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 UO₂ center and amido C(O)NH moieties provides an excellent receptor site for dihydrogen

Scheme 1

^a (a) TsO(CH₂CH₂O)₅Ts, Cs₂CO₃, MeCN; (b) Raney Ni, NH₂NH₃OH, EtOH; (c) ClCH₂C(O)Cl, Et₃N, CH₂Cl₂; (d) 2-(2-allyloxy)-3-hydroxybenzaldehyde, K₂CO₃, KI, MeCN; (e) Pd(OAc)₂, PPh₃, Et₃N, HCOOH, EtOH-H₂O, 4:1; (f) *cis*-1,2-cyclohexanediamine, UO₂(OAc)₂·2H₂O, MeOH.

phosphate (H₂PO₄[−]) and chloride (Cl[−]) anions⁹ and that the calix[4]arene crown-6 (1,3-alternate) fragment is capable of selective complexation of cesium ion (Cs⁺).¹⁰

Calix[4]arene diether **1** was prepared by alkylation of unsubstituted calix[4]arene¹¹ with *p*-(4-bromobutyl)nitrophenol in the presence of 1 equiv of K₂CO₃ as a base in refluxing acetonitrile in 61% yield. Alkylation of **1** with penta(ethylene glycol) ditosylate and Cs₂CO₃ 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 Et₃N

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Chart 1

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-hydroxybenzaldehyde¹² with **4** in the presence of K_2CO_3 and KI in 59% yield. Subsequent palladium-catalyzed deallylation¹³ 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 $\text{UO}_2(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ 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

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(14) Selected data for **7**: mp 244–245 °C; ^1H NMR (CDCl_3 - CD_3OD 5:1) δ 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 ($[\text{M} + \text{H}]^+$, calcd 1656.0). Details of the synthesis will be published in a full article.

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 , 0.05×10^{-7} mol m^{-2} s^{-1} , and for CsNO_3 , 0.02×10^{-7} mol m^{-2} s^{-1} . ^d Carrier in the membrane, 0.01 M. ^e No leakage of receptors was observed in blank experiments.

lipophilic cesium nitrate (CsNO_3) [$\Delta G^\circ_{\text{tr}}(\text{X}^-, \text{H}_2\text{O} \rightarrow \text{MeCN}) = 42.1$ and 21.0 kJ/mol for Cl^- and NO_3^- , respectively¹⁵] 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).

The transport processes for CsNO_3 and CsCl are different; NO_3^- is much more lipophilic¹⁵ 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 (5.5×10^{-7} mol m^{-2} s^{-1}) (Table 1) was observed, but the anion receptor **8**, which is not selective⁹ for NO_3^- , did not transport CsNO_3 . The flux was very low (0.02×10^{-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 0.07×10^{-7} and 0.42×10^{-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 (1.20×10^{-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 (0.89×10^{-7} mol m^{-2} s^{-1}) when compared with that observed for cation receptor **9** (5.50×10^{-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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(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 $[\text{Cl}^-]/[\text{NO}_3^-]$ ratio of $\sim 1:1$ was obtained. For comparison, a $[\text{Cl}^-]/[\text{NO}_3^-]$ ratio of 0.02:1 was observed¹⁷ in the competitive transport of potassium salts across a chloroform liquid membrane, mediated by dibenzo-18-crown-6.

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