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# Highly selective Ba²⁺ separations with acyclic, lipophilic di-[*N*-(X)sulfonyl carbamoyl] polyethers

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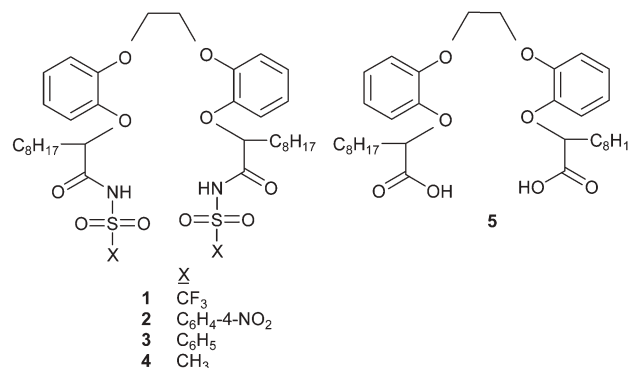
New lipophilic acyclic polyethers with two *N*-(X)sulfonyl carbamoyl groups of "tunable" acidity exhibit remarkable selectivity for Ba²⁺ over other alkaline earth metal ions in competitive solvent extraction and transport across polymer inclusion membranes.

Acyclic polyether ligands (podands) are important host molecules for a variety of ionic and neutral guest species.[1] They have found broad applications in separation processes involving organic and inorganic substances, phase transfer catalysis, chiral recognition, *etc.*[1] Acyclic polyethers have certain advantages over their cyclic analogues (crown ethers), such as their facile synthesis, which does not require high dilution techniques or use of a template effect. Also, complexation and decomplexation processes are generally faster in the acyclic systems and the pseudo-cavity usually has greater conformational flexibility.[1] Of particular interest are acyclic polyethers that contain proton-ionizable end groups. This interest was stimulated by the observation that monensin, nigericin, grisorixin, alborixin and emericid, which are well-characterized acyclic polyether carboxylic acid antibiotics, form strong complexes with metal ions, such as Ag⁺ and Ba²⁺.[1a] Thus, acyclic polyethers functionalized with pendant ionizable groups (carboxylic acid,[2] hydroxamic acid,[2e] phosphonic monoalkyl ester[2d]) are of special interest as potential ligands for separations of a variety of polyvalent metal ions by solvent extraction and membrane transport.[2c,d,3] Previous studies suggest that the identity of the ionizable functionality affects the selectivity and efficiency for solvent extraction of metal ions by acyclic polyether ligands. For example, lipophilic acyclic polyether di(hydroxamic acids) exhibit greater efficiency and selectivity for trivalent lanthanides than the corresponding di(carboxylic acids).[4] Therefore, developing new types of podands with a wider variety of proton-ionizable groups could potentially lead to additional applications of these compounds in metal ion separation processes.

In recent work, we have introduced the *N*-(X)sulfonyl carbamoyl function as a novel pendant proton-ionizable group in lariat ethers[5] and calix[4]arenes[6] to obtain macrocyclic ligands with "tunable" acidity by variation of X. Dibenzo-16-crown-5 lariat ethers were found to exhibit high Na⁺ selectivity in competitive solvent extraction of alkali metal cations,[5] while di-ionizable calix[4]arenes provided excellent extraction selectivity for Pb²⁺ and Hg²⁺ over alkali metal, alkaline earth and many other transition metal cations.[6] We now report the synthesis of acyclic polyethers **1–4** and application of these novel, lipophilic, di-ionizable podands in competitive solvent extraction and

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membrane transport of alkaline earth metal cations. These new acyclic ligands with two proton-ionizable groups are expected to be effective for extraction of divalent metal ions from aqueous solutions.



|   | X |
|---|---|
| **1** | CF₃ |
| **2** | C₆H₄-4-NO₂ |
| **3** | C₆H₅ |
| **4** | CH₃ |

The acyclic di-ionizable polyethers **1–4** were prepared in good yields by two-step reactions from the lipophilic acyclic polyether di(carboxylic acid) **5**.[2e] The general procedure for the conversion of **5** into ligands **1–4** is as follows: To a suspension of **5** (2.93 g, 5.0 mmol) in 30 ml of benzene at 0 °C under nitrogen, oxalyl chloride (5.0 ml, 57 mmol) was added dropwise. The mixture was stirred for 1 hour at room temperature then for 1 hour at 60–70 °C and evaporated *in vacuo*. The resultant di(acid chloride) was dissolved in THF (30 ml) and added to a mixture of sodium hydride (1.20 g, 50.0 mmol) and the appropriate sulfonamide (11.0 mmol) in THF (40 ml). The mixture was stirred at room temperature for 10 hours under nitrogen. Water was added carefully to destroy the excess of NaH and the THF was evaporated *in vacuo*. Water was added to the residue and the mixture was extracted with ethyl acetate. The ethyl acetate layer was washed with water, dried over sodium sulfate and evaporated *in vacuo* to give the crude product, which was purified by column chromatography on silica gel with dichloromethane→ethyl acetate–dichloromethane (1 : 5) as eluent to give the solid sodium salt of the ionized ligand. The solid was dissolved in chloroform and washed with 1 M hydrochloric acid (100 ml). Evaporation of the chloroform *in vacuo* gave podands **1–4** in 55–80% yields.† (For **2**, a shorter 1-hour reaction of the di(acid chloride) with the sodium 4-nitrobenzenesulfonamidate gave a cleaner crude product.)

Solvent extractions of alkaline earth metal cations from aqueous solutions into chloroform by acyclic polyether di[*N*-(X)sulfonyl carboxamides] **1–4** and the corresponding di(carboxylic acid) **5** were performed using a reported procedure[2c,d] with determination of alkali metal cation concentrations in the acidic aqueous strippant by ion chromatography. Results from competitive
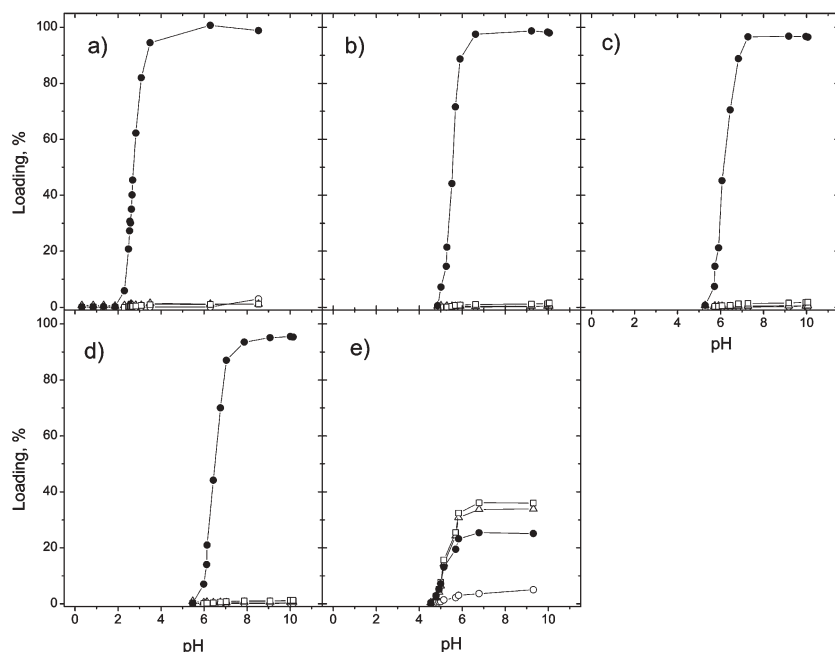
**Fig. 1** Metals loading of the organic phase *versus* pH of the aqueous phase for competitive solvent extraction of alkaline earth metal cations (20 mM in each) with chloroform solutions (5.0 mM) of lipophilic, di-ionizable, acyclic polyethers a) **1**, b) **2**, c) **3**, d) **4**, and e) **5**. ($\bigcirc$ = $Mg^{2+}$, $\triangle$ = $Ca^{2+}$, $\square$ = $Sr^{2+}$, $\bullet$ = $Ba^{2+}$)

extractions of aqueous solutions containing 20 mM (in each) of the alkaline earth metal cations with 5.0 mM chloroform solutions of **1–4** are presented in Fig. 1.

As can be seen from the data shown in Fig. 1a–d, lipophilic di-ionizable polyethers **1–4** are efficient extractants with very high selectivity for $Ba^{2+}$. The maximum loading was 95–100% as calculated for formation of 1 : 1 ionized podand–metal ion complexes. As expected, acidities of the new acyclic polyether ligands are appreciably influenced by the electron-withdrawing ability of X in the *N*-(X)sulfonyl carbamoyl group. The extraction profiles reveal that the acidity of the acyclic polyether ligands decreases in the order **1** > **2** > **3**, **4**. The efficiencies with which **1** and **2** extract $Ba^{2+}$ from acidic aqueous solutions are remarkable.

Comparison of the extractions profile in Fig. 1e for lipophilic, acyclic polyether di(carboxylic acid) **5** with those for the analogous di[*N*-(X)sulfonyl carboxamides] **1–4** reveals a profound influence of the ionizable group identity upon the selectivity of alkaline earth metal cation extraction. Thus, the competitive extraction selectivity of $Sr^{2+}$ $\sim$ $Ca^{2+}$ > $Ba^{2+}$ > $Mg^{2+}$ observed for ligand **5** is in sharp contrast with the very high $Ba^{2+}$ selectivity exhibited by ligands **1–4**.

The ability of lipophilic, acyclic, polyether di[*N*-(X)sulfonyl carboxamides] **1–4** to serve as carriers for transport of alkaline earth metal cations across polymeric inclusion membranes[7,8] was also examined.‡ Results from competitive transport of alkaline earth metal cations (0.20 M in each) in bis-tris/bis-tris·HCl buffer at pH 5.1 across cellulose triacetate–poly(vinyl chloride)–*o*-nitrophenyl octyl ether (CTA–PVC–NPOE) polymer inclusion membranes by di-ionizable carriers **1–4** are presented in Table 1. From these data, high $Ba^{2+}$ transport selectivity is clearly evident. The transport efficiency decreases as the X group of the carrier is changed in the order **1** > **2** > **4** > **3**.

**Table 1** Fluxes for competitive alkaline earth metal cation transport across CTA–PVC–NPOE polymer inclusion membranes by carriers **1–4**

| Carrier | Flux ($\mu$mol/m$^2$ s)[a] | | | |
| | $Mg^{2+}$ | $Ca^{2+}$ | $Sr^{2+}$ | $Ba^{2+}$ |
|---|---|---|---|---|
| **1** | 0.009 | 0.080 | 0.099 | 4.42 |
| **2** | U[b] | U | U | 2.54 |
| **3** | U | 0.020 | 0.057 | 0.687 |
| **4** | U | U | U | 0.025 |

[a] Average flux for transport experiments across two different CTA–PVC membranes. Reproducibility is $\pm 10\%$ of the stated value. [b] Undetectable in the aqueous receiving phase.

Further investigations of the metal ion separation properties of these novel acyclic di-ionizable polyethers are in progress.

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## Notes and references

† Selected data for **1**: oil which solidified on standing (Calc. for $C_{36}H_{50}F_6N_2O_{10}S_2$: C, 50.96; H, 5.93; N, 3.30. Found: C, 51.07; H, 5.61; N, 3.31%); $\nu_{max}$ (deposit from $CH_2Cl_2$ solution onto a NaCl plate)/cm$^{-1}$ 3215, 1757, 1255; $\delta_H$(CDCl$_3$, 300 MHz) 0.87 (t, *J* 6.6, 6H), 1.25 (s, 20H), 1.51–1.54 (m, 4H), 1.92–1.99 (m, 4H), 4.43–4.58 (m, 6H), 6.98–7.14 (m, 8H), 10.36 (s, 2H). For **2**: mp 93–95 °C (Calc. for $C_{36}H_{56}N_2O_{10}S_2$: C, 58.36; H, 7.62; N, 3.78. Found: C, 58.40; H, 7.73; N, 3.53%); $\nu_{max}$ (deposit from $CH_2Cl_2$ solution onto a NaCl plate)/cm$^{-1}$ 3250, 1718, 1255; $\delta_H$ (CDCl$_3$,

300 MHz) 0.87 (t, $J$ 6.5, 6H), 1.26 (s, 20H), 1.51–1.55 (m, 4H), 1.86–1.99 (m, 4H), 3.19 (s, 6H), 4.40–4.58 (m, 6H), 6.94–7.09 (m, 8H), 10.19 (s, 2H). For **3**: oil which solidified on standing (Calc. for $C_{46}H_{60}N_2O_{10}S_2$: C, 63.86; H, 6.99; N, 3.24. Found: C, 63.69; H, 7.74; N, 3.04%); $v_{max}$ (deposit from $CH_2Cl_2$ solution onto a NaCl plate)/cm$^{-1}$ 3246, 1718, 1254; $\delta_H$ (CDCl$_3$, 300 MHz) 0.86 (t, $J$ 6.6, 6H), 1.23 (s, 20H), 1.24–1.35 (m, 4H), 1.79–1.87 (m, 4H), 4.42–4.46 (m, 4H), 6.89–6.93 (m, 4H), 7.09–7.18 (m, 4H), 7.40–7.59 (m, 6H), 7.90–7.93 (m, 4H), 10.25 (s, 2H). For **4**: mp 114–116 °C (Calc. for $C_{46}H_{58}N_4O_{14}S_2$: C, 57.85; H, 6.12; N, 5.87. Found: C, 58.00; H, 6.07; N, 5.73%); $v_{max}$ (deposit from $CH_2Cl_2$ solution onto a NaCl plate)/cm$^{-1}$ 3242, 1725, 1255; $\delta_H$ (CDCl$_3$, 300 MHz) 0.86 (t, $J$ 6.6, 6H), 1.23 (s, 20H), 1.23–1.40 (m, 4H), 1.74–1.84 (m, 4H), 4.43–4.47 (m, 2H), 4.61 (s, 4H), 6.87–6.98 (m, 4H), 7.12 (t, $J$ 3.7, 4H), 8.08–8.18 (m, 4H), 8.24–8.28 (m, 4H), 10.36 (s, 2H).

‡ The membrane was clamped between the chambers of the transport cell using an O-ring and a finger clamp. In the next step, 40.0 mL of 1.0 M hydrochloric acid solution was introduced into the receiving phase chamber and 40.0 mL of the source phase was poured into the source phase chamber. The composition of the source phase was 0.20 M (each) in barium, calcium, strontium and magnesium chlorides in bis-tris/bis-tris·HCl buffer at pH 5.1. Both the source and the receiving phases were stirred at 200 rpm. Samples were removed from the receiving phase at 24 hour intervals over a 5-day period (sometimes more samples were taken at shorter intervals) and analyzed by ion chromatography after dilution. In the case of carrier **1**, the pH of the source phase was maintained at 5.1 by addition of saturated calcium hydroxide solution into the source phase with a Sage Syringe Pump Model 361 controlled by a Cole-Parmer Jenco Model 3672 pH/OPR Controller.

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