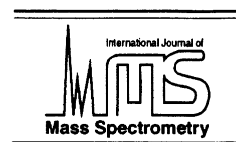

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Noncovalent inclusion complexes of protonated amines with crown ethers

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Abstract

The formation of stable noncovalent inclusion complexes in the gas phase between crown ethers and protonated amines has been investigated by the use of quadrupole ion trap mass spectrometry. The effect of varying the substituents on protonated amines of the type $[RNH_3]^+$ ($R = CH_3(CH_2)_2$, $C_6H_5(CH_2)_2$, $O_2NC_6H_4(CH_2)_2$ or $C_6H_5CH_2C(H)COOH$) was found to have a strong influence on the relative intensities of the inclusion complexes formed with crown ethers in competitive gas-phase reactions. Relative intensity measurements indicate that the introduction of an aromatic ring on the protonated amine or crown ether results in the formation of a less stable complex than the nonaromatic protonated propylamine/18-crown-6 adduct. The relative affinities of protonated propylamine and phenethylamine for 18-crown-6 and of phenylalanine for phenyl-18-crown-6 and 18-crown-6 are supported by tandem mass spectrometric and ligand exchange data. The overall order of stabilities for the noncovalent complexes investigated by ion trap mass spectrometry can be assigned tentatively as: $[p + H + 18\text{-crown-6}]^+ > [p + H + \text{benzo-18-crown-6}]^+ \sim [(r)\text{-phenyl} + H + 18\text{-crown-6}]^+ = [(s)\text{-phenyl} + H + 18\text{-crown-6}]^+ > [(s)\text{-phenyl} + H + (s)\text{-phenyl-18-crown-6}]^+ > [\text{nitro} + H + 18\text{-crown-6}]^+ > [\text{phen} + H + 18\text{-crown-6}]^+ \sim [\text{phen} + H + \text{benzo-18-crown-6}]^+$, where p = propylamine, phen = phenethylamine, phenyl = phenylalanine, and nitro = 4-nitrophenylalanine. (Int J Mass Spectrom 188 (1999) 53–61) © 1999 Elsevier Science B.V.

Keywords: Crown ethers; Amines; Inclusion complexes; Ion trap mass spectrometry

1. Introduction

The study of host–guest chemistry in the gas phase has received considerable interest only in recent years, despite extensive investigations in the solution phase since the discovery of crown ethers in 1967 [1,2]. Crown ethers are particularly useful in modelling biologically relevant ion transport processes, antibody–antigen association, and enzyme catalysis. Intermolecular and intramolecular hydrogen bonds and other electrostatic interactions are also important interactions in solution chemistry molecular recognition. The study of the gas-phase chemistry of inclusion complexes in the mass spectrometer is particularly important, because these noncovalent interactions may be observed in the absence of solvent effects, which opens up new avenues for understanding some of the fundamental details of molecular recognition.

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Dedicated to Brian Green for his many innovative contributions to mass spectrometry instrument development and for his tireless help in teaching us how to take advantage of them.

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The area of host–guest chemistry in the mass spectrometer has been reviewed recently [3]. The first reports of gas-phase formation of crown ether complexes were published in the mid-1980s and describe the reactions of transition metal ions with 12-crown-4 in a Fourier transform-ion cyclotron resonance (FT-ICR) mass spectrometer [4,5]. In the same year the formation of host–guest complexes between RNH_3^+ ($R = CH_3$, c-C_6H_{11}), $[(CH_3)_3NH]^+$, and $[\text{pyridine} + H]^+$ and the crown ethers (12-crown-4, 15-crown-5, and 18-crown-6) were described [6]. These crown ethers were observed to be much more efficient ligands than their acyclic analogues. There have been several other reports in recent years on the interaction of crown ethers with alkali metal ions [7–9], other metal ions [10], and anions [11,12].

The ammonium ion has been shown to demonstrate unusually high gas-phase affinities for the crown ethers 18-crown-6 and 21-crown-7 relative to the acyclic ethers [13,14]. This is attributed to the large cavity sizes (1.34–1.43 Å and 1.68–2.12 Å, respectively) being more able to accommodate the configuration necessary for optimum hydrogen bond interaction to the bulky tetrahedral ammonium ion (radius = 1.43 Å). The kinetic method [15] and the ligand exchange technique [16] were used to determine this high affinity of the ammonium ion for 18-crown-6 and 21-crown-7 [17].

There have been few accounts of the gas phase mass spectrometric complexation reactions between crown ethers and protonated amine ions since Meotner's preliminary investigations [6]. A study on the noncovalent inclusion complexes formed between a variety of protonated amines and the crown ethers 12-crown-4, 15-crown-5, and 18-crown-6 has been reported [18], in which the nature of the hydrogen bond interactions of the ion complexes was evaluated by comparison of their collisionally activated dissociation (CAD) spectra. The amines investigated were propylamine, 2,5-dimethylpyrrole, 2-chloro-6-methylpyridine, 2-methylaziridine, pyridine, 2-aminoethanol, 3-aminopropanol, diethylamine, 3,5-lutidine, ethylene diamine, and 4- and 5-aminobutanol. Weakly bonded complexes were found to dissociate following collisional activation to form intact protonated polyether molecules and/or ammonium ions by simple hydrogen bond cleavage. These weakly bonded complexes included all the 12-crown-4 inclusion complexes and all the 15-crown-5 complexes except those formed with propylamine, 2-methylaziridine, 2-aminoethanol, and ethylene diamine. Those complexes strongly bond by multiple hydrogen bonds, such as the complexes between 18-crown-6 and propylamine, 2-methylaziridine, 2-aminoethanol, 3-aminopropanol, and ethylene diamine dissociate not only to form the protonated polyether and/or ammonium ions, but also by extensive covalent bond cleavage of the protonated ether skeleton. It is only with the larger crown ethers that the multiple hydrogen bonding needed for the formation of a strongly noncovalently bonded complex can occur. In cases where the crown ether host can only bind to the amine part of the molecule, such as ion complexes of crown ethers with methylhydrazine and tosylhydrazine, covalent bond cleavage of the nitrogen–sulphur bond of the guest substrate occurs [19]. These results suggest that the association energy for the multiple hydrogen-bonding interactions of the crown ether/ammonium ion complex is of the same order as the covalent macrocyclic or nitrogen–sulphur bonds.

Recently, complexation reactions between modified crown ethers and substituted ammonium ions have been used to enable chiral recognition by mass spectrometry. Fast atom bombardment (FAB) and FT-ICR mass spectrometry have been used in enantioselective recognition of diastereomeric host–guest complexes between chiral crown ether hosts and chiral organic ammonium guests on the basis of the relative peak intensity (RPI) [20]. This work has included chiral differentiation of the enantiomers of phenylalanine methyl esters [21,22] and [1-(1-naphthyl)ethyl]amine [23,24].

This article reports a study of the gas-phase interactions of a range of crown ethers with aromatic and aliphatic protonated amines in a quadrupole ion trap. The effect of amine and crown ether structure on the stability of the crown ether/amine complexes has been investigated by competitive gas-phase reactions, tandem mass spectrometry, and ligand exchange experiments in the ion trap.

2. Experimental

Experiments were performed by using a quadrupole ion trap mass spectrometer (Finnigan MAT ITMS, San Jose, CA), operated at 120 °C. Helium bath gas pressure was maintained at 1×10^{-4} torr (uncorrected) measured by the ion trap vacuum chamber ion gauge. All chemicals were obtained from Aldrich Chemical Co. (Dorset, UK) except (s)-phenyl-18-crown-6, which was obtained from Dr. G.R. Stephenson (School of Chemical Sciences, University of East Anglia, Norwich, UK), and were used without further purification. Reaction times were varied by using key sequences [25] to increase the reaction period automatically. Total reaction times were calculated from the end of the protonated amine isolation period, taking into account electron multiplier warmup and the time taken to eject the $[M + H]^+$ ion. Key sequences were also employed in the tandem mass spectrometry studies of the inclusion complexes involving the variation of the auxiliary rf tickle voltage (0–3 V) applied to the end cap electrodes to optimise product ion yields [26]. Isolation of the inclusion complexes was achieved by using the filtered noise technique [27], with a low mass cut off of 50 amu.

Propylamine was introduced via a leak valve (Meggit Avionics, Portsmouth, UK) at a pressure of 4×10^{-6} torr (uncorrected). Phenethylamine (0.05 M), 4-nitrophenylethylamine (0.05 M), 18-crown-6 (0.1 M), and benzo-18-crown-6 (0.1 M) were prepared as solutions in dichloromethane. In a typical experiment a 1 μl aliquot of the appropriate amine solution was placed on the direct insertion probe together with a 1 μl aliquot of crown ether solution. The solvent was removed and the probe inserted into the mass spectrometer vacuum system and heated to 110 °C. The amines were ionised by electron ionisation and held in the trap for 50 ms to form a protonated $[M + H]^+$ ion by self-chemical ionisation (CI) [28]. The $[M + H]^+$ ion was isolated by using the filtered noise technique and allowed to react with the neutral crown ether vapour for ~100 ms before mass spectral acquisition by using a mass-selected instability scan. For the experiments comparing the relative stabilities of the protonated propylamine and phenylethylamine complexes with crown ethers, the intensities of protonated amine ions were adjusted to obtain similar ion counts before reaction with the crown ether.

A constant pressure of (r)- or (s)-phenylalanine was achieved inside the mass spectrometer by heating a solid sample of phenylalanine to 300 °C on the solids probe. The ionisation period (typically 1 ms) was adjusted to ensure similar intensities for the $[M + H]^+$ ion for both (r) and (s)-phenylalanine. In experiments comparing the relative affinity of protonated phenylalanine for (s)-phenyl-18-crown-6 and 18-crown-6, a 1 μL sample of the 0.05 M solution containing equimolar amounts of 18-crown-6 and (s)-phenyl-18-crown-6 was introduced on the solids probe and heated to 150 °C. The inclusion complex between either protonated phenylalanine and (s)-phenyl-18-crown-6 or protonated phenylalanine and 18-crown-6 was then isolated by using the filtered noise technique and retained in the trap for 100 ms. The ions were then ejected from the trap and a spectrum was acquired (40 scans averaged).

3. Results and discussion

3.1. Reactions of protonated amines with benzo-18-crown-6 and 18-crown-6

Host–guest complexes between protonated amines and crown ethers are formed readily in the ion trap. An example of the variation in adduct ion intensity with reaction time is shown in Fig. 1 for the formation of the protonated propylamine/benzo-18-crown-6 adduct. The product ion intensity (*m/z* 372) increases rapidly as the reaction approaches equilibrium in the ion trap and reaches a steady state after ~100 ms. At longer reaction times (>200 ms) the product ion intensity in the trap is affected by losses arising from competing ion–molecule reactions and ion scattering, which are species and mass dependent. The reaction profiles and time scales for other protonated ether/crown ether combinations studied were similar with little change in ion intensities at times greater than

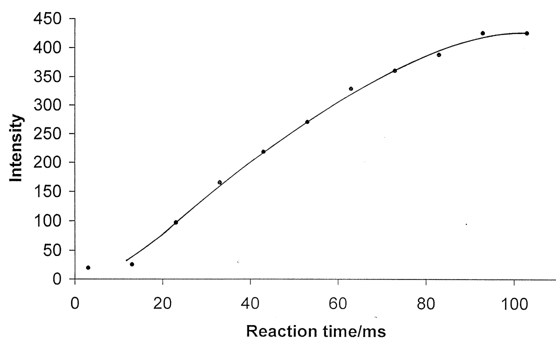

Fig. 1. Variation of adduct ion intensity (*m/z* 372) with reaction time for the reaction of protonated propylamine with benzo-18-crown-6.

100 ms. Product ion ratios for competitive reactions also showed little variation at longer reaction times (<200 ms). Because these variations were small, the observed complex ion intensity ratios at ~100 ms were not corrected for the effects of competing ion–molecule and scattering processes.

The relative affinities of 18-crown-6 and benzo-18-crown-6 for the protonated amines in the ion trap were investigated by competitive gas-phase reactions of $[R–CH_2CH_2NH_3]^+$ (where R = CH_3, C_6H_5, or $O_2NC_6H_4$) with these crown ethers. Isolation of the $[M + H]^+$ ions for propylamine and phenethylamine in the ion trap, for 100 ms in the absence of crown ether gave a spectrum [Fig. 2(a)] in which the ions at *m/z* 60 ($[C_3H_7NH_3]^+$) and *m/z* 122 ($[C_6H_5(CH_2)_2NH_3]^+$) have similar ion intensities. However, the spectrum observed following the competitive reaction with benzo-18-crown-6 present [Fig. 2(b)], showed adduct ions for both propylamine and phenethylamine at *m/z* 372 and *m/z* 434, respectively. There is also a small amount of protonated benzo-18-crown-6 at *m/z* 313, because of either the loss of neutral amine from the complexes or direct proton transfer from the protonated amine to the crown ether. The higher intensity of the benzo-18-crown-6 complex ion at *m/z* 372 indicates that this crown ether has a greater affinity for protonated propylamine than protonated phenethylamine, if the ion intensities are taken to represent relative affinities under the conditions of the ion trap experiment. The stability of the phenylethylamine adduct is therefore reduced compared to the protonated propylamine/benzo-18-crown-6 complex as a result of the presence of the aromatic ring on the amine.

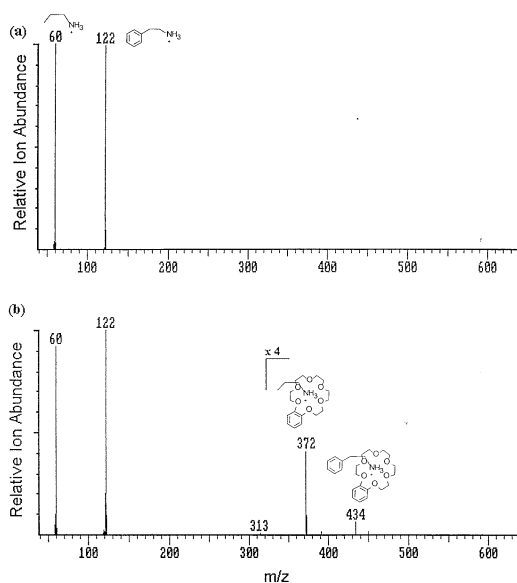

Fig. 2. Product ion mass spectra resulting from the reaction between the isolated MH^+ ions of propylamine and phenethylamine with (a) no crown ether present and (b) benzo-18-crown-6 present.

The relative intensities of the protonated propylamine and phenethylamine complexes with 18-crown-6 were studied by using a similar experimental procedure. The resulting spectrum (Fig. 3) shows an increased intensity for the protonated propylamine/18-crown-6 inclusion complex (*m/z* 324) compared to the protonated phenethylamine/18-crown-6 complex (*m/z* 386). This indicates that the 18-crown-6 also has

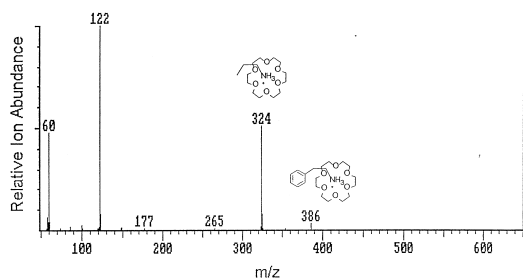

Fig. 3. Product ion mass spectrum resulting from the reaction (100 ms) of the MH^+ ions of propylamine and phenethylamine with 18-crown-6.

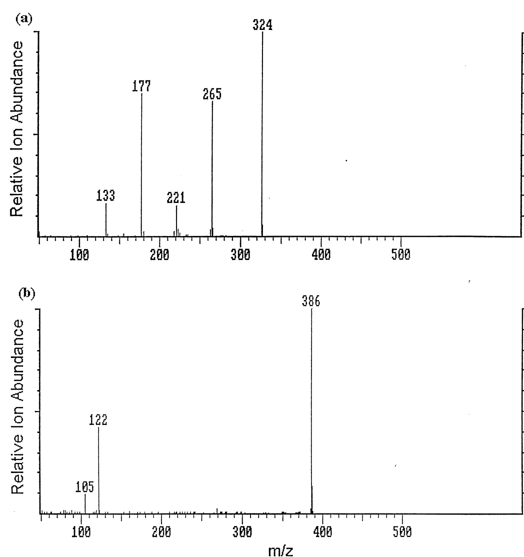

Fig. 4. Tandem mass spectrometry of the inclusion complexes between 18-crown-6 and (a) MH^+ of propylamine (*m/z* 324) and (b) MH^+ of phenethylamine (*m/z* 386).

a greater affinity for the propylamine than for phenethylamine because the aromatic ring on phenethylamine destabilises the crown ether adduct. The result of the relative intensity experiment was supported by tandem mass spectrometry of the two inclusion complexes using collisionally activated dissociation that yield significantly different product ion spectra (Fig. 4). The product ion spectrum of the protonated propylamine/18-crown-6 inclusion complex [Fig. 4(a)] showed fragment ions at *m/z* 265 (loss of neutral propylamine), and at *m/z* 221, *m/z* 177, and *m/z* 133 that correspond to the loss of 1–3 ethylene oxide units, respectively, together with neutral propylamine from the crown ether ring. This fragmentation of the crown ether is associated with a strongly bonded crown ether adduct [18]. In comparison, the product ion spectrum of the protonated phenethylamine/18-crown-6 inclusion complex ion at *m/z* 386 [Fig. 4(b)] gave two fragment ions at *m/z* 122, arising from the loss of the neutral 18-crown-6 to form protonated phenethylamine, and a less intense product ion at *m/z* 105. The *m/z* 122 product ion suggest a weakly bonded crown ether complex [18], arising from the poor interaction of the quaternary ammonium ion and the crown ether in the presence of the aromatic ring. The *m/z* 105 ion may arise from loss of 18-crown-6 and ammonia, or cleavage of the amine C–N bond. If the latter process occurred, then this would suggest a more strongly bound ammonium ion. However, the absence of fragmentation products from the crown ether ring and the prominence of the *m/z* 122 ion indicates that the phenethylamine ion is less strongly bonded than the propylamine adduct [18].

The effect of introducing a nitro substituent into the aromatic ring was investigated for the reactions of phenethylamine and 4-nitrophenethylamine with benzo-18-crown-6. The presence of an electron deficient aromatic group in 4-nitrophenethylamine might be expected to enhance the π–π interaction with the aromatic group on the benzo-18-crown-6. The spectrum obtained following the reaction of phenethylamine and 4-nitrophenethylamine with benzo-18-crown-6 produced a slightly greater intensity for the complex between 4-nitrophenethylamine and benzo-18-crown-6 at *m/z* 479 compared to the unnitrated inclusion complex at *m/z* 434. The greater intensity of the protonated 4-nitrophenethylamine/benzo-18-crown-6 inclusion complex suggests weak π–π bonding increases the stability of this complex.

The increased stability of the protonated propylamine inclusion complexes with 18-crown-6 and benzo-18-crown-6 compared to the corresponding phenethylamine complexes (Figs. 2 and 3), inferred from ion trap intensity ratios, suggests that introduction of the aromatic ring into the amine lowers the stability of the complex significantly. This is further supported by the observation of product ions corresponding to a strongly bonded complex for the protonated propylamine/benzo-18-crown-6 ion and product ions corresponding to a less strongly bonded complex for the protonated phenethylamine/benzo-18-crown-6 adduct. The increased stability of the 4-nitrophenethylamine/benzo-18-crown-6 inclusion complex compared to the phenethylamine/benzo-18-crown-6 complex indicates that the stability of the protonated 4-nitrophenethylamine/benzo-18-crown-6 inclusion complex lies between that of the inclusion complexes formed between propylamine/benzo-18-crown-6 and phenethylamine/benzo-18-crown-6.

These observations suggest the following order of affinity for the crown ether/amine noncovalent inclusion complexes based on ion trap intensity ratios and tandem mass spectrometric data: $[p + H + 18\text{-crown-6}]^+ > [\text{phen} + H + 18\text{-crown-6}]^+$; and $[p + H + \text{benzo-18-crown-6}]^+ > [\text{nitro} + H + \text{benzo-18-crown-6}]^+ > [\text{phen} + H + \text{benzo-18-crown-6}]^+$, where p = propylamine, nitro = 4-nitrophenethylamine, and phen = phenethylamine.

3.2. Reactions of phenylalanine with (s)-phenyl-18-crown-6 and 18-crown-6

The noncovalently bonded inclusion complexes formed between protonated amines and crown ethers were further investigated for the reactions of (s) and (r)-phenylalanine ($R_1R_2R_3C\text{–}NH_3^+$ ion, where $R_1 = C_6H_5CH_2$, $R_2 = H$, $R_3 = COOH$) with (s)-phenyl-18-crown-6 and 18-crown-6. Isolation of the $[M + H]^+$ (*m/z* 166) ion from (s)-phenylalanine in the absence of crown ether in the mass spectrometer, yielded only the *m/z* 166 ion. In comparison, the spectrum resulting from the introduction of (s)-phenyl-18-crown-6 into the mass spectrometer showed the formation of an inclusion complex at *m/z* 506. Fragment ions were also present at *m/z* 386, as a result of the elimination of $C_6H_5C_2H_3O$ from the adduct, at *m/z* 341, assigned to protonated (s)-phenyl-18-crown-6 resulting from the loss of (s)-phenylalanine, and at *m/z* 221, *m/z* 177, *m/z* 133 corresponding to the loss of 1, 2, or 3 ethylene oxide units together with the elimination of phenylalanine and $C_6H_5C_2H_3O$. These fragment ions are analogous to those seen in the low energy collisionally activated dissociation mass spectra of the 18-crown-6/ammonium ion complex reported by Maleknia and Brodbelt [19] and this extensive fragmentation of the inclusion complex suggests adduct formation may be strongly exothermic. An alternative explanation is that the observed fragmentation may arise because the protonated phenylalanine ions were not thermalised prior to reaction with the crown ether. It is unlikely that ions retained in the trap have a fully thermalised energy distribution because of the translational excitation of the applied rf trapping potential. However, recent measurements of the effective ion temperatures in the presence of helium buffer gas suggest that the internal energy of the trapped ions following collisional cooling is close to thermal [29].

The reaction of the $[M + H]^+$ ion of (s)-phenylalanine with (s)-phenyl-18-crown-6 and 18-crown-6 produced two inclusion complex ions at *m/z* 506 and *m/z* 430, respectively. Ions at *m/z* 341 and *m/z* 265 were also observed, relating to the protonated crown ethers that arise from direct proton transfer or elimination of (s)-phenylalanine from the inclusion complexes. Fragment ions at *m/z* 89, *m/z* 133, *m/z* 177, *m/z* 221, and *m/z* 386 were also observed. The $[M + H]^+$ from (s)-phenylalanine appears to have a greater affinity for 18-crown-6 compared to (s)-phenyl-18-crown-6, on the basis of the product ion intensity ratios, and this would suggest little π–π interaction between the aromatic rings. This is consistent with the earlier observation that the $[M + H]^+$ ion from propylamine has a greater affinity for benzo-18-crown-6 than the $[M + H]^+$ ion from phenethylamine. The possibility of chiral recognition of (r) and (s)-phenylalanine by (s)-phenyl-18-crown-6 was investigated by the relative peak intensity method [20]. In this approach the peak intensity of the target host (M)-guest (A^+) complex ion, $I([M + A]^+)$, is compared to that of an internal standard (18-crown-6) host (R)-guest (A^+) ion $I([R + A]^+$: the RPI value = $I([M + A]^+)/I([R + A]^+)$. The RPI values (averaged over three experiments) were calculated to be 0.180 ± 0.020 and 0.209 ± 0.013 for the (s)- and (r)-phenylalanine, respectively. The RPI values for the two enantiomers therefore show a small, but probably not significant difference in affinity for the (s)-phenyl-18-crown-6.

Tandem mass spectrometry of the (s)-phenylalanine/(s)-phenyl-18-crown-6 inclusion complex using collisionally activated dissociation with resonance excitation was employed to investigate this adduct further. The main product ion at *m/z* 341 (44% of precursor ion) resulted from the elimination of phenylalanine from the ring. The formation of low intensity product ions at *m/z* 89 (2%), *m/z* 133 (7%), *m/z* 177 (1%), and *m/z* 221 (5%) are because of fragmentation of the ring following elimination of

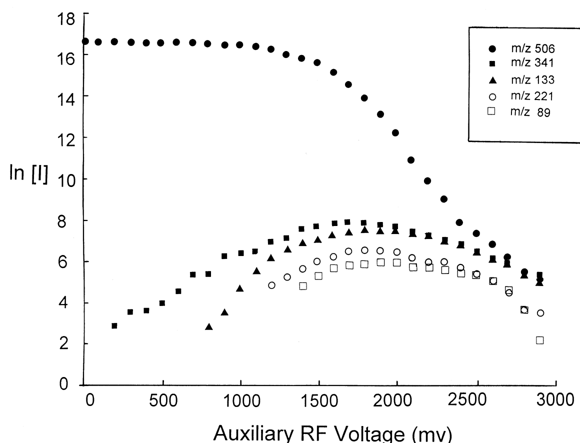

Fig. 5. Variation of ion intensity with CAD auxiliary rf voltage for the [s-phenylalanine + H + s-phenyl-18-crown-6]$^+$ inclusion complex.

$C_6H_5C_2H_3O$ and phenylalanine. A small amount of protonated (s)-phenylalanine at *m/z* 166 (4%) was also present in the spectrum. The main product ion being the decomplexation of phenylalanine from the crown ether would suggest a weakly bonded complex, however the formation of low intensity skeletal fragment ions would suggest that the stability of this complex lies between that of the propylamine/benzo-18-crown-6 and phenethylamine/18-crown-6 complexes [18].

The effect of the variation of auxiliary rf (tickle) voltage at a constant tickle time (1 ms) and working point (q_z = 0.1) on the CAD spectra of the [(s)-phenylalanine + H + (s)-phenyl-18-crown-6]$^+$ ion (*m/z* 506) was evaluated to obtain additional information about the dissociation of the complex (Fig. 5). As the amplitude of the auxiliary voltage is increased, the average internal energy deposition should also increase. Comparison of the relative appearance thresholds for the decomplexation process and the ring fragment ions reveals a small offset between the threshold for decomplexation (formation of *m/z* 341) at <250 mV and the threshold for skeletal fragmentation (formation of *m/z* 221, 133, and 89) at 800 mV (Fig. 5). These observations confirm that there is a significant difference in the energy needed to promote decomplexation versus skeletal fragmentation. This is consistent with the energy resolved mass spectra of the [15-crown-5 + H + 2-aminoethanol]$^+$ complex, where a threshold of about 20 mV activation voltage was reported [18]. The tandem mass spectrometry of the [(r)-phenylalanine + H + (s)-phenyl-18-crown-6]$^+$ inclusion complex showed virtually identical fragment ions with a similar energy resolved mass spectrum to the S,S inclusion complex.

The ligand exchange technique [17] was also employed to give an indication of the relative ion binding affinities of the inclusion complexes of phenylalanine with phenyl-18-crown-6 and 18-crown-6. In this method a protonated amine/crown ether inclusion complex is isolated and allowed to interact with a second uncomplexed crown ether molecule. Observation of the transfer of the protonated amine to the second crown ether indicates that this second crown ether has a higher gas-phase affinity for the protonated amine. The reaction needs to be done in the reverse direction to confirm the order of affinities and the concentrations of the two crown ethers must be approximately equal. The order of affinities for ammonium ion/crown ether systems determined by the ligand exchange technique have been shown to agree with the order established by using equilibrium methods in a high pressure mass spectrometer [17].

The spectrum resulting from the isolation of the [(s)-phenylalanine + H$^+$(s)-phenyl-18-crown-6]$^+$ noncovalent inclusion complex followed by a 100 ms reaction time in the presence of neutral 18-crown-6 [Fig. 6(a)], produced a [(s)-phenylalanine + H + 18-crown-6]$^+$ ion at *m/z* 430, formed by abstraction of protonated phenylalanine from the (s)-phenyl-18-crown-6 complex. However, ligand exchange is not observed for the reverse reaction between the [(s)-phenylalanine + H + 18-crown-6]$^+$ inclusion complex and neutral (s)-phenyl-18-crown-6, shown in Fig. 6(b), that indicates the greater affinity of 18-crown-6 for [(s)-phenylalanine + H]$^+$. This order of affinities therefore supports the data obtained by using the relative ion intensity approach.

The increased stability of the protonated phenylalanine/18-crown-6 noncovalent inclusion complex compared to the protonated phenylalanine/(s)-phenyl-18-crown-6 indicates the aromatic ring on (s)-phenyl-

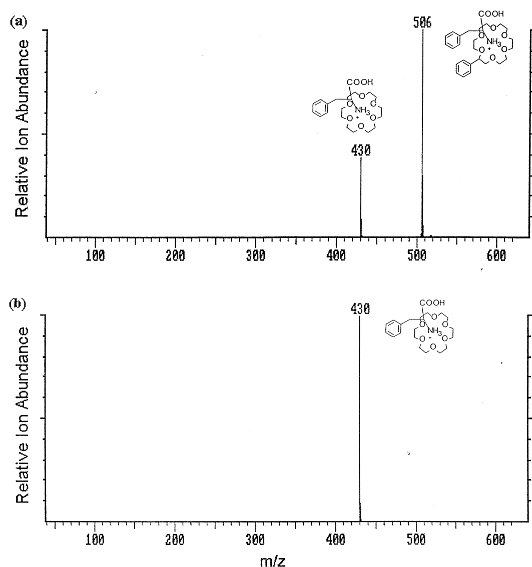

Fig. 6. Ligand exchange experiments between the MH^+ ion of (s)-phenylalanine and (s)-phenyl-18-crown-6 and 18-crown-6. (a) Isolation of the inclusion complex between (s)-phenylalanine and (s)-phenyl-18-crown-6 followed by a 100 ms reaction time in the presence of neutral 18-crown-6. (b) Isolation of the inclusion complex between (s)-phenylalanine and 18-crown-6 followed by a 100 ms reaction time in the presence of (s)-phenyl-18-crown-6.

18-crown-6 leads to the formation of a more weakly bound inclusion complex. This is consistent with the greater affinity of protonated propylamine for 18-crown-6 than benzo-18-crown-6. The observation of skeletal fragment ions in the product ion spectrum of the protonated phenylalanine/(s)-phenyl-18-crown-6 ion suggests that the stability of this complex lies between the stability of the propylamine/benzo-18-crown-6 and phenethylamine/18-crown-6 complexes. The overall order of the stabilities of the amine/crown ether noncovalent complexes can be tentatively assigned as: $[p + H + 18\text{-crown-}6]^+ > [p + H + \text{benzo-}18\text{-crown-}6]^+ \sim [(r)\text{-phenyl} + H + 18\text{-crown-}6]^+ = [(s)\text{-phenyl} + H + 18\text{-crown-}6]^+ > [(s)\text{-phenyl} + H + (s)\text{-phenyl-}18\text{-crown-}6]^+ > [\text{nitro} + H + 18\text{-crown-}6]^+ > [\text{phen} + H + 18\text{-crown-}6]^+ \sim [\text{phen} + H + \text{benzo-}18\text{-crown-}6]^+$, where p = propylamine, phen = phenethylamine, phenyl = phenylalanine, and nitro = 4-nitrophenylalanine.

4. Conclusion

Crown ethers form stable, noncovalent inclusion complexes with protonated amines in a quadrupole ion trap spectrometer. Structural recognition of amino-containing analytes is possible by using this approach, by isolation of the $[M + H]^+$ ion in the presence of a crown ether host followed by tandem mass spectrometry. The effect of varying the substituents on protonated amines of the type $[RNH_3]^+$ (R = $CH_3(CH_2)_2$, $C_6H_5(CH_2)_2$, $O_2NC_6H_4(CH_2)_2$ or $C_6H_5CH_2C(H)COOH$) can have a marked effect on the relative intensities of the complexes formed in competitive gas-phase experiments. These reactions have been used to assign the relative stabilities of the protonated amine/crown ether inclusion complexes. Relative intensity measurements suggest that introduction of an aromatic ring on the protonated amine or crown ether reduces the stability of the complex formed and these observations are supported by ligand exchange and tandem mass spectrometric experiments.

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