First insights into the protonation of dissymetrically disubstituted di-iron azadithiolate models of the [FeFe]H_2ases active site†

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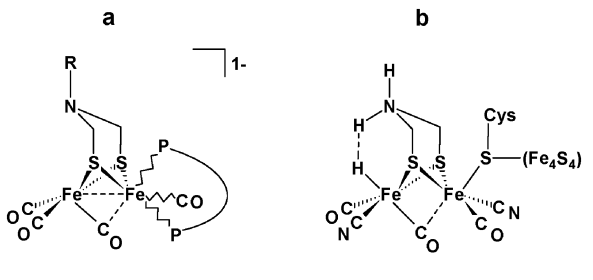
Dissymetrically disubstituted di-iron azadithiolate complexes [$Fe_2(CO)_4(\kappa^2$-LL){μ-$SCH_2N(^iPr)CH_2S$}] (LL = dppe, phen) protonate exclusively at the N atom of the bridge, like the hexacarbonyl precursor but in contrast to symmetrically disubstituted analogues; substitution of dppe for two CO groups noticeably increases the kinetics of the electrocatalytic proton reduction process.

Efforts of synthetic chemists to design model compounds that would reproduce some of the key features of the H cluster, the organometallic active site of the iron-only hydrogenase enzymes ([FeFe]H_2ase)[1,2] led to a variety of complexes, built on {2Fe2S} or {2Fe3S} frameworks.[3] However, while the pyramids enclosing the iron atoms are eclipsed in the model complexes, they are inverted in the H cluster, in which this thermodynamically less favourable arrangement[4] is stabilised by the surrounding protein.[5] DFT calculations recently indicated that the introduction of electron-donor ligands at a single Fe site should favour the "rotated" geometry.[4,6] This led us[7–9] and others[6,10–14] to investigate the synthesis and the reactivity of asymmetrically-disubstituted diiron dithiolate complexes. We recently reported that the protonation of [$Fe_2(CO)_4(\kappa^2$-dppe)(μ-pdt)] [dppe = $Ph_2P(CH_2)_2PPh_2$; pdt = $S(CH_2)_3S$] proceeds *via* the transient formation of terminal hydride ligands.[8] We also showed that the electrochemical reduction of [$Fe_2(CO)_4(\kappa^2$-dppe)(μ-pdt)] and of its azadithiolate-bridged analogues gives rise to an electron-transfer catalysed rearrangement to the symmetrical isomer, whose mechanism might involve an anionic intermediate with a rotated geometry (Scheme 1a).[15] Taken together, these results suggested that the reduction of [$Fe_2(CO)_4(\kappa^2$-dppe)-{μ-$SCH_2N(R)CH_2S$}] in the presence of acid may bring a situation allowing a proton–hydride interaction that would be similar to that postulated to occur at the H cluster (Scheme 1b).[16]

We therefore undertook to investigate the reactivity of the asymmetric [$Fe_2(CO)_4(\kappa^2$-dppe){μ-$SCH_2N(^iPr)CH_2S$}] and [$Fe_2(CO)_4(\kappa^2$-phen){μ-$SCH_2N(^iPr)CH_2S$}] complexes **1** and **2** (phen = 1,10-phenanthroline) with protons in order to assess whether this would produce a species with a protonated N bridgehead atom and a terminal hydride. The finding that **1** behaves differently from the pdt analogue in acidic medium and catalyses the reduction of protons at a relatively mild potential prompted us to present our results in a preliminary form.

The chelated compounds **1** and **2** were prepared from the hexacarbonyl precursor [$Fe_2(CO)_6$){μ-$SCH_2N(^iPr)CH_2S$}] according to well known procedures.[9,15] The synthesis and spectroscopic data of the novel phenanthroline complex **2** are reported in the ESI.† The ν(CO) absorptions of **2** (2008, 1938 and 1895 cm^{-1}) in dichloromethane are very close to those observed for the pdt analogue,[9] suggesting that the iron centres might be possible sites of protonation as it has been observed in the pdt series.[7–9] The structure of **2** was confirmed by an X-ray analysis of a single crystal obtained from a hexane–dichloromethane solution (Fig. 1) and this reveals a basal–basal coordination of the phenanthroline to one iron atom.‡

IR monitoring of the protonation of **1** in the presence of three equiv. of $HBF_4{\cdot}Et_2O$ in CH_2Cl_2 at 298 K revealed the quick replacement of the carbonyl bands of the starting material by three new absorptions at 2039(s), 1976(s) and 1929(sh) cm^{-1} assigned to a protonated species. These bands are shifted by *ca.* 20 cm^{-1} to a higher energy relative to those of **1**, consistent with a N-protonation.[17] Attempts to isolate the protonated product were unsuccessful. Further protonation experiments at low temperature were monitored by ^1H



R = ^{i}Pr, P⌒P = $Ph_2P(CH_2)_2PPh_2$

Scheme 1

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† Electronic supplementary information (ESI) available: Experimental details, spectroscopic data of **2**, acid-dependence of the reduction current for **1** and crystallographic data in CIF or other electronic format (CCDC 675690). See DOI: 10.1039/b801373j

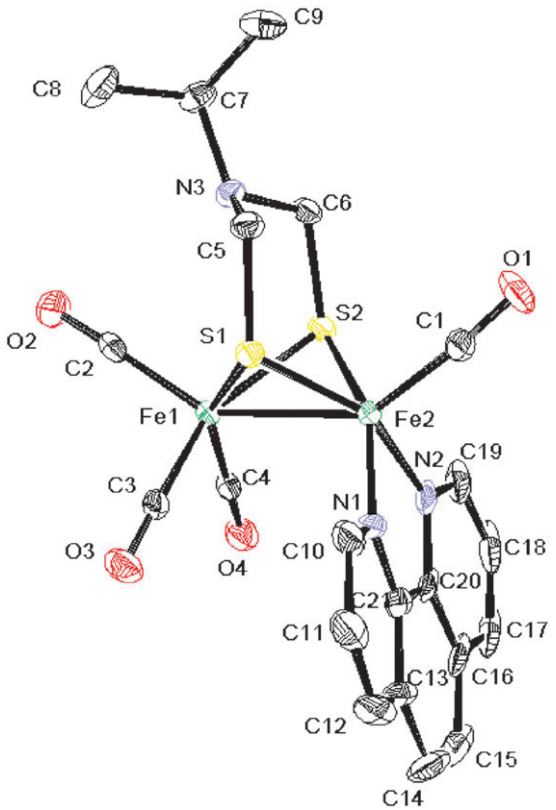

Fig. 1 Ortep view (ellipsoids at 30% of probability level) of $[Fe_2(CO)_4(\kappa^2\text{-phen})\{\mu\text{-SCH}_2\text{N}(^i\text{Pr})\text{CH}_2\text{S}\}]$ (**2**). Selected bond lengths (Å) and angles (°): Fe(1)–Fe(2), 2.5354(8); Fe(2)–N(1), 1.989(3); Fe(2)–N(2), 1.983(3); Fe(1)–S(1), 2.2582(11); Fe(2)–S(1), 2.2084(11); Fe(1)–S(2), 2.2667(10); Fe(2)–S(2), 2.2087(11); Fe(1)–S(1)–Fe(2), 69.16(3); Fe(1)–S(2)–Fe(2), 69.00(3); N(1)–Fe(2)–N(2), 81.79(16).

and ^{31}P NMR spectroscopy. Treatment of **1** with three equiv. of $HBF_4{\cdot}Et_2O$ in a CD_2Cl_2 solution at 183 K did not result in any signal that would be typical of a terminal hydride. It is worth noting that under the same reaction conditions, the slow protonation of $[Fe_2(CO)_4(\kappa^2\text{-dppe})(\mu\text{-pdt})]$ afforded terminal hydride intermediates.[8] ^{31}P-{^{1}H} NMR spectroscopy revealed the presence of two new signals at 94.6 and 87.7 ppm, indicating complete transformation of the starting material.[15] A two-dimensional ^{31}P–^{31}P NMR spectrum showed that these two signals correlate, indicating that they have to be assigned to a single product having a dppe ligand in a basal–apical position (Fig. a, ESI†).[18] Treatment of **2** with five equiv. of $HBF_4{\cdot}Et_2O$ in acetone gave results similar to those obtained for **1**, with carbonyl bands at 2024, 1956, 1930 cm^{-1} suggesting N-protonation. ^{1}H NMR spectrum of an acidic solution of **2** at 298 K or at 188 K revealed the formation of a new product existing as two isomers in a 7 : 3 ratio (see Table 1, ESI†).[20] No signal that could be assigned to a terminal or bridging hydride was observable. Thus, although the formation of metal hydrides previously indicated that the ligand set provides enough basicity for the Fe–Fe site of the pdt analogues of **1** and **2** to undergo protonation, complexes **1** and **2** protonate at the N atom of the bridge and we obtained no evidence of a subsequent proton transfer from the azadithiolate bridge to the metal site, nor a second protonation occurring at the metal

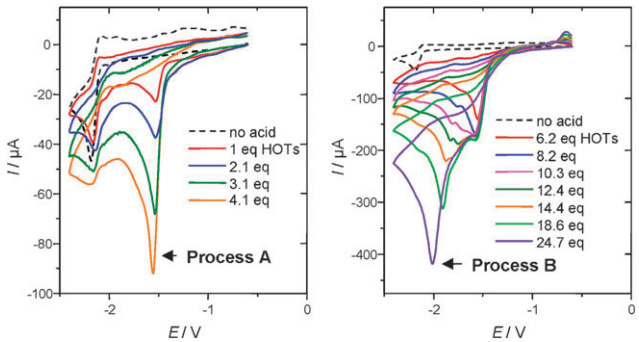

Fig. 2 Cyclic voltammetry of $[Fe_2(CO)_4(\kappa^2\text{-dppe})\{\mu\text{-SCH}_2\text{N}(^i\text{Pr})\text{CH}_2\text{S}\}]$ (**1**) (1 mM) in the absence and in the presence of HOTs (MeCN–$[NBu_4][PF_6]$; vitreous carbon electrode, v = 0.2 V s^{-1}; potentials are in V *vs.* Fc^+/Fc).

centre, which contrasts with the reactions reported for symmetrically PMe_3-disubstituted azadithiolate species.[21–23]

Nevertheless, even though the chelating ligation of dppe or 1,10-phenanthroline does not induce a proton–hydride interaction (Scheme 1b) nor protonation at the metal site at the Fe^IFe^I level, this might arise upon reduction of the N-protonated cation in the presence of an excess of acid. The positive shift of the reduction peak from *ca.* −2.0 V to −1.53 V (*vs.* Fc^+/Fc) upon addition of the first equivalent of HOTs to a MeCN–$[NBu_4][PF_6]$ solution of **1** (Fig. 2) is entirely consistent with protonation occurring at the nitrogen atom of the bridge as shown by the NMR and FTIR experiments. Note that the reduction of the symmetrically disubstituted analogues, $[Fe_2(CO)_4(PMe_3)_2\{\mu\text{-SCH}_2\text{NH(R)CH}_2\text{S}\}]^+$, is observed at a similar potential (R = CH_2Ph, E_p^{red} = −1.55 V;[21] R = $CH_2C_6H_4$-2-Br, E_p^{red} = −1.49 V[22]). Further additions of acid to **1** led to a linear increase of the reduction current at −1.53 V, indicative of proton reduction catalysis at this potential (Fig. 2, Process A).

The current of process A levels off after 8–10 equiv. HOTs have been added and a second acid-dependent reduction is then observed (Fig. 2, Process B). These features are qualitatively similar to those observed for the hexacarbonyl precursor of **1**, $[Fe_2(CO)_6\{\mu\text{-SCH}_2\text{N}(^i\text{Pr})\text{CH}_2\text{S}\}]$.[24] The fact that both complexes protonate only at the N atom at the Fe^IFe^I level suggests that the mechanisms of process A may be analogous for **1** and for $[Fe_2(CO)_6\{\mu\text{-SCH}_2\text{N}(^i\text{Pr})\text{CH}_2\text{S}\}]$. This provides the opportunity of assessing the effect of the dissymetric disubstitution on the characteristics of proton reduction catalysed by azadithiolate-bridged complexes. As expected, the reduction potential of the N-protonated derivative is negatively shifted (0.31 V, *ca.* 30 kJ mol^{-1}) upon substitution of dppe for two CO ligands at a single iron centre. However, for similar concentrations of **1** and of $[Fe_2(CO)_6\{\mu\text{-SCH}_2\text{N}(^i\text{Pr})\text{CH}_2\text{S}\}]$, the plateau reduction current for process A is about twice larger for the dppe complex than for its hexacarbonyl parent when HOTs is present in excess (Fig. b, ESI†). This indicates faster kinetics in the case of **1**. While the substitution enhances the basicity[23] of **1** compared to $[Fe_2(CO)_6\{\mu\text{-SCH}_2\text{N}(^i\text{Pr})\text{CH}_2\text{S}\}]$, which increases the thermodynamic driving force of the protonation steps, it may also affect the rate of H_2 elimination from the $\{2H^+/2e^-\}$ reduced

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species that was proposed to be limiting for $[Fe_2(CO)_6\{\mu\text{-}SCH_2N(^iPr)CH_2S\}]$ when the acid was present in excess.[24] If this reaction is also the rate limiting step of process A in the case of **1**, the increase by a factor 2 of the plateau current for **1** with respect to $[Fe_2(CO)_6\{\mu\text{-}SCH_2N(^iPr)CH_2S\}]$ would indicate that catalysis is about 4 times faster for the disubstituted complex **1** than for the hexacarbonyl parent.[25] Whether this kinetic gain arises from structural factors, that is a more favourable $H^+\cdots H^-$ disposition such as that in Scheme 1b, or from a better match of the pK_a of the dihydrogen ligand and of the protonated site in the $\{2H^+/2e^-\}$ reduced species is presently not known.

Further studies aimed at clarifying the mechanisms of protonation and of electrocatalytic proton reduction by complex **1** and by its symmetric isomer are in progress in our laboratory.

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Notes and references

‡ Crystal data for **2**: $C_{21}H_{19}Fe_2N_3O_4S_2$. M 553.21, triclinic, $P\bar{1}$, a = 9.4906(13), b = 10.2311(15), c = 12.8702(19) Å, α = 67.315(7), β = 89.583(8), γ = 73.043(8)°, Z = 2, V = 1095.0(3) Å^3; ρ_{cal} = 1.678 g cm^{-3}; μ(Mo-K$_\alpha$) = 1.55 mm^{-1}; λ = 0.71073 Å, T = 100(2) K. 16375 reflections measured, 4963 unique (R_{int} = 0.0513) used in refinement. $R1$ [4198 with $I > 2\sigma(I)$] = 0.0513, w$R2$ (all data) = 0.1096.[26]

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