Macrocyclic Tetranuclear Clusters with 28-, 32-, 36-, 40-, and 44-Membered Rings as High-potential Iron–Sulphur Protein Analogues

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A new series of Fe_4S_4 active-site analogues for high-potential iron–sulphur proteins have been prepared from $[Fe_4S_4(SBu^t)_4]^{2-}$ and macrocyclic tetra-aza tetrathiol ligands where the active-site cores are composed of an intramolecular hydrophobic domain formed by 28-, 32-, 36-, 40-, and 44-membered rings having methylene backbones. The compounds were obtained in good yields (70–90%) as black powders with m.p. > 300 °C. They dissolve in dimethylformamide and dimethyl sulphoxide, but are almost insoluble in most common organic solvents and water. A remarkable positive shift of the 1− to 2− redox couple has been observed for all the macrocyclic clusters examined. There is also a notable stabilization and ring-size effect upon the reaction of these clusters with molecular oxygen.

Novel biologically active materials may be derived from interactions between organic compounds and certain metal ions. Among well known examples are a number of metalloenzymes,[1] bleomycin,[2] cisplatin *cis*-$[Pt(NH_3)_2Cl_2]$,[3] and anticancer platinum greens.[4]

In previous work from this laboratory a new family of synthetic Fe_4S_4 active-site analogues of iron–sulphur proteins was introduced with tetrathiol compounds anchored to 36- and 38-membered rings consisting of a methylene backbone and a cyclophane skeleton, respectively.[5–7] Characteristic features observed in the macrocyclic Fe_4S_4 clusters were remarkable positive shifts of half-wave potentials and a stabilisation effect on the cores embedded in the intramolecular hydrophobic environment provided by the macrocyclic tetrathiol ligands.[6–8] We further found that such analogues can be efficient catalysts in the reactions of electrochemical CO_2 fixation.[9] As very few reports were available on the environmental effect on active-site cores,[10–12] we began a study of the synthesis of macrocyclic tetrathiol ligands and their application to Fe_4S_4 cluster preparations[5–8,13–15] for the purpose of determining this effect. We report herein the synthesis of a series of Fe_4S_4 clusters with macrocyclic tetrathiol ligands attached between the 28- and 44-membered rings. Also described are results on the half-wave potentials and on the stability of Fe_4S_4 cores towards molecular oxygen.

Results and Discussion

Synthesis of Tetrathiol Ligands (**12**)—(**16**) *and Macrocyclic* Fe_4S_4 *Clusters* (**18**)—(**22**).—Corey–Pauling–Kolutan (CPK) model examinations suggested that a pore size of at least 10 Å was necessary to incorporate the Fe_4S_4 core snugly inside the intramolecular hydrophobic domain (Table 1). It was therefore decided to synthesize macrocycles with a 28-membered ring (pore size approximately 11 Å) and greater.

Large macrocyclic tetra-amine compounds [(**1**)—(**5**), Scheme] as a key starting material were prepared without difficulty according to previously reported procedures by a double-condensation reaction between the corresponding dibromide and ditosylamide derivatives.[5,6,13] A slightly modified synthetic route developed for the 36-membered analogues[5,6] would also be applicable to the present synthetic work. Namely, for the preparation of macrocyclic tetra-acetylthio derivatives (**7**)—(**11**), simultaneous coupling reactions at four amine sites in the cyclic tetra-amines (**1**)—(**5**) were performed with 3-acetylthio-3-methylbutanoyl chloride (**6**).[5,6] Yields were roughly the same (60—70%, Table 1) for all the ring sizes with K_2CO_3 as a base in CH_2Cl_2. Subsequent deprotection (deacetylation) of (**7**)—(**11**) proceeded very smoothly under acidic conditions with 1 mol dm^{-3} HCl–MeOH at 60 °C, and the corresponding tetrathiol ligands anchored to macrocyclic rings were readily obtained in almost quantitative yields. The presence of SH and amide groups was exhibited around 2 570 and 1 620 cm^{-1}, respectively, in the i.r. spectra in $CHCl_3$ solutions. Proton n.m.r. spectra (200 MHz) of compounds (**12**)—(**16**) in $CDCl_3$ showed a singlet resonance of SH around δ 2.7 with an appropriate integration, which is reasonable compared with the previous results observed for the 36- and 38-membered analogues.[5–7]

Table 1. Yields and estimated pore sizes

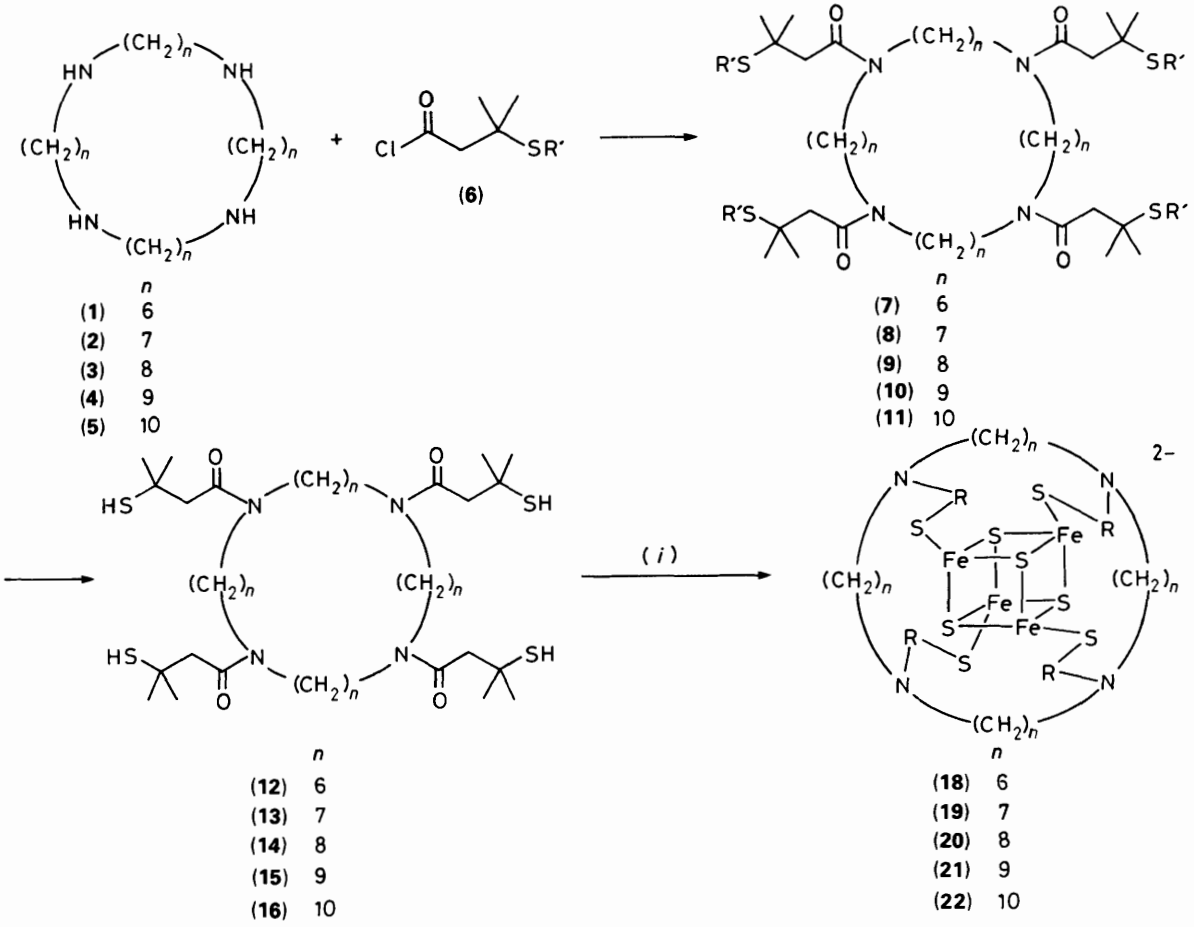
n (Ring size)	Pore size (Å)[a]	Compound (yield/%)			Remarks
6 (28)	11	(**7**) (56)	(**12**) (98)	(**18**) (85)	This work
7 (32)	13	(**8**) (61)	(**13**) (95)	(**19**) (83)	This work
8 (36)	14	(**9**) (68)	(**14**) (89)	(**20**) (70)	Refs. 5, 6
9 (40)	16	(**10**) (57)	(**15**) (98)	(**21**) (86)	This work
10 (44)	17	(**11**) (63)	(**16**) (91)	(**22**) (62)	This work

[a] Estimated from CPK model examination; *cf.* related data on core size from ref. 17 are Fe–Fe (2.8), S–S (3.6), and Fe–S (2.3 Å).

Then a series of Fe_4S_4 active-site analogues (**18**)—(**22**) was prepared by a ligand-substitution reaction[16] using the above tetrathiol compounds (**12**)—(**16**), and $[Fe_4S_4(SBu^t)_4]^{2-}$ (**17**).[17] The reaction was performed in dimethylformamide (dmf), and all manipulations were carried out under pure nitrogen. Typical experimental procedures were as follows.

A slight excess (1.02 equivalents) of tetrathiol compound [*e.g.* (**12**) in dmf was added to a MeCN solution of (**17**), and the mixture was kept at 40 °C for 1.5 h under reduced pressure with stirring to remove the liberated Bu^tSH. A mixture of ethyl acetate–n-hexane (1:4) was then added, kept at −20 °C overnight, and the resultant black-brown precipitate was collected by filtration. After gel filtration over Sephadex LH-20 with dmf, reprecipitation from dmf–ethyl acetate–hexane gave a black-brown powder with m.p. > 300 °C.

Thus, in the same manner, a series of novel Fe_4S_4 clusters with 28-, 32-, 36-, 40-, and 44-membered macrocyclic tetrathiol ligands (**18**)—(**22**) was obtained in good yields (62—86%, Table 1). These clusters dissolve in dmf and dimethyl sulphoxide



Scheme. Synthetic routes to macrocyclic clusters. R = $C(O)CH_2CMe_2$, R′ = MeCO. (*i*) $[Fe_4S_4(SBu^t)_4]^{2-}$ (**17**).

Table 2. Absorption spectral data in dmf, and half-wave potentials in dmso *

Compound	$\lambda_{max.}$/nm ($10^3\varepsilon$/dm^3 mol^{-1} cm^{-1})	$E_{\frac{1}{2}}$/V *vs.* s.c.e.	
		1− to 2−	2− to 3−
(**18**)	295 (20.1), 419 (15.3)	+0.24	−1.25
(**19**)	297 (20.1), 419 (15.4)	+0.24	−1.29
(**20**)	297 (19.9), 419 (15.4)	+0.23	−1.29
(**21**)	296 (20.4), 416 (15.4)	+0.26	−1.25
(**22**)	293 (21.8), 417 (15.4)	+0.25	−1.30

* Cluster (1 mmol dm^{-3}) in dmso and $NBu^n_4BF_4$ (0.2 mol dm^{-3}) as an electrolyte; cyclic voltammograms were measured at room temperature.

(dmso), but are practically insoluble in most common organic solvents such as MeCN, ethyl acetate, CH_2Cl_2, diethyl ether, tetrahydrofuran (thf), EtOH, MeOH, and water. The possibility of polymer formation cannot be ruled out completely for the above complexes, since no single crystals suitable for *X*-ray analysis have been obtained.

Absorption Spectra and Half-wave Potentials.—Electronic spectra of the above macrocyclic clusters in dmf are summarised in Table 2. Two absorption maxima around 300 and 420 nm were observed for each cluster with similar molar absorption coefficients (*ca.* 20×10^3 and 15×10^3 dm^3 mol^{-1} cm^{-1}, respectively). These spectra are essentially the same as that of the corresponding unclad Fe_4S_4 cluster (**17**), which suggests also the presence of Fe_4S_4 cluster chromophores in the cyclic analogues. Moreover, conversion of (**19**) into $[Fe_4S_4(SPh)_4]^{2-}$ by the addition of excess of PhSH has been shown from u.v.–visible spectra (*cf.* ref. 5).

As is well known, non-haem iron sulphur proteins are found in a wide variety of living creatures from bacteria to mammals.[18] One of the most important functions of iron–sulphur proteins is their electron-transfer ability in nature. They are involved in many kinds of biosyntheses and contribute directly to material conversion reactions *in vivo*.[18] Among them, high-potential proteins[19] exhibit their half-wave potentials (1− to 2−) near +0.35 V (*vs.* n.h.e. at pH 7) in water, whereas the structure of the Fe_4S_4 active core itself is very similar to that of low-potential 4Fe ferredoxins which show the redox potentials to be the most stable (2− to 3−) near −0.4 to −0.6 V.[18,20] It has been found that the active site of high-potential proteins is surrounded by proteins consisting of largely hydrophobic amino acids,[21] therefore this hydrophobic environment is expected to make an important contribution to the stabilization of Fe_4S_4 cores in the high-potential proteins.

Eventually, our preliminary studies demonstrated promising results using 36-membered clusters. Namely, among the three kinds of 36-membered complexes with phenyl, benzyl, and butyl type ligands, the t-butyl analogue (**20**) showed the most positive half-wave potential for a 1− to 2− redox cycle at +0.25 V (*vs.* saturated calomel electrode, s.c.e.) in dmso.[6,8] Therefore, we next investigated half-wave potentials of t-butyl Fe_4S_4 clusters with a series of ring sizes (**18**)—(**22**) by measuring cyclic voltammograms.

The respective potentials of 1− to 2− and 2− to 3− couples appeared around +0.24 and −1.29 V. It should be emphasized,

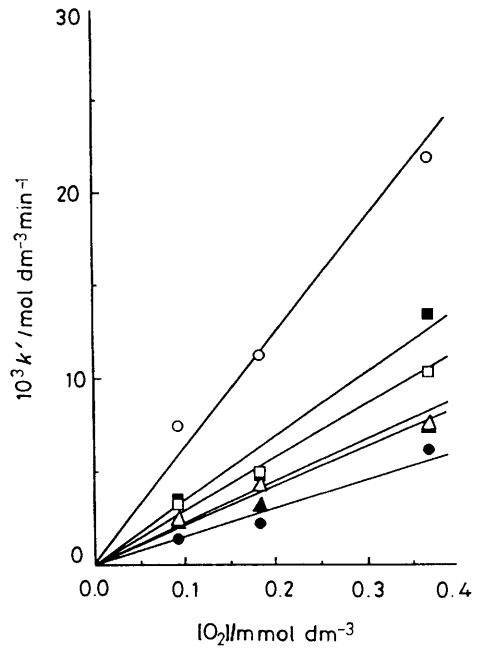


Figure. Plots of pseudo-first-order rate constant (k') as a function of [O_2] for the compounds (**17**) (○), (**18**) (□, 28-), (**19**) (△, 32-), (**20**) (●, 36-), (**21**) (▲, 40-), and (**22**) (■, 44-membered ring)

Table 3. Rate constants and half-lives of the t-butyl type macrocyclic clusters towards molecular oxygen[a]

Compound	Ring size	10^3k[b]/min^{-1}	Half-life, $t_{\frac{1}{2}}$[c]/min	Ratios of $t_{\frac{1}{2}}$
(**17**)	None	58.2 (0.990)	11.9	100
(**18**)	28	27.6 (0.993)	25.1	211
(**19**)	32	20.6 (0.988)	33.6	282
(**20**)	36	16.7 (0.976)	41.5	349
(**21**)	40	20.1 (0.987)	34.5	290
(**22**)	44	36.3 (0.969)	19.1	161

[a] Total volume of the reaction vessel 53 cm^3; cluster (0.5 mmol dm^{-3}) in dmf solution (2 cm^3). [b] First-order rate constant determined from plots of k' *vs.* [O_2] using the least-squares method. Figures in parentheses represent the regression coefficient. See text for further details. [c] Defined as $t_{\frac{1}{2}} = \ln 2/k$.

however, that remarkable positive shifts of the 1− to 2− couple have been observed for all the macrocyclic clusters synthesized here, since the corresponding potentials of unclad (**17**) were −0.11 and −1.40 V, respectively, for the 1− to 2− and 2− to 3−couples (refs. 6 and 8 and this work). Slight positive shifts of the 2− to 3− couple have also been observed for the macrocyclic clusters. This clearly shows that the phenomenon is very common for the present Fe_4S_4 clusters embedded in an intramolecular hydrophobic environment provided by macrocyclic tetrathiol ligands. Thus it is considered that the present clusters may be a good model for high-potential iron–sulphur proteins. It is rather curious that no particular differences in the potentials have resulted for these five analogues (**18**)—(**22**). This may mean that the electron transfer is not greatly affected by environmental differences within the ring sizes examined (cavity sizes *ca.* 11—17 Å formed by 28- to 44-membered rings) (Table 2).

Stability of Macrocyclic Fe_4S_4 *Clusters towards Molecular Oxygen.*—Another important feature is the fact that the active sites of the iron–sulphur proteins are known not to be particularly stable towards oxygen.[22] A hydrophobic environment may affect the stability of the core towards molecular oxygen, since in nature the domain formed by rather hydrophobic peptide chains stabilizes the 1− to 2− couple of high-potential proteins in a remarkably positive region.[19]

The stability of the above macrocyclic clusters (0.5 mmol dm^{-3} in dmf) towards molecular oxygen was evaluated by observing the decrease in absorbance at $\lambda_{max.}$(420 nm). Pseudo-first-order rate constants (k') for decomposition of the clusters were obtained in the form of initial rates (slope = $\Delta A/\Delta t$) from logarithmic plots of the absorbance as a function of time at different oxygen concentrations. Then the first-order rate constants (k) were determined from plots of k' *vs.* [O_2] by the least-squares method as shown in the Figure. The half-life defined as $t_{\frac{1}{2}} = \ln 2/k$ was also computed. These data are summarized in Table 3 together with ratios of the half-life.

The Figure clearly shows the stabilizing effects of the cyclic ligands on Fe_4S_4 cubane cores: for instance, the rate constants (k) for the decay of the clusters with macrocycle were 1.6—3.5 times smaller than that of the non-cyclic cluster (**17**). It is particularly of interest that the most stable cluster among those studied was the complex with a 36-membered ring, (**20**), and this may be consistent with the results of CPK model examination; that is, co-ordination of the Fe_4S_4 core with the 36-membered tetra(butanethiol) derivative seemed to fit best.[5,6] A ring-size effect was obvious, *viz.* both the larger and smaller rings stabilized less the Fe_4S_4 cores; for instance, the complexes with 32- and 40-membered rings had lower stability with very similar k values. It is probable that the macrocycles larger than 36-membered ones cause the core environment to loosen, and a more feasible reaction with molecular oxygen can be expected. With the smaller ring ligands, the core part sits inside the domain well and is still protected from the reactant, so that the extent of the effect seemed less. Thus the order of stability toward oxygen was (**20**) (36-membered ring) > (**21**) (40) = (**19**) (32) > (**18**) (28) > (**22**) (44) > (**17**) (unclad), with the ratio of 349:290:282:211:161:100 in terms of half-life.

Conclusion

We have synthesized tetra(butanethiol) ligands anchored to various sizes of macrocycles composed of a methylene backbone which are suitable for capturing cubane-type cluster cores. Ligand-substitution reactions afforded a series of Fe_4S_4 clusters surrounded by an intramolecular hydrophobic domain, (**18**)—(**22**). Redox processes were examined, and a remarkable positive shift of the potentials for the 1− to 2− couple was observed. We have also demonstrated for the first time the marked stabilization effect of the macrocyclic Fe_4S_4 clusters towards molecular oxygen. From these results we consider that the complexes studied here are a new model of high-potential iron–sulphur proteins. Measurements of Mössbauer spectra and magnetic susceptibility are in progress.

Experimental

General Methods.—Manipulations and measurements involving Fe_4S_4 clusters and thiols were carried out in an atmosphere of N_2 or Ar. Flash chromatographic separations were carried out as described[23] on silica gel 60 (230—400 mesh). Tetrahydrofuran (thf) and diethyl ether were distilled from sodium benzophenone ketyl; dmf, CH_2Cl_2, MeCN, benzene, hexane, and $CHCl_3$ from CaH_2, EtOH and MeOH from Mg, and ethyl acetate and acetone were purified by distillation. Other materials were purchased from appropriate sources and used as received. 3-Acetylthio-3-methylbutanoyl chloride[5,6] and the cluster (**17**) were prepared according to the literature procedures.[24] The 36-membered ring compounds (**3**), (**9**), (**14**), and (**20**) were prepared as described elsewhere.[5,6]

Physical Measurements.—Absorption spectra were recorded on a Hitachi U-3200 spectrophotometer, i.r. spectra with a JASCO IR-440. N.m.r. spectra were obtained on a Bruker AC-200 or a Hitachi R-40 spectrometer, and chemical shifts are relative to $SiMe_4$ as internal reference. Redox potentials were determined by obtaining cyclic voltammograms with a Hokuto Denko HA-501 instrument. The cluster concentration was 1 mmol dm^{-3} in 0.2 mol dm^{-3} solutions of $NBu^n_4BF_4$, and platinum and a saturated calomel electrode were used as the working electrode and the reference, respectively. The scan rate was 100 mV/s^{-1}.

Preparation of S-Acetyl Tetrathiol Compounds.—1,8,15,22-*Tetra*(3′-*acetylthio*-3′-*methylbutanoyl*)-1,8,15,22-*tetra-azacyclo-octacosane* (**7**). To a mixture of 1,8,15,22-tetra-azacyclo-octacosane (**1**) (200 mg, 0.504 mmol) and anhydrous K_2CO_3 (244 mg, 1.77 mmol) in dry CH_2Cl_2 (17 cm^3) was added dropwise a solution of 3-acetylthio-3-methylbutanoyl chloride (**6**) (589 mg, 3.03 mmol) in dry CH_2Cl_2 (17 cm^3) over a period of 40 min at 0 °C. The reaction mixture was then gradually warmed to room temperature and stirred for 3 d. The solution was washed with saturated $NaHCO_3$, water, and brine, and dried ($MgSO_4$). After removal of the solvent the residue was purified by chromatography over silica gel eluted with benzene–ethyl acetate (1:2) to give a colourless viscous oil in 56% yield (287 mg). $\nu_{max.}$ 1 665vs (CH_3CO), 1 620vs (CO–N), and 1 100vs (C–S) cm^{-1} ($CHCl_3$); δ_H($CDCl_3$) 1.2—1.8 (m, 32 H, CH_2), 1.57 (s, 24 H, CH_3), 2.23 (s, 12 H, $COCH_3$), 2.92 (s, 8 H, $COCH_2$), and 3.2—3.5 (m, 16 H, $N_\alpha CH_2$) (Found: C, 57.80; H, 8.85; N, 5.10. $C_{52}H_{92}N_4O_8S_4 \cdot 3H_2O$ requires C, 57.65; H, 9.10; N, 5.15%).

The following compounds were similarly prepared.

1,9,17,25-*Tetra*(3′-*acetylthio*-3′-*methylbutanoyl*)-1,9,17,25-*tetra-azacyclodotriacontane* (**8**). With 1,9,17,25-tetra-azacyclodotriacontane (**2**) (250 mg, 0.552 mmol) and anhydrous K_2CO_3 (267 mg, 1.93 mmol) in dry CH_2Cl_2 (18 cm^3); acid chloride (**6**) (645 mg, 3.31 mmol) in dry CH_2Cl_2 (18 cm^3); silica gel column eluted with benzene–ethyl acetate (1:1); 365 mg (61%) of colourless viscous oil. $\nu_{max.}$ 1 665vs (CH_3CO), 1 615vs (CO–N), and 1 100vs (C–S) cm^{-1} ($CHCl_3$); δ_H($CDCl_3$) 1.1—1.8 (m, 40 H, CH_2), 1.56 (s, 24 H, CH_3), 2.23 (s, 12 H, $COCH_3$), 2.92 (s, 8 H, $COCH_2$), and 3.2—3.5 (m, 16 H, $N_\alpha CH_2$) (Found: C, 62.20; H, 9.50; N, 5.00. $C_{56}H_{100}N_4O_8S_4$ requires C, 61.95; H, 9.30; N, 5.15%).

1,11,21,31-*Tetra*(3′-*acetylthio*-3′-*methylbutanoyl*)-1,11,21,31-*tetra-azacyclotetracontane* (**10**). With 1,11,21,31-tetra-azacyclotetracontane (**4**) (300 mg, 0.531 mmol) and anhydrous K_2CO_3 (257 mg, 1.86 mmol) in dry CH_2Cl_2 (18 cm^3); acid chloride (**6**) (620 mg, 3.18 mmol) in dry CH_2Cl_2 (18 cm^3); silica gel column eluted with benzene–ethyl acetate (3:1); 362 mg (57%) of colourless viscous oil. $\nu_{max.}$ 1 665vs (CH_3CO), 1 610vs (CO–N), and 1 100vs (C–S) cm^{-1} ($CHCl_3$); δ_H($CDCl_3$) 1.2—1.7 (m, 56 H, CH_2), 1.59 (s, 24 H, CH_3), 2.25 (s, 12 H, $COCH_3$), 2.92 (s, 8 H, $COCH_2$), and 3.2—3.5 (m, 16 H, $N_\alpha CH_2$) (Found: C, 64.00; H, 9.85; N, 4.50. $C_{64}H_{116}N_4O_8S_4$ requires C, 64.15; H, 9.75; N, 4.70%).

1,12,23,34-*Tetra*(3′-*acetylthio*-3′-*methylbutanoyl*)-1,12,23,34-*tetra-azacyclotetratetracontane* (**11**). With 1,12,23,34-tetra-azacyclotetratetracontane (**5**) (200 mg, 0.322 mmol) and anhydrous K_2CO_3 (157 mg, 1.13 mmol) in dry CH_2Cl_2 (11 cm^3); acid chloride (**6**) (376 mg, 1.93 mmol) in dry CH_2Cl_2 (11 cm^3); silica gel column eluted with benzene–ethyl acetate (3:1); 253 mg (63%) of colourless viscous oil. $\nu_{max.}$ 1 665vs (CH_3CO), 1 610vs (CO–N), and 1 105vs (C–S) cm^{-1} ($CHCl_3$); δ_H($CDCl_3$) 1.1—1.7 (m, 64 H, CH_2), 1.59 (s, 24 H, CH_3), 2.24 (s, 12 H, $COCH_3$), 2.92 (s, 8 H, $COCH_2$), and 3.2—3.5 (m, 16 H, $N_\alpha CH_2$).

Preparation of Macrocyclic Tetrathiol Ligands.—1,8,15,22-*Tetra*(3′-*mercapto*-3′-*methylbutanoyl*)-1,8,15,22-*tetra-azacyclo-octacosane* (**12**). The acetyl derivative (**7**) (100 mg, 97 μmol) in 1 mol dm^{-3} HCl–MeOH (10 cm^3) was heated at 60 °C for 2 h under nitrogen. The solvent was then removed *in vacuo*, and the residue was poured into brine and extracted with CH_2Cl_2 three times. After drying ($MgSO_4$) and evaporation of the solvent, 82 mg (98%) of colourless viscous oil were obtained. $\nu_{max.}$ 2 580w (SH) and 1 625vs (CO–N) cm^{-1} ($CHCl_3$); δ_H($CDCl_3$) 1.2—1.8 (m, 32 H, CH_2), 1.53 (s, 24 H, CH_3), 2.63 (s, 8 H, $COCH_2$), 2.66 (s, 4 H, SH, D_2O exchangeable), and 3.1—3.5 (m, 16 H, $N_\alpha CH_2$).

The following compounds were similarly prepared.

1,9,17,25-*Tetra*(3′-*mercapto*-3′-*methylbutanoyl*)-1,9,17,25-*tetra-azacyclodotriacontane* (**13**). With compound (**8**) (120 mg, 111 μmol) in 1 mol dm^{-3} HCl–MeOH (12 cm^3), 60 °C, 2 h; extracted with CH_2Cl_2 three times; colourless viscous oil, 96 mg (95%). $\nu_{max.}$ 2 570w (SH) and 1 620vs (CO–N) cm^{-1} ($CHCl_3$); δ_H($CDCl_3$) 1.2—1.7 (m, 40 H, CH_2), 1.52 (s, 24 H, CH_3), 2.59 (s, 8 H, $COCH_2$), 2.68 (s, 4 H, SH, D_2O exchangeable), and 3.1–3.4 (m, 16 H, $N_\alpha CH_2$).

1,11,21,31-*Tetra*(3′-*mercapto*-3′-*methylbutanoyl*)-1,11,21,31-*tetra-azacyclotetracontane* (**15**). With compound (**10**) (100 mg, 83.5 μmol) in 1 mol dm^{-3} HCl–MeOH (8.5 cm^3), 60 °C, 2 h; extracted with CH_2Cl_2 three times; colourless viscous oil, 84 mg (98%). $\nu_{max.}$ 2 580w (SH) and 1 620vs (CO–N) cm^{-1} ($CHCl_3$); δ_H($CDCl_3$) 1.2–1.7 (m, 56 H, CH_2), 1.53 (s, 24 H, CH_3), 2.61 (s, 8 H, $COCH_2$), 2.69 (s, 4 H, D_2O exchangeable), and 3.1—3.4 (m, 16 H, $N_\alpha CH_2$).

1,12,23,34-*Tetra*(3′-*mercapto*-3′-*methylbutanoyl*)-1,12,23,34-*tetra-azacyclotetratetracontane* (**16**). With compound (**11**) (100 mg, 79.7 μmol) in 1 mol dm^{-3} HCl–MeOH (8 cm^3), 60 °C, 2 h; extracted with CH_2Cl_2 three times; colourless viscous oil, 79 mg (91%). $\nu_{max.}$ 2 570w (SH) and 1 620vs (CO–N) cm^{-1} ($CHCl_3$); δ_H($CDCl_3$) 1.2—1.7 (m, 64 H, CH_2), 1.53 (s, 24 H, CH_3), 2.61 (s, 8 H, $COCH_2$), 2.70 (s, 4 H, SH, D_2O exchangeable), and 3.1—3.4 (m, 16 H, $N_\alpha CH_2$).

Preparation of Macrocyclic Clusters.—*Bis*(*tetraethylammonium*) *tetra*-μ_3-*sulphido*-[1,8,15,22-*tetra-azacyclo-octacosane*-1,8,15,22-*tetrakis*(1′,1′-*dimethyl*-3′-*oxopropanethiolato*-SS′S″S‴)]-tetrahedro-*tetraferrate* (**18**). All operations were carried out in a dry pure nitrogen atmosphere with the use of thoroughly degassed solvents and reagents. To a stirred solution of $[NEt_4]_2[Fe_4S_4(SBu^t)_4]$ (**17**) (87 mg, 89.8 μmol) in MeCN (45 cm^3) was added dropwise the tetrathiol ligand (**12**) (81 mg, 94.0 μmol) in dmf (10 cm^3) at 40 °C. The mixture was stirred under dynamic vacuum for 1.5 h, and dmf (10 cm^3) was added to dissolve the resulting black oily product. Ethyl acetate (50 cm^3) and n-hexane (200 cm^3) were then added to the mixture, which was kept at −20 °C overnight. The black-brown precipitate was collected by filtration, washed with hot CH_2Cl_2 and hot MeCN, and dried *in vacuo*. After gel filtration over Sephadex LH-20 with dmf, reprecipitation from dmf–ethyl acetate–n-hexane afforded a black-brown powder (112 mg, 85%), m.p. >300 °C; $\lambda_{max.}$(dmf) 295 (ε 20 100) and 419 nm (15 300 dm^3 mol^{-1} cm^{-1}); $E_{\frac{1}{2}}$ (1− to 2−, 2− to 3−) (*vs.* s.c.e., dmso) +0.24 and −1.25 V.

The following compounds were similarly prepared.

Bis(*tetraethylammonium*) *tetra*-μ_3-*sulphido*-[1,9,17,25-*tetra-azacyclodotriacontane*-1,9,17,25-*tetrakis*(1′,1′-*dimethyl*-3′-*oxo-propanethiolato*-SS′S″S‴)]-tetrahedro-*tetraferrate* (**19**). With compound (**17**) (96 mg, 99.1 μmol) in MeCN (49 cm^3) and (**13**) (95 mg, 103.5 μmol) in dmf (10 cm^3); stirred under vacuum for 2 h; dmf (10 cm^3) added; ethyl acetate (50 cm^3) and n-hexane (200 cm^3) to precipitate out a black-brown solid; yield 125 mg (83%), m.p. >300 °C; $\lambda_{max.}$(dmf) 297 (ε 20 100) and 419 nm (15 400 dm^3 mol^{-1} cm^{-1}); $E_{\frac{1}{2}}$ (1− to 2−, 2− to 3−) (*vs.* s.c.e., dmso) +0.24 and −1.29 V.

Bis(*tetraethylammonium*) *tetra*-μ_3-*sulphido*-[1,11,21,31-*tetra-azacyclotetracontane*-1,11,21,31-*tetrakis*(1′,1′-*dimethyl*-3′-*oxo*-

propanethiolato-SS'S''S''')]-tetrahedro-*tetraferrate* (**21**). With compound (**17**) (74 mg, 76.4 μmol) in MeCN (38 cm^3) and (**15**) (83 mg, 80.6 μmol) in dmf (8 cm^3); stirred under vacuum for 1 h; dmf (10 cm^3) added; ethyl acetate (150 cm^3) and n-hexane (150 cm^3) to precipitate out a black-brown solid; yield 114 mg (86%), m.p. > 300 °C; $\lambda_{max.}$(dmf) 296 (ε 20 400) and 416 nm (15 400 dm^3 mol^{-1} cm^{-1}); $E_{\frac{1}{2}}$ (1− to 2−, 2− to 3−) (*vs.* s.c.e., dmso) +0.26 and −1.25 V.

Bis(*tetraethylammonium*) *tetra*-μ_3-*sulphido*-[1,12,23,34-*tetraazacyclotetratetracontane*-1,12,23,34-*tetrakis*(1',1'-*dimethyl*-3'-*oxopropanethiolato*-SS'S''S''')]-tetrahedro-*tetraferrate* (**22**). With compound (**17**) (66 mg, 68.1 μmol) in MeCN (34 cm^3) and (**16**) (78 mg, 71.8 μmol) in dmf (7 cm^3); stirred under vacuum for 1.5 h; dmf (10 cm^3) added; ethyl acetate (100 cm^3) and n-hexane (300 cm^3) to precipitate a black-brown solid; yield 71 mg (62%), m.p. > 300 °C; $\lambda_{max.}$ 293 (ε 21 800) and 417 nm (15 400 dm^3 mol^{-1} cm^{-1}); $E_{\frac{1}{2}}$ (1− to 2−, 2− to 3−) (*vs.* s.c.e., dmso) +0.25 and −1.30 V.

Core Stability towards Molecular Oxygen.—The reaction vessel was a round-bottomed flask to which a u.v. cell (quartz, pathlength 2 mm) was connected through a three-way stopcock under N_2. The total inner volume of the system was 53 cm^3, and a cluster (0.5 mmol dm^{-3}) in dmf solution (2 cm^3) was used throughout the experiments. An appropriate amount of oxygen was injected, and the decrease in absorbance at a maximum was followed. Then the first-order rate constant for decomposition of the clusters was determined as mentioned in the text. The half-life defined as $t_{\frac{1}{2}} = \ln 2/k$ was also computed. These data are given in Table 3.

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