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Exchange of Dinitrogen between Iron and Molybdenum Centers and the Reduction of Dinitrogen Bound to Iron: Implications for the Chemistry of Nitrogenases

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The recent discovery of the vanadium-iron nitrogenase[1] and of a nitrogenase that apparently contains only iron[2] suggests that vanadium and iron, as well as molybdenum of the conventional nitrogenase,[3,4] may mediate the reduction of dinitrogen in vivo. We present here chemical data that show that the metal species common to the three nitrogenases, namely, iron, is itself capable of mediating the reduction of dinitrogen under mild conditions in vitro. This would lend support to the contention that iron may constitute the active site in all kinds of nitrogenases.

We have recently prepared the iron(II) dinitrogen complex $[FeH(N_2)(dmpe)_2]^+$ (dmpe = 1,2-bis(dimethylphosphino)ethane) by direct reaction of N_2 with $[FeH(H_2)(dmpe)_2]^+$.[5] This N_2 complex reacts with bases such as KOBu^t to produce an unstable iron(0) complex which we formulate as $[Fe(N_2)(dmpe)_2]$. This

$$[FeH(N_2)(dmpe)_2]^+ \xrightarrow{OBu^{t-}} [Fe(N_2)(dmpe)_2] + Bu^tOH$$

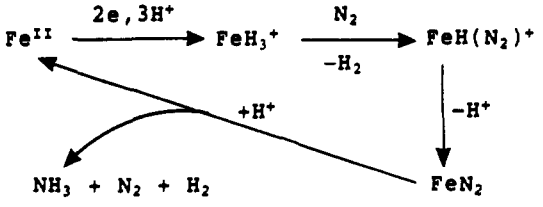
product has been characterized in solution by IR spectroscopy and $^{31}P\{^1H\}$ spectroscopy. (IR: $\nu(^{14}N_2)$ 1975, $\nu(^{15}N_2)$ 1917 cm^{-1}, THF. $^{31}P\{^1H\}$ NMR (THF/C_6D_6) A_2B_2 system, P_A -60.02, P_B -74.17 ppm (P(OMe) standard), $^2J_{PP}$ = 26 Hz.) This compound slowly loses N_2, and if the deprotonation is carried out under vacuum or zero partial pressure of N_2, all N_2 is rapidly lost. However, treatment of the solution of $[Fe(N_2)(dmpe)_2]$ with acids yields ammonia, and this was estimated quantitatively after base distillation, as shown in Table I. An approximately molar solution of HCl in Et_2O was generated from Me_3SiCl and MeOH, and this was used to ensure an HCl:Fe ratio of ca. 10:1. Because of the lability of the N_2 in $[Fe(N_2)(dmpe)_2]$, we were unable to devise a method to obtain a nitrogen balance in dinitrogen plus ammonia, but with HCl the ultimate iron product is $[FeCl_2(dmpe)_2]$ as determined by IR, UV, and $^{31}P\{^1H\}$ NMR spectroscopy and comparison with an authentic sample. The yield of $[FeCl_2(dmpe)_2]$ is of the order of 80%, but the dichloro complex itself reacts slowly with HCl. This system under optimal conditions can supply only two electrons per dinitrogen since the iron changes from iron(0) to iron(II), so that the maximum yield of ammonia should be $^2/_3NH_3$/initial mole of $[FeH(N_2)(dmpe)_2]^+$. Our best yields are currently of the order of 18%, but yields have yet to be optimized (Table I). Only trace amounts of hydrazine were observed, and then only in the presence of magnesium chloride, which was added in order to parallel some systems in which metal-N_2-magnesium interactions have been observed.[6] Protonation reactions carried out in vacuo yielded N_2 and H_2, 1 molar equiv of each.

Table I

compd or system	solvent[a]/acid	concn[b] of recovered NH_3, mM	yield[c] of NH_3, %
$[FeH(N_2)(dmpe)_2][BPh_4]$	THF/HCl	0	0
$[FeH(N_2)(dmpe)_2][BPh_4]$	THF/H_2SO_4	1.4	3.6
$[FeH(N_2)(dmpe)_2][BPh_4]$ + LiPh (5 molar equiv)	THF/H_2SO_4	1.0	2.6
$[Fe(N_2)(dmpe)_2]$	THF/H_2SO_4	3.4	8.6
$[Fe(N_2)(dmpe)_2]$	THF/HCl	4.8	12
$[Fe(N_2)(dmpe)_2]$	Et_2O/HCl	3.8	9.6
$[Fe(N_2)(dmpe)_2]$[d] + $MgCl_2$ (10 molar equiv)	THF/HCl	2.6	6.6

[a] THF = tetrahydrofuran. [b] Concentration of solution after base distillation and making up to 25 cm^3 starting from 1 mmol of Fe complex. Ammonia determination by the indophenol test. These values are corrected for blanks consisting of $[FeH(H_2)(dmpe)_2][BPh_4]$ treated as necessary with base and/or acid in the appropriate solvent under argon. Under such circumstances background concentrations of ca. 0.15 mM ammonia were obtained. [c] Yield expressed as (moles of NH_3/moles of $[FeH(N_2)(dmpe)_2][BPh_4]$) × 100. In terms of electrons, these yields need to be multiplied by $^3/_2$, since $Fe^0 \rightarrow Fe^{II}$ provides two electrons and $^1/_2N_2 \rightarrow NH_3$ requires three. [d] In only this case was any hydrazine observed (*p*-(dimethylamino)benzaldehyde test). Yield 0.4% based on initial iron complex.

Scheme I



These results show that it is possible to construct a reductive cycle for dinitrogen on iron solely by changing the hydrogen ion concentration (Scheme I).

We do not yet understand the mechanistic details of these reactions, but the system differs significantly from any iron nitrogen-fixing systems in the literature,[7] all of which employ strong reducing agents such as Grignard reagents, as well as nonprotic media. Our system does not require a reducing agent stronger than borohydride, which can function in protic solvents such as alcohols, and the effect of which could be mimicked in a protein by changing the relative fluxes of protons and electrons reaching a metal center.

We attempted to make compounds containing dinitrogen bridging between iron and molybdenum[8] by reaction of $[FeH(H_2)(dmpe)_2]^+$ with $[Mo(N_2)_2(dppe)_2]$ (dppe = 1,2-bis(diphenylphosphino)ethane) under Ar in tetrahydrofuran. What we observed is the metathetical reaction shown below, the known products being recovered in about 70% yield, but as judged by IR spectroscopy, the reaction appears quantitative.

$$2[FeH(H_2)(dmpe)_2]^+ + [Mo(N_2)_2(dppe)_2] \rightarrow 2[FeH(N_2)(dmpe)_2]^+ + [MoH_4(dppe)_2]$$

This reaction occurs despite the fact that $[FeH(N_2)(dmpe)_2]^+$ and $[Mo(N_2)_2(dppe)_2]$ have $\nu(N_2)$ at 2094 and 1977 cm^{-1}, respectively, which by the criterion normally used implies that N_2 is more strongly bound to molybdenum than to iron.[9] The molybdenum-hydrogen binding presumably provides the driving force,

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which must be considerable since the iron system will even abstract dinitrogen (although more slowly and less cleanly) from [W-$(N_2)_2$(depe)$_2$] (depe = 1,2-bis(diethylphosphino)ethane), to which it is particularly strongly bound.[10,11]

The reaction rate exhibits first-order dependence on the concentration of both iron and molybdenum complexes, but currently we cannot speculate about the mechanism of the H_2/N_2 exchange.[12]

These observations suggest an alternative interpretation of the functions of iron, molybdenum, and vanadium in the nitrogenases. Iron is believed to be involved in electron transfer, ultimately to the active site, but it may also mediate the reduction of dinitrogen under mild conditions analogous to those we have used here.[13] Molybdenum and vanadium (neither of which has been observed to change oxidation state when the appropriate proteins are reduced)[14] could have the function of trapping N_2 and passing it to iron. Indeed, the third (iron?) nitrogenase could be the ancestral nitrogenase, the vanadium and molybdenum nitrogenases being more efficient, younger variants. Structural[15] and abundance data[16] are at least consistent with this interpretation.

Acknowledgment. We acknowledge support of the European Economic Community, Grant ST2*410, for this work.

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(11) Hussain, W.; Leigh, G. J.; Mohd.-Ali, H.; Pickett, C. J. *J. Chem. Soc., Dalton Trans.* **1988**, 553.
(12) A similar exchange of H_2 and N_2 was reported from the reaction of [$FeH_4(PEt_2Ph)_3$] and [$Mo(N_2)_2$(dppe)$_2$], though the products were incorrectly formulated. This interesting observation has been ignored. See: Aresta, M.; Sacco, A. *Gazz. Chim. Ital.* **1972**, *102*, 755.
(13) The nitrogen-fixing function of iron in nitrogenase is not a new idea. It was suggested, without experimental support, many years ago. See: Winfield, M. E. *Rev. Pure Appl. Chem.* **1955**, *5*, 217.
(14) See: Zimmermann, R.; Trautwein, A. X., in ref 4, pp 63-81.
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Total Synthesis of Allosamidin: An Application of the Sulfonamidoglycosylation of Glycals

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Chitin[1] (**1**) is a major structural constituent of the exoskeleton of arthropods[2] and fungal cell walls.[3] Molecules that are able to inhibit chitin synthases and chitinases might function as insecticides[4] or fungicides[5] since a proper balance is necessary to control the morphology of insects[6] and fungi.[7] Interestingly, chitinases appear to operate defensively against fungal pathogens in plants[8] and may aid digestion in some vertebrates.[9] Thus, compounds that selectively inhibit the ability of specific organisms to degrade chitin could well be advantageous.

Allosamidin (**2**), isolated from mycelial extracts of *Streptomyces* sp. 1713, is an encouraging first success in screening for selective chitinase inhibitors.[10] The original structural formulation[11] of allosamidin was revised[12,13] to a chitin "look alike" consisting of 3,3′-*epi*-chitobiose β-linked to a novel aglycon sector termed "allosamizoline", which was recently synthesized in racemic form by Trost.[14] While allosamidin may be a transition-state analogue

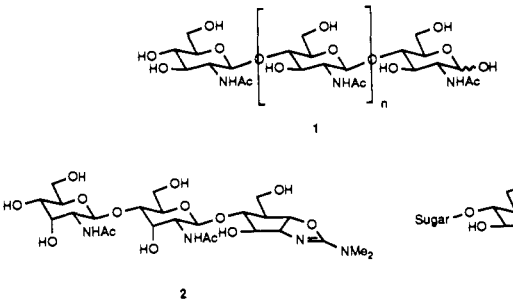
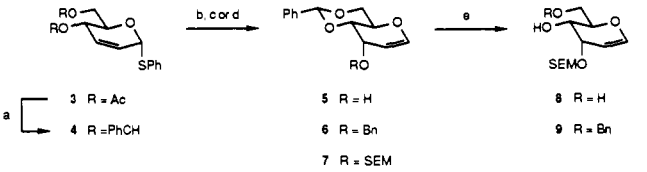


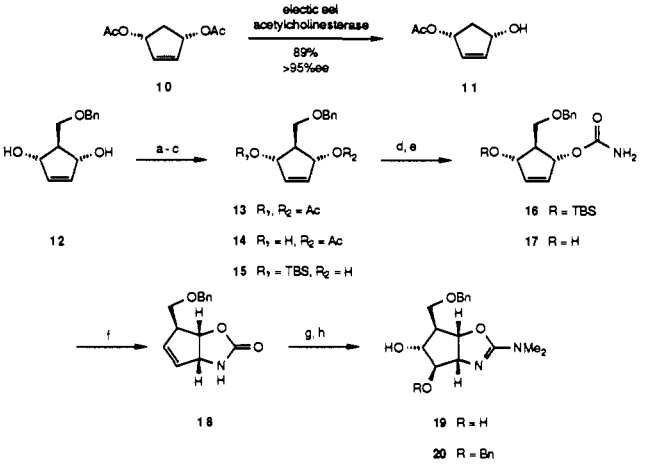
Figure 1

Scheme I[a]



[a] (a) NaOMe, MeOH; $PhCH(OMe)_2$, TsOH, DMF, 71%; (b) 2,2-dimethyldioxirane, CH_2Cl_2, −78 °C; Et_2NH, THF, 96%; (c) NaH, THF; BnBr, Bu_4NI, 96%; (d) SEMCl, *i*-Pr_2NEt, CH_2Cl_2, 100%; (e) Na, NH_3; Bn_2SnO, MeOH, reflux; CsF, BnBr, DMF, 69% (21% of recovered **8**).

Scheme II[a]



[a] (a) Ac_2O, Et_3N, DMAP, CH_2Cl_2, 89%; (b) electric eel acetylcholinesterase, NaN_3, pH 6.9 phosphate buffer, 95%, >95% ee; (c) TBSCl, imidazole, CH_2Cl_2; NH_3, MeOH, 100%; (d) $ClCO_2Ph$, pyridine, CH_2Cl_2, 0 °C; NH_3, MeOH, 82%; (e) aqueous HF, CH_3CN, 94%; (f) Et_3N, TFAA, THF, −78 °C → room temperature, 63%; (g) MeOTf, CH_2Cl_2; Me_2NH, 87%; CF_3CO_3H, TFA; TFA, H_2O, 44%; (h) Bu_2SnO, MeOH, reflux; BnBr, CsF, DMF, 46%.

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