plexation process should still be viewed essentially as one in which the solvent molecules are replaced in a stepwise fashion by ligand donor atoms, with a significant amount of the solvation energy being compensated for by the ligand binding energy during complexation.[50]

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Registry No. Ca, 7440-70-2; Sr, 7440-24-6; Ba, 7440-39-3; Me_2SO, 67-68-5; MeOH, 67-56-1; DMF, 68-12-2; PC, 108-32-7; (2,1,1), 31250-06-3; (2,2,1), 31364-42-8; (2,2,2), 23978-09-8; (2_B,2,2), 31250-18-7; (2_B,2_B,2), 40471-97-4.

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[50] Diebler, H.; Eigen, M.; Ilgenfritz, G.; Maass, G.; Winkler, R. *Pure Appl. Chem.* **1969**, *20*, 93.

Crystal and Molecular Structure of the Complex between *sym*-Dibenzo-14-crown-4-oxyacetate and Li$^+$, $[C_{20}H_{21}O_7]^-\cdot Li^+\cdot 7.5H_2O$

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Abstract: The synthesis and crystal structure of the title compound are described. Single crystal X-ray diffractometry indicates 8 formula units in the unit cell of parameters a = 20.779 Å, b = 17.845 Å, c = 13.903 Å, β = 98.19°. The space group is monoclinic $C2/c$. Direct methods yielded the structure, which was refined by least-squares techniques to a final R factor of 0.077 for 3124 independent observations. The lithium cation forms a 1:1 neutral complex with the carboxylic crown ether. In this complex, Li$^+$ is pentacoordinated with 4 crown oxygens (av. Li–O is 2.06 Å) and an apical water molecule (Li–O, 1.91 Å) in a nearly square pyramidal geometry. This apical water molecule forms a bridge between the Li$^+$ cation and the negatively charged carboxylate group. In the crystal structure we find an extensively ordered solvent (water) network which is dominated by O_5 pentagons. The crystal packing is formed of hydrophilic regions, linked together by water "channels", and hydrophobic regions, consisting mainly of the benzo rings.

Since Pedersen's introduction[1] of synthetic macrocyclic ionophores capable of forming stable complexes with alkali and alkali earth metal ions, considerable attention has been devoted to the exploitation of the cationic selectivity of these neutral coronands.[2–6] Crown ethers are of potential utility for many applications where cationic selectivity and solubility in nonpolar solvents or membranes are necessary. Properties that influence this selectivity include the charge, size, and electronic structure of the cations as well as the associated counterions. However, it is usually found that the strongest complex of an ionophore and a cation is one where the diameter of the cation best matches the diameter of the cavity formed by the polyether ring upon complexation.[1]

The nature of the interaction of lithium cations with neutral ionophores has received relatively little attention. Complexation tendencies toward lithium have been reported for 12- to 18-membered-ring crown ethers,[1,7–12] as well as (2.1.1)cryptand[13,14] and some acyclic quadridentate amido ethers.[15,16] Some of these complexing agents display a significant selectivity toward lithium cations.[11,12,15,16] In addition, crystal structure analyses have been presented for lithium complexes with the (2.1.1)cryptand,[14] some 12–18-membered-ring macrocycles,[17–20] and recently the crown ethers benzo-13-crown-4 (B-13-C-4)[21] and dibenzo-14-crown-4 (DB-14-C-4) (**1**).[22] In the latter two crystal structures, the coordination polyhedron of the lithium cation is 5-coordinate square pyramidal with the metal ion being positioned 0.7–0.8 Å above the plane of the four ethereal oxygens of the coronand. The counterion occupies the fifth (apical) coordination site.

A series of macrocyclic polyethers possessing ligating arms was reported recently by Gokel,[23] who identifies such compounds as

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(1) Pedersen, C. J. *J. Am. Chem. Soc.* **1967**, *89*, 2495, 7017.

(2) Lehn, J. M. *Struc. Bonding (Berlin)* **1973**, *16*, 1–69.

(3) Pedersen, C. J. In "Synthetic Multidentate Macrocyclic Compounds"; Izatt, R. M., Christensen, J. J., Eds.; Academic Press: New York, 1978; pp 1–51.

(4) Poonia, N. S.; Bajaj, A. V. *Chem. Rev.* **1979**, *79*, 389.

(5) Weber, E.; Vögtle, F. In "Host Guest Complex Chemistry I. Topics in Current Chemistry"; Boschke, F. L., Ed.; Springer-Verlag: New York, 1981; Vol. 98, pp 1–41.

(6) Hilgenfeld, R.; Saenger, W. In "Host Guest Complex Chemistry II. Topics in Current Chemistry"; Boschke, F. L., Ed.; Springer-Verlag: New York, 1982; Vol. 101, pp 1–82.

(7) Dale, J.; Krane, J. *J. Chem. Soc., Chem. Commun.* **1972**, 1012.

(8) Anet, F. A. L.; Krane, J.; Dale, J.; Daasvatn, K.; Kristiansen, P. O. *Acta Chem. Scand.* **1973**, *27*, 3395.

(9) Pedersen, C. J.; Frensdorff, H. K. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 16.

(10) Smetana, A. J.; Popov, A. I. *J. Soln. Chem.* **1980**, *9*, 183.

(11) Olsher, U.; Jagur-Grodzinski, J. *J. Chem. Soc., Dalton Trans.* **1981**, 501.

(12) Olsher, U. *J. Am. Chem. Soc.* **1982**, *104*, 4006.

(13) Lehn, J. M.; Sauvage, J. P. *J. Chem. Soc., Chem. Commun.* **1971**, 440.

(14) Moras, D.; Weiss, R. *Acta Crystallogr., Sect. B* **1973**, *B29*, 400.

(15) Kirsch, N. N.; Funck, R. J. J.; Pretsch, E.; Simon, W. *Helv. Chim. Acta* **1977**, *60*, 2326.

(16) Olsher, U.; Elgavish, G.; Jagur-Grodzinski, J. *J. Am. Chem. Soc.* **1980**, *102*, 3338.

(17) Bhagwat, V. W.; Manohar, H.; Poonia, N. S. *Inorg. Nucl. Chem. Lett.* **1980**, *16*, 373.

(18) Groth, P. *Acta Chem. Scand., Ser. A* **1981**, *A35*, 460, 463.

(19) Groth, P. *Acta Chem. Scand., Ser. A* **1982**, *A36*, 109.

(20) Groth, P. *Acta Chem. Scand., Ser. A* **1983**, *A37*, 71.

0002-7863/84/1506-1280$01.50/0

lariat ethers. The conformationally mobile arms present a potential for axially directed ligation, and were found to enhance cation binding. Likewise, crown ethers with pendant carboxylic acid groups have been synthesized and utilized in the solvent extraction of cations from aqueous into organic phases.[24-26] These ionizable crown ethers possess a distinct advantage over the neutral coronands previously studied in that cationic extraction does not require a concomitant phase transfer of the counterion. In a search for possible enhancement of the lithium selectivity which has been observed with DB-14-C-4 (**1**), the crown ether has been modified by adding a pendant ethereal arm which bears a carboxylic acid terminus. By providing an intramolecular carboxylate counterion to occupy the apical coordination site of the lithium, this crown ether carboxylic acid might possess a highly favorable entropy of complexation. Herein we report the synthesis of *sym*-dibenzo-14-crown-4-oxyacetic acid (**2**) and the crystal structure of its neutral complex with a lithium cation (**2a**).

Experimental

Synthesis. 1,3-Bis(2-hydroxyphenoxy)propane. Under nitrogen, a solution of NaOH (5.0 g, 125 mmol) in water (5 mL) was added over 1 h to a mechanically-stirred solution of catechol (11.0 g, 100 mmol) and 1,3-dibromopropane (6.0 mL, 59 mmol) which had been heated to 120 °C. The resulting mixture was heated at this temperature and stirred for 8 h. While still fluid the mixture was poured into water and 5 N NaOH solution (50 mL) and CH_2Cl_2 were added. Solid material was removed by filtration, and the aqueous layer of the filtrate was separated, neutralized with concentrated HCl, and extracted with CH_2Cl_2 (additional product was recovered by suspending the filtered solid in CH_2Cl_2 and adding concentrated HCl with stirring until the solid dissolved). The CH_2Cl_2 solutions were combined, dried over $MgSO_4$, and passed through a short column of silica gel to remove the polymeric contaminants. Evaporation of the CH_2Cl_2 in vacuo gave 1,3-bis(2-hydroxyphenoxy)-propane (4.5 g, 35%): mp 130–131 °C; IR (KBr) 3350 cm^{-1} (OH); ^1H NMR (CD_3COCD_3) δ 2.25 (2 H, m), 4.22 (4 H, t), 5.93 (2 H, br s), 6.80 (8 H, s). Anal. Calcd for $C_{15}H_{16}O_4$: C, 69.23; H, 6.15. Found: C, 68.99; H, 6.27.

***sym*-Hydroxydibenzo-14-crown-4.** Under nitrogen 1,3-bis(2-hydroxyphenoxy)propane (4.0 g, 16 mmol) and LiOH (0.71 g, 30 mmol) together in water (380 mL) were heated at 90 °C to achieve solution and the solution was cooled to 55 °C. Over 3 h, epichlorohydrin (1.2 mL, 15 mmol) was added, and heating at this temperature and stirring were continued for 10 h. After adding LiOH (0.71 g, 30 mmol) in one portion, additional epichlorohydrin (1.2 mL, 15 mmol) was introduced into the heated and stirred reaction mixture over 3 h and heating and stirring were continued for another 10 h. After cooling, the solid material was separated by filtration and dissolved in CH_2Cl_2. The CH_2Cl_2 solution was dried with $MgSO_4$, reduced to a small volume in vacuo, and loaded onto a short column of silica gel. Elution with Et_2O separated the product from contaminating polymeric materials. Evaporation of the eluate in vacuo gave *sym*-hydroxydibenzo-14-crown-4 (3.4 g, 70%): mp 153–154 °C (lit.[27] mp 153–154 °C); IR (KBr) 3560–3200 cm^{-1} (OH); ^1H NMR ($CDCl_3$ + CD_3COCD_3) δ 2.26 (2 H, m), 2.92 (1 H, br s), 4.0–4.6 (9 H, m), 6.95 (8 H, m).

***sym*-Dibenzo-14-crown-4-oxyacetic Acid (2).** After removal of the protecting mineral oil from sodium hydride (8.5 g of 50% sodium hydride, 180 mmol) by washing with *n*-pentane under nitrogen, THF (1000 mL) was added. *sym*-Hydroxydibenzo-14-crown-4 (9.5 g, 30 mmol) was added and the reaction mixture was stirred for 0.5 h at room temperature. Bromoacetic acid (8.4 g, 60 mmol) in THF (100 mL) was added dropwise to the stirred mixture over 0.5 h followed by continuous stirring at room temperature for 3 h. A small amount of water was carefully added to destroy the unconsumed sodium hydride. Additional water (100 mL) was introduced and the THF was evaporated in vacuo from the aqueous THF mixture. The residual alkaline aqueous mixture was extracted with CH_2Cl_2. The resultant aqueous layer was acidified to pH 1 with concentrated HCl and extracted with CH_2Cl_2. The organic solution was dried over $MgSO_4$ and evaporated in vacuo to yield *sym*-dibenzo-14-crown-4-oxyacetic acid (**2**) (9.0 g, 80%); mp 140–141 °C (from Et_2O); IR (KBr) 3500–2200 (CO_2H), 1700 cm^{-1} (C═O); ^1H NMR (CD_3COCD_3) δ, 2.25 (2 H, m, 3.90–4.55 (11 H, m), 5.6 (1 H, br s), 6.97 (8 H, m). Anal. Calcd for $C_{20}H_{22}O_7$: C, 64.17; H, 5.88. Found: C, 63.93; H, 6.08.

Table I. Positional Parameters

	x/a	*y/b*	*z/c*
O(1)	0.6259 (1)	0.2135 (1)	0.5447 (1)
O(2)	0.5323 (1)	0.1380 (1)	0.6343 (1)
O(3)	0.6092 (1)	0.0275 (1)	0.6559 (1)
O(4)	0.7054 (1)	0.1047 (1)	0.5799 (1)
C(1)	0.5774 (2)	0.2709 (2)	0.5261 (3)
C(2)	0.5356 (2)	0.2695 (2)	0.6068 (3)
C(3)	0.4927 (2)	0.2021 (2)	0.6074 (4)
C(4)	0.5020 (1)	0.0693 (2)	0.6272 (2)
C(5)	0.4357 (1)	0.0579 (3)	0.6108 (2)
C(6)	0.4114 (2)	−0.0137 (3)	0.6049 (3)
C(7)	0.4527 (2)	−0.0740 (3)	0.6160 (3)
C(8)	0.5204 (2)	−0.0640 (2)	0.6326 (2)
C(9)	0.5443 (1)	0.0083 (2)	0.6388 (2)
C(10)	0.6547 (2)	−0.0336 (2)	0.6666 (3)
C(11)	0.7228 (1)	−0.0019 (2)	0.6842 (2)
C(12)	0.7430 (2)	0.0381 (2)	0.5969 (3)
C(13)	0.7108 (1)	0.1440 (2)	0.4952 (2)
C(14)	0.7553 (2)	0.1281 (2)	0.4338 (3)
C(15)	0.7548 (2)	0.1723 (3)	0.3506 (3)
C(16)	0.7122 (2)	0.2294 (3)	0.3314 (3)
C(17)	0.6682 (2)	0.2459 (2)	0.3939 (3)
C(18)	0.6674 (1)	0.2035 (2)	0.4766 (2)
O(5)	0.7280 (1)	0.0443 (1)	0.7683 (1)
C(19)	0.7928 (2)	0.0564 (2)	0.8125 (3)
C(20)	0.7942 (2)	0.0978 (2)	0.9073 (3)
O(6)	0.8485 (1)	0.0985 (2)	0.9611 (2)
O(7)	0.7445 (2)	0.1290 (2)	0.9256 (2)
Li	0.6329 (3)	0.1384 (3)	0.6590 (4)
OW(0)	0.6582 (1)	0.1895 (1)	0.7789 (2)
OW(1)	0.5823 (2)	0.5719 (2)	0.8484 (3)
OW(2)	0.9338 (1)	−0.0188 (2)	0.9645 (2)
OW(3)	0.6451 (2)	0.3377 (2)	0.8511 (2)
OW(4)	0.5659 (1)	0.4421 (2)	0.7353 (2)
OW(5)	0.7004 (2)	0.1973 (2)	1.0773 (3)
OW(6)	0.5856 (2)	0.2727 (3)	1.1186 (3)
OW(7)	0.5000 (0)	0.6809 (4)	0.7500 (0)

Crystal Data. The crystal data were obtained by using Cu Kα radiation, $\lambda = 1.54178$ Å, $[C_{20}H_{21}O_7]^{-}\cdot Li^{+}\cdot 7.5H_2O$, $M = 515.44$, space group $C2/c$, monoclinic, $a = 20.779(5)$ Å, $b = 17.845$ (6) Å, $c = 13.903$ (4) Å, $\beta = 98.19$ (2)°, $V = 5102$ (2) Å^3, $Z = 8$, $D_c = 1.34$ g/cm^3, $D_m = 1.33 \pm 0.02$ g/cm^3, μ(Cu Kα) = 8.79 cm^{-1}.

Structure Determination. Single crystals were grown by slow evaporation from a 1:1 (volume) solution of water and methanol formed by mixing equimolar amounts of LiOH in water and coronand **2** in methanol. The integrated intensities of 3471 unique reflections ($3° \leq 2\vartheta \leq 130°$) were measured at room temperature on a Syntex $P2_1$ automated four-circle diffractometer. Corrections were made for background and Lorentz and polarization effects. It was unnecessary to make corrections for radiation decay or absorption. Only 3124 reflections (90% of the total) with $F_o \geq 2.0\sigma(F_o)$ were included in further calculations. The structure was elucidated by direct methods[28] and refined by a block-diagonal least-squares procedure.[29] Most of the non-hydrogen atoms of the coronand could be located from the initial MULTAN[28] *E* map. The rest of the coronand atoms, including all hydrogen atoms and the eight solvent molecules (H_2O), were located in the following difference electron density maps. About two-thirds of the hydrogen atoms in the water molecules could be assigned in the final difference maps, but since refinement of their positional parameters and temperature factors did not proceed smoothly, it was decided not to include them in the final model. The hydrogen atoms of the coronand were refined isotropically. All

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(21) Shoham, G.; Lipscomb, W. N.; Olsher, U. *J. Am. Chem. Soc.* **1983**, *105*, 1247.

(22) Shoham, G.; Lipscomb, W. N.; Olsher, U. *J. Chem. Soc., Chem. Commun.* **1983**, 208.

(23) Gokel, G. W.; Dishong, D. M.; Diamond, C. J. *J. Chem. Soc., Chem. Commun.* **1980**, 1053.

(24) Strzelbicki, J.; Bartsch, R. A. *Anal. Chem.* **1981**, *53*, 1894, 2247, 2251.

(25) (a) Charewicz, W. A.; Heo, G. S.; Bartsch, R. A. *Anal. Chem.* **1982**, *54*, 2094. (b) Charewicz, W. A.; Bartsch, R. A. *Ibid.* **1982**, *54*, 2300.

(26) Bartsch, R. A.; Heo, G. S.; Kang, S. I.; Liu, Y.; Strzelbicki, J. *J. Org. Chem.* **1982**, *47*, 457.

(27) Heo, G. S.; Bartsch, R. A.; Schlobohm, L. L.; Lee, J. G. *J. Org. Chem.* **1981**, *46*, 3574.

(28) "MULTAN-78, A System of Computer Programs for the Automatic Solution of Crystal Structure"; Main, P.; Hull, S. E.; Lessinger, L.; Germain, G.; Declercq, J. P.; Woolfson, H. M.; Universities of York and Louvain, 1978.

(29) Sheldrick, G. "Programs for Crystal Structure Determination"; Cambridge, England, 1975.

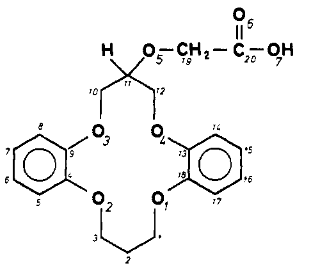

Figure 1. Molecular scheme and numbering system for **2**.

non-hydrogen atoms were refined by using anisotropic thermal parameters. Because one of the water molecules (W7) lies on a twofold axis, its positional and thermal parameters were appropriately restricted. Refinement converged to $R = 0.077$ and $R_\omega = 0.092$. In the final cycle of refinement the highest ratio of shift to estimated standard deviation was less than 0.02 (av, 0.002), and in the final difference electron density map the largest peak was 0.39 e/Å^3 (min, −0.30 e/Å^3).

Results

The molecular numbering scheme for the uncomplexed coronand **2** is presented in Figure 1. The final coordinates for all non-hydrogen atoms of the lithium complex **2a** and solvent molecules are listed in Table I. A stereoview of the final structure of the complex is depicted in Figure 2. As in the lithium complexes of B-10-C-4[21] and DB-14-C-4[22] (**1a**), the Li cation in the inclusion complex with **2** is present in a 5-coordinate, square-pyramidal geometry. It is coordinated by the four ethereal oxygens of the coronand proper and an axial water molecule, which in turn participates in a bifurcated hydrogen bond to the ethereal oxygen of the pendant oxyacetate moiety and the carboxylate terminus itself. Therefore, the entire complex is an electronically neutral zwitterion, with the lithium/carboxylate ion pair being bridged by a water molecule. The position of this apical water molecule corresponds to the location of the anion proper in the related structures of B-13-C-4 and DB-14-C-4 complexes with lithium.[21,22] Thus, this compound is a potential lithium carrier for aqueous-organic phase transfers where concomitant transfer of the aqueous phase anion is not desired.

Table II. Bond Lengths (Å)

C(1)–O(1)	1.433 (5)	C(18)–O(1)	1.380 (5)
Li–O(1)	2.067 (7)	C(3)–O(2)	1.427 (6)
C(4)–O(2)	1.376 (5)	Li–O(2)	2.068 (7)
C(9)–O(3)	1.378 (4)	C(10)–O(3)	1.437 (5)
Li–O(3)	2.038 (7)	C(12)–O(4)	1.424 (5)
C(13)–O(4)	1.389 (4)	Li–O(4)	2.077 (7)
C(2)–C(1)	1.513 (7)	C(3)–C(2)	1.497 (7)
C(5)–C(4)	1.380 (5)	C(9)–C(4)	1.394 (6)
C(6)–C(5)	1.373 (8)	C(7)–C(6)	1.371 (8)
C(8)–C(7)	1.404 (7)	C(9)–C(8)	1.380 (6)
C(11)–C(10)	1.510 (6)	C(12)–C(11)	1.518 (6)
O(5)–C(11)	1.422 (5)	C(14)–C(13)	1.375 (6)
C(18)–C(13)	1.394 (5)	C(15)–C(14)	1.399 (7)
C(16)–C(15)	1.351 (8)	C(17)–C(16)	1.380 (7)
C(18)–C(17)	1.378 (6)	C(19)–O(5)	1.415 (5)
C(20)–C(19)	1.508 (6)	O(6)–C(20)	1.262 (5)
O(7)–C(20)	1.231 (6)	OW(0)–Li	1.908 (7)
H(11)–C(1)	0.93 (4)	H(12)–C(1)	1.01 (4)
H(21)–C(2)	0.98 (1)	H(22)–C(2)	1.19 (1)
H(31)–C(3)	0.99 (6)	H(32)–C(3)	0.84 (5)
H(51)–C(5)	0.99 (6)	H(61)–C(6)	1.07 (5)
H(71)–C(7)	1.07 (5)	H(81)–C(8)	0.95 (5)
H(101)–C(10)	1.00 (4)	H(102)–C(10)	0.96 (5)
H(111)–C(11)	0.95 (4)	H(121)–C(12)	0.89 (4)
H(122)–C(12)	1.01 (4)	H(141)–C(14)	0.94 (5)
H(151)–C(15)	0.86 (5)	H(161)–C(16)	0.85 (6)
H(171)–C(17)	0.88 (5)	H(191)–C(19)	1.04 (6)
H(192)–C(19)	1.13 (5)	H(901)–OW(0)	0.99 (1)
H(902)–OW(0)	0.91 (1)		

Table III. Bond Angles (deg)

C(18)–O(1)–C(1)	117.4 (3)	Li–O(1)–C(1)	124.9 (3)
Li–O(1)–C(18)	117.4 (3)	C(4)–O(2)–C(3)	117.1 (3)
Li–O(2)–C(3)	124.9 (3)	Li–O(2)–C(4)	117.1 (3)
C(10)–O(3)–C(9)	116.2 (3)	Li–O(3)–C(9)	118.2 (3)
Li–O(3)–C(10)	125.5 (3)	C(13)–O(4)–C(12)	117.0 (3)
Li–O(4)–C(12)	125.2 (3)	Li–O(4)–C(13)	117.1 (3)
C(2)–C(1)–O(1)	108.5 (4)	C(3)–C(2)–C(1)	115.0 (4)
C(2)–C(3)–O(2)	108.9 (3)	C(5)–C(4)–O(2)	125.4 (4)
C(9)–C(4)–O(2)	114.4 (3)	C(9)–C(4)–C(5)	120.2 (4)
C(6)–C(5)–C(4)	119.8 (4)	C(7)–C(6)–C(5)	120.3 (4)
C(8)–C(7)–C(6)	121.0 (5)	C(9)–C(8)–C(7)	118.2 (4)
C(4)–C(9)–O(3)	114.3 (3)	C(8)–C(9)–O(3)	125.3 (4)
C(8)–C(9)–C(4)	120.4 (4)	C(11)–C(10)–O(3)	108.7 (3)
C(12)–C(11)–C(10)	113.9 (3)	O(5)–C(11)–C(10)	108.1 (3)
O(5)–C(11)–C(12)	112.8 (3)	C(11)–C(12)–O(4)	108.5 (3)
C(14)–C(13)–O(4)	124.4 (4)	C(18)–C(13)–O(4)	114.4 (3)
C(18)–C(13)–C(14)	121.1 (4)	C(15)–C(14)–C(13)	118.1 (4)
C(16)–C(15)–C(14)	121.1 (5)	C(17)–C(16)–C(15)	120.7 (5)
C(18)–C(17)–C(16)	119.8 (4)	C(13)–C(18)–O(1)	115.0 (3)
C(17)–C(18)–O(1)	125.8 (4)	C(17)–C(18)–C(13)	119.2 (4)
C(19)–O(5)–C(11)	113.7 (3)	C(20)–C(19)–O(5)	110.6 (4)
O(6)–C(20)–C(19)	115.3 (4)	O(7)–C(20)–C(19)	119.3 (4)
O(7)–C(20)–O(6)	125.3 (4)	O(2)–Li–O(1)	85.2 (3)
O(3)–Li–O(1)	128.5 (3)	O(3)–Li–O(2)	76.0 (2)
O(4)–Li–O(1)	76.0 (3)	O(4)–Li–O(2)	134.7 (3)
O(4)–Li–O(3)	84.2 (3)	OW(0)–Li–O(1)	110.0 (3)
OW(0)–Li–O(2)	107.0 (3)	OW(0)–Li–O(3)	121.2 (4)
OW(0)–Li–O(4)	118.1 (3)		

The ethereal oxygens of the macrocyclic part of **2a** are nearly planar with an average deviation from planarity of 0.046 Å (Table IV). The lithium cation is 0.84 Å above the center of this plane. In general, the two "halves" of the DB-14-C-4 skeleton are very nearly planar, and form a "V" shape at an angle of 118.6° with each other. The unmodified DB-14-C-4 complex with lithium (**1a**) displays a similar planarity of the macrocyclic ethereal oxygens and an angle between the two "V" shaped halves of 121°. Also, in **1a** the Li cation is 0.79 Å above the center of the plane of the four ethereal oxygens. The average diagonal distance between the opposite oxygen atoms across the macrocyclic ring in **2a** is 3.76 Å (O1–O3, 3.70 Å; O2–O4, 3.83 Å). The effective cavity size is therefore too small to accommodate the Li$^+$ cation within the plane of the four macrocyclic ethereal oxygens. The empirical effective diameter for a 5-coordinated Li$^+$ ion is shown to be in the range of 1.18–1.52 Å,[31] while the adjusted van der Waals diameter of the cavity in **2a** is 0.96 Å.[32] A similar treatment, set forth by Myers,[34] employs coordination diameters

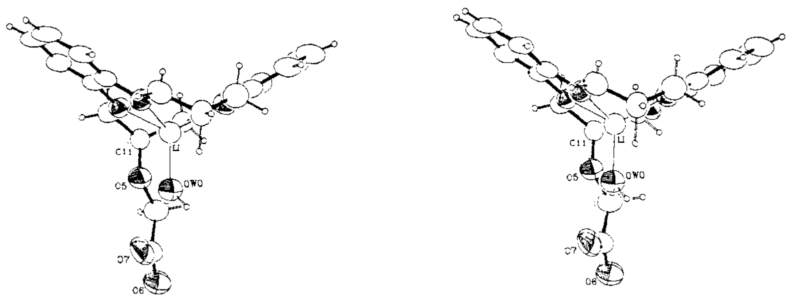

Figure 2. Stereo drawing (ORTEP) of complex **2a**.

Table IV. Least-Squares Planes in the Crystal Structure

a. Definition of the Planes

plane	atoms in the plane	av atomic deviation from planarity, Å
I	C2, C3, O2, C4, C5, C6, C7, C8, C9, O3, C10, C11	0.053
II	C11, C12, O4, C13, C14, C15, C16, C17, C18, O1, C1, C2	0.055
III	O1, O2, O3, O4	0.046
IV	C11, O5, C19, C20, O6, O7	0.063
V	O5, O7, OW0, OW3, Li	0.116

b. Dihedral Angles between Planes (deg)

plane I–plane II	61.44	plane III–plane IV	96.64
plane I–plane III	30.32	plane III–plane V	91.19
plane I–plane IV	121.71	plane IV–plane V	41.44
plane I–plane V	121.07		

Table V. Selected Torsion Angles (deg)

C17–C18–O1–C1	2.76
C18–O1–C1–C2	177.24
O1–C1–C2–C3	−69.14
C1–C2–C3–O2	69.52
C2–C3–O2–C4	−172.22
C3–O2–C4–C5	−10.49
C8–C9–O3–C10	0.88
C9–O3–C10–C11	179.75
O3–C10–C11–C12	−68.56
C10–C11–C12–O4	68.18
C11–C12–O4–C13	−171.68
C12–O4–C13–C14	−8.36
O3–C10–C11–O5	57.63
O4–C12–C11–O5	−55.52
C10–C11–O5–C19	159.30
C12–C11–O5–C19	−73.83
C11–O5–C19–C20	−173.21

rather than simple van der Waals diameters or formal ionic crystal diameters; this treatment yields similar qualitative results (1.42 Å for the cavity size and 1.92 Å for the Li$^+$ size). It is, therefore, of no surprise that the lithium cation in **2a** lies above the cavity plane and prefers five-coordination geometry as has been noted previously.[18,21,22] The observed mean Li–O distance of 2.06 Å (Table II) to the macrocyclic oxygens is consistent with the usual lithium–ethereal oxygen bond lengths in pentacoordinated complexes with macrocyclic ligands.[18,21,22] The rather short Li–O distance of the fifth apical water ligand (1.91 Å) suggests the possibility of a partial transfer of the charge of the carboxylate anion through this water molecule, causing the lithium cation to see it as the effective "counterion". Additionally, the different dipole moment of the water molecule and the special apical position could account for this shorter Li–O distance. A similar system involving a counterion which is interacting with an alkali metal cation through a water molecule is observed in the crystal structure of the 18-crown-6/sodium thiocyanate complex,[35] where a relatively shortened $H_2O–M^+$ linkage also occurs; this water molecule is also hydrogen bonded to the N terminus of the thiocyanate anion.

All bond lengths (Table II) and bond angles (Table III) are within the expected ranges,[33,36] with the exception of the relatively short aliphatic C–C distances (mean value 1.51 Å). Such short C–C distances were observed in similar macrocyclic systems previously reported[33,37] and may be due to the interaction with adjacent C–O ethereal linkages.[6] Selected torsion angles are listed in Table V. The average C–C–O–C torsion angle is 175.2° (the antiperiplanar (trans) conformation is 180.0°), and the average C–C–C–O torsion angle is 68.8° (the synclinal (gauche) conformation is 60.0°). These values are similar to those of larger complexed and uncomplexed crown ethers[4,6,33] and do not indicate that any significant ring strain is encountered by the coronand upon complexation. All structural and conformational parameters are also similar to those of **1a**.[22] No significant structural interaction between the basic crown ring system and the pendant arm is indicated, at least in the complex.

Table VI. Intramolecular and Intermolecular H-Bond Interactions (including equivalent positions)[a]

O5···OW0	2.98	OW1···OW4	2.79
O6···OW2	2.74	OW1···OW7	2.81
O6···OW3'	2.83	OW2···OW2''	2.87
O6···OW6'	2.97	OW2···OW4'	2.87
O7···OW0	2.74	OW3···OW4	2.83
O7···OW5	2.71	OW4···OW4''	2.82
OW0···OW3	2.85	OW5···OW6	2.87
OW1···OW2'	2.83	OW6···OW7'	2.85

[a] Only bond distances of less than 3 Å are presented (in Å) and standard deviations are <0.01 Å.

Discussion

In general, the conformation of the coronand skeleton in complex **2a** closely resembles that of the unmodified coronand (in **1a**). The novel aspect of the coronand modified with oxyacetic acid concerns the conformation of the pendant group. As far as we know this is the first direct demonstration, using crystallographic methods, of a negatively charged intramolecular flexible arm that is involved in the coordination and binding of a cation to a crown-type molecule. However, both the crystal structure (Figure 2) and molecular models clearly show that the carboxylate moiety is much too distant from the anticipated apical coordination position of the lithium cation, thereby precluding its direct interaction with the cation to form an ionic, yet electronically neutral, complex. Nevertheless, it apears that the negative charge of the carboxylate group is partially delocalized through the apical water ligand which is tightly coordinated to the lithium cation. This water molecule is in an anti orientation with respect to the carboxylate moiety.

The relative rigidity of the macrocyclic portion of **2a** and the rather short pendant arm apparently prevent a perfect covering of the large exposed apical area. Therefore in addition to the inclusion of a bridging apical water molecule, the complex prefers a "double coronand–double lithium cation" complementary system linked by water molecules (Figure 3). Furthermore, the arrangement of the complexed crown molecules and solvent molecules within the crystallographic unit cell (Figure 4) is of interest. The coronands are assembled in a hydrophobic sphere, interacting with each other through the aromatic rings, while the carboxylate groups, the lithium ions, and the water molecules form a hydrogen-bonded "network" filling the interior. Closer examination of the complicated water "network" (Figure 5) reveals an ordered polygon-like assembly in which the oxygens of the water molecules form five- and six-membered intermolecular rings. Among these edge-sharing rings the O_5 pentagons dominate. This phenomenon has been reported for the water clathrates[38,39] and similarly ordered water–organic structures.[40–47] The O···O distances in the

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(30) Johnson, C. K. "ORTEP-II, a Fortran Thermal-Ellipsoid Plot Program for Crystal Structure Illustrations"; Oak Ridge National Laboratory Report ORNL-5138, 1976.

(31) Shannon, R. D. *Acta Crystallogr., Sect. A* **1976**, *A32*, 751.

(32) The average distance between opposite oxygen atoms across the cavity, after subtracting the size of the oxygen atoms (see also ref 33).

(33) Dalley, M. D. In "Synthetic Multidentate Macrocyclic Compounds"; Izatt, R. M., Christensen, J. J., Eds.; Academic Press: New York, 1978; pp 207–243.

(34) Myers, R. T. *Inorg. Nucl. Chem. Lett.* **1980**, *16*, 329.

(35) Dobler, M.; Dunitz, J. D.; Seiler, P. *Acta Crystallogr., Sect. B* **1974**, *B30*, 2741.

(36) Dunitz, J. D.; Dolber, M.; Seiler, P.; Phizackerley, R. P. *Acta Crystallogr., Sect. B* **1974**, *B30*, 2733.

(37) Maverick, E.; Seiler, P.; Schweizer, W. B.; Dunitz, J. D. *Acta Crystallogr., Sect B* **1980**, *B36*, 615.

(38) Jeffrey, G. A.; McMullan, R. K. *Prog. Inorg. Chem.* **1967**, *8*, 43.

(39) Jeffrey, G. A. *Acc. Chem. Res.* **1969**, *2*, 344.

(40) Schwarzenbach, D. *J. Chem. Phys.* **1968**, *48*, 4134.

(41) Jeffrey, G. A.; Shen, M. S. *J. Chem. Phys.* **1972**, *57*, 56.

(42) Boer, F. P.; Neuman, M. A.; Van Remoortere, F. P.; Steiner, E. C. *Inorg. Chem.* **1974**, *13*, 2826.

(43) Jeffrey, G. A.; Mastropaolo, D. *Acta Crystallogr., Sect. B* **1978**, *B34*, 552.

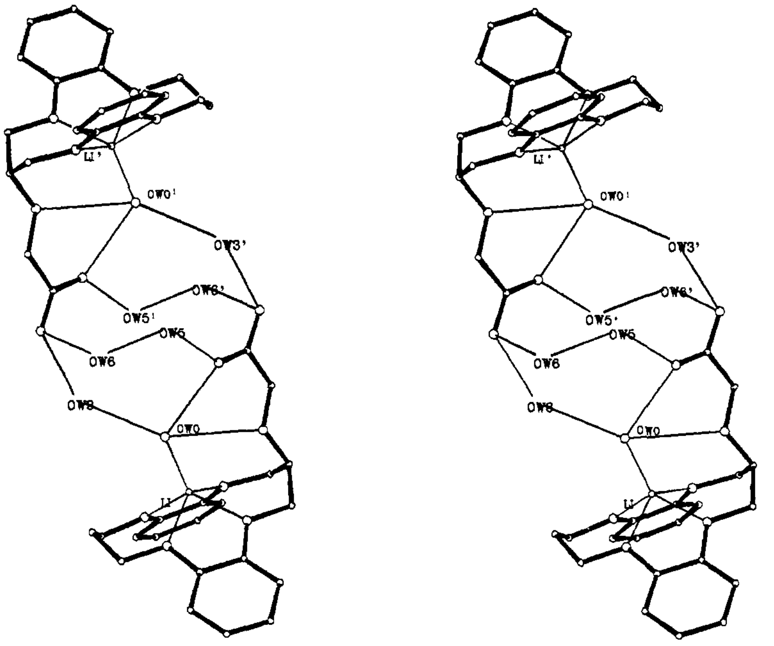

Figure 3. Stereoview of the "double coronand–double lithium cation" system.

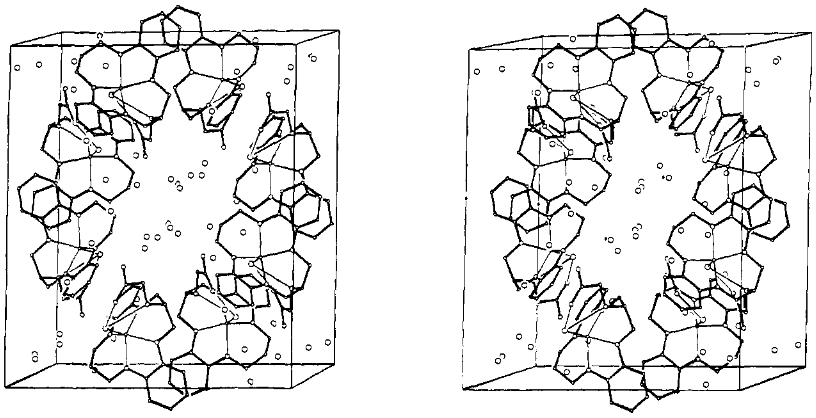

Figure 4. Stereo drawing of the unit cell packing of **2a**.

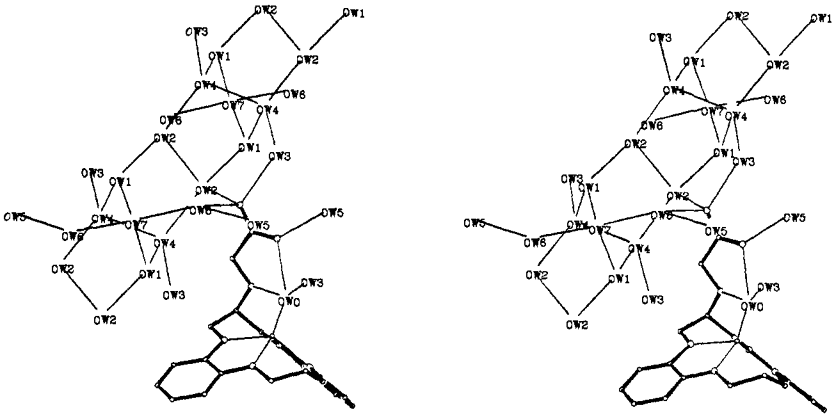

Figure 5. Stereo drawing of a part of the water "network" in the crystal structure of **2a**.

cross-linked network are in the range 2.71–2.98 Å (Table VI) with an average distance of 2.83 Å, in agreement with values in similar structures[38-48] and indicating a fairly strong hydrogen-bonding system. In fact this polygon network of water molecules forms infinite solvent channels (or "pleated ribbons") along the crystal (Figures 4 and 5). The coronand complex molecules interact with the water molecule network through the two carboxylate oxygens and the lithium bound water molecule (Figure 5). This special hydrogen-bonding interaction in the hydrophilic regions may be one of the primary forces which holds the crystallographic assembly together, and it could be a significant factor in the thermodynamic stability of the complex. Analogous structures which have alternate layers of ordered water and organic molecules

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(44) Saenger, W. *Nature (London)* **1979**, *279*, 343.

(45) Neidle, S.; Berman, H. M.; Shieh. H. S. *Nature (London)* **1980**, *288*, 129.

(46) Mootz, D.; Wussow, H. G., *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 552.

(47) Von Dreele, R. B. *Acta Crystallogr., Sect. B* **1981**, *B37*, 93.

(48) Van Remoortere, F. P.; Boer, F. P. *Inorg. Chem.* **1974**, *13*, 2071.

have been seen previously in the complexes of 12-crown-4[42,48] and other systems.[45,46] Similar yet disordered hydrophilic "channels" have been reported recently as well.[49] With regards to the relation between this crystal structure and the structure of the complex in solution, we feel that the crystal structure should resemble fairly closely that in aqueous solution because of the large number of water molecules present and the "aqueous-like" environment in the crystal. However, the structure of the complex in organic solvents or synthetic membranes is probably quite different.

Attempts to isolate suitable single crystals of un-ionized **2** with other lithium salts at neutral pH or in water-free solutions have been unsuccessful. A pH dependence of complexation tendencies is implied a priori by the presence of an ionizable carboxylic acid. It is most reasonable that at alkaline pH, the complexation of lithium cations by **2** will be independent of the counterion that is present in the aqueous solution.

Of primary concern for the ability of **2** to function as an effective phase-transport reagent for lithium ions is the apical water molecule which is required to complete the coordination polyhedron of the metal cation. This "exposed" water molecule would certainly affect the stability of the complex in an organic phase, and the results of preliminary solvent polymeric membrane transport studies with **2** indicate that Na^+ and K^+ (and in some conditions Rb^+ and Cs^+) are transported more readily than Li^+.[50] Perhaps these larger cations (effective diameters[31] in the range of 1.98 Å (Na^+) to 3.56 Å (Cs^+)) do not require an intervening water molecule for favorable pentavalent coordination to **2**. If one constructs a three-dimensional "cavity" from the four ethereal oxygens (O1–O4) and O7 of the carboxylate group (and a possible solvent molecule, or two, to complete a 6- or 7-coordination shell), the adjusted diameter of this "cavity"[32] is ≈2.8 Å (O1–O7, 5.72 Å; O2–O7, 5.55 Å). This diameter compares rather well with the effective diameter of K^+ (2.74–2.92 Å for 4–7-coordinated K^+).[31] The assumption of this argument, that the conformation of the molecule remains similar to the one described for **2a**, requires further study. An additional factor which may relatively disfavor Li^+ complexation may be the differing nature of interaction in an organic environment (such as that in the synthetic polymeric membranes) between the coronand, the cation, and the surroundings. Thus, even the structure may be modified by the organic environment.

It does seem likely that a longer, and perhaps less flexible, pendant moiety would allow for more favorable Li^+ complexation relative to the other alkali metal cations. The binding of larger divalent metals to **2** is strongly disfavored,[50] as has been described previously for the DB-14-C-4 system.[12,22] This is an important quality in the molecular design of lithium-selective compounds for industrial and medical applications.[51,52]

Synthetic attempts are now underway to create a coronand which has a longer pendant carboxylate arm so that its complexation with Li^+ can be studied. Examination of molecular models suggests that some oxy-benzoic acid derivatives of DB-14-C-4 would also meet the structural requirements outlined above, and this may allow a more favorable syn orientation of the lithium cation to the carboxylate.

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Registry No. 2, 80186-73-8; **2a**, 88271-61-8; *sym*-hydroxydibenzo-14-crown-4, 42397-72-8; *sym*-hydroxydibenzo-14-crown-4, 78328-81-1; catechol, 120-80-9; 1,3-dibromopropane, 109-64-8; epichlorohydrin, 106-89-8; bromoacetic acid, 79-08-3.

Supplementary Material Available: A list of observed and calculated structure factors (Table S1), anisotropic temperature factors for non-hydrogen atoms (Table S2), and coordinates and temperature factors for all hydrogen atoms (Table S3) (21 pages). Ordering information is given on any current masthead page.

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(49) Hanson, I. R.; Truter, M. R. *J. Chem. Soc., Perkin Trans. 2* **1981**, 1.

(50) Simon, W., personal correspondence, 1982.

(51) Meier, P. C.; Ammann, D.; Osswald, H. F.; Simon, W. *Med. Prog. Technol.* **1977**, *5*, 1.

(52) Güggi, M.; Fiedler, U.; Pretsch, E.; Simon, W. *Anal. Lett.* **1975**, *8*, 857.

Molecular Structure of Ferric Neurosporin, a Minor Siderophore-like Compound Containing N^{δ}-Hydroxy-D-ornithine

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Abstract: Ferric neurosporin, $FeC_{33}H_{51}N_6O_{15}\cdot 6CH_3CN$, or the ferric chelate of the cyclic triester of N^{α}-acetyl-N^{δ}-hydroxy-N^{δ}[(*R*)-3-hydroxybutyryl]-D-ornithine, is a new minor fusarinine-type siderophore-like compound isolated from cultures of *Neurospora crassa* (ATCC 10816). The compound was characterized chemically and spectroscopically and crystallized from ethanol equilibrated with acetonitrile at 0 °C in the rhombohedral space group *R*3 of the dimensions, hexagonal setting, $Z = 3$, $a = b = 19.774$ (18) Å, $c = 12.017$ (17) Å, $V = 4069.3$ Å^3, at −135 (2) °C. The structure was solved from a three-dimensional Patterson map and direct methods and refined to an *R* factor of 0.058. The molecule is flat (2.90-Å thickness) and assumes the Λ-cis absolute configuration about the central ferric ion, as determined from anomalous dispersion and circular dichroism measurements; the D configuration of ornithine was also proved by nonreductive hydrolysis–CD experiments. Conformationally, the N^{α}-acetylornithinyl groups are similar to those in ferric N,N',N''-triacetylfusarinine, indicating that the stereochemistry of the ornithine residue asymmetrically induces the chirality at the metal ion in the fusarinines.

The N^{δ}-hydroxy analogue of the amino acid ornithine, $HON(H)CH_2CH_2CH_2CH(NH_3^+)COO^-$, is the fundamental structural unit for two classes of fungal cyclic trihydroxamate-type siderophores (the ferrichromes and fusarinines), or low molecular weight, high affinity Fe(III)-selective chelating agents responsible for the acquisition and active translocation of ferric ion across the fungal

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