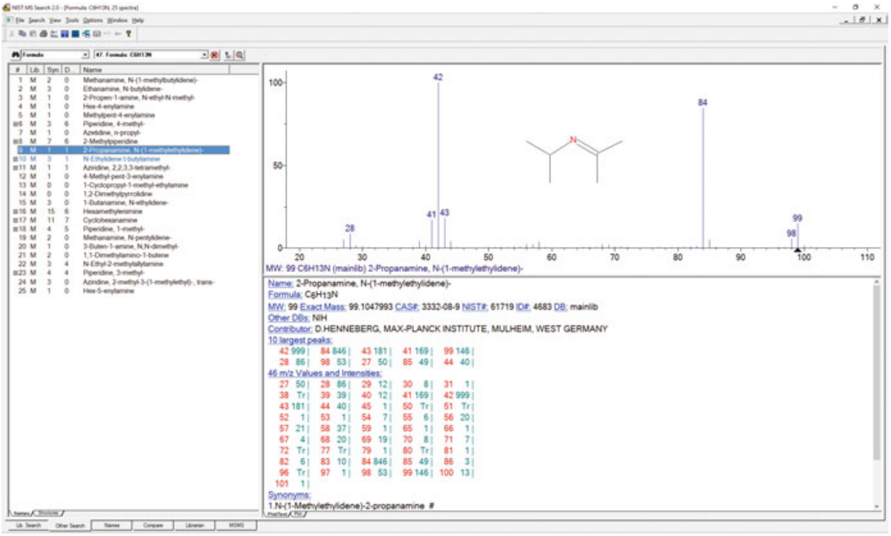
5.9.1 NIST/EPA/NIH Mass Spectral Database

The 2014 version of the NIST/EPA/NIH Mass Spectral Database [69, 75] contains about 276,000 EI spectra of more than 242,000 compounds plus roughly 34,000 replicate spectra. For almost 83,000 compounds there is a compilation of 386,000 *Kovats retention index* (KRI) values as determined on nonpolar and polar columns. Since 2005, this database also offers CID spectra, which actually sum up to 193,000 spectra of 44,000 precursor ions generated from about 8,300 different compounds. The reason for the larger number of spectra over the number of ions is the inclusion of multiple spectra for a given ionic species as obtained by skimmer-CID, and CID on triplequadrupole and quadrupole ion trap instruments, respectively [76]. The NIST/EPA/NIH Mass Spectral Database is available as a stand-alone solution and also with – most probably – any commercial mass spectrometer that can be equipped with an EI ion source.

Searching the NIST/EPA/NIH mass spectral database The NIST/EPA/NIH mass spectral database (Vers. 2.0, 2011) was searched for spectra corresponding to the molecular formula $C_6H_{13}N$ and twenty-five compounds were found. Figure 5.20 shows the screenshot where the spectrum of *N*-(1-methylethylidene)-2-propanamine was selected for display. The structural formula is included in the spectral plot, while compound name, formula, molecular weight, CAS number, a tabular listing of the peaks, and a (here truncated) collection of synonyms are presented in the text window. To a certain extent it is possible to customize the information to be displayed in a specified window and to adjust the formatting.

Built-in or stand-alone

EI mass spectral databases can optionally be included in the software package of mass spectrometers. Thus, the EI spectra measured are directly searchable in the database by similarity search typically yielding a list of several hits. Alternatively, stand-alone solutions allow for sophisticated search algorithms and strategies (Table 5.2) [77–79].



#	Lib.	Syn	D...	Name
1	M	2	0	Methanamine, N-(1-methylbutylidene)-
2	M	3	0	Ethanamine, N-butylidene-
3	M	1	0	2-Propen-1-amine, N-ethyl-N-methyl-
4	M	1	0	Hex-4-enylamine
5	M	1	0	Methylpent-4-enylamine
6	M	3	6	Piperidine, 4-methyl-
7	M	1	0	Azetidine, n-propyl-
8	M	7	6	2-Methylpiperidine
9	M	1	1	2-Propanamine, N-(1-methylethylidene)-
10	M	3	1	N-Ethylidene-t-butylamine
11	M	1	1	Aziridine, 2,2,3,3-tetramethyl-
12	M	1	0	4-Methyl-pent-3-enylamine
13	M	0	0	1-Cyclopropyl-1-methyl-ethylamine
14	M	0	0	1,2-Dimethylpyrrolidine
15	M	3	0	1-Butanamine, N-ethylidene-
16	M	15	6	Hexamethyleneimine
17	M	11	7	Cyclohexanamine
18	M	4	5	Piperidine, 1-methyl-
19	M	2	0	Methanamine, N-pentylidene-
20	M	1	0	3-Buten-1-amine, N,N-dimethyl-
21	M	2	0	1,1-Dimethylamino-1-butene
22	M	3	4	N-Ethyl-2-methylallylamine
23	M	4	4	Piperidine, 3-methyl-
24	M	3	0	Aziridine, 2-methyl-3-(1-methylethyl)-, trans-
25	M	1	0	Hex-5-enylamine

Name: 2-Propanamine, N-(1-methylethylidene)-
Formula: $C_6H_{13}N$
MW: 99 Exact Mass: 99.1047993 CAS#: 3332-08-9 NIST#: 61719 ID#: 4683 DB: mainlib
Other DBs: NIH
Contributor: D.HENNEBERG, MAX-PLANCK INSTITUTE, MULHEIM, WEST GERMANY
10 largest peaks:

```
   42 999 |   84 846 |   43 181 |   41 169 |   99 146 |
   28  86 |   98  53 |   27  50 |   85  49 |   44  40 |
```

46 m/z Values and Intensities:

```
   27  50 |   28  86 |   29  12 |   30   8 |   31   1 |
   38  Tr |   39  39 |   40  12 |   41 169 |   42 999 |
   43 181 |   44  40 |   45   1 |   50  Tr |   51  Tr |
   52   1 |   53   1 |   54   7 |   55   6 |   56  20 |
   57  21 |   58  37 |   59   1 |   65   1 |   66   1 |
   67   4 |   68  20 |   69  19 |   70   8 |   71   7 |
   72  Tr |   77  Tr |   79   1 |   80  Tr |   81   1 |
   82   6 |   83  10 |   84 846 |   85  49 |   86   3 |
   96  Tr |   97   1 |   98  53 |   99 146 |  100  13 |
  101   1 |
```

Synonyms:
1.N-(1-Methylethylidene)-2-propanamine #

Fig. 5.20 Screenshot of NIST/EPA/NIH mass spectral database (V 2.0, 2011) after a formula search for spectra corresponding to $C_6H_{13}N$. Among 25 candidates, the spectrum of *N*-(1-methylethylidene)-2-propanamine has been selected for display. The database not only delivers the EI mass spectrum but also CAS number, contributor, listing, synonyms etc.

Table 5.2 Types of searches in the NIST/EPA/NIH Mass Spectral Database

Type of search	Explanation
Formula	Searches spectra corresponding to a chemical formula. Parentheses are resolved, e.g., $CH_3CH(C(CH_3)_3)_2$ is converted to $C_{10}H_{22}$. Constraints like name fragment or certain peaks can be selected
Molecular weight	Searches for spectra belonging to a defined molecular weight. Constraints like elements, required peaks etc. may be selected
Any peaks	A search based on a small number of peaks. Spectra can be searched using the largest peaks, or peaks in certain ranges of total intensity
Sequential search	Search through database for matches that satisfy the constraints selected by the user
CAS number	Search for compounds with specified CAS number
NIST number	The NIST number identifies a unique spectrum. Search used to retrieve such a spectrum for repeated examination
ID number	Each library spectrum has an additional identification number to correctly deal with user-edited spectra

5.9.2 Wiley Registry of Mass Spectral Data

The Wiley Registry of Mass Spectral Data dates back to the early 1960s when Stenhagen, Abrahamsson, and McLafferty started collecting mass spectra to be published in printed volumes of the Atlas of Mass Spectral Data in 1968 [65–67]. Different from the American Petroleum Institute's (API) spectral library, this project collected more spectra while applying lower restrictions to spectral quality. The reasoning behind that concept being that the probability to find a spectrum similar to that just measured in ones' own laboratory would be higher and that the spectrum of a similar compound may also provide useful guidance for the final elucidation of the unknown structure.

The Wiley Registry, 11th Edition as of 2014 contained more than 1.2 million spectra, about 943,000 chemical structures and EI spectra of 707,500 unique compounds. The Wiley Registry also provides tandem mass spectra of 45,298 ions. It may be obtained in a package combined with the NIST 2014 mass spectral data base and search software to provide the largest available general-purpose MS library.

In addition, specialty libraries for compound classes are available, e.g., the Mass Spectra of Pharmaceuticals and Agrochemicals by Kühnle, the Maurer/Pfleger/Weber Mass Spectral & GC Data of Drugs, Poisons, Pesticides, Pollutants, and their Metabolites or the Mass Spectra of Designer Drugs [80].

Searching for databases

There are several mass spectral databases available on the market today [80]. As collections and packages in the software world are subject to rapid changes, it is recommended to do a quick internet search for something like "EI mass spectral database" or "mass spectral library" to identify current options in this field.

5.9.3 Mass Spectral Databases: General Aspects

Although the coverage of these databases is enormous, and an easy-to-use interface is provided, one should be aware of potential pitfalls. The high score of a hit can be wrong, simply because the spectrum of the actual compound is still not included in database. A spectrum may be flawed by superimposition with some impurity peaks, which can in turn mislead the search. As a result, the unknown can generally not be perfectly identified by simple comparison with a library spectrum [75]. Nonetheless, mass spectral databases are highly useful, because even under unfavorable circumstances, they deliver spectra of similar compounds or isomers for comparison, or at least afford some characteristics of spectra of a compound class under investigation [73]. Ultimately, one should always cross check the hits from the database. Again: even the highest score hit can be wrong, so adequate interpretational skills are still indispensable (Chap. 6).

5.10 EI in a Nutshell

Basic Principle

Energetic electrons are capable of ionizing molecules in the (highly) dilute gas phase, i.e., in high vacuum. The process of *electron ionization* (EI) yields positive radical ions possessing rather high internal energy (Chap. 2). The initial molecular ion, $M^{+\bullet}$, therefore tends to undergo numerous competing fragmentation reactions leading to fragment ions either by elimination of a radical or a molecule.

Hardness of Ionization

EI is generally considered a hard ionization method because it results in fragmentation of analyte molecular ions. The amount of fragmentation can be reduced by low-energy low-temperature techniques to some degree but it cannot be fully excluded. Soft ionization methods (Chaps. 7, 8, 10, 11, 12, and 13) are therefore recommended to complement EI mass spectral data.

Polarity

EI is a purely positive-ion method. The analyte can normally be detected by its molecular ions, $M^{+\bullet}$, accompanied by numerous fragment ions thereof. Occasionally, $[M+H]^+$ ions can occur, in addition, by auto-protonation.

Analytes for EI

As EI requires gaseous samples for ionization, the analytes need to be volatile at least to some extent. EI can be employed for nonpolar to medium polar analytes. It is capable of analyzing molecules as small as hydrogen and up to about 800 u, in rare cases when low polarity and thermal stability are combined it may also work up to 1300 u. Nowadays, the use of EI is often restricted to smaller molecules of less than 600 u and to GC-MS applications.

Sample Introduction

Gases and liquids can directly be introduced by means of a reservoir inlet or after separation via a gas chromatograph. Solids are generally introduced using a direct insertion probe. Sufficient volatility provided, dilute solutions of solids can also be subjected to gas chromatography and analyzed by EI upon elution from the chromatographic column.

Instrumentation

Early on, EI-MS and MS in general employed magnetic sector analyzers. Later, upon commercial availability, linear quadrupole and quadrupole ion trap mass analyzers were frequently equipped with EI sources, especially for GC-MS applications due to their superior scan speed. During the last decade, oaTOF instruments, Q-TOF hybrids, and recently even Orbitrap analyzers have become available (mainly) for GC-MS as they combine fast spectral acquisition with the ability to deliver accurate mass data.

Accurate Mass

Due to stable and long-lasting ion currents, EI is well suited for high-resolution and accurate mass measurements. Internal mass calibration is generally required. The mass calibrant (PFTBA or PFK) is then admitted via the reservoir inlet. In GC-MS, background peaks from column bleed can also serve as internal mass calibrants.

Dissemination and Availability

EI paved the way for MS to become an analytical technique in organic chemistry. From the 1950s until the late 1970s, EI was the preferred ionization method for organic MS. As EI can be combined with a variety of mass analyzers, it has found widespread application – from past to present.

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