Dynamic ligation at the first amine-coordinated iron hydrogenase active site mimic†

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Received (in Cambridge, UK) 14th June 2006, Accepted 2nd August 2006
First published as an Advance Article on the web 24th August 2006
DOI: 10.1039/b608260b

The first model of the iron hydrogenase active site has been prepared in which an amine ligand is loosely coordinated to an Fe^{I} centre, and can be replaced by a solvent molecule; irrespective of the ligand set, the one electron reduction of both complexes is chemically reversible and is shown to proceed through the same species which features a bridging CO ligand.

Fe-only hydrogenases (Fe H_2ase) are a naturally occurring class of metalloenzymes which catalyze the reversible reduction of protons to molecular hydrogen.[1] Their active site consists of a $[Fe_4S_4]$ cluster which is linked to an unusual diiron subsite by a cysteine residue.[2,3] The diiron unit is decorated by carbon monoxide and cyanide ligands, and by a non-proteic dithiolate which tethers the two low-valent iron centres. In the X-ray crystallographic analysis of the Fe H_2ases, one of the CO ligands was found in a bridging position between the two iron centres. Furthermore, structural biology suggests a loosely bound ligand in the coordination sphere of the distal iron Fe^{d} (denoted as L in Chart 1). It is here where molecular hydrogen can coordinate during the oxidation event,[4] and where a proton can oxidatively add in the initial step of the reduction process.[5] The site unoccupied by a permanent ligand is thus of crucial importance for the activity of the enzyme. In fact, it has been shown that exogenous carbon monoxide occupies this coordination site and inhibits the hydrogen evolution activity.[6–8]

Although the structural models of the Fe H_2ase active site have matured considerably over recent years,[9–11] little attention has been devoted to the role of the dynamic coordination at Fe^{d}.[12] This may however be not too surprising, since synthetic diiron complexes of type $[(\mu\text{-pdt})Fe_2(CO)_5(L)]$ (L = ligand, pdt = propyldithiolate) with loosely bound ligands are difficult to isolate and inherently unstable.[13] Apart from trimethylamine oxide which is a well-established reagent to remove carbon monoxide ligands,[14] we have recently found that primary amines such as *n*-propylamine exhibit a similar decarbonylation behaviour and facilitate ligand substitution reactions on Fe H_2ase active site model complexes.[15] We have now isolated and characterized $[(\mu\text{-pdt})Fe_2(CO)_5(H_2NPr)]$ **1** (Chart 1b), studied the liberation of a coordination site by IR spectroscopy and electrochemistry, and investigated the structural changes of the complex upon electrochemical reduction.

Confirming our previous observations, tlc analysis of a solution of $[(\mu\text{-pdt})Fe_2(CO)_6]$[16] in *n*-propylamine indicated complete consumption of the starting material and the appearance of a defined new product after a few hours of heating to reflux. We were delighted to find that the product possesses a remarkable stability in non-coordinating solvents such as pentane or toluene, and can be isolated and purified by column chromatography and recrystallization. The composition of the amine-coordinated $[(\mu\text{-pdt})Fe_2(CO)_5(H_2NPr)]$ (**1**) could be unambiguously established by single crystal X-ray analysis which showed that the *n*-propylamine coordinates to one iron centre at a basal position.†‡

Whereas the IR spectrum of complex **1** in non-coordinating solvents remains unchanged over time, the appearance of a new spectrum can be observed when the same experiment is conducted in CH_3CN. Complex **1** is consumed entirely and a defined product **2** is formed that is characterized by an IR spectrum similar in shape to that of **1**, however shifted towards higher energy (Fig. 1).

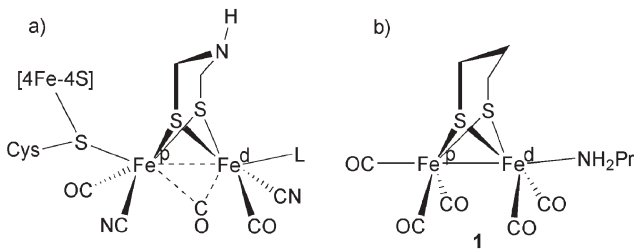

Chart 1

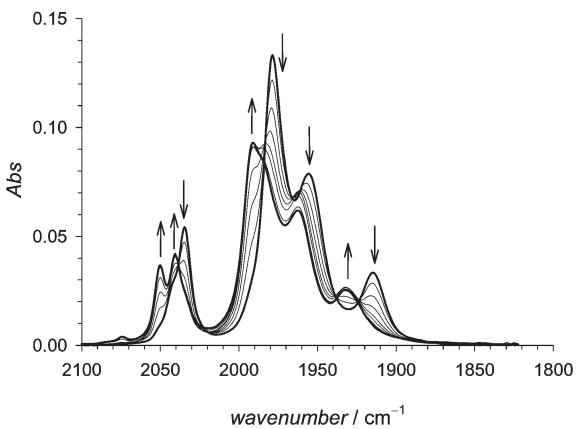

Fig. 1 Reversible transformation of $[(\mu\text{-pdt})Fe_2(CO)_5(H_2NPr)]$ (**1**), dissolved in acetonitrile, into $[(\mu\text{-pdt})Fe_2(CO)_5(NCCH_3)]$ (**2**). Shown are the spectral changes in the carbonyl region of the IR spectrum.

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† Electronic supplementary information (ESI) available: X-ray crystal structure of complex **1**. See DOI: 10.1039/b608260b

Expecting a certain lability of the amine ligand, we suspected that a solvent molecule may replace the propylamine in the coordination sphere of **1**. This notion is further supported by the fact that complex **1** can be quantitatively recovered by treatment of **2** with excess *n*-propylamine, as evidenced by the fully restored IR spectrum of complex **1**. A similar ligand substitution of a carbon monoxide ligand by CH_3CN has recently been reported for diferrous phosphane thiolates.[12]

The cyclic voltammogram of **2**[17,18] shows a reduction at E_{pc} = −1.68 V *vs.* $Fc^{+/0}$ (Fig. 2b) in the same region as that of the hexacarbonyl analogue [(μ-pdt)$Fe_2(CO)_6$] (E_{pc} = −1.67 V).[19] On the reverse scan, the voltammogram of complex **2** features one defined wave that can be associated with the oxidation of the product generated upon reduction of **2**. Remarkably, multiple scans do not show any detectable degradation, pointing towards a chemical reversibility of the electrochemically triggered processes on the typical voltammetry timescale (~10 s). The reduction of complex **1** (Fig. 2a), obtained from **2** by the addition of excess *n*-propylamine,[18] proceeds at E_{pc} = −1.80 V, and is thereby shifted by 120 mV compared to that of the CH_3CN substituted analogue **2**. This shift can be rationalized by the better π-acceptor capacity of the acetonitrile ligand, rendering the amine the stronger overall donor. Controlled potential electrolysis of complexes **1** and **2** clearly shows that both reductions are one electron processes. Even on the timescale of these experiments (*ca.* 10 min), 60–70% of the starting material can be recovered after re-oxidation. Similar to the oxidation behaviour of reduced **2**, the re-oxidation of reduced **1** is characterized by one defined wave and no degradation can be detected even after a number of scans. Moreover, the re-oxidation of both reduced forms occurs at the same potential at E_{pa} = −1.28 V, suggesting that the species formed after reduction of **1** is identical to that formed after reduction of **2**.

Further proof of this hypothesis as well as structural information on the reduced species was sought from FTIR-spectroelectrochemistry. The starting spectrum and the end spectrum after the electrochemical reduction of complexes **1** and **2** at −1.98 V and −1.78 V, respectively, are shown in Fig. 3. From an inspection of the end spectra, it is clear that the same species $\mathbf{3}^-$ is formed after electrochemical reduction, irrespective of the ligand set at the start

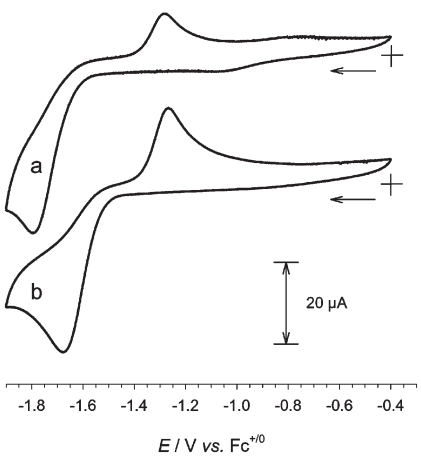


Fig. 2 Cyclic voltammogram (100 mV/s) of a 2 mM solution of complex **1** (a, obtained in the presence of excess *n*-propylamine) and **2** (b) in CH_3CN, containing 0.1 M $(Bu)_4NPF_6$.

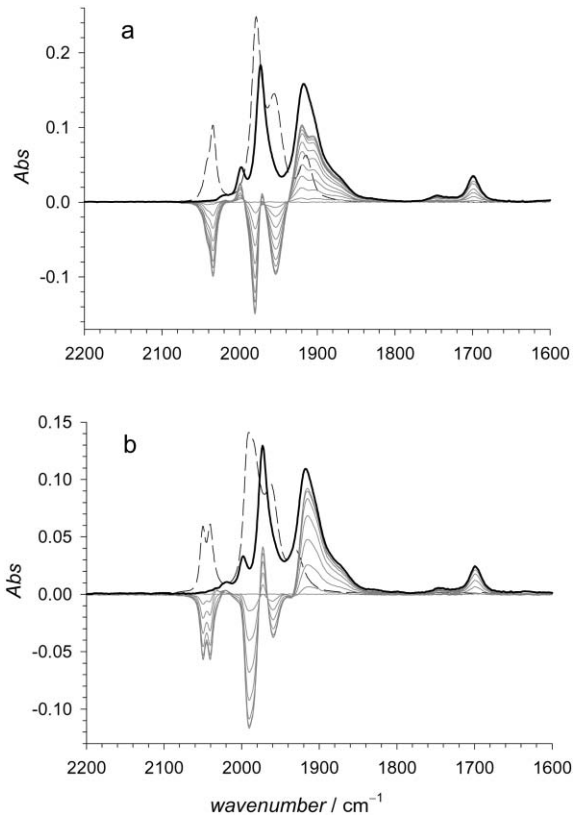
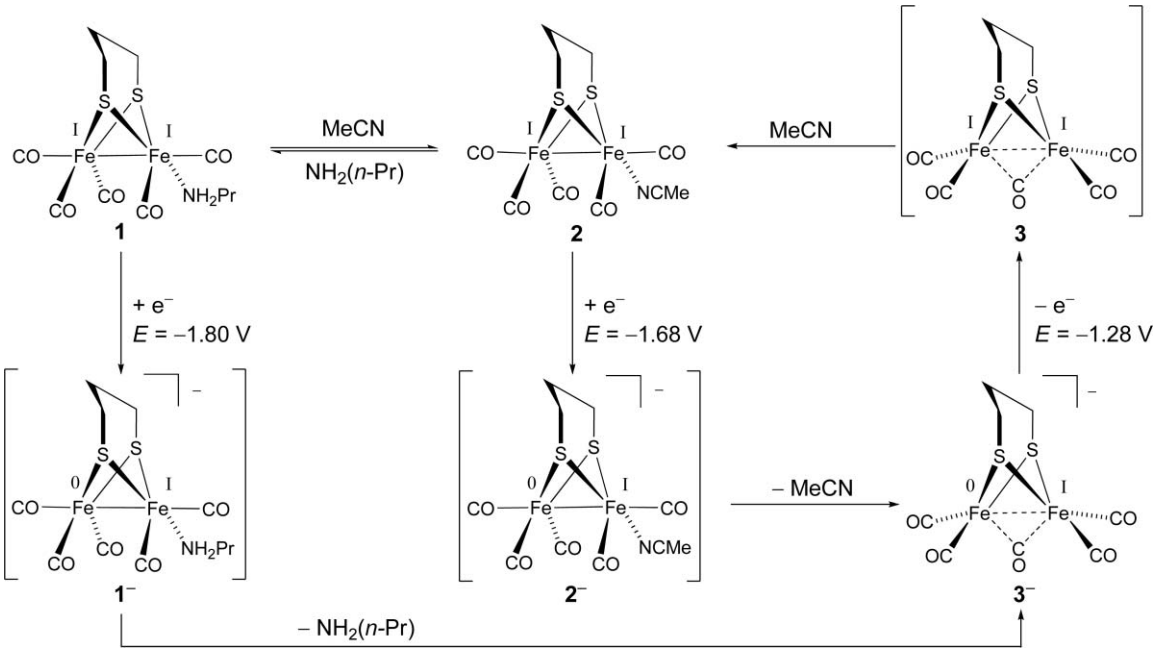


Fig. 3 IR spectrum of complex **1** (a) and **2** (b) before (dashed line) and after (solid line) the electrochemical reduction at −1.98 and −1.78 V, respectively. Grey traces are difference spectra recorded during the course of the electrolysis.

of the experiment (Scheme 1). Both reductions produce a species that is characterized mainly by two strong absorptions at 1973 cm^{-1} and 1917 cm^{-1} and a weaker band at 1699 cm^{-1}. Whereas the latter absorption is characteristic of a carbon monoxide ligand bridging the two iron centres, the concrete number of ligands at $\mathbf{3}^-$ cannot be deduced from the IR spectrum alone. It can, however, be anticipated that a change in the coordination sphere is responsible for the large separation of peak potentials of 520 mV and 400 mV between the reduction potential of **1** and **2** and the oxidation potential of $\mathbf{3}^-$, respectively. Since the oxidation of $\mathbf{3}^-$ proceeds at much milder potential than the reductions of **1** or **2**, species $\mathbf{3}^-$ is presumably ligated by fewer electron donating ligands. Taking the chemical reversibility of the reductions into consideration, we propose that all five carbon monoxide ligands remain at the diiron site and that the weakly coordinated amine in **1**, and CH_3CN in **2**, are expelled in order to stabilize the lower oxidation state in $\mathbf{3}^-$. This interpretation is consistent with recent findings that [(μ-pdt)$Fe_2(CO)_6$], which does not contain a loosely bound ligand, is forced to stabilize its lower oxidation states by irreversible structural changes.[20] Closing the cycle proposed in Scheme 1, re-oxidation of $\mathbf{3}^-$ results in the formation of intermediate **3** which quickly rearranges and saturates its coordination sphere by the addition of the respective ligand to form **1** or **2**.

In summary, we have synthesized and characterized the first amine-coordinated iron hydrogenase active site model complex.



Scheme 1 (Electro)chemical transformations of complex **1**.

Owing to the low binding strength of the amine, we gained access to a new ligand motif that can mimic the function of the flexible coordination site in the H_2ase enzyme. Complex **1** is therefore not only a useful synthon for future structural modelling challenges, it will also enable us to study the effect of water and H-derived ligands in future functional studies. Furthermore, the ligand flexibility allows the stabilisation of the mixed valence complex $\mathbf{3}^-$ after electrochemical reduction, the EPR spectroscopic investigations of which will be of relevance to the natural system. In the context of our long-standing goal to drive the reduction of protons photochemically,[21] the IR and EPR spectral signatures of the reduced diiron complex $\mathbf{3}^-$ are valuable references with which we can compare the data we will obtain in our photochemical experiments.

We wish to thank Dr Lars Eriksson for the acquisition of the X-ray data. Financial support for this work was provided by the Swedish Energy Agency, the Swedish Research Council and NEST-STRP: SOLAR-H (EU contr. nr. 516510).

Notes and references

‡ **[(μ-pdt)Fe_2(CO)$_5$($H_2NCH_2CH_2CH_3$)] (1)**. [(μ-pdt)Fe_2(CO)$_6$] (357 mg, 0.925 mmol) was dissolved in 17 ml *n*-propylamine under nitrogen atmosphere. After 6 h of refluxing, the solvent was removed *in vacuo*. Purification by column chromatography (pentane/toluene, 60/40) (165 mg, 43%). Single crystals suitable for X-ray analysis were obtained from hexane solutions. Anal. calculated for $C_{11}H_{15}Fe_2NO_5S_2$: C, 31.68; H, 3.63; N, 3.36. Found: C, 31.49; H, 3.57; N, 3.25%. IR (THF, cm^{-1}): ν_{CO} = 1980, 1943, 1907, 1892 (sh). Crystallographic data of **1**: Monoclinic, a = 11.279(1) Å, b = 13.631(1) Å, c = 12.135(1) Å, β = 113.86(1)°, V = 1706.4(3) $Å^3$, T = 291(2) K, $P2_1/a$, Z = 4, μ = 1.960 mm^{-1}, $N_{measured}$ = 28673, $N_{unique,\ all\ data}$ = 5528, $N_{unique,\ (I \geqslant 2\sigma(I))}$ = 3597, R_{int} = 0.0619, $wR2$ = 0.1455 (all data), $R1$ = 0.0492 ($I \geqslant 2\sigma(I)$). CCDC 612633. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b608260b

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