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{2Fe3S} clusters related to the di-iron sub-site of the H-centre of all-iron hydrogenases

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The first synthetic {2Fe3S} clusters structurally related to the sub-site of the H-centre of the all-iron hydrogenases are described: tripodal dithiolate thioether ligands allow the synthesis of di-iron pentacarbonyls with differential (2 : 3) S ligation of the Fe atoms.

X-Ray crystallographic data for Fe-only hydrogenases isolated from *Desulfovibrio desulfuricans*[1] and *Clostridium pasteurianum*[2] together with IR evidence show that the active centre of the enzyme possesses an unprecedented {2Fe3S} sub-site at which CO and CN ligands are bound.[3] The two Fe atoms of the sub-site share two bridging sulfur ligands of a propanedithiolate or related unit[4] with one of the Fe atoms additionally sulfur ligated by a cysteinyl ligand bridged to a {4Fe4S} cluster, Fig. 1(a). Molecules with a {2Fe2S} propanedithiolate core and CO/CN ligation have been synthesised[5] which possess structural elements of the CO inhibited sub-site.[6] We now show that formal backbone modification of the propanedithiolate ligand allows access to carbonyls with a {2Fe3S} core with differential S-ligation of the iron atoms, Fig. 1(b).

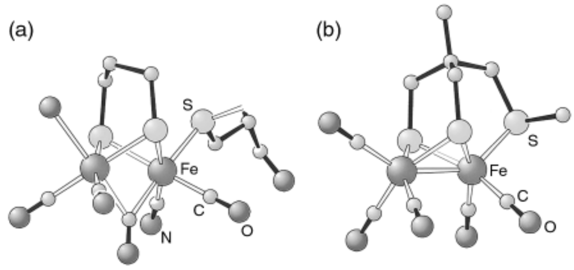
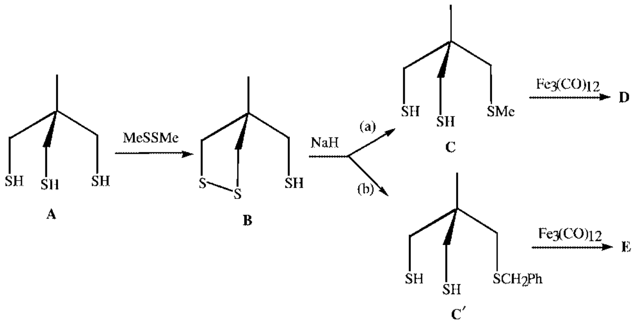


Fig. 1 (a) Proposed structure of the H-centre of Fe-only hydrogenases; this is a composite model combining features reported by Peters (PDB code 1FEH) and Nicolet (code 1HFE). (b) View of a molecule of the product **D**.

Two thiolate sulfur ligands of the tripodal thiolate **A**[7] are readily coupled with dimethyl disulfide with formation of a stable five-membered ring **B**, Scheme 1. This allows chemistry to be carried out on the unprotected thiol group. Reaction with MeI gives the thioether derivative, and subsequent reductive cleavage of the disulfide bond gives the backbone functionalised propanedithiol ligand **C**, Scheme 1.† The ligand reacts with $[Fe_3(CO)_{12}]$ to yield the {2Fe3S}-carbonyl **D** which has been fully characterised by X-ray crystallography, Fig. 1(b), and spectroscopy.‡



Scheme 1 Routes to ligands and complexes. *Reagents*: (a) i, MeI; ii, $LiAlH_4$; iii, H_2SO_4; (b) i, $PhCH_2Br$; ii, $LiAlH_4$; iii, H_2SO_4.

There are two independent molecules (plus their mirror image molecules) in crystals of **D**. The two molecules are essentially identical, and in each, the Fe–Fe distance is short, mean value 2.512(4) Å, indicative of an iron–iron bond. Each iron atom has five other contacts, in a square pyramidal coordination pattern, with the iron atom displaced (mean) 0.382(10) Å from the mean base plane towards the apical carbonyl ligand and 0.322(5) Å towards the thioether S atom. In each molecule, the normals to the square base planes are inclined at (mean) 74.7(6)° and the planes are hinged through the two bridging thiolate sulfur atoms of the S_3 ligands; the Fe–$S_{bridging}$ distances have a mean value of 2.254(1) Å. The third S atom, the thioether S, is coordinated to one of the iron atoms at a similar, mean distance of 2.254(3) Å and occupies the apical coordination site. Two carbonyl ligands occupy the base planes on each iron and one occupies the apical site of the second iron atom. The S_3 ligand thus lies atop the $Fe_2(CO)_5$ unit and is symmetrically arranged (with a pseudo-mirror plane through the iron atoms and the apical groups) except for the thioether methyl group which veers to one side or the other of the mirror plane. Both enantiomers are present in these centrosymmetric crystals.

The structural similarities between the enzyme sub-site and the model compound are evident from Fig. 1. The Fe···Fe bond distance in **D** and the average bridging Fe–S bond lengths are similar to those distances estimated from the protein crystallographic data, which are 2.6 and 2.3 Å, respectively[1,2] but the thioether Fe–S distance in **D** is shorter than the corresponding sub-site Fe–$S_{cysteine}$ distance in the enzyme which is *ca* 2.5 Å.

The benzyl analogue **E** is obtained by straightforward modification of the synthesis, Scheme 1. Its crystal structure, Fig. 2, confirms a conformation very similar to that of **D** with only very minor differences in bond angles and dimensions.‡

We have monitored the reaction of complex **D** with 2 equivalents of cyanide [K^+(18-crown-6) salt; MeCN]. This reveals its conversion within 30 min to a new species **F** which shows two distinct CN stretches, three terminal CO bands and a bridging CO band at 1780 cm^{-1}, Scheme 2. **F** is indefinitely stable in MeCN at 0 °C but on standing for 18 h at RT it slowly transforms to a new species **G** . The IR pattern and frequencies of **G** very closely resemble those of $[Fe_2(CO)_4(CN)_2$-

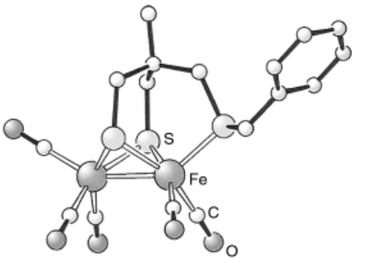


Fig. 2 View of the molecule of the product **E**.

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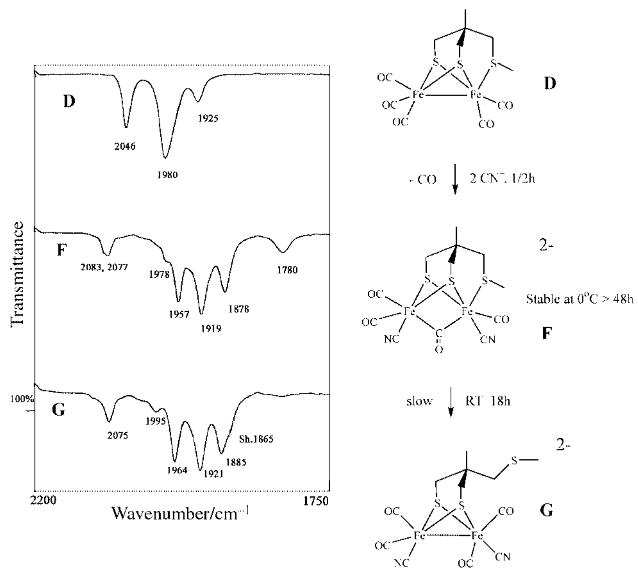

Scheme 2 Solution IR time course for reaction of **D** with cyanide in MeCN and proposed pathway to the species **F** and **G**.

$(SCH_2CH_2S)]^{2-}$,[5] showing a single ν(CN) at 2075 cm^{-1}, Scheme 2. FAB-MS of **G** shows a strong parent ion at 759 for $\{(K^+18\text{-crown-6})[Fe_2(CO)_4(CN)_2\{MeSCH_2C(Me)(CH_2S)_2\}]\}$. These preliminary results are consistent with the initial formation of a CO bridged di-cyanide species **F** which slowly isomerises to the metal–metal bonded terminal carbonyl species **G** with dissociation of the methyl thioether group, Scheme 2. This provides the first tentative evidence for the genesis of a model complex with all the principal structural features of the CO inhibited form of the natural sub-site: two cyanide groups, terminal and bridging CO ligands, and a {2Fe3S} core.§

Finally, we see in the preparation of **E** that a thiolate-*protected* rather than -*blocked* group can been introduced at one of the iron atoms: this or other S-protection/deprotection approaches should open up further chemistry of the synthetic sub-site.

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Notes and references

† *Spectroscopic and analytical* data. $MeC(CH_2S)_2CH_2SH$: ^1H NMR (400 MHz, $C_6D_5CD_3$): δ 0.73 (3H, s, CH_3), 0.89 (1H, t, ^3J 9 Hz, SH), 2.07 (2H, d, ^3J 9 Hz, C*H*$_2$SH), 2.27 [2H, d, ^2J 11.2 Hz, (C*H*HSSC*H*H)], 2.48 [2H, d, ^2J 11.2 Hz, (CH*H*SSCH*H*)]. FTIR (KBr): ν(SH) 2551m, br cm^{-1}. EIMS: *m*/*z* 166 {M}$^+$, 133 {M – SH}$^+$, 119 {M – CH_2SH}$^+$. Microanal.: $C_5H_{10}S_3$, found(calc.): C, 36.48(36.12); H, 6.14(6.06); S, 57.6(57.9)%. Yield 91%.

$MeC(CH_2SH)_2CH_2SMe$: ^1H NMR (400 MHz, CD_2Cl_2): δ 1.03 (3H, s, CH_3), 1.32 (2H, t, ^3J 9 Hz, SH), 2.13 (3H, s, SCH_3), 2.63 (2H, s, C*H*$_2$SCH$_3$), 2.63 [4H, d, ^3J 9 Hz, (HSC*H*$_2$CC*H*$_2$SH)]. EIMS: *m*/*z* 182 {M}$^+$, 101 $\{CH_3C(CH_2)_2CH_2S\}^+$, 87 $\{CH_3C(CH_2)CH_2S\}^+$, 69 $\{CH_3C(CH_2)_3\}^+$, 61 $\{CH_3CCH_2\}^+$, 47 $\{CH_2SH\}^+$. Microanal.: $C_6H_{14}S_3$, found(calc.): C, 39.26(39.56); H, 7.70(7.59); S, 53.0(52.8)%. Yield 55%.

$MeC(CH_2SH)_2CH_2SCH_2Ph$: ^1H NMR (400 MHz, CD_2Cl_2): δ 0.90 (3H, s, CH_3), 1.11 (1H, t, ^3J 9 Hz, SH), 2.46 (2H, s, C*H*$_2$SCH$_2$Ph), 2.47 [4H, d, ^2J 9 Hz, (HSC*H*$_2$CC*H*$_2$SH)], 3.63 (2H, s, SC*H*$_2$Ph), 7.24 (5H, m, SCH$_2$C$_6$*H*$_5$). EIMS: *m*/*z* 258 {M}$^+$, 166$\{CH_3C(CH_2S)_2CH_2SH\}^+$, 133$\{CH_3C(CH_2S)_2CH_2\}^+$, 101$\{CH_3C(CH_2)_2CH_2S\}^+$, 91$\{CH_2Ph\}^+$, 69$\{CH_3C(CH_2)_3\}^+$. Yield 31%.

$[Fe_2(CO)_5\{MeSCH_2C(Me)(CH_2S)_2]$: ^1H NMR (400 MHz, CD_2Cl_2): δ 0.90 (3H, s, CH_3), 1.65 [2H, d, ^2J 14 Hz, (*H*HCCCH*H*)], 2.05 (2H, br, C*H*$_2$SCH$_3$), 2.23 [2H, d, ^2J 14 Hz, (H*H*CCC*H*H)], 2.64 (3H, s, SCH_3). FTIR (in CH_3CN): ν(CO) 1925w, 1979s, br and 2046s cm^{-1}. EIMS: *m*/*z* 432 {M}$^+$, 404{M – CO}$^+$, 376{M – 2CO}$^+$, 348{M – 3CO}$^+$, 320{M – 4CO}$^+$, 292{M – 5CO}$^+$, 180$\{MeC(CH_2S)_2CH_2SMe\}^+$, 176$\{Fe_2S_2\}^+$, 61 $\{CH_3CCH_2\}^+$. Microanal.: $C_{13}H_{12}O_5S_3Fe_2\cdot(0.1C_6H_{14})$ found(calc.): C, 31.60(31.59); H, 3.05(3.04); S, 20.8 (21.8)%. Yield 49% (recrystallised from hexane).

$[Fe_2(CO)_5\{PhCH_2SCH_2C(Me)(CH_2S)_2]$: ^1H NMR (400 MHz, CD_2Cl_2): δ 0.90 (3H, s, CH_3), 1.70 [2H, d, ^2J 14 Hz, (H*H*CCC*H*H)], 1.82 (2H, s, C*H*$_2$SCH$_2$Ph), 2.28 [2H, d, ^2J 14 Hz, (*H*HCCCH*H*)], 4.12 (2H, s, SC*H*$_2$Ph), 7.40 (5H, m, SCH$_2$C$_6$*H*$_5$). FTIR (in CH_3CN): ν(CO) 1925w, 1981s, br, 2046s and 2073vw cm^{-1}. EIMS: *m*/*z* 508 {M}$^+$, 480{M – CO}$^+$, 452{M – 2CO}$^+$, 424{M – 3CO}$^+$, 396{M – 4CO}$^+$, 368{M – 5CO}$^+$, 267$\{Fe_2SSCH_2Ph\}^+$, 231$\{Fe_2SCH_2C(Me)CH_2S\}^+$, 176$\{Fe_2S_2\}^+$, 91$\{CH_2Ph\}^+$. Microanal.: $C_{19}H_{16}O_5S_3Fe_2$, found(calc.): C, 40.26(40.16); H, 3.57(3.15); S, 15.9(18.9)%. Yield 73% (recrystallised from MeCN).

‡ *Crystal structure* analyses. $[Fe_2(CO)_5\{MeSCH_2C(Me)(CH_2S)_2\}]$: *crystal data:* $C_{11}H_{12}Fe_2O_5S_3$, $M = 432.1$, monoclinic, space group $P2_1/n$ (equiv. to no. 14), $a = 18.467(2)$, $b = 10.9622(12)$, $c = 16.906(2)$ Å, $\beta = 105.267(8)°$, $V = 3301.6(6)$ Å^3, $Z = 8$, $D_c = 1.739$ g cm^{-3}, $F(000) = 1744$, $T = 293$ K, μ(Mo-Kα) = 21.5 cm^{-1}, λ(Mo-Kα) = 0.71069 Å.

Deep red, irregular fragment of a diamond-shaped plate crystal, sealed in a capillary. Preliminary photographic examination, then Nonius CAD4 diffractometer. 3528 Unique reflections to $\theta_{max} = 21°$, the limit of measurable intensities; 2614 'observed' with $I > 2\sigma_I$. Corrections for slight deterioration, absorption (semi-empirical ψ-scan methods) and elimination of negative net intensities (Bayesian statistical methods). Structure determination by direct methods in SHELXS[8] (A), refinement by full-matrix least-squares methods, on F^2, in SHELXL[9] (B). Final $wR_2 = 0.061$, $R_1 = 0.046$ (B) for all 3528 reflections weighted $w = \sigma^{-2}(F_o^2)$; for the 'observed' data, $R_1 = 0.028$. Highest difference peaks (*ca.* 0.24 e Å^{-3}) close to a carbonyl ligand.

$[Fe_2(CO)_5\{PhCH_2SCH_2C(Me)(CH_2S)_2\}]$: *crystal data:* $C_{17}H_{16}Fe_2O_5S_3$, $M = 508.2$, triclinic, space group $P\bar{1}$ (no. 2), $a = 9.8755(11)$, $b = 11.3853(13)$, c = 10.3912(13) Å, $\alpha = 110.555(10)$, $\beta = 92.983(9)$, $\gamma = 104.374(9)°$, $V = 1047.2(2)$ Å^3, $Z = 2$, $D_c = 1.612$ g cm^{-3}, $F(000) = 516$, $T = 293(1)$ K, μ(Mo-Kα) = 17.1 cm^{-1}, λ(Mo-Kα) = 0.71069 Å.

Very thin, red-brown plate mounted on a glass fibre. Similar diffractometer procedure and processing, giving 3686 unique reflections to $\theta_{max} = 25°$ (2715 'observed' with $I > 2\sigma_I$). No deterioration correction necessary. Final $wR_2 = 0.105$ and $R_1 = 0.053$ (B) for all 3686 reflections weighted $w = [\sigma^2(F_o^2) + (0.0579P)^2]^{-1}$, with $P = (F_o^2 + 2F_c^2)/3$; for the 'observed' data only, $R_1 = 0.037$. Highest difference peaks (to *ca.* 0.4 e Å^{-3}) all in the cluster core region.

CCDC 156989 and 161064. See http://www.rsc.org/suppdata/cc/b1/b102244j/ for crystallographic data in .cif or other electronic format.

§ Well-resolved IR data for the *oxidised* CO inhibited H-centre have been reported recently by De Lacey *et al.*[10] giving: ν(CN) at 2096 and 2089 cm^{-1}; ν(CO$_{terminal}$) at 2016, 1972 and 1963 cm^{-1}; and ν(CO$_{bridging}$) at 1811 cm^{-1}. In this paramagnetic state the di-iron sub-site is magnetically described as a localised mixed-valence state, though critically whether Fe^{II}–Fe^{III} or Fe^{I}–Fe^{II} was undecided.[11] The data we have at hand for the Fe^{I}–Fe^{I} species **F** show: ν(CN) at 2083 and 2077 cm^{-1}; ν(CO$_{terminal}$) at 1957, 1919 and 1878 cm^{-1}; and ν(CO$_{bridging}$) at 1780 cm^{-1}. Thus Δν(CO$_{terminal}$) corresponds to 59, 53 and 85 cm^{-1} respectively with Δν(CO$_{bridge}$) = 31 cm^{-1}. These magnitudes are consistent with the oxidised CO-form of the sub-site having the Fe^{I}–Fe^{II} configuration (*i.e.* it is one-electron oxidised with respect to **F**) and lends support to the deduction of De Lacey *et al.* that proximal iron atom is in the Fe ^{II} state {Δν(CO) = 85 cm^{-1}} with the less perturbed distal iron atom {Δν(CO) = 59, 53 cm^{-1}} in the Fe^{I} state.

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