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Multi-capillary-column proton-transfer-reaction time-of-flight mass spectrometry☆

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ABSTRACT

Proton-transfer-reaction time-of-flight mass-spectrometry (PTR-TOFMS) exhibits high selectivity with a resolution of around 5000 $m/\Delta m$. While isobars can be separated with this resolution, discrimination of isomeric compounds is usually not possible. The coupling of a multi-capillary column (MCC) with a PTR-TOFMS overcomes these problems as demonstrated in this paper for the ketone isomers 3-heptanone and 2-methyl-3-hexanone and for different aldehydes. Moreover, fragmentation of compounds can be studied in detail which might even improve the identification. LODs for compounds tested are in the range of low ppb_v and peak positions of the respective separated substances show good repeatability (RSD of the peak positions <3.2%). Due to its special characteristics, such as isothermal operation, compact size, the MCC setup is suitable to be installed inside the instrument and the overall retention time for a complete spectrum is only a few minutes: this allows *near real-time* measurements in the optional MCC mode. In contrast to other methods that yield additional separation, such as the use of pre-cursor ions other than H_3O^+, this method yields additional information without increasing complexity.

1. Introduction

Proton-transfer-reaction mass-spectrometry (PTR-MS) has become a widely used technique in environmental science and biological research, permitting the monitoring of trace volatile organic compounds (VOCs) [1•3]. PTR-MS allows real-time analysis of breath, down to breath-to-breath resolution [4•10]. Replacing the quadrupole in a PTR-MS as a mass filter by Time-Of-Flight (TOF) mass separation opened new horizons to yield faster measurements, higher mass-range, and much more detailed information [11,12]. Quadrupole based PTR-MS instruments have unity mass resolution and compounds with the same nominal mass cannot be distinguished. PTR-TOFMS instruments possess a mass resolving power ($m/\Delta m$) of over 5000, where m is the respective mass (or m/z, more precisely) of the signal in the spectrum and Δm is the width (FWHM) of the peak. This high resolution represents a great step toward separation and identification of isobaric compounds, according to their exact mass.

However, the problem remains for compounds with the same molecular composition and thus the same exact mass. Employing different precursor ions for ionization such as O_2^+ or NO^+ can be used for the differentiation of isomeric compounds [13]. While this can be of great use for target analysis of a certain limited number of compounds, this method usually fails for rich samples, where the comparison of the spectra for different pre-cursors becomes too complex.

Concerning fragmentation, the strength of dissociation depends on the difference in proton affinities between the analytes and the precursor ions (in the present study H_3O^+; 165.0 kcal mol^{-1}) and the collision energy (E/N) in the reaction chamber. For humid sample typically a high E/N is chosen to suppress the formation clusters, which however, leads to more fragmentation and thus, to more complicated data.

Another method to gather additional information on sample composition is gas chromatography by adding another dimension of separation to the spectrum, based on the chemical properties of the compound. TOF-MS with electron impact (EI) ionization counts by now as standard GC detection technique.

The idea of coupling a PTR-MS to a commercial GC system has been implemented by several groups. As an example Lindinger et al. combined separation of VOCs by GC with parallel and simultaneous

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detection with PTR-MS and EI MS detection [14], respectively. However, in spite of the advantage of using a gas chromatographic separation regarding the increased selectivity of a GC-PTR-MS, this combination diminishes an important advantage of PTR instruments: their capability for real-time detection due to the long cycle period of GC measurements.

Sacrificing some of the temporal resolution of a regular GC, smaller size and shorter cycle times can be obtained by using a multi capillary column (MCC) instead. These columns have already successfully been implemented with other VOC gas analyzers [15,16]. Normally, a multi capillary column consists of around 1000 parallel capillaries bundled in a stainless steel tube. The inner surface of each capillary is covered by a film of a stationary liquid phase. Different models regarding the shape (straight or coiled) and different stationary phases are commercially available. The length of the column is normally between 40 and 250 mm permitting a smaller pressure difference across the column compared to packed and single capillary columns (e.g. with a length of 30 m). The bundle of capillaries enables a higher load capacity that can be used to get a higher sensitivity. The higher flow range of a MCC between 20 and 150 ml/min allows for isothermal separation and a simple and compact heating setup can be realized. Moreover, the high flow is favorable for the coupling to a PTR drift-tube, which requires a flow larger than 30 ml/min.

An MCC enables a fast gas chromatographic separation in near real-time and it is small enough to be installed inside a PTR-TOFMS instrument. The presented setup allows switching a PTR-TOFMS into an MCC-mode without adaptation to the instruments sampling procedure. From the construction point of view the use of an MCC is less expensive and less bulky than the coupling of a commercial GC system to a PTR-TOFMS.

We will present the employed setup and exemplify its capabilities. Two applications for measurements of complex VOC mixture such as human breath and human skin emission were selected and will be discussed. PTR-MS has already previously been applied in both fields [17•20]. With the present setup a more exact quantification of the single VOCs can be achieved, since addition of the signals from fragment ions arising from different compounds (e.g. in case of aldehydes emanated through skin) can be eliminated, and moreover, isomeric compounds can be separated.

2. Materials and methods

2.1. MCC-PTR-TOFMS

The following part describes the installation of a multi-capillary column in a PTR-TOFMS (PTR-TOF 8000, Ionicon Analytik, Innsbruck, Austria) [21]. Important instrumental parameters and reaction conditions of the PTR-TOFMS are listed in Table 1. The principles of operation of the instrument are described extensively elsewhere [11,22].

An important objective of the presented work was to implement a MCC for sample separation (1) without changing the normal operation parameters of the PTR-TOFMS and (2) while using the normal continuous sample gas inlet.

For operation of the PTR-TOFMS, we installed additional components in the PTR-TOFMS sample inlet system, as depicted in Fig. 1: the MCC, a 6-port-valve (ring), a sampling loop made of Teflon tubing (volume 5 ml), and an additional small 3-way-valve made of PEEK (3-way flipper valve Type 6650, Bñ/4rkert, Ingelfingen, Germany). The MCC (S2-40/OV-1/0.2, Multichrom, Ltd., Novosibirsk, Russia) used in our setup is 20 cm long, coated with 0.2 α/4m polydimethylsiloxane film as the stationary phase. In this prototype setup the 6-port valve is made of stainless steel, but should ideally be made of inert material, i.e. stainless-steel coated with Silconert2000®r).

Table 1
Analysis parameters for VOCs detection using MCC-PTR-TOF.

Parameter	Analysis of aldehydes/skin sample	Analysis of ketone isomers/breath sample
Drift inlet pressure	2.14 mbar	
Drift inlet temperature	80 °C	
Transfer line temperature	120 °C	
Drift Field (and resulting E/N)	600 V (140 Td)	
Inlet flow for rinsing the loop	20 ml/min	
Pressure TOF lens	6.4 í 10−6 mbar	
MCC temperature	50 °C	40 °C
Carrier gas flow	50 ml/min	20 ml/min
TOF extraction frequency	25 kHz	
Number of scans per analysis	240	
Analysis time	4 min	
Mass range	*m/z* 0.0•508.47	

In order to control the MCC operating temperature, the multi-capillary column has been packed in an aluminum housing. Peltier elements between the aluminum housing and a heat sink allow the heating AND cooling of the column between 40 and 120 °C. This "mini-oven" is installed directly at the outside wall of the PTR-MS climate chamber. Therefore the sample gas connections to the MCC are still cold-spot free.

As displayed in Fig. 1, three different configurations of the valves are needed to operate the MCC-PTR-TOFMS:(a) *PTR-TOFMS mode*: This is the normal, real-time mode of the PTR-TOFMS only that in this setup the sample gas has to pass through the additional valves. The sample gas enters through the instruments normal sampling inlet and around 30 ml/min are drawn toward the pressure controller (PC) and the reaction chamber in total. To increase sample inlet flow, the inlet flow controller ("Inlet-FC") can draw additionally between 0 and 1000 ml/min.

In this configuration the sample loop and the MCC are rinsed by a defined flow of N_2 (nitrogen, purity 99.9999%), which is controlled by an additionally installed mass flow controller (not shown in Fig. 1, El_Flow, Bronkhorst High-Tech B.V., Ruurlo, The Netherlands).(b) *Sample-loop loading mode*: In this configuration the sample loop is flushed and is filled with sample gas after a few seconds. The Inlet FC can be used for faster filling of the sample loop.

Preferably, the small valve is already switched to direct clean N_2 into the reaction chamber, to insure a low background.(c) *MCC mode*: In this mode the sample gas in the sampling loop is injected and pressed through the MCC by the flow of N_2. The PTR-TOFMS now records the MCC chromatogram.

Following this protocol, the entire volume of the sampling loop is injected into the column, which defines the initial peak width. By switching back to configuration b) after a defined delay, the amount of sample gas injected and thus the initial peak width can be controlled. After injection the MCC measurement can be continued in configuration b) as well.

2.2. Preparation of test gases

3-Methylbutanal, hexanal, nonanal, octanal, 2-ethyl-1-hexanol, 3-methyl-2 hexanone, and decanal were purchased from Sigma•Aldrich (Steinheim, Germany), 3-heptanone from (Alpha Aesar GmbH Co KG (Karlsruhe, Germany).

For determination of the retention time and calibration of the compounds gaseous standards were prepared by evaporating liquid substances in glass bulbs. Each bulb (Supelco, Bellefonte, PA, USA) was cleaned with methanol (Sigma•Aldrich, Steinheim, Germany), dried at 85 °C for at least 20 h, purged with clean