A New Rigid Benzene-Bridged Macrotricyclic Ligand

Krzysztof E. Krakowiak* [a], Guoping Xue [b], Jerald S. Bradshaw [b], N. Kent Dalley [b], Alexander Y. Nazarenko [b], Xian X. Zhang [b], and Reed M. Izatt [b]

[a] IBC Advanced Technologies, Inc., American Fork, UT, 84003, USA [b] Department of Chemistry and Biochemistry, Brigham Young University, Provo, UT, 84602, USA
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Dedicated to the memory of Professor Raymond N. Castle

A macrotricyclic ligand composed of two benzene rings connected by four 2,2'-oxydiphenoxide bridges (**2**) has been prepared by treating 1,2,4,5-tetrakis[2-(2-hydroxyphenoxy)phenoxymethyl]benzene with 1,2,4,5-tetrakis(bromomethyl)benzene in acetonitrile in the presence of potassium carbonate. Ligand **2** is of interest because of its similarity to macrocycle **1** which interacts strongly with cesium ions. The proposed more direct route of treating an excess of 2,2'-oxydiphenol with 1,2,4,5-tetrakis(bromomethyl)benzene to prepare **2** did not give the desired macrocycle but gave bis(tribenzo-11-crown-3) (**8**). An X-ray crystal structure study of **2** showed that the benzene rings which are linked by the four 2,2'-oxydiphenoxide bridges are connected in a nonsymmetric pattern. The structure of **8** was also determined using X-ray diffraction methods, and is reported.

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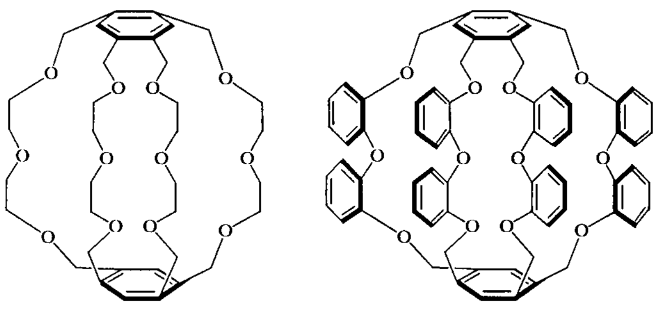
Nuclear waste facilities hold huge amounts of radioactive waste in which cesium 137 is one of the major radionuclides. It is very difficult to remove cesium from nuclear waste that has high concentrations of sodium and other base metal ions. To achieve this goal, the stability constant for cesium should be at least four orders of magnitude higher than it is for sodium [1]. The best selectivities for cesium have been reported for the bis-crown-6-calix[4]arene family of ligands and other calixerenes [2-5].

A few years ago, we published the synthesis of compound **1** (Figure 1) for cesium extraction [6]. That barrel-like molecule had two benzene rings connected by four diethylene glycol bridges. Ligand **1** had a strong interaction with cesium ions (log K = 3.5, valid in 80% methanol-20% water) and no apparent interaction with sodium ions. We now report the synthesis of macrocycle **2** which has two benzene rings connected by four 2,2'-oxydiphenoxide bridges. Thus, this macrotricyclic ligand has 8 additional benzene rings. This new macrotricyclic ligand should have increased selectivity for cesium over sodium since the molecule is more rigid and the phenyl ether rings may also interact with cesium. Unfortunately, ligand **2** is not soluble in methanol, so no comparison complexation studies have been carried out.



1 2

Figure 1. Macrotricyclic ligands.

Different strategies for the preparation of barrel-like molecules have been published [6-10]. Barrel-like molecule **2** was prepared starting from diphenol **3** as shown in Scheme 1. An excess of **4** was treated with tetrakis(bromomethyl)benzene (**5**) in acetonitrile in the presence of potassium carbonate to form tetrasubstituted benzene **6** with an 80% yield. After removing the protecting groups of **6** to form **7**, tetraphenol **7** was treated with **5** in acetoni-

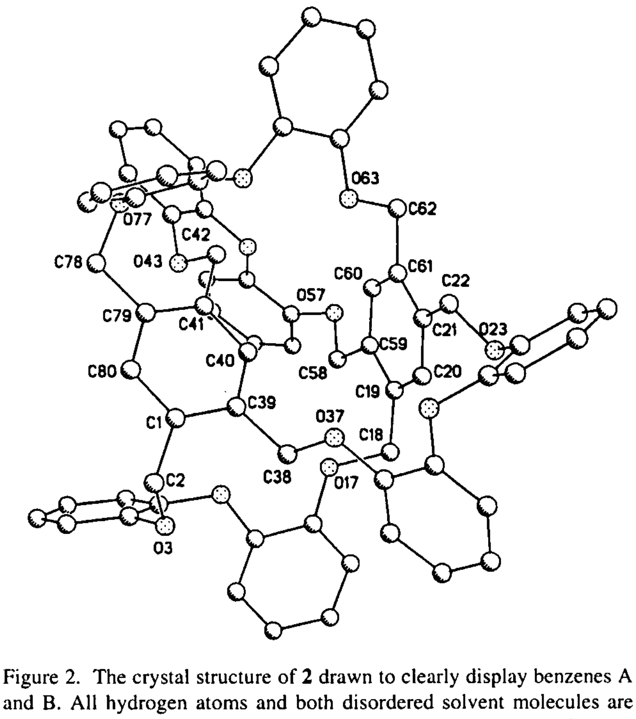
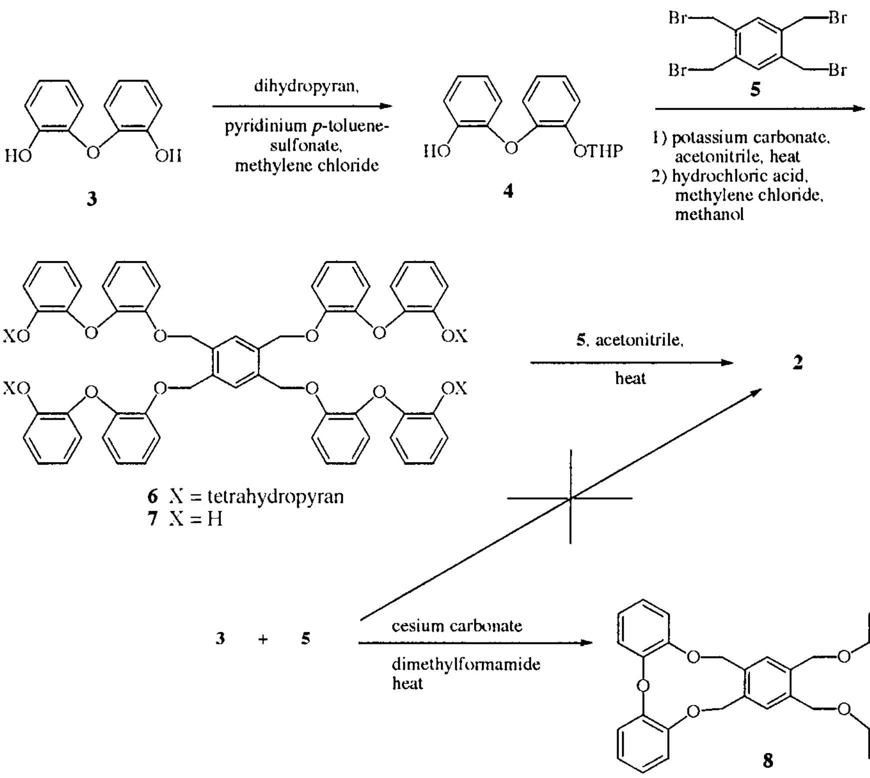


Figure 2. The crystal structure of **2** drawn to clearly display benzenes A and B. All hydrogen atoms and both disordered solvent molecules are omitted for clarity. Labels for most of the atoms are also omitted to improve the quality of the figure.

Scheme I



trile in the presence of potassium carbonate to form desired ligand **2** in an 8.5% yield. A one-step approach treating **5** with an excess of **3** did not give **2** but instead gave only bis(tribenzo-11-crown-3) **8** in a 70% yield. The identity and structure of **8** were established by an X-ray structure study of the compound (see Figure 3).

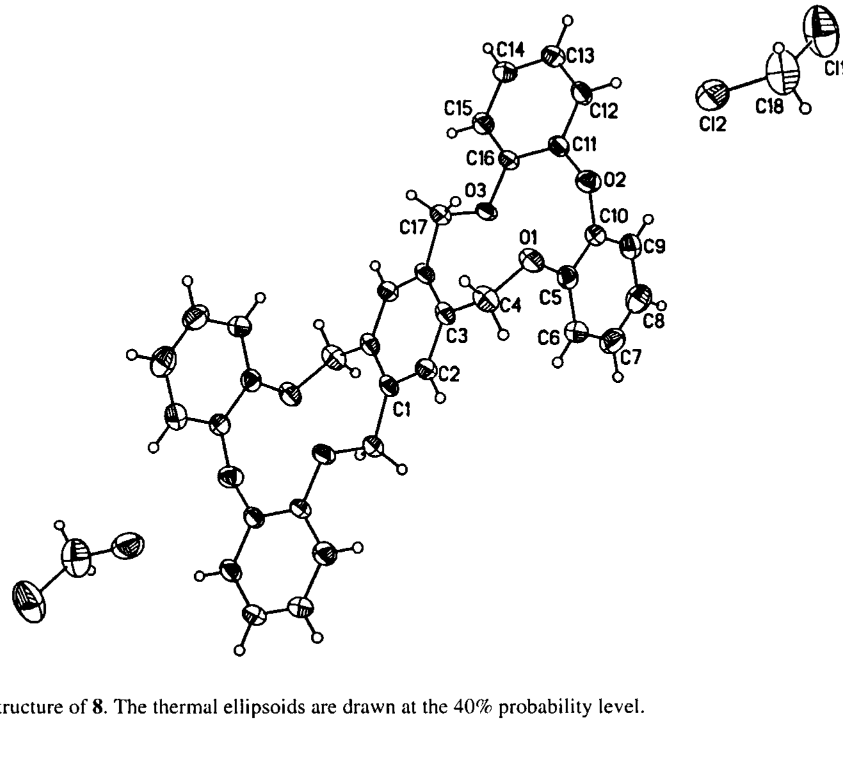


Figure 3. The crystal structure of **8**. The thermal ellipsoids are drawn at the 40% probability level.

The X-ray crystal structure of compound **2** confirmed the presence of the two benzene rings which are connected by four 2,2'-oxydiphenoxide bridges. These two benzene rings, benzene A, consisting of C1, C39, C40, C41, C79 and C80 and benzene B, consisting of C19, C20, C21, C61, C60 and C59, are shown in Figure 2. The figure shows the presence of the nonsymmetrical connections between benzene A and benzene B. For example, the linkages which join adjacent carbon atoms in benzene A, C1 and C39, are attached to nonadjacent carbon atoms, C19 and C21, in benzene B. This pattern is consistent throughout the structure.

EXPERIMENTAL

The ^{1}H and ^{13}C nmr spectra were recorded on Varian Gemini 200 MHz or Varian 300 MHz spectrometers using deuterated chloroform and dimethylsulfoxide-d_6 as solvents. Mass spectra were obtained on a Finnegan 8430 high resolution mass spectrometer using chemical ionization (ci), and fast atom bombardment (fab) methods. 2,2'-Oxydiphenol (**3**) was prepared as reported [9]. Solvents and starting materials were purchased from commercial sources where available.

Preparation of 2-(2-Tetrahydropyranyloxyphenoxy)phenol (**4**).

3,4-Dihydro-2*H*-pyran (4.2 g, 0.05 moles) was added dropwise to a solution of 2,2'-oxydiphenol (**3**) (10.1 g, 0.05 moles) and pyridinium *p*-toluenesulfonate (1.26 g, 5 mmoles) in 50 ml of methylene chloride. After stirring for 20 hours at room temperature, the solution was washed with a saturated sodium bicarbonate solution (50 ml), brine (50 ml) and water (50 ml). The organic solvent was dried over anhydrous magnesium sulfate and evaporated. The crude oil was purified by chromatography on silica gel using methylene chloride as the eluent. Compound **4** was obtained as a colorless viscous oil (8.6 g, 60%); ^{1}H nmr: 7.30-6.80 (m, 8H), 5.42 (m, 1H), 3.82-3.52 (m, 2H), 1.89-1.44 (m, 6H); ms: (ci) m/z 286 (M^+). This material was used without further purification.

Preparation of 1,2,4,5-Tetrakis[2-(2-tetrahydropyranyloxyphenoxy)phenoxymethyl]benzene (**6**).

A mixture of **4** (8.58 g, 30 mmoles), anhydrous potassium carbonate (41.4 g, 0.30 moles) and 100 ml of acetonitrile was stirred for 2 hours. A solution of 1,2,4,5-tetrakis (bromomethyl) benzene (2.25 g, 5 mmoles) in 50 ml of acetonitrile was added dropwise at reflux temperature and the resulting mixture was stirred for two days. The cooled mixture was filtered and the solvent was evaporated. The residue was recrystallized twice in chloroform and ethanol (1:1) to give **4** as a white crystal; (6.35 g, 80%); mp 160-161°; ^{1}H nmr: 7.24-6.82 (m, 34H), 5.28 (m, 4H), 5.10 (s, 8H), 3.78-3.58 (m, 8H), 1.58-1.28 (m, 24H), ms: (fab) m/z 1293 (MNa^+).

Anal. Calcd. for $C_{78}H_{78}O_{16}$: C, 73.68; H, 6.18. Found: C, 73.46; H, 6.26.

Preparation of 1,2,4,5-Tetrakis[2-(2-hydroxyphenoxy)phenoxymethyl]benzene (**7**).

To a solution of **6** (6.1 g, 4.8 mmoles) in 80 ml of methylene chloride and 80 ml of methanol was added 20 ml of concentrated hydrochloric acid. The resulting mixture was stirred overnight at room temperature. The white precipitate was filtered and washed with 50 ml of methanol and recrystallized from methylene chloride and ethanol (1:2) to give a white crystal; (4.25 g, 95%); mp 179-

Table 1

Crystal Data and Experimental Data for the Structural Study of **2** and **8**

	2	**8**
Formula	$C_{68}H_{52}O_{12}\cdot 2C_4H_8O$	$C_{34}H_{26}O_6\cdot 2CH_2Cl_2$
Formula weight	1205.37	700.40
F(000)	1272	724
Crystal system	Triclinic	Monoclinic
Space Group	$P\bar{1}$	$P2_1/n$
Unit cell dimensions	a = 14.155(4) Å, α = 66.607(7)° b = 15.692(3) Å, β = 86.20(2)° c = 16.908(4) Å, γ = 65.27(2)°	a = 9.5240(10) Å,α = 90° b = 12.2380(10) Å, β = 100.020(10) c = 14.2900(10) Å, γ = 90°
Volume	3108.3 $Å^3$	1640.2 (2) $Å^3$
Z	2	2
Density calc	1.288 Mg/m^3	1.418 Mg/m^3
Absorption coefficient	0.091 mm^{-1}	0.407 mm^{-1}
Crystal size	0.4 x 0.3 x 0.2 mm	0.5 x 0.3 x 0.25mm
θ range	2.4 to 20.0°	2.2 to 25.0°
Limiting indices	$-13 \le h \le 0, -13 \le k \le 12, -16 \le l \le 16$	$0 \le h \le 4, 0 \le k \le 14, -17 \le l \le 16$
Reflections collected	5824	1748
Independent reflections	5527 (R_{int} = 0.0403)	1568 (R_{int} = 0.0249)
Refinement methods	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	5525/0/778	15681/0/204
Goodnes-of-fit on F^2	1.062	1.030
Final R indices [I > 2 σ(I)]	R = 0.0801 wR^2 = 0.1915	R = 0.0476 wR^2 = 0.1038
R indices (all data)	R = 0.1561 wR^2 = 0.2486	R = 0.0826 wR^2 = 0.1248
Extinction coefficient	0.0017 (9)	0.0031(10)
Largest diff peak	0.451 $eÅ^{-3}$	0.215 $eÅ^{-3}$
Largest diff hole	-0.347 $eÅ^{-3}$	-0.201 $eÅ^{-3}$

Table 2

Atomic Coordinates [x 10^4] and Equivalent Isotropic Displacement Parameters [$Å^2$ x 10^3] for **2**. U(eq) is Defined as One Third of the Trace of the Orthogonalized U_{ij} Tensor.

Atom	x	y	z	U(eq)
C1	5742(6)	3640(6)	5007(6)	45(2)
C2	6332(7)	3758(7)	5631(6)	60(3)
O3	7452(5)	3202(5)	5654(4)	60(2)
C4	7849(7)	2149(8)	6002(6)	51(2)
C5	7817(8)	1597(9)	6855(7)	71(3)
C6	8309(9)	522(11)	7184(8)	90(4)
C7	8814(9)	8(9)	6676(9)	87(4)
C8	8844(8)	580(10)	5835(9)	80(3)
C9	8371(8)	1646(9)	5491(7)	58(3)
O10	8386(5)	2194(5)	4603(4)	72(2)
C11	9313(7)	2268(7)	4344(7)	51(3)
C12	10164(8)	1935(8)	4878(6)	67(3)
C13	11026(8)	2063(9)	4549(7)	85(4)
C14	11038(8)	2527(9)	3680(8)	83(4)
C15	10167(7)	2861(7)	3120(6)	64(3)
C16	9299(7)	2734(7)	3449(6)	47(2)
O17	8401(4)	3023(5)	2943(4)	58(2)
C18	8293(7)	3633(7)	2033(6)	55(3)
C19	7201(7)	3917(8)	1688(5)	45(2)
C20	6439(8)	4920(7)	1412(5)	48(2)
C21	5410(7)	5198(7)	1156(5)	38(2)
C22	4596(7)	6262(8)	956(6)	64(3)
O23	5069(5)	6956(5)	677(4)	65(2)
C24	4399(8)	7942(8)	562(7)	56(3)
C25	3899(8)	8668(9)	-241(7)	74(3)
C26	3262(9)	9658(9)	-361(7)	84(3)
C27	3110(9)	9929(8)	326(8)	83(3)
C28	3608(8)	9210(9)	1152(7)	74(3)
C29	4262(7)	8216(8)	1259(7)	54(3)
O30	4756(5)	7482(5)	2091(4)	65(2)
C31	5836(8)	7149(8)	2211(6)	51(3)
C32	6299(8)	7792(7)	1800(6)	62(3)
C33	7366(9)	7452(8)	1939(6)	66(3)
C34	7960(8)	6459(9)	2476(6)	62(3)
C35	7507(7)	5790(7)	2890(6)	52(2)
C36	6435(7)	6124(7)	2785(5)	46(2)
O37	5917(4)	5533(5)	3166(4)	54(2)
C38	6574(7)	4488(7)	3738(6)	59(3)
C39	5909(6)	3927(6)	4135(6)	46(2)
C40	5531(7)	3583(7)	3637(6)	52(3)
C41	4918(7)	3036(7)	3951(6)	50(2)
C42	4661(8)	2552(8)	3421(6)	61(3)
O43	5234(5)	1461(5)	3870(4)	65(2)
C44	4868(8)	896(7)	3622(6)	55(3)
C45	4069(8)	654(9)	4012(6)	74(3)
C46	3745(9)	37(10)	3828(8)	83(3)
C47	4233(10)	-335(8)	3232(8)	79(3)
C48	5013(9)	-90(8)	2815(7)	74(3)
C49	5355(8)	489(8)	3032(7)	57(3)
O50	6088(6)	809(5)	2606(4)	77(2)
C51	7110(8)	79(8)	2682(6)	56(3)
C52	7472(9)	-958(8)	3168(6)	67(3)
C53	8507(9)	-1616(8)	3174(7)	74(3)
C54	9156(8)	-1214(9)	2726(7)	80(3)
C55	8803 (9)	-186(10)	2263 (7)	77 (3)
C56	7789(9)	458(8)	2219(6)	59(3)
O57	7390(5)	1510(5)	1707(4)	67(2)
C58	7693(8)	2054(8)	2036(7)	77(3)
C59	6914(7)	3173(7)	1672(5)	46(2)
C60	5879(7)	3462(7)	1378(5)	47(2)

Table 2 (continued)

Atom	x	y	z	U(eq)
C61	5128(6)	4460(8)	1131(5)	42(2)
C62	4035(6)	4698(7)	858(5)	48(2)
O63	3438(5)	4748(5)	1575(3)	62(2)
C64	2414(7)	4939(7)	1452(6)	49(2)
C65	1863(7)	5239(7)	679(6)	66(3)
C66	826(8)	5422(8)	620(8)	82(3)
C67	340(8)	5293(9)	1364(9)	87(4)
C68	881(8)	4972(8)	2142(7)	73(3)
C69	1892(7)	4811(7)	2205(6)	56(3)
O70	2491(5)	4473(6)	2973(4)	85(2)
C71	2011(8)	4714(10)	3649(7)	62(3)
C72	1359(9)	5700(9)	3524(8)	79(3)
C73	944(8)	5885(9)	4216(9)	81(3)
C74	1196(9)	5125(11)	5027(8)	80(3)
C75	1855(9)	4152(9)	5138(7)	67(3)
C76	2292(7)	3930(8)	4461(6)	47(2)
O77	2919(5)	2924(5)	4568(4)	53(2)
C78	3889(7)	2417(7)	5146(5)	54(3)
C79	4624(7)	2895(6)	4784(5)	45(2)
C80	5070(7)	3168(6)	5304(6)	47(2)

Table 3

Average Bond Lengths for the Atoms of **2**

atoms	Bond Length (Å)
aromatic carbon-aromatic carbon	1.38 (2)
aromatic carbon-oxygen	1.39 (1)
aromatic carbon-aliphatic carbon	1.50 (1)
aliphatic carbon-oxygen	1.43 (2)

Table 4

Atomic coordinates [x 10^4] and equivalent isotropic displacement parameters [$Å^2$ x 10^3] for **8**. U(eq) is defined as one-third of the trace of the orthogonalized U_{ij} tensor.

	x	y	z	U(eq)
C1	-5810(11)	5178(4)	10729(4)	43(4)
C2	-4336(11)	5107(4)	10907(5)	48(5)
C3	-3499(11)	4938(4)	10215(4)	45(3)
C4	-1909(10)	4944(4)	10493(4)	60(4)
O1	-1181(4)	4127(3)	10037(2)	57(1)
C5	-1457(6)	3050(4)	10173(3)	48(2)
C6	-2061(7)	2626(4)	10914(3)	57(2)
C7	-2259(7)	1514(5)	10965(4)	70(2)
C8	-1876(7)	825(4)	10302(4)	74(2)
C9	-1295(7)	1241(4)	9562(3)	59(2)
C10	-1097(6)	2339(4)	9495(3)	47(2)
O2	-429(4)	2781(3)	8780(2)	57(1)
C11	-1194(9)	2788(4)	7854(3)	45(3)
C12	-464(7)	2448(4)	7144(3)	52(2)
C13	-1132(9)	2497(4)	6203(4)	57(3)
C14	-2507(9)	2845(4)	5980(4)	56(3)
C15	-3231(7)	3182(4)	6686(3)	53(2)
C16	-2557(9)	3168(4)	7629(3)	46(3)
O3	-3304(4)	3482(2)	8340(2)	48(1)
C17	-3429(7)	4653(4)	8449(3)	56(2)
C18	4852(10)	1435(6)	8794(5)	118(3)
Cl1	5230(3)	377(2)	8120(2)	151(1)
Cl2	3130(3)	1901(2)	8544(1)	109(1)

181°; ^{1}H nmr: 9.40 (b, 4H, disappeared in D_2O), 7.32-6.63 (m, 34H), 5.13 (s, 8H), ^{13}C nmr: 148.8, 148.0, 145.9, 144.4, 134.8, 128.7, 123.9, 123.7, 121.4, 119.4,118.8, 118.6, 116.9, 114.5, 67.6; ms: (fab) m/z 957 (MNa$^+$).

Anal. Calcd. for $C_{58}H_{46}O_{12}$: C, 74.51; H, 4.96. Found: C, 74.51; H, 5.05.

Preparation of Benzene-Bridged Macrotricyclic Polyether **2**.

1,2,4,5-Tetrakis(bromomethylbenzene) (0.90 g, 2 mmoles) was dissolved in 200 ml of acetonitrile and placed in an addition funnel. To a second addition funnel was added tetraphenol **7** (1.87 g, 2 mmoles) in 200 ml of acetonitrile. The two solutions were simultaneously added to 350 ml of acetonitrile containing potassium carbonate (11.04 g, 80 mmoles) at reflux temperature over a 20-hour period. The resulting mixture was refluxed for 3 days. The cooled mixture was filtered and the filtrate was evaporated. The residue was purified by chromatography on silica gel using chloroform and methanol (10:1) as eluent to give **2** (0.20 g, 8.5%) as a white solid; mp > 290° (dec.); ^{1}H nmr: 7.30-6.43 (m, 36H), 5.70-4.50 (m, 16H); ^{13}C nmr: 151.0, 149.5, 149.2, 149.0, 148.0, 147.7, 146.5, 137.4, 137.2, 135.0, 132.9, 129.4, 126.2, 125.2, 124.5, 124.2, 124.0, 122.6, 122.1, 121.2, 120.3, 115.2, 113.7, 112.5, 73.1, 71.2, 68.9, 66.8; ms: (fab) m/z 1083 (MNa$^+$). Single crystals suitable for X-ray studies were crystallized from tetrahydrofuran and chloroform.

Anal. Calcd. for $C_{68}H_{52}O_{12}$: C, 76.97; H, 4.94. Found: C, 76.85; H, 4.96.

Preparation of Bis(tribenzo-12-crown-3) (**8**).

To a mixture of 2,2'-oxydiphenol (**3**) (2.83 g, 14 mmoles) and cesium carbonate (45.6 g, 140 mmoles) in 500 ml of dimethylformamide was added 1,2,4,5-tetrakis(bromomethyl)benzene (**5**) (3.15 g, 7 mmoles) in 300 ml of dimethylformamide. The resulting mixture was stirred at 80-90° for 7 days. The cooled mixture was filtered, the filtrate was evaporated under vacuum, and the residue was dissolved in water and chloroform. After the organic layer was separated, the aqueous layer was extracted with chloroform. The combined organic solution was dried over magnesium sulfate and evaporated. The residue was recrystallized in chloroform and ethanol (2:1) to give a white crystal (2.60 g, 70%); mp 273-275%; ^{1}H nmr: 7.5 (s, 2H), 7.05-6.95 (m, 16H), 5.22 (s, 8H); ^{13}C nmr: 150.8, 149.2, 136.3, 134.0, 124.4, 123.9, 121.7, 121.1, 71.8; ms: (ci) m/z 530 (M$^+$).

Anal. Calcd. for $C_{34}H_{26}O_6$: C, 76.97; H, 4.94. Found: C, 76.82; H, 5.02.

X-ray Crystal Structure Analysis for **2** and **8**.

Suitable crystals for an X-ray study of **2** were crystallized from tetrahydrofuran while those of **8** were crystallized from methylene chloride. Crystal and intensity data for both structural studies were obtained using a Bruker P4 automated diffractometer which utilized MoKα radiation (λ = 0.71073 Å). Both sets of intensity data were corrected for secondary extinction. Crystal data and experimental details for the studies are listed in Table 1. Both structures were solved using direct methods and the structures were refined using a full-matrix, least squares procedure. All programs used in the solution, refinement and display of the structures are contained in the program package supplied by Bruker Analytical X-ray Systems [11].

During the initial stage of the refinement of **2**, it became apparent that the unit cell also contained two highly disordered tetrahydrofuran solvent molecules. Some of the peaks in the difference map were larger than 2 eÅ^{-3}. Atoms were placed at the positions of the larger difference map peaks but in as much as the emphasis of the study was on molecule **2**, no effort was made to resolve the structures of the disordered solvent molecules. All of the nonhydrogen atoms of **2** were refined anisotropically while the atoms of the disordered solvent molecules were refined isotropically. Positions for the hydrogen atoms bonded to the carbon atoms of **2** were calculated based on the molecular geometry and these atoms were allowed to ride on their neighboring carbon atoms during the refinement process. Positional and thermal parameters of the nonhydrogen atoms of **2** are listed in Table 2. Because of the large number of atoms in **2**, the bond lengths and angles are not included in the paper but their values may be obtained from the authors. Average bond lengths for **2** are listed in Table 3.

The structure of **8** contained a center of inversion and as a result the asymmetric unit consisted of one-half of the molecule and one methylene chloride molecule. The positions of the nonhydrogen atoms of **8** are listed in Table 4. All nonhydrogen atoms of the structure were refined anistropically. The bond lengths and angles of **8** are normal.

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