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Rhodium-Catalyzed Selective Mono- and Diamination of Arenes with Single Directing Site "On Water"

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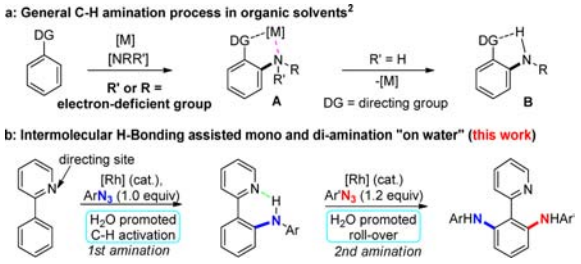
Supporting Information

ABSTRACT: A Rh(III)-catalyzed selective C−H amination of 2-phenylpyridine derivatives is reported. With pyridine as a directing group, the reaction has high mono- or diamination selectivity, and a wide range of effective substrates, including electron-deficient and -rich aryl azides. Water helps to promote C−H activation, and the concept of a water promoted rollover mechanism is postulated for the diamination step. The reactions were conducted using a Schlenk flask and proceeded smoothly "on water" under atmospheric conditions with nitrogen gas as the only byproduct.

Transition-metal catalyzed C−H amination is one of the most powerful and facile methods to construct amine derivatives, which have great potential applications in synthetic organic and medicinal chemistry.[1−3] A major advantage of such methods is the absence of a requirement for prefunctionalized starting materials. This allows simplification and abbreviation of synthetic procedures. Among these methods, C−H activation directed by functional groups has been successfully developed by Sukbok Chang and others with an appropriate combination of metal catalysts and chelate groups.[2,4] Although having many benefits, these reported protocols suffer from a selective and diminished substrate scope. For example, the reactions work well with electron-deficient nitrene sources because it helps to dissociate the catalyst from the product by reducing the coordination ability of a newly formed amino group (Intermediate **A**, Scheme 1a). The coordination ability of the directing group (DG) is lost because of intramolecular H-bonding if the formed products are secondary amines (Structure **B**, Scheme 1a); thus, only monoaminated products are formed for most substrates bearing conventional chelating groups even though excess equivalents of sources of amino groups are used.[5] These phenomena become more critical when two different amino groups need to be introduced while only one directing group is present. Therefore, a general and efficient method with a broad substrate scope, versatility in selectivity, and freedom from the aforementioned drawback is still needed.

Scheme 1. Metal Catalyzed Functional Group Directed C−H Amination



Water is inexpensive, nonpolluting, and nontoxic and can be handled safely compared to organic solvents.[6] It plays a critical role in biological and other systems due in part to its multiple H-bonding capabilities.[7] Due to the low stability of metal catalysts and ligands in water, direct metal catalyzed C−H amination in or on water has been developed minimally[8] although C−H functionalization in/on water has significant importance.[9] We recently reported mono-C−H amidation "on water" with *tert*-butyl 2,4-dinitrophenoxycarbamate as an electron-deficient nitrene source,[8] and Jones reported the "rollover" metalation of bipyridine rings of rhodium complexes through C−H activation with water as solvent.[10] Inspired by these studies,[8,10] we herein report water promoted rhodium-catalyzed direct amination of arenes with a variety of aryl azides having both electron-donating and -withdrawing substituents (Scheme 1b). As the starting materials, catalyst, and additive are not particularly soluble in water, the reactions are conducted "on water".[11] Another exciting and important part of this investigation is diamination. The diamination, recently reported by Chang et al., is achieved by rollover assisted by intramolecular H-bonding which provides access to another C−H bond for catalytic amination. A limited amount of azide is used for selective mono-C−H amination and an excess amount of azide for the secondary C−H amination step and a carefully designed purine as the directing group.[5] Our method however works well with a stoichiometric amount of aryl azide in both the first and second amination reactions using pyridine as a directing group. Therefore, we postulate a water promoted rollover mechanism

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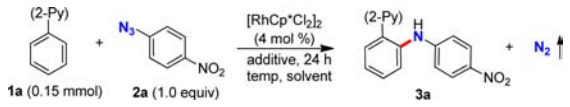
through intermolecular H-bonding, which can provide access to another C−H bond for amination.

Azides have unique advantages in C−H aminations, including ready availability, generation of N_2 gas as the sole byproduct, and neutral reaction conditions without additional oxidative or basic reagents.[2a,12,13] Therefore, we have conducted our investigation with 2-phenylpyridine (**1a**) and 1-azido-4-nitrobenzene (**2a**) in the presence of $[RhCp^*Cl_2]_2$ and other additives listed in Table 1. Extensive screening of the reaction conditions revealed that

Table 1. Optimization of Reaction Conditions



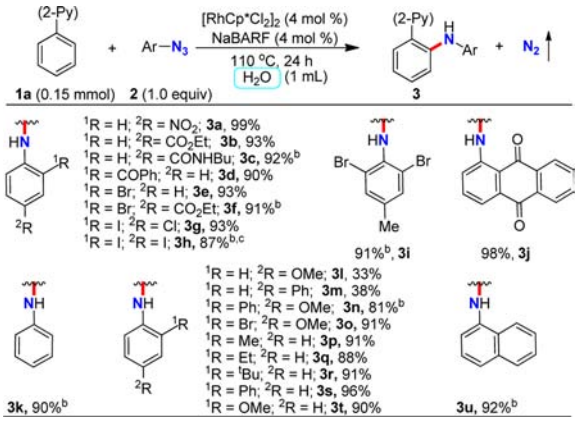
entry	additive (mol %)	solvent	temp (°C)	yield[a] (%)
1	$AgSbF_6$ (16)	H_2O	80	50
2	none	H_2O	80	2
3	$AgCO_3$ (16)	H_2O	80	11
4	$AgBF_4$ (16)	H_2O	80	88
5	NaBARF (16)	H_2O	80	95
6	NaBARF (4)	H_2O	80	90
7	NaBARF (16)	H_2O	110	99
8	**NaBARF (4)**	**H_2O**	**110**	**99**
9[b]	NaBARF (2)	H_2O	110	74
10[c]	NaBARF (4)	H_2O	110	80
11[d]	**NaBARF (4)**	**organic solvents**	**110**	**<10**
12	NaBARF (4)	neat	110	<5

[a]Yield was detected by crude NMR. [b]$[RhCp^*Cl_2]_2$ (2 mol %) was used. [c]For 12 h. [d]DCE, dioxane, THF, toluene, DMF, DMSO, hexane, or isopropanol was used as solvent.

use of 4 mol % of $[RhCp^*Cl_2]_2$ along with 4 mol % of NaBARF [sodium tetrakis(3,5-bis(trifluoromethyl)phenyl)borate] at 110 °C provides essentially quantitative conversion (entry 8). Addition of silver salts can increase the yield up to 88% (entries 1, 3, and 4), and organic solvents or neat conditions that were investigated failed to give acceptable yields (entries 11, 12).

With these optimized reaction conditions, we explored the substrate scope with substituted aryl azides (Scheme 2). As anticipated, various electron-deficient aryl azides, including sterically hindered 2-azido-1,3-dibromo-5-methylbenzene and the electron-deficient 1-azidoanthracene-9,10-dione work well

Scheme 2. Substrate Scope of Arylazides[a]



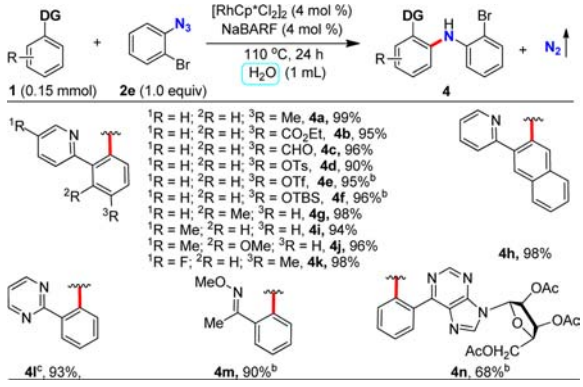
[a]Isolated yields. [b]For 48 h. [c]95% purity of azide.

resulting in high yields of the corresponding diaryl amines (**3a**−**j**). Although aryl azide lacking substituents in the aryl ring provided the desired product in high yield (**3k**), the reaction became sluggish when azides containing electron-rich functional groups at the *para* position were used (**3l**, **3m**). This possibly results from deactivation of the catalyst due to the strong coordination of the electron-rich amino group in the products as was mentioned in Scheme 1a. Fortunately, electron-rich azides containing functional groups at the *ortho* position give good yields (**3n**−**t**), presumably because steric hindrance at the *ortho* position facilitates the release of the catalyst from the products. Similarly, the highly sterically hindered aryl azide was also reacted efficiently (**3r**). 1-Azidonaphthalene can also be used as an efficient amino source (**3u**), and various functional groups, such as NO_2, CO_2Et, CONHBu, COPh, Br, and OMe, are well tolerated.

To confirm that the electron-rich products deactivate the catalyst, we performed the reactions of 2-phenylpyridine (**1a**) with ethyl 4-azidobenzoate in the presence of electron-deficient *N*-(4-nitrophenyl)-2-(pyridin-2-yl)aniline (**3a**, 0.4 equiv) or electron-rich *N*-(4-methoxyphenyl)-2-(pyridin-2-yl)aniline (**3l**, 0.4 equiv) (eqs S1, S2 in Supporting Information (SI)). The reaction with **3a** produced 62% of the product (**3b**) whereas reaction with **3l** gave only 6% of the desired product (**3b**) which supports the assumption. Interestingly, we have also found that the electron-rich azides (4-methoxyphenyl azide or 2-methoxyphenyl azide) react faster than an electron-deficient azide (4-nitrophenyl azide) in the intermolecular competitive reactions (eqs S3, S4 in SI).

We performed the reactions of substituted 2-arylpyridines and substrates with directing groups other than pyridine (Scheme 3).

Scheme 3. Substrate Scope of 2-Phenylpyridine Derivatives[a]



[a]Isolated yield. [b]For 48 h. [c]With *p*-NO_2PhN_3 instead of **2e**.

2-Phenylpyridines (**1**) with substituents on the arene ring work well, providing the desired products (**4a**−**h**) in excellent yield, irrespective of the electronic nature of the substituents. Transformable functional groups such as ester, aldehyde, OTs, OTf, and OTBS are well tolerated (**4b**−**f**). Substrates with substituents on both the arene and the pyridine rings also underwent reactions with 2-bromophenyl azide (**2e**) resulting in >90% yield of the desired aminated products (**4j**−**k**). Other directing groups such as pyrimidine, *O*-methyl oxime, and nucleoside[14] derivatives react under the same conditions leading to high yields of corresponding products (**4l**−**n**).

We examined whether diaminations are also possible and found that, like monoaminations, diaminations also proceed well under these reaction conditions (Scheme 4). Symmetrical (**5a**)

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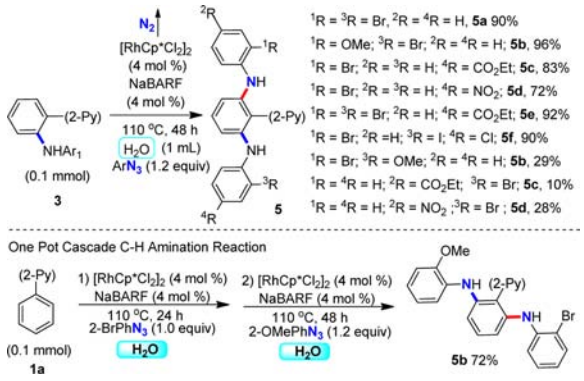
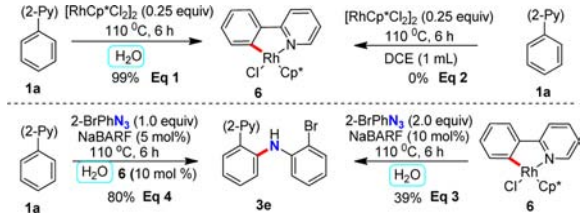
Scheme 4. Scope of Diamination



and unsymmetrical diaminated products (**5b**−**f**) could be obtained in high yields from a series of monoaminated compounds. Functional groups such as OMe, NO_2, CO_2Et, and halogens are well tolerated. We observed that electron-rich azides should be used in the second step; otherwise, the reaction provides a lower yield of the desired products (**5b**−**d**). This is because the electron-rich monoaminated compounds deactivate the catalyst as we have already observed during the monoamination reaction (eq S2). It is worthwhile to note that the two-step reaction from **1a** to **5b** can be performed in "one pot" and the desired product can still be obtained in 72% yield.

To gain insight into a possible reaction mechanism, a series of additional experiments were performed and are shown in Scheme 5 and the SI. The reactions of 2-phenylpyridine (**1a**)

Scheme 5. Preliminary Mechanistic Study

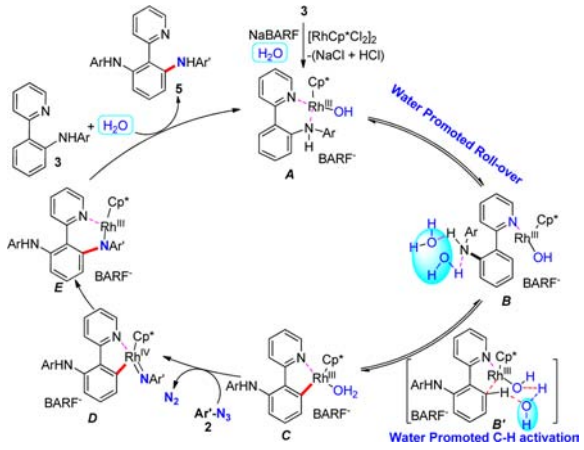


with $[RhCp^*Cl_2]_2$ were carried out in DCE and on water. On water, we obtained a 99% yield of rhodacycle **6** but in DCE no reaction was observed (eqs 1 and 2). When we treated **6** with 2-bromophenyl azide (**2e**) on water a 39% yield of the desired product was obtained (eq 3). When **6** was used as a catalyst it was found to be almost as efficient as a rhodium catalyst in the presence of NaBARF (eq 4), but in the absence of NaBARF it is inefficient (eq S5). The stoichiometric reaction gives a lower yield than the catalytic reaction because in the latter, the starting material, 2-phenylpyridine perhaps acts as a proton source and helps to release the product from the rhodium complex.[4f] We performed H/D scrambling studies. Both of the protons at the *ortho* position of **1a** were exclusively deuterated by D_2O in the presence of a rhodium catalyst within a 10 min reaction time (eq S6), implying that the C−H activation step is reversible. The same reaction in the presence of 2-bromophenyl azide provides **1a** with 27% deuterium incorporation and the desired monoaminated product **3e** with 26% deuterium incorporation (eq S7) which suggests that the C−H activation step is faster than the product formation step. Like monoamination, when we treated the monoaminated starting material **3e** with a rhodium catalyst on D_2O, almost quantitative incorporation of deuterium at the *ortho* position of **3e** was observed after 12 h of reaction time (eq S8). This observation suggests that the water promotes the necessary rollover to access the C−H bond for activation. The reaction of **3e** in the presence of 2-bromophenyl azide provides 41% of the diaminated product (**5a**) and 55% of the deuterated starting material (**3e**) (eq S9) which is also evidence for a water promoted rollover mechanism.[10]

Based on the results from stoichiometric reactions and H/D scrambling experiments we have found that the water plays at least two critical roles in this reaction. First, it helps to form the intermediate rhodacycle (**6**) which is an active intermediate in these reactions.[15] The dangling hydroxyl groups[16] present on the hydrophobic interfaces help to abstract a proton giving access to the desired rhodacycle (**6**). Second, it promotes the indispensable rollover step possibly by intermolecular H-bonding. Otherwise the directing site is occupied as a result of intramolecular H-bonding, and only monoaminated products are observed even with an excess amount of azides in previous catalytic systems.[5]

Based on these experimental results and a previously reported reaction pathway of monoamination in organic solvents[2,4] and amidation "on water",[8] a mechanism of diamination has been proposed (Scheme 6). The monoaminated starting material **3**

Scheme 6. Proposed Mechanistic Pathway of Diamination



can form the intermediate ***A*** with an active Rh-catalyst simply by acting as a bidented ligand. ***A*** then may undergo intermolecular H-bonding assisted and water promoted rollover to give the isomeric structure ***B***. ***B*** can give the intermediate ***C*** after C−H activation via transition state ***B′***. ***C*** can react with azide to form ***D***, and ***D*** can generate the bis-aminated structure (**E**) after nitrene transfer. Finally, in the presence of monoaminated starting material (**3**), ***E*** can generate the active catalyst ***A*** and the diaminated product (**5**) to complete the catalytic cycle.

In conclusion, we have successfully harvested water as a reaction medium to solve the selectivity issue in metal-catalyzed direct C−H amination. Using simple pyridine derivatives as the directing functional groups, highly selective mono- or diamination was achieved in a reaction involving an intermolecular H-bonding interaction with water. Using aryl azides as an amine source, the method works well with a wide range of substrates and without the addition of silver salts, acids, or bases. A water-promoted rollover mechanism was proposed through intermolecular H-bonding for the high yielding secondary functionalization reaction. This strategy may be very useful in catalysis and in the synthetic chemistry of C−H functionalization.

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■ ASSOCIATED CONTENT

Supporting Information

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Experimental details, characterization data for the products, and NMR spectra (PDF)

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Author Contributions

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For reviews of C−H amination through a C−H insertion pathway, see: (a) Starkov, P.; Jamison, T. F.; Marek, I. *Chem. - Eur. J.* **2015**, *21*, 5278. (b) Driver, T. G. *Nat. Chem.* **2013**, *5*, 736. (c) Roizen, J. L.; Harvey, M. E.; Du Bois, J. *Acc. Chem. Res.* **2012**, *45*, 911. (d) Dequirez, G.; Pons, V.; Dauban, P. *Angew. Chem., Int. Ed.* **2012**, *51*, 7384. (e) Collet, F.; Lescot, C.; Dauban, P. *Chem. Soc. Rev.* **2011**, *40*, 1926. (f) Collet, F.; Dodd, R. H.; Dauban, P. *Chem. Commun.* **2009**, 5061. (g) Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417. (h) Muller, P.; Fruit, C. *Chem. Rev.* **2003**, *103*, 2905.

(2) For reviews of C−H amination through a C−H activation pathway, see: (a) Shin, K.; Kim, H.; Chang, S. *Acc. Chem. Res.* **2015**, *48*, 1040. (b) Subramanian, P.; Rudolf, G. C.; Kaliappan, K. P. *Chem. - Asian J.* **2016**, *11*, 168. (c) Louillat, M. L.; Patureau, F. W. *Chem. Soc. Rev.* **2014**, *43*, 901. (d) Kuhl, N.; Schröder, N.; Glorius, F. *Adv. Synth. Catal.* **2014**, *356*, 1443. (e) Thirunavukkarasu, V. S.; Kozhushkov, S. I.; Ackermann, L. *Chem. Commun.* **2014**, *50*, 29. (f) Song, G. Y.; Wang, F.; Li, X. W. *Chem. Soc. Rev.* **2012**, *41*, 3651. (g) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068.

(3) For some studies, see: (a) Sun, C.-J.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2011**, *111*, 1293. (b) Ricci, A., Ed. *Amino Group Chemistry, From Synthesis to the Life Sciences*; Wiley-VCH: Weinheim, 2007. (c) Lawrence, S. A., Ed. *Amines: Synthesis Properties and Applications*; Cambridge University Press: Cambridge, 2004.

(4) For selected examples: (a) Park, Y.; Park, K. T.; Kim, J. G.; Chang, S. *J. Am. Chem. Soc.* **2015**, *137*, 4534. (b) Kim, H.; Shin, K.; Chang, S. *J. Am. Chem. Soc.* **2014**, *136*, 5904. (c) Wang, H.; Yu, Y.; Hong, X.-H.; Tan, Q.-T.; Xu, B. *J. Org. Chem.* **2014**, *79*, 3279. (d) Du, J. J.; Yang, Y.-X.; Feng, H.-J.; Li, C.-Y.; Zhou, B. *Chem. - Eur. J.* **2014**, *20*, 5727. (e) Kim, J.; Chang, S. *Angew. Chem., Int. Ed.* **2014**, *53*, 2203. (f) Kang, T.; Kim, Y.; Lee, D.; Wang, Z.; Chang, S. *J. Am. Chem. Soc.* **2014**, *136*, 4141. (g) Zhou, B.; Du, J.-J.; Yang, Y.-X.; Feng, H.-J.; Li, C.-Y. *Org. Lett.* **2013**, *15*, 6302. (h) Shin, K.; Baek, Y.; Chang, S. *Angew. Chem., Int. Ed.* **2013**, *52*, 8031. (i) Ryu, J.; Shin, K.; Park, S. H.; Kim, J. Y.; Chang, S. *Angew. Chem., Int. Ed.* **2012**, *51*, 9904. (j) Kim, J. Y.; Park, S. H.; Ryu, J.; Cho, S. H.; Kim, S. H.; Chang, S. *J. Am. Chem. Soc.* **2012**, *134*, 9110. (k) John, A.; Nicholas, K. M. *J. Org. Chem.* **2011**, *76*, 4158. (l) Xiao, B.; Gong, T.-J.; Xu, J.; Liu, Z.-J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 1466. (m) Shuai, Q.; Deng, G.-J.; Chua, Z.-J.; Bohle, D. S.; Li, C.-J. *Adv. Synth. Catal.* **2010**, *352*, 632. (n) Thu, H.-Y.; Yu, W.-Y.; Che, C.-M. *J. Am. Chem. Soc.* **2006**, *128*, 9048. (o) Uemura, T.; Imoto, S.; Chatani, N. *Chem. Lett.* **2006**, *35*, 842. (p) Chen, X.; Hao, X.-S.; Goodhue, C. E.; Yu, J.-Q *J. Am. Chem. Soc.* **2006**, *128*, 6790.

(5) Kim, H.-J.; Ajitha, M. J.; Lee, Y. J.; Ryu, J. Y.; Kim, J.; Lee, Y. H.; Jung, Y. S.; Chang, S. *J. Am. Chem. Soc.* **2014**, *136*, 1132.

(6) (a) Butler, R. N.; Coyne, A. G. *Chem. Rev.* **2010**, *110*, 6302. (b) Chen, L.; Li, C.-J. *Adv. Synth. Catal.* **2006**, *348*, 1459. (c) Li, C.-J. *Acc. Chem. Res.* **2002**, *35*, 533.

(7) (a) Butler, R. N.; Coyne, A. G. *Chem. Rev.* **2010**, *110*, 6302. (b) Franks, F. *Water: A Matrix of Life*, 2nd ed.; Royal Society of Chemistry: Cambridge, 2000. (c) Robinson, G. W. *Water in Biology, Chemistry, and Physics: Experimental Over Views and Computational Methodologies*; World Scientific: Singapore, 1996. (d) Ball, P. *Life's Matrix: A Biography of Water*, 1st ed.; Farrar Straus and Giroux: New York, River Edge, NJ, 1996.

(8) Ali, M. A.; Yao, X.; Sun, H.; Lu, H. *Org. Lett.* **2015**, *17*, 1513.

(9) For selected reviews: (a) Li, B.; Dixneuf, P. H. *Chem. Soc. Rev.* **2013**, *42*, 5744. (b) Fischmeister, C.; Doucet, H. *Green Chem.* **2011**, *13*, 741. (c) Herrerias, C. I.; Yao, X.; Li, Z.; Li, C.-J. *Chem. Rev.* **2007**, *107*, 2546. For selected examples: (d) Arockiam, P. B.; Fischmeister, C.; Bruneau, C.; Dixneuf, P. H. *Green Chem.* **2013**, *15*, 67. (e) Ackermann, L.; Wang, L.; Wolfram, R.; Lygin, A. V. *Org. Lett.* **2012**, *14*, 728. (f) Ackermann, L.; Lygin, A.-V. *Org. Lett.* **2012**, *14*, 764. (g) Fu, X.-P.; Liu, L.; Wang, D.; Chen, Y.-J.; Li, C.-J. *Green Chem.* **2011**, *13*, 549. (h) Ohnmacht, S. A.; Culshaw, A. J.; Greaney, M. F. *Org. Lett.* **2010**, *12*, 224. (i) Nishikata, T.; Abela, A. R.; Lipshutz, B. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 781. (j) Joucla, L.; Batail, N.; Djakovitch, L. *Adv. Synth. Catal.* **2010**, *352*, 2929. (k) Arockiam, P. B.; Fischmeister, C.; Bruneau, C.; Dixneuf, P. H. *Angew. Chem., Int. Ed.* **2010**, *49*, 6629. (l) Nishikata, T.; Lipshutz, B. H. *Org. Lett.* **2010**, *12*, 1972. (m) Arockiam, P. B.; Poirier, V.; Fischmeister, C.; Bruneau, C.; Dixneuf, P. H. *Green Chem.* **2009**, *11*, 1871. (n) Ohnmacht, S. A.; Mamone, P.; Culshaw, A. J.; Greaney, M. F. *Chem. Commun.* **2008**, 1241. (o) Baslé, O.; Li, C.-J. *Green Chem.* **2007**, *9*, 1047. (p) Turner, L.; Morris, J. A.; Greaney, M. F. *Angew. Chem., Int. Ed.* **2007**, *46*, 7996.

(10) Manbeck, K. A.; Brennessel, W. W.; Jones, W. D. *Inorg. Chim. Acta* **2013**, *397*, 140.

(11) (a) Yu, J.-S.; Liu, Y.-L.; Tang, J.; Wang, X.; Zhou, J. *Angew. Chem., Int. Ed.* **2014**, *53*, 9512. (b) Sengoden, M.; Punniyamurthy, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 572. (c) Mellouli, S.; Bousekkine, L.; Theberge, A. B.; Huck, W. T. S. *Angew. Chem., Int. Ed.* **2012**, *51*, 7981. (d) Narayan, S.; Muldoon, J.; Finn, M. G.; Fokin, V. V.; Kolb, H. C.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2005**, *44*, 3275. (e) Klijn, J. E.; Engberts, J. B. F. N. *Nature* **2005**, *435*, 746.

(12) For selected reviews: (a) Intrieri, D.; Zardi, P.; Caselli, A.; Gallo, E. *Chem. Commun.* **2014**, *50*, 11440. (b) Lu, H.; Zhang, X. P. *Chem. Soc. Rev.* **2011**, *40*, 1899. (c) Che, C. M.; Lo, V. K. Y.; Zhou, C. Y.; Huang, J. S. *Chem. Soc. Rev.* **2011**, *40*, 1950. (d) Driver, T. G. *Org. Biomol. Chem.* **2010**, *8*, 3831. (e) Cenini, S.; Gallo, E.; Caselli, A.; Ragaini, F.; Fantauzzi, S.; Piangiolino, C. *Coord. Chem. Rev.* **2006**, *250*, 1234. (f) Katsuki, T. *Chem. Lett.* **2005**, *34*, 1304.

(13) Our related studies using azides in C−H aminations: (a) Zhang, T.; Hu, X.; Wang, Z.; Yang, T. T.; Sun, H.; Li, G.; Lu, H. *Chem. - Eur. J.* **2016**, *22*, 2920. (b) Lu, H.; Li, C. Q.; Jiang, H.; Lizardi, C. L.; Zhang, X. P. *Angew. Chem., Int. Ed.* **2014**, *53*, 7028.

(14) Hocek, M.; Nauš, P.; Pohl, R.; Votruba, I.; Furman, P. A.; Tharnish, P. M.; Otto, M. J. *J. Med. Chem.* **2005**, *48*, 5869.

(15) Park, S. H.; Kwak, J.-S.; Shin, K.-M.; Ryu, J. Y.; Park, Y. S.; Chang, S. *J. Am. Chem. Soc.* **2014**, *136*, 2492.

(16) (a) Jung, Y.; Marcus, R. A. *J. Am. Chem. Soc.* **2007**, *129*, 5492. (b) Shen, Y. R.; Ostroverkhov, V. *Chem. Rev.* **2006**, *106*, 1140. (c) Molina, M. J. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1778. (d) Du, Q.; Freysz, E.; Shen, Y. R. *Science* **1994**, *264*, 826.

DOI: 10.1021/acs.orglett.6b00318
Org. Lett. 2016, 18, 1386−1389