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ARTICLE

Separation of Asparagine, Valine and Tetraethylammonium ions Overlapping in an Ion Mobility Spectrometer by clustering with Methanol introduced as a Modifier in the Buffer Gas

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We introduced methanol into the buffer gas of an ion mobility spectrometer with an electrospray ionization source, coupled to a quadrupole mass spectrometer, and mobilities of selected compounds changed to different extents, depending on their structures, due to formation of slow ion-methanol clusters. This differential change in ion mobility was applied to the baseline separation of a mixture of valine, asparagine, and tetraethylammonium ions (TEA) that overlapped in the mobility spectrum; the drift time of TEA did not increase due to steric hindrance to attachment of methanol molecules to its positive charge by TEA's four ethyl substituents; valine ion extensively clustered because its positive charge is more accessible for clustering with methanol and, therefore, its drift time increased the most, allowing resolution from TEA and asparagine; asparagine had an intermediate increase in drift time due to formation of intramolecular bridges that hid the positive charge from methanol molecules and delocalized it, for which asparagine had less clustering than valine. Other results show that when methanol concentration increased from 0.0 to 6.3 mmol m⁻³, changes in ion mobilities were: -5.0% (valine), -4.2% (phenylalanine), -3.2% (asparagine), -1.5% (glutamine), -1.4% (2,4-lutidine), -0.9% (arginine), -0.3% (2,6-di-tert-butylpyridine, DTBP), -0.2% (tetramethylammonium ion), and 0.0% (other tetraalkylammonium ions). Methanol in the buffer gas produced ion clusters with one to three methanol molecules in compounds with little steric hindrance in the charge as ethanolamine. The introduction of buffer gas modifiers has the potential of a tool for resolution of complex mixtures in ion mobility spectrometry.

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Introduction

Drift tube ion mobility spectrometry (IMS) is a time-of-flight analytical technique that separates gas-phase ions according to their size to charge ratios. IMS is the technique of choice for the detection of illegal substances in airports and customs. To cope with overlapping peaks, one disadvantage of IMS and most analytical techniques, buffer gas modifiers are introduced into the buffer gas of mobility spectrometers to selectively change the ion mobilities and produce their resolution. Buffer gas modifiers are polar volatile compound introduced into the buffer gas that selectively cluster with analytes and change their mobilities depending on the size and steric hindrance on the charge of analyte ions. These clusters have different sizes and spend different times inside the drift tube which may be used to separate analytes that overlap in IMS.¹ Eiceman *et al.* used ketones in the carrier gas to cluster hydrazine and monomethylhydrazine in air, avoiding the interference of ammonia.² Later, Gan and Corino introduced 4-heptanone in the carrier gas to detect alkanolamines in the presence of interferences as ammonia, Freon 22, and diesel fuel vapors.³

Separations with the addition of modifiers to the buffer gas are a potential tool for the resolution of complex mixtures in IMS. Dwivedi *et al.* started introducing modifiers in the buffer gas by the end of the drift tube; they separated enantiomers of amino acids introducing 10 ppm of (S)-2-butanol modifier into the buffer gas using electrospray ionization-ion mobility spectrometry-quadrupole mass spectrometry.⁴ Using this methodology, we demonstrated the formation of analyte:2-butanol modifier clusters and separated the overlapping α -amino acid serine and the drug valinol adding 6.8 mmol m⁻³ of 2-butanol modifier to the buffer gas; this separation was possible because differences in clustering behavior due to the different valinol and serine structures produced different changes in mobility (13.6% for serine and 9.8% for valinol), enough to resolve the peaks of these compounds.⁵ Ethyl lactate, nitrobenzene, and 2-butanol were used as modifiers to separate arginine and phenylalanine in a mobility spectrometer; the separation was possible through the formation of gas-phase intramolecular bridges between the two amine moieties in arginine; the bridges delocalized the ion charge which hindered the attachment of modifier molecules making the arginine ions travel faster the drift tube while there was not such hindrance in phenylalanine; ligand-saturation on the positive ions with modifier molecules occurred at high concentrations of modifier; when saturated, no additional reduction in analyte mobilities occurred when the concentration of modifier was further increased.⁶ The formation of analyte:modifiers clusters, or its absence, was also illustrated for tetraalkylammonium ions, pyridines, and α -amino acids using trifluoromethyl benzyl alcohol, methyl 2-chloropropionate, and water as modifiers; the relative insensitivity of tetraalkylammonium ions and DTBP mobilities to the introduction of 2-butanol into the buffer gas was due to steric hindrance of the four alkyl substituents in tetraalkylammonium ions and the two tert-butyl groups in DTBP; the substituents shielded the nitrogen positive atom of the ion from the attachment of 2-butanol modifier molecules; low buffer gas temperatures of 100 °C produced large reductions in mobilities by increasing ion:2-butanol interactions and formation of clusters; temperatures of 250 °C hindered the formation of clusters with analytes, and no reduction in ion mobility was obtained.⁷ In other work, TEA and valinol were separated introducing nitrobenzene in the buffer gas from 0.0 to 1.0 mmol m⁻³, which increased valinol drift times from 19.49 to 24.08 ms, a 24% increase, while TEA only increased 0.2%; ion clusters with one or two nitrobenzene molecules were found in compounds with little steric hindrance such as ethanolamine.⁸ Theoretical

calculations (B3LYP and the set 6-31G(d,p) with the GAMESS program) were applied to study the interaction of two overlapping analyte ions, caffeine and glucosamine, with a buffer gas modifier, ethyl lactate; it was found that ethyl lactate clustered more to protonated glucosamine than to caffeine and preferentially through the carbonyl group followed by the hydroxyl group, through hydrogen bonds, as expected for most experiments with modifiers.⁹ Puton *et al.* (2008) reviewed the use of modifiers in IMS and other type of additives in the drift tube.¹⁰

The separation of amino acids is important in nutritional assessment, analyses of complex biological samples¹¹ and meteorites,¹² diagnosis of neonatal metabolic disorders¹³ such as phenylketonuria and maple syrup urine disease,^{14,15} and other diseases.¹⁶⁻²⁰ In this work, the differential clustering of methanol with different ions was applied to the baseline separation of a mixture of TEA, asparagine, and valine, whose peaks overlapped in the mobility spectrum, by introducing methanol in the buffer gas.

Experimental

The methodology has been described in detail elsewhere for which only a brief summary is given.^{7,21}

Apparatus

The ion mobility spectrometer was built at Washington State University. Operating conditions routinely used for this instrument were: sample flow, 3 μ l min⁻¹; drift tube length, 25.0 cm; ionization region length, 7.5 cm; ESI voltage, 15.6 kV; voltage at first ring, 12.1 kV; voltage at the gate, 10.80 $\pm$ 0.01 kV; gate closure potential, $\pm$ 40 V; gate pulse width, 0.1 ms; scan time, 35 ms; number of averages for spectrum, 250-1000; pressure, 685-710 Torr; nitrogen flow, 0.94 liter min⁻¹; buffer gas temperature, 150 $\pm$ 2 °C; methanol flow rate, 0.31, 3.1 or 6.3 μ l min⁻¹.

The IMS instrument comprised an electrospray ionization source and a drift tube operated at ambient pressure (690-710 Torr in Pullman, WA, USA). The instrument was operated in single ion monitoring ion mobility spectrometry (SIM-IMS, only ions of a given mass to charge ratio or a range of masses are detected), radiofrequency-only ion mobility spectrometry (IMS, the total ion mobility spectrum is obtained), and mass spectrometry (MS, mass spectra are obtained).

Reagents

Phenylalanine, asparagine, arginine, glutamine, valine, 2,4-dimethyl pyridine (2,4-lutidine), DTBP, methanol, water, acetic acid, tetrabutylammonium (TBA), tetraproylammonium (TPA), tetraethylammonium (TEA), and tetramethylammonium (TMA) chlorides (ACS reagent grade, $\geq$ 97 or 98% purity) were purchased from Sigma Aldrich Chemical Co. (Milwaukee, WI, USA); see Fig. S1 (Electronic supplementary Information) for structures. These analytes were selected due to their different molecular weights and steric properties required to test the effects of size and steric hindrance on the mobilities of these molecules with the introduction of methanol into the buffer gas. Tetraalkylammonium ions were selected because they are ionic compounds, commonly used in IMS as chemical standards, and do not suffer from charge competition in ESI-IMS, for which a high sensitivity is expected for these compounds. DTBP and 2,4-lutidine were selected for these experiments also because they are used as chemical standards.

Analyte solution preparation, analyte identification, and calibration

Solutions of the analytes were prepared at 10 or 50 μM concentrations in ESI solution (47.5 % methanol: 47.5% water: 5% acetic acid) and were continuously injected and ionized by electrospray using a 15.6 kV voltage, a difference of 3.5 kV with respect to the target screen. Methanol, at concentrations up to 6.3 mmol m^{-3} , was introduced into the buffer gas before the buffer gas heater. Analytes were identified by mass spectrometry and comparing their reduced mobilities with those from literature. Additionally, SIM-IMS mode was used on the analytes and their clusters to identify IMS peaks. Reduced mobilities were determined from the known reduced mobilities of standards²² using the equation:

$$K_{o(\text{unknown})} t_{d(\text{unknown})} = t_{d(\text{standard})} K_{o(\text{standard})}$$

where K_0 is the reduced mobility in $\text{cm}^2 \text{V}^{-1} \text{s}^{-1}$ and t_d the drift time in ms. Contamination was detected using 2-4, lutidine and then TBA was used as a chemical standard.⁷

Results and Discussions

The percent changes in reduced mobilities, $\% \Delta K_0$, when 6.3 mmol m^{-3} of methanol was introduced into the buffer gas were: -5.0% (valine), -4.2% (phenylalanine), -3.2% (asparagine), -1.5% (glutamine), -1.4% (2,4-lutidine), -0.9% (arginine), -0.3% (2,6-di-tert-butylpyridine, DTBP), -0.2% (TMA), and 0.0% (TEA, TPA, and TBA). $\% \Delta K_0$ was defined as the percentage difference between K_0 in N_2 buffer gas and K_0 when the mixture methanol modifier/ N_2 was introduced into the drift tube at a given concentration. $\% \Delta K_0$ value for TMA was not statistically different from zero. Only differences greater than 0.5% for TMA and 0.15% for DTBP were significant; these values were calculated from the maximum relative standard deviations of the drift times for TMA and DTBP and are shown in Electronic Supplementary Information.

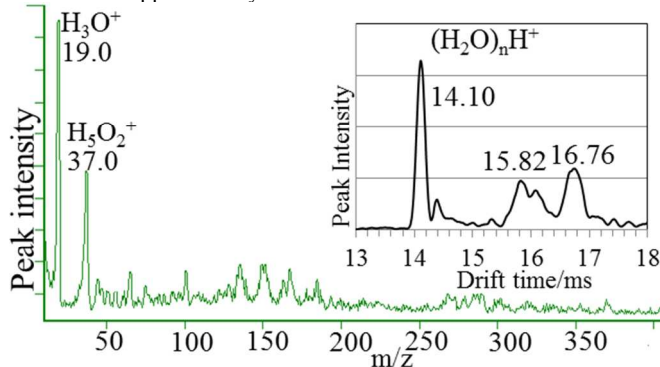


Fig. 1 MS spectra of the ESI solution in nitrogen buffer gas. The inset shows the main reactant ion peak in the IMS spectrum, $(\text{H}_2\text{O})_n\text{H}^+$ ($2.48 \text{ cm}^2 \text{V}^{-1} \text{s}^{-1}$); the peaks after 15 ms may be $(\text{CH}_3\text{OH})_n\text{H}^+$ ions and sodium adducts. The simple MS and IMS spectra indicate a clean instrument without contamination.

The blank spectra of the ESI solvent, before introducing methanol in the buffer gas, is shown in Fig. 1; the mass spectrum of the ESI solvent (obtained in MS mode), shows the main reactant ions peaks at m/z 19 and 37 and the absence of contamination, because peaks after m/z 37 amu are small; contamination control is required to avoid changes in analyte mobilities by clustering with contaminants. The IMS spectra in the inset, obtained in IMS mode, show the main reactant ion peak, $(\text{H}_2\text{O})_n\text{H}^+$, at 14.10 ms ($2.47 \text{ cm}^2 \text{V}^{-1} \text{s}^{-1}$). Other reactant ions after 15 ms may be combinations of water, methanol

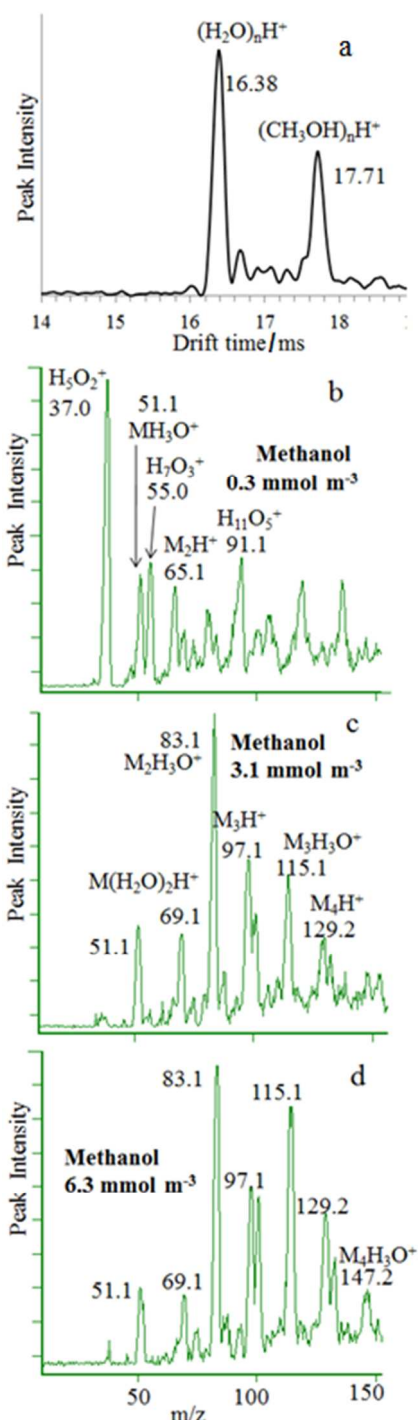


Fig. 2 IMS (a) and MS (b-d) spectra of the ESI solution adding methanol into the buffer gas at 150°C. (a) Methanol 0.31 mmol m^{-3} ; the main reactant ion peaks in the IMS spectrum were $(\text{H}_2\text{O})_n\text{H}^+$ ($2.18 \text{ cm}^2 \text{V}^{-1} \text{s}^{-1}$) and $(\text{CH}_3\text{OH})_n\text{H}^+$ ($2.01 \text{ cm}^2 \text{V}^{-1} \text{s}^{-1}$); the water mobility decreased with respect to those in Fig. 2 due to clustering with methanol. (b) Methanol 0.31 mmol m^{-3} . (c) Methanol 3.1 mmol m^{-3} ; the H_5O_2^+ peak in 2b disappeared due to clustering with methanol and the methanol cluster peaks $\text{M}_2\text{H}_3\text{O}^+$, M_3H^+ , $\text{M}_3\text{H}_3\text{O}^+$, and M_4H^+ appeared. (d) Methanol 6.3 mmol m^{-3} ; $\text{M}_2\text{H}_3\text{O}^+$, M_3H^+ , $\text{M}_3\text{H}_3\text{O}^+$, and M_4H^+ peaks increased with respect to water peaks due to clustering with methanol. Only the regions of the spectra with peaks are shown. M=Methanol.

(from the ESI solvent), nitrogen, and concomitants ions such as ammonium and sodium. All water clusters traveled across the drift tube rapidly interconverting into each other, back and forth, multiple times, coalescing into one single mobility peak at 14.10 ms in the IMS spectrum due to the equilibria:



This IMS peak had a weighted average of the ion mobilities of all water ions, due to the rapid equilibrium in the buffer gas between the clusters.

Fig. 2 shows the solvent spectra when methanol modifier was introduced to the buffer gas; the IMS spectrum shows a large mobility decrease (-12,1%) for the water peak with respect to Fig. 1, from 2.48 to 2.18 $cm^2 V^{-1}s^{-1}$, due to clustering equilibria with methanol; this large decrease (the largest found in this work) was due to the small mass of water: the smaller the ion the larger the mobility decrease when a modifier attaches.⁵ The mass spectra show that water cluster peaks disappeared due to a complete clustering with methanol modifier; also, due to attachment of methanol molecules: i) the peaks were shifting to higher masses and ii) the clusters had an increasing number of methanol molecules as the methanol concentration increased in the buffer gas.

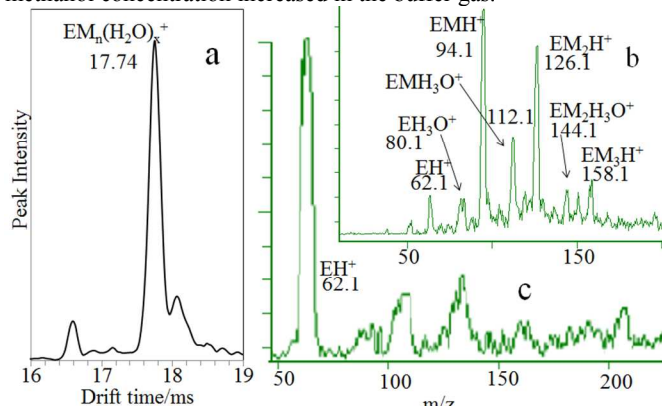
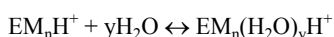
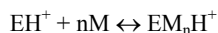


Fig. 3 IMS (a) and MS spectra (b) of a 100- μM ethanolamine, E, solution when 6.3 $mmol m^{-3}$ of methanol, M, was introduced into the buffer gas. (a) Ethanolamine cluster ions, EMH^+ , EM_2H^+ , EM_3H^+ , and EMH_3O^+ , coalesced at 17.74 ms (2.01 $cm^2 V^{-1}s^{-1}$) into a single peak due to the equilibrium of these ions in the drift tube. (b) Up to three methanol molecules attached to ethanolamine ions. The MS spectrum of ethanolamine in pure N_2 buffer gas is shown in (c) for comparison. The ion mobility spectrum for ethanolamine without introduction of methanol is shown in fig. 4A, reference 8.

Fig. 3 shows the IMS and MS spectra of ethanolamine when methanol was introduced into the buffer gas. Fig. 3b shows ethanolamine:methanol, ethanolamine:methanol:water, and ethanolamine:water clusters in the mass spectrum and a protonated ethanolamine peak largely reduced, due to clustering with methanol; however, only a single peak appeared in the IMS spectrum for all EH_3O^+ , EM_nH^+ and $EM_nH_3O^+$ ions indicating that they were in equilibrium in the buffer gas; $EM_2H_3O^+$ and EH^+ were not tested but they should be in equilibrium with the other clusters. All EH^+ , EM_nH^+ and $EM_nH_3O^+$ clusters probably traveled the drift tube continuously interconverting between each other as in the following equilibria:



Other equilibria might be present. As before, this single IMS peak, where the ethanolamine species coalesced, had a weighted average of the mobilities of the ethanolamine clusters and ions, due to the fast equilibrium in the drift tube between EH^+ and the clusters. Ethanolamine clustered with up to three methanol molecules (Fig. 3); clusters with up to three modifier molecules have been found before, one molecule for every partially positive charged hydrogen in the charged nitrogen,^{1,5-7} what we call the *Bollan-Eiceman rule*, not valid for small modifiers such as water.⁷ A result of these equilibria is that the mobility of analytes decrease when modifiers are injected in the drift tube.¹⁻⁸ Theoretical studies have shown that analytes attach by bonds between the positively charged hydrogens in the amine group and the carbonyl and hydroxyl groups in the modifiers.⁹

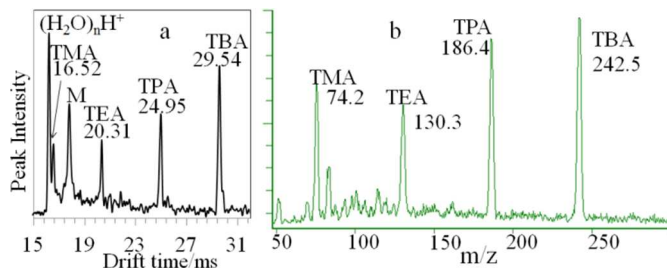


Fig. 4 (a) IMS and (b) MS spectra of 100- μM solutions of tetraalkylammonium ions when 3.1 $mmol m^{-3}$ of methanol were added to the buffer gas. The four bulky substituents in the positive nitrogen of tetraalkylammonium ions deterred clustering; therefore, methanol cluster peaks did not form; well-defined IMS peaks indicate that tetraalkylammonium ions did not fragment or cluster in the drift tube. W and M are the water and methanol cluster peaks, respectively.

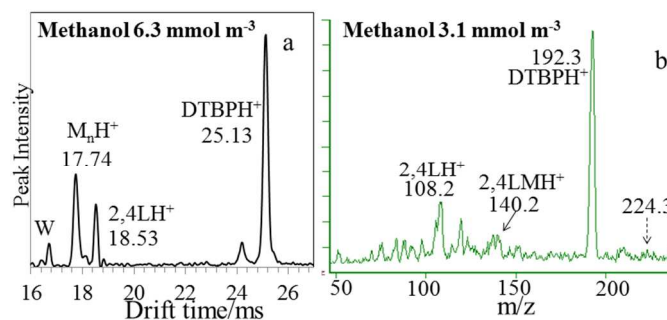


Fig. 5 IMS (a) and MS spectra (b) of a 10- μM mixture of pyridines adding 6.3 $mmol m^{-3}$ (a) or 3.1 $mmol m^{-3}$ (b) of methanol modifier into the buffer gas. 2,4LH⁺ appears at 18.53 ms (1.92 $cm^2 V^{-1}s^{-1}$) and DTBPH⁺ at 25.13 ms (1.42 $cm^2 V^{-1}s^{-1}$) in the mobility spectrum. Clustering between methanol and DTBPH⁺ ions was deterred by the two bulky tertbutyl substituents on DTBP: the DTBPH⁺:methanol cluster peak at m/z 224.3 did not appear but 2,4LH⁺ showed a small cluster peak, 2,4LMH⁺, at m/z 140.2. Ion mobility information for ethanolamine, tetraalkylammonium ions, DTBP and 2,4-lutidine without introduction of methanol is shown in Electronic Supplementary Information.

Tetraalkylammonium ions did not form clusters with methanol (Fig. 4) because four bulky alkyl substituents attached to the positive nitrogen hindered clustering of methanol molecules; therefore, the MS spectrum did not show methanol clusters at m/z 106.2 ($TMAM^+$), 162.3 ($TEAM^+$), 218.4 ($TPAM^+$), and 274.5 ($TBAM^+$), the same behavior reported before for tetraalkylammonium ions with other modifiers.^{5,7} Delocalization of the positive charge by these bulky substituents also limited clustering.^{23,24}

To compare the behavior of clustering ($2,4\text{LH}^+$) and non-clustering compounds (DTBP), a mixture of pyridines was analyzed when methanol was added to the buffer gas. The two bulky tert-butyl substituents around the positive charge on DTBP ions at positions 2 and 6 on the ring hindered clustering with methanol (Fig. 5); consequently, there was not a DTBPMH^+ cluster peak at m/z 224.3 in the MS spectrum; however, $2,4\text{LH}^+$ formed the cluster $2,4\text{LMH}^+$ at m/z 140.2 whose drift time coincided with that of $2,4\text{LH}^+$ which demonstrates that it was a cluster of this pyridine; clustering in $2,4\text{LH}^+$ and not in DTBP was a result of less steric hindrance due to the presence of only small methyl substituents in 2,4-lutidine which are farther away from the positive charge than in the case of DTBP. The drift times of the $2,4\text{LH}^+$ and $2,4\text{LMH}^+$ coincided by a type of equilibria as those shown above. In general, when the ion mobility of compounds was not affected or only slightly affected by the addition of methanol in the buffer gas (atenolol –see Fig. S2 Electronic supplementary Information -, tetraalkylammonium ions, DTBP, and arginine), they did not show clusters in the mass spectrum; when the ion mobilities decreased (2,4-lutidine, ethanolamine, phenylalanine, and valine), clusters with methanol were observed in the mass spectra in a number and intensity proportional to $\% \Delta K_0$. Only one methanol molecule attached to 2,4-lutidine according to the *Bollan-Eiceman rule*.

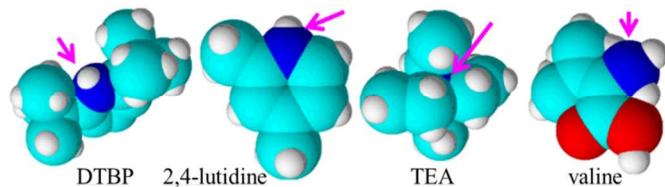


Fig. 6 3D structures of DTBP, 2,4-lutidine, TEA and valine. The positive charge, in the nitrogen atom, is sterically hindered by the alkyl substituents in DTBP and TEA, slightly hindered in 2,4-lutidine and little hindered in valine. The structures were generated with Chem3D Pro 11.0 (PerkinElmer, Waltham, MA, USA). Hydrogen: gray; Carbon: light blue; Nitrogen: dark blue; Oxygen: red. The arrows show the positively charged nitrogen.

Fig. 6 shows four tridimensional structures to explain the steric hindrance in non-clustering compounds such as DTBP and TEA; this Figure illustrates how the positive charge in the nitrogen atom is sterically hindered by bulky alkyl substituents in TEA and DTBP and is more accessible in valine and 2,4-L. Fig. 7 plots the mobility decrease of the analytes when methanol was introduced in the buffer gas; this figure shows that the largest mobility decrease was obtained at the beginning, with the first introduction of methanol, for valine, phenylalanine, asparagine, and 2,4-lutidine and that a plateau was obtained with the following increases of methanol concentration. This plateau was due to a steric limitation for the attachment of additional methanol molecules when the positive charge of analytes was becoming saturated with methanol.⁶ Changes in mobilities are influenced by steric hindrance on the charge and the size of ions (proportional to mass). To explain the origin of changes in mobilities in Fig. 7 ions must be divided in groups to be compared: diamines, tetraalkylammonium ions, and ions with steric hindrance on the charge or “without” it. The order of mobility decrease in diamines, which form intramolecular bridges with a non-clustering effect explained above, followed the mass of the molecule: Arginine 174.2 amu < Glutamine 146.2 amu < Asparagine 132.1 amu; the same was true for tetraalkylammonium ions (TBA 242.5 amu, TPA 186.4 amu, TEA 130.3 amu < TMA 74.2 amu), ions “without” steric hindrance (Phenylalanine 165.2 amu < Valine 117.1 amu) and ions with steric hindrance on the charge (DTBP 191.3 amu < 2,4-Lutidine 107.2 amu).

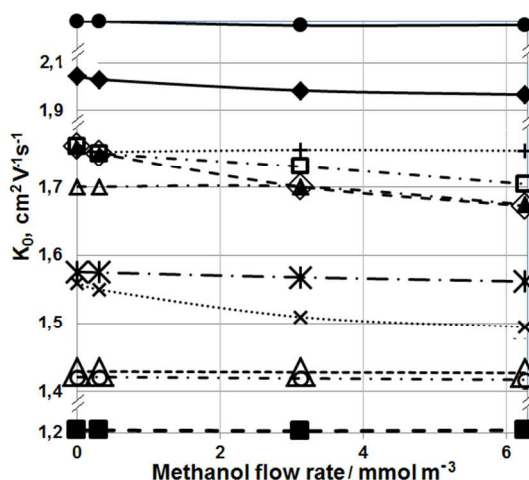


Fig. 7 Effect of methanol concentration in the buffer gas in the mobility of ions at 150°C. TMA (●), 2,4-lutidine (◆), TEA (+), asparagine (□), valine (◇), glutamine (▲), arginine (*), phenylalanine (x), TPA (Δ), DTBP (○), TBA (■); the formation of analyte:methanol clusters decreased the reduced mobilities of 2,4-lutidine and amino acids as methanol concentration increased in the buffer gas. The mobility values for this figure are shown in Table S1 (Electronic Supplementary Information).

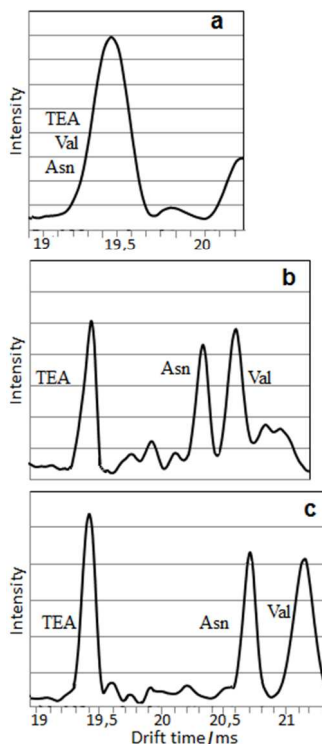


Fig. 8 Separation of TEA, asparagine (Asn), and valine (Val) ions by addition of methanol modifier to the buffer gas in a mobility spectrometer; concentrations of (a) 0.0, (b) 3.1 and (c) 6.3 mmol m^{-3} of methanol were used; the drift time of TEA did not change due to steric hindrance to modifier attachment caused by the four ethyl substituents. Valine extensively clustered and, therefore, its drift time increased from 19.49 ms to 21.16 ms, allowing the resolution from TEA and Asn.

The differential clustering of methanol with different ions was applied to the separation of a 100 μM mixture of TEA, asparagine, and valine (Fig. 8) by introducing methanol in the buffer gas. When methanol was not added to the N_2 buffer gas (a), the peaks of these compounds overlapped at 19.4 ms. When methanol concentration increased to 3.1 mmol m^{-3} (b), the drift time of asparagine increased to 20.33 ms and that of valine to 20.61 ms. With 6.3 mmol m^{-3} of methanol (c), the drift time of asparagine reached 20.60 ms and that of valine 21.16 ms which yielded a baseline separation of these compounds. However, the drift time of TEA did not change with the increasing concentration of methanol due to steric hindrance to attachment of methanol molecules caused by the four bulky ethyl substituents. Valine ion extensively clustered because its positive charge is more accessible to methanol for clustering (Fig. 7) and, therefore, it was the ion whose drift time increased the most, from 19.49 ms to 21.16 ms, allowing the resolution from TEA and asparagine. Asparagine had an intermediate increase in drift time, between those of TEA and valine, because it has a molecular weight larger than that of valine for which its mobility was less affected by attachment of modifier molecules than valine as has been demonstrated before;⁵ additionally, asparagine is a diamine that may form intermolecular bridges that hide the positive charge from methanol modifier molecules and delocalize it²⁴ for which there was less clustering to this amino acid. Separation of amino acids is important in analyses such as biological samples,¹¹ and meteorites,¹² especially because IMS has been integrated to space exploration and proposed for space search of amino acids.²⁵

Conclusions

The resolution of overlapping compounds can be obtained in IMS using costly and cumbersome instrumental alternatives such as longer drift tubes or increasing drift tube voltages or through an inexpensive choice as adding modifiers to the buffer gas of mobility spectrometers. We separated a mixture of TEA, asparagine, and valine, which overlapped in the IMS spectrum, by applying the different clustering behaviors of these analytes with methanol. Methanol, a modifier with a low molecular weight, produced a small change in the mobility of ions when compared to other modifiers⁵ and similar to water or ammonia, other low molecular weight modifiers.^{7,26}

Electronic Supplementary Information (ESI) available: $\% \Delta K_0$ calculation. Ion mobility information for ethanolamine, tetraalkylammonium ions, DTBP and 2,4-lutidine without introduction of methanol. Table S1 Change in analytes mobilities when methanol was introduced into the buffer gas at different concentrations. Fig. S1 Structure of compounds used in this work. Fig. S2 IMS and mass spectrum of atenolol when methanol was introduced in the buffer gas.

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