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J. Am. Chem. Soc., Just Accepted Manuscript • DOI: 10.1021/jacs.9b01262 • Publication Date (Web): 23 Apr 2019

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Catalytic C–H Amination Mediated by Dipyrrin Cobalt Imidos

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ABSTRACT: Reduction of $(^{Ar}L)Co^{II}Br$ ($^{Ar}L = 5$ -mesityl-1,9-(2,4,6-Ph₃C₆H₂)dipyrrin) with potassium graphite afforded the novel Co^I synthon (^{Ar}L)Co^I. Treatment of (^{Ar}L)Co^I with a stoichiometric amount of various alkyl azides (N₃R) furnished three-coordinate Co^{III} alkyl imidos (^{Ar}L)Co(NR) as confirmed by single crystal X-ray diffraction (R: CMe,Bu, CMe₂(CH₂)₂CHMe₂). The exclusive formation of four-coordinate cobalt tetrazido complexes (^{Ar}L)Co(κ^2 -N₄R₂) was observed upon addition of excess azide, inhibiting any subsequent C-H amination. However, when a weak C-H bond is appended to the imido moiety, as in the case of (4-azido-4-methylpentyl)benzene, intramolecular C-H amination kinetically outcompetes formation of the corresponding tetrazene species to generate 2,2-dimethyl-5-phenylpyrrolidine in a catalytic fashion without requiring product sequestration. The imido (^{Ar}L)Co(NAd) exists in equilibrium in the presence of pyridine with a four-coordinate, cobalt imide (^{Ar}L)Co(NAd)(py) (K_a = 8.04 M⁻¹) as determined by ¹H NMR titration experiments. Kinetic studies revealed that pyridine binding slows down the formation of the tetrazido complex by blocking azide coordination to the Co^{III} imido. Further, (^{Ar}L)Co(NR')(py) displays enhanced C-H amination reactivity compared to the pyridine-free complex enabling higher catalytic turnover numbers under milder conditions. The mechanism of C-H amination was probed via kinetic isotope effect (KIE) experiments $[k_{\rm H}/k_{\rm D} = 10.2(9)]$ and initial rate analysis with parasubstituted azides suggesting a two-step radical pathway. Lastly, the enhanced reactivity of (ArL)Co(NR')(py) can be correlated to a higher spin state population, resulting in a decreased crystal field due to a geometry change upon pyridine coordination.

1. INTRODUCTION

Direct incorporation of a nitrene functionality into unreactive C–H bonds is a challenging¹⁻² but appealing transformation given the ubiquity of *N*-functionalities in natural products,³ agrochemicals, and synthetic precursors.⁴ Thus, as an alternative to the traditional approach utilizing pre-activated substrates, transition metal catalyzed C–H amination has received great attention.⁵⁻⁹ More specifically, the synthesis of late, firstrow transition metal-bound nitrene complexes (e.g., imido, M(NR^{2–});¹⁰⁻¹² iminyl, M(²NR[–]);¹³⁻²² nitrene adducts, M(³NR)²³⁻²⁵) is of interest as such species have been invoked as viable and cost-effective nitrene group transfer reagents.

Towards this end, our group has recently demonstrated intermolecular C–H amination mediated by a threecoordinate dipyrrinato Fe^{III} imido, ascribing its reactivity to an atypical high-spin electronic configuration.²⁶ Cobalt imidos, specifically those featuring a covalently bound NR^{2–}fragment (i.e., Co^{III}(NR)), however, have been relatively less explored in the field of C–H amination as the majority of these species feature closed-shell electronic configurations, resulting in remarkably stable compounds.²⁷⁻³⁴ Although a handful of cobalt imidos display C–H activation or functionalization, such reactivity is still limited to ligand functionalization, precluding productive C–N bond formation. For example, a Co^{III} imido (Tp^{tBu,Me})Co^{III}(NAd) reported by Theopold displays amination of one of the peripheral tert-butyl C-H bonds of the tris(pyrazolyl)borate ligand.³⁵ The amination reactivity is ascribed to a thermally accessible triplet spin state which serves to destabilize the Co-imido bond, rendering it more reactive. Recently, three-coordinate (IMes)Co^{IV}(NDipp)₂ and [(IMes)Co^V(NDipp)₂][BAr^F₄] bis-imido complexes have been reported from the Deng group.³⁶ Interestingly, the Co^{IV} imido (S = $\frac{1}{2}$) undergoes intramolecular C-H activation of a benzylic C-H bond from the IMes ligand (with a subsequent C–N forming step), whereas the analogous Co^{V} imido (S = o) is relatively inert. A leading feature of reactive cobalt imidos is their open-shell spin ground state or thermally accessible low-lying excited states that gives rise to radical character along the metalimido bond vector, to generate more reactive entities.

Similarly, our group has reported the synthesis of threecoordinate dipyrrinato Co^{III} imidos featuring open-shell electronic configurations.³⁷ Studies revealed that $(^{Ar}L)Co^{III}(N^{r}Bu)$ $(^{Ar}L = 5$ -mesityl-1,9-(2,4,6-Ph₃C₆H₂)dipyrrin) exhibits thermal population of spin excited states ($S = o \rightarrow 2$), while the mesityl analogue

 $(^{Ar}L)Co^{III}(NMes)$ adopts an S = 1 electronic ground state. (^{Ar}L)Co^{III}(N^tBu) displays typical two-electron nitrene group transfer reactivity with PMe₂Ph to quantitatively generate phosphinimide PhMe₂P(N^tBu); however, no C-H bond activation was observed. In contrast, (ArL)Co^{III}(NMes) readily undergoes intramolecular benzylic C-H activation to afford a metallacycloindoline $(ArL)Co(\kappa^2-NHC_6H_2-2,4-$ Me₂-6-CH₂). Although neither imido complex is competent for intermolecular C-H activation, we hypothesized that given their propensity to adopt openshell electronic configurations, such cobalt imidos might manifest intramolecular C-H amination reactivity instead. We have previously demonstrated the catalytic synthesis of substituted N-heterocycles from linear alkyl azides via intramolecular C-H amination mediated by dipyrrinato Fe^{III} iminyl intermediates.^{14, 38} Likewise, we envisioned that a cobalt linear alkyl imido complex could generate the substituted pyrrolidine product upon intramolecular C-H amination. Thus, we sought to examine the following questions: (1) can we synthesize dipyrrinato Co^{III} imido complexes using linear alkyl azide substrates? (2) If possible, are these imidos competent for intramolecular C-H amination to afford substituted pyrrolidines? Furthermore, (3) is the amination reaction catalytic? To this end, we report herein the intramolecular catalytic C-H amination mediated by dipyrrinato Co^{III} imidos to afford N-heterocyclic products. In addition to the structural evidence of a Co^{III} imido as the species responsible for the desired reactivity, kinetic studies were conducted to elaborate mechanistic details of the Co^I/Co^{III} catalytic cycle. Lastly, our findings on ligand-accelerated C-H functionalization reactivity will be discussed.

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2. RESULTS AND DISCUSSION

2.1. Synthesis of Cobalt Synthons. We have previously reported the preparation of dipyrrinato Co^{II} and Co^I complexes, (ArL)CoCl(py) and (ArL)Co(py), respectively, which possess one equivalent of pyridine bound to the metal center.37 In an attempt to synthesize a more sterically-accessible cobalt synthon, we employed a metalation protocol used for our recently described solvent-free dipyrrin Fe congener.²⁶ As such, refluxing (ArL)Li with anhydrous CoBr, in toluene for 15 h produced the three-coordinate Co^{II} complex (^{Ar}L)Co^{II}Br (1) as determined by X-ray crystallographic analysis of single crystals grown from a saturated solution of 1 in a hexane/benzene mixture (2:1) stored at -35 °C (Figure 1a). Chemical reduction of 1 with potassium graphite (KC₈) in a thawing benzene solution cleanly afforded the reduced compound (ArL)Co^I (2) (Scheme 1). Crystals suitable for Xray diffraction were grown from a 2:1 hexane/benzene mixture at -35 °C and the solid state structure is shown in Figure 1b.

Interestingly, **2** exhibits identical ¹H NMR chemical shifts to those observed for the pyridine-bound Co¹ analogue, (^{Ar}L)Co(py). However, the solid-state structure of **2** is distinct from that of (^{Ar}L)Co(py),³⁷ displaying an intramolecular η^6 -arene interaction between the cobalt and one of the *ortho*-phenyl substituents from the 2,4,6-

$Ph_{3}C_{6}H_{2}$ aryl groups. (Figure 1b).

Scheme 1. Synthesis of 2



2.2. Reactivity of (^{Ar}L)**Co (2) with Alkyl Azides.** With the Co^I starting material **2** in hand, we sought to explore its reactivity with a variety of substituted linear alkyl azides. We envisioned that treatment of **2** with a linear alkyl azide would furnish the corresponding Co^{III} imido which could subsequently generate the substituted pyrrolidine via intramolecular C–H amination.

To test our hypothesis, we subjected a series of aliphatic azides such as 1-azidopentane, 1-azido-4-methylpentane, and (4-azidobutyl)benzene to a solution of 2 in benzene d_6 . In each instance, we observed immediate consumption of the azides and formation of the corresponding linear imine along with regeneration of 2 instead of our anticipated cyclized products (Scheme 2). We postulated that the imines are generated via a rapid α -H atom abstraction (α -HAA) via a Co^{III} imido intermediate.³⁹ To such undesired reactivity, α -gem-dimethyl avoid substituted alkyl azides were employed. As a result, slow addition of one equivalent of 2-azido-2-methylhexane or 2azido-2,5-dimethylhexane to a solution of 2 cleanly afforded a new paramagnetic species by ¹H NMR spectroscopy. Single crystals of these species suitable for Xray diffraction were obtained from a benzene/hexane solution at -35 °C to confirm formation of the corresponding Co^{III} imidos (3) and (4), respectively (Scheme 2). The X-ray crystal structures of both 3 and 4 revealed a trigonal planar geometry around the cobalt center, which is consistent with our previously reported Co imido, (ArL)Co^{III}(N^tBu) (Figures 1c, S-44).³⁷ Complexes 3 and 4 display Co-N_{imido} distances (3, 1.616(3); 4, 1.634(5) Å) and Co-N_{imido}-C angles (3, 177.5(3)°; 4, 178.5(5)°) consistent with metrics for (ArL)Co^{III}(N^tBu) (Co-N_{imido}: 1.609(3) Å, Co-N_{imido}-C angle: 178.8(1)°).

Gratifyingly, heating each of the isolated imidos 3 and 4 to 100 °C in benzene- d_6 furnished the cyclized products, 2,2,5-trimethylpyrrolidine and 2,2,5,5tetramethylpyrrolidine, in 13% and 9% yield, respectively, as determined by ¹H NMR. Although the yields are low, the formation of *N*-heterocycles demonstrates the capability of 3 and 4 to perform intramolecular C–H amination. Moreover, regeneration of 2 was observed by ¹H NMR upon consumption of the imidos which suggests the potential viability of 2 as a catalyst.

To test whether 2 can indeed serve as a catalyst, a 10 mol% benzene- d_6 solution of 2 was exposed to 2-azido-2-

 methylhexane or 2-azido-2,5-dimethylhexane. Surprisingly, in each case, formation of new paramagnetic

species distinct from the corresponding imido complex was



Figure 1. Solid-state structures for (a) (^{Ar}L)Co^{II}Br (1), (b) (^{Ar}L)Co^I (2), (c) (^{Ar}L)Co(NR) (3), $R = C(CH_3)_2(CH_2)_3CH_3$ and (d) (^{Ar}L)Co(κ^2 -N₄R₂) (5), $R = C(CH_3)_2(CH_2)_3CH_3$ at 100 K with the thermal ellipsoids set at the 50% probability level (hydrogen atoms and solvent molecules are omitted for clarity; Co aquamarine, C gray, N blue). Selected bond lengths (Å) and angles (°) for (3): Co-N1, 1.931(3); Co-N2, 1.926(3); Co-N₁_{imido}, 1.616(3); Co-N_{imido}-C, 177.5(3).

Scheme 2. Reactivity between 2 and various linear alkyl azides



observed via ¹H NMR and no desired cyclized product was detected. The same paramagnetic species can be independently prepared either from reaction of 2 with two equivalents of azide or from reaction of the isolated imido with one additional equivalent of azide in benzene at room temperature (Scheme 2). The X-ray crystal structures of these species revealed the formation of four-coordinate cobalt tetrazido complexes, (^{Ar}L)Co(κ^2 -N₄R₂) (R: CMe₂Bu, 5; CMe₂(CH₂)₂CHMe₂, 6) (Figures 1d, S-47). Similar reactivity was previously reported by our group utilizing the same ligand platform with both iron²⁶ and cobalt.³⁷ Such four-coordinate tetrazido species are presumably generated via a rapid trapping of a second equivalent of azide by a three-coordinate imido.⁴⁰⁻⁴² Unfortunately, these cobalt tetrazido complexes are remarkably stable. No decay to the corresponding imido or pyrrolidine was observed upon heating **5** or **6** to 100 °C in benzene- d_6 . Likewise, heating either tetrazido complex in the presence of excess alkyl azides yields no reaction.

The foregoing results demonstrate that under catalytic conditions, the *in situ* generated cobalt imido is rapidly converted into catalytically inactive tetrazido species before undergoing intramolecular C–H bond activation, thus preventing potential catalytic turnover. Therefore, to achieve the desired catalytic intramolecular C–H amination, the C–H bond activation step must kinetically outcompete formation of the tetrazido species. We hypothesized that cleavage of relatively weak C–H bonds

such as benzylic C–H bonds may lower the activation energy barrier for C–H activation such that intramolecular cyclization occurs faster than bimolecular tetrazido formation.

Scheme 3. Intramolecular C–H amination of benzylic C–H bonds



2.3. Catalytic C–H Amination. To test this hypothesis, we studied the reactivity of **2** with (4-azido-4-methylpentyl)benzene (**7**) where a potential benzylic C–H amination could take place to generate **2**,**2**-dimethyl-5-phenylpyrrolidine (**9**) as a product (Scheme 3).

The reaction progression of azide 7 with 10 mol% of 2 in benzene-d₆ was monitored by ¹H NMR spectroscopy at temperatures ranging from 25 °C to 80 °C. A time progression for the reaction performed at 50 °C highlights the paramagnetically shifted resonances for 2 (Figure 2a); the conversion of 2 to the corresponding imido (8) upon addition of azide 7 (10 equiv.) initially (Figure 2b, Scheme 3) and after 1 h (Figure 2c); and the final spectrum for the tetrazido complex (Figure 2d). As illustrated in Figure 2a-d, consumption of 8 occurred via two different pathways over time: (1) formation of catalytically inactive tetrazido species and (2) generation of the desired product 9 along with regeneration of 2 which is rapidly re-oxidized to 8 (Figure 2c), indicating that 8 is the catalytic resting state. Once all imido 8 is converted to the tetrazido species, there is no further consumption of azide 7 and the reaction stops (Figure 2d).

As the reaction temperature increases, the yield of pyrrolidine **9** increases as well, reaching a maximum of 78% at 80 °C. To better understand the amination reaction's temperature dependence, we surveyed the ratio between unreacted azide **7** and pyrrolidine **9** as a function of temperature by ¹H NMR (Figure 3). At low temperature, a considerable amount of unconsumed azide **7** is present as C–H amination is slow. As a result, the imido intermediate **8** is exposed to large concentrations of azide **7** leading to predominant formation of the corresponding tetrazido complex. As the temperature increases, however, the amination pathway becomes more favorable, promoting faster consumption of **7**, higher yields of **9**, and minimizing formation of the tetrazido complex.



Figure 2. (a) 'H NMR spectrum of **2** in benzene- d_6 (b) 'H NMR spectrum taken following addition of 10 equiv. of azide **7** in benzene- d_6 , Paramagnetic chemical shifts corresponding to imido **8** are colored in blue. (c) 'H NMR spectrum taken after 1 h and the chemical shifts corresponding to tetrazene (ArL)Co(κ^2 -N₄R'₂) are colored in red. (d) Reaction completed.



Figure 3. Diamagnetic region in 'H NMR spectra of the reactions conducted at various temperatures. The singlet at 3.3 ppm corresponds to 1,3,5-trimethoxybenzene which was used as an internal standard for integration.

2.4. Kinetic Analysis of Catalytic C–H Amination. To establish a detailed mechanism for the catalytic amination reaction, we performed various kinetic experiments. As shown in Figure 2b, the oxidation of 2 with excess azide 7 quantitatively affords imido 8 instantaneously, allowing us to estimate the concentration of 8 based on the initial concentration of catalyst 2. Furthermore, the initial concentration of 8 remains constant during early stages of the catalytic reaction since the concentration of azide 7 is high enough to re-oxidize 2 to 8 upon pyrrolidine f ormation, enabling initial rate kinetic analysis under pseudo steady-state conditions. Additionally, the initial rate kinetic analysis was necessary to exclude rate diminishing caused by

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Figure 4. (a) First order dependence on the concentration of **8** at 50 °C in C_6D_6 . (b) Zeroth order dependence on the concentration of **7** at 50 °C in C_6D_6 . (c) KIE study employing 7/7- d_a at 50 °C in benzene- d_6 .



Figure 5. (a) Solid-state structure of (^{Ar}L)Co(NAd) (**10**) at 100 K with the thermal ellipsoids set at the 50% probability level (hydrogen atoms and solvent molecules are omitted for clarity; Co aquamarine, C gray, N blue). (b) Job plot of **10** and pyridine at 25 °C. In all cases, [**10**] + [py] = 4.25 mM in benzene- d_6 . (c) ¹H NMR titration curve of **10** at 25 °C in benzene- d_6 . Black dashed line represents a result of fitting based on 1:1 binding isotherms.



Figure 6 (a) Solid-state structure of $(^{Ar}L)Co(\kappa^2-N_4Ad_2)$ (11) at 100 K with the thermal ellipsoids set at the 50% probability level (hydrogen atoms and solvent molecules are omitted for clarity; Co aquamarine, C gray, N blue). (b) Observed rates of formation of 11 as a function of [py-d₅] at 25 °C. In all cases, [10] = 8.50 mM and [N₃Ad] = 85.0 mM in benzene-d₆. (c) Observed rates of formation of 9 as a function of [py-d₅] at 25 °C. In all cases, [2] = 4.25 mM and [7] = 85.0 mM in benzene-d₆.

slow formation of the catalytically inactive tetrazido species. We first examined the reaction order of amination with respect to **8** by varying the catalyst loading. The rates were determined by measuring the concentration of product **9** (< 10% yield) over time at 50 °C in benzene- d_6 via 'H NMR spectroscopy. As shown in Figure 4a, a plot of the concentration of the imido (i.e., [**8**]) versus rates of product formation displays a linear correlation suggesting that C– H amination is first order in imido **8**.

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A similar kinetic analysis was conducted holding the catalyst concentration constant and varying azide concentration ([7]) to reveal a zeroth order dependence in azide 7 (Figure 4b), corroborating the unimolecular nature of the amination reaction. Lastly, we performed a kinetic isotope effect (KIE) experiment to investigate the ratedetermining step during catalysis. The KIE value was evaluated by comparing the initial rates of 5 mol% of 2 with 7 and its bis-deuterated form at the benzylic site (4-azido-4-methylpentyl-1,1- d_2)benzene (7- d_2). The observed ratio of the rate constants $(k_{\rm H}/k_{\rm D})$ was determined to be 7.6(2), which is in agreement with the C-H bond activation step being rate-determining (Figure 4c).43 Similarly, the intramolecular KIE value obtained by employing a stoichiometric amount of mono-deuterated azide $7-d_1$ showed three times greater selectivity for the C-H over the C-D bond (Figure S-10).

Given all the kinetic data, we propose the following catalytic sequence: (1) fast oxidation of **2** by an alkyl azide affords Co^{III} imido **8**; (2) **8** undergoes intramolecular H–atom abstraction to generate a transient Co^{II} amide (**Int**, Scheme 4); followed by (3) rapid radical recombination to afford the cyclized product **9**. Alternatively, a direct C–H insertion pathway from the Co^{III} imido cannot be fully excluded (Figure S-3).

2.5. Mechanism-driven Improvement of Catalytic Performance. To the best of our knowledge, this is the first example of catalytic C-H amination mediated by a spectroscopically observable Co^{III} imido, whose identity can be inferred from the structurally characterized analogues 3 and 4. Furthermore, it is noteworthy that the catalytic C-H amination we describe herein displays a distinct kinetic profile from the similar ring-closing catalysis mediated by a Co^{III} iminyl radical intermediate (in particular the system reported by Zhang, de Bruin, and coworkers) as opposed to a Co^{III} imido species.44-46 Specifically, as suggested by the KIE experiments, we have observed that the C-H activation step as opposed to activation of the azide moiety is the rate-determining. Additionally, in contrast to our previously reported Febased catalysis which requires Boc-protection of the pyrrolidine products to regenerate the active catalyst,^{14, 38} the Co^I/Co^{III} catalytic cycle showcased herein is capable of yielding free saturated cyclic amines without requiring product sequestration to eliminate product inhibition. Encouraged by these results, we attempted to further optimize the reaction conditions. Lowering the catalyst loading to 5 mol%, however, afforded 31% of pyrrolidine 9 at 80 °C, a significantly diminished yield compared to 78% obtained using 10 mol% of 2. The diminished yield is consistent with our proposed mechanism that formation of tetrazido complex is favored at relatively high concentrations of azide. Thus, while catalysis should be most effective under slow addition of the azide substrate or dilute reaction conditions, reaction time and volumetric throughput would therefore be limited, respectively. An alternative strategy to suppress tetrazido formation is to employ an ancillary ligand that would competitively bind the imido intermediate, thereby retarding or eliminating tetrazido formation.

To this end, pyridine was a suitable option given its modular steric and electronic profile. To study the binding dynamics between pyridine and a three-coordinate Co^{III} imido without concern for subsequent H–atom abstraction, an adamantyl substituted imido (**10**) was prepared as a model complex. Stoichiometric reaction of **2** with 1-azidoadamantane (N₃Ad) cleanly produced (^{Ar}L)Co(NAd) **10** in 87% isolated yield. Akin to imidos **3** and **4**, the solid-state structure of **10** displays a trigonal-planar geometry with a Co–N_{imido} distance of 1.620(7) Å and a nearly linear Co–N_{imido}–C angle of 171.4(6)° (Figure 5a).

 $\label{eq:Table 1. Effect of pyridine concentration on C-H amination reactivity^c$

Entry	[py-d ₅] (mM)	Rate (mM/min)	Yield (%)ª
1	0	N/A ^b	< 10
2	4.3	0.52(3)	21
3	8.5	0.70(5)	22
4	26	0.813(5)	35
5	89	1.12(2)	89
6	174	1.45(4)	91
7	300	1.63(4)	93
8	430	1.77(3)	93

^a¹H NMR yields using 1,3,5-trimethoxybenzene as internal standard. ^bInitial rate is not available due to a slower formation of **9** at 25 °C. ^cReactions were conducted with pyridine- d_5 to manipulate kinetic experiments with ¹H NMR spectroscopy. In all cases, [2] = 4.25 mM and [7] = 85.0 mM in benzene- d_6 at 25 °C.

With **10** in hand, we examined the complexation ratio between the three-coordinate imido and pyridine in solution using a Job plot analysis.⁴⁷ The maximum value in the Job plot (Figure 5b) appeared at 0.5 mole fraction of **10** and pyridine suggesting a 1:1 binding stoichiometry to afford (**10-py**) in solution. Furthermore, the binding equilibrium constant of pyridine to **10** (K_a = 8.04 M⁻¹) was determined by tracking the changes in ¹H NMR chemical shifts of **10** as a function of pyridine concentration (Figure 5c).⁴⁸

Although the binding affinity of pyridine is weak, the

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potential kinetic effect resulting from pyridine coordination on the rate of formation of the tetrazido *Scheme 4*

complex may still



be significant. Thus, we measured the conversion rate of isolated imido **10** to the corresponding tetrazido complex $(^{Ar}L)Co(\kappa^2-N_4Ad_2)$ (**11**, Figure 6a) as a function of pyridine- d_5 concentration. The rate obtained in the absence of pyridine was defined as 1 and the following relative rates (k_{rel}) were determined at 50% formation of **11**.

Indeed, a slower formation of **11** was observed at higher concentrations of pyridine- d_5 , indicating that, as more pyridine-bound imido **10-py** is present in solution, formation of the tetrazido complex is diminished (Figure 6b). These results support our original hypothesis that blocking the fourth coordination site of a three-coordinate imido with an additional ligand offers steric protection against tetrazido formation.

Given these findings, we anticipated that yields of **9** may be improved in the presence of pyridine. Indeed, a 5 mol% catalytic reaction with 7 in the presence of 10 equivalents of pyridine- d_5 with respect to 2 afforded 90% of 9 at 80 °C, greatly exceeding the amount of pyrrolidine product formed in the absence of pyridine. Furthermore, as the formation of the corresponding tetrazido complex is suppressed, regenerated Col catalyst (ArL)Co(py) is observed when the reaction is completed (Figure S-19). More surprisingly, not only were improved yields of **9** observed, but increased rates of C-H amination were also detected, implying enhanced amination reactivity of the pyridine-bound imido (8-py) relative to the threecoordinate imido 8. Similar to the kinetic experiments described in Section 2.4, initial rates of the C–H amination were measured at varying concentrations of pyridine- d_5 under pseudo steady-state conditions as the oxidation of 2 by azide 7 remained instantaneous and quantitative with pyridine- d_5 in solution (Table 1).

As shown in Table 1, in the absence of pyridine, an attempt to measure the initial rate of amination at 25 °C was not successful since the conversion of imido **8** to **9** is too slow to be measured at this temperature (Table 1, entry

1). In contrast, an increased rate is noted at the same temperature in the presence of 5 mol% of pyridine- d_5 (Table 1, entry 2). Likewise, the resulting initial rate increases as the concentration of pyridine- d_5 increases, displaying an overall saturation kinetic behavior in pyridine- d_5 (Figure 6c). Furthermore, pyridine- d_5 can used as a solvent to produce 92% of **9** with 1 mol% of catalyst **2** at 80 °C. To summarize, pyridine slows down the formation of the undesired tetrazido complex and functions as a cocatalyst, permitting higher catalytic turnover numbers under milder reaction conditions.

2.6. Mechanistic Study of C-H amination in the Presence of Pyridine. Excited by the enhanced C-H functionalization reactivity of 8-py, we investigated whether the mechanism of C-H activation changes in the presence of pyridine. A KIE value of 10.2(9), which is above the classical limit was observed in the presence of 10 equivalents of pyridine- d_5 with respect to 2 suggesting a stepwise radical pathway for C–H amination (Figure S-9).49 To further support a radical pathway, initial rates of amination were measured for a series of para-substituted azides under the same conditions. As a result, both electron-donating and electron-withdrawing substituted azides displayed slightly increased rates compared to the parent azide 7 (Table 2), suggesting stabilization of benzylic carboradical intermediates (Int or Int-py) upon H-atom abstraction. Plotting log $k_{\rm R}$ versus σ^+ parameters (Figure S-12) results in a non-linear correlation between reaction rate and electron-donating ability of the parasubstituent on 7-X. However, plotting log $k_{\rm R}$ versus the spin delocalization parameters (σ_{mb} , σ_{ii}) developed by Jiang and coworkers⁵⁰ yields a more linear relationship (Figure 7). Multiple coefficient linear regression for the dual-parameter equation log $k_{\rm R} = \rho_{\rm mb}\sigma_{\rm mb} + \rho_{jj}\bullet_{jj}$ provided $\rho_{\rm mb}$ = -0.25 and $\rho_{\rm ii}^{\bullet}$ = 0.72. The positive value of $\rho_{\rm ii}^{\bullet}$ indicates that the para-substituent (X) delocalizes spin in the transition state. Furthermore, the large $|\rho_{ij}^{\bullet}/\rho_{mb}|$ value of 2.9 indicates that the spin delocalization effect dominates

in the amination reaction, similar to the previously reported iron catalyzed amination reaction.39

Table 2. Initial rates and final yields of 9 with para-substituted azide substrates







Figure 7. Linear free energy correlation of log k_{R} vs. $(\sigma_{\text{mb}}, \sigma_{jj})$ for the amination reaction of *p*-substituted aryl azide substrates listed in Table 2 where $\rho_{mb} = -0.25$, $\rho_{ij}^{\bullet} = 0.72$.

Taking all mechanistic studies together, our proposed catalytic cycle for the intramolecular C-H amination in the presence of pyridine is illustrated in Scheme 4. Several mechanistic features are of note: (1) both 8 and 8-py are competent species for catalytic C-H amination to afford substituted pyrrolidine **9** in a two-step radical-type pathway; (2) 8-py displays drastically improved rate of amination compared to 8 along with slower formation of the catalytically inactive tetrazido complex; (3) 2 exhibits equilibrium with pyridine, existing as either an

(^{Ar}L)Co(py), or (^{Ar}L)Co(py), both of which are active catalysts to readily furnish 8-py.

2.7. Catalysis with Substituted Pyridines. Given the utility of added pyridine to facilitate the intramolecular amination catalysis, we sought to determine the impact of changing the pyridine donor on catalysis. To this end, the amination reaction was run with azide 7 using 1 mol% 2 in the presence of 20 equivalents of dimethylaminopyridine $(4-Me_2N)py$) in benzene- d_6 . The reaction afforded 91% of **9** at 80 °C, similar to the yield obtained from the reaction conducted in neat pyridine. Motivated by this result, we sought to investigate the effect of the para-substituent on pyridine on the reaction rates and yields of C-H amination. Specifically, we attempted to establish differences in values of k_2 among a series of *para*-substituted pyridines, where k_1 and k_2 are the first order rate constants of C–H amination mediated by 8 and 8-py', respectively (eq 1).⁵¹ Assuming that k_1 is negligible at 25 °C based on our experimental results (Table 1, entry 1), the rate law can be further simplified (eq 2).

$$\frac{d[\mathbf{9}]}{dt} = k_1[\mathbf{8}] + k_2[\mathbf{8} - \mathbf{py'}] \qquad (eq)$$

$$\frac{d[\mathbf{9}]}{dt} \approx k_2[\mathbf{8} - \mathbf{py'}] \text{ at } 25 \text{ °C} \qquad (eq)$$

dt

As shown in Table 3, electron-rich pyridines such as $4^{-t}Bu$)py and $(4^{-Me_2}N)$ py exhibit faster conversions as well as higher yields of 9 compared to pyridine. Both [8**py**'] and k_2 of each of the *para*-substituted pyridines were calculated based on the independently determined equilibrium binding constants using imido 10 (K_a, Table 3). As a result, the values of k_2 for pyridine, $4^{-t}Bu$)py, and 4–Me₂N)py are similar suggesting that the improved rates are mostly attributable to the higher concentration of the corresponding pyridine-bound imido complex, not to k_2 . Interestingly, we found that the electron-poor $4-(F_2C)py$ displays a stronger binding affinity than the unsubstituted pyridine, yet slows formation of 9, resulting in a considerably smaller k_2 relative to the electron-rich pyridines (Table 3, entry 4). The diminished rate employing $4-(F_2C)$ py suggests that electronic effects may also influence the reactivity of the pyridine-bound imidos, albeit additional studies are necessary to evaluate such contributions.



Figure 8. (a) Solution magnetic moments of mixture of (10) and (10-(4-Me₂Npy)) as a function of [4-Me₂Npy] at 25 °C in benzene- d_6 . (b) Frontier MO description of (^{Ar}L)Co(NR'). (c) Frontier MO description of (^{Ar}L)Co(NR')(py).

Table 3. Catalytic activity of 2 with para-substituted pyridines

	<i>р-</i> R C ₄ H ₄ N	K _a (M ⁻¹) ^a	$k_{ m R}/k_{ m H}$	NMR yield (%) ^b	k_2 (min ⁻¹)
1	Н	8.04	1.00	36.4	1.25
2	^t Bu	12.9	1.7(4)	89.4	1.42
3	NMe ₂	41.8	3.1(7)	90.8	1.24
4	CF ₃	12.5	0.36(2)	20.4	0.31

^aBinding constants at 25 °C in benzene-*d*₆. ^bH NMR yields using 1,3,5-trimethoxybenzene as internal standard.

2.8. Spin State Consideration of the Pyridine-bound Imido. We sought to determine if the pyridine-bound imido displays a different electronic structure as compared to the three-coordinate, pyridine-free imido. Our attempts to isolate **10-py** were unsuccessful due to the weak binding affinity of pyridine. Thus, we measured the solution magnetic moment of **10** as a function of concentration of $4-(Me_2N)py$, assuming that the total magnetic moment (μ_{eff}) is the summation of two individual components, μ'_{eff} and μ''_{eff} arising from **10** and **10-(4-Me_2Npy)**, respectively (eq 3). The mole fraction (χ) of each species at a given concentration of $4-(Me_2N)py$.

$$\mu_{\text{eff}} = \mu'_{\text{eff}}(\chi^{\text{10}}) + \mu''_{\text{eff}}(\chi^{\text{10 - dmap}}) \qquad (\text{eq 3})$$

In the absence of 4-(Me₂N)py, where μ_{eff} is the same as μ'_{eff} , **10** shows a μ_{eff} of 2.5 μ_{B} resulting from its *S* = 0 ground state (by analogy to (^{Ar}L)Co(N^tBu)) and population of thermally accessible excited states (e.g., *S* = 2). As the concentrations of 4–(Me₂N)py increases, the total solution magnetic moment of the mixture increases (Figure 8a) resulting in a μ''_{eff} of 4.0 μ_{B} . The μ''_{eff} value suggests that the pyridine-bound imido complex could change the spin ground state from the singlet, three-coordinate imidos

(e.g., S = 1, 2), or pyridine coordination could make the spin excited states thermally more accessible.

The observed changes in solution magnetic moments of 10 as a function of 4-(Me₂N)py concentration can be rationalized by considering the frontier molecular orbitals (FMOs). We have previously proposed a qualitative FMO description of a three-coordinate cobalt imido (ArL)Co(NtBu) to describe its thermal behavior (Figure 8b).37 Those FMOs would be further perturbed upon coordination of a fourth ligand, and thus give rise to a different electronic configuration. Pyridine coordination could result in either a trigonal monopyramidal geometry if the pyridine simply associates axially, or the geometry could undergo a tetrahedral distortion as has been observed for pyridine coordination in Holland's iron-imido work.52-54 To this end, we have performed geometry optimizations for **10-py** considering an S = 0, 1, or 2 spin ground state, and the results suggest a trigonal monopyramidal geometry for all cases (Table S-10). Moreover, at the optimized geometries of 10-py corresponding to the S = 1 and 2 spin ground states were found to be more stable than that for the S = 0 spin state by 6.1 and 7.7 kcal/mol, respectively. As such, we will present our FMO analysis using the S = 2 spin ground state as an example, although we cannot fully exclude of the possibility for an S = 1 spin ground state given the subtle energy difference between the S = 1 and 2 spin states.

A geometry change from trigonal planar to trigonal monopyramidal upon pyridine coordination impacts both the σ and π -bonding within the molecule. Assuming that pyridine approaches along the y-axis, the imide fragment falls below the *xz* plane (Figure 8c). Consequently, the π -overlap between the Co and imido N (Co 3 d_{xz} + N 2 p_x; Co 3 d_{yz} + N 2 p_y) is diminished, lowering both d_{xz} (σ L⁺ + π Nx^{*}) and d_{yz} (π Ny^{*}) in energy. In contrast, 3 d_z² and 3 d_{x²-y²} (π Ny^{*}) are destabilized (σ ^{*}_{Co-Npy}), while d_{xy} remains nominally non-bonding. The net result of the geometric configuration is to decrease the overall 3 d energy gap (i.e., Δ (3d_{xz} - 3d_{xy}) is diminished), leading to the higher spin

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state populations observed (Figure 8a). The qualitative orbital interaction analysis agrees with the DFT results (Figure S-55); however, further studies will be necessary to quantitatively analyze the frontier molecular orbital compositions given the extent of $Co-N_{imido} \pi$ -interaction varies as a function of the imido fragment deviation from the *xz* plane.

2.9. Origin of the Enhanced Reactivity of the Pyridine-bound Imido. Many transition metal complexes featuring metal-ligand multiple bonds display enhanced group transfer reactivity upon coordination of an exogenous ligand.55-58 For example, epoxidation of olefins mediated by either a CrV-oxo59 or MnV-oxo60 complex proceeds more efficiently upon ligation of pyridine *N*-oxide to these metal-oxo active species. This effect has also been observed for H-atom abstraction reactivity, however, the reported transition metal complexes are not capable of productive group transfer. The Goldberg group has demonstrated the enhanced H-atom abstraction reactivity of a Mn^V-oxo corrolazine complex in the presence of halide anions.⁶¹ Similarly, the Holland group showcased that an iron imido complex (MeL)Fe(NAd) undergoes H-atom transfer only upon ligation of 4–(^tBu)py.⁵¹

Given these precedents, we propose the following potential explanation to understand how pyridine influences the rate of C–H amination in this study. Based on our FMO analysis and the theoretical studies conducted on **10-py** (Section 2.8), we propose that the pyridinebound, four-coordinate Co imido complex features an attenuated Co–N bond order by accessing higher spin states as compared to the three-coordinate analogue. Furthermore, as the DFT results suggest, the trigonal monopyramidal geometry obtained upon pyridine ligation may resemble the structure of the transition state for H–atom abstraction more closely. As such, the H-atom abstraction step should be more kinetically favored.

3. CONCLUSIONS

The foregoing results demonstrate catalytic C–H amination mediated by dipyrrin-supported, Co^{III} imidos to afford substituted pyrrolidines from alkyl azides. Although our previously reported cobalt-based alkyl imido (^{Ar}L)Co(N^tBu) does not display intermolecular C–H activation reactivity, our strategy to introduce

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intramolecular benzylic C-H bonds proximal to the imido moiety promoted C-H bond amination. Kinetic studies support the viability of the structurally characterized three-coordinate dipyrrinato Co^{III} imido as a competent nitrene-group transfer species. Furthermore, the desired C-H amination reactivity was improved in the presence of pyridine. We found that pyridine plays critical roles during the catalytic reaction: (1) pyridine coordination prevents formation of a catalytically-inactive, four-coordinate cobalt tetrazido complex and, more importantly, (2) the resulting pyridine-bound CoIII imido displays enhanced rate of C-H amination. As a result, we were able to accomplish greater catalytic performance under milder conditions with pyridine as a co-catalyst. We rationalize the improved nitrene group transfer reactivity of the pyridine-bound imido might be resulting from perturbations in its geometric and electronic structures along with potential changes in reaction thermodynamics. We believe this study demonstrates the importance of understanding the salient features of such transition metal ligand multiple bonds to better design new catalysts. Given our findings, we are currently interested in further tailoring our systems to expand the group transfer catalysis protocol.

ASSOCIATED CONTENT

Supporting Information. General experimental considerations and procedures, multinuclear NMR data, solid state molecular structures, crystallographic CIF files, and crystallography data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

This work was supported by a grant from the NIH (GM-115815), the Dreyfus Foundation (Teacher-Scholar Award to T.A.B.), and Harvard University. Y.B. gratefully acknowledges a Kwanjeong Graduate Student Fellowship.

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