Analytica Chimica Acta 973 (2017) 59–67

Contents lists available at ScienceDirect

Analytica Chimica Acta

journal homepage: www.elsevier.com/locate/aca

Non-proximate mass spectrometry using a heated 1-m long PTFE tube and an air-tight APCI ion source

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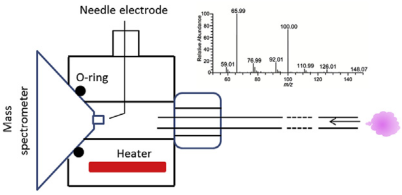
HIGHLIGHTS

- Non-proximate mass spectrometry for the trace-level gas analysis was developed.
- Using a 1-m long flexible PTFE tube, it can be applicable to complicated-shape real-world samples.
- By atmospheric pressure chemical ionization in the airtight ion source, sub-pg limits of detection were attained.
- Adsorption of less-volatility compounds was negligible with the tube temperature at 130° C.
- Novel experimental results obtained were fully examined by density functional theory calculations.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 15 January 2017
Received in revised form
19 March 2017
Accepted 24 March 2017
Available online 10 April 2017

Keywords:
Non-proximate mass spectrometry
Gas analysis
APCI
Rice hopper
Hydrogen peroxide
DFT calculations

ABSTRACT

Direct and rapid trace-level gas analysis is highly needed in various fields such as safety and security, quality control, food analysis, and forensic medicine. In many cases, the real samples are bulky and are not accessible to the space-limited ion source of the mass spectrometer. In order to circumvent this problem, we developed an airtight atmospheric-pressure chemical ionization (APCI) ion source equipped with a flexible 1-m-long, 2-mm-i.d. PTFE sniffing tube. The ambient air bearing sample gas was sucked into the heated PTFE tube (130 °C) and was transported to the air-tight ion source without using any extra pumping system or a Venturi device. Analytes were ionized by an ac corona discharge located at 1.5 mm from the inlet of the mass spectrometer. By using the airtight ion source, all the ionized gas in the ion source was introduced into the vacuum of the mass spectrometer via only the evacuation of the mass spectrometer (1.6 l min^{-1}). Sub-pg limits of detection were obtained for carbaryl and trinitrotoluene. Owing to its flexibility and high sensitivity, the sniffing tube coupled with a mass spectrometer can be

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http://dx.doi.org/10.1016/j.aca.2017.03.044

used as the stethoscope for the high-sensitive gas analysis. The experimental results obtained for drugs, hydrogen peroxide and small alkanes were discussed by DFT calculations.

1. Introduction

For the analysis of samples that are not accessible to the mass spectrometers, various techniques have been developed for remote sampling methods. In 2002, Chang et al. developed fused-droplet electrospray ionization mass spectrometry [1]. Ultrasonically nebulized sample solution was transported to the electrospray ionization ion source through a 50-cm-long, 0.9-cm-i.d. PTFE tube. The plume was fused with electrospray charged droplets in the ion source. This technique was well suited for remote sampling followed by electrospray ionization just in front of the mass spectrometer inlet. The remote sampling coupled with electrospray ionization was widely applied not only to the nebulized liquid samples [2] but also to laser-ablated plumes [3], desorbed/gasified molecules [4–6], particulates [7] and expiration [8].

Cooks and his coworkers developed non-proximate detection of explosives and chemical warfare agent simulants by desorption electrospray ionization (DESI) mass spectrometry [9,10]. In their work [10], the remote DESI source and the mass spectrometer were connected directly by a long 1.8-mm-i.d. stainless steel ion transport tube which allowed the transport of ions generated by DESI to the mass spectrometer. They found that ion intensities decreased by two and three orders of magnitude with the ion transfer tube lengths of 1 m and 3 m compared with that measured near the inlet with 2 mm distance [11]. This is due to neutralization of ions on the wall of the metal capillary. This diffusion loss of ions can be suppressed if the carrier gas velocity is increased by using an extra pumping or a Venturi devise. In 2007, Dixon et al. coupled a Venturi device as an extra suction of air to transport remotely generated ions from the ESI and DESI source [12]. They claimed that this technique should be readily applicable to other direct ionization methods. In 2009, Schaefer et al. discovered that rapid evaporation of biological tissues using an electrosurgical knife yielded gaseous molecular ions of the major tissue components, e.g., phospholipids [13]. Evaporated ionic plume was transported to a distant mass spectrometer employing a Venturi device and 1–2 m long PTFE tubing. This technique coupled with an endoscope was applied to in vivo diagnosis of gastrointestimal tissues [14]. He et al. designed air flow assisted ionization (AFAI) for remote-sampling ambient mass spectrometry [15]. By using an extra pumping system, the effective capture and remote transport of charged droplets leading to significant improvement of detection sensitivity were attained. Garimèlla et al. made a detailed analysis of gas-flow assisted ion transfer by means of additional pumping system [16]. Hydrodynamic simulations and experimental tests demonstrated that laminar flow can transfer ions over a distance as long as 6 m. The larger the inner diameter of the tube and the higher the gas velocity, the higher the transfer efficiency.

For the non-proximate mass spectrometry for trace gas analysis, various methods have been developed. In SIFT-MS, trace gas molecules in air/breath samples introduced into the helium carrier gas through the heated sampling line were ionized by selected reagent ions of H_3O^+, NO^+, or O_2^+. Absolute concentrations of trace gases can be determined down to ppb levels without sample collection and calibration. Smith and Španěl showed versatility of SIFT-MS in many areas of research and enterprise such as physiology, halitosis, addiction, renal failure, bacterial infection, cancer, diabetes, inflammatory bowel disease, food science, environmental health and security [17]. Prince, Milligan and McEwan made real-time atmospheric monitoring of volatile organic chemicals (VOCs) in air by the new generation of SIFT-MS instruments [18]. Five VOCs, ethene, ethanol, 1,3-butadiene, benzene and toluene, were continuously monitored from a stationary sampling point over a 4-days period. 1,3-butadiene was detected at a concentration of 9 pptv level [18]. More recently, Kumar et al. [19] applied SIFT-MS to the analysis of exhaled breath for volatile organic compound profiling of esophago-gastric cancer. They made quantification of VOCs in the exhaled breath from 3 groups of patients: esophago-gastic cancer, noncancer diseases of the upper gastro-intestinal tract and a healthy upper gastrointestinal tract cohort. Among 17 VOCs investigated, the concentrations of 4 VOCs, hexanoic acid, phenol, methyl phenol and ethyl phenol, were found to be significantly different among cancer and positive control groups.

Proton-transfer reaction mass spectrometry (PTR-MS) is a modified version of SIFT-MS [20,21]. The mass filter that is employed in SIFT is dispensed with a hollow-cathode discharge source that generates H_3O^+. This modification resulted in some two orders of magnitude higher sensitivity for PTR-MS than for SIFT-MS [21]. PTR is based on reactions of H_3O^+ ions, which provoke non-dissociative proton transfer to most of common VOCs. Because the proton donor concentration is largely unchanged by the addition of the trace-level analyte sample, measurement of the (proton donor)/(proton acceptor) ion signal ratio allows the absolute concentration of the acceptor molecules to be calculated from a simple kinetic analysis [21]. Consequently, it is possible to quantify individual organic gasses on a relatively short time scale and with a sensitivity that can reach well into the pptv mixing regime. Owing to its versatility and high sensitivity, PTR-MS has been widely used for atmospheric chemistry, plant studies, food science, and medical application [21,22].

APCI is an alternative and well-trodden method for the trace gas analysis. When APCI or API is operated in the open air or extra pumping is used for the transportation of gas samples, only some fraction of the sample can be introduced into the mass analyzer leading to the sacrifice of the detection sensitivity. In order to avoid such sample loss, several attempts have been made in which all the ionized gas can be introduced into the vacuum of the mass spectrometer. Cotte-Rodríguez, Mulligan and Cooks developed non-proximate detection of small and large molecules by desorption electrospray ionization and desorption atmospheric pressure chemical ionization mass spectrometry [10,11]. Flexible conductive silicone tubing (4.83 mm i.d., 1–3 m long) was directly connected to the inlet of a mass spectrometer. Low nanogram detection limits were obtained for the compounds studied from a wide variety of surfaces, even those present in complex matrixes. Chen et al. developed an ambient sampling chemi/chemical ion source with dielectric barrier discharge (DBD) [23]. The ambient air containing gaseous samples was sniffed into an enclosed ionization chamber which was of sub-ambient pressure, and was subsequently mixed with metastable helium atoms generated by helium DBD in front of the ion inlet of the mass spectrometer. Consumption of helium could be kept minimal for maintaining the stable discharge. This method was applied to non-proximate sample gas analysis, determination of active ingredients in drug tablets, and detection of