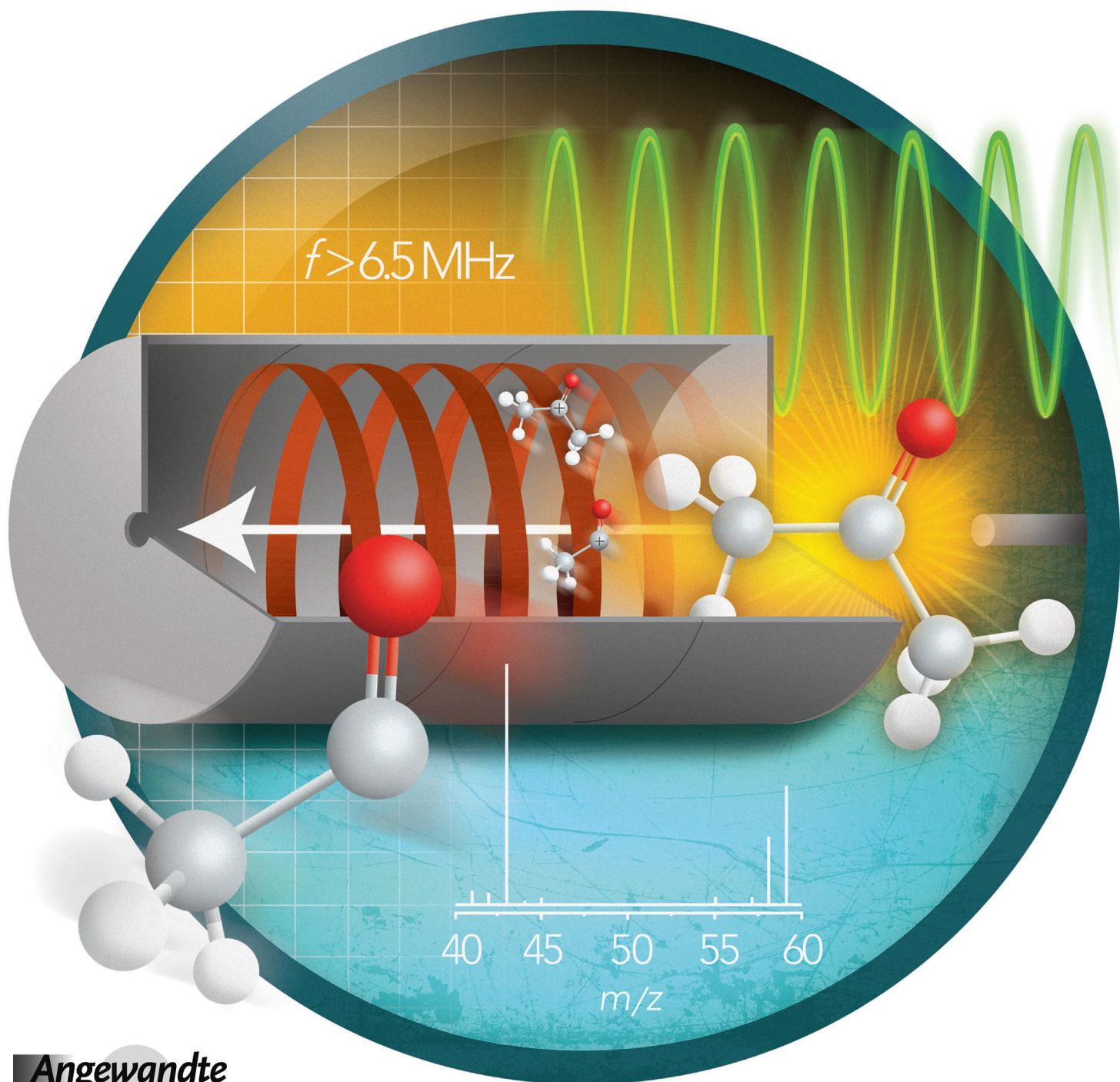


Radio-Frequency Ionization of Organic Compounds for Mass Spectrometry Analysis**

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Achieving the optimum analytical performance in mass spectrometry (MS) experiments depends partly on the efficiency of the ionization method(s). The ionization methods can be grouped into various types (e.g., ionization of gases, liquids, and solids) and a conventional approach is to cluster them into two major categories of “soft” and “hard” ionization approaches.^[1] Some of the “hard” ionization methods that yield extensive ion fragmentation include electron impact (EI) ionization,^[2] ²⁵²Cf desorption,^[3] and laser desorption.^[4] These “hard” ionization methods offer the advantage of providing additional functional group and structural information. However, often it is advantageous to avoid ion fragmentation to simplify the MS complexity and increase the signal-to-noise (S/N) ratio for identification of an unknown through the identification of intact molecular ions. Therefore, the “soft” ionization methods such as chemical ionization (CI),^[5] field desorption,^[6] matrix-assisted laser desorption/ionization (MALDI),^[4,7,8] and electrospray ionization (ESI)^[9,10] are also valuable methods to produce intact molecular ions of small molecules and macromolecular biopolymers.^[11]

Herein, we report a novel ionization method for the MS analysis of volatile and semivolatile organic molecules using radio-frequency (RF) signals. This ionization method was discovered in the process of investigating the possibility of injecting low m/z ions (i.e., $m/z < 100$) into the trap cell of a Fourier transform ion cyclotron resonance (FT-ICR) mass spectrometer located within a high magnetic field (e.g., 9.4 tesla).^[12] We demonstrate that under a specific set of experimental conditions, by applying an RF signal to the quadrupole ion guide (QIG) rods, we can generate ions with very high efficiency.

A systematic study of the RF ionization (RFI) process and analysis of the MS results showed that the RFI-generated ions were formed “off-axis” and radially away from the center of the ICR quadrupole trapping plate (QTP). To confirm the “off-axis” ion generation, we used appropriate trapping parameters to guide the ions into the ICR cell through various small circular entrance apertures (diameter 0.4 cm), positioned 1 mm away (axially) from the QIG rods. For this purpose, we conducted several experiments in which we replaced the original gold-plated copper QTP of the ICR cell with aluminum (Al) plates of various configurations (Figure 1) and leaked in the analyte of interest into the FT-ICR mass spectrometers’ vacuum chambers. The Al plates were made of eight layers of Al foil (each with a thickness of 200 μm and an outer diameter of 7.2 cm).

Figure 1a,b shows schematic views of the Al plates, positions of the QTP openings (circular apertures) into the ICR cell, and the positions of the QIG rods with respect to the

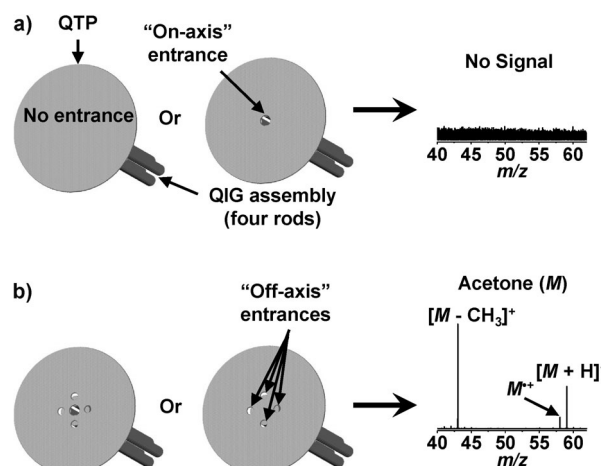


Figure 1. a,b) Schematic representations of the QTP modifications in the ICR cell (left and middle) and the resulting RFI/FT-ICR mass spectra of acetone (right) for various aperture positions on the QTP.

QTP. The corresponding RFI/FT-ICR mass spectra are shown in the right panels of Figure 1a,b. Eight sets of experiments were conducted to evaluate the ion entrance/generation positions using the modified QTPs. In each experiment after the original QTP had been replaced with an Al plate, a series of RFI/FT-ICR mass spectra were collected and inspected for the presence or absence of representative acetone (or background) ions. For each of the experiments, we also acquired internal EI mass spectra to ensure the integrity of all electronic connections on the ICR cell for ion signal detection.

To acquire the RFI/FT-ICR mass spectra with the Al QTPs (Figure 1, right panels), acetone, from the expansion volume reservoir of the sample introduction assembly,^[13,14] was leaked into the vacuum chamber for 3 ms (corresponding to an instantaneous acetone partial pressure of 1.0×10^{-7} torr). To ionize the neutral acetone molecules, an RF signal of 6.5 MHz (200 V_{bp}) was applied to the QIG rods for 500 ms.

When the Al QTPs with the configurations shown in Figure 1a were used, no acetone (or background) ion signals were observed in the mass spectrum. These MS experiments suggested that either ions were not formed near the center of the QIG assembly or if they were formed, these ions could not be transferred into the ICR cell.

When the Al QTPs with the configurations shown in Figure 1b were used, RFI-generated ions from acetone at m/z values of 43 (a major fragment ion, $[M - \text{CH}_3]^+$), 58 (M^+), and 59 ($[M + H]^+$ or the self-CI product of acetone^[13]) were observed. We also used four additional Al plate configurations in which only one of the “off-axis” entrances was open and the other three were blocked; with these additional QTP configurations we also observed ion signals for acetone. Compared to the RFI/FT-ICR mass spectra acquired with QTPs with a single “off-axis” entrance window open, those acquired with all of the five QTP entrances open into the ICR cell showed a twofold increase in the S/N ratio. The RFI MS results from Figure 1a and b suggested that the potential

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locations for ion generation and entrance (into the ICR cell) were “off-axis” between the QIG rod ends and QTP.

The acquisition of RFI/FT-ICR mass spectra using the “off-axis” entrances of the ICR cell QTP (Figure 1b) was associated with the following three nonideal features: 1) the presence of the peak splitting and side bands in the acquired RFI/FT-ICR mass spectra, 2) the failure to trap the ions inside the ICR cell for longer than 1 s (i.e., trapped ions were lost shortly after their introduction into the ICR cell), and 3) the necessity to use (optimized) asymmetric electrical potentials on the ICR cell trapping plates for efficient trapping of the RFI-generated ions (e.g., QTP voltage of 30 V and filament trapping plate (FTP) voltage of 0.0 V). To overcome these three nonideal features, we used a copper wire (200 μm diameter) ion guide (WIG) device.^[15] To acquire the RFI/FT-ICR mass spectrum of acetone using the WIG, the direct current (DC) voltage on the WIG was initialized to an optimized value of -17 V and then pulsed to 0.0 V during the ion excitation and detection events.

Figure 2a shows a schematic view of the ICR cylindrical cell and the “on-axis” position of the suspended WIG inside the ICR cell (marked by the black solid line parallel to the magnetic field lines). Each end of the 15 cm long copper WIG was attached to the center of one of the two end trapping plates of the ICR cell using ceramic washers (for electrical isolation) and two sets of brass screws and nuts.

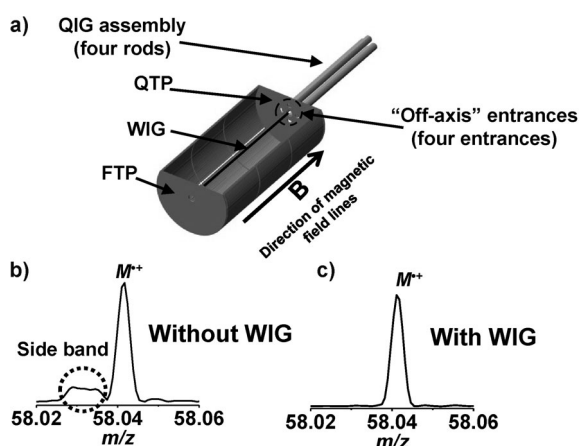


Figure 2. a) Schematic representation of the cylindrical ICR cell showing the position of the WIG. The expanded views of the m/z range from 58.02 to 58.06 for RFI/FT-ICR mass spectra of acetone b) without WIG and c) with WIG.

Figure 2b,c contains the expanded views of the m/z range from 58.02 to 58.06 for the RFI/FT-ICR mass spectra of acetone acquired without and with the WIG, respectively. The MS peak for the M^+ species from acetone (m/z 58.0413) in Figure 2b has a shoulder at the lower m/z side (i.e., peak labeled as “Side band” and marked with the dotted circle in Figure 2b); this side band disappeared when the WIG was used to guide the ions towards the center of the ICR cell (Figure 2c). When the WIG was used, the RFI-generated ions could be trapped inside the ICR cell for longer periods (e.g., more than 20 s, as compared to the maximum possible

trapping time of 1 s without using the WIG). The enhanced quality of the RFI/FT-ICR mass spectra (acquired in the presence of a WIG) confirmed our observations in Figure 1, suggesting the “off-axis” generation/entrance of the RFI-generated ions. Moreover, when a WIG was used, the RFI-generated ions could be trapped inside the ICR cell by applying symmetric (rather than asymmetric) electrical potentials on the ICR cell trapping plates.

In an attempt to generate ions “on axis”, we also performed experiments by spot-welding two rhenium ribbons (99.97 % purity, 10 mm long, 0.76 mm wide, 0.038 mm thick) on one of the QIG rods and the other on the central opening of the original QTP. The Re ribbon welded to the QIG rod was extended inward and its tip was at the exact center of the “on-axis” opening aperture of QTP and 2 mm away from the Re ribbon welded to the QTP. Only by using this new setup were we able to observe MS signals with the “on-axis” window open (data not shown).

We also compared the patterns and S/N ratios of FT-ICR mass spectra of acetone obtained using RFI (6.5 MHz, 200 V_{bp}) and EI (70 eV) (data not shown). The RFI/FT-ICR and EI/FT-ICR mass spectra of acetone showed comparable patterns. However, under the identical ionization time duration, RFI yielded a sixfold higher S/N ratio than EI.

The extent of ion fragmentation in RFI could be controlled by adjusting the RF ionization time duration. This suggests that RFI could be operated as both “soft” and “hard” ionization methods. Figure 3 shows the plots of

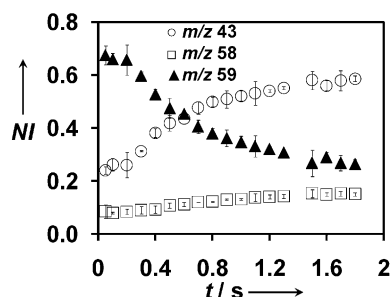


Figure 3. Plots of normalized intensities (NIs) for the $[M+H]^+$ (m/z 59), M^+ (m/z 58), and $[M-CH_3]^+$ (m/z 43) species generated from acetone as a function of RFI duration (t). The data points correspond to average values (three trials) and the error bars are calculated at the 95 % confidence limit.

normalized intensities for the $[M-CH_3]^+$ (empty circles), M^+ (empty squares), and $[M+H]^+$ species (filled triangles) generated from acetone (M) versus the time duration of RF signal applied to the QIG rods. As shown in Figure 3, when the RF ionization time was increased from 0.05 s to 1.8 s, the ion abundance for $[M+H]^+$ (m/z 59) decreased but the ion abundance for $[M-CH_3]^+$ (m/z 43) increased (e.g., the normalized intensity of m/z 43 increased from $(24 \pm 1)\%$ to $(60 \pm 1)\%$). Although the trapping conditions can influence the appearance of the mass spectra, our preliminary results suggest enhanced ion fragmentations as a function of RFI period.

To demonstrate the broad applicability of RFI, we also acquired the RFI/FT-ICR mass spectra of a semivolatile silicone polymer from a Varflex electrical insulating sleeving (IS) (type 5, Varflex Corp., Rome, NY). A 2 cm × 2 cm piece of the IS material was placed on the end terminal of the QIG assembly in proximity to the ICR cell QTP to cover the four rods (Figure 4, right).

Figure 4 (left) shows the RFI/FT-ICR mass spectrum acquired after the placement of the IS. The assigned MS peaks ($[C_7H_{21}O_4Si_4]^+$ (m/z 281.0509), $[C_9H_{27}O_5Si_5]^+$ (m/z 355.0708), and $[C_{11}H_{33}O_6Si_6]^+$ (m/z 429.0879)) with an average mass

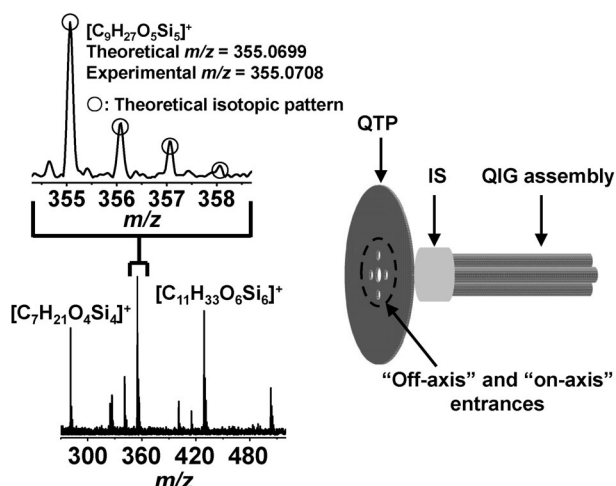


Figure 4. Right: Schematic view of the position of the insulating sleeving on the QIG rods. Left: RFI/FT-ICR mass spectrum of the cyclic PDMS compounds in type 5 Varflex IS.

measurement error of ≈ 1.7 ppm indicate the presence of cyclic poly(dimethylsiloxane) (PDMS) compounds. To confirm our peak assignments, we also compared the experimental isotopic patterns of the species assigned as $[C_7H_{21}O_4Si_4]^+$, $[C_9H_{27}O_5Si_5]^+$, and $[C_{11}H_{33}O_6Si_6]^+$ with their corresponding theoretical isotopic patterns. For example, as shown in Figure 4 (inset), the experimental isotopic pattern of the species at m/z 355.0708 matches the theoretical isotopic pattern for the assigned species as $[C_9H_{27}O_5Si_5]^+$ (Figure 4, empty circles).

The mechanism of ionization in RFI is not completely understood at this time; however, our initial investigations suggest that the mechanism(s) in RFI is different than the ionization mechanism in RF glow discharge (GD).^[16–18] For instance, ionization process in RF-GD requires maintaining a high pressure (e.g., 100–500 mtorr) of an inert gas (e.g., Ar) in the ion source. In contrast, RFI takes place in ultrahigh vacuum (1.0×10^{-9} torr) and does not require the use of an inert gas for ionization. We are currently investigating the

ionization mechanism(s) of RFI using a prototype RFI ion source and the details of the potential RFI mechanisms will be reported in the future.

Experimental Section

The mass spectra were acquired using two independent IonSpec FT-ICR mass spectrometers (former IonSpec Corp., now a division of Agilent Technologies, Santa Clara, CA) (ESI/FT-ICR^[19] and gas chromatography (GC)/FT-ICR^[14]). The two instruments shared a 9.4 tesla magnet (Cryomagnetics Inc., Oakridge, TN) and could be operated independently and one at a time. We used a previously reported home-built RF power supply to generate the RF signals^[12] for RFI. A transistor–transistor logic (TTL) relay switch was used to control the “on”/“off” states of the RF signals on the QIG rods. The RF signal was only applied to the QIG rods when the TTL signal was received from the IonSpec Omega software (version 8.0).

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