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A Pyridine Cage as a Bireceptor: Inclusion of Cations and Anions

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Abstract

The bireceptor molecule **1** was synthesized in an one-step procedure. It binds cations under neutral conditions and anions in acidic media. The structure of $K^+ \subset$ **1** was clarified by X-ray crystallographic analysis.

Key Words: Cryptand, Host compound, Cyclophane, Macrocycle, Inclusion

Recent advances in host-guest chemistry deals with cations and anions as guests have developed more sophisticated host molecules and demands higher selectivity for guest species. Although many host molecules have been synthesized for this purpose, the developments of hosts for the anion guests are less active than that of the cations.[1]

In previous reports, we clarified that cage compounds which contain six or four pyridine rings showed strong complexation abilities toward cations. Under acidic conditions, the cage compound complexed with Cl^- ion, and anions larger than Cl^- were not included in the cavity.[2] The rigid structure affected the selectivity of the guest species.

In the next step, we planned the synthesis of a multidentate bireceptor containing nitrogen and oxygen as donor atoms. The cage **1** was obtained as its potassium complex from the direct

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coupling reaction between 2,6-bis (bromomethyl)pyridine and 1,5-diamino-3-oxapentane under phase transfer conditions (CH_2Cl_2, Bu_4NBr/ aq. KOH).[3] Figure 2 shows the crystal structure of $K^+ \subset$ **1**.[4] The pyridine nitrogens and oxygen atoms are octahedrally coordinated to K^+, and the bridgehead nitrogens are also coordinated to K^+ in a tetrahedral fashion. The N···N distances of the bridgehead nitrogen atoms are in the range of 5.024 ~ 5.341 Å indicating that four nitrogen atoms are in a tetrahedral arrangement. The potassium ion is placed at the center of the cavity. The average distance between the potassium and pyridine nitrogen is 3.150Å and is comparable to that of potassium and the bridgehead nitrogen (3.177Å). On the other hand, the average distance between potassium and the oxygen atoms is shorter (3.039 Å) than that of the K^+···N. Representative bond lengths and angles are shown in Table 1.

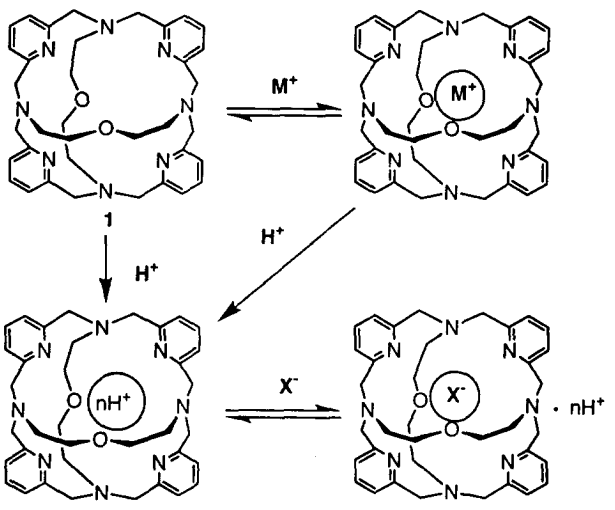

Figure 1 Cation and anion inclusions by cage compound **1**.

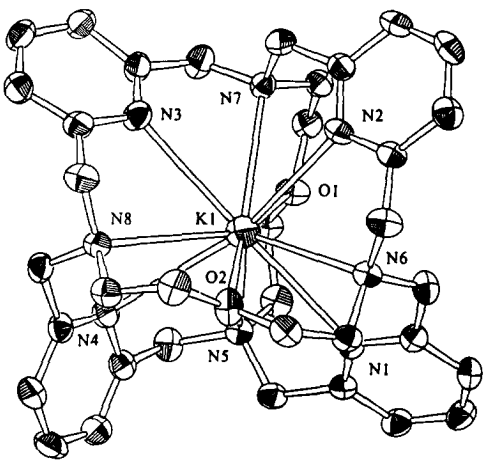

Figure 2 Crystal structure of $K^+ \subset$ **1**.

The inclusion properties toward anions were estimated in 10 % D_2SO_4. After the addition of Me_4NCl to a solution of **1** · nD^+, new signals corresponding to the $Cl^- \subset$ **1** · nD^+ appeared; the exchange rate of Cl^- was sufficiently slow in the solution. The binding constant, K_s = 24 ± 2 M^{-1}, was obtained by comparison of the intensities of both peaks. The thermodynamic data, ΔG (-1.8 kcal/mol), ΔH (-2.9 kcal/mol), and ΔS (-3.9 cal/K · mol) of the Cl^- inclusion were estimated by the van't Hoff's plots using K_s values at different temperatures obtained from variable temperature NMR spectra. In the case of the F^- ion complexation, the exchange rate of F^- was very fast compared to that of the Cl^-. The methylene signals were slightly shifted to

Table 1 Representative atomic distances (AD, Å) and angles (°) of the crystal structure of $K^+ \subset$ **1**.

	AD (Å)		angles (°)
K(1) - N(1)	3.130 (3)	N(1)-K(1)-N(3)	172.77 (8)
K(1) - N(2)	3.107 (3)	N(2)-K(1)-N(4)	162.87 (8)
K(1) - N(3)	3.091 (3)	N(5)-K(1)-N(7)	109.43 (7)
K(1) - N(4)	3.271 (3)	N(6)-K(1)-N(8)	111.17 (7)
K(1) - N(5)	3.268 (3)	O(1)-K(1)-O(2)	161.64 (7)
K(1) - N(6)	3.115 (3)		
K(1) - N(7)	3.068 (3)		
K(1) - N(8)	3.255 (3)		
K(1) - O(1)	3.059 (3)		
K(1) - O(2)	3.018 (3)		
N(5) - N(6)	5.179 (4)		
N(6) - N(7)	5.024 (5)		
N(7) - N(8)	5.154 (4)		
N(5) - N(7)	5.173 (4)		
N(5) - N(8)	5.341 (4)		
N(6) - N(8)	5.256 (4)		

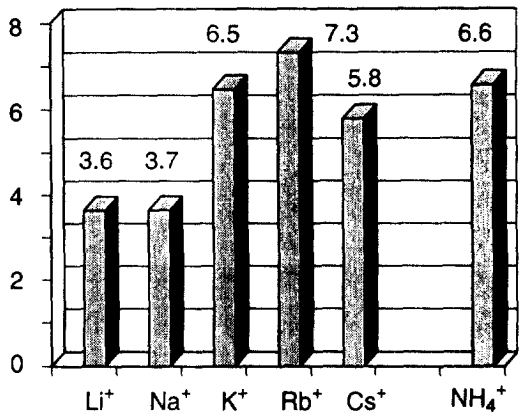

Figure 3

Plots of logK_s for $M^+ \subset$ **1** (Errors are within 5%).

upper field upon the addition of F^-, and this signal was used for the determination of K_s. The binding constant, K_s = 23 ± 3 M^{-1}, was obtained by the NMR titration experiment. In both cases, the 1:1 complex formations with Cl^- and F^- were observed.[5] The anions larger than Cl^- (Br^-, I^-, BF_4^-) were not complexed with $nD^+ \cdot$ **1**. In the case of cation inclusion, the binding constant K_s of $K^+ \subset$ **1** was estimated by a competition experiment using $K^+ \subset$ **1** and 18-crown-6. Since the K_s of $K^+ \subset$ 18-crown-6 in DMSO is known,[6] the K_s of $K^+ \subset$ **1** was calculated using the integral ratios of the signals of $K^+ \subset$ **1** and newly appeared metal-free **1**. The K_s values for other alkali metal cations were estimated in DMSO-d_6 by mixing $K^+ \subset$ **1** and Mpic (M = Li^+, Na^+, Rb^+, Cs^+). The new signals correspond to the $M^+ \subset$ **1** that appeared at different positions. The difference in the chemical shift, $\Delta\delta$, depends on the size of the cations; Cs^+ showed the largest $\Delta\delta$ and Li^+ showed the smallest. The binding constants of the cations are larger than that of the pyridine analog **2a**, but selectivity is similar to it (Figure 3).[7] The decadentate cryptand possessing N and O atoms as binding sites showed stronger cation affinity than parent pyridine analog **2a**.

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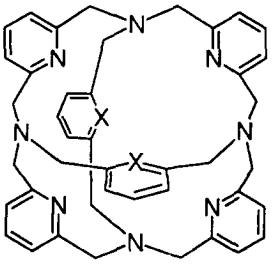
References and Notes

[1] a) Schmidtchen, F. P.; Berger, M. *Chem. Rev.* **1997**, *97*, 1609-1646. b) Ichikawa, K; Hossain, Md. A. *J. Chem. Soc., Chem. Commun.* **1996**, 1721-1722. c) Hossain, Md. A.; Ichikawa, K. *Chem. Lett.* **1996**, 553-554.

[2] a) Takemura, H.; Inazu, T. *J. Syn. Org. Chem. Jpn.*, **1998**, *56*, 604-614. b) Takemura, H.; Kon, N.; Tani, K.; Takehara, K.; Kimoto, J.; Shinmyozu T.; Inazu, T. *J. Chem. Soc., Perkin Trans. 1* **1997**, 239-246. c) Takemura, H.; Shinmyozu, T.; Inazu, T. *Coord. Chem. Rev.* **1996**, *156*, 183-200. d) Takemura, H.; Osada, S.; Shinmyozu, T.; Inazu, T. *J. Chem. Soc., Perkin Trans. 1* **1996**, 277-280. e) Takemura, H.; Shinmyozu, T.; Inazu, *J. Am. Chem. Soc.* **1991**, *113*, 1323-1331. f) Takemura, H.; Shinmyozu, T.; Inazu, *Tetrahedron Letters* **1988**, *29*, 1789-1792. g) Takemura, H.; Hirakawa, T.; Shinmyozu, T.; Inazu, T. *Tetrahedron Letters* **1984**, *25*, 5053-5056.



Pyridine analog of **1**.
2a: X = CH, **2b**: X = N

[3] The synthesis of the cage **1** will be described elsewhere.

[4] X-ray crystallographic data: Crystal data for **1**: $C_{36}H_{44}N_8O_2KBr$, Mr = 739.80 $gmol^{-1}$, colorless prismatic crystal (grown from CH_2Cl_2-DMSO mixture), size 0.80 × 0.80 × 0.50 mm, triclinic, space group $P\bar{1}$ (#2), a = 13.788(9), b = 13.96(1), c = 12.452(3) Å, α = 112.03(4), β = 112.73(4)°, γ = 52.13(4), V = 1713.72(1) $Å^3$, Z = 2, $\rho_{calcd.}$ = 1.434 gcm^{-3}, μ(Mo-Kα) = 13.71 cm^{-1}, F(000) = 772.00, T = 15 ± 1 °C using the ω -2θ scan technique to a maximum 2θ value of 55.2°. A total of 6396 reflections were collected. The final cycle of the full-matrix least-squares refinement was based on 5501 observed reflections (I > 3.00σ (I)) and 610 variable parameters and converged with unweighted and weighted agreement factors of R = 0.058, Rw = 0.091, and *GOF* = 1.29. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.56 and -1.06 $e^-/Å^3$, respectively. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 107664. Copies of the data can be obtained free of charge upon application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: +44(1223)336-033; E-mail: deposit@ccdc.cam.ac.uk].

[5] The components of the Cl^- and F^- complexes were determined by Job's plot and a Benesi-Hildebrand analysis of the NMR data.

[6] Kohltoff, I. M.; Chantooni, M. K., Jr. *Anal. Chem.* **1980**, *52*, 1039-1044.

[7] The binding constants of the pyridine analog of **1** (compound **2a**) toward cations are as follows; log*Ks* = 2.7 (Li^+), 3.5 (Na^+), 5.1 (K^+), 6.2 (Rb^+), 4.2 (Cs^+), 6.1 (NH_4^+).