Synthesis, structure and metal ion binding of di-(1,8-naphtho)-16-crown-4 compounds

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Abstract

The syntheses of two di(1,8-naphtho)-16-crown-4 compounds are described. In the X-ray structure of di(1,8-naphtho)-16-crown-4, the compound crystallizes in the orthorhombic space group $Pna2_1$ with four molecules per asymmetric unit. Alkali metal cation selectivities of the ionophores are assessed in solvent polymeric membrane electrodes.

Keywords: Small-ring crown ether, solid-state structure, alkali metal cation complexation

Introduction

Macrocyclic polyethers (crown ethers) are well known for their strong interactions with alkali metal and alkaline earth metal cations.[1-4] Small-ring crown ethers with four oxygens (*i.e.*, crown-4 compounds) often exhibit selective complexation of Li^+. In the past, we have reported studies of dibenzo-14-crown-4 **1** (Figure 1) and its derivatives with one or two substituents attached to the central carbon atoms of three-carbon bridges.[5-7] Due to rigidity in this ligand system, solid-state structures of its complexes provide insight into interactions of Li^+ with oxygen donor atoms. To probe the effect of expanding the crown ether ring from one with two 2-carbon and two 3-carbon bridges in dibenzo-14-crown-4 to four 3-carbon bridges, the synthesis of di-(1,8-naphtho)-16-crown-4 **2** was undertaken. We now describe the results of the synthetic endeavors, as well as the solid-state structure of **2** and its alkali metal cation selectivity in synthetic polymeric membrane electrodes.
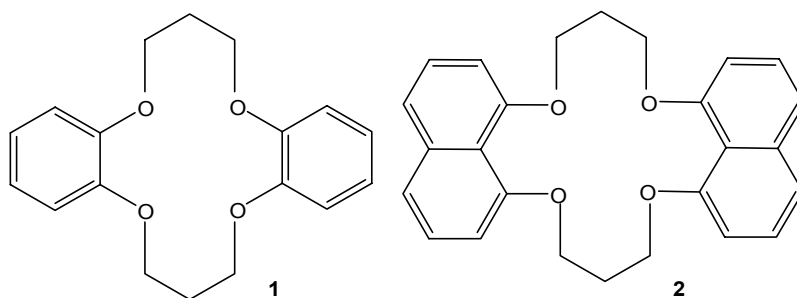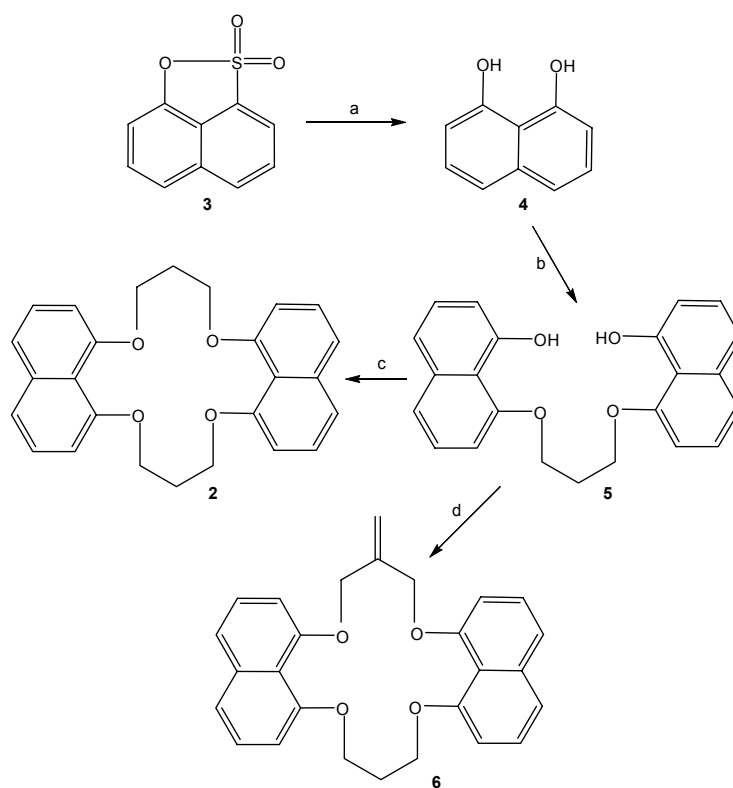
Figure 1. Structures of dibenzo-14-crown-4 **1** and di-(1,8-dinaphtho)-16-crown-4 **2**.

Results and Discussion

Synthesis
The preparative route to **2** is presented in Scheme 1.

Scheme 1. Synthesis of di-(1,8-naphtho)-16-crown-4 **2** and *sym*-(methylene)-di-(1,8-naphtho)-16-crown-4 **6**: (a) i) KOH, 250 ^{o}C, 2 h; ii) 6 N HCl; (b) 1,3-dibromopropane (0.5 equiv), K$_2$CO$_3$, MeCN, reflux, 8 h; (c) MsO(CH$_2$)$_3$OMs (1 equiv), Cs$_2$CO$_3$, MeCN, 80 ^{o}C, overnight; (d) (ClCH$_2$)$_2$C=CH$_2$, Cs$_2$CO$_3$, MeCN, 80 ^{o}C, overnight.

Reaction of commercially available 1,8-naphthosultone **3** with KOH at 250 ^{o}C for 2 hours followed by treatment of the resultant mixture with 6 N HCl gave a 54% yield of 1,8-dihydroxynaphthalene **4**. Dropwise addition of a solution of **4** and 0.5 equivalent of 1,3-dibromopropane in MeCN to a mixture of K_2CO_3 in MeCN at reflux followed by refluxing for 8 hours produced a 71% yield of the dinaphthol ether **5**. Slow addition by syringe pump of a solution of equivalent amounts of **5** and the dimesylate of 1,3-propanediol in MeCN to a mixture of Cs_2CO_3 in MeCN at reflux followed by overnight reflux gave a 71% yield of di-(1,8-naphtho)-16-crown-4 **2**.

Similar simultaneous addition of equivalent amounts of **5** and 3-chloro-2-chloromethyl-1-propene in MeCN to a mixture of Cs_2CO_3 in MeCN at reflux then refluxing overnight provided a 71% yield of *sym*-(methylene)-di-(1,8-naphtho)-16-crown-4 **6**.

Other attempted cyclizations to form di-(1,8-naphtho)-16-crown-4 compounds were unsuccessful, including: i) reaction of **5**, 3-chloro-2-chloromethyl-1-propene and LiH in THF; ii) reaction of **5**, 1,3-dichloroacetone and LiH in THF; and iii) reactions of **5** and epichlorohydrin with LiOH in H_2O or aqueous THF, with NaH in DMF or with Cs_2CO_3 in MeCN. Recovery of starting material **5** or evidence of decomposition products was observed in these cases.

Solid-state structure of 2

Compound **2** crystallized in the orthorhombic space group *Pna*2_1 with four molecules per asymmetric unit (Figure 2). While the 1,8-naphthalenedioxy moieties are well-behaved in all four independent molecules, the aliphatic 3-carbon bridges show signs of disorder (elongated thermal ellipsoids and relatively high residual electron density maxima in the vicinity). For the three of those disorders that could be resolved, the occupancy ratios of the two respective components were refined freely, while constraining the sum of the occupancies to unity. To counteract correlation effects arising from the disorders, similarity restraints on 1-2 and 1-3 distances and displacement parameters, as well as rigid bond restraints for anisotropic displacement parameters, were applied to all atoms. The disordered structure of one of the independent molecules is presented in Figure 3.

Altogether the structure of compound **2** is not well behaved. The diffraction pattern shows signs of non-merohedral twinning and the metric symmetry of the unit cell suggests the possibility of cell-doubling in the *b*-direction, especially when taking into account that the asymmetric unit contains four molecules. Neither suspicion could be corroborated, however. Extensive searches for alternative unit-cells and cell settings, as well as multiple orientations of the same unit-cell all performed with the program cell_now[8] did not yield any usable results. Nevertheless, the refinement is reasonably stable and we are confident that the molecular model determined by means of this diffraction experiment reflects the chemistry of the compound accurately.
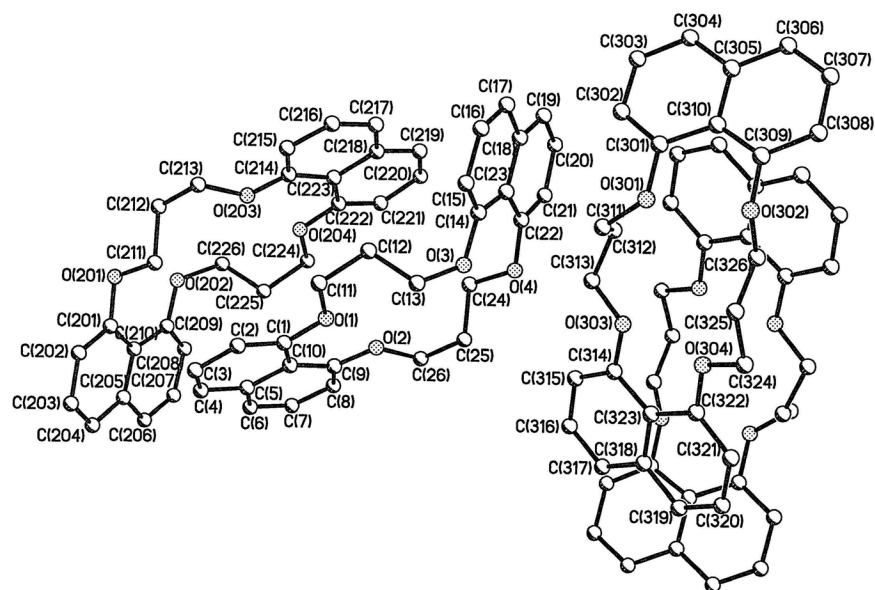
Figure 2. Ball-and-stick representation of the four crytallographically independent molecules with atomic labeling schemes for three of them. In the interest of clarity, the labels for the fourth molecule were omitted, but the labeling scheme follows the same principle as those of the other three molecules. Hydrogen atoms and atoms of the minor components of the disorders were omitted, as well.
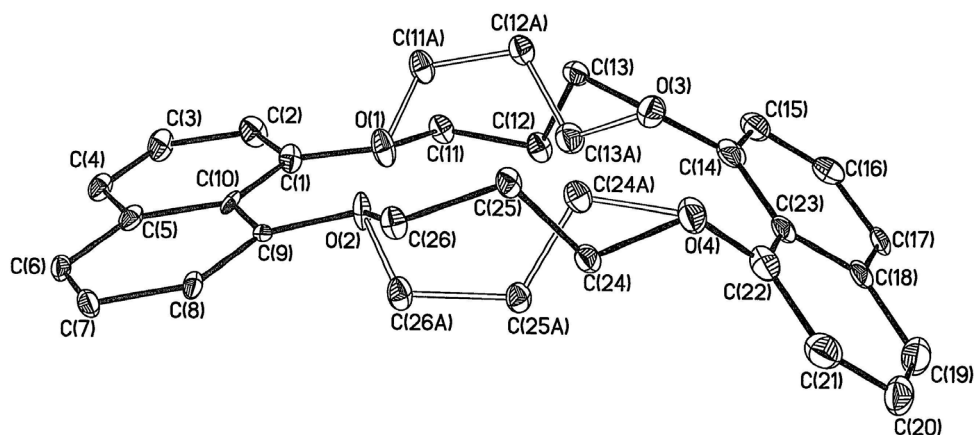

Figure 3. 50% probability representation of one of the four independent molecules, showing the disorder of the aliphatic linkers (open lines for bonds between atoms in the minor component of the disorders). Hydrogen atoms were omitted for clarity

Ionophoric response
Using a previously described procedure,[9] new crown-4 compounds **2** and **6** were incorporated into solvent polymeric membranes in which PVC was the polymer and *o*-nitrophenyl octyl ether (NPOE) was the membrane solvent. For ion-selective electrodes (ISEs) prepared from the

membranes, potentiometric selectivities for one of the alkali metal cation relative to another were determined by the fixed interference method.[10]

Although it had been anticipated that the small cavity sizes of di-(1,8-naphtho)-16-crown-4 **2** and *sym*-(methylene)-di-(1,8-naphtho)-16-crown-4 **6** would favor complexation of small alkali metal cations, preliminary experiments determined the greatest potentiometric response to Cs^+ among the five alkali metal cations. Therefore, Cs^+ was employed as the primary ion to which the other alkali metal cation responses were compared.

The potentiometric selectivities for Cs^+/M^+ (-log $K_{Cs,M}^{Pot}$) for crown ethers **2** and **6** are recorded in Table 1. A larger value of -log $K_{Cs,M}^{Pot}$ means a greater difference between the potentiometric response of the ionophore to the primary metal ion Cs^+ and that of the competing metal ion M^+. The potentiometric selectivities reveal a metal ion binding strength ordering of $Cs^+ > Rb^+ > K^+ > Li^+ > Na^+$ for both **2** and **6**. This ordering is consistent with 2:1 (crown ether:metal ion) complexation in which the metal ion is sandwiched between two crown ether molecules.

Table 1. Potentiometric selectivities for di-(1,8-naphtho)-16-crown-4 compounds **2** and **6**

		-log $K_{Cs,M}^{Pot}$				
Compound	M^+ =	Li^+	Na^+	K^+	Rb^+	Cs^+
2		1.95 ± 0.05^a	2.12 ± 0.02	1.00 ± 0.05	0.54 ± 0.05	0.0
6		2.09 ± 0.05	2.46 ± 0.05	1.15 ± 0.05	0.58 ± 0.05	0.0

[a]Standard deviations from four measurements, duplicate determinations with each of two ISEs.

Experimental Section

General. The ^1H and ^{13}C NMR spectra were recorded with IBM AF-200 or AF-300 spectrometers in $CDCl_3$ with Me_4Si (TMS) as internal standard. Chemical shifts (δ) are given in parts per million downfield from TMS and coupling constant (*J*) values are in hertz. IR spectra were recorded with a Perkin-Elmer model 1600 FT-IR spectrophotometer as deposits from CH_2Cl_2 solutions onto NaCl plates. Melting points were determined with a Mel-Temp melting point apparatus. Elemental analysis was performed by Desert Analytics Laboratory (now Columbia Analytical Services) of Tucson, Arizona.
Reagents and solvents were obtained from commercial suppliers and used directly unless otherwise noted. MeCN was dried over 4A molecular sieves. Powdered anhydrous Cs_2CO_3 was purchased from Chemmetall GMBH of Germany through CM Chemical Products, Inc. (Berkeley Heights, NJ).

Synthesis of 1,8-dihydroxynaphthalene (4). KOH (30.0 g, 0.53 mol) was dissolved in water (10 mL) and added to a preheated ceramic crucible containing 1,8-naphthosultone (6.00 g, 29.12 mmol). The mixture was heated in an oven at 250 °C for 2 h. The black viscous mixture was

cooled to room temperature and treated with 6 N HCl (300 mL). The mixture was extracted with CH_2Cl_2 (4 X 50 mL) and the combined extracts were dried over $MgSO_4$. Activated carbon (5 g) was added and the mixture was stirred and filtered. The filtrate was concentrated *in vacuo*. The residue crystallized to produce a 54% yield of **4** as light yellow needles with mp 138 ^{o}C (lit[11] mp 140 ^{o}C. IR 3280 (O-H) cm^{-1}. ^{1}H NMR δ 6.73-6.80 (m, 2H), 7.26-7.31 (m, 4H), 10.87 (s, 2H).

Synthesis of bis-1,3-(8-hydroxy-1-naphthoxy)propane (5). Under nitrogen, a solution of **4** (5.00 g, 31.25 mmol) and 1,3-dibromopropane (3.47 g, 17.18 mmol) in MeCN (150 mL) was added dropwise during a 2-h period to a stirred and refluxing mixture of K_2CO_3 (6.46 g, 46.0 mmol) in MeCN (15 mL). After the addition was completed, refluxing was continued for 8 h. The mixture was cooled to room temperature and the solvent was removed *in vacuo*. To the residue was added CH_2Cl_2 and water. The mixture was acidified with 6 N HCl and extracted with CH_2Cl_2 (3 X 50 mL). The combined extracts were dried over $MgSO_4$ and evaporated *in vacuo*. The residue crystallized to give a 85% yield of **5** as a white solid with mp 137 ^{o}C. IR 3290 (O-H) cm^{-1}. ^{1}H NMR δ 2.55 (pen, J=6.1 Hz, 2H), 4.44 (t, J=6.1 Hz, 4H), 6.78-6.94 (m, 4H), 7.23-7.45 (m, 8H), 9.28 (s, 2H). ^{13}C NMR δ 29.0, 65.7, 105.1, 110.4, 115.0, 119.0, 122.2, 125.6, 127.7, 136.7, 154.2, 154.9. Anal. Calcd for $C_{23}H_{20}O_4$: C, 76.63; H, 5.59. Found: C, 76.83; H, 5.52.

Synthesis of di-(1,8-naphtho)-16-crown-4 (2). Under nitrogen, a solution of **5** (1.00 g, 2.77 mmol) and the dimesylate of 1,3-propanediol (0.64 g, 2.77 mmol) in MeCN (75 mL) was added with a syringe pump over an 8-h period to a flask (equipped with a condenser and a Dean-Stark trap) containing a refluxing and stirred mixture of Cs_2CO_3 (2.25 g, 6.92 mmol) and MeCN (15 mL). During the addition, the volume in the flask was maintained at 30-35 mL by removal of solvent with the Dean-Stark trap. After the addition was completed, the mixture was stirred overnight at 80 ^{o}C and then evaporated *in vacuo*. Water (30 mL) was added and the mixture was extracted with CH_2Cl_2 (4 X 50 mL). The combined extracts were dried over $MgSO_4$ and the filtrate was passed through a short bed of alumina with CH_2Cl_2-hexane (1:5) as eluent. The eluate was evaporated *in vacuo* and the residue was crystallized from CH_2Cl_2-hexane to give a 71% yield of white solid with mp 194 ^{o}C (dec). ^{1}H NMR δ 2.57 (pen, J=6.3 Hz, 4H), 4.33 (t, J=6.3 Hz, 8H), 6.92-6.98 (m, 4H), 7.24-7.46 (m, 8H). ^{13}C NMR δ 30.1, 68.3, 76.7, 77.0, 77.3, 110.9, 119.8, 121.9, 126.3, 137.4, 155.9. Anal. calcd for $C_{26}H_{24}O_4$: C, 77.96; H, 6.04. Found: C, 77.72; H, 5.87.

Synthesis of *sym*-(methylene)-di-(1,8-naphtho)-16-crown-4 (6). Using the same procedure as described above for the synthesis of **2** but with 3-chloro-2-chloromethyl-1-propene in place of the dimesylate of 1,3-propanediol, the eluate from the short alumina column was evaporated *in vacuo* and the residue was crystallized from CH_2Cl_2-EtOAc to give a 71% yield of white crystals with mp 163 ^{o}C. ^{1}H NMR δ 2.46 (pen, J=6.2 Hz, 2H), 4.30 (t, J=6.2 Hz, 4H), 4.77 (s, 4H), 5.63 (s, 2H), 6.92-6.98 (m, 4H), 7.24-7.46 (m, 8H). ^{13}C NMR δ 30.2, 68.6, 71.2, 110.2, 111.5, 117.3, 119.8, 121.7, 121.9, 126.1, 126.4, 137.4, 141.7, 155.6, 156.6. Anal. calcd for $C_{27}H_{24}O_4$: C, 78.61; H, 5.57. Found: C, 78.87; H, 5.89.

Solid-state structure determination for (2). A suitable crystal for structure determination of **2** was obtained by crystallization from CH_2Cl_2-MeOH. Low temperature diffraction data were collected using a Siemens Platform three-circle diffractometer coupled to a Bruker-AXS Smart Apex CCD detector with graphite monochromated Mo Kα radiation ($\lambda = 0.71073$ Å), performing φ- and ω-scans. Data reduction was performed with the program SAINT, version 7.12[12] and semi-emperical absorption correction was performed using SADABS.[13] The structure was solved by direct methods using SHELXL[14] and refined against F^2 on all data by full-matrix least squares with SHELXL-97.[15] All non-hydrogen atoms were refined anisotropically; all hydrogen atoms were included into the model at their geometrically calculated positions and refined using a riding model. The crystal data and experimental details are listed in Table 2.

Table 2. Crystallographic information about the structure and refinement of **2**.

Empirical formula	$C_{26}H_{24}O_4$
Formula weight (g mol^{-1})	400.45
Temperature (K)	100
Crystal system	orthorhombic
Space group	$Pna2_1$
a (Å)	16.927(3)
b (Å)	35.950(7)
c (Å)	13.137(3)
α (^{o})	90
β (^{o})	90
γ (^{o})	90
Volume (Å^3)	7994(3)
Z	16
Density (calc) (g/cm^3)	1.331
Crystal size (mm)	0.50 x 0.50 x 0.30
Theta range (^{o})	1.13 to 26.37
Reflections collected	142114
Independent reflections (R_{int})	16331 (0.0441)
Completeness (%)	99.9
Data / restraints / parameters	16331 / 2447 / 1165
Goodness-of-fit on F^2	1.125
Final R1 for $I>2\sigma(I)$	0.0859
Largest difference peak and hole (eÅ^{-3})	1.238 and -0.448

The crystallographic data have been deposited with the Cambridge Crystallographic Data Centre (deposition number CCDC 623942) and can be obtained free of charge via www.ccdc.cam.ac.jk/data_request/cif.

Preparation of PVC membranes and potentiometric measurements were performed as reported,[9] but with Cs^+ as the primary ion instead of Na^+ and measurements for five alkali metal cation species instead of just Li^+, Na^+ and K^+.

Acknowledgements

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