
Differentiation of Isomeric Compounds by Two-Stage Proton Transfer Reaction Time-of-Flight Mass Spectrometry

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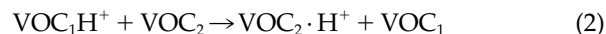
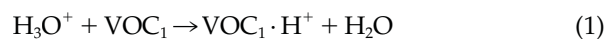
We investigated a two-stage ion source for proton transfer reaction (PTR) ionization to achieve more selective mass spectrometric (MS) detection of selected volatile organic compounds (VOCs) than that achieved with commonly used PTR-MS instruments, which are based on single-step PTR ionization with H_3O^+ . The two-stage PTR ion source generated reagent ions other than H_3O^+ by an initial PTR between H_3O^+ and a selected VOC, and then a second PTR ionization occurred only for VOCs with proton affinities larger than the affinity of the reagent VOC. Acetone and acetonitrile were useful as reagent VOCs because they provided dominant peaks as a protonated form. Using two-stage PTR-MS, we differentiated isomeric VOCs (for example, ethyl acetate and 1,4-dioxane) by means of differences in their proton affinities; protonated acetone formed the $[\text{M} + \text{H}]^+$ ion from ethyl acetate but not from 1,4-dioxane. The PTR-MS-derived concentrations agreed quantitatively with those independently determined by Fourier transform infrared spectroscopy (FT-IR) at parts per million by volume (ppmv) levels. In addition, interfering fragment ions formed from alkyl benzenes at m/z 79 (C_6H_7^+) could be distinguished from the m/z 79 ion arising from protonation of benzene, and therefore this method would prevent overestimation of benzene concentrations in air samples in which both benzene and alkyl benzenes are present. This two-stage PTR ionization may be useful for distinguishing various isomeric species, including aldehydes and ketones, if appropriate reagent ions are selected. (J Am Soc Mass Spectrom 2008, 19, 325–331) © 2008 American Society for Mass Spectrometry

Proton transfer reaction mass spectrometry (PTR-MS) is widely used for the rapid and sensitive determination of trace amounts of volatile organic compounds (VOCs) in air [1–3]. PTR ionization is a type of chemical ionization (CI) [4] that permits soft ionization of chemical species that have proton affinities (PAs) greater than that of the reagent species. The hydronium ion (H_3O^+) is commonly used as a primary ion because it undergoes PTRs with most VOCs but not with the major components of the atmosphere (such as N_2 , O_2 , and CO_2). If an appropriate reagent ion other than H_3O^+ is chosen for PTR ionization, designated chemical species can be detected selectively [3]. However, little research has been done on this technique, probably because few methods are available for the selective production of other reagent ions.

Reagent ions such as $(\text{C}_2\text{H}_5\text{OH})_n\cdot\text{H}^+$ and $(\text{CH}_3\text{COCH}_3)_2\cdot\text{H}^+$ have been used for the detection of ammonia in air by chemical ionization mass spectrometry (CI-MS) [5–7]. $(\text{C}_2\text{H}_5\text{OH})_n\cdot\text{H}^+$ and $(\text{CH}_3\text{COCH}_3)_2\cdot\text{H}^+$ ions were generated in radioactive ion sources from ethanol ($\text{C}_2\text{H}_5\text{OH}$) and acetone (CH_3COCH_3), respectively, diluted in N_2 . Because flow tube reactors were used, the

predominant primary ions were cluster ions. Ammonia was ionized not only by the PTR, which generated NH_4^+ , but also by CI, which produced cluster ions such as $\text{C}_2\text{H}_5\text{OH}\cdot\text{NH}_4^+$ and $(\text{CH}_3\text{COCH}_3)_2\cdot\text{NH}_4^+$; as a result, the interpretation of the resulting mass spectra was often complicated.

In this study, we developed a new ion source for PTR-MS in which designated reagent ions other than H_3O^+ are produced through protonation by H_3O^+ ions. In the first stage, PTR between H_3O^+ and a designated VOC (VOC_1) selectively produces reagent ions $\text{VOC}_1\cdot\text{H}^+$; when a second VOC (VOC_2) with a PA larger than that of VOC_1 is present in a sample, a second PTR ionization occurs to produce $\text{VOC}_2\cdot\text{H}^+$ ions:



Note that soft ionization is used for the production of the reagent ion, as well as for the ionization of the VOCs in the sample. The performance of this ion source was tested with several VOC_1 candidates. The ion source was used to differentiate isomeric VOCs (VOC_2); we identified the isomeric VOCs from the mass signals of their parent ions (i.e., the protonated VOCs). Therefore, this technique is unlike the collision-induced dissociation

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Table 1. Primary product ions for two-stage PTR with several reagent VOCs

VOC ₁ (M)	CH ₃ CN	C ₆ H ₅ CH ₃	(CH ₃) ₂ CO	(C ₂ H ₅) ₂ CO
PA (kJ mol ⁻¹) ^a	779	784	812	837
MH ⁺ (counts) ^b	1.2 × 10 ⁶	1.4 × 10 ⁶	1.8 × 10 ⁶	1.1 × 10 ⁶
H ₃ O ⁺ (counts) ^b	1.5 × 10 ³	2.8 × 10 ⁴	6.6 × 10 ³	1.5 × 10 ⁴
[MH + H ₂ O] ⁺ (counts) ^b	9.3 × 10 ³	—	6.6 × 10 ³	9.3 × 10 ³
[MMH - H ₂ O] ⁺ (counts) ^b	—	—	3.5 × 10 ⁴	—
[MMH] ⁺ (counts) ^b	1.2 × 10 ⁴	—	1.4 × 10 ⁴	3.4 × 10 ⁵
Other significant product ions ^c		<i>m/z</i> 77 (9)		<i>m/z</i> 45 (9)

^aReference [15].^bData were integrated over a period of 1 min at a repetition rate of 10 kHz (6 × 10⁵ scans).^cValues in parentheses show percentage intensity relative to that of MH⁺.

tion (CID) technique in PTR ion trap mass spectrometry [8, 9] and the CI-MS technique that uses O₂⁺ and NO⁺ as reagent ions [10, 11], both of which make use of fragment ions for the identification of isomeric VOCs.

Experimental

The instrument used in this study was a custom-built proton transfer reaction time-of-flight mass spectrom-

eter (PTR-TOFMS). The details of the instrumental set-up have been described elsewhere [12, 13]. In the two-stage mode, a reagent VOC (VOC₁) (acetonitrile, toluene, acetone, or diethyl ketone) was introduced from the port between the ED3 and ED4 electrodes (the VOC₁ port), and the sample gas was introduced from the newly inserted port between the ED4 and ED5 electrodes (the sampling port). In the one-stage mode, in which the reagent ion was H₃O⁺, nitrogen gas was

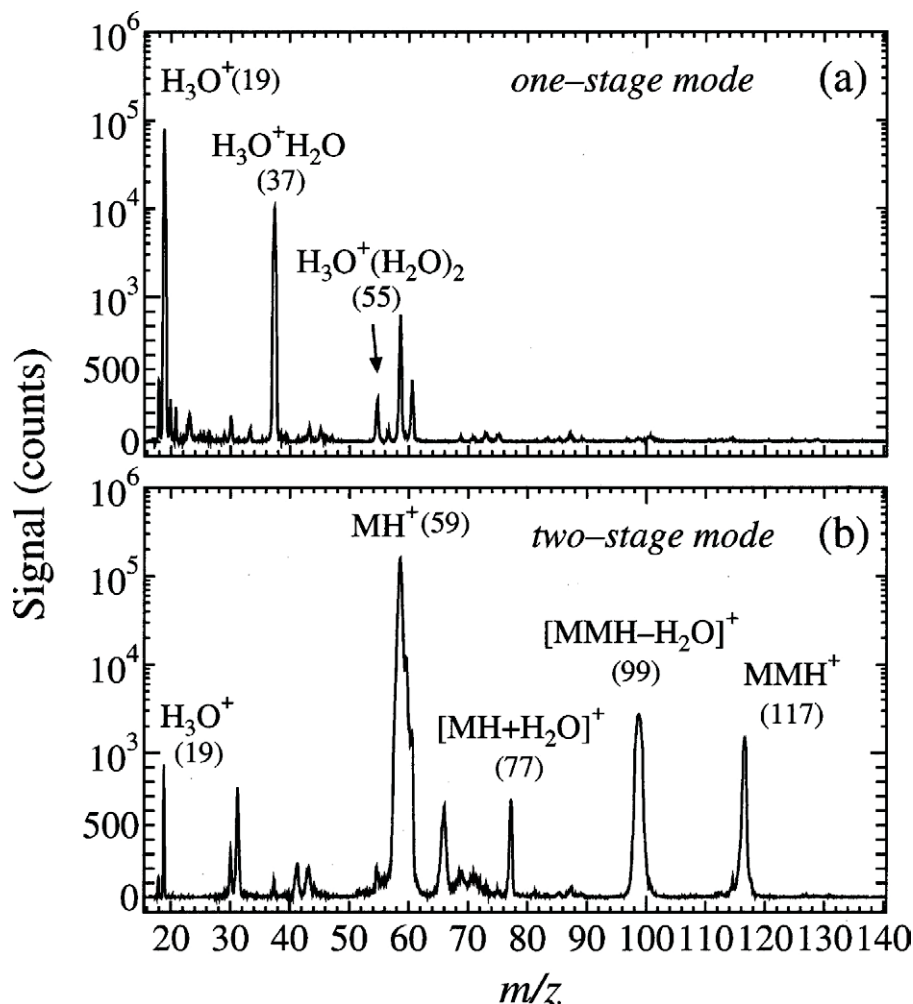


Figure 1. Background mass spectra obtained in the (a) one-stage mode and (b) two-stage mode with acetone as the reagent VOC₁. M = (CH₃)₂CO.

introduced from the VOC₁ port by means of a three-way ball valve. Switching between the one-stage and two-stage modes did not affect the discharge between the ED1 and ED3 electrodes. The VOC₁ reagents were introduced into the drift tube at pressures of 0.22, 0.45, 0.04, and 0.15 mTorr for acetonitrile, toluene, acetone, and diethyl ketone, respectively. All experiments were carried out at a drift-tube field strength of 100 Td.

The gases and chemicals used were as follows: N₂ (>99.99,995%) and (CH₃)₂CO/air (0.0197%) from Japan Fine Products, Kawasaki, Japan; CH₃CN/N₂ (0.104%), toluene/N₂ (0.0991%) and (C₂H₅)₂CO/N₂ (0.09,888%) from Takachiho, Tokyo, Japan; ethyl acetate (1.00 ppmv)/1,4-dioxane (0.96 ppmv)/N₂ from Sumitomo Seika, Tokyo, Japan; and ethyl acetate (>99.5%) and 1,4-dioxane (>99.0%) from Wako Chemicals, Osaka, Japan.

To determine whether the isomer concentrations could be differentially and quantitatively obtained by the present technique, we prepared 50:50 mixtures of ethyl acetate and 1,4-dioxane in a bakeable and evacuable 6-m³ photochemical chamber [14], and introduced the mixtures into the PTR-TOFMS instrument for analysis. Before each experiment, the photochemical chamber was filled with 800 torr of purified air. The reagents, ethyl acetate and 1,4-dioxane, were degassed by successive freeze-pump and thaw cycles, and the reagent vapors were collected in a calibrated glass bulb and then directed into the chamber with N₂ as a carrier gas.

During the introduction of the samples, the air in the chamber was mixed with an internally located fan. The chamber wall was temperature controlled at 25 °C (±1 °C). The concentrations of ethyl acetate and 1,4-dioxane in the chamber were monitored with an FT-IR spectrometer (Nicolet Nexus 670, Thermo, Waltham, MA) combined with a multireflection mirror system (optical path length = 221.5 m) [14]. The spectral resolution was 1.0 cm⁻¹. The peaks at 1759 cm⁻¹ and 881 cm⁻¹ were used for the determination of the concentrations of ethyl acetate and 1,4-dioxane, respectively. The precision of the FT-IR data were typically 0.5%, and the detection limit for ethyl acetate and 1,4-dioxane was ~4 parts per billion by volume (ppbv) at a signal-to-noise ratio (S/N) of 2.

Results and Discussion

The intensities of primary product ions obtained in the two-stage mode with acetonitrile, toluene, acetone, and diethyl ketone as reagents VOC₁ are listed in Table 1. The intensity of H₃O⁺ in the one-stage mode was 6.5 × 10⁵ counts for 1 min integration at a repetition of 10 kHz. For acetonitrile and acetone, the ion signal of H₃O⁺ at *m/z* 19 almost disappeared, and protonated acetonitrile (CH₃CN·H⁺) and protonated acetone ((CH₃)₂CO·H⁺) predominated. The intensities of the signals for these two species were approximately

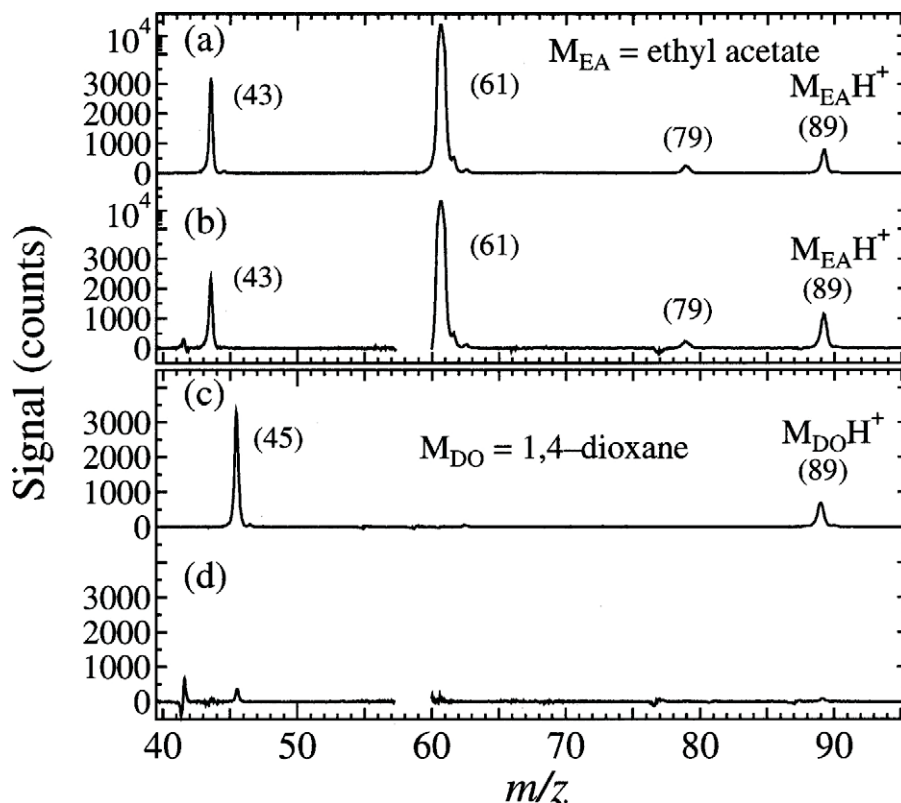


Figure 2. Mass spectra of ethyl acetate (M_{EA} , mass 88) and 1,4-dioxane (M_{DO} , mass 88) obtained in the one-stage mode (a) and (c), respectively, and the two-stage mode (b) and (d), respectively. VOC₁ = acetone.

twice the intensity of the signal for H_3O^+ , which is probably the result of the mass-dependent transmission efficiency of the TOFMS [13]. Background mass spectra obtained in the one-stage mode and the two-stage mode using acetone as the reagent VOC_1 are shown in Figure 1a and b, respectively. In the two-stage mode, the ion signals of $\text{H}_3\text{O}^+(\text{H}_2\text{O})_n$, $n = 0, 1, 2$ at m/z 19, 37, and 55 almost disappeared, and a strong peak for protonated acetone, $(\text{CH}_3)_2\text{CO}\cdot\text{H}^+$, was observed at m/z 59. The peak was broad because the relatively low mass resolution of our instrument, $m/\Delta m = \sim 100$, did not allow resolution of the isotopes. Small peaks assigned to $[(\text{CH}_3)_2\text{CO}\cdot\text{H} + \text{H}_2\text{O}]^+$, $[(\text{CH}_3)_2\text{CO}]_2\cdot\text{H} - \text{H}_2\text{O}]^+$, and $((\text{CH}_3)_2\text{CO})_2\cdot\text{H}^+$ were observed at m/z 77, 99, and 117, respectively, with intensities of at most 2% of the intensity of $(\text{CH}_3)_2\text{CO}\cdot\text{H}^+$.

In the case of toluene and diethyl ketone, strong ion signals of protonated molecules were observed, but the formation of fragment ions was also observed with very intense peaks at m/z 77 (probably C_6H_5^+) and 45 (probably $\text{C}_2\text{H}_5\text{O}^+$) (Table 1), respectively. In particular, the ion signal for $[\text{MMH}]^+$ was appreciable in the case of diethyl ketone because of its higher boiling point (375 K) compared with the boiling points of other reagent VOCs (e.g., 329 K for acetone) [15]. These results suggested that

of the VOCs examined in this study, acetonitrile and acetone were suitable for use as reagent VOCs.

Two isomeric VOCs of molecular weight 88, ethyl acetate ($\text{CH}_3\text{C}(\text{O})\text{OC}_2\text{H}_5$) and 1,4-dioxane (cyclo- $\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2$), the PAs of which are 836 and 798 kJ mol^{-1} , respectively [15], were introduced as samples (VOC_2). Acetone was chosen as VOC_1 . The PA for ethyl acetate is higher than the PAs for H_2O (691 kJ mol^{-1}) and acetone (812 kJ mol^{-1}) [15], whereas the PA of 1,4-dioxane lies between the PAs of H_2O and acetone. In the sample mass spectrum of ethyl acetate with the background mass spectrum subtracted in the one-stage mode (Figure 2a), signals of protonated ethyl acetate and fragment ions assigned to CH_3CO^+ , $\text{CH}_3\text{C}(\text{O})\text{OH}\cdot\text{H}^+$, and $\text{CH}_3\text{C}(\text{O})\text{OH}\cdot\text{H}_3\text{O}^+$ were observed at m/z 89, 43, 61, and 79, respectively. A similar mass spectrum was obtained in the two-stage mode (Figure 2b). (Ion signals between m/z 58 and 60 were masked because they were scattered by subtraction of the background mass spectrum.) Signals for protonated 1,4-dioxane and a fragment ion assigned as $\text{C}_2\text{H}_5\text{O}^+$ were observed at m/z 89 and 45, respectively, in the one-stage mode (Figure 2c), but these signals were not observed in the two-stage mode (Figure 2d). These results clearly show that, as a result of the difference in the PAs of the

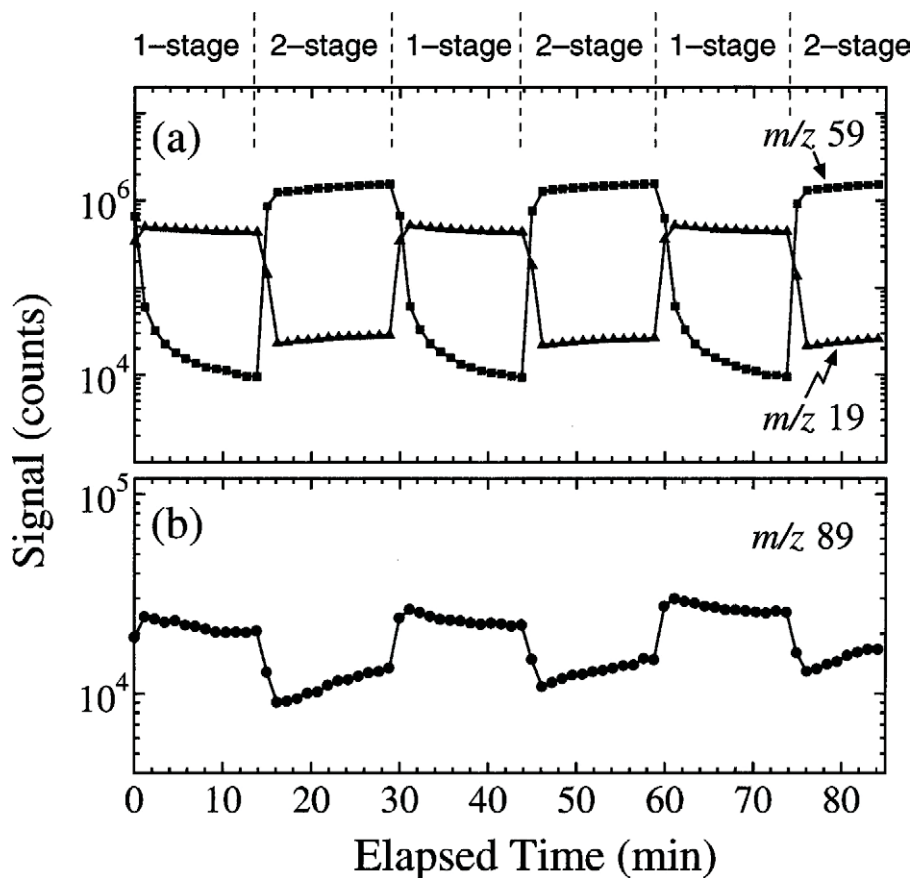


Figure 3. Temporal variations in the ion signals for (a) primary ions H_3O^+ (m/z 19) and $(\text{CH}_3)_2\text{CO}\cdot\text{H}^+$ (m/z 59) and (b) product ions at m/z 89 from a mixture of ethyl acetate and 1,4-dioxane, obtained by switching between operating modes. $\text{VOC}_1 =$ acetone.

Table 2. Normalized signal Intensities obtained in one-stage and two-stage modes for 50:50 mixtures of ethyl acetate and 1,4-dioxane

[Ethyl acetate] (ppmv)	[1,4-Dioxane] (ppmv)	$I_{\text{one-stage}}$ (10^3 ncounts) ^{a,c}	$I_{\text{two-stage}}$ (10^3 ncounts) ^{b,c}
Cylinder			
1.00	0.96	45.9 ± 1.5	8.6 ± 0.6
Chamber (FT-IR) ^d			
0.97	1.00	49.2 ± 2.2	8.7 ± 0.9
0.63	0.66	29.6 ± 0.3	5.1 ± 0.3
0.32	0.33	14.4 ± 0.9	2.5 ± 0.3

^aSignal intensities at m/z 89 obtained in one-stage mode normalized to 10^6 counts of H_3O^+ .

^bSignal intensities at m/z 89 obtained in two-stage mode normalized to 10^6 counts of $(\text{CH}_3)_2\text{CO}\cdot\text{H}^+$. $\text{VOC}_1 = \text{acetone}$.

^cError bars represent 95% confidence levels by t -test.

^dExperiments with each compound alone were performed, and the following results were obtained: $I_{\text{one-stage}} = (14.8 \pm 0.6) \times 10^3$ ncounts and $I_{\text{two-stage}} = (8.2 \pm 0.7) \times 10^3$ ncounts for 0.97 ppmv of ethyl acetate; and $I_{\text{one-stage}} = (32.3 \pm 2.8) \times 10^3$ ncounts and $I_{\text{two-stage}} = (0.2 \pm 0.4) \times 10^3$ ncounts for 0.98 ppmv of 1,4-dioxane.

two VOC_2 samples, a second PTR ionization occurred for ethyl acetate but not for 1,4-dioxane.

Figure 3a shows the temporal variations in the primary ions H_3O^+ (m/z 19) and $(\text{CH}_3)_2\text{CO}\cdot\text{H}^+$ (m/z 59) obtained when the two modes were switched at ~ 15 -min intervals. When we changed the operating mode from the one-stage mode to the two-stage mode at ~ 15 min intervals, the ion signals of H_3O^+ (m/z 19) decreased rapidly, and those of $(\text{CH}_3)_2\text{CO}\cdot\text{H}^+$ (m/z 59) increased rapidly. However, when the operating mode was switched from the two-stage mode to the one-stage mode, ion signals of $(\text{CH}_3)_2\text{CO}\cdot\text{H}^+$ decreased slowly, probably because acetone remained on the surface of the drift tube or the gas line or both. Figure 3b shows the temporal profile of ion signals at m/z 89 when a 50:50 mixture of ethyl acetate and 1,4-dioxane prepared in a cylinder was added (the concentration of each compound was 1.0 ppmv). When the mode was switched, the ion intensity changed markedly. In the one-stage mode, the intensity was high, and both ethyl acetate and 1,4-dioxane were detected, whereas in the two-stage mode, the intensity was low, and only ethyl acetate was detected.

The 50:50 mixtures of ethyl acetate and 1,4-dioxane at three concentrations (~ 1.0 , 0.66, and 0.33 ppmv) were prepared in a 6 m^3 photochemical chamber and were introduced into the PTR-TOFMS instrument. The normalized signal intensities obtained in the one-stage and two-stage modes are listed in Table 2. By using the values of $(45.9 \pm 1.5) \times 10^3$ ncounts for the one-stage mode ($S_{\text{one-stage}}$) and $(8.6 \pm 0.6) \times 10^3$ ncounts for the two-stage mode ($S_{\text{two-stage}}$), obtained from the cylinder of the 50:50 mixture of ethyl acetate and 1,4-dioxane, we determined the mixing ratios of ethyl acetate in the chamber by means eq 3:

$$[\text{ethyl acetate}] (\text{ppmv}) = I_{\text{two-stage}}/S_{\text{two-stage}} \quad (3)$$

And the mixing ratios of 1,4-dioxane were obtained from eq 4:

$$[\text{1,4-dioxane}] (\text{ppmv}) = I_{\text{one-stage}}/S_{\text{one-stage}} - [\text{ethyl acetate}] \quad (4)$$

The ethyl acetate and 1,4-dioxane concentrations determined from the two-stage PTR-TOFMS were compared with those obtained by FT-IR (Figure 4). Note that the concentrations for both ethyl acetate and 1,4-dioxane were determined independently; PTR-TOFMS was based on gravimetrically prepared gas standards, and FT-IR was based on absorption photometry. These results generally agreed within their measurement uncertainties, which suggest that by switching the reagent ions, we can differentiate isomeric VOCs by means of the mass signals of their protonated molecules.

This method could also be used to differentiate ion signals when the signal for a fragment ion overlaps with that for a protonated molecule. For example, in the mass spectrum of ethyl benzene ($\text{PA} = 788 \text{ kJ mol}^{-1}$ [15]) in the one-stage mode (Figure 5a), in addition to a large peak of protonated molecules at m/z 107, a small fragment peak was observed at m/z 79, and the intensity

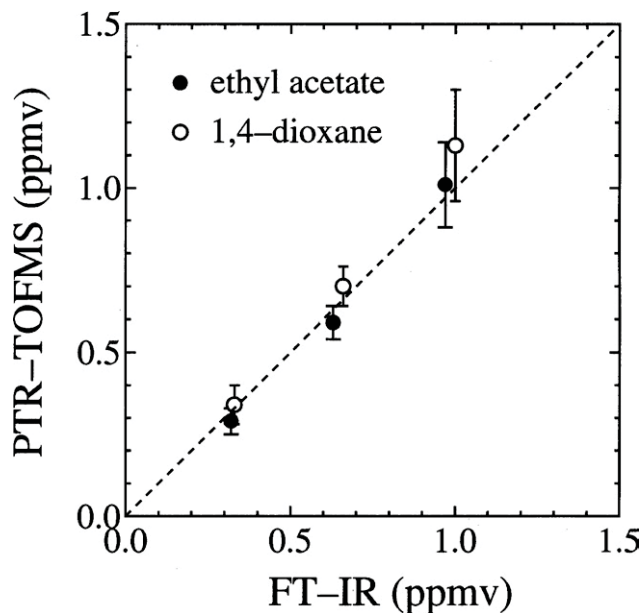


Figure 4. Comparison of ethyl acetate and 1,4-dioxane concentrations determined by two-stage PTR with those obtained by FTIR. The dashed line represents an $x = y$ line. $\text{VOC}_1 = \text{acetone}$.

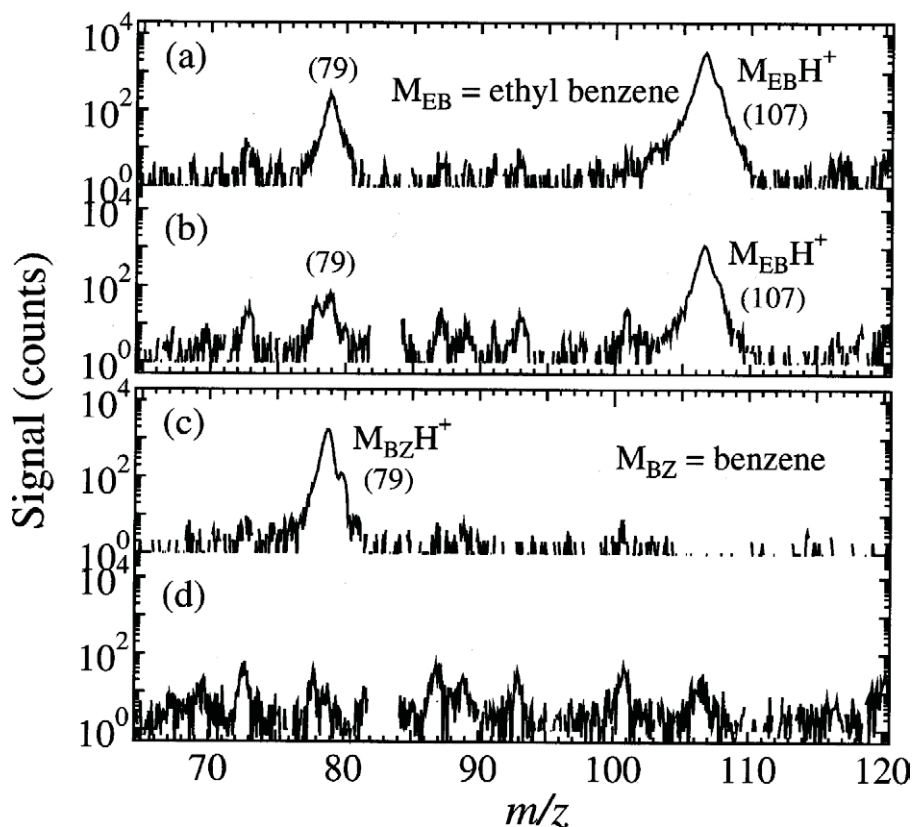


Figure 5. Mass spectra of ethyl benzene (M_{EB} , mass 106) and benzene (M_{BZ} , mass 78) obtained in the one-stage mode ((a) and (c), respectively), and the two-stage mode ((b) and (d), respectively). VOC_1 = acetonitrile.

of this peak was 0.07 relative to that at m/z 107. In the two-stage mode with acetonitrile as a reagent VOC, a similar mass spectrum was observed, although the total ion counts were reduced by approximately half (Figure 5b). The intensity of the ion signal at m/z 79 was 0.05 relative to that at m/z 107. The mass spectrum of benzene (PA = 750 kJ mol⁻¹ [15]) in the one-stage mode (Figure 5c) showed a single peak for the protonated molecule at m/z 79. In contrast to the result for ethyl benzene (Figure 5b), the peak at m/z 79 disappeared for benzene in the two-stage mode (Figure 5d). These results suggest that the use of $CH_3CN \cdot H^+$ as a reagent ion would allow us to distinguish benzene from alkyl benzenes that produce fragment ions at m/z 79 [3, 16–19] and would prevent possible overestimation of benzene concentrations in samples in which the relative abundances of benzene and alkyl benzenes are unknown.

Conclusions

A two-stage PTR ionization source was developed to generate reagent ions other than H_3O^+ , and the feasibility of the source for selectively detecting VOCs was examined. We tested protonation reactions of H_3O^+ with acetone and acetonitrile and found that both reagents gave a single strong peak, which corresponded

to the protonated target VOCs. By switching reagent ions between H_3O^+ and the designated $VOC_1 \cdot H^+$, we could differentiate isomeric VOCs with the same molecular weight but different PAs by monitoring the ion signals of their protonated molecules. This two-stage PTR ionization approach may be applicable to other isomeric species including aldehydes and ketones if the appropriate reagent ions for those pairs are selected.

Acknowledgments

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