Zhuang, C. S. Brook, Q. Lin, W. H. Moser, R. E. Lee Trout, A. M. Boldi, *Tetrahedron Lett.* **1997**, *38*, 8671–8674; c) A. B. Smith III, Q. Lin, K. Nakayama, A. M. Boldi, C. S. Brook, M. D. McBriar, W. H. Moser, M. Sobukawa, L. Zhuang, *Tetrahedron Lett.* **1997**, *38*, 8675–8678; d) the synthesis of a C39–C51 model compound and the corresponding cytotoxicities were recently reported: A. B. Smith III, Q. Lin, G. R. Pettit, J.-C. Chapuis, J. M. Schmidt, *Bioorg. Med. Chem. Lett.* **1998**, *8*, 567–568.

[13] K. C. Nicolaou, W.-M. Dai, R. K. Guy, *Angew. Chem.* **1994**, *106*, 38–69; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 15–44, and references therein.

[14] a) G. Höfle, N. Bedorf, H. Steinmetz, D. Schomburg, K. Gerth, H. Reichenbach, *Angew. Chem.* **1996**, *108*, 1671–1673; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 1567–1569; b) L. Wessjohann, *Angew. Chem.* **1997**, *109*, 739–742; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 739–742, and references therein.

[15] G. R. Pettit, *Prog. Chem. Org. Nat. Prod.* **1991**, *57*, 153–195, and references therein.

# New Developments in Nitrogen Fixation

**Felix Tuczek* and Nicolai Lehnert**

The prospect of producing ammonia from dinitrogen at room temperature and ambient pressure in analogy to nature has fascinated coordination chemists for a long time. Modeling the conditions present in the enzyme with low-molecular weight compounds, however, is extremely difficult in this case. So far, the iron–molybdenum cofactor (FeMoco), which is the center of bonding and reduction of dinitrogen in the enzyme nitrogenase,[1] has not been synthesized.[2] Furthermore, this cofactor does not bind $N_2$ in isolated form. It therefore appears more promising to realize a catalytic cycle based on the mono- and binuclear transition metal $N_2$ compounds that give $NH_3$ or $N_2H_4$ upon protonation. On the other hand, a "biomimetic" approach is important for understanding aspects of the function of the enzyme on a molecular level.[3] The results of these two different research directions, however, have always been considered as closely related.

Through coordination to one or more metal centers, the dinitrogen ligand, which is extremely inert in free form, acquires a different degree of "activation" (Figure 1).[4] In principle, systems suitable for protonation reactions are those with "moderate" to "strong" activation as well as compounds which cleave the $N_2$ molecule upon coordination. However, if the aim is to achieve relevance to the biological process, "mild" conditions are important. "Nonactivated" systems, although not protonable, may also provide information fundamental to an understanding of the metal–$N_2$ bond. Besides the two mentioned, central problems, "nitrogen fixation" also involves reactions of the dinitrogen ligand or its partly reduced, complex-bound derivatives leading to the incorporation of nitrogen from $N_2$ into (mostly organic) compounds. Recently, there has been important progress in each of these areas, which will be reported here in the order of increasing activation of $N_2$.

$N_2$-containing systems in which the N–N distances are similar to that in free dinitrogen are termed "nonactivated" and are found among compounds exhibiting an *end-on* coordination of $N_2$ to transition metals, for example $Fe^{II}$. It appears that there is now a further bonding mode possible in this category: the nonactivating *side-on* coordination to lanthanide and actinide centers. Up to now, this bonding mode had been known only for a $Sm^{III}$ complex.[5] The recent isolation and structural characterization of the *side-on* $N_2$-bridged complex $[\{U(NN'_3)\}_2(\mu\text{-}\eta^2\text{:}\eta^2\text{-}N_2)]$ ($NN'_3 = N(CH_2$

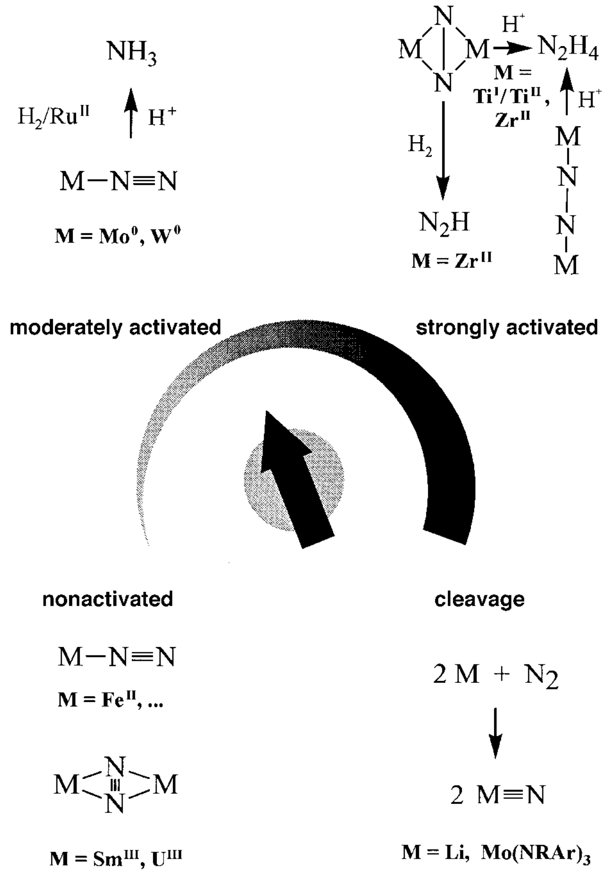


Figure 1. "Tuning" the activation of the $N_2$ ligand by the choice of the coordinating metal. The activation scale may be divided into four regimes; typical representatives mentioned in the text are indicated. The arrow points to the minimal degree of activation necessary for protonation.

---

[*] Dr. habil. F. Tuczek, Dipl.-Chem. N. Lehnert
Institut für Anorganische und Analytische Chemie der Universität
Staudingerweg 9, D-55099 Mainz (Germany)
Fax: (+49) 6131-39-2990
E-mail: Tuczek@iacgu7.chemie.uni-mainz.de

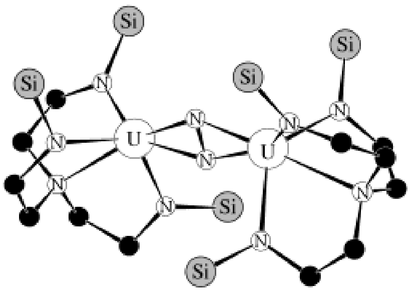


Figure 2. The complex $[\{U(NN'_3)\}_2(\mu\text{-}\eta^2{:}\eta^2\text{-}N_2)]$ ($NN'_3 = N(CH_2CH_2NSiBu\textit{t}Me_2)_3$); the terminal residues on the silyl groups are omitted for clarity.

$CH_2NSiBu\textit{t}Me_2)_3$; Figure 2), however, proved that actinides are also able to bind dinitrogen in this geometry.[6] The N–N distance of 1.109(7) Å is comparable to that in free $N_2$ (1.0975 Å). This is in sharp contrast to the *side-on-* or *edge-on*-bridged complexes of the early transition metals such as titanium and zirconium which belong to the most highly activated $N_2$ compounds (see below). While the reduction of $N_2$ in these systems is caused by electron donation from the metals into the *antibonding* $\pi^*$ orbitals of this ligand (Figure 3), the *side-on* coordination in the lanthanide and actinide systems is probably due to a σ-donor interaction of the *bonding* $\pi^b$ orbital. The exact nature of this bond, however, is as yet not entirely understood. As the *side-on* mode is preferred over the much more common *end-on* coordination, the σ-donor interaction of $p_\sigma$ with the metal must be energetically less favorable than the *side-on* coordination through $\pi^b$ (Figure 3). Possibly this is a consequence of the extremely weak σ-donor capability of the $N_2$ ligand through $p_\sigma$ which is also known from the complexes of the d-block metals.

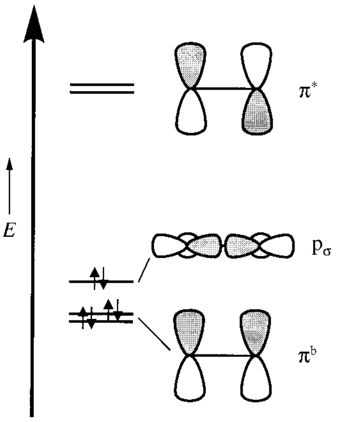
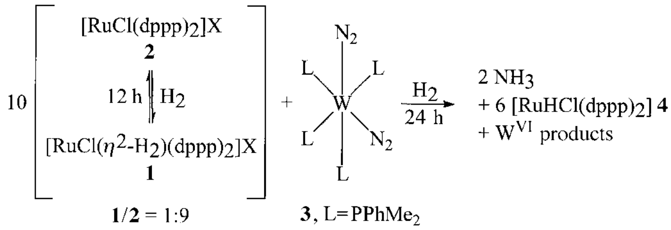


Figure 3. Frontier orbitals of the $N_2$ molecule.

"Moderately activated" systems are those which are protonable, but do not exhibit drastically increased N–N bond lengths (or lowered N–N stretching frequencies) over free $N_2$. Among this category are the *trans* and *cis*-dinitrogenmolybdenum and -tungsten complexes, some of which give $NH_3$ with mineral acids. In other cases, well-defined, complex-bound intermediates $N_2H_x$ ($x = 1-3$) of the protonation to $NH_3$ can be isolated.[7–9] This chemistry, which is probably most relevant to nitrogenase, has now been extended by Hidai and co-workers who effected the protonation of the complex-bound $N_2$ not with mineral acids but with a $H_2$ complex, *trans*-$[RuCl(\eta^2\text{-}H_2)(dppp)_2]X$ (**1**) (dppp = 1,2-bis(diphenylphosphanyl)propane; X = $PF_6$, $BF_4$, OTf($OSO_2CF_3$), $BPh_4$).[10] The $H_2$ complex **1** is slowly generated in situ from $[RuCl(dppp)_2]X$ (**2**) under $H_2$ (1 atm); compounds **1** and **2** are present under equilibrium conditions in the ratio 1:9 (Scheme 1). The $N_2$ complex *cis*-$[W(N_2)_2(PMe_2Ph)_4]$ (**3**) reacts with a ninefold excess of this mixture under $H_2$ to give two equivalents of $NH_3$. In the most favorable case a 55% yield with respect to tungsten is achieved. The reaction mixture also contains $[RuHCl(dppp)_2]$ (**4**) as well as free $PMe_2Ph$-ligand. Since **4** does not bind $H_2$, however, the reaction cannot be made cyclic with respect to hydrogen.



Scheme 1. Synthesis of **1** (from **2**) and its reaction with **3** to give **4** and $NH_3$.

Of particular interest with regard to this reaction is the problem of how the formation of the N–H bond proceeds: does the ruthenium–$H_2$ complex act as a metal acid; that is, is the $N_2$ ligand protonated in analogy to the reactions with mineral acids, or is there an initial, direct interaction between $N_2$ and $H_2$ mediated by the metal? The first possibility is supported by the fact that the $H_2$ complex **1** is markedly acidic ($pK_a = 4.4$). With a similar compound, protonation of the $N_2$ ligand in *trans*-$[W(N_2)_2(dppe)_2]$ (**5**) to the "hydrazido(2–)" stage had been evidenced before (dppe = 1,2-bis(diphenylphosphanyl)ethane).[11] This reaction as well as further reduction of "hydrazido(2–)" to $NH_3$ can likewise be achieved with the mixture of **1** and **2**. Also in favor of a close mechanistic relationship between the protonation with mineral acids and the $Ru^{II}$-mediated reaction with $H_2$ is the observation that the nature of the counterion X strongly influences the yield of $NH_3$. Finally, the presence of free phosphane in the reaction mixture indicates that in the later stages of the protonation reaction phosphane ligands are lost as well. The alternative mechanism, N–H bond formation through interaction between $N_2$ and $H_2$, has recently been demonstrated by Fryzuk et al. for a $Zr^{II}$ $\mu\text{-}\eta^2{:}\eta^2\text{-}N_2$ complex.[12] In contrast to the reaction system of Nishibayashi et al., which requires *two* different metal centers for bonding and activation of $N_2$ and $H_2$, both molecules are bound to *one* complex in this case. However, the $N_2$ *side-on-* or *edge-on*-coordinating $Zr^{II}$ and $Ti^{I}/Ti^{II}$ complexes belong to the "strongly activated" systems (Figure 1);[13] besides the arrangement of both molecules in one ligand sphere, this high degree of activation certainly contributes to facilitating the reaction between $N_2$ and $H_2$.

If the reaction of the *cis* tungsten complex **3** with the mixture of **1** and **2** under $H_2$ (1 atm) is carried out in the presence of acetone, acetone-azine $Me_2C{=}N{-}N{=}CMe_2$ is formed. It also should be possible to initiate other reactions of the Mo/W–$N_2H_x$ complexes by protonation of the $N_2$ precursors with the $H_2$/$Ru^{II}$ system. Recently, Mori et al. reported an alternative to incorporate nitrogen into organic substrates.[14] A solution of a $Ti^{IV}$ compound $TiX_4$ (X = Cl, O*i*Pr) in THF was stirred with an excess of trimethylsilyl chloride (TMSCl) and Li under dry air for 24 h, hydrolyzed with 10% HCl, and made basic with $K_2CO_3$. If, for example, PhCOCl was added to this mixture, $PhCONH_2$ was obtained in 88% yield. N-heterocycles can also be synthesized in this way. The authors assume that intermediates of the type $[TiX_m\{N(TMS)_n\}_o]$ are formed. Thus, the catalytic function of titanium would not be involved in a fixation or activation of $N_2$, but rather in a bonding of amide which results from an initial cleavage of $N_2$ by lithium. Interestingly, the related formation of nitride from $N_2$ by transition metal complexes has been evidenced only recently.[15] These $N_2$-cleaving systems mark the upper end of the activation scale (Figure 1).

What is the significance of the reported studies with respect to the two goals mentioned initially, the understanding of nitrogenase activity and the realization of a corresponding catalytic cycle in vitro? First these results deepen our knowledge about the metal–$N_2$ bond and its reactivity as a function of the metal center. Both *side-on* and *end-on* coordination, which are both candidates for the bonding of $N_2$ to FeMoco, may lead to very strong or no activation at all depending on the coordinating metal center. The reaction of the complex-bound $N_2$ molecule with $H_2$ is novel and this molecule may also be activated by coordination to a transition metal center. Finally, further progress has been made to understand the reactivity of the complex-bound $N_2$ molecule beyond protonation. All of these findings are relevant to the investigation of the nitrogenase function. In terms of the goal of transforming one of the most inert molecules at ambient conditions in chemical reactions, nitrogen fixation continues to play a pioneering role. The vision remains of integrating in particular the protonation to $NH_3$ into a catalytic cycle.

German version: *Angew. Chem.* **1998**, *110*, 2780–2782

**Keywords:** bioinorganic chemistry · metalloenzymes · nitrogen fixation · nitrogenases · protonations

---

[1] See, for example: J. B. Howard, D. C. Rees, *Chem. Rev.* **1996**, *96*, 2965; B. K. Burgess, D. J. Lowe, *Chem. Rev.* **1996**, *96*, 2983; R. R. Eady, *Chem. Rev.* **1996**, *96*, 3013.

[2] A. Müller, E. Krahn, *Angew. Chem.* **1995**, *107*, 1172; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1071.

[3] See, for example: a) *Molybdenum Enzymes, Cofactors and Model Systems* (Eds.: E. Stiefel, D. Coucouvanis, W. E. Newton), American Chemical Society, Washington, DC, **1993**, chapters 20–23; b) R. N. F. Thorneley, D. J. Lowe, *J. Biol. Inorg. Chem.* **1996**, *1*, 576; D. Sellmann, J. Sutter, *Acc. Chem. Res.* **1997**, *30*, 460; D. Coucouvanis, *J. Biol. Inorg. Chem.* **1996**, *1*, 594; c) R. L. Richards, *Coord. Chem. Rev.* **1996**, *154*, 83; R. L. Richards, *Pure Appl. Chem.* **1996**, *68*, 1521.

[4] This term is generally understood with respect to protonation or other reactions involving electrophilic attack to the $N_2$ unit.

[5] W. J. Evans, T. A. Ulibarri, J. W. Ziller, *J. Am. Chem. Soc.* **1988**, *110*, 6877.

[6] P. Roussel, P. Scott, *J. Am. Chem. Soc.* **1998**, *120*, 1070.

[7] M. Hidai, Y. Mizobe, *Chem. Rev.* **1995**, *95*, 1115.

[8] G. J. Leigh, *Acc. Chem. Res.* **1992**, *25*, 177.

[9] R. A. Henderson, G. J. Leigh, C. J. Pickett, *Adv. Inorg. Chem. Radiochem.* **1983**, *27*, 197.

[10] Y. Nishibayashi, S. Iwai, M. Hidai, *Science* **1998**, *279*, 540

[11] G. Jia, R. H. Morris, C. T. Schweitzer, *Inorg. Chem.* **1991**, *30*, 594.

[12] M. D. Fryzuk, J. B. Love, S. J. Rettig, V. G. Young, *Science* **1997**, *275*, 1445.

[13] See also: R. Duchateau, S. Gambarotta, N. Beydoun, C. Bensimon, *J. Am. Chem. Soc.* **1991**, *113*, 8986.

[14] M. Mori, K. Hori, M. Akashi, M. Hori, Y. Sato, M. Nishida, *Angew. Chem.* **1998**, *110*, 659; *Angew. Chem. Int. Ed.* **1998**, *37*, 636.

[15] C. E. Laplaza, C. C. Cummins, *Science* **1995**, *268*, 861.