Calix[4]arenes with a novel proton-ionizable group: synthesis and metal ion separations

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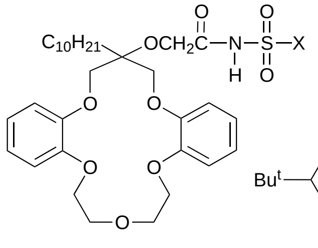
New calix[4]arenes with two *N*-(X)sulfonyl carboxamide groups of 'tunable' acidity are synthesized from the corresponding calixarene dicarboxylic acid and exhibit good to excellent extraction selectivity for Pb^{2+} over most alkali, alkaline earth and transition metal ions.

Calixarenes are an important class of macrocyclic host molecules that efficiently and selectively bind a variety of ionic and neutral guest species.[1–4] They find applications in separation processes involving organic and inorganic substances, phase transfer catalysis, chromatography, ion-selective electrodes, *etc.*[2] Calixarenes functionalized with pendent proton-ionizable groups (carboxylic acid, hydroxamic acid, phosphonic acid and phosphonic acid monoalkyl ester) are of special interest as potential agents for separations of polyvalent metal ions by liquid extraction and membrane transport[5–10] or sorption when immobilized on polymer matrices.[11–14] The ligation properties of such compounds are controlled by the nature of the ionizable groups, in particular their acidity. For example, calixarene carboxylic acids[5] were found to be much more efficient interphase carriers for alkaline earth cations than related nonfunctionalized calixarenes which contain phenolic groups on the lower rim. Developing new types of calixarenes with a wider variety of proton-ionizable functions may lead to additional applications of these compounds in metal ion separation processes.

In recent work, we have introduced the *N*-(X)sulfonyl carboxamide moiety as a novel pendent proton-ionizable group in lariat ethers **1** to obtain macrocyclic ligands with 'tunable' acidity that exhibit high Na^+ selectivity in competitive solvent extraction of alkali metal cations.[15] We now report the synthesis and application in metal ion extraction of a new type of calixarenes, the calix[4]arene bis[*N*-(X)sulfonyl carboxamides] **2**–**5**. It was anticipated that these new ligands would exhibit appreciable acidity and effectiveness in extracting divalent metal ions from aqueous solutions.

Calix[4]arenes **2**–**5**‡ were prepared in two steps from the calixarene dicarboxylic acid **6**.[16]§ The positions and shapes of the signals in the ^1H NMR spectra of **2**–**5** were found to vary with the identity of the solvent and concentration, which demonstrates that the calixarenes exist in solution as mixtures of conformers and also associate by NH··O=C hydrogen bonding. The conformational and associative behavior is especially pronounced for **5**. Solution and solid-state structures of the new ligands are under continued investigation.

The new di-ionizable calixarenes **2**–**5** efficiently extract Pb^{2+} from acidic (HNO_3) solutions into $CHCl_3$¶ (Fig. 1). The acidities of the new calixarene ligands are expected to be strongly influenced by the electron-withdrawing ability of X in the *N*-(X)sulfonyl group. Values of the pH for half-extraction ($\mathrm{pH}_{1/2}$) in the extraction profiles are found to vary with X in the order: CF_3 (2.0) > Ph (5.2) > 4-$O_2NC_6H_4$ (5.3) > Me (5.5). Although the $\mathrm{pH}_{1/2}$ values for **2**–**4** fall in the anticipated ordering for the electron-withdrawing ability of X,[15] that for **5** with X = 4-nitrophenyl is considerably less acidic than expected. It is suggested that the reduced acidity of **5** in $CHCl_3$ arises from inter- or intra-molecular NH··O=C hydrogen bonding or by conformational peculiarities of the compound that hinder metal ion complexation.



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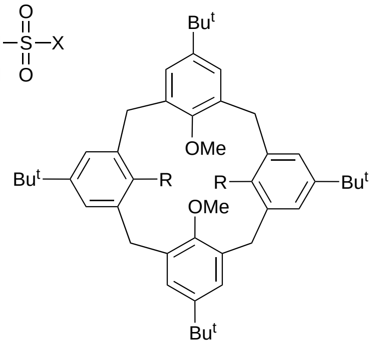
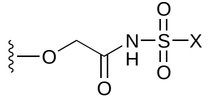
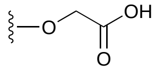


2–**5** R =



2 X = CF_3
3 X = Me
4 R = Ph
5 X = 4-$O_2NC_6H_4$

6 R =



The extraction selectivity of **2** at pH 2.5 was examined for equimolar binary mixtures of Pb–M,‖ where M is Na^+, K^+, Cs^+, Sr^{2+}, Cu^{2+}, Ni^{2+}, Co^{2+}, Zn^{2+}, Cd^{2+} or Hg^{2+} (Fig. 2). High selectivity is observed for Pb^{2+} over K^+, Cs^+ and all of the transition metal ions examined except Hg^{2+}. Good extraction selectivity for Pb^{2+} over Na^+ and Sr^{2+} is also evident. Interference to Pb^{2+} extraction by the presence of Hg^{2+} was significantly reduced by the addition of chloride ions to the aqueous solution.

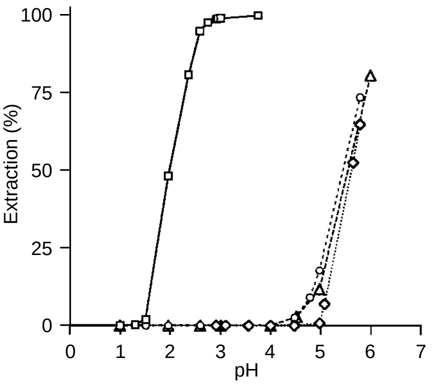


Fig. 1 pH profiles for Pb^{2+} extraction from 0.50 mM aq. $Pb(NO_3)_2$ into $CHCl_3$ with 1.00 mM calix[4]arene *N*-(X)sulfonyl carboxamides (□ **2**, (◇) **3**, (○) **4** and (△) **5**

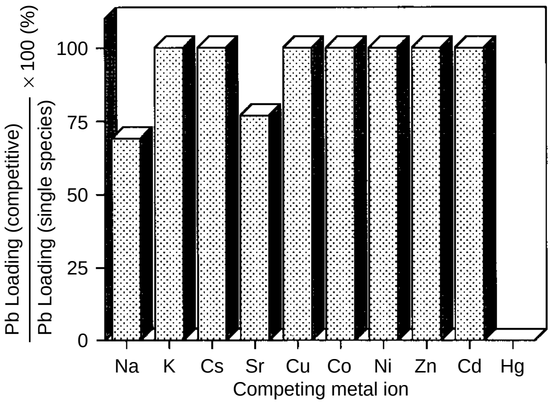


Fig. 2 Pb^{2+} loading of **2** in competitive extraction of 0.50 mM Pb^{2+} and 0.50 mM competing metal ion from an aqueous nitrate solution at pH 2.5 relative to the Pb^{2+} loading for extraction of Pb^{2+} under the same conditions, but in the absence of the competing metal ion

Further investigations of the metal ion separation properties of these novel proton-ionizable calixarenes are in progress.

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Notes and References

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‡ *Selected data* for **2**: mp 233–234 °C (Calc. for $C_{52}H_{64}F_6N_2O_{10}S_2$: C, 59.19; H, 6.11; N, 2.65. Found: C, 59.39; H, 6.19; N, 2.65%); ν_{max}(deposit from CH_2Cl_2 solution onto a NaCl plate)/cm^{-1} 3324, 3240, 1758, 1300, 1131, 1205, 1057; δ_H (300 MHz, [$^2H_6$]DMSO) 0.93 (br s, 18 H), 1.30 (s, 18 H), 3.68 (br m, 18 H), 6.80 (br m, 8 H), 10.31 (br s, 2 H). For **3**: mp 268–270 °C (Calc. for $C_{52}H_{70}N_2O_{10}S_2$: C, 65.93; H, 7.45; N, 2.96. Found: C, 65.56; H, 7.66; N, 2.95%) ν_{max} (deposit from CH_2Cl_2 solution onto a NaCl plate)/cm^{-1} 3355, 3241, 1731, 1347, 1151, 1199, 1122; δ_H(300 MHz, [$^2H_6$]DMSO) 0.99 (s, 18 H), 1.30 (s, 18 H), 3.74 (br m, 24 H), 6.55 (br m, 4 H), 7.15 (br s, 4 H), 11.80 (br s, 2 H). For **4**: mp 233–235 °C (Calc. for $C_{62}H_{74}N_2O_{10}S_2$: C, 69.50; H, 6.96. N, 2.61. Found: C, 69.77; H, 6.90; N, 2.55%); ν_{max}(deposit from CH_2Cl_2 solution onto a NaCl plate)/cm^{-1} 3352, 3248, 1732, 1361, 1163, 1196, 1089; δ_H(300 MHz, [$^2H_6$]DMSO) 0.96 (br s, 18 H), 1.22 (br s, 18 H), 3.63 (br m, 18 H), 6.47 (br m, 4 H), 7.10 (s, 4 H), 7.65 (m, 6 H), 8.00 (br s, 4 H), 12.39 (br s, 2 H). For **5**: mp 238–240 °C (Calc. for $C_{62}H_{72}N_4O_{14}S_2$: C, 64.12; H, 6.25; N, 4.82. Found: C, 63.74; H, 6.51; N, 4.48%); ν_{max}(deposit from CH_2Cl_2 solution onto a NaCl plate)/cm^{-1} 3346, 1719, 1350, 1162, 1197, 1089, 1532, 1350; δ_H(300 MHz, [$^2H_6$]DMSO 0.95 (br s, 18 H), 1.20 (br s, 18 H), 3.56 (br m, 18 H), 6.73 (br m, 8 H), 8.26 (s, 4 H), 8.46 (m, 4 H), 12.78 (br s, 2 H).

§ *Typical procedure* for conversion of **6** into the corresponding bis(*N*-trifluoromethanesulfonyl carboxamide) **2**: To a solution of **6** (2.50 g, 3.15 mmol) in dry benzene (50 ml) was added oxalyl chloride (3.25 ml, 37.4 mmol). The reaction mixture was refluxed for 4 h under nitrogen and evaporated *in vacuo*. The resultant acid chloride was dissolved in dry THF (50 ml) and added to a mixture of pentane-washed KH (35% in mineral oil, 3.63 g, 31.7 mmol) and trifluoromethanesulfonamide (1.38 g, 9.3 mmol) in dry THF (25 ml). The mixture was stirred at room temperature for 10 h (1 h for **5**) under nitrogen, then water (15 ml) was carefully added to destroy the residual KH. The THF layer was separated and diluted with EtOAc (100 ml). The organic solution was washed with a 10% aq. K_2CO_3 (3 × 50 ml) and evaporated *in vacuo*. Column chromatography on alumina with CH_2Cl_2 and then MeOH–CH_2Cl_2 (1 : 9) as eluents gave a white solid which was dissolved in CH_2Cl_2 (50 ml) and washed with 1 M HCl (50 ml). The CH_2Cl_2 solution was dried over $MgSO_4$ and evaporated *in vacuo* to give a white solid which was recrystallized from Et_2O–hexanes to give **2** (2.35 g, 71%). Calixarenes **3**–**5** were prepared similarly in 60, 80 and 70% yields, respectively.

¶ A 1.0 mM solution of the calixarene in $CHCl_3$ (5.0 ml) and 5.0 ml of 0.50 mM aq. $Pb(NO_3)_2$ (pH adjusted with dil. HNO_3) in a 15 ml, metal-free capped plastic centrifuge tube was shaken on a vortex mixer for 5 min, allowed to stand for 5 min, and shaken for another 5 min. The mixture was centrifuged for 5 min and an aliquot of the aqueous phase was removed and diluted with deionized water for Pb^{2+} analysis by atomic absorption spectrophotometry.

|| A 5.0 mM solution of **2** in $CHCl_3$ (5.0 ml) and 5.0 ml of an aqueous mixture (pH 2.5, HNO_3) which was 0.50 mM (each) in Pb^{2+} and the other metal nitrate was shaken on a vortex mixer for 5 min, allowed to stand for 5 min, and shaken again for 5 min. The mixture was centrifuged for 5 min and an aliquot was removed and diluted with deionized water. The Pb^{2+} concentration in the diluted aqueous phase was determined by atomic absorption spectrophotometry and compared with the result of Pb^{2+} extraction from the aqueous solution of 'pure' $Pb(NO_3)_2$ under the same conditions.

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