

ORGANO-NITROGEN COMPOUNDS FROM MOLECULAR NITROGEN

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INTRODUCTION

Industrial nitrogen fixation plays an important role in sustaining approximately 40% of the Earth's population through generation of synthetic fertilizers. Annually, ca. 500 million tons of anhydrous ammonia, ammonium nitrate, and urea are produced through the Haber-Bosch process, which requires harsh conditions (200 atm, 450-500°C) and affords low yields 10-20%. It has been estimated that this accounts for 1% of the world's annual energy consumption.¹ An efficient, mild method for fixating molecular nitrogen would be of great worth not only due to the immediate energy savings but it would also serve to provide novel reactivity possibly capable of generating organo-nitrogen compounds from molecular nitrogen.

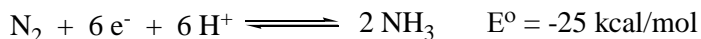
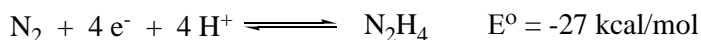
The first, stable dinitrogen coordination complex, $[\text{Ru}(\text{NH}_3)_5(\text{N}_2)]^{2+}$, was isolated in 1965 by Allen and Senoff,² and this initial observation has led to the development of many systems (primarily based on molybdenum, tungsten, and titanium) for incorporating molecular nitrogen into organic molecules.³ This review will focus on the various methods for generation of nitrogen-containing organic molecules based on synthetic nitrogen fixation processes.

Background

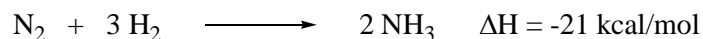
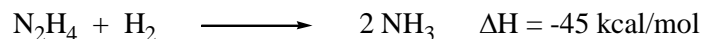
Thermodynamically, the fixation of nitrogen is an exothermic process for both protonation and hydrogenation steps (Scheme 1). However, as is evident from the hydrogenation of N_2 to N_2H_2 , the

Scheme 1: Thermodynamics of Nitrogen Fixation

Reduction/Protonation:



Hydrogenation:



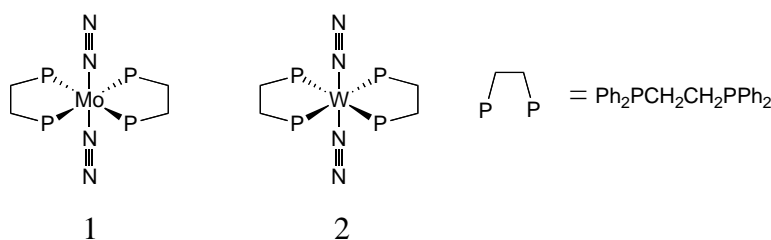
$$\Delta G^\circ = -7.7 \text{ kcal/mol}$$

96% product @ 298 K

0.2% product @ 723 K

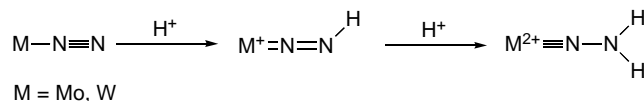
initial breaking of the triple bond in the nitrogen molecule is largely an endothermic process. This energy difference of 51 kcal/mol illustrates the necessity for the extreme heat and pressure crucial for the Haber-Bosch process. Reduction and protonation of molecular nitrogen at STP as demonstrated by nitrogenase enzymes offers the potential for a milder method of nitrogen fixation.

Molybdenum (**1**) and tungsten (**2**) catalysts were originally developed for the production of ammonia from dinitrogen in acidic media.^{4,5} Isolation of several intermediates on this reaction pathway lends mechanistic insight and serves as a starting point for the design of new systems for generating nitrogen-containing organic molecules from molecular nitrogen. The Group 6 transition metals (W, Mo, Cr) are believed to have the greatest orbital-overlap with end-on bound molecular nitrogen. The nitrogen molecule associates with the metal center of either electron rich low valent metals or electron deficient metals in high oxidation states. The electron rich cases will be described herein. π -Backbonding from electron rich metal centers is the reason for the stability of molecular nitrogen association and the σ -bond from the lone-pair on dinitrogen is the stabilizing interaction for electron deficient metal centers.



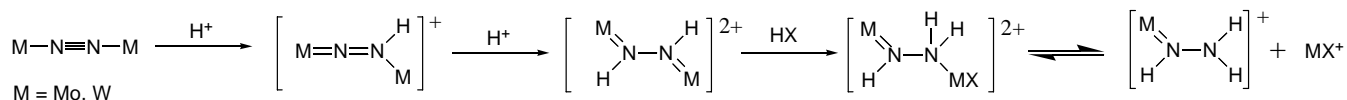
Several reaction intermediates have been isolated along the reaction pathway to ammonia production (Scheme 2). Isolation of various intermediates provides mechanistic insight and identification of complexes possibly suitable to be utilized for the generation of organo-nitrogen compounds. These intermediates show protonation occurring first at the terminal nitrogen of the complexes. A computational study has suggested the largest charge density resides on the terminal nitrogen of end-on bound dinitrogen.⁶ This data supports a bonding scheme in which the dinitrogen ligand is stabilized by π -back bonding from the metal, aiding in the protonation of the terminal nitrogen. Many molybdenum and tungsten hydrazido complexes with various ligand systems have been isolated (i.e. P, S, monodentate and bidentate); the hydrazido intermediate appears to be common to many nitrogen fixation systems.³

Scheme 2: Hydrazido(2-) Complex Generation



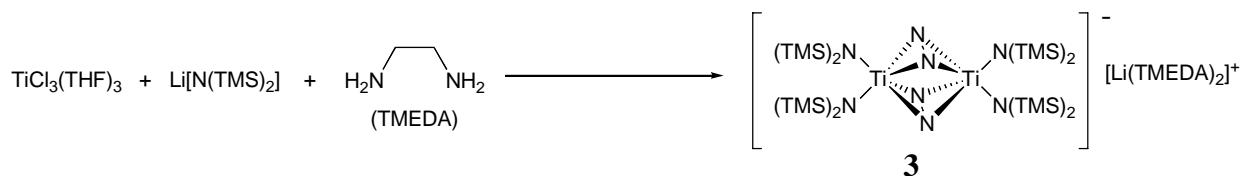
The systems discussed thus far all contain an end-on bound dinitrogen ligand which facilitates electron transfer from the metal. However, other catalysts are believed to operate through multiple metal center end-on binding (Scheme 3).^{7,8} Several of the starting $\mu-N_2$ bound complexes, typically from electron deficient metals have been isolated and shown to produce hydrazine under acidic conditions in low yields (ca. 20%), however; no intermediates have been characterized.

Scheme 3. Speculative Bimetallic Mechanism.



Titanium complexes are known to bind nitrogen in a multiple-metal, non-end-on fashion (Scheme 4).⁹ Complex **3** forms from ammonia and offers the first system capable of achieving catalyst turnover through the reaction of molecular nitrogen to tris(trimethylsilyl)amine. Considerable uses have been developed for the incorporation of the amine product in organometallic reagents.

Scheme 4. Generation of Non-end-on Bound Nitrogen.

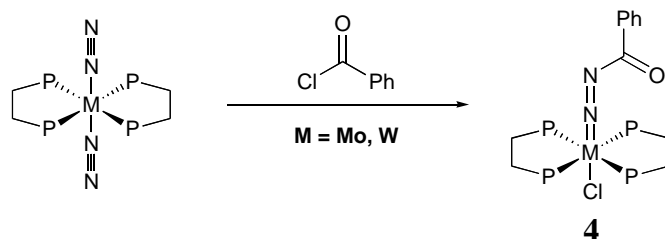


ORGANO-NITROGEN LIGAND GENERATION

The relatively large negative charge density build up on the terminal nitrogen of end-on mono-metallic complexes (i.e. **1** and **2**) may be exploited to incorporate organic molecules into the ligand environment of the metal. The first such reaction was demonstrated between an acid chloride and complexes **1** and **2** to generate complex **4** (Scheme 5).¹⁰ Complex **4** is known to form the hydrazido (2-) complex upon addition of HCl. It was later found that the terminal nitrogens of complexes **1** and **2** are

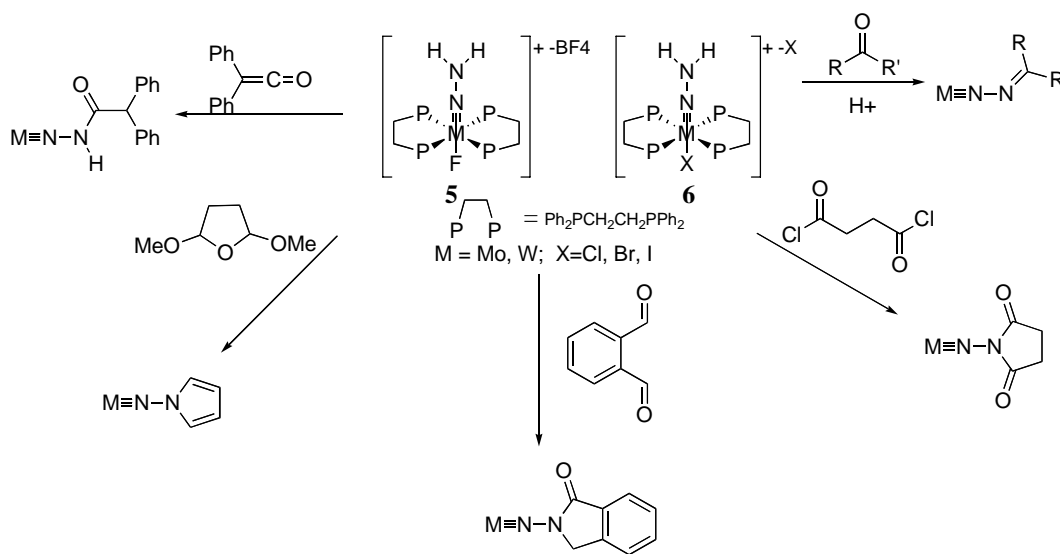
sufficiently nucleophilic to undergo mono- and di- alkylation with a variety of alkyl halides in moderate yields (75-41%).¹¹ Interestingly, mono-alkylation is selectively achieved over di-alkylation in the presence of excess alkyl halide. Gem-dibromides are also reactive with complexes **1** and **2** for the generation of the corresponding hydrazido (2-) complex.¹²

Scheme 5. First Organo-Nitrogen Ligand from Dinitrogen.



If an acid is employed to generate a hydrazido (2-) complex such as the product shown in Scheme 1, the reactivity of the terminal nitrogen parallels that of amines. Hidai demonstrated the addition to carbonyl compounds for a variety of carbonyls as seen in Scheme 6 from complexes **5** and **6**.³ Metal-bound amide type bonds may be formed from ketenes and phthalaldehyde. Pyrrole synthesis is possible from succinaldehyde. Ketones and aldehydes react readily to form imines, and finally diacid chlorides react readily to form imides.

Scheme 6. Carbonyl Reactivity with Hydrazido(2-) Complexes.



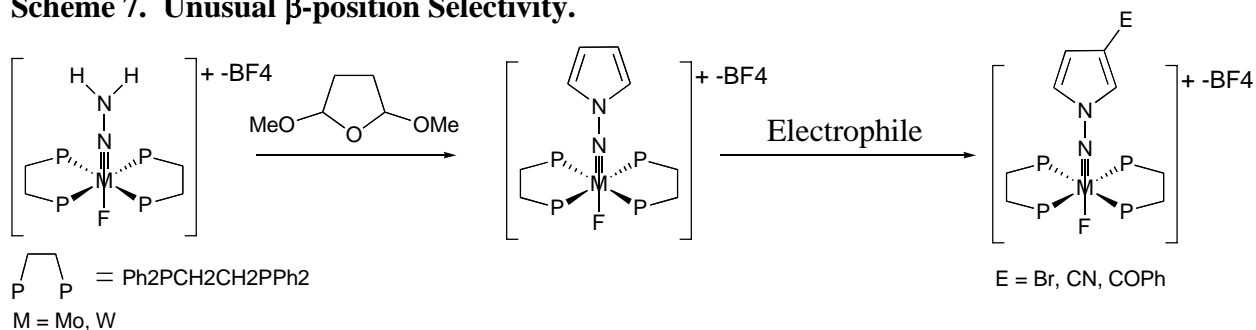
GENERATION OF ORGANO-NITROGEN COMPOUNDS

Tungsten and Molybdenum

Although the reactivity of metal bound dinitrogen with organic compounds is known without liberation of the nitrogen containing organic moiety, the utility of the reaction is narrowly limited to the synthesis of specific hydrazido (2-) metal complexes. In 1977, Chatt reported the first examples of the liberation of organic compounds from various alkylated hydrazido (2-) complexes formed from **1** and **2**, through the destruction of the metal complex with LiAlH_4 .¹³ An aqueous workup is necessary for good yields of the resulting amine. Chatt also noted that if only LiAlH_4 and MeOH were used under anhydrous conditions, approximately 30% of the desired amine was isolated. Under these conditions $\text{WH}_4(\text{dppe})_2$ is the major tungsten source isolated, which may be converted to **2** giving a cyclic process for nitrogen fixation. Leigh demonstrated through non-destructive electrochemical reduction, that alkylated complexes of **1** could reform complex **1** and a dialkylhydrazine.¹⁴

Hidai demonstrated pyrrole could be formed from succinaldehyde and either complex **1** or **2** in good yield (58% and 65%, respectively) upon treatment with LiAlH_4 .¹⁵ Interestingly, a variety of electrophiles could be added to functionalize the electron rich π -system of pyrrole selectively at that β -position (Scheme 7). This result stands in contrast to the usual α -position selectivity seen for free pyrrole. The harsh conditions needed to liberate the organo-nitrogen compound greatly limit the scope of substituted pyrroles that may be isolated. Unusual reactivity such as this provides incentive for future research due to the complementary selectivities seen (in relation to free pyrroles) for the bound 1-pyrrolylimido complexes due to steric encumbrance.

Scheme 7. Unusual β -position Selectivity.

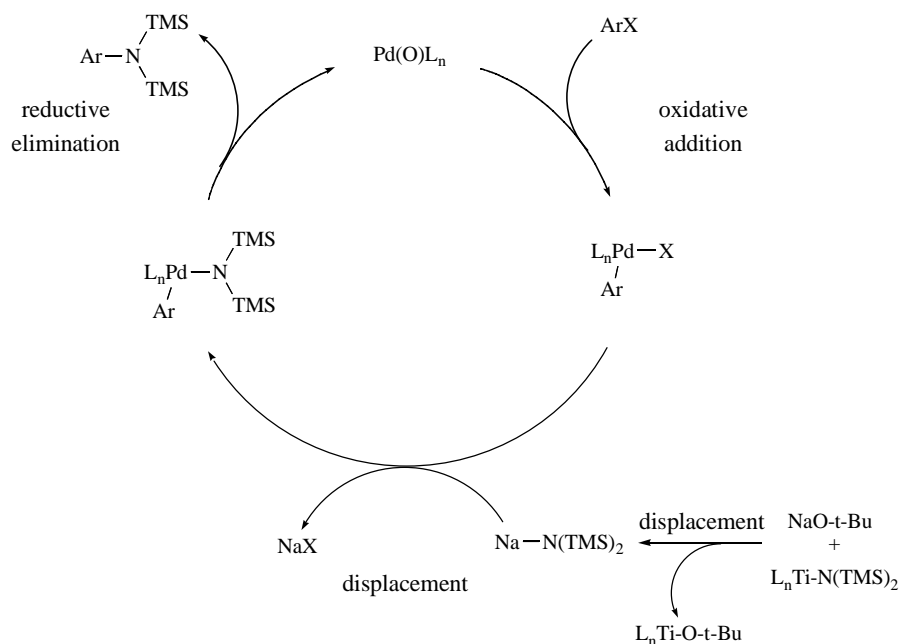


Titanium Based Reagents

Non-end-on bound molecular nitrogen fixation is possible with titanium complexes as previously stated. Mori has shown that, TiCl_4 or $\text{Ti}(\text{OiPr})_4$, in combination with Li, TMSCl and dinitrogen form

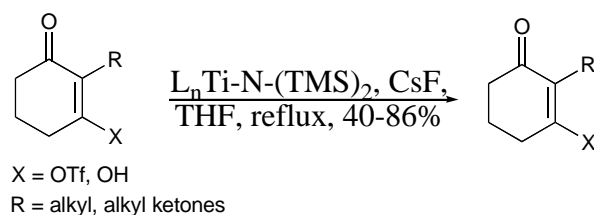
$L_n\text{Ti-N}(\text{SiMe}_3)_2$ complex (**7**). Upon addition of an aryl halide, $\text{Pd}_2(\text{dba})_3$, dppf, and NaOtBu , displacement with the $\text{N}(\text{SiMe}_3)_2$ group is facilitated after an oxidative addition of an aryl halogen bond on a $\text{Pd}(0)$ complex.¹⁶ The reductive elimination and subsequent in situ deprotection yields the anilines in good to low yields (11%-77%). The yields are highly dependent on the aryl ring substituent with electron-rich rings affording the lowest yields. The proposed catalytic cycle is shown in Scheme 8.¹⁶

Scheme 8. Catalytic Cycle for Aniline Formation.



Mori later extended the substrate scope to include β -keto enol triflates or 1,3-diketones through the use of CsF as an activator instead of sodium tert-butoxide (Scheme 9). Higher yields are observed for compounds capable of forming cyclic enamine and alkyl ketones to generate tri and tetra substituted pyrroles.

Scheme 9. Enaminone Synthesis.

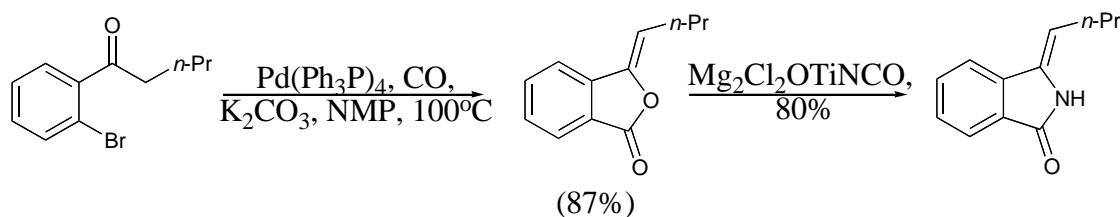


The $\text{Ti/Li/N}_2/\text{TMSCl}$ system constitutes a catalytic method for nitrogen fixation provided 50 equiv. of both Li and TMSCl are used; 2.5 turnovers are observed per titanium atom to give

tris(trimethylsilyl)amine.¹⁷ This marked the first generation of an organo-nitrogen compound in situ with molecular nitrogen as the nitrogen source for which a stoichiometric amount of a metal complex was not needed; however, it certainly was not the first generation of tris(trimethylsilyl)amine from a catalytic amount of a transition metal complex (*cis*-[Mo(N₂)₂(PMe₂Ph)₄], up to 24 turnovers).¹⁸

TiCl₄ in combination with Mg and N₂ (1 atm or atmospheric) in THF generates a complex of formula [THF/Mg₂Cl₂/TiN], which upon addition of CO₂ affords the isocyanate complex [3THF/Mg₂Cl₂O/TiNCO] (**8**). Complex **8** provides access to a novel pathway for formation of lactams from ortho halide substituted benzylic ketones. The stepwise process is shown in Scheme 10. The reaction may also be run as a one-pot single addition of all required reagents to afford the same yield as the two-step process.¹⁹

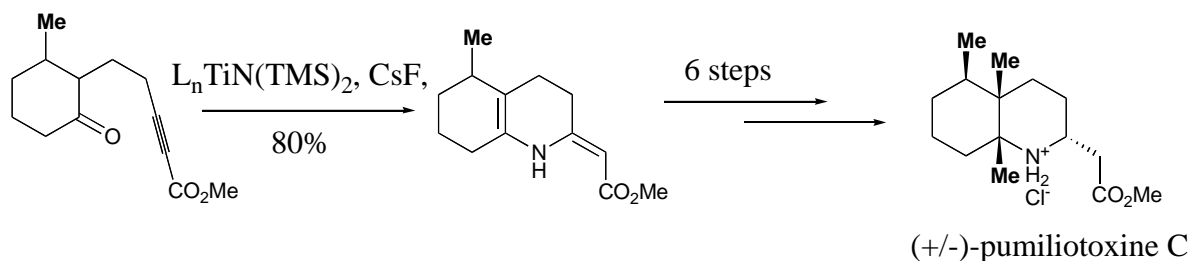
Scheme 9. Novel Lactam Synthesis.



Nitrogen Fixation Total Synthesis Example

Mori reported the total synthesis of (+/-)-pumiliotoxin C from a keto-alkyne and $\text{L}_n\text{TiN}(\text{TMS})_2$ as shown in Scheme 11. The key transformation of the synthesis is the formation of the six membered heterocycle through the use of the titanium complex derived from molecular nitrogen. The *z*-olefin configuration is rationalized based on hydrogen bonding between the ester and amine.²⁰

Scheme 11. Key Transformation in the Total Synthesis of Pumiliotoxin C



CONCLUSIONS:

Transition metal-derived complexes **5** and **7** have allowed for the synthesis of organo-nitrogen molecules through novel transformations beginning with molecular nitrogen. Although interesting chemistry is being developed for the incorporation of dinitrogen into organo-nitrogen compounds, these methods are not competitive with traditional methods for introducing nitrogen. Until the realization of a catalytic system, novel transformations with complexes derived from molecular nitrogen will continue to be of the most practical value for the generation of organo-nitrogen compounds.

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