

Ultrahigh Sensitivity PTR-MS Instrument with a Well-Defined Ion Chemistry

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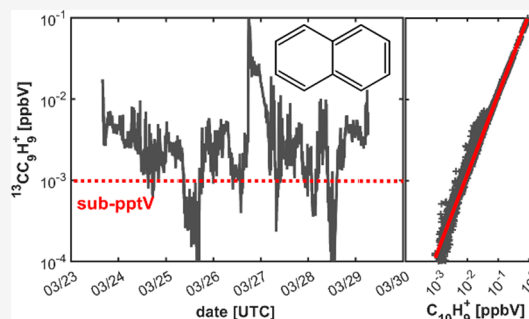


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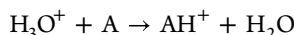


Supporting Information

ABSTRACT: Proton-transfer-reaction mass spectrometry (PTR-MS) is widely used for measuring organic trace gases in air. In traditional PTR-MS, both nonpolar and polar analytes are ionized with unit efficiency, as predicted from ion-molecule collision theories. This well-defined ion chemistry allows for direct quantification of analytes without prior calibration and therefore is an important characteristic of PTR-MS. In an effort to further increase the sensitivity, recently developed ultrahigh sensitivity chemical ionization mass spectrometry (CIMS) analyzers have, however, been reported to have sacrificed unit ionization efficiency for selected analytes or classes of analytes. We herein report on the development of a novel ultrasensitive PTR-MS instrument, the FUSION PTR-TOF 10k, which exhibits the same universal unit response as conventional PTR-MS analyzers. The core component of this analyzer is the newly designed FUSION ion-molecule reactor, which is a stack of concentric ring electrodes generating a static longitudinal electric field superimposed by a focusing transversal radiofrequency (RF) field. The FUSION PTR-TOF 10k instrument is equipped with an improved ion source, capable of switching between different reagent ions (H_3O^+ , O_2^+ , NO^+ , NH_4^+) in less than one second. The improved time-of-flight mass spectrometer analyzes m/z signals with a mass resolution in the 10000–15000 range. FUSION PTR-TOF 10k achieves sensitivities up to 80000 cps ppbV^{-1} and detection limits down to 0.5 pptV for a 1 s measurement time. We show time-series of naphthalene and ^{13}C -naphthalene as measured in ambient air in Innsbruck for demonstrating the sub-pptV detection capability of this novel FUSION PTR-TOF 10k.



Proton-transfer-reaction mass spectrometry (PTR-MS) is widely used for measuring organic trace gases in air.^{1–4} In PTR-MS, ionization is effected by proton transfer reactions from gaseous hydronium (H_3O^+) ions to neutral analyte molecules A:



While some protonated analytes may be subject to ionic fragmentation (e.g., abstraction of neutral water), it is a key feature of PTR-MS that AH^+ do not undergo reverse hydration or secondary reactions.⁵ This greatly simplifies the ion chemistry in PTR-MS compared to other chemical ionization mass spectrometry (CIMS) methods. In the original PTR-MS instrument,⁶ AH^+ ions are formed in a drift tube, i.e., a stack of ring electrodes generating a homogeneous longitudinal electric field along the axial ion path in the cylindrical ion-molecule reactor. Due to the high velocity imparted by the electric field, ions spend only $\sim 100 \mu\text{s}$ in the drift tube, which leaves no time for reverse or secondary reactions of AH^+ ions. Hydrated ions are efficiently dissociated in energetic collisions with the background gas molecules. Importantly, proton transfer reactions proceed at the collisional limit if the proton affinity (PA) difference between the donor and acceptor molecules exceeds 10 kcal mol^{-1} .⁷ Since most organic molecules have a $\text{PA} > 175 \text{ kcal mol}^{-1}$, PTR-MS analyzers detect almost all

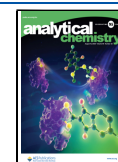
organic analytes, both nonpolar and polar, with unit efficiency, i.e., the collision rate equals the reaction rate. Exceptions include small saturated hydrocarbons, formaldehyde, and glyoxal. This universal detection capability makes PTR-MS unique among the CIMS methods. Since the collision rate of H_3O^+ ions with a neutral molecule A can be calculated,⁸ the sensitivity of PTR-MS to an analyte A can be inferred with an uncertainty of $\pm 30\%$. This is particularly useful if an external calibration is not possible.

Recently developed H_3O^+ -CIMS analyzers, including radiofrequency (RF) focusing fields, are more sensitive than conventional PTR-MS analyzers. Hence, in a focusing ion-molecule reactor (FIMR) instrument, an RF focusing quadrupole field is added to the electrostatic drift field and sensitivities $> 10000 \text{ cps ppbV}^{-1}$ are achieved.⁹ In the PTR3 instrument, only a transversal RF field is applied and sensitivities up to $19000 \text{ cps ppbV}^{-1}$ are achieved.¹⁰ It has,

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however, been reported that these analyzers suffer from a nonunit ionization efficiency for selected analytes or classes of analytes.^{11,12} Herein we present a new PTR-MS analyzer, the FUSION PTR-TOF 10k, which achieves ultrahigh sensitivity without losing the universal unit response that is typical for conventional PTR-MS analyzers. Additionally, we show subsecond switching between different reagent ions with the new improved ion source of this instrument.

EXPERIMENTAL SECTION

The new FUSION PTR-TOF 10k instrument (Figure 1) includes (i) an optimized ion source capable of switching

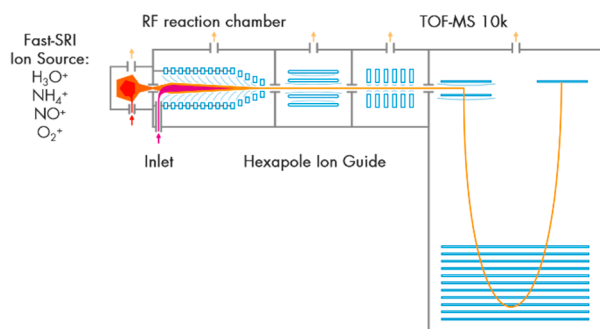


Figure 1. Schematic of the new FUSION PTR-TOF 10k analyzer.

between different reagent ions (H_3O^+ , O_2^+ , NO^+ , NH_4^+) in approximately 1 s and below (“Fast-SRI source”; SRI: Selective Reagent Ionization), (ii) a newly developed ion-molecule reactor (“FUSION reactor”), in which reagent ions react with neutral analyte molecules to form analyte ions, (iii) a hexapole ion guide and electrostatic lens system for transferring ions from the ion-molecule reactor to the mass analyzer, and (iv) an orthogonal acceleration reflectron time-of-flight mass spectrometer (ToF-MS) for m/z analysis of the ions at high mass resolution. In the following section, these components are described in more detail.

Fast-SRI Ion Source. The fast-SRI ion source is based on the glow discharge design originally developed at the University of Innsbruck, which was later optimized by IONICON. Currently, four types of reagent ions, H_3O^+ , NH_4^+ , NO^+ , and O_2^+ , can be produced in this ion source. The reagent gases used for generating these ions are water vapor, a mixture of nitrogen and water vapor,¹³ synthetic air, and pure oxygen, respectively. The fast-SRI ion source includes a novel reagent gas supply system, which allows one to rapidly switch between the different types of primary ions listed above (patent application submitted).

FUSION Reactor. The FUSION reactor is the core component of the new FUSION PTR-TOF 10k instrument. The ion-molecule reaction chamber is composed of a stack of 48 evenly spaced electrodes with a constant diameter. A DC voltage (up to 850 V) is applied to the ring electrodes across a resistor chain. In addition to the DC voltage, an RF voltage with a maximum peak-to-peak amplitude (V_{pp}) of 250 V and a typical frequency of 900 kHz can be applied to the ring electrodes. The application of an RF field has a well-known ion focusing effect, which increases the instrument sensitivity by a factor of 5–10. Ions are extracted from the ion-molecule reactor via an ion funnel, which is a stack of 20 closely spaced ring electrodes with decreasing internal diameters. The FUSION reactor is mounted inside a vacuum chamber

(volume: $\sim 70 \text{ cm}^3$) that is pumped by a scroll pump (HiScroll 6, Pfeiffer Vacuum, Aßlar, Germany). The typical pressure in the vacuum chamber ranges from 2.5 to 4.0 mbar. The sample flow through the FUSION reactor is $\sim 100 \text{ mL min}^{-1}$. All wetted metal surfaces are treated with IONICON’s extended volatility range (EVR) technology, which has been shown to improve the temporal response to low-volatility analytes and prevents the decomposition of labile species (e.g., peroxides).¹⁴ The vacuum chamber and the capillary inlet system are mounted in a heated enclosure (40–130 °C).

TOF-MS 10k. The TOF-MS 10k mass analyzer is the next evolution of IONICON’s orthogonal acceleration TOF-MS series that was introduced a decade ago.¹⁵ This TOF-MS 10k includes a hexapole ion-guide¹⁶ and a compact lens system for guiding the ions into the orthogonal acceleration TOF-MS. Ions are detected with a Multi-Channel Plate Detector (MCP) and signals are digitized with an analog-to-digital converter (ADC; ADQ7DC; Teledyne Signal Processing Devices Sweden AB, Linköping, Sweden) operated in pulse detection mode. The typical mass resolution of the ToF-MS at full width half-maximum is $>10000 m/\Delta m$. The typical resolution of the reported data is between 10000 and 12000 $m/\Delta m$ (Figure S1). At reduced sensitivity, a mass resolution up to 15000 can be achieved. For the measurements presented herein, the ToF-MS analyzer was operated with an upper m/z limit in the m/z range of 410 to 460 range.

PTR-TOF Data Evaluation. The PTR-TOF Viewer (v4.4) was used for the evaluation of instrumental sensitivities and limits of detection (LODs). The IONICON Data Analyzer IDA (v2.012 to v2.121) was used for high mass and time resolution data analysis and quantification of unknown compounds based on assigned chemical compositions. Custom Julia (<https://julialang.org/>) and MATLAB (2022b; The Mathworks Inc., MA, U.S.A.) scripts were developed for further analysis and visualization.

Performance Characterization. The FUSION PTR-TOF 10k instrument includes a calibration system in which calibration gas can be added to the inlet via a multiport inlet valve. The calibration gas can be diluted dynamically, using a dilution gas mass flow controller ($0\text{--}1000 \text{ mL min}^{-1}$) and a calibration gas mass flow controller ($0\text{--}20 \text{ mL min}^{-1}$) (Bronkhorst High-Tech B.V., Ruurlo, The Netherlands). For dilution, we used pure air generated with a Precision Zero Air 30L gas generator (Peak Scientific Instruments Ltd., Inchinnan, Scotland). Two standard gas mixtures were used: a 12-component mix ($\sim 1 \text{ ppmV}$ each), and a 10-component mix ($\sim 100 \text{ ppbV}$ each; both Società Italiana Acetilene and Derivati S.I.A.D. S.p.A., Bergamo, Italy). The properties of both standards are summarized in Table S1. For testing the effect of varying humidity on the instrumental response, the 12-component mix was diluted with zero air of variable relative humidity (RH). Different levels of RH (0–100%) were generated by passing a fraction of zero air through a bubbler filled with HPLC grade water (Sigma-Aldrich, Vienna, Austria). For testing the potential oxidation of a highly reactive compound inside the FUSION PTR-TOF 10k analyzer, the instrument sampled from a Teflon bag containing zero air with trace amounts ($\sim 10 \text{ ppbV}$) of limonene. Only the headspace of R(+)-limonene (97%; Sigma-Aldrich, Vienna, Austria) was sampled for preparing the bag.

Ambient Air Measurements. The FUSION PTR-TOF 10k instrument sampled ambient air in Innsbruck (Austria) for six consecutive days in March 2023. The inlet system consisted

Table 1. Sensitivities (in Counts per Second per Parts per Trillion, cps pptV⁻¹; 1 pptV = 10⁻⁹ v/v) and 3 σ LODs (1 s Signal Integration, 1 Min Signal Integration) for 15 Selected Analyte VOCs

compound	formula	A.H ⁺ [<i>m/z</i>]	sensitivity (cps/pptV)	LOD@1 s (pptV)	LOD@1 min (pptV)
methanol	CH ₃ O	33.034	4.2	30.17	3.42
acetonitrile	C ₂ H ₃ N	42.034	22.5	2.32	0.26
acetone	C ₃ H ₆ O	59.050	34.3	17.81	2.3
			38.9	N/A	N/A
isoprene	C ₅ H ₈	69.070	21.1	5.34	0.71
			25.5	3.88	0.9
methyl vinyl ketone	C ₄ H ₆ O	71.050	36.7	2.56	0.46
methyl ethyl ketone	C ₄ H ₈ O	73.065	39.0	3.91	0.54
			14.4	4.37	0.55
benzene	C ₆ H ₆	79.055	15.4	3.93	0.59
methyl propyl ketone	C ₅ H ₁₀ O	87.081	31.3	1.51	0.29
			25.8	1.71	0.29
toluene	C ₇ H ₈	93.070	28.7	1.48	0.24
butyl methyl ketone	C ₆ H ₁₂ O	101.097	44.3	1.15	0.07
			39.5	0.95	0.13
xylene	C ₈ H ₁₀	107.086	40.9	0.92	0.16
trimethylbenzene	C ₉ H ₁₂	121.102	45.7	0.76	0.13
2-octanone	C ₈ H ₁₆ O	129.128	59.8	1.04	0.32
(+) α -pinene	C ₁₀ H ₁₆	137.133	47.1	1.25	0.1
D5-siloxane	C ₁₀ H ₃₀ O ₅ Si ₅	371.102	73.5	0.54	0.07

of a 1.5 m long 0.040 in. ID 1/16 in. OD Sulfinert tubing (Restek Corp., Bellefonte, PA, U.S.A.) heated to 90 °C. Automatic zeros were performed by adding clean zero air to the tip of the inlet for 5 min every 5 h. The FUSION reactor was operated at an E/N of 100 Td (1 Td = 10⁻¹⁷ V cm²) and at a temperature of 110 °C. Data acquisition rates were set to 1 Hz.

RESULTS AND DISCUSSION

Sensitivity and Limit of Detection. Table 1 shows the figures of merit of the new FUSION PTR-TOF 10k instrument. The table lists the sensitivity and limits of detection (LOD, 3 σ ; in pptV) for 15 VOCs. LODs are reported for a 1 s and a 1 min signal integration time, respectively.

Table 1 shows that LODs are typically in the single digit pptV regime for a 1-s signal integration time. Only methanol and acetone have higher LODs due to a higher instrumental background. For a 1-min signal integration time, LODs are in the sub-pptV regime (hundreds of ppqV). Sensitivities are in the range between 4.2 and 73.5 cps pptV⁻¹. Similar to all PTR-MS analyzers, the instrument discriminates against low *m/z* ions, and the mass discrimination function (often also referred to as the relative transmission function) is shown in Figure 2. Maximum transmission is reached for ions with *m/z* > 120, and in the higher *m/z* range it is mainly the polarity of the analyte that determines the instrumental response factor. Trimethylbenzene (*m/z* = 121.102) is a low polarity compound that is detected with a sensitivity of 45.7 cps pptV⁻¹. Octanone (*m/z* = 129.128) is a polar compound that is detected with a sensitivity of 59.8 cps pptV⁻¹.

It is important to note that the sensitivity also depends on the upper *m/z* limit set for the mass spectrometric analysis. The sensitivities listed in Table 1 were obtained with an upper *m/z* limit of 440. Reducing the upper *m/z* limit to 250 would result in a ~ 30% higher sensitivity (~60.0 cps pptV⁻¹ for trimethylbenzene; ~ 80.0 cps pptV⁻¹ for octanone). It is also important to note that the differences in sensitivities can be

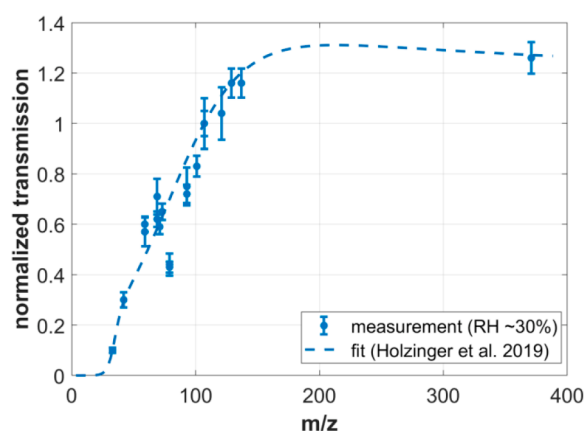


Figure 2. Normalized transmission for all analytes in two calibration gas standards was measured at a relative humidity of approximately 30% (at ambient temperature). The dashed line represents a transmission fit, as introduced by Holzinger et al. (2019).

entirely explained by the mass discrimination function (Figure 2) and the difference in the collision rates of H₃O⁺ ions with the respective analytes, which include both nonpolar and polar compounds. This means that the FUSION PTR-TOF 10k analyzer exhibits the same universal unit response as the conventional PTR-MS analyzer. Hence, uncalibrated compounds can be quantified with high accuracy based on ion-molecule collision kinetics. Other CIMS instruments for organic analytes (including the FIMR and PTR3 analyzer) have been reported to suffer from a nonunit ionization efficiency for selected analytes or classes of analytes.^{11,12}

Dynamic Range. An ultrahigh sensitivity has the drawback that nonlinearity effects appear at low analyte volume mixing ratios. The ADC in the FUSION PTR-TOF 10k analyzer saturates at ion count rates >2.5 × 10⁶ cps. With sensitivities in the range between 40 and 80 cps pptV⁻¹ range, saturation occurs at 30–60 ppbV (see Figure S2 with an example of limonene). This is well above the typical mixing ratios of trace

organic analytes in ambient air. Figure 3 confirms the response of the Instrument via a multistep calibration with the 12-

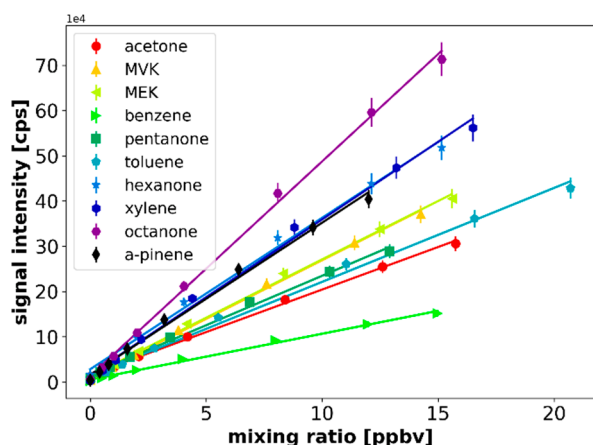


Figure 3. Calibration curves showing the linear response of the FUSION PTR-TOF 10k to 10 selected VOCs over the 0–15 ppbV range.

component standard (with total VOC concentrations of up to ~192 ppbV, i.e., the sum of all compounds in the VOC standard). It is important to note that the linearity range can be extended by more than 1 order of magnitude if the ion molecule reactor and/or the ion funnel are operated without RF (see Figure S2).

To put the results into perspective, in conventional PTR-MS analyzers, the pseudo-first-order ion kinetics approximation holds up to analyte mixing ratios in the single-digit ppmV regime. In the FUSION PTR-TOF 10k analyzer, the linear approximation breaks down at triple-digit ppbV levels due to the increased ion residence time in the FUSION reactor. Turning off the RF and increasing the DC voltage are options to overcome this limitation.

Humidity Dependence. Conventional PTR-MS analyzers exhibit a humidity-dependent decrease in sensitivity for a few analytes, even if their PA exceeds 175 kcal mol⁻¹. The most prominent examples are the aromatic compounds benzene and toluene. The underlying reason is that H₃O⁺(H₂O) ions do not react with benzene and react with reduced efficiency with toluene. If the electric field strength in the drift tube is kept low for reducing the fragmentation of analyte ions, then a fraction of the H₃O⁺ ions is converted to H₃O⁺(H₂O) ions. As a consequence, the sensitivities of benzene and toluene decrease with increasing humidity. Oxygenated organics such as ketones react at a collisional rate with H₃O⁺ and H₃O⁺(H₂O) ions, which is why the response to such analytes is humidity independent.

As shown in Figure 4, the FUSION PTR-TOF 10k analyzer exhibits a humidity-dependent response similar to that of conventional PTR-MS instruments. The response to benzene decreases by ~50–55% when increasing the RH from 0 to 100%. Please note that the humidity dependence can be decreased by elevating the E/N with an increase of the DC fraction. The response to, e.g., acetone and most other compounds is independent of humidity.

Ion Source Performance. One option to improve the selectivity of PTR-MS analyses is to switch between different reagent ions (H₃O⁺, NH₄⁺, NO⁺, O₂⁺). Since PTR-MS is an

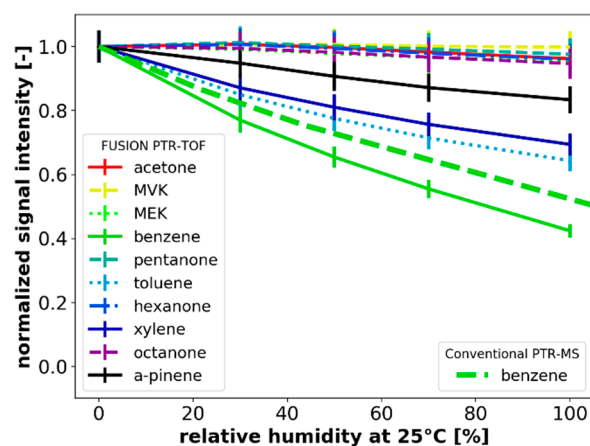


Figure 4. Humidity-dependent decrease in the instrumental response to a series of VOCs, as measured for the FUSION PTR-TOF 10k, and for benzene for a conventional PTR-MS analyzer.

online and real-time instrument, it is desirable that the switching between ions occurs as fast as possible.

Figure 5 (upper panel) shows data from an experiment in which benzene was sequentially measured via electron transfer

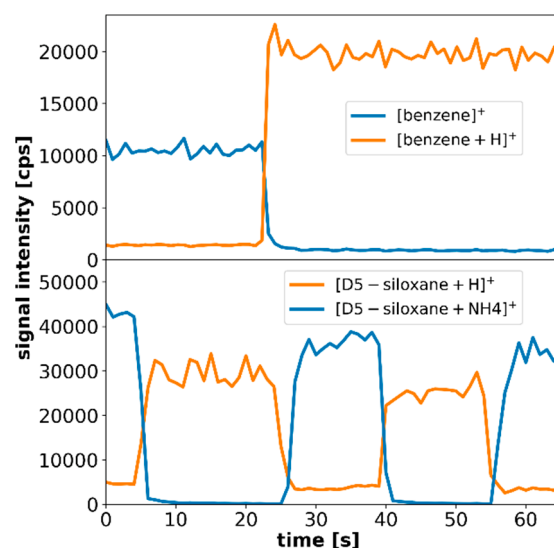


Figure 5. Upper panel: Fast switching from O₂⁺ to H₃O⁺ reagent ions to detect benzene as a molecular ion and a protonated molecule, respectively. Lower panel: Fast switching between NH₄⁺ and H₃O⁺ reagent ions to detect D₅-siloxane as an ammonium adduct and in its protonated form, respectively.

reactions to O₂⁺ ions to form C₆H₆⁺ ions and via proton transfer reactions from H₃O⁺ ions to form C₆H₇⁺ ions. Figure 5 (lower panel) shows how D₅-siloxane was alternately detected in its protonated form (via proton transfer from H₃O⁺) and as an ammonium (NH₄⁺) adduct. The switching between different detection modes occurs in less than 1 s. Only for the switching from H₃O⁺ to NH₄⁺ reagent ions, about 2 s is needed for signal stabilization. Please note, all SRI modes conserve the >98% reagent ion purity that is typical for PTR-MS (Table S2).

One important aspect that has not received sufficient attention from the PTR-MS community in the past is the fact that plasma ion sources generate radicals (e.g., OH radicals are formed in a water plasma) in high abundance. These

radicals may react with organic analytes in the instrument itself (“intrinsic oxidation”), thereby generating a positive measurement artifact for oxidized species. For probing potential measurement artifacts, we supplied 10 ppbV of limonene to the FUSION PTR-TOF 10k analyzer operated with H_3O^+ as the reagent ion. Limonene is highly reactive toward OH radicals, mainly forming 4-acetyl-1-methyl-cyclohexene (m/z 139.112), limononaldehyde (m/z 169.122), and other high molecular weight oxidation products. Figure S3 shows that the relative abundance of signals $\geq m/z$ 139 is less than 0.4% of the total limonene signal (m/z 81.070 + 95.086 + 137.132).

Ambient Air Measurements at ppqV Levels. For demonstrating the sub-pptV detection capability of the FUSION PTR-TOF 10k analyzer, we show the time series of naphthalene and ^{13}C -naphthalene as measured in ambient air in Innsbruck during a one-week measurement period (Figure 6).

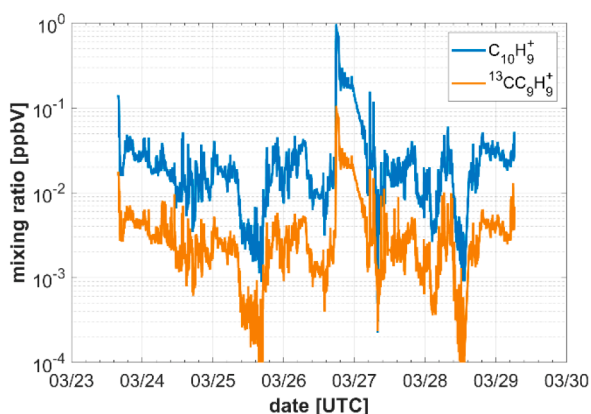


Figure 6. Time series (1 min averages) of naphthalene and ^{13}C -naphthalene, as measured in ambient air in Innsbruck (Austria) in March 2023.

Naphthalene mixing ratios range from 0.9 pptV to 0.9 ppbV, spanning 3 orders of magnitude in range. The ^{13}C -naphthalene time series shows the sub-pptV detection capability even better, with mixing ratios ranging from 0.1 pptV to 0.1 ppbV. It is important to note that this sub-pptV linearity is achieved despite complex isobaric interferences (Figure S4) that were present in ambient air. A correlation of naphthalene and the ^{13}C -naphthalene demonstrates instrumental linearity down to low triple digit ppqV levels (Figure S5).

CONCLUSIONS

It is an important and unique characteristic of PTR-MS that nonpolar and polar analytes are ionized with unit efficiency as predicted from ion–molecule collision theories. We have shown that the novel FUSION PTR-TOF 10k analyzer exhibits the same well-defined ion chemistry as conventional PTR-MS analyzers, making it the most sensitive PTR-MS instrument that strictly fulfills this characteristic. The FUSION PTR-TOF 10k analyzer reaches sensitivities up to 80000 cps ppbV^{-1} and detection limits in the 0.5 to 5 pptV range for a 1 s measurement time. The analytical power of this instrument is further improved by the implementation of a novel ion source (capable of switching between different reagent ions in less than 1 s) and of a high resolution ($m/\Delta m = 10000\text{--}15000$) mass analyzer.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.analchem.3c02669>.

Supporting tables include information on the calibration gas standards and the reagent ion purity. Supporting figures demonstrate the mass resolution, the dynamic range, and the low amount of OH-induced interferences, and depicts a mass-spectrum of naphthalene and its isotope and a cross-correlation of the respective two signals during 6 days of ambient measurements (PDF)

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Author Contributions

A.J. had the initial idea to develop the instrument described herein. M.M. and T.R. further improved this concept and conceived the fast-SRI ion source. M.L., M.M., and T.R. conducted the measurements, analyzed the data, and wrote the manuscript. A.W. contributed via discussions and wrote the final manuscript. All authors have given approval to the final version of the manuscript.

Notes

The authors declare the following competing financial interest(s): A.J., M.L., M.M., and T.R. work for IONICON Analytik, which is commercializing FUSION PTR-TOF 10k.

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