Calix[6]arene Bearing Carboxylic Acid and Amide Groups in Polymeric CTA Membrane

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Calix[6]arene having both carboxylic acid (1,3,5-) and carboxamide (2,4,6-) in an alternative way was synthesized. Transport rates of alkali and alkaline-earth metal ions were tested in bulk liquid membrane and polymer inclusion membrane. Ba^{2+} ion was found to give the highest transport rate among tested metal ions in both BLM and PIM systems. In PIM system, high durability (longer than 30 days) of the membrane was observed.

Key words : Calix[6]arene, Membrane, Transport experiment, Polymer inclusion membrane

Introduction

Calixarenes, which are macrocyclic compounds available in a variety of ring sizes, are of particular interest as inclusion hosts for ions and specific molecules.[1-3] While crown ethers and azacrown ether attached calix[4]arenes have long been interesting to chemists for synthesis as well as for their metal ion recognition,[4] calix[6]arene was not that attractive not only because synthesis of the calix[6]arene derivatives is difficult but also because the conformations of the product is too complicated to be assigned. Recently, these calix[6]arenes having both carboxamide and carboxylic acid tails by alternative pattern have been intensively stuided in selective separation of the lanthanides and actinides which can exist in atomic nuclear wastes.[5] Am^{3+} selectivity (separation factor) over lanthanides in two-phase extraction experiment was found to be 108 at pH 3.0.[5] However, transport through polymer inclusion membrane (PIM) and bulk liquid membrane (BLM) of the metal ions using the calix[6]arene derivatives have not been reported yet.

Simple two phase extraction, bulk liquid membrane (BLM), and supported liquid membrane (SLM) using calixcrown derivatives has been explored to investigate binding capabilities, transport rates, and transport permeability for the cesium ion.[6] As one of the membrane technologies, polymeric inclusion membrane (PIM) system has been recently investigated taking advantages of (i) easy setup, (ii) high selectivity, and (iii) high durability, has been developed.[7,8] PIMs with cellulose triacetate (CTA) polymer as a supporter, together with a hydrophobic non-volatile organic solvent (*e.g.*, NPOE) as a plasticizer and an organic carrier were found to cover the several problems occurred in SLM system such as loss of organic carrier with plasticizer into aqueous solution, slow transport rate, and low durability.[6-8] We now report the experimental results of the transport flux values for the metal ions using calix[6]arene derivative **4** in PIMs system (single and competitive ion experiments) along with permeability coefficient (P).

Experimental Section

Unless specified otherwise, reagent-grade reactants and solvents were obtained from chemical suppliers and used as received. Deionized water was prepared by passing distilled water through an Organo G-10 cartridge. Calix[6]arene derivative **1** was prepared by the adaptation of the reported procedures.[5]

Syntheses.

*1,3,5-Trimethyl-2,4,6-tricarboxamide-p-tert-butylcalix[6] arene (**2**)*: A mixture of 1.0 g (0.98 mmole) of 1,3,5-trimethyl-*p*-*tert*-butylcalix[6]arene, 0.497 mL (3.92 mmole) of *N*,*N*-diethyl-2-chloroacetamide, and 0.542 g (3.92 mmole) of K_2CO_3 in 150 mL of acetonitrile refluxed for 20 hrs. The crude mixture was dissolved in CH_2Cl_2 and the treated with 10% HCl solution. The organic layer was dried over $MgSO_4$. Recrystallization of the product from CH_2Cl_2/ MeOH (9:1) gave a white crystal in 80% yield. IR (KBr pellet, cm^{-1}): 3452, 2985.5, 2370.8, 1637.2, 1482.7, 1019.4. ^1H NMR (300 MHz, $CDCl_3$): δ 7.2-7.3 (d, 6H, Ar*H*), 6.59-6.68 (s, 6H, Ar*H*), 4.6 (s, 6H, O*CH*$_2$C), 3.56-4.55 (m, 12H, Ar*CH*$_2$Ar), 2.2 (s, 9H, -*CH*$_3$), 1.15-1.33 (q, 9H, NCH$_2$*CH*$_3$), 1.38 (s, 27H, *t*-Bu), 0.77 (s, 27H, *t*-Bu). FAB-MS *m/z* (M^+) calcd. 1454.92, found 1454.90.

*1,3,5-Tricarboxamide-p-tert-butylcalix[6]arene (**3**)*: Under nitrogen atmosphere, a mixture of 1.0 g (0.74 mmole) of 1,3,5-trimethyl-2,4,6-tricarboxamide-*p*-*tert*-butylcalix[6]arene, 0.70 mL (4.94 mmole) of iodotrimethylsilane, 0.36 g (2.95 mmole) of sodium perchlorate in 150 mL of chloroform refluxed for 4 hrs. After the chloroform was removed *in*

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vacuo, the crude mixture was dissolved in CH_2Cl_2 and the treated with 10% HCl solution. The organic layer was dried over $MgSO_4$. Recrystallization of the product from EtOAc : hexane (1:4) gave a white crystal in 66% yield. IR (KBr pellet, cm^{-1}): 3414.3, 2965.5, 2347.7, 1652.6, 1482.7, 1204.7; ^{1}H NMR ($CDCl_3$): δ 7.26-6.84 (t, 12H, Ar*H*), 4.59-4.47 (m, 6H, -CH_2C), 4.28-3.44 (m, 12H, ArCH_2Ar), 3.38-3.28 (m, 12H, N$CH_2$$CH_3$), 1.25-0.99 (m, 9H for $NCH_2$$CH_3$, 54H for *t*-Bu). FAB-MS *m/z* (M^+) calcd. 1312.84, found 1312.80.

1,3,5-Tricarboxylic acid-2,4,6-tricarboxamide-p-tert-butylcalix[6]arene (4): Under nitrogen atmosphere, to a solution of 1.0 g (0.76 mmole) of 1,3,5-triamide-*p*-*tert*-butylcalix[6]arene in THF, 0.547 g (22.8 mmole) of sodium hydride was added slowly at 0 °C. 0.63 g (4.56 mmole) of bromoacetic acid in 10 mL of THF was added dropwise at 0 °C. Upon the complete addition, the reaction mixture was refluxed for 10 hrs. After the THF was removed *in vacuo*, the crude mixture was dissolved in CH_2Cl_2 and the treated with 10% HCl solution. The organic layer was dried over $MgSO_4$. Recrystallization of the product from CH_2Cl_2/MeOH (9:1) gave a colorless crystal in 82% yield. IR (KBr pellet, cm^{-1}): 2965.5, 1753, 1644.9, 1482.7, 1197, 1119.8, 1058; ^{1}H NMR ($CDCl_3$): δ 7.12-7.0 (s, 6H, Ar*H*), 6.9-6.8 (s, 6H, Ar*H*), 5.3 (s, 3H -O*H*), 4.5 (s, 12H, OCH_2C), 3.8 (m, 6H, ArCH_2Ar), 3.4 (m, 6H, for ArCH_2Ar, 12H for N$CH_2$$CH_3$), 1.21-1.16 (m, 18H for $NCH_2$$CH_3$, 27H for *t*-Bu), 1.05 (s, 27H, *t*-Bu). FAB MS *m/z* (M^+): calcd 1486.95, found 1486.60.

Bulk Liquid Membrane. Membrane transport experiments were carried out using a bulk liquid membrane cell based on the concept of the Schulman bridge at 25 °C.[9] The bottom half of the cell was filled with 3.0 mL of 1.0 mM solution of the organic ligand **4** in chloroform and a glass tube is inserted. The interior of the tube above the organic media is filled with a 0.8 mL of 0.1 M metal ion solution as a source phase. The outer cylinder is filled with 5.0 mL of deionized water as a receiving phase. The details of the transport conditions are summarized in the footnotes of Table 1. The receiving phase was sampled after 24 hours stirring with 120 rpm at 25 °C and analyzed for cation concentration using an atomic absorption spectrometer.

CTA Membrane and transport experiment. Cellulose triacetate, CTA (0.062 g) in 5.0 mL of CH_2Cl_2 was mixed with 3.0 mL of 10% (v/v) NPOE (2-nitrophenyloctyl ether) in CH_2Cl_2 and 0.50 mL of 10% (v/v) tris(2-butoxyethyl) phosphate (TBEP) in CH_2Cl_2, and 2.0 mL of the ligand **4** (1.0 mM) in CH_2Cl_2. The NPOE and TBEP were used as membrane plasticizers. The solvent of this mixed solution was allowed to slowly evaporate in a 9.0 cm diameter petri dish which was covered by a watch glass. After 18-hour evaporation, a few drops of water were swirled on top of the film to help loosen it from the glass.[7] The polymer film was then carefully peeled off the petri dish. The thickness of the membrane film was 30 μm. The membrane was placed between 200 mL of two cylindrical glass vessels. The area of the membrane was 19.6 cm^2. Both source and receiving aqueous phase were stirred with glass stirrers at about 600 rpm by synchronous motors at 25 °C. The initial concentration of $LiNO_3$, $NaNO_3$, KNO_3, $RbNO_3$, $CsNO_3$, $Mg(NO_3)_2$, $Ca(NO_3)_2$, $Sr(NO_3)_2$, and $Ba(NO_3)_2$ was 0.010 M, respectively. 5.0 mL from the receiving phase was periodically taken and the metal cations transported from source phase into receiving phase through PIM were determined by atomic absorption spectrometer. Three independent experiments were employed in the determination of each cation transport rate and permeability constant. The standard deviations were less than ±10%.

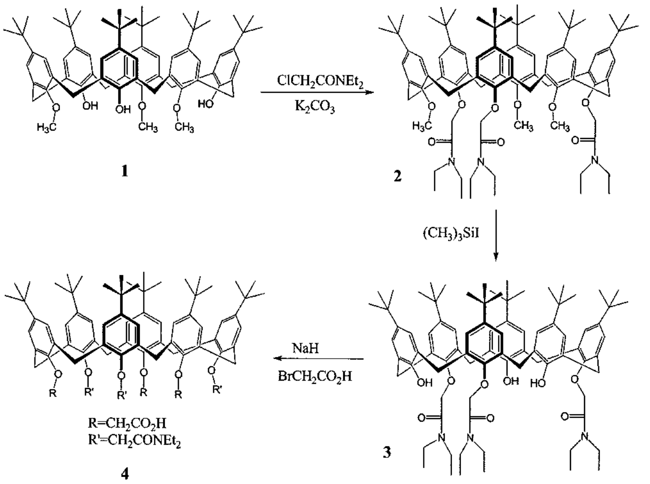
Table 1. Single ion transport values for alkali metal ions and alkaline-earth metal ions through a bulk liquid membrane using **4**[a]

Metal	Transport rate (10^{-8} mol·s^{-1}·m^{-2})[b]								
	Li^+	Na^+	K^+	Rb^+	Cs^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
	5.94	7.18	14.28	2.05	1.24	2.23	8.93	14.75	21.33

[a]Transport condition: source phase (aqueous solution of metal nitrate, 0.8 mL, 0.1 M); membrane phase ($ClCH_2CH_2Cl$, 3.0 mL), (carrier) = 1.0 mM; i.d. of glass vial = 18 mm, stirred by 13 mm Teflon-coated magnetic stirring bar driven by a Hurst Synchronous motor; receiving phase (deionized water, 5.0 mL). [b]The average value of three independent determinations. The experimental values deviate from the reported values by an average of 10%.

Results and Discussion

The synthetic scheme for **4** is shown in Scheme 1. Synthetic procedures for the target molecule were followed the method for *para-tert*-octylcalix[6]arene derivatives already reported.[5] To attach the three carboxylic acids on lower rim of the calix[6]arene unit by 1,3,5-alternative type, selective methylation should be carried out in advance. Alkylation of **1** with ethyl 2-bromoacetate in the presence of metal carbonate gave a low yield (less than 10%). So, we carried out amidoalkylation using *N,N*-diethyl 2-chloroacetamide prior to attaching the three carboxylic acids, then we obtained compound **2** in 80% yield. Demethylation of **2** using iodotrimethylsilane and sodium perchlorate gave **3** as a white crystal in 66% yield. Alkylation of **3** using 2-bromoacetic acid and NaH as a base in THF gave the desired target



Scheme 1. Synthetic scheme for **4**.

Table 2. Transport rates of alkali metal ions and alkaline-earth metal ions through a PIM using **4**

	Transport rate (10^{-5} mol·h^{-1}·m^{-2})[a]								
	Li^+	Na^+	K^+	Rb^+	Cs^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
4	0	6.10	8.45	0	1.64	3.22	6.73	10.57	124.88

[a]Transport condition: source phase (aqueous solution of metal nitrate 10 mM); membrane phase (CTA membrane), [carrier] =1.0 mM; receiving phase: deionized water.

molecule **4** as a white solid in 82% yield.

To measure the binding ability of the **4** toward alkali and alkaline-earth metal ions, firstly we used a bulk liquid membrane (BLM) system. The results of the measurement of single ion transport rate are described in Table 1. Among alkali metal ions, K^+ ion was found to move the most rapidly from source into receiving phase through bulk organic medium by a rate of 14.28×10^{-8} mol s^{-1} m^{-2}. For alkaline-earth metal ions, the transport rate of Ba^{2+} ion was the largest by 21.33×10^{-8} mol s^{-1} m^{-2}. So, it is presumed that Ba^{2+} ion is selectively bound to the calix[6]arene **4**, then demetalation rate from organic medium into the receiving phase is also fast although the rate-determining step between two process (complexation and decomplexation) could not be determined.

To study the binding ability of the **4** considering transport rate from source phase into receiving phase by an organic medium, we used a polymeric inclusion membrane (PIM) which is modeled after the diketone-containing membranes developed by Sugiura.[7] They are formed by the polymerization of cellulose triacetate (CTA) to give a thin film.[7] The PIM is then placed between an aqueous source and a receiving phase. While PIM can effectively separate two aqueous phases, they are independent of the organic solvents in maintaining phase separation and in allowing continuous transport. Transport rates of the alkali and alkaline-earth metal ions through PIM when ligand **4** were used are listed in Table 2. Like in the case of BLM, Ba^{2+} ion was found to give a selective transport through the PIM. Selectivity of Ba^{2+}/Mg^{2+} is more than 40 which is the largest value ever known so far. In a control experiment, no transport rate was detected in the absence of the ligands during more than 60-hour continuous run.

Permeability coefficient (*P*, m·s^{-1}) was determined by plotting the logarithm of Cs/Co *vs* time according to Eq. (1)

$$\ln(Cs/Co) = -(P\,S/V)\,t \qquad (1)$$

where Co is the initial concentration of the cation in the source phase, Cs denotes the metal ion concentration in the source phase as a function of time. V and S are for volume of source phase and for membrane area, respectively.[8] To obtain the permeability coefficient of the alkali and alkaline-earth metal ions, several different experimental sets were performed. The results are listed in Table 3 and depicted in Figure 1 and Figure 2. The slope for ln(Cs/Co)/(S/V) *vs* time (h) indicates the permeability coefficient (*P*). Potassium ion provided the largest permeability coefficient (-5.0) among alkali metal ions. In the case of alkaline-earth metal ions, barium ion gave -4.0 of permeability coefficient that is the largest among alkaline-earth metal ions. The Log *P* values increased with carrier concentration and reach a maximum

Table 3. Logarithm of permeability coefficients of alkali metal ions and alkaline-earth metal ions using **4**

Metal	Log P (m·s^{-1})[a]								
	Li^+	Na^+	K^+	Rb^+	Cs^+	Mg^{2+}	Ca^{2+}	Sr^{2+}	Ba^{2+}
	0	-5.10	-5.00	0	-5.70	-5.40	-5.10	-5.00	-4.00

[a]Transport condition: source phase (aqueous solution of metal nitrate 10 mM); membrane phase (CTA membrane); [carrier] = 1.0 mM; receiving phase: deionized water.

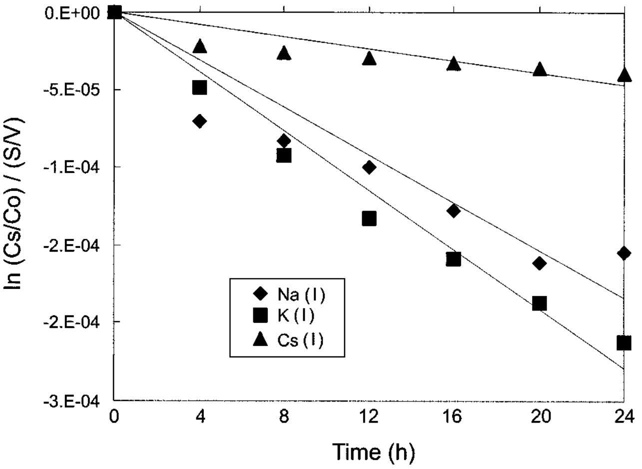


Figure 1. Kinetic plot of the permeability for alkali metal ions as a function of time (h) through a PIM. Source phase: aqueous solution of 10 mM metal nitrate; membrane phase: CTA membrane; [carrier] = 1.0 mM; receiving phase: deionized water.

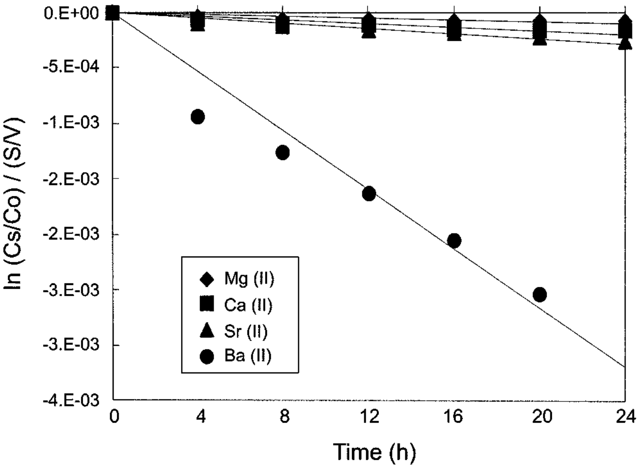


Figure 2. Kinetic plot of the permeability for alkaline-earth metal ions as a function of time (h) through a PIM. Source phase: aqueous solution of 10 mM metal nitrate; membrane phase: CTA membrane; [carrier] = 1.0 mM; receiving phase: deionized water.

at 10 mM of **4**. This relationship also complies with the diffusion-based mathematical model for organic ligand across a liquid membrane described by McBride.[10] To examine the long-term stability of the PIMs, same membrane containing **4** was repeatedly reloaded in successive experiments. Measurement of the transport flux every 4-hour gave constant values up to 30 days. After 30 days we observed some rust in the membrane, then observed small decline of permeability. PIM system retained a transparent solution without any loss of the organic materials into aqueous solutions during 30-days of stirring, indicating its excellent durability.

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