# Atmospheric pressure gas-phase ammonium/alkyl ammonium exchange studies of some crown ethers complexes using ion mobility spectrometry: A thermodynamic investigation and collision cross section measurements

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## ABSTRACT

A systematic evaluation of the intermolecular binding forces responsible for the association of crown ethers (hosts) with alkyl amines (guests) is presented by exchanging the ammonium and alkyl ammonium in the ion source of atmospheric pressure ion mobility spectrometry. The hydrogen bonding interactions of crown ether/alkyl ammonium ion complexes are examined with respect to the macrocyclic size effects of five crown ethers (12-crown-4, 15-crown-5, benzo-15-crown-5, 18-crown-6 and aza-18-crown-6) and the gas-phase basicities of five homologous series of alkyl amines. Our approach is based on a formalism assuming an equilibrium: $[host + NH_4]^+ + [guest + H]^+ \leftrightarrow [host + guestH]^+ + [NH_4]^+$. The exchange equilibrium constant for this process was calculated using the relative peak intensities of the corresponding species in the IMS spectra. Determination of the equilibrium constants at different temperature via Van't Hoff plots led to the standard molar enthalpy change $\Delta H^\circ$ that is equivalent to the guest-exchange affinity of different crown ethers. The collision cross-sections are measured for the formation of complexes ions and different alkyl ammonium ions, which are produced. Complexes of 15C5 with two different normal and iso-alkyl amine showed a gas phase selectivity binding to normal alkyl amines relative to iso-alkyl amines.

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## 1. Introduction

Studies on host–guest complexations in the gas phase lead to understanding the nature of the intrinsic binding interactions, which are involved in the molecular recognitions [1]. A large number of studies have been devoted to investigate the ion binding affinities and stability constants of model hosts, such as crown ethers, with two noteworthy guests of the protons and the ammonium ions [2,3] in the gas phase. Crown ethers are particularly useful in modeling biologically relevant ion transport processes, antibody–antigen associations, and enzyme catalysis. Complexing ammonium ions with crown ethers serve as a model for the interactions of ions with biological membranes, as well as with the interior of enzymes [4,5]. Among the available techniques, mass spectrometry has been extensively employed to investigate the crown ether inclusion complexes and host–guest interactions in the gas phase [6,7]. Since the driving force for the formation of inclusion complexes in solution is the so-called "hydrophobic effect", investigating the gas-phase chemistry of inclusion complexes is particularly important to probe the intrinsic properties of non-covalent interactions in the absence of complicating effect of solvent molecules.

Assessing the strength of hydrogen bonding interactions and correlating the interactions with structural factors should lead to a better understanding of the stabilities of non-covalent complexes in the gas phase. It is noted that the strengths of hydrogen bonds between the alkyl ammonium ion donors and the oxygen receptor sites dominate the stability of crown/amine complexes in the gas phase. Based on energy-variable collision-induced dissociation (CID) measurements, the interaction energy of an alkyl ammonium ion with a polyether could be as much as 45 kcal/mol [8–10].

Dearden and Chu studied exchange equilibrium constant of the alkyl amine guest between unsubstituted 18-crown-6 and isomers of dicyclohexano-18-crown-6 host using Fourier transform ion cyclotron resonance mass spectrometry and semi-empirical calculations [11]. Both methods revealed that the sterically unhindered ammonium cations bind dicyclohexano-18-crown-6 in preference to 18-crown-6, but the preferences are decreased or vanished for the ammonium cations branched at the carbon sites.

Ion mobility spectrometry (IMS) also provides an ideal environment to monitor gas-phase reactions, evaluates kinetic [12] and thermodynamic data for reaction mechanisms [13], and

determinates binding affinities. Tabrizchi and Shooshtari [14] used atmospheric pressure IMS for the first time to determine the relative gas-phase proton affinities by measuring the ion equilibrium concentration as a function of temperature. It is important to note that IMS has been used to investigate the polyether complexes since 1995 [15–17]. Bowers and co-workers have studied the conformation of alkali metal cationised linear and cyclic polyethers using low-pressure IMS [18]. Creaser et al. investigated the gas-phase structural analysis of polyether/protonated amine complexes using a tandem quadrupole ion trap/low-pressure drift tube [19,20] and atmospheric pressure ion mobility spectrometry [21]. Moreover, Colgrave et al. [22] studied the ligand–receptor complexations of cyclic and acyclic polyethers with amino acids and peptides by nano-electrospray ionization-IMS and ion trap mass spectrometry. They demonstrated small variations in reduced mobilities and collision cross-sections arising from small changes in the conformation of ligand–receptor complexes which led to differences in the reduced mobilities not only between cyclic and acyclic polyethers but also between their complexes with isomeric amines or biomolecules. The reduced mobilities of complexes were lower for the acyclic polyethers with respect to their cyclic analogues. Dearden et al. [23] investigated Shape-selective complexations between cucurbit [6] uril and phenylenediamine isomers in the gas-phase. This complexation arises from the reactivity of each of the complexes with *tert*-butyl amine, in which the *ortho*- and *meta*-phenylenediamine complexes exchange with *tert*-butyl amine whereas the *para*-phenylenediamine complex undergoes two slow additions without displacement. They used computational methods, Fourier transform ion cyclotron resonance mass spectrometry and ion mobility spectrometry to verify that the lowest energy binding sites for *ortho*- and *meta*-phenylenediamine are on the exterior of cucurbit [6] uril whereas *para*-phenylenediamine preferentially binds in the interior. Crown ethers have been also employed as shift reagents for separating a series of peptide ions by IMS [24]. Ion-molecule complexes between crown ethers and peptide ions cause shifting the mobilities of peptide ions, which initially have similar masses and charge states but they are not resolved well.

The main goal of this study is to determining the effect of crown ring size on the guest-exchange affinity by exploring the complexational behavior of some crown ether–ammonium complexes with a variety of alkyl amines in the gas phase. To this aim, guest-exchange in a crown ether host has been evaluated by the mean of variable-temperature equilibrium technique using atmospheric pressure ion mobility spectrometry.

## 2. Experimental

The alkyl amines, hereafter abbreviated as A, including: alylamine, n-propyl amine, isopropyl amine, n-butyl amine, and iso-butyl amine and the crown ethers including: 12-crown-4 (12C4), 15-crown-5 (15C5), 18-crown-6 (18C6), benzo 15-crown-5 (B15C5) were considered in this study. All chemicals were of analytical grade from Merck (Darmstadt, Germany).

All experiments were performed using an ion mobility spectrometer (model 1000, Isfahan University of Technology, Iran) with corona ionization source at 3000 V potential. The ions were then pulsed each 300 μs into a drift tube with potential 7500 V. The drift and carrier gas were both nitrogen at flow rates of 500 ml min$^{-1}$ and 150 ml min$^{-1}$ respectively, and passed through a 13X molecular sieves (Fluka) trap to remove its water vapor and other possible contaminations before entering into the IMS cell. The injector temperature was 473 K and the IMS cell was housed in a thermostated oven, in which the temperature was controlled within ±1 K. Ammonium carbonate was used to generate ammonia as a dopant to drift

gas streams. A small cap vessel filled with ammonium carbonate was connected to the carrier gas via a capillary tube whereas nitrogen was flowing into the vessel at a flow rate of about 20 ml min$^{-1}$. The solid ammonium carbonate is in equilibrium with the gaseous ammonia. This method ensures continuous introduction of a constant amount of ammonia into the reaction region. There is not an accurate value for the ammonium concentration, but the optimum flow rate was chosen when the $H_3O^+$ peak was eliminated and the $NH_4^+$ peak appeared in full height. The concentration of ammonia is believed to be in the order of few ppm [25].

In order to produce a constant current of reactant ions, a separate high voltage was used for the corona discharge. The needle voltage was adjusted accordingly to keep the corona current constant during all experiments. The spectrometer was operated in a positive mode, signal was averaged over 100 scans, and the resulting ion mobility spectrum was then displayed on the monitor. In all experiments, sample solutions containing 0.1 mM of alkyl amine and 0.1 mM of crown ether dissolved in methanol were directly infused into the injection port of IMS using a two-path syringe pump. The relative intensities of two peaks assigned to crown ether.alkyl amine.H$^+$ (C.A.H$^+$) and crown ether.NH$_4^+$ (C.NH$_4^+$) complexes were measured at different pumping speeds (1–60 μL min$^{-1}$). At a pumping speed of $\geq$40 μL min$^{-1}$, high enough to meet equilibrium conditions ($\geq$1.4 ppm V/V). The ratio of ([C.A.H$^+$]/[C.NH$_4^+$]) was assumed to be independent of the flow rate and is directly proportional to the equilibrium constant. Experiments were performed at different temperatures (333–403 K) with a fixed pumping speed (steady state conditions) and enthalpy change of reaction was obtained from the temperature dependency of equilibrium constants using the Van't Hoff relation.

## 3. Results and discussion

It is well known that the ring size, nature, and position of the donor atoms of crown ether have a strong influence on the complex formation with different compounds. The influences of different crown ethers (12C4, 15C5, B15C5, 18C6, aza18C6) on the complexation with some alkyl amines (alylamine, n-propyl amine, iso-propyl amine, n-butyl amine and iso-butyl amine) have been examined. IMS spectra were obtained for the mixture of crown ether and alkyl amine, which were introduced in the ionization source of IMS with ammonia drift gas dopant from two separate paths of a syringe pump.

For identification purposes, reduced mobility ($K_0$) is often used instead of drift time. The values of reduced mobilities are calculated for the positive ion mode using ($NH_4^+$) as the calibrant. The reduced mobility was calculated using Eq. (1) in a normalized standard pressure (760 torr) and temperature (273 K)

$$K_0(\text{unknown}) = \frac{K_0(\text{standard}) \times t_d(\text{standard})}{t_d(\text{unknown})} \qquad (1)$$

where $K_0$ is the reduced mobility with the units of (cm$^2$ V$^{-1}$ s$^{-1}$), and $t_d$ is the drift time. Peak assignments were carried out through separate injections of crown ethers and alkylamines (a typical spectrum in the absence and presence of ammonia drift gas dopant was shown for 12C4–butylamine in Fig. 1A). The observed peaks in the corona discharge IMS spectra could be assigned to ions formed by proton transfer for butylamine and complexing crown ethers with ammonium, respectively. With the exception of 18C6 in all cases, two peaks were observed in the IMS spectrum for crown ethers, which are assigned to the monomer (C.NH$_4^+$) and dimer (C.NH$_4^+$.C), respectively (Fig. 1B). By increasing the temperature, the peak intensity for the monomer adducts are also increased but the intensity of dimer are decreased.

In the presence of ammonia drift gas dopant, $NH_4^+$ is the major reactant ion present in this condition [26]. Under the ammonia
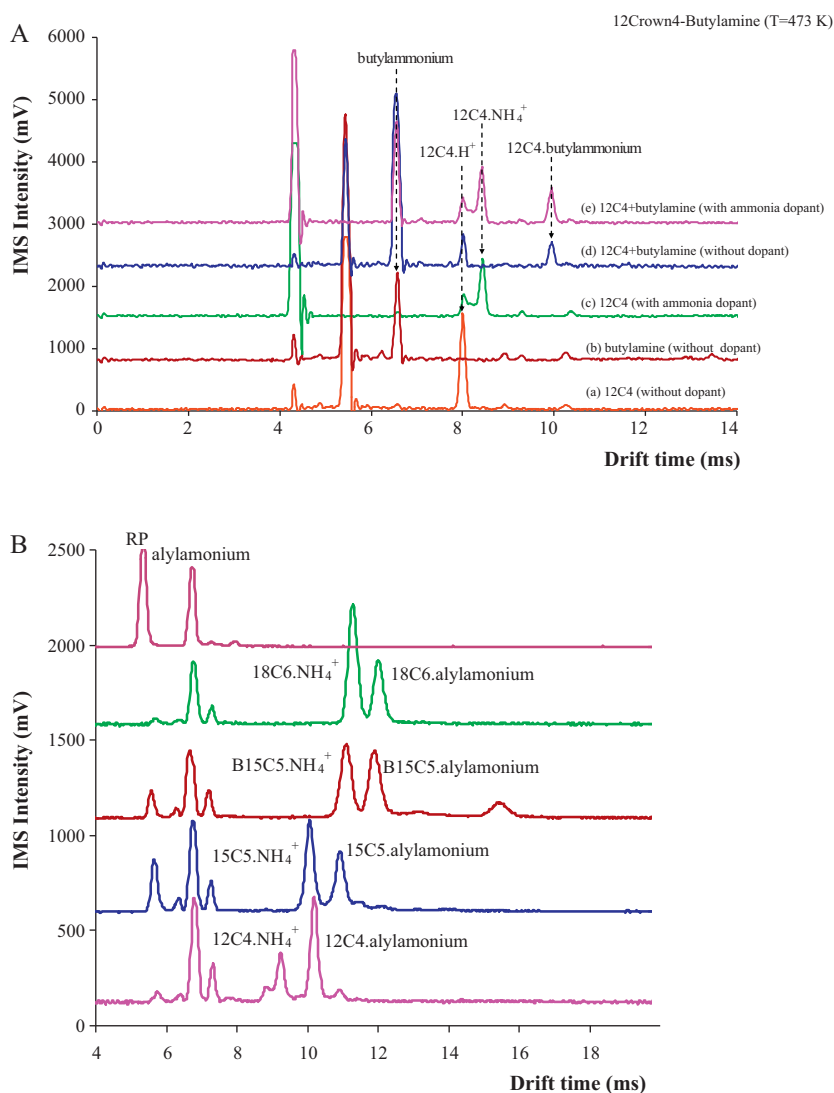
**Fig. 1.** (A) Peak assignment for 12C4–butylamine complex at cell temperature 473 K (a) 12C4, (b) butylamine and (d) 12C4–butylamine in the absence of drift gas dopant (c) 12C4 and (e) 12C4–butylamine in the presence of ammonia drift gas dopant. (B) Peak assignment for different crown ether–alylamine complexes at cell temperature 403 K.

doping, the proton or ammonium ion could adduct with crown ethers as shown in Eqs. (2) and (3). Liou and Brodbelt [9] compared gas-phase proton and ammonium ion affinities of crown ethers by the kinetic method with quadrupole mass spectrometer. They demonstrated that the crown ethers with large cavity sizes have dramatically higher relative affinities for the ammonium ion with respect to the proton ion. This preference was attributed to the favorable ability of the crown ethers to form multiple hydrogen-bonding interactions to the bulky tetrahedral ammonium ion with overall lower entropy of complexation. In contrast, the optimal hydrogen bonding geometry for proton attachment to polyethers involves an O–H$^+$–O bond angle of 180° [16]. Such geometry of proton coordination causes the lower proton affinity of the rigid crown ethers. Therefore, the main predicted species would be the non-covalent complex, which is formed between the host crown ether and the guest ammonium ion as C.NH$_4^+$, Eq. (3). It is obvious from Fig. 1A that the position of main peak assigned to 12C4 in the absence (a) and in the presence (c) of ammonia drift gas dopant are different, so various ion products would be formed at these two instrumental conditions. In the absence of ammonia drift gas dopant, the major reactant ion would be H$_3$O$^+$.$n$H$_2$O and all crown ethers either would undergo a proton transfer with H$_3$O$^+$ or would

adduct with H$_3$O$^+$ as C.H$^+$ or C.H$_3$O$^+$, respectively. Alkyl amines also undergo a proton transfer reaction directly with NH$_4^+$ reactant ion-owing to their higher proton affinity than that of ammonia- to produce protonated amine as shown in Eq. (4).

$$C + NH_3.H^+ \leftrightarrow C.H^+ + NH_3 \tag{2}$$

$$C + NH_3.H^+ \leftrightarrow C.NH_3.H^+ \tag{3}$$

$$A + NH_3.H^+ \leftrightarrow A.H^+ + NH_3 \tag{4}$$

What would happened when the incorporating ammonium–crown ether complexes accompanied by an alkyl amine in the ionization source of IMS? To answer this question we should take a look at the IMS spectrum shown in Fig. 1, in which a new peak assigned to the [C.AH]$^+$ are appeared for different crown ether–alylamine mixture as well as a decrease in intensity of other presented peaks, which assigned to reactant ion, protonated-alylamine, and crown–NH$_4^+$ adduct peak in a separately assignment experiments. A guest-exchange reaction occurs because of the interaction between the crown ether–ammonium complex and the alkyl amine. The ammonium is displaced by the alkyl amine (A) in a guest exchange reaction to produce a new crown ether-protonated amine complex [C.AH]$^+$. The formation of

**Table 1**
The reduced mobility (cm$^2$ V$^{-1}$ s$^{-1}$) and collision cross-sections (Å$^2$) of ions together with their corresponding mass-to-mobility.

| Guest | Host | | | | | |
|---|---|---|---|---|---|---|
| | $K_0{}^a$/mass$^b$/$\Omega_D{}^c$ | Amine (17) | 12C4 (176)$^d$ | 15C5 (220) | B15C5 (268) | 18C6 (264) |
| NH$_4$ | $K_0$ | 2.960 | 1.659 | 1.510 | 1.354 | 1.346 |
| | mass | 37, $n = 1^e$ | 202 | 238 | 284 | 311 |
| | $\Omega_D$ | 91.7 | 109.5 | 118.9 | 131.4 | 132.3 |
| Alyl (57)$^d$ | $K_0$ | 2.335 | 1.486 | 1.388 | 1.265 | 1.272 |
| | mass | 95, $n = 2$ | 245 | 273 | 314 | 311 |
| | $\Omega_D$ | 88.6 | 121.0 | 128.4 | 140.0 | 139.2 |
| n-Propyl (59) | $K_0$ | 2.311 | 1.476 | 1.382 | 1.255 | 1.245 |
| | mass | 98, $n = 2$ | 248 | 274 | 317 | 321 |
| | $\Omega_D$ | 89.0 (68.7)$^f$ | 121.7 | 128.9 (130.2)$^f$ | 141.1 | 142.2 |
| Isopropyl (59) | $K_0$ | 2.346 | 1.481 | 1.386 | 1.259 | 1.265 |
| | mass | 95, $n = 2$ | 246 | 275 | 317 | 314 |
| | $\Omega_D$ | 87.7 (63.8)$^f$ | 121.3 | 128.5 (121.1)$^f$ | 140.6 | 140.0 |
| n-Butyl (73) | $K_0$ | 2.121 | 1.410 | 1.312 | 1.206 | 1.209 |
| | mass | 121, $n = 2$ | 267 | 298 | 335 | 334 |
| | $\Omega_D$ | 94.0 | 126.1 | 135.5 | 146.4 | 146.1 |
| Iso-butyl (73) | $K_0$ | 2.150 | 1.420 | 1.320 | 1.209 | 1.215 |
| | mass | 117, $n = 2$ | 264 | 295 | 334 | 332 |
| | $\Omega_D$ | 92.8 | 127.0 | 134.7 | 146.1 | 145.5 |

$^a$ Reduced ion mobility (cm$^2$ V$^{-1}$ s$^{-1}$).
$^b$ Cross-sections (Å$^2$).
$^c$ Mass-to-mobility (a.m.u) calculated from Eq. (7) with relative errors < 7%.
$^d$ Mass (a.m.u).
$^e$ $n$ = number of hydration or ammonia.
$^f$ Theoretical calculation.

these complexes in the ionization source of IMS were confirmed based on the IMS-MS evidences [19], in which the mass spectral data were used to confirm the IMS peak assignments and they were also used to demonstrate the presence of a dominant ion in a $m/z$ ratio corresponding to the crown ether-protonated amine complex. Two major mechanisms could be proposed for this gas-phase guest-exchange reaction. In the first proposed mechanism (Eq. (5)), the net reaction is the proton transfer between the ammonium and the unprotonated-alkyl amine. The ammonium is lost as a neutral species and the resulting protonated species remains coordinated to the crown ether whereas the neutral species leaves. The second proposed mechanism (Eq. (6)) involves the protonated amine transfer, in which the alkyl amine should be protonated at first. Since the concentration of alkyl amine is much greater than that of the ionic reactants A.H$^+$ in the ionization source of IMS at any instant of reaction, the first mechanism predicted would be more likely. However, for the purpose of this study, it is no matter whether (5) or (6) mechanism predominate.

$$C.NH_3.H^+ + A \xleftrightarrow{K5} C.A.H^+ + NH_3 \qquad (5)$$

$$C.NH_3.H^+ + A.H^+ \xleftrightarrow{K6} C.A.H^+ + NH_4^+ \qquad (6)$$
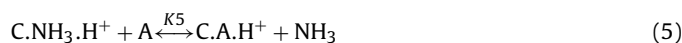
Similar results were obtained for other alkyl amines with 12C4, 15C5, B15C5, and 18C6, after complete mixing of the two solutions, the reduced mobilities are summarized in Table 1.

Different mass–mobility correlation curves have been published in the last few years [27–31]. The regression equation of the mass-to-mobility correlation curve for corona discharge IMS, Eq. (7), is in good agreement with the investigations of Bell et al. [27].

$$\log m = -0.52K_0 + b \qquad (7)$$

The regression equation of the mass-to-mobility correlation curve shows good mass values with $b = 3.11$ for different product ions (relative errors $< \pm 7\%$). The calculated masses for the (C. NH$_4^+$) and (C.A.H$^+$) complexes are given in Table 1.

The mobility of an ion is dependent on the number of collisions it encounters with the buffer gas. Measuring the mobility of ion yields information about the ion's shape and size or, in other words, collision cross section, could be determined. The relationship between the mobility of a product ion and its collision cross section has been derived in detail using kinetic theory [32–34] and is given by:

$$\Omega_D = \frac{3q}{16N_0K_0} \times \left( \frac{2\pi}{\mu k_B T} \right)^{0.5} \qquad (8)$$

where $\Omega_D$ is the collision cross section of the ion, $q$ is the ion charge, $N_0$ is the buffer gas density at standard temperature and pressure (STP), $K_0$ is the reduced mobility, $\mu$ is the reduced mass of the analyte ion and buffer gas, $k_B$ is the Boltzmann constant, and $T$ is the absolute temperature.

The calculated reduced mobilities, masses, and collision cross-sections for the different product ions are given in Table 1. The mobilities of the normal alkyl amines and crown complexes were found to be smaller than the branched isomer. For example, the reduced mobilities of propyl amine and 18C6 complexes are increased from 1.476 to 1.481 cm$^2$ V$^{-1}$ s$^{-1}$ and from 1.245 to 1.265 cm$^2$ V$^{-1}$ s$^{-1}$ for normal and branch isomer respectively. The collision cross-sections calculated for the normal-alkyl isomers and their complexes in all cases were greater than the iso-alkyl amines and complexes. Ion mobilities for the (C.NH$_4^+$) and (C.A.H$^+$) complexes are shown to be decreased by increasing the size of crown ether and guest ion. This may be attributed to the higher collision cross-section of the larger crown ether/guest complexes as well as their higher masses, as predicted by the Mason–Schamp equation [32]. The equilibrium constant for the amine-exchange reaction according to Eqs. (5) and (6) are defined by:

$$K_5 = \frac{[C.A.H^+][NH_3]}{[C.NH_3.H^+][A]} \qquad (9)$$

$$K_6 = \frac{[C.A.H^+][NH_4^+]}{[C.NH_3.H^+][A.H^+]} \qquad (10)$$

As the system is a flowing reaction, the reaction equilibrium occurs in a certain distance from the starting point, i.e. the corona needle. This distance depends on the concentration of the reactants.
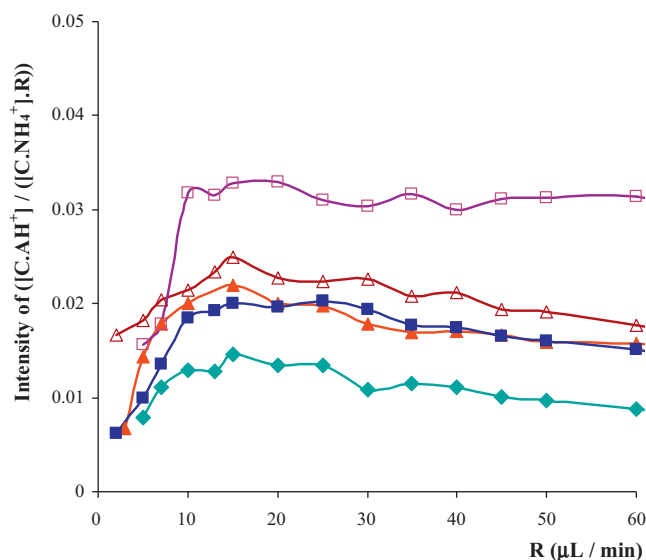
**Fig. 2.** The ratio of [C.A.H⁺]/([C.NH₄⁺].R) as a function of pumping speed (R) at cell temperature 403 K; (□) 15C5-n-propyl amine, (♦) 18C6-alyl amine, (■) 18C6-n-propyl amine, (△) 18C6-n-butyl amine, (▲) 18C6-iso-butyl amine.

The reaction should reach to equilibrium before the ions strike the shutter grid. Hence, the concentration of alkyl amine and crown should be high enough to fulfill this condition. The relative peak intensity of the crown ether-protonated amine complex versus that of the crown ether–ammonium complex ([C.A.H⁺]/[C.NH₄⁺]) is directly proportional to the equilibrium constant under a constant concentration ratio of [NH₃]/[A] or [NH₄⁺]/[AH⁺], which is achieved at a steady state pumping speed that determined by monitoring the ratio of [C.A.H⁺]/([C.NH₄⁺].pumping speed) as the pumping speed was varied.

By increasing the pumping speed, the concentration of both alkyl amine and crown ether in the IMS are increased until reactions (5) or (6) reach to equilibrium in the ionization source and a steady state. Therefore, as shown in Fig. 2, the plotted curve of [C.A.H⁺]/([C.NH₄⁺].pumping speed) versus pumping speed, which is proportional to the alkyl amine concentration, approaches an asymptote at the steady state condition. At each temperature, ion mobility spectra were then obtained at a constant pumping speed, in which $d([C.A.H^+]/([C.NH_4^+])/dR \approx 0$. Fig. 3 illustrates the behavior of temperature dependency of product ions for different crown ether–alkyl amine complexes. As expected, all peaks shift towards shorter drift times as the temperature increases. It is obvious from Fig. 3 that the relative intensity of the product ion response peaks changes as a function of temperature. There is a decrease in intensity of the C.A.H⁺ response and an increase in that of C.NH₄⁺ by

increasing the temperature. These observations reveal that the mentioned exchange reaction is an exothermic reaction. In addition, a peak in drift time longer than that of C.A.H⁺ peak, which assigned to dimmer form of C.NH₄⁺.C, is decreased as the temperature is increased. The presence of dimer of crown ether does not have any interference in the exchange equilibrium.

The relative stability constants of crown ether–alkyl ammonium complexes values were calculated and the results are summarized in Table 2. A look at Table 2 reveals that the relative stabilities of complexes under IMS conditions very significantly depend on the size of both the alkyl ammonium cation and the crown ether. The enthalpy changes of reactions (5) or (6) are referred to the guest-exchange affinity of given crown ethers. To obtain $\Delta H^\circ$ values, the mentioned reaction should be preceding under the equilibrium condition, which is achieved based on Tabrizchi work [14] for relative proton affinity measurement.

At experimentally steady state condition, slope of ln ([C.A.H⁺]/[C.NH₄⁺]) versus 1/T directly gives the enthalpy change related to the guest-exchange affinity for displacement of ammonium with alkyl amine for selected crown ethers and alkyl amines. Van't Hoff plots (Fig. 4) yield the $\Delta H^\circ$ values (Table 2). Obtained guest-exchange affinity reveals that increasing cavity size of crown ethers would result in the decrease of ammonium-exchange affinity. Generally, the observed order of ammonium-exchange-affinities of crown ethers is as follows: 12C4 > B15C5 ∼ 15C5 > 18C6. This trend is valid for all of five selected amine in similar values and it is inversely proportional to the order of gas phase ammonium affinity of each crown by previously studies [9], which is also employed as a verification for our proposed mechanism.

Liou [9,10] showed that the crown ethers with larger cavity sizes demonstrate the greatest ammonium affinities among all of the polyethers. The hydrogen bonding strength in adduct 18C6–NH₄⁺ is so strong that the displacement of ammonium with any alkyl amine is difficult, consequently 18C6 shows low tendency to undergo any guest-exchange reaction and yields the lowest ammonium-exchange affinity among the crown ethers whereas 12C4 shows the greatest guest-exchange affinity among our considered crown ethers. It is noted that 12C4 has the lowest ammonium affinity among crown ethers, which is attributed to its smaller cavity size (0.6–0.75 Å) relative to the ammonium ion (1.43 Å) and it has four oxygen atoms for possible participations in the hydrogen bonding with ammonium ion. Therefore, the ammonium ion in this weakly bound complex is easily exchanged with the alkyl amines. Furthermore, the critical energies for the fragmentation of crown ether–ammonium ion complexes have been estimated by Colorado et al. [35] using threshold collisional activation measurements in a quadrupole ion trap mass spectrometer. The obtained data show an increase in the number of donor oxygen atoms, which lead to optimal hydrogen bonds, imparts greater ammonium ion–crown ether binding energy to the non-covalent complexes. The presence

**Table 2**
The relative stability constants of crown ether–alkyl ammonium complexes values at 400 K and enthalpy change of the guest-exchange affinity (displacement of ammonium with alkyl amine for different crown ethers), Eq. (5).

| Crown | Amine | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 12C4 | | 15C5 | | B15C5 | | 18C6 | |
| | $K_n/K_{iso}$ | $-\Delta H^\circ$ kJ mol⁻¹ | $K_n/K_{iso}$ | $-\Delta H^\circ$ kJ mol⁻¹ | $K_n/K_{iso}$ | $-\Delta H^\circ$ kJ mol⁻¹ | $K_n/K_{iso}$ | $-\Delta H^\circ$ kJ mol⁻¹ |
| Alyl | – | 43.23 | – | 30.18 | – | 31.59 | – | 20.74 |
| n-Propyl | 0.25 | 44.39 | 13.32 (33.9)[b] | 23.69 | 0.61 | 30.18 | 2.16 | 18.54 |
| Isopropyl | $(0.08/T-1.4)$[a] | 43.73 | $(-0.31/T+2.59)$[a] | 26.27 | $(-0.04/T-0.49)$[a] | 30.51 | $(-0.28/T+0.77)$[a] | 21.37 |
| n-Butyl | 3.56 | 40.82 | 0.18 | 28.85 | 2.66 | 27.69 | 0.58 | 19.70 |
| Iso-butyl | $(-0.27/T+1.27)$[a] | 43.07 | $(-0.16/T+1.72)$[a] | 31.01 | $(-0.49/T+0.98)$[a] | 31.76 | $(0.3/T-0.55)$[a] | 17.21 |

[a] Equation in brackets show temperature dependency of relative logarithm of stability constants (ln $K_n/K_{iso}$).
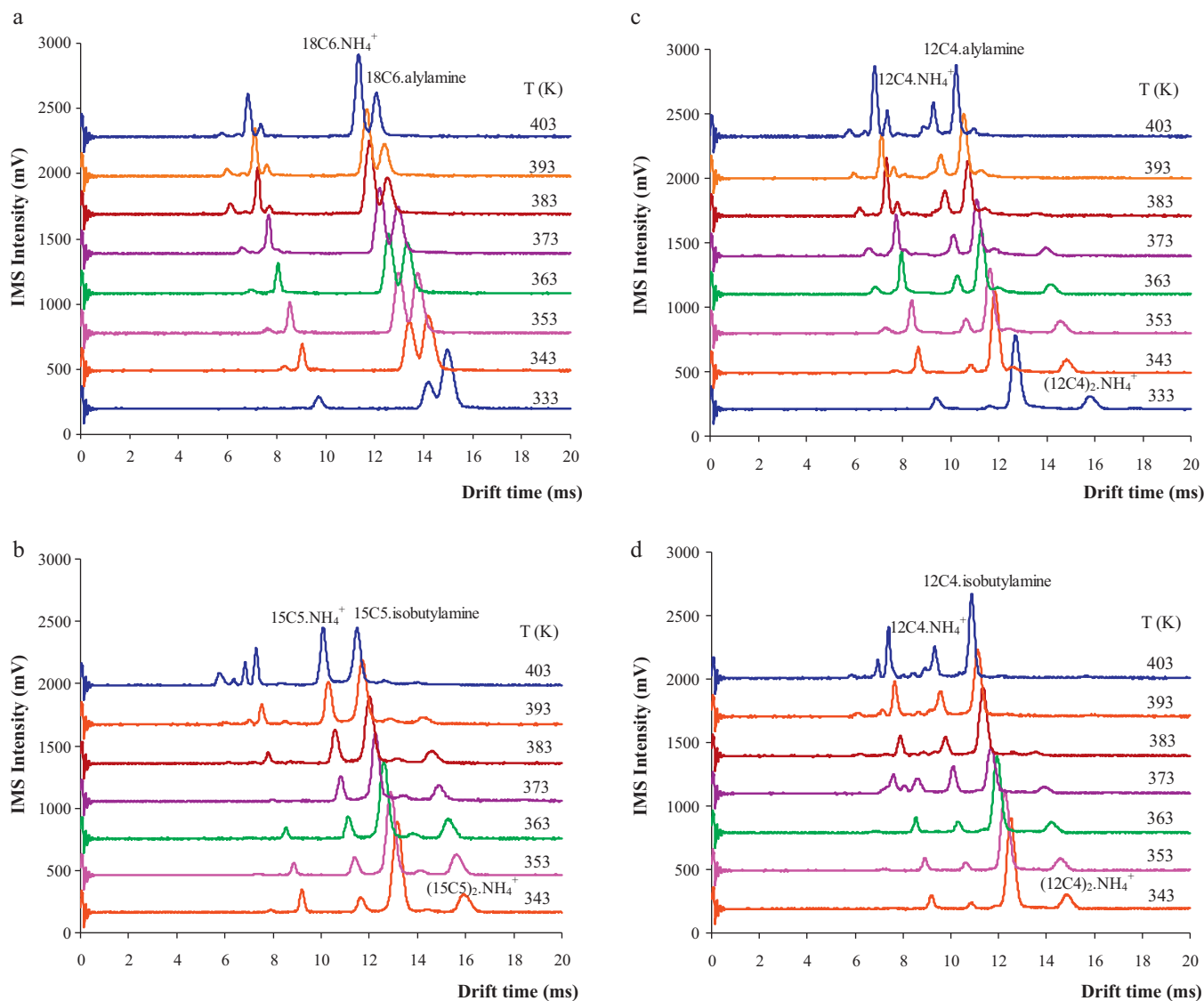[b] Theoretical calculation.

**Fig. 3.** The temperature behavior dependency of product ion response (a) 18C6–alylamine, (b) 15C5–iso-butlamine, (c) 12C4–alylamine and (d) 12C4–iso-butyl amine at different temperatures.

of benzene ring in crown ether does have significant influences on the ammonium-exchange affinity of B15C5 relative to 15C5. Overall ordering of ammonium-exchange affinities for B15C5 and 15C5 are parallel with each other with the exception of the iso and n-propylamine complexes. This finding confirms that the conformational structures of crown ethers have significant influences on the ammonium-exchange affinity in the gas phase. In addition to the ammonium-exchange affinity, the reduced mobility and collision cross section values for 15C5 and B15C5 alkyl ammonium complexes also differ with each other. In all cases, B15C5–alkyl ammonium complexes have higher collision cross section values than 15C5–alkyl ammonium complexes.

The differences in guest-exchange affinities between the lowest and highest members of the series of crown ether complexes also varies with the guest species in the order of normal-alkyl amine < iso-alkyl amine (Table 2). The enthalpy of guest-exchange affinity of crown ethers for the iso-alkyl amine isomers are more negative than the normal-alkyl amine, and the results are in good agreements with the decrease of collision cross-section.

In the case of aza18C6, no complex formation was observed with alkyl amine. Obviously, the formation of new complexes is not favored. This observation is consistent with the result previously established by Julian and Beauchamp [36] who investigated the abilities of 18C6, aza18C6, and a simple lariat crown ether derivative of aza18C6 to form adducts in the gas phase with small, lysine containing peptides. Their study revealed that 18C6 selectively forms adducts in the gas phase while substitution of nitrogen for oxygen inhibits the formation of non-covalent adducts with the model peptides. They attributed this to the high proton affinity of aza18C6, which serves to preferentially remove a proton from any alkyl ammonium ion upon introduction to the gas phase. The proton affinity of aza18C6 is determined by the kinetic method to be $250 \pm 1$ kcal/mol, which is nearly 20 kcal/mol higher than the proton affinity of 18C6. Through protonation of aza18C6, a highly symmetrical structure is generated, in which three most distant oxygens are able to fold back and hydrogen bond with the proton, which is localized on the nitrogen and causes contraction of the guest cavity, which will lead to the loss of any interaction with a proximate primary amine. This structure for protonated aza18C6 could be confirmed through comparison of reduced mobility and collision cross-section values for protonated aza18C6 ($K_0 = 1.407$ cm$^2$ V$^{-1}$ s$^{-1}$, $\Omega_D = 127.0$ Å$^2$) and 18C6.NH$_4^+$
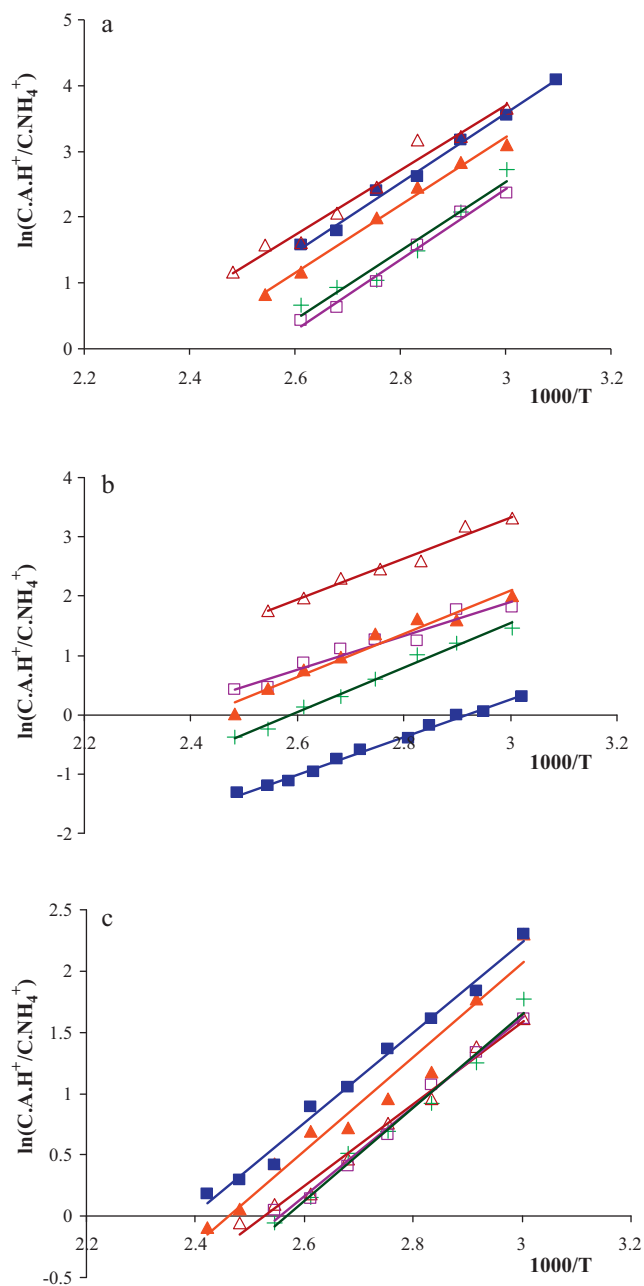
**Fig. 4.** Van't Hoff plot for the guest-exchange reaction between ammonium/alkyl amine (a) 12C4, (b) 15C5 and (c) B15C5 complexes; (+) alyl amine, (□) n-propyl amine, (■) iso-propyl amine, (▲) iso-propyl amine, (△) n-butyl amine.

($K_0 = 1.346\,cm^2\,V^{-1}\,s^{-1}$, $\Omega_D = 132.3\,\text{Å}^2$). Since protonated aza18C6 has symmetrical structure and lower mass due to adduction with proton instead of ammonium (results was not shown for aza18C6 in Tables), its collision cross-section is lower than that of 18C6.NH$_4$$^+$.

In order to investigating the dependencies of the stability and structure of crown–alkyl amine complexes to dimension of the alkyl ammonium ion, pairs of isopropyl and n-propyl ammonium cations were selected that there have a same mass and theoretical calculations were carried out on their 15-crown-5 complexes. The operating conditions were the same in both cases, so the observed variation in the complexation must arise from differences in collision cross-section (87.7 and 89.0 Å$^2$ for iso-propyl and n-propyl ammonium respectively) and, presumably, in the gas-phase conformations of these ions. Ab initio studies using HF/6-31G* optimization, without any constraint of host, guests and its

propyl ammonium complexes confirm that low energy conformers of protonated n-propyl amine/15-crown-5 relative to the protonated iso-propyl amine/15-crown-5 complexes with an estimated collision cross-section that is smaller than experimental values (Table 1). The initial structures of 15-crown-5, iso-propyl and n-propyl ammonium molecules were created by using HyperChem [37]. All ab initio calculations were carried out using the GAUSSIAN-98 package [38].

From the theoretical data, the cross section area and thermodynamic parameters of iso- and n-propyl ammonium complex formation reactions with 15-crown-5 in gas phase were calculated. It is noteworthy that a comparison between the relative stability constants value reported in Table 2 with the corresponding relative stability constants obtained in atmospheric pressure gas phase, there is a good agreement between theoretical and experimental relative stability constants values.

## 4. Conclusion

Non-covalent crown ether–ammonium ion complexes bound only by hydrogen bonds can be generated in the gas phase by ion mobility spectrometry and in the presence of an alkyl amine proceed a guest-exchange reaction. The value of guest-exchange affinity of crown ethers estimated from the standard enthalpy change for mentioned above reaction. Comparisons of obtained value of guest-exchange affinities for given crown ether–ammonium ion complexes reveal a general inverse relationship between the primary complex stability, which is directly proportional to ammonium affinity of these crown ethers and guest-exchange affinity. 18C6–ammonium and 12C4–ammonium complexes show the lowest and the highest guest-exchange-affinity respectively, among the series compared in this study. This trend suggests that the dissociation of primary crown ether–ammonium complexes is the determinant step in guest-exchange reaction even though a new more strongly bound complex formed. Complexes of 15C5 with two different normal and iso-alkyl amines showed a gas phase selectivity binding to normal-alkyl amines relative to iso-alkyl amines.

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