Rational Design of Cesium-Selective Ionophores: Dihydrocalix[4]arene Crown-6 Ethers

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Molecular mechanics calculations performed on calix[4]arene crown-6 ethers predict that the 1,3-dihydro derivatives will exhibit greater complementarity for potassium and cesium ions than the parent 1,3-bis(alkyloxy) calixcrowns. The X-ray crystal structures of 1,3-*alt*-bis(octyloxy)calix[4]arene benzocrown-6 ether, dihydrocalix[4]arene benzocrown-6 ether, and the cesium nitrate complex of dihydrocalix[4]arene benzocrown-6 ether were determined. The structure of the cesium complex corresponds closely to the structure predicted by molecular mechanics. The dihydrocalix[4]arene crown-6 ethers exhibit enhanced cesium selectivity in the extraction of alkali-metal salts.

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Introduction

Recent developments in calixarene chemistry[1] have led to remarkable advances in ionic recognition and separations.[2] Of particular significance is the development of calix[4]arene crown-6 ethers as highly efficient and selective cesium complexing agents,[3,4] with properties of tremendous value in the field of nuclear-waste remediation.[5] ^{137}Cs is a highly radioactive fission product present in irradiated nuclear fuels and represents a significant environmental, health and safety concern,[6] and therefore the separation and analysis of cesium has received much attention.[7] Calix[4]arene crown-6 ethers coordinate to cesium cations more strongly (by more than a factor of 100) and selectively than alkylated derivatives of dibenzo-21-crown-7,[8] previously considered to be the best crown ethers for cesium separations.[9] Accordingly, separation processes for removal of cesium from reprocessing wastes have been developed using calix[4]arene crown-6 ethers.[10] However, while cesium-to-sodium selectivities typically exceed 10^4, the observed cesium-to-potassium selectivities (100−400) limit the utility of these compounds when potassium is present in a large excess ($> 10^3$) over cesium,[8] as it is in certain contaminated groundwaters and neutralized reprocessing wastes. Consequently, improvement in the cesium-to-potassium selectivity of calixarene crown ethers has the potential to beneficially impact the monitoring and remediation of cesium contamination in the environment and treatment of nuclear-fuel reprocessing wastes.

In a recent survey of alkali metal nitrate extraction by calix[4]arene crown ethers,[11] it was observed that for bis(alkyloxy)calix[4]arene monocrown ethers (**1a**, **1b**, **2a**, and **2b** in Figure 1), reducing the size of the alkoxy substituent from octyl to allyl increased the cesium extraction efficiency by 10−30 % and the cesium-to-potassium selectivity by 20−40 %. Little impact on cesium-to-sodium selectivity was observed. Encouraged by these results, we embarked on an effort to investigate the basis for these effects and to develop calixarene crown ethers exhibiting enhanced cesium selectivities. These studies have resulted in the development of a new series of calix[4]arene crown ethers that exhibit enhanced selectivity for cesium over sodium, potassium, and rubidium,[12] facilitating the development of a fluorescence chemosensor with enhanced cesium response and selectivity.[13] We report herein the design and synthesis of these new calix[4]arene crown ethers along with the results of structural and extraction studies.

Results and Discussion

Molecular Modeling

To evaluate the potential impact of substituent size on cation binding by calix[4]arene crown ethers, a molecular modeling study was performed on 1,3-*alt*-calix[4]arene monocrown-6 ethers. Although four calix[4]arene conformations are possible,[1,14] we limited this study to the 1,3-*alt* conformer,[15] which is known to yield the maximum cesium

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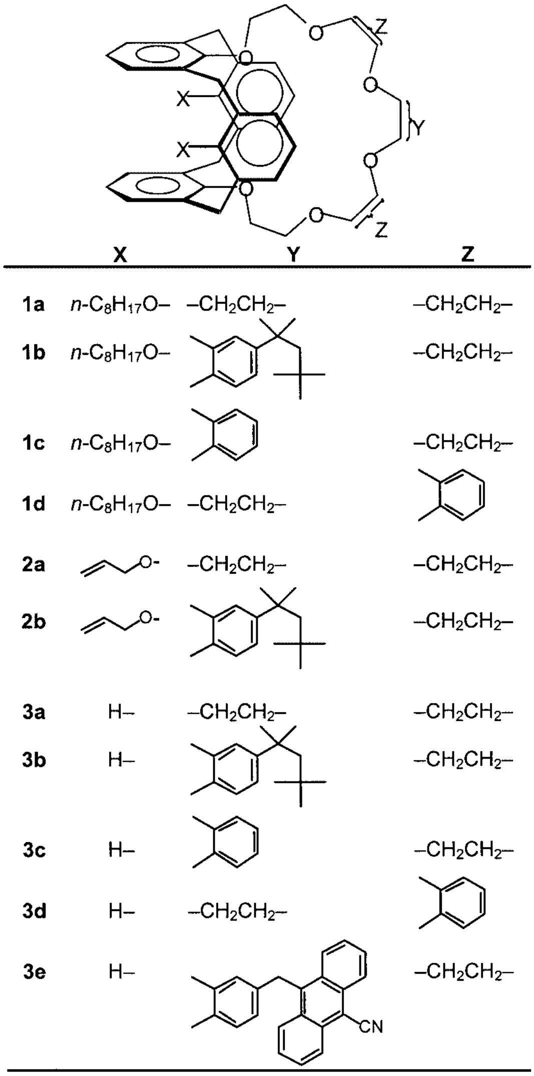

Figure 1. Calix[4]arene crown-6 ethers used in this study

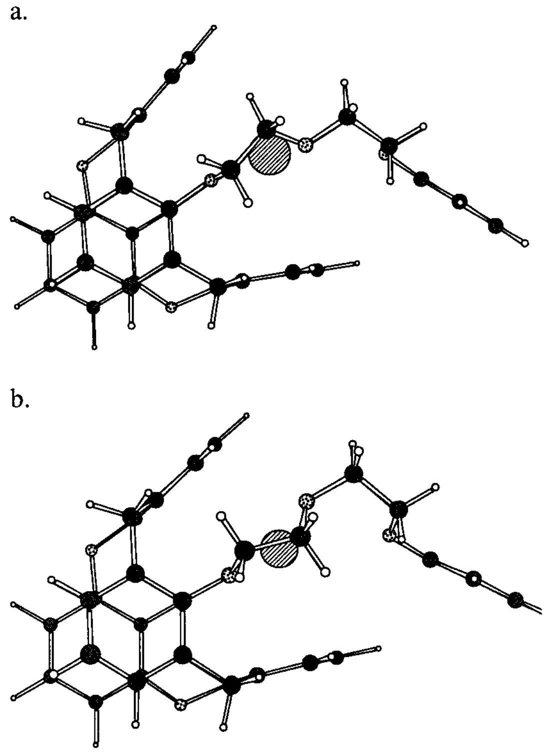

Figure 2. MM-derived crown ether conformations for complexes of a rigidified calix[4]arene benzocrown-6 ether; (a) lowest-energy Cs^+ complex, crown ether conformation:[21] *a,g-,a,a,g,a,a,0,a,a,g-,a,a,g,a*; (b) lowest-energy K^+ complex, crown ether conformation:[25] *a,g,a,g,g,a,a,0,a,a,g-,g-,a,g-,a*

binding by calix[4]arene crown-6 ethers.[3a] Because the flexible crown ether chain can adopt many conformations,[16] conformational analyses[17] were first performed on the K^+ and Cs^+ complexes of a model derivative of 1,3-*alt*-calix[4]arene benzocrown-6 ether. In this model, the conformation of the calix[4]arene macrocycle was constrained to the 1,3-*alt* conformation by inserting a 1,3-dioxybenzene moiety as a bridge between the X positions of the molecule shown in Figure 1. This analysis was done with the stochastic search option[18] of the MM3 program,[19] where the default MM3 parameter set was extended to treat the cation−ether interactions.[20] A total of 800 trial structures was examined for each complex, and over 50 conformers were located for each cation.

In support of the MM3 parameterization and the particular choice of model compound, the lowest-energy crown ether conformation found for the complex of the model-bridged 1,3-*alt*-calix[4]arene benzocrown-6 ether model with Cs^+ (Figure 2, a[21]) corresponds to the conformation found in the crystal structure reported previously for the cesium complex of 1,3-*alt*-calix[4]arene bis(benzocrown-6).[22] This conformation was not, however, a low-energy conformer for the K^+ complex. In contrast, the lowest-energy crown ether conformation for K^+ (Figure 2, b) was located as a low-energy conformer for Cs^+, lying 1.2 kcal/mol above the minimum for the lowest energy conformer for Cs^+.

Our standard modeling approach[23,24] was used to analyze the complementarity[25] of the calixcrown cavity towards potassium and cesium. MM3 optimizations were performed by modifying the K^+ and Cs^+ complexes above, replacing the 1,3-dioxybenzene substituent with *tert*-butoxy, methoxy, or hydrogen groups. The metal ion was removed, and the steric energy of the ligand in its bound form was calculated (U_{bound}). The ligand was then optimized, and the steric energy of the ligand in its binding conformation was determined (U_{bind}). A measure of complementarity, ΔU_{comp}, was obtained as the difference between these two steric energies.[23,24]

The calix[4]arene crown-6 ligand can interact with a complexed metal ion through π−cation interactions with two benzene rings of the calixarene as well as coordination to the six oxygen atoms of the crown ether. In addition to the ligand strain ΔU_{comp}, associated with cation complexation, summing each $[M^+]-C_{\text{arene}}$ interaction energy[26] provides a measure of the strength of the π−cation interactions E_π,

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which can be combined with ΔU_{comp} to rank a series of ligands with respect to their complementarity for a given cation. We used the same potential function for each ligand, neglecting that the interaction of the phenyl groups bearing alkoxy (methoxy or *tert*-butoxy) with the cation will be somewhat different from that of those bearing the hydrogen substituent.

Using the sum of ΔU_{comp} and E_π as our gauge, we observed (Table 1) that complementarity for both cations is best when the substituents are hydrogen and decreases in the order hydrogen > methoxy > *tert*-butoxy, consistent with our previous observation that smaller substituents resulted in increased cesium extraction.[11] Examination of the structures provided a clear explanation for this trend in terms of the geometric features associated with the π−cation interactions. The bonding interactions between a cation and arene can be characterized with two geometric parameters: the distance *d*, between the cation and the centroid of the arene ring and the tilt angle Ψ defined as the angle between the cation−centroid vector and the normal to the arene plane. These geometric parameters have recently been evaluated by MP2/6−311+G* calculations on 1:1 complexes of the alkali cations with benzene[27a] and methoxybenzene.[27b] The results (shown in Table 2) reveal that the cation−centroid distances are only slightly influenced by the addition of the methoxy group and that the most stable complexes result when the tilt angle is 0°. Additional coordination with the cation center should force the arene ligand farther from the cation and, thus, the cation−centroid distances in these 1:1 complexes represent a minimum distance one would expect to see in calix(4)arene crown ether structures.

Examination of the geometric parameters for the two cation−arene interactions in each calixarene complex (Table 2) suggest a general trend for the two cations. That is, increasing the steric bulk of the substituent results in an increase to the tilt angles Ψ. The geometric parameters of the π−cation interactions are closest to those computed for the 1:1 complexes when the substituent is hydrogen. Hydrogen substitution permits the cavity to open, thereby allowing the two arene donor groups to approach their preferred orientation with respect to the cation.

Table 1. MM energies in kcal/mol for potassium and cesium complexes of calix[4]arene benzocrown-6 ethers

	Potassium conformer			Cesium conformer		
	ΔU_{comp}	E_π	Sum	ΔU_{comp}	E_π	Sum
−H	6.88	−8.96	−2.08	5.93	−5.04	0.89
$-OCH_3$	7.64	−8.23	−0.059	7.18	−4.30	2.88
$-OC(CH_3)_3$	7.44	−7.48	−0.04	6.99	−3.90	3.09

Table 2. Cation-arene centroid distances, *d* (Å), and tilt angles, Ψ (°)

Arene	Source[a]	K⁺ d	Ψ	Cs⁺ d	Ψ
Benzene	QM[27a]	2.89	0	3.41	0
Methoxybenzene	QM[27b]	2.87	0	3.44	0
H-Substituted calix-crown (**3c**)	MM	3.27	16	3.87	15
		3.17	8	3.36	3
H-Substituted calix-crown (**3c**)	X-ray			3.88	12
				3.42	8
CH_3O-Substituted calix-crown	MM	3.33	21	3.75	22
		3.23	16	3.43	15
$(CH_3)_2CHO$-Substituted calix-crown	X-ray[3b]			3.80	20
				3.52	14
$(CH_3)_3CO$-Substituted calix-crown	MM	3.43	30	3.85	28
		3.19	25	3.56	24

[a] QM, MM, and X-ray respectively denote quantum mechanics, molecular mechanics, and X-ray crystallography.

Solid-State Structures

Crystals of **1c**, **3c**, and the cesium nitrate complex of **3c** {[Cs⁺]·**3c**}, suitable for single-crystal X-ray diffraction, were obtained (Figure 3−5), respectively. In all three structures, the calixarene adopts the 1,3-alternate conformation, but the crown conformation varies. The structures of the uncomplexed calix-crown molecules (**1c** and **3c**) can be compared to that of 1,3-calix[4]arene bis(naphthocrown-6),[28] the only previously published structure of an uncomplexed calix[4]arene crown-6 ether. The crown cavity is collapsed in on itself in both structures, as is typically observed for large uncomplexed crown-ether molecules.[29] Both **1c** and **3c** exhibit two molecules in the asymmetric unit, each with a distinct crown conformation. Additionally, both

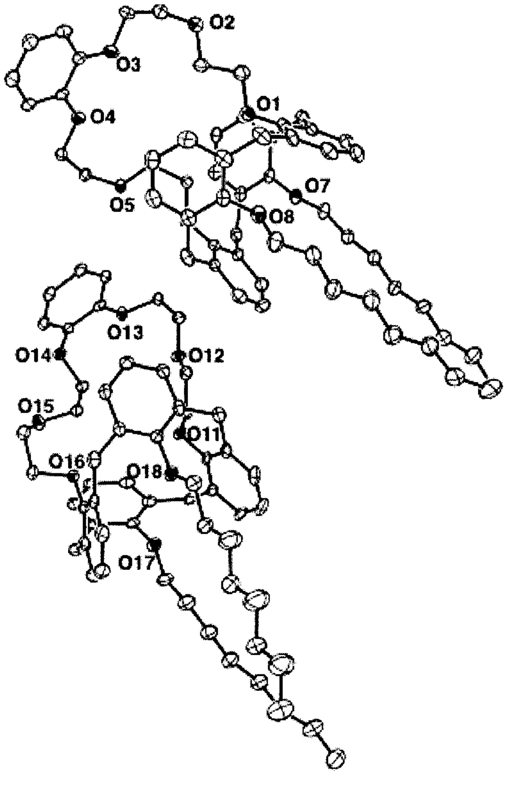

Figure 3. ORTEP drawing (50 % probability ellipsoids) of bis(*n*-octyloxy)calix[4]arene benzocrown-6 (**1c**); hydrogen atoms are omitted for clarity

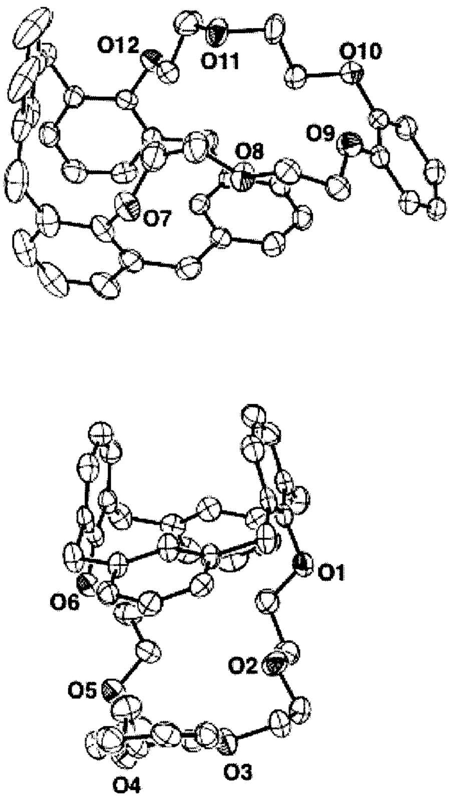

Figure 4. ORTEP drawing (50 % probability ellipsoids) of calix[4]arene benzocrown-6 (**3c**); minor disorder components and hydrogen atoms are omitted for clarity

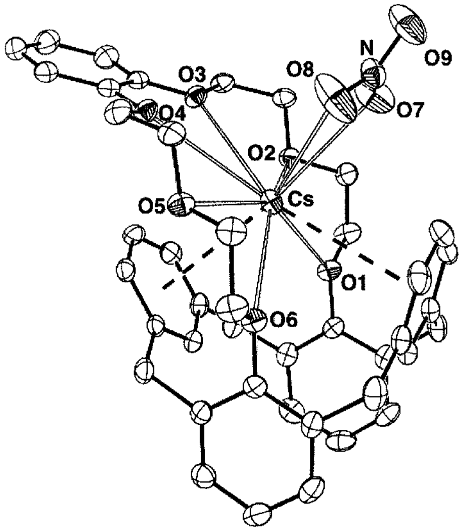

Figure 5. ORTEP drawing (50 % probability ellipsoids) of [Cs{calix[4]arene} benzocrown-6][NO_3]·2-methoxyethanol {[Cs^+]·**3c**}; minor disorder components, methoxyethanol, and hydrogen atoms are omitted for clarity

structures observed for **3c** are disordered in the crown ring, although the minor disorder component for one molecule is the same conformation as the major disorder component of the second molecule. Including the previously published naphthocrown structure,[28] a total of six distinct crown conformations are observed for these uncomplexed calix[4]arene crown-6 molecules, suggesting that several low-energy conformations are possible.

Comparison of the structures of **1c** and **3c** reveals that replacement of the octyloxy groups by hydrogen atoms (**1c** → **3c**) results in a change in the orientation and distance between opposing pairs of phenyl rings on the calixarene. The angle between the phenyl rings bearing the crown ether substituent flattens, from about 30° to −20°, allowing the O1−O6 distance to increase by about 1.3 Å. Furthermore, the angle between the two phenyl rings lying over the crown ether cavity increases, moving the arenes apart by 2−3 Å.

The crown conformation in [Cs^+]·**3c** is similar to previously reported Cs complexed calix[4]arene benzocrown-6 structures.[22] Upon Cs^+ binding to **3c**, the O1−O6 distance decreases by about 0.8 Å to 5.066(3) Å, and Cs−O distances are 3.292(2) Å and 3.249(2) Å for O1 and O6, respectively. The corresponding distances for Cs·**1c** are not available, as that structure has not yet been determined, but the O1−O6 distance for previously reported Cs·calix[4]arene crown-6 structures ranges from 4.7 to 4.9 Å, and typical $Cs-O_{phenyl}$ distances are observed between 3.2 and 3.3 Å.[22] Thus, the $Cs-O_{phenyl}$ distances of [Cs^+]·**3c** are similar to those observed for previously studied calix[4]arene crown-6 ethers, but the separation of the two phenyl ether oxygen atoms is greater. The remaining $Cs-O_{crown}$ distances are in the range 3.217(2)−3.378(2) Å, which at first glance appears entirely consistent with the reported range 3.00−3.57 Å, with a mean value 3.29(14) Å.[22] Closer examination of individual bond lengths shows that, while the Cs−O bond lengths to the benzo oxygen atoms [3.352(2) Å for O3; 3.378(2) for O4] are the longest observed in this structure, they are more than 0.1 Å shorter than those in previously reported Cs complexed calix[4]arene benzocrown-6 structures.[30] This shortened distance may explain some of the dramatic fluorescence enhancement reported previously.[13]

As discussed above, the bonding interactions between cesium and the two unsubstituted calix[4]arene rings in [Cs^+]·**3c** can be characterized by the distance (*d*) and angle (Ψ) between the cation and the centroid of the arene ring. As listed in Table 2, these distances are 3.42 Å and 3.88 Å for the rings opposite (C8−13) and adjacent (C22−27) to nitrate, respectively. These distances lie just outside the extremes of published values for calix[4]arene crown-6 complexes with Cs^+, which range from 3.46 to 3.80 Å.[3b,31] The angles Ψ are 8° and 12° in [Cs^+]·**3c**.

Remarkably, the structure predicted for [Cs^+]·**3c** in the molecular-modeling study is very similar to that found in the crystal structure. Despite the absence of the counter anion in the MM generated structure, the metrical parameters (Table 2) are nearly identical. Additionally, there is good correlation between the metrical parameters of the structure predicted for [Cs^+]·**3c** and the previously published structure of 1,3-bis(isopropoxy)calix[4]arene crown-6·cesium picrate (Table 2).[3b] Based on comparisons with structures of other free and cesium complexed calix[4]arene crown-6 molecules,[22] it appears, not surprisingly, that **3c**

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undergoes greater conformational reorganization upon cesium complexation.

Solution Conformation

Whereas **3c** adopts the 1,3-*alt* conformation in the solid state, previous studies of deoxygenated calix[4]arenes have indicated that the deoxygenated phenyl rings can rotate freely through the annulus of the calix[4]arene cavity[32] and no evidence of coalescence was observed in the VT NMR of **3d** over the temperature range 130−450 K.[12] The room-temperature NOESY confirms the conformational interconversion of the deoxygenated arene rings in **3b** (Figure 6). The proton at δ = 6.0 ppm exhibits crosspeaks with the protons of the crown ether methylene nearest to the calixarene (δ = 3.2 ppm) and with the *meta* protons of the phenolic arene groups (δ = 6.9 ppm). The δ = 6.0/3.2 ppm crosspeak is indicative of a *syn* orientation of the deoxygenated rings with the phenolic arenes, while the δ = 6.1/6.9 ppm crosspeak reveals the *anti* orientation. Presence of both crosspeaks indicates the presence of both conformers, consistent with conformational interconversion.

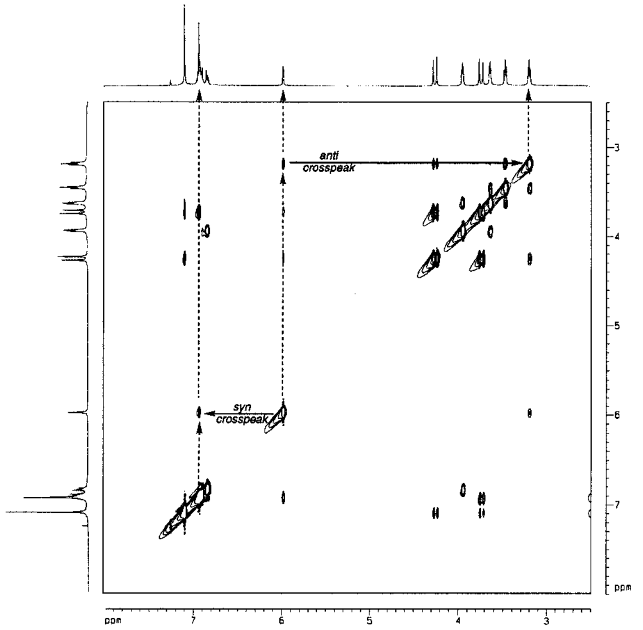

Figure 6. 400 MHz NOESY of **3c** at 295 K; the crosspeak of the calixarene proton at δ = 6.0 ppm with the methylene protons at δ = 3.2 ppm results from a *syn* orientation of the calixarene aryl groups, while the crosspeak at δ = 6.0/6.9 ppm results from the *anti* orientation

Liquid−Liquid Extraction

Crown ethers **3a**−**3e**, derived from dihydrocalix[4]arene, were earlier found to extract cesium nitrate roughly 10-fold less strongly than the corresponding calixcrown ethers bearing octyloxy substituents[12] (see Table 3). Accurate selectivity measurements as given by separation factors (defined as $S = D_{Cs}/D_M$) could not be determined from those earlier measurements, which employed a mixed aqueous solution of alkali metal nitrates, because the extraction of the metals other than cesium was near or below detection limits.[12] To boost the extractability of these metals, the experiment was repeated using **3a**−**3d** with an aqueous phase in which the potassium nitrate was replaced with potassium perchlorate. With use of 0.10 M perchlorate in the mixture and an extractant (calixcrown) concentration of 0.025 M, it was expected that perchlorate would be the predominant anion extracted into the organic phase, as it is approximately 1000-fold more lipophilic than nitrate.[33]

The results shown here (Table 3) clearly reflect the expected boost in metal cation extraction and in so doing reveal an increase in selectivity for cesium over rubidium and potassium for the dihydrocalix[4]arene crown ethers **3a**−**3d**. Of particular note, Cs/K separation factors in excess of 1500 were observed for all four extractants, a fivefold increase over the Cs/K selectivity of comparable bis(alkyloxy)-calix[4]arene crown-6 ethers. The Cs/Na separation factors of 10^4−10^5 observed here are at or above the practical limit of determination and are within the range of separation factors found for calix[4]arene crown ethers reported previously.[3a,8,11]

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

[a]	**3a**	**3b**	**3c**	**3d**	**1a**	**1b**	**1c**	**1d**
D_{CsNO_3} [b]	0.403	0.505	0.383	0.116	4.91	4.96	4.04	1.61
D_{CsClO_4} [c]	11.3	9.08	8.52	2.15				
D_{RbClO_4} [c]	0.136	0.131	0.108	0.0297				
D_{KClO_4} [c]	0.00510	0.00613	0.00514	0.00103				
D_{NaClO_4} [c]	2×10^{-4}	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$	$< 1 \times 10^{-4}$				
D_{LiClO_4} [c]	1.1×10^{-5}	$< 1 \times 10^{-5}$	$< 1 \times 10^{-5}$	$< 1 \times 10^{-5}$				
$S_{Cs/Rb}$	83	69	79	75				
$S_{Cs/K}$	2200	1500	1700	2100				
$S_{Cs/Na}$	60,000	> 90,000	> 90,000	> 20,000				

[a] Calixarene concentration: 2.5×10^{-2} M in 1,2-dichloroethane. Conditions: 25 °C; organic-to-aqueous phase ratio = 1. [b] Initial salt concentrations: $[CsNO_3] = 0.001$ M, $[RbNO_3] = 0.002$ M, $[KNO_3] = 0.1$ M, $[NaNO_3] = 1$ M, $[LiNO_3] = 1$ M. [c] Initial salt concentrations: $[CsNO_3] = 0.001$ M, $[RbNO_3] = 0.002$ M, $[KClO_4] = 0.1$ M, $[NaNO_3] = 1$ M, $[LiNO_3] = 1$ M.

Experimental Section

General: All reagents were obtained from commercial sources and used as received, unless otherwise noted. Calixarene crown ethers **1a–d**,[3b,11,31] **2a**,[11] and **2b**,[11] were prepared according to literature methods, as were dihydrocalix[4]arene,[34] 1,2-bis[2′-(2"-chloroethoxy)ethoxy]benzene, 1,2-bis[2′-(2"-chloroethoxy)ethoxy]-*tert*-octylbenzene, and bis-1,2-[2′-(2′′−hydroxyethoxy)phenoxy]ethane di-*p*-toluenesulfonate.[11] Reactions were monitored by TLC on Silica Gel 60 with ethyl acetate/hexanes as eluent, unless otherwise noted, and preparative chromatography performed on Silica Gel 60 (60−200 mesh). NMR spectra were obtained with a Bruker MSL400 spectrometer and data processed using SwaN-MR.[35]

Dihydrocalix[4]arene Crown-6 (3a): A mixture of dihydrocalix[4]arene (2.00 g, 5.10 mmol), pentaethylene glycol di-*p*-toluenesulfonate (3.0 g, 5.5 mmol), and cesium carbonate (3.26 g, 10.0 mmol) in acetonitrile (100 mL) was refluxed under argon overnight. The acetonitrile was evaporated in vacuo, and the residue dissolved in chloroform. The chloroform was washed sequentially with water, 1 N HCl, and saturated sodium hydrogen carbonate, dried with sodium sulfate, and the solvents evaporated in vacuo. Chromatography on silica gel with chloroform eluent yielded dihydrocalix[4]arenecrown-6 (2.0 g, 65.9 %) as an oil which was triturated with hexanes (1.64 g, 54.1 %). R_f = 0.34 (ethyl acetate/hexanes, 1:2); m.p. 79−81 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$, 23 °C, $CHCl_3$): δ = 7.22 (t, $^3J_{H,H}$ = 7.3 Hz, 2 H, ArH), 7.14 (d, $^3J_{H,H}$ = 7.3 Hz, 4 H, ArH), 6.91 (m, 6 H, ArH), 5.99 (s, 2 H, ArH), 4.28 (d, $^3J_{H,H}$ = 16.1 Hz, 4 H, Ar_2CH_2), 3.73 (d, $^3J_{H,H}$ = 16.1 Hz, 4 H, Ar_2CH_2), 3.39−3.50 (m, 16 H, OCH_2), 3.25 (t, $^3J_{H,H}$ = 4.6 Hz, 4 H, $ArOCH_2$) ppm. ^{13}C NMR (100.613 MHz, $CDCl_3$, 23 °C, $CDCl_3$): δ = 155.5, 142.1, 132.8, 130.5, 127.5, 126.8, 125.9, 123.8, 72.5, 70.9, 70.5, 70.1, 35.2 ppm. $C_{38}H_{42}O_6$ (594.74): calcd. C 76.74, H 7.12, O 16.14; found C 76.25, H 7.24.

Dihydrocalix[4]arene *tert*-Octylbenzocrown-6 (3b): A mixture of dihydrocalix[4]arene (1.00 g 2.55 mmol), 1,2-bis[2′-(2"-chloroethoxy)ethoxy]-*tert*-octylbenzene (1.11 g, 2.54 mmol), cesium carbonate (1.65 g, 5.08 mmol), and cesium iodide (0.10 g, 0.38 mmol) in acetonitrile (50 mL) was refluxed under argon for three days. The acetonitrile was evaporated in vacuo, and the residue dissolved in dichloromethane. The dichloromethane was washed sequentially with water and 1 N HCl, dried with sodium sulfate, and the solvents evaporated in vacuo. Chromatography on silica gel with dichloromethane/hexanes eluent gave dihydrocalix[4]arene *tert*-octylbenzocrown-6 (1.2 g, 62 %) as an oil which crystallized from acetonitrile (0.590 g, 30.6 %). R_f = 0.70 (ethyl acetate/hexanes, 1:4); m.p. 94−96 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$, 23 °C, $CHCl_3$): δ = 7.12 (m, 6 H, ArH), 6.92−6.98 (m, 6 H, ArH), 6.87−6.92 (m, 2 H, ArH), 6.74 (d, $^3J_{H,H}$ = 9.0 Hz, 1 H, ArH), 6.00 (s, 2 H, ArH), 4.26 (d, $^3J_{H,H}$ = 8.1 Hz, 2 H, Ar_2CH_2), 4.25 (d, $^3J_{H,H}$ = 8.1 Hz, 2 H, Ar_2CH_2), 3.90−3.96 (m, 4 H, OCH_2), 3.74 ppm [d, J(H,H) = 16.1 Hz, 4 H, $ArCH_2$), 3.62 (m, 4 H, OCH_2), 3.47 (m, 4 H, CH_2), 3.24 (t, $^3J_{H,H}$ = 4.9 Hz, 2 H, $ArOCH_2$), 3.18 (t, $^3J_{H,H}$ = 5.0 Hz, 2 H, $ArOCH_2$), 1.69 (s, 2 H, CH_2),1.33 (s, 6 H, CH_3), 0.72 (s, 9 H, CH_3) ppm. ^{13}C NMR (100.613 MHz, $CDCl_3$, 23 °C, $CDCl_3$): δ = 155.4, 147.7, 146.6, 143.3, 141.9, 141.8, 132.6, 130.6, 127.5, 126.4, 125.8, 123.7, 119.2, 114.0, 113.2, 72.4, 72.2, 70.5, 70.3, 69.8, 69.6, 69.3, 69.3, 56.8, 38.0, 35.3, 32.1, 31.6, 31.3 ppm.$C_{50}H_{58}O_6$ (754.99): calcd. C 79.54, H 7.74, O 12.71; found C 79.20, H 7.80.

Dihydrocalix[4]arene Benzocrown-6 (3c): A mixture of dihydrocalix[4]arene (1.10 g, 2.80 mmol), 1,2-bis[2′-(2"-chloroethoxy)ethoxy]benzene (0.909 g, 2.81 mmol), cesium carbonate (2.11 g, 6.47 mmol), and cesium iodide (0.170 g, 0.654 mmol) in acetonitrile (50 mL) was refluxed under argon for three days. The acetonitrile was evaporated in vacuo, and the residue dissolved in dichloromethane. The dichloromethane was washed sequentially with 1 N HCl, water, and saturated sodium hydrogen carbonate, dried with sodium sulfate, and the solvents evaporated in vacuo to obtain 1.8 g of a brown solid (100 %). Crystallization from hexanes provided dihydrocalix[4]arene benzocrown-6 (1.51 g, 83.8 %). R_f = 0.43 (ethyl acetate/hexanes, 1:4); m.p. 103−105 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$, 23 °C, $CHCl_3$): δ = 7.11 (s, 6 H, ArH), 6.89−7.00 (m, 8 H, ArH), 6.83−6.89 (m, 2 H, ArH), 6.01 (s, 2 H, ArH),4.27 (d, $^3J_{H,H}$ = 16.1 Hz, 4 H, Ar_2CH_2), 3.96 (t, $^3J_{H,H}$ = 4.4 Hz, 4 H, $ArOCH_2$), 3.74 (d, $^3J_{H,H}$ = 16.1 Hz, 4 H, Ar_2CH_2), 3.65 (t, $^3J_{H,H}$ = 4.4 Hz, 4 H, OCH_2), 3.48 (t, $^3J_{H,H}$ = 4.9 Hz, 4 H, OCH_2), 3.22 (t, $^3J_{H,H}$ = 4.9 Hz, 4 H, $ArOCH_2$) ppm. ^{13}C NMR (100.613 MHz, $CDCl_3$, 23 °C, $CDCl_3$): δ = 155.5, 148.8, 142.0, 132.7, 130.6, 127.6, 126.5, 125.8, 123.8, 121.5, 114.3, 72.3, 70.5, 69.5, 69.4, 35.3 ppm. $C_{42}H_{42}O_6$ (642.78): calcd. C 78.48, H 6.59, O 14.93; found C 78.37, H 6.73.

Dihydrocalix[4]arene Bisbenzocrown-6 (3d): A mixture of dihydroxycalix[4]arene (0.79 g, 2.0 mmol), bis-1,2-[2′-(2′′−hydroxyethoxy)phenoxy]ethane di-*p*-toluenesulfonate (1.3 g, 2.0 mmol), cesium carbonate (1.5 g, 4.6 mmol), and acetonitrile (15 mL) was refluxed under argon for three days. The acetonitrile was evaporated in vacuo, and the residue dissolved in chloroform. The chloroform was washed twice with 1 N HCl and twice with 1 N NaOH, dried with sodium sulfate, and the solvents evaporated in vacuo. Column chromatography on silica gel with ethyl acetate/hexanes eluent, followed by crystallization from ethyl acetate gave dihydrocalix[4]arene bisbenzocrown-6 (0.443 g, 31.9 %). R_f = 0.63 (ethyl acetate/hexanes, 1:4); m.p. 198 °C. ^{1}H NMR (400.13 MHz, $CDCl_3$, 23 °C, $CHCl_3$): δ = 7.09 (m, 2 H, ArH), 6.93−7.02 (m, 16 H, ArH), 6.88 (d, $^3J_{H,H}$ = 7.8 Hz, 2 H, ArH), 5.98 (s, 2 H, ArH), 4.23 (d, $^3J_{H,H}$ = 16.1 Hz, 4 H, Ar_2CH_2), 4.11 (s, 4 H, $ArOCH_2$), 3.83 (t, $^3J_{H,H}$ = 5.3 Hz, 4 H, $ArOCH_2$), 3.72 (d, $^3J_{H,H}$ = 16.1, 4 H, Ar_2CH_2), 3.15 (t, $^3J_{H,H}$ = 5.3 Hz, 4 H, $ArOCH_2$) ppm. ^{13}C NMR (100.613 MHz, $CDCl_3$, 23 °C, $CDCl_3$): δ = 155.4, 149.8, 148.1, 141.9, 132.8, 130.7, 127.6, 126.6, 125.9, 123.8, 122.7, 121.8, 118.6, 114.9, 71.0, 69.0, 67.5, 35.3 ppm. $C_{46}H_{42}O_6 \cdot 1/2H_2O$(699.83): calcd. C 78.95; H 6.19; O 14.86; found C 78.87, H 6.20.

X-ray Crystallography: CCDC-133729, -167717 and -167718 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) +44−1223/336−033; E-mail: deposit@ccdc.cam.ac.uk].

Data were obtained using a Nonius CAD4 diffractometer fitted with a 1.1-mm collimator using Mo-K_α radiation (λ = 0.71073 Å). Intensities were corrected for Lorentz and polarization effects, and empirical absorption corrections were applied (only for **3c** and [Cs^+]·**3c**) based on a set of ψ scans. Calculations were carried out using XCAD4[36] (data reduction), SHELXTL[37] (absorption correction, structure solution/refinement, and molecular graphics), and PLATON[38] (structure analysis). Each H atom was placed in a calculated position, refined using a riding model, and given an isotropic displacement parameter equal to 1.2 (C*H*, C*H*$_2$) or 1.5 (C*H*$_3$) 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 of all data against $|F|^2$ of the quantity $\Sigma\omega(F_o^2 - F_c^2)^2$ was used to adjust the positions and anisotropic thermal parameters of all non-hydrogen atoms.

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Table 4. Summary of crystallographic data

Complex	**1c**	**3c**	[Cs$^+$]·**3c**
Crystal size	0.66 × 0.60 × 0.08	0.56 × 0.49 × 0.17	0.71 × 0.53 × 0.20
Crystal system	triclinic	triclinic	triclinic
Space group	$P\bar{1}$ (No. 2)	$P\bar{1}$ (No. 2)	$P\bar{1}$ (No. 2)
a (Å)	10.2619(17)	10.634(3)	10.4672(13)
b (Å)	20.797(3)	17.432(4)	13.910(16)
c (Å)	25.997(5)	19.578(4)	14.807(2)
α (deg)	110.489(13)	70.959(17)	101.837(10)
β (deg)	99.702(14)	89.846(17)	94.453(11)
γ (deg)	92.356(13)	77.52(2)	94.602(10)
V (Å^3)	5092.5(15)	3340.6(13)	2093.4(5)
$\rho_{\mathrm{calcd.}}$ (g·cm^{-3})	1.17	1.28	1.45
$2\theta_{\mathrm{max.}}$ (deg)	43	44	55
Scan mode	ω	ω	ω
T (K)	100	173	150
Reflections collected	12010	10291	12738
Independent reflections	11678 (R_{int} = 0.041)	8182 (R_{int} = 0.020)	8950 (R_{int} = 0.017)
μ (mm^{-1})	0.076	0.084	0.95
Max./min. transmission	0.994/0.951	0.977/0.961	0.833/0.553
Parameters	1193	896	525
R	0.048	0.043	0.035
wR_2	0.125	0.117	0.091
Residual e$^-$ density (e$^-$·Å^{-3})	0.28	0.26	1.6

Liquid−Liquid Extraction: The extraction experiments were performed as described previously.[12] Equal volumes (0.5 mL each) of organic phase (0.025 M of extractant in 1,2-dichloroethane) and aqueous phase (mixture of metal salts: 1 M LiNO$_3$, 1 M NaNO$_3$, and 0.1 M KX, where X = NO$_3$ or ClO$_4$, 0.002 M RbNO$_3$, and 0.001 M CsNO$_3$) were equilibrated in capped vials by repeated inversion on a Glas-Col® laboratory rotator in a constant-temperature air box at 25.0 (± 0.2) °C for two hours. This procedure was determined previously to be sufficient to ensure equilibrium. The equilibrated samples were centrifuged for five to ten minutes before subsampling for analysis. Metal ion concentrations were determined for both phases, from which distribution ratios D_{M} = [M$^+$]$_{\mathrm{organic}}$/[M$^+$]$_{\mathrm{aqueous}}$ were calculated directly. Cesium was analyzed directly by gamma scintillation spectrometry for both phases. Lithium, sodium, potassium, and rubidium were analyzed only for the organic phase, subsequent to stripping, by inductively coupled plasma atomic emission spectrometry (IRIS model, Thermo Jarrell Ash). Stripping was achieved by diluting a portion of loaded organic phase with three portions of benzene, followed by two contacts with 1.0 m M HNO$_3$ at an organic-to-aqueous phase ratio of 1:2. Based on the limits of measurement and dilution factors, lower analytical limits on measurement of distribution ratios were estimated to be D_{Li}, 5.8 × 10^{-7}; D_{Na}, 2.5 × 10^{-6}; D_{K}, 9.6 × 10^{-5}; and D_{Rb}, 0.0070. Due to the difficulty in completely avoiding entrainment and contamination, however, the practical lower limit for D_{M} is regarded to be 1 × 10^{-4} for sodium and 1 × 10^{-5} for lithium. Values of D_{M} greater than this limit have an estimated uncertainty of ± 5 %. Teflon FEP® containers were used for all extractions and for storage of organic solutions. Polypropylene vials and containers were used for storage of aqueous solutions.

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