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Calix[4]arene-bis(dibenzocrown-6-ethers) with one proton-ionizable group

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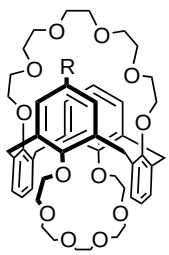
Abstract—Two 1,3-alternate calix[4]arene-biscrowns with one proton-ionizable group and two dibenzocrown-6-ether units are synthesized. The compounds exhibit high Cs^+ extraction efficiency and selectivity. Cs^+/Na^+ and Cs^+/K^+ selectivities for the new *N*-(trifluoromethylsulfonyl)carbamoyl-substituted calix[4]arene-bis(dibenzocrown-6) are found to be higher than those for an analog with no benzo group substituents in the crown ether units.

Intense studies of 1,3-alternate calix[4]arene-crown-6-ethers have been stimulated by the need to develop selective extractants for Cs^+ separation from radioactive liquid nuclear waste.[1,2] Although these compounds exhibit high Cs^+/Na^+ selectivities in solvent extraction and liquid membrane transport,[3–5] implementation of the ligands in practical separation processes is hampered by low extraction efficiency of their cesium salt complexes into organic solvents of low polarity.[6–8]

Recently we reported[9] the synthesis of novel 1,3-alternate calix[4]arene-bis(crown-6-ethers) **2** and **3** with a proton-ionizable group positioned in front of one crown ether unit. The ligands possessed markedly enhanced Cs^+ extraction efficiency compared to analog **1** without a proton-ionizable group. The Cs^+/Na^+ selectivities of these ligands were found to be at the same level as that of the non-ionizable analog **1**.



1: R = H
2: R = CO_2H
3: R = $CONHSO_2CF_3$

1,3-Alternate calix[4]arene-bis(crown-6-ethers) with one or more aromatic group incorporated into the polyether chains are reported to exhibit higher Cs^+/Na^+ selectivity compared to analogs with glycolic polyether chains.[3,5,10,11] Therefore, we undertook the synthesis and evaluation of analogs of **2** and **3** in which two ethylene bridges in each polyether unit have been replaced by two *o*-phenylene groups.

Synthesis of the new proton-ionizable calixbiscrowns **6** and **7** was performed as shown in Scheme 1. First, bromocalix[4]arene-bis(dibenzocrown-6-ether) **5** was prepared from bromocalix[4]arene[12] by reaction with ditosylate **4**[11] and Cs_2CO_3 in acetonitrile.[13] The 1,3-alternate conformation of the calix[4]arene moiety in **5** was verified by NMR spectroscopy. Thus, singlets at 3.72 and 3.74 ppm and two signals at 37.6 and 38.0 ppm were observed in the ^1H and ^{13}C NMR spectra, respectively, for the Ar-CH_2-Ar methylene groups of **5**. A carboxylic acid group was introduced into the calixbiscrown unit by treatment of **5** with BuLi and then with CO_2 giving rise to **6**. The presence of carboxylic group in **6** was verified by its IR and ^{13}C NMR spectra.[14] The *N*-(trifluoromethylsulfonyl)carbamoyl-substituted ligand **7**[15] was prepared by conversion of carboxylic acid **6** into the corresponding acid chloride followed by reaction with trifluoromethanesulfonamide and NaH.

The alkali metal cation (AMC) binding propensities of the new proton-ionizable calixbiscrowns **6** and **7** were evaluated by competitive extractions of Li^+, Na^+, K^+, Rb^+ and Cs^+ from aqueous nitrate/hydroxide solutions (0.10 mM in each AMC, pH 9.8) into 0.10 mM solutions of the ligands in chloroform.[16] As evident from

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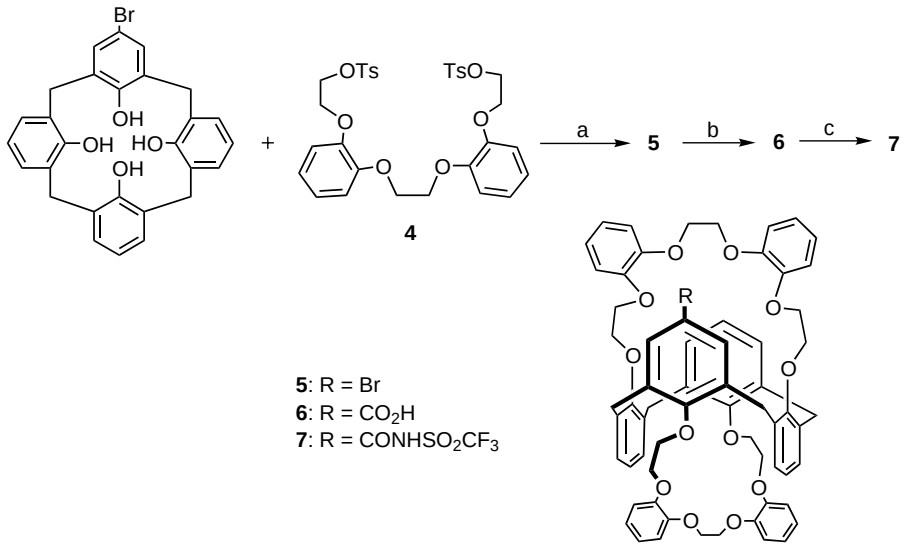

Scheme 1. (a) Cs_2CO_3, MeCN, reflux, 6 days; (b) (i) BuLi, THF, −75°C, 10 min; (ii) CO_2, THF, −75°C, 15 min; (c) (i) $(COCl)_2$, C_6H_6, 70°C, 5 h; (ii) $CF_3SO_2NH_2$, NaH, THF, rt, 12 h.

the results presented in Fig. 1, both of the calixbiscrowns exhibit preferential Cs^+ binding. The *N*-(trifluoromethylsulfonyl)carboxamide **7** is a significantly more efficient AMC extractant than the carboxylic acid **6**. The extraction efficiency for calixbiscrown **7** is found to be close to that of the earlier reported analog **3**.

For practical application in nuclear waste treatment, the ability of the ligand to separate Cs^+ from aqueous solutions containing large excesses of Na^+ and K^+ is very important. To compare the Cs^+ selectivity of **7** with that of analog **3**, which has no benzo groups in the crown ether moieties, competitive extraction of 0.10 mM Cs^+, 0.10 M K^+, and 1.0 M Na^+ aqueous nitrate solutions at pH 6.5 with 0.10 mM calixbiscrowns in chloroform was performed. The distribution coefficients, *D*, and their ratios presented in Table 1 show that ligand **7** with the dibenzocrown-6 units exhibits higher Cs^+/Na^+ and Cs^+/K^+ selectivities than ligand **3**.

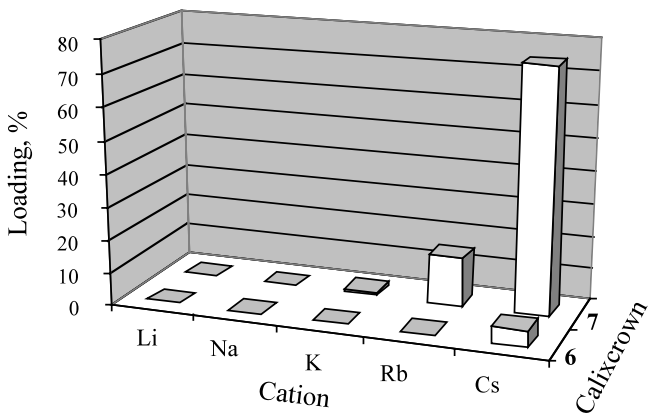

Figure 1. Competitive extractions of AMC from 0.10 mM (in each) aqueous nitrate solutions (pH 9.8) into chloroform with 0.10 mM calixbiscrowns **6** and **7**.

In conclusion, new proton-ionizable 1,3-alternate calix[4]arene-bis(dibenzocrown-6-ethers) **6** and **7** are found to exhibit high Cs^+ extraction efficiency and selectivity. The *N*-(trifluoromethylsulfonyl)carbamoyl-substituted calix[4]arene-bis(dibenzocrown-6-ether) **7** exhibits higher Cs^+/Na^+ and Cs^+/K^+ selectivities than the analogous proton-ionizable calixbiscrown **3** with no benzo groups in the crown ether units.

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Table 1. Competitive extraction of 0.10 mM Cs^+, 0.10 M K^+, and 1.0 M Na^+ aqueous nitrate solutions (pH 6.5) with 0.10 mM calixbiscrowns in $CHCl_3$

Calixbiscrown	D_{Cs}	D_{Na}	D_K	D_{Cs}/D_{Na}	D_{Cs}/D_K
3	0.14	5.0×10^{-5}	5.6×10^{-4}	2.8×10^{3}	250
7	0.28	4.0×10^{-5}	6.3×10^{-4}	7.0×10^{3}	440

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13. Preparation of **5.** A mixture of bromocalix[4]arene (2.45 g, 4.56 mmol), Cs_2CO_3 (3.72 g, 11.4 mmol), ditosylate **4** (2.93 g, 4.56 mmol) and acetonitrile (200 mL) was refluxed under nitrogen for 3 days. The same quantities of Cs_2CO_3 and ditosylate **4** were added again and refluxing was continued for another 3 days. The solvent was evaporated in vacuo and CH_2Cl_2 and 10% aqueous HCl (to pH<1) were added to the residue. The organic layer was washed with water, dried ($MgSO_4$) and evaporated in vacuo. Chromatography of the residue on silica gel with ethyl acetate–hexanes (1:4) as eluent gave **5** as a white solid. Yield 3.25 g (65%), mp 163–165°C; ^{1}H NMR (499.7 MHz, $CDCl_3$, 23°C): δ 3.28 (t, $J=6.9$, 2H), 3.46 (s, 4H), 3.50–3.64 (m, 10H), 3.72 s+3.74 s (8H), 4.37 s+4.24–4.46 m (8H), 6.47–6.52 (m, 1H), 6.55–6.62 (m, 4H), 6.68–6.75 (m, 4H), 6.88–7.13 (m, 13H); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (selected) 37.6 (Ar*C*H_2Ar), 38.0 (Ar*C*H_2Ar). Anal. calcd for $C_{64}H_{59}BrO_{12}$: C, 69.88; H, 5.41; Br, 7.26. Found: C, 69.49; H, 5.25; Br, 7.03%.
14. Preparation of **6.** To a solution of **5** (1.85 g, 1.68 mmol) in THF (30 mL), BuLi (5.05 mmol) in hexanes was added at −75°C with stirring under nitrogen. After 10 min at −75°C, CO_2 was bubbled through the solution for 10 min. After another 15 min at −75°C, the mixture was allowed to warm to ambient temperature. The solvents were evaporated in vacuo and CH_2Cl_2 was added to the residue. The organic layer was washed with aqueous Na_2CO_3, dried (Na_2SO_4) and evaporated in vacuo. The residue was chromatographed on silica gel with CH_2Cl_2–MeOH (96:4) as eluent. The resultant solid was dissolved in CH_2Cl_2. The solution was washed with 10% aqueous HCl and water, dried ($MgSO_4$) and evaporated in vacuo to give **6** as a white solid. Yield 1.20 g (67%), mp 151–153°C; IR (deposit from CH_2Cl_2 solution on a NaCl plate, cm^{-1}): ν 1710 (C=O); ^{1}H NMR (499.7 MHz, $CDCl_3$, 23°C): δ 3.37 (t, $J=6.6$, 2H), 3.42–3.63 (m, 6H), 3.72 (d+d, $J=17.5$, 4H, ArCH_2Ar), 3.83 (d, $J=16.2$, 2H, ArCH_2Ar), 3.92 (d, $J=16.2$, 2H, ArCH_2Ar), 4.20 (m, 4H), 4.38 (s, 4H), 6.48–6.53 (m, 1H), 6.57–6.64 (m, 4H), 6.72 (d, $J=6.8$, 2H), 6.77 (d, $J=6.3$, 2H), 6.85–7.07 (m, 14H), 7.08–7.14 (m, 2H), 7.73 (s, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (selected) 37.9 (Ar*C*H_2Ar), 38.0 (Ar*C*H_2Ar), 170.6 (*C*O_2H). Anal. calcd for $C_{65}H_{60}O_{14}$: C, 73.49; H, 5.68. Found: C, 73.46; H, 5.71%.
15. Preparation of **7**. A solution of **6** (0.55 g, 0.52 mmol) and oxalyl chloride (0.20 g, 1.55 mmol) in C_6H_6 (20 mL) was stirred under nitrogen at 70°C for 5 h and the solvent was removed in vacuo. A solution of the residue in THF was added to a mixture of a trifluoromethanesulfonamide (0.15 g, 1.03 mmol) and NaH (0.08 g, 3.3 mmol) in THF. The mixture was stirred under nitrogen at room temperature for 12 h. Then 0.5 mL of H_2O was added and the THF was evaporated in vacuo. The residue was dissolved in CH_2Cl_2 and the resulting solution was washed with aqueous Na_2CO_3, dried (Na_2SO_4) and evaporated in vacuo. The residue was washed with Et_2O, and then dissolved in CH_2Cl_2. The solution was washed with 10% aqueous HCl and water, dried ($MgSO_4$) and evaporated in vacuo to give **7** as off-white solid. Yield 0.56 g (90%), mp 137–139°C; ^{1}H NMR (499.7 MHz, $CDCl_3$, 23°C): δ 3.30–3.44 (m, 4H), 3.46–3.67 (m, 12H), 3.72 (d, $J=16.3$, 2H, ArCH_2Ar), 3.79 (d, $J=16.3$, 2H, ArCH_2Ar), 3.83 (d, $J=16.7$, 2H, ArCH_2Ar), 3.87 (d, $J=16.7$, 2H, ArCH_2Ar), 4.22–4.29 (m, 2H), 4.31–4.40 (m)+4.38 (s) (4H), 6.61–6.68 (m, 3H), 6.74–6.82 (m, 6H), 6.88–6.99 (m, 8H), 7.02–7.13 (m, 8H), 7.45 (s, 2H); ^{13}C NMR (125.7 MHz, $CDCl_3$): δ (selected) 37.8 (Ar*C*H_2Ar), 37.9 (Ar*C*H_2Ar), 165.1 (*C*ONH). Anal. calcd for $C_{66}H_{60}F_3NO_{15}S$: C, 66.27; H, 5.06; N, 1.17. Found: C, 66.54; H, 5.17; N, 1.17%.
16. After extraction, the organic phase was stripped with aqueous 0.1N HCl and the AMC concentrations in the strippant were determined by ion chromatography.