Nitrogen Fixation

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Catalytic Ammonia Synthesis in Homogeneous Solution—Biomimetic at Last?

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Substantial advances in nitrogen fixation apparently occur every decade. Perhaps the best illustration of this conjecture is provided by the elucidation of the structure of the iron molybdenum cofactor (FeMoco), the reactive center of the enzyme nitrogenase at which dinitrogen is reduced to ammonia. The first crystal structures of the molybdenum iron protein appeared in 1992, showing the FeMoco as an assembly of two defect Fe_4S_3 and $MoFe_3S_3$ cubane units connected by three μ_2-sulfido bridges (Figure 1).[1] The

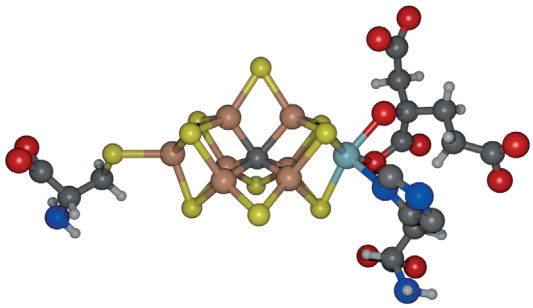

Figure 1. Structure of the FeMoco of nitrogenase with the interstitial C atom and terminal ligands (homocitrate and histidine on Mo, cysteine on Fe); C gray, O red, N blue, S yellow, Fe brown, Mo light blue, H light gray.

remarkable feature of this structure that inspired many synthetic and theoretical chemists was the fact that iron appeared to be three-coordinate. Ten years later, in 2002, it was found that an atom X at the center of the cluster had been overlooked (X = C, N, or O),[2] and thus the iron centers of the FeMoco were assigned the more conventional tetracoordination. Again almost ten years later, in 2011, X was shown to be C.[3] While this finding first appeared even more surprising than the empty cavity of the initial structure, we are now beginning to learn how this "interstitial" C atom is incorporated into the FeMoco.[4]

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Major breakthroughs regarding the homogeneously catalyzed synthesis of ammonia from N_2 under ambient conditions, in analogy to nitrogenase, appear to occur in similar time intervals. A fundamental discovery in this respect was certainly the cyclic generation of ammonia based on a tungsten dinitrogen complex published in 1985 by Pickett and Talarmin.[5] Although at that time already more than twenty years of research had been dedicated to nitrogen fixation in solution,[6] this paper for the first time established a clear connection between a set of well-defined nitrogen-containing intermediates (in this case making up the "Chatt cycle") and a cyclic, potentially catalytic formation of ammonia in homogeneous solution through the transfer of protons and electrons to such species. The actual activity of the system was, however, low (yield 0.73 mol NH_3 per W atom after three cycles). It was only at the beginning of the new millennium (2003), about twenty years after Pickett and Talarmin's seminal study, that the first truly catalytic ammonia synthesis in homogeneous solution was established. Based on a molybdenum triamidoamine system, Yandulov and Schrock were able to demonstrate the formation of ammonia from N_2 with a turnover number (TON) of 4 using a special lutidinium salt as an acid and decamethylchromocene as a reducing agent.[7] In 2011 Nishibayshi and co-workers increased the turnover number of a catalytic model system of nitrogenase to 12, again on the basis of a molybdenum complex.[8]

A potentially disappointing aspect of the Schrock, Nishibayashi, and Chatt systems was, however, that they were entirely abiological and in no way related to nitrogenase, except for the fact that they contained molybdenum. Nowadays it is considered very unlikely that N_2 is bound to this metal in the FeMoco, and dinitrogen is rather assumed to coordinate to the iron atoms of the central trigonal prism of the FeMoco (cf. Figure 1).[9] It was therefore difficult to draw conclusions from the reactive cycles of the model systems to apply to the mechanism of nitrogenase, which is still far from being fully understood.[9] From that perspective it is highly welcome that now, ten years after Yandulov and Schrock's *Science* paper, Peters and co-workers have published the first catalytic ammonia synthesis in homogeneous solution based on an iron complex, making it possible to relate these inorganic model systems more closely to the enzyme.[10]

In the last years the Peters group has been involved in the synthesis and reactivity of iron dinitrogen complexes with tripodal phosphine ligands. In particular, tris(phosphine)

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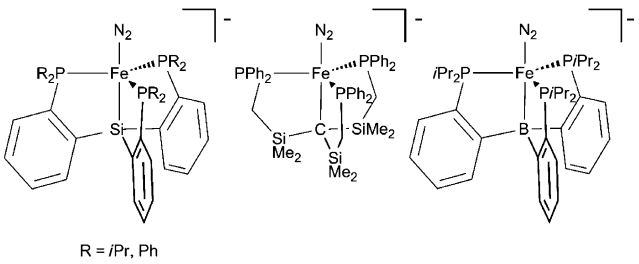
ligands with central silyl, carbon, and boron groups have been investigated.[10,11] Iron dinitrogen complexes with the corresponding [SiP^R_3], [$C^{Si}P^{Ph}_3$], and tris(phosphino)borane (TBP) ligands are shown in Scheme 1. It is with the last system (Scheme 1, right) that the catalytic generation of ammonia



Scheme 1. Iron dinitrogen complexes $[Fe(N_2)(SiP^R_3)]^-$ (R = *i*Pr, Ph), $[Fe(N_2)(C^{Si}P^{Ph}_3)]^-$, and $[Fe(N_2)(TBP)]^-$ (from left to right).

from N_2 could be effected. To this end the Fe^0 complex $[(TBP)Fe(N_2)][Na(12\text{-crown-}4)_2]$ was suspended in diethyl ether at −78 °C, followed by the sequential addition of excess acid ($HBAr^F_4 \cdot 2\,Et_2O$; $BAr^F = B[3,5\text{-}(CF_3)_2C_6H_3]_4$) and excess reducing agent (KC_8). Ammonia was identified by the indophenol method and as NH_4Cl by ^1H NMR spectroscopy. Average yields from 16 runs were about 7.0 equiv NH_3 per Fe equiv, and under these conditions 44 % of the protons were delivered to N_2 to produce NH_3.[10]

For comparison, the complex $[(SiP^{iPr}_3)Fe(N_2)][Na(12\text{-crown-}4)_2]$, which is isostructural to $[(TBP)Fe(N_2)][Na(12\text{-crown-}4)_2]$ but in which the B atom of TBP is replaced by Si (Scheme 1, left), was subjected to comparable reaction conditions. A major difference between the (TBP)Fe and $(SiP^{iPr}_3)Fe$ complexes is that the Fe–B bond in *trans* position to the apical ligand is far more flexible than the corresponding Fe–Si bond. However, only substoichiometric formation of ammonia was detected with the Si system, demonstrating that the higher structural flexibility of the boron congener is critically important for the catalytic activity.

In another recent paper, Peters et al. investigated iron complexes supported by the carbon-centered analogue of $[SiP^R_3]$, the $[C^{Si}P^{Ph}_3]$ ligand, in more detail.[11c] With a carbon atom in *trans* position to the apical ligand, the dinitrogen complex $[(C^{Si}P^{Ph}_3)Fe(N_2)]$ (Scheme 1, middle) provides a coordination environment which could be similar to that of N_2 in the FeMoco of nitrogenase. Both the electronic and the geometric structures of the Si and C systems are, however, characteristically different. Whereas the Fe^{II} complex $[(SiP^{iPr}_3)FeCl]$ has an intermediate spin ($S = 1$), the corresponding complex $[(C^{Si}P^{Ph}_3)FeCl]$ with a carbon-centered ligand is high-spin ($S = 2$). This difference can be traced back to a particularly long Fe–C bond in the latter complex, which in turn is associated with a high degree of ionic character in the $Fe–C_{alkyl}$ bond made possible by the three silyl substituents bonded to the C atom. A mechanistic implication of this feature becomes evident from the fact that the trigonal–bipyramidal complex $[(C^{Si}P^{Ph}_3)Fe]$ upon reduction in a nitrogen atmosphere undergoes a $Fe–C_{alkyl}$ bond lengthening along with N_2 binding *trans* to the C atom. This elongation can be taken as support for the hypothesis that an $Fe–C_{interstitial}$ bond in the central trigonal prism of the FeMoco might be modulated as a means of facilitating N_2 binding and reduction at a single Fe site.

In summary, by mediating a catalytic process of ammonia synthesis and establishing new structural motifs related to nitrogenase, the iron-based nitrogenase models developed by the Peters group have provided important insights into key features of biological nitrogen fixation, in particular with respect to the binding of dinitrogen to the four-coordinate iron centers of the FeMoco. Despite these major advances, however, a fundamental question in our understanding of the enzymatic reaction remains open. Notably the FeMoco can be transferred from the "semireduced" $S = 3/2$ state to the "reduced", substrate-reducing state at roughly −1.0 V vs. NHE.[12] This is in marked contrast to the reductant KC_8 employed in the catalytic model system (vide supra). Associated with this issue is the fact that the iron centers of the FeMoco most probably will not become reduced below Fe^{2+} (a second reduction of thiophenolate-bound FeMoco at −1.13 V vs. NHE presumably involves the Mo center),[13] in contrast to the model system which relies on the zero-valent state of iron and below to reduce N_2.[10,11e] This in turn is consistent with the fact that low-molecular-weight Fe^{II} complexes do not activate N_2.[14] To elucidate how nitrogenase gets around this limitation will require a lot of further model chemistry, along with detailed spectroscopic and mechanistic investigations on the enzyme.[3,9]

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