

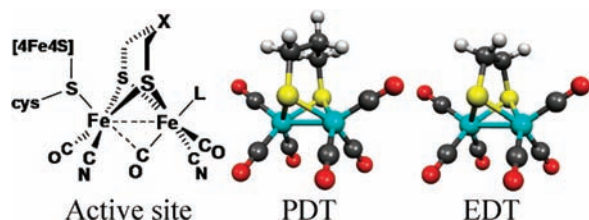
## One- to Two-Electron Reduction of an [FeFe]-Hydrogenase Active Site Mimic: The Critical Role of Fluxionality of the [2Fe2S] Core

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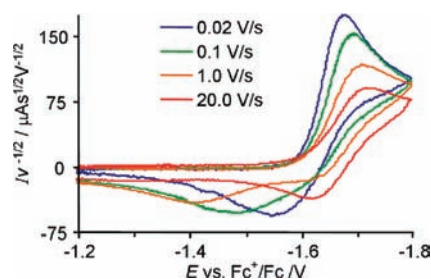
Iron–sulfur clusters mediate numerous electron transfer and reduction/oxidation (redox) processes in Nature.<sup>1</sup> In the important example of [FeFe]-hydrogenase enzymes, [4Fe4S] cluster cubanes transfer electrons through a cysteinyl sulfur to a [2Fe2S] cluster that is in a butterfly arrangement (Figure 1).<sup>2</sup> The [2Fe2S] cluster



**Figure 1.** A generalized representation of the active site of [FeFe]-hydrogenase enzymes and the active site mimics  $\mu$ -(SCH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>S)Fe<sub>2</sub>(CO)<sub>6</sub> (PDT), and  $\mu$ -(SCH<sub>2</sub>CH<sub>2</sub>S)Fe<sub>2</sub>(CO)<sub>6</sub> (EDT).

then serves as the active site for reversible reduction of protons to molecular hydrogen.<sup>3</sup> Because the development of robust, inexpensive, and efficient catalysts for production of hydrogen would be a major step toward a sustainable, carbon-free energy economy, synthetic complexes inspired by this active site are receiving much attention.<sup>4</sup> Even the simplest of these active site mimics,  $\mu$ -(1,3-propanedithiolato)diironhexacarbonyl (PDT) and  $\mu$ -(1,2-ethanedithiolato)diironhexacarbonyl (EDT), shown in Figure 1, provide complex chemical cycles of electron/proton uptake on the route to hydrogen production.<sup>5–7</sup> This work reports a cyclic voltammetry (CV) study of one of the simplest hydrogenase active site mimics, EDT, in which variable electron uptake with scan rate is observed. Through analysis of this rate dependence we have discovered evidence for a dynamic fluxionality and distortion of the [2Fe2S] core that facilitates uptake of the second electron at a potential less negative than that for uptake of the first electron (known as potential inversion). This structural rearrangement of the [2Fe2S] core offers an alternative to the current paradigm for the production of molecular hydrogen using these types of systems, as it is generally considered that the butterfly [2Fe2S] structure is largely conserved throughout the redox processes.

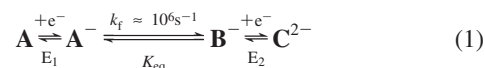
PDT has been reported to undergo a slightly greater than one-electron reduction at very slow scan rates (0.04 V/s).<sup>7</sup> In contrast, reduction of EDT at different scan rates encompasses a full range of electron uptake, from one electron to two electrons, smoothly transitioning between the extreme cases (see Figure 2 and Supporting Information (SI)). The two-electron process is attributed to a potential inversion and suggests a substantial intramolecular structural rearrangement.<sup>8</sup> The rate of transition to the two-electron process increases with increasing temperature (temperature studies shown in SI-9 to SI-12), indicating that there is a slight activation energy along the path of the structural transformation that leads to potential inversion.



**Figure 2.** Scan rate variation voltammograms of 1.0 mM EDT in CH<sub>3</sub>CN containing 0.10 M Bu<sub>4</sub>NPF<sub>6</sub> on a glassy carbon working electrode (GCE), under a CO atmosphere.

The ability to observe the shift from a one-electron to a two-electron process as the scan rate is slowed depends on the time scale of several possible processes, and EDT presents a fortuitous situation. Both spectroelectrochemistry (SEC)<sup>9</sup> and chemical synthesis indicate that a dimer is the ultimate product of reduction of PDT and EDT; however, this process is retarded under the conditions of this experiment with a CO atmosphere,<sup>7,10,11</sup> and the varied degradation and dimerization pathways of EDT for the most part have not had time to occur.<sup>10</sup> Nonetheless, as an additional check of possible bimolecular processes, the reduction of EDT was studied at varied concentrations of the complex (see SI-4–8). A second-order reaction would yield a 9-fold change in rate upon the trebling of concentration, but there is essentially no change in the one-electron to two-electron process.

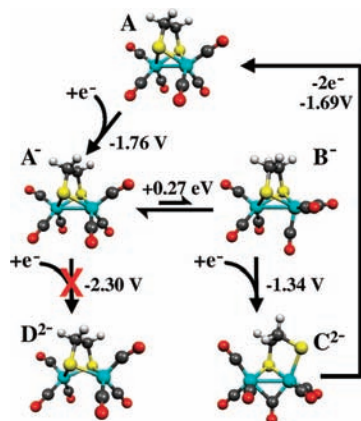
On the time scale of these electrochemical measurements of EDT the simplest representation for a mechanism that is consistent with the scan rate and temperature dependence has the general form of eq 1. Here species **A** is reduced by one electron to species **A**<sup>−</sup>, which in its initial form can only accept a



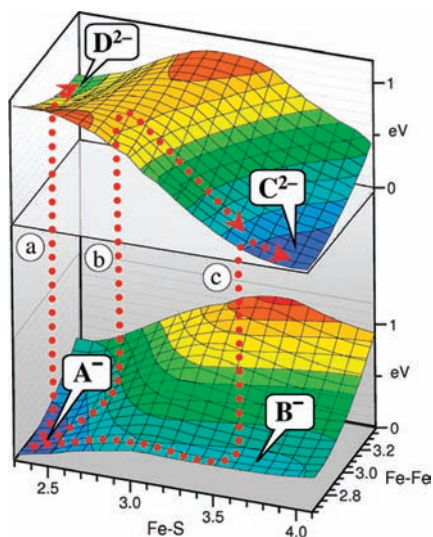
second electron at a potential more negative than  $E_1$ . In this mechanism species **A**<sup>−</sup> can kinetically undergo a transformation and reach equilibrium with a structure **B**<sup>−</sup> that is at higher energy than **A**<sup>−</sup>, but which can accept a second electron at a potential  $E_2$  that is less negative than  $E_1$  to proceed to **C**<sup>2−</sup>. The scan-rate and temperature dependence of the two-electron process depends on the kinetic and thermodynamic relationships of species **A**<sup>−</sup> and **B**<sup>−</sup>.

DFT computations that have been successful in modeling the physical and chemical properties of this and related molecules (see SI) give insight into the possible structures and relative free energies of the species in this mechanism.<sup>12</sup> The key results are shown in Scheme 1 for structures at optimal points on the potential energy surfaces of the one-electron and two-electron reduction events.

**Scheme 1.** DFT Optimized Pathways for the Primary Reduction Events of EDT



These structures and their relative energies are similar to those described in more detail in a previous report.<sup>10b</sup> Structure A is the optimized structure of the neutral EDT catalyst. The initial one-electron reduction, calculated here to occur at  $-1.76$  V, yields structure  $A^-$ . By cluster electron counting rules, the addition of electrons to the butterfly [2Fe2S] structure of the neutral molecule should lead to a lengthening or breaking of a cluster bond. Typically this involves opening of the butterfly arrangement toward a square arrangement, most often by lengthening of a metal–metal bond.<sup>6,13</sup> Consistent with this model, the Fe–Fe distance in  $A^-$  is  $2.79$  Å compared to  $2.51$  Å in A. Direct reduction of  $A^-$  gives structure  $D^{2-}$  with a very long  $Fe\cdots Fe$  distance of  $3.35$  Å. However, the reduction potential to this structure from the anion  $A^-$  is calculated to be  $-2.30$  V, a value much too negative to account for the potential inversion and two-electron process observed at slow scan rates. Instead, as the potential energy surfaces in Figure 3 show, the anion  $A^-$  can alternatively distort to structure  $B^-$ . Reduction from structure  $B^-$  strongly favors the lengthening and breaking of an Fe–S bond and the movement of a carbonyl ligand to a fully



**Figure 3.** Segments of the potential energy surfaces of the anion (bottom) and dianion (top) of EDT as a function of the Fe–S and Fe–Fe distances in Å (see SI for computational details). Reduction from near the optimum structure of  $A^-$  at high negative potential leads to structure  $D^{2-}$  with a long  $Fe\cdots Fe$  distance as shown by path (a), whereas reduction from structures of  $A^-$  distorted toward  $B^-$ , as shown by paths (b) and (c), leads to structure  $C^{2-}$  with a long  $Fe\cdots S$  distance, a bridging carbonyl ligand, and potential inversion.

bridging position shown by the structure of  $C^{2-}$  in Scheme 1. Potential inversion will occur for any structure of the fluxional anion that reduces to a point on the potential energy surface of the dianion within the well of structure  $C^{2-}$ , as shown in Figure 3. The calculated potential for the second reduction of EDT from structure  $B^-$  to structure  $C^{2-}$  is  $-1.34$  V compared to  $-1.76$  V for the first reduction from A to  $A^-$ , showing strong potential inversion.

The free energies determined by the calculations for this mechanism are consistent with the potentials, equilibrium constants, and rate constants obtained from simulation of the electrochemical data (see SI). The rate constant  $k_f$  obtained from the simulation for the transformation of  $A^-$  to  $B^-$  is  $\sim 10^6$  s<sup>-1</sup>, which indicates a fluxional molecule. The combination of the rate and equilibrium constant for the process  $A^- \rightleftharpoons B^-$  is consistent with the free energy surface between these species obtained from the electronic structure calculations shown in Figure 3.

The facile two-electron reduction made possible by the fluxionality of the metal carbonyl and the lengthening of an Fe–S distance in the [2Fe2S] core allows an increase in electron richness in the metal–sulfur cluster without an increase in the reduction potential for this class of molecules. There is no suggestion in the biophysical literature that the [FeFe]-hydrogenase sites operate at these highly reduced states, but the fluxionality of the iron–sulfur core may be an important factor in the redox behavior and catalytic activity of other iron–sulfur clusters. Further studies on other molecules are underway.

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**Supporting Information Available:** Experimental procedures, computational details, and CV data and simulations. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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