$La[N(SiMe_3)_2]_3$ – Catalyzed Deoxygenative Reduction of Amides with Pinacolborane. Scope and Mechanism.

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Tris[N,N-bis(trimethylsilyl)amide]lanthanum (La^{NTMS}) is an efficient and selective homogeneous catalyst for the deoxygenative reduction of tertiary and secondary amides with pinacolborane (HBpin) at mild temperatures (25-60 °C). The reaction, which yields amines and $O(Bpin)_2$, tolerates nitro, halide, and amino functional groups well, and this amide reduction is completely selective for both inter- and intramolecular alkene/alkyne hydroboration. Kinetic studies indicate that amide reduction obeys an unusual mixed-order rate law which is proposed to originate from saturation of the catalyst complex with HBpin. Kinetic and thermodynamic studies, isotopic labeling, and DFT calculations using energetic span analysis suggest the role of a $[(Me_3Si)_2N]_2La\text{-}OCHR(NR'_2)[HBpin]$ active catalyst, and hydride transfer is proposed to be ligand-centered. These results add to the growing list of transformations that commercially-available La^{NTMS} is competent to catalyze, further underscoring the value and versatility of lanthanide complexes in homogeneous catalysis.

Introduction

The deoxygenative reduction of amides to amines is an important transformation in academic, pharmaceutical, and industrial synthetic chemistry (Figure 1A).[1-5] The natural prevalence and synthetic accessibility of amides makes them valuable precursors to amines, but the inertness of the resonance-stabilized amide C=O bond generally necessitates the use of harsh reductants such as $LiAlH_4$, BH_3, and pressurized H_2.[6-9] These reagents present significant safety concerns and often suffer from poor functional group tolerance, particularly with nitro groups and alkenes/alkynes. As such, novel methods enabling the safe, selective and efficient reduction of amides would be valuable additions to the synthetic chemist's toolkit.[10] Significant progress has been made in this area, with much of the focus directed towards catalytic hydrosilylation.[11-13] Interestingly, amide reduction via catalytic hydroboration (with mild, easily handled boranes such as HBpin, Figure 1B) is largely unexplored, especially with lanthanide catalysts,[14-17] despite extensive precedent for the use of boranes as reductants for ketones and aldehydes,[14, 18-26] as well as the intense recent interest in the more-challenging reduction of esters via hydroboration.[14, 27-31] Recently, we reported that the homoleptic lanthanide amide $La[N(SiMe_3)_2]_3$ (La^{NTMS}, Figure 1B) displays extremely high catalytic activity for a variety of carbonyl reductions using HBpin, with 25 -60 °C turnover frequencies as high as 40,000 h^{-1} for ketones and aldehydes and 400 h^{-1} for esters.[31-32] With these results in mind, we sought to explore the La^{NTMS}-catalyzed hydroboration of more challenging amides.

Tris[*N*,*N*-bis(trimethylsilyl)amido]lanthanide complexes ($Ln[N(SiMe_3)_2]_3$, abbreviated here as Ln^{NTMS}) are encountered

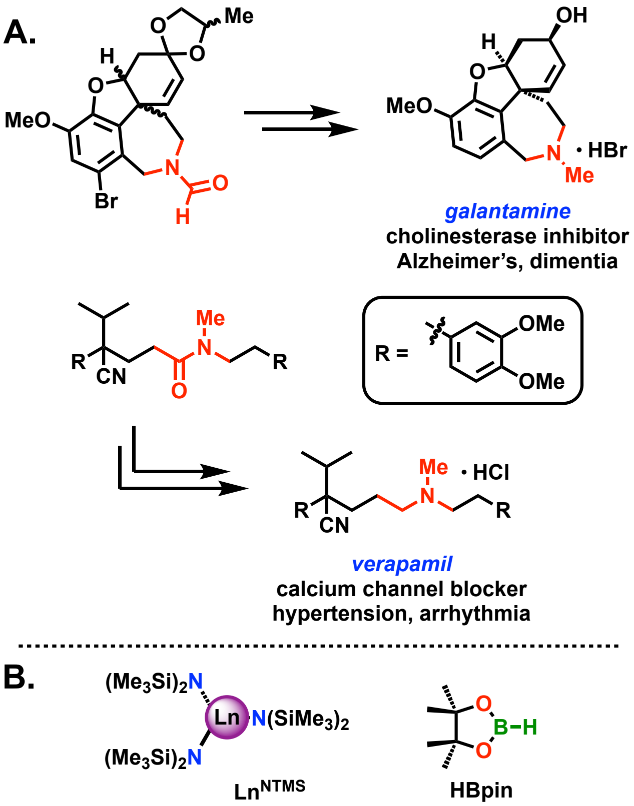


Figure 1. **A**. Examples of selective deoxygenative amide reductions practiced at scale.[1] **B.** Structures of tris[N,N-bis(trimethylsilyl)amido]lanthanide complexes (Ln^{NTMS}), where Ln = any lanthanide, and pinacolborane (HBpin).

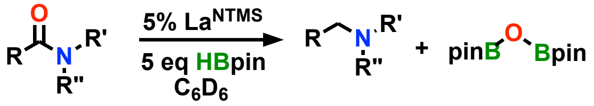
frequently in the lanthanide catalysis literature, both as precursors to more complex lanthanide organometallics[33-43] and as homogeneous catalysts, particularly for hydro-functionalization/reduction of alkenes and alkynes.[44-56] These complexes are commercially available for many lanthanides, or can be readily synthesized and purified, rendering them highly accessible and of great interest to the synthetic methods community.[57-59] A report from this Laboratory showed that it is possible to carry out the catalytic *synthesis* of amides with Ln^{NTMS},[60] but the La^{NTMS}-catalyzed *reduction* of amides had not yet been investigated. Given this, and the proven ability of La^{NTMS} to catalyze carbonyl hydroboration, La^{NTMS}-catalyzed amide hydroboration was an intriguing target.

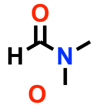
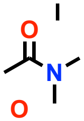
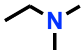
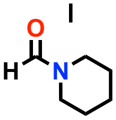
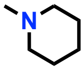
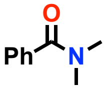
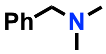
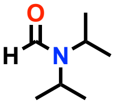
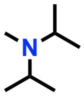
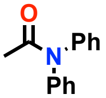
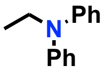
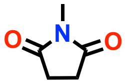
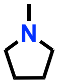
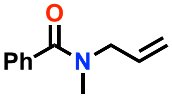
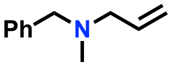
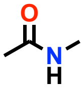
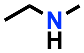
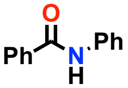
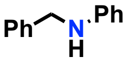
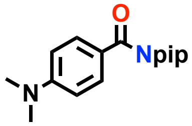
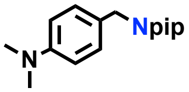
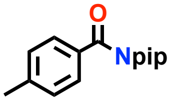
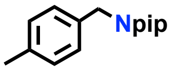
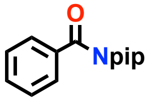
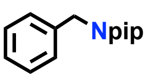
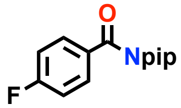
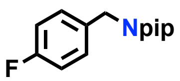
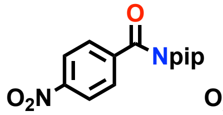
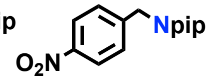
Here we report that La^{NTMS} effectively mediates the deoxygenative reduction of a variety of alkyl and aryl amides to the corresponding amines. This system, which utilizes a commercially available catalyst, mild reaction conditions, and easily-handled HBpin, constitutes a significant advance over traditional amide reduction methods, and is the first report of a borane-based amide reduction catalyzed by a lanthanide complex. We discuss here the scope of this transformation, as well as a proposed mechanism informed by a combined experimental-theoretical investigation.

Results and Discussion

Hydroboration Scope. Amide reduction is found to occur *via* deoxygenation to yield the corresponding amine and bis-(pinacolboryl)oxide (pinB-O-Bpin, ^{1}H-NMR: δ 1.00 ppm, ^{11}B-NMR: δ 21.7 ppm in C_6D_6) as a co-product (Table 1), analogous to that reported for other borane- and silane-based reductions.[13, 15, 61] Near quantitative conversion of amide to amine is observed for each of the substrates examined (Table 1) at a catalyst loading of 5 mol%, and acidic workup of preparative reactions (0.5 gram scale) affords the amine hydrochloride product in good yields without the need for column chromatography (see SI for details). Although only 2 equiv. HBpin (relative to amide) are formally required by stoichiometry for complete amide reduction, 5 equiv. were typically found necessary to achieve full conversion over the time and temperature range selected. This is likely attributable to reversible formation of transient amide-borane and amine-borane adducts which, once formed, would effectively reduce the amount of active HBpin available in solution. Considering the DFT-derived geometries in the proposed catalytic cycle, bulky HBpin-amide or HBpin-amine adducts would be expected to approach the catalyst complex and participate in amide reduction with greater difficulty. Such effects were previously observed in similar reductions, and other catalytic systems require HBpin to be held in even greater excess.[15] Tertiary amides are reduced cleanly at 25 °C, although sterically encumbered, and cyclic amides require elevated temperature (60 °C) for rapid reduction. Formamides (R = H) generally react more rapidly than amides (R ≠ H; e.g., Table 1, entry 1 vs. 2). Similarly, steric encumbrance at the R' and R" positions depresses the turnover rate (e.g., Table 1, entry 1 vs. 5). Even with HBpin in excess, the reduction of amides is completely chemoselective over the hydroboration of alkenes and alkynes in intermolecular competition experiments (Scheme 1). Likewise, no intramolucular alkene hydroboration products were observed during the reduction of *N*-allyl-*N*-methylbenzamide (Table 1, entry 8). In addition to La^{NTMS}, the catalytic activity of commercially available Sm^{NTMS} and Y^{NTMS} was also investigated for the reduction of *N,N*-dimethylbenzamide (Table 1, entry 4[c,d]). While the reaction proceeds similarly in all three cases, the observed rate of reduction not unexpectedly diminishes as

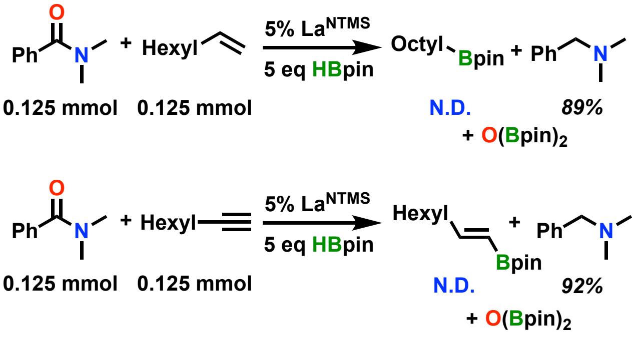
Table 1. Scope of La^{NTMS}-catalyzed amide reduction with pinacolborane[a]



#	Substrate	Product	T/°C	t/h	Yield[b]
1			25	1	97
2			25	6.5	94
3			25	1	99
4			25 25[c] 25[d] 60	17 25 36 2	>99 >99 >99 >99
5			25 60	96 24	>99 >99
6			25 60	20 0.5	>99 >99
7[e]			25 60	72 24	>99 >99
8			25 60	14 1	>99 >99
9			25 60	72 24	<1 70
10			25 60	72 48	<1 90
11			25 60	1 2	9 95
12			25 60	1 2	18 >99
13			25 60	1 2	28 99
14			25 60	1 1	38 97
15			25 60	1 1	68 >99

[a]Reaction conditions: La^{NTMS} (12.5 μmol), amide (0.25 mmol), and HBpin (1.25 mmol, 5 equiv.) in C_6D_6 (1 mL total volume). [b]% yields of amine products calculated by integration vs a hexamethylbenzene internal standard. [c]Sm^{NTMS}. [d]Y^{NTMS}. [e]10 equiv. HBpin.

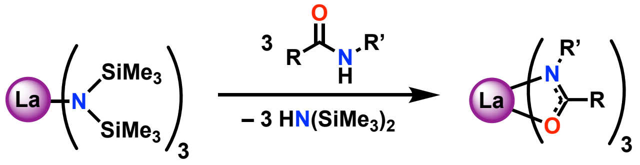
Scheme 1. Selective reduction of *N,N*-dimethyl-benzamide in the presence of 1-octene (top) and 1-octyne (bottom)[a]



[a]Yields calculated via ^{1}H-NMR of crude reaction mixtures. N.D. = not detected. Conditions: 1.00 mL C_6D_6, 60 °C, 2h.

the ionic radius of the central metal decreases (i.e., La > Sm > Y).

Secondary amides proved somewhat more challenging, requiring both elevated temperatures and longer reaction times to reach satisfactory yields (Table 1, entries 9 and 10). This is likely attributable to the rapid conversion of La^{NTMS} to a lanthanide tris-amidate species *in situ*, possibly hindering formation of the active catalyst for amide reduction (Scheme 2). Such a reactivity pattern has been reported previously[62] and is supported by the presence of free $HN(SiMe_3)_2$ in the ^{1}H-NMR spectrum of the secondary amide reaction mixture. In an attempt to fully characterize these tris-amidate complexes, the stoichiometric reaction of La^{NTMS} and benzanilide (1:3) was conducted. Upon mixing, the ^{1}H-NMR spectrum shows the complete conversion of the La^{NTMS} signal (δ 0.29 ppm, C_6D_6) to a new signal corresponding to $HN(SiMe_3)_2$ (δ 0.10 ppm, C_6D_6). Additionally, upon complexation, the aromatic proton signals belonging to benzanilide become quite broad when compared to the ^{1}H-NMR spectrum of the secondary amide alone (Figure S8, S9). Variable temperature (VT) NMR studies were next performed in toluene-d_8 due to the superior temperature profile enabled by toluene vs. benzene. However, the aromatic proton signals of the La-benzanilide tris-amidate species do not sharpen or coalesce with increasing temperature (up to 100 °C in toluene-d_8). Thus, integrations of these spectra provide minimal information. However, *in situ* studies conducted by adding amide and HBpin to the aforementioned 1:3 mixture of La^{NTMS} and benzanilide (i.e., forming the lanthanide tris-amidate species *in situ*) suggest this species is a less active but nevertheless competent amide reduction catalyst (Figure S10). Our attempts to isolate these tris-amidate complexes were unsuccessful. Reduction does not occur with the two primary amides tested (acetamide and benzamide), and instead an intractable, off-white precipitate is formed. While ligand insertion into carbon-heteroatom double bonds has been observed previously with similar rare earth silylamide complexes,[63] DFT studies indicate that, in this system, a ligand insertion pathway is energetically unfavorable (see SI). Furthermore, spectroscopic studies reveal that upon addition of benzamide to La^{NTMS}, $HN(SiMe_3)_2$ is produced instantaneously with precipitation of a catalytically inactive La-amide species. Characterization of this marginally soluble species by ^{1}H- and ^{29}Si-NMR spectroscopy suggests that it is a La-hemiaminalate complex, e.g., $[(Me_3Si)_2N]_2La\{\eta^2\text{-}OC(NH)Ph\}$ (monomeric or oligomeric; see SI). [64] Formation of this marginally soluble complex likely precludes the HBpin coordination necessary for efficient reduction to take place.



Scheme 2. Observed reaction of La^{NTMS} with secondary amides.

Kinetics and Mechanism. To probe the mechanism of this reaction, the rate law for catalytic *N,N*-dimethylbenzamide reduction was determined by a combination of initial rates analysis at various catalyst concentrations (for the order in La^{NTMS} concentration) and by monitoring substrate consumption under pseudo-first order conditions (see SI for details). Amide reduction is found to proceed with a first-order dependence on the La^{NTMS} concentration and zero-order dependence on the amide concentration. The order in HBpin was not amenable to determination under pseudo-zero order conditions (10 equiv. amide), as evidenced by a non-linear correlation for 0th, 1st and 2nd order plots (see SI). Initial rates analysis reveals that at low HBpin concentrations ([HBpin] < 1.67 *M*, 5-7 equiv. vs. amide), the rate has a first order dependence on HBpin concentration; however, a transition occurs when [HBpin] ≥ 1.67 *M* (≥ 8 equiv. vs. amide), and the order in HBpin becomes 0. This mixed-order system (eq. 1) is reminiscent of Michalis-Menten kinetics,

$$\text{Rate} = k[\text{LaNTMS}]^1[\text{Amide}]^0[\text{HBpin}]^{1/0} \qquad (1)$$

wherein the turnover-limiting step in the catalytic cycle depends on an equilibrium involving a substrate-catalyst complex.[65] While this regime is not frequently encountered outside of enzyme catalysis,[66] there are a few notable examples where saturation kinetics are observed in hydroelementation reactions.[30, 67-69] The presence of an equilibrium between a La complex and HBpin in or immediately preceding the turnover limiting step could explain the unusual rate behavior observed above. However, a non-equilibrium process, such as the availability of two different turnover-determining transition states, the relative energies of which depend on [HBpin], could also explain this rate law. As such, activation parameters for the reduction of *N,N*-dimethylbenzamide were determined at both low [HBpin] (5 equiv. HBpin vs. amide) and high [HBpin] (10

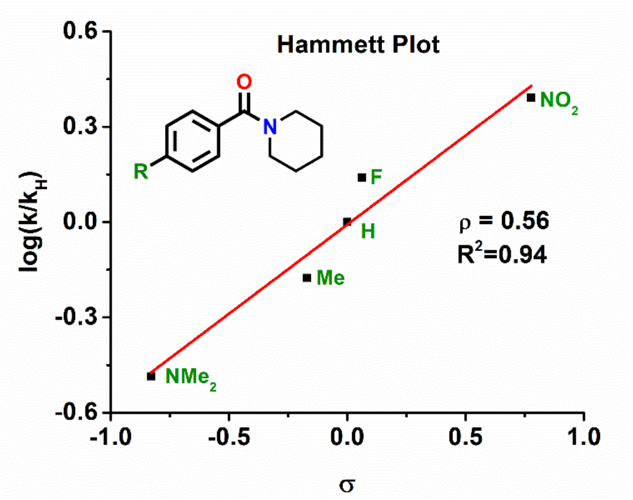


Figure 2. Hammett plot generated from the reduction of para-substituted *N*-benzoylpiperidines with HBpin. Rates determined via integration of product ^{1}H-NMR signals relative to a hexamethylbenzene internal standard.

equiv. HBpin vs. amide) conditions over a temperature range of 30-70 °C. Both low and high [HBpin] conditions yield very similar activation parameters consisting of relatively small and positive enthalpies ($\Delta H^\ddagger$ = 10.3 and 11.3 kcal/mol, respectively) and extremely large and negative entropies ($\Delta S^\ddagger$ = -49.7 and -46.4 e.u., respectively). These data support assignment of a transition state that is highly organized, sterically congested, and associative, and they strongly suggest the same rate-determining step is operative in low and high [HBpin] reactions, indicating the mixed-order rate law is most likely due to saturation of the catalyst complex with HBpin at ~8 equiv. HBpin vs amide (i.e., the reaction becomes pseudo-first order at this point; *vide infra* for a closer examination with DFT techniques).

To gauge the impact of electron density at the carbonyl carbon on the rate of amide reduction, a Hammett plot (Figure 2) was created using a series of *para*-substituted benzoyl piperidines. A slight increase in activity is observed for substrates with electron-withdrawing substituents at the R position, as indicated by a small, positive value for the Hammett parameter ρ of 0.56. Additional mechanistic details were obtained from isotopic labeling studies. Replacing HBpin with DBpin (see SI for details) leads to complete disappearance of the RCH_2NR'R'' ^{1}H NMR resonance when DBpin is the reductant. Rate studies with DBpin and HBpin give a kinetic isotope effect (KIE) of 1.50 for reduction of *N,N*-dimethylbenzamide.

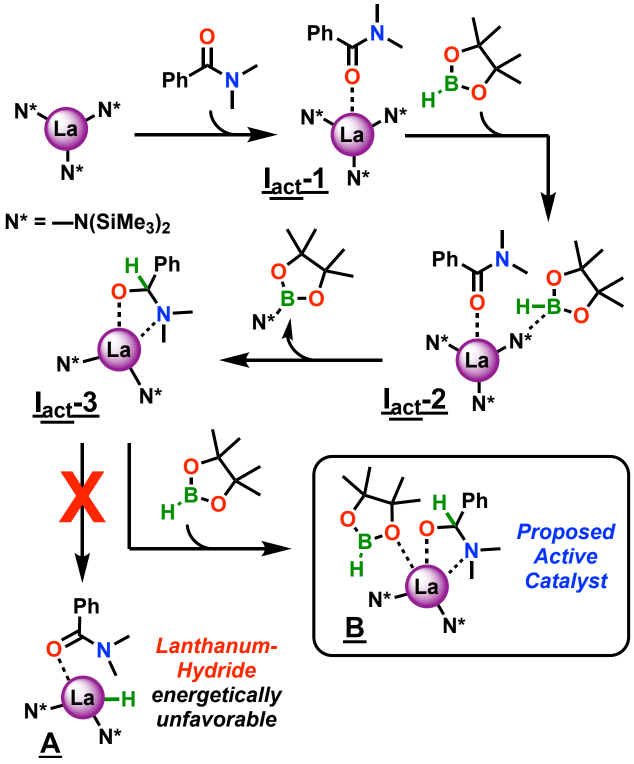


Figure 3. Proposed catalyst activation process for the hydroboration/reduction of amides catalyzed by La^{NTMS}.

Computational Mechanistic Analysis. Informed by the above kinetic and thermodynamic data, DFT modeling was next employed to better understand the mechanism of La^{NTMS}-catalyzed amide hydroboration. It will be seen that the active catalyst for this transformation is found to be the lanthanum hemiaminal species [$(Me_3Si)_2N]_2$La-OCHR(NR'$_2$)-[HBpin] (Figure 3, **B**), a species which bears a striking resemblance to the active catalyst this Laboratory found recently for La^{NTMS}-catalyzed ester hydroboration.[31] While the transient nature of this complex (*vide infra*) precludes its NMR spectroscopic observation *in situ*, the formation of this species is supported by the appearance of 1.0 equiv. (relative to La^{NTMS}) of pinB-N(SiMe$_3$)$_2$ in the ^{1}H-NMR spectra of catalytic reactions (at δ 1.03 and δ 0.37 ppm),[70] indicating that the hydroboronolysis of a single -N(SiMe$_3$)$_2$ precatalyst ligand occurs. The formation of pinB-N(SiMe$_3$)$_2$ could also be indicative of a metal-hydride active catalyst (e.g., [(Me$_3$Si)$_2$N]$_2$La-H]), (**A**, Figure 3) however the energy required to form such a species (+20.5 kcal/mol vs -21.2 kcal/mol barrierless for structure **B**) makes its presence in the catalytic cycle highly unlikely. Moreover, no spectroscopic evidence indicating the presence of a La-H species is observed. Attempts to isolate complex **B** were unsuccessful due to the formation of an off-cycle product containing ring-opened pinacolborane (see SI for characterization details) that predominates at the low substrate concentrations required for stoichiometric studies. This is identical to the deactivation product observed for La^{NTMS}-catalyzed ester hydroboration and is analogous to that found in lanthanocene-catalyzed pyridine dearomatization (Figure 4).[31, 71] In an attempt to further investigate the proposed catalyst activation process shown in Figure 3, NMR-monitored stoichiometric experiments were conducted. Species **I$_{act}$-1** was obtained from a 1:1 mixture of La^{NTMS} and *N,N*-dimethylbenzamide. Full conversion of the La[N(Si*Me*$_3$)$_2$]$_3$ proton signal at δ 0.29 ppm (C$_6$D$_6$) to a new signal at δ 0.41 ppm (C$_6$D$_6$) indicates the formation of what is presumed to be **I$_{act}$-1** (Figures S27, S28). Regarding species **I$_{act}$-2** and **I$_{act}$-3**, we attempted to isolate and characterize these intermediates by adding 1 equiv. of HBpin to a 1:1 mixture of La^{NTMS} and *N,N*-dimethylbenzamide (**I$_{act}$-1**), however, the resulting spectra revealed a complex mixture of products and obvious decomposition. The ratios of La^{NTMS}, amide, and HBpin were also varied but these too yielded mixtures of products. Additionally, adding 1 equiv. of amide to a solution of a precoordinated HBpin-La^{NTMS} complex was carried out, but attempts to isolate or unambiguously characterize **I$_{act}$-2** or **I$_{act}$-3** were ultimately unsuccessful.

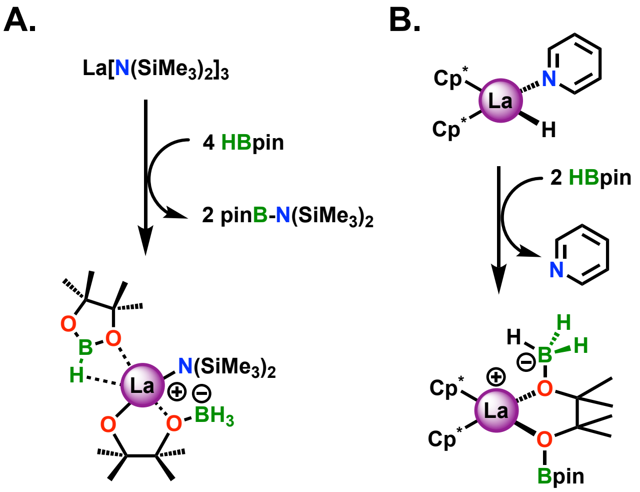


Figure 4. **A**. Off-cycle product observed in stoichiometric studies of both amide and ester hydroboration catalyzed by La^{NTMS}.[31] **B**. Comparable deactivation product reported for [Cp*$_2$LaH]$_2$-catalyzed pyridine dearomatization; Cp* = η^5-pentamethylcyclopentadienyl and characterized by single-crystal x-ray diffraction.[69]

The proposed mechanistic pathway consists of four major steps (Figure 5). First, coordination of an additional amide molecule and approach of the Lewis acidic boron center of the coordinated HBpin molecule towards the hemiaminal oxygen of

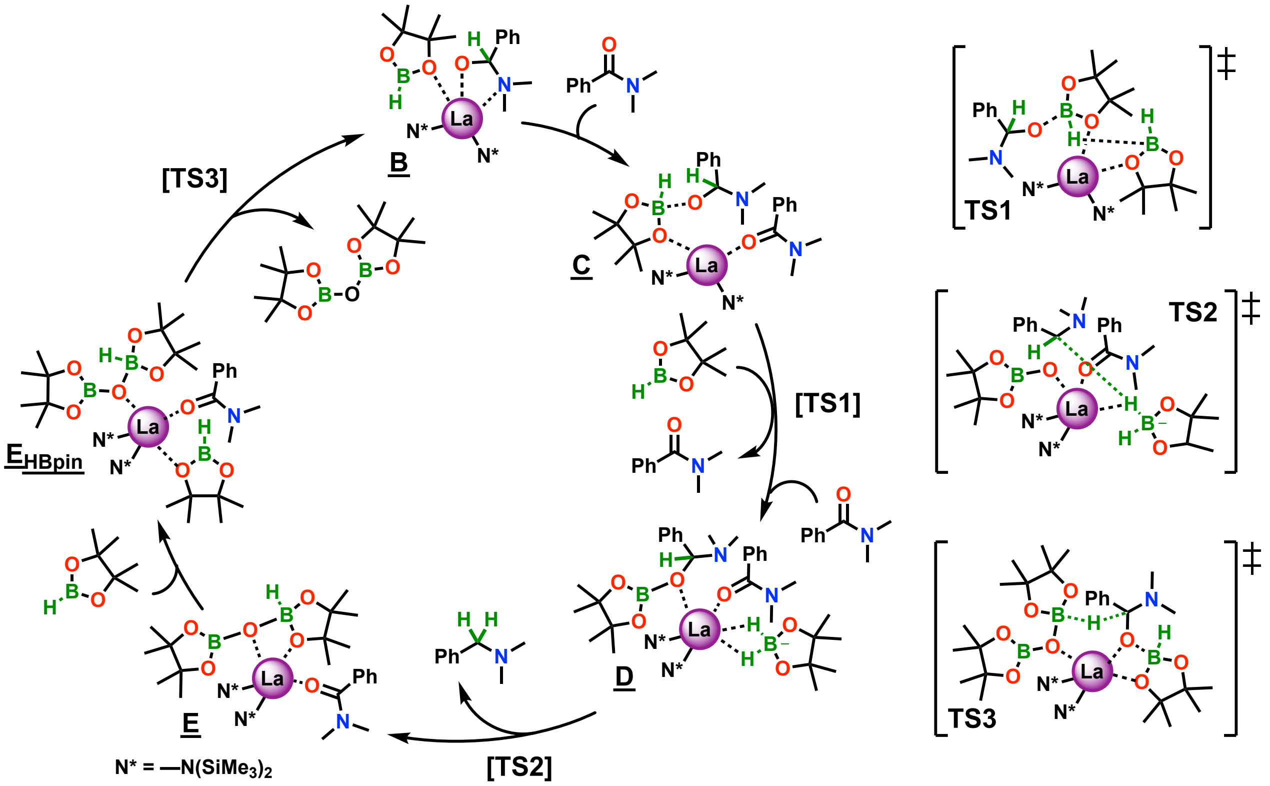


Figure 5. Proposed DFT-computed catalytic cycle and transition states for the catalytic hydroboration/reduction of *N,N*-dimethylbenzamide catalyzed by La^{NTMS}.

active catalyst **B**, leads to the formation of a new B-O bond and dissociation of the La-O bond. This step, which yields a La-coordinated pinacolborate species, proceeds spontaneously, providing an overall stabilization energy of 19.4 kcal/mol and producing **C** as a relative minimum in the energetic profile (Figure 6). Next, a HBpin molecule approaches the catalyst complex. Hydride transfer from the La-coordinated hemiaminal-hydroborate species to the coordinated HBpin forms La-coordinated H_2Bpin^-, a species often proposed to facilitate hydride transfer in HBpin-mediated reductions.[29-30, 72-75] With reorganization, and the approach and subsequent coordination of an additional amide substrate after **TS1,** the complex then forms species **D** with a stabilization energy of 16.3 kcal/mol. A significant portion of this stabilization energy coming from amide coordination alone (Figure 6). Third, C-O bond scission of the hemiaminal-borane species **D** results in a transient carbocationic species and La-bound-OBpin (**TS2**). The carbocationic species is subsequently reduced by $[H_2Bpin]^-$ to yield free amine. This step proceeds with a 4.0 kcal/mol barrier and is highly exergonic (-41.3 kcal/mol) forming species **E**. Next, a second HBpin molecule approaches the catalyst complex forming complex **E**$_{\mathbf{HBpin}}$. Even though this step is slightly exoenthalpic (ΔH =-3.2 kcal/mol), the entropy gain related to the association process shifts up the energy value along the Gibbs free energy profile (ΔG = 4.7 kcal/mol). Finally, hydride transfer from the activated HBpin of **E**$_{\mathbf{HBpin}}$ to the coordinated amide substrate acquired in the second step allows for the formation of the pinB-O-Bpin co-product and restoration of the active catalyst **B**. It is worth noting that because the reaction described warrants an excess of HBpin, it is plausible that an equilibrium exists between catalyst-amide and catalyst-HBpin coordination. For this reason, it is likely that other intermediates which are not shown in Figure 6 do exist within the proposed catalytic cycle. DFT calculation also supports this notion (Figure S19). However, the proposed catalytic cycle includes only the most stable intermediates and transition states, as these species are the largest contributors to the thermodynamic and kinetic behavior experimentally observed. In the transition state structure (**TS3**), HBpin interacts weakly with the carbonyl oxygen of the coordinated amide. This step is isoergonic and proceeds with an energy barrier of 20.3 kcal/mol. The above energetic profile shows that species **E** can be assigned as the turnover-determining intermediate (TDI) and **TS3** can be assigned as the turnover-determining transition state (TDTS). The computed $\Delta H^{\ddagger}$ = 10.9 kcal/mol and $\Delta S^{\ddagger}$ ≈ -35 e.u., parameters agree well with the experimental findings. Moreover, the formation of the **E**$_{\mathbf{HBpin}}$ complex convincingly explains the shift from first to zero order [HBpin] experimentally observed by increasing the HBpin concentration (Figure S4).

A first-order dependence on [HBpin] is expected, as HBpin enters the catalytic cycle between the **TDI** and **TDTS**, in agreement with the low-[HBpin] rate law determined experimentally, Rate = $k[\mathrm{La}]^1[\mathrm{Amide}]^0[\mathrm{HBpin}]^1$ (*vide supra*). However, that a high HBpin concentration can induce saturation of the catalyst complex with HBpin (effectively eliminating **E**$_{\mathbf{HBpin}}$ from the energetic profile) likely underlies the first-to-zero order transition observed for [HBpin] in the rate law.

In addition to the activation parameters discussed above, other experimental observations point to **E** and **TS3** as the TDI and TDTS, respectively. Steric encumbrance on the amide substrate strongly depresses reaction rates at 25 °C, which is to be expected for an associative, crowded transition state such as **TS3**. A small, positive Hammett ρ value (ρ = 0.56, Figure 2) indicates that the transition state is stabilized by withdrawal of electron density from the carbonyl carbon, but to a much lesser extent than is observed for typical base-catalyzed ester cleavages (ρ

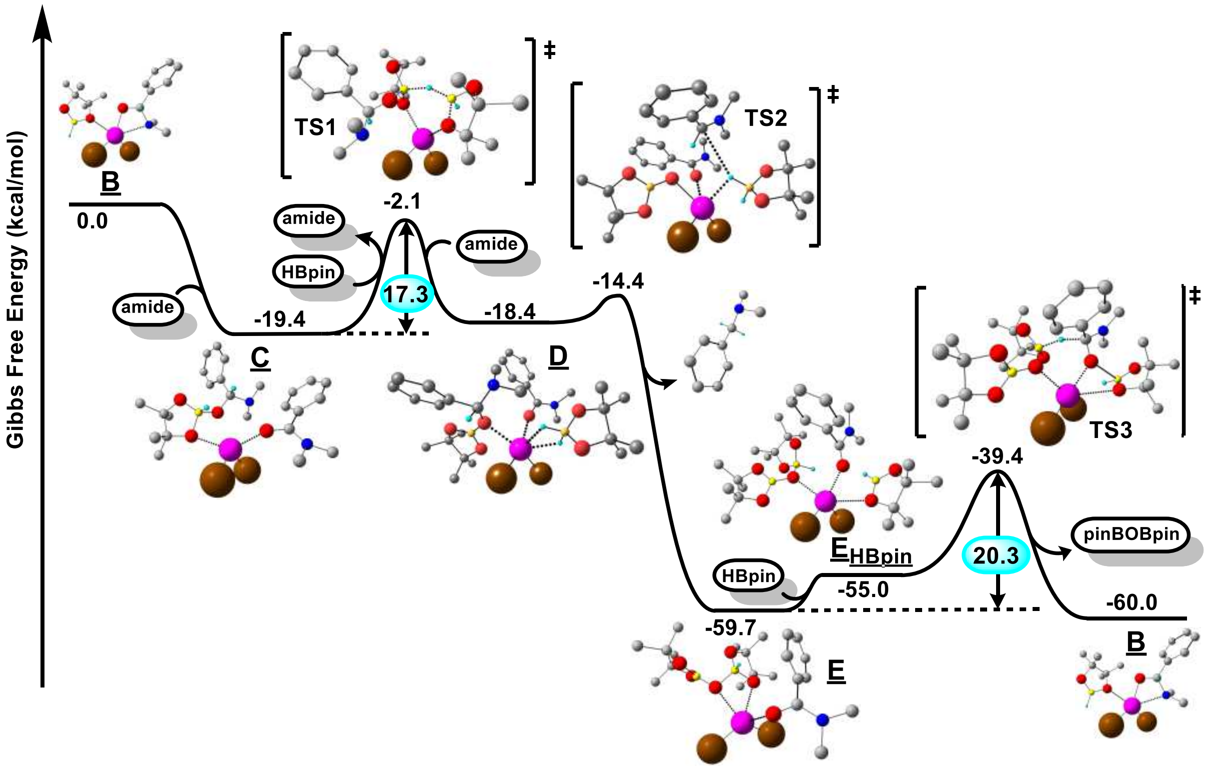


Figure 6. DFT-computed Gibbs free energy profile/catalytic cycle for the hydroboration/reduction of *N,N*-dimethylbenzamide catalyzed by $\mathrm{La}^{\mathrm{NTMS}}$.

=1.9-2.5).[19] This supports the present assignment that the turnover-limiting step involves nucleophilic hydride attack on a carbonyl bond that has been activated, in this case by simultaneous C=O coordination to both HBpin and La, priming the acyl carbon for nucleophilic attack and diminishing ρ. Similar results ware recently found for the analogues ester hydroboration process.[31] Finally, the observed HBpin/DBpin KIE of 1.50 indicates a bond to an HBpin-derived hydride is broken or formed during the rate-determining step.[76] No other KIEs have been reported for amide hydroboration, making direct comparison impossible, but this value is significantly smaller than KIEs found for several comparable reactions.[77-80] However, this Laboratory recently reported a nearly identical KIE (1.49) for ester hydroboration.[31] Notably, in the TDTS of both systems, the B-H bond of a coordinated hemiaminal-/hemiacetal-hydroborate is broken, and a new C-H bond is formed.

Conclusions

The scope and mechanism of $\mathrm{La}^{\mathrm{NTMS}}$-catalyzed, pinacolborane-based deoxygenative reduction of a diverse group of variously substituted amides is reported. The catalyst shows complete selectivity for amide reduction over nitro groups, alkenes, and alkynes, even at temperatures as high as 60 °C and catalyst loadings of 5 mol%. A combined experimental/theoretical analysis of the mechanism of this reaction reveals an unusual catalytic cycle involving ligand-centered hydride transfer. This gives rise to a rate law that is mixed order with respect to HBpin: Rate = $k[\mathrm{La}]^1[\mathrm{Amide}]^0[\mathrm{HBpin}]^1$ at low [HBpin] and Rate = $k[\mathrm{La}]^1[\mathrm{Amide}]^0[\mathrm{HBpin}]^0$ at high [HBpin]. This represents the first time a lanthanide catalyst has been employed for the pinacolborane-based reduction of amides, and it is the first attempt at a computationally-aided analysis of the mechanism of amide hydroboration. By combining a mild reductant such as HBpin with a highly active and readily accessible catalyst like $\mathrm{La}^{\mathrm{NTMS}}$, a safer, more selective and convenient route to amide reduction has been realized, highlighting the important role lanthanide catalysis can play in experimental chemical synthesis.

ASSOCIATED CONTENT

Supporting Information (SI): Experimental details, kinetic and thermodynamic data, computation details, and product characterization. This material is available free of charge via the Internet at http://pubs.acs.org.

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