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C3-cyclotriveratrylenes bearing pendant thiol substituents: New biofunctional ligands for the complexation of iron-sulfur clusters

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We report the synthesis of two new C3-cyclotriveratrylenes (LS_3) bearing three pendant arms ending either with a *n*-propyl thiol (1) or a *m*-substituted benzene thiol (2). The X-ray crystal structure of 1 and molecular modelling studies of a complex of 2 with Fe_4S_4 show that these molecules have the correct geometry to function as tridentate ligands towards this cluster. The reaction of 1 and 2 with $[Fe_4S_4(SR)_4]^{2-}$ (R = ethyl, t-butyl) actually results in a quantitative capture of these clusters and the formation of new stable species of the type $[Fe_4S_4(LS_3)(SR)]^{2-}$.

INTRODUCTION

One of the recent developments in molecular recognition chemistry is the chemical modelling of active sites in metalloenzymes, with the purpose of gaining a better knowledge on their structures and functions than with simpler synthetic analogs. This may also lead to the design of artificial supramolecular catalysts that mimic some of the properties of their natural models. There is increasing evidence that, within the enzyme pocket, the basic properties of the metal ion(s) or cluster, particularly their redox potential and in turn their ability to exchange electrons, are strongly dependent on the immediate protein environment, such as the presence of aromatic, phenolic, acidic or basic residues. These groups are capable of modulating the hydrophobicity of the pocket, or the number of hydrogen bonds with the metal site(s), and of modifying thereby the electron density at the latter. Moreover, the three-dimensional structure of the enzyme pocket conveys most of the size, shape, and topological dependence of the substrate-metal interactions, resulting in substrate specificity and in the stereoselectivity of the chemical transformations mediated by the enzyme. In recent years, a number of artificial metallohosts have been designed with the purpose of reproducing the environment of the metal sites in such proteins. Capped porphyrins have been used as cytochrome P450 models,[1] while modified cyclodextrins,[2] cyclophanes,[3] crown-ethers,[4] cavitands based on hexa-substituted benzenes,[5] and concave-shaped macrocycles[6] have been used as ligands for iron-sulfur protein models, and macrobicyclic bicapped ligands have been designed as siderophore models.[7] Some relevant properties of the active sites of the natural enzymes have been achieved in part with these ligands, such as asymmetric epoxydation or oxydation of olefins,[1] subsite specificity,[4,5] positioning of the metal center into a partly hydrophobic environment[2,3,7] or increased stability of iron-sulfur clusters in aqueous solution.[2]

In connection with our current work on the structure of the active site in aconitases and related iron-sulfur proteins,[8] we report here the design, synthesis and some properties of model systems in which new C3-cyclotriveratrylenes,[9] bearing three pendant arms terminated by a thiol group, provide ligands (LS_3) capable of binding to Fe_4S_4 iron-sulfur clusters. Examination of CPK models and molecular modelling studies both suggest that the size, shape and C3-symmetry of the rigid cyclotriveratrylene subunit are well suited for inserting an iron-sulfur cluster in the concave region of the host (Scheme I, X = OCH_3, Y = O, R = Et, t-Bu), and hence for providing an aromatic environment and an efficient protection from the solvent to at least part of the cluster.

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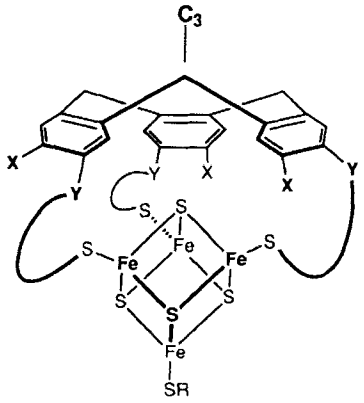
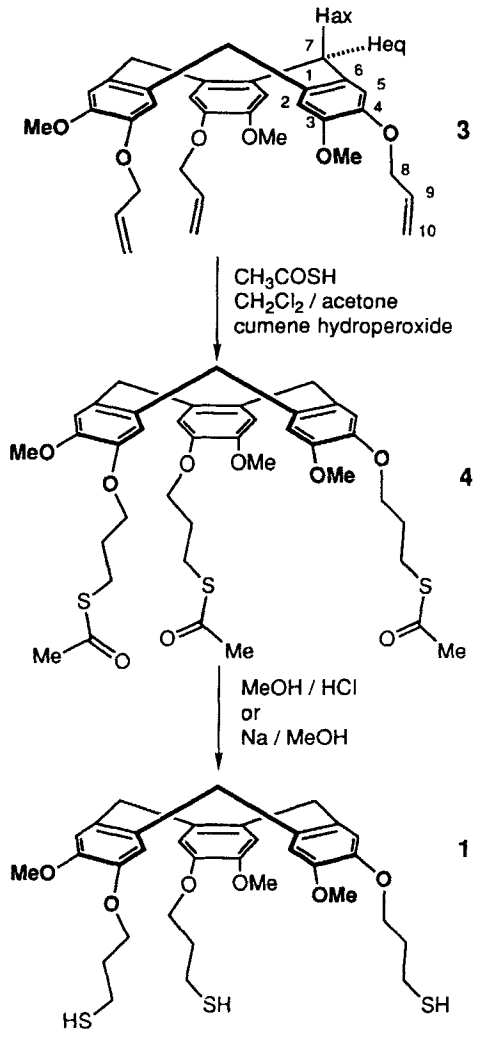


Scheme I

In the hosts considered in this paper (**1** and **2**, Schemes II and III, respectively), the structure of the pendant arms (O-$(CH_2)_3$-SH for **1** and O-CH_2-*m*-C_6H_4-SH for **2**) was chosen so as to allow a control of the degree of embedding of the metal cluster inside the aromatic pocket of the cyclotriveratrylene unit.

RESULTS AND DISCUSSION

Ligand **1** was synthesized as depicted in Scheme II, starting from the known tris-O-allyl derivative **3**.[10] Anti-Markownikov addition of thioacetic acid to the allylic double bonds of **3** to give **4** was achieved in 75% yield by using a method recently developed for the addition of thioacids to unsaturated carbohydrates.[11] Cleavage of the acetyl groups of **4** to generate the desired trithiol **1** could then be satisfactorily achieved either by reaction with sodium in methanol (80%), or with HCl in methanol (77%).[3b]



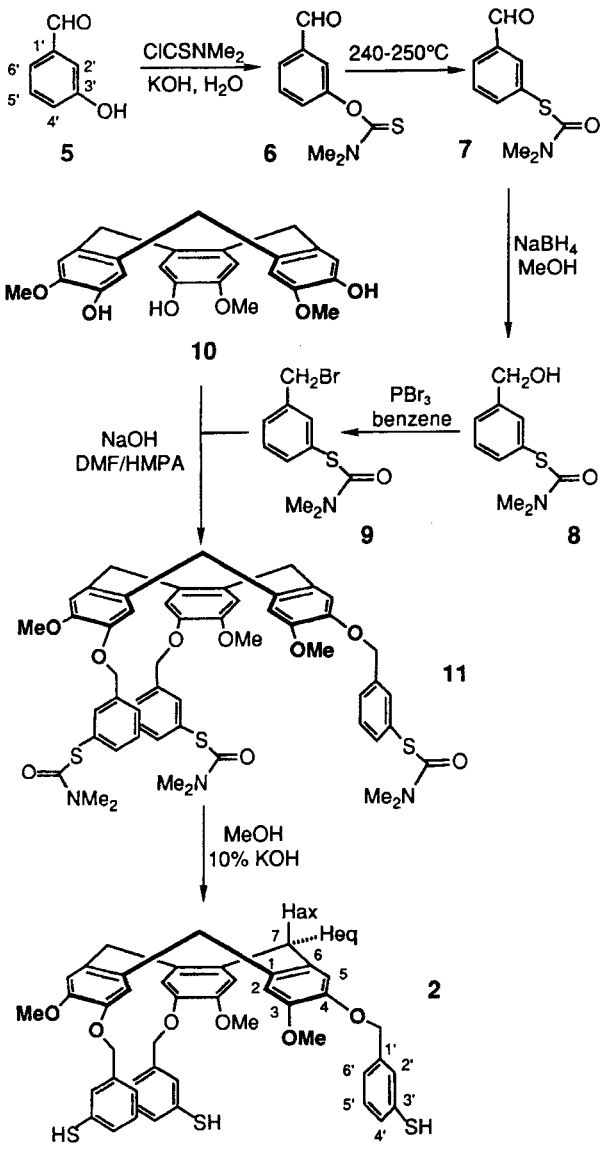
Scheme II

Ligand **2**, which bears three aromatic thiol side chains, was prepared by O-alkylation of the phenol groups of cyclotriguaiacylene[10] **10** with the benzyl bromide derivative **9**, followed by hydrolysis of the dimethylthiocarbamoyl groups to the free thiols (Scheme III).

For the synthesis of intermediate **9**, 3-hydroxybenzaldehyde **5** was thioesterified by N,N-dimethylthiocarbamoylchloride to give **6** (82%). A Newman-Kwart rearrangement[12,13] of **6** (250 °C, 2 h, 79%) then gave **7**, which led to the benzyl alcohol **8** (54%) upon reduction with $NaBH_4$. Bromination of the latter by PBr_3[14] produced **9** in 86% yield. Then, reaction of **9** with the sodium phenoxide derivative of **10** in DMF/HMPA, gave **11** quantitatively,[15] and hydrolysis of the thioesters of **11** (KOH in methanol, 81%) eventually afforded the desired ligand **2**.

Intermediates **6–9** gave spectroscopic data in agreement with their structures (see Experimental section). The ^1H- and ^{13}C-NMR spectra of ligand **1** and **2** showed all the required characteristics for a C3-cyclotriveratrylene in the rigid crown conformation[9]. The chemical shifts and multiplicities of all proton and carbon resonances in these compounds were assigned by suitable 2D-experiments (COSY, NOE, XHCORR, HMBC); full details on these structural studies will be reported separately.[16]

The structure of **1** was confirmed by X-ray crystallography. Good quality crystals were obtained by slow vapor diffusion of diethylether in a dichloromethane solution of the ligand. A view of the molecular structure is presented in Figure 1. The bond distances and angles are similar to those reported for other cyclotriveratrylenes[17] and cryptophanes (hosts containing two cyclotriveratrylene subunits).[18] As expected, the cyclononatriene ring adopts the crown conformation, indicated by the values of the angles at C_1, C_2 and C_3 (109.3°, 114°, 115.2°). The *n*-propyl side chains supporting the thiol functions are fully extended and lie (approximately) within the planes of the benzene rings to which they are bonded. In the crystal, the molecules are stacked in columns along the *c*



Scheme III

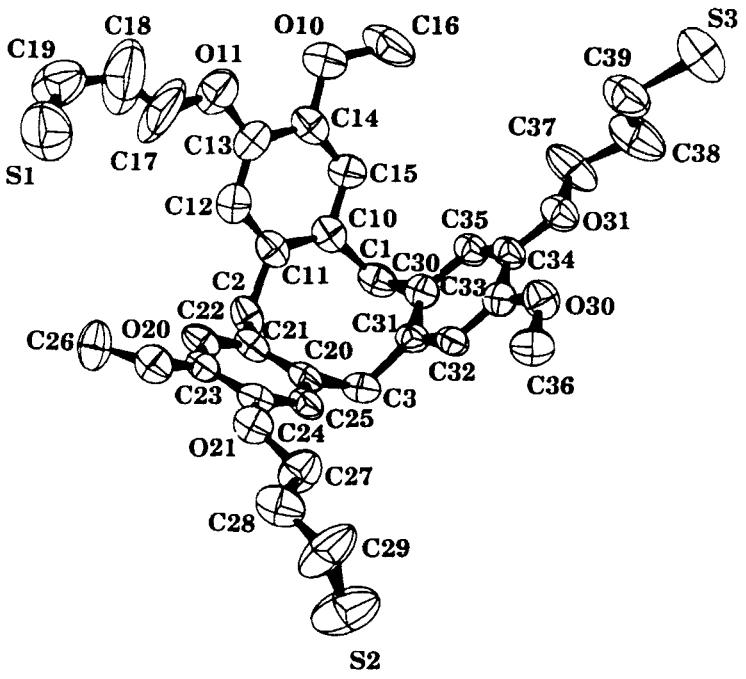
axis. All molecules in a column have the same chirality and the same upside or downside orientation of the cones with respect to the column axis; within a column each molecule is rotated by 60° with respect to the adjacent molecules. The packing consists of parallel, enantiomerically related columns, showing an alternate orientation of the cones, as shown in the stereoview at the bottom of Figure 1. Packing effects also bring short intermolecular contacts due to hydrogen bonding between the thiol groups; in each molecule, S_1 is at 4.07 Å from the S_2 of a neighboring molecule, while S_2 and S_3 are both at 3.84 Å from the S_3 and S_2 of two other molecules.

Evidence that ligands **1** and **2** are capable of capturing a Fe_4S_4 cluster in solution was first obtained when monitoring the reaction by ^{1}H-NMR spectroscopy. Upon stepwise addition of 0.5, 0.8, 1.0 and 1.5 equivalents of **2** to a solution of $[Fe_4S_4(SR)_4]^{2-}$ (R = Et, *t*-Bu) in DMF-d_7

Table 1 Atomic positional parameters for trithiol **1**.

	X	*Y*	*Z*	*BEQ*
C 1	2273 (3)	5276 (6)	7744 (4)	4.82
C 2	2923 (3)	4596 (6)	6294 (3)	4.80
C 3	3861 (3)	4412 (6)	7874 (3)	4.60
C 10	1901 (3)	4440 (6)	7080 (4)	4.14
C 11	2198 (3)	4070 (7)	6455 (4)	4.25
C 12	1840 (4)	3182 (7)	5916 (4)	5.00
C 13	1164 (4)	2632 (7)	6002 (4)	5.09
C 14	862 (4)	3018 (7)	6641 (4)	4.81
C 15	1222 (4)	3917 (7)	7162 (4)	4.76
O 10	185 (2)	2452 (5)	6683 (3)	6.45
C 16	-18 (5)	2459(10)	7419 (6)	10.25
O 11	773 (3)	1724 (5)	5496 (3)	7.45
C 17	1143 (7)	1255(16)	4900 (7)	15.54
C 18	833 (8)	792(24)	4380 (7)	19.31
C 19	1058 (5)	279(10)	3644 (5)	10.00
S 1	1885 (1)	-596 (3)	3669 (1)	12.08
C 20	3962 (3)	3506 (6)	7215 (4)	4.04
C 21	3544 (3)	3596 (6)	6484 (4)	4.22
C 22	3701 (3)	2750 (6)	5897 (4)	4.33
C 23	4261 (4)	1819 (7)	6037 (4)	4.53
C 24	4680 (3)	1718 (6)	6767 (4)	4.09
C 25	4536 (3)	2553 (6)	7348 (4)	4.54
O 20	4455 (2)	962 (4)	5486 (3)	5.40
C 26	4156 (4)	1259 (8)	4706 (4)	6.51
O 21	5249 (2)	793 (4)	6851 (2)	5.13
C 27	5802 (4)	922 (8)	7532 (4)	6.36
C 28	6458 (4)	61 (8)	7429 (5)	7.34
C 29	7044 (5)	-15(11)	8121 (6)	11.48
S 21	7137 (7)	705(19)	8811 (3)	8.40
S 2	7405 (2)	1632 (4)	8414 (3)	12.28
C 30	2649 (4)	4335 (6)	8361 (4)	4.43
C 31	3353 (3)	3871 (6)	8392 (4)	4.24
C 32	3636 (3)	2882 (6)	8945 (4)	4.25
C 33	3220 (4)	2372 (7)	9443 (4)	4.49
C 34	2504 (3)	2857 (7)	9411 (4)	4.54
C 35	2231 (3)	3828 (6)	8881 (4)	4.38
O 30	3450 (2)	1417 (4)	9999 (2)	5.53
C 36	4180 (3)	915 (7)	10041 (4)	5.78
O 31	2131 (2)	2282 (4)	9954 (2)	5.44
C 37	1420 (4)	2760 (9)	9949 (5)	8.36
C 38	1180 (5)	2107 (9)	10685 (6)	9.58
C 39	1019 (5)	690 (9)	10531 (5)	8.46
S 3	687 (1)	-83 (2)	11349 (1)	9.36

(the reaction is driven by removal of the displaced thiol HSR under vacuum), the resonances of the coordinated thiolate RS^- (δ 2.64 for the CH_3 of S-*t*-Bu, and 12.53 and 2.33 for the CH_2 and CH_3 of SEt, respectively) were found to decrease in intensity (but never disappeared completely), while those of the corresponding free thiol RSH appeared (δ 1.37 for HS-*t*-Bu, 2.50 and 1.27 for HSEt). This experiment indicates that the initially coordinated thiolates RS^- were progressively displaced by the incoming aromatic trithiol **2**. No further changes were observed in the NMR spectra when more than one equivalent of trithiol **2** was added, suggesting thus the formation of a 1:1 species of the type $[Fe_4S_4(\mathbf{2})(SR)]^{2-}$. Identical spectra were obtained when the reaction product was first isolated (see Experimental section) and then redissolved in DMSO-d_6. The overall NMR spectrum is consistent with the same trigonally symmetric C3 conformation (on the spectrometer time scale) as in the free trithiol. The resonances belonging to coordinated trithio-



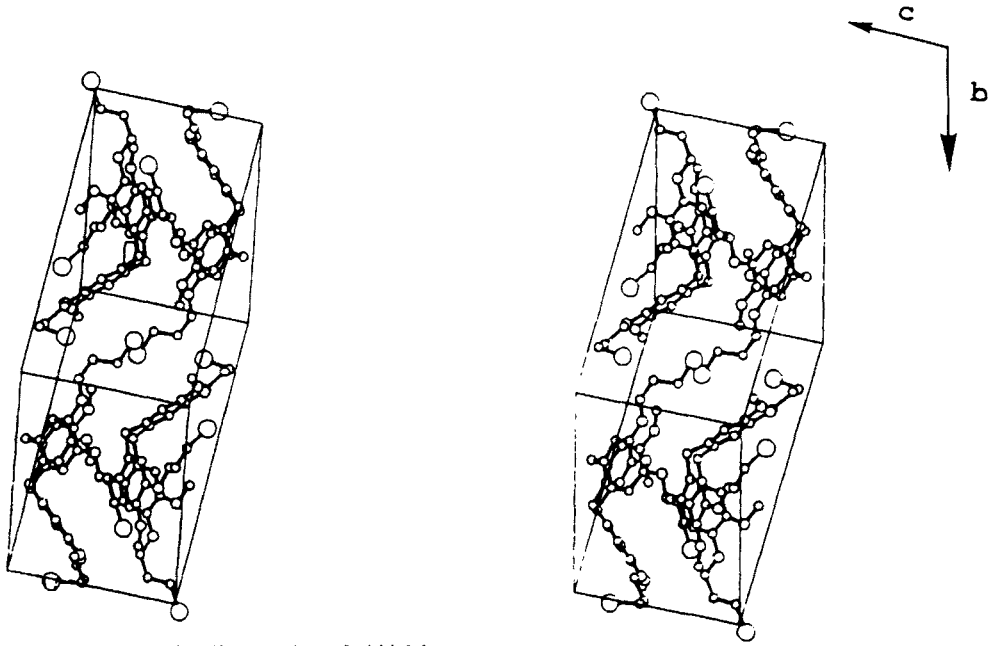


Figure 1 Molecular structure and unit cell stereoview of trithiol **1**.

late **2** were all broadened, as is usual in paramagnetic complexes. They were assigned by COSY, NOESY, TOCSY experiments and T_1 measurements, as well as by comparison with reported data[19] for $[Fe_4S_4(S\text{-}m\text{-}tol)_4]^{2-}$. The proton resonances of the cyclotriveratrylene unit (aromatic H_2 and H_5, OCH_3, OCH_2, and CH_2 bridge) are downfield shifted, a feature consistent with the fact that complexation to the iron-sulfur cluster has an electron withdrawing effect. Close attention was paid to the OCH_2 resonance in the TOCSY sequence, to verify that, although broad, it is indeed a single peak. This means that in the final complex the three side chains are

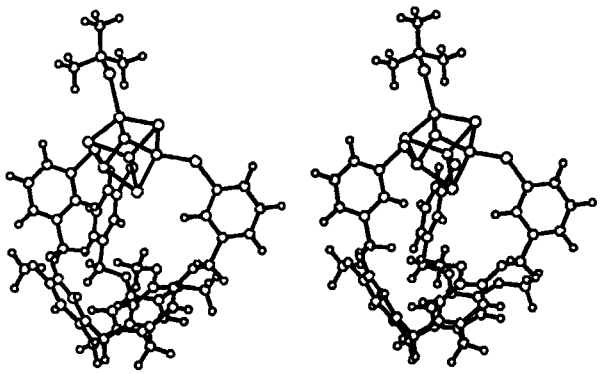


Figure 2 Molecular modelling of Fe_4S_4 complex with trithiol **2.**

bonded to a Fe-S core, that they all have the same orientation toward the top of the cyclotriveratrylene bowl, and therefore that they are most probably bonded to the same Fe-S core. These observations are in support of the formation of a species that is monomeric rather than bridged or polymeric. The observed upfield and downfield shifts for respectively the *ortho* (and *para*) and the *meta* protons of the aromatic thiol side chains indicate a dominant contact shift mechanism, as generally found[19] for ligands bonded to a paramagnetic Fe_4S_4 core. The resonance assigned to $H_{4'}$, the closest to the cluster, exhibits the greatest isotropic shift (ca. -1.8 ppm), whereas $H_{2'}$, which is just as close to the cluster, exhibits a smaller shift (-1.3 ppm), probably because of the presence of the nearby OCH_2 group. The proton $H_{6'}$, in the *para* position, is upfield shifted by approximately the same magnitude as for $H_{2'}$. On the contrary, $H_{5'}$, in the *meta* position, is downfield shifted by +1 ppm. The magnitude of these shifts is similar to those observed[19] for $[Fe_4S_4(S\text{-}m\text{-}tol)_4]^{2-}$ and for hexa-substituted benzene cavitands bound to a Fe_4S_4 cluster.[5] Similar results were obtained in the case of the reaction of $[Fe_4S_4(SR)_4]^{2-}$ with the aliphatic trithiol **1**.

Comparison of the electronic spectrum of the isolated product $[Fe_4S_4(\mathbf{2})(SR)]^{2-}$ with that of the starting cluster $[Fe_4S_4(StBu)_4]^{2-}$ shows that the absorption at 418 nm, due to ligand-metal charge transfer (LMCT) from S to Fe and characteristic of Fe_4S_4 cores, is shifted to 456 nm. This indicates that the Fe_4S_4 core retains its structure during the ligand exchange reaction, while replacement of StBu by the aromatic trithiol **2** accounts for the observed shift to lower energies.

Molecular modelling studies of the postulated $[Fe_4S_4(\mathbf{2})(SR)]^{2-}$ complex have been performed with the SYBYL[20] software. The geometry of the Fe_4S_4 core was based on crystallographic data[21] and was kept fixed during the energy minimization; no solvent was included, since no solvent resonances were detected in the NMR spectra. The predicted final structure is shown in Figure 2. This simulation supports the idea that ligand **2** is indeed capable of accomodating a single Fe_4S_4 in the way pictorially shown in Scheme I, and makes clear that the presence of the cyclotriveratrylene unit and of the side chains restricts the accessibility to the three lower faces of the cluster. Full characterization and detailed studies of the physico-chemical properties of these new complexes will be reported in due course[25].

EXPERIMENTAL

Cyclotriveratrylenes (**3**) and (**10**),[10] and iron-sulfur clusters $[NEt_4]_2[Fe_4S_4(StBu)_4]$ and $[AsPh_4]_2[Fe_4S_4(SEt_4,],$[22] were prepared as previously described. All solvents were used as purchased, except DMF, CH_2Cl_2 and THF which, when used for the cluster capture reactions, were distilled under argon over respectively $MgSO_4$, CaH_2 and Na/benzophenone. Cluster capture reactions were carried out in an argon-filled Jacomex glovebox equipped with a Hermann-Moritz oxymeter. Thin-layer chromatography (TLC) was performed on silica gel 60 F254 plates with aluminum backing (Merck). Column chromatography was performed on silica gel 60 (230 – 400 mesh, Merck). Elemental analyses were performed by the Service Central d'Analyses, CNRS, Vernaison (France). Melting points were measured on a Perkin-Elmer DSC7 microcalorimeter with simultaneous check of purity. Infrared spectra were recorded, on a Perkin Elmer FTIR 1600, as KBr pellets. ^1H and ^{13}C NMR spectra of the free ligands were taken in $CDCl_3$ (Bruker AM300). The residual $CHCl_3$ peak was set at 7.24 ppm and used as an internal standard for proton spectra. The main $CDCl_3$ peak was set at 76.9 ppm as a reference for carbon spectra. The XHCORR, DEPT, COSY and NOE sequences for the free ligands were run on the Bruker AM300. The NOE experiments for the free ligands were carried out by the difference method (NOEDIFF): a set of free induction decays was recorded upon saturation of the proton of interest, followed by a control which was recorded by applying an off-resonance irradiation. The HMBC sequence, as well as the COSY, TOCSY, NOESY and T_1 experiments (in DMF-d_7 or DMSO-d_6) for the cluster complexation reactions, were run on a Varian Unity 400 at 400 MHz for ^1H and 100 MHz for ^{13}C. Molecular modelling studies were performed with SYBYL 6.0 software[20] on a Control Data workstation.

Crystal structure determination

Compound **1** [$C_{33}H_{42}O_6S_3$, MW 630.55] crystallizes from dichloromethane/ether as clear slightly elongated blocks. Crystal data: monoclinic, space group $P2_{1/n}$, a = 18.684(7), b = 9.860(4), c = 17.685(7) Å, β = 99.53(1), V = 3213.04 Å^3, Z = 4. X-Ray diffraction experiments

were carried out on a small crystal of 0.30 × 0.35 × 0.20 mm, on a Enraf-Nonius CAD4 diffractometer (graphite monochromator, Mo K_α = 0.7107 Å). The intensities ($2\theta_{max}$ = 55°, 8042 measured data) were corrected for Lorentz and polarization effects, but not for absorption. The structure was solved by direct methods, using the SHELX86 package[23], which showed 36 out of 42 non-hydrogen atoms. It was completed by Fourier difference maps. The parameters were refined by full-matrix least-squares methods with the SHELX76 package.[24] The hydrogen positions were calculated with the geometrical constraint C-H 1.08 Å, and refined "riding" on their C atoms. Convergence for 2732 unique reflections having $|F_0| > 4\sigma(|F_0|)$ and 423 variables was reached at R_F = 0.075 and R_{WF} = 0.062 (weighting scheme w = $1/\sigma^2(|F_0|)$). Atomic positional parameters are listed in Table 1.

2,7,12-Trimethoxy-3,8,13-tris[(3-acetylthiopropyl)oxy]-10,15-dihydro-5H-tribenzo[a,d,g]cyclononene (4)

To a solution of **3** (20.8 g, 39.4 mmol) in a 1:1 mixture of dichloromethane and acetone (200 mL), 2 mL (13.5 mmol) of cumene hydroperoxide and 28 mL (378.2 mmol) of freshly distilled thioacetic acid were added. After stirring overnight at room temperature, the reaction mixture was washed with 3 × 100 mL of water. The organic layer was dried over sodium sulfate, and the solvent evaporated under reduced pressure. The solid residue was digested in ether to give 20.98 g (75%) of **4**, as a white solid, mp 86 °C, pure by TLC (dichloromethane/ether 9:1); IR: 1689($\nu_{SC=O}$); ^{1}H NMR ($CDCl_3$, see Scheme II for atom numbering); δ 2.05 (quint, 2H, H_9), 2.30 (s, 3H, $COCH_3$), 3.02 (t, 2H, CH_2S), 3.50 (d, 1H, H_{7eq}, J = 13.7 Hz), 3.81 (s, 3H, OCH_3), 3.97 (m, 2H, H_8), 4.71 (d, 1H, H_{7ax} J = 13.7 Hz), 6.82 (s, 1H, H_2), 6.83 (s, 1H, H_5); ^{13}C NMR ($CDCl_3$) δ 25.63 (C_{10}), 29.07 (C_9), 30.38 ($SCO\underline{C}H_3$), 36.17 (C_7), 56.0 (OCH_3), 67.55 (C_8), 113.55 (C_2), 115.47 (C_5), 131.60 (C_6), 132.25 (C_1), 146.67 (C_4), 148.14 (C_3), 195.46 (CO). Anal. Calcd for $C_{39}H_{48}O_9S_3$: C, 61.90; H, 6.35; O, 19.05; S, 12.70. Found: C, 62.07; H, 6.32; O, 19.13; S, 12.71.

2,7,12-Trimethoxy-3,8,13-tris[(3-mercaptopropyl)oxy]-10,15-dihydro-5H-tribenzo[a,d,g]cyclononene (1)

Compound **4** (2 g, 2.64 mmol) was refluxed for three hours under argon in a 1.5 M solution of HCl in methanol (700 mL). After cooling to room temperature, a white solid precipitated and was filtered to provide 1.27 g (77%) of the pure trithiol **1**, mp 154 °C; IR: 2414(ν_{S-4}); ^{1}H NMR ($CDCl_3$, see Scheme II for atom numbering); δ 1.38 (t, 1H, SH), 2.06 (m, 2H, H_9), 2.69 (q, 2H, H_{10}), 3.52 (d, 1H, H_{7eq}, J = 13.7 Hz), 3.80 (s, 3H, OCH_3), 4.07 (m, 2H, H_8), 4.73 (d, 1H, H_{7ax}, J = 13.7 Hz), 6.81 (s, 1H, H_2), 6.86 (s, 1H, H_5); ^{13}C NMR ($CDCl_3$) δ 21.04 (C_{10}), 33.04 (C_9), 36.22 (C_7), 56.10 (OCH_3), 67.16 (C_8), 113.83 (C_2), 115.72 (C_5), 131.78 (C_6), 132.36 (C_1), 146.68 (C_4), 148.30 (C_3). Anal. Calcd for $C_{33}H_{42}O_6S_3$: C, 62.86; H, 6.67; O, 15.24; S, 15.24. Found: C, 63.05; H, 6.70; O, 15.59; S, 14.80.

3-(N,N-dimethylthiocarbamoyloxy)benzaldehyde (6)

A solution of N,N-dimethylthiocarbamoylchloride (21.8 g, 176 mmol) in THF (50 mL) was added dropwise at 0°C to a solution of 3-hydroxybenzaldehyde (**5**) (21.49g, 176 mmol) and potassium hydroxide (10.84 g, 193 mmol) in water (126 mL). The reaction mixture was stirred for 15 minutes at room temperature. The resulting precipitate was collected by suction filtration, washed with 10% aqueous potassium hydroxide (200 mL), then water (200 mL), and dried overnight under vacuum. The pale yellow solid (31.5 g) was recrystallized from diisopropylether and afforded colourless crystals (30.1 g, 82%) of **6**, mp 73.2 °C; IR: 1665($\nu_{OC=S}$), 1698($\nu_{HC=O}$); ^{1}H NMR ($CDCl_3$, see Scheme III for atom numbering); δ 3.33, 3.42 (2s, 6H, $N(CH_3)_2$), 7.31 (ddd, 1H, $H_{4'}$), 7.50 (t, 1H, $H_{5'}$), 7.54 (t, 1H, $H_{2'}$), 7.74 (dt, 1H, $H_{6'}$), 9.94 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$) δ 38.59, 41.12 ($N(CH_3)_2$), 123.27 ($C_{2'}$), 127.07 ($C_{6'}$), 127.91 ($C_{4'}$), 129.54 ($C_{5'}$), 137.39 ($C_{1'}$), 154.38 ($C_{3'}$), 187.03 (OCS), 190.90 (CHO). Anal. Calcd for $C_{10}H_{11}NO_2S$: C, 57.41; H, 5.26; O, 15.31; S, 15.31; N, 6.70. Found: C, 57.49; H, 5.38; O, 15.60; S, 15.11; N, 6.76.

3-(N,N-dimethylcarbamoylthio)benzaldehyde (7)

A solution of **6** (15.05 g, 71.9 mmol) in diphenylether (200 mL) was heated at 240 – 250 °C for 2 – 3 hrs under argon, and the isomerization reaction was followed by TLC with dichloromethane as eluent. After cooling to 90 °C, the diphenylether was distilled off under vacuum. The brown oily residue solidified overnight in the refrigerator. Recrystallization from diisopropylether (200 mL) gave 11.85 g (79%) of colourless crystals of 7; mp 79 °C; IR: 1548 ($\nu_{SC=O}$), 1706 ($\nu_{HC=O}$); ^{1}H NMR ($CDCl_3$, see Scheme III for atom numbering); δ 3.00, 3.07 (2s, 6H, $N(CH_3)_2$), 7.52 (t, 1H, $H_{5'}$), 7.72 (dt, 1H, $H_{4'}$), 7.87 (dt, 1H, $H_{6'}$), 7.96 (t, 1H, $H_{2'}$), 9.97 (s, 1H, CHO); ^{13}C NMR ($CDCl_3$) δ 36.77 ($N(CH_3)_2$), 129.30 ($C_{5'}$), 129.62 ($C_{6'}$), 130.38 ($C_{3'}$), 136.76 ($C_{1'}$) 136.84 ($C_{2'}$), 141.24 ($C_{4'}$), 165.71 (SCO), 191.23 (CHO). Anal. Calcd for $C_{10}H_{11}NO_2S$: C, 57.41; H, 5.26; N, 6.70; O, 15.31; S, 15.31. Found: C, 56.67; H, 6.26; N, 6.72; O, 16.29; S, 14.64.

3-(N,N-dimethylcarbamoylthio)benzylalcohol (8)

Sodium borohydride (2.270 g, 60 mmol) was slowly added to a solution of **7** (11.85 g, 56.7 mmol) in 200 mL of methanol, and the reaction mixture was vigorously stirred overnight. The solvent was removed under vacu-

um, and dichloromethane (200 mL) and water (200 mL) were added to the solid residue. After the aqueous phase was acidified with concentrated HCl, the organic extract was washed with water until it was neutral, dried over Na_2SO_4 and evaporated to dryness to give compound **8** as an oil, which transformed into a pale yellow solid upon refrigeration. The latter (11.07 g) was recrystallized from diisopropylether to give 6.84 g (57%) of colourless crystals of pure **8**, mp 73 °C; IR: 1654 ($\nu_{SC=O}$), 3234 (ν_{O4}), 3471 (ν_{O4}); ^{1}H NMR ($CDCl_3$, see Scheme III for atom numbering); δ 2.85 (broad s, 1H, OH), 2.99, 3.04 (2s, 6H, $N(CH_3)_2$), 4.58 (s, 2H, CH_2), 7.33 (m, 3H, $H_{4',5',6'}$), 7.44 (s, 1H, $H_{2'}$); ^{13}C NMR ($CDCl_3$) δ 36.77 ($N(CH_3)_2$), 64.47 (CH_2), 127.63 ($C_{6'}$), 128.62 ($C_{3'}$), 128.82 ($C_{5'}$), 133.97 ($C_{4'}$), 134.45 ($C_{2'}$), 141.92 ($C_{1'}$), 166.96 (SCO). Anal. Calcd for $C_{10}H_{13}NO_2S$: C, 56.85; H, 6.16; N, 6.63; O, 15.16; S, 15.16. Found: C, 57.00; H, 6.22; N, 6.84; O, 16.09; S, 14.64.

3-(N,N-dimethylcarbamoylthio)benzyl bromide (9)

To a solution of **8** (4.05 g, 19. mmol) in benzene (75 mL) under argon, 1.78 g (19.2 mmol) of PBr_3 were added. The reaction mixture was stirred under argon for one hour, and 100 mL of diethylether were added. The organic phase was washed with 100 mL of saturated aqueous K_2CO_3, then with 2 × 100 mL of brine, and dried over sodium sulfate. After evaporation of the solvents, 4.52 g (86%) of **9** were obtained as a white microcrystalline solid, pure by TLC, mp 60 °C; IR: 1667 ($\nu_{SC=O}$); ^{1}H NMR ($CDCl_3$, see Scheme III for atom numbering); δ 3.03 (s, 6H, $N(CH_3)_2$), 4.46 (s, 2H, CH_2), 7.30-7.44 (m, 3H, $H_{4',5',6'}$), 7.51 (s, 1H, $H_{2'}$); ^{13}C NMR ($CDCl_3$) δ 32.54 (CH_2), 36.74 ($N(CH_3)_2$), 129.06, 129.60 ($C_{5'}$, $C_{6'}$), 129.31 ($C_{3'}$), 135.37, 135.79 ($C_{2'}$, $C_{4'}$), 138.30 ($C_{1'}$), 166.24 (SCO). Anal. Calcd for $C_{10}H_{12}BrNOS$: C, 43.79; H, 3.65; Br, 29.20; N, 5.11; O 5.84; S, 11.68. Found: C, 43.94; H, 4.46; Br, 28.68; N, 5.10; O, 6.06; S, 10.92.

2,7,12-Trimethoxy-3,8,13-tris[3-(N,N-dimethylcarbamoylthio) benzyloxy]-10,15-dihydro-5H-tribenzo[a,d,g]cyclononene (11)

To 2.5 g (6.13 mmol) of **10** in 150 mL of DMF/HMPA (1:1, v/v), 3 mL of aqueous NaOH were added, and the mixture was stirred for 10 minutes under argon, followed by addition of **9** (5.0 g, 18.25 mmol). After stirring at room temperature for one hour, further amounts of NaOH (1.5 mL) and of **9** (2.5 g) were added. After one more hour, the reaction mixture was poured into water, and the precipitate of **11** was isolated by suction filtration, washed with water and dried under vacuum; yield 6 g (99%), mp 141 °C. This product was used without further purification for the next step; IR: 1674 ($\nu_{SC=O}$); ^{1}H NMR ($CDCl_3$, see Scheme III for atom numbering); δ 3.04 (broad s, 6H, $N(CH_3)_2$), 3.46 (d, 1H, H_{7eq}, J = 13.8 Hz), 3.71 (s, 3H, OCH_3), 4.66 (d, 1H, H_{7ax}, J = 13.8 Hz), 5.06 (s, 2H, OCH_2), 6.70 (s, 1H, H_2), 6.82 (s, 1H, H_5), 7.30-7.53 (m, 3H, $H_{4',5',6'}$), 7.53 (s, 1H, $H_{2'}$); ^{13}C NMR ($CDCl_3$) δ 36.32 (C_7), 36.80 ($N(CH_3)_2$), 56.25 (OCH_3), 76.48 (OCH_2), 113.98 (C_2), 116.73 (C_5), 127.84 ($C_{6'}$), 128.99 ($C_{5'}$, $C_{3'}$), 131.74 (C_6), 132.96 (C_1), 134.10 ($C_{4'}$), 134.85 ($C_{2'}$), 138.46 ($C_{1'}$), 147.04 (C_4), 148.60 (C_3), 166.57 (SCO). Anal. Calcd for $C_{54}H_{57}N_3O_9S_3$: C, 65.65; H, 5.77; N, 4.25; O 14.59; S, 9.73. Found: C, 65.76 H, 5.76; N, 4.31; O, 14.98; S, 9.62.

2,7,12-Trimethoxy-3,8,13-tris[(3-mercaptobenzyl)oxy]-10,15-dihydro-5H-tribenzo[a,d,g]cyclononene (2)

A slurry of 6.04 g (6.12 mmol) of **11** in 300 mL of methanol was refluxed under argon until complete dissolution; 20 mL of 10% aqueous KOH were then added. The solution was stirred under argon for one hour and an additional amount of KOH (20 mL) was added. After one more hour, the solution was allowed to cool to room temperature, and concentrated HCl was added until neutrality. The white precipitate of **2** was isolated by suction filtration, washed with ether and dried under vacuum; yield 3.84 g (81%); mp 152 °C; IR: 3273 (ν_{S-4}); ^{1}H NMR ($CDCl_3$, see Scheme III for atom numbering); δ 3.43 (s, 1H, SH), 3.44 (d, 1H, H_{7eq}, J = 13.7 Hz), 3.70 (s, 3H, OCH_3), 4.67 (d, 1H, H_{7ax}, J = 13.7 Hz), 5.02 (s, 2H, OCH_2), 6.65 (s, 1H, H_2), 6.79 (s, 1H, H_5), 7.17-7.24 (m, 3H, $H_{4',5',6'}$), 7.31 (s, 1H, $H_{2'}$); ^{13}C NMR ($CDCl_3$) δ 36.27 (C_7), 56.08 (OCH_3), 76.13 (OCH_2), 113.76 (C_2), 116.32 (C_5), 124.02 ($C_{6'}$), 127.56 ($C_{2'}$), 128.50 ($C_{4'}$), 129.00 ($C_{5'}$), 131.10 ($C_{3'}$), 131.56 (C_6), 132.70 (C_1), 138.50 ($C_{1'}$), 146.80 (C_4), 148.37 (C_3). Anal. Calcd for $C_{45}H_{42}O_6S_3$: C, 69.76; H, 5.43; O 12.40; S, 12.40. Found: C, 69.78 H, 5.46; O, 12.51; S, 12.22.

Cluster capture reactions.

The following analytical and preparative procedures were used for the complexation of iron-sulfur clusters to **1** and **2**.

(i) *Analytical.* In a 5-mm NMR Young tube, 14.4 mg (0.015 mmol) of $[NEt_4]_2[Fe_4S_4(StBu)_4]$ (or 51.8 mg (0.038 mmol) of $[AsPh_4]_2$ $[Fe_4S_4(SEt_4)]$) were dissolved in 1 mL of DMF-d_7, and 0.5, 0.8, 1.0 and 1.5 equivalents of solid **1** (or **2**) were added stepwise to the solution. The thiol/thiolate exchange reaction was driven by removing the released thiol (HSEt, HStBu) under reduced pressure. ^{1}H NMR spectra were recorded at room temperature, 20 minutes after each addition of **1** or **2**.

(ii) *Preparative.* To a solution of 0.258 mmol of the starting cluster $[NEt_4]_2[Fe_4S_4(StBu)_4]$ or $[AsPh_4]_2[Fe_4S_4(SEt_4)]$ in 20 mL of DMF was added a solution of 0.258 mmol of **2** in 20 mL of dichloromethane. The resulting solution was stirred under dynamic vacuum for 3 hours. THF (50 mL) was then added

and the solution was stored overnight at -20 °C. The black microcrystalline solid was filtered off, washed with THF and dried under vacuum; UV-Vis (DMF) 456 nm; ^{1}H NMR (d_6-DMSO) δ 1.05 ($NCH_2C\underline{H}_3$, T_1 = 61 10^{-3}s), 2.55 (S-*t*-Bu), 2.94 ($NC\underline{H}_2CH_3$, T_1 = 0.026s), 3.55 (H_{7eq}, T_1 = 0.062s), 3.78 (OCH_3, T_1 = 0.034s), 4.63 (OCH_2, T_1 = 0.036s), 4.78 (H_{7ax}, T_1 = 0.036s), 5.34 ($H_{4'}$, $H_{2'}$, $H_{6'}$, T_1 = 0.026s), 6.0 (T_1 = 0.009s), 7.12, 7.23 (H_2, H_5, T_1 = 0.105s), 8.2 ($H_{5'}$, T_1 = 0.010s).

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