Synthesis, characterisation and X-ray diffraction studies of new lower rim calix[4]arene derivatives containing mixed donor atoms

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New lower rim *p-tert*-butylcalix[4]arene derivatives containing tetrathiophene functional groups as well as derivatives with two different pendant arms alternately arranged, one of which is in all cases a methylsulfanyl substituent whilst the other is either a tertiary amine (aliphatic of alicyclic) or a methylthiophene or an amide substituent, have been synthesised and characterised by ^{1}H and ^{13}C NMR spectroscopy in chloroform at 298 K. The use of phase transfer catalysis in the synthesis of calixarene derivatives is discussed. X-Ray diffraction studies of 5,11,17,23-tetrakis-(1,1-dimethylethyl)-25,26,27,28-tetrakis-[2-(thienyl)methoxy]calix[4]arene 1a and 5,11,17,23-tetrakis-(1,1-dimethylethyl)-25,27-bis[(2-methylsulfanyl)ethoxy]-26,28-bis[2-(diethylamino)ethoxy]calix[4]arene 2b are reported.

Introduction

Calixarenes are cyclic oligomers resulting from the base catalysed condensation of *p*-substituted phenols and formaldehyde. Functionalisation of the phenolic hydroxys at the lower rim of *p-tert*-butylcalix[*n*]arenes ($n = 4$, 6, 8) provides an interesting building block upon which ligating arms (containing donor atoms able to interact with metal cations) can be attached. Of particular interest are the calix[4]arene derivatives (cone conformation) characterised by an 'enforced' hydrophobic cavity between the aromatic rings and a hydrophilic region capable of complexing metal cations. The interaction of these derivatives with a particular group of cations is largely dependent on the nature and accessibility of the donor atoms of the ligating arms. Thus, derivatives containing ether, ester, amide or ketone functionalised groups are selective receptors for alkali, alkaline-earth and lanthanide cations.[1,2,3] However, an area of increasing interest is the search for ligands with selective properties for soft metal cations, particularly those with environmental interest such as mercury, lead and cadmium. Representative examples of lower rim functionalised calix[4]arenes with side chains containing soft donor atoms are those reported by Ting *et al.*,[4] Cobben *et al.*,[5] Beer *et al.*,[6] O'Connor *et al.*,[7] Gibbs and Gutsche,[8] Malinowska *et al.*,[9] Koh *et al.*,[10] Yordanov *et al.*,[11] Delaigue *et al.*,[12] Wròblewski *et al.*[13] and Sone *et al.*[14]

We recently reported[15] the synthesis, characterisation and acid-base properties of a series of lower rim functionalised calix[4]arenes containing aliphatic and alicyclic amines and demonstrated that the attachment of amino functional groups provides a suitable arrangement for interaction with toxic metal cations (Cd^{2+}, Hg^{2+} and Pb^{2+}), while cations such as Na^+, K^+ and Ba^{2+} are discriminated against. A further advantage of these ligands relative to others previously synthesised is that in their protonated form they can serve as efficient anion binders.[16]

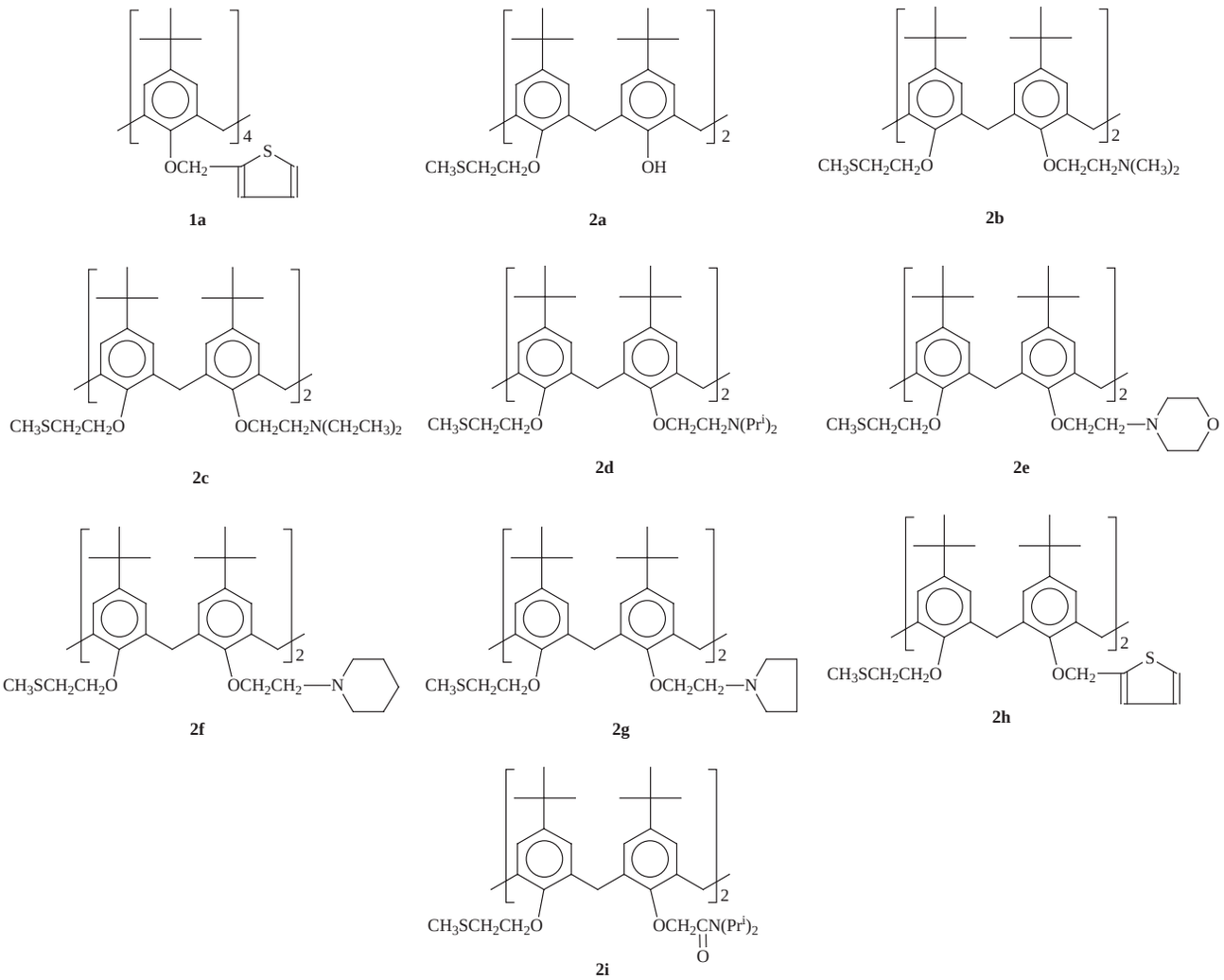
In this paper we report (i) the synthesis and ^{1}H and ^{13}C NMR spectroscopic characterisation of new lower rim derivatives of *p-tert*-butylcalix[4]arene containing tetrathiophene functional groups (**1a**) as well as derivatives with two different pendant arms alternately arranged, one of which is in all cases a methylsulfanyl substituent, whilst the other is either a tertiary amine (aliphatic, **2b**, **2c**, **2d**; alicyclic, **2e**, **2f**, **2g**) or a methylthiophene (**2h**) or an amide (**2i**) substituent; (ii) the use of phase transfer catalysts for the preparation of a previously reported macrocycle, **2a**; (iii) the X-ray structures of **1a** and **2b**.

Results and discussion

Use of a phase transfer catalyst in the synthesis of 2a

There is only one report in the literature[17] in which (for the synthesis of a di-substituted calix[4]spherand, namely, calix[4]-spherandiol), 18-crown-6 has been used for the preparation of the polyanion of *p-tert*-butylcalix[4]arene using sodium hydride and tetrahydrofuran as solvent. We have recently used crown ethers for the synthesis of calix[4]arene ester derivatives. In doing so, two important factors were considered, the solvent, and the selectivity of the crown ether for the cation as reflected in the stability constant data. Thus, acetonitrile was selected as the solvent because it offers a higher permittivity medium ($\varepsilon = 37.5$) than tetrahydrofuran ($\varepsilon = 7.6$).[18] Therefore the former solvent is a more suitable medium for the formation of the naked anions of *p-tert*-butylcalix[*n*]arenes ($n = 4$, 6, 8) than the latter, in which extensive ion-pair formation is likely to take place in solution. Since the selectivity of 18-crown-6 for potassium is greater by a factor of 10 than that for sodium in acetonitrile,[19] the potassium salt was used. Several advantages were found with respect to methods previously used and therefore 18-crown-6 was used for the synthesis of the **2a** derivative, as described in the Experimental section. This derivative was previously synthesised by Cobben *et al.*[5] and by Beer *et al.*[6] in the absence of a phase transfer catalyst. Advantages found in the use of 18-crown-6 are that (i) the alkylating agent is employed in equivalent quantities with respect to the phenolic units of the parent calixarenes; (ii) a chromatographic separation is not required; (iii) the yield is considerably higher than that reported by Beer *et al.*;[6] (iv) the refluxing period is much shorter.

The above examples illustrate that the use of phase transfer catalysts in the synthesis of calixarene derivatives should be further explored, particularly for the stepwise functionalisation of the parent calixarenes by using the respective equivalent quantities of base and alkylating agent required for their preparation. In addition, the above comments underline the importance of considering the physical properties of the solvent and the selective properties of the catalyst (in the case of crown ethers) in synthetic organic chemistry.



X-Ray crystal structure of 1a and 2b

Crystallographic parameters of this tetra-thiophene substituted calix[4]arene derivative are given in Table 1.† The structure of the molecule and the atom numbering system are depicted in Fig. 1. Selected intramolecular distances are given in Table 2.

As far as **2b** is concerned, crystallographic parameters for this nitrogen–sulfur mixed donor calix[4]arene derivative are given in Table 3. The structure of the molecule and the atom numbering are depicted in Fig. 2. Selected intramolecular distances are given in Table 4.

In the solid state **1a** and **2b** present a distorted cone conformation as observed for other derivatives.[20]

^{1}H and ^{13}C NMR spectroscopic studies

A relevant information regarding the conformation adopted in $CDCl_3$ for these derivatives is the non-equivalence shown between the axial (ax) and the equatorial (eq) hydrogens of the methylene bridge reflected by the pair of doublets which indicates that these compounds in this solvent adopt a 'cone' conformation.[2,3] This statement is reinforced by the ^{13}C NMR spectra where the carbon signal connecting two adjacent phenyl moieties is found at about 31.0 ppm.[21] As discussed by Gutsche,[3] the differences between the axial and equatorial protons of the methylene bridge ($\Delta\delta = H_{ax} - H_{eq}$) gives an indication of the symmetry of the cone conformation. A comparison between the $\Delta\delta$ value for *p-tert*-butylcalix[4]arene in $CDCl_3$ at 298 K (0.75 ppm) with the corresponding data for **2a** (0.99 ppm), **2b**–**2h** (1.19–1.28 ppm) and **2i** (1.34 ppm) appears to indicate that as the steric crowding between the substituents in the lower rim increases, $\Delta\delta$ values increase, suggesting that the aromatic rings adopt a relatively more parallel position. Again, a common feature of the spectra for derivatives **2b**–**2g** are the four multiplets or 'triplets' which can be seen between 4.3 and 2.9 ppm. These signals arise from the protons of the ethylene bridge between the two different heteroatoms (O, N) on each of the lower rim substituents. Lorentzian/Gaussian

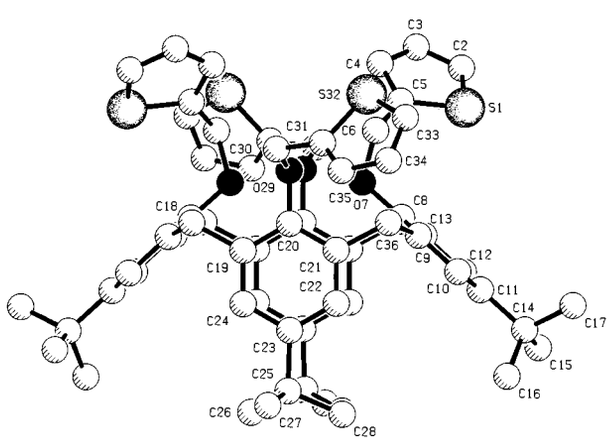


Fig. 1 Atom numbering scheme for **1a**. Structural disorder is not shown.

† Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC Web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature citation and the reference number 207/233.

Table 1 Crystal data and refinement details for **1a**

Molecular formula	$C_{64}H_{72}O_4S_4$
Molecular weight	1033.46
Crystal size (mm)	0.90 × 0.58 × 0.40
Colour	Colourless
Crystal system	Monoclinic
Space group	*C*2/c
a (Å)	11.973(5)
b (Å)	23.640(6)
c (Å)	20.974(4)
β (°)	93.26(2)
V (Å^3)	5927(3)
Z	4
D_c (g cm^{-3})	1.158
F(000)	2208
μ(MoKα) (mm^{-1})	0.21
Temperature (K)	293(2)
Wavelength (Å)	0.710 69
Scan mode	*ω*/2*θ*
θ Angular range (°)	1–25
Index range	−14/14, 0/28, 0/24
Unique reflections	5213
No. refined parameters	343
$R_w(F^2)$ (all data)	0.191
$R(F)$ [$I > 2\sigma(I)$]	0.057 (3594)
$R(F)$ (all data)	0.080
$w = [\sigma^2(F_o^2) + (0.1147P)^2 + 1.0187P]^{-1}$ where $P = [\text{Max}(F_o^2, 0) + 2F_c^2]/3$	—
Max/min electron density (e Å^{-3})	0.34/−0.29

Table 2 Selected intramolecular distances for **1a** (Å)

O(7)···O(7)[a]	3.410(3)
O(29)···O(29)[a]	5.370(3)
O(7)···O(29)	3.149(2)
O(7)···O(29)[a]	3.244(3)
O(7)···S(1)	3.454(3)
O(29)···S(32)	3.357(3)

[a] −x, y, 0.5−z

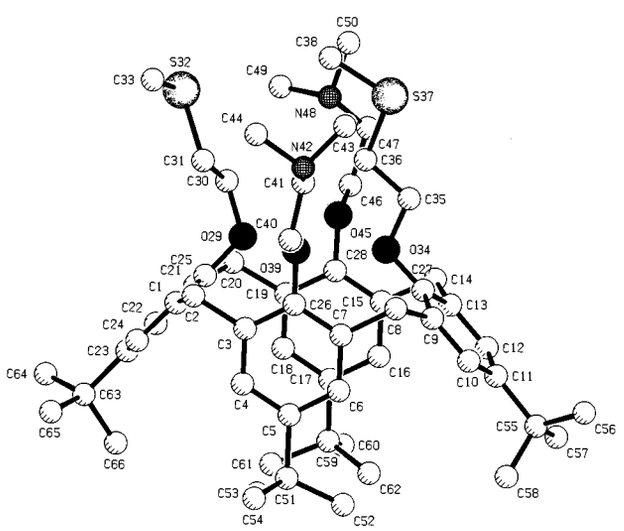


Fig. 2 Atom numbering scheme for **2b**. Structural disorder is not shown.

resolution enhancement and expansion of these 'triplets' revealed their full structure. Their complex structure are the results of restricted rotation around the C–C bond of the ethylene group which is caused by steric crowding between the lower rim substituents. For the effective starting material of these derivatives, **2a**, steric crowding does not occur and classical 1:2:1 intensity triplet signs are seen. Restricted rotation between two different heteroatoms produces non-equivalent protons on each methylene (OCH_2CH_2S and OCH_2CH_2N) creating an: AA′BB′ coupling system and the observed fine structure.

Table 3 Crystal data and refinement details for **2b**

Molecular formula	$C_{58}H_{86}O_4S_2N_2$
Molecular weight	939.41
Crystal size (mm)	0.54 × 0.25 × 0.22
Colour	Colourless
Crystal system	Monoclinic
Space group	$P2_1$/n
a (Å)	15.473(4)
b (Å)	19.752(6)
c (Å)	19.987(17)
β (°)	107.51(5)
V (Å^3)	5825(5)
Z	4
D_c (g cm^{-3})	1.072
F(000)	2048
μ(MoKα) (mm^{-1})	0.13
Temperature (K)	298(2)
Wavelength (Å)	MoKα 0.710 69
Scan mode	*ω*/2*θ*
θ Angular range (°)	1–25
Index range	−18/17, 0/23, 0/23
Unique reflections	10 214
No. refined parameters	571
$R_w(F^2)$ (all data)	0.206
$R(F)$ [$I > 2\sigma(I)$]	0.081 (2383)
$R(F)$ (all data)	0.303
$w = [\sigma^2(F_o^2) + (0.0892P)^2]^{-1}$, where $P = [\text{Max}(F_o^2, 0) + 2F_c^2]/3$	—
Max/min electron density (e Å^{-3})	0.28/−0.18

Table 4 Selected intramolecular distances for **2b** (Å)

O(29)···O(34)	3.603(6)
O(39)···O(45)	5.437(7)
O(29)···O(39)	3.331(6)
O(29)···O(45)	3.283(6)
O(34)···O(39)	3.316(6)
O(34)···O(45)	3.163(6)
O(29)···S(32)	3.994(5)
O(34)···S(37)	3.952(5)
O(39)···N(42)	3.661(8)
O(45)···N(48)	2.937(7)
S(32)···S(37)	5.229(6)
N(42)···N(48)	8.618(11)
N(42)···S(32)	6.410(8)
N(42)···S(37)	5.212(8)
N(48)···S(32)	4.783(8)
N(48)···S(37)	4.274(7)

The presence of two *tert*-butyl and two *m*-aromatic proton signals, which have not been differentiated in terms of assignment with regards to their lower di-substituent, show the existence of large structural and through space effects. Both sets of signals have a shift difference ($\Delta\delta$) of approximately 0.45 ppm. This significant shift difference cannot be attributed to substituent electronic effects as they occur too far away. Comparison of the spectral data of **2c** with those previously reported for lower rim calix[4]arenes derivatives containing exclusively diethylamine lower rim moieties {tetrakis-[(2*N*,*N*-diethylamino)ethoxy]-*p*-*tert*-butylcalix[4]arene}[15] or 2-(methylsulfanyl)ethoxy moieties {5,11,17,23-tetrakis(1,1-dimethylethyl)-25,26,27,28-tetrakis[(2-methylsulfanyl)ethoxy]calix[4]arene}[5,6] shows that the equivalent signals seen for these compounds lie between the two signals for each group of **2c**, making assignment difficult. The whole calixarene structure is a rigid system. The ^{1}H NMR spectroscopy performed in [$^2H_6$]DMSO at 298 and 373 K revealed no significant changes in the spectra. Some convergence of the *tert*-butyl and the *m*-aromatic proton's signals would have been expected for a non-rigid system.

In order to assign the four signals from the eight methylenes between the two heteroatoms on the lower rim, ligand **2c** was titrated with perchloric acid (or trifluoroacetic acid) in CD_3OD and single frequency homonuclear decoupling experiments were performed and coupled pairs were established. The results

are discussed in terms of the resonance protons corresponding to (i) the amine ligating atoms; and (ii) the methylene ligating atoms since these show distinctive features.

(i) Due to the protonation of the nitrogen atoms, the proton resonance positions of the two methylene groups were deshielded ($OC\mathbf{H}_2CH_2N$, $\Delta\delta = +0.42$ ppm, $OCH_2C\mathbf{H}_2N$, $\Delta\delta = +0.60$ ppm) and assigned. However, these downfield shifts are larger than expected, and therefore the possibility for the formation of a five membered ring with the oxygen atom, which links the substituent to the macrocycle *via* hydrogen bond, cannot be ruled out. The resonance positions of the methylene hydrogens adjacent to the oxygen and sulfur atoms only shift slightly upfield ($OC\mathbf{H}_2CH_2S$, $\Delta\delta = -0.02$ ppm and $OCH_2C\mathbf{H}_2S$, $\Delta\delta = -0.13$ ppm).

(ii) The protons of the two methylene groups of the (methylsulfanyl)ethyl ether functionalised arm now show free rotation; the methylene's AA′BB′ coupling system collapses into 1:2:1 intensity triplets. This indicates the possibility of conformational changes producing a less sterically hindered lower rim.

Large structural changes are also noted as the two *m*-aromatic ($\Delta\delta = +0.24$ and -0.15 ppm) and the two *tert*-butyl signals ($\Delta\delta = -0.13$ and $+0.15$ ppm) move towards each other, showing that the aromatic rings in the macrocyclic structure become closer to being equivalent.

Final remarks

Preliminary conductance studies carried out in methanol show that the new calix[4]arene ligands interact with Hg^{2+}, Cd^{2+}, Pb^{2+}, Cu^{2+} and Ag^{+}. We are now proceeding with thermodynamic studies involving these ligands and cations in a variety of solvents.

Experimental

General

^{1}H NMR measurements were recorded at 298 K using a Bruker AC-300E pulsed Fourier transform NMR spectrometer. Typical operating conditions for routine proton measurements involved 'pulse' or flip angle 30°, spectral frequency (SF) of 300.135 MHz, delay time 1.60 s, acquisition time (AQ) of 1.819, line broadening 0.55 Hz, sweep width 15 ppm ($^+$14 to -1 ppm). Solutions of **1a**, **2a**–**2i** in the appropriate solvent were placed in 5 mm NMR tubes using TMS as the internal reference to measure the spectra of the ligands. *J* Values are given in Hz.

^{13}C NMR spectra were recorded at the same temperature; typical operating conditions for routine carbon measurements involved 'pulse' or flip angle 60°, spectral frequency (SF) of 75.47 MHz, delay time 0.3 s, acquisition time (AQ) of 0.7, line broadening 1.4 Hz, sweep width 250 ppm ($^+$230 to -20 ppm). TMS was used as an internal reference. *p-tert*-Butylcalix[4]-arene, thiophene, 18-crown-6 (99%), 2-chloroethyl methyl sulfide (97%), 2-dimethylaminoethyl chloride hydrochloride (99%), 2-diethylaminoethyl chloride hydrochloride (99%) and sodium hydride (95%) were purchased from Aldrich and used without further purification. 2-*N*,*N*-diisopropylbromoacetamide was prepared by adding bromoacetyl bromide to diisopropylamine in chloroform; these chemicals were also purchased from Aldrich. 1-(2-Chloroethyl)pyrrolidine hydrochloride (98%), 2-diisopropylaminoethyl chloride hydrochloride (98%), 4-(2-chloroethyl)morpholine hydrochloride (99%) and 1-(2-chloroethyl)piperidine hydrochloride (98%) were purchased from Lancaster. 2-Chloromethylthiophene was prepared using a HCl generator and thiophene. Sodium hydrogen carbonate (99%) and calcium chloride (90%) from BDH were used.

N,*N*-Dimethylformamide (Fisher), tetrahydrofuran (Aldrich), hexane (Fisher), ethyl ethanoate (Fisher), acetonitrile (Fisher), dichloromethane (Fisher), ethanol (Hayman), methanol (Fisher), chloroform (Fisher), were purified as described elsewhere.[22,23]

For NMR measurements, $CDCl_3$, tetramethylsilane and trifluoroacetic acid, were all purchased from Aldrich chemical company.

5,11,17,23-Tetrakis-(1,1-dimethylethyl)-25,26,27,28-tetrakis[(2-thienyl)methoxy]calix[4]arene 1a

p-tert-Butylcalix[4]arene (2.7 g) was stirred under a nitrogen atmosphere in a DMF–THF (10:70) solvent mixture for 15 minutes. To the suspension, dry NaH (2 g) was added and this was followed by the addition of 2-chloromethylthiophene (5.25 ml). The reaction mixture was then refluxed for a period of 12 hours at 50 °C. The course of the reaction was monitored by TLC using a hexane–ethyl acetate (4:1) mixture as the developing solvent. The mixture was cooled and the solvent was removed under reduced pressure using a rotary evaporator. The residue was dissolved in CH_2Cl_2 and extracted with HCl (2 mol dm^{-3}), $NaHCO_3$ (saturated aqueous solution) and distilled water. The organic phase was dried with $CaCl_2$ and again the solvent was removed under reduced pressure. The remaining oil was recrystallised from hot acetonitrile and dichloromethane. The resulting crystals were dried under vacuum at 100 °C. Tetra-thiophene derivative **1a** yield 53%; mp, 255–257 °C; δ_H(300 MHz; $CDCl_3$) 7.25 (m, 1H), 6.94 (m, 1H), 6.69 (m, 1H), 6.69 (s, 2 H), 5.10 (s, 2 H), 4.14 (d, *J* 12.8, 1H), 2.89 (d, *J* 12.8, 1H), 1.06 (s, 9H); δ_C($CDCl_3$) 152.3, 140.5, 134.1, 124.8 (Ar), 144.7, 128.1, 126.5, 125.9 (thiophene), 69.3 (OCH_2), 33.8 [$C(CH_3)_3$], 31.9 ($ArCH_2Ar$), 31.4 [$C(CH_3)_3$] (Anal. calc. for $C_{64}H_{72}O_4S_4$; C, 74.39; H, 7.02; found, C, 74.34; H, 7.05%).

5,11,17,23-Tetrakis-(1,1-dimethylethyl)-25,27-dihydroxy-26,28-bis[2-(methylsulfanyl)ethoxy]calix[4]arene 2a

2a was prepared by adding *p-tert*-butylcalix[4]arene (8 g), potassium carbonate (6.9 g), 18-crown-6 (0.6 g) to freshly distilled acetonitrile (dried over CaH_2). The mixture was stirred for 15 minutes and then 2-chloroethyl methyl sulfide (5 g) was added. The reaction mixture was refluxed at 90 °C for 12 hours. The reaction was monitored by TLC using hexane–ethyl acetate (4:1) as the developing solvent.

Upon cooling the solvent was removed under reduced pressure by rotary evaporation. The residue was dissolved in dichloromethane and extracted with HCl (2 mol dm^{-3}), $NaHCO_3$ (saturated aqueous solution) and distilled water. The organic phase was dried with $CaCl_2$ and again the solvent was removed under pressure. The remaining oil was recrystallised from a hot ethanol–dichloromethane solvent mixture. The solid was dried under vacuum at 100 °C. 1,3-Bis[(methylsulfanyl)-ethyl] ether derivative yield 65%; mp, 226–227.5 °C; δ_H(300 MHz; $CDCl_3$) 7.06, 6.75 (s, 4H), 7.00 (s, 1H), 4.31 (d, *J* 13.0, 2H), 4.13 (t, *J* 7.0, 2H), 3.32 (d, *J* 13.0, 2H), 3.06 (t, *J* 7.0, 2H), 2.29 (s, 3H), 1.29, 0.96 (s, 18H); δ_C($CDCl_3$) 150.5, 149.9 (s, Ar, 25, 26, 27, 28), 146.9, 141.5 (s, Ar, 5, 11, 17, 23), 132.3, 127.8 (s, Ar, 1, 3, 5, 7, 9, 13, 15, 19, 21), 125.5, 125.0 [s, Ar (*C*-H)], 75.4 (CH_2CH_2S), 33.9, 33.7 [$C(CH_3)_3$], 33.5 (CH_2CH_2S), 31.7, 31.0 [$C(CH_3)_3$], 31.6 ($ArCH_2Ar$), 16.4 (SCH_3) (Anal. calc. for $C_{50}H_{68}O_4S_2$; C, 75.33; H, 8.60; found, C, 75.29; H, 8.40%).

5,11,17,23-Tetrakis-(1,1-dimethylethyl)-25,27-bis[(2-methylsulfanyl)ethoxy]-26,28-bis[2-(dimethylamino)ethoxy]calix[4]-arene 2b

The **2b** derivative was prepared by adding the 1,3-bis[(methylsulfanyl)ethyl] ether derivative **2a** (0.75 g), dry NaH (0.23 g) to freshly distilled THF (70 ml dried over potassium/benzophenone ketal) and DMF (20 ml, HPLC grade). The resulting suspension was stirred for 10 minutes whereupon 2-dimethylaminoethyl chloride hydrochloride (0.81 g, dried under vacuum over $CaCl_2$) was added slowly. The reaction mixture was then refluxed at 90 °C under a nitrogen atmosphere for 12 hours. The reaction was monitored by TLC using a hexane–ethyl acetate (4:1) solvent mixture as the developing solvent. After cooling, the solvent mixture was removed under reduced pressure by

rotary evaporation, the residue was dissolved in dichloromethane and extracted with $NaHCO_3$ (saturated aqueous solution) and distilled water. The organic phase was dried with $CaCl_2$ and again the solvent was removed under reduced pressure. The remaining oil was recrystallised from a hot methanol–dichloromethane mixture. The resulting crystals were dried under vacuum at 100 °C. The bis-dimethylamine derivative was obtained in 50% yield; mp, 207–210 °C; δ_H(300 MHz; $CDCl_3$) 7.06, 6.50 (s, 4H), 4.39 (d, *J* 12.5, 2H), 4.17 (t, *J* 8.3, 2H), 3.85 (t, *J* 6.8, 2H), 3.23 (t, *J* 6.4, 2H), 3.14 (d, *J* 12.6, 2H), 2.82 (t, *J* 6.8, 2H), 2.33 (s, 6H), 2.22 (s, 3H), 1.29, 0.84 (s, 18H); δ_C($CDCl_3$) 152.8, 149.9 (s, Ar, 25, 26, 27, 28), 144.1, 143.3 (s, Ar, 5, 11, 17, 23), 134.2, 131.1 (s, Ar, 1, 3, 7, 9, 13, 15, 19, 21), 124.4, 123.6 (s, Ar*C*-H), 72.3 (CH_2CH_2S), 72.1 (CH_2CH_2N), 58.2 (CH_2N), 45.0 ($NCH_3)_2$, 33.0, 32.6 [$C(CH_3)_3$], 31.6 (CH_2S), 30.6, 30.1 [$C(CH_3)_3$], 30.0 ($ArCH_2Ar$), 16.7 (SCH_3) (Anal. calc. for $C_{58}H_{86}O_4S_2N_2$; C, 74.15; H, 9.28; N, 2.23; found, C, 74.15; H, 9.32; N, 2.05%).

5,11,17,23-Tetrakis-(1,1-dimethylethyl)-25,27-bis[(2-methylsulfanyl)ethoxy]-26,28-bis[2-(diethylamino)ethoxy]calix[4]arene 2c

2c was prepared according to the procedure described for **2b** using 2-diethylaminoethyl chloride hydrochloride (2.20 g). The final product was recrystallised from a methanol–dichloromethane solvent mixture. Yield 65%; mp, 192–198 °C; δ_H(300 MHz; $CDCl_3$) 7.09, 6.47 (s, 4H), 4.36 (d, *J* 12.5, 2H), 4.17 (m, 2H), 3.85 (t, *J* 7.4, 2H), 3.20 (m, 2H), 3.14 (d, *J* 12.3, 2H), 3.02 (t, *J* 7.4, 2H), 2.61 (q, *J* 7.1, 4H), 2.22 (SCH_3, 3H), 1.07 (t, *J* 7.2, 3H), 1.31, 0.84 (s, 18H); δ_C($CDCl_3$) 153.6, 152.2 (s, Ar, 25, 26, 27, 28), 145.2, 144.3 (s, Ar, 5, 11, 17, 23), 135.3, 131.9 (s, Ar, 1, 3, 7, 9, 13, 15, 19, 21), 125.5, 124.5 (s, Ar*C*-H), 73.5 (CH_2-CH_2N), 73.3 (CH_2CH_2S), 52.8 (CH_2CH_2N), 47.6 [$N(CH_2$-$CH_3)_2$], 34.1, 33.6 [$C(CH_3)_3$], 32.7 (CH_2CH_2S), 31.7, 31.1 [$C(CH_3)_3$], 30.1 ($ArCH_2Ar$), 15.7 (SCH_3), 11.7 [$N(CH_2CH_3)_2$] (Anal. calc. for $C_{62}H_{94}O_4S_2N_2$; C, 74.80; H, 9.52; N, 2.81; found, C, 74.79; H, 9.92; N, 2.77%).

5,11,17,23-Tetrakis-(1,1-dimethylethyl)-25,27-bis[(2-methylsulfanyl)ethoxy]-26,28-bis[2-(diisopropylamino)ethoxy]calix[4]arene 2d

2d was prepared by adding the adduct 2-diisopropylaminoethyl chloride hydrochloride (1.51 g) to **2a**. The final product was recrystallised from a methanol–dichloromethane solvent mixture. Yield 55%; mp, 234–236 °C; δ_H(300 MHz; $CDCl_3$) 7.12, 6.44 (s, 4H), 4.35 (d, *J* 12.5, 2H), 4.22 (t, *J* 8.4, 2H), 3.67 (t, *J* 8.0, 2H), 3.25 (m, 2H), 3.16 (d, *J* 12.6, 2H), ≈3.0 (m, 4H), ≈3.0 (m, 4H), 2.22 (s, 3H), 1.33, 0.81 (s, 18H), 1.04 (d, *J* 6.5, 12H); δ_C($CDCl_3$) 154.0, 152.0 (s, Ar, 25, 26, 27, 28), 145.3, 144.1 (s, Ar, 5, 11, 17, 23), 135.6, 131.7 (s, Ar, 1, 3, 7, 9, 13, 15, 19, 21), 125.5, 124.5 (s, Ar, *C*-H), 76.9 (CH_2CH_2N), 73.3 (CH_2CH_2S), 49.9 [$CH(CH_2)_2$], 45.1 (CH_2CH_2N), 34.1, 33.6 [$C(CH_3)_3$], 32.8 (CH_2CH_2S), 31.7, 31.1 [$C(CH_3)_3$], 31.1 [$ArCH_2Ar$], 20.8 [$CH(CH_3)_2$], 15.7 (SCH_3) (Anal. calc. for $C_{66}H_{102}N_2O_4S_2$; C, 75.38, H, 9.78; N, 2.66; found, C, 75.42, H, 9.69, N, 2.69%).

5,11,17,23-Tetrakis-(1,1-dimethylethyl)-25,27-bis[(2-methylsulfanyl)ethoxy]-26,28-bis[2-(morpholino)ethoxy] calix[4]arene 2e

The **2e** derivative was prepared according to the procedure for **2b** using 4-(2-chloroethyl)morpholine hydrochloride (1.05 g). The final product was recrystallised from a methanol–dichloromethane solvent mixture. Yield 50%; mp, 173–177 °C; δ_H(300 MHz; $CDCl_3$) 7.06, 6.50 (s, 4H), 4.41 (d, *J* 12.5, 2H), 4.18 (t, *J* 8.1, 2H), 3.90 (t, *J* 6.4, 2H), 3.75 (m, 4H), 3.20 (t, *J* 8.5, 2H), 3.13 (d, *J* 12.6, 2H), 2.84 (t, *J* 6.4, 4H), 2.54 (m, 4H), 2.20 (s, 3H), 1.29, 0.86 (s, 18H); δ_C($CDCl_3$) 153.6, 152.3 (s, Ar, 25, 26, 27, 28), 145.2, 144.5 (s, Ar, 5, 11, 17, 23), 135.2, 134.1 (s, Ar, 1, 3, 7, 9, 13, 15, 19, 21), 125.5, 124.6 (s, Ar, *C*-H), 73.3 (CH_2CH_2S), 71.7 (CH_2CH_2N), 67.0 [$(CH_2)_2O$], 58.7 (CH_2CH_2N), 54.2 [$N(CH_2)_2$], 34.1, 33.6 [$C(CH_3)_3$], 33.0 (CH_2CH_2S), 31.6, 31.1 [$C(CH_3)_3$], 31.1 ($ArCH_2Ar$), 15.9 (SCH_3) (Anal. calc. for $C_{62}H_{90}O_6S_2N_2$; C, 72.76; H, 8.86; N, 2.74; found, C, 72.56; H, 9.21; N, 2.85%).

5,11,17,23-Tetrakis-(1,1-dimethylethyl)-25,27-bis[(2-methylsulfanyl)ethoxy]-26,28-bis[2-(piperidino)ethoxy]calix[4]arene 2f

The procedure used for the preparation of **2f** is the same as that described for **2b** using 1-(2-chloroethyl)piperidine hydrochloride (1.40 g). The final product was recrystallised from a methanol–dichloromethane solvent mixture. Yield 61%, mp, 239–241 °C; δ_H(300 MHz; $CDCl_3$) 7.06, 6.49 (s, 4H), 4.39 (d, *J* 12.5, 2H), 4.17 (t, *J* 8.2, 2H), 3.89 (t, *J* 7.0, 2H), 3.22 (m, 2H), 3.13 (d, *J* 12.6, 2H), 2.86 (t, *J* 7.0, 2H), 2.47 (m, 4H), 2.22 (s, 3H), 1.61 (m, 4H), 1.44 (m, 2H), 1.30, 0.85 (s, 18H); δ_C($CDCl_3$) 153.8, 152.3 (Ar, 25, 26, 27, 28), 145.0, 144.2 (Ar, s, 5, 11, 17, 23), 135.3, 132.0 (Ar, 1, 3, 7, 9, 13, 15, 19, 21), 125.4, 124.5 (Ar, *C*-H), 73.2 (CH_2CH_2S), 72,6 (CH_2CH_2N), 58.8 (CH_2CH_2N), 55.2 [$N(CH_2)_2$], 34.0, 33.5 [$C(CH_3)_3$], 32.8 (CH_2CH_2S), 31.6, 31.1 [$C(CH_3)$], 31.1 ($ArCH_2Ar$), 26.0 ($NCH_2CH_2CH_2$), 24.3 ($NCH_2CH_2CH_2$), 15.8 (SCH_2) (Anal. calc. for $C_{64}H_{94}O_4S_2N_2$; C, 75.39; H, 9.29; N, 2.75; found, C, 75.50; H, 9.67; N, 2.77%).

5,11,17,23-Tetrakis-(1,1-dimethylethyl)-25,27-bis[(2-methylsulfanyl)ethoxy]-26,28-bis[2-(1-pyrrolidinyl)ethoxy]calix[4]arene 2g

In the preparation of **2g** the procedure used for the synthesis of **2b** was followed using 1-(2-chloroethyl)pyrrolidine (1.28 g). The final product was recrystallised from a methanol–dichloromethane solvent mixture. Yield 53%; mp, 185–188 °C; δ_H(300 MHz; $CDCl_3$) 7.07, 6.50 (s, 4H), 4.40 (d, *J* 12.5, 2H), 4.16 (m, 2H), 3.90 (t, *J* 7.0, 2H), 3.21 (m, 2H), 3.14 (d, *J* 12.5, 2H), 3.00 (t, *J* 7.2, 2H), 2.60 (m, 4H), 2.22 (s, 3H), 1.81 (m, 4H), 1.30, 0.85 (s, 18H); δ_C($CDCl_3$) 153.9, 152.3 (s, Ar, 25, 26, 27, 28), 145.1, 144.3 (s, Ar, 5, 11, 17, 23), 135.3, 132.2 (s, Ar, 1, 3, 7, 9, 13, 15, 19, 21), 125.4, 124.5 (s, Ar, *C*-H), 74.0 (CH_2CH_2N), 73.3 (CH_2CH_2S), 56.0 (CH_2CH_2N), 54.6 (NCH_2CH_2), 34.1, 33.6 [$C(CH_3)_3$], 32.7 (CH_2CH_2S), 31.7, 31.2 [$C(CH_3)_3$], 31.1 ($ArCH_2Ar$), 23.6 (NCH_2CH_2), 15.8 (SCH_3) (Anal. calc. for $C_{62}H_{90}N_2O_4S_2$; C, 75.10; H. 9.15; N, 2.83; found, C, 75.07; H, 9.52; N, 2.86%).

5,11,17,23-Tetrakis-(1,1-dimethylethyl)-25,27-bis[(2-methylsulfanyl)ethoxy]-26,28-bis[(2-thienyl)methoxy]calix[4]arene 2h

For the preparation of **2h** the procedure used is that outlined for the synthesis of **2b** except that 2-chloromethylthiophene (0.5 ml) was added. The product was recrystallised from a methanol–dichloromethane solvent mixture. Yield 48%; mp, 249–259 °C; δ_H(300 MHz; $CDCl_3$) 7.34 (d, *J* 5.0, 2H), 7.07 (d, *J* 3.3, 1H), 7.02 (m, 1H), 7.10, 6.47 (s, 4H), 4.86 (s, 2H), 4.35 (d, *J* 12.5, 4H), 4.02 (m, 2H), 3.11 (d, *J* 12.6, 4H), 2.88 (m, 2H), 1.95 (s, 3H), 1.32, 0.83 (s, 18H); δ_C($CDCl_3$) 154.0, 151.6 (s, Ar, 25, 26, 27, 28), 145.2, 144.9 (s, Ar, 5, 11, 17, 23), 139.7 [CH_2C(CH)S], 135.4, 132.1 (s, Ar, 1, 3, 7, 9, 13, 15, 19, 21), 127.9, 126.9, 126.4 (thiophene), 125.5, 124.8 [s, Ar (*C*-H)], 73.3 (OCH_2S), 71.0 (OCH_2CH_2S), 34.1, 33.6 [$C(CH_3)_3$], 32.5 (OCH_2CH_2S), 31.7, 31.2 [$C(CH_3)_3$], 31.1 ($ArCH_2Ar$), 15.4 (SCH_3) (Anal. calc. for $C_{60}H_{76}S_4O_4$; C, 72.83; H; 7.74; found, C, 72.86; H, 7.96%).

5,11,17,23-Tetrakis-(1,1-dimethylethyl)-25,27-bis[(2-methylsulfanyl)ethoxy]-26,28-bis[(2-diisopropylamino)-2-oxoethoxy]-calix[4]arene 2i

The same procedure was used as outlined for the preparation of **2b** except that 2-*N*,*N*-diisopropylacetamide chloride (0.75 ml) was added to **2a** in order to synthesise this derivative. The diisopropylacetamide adduct was prepared by adding chloroacetyl chloride to diisopropylamine in diethyl ether, the reaction temperature being held at 0 °C. The product was recrystallised

from a methanol–dichloromethane solvent mixture. Yield 17%; mp, 274–282 °C; δ_H(300 MHz; $CDCl_3$) 7.11, 6.46 (s, 4H), 4.49 (d, *J* 12.5, 2H), 4.35 (s, 2H), 4.30 (m, 2H), ≈3.7 (br m, 2H), 3.35 (m, 2H), 3.15 (d, *J* 12.6, 2H), 2.31 (s, 3H), 1.42, 1.17 (br m, 12H), 1.34, 0.82 (s, 18H); δ_C($CDCl_3$) 166.4 (*C*=O), 154.3, 152.2 (s, Ar, 25, 26, 27, 28), 144.9, 144.5 (s, Ar, 5, 11, 17, 23), 135.6, 131.8 (s, Ar, 1, 3, 7, 9, 13, 15, 19, 21), 125.5, 124.7 [s, Ar(C-H)], ≈73.8 (CH_2CH_2S), ≈73.8 [$OCH_2C(O)$], 34.1, 33.6 [$C(CH_3)_3$], 32.0 (CH_2CH_2S), 31.7, 31.1 [$C(CH_3)_3$], 31.3 ($ArCH_2Ar$), 29.7 [$CH(CH_3)_2$], 21.0 [br, $CH(CH_3)_2$], 15.3 (SCH_3) (Anal. calc. for $C_{66}H_{98}N_2S_2O_6$; C, 73.43; H, 9.15; N, 2.59; found, C, 73.49; H, 9.73; N, 2.45%).

X-Ray crystallography

$C_{64}H_{72}O_4S_4$ **1a**. A suitable colourless prismatic crystal was selected and mounted on an Enraf Nonius CAD4 diffractometer. Unit cell parameters were determined from automatic centring of 25 reflections ($11.5 \leq \theta \leq 14.1$) and refined by the least-squares method. Three reflections measured every 2 h as orientation and intensity control showed no significant decay during data collection. Lorentz-polarisation corrections but no absorption corrections were made. The structure was solved by direct methods using the SHELXS-86 program[24] and refined on F^2 for all reflections by the full-matrix least-squares method using the SHELXL-97 program.[25] The asymmetric unit is half a molecule. Both thiophene rings present in the asymmetric unit were disordered and two opposite conformations were located for each one with site occupancy factors of 0.6/0.4 and 0.7/0.3. Restrictions were applied to their geometries. One *tert*-butyl group showed rotational disorder. Two sets of methyl groups were defined with site occupancy factors of 0.5 and refined as rigid bodies. Benzene rings were also refined as rigid bodies. H atoms were placed in calculated positions with isotropic temperature factors 1.5 (methyl hydrogens) or 1.2 (the rest) times U_{eq} of corresponding carbons. Non-hydrogen atoms were refined anisotropically.

$C_{50}H_{86}N_2O_4S_2$ **2b**. A suitable colourless prismatic crystal was selected and mounted on an Enraf Nonius CAD4 diffractometer. Unit cell parameters were determined from automatic centring of 25 reflections ($8.5 \leq \theta \leq 11.9$) and refined by the least-squares method. Three reflections measured every 2 h as orientation and intensity control showed no significant decay during data collection. Lorentz-polarisation corrections but no absorption corrections were made. The structure was solved by direct methods using SHELXS-86 program[24] and refined on F^2 for all reflections by the full-matrix least-squares method using the SHELXL-97 program.[25] Benzene rings were refined as rigid bodies. The four *tert*-butyl groups showed rotational disorder. Two or three sets of methyl groups were defined with site occupancy factors of 0.5/0.5, 0.4/0.3/0.3, 0.7/0.3 and 0.5/0.5 respectively and refined as rigid bodies. One NMe_2 group also shows structural disorder, two conformations were found with site occupancy factors of 0.6/0.4. H atoms were placed in calculated positions with isotropic temperature factors 1.5 (methyl hydrogens) or 1.2 (the rest) times U_{eq} of corresponding carbons. Non-hydrogen atoms (except the most disordered *tert*-butyl carbons) were refined anisotropically.

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