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The Effect of Benzene Moiety Fused with Macrocyclic Ring on the Proton Affinity of Crown Ethers Studied in MS/MS Experiment

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ABSTRACT

In this paper we address the question how the presence of an aromatic moiety affects the proton affinity of crown ethers. In order to compare the proton affinities of crown ethers studied (M), we compared the abundances of protonated crown ethers ($[M + H]^+$ ions) with the abundance of the ion $[NH_2\text{-B15C5} + H]^+$ (formally also protonated crown ether). Both $[M + H]^+$ and $[NH_2\text{-B15C5} + H]^+$ were formed as a result of decomposition of $[NH_2\text{-B15C5} + H + M]^+$. The presence of a benzene moiety fused with a macrocyclic ring strongly decreases the ratio $[M + H]^+/[NH_2\text{-B15C5} + H]^+$. Thus, the higher ring strain caused by the benzene moiety leads to a substantial lowering of the proton affinity of crown ethers. It is also suggested that for protonated benzo-crown ethers the ring strain is partly compensated by the proton-π interaction. The presence of an NO_2 group decreases the electron density on the aromatic ring and, consequently, the proton-π interaction is suppressed. As expected, the proton affinity of benzo-crown ethers increases with increasing size of their cavity since the ring strain is lower for larger molecules. An unexpectedly high proton affinity of dicyclohexano-18-crown-6 (DC18C6) has been observed.

Keywords: crown ethers, proton affinity, mass spectrometry

INTRODUCTION

In the field of supramolecular chemistry, crown ethers belong to the most popular hosts since their inclusion complexes have found a vast number of practical applications, for example, crown ethers are used in a number of types of chromatography [1].

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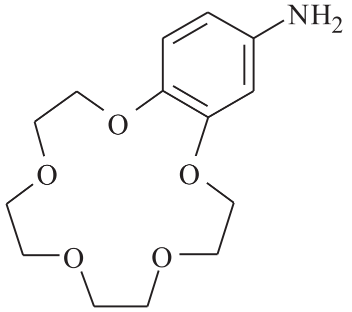
It is well known that the sizes of the guest and the crown ether cavity are of crucial importance for stability of the complexes. The presence of a benzene moiety fused with macrocyclic system yields a less flexible structure. Therefore, although the cavity size of dibenzo-18-crown-6 (DB18C6) is similar to that of 18-crown-6 (18C6), it seems that the cavity of DB18C6 is effectively smaller [2,3]. On the other hand, aromatic moieties are sources of π electrons, which enables complexes with cation-π [4] or π-π interactions [5] to be obtained.

Crown ethers are not prone to attach protons but, from the chemical point of view, crown ether complexes with the smallest cation are interesting. However, protonated crown ethers have not been widely studied. It has been found that their proton affinity increases with the increasing size of their cavity, namely, 12C4 < 15C5 < 18C6 [6,7]. The proton is attached inside the macrocyclic system, there is an intramolecular hydrogen bond and the ring strain is lower for larger molecules [7]. As expected, proton affinity of aza-crown ether is much higher that that of simple crown ethers [8].

In this paper we address the question how the presence of an aromatic moiety affects the proton affinity of crown ethers. It is expected that benzo-crown ethers have lower proton affinity than crown ethers. Since the former have more rigid molecules, the ring strain in them is expected to be greater than in the latter. On the other hand, the presence of π electrons may increase the proton affinity because of the proton-π interactions. Benzo-crown ethers can be regarded as compounds containing dialkoxy-substituted benzene moiety. The presence of alkoxy groups substantially increases the proton affinity of the benzene moiety [9,10].

One of the best experimental methods allowing evaluation of the proton affinity is the kinetic method originally proposed by Cooks [11,12]. The method consist in performing an MS/MS experiment for the ion $[M + H + B]^+$ (so called mass selected experiment), where B is a reference compound and M is a compound or compounds of interest [13]. This ion yields two fragment ions $[M + H]^+$ and $[B + H]^+$. If M and B are of similar chemical structure (entropic effect is negligible), the abundances of $[M + H]^+$ and $[B + H]^+$ are proportional to the M and B proton affinities, respectively [14].

Crown ethers form stable complexes with protonated amines [15,16], therefore, crown ether containing $-NH_2$ group can be good candidates for reference compounds. Aliphatic amines have much higher proton affinities than crown ethers [7,10] but aromatic amines such as aniline have lower proton affinities compared with aliphatic amines [17,18]. Hence, for the complexes of protonated aniline derivatives with crown ethers, both desired fragment ions should be observed. The reference compound we have chosen to use was 3-*amino*-benzo-15-crown-5 (Schematic 1, NH_2-B15C5).



Schematic 1. 3-*amino*-benzo-15-crown-5 (NH_2-B15C5).

EXPERIMENTAL

The mass spectra were obtained on a Waters/Micromass (Manchester, UK) Q-tof Premier mass spectrometer (software MassLynx V4.1, Manchester, UK). The sample solutions were prepared in methanol (most common solvents for electrospray ionization) at the crown ether concentration of 10^{-6} mol/dm^3. The sample solutions were infused into the ESI source by a syringe pump at a flow rate of 5 μl/min. The electrospray voltage was 3.5 kV. Figures 1 and 2 were obtained at a cone voltage adjusted to obtain the maximum abundances of the ions $[NH_2\text{-B15C5} + H + M]^+$ (about 45 V for M being 18C6 and its derivatives and larger crown ethers, about 30 V for 12C4, 15C5 and their derivatives), and at the source and desolvation temperatures of 80°C and 250°C, respectively, but other cone voltage and temperature values were also used. Nitrogen was used as the cone gas and desolvating gas at the flow-rates of 50 and 800 lh^{-1}, respectively. Argon was used as a collision gas, Figure 1 and 2 were obtained at the flow-rate 0.5 ml/min in the collision cell (lower flow rates were also used). MS/MS experiments were performed at different collision energies. Figure 2 was prepared on the grounds of the MS/MS spectra obtained at the collision energy of 10 eV for the ions $[NH_2\text{-B15C5} + H + \text{12C4}]^+$ and $[NH_2\text{-B15C5} + H + \text{B12C4}]^+$, 15 eV for $[NH_2\text{-B15C5} + H + \text{15C5}]^+$, $[NH_2\text{-B15C5} + H + \text{B15C5}]^+$ and $[NH_2\text{-B15C5} + H + NO_2\text{-B15C5}]^+$, 20 eV for all other ions $[NH_2\text{-B15C5} + H + M]^+$ (Figure 1 and 2). In such conditions, the ion $[NH_2\text{-B15C5} + H]^+$ was usually the base peak in the MS/MS spectrum obtained, with three exceptions: in the MS/MS spectra of ions $[NH_2\text{-B15C5} + H + \text{DB24C8}]^+$, $[NH_2\text{-B15C5} + H + \text{DC18C6}]^+$ and $[NH_2\text{-B15C5} + H + \text{DB30C10}]^+$ the base peak was the selected parent ion (Figure 2).

RESULTS AND DISCUSSION

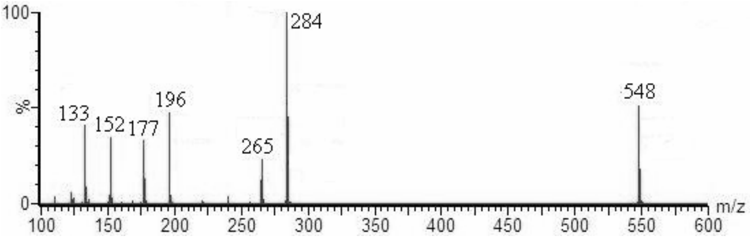
As a result of the MS/MS experiment performed for the ion $[NH_2\text{-}B15C5 + H + 18C6]^+$ (m/z 548), the ions $[NH_2\text{-}B15C5 + H]^+$ (m/z 284) and $[H + 18C6]^+$ (m/z 265) were formed with reasonable abundances (Figure 1a). There were also fragment ions formed as a result of decomposition of the ions $[NH_2\text{-}B15C5 + H]^+$ and $[18C6 + H]^+$. Different collision energies were applied but subsequent efficient fragmentation of $[NH_2\text{-}B15C5 + H]^+$ and $[18C6 + H]^+$ could not be eliminated. Other experimental parameters which can affect the dissociation of studied ions, namely collision gas pressure (to allow single collision regime), source and desolvation temperature, cone voltage, were also varied but subsequent dissociation of $[NH_2\text{-}B15C5 + H]^+$ and $[18C6 + H]^+$ was always observed. By performing MS/MS experiments for the ions $[NH_2\text{-}B15C5 + H]^+$ and $[H + 18C6]^+$ it was found that the ions at m/z 133, m/z 177 originated from $[18C6 + H]^+$ and those at m/z 152, 178 and 196 originated from $[NH_2\text{-}B15C5 + H]^+$. The ion $[NH_2\text{-}B15C5 + H]^+$ was also generated with high abundance from the electrosprayed solution, therefore, the MS/MS experiment for this ion was workable. In order to perform the MS/MS experiment for $[18C6] + H]^+$, the cone voltage was increased to about 60 V and, as a result of the so-called collision induced dissociation “in-source”, the ion $[18C6 + H]^+$ was formed from $[NH_2\text{-}B15C5 + H + 18C6]^+$ and then the MS/MS experiment for $[18C6 + H]^+$ was performed. Detailed description of the mass spectrometric fragmentation pathway of a protonated crown ether molecule is not a goal of this paper.

In order to compare the proton affinities of the crown ethers studied, we compared the abundances of protonated crown ethers studied ($[M + H]^+$ ions) with the abundance of the ion $[NH_2\text{-}B15C5 + H]^+$. Both $[M + H]^+$ and $[NH_2\text{-}B15C5 + H]^+$ were formed as a result of decomposition of $[NH_2\text{-}B15C5 + H + M]^+$, where M corresponded to the following crown ethers: 12-crown-4 (12C4), benzo-12-crown-4 (B12C4), 15-crown-5 (15C5), benzo-15-crown-5 (B15C5), and 3-*nitro*-benzo-15-crown-5, 18-crown-6 (18C6), dibenzo-18-crown-6 (DB18C6), 3-*nitro*-benzo-18-crown-6 (NO_2-B18C6), dicyclohexano-18-crown-6 (DC18C6), dibenzo-21-crown-7 (DB21C7), dibenzo-24-crown-8 (DB24C8), dibenzo-30-crown-10 (DB30C10). Because the reference compound and M are of similar chemical structure, the entropic effect is negligible, the abundances of $[M + H]^+$ and $[NH_2\text{-}B15C5 + H]^+$ are proportional to the M and NH_2-B15C5 proton affinities, respectively [14].

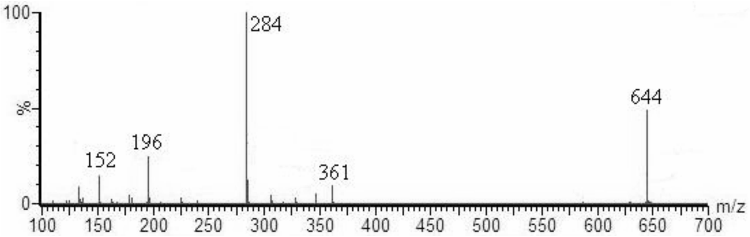
It is reasonable to assume that the ions $[NH_2\text{-}B15C5 + H + M]^+$ contain a protonated NH_2 group inside the crown ether cavity (ions of the type $[M_1 + H + M_2]^+$, where M_1 and M_2 correspond to the crown ethers studied). Therefore, the stability of the ions $[NH_2\text{-}B15C5 + H + M]^+$, decreases with decreasing cavity of M (lower collision energy is required to induce efficient decomposition of the ion $[NH_2\text{-B15C5} + H + 12C4]^+$ than the ion $[NH_2\text{-B15C5} + H + 15C5]^+$).

Figure 1 shows the MS/MS spectra obtained for the complexes of 18C6 and its three derivatives (DB18C6, NO_2-B18C6, DC18C6).

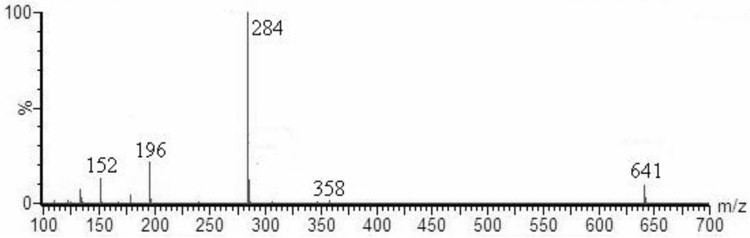
a) $[NH_2\text{-B15C5} + H + 18C6]^+$ m/z 548, $[18C6 + H]^+$ m/z 265



b) $[NH_2\text{-B15C5} + H + DB18C6]^+$ m/z 644, $[DB18C6 + H]^+$ m/z 361



c) $[NH_2\text{-B15C5} + H + NO_2\text{-B18C6}]^+$ m/z 641, $[NO_2\text{-18C6} + H]^+$ m/z 358



d) $[NH_2\text{-B15C5} + H + DC18C6]^+$ m/z 656, $[DC18C6 + H]^+$ m/z 373

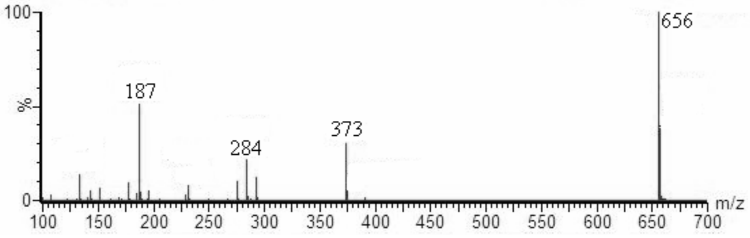


Fig. 1. MS/MS spectra of some of the ions $[NH_2\text{-B15C5} + H + M]^+$ ($[NH_2\text{-B15C5} + H]^+$ m/z 284).

Figure 2 shows relative abundances of $[M + H]^+$ and $[NH_2\text{-B15C5} + H]^+$ taken from the MS/MS spectra of the ions $[NH_2\text{-B15C5} + H + M]^+$. We also wanted to take into account the sums of the abundances of protonated crown ethers ($[M + H]^+$ and $[NH_2\text{-B15C5} + H]^+$) and the fragment ions derived from them but the respective relative proportions were similar to those obtained for the comparison of those of $[M + H]^+$ and $[NH_2\text{-B15C5} + H]^+$.

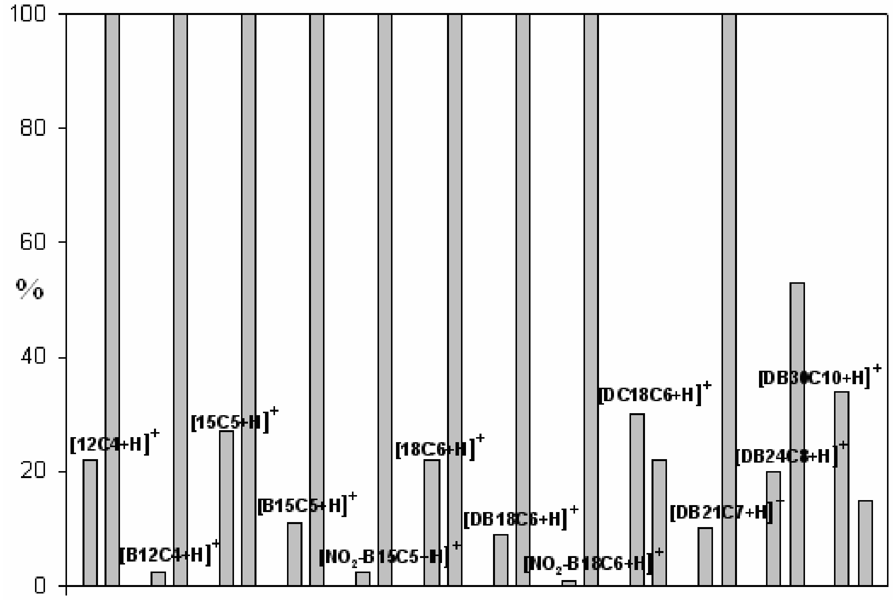


Fig. 2. Relative abundances of the ions $[M + H]^+$ and $[NH_2\text{-B15C5} + H]^+$ taken from MS/MS spectra of $[NH_2\text{-B15C5} + H + M]^+$. The bars of the ions $[M + H]^+$ are assigned and the neighbouring bars correspond to the ions $[NH_2\text{-B15C5} + H]^+$.

As clearly results from Figures 1 and 2, the presence of a benzene moiety fused with a macrocyclic ring strongly decreases the ratio $[M + H]^+/[NH_2\text{-B15C5} + H]^+$ namely $[12C4 + H]^+/[NH_2\text{-B15C5} + H]^+ >$ $[B12C4 + H]^+/[NH_2\text{-B15C5} + H]^+$, $[15C5 + H]^+/[NH_2\text{-B15C5} + H]^+ >$ $[B15C5 + H]^+/[NH_2\text{-B15C5} + H]^+$, $[18C6 + H]^+/[NH_2\text{-B15C5} + H]^+ >$ $[DB18C6 + H]^+/[NH_2\text{-B15C5} + H]^+$. Thus, the conclusion can be drawn that the higher ring strain caused by the benzene moiety leads to a substantial lowering of the proton affinity of crown ethers (the proton is attached inside the macrocyclic system and there is an intramolecular hydrogen bond [7]). Proton-π interaction seems to be of minor importance. However, it is also suggested that such interactions exist. It is well known that the NO_2 group is a strong electron withdrawing group. Thus, the presence of NO_2 group decreases electron density on the aromatic ring, but it has to be stressed that the proton affinity of nitrobenzene is higher than that of benzene (NO_2 group attaches the proton) [9]. As clearly results from Figure 1 and 2, the presence of an NO_2 group strongly decreases the proton affinity of benzo-crown ethers, namely $[B15C5 + H]^+/[NH_2\text{-}B15C5 + H]^+ > [NO_2\text{-}B15C5 + H]^+/[NH_2\text{-}B15C5 + H]^+$, $[DB18C6 + H]^+/[NH_2\text{-}B15C5 + H]^+ > [NO_2\text{-}B18C6 + H]^+/[NH_2\text{-}B15C5 + H]^+$. It seems reasonable to conclude that for protonated benzo-crown ethers the ring strain is partly compensated by the proton-π interaction. The presence of an NO_2 group decreases the electron density on the aromatic ring and, in consequence, the proton-π interaction is suppressed. The proton affinity of B15C5 is higher than that of NO_2-B15C5 and the proton affinity of DB18C is higher that that of NO_2-B18C6 (NO_2-B18C6 contains only one benzene moiety and DB18C6 contains two benzene moieties, thus a higher ring strain is expected for the latter).

In order to increase the proton-π interaction, it would be useful to use benzo-crown ethers with an electron donor substituent on the aromatic ring. However, benzo-crown ethers contain two alkoxy groups (two strong electron donor substituents) on the benzene moiety. In order to substantially increase the electron density on the aromatic ring, the third substituent should have stronger electron donor properties than that of the alkoxy group. Thus, the third substituent should be, for example, $-NH_2$ or $-N(CH_3)_2$ group. However, the proton will not be attached inside the macrocyclic system but will be captured by the amino groups.

As expected, the proton affinity of benzo-crown ethers increases with the increasing size of their cavity ($[DB30C10 + H]^+/[NH_2\text{-}B15C5 + H]^+ > [DB24C8 + H]^+/[NH_2\text{-}B15C5 + H]^+ > [DB21C7 + H]^+/[NH_2\text{-}B15C5 + H]^+ > [DB18C6 + H]^+/[NH_2\text{-}B15C5 + H]^+$, Figure 2) since the ring strain is lower for larger molecules. An unexpectedly high proton affinity of dicyclohexano-18-crown-6 (DC18C6) has been observed ($[DC18C6 + H]^+/[NH_2\text{-}B15C5 + H]^+ > [DB24C8 + H]^+/[NH_2\text{-}B15C5 + H]^+$). It is difficult to rationalize, most probably DC18C6 is very prone to assume a conformation favouring the intramolecular hydrogen bond formation.

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