Iron–Sulphur Dimers with Bidentate Carboxylate–Thiolate Terminal Ligands

Peter Beardwood and John F. Gibson*

Department of Chemistry, Imperial College of Science and Technology, London SW7 2AY, U.K.

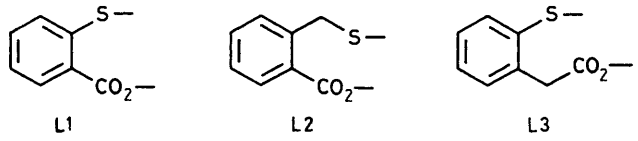
The mixed-donor carboxylate–thiolate chelate ligands L1, L2 and L3 co-ordinate $[2Fe–2S]^{2+}$ in a ligand exchange reaction with $[Fe_2S_2Cl_4]^{2-}$ and the resulting complexes are characterised by electronic, n.m.r., i.r., and Raman spectroscopy and shown to undergo a quasi-reversible one-electron reduction to the corresponding trianion, the e.s.r. spectra of which are compared with those for $[2Fe–2S]^{+}$ proteins of the Rieske type.

The Rieske iron–sulphur protein from *Thermus thermophilus* shows strong evidence for partial co-ordination of its two [2Fe–2S] clusters by non-cysteine ligands.[1] These [2Fe–2S] centres possess notably anomalous properties compared with those co-ordinated by a full complement of four thiolate ligands, for example: (i) averaged *g*-values ($g_{av.}$) of *ca.* 1.91 in the $[2Fe–2S]^{+}$ oxidation state compared to *ca.* 1.96 for ferredoxins; (ii) a 400—600 mV positive shift in redox potential; (iii) a large inequivalence of the isomer shifts and quadrupole splittings for the two Fe^{3+} ions in the Mössbauer spectra of the oxidised form; and (iv) a red-shifted electronic spectrum. Several other [2Fe–2S] proteins in mammals, plants, and bacteria show similar properties[2] and it is now of considerable interest to synthesise [2Fe–2S] model complexes having a variety of terminal ligands departing from the well characterised $[Fe_2S_2(SR)_4]$ cluster. Tetra-phenolate[3—5] and tetra-pyrrolate[3] co-ordinated [2Fe–2S] clusters have recently been reported. In this communication we describe the preparation and some properties of three $[Fe_2S_2L_2]^{2-}$ complexes involving bidentate carboxylate–thiolate ligands: (**1**), L = L1 (2-thiolatobenzoate); (**2**), L = L2 (2-thiolatomethylbenzoate);† (**3**), L = L3 (2-thiolatophenylacetate).[6]

$AsPh_4$ and NEt_4 salts of the dimeric complexes were prepared by adding stoicheiometric quantities of the ligands deprotonated with NaH in dimethylformamide (dmf) to the requisite $[Fe_2S_2Cl_4]^{2-}$ salt[7] also in dmf, filtering, and precipitating with Et_2O. Two recrystallisations from dmf–Et_2O gave the microcrystalline products with satisfactory elemental analyses in the following approximate yields: 70—80% of (**1**), 30—40% of (**2**), and 60—70% of (**3**). The complexes dissolve easily in dmf, *N*-methylpyrrolidinone (*N*mp), or dimethyl sulphoxide (dmso), but less readily in acetonitrile, and in the absence of dioxygen are stable in solution for prolonged periods. Addition of a small excess of benzenethiol in the presence of triethylamine quantitatively converted the carboxylate–thiolate dimers into $[Fe_2S_2(SAr)_4]^{2-}$, as monitored by optical spectrophotometry.

Figure 1 shows electronic absorption spectra for the complexes in dmf. They are characterised by the following features, λ/nm ($10^{-3}\varepsilon$/dm^3 mol^{-1} cm^{-1}): (**1**) ~560 sh. (7.1), 505 (7.9), and 313 (23.0); (**2**) ~550 sh. (5.1), 471 (6.1), and 325 sh. (15.2); (**3**) ~570 sh., 480 (8.3), 410 sh. (9.7), and 332 (15.5). There are some similarities to the optical spectra of $[Fe_2S_2(SR)_4]^{2-}$ complexes[8—11] which have a high energy band at *ca.* 330 nm (10^{-3} ε 15—22) and broad maxima in the region 400—600 nm tailing off in intensity towards longer wavelengths. In particular the spectrum of (**1**) is qualitatively very similar to that of $[Fe_2S_2(SAr)_4]^{2-}$. Thus, it is reasonable to suppose that the spectra in Figure 1 are dominated by charge-transfer transitions originating from the bridging and thiolate sulphurs. Notably the spectrum of $[Fe_4S_4(OAc)_4]^{2-}$ has been reported to be featureless in the interval 400—700 nm.[12] The low extinction of (**1**)—(**3**) in the region 400—600 nm compared to $[Fe_2S_2(SR)_4]^{2-}$ complexes may be attributed to there being half the number of thiolate sulphurs giving rise to charge transfer.

^{1}H N.m.r. spectra of the complexes in $(CD_3)_2SO$ have isotropically-shifted and dipolar-broadened resonances from ligand protons, δ: (**1**), −10.33 (ring position 6), −10.04 (4), −4.67 (3), and −4.16 (5); (**2**), −33.0 ($-CH_2S-$); (**3**), −9.90 (6), −9.47 (4), −3.95 (3), −2.4 (5), and −8.0 ($-CH_2CO_2-$). The widths of the peaks, ($-CH_2S-$) > ($-CH_2CO_2-$) > (3) > (6) > (4) ~ (5), are in keeping with the expected distances of the protons from the iron. The spin delocalisation through the carboxylate is small, as shown by the unexceptional isotropic shift for $-CH_2-$ in (**3**) (*ca.* −4.3), which can largely be attributed to delocalisation through the thiolate,[9] and by the position of phenyl-proton resonances in (**2**), centred at δ *ca.* 7.27 compared to δ *ca.* 7.23 for the deprotonated ligand. Thus the isotropic-shifts of the phenyl protons in (**1**) and (**2**) are dominated by contact interactions through the thiolate co-ordination to the iron. These shifts are in most cases larger than those for $[Fe_2S_2(SAr)_4]^{2-}$ complexes.[9] The position of the broad $-CH_2-$ resonance in (**2**) at δ −33.0 is similar to that for $[Fe_2S_2(SEt)_4]^{2-}$ at δ −32.0[10] and comparable to that for $[Fe_2S_2(S_2\text{-}o\text{-xylyl})_2]^{2-}$ at δ −39.6.[13] Intensities of the resonances for ligand protons in the three complexes relative to



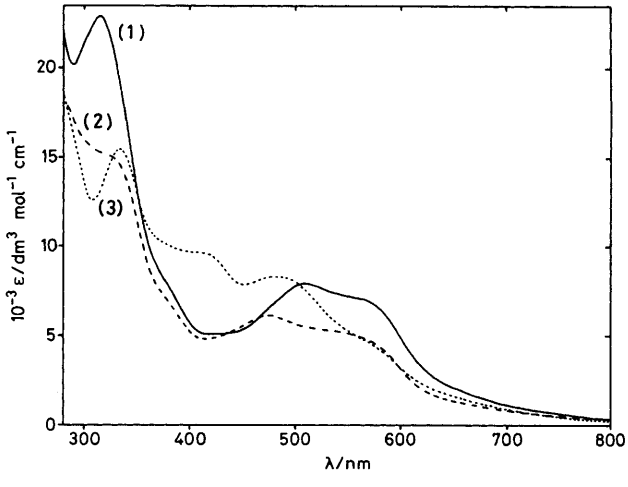


Figure 1. Electronic absorption spectra for (**1**)—(**3**) in dmf.

† Prepared from *o*-toluic acid *via* bromination of the methyl group with *N*-bromosuccinimide in CCl_4 followed by conversion into the isothiuronium salt with thiourea in H_2O–EtOH, and hydrolysis with NaOH to give the thiol after acidification.

those for their cations are consistent with the expected co-ordination of one ligand per iron.

Strong i.r. absorptions are observed from the co-ordinated carboxylate: ν(C=O) 1623 for (**1**), NEt_4; 1613 for (**2**), $AsPh_4$; 1623 cm^{-1} for (**3**), NEt_4; ν(C–O) 1308 for (**1**), 1323 for (**2**), and 1310 cm^{-1} for (**3**). The frequency separation of these modes, 290—315 cm^{-1}, is characteristic of unidentate co-ordination of the carboxylate group.[14] Thus the spectroscopic and analytical data support the expected co-ordination of each Fe^{3+} ion by a single S–O chelate. Although in the solid state a *cis* or *trans* arrangement of ligands may be favoured, their lability makes it unlikely that any preferred arrangement is retained in solution. Resonance Raman spectra of (**1**) and (**2**) have intense peaks at 373 and 394 cm^{-1} respectively from the symmetric stretch of the Fe_2S_2 bridge.

At a rapid dropping-mercury-electrode (r.d.m.e., *ca.* 6 drops/s) the dimers in dmf show two one-electron d.c. polarographic reduction waves with similar diffusion currents: (**1**), $E_{\frac{1}{2}}$ −1.02 (referred to saturated calomel electrode) and −1.84 V; (**2**), −1.15 and −1.53 V; (**3**), −1.08 and −1.66 V. We have measured half-wave potentials for some $[Fe_2S_2(SR)_4]^{2-}$ complexes under the same conditions, rather than use literature values,[8—10] in order to make more accurate comparisons without the interference of instrumental variables, in particular liquid junction potentials: (**4**), $[NEt_4]_2[Fe_2S_2(SPh)_4]$, $E_{\frac{1}{2}}$ −1.14 and −1.45 V; (**5**), $[NEt_4]_2[Fe_2S_2(S\text{-}oxylyl)_2]$, −1.51 and −1.79 V; (**6**), $[Me_3NCH_2Ph]_2[Fe_2S_2(SEt)_4]$, −1.44 and −1.69 V. The change in $E_{\frac{1}{2}}$ for the first reduction, assigned to $[2Fe\text{–}2S]^{2+/1+}$, on substituting two thiolate ligands with carboxylate is in the range +60 for (**3**) − (**4**) to +360 mV for (**2**) − (**5**). The latter could be argued to be the more valid comparison since the ligands are the most comparable. The complex (**2**), having alkyl- rather than aryl-thiolate co-ordination, is also more relevant to the likely cysteinyl co-ordination of the Rieske proteins, which have +400 to +600 mV shifts in redox potential compared to normal $[Fe_2S_2(SR)_4]$ ferredoxins. Complete substitution of the thiolate in $[Fe_4S_4(SR)_4]^{2-}$ by acetate leads to shifts in the first reduction potential of +100 (R = Ph) and +330 mV (R = CH_2Ph).[12] For the first reduction waves of (**1**)—(**3**), plots of $\log[i/(i_d - i)]$ against E have slopes in the range −60 to −65 mV. Cyclic voltammetry at glassy-carbon or platinum electrodes give well-formed pairs of cathodic current maxima and anodic minima for this redox process centred at potentials very close to those observed at the r.d.m.e. For (**1**) and (**3**) the anodic peak current is approximately equal to the cathodic peak current using a 100 mV/s scan rate, but for (**2**) it is somewhat smaller indicating greater departure from reversibility. This behaviour contrasts with the gross irreversibility of the first reduction process in monodentate-ligated $[Fe_2S_2(XR)_4]^{2-}$ (XR = SPh, SEt, or OPh) complexes and is reflected in the relative stability of the products of bulk chemical reduction.

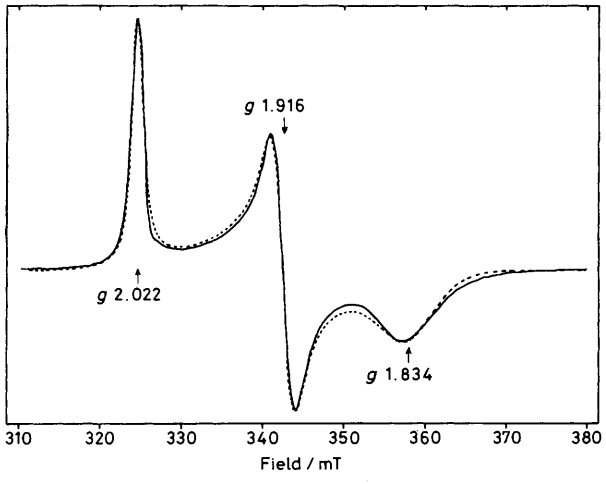


Figure 2. E.s.r. spectrum (9.19 GHz) of $[Fe_2S_2(2\text{-thiolatobenzoate})_2]^{3-}$ [reduced (**1**)] in dmf containing 0.1 M $NBu^n_4ClO_4$ at 77 K, together with a simulated spectrum (dashed line).

Reduction with a small excess of sodium acenaphthylenide, in the manner used for the $[Fe_2S_2(SR)_4]^{2-}$ clusters,[11] gives the following e.s.r. g values (determined by simulation[11]) for frozen solution samples: (**1**), 2.022, 1.916, 1.834 (dmf), 2.022, 1.911, 1.841 (*N*mp); (**2**), 2.021, 1.895, 1.874 (dmf), 2.023, 1.893. 1.877 (*N*mp); (**3**) 2.014; 1.882, 1.882 (dmf), 2.017, 1.900, 1.876 (*N*mp). A spectrum of (**1**) reduced in dmf is shown in Figure 2. The data given are for solvents containing 0.1 M (dmf) or 0.2 M (*N*mp) $NBu^n_4ClO_4$, which freeze as glasses. Similar, but in some cases rather broader, spectra were obtained using pure solvents. This behaviour is in contrast to that of monodentate-thiolate $[Fe_2S_2(SR)_4]^{2-}$ complexes which, on reduction, give ferredoxin-like e.s.r. spectra when the frozen solvent is non-vitreous but in some cases give Rieske-like spectra when the solvent freezes as a glass, the latter probably being due to a ligand substitution reaction at the Fe^{2+} ion.[11,15] Reduced (**1**) has the greatest stability of any synthetic $[2Fe\text{–}2S]^+$ complex we have so far examined, with a concentration dependent half-life of *ca.* 30 min at room temperature and long-term stability at −50 °C. Double integration of the e.s.r. spectrum in comparison to a Cu–ethylenediaminetetra-acetate standard indicates that careful reduction of (**1**) proceeds with nearly quantitative yield (up to 95%). Compounds (**3**) (yield *ca.* 60%) and in particular (**2**) (*ca.* 40%) are considerably less stable on reduction, decaying to only a few percent of their initial concentrations after several minutes at room temperature. Both sometimes show a small (*ca.* 5%) impurity signal with g values *ca.* 2.005, 1.998, and 1.955. A plot of g_y and g_x against $(g_y - g_x)$ for the six sets of g values of (**1**), (**2**), and (**3**) reduced in dmf or *N*mp shows a reasonable correlation according to the analysis of Bertrand and Gayda[16] for $[2Fe\text{–}2S]^+$. The intersection at $g_y = g_x$ is *ca.* 1.887, which is intermediate between the values of 1.94 for $[Fe_2S_2(SR)_4]^{3-}$ species[11,16] and 1.87 for reduced $[Fe_2S_2(OPh)_4]^{2-}$ and the Rieske type proteins.[5,15] Fee *et al.*[1] have suggested two bonding schemes for the co-ordination of the [2Fe–2S] centre in the Rieske protein from *T. thermophilus* by two cysteines and two non-cysteines (X and Y = phenolate, carboxylate, or imidazolate): (A) $(RS)_2Fe_2S_2FeXY$ or (B) $(RS)XFeS_2FeY(RS)$. The model compounds in this report are of type (B) with X = Y = carboxylate. The difference between the $g_y = g_x$ intersection of their g_y and g_x against $(g_y - g_x)$ plot and that of the Rieske type proteins[15] indicates that the latter have co-ordination of type (A) as suggested by their Mössbauer spectra. We are currently investigating ways of reproducing this type of co-ordination synthetically.

Added in proof. Recently reported electron double nuclear resonance and electron spin echo measurements for the Rieske iron–sulphur protein from *T. thermophilus* indicate co-ordination of the $[2Fe\text{–}2S]^+$ centre by one or more nitrogen ligands, probably from the imidazole ring of a histidine amino-acid residue (J. F. Cline, B. M. Hoffman, W. B. Mims, E. LaHaire, D. P. Ballou, and J. A. Fee, *J. Biol. Chem.*, 1985, **260**, 3251). It remains possible that the co-ordination at the Fe^{2+} in this protein also involves an oxygen ligand (phenolate or carboxylate) and that for some of

the [2Fe–2S]$^{+}$ proteins with $g_{av.}$ *ca.* 1.91 the Fe^{2+} ion is terminally co-ordinated solely by oxygen donors.

Received, 22nd April 1985; Com. 525

References

1 J. A. Fee, K. L. Findling, T. Yoshida, R. Hille, G. E. Tarr, D. O. Hearshen, W. R. Dunham, E. P. Day, T. A. Kent, and E. Munck, *J. Biol. Chem.*, 1984, **259**, 124.

2 P. J. Geary, F. Saboowalla, D. Patil, and R. Cammack, *Biochem. J.*, 1984, **217**, 667; P. J. Geary and D. P. E. Dickson, *ibid.*, 1984, **195**, 199; K. Sauber, C. Frohner, G. Rosenberg, J. Eberspacher, and F. Lingens, *Eur. J. Biochem.*, 1977, **74**, 89; H. Twilfer, F-H. Bernhardt, and K. Gersonde, *ibid.*, 1981, **119**, 595; B. L. Trumpower and C. A. Edwards, *J. Biol. Chem.*, 1979, **254**, 8697; S. de Vries, S. P. J. Albracht, and F. J. Leeuwerik, *Biochim. Biophys. Acta*, 1979, **546**, 316; R. Malkin and A. J. Bearden, *ibid.*, 1978, **505**, 147; W. D. Bonner and R. C. Prince. *FEBS Lett.*, 1984, **177**, 47.

3 D. Coucouvanis, A. Salifoglou, M. G. Kanatzidis, A. Simopoulos, and V. Papaefthymiou, *J. Am. Chem. Soc.*, 1984, **106**, 6081.

4 W. E. Cleland and B. A. Averill, *Inorg. Chem.*, 1984, **23**, 4192.

5 P. Beardwood and J. F. Gibson, *J. Chem. Soc., Chem. Commun.*, 1985, 102.

6 I. Pascal and D. S. Tarbell, *J. Am. Chem. Soc.*, 1957, **79**, 6015.

7 Y. Do, E. D. Simhon, and R. H. Holm, *Inorg. Chem.*, 1983, **22**, 3809.

8 J. J. Mayerle, S. E. Denmark, B. V. DePamphilis, J. A. Ibers, and R. H. Holm, *J. Am. Chem. Soc.*, 1975, **97**, 1032.

9 J. G. Reynolds and R. H. Holm, *Inorg. Chem.*, 1980, **19**, 3257.

10 K. S. Hagen, A. D. Watson, and R. H. Holm, *J. Am. Chem. Soc.*, 1983, **105**, 3905.

11 P. Beardwood and J. F. Gibson, *J. Chem. Soc., Dalton Trans.*, 1983, 737.

12 R. W. Johnson and R. H. Holm, *J. Am. Chem. Soc.*, 1978, **100**, 5338.

13 W. O. Gillum, R. B. Frankel, S. Foner, and R. H. Holm, *Inorg. Chem.*, 1976, **15**, 1095.

14 K. Nakamoto, 'Infrared and Raman Spectra of Inorganic and Coordination Compounds,' Wiley, New York, 3rd edn., 1978, p. 232.

15 P. Bertrand, B. Guigliarelli, J. P. Gayda, P. Beardwood, and J. F. Gibson, *Biochim. Biophys. Acta*, submitted for publication.

16 P. Bertrand and J. P. Gayda, *Biochem. Biophys. Acta*, 1979, **579**, 107.