

# Development of ambient sampling chemi/chemical ion source with dielectric barrier discharge

Lee Chuin Chen,<sup>a\*</sup> Zhan Yu,<sup>a,b</sup> Hiroko Furuya,<sup>b</sup> Yutaka Hashimoto,<sup>a</sup> Kenichi Takekawa,<sup>c</sup> Hiroaki Suzuki,<sup>d</sup> Osamu Ariyada<sup>d</sup> and Kenzo Hiraoka<sup>a\*</sup>



The development of a new configuration of chemical ionization (CI)-based ion source is presented. The ambient air containing the gaseous sample is sniffed into an enclosed ionization chamber which is of sub-ambient pressure, and is subsequently mixed with metastable species in front of the ion inlet of the mass spectrometer. Metastable helium atoms ( $\text{He}^*$ ) are used in this study as the primary ionizing agents and are generated from a dielectric barrier discharge (DBD) source. The DBD is powered by an AC high-voltage supply and the configuration of the electrodes is in such a way that the generated plasma is confined within the discharge tube and is not extended into the ionization chamber. The construction of the ion source is simple, and volatile compounds released from the bulky sample can also be analyzed directly by approaching the sample to the sampling nozzle. When combined with heated nitrogen or other desorption methods, its application can also be extended to non-volatile compounds, and the consumption for helium can be kept minimum solely for maintaining the stable discharge and gas phase ionization. Applications to non-proximate sample analysis, direct determination of active ingredients in drug tablets and the detection of trace explosive such as hexamethylene triperoxide diamine are demonstrated. Copyright © 2010 John Wiley & Sons, Ltd.

Supporting information may be found in the online version of this article.

**Keywords:** ambient sampling; Penning ionization; chemical ionization; dielectric barrier discharge; HMTD explosive

## Introduction

Besides the original atmospheric pressure chemical ionization (APCI) and its variants (e.g. desorption-APCI<sup>[1]</sup> and atmospheric pressure solids analysis probe<sup>[2]</sup>), ionization of volatile and non-volatile compounds could also be achieved by Penning ionization alone, or followed by the subsequent chemical ionization using metastable species.<sup>[3–8]</sup> One prominent example is the commercial direct analysis in real time (DART) ion source,<sup>[7,8]</sup> where the sample is placed under the heated metastable helium ( $\text{He}^*$ ) stream directed toward the ion inlet of the mass spectrometer. Modification on the DART design with a radio-frequency discharge source also exists.<sup>[9]</sup> Besides ionization, desorption of non-volatile compounds can also be achieved directly by the flowing afterglow of a DC atmospheric pressure glow discharge and radio-frequency plasma torch.<sup>[10–12]</sup>

Desorption/ionization of sample deposited on one of the electrodes of dielectric barrier discharge (DBD) has also been introduced by Zhang.<sup>[13]</sup> Recently, an extended version of DBD ionization (DBDI) using DBD torch has been reported by Zhang's and Cooks's groups in which they call it low-temperature plasma probe (LTP).<sup>[14,15]</sup> Although the desorption process may differ, those ion sources that use the flowing metastable helium in ambient air likely share the same ionization mechanism. For example, the Penning ionization of the ambient gas such as water molecules by  $\text{He}^*$  produces reactant ions, e.g. protonated water clusters ( $[\text{H}_2\text{O}]_n\text{H}^+$ ), and the chemical ionization takes place similarly to that of APCI.<sup>[16]</sup>

Recently, we have also introduced a DART-like ion source using DBD for the generation of metastable helium.<sup>[17,18]</sup> Although DBD produces LTP with the gas temperature ranges below 700 K, the electron temperature is much higher ( $> 10\,000\text{ K}$ ),<sup>[19]</sup> posing possible damage or unwanted reaction with the sample. A strategy similar to the DART ion source has been adopted to keep the sample from the electric discharge by suitable configuration of the discharge electrodes. In our previous DBD ion source,<sup>[17]</sup> the gas heater was located before the discharge tube to prevent the annihilation of  $\text{He}^*$  due to the collision with the metallic wall along its steam path. Nevertheless, similar to other API ion sources that use flowing metastable helium, the typical flow rate of helium usually exceeds 0.5 l/min, thus, raising the concern of long-term operating cost of these instruments.

\* Correspondence to: Kenzo Hiraoka and Lee Chuin Chen, Clean Energy Research Center, University of Yamanashi, 4-3-11 Takeda, Kofu, Yamanashi 400-8511, Japan.

E-mail: hiraoka@yamanashi.ac.jp; leechuin.yamanashi@gmail.com

a Clean Energy Research Center, University of Yamanashi, 4-3-11 Takeda, Kofu, Yamanashi 400-8511 Japan

b College of Chemistry and Biology, Shenyang Normal University, Shenyang 110034, China

c Forensic Science Laboratory, Yamanashi Prefectural Police Headquarters, 312-4 Kubonakajima, Isawa, Fuefuki, Yamanashi 406-0036, Japan

d Arios Inc., Musashino 3-2-20, Akishima, Tokyo 196-0021, Japan

As has also been pointed out by Cody,<sup>[8]</sup> the discharge and ionization can be sustained at much lower helium flow rate, but considerable amount of helium needs to be consumed as the carrier gas to desorb and deliver the ionized sample to the ion-sampling orifice. Placing the discharge source closer to the orifice (with distance  $<3$  mm) could minimize the flow rate, but it would also limit the space where the sample needed to be located.

In this article, we present a new configuration of the DBD ion source of which, instead of blowing the sample with  $\text{He}^*$  in the open space, the neutral gaseous sample together with the ambient air is sniffed into an enclosed ionization chamber to react with  $\text{He}^*$  before the ion inlet of the mass spectrometer. Volatile compounds evaporated from sample could be easily detected in real time by approaching the sample close to the sampling nozzle. Non-volatile compound can also be analyzed with combination of hot carrier gas flowing toward the sniffing probe.

The use of sniffing type ion source is not new. Early work can date back to McLuckey's atmospheric sampling glow discharge ionization (ASGDI) ion source where the sample gas was leaked into a DC discharge chamber for ionization.<sup>[20]</sup> Converted GC-MS with the GC column replaced by a modified sample inlet also existed commercially for chemical sensing.<sup>[21]</sup> Recent examples include the secondary electrospray and APCI ion sources with external pumping system.<sup>[22,23]</sup> In our present configuration, the discharge is separated from the reaction/ionization chamber, and it can be adapted to the commercial ESI mass spectrometer without external pump. As both chemi (i.e. Penning) and chemical ionizations are the primary processes taking place in the present ion source, it will be referred as ambient sampling chemi/chemical ionization throughout this article.

## Experimental

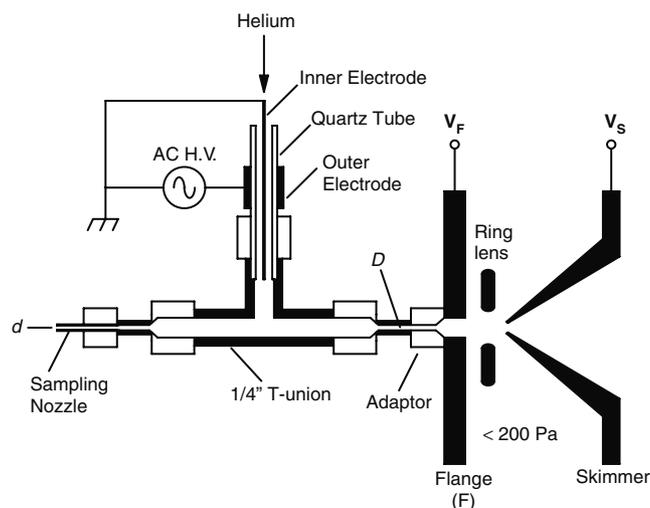
### Mass spectrometer

The experiments were performed using an orthogonal-acceleration time-of-flight mass spectrometer (AccuTOF, JEOL, Tokyo, Japan). The original cone shape ion-sampling orifice of the AccuTOF was replaced by a custom-made flange with a threaded hole situated at the center, which was coaxial with the skimmer of the mass spectrometer (Fig. 1). The internal electrodes of the mass spectrometer remained unchanged. The potential difference between the vacuum flange and the skimmer ( $|V_F - V_S|$ ) was tuned within 10–30 V during the operation. Design parameters of the ion source were chosen to ensure the pressure before the skimmer would not exceed 200 Pa, to maintain a proper operation of separation and transportation of ions inside the mass spectrometer.

### Ion source

The ion source was constructed from the commercially available stainless steel tubes and fittings and was attached to the vacuum flange via an adaptor. Stainless steel tubes were obtained from GL Scientific (Tokyo, Japan), and the fittings were from Swagelok (Nippon Swagelok FST Inc., Hyogo, Japan). All the parts are replaceable, allowing us to test different design and tubing dimension easily.

Figure 1 shows the configurations of the ion source, in which metastable helium atoms ( $\text{He}^*$ ) generated from a DBD source react

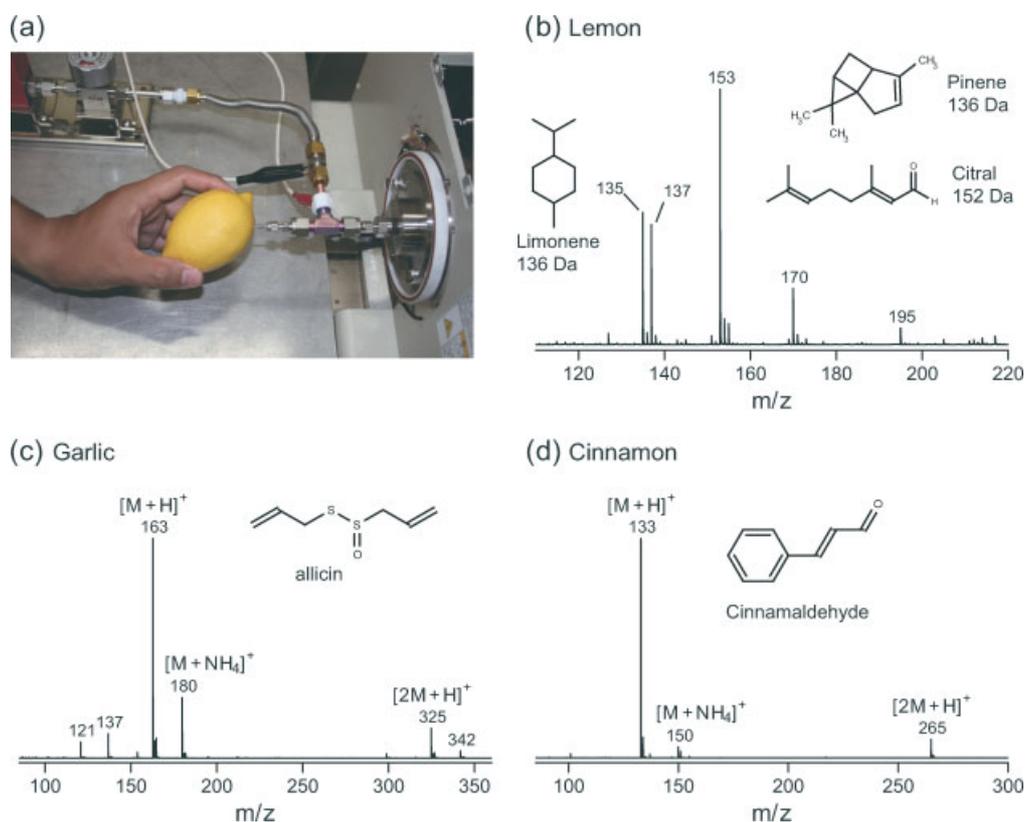


**Figure 1.** Schematic of the ambient sampling ion source using DBD for the generation of metastable helium atoms ( $\text{He}^*$ ). The ionization chamber formed by the stainless steel T-union is electrically shorted to the vacuum flange of the mass spectrometer. The distance from the center of the T-union to the flange (F) is 5 cm. In the default condition, the inner diameters for the sampling nozzle ( $d$ ) and ion transport channel ( $D$ ) are 0.25 and 0.8 mm, respectively, and AC HV is 2 kV peak-to-peak.

with the sample and ambient gases in the junction of a stainless steel T-union. The mixture of gases and ions was sucked into the vacuum via a channel with an inner diameter defined by  $D$ . Another closely related design parameter is  $d$ , the aperture size of the sampling nozzle. The combination of these parameters ( $d$  and  $D$ ) would affect the operating pressure inside the ionization chamber (T-union). Unless otherwise stated, the default dimensions for  $d$  and  $D$  are 0.25 and 0.8 mm, respectively. Ionization of sample presumably starts at the junction of the T-fitting which is of the same electric potential with the vacuum flange (F).

The DBD tube was a high-grade quartz tube (Vitreosil) with 6 mm outer diameter (OD) and 4 mm inner diameter (ID). The electrodes for the DBD consisted of a platinum wire (inner electrode), and a copper strip (outer electrode) that was adhered on the outer surface of the quartz tube. The sinusoidal signal of 20 kHz generated from a function generator was amplified by a power amplifier and was stepped up by a transformer to an AC high voltage (AC HV). The outer electrode was applied with the AC HV, and the inner electrode was held at ground potential. The resultant discharge direction was perpendicular to the helium flow, and could be confined within the DBD tube by adjusting the location of the external electrode, and extending the inner electrode toward the exit of the quartz tube. The extent of ionization and the total ion current (TIC) increased with the applied AC HV, but the abundance of ions would reach a plateau when the voltage exceeded 2000 V peak-to-peak (Fig. S1 in the supporting information). Throughout the experiment, the AC HV was set at approximately 2000 V peak-to-peak.

The flow rate of helium gas (99.999%) was monitored and controlled by a mass flow controller (Horiba, Kyoto, Japan). During the starting up of the ion source, the flow rate of helium was set at 400 ml/min for a few seconds to purge the unwanted impurities trapped within the discharge source, and after that, the flow rate was reduced to 80 ml/min for typical operation. During the experiment, the helium flow rate could be increased



**Figure 2.** (a) Photograph showing the operation of the ion source for the direct analysis of volatile compounds for bulk sample. (b–d) Direct analyses of the primary volatile compounds for lemon, garlic and cinnamon powder, respectively.

up to 900 ml/min without affecting the vacuum of the mass spectrometer.

For the measurement of the operating pressure of the ion source, the T-union was replaced by a four-way cross-union, and the additional channel was connected with a Baratron capacitance manometer (MKS Instruments, Andover, MA, USA). The operating pressure depended on the design parameters and the helium flow rate (Fig. S2 in the supporting information). For the default condition ( $d = 0.25$  mm,  $D = 0.8$  mm and helium flow rate of 80 ml/min), the operating pressure was about 70 Torr.

### Chemicals and sample preparation

Solvents and buffer solutions were of reagent grade and were used without further purification. Pure water was prepared using Milli-Q system (Millipore, Bedford, MA, USA). Natural samples (lemon, garlic, etc.), cigarette and beverage were obtained from local groceries stores. Decahydronaphthalene, 3-aminopropyltriethoxy silane and perfluorooctyltriethoxy silane were purchased from Sigma–Aldrich (St Louis, MO, USA). Hexamethylene triperoxide diamine (HMTD) and methamphetamine hydrochloride were synthesized in the laboratory according to the explosive and drug handling procedures approved by the Japan Police Department.

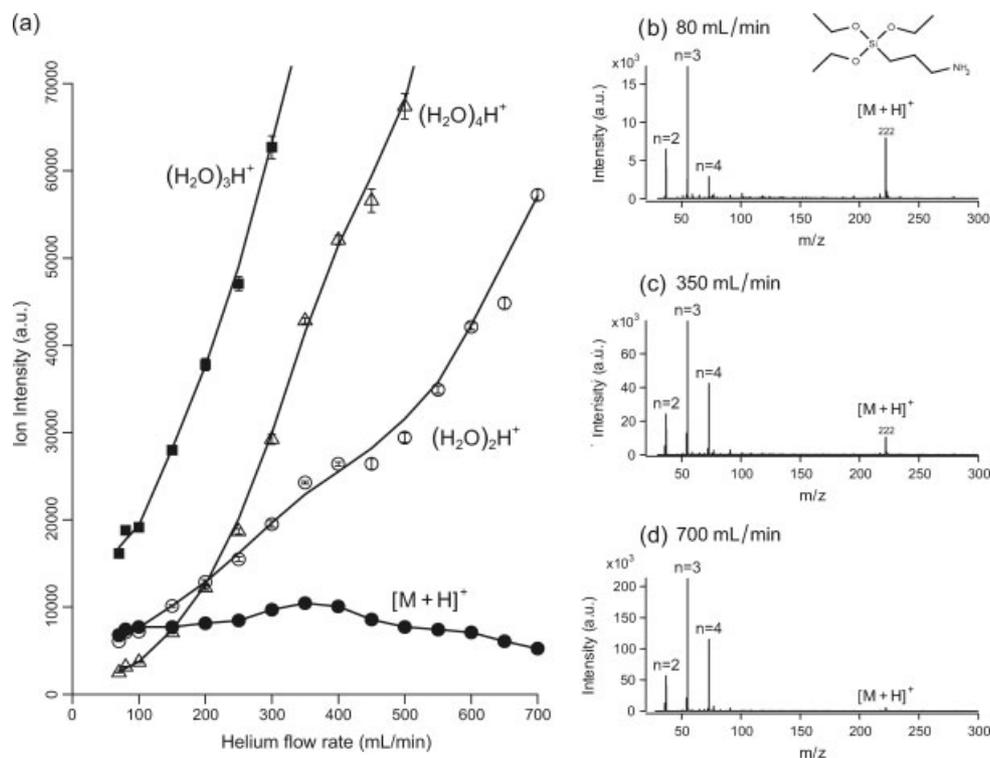
For the detection of methamphetamine, the hydrochloride salt of methamphetamine was dissolved and diluted in water. The initially prepared samples were of neutral pH, and the drug compound was in their ionic forms. The uncharged free form of the drug was volatile and could be easily released from the solution by pH adjustment of the liquid solution using NaOH.

## Results and Discussion

### Detection of volatile compounds

Detection of volatile compounds using the present ion source could be conducted directly by approaching the sample close to the sampling nozzle as illustrated in Fig. 2a. Due to the spatial clearance before the ion source, bulky object could be analyzed directly, and no additional carrier gas was necessary during the sampling process. Figure 2b–d shows the direct analyses of primary volatile compounds for lemon, garlic and cinnamon powder, respectively. The surface of the lemon peel was slightly scratched by hand to release the fragrance of lemon, which was primarily consisted of terpenes such as limonene and citral. The peaks at  $m/z$  135 and 137 in Fig. 2b are likely due to the hydride abstracted ( $[M-H]^+$ ) and protonated ( $[M+H]^+$ ) molecules of limonene. Verification measurement on pure limonene oil also showed these major peaks (data not shown). Contribution from pinene that is of the same molecular weight as limonene was also possible. The protonated citral ( $m/z$  153) was also detected in high abundance.

For freshly sliced garlic, allicin, a thiosulfate that was formed from the decomposition of alliin with the presence of alliinase (a garlic enzyme) when the garlic tissue was damaged,<sup>[24]</sup> was detected with high abundance as protonated molecule (Fig. 2c). Allicin can also form adduct with ammonium ions originated from the ammonia released from the sliced garlic,<sup>[24]</sup> or presence in the ambient air. In Fig. 2d, cinnamaldehyde that gives cinnamon its flavor and odor was detected as the protonated molecule at  $m/z$  133.



**Figure 3.** (a) Ion intensities for the protonated 3-aminopropyltriethoxy silane and the background ions originated from protonated water clusters ( $[\text{H}_2\text{O}]_n\text{H}^+$ ,  $n = 2, 3, 4$ ) at different helium flow rate using ambient sampling chemi/chemical ion source. (b–d) The corresponding mass spectra at the helium flow rate of 80, 350 and 700 ml/min, respectively.

### Dependence on helium flow rate

Figure 3a shows the effect of helium flow rate on the measured ion intensities for protonated analyte and the protonated water clusters ( $[\text{H}_2\text{O}]_n\text{H}^+$ ,  $n = 2, 3, 4$ ) background ions. The results were obtained from a single run of measurement with varying helium flow rate. The sample used here is 3-aminopropyltriethoxy silane, which was released to the ambient air by placing the bottle containing the analyte at about 0.5 m away from the ion source. A fan was used to circulate the air around the sampling nozzle. The corresponding mass spectra obtained at different helium flow rate are shown in Fig. 3b–d.

Stable glow discharge and ionization can be sustained at a minimum flow rate of 70 ml/min. As the helium flow rate increases, the ion abundances of protonated water clusters rise drastically. For example, at 700 ml/min (Fig. 3d), the ion signal for  $[\text{H}_2\text{O}]_3\text{H}^+$  was an order of magnitude stronger than that of 80 ml/min (Fig. 3b). On the contrary, the ion intensity for protonated analyte remained relatively constant with the change in helium flow rate. Although it has a maximum point at approximately 350 ml/min, satisfactory result could be obtained with less helium flow rate (e.g. 80–100 ml/min). Similar relationship was also observed for some of the background ions originated from the trace amount of plasticizers [e.g. bis(2-ethylhexyl) phthalate and dibutyl phthalate], which were present in the ambient air.

### Effect of ammonia for the detection of amines

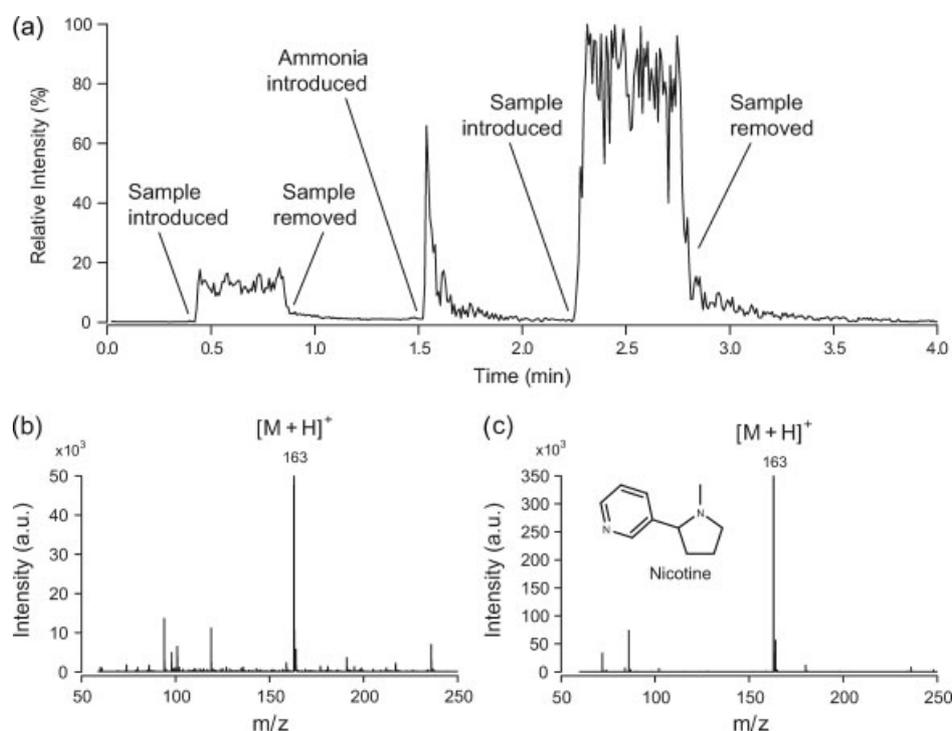
Because the ionization of samples took place in an enclosed ionization chamber, the detection of certain polar compounds such as amines could be affected due to its high adsorption on the metallic surface. Long retention and memory effect of these

compounds were observed particularly when the ion source was operated at room temperature. Besides heating the ion source to approximately 70–90 °C, we found that the addition of ammonia gas could greatly enhance the detection sensitivity for amines with reduced memory effect on the ion source.

A demonstration is given in Fig. 4 for the detection of nicotine from unlit cigarette. The ion source was not heated in this experiment to highlight the effect. Figure 4a shows the extracted ion chromatogram for the protonated nicotine at  $m/z$  163. The measurement was first performed without ammonia, and the sample was then taken away from the sampling nozzle. The ion source was kept idle for approximately 45 s, and ammonia was introduced into the ion source by placing a bottle containing ammonia solution ( $\text{NH}_4\text{OH}$ ) close to the sampling nozzle. The abundance of the protonated nicotine increased sharply at the moment when ammonia was introduced and decayed gradually. By maintaining the ammonia supply, the sample was reintroduced again into the ion source. The acquired mass spectra without and with the presence of ammonia are shown in Fig. 4b and c.

The addition of ammonia into the ion source could have two possible outcomes. One is the provision of proton donor (e.g.  $\text{NH}_4^+$ ) for the ionization. However, as ammonia has higher proton affinity than water, the protonation efficiency from  $\text{NH}_4^+$  ought not to be superior to the water-related reactant ions. Furthermore, ion signal enhancement was not observed for other non-amine compounds used in this study. Thus, the more possible and dominant effect of the ammonia gas was on the deactivation of the ion source for amines.

As ammonia molecules could compete with amines for the adsorption sites on the inner metallic wall surface of the ion source, the presence of ammonia could thus reduce or prevent



**Figure 4.** Detection of nicotine from unlit cigarette using the ambient sampling chemi/chemical ion source with the presence of ammonia in the ambient air. (a) Ion chromatogram for the protonated nicotine ( $m/z$  163,  $[M+H]^+$ ). (b and c) The corresponding averaged mass spectra of the unlit cigarette without (b) and with (c) the introduction of ammonia in the ambient air.

the adsorption loss of amines. Evidence to this conjecture was the finding that the introduction of ammonia gas had a 'cleaning effect' to the ion source (i.e. it could effectively remove the 'memory' of amine left from the previous measurement). For example, when we introduced a high concentration of nicotine to the ion source, the nicotine ion signal could be detected for prolonged period even the sample was completely removed away from the sampling nozzle. The inner surface of the ion source was presumed to be covered by amines, but they are spontaneously desorbed and re-adsorbed. The presence of ammonia in sufficient concentration could prevent the re-adsorption of amine back to the surface, and eventually purged the amine to the gas phase. This may explain the sudden increase and decay of nicotine ions as shown in Fig. 4a even without the introduction of the sample. It should be noted that the finding of this deactivation effect is not novel, as it had long been exploited in GC using ammonia carrier gas for reducing the sample retention.<sup>[25–27]</sup> However, it is fruitful for the optimization of the present ion source for the detection of high-polar analytes such as amines.

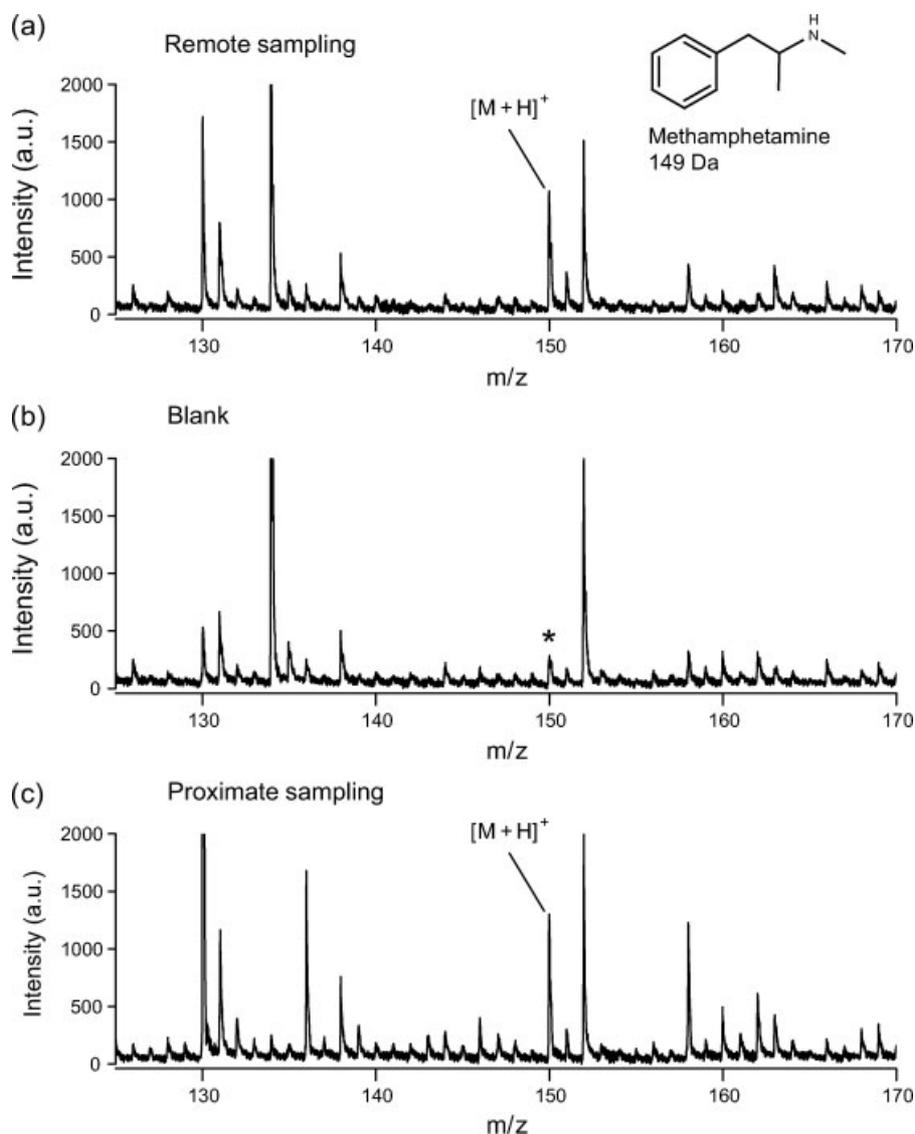
### Non-proximate analyte detection

Non-proximate analyte detection has been reported by several groups by remote sampling of ions produced by electrospray ionization (ESI) and desorption electrospray ionization (DESI).<sup>[28–30]</sup> However, it should be noted that the survival of ESI generated ions over a long ion transport tube could be very different from those generated by pure gaseous ionization methods, because a proportion of the detected ions could be originated from the desolvation of charged droplets that are co-sampled into the ion transport tube.<sup>[28]</sup> For gaseous ion, the transmission loss is more pronounced due to higher collision and thus, neutralization rate with the inner wall of the transport tube.

Rather than ions, the non-proximate analyte detection was demonstrated with the present ion source by remote sampling of neutral sample gas, over a long distance from the mass spectrometer. It was achieved by simply connecting the sampling nozzle to the T-union of the ion source via a 1-m long stainless steel tube (1/4" OD and 1/5" ID), while maintaining a short distance between the ionization chamber and the mass spectrometer. The sample transfer tube was further heated to 150 °C by a temperature controlled heater.

Application example of non-proximate analyte detection with the present ion source for the remote *in vivo* analysis of odor is depicted in Fig. S3 in the supporting information. Odor or breath analysis using mass spectrometric method is not new (examples can be found for conventional GC-MS,<sup>[31]</sup> or more recently for extractive electrospray ionization<sup>[32]</sup>), but the technique used here does not require the blowing of breath toward the ion source.

A comparison of sensitivity of the ion source with and without the extended sample transfer tube is shown in Fig. 5. The measurement was performed for an aqueous solution containing methamphetamine at a low concentration which was close to the detection limit of the mass spectrometer. The sample stocks were prepared in microtubes with pure water and were diluted subsequently. Sodium hydroxide was added to the final stock of the solution to adjust its pH to approximately 11 so that the drug compound was completely in their uncharged free form. Ammonium hydroxide was also added to the sample to provide the ammonia gas that could reduce the adsorption of methamphetamine onto the sampling tube during the sample transportation. The free form of methamphetamine was highly volatile and the cap of the microtube was closed immediately after the addition of NaOH and NH<sub>4</sub>OH mixtures. The mixture was vortexed and slightly warmed to accumulate the



**Figure 5.** (a) Mass spectrum for 20  $\mu\text{l}$  of 3 ng/ml (3 ppb) methamphetamine in NaOH and ammonia aqueous solution at a distance of 1 m away from the mass spectrometer using remote sampling chemi/chemical ion source. (b) Verification of the background ion signal with a blank sample. (c) Measurement of the methamphetamine of the same concentration without the extension of the sampling tube (default configuration).

methamphetamine in the headspace. A small hole was pierced through the microtube, and the measurement was made by sniffing the headspace above the liquid solution by the sampling nozzle.

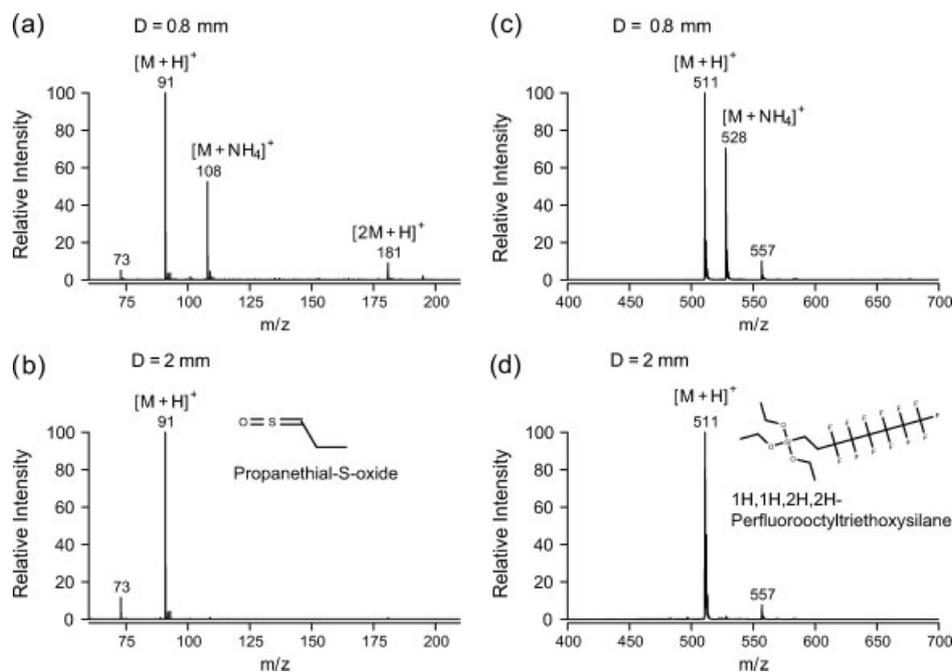
Figure 5a shows the mass spectrum of 3 ng/ml methamphetamine in 20  $\mu\text{l}$  aqueous solution obtained by remote sampling of the analyte with a 1-m long sample transfer tube. The verification of the background ions for a blank sample (containing same concentration of NaOH and  $\text{NH}_4\text{OH}$ , but without analyte) is depicted in Fig. 5b. A background peak labeled with asterisk (\*) coincides at the same  $m/z$  of the analyte, which could partly be due to the contamination during the sample preparation. The measurement of the sample with the same concentration and preparation procedure was repeated without the extended sampling tube and the mass spectrum obtained is shown in Fig. 5c. Both spectra (Fig. 5a and c) produce the analyte peaks with near equal signal to noise (S/N) ratio. In sum, unlike ions, it is demonstrated that low-loss transportation of neutral sample gases for the present ion source

could be achieved with sufficient heating and deactivation of the transport tube.

#### Design parameters for the ion source

Changing the design parameters that affects the operating pressure of the ion source could influence the observed mass spectra. For example, increasing the bore size of the ion transport channel,  $D$  from the default value of 0.8–2 mm, as an attempt to increase the ion transmission to the mass spectrometer, would also reduce the operating pressure in the ionization chamber (Fig. S2 in the supporting information).

The detection of propanethial-S-oxide released from freshly cut onion for  $D = 0.8$  and 2 mm is shown, respectively, in Fig. 6a and b. The measurements of 1H, 1H, 2H, 2H perfluorooctyltriethoxy silane, which has more oxygen atoms, are depicted in Fig. 6c and d, respectively. The inner diameter for the sampling nozzle ( $d$ ) in these measurements remained to be 0.25 mm. The significant feature of lower operating pressure is the near absence of ammonium adduct



**Figure 6.** Differences in mass spectra obtained with different design parameters. (a and b) Mass spectra of propanethial-S-oxide released from the freshly cut onion obtained by the ambient sampling ion source with different dimensions:  $D = 0.8$  mm (a) and  $D = 2$  mm (b), for the ion source. (c and d) Mass spectra of 1H, 1H, 2H, 2H-perfluorooctyltriethoxy silane obtained with  $D = 0.8$  mm (c) and  $D = 2$  mm (d). The inner diameter for the sampling nozzle (d) in these measurements remained to be 0.25 mm.

ions  $[M+NH_4]^+$  even with the presence of ammonia impurity in the ambient air. Same observation was also found for other analytes such as alliin, cinnamaldehyde and the oxygen-rich 18-crown-6 ether. The ion signal originated from the dimer in the case of lower operating pressure was also found to be weak, indicating less clustering of analytes.

In certain cases, operating the ion source at lower pressure is advantageous as it produces simpler mass spectra which are easier to interpret. However, for the conditions with  $D = 2$  mm, the required flow rate for helium to maintain satisfactory ionization efficiency is about four to five times higher compared to the default condition ( $D = 0.8$  mm). It also poses a problem if it is desirable to promote the ammonium adduct ions for the compounds that are more difficult to be protonated. Thus, depending on the analyte, there is a trade-off in selecting the optimum and yet cost-effective operating condition for the ion source. Nevertheless, the results here suggest that, as a future improvement in the present ion source, the tunability of these physical parameters and the operating pressure of the ion source should be made available to optimize the ionization of different compounds.

### Analysis for non-volatile compounds

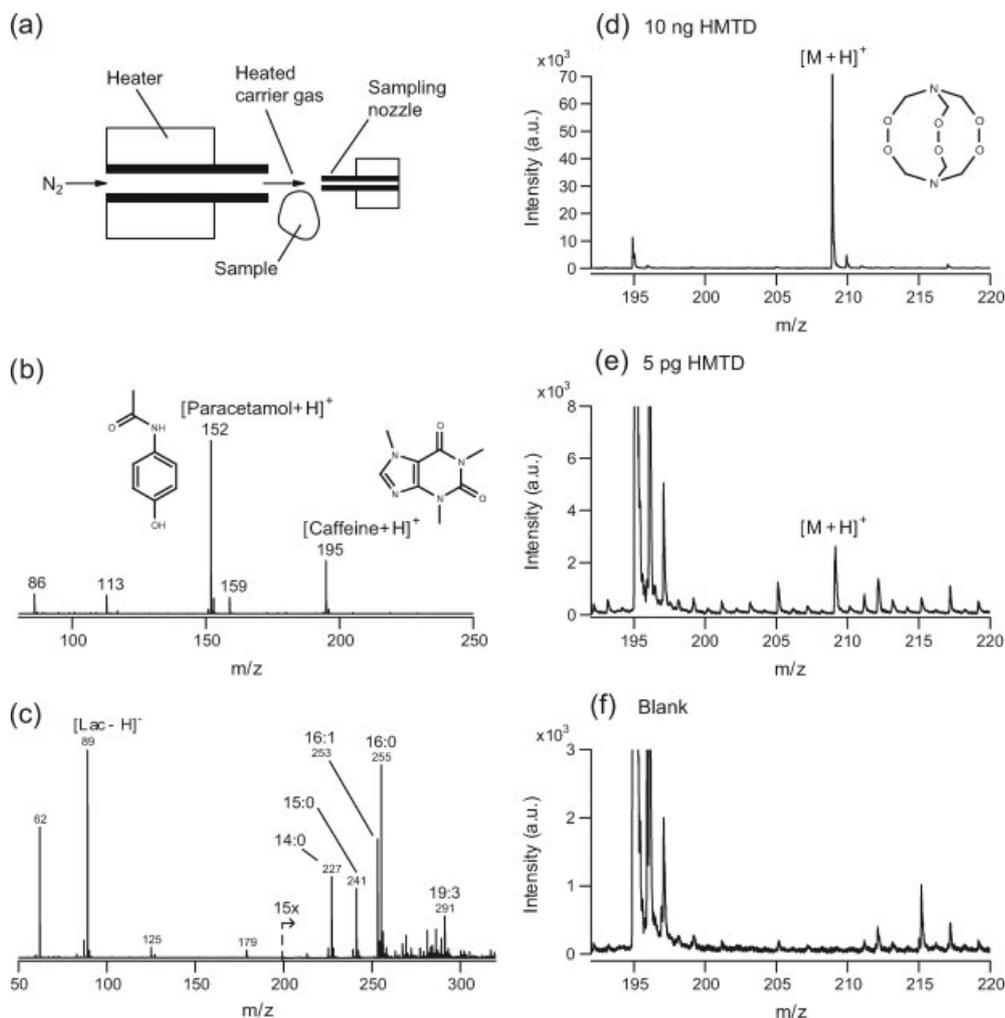
DART-like operation using the present ion source can be realized using an additional gas heater placed in front of the sampling nozzle as shown in Fig. 7a. Nitrogen was used as the carrier gas and was flowed through the gas heater heated at 150–200 °C. Similar to DART, direct analysis of solid and non-volatile compounds could be performed in real time by placing the sample within the flow stream of the hot carrier gas. The flow rate of nitrogen was adjusted between 0.5 and 1 l/min, whereas the flow rate for helium was kept at 80–100 ml/min. The ion source was also heated to approximately 90 °C to reduce the sample retention and memory effect.

Figure 7b shows the direct analysis of a local brand pharmaceutical tablet for common cold which consists of paracetamol and caffeine as its primary ingredients. Figure 7c is a negative ion mass spectrum of thumbprint pressed on a clean aluminum foil. The strongest ion signal originated from the deprotonated lactic acid ( $[Lac-H]^-$ ). Lactic acid is highly volatile and can be detected in high abundance even without heating. Dominant peaks in the high-mass region are due to the deprotonated molecules of free fatty acids such as palmitic acid (16:0), which are the secretion from the human skin glands.<sup>[33]</sup>

Trace analysis of HMTD, which is an explosive suspected for the 2005 London bombings,<sup>[34]</sup> was also performed with the present ion source using heated nitrogen carrier gas for thermal desorption. The HMTD was dissolved in acetone and a 1- $\mu$ l diluted sample solution was deposited on the clean glass substrate. The mass spectra for 10 ng and 5 pg HMTD are depicted in Fig. 7d and e, respectively. Verification of the background ions from the glass substrate deposited with blank sample (acetone solution without HMTD) is shown in Fig. 7f. The background spectrum shows no sign of the analyte, thus confirming the detection limit for this explosive in the picogram level.

### Conclusion

We have demonstrated an ambient sampling ion source that has a close resemblance to CI ion source in which the ionization takes place in an enclosed chamber which is of sub-ambient pressure. Because the ions are generated in the region close to the mass spectrometer, the survival of ions will not be affected in the operation of non-proximate analyte detection. Efficient transportation of neutral sample gases over a long distance is also



**Figure 7.** (a) Schematic of the ion source for the analysis of non-volatile compounds. The sample was placed in between the gas heater and the ion source, and the sample was thermally desorbed and delivered to the sampling nozzle by the flowing stream of heated nitrogen. (b) Real time and direct analysis of a pharmaceutical tablet for common cold. (c) Negative ion mode mass spectrum for finger print pressed on a clean aluminum foil. (d and e) Direct detection of 10 ng (d) and 5 pg (e) HMTD deposited on a glass substrate. (f) Background ions of a blank sample to verify for the trace detection of HMTD.

possible with sufficient heating and deactivation of the sample transfer tube. Regarding the limit of detection, at this stage, it is about 1 ppb for the methamphetamine in solution and 5 pg for solid HMTD. Overall, the sensitivity is about five times higher than our previously published ion source<sup>[17,18]</sup> that used flowing metastable helium in the atmospheric pressure. Quantitative analysis can be done by the addition of suitable compound that acts as the internal standard to the sample during the measurement.

### Acknowledgements

This work was funded by the Safety/Security S & T Project from the Japanese Ministry of Education, Culture, Sports, Science and Technology. L. C. C. was supported by the Japan Society for the Promotion of Science (JSPS).

### References

- [1] S. Peng, N. Ahlmann, K. Kunze, W. Nigge, M. Edler, T. Hoffmann, J. Franzke. Thin-layer chromatography combined with diode

laser desorption/atmospheric pressure chemical ionization mass spectrometry. *Rapid Commun. Mass Spectrom.* **2004**, *18*, 1803.

- [2] C. N. McEwen, R. G. McKay, B. S. Larsen. Analysis of Solids, Liquids, and Biological Tissues Using Solids Probe Introduction at Atmospheric Pressure on Commercial LC/MS Instruments. *Anal. Chem.* **2005**, *77*, 7826.
- [3] D. Faubert, G. J. C. Paul, J. Giroux, M. J. Bertrand. Selective fragmentation and ionization of organic compounds using an energy-tunable rare-gas metastable beam source. *Int. J. Mass Spectrom. Ion Process.* **1993**, *124*, 69.
- [4] M. Tsuchiya, H. Kuwabara. Liquid ionization mass spectrometry of nonvolatile organic compounds. *Anal. Chem.* **1984**, *56*, 14.
- [5] K. Hiraoka, S. Fujimaki, S. Kambara, H. Furuya, S. Okazaki. Atmospheric-pressure Penning ionization mass spectrometry. *Rapid Commun. Mass Spectrom.* **2004**, *18*, 2323.
- [6] K. Hiraoka, H. Furuya, S. Kambara, S. Suzuki, Y. Hashimoto, A. Takamizawa. Atmospheric-pressure Penning ionization of aliphatic hydrocarbons. *Rapid Commun. Mass Spectrom.* **2006**, *20*, 3213.
- [7] R. B. Cody, J. A. Laramée, H. D. Durst. Versatile New Ion Source for the Analysis of Materials in Open Air under Ambient Conditions. *Anal. Chem.* **2005**, *77*, 2297.
- [8] R. B. Cody. Observation of Molecular Ions and Analysis of Nonpolar Compounds with the Direct Analysis in Real Time Ion Source. *Anal. Chem.* **2009**, *81*, 1101.

- [9] Y. Cho, C. Lin, J. Shiea. Direct analysis in real time/mass spectrometry for continuously monitoring the states of ongoing chemical reactions involved with volatile compounds. *56th ASMS Conference on Mass Spectrometry*. Denver, Colorado, **2008**.
- [10] F. J. Andrade, J. T. Shelley, W. C. Wetzel, M. R. Webb, G. Gamez, S. J. Ray, G. M. Hieftje. Atmospheric Pressure Chemical Ionization Source. 1. Ionization of Compounds in the Gas Phase. *Anal. Chem.* **2008**, *80*, 2646.
- [11] F. J. Andrade, J. T. Shelley, W. C. Wetzel, M. R. Webb, G. Gamez, S. J. Ray, G. M. Hieftje. Atmospheric Pressure Chemical Ionization Source. 2. Desorption-Ionization for the Direct Analysis of Solid Compounds. *Anal. Chem.* **2008**, *80*, 2654.
- [12] L. V. Ratcliffe, F. J. M. Rutten, D. A. Barrett, T. Whitmore, D. Seymour, C. Greenwood, Y. Aranda-Gonzalvo, S. Robinson, M. McCoustra. Surface Analysis under Ambient Conditions Using Plasma-Assisted Desorption/Ionization Mass Spectrometry. *Anal. Chem.* **2007**, *79*, 6094.
- [13] N. Na, M. Zhao, S. Zhang, C. Yang, X. Zhang. Development of a Dielectric Barrier Discharge Ion Source for Ambient Mass Spectrometry. *J. Am. Soc. Mass Spectrom.* **2007**, *18*, 1859.
- [14] Y. Zhang, X. Ma, S. Zhang, C. Yang, Z. Ouyang, X. Zhang. Direct detection of explosives on solid surfaces by low temperature plasma desorption mass spectrometry. *Analyst* **2009**, *134*, 176.
- [15] J. D. Harper, N. A. Charipar, C. C. Mulligan, X. Zhang, R. G. Cooks, Z. Ouyang. Low-Temperature Plasma Probe for Ambient Desorption Ionization. *Anal. Chem.* **2008**, *80*, 9097.
- [16] J. A. Laramee, R. B. Cody. Chemi-ionization and direct analysis in real time (DART) mass spectrometry. In *The Encyclopedia of Mass Spectrometry – Volume 6: Ionization Methods*, M. L. Gross, R. M. Caprioli (Eds). Elsevier: Oxford, UK, **2007**, pp. 377–387.
- [17] L. C. Chen, Y. Hashimoto, H. Furuya, K. Takekawa, T. Kubota, K. Hiraoka. Rapid detection of drugs in biofluids using atmospheric pressure chemi/chemical ionization mass spectrometry. *Rapid Commun. Mass Spectrom.* **2009**, *23*, 333.
- [18] L. C. Chen, H. Suzuki, K. Mori, O. Ariyada, K. Hiraoka. Mass Spectrometric Detection of Gaseous Hydrogen Peroxide in Ambient Air Using Dielectric Barrier Discharge as an Excitation Source. *Chem. Lett.* **2009**, *38*, 520.
- [19] C. Tendero, C. Tixier, P. Tristant, J. Desmaison, P. Leprince. Atmospheric pressure plasmas: A review. *Spectrochim. Acta B* **2006**, *61*, 2–30.
- [20] S. A. McLuckey, G. L. Glish, K. G. Asano, B. C. Grant. Atmospheric sampling glow discharge ionization source for the determination of trace organic compounds in ambient air. *Anal. Chem.* **1988**, *60*, 2220.
- [21] R. Marsili. Combining mass spectrometry and multivariate analysis to make a reliable and versatile electronic nose. In *Flavor, Fragrance, and Odor Analysis*. R. Marsili (Ed). Marcel Dekker: New York, **2002**, pp. 349–374.
- [22] P. Martínez-Lozano, J. F. de la Mora. On-line Detection of Human Skin Vapors. *J. Am. Soc. Mass Spectrom.* **2009**, *20*, 1060.
- [23] H. Inoue, H. Hashimoto, S. Watanabe, Y. T. Iwata, T. Kanamori, H. Miyaguchi, K. Tsujikawa, K. Kuwayama, N. Tachi, N. Uetake. Thermal desorption counter-flow introduction atmospheric pressure chemical ionization for direct mass spectrometry of ecstasy tablets. *J. Mass Spectrom.* **2009**, *44*, 1300.
- [24] U. B. Pandey. Garlic. In *Handbook of Herbs and Spices*, K. V. Peter (Ed). CRC Press: Boca Raton, **2001**, pp. 180–194.
- [25] M. Abdel-Rehim, M. Hassan, H. Ehrsson. Capillary gas chromatography of amines with ammonia as carrier gas. *J. High Resolut. Chromatogr.* **1990**, *13*, 252.
- [26] M. Abdel-Rehim, L. Zhang, M. Hassan, H. Ehrsson. Mixture of ammonia and helium as a carrier gas for capillary gas chromatography. *J. Microcolumn Sep.* **1993**, *5*, 537.
- [27] L. Ghaoui, K. Pell, K. Chritz, R. N. Loomis. Analysis of amine compounds by capillary gas chromatography using ammonia-helium carrier gas. *J. High Resolut. Chromatogr.* **1995**, *18*, 157.
- [28] B. Lin, J. Sunner. Ion transport by viscous gas flow through capillaries. *J. Am. Soc. Mass Spectrom.* **1994**, *5*, 873.
- [29] I. Cotte-Rodriguez, R. G. Cooks. Non-proximate detection of explosives and chemical warfare agent simulants by desorption electrospray ionization mass spectrometry. *Chem. Commun.* **2006**, 2968.
- [30] R. B. Dixon, M. S. Bereman, D. C. Muddiman, A. M. Hawkrige. Remote Mass Spectrometric Sampling of Electrospray- and Desorption Electrospray-Generated Ions Using an Air Ejector. *J. Am. Soc. Mass Spectrom.* **2007**, *18*, 1844.
- [31] I. Blank. Gas chromatography-olfactometry in food aroma analysis. In *Flavor, Fragrance, and Odor Analysis*, R. Marsili (Ed). Marcel Dekker: New York, **2002**, pp. 297–331.
- [32] J. Ding, S. Yang, D. Liang, H. Chen, Z. Wu, L. Zhang, Y. Ren. Development of extractive electrospray ionization ion trap mass spectrometry for in vivo breath analysis. *Analyst* **2009**, *134*, 2040.
- [33] T. Takemura, P. Wertz, K. Sato. Free fatty acids and sterols in human eccrine sweat. *Br. J. Dermatol.* **1989**, *120*, 43.
- [34] London bombers used everyday materials – US police. *Reuters*. 4 Aug **2005**.