International Journal for Ion Mobility Spectrometry
https://doi.org/10.1007/s12127-019-00246-y

ORIGINAL RESEARCH

Influence of gas modifiers on the TIMS analysis of familiar explosives

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Received: 12 February 2019 / Revised: 22 February 2019 / Accepted: 22 February 2019

Abstract

In the present work, we studied the influence of the bath composition (e.g., organic modifiers) on the mobility resolving power, resolution, and lifetime of familiar explosives during trapped ion mobility spectrometry (TIMS). Experimental results showed the dependence of the mobility with the organic modifiers (mass and size) for the case of TIMS-MS. Different from trends observed in drift tube like IMS devices, no correlation between the mobility resolving power and resolution in TIMS was observed with the bath gas composition (e.g., air, air + methanol, air +2-propanol, and air + acetone). Time decay plots showed that common explosives with adduct complexes signal decrease over time as a function of the trapping time, without any significant improvement with the addition of the organic modifiers. Theoretical calculation of potential clustering and dissociation pathways supported the time decay findings since no major energetic differences between the pathways were observed as a function of the organic modifiers. Our findings suggest that beside the size of the collision partner, there are specific intermolecular dynamics that drive the trapping behavior of familiar explosives.

Keywords Trapped ion mobility mass spectrometry · Common explosives · Organic modifiers

Introduction

Ion mobility spectrometry (IM) is based on the separation of charged species due to differences in their mobility under the influence of an electric field in a bath gas. In a conventional drift tube, the separation of chemical species results from numerous, near-thermal collision between analyte ions and a chemically-inert drift gas. The bath gas composition affects the separation efficiency. For example, in high-field asymmetric waveform ion mobility spectrometry (FAIMS) and differential mobility spectrometry (DMS), the carrier gas composition is commonly altered to increase the resolution for closely spaced analytes. For conventional low field IM techniques such as drift tube (DTIMS) this practice is also utilized. Hill and coworkers demonstrated enhanced analyte selectivity on an ambient pressure drift tube when varying the drift gas from low to high polarizability (helium, nitrogen, argon, and carbon dioxide) [1–4]. Yost and coworkers demonstrated increased resolving power for several isobaric steroids, analyzed in a reduced-pressure drift tube instrument, using CO2 as the drift gas. Fjeldsted and coworkers investigated the separation of isomeric carbohydrates, fluoroalkyl phosphazenes, and various small molecule pesticides under various drift gases (He, N_2, Ar, CO_2, N_2O, SF_6). In addition, gas modifiers have been used to increase the analytical power of IMS by increasing the size of the collision partner or inducing higher order multi-pole interactions, [5–10].

We have recently reported on the effect of bath gas modifiers on the conformational space of peptides and heme proteins during trapped ion mobility spectrometry (TIMS). [11, 12] Different from other IMS separations, in the case of TIMS, ion are held stationary under the influence of an electric field that compensated a drift force induced by a moving gas. [1–3, 13, 14] In TIMS, the increase in size of the collision partner size leads to a larger electric field require to trap the ions and subsequently an increase in the resolution. However, since recent experiments showed, the interaction between charge species and bath gas modifiers can lead to the formation of meta-stable complexes, that can lead to conformational rearrangement. [11]

In the present study we further investigate the role of bath gas modifiers during TIMS experiments for the case of familiar explosives. In particular, molecular ion species formed by

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Electronic supplementary material The online version of this article (https://doi.org/10.1007/s12127-019-00246-y) contains supplementary material, which is available to authorized users.

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HMX and PETN are studied as a function of the bath gas composition and trapping time. Previous studies have also shown that in the case of the molecular ion of familiar explosives, the ion abundances decreases with the trapping time. [4] Several dissociation pathways are considered theoretically to understand the dissociation reactions.

Experimental methods

Materials and reagents Individual standards of 3-nitrooxy-2,2-bis-(nitrooxymethyl) propyl nitrate (PETN) and octahydro-1,3,5,7-tetranitro-1,3,5,7-tetrazocine (HMX) were obtained from AccuStandard (New Haven, CT) and used as received. Ammonium chloride, ammonium formate, and ammonium nitrate salts and chromatography grade water, methanol and acetonitrile solvents were obtained from Fisher Scientific (Suwanee, GA) and used as received. HMX was dissolved in 1: 1 water: methanol *v/v* ratio, and PETN was dissolved in 1: 1: 1 water: methanol: acetonitrile *v*/v ratio to a final concentration of 1 μM. Each ammonium salt containing solution was prepared separately and added to each explosive solution to a final concentration of 10 mM of ammonium salt. A Tuning Mix calibration standard (G24221A) was obtained from Agilent Technologies (Santa Clara, CA) and used as received.

Trapped ion mobility spectrometry – Mass spectrometry analysis (TIMS-MS) Details regarding the TIMS operation and specifics compared to traditional IMS can be found elsewhere. [1–3, 13, 14] Briefly, mobility separation in TIMS is based on holding the ions stationary against a moving gas using an electric field. The separation in a TIMS device can be described in the center of the mass reference frame using the same principles as in a conventional IMS drift tube. [15] Since mobility separation is related to the number of ion-neutral collisions (or drift time in traditional drift tube cells), the mobility separation in a TIMS device depends on the bath gas drift velocity, ion confinement and ion elution parameters. The reduced mobility, *K*, of an ion in a TIMS cell is described by:

$$K = \frac{V_g}{E} \approx \frac{A}{(V_{elution} - V_{out})}$$

where v_g and E are the velocity of the gas and the applied electric field across the TIMS analyzer region. $V_{elution}$ is the voltage when the ions elute in the V_{ramp} sweep and V_{out} is the voltage applied at the end of the TIMS analyzer region. A is a constant that relates to the velocity of the bath gas and electric field axial distribution and can be calculated using mobility standards. Notice that, once A is calculated for a given bath gas (e.g., Tuning Mix as calibrants for N_2 bath gas), it will not change when using gas modifiers since the pressure difference between P1 and P2 are kept the same (see details in Fig. 1).

A custom-built, pulled capillary nanoESI source was utilized for all the experiments. Quartz glass capillaries (O.D.: 1.0 mm and I.D.: 0.70 mm) were pulled utilizing a P-2000 micropipette laser puller (Sutter Instruments, Novato, CA) and loaded with 10 μL aliquot of the sample solution. A typical nanoESI source voltage of ± 600–1200 V was applied between the pulled capillary tips and the TIMS-MS instrument inlet. Ions were introduced via a stainless-steel tube (1/16 × 0.020″, IDEX Health Science, Oak Harbor, WA) held at room temperature into the TIMS cell. It should be noted that all solvent studies were performed with nitrogen as the bath gas.

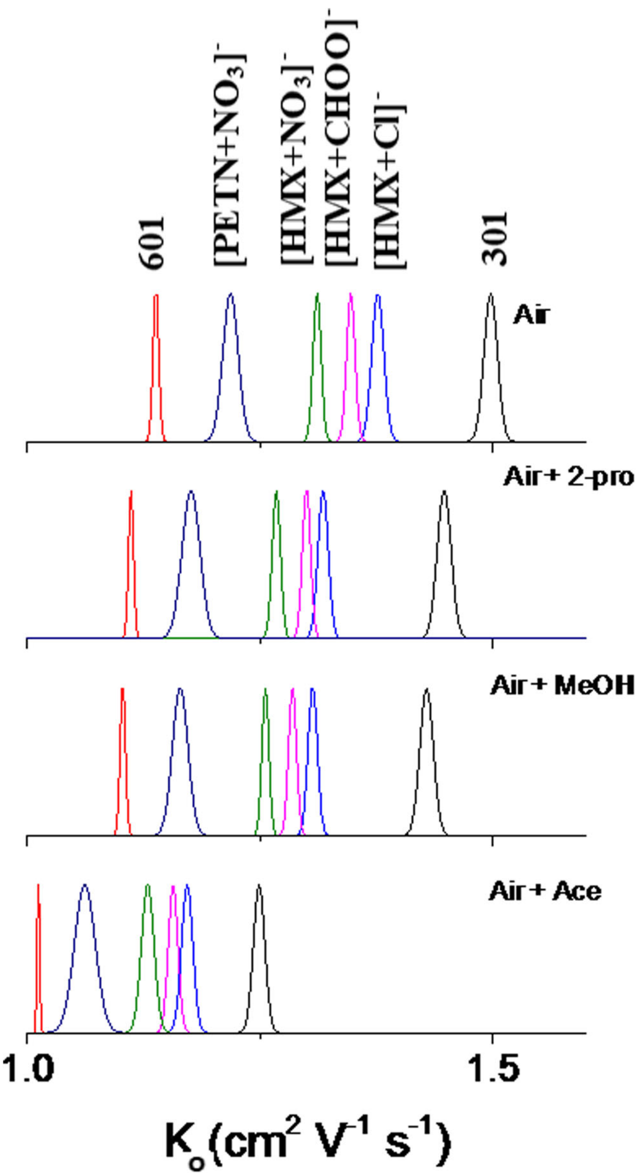

Fig. 1 Typical reduced mobility profiles as a function of the bath gas composition for Tuning Mix standards (301 and 601 m/z) and four familiar explosives molecular ions (HMX + Cl, HMX + CHOO, HMX + NO_3 and PETN + NO_3)

Table 1 Mobility and resolving power for familiar explosives molecular ions as a function of the bath composition

	Air			Air + MeOH			Air +2-propanol			Air + Acetone		
	K	ΔK	R	K	ΔK	R	K	ΔK	R	K	ΔK	R
$[HMX + Cl]^-$	1.376	0.012	107	1.306	0.009	133	1.317	0.011	119	1.171	0.012	97
$[HMX + CHOO]^-$	1.347	0.008	150	1.284	0.008	152	1.299	0.00869	149	1.156	0.010	114
$[HMX + NO_3]^-$	1.310	0.008	153	1.255	0.007	168	1.267	0.00877	144	1.129	0.013	84
$[PETN+NO_3]^-$	1.217	0.016	74	1.163	0.016	70	1.175	0.01924	61	1.061	0.022	47
301	1.497	0.014	104	1.428	0.014	100	1.447	0.01485	97	1.248	0.012	102
601	1.137	0.006	187	1.102	0.005	194	1.111	0.0067	165	1.011	0.002	354

Mobility calibration was performed using the Tuning Mix calibration standard (G24221A, Agilent Technologies, Santa Clara, CA) in positive ion mode (e.g., $m/z = 322$, $K_0 = 1.376\ cm^2\ V^{-1}\ s^{-1}$ and $m/z = 622$, $K_0 = 1.013\ cm^2\ V^{-1}\ s^{-1}$). [3] The A constant obtained in positive mode was used for negative ion mode mobility calculations. TIMS operation was controlled using in-house software, written in National Instruments Lab VIEW, and synchronized with the maXis Impact Q-ToF acquisition program. [13, 14] Gas modifiers were introduced at the entrance of the TIMS cell via vaporization of the respective solvents (e.g., methanol, 2-propanl or acetone) at a ratio of 2:1 air: air modified mix (scheme shown in Fig. S1); this method was preferred to guarantee reproducibility across the experiments and simplified mobility calibration (i.e., constant gas flow in the TIMS analyzer). Room humidity was kept at 60% during all the experiments. For simplified mobility calibration, the gas velocity was kept constant in all experiments (P1 and P2 values). For TIMS, the resolving power (R) and resolution (r) are defined as R = K/w and r = 1.18*(K2 − K1)/(w1 + w2), respectively, where w is the full peak width at half-maximum (w).

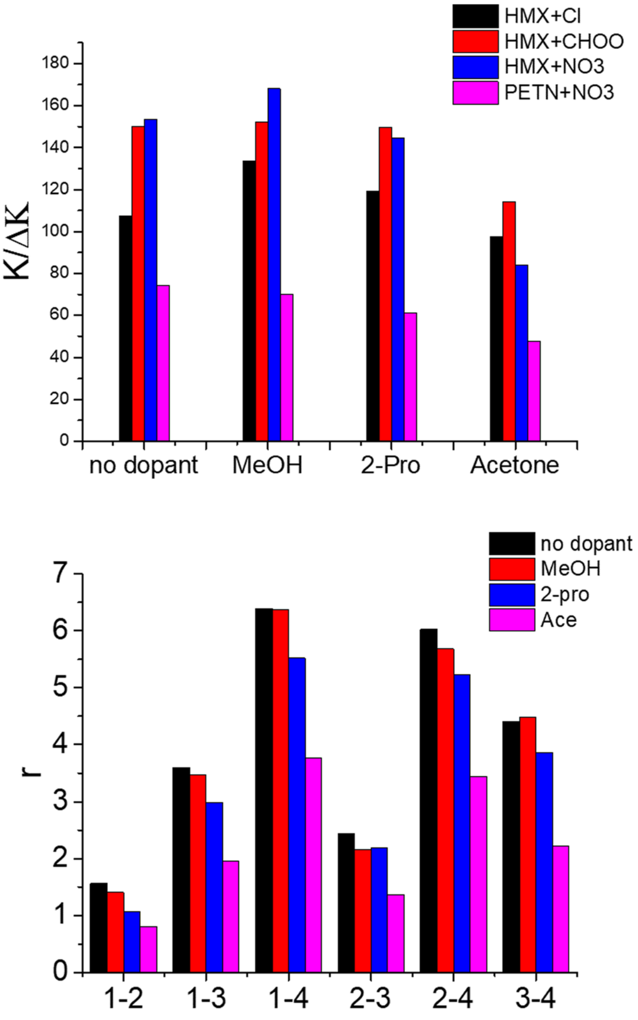

Fig. 2 Dependence of the mobility resolving power and the mobility resolution as a function of the bath gas composition. For the resolution calculation, the following nomenclature was used 1-HMX + Cl, 2-HMX + CHOO, 3-HMX + NO_3 and 4-PETN + NO_3 (more details in Table 2)

Theoretical calculations

Candidate structures were generated, and energy minimized for the parent and characteristic complexes at the DFT/B3LYP/6–31 + g(d) level using the Gaussian 09 software [16]. Vibrational frequencies were calculated to guarantee that the optimized structures correspond to real minima in the energy space.

Results and discussion

The nESI-TIMS-MS analysis of HMX and PETN in the presence of various salts resulted in the observation of mainly four adducts species: 1-HMX + Cl, 2- HMX + CHOO, 3-HMX + NO_3 and 4-PETN + NO_3. While these species are easily resolved in the 2D IMS-MS space, our discussion is based on the effect of the bath gas composition on the resolving power, resolution and lifetime as a function of the trapping time. Inspection of Fig. 1 shows that in the TIMS trapping experiments, the increase in size

Table 2 Mobility resolution for familiar explosives molecular ions as a function of the bath composition

	Bath Gas Modifier			
Molecular species	Air	Air + MeOH	Air +2-propanol	Air + Acetone
1–2	1.56	1.40	1.06	0.80
1–3	3.59	3.47	2.99	1.96
1–4	6.39	6.36	5.52	3.77
2–3	2.44	2.15	2.18	1.36
2–4	6.02	5.68	5.23	3.44
3–4	4.40	4.48	3.85	2.22
301–601	20.7	19.4	18.4	18.5

For the resolution calculation, the following nomenclature was used 1-HMX + Cl, 2- HMX + CHOO, 3-HMX + NO_3 and 4-PETN + NO_3

of the collision partner leads to an increase of electric field require to hold the ions for a constant bath gas velocity. That is, an effective change in the mobility of the ions as a function of the size of the collision partner (see Fig. 1) is observed. In the case

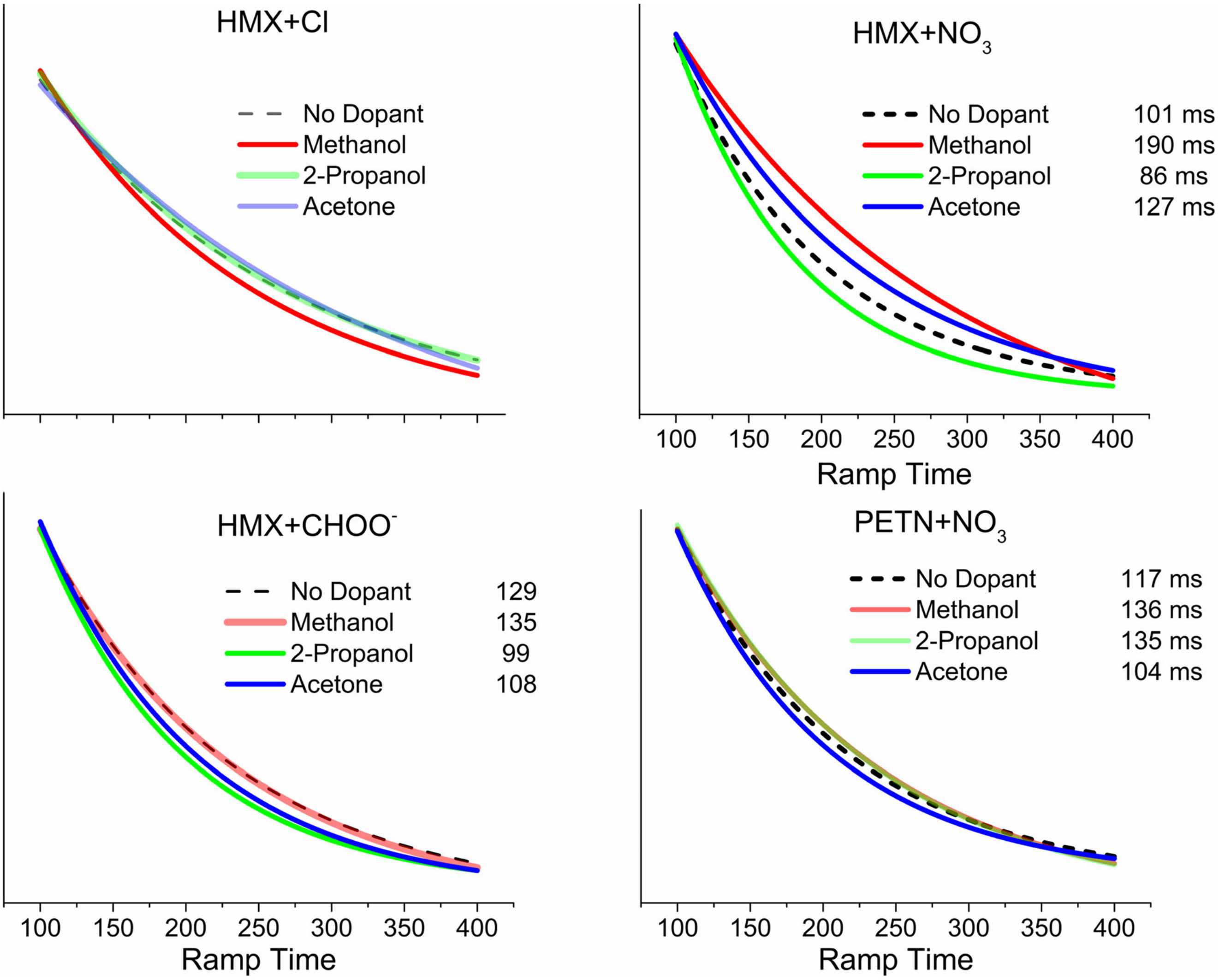

Fig. 3 Relative abundance of familiar explosive molecular ions as a function of the trapping time and bath gas compositions: (**a**) HMX + Cl, (**b**) HMX + CHOO, (**c**) HMX + NO_3 and (**d**) PETN + NO_3

Table 3 Time decays of familiar explosive molecular ions as a function of the trapping time and bath gas composition

	Air τ (ms)	Air + MeOH τ (ms)	Air +2-propanol τ (ms)	Air + Acetone τ (ms)
$[HMX + Cl]^-$	172	150	170	228
$[HMX + CHOO]^-$	129	135	99	108
$[HMX + NO_3]^-$	101	190	86	127
$[PETN+NO_3]^-$	117	136	135	104

considered, as the bath composition changes from air to air doped with methanol, 2-propanol and acetone, a reduction in mobility (or increase in CCS) is observed for all the familiar explosive complexes (see Table 1).

The dependence of the resolution and resolving power as a function of the bath composition is summarized in Fig. 2 and Tables 1 and 2. Differences in resolution are observed as a function on the adduct form and of the bath gas composition. We attribute these differences to the flexibility of the different adduct forms in the gas-phase and to the interaction of the molecular complexes with the bath gas dopants. In the case of resolution, a significant decrease (up to 2x fold) in resolution is observed for all the familiar explosives in the presence of the bath gas dopants (see Fig. 2). Under the same conditions, the resolution of the tuning mix ions (301 and 601 m/z) only showed minor variations with the bath gas composition (see Table 2). These effects suggest that there is a strong interaction between the familiar explosive complexes and the residual bath gas molecules.

The analysis of the relative abundance of the familiar explosives as a function of the trapping time is summarized in Fig. 3 and Table 3. Only small changes in the lifetimes are observed in the stability curves of the familiar explosives in the presence of the dopants. These observations are in good agreement with the theoretical clustering and dissociation reactions presented in Table 4 and Fig. S2. In our previous report [4], we suggested that the familiar explosive complex stability could be driven by bath gas impurities, where bath gas molecules could act as scavengers of the adducted anions. Inspection of Fig. 3 and Tables 3 and 4 suggest that the presence of water and/or other organic molecules does not changes dramatically the energy for clustering and dissociation of the complexes. However, the larger the number of clustering molecules, the higher the stability of the complex. If the clustering mechanism involves several neutral molecules, a higher stability of the complex can be reached in a clustering / declustering dynamics. This proposed mechanism will also explain the trends in resolving power and resolution shown in Figs. 1 and 2 for the case of the familiar explosives, where the increase in size of the bath gas dopant did not lead to an increase in resolution. The comparison between the different adducts for the case of HMX in the presence of different bath gas dopants suggested that beside the size, there are specific intermolecular dynamics that drive the trapping behavior.

Table 4 Energies associated to adduct formation and dissociation in the presence of water, methanol, acetone and 2-propanol molecules for $[HMX + X]^-$ where X = Cl / CHOO /NO_3

$HMX+[X]^- + H_2O$	→	$[HMX + X]^- + H_2O$ −44/−46/−38 kJ/mol	→	$[HMX + X + H_2O]^-$ −53/−56/−46 kJ/mol	→	$HMX+[X + H_2O]^-$ −14/−16/−14 kJ/mol
Methanol				$[HMX + X + CH_3OH]^-$ −53/−57/−47 kJ/mol		$HMX+[X + CH_3OH]^-$ −14/−16/−13 kJ/mol
Acetone				$[HMX + X+(CH_3)_2CO]^-$ −52/−54/−44 kJ/mol		$HMX+[X+(CH_3)_2CO]^-$ −14/−15/−14 kJ/mol
2-Propanol				$[HMX + X+(CH_3CHOHCH_3)]^-$ −53/−56/−45 kJ/mol		$HMX+[X+(CH_3CHOHCH_3)]^-$ −15/−17/−14 kJ/mol
$HMX+[X]^- + (H_2O)_2$	→	$[HMX + X]^- + (H_2O)_2$ −44/−46/−38 kJ/mol	→	$[HMX + X+(H_2O)_2]^-$ −60/−65/−56 kJ/mol	→	$HMX+[X+(H_2O)_2]^-$ −25/−31/−25 kJ/mol
Methanol				$[HMX + X+(CH_3OH)_2]^-$ −61/−66/−55 kJ/mol		$HMX+[X+(CH_3OH)_2]^-$ −27/−30/−25 kJ/mol
Acetone				$[HMX + X+((CH_3)_2CO)_2]^-$ −58/−60/−55 kJ/mol		$HMX+ [X+((CH_3)_2CO)_2]^-$ −25/−25/−22 kJ/mol
2-Propanol				$[HMX + X+(CH_3CHOHCH_3)]^-$ −60/−65/−54 kJ/mol		$[HMX + X+(CH_3CHOHCH_3)]^-$ −27/−31/−25 kJ/mol

Conclusions

A systematic study of the influence of the bath gas composition using organic modifiers on the analytical performance of trapped IMS (TIMS) is described for two familiar explosives: HMX and PETN. In the presence of salts in the starting solution, the nESI process leads to the formation of single charged characteristic molecular complexes of the form: 1-HMX + Cl, 2- HMX + CHOO, 3-HMX + NO_3 and 4-PETN + NO_3. Experimental results show the dependence of the mobility with the organic modifiers (mass and size). Different from trends observed in drift tube like IMS devices with the use of bath gases of varying size, no direct correlation and no significant improvement in mobility resolving power and resolution is observed under the conditions considered (e.g., air, air + methanol, air +2-propanol, and air + acetone). Time decay plots showed that common explosives with adduct complexes signal decrease over time as a function of the trapping time, without any significant improvement with the addition of the organic modifiers. Theoretical calculation of potential dissociation pathways showed that there are minor energetic differences between the processes considered with the organic modifiers in the presence of water contaminants. However, if the clustering mechanism involves several neutral molecules, a higher stability of the complex can be reached in a clustering / de-clustering dynamics. This proposed mechanism will also explain the non-expected trends in resolving power and resolution with the increase in the collision partner size.

Acknowledgements This work was supported by the National Science Foundation Division of Chemistry, under CAREER award CHE-1654274, with co-funding from the Division of Molecular and Cellular Biosciences to F.F.-L. The authors will also like to acknowledge the helpful discussions and technical support from Dr. Mark E. Ridgeway and Dr. Melvin A. Park from Bruker Daltonics Inc. during the development and installation of the custom-built TIMS-TOF MS instrument. We will also like to acknowledge Dr. Alexander Mebel support for the theoretical calculations.

References

1. Schenk ER, Ridgeway ME, Park MA, Leng F, Fernandez-Lima FA (2014) Isomerization kinetics of AT hook Decapeptide solution structures. Anal Chem 86(2):1210–1214
2. Schenk ER, Mendez V, Landrum JT, Ridgeway ME, Park MA, Fernandez-Lima FA (2014) Direct observation of differences of carotenoid polyene chain cis/trans isomers resulting from structural topology. Anal Chem 86(4):2019–2024
3. Hernandez DR, DeBord JD, Ridgeway ME, Kaplan DA, Park MA, Fernandez-Lima FA (2014) Ion dynamics in a trapped ion mobility spectrometer. Analyst 139(8):1913–1921
4. McKenzie A, DeBord JD, Ridgeway ME, Park MA, Eiceman GA, Fernandez-Lima F (2015) Lifetimes and stabilities of familiar explosives molecular adduct complexes during ion mobility measurements. Analyst 140(16):5692–5699
5. B. Schneider, T. Covey, E. Nazarov, DMS-MS separations with different transport gas modifiers, 2013
6. Kafle A, Coy SL, Wong BM, Fornace AJ Jr, Glick JJ, Vouros P (2014) Understanding gas phase modifier interactions in rapid analysis by differential mobility-tandem mass spectrometry. J Am Soc Mass Spectrom 25(7):1098–1113
7. Levin DS, Vouros P, Miller RA, Nazarov EG, Morris JC (2006) Characterization of gas-phase molecular interactions on differential mobility ion behavior utilizing an electrospray ionization-differential mobility-mass spectrometer system. Anal Chem 78(1): 96–106
8. Porta T, Varesio E, Hopfgartner G (2013) Gas-phase separation of drugs and metabolites using modifier-assisted differential ion mobility spectrometry hyphenated to liquid extraction surface analysis and mass spectrometry. Anal Chem 85(24):11771–11779
9. R. Fernández-Maestre, C. Wu, H.H. Hill, Buffer gas modifiers effect resolution in ion mobility spectrometry through selective ion-molecule clustering reactions, Rapid Commun Mass Spectrom : RCM, 26 (2012) 2211–2223, 19
10. Waraksa E, Gaik U, Namieśnik J, Sillanpää M, Dymerski T, Wójtowicz M, Puton J (2016) Dopants and gas modifiers in ion mobility spectrometry, vol 82, pp 237–249
11. Butcher D, Miksovska J, Ridgeway ME, Park MA, Fernandez-Lima F The effects of solution additives and gas-phase modifiers on the molecular environment and conformational space of common heme proteins. Rapid Commun Mass Spectrom 0
12. Garabedian A, Leng F, Ridgeway ME, Park MA, Fernandez-Lima F (2018) Tailoring peptide conformational space with organic gas modifiers in TIMS-MS. Int J Ion Mobil Spectrom 21(1-2):43–48
13. Fernandez-Lima FA, Kaplan DA, Park MA (2011) Note: integration of trapped ion mobility spectrometry with mass spectrometry. Rev Sci Instrum 82(12):126106
14. Fernandez-Lima FA, Kaplan DA, Suetering J, Park MA (2011) Gas-phase separation using a trapped ion mobility spectrometer. Int J Ion Mobil Spectrom 14(2-3):93–98
15. E.W. McDaniel, E.A. Mason, Mobility and diffusion of ions in gases, John Wiley and Sons, Inc., New York, New York, 1973
16. M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J. Montgomery, J.A.T. Vreven, K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, V. Bakken, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, C. Gonzalez, J.A. Pople, Gaussian 03, revision C.02, in: Gaussian, Inc., Wallingford CT, 2004