International Journal of Mass Spectrometry 289 (2010) 170–172

Contents lists available at ScienceDirect

International Journal of Mass Spectrometry

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

Short communication

Interferences in the determination of formaldehyde via PTR-MS: What do we learn from m/z 31?

Tobias Schripp*, Christian Fauck, Tunga Salthammer

Fraunhofer Wilhelm-Klauditz-Institut (WKI), Material Analysis and Indoor Chemistry, Bienroder Weg 54E, D-38108 Braunschweig, Lower Saxony, Germany

ARTICLE INFO

Article history:
Received 19 October 2009
Received in revised form 29 October 2009
Accepted 2 November 2009
Available online 12 November 2009

Keywords:
Formaldehyde
Breath analysis
PTR-MS
Fragmentation

ABSTRACT

The determination of trace levels of formaldehyde in air via Proton-Transfer-Reaction-Mass-Spectrometry (PTR-MS) has been reported in several publications. Especially in case of breath analysis – an important field for PTR-MS measurements – relatively high formaldehyde concentrations were found. However, due to the low mass of the target compound interferences from fragment ions of larger molecules are likely. In this study breath analysis aiming at the determination of formaldehyde via PTR-MS and online-formaldehyde analysis (basing on the Hantzsch reaction) is performed. The presence of alcohols obviously increased the amount of detected m/z 31 while no change of the online-analyzer signal occurred. Additionally, the determination of the rate constant k_f of the formaldehyde ionization in the PTR-MS is performed on the basis of emission chamber tests. The results illustrate the vast complications when quantifying formaldehyde in air via PTR-MS at m/z 31.

1. Introduction

The development of modern analytical devices opens up the opportunity for the continuous analysis of indoor and outdoor atmospheric volatile organic compounds (VOC). Especially the analysis of human breath, which is currently aiming at possible correlations between exhaled compounds and human diseases (e.g., lung cancer), is an increasing and relevant research field. Proton-Transfer-Reaction-Mass-Spectrometry (PTR-MS) [1] is widely applied in breath analysis because this technique enables the monitoring of selected mass fragments in exhaled air with sufficient sensitivity and time resolution.

Formaldehyde has been reported to be also detectable via PTR-MS. The main problem of measuring formaldehyde via PTR-MS is the backward reaction of the protonated formaldehyde into the non-protonated form. The energy dependencies of this phenomenon have been intensively discussed in the literature [2]. However, some publications face the data for formaldehyde critically [3,4]. The topic has drawn considerable interest after Moser et al. [5] reported a maximum value of 73 ppbv formaldehyde during the breath analysis of 344 people. The origin of this large amount has not been discussed by the authors, although serious amounts of other organic compounds (e.g., methanol) were also found in the exhaled air. For such case, the overlap of spectra in the PTR-MS has been reported [6]; e.g., for formaldehyde (m/z 31) $^{15}N^{16}O^+$ can be expected. This artifact can be corrected by measuring m/z 30 and using the isotopic ratio to determine the influence on the signal of m/z 31.

This publication will summarize the main issues connected to the analysis of formaldehyde via PTR-MS and the use of m/z 31 as targeting mass. Additionally, a comparison of PTR-MS measurements and the common Hantzsch technique [7] for the quantification of formaldehyde in air is presented.

2. Materials and methods

2.1. Breath analysis

The breath analysis sampling was performed using a 3 L glass chamber which was continuously flushed with 200 mL/min pure nitrogen to reduce condensation (see Fig. 1). Three healthy male non-smokers (weight 87–98 kg) were asked to exhale for 5 min through an unheated glass tube into the chamber while inhaling through the nose. The inhaled laboratory air contains ~7 ppb formaldehyde. Two measuring devices were attached to the chamber: (a) a high-sensitivity PTR-MS (Ionicon Analytik, Innsbruck) and (b) an AL4021 formaldehyde-autoanalyzer (Aero-Laser, Garmisch-Partenkirchen). The PTR-MS measured m/z 31 while the AL4021 measured formaldehyde via the Hantzsch reaction. Then, the three test persons consumed 6 cL of vodka (40%) within the following hour and the experiment was repeated.

---

* Corresponding author. Tel.: +49 531 2155 249; fax: +49 531 2155 905.
E-mail address: tobias.schripp@wki.fraunhofer.de (T. Schripp).

1387-3806/$ – see front matter © 2009 Elsevier B.V. All rights reserved.
doi:10.1016/j.ijms.2009.11.001

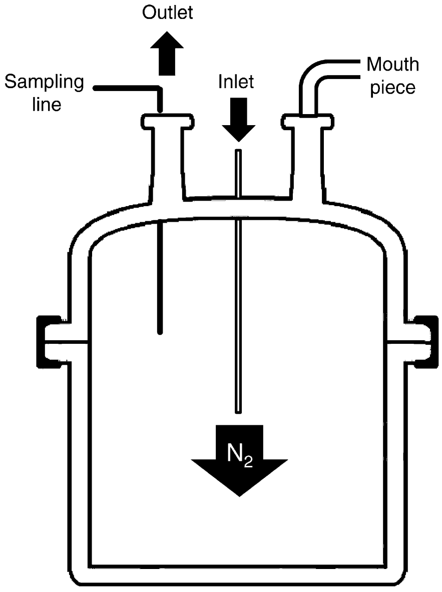

Fig. 1. Scheme of the 3 L cylindric glass chamber flushed with pure nitrogen (200 mL/min).

2.2. Emission chamber test

Two 1 m^3 glass emission test chambers, that fulfill the specifications of ISO 16000-9, were equipped each with two OSB (oriented strand board) panels (loading factor 1 m^2/m^3) at an air exchange rate of 1 h^{-1} (chamber 1) and 0.5 h^{-1} (chamber 2) respectively. The temperature was set to 23 °C and the air humidity was set to 45–50% r.h. The AL4021 and the PTR-MS were attached to the chamber seven days after loading. On the basis of the formaldehyde concentration determined by the AL4021 the rate constant k_f for the protonation reaction (see Eq. (1)) is calculated [8]. The ratio between the forward and backward reaction of the formaldehyde protonation is expected to be in the range of $k_f/k_b \approx 6000$ [9]:

$$\mathrm{HCHO} + \mathrm{H_3O^+} \underset{k_b}{\overset{k_f}{\rightleftarrows}} \mathrm{H_2COH^+} + \mathrm{H_2O} \tag{1}$$

The rate constant k_f is derived from Eq. (2), which is the calculative basis of the concentration given by the PTR-MS-Software. It is important to note that this approach does not consider the backward reaction for the given conditions and, thus, k_f must not represent the real reaction constant but a superposition of the forward and backward reaction constant:

$$c\,[\mathrm{ppb}] = \frac{n_{31} \cdot U \cdot T \cdot \mathrm{tr}_{21}}{k_f \cdot n_{21} \cdot p_d^2 \cdot \mathrm{tr}_{31}} \cdot 1.69241 \times 10^{-11} \tag{2}$$

Here, n_{21} [cps] and n_{31} [cps] are the numbers of detected ions, U [V] is the drift voltage, T [K] is the temperature, k_f [cm^3/s] is the rate constant of the protonation reaction, p_d [mbar] is the drift tube pressure, tr_{21} and tr_{31} are the transmission factors of the respective ions.

3. Results and discussion

The PTR-MS has been designed for the soft ionization of volatile organic compounds without major fragmentation of the molecule under observation. In reality, breakup of molecules can be observed [10]. If substances of high concentration are present in the sample air, the fragmentation masses of these compounds can interfere with the detection of other compounds in trace amounts. The performed experiment proved the interference of exhaled alcohol during breath analysis on m/z 31. In case of the three test persons the PTR-MS showed an increase in the signal of m/z 31 in the presence of alcohol while the reference method (Hantzsch reaction) showed no change in formaldehyde concentration at all (see Fig. 2). The exhaled concentration was expected to be lower than the laboratory background [11] beside the effect of constant flushing of the chamber which was chosen to prevent water condensation while just slightly reducing the formaldehyde concentration.

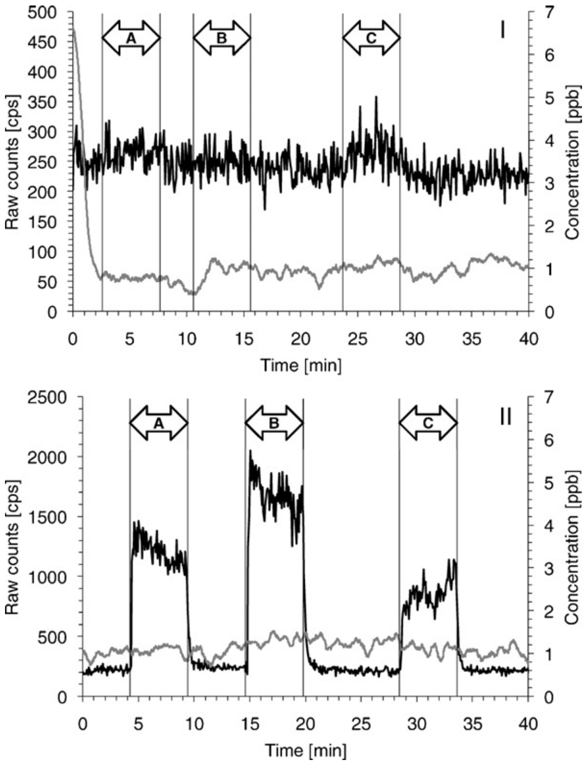

Fig. 2. Breath analysis of three probands (A–C) using a PTR-MS (black line; m/z 31 (raw data); left axis) and an online-Hantzsch-Analyser (grey line; right axis) without alcohol (I) and with alcohol (II).

For the identification of the interfering compound a gas chromatographic analysis (headspace injector, flame-ionization detector) of the consumed alcohol revealed the presence of low amounts of methanol (0.003% of ethanol content). The interference of both alcohols – methanol and ethanol – due to the reaction with O_2^+ on m/z 31 is known from the literature [9,12]. A complete scheme for the reaction of H_3O^+ and formaldehyde in the presence of alcohols is given in Ref. [9]. To illustrate the impact of the presence of O_2^+ on the results, 1 μL pure liquid ethanol was injected in a tedlar bag (5 L) filled with nitrogen and a second bag filled with synthetic air. The increase in the PTR-MS signals for the target mass of ethanol (m/z 47) and m/z 31 is shown in Fig. 3. The ratio of O_2^+/H_3O^+ for the synthetic air sample is 1.5% while the laboratory background is slightly lower (1%). In case of the nitrogen-filled bag the ratio is significantly lower (<0.1%) which also represents the starting conditions of the breath analysis. In the absence of oxygen the signal for m/z 31 does not change during the measurement of ethanol while this is the case for the experiment in synthetic air. This proves – as expected – the interference of ethanol in the presence of ionized oxygen on m/z 31. The increase in m/z 31 is 1.65% of the increase in m/z 47. During the experiments, the signal for the primary ions (m/z 21) does not change significantly due to sufficient dilution.

The most relevant factor when calculating the concentration of formaldehyde in air from the raw data of the PTR-MS is the reaction constant of the proton transfer reaction. However, this factor is strongly depending on the environmental conditions but

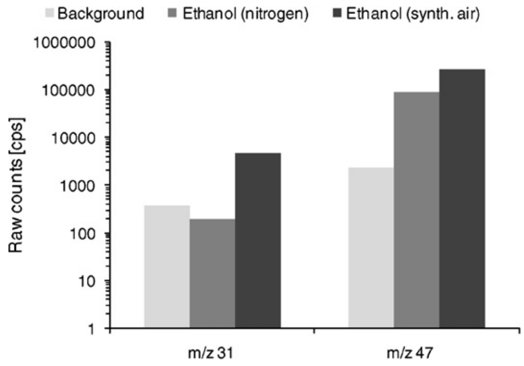

Fig. 3. PTR-MS signals for ethanol in nitrogen and synthetic air (mean of 30 cyles).

also on the device settings. The mean relative kinetic energy of the reactants for the given analytical conditions has to be determined and then transferred into rate constants [2,4]. Steinbacher et al. [4] – for example – reported $k_f = 1.5 \times 10^{-9}$ cm^3/s (forward reaction) and $k_b = 2.8 \times 10^{-11}$ cm^3/s (backward reaction) for a relative kinetic energy of 0.17 eV. Even higher rate constants, like 3×10^{-9} cm^3/s [13], are used. As mentioned above, the analytical results depend on the sampling conditions. In case of breath analysis the sampled air features high humidity. The humidity effect is not limited to changes in the reaction conditions but could also produce interfering ions (e.g., *m*/*z* 37 for the dimeric water cluster) which complicate the quantification.

In the present study, the rate constant is determined via external calibration. The AL 4021-Autoanalyzer measured the formaldehyde concentration in the emission test chambers and the rate constant is calculated from the raw counts of the PTR-MS. For our instrumental setup [*U* (drift tube) = 600 V; *T* (drift tube) = 60 °C; *p* (drift tube) = 2.025 mbar; transmission factor (*m*/*z* 21) = 0.3358; transmission factor (*m*/*z* 31) = 0.3634] the rate constant results to 4.30×10^{-10} cm^3/s (chamber 1; $c_{\mathrm{HCHO}} = 91$ ppb) and 3.95×10^{-10} cm^3/s (chamber 2; $c_{\mathrm{HCHO}} = 160$ ppb). This rate constant is much lower than the previously reported which might result from different reaction conditions.

For the presented breath analysis the PTR-MS would result in a fault concentration of formaldehyde in the range of 40 ppb (basing on a rate constant of 4×10^{-10} cm^3/s) due to the presence of alcohol in the exhaled air. Therefore, the determination of formaldehyde in the presence of high concentrated common volatile organic compounds is not possible via PTR-MS without sufficient knowledge about the ion-chemistry of the target compound and extensive calibration.

4. Conclusions

The PTR-MS is basically not able to identify compounds because it cannot distinguish between the different origins of mass fragments. This limitation is important if surplus compounds are present in the sample. Fragment ions of these compounds can interfere on other *m*/*z* than the protonated molar mass. Then, trace analysis of other compounds is not possible.

If side reactions – like the ionization of alcohols in the presence of O_2^+ – occur during the analysis, the effect has to be considered during calibration. Within the presented breath analysis the ratio O_2^+/H_3O^+ fluctuates due to loss of exhaled oxygen from the chamber by the nitrogen flux. In that case, the calibration of the PTR-MS has to be performed under exactly the same conditions and a measurement of the pure compound in a tedlar bag, like presented above, is insufficient.

In case of formaldehyde, the analysis is additionally complicated by the equilibrium between protonated and non-protonated molecules. The rate constant of this reaction has to be determined precisely for the present instrument and measuring condition to calculate the air concentration without vast error. However, if the calibration and validation of the PTR-MS is necessary by another high-time resolved reference method, the advantage of the PTR-MS for online formaldehyde monitoring does not apply. The PTR-MS is feasible for the determination of formaldehyde if the reaction scheme during ionization is known and the quantitative results are corrected by additional calibration of the effects of the oxygen concentration [9], the air humidity [14], and the concentration of CO_2 [15]. Nevertheless, this extensive calibration increases the effort and the uncertainties of the measurement considerably against common online techniques.

Acknowledgments

The authors are grateful to the three test persons for their time and effort.

References

[1] W. Lindinger, A. Hansel, A. Jordan, On-line monitoring of volatile organic compounds at pptv levels by means of proton-transfer-reaction mass spectrometry (PTR-MS) medical applications, food control and environmental research, International Journal of Mass Spectrometry and Ion Processes 173 (1998) 191–241.

[2] A. Hansel, W. Singer, A. Wisthaler, M. Schwarzmann, W. Lindinger, Energy dependencies of the proton transfer reactions $H_3O^+ + CH_2O$ [double arrow] $CH_2OH^+ + H_2O$, International Journal of Mass Spectrometry and Ion Processes 167–168 (1997) 697–703.

[3] J. de Gouw, C. Warneke, Measurement of volatile organic compounds in the earth's atmosphere using proton-transfer-reaction mass spectrometry, Mass Spectrometry Reviews 26 (2007) 223–257.

[4] M. Steinbacher, J. Dommen, C. Ammann, C. Spirig, A. Neftel, A.S.H. Prevot, Performance characteristics of a proton-transfer-reaction mass spectrometer (PTR-MS) derived from laboratory and field measurements, International Journal of Mass Spectrometry 239 (2004) 117–128.

[5] B. Moser, F. Bodrogi, G. Eibl, M. Lechner, J. Rieder, P. Lirk, Mass spectrometric profile of exhaled breath—field study by PTR-MS, Respiratory Physiology & Neurobiology 145 (2005) 295–300.

[6] B. Thekedar, W. Szymczak, V. Höllriegel, C. Hoeschen, U. Oeh, Investigations on the variability of breath gas sampling using PTR-MS, Journal of Breath Research 3 (2009) 027007.

[7] T. Salthammer, Photophysical properties of 3,5-diacetyl-1,4-dihydrolutidine in solution: application to the analysis of formaldehyde, Journal of Photochemistry and Photobiology A: Chemistry 74 (1993) 195–201.

[8] T. Kelly, C. Fortune, Continuous monitoring of gaseous formaldehyde using an improved fluorescence approach, International Journal of Environmental Analytical Chemistry 54 (1994) 249–263.

[9] P. Španěl, D. Smith, Quantification of trace levels of the potential cancer biomarkers formaldehyde, acetaldehyde and propanol in breath by SIFT-MS, Journal of Breath Research 2 (2008) 046003.

[10] Ionicon, Proton Affinities and Fragmentation List, 2008, www.ptrms.com.

[11] T. Wang, A. Pysanenko, K. Dryahina, P. Spanel, D. Smith, Analysis of breath, exhaled via the mouth and nose, and the air in the oral cavity, Journal of Breath Research 2 (2008) 037013.

[12] I. Kushch, K. Schwarz, L. Schwentner, B. Baumann, A. Dzien, A. Schmid, K. Unterkoffler, G. Gastl, P. Spanel, D. Smith, A. Amann, Compounds enhanced in a mass spectrometric profile of smokers' exhaled breath versus non-smokers as determined in a pilot study using PTR-MS, Journal of Breath Research 2 (2008) 026002.

[13] K. Schwarz, W. Filipiak, A. Amann, Determining concentration patterns of volatile compounds in exhaled breath by PTR-MS, Journal of Breath Research 3 (2009) 027002.

[14] S. Inomata, H. Tanimoto, S. Kameyama, U. Tsunogai, H. Irie, Y. Kanaya, Z. Wang, Technical note: determination of formaldehyde mixing ratios in air with PTR-MS: laboratory experiments and field measurements, Atmospheric Chemistry and Physics 8 (2008) 273–284.

[15] L. Keck, C. Hoeschen, U. Oeh, Effects of carbon dioxide in breath gas on proton transfer reaction-mass spectrometry (PTR-MS) measurements, International Journal of Mass Spectrometry 270 (2008) 156–165.