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The first synthesis of a calix[4](diseleno)crown ether as a sensor for ion-selective electrodes

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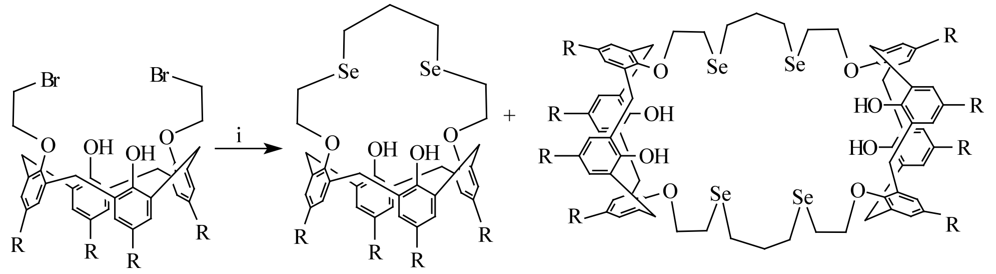
Abstract—Two calix[4](diseleno)crown ethers **3** and **4** were synthesized by reaction of the disodium salt of 1,3-propanediselanol with the preorganized 1,3-dibromoethoxylcalix[4]arenes **1** and **2**. Compound **3** forms an interesting infinite sheet aggregate via self-inclusion and intermolecular Se···Se interactions in the solid state. Preliminary evaluation of **3** and **4** as ionophores for ion-selective electrodes (ISEs) is reported. © 2001 Elsevier Science Ltd. All rights reserved.

With the aim of advancing chemical sensor technology, considerable recent attention has focused on a new generation of abiotic host molecule calixarenes.[1] The preorganized three-dimensional structures of this type of metacyclophane largely benefit their receptor properties for neutral molecules and ionic species. For improving its ion affinities, a number of calixcrown ethers with enforced cavities for binding ions were synthesized in the past decade.[2] With the introduction of different numbers of binding sites and by varying the ring size of the crown loops, some of them exhibit a strong affinity for Na^+, K^+ and Cs^+. More recently, some endeavours have been focused on the synthesis of nitrogen incorporated calixcrown ethers for improving their affinity for transition metal ions.[3]

Aiming at constructing calix[4]arene-based receptor molecules containing N, S or P donors, which are sensitive to transition metal ions in analytical chemistry due to their biomedical, environmental and industrial significance, we have synthesized a series of tweezer-like calix[4]arene derivatives containing sulfur and nitrogen atoms. This type of calix[4]arene exhibits a good Ag^+-selectivity against most interfering ions.[4] These results encouraged us to investigate some novel ionophores containing other soft donors such as selenium atoms, and compare their ion-selective behaviours with our previous work for further understanding the complicated ion-selectivity mechanism in ionophore-based ISEs. To this end, we report herein on the synthesis of two novel calix[4](diseleno)crown ethers **3** and **4** and



1, 2 **3, 4** **5**

1, **3**: R = H; **2**, **4**: R = *t*-Bu; **5:** R = *t*-Bu.

Scheme 1. (i) Disodium salts of 1,3-propanediselanol, ethanol/THF refluxed for 6 h.

Keywords: calix[4]arenes; crown ethers; selenium and compounds; aggregation; ionophore; electrodes.

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their Ag$^+$ selectivity behaviours monitored by electromotive force measurements of polymer membrane electrodes based on these novel Ag$^+$-selective ionophores.

According to Scheme 1, calix[4](diseleno)crown ethers **3** and **4** were synthesized in yields of 29 and 33%, respectively, by the reaction of 25,27-bis(bromoethoxyl)-26,28-dihydroxyl-calix[4]arene **1**[5b] and **2**[5a] with the disodium salt of 1,3-propanediselenol, which was prepared in situ by the reaction of 1,2-diselenocyclopentane with sodium borohydride in the presence of NaOH. Double bridged biscalix[4](tetraseleno)crown ether **5** was obtained as a byproduct in 4% yield in the preparation of **4**. Interestingly, when the disodium salt of 1,3-propanediselenol was slowly added into the refluxed THF solution of **2**, the yield of **5** increased to 10%. ^{1}H NMR spectra indicate that calix[4]crown **3** keeps the cone conformation.[6] Two doublets of the protons within the methylene bridge of the calix[4]arene framework at 4.38 and 3.38 ppm with $J=13.1$ Hz and the separation of the aryl protons of calix[4]arene skeleton (7.10 and 6.70 ppm of the *meso*-Ph-H, 6.72 and 6.67 ppm of the *para*-Ph-H) suggest that **3** is in a 'pinched' cone conformation. Two doublets at 4.29 and 3.27 ppm with $J=13.0$ Hz for the protons of the methylene bridge of the calix[4]arene skeleton, and the separation of the *tert*-butyl resonances at 1.28 and 0.81 ppm, respectively, as well as the separation of the aryl protons of the calix[4]arene skeleton at 7.05 and 6.61 ppm, respectively, indicated that **4** was also in a 'pinched' cone conformation. The ^{1}H NMR spectra of **5** are similar to those of **4**, but their R_f values in TLC are obviously different. Compound **5** was further confirmed by FAB-MS spectra.

Calix[4]crown ether **3** adopts the cone conformation (Fig. 1a).[7] The intramolecular distance of Se(1)···Se(2) is 5.81 Å. The torsion angles of O(2)–C(35)–C(34)–Se(2), O(1)–C(29)–C(30)–Se(1), Se(1)–C(31)–C(32)–C(33), C(31)–C(32)–C(33)–Se(2) and C(32)–C(33)–Se(2)–C(34) of the crown loop are −87.3, −93.6, 173.2, −173.0 and −65.2°, respectively. The interplanar angles between the adjacent four aromatic arenes are between 79.5 and 103.4°. Two opposite arenes bearing the crown loop have an interplanar angle of 27.7°, while the other two aromatic rings were tilted away from the calix cavity with an interplanar angle of 107.1°. As shown in Fig. 1(b and c) **3** forms a dimer structure via self-inclusion of the two cavities, namely one of the four phenyl groups of one cavity embedded into another cavity. The attraction leading to the supramolecular structure is π–π stacking, which is formed by the partial overlapping of the two aromatic groups, and with an interplanar angle of 0°, as well as a distance of 3.35 Å between the two arenes. The centroid···centroid distance of the two aromatic rings capping each other is 4.24 Å, which is lower than 4.6 Å being defined for the extreme condition of this type of partially overlapped π–π stacking by molecular modeling.[8] It is interesting to note that this dimeric structure further assembled into a two-dimensional aggregate via intermolecular weak Se···Se interactions, as shown in Fig. 2. The intermolecular Se···Se distances are 3.826 Å between Se(1) and Se(2B); 3.818 Å between Se(1) and Se(1D), which are shorter than the sum of the van der Waals radii of two selenium atoms (4.00 Å).

Calix[4](diseleno)crown ethers **3** and **4** were found to be good ionophores for silver ion-selective electrodes. It was found that electrodes based on ionophores **3** and **4** gave a good Nernstian response of 57 mV decade^{-1} to the activity of Ag$^+$ ion in the concentration range 5×10^{-6} –10^{-2} M $AgNO_3$, within the limits of detection of between $10^{-5.5}$ and $10^{-5.8}$ M.

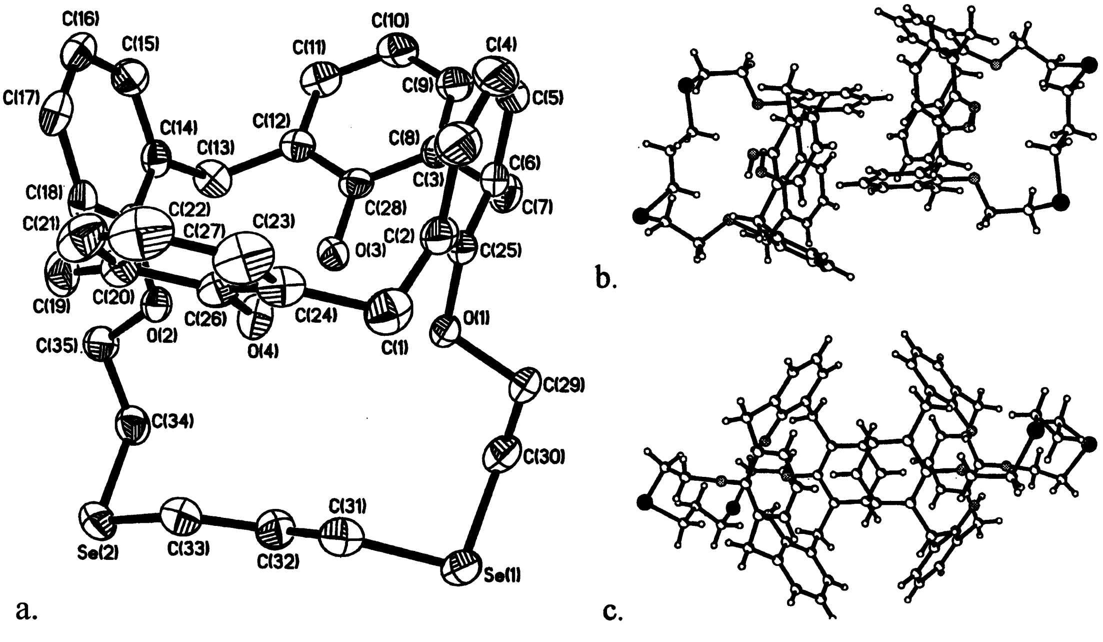

Figure 1. X-Ray crystallography of calix[4]crown ether **3**. (a) Labelling of **3**, all hydrogen atoms were omitted for clarity. (b) and (c) Two views of the self-assembly of **3** via parallel-displaced π–π stacking.

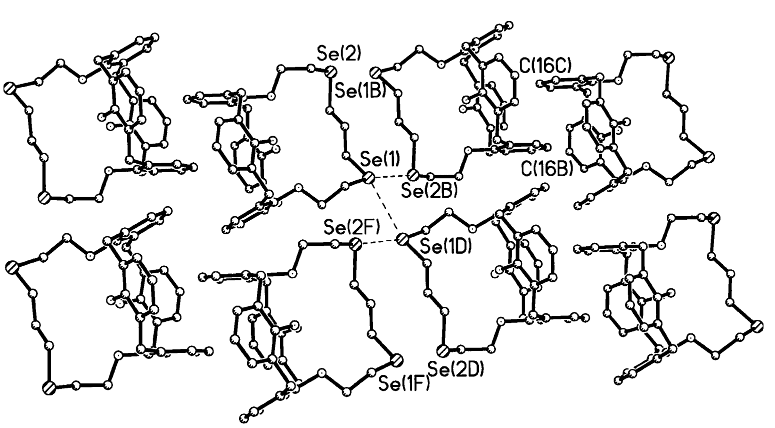

Figure 2. Infinite sheet aggregate of calix[4]crown ether **3** via self-inclusion of the hydrophobic cavities and intermolecular selenium···selenium contacts. All hydrogen atoms were omitted for clarity.

Table 1. Selectivity coefficient (log $K_{Ag,M}^{pot}$) of the electrodes based on ionophores **3** and **4**[9]

Ion		Ag^+	Na^+	K^+	NH_4^+	Ca^{2+}	Mg^{2+}	Ni^{2+}	Cu^{2+}	Zn^{2+}	Cd^{2+}	Pb^{2+}	Hg^{2+}
$K_{Ag,M}^{pot}$	**3**	0	−4.2	−4.0	−3.7	−5.0	−5.0	−4.7	−4.7	−4.5	−4.6	−4.4	−2.1
	4	0	−3.6	−4.1	−4.0	−5.0	−5.1	−5.3	−4.9	−4.4	−4.9	−5.2	−2.3

Potentiometric selectivity coefficients (log $K_{Ag,M}^{pot}$) of polymeric membrane electrodes based on the two ionophores were evaluated (Table 1). The potentiometric selectivity coefficients were measured by the fixed interference method. As shown in Table 1, the polymer membranes containing calix[4]crown ethers **3** and **4** as ionophores gave excellent log $K_{Ag,M}^{pot}$ values (≤ -3.6) against most of the interfering cations examined (i.e. Na^+, K^+, NH_4^+, Mg^{2+}, Ca^{2+}, Ni^{2+}, Zn^{2+}, Cu^{2+}, Cd^{2+} and Pb^{2+}), except that Hg^{2+} exhibited relatively weak interfering (log $K_{Ag,M}^{pot} \leq -2.1$). The fact that polymer membranes containing ionophores **3** and **4** gave excellent log $K_{I,M}^{pot}$ values against Na^+, K^+, NH_4^+, Ca^{2+}, Mg^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, Cd^{2+} and Pb^{2+} means that **3**- and **4**-based ISEs possess high Ag^+ selectivity and only respond weakly to the above interfering ions. The strong Hg^{2+} interference in some ionophore-based ISEs[5b] and traditional Ag_2S-based ISE is largely eliminated in the present ISEs. One possible explanation is that those ions with high hydration energies, such as Na^+, K^+, NH_4^+, Ca^{2+}, Mg^{2+}, Pb^{2+} and most divalent transition metal ions, cannot strongly interact with selenium donors in the ionophores, while less heavily hydrated soft Ag^+ coordinate to soft selenium donors selectively.

In summary, two novel selenium functionalized calix[4]crowns were synthesized and characterized. Potentiometric selectivity evaluation showed that they are good Ag^+-selective ionophores in ISEs. Their structure–selectivity relationships and comparative experiments with other ionophores containing N and S donors are now being investigated and will be reported in due course.

Acknowledgements

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6. Selected data for compound **3**: ^{1}H NMR (200 MHz, $CDCl_3$): 7.10 (d, 4H, $J=7.4$ Hz), 6.90 (s, 2H, OH), 6.72 (t, 2H, $J=9.2$ Hz), 6.70 (d, 4H, $J=9.2$ Hz), 6.67 (t, 2H, $J=7.4$ Hz), 4.38 (d, 4H, $J=13.1$ Hz), 4.22 (t, 4H, $J=6.4$ Hz), 3.39 (d, 4H, $J=13.1$ Hz), 3.19 (t, 4H, $J=6.4$ Hz), 3.10 (t, 4H, $J=6.4$ Hz), 2.42 (m, 2H, $J=6.4$ Hz). Calcd for $C_{35}H_{36}O_4Se_2{\cdot}0.5CH_2Cl_2$: C, 59.13; H, 5.17. Found: C, 59.51; H, 5.60. Selected data for compound **4**: ^{1}H NMR (200 MHz, $CDCl_3$): 7.05 (s, 4H), 6.61 (s, 4H), 6.45 (s, 2H), 4.29 (d, 4H, $J=13.0$ Hz), 4.18 (t, 4H, $J=6.7$ Hz), 3.27 (d, 4H, $J=13.0$ Hz), 3.19 (t, 4H, $J=6.7$ Hz), 3.05 (t, 4H, $J=6.4$ Hz,), 2.27 (m, 2H, $J=6.4$ Hz), 1.28 (s, 18H), 0.811 (s, 18H). Calcd for $C_{51}H_{68}O_4Se_2{\cdot}0.5CH_2Cl_2$: C, 65.41; H, 7.36. Found: C, 65.38; H, 7.17. Selected data for compound **5**: ^{1}H NMR (200 MHz, $CDCl_3$): 7.70 (s, 4H), 6.98 (s, 8H), 6.82 (s, 8H), 4.29 (d, 8H, $J=12.5$ Hz), 4.12 (t, 8H, $J=6.5$ Hz), 3.32 (d, 8H, $J=12.5$ Hz), 3.10 (t, 8H, $J=6.5$ Hz), 2.98 (t, 8H, $J=8.0$ Hz), 2.24 (m, 4H), 1.35 (s, 18H), 1.25 (s, 36H), 0.95 (s, 18H). FAB$^+$-MS: 1817.9 (M^++1). Calcd for $C_{102}H_{136}O_8Se_4{\cdot}CH_2Cl_2$: C, 59.13; H, 5.17. Found: C, 59.42; H, 5.35.
7. Single-crystal diffraction measurement of crystal on a Bruker Smart 1000 diffractometer with Mo-Kα ($\lambda=0.71073$ Å) at 293 K. Data for **3**: $C_{35}H_{36}O_4Se_2{\cdot}0.5CH_2Cl_2$, $M=771.02$, crystal in triclinic, space group $P\bar{1}$, $Z=2$, $a=10.4953(17)$, $b=11.7650(19)$, $c=15.136(3)$ Å, $\beta=77.690(3)°$, $V=1632.6(5)$ Å^3, $D_{\text{calcd}}=1.467$ mg/mm^3, $\mu=2.384$ mm^{-1}, $F(000)=734$. A total of 6676 reflections were measured, 5624 unique. The structure was solved by direct method and refined on F^2 using SHELXTL software (Sheldrick, G. M. Göttingen, Germany). Final $wR_2=0.1571$, with a conventional $R_1=0.0573$ (reflections with $I>2\sigma(I)$) and a GOOF$\,=1.039$ for 409 refined parameters. Crystallographic data (excluding structure factors) for the structure reported here have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 172268. CCDC-copies of the data can be obtained on application to CCDC, 12 Union Rd., Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033); e-mail: deposit@ccdc.cam.ac.uk).
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9. The polymeric membrane was prepared as follows. Calix[4](diseleno)crown ether (4 mg), dibutyl phosphate (263 mg), PVC (132 mg) and potassium tetrakis(*p*-chlorophenyl)borate (75 mol% relative to ionophore content) were dissolved in tetrahydrofuran (THF). The well-distributed PVC–THF syrup was poured into a glass mould and the organic solvent was allowed to evaporate at ambient temperature over 24 h. The final flexible, transparent membrane with thickness of 0.2–0.4 mm was cut into discs of 6 mm diameter with a cork borer. The discs were pasted onto the PVC tips and clipped to the end of the electrode body, which consisted of an Ag–AgCl wire immersed in an internal solution of 0.01 M silver nitrate. The PVC membrane electrodes were preconditioned by immersion in a 0.01 M silver nitrate solution at least 12 h prior to use. The representative electrochemical cell for the EMF measurement was as follows: Ag, AgCl|int. soln (0.01 M $AgNO_3$)|PVC membrane|sample|salt bridge (1 M KNO_3)|3MKCl|Hg_2Cl_2, Hg.