Synthesis, Structure, and Extraction Properties of *paco*-Calix[4]arene Crown-6 Ethers *

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Abstract

anti-25,27-Bis-*n*-octyloxycalix[4]arene, the *paco*-isomer of 25,27-bis-*n*-octyloxycalix[4]arene crown-6 ether, and the *paco*- and 1,3-*alt* isomers of 25,27-bis-*n*-octyloxycalix[4]arene *t*-butylbenzocrown-6 ether were prepared. The crystal structures of *anti*-25,27-bis-*n*-octyloxycalix[4]arene, *paco*-25,27-bis-*n*-octyloxycalix[4]arene crown-6, and 1,3-*alt*-25,27-bis-*n*-octyloxycalix[4]arene crown-6 were determined and the solution structure of *anti*-25,27-bis-*n*-octyloxycalix[4]arene was studied by 2D- and VT-NMR. The extraction of alkali metal nitrates by the *paco*-25,27-bis-*n*-octyloxycalix[4]arene crown-6 and *t*-butylbenzocrown-6 ethers in 1,2-dichloroethane was compared to that of the corresponding 1,3-*alt* isomers.

Introduction

The development of calixarene chemistry [1], and the subsequent marriage with crown ethers [2] has resulted in significant advances in ion recognition [3]. Of particular interest is the role that calixarene conformation plays in shaping these molecules. Calix[4]arene, for instance, can adopt four different conformations: cone, partial cone (*paco*), 1,2-alternate (1,2-*alt*), and 1,3-alternate (1,3-*alt*), as determined by the relative orientations of the phenolic rings [4]. While calix[4]arene is conformationally mobile, substituents on the phenolic oxygens larger than ethyl block the interconversion [5], and methods have been developed to obtain each of the individual conformations selectively [5, 6]. This is significant since the calixarene conformation strongly influences the specific recognition properties of calix[4]arene derivatives. For example, diethoxy, tetra-*t*-butylcalix[4]arene crown-5 ether was reported to bind potassium with a selectivity that varied depending on the calixarene conformation in the order: *paco* > 1,3-*alt* > *cone* [7]. Subsequently, it was shown that removal of the *t*-butyl groups from the calix[4]arene resulted in crown ether derivatives that exhibited optimum potassium (crown-5) and cesium (crown-6) binding when in the 1,3-*alt* conformation [8].

In the course of our work on calix[4]arene crown-6 ethers as cesium extractants for decontamination of neutralized nuclear fuel reprocessing wastes [9], we isolated the *syn* and *anti* isomers of 25,27-bis-*n*-octyloxycalix[4]arene (**1a** and **1b** in Figure 1), from which we prepared the *paco*- and 1,3-*alt*-25,27-bisoctyloxycalix[4]arene crown-6 ethers **2a**, **2b**, **3a**, and **3b** shown in Figure 1 for evaluation as cesium-selective extractants [10]. In this paper, we report their syntheses, the crystal structures of **1b**, **2a**, and **2b**, and the alkali cation extraction properties of **2a**, **2b**, **3a**, and **3b** [11].

Experimental

General

The syntheses of **1a** and **2a** have been reported previously [11]. The synthesis of **1b**, **2b**, **3a**, and **3b** are described below. All reagents were obtained from commercial sources and used as received, unless otherwise noted. Metal nitrates were dried for 48 hours at 150 °C over P_2O_5. Reactions were monitored by TLC on Silica Gel 60 using ethyl acetate/hexanes eluent, unless otherwise noted, and preparative chromatography was performed on Silica Gel 60 (60–200 mesh). ^{1}H NMR data were obtained on a Bruker MSL400 spectrometer and data processed using SwaN-MR [12]. The 2D COSY was obtained on a Bruker AVANCE 600 spectrometer.

Synthesis

anti-25,27-Bisoctyloxycalix[4]arene **1b**

A mixture of 25,27-bisallyloxycalix[4]arene (1.0 g, 2.0 mmol), 1-iodooctane (2.4 g, 10 mmol), and K_2CO_3 (1.5
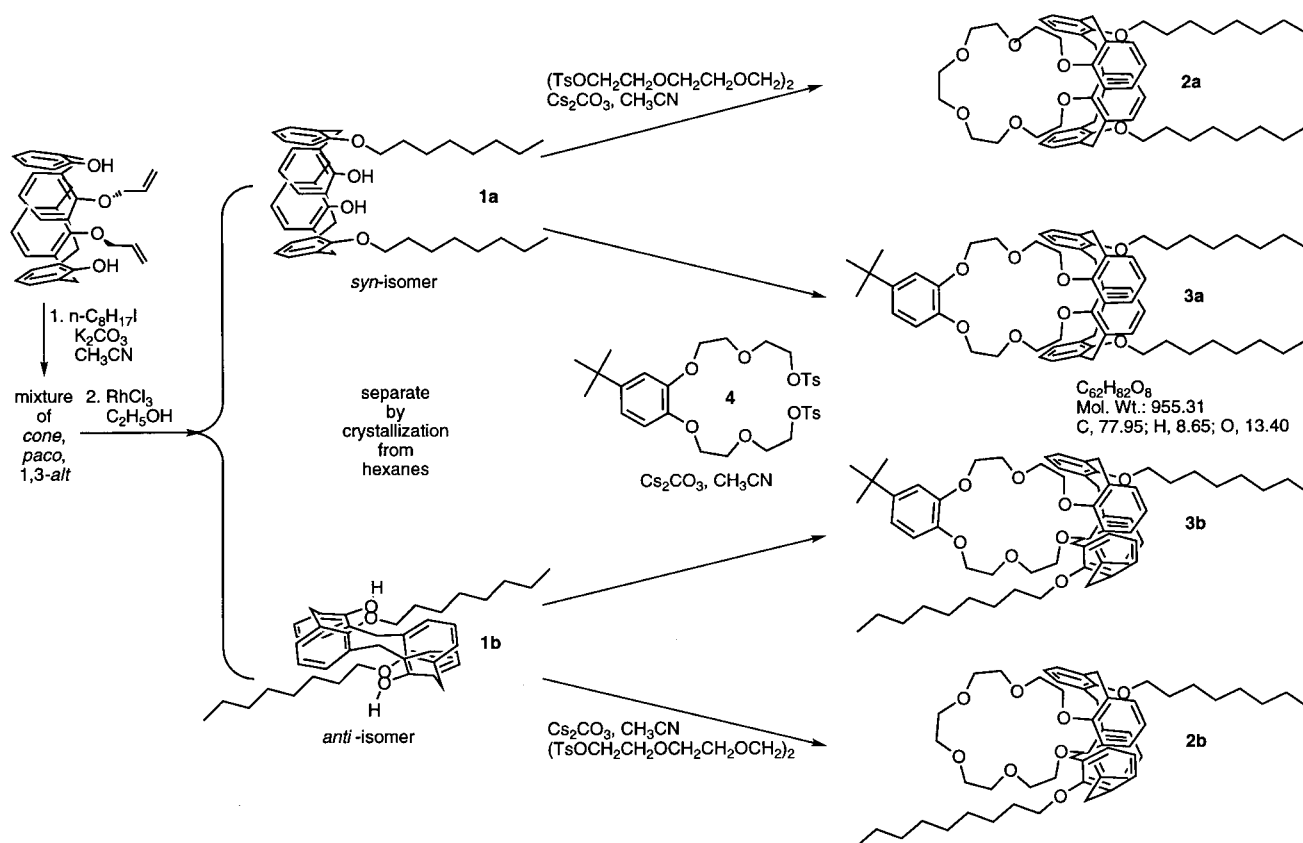
Figure 1. Synthetic scheme and structures of compounds.

g, 11 mmol) in acetonitrile (200 mL) was heated at reflux for three days. The solvent was evaporated *in vacuo*; the residue was dissolved in hexanes, and adsorbed onto a short column of silica gel. Excess iodooctane was eluted with hexanes, after which the product was eluted with 1:1 ethyl acetate:hexanes. After solvent evaporation, the mixture of 25,27-bisallyloxy-26,28-bis-*n*-octyloxy calix[4]arene isomers was dissolved in ethanol/ethyl acetate (10 mL/10 mL), RhCl$_3$ was added, and the solution heated at reflux for four days. Following evaporation *in vacuo* the crude mixture was dissolved in hexanes (10 mL) and placed in the refrigerator (~5 °C) overnight. The colorless crystals were filtered and air-dried to obtain 0.30 g (23%) of **1b**. ^{1}H (400.13 MHz, CDCl$_3$, 23 °C, CHCl$_3$): δ = 0.68 (4H, p, J = 7.5, OCH$_2$CH$_2$C*H$_2$*CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$), 0.87 (6H, t, J = 7.2, OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$C*H$_3$*), 0.94 (4H, m, OCH$_2$CH$_2$CH$_2$C*H$_2$*CH$_2$CH$_2$CH$_2$CH$_3$), 1.01 (8H, m, OCH$_2$C*H$_2$*CH$_2$CH$_2$C*H$_2$*CH$_2$CH$_2$CH$_3$), 1.13 (4H, m, OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$C*H$_2$*CH$_2$CH$_3$), 1.24 (4H, m, OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$C*H$_2$*CH$_3$), 3.57 (4H, t, J = 7.2, OC*H$_2$*CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_2$CH$_3$), 3.75 (4H, d, J = 15.5, ArC*H$_2$*Ar), 3.97 (4H, d, J = 15.5, ArC*H$_2$*Ar), 6.74 (2H, t, J = 7.5, ArH^4), 6.99 (2H, t, J = 7.5, ArH^4), 7.06 (4H, d, J = 7.5, ArH^3), 7.16 (4H, d, J = 7.5, ArH^3), 7.42 (2H, s, ArO*H*); ^{13}C (100.613 MHz, CDCl$_3$, 23 °C, CDCl$_3$): δ = 14.1, 22.7, 24.9, 28.7, 28.9, 29.3, 31.8, 34.9, 74.0, 119.7, 124.7, 127.6, 128.2, 128.7, 133.6, 153.2, 153.3; elemental analysis calcd. (%) for C$_{44}$H$_{54}$O$_4$ (646.91): C 81.44, H 8.70, O 9.86; found C 81.43, H 8.68.

Bis-1,2-[2′(2″-hydroxyethoxy)ethoxy]-4-t-butylbenzene **5**

A suspension of 4-*t*-butylcatechol (10.0 g, 60.2 mmol), 2-chloroethoxyethanol (26 mL, 180 mmol), and K$_2$CO$_3$ (80 g, 533 mmol) in dimethylformamide (150 mL) was heated at 80 °C with stirring under argon overnight. The dimethylformamide was evaporated *in vacuo*, the residue dissolved in ethyl acetate, filtered, and concentrated *in vacuo*. The crude product was purified by chromatography on silica gel, eluting sequentially with hexanes, then ether, then ethyl acetate to obtain **5** (16.6 g, 71%) as a yellow oil. ^{1}H (400.13 MHz, CDCl$_3$, 23 °C, CHCl$_3$): δ = 1.26 (9H, s, (CH$_3$)$_3$C–), 3.62–3.67 (4H, m, Bz-OCH$_2$CH$_2$OC*H$_2$*CH$_2$OH), 3.70–3.75 (4H, m, Bz-OCH$_2$CH$_2$OCH$_2$C*H$_2$*OH), 3.83 (2H, br s, –OH), 3.84–3.89 (4H, m, Bz-OCH$_2$C*H$_2$*OCH$_2$CH$_2$OH), 4.10–4.14 (2H, m, Bz-OC*H$_2$*CH$_2$OCH$_2$CH$_2$OH), 4.14–4.18 (2H, m, Bz-OC*H$_2$*CH$_2$OCH$_2$CH$_2$OH), 6.78 (1H, d, J = 8.1, BzH^6), 6.88 (1H, d, J = 2.2, BzH^3), 6.88–6.90 (1H, m, BzH^5); ^{13}C (100.613 MHz, CDCl$_3$, 23 °C, CDCl$_3$): δ = 32.1, 34.0, 61.1, 68.1, 68.2, 69.0, 69.1, 72.5, 72.6, 111.3, 112.7, 117.7, 144.3, 145.8, 147.5.

Bis-1,2-[2′(2″-hydroxyethoxy)ethoxy]-4-t-butylbenzene di-p-toluenesulfonate **4**

Bis-1,2-[2′(2″-hydroxyethoxy)ethoxy]-4-*t*-butylbenzene, **5**, (14.4 g, 42.1 mmol) was added to a solution of *p*-toluenesulfonyl chloride (19 g, 97 mmol) in pyridine (80 mL). After standing at room temperature for 5 hours, water (300 mL) was added and the solution was extracted twice with ether (300 mL; 150 mL). The combined ether
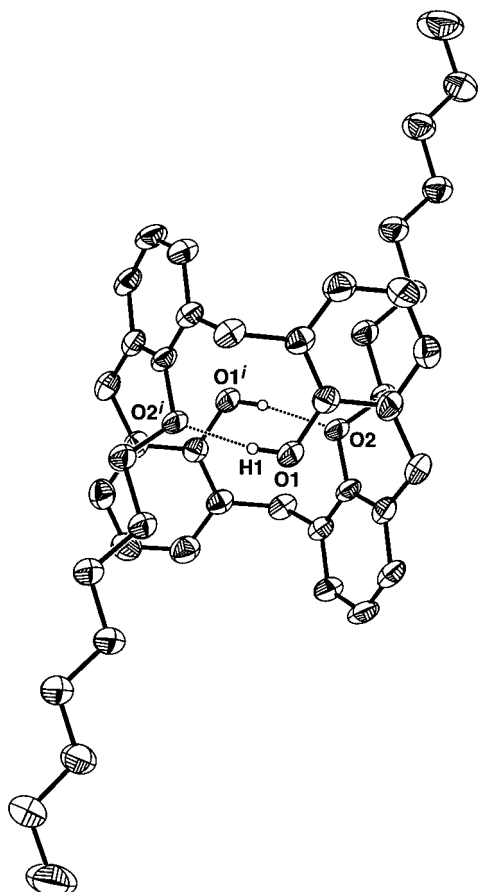
Figure 2. ORTEP representation with 50% probability ellipsoids of *anti*-1,3-bisoctyloxycalix[4]arene (**1b**). Unlabelled atoms are carbon. Hydrogen atoms, except the hydroxyl H atom, are omitted for clarity. Symmetry code: (i) $-x, 2-y, -z$.
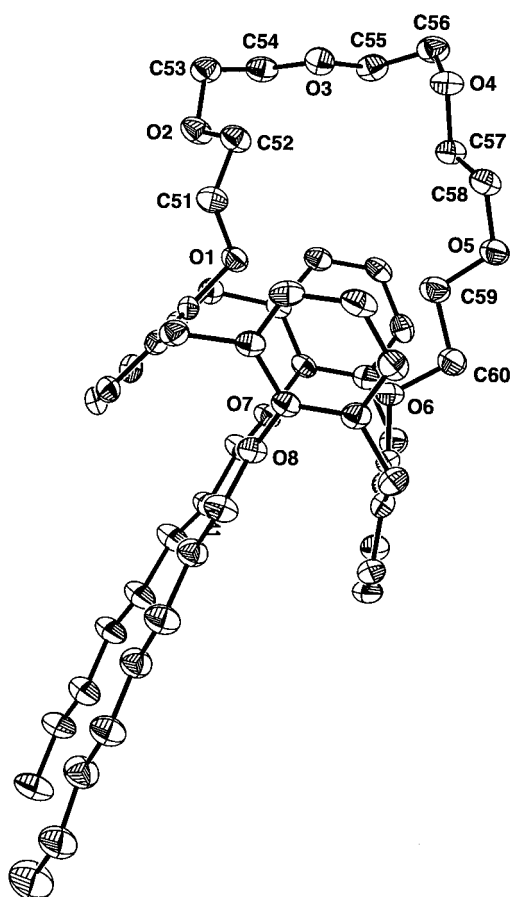

Figure 3. ORTEP representation with 50% probability ellipsoids of 1,3-alt-bis-*n*-octyloxycalix[4]arene crown-6 (**2a**). Unlabelled atoms are carbon. Hydrogen atoms are omitted for clarity.

extract was washed twice with 1 N HCl (200 mL each), once with water (200 mL), dried over MgSO$_4$, filtered, and evaporated *in vacuo* to obtain **5** (18 g, 67%) as a brown oil. ^{1}H (400.13 MHz, CDCl$_3$, 23 °C, CHCl$_3$): δ = 1.27 (9H, s, (CH$_3$)$_3$C–), 2.38 (6H, s, SO$_2$Ar–C*H*$_3$), 3.71–3.77 (8H, m, Bz-OCH$_2$C*H*$_2$OC*H*$_2$CH$_2$O-Ts), 4.02 (2H, t, J = 4.7, Bz-OC*H*$_2$CH$_2$OCH$_2$CH$_2$O-Ts), 4.07 (2H, t, J = 4.7, Bz-OC*H*$_2$CH$_2$OCH$_2$CH$_2$O-Ts), 4.12–4.18 (4H, m, Bz-OCH$_2$CH$_2$OCH$_2$C*H*$_2$O-Ts), 6.78 (1H, d, J = 8.1, BzH^6), 6.90 (1H, d/d, J = 2.2/8.1, BzH^5), 6.92 (1H, d, J = 2.2, BzH^3), 7.27 (4H, m, SO$_2$Ar–H), 7.76 (4H, d/d, J = 8.3/1.8, SO$_2$Ar–H); ^{13}C (100.613 MHz, CDCl$_3$, 23 °C, CDCl$_3$): δ = 21.5, 31.4, 34.2, 61.1, 68.8, 68.9, 69.2, 69.3, 70.0, 79.9, 113.3, 114.5, 118.4, 127.9, 129.7, 133.1, 144.7, 145.0, 146.7, 148.3.

paco-25,27-Bis-n-octyloxycalix[4]arene crown-6 **2b**

A suspension of **1b** (0.20 g, 0.31 mmol), pentaethyleneglycol ditosylate (0.17 g, 0.85 mmol), and Cs$_2$CO$_3$ (1.5 g, 4.6 mmol) in acetonitrile (50 mL) was heated with stirring under argon at reflux for two days. The solvent was removed *in vacuo*, and the residue was partitioned between dichloromethane (30 mL) and 1 N HCl (30 mL). The organic phase was washed twice with water (20 mL), dried over Na$_2$SO$_4$, and evaporated *in vacuo*. Chromatography on
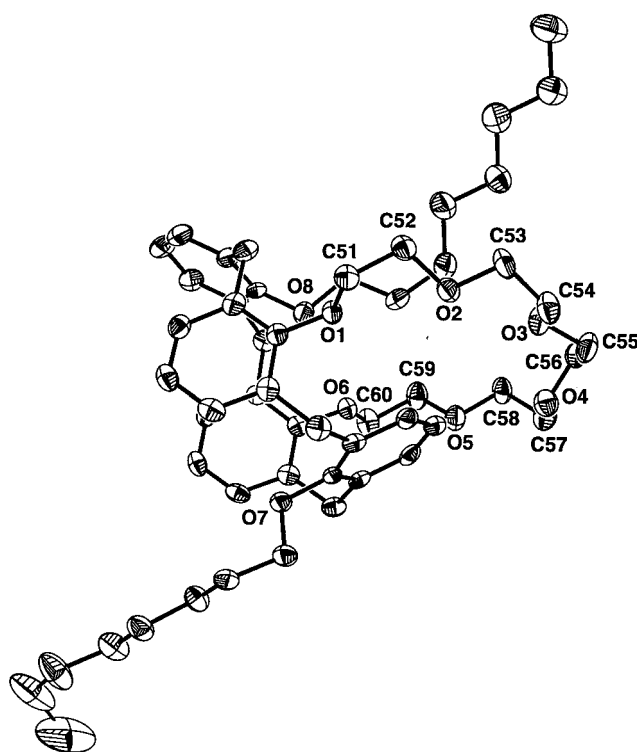

Figure 4. ORTEP representation with 50% probability ellipsoids of *paco*-bis-*n*-octyloxycalix[4]arene crown-6 (**2b**). Unlabelled atoms are carbon. Hydrogen atoms and the minor disorder component are omitted for clarity.

silica gel (ethyl acetate/hexanes gradient elution) provided 165 mg (63%) of **2b**. ^{1}H (400.13 MHz, CDCl$_3$, 23 °C, CHCl$_3$): δ = 0.85 (3H, t, J = 7.1, OCH$_2$CH$_2$(CH$_2$)$_5$CH_3), 0.88 (3H, t, J = 6.7, OCH$_2$CH$_2$(CH$_2$)$_5$CH_3), 1.05–1.38 (20H, m, OCH$_2$CH$_2$(CH_2)$_5$CH$_3$), 1.40–1.52 (2H, m, OCH$_2$CH_2(CH$_2$)$_5$CH$_3$), 1.52–1.65 (2H, m, OCH$_2$CH_2(CH$_2$)$_5$CH$_3$), 3.09 (2H, d, J = 13.0, ArCH_2Ar), 3.27 (2H, t, J = 6.8, OCH_2CH$_2$(CH$_2$)$_5$CH$_3$), 3.60–3.89 (24 H, m), 4.01–4.08 (2 H, m), 4.19 (2H, d, J = 13.0, ArCH_2Ar), 6.51–6.59 (4H, m, ArH^3 + ArH^4), 6.78 (2H, t, J = 7.5, ArH^4), 6.92 (2H, d/d, J = 2.5/6.6, ArH^3), 6.98 (2H, d, J = 7.5, ArH^3), 7.1 (2H, t, J = 7.5, ArH^4), 7.48 (2H, d, J = 7.5, ArH^3); ^{13}C (100.613 MHz, CDCl$_3$, 23 °C, CDCl$_3$): δ = 14.1, 22.6, 22.7, 26.0, 26.1, 28.9, 29.3, 29.5, 29.6, 29.9, 30.6, 31.0, 31.8, 31.9, 36.5, 70.5, 70.7, 71.3, 71.4, 72.2, 72.7, 73.2, 122.0, 122.1, 122.2, 128.4, 128.6, 129.3, 131.3, 132.8, 133.2, 134.0, 136.4, 155.4, 155.9, 156.7; elemental analysis calcd. (%) for C$_{44}$H$_{76}$O$_8$ (865.19): C 76.35, H 8.85, O 14.79; found C 76.02, H 8.80.

1,3-alt-25,27-Bis-n-octyloxycalix[4]arene 4′-t-butylbenzocrown-6 **3a**

A suspension of **1a** (0.36 g, 0.55 mmol), **4** (0.40 g, 0.61 mmol), and Cs$_2$CO$_3$ (1.6 g, 5.0 mmol) in acetonitrile (100 mL) was heated with stirring under argon at reflux for two days. The solvent was removed *in vacuo*, and the residue was partitioned between dichloromethane (30 mL) and 1 N HCl (30 mL). The organic phase was washed twice with water (20 mL), dried over Na$_2$SO$_4$, and evaporated *in vacuo*. Chromatography on silica gel (ethyl acetate/hexanes gradient elution) provided 340 mg (64%) of **3a**. ^{1}H (400.13 MHz, CDCl$_3$, 23 °C, CHCl$_3$): δ = 0.91 (6H, t, J = 6.6, OCH$_2$CH$_2$(CH$_2$)$_5$CH_3), 1.11–1.20 (4H, m, OCH$_2$(CH$_2$)$_5$CH_2CH$_3$), 1.20–1.37 (20H, m, OCH$_2$(CH_2)$_5$CH$_2$CH$_3$), 1.32 (6H, s, C(CH_3)$_3$), 3.44 (4H, t, J = 7.4, OCH_2(CH$_2$)$_5$CH$_2$CH$_3$), 3.51 (2H, t, J = 5.8, Ar-OCH$_2$CH$_2$OCH_2CH$_2$O-Bz), 3.54–3.65 (8H, m Ar-OCH_2CH_2OCH$_2$CH$_2$O-Bz), 3.71 (2H, t, J = 4.7, Ar-OCH$_2$CH$_2$OCH_2CH$_2$O-Bz), 3.75 (8H, s, Ar-CH_2-Ar), 4.09–4.14 (4H, m, Ar-OCH$_2$CH$_2$OCH$_2$CH_2O-Bz), 6.64 (2H, t, J = 7.4, ArH^4), 6.77 (2H, t, J = 7.4, ArH^4), 6.90 (1H, d, 8.4, BzH^6), 6.96–7.07 (10H, m, BzH^3 + BzH^5 + ArH^3); ^{13}C (100.613 MHz, CDCl$_3$, 23 °C, CDCl$_3$): δ = 14.1, 22.7, 25.8, 29.3, 29.4, 29.6, 31.4, 31.5, 31.9, 34.3, 37.8, 69.6, 70.0, 70.1, 70.2, 70.3, 70.4, 70.6, 70.7, 114.5, 114.6, 118.7, 122.0, 122.1, 129.7, 129.8, 129.9, 133.8, 134.0, 134.1, 145.0, 147.1, 148.2, 156.3, 156.4, 156.8; elemental analysis calcd. (%) for C$_{62}$H$_{82}$O$_8$ (955.31): C, 77.95 H, 8.65, O 13.40; found C 77.61, H 8.78.

paco-25,27-Bis-n-octyloxycalix[4]arene 4′-t-butylbenzocrown-6 **3b**

A suspension of **1b** (0.50 g, 0.77 mmol), **4** (0.55 g, 0.85 mmol), and Cs$_2$CO$_3$ (2.0 g, 6.1 mmol) in acetonitrile (135 mL) was heated with stirring under argon at reflux for two days. The solvent was removed *in vacuo*, and the residue was partitioned between dichloromethane (30 mL) and 1 N HCl (30 mL). The organic phase was washed twice with water (20 mL), dried over Na$_2$SO$_4$, and evaporated *in vacuo*. Chromatography on silica gel (ethyl acetate/hexanes gradient elution) provided 530 mg (72%) of **3b**. ^{1}H (400.13 MHz, CDCl$_3$, 23 °C, CHCl$_3$): δ = 0.80 (3H, t, J = 6.9, OCH$_2$CH$_2$(CH$_2$)$_5$CH_3), 0.90 (3H, t, J = 6.9, OCH$_2$CH$_2$(CH$_2$)$_5$CH_3), 1.31 (20H, m, OCH$_2$CH$_2$(CH_2)$_5$CH$_3$), 1.55–1.69 (4H, m, OCH$_2$CH_2(CH$_2$)$_5$CH$_3$), 3.11 (2H, d, J = 13.0, ArCH_2Ar), 3.48 (2H, t, J = 6.5, OCH_2CH$_2$(CH$_2$)$_5$CH$_3$), 3.59–3.78 (8H, m), 3.83–4.01 (6 H, m), 4.15–4.44 (10 H, m), 6.48 (2H, m, ArH^3), 6.54 (2H, t, J = 7.4, ArH^4), 6.85 (1H, t, J = 7.5, ArH^4), 6.87 (2H, d, J = 8.4, BzH^6), 6.92 (1H, d/d, J = 2.1/8.4, BzH^5), 6.93 (2H, m, ArH^3), 7.00 (1H, d, J = 2.1, BzH^3), 7.04 (2H, d, J = 7.5, ArH^3), 7.07 (2H, t, J = 7.5, ArH^4), 7.47 (2H, d, J = 7.5, ArH^3); ^{13}C (100.613 MHz, CDCl$_3$, 23 °C, CHCl$_3$): δ = 14.0, 14.1, 22.6, 22.7, 26.0, 26.1, 28.7, 29.3, 29.4, 29.6, 29.8, 30.7, 31.1, 31.5, 31.8, 34.3, 36.4, 67.9, 70.8, 71.0, 72.5, 72.8, 73.4, 73.5, 111.0, 112.4, 117.5, 122.0, 122.1, 122.3, 128.5, 128.7, 129.3, 131.3, 131.4, 132.8, 133.0, 133.1, 133.8, 136.6, 144.1, 146.55, 148.1, 155.4, 155.8, 156.7; elemental analysis calcd. (%) for C$_{62}$H$_{82}$O$_8$.H$_2$O (973.32): C, 76.51 H, 8.70 O, 14.79; found C 76.36, H 8.78.

X-ray crystallography

The structures were determined by single-crystal X-ray diffraction methods. Intensity data were obtained using a Nonius CAD4 diffractometer fitted with a 1.1 mm collimator using Mo-Kα radiation (λ = 0.71073 Å) and a Oxford Cryosystems 600 series low temperature device. Calculations were carried out using XCAD4 [13] (data reduction), SHELXTL [14] (absorption correction, structure solution/refinement, and molecular graphics), and PLATON [15] (structure analysis). With the exception of the hydroxyl H atom in **1b**, each H atom was placed in a calculated position, refined using a riding model, and given an isotropic displacement parameter equal to 1.2 (CH, CH_2) or 1.5 (CH_3) times the equivalent isotropic displacement parameter of the atom to which it is attached. When warranted, methyl H atomic positions were allowed to rotate about the adjacent C—C bond. Full-matrix least-squares refinement against $|F|^2$ of the quantity $\sum w(F_o^2 - F_c^2)^2$ was used to adjust the refined parameters. A summary of parameters associated with the structure determinations is given in Table 1, and selected torsion angles in Table 2. Positional and isotropic equivalent thermal parameters are provided in the supplementary data.

anti-25,27-Bis-n-octyloxycalix[4]arene **1b**

X-ray quality crystals were obtained by recrystallization from diethyl ether. Only half of the molecule makes up the asymmetric unit, the other half being generated by symmetry. The atomic coordinates of the hydroxyl H atom were allowed to refine, as was its isotropic thermal parameter.
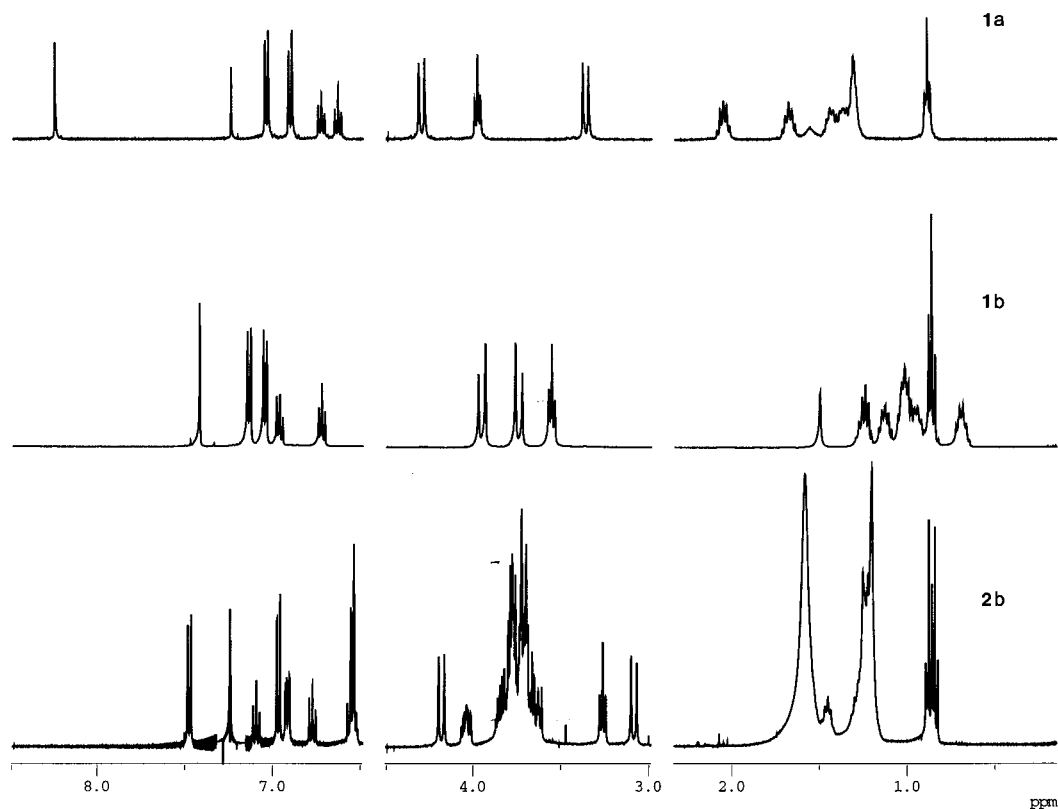
Figure 5. Overlay of NMR spectra of **1a** (top), **1b** (middle), and **2b** (bottom).

Table 1. Crystal data and summary of intensity data collection and structure refinement

| Compound	**1b**	**2a**	**2b**
Formula	$C_{44}H_{56}O_4$	$C_{54}H_{74}O_8$	$C_{54}H_{74}O_8$
Formula weight	648.9	851.1	851.1
Temp., °C	−110	−110	−110
Crystal dimensions (mm^3)	$0.74 \times 0.21 \times 0.11$	$0.56 \times 0.51 \times 0.31$	$0.59 \times 0.36 \times 0.16$
Crystal system	monoclinic	triclinic	monoclinic
Space group	$P2_1/c$	$P\bar{1}$	Cc
a (Å)	11.6983(11)	9.937(2)	24.410(4)
b (Å)	17.726(2)	10.674(2)	13.957(2)
c (Å)	9.0652(7)	24.792(4)	15.665(3)
α (deg)		99.157(14)	
β (deg)	92.130(9)	93.486(13)	110.46(2)
γ (deg)		110.51(2)	
V (Å^3)	1878.5(3)	2412.2(8)	5000.3(13)
Z	2	2	4
D_{calc} (g cm^{-3})	1.15	1.17	1.13
μ (cm^{-1})	0.71	0.77	0.74
2θ range (deg)	$4 \leq 2\theta \leq 48$	$4 \leq 2\theta \leq 50$	$4 \leq 2\theta \leq 48$
Reflections measured	4405	11118	4579
Independent reflections	2938 [$R_{int} = 0.056$]	8461 [$R_{int} = 0.024$]	4066 [$R_{int} = 0.044$]
R [$F^2 > 2\sigma F^2$]	0.045	0.041	0.039
wR (F^2)	0.12	0.11	0.10
GOF	1.01	1.02	1.05
Largest feature in final diff. map (e$^-$ Å^{-3})	0.22	0.19	0.16
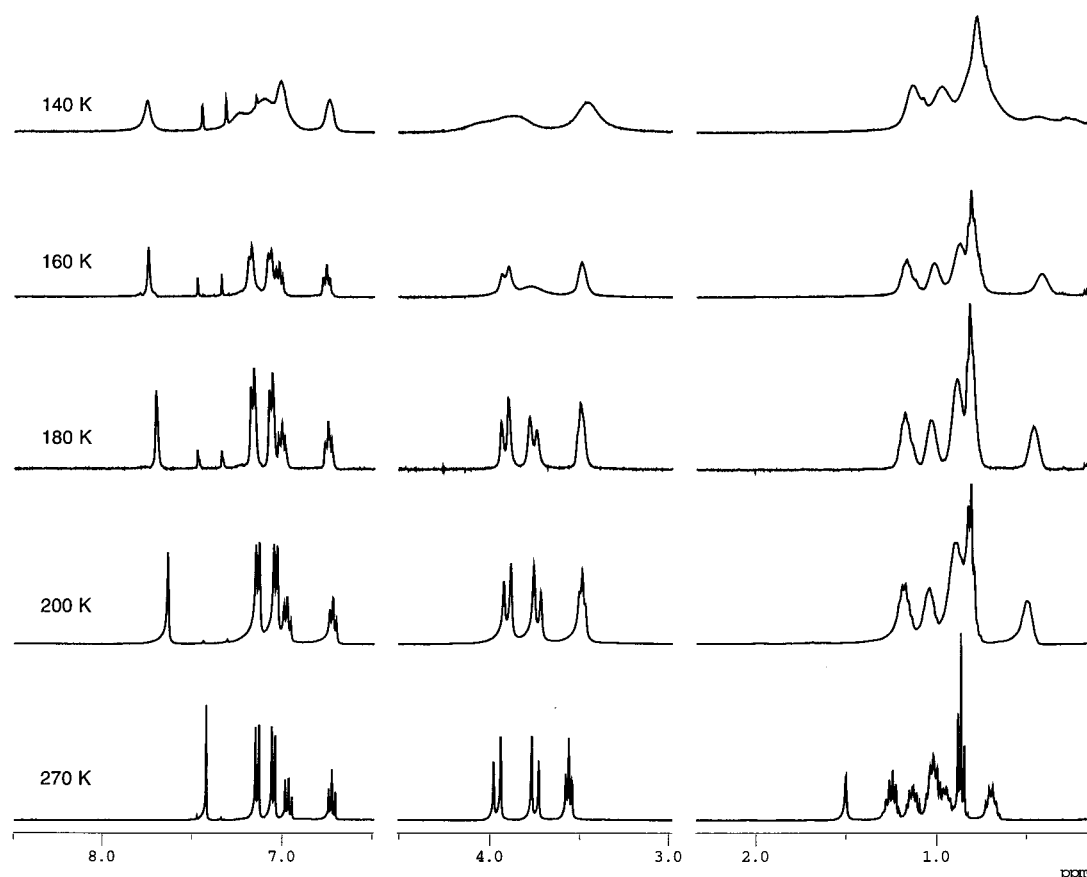
Figure 6. VT-NMR of **1b** (10 mg **1b**/0.7 mL d_1-dichlorofluoromethane).

1,3-alt-25,27-Bis-n-octyloxycalix[4]arene crown-6 **2a**

X-ray quality crystals were obtained by recrystallization from a methanol/diethyl ether solution. An absorption correction, based on a set of psi-scans was applied.

paco-25,27-Bis-n-octyloxycalix[4]arene crown-6 **2b**

X-ray quality crystals were obtained by recrystallization from a methanol/diethyl ether solution. Minor disorder is apparent on both *n*-octyl chains. C41 and C42 are modeled with 2-fold positional disorder (80:20). C37 and C38 exhibit a more complex disorder, but are modeled only as 2-fold (55:45). Restraints are applied to bond distances and angles, as well as U_{ij} components, involving the disordered atoms. Despite the restraints, some of the disordered atoms have unusual elongation. Determination of the absolute structure proved inconclusive, as the Flack parameter [16] refined to a value of 0.1(12).

Table 2. Selected torsion angles (deg)

	2a	2b
O1–C51–C52–O2	76.3(2)	62.0(4)
C51–C52–O2–C53	167.8(2)	170.8(3)
C52–O2–C53–C54	82.6(2)	172.8(3)
O2–C53–C54–O3	−77.9(2)	−74.8(4)
C53–C54–O3–C55	173.6(2)	−163.7(4)
C54–O3–C55–C56	171.6(2)	176.7(4)
O3–C55–C56–O4	54.0(2)	85.0(4)
C55–C56–O4–C57	60.6(2)	168.1(3)
C56–O4–C57–C58	164.1(2)	86.1(5)
O4–C57–C58–O5	−177.6(2)	82.2(5)
C57–C58–O5–C59	−78.1(2)	177.9(3)
C58–O5–C59–C60	−175.8(2)	174.6(3)
O5–C59–C60–O6	−172.7(2)	−71.3(4)

Solvent extraction

Equal volumes (1.0 mL each) of organic phase (0.002, 0.005, or 0.010 M of calixarene-crown ether in 1,2-dichloroethane) and aqueous phase (mixture of [CsNO₃] = 0.010 M, [RbNO₃] = 0.020 M, [KNO₃] = 0.10 M, [NaNO₃] = 0.50 M, [LiNO₃] = 2.0 M) were equilibrated by repeated inversion on a rotating device in a thermostatic air box at 25.0 °C (±0.5 °C) for a minimum of 2 hours; this procedure was determined previously to be sufficient to ensure equilibrium.

The samples were centrifuged at 3000 rpm for 10 minutes. An aliquot of the organic phase (0.5 mL) was removed, diluted with 1.5 mL of *iso*-amylbenzene, and contacted with 6.0 mL of water, following the same procedure as for the extraction. This back-extraction sample was centrifuged, and 5.0 mL of the aqueous phase was removed for analysis by ion chromatography. All equilibrations were performed in triplicate, as were the blank runs of crown ether solution
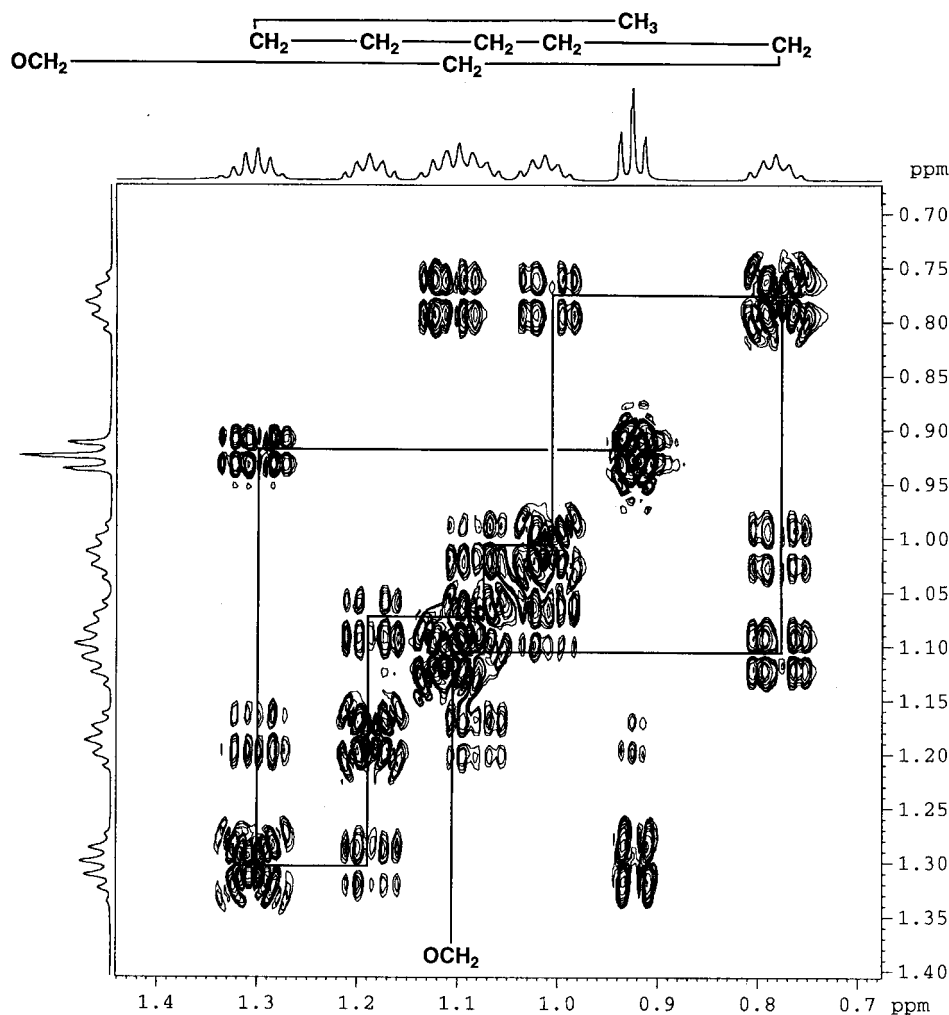
Figure 7. Alkyl region from COSY of **1b**.

against deionized water, 1,2-dichloroethane against metal nitrate solution, and 1,2-dichloroethane against water.

Metal cation analysis of aqueous solutions was performed on a Dionex 2020i ion chromatography system equipped with a autosampler, AI-450 workstation, and conductivity detector, using a Dionex IonPac CS12 cation exchange column with 0.16 m methanesulfonic acid as the eluent. Calculations were based on an average of three injections for each sample using the external-standard method. Detection limits for Li^+, K^+, Rb^+, and Cs^+ were $[M^+] \leq 3 \times 10^{-6}$ M; the detection limit for Na^+ was $[Na^+] \leq 10^{-4}$ M, as a result of the high background of Na^+ in the controls. Acid-treated polypropylene vials and containers were used for both extraction and storage of aqueous solutions. All organic solutions were stored in Teflon® containers.

Results and discussion

Synthesis

Cone and *paco* calix[4]arene crown ethers have been prepared previously from dihydroxycalix[4]arene crown ethers [7], specifically by demethylation of a 25,27-bismethoxy

calix[4]arene crown ether, followed by dialkylation. Use of sodium base in the dialkylation reaction provided the *cone* isomer, while use of potassium base gave the *paco* isomer. During our synthetic work on calixarenes and calixarene crown ethers, we alkylated *syn*-25,27-bisallyloxy calix[4]arene [4] as shown in Scheme 1. The allyl group was of interest since it could provide a site for functionalization or immobilization, be readily removed [17], or used to functionalize the *p*-position of the calixarene *via* Claisen rearrangement [18]. Use of potassium base in the dialkylation reaction was expected to provide predominantly the partial cone conformer; however, a mixture of conformational isomers was obtained. Deallylation gave a 1:1 mixture of *syn*- and *anti*-25,27-bisoctyloxycalix[4]arene. Fortuitously, the *anti*-25,27-bis-*n*-octyloxycalix[4]arene precipitated as a single pure compound from hexanes [19]. This compound was used to prepare the two paco-calix[4]arene crown ethers **2b** and **3b**.

X-ray crystal structures

Crystal structures of *anti*-25,27-bis-*n*-octyloxycalix[4]arene (**1b**), 1,3-*alt*-bis-*n*-octyloxycalix[4]arene crown-6 (**2a**), and *paco*-bis-*n*-octyloxycalix[4]arene crown-6 (**2b**) (Figures 2–

Table 3. Distribution ratios (D_M) for the extraction of alkali metal nitrates from water to 1,2-dichloroethane by calix[4]arene crown-6 ethers[a] and the corresponding selectivity factors (S) for Cs^{+} over Rb^{+}, K^{+}, and Na^{+} ions

	$D_{Cs} \times 10^3$	$D_{Rb} \times 10^3$	$D_K \times 10^3$	$D_{Na} \times 10^6$	$D_{Li} \times 10^6$	$S_{Cs/Rb}$	$S_{Cs/K}$	$S_{Cs/Na}$
2a								
2.0 mM	104	16.8	0.831	1.6	0.50	6.2	120	64,000
5.0 mM	227	41.1	2.12	21	1.8	5.5	110	11,000
10 mM	396	86.2	4.98	61	5.7	4.6	79	6,500
2b								
2.0 mM	2.44	1.35	0.249	36	0.62	1.8	9.8	69
5.0 mM	4.72	2.49	0.467	65	1.8	1.9	10	73
10 mM	8.34	3.95	0.746	95	2.6	2.1	11	88
3a								
2.0 mM	91.7	16.6	0.638	0.6	0.02	5.5	140	150,000
5.0 mM	208	41.9	1.77	5.8	0.58	5.0	120	36,000
10 mM	359	83.5	3.95	9.2	1.1	4.3	91	39,000
3b								
2.0 mM	1.29	1.13	0.135	17	0.20	1.2	9.6	78
5.0 mM	2.42	1.93	0.250	20	0.46	1.2	9.7	120
10 mM	4.22	3.04	0.391	27	1.3	1.4	11	160

[a][CsNO$_3$] = 0.010 M, [RbNO$_3$] = 0.020 M, [KNO$_3$] = 0.10 M, [NaNO$_3$] = 0.50 M, [LiNO$_3$] = 2.0 M; conditions: 25 °C, O/A = 1.

4) were determined and a summary of X-ray diffraction data is presented in Table 1.

All previously reported structures of calix[4]arene molecules containing free OH groups are observed to adopt the cone conformation, which is attributed to stabilization by intramolecular hydrogen bonds [3d]. In sharp contrast, the structure of *anti*-bis-*n*-octyloxycalix[4]arene (**1b**) is observed in the 1,2-alternate conformation. This conformation is particularly rare in crystal structures of calix[4]arene molecules; of the few examples being reported [6b, 20] only the 1,2-*alt*-25,27-dimethoxythiacalix[4]arene contains free OH groups on the calixarene [21]. Only half of the molecule is present in the asymmetric unit, the other half being generated by crystallographic symmetry. Hydrogen bonding is observed between the phenolic hydrogen and an adjacent ether oxygen atom (H···O = 1.91(3) Å, O···O = 2.749(2) Å, ∠O–H···O = 169(2)°). The long H···O distance suggests that this interaction may be relatively weak.

In the 1,3-alternate conformation of **2a**, the *n*-octyl groups are fully extended, that is, all torsion angles for those substituents are *anti*. This contrasts with the partial cone isomer **2b**, which exhibits at least one *gauche* angle on each octyl group. Aside from the different calix[4]arene conformations in **2a** and **2b**, the greatest conformational variability is observed in the crown ether segments. The relative arrangement of these rings can be determined by examination of their torsion angles (Table 2) [22, 23]. Expressed in terms of *anti* (*a*) and *gauche* (*g*), and beginning with O1–C51–C52–O2, the crown fragments in **2a** and **2b** have *gag g⁻aa gga ag⁻a a* and *gaa g⁻aa gag gaa g⁻* conformations, respectively. These two conformations are clearly different from each other and are also unique when compared to other structures of uncomplexed calix[4]arene-crown-6 molecules [24, 25]. This conformational diversity suggests that several low-energy conformations are possible for these molecules. None of the crown conformations reported thus far match the two conformations that are observed in the structures of calix[4]arene-crown-6-ether complexes with either alkali metal ions or polar organic molecules. The binding conformations in these host–guest complexes always exhibit gauche O–C–C–O angles, and *anti* C–O–C–C angles (the pattern *gaa* repeated around the ring) [25, 26b], however the conformation observed in **2b** comes quite close, with the only deviation being the *gauche* C56–O4–C57–C58 angle. The observed crown ether conformation of **2b** may be attributed to the partial filling of the crown cavity by the *n*-octyloxy group. This is often observed for more electropositive guests, such as the methyl groups on acetonitrile or nitromethane [26b]. We believe this is the first example of a structurally characterized crown complex of an aliphatic group (albeit *intra*molecular), even through no C–H···O interactions are observed between the *n*-octyl group and the crown ether oxygen atoms.

Solution NMR

1a is known to prefer the cone conformation in solution [11], as well as in the solid state and the 400 MHz room temperature ¹H NMR spectrum is consistent with this assignment. The ¹H NMR spectrum of **1b**, on the other hand, is not so readily interpreted. The *anti* orientation of the alkyl substituents precludes the *cone* or 1,3-*alt* conformers, however the observed NMR spectrum is inconsistent with either the *paco* or 1,2-*alt* conformations. As shown in Figure 5, the methylene protons of the calixarene in **1b** appear as a pair of doublets at 4.1 and 3.8 ppm (J = 15.5 Hz), similar to the observations reported previously for *anti*-25,27-bisethoxy, tetra-*t*-butylcalix[4]arene [6c]. The *meta* protons of the calixarene show up at precisely the chemical shifts reported for *anti*-25,27-bisethoxy, tetra-*t*-butylcalix[4]arene (7.06 and 7.16 ppm), in this case as a pair of doublets coupled to the *para* protons (triplets, J = 7.5 Hz) at 6.74 and 6.99

ppm. Groenen *et al.* suggested a symmetric conformation for *anti*-25,27-bisethoxy, tetra-*t*-butylcalix[4]arene where the two phenolic groups are convergent with their respective arenes lying coplanar with the calixarene methylenes [6b]. A more likely explanation is a rapid interconversion between the *paco* and 1,2-*alt* conformers, as reported for the *anti*-25,27-bisethoxy, tetra-*t*-butylcalix[4]arene bisquinone [27]. Evidence for the dynamic behavior **1b** was obtained by VT-NMR (see Figure 6). Upon cooling a solution of **1b** in CDFCl$_2$, little change was observed down to 190 K. Below this temperature peak broadening occurred with coalescence at ∼140 K. Unfortunately, the limit of slow exchange was not reached before the solvent froze at ∼130–135 K, so it is not possible to unambiguously assign the conformation. However, this observation does reveal the fluxional nature of this molecule and represents a remarkably low barrier for interconversion of a calixarene bearing hydroxyl groups capable of hydrogen bonding to adjacent oxygens.

The methylene resonances of the octyl groups in **1b** are interesting; they appear consistently upfield of those in **1a** (Figure 5). The COSY spectrum of **1b** (Figure 7) allows assignment of the multiplet at 0.68 to the third methylene from the phenolic oxygen, 1.39 ppm upfield of the corresponding proton in **1a**. A similar deshielding was observed for the methyl protons in *anti*-25,27-bisethoxy, tetra-*t*-butylcalix[4]arene [6b]. Remarkably, these upfield shifts are not observed in the *paco* crown ether derivative **2b** (see Figure 5), suggesting that the environment of the alkyl substituents is different for **1b** than for **2b**. Indeed, in the crystal structure of **2b**, the methylene groups of the anti-octyloxy substituent are oriented away from the calixarene cavity, in contrast to the situation observed in **1b**.

Solvent extraction

The competitive extraction of alkali metal nitrates by **2a**, **2b**, **3a**, and **3b** was performed at three different concentrations of calix[4]arene crown-6 ethers in 1,2-dichloroethane (DCE). The extraction results reported in Table 3 clearly show the cesium selectivity expected for these extractants, as well as the differences between the *paco* and 1,3-*alt* conformers. In each case, the 1,3-*alt* isomer exhibits significantly stronger extraction than the *paco* isomer for the larger cations, K, Rb, and Cs. Only in the case of sodium does the *paco* isomer extract more strongly than the 1,3-*alt*, and the differences are relatively minor. The decreased extraction efficiency of the *paco* calix[4]arene crown ethers has a significant impact on the selectivity factors (S) as well. Whereas **2a** and **3a** both show cesium-to-sodium selectivity factors ($S_{Cs/Na}$) exceeding 1000 and $S_{Cs/K} \sim 100$, the corresponding S values of **2b** and **3b** are ∼100 and ∼10, respectively.

These observations are consistent with studies of bisalkoxycalix[4]arene crown ethers reported previously [7, 8, 10]. For bisalkoxycalix[4]arene crown-5 ethers that exhibit potassium selectivity, the 1,3-*alt* conformer is a stronger extractant that the *paco* isomer. However, the *paco* isomer exhibits slightly higher selectivity for potassium over the larger rubidium and cesium ions than the 1,3-*alt* isomer, in contrast to the results for the crown-6 ethers.

The decreased extraction efficiency of the *cone*- and *paco*-bisalkoxycalix[4]arene crown-5 ethers relative to the 1,3-*alt* isomer was attributed in part to steric hindrance of the crown cavity by the ether substituents. Steric hindrance of the crown ether cavity by the *n*-octyl groups of **2b** is clearly observable in the crystal structure shown above, providing structural evidence for the steric contribution to the extraction properties of the conformational isomers of calix[4]arene crown-6 ethers.

Acknowledgements

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