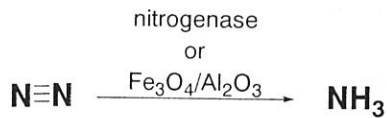


Nitrogen Fixation

Yamaguchi A. (D2)
2009 Feb. 21st

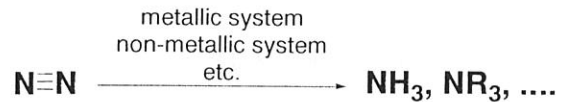
traditional method



nitrogenase → · catalytic
· homogeneous
· <1 atm N₂
· 170 x 10⁹ kg/year (estimated)
Fe or Mo as center metal

Fe₃O₄/Al₂O₃ → · developed in 1922
(Haber-Bosch) · catalytic
· heterogeneous
· high pressure, temperature
· 80 x 10⁹ kg/year (1995)

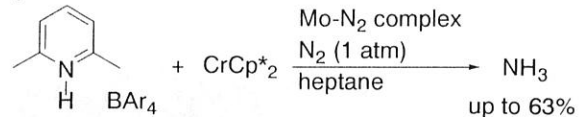
recent achievement



[directions]

- mild conditions (low pressure, temperature)
- catalytic (rare)
- H₂ as H source
- functionalization (N-C, N-X bond formation)
- different mechanism

e.g.

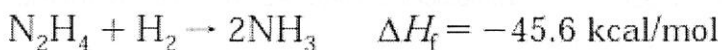
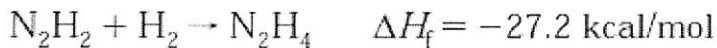
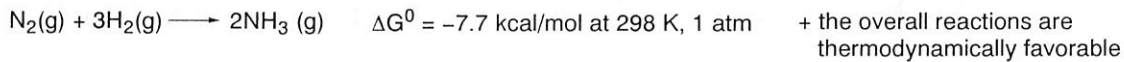


Contents

- general feature of N₂ fixation
- biological N₂ fixation (nitrogenase)
- artificial N₂ fixation system

1. general feature of N₂ fixation Chem. Rev. 1996, 96, 2965.

reduction to NH₃



ΔH_f: enthalpies of formation

realization of ammonia synthesis is complicated by kinetic stability of nitrogen-nitrogen triple bond

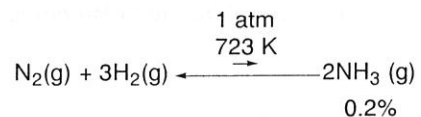
⇒ the primary energetic barrier to N₂ reduction is the triple bond

cf.

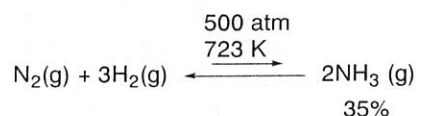
Haber-Bosch process

+ dissociation of N₂ to atomic nitrogen on the active crystal face of the iron catalyst at 600-800 K

exothermic reaction |
high temperature | → equilibrium shifts toward the reactants



↓ increase of pressure



2. biological N₂ fixation

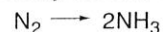
Chem. Rev. 1996, 96, 2965.
Acc. Chem. Res. 2005, 38, 208.
Dalton Trans. 2006, 2277.

+ biological N₂ fixation is performed by **nitrogenase (metalloenzyme)**

0.8 atm (N₂), 290 K

a group of prokaryotic organism

catalyzes following reactions



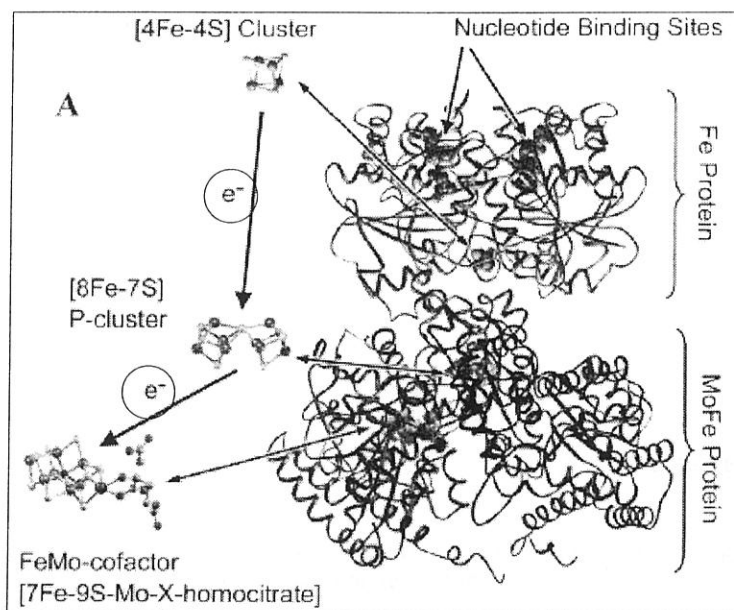
reduction of acetylene, azide, cyanide...

at least four different types of nitrogenase have been characterized

* where and how do substrates interact with the active site?

* what is the nature of reaction intermediate along the reduction pathway?

⇒ focus of the intense study
for more than 50 years...

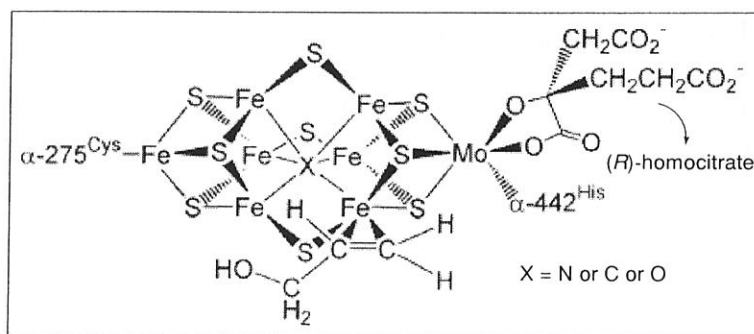
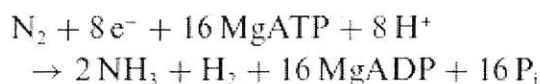


one half of the nitrogenase complex

The most widely distributed and studied types of nitrogenase is composed of two component proteins, **Fe protein** and **MoFe protein**

reduction sequence

- (i) reduction of Fe protein by electron carriers such as ferredoxins (Fd) and flavodoxins
- (ii) transfer of single electrons from Fe protein to MoFe protein in a MgATP-dependent process
- (iii) electron transfer to the substrate at the active site within the MoFe protein (**FeMo-cofactor**)



allyl alcohol-bound FeMo-cofactor

+ (R)-homocitrate provides two O-ligands to the Mo

+ the cofactor is covalently attached to the protein through coordination of the terminal Fe by the side chain of $\alpha\text{-275}^{\text{Cys}}$ and coordination of the Mo by the side chain of $\alpha\text{-442}^{\text{His}}$

elucidation of the mechanism

mutation

e.g. substitution of $\alpha\text{-70}^{\text{Val}}$ to Ala enable binding and reduction of larger substrates such as propargyl alcohol, hydrazine etc.

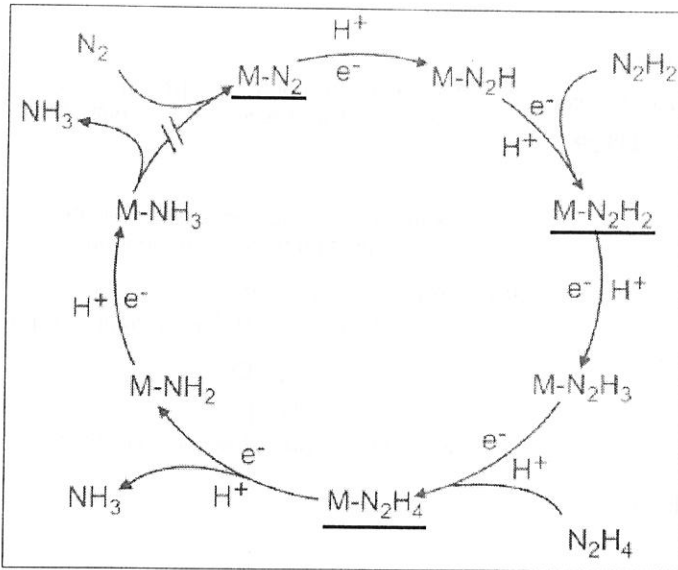
⇒ elucidation of binding site

trapping intermediates

freezing the MoFe protein during the course of reduction and analysing by EPR and ¹⁵N ENDOR spectroscopy

↓
Electron-Nuclear DOuble Resonance

using both to detect FeMo-cofactor species at different levels of reduction



putative intermediates bound to FeMo-cofactor during N_2 reduction

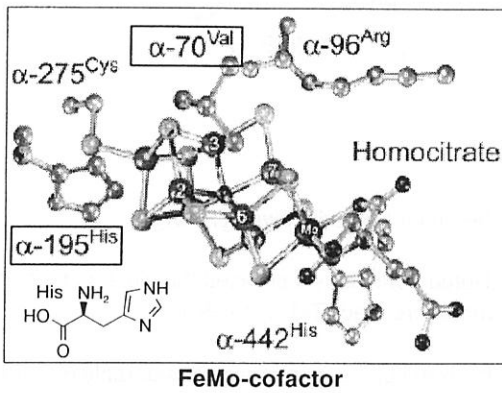
- + traces of hydrazine can be detected when nitrogenase is acid- or base-quenched while actively reducing N_2
- + hydrazine can be reduced to NH_3 by nitrogenase
- + a reasonable starting point was to consider N_2 reduction on the FeMo-cofactor as proceeding through successive protonation/reduction with bound intermediates similar to those in the Chatt cycle (proposed catalytic cycle for reduction of N_2 by artificial catalyst)
- + trapped intermediates are hydrazine, diazene and N_2

[Hydrazine] *Biochemistry*, 2005, 44, 8030.

* substitution of α -195^{His} to Gln and α -70^{Val} to Ala

believed to be the proton donor

Handwritten note: α -70 Val to Ala \Rightarrow opening the protein environment for H_2NNH_2 binding
disrupting proton delivery (inhibition of turnover)



trapping hydrazine complex

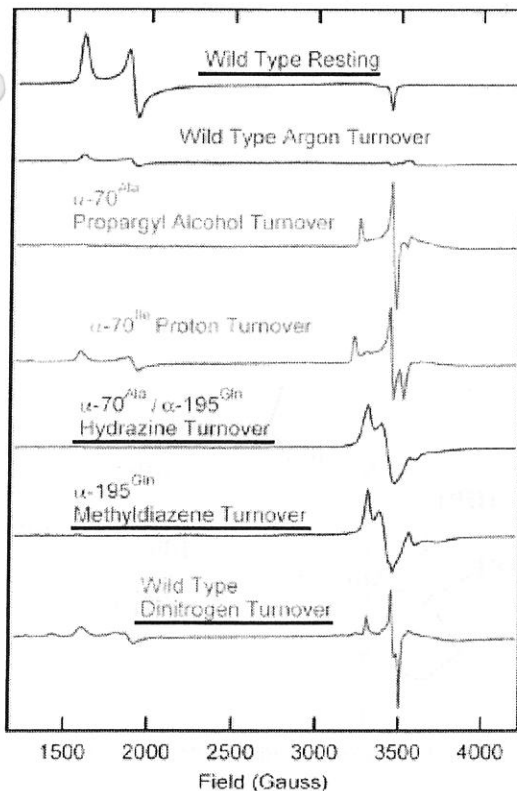
MoFe-protein, Fe-protein, hydrazine, MgATP, dithionite, buffer

rt, 30 sec

freezing with liq. N_2

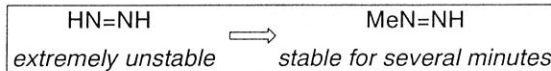
- + new $S = 1/2$ EPR state (different from resting state)
- + ^{15}N -ENDOR suggested that hydrazine (or derivative) was bound to the FeMo-cofactor

\Rightarrow the first nitrogenous substrate species had been trapped on the FeMo-cofactor in high yield



EPR signals of nitrogenase

[diazene] *J. Am. Chem. Soc.* 2005, 127, 14960.



J. Am. Chem. Soc. 1968, 90, 7173.

* substitution of α -195^{His} to Gln (α -195^{Gln} MoFe protein)

- + novel $S = 1/2$ EPR signal (not identical to that observed for hydrazine)
- + $H^{15}N=NH$ (or derivative) was bound to the FeMo-cofactor (^{15}N -ENDOR)
- + $^{1,2}H$ -ENDOR indicated the presence of exchangeable protons

[dinitrogen] *J. Am. Chem. Soc.* 2005, 127, 14960.

* using wild type MoFe protein

- + novel $S = 1/2$ EPR signal (not identical to that observed for hydrazine and methyl diazene)
- + single ^{15}N was observed coupled to the FeMo-cofactor for the N_2 trapped state (^{15}N -ENDOR)
- + $^{1,2}H$ -ENDOR indicated the absence of exchangeable protons

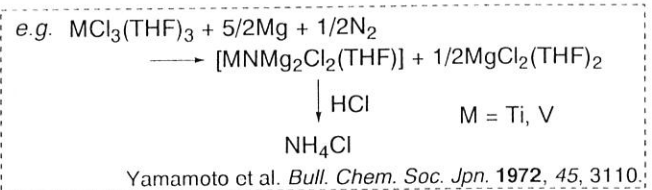
3. artificial N₂ fixation system

mainly realized by metal-dinitrogen complex (like nitrogenase)

- (a) N₂ is isoelectronic to CO, but weaker σ-donor and π-acceptor
- (b) π-acceptor ability is important for the stability of N₂ complex
- (c) strong π-back donation can stabilize N₂ complex
- (d) usual binding mode is end-on (η¹)
- (e) free N₂: 2331 cm⁻¹, bound N₂: 1900-2200 cm⁻¹

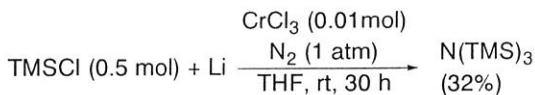
the first N₂ complex → [Ru(NH₃)₅N₂]²⁺
J. Chem. Soc., Chem. Commun. **1965**, 621.

various dinitrogen complexes and their reduction have been reported



catalytic conversion of molecular dinitrogen into silylamines

* earlier report by Shiina *J. Am. Chem. Soc.* **1972**, *94*, 9266.



* Hidai's work *Hidai et al. J. Am. Chem. Soc.* **1989**, *111*, 1939.

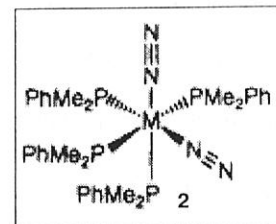


Table II. Effects of Transition-Metal Complexes on the Conversion of Dinitrogen into Silylamines^a

complex	time (h)	conv (%)	yield (%) ^b (turnover number) ^c		
			N(SiMe ₃) ₃	HN(SiMe ₃) ₂	(SiMe ₃) ₂
none	4	10	0 (0)	0 (0)	2.7
3	4	>95	23.7 (7.5)	1.2 (0.6)	45.1
3 ^d	4	84	6.9 (2.4)	0.2 (0.1)	53.4
3 ^e	4	>99	21.4 (14.4)	0.9 (0.9)	50.7
3 ^f	15	>99	36.6 (24.3)	1.1 (1.1)	39.0
[Mo(N ₂) ₂ (dpe) ₂]	4	>99	9.7 (3.2)	0.8 (0.4)	53.9
2	4	>99	2.9 (0.9)	1.6 (0.8)	71.8
[W(N ₂) ₂ (dpe) ₂]	4	>95	3.3 (1.1)	1.4 (0.7)	50.7
CrCl ₃ ^d	4	51	6.3 (2.2)	0.3 (0.2)	25.1
CrCl ₃ ^f	4	37	0.6 (0.2)	0.9 (0.4)	1.4

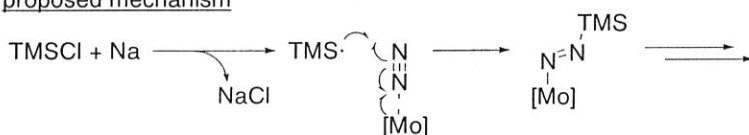
^a Reaction conditions; TMSCl (10 mmol), Na microdispersion (10 mmol), THF (6.5 ml) catalyst (0.1 mmol), under N₂, 30 °C ^b determined by GLC; (TMSCl converted into the compound/(TMSCl charged) × 100 ^c mol per metal atom ^d Li chips instead of Na ^e catalyst (0.05 mmol) ^f THF (32.5 ml), catalyst (0.05 mmol)

+ the major byproduct was (TMS)₂

+ diluted conditions increased the yield up to 37% and decreased (TMS)₂ to 39%

+ this reaction system has a considerably greater reaction rate and selectivity toward silylamine than previous Shiina's system

proposed mechanism

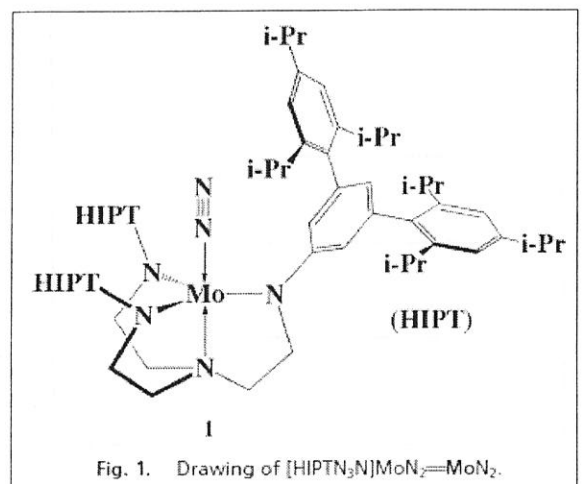


catalytic reduction of dinitrogen to ammonia

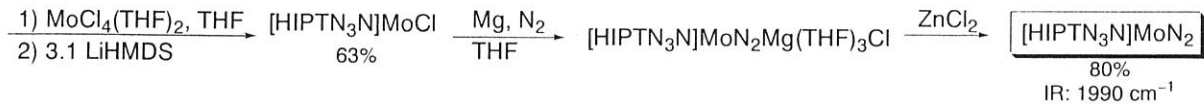
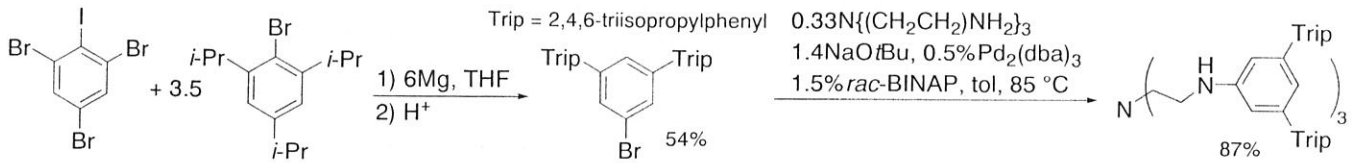
Schrock et al. *Science*, **2003**, *301*, 76.
Proc. Natl. Acad. Sci. USA **2006**, *103*, 17099.

[HIPTN₃N]MoN₂ catalyzed the reduction of N₂ to NH₃, using CrCp*₂ and (2,6-lut)BAR₄ as electron and proton source, respectively

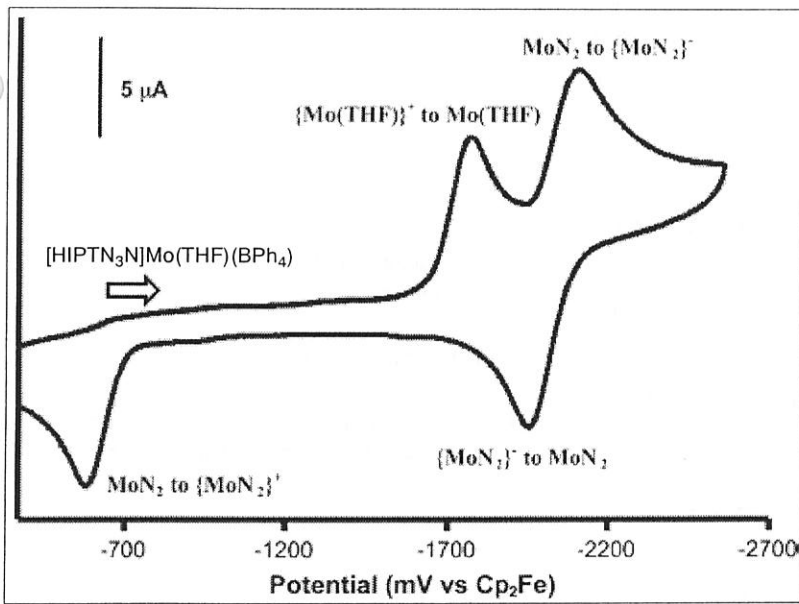
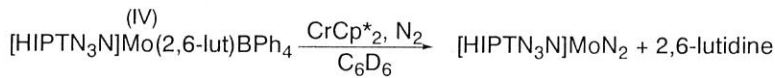
- [HIPTN₃N]³⁻ →
- + prevent any bimetallic reactions (aside from electron transfer)
 - + maximize steric protection of a metal coordination site in a monometallic species
 - + provide increased solubility of intermediates in nonpolar solvents



synthesis



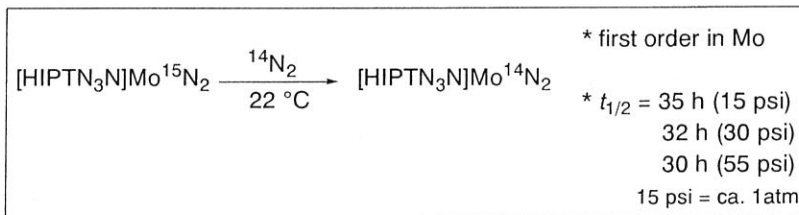
ligand exchange



cyclic voltammogram of $[HIPTN_3N]Mo(THF)BPh_4$

- + reduction of $[HIPTN_3N]Mo(THF)^+$ to $[HIPTN_3N]Mo(THF)$ yields $[HIPTN_3N]MoN_2$ in a few second
- + reoxidation of $[HIPTN_3N]Mo(THF)$ to $[HIPTN_3N]Mo(THF)^+$ is not observed on the reverse sweep

\Rightarrow replacement of other ligands with N_2 easily take place
 "probably π -back donation is important"



\Rightarrow exchange of $^{15}N_2$ for $^{14}N_2$ is independent of dinitrogen pressure up to 55 psi
 "dissociative ligand exchange"

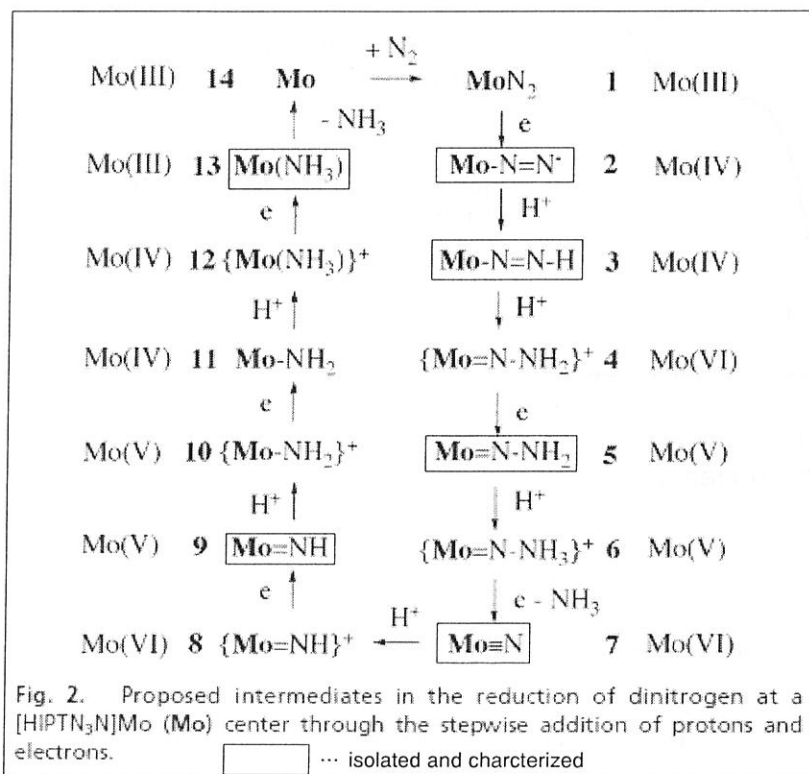
+ $[HIPTN_3N]MoN_2$ can release N_2 without addition of extra ligand

+ only 3 frontier orbitals are readily available in the coordination pocket, and an intermediate or transition state that contains two N_2 would require that at least 4 orbitals be used (2σ and 2π)

Table 1. The results of catalytic reduction of N₂. Unless otherwise indicated, all runs were done at 23° to 25°C and (1 atm) of N₂, by dropwise addition with constant stirring of 10.0 mL of a solution of CrCp*₂ in heptane (36 equivalents relative to Mo) at a rate of 1.7 ml per hour to a mixture of the Mo compound, 48 equivalents of [LutH](BAR'₄) and 0.6 ml of heptane, followed by stirring for 1 hour. Ammonia was isolated as a mixture of solid NH₄Cl and 2,6-LutHCl and analyzed by the indophenol method (38–40). The theoretical yield is based on the amount of NH₃ possible with the reducing equivalents available. Numbers in parentheses in columns 2 and 4 are the standard deviations, σ. Equiv., equivalents; expt, experimental. (Ar' = 3,5-dtCF₃C₆H₃)

Mo compound	Equiv. NH ₃ (expt/theory)	No. of runs	Yield NH ₃ , %
[HIPTN ₃ N]Mo(N ₂) (1)	7.56 (11)/12	6*	63(1)
[HIPTN ₃ N]Mo(N=NH) (2)	7.73 (15)/12.33	4†	63(1)
[HIPTN ₃ N]Mo≡N (4)	7.97 (23)/12	3‡	66(2)
[[HIPTN ₃ N]Mo(NH ₃)](BAR' ₄) (6)	8.06 (21)/12.67	3§	64(2)
[HIPTN ₃ N]Mo(¹⁵ N= ¹⁵ NH) under ¹⁵ N ₂	8.18/12.33	1	66
[HIPTN ₃ N]Mo(N ₂)¶	2.83/12	1	24

*Two runs outside the drybox (7.54 and 7.62 equivalents), two runs inside (7.55 and 7.62 equivalents), and two runs inside in the dark (7.69 and 7.36 equivalents); average = 7.56 equivalents, σ = 0.11. †7.75, 7.93, 7.61, and 7.62 equivalents; average = 7.73, σ = 0.15. ‡8.22, 7.95, and 7.75 equivalents; average = 7.97, σ = 0.23. §8.08, 8.26, and 7.84 equivalents; average = 8.06, σ = 0.21. ||>98% ¹⁵NH₄Cl by ¹H NMR, as described in the text and Fig. 2. ¶CrCp*₂ was added over a period of 25 s, followed by stirring for 7 hours.

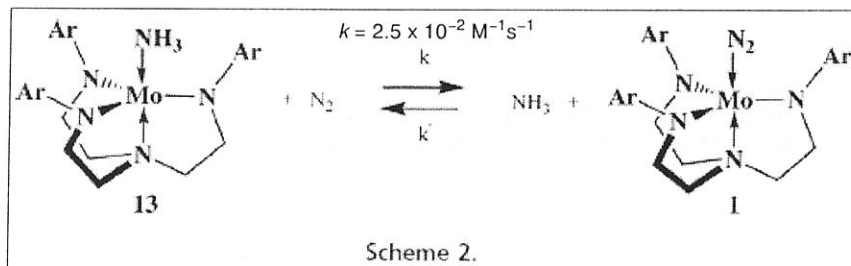


+ some of intermediates were isolated and characterized

+ CrCp*₂ was slowly added

+ the major sideproduct was H₂ (ca. 33%)
CrCp*₂ + (2,6-lut)BAR'₄ \longrightarrow H₂

ligand exchange between NH₃ and N₂



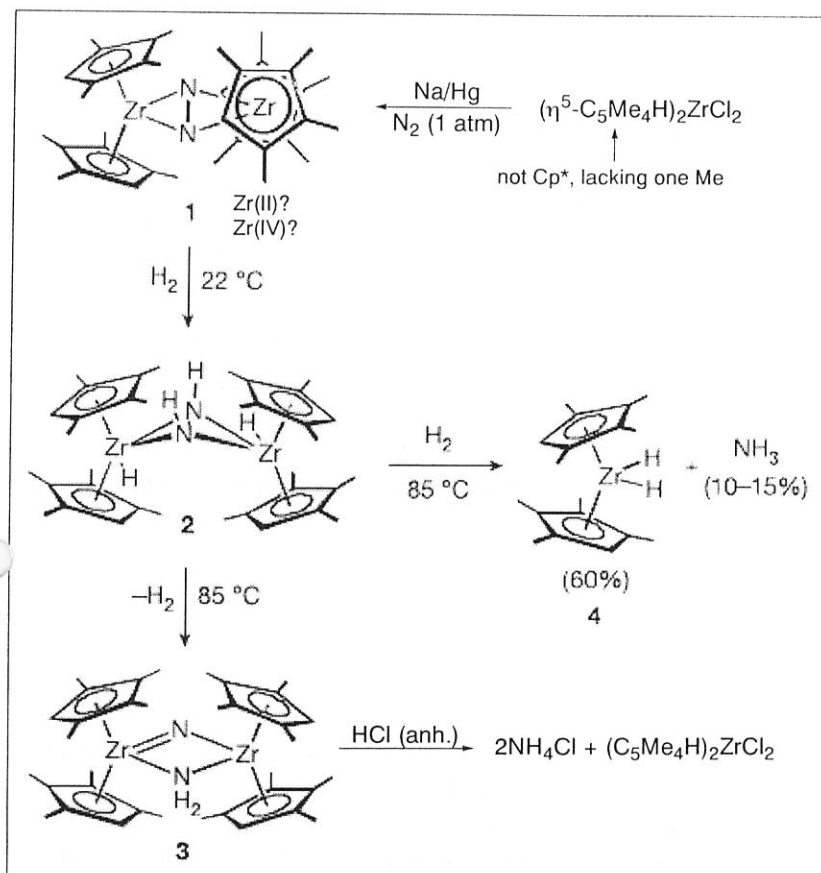
$$K_{eq} = \frac{[[\text{HIPTN}_3\text{N}]\text{MoN}_2][\text{NH}_3]}{[[\text{HIPTN}_3\text{N}]\text{Mo}(\text{NH}_3)][\text{N}_2]} = 0.1 \quad (22^\circ \text{C})$$

[HIPTN₃N]Mo(NH₃) is slowly converted to [HIPTN₃N]MoN₂

addition of BPh₃ accelerate conversion NH₃ complex to N₂ complex
→ NH₃ is scavenged by BPh₃

adding H₂ to a metal-N₂ complex tends to result in the formation of N₂ and metal-hydrogen bonds...

⇒ adjustment of ligands in Zr complex allowed direct observation of N-H bond formation from N₂ and H₂



+ $(\eta^5\text{-C}_5\text{Me}_4\text{H})_2\text{Zr}(\mu_2, \eta^2, \eta^2, \text{-N}_2)$ (**1**) has a side-on N₂ ligand

+ N-N bond length of 1.377 Å is elongated substantially compared to free N₂ (1.098 Å) and the related end-on bound N₂ complex such as $[\text{Cp}^*\text{Zr}(\eta^1\text{-N}_2)]_2(\mu_2, \eta^1, \eta^1\text{-N}_2)$

+ **1** reacted with 1 atm H₂ at ambient temperature to give **2** having side-on diazenido ligand

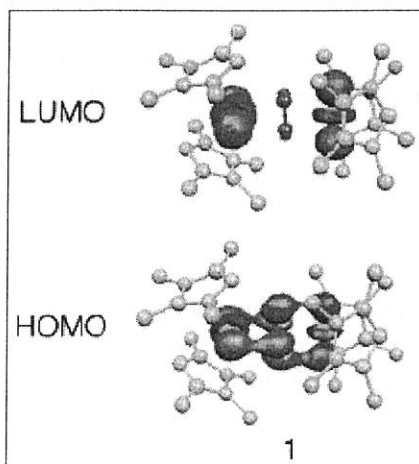
+ heating solution of **2** resulted in loss of H₂ and cleavage of N-N bond

+ treatment of **3** with HCl yielded NH₄Cl

+ gentle warming of **2** under 1 atm H₂ resulted in formation of ammonia, albeit in low yield

hydrogenation and cleavage of N₂

origin of dinitrogen hydrogenation promoted by $(\eta^5\text{-C}_5\text{Me}_4\text{H})_2\text{Zr}(\mu_2, \eta^2, \eta^2, \text{-N}_2)$



frontier molecular orbitals of $(\eta^5\text{-C}_5\text{Me}_4\text{H})_2\text{Zr}(\mu_2, \eta^2, \eta^2, \text{-N}_2)$

+ the LUMO of **1** is an in-phase linear combination of two zirconocene 1a₁ orbitals which is well-suited to accommodate incoming H₂ molecules

+ HOMO is the corresponding out-of-phase linear combination of zirconocene 1a₁ orbitals and engaged in π-bonding with a π* orbital of the N₂ ligand

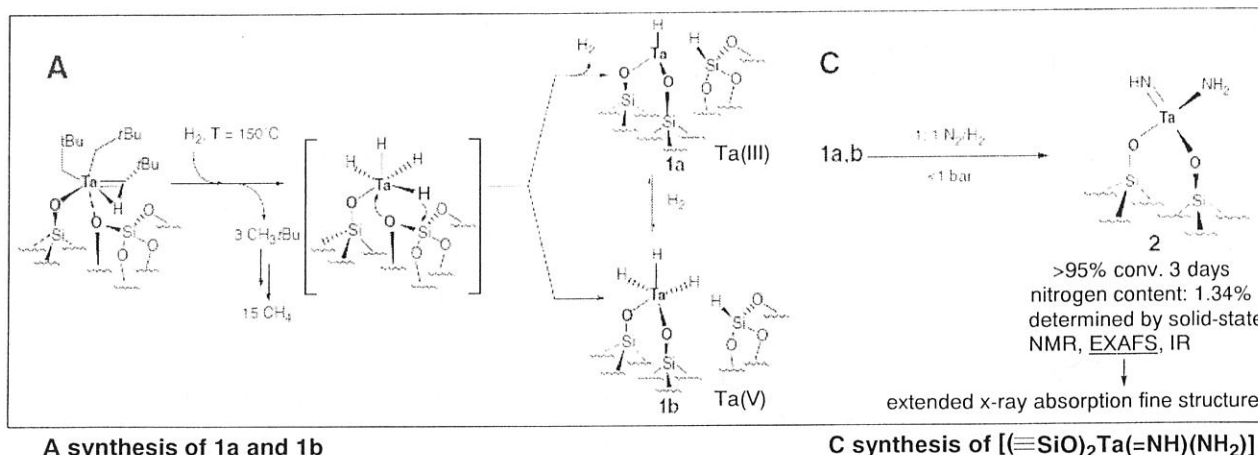
→ reminiscent of group 4 transition metal imido complex and suggests significant Zr=N character

twisted ground state structure allows opposite phase 1a₁ zirconocene orbitals to overlap with the orthogonal lobes of the N₂ π* molecular orbital, imparting significant imido character into the Zr-N bonds and thereby enabling 1,2-addition of H₂

other examples of dinitrogen hydrogenation with H₂: Fryzuk et al. *Science*, 1997, 275, 1445.

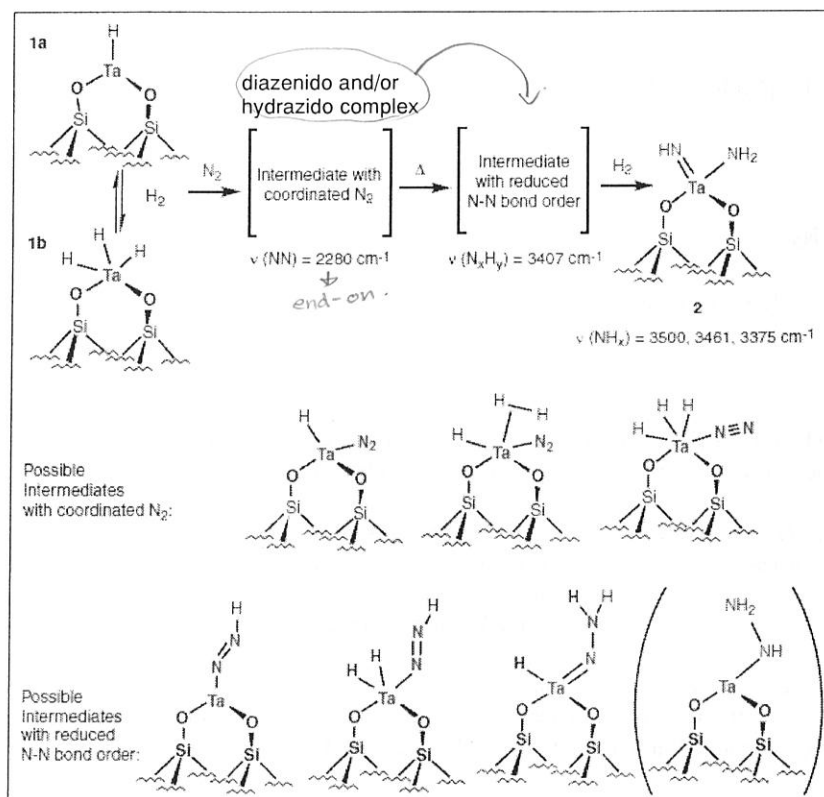
J. Am. Chem. Soc. 2007, 129, 10895.

cleavage of dinitrogen at 250 °C and 1 atm by dihydrogen on isolated silica surface-supported tantalum hydride centers
 # mechanism is distinct from others (enzymatic and artificial organometallic N₂ activating system)



the reaction of 1 with N₂ was studied by *in situ* IR

proposed reaction mechanism



+ Ta(N₂) stretching band (2280 cm⁻¹) suggest end-on coordination of N₂

+ upon heating, $\nu = 3400 \text{ cm}^{-1}$ (TaN_xH_y) and trace amount of final product appeared

+ addition of H₂ resulted in formation of 2

+ IR spectral evidence is consistent with the formation of diazenido and/or hydrazido complex

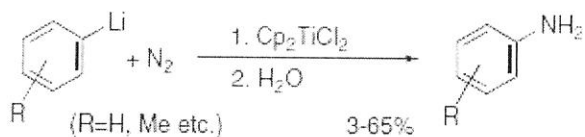
+ does not require extra proton or electron source

+ Ta-promoted heterolytic cleavage on a Ta dinitrogen adduct or unprecedented N₂ insertion in a Ta-H bond?? → unclear

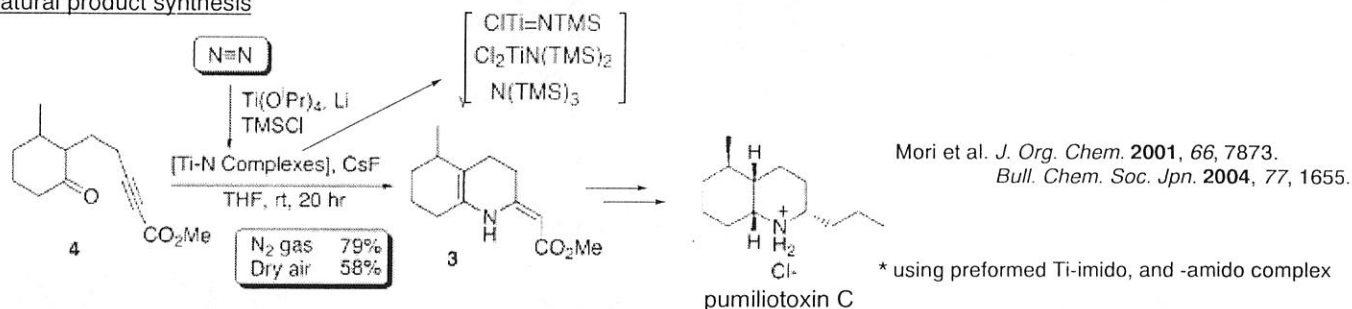
- + generally, multimetallic cooperation is needed for N₂ activation (exception: Schrock's mononuclear Mo complex)
- + surface organometallic approach yields isolated Ta^{III/IV} centers protected against bimetallic decomposition by the the strong and inert siloxy bonds to the rigid silica surface
- + highly uncoordinated, electronically unsaturated, highly thermally stable, isolated Ta
 → enabling cleavage of N≡N
- + involving both nitrogen atoms during the reduction

C-N bond formation using N₂ as a nitrogen source

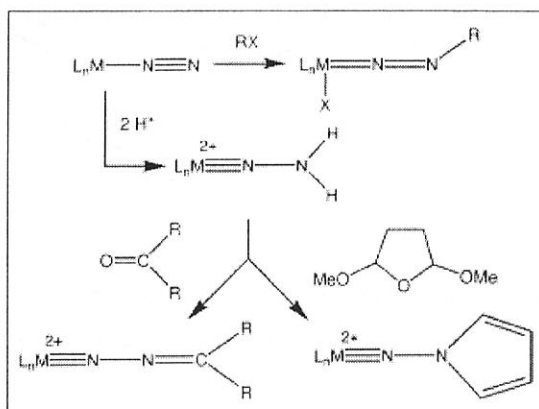
the first C-N formation using N₂



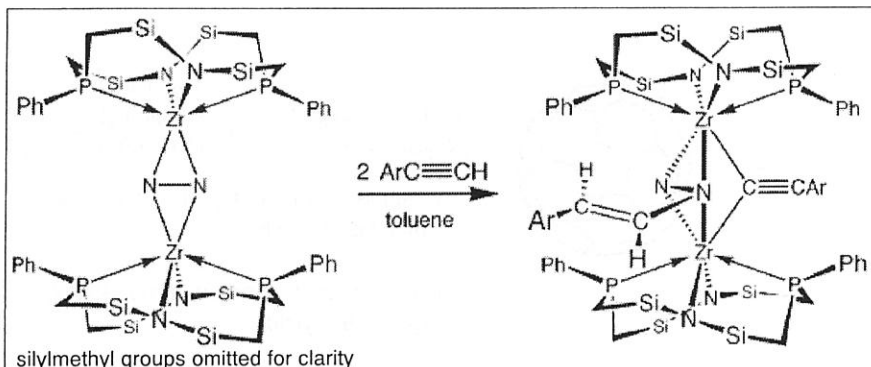
natural product synthesis



⇒ limited to the reaction with *electrophilic agent*

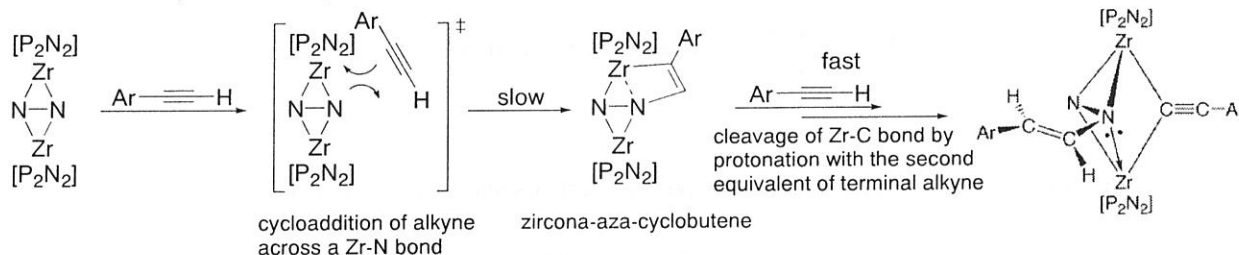


reaction with terminal alkyne Fryzuk et al. *J. Am. Chem. Soc.* **2004**, 126, 9480.

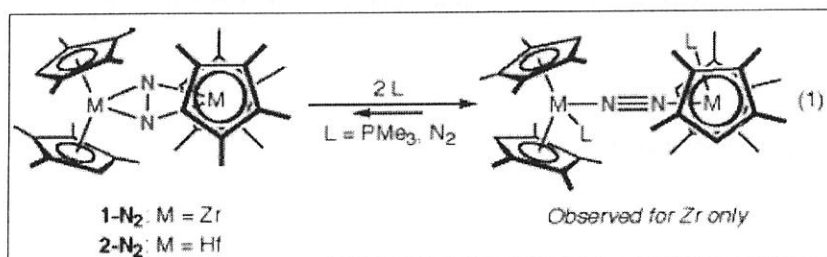


+ displacement of N₂ must be avoided
+ one acetylide as a bridging unit

lack of kinetic isotope effect using Ar-C≡D → initiation is not deprotonation of acetylenic proton



reaction with isocyanate Chirik et al. *J. Am. Chem. Soc.* **2006**, 128, 10696.



+ reaction of 1-N₂ with alkyne
→ zirconacycle and N₂ loss

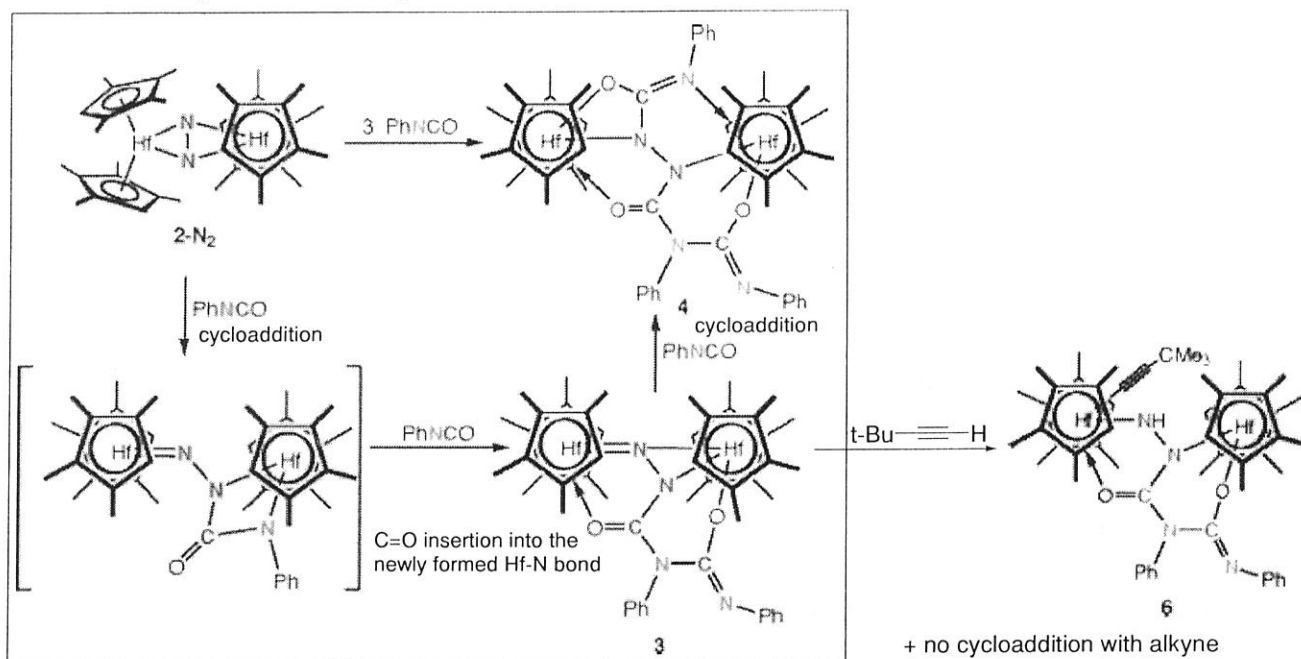
+ reaction of 1-N₂ with PhNCO
→ complex mixture and N₂ loss

+ ligand-induced side-on, end-on isomerization (using, PMe₃, only for Zr)

$2-N_2 \rightarrow$

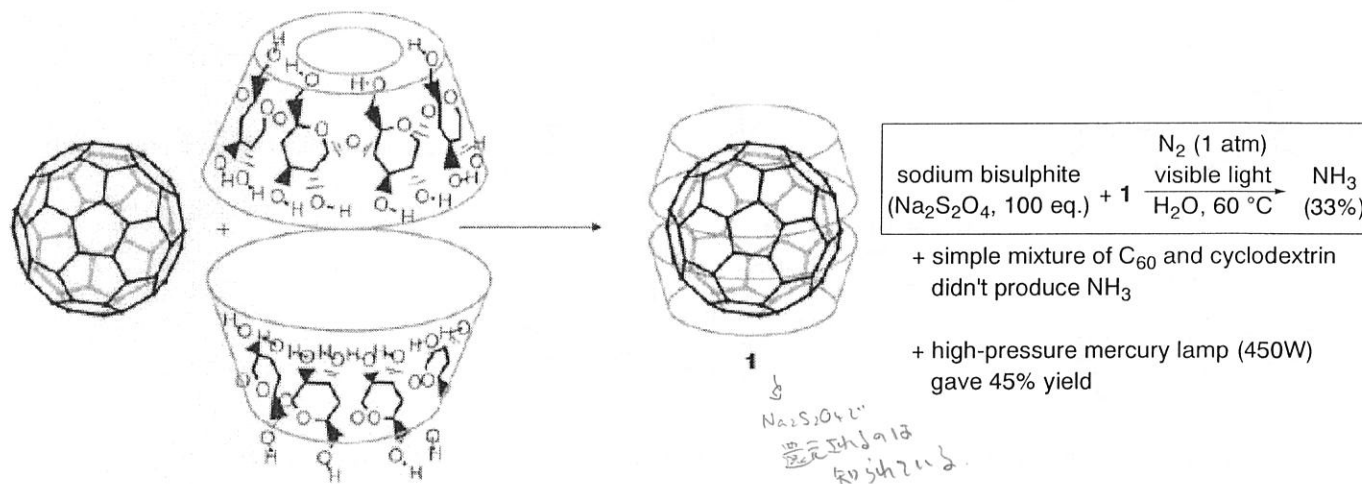
- + hafnium congener
- + shorter Hf-N bonds and elongated N-N linkage
- + blue-shifted LMCT band relative to $1-N_2$

 \Rightarrow suggesting increased imido character in the M-N bond
 Ligand to Metal Charge Transfer



non-metal system for N_2 fixation Uemura, Nishibayashi, Yoshida et al. *Nature*, 2004, 428, 279.

water-soluble C_{60}/γ -cyclodextrin (1:2) complex and light under 1 atm N_2



buckminsterfullerene + γ -cyclodextrin $\xrightarrow[118^\circ\text{C}]{\text{H}_2\text{O}/\text{toluene}}$ bicapped buckminsterfullerene **1**

mechanistic investigation

- + **1** has strong absorption in the UV region and weaker but significant bands in the visible region
- + charge transfer between N_2 and reduced and excited **1** (exciplex formation) is probably involved
- + cyclic voltammogram of **1** in $H_2O \rightarrow$ reversible wave at $-0.61V$ (C_{60}/C_{60}^-) and irreversible wave at $-1.09V$ (C_{60}^-/C_{60}^{2-})
- + IR and NMR spectra were not informative
- + N_2 coordinate to the surface of the C_{60} molecule in **1** in end-on mode