Nitrogen–Carbon Bond Formation

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Activation of Dinitrogen-Derived Hafnium Nitrides for Nucleophilic N–C Bond Formation with a Terminal Isocyanate**

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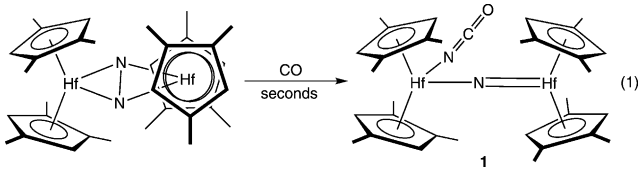
Synthetic methods for the assembly of nitrogen-carbon bonds are of fundamental and practical importance given the prevalence of this linkage in amino acids, pharmaceuticals, agrochemicals, and polymers.[1] Because of its high atmospheric abundance and non-toxicity, molecular nitrogen is an attractive synthon for the construction of N–C bonds if the kinetic and thermodynamic barriers associated with N_2 reduction can be surmounted. Inspired by reports by Sobota[2] and Fryzuk,[3] our laboratory has been exploring "ligand-induced N_2 cleavage", whereby a reducing transition metal is combined with an incoming ligand to supply the requisite six electrons to cleave the N≡N bond.[4] With strongly activated zirconocene[5] and hafnocene[6] dinitrogen complexes, this approach has proven to be a general method for nitrogen–carbon bond formation using carbon monoxide as the incoming ligand.

The formation of molecular nitrides from N_2 cleavage using a variety of reducing transition-metal complexes from across the transition series is now well-documented.[7–12] In most instances, the resulting metal nitride product is inert,[8d,13] rendering further functionalization, particularly N–C bond forming reactions, problematic.[9] Using CO-induced dinitrogen cleavage, our laboratory has reported the synthesis of a rare example of a bridging hafnium nitride, $[\{(\eta^5\text{-}C_5H_2\text{-}1,2,4\text{-}Me_3)_2Hf\}_2(NCO)(\mu_2\text{-}N)]$ (**1**), from addition of one equiv of CO to the corresponding hafnocene dinitrogen complex, $[\{(\eta^5\text{-}C_5H_2\text{-}1,2,4\text{-}Me_3)_2Hf\}_2(\mu_2,\eta^2,\eta^2\text{-}N_2)]$ [Eq. (1)].[14,15]



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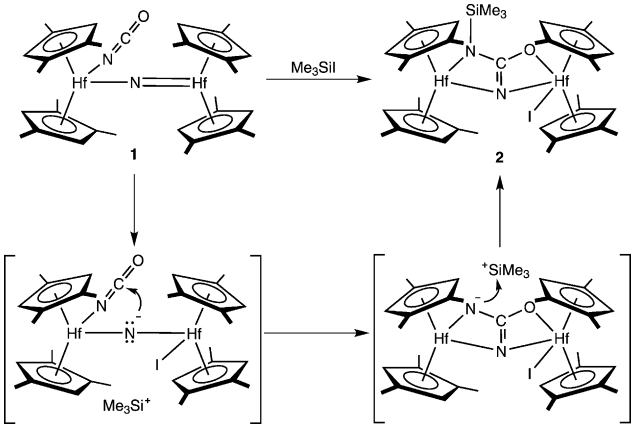
This compound provides a rich platform for elaboration of the N_2-derived nitride, overcoming the reactivity challenges typically encountered with bridging nitride complexes.[13] Subsequent carbonylation furnished oxamidide ($[N_2C_2O_2]^{4-}$) ligands[16] while treatment with cyclooctyne at ambient temperature resulted in N–C bond formation by cycloaddition.[14] Notably, heating of the cycloaddition product engaged the terminal isocyanate ligand, resulting in an additional N–C bond-forming event. Likewise, organic nitriles underwent insertion into the bridging hafnium nitride, and the resulting carbodiimide ligand engaged in additional N–C bond formation with the terminal isocyanate ligand. These results suggested that terminal isocyanates, which are often viewed as pseudohalides and typically inert in transition-metal compounds,[17–19] are potential platforms for additional N–C bond forming chemistry. Herein we describe a new strategy for activation of a bridging hafnocene nitride by anion abstraction from silyl halides and alkyl triflates that in turn increases the nucleophilicity of the nitrogen atom promoting N–C bond formation with a typically inert terminal isocyanate. This cascade allows the synthesis of otherwise challenging-to-prepare mono-substituted ureas from N_2, CO, and the appropriate electrophile.

Addition of one equiv of Me_3SiI to a freshly prepared solution of **1** in [D_6]benzene furnished a new C_s symmetric hafnocene compound containing a [$SiMe_3$] substituent. Repeating the silylation with the ^{15}N, ^{13}C isotopologue, [^{15}N,^{13}C]-**1**, prepared from $^{15}N_2$ and ^{13}CO gases, respectively, revealed that the new compound was not the expected iodo isocyanate dihafnocene silylimido complex but rather the dihafnocene silyl ureate complex, $[\{(\eta^5\text{-}C_5H_2\text{-}1,2,4\text{-}Me_3)_2Hf\}_2(I)(\mu_2\text{-}NCONSiMe_3)]$ (**2**) arising from additional N–C bond formation from the terminal isocyanate (Scheme 1).



Scheme 1. Formation of **2** from **1**, and likely pathway of formation.

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The ^{15}N NMR spectrum of [^{15}N,^{13}C]-**2** in C_6D_6 was diagnostic for additional N–C bond formation involving the terminal isocyanate. Two doublets were observed. One is centered at 133.7 ppm with a small $^1J_{CN}$ coupling of 1.6 Hz and is assigned as the silylated nitrogen; the other appears at 225.1 ppm with a larger $^1J_{CN}$ coupling of 5.1 Hz. The ^{13}C NMR spectrum of [^{15}N,^{13}C]-**2** in C_6D_6 was likewise informative, as the resonance typically associated with a terminal hafnium isocyanate was absent, and a single ^{13}C-labeled resonance was observed at 163.6 ppm for the central atom in the ureate core. This peak appears as an apparent doublet with $^1J_{CN} = 5.1$ Hz, indicating that the smaller coupling to the nitrogen of the [$^{15}NSiMe_3$] fragment was not resolved.

The solid-state structure of **2** was established by X-ray diffraction, and a representation of the molecule is presented in Figure 1.[22] The crystallographic data confirm formation of

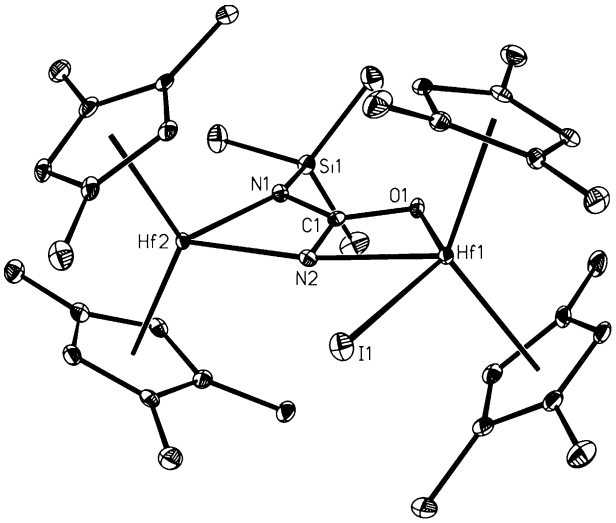
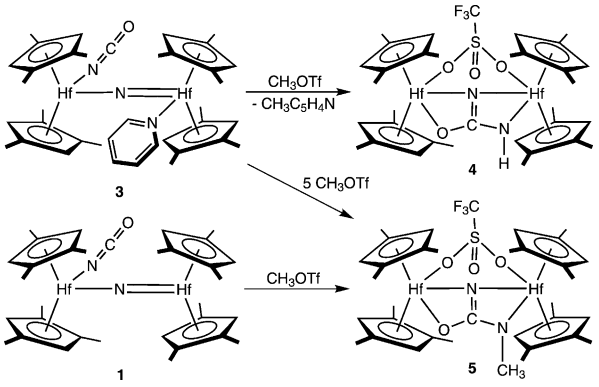


Figure 1. Representation of molecular structure of **2**. Ellipsoids are set at 30% probability; one molecule of fluorobenzene solvate and hydrogen atoms omitted for clarity.

the silylureate core arising from N–C bond formation from the bridging hafnocene nitride and the terminal isocyanate. The iodide ligand and the silyl group on the ureate are placed in a *transoid* arrangement in the core of the molecule. The C1–N1 and C1–N2 bond distances of 1.372(5) and 1.351(5) Å are between single and double C–N bonds, which is consistent with delocalization within the core. Chemical methods were also used to confirm ureate formation from CO-induced dinitrogen cleavage. Treatment of a C_6D_6 solution of **2** with excess methanol liberated urea, $H_2NC(O)NH_2$, which most likely arises from concomitant cleavage of the N–Si bond under the conditions of the protonolysis. Attempts to extend this cascade-type reactivity to CH_3I were unsuccessful, as decomposition of the hafnocene complex was observed immediately following addition of the alkyl halide to **1**.

A possible pathway for the formation of **2** is presented in Scheme 1. The first step is likely halogen atom abstraction by **1** to generate a formally anionic dihafnocene bridging nitride and a transient silyl cation. Coordination of an anionic (X-type) ligand reduces hafnium–nitrogen multiple bonding and likely increases the nucleophilicity of the nitride. This in turn promotes N–C bond formation with the terminal isocyanate to assemble the ureate core, which is trapped by $[Me_3Si]^+$ to yield **2**. Because **1** can only be generated for short periods in solution, subsequent studies were conducted with the pyridine-stabilized dihafnocene nitride, [{(η^5-C_5H_2-1,2,4-Me_3)$_2$Hf}$_2$(NCO)(pyridine)(μ_2-N)] (**3**), as this compound can be isolated and stored in the solid state.[15] Notably, silylation of **3** to yield **2** was much slower than with **1** and required 18 h to reach completion. This observation suggests pyridine dissociation precedes halide atom abstraction.

Observation of a cascade reaction resulting in ureate formation upon silylation of **1** prompted exploration of the generality of the transformation among other electrophiles. Monitoring the addition of one equivalent of CH_3OTf to a C_6D_6 solution of **3** by ^1H NMR spectroscopy revealed formation of a new C_s symmetric hafnocene product **4** (Scheme 2). A notable feature of the ^1H NMR spectrum



Scheme 2. Reactions of **1** and **3** with methyl triflate.

was the observation of a broad singlet at 3.39 ppm corresponding to a single proton. Notably absent was any resonance attributable to a N–CH_3 group. Repeating the CH_3OTf addition with [^{15}N,^{13}C]-**3** resulted in the splitting of the singlet at 3.39 ppm into a doublet of doublet of doublets ($^1J_{NH} = 75.2$, $^2J_{CH} = 4.8$, $^3J_{NH} = 2.1$ Hz), confirming N–H bond formation and assembly of a ureate core. Consistent with this finding was the observation of a doublet of doublet of doublets ($^1J_{NH} = 75.2$, $^1J_{CN} = 5.4$, $^2J_{NN} = 1.7$ Hz) centered at 110.9 ppm in the ^{15}N NMR spectrum (Figure 2) assigned as

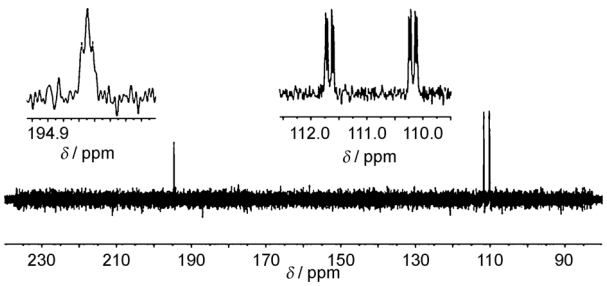


Figure 2. ^{15}N NMR spectrum of [^{15}N,^{13}C]-**4** in C_6D_6.

the protonated nitrogen. A second resonance was observed as a pseudo triplet ($^1J_{CN} = {}^2J_{NN} = 1.7$ Hz) at 194.6 ppm attributed to the central nitrogen atom of the ureate core. Solution IR spectroscopy also confirmed N–H bond formation, as a moderate-intensity N–H band was observed at 3405 cm^{-1} that shifted to 3398 cm^{-1} (3397 cm^{-1} expected from harmonic oscillator) upon ^{15}N labeling.

Colorless single crystals of **4** were obtained from a fluorobenzene–pentane solution chilled to −35 °C. The solid-state structure is presented in Figure 3 and established the identity

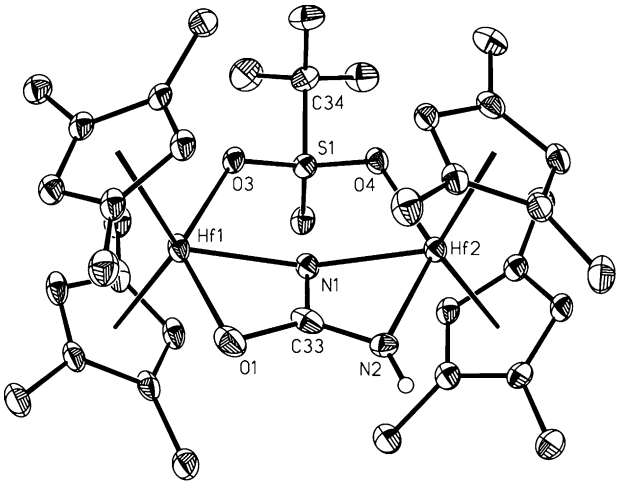
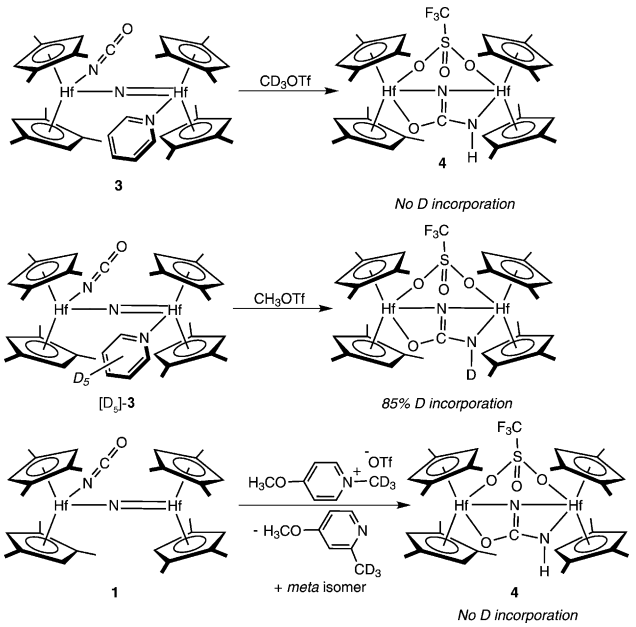


Figure 3. Representation of the molecular structure of **4**. Ellipsoids are set at 30%; hydrogen atoms, except those attached to N2, and one molecule of toluene solvate omitted for clarity.

of **4** as the dihafnocene ureate complex, [{(η^5-C_5H_2-1,2,4-Me_3)$_2$Hf}$_2$(μ_2-OTf)(μ_2-NCONH)].[22] The hydrogen atom on the ureate core was located in the difference map and there was no evidence for a methyl group from the CH_3OTf addition. The core of the molecule contains a bridging parent ureate ligand, $[NCONH]^{3-}$, along with a triflate anion that spans both hafnium atoms. The C33–N1, C33–N2, and C33–O1 distances of 1.343(8), 1.326(9), and 1.332(7) Å are similar and again indicate delocalization of electron density throughout the ureate fragment.

Formation of an $[NCONH]^{3-}$ ligand from methyl triflate addition to **3** raised the question of the source of the proton. The product, **4**, was isolated in 80% yield, suggesting that contamination of the CH_3OTf with HOTf was unlikely. Nevertheless, CH_3OTf was freshly synthesized from AgOTf and CH_3I and the yield of **4** was unchanged from batch to batch. Performing the addition of CH_3OTf to **3** in the presence of excess 2,6-di-*tert*-butylpyridine also produced **4** in quantitative yield as judged by ^1H NMR spectroscopy. Additionally, analysis of the organic products following treatment of **3** with CH_3OTf by GC-MS established formation of isomers of methylpyridine.

Isotopic labeling experiments were performed to determine the source of the proton responsible for N–H bond formation (Scheme 3). Addition of one equiv of CD_3OTf to a benzene solution of **3** and analysis of the product mixture by ^1H and ^2H NMR spectroscopies established no incorporation



Scheme 3. Deuterium labeling experiments.

of deuterium in the N–H position of **4**. A second experiment was conducted whereby [D_5]-**3** was prepared from [D_5]pyridine and treated with CH_3OTf. Analysis of the product by NMR spectroscopy established formation of [D_1]-**4** where the N–H position of the ureate core was labeled with deuterium (Scheme 2). The ^2H NMR spectrum also revealed formation of a small quantity of [*N*-CH_3-C_5D_5N]-[OTf] (see the Supporting Information). Thus, the isotopic labeling experiments suggest that formation of **4** likely proceeds by initial methylation of the coordinated pyridine to form [*N*-CH_3-C_5H_5N][OTf] and **1**. Coordination of the triflate anion generates a nucleophilic hafnium nitride poised to engage in N–C bond formation with the terminal isocyanate ligand akin to formation of **2** from Me_3SiI addition to **1**. Deprotonation of the *ortho* position of the pyridinium triflate furnished the observed product, **4**. It is known that methylation of pyridine derivatives increases the acidity of the *ortho* C–H bonds, rendering protonation competitive with alkylation.[20] Additional support for this hypothesis was provided by the addition of [*N*-CD_3-*p*-(CH_3O)C_5H_4N][OTf] to a C_6D_6 solution of **1**. Analysis of the product by NMR spectroscopy established clean formation of **4** with less than 5% deuterium in the N–H position of the ureate ligand. Analysis of the organic products by ^2H NMR spectroscopy revealed formation of the *ortho* and *meta* isomers of the 4-methoxymethylpyridine.

Also consistent with this rationale is the dependence of the product distribution on the quantity of added methyl triflate. Performing the addition to **3** with five equivalents of CH_3OTf produced a new C_s symmetric hafnium product identified as the expected methylated ureate, [{(η^5-C_5H_2-1,2,4-Me_3)$_2$Hf}$_2$(μ_2-OTf)(μ_2-NCONMe)] (**5**) in 70% yield of isolated product. The NMR spectroscopic features of **5** are similar to **4** with the notable absence of the singlet at 3.39 for the N–H and the addition of a new resonance at 2.88 ppm

assigned to the N–CH_3. Upon labeling with $^{13}CH_3OTf$ and $^{15}N_2$, this signal appears as a doublet of doublets ($^1J_{CH}$ = 133.7 Hz, $^2J_{NH}$ = 5.9 Hz), confirming methylation of an N_2-derived nitrogen atom. Although the ^{15}N NMR spectrum of [^{15}N,^{13}C]-**5** featured only broad singlets at 107.2 and 195.2 ppm, the ^{13}C NMR data clearly establish formation of the ureate core, with the resonance corresponding to the central carbon atom appearing as a doublet of doublets centered at 165.7 ppm ($^1J_{CN}$ = 6.5 Hz, $^2J_{CC}$ = 2.2 Hz). A more rational synthesis of **5** is from addition of CH_3OTf to a C_6D_6 solution of **1** (Scheme 2). In the absence of *N*-alkylated pyridinium, no competing protonation is possible and hence no **4** was observed. More significantly, alkylation of either **1** or **3** provides a route to asymmetric ureas directly from N_2, CO, and the appropriate electrophile. Given the utility of asymmetric ureas in agricultural and medicinal chemistry, methods that obviate the use of phosgene are attractive.[21] Buchwald and co-workers recently reported a palladium-catalyzed cross-coupling reaction for the synthesis di- and tri-substituted aryl ureas, although preparation of mono-alkyl substituted ureas were not described.[21b]

Introduction of other alkyl groups onto the ureate core was also examined. Treatment of **3** with ethyl trifluoromethanesulfonate (EtOTf) produced no reaction, raising the possibility that the longer alkyl group may be too large to alkylate coordinated pyridine. However, addition of *N*-ethylpyridinium triflate to a C_6D_6 solution of **1** produced an intractable mixture of products after one hour. These products are the same as those observed from decomposition of **1** in solution in the absence of added reagents, suggesting that ethylation of the pyridine also inhibits deprotonation of the *ortho* position of the heterocycle.

Direct alkylation of **1** was successful, as addition of EtOTf to a C_6D_6 solution of the hafnocene nitride cleanly furnished [{(η^5-C_5H_2-1,2,4-Me_3)$_2$Hf}$_2$(μ_2-OTf)(μ_2-NCONEt)] (**6**) as a white solid in 86% yield. The ^1H NMR spectrum of **6** in C_6D_6 has six cyclopentadienyl methyl and four cyclopentadienyl hydrogen resonances, which is consistent with an averaged C_s symmetry in solution. The methylene protons of the *N*-ethyl group appear as a quartet at 3.24 ppm, which is consistent with nitrogen alkylation. The ^{13}C NMR spectrum of [^{15}N,^{13}C]-**6** established ^{15}N coupling to the ethyl methylene resonance at 39.2 ppm ($^1J_{CN}$ = 2.4 Hz). The ureate carbon derived from ^{13}CO appears as a doublet at 166.3 ppm ($^1J_{CN}$ = 6.0 Hz). The ^{15}N NMR spectrum has similar features to that of **5**, with a doublet centered at 197.9 ppm ($^1J_{CN}$ = 1.4 ppm) corresponding to the μ_2-ureate nitrogen. A complex multiplet was also located at 121.8 ppm with unresolved N–H and N–C coupling for the *N*-ethylated nitrogen atom. X-ray diffraction experiments also corroborated the identity of **6** (a representation of the structure is given in the Supporting Information).[22] Release of the functionalized ureate was achieved by treatment of **6** with four equivalents of anhydrous hydrochloric acid and furnished *N*-ethyl urea in 79% yield.

In summary, the base-free dihafnocene nitride, prepared from CO-induced N_2 cleavage, is a versatile substrate for the construction of N–C bonds. Anion abstraction from Me_3SiI or alkyl triflates generates a nucleophilic bridging nitride that engages a terminal hafnocene isocyanate to assemble ureate cores. Introduction of pyridine into the coordination sphere of the hafnium provides an unusual method for ureate protonation as alkylation of the heterocycle renders the *ortho* C–H bonds sufficiently acidic to engage hafnium intermediates. Promoting new reactivity of metal nitrides as well as the ubiquitous isocyanate ligand in transition-metal chemistry will inspire new approaches to N–C bond formation and also provide new avenues of exploration in dinitrogen functionalization.

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[22] CCDC 949474 (**2**), 949475 (**4**), and 949476 (**6**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

