Synthesis and X-Ray Structure of a Novel Concave Tetradentate Sulphur Ligand System: Electrochemical Characterisation of a Semi-encapsulated [4Fe–4S]$^{2+}$ Cluster Complex

Constantinus F. Martens,[a] **Henk L. Blonk,**[b] **Thijs Bongers,**[b] **Johannes G. M. van der Linden,**[b] **Gezina Beurskens,**[c] **Paul T. Beurskens,**[c] **Jan M. M. Smits**[c] **and Roeland J. M. Nolte***[a]

[a] *Department of Organic Chemistry,* [b] *Department of Inorganic Chemistry and* [c] *Department of Crystallography, University of Nijmegen, Toernooiveld, 6525 ED Nijmegen, The Netherlands*

An Fe_4S_4-cluster, partly encapsulated by a concave, tetradentate ligand, mimics certain electrochemical properties of metalloproteins.

Current efforts in the design of iron–sulphur protein analogues focus on the use of cavitands and other macrocyclic ligand systems to coordinate the Fe_4S_4-core. Recent examples include modified cyclodextrines,[1] macrocycles[2] and cavitands based on hexa-substituted benzenes.[3] A variety of goals are being persued, *inter alia* the improvement of the aqueous solubility of the formed cluster, the creation of a specific iron-subsite, and the mimicking of the hydrophobicity in the protein pocket.

As part of our programme aimed at the development of metallohosts[4] from the building block diphenylglycoluril we describe a novel concave, tetradentate thiol ligand system **1**, which forms a 1 : 1 complex with an Fe_4S_4-cluster **2**. In the cluster complex the Fe_4S_4-core is partly shielded from its environment giving rise to electrode phenomena previously encountered with proteins.

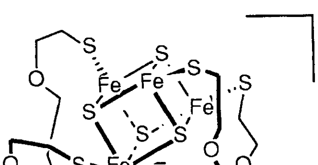
The protected tetra thiol ligand **1a** was synthesised using previously described procedures.[4,5] Its structure (see stereoview; Fig. 1) was determined by X-ray crystallography.† Host **1a** has a cavity formed by two fused 2-imidazolidone rings, which are flanked by two *o*-xylylene units. Its overall shape is concave and its convex side is shielded by two phenyl substituents.

Quantitative deprotection of **1a** into **1b** was easily achieved using sodium methanolate. Exchange reactions of $(Bu_4N)_2$-$[Fe_4S_4Cl_4]$[7] with a suspension of **1b** in dimethylformamide (DMF) were conducted under a nitrogen atmosphere in very dilute solutions to avoid the formation of polymeric products, eqn. (1).

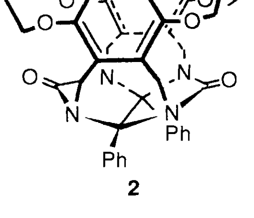
$$[Fe_4S_4Cl_4]^{2-} + \underset{\mathbf{1b}}{L(Na)_4} \rightarrow \underset{\mathbf{2}}{[Fe_4S_4(L)]^{2-}} + 4\,NaCl \qquad (1)$$

During the course of the reaction a colour change was observed from purple-black to brown-black. The progress of the exchange reaction was followed with cyclic voltammetry (CV) and differential pulse polarography (DPP) by monitoring the disappearance of the 2–/3– wave of the $Fe_4S_4Cl_4{}^{2-}$ reduction at −1.34 V (*vs.* $F_c{}^{+,0}$) and the simultaneous appearance of the 2–/3– reduction wave of the newly formed product at −1.70 V in samples, obtained from the reaction mixture. The complex **2** was isolated through precipitation with diethyl ether or evaporation of the solvent. The samples thus obtained were characterised further using various physical methods.

First of all CV was used to identify the nature of our product. Remarkably, the current response of the new wave was very small, a phenomenon noted earlier for the electrochemical reduction of a variety of redox-active metalloproteins in water.[8] With the addition of a modulator (Ba^{2+} or Na^+) a considerable increase in the current response was noted in the CV and DPP of **2**. This was observed for all four electrodes we used, *viz.* Au, Pt, pyrolytic graphite edge (PGE) and pyrolytic graphite basal (PGB), indicating that not only the electrode material, but also the modulator plays an important role in the 2–/3– reduction process. We believe that association and dissociation processes of cluster **2** with the Ba^{2+} ions occurring in the interfacial electrode layer (probably through coordination at the ether and carbonyl oxygen atoms present in our ligand system) enhance the electron transfer rate considerably. This can be concluded from the 70 mV redox potential shift from −1.70 to −1.63 V that is observed when Ba^{2+} is added, while no potential shift is noted for the ferrocene oxidation or for the reduction of other simple thiolate cluster compounds under the same conditions. As with the natural systems, a maximum response was observed when the Ba^{2+} concentration is approximately 25 mmol dm^{-3} (Table 1). Similarly, like with the metalloproteins,[8] monovalent cations did not improve the current response to the same extent as did divalent cations. With the modulator present a nearly chemically reversible wave was obtained with $i_b/i_f \approx 0.80$ and a cathodic–anodic peak separation close to the



L: R = $(OCH_2CH_2)_2S^-$
1a; R = $(OCH_2CH_2)_2SC(O)Me$
1b; R = $(OCH_2CH_2)_2SNa$



2

---

† *Crystal data* for **1a**: $C_{56}H_{66}N_4O_{14}S_4$, M_r = 1147.4, T = 293 K, triclinic, $P\bar{1}$, a = 14.030(1), b = 14.828(1), c = 15.588(1) Å, α = 102.77(1), β = 111.19(1), γ = 97.18 (1)°. V = 2873.2(5) Å^3, Z = 2, D_c = 1.326 g cm^{-3}, Mo-Kα radiation, μ = 2.22 cm^{-1}. The crystal (0.50 × 0.16 × 0.21 mm) was obtained by recrystallisation from acetone. Unit cell dimensions were determined from 25 reflections with 10° < θ < 12°. Intensity data were collected for 20154 reflections (complete sphere up to θ = 25°). The structure was determined using vector search methods (ORIENT) with **1**, R = O^{6a} as a model, automatically followed by direct methods (DIRDIF) with the orientated fragment given as input, which gave the rest of the non-hydrogen atoms. Least-square refinement (SHELX) converged to R = 0.078 and R_w = 0.108 for 4619 observed reflections and 705 variables. Standard experimental and computational details, and references to ORIENT, DIRDIF and SHELX are given in ref. 6(*b*). Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

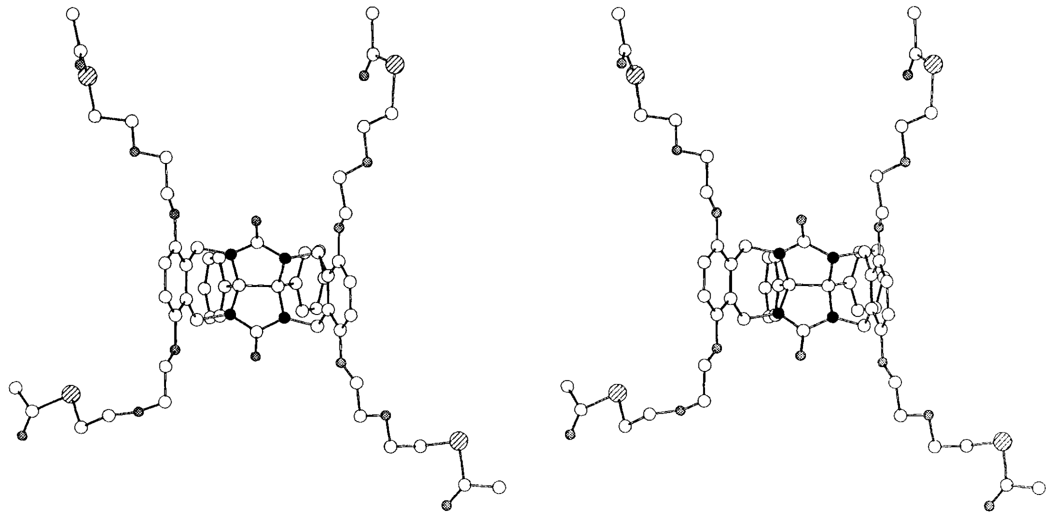


Fig. 1 Stereoview of **1a**

Table 1 Electrochemical properties of cluster compound **2**[a]

$[Ba(ClO_4)_2]$/ mmol dm^{-3}	$E_{1/2}$/V[b]	i_{pc}[c]	i_{pa}[c]	i_{pa}/i_{pc}
0	−1.70	1.15	—	—
5	−1.67	2.7	2.3	0.85
10	−1.66	4.2	3.2	0.76
25	−1.64	5.2	4.1	0.79
50	−1.63	4.7	2.9	0.62

[a] 2−/3− Reduction at *ca.* 25 °C in DMF using a PGE-working electrode, a platinum auxiliary electrode, a Ag/AgCl reference electrode and 0.1 mol dm^{-3} tetrabutylammonium hexafluorophosphate (TBAH) as the supporting electrolyte. [b] Potentials *vs.* Fc^+/Fc in DMF. [c] Arbitrary units.

theoretical value for a reversible one-electron process (*ca.* 65 mV is observed). This might indicate that the complex is monomeric. The reduction at the platinum working electrode is diffusion controlled as can be concluded from the linear response of i_{pc} on $v^{1/2}$ (see Fig. 2). The redox potential of the 2−/3− reduction process of the newly formed cluster **2** is close to that of the known $[Fe_4S_4(SEt)_4]^{2-}$ cluster supporting the formation of the former compound.[9] Also the UV–VIS spectra of both clusters are very similar.‡ Further information that **2** had been formed, comes from IR spectroscopy, which showed the disappearance of the intense Fe–Cl vibration at 352 cm^{-1} (solid CsI, comparison of **2** with $[Fe_4S_4Cl_4]^{2-}$). ^1H NMR revealed the presence of two sets of the CH_2S-protons in complex **2**, *viz.* at δ 13.25 (6H) and 14.25 (2H), respectively. This suggests that one of the corners of the Fe_4S_4-cube points towards the cavity as indicated schematically in drawing

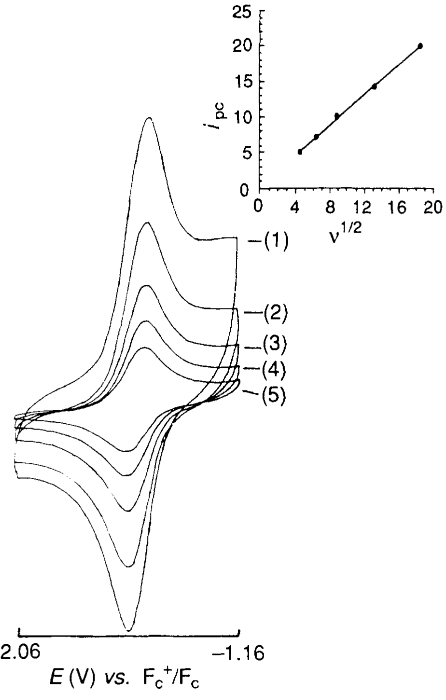


Fig. 2 Cyclic voltammograms of cluster compound **2** recorded as a function of the scan rate *v*; 400 mV s^{-1} (1), 200 mV s^{-1} (2), 100 mV s^{-1} (3), 50 mV s^{-1} (4), 25 mV s^{-1} (5). Measurements were conducted at *ca.* 25 °C in DMF using a platinum disk working electrode, a platinum auxiliary electrode and Ag/AgCl reference electrode (0.32 mmol dm^{-3} of cluster compound **2**, 0.1 mol dm^{-3} tetrabutylammonium hexafluorophospate (TBAH) as the supporting electrolyte, 20 mmol dm^{-3} $Ba(ClO_4)_2$ as modulator). Inset: plot of the peak current for the reduction process at the Pt-electrode *vs.* the square-root of the scan rate, $v^{1/2}$, verifying the predominance of linear diffusion for cluster compound **2**.

---

‡ ^1H NMR **1a**: (400 MHz, $CDCl_3$) δ 2.33 [s, 12H, $SC(O)CH_3$], 3.12 (t, 8H, $OCH_2C\mathit{H}_2S$), 3.70 (m, 8H, $OC\mathit{H}_2CH2S$), 3.80 (m, 8H, $OCH_2C\mathit{H}HO$ and $NC\mathit{H}H$), 3.89 (m, 4H, $OCH_2CH\mathit{H}O$), 3.99 (m, 4H, $OC\mathit{H}HCH_2O$), 4.08 (m, 4H, $OCH\mathit{H}CH_2O$), 5.53 (d from AB, 4H, $NCH\mathit{H}$), 6.67 (s, 4H, XyH), 7.09 (m, 10H, PhH). ^{13}C NMR **1a**: ($CDCl_3$) δ 29.02 ($OCH_2\mathit{C}H_2S$), 30.52 ($\mathit{C}H_3C(O)S$), 37.06 ($N\mathit{C}H_2Ar$), 69.82 ($OCH_2\mathit{C}H_2O$ and $O\mathit{C}H_2CH_2S$), 70.04 ($O\mathit{C}H_2CH_2CH_2O$), 85.18 ($N\mathit{C}(N)Ar$), 114.57 (Xy*C*), 128.17 (Ar*C*), 128.32 (Ar*C*), 128.42 (Ar*C*), 134.08 (Ar*C*), 150.85 (Ar*C*), 157.75 [NC(O)N], 195.50 [$S\mathit{C}(O)CH_3$]. UV–VIS (DMF) λ_{max}/nm (ε) for $Fe_4S_4(S\text{–}Et)_4$-$(Bu^n{}_4N)_2$: 297 (23 300), 418 (17 200); λ_{max}/nm (ε) found for (**2**)·$Bu^n{}_4N)_2$: 295 (25 500), 412 (13 100). ^1H NMR **2** ([$^2H_6$]DMSO δ 0.94 (m, 24H, $NCH_2\mathit{C}H_2CH_2C\mathit{H}_3$), 1.32 (m, 16H, $NCH_2CH_2C\mathit{H}_2CH_3$), 1.58 (m, 16H, $NCH_2C\mathit{H}_2CH_2CH_3$), 3.17 (m, 16H, $NC\mathit{H}_2CH_2CH_2CH_3$), 3.68–4.08 (m, 28H, $OC\mathit{H}_2C\mathit{H}_2OC\mathit{H}_2$ and $NC\mathit{H}H$), 5.50 (s, 4H, $NC\mathit{H}H$), 6.87 (s, 4H, XyH), 7.10 (s, 10H, PhH), 13.25 (br, 6H, $OCH_2C\mathit{H}_2S$), 14.25 (br, 2H, $OCH_2C\mathit{H}_2S$).

2. Corey–Pauling–Koltun models show that in this way the cluster and ligand are well matched. A temperature-dependence shift experiment ([$^2H_6$]DMSO, temperature range 25–50 °C) showed that each of the two sets of CH_2S-protons in **2** shift 0.75 ppm downfield when the temperature is increased by 25 °C. This shift value is in good agreement with values reported for other iron–sulphur clusters.[10] It suggests that the Fe_4S_4-core in **2** is intact. The same conclusion was drawn from a core extrusion experiment: addition of a slight excess of PhSH to **2** generated the cluster $[Fe_4S_4(S\text{–}Ph)_4]^{2-}$, which was detected by ^1H NMR [measured ([$^2H_6$]DMSO), lit.[10] (CD_3CN) δ 5.50, 5.28 (*p*-PhH); 5.80, 5.88 (*o*-PhH); 8.20, 8.18 (*m*-PhH)].

In summary, we may conclude that we have synthesised a new semi-encapsulated iron–sulphur cluster, which displays electrochemical behaviour previoulsy only encountered in metalloproteins. Currently, our research is being focused on the synthesis of diphenylglycoluril ligand systems capable of fully encapsulating an Fe_4S_4-core.

We thank Professor J. J. Steggerda for stimulating discussions.

Received, 19th April 1991; Com. 1/01848E

References

1 Y. Kuroda, Y. Sasaki, Y. Shiroiwa and I. Tabushi, *J. Am. Chem. Soc.*, 1988, **110**, 4049.
2 Y. Okuno, K. Uoto, Y. Sasaki, O. Yonemitsu and T. Tomohiro, *J. Chem. Soc., Chem. Commun.*, 1987, 874.
3 T. D. P. Stack and R. H. Holm, *J. Am. Chem. Soc.*, 1988, **110**, 2484.
4 F. G. M. Niele, C. F. Martens and R. J. M. Nolte, *J. Am. Chem. Soc.*, 1989, **111**, 2078.
5 B. Strijtveen and R. M. Kellogg, *J. Org. Chem.*, 1986, **51**, 3664.
6 (*a*) R. P. Sybesma, G. Beurskens, P. T. Beurskens and R. J. M. Nolte, to be published; (*b*) J. M. M. Smits, H. Behm, W. P. Bosman and P. T. Beurskens, *J. Crystallgr. Spectrosc. Res.*, 1988, **18**, 447.
7 G. B. Wong, M. A. Bobrik and R. H. Holm, *Inorg. Chem.*, 1978, **17**, 578.
8 F. A. Armstrong, A. M. Bond, A. O. Hill, B. N. Oliver and I. S. M. Psalti, *J. Am. Chem. Soc.*, 1989, **111**, 9185; F. A. Armstrong, A. O. Hill and N. J. Walton, *Acc. Chem. Res.*, 1988, **21**, 407; F. A. Armstrong, A. P. Cox, A. O. Hill, V. J. Lowe and B. N. Oliver, *J. Electroanal. Chem.*, 1987, **217**, 331.
9 B. V. Depamphilis, B. A. Averill, T. Herskovitz and L. Que, *J. Am. Chem. Soc.*, 1974, **96**, 4159.
10 R. H. Holm, W. D. Phillips, B. A. Averill, J. J. Mayerle and T. Herskovitz, *J. Am. Chem. Soc.*, 1974, **96**, 2109.