

Synthesis of Crown Ethers Based on 9,9-Bis-(4-hydroxyphenyl)fluorene and Structural Determination by X-Ray Single Crystallography

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We report the synthesis and characterization of [38], [57], [76] and [48]-membered crown ethers including bis-(hydroxyphenyl)fluorene in the macroring. Four crown ethers **1-4** are characterized by MALDI-mass spectral data and $^1\text{H-NMR}$ data. Also, structural determination of [38]-membered crown ether **1** has been performed by X-ray crystallography.

Keywords : Crown ethers, 9,9-Bis-(4-hydroxyphenyl)fluorene. X-ray single crystallography.

Introduction

The first viable syntheses of cyclic polyethers, crown ethers, were reported by Pedersen in 1967.¹ Since the first syntheses of dibenzo-18-crown-6, 18-crown-6, and other crown ether macrocycles,¹⁻⁴ there has been a tremendous growth in the research activities pertaining to synthesis of macrocyclic molecules analogous to the crown ethers.^{5,6} The interest in such macrocycles is derived from the knowledge that such compounds show selectivity in complexing with a variety of neutral and ionic substrates. Modifications of such crown ether structural parameters as size of the cavity, number of ether oxygen atoms, length of aliphatic chains connecting ether oxygens, aromatic groups in the structure, and substitution of oxygen by heteroatoms such as N or S as a part of aliphatic or aromatic units have been reported.^{5,6} The selectivity of the complexation is dependent on the above-mentioned parameters as well as other chemical interactions that may be present, thus giving new directions to the subject of molecular recognition.

Of these factors, we have been interested in the effects of changing the spatial arrangement of donor atoms by introducing 9,9-bis-(4-hydroxyphenyl)fluorene groups into a crown ether to give a less rigid aromatic region. More recently, the interest in large (>[24]-membered) crown ethers⁷ stems from their utilization in the synthesis of (pseudo) rotaxanes in which one component is thread through the cavity of the crown ether structure.⁸ Herein we report the synthesis, characterization of [38], [57], [76], and [48]-membered crown ethers including 9,9-bis-(4-hydroxyphenyl)fluorene in the macroring.⁹

Results and Discussion

Thus, reaction of 9,9-bis-(4-hydroxyphenyl)fluorene with 1 equiv of tri(ethylene glycol) di-*p*-tosylate in the presence of 3 equivs of Cs_2CO_3 in refluxing acetonitrile for 20 h gave

[38]-membered crown ether **1** (32%), [57]-membered crown ether **2** (13%), and [76]-membered crown ether **3** (4%), and were characterized by IR, $^1\text{H-NMR}$, Matrix-Assisted Laser Desorption/Ionization (MALDI) MS, and X-ray analysis. Similarly reaction of 9,9-bis-(4-hydroxyphenyl)fluorene with 1 equiv of di(ethylene glycol) di-*p*-tosylate gave very low yield of [48]-membered crown ether **4** (1%) and mostly polymeric materials (Scheme 1). Attempt to increase the yield of **4** when using K_2CO_3 or Rb_2CO_3 as base was unsuccessful.

Further studies into the complexation with these crown ethers and dibenzylammonium ions or di-*n*-butylammonium ions, and the investigation of the possibility of existence in pseudorotaxane forms are underway.

X-Ray Structural Description. The ORTEP diagrams of crown ether **1** with different views are shown in Figure 1 and 2. The center of a macrocyclic molecule is located on the crystallographic inversion center and therefore, only half of molecule resides on an asymmetric unit. The overall structure of molecule can be described as [38]-membered macrocyclic ring with two fluorene groups attached almost perpendicularly. Four atoms (C1, C31, C1a, and C31a) in a macrocyclic ring form a nearly perfect plane and the angle between this plane and fluorene ring is 84.78° . The longest diameter (C22-C22a distance) for a macrocyclic ring is 18.442 Å and the shortest one (C28-C28a distance) is 5.452 Å. Within a macrocyclic ring, there are two equivalent semi pores which consist of four oxygens (O1, O2, O3a, and O4a) and four carbons (C20, C21, C29a, and C30a). The distances between diagonally positioned oxygen atoms, in semi pore, are 4.408 Å for O1-O4a and 4.693 Å for O2-O3a, respectively, and those between adjacent oxygen atoms are ranged from 2.876 Å to 3.635 Å. In contrast to a non-polar covalent central pore which consists of C18, C27, C27a, and C18a atoms, two semi pores composed with four oxygen atoms can accommodate polar molecules and cations of suitable size, such as alkali metals, alkaline earth metals, or organic ions, due to polar nature in the cavity. The crystal data and refinement parameters are listed in Table 1. Selected bond lengths and angles are presented in Table 2.

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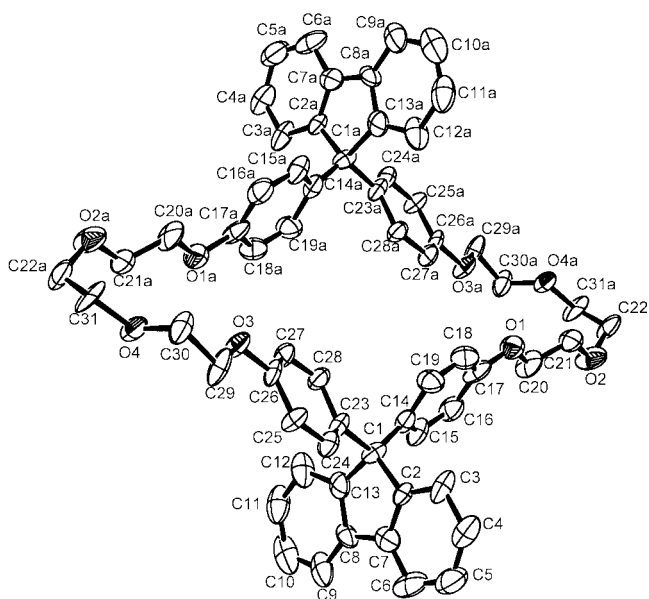
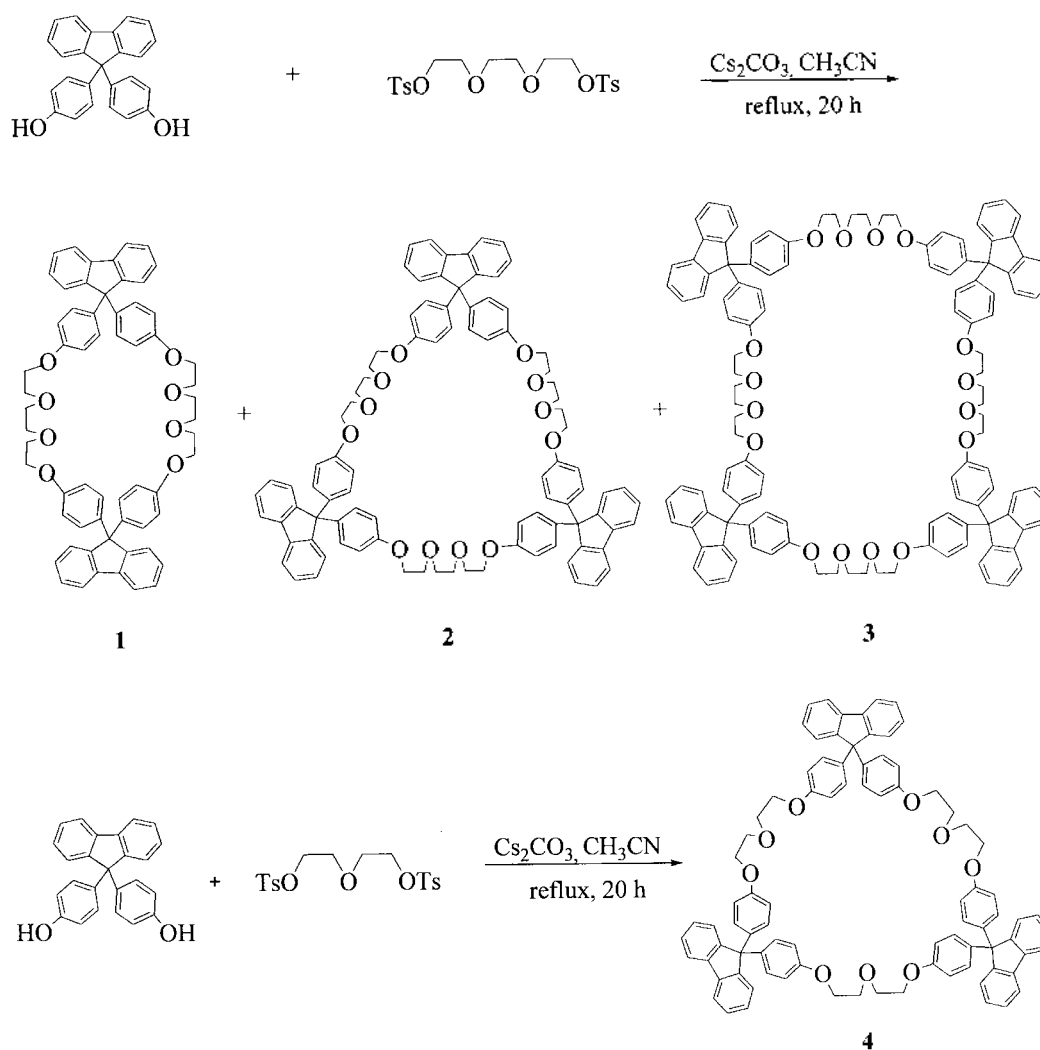


Figure 1. ORTEP diagram of crown ether 1. Hydrogen atoms are omitted for clarity.

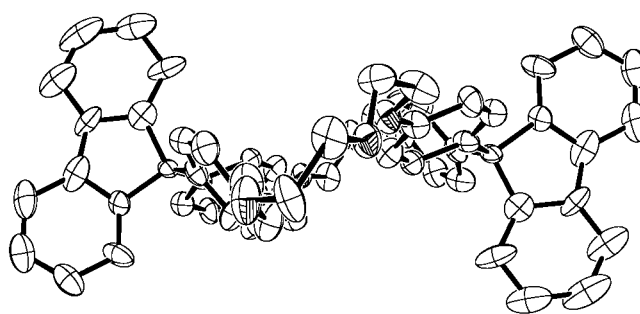


Figure 2. Side view of ORTEP diagram.

Experimental Section

All reagents and solvents were reagent grade or were purified by standard methods before use and the reactions were routinely carried out under an inert atmosphere. Silica gel 60 (70-230 mesh ASTM) used for column chromatography was supplied by E. Merck. Analytical thin layer chromatography (TLC) was performed on silica gel with fluorescent indicator coated on aluminium sheets. Melting

Table 1. Crystal Data and Structure Refinement for **1**

Empirical formula	C ₆₂ H ₅₆ O ₈
Formula weight	929.12
Temperature	293 (2) K
Wavelength	0.71073 Å
Crystal system	monoclinic
Space group	P2 ₁ /c
Unit cell dimensions	a = 15.245 (4) Å b = 22.216 (7) Å c = 8.973 (2) Å β = 96.66 (1)°
Volume	3018.5(14) Å ³
Z	2
Density (calculated)	1.154 Mg/m ³
Absorption coefficient	0.074 mm ⁻¹
F(000)	1104
Theta range for data collection	1.83 to 22.50 deg.
Index ranges	-16 ≤ h ≤ 16, -23 ≤ k ≤ 0, 0 ≤ l ≤ 9
Independent reflections	3906 [R (int) = 0.1009]
Refinement method	Full-matrix least-squares on F ²
Data/restraints/parameters	3905/0/380
Goodness-of-fit on F ²	1.003
Final R indices [I > 2σ(I)]	R = 0.1239, R _w = 0.3119
Largest diff. peak and hole	0.296 and -0.344 e/Å ³

$R = \frac{\sum ||F_o| - |F_c||}{\sum |F_o|}$, $R_w = \frac{[\sum w(|F_o| - |F_c|)^2]}{[\sum w(|F_o|)^2]}^{1/2}$, where $w = 1/\sigma^2(|F_o|)$.

points were taken using an Electrothermal melting point apparatus and are uncorrected. Infrared spectra were recorded on a Nicolet Magna 550 FTIR spectrometer and ¹H NMR spectra were measured on a Gemini 300 spectrometer. All chemical shifts are reported in parts per million (δ) relative to tetramethylsilane.

The tri(ethylene glycol) di-*p*-tosylate and di(ethylene glycol) di-*p*-tosylate were prepared following the literature procedure.¹⁰

Preparation of Crown Ethers 1-3. 9,9-Bis-(4-hydroxyphenyl)fluorene (1.08 g, 3 mmol), Cs₂CO₃ (2.96 g, 9 mmol) and CH₃CN (100 mL) were introduced into a 500 mL three-necked flask equipped with a magnetic stirrer, reflux condenser, dropping funnel, and nitrogen inlet tube. Tri(ethylene glycol) di-*p*-tosylate (1.38 g, 3 mmol) in CH₃CN (30 mL) was then added dropwise to the stirred mixture over 30 min., and stirring was continued for 20 h at reflux temperature. After cooling the precipitated solid was filtered off and the filtrate was removed on a rotary evaporator. The residue was chromatographed on silica gel column eluted with hexane-EtOAc (7 : 1) to give product **1-3** in the order.

Crown ether **1**: yield 32%; white solid, mp 236 °C; IR (KBr) 2928, 2869, 1603, 1506, 1444, 1242, 1176, 1118, 1060, 827, 741 cm⁻¹; ¹H-NMR (CDCl₃) δ 3.71 (s, 8H, CH₂), 3.81 (t, 8H, *J* = 4.7, CH₂), 4.06 (t, 8H, *J* = 4.7, CH₂), 6.77 (d, 8H, *J* = 8.8, ArH), 7.10 (d, 8H, *J* = 8.8, ArH), 7.23-7.39 (m, 12H, ArH), 7.55 (d, 4H, *J* = 7.3, ArH); MALDI MS *m/z* Calcd. 928.39. Found 928.05.

Table 2. Selected Bond lengths [Å] and angles [deg] for **1**

O(1)-C(17)	1.36(2)	C(8)-C(9)	1.35(2)
O(1)-C(20)	1.42(2)	C(8)-C(13)	1.43(2)
O(2)-C(22)	1.40(2)	C(9)-C(10)	1.34(3)
O(2)-C(21)	1.43(2)	C(10)-C(11)	1.43(3)
C(1)-C(14)	1.47(2)	C(11)-C(12)	1.41(2)
C(1)-C(13)	1.54(2)	C(12)-C(13)	1.38(2)
C(1)-C(2)	1.56(2)	C(14)-C(15)	1.37(2)
C(2)-C(3)	1.35(2)	C(14)-C(19)	1.42(2)
C(2)-C(7)	1.39(2)	C(15)-C(16)	1.36(2)
C(3)-C(4)	1.38(2)	C(16)-C(17)	1.43(2)
C(4)-C(5)	1.36(2)	C(17)-C(18)	1.34(2)
C(5)-C(6)	1.38(2)	C(18)-C(19)	1.36(2)
C(6)-C(7)	1.46(2)	C(20)-C(21)	1.41(2)
C(7)-C(8)	1.41(2)	C(22)-C(31a)	1.49(2)
C(17)-O(1)-C(20)	121.9(12)	C(9)-C(10)-C(11)	121(2)
C(22)-O(2)-C(21)	117.1(11)	C(12)-C(11)-C(10)	118(2)
C(14)-C(1)-C(13)	114.6(10)	C(13)-C(12)-C(11)	119(2)
C(14)-C(1)-C(2)	111.7(10)	C(12)-C(13)-C(8)	119(2)
C(13)-C(1)-C(2)	99.5(10)	C(12)-C(13)-C(1)	128.5(13)
C(14)-C(1)-C(23)	115.4(10)	C(8)-C(13)-C(1)	112.0(12)
C(13)-C(1)-C(23)	106.7(10)	C(15)-C(14)-C(19)	114.5(13)
C(2)-C(1)-C(23)	107.5(9)	C(15)-C(14)-C(1)	123.7(13)
C(3)-C(2)-C(7)	123.4(13)	C(19)-C(14)-C(1)	120.8(12)
C(3)-C(2)-C(1)	127.7(12)	C(16)-C(15)-C(14)	126(2)
C(7)-C(2)-C(1)	108.5(12)	C(15)-C(16)-C(17)	117.6(14)
C(2)-C(3)-C(4)	118(2)	C(18)-C(17)-O(1)	119(2)
C(5)-C(4)-C(3)	122(2)	C(18)-C(17)-C(16)	117.2(14)
C(4)-C(5)-C(6)	121(2)	O(1)-C(17)-C(16)	123.6(12)
C(5)-C(6)-C(7)	118(2)	C(17)-C(18)-C(19)	124(2)
C(2)-C(7)-C(8)	113.5(13)	C(18)-C(19)-C(14)	120.1(13)
C(2)-C(7)-C(6)	117(2)	C(21)-C(20)-O(1)	108.9(14)
C(8)-C(7)-C(6)	129(2)	C(20)-C(21)-O(2)	111.5(13)
C(9)-C(8)-C(7)	132(2)	O(2)-C(22)-C(31a)	116.3(14)
C(9)-C(8)-C(13)	121(2)	C(24)-C(23)-C(1)	124.4(11)
C(7)-C(8)-C(13)	105.8(13)	C(28)-C(23)-C(1)	115.1(11)
C(10)-C(9)-C(8)	120(2)		

Symmetry transformations used to generate equivalent atoms.

Crown ether **2**: yield 13%; white solid, mp 129 °C; IR (KBr) 2924, 2866, 1607, 1506, 1448, 1250, 1176, 1118, 1064, 823, 745 cm⁻¹; ¹H-NMR (CDCl₃) δ 3.69 (s, 12H, CH₂), 3.79 (t, 12H, *J* = 4.7, CH₂), 4.03 (t, 12H, *J* = 4.7, CH₂), 6.73 (d, 12H, *J* = 8.8, ArH), 7.08 (d, 12H, *J* = 8.8, ArH), 7.22-7.36 (m, 18H, *J* = 7.3, ArH), 7.73 (d, 6H, *J* = 7.3, ArH); MALDI MS *m/z* Calcd. 1392.59. Found 1393.04.

Crown ether **3**: yield 4%; white solid, mp 127-129 °C; IR (KBr) 2920, 2877, 1607, 1506, 1444, 1242, 1176, 1130, 1110, 823, 749 cm⁻¹; ¹H-NMR (CDCl₃) δ 3.68 (s, 16H, CH₂), 3.79 (t, 16H, *J* = 4.7, CH₂), 4.03 (t, 16H, *J* = 4.7, CH₂), 6.73 (d, 16H, *J* = 8.5, ArH), 7.08 (d, 16H, *J* = 8.5, ArH), 7.23-7.38 (m, 24H, ArH), 7.72 (d, 8H, *J* = 7.3, ArH); MALDI MS *m/z* Calcd. 1856.79. Found 1854.77.

Preparation of Crown Ether 4. Compound **4** was prepared from 9,9-bis-(4-hydroxyphenyl)fluorene (1.08 g, 3 mmol) and di(ethylene glycol) di-*p*-tosylate (1.24 g, 3 mmol) in the presence of Cs₂CO₃ (2.96 g, 9 mmol) in CH₃CN according to the procedure described above. Column chromatography of residue gave 0.01 g (1%) of **4**: white solid, mp 170 °C; IR (KBr) 2932, 2873, 1615, 1503, 1444, 1246, 1176, 1130, 1060, 819, 745 cm⁻¹; ¹H-NMR (CDCl₃) δ 3.86 (t, 12H, *J* = 4.6, CH₂), 4.08 (t, 12H, *J* = 4.6, CH₂), 6.75 (d, 12H, *J* = 8.8, ArH), 7.08 (d, 12H, *J* = 8.8, ArH), 7.24-7.29 (m, 18H, ArH), 7.73 (d, 6H, *J* = 7.0, ArH); MALDI MS *m/z* Calcd. 1261.04. Found 1260.52.

X-Ray Single Crystallography of Crown Ether 1. Single crystal of crown ether **1** was mounted into glass capillary under N₂ atmosphere and then sealed. Diffraction data were collected at ambient temperature on Bruker P4 four circle diffractometer using Mo-Kα radiation. Intensity data were collected by using a θ -2 θ step scan technique and for all data sets the condition of the crystal was monitored by measuring 2 standard reflections. The solution of structure **1** was carried out by a combination of heavy atom Patterson techniques, direct methods, and Fourier techniques. The refinement of the structures by full matrix least squares methods was based on 3905 unique reflections ($2\theta = 45$, $I > 2\sigma$). At the current stage of refinement on 380 parameters all atoms present in the asymmetric units, $R = 0.1239$, $R_w = 0.3119$.

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