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High-Pressure Ion Mobility Spectrometry

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Abstract

The effects of above-ambient pressure on ion mobility on resolving power, resolution, and ion current were investigated using a small, stand-alone ion mobility spectrometer (IMS). This work demonstrates the first example of ion mobility spectrometry at pressures above ambient. Ion mobility spectra of chemical warfare agent (CWA) stimulant dimethyl methylphosphonate (DMMP) and several other standard compounds are shown for superambient conditions. The IMS was operated at pressures from 700 to 4560 Torr. An optimal resolving power was obtained at a specific voltage as a function of pressure, with higher optimal resolving powers obtained at higher voltages, as predicted from standard IMS theory. At high pressures, however, resolving power did not increase as much as theory predicted, presumably due to ion clustering. Nevertheless, an increase in pressure was found to improve resolution in IMS. One example where high pressure improved resolution was the separation of cyclohexylamine ($K_0 = 1.83$) and 2-hexanone ($K_0 = 1.86$) (where K_0 is the reduced mobility value). The product ions of these two compounds could not be separated at ambient pressure but could be nearly baseline separated when the pressure of the buffer gas was raised to 2280 Torr. Total ion current was also examined at pressures from ambient up to 4560 Torr. Total ion current, when investigated with pressure, was found to reach a maximum, initially rising with increased pressure.

Ion mobility spectrometry (IMS) is an analytical technique most commonly used for explosive and illicit drug detection.^{1,2} It is a rapid, gas-phase separation method wherein ions are separated based on their size, shape, charge, and ion-neutral interaction potential. Size-based separation along with rapidity and ease of measurements give IMS useful applications in environmental monitoring,³ metabolomics,⁴ proteomics,^{5,6} and industrial process control.¹

The mobilities of ions were first measured in buffer gases at pressures of 1–10 Torr, primarily to study ion-neutral interactions in the gas phase. First developed in the 1970s,⁷ ambient pressure ion IMS (also known as plasma chromatography) has become the method of choice for the detection of explosives, drugs, and chemical warfare agents.¹ Conducting ion mobility experiments at atmospheric pressure not only simplified the experiment because large and cumbersome vacuum pumps were no longer needed, but resolving power and resolution were improved over those obtained with reduced pressure instruments. In addition to the common stand-alone IMS instruments used today, both subambient and ambient pressure IMS cells have received considerable attention lately as an interface for mass spectrometry.⁸ The ability of IMS to separate isomers and biological conformers adds a new dimension of information that may be obtained from mass spectrometry.^{4,9} For application to biological systems, subambient IMS (when coupled to mass spectroscopy) has the advantage of possible ion focusing, improved ion transmission, and ease of interface to a mass spectrometer. However, ambient or near-ambient pressure IMS instruments gain an increase in ion–molecule interactions,

allowing greater separation selectivity.⁸ Although the effects of temperature, voltage, and drift gases⁹ have been investigated with respect to IMS resolution, selectivity, and resolving power, few systematic experiments have been conducted in which pressure has been varied to improve resolution.

In a recent paper, Tabrizchi and Rouholahnejad investigated the effect of pressure on IMS resolution from high vacuum to atmospheric pressure.¹⁰ In this study, the authors noted an increase in resolving power as pressure increased, but this gain was accompanied by a significant loss in signal. Tabrizchi and Rouholahnejad constructed an IMS cell in which the internal pressure could be controlled from high vacuum up to atmospheric pressure. The authors noted an increase in ion current and dynamic range as the pressure decreased¹¹ but an inverse relationship on resolving power and resolution. The authors varied the gate pulse width (50–225 μ s) and the pressure of the cell (0–800 hPa) and measured the resolving power. In this limit, resolving power was shown to increase toward a maximum, dependent upon the initial pulse of ions allowed into the drift region of the cell.

Nazarov et al. evaluated the effect of pressure on differential mobility spectrometry.⁶ In this study, ion transmission, peak width, and peak intensity were studied in a differential mobility spectrometer (DMS) at 0.42, 0.76, and 1.55 atm. The authors found a change in peak position that was explained through the description of the instrumental conditions in townsend (E/N) instead of separate terms of pressure, temperature, and electric field. For DMS, a decreased pressure was found to be favorable due to the increased E/N value, allowing for an increase in resolution as well as a decrease in both required operating voltages and the probability of electrical breakdown of the inert carrier gas.⁶

There have been several endeavors to reduce the size of an ion mobility spectrometer, and several miniaturized IMS instruments have been developed and reported.¹² In every case, however, the resolving power of an IMS is reduced as the size of the IMS is decreased. One approach to improve the resolving power of a small IMS sensor may be to increase pressure. To date, no investigations of high pressure (buffer gas pressures above ambient pressure) have been conducted. Thus, the objective of this study was to provide initial information on how ions behave at elevated pressures, especially with respect to analytical figures of merit such as resolving power, resolution, separation, and sensitivity.

IMS THEORY AND PREDICTION OF HIGH-PRESSURE EFFECTS

Analytes measured in IMS are commonly characterized by their reduced mobility value (K_0), as defined:¹³

$$K_0 = \frac{L^2}{V t_d} \left(\frac{P}{760} \right) \left(\frac{273.15}{T} \right) \quad (1)$$

IMS separation is characterized through two parameters: resolving power (R_p) and resolution. Previous studies have shown the relation and advantage of manipulating the drift gas⁹ and temperature¹ in order to increase resolution and resolving power; and as previously stated, one study has demonstrated the effect of pressure on resolving power from high vacuum up to atmospheric pressure.¹⁰ Primarily affecting resolution and R_p , IMS ion peaks are broadened primarily through two distinct mechanisms: simple diffusion (represented as t_{diff}) and the initial width of the ion packet (t_g) introduced into the tube. These mechanisms are summed through the following relation:¹³

$$w^2 = t_g^2 + t_{\text{diff}}^2 \quad (2)$$

Thus, resolving power in an IMS may be reduced to contributions implied by the diffusion and gate pulse limited regimes as described previously:¹³

$$R_c^{-2} = R_g^{-2} + R_{\text{diff}}^{-2} \quad (3)$$

where R_c is defined as the conditional resolving power, R_{diff} is the diffusion-limited resolving power, and R_g is the gate pulse limited resolving power. Using the above equation with terms found in Siems et al.¹³ and Kanu et al.¹⁴ the following equation may be derived:

$$R_c = \frac{1}{\sqrt{\frac{t_g^2 K^2 V^2}{L^4} + \frac{16k_B T \ln(2)}{qV}}} \quad (4)$$

In order to more easily predict resolving power from literature data reduced mobility was substituted for the mobility term in eq 4:

$$R_c = \frac{1}{\sqrt{\frac{760}{273} \frac{t_g^2 K_0^2 P^2}{L^4 T^2} + \frac{16k_B T \ln(2)}{qV}}} \quad (5)$$

This equation demonstrates that there is a maximal resolving power which is dependent upon the voltage applied to the beginning of the drift region, as shown in Figure 1A. However, the optimal voltage changes with pressure, due to the pressure dependence inherent in the R_c equation. This is apparent if the derivative of eq 5 is obtained with respect to voltage and set equal to zero to find the maximum:

$$V_{\text{opt}} = 0.0395 \left[\frac{L^4 P^2}{t_g^2 K_0^2 T} \right]^{1/3} \quad (6)$$

Within this equation, the pressure dependence of the voltage optimum is explicitly described. Operating the IMS at the optimal voltage should provide the maximal obtainable resolving power for that given pressure and temperature. Additionally, at a given voltage, resolving power asymptotically approaches a maximum with increasing pressure (Figure 1B). Thus, the resolving power of an IMS instrument may be optimized through the manipulation of both the voltage applied to and the pressure of the drift tube. Theoretically, a 6.8 cm drift tube operated at atmospheric pressure, as used in this study, and 1360 V provides a maximum resolving power of approximately 60. However, at 2040 V, the maximal resolving power is about 80 and not reached until about 4000 Torr.

Theory predicts that R_p can be improved with pressure, and because ion mobility spectra do not exist at elevated pressures, the objectives of this project were to construct a high-pressure ion mobility apparatus, to determine if ion mobility spectra could be obtained at pressures above ambient, and to compare the experimentally obtained resolving powers with theory.

EXPERIMENTAL SECTION

Materials and Chemicals Used

All chemicals and reagents were reagent grade and were used as obtained as neat samples. Ultrahigh purity nitrogen was used for both drift and carrier gas.

Ion Mobility Spectrometer

The IMS was similar to a previous design used in this laboratory and has been described in detail elsewhere.³ In general the IMS consisted of a stacked stainless steel (alloy 304) and Macor (Astro-Met, Cincinnati, OH) ring design having an ionization region and a drift region which were separated by a Bradbury–Nielsen type ion gate. The ionization region contained a 15 mCi ⁶³Ni foil. Overall length of the tube was 11.3 cm (17 rings), with a 4.5 cm reaction region (5 rings) and a 6.8 cm drift region (12 rings). A Bradbury–Nielsen gate was used to introduce a finite pulse of ions into the drift region. The entire assembly was wrapped in a heat-shrink plastic polymer in order to create a sealed barrier to the ambient atmosphere. However, this plastic prevented heating of the instrument due to outgassing from the plastic shell at elevated temperatures. A gold-sputtered Faraday plate was used with National Instrument's LabView in-house programmed software for ion detection, data acquisition, and data processing. The instrument was operated in positive ion mode at room temperature throughout the experiment.

Pressure Chamber

A pressure chamber (Figure 2, parts A and B) was constructed at Washington State University (WSU), Pullman to enable ion mobility spectrometry at elevated pressures. Total internal volume of the chamber was 8980 cm³, and the chamber was rated to conduct experiments up to 175 psig (9044 Torr), with a maximum pressure rating set above a pressure release valve set at 225 psig (11 628 Torr) to ensure experimenter safety. The chamber contained four gas connections: one each for carrier gas, drift gas, pressure regulation, and pressure measurement. Pressure was monitored using an Ashcroft 1008S pressure gauge with a range of 0–300 psig (Stratford, CT). IMS tube electrical connections were created with six feed-throughs inserted into the side of the chamber, rated at 10 000 V. A BNC connector was used for signal transfer between the instrument and signal amplifier. Pressure was regulated by holding constant the in-flow of carrier and drift gas (0.45 and 1.00 L/min, respectively) and adjusting the drift gas out-flow from the chamber using a valve. Pressures were maintained to within ± 1 psi (51.7 Torr) using this technique.

Sample Introduction and Ionization

All samples used were semivolatile organic compounds and are listed with structures and reduced mobility values (K_0) in Table 1. An amount of 1 μ L of neat sample was applied to a small piece of filter paper and placed into a separate high-pressure sample chamber (see Figure 2) which was situated outside of the instrument pressure chamber. Carrier gas flowed over the sample, and volatile vapors were swept into the reaction region where they were ionized by the above-mentioned ⁶³Ni foil.

RESULTS AND DISCUSSION

Resolving Power

An example of a high-pressure IMS positive mode spectrum of dimethyl methylphosphonate (DMMP) is shown in Figure 3. Peaks A, B, and C are the reactant ion peak (RIP), DMMP monomer product ion, and DMMP proton-bound dimer product ion, respectively.¹⁵ As shown in Figure 4A, the resolving power of the [DTBP + H]⁺ ion followed the expected gate pulse

to diffusion-limited trend that theory predicted, demonstrating an optimal value for the drift voltage at pressures of 1140 and 2280 Torr to maximize resolving power. However, at 4560 Torr, the resolving power decreased and did not increase. This may have been due the inability to heat the system, increasing ion–molecule clustering within the drift tube and thus decreasing the resolving power by increasing the peak width. Although in theory resolving power increases as temperature decreases, in practice resolving power often decreases with decreasing temperature due to the formation of ion-neutral clusters at low temperatures.^{16,17} If ion-neutral clustering is the primary reason for reduced resolving power, heating the tube should decrease clustering and increase resolving power. The IMS tube used in this study, however, was limited to operation under ambient temperature conditions because of the construction materials. Nevertheless, these spectra demonstrated for the first time that elevated pressure ion mobility spectra can be generated and resolving power may be increased.

As shown in Figure 4B, an optimum pressure for this instrument (at 5000 V) was determined to be 2394 Torr. Resolving power increased up to 35 at this pressure and decreased above this pressure. As discussed in Figure 4A, the decrease in R_p with further increasing pressure may have been due to ion-neutral clustering, with the pressure driving the formation of clustered ions.

Separation of Compounds with Similar Reduced Mobility Values (K_0)

Assuming that pressure does not alter the reduced mobility of an ion, Figure 5A shows the theoretical and actual effect of pressure on mobility of two compounds tested in this study in positive mode IMS: DMMP dimer and monomer, and RIP. As shown, mobility is inversely proportional to pressure. However, the theoretical data shows a lower slope than that observed for the experimental data. This indicates as pressure increases the mobility become decreasingly smaller than predicted from theory, which is in agreement with the explanation that ion–molecule clusters are being formed at higher pressures. In Figure 5A, it may be noted that DMMP dimer showed less clustering than either the RIP or DMMP monomer, indicating that its dimer configuration inhibits the clustering of the molecule. However, RIP and DMMP monomer, being single, unclustered ions, show a significant tendency to cluster with neutral drift gas molecules as they fly through the drift tube. Thus, since temperature has been previously shown to reduce clustering reactions at atmospheric pressure, it is proposed that temperature should help to increase the correlation between theoretical and experimental data of inverse mobility verses pressure.

Figure 5B shows the experimental results of two compounds: cyclohexylamine (CHA, $K_0 = 1.86$) and 2-hexanone (2-HN, $K_0 = 1.83$). In this figure, slightly different slopes indicate that a separation of these two compounds may be possible at higher pressures, whereas at atmospheric pressure they coelute. Figure 6 shows the ion mobility spectra of these two compounds. Figure 6A shows an overlay of these compounds at atmospheric pressure demonstrating that they have nearly the same drift time and could not be separated in a mixture. Figure 6B is an ion mobility spectrum of a mixture of these two compounds at atmospheric pressure demonstrating that, indeed, they cannot be separated. Parts C and D of Figure 6 are ion mobility spectra of the same mixture at elevated pressures. The compounds were separated at 1279 Torr (Figure 6C) and nearly baseline resolved at 2310 Torr (Figure 6D). In this experiment, the slower drifting ion was CHA, as expected due to its lower K_0 value. The specific mechanism through which these compounds were resolved is not yet clear. Resolution may have been due to a relative change in mobility with pressure or to an increase in resolving power. However, the resolution of these compounds provides a first example of the potential use of elevated pressure to improve ion mobility spectrometry.

Total Ion Current

The total ion current of the instrument was measured across an applied voltage range of 2000–8000 V and pressures of 1140, 2280, and 4560 Torr (Figure 7A) and a pressure range of 700–4560 Torr and voltages of 3000, 5000, and 6000 V (Figure 7B). As shown in Figure 7A, the total ion current increased proportionally at low voltage ranges to an asymptotic maximum, but the curves for each pressure were dissimilar. At 8000 V, the current seen at the detector was higher at 2280 Torr than at 1140 Torr, but lower at 4560 Torr. This phenomenon was further investigated in Figure 7B, where the maximal ion current occurred at different pressures for each electric field.

The dependence of ion current on pressure may be due to an ionization efficiency effect. As pressure increases, the β -particles emitted from the ^{63}Ni source collide with more neutral drift gas molecules due to their higher number density. This causes an increase in ions formed initially and thus an increase in total ion current moving through the system. The maximal current was also seen to increase with electric field. This was an expected result to the decrease in migration time for the ions in the tube. With less time, the diffusional term of eq 2 decreases, thus decreasing the observed peak width and the observed resolving power.

CONCLUSIONS

The feasibility and utility of operating an IMS at elevated pressures has been demonstrated. Increased pressure improved resolving power, total ion current, and the ability to resolve compounds with very similar K_0 values while using a small, typically low-resolution instrument. Thus, the exploitation of pressure with an IMS system demonstrates that it may be possible to construct small but high-resolution sensors or may be used to increase the resolving power of large high-resolution laboratory instruments. An increase in clustering effects at high pressure is believed to cause a deviation from the expected increase in resolving power, but this may be corrected when a heated instrument is used. In conclusion, pressure may be used as an additional instrumental parameter in accordance with temperature, gate pulse, and electric field. In so doing, the operating characteristics of an ion mobility spectrometer may be altered and optimized for a specific compound or application. Although a large pressure chamber was used in these studies, it is envisaged that a self-contained, pressurized IMS could be constructed for improved resolutions in a small size.

Acknowledgments

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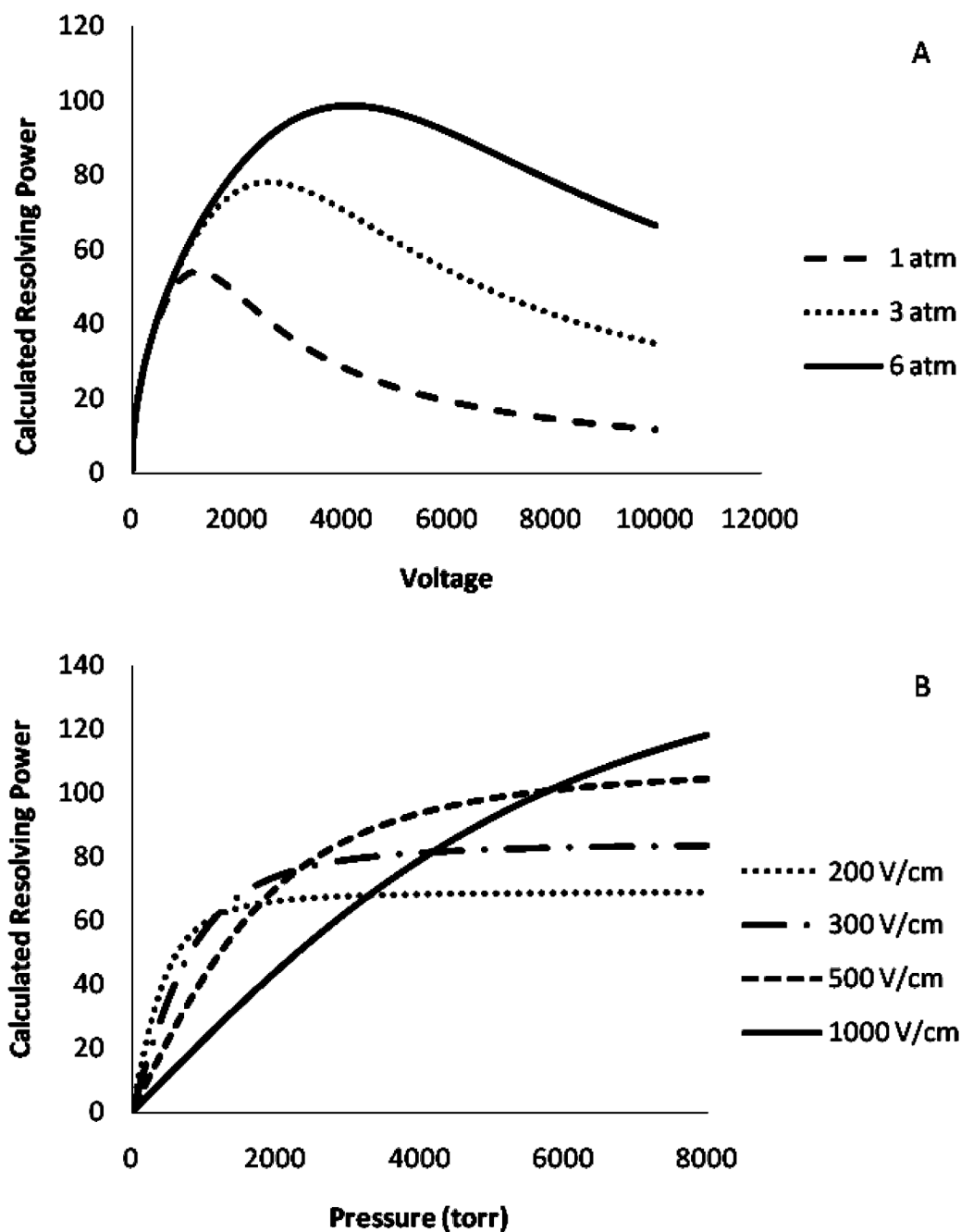


Figure 1.

Theoretical resolving power for a 6.8 cm drift tube. (A) Resolving power vs voltage at 700, 2280, and 4560 Torr as calculated from eq 5. (B) Resolving power vs pressure at 200, 300, 500, and 1000 V/cm. Calculated values take into account a changing mobility value as pressure increases but neglect any change in the collision integral with pressure. An increase in maximum resolving power is theoretically shown with an increase in pressure.

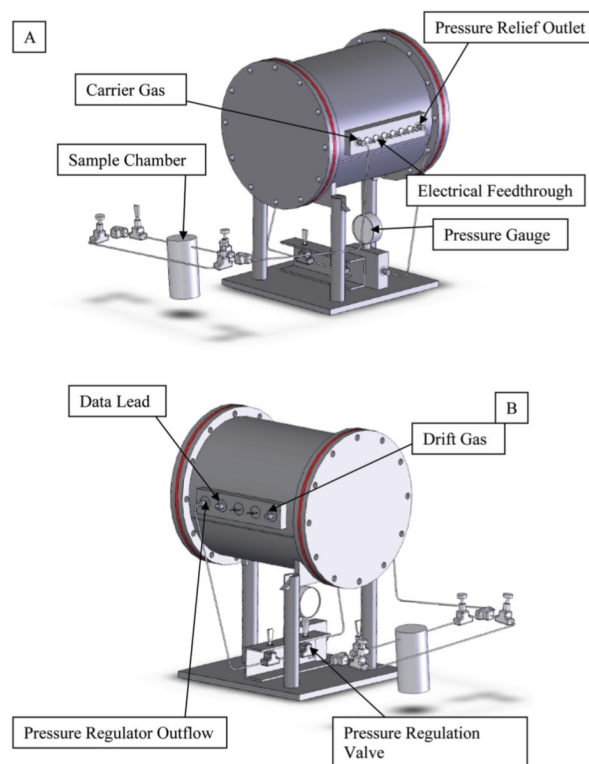


Figure 2.

Pressure chamber viewed from the right (A) and left (B) sides. Computer-rendered drawings of the high-pressure chamber used to perform high-pressure ion mobility spectrometry. Internal volume of 8980 cm³ allowed a small IMS to be placed within the chamber. The sample introduction chamber is also shown. The chamber was custom built on site, capable of 175 psi (9044 Torr).

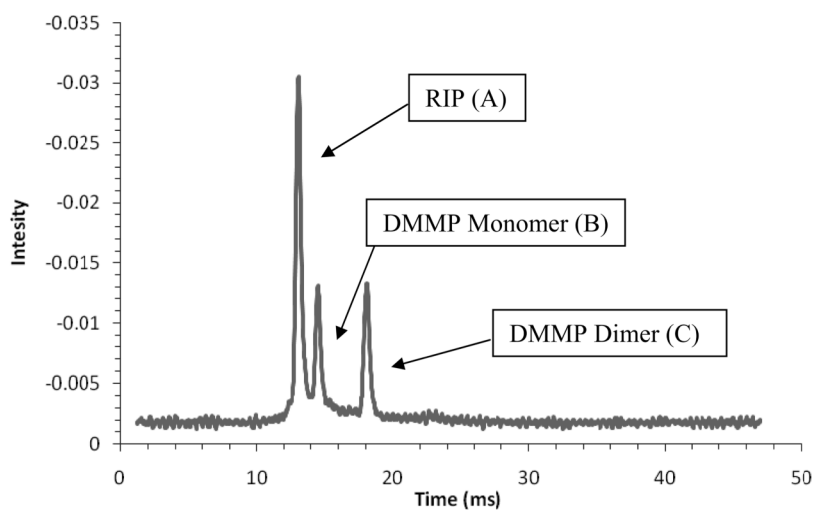
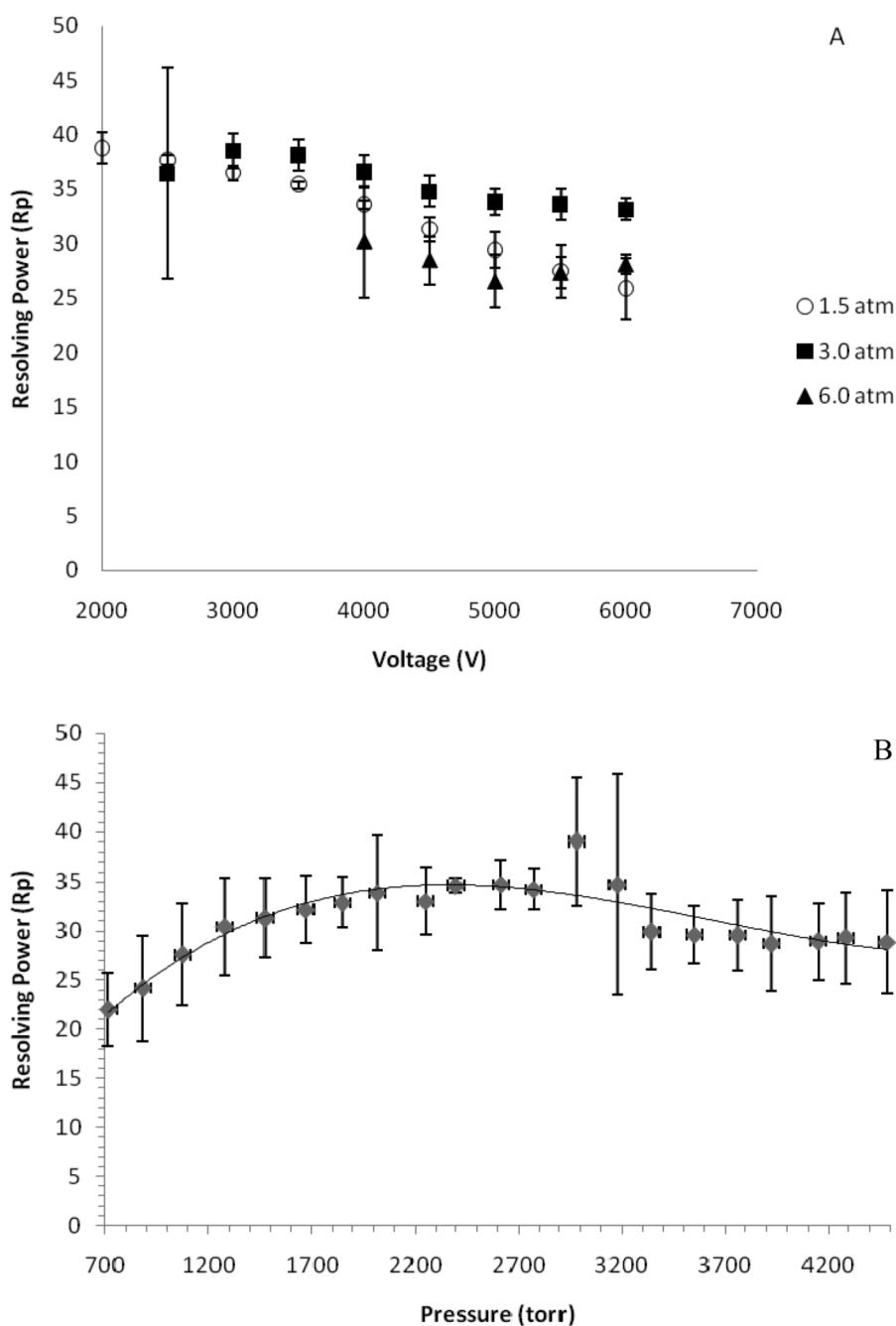


Figure 3. IMS Spectrum of dimethyl methylphosphonate. This spectrum was obtained at 4500 V, 0.2 ms gate pulse, and 2280 Torr with Faraday plate detection. This is the first example of an IMS spectrum taken under superambient conditions.

**Figure 4.**

Resolving power of the IMS measured using DTBPH⁺ ion. (A) Resolving power at 1140, 2280, and 4560 Torr. The large error bar at 2280 Torr and 2500 V is due to the limit of detection for that pressure. An increase in optimal drift voltage was noted as pressure increased, but the expected resolving power increase was minimal. (B) Resolving power vs pressure at 5000 V with a 200 μ s gate pulse width. At this gate voltage, pressure tends to increase resolving power to a maximum, after which the resolving power decreases due to increased clustering. Error bars indicate 1 standard deviation of triplicate measurements.

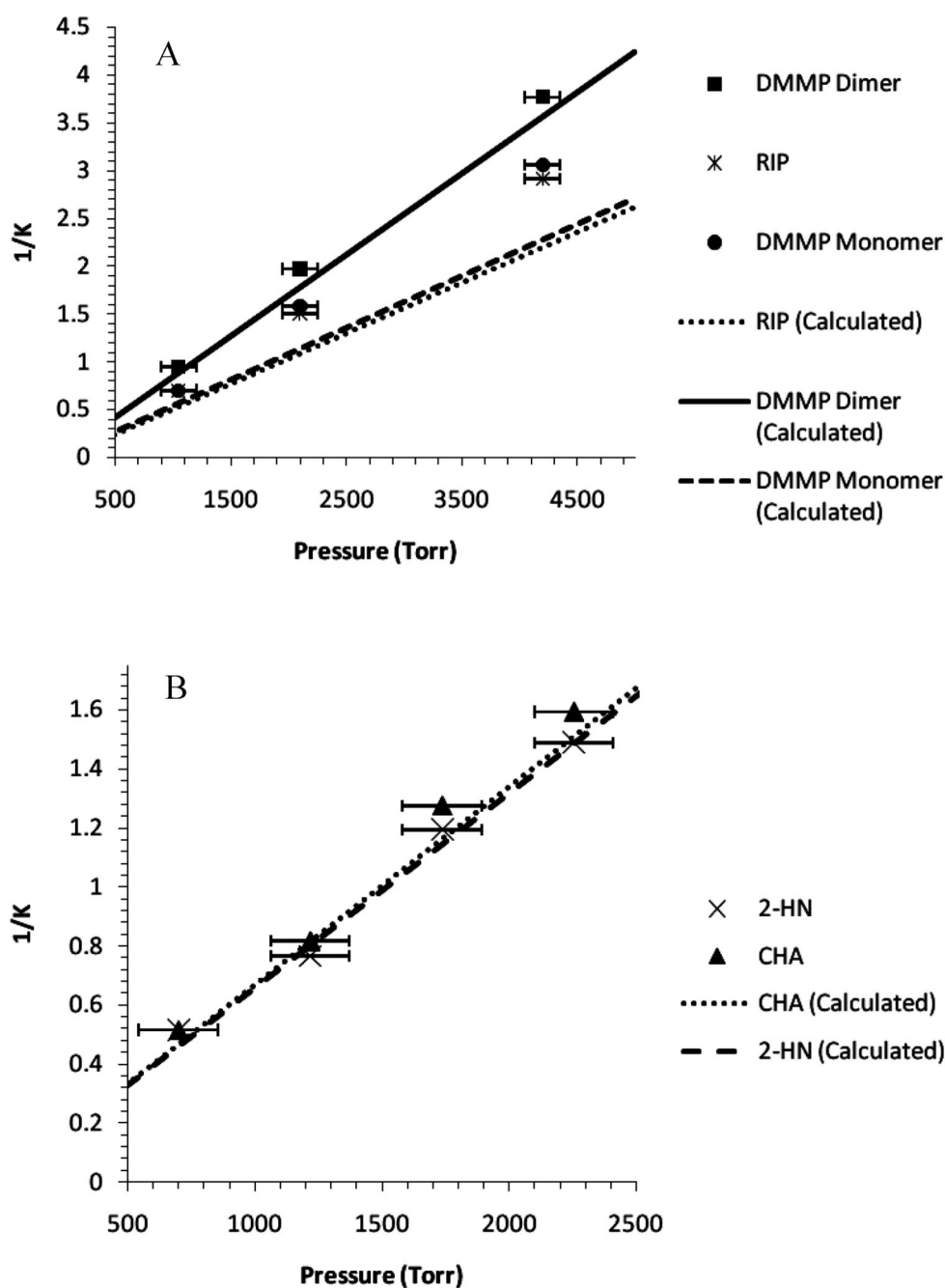


Figure 5.

Calculated and experimental $1/K$ vs pressure. (A) This data was obtained by calculating mobility with collision cross section values of (from top to bottom) 3, 2, 1.5, 1.2, 1.1, and 1. This assumes mobility does not change with pressure. (B) Lines are linear regression best fit of the data, and error bars indicate the ± 3 psi inherent in the pressure gauge used. The differing slopes and intercepts indicate a change in mobility as pressure increases.

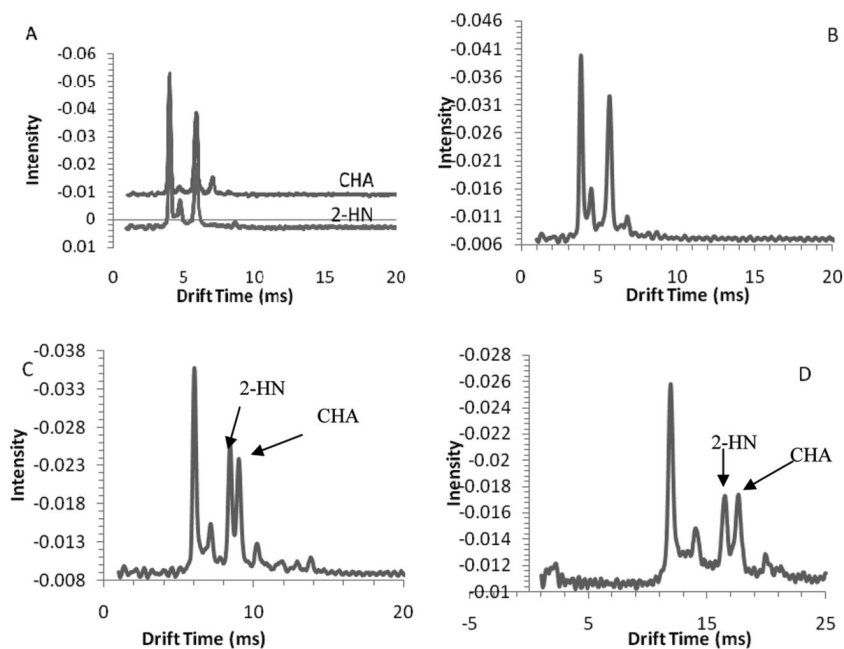


Figure 6.

IMS spectrum of a mixture of CHA and 2-HN. (A) Overlay of CHA and 2-HN at atmospheric pressure. (B) Mixture of CHA and 2-HN at atmospheric pressure. (C) Mixture of CHA and 2-HN at 1279 Torr. (D) Mixture of CHA and 2-HN at 2310 Torr. Reduced mobility values are 1.83 and 1.86 V/cm^2 , respectively (at atmospheric pressure). Increased separation at 2310 Torr is due to CHA drifting slower at high pressure than 2-HN.

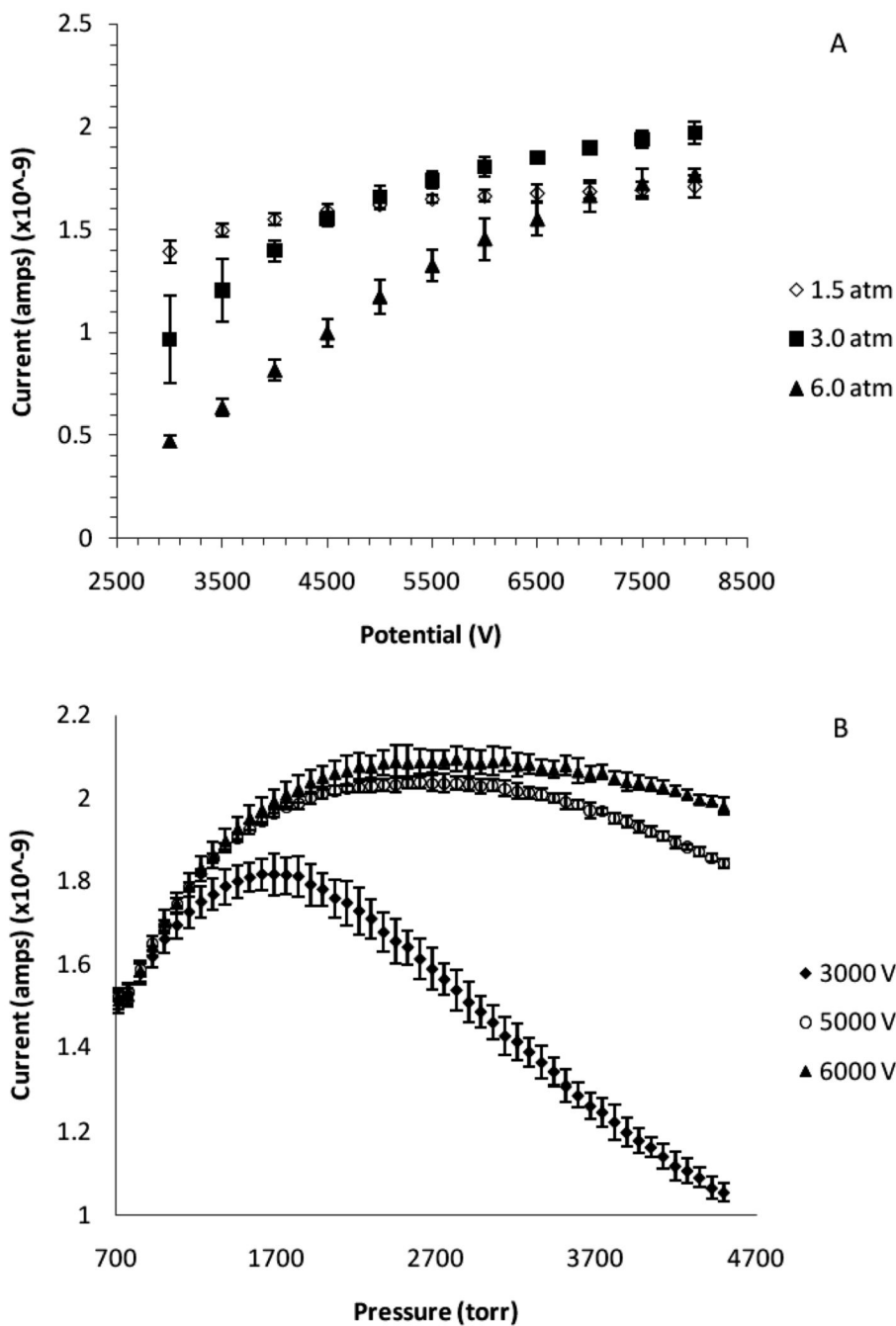
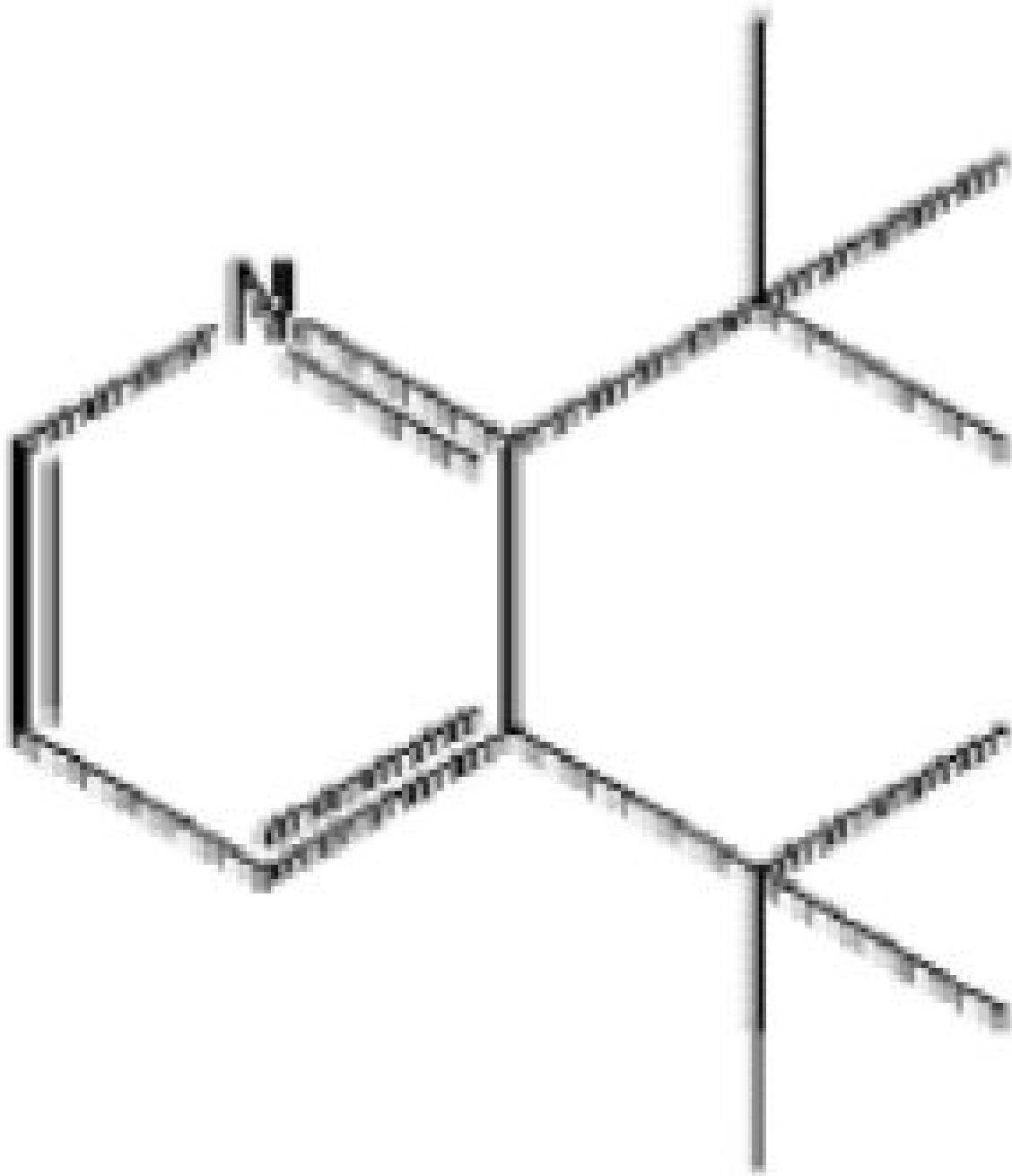


Figure 7.

Total ion current of an IMS in nitrogen, for three different pressures (A) and at three different voltages (B). Error bars indicate 1 standard deviation of triplicate measurements. At each given electric field, there exists an ideal pressure to maximize total ion current reaching the Faraday plate detector.

Table 1Volatile Organic Compounds Used in This Experiment^a

Name	Di- <i>tert</i> -butyl-pyridine	D
Abbreviation	DtBP	methy
K ₀	1.42 ¹	
Structure		

Name	Di- <i>tert</i> -butyl-pyridine	I methy

^a *K*₀ values reported as found in cited literature.