Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

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To cite this Article Wang, Chuan , Huszthy, Peter , Bradshaw, Jerald S. , Lamb, John D. , Olenyuk, Bogdan , Bearss, David and Izatt, Reed M.(1995) 'Alkoxymethyl-Substituted 18-Crown-6 and 21-Crown-7 Ligands: Synthesis, Complexation Properties, and Metal Ion Membrane Separations', Separation Science and Technology, 30: 7, 1589 — 1607

To link to this Article: DOI: 10.1080/01496399508010364

URL: http://dx.doi.org/10.1080/01496399508010364

SEPARATION SCIENCE AND TECHNOLOGY, 30(7-9), pp. 1589-1607, 1995

ALKOXYMETHYL-SUBSTITUTED 18-CROWN-6 AND 21-CROWN-7 LIGANDS: SYNTHESIS, COMPLEXATION PROPERTIES, AND METAL ION MEMBRANE SEPARATIONS

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ABSTRACT

Three novel alkoxymethyl-substituted 18-crown-6 (8-10) and one new alkoxymethyl-substituted 21-crown-7 (11) ligands have been prepared. First, 1-*O*-tritylpropanetriol (1) and penta- or hexaethylene glycol ditosylate were cyclized in the presence of an alkali metal hydride. The resulting trityloxymethyl-substituted crowns were deprotected to give the hydroxymethyl-substituted 18-crown-6 (6) and hydroxymethyl-substituted 21-crown-7 (7). The latter compounds were alkylated using sodium hydride and the appropriate 1-bromoalkane to form 8-11. Complexation properties of these new ligands with the alkali metal cations were studied by a calorimetric titration technique. Compared with the parent 18-crown-6 and 21-crown-7 ligands, the substituted 18-crown-6 ligands demonstrate superior selectivity for K^+, while the substituted 21-crown-7 ligand demonstrated less selectivity for Cs^+ over other alkali cations. Solvent extraction and membrane separation experiments using these new ligands were also carried out. The results demonstrated that the structural features of these new ligands have a significant influence on cation complexation selectivity and separations potential.

INTRODUCTION

Membranes have received considerable attention in recent years because of their potential for performing novel separations of chemical species (1). One of the powerful challenges in membrane research has been designing high chemical selectivity into the separation system (2). Our research program has focused on the development of separation methodology for metal cations using macrocyclic ligands. Macrocyclic ligand carrier-mediated liquid membrane transport offers considerable promise in metal cation separations because of the excellent selectivity characteristics of these ligands (3).

In order for macrocyclic ligands to serve as viable liquid membrane carriers, they must be relatively hydrophobic to avoid loss from the membrane phase to the adjacent aqueous solutions. Our previous work (4) has demonstrated that hydrophobic substituents on the macrocyclic ligand can influence membrane performance both in terms of flux and selectivity. This effect may result from the influence of the hydrophobic moiety on cation complexation properties or on the partition coefficient of the ligand between water and the liquid membrane. The work of Hancock et al. (5) showed that addition of substituent groups bearing neutral oxygen donors increases ligand selectivity for large, relative to small, metal cations. He emphasized that oxygen donors do not have to be part of a macrocyclic ring in order to provide selectivity for large metal ions.

In light of these principles, we have synthesized a series of ligands which should have desirable selectivity and partition characteristics to make separations among certain metal cations. All these ligands have either the 18-crown-6 or 21-crown-7 parent structure and contain a different length of aliphatic substituent containing a neutral oxygen donor atom. The aim of this work has been to investigate the utility of including the neutral oxygen donor atom on the ligand side arm, as well as to elucidate the effect of chain length both on complexation properties and membrane separation efficiency. In the present study, competition titration calorimetry (6) was employed to measure complex equilibrium constants, and a dual-module hollow-fiber (DMHF) membrane contactor system (7) was used to perform alkali metal cation separations. Furthermore, the separation equilibria were examined by determination of extraction equilibrium constants.

EXPERIMENTAL

Materials and Solution Preparation

All commercial chemicals were reagent grade and used as supplied from the manufacturer without further purification. 2-Octanone (Aldrich) was used as the organic solvent in all DMHF contactor and solvent extraction experiments. The DMHF source phases and/or aqueous extraction phases were prepared from $NaNO_3$ (Fisher), KNO_3 (J.T.Baker), $RbNO_3$ (Aldrich), and $CsNO_3$ (Aldrich) using distilled, deionized water. The receiving phases in the membrane experiments and the aqueous phases in the back extraction steps of the solvent extraction experiments were distilled deionized water. The macrocycles used are shown in Figure 1. The concentration of the ligand carriers in all experiments was 1.0 m*M*.

Synthesis of Ligands

1-*O*-tritylpropanetriol (1) (Scheme IA). Compound **1** was prepared in 60% yield as reported (8) with minor modifications: (a) the reaction was carried out under argon; (b) instead of column chromatography, the crude product was purified by recrystallization, first from toluene, then from isopropyl ether, mp 108°, reported: 108° (8).

Preparation of oligoethylene glycol ditosylates **2** and **3** (Scheme IB). Ditosylates **2** and **3** were prepared in a manner similar to that reported (9) for other oligoethylene glycol ditosylates by adding 0.025 mol of the appropriate oligoethylene glycol and 11.63 g (0.061 mol) of tosyl chloride dissolved together in 125 mL of pure THF to a vigorously stirred suspension of 8.4 g (0.13 mol, 87%) of finely powdered KOH in 100 mL of pure THF. Ditosylate **2** (12.55 g, 92%) solidified on standing, mp: 38-40°; ir (KBr): 1359, 1190, 1175, 1112 cm^{-1}; ^1H nmr: δ 2.43 (s, 6 H), 3.57 (s, 8 H), 3.59 (s, 4 H), 3.68 (t, 4 H, J = 5 Hz), 4.15 (t, 4 H, J = 5 Hz), 7.34 (d, 4 H, J = 8 Hz), 7.78 (d, 4 H, J = 8 Hz); ms (CI): 547 $(M + 1)^+$. *Anal.* Calcd. for $C_{24}H_{34}O_{10}S_2$: C, 52.73; H, 6.27. Found: C, 53.00; H, 6.37. Ditosylate **3** (13.71 g, 93%) was an oil, ir (neat): 1356, 1189, 1177, 1097 cm^{-1}; ^1H nmr: δ 2.44 (s, 6 H), 3.58 (s, 8 H), 3.62 (s, 8 H), 3.68 (t, 4 H, J = 5 Hz), 4.15 (t, 4 H, J = 5 Hz), 7.34 (d, 4 H, J = 8 Hz), 7.79 (d, 4 H, J = 8 Hz); ms (CI): 591 $(M + 1)^+$. *Anal.* Calcd. for $C_{26}H_{38}O_{11}S_2$: C, 52.87; H, 6.48. Found: C, 52.80; H, 6.43.

Preparation of trityloxymethyl-substituted crown ethers **4** and **5** using sodium hydride as a base (Scheme IIA). To a vigorously stirred mixture of 1.77 g (59 mmol, 80% dispersion in mineral oil) of NaH and 250 mL of pure and dry THF at 0° and under argon, was added dropwise, 6.15 g (18.4 mmol) of **1** dissolved in 500 mL of pure and dry THF. After addition, the reaction mixture was stirred at 0° for 10 min, at rt for

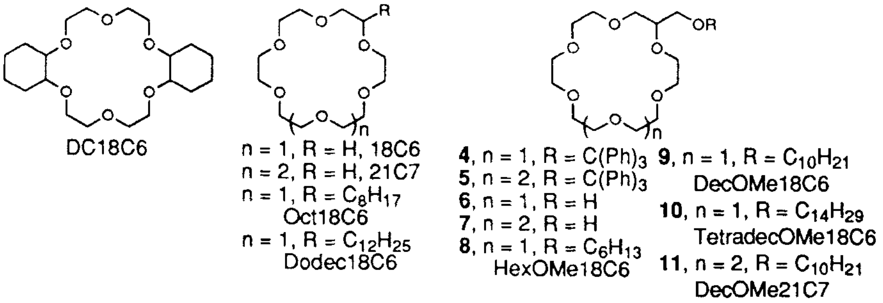
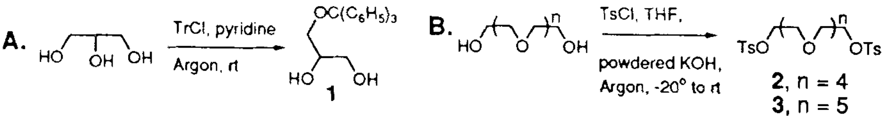
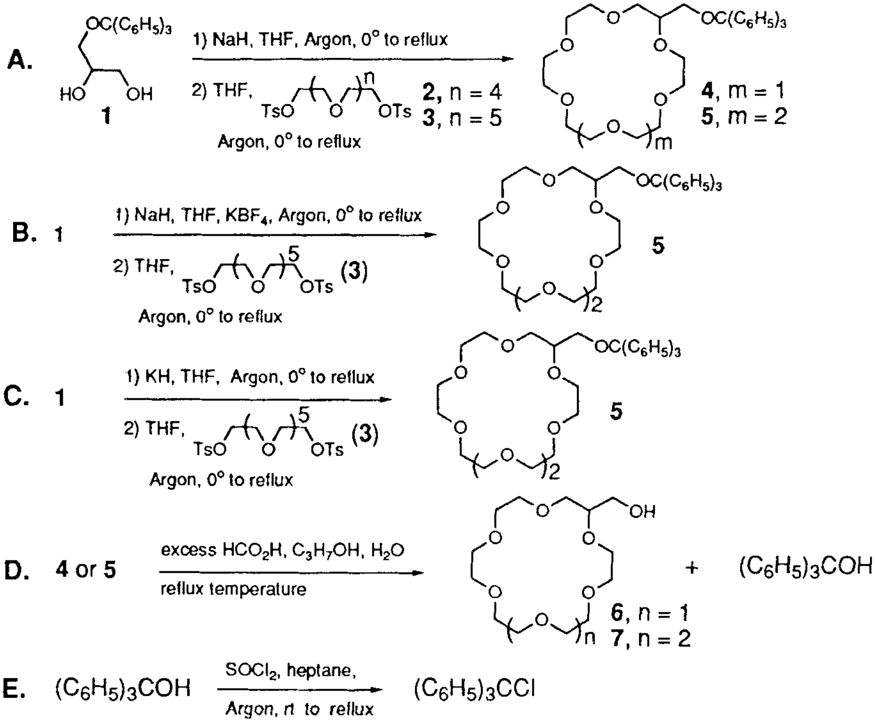


FIGURE 1. Macrocyclic ligands used in this study.



SCHEME 1. Syntheses of starting materials 1-3.

30 min, and refluxed for 6 h. The reaction mixture was cooled to 0°, and 19.4 mmol of **2** or **3** dissolved in 500 mL of pure and dry THF was added dropwise. The reaction mixture was stirred at rt for 1 d and then refluxed for 4 d. The solvent was evaporated under reduced pressure, and the residue was dissolved in a mixture of 500 mL of ether, 80 g of ice, and 80 mL of water and shaken well. The phases were separated, and the aqueous phase was shaken 3 times with 200-mL portions of ether. The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and the solvent was removed under reduced pressure to give crude **4** and **5**. Crude 2-[(triphenylmethoxy)methyl]-1,4,7,10,13,16-hexaoxacyclooctadecane (**4**) (9.72 g) was purified by column chromatography on aluminum oxide using toluene and then a 1/100 ethanol/toluene mixture as eluents to give 6.12 g (62%) of pure **4** as a clear oil; ir (neat): 3085, 3057, 3031, 1596, 1490, 1249, 1124, 1033 cm^{-1}; ^1H nmr: δ 3.11-3.25 (m, 2 H), 3.51-3.86 (m, 23 H), 7.18-7.51 (m, 15 H); ms (low volt) m/e: 536 (M^+). Satisfactory elemental analyses were obtained for **8-10** which are derivatives of **4**. Crude 2-[(triphenylmethoxy)methyl]-1,4,7,10,13,16,19-heptaoxacycloheneicosane (**5**) (10.24 g)



SCHEME II. Syntheses of hydroxymethyl-substituted crown ethers.

was purified as above for **4** to give 2.48 g (23%) of **9** as a clear oil, ir (neat): 3085, 3057, 3031, 1596, 1490, 1250, 1120, 1033 cm^{-1}; ^{1}H nmr: δ 3.10-3.25 (m, 2 H), 3.53-3.82 (m, 27 H), 7.19-7.50 (m, 15 H); ms (low volt) m/e: 580 (M$^+$). A satisfactory elemental analysis was obtained for **11**, a derivative of **5**.

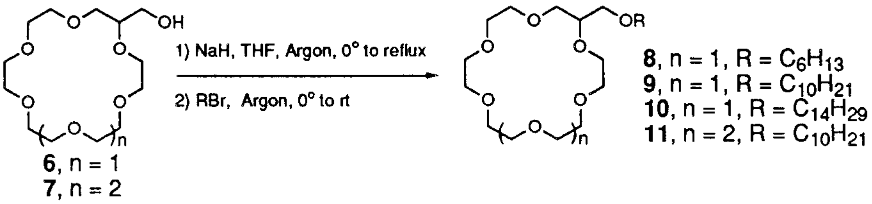
Preparation of **5** using sodium hydride and potassium tetrafluoroborate (Scheme IIB). Following the procedure above using 1.77 g (59 mmol) NaH, 11.0 g (87.4 mmol) of KBF_4 (dried at 50° in a vacuum oven over P_2O_5), 4.55 g (13.6 mmol) of **1**, and 8.5 g (14.4 mmol) of **3**, 7.88 g of crude product was obtained. This material was purified by column chromatography, first on aluminum oxide using toluene and a 1/100 ethanol/toluene mixture as eluents and then on silica gel using 1/8 ethanol/toluene as eluent to give 1.18 g (15%) of **5**, which was identical to **5** above.

Preparation of **5** using potassium hydride as a base (Scheme IIC). To a vigorously stirred mixture of 10.31 g (90 mmol, 35% dispersion in mineral oil) of KH and 250 mL of pure and dry THF at 0° and under argon, was added dropwise 6.15 g (18.4 mmol) of **1** dissolved in 500 mL of pure THF. The reaction mixture was stirred at 0° for 10 min, at rt for 30 min, and refluxed for 14 h. The reaction mixture was cooled to 0°, and 11.46 g (19.4 mmol) of **3** dissolved in 500 mL of pure THF was added dropwise. The reaction mixture was stirred at rt for 6 h then refluxed 4 d. The reaction mixture was cooled to 0°, and 200 mL of a 1/1 t-butyl alcohol/THF mixture was added. The resulting mixture was stirred at 0° for 10 min, at rt for 30 min, and refluxed for 2 h to destroy the excess KH. The solvent was evaporated (reduced pressure), and the residue was purified as described above to give 2.24 g (21%) of **5**, which was identical to **5** above.

Preparation of hydroxymethyl-substituted crown ethers **6** and **7** from **4** and **5** (Scheme IID). To 3.54 mmol of **4** or **5** was added a mixture of 5 mL of 88% formic acid, 15 mL of water, and 40 mL of propyl alcohol, and the resulting mixture was stirred and refluxed for 5 min. The excess reagents and solvents were removed under reduced pressure. Traces of volatile materials were removed under reduced pressure (0.05 mm Hg) at 60°, and the residue was dissolved in a mixture of 40 mL of water and 80 mL of ether. The mixture was shaken and separated. The aqueous phase was shaken twice with 40-mL portions of ether. The combined organic phase was dried ($MgSO_4$), filtered and the solvent was removed under reduced pressure to give crude trityl alcohol contaminated with propyl trityl ether. The aqueous phase was evaporated under reduced pressure. The residue was kept in a vacuum oven under 0.05 mm Hg at 60° over P_2O_5 for 6 h to give crude **6** and **7**. Crude 2-(hydroxymethyl)-1,4,7,10,13,16-hexaoxacyclooctadecane (**6**) (1.03 g) was purified by column chromatography on aluminum oxide using toluene and then a 1/40 ethanol/toluene mixture as eluents to give 0.97 g (93%) of **6** as a clear oil. ir (neat): 3454, 2875, 1458, 1353, 1296, 1250, 1110, 953, 837 cm^{-1}; ^1H nmr: δ 2.62 (s, broad, disappeared in D_2O, 1 H), 3.51-3.90 (m, 25 H); ms (low volt) m/e: 294 (M^+). Crude 2-(hydroxymethyl)-1,4,7,10,13,16,19-heptaoxacycloheneicosane (7) (1.18 g) was purified as above for **6** to give 1.10 g (92%) of **7** as a clear oil; ir (neat): 3456, 2868, 1456, 1350, 1296, 1254, 1104, 949, 844 cm^{-1}; ^1H nmr: δ 2.93 (s, broad, disappeared in D_2O, 1 H), 3.51-3.93 (m, 29 H); ms (low volt) m/e: 338 (M^+).

Trityl chloride from crude trityl alcohol (Scheme IIE). To a stirred mixture of 3.2 g (12 mmol) of crude trityl alcohol contaminated with trityl propyl ether (Scheme IID) and 16 mL of heptane at rt and under argon, was added dropwise, 1.28 mL (2.09g 17.5 mmol) of thionyl chloride. After addition, the reaction mixture was stirred at rt for 10 min then refluxed for 6 h. The reaction mixture was kept at rt for 6 h and in a refrigerator for 2 d. The crystals were filtered and dried in a vacuum desiccator over KOH pellets to give 2.78 g of trityl chloride. The mother liquor was condensed to 6 mL and treated as above to give an additional 0.22 g of trityl chloride. The combined yield was 3.0 g (90%). This material was identical to reported trityl chloride (10).

Preparation of alkoxymethyl-substituted crown ethers **8-11** (Scheme III). To a vigorously stirred mixture of 0.24 g (8 mmol, 80% dispersion in mineral oil) of NaH and 5 mL of dry and pure THF at rt and under argon, was added dropwise, 2 mmol of **6** or **7** dissolved in 30 mL of THF. The reaction mixture was stirred at rt for 10 min then it was refluxed for 4 h. The reaction mixture was cooled to 0° and 3 mmol of the appropriate 1-bromoalkane was added dropwise. The reaction mixture was stirred at 0° for 1 h then at rt for 2 d. The solvent was evaporated under reduced pressure and at the residue was treated cautiously with 20 g of ice. After excess NaH was destroyed, 100 mL of ether was added and the resulting mixture was mixed well and separated. The aqueous phase was shaken 3 times with 50-mL portions of ether. The combined organic phase was dried over anhydrous $MgSO_4$, filtered, and the solvent was removed under reduced pressure. The crude products were purified by column chromatography on silica gel using toluene and then a 1/8 ethanol/toluene mixture as eluents to give **8-11** as follows. 2-(Hexoxymethyl)-1,4,7,10,13,16-hexaoxacyclooctadecane (**8**) (0.67 g, 88%) was obtained as a clear oil; ir (neat): 2930, 2860, 1466, 1351, 1296, 1250, 1120, 992, 946, 851, 728 cm^{-1}; ^1H nmr: δ 0.88 (t, 3 H, J = 7 Hz), 1.23-1.40 (m, 6 H), 1.45-1.64 (m, 2 H), 3.37-3.85 (m, 27 H); ms (low volt) m/e: 378 (M^+). *Anal.* Calcd. for $C_{19}H_{38}O_7$: C, 60.29; H, 10.12. Found: C, 60.08; H, 9.94. 2-(Decoxymethyl)-1,4,7,10,13,16-hexaoxacyclooctadecane (**9**) (0.80 g, 92%) was obtained as a clear oil; ir (neat): 2925, 2856, 1466, 1351, 1296, 1250, 1120, 991, 947, 850, 730, 700 cm^{-1}; ^1H nmr: δ 0.88 (t, 3 H, J = 7 Hz), 1.19-1.41 (m, 14 H), 1.44-1.63 (m, 2 H), 3.36-3.84 (m, 27 H); ms (low volt) m/e: 434 (M^+). *Anal.* Calcd. for $C_{23}H_{46}O_7$: C, 63.56; H, 10.67. Found: C, 63.40; H, 10.41. 2-(Tetradecoxymethyl)-1,4,7,10,13,16-hexaoxacyclooctadecane (**10**) (0.91 g, 93%) was obtained as a white solid, mp: 39-40° (hexane);



SCHEME III. Syntheses of alkoxymethyl-substituted crown ethers 8-11.

ir (KBr): 2918, 2851, 1468, 1353, 1287, 1250, 1106, 969, 839, 721, 699 cm^{-1}; ^{1}H nmr: δ 0.88 (t, 3 H, J = 7 Hz), 1.16-1.44 (m, 22 H), 1.45-1.64 (m, 2 H), 3.37-3.86 (m, 27 H); ms (low volt) m/e: 490 (M$^+$). *Anal.* Calcd. for $C_{27}H_{54}O_7$: C, 66.09; H, 11.09. Found: C, 66.01; H, 10.82. 2-(Decoxymethyl)-1,4,7,10,13,16,19-heptaoxacycloheneicosane (**11**) (0.77 g, 80%) was obtained as a clear oil, ir (neat): 2924, 2856, 1465, 1350, 1297, 1250, 1118, 994, 946, 849, 722 cm^{-1}; ^{1}H nmr: δ 0.88 (t, 3 H, J = 7 Hz), 1.20-1.43 (m, 14 H), 1.45-1.63 (m, 2 H), 3.38-3.86 (m, 31 H); ms (low volt) m/e: 478 (M$^+$). *Anal.* Calcd. for $C_{25}H_{50}O_8$: C, 62.73; H, 10.53. Found: C, 62.98; H, 10.25.

Calorimetric Procedures

Log *K*, Δ*H*, and Δ*S* values were determined by direct and competitive calorimetric titrations with a Tronac titration calorimeter using described procedures (6,11). In the case of the interaction of K$^+$ with the 18-crown-6-type ligands, the log *K* value was larger than 5. Hence, a competitive procedure involving the titration of K$^+$ against the Na$^+$ ligand complex was used to determine log *K* for the K$^+$ ligand complex.

Membrane Separation Experiments

The DMHF membrane system (Figure 2) consisted of a glass 250-mL reservoir containing the source phase and another of equal volume containing the receiving phase. These aqueous phases were circulated by means of C-Flex or Norprene (Cole-Parmer) tubing and a Masterflex (Cole-Parmer) peristaltic pump through the lumen of a hollow-fiber bundle. Each fiber bundle was constructed of 60 lengths of polypropylene

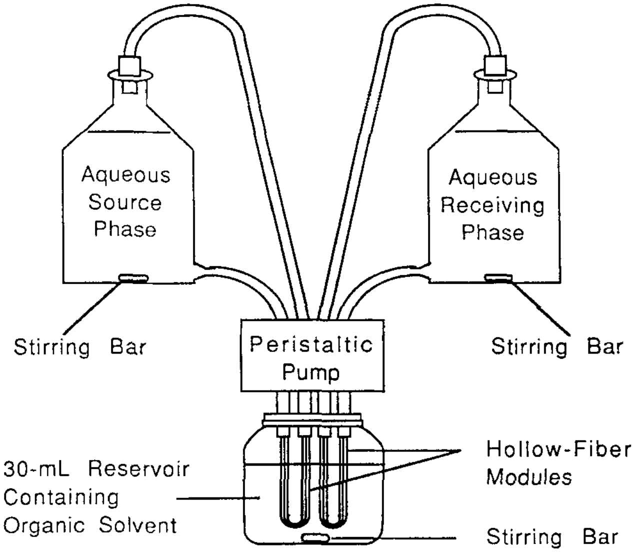


FIGURE 2. Schematic of the dual hollow-fiber membrane system.

microporous hollow-fibers, secured using polyethylene tubing connectors and silicone glue (Dow Corning and Mechanics Helper, Inc.). The fibers used, Celgerd X20 (Hoechst Celanese), have an inside diameter of 400 μm, an outside diameter of 456 μm, an effective pore size of 0.03 μm, and 40% porosity (manufacturer's specifications). Each fiber bundle was 15 cm in length, excluding the polypropylene tubing connectors. Two fiber bundles were held in a U-shape and immersed in a 60-mL membrane reservoir containing 25 mL of the membrane solvent/macrocycle solution. The average outside surface area of each bundle in 500 mL of pure and dry THF was added dropwise. The reaction mixture was stirred at rt for 1 d and then refluxed for 4 d. The solvent was evaporated under reduced pressure, and that was exposed to the solvent was 71 cm^2. Solvent and aqueous reservoirs were continuously stirred with Teflon-coated magnetic stirring bars and synchronous stirring motors at 600 rpm (Hurst Manufacturing Co.).

Each membrane experiment was run for at least 12 h. Samples for analysis were taken periodically (usually hourly) from the receiving phase. New hollow-fiber bundles were made for each experiment. The samples were analyzed for metal cation content using either AA spectrophotometry (Perkin Elmer Model 603) or ICP spectrophotometry (Perkin Elmer Model Plasma II). All experiments were performed in duplicate. Membrane and solvent extraction blank experiments, run in the absence of the macrocycle, were performed in each case to test for transport or extraction of cations not mediated by the macrocycle.

Solvent Extraction Experiments

Solvent extraction experiments were performed to determine equilibrium constant (K_{ex}) values for the reaction

$$M^{+}_{aq} + A^{-}_{aq} + L_{org} = MLA_{org}$$

for each metal ion, where M^+ = Na^+, K^+, Rb^+, or Cs^+, and A^- = NO_3^-, L was any of the four alkoxymethyl-substituted 18-crown-6 and 21 crown-7 ligands examined in this study. The organic diluent was 2-octanone. Equal volumes (5 mL) of the aqueous and organic phases were shaken by a Burrell Wrist Action shaker (model 75) until equilibrium of the organic phases (no changes in phase composition) was achieved. The cations were then stripped from the organic phase by back extraction to an aqueous receiving phase (distilled, deionized water). The measured changes in species concentration (M^{+}_{aq}) were used to determine K_{ex} values by the method of Ouchi et al. (12), which has been used for the extraction of cations plus coanions by neutral macrocycles.

RESULTS AND DISCUSSION

Synthesis of Ligands

There are two basic routes to prepare the alkoxymethyl-substituted macrocycles. Cyclization can be carried out with a precursor which already contains the desired alkoxymethyl unit. These cyclizations can be intramolecular (13) or intermolecular (14). Another approach to prepare these alkoxymethyl-substituted crown compounds is by using a protecting group on the precursor containing the hydroxymethyl moiety (15,16). After cyclization, the protecting group is removed and the resulting hydroxymethyl crown ether is alkylated. We used the latter synthetic pathway (Scheme II) to prepare alkyloxymethyl-substituted crown ligands (**8-11**) using the trityl group for protection (to form **4** and **5**). We chose the trityl group because it is easily removed (17,18) and it makes the crown ether more lipophilic so less polar solvents can be used for isolation and purification.

The starting materials for the trityloxymethyl-substituted crowns were prepared (Scheme I). 1-*O*-Tritylpropanetriol (**1**) was prepared as reported (8) with minor modifications. Ditosylates **2** and **3** were prepared from the appropriate oligoethylene glycol and tosyl chloride using an excess of powdered potassium hydroxide as a base in THF (9). This method produced pure products. Crude **2** solidified after standing for several days. To our knowledge, **2** has not been reported as a solid material.

Hydroxymethyl-substituted crowns **6** and **7** were prepared (Scheme II). Cyclization of **1** with **2** in the presence of NaH in THF gave trityloxymethyl-substituted 18-crown-6 (**4**, 62%) and with **3**, trityloxymethyl-substituted 21-crown-7 (**5**, 24%). The yield of this latter cyclization was not improved when the reaction was carried out in the presence of KBF_4 (Scheme IIB, 15%) or when KH was used instead of NaH (Scheme IIC, 21%). Compounds **4** and **5** were deprotected in a mixture of excess formic acid, propanol, and water to give hydroxymethyl-substituted crown ethers **6** (93%) and **7** (92%), respectively (Scheme IID). The side product, trityl alcohol, contaminated with a small amount of propyl trityl ether, was transformed into trityl chloride (90%, Scheme IIE). Thus, the expensive trityl chloride can be recycled in these synthetic procedures. It is relevant to note that **7** has been prepared previously through the benzyloxymethyl-substituted 21-crown-7 which was deprotected by catalytic hydrogenation (19-21).

Scheme III shows the preparation of alkoxymethyl-substituted 18-crown-6 ligands **8** (88%), **9** (92%), and **10** (93%), and decoxymethyl-substituted 21-crown-7 (**11**, 80%) starting from hydroxymethyl-substituted crowns **6** and **7** and the appropriate 1-bromoalkane. The overall yields of these products (50-55% for **8-10** and 18% for **11**) show that this is a valuable method to prepare these lipophilic macrocyclic ligands.

Binding of Metal Cations

Table 1 lists log K, ΔH, and $T\Delta S$ values determined in methanol at 25 °C for the reaction of the macrocyclic ligands studied with alkali metal cations. These ligand-cation systems illustrate in a systematic fashion the effect on cation binding of

TABLE 1. LOG *K*, ΔH, AND $T\Delta S$ VALUES FOR REACTIONS OF Na^+, K^+, Rb^+, AND Cs^+ WITH VARIOUS 18-CROWN-6 LIGANDS IN METHANOL AT 25°C

Ligand	Cation	Log *K*	ΔH(KJ/mol)	$T\Delta S$(KJ/mol)
18C6[a]	Na^+	4.32	-34.0	-9.5
DC18C6[a]		4.27	-19.9	5.2
Oct18C6[b]		3.91		
Dodec18C6[b]		3.93		
HexOMe18C6		3.81±0.12	-32.2	-10.4
DecOMe18C6		3.90±0.17	-29.6	-7.3
TetradecOMe18C6		3.96±0.14	-35.4	-12.8
18C6[a]	K^+	6.07	-56.8	-22.1
DC18C6[a]		5.63	-45.2	-13.1
Oct18C6[b]		5.03		
Dodec18C6[b]		5.28		
HexOMe18C6		6.21±0.13	-35.6	-0.15
DecOMe18C6		6.04±0.16	-33.6	0.88
TetradecOMe18C6		5.86±0.15	-38.8	-5.34
18C6[a]	Rb^+	5.82	-47.1	-13.8
DC18C6[a]		4.88	-35.7	-7.8
HexOMe18C6		4.83±0.16	-46.3	-18.7
DecOMe18C6		4.96±0.15	-46.9	-18.6
Tetradec18C6		4.88±0.18	-46.8	-18.9
18C6[a]	Cs^+	4.44	-49.9	-24.5
DC18C6[a]		4.25	-32.1	-7.83
HexOMe18C6		4.23±0.10	-45.4	-21.3
DecOMe18C6		4.22±0.18	-43.4	-19.3
TetradecOMe18C6		4.23±0.11	-46.8	-22.6

[a]Ref. 26 [b]Ref. 27

macrocycle substitutent chain length as well as the presence of the neutral oxygen donor-atom in the chain. In general, addition of carbon chain substituents to the crown ether ring results in a small decrease in complex stability with alkali metal ions compared to 18-crown-6. This decrease in stability is also observed when dicyclohexano units (DC18C6) or single aliphatic chains (Oct18C6 or Dodec18C6) are added to make the ligand hydrophobic. The drop in stability of complexes of crown ethers upon addition of hydrophobic substituents results from steric hindrances or changes in the macrocyclic ring conformation upon cation complexation and/or the lowering of solvation energy of the resulting complex (22).

The stability constant of the HexOMe18C6-K^+ complex is slightly higher than that of the 18C6-K^+ complex and much higher than the complexes of Oct18C6 and Dodec18C6 (see Figure 3). This result implies that, under the right conditions, the neutral oxygen atom in the side chain can participate in the binding of the cation. In terms of enthalpy and entropy contributions to stability, all the ligands studied formed strong enthalpy-stabilized complexes with the alkali metal cations. Since the atomic radius of Na^+ is smaller than the 18C6 cavity, Na^+ is not held strongly in the ligand cavity and the oxygen containing side arm does not assist in complexation. For this reason, the Na^+- ligand complexes have relatively small ΔH values.

Data in Table 2 show that the neutral oxygen donor in the ligand side chain can enhance the size-match selectivity for metal cations. Addition of the hexoxymethyl side chain increases ligand selectivity for K^+ (see Figure 3). As the substituent chain length increases in this series, the selectivity for K^+ over the other alkali cations decreases due to the greater steric destabilizing effect of longer chains mentioned above.

The data in Table 3 show that of the alkali metal cations, Cs^+ is bound most strongly by 21-crown-7 macrocycles. This results from the match of the ionic crystal radius of Cs^+ to the size of the 21-crown-7 cavity. However, DecOMe21C7 does not show the selectivity enhancement for Cs^+ over 21-crown-7 that the substituted 18-crown-6 compounds did for K^+ over 18-crown-6 (see Table 2). This is likely because the 21-crown-7 ring has greater ring flexibility than 18-crown-6 and can more easily complex the smaller cations by wrapping around them.

Membrane Separations

In a multiphase separation system, the hydrophobic substitutent in these new ligands is designed to improve the partition properties of the ligand so that it will

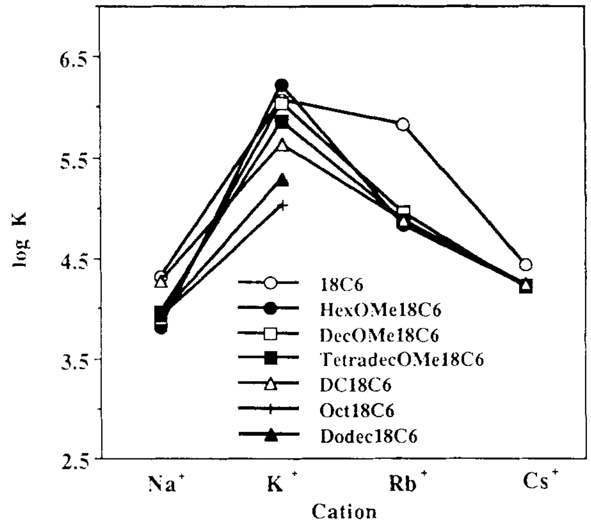


FIGURE 3. Comparison of alkali metal log K values for various ligands in methanol at 298.16 K.

TABLE 2. COMPARISON OF THE METAL ION SELECTIVITY[a] FOR DIFFERENT 18-CROWN-6 LIGANDS

Ligand	ΔLog*K*(K^+/Na^+)	ΔLog*K*(K^+/Rb^+)	ΔLog*K*(K^+/Cs^+)
18C6	1.75	0.25	1.63
DC18C6	1.36	0.75	1.38
HexOMe18C6	2.40	1.39	1.98
DecOMe18C6	2.14	1.08	1.82
TetradecOMe18C6	1.90	0.98	1.63

[a] ΔLog*K*(K^+/Na^+) = Log*K*(K^+) - Log*K*(Na^+)

TABLE 3. LOG *K*, Δ*H*, AND TΔ*S* VALUES FOR REACTIONS OF Na^+, K^+, Rb^+, AND Cs^+ WITH VARIOUS 21-CROWN-7 LIGANDS IN METHANOL AT 25°C

Ligand	Cation	Log *K*	Δ*H*(KJ/mol)	TΔ*S*(KJ/mol)
21C7[a]	Na^+	1.73	-43.4	-33.4
DecOMe21C7		1.6±0.2	-20.0	-11.1
21C7[a]	K^+	4.22	-35.9	-11.8
DecOMe21C7		3.8±0.2	-45.3	-23.8
21C7[a]	Rb^+	4.86	-40.4	-12.7
DecOMe21C7		4.4±0.2	-48.2	-23.2
21C7[a]	Cs^+	5.01	-46.8	-18.2
DecOMe21C7		4.4±0.1	-47.1	-21.9

[a] Ref. 26

remain in the organic phase. Membrane separation experiments were conducted using a dual-module hollow-fiber (DMHF) membrane contactor (Figure 2). In the present study, it was desired to show that the improved selectivities determined by log *K* values would be reflected in membrane fluxes.

Table 4 shows cation fluxes for all ligands studied from a neutral source solution containing equimolar amounts of the alkali metal nitrate salts. In each case, the selectivities determined by titration calorimetry were maintained. Experiments using alkoxymethyl-substituted 18-crown-6 ligands showed selectivity of K^+ over Rb^+, Na^+, and Cs^+. This is shown for HexOMe18C6 in Figure 4. As expected, experiments that employed alkoxymethyl-substituted 21-crown-7 as a carrier resulted in selectivity of Cs^+ over the other alkali metal cations. As a result, 18-crown-6-based ligands can effectively be used to separate K^+ ions from the other alkali metal cations, while 21-crown-7-based ligands are effective in the separation of Cs^+ from the other alkali metal cations.

Due to the higher K^+ selectivity of HexOMe18C6 over DecOMe18C6, HexOMe18C6 is a more effective carrier than DecOMe18C6. TetradecOMe18C6

TABLE 4. COMPETITIVE TRANSPORT OF METAL CATIONS ACROSS A 2-OCTANONE MEMBRANE FROM A NEUTRAL SOURCE PHASE[a]

Carrier Transport	Average Cation Flux and Standard Deviation (mol·s^{-1}·m^{-2}) x 10^{-7}	Total Cation Flux (mol·s^{-1}·m^{-2}) x 10^{-7}	Selectivity Order
HexOMe18C6	K^+(2.7±0.2) Rb^+(0.57±0.04) Na^+(0.33±0.05) Cs^+(0)	3.6	$K^+>Rb^+>Na^+>Cs^+$
DecOMe18C6	K^+(2.2±0.2) Rb^+(1.0±0.7) Na^+(0.067±0.004) Cs^+(0)	3.3	$K^+>Rb^+>Na^+>Cs^+$
TetradecOMe18C6	K^+(2.8±0.4) Rb^+(0.44±0.03) Na^+(0.065±0.004) Cs^+(0)	3.3	$K^+>Rb^+>Na^+>Cs^+$
DecOMe21C7	Cs^+(1.6±0.5) Rb^+(0.96±0.04) K^+(0.45±0.04) Na^+(0.10±0.03)	3.1	$Cs^+>Rb^+>K^+>Na^+$

[a] Transport in a 0.1 *M* $NaNO_3$, 0.1 *M* KNO_3, 0.1 *M* $RbNO_3$, or 0.1 *M* $CsNO_3$/1.0 m*M* ligand in a 2-octanone/H_2O liquid membrane.

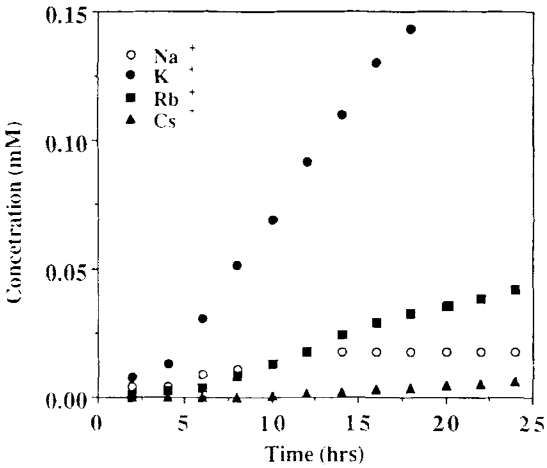


FIGURE 4. Transport of cations with the DMHF system using HexOMe18C6 as a carrier.

TABLE 5. EXTRACTION EQUILIBRIUM CONSTANTS FOR INTERACTION OF SOME ALKOXYMETHYL-SUBSTITUTED 18-CROWN-6 AND 21-CROWN-7 LIGANDS WITH ALKALI METAL CATIONS

Macrocycle	K_{ex}[a]			
	Na^+	K^+	Rb^+	Cs^+
HexOMe18C6	0.09	2.04	0.51	0.10
DecOMe18C6	0.09	2.04	0.52	0.10
TetradecOMe18C6	0.19	2.10	0.53	0.13
DecOMe21C7	0.10	0.04	0.13	1.76

[a] Extraction equilibrium constant, $M^+(aq) + A^-(aq) + L(org) = MLA(org)$

demonstrates approximately the same efficiency as HexOMe18C6 as a membrane carrier. Because TetradecOMe18C6 has a longer hydrophobic chain, it is retained more completely in the organic phase and offers greater potential for use in membranes. The 21-crown-7-based ligand reveals less selectivity for Cs^+ in the membrane, as was also true in homogeneous solution equilibria.

Solvent Extractions

In order to understand the membrane separation behavior, extraction equilibrium constants (K_{ex}) were determined by solvent extraction experiments for the different alkoxymethyl-substituted crown ether ligands with alkali metal cations. Results are summarized in Table 5. For each 18C6-based ligand, the extraction sequence is K^+ > Rb^+ > Na^+, Cs^+; for the 21C7-based ligand; the extraction sequence is Cs^+ > Rb^+ > Na^+, K^+. These extraction sequences are consistent with the sequences determined from membrane experiment flux values. Transport of cations and accompanying anions by neutral macrocycles has been shown to be diffusion-limited in the boundary area (7,23,24,25). Based on this fact, we have developed a model (25) to predict cation fluxes and selectivities for the hollow-fiber-supported liquid membrane system. At special experimental conditions, the model parameters, other than K_{ex} values, can be considered as constant. The selectivity in cation transport then will be proportional to the extraction order. The results in this study further demonstrate the usefulness of our model. Since the K_{ex} value is influenced by many factors of the system, it needs to be explored in more detail.

ACKNOWLEDGMENTS

We wish to thank the Department of Energy, Office of Basic Energy Sciences for Grant No. DE-FG02-86ER-13463. We appreciate the help of undergraduate Randy Peterson who made some of the membrane separation experiments.

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