Mechanism of Transition-Metal-Mediated Nitrogen Fixation: Where Does the Third Proton Go?

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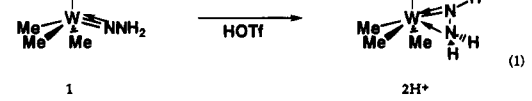
Received July 25, 1994

Nitrogen fixation, the process necessary to transform atmospheric dinitrogen into a form usable for the synthesis of life-sustaining biomolecules, occurs only in the presence of a suitable catalyst. A small class of organisms, termed diazatrophs, contains such catalysts, called nitrogenase enzymes.[1] In attempts to mimic the operation of these enzymes, many transition-metal complexes containing N_2H_x ligands ($x = 0-4$) have been prepared and interconverted[2,3] by the addition or subtraction of protons and electrons. The formation of NNH_2 ligands by the addition of two protons to η^1 N_2 ligands is well established;[2,4] less clear in the sequence of events leading to ammonia is the location and timing of the third protonation. Because coordination to a metal can greatly decrease the rate at which oxygens and nitrogens exchange protons,[5] we hoped that the various protonation sites in N_2H_x ligands would be separately observable and that we could study in detail the proton transfer reactions involved in N_2 reduction.

A system reported by Schrock in 1990[6] seemed ideal. Protonation of the bridging dinitrogen complex $[MoCp^*Me_3](\mu\text{-}N_2)[WCp'Me_3]$ ($Cp^* = C_5Me_5$, $Cp' = C_5Me_4Et$) in the presence of zinc amalgam yielded up to 1.86 equiv of ammonia. Later, $WCp^*Me_3(NNH_2)$ (**1**), a possible reduction intermediate analogue, was isolated and protonated to give $[WCp^*Me_3(\eta^2\text{-}NHNH_2)]OTf$ ($[\mathbf{2H}^+]OTf$) (eq 1).[7]



1 2H+ (1)

The structural rearrangement involved in this protonation suggested that its rate would be slow. One clue to its mechanism came from the low-temperature deprotonation of $\mathbf{2H}^+$ reported by Schrock in 1992.[8] As shown in Scheme 1, deprotonation of $\mathbf{2H}^+$ at low temperatures leaves a bent, η^2, hydrazido complex, $WCp^*Me_3(\eta^2\text{-}NNH_2)$ (**2**);[9] upon warming, **2** opens to the η^1-hydrazido complex **1**. In order to see whether the reverse process (the protonation of **1** to $\mathbf{2H}^+$) also proceeds through **2**, we have studied the interconversion of $\mathbf{2H}^+$ and **1** with a variety of acids and bases, and we have found *two* reaction pathways. This bifurcated mechanism gives a result that is counterintuitive: a reaction involving proton removal that *slows down* with more powerful bases.

We have established the existence of two equilibria. First, the ^1H NMR peak positions of $\mathbf{2/2H}^+$ mixtures are an average of the peak positions of **2** and $\mathbf{2H}^+$ and depend on the ratio of **2** to $\mathbf{2H}^+$; therefore **2** and $\mathbf{2H}^+$ are in rapid equilibrium at low temperatures.[10] Observing this equilibrium with 2,4-lutidine in CD_2Cl_2 at −65 °C allowed us to calculate a pK_a for $\mathbf{2H}^+$ of 14.7 in CH_3CN.[11−13] Second, at room temperature in CD_3CN separate peaks can be observed for $\mathbf{2H}^+$ and **1**, and an equilibrium constant for their interconversion can be measured by ^1H NMR. Performing the deprotonation of $\mathbf{2H}^+$ with 2,6-di-*tert*-butyl-4-methylpyridine resulted in a pK_{eq} of 12.8 between $\mathbf{2H}^+$ and **1**.[14]

Most intriguing, though, was that when $\mathbf{2H}^+$ was deprotonated by 2,4-lutidine in CD_3CN at −23 °C, the formation of **1** was too fast for kinetic study: at least 10 times faster than the measured rate constant for **2** → **1** (k_{-3} below). This observation implied a second pathway for $\mathbf{2H}^+$ → **1**, one in which opening of the η^2-hydrizido ligand precedes deprotonation. Both pathways are shown in Scheme 2.

If we assume that the $\mathbf{2/2H}^+$ equilibrium is rapidly maintained and make the steady state approximation for $\mathbf{1H}^+$,[15] the rate law for complete conversion of $\mathbf{2H}^+$ to **1** is eq 2.

$$\frac{d[\mathbf{1}]}{dt} = \frac{k_1k_2[B]}{k_{-1} + k_2[B]}\left(\frac{[BH^+]}{[BH^+] + K[B]}\right)[T] + k_{-3}\frac{K[B]}{[BH^+] + K[B]}[T] \quad \text{where} \quad [T] = [\mathbf{2H}^+] + [\mathbf{2}] \quad (2)$$

The first term represents the k_1k_2 path, $\mathbf{2H}^+ \rightleftharpoons \mathbf{1H}^+ \rightarrow \mathbf{1}$; the second term represents the k_{-3} path, $\mathbf{2H}^+ \rightleftharpoons \mathbf{2} \rightarrow \mathbf{1}$. The extent

(1) The biological nitrogen fixation literature is summarized in the recent report of the structures of the iron and molybdenum−iron proteins: Kim, J.; Rees, D. C. *Biochemistry* **1994**, 33, 389−397.

(2) For reviews on the subject, see: (a) Chatt, J.; Dilworth, J. R.; Richards, R. *Chem. Rev.* **1978**, *78*, 589−625. (b) Leigh, G. J. *Acc. Chem. Res.* **1992**, *25*, 177−181.

(3) (a) Allen, A. D.; Senoff, C. V. *Chem. Commun.* **1965**, 621−622. (b) Sellmann, D.; Brandl, A.; Endell, R. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 1019. (c) Huttner, G.; Gartzke, W.; Allinger, K. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 822−823. (d) Heath, G. A.; Mason, R.; Thomas, K. M. *J. Am. Chem. Soc.* **1974**, *96*, 259−260. (e) Henderson, R. A.; Oglieve, K. E. *J. Chem. Soc., Dalton Trans.* **1990**, 1093−1096. (f) Sellmann, D.; Kern, W.; Pöhlmann, G.; Knoch, F.; Moll, M. *Inorg. Chim. Acta* **1991**, *185*, 155−162. (g) Vogel, S.; Barth, A.; Huttner, G.; Klein, T.; Zsolnai, L.; Kremer, R. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 303−304. (h) Collman, J. P.; Hutchison, J. E.; Ennis, M. S.; Lopez, M. A.; Guilard, R. *J. Am. Chem. Soc.* **1992**, *114*, 8074−8080. (i) Sellmann, D.; Soglowek, W.; Knoch, F.; Ritter, G.; Dengler, J. *Inorg. Chem.* **1992**, *31*, 3711−3717. (j) Evans, W. J.; Kociok-Köhn, G.; Ziller, J. W. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1081−1082. (k) Evans, W. J.; Kociok-Köhn, G.; Leong, V. S.; Ziller, J. W. *Inorg. Chem.* **1992**, *31*, 3592−3600. (l) Smith, M. R.; Cheng, T.-Y.; Hillhouse, G. L. *J. Am. Chem. Soc.* **1993**, *115*, 8638−8642. (m) DeBord, J.; George, T. A.; Chang, Y.; Chen, Q.; Zubieta, J. *Inorg. Chem.* **1993**, *32*, 785−786. (n) Cheng. T.-Y.; Peters, J. C.; Hillhouse, G. L. *J. Am. Chem. Soc.* **1994**, *116*, 204−207.

(4) George, T. A.; Kaul, B. B.; Chen, Q.; Zubieta, J. *Inorg. Chem.* **1993**, *32*, 1706−1711 and references therein.

(5) (a) Kramarz, K. W.; Norton, J. R. *Prog. Inorg. Chem.* **1994**, *42*, 1. (b) Carroll, J. M.; Norton, J. R. *J. Am. Chem. Soc.* **1992**, *114*, 8744−8745.

(6) Schrock, R. R.; Kolodziej, R. M.; Liu, A. H.; Davis, W. M.; Vale, M. G. *J. Am. Chem. Soc.* **1990**, *112*, 4338−4345.

(7) Schrock, R. R.; Liu, A. H.; O'Regan, M. B.; Finch, W. C.; Payack, J. F. *Inorg. Chem.* **1988**, *27*, 3574−3583.

(8) Glassman, T. E.; Vale, M. G.; Schrock, R. R. *J. Am. Chem. Soc.* **1992**, *114*, 8098−8109.

(9) Bold numbers (**1** or **2**) indicate whether the hydrazido ligand is η^1 or η^2, and $\mathbf{H}^+$ indicates that the hydrazido ligand is protonated. In Schemes 1 and 2, each tungsten is also bound to three methyl ligands and one C_5Me_5 = Cp* ligand. These ancillary ligands are omitted for clarity.

(10) The speed of proton exchange between **2** and $\mathbf{2H}^+$ is not surprising because it involves a simple proton transfer between lone pairs on N_α; no rehybridization is necessary. See ref 5a and the following: Kristjansdóttir, S. S.; Norton, J. R. In *Transition Metal Hydrides*; Dedieu, A., Ed.; VCH: New York, 1992; Chapter 9.

(11) An NMR tube was charged with $\mathbf{2H}^+$ and 800 μL of CD_2Cl_2, and an appropriate amount (2.2 equiv with 6 μmol of $\mathbf{2H}^+$, or 7.5 equiv with 8 μmol of $\mathbf{2H}^+$) of 2,4-lutidine was added by vacuum transfer at 77 K. After warming to −65 °C, the chemical shift observed for the cis methyl ligand in the mixture was compared with those of pure **2** (δ −0.63) and pure $\mathbf{2H}^+$ (δ 0.31). The ratio of **2** to $\mathbf{2H}^+$ thus obtained was used to calculate the equilibrium constant K as 0.20(7). If we assume (because both acid/base pairs are large[12]) that K is approximately the same in CH_3CN, neglect its temperature dependence, and use the known pK_a of 2,4-lutidine in CH_3CN (14.05),[13] we can estimate the 25 °C pK_a of $\mathbf{2H}^+$ in CH_3CN.

(12) The same assumption has been made in other cases: Jia, G.; Morris, R. H. *Inorg. Chem.* **1990**, *29*, 581−582. See also ref 10.

(13) Chantooni, M. K., Jr.; Kolthoff, I. M. *J. Am. Chem. Soc.* **1968**, *90*, 3005.

(14) An NMR tube was charged with 15 μmol of $\mathbf{2H}^+$ and 1 equiv of 2,6-di-*tert*-butyl-4-methylpyridine in CD_3CN. The equilibrium concentrations of **1** and $\mathbf{2H}^+$ were measured by ^1H NMR integration. The resulting equilibrium constant, 0.58, agreed within experimental error with that obtained when the equilibrium was approached from the opposite direction. The pK_{eq} was then determined by taking the pK_a of 2,6-di-*tert*-butyl-4-methylpyridinium triflate as 12.6 (obtained by analyzing the ^1H NMR peak positions of equilibrium mixtures of this acid with 2,4-lutidine).

(15) No $\mathbf{1H}^+$ is observed during the reaction.

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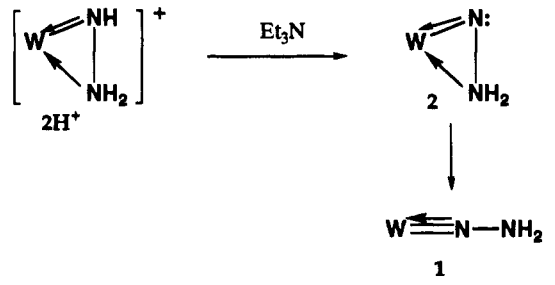
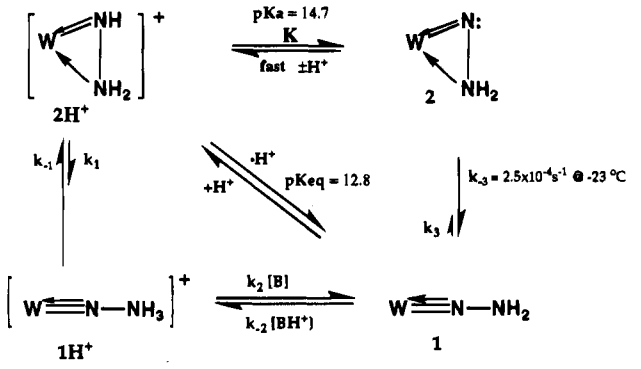
Scheme 1



Scheme 2



to which each path occurs depends on the $2H^+/2$ equilibrium. To the extent that all the $2H^+$ is converted to **2**, the reaction will occur only through the k_{-3} path; to the extent that none of the $2H^+$ is converted to **2**, the reaction will occur only through the k_1k_2 path. Because the k_{-3} path is inherently slower than the k_1k_2 path, the overall rate of $2H^+ \rightarrow 1$ *decreases* when the base shifts the $2H^+/2$ equilibrium to the right.

For sufficiently small [B], k_2[B] should be $\ll k_{-1}$ and K[B] $\ll$ [BH^+], and the first term in eq 2 should increase linearly with added base. For sufficiently large [B], k_2[B] should be $\gg k_{-1}$ and K[B] $\gg$ [BH^+], and the first term in eq 2 should be proportional to [B]$^{-1}$. The predicted behavior was observed when $2H^+$ (4.7 μmol in 800 μL of CD_2Cl_2) was treated with varying amounts of 2,4-lutidine. The formation of **1** and the disappearance of $2/2H^+$ were monitored at −53 °C by ^{1}H NMR. The relationship between the resulting rate constants and the concentration of 2,4-lutidine was fitted with the first term of eq 2 (the formation of **1** through **2**, the k_{-3} path, is negligible at this temperature). The experimental data, the best fit, and the resulting parameters for k_1 and k_{-1}/k_2 are shown in Figure 1.

Scheme 2 requires that the value of the rate constant k_1 for the opening of the η^2-hydrazido ligand be independent of the nature of the base. Indeed, the use of pyridine gave approximately the same value for k_1[16] as that obtained with 2,4-lutidine.

Two pathways are also available to the reverse process, the conversion of **1** to $2H^+$. Protonation of **1** can occur either directly to give $1H^+$, followed by closure to $2H^+$, or after closure of the hydrazido ligand in **1** (**1** → **2**). However, direct ^{1}H NMR observation of **2** → **1** shows that k_{-3} is only 2.5×10^{-4} s^{-1} at −23 °C in CH_3CN, and k_3 must be even slower.[17] (No **2** can be detected by ^{1}H NMR after it is allowed to come

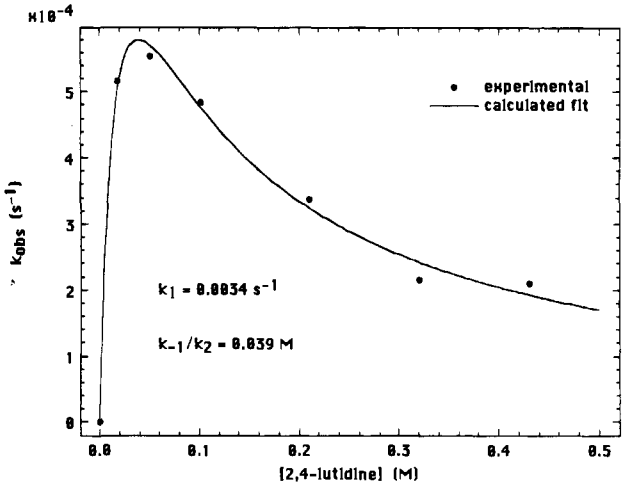


Figure 1. Dependence of the rate of $2H^+ \rightarrow 1$ on the concentration of 2,4-lutidine in CD_2Cl_2 at −53 °C.

to equilibrium with **1**, and the pK_{eq} and pK_a of $2H^+$ give an estimate of k_{-3}/k_3 as >80 in CH_3CN at 25 °C). As conversion of **1** to $2H^+$ with pyridinium triflate in CD_3CN is complete within 5 min at −37 °C, it must occur via $1H^+$.

The protonation of **1** to $1H^+$ is facile; its rate with weak acids can be directly measured. The ^{1}H NMR resonance due to the β hydrogens of **1** broadens when a CD_3CN solution is treated with [Me_3NH][ClO_4], although there is no net reaction. This broadening is proportional to the concentration of Me_3NH^+ and must be due to the operation of eq 3. At room temperature k_{-2} is 2600 M^{-1} s^{-1}.[18]

$$W{\equiv}NNH_2 + Me_3NH^+ \underset{k_2}{\overset{k_{-2}}{\rightleftharpoons}} W{\equiv}NNH_3^+ + Me_3N: \quad (3)$$

In an effort to determine the structure of $1H^+$ we have treated **1** with various acids at low temperatures. With HOTf in CD_2Cl_2, $2H^+$ is formed immediately at −75 °C. However, with [$(Et_2O)_2H$][$B(Ar_F)_4$][19] at −50 °C in THF-d_8, **1** is converted into a species with only a single NH resonance (3H, broad, δ = 10.32). This species rearranges to $2H^+$ above −40 °C and is presumably the $1H^+$ in Scheme 2. The fact that one nitrogen of $1H^+$ bears all three protons has been confirmed: in the proton NMR spectrum the NH resonance appears as a doublet, $^1J_{NH}$ = 77 Hz, when $1H^+$ is prepared from **1**-^{15}N.[20,21]

It is thus clear that the β *nitrogen* of **1** is the kinetic site of protonation. Still unsolved is the question of how $1H^+$ rearranges to $2H^+$.

Acknowledgment. We thank Professor Richard Schrock, Dr. Mike Vale, and Dr. Timothy Glassman for stimulating discussions. We also thank Dr. Mike Vale for providing a generous sample of **1**, Anthony Lupinetti for experimental assistance, and Dr. Chris Rithner for assistance with NMR studies. Financial support has been provided by NSF Grant CHE-9120454.

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(16) When the 2,4-lutidine concentration exceeds 0.3 M, k_1 becomes rate limiting the $k_{obs} \cong k_1([BH^+])/([BH^+] + K[B])$. If we assume that k_2 is at least as large for pyridine as for 2,4-lutidine, the same expression will hold for [py] > 0.3 M. Thus we have estimated k_1 from k_{obs} for $2H^+ \rightarrow 1$ with [py] of 0.3 and 0.6 M.

(17) The deprotonation of $2H^+$ to **2** was performed with three bases: triethylamine, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), and morpholine. The observed rate constants for **2** → **1** were equivalent (between 2.4 and 2.6×10^{-4} s^{-1}) and thus independent of the nature of the base, suggesting that the k_1k_2 path is inoperative under these conditions.

(18) The line width of the $N_\beta H_2$ resonance of **1** was measured in the presence and absence of Me_3NH^+. The lifetime τ of the $N_\beta H_2$ protons was then obtained from $\tau^{-1} = \pi(\Delta\nu_{excess})$. Because only two-thirds of the H^+ transfers in eq 3 lead to line broadening, k_{-2}[Me_3NH^+] = $(3/2)\tau^{-1}$ = $(3/2)\pi(\Delta\nu_{excess})$.

(19) Brookhart, M.; Grant, B.; Volpe, A. F., Jr. *Organometallics* **1992**, *11*, 3920.

(20) The fact that $1H^+$ cannot be observed in less coordinating solvents suggests that it coordinates THF when generated in that solvent.

(21) A tungsten complex with a hydrazidium (N−NH_3^+) ligand has been previously reported: (a) Galindo, A.; Hills, A.; Hughes, D. L.; Richards, R. L. *J. Chem. Soc., Chem. Commun.* **1987**, 1815−1816. (b) Galindo, A.; Hills, A.; Hughes, D. L.; Richards, R. L.; Hughes, M.; Mason, J. *J. Chem. Soc., Dalton Trans.* **1990**, 283−288.