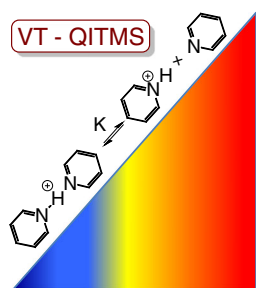


RESEARCH ARTICLE

Development and Evaluation of a Variable-Temperature Quadrupole Ion Trap Mass Spectrometer

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Abstract. A new, variable-temperature mass spectrometer system is described. By applying polyimide heating tape to the end-cap electrodes of a Bruker (Bremen, Germany) Esquire ion trap, it is possible to vary the effective temperature of the system between 40 and 100°C. The modification does not impact the operation of the ion trap and the heater can be used for extended periods without degradation of the system. The accuracy of the ion trap temperatures was assessed by examining two gas-phase equilibrium processes with known thermochemistry. In each case, the variable-temperature ion trap provided data that were in good accord with literature data, indicating the effective temperature in the ion trap environment was being successfully modulated by the changes in the set-point temperatures on the end-cap electrodes. The new design offers a convenient and effective way to convert commercial ion trap mass spectrometers into variable-temperature instruments.

Keywords: Ion trap, Variable temperature

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Introduction

Early modeling of ion trap mass spectrometers indicated that ions would equilibrate to temperatures near that of the buffer gas and would not be substantially heated by the trapping potential [1–5]. In 1998, we provided experimental evidence that supported that conclusion and reported an effective temperature of 310 ± 20 K under ambient conditions [6]. This also suggested that the temperature of the ion trap environment could be manipulated by heating/cooling the ion trap. Expected residence times and collision rates also indicated that this is a viable approach. [With typical reagent pressures, the ions will collide with helium roughly 1000 times for every collision with a neutral reagent. Given its mean velocity and trap design, a helium atom will collide with the walls on the order of once every 10 μ s and have a residence time in the trap on the order of 10 ms. Evidence that this is sufficient comes from Glish who has shown that collisional cooling rates in the ion trap are in excess of 100 s⁻¹ at normal helium pressures (pseudo first order

reaction rates are generally in the 1 s⁻¹ range in our system)] [7]. Most importantly, Glish and co-workers have used innovative designs and demonstrated that heating or cooling the ion trap electrodes leads to ions whose behavior is consistent with altered internal energies [8–11]. For our development of a variable-temperature mass spectrometer, we have turned to a different design than the Glish systems. We have opted to directly heat the end-cap electrodes of a Bruker Esquire 3000 Plus quadrupole ion trap and have developed a system that operates over a 60°C range (~40–100°C) with reproducible control of the heating of the ion trap environment.

Design and Methods

In the Bruker Esquire, the ring electrode is suspended between the end-cap electrodes by a pair of electrical insulators. We found that materials applied to the outer surface of the ring electrode interfered with the proper function of the Bruker ion trap, so we focused on the end-cap electrodes. We decided that heating only the end-cap electrodes would be sufficient given that all of the ring electrode's physical contacts, aside from its electrical feed-through, are sunk to the end-caps. This simplifies the design of a heating system and avoids contact with the ring electrode. The working hypothesis is that in the low-

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pressure environment of the vacuum manifold, the temperature gradients would be modest in the ion trap. In our design, we applied polyimide-coated heating elements to the end-cap electrodes of the Bruker ion trap (Figure 1). The heating elements are flexible and the polyimide provides high thermal conductance. The two heating elements are Minco (Minneapolis, MN, USA) HK5205 R40.7L 12A units. Several options were explored for attaching the heating element to the electrodes. In attaching the heating elements, degassing and degradation of plastic and other polymeric materials proved problematic at elevated temperatures. In the final design, the heating elements were secured to the end-caps by multiple layers of high-grade Teflon and clamped with a stainless steel cable tie (entrance end-cap) or a stainless steel worm-drive clamp (detection end-cap). A stainless steel tee was added to the vacuum manifold port normally bearing the instrument's ion gauge. The tee allowed for electrical feed-throughs and a feed-through for the helium buffer gas restriction capillary (Figure 1).

To monitor the temperature of the end-caps, a Minco RTD temperature sensor (S17624PDZT40A) was applied to each end-cap (isolated from heating elements). The end-caps are heated separately using independent temperature controllers, which cycle the electrode heating to maintain the same set-point temperature on each end-cap. All the components in the design are rated to at least 200°C and the combined heating elements provide up to 14 W of power. The temperature at the end caps can be shifted 10°C in a matter of minutes, but in these studies, the system was allowed sufficient time to thermally equilibrate. The system readily maintains temperatures between 40 and 100°C without degradation of instrument performance or unacceptable chemical noise from background gases. It has been run continuously for over 24 months.

The modifications needed for doing gas-phase ion/molecule reactions in the ion trap are very similar to those that we have previously developed for Thermo LCQ and DECA ion traps [12]. In short, liquid reagents are introduced via a syringe pump into a flow of helium. A small portion of the reagent/helium mixture is metered into the ion trap via a restriction capillary (through the added tee on the vacuum manifold). The flow of helium in the mixing manifold is maintained by a mass flow controller and the pressure in the manifold is measured by an absolute pressure barometer (the helium pressure is varied via a needle valve at the exhaust port of the mixing manifold). The pressure and flow in

the mixing manifold are manipulated to maintain the vacuum manifold pressure advised by Bruker. Reagent pressures in the ion trap are calculated from the estimated helium pressure in the trap, the mixing ratio of the neutral reagent to helium in the mixing manifold, and a theoretical correction for differential effusion from the ion trap. The estimated helium pressure in the ion trap is routinely calibrated by examining reaction systems that have known rate constants at ambient temperature [13]. The absolute rate constants and equilibrium constants have estimated uncertainties of approximately $\pm 30\%$, but relative measurements should be considerably more accurate ($\pm 10\%$).

For the present work, multiple approaches were used to analyze the data and calculate equilibrium constants. The differences involved how ion discrimination was assessed and how the intensities were extrapolated to infinite reaction time. Variation in instrument sensitivity (ion discrimination) is a critical issue because the data suggest that it is temperature-dependent (described in the section *Temperature-Dependent Ion Discrimination*). In the reactions in this study, a single product is formed so it was assumed that any change in the total spectrum intensity as the system approached equilibrium was due to ion discrimination. The dimensionless equilibrium constant (i.e., product/reactant ion) was determined by fitting the observed reactant ion intensity to the functional form of a first-order system reaching equilibrium (the neutral reagent to ion ratio is at least 10^5 so first-order behavior is expected). We prefer this approach because it averages out experimental variations in the measured intensity at the various time points and can correct for conditions where equilibrium might not be fully attained in the timeframes used in the experiments. The reported equilibrium constant incorporates the calculated neutral reagent pressure and the inferred ion discrimination factor.

Reaction Systems

To evaluate the ability of the modified ion trap to characterize chemical reactivity as a function of temperature, we have turned to reaction systems that have been previously examined in the gas phase using instruments with variable-temperature capabilities, specifically high-pressure mass spectrometers. As we had noted in earlier work on ion trap temperatures [6], adduct-forming processes are ideal because the large magnitude of the enthalpic change (balanced by a large entropic change) leads to a high level



Figure 1. Modified Bruker Esquire ion trap: (a) ion trap with attached heating elements on end caps, (b) vacuum manifold, and (c) tee used for electrical and helium feed-throughs

of temperature dependence in the equilibrium constant. However, our system has a relatively limited range of neutral reagent pressures ($\sim 10^5$ – 10^8 torr), so we are only able to characterize adduct-forming reactions with free energy changes of about -13 ± 3 kcal/mol. Additionally, our system is constrained by the method of reactant ion formation (electrospray ionization) and the volatility of the neutral reagent (boiling point below about 200°C to provide the needed partial pressure in the manifold). Finally, it would be valuable to have validation systems that have been analyzed independently in the past by more than one research group. These criteria greatly limit the pool of potential reaction systems. The optimum choice is the reaction of the pyridinium cation with pyridine (Figure 2). It has been studied several times in variable-temperature instruments and has a free energy of reaction near the center of our useful range [14–17]. To augment the data from this system, we have also examined the reaction of 2-methylpyridinium with 2-methylpyridine (Figure 2). Here we rely on previous data from only one source [15], but it is ideal by other criteria.

Results and Discussion

Equilibrium Measurements

Sample plots of the raw intensities for the pyridinium cation and the pyridinium/pyridine adduct at two temperatures are shown in Figure 3. In each of these cases, the pyridinium ion was isolated initially in the ion trap via a MS^n scan function and allowed to reach equilibrium with the adduct, but the data used for the thermochemical analyses below included runs where the adduct instead was initially isolated by an MS^n scan function. The impact of the temperature change is evident and, as expected, a multi-fold shift in the ratio of equilibrium intensities is observed. In the plot for 40°C , mass discrimination is very evident in the much lower final intensity for the adduct compared with the initial pyridinium intensity. The magnitude of the ion discrimination is unusual for the ion trap and undoubtedly related to the fragile nature of the adduct and the potential for it to be lost during the mass spectrum scan function [12, 18, 19].

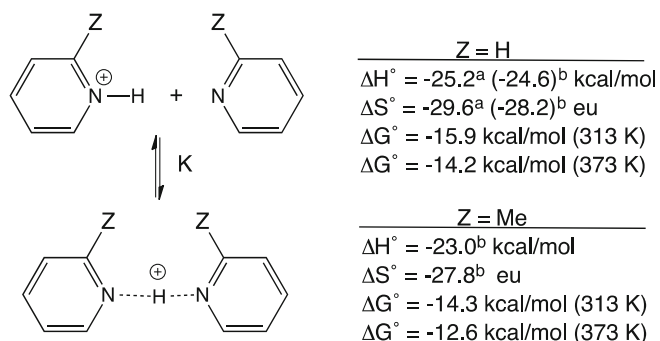


Figure 2. Reaction systems. Data taken from (a) reference 14 and (b) reference 15. For pyridine (Z = H), enthalpy/entropy values of -23.7 – -28.0 [16] and -26.3 – -32.1 [17] have also been reported

Enthalpy/Entropy Measurements

To test the accuracy of the apparent ion trap temperatures, as measured by the sensors at the end-cap electrodes, we have generated data for van't Hoff plots in the general temperature range from 40 to 100°C for both of the reactions outlined in Figure 2. The van't Hoff plots for both systems are presented in Figure 4. The plots show very good linearity over the temperature range. This is particularly true for pyridine. This system was most suitable for the available temperature range, and we collected considerably more useable data for it. The slight curvatures in the plots are likely from random errors, particularly because the perceived curvature in one case is concave down (pyridine) and in the other (2-methylpyridine), it is concave up. For pyridine, the derived enthalpies correspond well with the literature data. The enthalpy is -25.5 ± 0.6 kcal/mol versus the value of -25.2 ± 1.0 kcal/mol from Mautner's 1992 study [14]. Pyridine was also included in Mautner and Sieck's 1983 study [15] and their earlier reported enthalpy was -24.6 ± 1.0 kcal/mol, which is 0.9 kcal/mol away from our ion trap value. As a final comparison, our measured enthalpy for pyridine is also consistent with Holland and Castleman's value of -26.3 ± 0.2 kcal/mol [17]. The good consistency with literature values indicates that the variable-temperature ion trap is providing an environment with suitably accurate temperature control. Focusing on the data from Mautner, the slightly higher enthalpy measurements might be related to the difference in the temperature ranges of the instruments: 313 – 373 K for the ion trap and ~ 400 – 500 K for the high-pressure mass spectrometer. The vibrational properties of the proton-bound dimer are very different than those of the rigid reactants. With the adduct having more accessible degrees of freedom and a higher heat capacity than the combined reactants, the enthalpy of reaction is expected to show some temperature dependence. A simple analysis using enthalpy contributions computed at the M06/6-31+G* level for the pyridine system suggests a 0.6 kcal/mol drop in the magnitude of the enthalpy change in going from 313 K to 500 K. Modeling of the curvature resulting from this effect indicates that it would be very subtle and could easily be hidden by the uncertainties of the equilibrium measurements.

Comparing the measured entropy changes for the pyridine reaction, we see that the ion trap gives values that are 4 – 5 eu higher than those reported previously by Mautner [14, 15]. The difference is smaller (1.8 eu) when comparing to Holland and Castleman's value for pyridine [17]. Unlike the enthalpy measurements, the entropy values are directly linked to the absolute equilibrium constant measurements and, therefore, subject to systematic errors related to the accuracy of the neutral reagent pressure determination and the mass discrimination correction of the instrument. As a result, higher errors are likely in the entropy change measurement. However, the 4 – 5 cal/mol/K difference is at the edge of the combined uncertainties of the current and previous experiments. As with the enthalpy, it is predicted that the entropy will also have temperature dependence in these reactions. Using the same computational approach to estimate this effect, the magnitude of the entropy change drops by 1.5 cal/mol/K in going from 313 to 500 K for

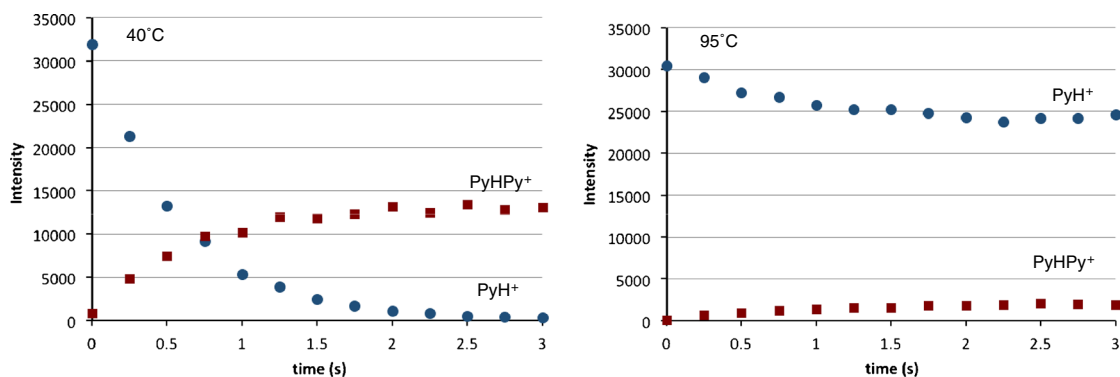


Figure 3. Plots of signal intensity versus time for the equilibrium between pyridinium (PyH^+ , blue) and its adduct with pyridine (PyHPy^+ , red). The left panel is 40°C and the right is 95°C

the pyridine system. Although this does not explain the entire discrepancy with Mautner's data, it brings the results well within the expected experimental uncertainties and again suggests that the variable-temperature ion trap is capable of producing reasonably accurate thermochemical data. [We modeled the effect of temperature inaccuracy on the derived entropy values. To force the data to give Mautner's entropy and enthalpy values, the effective ion temperature would need to be higher than the measured temperature at the end-cap, and this gap would have to increase with temperature (by about 6° across the range). This is counterintuitive in that one would expect the efficiency of heating to drop rather than increase with higher set points. The uncertainties in the previous experimental work also make it impossible to back-calculate effective temperatures from the current equilibrium measurements. Absolute uncertainties in excess of ± 30 K result from this approach. By attempting to reproduce previous thermochemical measurements, one gains a better measure of the system's capabilities relative to established approaches.]

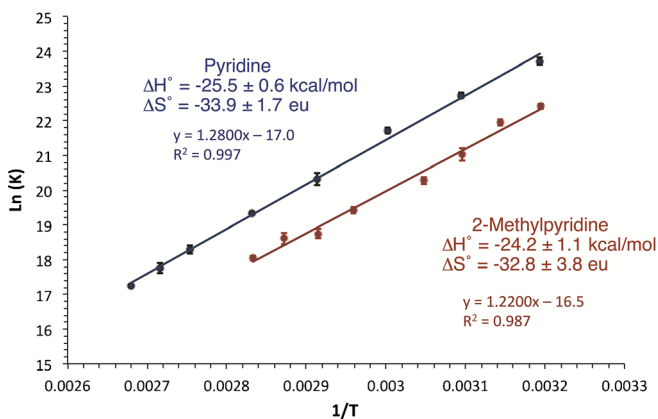


Figure 4. Van't Hoff plots for proton-bound dimer formation for pyridine and 2-methylpyridine. Uncertainties in $\ln(K)$ values are derived from standard deviations in repeated measurements. Uncertainties in enthalpy and entropy include contributions from the plots as well as an estimate of the potential systematic error in the neutral reagent number density measurement ($\pm 30\%$). Temperature in K

With 2-methylpyridinium, data are only shown up to 80°C because the adduct is more weakly bound and data quality deteriorated at the higher temperatures where little adduct was present. In this system, the ion trap value is -24.2 ± 1.1 kcal/mol compared with -23.0 ± 1.0 kcal/mol from Mautner and Sieck's 1983 study [15]. The gap here is 1.2 kcal/mol, but that is well within the combined uncertainties of the experiments. It should be noted that Mautner and Sieck's 1983 [15] enthalpy value for the pyridine system is also lower in magnitude than the ion trap value (by 1.1 kcal/mol). Therefore, when using the same data set for comparison (i.e., Mautner's 1983 paper), we find that the measured enthalpies for both reactions are about 1 kcal/mol higher in magnitude in our system. As in the pyridine system, the ion trap value for the entropy change is about 5 eu higher, but still within the reported uncertainties of the experiments.

Temperature-Dependent Ion Discrimination

In the course of these studies, it was obvious that the instrument was less sensitive in determining the ion concentration of the proton-bound dimer relative to the protonated precursor. When starting with the protonated precursor, the total ion count dropped sharply as equilibrium was reached (see Figure 2, 40°C). Although this may partially be a mass discrimination effect, it is also related to the stability of the proton-bound dimer. With ion traps, it is well known that fragile ions (e.g., noncovalent complexes) can dissociate during the mass scan function and not be detected at the appropriate m/z value [12, 18, 19]. What is novel in this system is that the ion discrimination is temperature-dependent. This is illustrated in Figure 5. The sensitivity ratio is calculated as the absolute value of the change in the protonated precursor signal intensity divided by the change in the protonated dimer signal intensity as the reaction moves to equilibrium ($|(I_{\text{eq}}^{\text{PyH}^+} - I_0^{\text{PyH}^+}) / (I_{\text{eq}}^{\text{PyHPy}^+} - I_0^{\text{PyHPy}^+})|$). There is considerable scatter in the data because in some cases the ratios involve relatively small changes in intensity. The key points though are that the ion discrimination is large (2- to 4.5-fold) and can increase by up to 50% across our

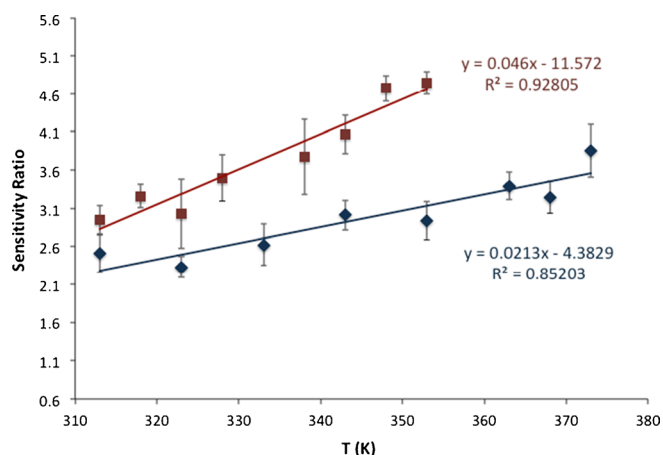


Figure 5. Plots of instrument sensitivity ratio versus temperature (the blue data are for pyridine and the red data are for 2-methylpyridine). The sensitivity ratio is calculated as the absolute value of the change in the protonated precursor signal intensity divided by the change in the protonated dimer signal intensity as the reaction moves to equilibrium ($|(I_{\text{eq}}^{\text{PyH}^+} - I_0^{\text{PyH}^+}) / (I_{\text{eq}}^{\text{PyHPy}^+} - I_0^{\text{PyHPy}^+})|$). Uncertainties are based on the standard deviations of repeated measurements

accessible temperature range. Correction for ion discrimination is critical; without doing so, the magnitude of the observed enthalpy change would increase by up to 2 kcal/mol (8 cal/mol/K in entropy). As a result, one must carefully account for ion discrimination when carrying out studies with fragile species in ion traps.

Conclusion

By applying polyimide-coated heating elements to the end-cap electrodes of a Bruker Esquire ion trap system, it is possible to use the instrument as a variable-temperature mass spectrometer. The present configuration is able to operate with set-point temperatures between 40 and 100°C without degradation of its performance as a mass spectrometer. Two systems with known thermochemistry were used to evaluate the effective temperature measurement in the ion trap. In both adduct-forming reactions, the temperature-dependent variations in the equilibrium constants were consistent with previous data and indicate that the system is providing a reaction environment acceptably close to the set-point temperature of the end-cap electrodes. The new design will allow researchers a straightforward way of converting existing instrumentation into variable-temperature mass spectrometers.

Acknowledgments

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References

- Goeringer, D.E., Mcluckey, S.A.: Evolution of ion internal energy during collisional excitation in the Paul ion trap: a stochastic approach. *J. Chem. Phys.* **104**, 2214–2221 (1996)
- Hart, K.J., Mcluckey, S.A.: Relative dissociation-energy measurements using ion-trap collisional activation. *J. Am. Soc. Mass Spectrom.* **5**, 250–259 (1994)
- Lunney, M.D.N., Buchinger, F., Moore, R.B.: The temperature of buffer-gas cooled ions in a Paul trap. *J. Mod. Opt.* **39**, 349–360 (1992)
- Goeringer, D.E., Asano, K.G., Mcluckey, S.A.: Ion internal temperature and ion trap collisional activation: protonated leucine enkephalin. *Int. J. Mass Spectrom.* **182**, 275–288 (1999)
- Goeringer, D.E., Mcluckey, S.A.: Relaxation of internally excited high-mass ions simulated under typical quadrupole ion trap storage conditions. *Int. J. Mass Spectrom.* **177**, 163–174 (1998)
- Gronert, S.: Estimation of effective ion temperatures in a quadrupole ion trap. *J. Am. Soc. Mass Spectrom.* **9**, 845–848 (1998)
- Black, D.M., Payne, A.H., Glish, G.L.: Determination of cooling rates in a quadrupole ion trap. *J. Am. Soc. Mass Spectrom.* **17**, 932–938 (2006)
- Jue, A.L., Racine, A.H., Glish, G.L.: The effect of ion trap temperature on the dissociation of peptide ions in a quadrupole ion trap. *Int. J. Mass Spectrom.* **301**, 74–83 (2011)
- Payne, A.H., Glish, G.L.: Thermally assisted infrared multiphoton photodissociation in a quadrupole ion trap. *Anal. Chem.* **73**, 3542–3548 (2001)
- Racine, A.H., Payne, A.H., Remes, P.M., Glish, G.L.: Thermally assisted collision-induced dissociation in a quadrupole ion trap mass spectrometer. *Anal. Chem.* **78**, 4609–4614 (2006)
- Remes, P.A., Glish, G.L.: Collisional cooling in a quadrupole ion trap at sub-ambient temperatures. *Int. J. Mass Spectrom.* **265**, 176–181 (2007)
- Gronert, S.: Quadrupole ion trap studies of fundamental organic reactions. *Mass Spectrom. Rev.* **24**, 100–120 (2005)
- Gronert, S., Depuy, C.H., Bierbaum, V.M.: Deuterium-isotope effects in gas-phase reactions of alkyl-halides—distinguishing E2 and Sn2 pathways. *J. Am. Chem. Soc.* **113**, 4009–4010 (1991)
- Meotner, M.: Intermolecular forces in organic clusters. *J. Am. Chem. Soc.* **114**, 3312–3322 (1992)
- Meotner, M., Sieck, L.: The ionic hydrogen-bond. 1. Sterically hindered bonds—solvation and clustering of protonated amines and pyridines. *J. Am. Chem. Soc.* **105**, 2956–2961 (1983)
- Meotner, M.: Ion thermochemistry of low-volatility compounds in the gas-phase. 2. Intrinsic basicities and hydrogen-bonded dimers of nitrogen heterocyclics and nucleic bases. *J. Am. Chem. Soc.* **101**, 2396–2403 (1979)
- Holland, P.M., Castleman, A.W.: The thermochemical properties of gas-phase transition-metal ion complexes. *J. Chem. Phys.* **76**, 4195–4205 (1982)
- Vachet, R.W., Hartman, J.R., Gertner, J.W., Callahan, J.H.: Investigation of metal complex coordination structure using collision-induced dissociation and ion-molecule reactions in a quadrupole ion trap mass spectrometer. *Int. J. Mass Spectrom.* **204**, 101–112 (2001)
- Cleven, C.D., Cooks, R.G., Garrett, A.W., Nogar, N.S., Hemberger, P.H.: Radial distributions and ejection times of molecular ions in an ion trap mass spectrometer: a laser tomography study of effects of ion density and molecular type. *J. Phys. Chem.* **100**, 40–46 (1996)