Lariat ethers with a novel proton-ionizable group. Synthesis and solvent extraction of alkali metal cations

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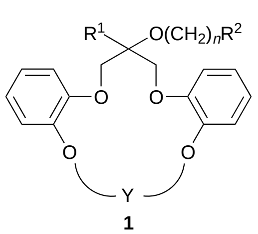
Novel lariat ethers with pendent *N*-alkyl- and *N*-arylsulfonyl carbamoyl groups are synthesized in two steps from *sym*-(decyl)dibenzo-16-crown-5-oxyacetic acid; for competitive solvent extraction of alkali metal cations from aqueous solutions into chloroform by these proton-ionizable lariat ethers with 'tunable' acidity, the selectivity order is $Na^+ \gg K^+$ with no detectable extraction of Li^+, Rb^+ or Cs^+.

A wide variety of macrocyclic polyether compounds (crown ethers) has been developed for the complexation and separation of metal ions. Many of these crown compounds show superior binding and selectivity towards Group 1 and 2 metal cations compared to other ligands.[1–3] The binding efficiency and selectivity of crown compounds may be increased by the addition of a ligand-bearing side arm to form a lariat ether.[4] Unlike their crown ether analogues, lariat ethers possess three-dimensional cavities for the coordination of metal cations.[5] The properties of these pendent ligation sites, *i.e.* their Lewis basicity and whether they are neutral or ionizable, plays an important role in determining the metal-ion binding properties of the lariat ether.

Previously we have prepared substituted lariat ethers **1** and investigated their applications in solvent extraction and liquid membrane transport of alkali metal cations, as well as their use in polymeric membrane electrodes.[6–8] The R^1 substituent on the three-carbon bridge (hydrogen, alkyl, perfluoroalkyl or aryl) affects not only the lipophilicity of the lariat ether, but also the preorganization of the binding site.[9] Moreover, the ligand substituent R^2 can be ionizable or neutral, *e.g.* a carboxylic acid or an amide, respectively, depending on the target metal ion and the particular application of interest.[10,11] Proton-ionizable lariat ether carboxylic acids and phosphonic acid monoethyl esters are particularly effective in metal ion separation processes.[12]

We are now investigating a novel type of proton-ionizable lariat ether in which the acidity of the pendant function is 'tunable'. In *N*-alkyl- or *N*-aryl-sulfonylcarbamoyl lariat ethers such as **2**, variation of the X group (alkyl, perfluoroalkyl or aryl) should influence the acidity of the pendent group. We now report a synthetic route to dibenzo lariat ethers **3**–**6** and the application of these novel lipophilic proton-ionizable lariat ethers in the solvent extraction of alkali metal cations.

The lariat ether **3**–**6** are prepared in two steps from the lipophilic lariat ether oxyacetic acid **7**.[13] A general procedure for the conversion of lariat ether carboxylic acid **7** into the corresponding *N*-trifluoromethylsulfonyl amide **3** is as follows: Benzene (25 ml) was added to **7** (2.00 g, 3.68 mmol) followed by oxalyl chloride (1.90 ml, 22.0 mmol). The resulting mixture was stirred at room temperature under nitrogen for 6 h then evaporated *in vacuo*. The resultant acid chloride was dissolved in dry THF (25 ml) and added to a mixture of pentane–washed potassium hydride (2.10 g, 18.4 mmol) and trifluoromethane sulfonamide (0.66 g, 4.40 mmol) in dry THF (25 ml). The mixture was stirred at room temperature for 10 h under nitrogen and then water (10 ml) was carefully added to destroy the remaining potassium hydride. The THF solution was separated from the aqueous layer and diluted with ethyl acetate (100 ml). The resulting organic solution was washed with 10% aqueous potassium carbonate (2 × 30 ml), dried over magnesium sulfate and evaporated *in vacuo*. The residue was washed with hexanes and purified by column chromatography (Al_2O_3, $CH_2Cl_2 \rightarrow$ 2% $MeOH–CH_2Cl_2$) to give the potassium salt of ionized **3** as a white solid which was dissolved in $CHCl_3$ and washed with 1 M HCl (50 ml). Evaporation of the $CHCl_3$ *in vacuo* gave **3** as a white solid (2.03 g, 82% yield).† Similar procedures were utilized to prepare acetamides **4**–**6**. (For the preparation of **6**, a shorter, 1 h reaction of the lariat ether oxyacetyl chloride with the potassium sulfonamidate gave a cleaner crude product.)



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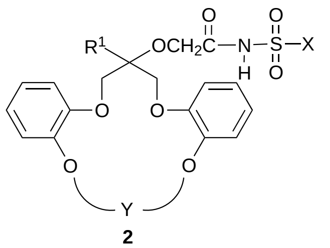

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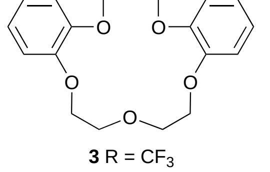
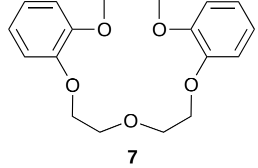


3 R = CF_3
4 R = Me
5 R = Ph
6 R = $4\text{-}NO_2C_6H_4$



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A single crystal of the proton-ionizable lariat ether **3** suitable for X-ray diffraction analysis was grown and its solid-state structure determined. In the structure, the functional side arm is oriented over the polyether cavity, as noted previously for lariat ether carboxylic acid **7**.[14] Thus the presence of the geminal decyl group in **3** preorganizes the coordinating side arm for metal ion complexation.[9]

Solvent extractions of alkali metal cations from aqueous solutions into chloroform by the lariat ether carboxamides were performed.‡ Results from competitive extractions of aqueous solutions containing 20 mM (each) of the alkali metal cations with 5 mM chloroform solutions of **3**–**6** are presented in Fig. 1. Metal ion loadings at pH 11 and selectivity factors are given in Table 1.

The lariat ether oxyacetamide **3**–**6** are found to be efficient extractants with very high selectivity for Na^+. The maximal loading is 96–100% as calculated for the formation of 1 : 1 ionized lariat ether–metal ion complexes. Only Na^+ and K^+ are detectably extracted into the chloroform phase and the Na^+/K^+ selectivity is 47–49 under conditions of high loading. The similarity of extraction selectivities for the four extractants indicates that changing X does not exert an appreciable steric

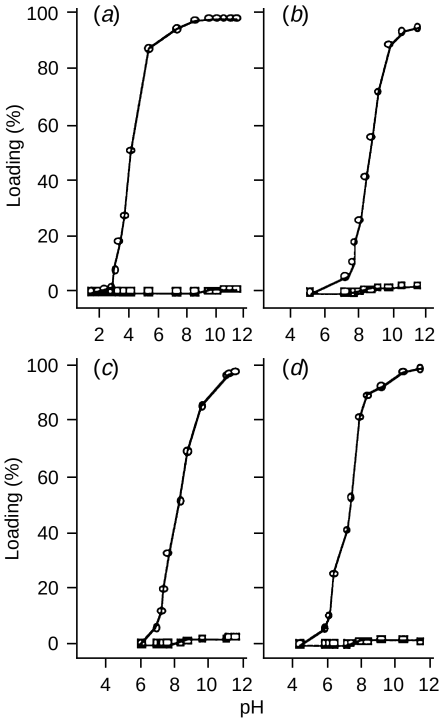

Fig. 1 Metal loadings of the organic phase *vs.* the pH of the aqueous phase for competitive solvent extractions of 20 mM (each) solutions of alkali metal cations with 5 mM chloroform solutions of (*a*) **3**, (*b*) **4**, (*c*) **5** and (*d*) **6**, with (○) Na$^+$ and (☐) K$^+$

Table 1 Loading and selectivity factors for extraction of alkali metal cations by proton-ionizable lariat ethers **3**–**6** at pH 11[a]

Extractant	Total loading (%)	Selectivity Na$^+$/K$^+$
3	100	49
4	96	47
5	97	48
6	100	49

[a] Concentrations of extracted Li$^+$, Rb$^+$ and Cs$^+$ were below detection limits.

effect. However, the variation of X does appreciably influence the side arm acidity. As judged from the extraction profiles, the acidities of the proton-ionizable lariat ethers decrease in the order: **3** > **6** > **4**, **5**. The efficiency with which **3** extracts Na$^+$ from acidic aqueous solutions is noteworthy.

Further investigations of metal ion separations with such ‘tunable’ proton-ionizable lariat ethers are in progress.

This research was supported by the Division of Chemical Sciences of the Office of Basic Energy Sciences of the U.S. Department of Energy. We thank Dr Frederick J. Brown of Zeneca Pharmaceuticals for the suggestion that *N*-alkyl- and *N*-aryl-sulfonylcarbamoyl groups be incorporated into proton-ionizable lariat ethers. We also thank Dr Carey E. Bauer of Northern Illinois University and Dr Robin D. Rogers of the University of Alabama, Tuscaloosa, for determining the X-ray crystal structure of **3**.

Footnotes and References

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† Spectra (^{1}H and ^{13}C NMR and IR) of compounds **3**–**6** are consistent with their structural assignments and will be reported in a more detailed publication. *Selected data* for **3**: mp 100 °C; calc. for $C_{32}H_{49}F_3NO_9S$: C, 56.88; H, 6.56; N, 2.07. Found: C, 56.99; H, 6.83; N, 2.06%. For **4**: 75% yield of white solid, mp 43–45 °C; calc. for $C_{32}H_{47}NO_9S \cdot 0.1\ CH_2Cl_2$: C, 61.17; H, 7.55; N, 2.22. Found: C, 61.36; H, 7.76; N, 2.10%. For **5**: 81% yield of white solid, mp 52–54 °C; calc. for $C_{37}H_{49}NO_9S$: C, 64.99; H, 7.22; N, 2.05. Found: C, 64.75; H, 7.32; N, 2.00%. For **6**: 80% yield of yellow solid, mp 54–57 °C; calc. for $C_{37}H_{48}N_2O_{11}S$: C, 60.97; H, 6.64; N, 3.84. Found: C, 60.62; H, 6.69; N, 3.72%.

‡ Into a capped, metal-free, plastic 15 ml centrifuge tube was added 2.0 ml of an aqueous solution which was 20.0 mM (each) in sodium, potassium, rubidium and cesium chlorides and 20.0 mM in lithium (chloride + hydroxide). [Due to the higher acidity of **3**, some of the extracted aqueous solutions for this ligand were 20.0 mM (each) in lithium, sodium, potassium, rubidium and cesium chlorides with added HCl.] A 5.0 mM solution of the proton-ionizable lariat ether (2.0 ml) was added and the tube was shaken on a vortex mixer for 4 min and then centrifuged for 4 min to promote complete phase separation. The aqueous phase was removed with a syringe and the equilibrium pH of this aqueous phase was measured with a combination microelectrode. Of the organic phase, 1.5 ml was transferred by syringe into a new plastic centrifuge tube. After adding 3.0 ml of 0.1 M HCl, the tube was shaken on a vortex mixer for 4 min and then centrifuged for 4 min. A portion of the aqueous phase was removed with a syringe and diluted with deionized water for alkali metal cation analysis by ion chromatography.

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Received in Corvallis, OR, USA, 6th May 1997; 7/03106H