

Simultaneous Binding of Boron and Ammonium Cation by a Pseudocryptand: Synthesis, X-Ray Analysis and Solution Studies by NMR Spectroscopy

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Treatment of the macrocyclic compound **1** bearing two catecholate moieties with equimolar amounts of $B(OH)_3$ and aqueous NH_3 in a H_2O -EtOH mixture gave exclusively the ammonium inclusion complex **2** which was then studied both in solution and in the solid state; the selectivity sequence $NH_4^+ > Na^+ > Cs^+$ in CD_3OD solution was obtained and the ammonium ion complex **2** was found to be more stable than the $\{[222], NH_4^+\}$ complex by at least 3 orders of magnitude.

Owing to the fundamental importance of ammonium cations in living organisms, the molecular recognition of these organic cations has been widely investigated over the past 25 years.¹⁻⁵ Although many thermodynamic measurements are available for ammonium cation complexes,⁶ few structural data for the complexes in the solid state have been reported. In particular, only a few structural analyses of the binding of the simplest ammonium cation, *i.e.* the NH_4^+ cation, by crown ethers,⁷ macrobicyclic⁸ and macrotricyclic⁹ cryptands and by antibiotics such as nonactin¹⁰ and tetraactin¹¹ have been published. All the above mentioned ligands, except the crown ether bearing a *p*-nitrophenate moiety,^{7d} are neutral and the complexation of the cation is associated with the presence of a counter anion.

Our approach to the design of compound **1** was inspired by naturally occurring antibiotics such as boromycin¹² and aplasmomycin,¹³ both bearing a borate ester moiety. For this purpose, we synthesised compound **1**,¹⁴ a pseudocryptand, which combines the [2.2] macrocyclic core¹⁵, as found in the [2.2.2.] cryptand,¹⁶ with two bidentate dianionic catecholate units to make a binucleating ligand. Upon binding of B^{III} to the two catecholate moieties a negatively charged complex of the Böeseken type is formed.¹⁷ The latter, a cryptand possessing a preorganised cavity, binds in its turn alkali metal cations with remarkable stability and selectivity.¹⁸ The driving forces for the complex formation are the attractive charge-charge and charge-dipole interactions. A similar analysis has been previously reported for the complexation of alkali metal cations by podands and coronands,¹⁹ and must apply also to complexes of triaza- and tetraaza-macrocycles bearing three and four pendant catecholate units²⁰ as well as of macrobicyclic tris-catecholate ligands.²¹

We now report solution studies as well as structural features of the ammonium ion inclusion complex **2**.

Treatment of **1**¹⁴ in EtOH with 1 equiv. of $B(OH)_3$ and 1 equiv. of aqueous NH_3 in H_2O -EtOH mixture at room temp. and under argon exclusively gave complex **2**. A single recrystallisation afforded the pure compound. For the $(1^{4-}, B^{3+}, K^+)$ complex, both proton and carbon signals were assigned completely by 1H - ^{13}C correlation experiments, and we assumed that the same assignment for **2** would hold. ^{11}B NMR spectroscopy (160.46 MHz) showed a single signal at 12.68 ppm ($BF_3 \cdot Et_2O$ as external reference) with a line width of *ca.*

16 Hz. Complex **2** was shown to be chemically stable. Indeed, even in a solvolyzing solvent such as CD_3OD , no alteration of its 1H spectrum was detected over several weeks time. Although the acidity constant for the complexed NH_4^+ cation was not measured, it is reasonable to suggest that upon complexation, its value would be greatly decreased with respect to the free cation. This may be an explanation to the absence of transprotonation taking place between the complexed NH_4^+ and the two tertiary amines of the ligand. Indeed, whereas in the solid state this was established by X-ray analysis, in solution, the 1H NMR data for **2**, when compared to the data obtained for the alkaline cation complexes, suggested the same fact.

Since we have previously observed that the proton chemical shifts for the alkali metal complexes of the type $(1^{4-}, B^{3+}, M^+)$ were strongly dependent on the nature of the cation,¹⁸ the binding features of **2** were also studied by 1H NMR spectroscopy in $CDCl_3$ and in CD_3OD (Fig. 1). In CD_3OD , the 1H NMR spectrum of **2** in the δ 3.8–4.4 region was composed of a triplet at 4.0 ppm (10.5 Hz) for the OCH_2CHOCH_2 and a doublet at 4.31 ppm (11.7 Hz) for one of the two benzylic CH_2N protons [Fig. 1(a)]. Upon addition of alkaline cations to **2**, changes were observed. Competition experiments between **2** and Na^+ (4–23 equiv. of NaI added to **2**) gave a selectivity of *ca.* 40 in the favour of NH_4^+ [Fig. 1(b)]. The selectivity of *ca.* 40 in CD_3OD observed for **2** is one order of magnitude higher than the factor 4 reported in H_2O for the [2.2.2.] cryptand.^{8,15} Competition between **2** and K^+ in CD_3OD showed that upon addition of 1.1 equiv. of KI, the NH_4^+ cation was totally displaced by K^+ leading thus to the $(1^{4-}, B^{3+}, K^+)$ complex [Fig. 1(b)]. Since the stability of the latter was extremely high,¹⁸ we have not been able so far to determine the selectivity factor between NH_4^+ and K^+ . With the NH_4^+ vs. Cs^+ cation, the same type of competition experiments (ratio $CsBr/2$ varied for 11.7 to

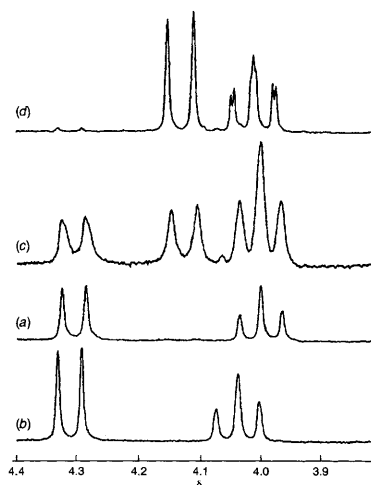
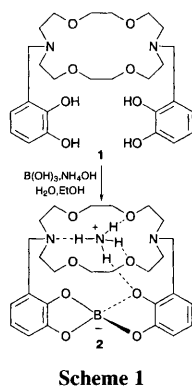


Fig. 1 1H NMR (300 MHz) studies of the binding features of **2**. Selected region (1.8–4.4 ppm) in CD_3OD . (a) The NH_4^+ complex **2**, (b) **2** + 1.1 equiv. KI, the signals observed are the same as those obtained for the pure $(1^{4-}, B^{3+}, K^+)$ complex, (c) **2** + 5.2 equiv. of NaI, (d) for comparison purposes the $(1^{4-}, B^{3+}, Na^+)$ complex.

53) revealed a factor of *ca.* 100 in the favour of the NH_4^+ cation. Addition of up to 15 equiv. of the [2.2.2] cryptand to a solution of **2** (5×10^{-3} mol dm^{-3}) in CDCl_3 caused no changes to the resonances due to the original complex **2**, indicating that **2** is more stable than the ([2.2.2] NH_4^+) complex by at least 3 orders of magnitude.

In the solid state, the inclusive nature of the NH_4^+ complex **2** was demonstrated by an X-ray study of the crystals obtained from a CH_2Cl_2 -hexane mixture.[†] Because of the tetrahedral coordination around boron, both *R*- and *S*-isomers are present in the unit cell. The X-ray analysis of the racemate revealed the following features (Fig. 2): (i) a slightly deformed tetrahedral geometry around boron with OBO angles varying from 104.2 to 112.9° (average 109.5°) and an average B–O distance of *ca.* 1.47 Å; (ii) since all four protons around the nitrogen atom of the substrate were localised, the bond distance analysis revealed that the substrate was indeed the NH_4^+ cation. The coordination geometry around the nitrogen atom is a distorted tetrahedron with an average N–H distance of *ca.* 1.07 Å and an average NHN angle of *ca.* 109.6°, (NHN angle values varied from 103.2 to 122.4°); (iii) both lone pairs of the two bridgehead nitrogen atoms are oriented towards the interior of the cavity (in, in conformation), (iv) the NH_4^+ cation is located within the cavity formed by the negatively charged cryptand; (v) the nitrogen atom of the NH_4^+ cation is located almost at equal distances from the two bridgehead nitrogen atoms [N(1)–N⁺ and N(10)–N⁺ 3.126 and 3.072 Å respectively, N–N⁺–N angle 178°]; (vi) in the complex **2**, the NH_4^+ cation is surrounded by three oxygen atoms (average N⁺–O distance of *ca.* 2.87 Å, average N⁺–HO angle of *ca.* 165.6°) and one nitrogen atom (N⁺–N distance of 3.072 Å, N⁺–HN angle of 166.5°) leading to tetrahedral coordination around the molecular cation. Thus, as in the case of the (2.2.2, NH_4^+) complex,⁸ of the eight oxygen atoms present in **2**, only three of them composed of the two ether junctions and one borate oxygen atom, are localised within a bonding distance of NH_4^+ . The average N⁺–O and N⁺–N distances observed for **2** are perfectly compatible with average distances reported for other ammonium complexes.^{7–12}

In conclusion, binding of B^{III} by the macrocycle **1** affords an anionic cryptand displaying the selectivity sequence for cation binding $\text{NH}_4^+ > \text{Na}^+ > \text{Cs}^+$ in CD_3OD . The NH_4^+ inclusion complex **2** appears to be more stable, by at least 3 orders of magnitude, than the ([2.2.2], NH_4^+) complex.

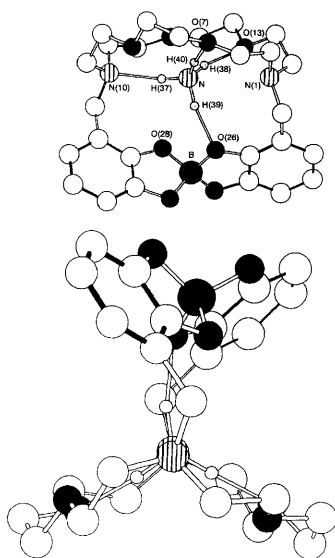


Fig. 2 Crystal structure of **2** (arbitrary isomer). For the sake of clarity, hydrogen atoms, except those belonging to the NH_4^+ cation, are not presented. Selected distances (Å): N⁺–N(10) 3.072, N⁺–O(7) 2.852, N⁺–O(13) 2.900, N⁺–O(26) 2.879.

We thank the CNRS and the Institut Universitaire de France (IUF) for financial support.

Received, 9th May 1995; Com. 5/02900G

Footnote

[†] Crystal data for **2**; $\text{C}_{26}\text{H}_{34}\text{BN}_2\text{O}_8 \cdot \text{NH}_4 \cdot \text{CH}_2\text{Cl}_2$ colourless crystals, -100°C , $M = 616.4$, monoclinic, $a = 11.720(3)$, $b = 15.603(4)$, $c = 17.348(5)$ Å, $\beta = 106.04(2)^\circ$, $U = 3048.9$ Å³, space group $P2_1/c$, $Z = 4$, $D_c = 1.343$ g cm^{-3} , Cu-K α graphite monochromated, $\mu = 23.664$ cm^{-1} , 2557 data with $I > 3\sigma(I)$, $R = 0.067$, $R_w = 0.093$. The structure was solved using MULTAN. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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