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Mobility shifts when buffer gas temperature increases in ion mobility spectrometry are affected by intramolecular bonds

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ABSTRACT

When buffer gas temperatures increase in ion mobility spectrometry (IMS), ions lose hydration molecules and their mobilities increase. Also, shift reagents (SRs, dopants or modifiers) introduced in the buffer gas, form adducts with the ions and their ion mobilities decrease. Some ions, such as methionine and diamines, are not largely influenced by the introduction of SRs or the buffer gas temperatures because they form intramolecular hydrogen bonds (IHBs). We used electrospray ionization IMS coupled to quadrupole mass spectrometry to study the drift behavior of these ions using data obtained at different temperatures or with different SRs. In this study, we explain the unusually small mobility shifts in methionine and diamine ions when buffer gas temperature increases in IMS based on the breaking of IHBs that increase the ions' collision cross-sections. We also explain the small mobility shifts in these ions when buffer gas SRs are introduced in the drift tube based on the formation of these IHBs, This study is important because when temperature increases in IMS, mobility shifts had been considered to be affected exclusively by declustering and the increase in collision frequency. This information will help understand the behavior of IHB-forming ions in IMS at different temperatures and when buffer gas SRs are introduced in the drift tube, and could be used to demonstrate the presence of these bonds and measure their binding energy.

1. Introduction

Ion mobility spectrometry is an analytical technique that separates ions based on their size to charge ratio under the influence of an electric field. In IMS, the electric field accelerates the ions, while collisions with the buffer gas decelerate them [1]. The time the ions take to reach the detector is proportional to their size (collision cross section, CCS) because the larger they are the more they collide.

Thermal energy affect the velocity of the ions and the formation and breaking of IHBs:

$$E = \frac{3KT}{2} \tag{1}$$

where T is the temperature in Kelvin and k the Boltzmann constant, 1.38×10^{-23}. At 250 °C thermal energy is 1.6 Kcal/mol. Part of this energy can be transferred to the analyte ions traveling through the nitrogen drift gas by means of inelastic collisions. Due to the thousands of collisions against the buffer gas during the drift of the ions to the detector, this energy transfer add up to the breaking of weak IHBs which increase CCS. This is why the cleavage and formation of IHBs, defined as weak hydrogen bonds due to their low energy [2], is considered a short-time (less than one ns) dynamic process at room temperature in small molecules such as the alanine pentapeptide [3].

Ion mobility is related to thermal energy, mass and size by the fundamental IMS equation [4,5]:

$$K_0 = \frac{3e}{16N_0}\sqrt{\frac{2\pi}{\mu kT}}\frac{1}{\Omega} \tag{2}$$

where e is the ion charge, N_0 the buffer gas number density at P_0 and T_0, μ the ion and buffer gas reduced mass, k the Boltzmann constant, T the effective buffer gas temperature, and Ω the momentum transfer collision integral (the experimental ion's CCS). According to Eq. (2), temperature variation has three consequences: 1) N varies inversely with T, accounted for by using K_0 and N_0. 2) The average relative ion-neutral collision velocity increases with $T^{1/2}$, accounted for by the term in the radical; and 3) Ion size also depends on T accounted by including the average ion-neutral CCS. Factors 2 and 3 determine collision frequency, so the usual decrease in CCS with

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T tends to oppose the increase in collision frequency due to higher ion-neutral speed and the higher CCS due to breaking of IHBs.

The increase in reduced mobilities with the increase in buffer gas temperature reported by many authors has been explained by reduction of water adduction with temperature [6–8]. In line with this, Borsdorf and Eiceman considered that values for calculated mobilities must include the effects of moisture and temperature on the identity of product ions; they explained that mobility values are usually normalized to temperature and pressure and reported as reduced mobilities (K_0) but this normalization cannot compensate for changes in ion identity due to changes in adduction with temperature or moisture [9]. Apart from declustering, the increase in reduced mobility when buffer gas temperature is increased has been explained using the additional collision energy obtained by the ions that increase the collision frequency against the buffer gas molecules [5,6].

Some compounds do not show the mobility shifts expected when the buffer gas temperature is increased or SRs are introduced in the buffer gas [10]. Methionine and diamines have experienced only small mobility shifts when SRs have been injected in the buffer gas in IMS because of the low adduction of these ions with polar SRs [10–12]. This low clustering is due to a large size that decreases the effect of SR adduction on collision cross-section (atenolol) or IHBs that stabilize the positive charge and deter the approach of the SRs due to steric hindrance because the charge is buried in the structure (methionine and diamines) [11,12].

In this paper, we show that the small mobility shifts obtained with methionine and diamines when buffer gas temperature increases in IMS or when buffer gas SRs are introduced in the drift tube demonstrate the presence of IHBs and the breaking of these bonds with temperature. This may be the first time that the drift behavior of ions when the buffer gas temperature is increased has been explained using IHBs because this effect had been exclusively attributed to declustering and the increase in collision frequency as explained above. We also introduce here two concepts: $\Delta K_{0,c}$, the percentage difference between K_0 in pure buffer gas and K_0 when a SR is introduced into the buffer gas at a given concentration; and $\Delta K_{0,T}$,the percentage difference between K_0 at two different temperatures.

2. Experimental

The methodology has been described before [13] and a brief description is given here.

2.1. Instrument

The ion mobility spectrometer was built at Washington State University; it had an electrospray ionization source and a 25-cm drift tube coupled to a quadrupole mass spectrometer. Routine operating conditions and instrumental parameters were: ESI flow, 3 μl min^{-1}; reaction region length, 7.5 cm; ESI voltage, 15.6 kV; voltage at first ring, 12.1 kV; voltage at the gate, 10.80 ± 0.01 kV; electric field, 432 V cm^{-1}; gate closure potential, ±40 V; gate pulse width, 0.1 ms; scan time, 35 ms; pressure, 680–710 Torr; buffer gas, nitrogen; buffer gas temperature, 150 ± 2 °C; buffer gas flow, 0.93 l min^{-1}. The desolvation and drift regions were separated by a Bradbury-Nielsen ion gate; a countercurrent of dry, preheated N_2 buffer gas was introduced through the low voltage end of the drift tube. The ABB Extrel mass spectrometer (0–4000 amu) was operated in three modes. In single ion monitoring mode (SIM), only ions of a given mass to charge ratio or a range of masses are detected; in radiofrequency-only mode (IMS) total ion mobility spectra are obtained; and in mass spectrometry mode (MS), mass spectra are obtained.

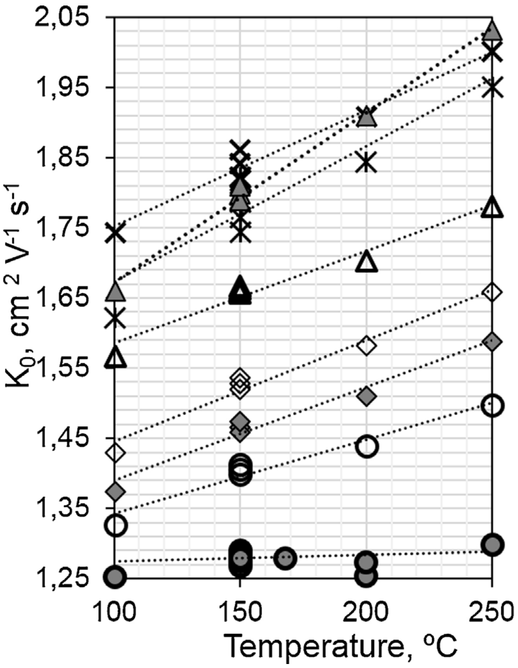

Fig. 1. Reduced mobility shifts with buffer gas (nitrogen) temperature. Atenolol showed little change with temperature and the slope for methionine was lower than that of phenylalanine or similar to that of tyrosine, compounds of larger mass (Table S3) because the increase in atenolol and methionine's K_0 was compensated by the decrease in K_0 produced by the breaking of intramolecular bonds. Valinol (x), serine (▲), threonine (∗), methionine (△), phenylalanine (◇), tyrosine (♦), tryptophan (o), atenolol (●). The number of experiments can be found in Table S4.

2.2. Reagents

Atenolol, methionine, 2,4-lutidine, 2,6-di-tert-butyl pyridine (DTBP), tetrabutylammonium chloride (TBA), water, and acetic acid (ACS reagent grade, ≥97 or 98% purity) were purchased from Sigma Aldrich Chemical Co. (Milwaukee, WI, USA, Fig. 1). Tetrabutylammonium chloride, 2,4-lutidine, and di-tert-butyl pyridine were used as the chemical standards because they are the most used in IMS [14].

2.3. Theoretical calculations

The density functional theory, using the hybrid functional X3LYP/6–311 + +(d,p), that accounts for the basis set superposition error, was used for theoretical calculations with the Gaussian 09 program at 150 °C [15,16]. Proton affinities were calculated subtracting protonated molecule energies from molecule energies [17].

2.4. Solutions preparation and injection

Analyte solutions were prepared at 50-μM concentrations in ESI solution (47.5% methanol: 47.5% water: 5% acetic acid). Liquid samples or blank solution (ESI solution) were injected continuously by ESI. Liquid SRs were injected as vapors into the buffer gas line before the buffer gas heater through a heated cross-junction. The structures of compounds used in this study are shown in Fig. S1.

3. Results and discussion

The mass and shape of ions affect K_0 through the CCS; this is, K_0 is governed by the reduced mass and size-to-charge ratio of the ion in the supporting atmosphere (Eq. (2)) [4]. However, in this discussion we used mass (proportional to CCS) instead of CCS because these data are derived from K_0, which is already used. CCS