International Journal of Mass Spectrometry 200 (2000) 285–312

Quadrupole ion trap mass spectrometry: a view at the turn of the century

Raymond E. March*

Department of Chemistry, Trent University, Peterborough ON K9J 7B8 Canada

Received 14 August 2000; accepted 15 August 2000

Abstract

A personal account of the quadrupole ion trap researches carried out in my laboratory and in collaboration with other laboratories. This account commences with the announcement, in 1983, of the first commercially available ion trap detector, manufactured by Finnigan MAT, and continues to the present day. Much of the ion trap mass spectrometry research that took place during the period following this announcement until 1994 has been discussed in detail in three volumes entitled *Practical Aspects of Ion Trap Mass Spectrometry* that were published in 1995. Except for those researches that impinged directly on our work during this period, no discussion of the contents of these three volumes is repeated here. The ion trap literature from 1994 to the present has been reviewed selectively so as to convey to the reader the dynamic nature of ion trap mass spectrometry and the wide variety of its application. (Int J Mass Spectrom 200 (2000) 285–312) © 2000 Elsevier Science B.V.

Keywords: Quadrupole ion trap; Mass spectrometry; Gaseous ions; Gas chromatography; Electrospray ionization

1. Introduction

In 1999, the *International Journal of Mass Spectrometry* published a special issue [1] on quadrupole ion trap mass spectrometry, which consisted of a collection of invited papers in honor of the scientific contributions of John Todd and Ray March. In that issue, Todd and March presented a retrospective review [2] of the developments in the theory, technology, and application of the Quistor (QUadrupole Ion STORe) in the time window defined broadly as the 1970s and up to the appearance of commercial quadrupole ion trap devices. In the review, the authors gave an account of the circumstances that drew them to pursue their researches. Here, I present a personal perspective of the field of quadrupole ion trap mass spectrometry from the advent of commercial ion trap devices to the present day. This article is an account of the researches in mass spectrometry carried out in my laboratory and in collaboration with other laboratories. While the principal technique employed in this research was that of mass spectrometry, this account is not one dealing exclusively with the quadrupole ion trap; from time to time, research was carried out with other mass spectrometers, particularly sector instruments.

2. Recognition of the quadrupole ion trap pioneers

The original public disclosure of the quadrupole ion trap in 1953 was made in the same patent as that

---

* Corresponding author. E-mail: rmarch@trentu.ca

PII S1387-3806(00)00345-6

in which Paul and Steinwedel first described the operating principles of the quadrupole mass filter; while not quite an afterthought of the inventors, the ion trap was, nevertheless, described as “still another electrode arrangement.” The principle of using strong focusing fields for mass analysis was recognized by Paul and his colleagues at the University of Bonn, and the first detailed account of the operation of the quadrupole ion trap appeared in the thesis of Berkling aus Leipzig in 1956 [3].

In the fall of 1989, the Royal Swedish Academy of Sciences awarded half of the Nobel Prize in Physics jointly to Wolfgang Paul of the University of Bonn and Hans Dehmelt of the University of Washington. The awards were made “for the development of the ion trap technique which has made it possible to study a single electron or single ion with extreme precision.” The remaining half was awarded to Norman Ramsay for “invention of the separated oscillatory fields method and its use in the hydrogen maser and other atomic clocks.” The ion trapping fraternity bathed in the reflected glory of the Nobel awards. The award brought recognition to an area in which activity had become intense since the advent of the commercial version of the ion trap as a mass spectrometer in 1983.

3. A new mass spectrometer

In 1983, the American Society for Mass Spectrometry held its thirty-first annual conference in Boston, MA. This conference proved to be memorable for three reasons. First, because renovations were being carried out on and about the conference building, attendees had to tread carefully along the temporary walkways through the construction zone and had to listen attentively to presentations while trying to filter out the various background construction noises. Second, attendees were invited, as a group, to attend a nearby performance of the Boston Pops, and so we walked from the construction site to the concert hall. Everybody thoroughly enjoyed the concert and was suitably impressed by the footnote in the concert program to the effect that “Members of the American Society for Mass Spectrometry are welcomed to this evening’s performance.” After the concert, we walked contentedly back to our hotels in a long, meandering stream. Third, Paul Kelley announced that Finnigan had produced a new commercial mass spectrometric device known as an Ion Trap Detector (ITD) [4]; the ITD was to serve as a mass-selective detector for a gas chromatograph [5].

Reference [4] is taken from a series of three volumes titled *Practical Aspects of Ion Trap Mass Spectrometry* [6] that were published in 1995. The idea of using a quadrupole ion trap for this purpose had been explored in our laboratory and described in a Master’s thesis [7]. However, there is an enormous amount of data generated, and the mass spectrometric operation of our quadrupole ion traps was cumbersome to say the least. Here was a new method of mass-selected axial ejection in which the quadrupole ion trap, shown in Fig. 1, acts as ion source, ion store, and mass spectrometer. It was an incredible idea that I thought would be revolutionary. Indeed, the advent of the ion trap significantly changed my life and that of John Todd and many others. Although Todd had known of the impending announcement (see Chap. 4 of [4]), it came as a surprise to me. I was delighted and realized immediately the future need for a primer on quadrupole ion traps. It was 6 yr later that this primer, authored by March, Hughes, and Todd, and published by Wiley, finally appeared [8].

3.1. The nature of a mass spectrometer

A mass spectrometer is an instrument in which positive or negative gas-phase ions formed from sample molecules can be analyzed according to their mass/charge (m/z) ratio. When a magnetic or electric field is scanned, ion signals can be obtained from a detector at a field value appropriate to the mass/charge ratio and with an intensity proportional to the ion number. Thus there is a source of ions, a mass-resolving element, and a detector. A mass spectrum is a graphical representation of the ion signal intensities versus the mass/charge ratio. With very few exceptions (e.g., ion cyclotron resonance mass spectrometers), this description of the function and output of a

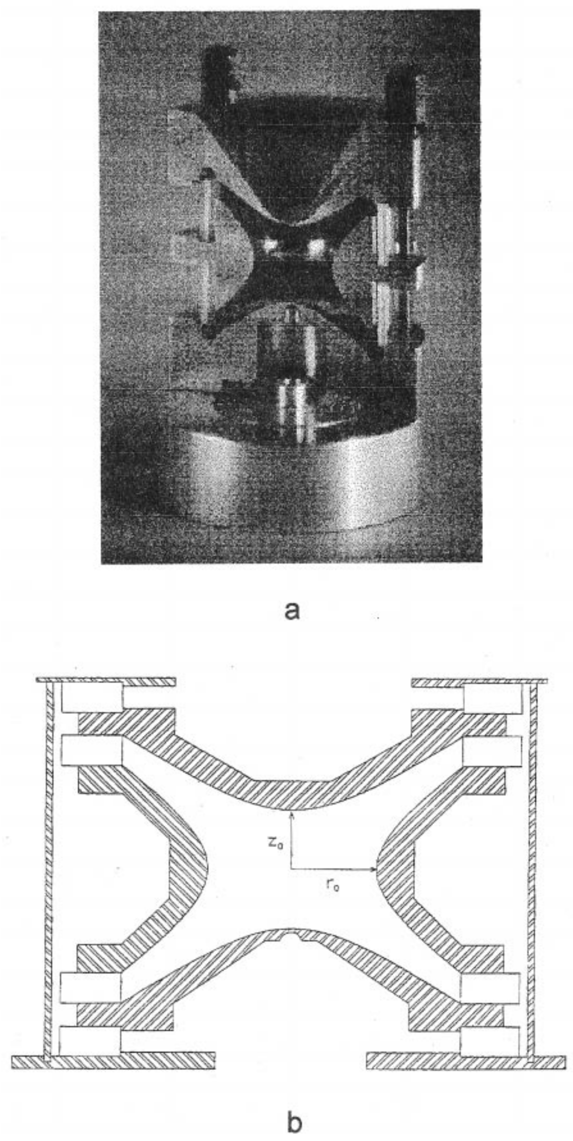

Fig. 1. Quadrupole ion trap; *a*, photograph of an ion trap cut in half along the axis of cylindrical symmetry, *b*, a schematic diagram of the three-dimensional ideal ion trap showing the asymptotes and the dimensions r_0 and z_0.

mass spectrometer generally applies. Yet the quadrupole ion trap mass detector as produced commercially initially did not have an ion source separate from a mass-resolving element; rather, the trajectories of ions were confined to a relatively small volume of 2–3 cm^3 rather than being directed through a sector instrument. Furthermore, the theory of ion confinement and mass-selective ion ejection from the trapping volume was completely new to the mass spectrometry community. Now the theory of operation of a quadrupole mass filter is similar to that of an ion trap, in that a two-dimensional quadrupole field is considered for a mass filter and a three-dimensional quadrupole field for an ion trap. However, most users of mass filters paid little heed to the theory of mass filter operation beyond consideration of a scan line passing through the apex of the triangular stability diagram. The theory of operation of a quadrupole ion trap with its odd-shaped four-sided stability diagram (Fig. 2) proved to be, by and large, an impediment to the adoption and exploration of ion trap instruments by established mass spectrometrists.

3.2. Ion trap detector

The announcement by Paul Kelley that Finnigan had produced a new commercial mass spectrometric device known as an Ion Trap Detector (ITD) [4] was followed, not surprisingly, by many orders for the instrument. Let us recall that the instrument was a tabletop model and consisted of a gas chromatograph and a mass-selective detector with a mass range of 10–650 Th [9]. Furthermore, the instrument and the data output were controlled and treated, respectively, by the accompanying computer.

The ion trap functions as a mass spectrometer when the field within the device is changed, so that the trajectories of simultaneously trapped ions of consecutive specific mass/charge ratio become sequentially unstable and ions leave the trapping field in order of their mass/charge ratio. On ejection from the ion trap, ions strike a detector and provide an output signal. This relatively simple method of mass-selective operation of the ion trap has led to a revolution in mass spectrometry. It is estimated that some 6000 ion trap instruments have been sold thus far at a total cost of about half a billion U.S. dollars; the volume of these sales has led to a reorganization of the mass spectrometry industry. The combination of a quadrupole ion trap interfaced with a gas chromatograph is now available commercially at a price that permits the

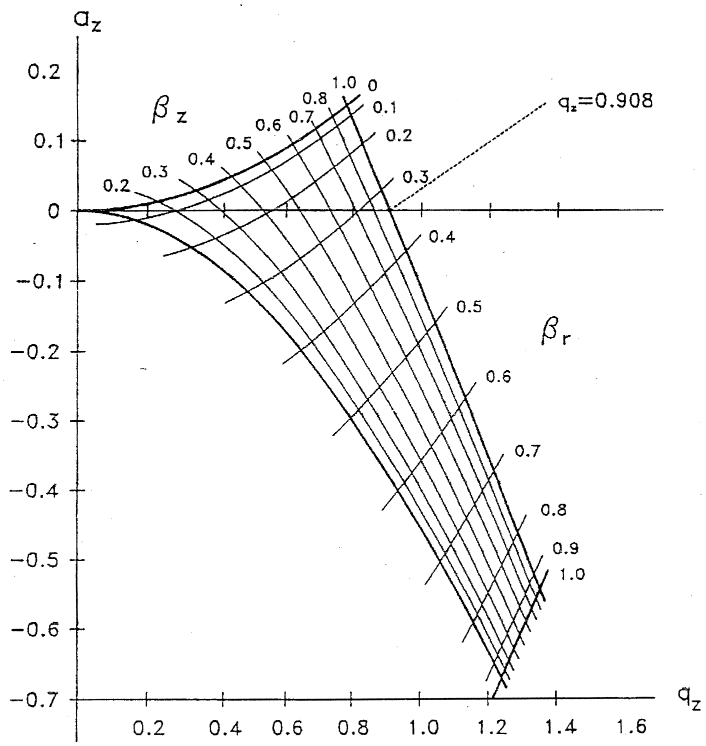

Fig. 2. Stability diagram in (a_z, q_z) space for the region of simultaneous stability in the r and z directions near the origin for the three-dimensional quadrupole ion trap; the iso-β_r and iso-β_z lines are shown in the diagram. The q_z-axis intersects the $\beta_z = 1$ boundary at $q_z = 0.908$, which corresponds to q_{max} in the mass-selective mode.

acquisition of these instruments by most academic departments of chemistry; thus, these instruments are now becoming accessible to relatively large numbers of students, at both graduate and undergraduate levels.

3.3. Electrospray ionization and the second-generation ion trap mass spectrometer

With the advent of new methods by which ions can be formed in the gas phase from polar as well as covalent molecules and introduced subsequently into an ion trap, the range of applications of the quadrupole ion trap is now considerable. The coupling of liquid chromatography (LC) with electrospray ionisation (ESI) and with mass spectrometry (MS) in the early 1980s, together with the rapid advancement in ion trap technology, have led to the development of new ion trap instruments for the analysis of nonvolatile, polar, and thermally labile compounds. In 1995, new ion trap instruments (Finnigan's LCQ and GCQ and Bruker-Franzen's ESQUIRE) were introduced, which employ external ion sources with injection of externally generated ions into the ion trap [10]. The major focus for the application of these new instruments, using LC/ES/MS, has been the analysis of high–molecular weight biopolymers such as proteins, peptides, and oligo-deoxyribonucleotides.

4. Quadrupole ion trap research

4.1. An international microconference

Let us pick up the story in August 1982, at the ninth International Mass Spectrometry Conference (IMSC), which was held in Vienna. At the conference, the first international but only quasi-official quadrupole ion trap meeting was held on a stone

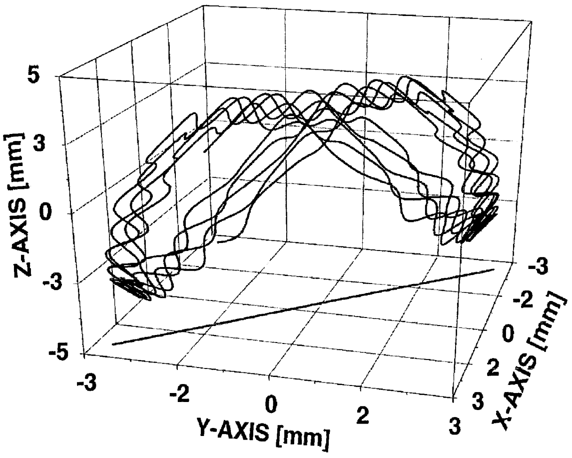

Fig. 3. Trajectory of a trapped ion of *m/z* 105. The initial position was selected randomly from a population with an initial gaussian distribution (FWHM of 1 mm); $q_z = 0.3$; zero initial velocity. The projection onto the x-y plane illustrates planar motion in three-dimensional space. The trajectory develops a shape that resembles a flattened boomerang. Taken from [316].

staircase facing a store that sold cold beer. Those in attendance were John Todd, Pradeep Ghosh from India, and Ray March. Todd and March had constructed homemade ion trap apparatuses with which they had carried out numerous experiments, while Ghosh had concentrated on ion trajectory simulations. The amicable discussion focused chiefly on the simulation of ion trap behavior by calculation of ion trajectories. Ghosh was interested in ion injection into the ion trap and had carried out numerous calculations that indicated that substantial path lengths could be found for ions injected in narrow initial RF phase windows [11]. As Kofel has explained [12], trapping of a particle injected into an ion trap under continuous trapping fields with constant amplitudes and in the absence of ion motion relaxation is impossible by definition. The definition of trapping implies that a particle must return to a position close to the starting point such that the trajectory of the particle can resemble a Lissajous figure, as shown in Fig. 3. The general conclusion of the meeting appeared to be that we should cooperate in carrying out further simulations of ion trajectories in the ion trap. However, electronic mail and facsimile machines were not readily available throughout the world at that time and, sadly, we did not collaborate further with Ghosh. Nevertheless, the ideas of further ion trajectory simulation and ion injection into a quadrupole ion trap prevailed.

4.2. Infrared multiphoton dissociation of gaseous ions

The sole presentation at the ninth IMSC of experimental work carried out with an ion trap concerned the dissociation of ions within an ion trap by infrared multiphoton absorption [13]. The idea of photodissociating ions in an ion trap had been stimulated by other workers engaged in research with ion cyclotron resonance (ICR) mass spectrometers, particularly Dunbar and coworkers [14–16], Braumann and coworkers [17], and Beauchamp and coworkers [18,19]. Each had presented their work at NATO conferences in La Baule, France, and/or in Vimeiro, Portugal; such conferences afforded excellent opportunities for discussion of research carried out and contemplated. Dunbar had used lasers in the ultraviolet to visible region, while Braumann and Beauchamp had used infrared lasers. The choice of laser for quadrupole ion trap research was facile; all grant applications had been refused, but Clive Willis of the National Research Council of Canada loaned March a continuous wave CO_2 laser.

The CO_2 laser had an output of $\sim 10^{22}$ photons/s, where each photon had an energy of 944 cm^{-1}. The first system to be examined consisted of the proton-bound dimers of 2-propanone [20] because it was known that 2-propanone formed such dimers and I had investigated the pulsed photolysis of 2-propanone (or acetone as it was known in the 1950s) for my doctoral work. The choice was serendipitous because proton-bound dimers of 2-propanone absorbed the IR photons so readily that the entire ion cloud could be photolysed in 20 ms. Because the laser beam with a $\sim$1.5-mm diameter was directed radially through the center of the ion trap, the rapid dissociation of the dimers supported the hypothesis that gaseous ions are focused to the center of the ion trap in momentum-dissipating collisions with neutrals in the ion trap.

Further investigation showed that proton-bound dimers of 2-propanone had the highest absorption coefficient of any of the systems examined in our laboratory. For this reason, proton-bound dimers of 2-propanone were used to facilitate alignment of the laser beam through the ion trap before the investigation of other systems.

The dissociation energy of proton-bound dimers of alcohols, ketones, and ethers had been shown [21] to be ~30 kcals/mol. Because the energy of an einstein of IR photon of 944 cm^{-1} is ~3 kcals/mol, dissociation of proton-bound dimers required some 10 photons. As the irradiated ions were contained in an ion trap, it was almost simply a matter of time before all the ions were photodissociated. It was possible to explore the opposing effects of stepwise photoexcitation and collisional cooling of nascent proton-bound dimer ions [20,22–26] and to determine absorption coefficients of IR photons at each of three wavelengths.

4.3. Ion trajectory simulations

Numerical integration of the Mathieu equation permits calculation of the trajectory of a charged species in an ideal quadrupole ion trap. Moreover, integration of the Mathieu equation permits the details of an ion trajectory to be calculated directly at any given point in time with great accuracy. Although integration of the Mathieu equation permitted calculation of an ion's trajectory, the performance of such a calculation in the 1960s and 1970s was not a trivial matter in that large stacks of punched computer cards had to be assembled, the calculations carried out—usually at a remote site, and the voluminous printout had to be examined and sorted by hand. Nevertheless, in 1968 Dawson and Whetten [27] reported the first application of numerical methods to the calculation of single ion trajectories. At that time, application was limited to the use of the quadrupole ion trap as a storage device for specific ions, not as a mass spectrometer [28,29]. Dawson and Whetten extended these early studies to an examination of ion ejection in which a range of ion masses was confined simultaneously [30].

It was on the occasion of a visit in 1974 by Jean Durup of l'Université de Paris-Sud, at Orsay, to our laboratory that we entered the fledgling ion trajectory simulation field. Monte Carlo methods were employed for the investigation of ion motion, with the ions undergoing momentum-dissipating collisions and charge exchange [31]. Recent experimental work had shown that the ratio of signal intensities for Ar^{+} and Ar^{2+}, when these species were ejected from a quadrupole ion trap, varied significantly from that expected for electron impact ionization; thus, the first system to be examined was that of Ar^{+} and Ar^{2+}. These studies indicated that ions migrate to the center of the ion trap with an accompanying loss in kinetic energy as a result of collisions with neutrals in the ion trap. Once ions have been focused to the ion trap center, they can be extracted from an ion trap with high efficiency [31,32]. It was realized later that collisional focusing of the ion cloud to the center of the ion trap by the use of helium buffer gas in the commercial device was essential to the mass-selective axial instability mode of operation of the ion trap as a commercial mass spectrometer. The use of Monte Carlo methods was extended to the study of an ensemble of two ion species [33]. An account of the development of calculations of ion trajectories in an ion trap is given elsewhere ([6], Vol. 1, Chap 6).

4.4. Homemade quadrupole ion trap

4.4.1. The competition

In 1985, the Finnigan MAT ion trap instruments began to appear in laboratories. The ITD, complete with gas chromatograph, was the standard GC/MS instrument, while the ITMS was a research instrument in which the ion trap assembly was mounted in a spacious vacuum housing. The ITD was constructed with DC power supplies for off-axis operation. This capability was found not to be necessary for normal GC/MS operation. The software determined the versatility of each instrument and, like the television cable operation of today, more versatility (or television channels) could be obtained at a price. Because of the greater versatility of the software for the ITMS, such as chemical ionization, ion isolation, tandem mass spectrometry, and later, resonance excitation, I tried to acquire such an instrument. Alas, in the 1980s in Canada, research funding was scarce and I was unsuccessful in obtaining funds, and, I found that I was competing with other research groups that had much superior instrumentation.

4.4.2. Ion trap construction

All of our laboratory work on the quadrupole ion trap up to 1992 had been carried out on homemade instruments where the vacuum housings and the ion traps were constructed in the Science Workshop at Trent University. Much of our early research was made possible only through the skill and perseverance of Ian Stuart, Wayne King, Ken Fowler, and George Wynn in fabricating and modifying the ion trap apparatuses. The hyperbolic ring and end-cap electrodes were polished to a mirror finish that required hours of polishing the electrodes by hand while they were rotated slowly in a lathe. The rose-colored ceramic spacers for the electrodes were machined from dull gray lava and then baked. Because the spacers usually shrank by ~6% (but not always) during the baking process, many such spacers had to be produced in order to obtain a matching set that would yield the required geometric arrangement of the electrodes, viz

$$r_0^2 = 2z_0^2, \tag{1}$$

where r_0 was the radius of the ring electrode and was set normally at 1 cm and $2z_0$ was the distance of closest approach of the two end-cap electrodes. Luckily, we needed to pay only for the material and not for the services of the technicians.

A small ion trap was constructed with $r_0 = 6$ mm together with several cylindrical ion traps where both the radius and height of the cylinder were varied [34–36]. One cylindrical ion trap, named the Gruyère cheese trap, was intended as a long-term environmental monitoring device that operated without a filament. The ion trap was named thus because several holes were drilled in the barrel of the cylindrical electrode. Ions were produced by field ionization at the burred edges of the holes, and in the presence of specific molecules, chemical ionization could occur to produce ions of interest that were pulsed regularly from the ion trap into a quadrupole mass filter [37].

The first RF power supply was built locally, and the second was an Extranuclear Corporation power supply for a quadrupole mass filter modified for an ion trap. All that was needed then were vacuum pumps, low-voltage DC power supplies for biasing electrodes, filament power supply, Channeltron electron multiplier (EM) detectors plus a high-voltage DC power supply, pulse generators (Hewlett-Packard, model 214A), a scan delay generator (Ortec-Brookdeal, model 9425A), a linear gate (Ortec-Brookdeal, model 9415), a Tektronix oscilloscope with four inputs to set up the timing sequence, and an x-y recorder (Hewlett-Packard, model 7044A). The oscilloscope had been classed as government surplus and was obtained for a nominal fee. The Channeltron EM detectors were donated by F. Field once the sensitivity of the detectors had dropped to 10^5; we learned how to regenerate the detectors by baking them for a few hours. The quadrupole ion trap was mounted in place of the normal ion source of a quadrupole mass filter (Vacuum Generators, QXK400). All of the electronics were mounted in two 19-in racks each ~2 m high that stood close to the vacuum housing.

4.4.3. Ion trap research

With this type of apparatus [38] at Trent University and at the University of Kent in the laboratory of J.F.J. Todd, it had been possible to carry out quite an impressive amount of chemical research and instrument development. The principal research contributions were the description of the novel quadrupole ion store (QUISTOR) [39] for the confinement of ions and subsequent mass spectrometric examination [40] and for chemical ionization [41], the study of ionic processes and chemical ionization reactions [42–44], and the collisional focusing of ions [31]. Later came the investigation of the relative efficiencies of confinement of Ar^+ and Ar^{2+} [45], the experimental determination of stability diagrams [36], the selective ion reactor (the forerunner of tandem mass spectrometric operation of the quadrupole ion trap) [46], and the investigation of ion chemistry and the determination of proton affinities [47–49].

4.4.4. Collisional focusing of ions

In the investigation of ion chemistry, some 20 to 30 compounds were examined in all. The ion chemistry of a compound consists of a description of the reactions that primary and higher-order ions undergo when trapped with parent molecules. The storage time was varied from some tens of microseconds to several hundreds of milliseconds. At the end of each storage period, all of the ions were ejected into a quadrupole mass filter for mass analysis. The mass filter was scanned slowly while the experiment was repeated at the same storage time until the desired mass range was covered. The experiment was then repeated with increasing storage times. In this manner, the thermodynamic cascade of ion/molecule reactions could be observed. A surprising feature of each compound examined [50] was the observed increase in the temporal variation of the total ion current at low storage times. It was shown later [31] that this increase was caused by the collisional migration of ions (with a corresponding reduction in ion energy) to the center of the ion trap from which they were ejected with enhanced efficiency. The collisional focusing of ions to the center of the ion trap can be shown theoretically [31] and experimentally [22] to occur both radially and axially. Because this effect occurs radially, it is clear that collisional focusing of ions to trajectories close to the central axis of a quadrupole mass filter should occur analogously. Two of the advantages of collisional focusing in a quadrupole mass filter are to reduce ion loss processes in transmission of the mass filter and to collimate the ion beam on leaving the mass filter [51].

4.4.5. Resonance excitation

The loan of a sweep generator (Wavetek, model 134) permitted exploration of mass-selective resonant excitation of trapped ions, and two experiments were carried out. The first experiment was akin to an ICR double-resonance experiment to probe specific ion/molecule mechanisms by exciting precursor ions with radiation and observing perturbations in the product ion distribution [52,53]. The second experiment involved the deviation of the experimental resonant frequency from the theoretical value for several species of ions stored simultaneously. From the change in frequency, $\Delta\omega$, both the space charge within the ion trap and the shift of the stability diagram can be calculated [54–56]. The first paper [57] was received by the Canadian Journal of Chemistry on January 15, 1979, and published in August of that year. The second [58], which showed that each ion species experienced the same space charge, we decided to submit to the *Journal of Vacuum Science and Technology* because some of the early papers of Dawson and Whetten (e.g. [27]) had been published in that journal. The manuscript was received on January 30, 1979, accepted for publication on May 31, 1979, and published in the July/August issue in 1980. We were fortunate that the paper was published at all, as the editor had died in the summer of 1979. A colleague of the editor found the manuscript in the spring of 1980, and it was published. Since that time, I have checked on the progress of each manuscript once every month.

5. Tandem mass spectrometry with a ZAB sector instrument

5.1. The Swansea ZAB-2F instrument of reverse geometry

In 1985, we had reached a turning point. The quadrupole ion trap apparatus was almost 12 yr old, and two applications for funds for a commercial ion trap apparatus had been rejected. I had spent a sabbatical leave with J.H. Beynon, F.R.S., at the Royal Society Research Unit in Swansea, and had become familiar with the operation of the ZAB-2FQ. The ZAB signifies that there are zero α and β focusing errors, while 2F signifies double focusing; this mass spectrometer is of reverse geometry in that the magnetic sector (B) precedes the electrostatic sector (E). This was a wonderful mass spectrometer for a chemist because ion species (a chemical) could be isolated in the magnetic sector and examined in the second field-free region 1.07 m in length. Metastable fragmentation, collision-induced dissociation [59,60], and neutralization–reionization reactions of mass-selected ion species could be studied. The electrostatic sector permitted determination of ion energy or, strictly, the mass/kinetic energy ratio. In addition, an argon ion laser could be used for photodissociation studies [61–64].

5.2. The Toronto ZAB-2FQ triple-sector instrument

In 1984, I had joined A.G. Harrison and R.K. Boyd in making application for funds for a ZAB-2FQ, that is, a ZAB-2F (as in the RSRU, Swansea) with a quadrupole collision cell (q) and a quadrupole mass filter (Q) following the electrostatic sector. The quadrupole mass filter after the electrostatic sector permitted unambiguous determination of the mass/charge ratio of decelerated ions. Thus, the ZAB-2FQ was a BEqQ instrument with three field-free regions for investigating ion chemistry. The only problem at that time was that Vacuum Generators had not solved the problem of decelerating the ions issuing from the electrostatic sector and about to enter the quadrupole mass filter. By 1986, the deceleration problem was solved and the application for funds was partially successful; as a result, we received a secondhand ZAB-2F with a new qQ addition. During the next few years, we carried out research on the ZAB-2FQ [65], investigating a variety of reactions, both unimolecular (decomposition) and bimolecular (collisions), of gaseous ions. The systems studied included the neutralization–reionization of $C_2H_2^+$ [66], the ethyne-d_1 cation [67], the site of protonation of aromatic compounds [68], and the question as to whether H_3O^+ survived neutralization–reionization [69]. It was found that, unlike D_3O, the neutral species H_3O was not stable, and H_3O^+ did not survive neutralization–reionization. We became interested in charge separation processes and the measurement of the kinetic energy released in such reactions because R.J. Hughes had found triply and quadruply charged molecular ions in benzo[*a*]pyrene. The charge separation reactions investigated were those of $C_3H_n^{2+}$ and $C_3D_n^{2+}$ ($n = 1$–6) [70] and of dications that produced overlapping kinetic energy releases [71], of multiply charged ions derived from polycyclic aromatic hydrocarbons [72], of dimethylanisoles [73], and of dimethylanilines [74], as well as the deconvolution of ion kinetic energy release signals from singly, doubly, and triply charged metastable ions [75].

An interest in the origin of artifact ion signals led to an investigation of the gas-phase ion chemistry of N_2O [76] and the dissociation in the accelerating region of ions derived from N_2O [77–80].

6. Quadrupole ion trap researches continued

6.1. Injection of externally generated ions

During this period, some ion trap research was carried out investigating ion chemistry [81] and proton affinity [82], but the apparatus had become quite rickety and subject to repeated breakdowns. The arrival of Urs Schlunegger from the University of Bern afforded an opportunity to try a new experiment that involved the addition of our quadrupole ion trap/quadrupole mass filter apparatus to an even more aged AEI MS30 EB mass spectrometer. The MS30 was a dual-beam instrument, and consequently, the detector housing was quite spacious. The conventional wisdom on the injection of ions into a quadrupole ion trap was that any ion injected would be ejected with equal energy. On the basis of our experience with ion collisional focusing in an ion trap, it was argued that a collision gas in the ion trap would bring about ion/neutral collisions that should reduce ion kinetic energy. Once the kinetic energy is less than that equivalent to the trapping potential, the ion would not be able to escape from the ion trap. First, the mass-selected ions of 4 keV kinetic energy had to be slowed by multiple collisions to a kinetic energy of some tens of electron volts. A second electrostatic analyzer in the detector housing served normally to direct one of the ion beams to a detector, and the other passed through a cylindrical channel, some 15 cm long, to the second detector. Helium gas was introduced both into the ion trap and through a hole drilled in the center of the channel. Mass-selected acetone-d_6 molecular ions of 4 keV suffered many collisions in the channel and were then directed into an ion trap along an asymptote; the admission of ions continued for 70 ms, the RF amplitude was 200 $V_{\text{p-p}}$, and the helium pressure was 2×10^{-6} Torr. Trapped ions were ejected in a succession of experiments into the mass filter, which was scanned slowly. The mass spectrum obtained on photographic paper showed the presence of CD_3^+, CO^+, CD_3CO^+, and even some $(CD_3)_2CO^+$ ions that had survived intact. The account [83] of the work was, I believe, the first in which the confinement of externally generated ions in a quadrupole ion trap was reported. These experiments were the final experiments with our homemade ion trap apparatus. In the early 1990s, commercial ion trap mass spectrometers with electrospray ionization (Finnigan LCQ and Bruker-Franzen ESQUIRE) necessarily used injection of externally generated ions, as did the Finnigan GCQ.

6.2. Simulation studies

In the late 1980s, our attention was directed to collaborative studies with colleagues at the University of Provence concerning the motion frequency spectrum of confined ions [84] and the influence of detection methods on the motion of confined ions [85–88]. We then embarked on the development of a series of simulation programs. Now that powerful benchtop computers were available, the objective was to simulate the motion of trapped ions subjected to resonant excitation in each of monopolar, quadrupolar, and dipolar modes [89–94]. Initially, the ions were considered to be trapped in an ideal quadrupole ion trap; this assumption permitted the ready calculation of the field at a point in the ion trap. Later, a field interpolation method (FIM) permitted calculation of the field in nonideal ion trapping devices [95,96]; we shall return to this point later. A simulation study was carried out of the mass-selective ion isolation process in a quadrupole ion trap [97,98]. A brief account of the computer simulation of single-ion trajectories in Paul-type ion traps has appeared [99] and was followed by a more detailed description of the simulation of single and multiple particles [100].

6.3. The stretched ion trap

In 1988, as a result of discussions started at the International Mass Spectrometry Conference in Bordeaux, France, D.K. Bohme and I made a successful application for funds for a commercial ion trap detector (Finnigan MAT ITD). The gas chromatograph was discarded and, through the efforts of a graduate student, Xiaomin Wang, the ITD was modified to extend the mass range of the instrument and to carry out resonant excitation of selected ion species. The objective was to use ion/molecule reactions within an ion trap to synthesize ions of intergalactic interest and to determine the structures of such ions by CID, using ions of known structure. The modification of the instrument progressed well, and the mass range was doubled with little problem. However, for the resonant excitation of selected ion species, Wang found that the calculated fundamental axial secular frequencies were 16%–18% lower than the experimental values. The problem remained unresolved for about a year—a year in which my colleague's confidence in the ion trap waned while Wang wrestled with the problem. It was in the summer of 1991 that the mass spectrometry community learned that early problems of mass assignment with the ion trap had been resolved by stretching the separation of the end-cap electrodes. Because the value of z_0 had been increased by some 10.6%, the relationship between r_0 and z_0 as given by Eq. (1) no longer held. Similarly, the definition of the trapping parameter, q_z, for an ideal quadrupole ion trap,

$$q_z = \frac{4eV}{mr_0^2\Omega^2}, \tag{2}$$

no longer held, where e is the electronic charge, V is the zero-to-peak amplitude of the RF storing potential, m is the mass of an ion, and Ω is the radial frequency of the RF potential. To compensate, in part, for the stretching of the ion trap, the $a_{r,z}$ and $q_{r,z}$ trapping parameters are now calculated using the actual values of z_0 and r_0, as follows:

$$a_r = \frac{8eU}{m(r_0^2 + 2z_0^2)\Omega^2}; \qquad q_r = \frac{-4eV}{m(r_0^2 + 2z_0^2)\Omega^2} \tag{3}$$

and

$$a_z = \frac{-16eU}{m(r_0^2 + 2z_0^2)\Omega^2}; \qquad q_z = \frac{8eV}{m(r_0^2 + 2z_0^2)\Omega^2}. \tag{4}$$

When $r_0^2 = 2z_0^2$ (Eq. [1]) is substituted into Eq. (4), we obtain the q_z trapping parameter given in Eq. (2). It should be noted that for the ion trap in the LCQ and GCQ instruments, $r_0 = 0.707$ cm and $z_0 = 0.785$ cm such that the geometry has been stretched by ~57%. A full account of the commercialization of the quadrupole ion trap and both the mass assignment problem and its resolution are given elsewhere [4]. Depending on the value of q_z, the value calculated for q_z from Eq. (4) is some 16%–18% greater than that calculated from Eq. (2). Thus, because the secular frequency, ω_z, is directly proportional to β_z, a trapping parameter, and is given by

$$\omega_z = \frac{\beta_z \Omega}{2}, \tag{5}$$

where β_z is approximately directly proportional to q_z, it is clear that the discrepancy in secular frequencies found by Wang is accounted for entirely by the stretching of the ion trap. Eventually, an initial presentation of Wang's work was made in 1992 [101] and was followed by other publications [102–104]. The ion trap proved to be ideally suited for the structure determination of, for example, $C_{14}H_{10}^+$, $C_{10}H_{10}^+$, and $C_{10}H_8^+$ ions formed in ion/molecule reactions from substituted ethynes [104], isolated and excited resonantly to produce characteristic fragment ions. However, so much effort and so many scant resources had been expended on the frequency discrepancy problem that the volume of research done was less than anticipated. The literature had been misleading, and I felt that confidence in my expertise had flagged. The thesis work was completed, Wang graduated and the collaborative venture languished. Some of our publishable "Thoughts on the stretched ion trap" appeared in 1992 [105].

7. A New Era in Ion Trap Research

In August 1991, I received a call from Greg Wells of Varian Associates. I learned that Varian Associates had negotiated with Finnigan to produce ion trap instruments under a licensing agreement. Greg invited my laboratory to become the research wing for the fledgling manufacturing operation at Varian: What an opportunity! Within months, Varian had donated to my laboratory two gas chromatography/ion trap instruments, first a Saturn I and later a QISMS (quadrupole ion store mass spectrometer). The Saturn I could be described as an old-fashioned ion trap instrument in that it came equipped with DC power supplies for operation of the ion trap away from the q_z axis of the stability diagram; this DC capability was used to advantage later. The initial task was to write a new software program that would permit full control of the experimental variables. The experimental variables were the duration of ionization, RF amplitude ramp rate, resonant excitation, axial modulation [106] (by which ions come into resonance with a fixed frequency shortly before ion ejection, thereby obviating space charge effects that perturb mass resolution), DC voltage, and DC voltage ramp rate.

Once the software program had been written by F. Londry, the Saturn I instrument was very versatile and powerful in terms of the specificity or informing power that could be obtained when the ion trap was combined with a gas chromatograph, that is, GC/MS/MS. Tandem mass spectrometry could be carried out to the *n*th degree and the variation of the RF voltage scan rate permitted variation of the mass resolution and the entire region of the first stability region could be explored. Let us examine first the importance of tandem mass spectrometry.

7.1. Tandem mass spectrometry

Tandem (Latin, meaning at length) mass spectrometry, MS/MS, is the practice of performing one mass-selective operation after another, much as the riders are seated on a tandem bicycle. The first mass-selective operation isolates an ion species designated as the parent ion, while the second determines the mass/charge ratios of the fragment, or product, ions formed by CID of the parent ions. MS/MS with a quadrupole ion trap, where successive mass-selective operations are carried out in time, offers a number of advantages. First, as the ion trap operates in a pulsed mode, mass-selected ions can be accumulated over time. Second, as CID is wrought by many collisions of mass-selected ions with helium atoms where the energy transferred per collision is small, dissociation channels of lowest activation energy are accessed almost exclusively. Third, all isolated ions can be dissociated, and fragment ions arising from some 90% of them can be confined. Fourth, a sequence of several mass-selective operations can be performed such as MS^2, MS^3, MS^4, and so forth.

At the time of writing, the uniqueness of the ion trap lies in its ability to perform tandem mass spectrometry to the *n*th degree [107]. While the ion trap has a mass range of up to several thousand Thomsons; has a high mass scan rate of >5000 amu/s; is compatible with gas chromatography, liquid chromatography, atmospheric pressure ionization, and electrospray ionization; and has a modest mass resolution that can be increased in “zoom” mode, it is unique only in its ability to perform mass spectrometry to the *n*th degree and at a reasonable cost.

7.2. High mass resolution

Until 1991, the ion trap had a mass resolution, defined as $m/\Delta m$, where m is the mass of the ion and Δm is the full width at half maximum (FWHM) of the ion signal, of $\sim 3 \times m$. In the next 2 yr, the mass resolution was increased in three enormous bounds [108]. First, Schwartz et al. [109] succeeded in reducing the RF voltage scan rate by a factor of 20, so that the time interval required to scan 1 Th was increased from 190 μs to $\sim$3.8 ms and observed a mass resolution of 33,000. Concurrently, Goeringer et al. [110] obtained mass resolution in excess of 45,000 at *m/z* 502 by scanning the resonance frequency; they observed a FWHM of 11 mTh. It should be pointed out that a value of mass resolution does not yield the width or FWHM of an ion signal peak; the mass must be known to establish the peak width. It is the peak width that determines the degree to which two neighboring peaks can be resolved. Similarly, considering a greater mass, provided the same FWHM can be sustained, can increase the mass resolution. Hence, it is more informative to refer to the FWHM in such discussions, but old habits die hard. Second, Cooks’ group at Purdue University achieved a FWHM of 3.5 mTh to yield a mass resolution of 1,130,000, with *m/z* 3510. In this work, the scan rate was reduced by a factor of 333. Third, Londry et al. [111,112] in 1993, reported mass resolutions of 0.8×10^7 and 1.2×10^7 for ions of *m/z* 414 (Fig. 4) and *m/z* 614, respectively. At the higher mass resolution, FWHM values of 52 μTh were observed when the scan rate had been reduced by a factor of 5.5×10^4. While the mass resolution was high, the mass assignment was not satisfactory. To improve the mass assignment, it was found necessary to phase lock the resonant ejection frequency with both the RF potential and the line potential. Under these conditions [113] and as shown in Fig. 5, mass resolution of 130,000 was observed with *m/z* 264 with excellent mass assignment. This level of performance has yet to be realized in a commercially available ion trap instrument.

7.3. The first stability region

The first stability region is shown in Fig. 2. The advent of waveform generators for resonance excitation over a wide range of frequencies has obviated the necessity of moving the working point of an ion species away from the q_z axis. Thus, the requirement for DC power supplies to cause the movement of the working point to nonzero a_z values no longer exists, and such power supplies are no longer a component of commercial ion traps. The DC power supplies on the Saturn I instrument were used to develop an empirical method for the prediction of the frequency at which optimum resonant excitation can be achieved [114].

The published research that appeared from our laboratory during the period in which we enjoyed collaboration with Varian Associates and, particularly, with Greg Wells, concerned our activities with high mass resolution as discussed above [111–

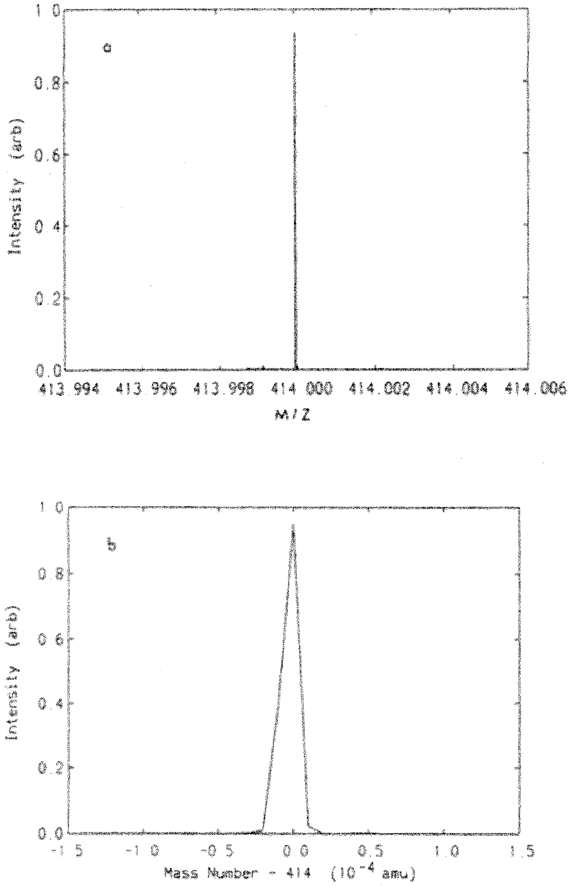

Fig. 4. (*a*) Partial electron impact mass spectrum of perfluorotributylamine showing *m/z* 414 with high resolution. (*b*) An expanded version of the mass spectrum shown in part (*a*) showing the FWHM peak width of *m/z* 414 to be 13.4 × 10^{-6} Da. In both parts of this figure, the center of the peak has been located at the nominal mass/charge ratio of the ion.

113,115] ion chemistry [116], simulations, and systems of environmental interest.

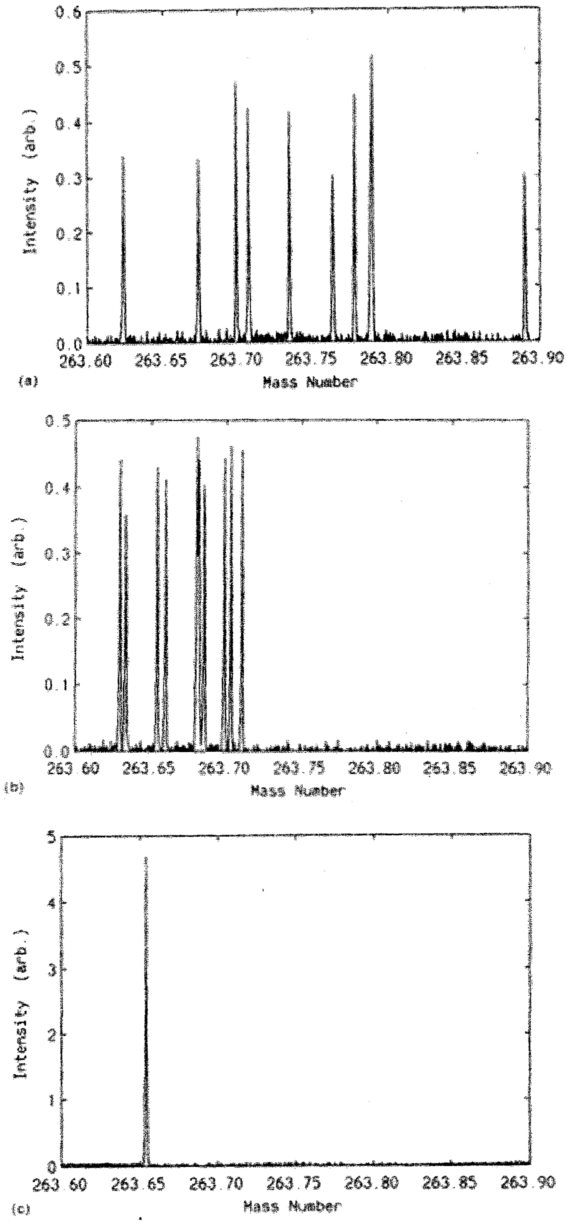

Fig. 5. The result of coadding 10 microscans of *m/z* 264 with $q_{z,\mathrm{eject}} = 0.78$: (*a*) with both phase locking and line locking disabled; (*b*) with phase locking enabled but line locking disabled; (*c*) with both phase locking and line locking enabled.

7.4. Boundary activated dissociation

The simulation of single ion trajectories led to two fruitful directions, boundary-activated dissociation [117] and the investigation of secular frequency change in a stretched ion trap. In a simulation study [93] of mass-selective isolation of ions in an ion trap, it was observed that ion kinetic energy increased rapidly when the working point of an ion moved to the vicinity of a boundary of the stability region. Ion/neutral collisions under these conditions could lead to ion dissociation. We communicated the result to P. Traldi, and he responded by sending some experimental data on daughter ion signal intensities acquired by boundary activation, that is, ion fragmentation in the absence of an applied resonance frequency. The results were published [118,119], and a patent was obtained [120]; unfortunately, as a civil servant, Traldi could not be a coholder of the patent. Although numerous papers have been published by the groups of Traldi, Creaser, and March [117], it is my personal belief that the combination of boundary excitation and periods of kinetic cooling has yet to be evaluated fully.

7.5. Secular frequency change

A second simulation, made possible by using the field interpolation method referred to earlier, allowed calculation of ion trajectories in a stretched ion trap [121]. Because the electrode separation was increased but the shapes of the electrodes were not changed, the field in the ion trap is no longer ideal and an interpolation method is required for calculation of the field. This second simulation permitted rationalization of two experimental observations. First, the ion fundamental axial secular frequency calculated by Eq. (5) differs by some 2–3 kHz from the experimentally optimized value; second, the form of the ion absorption curve is not symmetric. Trajectories were calculated for ions subjected to resonance excitation; when the ion excursion from the center of the ion trap reached 1 mm, the calculation was suspended and the trajectory was frequency analyzed. This procedure was repeated until the frequency analysis had been completed for an ion 7 mm from the ion trap center and close to an end-cap electrode. The axial secular frequency increases and the radial secular frequency decreases as the excursion of an ion from the ion trap center increases. This behavior explains both the frequency discrepancy and the form of the absorption curve.

7.6. Dioxins, furans, and PCBs

7.6.1. Dioxins and furans by GC/MS/MS

The research involving compounds of environmental interest was concerned mainly with the development of analytical protocols using GC/MS, GC/MS/MS, and chemical ionization. This work was carried out with the QISMS instrument. The GC/MS/MS analytical protocol for dioxins and furans involved the optimization of mass-selective isolation and of resonance excitation of the mass-selected ions. The protocol was simplified enormously by the observation that dioxin congeners (or furan congeners) having a common degree of chlorination could be fragmented efficiently by a common resonance excitation episode [122]. The development of Toolkit by Varian Associates permitted the creation of up to 200 individualized scan functions that could be run consecutively so as to permit the tandem mass spectrometric determination of coeluting dioxins and furans [123–125]. A comparison of three mass spectrometric methods for the determination of dioxins/furans has been presented [126]. The factors considered in this comparison were the tuning of each instrument, the preparation and comparison of calibration curves, the 2,3,7,8-T_4CDD detection limit for each instrument, average relative response factors, and ionization cross sections. In addition, ion signals caused by H_6CDDs obtained with each instrument from two real samples (air and pyrolyzed polychlorinated phenols) were presented.

7.6.2. PCBs by GC/MS/MS and chemical ionization

While it is possible to detect dioxins, furans, and PCBs in a single gas chromatographic run, it was not our objective to do so. In collaboration with C.D. Metcalfe of Trent University, we chose rather to concentrate on two problems. First, the development of an analytical protocol for the determination of the 39 PCBs that had the highest toxic equivalency factors as calculated by Kafafi et al. [127]; all 39 congeners had between four and seven chlorine atoms with either zero or one *ortho*-substituted chlorine atom. Second, an examination was made of coeluting PCB congeners 77 and 110. The GC/MS/MS method developed for the 39 congeners was based on the observation that non- and mono-*ortho*-substituted pentachlorobiphenyl compounds lost preferentially two chlorine atoms compared with single chlorine atom loss; the converse held for the di-*ortho*-substituted pentachlorobiphenyls [128,129].

PCB congener 77 (3,3′,4,4′-tetrachlorobiphenyl) is a coplanar non-*ortho* molecule found in concentrations generally lower than those of congener 110 (2,3,3′,4′,6-pentachlorobiphenyl); congener 77 is markedly more toxic than is congener 110, with which it coelutes. It was found that chemical ionization using the reagent ion $C_2H_5^+$, isolated from methane, produced protonated congeners with little, if any, fragmentation that allowed determination of each component. This method involved chemical ionization using a reagent ion that must be synthesized through ion/molecule reactions and isolated before reaction. $C_2H_5^+$ ions from ethane were found to be unsuitable because the reaction was so energetic that fragmentation of the protonated species occurred [130]. Another chemical ionization method that was developed was the determination of *n*-nitrosodimethylamine in complex environmental matrices [131].

An abridged review of the application of gas chromatography/mass spectrometry to the determination of dioxins and furans has been prepared [132], and a review of the application of quadrupole ion trap mass spectrometry to the determination of dioxins/furans and PCBs is to appear soon in an issue of *Mass Spectrometry Reviews* [133].

8. Collaborations

One of the great pleasures for a researcher is the opportunity to travel and visit other laboratories; in this respect, I have been most fortunate. Our collaboration with Todd has been well documented here and elsewhere [2], as has our collaboration, together and individually, with Fernande Vedel ([6], Vol. 1, Chap. 8; Vol. 2, Chap. 7) and Jacques André of the Université de Provence. An invitation from Tabet, of the Université Marie et Pierre Curie in Paris, to assist him in setting up an ion trap laboratory was accepted readily. This was an interlaboratory venture that entailed visits by students to the collaborating laboratory. The project involved instruction in the basics of quadrupole ion trap theory (in French), supervision of research, thesis examinations, and other pleasurable duties. From this collaboration came a series of publications concerned mainly with ion/neutral processes in the ion trap [134,135], ion chemistry [136–138], and negative-ion mass spectrometry in an ion trap [139–141].

Another collaboration with Traldi of the CNR in Padova, Italy, led to joint research (Peterborough, Paris, and Padova) on negative-ion mass spectrometry [141]. Cooks' group had shown by experiment and simulation that the energy of positive ions of *m/z* 134 ejected axially from the ion trap were accelerated by the RF field such that they could possess several hundreds of electron volts of kinetic energy [142]. It followed logically that negative ions stored simultaneously (or not) would be accelerated similarly under these conditions and, when their kinetic energies exceeded the decelerating potential of the detector, could be detected. The Padova connection led also to investigation of a novel sample introduction system [143].

9. The writing of texts, reviews, and encyclopedia articles

It has been discussed above that, during the presentation in 1983 by Paul Kelley of the new Finnigan MAT ITD, I had realized there would be a need for a quadrupole ion trap primer text. The only text in existence was that of Dawson [144], published in 1976: this publication has been reprinted recently as part of the series of "American Vacuum Society classics" by the American Institute of Physics under ISBN 1563964554. I was familiar with the magnitude of the problem faced by my graduate students as they strove to grasp the essentials of the field of quadrupole mass spectrometry. However, there is a great difference between seeing a need for something and supplying that something (modified by the restrictions of the real world) so as to satisfy the need. The first step was to prepare an outline for the primer and to discuss this outline with a publisher. The publisher, Wiley, required a text of at least 250 pages if it were to be published in the series of monographs on analytical chemistry and its applications. Such a task required assistance, and so Richard Hughes and John Todd joined the team; at this juncture, we had crossed the Rubicon and there was to be no turning back. The task became one of completing the voyage. Though the primer [8] grew from some 70 pages to 470 pages and was 6 yr in preparation, the book contained a full treatment of ion trap theory and was generally well accepted, particularly among graduate students. The historical account in this text by Todd has been expanded into a full-scale review [145].

Reviews on specific ion trap topics have been contributed by Cooks and coworkers [146,147], and a special collection of papers reporting on recent developments in quadrupole ion trap mass spectrometry has appeared in this journal [148]. The field of quadrupole ion trap mass spectrometry was reviewed extensively for the twelfth International Mass Spectrometry Conference [149] held in Amsterdam in 1991. In that same year, Todd and I agreed to coedit a new quadrupole ion trap text for CRC Press. The task of coediting a text differs considerably from that of authoring or coauthoring a text. Essentially, the task of a coeditor is to negotiate with the publisher and with the prospective contributors and to strive for harmony with one's coeditor. This task is akin to being the comanager of a virtual stable of racehorses, each of which has a unique personality and its own racing schedule. On top of that, the comanagers also want to race. It is a great tribute to the mass spectrometry community that 18 of the most active ion trap laboratories in the world at that time contributed 30 chapters in all. This splendid effort was achieved despite the many demands of research, teaching, administration, and writing applications for research funding on the contributors. Once we were enmeshed in the dynamic world of publishing, the project took on a life of its own, with the result that the single text grew to three volumes! It is noteworthy that no contributor was paid, and it was agreed that each contributor would receive a set of all three volumes.

The three volumes were published in 1995 in the CRC Series on Modern Mass Spectrometry and titled *Practical Aspects of Ion Trap Mass Spectrometry* [6]. Volume 1 of this series, subtitled *Fundamentals of Ion Trap Mass Spectrometry*, covers the history of the quadrupole ion trap, nonlinear ion traps, ion activation, ion/molecule reactions, and ion trajectory simulations. A detailed exposition of the mathematical basis of the operation of the ion trap is given in Chapter 2 of Volume 1. Volume 2 is subtitled *Ion Trap Instrumentation* and deals with enhancement of ion trap performance, ion trap confinement of externally generated ions, ion structure differentiation, ion photodissociation, lasers and the ion trap, and ion traps in the study of Physics. Volume 3 is subtitled *Chemical, Environmental and Biomedical Applications* and includes a review of fundamentals in addition to extensive expositions on gas chromatography/ion trap tandem mass spectrometry (GC/MS/MS) and liquid chromatography/ion trap tandem mass spectrometry (LC/MS/MS). It is impossible to review these three volumes in this paper, and I have not tried to do so. Rather, I have attempted to focus on the research activity that has occurred during the past 5–6 yr, that is, 1994–2000, in some of the areas of quadrupole ion trap mass spectrometry covered by the three volumes.

An introduction to the quadrupole ion trap written by this author in a tutorial form has appeared recently [150]. While the above texts have been quite well received, the cost of each volume can deter the interested graduate student from acquiring a personal copy. Thus, I have put together a series of lectures on quadrupole mass spectrometry into a primer of some 85 pages, rather along the lines that I envisaged initially in 1983 [151]. In 1998, two reviews of ion trap mass spectrometry appeared [152,153].

The final chapter of this writing adventure concerns the writing of articles for encyclopedias. While it is mildly flattering to be invited to contribute to an encyclopedia, I have a theory that one is invited to write such articles only when one has passed one's zenith of research activity and just before one enters the forgetfulness of senility. I have been able to complete three encyclopedia contributions; two have already appeared [154,155], and one is about to appear [156]. It is now almost 2 yr since the most recent invitation, and I am beginning to worry; perhaps my theory is not far from the truth.

10. A survey of recent research activity

10.1. Theory

It has long been recognized that a real ion trap, having truncated electrodes and perforations in the electrodes for admission of electrons and ejection of ions, does not have a pure quadrupole field. The physical requirements of a real ion trap introduce deviations from ideality such that the field within the ion trap is no longer linear (a requirement of a pure quadrupole field); these deviations have been called field faults or superpositions of higher-multipole fields. All rotationally symmetric fields without space charge can be described by a weighted sum of such multipoles. It was recognized by the early workers in this field, that is, by von Busch and Paul and by Dawson and Whetten, that field faults had a deleterious effect on the performance of instruments with two-dimensional quadrupole fields, as such field faults caused ion losses by so-called nonlinear resonances. Once the problem encountered by Finnigan of mass shifts in the ion trap had been overcome by the serendipitous stretching of the ion trap geometry, the problem was ascribed to the presence of nonlinear resonances in the ion trap. The following question arises: If such resonances (or field faults or superpositions of higher-multipole fields) cause undesirable ion losses, can this mechanism of ion loss be employed for the deliberate ejection of ions in a mass-selective manner? This question of the influence of nonlinear resonances has been considered at length by Franzen, Gabling, Schubert, and Wang ([6], Vol. 1, Chap. 3), and it has been shown that the influence on modern mass scanning methods of weak higher-multipole fields is surprisingly strong.

10.2. Applications of electrospray ionization

The most active areas of ion trap research in the past 5–6 yr have been applications of electrospray ionization ([6], Vol. 2, Chap. 3; Vol. 3, Chaps. 5, 6, and 14), environmental applications ([6], Vol. 3, Chaps. 12 and 13), ion chemistry ([6], Vol. 1, Chaps. 5 and 8; Vol. 3, Chaps. 8–19), and instrument development ([6], Vol. 2, Chaps. 2, 3, and 7; Vol. 3, Chaps. 1, 6, and 11).

Recent publications relating to the use of a quadrupole ion trap combined with ESI have covered a wide range of topics. The efficacy of this method is highly dependent on the efficiency with which externally generated ions may be injected into the ion trap. The contributions of Doroshenko and Cotter [157–159] to our understanding of this process have been acknowledged elsewhere [153]. Let us consider first the manipulation of a sample before the admission of ions to the ion trap. Barroso and de Jong have developed a method of sheathless preconcentration applied to peptide analysis using capillary electrophoresis/ESI/ion trap [160]. Nanospray ionization [161,162] and microscale ESI [163] have been reported for the investigation of peptides and protein digests. In the examination of small quantities of material, the rate of sample flow through the introduction system often precludes the opportunity to carry out more than one mass spectrometric operation. In an attempt to overcome this difficulty, Davis and Lee [164] have demonstrated a method whereby sample analysis times for components eluting from an LC have been increased greatly by “peak parking.” This procedure permits high mass resolution over a narrow mass range as well as MS^2 and MS^3 within the ion trap. Derivatization of alkenes and alkynes for ESI/MS has been described [165].

Kinetic studies have been concerned with hydroiodic acid attachment as a chemical probe of gaseous protein ion structure [166] and gas phase H/D exchange kinetics, DI versus D_2O [167–170]. Ion–ion interactions of protonated pyridine with multiply charged oligonucleotides have been investigated by McLuckey and coworkers [171–173]. The propensity of the ion trap for tandem mass spectrometry MS^n has been demonstrated with reference to structural elucidation of erythromycins using MS^5 [174], determination of the anomericity of the glycosidic bond in Zn(II)-diethylenetriamine-disaccharide complexes using MS^n [175], examination of the ESI/MS^n of poly(propylene oxide) [176], and an MS^n study of triterpenoid saponins [177]. Other structural studies include a comparative study of four mass spectrometric methods employed in the elucidation of structure and fragmentation mechanisms of isomeric T-rich oligodeoxynucleotides [178], isomeric photomodified oligodeoxynucleotides [179], and a collisional activation study of the gas-phase stability of double-stranded oligonucleotides and their noncovalent complexes [180]. Van Berkel and Zhou have reported on the observation of gas-phase molecular dications formed via the controlled-current electrolytic process inherent to ESI; in this work, they studied the effect of different metal ESI capillaries [181]. Operation of an ion trap in combination with time-of-flight ion analysis has been carried out by Purves and Li [182] and by Lubman and coworkers [183–187].

The dissociation of a range of ion species has been reported. These reports include the collisional activation of deprotonated deoxymononucleoside and deoxydinucleoside monophosphates [188], decompositions of odd- and even-electron anions derived from deoxy-polyadenylates [189], MS/MS of model peptides modified with *trans*-2-hexenal [190], fragmentation of phosphopeptides [191], the role of the sulfhydryl group on the gas-phase fragmentations reactions of protonated cysteine and cysteine-containing peptides [192], dissociation of doubly charged transition metal/polyether/pyridyl ligand complexes [193], and fragmentation pathways of selectively labeled uropranolol [194] and of propranolol-related β-fluorinated amines [195].

Additional contributions include the evaluation of metal complexation [196,197] as an alternative to protonation for ESI of pharmaceutical compounds [198], the identification and positional mapping of aflatoxin B_1-guanine adducts in oligonucleotides [199], comparison of GC/MS and HPLC/MS with an ion trap applied to the determination of polyhydroxyalkaloids in bluebells [200], characterization of supramolecular complexes by high mass resolution [201], determination of calcium binding sites in gas-phase small peptides [202], peptide sequencing [203], a tetrahedral supramolecular Ti_4L_4 cluster [204], linkage position determination in cobalt coordinated pentasaccharides [205], ion trap and solution study of cyclodextrin-catalyzed oxidation of glutathione [206], charge derivatization of peptides to simplify their sequencing [207], determination of trans-4-hydroxy-2-nonenal at cellular levels [208], and collisional activation of multiply protonated polypeptides where the disulfide linkage has been reduced [209] and of singly charged peptide ions [210].

Strategies for locating disulfide bonds in a monoclonal antibody [211] and the sequencing of antithyroxine monoclonal antibody Fab fragment [212] have been reported. Methods have been given for the determination of 5-methyl-2′-deoxycytidine in urine [213] and of phenothiazines in whole blood [214]. An investigation of poly [(R,S)-3-hydroxybutanoic acid] telechelics [215,216] has been reported together with mass spectra of some new 3,4-dihydro-2[H]-pyridones [217].

10.3. Environmental applications

Numerous publications pertaining to the environment have appeared in the past 5–6 yr. Clearly, great use is being made of the ion trap for the determination of many compounds of environmental interest. The publications are concerned with air analysis [218,219] and the determination of semivolatile organic compounds [220] and of polycyclic aromatic hydrocarbons [221,222]. The application of ion trap mass spectrometry to drinking water and river water has increased. It is the opinion of the author that there will be a significant growth in the application of mass spectrometry to natural waters. At present, there are concerns with pesticides in food, for example, chlormequat in pear extracts [223], herbicides, and farm run-off. There is growing concern with the levels of pharmaceutical and neutraceutical products (and their metabolites), surfactants and their decomposition products, and so forth in bodies of water from which drinking water supplies are drawn. For example, the determination of Bisphenol A and nonyl phenol in river water [224], the determination of persistent acid metabolites of nonylphenol ethoxylate surfactants [225], and the identification and characterization of Fenton oxidation products of surfactants by ESI/MS [226] have been reported recently. The chlorination of drinking water brings other problems necessitating the determination of organohalogen compounds [227,228] and determination of the main chlortoluron byproducts during water disinfection by chlorine [229]. The determination of oxygenated polar organic compounds poses a particular problem because of lack of suitable methodologies; derivatization has been explored as a means to obviate this problem [230].

The characterization of a nerve agent VX (O-ethyl S-2-diisopropylaminoethyl methyl phosphonothiolate) on the surfaces of concrete samples by ion trap secondary ion mass spectrometry [231] together with a GC/MS study of organic films on stone monuments [232] has been reported. A sensitivity enhancement for the detection of chlorophylls has been found using atmospheric pressure ionization [233]. Two publications have appeared dealing with mass spectrometric methods for the identification of chemical markers of bacteria [234,235].

10.4. Ion/molecule reactions

Much ion-chemistry research has been concerned with the reactions of ions, the kinetics of ion/molecule reactions, ion dissociation, and ion structure determination. The ions studied are the phenylium cation with small oxygen- and nitrogen-containing molecules [236], isomeric parent ions from the dissociation of dimethylpyrroles [237], protonated polyamines [238], gas-phase H/D exchange reactions of polyamine complexes [239], perfluorotri-*n*-butylamine fragment ions [240], cluster ions of the form $H^+(H_2SO_4)_m(H_2O)_n$ [241], silane/hydrocarbon mixtures [242], and sodium ion attachment reactions [243,244]. Kinetic studies of gas phase reactions of the ion $C_5H_5Fe^+$ [245] and of the dissociation of a transient intermediate [246] have been carried out. The ion chemistry of carbon suboxide has been studied [247]. A chemometric approach to the evaluation of the parameters affecting the determination of reaction rate constants [248] has been made, and the effective ion temperatures in an ion trap have been estimated [249]. An effect of buffer gas temperature on the distribution of product ions in high mass tandem mass spectrometry has been found [250]. A time-of-flight method has been used to estimate the kinetic energy of N^+ ions throughout the stability diagram [251].

The mass spectrometric investigation of antibiotics, for example, the postcolumn metal complexation of quinolone antibiotics [252], is commanding some attention, as was seen in the above discussion on the use of ESI with the ion trap. Chemical ionization reactions studied were of oxygenated CI reagents with Vincamine [253], determination of the double-bond position in functionalized monoenes using acetonitrile as CI gas [254], and ammonia CI for the structure determination of alkaloids [255]. The effects of functional group interactions on the gas-phase methylation and dissociation of acids and esters also have been reported [256]. Studies on the dissociation of ions have included alkali cationized polysaccharides [257], rearrangement of *n*-butylbenzene [258], the estimation of critical energies for ion dissociation via threshold collisional activation measurements [259], the dissociation of polyether-transition metal ion dimer complexes [260], the effects of heavy gases on CID of peptides [261], and the origin of the product ions observed [262]. Structure elucidation studies include those of radical cations [263], polyketide tetrasubstituted δ-lactones [264], and distinguishing the structural isomers of glutathione conjugates of estrone and estradiol [265] and of conjugated diene epoxides [266]. The sites of reaction of pilocarpine have been reported [267]. Elimination reaction studies are the deamination of protonated amines to yield protonated imines [268], denitration of nitroaromatic compounds by arylnitrile radical cations [269], and elimination of CF_2 from trifluorocresols [270]. It is encouraging to observe that a library has been established of atmospheric pressure ionization (API) daughter mass spectra based on wideband excitation in an ion trap [271].

10.5. Instrument development

There have been some interesting developments in the area of instrument development. An ion trap has been combined with capillary zone electrophoresis separation for the CVZE/MS/MS (QIT) structural analysis of chromophore-labeled disaccharides [272] and for characterization of β-agonists [273]. The Barinaga group has observed enhanced abundance sensitivity for the resonant ion excitation of atomic ions generated in an inductively coupled plasma combined with an ion trap [274]. An ion trap/ion mobility/time-of-flight mass spectrometer has been used to measure collision cross sections for 660 peptide ions [275]. Voyksner and Lee [276] have investigated the use of an octupole ion guide for ion storage and high-pass mass filtering to improve the quantitative performance of ESI with an ion trap. An ion trap has been employed as a secondary ion mass spectrometer [231,277], and a hybrid ion trap has been characterized [278]. Laser desorption has been optimized [279]. The uses of overtone and fundamental resonances for mass range extension have been compared [280].

The application of field-modulated selective ion storage that reduces ion loss [281], external customized waveforms [282], vector-summed sine wave–tailored waveforms for dipolar excitation of ions [283], automated strategies for obtaining standardized collisionally induced dissociation mass spectra [284], and a new ion ejection method [285] have been reported. Pulsed buffer gas introduction has been explored further [286,287], and a comparison of equilibrium ion density and trapping force in Penning, Paul, and combined ion traps [288] has been reported. Novel ion trap devices continue to attract interest [289–292], and a dual quadrupole ion trap mass spectrometer has been evaluated [293]. Features of unstable ion trajectories have been explored [294,295].

Two further publications concern the RF frequency and the effect of change of frequency on ion storage. The first [296] is an investigation of the effects of the RF frequency potential on the trapping of externally generated ions in an ion trap, while the second [297] concerns a frequency scan for the analysis of high mass ions (60–160 kDa) generated by matrix-assisted laser desorption/ionization in an ion trap, as shown in Fig. 6.

10.6. Drugs and drug metabolites

The determination of drugs and drug metabolites [298–301] is becoming increasingly important, and the ion trap finds application in this area. The high sensitivity of mass spectrometry permits detection and identification of minor impurities in drugs [302] and of unknown but related substances in commercial erythromycin samples [303]. The analysis of a commercial preparation of erythromycin estolates [304] and the identification of tetracycline antibiotics [305] have been reported. Last but not least, there is a report on an ion trap determination of anabolic steroids [306].

10.7. Proteins

It should be noted that some publications concerning proteins may have been discussed in the sections above. The sequence determination of citropin peptides from the skin glands of the Australian Blue Mountains tree frog, *Litoria citropa* [307,308], the analysis of noncovalent protein complexes up to 290 kDa [309], the electrospray-assisted modification of proteins as a radical probe of protein structure [310], and the identification of cysteine residues by isotopic labeling [311] have been reported.

10.8. Simulations

There has not been a great deal of activity in the simulation area. The use of commercial packages for the calculation of ion trajectories has, perhaps, precluded research in this area. The Cooks' group has carried out multiparticle simulations [312], Yoshinari has carried out a numerical analysis of the behavior of ions injected into an ion trap [313], and the March group has reported a comparison of three simulation programs for the calculation of ion trajectories in an ion trap [314].

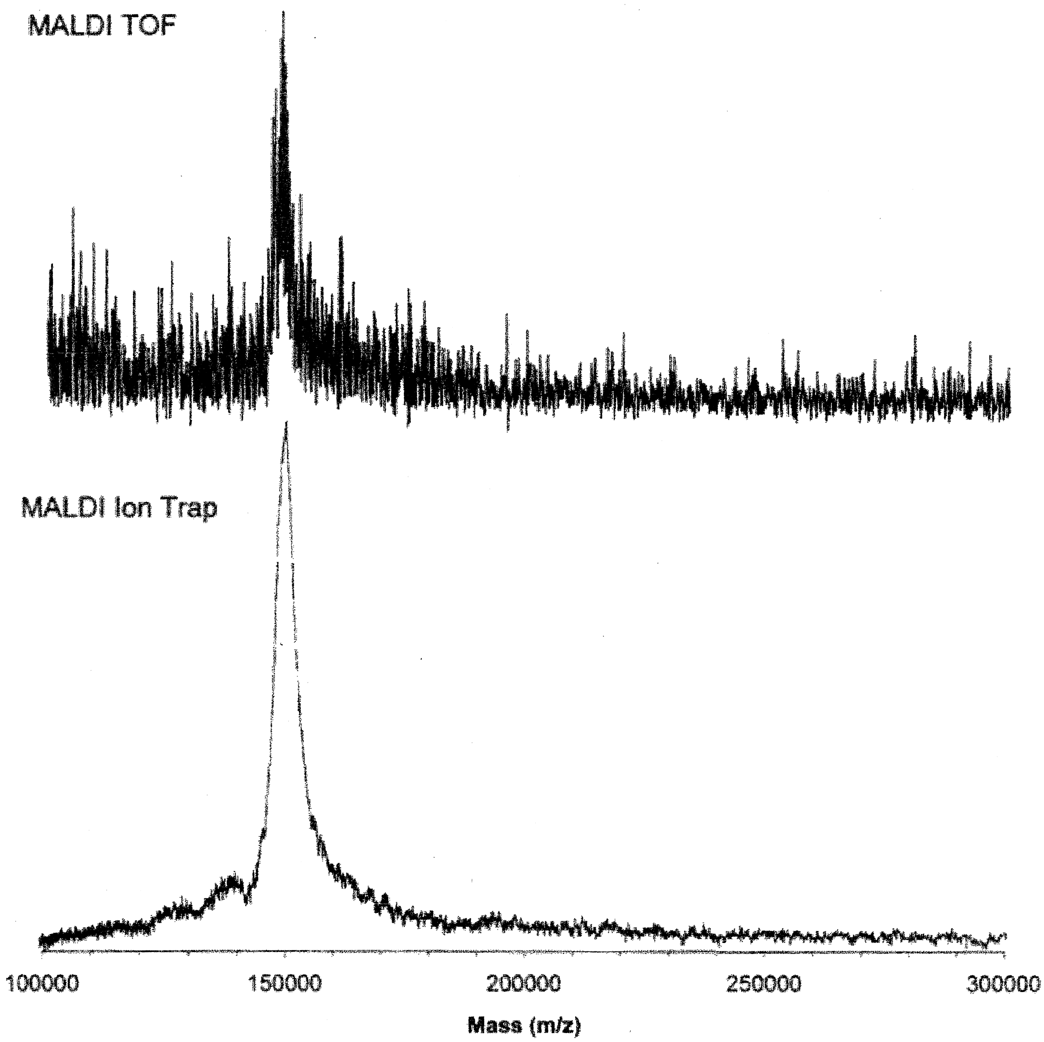

Fig. 6. Sensitivity comparison between a commercial TOF analyzer and an ion trap instrument on 0.1 pmol bovine IgG. The top mass spectrum is an average of 256 mass spectra, while the ion trap mass spectrum was produced by a single laser shot.

11. Conclusion

It has been a great pleasure to prepare this invited personal account of the mass spectrometric research with which I have been associated during the past 2 decades. Such an opportunity is only too rare. In 1991, I submitted a manuscript in which I mused on the present state of the ion trap and prospects for future applications [315]. In Dylan Thomas fashion, where his mythical village viewed in reverse means nothing at all, I left myself a face saver. The submission was entitled “A musing . . . ” If the manuscript was to be rejected, I could explain that I was simply amusing myself!

In the conclusion to that publication, it was stated that “it is obvious that ion trap mass spectrometry, with its demonstrated sensitivity, its ability to accumulate ions, its compatibility with a variety of ionization methods, mass range and resolution, now offers extraordinary versatility as we begin to tackle the myriad problems in structural biology, such as sequencing of proteins for cloning and the identification of post-translational modifications." This present review confirms my confidence in the quadrupole ion trap as an extraordinary instrument for the pursuit of mass spectrometry and its application in the twenty-first century. Thank you.

Acknowledgments

I wish to acknowledge and to thank John Todd of the University of Kent at Canterbury, England; John Beynon of the Royal Society Research Unit at Swansea University College, Wales; Jacques André and Fernande Vedel of the Université de Provence, Marseille, France; Alex Harrison of the University of Toronto, Canada; Diethard Bohme of York University, North York, Canada; Jean-Claude Tabet of the Université Pierre and Marie Curie, Paris, France; Pietro Traldi of the National Research Centre in Padova, Italy; and Chris Metcalfe of Trent University. In particular, I wish to thank Greg Wells of Varian Associates for the opportunity to pursue ion trap research in a directed and accelerated manner.

References

[1] A Special Issue, volume 190/191 of Int. J. Mass Spectrom., was published as *A Collection of invited papers in honour of the scientific contributions of John F.J. Todd and Raymond E. March*, ed. Scott A. McLuckey, August 1999.

[2] J.F.J. Todd, R.E. March, Int. J. Mass Spectrom. 190/191 (1999) 9.

[3] K. Berkling aus Leipzig, Physikalisches Institut der Universitat, Bonn, West Germany, 1956.

[4] J.E.P. Syka, In *Practical aspects of ion trap mass spectrometry: fundamentals*. R.E. March and J.F.J. Todd (Eds.), Modern mass spectrometry series, vol. 1. CRC Press, Boca Raton, FL (1995).

[5] P.E. Kelley, G.C. Stafford Jr., D.R. Stephens, U.S. Patent 4 540 884, 10 September 1985; Can. Patent 1 207 918, 15 July 1986.

[6] R.E. March and J.F.J. Todd (Eds.) *Practical aspects of ion trap mass spectrometry*, Modern mass spectrometry series, vol. 1, *Fundamentals*, (1995) vol. 2, *Instrumentation*, (1995); vol. 3, *Chemical, Biomedical, and Environmental Applications*, 1995, CRC Press, Boca Raton, FL (1995) 51.

[7] M.A. Armitage, Applications of quadrupole ion storage mass spectrometry, Trent University, Peterborough, ON, Canada, 1979.

[8] R.E. March, R.J. Hughes, with an historical review by J.F.J. Todd, *Quadrupole Storage Mass Spectrometry*. Chemical Analysis Series, vol. 102. Wiley, New York (1989).

[9] R.G. Cooks, A.L. Rockwood, Rapid Commun. Mass Spectrom. 5 (1991) 93.

[10] S.T. Quarmby, S.A. McLuckey, Int. J. Mass Spectrom. 190/191 (1999) 81.

[11] P.K. Ghosh, A.S. Arora, L. Narayan, Int. J. Mass Spectrom. Ion Phys. 23 (1977) 237.

[12] P. Kofel, In R.E. March and J.F.J. Todd (Eds.), *Practical aspects of ion trap mass spectrometry: instrumentation*. Modern Mass Spectrometry Series, vol. 2. CRC Press, Boca Raton, FL (1995).

[13] R.J. Hughes, R.E. March, A.B. Young, Proceedings of the 9th International Mass Spectrometry Conference, 29 August–3 September 1982, Vienna. Int. J. Mass Spectrom. Ion Phys. 47 (1983) 85.

[14] R.C. Dunbar, in M.T. Bowers (Ed.), Gas phase ion chemistry, vol. 2; Academic Press, London (1979), pp. 182–220.

[15] R.C. Dunbar, in H. Hartmann and K.-P. Wanczeck (Eds.), Lecture notes in chemistry, Springer, Berlin (1982), pp. 1–26.

[16] R.C. Dunbar, in M.T. Bowers (Ed.), Gas phase ion chemistry, vol. 3. Ions and light. Academic Press, London (1984), pp. 129–166.

[17] R.N. Rosenfeld, J.M. Jasinski, J.I. Braumann, J. Am. Chem. Soc. 101 (1979) 3999.

[18] D.S. Bomse, R.L. Woodin, J.L. Beauchamp, J. Am. Chem. Soc. 101 (1979) 5503.

[19] L.R. Thorne, J.L. Beauchamp, in M.T. Bowers (Ed.), Gas phase ion chemistry, vol. 3. Ions and light. Academic Press, London (1984), pp. 41–97.

[20] R.J. Hughes, R.E. March, A.B. Young, Int. J. Mass Spectrom. Ion Phys. 42 (1982) 255.

[21] P. Kebarle, Ann. Rev. Phys. Chem. 28 (1977) 445.

[22] R.J. Hughes, R.E. March, A.B. Young, Can. J. Chem. 61 (1983) 834.

[23] R.J. Hughes, R.E. March, A.B. Young, Can. J. Chem. 61 (1983) 824.

[24] R.E. March, NATO Advanced Study Institute, September 1982, Vimeiro, Portugal. Ionic processes in the gas phase. M.A.A. Ferreira (Ed.) Series C: Mathematical and Physical Sciences 118 (1983) 359–360.

[25] R.J. Hughes, R.E. March, A.B. Young, Int. J. Mass Spectrom. Ion Phys. 47 (1983) 85.

[26] A.B. Young, R.E. March, R.J. Hughes, Can. J. Chem. 63 (1985) 2324.

[27] P.H. Dawson, N.R. Whetten, J. Vac. Sci. Technol. 5 (1968) 1.

[28] P.H. Dawson, N.R. Whetten, Int. J. Mass Spectrom. Ion Phys. 2 (1969) 45.

[29] P.H. Dawson, N.R. Whetten, Int. J. Mass Spectrom. Ion Phys. 16 (1975) 269.

[30] P.H. Dawson, N.R. Whetten, Int. J. Mass Spectrom. Ion Phys. 14 (1974) 339.

[31] R.F. Bonner, R.E. March, J. Durup, Int. J. Mass Spectrom. Ion Phys. 22 (1976) 17.

[32] R.F. Bonner, R.E. March, Int. J. Mass Spectrom. Ion Phys. 25 (1977) 411.
[33] M.C. Doran, J.E. Fulford, R.J. Hughes, Y. Morita, R.F. Bonner, R.E. March, Int. J. Mass Spectrom. Ion Phys. 33 (1980) 139.
[34] R.F. Bonner, J.E. Fulford, R.E. March, G.F. Hamilton, Int. J. Mass Spectrom. Ion Phys. 24 (1977) 255.
[35] R.E. Mather, R.M. Waldren, J.F.J. Todd, R.E. March, Int. J. Mass Spectrom. Ion Phys. 33 (1980) 201.
[36] J.E. Fulford, R.E. March, R.E. Mather, J.F.J. Todd, R.M. Waldren, Can. J. Spec. 25 (1980) 85.
[37] M. Ikonomou, Honors Project, Trent University, 1983.
[38] J.F.J. Todd, G. Lawson, R.F. Bonner, in P.H. Dawson (Ed.), *Quadrupole Mass Spectrometry and Its Applications*. Elsevier, Amsterdam (1976) 181.
[39] G. Lawson, J.F.J. Todd, Mass Spectrometry Group Meeting, Bristol, 1971, Abstr. 44.
[40] G. Lawson, R.F. Bonner, J.F.J. Todd, J. Phys. E. Sci. Instrum. 6 (1973) 357.
[41] J.F.J. Todd, R.F. Bonner, G. Lawson, J. Chem. Soc. Chem. Commun. (1972) 1179.
[42] R.F. Bonner, G. Lawson, J.F.J. Todd, R.E. March, Adv. Mass Spectrom. 6 (1974) 377.
[43] G. Lawson, J.F.J. Todd, R.F. Bonner, Dyn. Mass Spectrom. 4 (1975) 39.
[44] G. Lawson, R.F. Bonner, R.E. Mather, J.F.J. Todd, R.E. March, J. Chem. Soc. Faraday Trans. I 72(3) (1976) 545.
[45] J.F.J. Todd, R.M. Waldren, R.E. Mather, G. Lawson, Int. J. Mass Spectrom. Ion Phys. 28 (1978) 141.
[46] J.E. Fulford, R.E. March, Int. J. Mass Spectrom. Ion Phys. 26 (1978) 155.
[47] G.B. DeBrou, J.E. Fulford, E.G. Lewars, R.E. March, Int. J. Mass Spectrom. Ion Phys. 26 (1978) 345.
[48] J.E. Fulford, J.W. Dupuis, R.E. March, Can. J. Chem. 56 (1978) 2324.
[49] M.A. Armitage, M.J. Higgins, E.G. Lewars, R.E. March, J. Am. Chem. Soc. 102 (1980) 5064.
[50] R.F. Bonner, G. Lawson, J.F.J. Todd, R.E. March, unpublished data.
[51] D.J. Douglas, J.B. French, J. Am. Soc. Mass Spectrom. 3 (1992) 398.
[52] L.R. Anders, J.L. Beauchamp, R.C. Dunbar, J.D. Baldeschweiler, J. Chem. Phys. 45 (1966) 1062.
[53] J.L. Beauchamp, L.R. Anders, J.D. Baldeschweiler, J. Am. Chem. Soc. 89 (1967) 4569.
[54] F.G. Major, H.G. Dehmelt, Phys. Rev. 170 (1968) 91.
[55] É.P. Sheretov, V.A. Zenkin, V.F. Samodurov, Sov. Phys. Tech. Phys. 18 (1973) 282.
[56] C. Schwebel, P.A. Möller, P.T. Manh, Rev. Phys. Appl. 10 (1975) 227.
[57] M.A. Armitage, J.E. Fulford, D.N. Hoa, R.J. Hughes, R.E. March, Can. J. Chem. 57 (1979) 2108.
[58] J.E. Fulford, D.N. Hoa, R.J. Hughes, R.E. March, R.F. Bonner, G. Wong, J. Vac. Sci. Technol. 17 (1980) 829.
[59] I.W. Griffiths, E.S. Mukhtar, R.E. March, F.M. Harris, J.H. Beynon, Proceedings of the Twenty-Ninth ASMS Conference on Mass Spectrometry and Allied Topics, Minneapolis, MN, p. 709 (1981).
[60] T.G. Morgan, A.G. Brenton, R.E. March, F.M. Harris, J.H. Beynon, Int. J. Mass Spectrom. Ion Processes 64 (1985) 299.
[61] E.S. Mukhtar, I.W. Griffiths, R.E. March, F.M. Harris, J.H. Beynon, Int. J. Mass Spectrom. Ion Phys. 41 (1981) 61.
[62] I.W. Griffiths, E.S. Mukhtar, R.E. March, F.M. Harris, J.H. Beynon, Int. J. Mass Spectrom. Ion Phys. 39 (1981) 125.
[63] I.W. Griffiths, I. Howe, R.E. March, J.H. Beynon, Int. J. Mass Spectrom. Ion Phys. 54 (1983) 323.
[64] T.G. Morgan, R.E. March, F.M. Harris, J.H. Beynon, Int. J. Mass Spectrom. Ion Processes 61 (1984) 41.
[65] A.G. Harrison, R.S. Mercer, E.J. Reiner, A.B. Young, R.K. Boyd, R.E. March, C.J. Porter, Int. J. Mass Spectrom. Ion Processes 74 (1986) 13.
[66] R.E. March, A.B. Young, Int. J. Mass Spectrom. Ion Processes 76 (1987) 11.
[67] R.E. March, J.G. MacMillan, Int. J. Mass Spectrom. Ion Processes 85 (1988) 91.
[68] A.W. McMahon, F. Chadikun, A.G. Harrison, R.E. March, Int. J. Mass Spectrom. Ion Processes 87 (1989) 275.
[69] R.E. March, A.B. Young, Int. J. Mass Spectrom. Ion Processes 85 (1988) 237.
[70] R.E. March, Org. Mass Spectrom. 22 (1987) 545.
[71] R.E. March, A.G. Harrison, A.B. Young, Org. Mass Spectrom. 22 (1987) 651.
[72] G.K. Koyanagi, R.E. March, Int. J. Mass Spectrom. Ion Processes 83 (1988) 245.
[73] A.G. Harrison, H. Camilleri, A.W. McMahon, R.E. March, Int. J. Mass Spectrom. Ion Processes 86 (1988) 303.
[74] J.-Y. Wang, R.E. March, S.J.A. Curtis, A.G. Harrison, Int. J. Mass Spectrom. Ion Processes 101 (1990) 355.
[75] G.K. Koyanagi, J.-Y. Wang, R.E. March, Rapid Commun. Mass Spectrom. 4 (1990) 373.
[76] R.E. March, G.K. Koyanagi, A.W. McMahon, Sixteenth Meeting of the British Mass Spectrometry Society, 6–9 September 1987, York University, pp. 21–4 (1987).
[77] G.K. Koyanagi, A.W. McMahon, R.E. March, Rapid Commun. Mass Spectrom. 1 (1987) 132.
[78] G.K. Koyanagi, A.W. McMahon, R.E. March, A.G. Harrison, Int. J. Mass Spectrom. Ion Processes 87 (1989) 249.
[79] R.E. March, R.J. Hughes, G.K. Koyanagi, A.W. McMahon, in P. Longevialle (Ed.), Proceedings of the Eleventh International Mass Spectrometry Conference, 29 August–2 September 1988, Bordeaux. Advances in Mass Spectrometry, vol. 11, London: Heyden & Son (1989) pp. 778–779.
[80] R.J. Hughes, R.E. March, Int. J. Mass Spectrom. Ion Processes 127 (1993) 27.
[81] A. Kamar, A.B. Young, R.E. March, Can. J. Chem. 64 (1986) 1979.
[82] A. Kamar, A.B. Young, R.E. March, Can. J. Chem. 64 (1986) 2368.
[83] J.E. Curtis, A. Kamar, R.E. March, U.P. Schlunegger, Proceedings of the Thirty-Fifth ASMS Conference on Mass Spectrometry and Allied Topics, 24–29 May 1987, Denver, CO, pp. 237–238 (1987).
[84] F. Vedel, M. Vedel, R.E. March, in A. Salin (Ed.), Proceedings of the Third European Conference on Atomic and Molecular Physics, 3–7 April 1989, University of Bordeaux I, p. 667 (1989).

[85] F. Vedel, M. Vedel, R.E. March, Proceedings of the Sixteenth International Conference on the Physics of Electronic and Atomic Collisions, 26 July–1 August 1989, New York, p. 119 (1989).

[86] F. Vedel, M. Vedel, R.E. March, Int. J. Mass Spectrom. Ion Processes 99 (1990) 125.

[87] M. Vedel, F. Vedel, R.E. March, Spectrométrie 150 (1990) 24.

[88] F. Vedel, M. Vedel, R.E. March, Int. J. Mass Spectrom. Ion Processes 108 (1991) R11.

[89] R.E. March, A.W. McMahon, F.A. Londry, R.L. Alfred, J.F.J. Todd, F. Vedel, Proceedings of the Thirty-Seventh ASMS Conference on Mass Spectrometry and Allied Topics, 21–26 May 1989, Miami Beach, FL, pp. 460–1 (1989).

[90] R.E. March, A.W. McMahon, F.A. Londry, R.L. Alfred, J.F.J. Todd, F. Vedel, Int. J. Mass Spectrom. Ion Processes 95 (1989) 119.

[91] R.E. March, A.W. McMahon, E. Tracey Allinson, F.A. Londry, R.L. Alfred, J.F.J. Todd, F. Vedel, Int. J. Mass Spectrom. Ion Processes 99 (1990) 109.

[92] R.E. March, F.A. Londry, R.L. Alfred, J.F.J. Todd, A.D. Penman, F. Vedel, M. Vedel, Int. J. Mass Spectrom. Ion Processes 110 (1991) 159.

[93] R.E. March, M.R. Weir, M. Tkaczyk, F.A. Londry, R.L. Alfred, A.M. Franklin, J.F.J. Todd, Org. Mass Spectrom. 28 (1993) 499.

[94] R.L. Alfred, F.A. Londry, R.E. March, Int. J. Mass Spectrom. Ion Processes 125 (1993) 171.

[95] R.E. March, M. Tkaczyk, F.A. Londry, R.L. Alfred, Int. J. Mass Spectrom. Ion Processes 125 (1993) 9.

[96] M. Splendore, M. Lausevic, Z. Lausevic, R.E. March, Rapid Commun. Mass Spectrom. 11 (1997) 228.

[97] R.E. March, F.A. Londry, R.L. Alfred, A.M. Franklin, J.F.J. Todd, Int. J. Mass Spectrom. Ion Processes 112 (1992) 247.

[98] R.E. March, M. Tkaczyk, F.A. Londry, R.L. Alfred, Int. J. Mass Spectrom. Ion Processes 125 (1993) 9.

[99] F.A. Londry, R.L. Alfred, R.E. March, J. Am. Soc. Mass Spectrom. 4(9) (1993) 687.

[100] R.K. Julian Jr., R.G. Cooks, R.E. March, F.A. Londry, in R.E. March and J.F.J. Todd (Eds.), *Practical aspects of ion trap mass spectrometry: fundamentals*. Modern Mass Spectrometry Series, vol. 1. CRC Press, Boca Raton, FL (1995) 221.

[101] X. Wang, D.K. Bohme, R.E. March, Proceedings of the Fortieth ASMS Conference on Mass Spectrometry and Allied Topics, 31 May–5 June 1992, Washington, DC, p. 230.

[102] X. Wang, D.K. Bohme, R.E. March, Can. J. Appl. Spectroscopy 38(2) (1993) 55.

[103] X. Wang, H. Becker, A.C. Hopkinson, R.E. March, L.T. Scott, D.K. Bohme, Int. J. Mass Spectrom. Ion Processes. 161 (1997) 69.

[104] X. Wang, R.E. March, A.C. Hopkinson, D.K. Bohme, Proceedings of the Forty-Third ASMS Conference on Mass Spectrometry and Allied Topics, Atlanta, Georgia, 21–26 May 1995, p. 79.

[105] R.E. March, F.A. Londry, R.L. Alfred, Org. Mass Spectrom. 27 (1992) 1151.

[106] J.E.P. Syka, J.N. Louris, P.E. Kelley, G.C. Stafford, W.E. Reynolds, US Patent 4 736 101 (1988).

[107] R.E. March, R.J. Strife, in R.E. March and J.F.J. Todd (Eds.), *Practical aspects of ion trap mass spectrometry: chemical, biomedical, and environmental applications*. Modern Mass Spectrometry Series, vol. 3. CRC Press, Boca Raton, FL (1995).

[108] J.D. Williams, K.A. Cox, J.C. Schwartz, R.G. Cooks, in R.E. March and J.F.J. Todd (Eds.), *Practical aspects of ion trap mass spectrometry: instrumentation*. Modern Mass Spectrometry Series, vol. 2. CRC Press, Boca Raton, FL (1995) 3.

[109] J.C. Schwartz, J.E.P. Syka, I. Jardine, J. Am. Soc. Mass Spectrom. 106 (1991) 79.

[110] D.E. Goeringer, S.A. McLuckey, G.L. Glish, Proceedings of the Thirty-Ninth Annual Conference on Mass Spectrometry and Allied Topics, p. 532, Nashville, TN, 1991.

[111] F.A. Londry, G.J. Wells, R.E. March, Rapid Commun. Mass Spectrom. 7 (1993) 43.

[112] F.A. Londry, G.J. Wells, R.E. March, Hyperfine Interactions 81 (1993) 179.

[113] F.A. Londry, R.E. March, Int. J. Mass Spectrom. Ion Processes 144 (1995) 87.

[114] M. Splendore, M. Lausevic, Z. Lausevic, R.E. March, Rapid Commun. Mass Spectrom. 11 (1997) 228.

[115] R.E. March, F.A. Londry, G.J. Wells, E.G. Marquette. U.S. Patent 5,397,894. Method of high mass resolution scanning for an ion trap mass spectrometer. 14 March 1995.

[116] J.B. Plomley, F.A. Londry, R.E. March, Rapid Commun. Mass Spectrom. 10 (1996) 200.

[117] P. Traldi, S. Catinella, R.E. March, C.S. Creaser, in R.E. March and J.F.J. Todd (Eds.), *Practical aspects of ion trap mass spectrometry: fundamentals*. Modern Mass Spectrometry Series, vol. 1. CRC Press, Boca Raton, FL (1995) 299.

[118] R.E. March, F.A. Londry, S. Fontana, S. Catinella, P. Traldi, Rapid Commun. Mass Spectrom. 7 (1993) 929.

[119] R.E. March, M.R. Weir, F.A. Londry, S. Catinella, P. Traldi, J.A. Stone, W.B. Jacobs, Can. J. Chem. 72 (1994) 966.

[120] F.A. Londry, R.E. March, S. Catinella, U.S. Patent 5,378,891. A method for selective collisional dissociation using border effect excitation with prior cooling time control. 3 January 1995.

[121] M. Splendore, F.A. Londry, R.E. March, R.J.S. Morrison, P. Perrier, J. André, Int. J. Mass Spectrom. Ion Processes 156 (1996) 11.

[122] J.B. Plomley, C.J. Koester, R.E. March, Org. Mass Spectrom. 29 (1994) 372.

[123] J.B. Plomley, R.S. Mercer and R.E. March, Fifteenth International Symposium on Chlorinated Dioxins and Related Compounds, Edmonton, Canada, 21–25 August 1995. Organohalogen Compounds 23 (1995) 7.

[124] J.B. Plomley, R.E. March, R.S. Mercer, Anal. Chem. 68 (1996) 2345.

[125] M. Splendore, J.B. Plomley, R.E. March, R.S. Mercer, Int. J. Mass Spectrom. Ion Processes. 165/166 (1997) 595.

[126] R.E. March, M. Splendore, E.J. Reiner, R.S. Mercer, J.B. Plomley, D.S. Waddell, K.A. MacPherson, Int. J. Mass Spectrom., Morrison Honour Issue, 194 (2–3) (2000) 235. Republished as an Erratum in *IJMS*, 197 (2000) 283.

[127] S.A. Kafafi, H.Y. Afeefy, A.H. Ali, H.K. Said, A.G. Kafafi, Environ. Health Persp. 101 (1993) 422.
[128] M. Lausevic, X. Jiang, C.D. Metcalfe, R.E. March, Rapid Commun. Mass Spectrom. 9 (1995) 927.
[129] M. Lausevic, M. Splendore, R.E. March, J. Mass Spectrom. 31 (1996) 1244.
[130] M. Lausevic, J.B. Plomley, X. Jiang, R.E. March, C.D. Metcalfe, Eur. Mass Spectrom. 1 (1995) 149.
[131] J.B. Plomley, C.J. Koester, R.E. March, Anal. Chem. 66 (1994) 4437.
[132] J.B. Plomley, M. Laušević, R.E. March, in W.M.A. Niessen (Ed.), *Current practice of gas chromatography–mass spectrometry*. Dekker, New York, in press.
[133] J.B. Plomley, M. Laušević, R.E. March, Mass Spectrometry Reviews. 19 (2000) 305.
[134] P. Liere, T. Blasco, R.E. March, J.-C. Tabet, Rapid Commun. Mass Spectrom. 8 (1994) 953.
[135] P. Liere, S. Bouchonnet, R.E. March, J.C. Tabet, Rapid Commun. Mass Spectrom. 9 (1995) 1594.
[136] N. Méchin, J. Plomley, R. March, T. Blasco, J.-C. Tabet, Rapid Commun. Mass Spectrom. 9 (1995) 5.
[137] P. Liere, R.E. March, T. Blasco, J.-C. Tabet, Int J. Mass Spectrom. Ion Processes 153 (1996) 101.
[138] P. Liere, V. Steiner, K. Jennings, R.E. March, J.-C. Tabet, Int. J. Mass Spectrom. Ion Processes 167/168 (1997) 735.
[139] S. Catinella, P. Traldi, X. Jiang, F.A. Londry, R.J.S. Morrison, R.E. March, S. Gregoire, J.-C. Mathurin, J.-C. Tabet, Rapid Commun. Mass Spectrom. 9 (1995) 1302.
[140] J.-C. Mathurin, S. Gregoire, A. Brunot, J.-C. Tabet, R.E. March, S. Catinella, P. Traldi, J. Mass Spectrom. 32 (1997) 829.
[141] S. Gregoire, J.-C. Mathurin, R.E. March, J.-C. Tabet, Can. J. Chem. 76 (1998) 452.
[142] H.-P. Reiser, R.E. Kaiser, P.J. Savickas, R.G. Cooks, Int. J. Mass Spectrom. Ion Processes 6 (1991) 237.
[143] D. Favretto, F. Cecchinato, P. Traldi, R.E. March, J. Mass Spectrom. 30 (1995) 1347.
[144] P.H. Dawson, *Quadrupole mass spectrometry and its applications*, Elsevier, Amsterdam, 1976.
[145] J.F.J. Todd, Mass Spec. Rev. 10 (1991) 3.
[146] B.D. Nourse, R.G. Cooks, Anal. Chim. Acta. 228 (1990) 1.
[147] R.G. Cooks, R.E. Kaiser Jr., Accounts Chem. Res. 23 (1990) 213.
[148] G.L. Glish, S.A. McLuckey (Eds.), *Quadrupole Ion Traps*, Int. J. Mass Spectrom. Ion Processes 106 (1991).
[149] R.E. March, Int. J. Mass Spectrom. Ion Processes 118/119 (1992) 71.
[150] R.E. March, J. Mass Spectrom. 32 (1997) 351.
[151] R.E. March, *Quadrupole Mass Spectrometry*. KathRay Enterprises, ON, English version, 1998. Chinese version, translated by Dr. Chunyan Hao, 1999.
[152] R.E. March, Rapid Commun. Mass Spectrom. 12 (1998) 1543.
[153] R.E. March. Advances in quadrupole ion trap mass spectrometry: instrument development and applications. Invited lecture presented at the Fourteenth International Mass Spectrometry Conference, Tampere, Finland, Aug. 25–29, 1997 Adv. Mass Spectrom., 14 (1998) 241, Elsevier, Amsterdam.
[154] R.E. March, in Robert Paehlke (Ed.), Encyclopedia of conservation and environmentalism. Garland Publishing, New York (1995) p. 425.
[155] R.E. March, in J. Lindon, G. Tranter, and J.L. Holmes (Eds.), Encyclopedia of Spectroscopy and Spectrometry, Academic Press, London (1999), pp. 1000–1009.
[156] R.E. March, *Encyclopedia of Analytical Chemistry*, Wiley, Chichester, 13 (2000) 11848.
[157] V.M. Doroshenko, R.J. Cotter, Rapid Commun. Mass Spectrom. 7 (1993) 822.
[158] V.M. Doroshenko in J.C. Miller and D.B. Geohegan (Eds.), Laser Ablation: Mechanisms and Applications. II. Proceedings of the Second International Conference on Laser Ablation, Knoxville, TN, 19–22 April 1993. AIP Press, New York (1994) p. 513.
[159] V.M. Doroshenko, R.J. Cotter, US Patent 5 399 857 (1995).
[160] M.B. Barroso, A.P. de Jong, J. Am. Soc. Mass Spectrom. 10 (1999) 1271.
[161] R. Körner, M. Wilm, K. Morand, M. Schubert, M. Mann, J. Am. Soc. Mass Spectrom. 7 (1996) 150.
[162] B. Feng, R.D. Smith, J. Am. Soc. Mass Spectrom. 11 (2000) 94.
[163] M.T. Davis, T.D. Lee, J. Am. Soc. Mass Spectrom. 9 (1998) 194.
[164] M.T. Davis, T.D. Lee, J. Am. Soc. Mass Spectrom. 8 (1997) 1059.
[165] G.J. Van Berkel, J.M.E. Quirke, C.L. Adams, Rapid Commun. Mass Spectrom. 14 (2000) 849.
[166] J.L. Stephenson, Jr., T.G. Schaaff, S.A. McLuckey, J. Am. Soc. Mass Spectrom. 10 (1999) 552.
[167] T.G. Schaaff, J.L. Stephenson, Jr., S.A. McLuckey, J. Am. Soc. Mass Spectrom. 11 (2000) 167.
[168] T. Felix, M. Reyzer, J.S. Brodbelt, Int. J. Mass Spectrom. 190/191 (1999) 161.
[169] G.E. Reid, R.J. Simpson, R.A.J. O'Hair, Int. J. Mass Spectrom. 190/191 (1999) 209.
[170] Y.A. Ranasinghe, G.L. Glish, Int. J. Mass Spectrom. 190/191 (1999) 295.
[171] W.J. Herron, D.E. Goeringer, S.A. McLuckey, J. Am. Soc. Mass Spectrom. 6 (1995) 525.
[172] J.L. Stephenson, Jr., G.J. Van Berkel, S.A. McLuckey, J. Am. Soc. Mass Spectrom. 8 (1997) 637.
[173] J.L. Stephenson, Jr., S.A. McLuckey, J. Am. Soc. Mass Spectrom. 9 (1998) 585.
[174] P.J. Gates, G.C. Kearney, R. Jones, P.F. Leadlay, J. Staunton, Rapid Commun. Mass Spectrom. 13 (1999) 242.
[175] S.P. Gaucher, J.A. Learie, J. Am. Soc. Mass Spectrom. 10 (1999) 269.
[176] A. Stolarzewicz, D. Neugebauer, J. Silberring, Rapid Commun. Mass Spectrom. 13 (1999) 2469.
[177] M. Cui, W. Sun, F. Song, Z. Liu, S. Liu, Rapid Commun. Mass Spectrom. 13 (1999) 873.
[178] Z. Wang, K.X. Wan, R. Ramanathan, J.S. Taylor, M.L. Gross, J. Am. Soc. Mass Spectrom. 9 (1998) 683.
[179] Y. Wang, J.-S. Taylor, M.L. Gross, J. Am. Soc. Mass Spectrom. 10 (1999) 329.
[180] K.X. Wan, M.L. Gross, T. Shibue, J. Am. Soc. Mass Spectrom. 11 (2000) 450.

[181] G.J. Van Berkel, F. Zhou, J. Am. Soc. Mass Spectrom. 7 (1996) 157.

[182] R.W. Purves, L. Li, J. Am. Soc. Mass Spectrom. 8 (1997) 1085.

[183] M.X. Li, J.-T. Wu, S. Parus, D.M. Lubman, J. Am. Soc. Mass Spectrom. 9 (1998) 701.

[184] Y. Chen, X. Jing, D. Misek, R. Hinderer, S.M. Hanash, D.M. Lubman, Rapid Commun. Mass Spectrom. 13 (1999) 1907.

[185] X. Jing, Y. Chen, D.M. Lubman, D. Misek, S.M. Hanash, Rapid Commun. Mass Spectrom. 13 (1999) 2327.

[186] J.-T. Wu, L. He, M.X. Li, S. Parus, D.M. Lubman, J. Am. Soc. Mass Spectrom. 8 (1997) 1237.

[187] P. Huang, D.B. Wall, S. Parus, D.M. Lubman, J. Am. Soc. Mass Spectrom. 11 (2000) 127.

[188] S. Habibi-Goudarzi, S.A. McLuckey, J. Am. Soc. Mass Spectrom. 6 (1995) 102.

[189] S.A. McLuckey, J.L. Stephenson Jr., R.A.J. O'Hair, J. Am. Soc. Mass Spectrom. 8 (1997) 148.

[190] A.G. Baker, D. Wiesler, M.V. Novotny, J. Am. Soc. Mass Spectrom. 10 (1999) 613.

[191] J.P. DeGnore, J. Qin, J. Am. Soc. Mass Spectrom. 9 (1998) 1175.

[192] R.A.J. O'Hair, M.L. Styles, G.E. Reid, J. Am. Soc. Mass Spectrom. 9 (1998) 1275.

[193] J. Shen, J.S. Brodbelt, J. Am. Soc. Mass Spectrom. 10 (1999) 126.

[194] A.L. Upthagrove, M. Hackett, W.L. Nelson, Rapid Commun. Mass Spectrom. 13 (1999) 534.

[195] A.L. Upthagrove, M. Hackett, W.L. Nelson, Rapid Commun. Mass Spectrom. 13 (1999) 1671.

[196] S.M. Blair, E.C. Kempen, J.S. Brodbelt, J. Am. Soc. Mass Spectrom. 10 (1999) 1049.

[197] B.J. Hall, J.S. Brodbelt, J. Am. Soc. Mass Spectrom. 10 (1999) 402.

[198] E.J. Alvarez, J.S. Brodbelt, J. Am. Soc. Mass Spectrom. 9 (1998) 463.

[199] L.A. Marzilli, D. Wang, W.R. Kobertz, J.M. Essigmann, P. Vouros, J. Am. Soc. Mass Spectrom. 9 (1998) 676.

[200] M.J. Egan, E.A. Porter, G.C. Kite, M.S.J. Simmonds, J. Barker, S. Howells, Rapid Commun. Mass Spectrom. 13 (1999) 195.

[201] G. Hopfgartner, F. Vilbois, C. Piguet, Rapid Commun. Mass Spectrom. 13 (1999) 302.

[202] O.V. Nemirovskiy, M.L. Gross, J. Am. Soc. Mass Spectrom. 10 (1999) 1020.

[203] L.C.M. Ngoka, M.L. Gross, J. Am. Soc. Mass Spectrom. 10 (1999) 732.

[204] S. König, C. Brückner, K.N. Raymond, J.A. Learie, J. Am. Soc. Mass Spectrom. 10 (1999) 1099.

[205] S. König, J.A. Learie, J. Am. Soc. Mass Spectrom. 9 (1998) 1125.

[206] W. Sun, J. Liu, M. Cui, F. Song, S. Liu, Rapid Commun. Mass Spectrom. 13 (1999) 950.

[207] M. Adamczyk, J.C. Gebler, J. Wu, Rapid Commun. Mass Spectrom. 13 (1999) 1413.

[208] A.M. Gioacchini, N. Calonghi, C. Boga, C. Cappadone, L. Masotti, A. Roda, P. Traldi, Rapid Commun. Mass Spectrom. 13 (1999) 1573.

[209] J.L. Stephenson, Jr., B.J. Cargile, S.A. McLuckey, Rapid Commun. Mass Spectrom. 13 (1999) 2040.

[210] J. Qin, B.T. Chait, Int. J. Mass Spectrom. 190/191 (1999) 313.

[211] R. Mhatre, J. Woodard, C. Zeng, Rapid Commun. Mass Spectrom. 13 (1999) 2503.

[212] M. Adamczyk, J.C. Gebler, J. Wu, Rapid Commun. Mass Spectrom. 14 (2000) 999.

[213] C.G. Zambonin, F. Palmisano, Rapid Commun. Mass Spectrom. 13 (1999) 2160.

[214] H. Seno, H. Hattori, A. Ishii, T. Kumazawa, K. Watanabe-Suzuki, O. Suzuki, Rapid Commun. Mass Spectrom. 13 (1999) 2394.

[215] H. Arslan, G. Adamus, B. Hazi, M. Kowalczuk, Rapid Commun. Mass Spectrom. 13 (1999) 2433.

[216] G. Adamus, M. Kowalczuk, Rapid Commun. Mass Spectrom. 14 (2000) 195.

[217] H. Acherki, C. Alvarez-Ibarra, M. Gutiérrez, R. Martin-Alvarez, M.L. Quiroga, Rapid Commun. Mass Spectrom. 14 (2000) 1123.

[218] G.L. Kok, M.E. Cisper, P.H. Hemberger, J. Am. Soc. Mass Spectrom. 7 (1996) 1172.

[219] A. Saba, A. Rafaelli, S. Pucci, P. Salvadori, Rapid Commun. Mass Spectrom. 13 (1999) 1899.

[220] C.G. Gill, A.W. Garrett, W.L. Earl, N.S. Nogar, P.H. Hemberger, J. Am. Soc. Mass Spectrom. 8 (1997) 718.

[221] S.M. Pyle, L.D. Betowski, A.B. Marcus, W. Winnik, R.D. Brittain, J. Am. Soc. Mass Spectrom. 8 (1997) 183.

[222] A.A. Mosi, W.R. Cullen, G.K. Eigendorf, Int. J. Mass Spectrom. 190/191 (1999) 195.

[223] C.S. Evans, J.R. Startin, D.M. Goodall, B.J. Keely, Rapid Commun. Mass Spectrom. 14 (2000) 112.

[224] A. Motoyama, A. Suzuki, O. Shirota, R. Namba, Rapid Commun. Mass Spectrom. 13 (1999) 2204.

[225] C. Hao, T.R. Croley, R.E. March, B.G. Koenig, C.D. Metcalfe, J. Mass Spectrom. 35 (2000) 818.

[226] A. Cuzzola, A. Raffaelli, A. Sabo, P. Salvadori, Rapid Commun. Mass Spectrom. 14 (2000) 834.

[227] P. Bocchini, R. Pozzi, C. Andaló, G.C. Galletti, Rapid Commun. Mass Spectrom. 13 (1999) 2049.

[228] P. Bocchini, C. Andaló, D. Bonfiglioli, G.C. Galletti, Rapid Commun. Mass Spectrom. 13 (1999) 2133.

[229] C.G. Zambonin, I. Losito, F. Palmisano, Rapid Commun. Mass Spectrom. 14 (2000) 824.

[230] P. Frazey, X. Rao, R. Spaulding, B. Beld, M.J. Charles, Int. J. Mass Spectrom. 190/191 (1999) 343.

[231] G.S. Groenewold, A.D. Appelhans, G.L. Gresham, J.E. Olson, M. Jeffery, M. Weibel, J. Am. Soc. Mass Spectrom. 11 (2000) 69.

[232] F. Di Angelis, A. Di Tullio, G. Mellerio, R. Quaresima, R. Volpe, Rapid Commun. Mass Spectrom. 13 (1999) 895.

[233] R.L. Airs, B.J. Keely, Rapid Commun. Mass Spectrom. 14 (2000) 125.

[234] M. Krahmer, K. Fox, A. Fox, Int. J. Mass Spectrom. 190/191 (1999) 321.

[235] A.D. Hendricker, C. Abbas-Hawks, F. Basile, K.J. Voorhees, T.L. Hadfield, Int. J. Mass Spectrom. 190/191 (1999) 331.

[236] Y.A. Ranasinghe, G.L. Glish, J. Am. Soc. Mass Spectrom. 7 (1996) 473.
[237] T. Lin, M.R. Asam, G.L. Glish, J. Am. Soc. Mass Spectrom. 7 (1996) 930.
[238] M.L. Reyzer, J.S. Brodbelt, J. Am. Soc. Mass Spectrom. 10 (1999) 1043.
[239] M.L Reyzer, J.S. Brodbelt, J. Am. Soc. Mass Spectrom. 11 (2000) 711.
[240] C.S. Creaser, S.K. West, J.P.G. Wilkins, Rapid Commun. Mass Spectrom. 14 (2000) 538.
[241] E.R. Lovejoy, Int. J. Mass Spectrom. 190/191 (1999) 231.
[242] P. Antoniotti, L. Operti, R. Rabezzana, G.A. Vaglio, P. Volpe, Int. J. Mass Spectrom. 190/191 (1999) 243.
[243] T. Faye, A. Brunot, M. Sablier, J.-C. Tabet, T. Fujii, Rapid Commun. Mass Spectrom. 14 (2000) 1066.
[244] A. Favre, F. Gonnet, J.-C. Tabet, Int. J. Mass Spectrom. 190/191 (1999) 303.
[245] G. Innorta, L. Pontoni, S. Torroni, J. Am. Soc. Mass Spectrom. 9 (1998) 314.
[246] M.R. Asam, G.L. Glish, J. Am. Soc. Mass Spectrom. 10 (1999) 119.
[247] O. Bortolini, L. Pandolfo, C. Tomaselli, P. Traldi, Int. J. Mass Spectrom. 190/191 (1999) 171.
[248] R. Carpignano, L. Operti, R. Rabezzana, G.A. Vaglio, J. Am. Soc. Mass Spectrom. 9 (1998) 938.
[249] S. Gronert, J. Am. Soc. Mass Spectrom. 9 (1998) 845.
[250] K.G. Asano, D.E. Goeringer, D.J. Butcher, S.A. McLuckey, Int. J. Mass Spectrom. 190/191 (1999) 281.
[251] M. Vedel, J. Rocher, M. Knoop, F. Vedel, Int. J. Mass Spectrom. 190/191 (1999) 37.
[252] J. Shen, J.S. Brodbelt, Rapid Commun. Mass Spectrom. 13 (1999) 1381.
[253] G.F. Bauerle, Jr., B.J. Hall, N.V. Tran, J.S. Brodbelt, J. Am. Soc. Mass Spectrom. 7 (1996) 250.
[254] N.J. Oldham, A. Svatoš, Rapid Commun. Mass Spectrom. 13 (1999) 331.
[255] H.M. Garraffo, T.F. Spande, T.H. Jones, J.W. Daly, Rapid Commun. Mass Spectrom. 13 (1999) 1553.
[256] J.J. Isbell, J.S. Brodbelt, J. Am. Soc. Mass Spectrom. 7 (1996) 559.
[257] M.R. Asam, G.L. Glish, J. Am. Soc. Mass Spectrom. 8 (1997) 987.
[258] T.R. Croley, R. Zemribo, B.C. Lynn, Jr., Int. J. Mass Spectrom. 190/191 (1999) 265.
[259] A. Colorado, J.S. Brodbelt, J. Am. Soc. Mass Spectrom. 7 (1996) 1116.
[260] E.J. Alvarez, V.H. Vartanian, J.S. Brodbelt, J. Am. Soc. Mass Spectrom. 8 (1997) 620.
[261] R.W. Vachet, G.L. Glish, J. Am. Soc. Mass Spectrom. 7 (1996) 1194.
[262] R.W. Vachet, K.L. Ray, G.L. Glish, J. Am. Soc. Mass Spectrom. 9 (1998) 341.
[263] R.J. Strife, Rapid Commun. Mass Spectrom. 13 (1999) 759.
[264] K.J. Weissman, G.C. Kearney, P.F. Leadley, J. Staunton, Rapid Commun. Mass Spectrom. 13 (1999) 2103.
[265] R. Ramanathan, K. Cao, E. Cavalieri, M.L. Gross, J. Am. Soc. Mass Spectrom. 9 (1998) 612.
[266] M. Sharifi, J. Einhorn, Int. J. Mass Spectrom. 190/191 (1999) 253.
[267] M. Satterfield, J.S. Brodbelt, J. Am. Soc. Mass Spectrom. 10 (1999) 209.
[268] D. Zhang, L.A. Gill, R.G. Cooks, J. Am. Soc. Mass Spectrom. 9 (1998) 1146.
[269] L.S. Riter, D.F. Fraley, R.G. Cooks, J. Am. Soc. Mass Spectrom. 11 (2000) 33.
[270] S. Tajima, S. Takahashi, O. Sekiguchi, Rapid Commun. Mass Spectrom. 13 (1999) 1458.
[271] C. Baumann, M.A. Cintora, M. Eichler, E. Lifante, M. Cooke, Rapid Commun. Mass Spectrom. 14 (2000) 349.
[272] D.T. Li, J.F. Sheen, G.R. Her, J. Am. Soc. Mass Spectrom. 11 (2000) 292.
[273] M. Gucek, R.J. Vreeken, E.R. Verheij, Rapid Commun. Mass Spectrom. 13 (1999) 612.
[274] G.C. Eiden, C.J. Barinaga, D.W. Koppenaal, J. Am. Soc. Mass Spectrom. 7 (1996) 1161.
[275] S.J. Valentine, A.E. Counterman, D.E. Clemmer, J. Am. Soc. Mass Spectrom. 10 (1999) 1188.
[276] R.D. Voyksner, H. Lee, Rapid Commun. Mass Spectrom. 13 (1999) 1427.
[277] G.S. Groenewold, A.D. Appelhans, J.C. Ingram, J. Am. Soc. Mass Spectrom. 9 (1998) 35.
[278] C.R. Arkin, B. Goolsby, D.A. Laude, Int. J. Mass Spectrom. 190/191 (1999) 47.
[279] D.B. Robb, M.W. Blades, Int. J. Mass Spectrom. 190/191 (1999) 69.
[280] C.S. Creaser, J.W. Stygall, Int. J. Mass Spectrom. 190/191 (1999) 145.
[281] G. Wells, C. Huston, J. Am. Soc. Mass Spectrom. 6 (1995) 928.
[282] R.W. Vachet, S.W. McElvany, J. Am. Soc. Mass Spectrom. 10 (1999) 355.
[283] V.A. Sarurkar, A.G. Menon, Rapid Commun. Mass Spectrom. 13 (1999) 469.
[284] L.L. Lopez, P.R. Tiller, M.W. Senko, J.C. Schwartz, Rapid Commun. Mass Spectrom. 13 (1999) 663.
[285] M. Splendore, E. Marquette, J. Oppenheimer, C. Huston, G. Wells, Int. J. Mass Spectrom. 190/191 (1999) 129.
[286] B.I. Coopersmith, R.A. Yost, J. Am. Soc. Mass Spectrom. 6 (1995) 976.
[287] T.L. Williams, J.L. Stephenson, Jr., R.A. Yost, J. Am. Soc. Mass Spectrom. 8 (1997) 532.
[288] G.-Z. Li, S. Guan, A.G. Marshall, J. Am. Soc. Mass Spectrom. 9 (1998) 473.
[289] Q. Ji, M.R. Davenport, C.G. Enke, J.F. Holland, J. Am. Soc. Mass Spectrom. 7 (1996) 1002.
[290] M. Aliman, A. Glasmachers, J. Am. Soc. Mass Spectrom. 10 (1999) 1000.
[291] Z. Ouyang, E.R. Badman, R.G. Cooks, Rapid Commun. Mass Spectrom. 13 (1999) 2444.
[292] V.S. Gurov, M.V. Dubkov, O.V. Korneeva, Rapid Commun. Mass Spectrom. 14 (2000) 454.
[293] Y. Zerega, P. Perrier, M. Carette, G. Brincourt, T. Nguema, J. André, Int. J. Mass Spectrom. 190/191 (1999) 59.
[294] É.P. Sheretov, O.W. Rozhkov, D.M. Kiryushin, A.E. Malutin, Int. J. Mass Spectrom. 190/191 (1999) 103.

[295] É.P. Sheretov, T.B. Karnav, A.V. Brykov, Int. J. Mass Spectrom. 190/191 (1999) 113.

[296] D.B. Robb, M.W. Blades, Rapid Commun. Mass Spectrom. 13 (1999) 1079.

[297] U.P. Schlunegger, M. Stoekli, R.M. Caprioli, Rapid Commun. Mass Spectrom. 13 (1999) 1792.

[298] G.J. Dear, J. Ayrton, R. Plumb, I.J. Fraser, Rapid Commun. Mass Spectrom. 13 (1999) 456.

[299] R.S. Plumb, J. Ayrton, G.J. Dear, B.C. Sweatman, I.M. Ismail, Rapid Commun. Mass Spectrom. 13 (1999) 845.

[300] G.J. Dear, R.S. Plumb, B.C. Sweatman, I.M. Ismail, J. Ayrton, Rapid Commun. Mass Spectrom. 13 (1999) 886.

[301] G. Bartolucci, G. Pieraccini, F. Villanelli, G. Moneti, A. Triolo, Rapid Commun. Mass Spectrom. 14 (2000) 967.

[302] J.-C. Wolff, S. Monté, N. Haskins, D. Bell, Rapid Commun. Mass Spectrom. 13 (1999) 1979.

[303] C. Govaerts, H.K. Chepkwony, A. Van Schepdael, E. Roets, J. Hoogmartens, Rapid Commun. Mass Spectrom. 14 (2000) 878.

[304] C.-C. Lai, P.-L. Tsai, C. Yu, G.-R. Her, Rapid Commun. Mass Spectrom. 14 (2000) 468.

[305] V.H. Vartanian, B. Goolsby, J.S. Brodbelt, J. Am. Soc. Mass Spectrom. 10 (1999) 1089.

[306] M.H. Choi, B.C. Chung, W. Lee, U.C. Lee, Y. Kim, Rapid Commun. Mass Spectrom. 13 (1999) 376.

[307] P.A. Wabnitz, J.H. Bowie, J.C. Wallace, M.J. Tyler, Rapid Commun. Mass Spectrom. 13 (1999) 1724.

[308] P.A. Wabnitz, J.H. Bowie, J.C. Wallace, M.J. Tyler, Rapid Commun. Mass Spectrom. 13 (1999) 2498.

[309] Y. Wang, M. Schubert, A. Ingendoh, J. Franzen, Rapid Commun. Mass Spectrom. 14 (2000) 12.

[310] S.M. Maleknia, M.R. Chance, K.M. Downard, Rapid Commun. Mass Spectrom. 13 (1999) 2352.

[311] M. Adamczyk, J.C. Gebler, J. Wu, Rapid Commun. Mass Spectrom. 13 (1999) 1813.

[312] R.K. Julian, M. Nappi, C. Weil, R.G. Cooks, J. Am. Soc. Mass Spectrom. 6 (1995) 56.

[313] K. Yoshinari, Rapid Commun. Mass Spectrom. 14 (2000) 215.

[314] M.W. Forbes, M. Sharifi, T.R. Croley, Z. Lausevic, R.E. March, J. Mass Spectrom. 34 (1999) 1219.

[315] R.E. March, Org. Mass Spectrom. 26 (1991) 627.

[316] M. Nappi, C. Weil, C.D. Cleven, L.A. Horn, H. Wollnik, R.G. Cooks, Int. J. Mass Spectrom. Ion Processes 161 (1997) 77.