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Accurate and reproducible ion mobility measurements for chemical standard evaluation

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ABSTRACT

Chemical standards are used to calibrate ion mobility spectrometers (IMS) for accurate and precise identification of target compounds. Research over the past 30 years has identified several positive and negative mode compounds that have been used as IMS standards. However, the IMS research community has not come to a consensus on any chemical compound(s) for use as a reference standard. Also, the reported K_0 values for the same compound analyzed on several IMS systems can be inconsistent. In many cases, mobility has not been correlated with a mass identification of an ion.

The primary goal of this work was to provide mass-identified mobility (K_0) values for standards. The results of this work were mass-identified K_0 values for positive and negative mode IMS chemical standards. The negative mode results of this study showed that TNT is a viable negative mode reference standard. New temperature-dependent K_0 values were found by characterizing drift gas temperature and water content; several examples were found of temperature-dependent changes for the ion species of several standards. The overall recommendation of this study is that proposed IMS standards should have temperature-dependent K_0 values quoted in the literature instead of using a single K_0 value for a compound.

1. Introduction

An ideal chemical standard used for ion mobility spectrometry (IMS) has been sought since the early 1980s. Early workers in the plasma chromatography (PC)/atmospheric pressure ion mobility spectrometry development area generated libraries of reduced mobility (K_0) values (unique values which identify compounds in IMS by the mid-1980s. [1,2] At the same time, many of these workers proposed compounds as IMS standards after reporting reproducibility of a compound's K_0 value.[2] At this time, the IMS standard 2,4-dimethyl pyridine (2,4-DMP) or 2,4-lutidine emerged as a compound to calibrate the reduced mobility scale. [2] 2,4-DMP was recommended as a standard because it produced a single protonated monomer ion at m/z 108.08 and has a strong proton affinity (969.2 kJ mol^{-1} vs. H_2O at 691 kJ mol^{-1}). [2,3] However, as later work would show, the K_0 value for the protonated monomer of 2,4-DMP changed with drift gas temperature and that increased concentrations of the neutral 2,4-DMP molecules caused a protonated 2,4-DMP dimer ion to form at m/z 215.15.[4,5]

In the 1990s, dimethyl methylphosphonate (DMMP) was proposed as an IM chemical standard; DMMP was already used to simulate the mobility behavior of the chemical warfare agent Sarin in IMS analyses [6,7]. Initial work showed that the K_0 values for the DMMP monomer and dimer ions depended slightly on temperature and that the DMMP monomer ion seemed to 'cluster' more with neutral water molecules (a variable that affects K_0 value determinations) than the 2,4-DMP monomer ion [7].

Another study introduced IMS chemical standards for use with ESI–IMS analyses [8]. This study illustrated the need for an ESI-IMS standard that would not change its ion chemistry with regard to solvent composition, gaseous impurities, and that would remain as a single ion species during an analysis [8,9]. Still others have proposed various chemical compounds, such as the hydrated proton ion, commonly referred to as the reactant ion peak (RIP), various amines, and fullerenes be used as positive mode standard compounds [10,11].

Guidelines were introduced for choosing a positive mode-active IMS standard and 2,6-Di-*tert*-butylpyridine (D*t*BP) was suggested as the IMS standard that best fits these guidelines. Among the guidelines listed, a positive mode IMS standard should have: a high proton affinity, a protonated monomer form stable at temperatures up to 250 °C; a low propensity to cluster with neutral water or drift gas molecules; and be easy to purchase across the world.[4]

A more recent study asserted that reference standards be classified as either 'chemical' or 'instrumental' reference standards [12]. The results of the study found that the K_0 value of D*t*BP was indifferent to

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organic chemical interferences in the IMS drift region while 2,4-DMP responded to organic chemical interferences with a change in K_0 value. D*t*BP was classified as an 'instrumental' reference standard compound, which could be used to monitor instrumental parameters that affect K_0 value determinations in an IMS. 2,4-DMP, a 'chemical' reference standard compound, was used to detect if the IMS had chemical interferences that could cluster with the analyte ions and shift analyte mobility values from predicted K_0 values found with the 'instrumental' reference standard. This study concluded that both types of reference standards should be used to calibrate mobility scales, especially when using electrospray ionization.

Currently, reported K_0 values for the same compound analyzed on several IMS systems can be inconsistent [13]. No previous study on chemical standards has provided simultaneous mass-identified mobility values to confirm the ion species produced by each compound. Very few literature reports have provided error values associated with the mobility values obtained for standard compounds [14,15].

Concurrently with work proposing and characterizing IMS standards, other studies refined how a measured mobility value depends upon the temperature of the IMS, [16–22] the pressure inside the IMS, [23–25] the electric field setup across the IMS, [19,26–28] the length of the IMS, [29] and the drift gas composition and water content inside the IMS [19,30–33]. The calculation of a K_0 value requires measurement of five quantities: the length of the IMS drift region (L), the ion gate voltage (V), drift time of the response ion of interest (t_d), experimental temperature, (T) and pressure (P). When combined, these parameters make up the standard reduced mobility equation:

$$K_0 = \left(\frac{L^2}{V\,t_d}\right)\left(\frac{T_0}{T}\right)\left(\frac{P}{P_0}\right) \tag{1}$$

where the squared length of the IMS drift region (L, (cm)) is divided by the voltage applied to pulse the ions into the IMS drift region (V, volts) multiplied by the analyte drift time (t_d, (seconds)) and corrected for standard temperature (T, (Kelvin)) and experimental pressure (P, (Torr)).[34]

A study which measured the error in mobility values from IMS systems provided a framework where the measured values in the K_0 expression can be evaluated along with their associated measurement uncertainties [15]. For example, the length of the IMS drift region (L) depends on temperature and the electric field homogeneity of the drift region. The concept of an effective drift length, L_{eff}, has been used to correct L due to changes in the IMS temperature [4]. Thus, the effective drift length at any experimental temperature can be calculated using the equation (modified):

$$L_T = L_{amb}(1 + C_T(T - T_{amb})) \tag{2}$$

where L_T is the length of the drift region at a certain temperature T, L_{amb} is the measured drift length at an ambient temperature T_{amb}, and C_T is the coefficient of thermal expansion for an insulating material between electrodes in the drift space [4]. Yet, this equation overlooks several key factors: the uncertainty of the measured temperature and its corresponding change in length value; the coefficient of thermal expansion for the electrode materials, and any other materials in the drift region that change size as a function of temperature.

A second way to calculate an unknown compound's K_0 value from the K_0 value of a standard compound:

$$K_{0,unk} = K_{0,std} \times \frac{t_{d,std}}{t_{d,unk}} \tag{3}$$

where $K_{0,\mathrm{unk}}$ is the K_0 value of the unknown compound, $K_{0,\mathrm{std}}$ is the K_0 value of the reference standard, $t_{d,\mathrm{std}}$ is the drift time (ms) of the reference standard and $t_{d,\mathrm{unk}}$ is the drift time (ms) of the unknown compound [4]. Many others have adopted this technique to calculate K_0 values [8,29,35,36].

However, there are two problems with the reference standard calibration method. First, the IMS community has not come to a consensus on one or more suitable compound(s) as reference standard(s). Second, K_0 values found with the reference calibration method only cancel out measurement uncertainty for a single IMS system; K_0 values generated by this method cannot be compared to values obtained on another instrument because measurement techniques vary.

A third method to obtain reduced ion mobility values used an "instrument specific factor" (F_{IMS}) to the calculation of a K_0 value such that:

$$K_0 = \frac{F_{IMS}}{t_d}; \quad F_{IMS} = \frac{L^2}{E}\left(\frac{T_0}{T}\right)\left(\frac{P}{P_0}\right) \tag{4}$$

where F_{IMS} is the instrument specific factor ($\mathrm{cm^{-2}\,V^{-1}}$), L is the squared length of the IMS drift region (L, cm), E is the electric field setup across the IMS drift region ($V\,\mathrm{cm^{-1}}$), t_d is the analyte drift time (seconds), and K_0 is corrected for temperature (T, (Kelvin)) and pressure (P, (Torr)) [14]. However, the use of this correction factor has several issues which may limit its use beyond routine, and well characterized IMS analyses. First, while this correction factor helps to obtain reproducible data for a single IMS instrument and can be implemented in data acquisition algorithms, it must be updated at regular intervals to check for variation in instrumental parameters. Second, the correction factor is calculated from the K_0 and drift time of the reactant ion peak (RIP), presumably the $(H_2O)_nH^+$ ion in the positive mode. Other work has shown that the RIP was not a good IMS standard because its K_0 value was not constant with temperature and increasing moisture content [4]. Finally, the accuracy of the normalized K_0 values produced from this study have not been confirmed by an ion mobility-mass spectrometry method.

The first goal of this work was to provide simultaneously mass-identified mobility values for IMS standard compounds and chemical warfare agent (CWA) structural simulants. The second goal was to provide a range of mass-identified mobility values, along with error values, for the standard compounds at several experimental temperatures and drift gas water content values. The third and final goal of this project was to compare simultaneously mass-identified mobility values found in this work with mobility values for standards found in previous work.

The compounds in this work were chosen for several reasons. First, this group of chemicals contained the most widely used compounds proposed as mobility standards for the positive ionization mode [11]. Second, while many of these same compounds were analyzed in an earlier study, the K_0 values were obtained over a smaller temperature range, there were no error values associated with the K_0 values, and no negative mode compounds were studied [4]. Methyl salicylate, a negative mode compound chosen for this study, purportedly is the most common internal calibrant for negative mode ions [11]. This compound is commonly used in commercial, standalone IMS systems (such as the Barringer/Smiths IONSCAN®) to create reactant ion peaks (RIPs) and to calculate subsequent K_0 values for unknown compounds. However, there are no published reports of MeS' K_0 value dependence on temperature or any other IMS parameters. Finally, dimethyl methylphosphonate (DMMP) and thiodiglycol (TDG) are both structural simulants for active chemical warfare agents Sarin (GB) and sulfur mustard (HD), respectively; these compounds and others have been used to estimate the mobility behavior of live chemical agents in standalone systems without implementing expensive control systems needed for the analyses [37,38].

The ultimate goal of this project aims to reduce measurement uncertainty of the parameters found in the K_0 expression so that more accurate and reproducible K_0 values can be reported for IMS reference standards and target compounds. These more accurate and precise K_0 values are needed to eventually generate a database of IMS standard compounds that have K_0 values characterized over a range of temperature and drift gas water content values.

2. Material and methods

2.1. Chemicals

All chemicals and solvents were purchased from Sigma–Aldrich (St. Louis, MO) and Alfa Aesar (Ward Hill, MA) and were used without further purification. Each IMS standard and CWA structural simulant were obtained as a $>95\%$ pure, neat liquid. Please note that these compounds may cause skin and eye irritation. Wear applicable personal protective equipment including safety goggles and follow all safety guidelines described in the material safety data sheets for each compound.

2.2. Instrumentation

An IM-TOFMS instrument (constructed at Washington State University and Ionwerks, Inc. (Houston, TX)) with a ^{63}Ni ionization source was used to obtain all mass-identified mobility measurements and has been previously described [39]. Briefly, ions were created in an 8.52 cm ion-molecule reaction region where they were pulsed into the 16.20 cm drift region by a Bradbury–Nielsen ion gate with a 200 μs pulse width. After traveling under a uniform electric field at ambient pressure, the ions traversed a 300 μm pin hole into a pressure interface region (1.6 Torr) and then into the ion focusing region (2.5×10^{-2} Torr) of the TOFMS. A series of ion lenses guided the ions towards the TOF extraction pulser where the ions were orthogonally extracted the V-shaped flight path of the TOFMS (1.7×10^{-6} Torr). A Burle multi channel plate detector was used for ion detection (Lancaster, PA). Spectra were generated by software developed at Ionwerks Inc. (Houston, TX) run on the ITT Visual Information Solutions IDL Virtual Machine platform (Boulder, CO). Background mass-to-charge ratio (m/z) spectra were obtained before each sample to ensure no carryover was present from the previous samples. Any fragmentation caused by the IMS–MS interface was monitored using the 2D IM-MS spectra and mobility values were reported for the primary ions. Overall, multiple mass-correlated mobility spectra were collected on a single day and over multiple days to eliminate instrumental variability. The reduced mobility values provided in the table were reported to $\pm1\sigma$ for a sample size (n) of 24.

2.2.1. Sample introduction

Samples were introduced via a modified electrode ring inside of the IM reaction region. This electrode ring was connected to a small, tubular stainless steel chamber via Swagelok fittings. A small amount of sample (usually 0.1 μL of the neat compound) was placed on a clean, glass slide inside the chamber and then the chamber was sealed. The chamber was heated by a resistive wire as described above and an in-line gas heater was also used to propel the sample vapor from inside the chamber through a 6 cm. length of 1/8″ stainless steel tubing and Swagelok fittings into the reaction region. This transfer area was insulated with fiberglass wool (Ace Hardware, Pullman, WA) to prevent any cold spots and to ensure adequate transport of the sample vapors into the IMS. Purified, dry air was used as a carrier gas and the gas introduction and metering system also helped to control the amount of vapor introduced into the reaction region of the IMS.

At the lower experimental temperatures (30 °C and 50 °C), the less volatile samples did not adequately produce enough vapors for satisfactory data acquisition. Thus, a different sample introduction device was used which involved the use of an in-line gas heater to heat a neat liquid sample deposited on glass wool inside a Pasteur pipette from VWR International, LLC (West Chester, PA). The Pasteur pipette was placed inside a stainless steel rod that was wrapped in a high temperature heating tape supplied by Omega (Stamford, CT) and this apparatus was setup so that any vapors evolving from the sample were introduced into the front of the IMS drift cell next to the ion source. This introduction assembly was used only for TDG at 30 °C and 50 °C and for MeS at 30 °C.

2.2.2. Temperature

The IM drift tube was heated above ambient temperature by four 175 W Watlow Firerod cartridge heaters supplied by Heatcon Inc. (Seattle WA), inserted into the outer aluminum case surrounding the IM tube. The IMS was insulated by Aerogel, supplied by Aspen Aerogels, Inc. (Northborough, MA). The IM drift region temperature was characterized by inserting two custom-made 1/16″ (1.59 mm) O.D. platinum resistive temperature devices (RTDs) (Isotech N.A., Colchester, VT) into the drift region of the IMS via modified electrode rings; the first RTD was positioned approximately 10 mm from the ion gate at the top of the IM drift region and the second RTD was positioned approximately 10 mm from the drift gas inlet at the bottom of the IM drift region (closest to the MS inlet). Both RTDs were positioned so that the RTD measurement tip was centered inside the IM drift region. Measurements were taken at several set points as defined by the temperature control unit (constructed in-house at WSU using two Omega 1/16 DIN MICROMEGA® PID temperature controllers (Stamford, CT)): 30 °C, 50 °C, 100 °C and 150 °C. Temperatures were recorded every 10 s for several hours using a F200 precision thermometer with data logging capability (Isotech N.A., Colchester, VT). These experiments were repeated across several days and used to obtain the temperature of the IM drift gas used in the calculation of K_0 values.

2.2.3. Pressure

Each ion mobility mass spectrum in this study had a unique pressure measurement associated with it. The ambient pressure was measured every 15 s and recorded after each ion mobility mass spectral data acquisition period (approximately every 1–5 min) by a PTC PRHTEMP101 pressure, humidity, and temperature recorder located approximately 5 m. from the IM-TOFMS. The pressure recorder measurements were checked against a Nova 230–7420 series mercury barometer located approximately 1 m. from the IM-TOFMS (NovaLynx Corp., Auburn, CA); station atmospheric pressure and weather observations were found from data recorded by an U.S. National Weather Service ASOS weather station located approximately 4.8 km. from the instrument lab at the regional airport. The average pressure inside the IM tube was 693.60 Torr with a pooled standard deviation of 1.92 Torr for a sample size (n) of 343; the pressure was not varied except for differences in atmospheric pressure due to changing weather in Pullman, WA.

2.2.4. Voltage

The K_0 values for each compound were collected at multiple voltage values to determine K_0 dependence on the electric field. Caddock MS type $1.00\pm1\%$ MΩ high temperature resistors were connected in series to setup the electric field across the IM tube (Riverside, CA). A Bertran 205B series dual polarity high voltage power supply provided the various voltages required for the electric field across the IM tube (Spellman, Hauppage, NY).

The voltage was measured at each voltage setting by a HPV-500 100 kV precision high voltage divider probe (CPS, Portland, OR) connected to a Fluke 8846 A precision digital multimeter (Everett, WA). Several uniform electric fields were used to study the effect of the electric field strength on the K_0 values; the average electric field values were 372.70 ± 2.50, 423.70 ± 1.70, 476.90 ± 2.50, and 530.50 ± 2.70 V cm^{-1} for $n = 24$ and the error values are given to $\pm 1\sigma$.

2.2.5. *Drift gas introduction and water content*

Purified, compressed air (A-L Compressed Gasses, Inc, Spokane, WA) was regulated at 25 psi and delivered at a flow rate of 1000 mL min^{-1} into the IMS by an Aalborg P-series rotameter (Orangeburg, NY); the drift gas was further purified using an Alltech moisture trap (W.R. Grace and Co., Deerfield, IL) that removed any gaseous impurities and reduced the drift gas water content below 4.0 mg m^{-3} H_2O. Water vapor was added to the drift gas via a stainless steel 'tee' from VICI Valco (Houston, TX) connected to a Hamilton 250 μL gas-tight sample syringe (Reno, NV) via a 30 cm. length of 60 μm I.D. × 145 μm O.D. fused silica capillary (Polymicro Technologies, LLC, Phoenix, AZ) and stainless steel fittings. The syringe injected water into the drift gas stream at a flow rate of 4 μL min^{-1} using a KD Scientific Inc. model 210 syringe pump (Holliston, MA). The drift gas moisture content, dew point, and relative humidity was measured using a GE Moisture Image Series 1 moisture analyzer (Billerica, MA) [40]. An external calibration of the moisture content was carried out by increasing the water flow rate at 0.5 μL increments from 0 to 5 μL min^{-1}. The drift gas was also preheated before introduction into the drift cell via a fiberglass-covered wrap-around heating cord (Omega, Stamford, CT). This heating cord was coiled around an approximately 40 cm. length of 1/8″ stainless steel drift gas tubing before entering the IM drift cell. Stainless steel regulators, flowmeter valves, tubing, and fittings were used in the drift gas setup to prevent trace moisture buildup on surfaces in contact with the drift gas; dry drift gas flowed through the drift gas system for several hours to ensure accurate dry drift gas measurements for mobility values [41].

2.2.6. *Length*

IM drift region distance measurements were calculated from engineering drawings as well as actual measurements within the ion mobility spectrometer. Coefficients of thermal expansion for the electrode material (304 stainless steel, 17.8×10^{-6} m/m K) and insulating material (99.7% aluminum oxide, 6.3×10^{-6} m/m K) that made up the IM tube were also included in the length determinations as a function of temperature [42].

3. Results and discussion

3.1. *Error analysis and error corrections*

The first step used to obtain precise K_0 values was to quantify the current error associated with each parameter in the reduced mobility equation (as listed in Table 1). This error analysis was prompted by a previous report's discussion of error in IMS analyses but that only listed possible sources of error for standalone systems [14].

For a typical standalone instrument, the error associated with the length was estimated at $\pm 5.0 \times 10^{-4}$ m due to thermal expansion. The error associated with the voltage was largely due to the high voltage supply ripple and was determined to be $\pm 1.0 \times 10^{-3}$ V according to instrumental specifications. The error associated with the drift time measurement was approximately $\pm 1.0 \times 10^{-5}$ s and was largely due to the clock rate of the data acquisition system. The error associated with temperature was approximately $\pm 6.0 \times 10^{-3}$ K if the change in temperature of the drift gas was estimated to be ± 3 K at 473 K (i.e. 200 °C, the maximum operating temperature of the IMS for this study). This estimate was based on initial gas temperature measurements in the drift region of the IM-TOFMS. This error is largely due to temperature changes (mostly due to HVAC) in the surrounding lab environment that may perturb the system from the temperature set by the temperature control unit. The error associated with pressure is largely due to the error controlling and measuring the pressure; the error value of $\pm 7.0 \times 10^{-4}$ Torr was estimated assuming ± 0.5 Torr change with an ambient, operating pressure of 700 Torr. The overall estimate of error, found by taking the square root of the sum of each squared error value, in a typical standalone in the WSU research lab ranged from ± 0.006 cm^2 V^{-1} s^{-1} to ± 0.012 cm^2 V^{-1} s^{-1} for K_0 values of 1.0–2.0 cm^2 V^{-1} s^{-1}, respectively. This range of values represents the best achievable precision with current instrumentation and techniques.

For the ion mobility–time of flight mass spectrometer used in this study, the error values were the same as above except for the errors associated with drift time, temperature, and pressure. The error associated with the drift time measurement is approximately $\pm 1.0 \times 10^{-7}$ s (two orders of magnitude lower than the standalone IMS system); this reduction in error is largely due to the much higher clock rate of the data acquisition system used by the TOF-MS. The error associated with temperature is approximately $\pm 2.0 \times 10^{-3}$ K vs. $\pm 6.0 \times 10^{-3}$ K in the standalone IMS. This reduction in error is due to better mitigation of temperature disturbances around this IM-TOFMS system by better insulation. The error associated with pressure ($\pm 1.0 \times 10^{-4}$ Torr) is also lower than what was estimated for the standalone system due to better control and measurement over a comparable standalone

Table 1

Current state of the art for the error associated with each parameter in the reduced mobility equation on a typical standalone IMS and IM-TOFMS used in this study.

Reduced mobility parameter	Standalone ion mobility spectrometer	Ion mobility-time-of-flight mass spectrometer	Major source(s) of error
Length L, (m)	$s_L = \frac{25\times10^{-6}\ m}{5\times10^{-2}\ m} = 0.5 \times 10^{-3}\ m$	$s_L = \frac{25\times10^{-6}\ m}{10\times10^{-2}\ m} = 0.25 \times 10^{-3}\ m$	Temperature, vibration
Drift time, t_d, (s)	$s_{t_d} = \frac{10^{-7}\ s}{10^{-2}\ s} = 0.01 \times 10^{-3}\ s$	$s_{t_d} = \frac{10^{-9}\ s}{10^{-2}\ s} = 0.0001 \times 10^{-3}\ s$	Data acquisition clock rate
Voltage V, (V)	$s_V = 10^{-3}\ V$	$s_V = 10^{-4}\ V$	voltage ripple in HV source
Pressure P, (Torr)	$s_P = \frac{0.5\ Torr}{700\ Torr} = 0.7 \times 10^{-3}\ Torr$	$s_P = \frac{0.1\ Torr}{700\ Torr} = 0.1 \times 10^{-3}\ Torr$	Measurement and control
Temperature T, (K)	$s_T = \frac{3\ K}{473\ K} = 6.0 \times 10^{-3}\ K$	$s_T = \frac{1\ K}{473\ K} = 2.0 \times 10^{-3}\ K$	Atmospheric disturbances
	$s_{K_0} = 0.006\ cm^2\ V^{-1}\ s^{-1}\quad For\ K_0 = 1$	$s_{K_0} = 0.002\ cm^2\ V^{-1}\ s^{-1}\quad For\ K_0 = 1$	
	$s_{K_0} = 0.012\ cm^2\ V^{-1}\ s^{-1}\quad For\ K_0 = 2$	$s_{K_0} = 0.004\ cm^2\ V^{-1}\ s^{-1}\quad For\ K_0 = 2$	

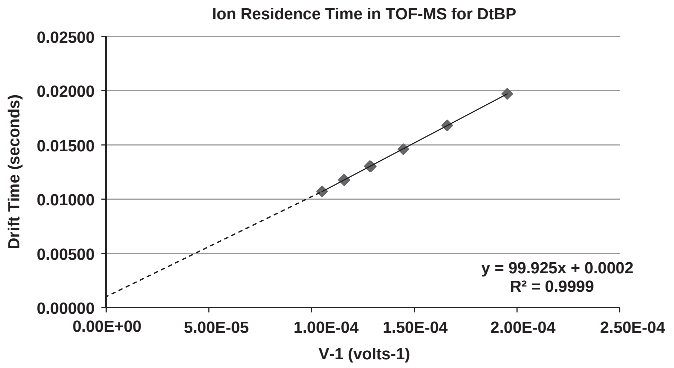


Fig. 1. Plot of mobility drift time (seconds) versus (voltage^{-1}). This plot allows you to determine the residence time of an ion in a mass spectrometer after the mobility separation by finding the y-intercept from the equation of the line.

IMS system. The overall estimate of error in the IM-TOFMS used in this study, found by taking the square root of the sum of each squared error value, ranged from $\pm 0.002\ \mathrm{cm^2\,V^{-1}\,s^{-1}}$ to $\pm 0.005\ \mathrm{cm^2\,V^{-1}\,s^{-1}}$ for K_0 values of 1.0–$2.0\ \mathrm{cm^2\,V^{-1}\,s^{-1}}$, respectively. This range of values represents the best achievable precision with current instrumentation and techniques.

3.2. *Drift time*

Fig. 1 shows a plot of the mobility drift time (seconds) of di-*tert*-butylpyridine plotted against several inverse values of the ion gate voltage (volts^{-1}). This plot was constructed to determine the average residence time of the D*t*BP ions in the TOF-MS; this time value was calculated so that it could be subtracted from mobility drift time measurements to correct the mobility drift time as measured by the TOF-MS. This experiment was conducted by changing the electric field strength across the IM cell by applying increasing voltage to the first electrode in the cell: 7.0 kV, 8.0 kV, 9.0 kV, 10.0 kV, and 11.0 kV. The residence time for D*t*BP was 1.930×10^{-4} s (193.0 μs) and was determined by calculating the *y*-intercept of the line found by plotting the drift time (seconds) versus V^{-1}. The TOF-MS residence times for other chemicals used in this study were also found and subtracted from mobility drift times to achieve accurate reduced mobility values.

3.3. *Effective length of the electric field*

Another source of error in an IM-MS, which was not found in the standalone IM instrument with aperture grids, was the effective length of the IMS drift region's electric field due to the MS pressure interface geometry. The last ring of the IM cell (which also introduced gas into the IMS) was separated from the pressure interface nozzle cone by a 2 mm ceramic spacer. Thus, the effective length of the drift region (i.e. the length of the electric field an ion 'sees' inside the drift region) was longer than the geometric length of the IM drift region. The error associated with this difference was corrected by subtracting the nozzle cone voltage from the ion gate voltage.

3.4. *Temperature studies*

Temperature stability achieved through a well-controlled drift gas temperature was essential to achieve accurate and reproducible reduced mobility values since the collision cross section, and thus the mobility, of an ion is temperature-dependent [43]. Fig. 2**a)** shows the IMS experimental drift gas temperature as a function of drift gas flow rate in an IM tube with an open-ended configuration; Fig. 2**b)** shows the same IM tube drift gas temperature profile once the ion source end was enclosed. The *x*-axis lists the measurement position of the temperature probe, either near the ion gate at the top of the drift region or near the drift gas inlet at the bottom of the drift region (near the MS inlet). The plots reveal several interesting characteristics of the drift gas temperature in the IM drift region. Fig. 2**a)** shows that in the open-ended configuration, at a high flow rate of 1300 mL min^{-1} air, the temperature at the ion gate was almost 10 °C higher than at the gas inlet. This result indicated that the temperature at the bottom of the drift region was lowered by the drift gas flow from the pressurized gas cylinder and that the drift gas was warming up as it traveled to the top of the drift region. The opposite effect occurred when the flow rate was lowered to 800 mL min^{-1} air. The temperature near the ion gate was lower than the temperature near the gas inlet, indicating that the ambient conditions outside the open end of the IM tube (typically 24 °C) were influencing the temperature near the ion gate whereas the IM temperature near the gas inlet was at a higher temperature since it was closed off to the outside atmosphere. A drift gas flow rate of 1000 mL min^{-1} air was the best flow rate to minimize the temperature gradient across the drift region, with the gas inlet and gate readings brought to within 1 °C of each other.

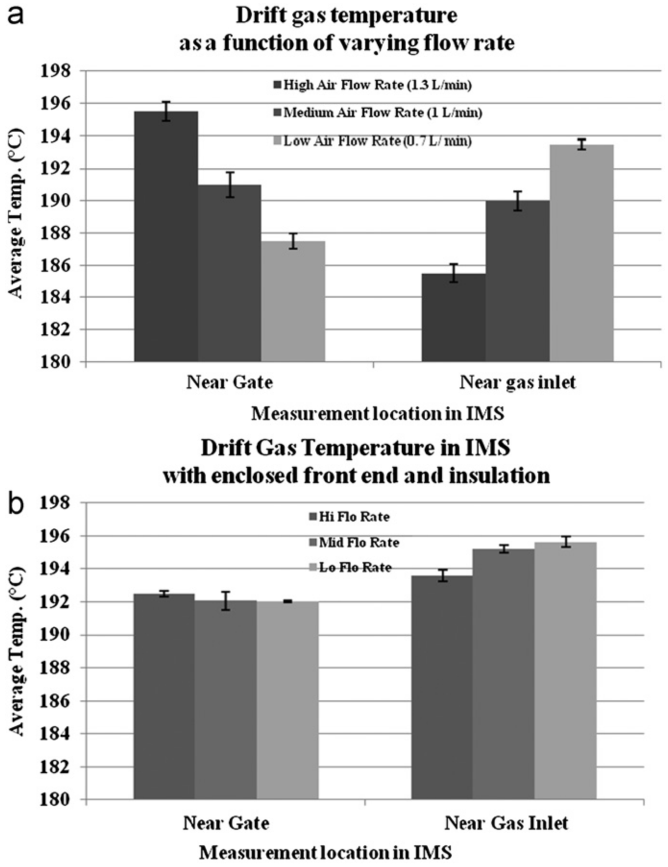
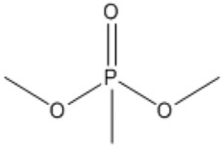
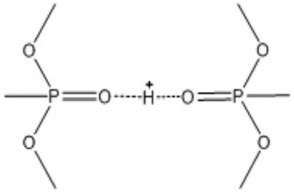
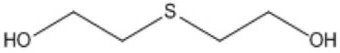
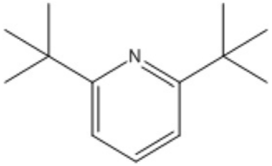
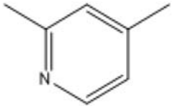


Fig. 2. **a)** Plot of the average IMS drift gas temperature (°C) versus temperature measurement location at three drift gas flow rates: Low-700 mL min^{-1} air, medium-1000 mL min^{-1} air, and high-1300 mL min^{-1} air. **b)** Plot of the average IMS drift gas temperature (°C) versus temperature measurement location at three drift gas flow rates: Low-700 mL min^{-1} air, medium-1000 mL min^{-1} air, and high-1300 mL min^{-1} air after the IM cell was sealed at the front of the cell and better insulated.

Fig. 2**b)** shows the effect on the drift gas temperature when the IM ion source end was enclosed and the entire tube was insulated with Aerogel, an inorganic insulating material. The results of this study found that the temperature at the gas inlet was always higher than that at the gate and that the highest flow rate at

Table 2

Common compound name, molecular weight, chemical formula, structure and experimental K_0 values found for four experimental temperatures: a) 34.80 °C ± 0.40 °C, b) 49.10 °C ± 0.50 °C, c) 96.90 °C ± 0.60 °C, and d) 145.30 °C ± 0.40 °C; errors are given to $\pm 1\sigma$ with a sample size $(n) = 24$. Ranges of literature values are given across several literature sources. An italicized K_0 value indicates a change in ion species from the previous K_0 value; these values cannot be directly compared due to the change in ion chemistry but are useful to understand how the ion type changes as a function of temperature.

Compound name	**MW** (g mol^{-1})	**Chemical formula**	**Structure**	**K_0 values 4.0 mg m^{-3} H_2O (cm^2 v^{-1} s^{-1})**	**K_0 values 2100.0 mg m^{-3} H_2O (cm^2 v^{-1} s^{-1})**	**Lit. K_0 value ranges (cm^2 v^{-1} s^{-1})**	**Ref.**
Dimethyl methylphosphonate-monomer (DMMP)H$^+$ = 125.04	124.08	$C_3H_9O_3P$		a) 1.600 ± 0.001 b) 1.710 ± 0.005 c) 1.820 ± 0.005 d) 1.890 ± 0.005	a) 1.520 ± 0.008 b) 1.670 ± 0.004 c) 1.810 ± 0.008 d) 1.860 ± 0.004	1.88–1.99; 1.65–2.0; 1.74–1.8	6,7, 29
Dimethyl methylphosphonate – dimer (DMMP)$_2$H$^+$ = 249.07	248.16	$C_6H_{19}O_6P_2$		a) 1.400 ± 0.001 b) 1.400 ± 0.001 c) 1.410 ± 0.001 d) 1.400 ± 0.008	a) 1.400 ± 0.003 b) 1.400 ± 0.001 c) 1.400 ± 0.001 d) 1.390 ± 0.001	1.40–1.41; 1.40–1.42; 1.38–1.39	6,7
Thiodiglycol (TDG) TDG+NH$_4^+$ = 140.07 TDG+H–H_2O^+ = 105.04	122.19	$C_4H_{10}O_2S$		a) 1.460 ± 0.008 b) 1.600 ± 0.006 c) 1.680 ± 0.006 d) 2.000 ± 0.008	a) 1.450 ± 0.002 b) 1.470 ± 0.004 c) 1.640 ± 0.002 d) 1.970 ± 0.006	1.90; 1.93	42,43
2,6-di-tert-butylpyridine (DtBP) (DtBP)H$^+$ =192.18	191.17	$C_{13}H_{21}N$		a) 1.400 ± 0.005 b) 1.410 ± 0.004 c) 1.410 ± 0.005 d) 1.400 ± 0.005	a) 1.390 ± 0.005 b) 1.400 ± 0.005 c) 1.400 ± 0.005 d) 1.390 ± 0.005	1.45–1.46; 1.42	6,29
2,4-dimethyl pyridine or 2,4-lutidine (2,4-DMP) (2,4-DMP)H$^+$ = 108.08	107.15	C_7H_9N		a) 1.730 ± 0.002 b) 1.780 ± 0.004 c) 1.890 ± 0.001 d) 1.950 ± 0.002	a) 1.600 ± 0.003 b) 1.750 ± 0.004 c) 1.860 ± 0.002 d) 1.920 ± 0.005	1.95; 1.85–1.96; 1.75–2.0	4, 6, 7

1300 mL min^{-1} air caused the smallest temperature gradient across the drift region. However, the above improvements to the IM cell still did not mitigate the problem of the temperature gradient across the drift region. This problem was solved by pre-heating the drift gas before it entered the IM gas inlet.

3.5. Accurate and precise reduced mobility values for positive ions

Positive mode-active compounds for IMS standards have been in use since the 1980s and a review has listed all the compounds proposed for use as a standard [2,11]. Table 2 shows four of the most common positive ionization mode mobility compounds. The table lists the compound's name and ion type(s), molecular weight, chemical formula, structure, and reduced mobility values at four experimental temperatures and two drift gas water contents (4.0 mg m^{-3} and 2100 mg m^{-3}); a typical literature reduced mobility value or range of literature reduced mobility values was also given for comparison purposes.

3.5.1. DMMP monomer

Temperature and drift gas moisture-dependent K_0 values were found for the compounds studied. The first row in Table 2 shows the experimental reduced mobility values for the DMMP monomer ion at m/z 125.04. The DMMP monomer ion formed by the following reaction:

$$DMMP+(H_2O)_nH^+ \rightarrow DMMPH^+(H_2O)_{n-x}+xH_2O$$

The K_0 values had an 18.0% difference in a drift gas with low water content (<4.0 mg m^{-3} H_2O) over the temperature range. The K_0 values had a greater percent difference of 22.4% in a drift gas with high water content (≥ 2100 mg m^{-3}) over the same temperature range. As shown in Table 3, this percent difference in K_0 values was larger than the percent difference that can be calculated from Eiceman et al.'s work for the DMMP monomer with a water content at 2.9 mg m^{-3}; however, since the moisture levels were higher in this study than Eiceman et al. the upward trend in the percent difference in the K_0 values can be expected [4]. A study by Ewing et al. was conducted with a wider range of drift gas water contents over a similar temperature range; this study found an estimated 11.1% difference at 4.42 mg m^{-3} and an estimated 21.2% difference at 1474.03 mg m^{-3} [5].

The range of K_0 values for the DMMP monomer ion found in this study agreed best with work by Ewing et al. and Viitanen et al. who also saw a temperature-dependent K_0 value for the DMMP monomer ion [5,29]. These results show that the DMMP monomer ion's K_0 value changed more with increasing drift gas water content and that these results fit within a trend shown by previous literature reports [4,5]. The change in K_0 value for a single ion species may be explained by an increase in the ion's size as the result of increased ion-induced dipole interactions from water molecules clustered around the ion [5,34].

Table 3
The percentage differences in K_0 values for the DMMP monomer ion ((DMMP)H$^+$ at m/z 125.04) between 35 °C and 215 °C and as a function of increasing drift gas water content (mg m^{-3}). The table shows an increasing trend for the K_0 values' percentage differences as the drift gas water content increases for the same temperature range.

Drift gas water content (mg m^{-3})	% difference in (DMMP)H$^+$ K_0 value between 35 °C and 215 °C	Source
2.90	10.6%	[4]
4.42	11.1%	[5]
4.0	18.0%	This study
1474.0	21.2%	[5]
2100.0	22.4%	This study

NB: The % difference values from the literature reports were calculated from values estimated from plots in the respective studies; actual values were not available from the reports.

3.5.2. DMMP dimer

The K_0 values for the protonated DMMP dimer ion at m/z 249.07 show good agreement with previously published literature reports [4,5,29]. The DMMP dimer ion formed by the following reaction:

$$DMMPH^+(H_2O)_n+DMMP \rightarrow DMMP_2H^+(H_2O)_{n-x}+xH_2O$$

Over the 120 °C temperature and 2000 mg m^{-3} drift gas water content ranges, the DMMP dimer's K_0 value only changed by 1.4%. This percentage difference is similar to what Ewing et al. found in their study when they showed only a 1.0% difference in the K_0 value for the DMMP dimer ion over a 25 °C–215 °C temperature range and from a 4.42–1474.03 mg m^{-3} drift gas water content [5].

3.5.3. Thiodiglycol

The thiodiglycol (TDG) results from this study showed that, along with ion size changes due to clustering, the K_0 value can also be affected by a change in the ion species. At a temperature between 96.9 °C and 145.3 °C, the ion species for TDG changed from TDG+NH_4^+ at m/z 140.07 to TDG+H–H_2O^+ at 105.04. The ammonium adduct ion formed by the following reaction:

$$TDG+NH_4^+ \rightarrow (TDG)NH_4^+$$

Only two previous reports were found listing a K_0 value for TDG but these reports used an electrospray (ESI) ion source with an IMS temperature at 200 °C [37,38]. At this experimental temperature, only the species at m/z 105.04 was present. However, many portable IMS chemical warfare agent detectors are operated at or near ambient temperature (25 °C) so the ammonium adduct species may be important at the lower temperatures [44,45].

The temperature dependence of the K_0 value for the TDG+NH_4^+ ion species, formed at temperatures below 145.3 °C was 15.1% for an average drift gas water content of 4.0 mg m^{-3} and 13.1% for an average drift gas water content of 2100 mg m^{-3}. The study did not determine the temperature dependence for the TDG+H–H_2O^+ ion species because only one temperature point was taken when this species was present in the analysis. However, the fact that the ion formed only at an elevated temperature at or around 145.3 °C indicated that TDG was susceptible to temperature-induced ion chemistry. At a temperature above 100 °C, ion-molecule reaction conditions changed so that the ammonia reactant ion (commonly seen in background air) was not the preferred ionization pathway but that proton addition followed by dehydration created the primary analyte ion for TDG as shown by the following reaction:

$$TDG+(H_2O)_nH^+ \rightarrow TDGH^+(H_2O) \rightarrow TDGH^+-H_2O$$

This reaction pathway was most likely only accessible at elevated temperatures and with lower probabilities for clustering with neutral and water molecules. As expected with an ion species that had a lower m/z and was found at higher temperatures, the K_0 value for the TDG+H–H_2O^+ species was larger than the K_0 values for the TDG+NH_4^+ species; the K_0 values also followed the same general trend of larger K_0 values in the 4.0 mg m^{-3} H_2O drift gas over the 2100 mg m^{-3} H_2O drift gas.

The K_0 values measured in this study were both larger than those listed in the ESI-IMS reports; the earlier reports listed the K_0 value for the TDG+H–H_2O^+ ion at 1.90 and 1.93 cm^2 V^{-1} s^{-1}, respectively.[37,38] The difference in values (1.90 and 1.93 cm^2 V^{-1} s^{-1} versus 2.000 cm^2 V^{-1} s^{-1} for the 4.0 mg m^{-3} drift gas water content and 1.97 cm^2 V^{-1} s^{-1}for the 2100 mg m^{-3} drift gas water content) were most likely due to increased clustering with the electrospray solvent molecules which could have increased the ion's effective size and caused measured mobilities to be lower than reported here.

3.5.4. DtBP

The K_0 value for the (DtBP)H$^+$ species at m/z 192.18 changed by less than 1% over the temperature range used in this study; this result agreed with previous literature reports which saw less than 1% change in the K_0 value for this compound [4]. Previous literature reports also found that DtBP was not susceptible to changes in IMS electric field strength, temperature, and drift gas water content [4]. This can be explained both by DtBP's high proton affinity (982.9 kJ mol^{-1} versus 691 kJ mol^{-1} for H_2O) which helps the ion to keep its charge and the position of the two *tert*-butyl groups that surround the charge on the nitrogen atom, the charge's most likely location [3]. The *tert*-butyl groups seem to 'shield' the ion's charge from clustering species that would cause changes to the ion's K_0 value by ion-induced dipole interactions. [34]

3.5.5. 2,4-DMP

The K_0 value for 2,4-dimethyl pyridine monomer ((2,4-DMP)H$^+$) at m/z 108.08 had a marked temperature dependence over the 120 °C temperature range studied. The percentage difference over the temperature range was 12.7% for the 4.0 mg m^{-3} H_2O drift gas and 20.0% for the 2100 mg m^{-3} H_2O drift gas. As shown in Table 4, a trend can be seen of increasing percentage differences as a function of increasing drift gas water content; this trend complements estimated percentage differences seen in a previous literature report [5]. K_0 value data was not collected for the 2,4-DMP dimer in this study (as has been previously reported in other accounts) because sample concentrations needed to form the dimer overwhelmed the detector and led to lengthy sample cleanup times [4].

The range of average K_0 values for 2,4-DMP in this study most closely aligned with previous work by Ewing et al. [5]. Earlier work by Karpas, who first used 2,4-DMP as an IMS standard compound, found that 2,4-DMP had a stable 1.95 cm^2 V^{-1} s^{-1} K_0 value between 150 °C and 250 °C [2]. The 1.95 cm^2 V^{-1} s^{-1} value was only seen in this study at 150 °C and in the 4.0 mg m^{-3} H_2O drift gas. The widely reported 1.95 cm^2 V^{-1} s^{-1} K_0 value for 2,4-DMP was most likely only valid at IMS cell temperatures $\geq$ 150 °C [11]. The K_0 values from Eiceman et al.'s study were not given for the two lower temperature points but, for the points near 100 °C and 150 °C, the values were within $\pm$0.01 cm^2 V^{-1} s^{-1} for the lowest water content drift gas [4].

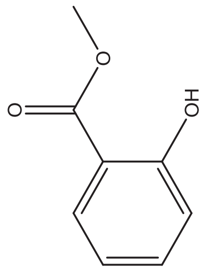
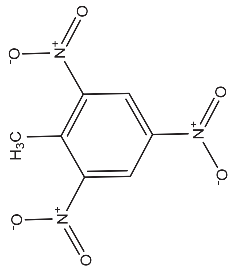
Overall, the K_0 values found for the positive mode compounds at four experimental temperatures and two drift gas water contents showed that temperature and drift gas water content can affect the mobility of an ion and, in some cases, the ion

Table 4
The percentage differences in K_0 values for the 2,4-DMP monomer ion ((2,4-DMP)H$^+$ at m/z 108.08) between 35 °C and 215 °C and as a function of increasing drift gas water content (mg m^{-3}). The table shows an increasing trend for the K_0 values' percentage differences as the drift gas water content increases for the same temperature range.

Drift gas water content (mg m^{-3})	% difference in (2,4-DMP)H$^+$ K_0 value between 35 °C and 215 °C	Source
4.42	5.3%	[5]
4.0	12.7%	This study
1474.0	14.3%	[5]
2100.0	20.0%	This study

NB: The % difference values from the literature reports were calculated from values estimated from plots in the respective studies; actual values were not available from the reports.

Table 5
Common compound name, molecular weight, chemical formula, structure and experimental K_0 values found for four experimental temperatures: a) 34.80 °C $\pm$ 0.40 °C, b) 49.10 °C $\pm$ 0.50 °C, c) 96.90 °C $\pm$ 0.60 °C, and d) 145.30 °C $\pm$ 0.40 °C; errors are given to $\pm 1\sigma$ with a sample size (n)=24. Ranges of literature values are given across several literature sources. An italicized K_0 value indicates a change in ion species from the previous K_0 value; these values cannot be directly compared due to the change in ion chemistry but are useful to understand how the ion type changes as a function of temperature.

Compound name and ion species (Th.)	MW (g mol^{-1})	Chemical formula	Structure	K_0 values low H_2O (cm^2 v^{-1} s^{-1})	K_0 values high H_2O (cm^2 v^{-1} s^{-1})	Lit. K_0 value (cm^2 v^{-1} s^{-1})	Ref.
Methyl salicylate (MeS) MeS–H$^-$ =151.04 MeS+CO_2^- =196.04	152.15	$C_8H_8O_3$		a) 1.360 $\pm$ 0.005 b) 1.470 $\pm$ 0.005 c) 1.590 $\pm$ 0.004 d) 1.650 $\pm$ 0.007	a) 1.340 $\pm$ 0.007 b) 1.450 $\pm$ 0.007 c) 1.580 $\pm$ 0.007 d) 1.650 $\pm$ 0.003	1.47 for MeS–H$^-$ at 51 °C; 1.62 at 92 °C	[36,46]
2,4,6-trinitrotoluene (TNT) TNT-H$^-$ =226.01	227.13	$C_7H_5N_3O_6$		a) 1.490 $\pm$ 0.005 b) 1.500 $\pm$ 0.004 c) 1.530 $\pm$ 0.001 d) 1.540 $\pm$ 0.004	a) 1.490 $\pm$ 0.004 b) 1.500 $\pm$ 0.004 c) 1.520 $\pm$ 0.002 d) 1.530 $\pm$ 0.003	1.45–1.54 for varying T.	[13]

chemistry used to form the ion. The study also generated the first simultaneously mass-identified mobility values for all the proposed standards in the above tables, revealing previously unreported analyte ion formation changes that affected the mobility values of the ion species. While not all of the K_0 values generated in this study agreed with literature reports, the same trend was observed of increasing mobility values with temperature and in a lower water content drift gas.[4]

3.6. *Accurate and precise reduced mobility values for negative ions*

While negative mode IMS has been extensively used since the 1970s for explosives detection in the negative mode, the development of negative mode-active compounds for IMS standards has lagged behind that of standard development for the positive mode and fewer compounds have been used as standards; all the compounds proposed for use as a negative mode standards have been listed in a review article [11]. The two compounds used in this study, methyl salicylate (MeS) and 2,4,6-trinitrotoluene (TNT), were chosen because they have been the most common compounds used as standards in IMS analyses [11].

Table 5 shows the shows two negative ionization mode mobility compounds listing the compound's name and ion type(s), molecular weight, chemical formula, structure, and reduced mobility values at four experimental temperatures and two drift gas water contents; a typical literature reduced mobility value or range of literature reduced mobility values was also given for comparison purposes.

3.6.1. *Methyl salicylate*

This study found that methyl salicylate showed a change in analyte ion chemistry for increasing temperature. For the experimental temperatures near 30 °C and 50 °C, the primary analyte ion for MeS was $MeS–H^-$ at m/z 151.04. Over this temperature range, the K_0 value for the proton abstracted species had an 8.1% percent difference in the 4.0 mg m^{-3} H_2O drift gas and an 8.2% difference in the 2100 mg m^{-3} H_2O drift gas. After the 50 °C temperature point, the primary analyte ion for MeS shifted to $MeS+CO_2^-$ at m/z 196.04. This species also exhibited a change in its K_0 value with temperature and drift gas moisture content; over a 100 °C to 150 °C range, the K_0 value for the CO_2 adduct had a percent difference of 3.8% in the 4.0 mg m^{-3} H_2O drift gas and a 4.4% difference in the 2100 mg m^{-3} H_2O drift gas. Over the entire temperature range, the measured K_0 values for MeS showed a 21.3% difference in a 4.0 mg m^{-3} H_2O drift gas and a 23.1% difference for the 2100 mg m^{-3} H_2O drift gas. The K_0 values all increased over the 120 °C temperature range.

3.6.2. *TNT*

TNT, by contrast with MeS, had much lower percent differences in its K_0 values (3.4% in the 4.0 mg m^{-3} H_2O drift gas and 2.7% in the 2100 mg m^{-3} H_2O drift gas) found across the temperature range. TNT also only produced a proton abstracted species, $TNT\text{-}H^-$, at m/z 226.01 across the entire temperature range. Fig. 3 highlights the changes in reduced mobility value versus temperature for MeS and TNT. The curves in the plot clearly show that MeS' K_0 value has a greater dependence on temperature than TNT's K_0 value. The stability of TNT's K_0 value may be due to the ion formation mechanism (the enthalpy change for the proton abstraction reaction with O_2^- is -37.1 kcal mol^{-1}) and the structure of the resultant ion species; the nitro groups on either side of the charge on the deprotonated methyl group may prevent ion-induced dipole interactions between the charge and neutral molecules, resulting in less cluster formation [47]. MeS may be more susceptible to clustering due to dipole-induced dipole interactions with the lone pair electrons on the oxygen atoms in the compound and that the charge, located most likely on the oxygen atom after a proton abstraction of the phenol (pKa = 10), may have greater ion-induced dipole interactions with neutral cluster molecules than the charge located on TNT ion [34].

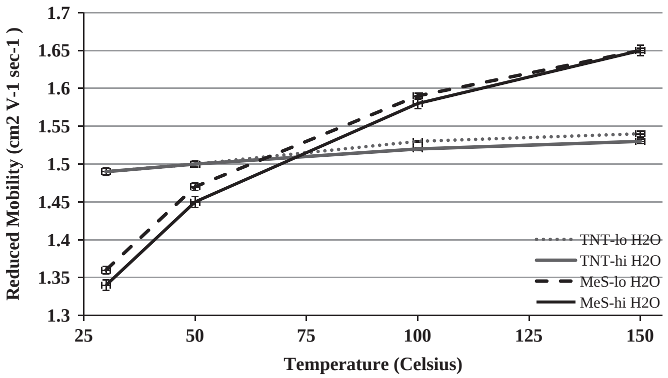


Fig. 3. Plot of reduced mobility (cm^2 V^{-1} s^{-1}) versus temperature (°C) for TNT at both low (red, dashed trace) and high (red trace) drift gas water content and methyl salicylate (MeS) at both low (black, dashed trace) and high (black trace) drift gas water content. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Overall, the study of proposed negative mode compounds showed temperature and drift gas water content dependence on each compound's K_0 values; the effect of these parameters was much greater on the K_0 values for MeS than for TNT. The study also revealed that temperature-dependent ion chemistry can affect MeS' ion species, and, thus, its K_0 values. The K_0 values generated in this study also provided much needed temperature-dependent mobility data which was not available from previous literature reports [4].

4. Conclusions

This study used IM-TOFMS to obtain mass-identified reduced mobility values for several proposed positive and negative mode IMS standards. The results showed that, over a 120 °C temperature range and an approximate 1800 mg m^{-3} drift gas water content range, the reduced mobility values for the positive mode compounds had percent differences that ranged from 1.4% for D*t*BP to 22.4% for the DMMP monomer ion. D*t*BP and the DMMP dimer ion had the lowest percent differences in their K_0 values over the temperature and drift gas water content ranges; these trends were seen in earlier reports but have now been reported with simultaneous mass identifications of the ion species and with previously unreported values of reproducibility. The study also showed previously unreported temperature-dependent changes to the ion species for several standards. These results indicate that TDG, used as a structural simulant for mustard gas in IMS, should not be used as a chemical standard due to temperature-dependent ion species changes. The same recommendation is also made for methyl salicylate. MeS not only had temperature-dependent ion species changes but also had a much greater percent difference in its reduced mobility values versus TNT (e.g. 2.7% for TNT and 23.1% for MeS in the 2100 mg $m^{-3}H_2O$ drift gas).

The overall recommendation of this study is that temperature-dependent reduced mobility values should be quoted in the literature for these compounds instead of using a single K_0 value for a compound. For example, a K_0^{303} for $DMMPH^+$ at 30 °C (303 K) is 1.60, while K_0^{323} for $DMMPH^+$ at 50 °C is 1.71. These reference standards have applicability not only in chemical warfare agent detection but also in other threat categories including explosives and toxic industrial chemicals as well as biological applications of IMS.

The results of this study also warrant recommending TNT as a viable negative mode reference standard while acknowledging that the K_0 value for TNT does change with temperature and drift gas water content; however, TNT's K_0 value changed by a much smaller degree than MeS. Development is still needed for negative mode reference compounds. D*t*BP and the DMMP dimer ion remain good IMS chemical reference standards since they both have K_0 values that changed $\leq 1.4\%$ over the temperature and drift gas water content ranges studied.

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