Nitrogen Fixation

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# Expanding Boundaries: $N_2$ Cleavage and Functionalization beyond Early Transition Metals

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Using molecular nitrogen ($N_2$) as a building block for the preparation of nitrogen-containing organic molecules is a grand challenge in chemical synthesis.[1] The strong NN bond (226 kcal mol$^{-1}$), the large HOMO–LUMO gap (10.8 eV), and the non-polarity render the molecule inert to most reagents.[2] To overcome this challenge, chemists have typically relied on highly reducing early-transition-metal compounds to provide electrons to weaken or even cleave the N$-$N bond to open reactivity. In a recent Communication, Schneider and co-workers[3] described a rhenium pincer complex that promotes $N_2$ cleavage, and the resulting metal nitride could be used to deliver the nitrogen atom for the stoichiometric synthesis of nitriles. This work will be the focus of this Highlight.

Why is dinitrogen an attractive building block for nitriles? The current industrial route to nitriles relies on the catalytic ammoxidation of propylene to yield acrylonitrile, a useful monomer for the generation of polyacrylonitrile plastics. Acetonitrile and hydrogen cyanide are byproducts of this process.[5] Whereas acetonitrile finds widespread use as a solvent, correlating its manufacture with polymer production has recently resulted in a disruption in supply.[4] The other byproduct, toxic hydrogen cyanide, is deprotonated on site to NaCN, a common CN$^-$ source in nucleophilic cyanation.[5] The direct catalytic synthesis of nitriles from $N_2$ could provide several practical and environmental advantages. As $N_2$ accounts for 78 % of the atmosphere, it is abundant and readily accessed as is the $^{15}N_2$ isotopologue, offering a potentially economic route to $^{15}$N-labeled compounds.

A possibly more stimulating intellectual and practical challenge is the use of dinitrogen as a surrogate for ammonia. A more holistic analysis of nitrile synthesis using the currently practiced ammoxidation process draws parallels with the modern airline industry. Instead of a "direct flight", where $N_2$ remains a constituent of a triple bond, dinitrogen is fully reduced to ammonia with tremendous energetic costs using the Haber–Bosch process and then, following this "layover", undergoes reoxidation with the alkene.[6–8] Approximately 20 % of the ammonia synthesized through the Haber–Bosch process is upgraded to nitrogen-containing organic molecules, including amino acids, nitriles, amides, and ureas.[9] One of the subtle, hidden costs associated with these routes is carbon dioxide pollution. Haber–Bosch ammonia synthesis, while enabling approximately 50 % of the world's food production, also accounts for 3 % of the global $CO_2$ emissions, principally from the steam reformation of methane, which is used to generate the $H_2$ gas required for nitrogen fixation. As concerns about global climate increase,[10] emphasis will be placed on developing carbon-neutral chemical processes of nitrogen fixation and ammoxidation that do not require, by reaction stoichiometry, a carbon dependency.

While a widely recognized contemporary challenge in modern small-molecule activation chemistry, examples of the direct incorporation of $N_2$ into organic molecules remain rare.[11–13] Among the many potential target transformations, the conversion of $N_2$ into organic nitriles is attractive, as a "triple bond metathesis" with an appropriate carbon source may be thermodynamically viable.[14] Similar reasoning may also be applied to the synthesis of isocyanates (RN=C=O) and carbodiimides (RN=C=NR′) where the formation of N=C double bonds also has thermodynamic benefits.[15,16] Furthermore, the versatility of these functional groups in organic synthesis inspires new and potentially transformative synthetic routes.[17]

The 1995 report by Laplaza and Cummins of low-temperature $N_2$ cleavage by a three-coordinate molybdenum complex demonstrated that coordination complexes could be tailored through rational ligand design to promote the cleavage of one of the strongest covalent bonds in chemistry.[18] Following this discovery, a number of other examples quickly ensued[19] although examples that yield terminal metal nitrides remain relatively uncommon. Representative examples with molybdenum,[20,21] niobium,[22] and most recently rhenium[23] are highlighted in Figure 1.

Although the cleavage of the strong N$-$N bond in $N_2$ was long perceived as the most challenging step for the synthesis of $N_2$-derived nitrogen-containing organic molecules, this proved not to be the case. As evidenced by the seminal Cummins discovery, the exergonicity of the $N_2$ cleavage reaction to form the corresponding monomeric molybdenum nitride suggests that the resulting Mo$-$N bond may in fact be stronger and therefore less reactive than $N_2$. This potential limitation was cleverly overcome by Cummins[24] and co-workers who exploited the polarity of [N($^t$Bu)Ar]$_3$MoN to promote reactions with electrophilic acyl chlorides, ultimately

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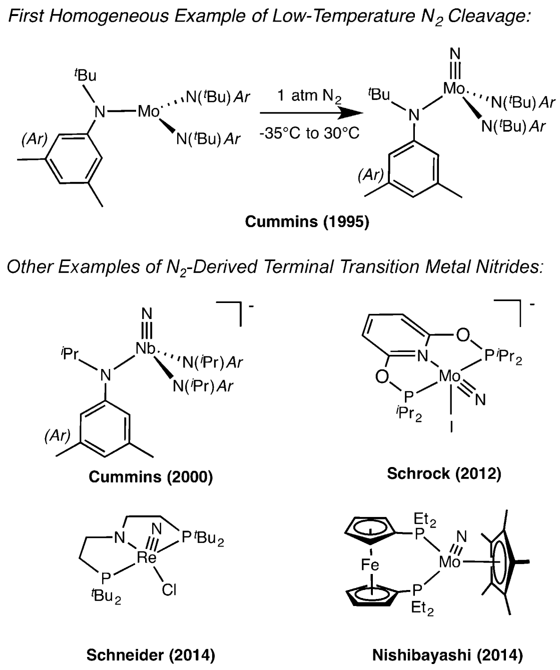
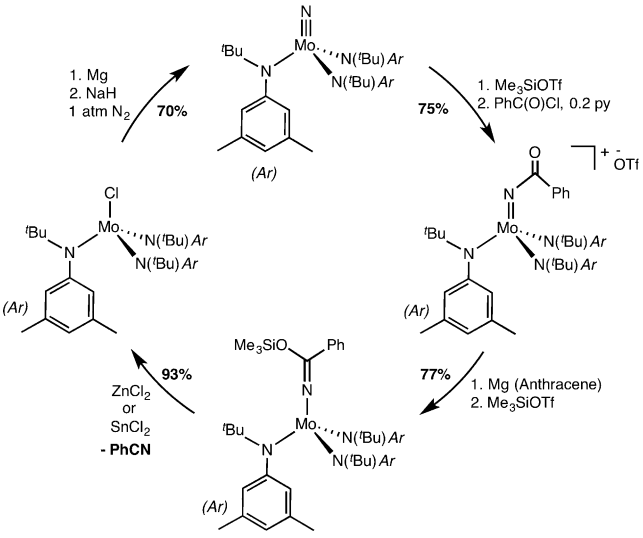


*Figure 1.* Terminal transition-metal nitrides derived from $N_2$.

resulting in a synthetic cycle for benzonitrile using $N_2$ as the nitrogen source (Scheme 1).

An alternative approach to dinitrogen cleavage and functionalization that has been explored in our own laboratory is known as "ligand-induced $N_2$ cleavage". This concept, whereby an incoming ligand serves both as a source of electrons as well as the substrate for N−C bond formation, was first described by Sobota and Janas,[25] where coordinated dinitrogen underwent carbonylation to form titanium isocyanates, and was later adopted by Fryzuk and co-workers to achieve rich dinitrogen functionalization chemistry with tantalum.[26] Our laboratory has since extended this approach



*Scheme 1.* Cummins' incorporation of atmospheric dinitrogen into an organic nitrile. py = pyridine, Tf = trifluoromethanesulfonyl.

to strongly activated, side-on $N_2$ complexes of zirconocene and hafnocene compounds.[27] Carbonylation of an *ansa*-hafnocene dinitrogen derivative resulted in $N_2$ cleavage with concomitant N−C and C−C bond formation, resulting in a rare bridging oxamidide ligand (Scheme 2a).[28] Notably, the $[N_2C_2O_2]^{4-}$ core was assembled from $N_2$ and CO—the diatomic compounds with the two strongest bonds in chemistry. Using a less sterically protected ligand scaffold to prevent competing cyclopentadienyl substituent cyclometalation, the synthesis and subsequent reactivity of a rare hafnium nitride was explored (Scheme 2b). This compound exhibits rich N−C bond-forming chemistry, providing access to cyanamide, carbodiimidyl, amidinato, ureate, isocyanate, and carbodiimide ligands where the nitrogen atom was derived from $N_2$ in each case (Scheme 2, bottom).[29]

These molybdenum and hafnium examples, along with related studies from the groups of Sita[15] and Nishibayashi,[21] demonstrated the dichotomy associated with azophilic early transition metals. Whereas the redox potentials of reduced early-transition-metal compounds provide a driving force for $N_2$ cleavage, the availability of empty $t_{2g}$ orbitals in the oxidized product strengthens the resulting $M{-}NR_x$ bonds and imposes significant kinetic and thermodynamic barriers for the liberation of the functionalized nitrogen-containing ligand from the coordination sphere of the metal. The rich chemistry of molybdenum with the various nitrogen ligand types relevant to nitrogen fixation[30] highlights this concept. Examples containing $N_2$, diazenido (−NNR), hydrazido (=$NNR_2$), nitride (≡N), imido (=NR), and amido (−$NR_2$) ligands are all known and are a result of the appropriate energy disposition and symmetry of the metal d orbitals.[31]

One strategy to overcome this challenge is to move to the right on the periodic table and use later transition metals for $N_2$ cleavage and functionalization.[32] In doing so, one must surmount the "nitrido wall", a concept analogous to Harry Gray's famous "oxo wall",[33] where the higher d electron count of lower-oxidation-state late transition metals populates M−N π* orbitals and disfavors metal–ligand multiple bonding (Figure 2).[34] As a result, the synthesis of terminal transition-metal nitrides using late metals poses a fundamental synthetic challenge. While rare, examples of such compounds have been reported for iron,[35] ruthenium,[36] iridium,[37] as well as rhodium[38] albeit not from $N_2$. Notably, the groups of Holland[32a] and Vogler[32b] demonstrated unique examples of dinitrogen cleavage by late metal systems using iron and ruthenium complexes, respectively.

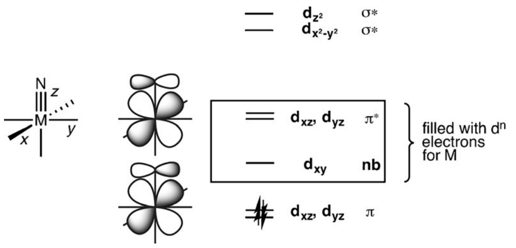
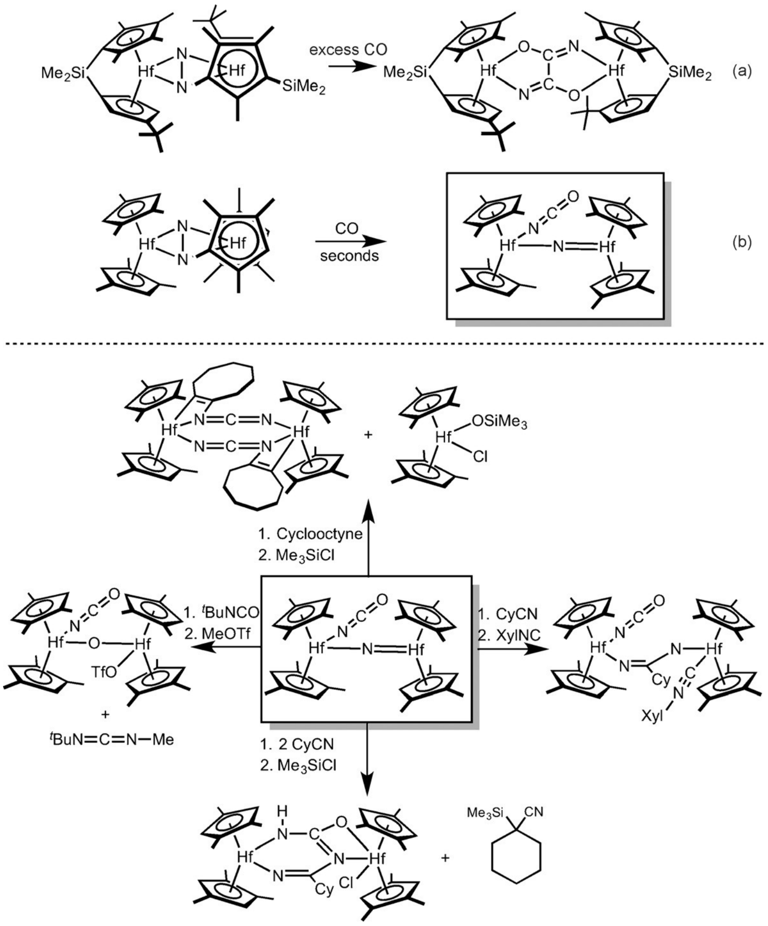
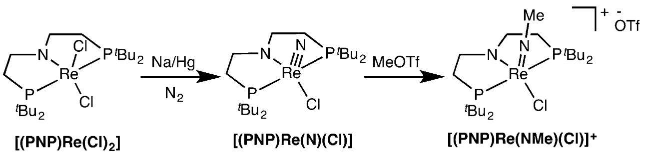


*Figure 2.* Qualitative d orbital splitting diagram for transition-metal nitrides in an octahedral coordination geometry.



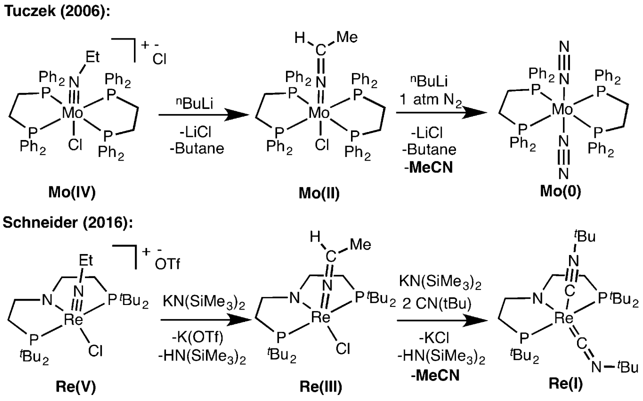
*Scheme 2.* a, b) CO-induced $N_2$ cleavage in activated dinitrogen hafnocene complexes and subsequent N−C and C−C bond-forming reactions of a base-free hafnium nitride. Cy = cyclohexyl, Xyl = xylyl.

Given the intense and long-standing interest in early-transition-metal dinitrogen chemistry, the rich rhenium dinitrogen chemistry discovered by Schneider and co-workers is both notable and refreshing. Treatment of the pincer-ligated rhenium dichloride precursor $[(PNP)ReCl_2]$ ($PNP = N(CH_2CH_2P^tBu_2)_2$) with strong reducing agents, such as Na(Hg) or $(\eta^5\text{-}C_5Me_5)_2Co$, resulted in dinitrogen cleavage and formation of a terminal rhenium nitride (Scheme 3).[23] The Re−N bond was then elaborated by treatment with methyl triflate to yield the formally rhenium(V) *N*-methylimido product, [(PNP)Re(NMe)(Cl)]OTf.



*Scheme 3.* Synthesis and reactivity of an $N_2$-derived rhenium nitride.

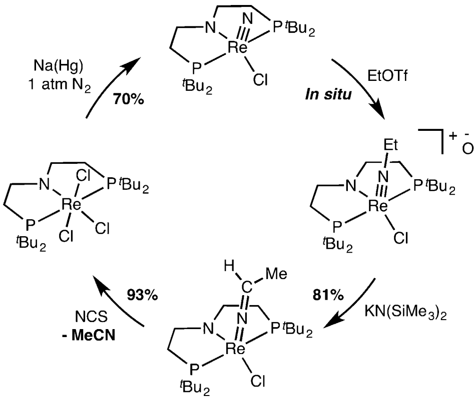
These initial promising findings provided the foundation for the most recent Communication,[3] where the reactivity of the analogous *N*-ethylimide rhenium complex, $[(PNP)Re(NEt)(Cl)]^+$, was explored in the context of nitrile synthesis. Analogous to the molybdenum chemistry pioneered by Tuczek and co-workers, where imido ligands were converted into nitriles through aldimido intermediates (Scheme 4), Schneider and co-workers employed a double-deprotonation strategy to liberate acetonitrile from the coordination sphere of rhenium while stabilizing the resulting $Re^I$ species with a strongly π-accepting isocyanate ligand. In both examples, the metal undergoes formal four-electron reduction, from



*Scheme 4.* Release of acetonitrile from molybdenum (top) and rhenium (bottom) imides by a double-deprotonation strategy.

$\mathrm{Mo^{IV}}$ to $\mathrm{Mo^{0}}$ and from $\mathrm{Re^{V}}$ to $\mathrm{Re^{I}}$. For the latter, the anionic, electron-donating amido-based pincer ligand is likely essential for creating a similar electronic environment as in the molybdenum example.

Having demonstrated the key four-electron reduction of $[\mathrm{(PNP)Re(NEt)(Cl)}]^+$ that results in the release of one equivalent of acetonitrile, conditions were explored for its release in a synthetic cycle. As shown in Scheme 5, oxidative conditions involving the treatment of the rhenium aldimide compound, $[\mathrm{(PNP)Re(NCHCH_3)(Cl)}$, with two equivalents of NCS resulted in the regeneration of $\mathrm{(PNP)ReCl_3}$. The addition of an appropriate reducing agent resulted in $N_2$ cleavage and formation of the rhenium nitride, $[\mathrm{(PNP)Re(N)(Cl)}]$, a compound known to engage in electrophilic N−C bond formation and subsequent deprotonation chemistry. Thus a synthetic cycle was completed where $N_2$ was used as the nitrogen source for acetonitrile.



***Scheme 5.*** Synthetic cycle for the incorporation of atmospheric dinitrogen into acetonitrile with a PNP rhenium system. NCS = *N*-chlorosuccinimide.

Whereas the use of strong reducing agents in combination with electrophiles poses a challenge for catalysis, the work of Schneider and co-workers is nevertheless a landmark contribution to the field of dinitrogen functionalization as $N_2$ cleavage and subsequent functionalization are no longer the exclusive privilege of early transition metals. Extending this type of reactivity to less azophilic transition metals will also provide fundamental concepts likely to extend beyond $N_2$ functionalization chemistry and open new opportunities in organometallic chemistry, catalysis, and small-molecule activation.

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