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Crystal and Molecular Structure of Benzo-13-crown-4 and Its Complex with Lithium Thiocyanate

G. Shoham,[†] W. N. Lipscomb,*[,†] and U. Olsher[‡]

Contribution from Gibbs Laboratory, Department of Chemistry, Harvard University, Cambridge, Massachusetts 02138, and the Department of Biological Chemistry, Harvard Medical School, Boston, Massachusetts 02115. *Received July 6, 1982*

Abstract: The crystal structures of the title compounds have been determined from single-crystal X-ray diffractometry data. There are 4 molecules of polyether in the unit cell of dimensions a = 8.014 Å, b = 8.309 Å, and c = 18.964 Å. The space group is $P2_12_12_1$. The structure was solved by direct methods and refined by least-squares methods to a value of 0.042 for R with use of 1243 independent observations. Crystals of the complex with LiSCN in the space group *Pbca* have 8 molecules in unit cell of dimensions a = 11.870 Å, b = 13.453 Å, and c = 19.105 Å. The structure was solved by Patterson and direct methods and refined by least-squares methods to 0.069 for R with use of 1612 independent observations. The free crown ether is "bent": three oxygens are pointing to the interior and one to the exterior of the macrocyclic ring. In the complex, Li is pentacoordinated to four crown oxygens and the N of the SCN anion. Li–O distances are in the range of 2.01–2.16 Å, and the Li–N distance is 1.945 Å. Complexation of the ether changes its conformation. A rotation of ~145° about the CC–CO bond in the C–C–C–O dihedral angle brings one of the oxygens inward, allowing simultaneous coordination of all four oxygens to the Li cation. All of the remaining torsion angles are similar to those which are typical in these systems. Also, the C–C aliphatic bonds are short (average C–C ~1.49 Å) in both molecular structures, in agreement with known structures of a similar kind.

A large number of crown ethers has been synthesized in the last 14 years, most of which form a wide variety of complexes with alkali and alkaline earth metal cations.[1-9] Since one main interest in this family of compounds is their analogous behavior to naturally occurring ionophores, most of the experiments in solution and crystal structure analysis have been focused upon complexes of these cyclopolyethers with Na^+ and K^+ cations. Parallel efforts have been made both to understand the nature of binding of these cations to macrocyclic ethers and to design new synthetic macrocycles that will form more stable and more selective complexes with a specific cation.

Relatively little work has been done on complexes of Li cations with crown ethers. Complexation capabilities with lithium by small 12–15-member ring crown ethers have been reported.[1,4,7,8] In particular benzo-13-crown-4[10] (I) is an effective and selective complexing agent for lithium.[11] In addition the (2.1.1) cryptand[12,13] and some acyclic quadridentate amido ethers preferentially complex lithium.[14,15] Among the naturally occuring macrocycles, antamamide (a cyclic decapeptide isolated from the poisonous mushroom *Amanita phalloides*) has been shown to complex preferentially with Li in semipolar solvents such as acetonitrile.[16,17] Crystal structure analysis has been made on the complexes of Li^+ with the (2.1.1) cryptand and antamanide[13,17] and more recently on some complexes of macrocyclic polyethers with Li^+.[18-21] In these structures Li cation occurs in various coordinations (tetra, penta, and hexa), and the Li–ligand bond distances vary from 1.86 to 2.29 Å.

NMR experiments indicate that the benzo-13-crown-4 forms a 1:1 complex with Li, in which Li fits exactly in the "cavity" of the crown ether. However, the effectiveness of binding depends on the counterion. For these reasons we have studied the detailed nature of the crown ether complex with Li^+ and of its interaction with the counteranion. In particular, we describe the crystal structure of benzo-13-crown-4 and its complex with LiSCN.

Experimental Section

Uncomplexed B-13-C-4 (I). Crystals of I were grown from *n*-heptane by slow cooling. A single crystal of approximate dimensions 0.4 × 0.25 × 0.2 mm was used for space group determination and data collection. Systematic absences indicated that the space group is $P2_12_12_1$ (orthorhombic).

Crystal data: $C_{13}H_{18}O_4$, mol wt = 238.29, space group $P2_12_12_1$, a = 8.014 (1) Å, b = 8.309 (1) Å, c = 18.964 (3) Å, V = 1262.9 (3) Å^3, ρ_{calcd} = 1.25 g cm^{-1}, ρ_{measd} = 1.26 ± 0.02 g cm^{-1}, Z = 4, μ(Cu Kα) = 6.74 cm^{-1}.

Table I. Positional Parameters for I

	x/a	y/b	z/c
O(1)	0.4007 (2)	0.2471 (2)	0.5290 (1)
O(2)	0.1871 (2)	0.2494 (2)	0.6366 (1)
O(3)	−0.0448 (3)	−0.0088 (2)	0.6661 (1)
O(4)	0.3129 (2)	−0.0867 (2)	0.5542 (1)
C(1)	0.4415 (3)	0.3375 (3)	0.5880 (1)
C(2)	0.3286 (3)	0.3385 (3)	0.6447 (1)
C(3)	0.3687 (4)	0.4286 (3)	0.7047 (1)
C(4)	0.5135 (4)	0.5171 (3)	0.7069 (1)
C(5)	0.6207 (4)	0.5192 (4)	0.6499 (1)
C(6)	0.5842 (3)	0.4262 (3)	0.5907 (1)
C(7)	0.0661 (4)	0.2541 (4)	0.6916 (1)
C(8)	−0.0812 (4)	0.1596 (3)	0.6684 (2)
C(9)	−0.0313 (4)	−0.0750 (4)	0.5979 (1)
C(10)	0.0739 (5)	−0.2219 (4)	0.5986 (2)
C(11)	0.2520 (4)	−0.1875 (4)	0.6106 (2)
C(12)	0.4717 (3)	−0.0232 (3)	0.5681 (1)
C(13)	0.5068 (3)	0.1100 (3)	0.5173 (1)

[†] Harvard University.

[‡] Harvard Medical School.

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Table II. Bond Lengths (Å) for I

C(1)-O(1)	1.387 (3)	C(13)-O(1)	1.438 (3)
C(2)-O(2)	1.363 (3)	C(7)-O(2)	1.425 (4)
C(8)-O(3)	1.430 (4)	C(9)-O(3)	1.410 (4)
C(11)-O(4)	1.444 (4)	C(12)-O(4)	1.402 (4)
C(2)-C(1)	1.404 (4)	C(6)-C(1)	1.361 (4)
C(3)-C(2)	1.401 (4)	C(4)-C(3)	1.374 (5)
C(5)-C(4)	1.380 (5)	C(6)-C(5)	1.394 (4)
C(8)-C(7)	1.485 (5)	C(10)-C(9)	1.484 (6)
C(11)-C(10)	1.473 (6)	C(13)-C(12)	1.493 (4)
H(03)-C(3)	1.08 (0)	H(04)-C(4)	1.08 (0)
H(05)-C(5)	1.08 (0)	H(06)-C(6)	1.08 (0)
H(07)-C(7)	1.08 (0)	H(17)-C(7)	1.08 (0)
H(08)-C(8)	1.01 (1)	H(18)-C(8)	1.10 (1)
H(09)-C(9)	0.95 (1)	H(19)-C(9)	1.06 (1)
H(010)-C(10)	1.01 (1)	H(110)-C(10)	1.11 (1)
H(011)-C(11)	1.08 (1)	H(111)-C(11)	1.08 (0)
H(012)-C(12)	1.08 (0)	H(112)-C(12)	1.08 (0)
H(013)-C(13)	1.08 (0)	H(113)-C(13)	1.08 (0)

Table III. Bond Angles (deg) for I

C(13)-O(1)-C(1)	114.4 (2)	C(7)-O(2)-C(2)	118.0 (2)
C(9)-O(3)-C(8)	115.1 (3)	C(12)-O(4)-C(11)	112.7 (2)
C(2)-C(1)-O(1)	117.9 (2)	C(6)-C(1)-O(1)	121.4 (2)
C(6)-C(1)-C(2)	120.6 (2)	C(1)-C(2)-O(2)	116.5 (2)
C(3)-C(2)-O(2)	124.9 (3)	C(3)-C(2)-C(1)	118.5 (3)
C(4)-C(3)-C(2)	120.2 (3)	C(5)-C(4)-C(3)	120.6 (3)
C(6)-C(5)-C(4)	119.5 (3)	C(5)-C(6)-C(1)	120.4 (3)
C(8)-C(7)-O(2)	108.0 (3)	C(7)-C(8)-O(3)	111.3 (3)
C(10)-C(9)-O(3)	110.8 (3)	C(11)-C(10)-C(9)	113.1 (3)
C(10)-C(11)-O(4)	109.0 (3)	C(13)-C(12)-O(4)	109.2 (2)
C(12)-C(13)-O(1)	112.1 (2)		

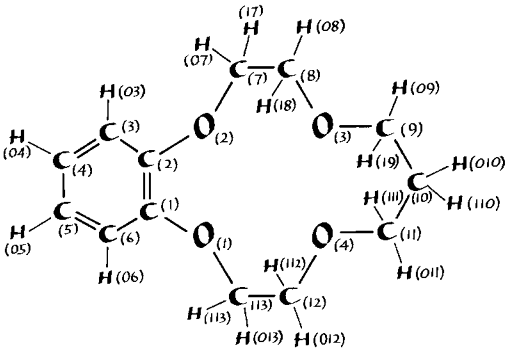

Figure 1. Numbering scheme in B-13-C-4.

Integrated intensities of 1362 independent reflections in the range of 3° ≤ 2θ ≤ 137° were measured in the $\theta/2\theta$ scan mode, with the use of graphite-crystal monochromatized Cu Kα radiation (λ_{mean} = 1.541 78 Å), on an automated four-circle Syntex P2_1 diffractometer. Corrections were applied for background, radiation damage, and Lorentz and polarization effects. Because of the small size of crystals no absorption corrections were made. Only 1243 observations (91%) with $F_o \geq 3.0\sigma(F_o)$ were included in further calculations.

Structure Determination. Fourteen of the seventeen non-hydrogen atoms were found by direct methods.[22] The other three non-hydrogen atoms and six hydrogen atoms were then located in difference electron-density maps. Refinement, including anisotropic thermal parameters for all non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms, was carried out by the use of block diagonal least-squares methods.[23] Successive refinement cycles, combined with difference electron-density maps, revealed the other 12 hydrogen atoms. Their positions were then idealized 1.08 Å away from their respective carbon atoms, and only their isotropic temperature factors were further refined.

Table IV. Positional Parameters for II

	x/a	y/b	z/c
S(1)	0.4560 (1)	0.1848 (1)	0.0318 (1)
C(14)	0.4654 (3)	0.2153 (3)	0.1148 (2)
N(1)	0.4722 (3)	0.2340 (3)	0.1725 (1)
Li	0.4769 (6)	0.2484 (5)	0.2738 (3)
O(1)	0.5095 (2)	0.0953 (2)	0.3019 (1)
O(2)	0.3390 (2)	0.2056 (2)	0.3318 (1)
O(3)	0.4165 (2)	0.3853 (2)	0.2985 (1)
O(4)	0.6180 (2)	0.2699 (2)	0.3302 (1)
C(1)	0.4437 (3)	0.0640 (3)	0.3578 (2)
C(2)	0.3512 (3)	0.1230 (3)	0.3731 (2)
C(3)	0.2787 (4)	0.0958 (4)	0.4263 (2)
C(4)	0.2998 (6)	0.0094 (4)	0.4626 (3)
C(5)	0.3887 (6)	−0.0482 (5)	0.4471 (3)
C(6)	0.4612 (5)	−0.0218 (4)	0.3943 (3)
C(7)	0.2757 (4)	0.2880 (3)	0.3578 (2)
C(8)	0.2989 (4)	0.3711 (4)	0.3078 (2)
C(9)	0.4660 (4)	0.4494 (4)	0.3492 (2)
C(10)	0.5924 (4)	0.4463 (4)	0.3419 (3)
C(11)	0.6472 (4)	0.3551 (4)	0.3701 (2)
C(12)	0.6609 (4)	0.1813 (4)	0.3596 (3)
C(13)	0.6285 (4)	0.0970 (4)	0.3131 (4)

Table V. Bond Lengths (Å) for II

C(14)-S(1)	1.641 (5)	N(1)-C(14)	1.134 (6)
Li-N(1)	1.945 (7)	O(1)-Li	2.164 (8)
O(2)-Li	2.059 (8)	O(3)-Li	2.033 (8)
O(4)-Li	2.012 (8)	C(1)-O(1)	1.387 (5)
C(13)-O(1)	1.428 (6)	C(2)-O(2)	1.371 (5)
C(7)-O(2)	1.429 (6)	C(8)-O(3)	1.420 (6)
C(9)-O(3)	1.424 (6)	C(11)-O(4)	1.419 (6)
C(12)-O(4)	1.414 (7)	C(2)-C(1)	1.387 (6)
C(6)-C(1)	1.365 (7)	C(3)-C(2)	1.381 (7)
C(4)-C(3)	1.377 (9)	C(5)-C(4)	1.342 (10)
C(6)-C(5)	1.373 (9)	C(8)-C(7)	1.496 (7)
C(10)-C(9)	1.507 (8)	C(11)-C(10)	1.489 (8)
C(13)-C(12)	1.491 (9)	H(04)-C(4)	0.85 (5)
H(03)-C(3)	0.91 (4)	H(06)-C(6)	0.88 (5)
H(05)-C(5)	0.84 (5)	H(17)-C(7)	1.01 (4)
H(07)-C(7)	0.97 (4)	H(18)-C(8)	0.89 (4)
H(08)-C(8)	0.96 (4)	H(19)-C(9)	0.97 (4)
H(09)-C(9)	0.93 (5)	H(110)-C(10)	0.92 (5)
H(010)-C(10)	0.95 (4)	H(111)-C(11)	0.98 (4)
H(011)-C(11)	1.03 (5)	H(112)-C(12)	0.97 (5)
H(012)-C(12)	1.02 (5)	H(113)-C(13)	0.92 (5)
H(013)-C(13)	1.01 (5)		

The refinement of the structure converged to a value of 0.042 for *R*. In the final cycle of refinement the largest ratio of shifts to estimated standard deviations was less than 0.003. A final difference synthesis had no peaks of magnitude greater than 0.2 e/Å^3. The final fractional coordinates of I are given in Table I, and bond lengths and bond angles are listed in Tables II and III. The numbering system is shown in Figure 1.

Complex of I with LiSCN (II). Crystals of II were grown from a 1:1 methanol–diethyl ether mixture by slow evaporation. No attempt was made to completely dry the LiSCN salt; thus traces of water molecules might have been present in the crystallization solution. A single crystal of approximate dimensions 0.25 × 0.20 × 0.08 mm was used for space group determination and data collection. Systematic absences indicated that the space group is *Pbca*.

Crystal data: $C_{14}H_{18}O_4NSLi$, mol wt = 303.31, space group *Pbca*, a = 11.870 (2) Å, b = 13.453 (2) Å, c = 19.105 (3) Å, V = 3050.8 (7) Å^3, ρ_{calcd} 1.32 g cm^{-1}, ρ_{measd} = 1.34 ± 0.02 g cm^{-1}, Z = 8, μ(Cu Kα) = 18.89 cm^{-1}.

Integrated intensities of 2865 reflections in the range of 3° ≤ 2θ ≤ 130° were measured as described above. Corrections were applied for background, radiation damage, and Lorentz and polarization effects.

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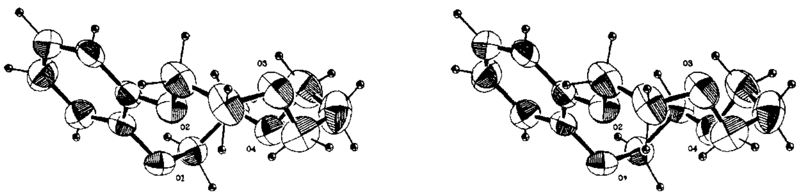

Figure 2. Stereo drawing of B-13–C-4.

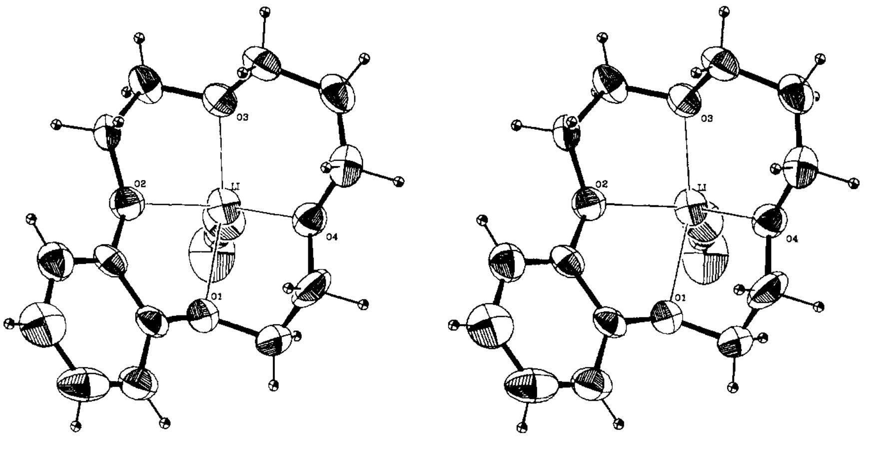

Figure 3. Stereo drawing of the complex B-13–C-4/LiSCN (top view).

Also, empirical absorption corrections were made.[24] Due to the small size of the crystal, the diffraction pattern was fairly weak and relatively poorly measured in the range $2\theta > 110°$, and therefore only 2049 observations with $F_o \geq 2.0\sigma(F_o)$ were used for further calculation.

Structure Determination. The sulfur atom was located from the Patterson function. However, the difference electron-density map did not reveal any recognizable fragment of the structure. Use of direct methods[22] then confirmed the sulfur position and revealed all other non-hydrogen atoms. All hydrogen atoms were then found from cycles of difference electron-density maps and block diagonal least-squares refinements.[23] In the final stage of refinement, only those 1612 reflections for which $F_o \geq 6.0\sigma(F_o)$ were included; all positional parameters were refined by using anisotropic thermal parameters for non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms. The refinement of the structure of II converged to values of 0.069 and 0.067 for R and R_w, respectively.

In the final cycle of refinement the largest ratio of shifts to estimated standard deviations was less than 0.003, and no peaks higher than 0.41 e/Å^3 around the sulfur atom and 0.32 e/Å^3 elsewhere were seen in the final difference electron-density map.

The final fractional coordinates of II are given in Table IV, and bond lengths and bond angles are listed in Tables V and VI. The numbering scheme is the same as that in Figure 1; C(14) is the carbon atom of the SCN$^-$ anion.

Results and Discussion

Structure of the Free Molecule. A stereo drawing of the structure (Figure 2) shows a rather large deviation of the molecule from planar configuration, more than was expected from NMR studies.[11] The macrocycle is asymmetrically "bent", forming an angle of 137° between the plane of the benzene ring plus the two catechol oxygens O(1) and O(2) (plane A) and the least-squares plane of the rest of the atoms (plane B). The four oxygens are not coplanar: three of them (O(1), O(2), O(4)) point to the interior of the cavity of the macrocycle (down in Figure 2), while the fourth oxygen (O(3)) points to the exterior of the cavity (up in Figure 2). The small ring may give rise to repulsion of the lone pairs on the oxygens in a hypothetical configuration in which all oxygens are pointing inward. Bond length and bond angles of the etheral bonds are similar to those found in other acyclic systems or in larger ring systems;[25-29] the average C–O distance is 1.42 Å, and the average C–O–C angle is 114°. The aliphatic C–C bonds (average 1.48 Å) are significantly shorter than the "expected" value[28] of 1.537 Å or the value of 1.523 Å reported for 1,4-dioxane[29] in the gas phase. This shortening has been found previously in the larger macrocyclic crown ethers and their complexes.[2,5,26,27]

Table VI. Bond Angles (deg) for II

N(1)–C(14)–S(1)	178.4 (4)	Li–N(1)–C(14)	172.4 (5)
O(1)–Li–N(1)	99.1 (3)	O(2)–Li–N(1)	119.0 (4)
O(2)–Li–O(1)	75.1 (3)	O(3)–Li–N(1)	108.1 (4)
O(3)–Li–O(1)	150.2 (4)	O(3)–Li–O(2)	81.2 (3)
O(4)–Li–N(1)	124.8 (4)	O(4)–Li–O(1)	81.7 (3)
O(4)–Li–O(2)	114.4 (3)	O(4)–Li–O(3)	92.2 (3)
C(1)–O(1)–Li	112.3 (3)	C(13)–O(1)–Li	101.4 (3)
C(13)–O(1)–C(1)	116.5 (4)	C(2)–O(2)–Li	116.9 (3)
C(7)–O(2)–Li	112.9 (3)	C(7)–O(2)–C(2)	118.9 (3)
C(8)–O(3)–Li	104.7 (3)	C(9)–O(3)–Li	124.2 (3)
C(9)–O(3)–C(8)	113.7 (4)	C(11)–O(4)–Li	127.4 (4)
C(12)–O(4)–Li	113.0 (4)	C(12)–O(4)–C(11)	112.3 (4)
C(2)–C(1)–O(1)	115.8 (4)	C(6)–C(1)–O(1)	124.3 (4)
C(6)–C(1)–C(2)	119.7 (4)	C(1)–C(2)–O(2)	115.2 (4)
C(3)–C(2)–O(2)	125.0 (4)	C(3)–C(2)–C(1)	119.8 (4)
C(4)–C(3)–C(2)	118.8 (5)	C(5)–C(4)–C(3)	121.3 (6)
C(6)–C(5)–C(4)	120.4 (6)	C(5)–C(6)–C(1)	120.0 (6)
C(8)–C(7)–O(2)	105.1 (4)	C(7)–C(8)–O(3)	111.2 (4)
C(10)–C(9)–O(3)	109.3 (4)	C(11)–C(10)–C(9)	115.1 (5)
C(10)–C(11)–O(4)	111.4 (4)	C(13)–C(12)–O(4)	108.1 (5)
C(12)–C(13)–O(1)	110.9 (5)		

Structure of the Complexed Molecule. Stereo drawings of the complex (II) are shown in Figures 3 and 4. The lithium is pentacoordinated to the four ethereal oxygens of the crown ether and to the SCN$^-$ anion. The macrocycle is still "bent" asymmetrically (the angle between plane A and plane B is 131°), and all four oxygens are directed toward the "convex" side of the molecule, allowing simultaneous coordination to the Li cation. The four oxygens are not completely coplanar; the mean deviation from the mean least-squares plane connecting them is 0.3 Å. The Li cation is 0.8 Å above the center of this plane, and the SCN$^-$

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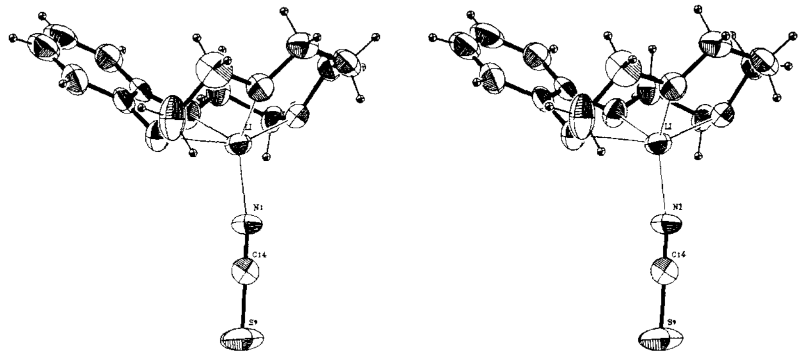

Figure 4. Stereo drawing of the complex (side view).

Table VII. Selected Torsion Angles (deg)

	free B-13-C-4	complexed B-13-C-4
C(6)-C(1)-O(1)-C(13)	69	51
C(1)-O(1)-C(13)-O(12)	74	73
O(1)-C(13)-C(12)-O(4)	68	55
C(13)-C(12)-O(4)-C(11)	−166	178
C(12)-O(4)-C(11)-C(10)	168	175
O(4)-C(11)-C(10)-C(9)	−61	−67
C(11)-C(10)-C(9)-O(3)	*−71*	*75*
C(10)-C(9)-O(3)-C(8)	*155*	*−171*
C(9)-O(3)-C(8)-C(7)	*−108*	*86*
O(3)-C(8)-C(7)-O(2)	70	52
C(8)-C(7)-O(2)-C(2)	175	−168
C(7)-O(2)-C(2)-C(3)	3	−24

anion is on the other side of the Li. Here again, the ethereal bond lengths (average C–O bond is 1.42 Å) and bond angles (average C–O–C angle is 113°) are typical,[25-29] and the average aliphatic C–C bond (1.50 Å)is again shorter than expected.

Conformation. Comparison between the corresponding bond lengths and bond angles in the uncomplexed and the complexed molecule (Tables II, III, V, VI) shows that they are basically the same within experimental error, except for small variation of angles around the "catechol" oxygens O(1), O(2). The main difference between the two forms is one of conformation. Selected torsion angles for both forms (Table VII) show that the main conformational difference is around O(3) and C(9). A 146° rotation around the C(9)–C(10) bond changes the C(11)–C(10)–C(9)–O(3) torsion angle from −71° in the free crown ether to +75° in the complexed one. This change brings C(9) "up" and O(3) "down" to the common side with the other three oxygens, thus forming the cavity that binds the Li cation (Figure 3).

Despite the small size of the macrocyclic ring and limited flexibility of the molecule due to the rigid cathecol group, the O–C–C–O aliphatic torsion angles are relatively close to 60° in both the complexed and uncomplexed molecule. This gauche conformation is also common in the larger polyether rings.[2,5] In the same way, the aliphatic C–C–O–C torsion angles in both structures are relatively close to the trans conformation (180°), the common "relaxed" form in larger crown ethers.[2,5] An exception is the C(9)–O(3)–C(8)–C(7) torsion angle, which is closer to the gauche conformation before and after the complexation. Probably this region of the molecule accounts for most of the strain in the ring both in the uncomplexed and in the complexed systems.

The best fit of the crown ethers in I and II by a least-squares rotation method[30] gives a total rms deviation of 0.46 Å between related atoms in the two structures. Superposition of the two structures after such rotation is shown in Figure 5, where the major difference around the O(3)–C(9) bond is exhibited.

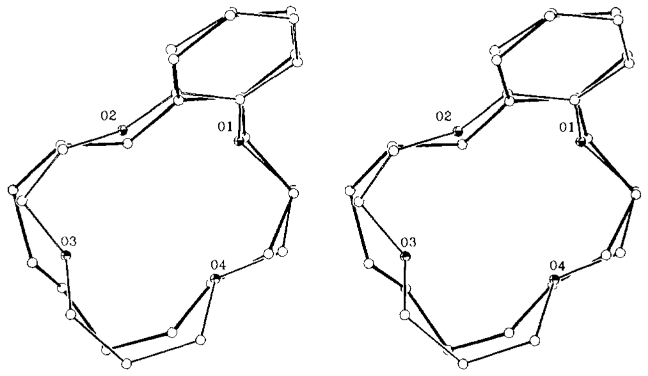

Figure 5. Stereoview of the crown ether in the complex (II) (thin line) superimposed on the stereoview of the free crown ether (I) (thick dark line).

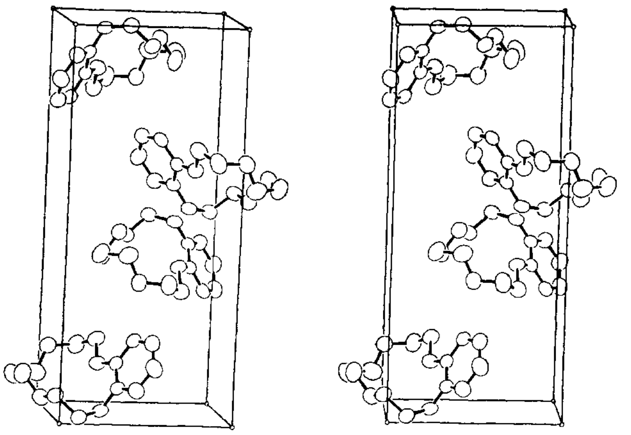

Figure 6. Stereoview of the unit cell packing of I.

Lithium Environment. From solution work on the complex of benzo-13-crown-4 with lithium salts and from inspection of the model, it was suggested[11] that the lithium cation fits nicely the size of the cavity in the crown ether (the ratio, *F*, of the diameter of Li$^+$ ion to the hole diameter of the crown was estimated as ~1.0). This type of complexation was classified later[5] as group 1. However, we show here that the lithium cation lies *above* the cavity of the cyclic polyether, coordinated on one side to the four ethereal oxygens, leaving its other side open for anion coordination. Indeed, the O(1)–O(3) distance in the complexed macrocycle of *4.05* Å and the O(2)–O(4) distance of 3.42 Å result in an adjusted diameter of the cavity of 0.62–1.25 Å.[31] These values are small compared to the effective diameter of the Li$^+$ cation (1.18–1.52 Å)[32] and thus favor the classification of group 2[5] for complexation.

The Li–O bond lengths, which range from 2.01 to 2.16 Å, average around 2.06 Å (Table V). However, the Li–O(1) bond (2.16 Å) is substantially longer than the others. The SCN$^-$ anion

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(30) (a) Kabsch, W. *Acta Crystallogr., Sect. A* **1976**, *A32*, 922. (b) Kabsch, W. *Ibid.* **1978**, *A34*, 827.

(31) Distance between opposite oxygens across the cavity, subtracting the size of oxygen atoms (see also ref 5).

(32) Effective radius for Li$^+$ cation was calculated to be 0.59 Å for four coordinated Li and 0.76 Å for six coordinated Li: Shannon, R. D. *Acta Crystallogr., Sect. A* **1976**, *A32*, 751.

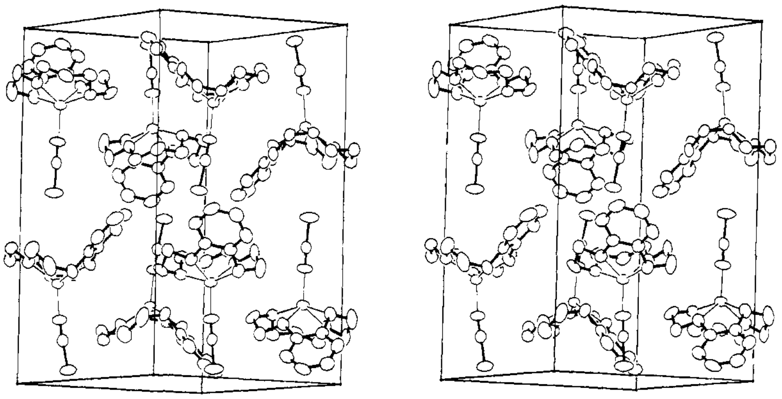

Figure 7. Stereoview of the unit cell packing of II.

coordinates to the lithium cation with its nitrogen atom, as commonly seen.[19,21,33,34] The Li–N–C angle is 172°. The Li–N distance (1.945 Å) is shorter than all Li–O distances and shorter than typical Li–N distances[13,17,19a] probably because of the unbalanced arrangement around the Li and the negative charge on the anion. A short Li–N distance has been observed previously in similar systems.[19b,21] The coordination geometry around Li is a distorted intermediate between the square pyramid and the trigonal bipyramid.

In inorganic compounds lithium is usually found in tetrahedral or octahedral coordination with average Li–O distances of 1.98 and 2.16 Å, respectively.[25] However, recent structural studies of Li macrocyclic multidentate complexes provide examples of pentacoordination. For example, in the Li–antamamide complex,[17] lithium is pentacoordinated to four carbonyl oxygens (average Li–O, 2.11 Å) and a nitrogen of a CH_3CN solvent molecule (Li–N, 2.07 Å) in a nearly square-pyramidal geometry. In both of the complexes of 16-crown-4 and 12-crown-4 with LiSCN[19] lithium is coordinated to the four ethereal oxygens (average Li–O, 2.08 Å) and SCN^- anion, giving a square-pyramidal coordination. Even in the complex of the double-loop macrocycle 18,18′-spirobi(19-crown-6), with LiI,[20] where the cavity is too large for one Li cation, lithium is pentacoordinated to three of the six ethereal oxygens of the crown ring and to two water molecules in a distorted trigonal-bipyramid geometry (average Li–O, 2.04 Å; 1.96 Å for the "equatorial" oxygens and 2.17 Å for the "apical" oxygens).

In addition, a few other Li–crown systems investigated in our laboratory[21] display five-coordinated Li complexes. The geometries vary from the square pyramid to less idealized distorted pentacoordination geometries.

Therefore, it seems likely that pentacoordination is a fairly general and stable coordination of the lithium cation with such macrocyclic ligands. The square-pyramidal geometry is the preferred geometry where possible. If indeed this is a general tendency, the distorted symmetry around the lithium and the difference in the Li–O distances in II might be caused by partial rigidity and strain in the macrocyclic ring system. Perhaps, then, one can design a more symmetrical ring system in order to favor a relaxed square-pyramidal coordination and then add an intramolecular tail that would occupy the apical position of the complex. This design would favor a more stable Li complex, which would be less sensitive to choice of anion or solvent.

With the assumption of tetrahedral hybridization on the oxygens, it appears that one lone pair (lp) on each oxygen atom is generally pointing toward the lithium cation (average Li–O–lp angle, ~18°). Again, the deviation from perfect collinearity of Li–lp–O might be caused by the limited conformational flexibility of the crown ether.

Crystal Packing. It is often argued that the conformation of a molecule determined by crystal structure analysis might be affected by crystal packing, lattice energy, and the solvent from which it was crystallized. However, in this study these effects probably do not play a significant role in the conformational energetics of the cyclic ether for the following reasons. (1) The molecule is relatively rigid. There is a very limited number of possible conformations, especially in the complexed form where there is strong interaction between the crown ether and the Li cation, and the macrocyclic part is basically "locked" into one conformation. (2) There are no solvent molecules in either of the cyrstals, in contrast to structural or directly complexed solvent molecules that have been found in crystal structures of the complexes of some larger crown ethers.[2,5,35] (3) No abnormal intermolecular contacts occur in either of the crystals (Figures 6 and 7). Also, there are no intermolecular distances shorter than 2.6 Å in the crystal structure of the uncomplexed molecule and 2.7 Å in the crystal structure of the complexed system. (4) A full optimization of all structural parameters in the uncomplexed molecule was done by semiempirical molecular orbital calculations (MNDO)[36] at the minimum basis set level, starting from the crystal structure coordinates and from distorted conformations as well. All calculations converged to the crystal structure conformation with total rms deviations of less than 0.15 Å.

Summary. The geometry of the binding site for Li^+ found here has revised an earlier proposal. The Li^+ is not in the plane of the four oxygens, but on one side of them, and coordinated also to the counterion SCN^-. In addition, Li^+ forms a 1:1 complex with B-13-C-4 in which Li^+ is pentacoordinated. The major conformational change under complexation is a 145° "flip" of one of the oxygen atoms. The complex is fairly compact and has the following properties and limitations.

(1) The cavity size is too small to bind Li^+ cation in the center of the molecule. (2) The macrocyclic ring is not flexible enough to arrange the oxygens in a symmetrical geometry equidistant from the lithium and to enable a collinear interaction of the oxygen lone pairs with the cation. (3) The fifth coordination is occupied by a nonspecific ligand—the anion, in this case.

Further studies, in order to remove these limitations on the macrocyclic molecule itself, may lead to a better and more selective ionophore for Li^+ and enable us to understand the role of the counteranion in these systems. Additional structural analysis of a series of B-13-C-4 complexes with Li^+ with different counteranions is now in progress in our laboratory, parallel to analogous investigations of the complexes of similar crown ethers with a set of Li salts in solution. Applications of these Li^+ chelating macrocyclic molecules include extraction of Li^+ from salt seas and, indirectly, regulation of Li^+ concentrations in the brain. Studies that improve the selectivity for Li^+ over other ions include variations of the macrocycle and of the counterion.

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Supplementary Material Available: Thermal parameters for non-hydrogen atoms (Table S1 for I, Table S4 for II), hydrogen atom positions and thermal parameters (Table S2 for I, Table S5 for II), and a listing of observed and calculated structure factors (Table S3 for I, Table S6 for II) (19 pages). Ordering information is given on any current masthead page.

Multifunctional Micellar Catalysis as a Model of Enzyme Action

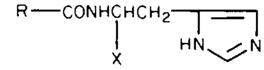
Yasuji Ihara,*[1] Mamoru Nango,[2] Yoshiharu Kimura,[2] and Nobuhiko Kuroki[2]

Contribution from the Yamaguchi Women's University, 3-2-1 Sakurabatake, Yamaguchi 753, Japan, and the Department of Applied Chemistry, University of Osaka Prefecture, Sakai, Osaka 591, Japan. *Received June 21, 1982*

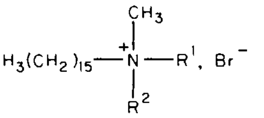
Abstract: The rate constants of both the acylation and deacylation processes in the hydrolyses of *p*-nitrophenyl acetate (PNPA) and hexanoate (PNPH) by imidazole catalysts (**1**) in the presence of surfactant micelles (**2**) have been directly determined under single turnover conditions at pH 7.30 in 0.02 M phosphate buffer and 25 °C. The major course of catalysis was the acylation followed by deacylation at the imidazole group. The kinetic analysis suggests that a multifunctional mode of action is involved in the catalytic ester hydrolysis; the acylation and deacylation rates are accelerated by carboxylate ion in the catalyst and by surfactant hydroxyl group, respectively.

The active site of α-chymotrypsin consists of the imidazole (His-57), hydroxyl (Ser-195), and carboxylate (Asp-102) groups. These three functional groups act as an esterolytic catalyst with mutual cooperation.[3] Many micellar enzyme models have been investigated in order to gain further insight into the nature of enzyme reactions[4] and, particularly, micellar bifunctional catalysts have been utilized successfully to elucidate certain aspects of the estrolytic enzyme reaction.[5]

The present study describes a kinetic analysis of multifunctional catalysis during the hydrolysis of *p*-nitrophenyl acetate (PNPA) and hexanoate (PNPH) by *N*-acylhistidine (**1**) in the presence of surfactant micelles (**2**). These micellar catalytic systems involve three functional groups and one can anticipate multifunctional interactions between them. The results obtained in this investigation demonstrate the first example of micellar catalysis with a triad of catalytic groups.



1a, R = CH_3; X = CO_2H
b, R = $CH_3(CH_2)_8$; X = CO_2H
c, R = $CH_3(CH_2)_8$; X = CO_2CH_3



$CH_3(CH_2)_{15}\overset{+}{N}(CH_3)(R^1)(R^2)$, Br^-

2a, $R^1 = R^2 = CH_3$
b, $R^1 = CH_3$; $R^2 = (CH_2)_2OH$
c, $R^1 = R^2 = (CH_2)_2OH$
d, $R^1 = CH_3$; $R^2 = (CH_2)_3OH$
e, $R^1 = CH_3$; $R^2 = CH(OH)CH_3$

Although there have been some investigations of the catalytic hydrolysis of *p*-nitrophenyl carboxylates by similar micellar catalytic systems, these investigations followed only the acylation process[6a] or acyl transfer during the reactions.[5a,b,6b] In this study, we directly measured deacylation rate constants of an acylated intermediate, as well as acylation rate constants during the course of the hydrolysis reactions.

Experimental Section

Materials. *p*-Nitrophenyl acetate (PNPA) and hexanoate (PNPH) were obtained from Tokyo Kasei Organic Chemicals. PNPA was purified by recrystallization from cyclohexane before use. Commercial *N*-acetylimidazole (Nakarai Chemicals Co.) was used without further purification. Functional surfactants (**2b–e**) were prepared by reaction of cetyl bromide and the corresponding tertiary amines in refluxing ethanol:[7] **2b**, mp 212–213 °C (lit.[7a] mp 208–210 °C); **2c**, mp 86–87 °C (lit.[7b] mp 85 °C); **2d**, mp 80–82 °C (lit.[7b] mp 82 °C); **2e**, mp 116–117 °C. Anal. ($C_{21}H_{46}O_2NBr$) C, H, N. Other materials have been described elsewhere.[8]

Kinetic Measurements. Reactions were generally monitored on a Hitachi 200 spectrophotometer or a Shimazu 140 spectrophotometer with a thermostated cell holder at 25 °C. In the general procedure, a solution (25 μL) of substrate in acetonitrile was added to a buffer solution (3.00 mL) containing the catalyst and surfactant at the desired concentrations. Details of the kinetic techniques and conditions may be found in the Results and Discussion. The spectra–time study of the reactions was monitored on a Hitachi 200 spectrophotometer with a wavelength program attachment.

Results and Discussion

Acyl Intermediates and the Reaction Traces. The spectra vs. time study of the reaction of PNPA with **1b** in the presence of **2a** was followed in the wavelength range 240–320 nm as shown in Figure 1. The spectra in Figure 1 consist of two phases: a fast reaction (acylation process) followed by a considerably slower reaction (deacylation process). We also observed good isosbestic points at 254 nm during the course of the acylation reaction. This reaction trace at a fixed wavelength (245 nm) is shown in Figure 2. However, although the reactions of PNPA with **1b** in the presence of **2a** or **2b** show different spectra–time behavior, we can

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(2) University of Osaka Prefecture.

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