

Unusual complex between 18-Crown-6 and tetramethylammonium cation—detection by electrospray ionization mass spectrometry

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Abstract Complexes between crown ethers and quaternary ammonium cations have been studied by electrospray ionization mass spectrometry (ESI-MS). The ESI-MS method has been shown to allow observation of not only stable inclusion complexes between large crown ethers and tetramethylammonium cation (e.g. [DB30C10 + (CH₃)₄N]⁺ ion) but also of unstable inclusion complexes between smaller crown ethers and quaternary ammonium cations which are difficult to observe by other methods, namely [18C6 + (CH₃)₄N]⁺ ion. Stability of the complexes between crown ethers containing aromatic ring and tetramethylammonium cation is enhanced by cation- Π interactions. The molecule of 18C6 does not contain aromatic rings, thus [18C6 + (CH₃)₄N]⁺ ion exists due to the formation of C–H \cdots O hydrogen bonds. Such a complex is quite unusual, since C–H \cdots O hydrogen bonds are very weak and usually coexist with other strong interactions.

Keywords Quaternary ammonium cations · Crown ethers · Inclusion complexes · Electrospray ionisation Mass spectrometry

Introduction

In the field of supramolecular chemistry, crown ethers (CE) belong to the most popular hosts since their inclusion complexes have found a vast number of practical applications [1]. They are able to form stable complexes not only with metal cations but also with ammonium cation and protonated amines [2–5]. Large crown ethers (e.g. dibenzo-30-crown-

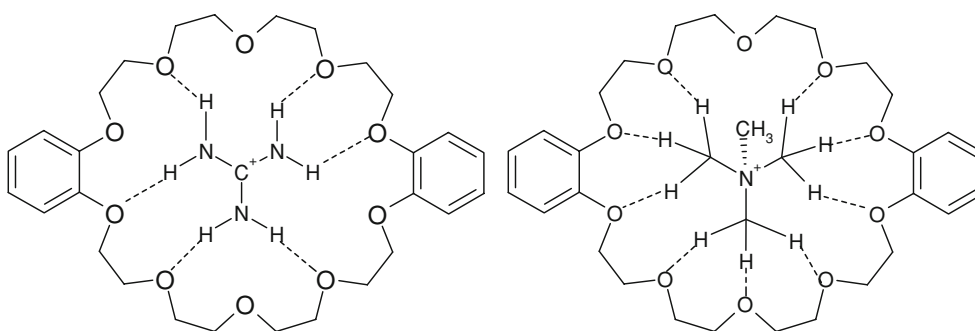
10 [DB30C10]) are able to form inclusion complexes with protonated guanidine and its derivatives [6–9]. Such complexes exist due to the formation of hydrogen bonds (Scheme 1). It is expected that large crown ethers will form analogous complexes with the tetramethylammonium cation ((CH₃)₄N⁺), as shown in Scheme 1. Although the C–H \cdots O hydrogen bonding was found in organic crystals more than 40 years ago, it was only in the second half of the 1990s when this interaction was generally accepted. Strong experimental evidence of the C–H \cdots O hydrogen bonding in solutions is difficult to obtain, since the C–H \cdots O hydrogen bonds usually coexist with other strong interactions and are typically weak [10–13].

Bartoli et al. [14] have shown by using ¹H NMR titration that dibenzo-24-crown-8 (DB24C8) form stable complexes with (CH₃)₄N⁺. On the other hand, dicyclohexano-24-crown-8, the molecule of almost the same cavity as DB24C8 but without aromatic rings, does not form complexes with (CH₃)₄N⁺. Thus, the cation- Π interaction is of crucial importance for formation of complexes between crown ethers and (CH₃)₄N⁺ (more important than the C–H \cdots O hydrogen bonding), e.g. for the complex shown in Scheme 1.

Formation of the complex between tetramethylammonium cation ((CH₃)₄N⁺) and smaller crown ether, namely 18-crown-6 (18C6), was not observed by calorimetric titration [3, 15], molecular mechanics calculations also did not imply formation of such a complex [3]. The lack of aromatic rings and a relatively small crown ether cavity prevent the 18C6–(CH₃)₄N⁺ complex formation. On the other hand, there are suggestions that the interactions between e.g. 18C6 and tetramethylammonium cation exist in solution [16].

In this communication we demonstrate (by using electrospray ionisation mass spectrometry) the existence of

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Scheme 1 Inclusion complex between protonated guanidine and tetramethylammonium cation and DB30C10—right, inclusion complex between dibenzo-30-crown-10 (DB30C10)—left, inclusion complex between

unstable complex between $(\text{CH}_3)_4\text{N}^+$ and 18C6, whose existence was declined by other methods. It is well known that ESI-MS is nowadays one of the best methods in host-guest chemistry, since this technique is very helpful in structure determination, allows obtaining thermochemical data in the gas phase and even permits chiral recognition [17].

Experimental

The ESI mass spectra were obtained on a Waters/Micromass (Manchester, UK) ZQ2000 mass spectrometer (single quadrupole type instrument, Z-spray, software MassLynx V3.5) as described earlier [7]. The sample solutions were prepared in methanol at the crown ether concentration 10^{-6} – 10^{-5} mol/dm³ with the three-fourfold excess quaternary ammonium hydroxide or salt, and mixed by using ultrasonic bath.

Both crown ethers and quaternary ammonium hydroxides and salts, PEG 500 were obtained from Sigma-Aldrich and used without further purification. We found that hydroxides contain fewer metal cations than the salts, thus for the presented study hydroxides are more appropriate, however for some tetraalkylammonium cations they are not commercially available.

The recorded spectra are shown in the mass range of interest, however, it has to be pointed out that at lower mass range, as expected, there were very abundant peaks of tetraalkylammonium cations.

Results and discussion

In order to get some intuition about the nature of complexes between crown ethers and tetraalkylammonium cations, at first the large crown ether, namely dibenzo-30-crown-10 (DB30C10), was taken for study. There was an intense peak of the complex between DB30C10 and tetramethylammonium

cation, namely $[\text{DB30C10} + (\text{CH}_3)_4\text{N}]^+$ at m/z 610. The cone voltage increase resulted in a dramatic lowering of the $[\text{DB30C10} + (\text{CH}_3)_4\text{N}]^+$ signal but the signals of $[\text{DB30C10} + \text{NH}_4]^+$, $[\text{DB30C10} + \text{Na}]^+$ and $[\text{DB30C10} + \text{K}]^+$ were held at the same level. Thus, in the gas phase, the complex between $(\text{CH}_3)_4\text{N}^+$ and DB30C10 is much less stable than the complexes between DB30C10 and NH_4^+ , Na^+ or K^+ . The complexes between DB30C10 and a larger quaternary ammonium cation, namely tetraethyl- and tetrapropylammonium, hexadecyltrimethylammonium, dihexadecyldimethylammonium cation were also observed but only at a low cone voltage 10–20 V. Thus, such complexes may exist in solution but are very unstable in the gas phase. A complex between DB30C10 and tetrabutylammonium cation was not observed. Complexes between tetraalkylammonium cations and smaller crown ethers (namely dibenzo-24-crown-8, dibenzo-21-crown-7 and dibenzo-18-crown-6) were also observed. As expected, the greater the crown ether the more abundant the complex detected. However, we must add that, on the basis of above briefly described results, it is hard to expect practical analytical application of crown ether-tetraalkylammonium cation complexes (e.g. for analysis of cationic surfactants or phosphatidylcholine constituent). For such a purpose it would be better to use another macrocyclic receptor, namely 2,11,20,29-tetraoxa[3.3.3.3] paracyclophane as recently described by Sarri et al. [18].

Figure 1 left shows the ESI mass spectrum obtained for the solution containing tetramethylammonium hydroxide and 18-crown-6 (18C6). At a low cone voltage value 10 V there is the abundant ion $[\text{18C6} + (\text{CH}_3)_4\text{N}]^+$ at m/z 338. This complex is unstable in the gas phase, and at the cone voltage of 30 V it was not detected.

The complex between 18C6 and $(\text{CH}_3)_4\text{N}^+$ cation was not observed by other methods [3, 15]. The question is if the ion observed on the ESI mass spectrum (Fig. 1 left) is a real inclusion complex or just structurally undefined electrostatic adduct formed due to the ion-dipole forces. Electrostatic attraction is enhanced in the gas phase (e.g. ESI-MS conditions) in comparison to that in solution [19],

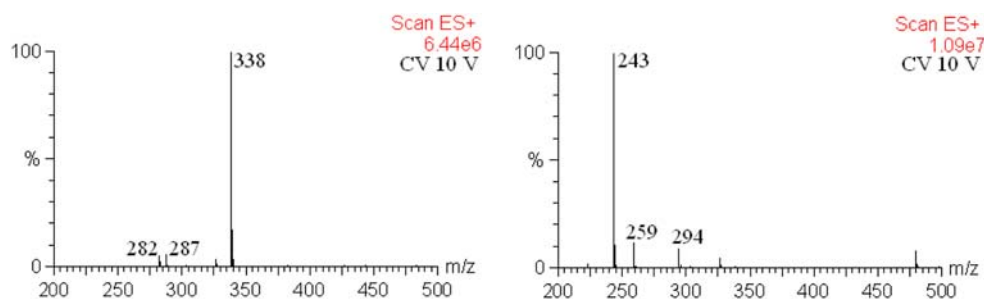


Fig. 1 ESI mass spectra obtained for the solution containing 18C6 and tetramethylammonium hydroxide—left, for the solution containing 15C5 and tetramethylammonium hydroxide—right. $[18C6 + H]^+ m/z$

265, $[18C6 + NH_4]^+ m/z$ 282, $[18C6 + Na]^+ m/z$ 287, $[18C6 + (CH_3)_4N]^+ m/z$ 338, $[15C5 + Na]^+ m/z$ 243, $[15C5 + K]^+ m/z$ 259, $[15C5 + (CH_3)_4N]^+ m/z$ 294

thus the $[18C6 + (CH_3)_4N]^+$ ion can be formed during the electrospray ionisation process. If the $[18C6 + (CH_3)_4N]^+$ ion is just an electrostatic adduct, not an inclusion complex, an analogous ion (of similar stability), should be observed for 15C5, namely ion $[15C5 + (CH_3)_4N]^+$ at m/z 294. As shown in Fig. 1 right, the $[15C5 + (CH_3)_4N]^+$ ion was detected at the cone voltage of 10 V, but it was characterized by low abundance. At the cone voltage of 20 V this ion was not detected, which means that its stability was very low, much lower than that of the $[18C6 + (CH_3)_4N]^+$ ion. The complex between 12-crown-4 and tetramethylammonium cation ($[12C4 + (CH_3)_4N]^+$ ion at m/z 250) was not detected at all. Therefore, it is reasonable to conclude that the $[18C6 + (CH_3)_4N]^+$ ion is a real inclusion complex. Obviously, the whole $(CH_3)_4N^+$ ion cannot be placed inside 18C6, but only one methyl group, analogously to protonated primary amines [4, 5]. It is worth adding that a small signal assigned to the $[18C6 + (C_2H_5)_4N]^+$ ion at m/z 394 was also observed, but the one assigned to $[18C6 + (C_3H_7)_4N]^+$ at m/z 450 was not.

The greater stability of the $[18C6 + (CH_3)_4N]^+$ ion in comparison to the $[15C5 + (CH_3)_4N]^+$ ion may result from the fact that the polarizability of the crown ether increases with increasing size as does the number of internal degrees of freedom of the complexes. Therefore, ESI mass spectra were also recorded for a solution containing $(CH_3)_4N^+$ cation and polyethylene glycol (PEG 500, a linear correspondent of crown ethers). The $[HO(CH_2CH_2O)_6H + (CH_3)_4N]^+$ ion was detected (m/z 356) at the cone voltage 10 V but at the cone voltage of 20 V this ion was not detected. It means that its stability was very low, much lower than that of the $[18C6 + (CH_3)_4N]^+$ ion, in spite of the fact that the linear molecule of $HO(CH_2CH_2O)_6H$ has more internal degrees of freedom than the cyclic 18C6 molecule. The $HO(CH_2CH_2O)_6H$ molecule contains one oxygen atom more than that of 18C6 thus the charge dipole-interaction cannot be the reason for the $[18C6 + (CH_3)_4N]^+$ ion stabilization. The greater stability of the $[18C6 + (CH_3)_4N]^+$ ion in comparison

the $[HO(CH_2CH_2O)_6H + (CH_3)_4N]^+$ ion is caused by well known entropic effect, which is characteristic of the inclusion complexes of macrocyclic compounds.

There is a large number of ESI-MS studies of complexes based on different types of hydrogen bonds [19]. To the best of our knowledge the $[18C6 + (CH_3)_4N]^+$ ion is the first example of a complex based exclusively on the C–H...O interaction which was successfully transferred to the gas phase.

Bartoli et al. [14] have shown that cation- π interaction is of crucial importance for formation of complexes between crown ethers and $(CH_3)_4N^+$, since a crown ether without aromatic rings, do not form complex with $(CH_3)_4N^+$. Formation of the inclusion complex between 18C6 and $(CH_3)_4N^+$ is strong evidence that the presence of the cation- π interaction is not a necessary condition to form complex between crown ethers and tetramethylammonium cation. Such a complex can exist due to the C–H...O hydrogen bonding.

In order to compare the contributions of the cation- π interactions and the C–H...O hydrogen bonding to the stability of the crown ethers- $(CH_3)_4N^+$ complexes, the solution containing dibenzo-18-crown-6, 18-crown-6 (DB18C6 and 18C6 at equal concentration!) and $(CH_3)_4N^+$ cation was analysed.

Figure 2 left shows the ESI mass spectrum of the methanol solution containing DB18C6 and 18C6 at the same concentrations of 5×10^{-6} mol/dm³. The peaks of cationized 18C6 molecule ($[18C6 + Na]^+$ and $[18C6 + K]^+$) are more intense than the peaks of cationized DB18C6 molecule. Although the cavity size of DB18C6 is similar to that of 18C6, it seems as though the cavity is effectively smaller as a result of its less flexible structure [20]. Thus, DB18C6 forms less stable 1:1 complexes with metal cations than 18C6 and, as a consequence, ions $[18C6 + Na]^+$ and $[18C6 + K]^+$ are more abundant than ions $[DB18C6 + Na]^+$ and $[DB18C6 + K]^+$. The obtained data are in good agreement with the results published by Anderson et al. [21]. When

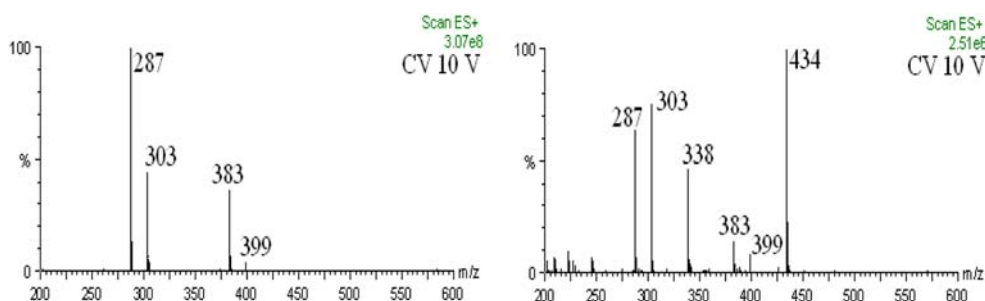


Fig. 2 ESI mass spectra obtained for solution containing 18C6 and DB18C6—left; 18C6, DB18C6 and tetramethylammonium hydroxide—right. $[18C6 + Na]^+ m/z$ 287, $[18C6 + K]^+ m/z$ 303, $[18C6 +$

$(CH_3)_4N]^+ m/z$ 338, $[DB18C6 + Na]^+ m/z$ 383, $[DB18C6 + K]^+ m/z$ 399, $[DB18C6 + (CH_3)_4N]^+ m/z$ 434

tetramethylammonium cation was added to the solution, the presence of its complexes with crown ethers was manifested in the ESI mass spectrum obtained (Fig. 2 right).

As shown in Fig. 2 right, the ion $[DB18C6 + (CH_3)_4N]^+$ is twice as abundant as $[18C6 + (CH_3)_4N]^+$. Thus, although the cation- π interaction is not a necessary condition to form complexes between crown ethers and tetramethylammonium cation, this type of interaction significantly increases the stability of such complexes in solution.

The fact that the ion $[DB18C6 + (CH_3)_4N]^+$ is more abundant than the ion $[18C6 + (CH_3)_4N]^+$ may be caused by higher surface activity of the former ion. However, many studies have demonstrated that the results of ESI-MS analysis of the host-guest complexes correlate well with measurements of the equilibria in solution and the ESI efficiencies for similar host-guest complexes, including the ones involving macrocycles are often close enough to be ignored [22].

As results from Fig. 2, the addition of tetramethylammonium hydroxide caused a drastic decrease in the abundances of alkali cation complexes. The latter are most probably suppressed by $(CH_3)_4N^+$ cation which is transferred to the gas phase (ESI condition) with very high efficiency.

Figure 2 was obtained at low cone voltage 10 V. When the cone voltage was increased to 30 V both ions $[18C6 + (CH_3)_4N]^+$ and $[DB18C6 + (CH_3)_4N]^+$ disappeared. In other words, the higher gas phase stability of the latter ion was not observed. Therefore, the cation- π interactions bring a significant contribution to formation of the complexes of interest in solution, but not in the gas phase. This observation is difficult to rationalize, since in the gas phase there is no competition of solvation.

Conclusion

It has been demonstrated that ESI-MS allows observation of unstable inclusion complexes between crown ethers and quaternary ammonium cations which are difficult to observe

by other methods, namely $[18C6 + (CH_3)_4N]^+$ ion. The stability of complexes between crown ethers containing aromatic ring and tetramethylammonium cation is enhanced by the cation- π interaction. 18C6 molecule does not contain aromatic rings, thus $[18C6 + (CH_3)_4N]^+$ ion exist due to the formation of the C-H \cdots O hydrogen bonds. Such a complex is quite unusual, since the C-H \cdots O hydrogen bonds are very weak and usually coexist with other strong interactions. The stability of complexes between crown ethers containing aromatic ring and tetramethylammonium cation is enhanced by the cation- π interaction in solution but not in the gas phase as results from a comparison of the complexes formed by 18-crown-6 and dibenzo-18-crown-6.

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