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Autonomous in Situ Analysis and Real-Time Chemical Detection Using a Backpack Miniature Mass Spectrometer: Concept, Instrumentation Development, and Performance

Paul I. Hendricks,[†] Jon K. Dalgleish,[†] Jacob T. Shelley,[†] Matthew A. Kirleis,[§] Matthew T. McNicholas,[§] Linfan Li,[‡] Tsung-Chi Chen,[‡] Chien-Hsun Chen,[‡] Jason S. Duncan,[†] Frank Boudreau,[†,∥] Robert J. Noll,[†,∥] John P. Denton,[§] Timothy A. Roach,[⊥] Zheng Ouyang,*[,‡,∥] and R. Graham Cooks*[,†,∥]

[†]Department of Chemistry, Purdue University, West Lafayette, Indiana 47907, United States

[‡]Weldon School of Biomedical Engineering, Purdue University, West Lafayette, Indiana 47907, United States

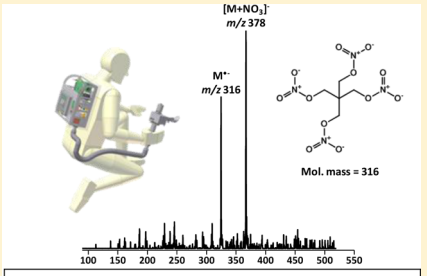
[§]Department of Electrical and Computer Engineering Technology, Purdue University, West Lafayette, Indiana 47907, United States

[∥]Center for Analytical Instrumentation Development, Discovery Park, Purdue University, West Lafayette, Indiana 47907, United States

[⊥]SOCOM, 1636 Regulus Ave., Virginia Beach, Virgina 23461, United States

Supporting Information

ABSTRACT: A major design objective of portable mass spectrometers is the ability to perform in situ chemical analysis on target samples in their native states in the undisturbed environment. The miniature instrument described here is fully contained in a wearable backpack (10 kg) with a geometry-independent low-temperature plasma (LTP) ion source integrated into a hand-held head unit (2 kg) to allow direct surface sampling and analysis. Detection of chemical warfare agent (CWA) simulants, illicit drugs, and explosives is demonstrated at nanogram levels directly from surfaces in near real time including those that have complex geometries, those that are heat-sensitive, and those bearing complex sample matrices. The instrument consumes an average of 65 W of power and can be operated autonomously under battery power for ca. 1.5 h, including the initial pump-down of the manifold. The maximum mass-to-charge ratio is 925 Th with mass resolution of 1−2 amu full width at half-maximun (fwhm) across the mass range. Multiple stages of tandem analysis can be performed to identify individual compounds in complex mixtures. Both positive and negative ion modes are available. A graphical user interface (GUI) is available for novice users to facilitate data acquisition and real-time spectral matching.



1 μg pentaethythritol tetranitrate (PETN) ionized from a surface using a low temperature plasma and analyzed using a backpack mass spectrometer

Mass spectrometry has become a preferred technique for chemical analysis because of its selectivity, sensitivity, speed of analysis, and applicability to a wide range of chemical compounds. Increasingly, critical applications in environmental monitoring,[1] food safety, public security,[2] therapeutic drug monitoring,[3,4] and tissue biopsy analysis[5−7] require decisions to be made in real time based upon analytical chemical information. These situations call for in situ analysis and portable instruments.

Traditionally, mass spectrometers are laboratory-based, with analysis time, cost, and complexity further increased through extensive use of separation methods and sample preparation. Bench-top, lab instrumentation will typically yield much better analytical performance than will miniature mass spectrometers, but the need for immediate actionable information at the point of care (POC) or point of analysis (POA) can mandate utilization of the just-adequate performance associated with portable mass spectrometers. Previously reported portable systems[8] have parts-per-million (ppm) to parts-per-billion (ppb) detection limits, mass ranges suitable for organic molecules (m/z 600), unit mass resolution, and capabilities for tandem mass spectrometry. They have been developed commercially[9−13] and academically[14−17] and used for in-field and in situ detection of explosives, illicit drugs, biological warfare agents,[18] food adulterants, pesticides, and toxic industrial compounds. Very few of these systems are capable of trace analysis of nonvolatile compounds from surfaces, a design goal of this work.

The two portable instruments described in this and the accompanying paper[19] utilize similar system components, but they are deployed differently, viz., either as a wearable backpack system (Mini S, shown in Figure 1 and Supporting Information Figure S1) or as a stand-alone single-unit instrument (Mini 12). They are based on experience with the earlier Mini 10 and Mini

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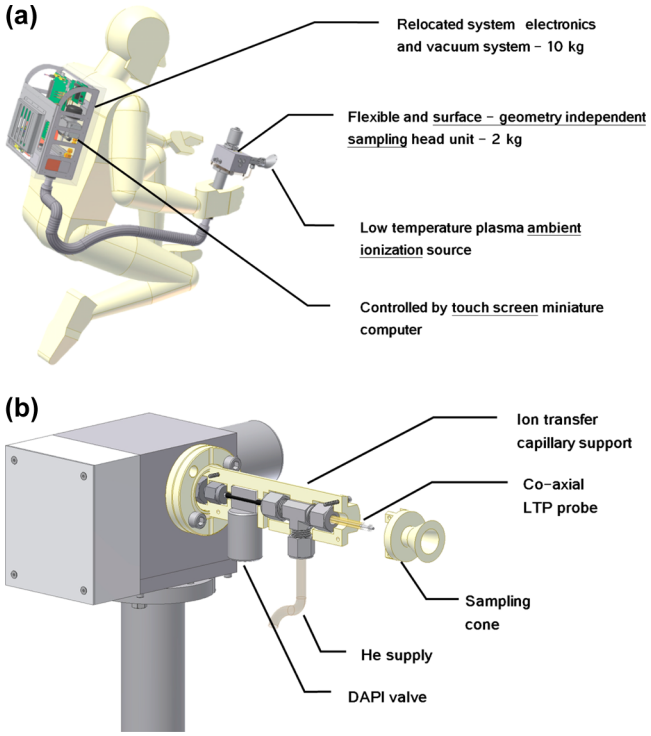

Figure 1. (a) Miniature mass spectrometer composed of two sections, a backpack section that houses the vacuum system and control electronics and hand-held head unit with an integrated LTP source for geometry-independent sampling. (b) Exploded view of the hand-held head unit head unit; note the linear integration of the ion source, ion transfer capillaries, DAPI, and mass analyzer. Helium supply generates a positive pressure inside the LTP source, and reactive ion species make contact with the sample surface. When the DAPI valve is actuated ions and neutrals are drawn through the ion transfer capillaries and into the mass analyzer.

11 platforms.[15,20] with the current systems utilizing similar mechanical and turbomolecular pumps, a discontinuous atmospheric pressure interface (DAPI),[14,21] and a rectilinear ion trap (RIT)[22] mass analyzer, as well as a multiplier and dynode assembly for detection of positive and negative ion species.[23] Principal design criteria include direct sampling of ions generated at atmospheric pressures, detection of both positively and negatively charged species, integration of the ionization source with the ion inlet, system portability, geometry-independent surface sampling, sampling from complex matrices of low-volatility components, stability of the system electronics, low operational power, automated operation, and automated data interpretation.

Performance of the miniaturized pumping system is balanced against the high ion/neutral conductance into the vacuum manifold from atmosphere through utilization of DAPI (Supporting Information, Figure S2), a key enabler when instrumentation is constrained by size, weight, and power. Although the pulsed DAPI system greatly reduces the instrument duty cycle, it allows sampling of ions generated at atmospheric pressures and hence the use of ambient ionization sources such as low-temperature plasma (LTP),[24] paper spray (PS),[25] and desorption electrospray ionization (DESI)[26] in addition to conventional atmospheric pressure sources, e.g., nanoelectrospray (nESI)[27] and atmospheric pressure chemical ionization (APCI).[28] Compatibility with a range of different ionization sources expands the classes of chemical compounds that can be analyzed relative to systems that are restricted to membrane-inlet sampling or solid-phase microextraction (SPME) columns.

The Mini S is designed for maximum portability and greatest flexibility for in situ analysis. The form factor comprises two sections: a wearable backpack unit housing the heaviest components of the instrument (i.e., the vacuum system, electronic control boards, batteries, and plasma discharge gas) and a separate hand-held head unit which contains the mass analyzer, ion-detection circuit, sample inlet, and ion source. A preliminary description of the concept of separating the sampling/ionization head unit from the vacuum and mass analysis system has been published.[29] The head unit designed for the Mini S contains an integrated LTP source (Supporting Information, Figures S1 and S2) with a novel coaxial arrangement of ion transport capillaries and mass analyzer, designed specifically for geometry-independent sampling of target analytes directly from surfaces bearing physically and chemically complex samples (e.g., human fingers, cloth, and cardboard) at levels as low as 2 $\mu g/cm^2$. The instrument consumes an average of 65 W of power and can be operated under battery power for approximately 1.5 h (single battery pack, 16 C-cell batteries). It takes ca. 15 min to bring a fully vented system to pressures suitable for operation. Multiple stages of tandem mass analysis can be performed. A graphical user interface (GUI) was developed for novice users which allows for automated instrumentation control, data acquisition, and data interpretation through customizable, user-generated, workflows that include library matching of mass spectral data.

INSTRUMENTAL DESIGN AND EXPERIMENTAL SECTION

Chemicals. Chemical reference standards (1000 $\mu g/mL$) for trinitrotoluene (TNT), pentaerythritol tetranitrate (PETN), and cyclotrimethylenetrinitramine (RDX) were purchased from AccuStandard (New Haven, CT). Reference standards (1000 $\mu g/mL$) for cocaine, methamphetamine, and 3,4-methylenedioxy-*N*-methylamphetamine (MDMA or ecstasy) were obtained from Cerilliant (Round Rock, TX). Chemical warfare simulants dimethy methylphosphonate (DMMP) and the alkyl phosphates were supplied from Sigma-Aldrich (St. Louis, MO); mipafox was supplied directly by the program sponsor. Reference standards from both chemical classes were used for detection from glass and other surfaces (paper, cardboard, human fingers, cloth) without further purification. The upper mass-to-charge limit for the instrument was determined with a mixture of poly(ethylene glycol) polymers (average molecular weights of approximately 100–600) in concentrations of 50–500 μM in 1×10^{-3} M NaOH and 100 $\mu g/mL$ cocaine, respectively; both compounds were ionized by electrospray using an nESI source.

Instrument Design Concept and Implementation. Fully assembled, the Mini S is composed of two major components: a wearable backpack and a hand-held head unit (Supporting Information, Figure S3). The backpack portion of the instrument weighs 10 kg when fully assembled. A KNF Neuberger (Trenton, NJ) mechanical pump (5 L/min) and a Pfeiffer Vacuum HiPace10 (Nashua, NH) turbomolecular pump (10 L/s) comprise the vacuum system and are mounted to a lightweight aluminum (5052) frame (30.5 cm × 29.5 cm × 12.5 cm) which forms the wearable backpack portion of the instrument (Supporting Information, Figure S3A). Integrated with the aluminum frame are provisions to mount an on-board

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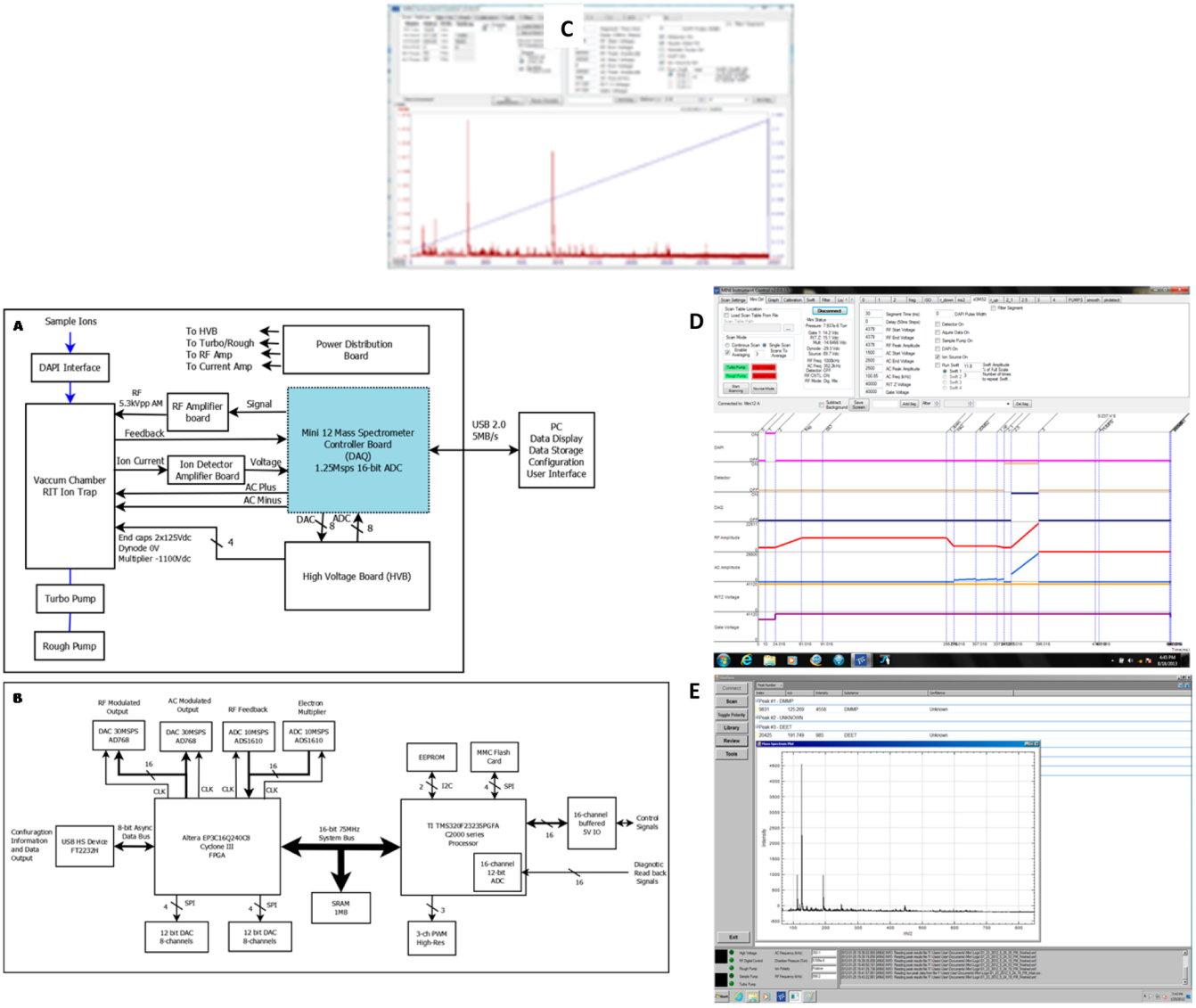

Figure 2. (A) Electronic control scheme for the Mini12 instrument. (B) Communication scheme for the DSP, FPGA, and on-board SRAM memory. (C) Output mass spectrum with rf ramp superimposed to track linearity. (D) Graphical representation of the instrument scan table as displayed inside the expert user software interface. This interface is used for setting the voltage control operation and timing for all of the instrument devices including the mass analyzer, ion detection circuit, source voltage, ion introduction, and data acquisition. In addition, all of the instrument ADCs, the rf frequency, and the rf PID controller are also tuned through this interface. The central display allows for the viewing of acquired data, a graphical view of the instrument method, i.e., voltage amplitudes with respect to time, and the visualization of the SWIFT notch in both frequency and time domains. (E) Image of the novice user interface software that provides MS library search capability, results reporting, instrument status information, and automated routines such as instrument startup, shutdown, and data acquisition.

gas regulator and miniature He tank (Leland Limited, Inc.; South Plainfield, NJ) for the LTP source, as well as 24 V rechargeable, nickel metal hydride battery (Powerizer; Richmond, CA) (Figure 1a).

The body of the hand-held head unit is an aluminum manifold (6061) (12 cm × 7.5 cm × 8.5 cm) and weighs 2 kg when fully assembled. This component is connected to the backpack portion of the instrument via a 76 cm long stainless steel vacuum bellows (Kurt J. Lesker; Clairton, PA). The head unit requires the mass analyzer, ion-transport capillaries, DAPI valve, and LTP ionization source to all be linearly integrated to allow for geometry-independent sampling, efficient ion introduction, and successful transmission of ions into the mass analyzer. The positions and alignment of the ion source, transfer capillaries, and DAPI valve are maintained by the use of a polymer support (constructed with rapid polymer prototyping) that surrounds these components and bolts directly to the manifold (Figure 1b).

The coaxial LTP ion source (Figure 1b) consists of a 42.5 mm long quartz tube (2 mm o.d., 4 mm i.d.) which serves as the dielectric barrier and which surrounds the ion-transfer capillary (stainless steel, 10 cm, 0.020 in. i.d., 0.0625 in. o.d.) and also serves as the primary ion inlet to the vacuum system. The high-voltage connection to the LTP is supplied to an electrode on the outside of the quartz tube, while the ion transfer capillary serves as the counter, grounded, electrode. In this configuration the discharge region is between the inside surface of the dielectric and the grounded inlet capillary. During operation the ionizing species generated by the plasma are in close proximity to both the sampling surface and the inlet to

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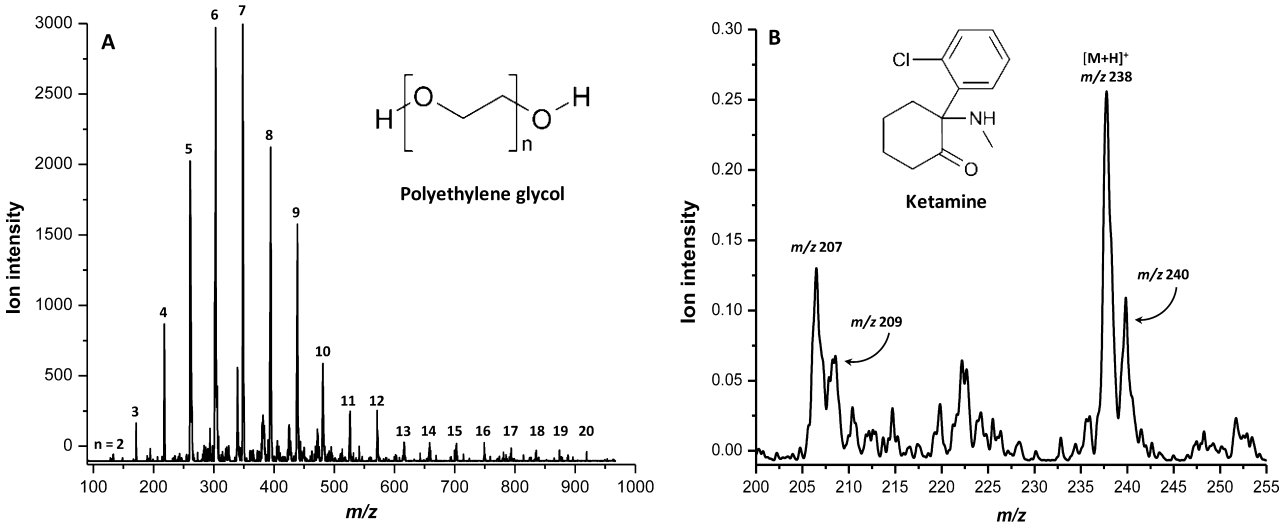

Figure 3. (A) nESI mass spectrum of poly(ethylene glycol) $[PEG + Na]^+$ demonstrating maximum detectable mass-to-charge 925 Th. (B) Ketamine, a controlled substance and common party drug, analyzed with the Mini-S and an LTP ion source. Three-scan average of 1 $\mu g/cm^2$ ketamine, m/z 238/240 $[M + H]^+$. Sample was ionized with LTP, 80 mL/min He, 500 V_{p-p} at 30 kHz (~1 W). Mass resolution of 1 amu (fwhm) is sufficient to separate the chlorine isotopic peaks by a valley of less than 10%. It should also be noted that fragments carrying the chlorine atom are formed during the ionization process (M − 31, m/z 207) which generates a full scan mass fingerprint that can be used by the automated library search software.

the mass spectrometer. Helium, the usual discharge gas, is supplied to the LTP source (80−120 mL/min) via a T-fitting that generates a positive pressure inside the plasma source which together with the electric field generated causes the discharge gas along with the ionizing species to directly impinge upon the sample surface allowing ionization of the target analyte and thermal energy transfer. The high-voltage waveform applied to the LTP probe was ca. 2 kV_{p-p} at 27−33 kHz. Input power of less than 1 W was used for most compounds analyzed. In specific circumstances, LTP input powers were increased to approximately 8 W to improve analyte thermal desorption. Ion injection into the mass analyzer occurs when the DAPI valve is actuated, driving ions and neutrals through the ion transfer capillaries and directly into the mass analyzer without the aid of additional lenses or ion focusing.

The bipolar detector consisting of a conversion dynode and channeltron electron multiplier[30] is housed in a metal tube within the vacuum manifold that houses the ion source (see photograph, Supporting Information Figure S3C). It is well-screened from the effects of electrical discharges in air, and it gives low-noise spectra in both the positive and negative ion modes.

Similar to earlier miniature mass spectrometers the Mini S utilizes an LC-tank circuit for voltage amplification of the main rf. In this instrument the rf signal is transferred from the backpack, containing the inductance coil (L), and the head unit containing the mass analyzer (C) (Figure 1, compare also Supporting Information Figure S1). This design requires an unusually long cable connection between these two components (adding additional capacitance to the LC circuit), and it represents a departure from the design typical of mass spectrometers in which the mass analyzer and inductance coil are spatially close together in an effort to minimize capacitance. This design is successful because of the low capacitance of the RIT mass analyzer (~22 pF) and a specially designed inductance coil (~300 μH), which allows a connection from the rf coil to the mass analyzer to be made with a low-capacitance high-voltage cable (RG62/U, 44.62 pF/m) and still allows the instrument to be operated at a drive frequency of 1 MHz.[8,31] A 20 pF adjustable capacitor in parallel with the rf circuit allows small changes to the capacitance of the circuit to be made so that the instrument can be tuned to operate at precisely 1 MHz.

The Mini-S rf amplifier circuit is capable of achieving a maximum output voltage of ~6 kV_{p-p} at 1 MHz. This corresponds to a maximum detectable mass-to-charge of 930. Given this performance the rf voltage amplitude is no longer a bottleneck to completing analysis of organic molecules such as explosives, chemical warfare agents, and illicit drugs. SAFETY NOTE: the normal care taken when working with high voltages should be strictly adhered to with this unusual instrument configuration.

Digital System Control: Design and Implementation. The instrument (Figures 1 and 2) was designed at Purdue University. Instrument design included development of the electronic control architecture, circuit design, printed circuit board (PCB) layout, instrument control software, mechanical design, and system electronics testing. Two six-layer PCBs house a digital signal processor (TMS320F28335PGFA, Texas Instruments; Dallas, TX) which is used in tandem with a field-programmable gate array (FPGA) (Cyclone III FPGA, Altera; San Jose, CA) to manage instrument-to-data system communications (5 MB/s), scan function execution, data acquisition (10 Msps), direct digital synthesis (DDS) waveform generation, stored waveform inverse Fourier transform[32] (SWIFT) signal generation and playback (Figure 3), and error correction to rf amplitude linearity.

The expert graphical user interface (Figure 2D) can be used to set all operating parameters and to display the time-dependent parameters as a scan table. This allows setting of operating voltage amplitudes and their timing for the mass analyzer, ion detector, LTP operation, ion introduction via the DAPI, and data acquisition. In addition, all of the instrument ADCs, the rf frequency, and the rf PID (proportional, integral differentiation) controller are also tuned through this interface. The central display also allows acquired data to be viewed. A

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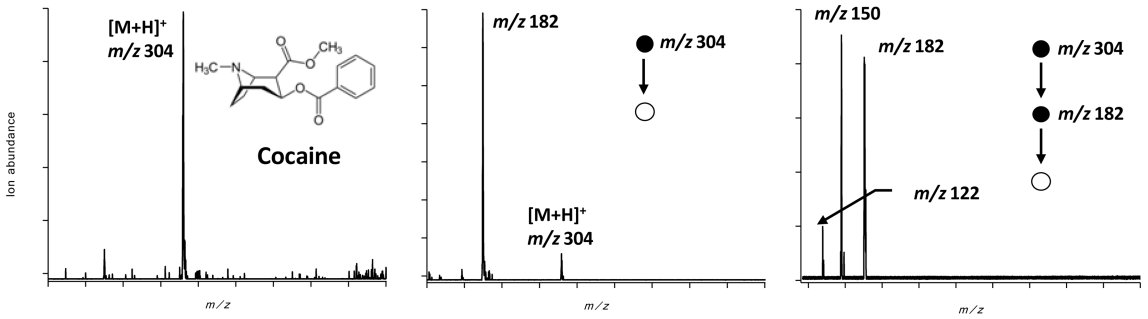

Figure 4. Multiple-stage product ion scan (MS/MS/MS) demonstrated using 100 ppm of the model compound cocaine.

digital controller for the main rf, which took advantage of the high-speed processing capabilities of the FPGA, was implemented for control of the main rf instead of employing a traditional analog feedback controller as used in our previous Mini instruments. In this design the feedback signal was obtained from the modulated rf through a series of capacitors, which was then converted to a digital value by an ADC (10 Msps) and used along with the setting values of modulating rf amplitude in a FPGA program module designed to perform the function of a PID controller. This system provides good rf linearity over the whole scan range (compare Figure 2C). Increased processor speed and available memory of the FPGA, relative to the earlier Mini 11 instrument, allows SWIFT signals (unavailable for Mini 11) to be generated with a user-defined notch in the frequency domain as a part of the instrument operation. A time-domain waveform is then calculated using up to 524 288 (2^{19}) data points each of 16-bit resolution in amplitude to implement the waveform with a specified frequency notch. It is stored on the static random-access memory (SRAM) and is available for playback at a speed up to 30 Msps in any segment(s) during a scan cycle. Up to four SWIFT waveforms can to be defined and stored with a compromise in the number of data points (i.e., 2^{17} vs 2^{19}), which can be output for different segments within a single scan. Supporting Information given in Figure S4 illustrates time-domain waveform and it application to isolate ions of interest prior to an rf scan. The expert user interface allows visualization of the SWIFT notch in both the frequency and time domains.

Software: Novice User Interface and Library Searching Software. In order to facilitate in-field instrument operation by novice users, two specialized features were integrated into the instrument. First, a lightweight tablet PC (HP Slate; Palo Alto, CA; Windows 7 OS) was utilized for data acquisition and processing, both of which could be executed via the touch screen display. Second, a novice user interface (image of GUI shown in Figure 2E) was developed to execute predefined methods for chemical analysis and process the data. Mounted to the handle of the head unit is a push-button trigger, which when activated, initiates data acquisition and execution of the predefined data analysis workflow (detailed in Supporting Information Figure S5). The analytical method and data processing workflow are preselected based on the targeted analysis. Analytical method and data processing workflows include the ability to complete a series of positive, negative, or polarity switching full mass scans, automatic MS/MS product ion scans of target m/z values, library peak matching, and quantitative analysis. To further simplify instrument operation and interpretation of mass spectral data colored LEDs on the hand-held head unit (Supporting Information, Figure S3D) provide a green−yellow−red color indicator to the operator to communicate the status of the instrument and data system and detection of a chemical threat.

RESULTS AND DISCUSSION

Quadrupole ion trap mass analyzers are excellent candidates for miniaturized instruments because they are compatible with miniaturized vacuum systems allowing the size, weight, and power consumption of the mass spectrometer to be reduced. Unique among mass analyzers, ion traps operate well even in the millitorr regime, several orders of magnitude higher than other mass analyzers. Collisions with small neutral molecules after ion injection kinetically cool the ions allowing the ion cloud to relax to the physical center of the mass analyzer. Buffering the motion of trapped ions traps increases trapping efficiency and gives a more dense ion cloud—simultaneously improving both the sensitivity and mass resolution of the device.[30]

Normal operating parameters produced a maximum mass-to-charge range of 100−925 amu, using resonance ejection (ac_{freq} = 369 kHz),[33,34] as verified with sodiated poly(ethylene glycol) ions, $[PEG + Na]^+$ (Figure 3A). Ion introduction periods were between 15 and 25 ms, during which time the vacuum manifold pressure increased to approximately 100 mTorr. After ion introduction the manifold pressure was allowed to drop to approximately 1.5 mTorr, which occurred 2 s after ion injection. Details of operating conditions are given in the Supporting Information, section 6. Briefly, for mass analysis, the rf amplitude was scanned at a rate of 12 000 amu/s. Total mass spectral scan times were 2.3 s; under these operating conditions and a mass resolution of 2 amu fwhm was obtained across the mass range. However, under the best operating conditions in which the number of ions introduced into the trap was carefully controlled and with appropriately tuned rf/ac amplitudes and frequencies, the fwhm for analyte peaks can have values of ca. 0.6 Th (Supporting Information, Figure S6). Figure 3B shows a mass spectrum of the controlled substance ketamine, a well-known drug of abuse, recorded using LTP as the ionization source. The isotopic pattern for ketamine clearly resolves the chlorine isotopes of the molecular ion with less than a 10% valley separating the ^{35}Cl isotope at m/z 238 from the ^{37}Cl isotope at m/z 240. A key functionality of ion trap mass analyzers is that multiple stages of tandem MS can be performed using a single analyzer,[35,36] allowing structural characterization, increased confidence in analyte identification (via fragment ions), and enhanced detection limits by improving the signal-to-noise ratio. This functionality is illustrated for the model compound cocaine in Figure 4.

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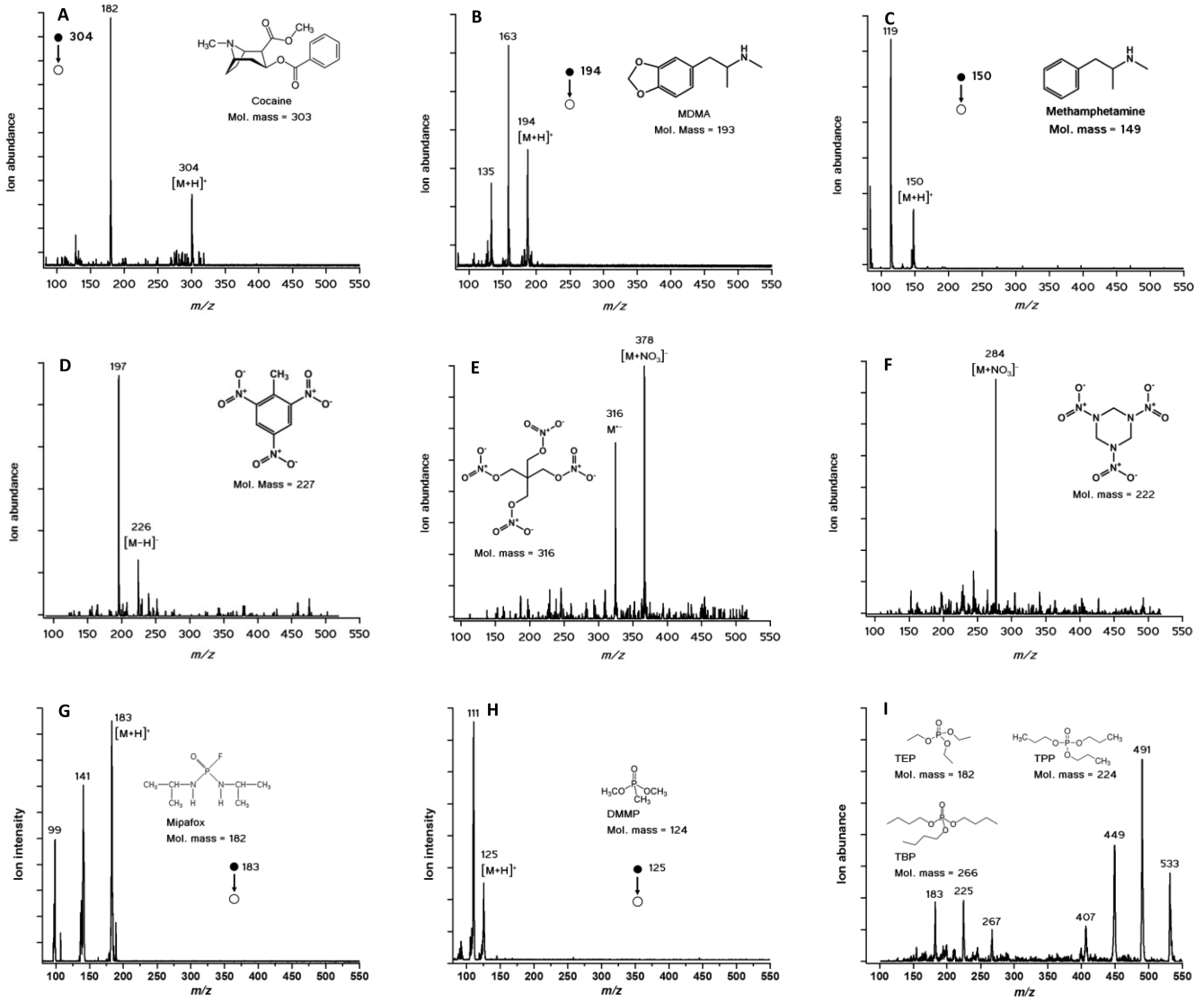

Figure 5. (A–F) Ionization and detection of nine compounds using a coaxial LTP ionization source integrated into a hand-held head unit, (D–F) in negative ion mode, others positive. (A) MS/MS spectrum, 2 μg/cm^2 cocaine sampled directly from human fingers. (B) MS/MS spectrum, 10 μg/cm^2 3,4-methylenedioxy-*N*-methylamphetamine (MDMA or ecstasy) sampled directly from the inside corners of a cardboard box. (C) MS/MS spectra, 10 μg/cm^2 sampled directly from textbook paper. (D–F) TNT, PETN, and RDX, <1 μg/cm^2 sampled directly from glass melting point tubes. Melting point tubes were dipped directly into the standard solution for approximately 2 s and then removed; amounts less than 1 μg were deposited on the surface. (G) MS/MS spectra, 1 μg/cm^2 mipafox sampled directly from a nitrile glove. (H) MS/MS spectrum, 1 μg/cm^2, dimethyl methylphosphonate (DMMP) sampled from cotton. (I) MS spectrum of a mixture of triethyl, tripropyl, and tributyl phosphate, 1 μg/cm^2, sampled from cotton.

Power consumption, rf amplitude, and manifold pressure were recorded over a series of three consecutive scans. The peak power draw for the instrument was 144 W and coincided with the maximum rf voltage output (~6.2 kV_{p-p}) generated during mass analysis (Supporting Information, Figure S7). The rf amplitude output was measured directly from the rf coil with a high-voltage rf probe (Tektronix p6015A (3.0 pF); Beaverton, OR) in parallel with the amplification circuit. More notable, however, is that the average power consumption is 65 W, over the three scans, much of which is used by the vacuum system in maintaining manifold pressures, which rise to 1×10^{-1} Torr when the DAPI valve is opened and then fall to about 10^{-3} Torr in 2 s when mass analysis is performed (Supporting Information, Figure S7). The cumulative current draw for the entire instrument was measured with a Fluke current clamp (Fluke; Everett, WA) placed between the ac/dc converter at the wall outlet and the main instrument-power input. It should be noted that monitoring power consumption in response to systemwide events, such as the rapid increase in manifold pressure (~100 mTorr; 15–25 ms DAPI pulse) during ion introduction, is of diagnostic value. In this case, the current draws from the mechanical and turbomolecular pump in response to elevated manifold pressures are identifiable, providing information about the performance of individual instrument components relative to system-level events and operational conditions. With a single battery pack (and helium tank) the instrument could be operated autonomously for up to 1.5 h, and this is limited by the power consumption of the vacuum system rather than the mass range used during analysis or the power necessary to operate the ion source. The 1.5 h of operation includes time and power consumption required to bring the manifold pressure from atmosphere to 1.0×10^{-5}

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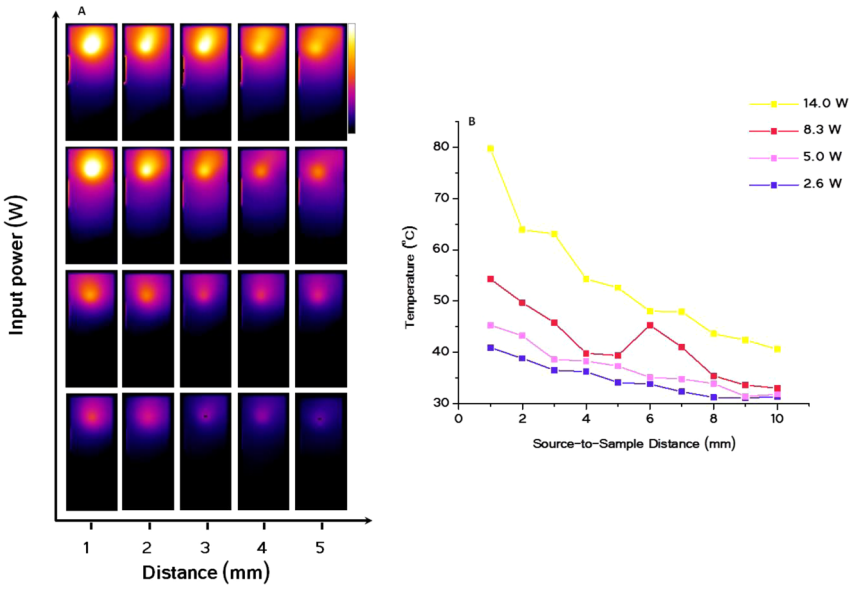

Figure 6. (A) Thermographic images of an LTP source with 1.14 cm diameter spot size (~1.0 cm^2) at four power input settings (2.6, 5.0, 8.3, and 14.0 W) and source stand-off distances of 1−5 mm: surface temperature range of ~35 °C (2.6 W at 5 mm) to 80 °C (14.0 W at 1 mm). (B) Maximum surface temperature plots at stand-off distances of 10 mm.

Torr and continuous operation of the source voltage, DAPI valve, and data system.

Mass spectrometer instrumentation is inherently complex due to heavily integrated electronic control that is needed in order to simultaneously, and synchronously, operate multiple processes to produce a single mass spectrum. Electronic systems utilized by these instruments include instrument state/status communication(s), event timing, waveform generation, voltage amplification, and data acquisition. Failure to execute the required process with high fidelity (e.g., nonlinear rf amplitude generation) will lead directly to poor mass resolution, incorrect mass assignments, and truncated mass ranges. In this implementation, the values for the proportional−integral−derivative (PID) controller are set through the software which avoids having to make hardware modifications to physical circuits that are sensitive to the tolerances of individual components and provides a method for error correction during periods of extended operation that may lead to mass drift caused by heat, component fatigue, or changes in the surrounding environment. Implementation of the PID controller provided a mass drift that ranged from 0.6 to −0.2 amu, whereas the analog feedback control circuit implemented in earlier instruments had a drift ranging from 1.7 to −0.5 amu; both tests were conducted over 1 h of continuous operation.[37] Furthermore, for portable instrumentation, updating feedback control parameters, or updating the entire feedback control algorithm itself using software as opposed to hardware modification(s), is particularly advantageous in situations where the instrument is deployed in an environment that is not immediately accessible to an operator or if the instrument is subject to an environmental change which requires preprogrammed or continuous updates.

A major objective of a portable instrument is the ability to perform in situ chemical analysis in which the target analyte(s), by definition, remain on the original substrate and in the natural environment. Thus, combining ambient ionization technology with a redesigned, highly portable, miniaturized mass spectrometer became a critical focus. Low-temperature plasma was selected as the primary ambient ionization source for this instrument because positive and negatively charged ions can be generated with roughly the same source conditions, plasmas are formed with low-amplitude voltage inputs, discharge gas flow rates are low, source fabrication is simple, and there is no requirement for additional solvents or chemical reagents to effect analyte ionization. Although the exact mechanisms of ionization for the analytes discussed here are unknown, it is generally accepted that the production of high-energy species such as helium metastables ultimately leads to the formation of water clusters that have direct roles in analyte ionization. For situations where increased thermal deposition was needed to assist desorption of compounds such as PETN and RDX[38] (vapor pressures at room temperature of 1.16×10^{-8} and 3.3×10^{-9} Torr, respectively), the source conditions could be tuned to supply additional input power (~8 W) to increase surface temperatures to as much as 50 °C at 1 mm standoff distance (Figure 5). Despite these advantages, helium is less dense than air and therefore has less contact with the sample surface and subsequent injection into the mass spectrometer during actuation of the DAPI valve at standoff distances larger than 5 mm, which was verified with Schlieren imaging of the coaxial LTP source connected to a Mini instrument. Nevertheless, the source and sampling conditions are sufficient to analyze compounds at sample-to-source distances between 1 and 5 mm.

Critical to in situ chemical detection is the ability to successfully analyze a wide range of compounds from various surface types without the need to change or reoptimize ion source or sampling conditions.[39] As a demonstration of this flexibility, CWA (mipafox) and CWA simulants (dimethyl methylphosphonate and a mixture of triethyl, tripropyl, tributyl phosphate), illicit drugs (cocaine, methamphetamine, and MDMA), and explosives (trinitro toluene, PETN, and RDX) were analyzed directly from surfaces that include human skin, nitrile gloves, cotton, cardboard, and glass (Figure 5). The data were taken in both the positive and negative ion modes. Molecular ions for every chemical target except PETN and RDX were detected using the coaxial LTP source coupled to

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the Mini S without adjustment to the ionization conditions. PETN and RDX, due to their low vapor pressures, required increased input power to increase the temperature of the plasma to aid in surface desorption (Figure 6); no other operating parameters were modified, and this functionality was easily incorporated into the novice user interface as a special mode of operation. When holding operating conditions constant typical spectra showed reproducibility in relative abundance of 10% for the main ions.

CONCLUSION

A new miniaturized and highly portable mass spectrometer has been developed and can be configured for deployment in multiple configurations that target in situ chemical analysis and real-time detection of illicit drugs, explosives, and pharmaceuticals. Implementation of new technologies and instrument design strategies, i.e., an on-board FPGA in tandem with a DSP for waveform generation and rf error correction, and coupling of DAPI to ambient ionization source(s), improves instrument performance and versatility while keeping size, weight, and power consumption low. Furthermore, instrument control software, which has been minimal in our previous Mini mass spectrometers, has been a significant portion of the development effort. In particular, the novice user interface enables autonomous data acquisition, processing, and report generation based upon predefined user workflows and without continued user input. Together, all the design concepts implemented have produced an instrument that is highly portable, designed for in situ analysis, and may be effectively operated (i.e., decision(s) can be made) by personnel not familiar with instrumentation or chemical analysis.

ASSOCIATED CONTENT

Supporting Information

Additional information as noted in text. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Authors

*E-mail: Ouyang@purdue.edu. Phone: 765-494-2214.
*E-mail: Cooks@purdue.edu. Phone: 765-494-5263.

Notes

The authors declare no competing financial interest.

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REFERENCES

(1) Lebedev, A. T. *Annu. Rev. Anal. Chem.* **2013**, *6*, 163−189.
(2) Moore, D. S. *Rev. Sci. Instrum.* **2004**, *75*, 2499−2512.
(3) Manicke, N. E.; Abu-Rabie, P.; Spooner, N.; Ouyang, Z.; Cooks, R. G. *J. Am. Soc. Mass Spectrom.* **2011**, *22*, 1501−1507.
(4) Wilkinson, G. R. *N. Engl. J. Med.* **2005**, *352*, 2211−2221.
(5) Liu, J. J.; Cooks, R. G.; Ouyang, Z. *Anal. Chem.* **2011**, *83*, 9221−9225.
(6) Schafer, K. C.; Balog, J.; Szaniszlo, T.; Szalay, D.; Mezey, G.; Denes, J.; Bognar, L.; Oertel, M.; Takats, Z. *Anal. Chem.* **2011**, *83*, 7729−7735.
(7) Schafer, K. C.; Szaniszlo, T.; Gunther, S.; Balog, J.; Denes, J.; Keseru, M.; Dezso, B.; Toth, M.; Spengler, B.; Takats, Z. *Anal. Chem.* **2011**, *83*, 1632−1640.
(8) Ouyang, Z.; Cooks, R. G. *Annu. Rev. Anal. Chem.* **2009**, *2*, 187−214.
(9) Lange, F.; Ludwig, T. Presented at the HEMS Workshop, St. Pete Beach, FL, 2011.
(10) Mino, W. K. J.; Spencer, M.; Wylde, J.; Raftery, D. Vancouver, Canada, 2012.
(11) Yang, M.; Kim, T.-Y.; Hwang, H.-C.; Yi, S.-K.; Kim, D.-H. *J. Am. Soc. Mass Spectrom.* **2008**, *19*, 1442−1448.
(12) Contreras, J. A.; Murray, J. A.; Tolley, S. E.; Oliphant, J. L.; Tolley, H. D.; Lammert, S. A.; Lee, E. D.; Later, D. W.; Lee, M. L. *J. Am. Soc. Mass Spectrom.* **2008**, *19*, 1425−1434.
(13) Spaeder, T. A.; Walton, R. B. *Abstr. Pap.—Am. Chem. Soc.* **2003**, *226*, U128−U128.
(14) Gao, L.; Li, G.; Nie, Z.; Duncan, J.; Ouyang, Z.; Cooks, R. G. *Int. J. Mass Spectrom.* **2009**, *283*, 30−34.
(15) Gao, L.; Song, Q.; Patterson, G. E.; Cooks, R. G.; Ouyang, Z. *Anal. Chem.* **2006**, *78*, 5994−6002.
(16) Patterson, G. E.; Guymon, A. J.; Riter, L. S.; Everly, M.; Griep-Raming, J.; Laughlin, B. C.; Ouyang, Z.; Cooks, R. G. *Anal. Chem.* **2002**, *74*, 6145−6153.
(17) Ecelberger, S. A.; Cornish, T. J.; Collins, B. F.; Lewis, D. L.; Bryden, W. A. *Johns Hopkins APL Tech. Dig.* **2004**, *25*, 14−19.
(18) Smith, J. N.; Keil, A.; Likens, J.; Noll, R. J.; Cooks, R. G. *Analyst* **2011**, *135*, 994−1003.
(19) Li, L.; Chen, T.; Ren, Y.; Hendricks, P. I.; Cooks, R.; Ouyang, Z. *Anal Chem* **2014**.
(20) Gao, L.; Sugiarto, A.; Harper, J. D.; Cooks, R. G.; Ouyang, Z. *Anal. Chem.* **2008**, *80*, 7198−7205.
(21) Gao, L.; Cooks, R. G.; Ouyang, Z. *Anal. Chem.* **2008**, *80*, 4026−4032.
(22) Ouyang, Z.; Wu, G.; Song, Y.; Li, H.; Plass, W. R.; Cooks, R. G. *Anal. Chem.* **2004**, *76*, 4595−4605.
(23) Sanders, N. L.; Kothari, S.; Huang, G. M.; Salazar, G.; Cooks, R. G. *Anal. Chem.* **2010**, *82*, 5313−5316.
(24) Harper, J. D.; Charipar, N. A.; Mulligan, C. C.; Zhang, X.; Cooks, R. G.; Ouyang, Z. *Anal. Chem.* **2008**, *80*, 9097−9104.
(25) Wang, H.; Liu, J. J.; Cooks, R. G.; Ouyang, Z. *Angew. Chem., Int. Ed.* **2010**, *49*, 877−880.
(26) Takats, Z.; Wiseman, J. M.; Cooks, R. G. *J. Mass Spectrom.* **2005**, *40*, 1261−1275.
(27) Wilm, M. S.; Mann, M. *Int. J. Mass Spectrom.* **1994**, *136*, 167−180.
(28) Horning, E. C.; Horning, M. G.; Carroll, D. I.; Dzidic, I.; Stillwell, R. N. *Anal. Chem.* **1973**, *45*, 936−943.
(29) Hou, K.; Xu, W.; Xu, J.; Cooks, R. G.; Ouyang, Z. *Anal. Chem.* **2011**, *83*, 1857−1861.
(30) Stafford, G. C., Jr.; Kelley, P. E.; Syka, J. E. P.; Reynolds, W. E.; Todd, J. F. J. *Int. J. Mass Spectrom. Ion Processes* **1984**, *60*, 85−98.
(31) March, R. E.; Todd, J. F. J. *Quadrupole Ion Trap Mass Spectrometry*; John Wiley & Sons, Inc.: Hoboken, NJ, 2005.
(32) Guan, S.; Marshall, A. G. *Int. J. Mass Spectrom. Ion Processes* **1996**, *157−158*, 5−37.
(33) Charles, M. J.; McLuckey, S. A.; Glish, G. L. *J. Am. Soc. Mass Spectrom.* **1994**, *5*, 1031−1041.
(34) Goeringer, D. E.; Whitten, W. B.; Ramsey, J. M.; McLuckey, S. A.; Glish, G. L. *Anal. Chem.* **1992**, *64*, 1434−1439.
(35) Louris, J. N.; Cooks, R. G.; Syka, J. E. P.; Kelley, P. E.; Stafford, G. C.; Todd, J. F. J. *Anal. Chem.* **1987**, *59*, 1677−1685.
(36) McLuckey, S. A. *J. Am. Soc. Mass Spectrom.* **1992**, *3*, 599−614.
(37) Kirleis, M. Thesis, Purdue University, West Lafayette, Indiana, 2011.
(38) Ostmark, H.; Wallin, S.; Ang, H. G. *Propellants, Explos., Pyrotech.* **2012**, *37*, 12−23.

(39) Garcia-Reyes, J. F.; Harper, J. D.; Salazar, G. A.; Charipar, N. A.; Ouyang, Z.; Cooks, R. G. *Anal. Chem.* **2010**, *83*, 1084−1092.