Tetrahedral Recognition of a Water Molecule by Heteroditopic Cryptands: X-ray Structural Studies

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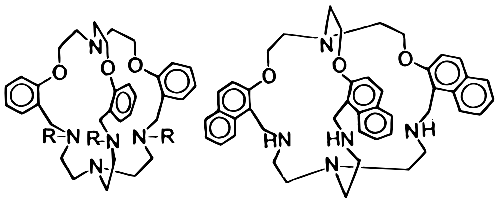
Molecular recognition represents one of the basic functional features of supramolecular chemistry.[1] Only recently have chemists shown interest toward this important area in order to get a clear understanding of different biochemical processes like cooperativity, allosterism, regulation, etc.[2−4] A supramolecular complex is formed when some specific information, which is stored in the host molecule, is read by the guest molecule, giving rise to attractive interactions that include H-bonding, aromatic−aromatic π-stacking, and electrostatic and hydrophobic forces.

Macropolycycles of appropriate binding sites and intramolecular cavities can be synthetically constructed to make them suitable hosts to form selective inclusion complexes. Oxazamacropolycycles are potential receptors for organic as well as inorganic cations,[5] anions,[6] and neutral molecules.[7] Natural antibiotics have been shown[8] to complex water molecules by H-bonding when they are free of metal ions. This complexation with water is believed to assist in the metal ion complexation by influencing the hydration shell of the metal ion. Complexation of water by crown ethers and by oxazamacrocycles is well documented.[9] Many of these systems have been characterized by X-ray crystallography; however, this is not so in the case of macrobicyclic cryptands.[10−13] Bianchi and co-workers[13] have recently described the crystal structure of a water inclusion complex where the water molecule is trapped inside the cavity of a diprotonated tetraazamacrobicycle. Takemura et al. have described the isolation and approximate structure of a water inclusion compound with a neutral cryptand.[12] In the present paper, we describe three heteroditopic cryptands (Figure 1), which readily take up a water molecule inside the cavity when they are diprotonated.



R = H (**L**$_1$)
= Me (**L**$_2$)

L$_3$

Figure 1. Heteroditopic cryptands **L**$_1$, **L**$_2$, and **L**$_3$ described in the paper; the water cryptates are designated as $[H_2\mathbf{L_1}\subset H_2O]^{2+}\cdot 2SCN^{-}\cdot 2H_2O$ (**A**), $[H_2\mathbf{L_2}\subset H_2O]^{2+}\cdot 2C_6H_2N_3O_7^{-}\cdot 0.5CH_3COCH_3$ (**B**), $[H_2\mathbf{L_2}\subset H_2O]^{2+}\cdot 2ClO_4^{-}$ (**C**), and $[H_2\mathbf{L_3}\subset H_2O]^{2+}\cdot 2ClO_4^{-}$ (**D**).

The water inclusion complex with **L**$_1$ was obtained in a serendipitious manner while its molecular recognition property toward ethylenediammonium, hydroxylammonium, and methylammonium cations was being investigated. Thus, **A** was isolated when ethylenediammonium dithiocyanate was treated with **L**$_1$. Two protons from the ethylenediammonium moiety are transferred to the secondary amino nitrogens; one water molecule present in the solvent enters the cavity and forms the inclusion complex. The aquophoric characteristic of the cryptand is not changed upon N-methylation of the secondary amino nitrogens. Also, in case of the water−cryptate **D**, the FAB-mass spectral results, when compared with that obtained in the case of **A**, strongly suggest that the cryptand is diprotonated with a water molecule inside the cavity. The cryptands do not get further protonated under the present experimental conditions. This unusual protonation behavior results from a cooperativity effect mediated by the water molecule—a phenomenon found earlier by Lehn[11] on the basis of NMR studies. The two bridgehead nitrogens have an in−in conformation in all three structures and possibly also in the case of **D**. Thus, further N-protonation will cause a substantial increase of the electrostatic repulsion among positive charges within the cavity.

A stereoview of the complex cation in **A** is shown in Figure 2. The molecule consists of the cation $[H_2\mathbf{L_1}\subset H_2O]^{2+}$ and two thiocyanate anions. Two water molecules are also present in the lattice. As can be seen in Figure 2, N(3) and N(4) are protonated. The two hydrogens of the water molecule are H-bonded to one bridgehead nitrogen and the unprotonated N(2) while protonated N(3) and N(4) are H-bonded to O1w. The bond angles around the oxygen atom (Table 2) do deviate somewhat from the ideal tetrahedral; however, the short O1w−N distances (range, 2.775−2.967 Å) signify strong H-bonding interactions. The atom O1w is 1.296 Å above the plane described by the three secondary amino nitrogens N(2), N(3), and N(4) while it is 1.656 Å below the plane described by the three ethereal oxygens. Thus, O1w is situated almost at the middle of the cavity. There are two more lattice water molecules which are outside the cavity and are H-bonded to the cryptand-protonated nitrogens, which are not involved in bonding with the water molecule inside the cavity. Further, the hydrogen atoms of the lattice water are bonded to the thiocyanate anions, forming a chainlike structure.

The solid state structures of **B** and **C** are very similar to the one present in **A**. One important difference is the

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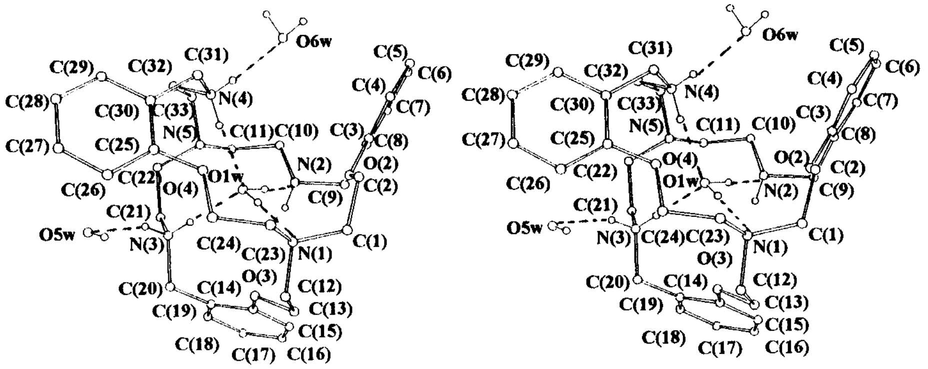

Figure 2. Stereoview of the complex cation in **A**.

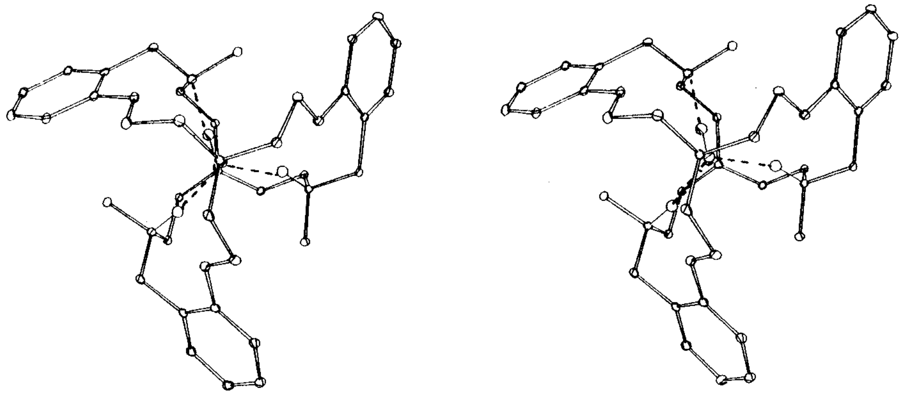

Figure 3. Stereoview along the two bridgehead nitrogen atoms (pseudo-3-fold axis) in **B**; **A** and **C** each have a similar view.

fact that there are no water molecules outside the cavity as there are no additional protons available on nitrogens to bind. Rather, a disordered acetone molecule is present in the lattice **B**. A pseudo-3-fold axis, which is along the two bridgehead N-atoms, is present in the cations in **A**−**C**. A stereoview along the two bridgehead nitrogens is shown in Figure 3. In contrast to our structures, the recently reported[13] crystal structure of a water cryptate shows that the O atom of the water molecule is held inside the cavity with five bonds. The ^{1}H-NMR data show that the water molecule is rapidly exchanging with the medium since the bonded water molecule does not show up in the spectrum, as studied in case of **A**.

Experimental Section

Syntheses of the cryptands $\mathbf{L_1}$ and $\mathbf{L_3}$ using Cs(I) ion as the template were reported earlier.[14] They have now been prepared in comparable yields without using any templating ions at room temperature following the literature.[15] This way, the cryptands can now be easily prepared on a multigram scale. The cryptand $\mathbf{L_2}$ has been prepared from $\mathbf{L_1}$ by the usual N-methylation technique using formic acid and formaldehyde, and its formation was confirmed by ^{1}H-NMR (80 MHz) data. FAB-mass (positive ion) data were recorded at the Central Drug Research Institute (CDRI), Lucknow, India, on a JEOL-SX 102/DA-6000 mass spectrometer/data systems at 298 K. ^{1}H-NMR data were recorded either on a Bruker WP-80FT instrument (at IIT Kanpur) or on a Bruker WM-400FT instrument (at CDRI).

Synthesis of $[H_2L_1\subset H_2O]^{2+}\cdot 2SCN^-\cdot 2H_2O$ (A). To a stirred solution of $\mathbf{L_1}$ (0.56 g; 1 mmol) in methanol (25 mL) was added solid ethylenediammonium dithiocyanate, and stirring was continued for another 8 h. The resulting solution was filtered and allowed to slowly evaporate, which afforded pale yellow prisms in 75% yield: ^{1}H-NMR (400 MHz, $CDCl_3$ + d_6-DMSO) δ 2.45 (s br, 6H), 2.7 (s br, 6H), 3.1 (s br, 6H), 3.95 (s, 6H), 4.25 (t, 6H), 7.01, 7.25, 7.45 (t, d, t, 12H); FAB-mass m/z 560 ($\mathbf{L_1}$ +1)$^+$, 582 ($H_2\mathbf{L_1}$ + H_2O + 3)$^+$.

Synthesis of $[H_2L_2\subset H_2O\,]^{2+}\cdot 2C_6H_2N_3O_7^-\cdot 1/2CH_3COCH_3$ (B). To an ethanolic solution of $\mathbf{L_2}$ (0.28 g; 0.5 mmol) was added 1 mmol of picric acid in 95% ethanol slowly with constant stirring at rt whereupon a bright yellow solid precipitated. The solid filtered and recrystallized from acetone at rt by slow evaporation, which afforded yellow prisms of **B** in 77% yield.

Synthesis of $[H_2L_2\subset H_2O]^{2+}\cdot 2ClO_4^-$ (C). The diperchlorate salt was obtained in a similar manner by adding aqueous perchloric acid to the cryptand at rt. The white precipitate was collected and recrystallized from MeCN to obtain **C** as colorless rectangular parallelopipeds in 62% yield.

Synthesis of the Water Inclusion Complex with the Cryptand $\mathbf{L_3}$ (D). When aqueous perchloric acid was allowed to react with the cryptand at rt, a white precipitate was obtained in 70% yield: FAB-mass m/z 732 ($\mathbf{L_3}$ + H_2O + 4)$^+$. Attempts to grow single crystals of the material were unsuccessful.

X-ray Crystallography. Cell parameters and reflection intensities were measured at 298 K on Nicolet R2m/V (for **A** and **B**) and Enraf-Nonius CAD4 Mach (for **C**) diffractometers using graphite-monochromated Mo Kα radiation. A summary of crystal data, data collection, and structure analysis and refinements are given in the Table 1. Intensity data were corrected for decay, Lorentz polarization, and absorption effects (analytical). The structures were solved by direct methods and refined on F by full-matrix least-squares techniques. For **A** and **B**, the SHELXTL-PLUS program package[16] on a DEC microvax-II computer and for **C** the XTAL 3.2 package[17] on a PC-486DX (PCL, India) computer were used for calculations. In each case, a few hydrogen atoms could be located in successive Fourier difference maps while others were added at calculated positions.

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Table 1. Crystal and Refinement Data of A, B, and C

	A	B	C
formula	$[C_{33}H_{47}N_5O_3{\cdot}H_2O]{\cdot}2SCN{\cdot}2H_2O$	$[C_{36}H_{53}N_5O_3{\cdot}H_2O]{\cdot}2C_6H_2N_3O_7{\cdot}0.5CH_3COCH_3$	$[C_{36}H_{53}N_5O_3{\cdot}H_2O]{\cdot}2ClO_4$
formula weight	730.99	1107.10	820.78
crystal dimens (mm)	0.5 × 0.5 × 0.6	0.42 × 0.42 × 0.3	0.32 × 0.38 × 0.4
crystal system	monoclinic	triclinic	triclinic
space group	Cc	$P\bar{1}$	$P\bar{1}$
Z	4	2	2
a (Å)	13.701(2)	12.674(3)	10.024(1)
b (Å)	15.284(2)	14.522(3)	10.061(1)
c (Å)	19.685(3)	17.101(4)	20.720(2)
α (deg)	90.0	111.82(1)	99.70(1)
β (deg)	107.61(3)	110.64(1)	102.34(1)
γ (deg)	90.0	90.56(1)	91.12(1)
V (Å^3)	1087(1)	2698(1)	2009(1)
d (calcd, g/cm^3)	1.236	1.363	1.357
$F(000)$	1564	1168	872
μ (cm^{-1})	1.86	1.05	1.07
$2\theta_{\max}$ (deg)	50	45	50
no. of data	3608	7063	4789
no. of data used	3098	4451	2862
no. of variables	449	719	495
R_f	0.033	0.067	0.056
R_w	0.046	0.067	0.062
S	0.84	1.41	2.181

Table 2. Selected Bond Lengths (Å), Angles (Deg), and Torsion Angles (Deg) for A, B, and C (in the case of A H3N and H4N are H3NA and H4NA)

	A	B	C
O(1w)−N(1)	2.967(2)	2.909(3)	2.880(3)
O(1w)−N(2)	2.828(3)	2.872(3)	2.928(2)
O(1w)−N(3)	2.842(2)	2.867(2)	2.816(2)
O(1w)−N(4)	2.775(2)	2.852(2)	2.770(2)
O(1w)−H(3N)	2.035(3)	1.904(3)	1.945(3)
O(1w)−H(4N)	1.905(3)	1.815(3)	1.920(3)
N(1) − H(1wA)	2.121(3)	1.911(3)	1.847(3)
N(2)−H(1wB)	2.024(4)	1.835(4)	2.106(4)
O(1w)−H(1wA)−N(1)	174.83(5)	171.03(2)	162.58(6)
O(1w)−H(1wB)−N(2)	158.68(4)	178.81(3)	163.22(4)
O(1w)−H(3NA)−N(3)	171.14(4)	153.85(4)	168.25(5)
O(1w)−H(4NA)−N(4)	173.09(5)	170.77(4)	158.25(3)
H(1wA)−O(1w)−H(1wB)	98.35(4)	112.02(5)	96.94(4)
H(1wA)−O(1w)−H(3N)	123.23(4)	107.88(4)	123.94(5)
H(1wA)−O(1w)−H(4N)	118.36(2)	124.64(3)	122.18(3)
H(1wB)−O(1w)−H(3N)	102.25(5)	95.88(3)	112.78(2)
H(1wB)−O(1w)−H(4N)	112.23(3)	103.24(4)	102.38(2)
H(3N)−O(1w)−H(4N)	104.63(4)	99.7(5)	98.22(3)
N(1)−H(1wA)−O(1w)−H(1wB)	−123(3)	122(2)	26(2)
N(1)−H(1wA)−O(1w)−H(1wB)	−12(2)	−134(3)	−147(2)
N(1)−H(1wA)−O(1w)−H(1wB)	119(2)	−3(2)	−68(2)
N(2)−H(1wB)−O(1w)−H(1wA)	171(3)	−87(2)	130(3)
N(2)−H(1wB)−O(1w)−H(1wA)	−67(3)	49(3)	−122(3)
N(2)−H(1wB)−O(1w)−H(1wA)	44(2)	161(2)	137(3)
N(3)−H(3N)−O(1w)−H(4N)	−83(3)	−19(2)	145(2)
N(3)−H(3N)−O(1w)−H(4N)	53(2)	119(3)	−84(2)
N(3)−H(3N)−O(1w)−H(4N)	162(3)	−125(2)	−87(2)
N(4)−H(4N)−O(1w)−H(1wA)	116(2)	100(2)	122(2)
N(4)−H(4N)−O(1w)−H(1wB)	5(2)	−29(3)	88(3)
N(4)−H(4N)−O(1w)−H(3N)	−105(3)	−130(2)	−150(3)

Anisotropic refinement of non-hydrogen atoms and isotropic refinement of hydrogen atoms associated with H-bonding were carried out. Analytical expressions of neutral-atom scattering factors were employed, and anomalous dispersion corrections were incorporated. All the atoms were included in the structure factor calculations. The relevant bond distances and angles along with torsional angles about the included water molecule for all the three complexes are collected in Table 2.[18]

In conclusion, the results of the present study show that $\mathbf{L_1}$, $\mathbf{L_2}$, and $\mathbf{L_3}$ are suitable to trap a molecule of water when diprotonated. The abnormal protonation behavior is the result of a cooperative effect mediated by the water molecule. The structures described here are the first diprotonated cryptands clearly shown to capture water *via* tetrahedral coordination in the central cavity. The molecular recognition property of these cryptands with different guest entities is currently being investigated.

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[18] The author has deposited atomic coordinates for $\mathbf{L_1}$, $\mathbf{L_2}$, and $\mathbf{L_3}$ with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.