

## Exploring the feasibility of N<sub>2</sub> fixation at single and multiple iron sites

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A key longstanding goal of coordination chemistry is to map the types of metal complexes that can be anticipated to have reasonable stability and to elucidate their reactivity patterns. Such information drives to the heart of mechanistic postulates for transformations that occur in metalloenzymes as complicated as nitrogenase. Of central interest to hypotheses concerning the possible roles for iron and/or molybdenum in biological nitrogen fixation are the accessible geometries and oxidation states of proposed intermediates along the reduction pathway. Inorganic coordination chemistry can play a critical role with respect to expanding our understanding of the N<sub>2</sub> chemistry available to both iron and molybdenum, and in testing the validity of chemical assumptions that are inherent to a given mechanistic pathway.

The presence of a single molybdenum center in the FeMo-cofactor, in addition to a wealth of structurally diverse functional model systems, has reinforced the suggestion that a single molybdenum site may be responsible for mediating N<sub>2</sub> uptake and reduction in FeMo-N<sub>2</sub>ase. Particularly attractive is a scheme akin to that originally put forward by Chatt<sup>1</sup> and later modified by Pickett<sup>2</sup> in which a vacant Mo<sup>III</sup> site, perhaps generated via homocitrate dechelation under electron loading conditions, binds N<sub>2</sub> to mediate its successive reduction to NH<sub>3</sub> by the successive transfer of protons and electrons. Significant in this regard is the recent work of Schrock and coworkers, elegantly detailed in his lecture at this conference, who have demonstrated that such a cycle can be accomplished in a small molecule synthetic system.<sup>3</sup> They have suggested that certain triamidoamine-supported molybdenum complexes are capable of catalytically shuttling between the various oxidation states Mo<sup>III</sup>/Mo<sup>IV</sup>/Mo<sup>V</sup>/Mo<sup>VI</sup> as nitrogen is taken-up and reduced to ammonia.

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<sup>1</sup> Chatt, J.; Dilworth, J. R.; Richards, R. L. *Chem. Rev.* **1978**, *78*, 589-625.

<sup>2</sup> Pickett, C. J. *J. Biol. Inorg. Chem.* **1996**, *1*, 601-606.

<sup>3</sup> Yandulov, D. V.; Schrock, R. R. *Science* **2003**, *301*, 76-78.

A related nitrogen reduction cycle that emphasizes iron as the key substrate binding site, rather than molybdenum, has also been proposed.<sup>4</sup> The proposed scheme mirrors that of the molybdenum postulate, but in this case invokes a hemi-labile role for the central light atom (located by the Rees group), rather than the homocitrate ligand. This hemi-lability serves to expose a low-valent iron site for N<sub>2</sub> uptake under electron loading conditions. Such a scenario would set the stage for the further reduction of N<sub>2</sub> to ammonia, perhaps via a Chatt-type Fe<sup>IV</sup> redox cycle based upon iron, or some bifurcating pathway wherein the chemical reduction path diverges to two or more iron centers subsequent to the initial N<sub>2</sub> binding/reduction step. Several suggestive intermediates are sketched out in the figure below to underscore each possibility. Depending on the degree to which the linkage between iron and the central light atom is broken during the cycle, both 4- and/or 5-coordinate complexes should be considered as appropriate starting points for model chemistry.

In this context, our own group has recently developed 4- and 5-coordinate, phosphine-rich iron systems.<sup>5,6,7</sup> While our use of phosphine co-ligands departs from the sulfur-rich environment of the cofactor, phosphines have so far proven uniquely reliable for generating the well-defined N<sub>2</sub> and N<sub>x</sub>H<sub>y</sub> iron complexes of interest to us.

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<sup>4</sup> Peters, J. C.; Mehn, M. P. In *Activation of Small Molecules*; Tolman, W. B., Ed.; Wiley: New York, **2006**, p 81-120.

<sup>5</sup> Hendrich, M. P.; Gunderson, W.; Behan, R. K.; Green, M. T.; Mehn, M. P.; Betley, T. A.; Lu, C. C.; Peters, J. C. *Proc. Natl. Acad. Sci. U. S. A.* **2006**, *103*, 17107

<sup>6</sup> (a) Brown, S. D.; Betley, T. A.; Peters, J. C. *J. Am. Chem. Soc.* **2003**, *125*, 322-323. (b) Betley, T. A.; Peters, J. C. *J. Am. Chem. Soc.* **2003**, *125*, 10782-10783. (c) Betley, T. A.; Peters, J. C. *J. Am. Chem. Soc.* **2004**, *126*, 6252-6254.

<sup>7</sup> Mankad, N. P.; Whited, M. T.; Peters, J. C. *Angew. Chem. Int. Ed.* **2007**, *47*, 5768.

The platforms we have developed exhibit (i) an unusual degree of redox flexibility for mononuclear iron systems, (ii) a fascinating propensity to populate low spin ground state configurations for pseudotetrahedral  $\text{Fe}^{2+}$ ,  $\text{Fe}^{3+}$ , and  $\text{Fe}^{4+}$  species, and (iii) a capacity to accommodate both strongly  $\pi$ -basic (e.g.,  $\text{N}^{3-}$ ,  $\text{NR}^{2-}$ ),  $\pi$ -acidic (e.g.,  $\text{N}_2$ ), and intermediate type (e.g.,  $\text{N}_2\text{R}^-$ ,  $\text{NR}_2^-$ ) ligands at a single coordination site. Collectively, these properties suggest that it should, in principle, be possible to identify a synthetic

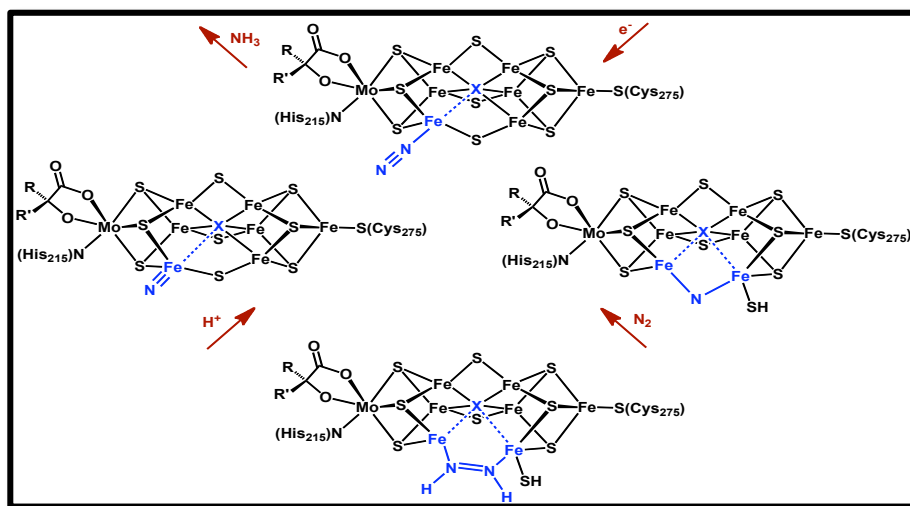


Figure 1. Line drawing representation of the FeMo-cofactor of nitrogenase schematically illustrating single-site and two-site iron-mediated pathways for nitrogen reduction. A role for the central light atom of the cluster (X) is suggestively forwarded as a hemi-labile ligand that exposes a reactive iron center upon partial or complete dissociation.

catalyst system that emphasizes a single iron site.

As a complementary path of study, we have more recently undertaken the study of bimetallic iron systems that accommodate reduced forms of nitrogen in varying states of oxidation at a position that bridges the two iron centers. For example, such systems include hydrazine ( $\text{N}_2\text{H}_4$ ), hydrazido ( $\text{N}_2\text{H}_2^{2-}$ ), diazene ( $\text{N}_2\text{H}_2$ ), amide ( $\text{NH}_2^-$ ), and imide ( $\text{NH}^-$ ) ligands.<sup>8</sup> It is plausible, and perhaps even likely, that the  $\text{N}_2$  substrate will sample both single site and diiron site binding modes as it traverses its path to complete reduction to ammonia.

While molybdenum model systems remain the best-studied and most mature class of synthetic complexes that mediate the reduction of nitrogen to ammonia, our view is

<sup>8</sup> Saouma, C. T.; Müller, P.; Peters, J. C. *J. Am. Chem. Soc.* **2009**, *131*, 10358.

that the stage is well set for synthetic iron systems to be placed on a similar footing. Clearly, success in this regard will depend on the many design details, and a bit of luck no doubt. But the ubiquitous presence of iron in all nitrogenase (and hydrogenase) cofactors, in addition to the rich biochemical and spectroscopic data now available,<sup>9</sup> provide ample impetus to focus on the possibility that iron plays a key catalytic role in biological nitrogen fixation.

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<sup>9</sup> Dean, D. R.; Hoffman, B.M.; Seefeldt, L.C. *Biochemistry* **2007**, *46*, 6784.