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Synthesis of new bis-calix[4]arenes with imine linkages. A search for new silver-selective sensors

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Abstract—We synthesized a series of new bis-calix[4]arenes with imine units in high yields by using a simple condensation procedure, and two of these bis-calix[4]arenes were tested as sensors in solid-state electrodes. High selectivity for Ag^+, even over that of Hg^{2+}, and excellent electrode properties were found. © 2001 Elsevier Science Ltd. All rights reserved.

There has been a lot of research activity on the synthesis of sensors for metal ions, anions and organic analytes.[1] Recently, one of us reported a silver(I) ion-selective PVC membrane based on a bis-pyridine tetramide macrocycle.[2] Progress has still to be made in relation to the design and synthesis of sensors for environmentally or biologically important cations like silver, which has use in cancer immunotherapy, and industrial interest in the separation of silver from waste stream effluents and the use of silver complexes in photographic materials. Calixarenes with appropriate appended groups are good candidates for this because they have been shown to be highly specific ligands[3] and their potential as sensing agents has received increasing interest.[4]

Recently, Reinhoudt et al.[5] have synthesized head-to-head-linked double calix[4]arenes that complex silver ions selectively and the selectivity of complexation was studied by chemically modified field-effect transistor measurements.

Previously, one of us reported the synthesis of different series of polyaza macrocycles and macrobicycles containing two or three 3,5-disubstituted pyrazole units linked to polyamine chains by imine or amine bonds.[6–8] In basic media, these ligands formed di- or tripyrazolate sodium salts from which di- and/or tetranuclear Zn(II) and Cu(II) complexes were formed.[7,9] The acid–base behavior of these polyamine has also been reported recently.[10] Now, following the synthetic procedure previously used by us[6–8,10] and using a [2+2] dipodal condensation of 5,11,17,23-tetrakis(1,1-dimethylethyl)-25,27 - bis(2 - aminoethoxy) - 26,28 - dihydroxycalix[4]-arene[11] in the cone conformation or cone-1,3-diamine **1**, with terephthaldialdehyde **2a**, or with isophthaldialdehyde **2b**, or with pyridine 2,6-dicarbaldehyde **2c**, or 2,6-diformyl-4-methylphenol **2d** or 2,6-diformyl-4-*tert*-butylphenol **2e**, in ethanol, we have obtained novel Schiff-base bis-calix[4]arenes (Scheme 1) with four imine groups in high yields (85–95%). The high yields were due to the insolubility of the products in ethanol. While this work was in progress Kim et al. reported the synthesis of bis-calix[4]arenes with imine units at the upper rim.[12] Although Kim has presented a good method for the synthesis of bis-calix[4]arenes, it is still restricted in many respects such as the difficulty in synthesizing the starting diamine, long reaction times and relatively drastic conditions. Compared to the method[13] reported by Kim,[12] our method has the following advantages: (1) the starting material, 25,27-di(aminoethoxy)-*p*-*tert*-butylcalix[4]arene, can be easily prepared by reducing 25,27-di(cyanomethoxy)-*p*-*tert*-butylcalix[4]arene in 80% yield[11] and is more reactive than the diaminocalix[4]arene used by Kim, and (2) the conditions are very mild and the reactions are complete in 20–30 min except for **3a** and **3b** where refluxing is required for 10 h. The ^1H NMR spectra of compounds **3a**–**e** could be assigned completely and are fully consistent with the capped structures. Compounds **3a**–**e** were deduced to be 1,3-bridged *p*-*tert*-butylcalix[4]arene derivatives because of the presence of only two singlets

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Keywords: bis-calix[4]arenes; silver(I) ions; sensors.

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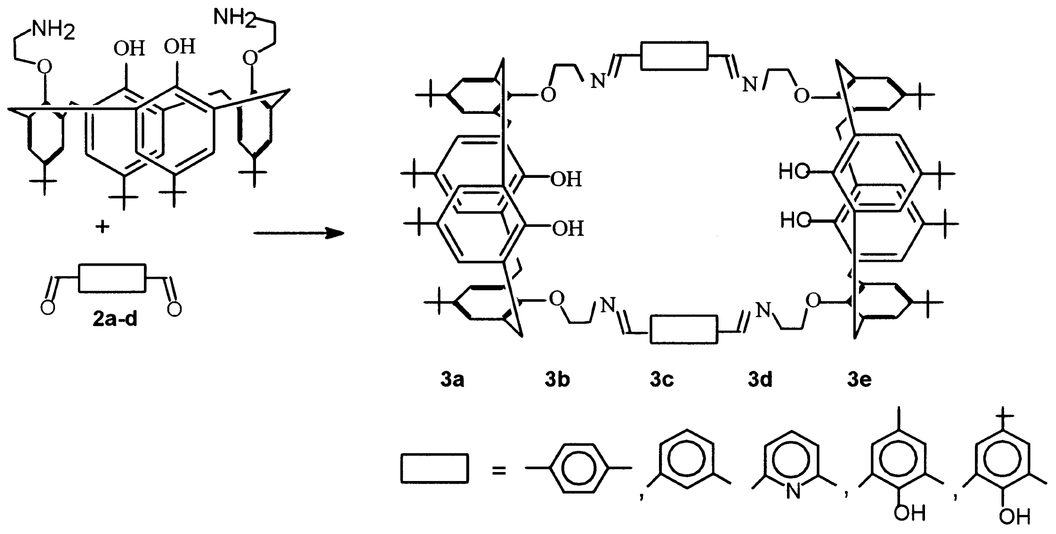

Scheme 1.

for the *tert*-butyl protons (0.95 and 1.30 ppm) for **3a**, 0.92 and 1.28 ppm for **3b**, 0.95 and 1.28 ppm for **3c**, 0.91 and 1.28 ppm for **3d** and 0.92 and 1.28 ppm for **3e**. Furthermore the imine protons appear at δ 8.35 for **3a**, 8.41 for **3b**, 8.74 for **3c**, 8.72 for **3d** and 8.78 for **3e**. In ^{13}C NMR spectra, the presence of a signal at δ 31.75 for all the compounds confirms that the Schiff-base calixarenes exist in the cone conformation. In the IR spectra an absorption band appears at 1645–1650 cm^{-1} for all compounds. In the FAB mass spectrum the parent ion peak is observed at M$^+$ in all compounds. On the basis of this spectroscopic evidence the transformation of **1** into **3a–e** occurs with the retention of the cone conformation of the *p*-*tert*-butylcalix[4]arene moiety.

A preliminary evaluation of the binding efficiencies of **3a–e** was carried out by two-phase solvent extraction of metal picrates (Na$^+$, K$^+$, Ca^{2+}, Pb^{2+} and Ag$^+$) into chloroform under neutral conditions. The results are summarized in Table 1. All the compounds were observed to extract Ag$^+$ ions more efficiently than other ions. We also used a bulk liquid membrane to measure the transport rates of metal ions from an aqueous source phase into an aqueous receiving phase through an organic bulk membrane. The measured transport rates are given in Table 1 and it is clear from these rates that the silver ion is preferentially transported by all the bis-calix[4]arenes. This silver-ion selectivity may be due to electrostatic interaction between the metal ion and the four highly preorganized soft-binding sites (imine units) surrounded by ethereal oxygen atoms. Attempts to obtain suitable crystals for X-ray crystallography were not successful. However, to elucidate the binding mode of **3a–e** with silver picrate, ^{1}H NMR and IR spectra of the complexes (**4a–e**) were recorded.[14] It has been observed that the complexation of **3a–e** with silver(I) shows different chemical shifts which indicate that the silver ion is interacting with different donor atoms in the bis-calix[4]arenes. The important changes were in the chemical shift of the imino protons and the protons attached to 'N' and 'O' which moved downfield in general on complexation with silver. In the IR spectra, the absorption band corresponding to the imine unit also moved to lower frequency.

Table 1. Solvent extraction[a] (transport rates[b,c] × 10^8 mol/24 h) results for metal ions using various organic ligands

	Extractability %[d] (transport rates)[b,c]				
Compound	Na$^+$	K$^+$	Ca^{2+}	Pb^{2+}	Ag$^+$
3a	2.76 (136.40)	11.86 (10.60)	1.93 (24.10)	20.53 (182.40)	49.52 (523.00)
3b	4.36 (39.20)	3.50 (46.40)	3.88 (36.90)	9.95 (98.30)	48.56 (966.30)
3c	28.03 (–)	23.44 (–)	17.69 (–)	37.48 (–)	72.92 (1118.00)
3d	45.64 (32.60)	40.48 (102.40)	28.72 (148.3 0)	38.53 (86.20)	55.26 (745.00)
3e	13.93 (56.90)	10.79 (62.80)	6.76 (297.90)	14.61 (261.30)	66.51 (1102.00)

[a] Source phase (aqueous solution of metal picrate, 2 mL), Mpic. = 1 mM (except lead picrate which is 0.5 mM); organic phase (CHCl$_3$, 2 mL), (carrier) = 0.1 mM.

[b] Transport conditions: Source phase (aqueous solution of metal picrates, 3 mL, 0.01 M); membrane phase (chloroform, 15 mL, (carrier) = 1.0 mM; i.d. glass vial = 20 mm; receiving phase: water 10 mL).

[c] The average value of three independent determinations. The experimental values deviate from the reported value by an average of 10%.

[d] Extractability = (concentration of extracted metal)/(concentration of organic ligand)×100%: the average value of three independent determinations.

Table 2. Composition and electrode characteristics of bis-calix[4]arene-based silver(I)-selective membrane sensors

Electrode	Calix[4]arenes[a,b]	PVC[a]	DOS[a,c]	Detection limit (M)	Slope (mV per decade)[d]
E3a	**3a**	32.0	66.5	1.0×10^{-5}	59.7
E3c	**3c**	32.1	66.4	5.0×10^{-5}	54.0

[a] Numbers indicate mass %.

[b] Bold characters indicate the calixarenes in Scheme 1.

[c] Dioctyl sebacate.

[d] Between detection limit and 1 mM.

Based on the results of these binding studies we envisaged that it should be possible to construct silver(I)-selective PVC membranes based on these bis-calix[4]arenes. Thus, sensor membranes for two ionophores were prepared and assembled as previously described.[2] These PVC membranes have been found to be superior than the conventional Ag_2S-based solid-state electrode and many calixarene[4]-based potentiometric ion-selective electrodes for silver(I). The composition of the membranes is listed in Table 2.

The PVC-based membranes of Schiff-base *p-tert*-butylcalix[4]arenes generated stable potentials when placed in contact with silver nitrate solution. The e.m.f. responses of the membranes in the presence of wide range of silver(I) ion solutions are shown in Fig. 1. The electrodes demonstrate a linear response for the Ag^+ ion in the concentration range of 1.0×10^{-5} to 1.0×10^{-1} M for all the membranes. The slopes of plots (Table 1) indicate the Nernstian nature of electrodes. In terms of lifetime of the PVC membrane electrodes, response stability was observed for over 6 months.

The response for the primary ion in the presence of various cations was measured in terms of the potentiometric selectivity coefficient ($\log K^{\mathrm{Pot}}{}_{\mathrm{A,B}}$) which has been evaluated by the fixed interference method at 1.0×10^{-2} M concentration of various interfering ions.

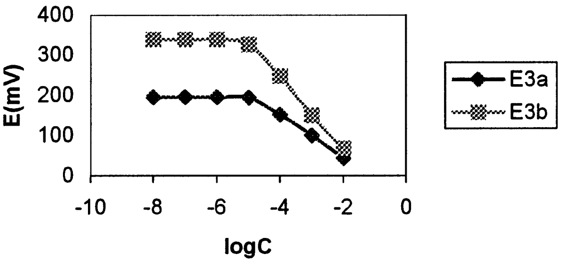

Figure 1. Typical potentiometric Ag^+ responses of the bis-calixarene-based PVC membrane electrodes: (◆) **E3a**, (■) **E3c**.

Table 3 shows the potentiometric selectivity coefficient data of Schiff-base *p-tert*-butylcalix[4]arene-based PVC membrane electrodes **E3a** and **E3c** for the interfering cations relative to silver(I). Among the calix[4]arenes, **E3c** shows the better responses and selectivity than **E3a** electrode. This is in agreement with the binding studies.

The selectivity coefficient $\log K^{\mathrm{Pot}}{}_{\mathrm{A,B}}$ values are quite low for divalent cations, indicating no interference if present with silver ion. Hg^{2+} exhibits comparable size and characteristics to that of Ag^+. The better selectivity of these sensors for Ag^+ compared with Hg^{2+} ($\log K^{\mathrm{Pot}}{}_{\mathrm{A,B}}=-3.3$) could be attributed to electronic factors and mobility problems inside the membrane. Compared to that of an Ag_2S-based electrode, the relative selectivity toward Ag^+ over Hg^{2+} ($\log K^{\mathrm{Pot}}{}_{\mathrm{A,B}}=-2.1$) is much improved. Heavy ions like Ba^{2+}, Cu^{2+}, Pb^{2+} and Co^{2+} do not disturb the functioning of this sensor. The selectivity of the two sensors is much improved over alkali metal ions especially over Na^+ in comparison to other calix[4]arene-based ion-selective electrodes reported in the literature.[4]

In conclusion, new Schiff-base bis-calix[4]arenes were synthesized with the cone conformation in high yield at room temperature. Complexation studies by two-phase extraction and transportation were carried out to show silver-ion selectivity. These bis-calix[4]arenes form silver-selective PVC membranes. This silver-ion selectivity may be due to electrostatic interaction between the metal ion and the aza crown cavity composed of oxygen and nitrogen atoms as donors.

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Table 3. The selectivity coefficients of electrodes **E3a** and **E3c** based on the membranes of Schiff-base *p-tert*-butylcalix[4]arenes **3a** and **3c**, respectively

Diverse ions (B)	Ag^+	K^+	Na^+	$NH_4{}^+$	Mg^{2+}	Ca^{2+}	Ba^{2+}	Ni^{2+}	Co^{2+}	Cu^{2+}	Pb^{2+}	Hg^{2+}
Log $K^{\mathrm{Pot}}{}_{\mathrm{A,B}}$ **E3a**	0	−1.90	−2.45	−2.20	−3.57	−3.55	−3.65	−3.27	−3.35	−3.15	−3.15	−2.29
Log $K^{\mathrm{Pot}}{}_{\mathrm{A,B}}$ **E3c**	0	−3.30	−2.95	−3.05	−3.92	−4.25	−4.17	−3.87	−4.00	−4.30	−3.80	−3.30

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13. *General procedure for the synthesis of* ***3a–e***: Calix[4]amine **1** (0.734 g, 1.00 mmol) and dialdehydes **2a**–**e** (1.00 mmol) were stirred (refluxed for 10 h in the cases of **3a** and **3b**) together in ethanol (100 ml). A solid separated which was filtered, washed and recrystallized from dichloromethane and methanol and dried under vacuum. Selected data is as follows. Compound **3a**: mp 260–262°C; ^{1}H NMR (200 MHz, CDCl$_3$): δ 0.95 [s, 36H, C(CH$_3$)$_3$], 1.30 [s, 36H, C(CH$_3$)$_3$], 3.31 [d, J = 15 Hz, 8H, ArCH$_2$Ar], 4.00 [t, J = 5 Hz, 8H, NCH$_2$], 4.25 [t, J = 5 Hz, 8H, OCH$_2$], 4.34 [d, J = 15 Hz, 8H, ArCH$_2$Ar], 6.75 [s, 8H, ArH], 7.05 [s, 8H, ArH], 7.25 [s, 4H, ArOH], 7.8 [s, 8H, ArH], 8.35 [s, 4H, HC=N]; FAB-MS (m/z): 1664 (M$^+$). Compound **3b**: mp >250°C; ^{1}H NMR (200 MHz, CDCl$_3$): δ 0.92 [s, 36H, C(CH$_3$)$_3$], 1.28 [s, 36H, C(CH$_3$)$_3$], 3.26 [d, J = 14 Hz, 8H, ArCH$_2$Ar], 4.01 [br, t, J = 5 Hz, 8H, NCH$_2$], 4.20–4.29 [m, 16H, OCH$_2$, ArCH$_2$Ar], 6.75 [s, 8H, ArH], 7.01 [s, 8H, ArH], 7.18 [s, 4H, ArOH], 7.32 [t, J = 6 Hz, 2H, ArH], 7.85 [d, J = 6 Hz, 4H, ArH], 8.02 [s, 2H, ArH], 8.41 [s, 4H, HC=N]; FAB-MS (m/z): 1664 (M$^+$). Compound **3c**: mp 242–244°C; ^{1}H NMR (200 MHz, CDCl$_3$): δ 0.95 [s, 36H, C(CH$_3$)$_3$], 1.28 [s, 36H, C(CH$_3$)$_3$], 3.26 [d, J = 12 Hz, 8H, ArCH$_2$Ar], 4.13–4.16 [m, 16H, NCH$_2$, OCH$_2$], 4.23 [d, J = 12 Hz, 8H, ArCH$_2$Ar], 6.79 [s, 8H, ArH], 7.02 [s, 8H, ArH], 7.32 [s, 8H, ArOH], 7.57 [t, J = 5.8 Hz, 2H, PyH], 7.97 [d, J = 8 Hz, 4H, PyH], 8.74 [s, 4H, HC=N]; FAB-MS (m/z): 1666 (M$^+$). Compound **3d**: mp 222–224°C; ^{1}H NMR (200 MHz, CDCl$_3$): δ 0.91 [s, 36H, C(CH$_3$)$_3$], 1.28 [s, 36H, C(CH$_3$)$_3$], 1.78 [s, 6H, CH$_3$], 3.25 [d, J = 12 Hz, 8H, ArCH$_2$Ar], 4.05–4.14 [m, 16H, NCH$_2$, OCH$_2$], 4.20 [d, J = 12 Hz, 8H, ArCH$_2$Ar], 6.74 [s, 8H, ArH], 7.02 [s, 8H, ArH], 7.08 [s, 4H, ArH], 7.27 [br, s, 4H, ArOH], 8.72 [s, 4H, HC=N]; FAB-MS (m/z): 1724 (M$^+$). Compound **3e**: mp 240°C (dec.); ^{1}H NMR (200 MHz, CDCl$_3$): δ 0.92 [s, 36H, C(CH$_3$)$_3$], 1.00 [s, 18H, C(CH$_3$)$_3$], 1.27 [s, 36H, C(CH$_3$)$_3$], 3.24 [d, J = 12 Hz, 8H, ArCH$_2$Ar], 4.03–4.34 [br, m, 24H, ArCH$_2$Ar, NCH$_2$, OCH$_2$], 6.76 [s, 8H, ArH], 6.99 [s, 8H, ArH], 7.18 [s, 4H, ArH], 7.64 [br, s, 4H, ArOH], 8.78 [s, 4H, HC=N]; FAB-MS (m/z): 1808 (M$^+$). All the compounds give satisfactory C, H and N analysis.
14. Compound **4a**: IR (CHCl$_3$): 1634 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 0.91 [s, 36H, C(CH$_3$)$_3$], 1.26 [s, 36H, C(CH$_3$)$_3$], 3.43 [d, J = 12 Hz, 8H, ArCH$_2$Ar], 4.08 [d, J = 15 Hz, 8H, ArCH$_2$Ar], 4.40 [br, s, 8H, NCH$_2$], 4.64 [br, s, 8H, OCH$_2$], 6.79 [s, 8H, ArH], 7.08 [s, 8H, ArH], 7.84 [s, 8H, ArH], 8.68, 8.92 [br, s, 4H, HC=N]. Compound **4b**: IR (CHCl$_3$): 1608 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 0.88 [s, 36H, C(CH$_3$)$_3$], 1.19 [s, 36H, C(CH$_3$)$_3$], 3.25 [d, J = 14 Hz, 8H, ArCH$_2$Ar], 3.90–4.35 [br, m, 24H, NCH$_2$, OCH$_2$, ArCH$_2$Ar], 7.67 [t, J = 6 Hz, 2H, ArH], 8.11 [d, J = 6 Hz, 4H, ArH], 8.32 [s, 2H, ArH], 8.64 [s, 4H, HC=N]. Compound **4c**: IR (CHCl$_3$): 1629 cm^{-1}. Compound **4d**: IR (CHCl$_3$): 1634 cm^{-1}; ^{1}H NMR (200 MHz, CDCl$_3$): δ 0.85 [s, 36H, C(CH$_3$)$_3$], 1.31 [s, 36H, C(CH$_3$)$_3$], 1.78 [s, 6H, CH$_3$], 3.30 [d, J = 12 Hz, 8H, ArCH$_2$Ar], 3.97–4.32 [m, 24H, NCH$_2$, OCH$_2$, ArCH$_2$Ar], 6.70 [s, 8H, ArH], 7.08 [s, 8H, ArH], 7.03 [s, 4H, ArH], 8.70 [s, 4H, HC=N]. Compound **4e**: IR (CHCl$_3$): 1634 cm^{-1}.