

Combined IMS and SIFT-MS Study of Phthalates

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Abstract. Phthalates are molecules used in industry as plasticisers, however, they represent a potential health risk for the human population. Several phthalates are classified and controlled under the EU regulations and thus it is important to evaluate their concentration in daily use products. Ion mobility spectrometry (IMS) is a technique suitable for real-time phthalate analysis. To understand the ion chemistry in the IMS, we used the IMS-MS and the SIFT-MS methods to study reactions of dimethyl phthalate, dimethyl isophthalate, dimethyl terephthalate, diethyl phthalate and dipropyl phthalate with the hydronium, H_3O^+ , reagent ions at variable humidity. Different isomerisation of the studied phthalates strongly affects formation of water clusters. No water clusters production was observed for 1,2 position of phthalate esters, which positively affect selectivity of identification of phthalates.

Introduction

Phthalates (esters of phthalic acid) are used as plasticizers in production of plastics. However, their negative health effect are now well understood [Halden, 2010; Benjamin *et al.*, 2015]. Phthalates are characterized as endocrine disruptors which represent a major hazard for pregnant woman and children under 3 years. Several the most dangerous phthalates (diethylhexyl phthalate, dibutyl phthalate, benzylbutyl phthalate, diisononyl phthalate, diisodecyl phthalate, and di-n-octyl phthalate) are under the EU regulations [EC, 2005] or are tracked by European Chemical Agency [EHCA]. However, the regulations do not cover daily use plastic products other than toys. Phthalates can be thus present in plastic containers [Shen, 2005], cosmetics [Juhasz and Marmur, 2014] or toothbrushes [Sadeghi *et al.*, 2015]. Hazard of contamination is coming from plastic producers located outside the area of regulations including China or India. Products imported into the EU must be therefore tested.

Several analytical techniques are used for detection of phthalates; mainly based on the liquid or gas chromatography — mass spectrometry (GC-MS / LC/MS) [Russo *et al.*, 2015] primary using electron ionization at 70 eV. The primary product of dissociative ionization observed in the mass spectrum is the protonated phthalate anhydride at mass to charge ratio m/z 149, characteristic for the most phthalates (NIST). Presence of phthalates can be confirmed by detection of phthalate anhydride ion; however, mass spectral analyses have poor selectivity between the different types of phthalates. Chromatography methods are additionally time consuming, requiring several minutes (10–15 min) to analyse one sample. Even with optimisation and automation the samples throughput is thus limited.

Soft chemical ionization (SCI) techniques providing high selectivity used mainly in real time detection of VOCs at trace levels [Smith and Španěl, 2011] can be potentially used for real time and accurate detection of phthalates contamination in plastics. Ion mobility spectrometry (IMS) is a suitable SCI technique for detection of phthalates. IMS is a device using operational pressure near atmospheric and can be used for detection of traces of molecules present at very low partial pressures such as explosives [Sabo *et al.*, 2014].

To describe the possibility of phthalate detection in the IMS, we have to understand the ion chemistry occurring during the detection. Therefore, we have carried out a combined IMS-MS and SIFT-MS study of several phthalates with focus on the phthalate ion chemistry with $\text{H}_3\text{O}^+(\text{H}_2\text{O})_n$ primary ions.

Experiment

Ion mobility spectrometry — mass spectrometry (IMS-MS)

Detail description of IMS-MS setup was reported previously [Sabo *et al.*, 2010] (Figure 1). Briefly, a corona discharge operating in positive mode (3 kV difference in potential between a wire electrode and

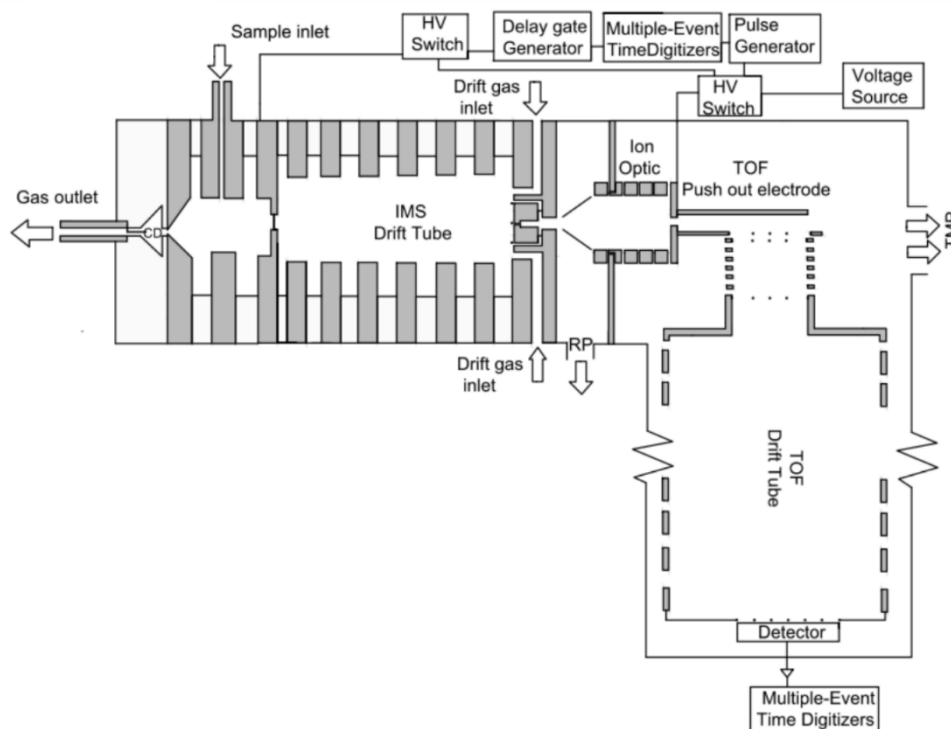


Figure 1. A schematic view of the IMS-MS experimental setup.

a planar electrode, usually at potential of about 8 kV across a drift tube) at atmospheric pressure in purified lab air producing reactant ions. The ion chemistry near to discharge quickly resulting mainly to H_3O^+ ions formation. Ions are then transferred into the reaction region where are reacting with sampled gas. Under the relatively high humidity H_3O^+ ions are quickly converted into a higher water clusters $\text{H}_3\text{O}^+(\text{H}_2\text{O})_n$ with $n < 4$. Trace amount of organic molecules with proton affinity higher as water and water clusters (165 kcal/mol for water (NIST)) react with hydronium ions via proton transfer forming protonated molecular ions and their water clusters. For higher analyte concentrations formation of dimers is also observed; another possibility is also fragmentation. Generated ions are introduced via a shutter grid into the drift tube (consisting of stainless steel electrodes insulated by Teflon and connected to a resistor chain) where they are separated according to their mobility in electric field. At the end of the drift tube the ions are transferred via a pinhole into the low pressure region of ToF-MS system where they are guided by ion optics into the drift tube of TOF. Here the ions are separated according to their flight time and detected using a multichannel plate, MCP. A combined IMS/MS spectrum is thus obtained with a possibility to characterize ion composition of the peaks observed in the IMS spectrum.

Selected ion flow tube — mass spectrometry (SIFT-MS)

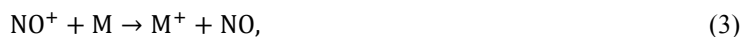
The SIFT-MS experiment [Smith and Španěl, 2005] (Figure 2) is using a microwave induced glow discharge in a mixture of water vapour and lab air to produce H_3O^+ , NO^+ and O_2^+ reagent ions. A specific ion type is then selected by a quadrupole mass filter and injected into the flow tube. Helium carrier gas at 1.5 mbar and room temperature is used to transfer the ions via the flow tube at a defined flow speed. Sample gas is introduced into the flow tube by an inlet port 1 cm downstream of the ion injector. Depending on the type of reagent ions, reactions with analyte molecules occur via several possible processes, including proton transfer for H_3O^+ reagent ions



charge transfer for O_2^+ reagent ions



and charge transfer or association for NO^+ reagent ions



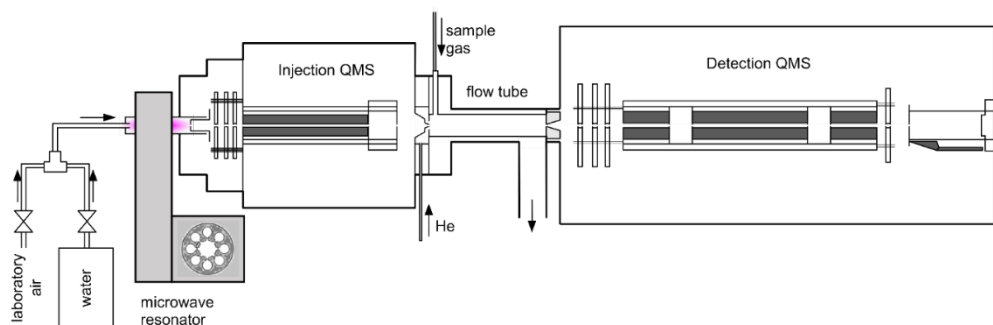


Figure 2. A schematic of the SIFT-MS experimental setup.

Table 1. Summary of the ionization energies (IE) and the proton affinities (PA) of reactants.

	H ₂ O	NO	O ₂	DMP	DMIP	DMTP	DEP	DPrP
IE (eV)	12.65 ^a	9.26 ^c	12.07 ^d	9.64 ^e	9.84 ^e	9.78 ^e	nd	nd
PA (eV)	7.16 ^b	5.51 ^b	4.36 ^b	nd	8.74 ^b	8.74 ^b	nd	nd

a — [Snow, 1990], b — [Hunter, 1998], c — [Reiser, 1988], d — [Tonkyn, 1989], e — [Kuhn, 1968], nd – no data

The product ions are at the end of the flow tube sampled into the detection quadrupole mass spectrometer and detected by electron multiplier. The ion chemistry in SIFT was investigated in dependence on variable humidity to achieve distribution of primary ions similar for IMS, where hydrated hydronium ions are present.

All investigated phthalates DMP (dimethyl phthalate), DMIP (dimethyl isophthalate), DMTP (dimethyl terephthalate), DEP (diethyl phthalate) and DPrP (dipropyl phthalate) were purchased from Sigma-Aldrich Co. Information about ionization energies and proton affinities is presented in Table 1.

Results

The combined IMS spectrum for DMP, DMIP and DMTP isomers is presented in Figure 3. Samples were heated up to 26°C for DMP and DMIP and 56°C for DMTP to enhance the sample evaporation. Spectra were recorded using the IMS/MS experiment in Bratislava using 497 V/cm drift field under the 343 K and 700 mbar in the drift tube. Reduced ion mobilities (K_0) were for each peak calculated according to peak maxima using the

$$K_0 = K \frac{p}{T} \frac{273 \text{ K}}{1013 \text{ hPa}} = \frac{l_d}{t_d E} \frac{p}{T} \frac{273 \text{ K}}{1013 \text{ hPa}}, \quad (5)$$

where K represents mobility, p and T stand for pressure and temperature in the drift tube, l_d and t_d represent drift length and drift time and E represents reduced electric field. The first detected peak with reduced mobility $K_0 = 2.04 \text{ cm}^2\text{V}^{-1}\text{s}^{-1}$ corresponds to ammonia. Hydronium water clusters, representing the reagent ion peak (RIP), are detected at $K_0 = 1.92 \text{ cm}^2\text{V}^{-1}\text{s}^{-1}$. For the investigated phthalates three characteristic peak regions were observed. Using MS, we have identified the first segment with $K_0 = 1.63 \text{ cm}^2\text{V}^{-1}\text{s}^{-1}$ as protonated phthalate ion MH^+ (M stands for phthalate isomer). This product was observed for the DMP isomer exclusively. Additional region with reduced mobility close to $1.40 \text{ cm}^2\text{V}^{-1}\text{s}^{-1}$ corresponded to hydrates of the protonated phthalate ion $\text{MH}^+(\text{H}_2\text{O})_n$. Only a minor contribution of water cluster products for the DMP isomer was observed. However, for the DMIP and DMTP isomers that water clusters of protonated phthalate ion were dominant. For DMIP the presence of $\text{MH}^+(\text{H}_2\text{O})_2$ ion and for DMTP the presence of $\text{MH}^+(\text{H}_2\text{O})$ ion are dominant. Finally, the reduced mobility around $1.05 \text{ cm}^2\text{V}^{-1}\text{s}^{-1}$ belongs to formation of protonated molecular dimers M_2H^+ and their water clusters $\text{M}_2\text{H}^+(\text{H}_2\text{O})_2$.

To summarize, location of ester groups on benzene core significantly changes clustering ability of phthalate isomers with water. 1,2 position (DMP) do not provide accessible and stable state for clustering with water. Presence of phthalate esters on 1,3 carbons (DMIP) allows effective association with two water molecules. Fully open 1,4 position of phthalate esters (DMTP) effectively attaches only one water molecule.

Using the SIFT-MS, we studied the ion chemistry of all dimethyl phthalate isomers as well as of diethyl phthalate (DEP) and dipropyl phthalate (DPrP) using H_3O^+ , NO^+ and O_2^+ reagent ions. Table 2 shows the main products in dry environment. Reaction with hydronium leads to proton transfer reaction forming MH^+ ion. Using of NO^+ reagent ion leads either to charge transfer forming M^+ ion or association forming $\text{M}\cdot\text{NO}^+$ ion. Reaction with O_2^+ reagent ion leads to charge transfer forming M^+ ion. The main dissociation channel is equivalent for all observed phthalates as well as for all ionization mechanisms forming M-OR^+ ion. For DPrP, more dissociation channels were observed as a result of decreasing ionization energy of larger hydrocarbons.

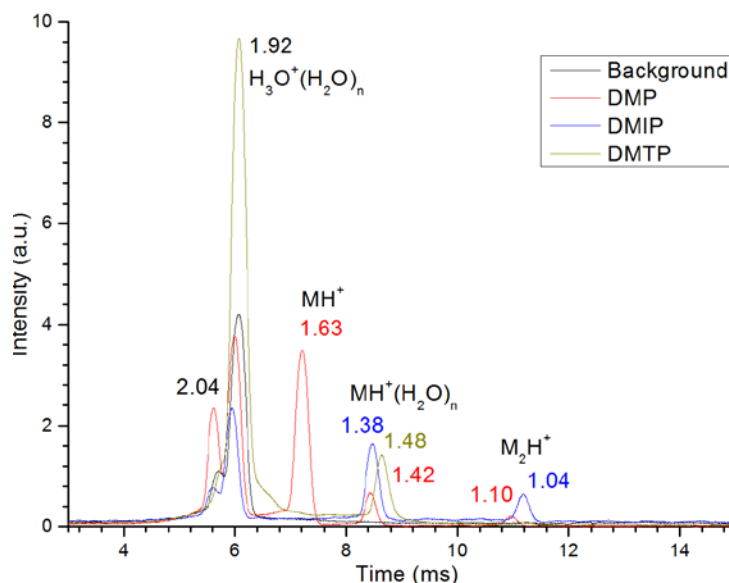


Figure 3. The IMS spectrum of DMP, DMIP and DMTP isomers. Reduced ion mobilities were for each peak calculated according to peak maxima. Ion types responsible for presence of peak were estimated using IMS/MS experiment. The first detected peak with reduced mobility $K_0 = 2.04 \text{ cm}^2 \text{V}^{-1} \text{s}^{-1}$ corresponds to ammonia.

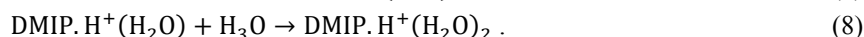
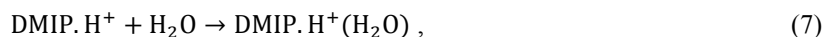
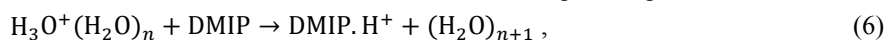
Table 2. Ion products of various phthalates interacting with H_3O^+ , NO^+ and O_2^+ reagent ions in the SIFT. Mass spectra were recorded under dry conditions. R stands for alkyl substituent varying for different phthalates.

Compound (MW)	m/z	br	H_3O^+	m/z	br	NO^+	m/z	br	O_2^+
DMP (194) 4.1 ^a 	163	37%	(DMP-OR) ⁺	163	86%	(DMP-OR) ⁺	163	83%	(DMP-OR) ⁺
	195	63%	DMP.H ⁺	194	3%	DMP ⁺	194	17%	DMP ⁺
				224	11%	DMP.NO ⁺			
DMIP (194) 12.8 ^a 	163	8%	(DMIP-OR) ⁺	163	63%	(DMIP-OR) ⁺	163	39%	(DMIP-OR) ⁺
	181	1%	(DMIP-(R-H)) ⁺	194	9%	DMIP ⁺	194	61%	DMIP ⁺
	195	82%	DMIP.H ⁺	224	28%	DMIP.NO ⁺			
	213	9%	DMIP.H ⁺ .H ₂ O						
DMTP (194) 14.1 ^a 	163	11%	(DMTP-OR) ⁺	163	79%	(DMTP-OR) ⁺	163	26%	(DMTP-OR) ⁺
	195	82%	DMTP.H ⁺	194	9%	DMTP ⁺	194	74%	DMTP ⁺
	213	7%	DMTP.H ⁺ .H ₂ O	224	12%	DMTP.NO ⁺			
DEP (222) 2.8 ^b 	177	36%	(DEP-OR) ⁺	177	73%	(DEP-OR) ⁺	177	69%	(DEP-OR) ⁺
	223	64%	DEP.H ⁺	222	5%	DEP ⁺	222	31%	DEP ⁺
				223	22%	*DEP.H ⁺			
DPrP (250) 	191	15%	(DPrP-OR) ⁺	191	22%	(DPrP-OR) ⁺	149	25%	C ₆ H ₄ (CO) ₂ OH ⁺
	223	2%	(DPrP-C ₂ H ₅) ⁺	209	5%	(DPrP-(R-H)) ⁺	167	10%	(DPrP-2(R-H)) ⁺
	251	83%	DPrP.H ⁺	251	6%	DPrP ⁺	191	12%	(DPrP-OR) ⁺
				280	67%	DPrP.NO ⁺	209	44%	(DPrP-(R-H)) ⁺
						250	9%	DPrP ⁺	

* impurity caused by presence of H_3O^+ reagent ions, br — branching ratio, MW — molecular weight, a — vapour pressure in 10^{-3} mbar at 25°C [Daubert, 1989], b — vapour pressure in 10^{-3} mbar at 25°C [Hinckley, 1990]

Effect of humidity on ion chemistry can be described as two phenomena. The first is the association of the reagent ions with water molecules forming hydrates which exhibit different ion chemistry. The second is presence of secondary reactions between the products of primary reactions and water molecules. Effect of humidity on ion chemistry was studied for H_3O^+ reagent ions, where it has the most significant impact. Results for DMP isomers are shown in Figure 4. Distribution of hydronium clusters (Figure 4a) is at high humidity dominated by presence of $\text{H}_3\text{O}^+(\text{H}_2\text{O})_3$ reagent ion similar as for the IMS measurement. Primary processes should be comparable in this region. Formation of water clusters depends strongly on the isomer geometry. For

DMP (1,2 position of phthalate ester groups) we observed no formation of protonated phthalate water clusters. For DMIP (1,3 position of phthalate ester groups) is formation of protonated phthalate water clusters very efficient. As water concentration increases, protonated *iso* isomer attaches two water molecules. According to the kinetic profile in Figure 4c, we can describe formation of water clusters as a sequential process



In contrast to DMIP, the fully open geometry of protonated DMTP (1,4 position of phthalate ester groups) attaches only one water molecule. That can suggest unsymmetrical geometry of esters or alkyl substituent in *trans* position or different charge distribution in comparison with *cis* geometry.

Discussion

Observed ion chemistry behaviour may be compared with previous studies of *Fales et al.* [1971], *George and Prest* [2002] or *Jeilani et al.* [2010] noting that the primary ions used in their studies had higher interaction energy. *Fales et al.* [1971] used methane and isobutene, *George and Prest* [2002] used methane and ammonia and *Jeilani et al.* [2010] methane chemical ionization. With phthalate anhydride (m/z 149) as a primary product, ion chemistry for these primary ions is comparable with electron ionization spectra [*Lacko et al.*, 2018]. Anyway, George confirmed loss of $-\text{OR}$ group. Intensity of the fragment decreases with increase of alkyl chain length. Jeilani et al. described fragmentation mechanism for formation of observed phthalate anhydride (m/z 149) and $\text{M}-(\text{R}-\text{H})^+$ (m/z 167) ions. Formation of $\text{M}-2(\text{R}-\text{H})^+$ ion however requires McLafferty rearrangement, which is not accessible for alkyls containing less than three carbons. Similar fragmentation was in our experiment observed only for DPrP, ionized by charge transfer from O_2^+ reagent ion.

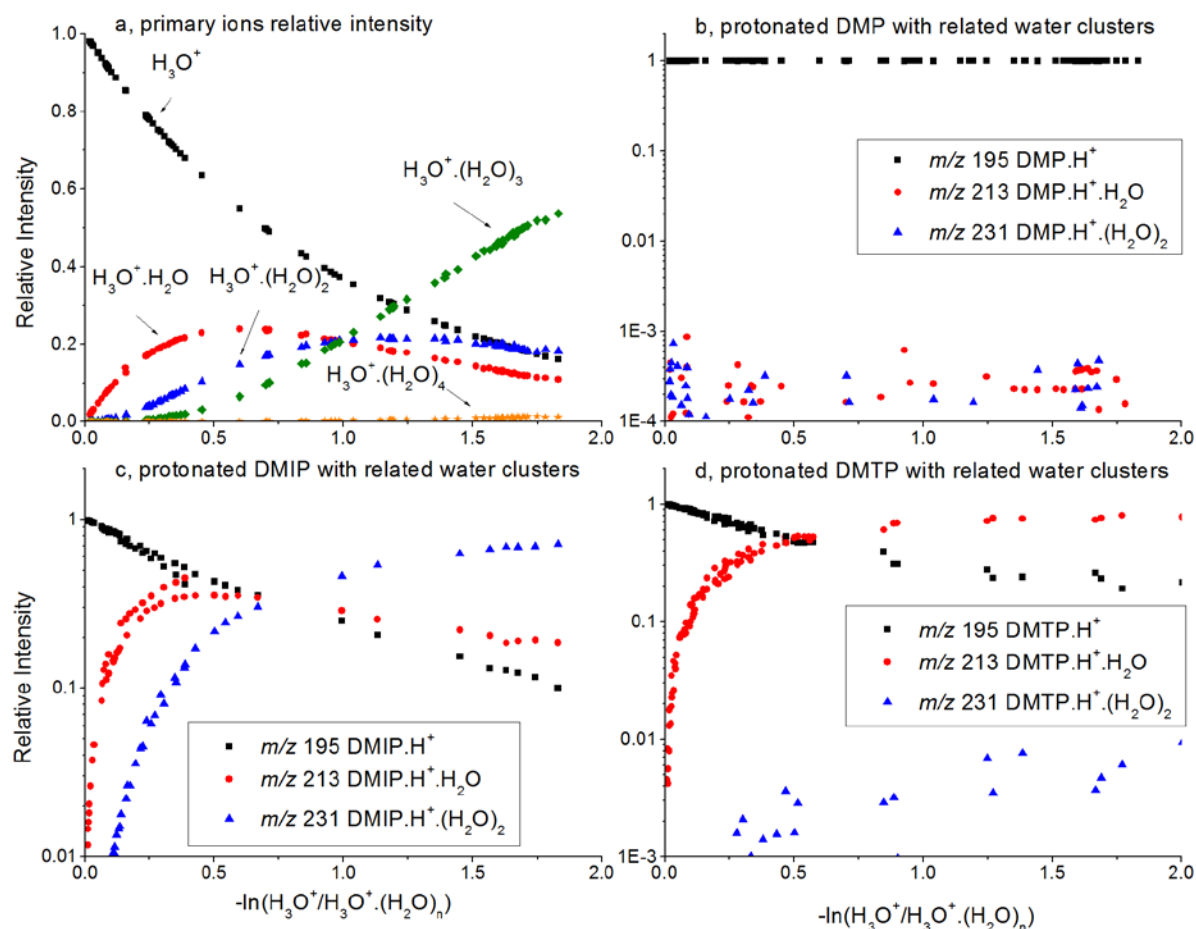


Figure 4. Relative intensity of selected ions as a function of water concentration in the SIFT: (a) evolution of H_3O^+ reagent ions and related water clusters and relative intensity of protonated DMP (b), DMIP (c) and DMTP (d) isomers with related water clusters formed by interaction with $\text{H}_3\text{O}^+(\text{H}_2\text{O})_n$ reagent ions. Humidity is expressed as a negative logarithm of ratio between hydronium ions and all hydronium water clusters.

According to our observations, dissociation induced by chemical ionization for short alkyl chains proceeds by loss of –OR group. Dissociation is active for both proton transfer as well as charge transfer ionization, but more efficient for charge transfer. Interaction of ionized phthalate molecule with neutral water represents a secondary process. Efficiency of such an interaction depends according to our observation on isomeric state of phthalates. Location of phthalate ester groups in 1,2 position and thus a close position of esters does not allow association of water molecules. Effect is observed even for phthalates with longer alkyl chains (up to C₃ for DPrP). *iso*- isomerization allows effective association of two neutral water molecules. The geometry of the association was not calculated; however, we can assume that both water molecules are attached to the ester oxygen containing proton. If proton lays in plane with benzene ring (ester to benzene dihedral angle is 0°), water molecules can be located out of the plane on both sides around the ester oxygen. When the ester group is rotated out of the benzene plane (ester to benzene dihedral angle is 90°) the molecule provides only a limited access to protonated oxygen and thus water attachment is restricted. That can be case of the *trans*- isomerization, where we observed effective association with only one water molecule.

The last observed phenomena are a lack of dissociation fragments is the IMS experiment. According to SIFT-MS observation, the loss of –OR group represents a reasonable channel, especially for DMP. Lack of the fragmentation can be however explained by different pressure conditions in both experiments. Pressure of 700 mbar present in IMS compared to 1.5 mbar in SIFT facilitates significantly more three-body reactions with the carrier gas. Three-body reactions can effectively remove energy excess during the proton transfer, which would otherwise lead to dissociation. Additionally, IMS operates with molecular nitrogen as a carrier gas providing additional rotational and vibrational states providing cooling of reactions even more effective (compare to He in SIFT).

Conclusion

A combined IMS-MS and SIFT-MS study of phthalate isomers (DMP, DMIP, DMTP) and additional SIFT-MS study of DEP and DPrP were carried out. The experiments were carried out primarily using the H₃O⁺(H₂O)_n reagent ions, but additionally the NO⁺ and O₂⁺ reagent ions were used in SIFT-MS. The IMS study uncovered differences in secondary processes of protonated phthalates with water molecules. Formation of water clusters strongly depends on isomerization of phthalates. Results were confirmed by study of chemical kinetic using SIFT-MS. According to different position of phthalate esters, for 1,2 position is water attachment impossible, for 1,3 position can phthalate effectively attach two water molecules, and for 1,4 position is effective only attachment of one water molecule. A geometry of structures would have to be investigated theoretically in future to explain these observations. The main dissociation channel observed for all reagent ions was the loss of the –OR group. Dissociation differed from the usually observed formation of phthalate anhydride ion (*m/z* 149) due to lower interaction energies and a short length of phthalate alkyl chains. Due to the higher pressure and the presence of diatomic carrier gas, fragmentation was absent in IMS. Results suggest very good selectivity for 1,2 phthalates, mostly resulting in only two major product ions for SCI-MS and only one MH⁺ product ion for IMS.

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