A theory for two-dimensional Fourier-transform ion cyclotron resonance mass spectrometry

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A theoretical model, based on the Lorentz equations for ion motion and the mass action law, is developed for two-dimensional Fourier-transform mass spectrometry known as 2D FT–ICR or 2D FTMS. The theory illustrates that the modulation of 2D FT–ICR ion signals in the additional time dimension comes from the modulation of the primary ion speed by the 2D excitation pulses. The modulation of the primary ion speed is found not to be sinusoidal and the modulation of the ion signals in 2D FT–ICR spectra is found to be complicated even in the simplest chemical system. The complex modulation creates higher harmonic components in the spectra. Based on the model, a data processing algorithm is proposed. The results show that the Fourier transformation should be performed stepwise in order to obtain complete information, and that the phase portion of the frequency domain generated by the second Fourier transformation should not be discarded since it contains useful information.

I. INTRODUCTION

Fourier-transform ion cyclotron resonance (FT–ICR) mass spectrometry is becoming a very useful tool in analytical chemistry.[1] Although many researchers cite the high resolution and wide mass range as basic advantages of the technique,[2] the capability for study of ion–molecule reactions and for determination of ion structures also plays an important role in its applications.[3]

The current understanding of ion–molecule reactions and ion structures should be partly credited to the introduction of tandem mass spectrometry.[4] One of the most attractive characteristics of FT–ICR is that one can perform tandem mass spectrometry experiments in a single trapped-ion cell.[5] Conventional mass spectrometry techniques require spatially distinct regions for the ion separations. In a FT–ICR experiment on the other hand, ions are formed by a variety of methods and the ions of interest can be isolated by ejection of the other ions. The speed of the isolated ion(s) can then be increased through acceleration with an excitation pulse(s). The accelerated ions collide with neutrals in the ICR cell to produce products which can be detected later by the usual excite–detect pulse sequence. The Fourier transform of the time-domain signal gives a frequency domain result that contains the mass-to-charge ratio information on the ions.

Although the experimental procedures stated above are suitable for the study of any type of ion–molecule reaction, they are most widely used in collision-induced dissociation (CID) experiments.[6] In a CID experiment, the collision of ions with collision gas atoms or molecules produces daughter ion fragments which carry structural information about the parent ions. Moreover, the structure of the parent ions may be deduced by analysis of the daughter fragmentation patterns. These tandem mass-spectrometry (MS) techniques with CID can be used to study ion–molecule reactions or to determine ion structures that involve a small number of ionic species. However, when a chemical compound becomes complicated or when a mixture is to be analyzed, the experimental procedures quickly become very complex and time consuming.

The technique of two-dimensional (2D) FT–ICR mass spectrometry was first introduced by Pfändler *et al.*[7] The techniques of 2D FT–ICR are very new. While its underlying principles have not been fully understood, it has great potential in that, in theory, it allows one to examine *all* the ion–molecule reactions in a system in one experiment. Future development of the method requires a breakthrough on theoretical as well as experimental aspects.

In this paper, we offer a comprehensive model based on the motion of ion packets and on the mass action law to interpret the modulation in the additional time dimension shown as t_1 in Fig. 1. The discussion does not attempt to include all the possible processes in 2D FT–ICR operations, but instead focuses on the modulation information transfer from the phase relations of the 2D FT–ICR excitation to the detected ion signals. The mass spectral characteristics are discussed and a data processing algorithm is proposed based on the model.

II. 2D FT–ICR EXPERIMENTAL PROCEDURES

The pulse sequence (Fig. 1) of a 2D FT–ICR chemical cycle is realized by inserting a pair of excitation pulses

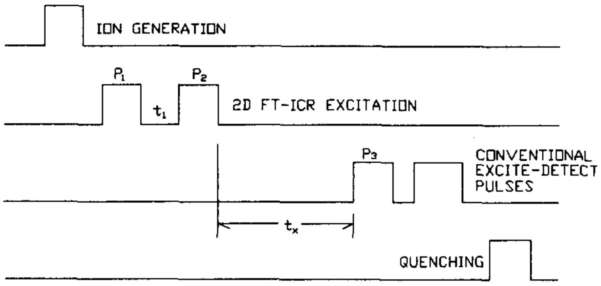

FIG. 1. The pulse sequence of 2D FT–ICR experiments differ from conventional 1D FT–ICR by the addition of pulses P_1 and P_2 with the evolution time t_1.

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(P_1, P_2) with a time delay t_1 between P_1 and P_2 after the ion-generation event but before the ion-reaction period. The time delay, t_1, the evolution time, provides another time dimension for the 2D FT–ICR spectrum. For a certain t_1, the basic excite–detect pulses generate a time-domain transient signal which can be Fourier transformed to give the frequency-domain mass spectrum which is assigned as ω_2, the ordinary FT–ICR frequency dimension. The magnitude spectrum measures the numbers of ions present in the ICR cell at the detection time. The phase portion of the frequency domain, which arises in response to the excitation pulse (P_3) does not usually give useful chemical information in 1D FT–ICR, and therefore is discarded. In 2D FT–ICR the evolution time t_1 can be incremented systematically and a series of time-domain transient signals in the detection time variable t_2 can be obtained. These time-domain ion transient signals are subject to Fourier transformation in dimension t_2 to give a series of spectra. We denote the series spectra as a function of both t_1 and ω_2, $S(t_1, \omega_2)$. The information in $S(t_1, \omega_2)$ can be Fourier transformed in the time dimension t_1 to give the two dimensional magnitude spectrum $S(\omega_1, \omega_2)$ and phase function $P(\omega_1, \omega_2)$.

III. MODULATION OF THE SPEED OF PRIMARY IONS

Since the spectra in the frequency dimension ω_2 are the very familiar 1D FT–ICR spectra, this discussion concentrates on the interpretation of the dimension t_1. To understand the physical significance of t_1, the simplest chemical system is used as shown in the following reaction:

$$A^+ + N \rightarrow B^+ + P. \tag{1}$$

Here A^+ represents the primary ion(s) present in the ICR cell before the reaction time starts. N represents the neutral molecules, and B^+ represents the ion(s) produced by the reaction (1) during the reaction time period, t_x.

In order to simplify the model, the following assumptions are made regarding the physical conditions of the experiment: (a) the combination of the pair of excitation pulses does not cause ion ejection; (b) any t_1 is less than the 2D excitation pulse length. The first assumption implies that a single 2D excitation pulse can only excite A^+ to an orbital with a diameter less than half of the cell dimension. The second condition assures that, during the short evolution time, the phase diffusion of the excited-ion packet is minimized and can be ignored in the model.

Figure 2 summarizes the model. Before the 2D excitation, the primary ions A^+ are trapped in the center of the ICR cell. The ions have a thermal velocity distribution (about 0.03 eV of kinetic energy). The first 2D excitation pulse (P_1) brings the ion packet into an orbital with increased kinetic energy (which may be 10 eV or more). The ions move coherently in the orbital during the evolution time period (t_1). The second excitation pulse further excites the ion packet into a higher-energy orbital or deexcites it into a lower orbital depending on the phase relationship of the two pulses at the cyclotron frequency of A^+. The modulation can be expressed as (see the Appendix):

$$V_A = V_{A0}\{2[1 + \cos(\omega_A t_1)]\}^{1/2}. \tag{2}$$

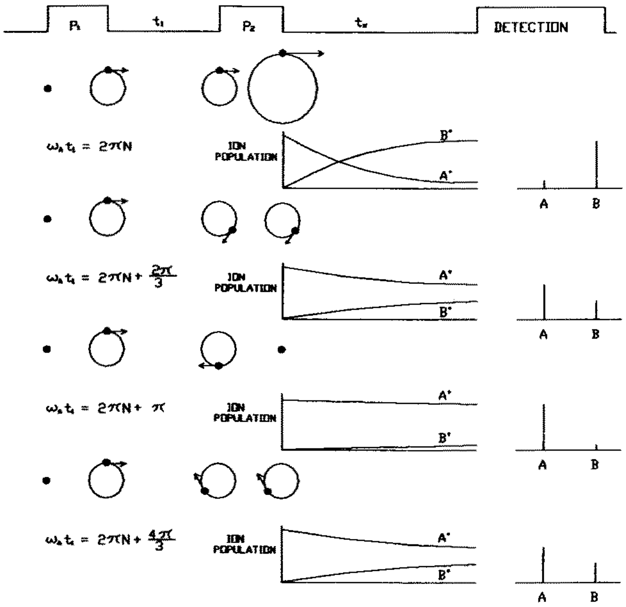


FIG. 2. The graphic representation of a simple theory for 2D FT–ICR shows that the product $\omega_A t_1$ controls the modulation of the speed of ion A^+. The ion reaction period t_x gives changes in the relative ion populations, and the signal detected at the end of t_x is transformed to give the mass spectrum showing relative intensities of A^+ and B^+.

Here V_A is the ion packet speed at the end of the excitation pulse P_2, V_{A0} is the speed of the ion packet A^+ at the end of the excitation pulse P 1. When the phase is equal to $2\pi n$ (with $n = 0,1,2,...$) or $\omega_A t_1 = 2\pi n$, the ion packet is excited into the highest orbital and $V_A = 2V_{A0}$. When the phase is equal to $\pi(2n+1)$ or $\omega_A t_1 = \pi(2n+1)$, the ion packet is deexcited back to its initial thermal state. Figure 2 contains further information on other cases. The result is that the speed of the primary ion packet is, therefore, modulated with the frequency ω_A.

IV. MODULATION OF ION SIGNALS

The population of ions A^+ at the end of the excitation pulses, P_1 and P_2, does not depend on t_1 since no ions are ejected and no significant reaction occurs. During the reaction period (t_x), the ions A^+ collide with neutrals in the ICR cell and are converted into B^+ ions. For clarity, we also assume that there is no ion loss in the reaction period, that all the ions can be detected by the final excite–detect pulse sequence, and that the reaction is endoergic (for example, that the product ions arise from primary ion dissociation as in a collision-induced dissociation experiment). During reaction under these conditions, the population of A^+ decreases and the population of B^+ increases. If the ion packet of A^+ is excited into a higher orbital, the ions A^+ will possess higher speed and will have a higher collision energy with the neutrals. Reaction (1) is then accelerated and an increase of the product ion abundance occurs as shown in the first case in Fig. 2. The second and fourth cases show no net increase in product formation after the second pulse. The pattern is illustrated in Fig. 2. Thus, the modulation of the speed of the primary ions A^+ at the beginning of the reaction period results in the modulation of populations of both the A^+ and B^+ ions. From this qualitative analysis, two conclusions can be drawn. First, the populations of both the primary ions (A^+) and the product ions (B^+) are modulated with the cyclotron frequency (ω_A) of the primary ions. The modulation of the ions A^+ results in a peak at (ω_A,ω_A) on the diagonal in the two-dimensional magnitude spectrum $S(\omega_1, \omega_2)$, and the modulation on the product ions results in an off-diagonal peak at (ω_B,ω_A) in $S(\omega_1, \omega_2)$ which provides evidence of the reaction (1). Second, the modulation of the primary ions and the modulation of the product ions are in opposite phases.

The speed modulation by the pair of excitation pulses P_1 and P_2 is not sinusoidal: a more complex modulation of the ion signals is expected from the model. For simplicity, we presume that the speed of A^+ does not change in the reaction period until the ions collide with neutrals to produce B^+, and also that the reaction cross section can be expressed as follows:

$$\sigma(E) = \begin{cases} 0, & E \leqslant E_{\text{threshold}} \\ \sigma_0, & E > E_{\text{threshold}}. \end{cases} \tag{3}$$

The assumption of the reaction cross section agrees with the rigid-sphere kinetic model with a threshold energy ($E_{\text{threshold}}$). Reaction (1) is a pseudo-first-order reaction for a constant pressure of neutrals, and the rate equation can be expressed as

$$-d[A^+]/dt = k[A^+][N], \quad k = V_{AN}\sigma(E). \tag{4}$$

Here V_{AN} is the relative speed of A^+ and N. It is approximately equal to the speed of A^+ in the laboratory frame. $\sigma(E)$ is the reaction cross section.

The solution of (4) is

$$[A^+] = [A^+]_0 e^{-kt_x[N]}, \tag{5}$$

where $[A^+]_0$ is the initial ion population of A^+ and t_x is the reaction time. Substituting (2) in the above equation gives

$$[A^+] = \begin{cases} [A^+]_0 \exp^{\{-c[1+\cos(\omega_A t_1)]^{1/2}\}}, & t_1|_{E > E_{\text{threshold}}} \\ [A^+]_0, & t_1|_{E \leqslant E_{\text{threshold}}} \end{cases} \tag{6}$$

and $c = (2)^{1/2} t_x \sigma_0 V_{A0}[N]$. The energy is given by $E = (1/2) m_A V^2 = m_A V_0^2 [1 + \cos(\omega_A t_1]$. By conservation of total ion numbers, we also have

$$[B^+] = \begin{cases} [A^+]_0 (1 - \exp^{\{-c[1+\cos(\omega_A t_1)]^{1/2}\}}, & t_1|_{E > E_{\text{threshold}}} \\ 0, & t_1|_{E \leqslant E_{\text{threshold}}} \end{cases}. \tag{7}$$

Since the modulation of the ion populations are not sinusoidal as seen in Eqs. (6) and (7), higher harmonic components in the spectra exist. The value of parameter c and the value of the threshold energy ($E_{\text{threshold}}$) in Eqs. (6) and (7) have an influence on the structure of the spectra obtained from the use of the additional dimension (t_1 or ω_1). Figure 3 shows three plots of function (6), each with its corresponding magnitude spectra obtained by Fourier transformation for the case with $E_{\text{theshold}} = 0$. This special case is the result of the rigid-sphere model with no threshold energy term.

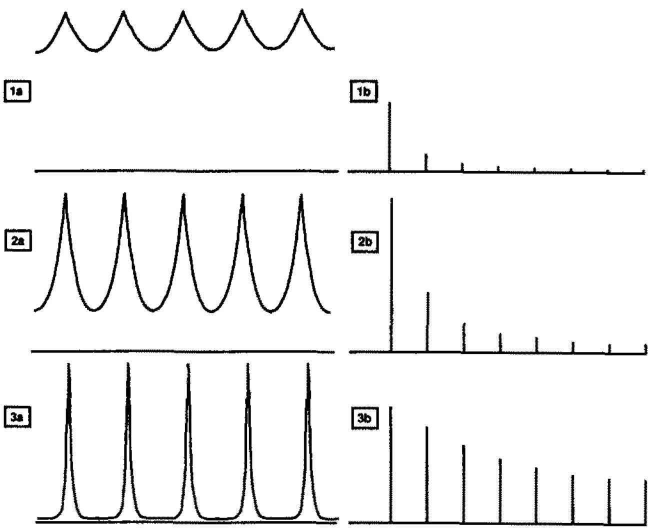


FIG. 3. Theoretical modulation functions of ion signal (with zero threshold energy) are shown in (a) with their magnitude spectra shown in (b) for the conditions in which parameter c has the following values: (1) 0.2, (2) 1.0, and (3) 5.0.

With an increase in reaction time (t_x) or an increase in the pressure of neutrals, the parameter c increases. The results in Fig. 3 illustrate that for the theoretical ion signal modulation function, $f(t) = \exp\{-c[1 + \cos\omega_A t]^{1/2}\}$, an increase in

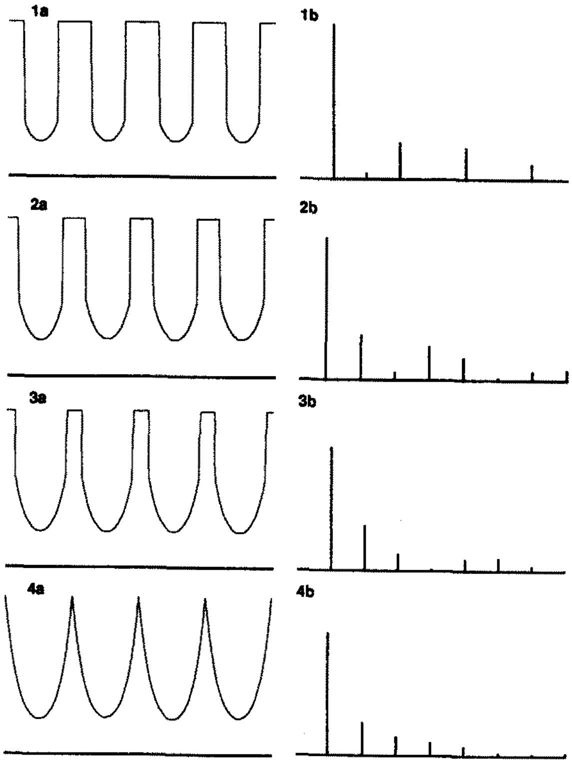


FIG. 4. Theoretical modulation functions of ion signal with parameter $c = 1$ are shown in (a) with their magnitude spectra shown in (b) for the conditions in which the threshold energy has the following values: (1) $E_{\text{threshold}} = 0.5E_{\max}$, (2) $E_{\text{threshold}} = 0.25E_{\max}$, (3) $E_{\text{threshold}} = 0.125E_{\max}$, and (4) $E_{\text{threshold}} = 0$. The maximum energy is defined as $2mV_0^2$.

parameter c gives an increase in the higher harmonic components. However, decreasing the magnitude of parameter c not only decreases the relative intensity of the higher harmonics, but decreases the absolute intensity of the fundamental frequency as well.

Figure 4 shows the spectral changes as a function of the threshold energy for the theoretical ion signal modulation function, $f(t) = \exp\{-c[1+\cos\omega_A t]^{1/2}\}$, with $t|_{E>E_{\text{threshold}}}$ and $P(t) = e$, with $t|_{E<E_{\text{threshold}}}$ $(E = \frac{1}{2}m_A V^2 = m_A V_0^2[1+\cos\omega_A t])$. The four plots of function (6) have the value of parameter c fixed $(c = 1.0)$ and the value of the threshold energy is changed from 0 to 0.5 of the maximum energy $(E_{\max} = 2mV_0^2)$. The introduction of the threshold energy term gives a truncation of the ion signal along t_1 and produces complexity in the magnitude spectrum.

The relative intensities of the harmonics shown in Figs. 3 and 4 depend on the experimental conditions and the nature of the chemical system. One more general conclusion can be drawn. The harmonics exist because the modulation on the ion signals is not sinusoidal.

V. DATA PROCESSING

As mentioned in Sec. I, the 2D FT–ICR experiment first generates a data array in two time dimensions (t_1, t_2). Only the magnitude spectra $S(t_1,\omega_2)$ from the fast Fourier transform on t_2 give useful information, and the phase portion of the frequency domains can be discarded. Therefore, any spectral analysis method which generates spectral density can be used for the first data processing step. One example is the maximum entropy method which promises to generate high-resolution spectral density.[8]

Fourier transform of $S(t_1,\omega_2)$ on t_1 yields a 2D magnitude spectrum $S(\omega_1,\omega_2)$ and a phase function $P(\omega_1,\omega_2)$. $S(\omega_1,\omega_2)$ gives basic information on the chemical system which includes the masses of the primary and product ions as well as the direction of reaction. $P(\omega_1,\omega_2)$ provides additional information on the reactions. In the model discussed above, the phase at (ω_A,ω_B) is 180° from that at (ω_A,ω_A). In experiments conducted under different experimental conditions from this model, the phase difference might be zero. For example, if the amplitude of the 2D FT–ICR excitation pulses is too high, the primary ions would be ejected during the second pulse for certain value of t_1. This would result in the modulation of population for the primary ions at the beginning of reaction period. The loss of the primary ions would cause a decrease of the product ion signals. In this case the modulation of product ion signal could be the same as (in phase with) the primary ions as observed in the previous experiments by Pfändler *et al.*[7(b)]. The model discussed here illustrates that the phase function contains useful information and should not be discarded. Since only the relative phase has physical significance, a phase reference should be established for comparison. Here we propose that the diagonal elements of the phase function $P(\omega_1,\omega_2)$ be set to zero for reference and others adjusted accordingly. That is,

$$P(\omega_1,\omega_2) - P(\omega_1,\omega_2)|_{\omega_2=\omega_1} \Rightarrow P_1(\omega_1,\omega_2) \quad \text{for all } \omega_1.$$

$P_1(\omega_1,\omega_2)$ is the adjusted new phase function.

VI. CONCLUSION

The model developed above shows that the introduction of the additional time dimension in 2D FT–ICR causes modulation of the primary ion speed. The propagation of the speed modulation to the ion signals is complicated. It depends heavily on the experimental conditions and the nature of the chemical system under study.

Although the model presented above is simplified, general conclusions can be drawn from it.

(1) 2D FT–ICR spectra in frequency domains come from the modulation of the primary ion speed;
(2) propagation of the speed modulation to the ion signals depends on the ion loss mechanism and ion chemistry;
(3) harmonic components exist in the 2D magnitude spectra;
(4) the phase function contains useful information about the chemical system.

APPENDIX

The motion of a charged particle with mass of m and charge of q in a static magnetic field B_0 along the z axis and an electric field along the x axis can be described by the Lorentz equations (the z-direction motion is discarded):

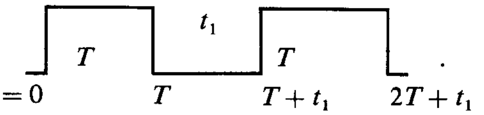
$$\frac{dv_x}{dt} = \left(\frac{q}{m}\right)E_x(t) + \omega_0 v_y, \tag{A1}$$

$$\frac{dv_y}{dt} = -\omega_0 v_x, \qquad \omega_0 = \frac{B_0 q}{m}. \tag{A2}$$

If (during the ion excitation) the electric field oscillates with the ion resonance frequency, $\omega_0/2\pi$, $E_x(t)$ can be expressed for 2D FT–ICR excitation pulses as

$$E_x(t) = \begin{cases} E_0 \sin\omega_0 t, & 0<t<T \quad \text{or} \quad T+t_1<t<2T+t_1 \\ 0, & \text{otherwise,} \end{cases} \tag{A3}$$

(A4)



The solutions of Eqs. (A1) and (A2) in absence of excitation are

$$v_x(t) = v_{x0}\cos\omega_0 t + v_{y0}\sin\omega_0 t, \tag{A5}$$

$$v_y(t) = -v_{x0}\sin\omega_0 t + v_{y0}\cos\omega_0 t. \tag{A6}$$

The solutions during the ion excitation are

$$v_x(t) = v_{x0}\cos\omega_0 t + v_{y0}\sin\omega_0 t + [(qE_0 t)/2m]\sin\omega_0 t, \tag{A7}$$

$$v_y(t) = -v_{x0}\sin\omega_0 t + v_{y0}\cos\omega_0 t + [(qE_0 t)/2m]\cos\omega_0 t - [(qE_0)/2m\omega_0]\sin\omega_0 t. \tag{A8}$$

The last term of Eq. (A8) can be ignored if the excitation runs more than ten cycles. We assume that the initial ion speed is zero $(t = 0)$ and the excitation pulse length (T) satisfies the relationship $\omega_0 T = 2n\pi$ (n is integer). The second assumption does not set any limitation on the generality of the result (see the results below).

The ion velocity at the end of the first excitation pulse ($t = T$) is obtained by Eqs. (A7) and (A8) with the initial conditions of $v_{x0} = 0$ and $v_{y0} = 0$:

$$v_x(T) = 0, \quad v_y(T) = v_0, \quad v_0 = qE_0T/2m. \qquad \text{(A9)}$$

The ion velocity at the end of the evolution time period ($t = T + t_1$) is given by Eqs. (A5) and (A6) with Eq. (A9) as the initial condition:

$$v_x(T + t_1) = v_0 \sin \omega_0 t_1,$$

$$v_y(T + t_1) = v_0 \cos \omega_0 t_1.$$

Repeating the procedures, we obtain the ion velocity at the end of the second excitation pulse ($t = 2T + t_1$):

$$v_x(T + t_1) = v_0 \sin \omega_0 t_1,$$

$$v_y(T + t_1) = v_0(1 + \cos \omega_0 t_1).$$

Therefore, the ion speed at the end of the excitation pulses can be expressed as:

$$v(t_1) = v_0[2(1 + \cos \omega_0 t_1)]^{1/2}.$$

If the pulse duration T does not satisfy the relation $\omega_0 T = 2n\pi$ ($n = 1,2,...$), the result will be

$$v(t_1) = v_0\{2[1 + \cos \omega_0(T - t_1)]\}^{1/2}.$$

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[1] *Fourier Transform Mass Spectrometry*, edited by M. V. Buchanan (American Chemical Society, Washington, D.C., 1987).

[2] D. Russell, Mass Spectrom. Rev. **5**, 167 (1986).

[3] M. L. Gross and D. L. Rempel, Science **226**, 261 (1984).

[4] *Tandem Mass Spectrometry*, edited by F. W. McLafferty (Wiley, New York, 1983).

[5] F. W. McLafferty and I. J. Amster, Int. J. Mass Spectrom. Ion Phys, **72**, 85 (1986).

[6] R. T. McIver, Jr. and W. D. Bowers, in Ref. 4 p. 286.

[7] (a) P. Pfändler, G. Bodenhausen, J. Rapin, R. Houriet, and T. Gäumann, Chem. Phys. Lett. **138**, 195 (1987); (b) P. Pfändler, G. Bodenhausen, J. Rapin, M. Walser, and T. Gäumann, J. Am. Chem. Soc. **110**, 5625 (1988).

[8] A. Rahbee, Int. J. Mass Spectrom. Ion Phys. **72**, 3 (1986).