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Hemi-labile Bridging Thiolates as Proton Shuttles in Bio-inspired H₂ Production Electrocatalysts

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Abstract

Synthetic analogues and computationally assisted structure-function analyses have been used to explore the features that control proton-electron and proton-hydride coupling in electrocatalysts inspired by the [NiFe]-hydrogenase active site. Of the bimetallic complexes derived from aggregation of the dithiolato complexes MN₂S₂ (N₂S₂ = bismercaptoethane diazacycloheptane; M = Ni or Fe(NO)) with (η^{5} - C_5H_5)Fe(CO)⁺ (the Fe' component) or (η^5 - C_5H_5)Fe(CO)₂⁺, Fe", which yielded Ni-Fe'⁺, Fe-Fe'⁺, Ni-Fe"⁺, and Fe-Fe"⁺, respectively, both Ni-Fe'⁺ and Fe-Fe'⁺ were determined to be active electrocatalysts for H₂ production in the presence of trifluoroacetic acid. Correlations of electrochemical potentials and H₂ generation are consistent with calculated parameters in a predicted mechanism that delineates the order of addition of electrons and protons, the role of the redox-active, non-innocent NO ligand in electron uptake, the necessity for Fe'-S bond breaking (or the hemi-lability of the metallodithiolate ligand), and hydrideproton coupling routes. Although the redox active ${Fe(NO)}^7$ moiety can accept and store an electron and subsequently a proton (forming the relatively unstable Fe-bound HNO), it cannot form a hydride as the NO shields the Fe from protonation. Successful coupling occurs from a hydride on Fe' with a proton on thiolate S and requires a propitious orientation of the H-S bond that places H^+ and H^- within coupling distance. This orientation and coupling barrier are redox-level dependent. While the Ni-Fe' derivative has vacant sites on both metals for hydride formation, the uptake of the required electron is more energy intensive than that in Fe-Fe' featuring the non-innocent NO ligand. The Fe'-S bond cleavage facilitated by the hemi-lability of thiolate to produce a terminal thiolate as a proton shuttle is a key feature in both mechanisms. The analogous Fe"-S bond cleavage on Ni-Fe" leads to degradation.

Introduction

Heterobimetallic molecular compositions utilizing thiolate-sulfurs as bridges are widespread in biology, especially in the active sites of metalloenzymes such as the [FeFe]- and [NiFe]-H₂ase and Acetyl CoA Synthase.^{1,2} That these biocatalysts facilitate organometallic-like transformations, using first-row/abundant transition metals, has inspired chemists to address the features that control their mechanisms of action through the synthetic-analogue approach. Synergy between synthesis and theory has developed by linking the mechanistic interpretation of assays, such as electrocatalytic proton reduction or hydrogen oxidation in the active sites of the hydrogenases, with those of the model

complexes.³ While the structures of individual components of the biocatalysts that are site-isolated by the protein are clear, functional reproductions in small molecule models have not been entirely successful. The role of a pendant amine base nearby an open site on iron was determined to be critical to the remarkable rates of hydrogen production in the [FeFe]-H₂ase² and has been successfully used to design H⁺ reduction and H₂ oxidation electrocatalysts in nickel-based complexes outfitted with



the PNP- and P₂N₂-type ligands of Dubois, et al.³⁻⁸ Their team has also provided dramatic, *bona fide* examples of heterolytic H₂ cleavage products in $(\eta^5-C_5H_4R)Fe^{II}(P_2N_2)^+$ complexes, suggesting that the P₂N₂ ligand in structure I, and its pendant base capabilities, might be considered as a surrogate for the Ni(SR)₄ metalloligand in the [NiFe]-H₂ase active site.⁹⁻¹¹ Thus, while the catalytic center of [NiFe]-H₂ase does not have a pendant amine as operative base, there is structural support from high resolution protein crystallography that a terminal cysteinyl thiolate on the nickel might serve in that capacity.^{12,13} Such a suggestion was made earlier in the mechanistic study of Niu and Hall.¹⁴ Other persistent questions regarding the requirement of two metals in such active sites are as follows: Do they assist each other by dual electron storage? Does one tune the electronic character and redox potential of the other? Is a metallodithiolate biology's ultimate redox-active, non-innocent ligand?

There is an extensive class of bi- and polymetallic complexes derived from transition metals, largely Ni^{II}, in tetradentate $E_2S_2^{2-}$ (E = N, P, S) binding sites that use excess lone pairs on the cis thiolate



sulfurs for binding in a bidentate manner to an additional metal, M'.^{15,16} Analogous to the $(\eta^5-C_5H_4R)Fe^{II}(P_2N_2)^+$ complexes described above, myriad heterobimetallics have been reported in a developing area that uses η^5 -cyclopentadienide $(\eta^5-C_5H_5 \text{ or } \eta^5-C_5Me_5 \text{ , i.e., } Cp \text{ and } Cp^*,$ respectively) or η^6 -arenes bound to $d^6 Fe^{II}$ or Ru^{II} , as M', which in combination with the bridging dithiolates from the NiN₂S₂ may offer a

single open site for reactivity at M', structure II.^{15,17-22} The tunability at the pi-ligand offers some control for oxidative addition in stoichiometric reactions, including both H₂ and O₂ activation.²³⁻²⁶ Reports of proton reduction under electrochemical conditions by such CpFe^{II} or CpRu^{II} entities are scarce in the literature; however, there are examples of an S'₂NiS₂ (S' = thioether sulfur; S = thiolate sulfur) metalloligand bound to CpFe' and Cp*Fe' that demonstrated modest electrocatalysis and H₂ production.^{18,20} The MN₂S₂ platform offers opportunity to modify a metallodithiolate ligand by changing only the M, retaining consistency in steric features such that the S-donor and M'-acceptor effects might be deconvoluted. Thus, we have designed experimental and computational protocols to analyze the

proton reduction possibilities of the heterobimetallics represented in Figure 1, with focus on the potential sites for electron and proton uptake, the order of their addition, and the requirements for hemi-lability and S-protonation of the MN₂S₂ metallodithiolate ligands at various redox levels.

Results

Svnthesis and Characterization. Scheme 1 displays the synthetic protocol used to prepare the bimetallic complexes, $MN_2S_2 \cdot CpFe(CO)^+BF_4^-$ (M = Fe(NO), Ni, the Fe in CpFe(CO) is Fe'), Fe-Fe'⁺ and Ni-Fe'⁺, in this work. The reaction of MN_2S_2 and $[CpFe(CO)_2(Solv)]^+$, prepared in situ from CpFe(CO)₂I and AgBF₄ in CH₂Cl₂, at 22°C, formed an intermediate species $MN_2S_2 \cdot CpFe(CO)_2^+BF_4^-$, Fe-Fe^{"+} and Ni-Fe^{"+} (the Fe in CpFe(CO)₂ is Fe"). Subsequent photolysis released CO and permitted bidentate binding of the metallodithiolate ligands. While the intermediate species, Fe-Fe"⁺ and Ni-Fe"⁺,

Scheme 1. The synthesis of $Fe-Fe'^+$ and $Ni-Fe'^+$ complexes as BF_4^- salts. The IR frequencies of CO and NO are in red and blue respectively.



are light and air sensitive, the **Fe-Fe**^{*} and **Ni-Fe**^{*} complexes are isolated as intensely colored crystalline BF_4^- salts that are thermally and air stable in the solid form. Stringent conditions (CO pressure of 11 bar and 50°C) partially return the MFe^{*+} to the MFe^{**}, see Figure S9.

X-ray diffraction analysis of crystalline Ni-Fe'⁺, Fe-Fe'⁺, and Ni-Fe''⁺ revealed molecular structures with typical piano-stool geometry about the CpFe'(CO)⁺ unit and butterfly-like [M(μ -SR)₂Fe'] cores in the Ni-Fe'⁺ and Fe-Fe'⁺ derivatives, Figure 1. Specifically, the bridging thiolate sulfur lone pairs impose a hinge angle (the intersection of the best N₂S₂ plane with the S₂Fe' plane) of ca. 125°. The mesocyclic diazacycloheptane framework in the MN₂S₂ portion of each provides similar N---N and S---S distances, and $\angle_{S-Fe'-S}$ of ca. 82°. In the Fe-Fe'⁺ complex the NO is transoid to the CO on the CpFe' unit; the \angle_{Fe-N-O} angle is 163.8°. The M^{...}Fe' distance in Fe-Fe'⁺ and Ni-Fe'⁺ are 3.203(1) and 3.016(1) Å, respectively. In contrast, the Ni-Fe''⁺ dicarbonyl complex finds the NiN₂S₂ plane is shifted away from where it was in the Ni-Fe'⁺, opening the Ni–S-Fe'' bond angle to ca. 121.4(1)° from ca. 85.44(3)° in the Ni-Fe'⁺, and yielding a Ni-Fe'' distance some 0.7 to 0.9 Å greater than in the bidentate MN₂S₂-Fe' complex. The Fe"-S dative bond distance in Ni-Fe"⁺ is 2.285(3) Å and the non-bonded thiolate S is at 3.999(3)Å from the Fe".



Figure 1. Molecular structures of **Ni-Fe**^{**}, **Fe-Fe**^{*+}, and **Ni-Fe**^{*+} complexes. The BF₄⁻ ions are omitted for clarity. ^{*a*}Bonded sulfur. ^{*b*} Non-bonded sulfur. ^{*c*} Average M-S distance

While the Ni-Fe^{*+} complex is diamagnetic, the Fe-Fe^{*+} has S = 1/2, consistent with the wellknown {Fe(NO)}⁷ electronic configuration.^{27,28} The 298 K, X-band EPR spectrum, shows an isotropic triplet of g value = 2.04 with hyperfine coupling constant of 15.3 G, and only minor differences to the free metalloligand.²⁹ Details of the low- and variable field Mössbauer spectra of the M-Fe^{*+} and M-Fe^{**+} complexes will be presented and discussed in a separate study.

Electrochemistry: Cyclic voltammograms (CV) of BF₄⁻ salts of **Fe-Fe**^{*+}, Figure S30, and **Ni-Fe**^{*+}, Figure S34, were recorded at 22° C under Ar. All scans are referenced to internal Fc^{0/+} at $E_{1/2} = 0.0$ V. Full scans of both complexes initiated in the positive direction as well as peak isolation and scan rate dependence can be found in the SI, Figures S30-S37. On initiating the electrochemical scan in the cathodic direction, two reduction events, and, upon reversal, two oxidation events were observed for both complexes within the MeCN solvent window. The initial reductive event, at -1.64 V in the case of the **Ni-Fe**^{*+}, is assigned to the Ni^{II/I} couple; its irreversibility is addressed in the computational section below. In contrast, for the **Fe-Fe**^{*+} complex, the first reduction is quasi-reversible and at a more positive position, -1.19 V; it is assigned to the {Fe(NO)^{7/8} redox couple. In both cases, the first observed or more positive reduction event is anodically shifted compared to the MN₂S₂ (free metalloligand) precursors, thus illustrating the electron-withdrawing nature of the [CpFe'(CO)]⁺ unit and its ability to modulate redox events on the MN₂S₂ unit.^{28,30} The second, more negative, irreversible reduction event in the **Fe-Fe**^{*+} complex is assigned to the Fe^{*II/I} couple in the [CpFe'(CO)]⁺ unit. For the **Ni-Fe**^{*+} complex, assignment of the more negative event is not straight-forward due to the irreversibility of the previous redox event;

computational studies, *vide infra*, indicate an intramolecular Ni^I to Fe^{II} electron transfer concomitant with structural rearrangement accounts for this irreversible behavior.

Addition of trifluoroacetic acid (TFA) to the electrochemical cell containing Ni-Fe'+ or Fe-Fe'+ increases the current of the initial reduction events described above. [N.B. Methanesulfonic acid gave similar results as TFA, see figure S38 - S39, however considerable fouling of the electrode surface discouraged extensive studies with this acid.] For the Ni-Fe'⁺ complex, this current continues to increase with additional equivalents of TFA, Figure 2A, while for the Fe-Fe'⁺ complex the initial reduction event's current is saturated after addition of 12 equiv. of TFA, With greater than 6 Figure 2B. equiv. of TFA, a new peak at -1.66 V



Figure 2. CV of 2 mM A) **Ni-Fe'**⁺ and B) **Fe-Fe'**⁺ under Ar in CH₃CN solutions containing 0.1 M [${}^{t}Bu_{4}N$][PF₆] as supporting electrolyte with addition of equivalents of trifluoroacetic acid. C) An overlay of **Ni-Fe'**⁺ and **Fe-Fe'**⁺ in the presence of 50 equivalents of TFA as well as 50 equivalents of TFA in the absence of either catalyst. The dotted line denotes the potential applied during bulk electrolysis, -1.56 V.

appears for the **Fe-Fe'**⁺ complex and its intensity increases with additional equiv. of TFA. An overlay of both complexes after addition of 50 equiv. of TFA as well as TFA in the absence of either catalyst is displayed in Figure 2C. The large current enhancement was attributed to the catalytic production of H₂, which was quantified by bulk electrolysis studies described below. From the CV experiments, turnover frequencies (TOFs) of 69 s⁻¹ and 52 s⁻¹ (experimental barriers: 14.9 and 15.1 kcal/mol at 298.15 K by Eyring equation) and overpotentials of 938 mV and 942 mV for the **Fe-Fe'**⁺ and **Ni-Fe'**⁺ complexes respectively, were obtained.³¹⁻³³ The calculation of TOFs and overpotentials follows the approach described by Helm, Appel, and Wiese, see the SI for specifics.^{33,34} It is noteworthy to mention the overserved barrier is a comprehensive parameter reflecting the activation of electron transfer, proton transfer and intra-/inter-molecular processes throughout the catalytic cycle. It is often higher than the calculated barriers of intramolecular processes, *vide infra*. The H/D kinetic isotope effects on **Fe-Fe'**⁺ and **Ni-Fe'**⁺ turnover frequencies (*k*_H/*k*_D) were determined to be 1.46 and 1.56, respectively. While *k*_H/*k*_D

isotope effects are known to vary widely, these relatively low ratios are consistent with the likely involvement of metal-hydride species in the catalytic cycles.^{35 36}

 Electrocatalytic H_2 production: The headspace of the bulk electrolysis setup was analyzed for H_2 using gas chromatography after applying a constant potential at -1.56 V (dotted line in Figure 2) in the presence of catalyst and 50 equivalents of TFA. Due to the overlap of the background TFA peak and the catalytic peaks, the H_2 evolving from the acid itself must be deducted, Table S3. All values obtained are an average of three separate bulk electrolysis experiments. After 30 min of electrolysis with the **Ni-Fe'**⁺ catalyst, 0.98 ± 0.04 Coulombs (after acid subtraction) was passed through the solution resulting in a turn-over-number (TON) of 0.26 ± 0.01 with a Faradaic efficiency of 96.0 ± 2.9 % for H_2 production, Table S4. Similarly in the presence of the **Fe-Fe'**⁺ catalyst, passage of 1.29 ± 0.06 Coulombs through the solution gave a TON of 0.33 ± 0.02 with a Faradaic efficiency of 77.2 ± 7.9 % for H_2 , Table S5. These results confirm that the current enhancement in the cyclic voltammogram is in fact due to the reduction of protons to H_2 by the **Ni-Fe'**⁺ catalysts in the presence of TFA.

Computational investigation: assignment of redox events and mechanistic studies

The complexities of the cyclic voltammograms of the **Ni-Fe'**⁺ or **Fe-Fe'**⁺ complexes in the presence of added acid, which indicate the existence of protonated and/or rearranged species, stimulated computational studies as complements to electrocatalytic proton reduction studies. A minimum of two chemical steps (C steps, *i.e.* protonation) and two electrochemical steps (E steps, *i.e.* reduction) is required to produce H₂ from protons and electrons. The exact order of C and E steps depends on the pK_a of the acid vs. catalyst and the redox potential of the catalyst, respectively; they often take place in an alternating order to prevent the accumulation of charges.³⁷ To computationally construct the E and C steps in catalytic cycles, structures of the precursor complexes from x-ray diffraction were compared to the calculated structures as validity checks, Table S11; the redox potentials (E^0 vs. Fc^{+/0}) and relative acidities ($\Delta pK_a = pK_a$ (CatH) – pK_a (CF₃COOH)) of components were predicted by calculations. Alternative sites for location of the added protons were carefully examined to determine which sites were lowest in energy. Detailed methodology information and optimized geometries (*xyz* files) are deposited in the SI.

Computational approaches to electrocatalytic proton reduction mechanisms have become fairly standard,³⁷⁻³⁹ especially for biomimetics of the hydrogenase active sites. From protein crystallography the features of the protein ensconced molecular catalysts and second coordination spheres are readily apparent but their roles are just beginning to be firmly established.¹ Hence, our starting points for the predicted mechanisms lie in paths deemed reasonable for the biocatalysts and for previous studies of biomimics; structures are accepted or rejected according to comparative energies (E^0 and pK_a) and

activation barriers between structures. The bimetallic constitution of our complexes, $\mathbf{Fe}-\mathbf{Fe}^{*+}$ and $\mathbf{Ni}-\mathbf{Fe}^{*+}$ enables them to buffer electrons, with additional stabilization from the non-innocent ligands, particularly NO in the case of $\mathbf{Fe}-\mathbf{Fe}^{*+}$.²⁹ At some point, typically after reduction(s), a complex must be able to accept a proton, convert it into a hydride on the metal, be poised to react with an additional proton, located on some basic site, to yield H₂. Our model complexes, however, lack an obvious built-in pendant base to serve as a proton reservoir, a role played by the bridgehead amine in [FeFe]-H₂ase, ^{1,38,40-42} or a terminal thiolate in the [NiFe]-H₂ase active site.^{1,12,13} Instead, the hemi-labile bridging thiolates on $\mathbf{Fe}-\mathbf{Fe}^{*+}$ and $\mathbf{Ni}-\mathbf{Fe}^{*+}$ may dissociate one of two Fe'-S bonds; the veracity of such a mono-dentate S-bridging species is supported by the isolated $\mathbf{Ni}-\mathbf{Fe}^{*+}$ shown in Scheme 1. Such dissociation creates reactive sites both on S and Fe'; i.e., a Lewis acid-base pair that can be used as proton and hydride storage depots is generated. Interestingly, the possibility of conversion of a bridging thiolate into an available proton base was inspired by the early theoretical studies of the [FeFe]-H₂ase.^{38,43} The advent of semi-synthetic approaches



Figure 3. The calculated electrocatalytic cycles for H₂ production on **Fe-Fe**^{*} in the presence of TFA. The relative Gibbs free energies are provided in kcal/mol and the reference point (G = 0) resets after every reduction or protonation. The redox potentials (E) are reported in V with reference to the standard redox couple Fc^{+/0} and the relative acidities (ΔpK_a) are reported with reference to TFA. Note: superscripts DN and UP on S refer to the positioning of the proton in S-protonated species.

to biohybrids in recent years that unambiguously identified a bridgehead amine in the S to S linker of the diiron unit in [FeFe]-H₂ase has established the pivotal role of this pendant base in proton transfer, thus negating the requirement for Fe-S bond cleavage in such functionalized dithiolates. ⁴⁴⁻⁴⁷

Figures 3 and 4 display the calculated electrocatalytic cycles for H₂ production with Fe-Fe'+ and Ni-Fe^{*}, respectively, as electrocatalysts. Α description of the former is as follows. In the absence of added acid, the CV scans of Fe-Fe'⁺ show two reduction first quasievents; the

reversible one was calculated to be -1.11 V (exp. -1.19V) and is assigned to the Fe(NO) unit, i.e., the redox couple $\{Fe(NO)\}^{7/8}$ -Fe^{'II}. Such an assignment was confirmed by the IR shifts of the diatomic ligands (exp.: -57 and -23 cm⁻¹; calc'd -84 and -31 for NO and CO respectively, Figure S11, Table S12). The resulting neutral **Fe-Fe'** has a linear triplet $\{Fe(NO)\}^8$ moiety, formed by high spin Fe^{II} antiferromagnetically coupled to high-spin NO⁻.^{29,48} It may be further reduced irreversibly, calculated at - 1.99 V (exp. - 2.07 V), to **Fe-Fe'**⁻, in which one S-Fe' bond dissociates to accommodate the added electron on Fe' with a final redox level of $\{Fe(NO)\}^8$ -Fe'^{II}.

In the presence of TFA the first reduction event at -1.19 V in the cyclic voltammogram was observed to increase in current without shifting position. This behavior is explained by the reaction of TFA with the reduced **Fe-Fe'** state and its depletion, thus enhancing diffusion of **Fe-Fe'**⁺ into the double layer at the electrode. By calculations, the thiolate S was determined to be the optimal protonation site. Other possibilities (Table S9) were considered, including the iron-bound NO which would produce the HNO ligand. It was found however to be thermodynamically less likely and also non-productive for subsequent H₂ formation as a metal-hydride is needed for the H⁺/H⁻ coupling. Upon protonation on sulfur the bond cleavage at Fe'-S immediately follows, stabilizing the system by 3.7 kcal/mol. The ΔpK_a (vs. TFA) values for ring-closed (**Fe-Fe'-S^{HH+}**) and ring-opened (**Fe-Fe'-S^{UP}H⁺**) sulfur-protonated species are -5.6 and -2.7, respectively, indicating slightly unfavorable thermodynamic processes. Thus, excess acid is needed to drive the protonation of **Fe-Fe'**, explaining why the observed saturation of current enhancement requires multiple equivalents (> 12 equiv.) of added acid and rules out the possibility of an immediate second protonation on **Fe-Fe'-S^{UP}H⁺** (to **Fe-Fe'H-S^{DN}H²⁺**, $\Delta pK_a = -14.3$). Despite the increase in current response, the electrochemical event at -1.11 V (-1.19 V exp.) is not catalytic as this reduction potential is insufficient (*vide infra*) to pass a second electron and close the catalytic cycle.

A second current enhancement, which appears in CV scans with added acid at -1.66 V (shifted by 0.41 V from - 2.07 V in the absence of acid), suggests reactions of new species, **Fe-Fe'-S^{UP}H**⁺, generated by protonation. One should be reminded that the production of **Fe-Fe'-S^{UP}H**⁺ is energetically unfavorable such that the reduction event of **Fe-Fe'-S^{UP}H**⁺ observed at -1.66 V becomes dominant only with the presence of more than 6 equiv. of TFA. The reduction of **Fe-Fe'-S^{UP}H**⁺ has a calculated potential of -1.32 V, changing the Fe^{II} of Fe' to Fe^I, a redox state capable of converting a proton into a hydride. The direct product of reduction, **Fe-Fe'-S^{UP}H** (*G* =1.4 kcal/mol) may transform into a hydride-bearing species **Fe-Fe'H** (*G* =1.7 kcal/mol) via the S-H inversion species **Fe-Fe'-S^{DN}H** (*G* = 0 kcal/mol) traversing two low-lying transition states (*G* = 4.2 and 7.6 kcal/mol). The **Fe-Fe'H** species is at the {Fe(NO)}⁸-Fe'^{III} redox level as the electrons forming the iron-hydride are donated by Fe^I of the reduced Fe'.

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There are two pathways shown in Figure 3 for addition of the second proton. Although Fe-Fe'-S^{DN}H is the dominant species, the next protonation step, either on S of Fe-Fe'H or on Fe' of Fe-Fe'-S^{DN}H, produces the same thiol-hydride, Fe-Fe'H-S^{DN}H⁺ and both protonations are thermodynamically favored, with $\Delta p K_a$ values of 6.6 or 5.3 kcal/mol, respectively. The spatial positioning of the hydride and the proton on Fe-Fe'H-S^{DN}H⁺ allows the coupling reaction over a barrier of G = 11.6 kcal/mol. The resulting H₂ σ -complex Fe-Fe'H₂⁺ then overcomes another barrier at G = 12.0 kcal/mol to dissociate H₂ and to regenerate the catalyst Fe-Fe'⁺. This catalyst cycle thus closes with an [ECEC] mechanism. This mechanism uses the thiolate sulfur as a proton relay. One may argue TFA may directly deliver the proton to the hydride of Fe-FeH' to accomplish an intermolecular coupling to form Fe-FeH₂⁺, skipping the intermediate Fe-FeH-S^{DN}H'⁺. The relatively high barrier at 16.2 kcal/mol (Figure S43) renders this



Figure 4. The calculated electrocatalytic cycles for H₂ production on Ni-Fe⁺ in the presence of TFA; see caption of Figure 3 for additional description. The Gibbs free energy of the barrier between Ni-Fe[']H₂ and Ni-Fe', G = -4.6 kcal/mol, as marked with an asterisk, is lower than that of Ni-Fe[']H₂, G = 1.2 kcal/mol. This is caused by the preference of solvation correction over the transition state. This transition may be accepted as barrierless.

possibility less likely. In contrast the delivery of proton into the sulfur open site only incurs a negligible barrier (Figure S43).

Alternatively, Fe-Fe'H-S^{DN}H⁺ may accept a third electron at a redox potential of -1.27 V and the highest reaction barrier for H_2 formation dramatically drops to 4.9 kcal/mol. In this case the reduced Fe-Fe' is regenerated instead of Fe-Fe'⁺ and closes an E[CECE] working catalytic cycle, in which the first reduction event essentially serves as an activation step. According to the calculations, the current enhancement with the associated second reduction event at -1.32 V (calc'd; observed at -1.66 V) is

considered to be catalytic and productive in either the slow or fast catalytic cycle as subsequent reduction events are all calculated to be less negative than -1.32 V.

The nickel species **Ni-Fe'** has mechanisms similar to those of **Fe-Fe'**⁺ with a few exceptions, Figure 4. The first reduction of **Ni-Fe'**⁺ is initially localized on the NiN₂S₂ moiety with its four-membered Ni(μ -SR)₂Fe' unit intact as was that of **Fe-Fe'**. However, the four-coordinate nickel lacks the electronic flexibility of Fe(NO) in **Fe-Fe'** and can only accommodate the added electron on nickel's highly destabilized antibonding $d_{x_{2}-y_{2}}$ orbital, achieving an oxidation state of Ni¹-Fe'^{II} in **Ni-Fe'***. As a result the calculated redox potential rises significantly to -2.00 V (exp. -1.64 V). Following the reduction, one S-Fe bond of the Ni(μ -SR)₂Fe' core breaks to open the Ni-S₂-Fe' ring. The electron previously added to the nickel is concomitantly transferred to the unsaturated (16-e⁻) Fe' with bond cleavage, bringing the electron counts back to a 16-e⁻ Ni^{II} and a 17-e⁻ Fe^I. This arrangement stabilizes the ring-opened species **Ni-Fe'** by 1.0 kcal/mol, accounting for observed irreversibility of the CV event. The experimental IR shift, -157 cm⁻¹ (Figure S10), upon the reduction of **Ni-Fe'⁺**, confirms **Fe-Fe'** (calc'd shift: -127 cm⁻¹, Table S12) is the reduced product, rather than **Fe-Fe'*** (calc'd shift: -43 cm⁻¹).

In the absence of acid, following the ring-opening process and intramolecular charge transfer, the successive reduction on **Ni-Fe'** puts the second electron again within the Ni^{II/I} couple. The calculations also affirm that the first redox potential is more negative than that of any subsequent steps in the catalytic cycles in the presence of TFA (Figure 4), so that the CV current enhancement at -1.64 V is acknowledged as catalytic. The follow-up protonation on **Ni-Fe'** goes directly to the reduced Fe' rather than S as the Fe^I has sufficient electron density to convert the proton into a Fe^{III}-hydride. The next steps are similar to those of **Fe-Fe'**⁺ in Figure 3. The **Ni-Fe'**⁺ may also have two working catalytic cycles, either [ECEC] or E[CECE] depending on the occurrence of a non-mandatory, third reduction event.

The homoconjugation of TFA,^{31,49} *i.e.* the stabilization of the conjugate base TFA⁻ by another molecule of H-TFA, was evaluated by calculations to enhance the the acidity by - 5.6 p K_a units (exp. - 3.9)³¹ on standard conditions. The acidity increase, though less significant when the acid concentration is low, may further facilitate these protonation processes outlined in Figure 3 and 4 at the cost of faster depletion of the available acid on the electrode surface. However, it may not be able to activate another route. An immediate second protonation requires a much stronger acid, *vide supra*.

By proceeding along the predicted mechanistic pathway, the mono-dentate species, Ni-Fe^{**}, breaks its single Fe-S bond upon reduction and the complex decomposes, as experimentally observed. The cleaved fragment, the \cdot FeCp(CO)₂ radical, is also catalytically active for H₂ production before its fast deactivation by dimerization.⁵⁰

Discussion

This work provides a paradigm for deconvoluting electrocatalytic proton-reduction mechanisms in dithiolate bridged bimetallics. Salient points to be made regarding the mechanistic features of the two $[MN_2S_2 \cdot CpFe(CO)]^+$ electrocatalysts are as follows:

• The initial electron uptake is at the M in the N₂S₂ pocket, rather than the CpFe'(CO)⁺, for both $M = Ni^{II}$ and {[Fe(NO)}⁷; the latter however presents a softer, delocalized landing for the electron, without permitting subsequent Fe-H formation, as the iron is not adequately basic (Table S9). Another key difference lies in the fact that the added electron is stored on the {[Fe(NO)}⁸ unit (within the Fe(NO)N₂S₂ metallo-ligand) throughout the catalytic cycle rendering that unit a "redox-active, spectator ligand"⁵¹ to the reactive center, the CpFe(CO) unit, in the preferred E[CECE] path. In contrast, the first-formed Ni¹N₂S₂ readily transfers its electron to Fe', with Ni^{II}-(μ -SR)₂-Fe¹' ring opening in advance of protonation. Thus, the Ni^{II} in the mono-dentate NiN₂S₂ metalloligand cannot accept a proton to form a Ni-H bond resembling the recent NMR characterized Ni-bound hydride in a Ni-R model, which contains a non-innocent ligand with Ni to buffer the electron.⁵² Besides, Fe is also protected from the proton by open sites on S and on reduced Fe'.

• The hemi-lability of the MN_2S_2 metallo-ligand, necessary for producing an open site on the active iron of the CpFe' unit (a site that is occupied by CO in the **Ni-Fe''**⁺ congener or procatalyst), as well as an available S-base site, is facilitated by reduction of the dithiolate bridged bimetallic.



Figure 5. Species featuring proximate proton-hydride pairs and the comparisons of H^+ - H^- distances. The τ value, a measure of square pyramid ($\tau = 0$) vs. trigonal bipyramid ($\tau = 1$) geometry in the

A further role for this hemi-lability is displayed in the mono-dentate bridging thiolate bound to the Fe^{,III}hydride in **Fe-Fe'H-S^{DN}H**⁺. The Fe^{,III} with a formal electron count of 17 is able to accept partial donation from an available π -donor pair on S, serving as a σ + π ligand, while Fe^{,III} in **Fe-Fe'H-S^{DN}H**⁺ is completely saturated and the S is merely a σ -donating ligand. (See Table S10 for Fe'-S bonding analysis.) This additional π bonding in the oxidized **Fe-Fe'H-S^{DN}H**⁺ species is exemplified by its short Fe'-S bond distance at 2.230 Å that elongates to 2.342 Å upon reduction to the **Fe-Fe'H-S^{DN}H** species.

• The H₂ evolution from the di-protonated, doubly or triply reduced species requires optimally oriented protonated thiol and iron hydride. In this regard it is instructive to compare H⁺---H⁻ distances in our calculated intermediate thiol-hydrides with experimental data from the doubly protonated $P_2N_2FeCpR(CO)$ complex of Liu, et al.,¹⁰ Figure 5, finding concurrence in the reduced **Fe-Fe'H-S^{DN}H** form (1.486Å) with that found in the amine pendant base complex (1.489 Å). Note that reduction of Fe- $Fe'H-S^{DN}H^+$ shortens the H⁺---H⁻ distance from 2.634Å to 1.486Å via structural shifts in the Fe(NO)N₂S(SH) metalloligand, involving both a rotation around the Fe'-S bond as well as a small change in the τ parameter⁵³ that defines the extent of square pyramid vs. trigonal bipyramid character in the Fe(NO)N₂S(SH) unit. These changes push the proton-hydride pair into a close position, creating an early transition state according to Hammond's postulate,⁵⁴ amenable for H₂ elimination via the E[CECE], low barrier path. In contrast at 2.634Å the H⁺/H⁻ coupling following the [ECEC] mechanistic path must surmount a much higher barrier. Note that the H^+ --- H^- coupling distance in the Fan and Hall calculated mechanism for proton reduction in the [FeFe]-H₂ase active site is 1.472Å, remarkably consistent with the experimental value from structure I, and the calculated value (1.486Å) for our reduced diprotonated intermediate **Fe-Fe'H-S^{DN}H** in Figure 5.³⁶ Notably, the proton/hydride pair recently characterized in the Ni-R state of the [NiFe]-H₂ase active site is at 2.45Å,¹² a distance related to the intermediate in our slow route for H₂ production, and perhaps consistent with the [NiFe]-H₂ase enzyme's bias towards H₂ uptake and oxidation rather than production.

In conclusion, the well-studied P_2N_2 ligand of Dubois, et al.⁴ has control of optimal proton placement via the chair/boat interconversion of the six-membered FeP₂C₂N cyclohexane-like ring described in Figure 5,¹⁰ a feature that was exploited in the design and development of further generations of the Ni(P₂N₂)₂ catalyst(s) and presaged by Nature's azadithiolate bidentate bridging ligand in the [FeFe]-H₂ase active site.¹ The heterobimetallics explored herein demonstrate the possibility for very stable bidentate ligands based on metallodithiolates (a metal-tamed S-donor or Nature's version of a phosphine P-donor) that respond to an electrochemical event by switching a coordinate covalent bond into a Lewis acid-base pair and concomitantly placing a proton and hydride within an optimal coupling distance. Easily accessible molecular motions and coordination sphere distortions are available to render the tethered thiolate into a pendant base of greater activity for proton delivery to the metal-hydride. The opportunities for tuning catalysts according to this approach lie both on the metal responsible for the hydride activity and, as we have also shown, the metal that holds and orients the pendant base. Our future plans are to optimize the catalysts via the bidentate S-M-S angle and to pursue experimental evidence for the thiol-hydride pair.

Supporting Information

Experimental, additional spectroscopic, electrochemical and computational details, X-ray crystallographic data (CIF) from the structure for complexes **Fe-Fe'**⁺, **Ni-Fe'**⁺, **Ni-Fe'**⁺, and computational *xyz* files. This material is available free of charge via the Internet at http://pubs.acs.org.

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