Synthesis and complexation study of (1,4-linked)-homothiaisocalixnaphthalenes†

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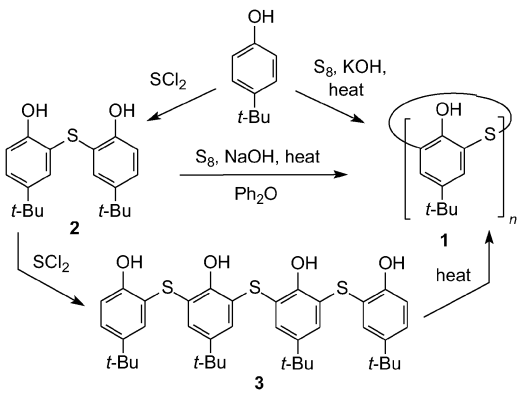
Received (in Montpellier, France) 12th February 2007, Accepted 13th March 2007
First published as an Advance Article on the web 2nd April 2007
DOI: 10.1039/b702152f

A series of new cavity-containing molecular receptors, ''homothiaisocalixnaphthalenes'' containing 2,3-dialkoxy-substituted naphthalene units, have been synthesized, and some of their complexation properties have been investigated. The syntheses of the octaethoxy- and *n*-octapropoxy-octahomotetrathiaisocalix[4]naphthalenes were accompanied by small amounts of the corresponding higher dodecahomohexathia homologues. All of the macrocycles which were synthesized were highly symmetrical and conformationally flexible. Although these new macrocycles were not effective hosts for C_{60}- and C_{70}-fullerenes or the tetramethylammonium cation, two of them were shown, in a limited study, to effectively bind with Ag^+ and only modestly with Hg^{2+}.

Introduction

Thiacalix[*n*]arenes such as **1** ($n = 4$) are calixarenes in which the methylene groups that link the phenolic units have been replaced by sulfur atoms. These compounds and their derivatives, which have recently been reviewed by Miyano *et al.*[1] and others,[2] are of considerable interest. The interest is due to their applications, among others, as molecular hosts for several different soft-to-intermediate hardness metal (*e.g.* Ag^+, Zn^{2+}, Cd^{2+}, Hg^{2+}), alkali or alkaline earth metal ions,[3] and as has recently been shown, for the selective removal of ^{226}Ra from gas-field-produced waters.[4] Thiacalix[4]arene itself has been prepared using either a one-step procedure,[5] from *para-tert*-butylphenol and sulfur, or more efficiently *via* the sulfur-bridged dimer **2**,[6] or by a less efficient multi-step process *via* the linear tetramer **3**[7] (Scheme 1).



Scheme 1

There are only a few examples of homothiacalixarenes which have been reported such as **4**,[8] **5a–c**,[9] **6**[10] and **7a–c**[11] (Fig. 1), in which the methylene bridges between the aromatic units are partly or completely replaced by various alkylthio or alkyldithio groups. These compounds have also been shown to be effective hosts for various metal ions. To date, such homothiacalixarenes have received much less attention than **1** and its derivatives. In this paper, we report the synthesis of some analogous 1,4-linked naphthalene-ring-based homothiacalixarenes and a limited study of some of their inclusion properties.

Results and discussion

We previously reported that the [1 + 1] coupling between the corresponding bis(mercaptomethyl)- **8** and bis(bromomethyl)-naphthalenes **9**, respectively, in basic and high dilution conditions produced tetrahomodithiacalix[4]naphthalenes **10** and **11**[12,13] in reasonable yields (Scheme 2). These new homodithiacalix[4]naphthalenes were used as precursors for the syntheses of the corresponding homocalix[4]naphthalenes *via* extrusion of the sulfur atoms,[11] and although these compounds were found to be able to complex with Ag^+ their complexation properties were not investigated in any detail at that time.

Based upon our experience with C_{60}- and C_{70}-fullerene complexation studies involving calixnaphthalenes[14] and their homologues such as **10** and **11**, and also with the structurally-unrelated, but sulfur-containing bowl-shaped corannulene macrocycles,[15] we hypothesized that octahomotetrathiaisocalix[4]naphthalenes such as **12a–d** (Fig. 2), the sulfur-containing analogues of ''Zorbarene''(**13**)[16] might also be effective receptors. This hypothesis was based upon CPK and molecular modeling[17] studies which suggested that these compounds had the prerequisite cavity dimensions for embracing C_{60}- and C_{70}-fullerenes. We therefore decided to synthesize and evaluate the potential fullerene complexation properties of **12a–d**, the

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† Electronic supplementary information (ESI) available: General experimental methods and spectra of all new compounds. See DOI: 10.1039/b702152f

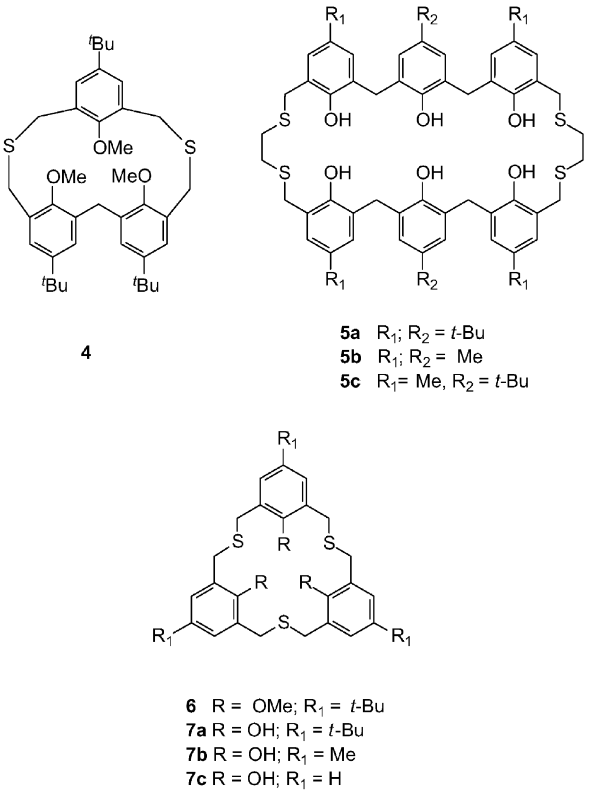


Fig. 1 Some homothiacalixarenes that have been reported.

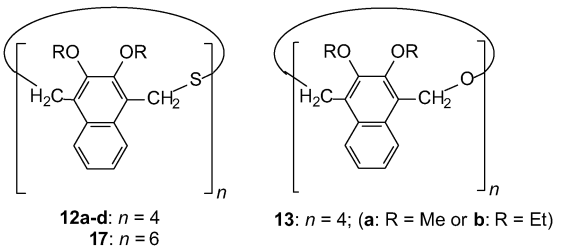


Fig. 2 Homothia- and homooxacalixnaphthalenes.

methoxy, ethoxy, *n*-propoxy and *n*-butoxy derivatives of **12**, respectively.

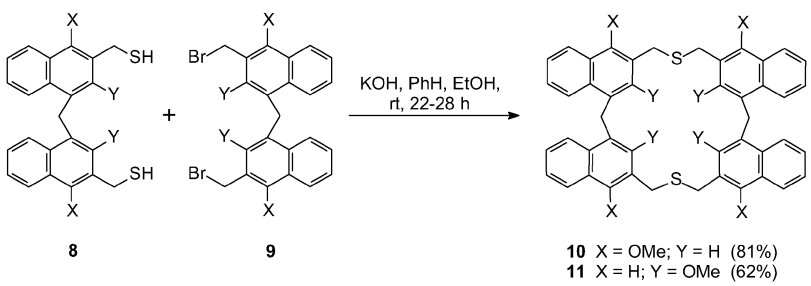
Octahomotetrathiaisocalix[4]naphthalenes and dodecahomohexathiaisocalix[6]naphthalenes

The syntheses of **12a–d** were achieved in a relatively straightforward approach, as outlined in Scheme 3, starting from the corresponding 2,3-dialkoxynaphthalenes (**14a–d**). Use of Bodwell's one-pot procedure[18] for the reactions of 1,4-bis(bromomethyl)-2,3-dialkoxynaphthalenes (**15a–d**) with Na_2S–Al_2O_3 to form the corresponding target macrocyclic products **12a–d** at ambient temperature did not yield any desired product formation, and upon heating, only resulted in decomposition of starting material. Employment of Ashram's procedure,[11] which he used to synthesize **7a–c**, also failed in our cases to afford any of our target compounds. An alternative procedure involving [2 + 2] coupling reactions between **15a–d** and 1,4-bis(mercaptomethyl)-2,3-dialkoxynaphthalenes (**16a–d**), respectively, was therefore used, and proved to be successful.

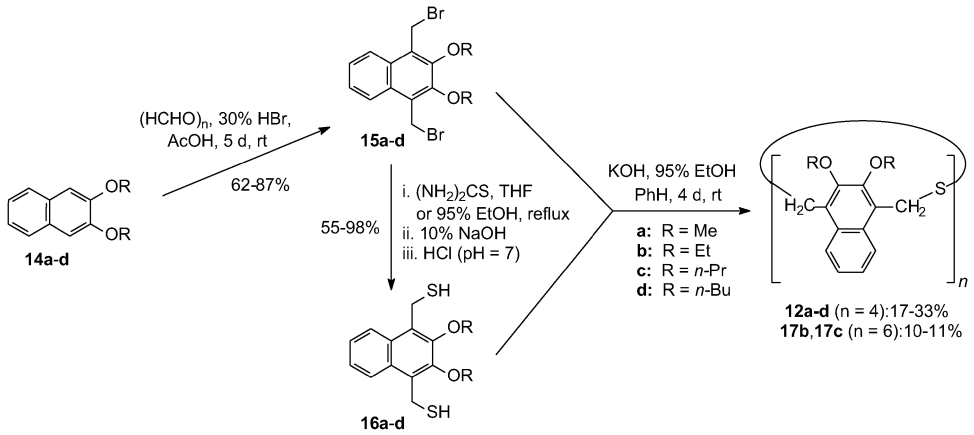
Treatment of **15a–d** with thiourea, followed by hydrolysis under basic conditions, gave intermediates **16a–d**, respectively, in 62–87% yields. Bis(mercaptolation) of **15d** in THF at either ambient or reflux temperatures however gave the crude products only as resinous mixtures, which after purification by chromatography afforded **16d** in very low (~2.5%) yields. Nevertheless, **16d** could be produced in a much better yield (62%) when 95% EtOH was employed as the reaction solvent. Coupling reactions under basic conditions using equimolar amounts, respectively **15a–d** with **16a–d**, afforded the corresponding "1,4-linked" octahomotetrathiaisocalix[4]naphthalenes (**12a–d**) in 18–33% isolated yields. Along with these cyclic tetrameric products, "1,4-linked" dodecahomohexathiaisocalix[6]naphthalenes ("hexathia-[3.3.3.3.3.3](1,4)-naphthalenophanes"), **17b** and **17c** were also isolated in 10 and 11% yields, respectively. Calix[4]naphthalenes **12b** and **12c** which are less polar than **17b** and **17c** could be relatively easily separated and purified. As anticipated, none of the dimeric [3.3](1,4)naphthalenophane products were produced.[19]

All of the new macrocyclic compounds **12a–d** were highly symmetrical as indicated by their relatively simple ambient temperature ^{1}H NMR spectra. Fast conformational equilibration in solution at ambient temperature was obvious from the fact that all of the signals were sharp, and that their bridging methylene groups appeared as singlets at δ 4.30, 4.30, 4.28 and 4.27 ppm, respectively, which are further upfield than those of the bridging methylene groups (singlets at δ 5.04–5.05 ppm) of the corresponding homooxaisocalix[4]naphthalenes **13a–d**.[16] Low-temperature VT-^{1}H NMR studies down to −65 °C did not reveal any coalescence temperatures for any of these new compounds.

Comparison of the chemical shifts of the alkoxy protons in the spectra of **12a–d** with those of their respective precursors



Scheme 2



Scheme 3

revealed significant differences only in the cases of **12a** and **12b**. The position of the methyl signal of the methoxy groups in **12a** at δ 3.65 ppm is higher upfield than those of the corresponding signals in the precursors **15a**, **14a** and **16a**, all of which are at approximately δ 4.00 ppm. The positions of the methylene and the methyl protons of the ethoxy groups in **13b** at δ 4.06 and 1.39 ppm, respectively, are also higher upfield than the corresponding signals of the precursors **15b**, **14b** and **16b**, which appear at approximately δ 4.22 and 1.48–1.54 ppm, respectively.

Complexation studies

With C_{60} and C_{70} as the guests. On the basis of their molecular architecture and molecular modeling we had hypothesized that these newly-synthesized macrocycles could be potential new hosts for C_{60} and/or C_{70}. To assess their potential binding abilities with these fullerenes, complexation studies using ^{1}H NMR spectroscopy were therefore undertaken. Since **12a** and **12b** had only very low solubilities in the usual fullerene solvents benzene or toluene, the studies could only be undertaken using CS_2, a solvent in which the solubilities of the fullerenes themselves are also known to be higher.[15] However, there was no sign of any complexation having occurred with C_{60} or C_{70} and any of the macrocycles tested, since there were no changes evident in either the colour of the solutions, or in any of the ^{1}H NMR signals.

There are clearly many factors which could account for why these compounds failed to show any supramolecular complexation with C_{60} or C_{70}. Included among these factors may also be the tendency for the sulfur atoms to be exodentate to the macrocyclic ring, by analogy with some thiacrown ethers which have been reported by others.[20] As a result, the sulfur atoms in **12a–d** may not be situated within the cavity and thus be unable to assist in the binding to the fullerenes to the same extent and manner which they can in the case of the sulfur atom-containing corannulene macrocycles.[15]

Binding studies with tetramethylammonium chloride (TMACl). Many studies have been reported in which quaternary ammonium salts have been used as guests in host–guest studies in lipophilic solvents involving various macrocyclic hosts, and which have demonstrated the importance of cation–π interactions.[21a–d] Since it has previously been shown that the octahomooxa compounds **13a** and **13b** were good and effective receptors with TMACl (tetramethylammonium chloride) in $CDCl_3$,[16] it was decided to conduct similar complexation studies with their thia analogues, **12a** and **12b**. However, when $CDCl_3$ solutions of either of these compounds were added to saturated $CDCl_3$ solutions of TMACl, no changes were observed with any of the chemical shifts of either the hosts or the guest molecules.

Comparison of the molecular mechanics-generated structures of either **12a** or **12b** with those of **13a** and **13b**[16] suggest that, in the latter cases, the fact that the oxygen atoms of the $–CH_2–O–CH_2–$bridges are situated within the cavity in contrast to the sulfur atoms, as also noted above, could also account for the apparent lack of binding abilities with TMA cation in these cases.

Binding studies with AgO_2CCF_3 and $HgCl_2$. Yamato *et al.* recently reported a highly selective binding for Ag^+ using their hexahomotrithiacalix[3]arene, **6**, with various metal picrates.[10] We therefore decided to employ Ag^+ as a guest for **12a** and **12b** using a mixture of 1 : 9 $CD_3CN–CDCl_3$ (v/v) as the solvent for the complexation investigation using ^{1}H NMR spectroscopy. To avoid any solvent effect, all host and guest solutions were prepared using the same solvent mixture. Upon addition of aliquots of solutions of Ag^+ ($\sim 5 \times 10^{-3}$ M) to the host solutions of **12a** or **12b** ($\sim 5 \times 10^{-4}$ M), the ^{1}H NMR spectra showed clear induced changes in the chemical shifts of all of the host signals. With [Guest] : [Host] ratios $\geq 10 : 1$, the observed chemical shifts leveled off very rapidly, so instead, the complexation studies were conducted at lower ratios, ranging from 0.54–2.87. In these ranges, addition of Ag^+ solutions to the host solutions resulted in shifts of all of the host signals to lower fields. The largest complexation-induced chemical shifts which were seen for **12a** and **12b** were for the $–CH_2–$ groups of their bridging $–CH_2SCH_2–$ groups ($\Delta\delta_{max}$ = 0.125 and 0.150 ppm, respectively). The chemical shift changes for their alkoxy group signals, *e.g.* OCH_3 or OCH_2, were smaller ($\Delta\delta_{max}$ = 0.088 and 0.035 ppm, respectively), as were those for their aromatic signals which were also smaller

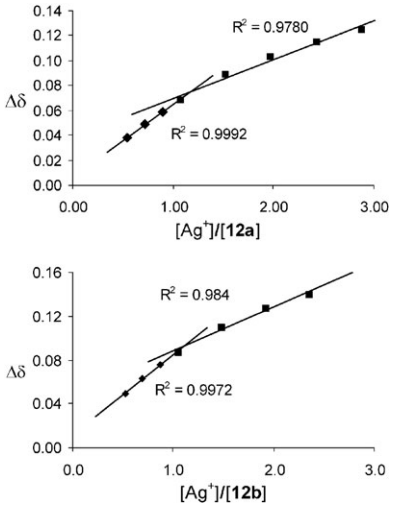


Fig. 3 Mole ratio plots showing the 1 : 1 stoichiometry of Ag^+ with **12a** (top) and **12b** (bottom).

($\Delta\delta_{max}$ = 0.012 and 0.100 ppm, respectively). These changes suggest that Ag^+, a "soft" cation, binds, as could be predicted, most tightly with the bridging sulfur atoms rather than with the oxygen atoms of the alkoxy groups, or the naphthyl sub-units. Hence, these larger induced chemical shift changes observed for the bridging methylenes were the ones used for determinations of the guest–host stoichiometries and also for determination of the K_{assoc} values.[22] The mole ratio plots, indicated the formation of 1 :1 host–guest complexes for receptors **12a** or **12b** (Fig. 3) with Ag^+ in the concentration ranges which were studied. Due to the generally smaller chemical shift changes observed with the limited amounts of the macrocycles and $HgCl_2$ and their respective solubility limitations, the determination of the mole ratio plots in these cases was more equivocal. Nevertheless, using a 1 : 1 binding isotherm model and non-linear curve fitting, reasonable, albeit much smaller, K_{assoc} values than those observed with Ag^+ could be derived. The tetraethoxy macrocycle **12b** again revealed the higher K_{assoc} values.

Apparent K_{assoc} values for complex formation between **12a** or **12b** with Ag^+ were initially calculated using both the Benesi–Hildebrand (B–H) and Foster–Fyfe (F–F) treatments, respectively (Table 1).[22] Although results from both methods showed reasonably good agreement for both receptors tested, more reliable values were conveniently obtained using non-linear curve fitting in all cases.[23] The K_{assoc} values with **12b** for the binding of Ag^+ are ~1.3-fold larger, and in the case of Hg^{2+} are ~2.4-fold larger, than those with **12a**.

Table 1 K_{assoc} values (M^{-1}) for $AgCF_3CO_2$ and $HgCl_2$ complexes with **12a** and **12b** in 1 : 9 CD_3CN–$CDCl_3$ at 298 K

Entry	Complexes	Run # 1 ([G]/[H])	Run # 2 ([G]/[H]	Average
1	Ag^+: **12a**	**592 ± 11** (0.54–15.9)	**581 ± 10** (0.54–15.9)	**587 ± 11**
2	Ag^+: **12b**	**727 ± 35** (0.2–4.1)	**790 ± 11** (0.35–13.7)	**759 ± 25**
3	Hg^{2+}: **12a**	**67 ± 23** (0.35–10.9)	**69 ± 28** (0.35–10.9)	**68 ± 26**
4	Hg^{2+}: **12b**	**148 ± 38** (0.35–11.0)	**173 ± 21** (0.35–11.0)	**161 ± 30**

Conclusions

A series of new macrocyclic molecular receptors ("homothiacalixnaphthalenes") based upon 2,3-dialkoxy-substituted naphthalene units, previously unreported have now been synthesized in synthetically useful yields, and some of their complexation properties have also been investigated. The syntheses of the octaethoxy and octa-*n*-propoxy macrocyclic compounds **12b** and **12c** were accompanied by small amounts of the corresponding higher hexaoxa homologues, **17b** and **17c**, respectively, but their complexation properties were not elucidated. The ^1H NMR spectra of all of the macrocycles obtained showed clearly that they were highly symmetrical and conformationally flexible. Although CPK models and molecular modeling suggested that these new receptors had the potential to be suitable hosts for the electron-deficient neutral guest molecules, C_{60}- and C_{70}-fullerenes, the solution complexation experiments did not demonstrate any such ability. As well, no complexation either was observed between these new homothia receptors and the TMA cation, however with the transition metal cations Ag^+ and Hg^{2+}, moderate-to-modest binding abilities could be determined. These results suggest that *e.g.* the Ag^+–π or Ag^+–sulfur (and to a lesser extent, the corresponding Hg^{2+}) interactions may be more effective than both the π–CH_3 interactions with the methyl groups of the TMA cation, and/or the π–π* interactions in the case of the host–fullerene complexations.

Experimental

Syntheses

1,4-Bis(mercaptomethyl)-2,3-dimethoxynaphthalene (16a). General procedure: a stirred mixture of the crude **15a** (1.87 g, 5.00 mmol) and thiourea (0.98 g, 13 mmol) in dry THF (150 mL) was heated at reflux with stirring for 36 h. After the reaction mixture was cooled to room temperature, the solvent was removed under reduced pressure. The resulting residue was dissolved in distilled water (100 mL), aqueous 10% NaOH solution (20 mL) was added and the mixture was heated at reflux for a further 24 h. After the reaction mixture was cooled to room temperature, the mixture was chilled in an ice bath and was neutralized by the addition of aqueous 10% HCl. The resulting precipitate was isolated by suction filtration and air-dried to give the crude product (1.22 g, 87% yield) as a light yellow powder, which was purified by chromatography (5 : 95 EtOAc–hexane) to yield **16a** (0.80 g, 64%) as a colourless powder: mp 120 °C ($CHCl_3$); ^1H NMR δ 1.94 (t, J = 6.8 Hz, 2H), 4.01 (s, 6H), 4.22 (d, J = 6.8 Hz, 4H), 7.51–7.53 (m, 2H), 7.97–7.99 (m, 2H); ^{13}C NMR δ 19.1, 61.4, 124.4, 125.9, 129.2, 150.0; GCMS m/z (relative intensity) 280 (M^+, 30), 247 (60), 214, 199 (60), 171, 128 (100), 115 (40).

1,4-Bis(mercaptomethyl)-2,3-diethoxynaphthalene (16b). Using the general procedure for **16a**, the reaction of the crude **15b** (0.69 g, 1.50 mmol) and thiourea (0.25 g, 3.3 mmol) in dry THF (50 mL) gave the crude product (0.38 g, 68%) as a light

yellow powder, which was purified by chromatography (2.5 : 97.5 EtOAc–hexane) to yield **16b** (0.22 g, 40%) as a colourless powder: mp 119–120 °C ($CHCl_3$); ^{1}H NMR δ 1.48 (t, J = 7.0 Hz, 6H), 1.93 (t, J = 7.0 Hz, 2H), 4.18–4.23 (m, 8H), 7.50–7.52 (m, 2H), 7.97–7.99 (m, 2H); ^{13}C NMR δ 16.2, 19.3, 69.8, 124.4, 125.7, 129.18, 129.21 149.0; GCMS m/z (relative intensity) 308 (M^+, 20), 275 (30), 185 (50), 157 (50), 128 (90), 115 (40).

1,4-Bis(mercaptomethyl)-2,3-dipropoxynaphthalene (16c). Using the general procedure for **16a**, the reaction of the crude **15c** (1.29 g, 3.0 mmol) and thiourea (0.58 g, 7.8 mmol) in dry THF (150 mL) gave the crude product (0.71 g, 71%) as a light yellow powder, which was purified by chromatography (2 : 98 EtOAc–hexane) to yield **16c** (0.42 g, 42%) as a colourless powder: mp 72–74 °C ($CHCl_3$); ^{1}H NMR δ 1.12 (t, J = 7.5 Hz, 6H), 1.86–1.95 (m, 6H), 4.08 (t, J = 6.5 Hz, 4H), 4.22 (d, J = 6.9 Hz, 4H), 7.50–7.52 (m, 2H), 7.97–7.99 (m, 2H); ^{13}C NMR δ 10.9, 19.3, 24.0, 75.8, 124.4, 125.7, 129.17, 129.24, 149.2; GCMS m/z (relative intensity) 336 (M^+, 10), 270 (25), 227 (100), 186 (70), 157 (50), 128 (90), 115 (40).

1,4-Bis(mercaptomethyl)-2,3-dibutoxynaphthalene (16d). Procedure 1: Using the general procedure for **16a**, **16d** was obtained from **15d** in only 2.5% yield as a colourless powder: mp 41–42 °C; ^{1}H NMR δ 1.03 (t, J = 7.4 Hz, 6H), 1.56–1.62 (m, 4H), 1.83–1.88 (m, 4H), 1.93 (t, J = 7.3 Hz, 2H), 4.12 (t, J = 6.3 Hz, 4H), 4.22 (d, J = 6.7 Hz, 4H), 7.50–7.52 (m, 2H), 7.97–7.99 (m, 2H); ^{13}C NMR δ 14.3, 19.3, 19.6, 32.8, 74.1, 124.4, 125.7, 129.1, 129.2, 149.2; GCMS m/z (relative intensity) 364 (M^+, 1), 298 (30), 241 (100), 225, 186 (100), 186 (100), 157 (50), 128 (70), 115 (41).

Procedure 2: (Reaction conducted at room temperature.) A solution of crude **15d** (0.23 g, 0.50 mmol) and thiourea (0.10 g, 1.3 mmol) in dry THF (25 mL) was stirred at room temperature under N_2 for 30 h. A solution of cold aqueous 10% NaOH (25 mL) was added and stirred for a further 2 h. The reaction mixture was chilled in an ice bath, acidified by aqueous 3 M HCl until the pH reached 2, extracted with $CHCl_3$ (3 × 20 mL), washed with distilled water (1 × 30 mL), brine (1 × 30 mL), dried over anhydrous $MgSO_4$ and filtered. After the solvent was removed under reduced pressure, the resulting residue was purified by chromatography (0.5 : 99.5 EtOAc–hexane) to yield **16d** (0.07 g, 39%) as a colourless powder having identical characterization data to those obtained from Procedure 1.

Procedure 3: (Using 95% EtOH as solvent.) A solution of crude **15d** (0.92 g, 2.00 mmol) and thiourea (0.40 g, 5.20 mmol) in 95% EtOH (100 mL) was heated at reflux with stirring under N_2 for 19 h. After cooling to room temperature, the reaction mixture was chilled in an ice bath, then aqueous 10% NaOH (100 mL) was added. The resulting mixture was stirred for a further 2.5 h, acidified with aqueous 3 M HCl until the pH reached 2, extracted with $CHCl_3$ (3 × 50 mL), dried over anhydrous $MgSO_4$ and filtered. After the solvent was removed under reduced pressure, the resulting residue was purified by chromatography (0.5 : 99.5 EtOAc–hexane) to yield **16d** (0.45 g, 62%) as a colourless powder having identical characterization data to those obtained from the Procedure 1.

Octahomotetrathiaisocalix[4]-2,3-dimethoxynaphthalene (12a). General procedure: To a stirred solution of KOH (0.20 g, 3.0 mmol) in 95% ethanol (20 mL) at room temperature, a solution of **15a** (187 mg, 0.500 mmol) and **16a** (140 mg, 0.500 mmol) in benzene (6 mL) was added over 3.0 h using a syringe pump. The mixture was stirred at room temperature for a further 4 d. After the solvents were evaporated, water (30 mL) was added and the residue was neutralized with aqueous 3 M HCl, extracted with $CHCl_3$ (3 × 50 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated, and the crude product was purified by PLC (3 : 7 EtOAc–hexane) to yield **12a** as a colourless powder (63 mg, 25%): mp > 250 °C (dec.); ^{1}H NMR δ 3.65 (s, 6H), 4.03 (s, 4H), 7.11–7.13 (m, 2H), 7.68–7.69 (m, 2H); ^{13}C NMR δ 27.4, 61.2, 124.5, 125.4, 126.3, 129.8, 150.1; (+)-APCI MS m/z (relative intensity) 985.3 (M^+, 60) calcd.: 985.3 for $C_{56}H_{56}O_8S_4$, 771.1 (10), 493.1 (100), 338.4 (80).

Octahomotetrathiaisocalix[4]-2,3-diethoxynaphthalene (12b) and dodecahomohexathiaisocalix[6]-2,3-diethoxynaphthalene (17b). Using the general procedure for **12a**, the coupling reaction between **15b** (201 mg, 0.500 mmol) and **16b** (154 mg, 0.500 mmol) gave the crude product, which was purified by PLC (2 : 8 EtOAc–hexane) to yield **12b** (76 mg, 28%) as a colourless powder: mp 250 °C (dec.); ^{1}H NMR δ 1.39 (t, J = 7.2 Hz, 6H), 4.06 (q, J = 6.8 Hz, 4H), 4.30 (s, 4H), 6.90–6.92 (m, 2H), 7.43–7.45 (m, 2H); ^{13}C NMR δ 16.1, 27.7, 70.0, 124.3, 125.3, 126.2, 130.0, 150.0; (+)-APCI MS m/z (relative intensity) 1097.4 (M^+, 100) calcd.: 1097.5 for $C_{64}H_{72}O_8S_4$; 789.3 (5), 549.3 (7), 338.4 (35); and **17b** (29 mg, 11%) as a colourless powder: mp > 180 °C (dec.); ^{1}H NMR δ 1.30 (t, J = 7.0 Hz, 6H), 4.06 (q, J = 7.1 Hz, 4H), 4.32 (s, 4H), 7.18–7.20 (m, 2H), 7.77–7.78 (m, 2H); ^{13}C NMR δ 16.0, 27.9, 69.9, 124.7, 125.3, 126.0, 130.0, 149.7; (+)-APCI MS m/z (relative intensity) 823.3 (M^{2+}, 15) calcd.: 1646.3 for $C_{96}H_{108}O_{12}S_6$, 423.5 (5%), 338.4 (100%).

Octahomotetrathiaisocalix[4]-2,3-dipropoxynaphthalene (12c) and dodecahomohexathiaisocalix[6]-2,3-*n*-propoxynaphthalene (17c). Using the general procedure for **12a**, the coupling reaction between **15c** (168 mg, 0.500 mmol) and **16c** (215 mg, 0.500 mmol) gave a product, which was purified by PLC (1 : 9 EtOAc–hexane) to yield **12c** (100 mg, 33%) as a colourless powder: mp >180 °C (dec.); ^{1}H NMR δ 1.06 (t, J = 7.7 Hz, 6H), 1.81–1.88 (m, 4H), 3.97 (t, J = 6.7 Hz, 4H), 4.28 (s, 4H), 6.85–6.87 (m, 2H), 7.39–7.41 (m, 2H); ^{13}C NMR δ 10.9, 23.9, 27.5, 76.0, 124.3, 125.2, 126.0, 129.7, 149.8; (+)-APCI MS m/z (relative intensity) 1029.4 (M^+, 74) calcd.: 1209.7 for $C_{72}H_{88}O_8S_4$, 617.2 (42), 341.2 (100), 338.4 (43); and **17c** (35 mg, 11%) as a colourless powder: mp >180 °C (dec.); ^{1}H NMR δ 0.89 (t, J = 7.3 Hz, 6H), 1.61–1.69 (m, 4H), 3.91 (t, J = 6.8 Hz, 4H), 4.32 (s, 4H), 7.19–7.21 (m, 2H), 7.81–7.82 (m, 2H); ^{13}C NMR δ 10.7, 23.7, 27.9, 75.9, 124.7, 125.3, 125.8, 130.1, 149.9; (+)-APCI MS m/z (relative intensity) 1813.4 (M^+, 15) calcd.: 1814.6 for $C_{108}H_{132}O_{12}S_6$, 715.6 (20), 382.5 (60) 338.4 (100).

Octahomotetrathiaisocalix[4]-2,3-*n*-dibutoxynaphthalene (12d). Using the general procedure for **12a**, the coupling reaction between **15d** (182 mg, 0.500 mmol) and **16d** (229 mg, 0.500

mmol) gave the crude product, which was purified by PLC (1 : 9 EtOAc–hexane) to yield **12d** (59 mg, 18%) as a colourless powder: mp > 200 °C (dec.); ^{1}H NMR δ 0.99 (t, J = 7.4 Hz, 6H), 1.49–1.56 (m, 5H, overlap with HOD signal), 1.78–1.84 (m, 4H), 4.01 (t, J = 6.4 Hz, 4H), 4.27 (s, 4H), 6.83–6.85 (m, 2H), 7.39–7.40 (m, 2H); ^{13}C NMR δ 14.3, 19.6, 27.5, 32.8, 74.3, 124.3, 125.2, 125.9, 129.7, 149.8; (+)-APCI MS m/z (relative intensity) 1322.5 (M^+, 100) calcd.: 1321.9 for $C_{80}H_{104}O_8S_4$, 957.3 (10), 705.4 (38), 419.2 (50), 338.4 (70).

Association constant determinations

Association constants (K_{assoc}) for the metal-binding studies in 1 : 9 CD_3CN–$CDCl_3$ between **12a** or **12b** with AgO_2CCF_3 were determined by ^{1}H NMR spectroscopy upon the changes in the chemical shift of the respective methylene bridge (–SCH_2–) signals. In the Benesi–Hildebrand treatment, K_{assoc} values were derived from plotting $(1/\Delta\delta)$ as a function of $1/[Ag^+]$, or using the Foster–Fyfe treatment, by plotting $\Delta\delta/[Ag^+]$ *vs.* $\Delta\delta$. For the non-linear curve fitting plots a 1 : 1 binding isotherm as described by Connors[23] was employed.

In a typical experiment, aliquots of the guest solutions, *e.g.* AgO_2CCF_3 (5.22×10^{-3} M ranging from 30–885 μL) in 1 : 9 CD_3CN–$CDCl_3$ (v/v) were added to individual NMR tubes which contained 600 μL of either **12a** (4.84×10^{-4} M), or **12b** (4.84×10^{-4} M). The resulting solutions were sonicated for approx. 5 min before NMR measurements were recorded at 298 K at 500 MHz. A similar methodology was employed with $HgCl_2$.

Acknowledgements

This research was supported by the Natural Sciences and Research Council of Canada (NSERC) and the Department of Chemistry, Memorial University of Newfoundland.

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