

Syntheses and ion-selective properties of 25,27-bis(2-hydroxyethylthioalkoxyl)-26,28-dihydroxycalix[4]arenes[†]

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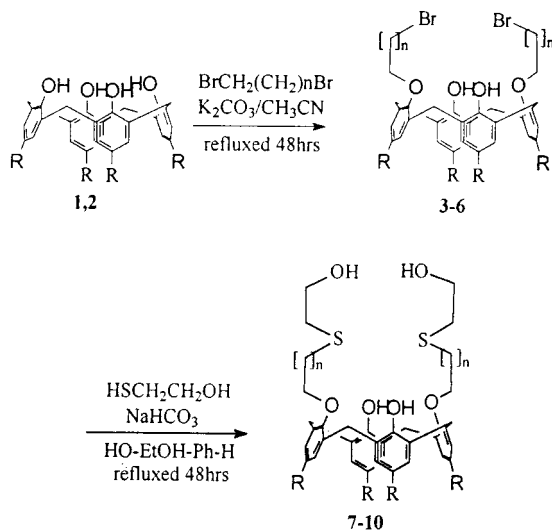
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25,27-Bis(2-hydroxyethylthioalkoxyl)-26,28-dihydroxycalix[4]arenes **7-10** were synthesized and the preliminary performance of **7-10** as ionophores for ion-selective electrode was also investigated.

In recent years, much has been written about calixarenes as excellent receptors for the specific binding of guest atoms and molecules. Derivatives containing a wide range of functional groups have been synthesized and shown to have different degrees of receptor ionophoric activity.¹⁻³ A number of calixarenes containing pendant ether, amide, ketonic, and ester groups as neutral carriers have been incorporated into ion-selective electrodes sensitive to alkali metal ions such as the sodium ion,⁴⁻⁷ potassium ion,^{8,9} and caesium ion.^{10,11} However, few papers have reported ion-selective electrodes based on calixarenes for heavy metal ions such as the silver ion,¹²⁻¹⁴ lead ion,^{15,16} and thallium ion.¹⁷ In the course of investigating polythio or polyaza functionalised calix[4]arenes as transition metal ion-selective electrodes,^{13,14} we report here the synthesis of 25,27-bis(2-hydroxyethylthioalkoxyl)-26,28-dihydroxycalix[4]arenes as a series of novel potential important intermediates for the synthesis of sulfur – containing calix[4]crown ethers and their ion-selective electrode properties.

K₂CO₃ gave calix[4]arenes **7-10**. At the same time, treatment of calix[4]arene dibromide **3** with 2-mercaptoethanol in benzene-water (1:1) in the presence of sodium hydrogencarbonate also gave **7** in high yield. Compounds **7-10** which adopt cone conformations were conventionally characterised by ¹H NMR spectra by the quadruplet of the ArCH₂Ar resonance.

Sulfur containing crown ethers, pendant ether¹⁸ and calix[4]arene based polythio compounds^{13,14} usually have silver-selective properties. Therefore, **7-10** were utilized as sensing components to prepare Ag⁺-selective polymer membrane electrodes. The membrane compositions were calix[4]arene diol 1wt%, plasticizer (DBP) 66wt%, PVC 33% and 100mol% KTC1PB relative to ionophore content. Response potentials of Ag⁺ were measured at ambient temperature (25±0.5°C). The representative electrochemical cell for the EMF measurement was as follows: Ag, AgCl / int. soln. (0.01M AgNO₃) / PVC membrane / sample / salt bridge (1M KNO₃) / 3M KCl / Hg₂Cl₂, Hg. Electrodes based on the ionophores **7-10** gave Nernstian responses of between 40 mV/decade and 52mV/decade to the activity of Ag⁺ ion within the concentration range 10⁻⁵–10^{-1.3}M AgNO₃, within the limits of detection of between 10^{-5.5} and 10^{-5.8}M.



Scheme 1

The synthetic route for the preparation of calix[4]arenes **7-10** is described in Scheme 1. Reaction of calix[4]arene **1** with BrCH₂CH₂Br in the presence of potassium carbonate in acetonitrile provided calix[4]arene dibromide **3** in 59% yield. Subsequently, treatment of calix[4]arene dibromides **3-6** with 2-mercaptoethanol in THF-H₂O (1:1) in the presence of

Table 1 Selectivity coefficient (logK_{ij}^{pot}, i=Ag⁺) of the electrodes based on ionophores **7-10**

Ion	Ionophores 7	8	9	10
Na ⁺	-2.0	-1.9	-1.8	-2.0
K ⁺	-2.2	-2.3	-2.4	-2.4
NH ₄ ⁺	-2.2	-2.3	-2.4	-2.4
Ca ²⁺	-3.4	-3.5	-3.3	-3.8
Mg ²⁺	-3.4	-3.5	-3.3	-3.8
Fe ³⁺	-3.6	-3.7	-3.9	-4.0
Cu ²⁺	-3.8	-3.9	-4.0	-3.8
Zn ²⁺	-3.8	-3.9	-4.0	-3.8
Ni ²⁺	-3.8	-3.9	-4.0	-3.8
Cd ²⁺	-3.8	-3.9	-4.0	-3.8
Co ²⁺	-3.8	-3.9	-4.0	-3.8
Hg ²⁺	0.9	1.0	0.9	1.0

1, 3, 5, 7, 9: R = H; 2, 4, 6, 8, 10: R = *t*-Bu

3,4,7,8: n=1; 5,6,9,10: n=2

Potentiometric selectivity coefficients (logK_{Ag/M}) of polymeric membrane electrodes based on the carriers were evaluated. The potentiometric selectivity coefficients were measured by a mixed solution method or for strong interfering ions by the separate solution method using 0.01M solutions of metal nitrates at a constant pH 4 (for mercury at pH 2). In this mixed-solution method, the concentration of the silver ion is varied while that of the interference ions such as Na⁺, K⁺, NH₄⁺, Ca²⁺, Mg²⁺ are 0.1M; Zn²⁺, Cd²⁺, Ni²⁺, Cu²⁺, Co²⁺, Fe²⁺, Hg²⁺ are 0.01M. The values of the selectivity coefficients are

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[†] This is a Short Paper, there is therefore no corresponding material in *J. Chem. Research (M)*.

summarised in Table 1. As it is evident from Table 1, that the alkali metal, alkaline earth metal, lead and some common transition metal ions except Hg^{2+} give no interference in the performance of the membrane electrodes. The soft heavy metal Hg^{2+} gave a strong interference towards Ag^+ ion.

In terms of the lifetime of the PVC membrane electrodes, response stability was observed for over a month without any considerable divergence in potential.

Experimental

^1H NMR spectra were recorded on Bruker AC 200 spectrometer in CDCl_3 with TMS as an internal standard. All solvents were dried and redistilled before use. 2-Mercaptoethanol and $\text{BrCH}_2(\text{CH}_2)_n\text{Br}$ were redistilled before use. All reactions were carried out under nitrogen atmosphere. Compounds **4**, **5** and **6**¹⁹ were prepared as described in the literature.

25,27-Bis(2-bromoethoxy)-26,28-dihydroxycalix[4]arene (**3**). Compound **1** (5.12g, 12 mmol) was added to a 300 ml round-bottomed flask, together with anhydrous potassium carbonate (3.23g, 23.5mmol), and 1,2-dibromoethane (100ml) in CH_3CN (100ml). The suspension was refluxed until the disappearance of **1** monitored by TLC. The mixture was cooled to room temperature, and the solvent was removed under reduced pressure. The solid residue was dissolved in 100ml CH_2Cl_2 and washed with water (100ml x 2). The organic layer was separated and dried with anhydrous sodium sulfate. After removing the solvent, the residual product was purified by column chromatography (CH_2Cl_2 : petroleum ether = 1:1). 4.5g of **3** was obtained as white powder in 59% yield, m.p. 268–271°C; ^1H NMR: 7.58(s, 2H, OH), 7.07(d, 4H, $J=7.4\text{Hz}$, $m\text{-Ar-H}$), 6.71(t, 2H, $J=7.4\text{Hz}$, $p\text{-Ar-H}$), 6.68(t, 2H, $J=7.4\text{Hz}$, $p\text{-Ar-H}$), 4.34(d, 4H, $J=12.9\text{Hz}$, $\text{Ar-CH}_2\text{-Ar}$), 4.35(t, 4H, $J=6.0\text{Hz}$, $\text{OCH}_2\text{CH}_2\text{Br}$), 3.90(t, 4H, $J=6.04\text{Hz}$, $\text{OCH}_2\text{CH}_2\text{Br}$), 3.41(d, 4H, $J=12.9\text{Hz}$, $\text{Ar-CH}_2\text{-Ar}$). Calc. For $\text{C}_{33}\text{H}_{30}\text{Br}_2\text{O}_4$: C, 60.21; H, 4.74. Found: C, 59.96; H, 4.82.

25,27-Bis(2-hydroxyethylthioethoxy)-26,28-dihydroxycalix[4]arene (**7**). Method A: calix[4]arene dibromide **3** (1.28g, 2mmol), was added to a 100ml reactor, was charged together with K_2CO_3 (0.55g, 4mmol), H_2O (30ml), THF (30ml), and 2-mercaptoethanol (1ml). The suspension was refluxed for 4 days under nitrogen atmosphere. Then, the solvent was removed under reduced pressure. The residue was extracted with chloroform (60ml), and washed with brine (50ml), and water (50ml) it was dried with anhydrous sodium sulfate, and filtered. After the solvent was removed, the residue was purified by column chromatography (petroleum ether: dichloromethane = 1:2). 1. g of **7** as white powder was obtained in 94% yield. ^1H NMR: 7.45(s, 2H, ArOH), 7.07(d, 4H, $J=7.5\text{Hz}$, $m\text{-Ar-H}$), 6.82(d, 4H, $J=7.5\text{Hz}$, $m\text{-Ar-H}$), 6.71(t, 2H, $J=7.5\text{Hz}$, $p\text{-Ar-H}$), 6.65(t, 2H, $J=7.5\text{Hz}$, $p\text{-Ar-H}$), 4.34(d, 4H, $J=13.3\text{Hz}$, $\text{Ar-CH}_2\text{-Ar}$), 4.14(t, 4H, $J=6.3\text{Hz}$, $\text{OCH}_2\text{CH}_2\text{S}$), 3.87 (t, 4H, $J=5.7\text{Hz}$, $\text{SCH}_2\text{CH}_2\text{OH}$), 3.37(d, 4H, $J=13.3\text{Hz}$, $\text{Ar-CH}_2\text{-Ar}$), 3.19 (t, 4H, $J=6.3\text{Hz}$, $\text{OCH}_2\text{CH}_2\text{S}$), 2.90(t, 4H, $J=5.7\text{Hz}$, $\text{SCH}_2\text{CH}_2\text{OH}$). Calc. For $\text{C}_{36}\text{H}_{40}\text{O}_6\text{S}_2$: C, 68.33; H, 6.37. Found: C, 68.16; H, 6.28.

Method B: To a 100ml reactor, was charged calix[4]arene dibromide **3** (1. g, 2mmol), NaHCO_3 (0.34g, 4mmol), H_2O (30ml), benzene (30ml), and 2-mercaptoethanol (1ml). The suspensions were refluxed for 48h under nitrogen atmosphere. Then, the solvent was removed under reduced pressure. The purification procedure was the same as Method A and 1.12g of **7** obtained in 88.5% yield.

The syntheses of **8–10** were subjected to the analogue procedure for the synthesis of **7** with method A.

25,27-Bis(2-hydroxyethylthioethoxy)-26,28-dihydroxy-5,11,17,23-tetra-*p-tert*-butylcalix[4]arene (**8**). **8** was obtained as white powder in 93.6% yield; m.p.204–206°C; ^1H NMR: 7.19(s, 2H, Ar-OH), 7.02(s, 4H, Ar-H), 6.66(s, 4H, Ar-H), 4.30(d, 4H, $J=12.7\text{Hz}$, $\text{Ar-CH}_2\text{-Ar}$), 4.07(t, 4H, $J=6.3\text{Hz}$, $\text{OCH}_2\text{CH}_2\text{S}$), 3.83(t, 4H, $J=6.3\text{Hz}$, $\text{SCH}_2\text{CH}_2\text{OH}$), 3.27(d, 4H, $J=12.7\text{Hz}$, $\text{Ar-CH}_2\text{-Ar}$),

3.10(t, 4H, $J=6.3\text{Hz}$, $\text{SCH}_2\text{CH}_2\text{OH}$), 2.88(t, 4H, $J=6.3\text{Hz}$, $\text{OCH}_2\text{CH}_2\text{S}$), 1.25(s, 18H, *t*-Bu-H), 0.84(s, 18H, *t*-Bu-H). Calc. For $\text{C}_{52}\text{H}_{72}\text{O}_6\text{S}_2$: C, 72.86; H, 8.47. Found: C, 72.67; H, 8.46.

25,27-Bis(2-hydroxyethylthioethoxy)-26,28-dihydroxycalix[4]arene (**9**). **9** was given as white foam in 77.7% yield. ^1H NMR: 8.02(s, 2H, Ar-OH), 7.05(d, 4H, $J=7.3\text{Hz}$, $m\text{-Ar-H}$), 6.89(d, 4H, $J=7.3\text{Hz}$, $m\text{-Ar-H}$), 6.72(t, 2H, $J=7.3\text{Hz}$, $p\text{-Ar-H}$), 6.65(t, 2H, $J=7.3\text{Hz}$, $p\text{-Ar-H}$), 4.28(d, 4H, $J=12.8\text{Hz}$, $\text{Ar-CH}_2\text{-Ar}$), 4.10(t, 4H, $J=6.3\text{Hz}$, $\text{OCH}_2\text{CH}_2\text{CH}_2\text{S}$), 3.78(t, 4H, $J=6.0\text{Hz}$, $\text{SCH}_2\text{CH}_2\text{OH}$), 3.38(d, 4H, $J=12.8\text{Hz}$, $\text{Ar-CH}_2\text{-Ar}$), 3.11(t, 4H, $J=6.3\text{Hz}$, $\text{OCH}_2\text{CH}_2\text{CH}_2\text{S}$), 2.82(t, 4H, $J=6.0\text{Hz}$, $\text{SCH}_2\text{CH}_2\text{OH}$), 2.54(s, 2H, CH_2OH), 2.31(m, 4H, $\text{OCH}_2\text{CH}_2\text{CH}_2\text{S}$). Calc. For $\text{C}_{38}\text{H}_{44}\text{O}_6\text{S}_2$: C, 69.06; H, 6.71. Found: C, 68.90; H, 6.42.

25,27-Bis(2-hydroxyethylthioethoxy)-26,28-dihydroxy-5,11,17,23-tetra-*p-tert*-butylcalix[4]arene (**10**). **10** was given as white foam in 79% yield. ^1H NMR: 7.50(s, 2H, Ar-OH), 7.03(s, 4H, Ar-H), 6.80(s, 4H, Ar-H), 4.26(d, 4H, $J=13.5\text{Hz}$, $\text{Ar-CH}_2\text{-Ar}$), 4.06(t, 4H, $J=5.7\text{Hz}$, $\text{OCH}_2\text{CH}_2\text{CH}_2\text{S}$), 3.79(t, 4H, $J=5.7\text{Hz}$, $\text{SCH}_2\text{CH}_2\text{OH}$), 3.31(d, 4H, $J=13.5\text{Hz}$, $\text{Ar-CH}_2\text{-Ar}$), 3.06(t, 4H, $J=6.8\text{Hz}$, $\text{OCH}_2\text{CH}_2\text{CH}_2\text{S}$), 2.80(t, 4H, $J=5.7\text{Hz}$, $\text{SCH}_2\text{CH}_2\text{OH}$), 2.37(s, 2H, CH_2OH), 2.26(m, 4H, $\text{OCH}_2\text{CH}_2\text{CH}_2\text{S}$), 1.26(s, 18H, *t*-Bu-H), 0.95(s, 18H, *t*-Bu-H). Calc. For $\text{C}_{54}\text{H}_{76}\text{O}_6\text{S}_2$: C, 73.26; H, 8.65. Found: C, 73.37; H, 8.51.

This work was supported by the National Nature Science Foundation of China (Project Grant No. 298720197).

Received 29 June 2000; accepted 15 September 2000
Paper 00/419

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