Second coordination sphere effects in [FeFe]-Hydrogenase mimics

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Proton relay effect in pyridyl appended hydrogenase mimics
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Introduction

Hydrogenases are metalloenzymes that perform the reversible proton reduction reaction at very high rates with overpotentials close to the thermodynamic limit. Among the three classes of hydrogenases known, those containing a di-iron active site are definitely the fastest enzymes. In recent years this class of enzymes gained lot of interest, also in the context of renewable energy and carbon neutral economy. It is not difficult to envision devices, such as fuel cells or electrolyzers, based on components inspired by nature.

The active site of the enzyme, the H-cluster, is embedded in a dense protein matrix that provides stability, substrate preorganization and geometrical preorganization, which forces the active site in the so-called rotated structure. Two cofactors are essential for the high operational rates of the enzyme; i) the Fe₄S₄ cluster bounded to the distal iron, responsible for shuttling electrons into the iron-iron core and ii) the azadithiolate cofactor, which acts as proton relay and thereby preorganizes the substrates (i.e. protons). The two cofactors are believed to work in synergy through proton coupled electron transfer steps (PCET). In stark contrast herewith, current synthetic ‘artificial’ model systems lack the protein environment and only a handful of reports describe efforts to combine the two cofactors mentioned. Most of the mimics are of the hexacarbonyl type due to their relative ease of preparation. Drawback is the generation of low-polarity complexes for which the electrochemistry can only be studied in organic solvents. Electrochemistry studies in aqueous media with di-iron-based models are scarce and usually hampered by insolubility of the complexes. Some relevant electrochemical data in water have been obtained using water-soluble complexes by functionalization of the ligands with appropriate groups such as sulfonates or by using water-soluble phosphine ligands such as PTA. However, analytical difficulties due to poor solubility, low activity and high overpotentials hampered detailed studies.

Recently our group reported an iron-iron model featuring a benzenedithiolate bridge and a phosphole ligand bearing two pyridine substituents. It has been shown that this particular ligand acts as an electron reservoir that actively partakes in the reduction of protons. The pyridyl ligands were also found to efficiently act as proton relays, allowing for a PCET step. The proposed proton reduction mechanism for this complex is shown in Figure 1. Furthermore, the presence of the pyridyl groups allowed for the dissolution of the complex in diluted acidic solutions, giving access to the study of this complex in aqueous media.
In this work, we set out to elucidate the role of proton-responsive ligands by decoupling this function from the redox-active properties of the dipyridylphosphole ligand, both in organic solvents and in acidic aqueous media. To this end we install trispyridylphosphine ligands onto synthetic iron-iron hydrogenase models featuring benzenedithiolate bridges. In order to overcome the loss of the redox-activity of the ligand, the electronic properties of the catalysts are tuned by i) modification of the benzenedithiolate bridge, ii) increasing the number of trispyridylphosphine ligands and iii) protonation of the pyridyl ligands. It is shown that in dichloromethane solution the mono-phosphine complexes do not display proton coupled electron transfer steps and their catalytic rates are about two orders of magnitude slower than the redox-active phosphole derivative; interestingly they operate at milder overpotentials. The positive effect of the proton-responsive trispyridylphosphine ligands becomes evident when the complexes are measured in diluted sulfuric acid solution. Pyridyl protonation counterbalances the electron-donating properties of the phosphines and preorganizes protons around the di-iron center, allowing for unprecedented proton reduction rates that reach values up to $10^8 \text{M}^{-1}\text{s}^{-1}$, far beyond the enzymatic rates.

**Figure 1.** Proposed mechanism of proton reduction by the dipyridylphosphole substituted benzenedithiolate di-iron complex in dichloromethane.\(^9\)
Strategy

In order to decouple the proton-responsive properties of the dipyridylphosphole ligand from its redox-active nature, the redox-innocent proton-responsive trispyridylphosphine was chosen as ligand for this study.

The electronic properties of the complexes are controlled in three ways, Scheme 1:

1. by modification of the electron withdrawing character of the benzenedithiolate bridge
2. by the number of trispyridylphosphine ligands connected to the di-iron core
3. by protonation of the pyridyl ligands

Scheme 1. Overview of the strategy and complexes that will be described.
A more electron-withdrawing bridge should decrease the electron density at the di-iron core while a higher number of phosphine ligands (acting as σ-donors and π-acceptors) should have the opposite effect. Aside from the structural modification of the complexes, protonation of the pyridyl moieties is potentially an extra handle to influence the overall electron density of the di-iron core. Furthermore, protonation of the pyridyl ligands should render the complexes soluble in acidic aqueous solutions allowing the study of proton reduction in aqueous media. Comparison of proton reduction in organic solvents, where the pyridyl ligands are in their unprotonated state, to similar studies in aqueous acidic media, with the pyridyl units being inherently protonated, could reveal the role of the proton-responsive ligand.

First the synthesis, characterization and analytical data of the complexes will be presented. Electrochemical analysis in dichloromethane in the absence of acid will elucidate the main redox behavior of the complexes. The subsequent section describes the electrochemical experiments aimed at understanding the follow-up reactivity of the complexes upon the first electron transfer. Lastly, the catalytic behavior of the complexes is described, starting with experiments performed in dichloromethane in the presence of weak acid followed by their behavior upon addition of stoichiometric amounts of strong acid and concluding with catalytic studies in acidic aqueous media.
Results and discussion

Synthesis and characterization

Tetrachlorobenzenedithiol\textsuperscript{18,19} and tetrafluorobenzenedithiol\textsuperscript{20} were prepared according to modified literature procedures. The di-iron dithiolate hexacarbonyl complexes 1-3 were prepared by reaction of the corresponding substituted benzenedithiol with the iron precursor Fe\textsubscript{3}(CO)\textsubscript{12} in hot toluene solution.

Complexes 1 and 2 have been reported and extensively characterized before.\textsuperscript{21,22} The novel compound 3 has been characterized thoroughly by NMR and FT-IR spectroscopy, HR-mass spectrometry, cyclic voltammetry and X-ray crystallography. Its solid state molecular structure is shown in Figure 2, the relevant analytical data for complexes 1-3 are shown in Table 1 while their IR spectra are shown in the appendix section.

![Figure 2. X-ray crystal structure of Fe\textsubscript{2}(F\textsubscript{4}bdt)(CO)\textsubscript{6} 3. Ellipsoids are set at 50% probability.](image-url)
Table 1. Analytical data for complexes 1-3.

<table>
<thead>
<tr>
<th></th>
<th>Fe$_2$(bdt)(CO)$_6$</th>
<th>Fe$_2$(Cl$_4$bdt)(CO)$_6$</th>
<th>Fe$_2$(F$_4$bdt)(CO)$_6$</th>
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</thead>
<tbody>
<tr>
<td><strong>Distances (Å)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fe-Fe</td>
<td>2.480</td>
<td>2.480</td>
<td>2.469</td>
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<td>Fe-S average</td>
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<td>2.270±0.004</td>
<td>2.281±0.008</td>
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<td>Fe-CO average</td>
<td>1.792±0.009</td>
<td>1.804±0.011</td>
<td>1.803±0.011</td>
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<tr>
<td><strong>CO Freq. in hexane (cm$^{-1}$)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2006</td>
<td>2014</td>
<td>2015</td>
</tr>
<tr>
<td></td>
<td>2044</td>
<td>2051</td>
<td>2052</td>
</tr>
<tr>
<td></td>
<td>2079</td>
<td>2084</td>
<td>2086</td>
</tr>
<tr>
<td><strong>Average CO</strong></td>
<td>2043</td>
<td>2049</td>
<td>2051</td>
</tr>
<tr>
<td><strong>E$_\frac{1}{2}$ (V vs. Ag/AgCl) in CH$_2$Cl$_2$</strong></td>
<td>-0.953</td>
<td>-0.834</td>
<td>-0.826</td>
</tr>
<tr>
<td><strong>n electrons</strong></td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>Potential Inversion</strong></td>
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<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td><strong>Reversibility</strong></td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
</tbody>
</table>
The hexacarbonyl complexes have been converted into the corresponding mono-tris(\textit{m}-pyridyl)phosphine derivatives 1a-3a by treatment with the decarbonylating agent trimethylamine N-oxide in the presence of one equivalent of phosphine ligand. Complexes 1a-3a have been purified by column chromatography and characterized by NMR and FT-IR spectroscopy, cyclic voltammetry, HR-mass spectrometry and X-ray crystallography. A second set of measurements has been carried out in diluted sulfuric acid to prove the stability of the species under aqueous acidic conditions. The molecular structures of these species are shown in Figure 3, with the relevant analytical data compiled in Table 2 and their IR shown in the appendix section.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figures.png}
\caption{X-ray crystal structures of Fe$_2$(bdt)(CO)$_5$PPy$_3$, 1a (top left), Fe$_2$(Cl$_4$bdt)(CO)$_5$PPy$_3$, 2a (top right), Fe$_2$(F$_4$bdt)(CO)$_5$PPy$_3$, 3a (bottom). Ellipsoids are set at 50\% probability.}
\end{figure}
Table 2. Analytical data for complexes 1a-3a.

<table>
<thead>
<tr>
<th></th>
<th>Fe&lt;sub&gt;2&lt;/sub&gt;(bdt)&lt;br&gt;(CO)&lt;sub&gt;5&lt;/sub&gt;PPy&lt;sub&gt;3&lt;/sub&gt;, 1a</th>
<th>Fe&lt;sub&gt;2&lt;/sub&gt;(Cl&lt;sub&gt;4&lt;/sub&gt;bdt)&lt;br&gt;(CO)&lt;sub&gt;5&lt;/sub&gt;PPy&lt;sub&gt;3&lt;/sub&gt;, 2a</th>
<th>Fe&lt;sub&gt;2&lt;/sub&gt;(F&lt;sub&gt;4&lt;/sub&gt;bdt)&lt;br&gt;(CO)&lt;sub&gt;5&lt;/sub&gt;PPy&lt;sub&gt;3&lt;/sub&gt;, 3a</th>
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<tr>
<td><strong>Distances (Å)</strong></td>
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<td></td>
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<td>Fe-Fe</td>
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<td>Fe-CO average</td>
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<td>1.789±0.017</td>
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<td>2.235</td>
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<td>2000</td>
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<tr>
<td></td>
<td>2003</td>
<td>2009</td>
<td>2010</td>
</tr>
<tr>
<td></td>
<td>2059</td>
<td>2063</td>
<td>2065</td>
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<tr>
<td><strong>Average CO</strong></td>
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<td>2023.7</td>
<td>2024.8</td>
</tr>
<tr>
<td><strong>&lt;sup&gt;31&lt;/sup&gt;P NMR CD&lt;sub&gt;2&lt;/sub&gt;Cl&lt;sub&gt;2&lt;/sub&gt; (ppm)</strong></td>
<td>49.3</td>
<td>48.0</td>
<td>48.5</td>
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<td><strong>E&lt;sub&gt;red&lt;/sub&gt; (V vs. Ag/AgCl) CH&lt;sub&gt;2&lt;/sub&gt;Cl&lt;sub&gt;2&lt;/sub&gt;</strong></td>
<td>-1.134</td>
<td>-1.021</td>
<td>-1.011</td>
</tr>
<tr>
<td>n electrons</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Disproportionation</td>
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<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Reversibility</td>
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<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td><strong>CO Freq. in H&lt;sub&gt;2&lt;/sub&gt;SO&lt;sub&gt;4&lt;/sub&gt; (cm&lt;sup&gt;-1&lt;/sup&gt;)</strong></td>
<td>2015</td>
<td>2019</td>
<td>2023</td>
</tr>
<tr>
<td></td>
<td>2005</td>
<td>2008</td>
<td>2012</td>
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<td></td>
<td>2069</td>
<td>2073</td>
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<tr>
<td><strong>Average CO</strong></td>
<td>2029.3</td>
<td>2033.4</td>
<td>2036.6</td>
</tr>
<tr>
<td><strong>&lt;sup&gt;31&lt;/sup&gt;P NMR D&lt;sub&gt;2&lt;/sub&gt;SO&lt;sub&gt;4&lt;/sub&gt; (ppm)</strong></td>
<td>57.6</td>
<td>55.9</td>
<td>54.9</td>
</tr>
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</table>
Second coordination sphere effects in [FeFe]-Hydrogenase mimics

Two bis-phosphine complexes 1b and 3b have been prepared by refluxing a toluene solution of the parent hexacarbonyl compounds in the presence of two equivalents of the phosphine ligand. Isolation of the clean compounds is achieved by recrystallization from DCM/hexane mixtures. Characterization of those compounds is done similarly as stated before for the mono-substituted ones. The molecular structures are shown in Figure 4, their analytical data is presented in Table 3 an their IR shown in the appendix section.

Figure 4. X-ray crystal structures of Fe₂(bdt)(CO)₄(PPy₃)₂ (left), 1b and Fe₂(F₄bdt)(CO)₄(PPy₃)₂ 3b (right). Ellipsoids are set at 50% probability
Table 3. Analytical data for complexes 1b and 3b.

<table>
<thead>
<tr>
<th>Distances (Å)</th>
<th>Fe₂(bdt) (CO)₄(PPy)₂ 1b</th>
<th>Fe₂(F₄bdt)(CO)₄(PPy)₂ 3b</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fe-Fe</td>
<td>2.463</td>
<td>2.479</td>
</tr>
<tr>
<td>Fe-S average</td>
<td>2.283±0.001</td>
<td>2.288±0.004</td>
</tr>
<tr>
<td>Fe-CO average</td>
<td>1.764±0.003</td>
<td>1.764±0.006</td>
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<tr>
<td>Fe-P average</td>
<td>2.226±0.005</td>
<td>2.229±0.004</td>
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<tr>
<td>CO Freq. in CH₂Cl₂ (cm⁻¹)</td>
<td>1950</td>
<td>1960</td>
</tr>
<tr>
<td></td>
<td>1966</td>
<td>1976</td>
</tr>
<tr>
<td></td>
<td>2010</td>
<td>2018</td>
</tr>
<tr>
<td>Average CO</td>
<td>1975.2</td>
<td>1984.8</td>
</tr>
<tr>
<td>³¹P NMR CD₂Cl₂ (ppm)</td>
<td>46.5</td>
<td>44.9</td>
</tr>
<tr>
<td>E₉ₑ₀ (V vs. Ag/AgCl) CH₂Cl₂</td>
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<td>-1.151</td>
</tr>
<tr>
<td>n electrons</td>
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<td>1</td>
</tr>
<tr>
<td>Further Reactivity</td>
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<td>✓</td>
</tr>
<tr>
<td>Reversibility</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>CO Freq. in H₂SO₄ (cm⁻¹)</td>
<td>1982</td>
<td>1992</td>
</tr>
<tr>
<td></td>
<td>1992</td>
<td>2001</td>
</tr>
<tr>
<td></td>
<td>2033</td>
<td>2041</td>
</tr>
<tr>
<td>Average CO</td>
<td>2002.4</td>
<td>2011.4</td>
</tr>
<tr>
<td>³¹P NMR D₂SO₄ (ppm)</td>
<td>56.2</td>
<td>53.5</td>
</tr>
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</table>

All the complexes were found to be relatively oxygen tolerant even in solution, but rapid decomposition was observed when aerobic solutions were exposed to either light or acetonitrile. The solid samples were found to be stable for extended periods of time at -20 °C. Among all the complexes presented, 2 and 2a were found to be the most unstable.

The molecular structures of the complexes in the solid state display the typical butterfly conformation of the di-iron core, where each iron is in a distorted octahedral coordination. The phosphine ligands are always located in the apical position, in agreement with similar literature on benzenedithiolate analogs. Analysis of the crystallographic data suggests negligible structural differences among complexes with the same number of CO ligands. Further-
more, the crystallographic data show that the complexes are rather similar in terms of bond lengths, even when a different number of phosphine ligands are coordinated. On the other hand, the IR data, particularly in the CO region show that the electronic properties of the complexes are significantly different, following the expected trend, in line with the electron-withdrawing properties of the dithiolate bridge and the electron-donating properties of the phosphines. A more electron-withdrawing bridge results in a minor shift of the CO bands to higher wavenumbers e.g. from 1 to 3 the average shift is about 8 cm\(^{-1}\). A higher number of phosphine ligands results in a major shift to lower wavenumbers e.g. from 1 to 1b the average shift is about 60 cm\(^{-1}\), in line with literature precedents.\textsuperscript{22-24}

**Cyclic voltammetry studies in CH\(_2\)Cl\(_2\)**

**Complexes 1-3**

As mentioned before, complexes 1 and 2 have been reported in literature and their voltammetric response has been thoroughly investigated under a wide variety of conditions.\textsuperscript{22,25-27} Here, only the cyclic voltammograms of the novel tetrafluorobenzenedithiolate derivative 3 in DCM solution in absence of acid are shown, Figure 5 (left). This complex displays a reversible single wave event at -0.826 V vs. Ag/AgCl. The electrochemical event is a two-electron process with potential inversion, as determined by isopoint analysis\textsuperscript{28} and bulk electrolysis, similarly to what is known for 1 and 2.

![Image of cyclic voltammograms](image)

**Figure 5.** Left: cyclic voltammograms of Fe\(_2\)(F\(_4\)bdt)(CO)\(_6\), 3 at different scan speeds. Right: comparison of voltammograms for complexes 1-3.
Proton relay effect in
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Figure 5 (right) shows an overlay of the reversible reduction events for complexes 1-3. Switching from the benzenedithiolate derivative 1 (electronegativity of H substituent: 2.1) to the more electron-withdrawing tetrachloro-derivative 2 (electronegativity of Cl substituent: 3.0) lowers the reduction potential of the complex by about 120 mV. Surprisingly, increasing the electronegativity of the benzene ring substituents even more with the tetrafluoro-complex 3 (electronegativity of F substituent: 4.0), lowers the reduction potential by a mere 8 mV, suggesting that there is a lower limit to the reduction potential of hexacarbonyl complexes by only increasing the electron-withdrawing properties of the benzene bridge.

Preliminary experiments in the presence of acid showed similar behavior between 3 and the other two complexes of the series, therefore further analysis and proton reduction data are here omitted.

Complexes 1a-3a

Complexes 1a-3a show a single reduction peak in the range -1.15 – -1.02 V vs. Ag/AgCl, as shown in Figure 6 (left). The reduction is electrochemically quasi-reversible with the back-oxidation trace showing two distinct peaks. Semi-integrative convolution plots for the complexes in the presence of equimolar amounts of ferrocene were analyzed indicating a one-electron process, Figure 6 (right). Even though it is known that this method introduces approximations and errors due to the lack of knowledge of the diffusion coefficients of the species, it gives a reasonable indication on the number of electrons involved in the process.\textsuperscript{29} We note that bulk electrolysis, which is typically a more accurate method to determine the number of electrons involved in a given process, is problematic in this case due to the follow-up reactivity of the complexes, as will be described in the next section.
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Unlike what was observed for the parent hexacarbonyls, the mono-phosphine derivatives undergo a one-electron reduction. The trend in the reduction potential of the three complexes is in line with what is observed for the parent complexes, in accordance with the electron-withdrawing character of the bridge.

Complexes 1b and 3b

The benzenedithiolate derivative 1b displays a single non-reversible reduction peak at -1.41 V vs. Ag/AgCl while the tetrafluoro-derivative 3b shows two non-reversible events at -1.15 V and -1.33 V. A comparison of the two complexes is shown in Figure 7 (left). Interestingly, the back-oxidation traces show overlapping peaks at -0.4 V that can be attributed to a common decomposition pathway of dithiolate dissociation. Semi-integrative convolution plots obtained from an equimolar solution of ferrocene and complexes 1b or 3b indicate a one-electron process for the first reduction event of both complexes, Figure 7 (right).

Figure 6. Left: cyclic voltammograms of the mono-phosphine derivatives 1a-3a. Right: cyclic voltammogram of 1a with equimolar amounts of ferrocene (black line) and semi-integrative plot (red line) showing similar plateau currents for the two species in solution.
**Proton relay effect in pyridyl appended hydrogenase mimics**

The single reduction event observed for complex 1b splits into two different events at relatively fast scan rates above 1 V/s. On the other hand, the two reduction events seen for complex 3b converge into one peak at relatively slow scan rates, below 20 mV/s. This phenomenon is tentatively attributed to a follow-up rearrangement of the complexes e.g. apical to basal phosphine orientation or loss of phosphine ligand upon reduction. If sufficient time is allowed after the mono-reduction (slow scan rates) the rearrangement can take place and the newly generated species cannot be further reduced a second time. On the contrary, when the rearrangement does not take place (fast scan rates) the mono-reduced complexes can be further reduced a second time. Figure 8 schematically shows the processes described, with the red arrow indicating the preferred pathway at conventional scan rates (around 100 mV/s).

**Figure 7.** Left: cyclic voltammograms of the bis-phosphine derivatives 1b and 3b. Right: cyclic voltammogram of 1b with equimolar amounts of ferrocene (black line) and semi-integrative plot (red line), showing similar plateau currents for the two species in solution.

**Figure 8.** Scheme of the reduction of 1b and 3b. The red arrow indicates the preferred pathway at scan rates around 100 mV/s. Species 1b* and 3b* are tentatively assigned to new species obtained after follow-up rearrangement e.g. apical to basal phosphine orientation or loss of phosphine ligand upon the first reduction. The species 1b2− can be observed at fast scan rates. Formation of 3b2− is avoided at slow scan rates.
Second coordination sphere effects in [FeFe]-Hydrogenase mimics

The electrochemical data presented for the reduction of the complexes 1-3, 1a-3a, 1b and 3b follow the general trend expected, in line with the FT-IR data presented before. Increasing the electron-withdrawing character of the bridge shifts the reduction potential of the complexes towards milder values by about 125 mV going from 1 to 3 or from 1a to 3a. Increasing the number of phosphine ligands has the opposite effect, lowering the reduction potential by about 180-200 mV per phosphine ligand. The average CO frequency of the three most intense carbonyl signals is often used as an indicator of the electron density at the di-iron core. The average CO shift thus obtained correlates well with the reduction potential of the complexes. Figure 9 summarizes this data for all the complexes presented here.

Reactivity of the complexes upon reduction

The cyclic voltammograms of complexes 1a-3a display a second minor reduction event in the range -1.15 – -1.35 V, about 150-200 mV after their main reduction discussed previously. The intensity of this particular peak depends on the scan rate, being more pronounced at slow rates, and the redox potential is found to be consistent with that of the bis-substituted complexes 1b-3b. In literature, the electrochemically induced disproportionation associated with intramolecular rearrangement of the mono-substituted bis-diphenylphosphinomethane (dppm) di-iron complex into its bis-substituted derivative, where the pendant free phosphine of dppm also coordinates to the iron center, has been previously suggested.\textsuperscript{31} Dissociation of a CO ligand upon mono-reduction of the complex allows for the coordination of the

\textbf{Figure 9.} Plot of the average CO shift against the reduction potential of the complexes.
free phosphine, already present nearby the iron center. Intrigued by this report and voltammograms obtained, we wondered if a similar intermolecular process could also occur with the complexes presented here.

Interestingly, we note that if more consecutive voltammetric cycles are measured for a solution of complex 1a, a third reduction event appears at -1.05 V, Figure 10 (left). This reduction event has a redox potential comparable to that of the hexacarbonyl species 1. Addition of 1 to this same solution indicates that the newly generated species has the same reduction potential as an authentic sample of 1, Figure 10 (right). This observation suggests that a disproportionation reaction associated with ligand exchange, triggered by the mono-reduction of the mono-phosphine complexes, takes place according to Scheme 2. A similar process is known for propane dithiolate, mono-substituted di-iron complexes.32,33

Figure 10. Left: repeated cyclic voltammograms for 1a, showing the appearance of 1 around -1.05 V and 1b around -1.4 V, at the second cycle. Right: overlap of the equimolar solution of 1 and 1a (black) and a solution of 1a at the third consecutive cycle, showing that the newly generated species at the surface of the electrode is consistent with being complex 1.

\[
\text{OC-Fe}^1\text{-Fe}^1\text{P} \xrightarrow{1\text{e}^-} 2 \left[ \text{OC-Fe}^0\text{-Fe}^1\text{P}^{-} \right] \xrightarrow{1\text{e}^-} \text{OC-Fe}^0\text{-Fe}^0\text{-CO}^{-2} + \text{P-Fe}^1\text{-Fe}^1\text{P}
\]

Scheme 2. Schematic disproportionation reaction of mono-phosphine derivatives upon mono-reduction. Benzenedithiolate bridge and remaining CO ligands are omitted for clarity.

Validation of our hypothesis came from spectroelectrochemistry coupled with FT-IR spectroscopy, which clearly reveals the simultaneous appearance of two distinct species upon reduction of the mono-phosphine derivatives. One species was found to be identical to the
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bis-phosphine complexes in their neutral form while the other can be ascribed to the doubly reduced hexacarbonyl parent complex. Figure 11 displays an overlay of the IR-spectroelectrochemistry data for the benzenedithiolate series of complexes 1, 1a and 1b.

![Figure 11. FT-IR spectroelectrochemistry data. In black IR of 1b. Red spectroelectrochemistry measurement for 1 after its reduction, showing the bleaching of 1 and the appearance of 12. Blue spectroelectrochemistry measurement for 1a showing its bleaching and simultaneous appearance of 12 and 1b.](image)

Although the electrochemical conversion of similar hexacarbonyl species into the mono- and bis-phosphine complexes has been reported before, the opposite process, which generates back the di-anion of the hexacarbonyl parent complex has not been observed yet for benzenedithiolate di-iron complexes. Furthermore, we suspected the existence of intricate equilibrium reactions at the electrode surface. In fact, during the cycling experiment described in Figure 10 (left), it was expected that the signal of the mono-phosphine derivative would progressively decrease with the number of cycles, while the signals of the hexacarbonyl and bis-phosphine complexes would both gradually increase according to the IR-spectroelectrochemistry measurements. Interestingly, it was observed that a steady state was quickly reached and after a couple of cycles the concentrations of the three species did not change significantly anymore. In addition, a separate cycling experiment using an equimolar solution of 1 and 1a showed no change of the voltammogram upon repeated voltammetric cycles, suggesting that the equilibrium has established, Figure 12 (left). Unexpectedly complex 1b was not clearly detected at any cycle. Although this could appear counterintuitive since the disproportionation equilibrium reaction involves all three species 1, 1a and 1b, we suspect that additional equilibrium reactions and decomposition pathways are present. However, if additional phosphine ligand is added in solution (about 25 equivalents), both signals for 1 and 1a gradually decrease while that of 1b increases, being the predominant species at the electrode surface, Figure 12 (right). Although about 12 equivalents of free phosphine ligand per
Proton relay effect in pyridyl appended hydrogenase mimics

di-iron complex are present in solution, a steady state is quickly reached. Since we do not observe clear accumulation of \(1b\) at the electrode, the collected experiments suggest that all complexes could undergo further rearrangement upon reduction.

\[
\begin{align*}
\text{Figure 12. Left: cycling experiment for an equimolar solution of } & \text{1 and 1a showing no change of the voltammogram upon repeated voltammetric cycles. Right: addition of phosphine ligand to an equimolar solution of 1 and 1a showing their gradual decrease while the signal for 1b increases upon repeated cycles.}
\end{align*}
\]

In line with this, a cycling experiment starting with a solution of complex 1b shows, already at the second cycle, the appearance of significant amounts of the mono-phosphine derivative, Figure 13 (left). In this case, a disproportionation event can be excluded since the triply substituted di-iron complex is not observed. To the best of our knowledge, no examples of (isolated) benzenedithiolate tris-phosphine di-iron complexes are reported. It is noted that in order to generate 1a from 1b an additional CO ligand is needed, likely coming from the decomposition of a second molecule of 1b and some free phosphine ligand must be liberated at the electrode surface. Although in lower amounts, also the hexacarbonyl derivative 1 is detected at the second cycle. The lower amount of this complex could be explained by its known reactivity, when in its doubly reduced state, with the free phosphine ligand, which is in this case generated at the electrode surface upon reduction of 1b.\(^{34}\)
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in [FeFe]-Hydrogenase mimics

Lastly, we measured an equimolar solution of complex 1 and 1b, Figure 13 right. At the first cycle only the two expected complexes are present, indicating that there is no fast reaction between the doubly reduced hexacarbonyl (1²) and 1b in its neutral form. Instead, at the second cycle, significant amounts of 1a are present. Interestingly both the intensity of 1 and 1b are now lower, suggesting that 1a is generated independently from the mono-reduction of 1b and from the reaction of 1² with the free phosphine liberated in solution after reduction of 1b. A summary of the reactivity described is simplified in Table 4 where the first column indicates the species present in solution before the electrochemical measurement and the second column contains the species that are detected at the surface of the electrode, at the second consecutive cycle that are different from those present in solution.

Table 4. Summary of the reactivity described. P indicates free phosphine ligand.

<table>
<thead>
<tr>
<th>Starting solution</th>
<th>Species detected at 2nd cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1 + P</td>
</tr>
<tr>
<td>2</td>
<td>1a</td>
</tr>
<tr>
<td>3</td>
<td>1b</td>
</tr>
<tr>
<td>4</td>
<td>1a + 1</td>
</tr>
<tr>
<td>5</td>
<td>1 + 1a + P</td>
</tr>
<tr>
<td>6</td>
<td>1+1b</td>
</tr>
</tbody>
</table>
Finally, we note that other literature reports on phosphine substituted benzenedithiolate complexes show similar voltammograms, indicating that such intricate reactivity upon reduction might be more general phenomenon for such type of compounds.\textsuperscript{30,35}

**Proton reduction from weak acid in CH\textsubscript{2}Cl\textsubscript{2}**

**Complexes 1a-3a**

When complexes 1a-3a are in the presence of the weak acid HNEt\textsubscript{3}PF\textsubscript{6} - this acid is not strong enough to protonate either the Fe-Fe bond of the neutral species or the basic nitrogen of the pyridine ligands - the first reduction peak of the complexes becomes completely irreversible and new oxidation peaks appear in the range -0.4 – -0.1 V, Figure 14. This behavior is consistent with the reduction of the complexes, followed by protonation of the Fe-Fe bond to yield a bridging hydride. When the potential window is increased to more reductive potentials, a new peak appears in the range -1.55 – -1.40 V. This peak increases in intensity with increasing aliquots of acid, revealing the catalytic nature of this process, Figure 14.

![Figure 14. Voltammetric response of 1a in the presence of increasing amounts of acid (HNEt\textsubscript{3}PF\textsubscript{6}) in dichloromethane.](image)

Combining the information obtained in the absence of acid for the first redox event, with the new information in the presence of acid, the overall proton reduction mechanism of 1a-3a can be summarized as an ECEC type, as proposed for similar complexes.\textsuperscript{30} This mechanism differs from the one demonstrated for the parent hexacarbonyl species, which operates via an EECEC mechanism.\textsuperscript{25} Foot-of-the-wave (FotW) analysis\textsuperscript{36} was employed to deduce the catalytic proton reduction rate constant and related turnover frequency.
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for the complexes. This analysis revealed a $k_{cat}$ in the order of $2\cdot10^3 \text{M}^{-1}\text{s}^{-1}$. Table 5 summarizes the relevant data for complexes 1a-3a used to build the Tafel plot in Figure 15.

Table 5. Catalytic parameters for complexes 1a-3a in DCM solution, in the presence of weak acid (HNEt$_3$PF$_6$). TOF$_{\text{max}}$ are extrapolated for a 1 M concentration of acid.

<table>
<thead>
<tr>
<th></th>
<th>Fe$_2$(bdt) (CO)$_3$PPy$_3$ 1a</th>
<th>Fe$_2$(Cl,bdt) (CO)$_3$PPy$_3$ 2a</th>
<th>Fe$_2$(F,bdt) (CO)$_3$PPy$_3$ 3a</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_{cat}$ ($\text{M}^{-1}\text{s}^{-1}$)</td>
<td>2.8$\cdot10^3$</td>
<td>2.4$\cdot10^3$</td>
<td>2.0$\cdot10^3$</td>
</tr>
<tr>
<td>Catalytic E$_{1/2}$ potential (V vs. Ag/AgCl)</td>
<td>-1.50</td>
<td>-1.45</td>
<td>-1.40</td>
</tr>
<tr>
<td>$\eta$ (V)</td>
<td>0.68</td>
<td>0.63</td>
<td>0.58</td>
</tr>
<tr>
<td>TOF$_{\text{max}}$ (s$^{-1}$)</td>
<td>5.5$\cdot10^3$</td>
<td>4.7$\cdot10^3$</td>
<td>3.9$\cdot10^3$</td>
</tr>
</tbody>
</table>

In contrast to the behavior of the redox-active and proton-responsive dipyridylphosphole complex, the trispyridylphosphine complexes 1a-3a do not allow for a PCET step in their mechanism. The trispyridylphosphine ligand is purely acting as a spectator, remaining in its neutral form over the entire catalytic cycle. As such, the trispyridylphosphine does not play a beneficial role as proton-responsive ligand and it also increases the operational overpotential of the complexes by roughly 100 mV compared to the respective more electron-deficient hexacarbonyl parent complexes. Interestingly, although the trispyridyl complexes are lacking any redox-active and proton-responsive properties, they require a milder overpotential.
Proton relay effect in pyridyl appended hydrogenase mimics

compared to the dipyridylphosphole complex. The importance of the redox-active ligand is evidenced by the catalytic rate of the dipyridylphosphole complex, which is roughly 200 times faster than the trispyridyl complexes. Upon reduction, the redox-activity of the dipyridylphosphole ligand allows for delocalization of some electron density onto the phosphorus based ligand itself, therefore increasing the basicity of the pyridyl moieties. The increased basicity of the pyridyl ligands allows for their protonation and therefore proton preorganization around the di-iron center. This process happens in a concerted PCET fashion.

The electron-withdrawing character of the bridge has a clear effect for the overpotential; complexes with electron-deficient di-iron cores display a milder first reduction potential and require milder catalytic potentials, but at the expense of lower proton reduction rates. In fact, moving from 1a to 3a the overpotential drops by about 100 mV while the catalytic activity decreases by roughly only 30%. Interestingly, while the reduction potentials of 2a and 3a are nearly identical in the absence of acid (Figure 6), we observe 50 mV difference in their catalytic potential, indicating that the first reduction potential of the complexes cannot be directly taken as a measure for the catalytic potential.

At this point we were also wondering whether the reductive disproportionation reactivity observed in the absence of acid is also relevant under catalytic conditions. We addressed this issue by comparison of the cyclic voltammograms for the hexacarbonyl species with those obtained for complexes 1a-3a in the presence of the weak acid. Our experiments indicate that in the presence of a few equivalents of acid (below about 4 equivalents) disproportionation still happens as a minor event. In the presence of higher amounts of acid (above about 8 equivalents) disproportionation is not observed, indicating that protonation and disproportionation have similar rates.

**Complexes 1b and 3b**

In the presence of HNEt$_3$PF$_6$, the reduction potential of 1b and 3b shifts anodically by about 100 mV, Figure 16. Despite the fact that the first reduction peak current increases slightly, the semi-integral plot and comparison with equimolar amounts of ferrocene indicate that this is still a one-electron process. Since the weak acid used protonates neither the Fe-Fe bond nor the pyridyl ligands, the large potential shift observed can be attributed to a proton coupled electron transfer step.
Increasing the potential window to more reductive potentials reveals the appearance of a new catalytic wave with the onset potential at -1.4 V and a peak potential at about -1.6 V. Similarly to the mono-phosphine complexes, the catalytic mechanism for the bis-phosphine complexes can be summarized as an ECEC mechanism where the first EC is a concerted step. Proton reduction rates for 1b and 3b were deduced from FotW analysis; the catalytic rate constant and relevant parameters are reported in Table 6 while Figure 17 shows the Tafel plot for the two bis-substituted complexes.

**Figure 16.** Voltammogram of 1b in absence of acid (black line) and in the presence of 8 equivalents of weak acid, showing a 100 mV potential shift indicating a PCET step. Proton reduction catalysis occurs at -1.4 V.

**Table 6.** Catalytic parameters for complexes 1b and 3b in DCM solution, in the presence of weak acid (HNEt₃PF₆). TOFₘₐₓ are extrapolated for a 1 M concentration of acid.

<table>
<thead>
<tr>
<th></th>
<th>Fe₂(bdt)(CO)₄(PPy)₂ 1b</th>
<th>Fe₂(F₄bdt)(CO)₄(PPy)₂ 3b</th>
</tr>
</thead>
<tbody>
<tr>
<td>$k_{cat}(M^{-1}s^{-1})$</td>
<td>3.6·10³</td>
<td>2.5·10³</td>
</tr>
<tr>
<td>Catalytic $E_{1/2}$ potential (V vs. Ag/AgCl)</td>
<td>-1.68</td>
<td>-1.60</td>
</tr>
<tr>
<td>$\eta$ (V)</td>
<td>0.86</td>
<td>0.78</td>
</tr>
<tr>
<td>TOFₘₐₓ (s⁻¹)</td>
<td>7.3·10³</td>
<td>5.0·10³</td>
</tr>
</tbody>
</table>
Figure 17. Tafel plot for complexes 1b and 3b in the presence of weak acid, in DCM. The value of $\text{TOF}_{\text{max}}$ is extrapolated for a 1 M concentration of substrate.

By comparing 1a to 1b it is clear that the coordination of a second phosphine ligand has a significant effect on the catalysis. The second phosphine makes the complex more electron-rich, which therefore requires about 200 mV higher overpotential to start the proton reduction reaction while the catalytic rates are only marginally higher. A similar observation can be made when comparing 3a to 3b. Regarding the electron-withdrawing character of the bridge, moving from 1b to 3b has a similar influence as seen for the mono-substituted derivatives; the overpotential is about 80 mV milder while the rate drops by only 30% as the di-iron core of the complex becomes more electron-deficient.

Exclusion of any follow-up reactivity for complexes 1b and 3b, upon mono-reduction in the presence of acid was confirmed by comparison of the voltammograms with those of the mono-phosphine and hexacarbonyl complexes. Such comparisons indicate that the bis-phosphine complexes behave differently than the mono-phosphine derivatives, as no back-oxidation peaks are detected for the former. Even when only small amounts of acid are added, any side reactivity is completely suppressed, possibly due to the inherently fast proton coupled electron transfer step. In addition, the main catalytic proton reduction catalysis for the bis-phosphine complexes happens at potentials about 200 mV cathodically shifted compared to their mono-substituted counterparts, in agreement with the higher electron density at the di-iron center.
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Study of the complexes in CH₂Cl₂ with strong acid

Next we studied proton reduction catalysis in the presence of HBF₄, a strong acid. This acid is sufficiently strong to protonate either the pyridyl groups or the iron-iron bond. However, reaction with a stoichiometric amount did not lead to a bridging hydride species, as indicated by ¹H NMR spectroscopy. This suggests that the pKₐ of the trispyridylphosphines is lower than that of the di-iron fragment.

Addition of one equivalent of strong acid to 1a causes the first reduction potential to anodically shift by about 230 mV. A second reduction is also present at potentials similar to that of the original reduction of the complex in absence of acid. Addition of a second equivalent of HBF₄ causes the first reduction potential to shift by an additional 150 mV, Figure 18. Exhaustive investigation is hampered by precipitation of the poorly soluble doubly protonated compound.

For complex 1b a similar trend is observed, with an anodic potential shift of about 520 mV upon addition of one equivalent of acid. As this complex showed PCET in the presence of weak acid, this shift is most likely due to a combination of ligand protonation and PCET. Detailed proof is hard to obtain due to the poor solubility of the mono-protonated species, Figure 18 (right).

These experiments indicate that ligand protonation has the beneficial effect of lowering the
Proton relay effect in pyridyl appended hydrogenase mimics

redox potential of the first electron transfer to milder values. Although also the second electron transfer appears to be anodically shifted, proper analysis and interpretation of the data is hampered by the poor solubility of the species involved.

Catalysis in diluted H₂SO₄

In contrast to the protonated species in dichloromethane, complexes 1a-3a, 1b and 3b dissolve well in acidic aqueous solutions. This allowed us to study electrocatalytic proton reduction at a glassy carbon working electrode in acidic aqueous media. The complexes were found to show very high activity under typical concentrations, therefore the experiments were performed at 25 µM catalyst concentration in 0.5 M H₂SO₄ solution. The previously presented analytical data (Tables 2 and 3) show the great stability of the complexes under such harsh acidic conditions, provided the combination of light and oxygen is avoided. The analytical data, in particular ¹H NMR and FT-IR spectroscopy, indicate that also in diluted sulfuric acid only protonation of the pyridyl ligands occurs, while the di-iron bond stays intact.

Under the described conditions, complexes 1a-3a show scan speed-independent plateau currents at -1.0 V, similar to their first reduction in organic solvents, Figure 19 left. The S-shaped voltammograms obtained indicate that the electrocatalysis occurs under pure kinetic control with negligible depletion of substrate. The DuBois method to obtain the catalytic rate constants $k_{cat}$ could therefore be employed.³⁷ The value of $k_{cat}$ can be accessed from the ratio $I_{pl}/I_{0p}$ where $I_{pl}$ is the plateau current at a given scan speed and $I_{0p}$ is the current in the absence of substrate, which can be easily calculated using the Randles–Sevcik equation.³⁸ The diffusion coefficients are obtained from ¹H-DOSY NMR experiments in 1 M D₂SO₄ in D₂O. A second method to estimate the same catalytic constant is the FotW analysis proposed by Savéant.³⁶ Application of this analysis at the different scan speeds recorded provides estimated reaction rates that are in good agreement with those obtained via the Dubois method. The calculated values of $k_{cat}$ were found to be as high as $10^7$ M⁻¹s⁻¹ for 1a and $10^5$ M⁻¹s⁻¹ for 3a. The relevant parameters are summarized in Table 7.
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Complexes 1b and 3b were also found to be extremely active under these conditions. Respective 25 µM solutions in 0.5 M H₂SO₄ display a diffusion-limited shape of the catalytic curve at potentials around -1.10 – -1.15 V vs. Ag/AgCl, Figure 19 (right). The shape of the voltammograms suggests a quick depletion of substrate, which is a first indication that these complexes are faster catalysts than their mono-substituted analogs.

In this case the catalytic rates were deduced by FotW analysis and found to reach unprecedented values in the order of 10⁸ M⁻¹s⁻¹. Table 7 summarizes the relevant data while Figure 20 shows a Tafel plot for the different complexes under acidic aqueous conditions.

Table 7. Catalytic parameters for complexes 1a-3a, 1b and 3b in 0.5 M H₂SO₄ solution. TOFₜₒₜₛ are extrapolated for a 1 M concentration of acid.

<table>
<thead>
<tr>
<th></th>
<th>1a</th>
<th>2a</th>
<th>3a</th>
<th>1b</th>
<th>3b</th>
</tr>
</thead>
<tbody>
<tr>
<td>k_cat (M⁻¹s⁻¹)</td>
<td>1.8·10⁷</td>
<td>9.2·10⁵</td>
<td>5.4·10⁵</td>
<td>2.7·10⁸</td>
<td>4.0·10⁶</td>
</tr>
<tr>
<td>Catalytic Eₚ potential (V vs. Ag/AgCl)</td>
<td>-1.08</td>
<td>-1.04</td>
<td>-1.03</td>
<td>-1.15</td>
<td>-1.10</td>
</tr>
<tr>
<td>η (V)</td>
<td>0.82</td>
<td>0.78</td>
<td>0.77</td>
<td>0.89</td>
<td>0.84</td>
</tr>
<tr>
<td>TOFₜₒₜₛ (s⁻¹)</td>
<td>3.6·10⁷</td>
<td>1.8·10⁶</td>
<td>1.1·10⁶</td>
<td>5.3·10⁸</td>
<td>8.0·10⁶</td>
</tr>
</tbody>
</table>
Proton relay effect in pyridyl appended hydrogenase mimics

In diluted H$_2$SO$_4$ protonation of the pyridyl ligands of the mono-phosphine derivatives 1a-3a, has the effect of shifting the average CO frequency by about 11 wavenumbers to higher values. For the bis-phosphine complexes 1b and 3b, the average shift for the CO bands is roughly doubled at 20 cm$^{-1}$. Addition of these data to the plot presented before for the average CO shift against the first reduction potential shows that pyridyl protonation has a large effect on the electronics of the complexes, effectively counterbalancing the increase in electron density caused by the phosphine substitution, Figure 21.

Figure 20. Tafel plot for complexes 1a-3a, 1b and 3b in 0.5 M H$_2$SO$_4$ solution. The value of TOF$_{max}$ is extrapolated for a 1 M concentration of substrate.

Figure 21. Plot of the average CO shift against the reduction potential of the complexes. In red are shown the data obtained in diluted sulfuric acid solution.
Second coordination sphere effects in [FeFe]-Hydrogenase mimics

In diluted sulfuric acid, proton reduction happens at the first reduction. Therefore, from the graph above, it might appear that the catalytic potential for proton reduction in aqueous media is particularly mild. Although the numerical values for the reduction potentials seem milder compared to the DCM ones, it is important to realize that the main working solvent and the type of acid employed are different. This translates in a different thermodynamic proton reduction potential and therefore a comparison of the overpotentials is needed. In diluted sulfuric acid, the overpotentials are found to be higher than in dichloromethane. For the mono-phosphine 1a, going from organic solvent solution and weak acid to acidic water has the effect of increasing the activity of the catalyst by four orders of magnitude, but at the expense of a significantly higher overpotential of about 140 mV, Figure 22 (left). The bis-phosphine complex 1b on the other hand shows about five orders of magnitude higher activity in sulfuric acid than in organic solvents while the overpotential increases by a mere 30 mV, Figure 22 (right).

The presence of the pyridyl moieties and their inherent protonation in acidic aqueous solutions results in preorganization of the protons proximal to the catalytic di-iron center, which drastically increases the activity of the complexes. Furthermore, pyridyl protonation has the beneficial effect of counterbalancing the electron-donating abilities of the phosphine ligands as electron transfer steps are facilitated because of positive charges of the complexes.
Conclusions

In conclusion, we have shown that modification of the electron-withdrawing properties of the benzenedithiolate bridge has a significant effect for catalysis. Complexes featuring strongly electron-deficient di-iron cores have lower catalytic proton reduction potentials while the decrease of their activity is modest.

Protonation of the pyridyl groups offers a good strategy to partially counterbalance the increase in the electron density of the di-iron core due to phosphine coordination. The positive effect of pyridyl protonation is best shown by comparison of complex 1b in dichloromethane and sulfuric acid. Moving to the acidic aqueous environment the activity of the complex increases by a factor of five, while the increase in overpotential is negligible.

This work demonstrates that the presence of a proton-responsive ligand that facilitates a PCET step is important to lower the first reduction potential of di-iron complexes bearing benzenedithiolate bridges. This is most important when the complex can perform catalysis at its first reduction so that the PCET step effectively lowers the catalytic overpotential. Interestingly, it is also shown that proton-responsive ligands alone are sufficient to achieve high catalytic rates.

Acknowledgments

Lukas Jongkind is acknowledged for the synthesis of mono-tris(m-pyridyl)phosphine. Wojciech Dzik is acknowledged for X-ray data collection and refinement of the crystal structures. Simon Mathew is thanked for fruitful discussion and suggestions.
Experimental

Materials and methods

General procedures: all synthetic procedures were carried out under an argon atmosphere using standard Schlenk techniques. All commercially available chemicals were used as received without further purification. Solvents used for synthesis were dried, distilled and degassed with the most suitable method. Column chromatography was performed open to air using solvents as received.

Electrochemistry: Cyclic voltammetry was performed on 1 mM solution of analyte (unless otherwise stated) using 0.1 M tetrabutylammonium hexafluorophosphate as supporting electrolyte. The voltammograms were recorded using a PG-STAT302N potentiostat at glassy carbon disk electrode (2 mm diameter). A platinum coil was used as auxiliary electrode and a leak free silver electrode (inner compartment 3 M KCl/Ag) as reference electrode.

Spectroelectrochemistry was performed in an optically transparent thin layer OTTLE cell with platinum working electrode, platinum auxiliary electrode and silver wire as reference electrode, using 0.2 M tetrabutylammonium hexafluorophosphate as supporting electrolyte.

Mass analysis: high resolution mass spectra for all compounds were collected on an AccuTOF GC v 4g, JMS-T100G-CV mass spectrometer (JEOL, Japan).

X-ray crystal structure determination: X-ray intensities were measured on a Bruker D8 Quest Eco diffractometer equipped with a Triumph monochromator (λ = 0.71073 Å) and a CMOS Photon 50 detector at a temperature of 150(2) K. Intensity data were integrated with the Bruker APEX2 software. Absorption correction and scaling was performed with SADABS. The structures were solved using intrinsic phasing with the program SHELXT. Least-squares refinement was performed with SHELXL-2013 against F² of all reflections. Non-hydrogen atoms were refined with anisotropic displacement parameters. The H atoms were placed at calculated positions using the instructions AFIX 13, AFIX 43 or AFIX 137 with isotropic displacement parameters having values 1.2 or 1.5 times Ueq of the attached C atoms.
Synthesis of complexes

Tetrachlorobenzenedithiol\textsuperscript{10,19} and tetrafluorobenzenedithiol\textsuperscript{20} were prepared according to modified literature procedures. \textit{m}-Trispyridylphosphine was prepared according to literature procedure.\textsuperscript{42}

General procedure for the preparation of the hexacarbonyl complexes \textbf{1-3}.

An oven-dried, argon-flushed round bottom Schlenk flask equipped with a reflux condenser was charged with Fe\textsubscript{3}(CO)\textsubscript{12} (4 mmol) and the dithiol precursor (1 equiv, 4 mmol). After addition of 200 mL of toluene, the reaction mixture was heated to 80 °C overnight in the dark. The reaction was cooled to room temperature and filtered through a plug of Celite before removing the volatiles under reduced pressure. The residue was dissolved in hexanes and chromatographed on silica gel to afford the clean compound.

\[\text{Fe}_{2}\text{(bdt)(CO)}_{6}, \textbf{1}: 1.09 \text{ g, yield 65\%.} \]
\[\text{\textsuperscript{1}H NMR (CD\textsubscript{2}Cl\textsubscript{2}, ppm) } \delta 7.22 \text{ (dd, } J = 5.7, 3.2 \text{ Hz, 2H), } 6.71 \text{ (dd, } J = 5.7, 3.2 \text{ Hz, 2H).} \]
\[\text{\textsuperscript{13}C NMR (CD\textsubscript{2}Cl\textsubscript{2}, ppm) } \delta 207.6, 147.4, 127.9, 126.7. \text{ FT-IR (hexane, } \nu) 2006, 2044, 2079 \text{ cm}^{-1}. \]

\[\text{Fe}_{2}\text{(Cl\textsubscript{4}bdt)(CO)}_{6}, \textbf{2}: 0.89 \text{ g, Yield 40\%.} \]
\[\text{\textsuperscript{13}C NMR (CD\textsubscript{2}Cl\textsubscript{2}, ppm) } \delta 209.1, 206.6, 148.4, 131.4, 131.2, 129.2, 127.1. \text{ FT-IR (hexane, } \nu) 2014, 2050, 2084 \text{ cm}^{-1}. \text{ HR FD-MS (m/z) found: 557.6581 expected: 557.6562, C}_{12}\text{Cl}_{4}\text{Fe}_{2}\text{O}_{6}S_{2}. \]

\[\text{Fe}_{2}\text{(F\textsubscript{4}bdt)(CO)}_{6}, \textbf{3}: 1.24 \text{ g, yield 63\%.} \]
\[\text{\textsuperscript{13}C NMR (CD\textsubscript{2}Cl\textsubscript{2}, ppm) } \delta 209.1, 206.4, 151.0 - 146.9 \text{ (m), } 145.9 - 143.7 \text{ (m), } 141.7 - 139.4 \text{ (m), } 138.0 - 136.1 \text{ (m), } 133.4 - 130.5 \text{ (m).} \text{\textsuperscript{19}F NMR (CD\textsubscript{2}Cl\textsubscript{2}, ppm) } \delta -131.05 \text{ (d, } J = 20.0 \text{ Hz), -153.43 (d, } J = 20.0 \text{ Hz). FT-IR (hexane, } \nu) 2015, 2052, 2086 \text{ cm}^{-1}. \text{ HR FD-MS (m/z) found: 491.7750 expected: 491.7772, C}_{12}\text{F}_{4}\text{Fe}_{2}\text{O}_{6}S_{2}. \]

General procedure for the preparation of the mono-trispyridyl phosphine complexes \textbf{1a-3a}.

An oven-dried, argon-flushed round bottom Schlenk flask was charged with the hexacarbonyl complex \textbf{1-3} (0.6 mmol), trispyridyl phosphine (1 equiv, 0.6 mmol) and dichloromethane 60 mL. In a separate flask Me\textsubscript{3}NO (1.5 equiv, 0.9 mmol) was dissolved in 2 mL of acetonitrile and this solution added to the first flask. After stirring the reaction mixture for 30 minutes at room temperature, in the dark the solvents were removed under reduced pressure. The residue was dissolved in minimal amount of DCM and chromatographed over silica gel with DCM:MeOH 94:6 to afford the clean compound.
Second coordination sphere effects in [FeFe]-Hydrogenase mimics

Fe₄(bdt)(CO)₅PPy₃ 1a: 299 mg, yield 76%. ¹H NMR (CD₂Cl₂, ppm) δ 8.76 – 8.64 (m, 6H), 7.87 (t, J = 9.4 Hz, 3H), 7.38 (t, J = 6.4 Hz, 3H), 6.63 (dd, J = 5.5, 3.2 Hz, 2H), 6.32 (dd, J = 5.5, 3.2 Hz, 2H). ³¹P NMR (CD₂Cl₂, ppm) δ 49.32. ³¹C NMR (CD₂Cl₂, ppm) δ 212.8, 212.7, 208.6, 153.0, 152.8, 151.3, 147.2, 140.2, 140.1, 130.4, 129.9, 127.71, 125.9, 123.7, 123.6. FT-IR (hexane, ν) 1992, 2003, 2059 cm⁻¹. ¹H NMR (CD₂Cl₂, ppm) δ 8.82 – 8.50 (m, 12H), 7.99 (t, J = 7.1 Hz, 3H), 6.44 (dd, J = 5.1, 3.0 Hz, 2H), 6.18 (dd, J = 5.1, 3.0 Hz, 2H). ³¹P NMR (CD₂Cl₂, ppm) δ 57.64. DOSY (1 M D₂SO₄, ν) logD=-9.461 m⁻³s⁻¹. FT-IR (1 M H₂SO₄, ν) 2015, 2005, 2069 cm⁻¹. HR FD-MS (m/z) found: 657.9080 expected: 657.9047, C₂₆H₁₆Fe₂N₃O₅PS₂.

Fe₄(Cl₄bdt)(CO)₅PPy₃ 2a: 233 mg, Yield 49%. ¹H NMR (CD₂Cl₂, ppm) δ 8.75 – 8.59 (m, 6H), 7.95 (t, J = 9.6 Hz, 3H), 7.46 (m, 3H). ³¹P NMR (CD₂Cl₂, ppm) δ 48.01. ³¹C NMR (CD₂Cl₂, ppm) δ 212.1, 207.6, 152.8, 152.6, 151.7, 148.3, 140.2, 140.1, 131.1, 130.2, 129.7, 129.2, 123.9. FT-IR (hexane, ν) 1999, 2009, 2063 cm⁻¹. ¹H NMR (CD₂Cl₂, ppm) δ 8.51 (d, J = 5.7 Hz, 3H), 8.48 – 8.37 (d, J = 6.3 Hz, 3H), 8.25 (t, J = 9.4 Hz, 3H), 7.84 – 7.60 (m, 3H). ³¹P NMR (CD₂Cl₂, ppm) δ 55.88. DOSY (1 M D₂SO₄, ν) logD=-9.739 m⁻³s⁻¹. FT-IR (1 M H₂SO₄, ν) 2019, 2008 2073 cm⁻¹. HR FD-MS (m/z) found: 795.7462 expected: 795.7445, C₂₆H₁₂Cl₄Fe₂N₃O₅PS₂.

Fe₄(F₄bdt)(CO)₅PPy₃ 3a: 328 mg, yield 75%. ¹H NMR (CD₂Cl₂, ppm) δ 8.96 – 8.56 (m, 6H), 7.97 (t, J = 10.0 Hz, 3H), 7.49 (m, 3H). ³¹P NMR (CD₂Cl₂, ppm) δ 47.64. ³¹C NMR (CD₂Cl₂, ppm) δ 211.9, 211.9, 207.5, 152.7, 151.8, 147.2, 143.8, 140.2, 140.1, 131.5, 129.7, 129.2, 124.0. ³¹F NMR (CD₂Cl₂, ppm) δ -131.16 (d, J = 19.5 Hz), -154.99 (d, J = 19.5 Hz). FT-IR (hexane, ν) 2000, 2010, 2065 cm⁻¹. ¹H NMR (CD₂Cl₂, ppm) δ 8.51 (m, 6H), 8.33 (t, J = 9.3 Hz, 3H), 7.74 (m, 3H). ³¹P NMR (CD₂Cl₂, ppm) δ 54.94. ³¹F NMR (CD₂Cl₂, ppm) δ -128.02 (d, J = 20.1 Hz), -150.72 (d, J = 20.1 Hz). DOSY (1 M D₂SO₄, ν) logD=-9.476 m⁻³s⁻¹. FT-IR (1 M H₂SO₄, ν) 2023, 2012, 2075 cm⁻¹. HR FD-MS (m/z) found: 729.8697 expected: 729.8670, C₂₆H₁₂F₄Fe₂N₃O₅PS₂.

General procedure for the preparation of the bis-trispyridyl phosphine complexes 1b and 3b.

An oven-dried, argon-flushed round bottom Schlenk flask was charged with the hexacarbonyl complex 1 or 3 (0.3 mmol), trispyridyl phosphine (2.5 molar equiv, 0.75 mmol) and toluene (60 mL). The reaction mixture was refluxed for 2 hours. After cooling the reaction mixture to room temperature the volatiles were removed under reduced pressure. The residue was dissolved in dichloromethane and the complexes precipitated with hexanes. After three recrystallizations the solids were washed with hexanes before drying under vacuum.

Fe₄(bdt)(CO)₅PPy₃ 1b: 233 mg, yield 87%. ¹H NMR (CD₂Cl₂, ppm) δ 8.64 (m, 12H), 7.85(t, J = 9.2 Hz, 6H), 7.34 (dd, J = 7.9, 4.8 Hz, 6H), 6.02 (dd, J = 5.4, 3.2 Hz, 2H), 5.91 (dd, J = 5.4, 3.2...
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Hz, 2H). 31P NMR (CD2Cl2, ppm) δ 46.57. 13C NMR (CD2Cl2, ppm) δ 214.0, 214.0, 213.9, 152.8, 152.8, 152.7, 150.9, 146.8, 140.1, 140.1, 140.0, 130.5, 130.1, 127.4, 124.9, 123.4, 123.4. FT-IR (DCM, ν) 1950, 1966, 2010 cm⁻¹. 1H NMR (1 M D2SO4, ppm) δ 8.73 (d, J = 5.8 Hz, 6H), 8.71 – 8.52 (m, 12H), 7.99 (t, J = 7.1 Hz, 6H), 6.20 – 5.61 (m, 4H). 31P NMR (1 M D2SO4, ppm) δ 56.18. DOSY (1 M D2SO4) logD = -9.482 m²s⁻¹. FT-IR (1 M H2SO4, ν) 1982, 1992 2033 cm⁻¹. HR FD-MS (m/z) found: 983.9783 expected: 983.9789. Fe2(F4bdt)(CO)4(Ppy)3, 3b: 237 mg, yield 82%. 1H NMR (CD2Cl2, ppm) δ 8.68 (m, 12H), 7.94 (t, J = 9.2 Hz, 6H), 7.43 (m, 6H). 31P NMR (CD2Cl2, ppm) δ 131.13 (d, J = 19.9 Hz), -156.52 (d, J = 19.9 Hz). 13C NMR (CD2Cl2, ppm) δ 213.0, 213.0, 212.7, 212.7, 212.5, 212.5, 212.5, 212.5, 212.5, 212.5, 212.5, 212.5, 212.5. FT-IR (DCM, ν) 1976, 2018 cm⁻¹.

Crystallographic details

Fe2(F4bdt)(CO)3, 3: C12F4Fe2O6S2, Fw = 491.94, orange plate, 0.91 × 0.44 × 0.12 mm, Monoclinic, P21/n (No: 14), a = 6.4785 (4), b = 15.2757 (9), c = 15.6631 (10) Å, β = 94.601 (3)°, V = 1545.08 (16) Å³, Z = 4, Dc = 2.115 g/cm³, μ = 2.22 mm⁻¹. 17623 reflections were measured up to a resolution of (sin θ/λ)max = 0.597 Å⁻¹. 2749 reflections were unique (Rint = 0.044), of which 2454 were observed [I>2σ(I)]. 235 parameters were refined with 0 restraints. R1/wR2 [I > 2σ(I)]: 0.0286/0.0983 R1/wR2 [all refl.]: 0.0346/0.1082. S = 0.93. Residual electron density between -0.49 and 0.36 e/Å³.

Fe2(bdt)(CO)3PPy3, 1a: C26H16Fe2N5O5PS2, Fw = 657.21, dark red block, 0.57 × 0.52 × 0.24 mm, Triclinic, P (No: 2), a = 9.8921 (4), b = 11.5320 (5), 12.4221 (5) Å, α = 90.689 (2), β = 92.882 (2), γ = 109.525 (2)°, V = 1333.26 (10) Å³, Z = 2, Dc = 1.637 g/cm³, μ = 1.35 mm⁻¹. 25473 reflections were measured up to a resolution of (sin θ/λ)max = 0.597 Å⁻¹. 4739 reflections were unique (Rint = 0.031), of which 4229 were observed [I>2σ(I)]. 352 parameters were refined with 0 restraints. R1/wR2 [I > 2σ(I)]: 0.0387/0.1286 R1/wR2 [all refl.]: 0.0324/0.1114. S = 1.09. Residual electron density between -0.60 and 0.83 e/Å³.

Fe2(Cl4bdt)(CO)3PPy3, 2a: C29H19Cl4Fe2N5O5PS2, Fw = 838.06, dark red plate, 0.74 × 0.36 × 0.15 mm, Triclinic, P (No: 2), a = 10.9935 (5), b = 11.6498 (5), c = 12.9988 (6) Å, α = 97.474 (2), β = 98.021 (2), γ = 96.445 (2)°, V = 1620.01 (13) Å³, Z = 2, Dc = 1.718 g/cm³, μ = 1.45 mm⁻¹. 38316
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Reflections were measured up to a resolution of \((\sin \theta/\lambda)_{\text{max}} = 0.597 \text{ Å}^{-1}\). 5742 reflections were unique (\(R_{\text{int}} = 0.046\)), of which 4820 were observed \([I > 2\sigma(I)]\). 416 parameters were refined with 2 restraints. \(R1/wR2 [I > 2\sigma(I)]\): 0.0398/0.1252 \(R1/wR2 [\text{all refl.}]\): 0.0512/0.1408. \(S = 1.13\). Residual electron density between –0.57 and 1.03 e/Å\(^3\).

\(\text{Fe}_2(\text{F}_4\text{bdt})(\text{CO})_5\) \(3\text{a}: C_{26}H_{12}F_4\text{Fe}_2\text{N}_3\text{O}_5\text{P}_2\). \(Fw = 729.18\), dark red block, \(0.71 \times 0.28 \times 0.19\) mm, Triclinic, \(P\) (No: 2), \(a = 8.6708 (7)\), \(b = 9.6912 (8)\), \(c = 17.5162 (15)\) Å, \(\alpha = 83.094 (4)\), \(\beta = 86.066 (4)\), \(\gamma = 71.838 (2)\) °, \(V = 1387.7 (2)\) Å\(^3\), \(Z = 2\), \(D_x = 1.745\) g/cm\(^3\), \(\mu = 1.32\) mm\(^{-1}\). 20532 reflections were measured up to a resolution of \((\sin \theta/\lambda)_{\text{max}} = 0.596 \text{ Å}^{-1}\). 4892 reflections were unique \((R_{\text{int}} = 0.035)\), of which 4230 were observed \([I > 2\sigma(I)]\). 388 parameters were refined with 0 restraints. \(R1/wR2 [I > 2\sigma(I)]\): 0.0331/0.1093 \(R1/wR2 [\text{all refl.}]\): 0.0424/0.1240. \(S = 0.97\). Residual electron density between –0.48 and 0.44 e/Å\(^3\).

\(\text{Fe}_2(\text{bdt})(\text{CO})_4(\text{PPy})_3\) \(1\text{b}: C_{40}H_{28}\text{Fe}_2\text{N}_6\text{O}_4\text{P}_2\). \(Fw = 894.44\), dark red plate, \(0.39 \times 0.18 \times 0.10\) mm, Orthorhombic, \(P2_12_12_1\) (No: 19), \(a = 12.0635 (9)\), \(b = 17.3488 (14)\), \(c = 18.0217 (14)\) Å, \(V = 3771.7 (5)\) Å\(^3\), \(Z = 4\), \(D_x = 1.575\) g/cm\(^3\), \(\mu = 1.02\) mm\(^{-1}\). 31187 reflections were measured up to a resolution of \((\sin \theta/\lambda)_{\text{max}} = 0.598 \text{ Å}^{-1}\). 6713 reflections were unique \((R_{\text{int}} = 0.074)\), of which 5857 were observed \([I > 2\sigma(I)]\). 505 parameters were refined with 0 restraints. \(R1/wR2 [I > 2\sigma(I)]\): 0.0509/0.1128 \(R1/wR2 [\text{all refl.}]\): 0.0385/0.1014. \(S = 0.82\). Residual electron density between –0.34 and 0.70 e/Å\(^3\).

\(\text{Fe}_2(\text{F}_4\text{bdt})(\text{CO})_4(\text{PPy})_3\) \(3\text{b}: C_{41}H_{26}Cl_2\text{Fe}_2\text{N}_6\text{O}_4\text{P}_2\). \(Fw = 1051.34\), dark red plate, \(0.34 \times 0.11 \times 0.05\) mm, Monoclinic, \(C2/c\) (No: 15), \(a = 40.2484 (15)\), \(b = 11.9538 (4)\), \(18.7485 (7)\) Å, \(\beta = 109.875 (1)°\), \(V = 8483.0 (5)\) Å\(^3\), \(Z = 8\), \(D_x = 1.646\) g/cm\(^3\), \(\mu = 1.05\) mm\(^{-1}\). 29490 reflections were measured up to a resolution of \((\sin \theta/\lambda)_{\text{max}} = 0.595 \text{ Å}^{-1}\). 7476 reflections were unique \((R_{\text{int}} = 0.037)\), of which 5640 were observed \([I > 2\sigma(I)]\). 569 parameters were refined with 0 restraints. \(R1/wR2 [I > 2\sigma(I)]\): 0.1121/0.2706 \(R1/wR2 [\text{all refl.}]\): 0.0929/0.2500. \(S = 2.08\). Residual electron density between –1.30 and 2.98 e/Å\(^3\).
Appendix

Figure 23. IR spectra of complexes 1 (Fe₂(bdt)(CO)₆), 2 (Fe₂(Cl₄bdt)(CO)₆) and 3 (Fe₂(F₄bdt)(CO)₆) in hexanes.

Figure 24. IR spectra of complexes 1a (Fe₂(bdt)(CO)₅PPy₃), 2a (Fe₂(Cl₄bdt)(CO)₅PPy₃) and 3a (Fe₂(F₄bdt)(CO)₅PPy₃) in hexanes.
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Figure 25. Ir spectra of complexes 1b (Fe₂(bdt)(CO)₅(PPy₃)₂) and 3b (Fe₂(F₄bdt)(CO)₅(PPy₃)₂) in dichloromethane.

Figure 26. Ir spectra of complexes 1a (Fe₂(bdt)(CO)₅(PPy₃)), 2a (Fe₂(Cl₄bdt)(CO)₅(PPy₃)) and 3a (Fe₂(F₄bdt)(CO)₅(PPy₃)) in 1 M H₂SO₄.
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Figure 27. Ir spectra of complexes \(1b\) (Fe\(_2\)(bdt)(CO)\(_4\)(PPy\(_3\))\(_2\)) and \(3b\) (Fe\(_2\)(F\(_4\)bdt)(CO)\(_4\)(PPy\(_3\))\(_2\)) in 1 M H\(_2\)SO\(_4\).
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References

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