# *Communications to the Editor*

## Bifunctional Recognition: Simultaneous Transport of Cations and Anions through a Supported Liquid Membrane

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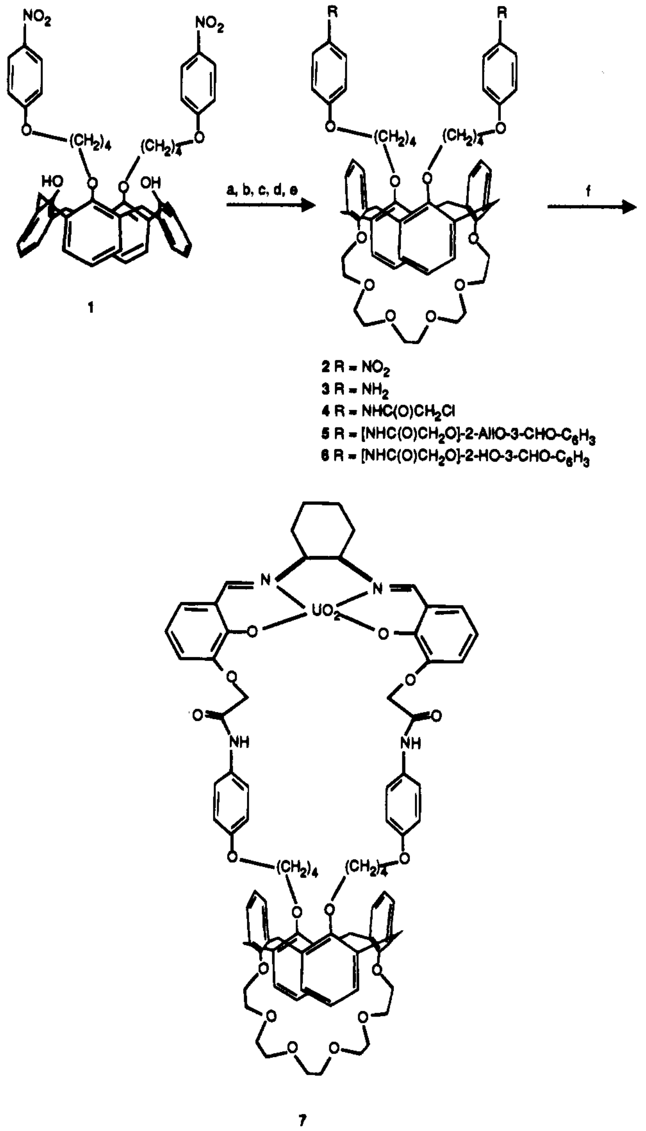
The design and synthesis of macrocyclic cation receptors is very well documented in supramolecular chemistry.[1] Despite anion recognition being a relatively new area of research, both positively charged and neutral receptors for anionic species have been prepared in the last few years.[2] Recently we described the synthesis of *neutral bifunctional receptors* for the *simultaneous complexation of hydrophilic anions and cations* in organic media.[3] In these receptors, the appropriate binding sites for both anionic and cationic species are covalently combined in a neutral molecule.[4] In this Communication, we report our preliminary results on simultaneous transport of cations and anions through a supported liquid membrane (SLM) assisted by a novel type of neutral bifunctional receptor. To the best of our knowledge, this is the first example of carrier-assisted cotransport, in which the anion and cation of a *hydrophilic* salt are *bound* and transported simultaneously through a membrane.[5-7]

Our synthetic strategy is based on the attachment of both cation and anion binding sites to the rigid lipophilic calix[4]arene platform (Scheme 1).[8] It is known that the covalent combination of a Lewis acidic $UO_2$ center and amido C(O)NH moieties provides an excellent receptor site for dihydrogen phosphate ($H_2PO_4^-$) and chloride ($Cl^-$) anions[9] and that the calix[4]arene crown-6 (1,3-alternate) fragment is capable of selective complexation of cesium ion ($Cs^+$).[10]

**Scheme 1**



[a] (a) $TsO(CH_2CH_2O)_5Ts$, $Cs_2CO_3$, MeCN; (b) Raney Ni, $NH_2NH_3OH$, EtOH; (c) $ClCH_2C(O)Cl$, $Et_3N$, $CH_2Cl_2$; (d) 2-(2-allyloxy)-3-hydroxybenzaldehyde, $K_2CO_3$, KI, MeCN; (e) $Pd(OAc)_2$, $PPh_3$, $Et_3N$, HCOOH, $EtOH$-$H_2O$, 4:1; (f) *cis*-1,2-cyclohexanediamine, $UO_2(OAc)_2{\cdot}2H_2O$, MeOH.

Calix[4]arene diether **1** was prepared by alkylation of unsubstituted calix[4]arene[11] with *p*-(4-bromobutyl)nitrophenol in the presence of 1 equiv of $K_2CO_3$ as a base in refluxing acetonitrile in 61% yield. Alkylation of **1** with penta(ethylene glycol) ditosylate and $Cs_2CO_3$ as a base in acetonitrile gave calix[4]arene **2** in the 1,3-alternate conformation in 57% yield. Subsequent reduction of **2** with Raney Ni in refluxing ethanol gave quantitatively the corresponding diaminocalix[4]arene **3**. Reaction of **3** with chloroacetyl chloride in the presence of $Et_3N$

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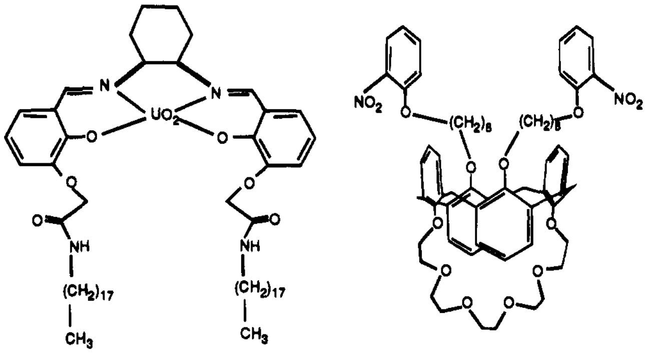
**Chart 1**



**8** **9**

in $CH_2Cl_2$ gave the corresponding 1,3-bis(chloroacetamido)calix[4]arene **4** in 69% yield. Dialdehyde **5** was obtained by alkylation of 2-(2-allyloxy)-3-hydroxybenzaldehyde[12] with **4** in the presence of $K_2CO_3$ and KI in 59% yield. Subsequent palladium-catalyzed deallylation[13] of calixarene **5** afforded dialdehyde **6** in quantitative yield, which was used without purification for the cyclization step. Reaction of **6** with *cis*-1,2-cyclohexanediamine and $UO_2(OAc)_2 \cdot 2H_2O$ in refluxing methanol under high dilution conditions gave receptor **7**, which was isolated in 11% yield after column chromatography.[14] Compound **7** has been used as a carrier to investigate the transport of hydrophilic cesium chloride (CsCl) and the more lipophilic cesium nitrate ($CsNO_3$) [$\Delta G^\circ_{tr}$ ($X^-$, $H_2O \rightarrow$ MeCN) = 42.1 and 21.0 kJ/mol for $Cl^-$ and $NO_3^-$, respectively[15] ] across a supported liquid membrane composed of a porous polymeric support (Accurel) impregnated with *o*-nitrophenyl *n*-octyl ether (NPOE).[5d] For comparison, the same experiment was performed with the receptors **8**[9] and **9**,[10] which have only either anion or cation binding sites, respectively (Chart 1) (Table 1).

**Table 1.** Salt Fluxes[a–c] through a Supported Liquid Membrane Measured for Different Carriers[d,e] in NPOE

| carrier | $CsNO_3$ flux | CsCl flux |
|---|---|---|
| **8** | 0.02 | 0.07 |
| **9** | 5.50 | 0.42 |
| **7** | 0.89 | 1.20 |

[a] Salt concentration, 0.1 mol $L^{-1}$. [b] Fluxes (in units of $10^{-7}$ mol $m^{-2}$ $s^{-1}$) after 24 h at 298 K. [c] Blank fluxes of the salts in NPOE, for CsCl, $0.05 \times 10^{-7}$ mol $m^{-2}$ $s^{-1}$, and for $CsNO_3$, $0.02 \times 10^{-7}$ mol $m^{-2}$ $s^{-1}$. [d] Carrier in the membrane, 0.01 M. [e] No leakage of receptors was observed in blank experiments.

The transport processes for $CsNO_3$ and CsCl are different; $NO_3^-$ is much more lipophilic[15] than $Cl^-$, and only $NO_3^-$ can easily follow the complexed $Cs^+$ cation through the hydrophobic membrane, even in the absence of anion carrier.[5d] With the cation carrier **9**, a high flux of $CsNO_3$ ($5.5 \times 10^{-7}$ mol $m^{-2}$ $s^{-1}$) (Table 1) was observed, but the anion receptor **8**, which is not selective[9] for $NO_3^-$, did not transport $CsNO_3$. The flux was very low ($0.02 \times 10^{-7}$ mol $m^{-2}$ $s^{-1}$) and comparable with the (blank) flux obtained without carrier. It implies that, probably, in the case of **9**, *only* the cation binding site is responsible for the transport.

The transport of CsCl by the monofunctional carriers **8** (anion) and **9** (cation) exhibits low flux values of $0.07 \times 10^{-7}$ and $0.42 \times 10^{-7}$ mol $m^{-2}$ $s^{-1}$, respectively (Table 1). Obviously, when one of the ionic species is complexed, the uncomplexed counterion cannot sufficiently penetrate the lipophilic membrane.

However, a significant flux ($1.20 \times 10^{-7}$ mol $m^{-2}$ $s^{-1}$) was observed for bifunctional carrier **7** with CsCl, which is much higher than the corresponding fluxes for the monofunctional carriers **8** and **9**. At the same time, carrier **7** showed a surprisingly low flux of $CsNO_3$ ($0.89 \times 10^{-7}$ mol $m^{-2}$ $s^{-1}$) when compared with that observed for cation receptor **9** ($5.50 \times 10^{-7}$ mol $m^{-2}$ $s^{-1}$). This proves that (i) *both* anion and cation binding sites of **7** are involved in the complexation and (ii) the presence of only an anion or a cation binding site in the receptor molecule is *not sufficient* for effective transport of a *hydrophilic* salt such as CsCl. But more important is that this suggests a *preference* of hydrophilic CsCl over lipophilic $CsNO_3$.[16]

These results indicate the unique feature of receptors in which both binding sites are *covalently* linked.

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[14] Selected data for **7**: mp 244–245 °C; $^1H$ NMR ($CDCl_3$–$CD_3OD$ 5:1) $\delta$ 9.21 (s, 2 H), 7.42 (d, $J$ = 8.2 Hz, 4 H), 7.17, 7.11 (2 × d, $J$ = 8.0 Hz, 4 H), 7.0–6.8 (m, 10 H), 7.71 (t, $J$ = 7.6 Hz, 2 H), 7.62 (t, $J$ = 8.0 Hz, 2 H), 6.50 (d, $J$ = 8.2 Hz, 4 H), 4.69 (s, 4 H), 4.6–4.5 (m, 2 H), 3.78 (s, 8 H), 3.54 (s, 4 H), 3.5–3.2 (m, 20 H), 3.15 (t, $J$ = 7.0 Hz, 4 H), 2.4–2.3 (m, 2 H), 2.1–1.9 (m, 8 H), 1.5–1.3 (m, 6 H); MS-FAB $m/z$ 1656.3 [(M + H)$^+$, calcd 1656.0]. Details of the synthesis will be published in a full article.

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[16] In competition experiments with **7**, utilizing equimolar quantities of CsCl and $CsNO_3$ (0.05 M each), the receiving phases were analyzed, and a [$Cl^-$]/[$NO_3^-$] ratio of ~1:1 was obtained. For comparison, a [$Cl^-$]/[$NO_3^-$] ratio of 0.02:1 was observed[17] in the competitive transport of potassium salts across a chloroform liquid membrane, mediated by dibenzo-18-crown-6.

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