Real-Time Flavor Analysis: Optimization of a Proton-Transfer-Mass Spectrometer and Comparison with an Atmospheric Pressure Chemical Ionization Mass Spectrometer with an MS-Nose Interface

Shane J. Avison*

Firmenich S.A., Rue de la Bergère 7, Meyrin 2, CH-1217 Geneva, Switzerland

ABSTRACT: Two techniques are recognized for the real-time analysis of flavors during eating and drinking, atmospheric pressure chemical ionization mass spectrometry (APCI-MS), and proton transfer reaction mass spectrometry (PTR-MS). APCI-MS was developed for the analysis of flavors and fragrances, whereas PTR-MS was originally developed and optimized for the analysis of atmospheric pollutants. Here, the suitability of the two techniques for real-time flavor analysis is compared, using a varied range of common flavor compounds. An Ionicon PTR-MS was first optimized and then its performance critically compared with that of APCI-MS. Performance was gauged using the capacity for soft ionization, dynamic linear range, and limit of detection. Optimization of the PTR-MS increased the average sensitivity by a factor of more than 3. However, even with this increase in sensitivity, the Limit of Detection was typically 10 times higher and the Dynamic Linear Range ten times narrower than that of the APCI-MS.

KEYWORDS: PTR-MS, APCI-MS, MS-nose, flavor

INTRODUCTION

Real-time analysis of flavors is a key technique for measuring flavor release and understanding the connection between release and perception. In general, analysis of volatiles in real time is a powerful technique with three main applications: (i) measuring exhaled metabolites for medical diagnostics; (ii) measuring atmospheric gases, including pollutants; and (iii) measuring volatile release from foods and fragrances. The challenges that this technique presents are very different from those of volatile analysis by gas chromatography: in real-time analysis, the volatiles are sampled continuously and without chromatography. In consequence, ion mass is the only identifier of the volatile, and so the ionization must be soft. Ideally, only the molecular ion is formed; otherwise, discrimination of the different volatiles becomes complicated or impossible. A compromise must be found between ionization conditions that are (i) too soft, which leads to low sensitivity due to insufficient ion formation and (ii) too energetic, which causes a reduction or complete loss of the molecular ion due to fragmentation, a consequence of which is a decrease in the limit of detection. The optimum conditions will depend on the molecule concerned. Smaller molecules of interest in the medical and atmospheric fields, for example, are less fragile, and so harder ionization conditions can be used without compromising performance. Thus, within real-time volatile analysis, different applications have different constraints. The best analytical conditions for analysis of atmospheric gases are not optimal for measuring volatiles during eating. In this study, we optimize and critically compare the two techniques that are most suitable for real-time analysis of volatiles in food during eating using an in vitro model.

The development of real-time measurements began in 1979 when Lovett et al.[1] created an interface for an atmospheric pressure chemical ionization mass spectrometer (APCI-MS) that could directly analyze volatiles in breath in real time.

However, interference from ammonia in the breath limited its use as a diagnostic tool. In 1983, Benoit et al.[2] created an interface that eliminated the problem of ammonia interference. However, its use required the patient to exhale through the mouth at a specific rate in order to maintain a sufficient pressure differential between the interface and the MS. Neither breathing through the mouth nor exhaling at a specific rate is natural during eating, and so this interface cannot be used for real time analysis of aroma. This problem was partially solved[3,4] by using a permeable membrane to maintain the vacuum of the MS while allowing volatiles present on the breath to pass into the MS. However, the membrane permeability was volatile dependent, making the interface less than ideal. In 1996, Taylor and Linforth[5] developed an active sampling interface. Breath was drawn into the ionization region by using the Venturi effect, which was induced by dilution gas. This improvement removed all of the drawbacks mentioned earlier: (i) ammonia was not a problem; (ii) the subject could breathe naturally through the nose; (iii) the pressure differential was maintained automatically, with no constraints on the subject's behavior; and (iv) no membrane was needed to maintain the vacuum. This interface measured the volatiles being released while eating and breathing normally through the nose. It has since been commercialized as the MS-NOSE. In this form, it has been used by a number of groups, particularly the groups at Firmenich S.A., NIZO Food Research and Quest International.[6−12] Others chose to create their own version of the MS-Nose[13−19] On the other hand, Haahr et al.[20−22] designed an interface based on the Venturi effect outside the ionization region. However, the flow rates into the MS were very low and

the temporal resolution was limited because the signal did not fall to baseline between breaths. Charles et al.[23] and Warscheid et al.[24] chose a completely different design: the gaseous sample was pumped at a constant rate into the APCI source and a liquid mobile phase caused ionization. The need for a constant flow rate means that this method is not ideal for breath-by-breath analysis. It is useful, however, for online monitoring of volatile production during a reaction,[23,24] where a constant flow of gas through the reaction vessel can be directed into the interface.

Proton transfer reaction mass spectrometry (PTR-MS) is an alternative to the MS-Nose. It was developed in 1995, mainly for the analysis of atmospheric pollutants and volatile compounds on the breath for medical diagnostic purposes,[25,26] but not for flavor release.[27−31] The key difference between breath analysis of metabolites and real time release measurement is the higher data sampling frequency, which is typically between 20 and 100 ms. However, more recently, PTR-MS has been used in the study of flavors and fragrances.[30,32−37]

As stated above, both PTR-MS and the APCI-MS have been shown to be suitable for real time analysis of flavor. However, the way in which each instrument introduces the volatiles into the ion sources and ionizes them are somewhat different. The APCI-MS introduces the volatiles into the atmospheric pressure ionization source using a venturi effect interface. The PTR-MS however uses the vacuum of the MS to introduce the volatiles into the ion source, which is within the vacuum region of the instrument. In both cases, ionization is achieved by proton transfer reactions with the H_3O+ ions generated within the ionization sources of each instrument. For APCI-MS, this occurs in a continuous manner at atmospheric pressure and for PTR-MS, this occurs in a semicontinuous manner under vacuum.[38] It should therefore be interesting to determine how these sample introduction methods and ionization sources perform when tested under the same real time conditions.

The aim of this comparison will therefore be to test the instruments under the same real time analysis conditions (data sampling rate of 1 data point every 20 ms) with flavor compounds that cover a wide range of log P, volatility and functional groups, the results of which should give some indication to the relative performance under "identical" operating conditions flow rate, optimal ionization, and laboratory environment. This comparison has not been done previously, as few laboratories are equipped with both instruments.

■ MATERIALS AND METHODS

Chemicals. Tests were made on eight common flavor compounds, which *were chosen to cover the different chemical classes (alcohols, ester, ketones acids, aldehydes, and hetrocyclic groups typically encountered in flavors) a wide range of log P (0.28−4.51) and a wide range of volatilities (127−91376 µg/L air).* They were obtained in-house: 2-butanone (CAS No. 78-93-3), E-2-hexenol (CAS No. 2305-21-7), hexanoic acid (CAS No. 142-62-1), benzaldehyde (CAS No. 100-52-7), 2,3-dimethyl pyrazine (CAS No. 5910-89-4), ethyl butyrate (CAS No. 105-54-4), iso-amyl acetate (CAS No. 123-92-2), and limonene (CAS No. 14576-08-0) with the exception of limonene (≥95% purity) all of the compounds are ≥98% purity.

Instrumentation. An MS-NOSE system (Micromass ZMD, Manchester, UK; APCI-MS (Quadrupole)) fitted with a homemade interface) and an Ionicon PTR-MS (Quadrupole) (Innsbruck, Austria) with a high sensitivity upgrade were used. In order to ensure equal transfer of volatiles from the headspace into the PTR-MS the interface

tubing (1 mm i.d. PEEK) within the heated transfer line was replaced with 0.5 mm i.d. deactivated fused silica tubing (SGE, Milton Keynes, UK), which reduced the minimum sampling flow rate to 44 mL/min. All measurements were made under the same laboratory conditions using the best operating conditions (manufacturer's recommendations) for both instruments. The dwell times and interchannel delays were set at 20 ms for both instruments.

Headspace Measurements. Headspace measurements were made on 100 mL of aqueous solution of a single volatile in a 500 mL Schott bottle. It was sealed with a plastic cap fitted with a sampling port and left to equilibrate for at least 1 h. Following equilibration, the sampling port was opened and the fused silica of the PTR-MS or the MS-NOSE was inserted. Sampling time was typically 30 s at a flow rate of 44 mL/min for both the PTR-MS and the MS-Nose. The baseline was allowed to return to normal between measurements.

Determination of the Optimum Cone and Drift Tube Voltages. First, the ions that were formed from each test compound were determined. The headspace above a 40 mg/L solution was measured. The effect of varying the drift tube voltage (PTR-MS) and the cone voltage (MS-NOSE) on the formation of the molecular ions was determined. The drift voltage was varied from 400 to 600 V in 50 V increments. The cone voltage was varied from 10 to 33 V in 1 V increments. Because of the software limitations of the PTR-MS, one voltage per scan file (m/z 30−250) was applied; thus, five separate scan files were needed to cover the 400−600 V range (400, 450, 500, 550, 600 V). For the MS-NOSE, it was possible to apply eight cone voltages within one scan file, therefore requiring only three scan files per volatile (scan file 1: CV10−17, scan file 2: CV 18−25, scan file 3: CV 26−33).

Experimental Design for Optimization of PTR-MS. The six key parameters of the PTR-MS (Table 1) were as follows: flow control of

Table 1. Parameters for Optimization of the PTR-MS and Their Range of Variation

parameter	range	units	Ionicon predicted effect on ionization[a]
USO	50−180	V	no effect
US	50−300	V	no effect
drift	400−600	V	biggest effect
UNC	0−10	V	no effect (already optimal)
FC	5−7	mL/min	can improve ionization
PC	320−370	mbar	can improve ionization

[a]Predicted effects are based on information from the instruction manual and discussions with Ionicon.

the water vapor into the ionization chamber (FC), pressure control of the drift tube (PC), source-out voltage (USO), source voltage (US), drift tube voltage (Drift), and nose cone voltage (UNC). These were optimized by experimental design (Design-Expert 7 Stat-Ease, Inc., Minneapolis, MN, USA). A D-optimal design was used with three levels for each factor. It consisted of 16 center edges, 21 vertices, 1 plane center, and 8 center points. The measurements for these experiments were carried out using 100 µg/L solutions of the test volatiles. The PTR-MS was operated in selected ion recording (SIR) mode. The SIR file contained the molecular ions and fragments identified in the initial experiments of the test volatiles.

■ RESULTS AND DISCUSSION

Preliminary Experiments. Before optimizing the PTR-MS, headspace measurements were made to determine which ions were formed when the volatiles are introduced into the ionization source/drift tube. The only variable for these experiments was the drift tube voltage, as this parameter is typically used for optimizing the ionization. It plays the same role as the cone voltage in APCI-MS: higher voltages increase ionization, breakdown, and ion declustering. For comparison, the same samples were also analyzed using the MS-NOSE while
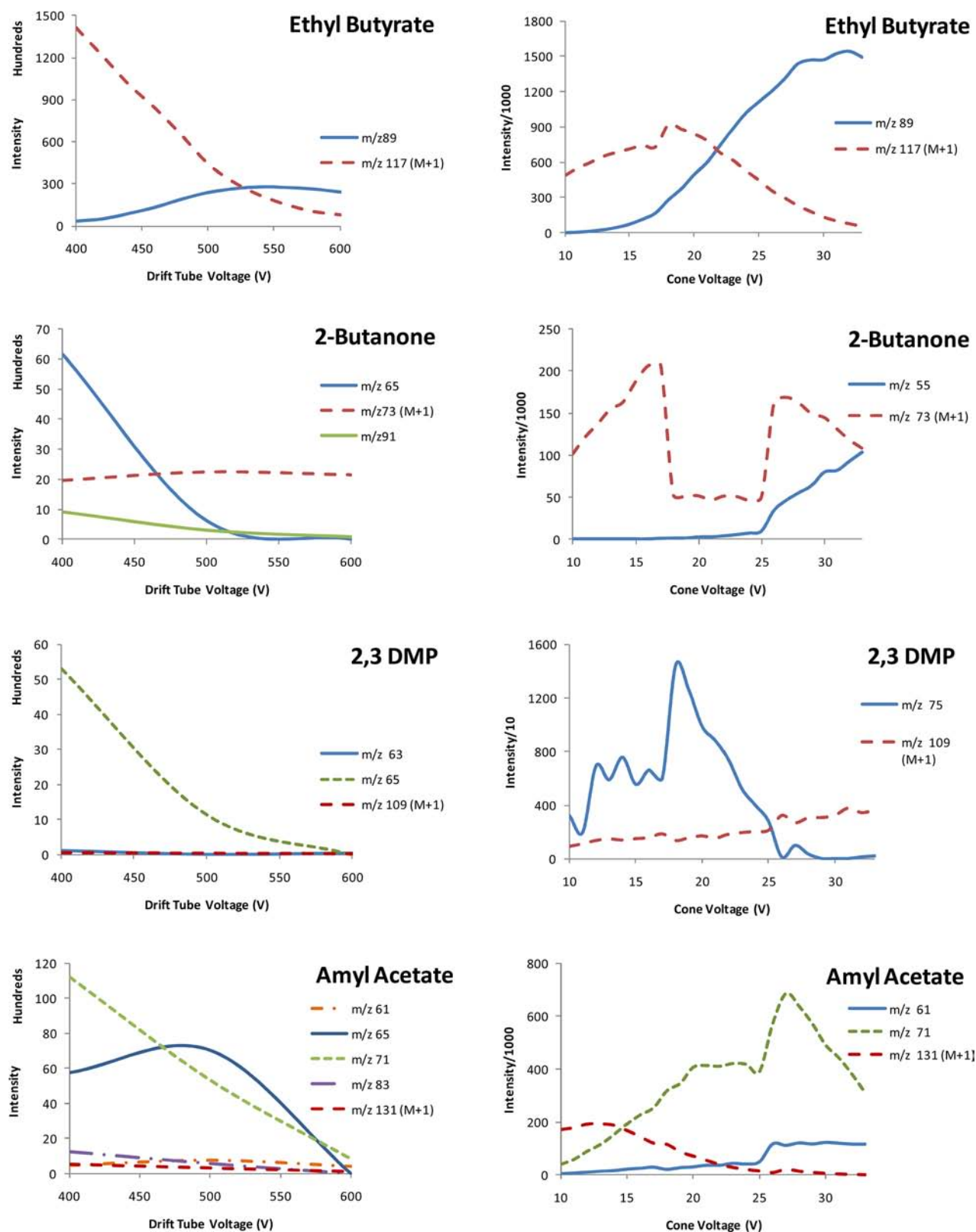
Figure 1. Effect of the key voltage on ionization. Left column: PTR-MS drift tube voltage. Right column: MS-NOSE cone voltage. The molecular ion of the flavor compound is labeled M+1.

the cone voltage was changed. For this instrument, all other parameters had been previously optimized. As expected, changing the drift tube voltage and the cone voltage altered the molecular ion intensity and the amount of breakdown of the volatile.

Figures 1 and 2 show the results for all eight volatiles, with PTR-MS results on the left and APCI-MS results on the right. Ideally, soft ionization should produce large amounts of the molecular ion. If present, then it is marked as M+1 in the legend. For the PTR-MS, the molecular ion was not observed
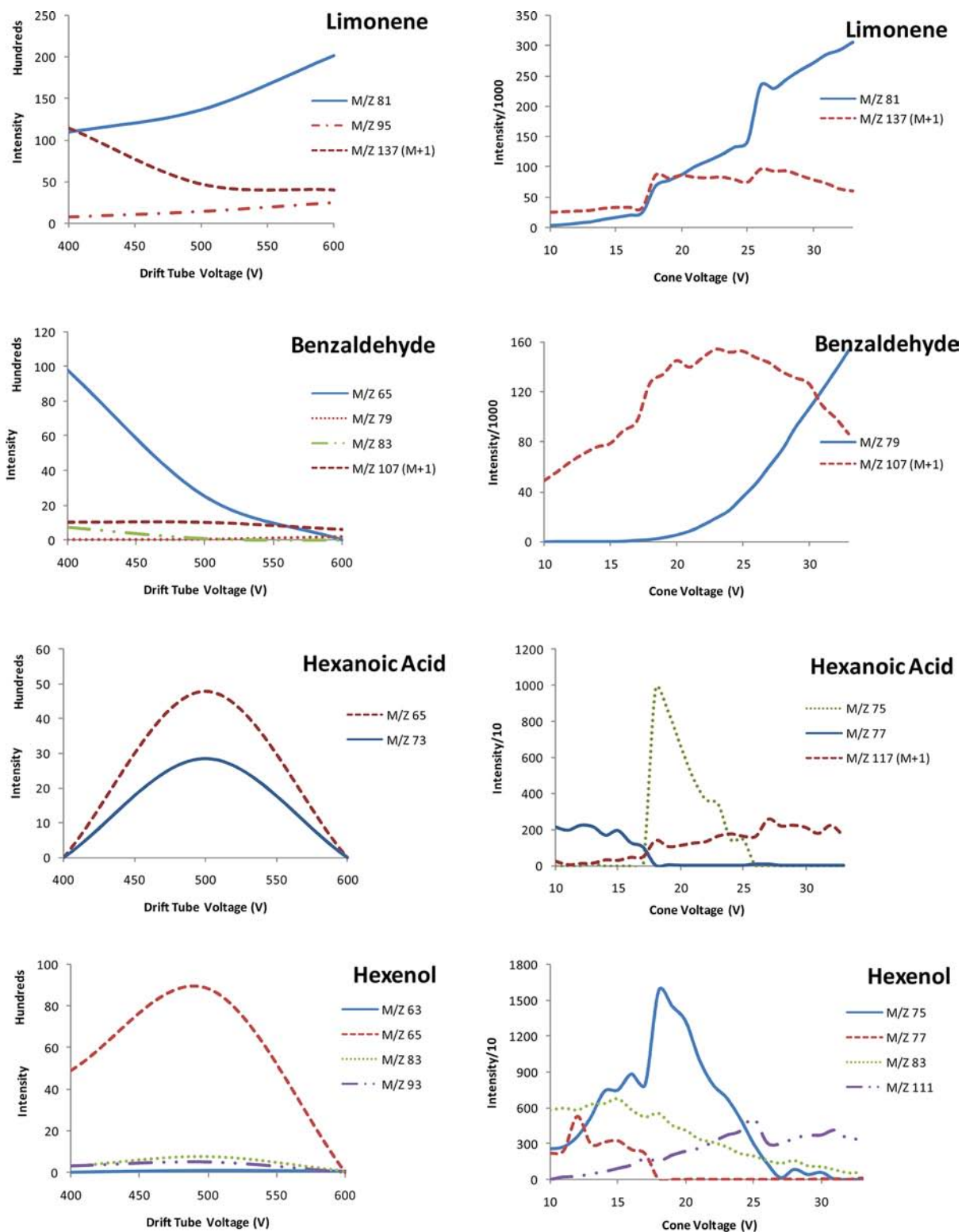
Figure 2. Effect of the key voltage on ionization. Left column: PTR-MS drift tube voltage. Right column: MS-NOSE cone voltage. The molecular ion of the flavor compound is labeled M+1.

for E-2-hexenol and hexanoic acid. For the other volatiles, the molecular ion was higher in abundance than its fragments only for ethyl butyrate. For the MS-NOSE, the molecular ion was observed for all volatiles except E-2-hexenol. In addition, the molecular ion was in higher abundance than its fragments. These results clearly demonstrate that ionization in the MS-NOSE is much softer than in the PTR-MS before optimization.

Experimental Design. The results of the design were first analyzed by using analysis of variance to determine the parameters with a statistically significant effect (>95% confidence) on the ionization characteristics of each volatile. We then created quadratic models for each volatile, using all first and second order effects (Design-Expert 7 Stat Ease, Inc.). After an initial analysis in which all factors were used, the

Table 2. Optimum Conditions in the PTR-MS for Production of Molecular or Fragment Ions

volatile[a]	FC		PC		USO		US		drift		UNC	
	std[b]	opt[c]	std	opt	std	opt	std	opt	std	opt	std	opt
2-butanone	7	7	335	335	80	158	100	161	400	400	5.7	7
amyl acetate	7	7	335	370	80	172	100	174	400	400	5.7	7
amyl acetate 71	7	7	335	344	80	180	100	164	400	400	5.7	6.9
benzaldehyde	7	5	335	335	80	141	100	163	400	400	5.7	7
C6 acid	7	7	335	348	80	172	100	50	400	400	5.7	5.1
C6 acid 73	7	5	335	351	80	180	100	159	400	532	5.7	8
2,3 DMP[d]	7	6	335	350	80	50	100	50	400	400	5.7	7
hexenol 83	7	7	335	363	80	163	100	169	400	400	5.7	7
limonene	7	7	335	370	80	169	100	167	400	400	5.7	7
limonene 81	7	6	335	342	80	180	100	163	400	400	5.7	7
ethyl butyrate	7	7	335	349	80	160	100	154	400	400	5.7	6

[a]A number after a volatile indicates the m/z of a fragment ion. [b]Std = manufacturer's standard conditions. [c]Opt = optimum conditions. [d]2,3 DMP = 2,3-dimethyl pyrazine.

models were simplified by eliminating all those with a significance of $p > 0.05$. Typically, almost all factors in the improved models were significant at the level $p < 0.0001$. A few remained at significance levels of 0.03, which is still highly significant. These models were then used to predict the optimum conditions for the production of the molecular ions or the largest fragment (hexanoic acid and E-2-hexenol) for all of the test volatiles. Table 2 shows these results in comparison to the manufacturer's standard conditions.

The results were surprising: the manufacturer states that the drift voltage in the PTR has the largest effect on the formation of the molecular ion, but it was found to have little influence. The optimum drift voltages were almost all 400 V, the lowest possible level. Hexanoic acid was the only exception with an optimum drift voltage of 532 V, although this was the optimum for a fragment ion (m/z 73) and not the molecular ion. The FC and PC do not change much and they have little effect on the ionization. Paradoxically, the factors that were not expected to affect the ionization (USO and US)[39] were those that had the greatest influence. The UNC, which should never change according to the manufacturer,[39] had a significant and positive effect on the amount of molecular ion. After optimization, the molecular ion of hexanoic acid was observed. Table 3 shows how optimization improved the performance. The average signal intensity was increased by a factor of 3.2 compared with the standard operating conditions.

Because the PTR-MS cannot have multiple settings during an analysis (this is not the case for APCI-MS), a compromise had to be made between the optimum settings for the various volatiles. The average value for each of the PTR-MS settings was chosen as a suitable compromise. To confirm that this compromise was valid, we reanalyzed the samples using standard (before optimization), optimum, and compromise settings. Table 3 shows that using compromise conditions gave an average signal intensity that was 2.4 times higher than the standard conditions. This confirms that the compromise was in fact a reasonable one.

Limits of Detection (LODs) and Dynamic Linear Range (DLR). Using the compromise conditions, the LOD and DLR of the different volatiles were determined. For each volatile, aqueous calibration solutions were made with concentrations of 0.001, 0.01, 0.1, 0.5, 1, 10, and 100 mg/L. They were made from stock solutions containing 200 μL of volatile in 10 mL of methanol, aliquots of which were then diluted in water. The corresponding headspace concentrations above the solutions

Table 3. Improvement of the PTR-MS Signal Intensity by Using the Optimum and Compromise Settings

volatile	factor[a]	
	optimized	compromise
2-butanone	2.0	1.7
amyl acetate	4.0	2.9
amyl acetate 71	3.3	2.6
benzaldehyde	3.1	2.6
C6 acid	4.6	2.9
C6 acid 73	3.4	2.3
2,3 DMP[b]	1.3	1.1
hexenol 93	4.3	3.2
limonene	4.1	2.9
limonene 81	3.3	2.6
ethyl butyrate	2.2	1.8
average factor	3.2	2.4

[a]Optimum or compromise signal intensity/standard signal intensity. [b]2,3 DMP = 2,3-dimethyl pyrazine.

were calculated using Henry's law constants; therefore, the LOD and DLR are quoted as headspace concentrations (ppbv). Table 4 shows that the MS-NOSE outperformed the Ionicon PTR-MS for all of the molecules in both the LOD and the DLR. However, it should be noted that the LODs in this comparison were determined with a dwell time of 20 ms, which is somewhat shorter than the 1 min of dwell time (factor of

Table 4. Comparison of Performance after Optimization: Limit of Detection (LOD) in ppbv and the Dynamic Linear Range (DLR)

volatile	Ionicon-PTR		MS-nose	
	LOD[a]	DLR[b]	LOD[a]	DLR[b]
2-butanone	9.1	1000	9.1	1000
E-2-hexenol	15.5	1000	1.5	10000
hexanoic acid	14.6	100	1.5	1000
benzaldehyde	1.3	1000	0.1	10000
2,3 DMP[c]	16.4	200	3.3	1000
ethyl butyrate	3.5	1000	3.5	10000
amyl acetate	41.9	1000	4.2	10000

[a]Minimum concentration measured with a signal-to-noise ratio >3. [b]Maximum concentration in the linear range/LOD. [c]2,3 DMP = 2,3-dimethyl pyrazine.

3000) that is typically used on a PTR-MS. This could explain why they are not in the low parts per trillion range that is typically quoted.

In conclusion, the PTR-MS is a sensitive machine in the application for which it was originally designed, i.e., measurement of atmospheric constituents that are unlikely to fragment.[39] However, this study shows that for fragrance and flavor molecules, its sensitivity is severely compromised by breakdown of the molecular ion and the very short dwell times. This was quite clearly demonstrated with the tests carried out here, as in not one of the tests did the PTR-MS come close to outperforming the MS-NOSE. However, this problem is not intrinsic to the PTR-MS technique. Its sensitivity could be improved in two ways: (1) increasing the amount of sample that enters the drift tube (without compromising vacuum), as currently only 14 mL/min of 44 mL/min actually enters the drift tube; (2) reducing the drift tube voltage to below 400 V. This should decrease the amount of breakdown; however, this parameter cannot currently be changed by the user.

From the point of view of instrument manufacturers, real-time analysis of flavors is a niche market. Therefore, as this study has shown, the recommended operating conditions may be far from optimum. In addition, because the optimum conditions for soft ionization of volatiles are molecule dependent, the right compromise conditions depend on which molecules are being measured. Therefore, users of PTR-MS who are willing to optimize the operating conditions will be rewarded with significant gains in performance. Finally, it is worth pointing out that all of these results are equally applicable to fragrance molecules.

■ AUTHOR INFORMATION

Corresponding Author
*Tel: +41 22 780 2186. Fax: +41 22 780 2735. E-mail: Shane.Avison@Firmenich.com.

Notes
The authors declare no competing financial interest.

■ ABBREVIATIONS USED

APCI-MS, atmospheric pressure chemical ionization mass spectrometry; PTR-MS, proton transfer reaction mass spectrometry; SIR, selected ion recording; LOD, limit of detection; DLR, dynamic linear range; FC, flow control of the water vapor into the ionization chamber; PC, pressure control of the drift tube; USO, source-out voltage; US, source voltage; drift, drift tube voltage; UNC, nose cone voltage

■ REFERENCES

(1) Lovett, A. M.; Reid, N. M.; Buckley, J. A.; French, J. B.; Cameron, D. M. Real-time analysis of breath using an atmospheric pressure ionization mass spectrometer. *Biol. Mass Spectrom.* **1979**, 6 (3), 91−97.
(2) Benoit, F. M.; Davidson, W. R.; Lovett, A. M.; Nacson, S.; Ngo, A. Breath analysis by atmospheric pressure ionization mass spectrometry. *Anal. Chem.* **1983**, 55 (4), 805−807.
(3) Soeting, W. J.; Heidema, J. A mass spectrometric method for measuring flavour concentration/time profiles in human breath. *Chem. Senses* **1988**, 13 (4), 607−617.
(4) Springett, M. B.; Rozier, V.; Bakker, J. Use of fiber interface direct mass spectrometry for the determination of volatile flavor release from model food systems. *J. Agric. Food Chem.* **1999**, 47 (3), 1125−1131.
(5) Taylor, A. J.; Linforth, R. S. T. Flavour release in the mouth. *Trends Food Sci. Technol.* **1996**, 7 (12), 444−448.
(6) Weel, K. G. C.; Boelrijk, A. E. M.; Alting, A. C.; van Mil, P. J. J. M.; Burger, J. J.; Gruppen, H.; Voragen, A. G. J.; Smit, G. Flavor

release and perception of flavored whey protein gels: Perception is determined by texture rather than by release. *J. Agric. Food Chem.* **2002**, 50 (18), 5149−5155.
(7) Weel, K. G. C.; Boelrijk, A. E. M.; Burger, J. J.; Verschueren, M.; Gruppen, H.; Voragen, A. G. J.; Smit, G. New device to simulate swallowing and in vivo aroma release in the throat from liquid and semiliquid food systems. *J. Agric. Food Chem.* **2004**, 52 (21), 6564−6571.
(8) Weel, K. G. C.; Boelrijk, A. E. M.; Burger, J. J.; Jacobs, M. A.; Gruppen, H.; Voragen, A. G. J.; Smit, G. Effect of emulsion properties on release of esters under static headspace, in vivo, and artificial throat conditions in relation to sensory intensity. *J. Agric. Food Chem.* **2004**, 52 (21), 6572−6577.
(9) van Loon, W. A. M.; Linssen, J. P. H.; Boelrijk, A. E. M.; Burgering, M. J. M.; Voragen, A. G. J. Real-time flavor release from french fries using atmospheric pressure chemical ionization mass spectrometry. *J. Agric. Food Chem.* **2005**, 53 (16), 6438−6442.
(10) Ruijschop, R. M. A. J.; Burgering, M. J. M.; Jacobs, M. A.; Boelrijk, A. E. M. Retro-nasal aroma release depends on both subject and product differences: A link to food intake regulation? *Chem. Senses* **2009**, 395−403.
(11) King, B. M.; Arents, P.; Bouter, N.; Duineveld, C. A. A.; Meyners, M.; Schroff, S. I.; Soekhai, S. T. Sweetener/sweetness-induced changes in flavor perception and flavor release of fruity and green character in beverages. *J. Agric. Food Chem.* **2006**, 54 (7), 2671−2677.
(12) Dronen, G. A. R. Rapid analysis of volatile release from powders using dynamic vapor sorption atmospheric pressure chemical ionization mass spectrometry. *J. Food Sci.* **2003**, 68 (7), 2158−2162.
(13) Buffo, R. A.; Zehentbauer, G.; Reineccius, G. A. Determination of linear response in the detection of aroma compounds by atmospheric pressure ionization mass spectrometry (API-MS). *J. Agric. Food Chem.* **2005**, 53 (3), 702−707.
(14) Gierczynski, I.; Laboure, H.; Semon, E.; Guichard, E. Impact of hardness of model fresh cheese on aroma release: in vivo and in vitro study. *J. Agric. Food Chem.* **2007**, 55 (8), 3066−3073.
(15) Gierczynski, I.; Laboure, H.; Guichard, E. In vivo aroma release of milk gels of different hardnesses: inter-individual differences and their consequences on aroma perception. *J. Agric. Food Chem.* **2008**, 56 (5), 1697−1703.
(16) Le Quéré, J. L.; Gierczynski, I.; Langlois, D.; Sémon, E. Nosespace with an ion trap mass spectrometer-quantitative aspects. In *Developments in Food Science Flavour Science Recent Advances and Trends*; Wender, L. P. B., Ed.; Elsevier: New York, 2006; Vol. 43pp 589−592.
(17) Pionnier, E.; Chabanet, C.; Mioche, L.; Le Quere, J. L.; Salles, C. In vivo aroma release during eating of a model cheese: relationships with oral parameters. *J. Agric. Food Chem.* **2004**, 52 (3), 557−564.
(18) Savary, G.; Semon, E.; Meunier, J. M.; Doublier, J. L.; Cayot, N. Impact of destroying the structure of model gels on volatile release. *J. Agric. Food Chem.* **2007**, 55 (17), 7099−7106.
(19) Zehentbauer, G.; Krick, T.; Reineccius, G. A. Use of humidified air in optimizing APCIMS response in breath analysis. *J. Agric. Food Chem.* **2000**, 48 (11), 5389−5395.
(20) Haahr, A. M.; Madsen, H.; Smedsgaard, J.; Bredie, W. L. P.; Stahnke, L. H.; Refsgaard, H. H. F. Flavor release measurement by atmospheric pressure chemical ionization ion trap mass spectrometry, construction of interface and mathematical modeling of release profiles. *Anal. Chem.* **2003**, 75 (3), 655−662.
(21) Haahr, A. M.; Bardow, A.; Thomsen, C. E.; Jensen, S. B.; Nauntofte, B.; Bakke, M.; dler-Nissen, J.; Bredie, W. L. P. Release of peppermint flavour compounds from chewing gum: Effect of oral functions. *Physiol. Behav.* **2004**, 82 (2−3), 531−540.
(22) Ovejero-Lopez, I.; Haahr, A. M.; van den Berg, F.; Bredie, W. L. P. Flavor release measurement from gum model system. *J. Agric. Food Chem.* **2004**, 52 (26), 8119−8126.
(23) Charles, L.; Riter, L. S.; Cooks, R. G. Direct analysis of semivolatile organic compounds in air by atmospheric pressure

chemical ionization mass spectrometry. *Anal. Chem.* **2001**, 73 (21), 5061−5065.

(24) Warscheid, B.; Kuckelmann, U.; Hoffmann, T. Direct quantitative analysis of organic compounds in the gas and particle phase using a modified atmospheric pressure chemical ionization source in combination with ion trap mass spectrometry. *Anal. Chem.* **2003**, 75 (6), 1410−1417.

(25) Hansel, A.; Jordan, A.; Holzinger, R.; Prazeller, P.; Vogel, W.; Lindinger, W. Proton transfer reaction mass spectrometry: On-line trace gas analysis at ppb level. *Int. J. Mass Spectrom. Ion Proc.* **1995**, *149/150*, 609−619.

(26) Hansel, A.; Singer, W.; Wisthaler, A.; Schwarzmann, M.; Lindinger, W. Energy dependencies of the proton transfer reactions. *Int. J. Mass Spectrom. Ion Proc.* **1997**, *167−168*, 697−703.

(27) Jordan, A.; Hansel, A.; Holziner, R.; Lindinger, W. *Acetonitrile and benzene in the breath of smokers and non-smokers investigated by proton transfer reaction mass spectrometry (PTR-MS)*. 148 ed.; 1995; p L1−L3.

(28) Lagg, A.; Taucher, J.; Hansel, A.; Lindinger, W. Applications of proton transfer reactions to gas analysis. *Int. J. Mass Spectrom. Ion Proc.* **1994**, *134* (1), 55−66.

(29) Lindinger, W.; Hansel, A.; Jordan, A. 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. *Int. J. Mass Spectrom. Ion Proc.* **1998**, *173* (3), 191−241.

(30) Taucher, J.; Hansel, A.; Jordan, A.; Lindinger, W. Analysis of compounds in human breath after ingestion of garlic using proton-transfer-reaction mass spectrometry. *J. Agric. Food Chem.* **1996**, *44* (12), 3778−3782.

(31) Williams, J.; Poschl, U.; Crutzen, P. J.; Hansel, A.; Holzinger, R.; Warneke, C.; Lindinger, W.; Lelieveld, J. An atmospheric chemistry interpretation of mass scans obtained from a proton transfer mass spectrometer flown over the tropical rainforest of surinam. *J. Atmos. Chem.* **2001**, *38* (2), 133−166.

(32) Mateus, M. L.; Lindinger, C.; Gumy, J. C.; Liardon, R. Release kinetics of volatile organic compounds from roasted and ground coffee: Online measurements by PTR-MS and mathematical modeling. *J. Agric. Food Chem.* **2007**, *55* (25), 10117−10128.

(33) Mayr, D.; Mark, T.; Lindinger, W.; Brevard, H.; Yeretzian, C. Breath-by-breath analysis of banana aroma by proton transfer reaction mass spectrometry. *Int. J. Mass Spectrom.* **2003**, *223−224*, 743−756.

(34) Pollien, P.; Lindinger, C.; Yeretzian, C.; Blank, I. Proton transfer reaction mass spectrometry, a tool for on-line monitoring of acrylamide formation in the headspace of maillard reaction systems and processed food. *Anal. Chem.* **2003**, *75* (20), 5488−5494.

(35) Pollien, P.; Jordan, A.; Lindinger, W.; Yeretzian, C. Liquid-air partitioning of volatile compounds in coffee: Dynamic measurements using proton-transfer-reaction mass spectrometry. *Int. J. Mass Spectrom.* **2003**, *228* (1), 69−80.

(36) Roberts, D. D.; Pollien, P.; Antille, N.; Lindinger, C.; Yeretzian, C. Comparison of nosespace, headspace, and sensory intensity ratings for the evaluation of flavor absorption by fat. *J. Agric. Food Chem.* **2003**, *51* (12), 3636−3642.

(37) Yeretzian, C.; Jordan, A.; Lindinger, W. Analysing the headspace of coffee by proton-transfer-reaction mass-spectrometry. *Int. J. Mass Spectrom.* **2003**, *223−224*, 115−139.

(38) Taylor, A. J.; Linforth, R. S. T. On line monitoring of flavour processes. In *Food Flavour Technology*, 2nd ed.; Wiley: New York, 2010; pp 272−279.

(39) Lindinger, C. *Proton Reaction Mass Spectrometer User's Manual* **2002**, 1−49.