

Mechanistic Studies on the Rh(III)-Mediated Amido Transfer Process Leading to Robust C–H Amination with a New Type of Amidating Reagent

Yoonsu Park,^{†,‡} Kyung Tae Park,^{†,‡} Jeung Gon Kim,^{*,‡,†} and Sukbok Chang^{*,‡,†}

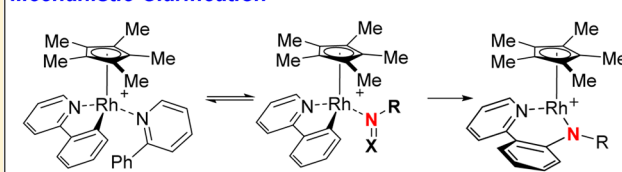
[†]Department of Chemistry, Korea Advanced Institute of Science and Technology (KAIST), Daejeon, 305-701, Republic of Korea

[‡]Center for Catalytic Hydrocarbon Functionalizations, Institute for Basic Science (IBS), Daejeon, 305-701, Republic of Korea

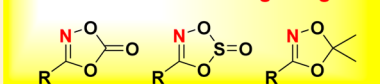
Supporting Information

ABSTRACT: Mechanistic investigations on the Cp^{*}Rh(III)-catalyzed direct C–H amination reaction led us to reveal the new utility of 1,4,2-dioxazol-5-one and its derivatives as highly efficient amino sources. Stepwise analysis on the C–N bond-forming process showed that competitive binding of rhodium metal center to amidating reagent or substrate is closely related to the reaction efficiency. In this line, 1,4,2-dioxazol-5-ones were observed to have a strong affinity to the cationic Rh(III) giving rise to dramatically improved amidation efficiency when compared to azides. Kinetics and computational studies suggested that the high amidating reactivity of 1,4,2-dioxazol-5-one can also be attributed to the low activation energy of an imido-insertion process in addition to the high coordination ability. While the characterization of a cationic Cp^{*}Rh(III) complex bearing an amidating reagent was achieved, its facile conversion to an amido-inserted rhodacycle allowed for a clear picture on the C–H amidation process. The newly developed amidating reagent of 1,4,2-dioxazol-5-ones was applicable to a broad range of substrates with high functional group tolerance, releasing carbon dioxide as a single byproduct. Additional attractive features of this amino source, such as they are more convenient to prepare, store, and use when compared to the corresponding azides, take a step closer toward an ideal C–H amination protocol.

Mechanistic Clarification



New Class of Amidating Reagents



- Strong Coordination
- Low Activation Barriers
- External Oxidant-Free
- Low Catalyst Loading

INTRODUCTION

Construction of a carbon–nitrogen bond is one of the most fundamental operations in nature and organic synthesis. The resulting amino compounds are widely present in natural products, pharmaceutical drugs, and functional materials. Thus, the development of efficient C–N bond-forming methods has been extensively explored.¹ While conventional synthetic approaches employ functionalized compounds such as alkenyl or aryl (pseudo)halides to react with nitrogen sources,² direct catalytic amination on carbon–hydrogen bonds has drawn significant attention based on a recent notable advance achieved in the C–H activation procedures.³ With a better understanding of C–H activation process dealing with high activation barriers and selectivity issues, the direct use of abundant carbon–hydrogen connections would eliminate prefunctionalization steps.⁴ In this regard, transition-metal-mediated C–H functionalization offers great promise to chemo-, regio-, and stereoselective synthetic procedures operating under mild conditions.

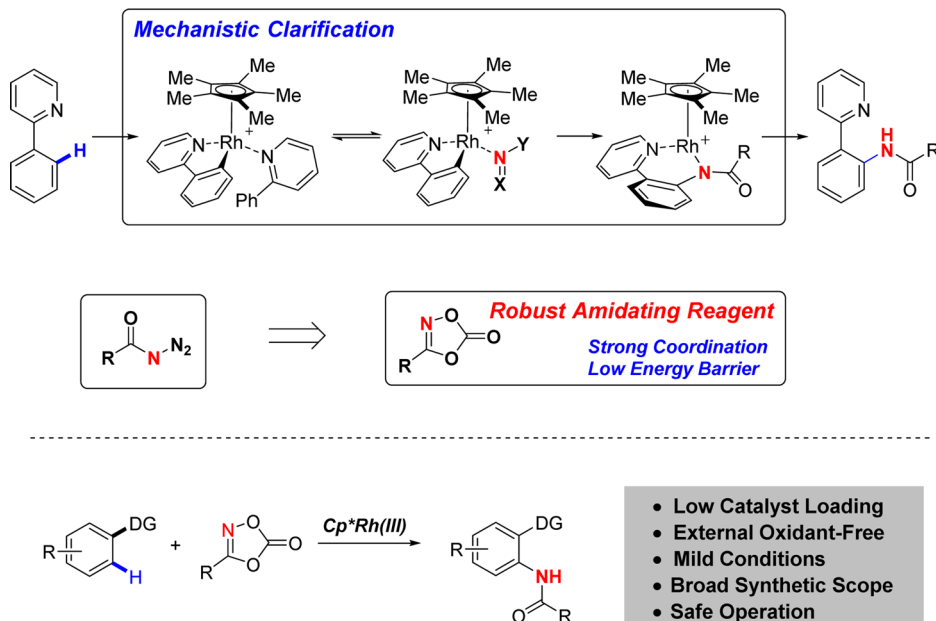
In case of C–H amination reactions, a seminal work by Breslow et al. using iminoiodinane with Fe- and Rh-based catalysts blazed a trail for the significant catalytic C–H amination procedures.⁵ Currently, major research efforts are

en route for an ideal catalytic C–H amidation system: coupling of unactivated hydrocarbons with amidating reagents which are readily available and convenient to use under mild conditions while producing minimal amounts of waste.³ We recently answered to those demands by utilizing organic azides as the unique amino source which also work as internal oxidants, thus not necessitating any external oxidants enabling an environmentally benign catalytic process.^{6,7} Our original development and detailed mechanistic studies on the Cp^{*}Rh(III)-catalyzed direct C–H amination using azides⁶ have been a stepping stone for the expansion to more efficient and selective catalytic systems showing broader synthetic applications.^{7,8}

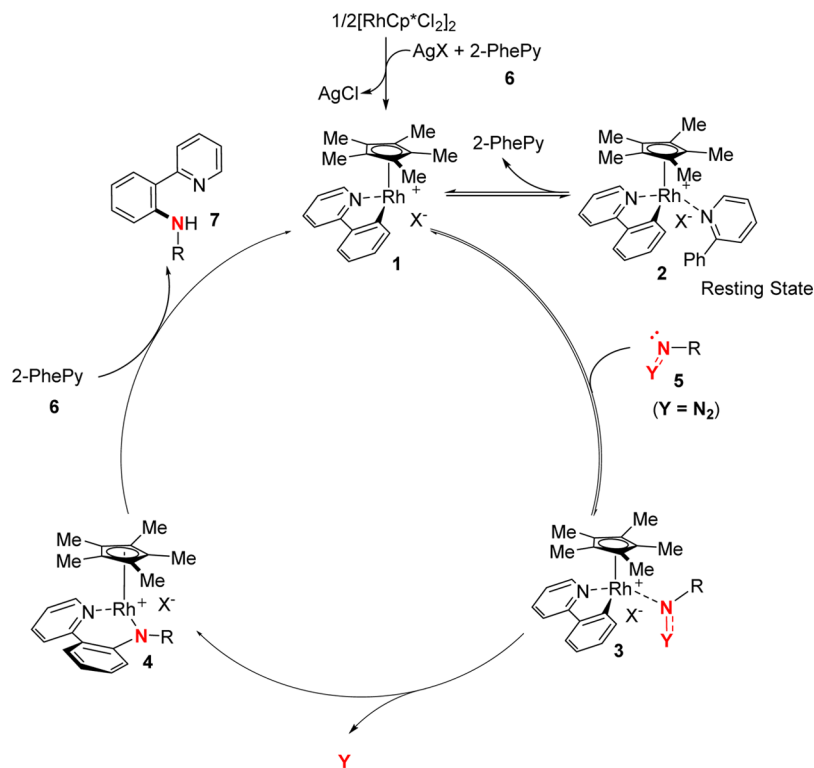
In our continuing mechanistic investigations on the C–H amination reactions, we were able to draw a more comprehensive picture on the C–N bond-forming process. Kinetics and coordination studies including the isolation of a key intermediate revealed that a competitive binding of a metal center to substrate or nitrogen source is directly related to the reaction efficiency. This breakdown study allowed us to introduce a robust catalytic system for the efficient C–H

Received: February 10, 2015

Scheme 1. Development of Highly Reactive C–H Amidation Driven by Mechanistic Studies



Scheme 2. Mechanistic Proposal on the Rh(III)-Catalyzed C–H Amination Using an Organic Azides



amidation reactions using 1,4,2-dioxazol-5-ones as the convenient amino source (Scheme 1). This new catalytic system allowed low catalyst loading, broad synthetic scope, and external oxidant-free mild reaction conditions releasing CO₂ as a single byproduct, altogether directing an ideal C–H amination protocol, which is described herein as follows.

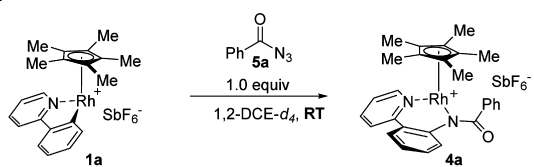
RESULTS AND DISCUSSIONS

Identification of a Rate-limiting Factor in the C–H Amidation using Azides. We previously reported the

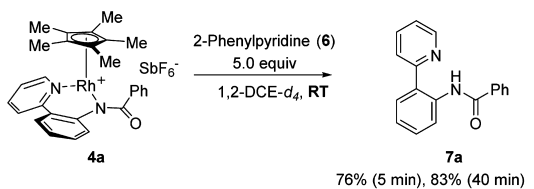
Rh(III)-catalyzed direct amidation of arene, alkene, and alkane C–H bonds using organic azides as the nitrogen source.^{6,7} Extensive experimental and computational studies allowed us to propose a preliminary mechanistic depiction (Scheme 2). During our subsequent investigations, one interesting observation especially caught our attention: while each of stoichiometric C–N bond formation of a rhodacycle (**1a**) with benzoyl azide (**5a**) (Scheme 3a) and protodemetalation of the consequent amido rhodium complex (**4a**) by using 2-phenylpyridine substrate (**6**) are facile at room temperature

Scheme 3. Analyses of Individual Stage

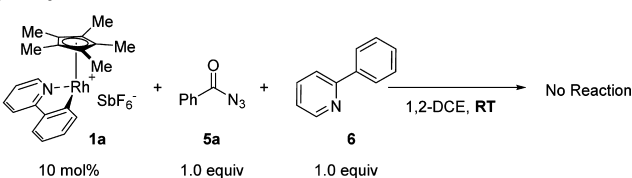
a) C–N Bond Formation



b) Protodemetalation



c) Catalytic Reaction at RT



(Scheme 3b), its catalytic conversion using a rhodacycle species (**1a**) did not take place (Scheme 3c).

We decided to initiate a detailed analysis on whole C–N bond-forming processes to find a clue to this nonreactivity under the catalytic conditions. We hypothesized that the C–H amination pathway can be divided into four individual stages (Scheme 2): (i) generation of a cationic rhodacycle **1** from the resting state species **2**; (ii) coordination of an azide to a metal center to form an intermediate **3**; (iii) insertion of an imido moiety into the rhodium–carbon bond to form the C–N bond, thus generating a metal–amido complex **4**; and (iv) protodemetalation with concomitant C–H bond activation of a second substrate to release product **7** with the regeneration of an active species **1**. The successful conversion from a rhodacycle **1a** to a product **7a** (Scheme 3a,b) led us to postulate that the above presupposed three stages (ii–iv) are facile under the applied conditions. Consequently, this reasoning warranted a further study especially with regard to the stage (i).

Ellman and co-workers observed the inhibitory effects of substrates in the Cp**Rh*(III)-catalyzed addition of 2-phenylpyridines to imines.⁹ We also figured out the analogous behavior of substrates in the *Rh*-catalyzed C–H amination reactions.⁶ As was revealed by our previous mechanistic studies,⁶ a substrate will occupy the vacant site of a cationic rhodacycle **1** to generate a resting species **2**, which accounts for an inverse first-order kinetics on 2-phenylpyridine (Scheme 2). Consistent with this reasoning, when **2a** was allowed to react with benzoyl azide **5a**, the amidation proceeded almost negligibly even after prolonged time (Figure 1). Again, this reactivity of **2a** is totally opposite when compared to a cationic rhodacycle **1a** having one vacant site that reacts promptly with benzoyl azide **6a** at room temperature (Scheme 3a).

The observed poor conversion of **2a** to a metal–amido complex **4a** implies that an organic azide is not capable of binding effectively to a metal center in the presence of 2-phenylpyridine. Under this circumstance, the effective concentration of a rhodium complex entering into an operating catalytic cycle can be regarded to be very low, while most of the

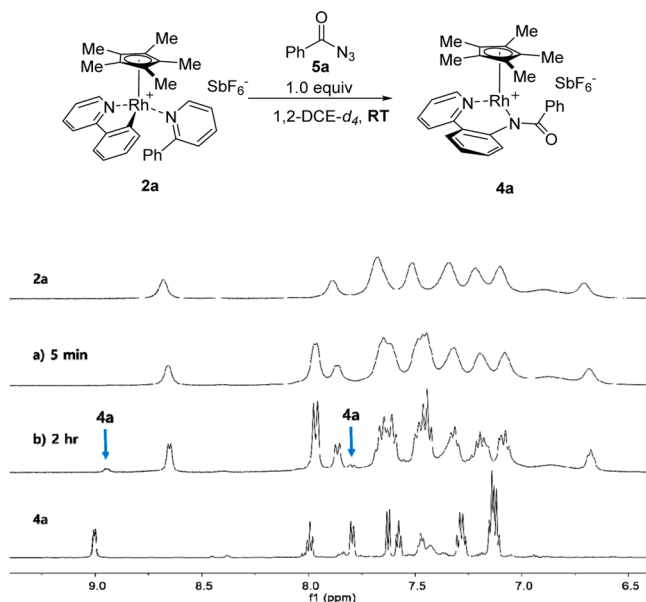


Figure 1. NMR study of C–N bond formation with a resting species **2a** (see the Supporting Information for details).

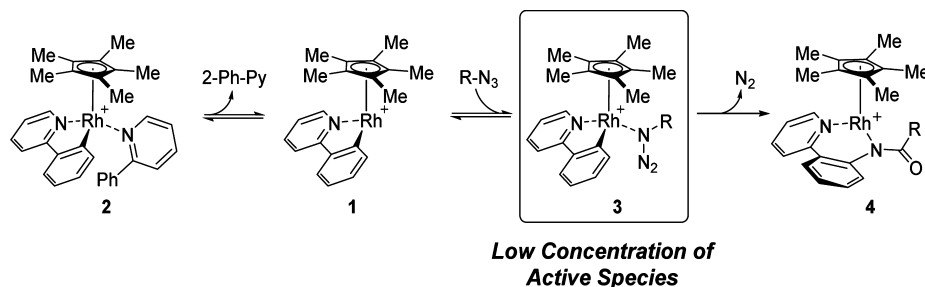
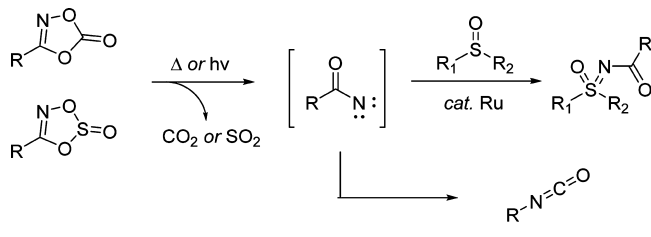
metal complex is present in the resting state **2**. This result led us to reason that one factor directly related to the reactivity is a coordination competition between substrate and azide to a metal center, and the facile generation of an azide-bound rhodacycle **3** becomes crucial for the efficient C–H amination (Scheme 4).

Finding a New Amino Source with Higher Affinity: 1,4,2-Dioxazol-5-one. We started to search for a different type of amino source with strong coordination ability, thus eventually leading to an efficient catalytic C–H amination reaction. In this research program, one class of dioxazole compounds especially caught our attention. In 1960s, Sauer and Meyer showed that *N*-acyl nitrenes can be generated from 1,4,2-dioxazol-5-one, 1,4,2-dioxazol-5-thione, and 1,3,2,4-dioxathiazole-2-oxide.¹⁰ Similar to acyl azides, those compounds undergo thermal or photo-initiated decomposition leading to *N*-acyl nitrenes (Scheme 5).^{10,11}

Recently, Bolm and co-workers elegantly demonstrated the synthetic utility of 1,4,2-dioxazol-5-ones for the synthesis of *N*-acyl sulfimides and sulfoximides via a light-induced catalytic method, in which a ruthenium *N*-acyl nitrene was proposed as a key intermediate.¹² Dubé also employed 1,4,2-dioxazol-5-ones as a safe alternative to acyl azides for the synthesis of isocyanates.¹³ On the basis of our previous development of the *Rh*(III)-catalyzed C–H amination using organic azides,⁶ we envisioned that dioxazoles could also be a good candidate as another type of efficient nitrene sources. Considering the observation by Ellman⁹ and Shi¹⁴ that imines displayed comparable binding ability with 2-phenylpyridine, we anticipated that dioxazoles would have stronger affinity than acyl azides, again contributing to the increase of amination efficiency.

To validate our working hypothesis, three different types of dioxazoles were examined along with benzoyl azide (Table 1). Initial tests were conducted with a cationic *Rh*(III) catalytic system generated *in situ* from [Cp**RhCl*]₂ and AgNTf₂. Benzoyl azide (**5a**) and 3-phenyl-5,5-dimethyl-1,4,2-dioxazole (**8a**) gave no detectable product at room temperature (entries 1–2). The latter, however, started to display reasonable

Scheme 4. Coordination Equilibrium of Cp*Rh(III) with 2-Phenylpyridine and Azide

Scheme 5. *N*-Acyl Nitrenes from Dioxazoles

reactivity upon heating (14% at 80 °C and 75% at 100 °C) (entries 3–4). We were pleased to observe that while 3-phenyl-1,4,2-dioxazol-5-thione (**8b**) exhibited satisfactory reactivity at ambient temperatures (entries 5–6), an amidation with its carbonyl analogue 3-phenyl-1,4,2-dioxazol-5-one (**8c**) was quantitative even at room temperature (entry 7).

As a result, this amidating reagent **8c** was chosen for further optimization studies. It should be mentioned that 1,4,2-dioxazol-5-ones can easily be prepared from the corresponding hydroxamic acids, and they can be stable to store and convenient to use without a special precaution.^{10–13} A

replacement of a counteranion of NTf_2^- by SbF_6^- or the use of a pregenerated cationic rhodium catalyst did not deteriorate the catalytic efficiency (entries 8–9). Significantly, the product yield was still well maintained at 40 °C even with 0.5 mol % of catalyst loading (entries 10–12). In a stark contrast, other catalytic systems such as $[\text{Ru}(p\text{-cymene})\text{Cl}_2]_2$ and $[\text{Cp}^*\text{IrCl}_2]_2$, previously shown to be effective on the direct C–H amidation in our studies,⁷ were not effective for the present amidation using 3-phenyl-1,4,2-dioxazol-5-one (**8c**) as an amidating reagent (entries 13–16).

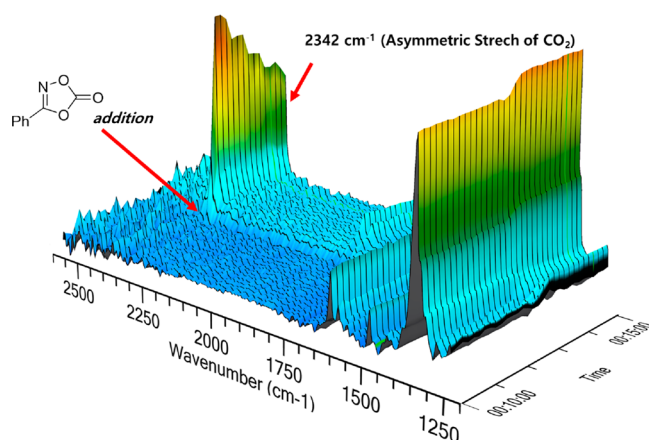
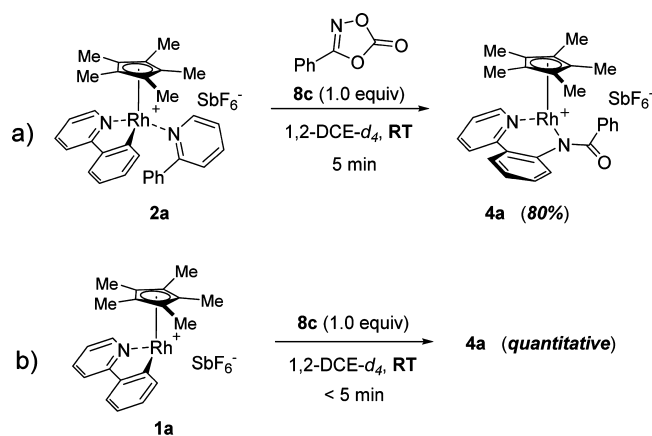
Origin of High Reactivity. To understand the origin of high reactivity of 1,4,2-dioxazol-5-ones, we conducted a series of experimental and computational studies. At first, the stoichiometric reactions of cationic $\text{Cp}^*\text{Rh(III)}$ complexes (**1a** and **2a**) with 3-phenyl-1,4,2-dioxazol-5-one (**8c**) were examined (Scheme 6). Both of **1a** and its resting species **2a** underwent instant conversion to the amido product **4a**. We also monitored the reaction of **1a** with **8c** using a time-resolved IR spectrometer (Figure 2). A new peak appeared at 2342 cm^{-1} upon the addition of dioxazolone into a solution of **1a**, and it was assigned to be an asymmetric stretching $\text{C}=\text{O}$ bond of

Table 1. Optimization of Direct C–H Amidation with Dioxazoles^a

entry	N source	catalyst (mol %)	additive (mol %)	temp (°C)	yield (%) ^b
1	5a	$[\text{Cp}^*\text{RhCl}_2]_2$ (5)	AgNTf_2 (20)	rt	<1
2	8a	$[\text{Cp}^*\text{RhCl}_2]_2$ (5)	AgNTf_2 (20)	rt	<1
3	8a	$[\text{Cp}^*\text{RhCl}_2]_2$ (5)	AgNTf_2 (20)	80	14
4	8a	$[\text{Cp}^*\text{RhCl}_2]_2$ (5)	AgNTf_2 (20)	100	74
5	8b	$[\text{Cp}^*\text{RhCl}_2]_2$ (5)	AgNTf_2 (20)	rt	75
6	8b	$[\text{Cp}^*\text{RhCl}_2]_2$ (5)	AgNTf_2 (20)	40	80
7	8c	$[\text{Cp}^*\text{RhCl}_2]_2$ (5)	AgNTf_2 (20)	rt	99 (97)
8	8c	$[\text{Cp}^*\text{RhCl}_2]_2$ (5)	AgSbF_6 (20)	rt	97
9	8c	$[\text{Cp}^*\text{Rh}(\text{MeCN})_3][\text{SbF}_6]_2$ (10)	–	rt	98
10	8c	$[\text{Cp}^*\text{RhCl}_2]_2$ (1)	AgNTf_2 (4)	rt	80
11	8c	$[\text{Cp}^*\text{RhCl}_2]_2$ (1)	AgNTf_2 (4)	40	99
12	8c	$[\text{Cp}^*\text{RhCl}_2]_2$ (0.5)	AgNTf_2 (2)	40	92
13	8c	$[\text{Ru}(p\text{-cymene})\text{Cl}_2]_2$ (5)	AgNTf_2 (20)	rt	<1
14	8c	$[\text{Ru}(p\text{-cymene})\text{Cl}_2]_2$ (5)	AgNTf_2 (20)	50	<1
15	8c	$[\text{Cp}^*\text{IrCl}_2]_2$ (5)	AgNTf_2 (20)	rt	4
16	8c	$[\text{Cp}^*\text{IrCl}_2]_2$ (5)	AgNTf_2 (20)	50	10

^a6 (0.20 mmol), nitrogen source **8** (0.22 mmol), catalyst, additive, and 1,2-dichloroethane (0.5 mL) at the indicated temperature. ^bNMR yields (internal standard: 1,1,2,2-tetrachloroethane, isolated yield in parentheses).

Scheme 6. Stoichiometric Reactions of 1,4,2-Dioxazol-5-one with Cp*Rh(III) Complexes

Figure 2. Time-resolved IR monitoring of a reaction of **1a** with **8c**.

released CO_2 in accordance with the precedent reports.^{15,16} The observed fast conversion of a resting species **2a** to an amido-inserted rhodacycle **4a** was in a stark contrast to the reaction of **2a** with benzoyl azide (**5a**) as shown in Figure 1, where much slower conversion was monitored. This result clearly showed that 1,4,2-dioxazol-5-one readily displaces bound 2-phenylpyridine from the resting species **2a** with much higher efficiency than benzoyl azide.

Interestingly, as benzoyl azide can react with **1a** to form **4a** via N_2 release (Scheme 3a), the same product can also be obtained from a reaction with 1,4,2-dioxazol-5-one upon release of CO_2 . To measure the reactivity difference between dioxazolone and azide in the reaction with **1a**, we performed

a direct competition reaction (Scheme 7). A cationic rhodium complex **1a** (1.0 equiv) was allowed to react with an equal mixture of dioxazolone **8c** (2.0 equiv) and deuterium-labeled d_5 -benzoyl azide **5a- d_5** (2.0 equiv) with the anticipation of tracing the origin of obtained product(s). After protonolysis, ^1H NMR analysis of the isolated product clearly showed no noticeable deuterium incorporation (**7a**:**7a- d_5** , >19:1). This result strongly suggests that the reactivity of 1,4,2-dioxazol-5-one excelled acyl azide under identical conditions.

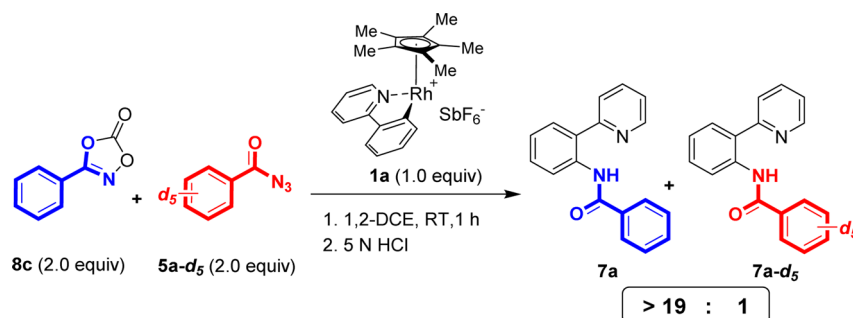
For a better understanding of the reactivity difference among amino sources, we conducted density functional theory (DFT) calculations to obtain thermodynamic parameters including Gibbs free energy for the equilibrium between a rhodacycle complex **2** (resting species bound to a substrate) and **3** (replaced by an amino precursor) employing various nitrogen sources (Table 2).^{17,18} It was seen that the replacement of 2-

Table 2. Calculated Coordination Equilibrium between 2-Phenylpyridine and Nitrogen Sources

entry	1	2	3	4
:N=X				
ΔG° (kcal/mol)	10.1	5.2	2.8	-1.2
K_{calcd}	3.7×10^{-8}	1.4×10^{-4}	8.2×10^{-3}	8.1

phenylpyridine with acetyl azide was thermodynamically least favorable among examined amino sources (entry 1). It was calculated to require 10.1 kcal/mol for this process, which will consequently yield low concentration of **3** where Y-N=X is acetyl azide ($K_{\text{calcd}} = 3.7 \times 10^{-8}$). Change of amino precursors from azide to dioxazolone or dioxathiazole resulted in significantly higher coordination propensity by the magnitude of 10^3 to 10^5 scales (entries 2 and 3, respectively), which is in a good agreement with our working hypothesis. Interestingly, in case of dioxazole (entry 4), the equilibrium lies favorably toward the replaced complex **3** ($\Delta G^\circ = -1.2$ kcal/mol). Since the subsequent migratory imido insertion of an isolated

Scheme 7. Competitive C–N Bond Formation between 1,4,2-Dioxazol-5-one and Acyl Azide



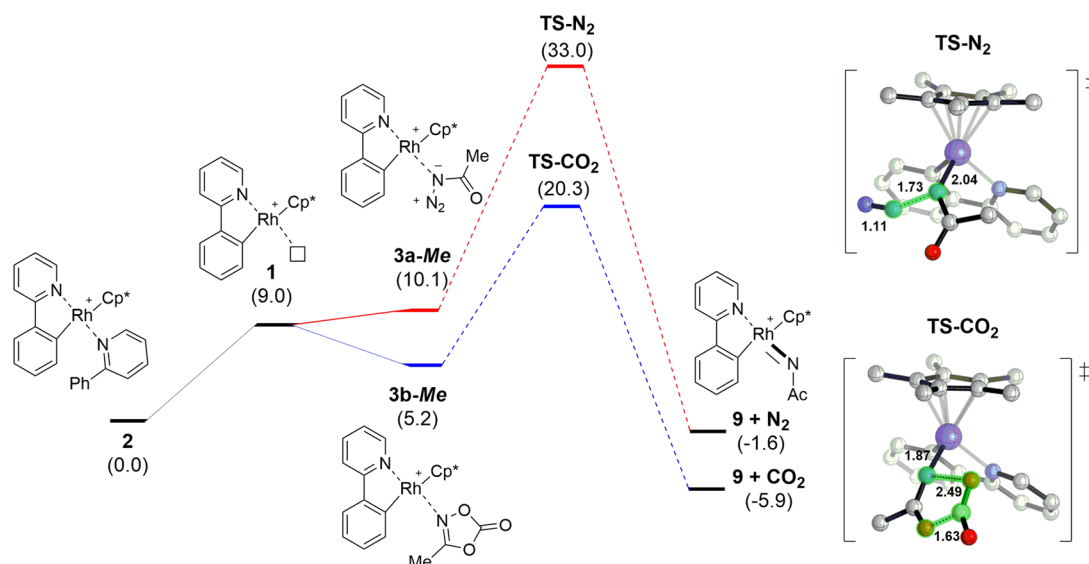


Figure 3. Potential energy surfaces for the formation of Rh-nitrenoid from a resting species **2** with azide or 1,4,2-dioxazol-5-one (see Supporting Information for details).

complex **3** ($Y-N=X$: 3-phenyl-5,5-dimethyl-1,4,2-dioxazole) did not occur at room temperature, we were able to obtain experimentally the equilibrium constant with 3-phenyl-5,5-dimethyl-1,4,2-dioxazole (**8c**) ($K_{exp} = 6.3$), which is within the range of the calculated number ($K_{cal}^{\circ} = 8.1$, entry 4).¹⁹

Extended calculations on the postulated subsequent metal-nitrenoid formation were also performed using acyl azide and 1,4,2-dioxazol-5-one as the amino sources (Figure 3). It revealed that ΔG^{\ddagger} in the formation of a rhodacyclic nitrene species (**9**) by a reaction of **2** with 1,4,2-dioxazol-5-one (CO_2 release) was lower by 12.7 kcal/mol than that with acyl azide (N_2 release): 20.3 and 33.0 kcal/mol, respectively. We reasoned this difference may be reflected in the reaction efficiency observed experimentally (Scheme 3 and Scheme 6). As a result, the high reactivity of 1,4,2-dioxazol-5-one as an amino source can be attributed to two synergistic effects: facilitation of the nitrenoid formation as well as more favorable replacement of a substrate in a resting species (shown in Table 2).

Isolation and Characterization of a Rhodacycle Bound to an Amino Source (3). Whereas mechanistic details on the C–H bond activation process have been well studied, experimental investigations on the C–N bond-forming step are still less explored mainly due to the highly labile nature of plausible intermediates.²⁰ In this line, while we recently cleared the mist in the direct C–H amidation reactions utilizing organic azides as the amino source,^{6b} there are still some issues remained unanswered, representatively the characterization of key intermediates. In fact, while several catalytic systems have been developed for the C–H amination, only a few examples are known reporting the isolation or identification of nitrogen-containing critical intermediates in the amido transfer process.^{21,22} In our case of using azide precursors, the immediate conversion of substrates to amido products under the developed amination conditions hampered an intermediate study.

Hinted by the favorable equilibrium shift toward the dioxazole-bound rhodacycle (Table 2, entry 4), we tried to obtain the anticipated intermediate. We were delighted to isolate indeed the desired intermediate **3c**, an adduct of a rhodacycle **1a** and 3-phenyl-5,5-dimethyl-1,4,2-dioxazole **8a**. As

expected, an X-ray crystallographic analysis clearly showed the coordination of a nitrogen atom to the rhodium center (Figure 4). The bond length of rhodium-dioxazole ($Rh1-N2$, 2.122 Å)

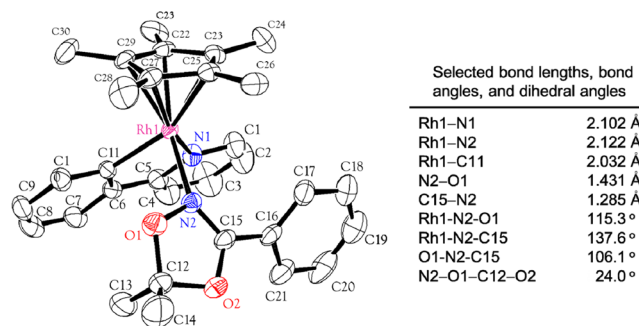
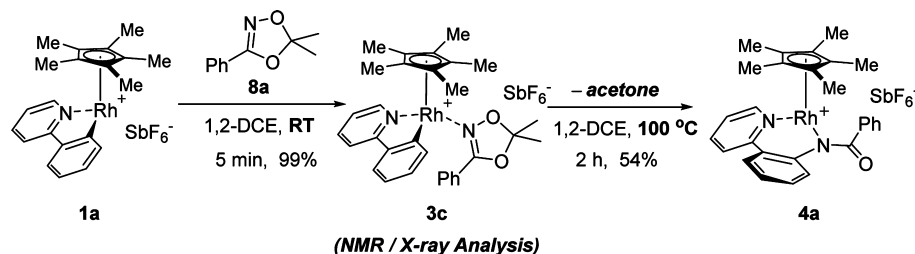
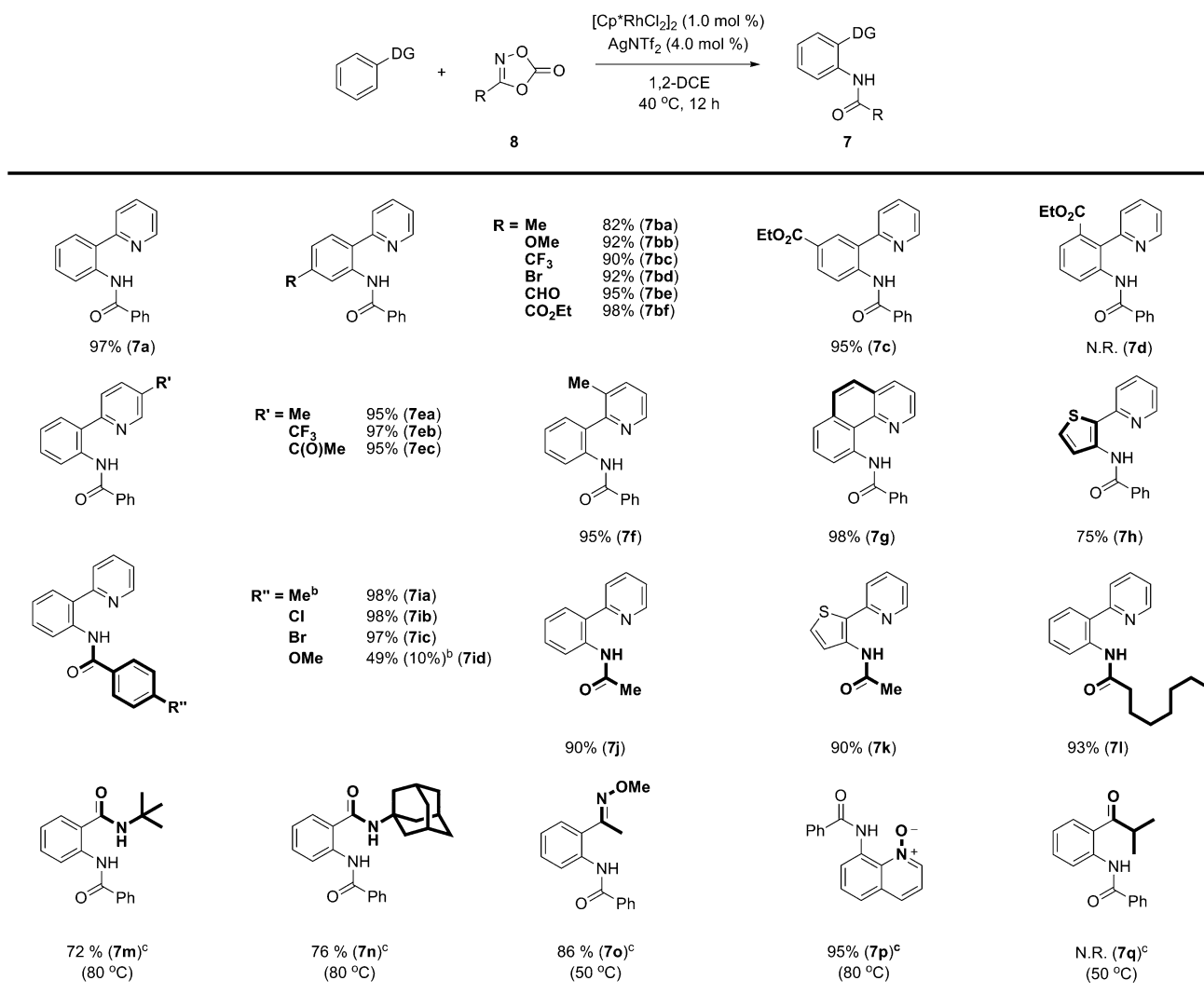


Figure 4. ORTEP of **3c** with selected bond lengths and angles. Thermal ellipsoid depicted at the 50% probability level. Hydrogen atoms and SbF_6^- anion are omitted for clarity.

is similar to that of rhodium-pyridyl nitrogen ($Rh1-N1$, 2.102 Å). Again, this result proved our working hypothesis that dioxazole derivatives would have a strong binding affinity. More pleasingly, this isolated species was observed to undergo an imido insertion smoothly at 100 °C to furnish the corresponding amido rhodacycle **4a** in 54% after 2 h. In this transformation, not surprisingly, acetone was observed to discharge by a NMR analysis (Scheme 8).

Synthetic Scope. With the optimized amidation condition in hand (Table 1 and also see the Supporting Information for screening additional reaction parameters), the scope of substrates was finally scrutinized (Scheme 9). The reaction occurred smoothly under mild conditions at 40 °C within 12 h by employing the dimeric rhodium catalyst in 1 mol % together with 4 mol % of $AgNTf_2$ in most cases. With 2-phenylpyridine derivatives, regardless of electronic and/or steric variations, excellent amidation efficiency was obtained (**7a–g**). Alteration on either phenyl or pyridyl ring did not degrade the catalytic activity. However, a substrate bearing an *ortho*-ester substituent in phenyl side was ineffective under the present conditions (**7d**). Functional group tolerance was found to be excellent, and

Scheme 8. Stepwise C–N Bond Formation

Scheme 9. Substrate Scope of C–H Amidations^a

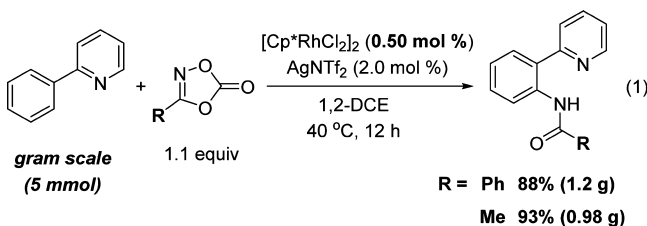
^aSubstrate (0.20 mmol) and **7** (0.22 mmol) in 1,2-dichloroethane (0.5 mL), otherwise indicated: isolated yields. ^bC–C amidation product (10%) was formed. ^c[Cp*RhCl₂]₂ (5.0 mol %) and AgNTf₂ (20 mol %) were applied.

a wide range of potentially chelating groups such as ester (**7bf** and **7c**), ketone (**7ec**), and aldehyde (**7be**) did not affect the reaction progress. The amidation of benzo[*h*]quinoline was almost quantitative (**7g**) and that on a heterocycle was also facile (**7h** and **7k**). A variation on the amidating reagent, 1,4,2-dioxazol-5-one, was subsequently examined. Whereas substituents at the phenyl moiety with electronically neutral or deficient property did not affect the excellent amidation efficiency (**7ia–ic**), a reaction with 1,4,2-dioxazol-5-one having 4-methoxyphenyl substituent was sluggish (**7id**, 49%) with a

contaminant C–C amidated side product (10%).^{7g} The introduction of alkyl *N*-acyl amide group is of special interest considering the fact that alkyl acyl azides, an alternative amidating reagent for giving rise to the same products by our previously developed procedures,^{7c} are less convenient to employ in that they are prone to rearrange into the corresponding isocyanates.^{7g} In addition, alkyl acyl azides of low molecular weight often cause a safety issue.^{13,23} In this regard, we envisioned that 1,4,2-dioxazol-5-one derivatives could be viewed as a more convenient and safer alternative to

the acyl azides. We were pleased to observe that a number of 1,4,2-dioxazol-5-ones having alkyl substituents at the 3-position were highly facile to afford alkyl amidated products in excellent yields (7j–l). An additional array of modified directing groups was also investigated to find out that amide (7m–n), ketoxime (7o), and *N*-oxide (7p) worked well albeit under slightly more demanding conditions. However, ketone, a weakly coordinating directing group, was not effective (7q).

The present arene C–H amidation with 1,4,2-dioxazol-5-ones was highly efficient under mild conditions to allow for a facile performance even in a large scale (eq 1). For instance, the



installation of acetamido and benzamido into 2-phenylpyridine could be conducted in a gram scale with excellent product yields (7a and 7j, respectively) with low catalyst loading (0.5 mol %).

CONCLUSIONS

We have described herein the development of a robust direct C–H amidation using a new type of amidating reagent. Stepwise analysis on the Cp*Rh(III)-catalyzed C–H amidation showed that competitive binding of rhodium metal center to amidating reagent or substrate is closely related to the reaction efficiency. In this line, 1,4,2-dioxazol-5-ones with a strong affinity could be employed as a new amidating reagent, thus resulting in excellent amidation efficiency. Experimental and computational works proved that the combination of the strong coordination ability of 1,4,2-dioxazol-5-ones and low activation energy of an imido insertion process is attributed to the origin of high reactivity. In addition, isolation and characterization of a cationic Cp*Rh(III) complex bearing an amino source were realized. The understanding of coordination propensity of metal center and nitrogen sources and the observation of its turnover to an amido inserted rhodacycle allowed a clear picture on the C–H amination process. The newly developed Cp*Rh(III)-catalyzed reaction with 1,4,2-dioxazol-5-ones was found to be highly efficient over a broad range of substrates with high functional group tolerance releasing carbon dioxide as a single byproduct. Additional attractive features of this amino source such that they are more convenient to prepare, store, and use when compared to the corresponding azides will make a step closer toward an ideal C–H amination protocol.

ASSOCIATED CONTENT

Supporting Information

Detailed experimental procedure and characterization of new compounds, Cartesian coordinates of computed structures, and X-ray analysis. This material is available free of charge via the Internet at <http://pubs.acs.org>.

AUTHOR INFORMATION

Corresponding Authors

*jeunggonkim@kaist.ac.kr

*sbchang@kaist.ac.kr

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank Dr. Sung-Woo Park, Dr. Jaesung Kwak, and Mr. Kwangmin Shin (Institute for Basic Science, Korea) for valuable discussions and Ms. Seohee Oh (KAIST) for XRD analysis. Y.P. is a recipient of Kwanjeong Educational Foundation scholarship. This research was supported by the Institute for Basic Science (IBS-R010-D1) in Korea.

REFERENCES

- (1) (a) *Amino Group Chemistry, From Synthesis to the Life Science*; Ricci, A., Ed.; Wiley-VCH; Weinheim, 2008. (b) Candeias, N. R.; Branco, L. C.; Gois, P. M. P.; Afonso, C. A. M.; Trindade, A. F. *Chem. Rev.* **2009**, *109*, 2703. (c) Hili, R.; Yudin, A. K. *Nat. Chem. Biol.* **2006**, *2*, 284.
- (2) (a) Ullmann, F. *Ber. Dtsch. Chem. Ges.* **1903**, *36*, 2382. (b) Monnier, F.; Taillefer, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 6954. (c) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054. (d) Paul, F.; Patt, J.; Hartwig, J. F. *J. Am. Chem. Soc.* **1994**, *116*, 5969. (e) Hartwig, J. F. *Acc. Chem. Res.* **2008**, *41*, 1534. (f) Guram, A. S.; Buchwald, S. L. *J. Am. Chem. Soc.* **1994**, *116*, 7901. (g) Surry, D. S.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2008**, *47*, 6338.
- (3) Selected reviews on C–H aminations: (a) Collet, F.; Dodd, R. H.; Dauban, P. *Chem. Commun.* **2009**, 5061. (b) Collet, F.; Lescot, C.; Dauban, P. *Chem. Soc. Rev.* **2011**, *40*, 1926. (c) Jeffrey, J. L.; Sarpong, R. *Chem. Sci.* **2013**, *4*, 4092. (d) Ramirez, T. A.; Zhao, B.; Shi, Y. *Chem. Soc. Rev.* **2012**, *41*, 931. (e) Armstrong, A.; Collins, J. C. *Angew. Chem., Int. Ed.* **2010**, *49*, 2282. (f) Louillat, M.-L.; Patureau, F. W. *Chem. Soc. Rev.* **2014**, *43*, 901. (g) Mahy, J.-P.; Ciesielski, J.; Dauban, P. *Angew. Chem., Int. Ed.* **2014**, *53*, 6862.
- (4) Selected reviews on C–H activations: (a) Labinger, J. A.; Bercaw, J. E. *Nature* **2002**, *417*, 507. (b) Fagnou, K.; Lautens, M. *Chem. Rev.* **2003**, *103*, 169. (c) Bergman, R. G. *Nature* **2007**, *446*, 391. (d) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173. (e) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335. (f) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (g) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Commun.* **2010**, *46*, 677. (h) Daugulis, O. *Top. Curr. Chem.* **2010**, *292*, 57. (i) Yeung, C. S.; Dong, V. M. *Chem. Rev.* **2011**, *111*, 1215. (j) McMurray, L.; O'Hara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885. (k) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (l) White, M. C. *Science* **2012**, *335*, 807. (m) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879. (n) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651. (o) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788. (p) Hartwig, J. F. *Acc. Chem. Res.* **2012**, *45*, 864. (q) Neufeldt, S. R.; Sanford, M. S. *Acc. Chem. Res.* **2012**, *45*, 936. (r) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. *Angew. Chem., Int. Ed.* **2012**, *51*, 8960. (s) Kuhl, N.; Hopkinson, M. N.; Wencel-Delord, J.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 10236. (t) Rouquet, G.; Chatani, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 11726. (u) Pan, S.; Shibata, T. *ACS Catal.* **2013**, *3*, 704. (v) Kuhl, N.; Schröder, N.; Glorius, F. *Adv. Synth. Catal.* **2014**, *356*, 1443. (w) Davies, H. M. L.; Morton, D. *Chem. Soc. Rev.* **2011**, *40*, 1857. (x) Newhouse, T.; Baran, P. S. *Angew. Chem., Int. Ed.* **2011**, *50*, 3362.
- (5) (a) Breslow, R.; Gellman, S. H. *J. Chem. Soc., Chem. Comm.* **1982**, 1400. (b) Breslow, R.; Gellman, S. H. *J. Am. Chem. Soc.* **1983**, *105*, 6728. (c) Svastits, E. W.; Dawson, J. H.; Breslow, R.; Gellman, S. H. *J. Am. Chem. Soc.* **1985**, *107*, 6427.
- (6) (a) Kim, J. Y.; Park, S. H.; Ryu, J.; Cho, S. H.; Kim, S. H.; Chang, S. *J. Am. Chem. Soc.* **2012**, *134*, 9110. (b) Park, S. H.; Kwak, J.; Shin, K.; Ryu, J.; Park, Y.; Chang, S. *J. Am. Chem. Soc.* **2014**, *136*, 2492.
- (7) (a) Ryu, J.; Shin, K.; Park, S. H.; Kim, J. Y.; Chang, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 9904. (b) Kim, J.; Kim, J.; Chang, S. *Chem.–Eur. J.* **2013**, *19*, 7328. (c) Ryu, J.; Kwak, J.; Shin, K.; Lee, D.; Chang, S. *J. Am. Chem. Soc.* **2013**, *135*, 12861. (d) Shin, K.; Baek, Y.; Chang, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 8031. (e) Kim, J.; Chang, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 8031.

- Chem., Int. Ed.* **2014**, *53*, 2203. (f) Hwang, H.; Kim, J.; Jeong, J.; Chang, S. *J. Am. Chem. Soc.* **2014**, *136*, 10770. (g) Shin, K.; Ryu, J.; Chang, S. *Org. Lett.* **2014**, *16*, 2010. (h) Lee, D.; Kim, Y.; Chang, S. *J. Org. Chem.* **2013**, *78*, 11102. (i) Kang, T.; Kim, Y.; Lee, D.; Wang, Z.; Chang, S. *J. Am. Chem. Soc.* **2014**, *136*, 4141. (j) Kang, T.; Kim, H.; Kim, J. G.; Chang, S. *Chem. Commun.* **2014**, *50*, 12073. (k) Shin, K.; Chang, S. *J. Org. Chem.* **2014**, *79*, 12197. (l) Kim, H.; Park, J.; Kim, J. G.; Chang, S. *Org. Lett.* **2014**, *16*, 5466. (m) Gwon, D.; Lee, D.; Kim, J.; Park, S.; Chang, S. *Chem.–Eur. J.* **2014**, *20*, 12421. (n) Figg, T. M.; Park, S.; Park, J.; Chang, S.; Musaev, D. G. *Organometallics* **2014**, *33*, 4076.
- (8) (a) Hou, W.; Yang, Y.; Ai, W.; Wu, Y.; Wang, X.; Zhou, B.; Li, Y. *Eur. J. Org. Chem.* **2015**, 395. (b) Shin, Y.; Han, S.; De, U.; Park, J.; Sharma, S.; Mishra, N. K.; Lee, E.-K.; Lee, Y.; Kim, H. S.; Kim, I. S. *J. Org. Chem.* **2014**, *79*, 9262. (c) Pan, C.; Jin, N.; Zhang, H.; Han, J.; Zhu, C. *J. Org. Chem.* **2014**, *79*, 9427. (d) Peng, J.; Xie, Z.; Chen, M.; Wang, J.; Zhu, Q. *Org. Lett.* **2014**, *16*, 4702. (e) Zhou, X.; Luo, P.; Long, L.; Ouyang, M.; Sang, X.; Ding, Q. *Tetrahedron* **2014**, *70*, 6742. (f) Ryu, T.; Min, J.; Choi, W.; Jeon, W. H.; Lee, P. H. *Org. Lett.* **2014**, *16*, 2810. (g) Wang, N.; Li, R.; Li, L.; Xu, S.; Song, H.; Wang, B. *J. Org. Chem.* **2014**, *79*, 5379. (h) Sun, B.; Yoshino, T.; Matsunaga, S.; Kanai, M. *Adv. Synth. Catal.* **2014**, *356*, 1491. (i) Jia, X.; Han, J. *J. Org. Chem.* **2014**, *79*, 4180. (j) Pan, C.; Abdulkader, A.; Han, J.; Cheng, Y.; Zhu, C. *Chem.–Eur. J.* **2014**, *20*, 3606. (k) Yadav, M. R.; Rit, R. K.; Sahoo, A. K. *Org. Lett.* **2013**, *15*, 1638. (l) Bhanuchandra, M.; Yadav, M. R.; Rit, R. K.; Kuram, M. R.; Sahoo, A. K. *Chem. Commun.* **2013**, *49*, 5225. (m) Zheng, Q.-Z.; Liang, Y.-F.; Qin, C.; Jiao, N. *Chem. Commun.* **2013**, *49*, 5654. (n) Yu, D.-G.; Suri, M.; Glorius, F. *J. Am. Chem. Soc.* **2013**, *135*, 8802.
- (9) (a) Tsai, A. S.; Tauchert, M. E.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2011**, *133*, 1248. (b) Tauchert, M. E.; Incarvito, C. D.; Rheingold, A. L.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2012**, *134*, 1482.
- (10) (a) Sauer, J.; Mayer, K. K. *Tetrahedron Lett.* **1968**, *9*, 319. (b) Sauer, J.; Mayer, K. K. *Tetrahedron Lett.* **1968**, *9*, 325. (c) Eibler, E.; Sauer, J. *Tetrahedron Lett.* **1974**, *15*, 2565. (d) Eibler, E.; Käsbauer, J.; Pohl, H.; Sauer, J. *Tetrahedron Lett.* **1987**, *28*, 1097.
- (11) (a) Middleton, W. J. *J. Org. Chem.* **1983**, *48*, 3845. (b) Zhong, C. L.; Tang, B. Y.; Yin, P.; Chen, Y.; He, L. *J. Org. Chem.* **2012**, *77*, 4271.
- (12) (a) Bizet, V.; Buglioni, L.; Bolm, C. *Angew. Chem., Int. Ed.* **2014**, *53*, 5639. (b) Boglioni, L.; Bizet, V.; Bolm, C. *Adv. Synth. Catal.* **2014**, *356*, 2209.
- (13) Dubé, P.; Nathel, N. F. F.; Vetelino, M.; Couturier, M.; Aboussafy, C. L.; Pichette, S.; Jorgensen, M. L.; Hardink, M. *Org. Lett.* **2009**, *11*, 5622.
- (14) (a) Li, Y.; Li, B.-J.; Wang, W.-H.; Huang, W.-P.; Zhang, X.-S.; Chen, K.; Shi, Z.-J. *Angew. Chem., Int. Ed.* **2011**, *50*, 2115. (b) Li, Y.; Zhang, X.-S.; Li, H.; Wang, W.-H.; Chen, K.; Li, B.-J.; Shi, Z.-J. *Chem. Sci.* **2012**, *3*, 1634.
- (15) Stevens, R. W., Jr.; Chuang, S. S. C. *J. Phys. Chem. B* **2004**, *108*, 696.
- (16) IR measurement of CO₂, dissolved in 1,2-DCE, showed a peak at 2342 cm⁻¹; see Supporting Information for details.
- (17) Selected examples of computed equilibrium constants analysis: (a) Zhao, Y.-L.; Bartberger, M. D.; Goto, K.; Shimada, K.; Kawashima, T.; Houk, K. N. *J. Am. Chem. Soc.* **2005**, *127*, 7964. (b) Schmidt, Y.; Lam, J. K.; Pham, H. V.; Houk, K. N.; Vanderwal, C. D. *J. Am. Chem. Soc.* **2013**, *135*, 7339. (c) Gómez-Bombarelli, R.; González-Pérez, M.; Pérez-Prior, M. T.; Calle, E.; Casado, J. *J. Phys. Chem. A* **2009**, *113*, 11423. (d) Guthrie, J. P.; Povar, I. *J. Phys. Org. Chem.* **2013**, *26*, 1077.
- (18) Computational equilibrium constants for the given reaction can be calculated by substituting the differences of standard Gibbs energy differences for equilibrium constant–Free energy relationship, $\Delta G^\circ = -RT \ln K^\circ$.
- (19) An experimental equilibrium constant was measured by mixing **2a** and 3-phenyl-5,5-dimethyl-1,4,2-dioxazole with ¹H NMR spectrometer; see the Supporting Information for details.
- (20) (a) Zhang, L.-L.; Li, L.-H.; Wang, Y.-Q.; Yang, Y.-F.; Liu, X.-Y.; Liang, Y.-M. *Organometallics* **2014**, *33*, 1905. (b) Dick, A. R.; Remy, M. S.; Kampf, J. W.; Sanford, M. S. *Organometallics* **2007**, *26*, 1365. (c) Ke, Z.; Cundari, T. R. *Organometallics* **2010**, *29*, 821. (d) Sau, Y.-K.; Yi, X.-Y.; Chan, K.-W.; Lai, C.-S.; Williams, I. D.; Leung, W.-H. *J. Organomet. Chem.* **2010**, *695*, 1399.
- (21) Kim, H.; Shin, K.; Chang, S. *J. Am. Chem. Soc.* **2014**, *136*, 5904.
- (22) Turlington, C. R.; White, P. S.; Brookhart, M.; Templeton, J. L. *J. Am. Chem. Soc.* **2014**, *136*, 3981.
- (23) Azide of low molecular weight (more than 25% nitrogen content) should be handled as a solution below 10%. *Bretherick's Handbook of Reactive Chemical Hazards*; Urben, P. G., Ed.; Butterworth-Heinemann Ltd.: Oxford, 1999.