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Cyclic Denitrogenation of N-Heterocycles Applying a Homogeneous Titanium Reagent

Alison R. Fout, Brad C. Bailey, John Tomaszewski, and Daniel J. Mindiola*

Department of Chemistry, Indiana University, Bloomington, Indiana 47405

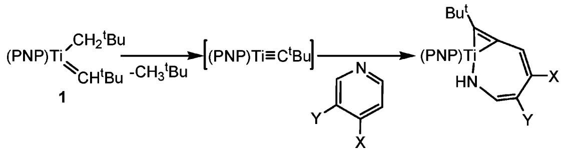
Received July 17, 2007; E-mail: mindiola@indiana.edu

Catalytic conversion of N-heterocycles present in petroleum or coal-based liquids to ammonia and nitrogen-free carbon based products, a process referred to as hydrodenitrogenation (HDN), is an important petrochemical transformation since it reduces the emissions of NO_x upon combustion of these fuels.[1] Unfortunately, the mechanism by which the HDN heterogeneous catalysts, typically a sulfided $CoMo/Al_2O_3$ or $NiMo/Al_2O_3$ surface, break the strong C−N bonds in N-heterocycles is far from being understood.[2] Although HDN, hydrodesulfurization (HDS), and hydrodeoxygenation (HDO) are procedures performed simultaneously during the hydrotreating process, current technology applies conditions optimized only for HDS.[1c,2a,3] As a result, sulfur removal is more efficient since HDN would only occur for a fraction of substrates such as aliphatic amines, given that these are easier to hydrodenitrogenate.[2b,3,4] Hence, the current practice of HDN needs to be understood and possibly optimized, since robust *N*-heterocycles often carry on untouched under the current standard conditions (2000 psi H_2, 300−450 °C).[1d] Understanding the intrinsic details behind some of the key steps in HDN, especially C−N bond cleavage, would benefit from prototypical homogeneous models which could ultimately perform the analogous transformation under much milder conditions.[1c,4c,5]

While studying intermolecular C−H activation reactions of hydrocarbons, we recently discovered that compound (PNP)Ti═CH^{t}Bu(CH$_2$^{t}Bu) (**1**)[6] (PNP = N[2-P(CHMe$_2$)$_2$-4-methylphenyl]$_2$ can ring-open both pyridine or picolines at room temperature over 12 h to afford azametallabicyclic systems of the type (PNP)Ti(C(^{t}Bu)CC$_4$H$_3$RNH) (R = H, **2a**; R = Me, **2b** and **2c**; Scheme 1).[7] In the case of 3-methylpicoline only one regioisomer, **2c**, was generated. The likely intermediates leading to **2a** have already been probed by independent experiments as well as high-level DFT analysis.[7] We report here that the former pyridine nitrogen of complexes such as **2a**−**c** can be denitrogenated, under mild conditions and in a cyclic manner, when treated with an electrophile such as (CH$_3$)$_3$SiCl. Synthetic, isotopic labeling and preliminary mechanistic studies addressing the denitrogenation process are presented.

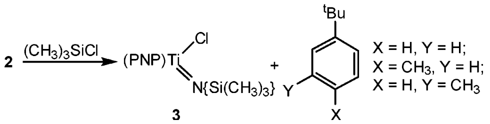
Despite compound **2** being remarkably stable to heat (120 °C for 4 days under N_2 or Ar), treatment of such with (CH$_3$)$_3$SiCl (excess or 1 equiv) over 72 h at 65 °C results in formation of (PNP)Ti═N{Si(CH$_3$)$_3$}(Cl) (**3**), concurrent with extrusion of the substituted arene ^{t}BuAr (Ar = C$_6$H$_5$, 4-MeC$_6$H$_4$, 3-MeC$_6$H$_4$) (Scheme 2). While the former product has been independently synthesized and characterized,[8] the latter organic side-material was confirmed by a combination of ^{1}H, and ^{13}C NMR spectral data. When using 1 equiv of electrophile, vacuum transfer of the volatiles reveals exclusive formation of the arene by multinuclear NMR spectroscopy with no other hydrocarbon-based products being detected by GC−MS, and ^{1}H NMR spectroscopy.[9] If the same reaction is monitored with the isotopomer (PNP)Ti(C(^{t}Bu)CC$_4$H$_4$^{15}NH) (**2a**)-^{15}N, derived from ^{15}N enriched pyridine[9] and **1** (^{15}N NMR: 131.8 ppm, $^1J_{N-H}$ = 58.4 Hz, $^3J_{N-H}$ = 6.0 Hz), the ^{15}N enriched imide (PNP)Ti═^{15}N{Si(CH$_3$)$_3$}(Cl) (**3**)-^{15}N is quantitatively formed (^{15}N NMR: 553.9 ppm, $^2J_{N-P}$ = 2.3 Hz)[8a] thus unarguably supporting the notion that the trimethylsilylimide nitrogen in **3** is derived from pyridine denitrogenation.

Scheme 1. Ring-opening of N-Heterocycles

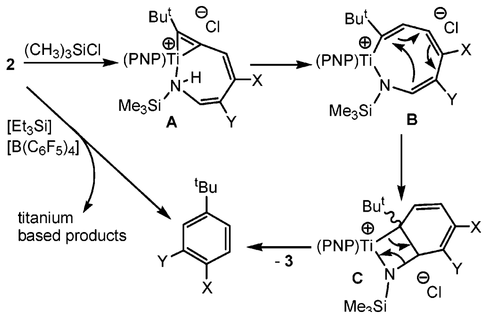


X = Y = H, **2a**; X = CH$_3$, Y = H, **2b**; X = H, Y = CH$_3$, **2c**

Scheme 2. Denitrogenation of N-Heterocycles



Scheme 3. Proposed Mechanism for the Denitrogenation of N-Heterocycles



Formation of **3** from **2a**−**c** and (CH$_3$)$_3$SiCl is proposed to occur first by silylation of the α-nitrogen composing the azametallabicyclic ring (intermediate **A**), followed by a ring expansion applying a 1,3-hydrogen shift to afford the eight-membered ring intermediate **B**. By means of an electrocyclic rearrangement, we then propose that **B** would ring-contract to generate intermediate **C**, which then would [2+2] retrocyclo-extrude the substituted arene product to finally engender formation of the imide, **3** (Scheme 3). Electrocyclic rearrangements involving cyclooctatriene to the bicyclic ring-fused system are well-known, and similar ring-contraction reactions in eight-azamembered metal rings have been documented previously by Wigley and co-workers.[10] We have found that the rate of the reaction for the **2a** → **3** conversion does not appear to be dependent on the concentration of the (CH$_3$)$_3$SiCl at 80 °C (0.018 M, k = 10.2(37) × 10^{-5} s^{-1}; 0.18 M, k = 9.18(23) × 10^{-5} s^{-1}; 79.9 M, k = 11.7(12) × 10^{-5} s^{-1})[9] thus implying that the proposed conversion, **2** → **A**, is likely not the slowest step in the denitrogenation sequence. We cannot however, rule out the possibility of a pre-equilibrium phenomena along the steps **2** → **C**.

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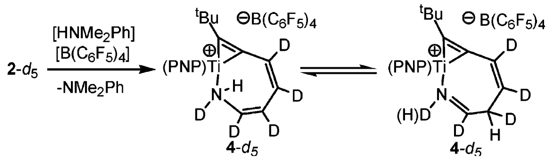
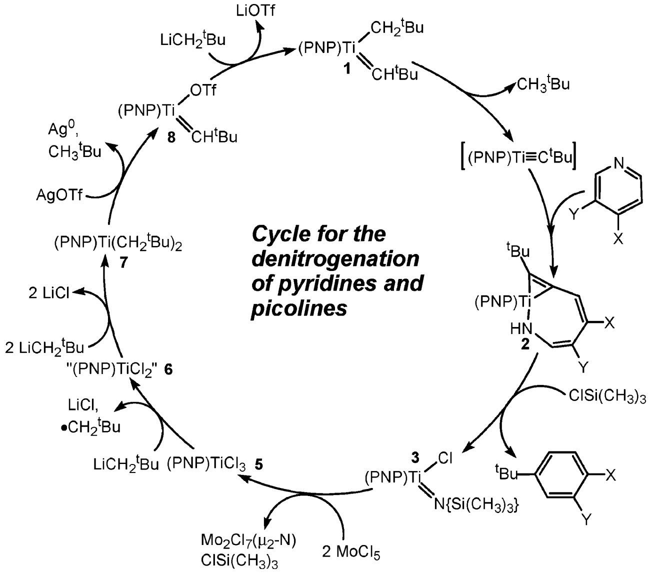
Scheme 4. Protonation of **2** and Subsequent Tautomerization



Scheme 5. Denitrogenation of N-Heterocycles Using a Recyclable Titanium Reagent



To ascertain if the electrophile adds to the α-N in compounds such as **2a** we explored a close analogue. Accordingly, we found that when complex **2a** is treated with an H^+ source such as $[HNMe_2Ph][B(C_6F_5)_4]$, denitrogenation does not occur. Instead, protonation and tautomerization ensues to produce $[(PNP)Ti(NH_2(C^tBu)C_5H_4)][B(C_6F_5)_4]$ (**4**), a complex characterized by a combination of ^1H, ^{13}C, ^{31}P, ^{11}B, and ^{19}F NMR spectra (Scheme 4). Formation of **4** and its tautomer were spectroscopically evident when $(PNP)Ti(C(^tBu)CC_4D_4ND)$ (**2a**)-d_5 (prepared from NC_5D_5) was treated with $[HNMe_2Ph][B(C_6F_5)_4]$ to yield the mixture of tautomers (**4**)-d_5 (Scheme 4). This result implies that an electrophile is likely to coordinate first to the former pyridine or picoline nitrogen in **2**. Changing the anion from Cl to $B(C_6F_5)_4$ does not appear to impede both the ring-expansion, the electrocyclic rearrangement, and ring-extrusion steps for the **A** → **B** → **C** → **3** sequence, since addition of $[Et_3Si][B(C_6F_5)_4]$ to **2a**−**c** also effects arene extrusion (Scheme 3).[9] However, we have been unable to characterize the metal-based byproduct for the latter reaction.[9]

We have also determined that product **3** can be deiminated with electrophiles such as $TiCl_4(THF)_2$, $NbCl_5$, and PCl_5 to afford the known complex $(PNP)TiCl_3$ (**5**).[11] In all cases however, separation of the imide oligomer from **5** was hampered by their similar solubilities. We speculated whether an insoluble product would facilitate purification of **3** for further reaction chemistries since substitution of an imide for two chlorides would allow us to possibly recycle **5** back to **1**. To achieve this goal, we turned our attention to $MoCl_5$, since the reported nitride $Mo_2Cl_7(\mu_2\text{-}N)$[12] is a highly insoluble compound. Gratifyingly, treatment of **3** with ∼2 equiv of $MoCl_5$ resulted in clean formation of **5** in 75% yield concurrent with precipitation of the black insoluble product that we propose to be $Mo_2Cl_7(\mu_2\text{-}N)$[12] $(ClSi(CH_3)_3$ was observed by ^1H NMR spectroscopy). Upon treatment of **5** with 3 equiv of $LiCH_2{}^tBu$, a reduction (presumably via formation of $(PNP)TiCl_2$ (**6**), Scheme 5), transmetallation transpires to afford the known Ti(III) bisalkyl precursor $(PNP)Ti(CH_2{}^tBu)_2$ (**7**)[11] (Scheme 5). One-electron oxidation of **6** with AgOTf furnishes $(PNP)Ti{=}CH^tBu(OTf)$ (**8**),[11] and subsequent treatment of the latter with 1 equiv with $LiCH_2{}^tBu$ produces **1**[6] thereby closing the homogeneous cycle for the denitrogenation of pyridine or picolines (Scheme 5). In fact, for the denitrogenation of pyridine, the overall yield for the recycling of titanium reagent was 18%.

The overall conversion of **1** to **3** in the presence of $(CH_3)_3SiCl$ advocates that a complete "C^tBu" for "N" metathetical reaction with pyridines and picolines has taken place, whereby a transient titanium alkylidyne, $(PNP)Ti{\equiv}C^tBu$, denitrogenates the N-heterocycles concurrent with transfer of the alkylidyne moiety. In the process, three strong C−N bonds composing the N-heterocycle ring have been cleaved under mild conditions and without the need of a reducing agent such as H_2. As a result, the hydrocarbon based-product generated in our set of denitrogenation reactions is not saturated. We speculate that the use of an electrophile such as $(CH_3)_3SiCl$ was needed to make formation of the titanium imide much more thermodynamically within reach. Our work therefore demonstrates that "N" removal of pyridine can be achieved under mild conditions and in a cyclic manner, and that such a process is promoted by an azophilic Ti center as well as highly polarized Ti−C multiple bond. We are currently performing more detailed kinetic studies on the **2** → **3** conversion.

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Supporting Information Available: Experimental preparation, reactivity (all compounds), and additional discussion. This material is available free of charge via the Internet at http://pubs.acs.org.

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