

Product ion distributions for the reactions of NO⁺ with some physiologically significant aldehydes obtained using a SRI-TOF-MS instrument



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ABSTRACT

Product ion distributions for the reactions of NO⁺ with 22 aldehydes involved in human physiology have been determined under the prevailing conditions of a selective reagent ionization time of flight mass spectrometry (SRI-TOF-MS) at an E/N in the flow/drift tube reactor of 130 Td. The chosen aldehydes were fourteen alkanals (the C₂–C₁₁ n-alkanals, 2-methyl propanal, 2-methyl butanal, 3-methyl butanal, and 2-ethyl hexanal), six alkenals (2-propenal, 2-methyl 2-propenal, 2-butenal, 3-methyl 2-butenal, 2-methyl 2-butenal, and 2-undecenal), benzaldehyde, and furfural. The product ion fragmentation patterns were determined for both dry air and humid air (3.5% absolute humidity) used as the matrix buffer/carrier gas in the drift tube of the SRI-TOF-MS instrument. Hydride ion transfer was seen to be a common ionization mechanism in all these aldehydes, thus generating (M–H)⁺ ions. Small fractions of the adduct ion, NO⁺M, were also seen for some of the unsaturated alkenals, in particular 2-undecenal, and heterocyclic furfural for which the major reactive channel was non-dissociative charge transfer generating the M⁺ parent ion. Almost all of the reactions resulted in partial fragmentation of the aldehyde molecules generating hydrocarbon ions; specifically, the alkanal reactions resulted in multiple product ions, whereas, the alkenals reactions produced only two or three product ions, dissociation of the nascent excited product ion occurring preferentially at the 2-position. The findings of this study are of particular importance for data interpretation in studies of aldehydes reactions employing SRI-TOF-MS in the NO⁺ mode.

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1. Introduction

It is well established that the human body generates a wide variety of volatile organic compounds (VOCs) some that are present in exhaled breath, emitted through the skin and released by urine samples. As human-specific signatures, these VOCs can be considered as non-invasive biochemical probes that can track normal and abnormal metabolic processes in the body, bacterial and inflammatory processes, and provide invaluable information on exposure to environmental pollutants and/or toxins [1–7].

Volatile aldehydes are widespread in human tissue and fluids and play important roles in functional processes. They have been reported to be common constituents of human urine [8–10], exhaled breath [11,12], and present in skin emanations [13–17]. Some members of this chemical class have been detected in human blood [12,18] and found to be released by in vitro human cell cultures [19–21]. In the medical context, volatile aldehydes have been suggested to be biomarkers of lung cancer [2,19,20,22–25], liver cancer [26], and breast cancer [27] (see Table 1). Some aldehydes are thought to be cytotoxic intermediates with several functions, such as signal transduction, gene regulation, and cellular proliferation [28,29]. Recently, efforts have been made to employ volatile aldehydes in safety and security applications [9,15,30–32]. Thus, there is growing evidence provided by a number of studies suggesting that chemical analysis of human odor could considerably improve effectiveness of search and rescue operations (USaR) organized after disasters resulting in building collapse (e.g., earthquakes, tropical storms, explosions). Although

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Table 1
Aldehydes under study, their occurrence in human fluids and tissues and their potential diagnostic use in medicine.

Compound	CAS	Detected in:	Potential marker of
Acetaldehyde	75-07-0	(a) Urine [10] (b) Breath [11,74,75] (c) Skin emanation [15,76–79] (d) Released by cell cultures: [20,21,24]	Lung cancer [20,24,25]
n-Propanal	123-38-6	(a) Urine [9–11,30] (b) Blood [12] (c) Breath [11,12,80] (d) skin emanation [15,77–79,81]	Lung cancer [2]
n-Butanal	123-72-8	(a) Skin emanation [15,81] (b) Breath [80]	Lung cancer [2]
n-Pentanal	110-62-3	(a) Urine [9,10,30] (b) Breath [23] (c) Skin emanation [15,79,81]	Lung cancer [2,22,23]
n-Hexanal	66-25-1	(a) Urine [8–10,30] (b) Blood [18,26] (c) Breath [23,80] (d) Skin emanation [14,15,81] (e) Released by cell cultures: [19,21]	Lung cancer [2,19,23] Liver cancer [26]
n-Heptanal	111-71-7	(a) Urine [10] (b) Blood [18,26] (c) Breath [27] (d) Skin emanation [14,79,81,82]	Lung cancer [2,19] Breast cancer [27]
n-Octanal	124-13-0	(a) Urine [9,10,15,30] (b) Breath [23] (c) Skin emanation [13–16,81–83]	Lung cancer [2,23]
n-Nonanal	124-19-6	(a) Urine [10,11] (b) Breath [23] (c) Blood [26] (d) Skin emanation [13–16,81–83]	Lung cancer [2,23]
n-Decanal	112-31-2	(a) Breath [23] (b) Skin emanation: [13,14,16,82,83]	
n-Undecanal	112-44-7	(a) Skin emanation [84,85]	
Propanal, 2-methyl-	78-84-2	(a) Urine [10,11,30] (b) Skin emanation [15,82]	
Butanal, 2-methyl-	96-17-3	(a) Urine [9–11] (b) Skin emanation [15,82]	
Butanal, 3-methyl-	590-86-3	(a) Urine [10,11] (b) Skin emanation [15]	
Hexanal, 2-ethyl-	123-05-7	(a) Contaminant from extracorporeal circuits [86]	
2-Propenal	107-02-8	(a) Urine [11] (b) Breath [11] (c) Blood [12] (d) Skin emanation [15]	
2-Propenal, 2-methyl-	78-85-3	(a) Urine [10,11] (b) Breath [11,86] (c) Skin emanation [15]	
2-Butenal, (E)-	123-73-9	(a) Urine [11] (b) Breath [11] (c) Skin emanation [15]	
2-Butenal, 2-methyl-		(a) Urine [10,11] (b) Skin emanation [82]	
2-Butenal, 3-methyl-	107-86-8	(a) Urine [11] (b) Skin emanation [15,16]	
2-Undecenal	53448-07-0	(a) human milk	
Furfural	98-01-1	(a) Urine [10,11]	Gastric cancer [87]
Benzaldehyde	100-52-7	(a) Urine [8,10] (b) Breath [11] (c) Skin emanation [13,15,16,82,83]	Lung Cancer [22]

the origin of some aldehydes in human organisms is unclear, several sources could explain their occurrence. These include (i) alcohols metabolism [33–35], (ii) reduction of hydroperoxides by cytochrome p450 [36], (iii) oxidative stress [14,37], (iv) diet [38,39] and (v) environmental exposure (e.g. tobacco smoking) [40]. Within this framework, a precise and reliable identification, and ultimately quantification, of volatile aldehydes is of importance for their potential exploitation in clinical and/or safety applications.

Proton-transfer reaction mass spectrometry (PTR-MS) [41,42] is frequently employed in biological, medical, and environmental studies for detecting and quantifying volatile organic compounds [43–50]. Its applicability stems from its versatility, excellent sensitivity (low pptv concentration levels), and real-time response. The application of a Time-of-Flight (TOF) mass analyser in PTR-MS instruments notably improves their resolving power and, thereby, the discrimination between isobaric compounds [5,51,52]. The recent employment of additional precursor (reagent) ions such as NO^+ , O_2^+ , and Kr^+ instead of the usual H_3O^+ (creating a selective reagent ionization time of flight mass spectrometry (SRI-TOF-MS)) has further enhanced the analytical possibilities of this technique [51,53].

The primary goal of the present work was to investigate the product ion distributions for the reactions with NO^+ ions of 22 aldehydes involved in human physiology and pathophysiology using a SRI-TOF-MS [51,53], a variant of the well-established PTR-MS technique [41,42]. The reactions of NO^+ with VOCs in SRI-TOF-MS are relatively poorly known, inhibiting their use for trace gas analysis, but it is certain that for most such reactions multiple product ions will result, as can also happen using H_3O^+ reagent ions in PTR-MS [54]. An interesting advantage of NO^+ as a reagent ion is that different chemical classes of VOCs have their typical reactions with NO^+ (charge/electron transfer, hydride ion (H^-), transfer, hydroxide ion (OH^-) transfer, alkoxide ion (OR^-) transfer, and NO^+ /analyte molecule association), as has been summarized in a detailed review paper [55]. This ion chemical variability is of potential value because it allows in some cases the separation of functional isomers [55]. 22 aldehydes were selected for inclusion in the present study as guided by the available literature that reports their presence in human urine, breath, blood, and skin emanation, as summarized in Table 1.

2. Experimental

2.1. Materials and standard mixtures

Single-compound standard mixtures were prepared from liquid aldehydes, the majority of which were purchased from Sigma-Aldrich (Austria); acetaldehyde (99%), n-propanal (97%), n-butanal (99%), n-pentanal (97%), n-hexanal (98%), n-heptanal (95%), n-octanal (99%), n-undecanal (97%), 2-methyl propanal (99.5%), 3-methyl butanal (97%), 2-ethyl hexanal (96%), 2-methyl 2-propenal (95%), and (E)-2-butenal (99%). Moreover, n-nonanal (95%), n-decanal (95%), 2-propenal (95%), and benzaldehyde (99%) were obtained from Fluka (Switzerland), whereas, 2-methyl butanal (90%), 3-methyl 2-butenal (97%), (E)-2-methyl 2-butenal (97%), (E)-2-undecenal (90%), and furfural (98%) were provided by SAFC (USA). The compound purities are also given in Table 2 for assistance in the interpretation of the product ion distributions of the NO^+ /aldehyde reactions.

The standard mixtures were produced in two steps. First, single-compound primary standards were prepared in 1-L glass bulbs (Supelco, Canada). Before usage, each bulb was thoroughly cleaned with methanol and dried at 70 °C under the flow of high-purity nitrogen for at least 12 h to remove potential contaminants. The bulb was then evacuated using a membrane vacuum pump and

approximately (0.5–1) μL of liquid analyte was injected through a rubber septum. Next, the bulb was heated to 100 °C for 30 min to ensure complete evaporation and then the pressure was balanced to ambient pressure with high-purity cylinder air. The desired standard mixtures were prepared by transferring appropriate volumes of the primary standard into 3-L volume transparent Tedlar bags (SKC Inc., USA) filled with predefined amounts of purified and humidified air, the latter being produced by a GasLab calibration mixtures generator (Breitfuss Messtechnik, Germany). Effectively, for each compound the product ion distribution was investigated using 3 distinct concentration levels of each aldehyde in air ranging approximately from 25 to 150 ppbv and at two different absolute humidity levels of essentially 0 and 3.5%.

2.2. SRI-TOF-MS analysis

The NO^+ /aldehyde reactions were studied using an Ionicon Analytik (Innsbruck, Austria) type 8000 SRI-TOF-MS instrument [56], a variant of the familiar PTR-MS flow-drift tube instruments [51,52,57,58]. The NO^+ precursor/reagent ions were generated by the ionization mechanism extensively described elsewhere [55,59], essentially by charging the hollow cathode discharge ion source with high purity dry air. The settings of the ion source were chosen as follows: ion source current 5 mA, source voltage (Us) 20 V, source-out voltage (Uso) 70 V, and source valve opening 40%. With these settings the major parasitic impurity ions, as detected downstream by the analytical TOF-MS, were H_3O^+ , O_2^+ , and NO_2^+ at relative levels (parasitic ion/ NO^+) of 0.3–0.6%, 1–1.5%, and 1–2%, respectively in the air carrier/buffer gas. The NO^+ /aldehyde reactions occurred in the carrier/aldehyde sample gases in the flow/drift tube at a total pressure of 2.23 mbar and a gas temperature of 60 °C. Moreover, the voltage along the drift section was set to 600 V leading to an E/N ratio of approximately 130 Td [54].

The high resolution realized by the TOF analyzer ranged from m/z 1 to 500 and were acquired at a time of 30 s by co-adding 750,000 single 40- μs long TOF-MS extractions recorded at a sampling frequency $1/\Delta t = 10$ GHz. This corresponds to a theoretical upper limit $m/\Delta m$ of $\approx 90,000$ at m/z 100 (the flight time of these ions being $\approx 18 \mu\text{s}$). However, the actual mass resolution obtained from the detected peaks was ≈ 4000 at m/z 100. This high resolution allows the separation of ions at nominally the same integer mass, for example, the nominally isobaric ions C_3H_7^+ and CH_3CO^+ ions that are sometimes produced simultaneously in the analysis of gaseous matrices containing hydrocarbons, aldehydes and ketones [57,58]. The mass calibration was based on three impurity peaks always present in the spectra: H_3O^+ (19.0178), $^{15}\text{NO}^+$ (30.9945), and NO_2^+ (45.9924).

The standard mixtures entered the flow/drift tube of the SRI-TOF-MS instrument at a steady flow rate of 10 mL/min via a two-meter-long, heated (40 °C) Teflon transfer line. The total duration of a single measurement was 5 min, which corresponds to 10 mass spectra acquired per concentration level. Effectively, the average of these 10 spectra was used to determine the percentages of the product ions resulting from each NO^+ /aldehyde reaction.

3. Results and discussion

Table 2 summarizes the product ions distribution for the 22 aldehyde/ NO^+ reactions. The channel percentages were calculated using the signal intensities corrected for the mass dependent discrimination of the instrument (“transmission”). Only product ions with abundance greater than 0.5% of the total signal were included in the table unless they clearly originated from the species under study (e.g., the small adduct ion in the benzaldehyde reaction), although the stated purities of the aldehydes (see Section 2.1),

Table 2
Product ion distributions for the reactions of NO⁺ with 22 aldehydes under dry and humid (AH 3.5%) air carrier gas in the SRI-TOF-MS instrument at a specific E/N of 130 Td. The ion products resulting from hydride ion transfer and (M–H)⁺ are indicated in **bold** type; those ions resulting in adduct formation NO⁺M are indicated in *italics*. Uncertain neutral products for the reactions are indicated by bracketing. The compound purities are given in %.

Compound	Formula	Purity [%]	MW	Reaction channel	Dry air [%]	Humid air [%]	Measured m/z [Th]	Expected m/z [Th]	Error [mTh]
Acetaldehyde	C ₂ H ₄ O	99	44.05	C ₂ H ₃ O ⁺ + HNO	100	100	43.0196	43.0179	1.7
n-Propanal	C ₃ H ₆ O	97	58.08	C ₃ H ₅ O ⁺ + HNO	76	100	57.0362	57.0335	2.7
				C ₂ H ₅ ⁺ + CO + HNO	18.6	0	29.0386	29.0386	0.1
				C ₂ H ₃ ⁺ + (CHO + H ₂) + NO	5.5	0	27.0225	27.0229	0.1
n-Butanal	C ₄ H ₈ O	99	72.11	C ₄ H ₇ O ⁺ + HNO	18.4	16.5	71.0529	71.0492	3.8
				C ₃ H ₇ ⁺ + CO + HNO	47	54	43.0563	43.0543	1.9
				C ₃ H ₅ ⁺ + CHO + (NO + H ₂)	32	28	41.0404	41.0386	1.8
				C ₃ H ₃ ⁺ + (CHO + NO + 2H ₂)	2.7	1.8	39.0253	39.0230	2.4
n-Pentanal	C ₅ H ₁₀ O	97	86.13	C ₅ H ₉ O ⁺ + HNO	14.9	15.9	85.0715	85.0648	5.9
				C ₄ H ₉ ⁺ + CO + HNO	65.5	69	57.0742	57.0699	2.7
				C ₃ H ₅ ⁺ + (C ₂ H ₃ O + H ₂ + NO)	17.9	14.2	41.0422	41.0386	1.2
				C ₃ H ₃ ⁺ + (C ₂ H ₃ O + 2H ₂ + NO)	1.7	1	39.0249	39.0230	1.2
n-Hexanal	C ₆ H ₁₂ O	98	100.16	C ₆ H ₁₁ O ⁺ + HNO	12.5	13.4	99.0856	99.0805	6.2
				C ₆ H ₉ ⁺ + (H ₂ O + HNO)	0.5	0.5	81.0770	81.0698	7.1
				C ₅ H ₁₁ ⁺ + CO + HNO	14.2	15.9	71.0902	71.0856	4.6
				C ₃ H ₇ ⁺ + C ₃ H ₅ NO ₂	44.5	48	43.0563	43.0543	2.1
				C ₃ H ₅ ⁺ + (C ₃ H ₅ NO ₂ + H ₂)	26.5	21.2	41.0407	41.0386	2.1
				C ₃ H ₃ ⁺ + (C ₃ H ₅ NO ₂ + 2H ₂)	1.8	1.1	39.0242	39.0230	1.2
n-Heptanal	C ₇ H ₁₄ O	95	114.18	C ₇ H ₁₃ O ⁺ + HNO	18.2	20	113.1031	113.0961	7.0
				C ₇ H ₁₁ ⁺ + (H ₂ O + HNO)	2.3	2.2	95.0924	95.0856	6.8
				C ₆ H ₁₃ ⁺ + CO + HNO	8.7	9.6	85.1076	85.1012	6.4
				C ₄ H ₉ ⁺ + (C ₃ H ₅ O + NO)	5.2	4.8	57.0730	57.0699	3.1
				C ₃ H ₇ ⁺ + (C ₄ H ₇ O + NO)	39	43	43.0562	43.0543	1.9
				C ₃ H ₅ ⁺ + (C ₄ H ₇ O + NO + H ₂)	25	19.6	41.0404	41.0386	1.8
				C ₃ H ₃ ⁺ + (C ₄ H ₇ O + NO + 2H ₂)	1.8	0.9	39.0239	39.0230	0.9
n-Octanal	C ₈ H ₁₆ O	99	128.22	C ₈ H ₁₅ O ⁺ + HNO	27	29.5	127.1204	127.1174	3.0
				C ₈ H ₁₃ ⁺ + (H ₂ O + HNO)	5.3	5.2	109.1086	109.1012	7.4
				C ₅ H ₇ ⁺ + (C ₃ H ₅ NO ₂ + 2H ₂)	1.5	1.5	67.0586	67.0542	4.4
				C ₄ H ₉ ⁺ + C ₄ H ₇ NO ₂	57	57	57.0734	57.0699	3.5
				C ₃ H ₅ ⁺ + (C ₅ H ₉ NO ₂ + H ₂)	8.5	7	57.0734	41.0386	2.1
n-Nonanal	C ₉ H ₁₈ O	95	142.24	C ₉ H ₁₇ O ⁺ + HNO	46.2	47.3	141.1373	141.1274	9.9
				C ₉ H ₁₅ ⁺ + (H ₂ O + HNO)	7.8	6.9	123.1257	123.1168	8.9
				C ₅ H ₁₁ ⁺ + C ₄ H ₇ NO ₂	8.4	8.2	71.0916	71.0856	6.0
				C ₄ H ₉ ⁺ + C ₅ H ₉ NO ₂	18	18.2	57.0748	57.0699	4.9
				C ₃ H ₇ ⁺ + C ₆ H ₁₁ NO ₂	15.7	13.7	43.0580	43.0543	3.8
				C ₃ H ₅ ⁺ + (C ₆ H ₁₁ NO ₂ + H ₂)	4.2	5.8	41.0405	41.0386	1.9
n-Decanal	C ₁₀ H ₂₀ O	95	156.3	C ₁₀ H ₁₉ O ⁺ + HNO	63	69	155.1576	155.1431	14.0
				C ₁₀ H ₁₇ ⁺ + (H ₂ O + HNO)	6	5.7	137.1454	137.1325	12.9
				C ₆ H ₁₃ ⁺ + (C ₄ H ₇ O + NO)	2	2.3	85.1099	85.1012	8.8
				C ₅ H ₁₁ ⁺ + (C ₅ H ₉ O + NO)	5.3	5	71.0909	71.0856	5.4
				C ₄ H ₉ ⁺ + (C ₆ H ₁₁ O + NO)	6.5	6	57.0731	57.0699	3.3
				C ₃ H ₇ ⁺ + (C ₇ H ₁₃ O + NO)	13	10	43.0555	43.0543	1.3
				C ₃ H ₅ ⁺ + (C ₇ H ₁₃ O + H ₂ + NO)	6.3	3.3	41.0399	41.0386	1.4
				C ₁₁ H ₂₂ O·NO ⁺	0.6	0.5	200.1802	200.1646	15.7
n-Undecanal	C ₁₁ H ₂₂ O	97	170.29	C ₁₁ H ₂₁ O ⁺ + HNO	85.6	87.4	169.1721	169.1587	13.4
				C ₁₁ H ₁₉ ⁺ + (H ₂ O + HNO)	5.2	4.7	151.1606	151.1482	12.5
				C ₇ H ₁₁ ⁺ + (C ₄ H ₇ O + 2H ₂ + NO)	7	5.8	95.0928	95.0856	7.3
				C ₆ H ₉ ⁺ + (C ₅ H ₉ O + 2H ₂ + NO)	1.4	0.6	81.07537	81.0699	5.5
				Propanal, 2-methyl-	C ₄ H ₈ O	99.5	72.11	C ₄ H ₇ O ⁺ + HNO	4.2
C ₃ H ₇ ⁺ + CHNO ₂	51.5	67	43.0576					43.0543	3.3
C ₃ H ₅ ⁺ + (CHNO ₂ + H ₂)	39.5	25.6	41.0420					41.0386	3.4
C ₃ H ₃ ⁺ + (CHNO ₂ + 2H ₂)	4.8	1.6	39.0269					39.0230	4.0
Butanal, 2-methyl-	C ₅ H ₁₀ O	90	86.13	C ₅ H ₉ O ⁺ + HNO	2.3	3.1	85.0694	85.0648	4.5
				C ₄ H ₉ ⁺ + CO + HNO	72.3	80.7	57.0743	57.0699	4.4
				C ₃ H ₅ ⁺ + (C ₂ H ₄ O + HNO)	23.2	14.8	41.0417	41.0386	3.0
				C ₃ H ₃ ⁺ + (C ₂ H ₃ O + NO + 2H ₂)	3	1.5	39.0266	39.0230	3.7
Butanal, 3-methyl-	C ₅ H ₁₀ O	97	86.13	C ₅ H ₉ O ⁺ + HNO	12.2	14.2	85.0706	85.0648	5.8
				C ₄ H ₉ ⁺ + CO + HNO	70	76.6	57.0738	57.0699	3.9
				C ₃ H ₅ ⁺ + (C ₂ H ₃ O + H ₂ + NO)	17.6	9.2	41.0419	41.0386	3.3
Hexanal, 2-ethyl-	C ₈ H ₁₆ O	96	128.12	C ₈ H ₁₅ O ⁺ + HNO	2.1	2.6	127.1219	127.1118	10.2
				C ₄ H ₉ ⁺ + (C ₄ H ₇ O + NO)	88	89	57.0726	57.0699	2.8
				C ₃ H ₅ ⁺ + (C ₅ H ₉ O + H ₂ + NO)	9.7	8	41.0398	41.0386	1.3

Table 2 (Continued)

Compound	Formula	Purity [%]	MW	Reaction channel	Dry air [%]	Humid air [%]	Measured m/z [Th]	Expected m/z [Th]	Error [mTh]
2-Propenal	C ₃ H ₄ O	95	56.06	C ₃ H ₄ O·NO ⁺	4.5	5.5	86.0287	86.0237	5.0
				C ₃ H ₃ O ⁺ + HNO	93	93.4	55.0212	55.0179	3.4
				C ₂ H ₃ ⁺ + CO + HNO	2.6	1.2	27.0266	27.0230	3.6
2-Propenal, 2-methyl-	C ₄ H ₆ O	95	70.09	C ₄ H ₆ O·NO ⁺	1.5	1.6	100.0488	100.0393	9.5
				C ₄ H ₅ O ⁺ + HNO	26	22	69.0377	69.0335	4.2
				C ₃ H ₅ ⁺ + CO + HNO	73	72	41.0419	41.0386	3.3
				C ₃ H ₃ ⁺ + (CHO + NO + H ₂)	10	4.5	39.0264	39.0230	3.4
2-Butenal	C ₄ H ₆ O	97	70.09	C ₄ H ₆ O·NO ⁺	0.6	0.6	100.047	100.0394	7.7
				C ₄ H ₅ O ⁺ + HNO	96	94	69.0371	69.0335	3.6
				C ₃ H ₅ ⁺ + CO + HNO	3.2	5	41.0406	41.0386	2.1
2-Butenal, 2-methyl-	C ₅ H ₈ O	97	84.12	C ₅ H ₈ O·NO ⁺	0.4	0.3	114.0648	114.0550	9.8
				C ₅ H ₇ O ⁺ + HNO	67	64	83.0546	83.0492	5.5
				C ₄ H ₇ ⁺ + CO + HNO	32	36	55.057	55.0543	2.8
2-Butenal, 3-methyl-	C ₅ H ₈ O	97	84.12	C ₅ H ₇ O ⁺ + HNO	98	98	83.0539	83.0492	4.8
				C ₄ H ₇ ⁺ + CO + HNO	2	2	55.0575	55.0543	3.3
2-Undecenal	C ₁₁ H ₂₀ O	90	168.28	C ₁₁ H ₂₀ O·NO ⁺	8	9.7	198.1665	198.1489	18
				C ₁₁ H ₁₉ O ⁺ + HNO	92	90.3	167.1588	167.1431	15.7
Furfural	C ₅ H ₄ O ₂	98	96.08	C ₅ H ₄ O ₂ ·NO ⁺	9	11	126.0273	126.0186	8.7
				C ₅ H ₄ O ₂ ⁺ + NO	51	54	96.0261	96.0206	5.5
				C ₅ H ₃ O ₂ ⁺ + HNO	39	35	95.0186	95.0128	5.9
Benzaldehyde	C ₇ H ₆ O	99	106.12	C ₇ H ₆ O·NO ⁺	0.2	0.4	136.0474	136.0393	8.1
				C ₇ H ₅ O ⁺ + HNO	98	98.2	105.0405	105.0335	6.9
				C ₆ H ₅ ⁺ + CO + HNO	1.7	1.4	77.0318	77.0386	6.8

which range from 90 to 99%, means that product ions percentages should be considered in the light of the specific purities of each aldehyde. The abundance percentages listed for each reaction are the averages of values obtained for 3 distinct mean concentrations (from 10 spectra) of the aldehydes in the dry air and the humid air, as indicated in Table 2.

There is a long history on the study of mechanisms of ion–molecule reactions, especially so at thermal and near-thermal interaction energies [60,61]. At these low interaction energies the reactions are generally considered to occur by an intimate ion–molecule interaction forming an excited intermediate complex, in the present reactions (NO⁺M)^{*}, which can either spontaneously undergo unimolecular decomposition back to the reactants or forward to fragmentation product ions, or be partially or totally stabilized by a third body collision (with the bath gas atoms and/or molecules in which the reaction occurs) resulting in the stable NO⁺M adduct ion. Looser or longer range interactions can occur, usually at higher interaction energies as in ion–neutral beams via the process of exothermic charge/electron transfer, but heavy particle exchange, such as hydride ion, H⁻, transfer, rarely occurs at long distance.

In all the reactions in the present series a significant, often dominant reaction mechanism is seen to be hydride ion transfer generating (M–H)⁺ ions, as indicated by the percentage product ions given as **bold** in Table 2. This is in accordance with earlier studies carried out under the thermalized condition of the SIFT and SIFT-MS [62–64]. This strongly implies that these NO⁺/aldehyde reactions in the thermalized SIFT-MS, and even the suprathreshold SRI-TOF-MS reactors, do proceed via close interactions and the initial formation of the intermediate (NO⁺M)^{*} excited complexes. In the SIFT experiments, the observed product ions for the saturated alkanals mostly result from H⁻ transfer, occasionally the partial formation of NO⁺M adduct ions in the case of the unsaturated alkenals, and rarely ions that result from chemical rearrangements within the excited complex [62,65]. However, it is known and expected from mechanistic considerations that the lifetimes of these (NO⁺M)^{*} complexes decreases with increasing interaction

energy and gas temperature [66] and so their lifetimes are expected to be shorter in SRI-TOF-MS flow/drift reactors than in thermalized SIFT-MS flow tube reactors (carrier gas temperature typically 25 °C). This will diminish the probability of seeing stabilized NO⁺M adduct ions in the SRI-TOF-MS reactor at similar carrier/buffer gas pressures but at the higher carrier gas temperature of 60 °C (see below).

In the present flow/drift tube experiments, significant percentages of fragment ions are also seen for both the alkanals and alkenals reactions, most often as hydrocarbon ions C_nH_m⁺, and this must be due to the elevated ion–molecule interaction energies in the flow/drift tube and the possible injection from the ion source of energetic ions such as N₂⁺ that will not be seen downstream by the analytical mass spectrometer because of reactive loss. Thus, fragmentation occurs in addition to hydride ion transfer for all these aldehyde reactions, as can be seen by the multiple product ions in many reactions, with the exception of the 2-undecenal and furfural reactions, seen in Table 2. This is particularly true for alkanals where 2–6 additional fragment ions are observed.

Ultimately, the energetics will determine the ion and neutral products of these reactions. Consider first the NO⁺/acetaldehyde reaction that results in only the CH₃CO⁺ product ion and an HNO neutral molecule. It is straightforward to show that this reaction is exothermic by 0.7 eV (electron volts) [67], yet this reaction is known to be relatively slow even under SIFT-MS conditions [62]; it is uncertain what its rate will be under PTR-MS conditions, but this would need to be ascertained if the NO⁺/acetaldehyde reaction is to be exploited for analysis. The fraction of (M–H)⁺ to the total product ions in the NO⁺/propanal reaction indicated in Table 2 and Fig. 1 is 100% for moist carrier/sample gas and <100% in dry air when obviously additional product ions are seen:



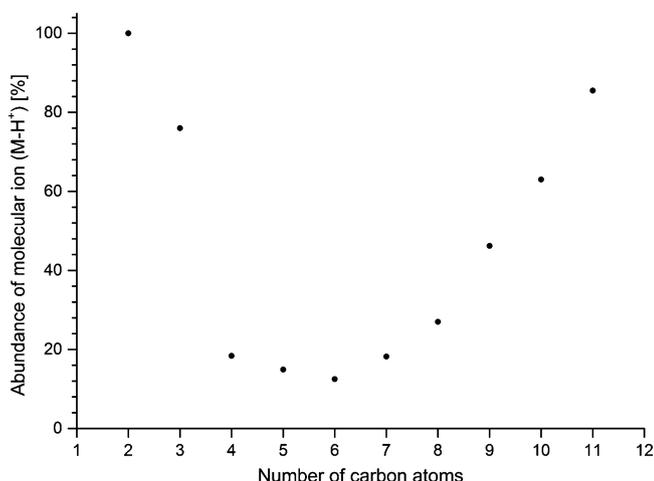


Fig. 1. Percentage of (M–H)⁺ product ions in the reactions of NO⁺ ions with n-alkanals in dry air in the SRI-TOF-MS instrument at an E/N of 130 Td.

Hydride ion transfer (1a) is exothermic by 1.1 eV and is thus more exothermic than in the analogous acetaldehyde reaction. But what are the neutral products of reactions (1b) and (1c)? The fragmentation channel (1b) leading to a closed shell hydrocarbon ion is calculated to be endothermic by >2 eV [67] to produce two radical neutrals HCO[•], and NO[•], and endothermic by only 1 eV to produce the closed shell molecules CO and HNO. Reaction (1c) is very endothermic by >4 eV to produce three neutral products CHO, H₂ and NO and this is very unlikely, but it is less endothermic at 3.2 eV to produce the two products indicated as CH₂O and HNO. Thus, it is problematic to identify the neutral products of these apparently very endothermic reactions, especially so because of the uncertainty in the kinetic energy distribution of the ions in the flow/drift tube (but which must depart from Maxwellian and is probably skewed toward the high energy tail), the vibrational state of the reactant NO⁺ ions, and the interaction energies of the reactant ions and aldehyde molecules. What is certain is that the interaction energies will be elevated above the thermal energies prevailing in SIFT studies [54] and this could drive endothermic reactions as apparently is the case for several of the reaction channels indicated for other reactions listed in Table 2. In support of the likely elevated interaction energies in the flow/drift tube reactors is the detailed analysis of hydrated hydronium ions, H₃O⁺(H₂O)_n, in PTR-MS flow/drift tube reactors by de Gouw et al. [54], which indicates that the monohydrate ion H₃O⁺H₂O, which has an H₃O⁺–H₂O binding energy of 1.4 eV, is entirely dissociated at an E/N of 130 Td as adopted in the present experiments. This implies that ions like C₂H₅CO⁺, such as may be formed in reaction (1a), could fully dissociate to C₂H₅⁺ and CO. Even so, it is difficult to see how reactions that are apparently endothermic by much more than 1 eV for ground vibronic state NO⁺ ions can occur. It is therefore futile to attempt to define the reactions fully or even to guess the neutral products for the minor channels of these reactions when their origins are so uncertain.

In summary, for the C3–C7 alkanal reactions, CO elimination is observed as a common fragmentation mode of the hydride ion product (M–H)⁺ leading to the observed closed shell hydrocarbon ions C_nH_{2n+1}⁺. For C6–C11 n-alkanals the hydride ion transfer process may be followed by the elimination of an H₂O molecule (or formation of dihydroxyamine H₃NO₂ as a single neutral product), but this could only be substantiated by detailed consideration of the energetics of the reactions; this uncertainty is indicated by bracketing the probable neutral products of each reaction in Table 2. The energy required for fragmentation of the primary product ion (M–H)⁺ to eliminate CO or H₂O molecules can be acquired

in multiple collisions with the N₂ and O₂ molecules that excites internal vibrational modes of (M–H)⁺ ions, since at an E/N of 130 Td the “effective temperature” of the interaction can be 500–800 K [68]. Interestingly, the possible H₂O molecule elimination is apparently not occurring for the branched alkanal reactions for which the major mechanism can be interpreted as the elimination of C_nH_(2n–1)O groups and the formation of hydrocarbon ions, C₃H₇⁺ and C₄H₉⁺ (see Table 2).

In the case of n-alkanals, the percentage (branching ratio) of the (M–H)⁺ hydride ion transfer products exhibits an interesting dependence on the number of carbon atoms in the molecule (see Fig. 1) that varies from 100% for the acetaldehyde reaction to a minimum percentage (13%) for the n-hexanal reaction. Heavier n-alkanals fragment considerably less. For instance, the percentage of (M–H)⁺ ions for the n-octanal reaction is 27%, whereas for the n-undecanal reaction it is about 85%. This phenomenon may assist identification of heavier alkanals in the SRI-TOF-MS(NO⁺) instrument, but it would be complicated for the analysis of real matrices that contain mixtures of aldehydes and other trace compounds. Why does the plot of (M–H)⁺ ion percentage signal levels have the form shown in Fig. 1? The answer must lie to some extent in the nature and the energetics of individual product channels of the NO⁺/M reactions, specifically the lifetime of the intermediate (NO⁺M)⁺ excited complexes and the accessibility of the other reaction channels. The production of (M–H)⁺ ions is exothermic for all the reactions, but others of the observed channels may also be exothermic, especially so for those reactions where (M–H)⁺ production is relatively small fraction of the total product ions. The lifetimes of the (NO⁺M)⁺ excited complexes are generally assumed to be shorter for small M and to increase with molecular weight of M, as a consequence of the increasing number of vibrational modes of the complex in which the binding energy can be temporarily dispersed [66]. A combination of these parameters could explain the increased efficiency of (M–H)⁺ production within the longer-lived complexes of the larger alkanals.

The presence of a side-chain in the aldehyde molecule promotes greater fragmentation of isomeric aldehydes, as can be seen in Table 2. However, this effect seems to occur only when the methyl (or ethyl) group is located at the second position of the main carbon chain. For example, the abundance of the (M–H)⁺ product ion of n-pentanal and 3-methyl butanal reactions is very similar at 14–15%, whereas the fraction of this ion in the 2-methyl butanal reaction is only 2%. A similar effect can be seen by comparing the n-butanal and the 2-methyl propanal reactions (18% vs 4%), and the n-octanal reaction with the 2-ethyl hexanal reaction (27% vs 2%). The same holds true for the alkenal reactions (e.g., 96% for 2-butenal vs 26% for 2-methyl 2-propenal). Consequently, the identification of 2-methyl(ethyl) aldehydes by SRI-TOF-MS(NO⁺) could be problematic in biological matrices using only this information. Unsaturated aldehydes showed a much lower degree of fragmentation.

A further interesting point is that in the reactions of NO⁺ with the largest alkanal, n-undecanal, in some unsaturated aldehydes, the heterocyclic furfural, and the aromatic benzaldehyde, small stable NO⁺M association product ions are observed, as indicated in *italics* in Table 2. The percentages are only small, but greatest for the furfural and 2-undecenal reactions where they reach approximately 10% of the total product ions. This reaction product channel has been seen previously for some unsaturated aldehydes in SIFT studies [62,63] and is attributed to the proximity of the ionization energies (IE) of the aldehydes with IE of NO, which results in “charge transfer complexing” that prolongs the lifetime of the (NO⁺M)⁺ intermediate complexes [63]. This interesting phenomenon is especially efficient in the association of NO⁺ ions with ketones in SIFT reactors [62,69,70]. It can also be reported here that a recent spot investigation of the NO⁺/n-undecanal reaction in a (thermalized)

SIFT experiment significantly revealed a 40% NO^+ /undecanal adduct ion together with a 60% hydride ion channel and no significant fragmentation channels [71].

Amongst all the aldehydes included in this study, charge transfer was only observed in the furfural reaction (50% of the total product ions), this process being marginally exothermic because the ionization energy, IE, of the furfural molecule at 9.22 eV [72] is just lower than the IE of NO (9.26 eV [72]). This charge transfer efficiency will be assisted by the increased NO^+ /furfural molecule interaction energy in the SRI-TOF-MS reactor.

The presence of water molecules in the sample/carrier gas has little or no effect on the product ion distributions for all these NO^+ /aldehyde reactions except for the n-propanal reaction (see Table 2) for which in humid air the only observed product ion is $(\text{M}-\text{H})^+$. This is probably due to the fact that the product C_2H_5^+ and C_2H_3^+ ions of the NO^+ /propanal reaction can rapidly react with water molecules in moist air and thus be eliminated from the reactor and not be seen by the downstream mass spectrometer. This will generally be the case for product ions of the type MH^+ , where M has a proton affinity (PA) lower than the PA of water molecules (691 kJ mol^{-1} [67]). This applies to protonated acetylene C_2H_3^+ (PA = 641.4 kJ mol^{-1}) and protonated ethylene C_2H_5^+ (PA = 680.5 kJ mol^{-1}), as appear in reactions (1b) and (1c). This observation is consistent with an analogous phenomenon in SIFT-MS reported by Francis et al. [73]. Significantly, the abundance of the C_3H_5^+ product ion for other aldehyde reactions reduced somewhat in the spectra obtained for the humid sample/carrier gas (see e.g., this product ion for the 2-methyl propanal and the 3-methyl butanal reactions). Although, the chemical structures of the particular C_3H_5^+ product ions are not established, three C_3H_4 underlying structural isomers are possible, all three having higher PA than water molecules (allene: 775 kJ mol^{-1} , propyne: 748 kJ mol^{-1} , and cyclopropene: 818.5 kJ mol^{-1}). Whilst the differences in these PA and that of water molecules is rather large and so proton transfer will be inhibited, it could be partially promoted by the elevated energies of the ion-molecule interactions in the SRI-TOF-MS flow/drift reactor and because of the very large number density of the H_2O molecules in the sample/carrier gas at an absolute humidity of 3.5%.

4. Concluding remarks

The results of the present study of the reactions of NO^+ with some 22 aldehydes, comprising several n-alkanals, several branched chain alkanals, and several alkenals, indicates that most of the reactions result in multiple ion products, but common $(\text{M}-\text{H})^+$ product ions are seen that result from hydride ion transfer with the fractional abundance of these ions increasing with the alkanal molecular mass. A series of hydrocarbon ions, C_nH_m^+ , appear at widely differing percentages of the total ion products at m/z values that reflect the complexity (atomicity) of the aldehyde molecules. More specifically, alkanals exhibited a higher degree of fragmentation than the alkenals and the branched aldehydes dissociated most commonly at the position 2. It must be emphasized that these ion product distributions will surely depend on the actual value of E/N used in the SRI-TOF-MS instrument. Whilst increasing the humidity of the sample/carrier gas had little effect on the product ion branching ratios, such serious fragmentation limits the value of SRI-TOF-MS using NO^+ reagent ions for the identification of aldehydes, especially when more than one of these compounds occur together in real samples such as exhaled breath and the headspace of biological fluids.

Analytical sensitivity is diminished when multiple ion products of the analytical reactions occur unless such is carefully accounted for. It is also imperative that the rate constants for the analytical

reactions be determined under the actual conditions of the reactor in order to obtain reliable quantification. This is especially so for these NO^+ reactions occurring in the flow/drift tube, because minor association channels are seen which is a clear warning of rate constants that can vary (usually decrease) with increasing interaction energy. In this regard, it is worthy of note that the rate constant for the NO^+ /acetaldehyde is much less than the collisional rate constant even under the thermal conditions of the SIFT system [62] and would most probably decrease with increasing E/N in the flow/drift tube of a SRI-TOF-MS system.

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