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Detection and Quantification of Chemical Warfare Agent Precursors and Surrogates by Selected Ion Flow Tube Mass Spectrometry

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The rate coefficients and branching ratios of 15 chemical warfare agent precursor and surrogate compounds reacting with H_3O^+ , NO^+ , and O_2^+ have been measured in the laboratory using the selected ion flow tube (SIFT) technique. Measurement of the relevant kinetic parameters for these agents has enabled quantitative monitoring using the SIFT-MS analytical technique. Thirteen of the 15 compounds studied were found to have real-time detection limits in the parts-per-trillion-by-volume concentration range when measured on a standard commercial Voice100 instrument, with specific compounds having detection limits below 100 parts-per-trillion-by-volume.

Chemical warfare agents (CWAs—also commonly known as chemical weapons agents) are extremely toxic compounds which are “intended for use in military operations to kill, seriously injure, or incapacitate man because of physiological effects.”¹ In 1997, the Chemical Weapons Convention (CWC) was enacted by the Organisation for the Prohibition of Chemical Weapons.² The convention severely restricts the production, stockpiling, transport, and use of chemical warfare agents.³ The CWC does not only control CWAs in their native form but also places controls on the precursors used in the production of CWAs. CWAs are often produced by combining precursor chemicals in specific ratios just prior to use⁴ as the CWA precursor compounds are less toxic and more easily transportable than their respective CWA. It is therefore important to be able to detect precursor compounds during their transportation and also disposal. The detection technique used must be highly selective, so as to minimize false positives or false negatives, be very rapid, to ensure minimal

human exposure, and have a detection limit low enough to detect the compound of interest to safe levels.⁵

Selected ion flow tube mass spectrometry (SIFT-MS) is a technique for the quantitative analysis of volatile organic compounds (VOCs) in whole air samples.^{6–8} SIFT-MS generally uses three reagent ions (H_3O^+ , NO^+ , and O_2^+) to chemically ionize and detect analytes at sensitivities in the low parts-per-billion-by-volume (ppbv) level for most analytes, and more recently the parts-per-trillion-by-volume (pptv) for specific analytes.⁹ Negative ions have also been used on occasions for specific analytes¹⁰ and are a useful addition to the technique. To properly utilize SIFT-MS as an analytical technique, at a level that will provide accurate analyte quantitation, a thorough understanding of the chemical kinetics of the analyte reacting with the three SIFT-MS reagent ions is required. This understanding involves measuring rate coefficients and branching ratios of each reagent ion and their respective water clusters with the analyte and knowledge of the chemistry of primary product ions reacting with water molecules. Currently the database of compounds which can be quantified by SIFT-MS contains over 500 compounds. The known compounds allow SIFT-MS to be applied to many applications such as breath analysis,^{6,11} environmental monitoring,¹² oil exploration,^{13,14} and the detection of peroxide-based explosives.¹⁵

The current study looks at the capabilities of SIFT-MS to quantitatively detect a range of compounds which are related to CWAs. SIFT-MS is restricted to analytes that have some volatility, though lowering detection limits are reducing this limitation. This is not a significant limitation for most CWAs as the agents are

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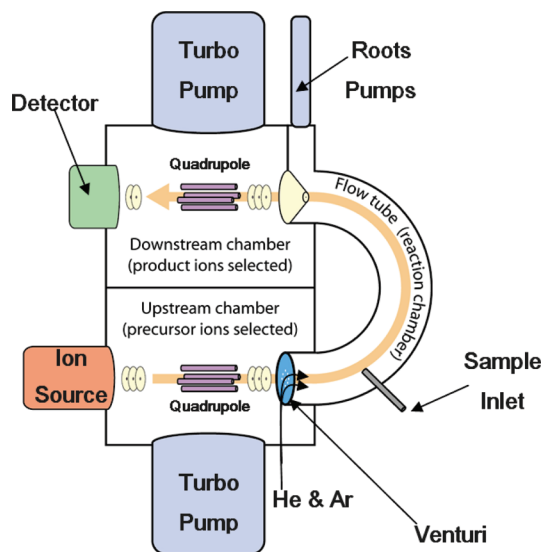


Figure 1. Schematic diagram of the Voice100 SIFT-MS instrument.

delivered as a vapor, but less volatile CWAs, e.g., VX, could be detected by degradation products or impurities. The compounds examined here are either CWA precursor compounds or lower toxicity chemical warfare agents (such as phosgene). To complement these compounds, a selection of common chemical warfare surrogates has been studied. Surrogate compounds are less toxic structural analogues of CWAs which are commonly used by other detection technologies (such as ion mobility spectrometry) to ensure the correct functioning of the instrument with a minimized risk of exposure to extreme toxicity.¹⁶ The CWA surrogate compounds have been studied to more fully demonstrate the detection limits expected for real CWAs.

EXPERIMENTAL SECTION

Three different SIFT-MS instruments have been used in the current study with the majority of measurements being made on a small commercial Voice100 SIFT-MS (Syft Technologies Ltd., Christchurch, New Zealand) analytical instrument (Figure 1). The other two instruments include a large laboratory-based instrument that has been described previously¹⁷ and a second-generation small commercial instrument, the Voice200 SIFT-MS (Syft Technologies Ltd.). The Voice100 has been mentioned in earlier papers,^{9,15} and more recently described in some detail,¹⁸ and therefore the instrumental operation will only be discussed briefly. The Voice100 instrument is similar to SIFT-MS instruments described previously by Smith and Spaul,⁸ this group,¹⁷ and Schoon et al.¹⁹ with a few subtle, yet important differences.

In the Voice100, the flow tube is approximately 30 cm long and 5 cm in diameter and is bent through 180°, so as to stack the downstream on the upstream chamber and therefore minimize the overall footprint of the instrument. The Venturi orifice used on the Voice100 is a dual-inlet system, where helium is used to create the Venturi effect on the inner annulus and argon is added

through the outer annulus on the Venturi plate. All experiments were performed with a flow tube pressure of 0.5 Torr and a 40% helium to 60% argon mixture. The Voice200 is a smaller and lighter version of the Voice100 where the roots pump has been replaced by a dry scroll pump (Edwards S35). It has a reaction time of about 5 ms and generally has a higher sensitivity than the Voice100. Three methods have been employed for determining the rate coefficients and branching ratios of the 15 CWA-related compounds studied. For compounds with high vapor pressures (greater than 3 Torr at 20 °C), rate coefficients and branching ratios were determined by the semilogarithmic plot of ion intensity against an absolute measurement of neutral flow,²⁰ hence termed “absolute kinetics”. However, for compounds with vapor pressures found to be less than 3 Torr, rate coefficients could only be measured relative to the H_3O^+ collision-limiting rate coefficient, using mixtures of the analyte in dry nitrogen. Branching ratios were determined where possible by diluting the analyte concentration and extrapolating the product ion intensity to zero flow. This “relative with dilutions” method was used for compounds which had partial vapor pressures less than 3 Torr but greater than 50 ppmv (~0.04 Torr partial vapor pressure).

The third method was dictated because of safety issues concerning transport. Phosgene could not be transported readily, and instead of synthesizing it we used a permeation tube (Kin-Tek Laboratories, Inc., 504 Laurel Dr., LaMarque, TX) which creates an accurate dynamic dilution in the single digit parts-per-million-by volume concentration range. The permeation tube was used in conjunction with a Dynacalibrator 150 (VICI Metronics Inc., Poughkeepsie, NY) permeation oven. This combination with the known concentration release of phosgene enables the rate coefficient and branching ratio to be found.

The method of determining rate coefficients of the water clusters ($\text{H}_3\text{O}^+\cdot\text{H}_2\text{O}$ $m/z = 37$, $\text{H}_3\text{O}^+\cdot 2\text{H}_2\text{O}$ $m/z = 55$, and $\text{H}_3\text{O}^+\cdot 3\text{H}_2\text{O}$ $m/z = 73$) reacting with the neutral analyte has been described previously.¹⁶

Table 1 lists the methods of measuring the kinetic parameters and their estimated absolute uncertainties (based on the known experimental uncertainties of the equipment used), as well as the governing body which restricts each compound. Figure 2 gives the molecular configuration.

The collision-limiting rate coefficients have been calculated using the method of Su.²¹ Dipole moments and polarizabilities have been obtained by quantum chemical calculations using the Gaussian 03W suite of software²² at the B3LYP/6-311+G(d,p) level of theory. As some of the studied molecules are quite large with many degrees of torsional freedom, there is a possibility that more than one conformer may be long-lived in the gas phase, and it is therefore necessary to Boltzmann-average the dipole moment and polarizability over these conformers. The initial conformational analysis was undertaken using an MM2/MM3 potential energy surface scan, altering a range of torsional angles. All conformers determined to be within 20 kJ mol⁻¹ of the lowest energy conformer were then optimized to the B3LYP/3-21G level of theory, and the Hessian was calculated to ensure each conformer was a true minimum. All true minima were then reoptimized using the 6-311+G(d,p) basis set. Collision-limiting

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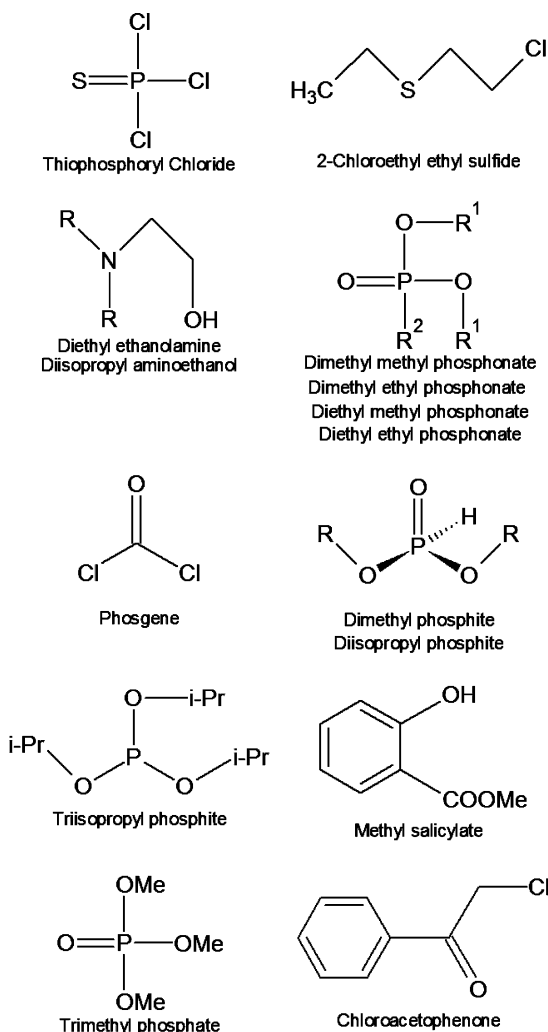
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Table 1. Compounds, Measurement Methods, and Their Uncertainties^a

compound	CAS no.	type ^b	method ^c	uncertainty ^d		
				k_{exp}^0 (%)	k_{exp}^n (%)	BR (%)
thiophosphoryl chloride	3983-91-0	surrogate	absolute	±10	±35	±20
2-chloroethyl ethyl sulfide	693-07-2	surrogate	absolute	±10	±35	±20
diethyl ethanolamine	100-37-8	CWC 2.11	absolute	±10	±35	±20
dimethyl methyl phosphonate	756-79-6	CWC 2.4	absolute with dilutions	±10	±35	±20
phosgene (carbonyl dichloride)	75-44-5	CWC 3.1	permeation tube	±15	±35	±20
dimethyl ethyl phosphonate	6163-75-3	CWC 2.4	relative with dilutions	±25	±50	±30
diethyl methyl phosphonate	683-08-9	CWC 2.4	relative with dilutions	±25	±50	±30
diethyl ethyl phosphonate	78-38-6	CWC 2.4	relative with dilutions	±25	±50	±30
diethyl phosphite	762-04-9	CWC 3.11	relative with dilutions	±25	±50	±30
diisopropyl phosphite	1809-20-7	CWC 3.11	relative with dilutions	±25	±50	±30
triisopropyl phosphite	116-17-6	CWC 3.11	relative with dilutions	±25	±50	±30
methyl salicylate	119-36-8	surrogate	relative with dilutions	±25		±30
trimethyl phosphate	512-56-1	surrogate	relative with dilutions	±25		±30
(diisopropylamino) ethanol	96-80-0	CWC 2.11	relative without dilutions	±25		±30
chloroacetophenone	532-27-4	tear gas	relative without dilutions	±25		±30

^a k_{exp}^n refers to the amount of uncertainty to add to the collision rate constant, k_{exp}^0 , for each water cluster. For example, the uncertainty in the reaction of $\text{H}_3\text{O}^+ \cdot 2\text{H}_2\text{O}$ with thiophosphoryl chloride has $\pm 10\%$ for k_{exp}^0 , then $\pm 35\%$ for each water cluster, which totals $\pm 80\%$. ^b Refers to the schedule of the CWC which restricts the compound, or whether the compound is a surrogate. Chloroacetophenone is tear gas (CN), which is not restricted but included for completeness. ^c Definitions discussed in text. ^d k_{exp}^0 refers to the uncertainty of the experimental rate coefficients of H_3O^+ , NO^+ , and O_2^+ reacting with the neutral analyte.

**Figure 2.** Representation of the molecular configuration of the molecules studied.

rate coefficients were determined for each conformer and then Boltzmann-averaged across all conformers using the standard

enthalpy also determined from the quantum chemical calculations. This method is a version of the approach taken by Schoon et al.²³ optimized for a desktop computer (P4, 2.4 GHz, 2GB RAM).

Chemicals. As mentioned above, phosgene was sourced in a permeation tube with a known permeation rate uncertainty of $\pm 2\%$ (a NIST calibrated standard). Methyl salicylate and trimethyl phosphate were donated by the Australian Defense Science and Technology Organisation (Fishermans Bend, Melbourne, Australia). All other compounds were purchased from Sigma-Aldrich (Sydney, Australia), with the purity of all compounds being 95% or greater. Compounds which were measured by the method of absolute kinetics were further purified by freeze–pump–thaw cycling.

RESULTS

Table 2 lists the experimental rate coefficients and calculated collision-limiting rate coefficients for each of the 15 compounds. Where an experimental rate coefficient is not given for H_3O^+ , the relative method has been used and we can assume the collision-limiting rate coefficient; however, where an experimental rate coefficient is not given for $\text{H}_3\text{O}^+ \cdot (\text{H}_2\text{O})_n$ ($n = 1-3$), the collision-limiting rate coefficient cannot be assumed as proton

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Table 2. Kinetic Parameters Measured at 298 K and 0.5 Torr

compound	μ_D/debye^a	$\alpha/\text{\AA}^3^a$	$k_{\text{exp}}[k_c]/10^{-9} \text{ cm}^3 \text{ s}^{-1}^b$					
			H_3O^+	$\text{H}_3\text{O}^+\cdot\text{H}_2\text{O}$	$\text{H}_3\text{O}^+\cdot 2\text{H}_2\text{O}$	$\text{H}_3\text{O}^+\cdot 3\text{H}_2\text{O}$	NO^+	O_2^{++}
thiophosphoryl chloride	0.85	11.81	2.3 [2.3]	0.32 [1.7]	0.06 [1.4]	0.06 [1.3]	1.1 [1.8]	1.7 [1.8]
2-chloroethyl ethyl sulfide	2.25	12.38	3.5 [3.4]	2.8 [2.6]	— [2.2]	— [2.0]	2.7 [2.8]	2.7 [2.7]
diethyl ethanolamine	1.69	12.99	2.9 [2.9]	2.6 [2.2]	— [1.9]	— [1.8]	2.3 [2.4]	2.2 [2.4]
dimethyl methyl phosphonate	2.27	10.05	2.8 [3.3]	3.5 [2.5]	— [2.2]	— [2.0]	2.2 [2.7]	1.8 [2.7]
phosgene (carbonyl dichloride) ^c	1.22	5.77	0.2 [2.1]	<0.01 [1.6]	<0.01 [1.4]	<0.01 [1.3]	<0.01 [1.7]	0.9 [1.7]
dimethyl ethyl phosphonate	2.04	11.74	[3.2]	2.1 [2.4]	— [2.1]	— [1.9]	2.1 [2.6]	2.1 [2.5]
diethyl methyl phosphonate	2.25	13.66	[3.4]	1.8 [2.6]	— [2.2]	— [2.0]	2.1 [2.8]	2.2 [2.7]
diethyl ethyl phosphonate	2.05	15.36	[3.3]	1.8 [2.5]	— [2.1]	— [1.9]	2.0 [2.7]	2.1 [2.6]
diethyl phosphite	2.37	11.82	[3.5]	3.2 [2.6]	— [2.3]	— [2.1]	2.8 [2.9]	2.8 [2.8]
diisopropyl phosphite	2.64	15.28	[3.9]	3.1 [2.9]	2.6 [2.5]	— [2.2]	2.8 [3.2]	2.7 [2.7]
triisopropyl phosphite	2.37	19.58	[3.8]	2.8 [2.8]	2.0 [2.4]	1.4 [2.1]	3.1 [3.1]	3.0 [3.0]
methyl salicylate	3.32	15.45	[4.5]	— [3.4]	— [2.9]	— [2.6]	2.1 [3.7]	2.7 [3.6]
trimethyl phosphate	3.87	10.34	[4.8]	— [3.6]	— [3.1]	— [2.8]	2.0 [4.0]	2.2 [3.9]
(diisopropylamino) ethanol	0.93	14.28	[2.5]	— [1.9]	— [1.6]	— [1.5]	1.3 [2.0]	0.9 [2.0]
chloroacetophenone	4.85	15.87	[6.0]	— [4.5]	— [3.9]	— [3.5]	4.4 [4.9]	2.8 [4.8]

^a All dipole moments and polarizabilities are the Boltzmann-averaged value across the lowest energy conformers as discussed in the Experimental Section. ^b Collision-limiting rate coefficients were calculated as described in the method of Su (ref 21). ^c Phosgene has known literature values of dipole moment (1.17 D) and polarizability (7.29 Å³) as discussed in the text (ref 24). Where the experimental rate coefficient is left blank assume the collision-limiting rate coefficient. Where the value is a hyphen “—” the rate was not measurable, and the collision rate cannot be assumed.

transfer may not be exothermic. Table 3 lists the product ions observed and the relative branching ratios for each ion reacting with the 15 compounds of interest. The branching ratios of all molecules containing chlorine and sulfur atoms were observed with the expected isotopic ratios.

DISCUSSION

Theoretical Calculations. The calculated value of dipole moment for phosgene (1.22 D) is approximately equal to the literature value of 1.17 D (± 0.02).²⁴ However, the B3LYP/6-311+G(d,p) value for polarizability calculated here (5.77 Å³) is approximately 20% lower than the literature value (7.29 Å³) tabulated by Maryott and Buckley.²⁹ The discrepancy may be attributed to the 6-311+G(d,p) basis set not correctly modeling the large chlorine atoms and/or the uncertainty (which is unknown) on the literature value. Using both literature values for dipole moment and polarizability, the value for the collision-limiting rate coefficient for H_3O^+ is only 5% faster than the value determined using calculated parameters, which is an acceptable discrepancy.

H_3O^+ Reactions. For all compounds for which the relative kinetic method was used, H_3O^+ was found to proton transfer to the compound; the reaction rate coefficient for H_3O^+ was

assumed to equal the calculated rate coefficient.³⁰ In support of this assumption, for all measured absolute rate coefficients, H_3O^+ was found to proton transfer at or very near to the empirical collision rate coefficient. Only phosgene (measured using a permeation apparatus) was observed to react more slowly than the collision-limiting rate coefficient with a reaction efficiency of $\sim 10\%$ and this is indicative of the reported proton affinity of phosgene being less than the proton affinity of H_2O as shown by the calculation.

On initial measurement, the reaction of H_3O^+ with phosgene gave rise to product ions corresponding to proton transfer (m/z 99, 101, and 103) with a rate coefficient substantially less than the collision-limiting rate coefficient ($3 \times 10^{-10} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$). The G4 “accurate energy” compound method²⁶ was employed to determine an accurate proton affinity/gas basicity of phosgene in an attempt to explain the observations. Proton affinities and gas basicities for both the carbonyl (oxygen bound) and chloride sites have determined and are given as Figure 3. However, as Figure 3 illustrates, even with the contribution from entropy, protonation at neither the carbonyl nor the chloride site will be an exergonic process with H_3O^+ (PA = 691 kJ mol⁻¹, GB = 660 kJ mol⁻¹). The observation of the protonated phosgene species is attributed to the presence of small amounts of ArH^+ present in the flow tube. The ArH^+ is formed by excited H_3O^+ species entering the flow tube and colliding with an argon atom before all the excitation energy has been dissipated by collisions with helium atoms. The effect of ArH^+ reacting with phosgene was subtracted from the measured rate coefficient to yield a final rate coefficient of $2 \times 10^{-10} \text{ cm}^3 \text{ molecule}^{-1} \text{ s}^{-1}$.

Table 3 shows that generally all phosphonate, phosphite, and phosphate compounds reacting with H_3O^+ give the protonated molecular ion, with very little or no fragmentation observable. One of the phosphonates, dimethyl methyl phosphonate

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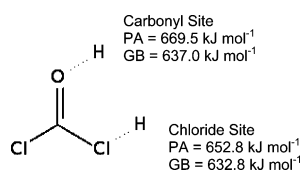
Table 3. Product Ion Branching Ratios Measures at 298 K and 0.5 Torr

compound	m/g mol ⁻¹	PA/kJ mol ⁻¹	IE/eV	H ₃ O ⁺			NO ⁺			O ₂ ^{•+}		
				ion	m/z	BR	ion	m/z	BR	ion	m/z	BR
thiophosphoryl chloride	169.41			PS ³⁷ Cl ₂ ³⁵ ClH ⁺	173	0.10	PS ³⁷ Cl ₂ ³⁵ Cl•NO ⁺	202	0.40	PS ³⁷ Cl ₂ ³⁵ Cl ⁺	172	0.05
				PS ³⁷ Cl ³⁵ Cl ₂ H ⁺	171	0.25	PS ³⁷ Cl ³⁵ Cl ₂ •NO ⁺	200	0.45	PS ³⁷ Cl ³⁵ Cl ₂ ⁺	170	0.20
				PS ³⁵ Cl ₃ H ⁺	169	0.30	PS ³⁵ Cl ₃ •NO ⁺	198	0.15	PS ³⁵ Cl ₃ ⁺	168	0.20
				P ³⁷ Cl ³⁵ Cl ₂ H ⁺	139	0.05				PS ³⁷ Cl ³⁵ Cl ⁺	135	0.10
				P ³⁵ Cl ₃ H ⁺	137	0.05				PS ³⁵ Cl ₂ ⁺	133	0.10
				PS ³⁷ Cl ³⁵ Cl ⁺	135	0.05				P ³⁷ Cl ³⁵ Cl ⁺	103	0.15
				PS ³⁵ Cl ₂ ⁺	133	0.10				P ³⁵ Cl ₂ ⁺	101	0.20
				P ³⁷ Cl ³⁵ Cl ⁺	103	0.05						
				P ³⁵ Cl ₂ ⁺	101	0.05						
				C ₄ H ₉ ³² S ³⁷ ClH ⁺	127	0.05	C ₄ H ₉ ³² S ³⁷ Cl ⁺	126	0.15	C ₄ H ₉ ³² S ³⁵ Cl ⁺	124	0.05
				C ₄ H ₉ ³² S ³⁵ ClH ⁺	125	0.20	C ₄ H ₉ ³² S ³⁵ Cl ⁺	124	0.40	C ₄ H ₉ ³² S ⁺	89	0.15
				C ₄ H ₉ ³⁴ S ⁺	91	0.05	C ₄ H ₉ ³² S ⁺	89	0.40	C ₃ H ₇ ³² S ⁺	75	0.75
2-chloroethyl ethyl sulfide	124.63			C ₄ H ₉ ³² S ⁺	89	0.65	C ₃ H ₇ ³² S ⁺	75	0.05	C ₂ H ₆ ³² S ⁺	62	0.05
				C ₃ H ₇ ³² S ⁺	75	0.05						
				C ₆ H ₁₄ NOH ₂ ⁺	118	0.85	C ₆ H ₁₄ NOH ⁺	117	0.05	C ₅ H ₁₂ N ⁺	86	1.00
				C ₆ H ₁₄ N ⁺	100	0.05	C ₆ H ₁₄ NO ⁺	116	0.05			
diethyl ethanolamine	117.19	1005 ^a	8.6	C ₄ H ₉ NOH ₂ ⁺	89	0.10	C ₅ H ₁₂ N ⁺	86	0.75			
							C ₂ H ₁₀ N ⁺	72	0.15			
dimethyl methyl phosphonate	124.08		10.0	C ₃ H ₉ PO ₃ H ⁺	125	0.95	C ₃ H ₉ PO ₃ •NO ⁺	154	1.00	C ₃ H ₉ PO ₃ ⁺	124	0.50
				(C ₂ H ₆ PO ₂ H) ⁺	94	0.05				C ₂ H ₇ PO ₂ ⁺	94	0.50
phosgene (carbonyl dichloride)	98.92	670 ^b		CO ³⁷ Cl•H ₂ O ⁺	83	0.15	no reaction			CO ³⁷ Cl ⁺	65	0.75
				CO ³⁵ Cl•H ₂ O ⁺	81	0.35				CO ³⁵ Cl ⁺	63	0.25
				CO ³⁷ Cl ⁺	65	0.15						
				CO ³⁵ Cl ⁺	63	0.35						
dimethyl ethyl phosphonate	138.10			C ₄ H ₁₁ PO ₃ H ⁺	139	1.00	C ₄ H ₁₁ PO ₃ •NO ⁺	168	1.00	C ₄ H ₁₁ PO ₃ ⁺	138	0.30
										C ₂ H ₇ PO ₃ ⁺	110	0.70
diethyl methyl phosphonate	152.13			C ₅ H ₁₃ PO ₃ H ⁺	153	1.00	C ₅ H ₁₃ PO ₃ •NO ⁺	182	1.00	C ₅ H ₁₃ PO ₃ ⁺	152	0.35
										C ₃ H ₁₀ PO ₃ ⁺	125	0.50
										C ₃ H ₉ PO ₂ ⁺	108	0.10
										CH ₃ PO ₃ H ₃ ⁺	97	0.05
										UPI ^c	125	0.80
diethyl ethyl phosphonate	166.16			C ₆ H ₁₅ PO ₃ H ⁺	167	1.00	C ₆ H ₁₅ PO ₃ •NO ⁺	196	1.00	C ₃ H ₉ PO ₂ ⁺	108	0.20
										C ₄ H ₁₁ PO ₃ ⁺	138	0.20
diethyl phosphite	138.10			C ₄ H ₁₁ PO ₃ H ⁺	139	1.00	C ₄ H ₁₁ PO ₃ •NO ⁺	168	1.00	UPI ^c	111	0.75
										UPI ^c	83	0.05
diisopropyl phosphite	166.16			C ₆ H ₁₅ O ₃ PH ⁺	167	1.00	C ₆ H ₁₅ O ₃ P•NO ⁺	196	0.95	UPI ^c	119	0.10
							C ₃ H ₇ O ⁺	59	0.05	UPI ^c	101	0.40
										UPI ^c	83	0.50
triisopropyl phosphite	208.24			C ₉ H ₂₁ PO ₃ H ⁺	209	0.50	unable to measure ^d			C ₉ H ₂₁ PO ₃ ⁺	208	0.10
				C ₆ H ₁₄ PO ₂ ⁺	149	0.50				UPI ^c	156	0.10
										C ₆ H ₁₄ PO ₂ ⁺	149	0.20
										UPI ^c	124	0.60
methyl salicylate	152.05		7.7	C ₈ H ₈ O ₃ H ⁺	153	1.00	C ₈ H ₈ O ₃ ⁺	152	1.00	C ₈ H ₈ O ₃ ⁺	152	0.60
										C ₇ H ₆ O ₃ ⁺	138	0.40
trimethyl phosphate	140.02	891	10.5	C ₃ H ₉ PO ₄ H ⁺	141	1.00	C ₃ H ₉ PO ₄ •NO ⁺	170	1.00	C ₃ H ₉ PO ₄ ⁺	140	0.30
										C ₃ H ₈ PO ₄ ⁺	139	0.70
(diisopropylamino) ethanol	145.12	971 ^a		C ₈ H ₁₉ NOH ⁺	146	0.95	C ₈ H ₁₉ NO•NO ⁺	175	0.35	C ₇ H ₁₆ NO ⁺	130	0.10
				C ₈ H ₁₈ N ⁺	128	0.05	C ₈ H ₁₉ NO ⁺	145	0.25	C ₇ H ₁₆ N ⁺	114	0.60
							C ₇ H ₁₆ N ⁺	114	0.35	C ₅ H ₁₂ NO ⁺	102	0.155
							C ₅ H ₁₂ NO ⁺	102	0.05	C ₆ H ₁₁ NO ⁺	72	0.15
chloroacetophenone	154.29		9.6	C ₈ H ₇ O ³⁷ ClH ⁺	157	0.25	C ₈ H ₇ O ³⁷ Cl•NO ⁺	186	0.25	(C ₆ H ₅)CO ⁺	105	1.00
				C ₈ H ₇ O ³⁵ ClH ⁺	155	0.75	C ₈ H ₇ O ³⁵ Cl•NO ⁺	184	0.75			

^a Proton affinities calculated by the CBS-4 M (ref 25) accurate energy compound method using the Gaussian 03W (ref 22) suite of software.

^b Proton affinity of phosgene calculated by the G4 (ref 26) accurate energy compound method using the Gaussian 03W (ref 22) suite of software. All other thermochemical parameters sourced from the NIST (refs 27 and 28) database. ^c "UPI" refers to a structurally unidentified product ion.

^d Association product at the limit of the Voice100 mass range.

**Figure 3.** Thermodynamics of phosgene protonation calculated by the G4 compound method in using the G03W suite of software.

(C₃H₉PO₃ = DMMP), has been the subject of other flow tube kinetic investigations with a wider range of reagent ions than

used in this study.^{10,31} There is, however, some uncertainty as to its dipole moment and therefore its collision capture rate. Midey et al.¹⁰ adjusted their calculated value of 4.8 D down to 3.76 D on the grounds that MP2 methods tend to overestimate the dipole moment. This is still significantly larger than our calculated value of 2.27 D corresponding to a capture rate coefficient of 3.3×10^{-9} cm³ s⁻¹. Other reported values for the dipole moment of

(31) Chatterjee, B. J.; Tosh, R.; Johnsen, R. *Int. J. Mass Spectrom. Ion Processes* **1991**, *103*, 81–92.

DMMP are 2.38³² and 2.86 D.³³ The dipole moment is a very sensitive function of the O–P–O angle, and small variations can lead to large differences in the calculated value. Our measured absolute rate coefficient of $2.8 \times 10^{-9} \text{ cm}^3 \text{ s}^{-1}$ is closer to the capture rate coefficient based on a lower dipole moment. This value was measured on both the larger laboratory instrument and on the Voice100 instrument and falls between the values reported by Chatterjee et al.³¹ and Midey et al.¹⁰ All studies of the reaction of H_3O^+ and DMMP confirm that proton transfer is the only product ion although we also observed a small 5% signal at m/z 94 corresponding to $\text{C}_2\text{H}_6\text{PO}_2\text{H}^+$ (i.e., loss of CH_3O), but we cannot attribute this as directly derived from H_3O^+ .

Trimethyl phosphate has a known proton affinity of $890.6 \text{ kJ mol}^{-1}$, and therefore with H_3O^+ it would yield a protonated molecular ion with $\sim 200 \text{ kJ mol}^{-1}$ excess energy. As only the protonated molecular ion is observed, it must be concluded that trimethyl phosphate has sufficient degrees of freedom to dissipate and transfer the excess energy in collisions with the carrier gas.

Discussion of $\text{H}_3\text{O}^+ \cdot n\text{H}_2\text{O}$ Reactions ($n = 1, 2, 3$). To measure the reaction rate coefficients of an analyte with the water clustering ions, significant analyte vapor must be generated such that the drop in the reagent ions intensity is large enough to measure. Rate coefficients of 11 of the 15 CWA precursor or surrogate analytes with $\text{H}_3\text{O}^+ \cdot \text{H}_2\text{O}$ have been measured. However, due to an inability to generate significant analyte vapor, the rate coefficients of $\text{H}_3\text{O}^+ \cdot 2\text{H}_2\text{O}$ and $\text{H}_3\text{O}^+ \cdot 3\text{H}_2\text{O}$ with only four and three analytes, respectively, have been measured. Midey et al.¹⁰ report collision rate reactions for $\text{H}_3\text{O}^+ \cdot \text{H}_2\text{O}$ yielding the proton-transfer product ion in agreement with this study.

Thiophosphoryl chloride was observed to react at the collision-limiting rate coefficient with H_3O^+ , at approximately 20% reaction efficiency with $\text{H}_3\text{O}^+ \cdot \text{H}_2\text{O}$, and at less than 5% reaction efficiency for the higher water clusters of the hydronium ion. Because of the observed decrease in reaction efficiency as the number of water molecules attached to H_3O^+ increases, it is not unreasonable to bracket the proton affinity of thiophosphoryl chloride to be greater than that of H_2O (691 kJ mol^{-1}), but less than 827 kJ mol^{-1} , the total of the proton affinity of H_2O and the enthalpy of reaction of H_2O clustering with H_3O^+ .²⁷

Discussion of NO^+ and O_2^+ Reactions. As expected, reactions of NO^+ reagent ions with the 15 CWA-related compounds were found to proceed by association, hydride abstraction, or electron transfer dependent on the thermodynamic constraints of the reaction. Two other flow tube studies of the reaction of NO^+ and DMMP agreed with the findings of this study in that the reaction occurs by rapid association.^{10,31}

The reactions of O_2^+ were generally found to occur via electron transfer with a large degree of fragmentation observed. The highly fragmented product ions occur due to the large difference in ionization potential between O_2 and the analyte,

which is generally greater than 2 eV, as the ionization potential of O_2 is 12.01 eV .²⁸

A few product ions for the reactions of O_2^+ with the phosphonate and phosphite species could not be assigned an ionic structure due to ambiguity in the product structures possible. Our results for DMMP are similar to those of Midey et al.¹⁰ except we have not included ion products at $<2\%$ level. Chatterjee et al.³¹ also report the same two major ion products for the O_2^+/DMMP reaction. The observed unassigned ion peaks from the reaction of O_2^+ with the other reagents are proposed to be thermodynamic minima, which have undergone complex rearrangement processes due to the presence of the phosphorus atom which can exist in multiple oxidation states. The unassigned peaks may be impurities in the sample; however, for diisopropyl phosphite the only product ions observed were unassignable. Further investigation is required to determine their identity; however, this investigation is outside the scope of the current study.

Limits of Detection. Recently, Milligan et al.⁹ published a method for determining the limit of detection on a SIFT-MS instrument. The limit of detection (LOD) is defined as the lowest concentration which can be detected at a known confidence level. When the confidence level is defined to be three standard deviations above background the limit of detection is calculated by eq 1, where b_μ is the mean background count rate (in counts s^{-1}), t is the time spent monitoring the background of the product ions intensity, and s is the instrument sensitivity for a specific analytes reagent ion/product ion pair (in counts $\text{s}^{-1} \text{ ppbv}^{-1}$). The value of s is dependent on the rate coefficient and branching ratio for the ion–molecule reaction of interest.

$$\text{LOD}_{\text{pptv}} = \frac{3000\sqrt{b_\mu t}}{st} \quad (1)$$

For example, DMMP has been measured in this study to associate with NO^+ at $2.0 \times 10^{-9} \text{ cm}^3 \text{ molecules}^{-1} \text{ s}^{-1}$. On a standard Voice100 instrument the NO^+ reagent ion intensity is approximately $1 \times 10^6 \text{ counts s}^{-1}$, which corresponds to a sensitivity of $6.2 \text{ counts s}^{-1} \text{ ppbv}^{-1}$. This value is found by solving the SIFT-MS concentration equation⁶ for the product ion intensity when all other parameters are known. The measured chemical background at m/z 154 is $0.8 \text{ counts s}^{-1}$; therefore, the limit of detection is 140 pptv (parts-per-trillion-by-volume) for an integration time of 10 s. DMMP was also measured on the newer Voice200 instrument which is generally more sensitive than the Voice100 instrument with count rates of reagent ions up to $20 \times 10^6 \text{ counts s}^{-1}$. However, for DMMP, the higher background in the Voice200 yielded a similar level of detection as quoted in Table 4.

In comparison to the limit of detection, the limit of quantitation is the minimum concentration which can be detected with acceptable precision.⁹ If the precision is defined as $\pm 20\%$, the limit of quantitation can be calculated by eq 2.

$$\text{LOQ}_{\text{pptv}} = 1000 \frac{25 + 5\sqrt{25 + 4b_\mu t}}{4st} \quad (2)$$

The limits of detection and limits of quantitation for each CWA-related analyte with the optimum precursor ion over a 10 s

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Table 4. LOD_{pptv} and LOQ_{pptv} for All 15 Measured Analytes

	reagent ion	product ion	b_{μ}^a	s^b	LOD _{pptv}	LOQ _{pptv}	TWA _{pptv} ^c
thiophosphoryl chloride	H ₃ O ⁺	PS ³⁵ Cl ₃ H ⁺	4.2	1.4	1400	2100	
2-chloroethyl ethyl sulfide	NO ⁺	C ₄ H ₉ ³² S ³⁵ Cl ⁺	0.50	9.1	75	180	
diethyl ethanolamine	H ₃ O ⁺	C ₆ H ₁₄ NOH ₂ ⁺	1.8	5.0	250	450	2 × 10 ⁶
dimethyl methyl phosphonate	NO ⁺	C ₃ H ₉ PO ₃ •NO ⁺	0.83	2.4	140	240	
phosgene (carbonyl dichloride)	O ₂ ⁺	CO ³⁷ Cl ⁺	46	1.8	3600	4600	2 × 10 ⁴
dimethyl ethyl phosphonate	NO ⁺	C ₄ H ₁₁ PO ₃ •NO ⁺	0.65	7.0	110	250	
diethyl methyl phosphonate	NO ⁺	C ₅ H ₁₃ PO ₃ •NO ⁺	0.35	7.0	80	220	
diethyl ethyl phosphonate	NO ⁺	C ₆ H ₁₅ PO ₃ •NO ⁺	0.10	6.7	45	200	
diethyl phosphite	NO ⁺	C ₄ H ₁₁ PO ₃ •NO ⁺	0.65	9.4	81	180	
diisopropyl phosphite	NO ⁺	C ₆ H ₁₅ PO ₃ •NO ⁺	0.10	9.4	32	140	
triisopropyl phosphite	H ₃ O ⁺	C ₉ H ₂₁ PO ₃ H ⁺	0.05	3.8	55	340	
(diisopropylamino) ethanol	H ₃ O ⁺	C ₈ H ₁₉ NOH ⁺	1.36	4.9	230	420	
chloroacetophenone	NO ⁺	C ₈ H ₇ O ³⁵ Cl•NO ⁺	0.70	11.1	72	160	5 × 10 ⁴
methyl salicylate	NO ⁺	C ₈ H ₈ O ₃ ⁺	0.65	7.0	110	250	
trimethyl phosphate	NO ⁺	C ₃ H ₉ PO ₄ •NO ⁺	1.35	6.7	160	310	

^a b_{μ} (in units of counts s⁻¹) measured over 10 s of sampling chemical background. ^b s (in units of counts s⁻¹ pptv⁻¹) determined at H₃O⁺, NO⁺, and O₂⁺ reagent ion intensities of 6 × 10⁵, 1 × 10⁶, and 8 × 10⁵ counts s⁻¹, respectively. ^c 8 h time-weighted average values are given where available.

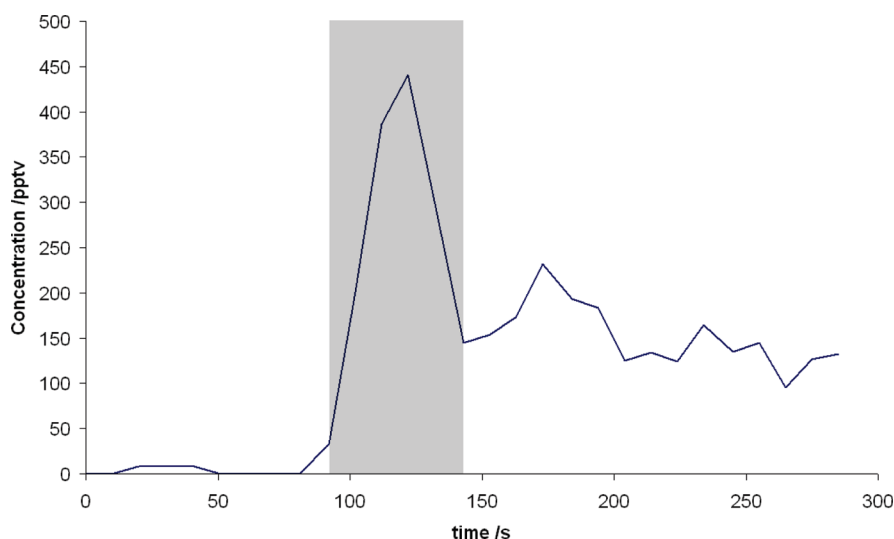


Figure 4. Detection of a sample of diisopropyl phosphite in the parts-per-trillion-by-volume concentration range. The shaded area represents the equilibration time following sample valve opening.

background sampling time and 20 s analyte sampling time is given as Table 4. Values of b_{μ} and s are determined on a standard Voice100 instrument. LOQ_{pptv} values have been found to be below the 8 h time-weighted-average (TWA) values for safe exposure for each of the three compounds which have been assigned.³⁴

The data presented in Table 4 can also be compared with other CWA detection technologies which have published limits of detection. Black and Read³⁵ quoted the limit of detection for (diisopropylamino) ethanol on an LC–APCI–MS to be ≤1200 pptv (≤10 ng mL⁻¹ of analyte in water), which is ~5 times greater than measured for a Voice100 in this study. Chen et al.³⁶ measured dimethyl methyl phosphonate using ESI–MS–MS and determined the limit of detection to be in the low part-per-

billion-by-volume range. Patel et al.³⁷ measured the same compound using a chemicapacitive microsensors and found the limit of detection to be 180 ppbv (180 000 pptv), which is an order of magnitude greater than determined here, and Mukherjee et al. used photoacoustic spectroscopy to also find a limit in the sub-part-per-billion-by-volume range.³⁸

An example of the quantitation of diisopropyl phosphite in dry air in the part-per-trillion-by-volume concentration range is given as Figure 4. The measured concentration was found to be 150 pptv, with a chemical background of less than 10 pptv.

CONCLUSION

The measurement of the kinetic parameters for 15 important CWA precursor and simulant compounds has expanded the range of SIFT–MS such that quantitative detection is now available for

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each compound measured in the present study. For 13 of the 15 measured compounds, the LOD and LOQ were found to be in the parts-per-trillion-by-volume concentration range when using appreciably short detection times.

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