Organic LETTERS

Letter

Cite This: Org. Lett. XXXX, XXX, XXX−XXX

pubs.acs.org/OrgLett

Cu-Catalyzed Denitrogenative Ring-Opening of 3-Aminoindazoles for the Synthesis of Aromatic Nitrile-Containing (Hetero)Arenes

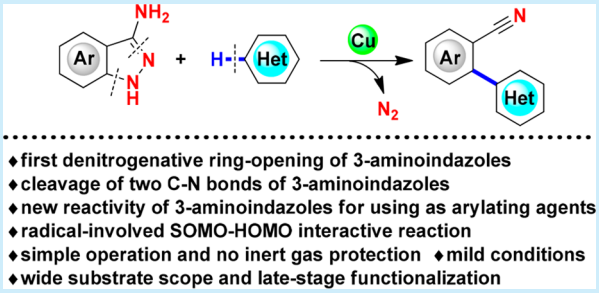
Yao Zhou,[†] Shuilin Deng,[†] Shaoyu Mai,[†] and Qiuling Song*[,†,‡]

[†]Institute of Next Generation Matter Transformation, College of Chemical Engineering, Huaqiao University, 668 Jimei Boulevard, Xiamen, Fujian 361021, P. R. China

[‡]College of Pharmaceutical Sciences, Zhejiang University of Technology, Hangzhou, 310014, P.R. China

Supporting Information

ABSTRACT: An unprecedented Cu-catalyzed oxidative cleavage of two C−N bonds of 3-aminoindazoles is reported herein, which represents the first example for denitrogenative ring-opening of 3-aminoindazoles. This novel reactivity of 3-aminoindazoles enables the production of diverse aromatic nitrile-containing (hetero)-arenes via C−H arylation of (hetero)arenes with wide subsrate scope under mild conditions.

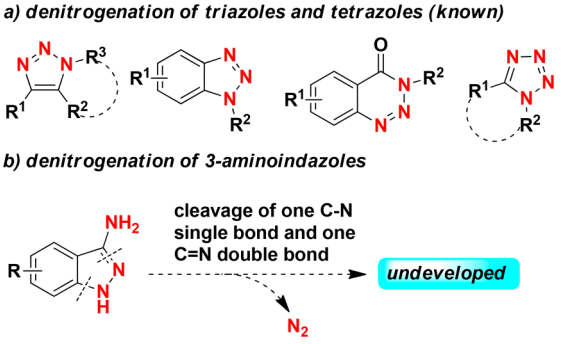


The transition-metal-catalyzed denitrogenative reaction is one of the most significant achievements in synthetic chemistry. Because triazoles are well-known as precursors to generate α-imino metal carbenoid species, during the past decades, a great deal of work based on the transition-metal-catalyzed denitrogenation of triazoles has been reported.[1] In addition to triazoles, the denitrogenative ring-opening of benzotriazoles,[2] benzotriazinones[3] and tetrazoles[4] were also explored by chemists. Although remarkable progress has been made on the denitrogenation of polynitrogen heterocycles (Scheme 1a), to our knowledge, the denitrogenative ring-opening of 3-aminoindazoles has never been documented to date (Scheme 1b).

Heterobiaryls are privileged core structural motifs as they widely distribute in biologically active molecules, peptide mimetics, drugs and optoelectronic materials.[5] A huge number of transition-metal-catalyzed arylations of the innate C−H bond of heteroarenes have been excavated to forge these ubiquitous heterobiaryls[6] because direct C−H arylation overcomes preactivation of heteroaromatics, which is cost-effective for the step-economical diversification of heteroarenes. In this regard, C−H arylation of (hetero)arenes using aryl halides as coupling partners is dominant in organic chemistry.[7] As alternative strategies, C−H arylation using highly reactive arylation agents (such as hypervalent iodine reagents,[8] diazonium salts,[9] organoboranes,[10] and others[11]), transition-metal-free process,[12] C−H/C−H cross-coupling,[13] and photoinduced C−H arylation[14] have also been developed by chemists in recent years. Despite great progress achieved in the field of C−H arylation of (hetero)arenes, most of the previous methods often suffer from inert gas protection and high reaction temperature ranging from 100 to 200 °C. Given this point, the development of facile tactics and novel arylation agents is in demand and is desirable to accomplish C−H arylation of (hetero)arenes concomitant with the installation of additional functionalities, which could be converted to expand the molecular complexity. In this Letter, we endow a new reactivity of 3-aminoindazoles for use as arylating agents in C−H functionalization of (hetero)arenes under mild conditions (Scheme 2).

We commenced our study by exploring suitable systems for the envisioned denitrogenation of 3-aminoindazoles. Several oxidative systems were investigated initially by using commercially available 3-amino-1*H*-indazole (**1a**) and 2-phenyl-1*H*-indole (**2a**) as model substrates (Table S1, entry 1−6). To our delight, the denitrogenative ring-opening of 3-aminoindazole was indeed observed when the reaction was conducted with the Cu/[O] catalyst system. After thoroughly screening the reaction parameters, the desired product 2-(2-

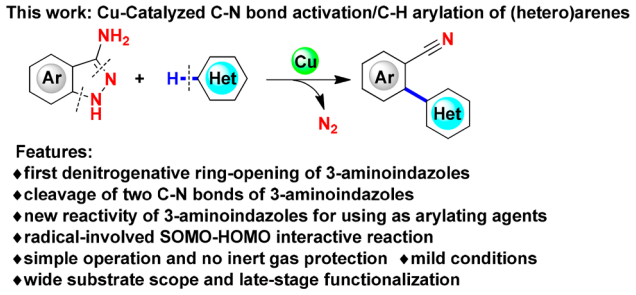
Scheme 1. Denitrogenation of Polynitrogen Heterocycles



Received: August 17, 2018

DOI: 10.1021/acs.orglett.8b02629
Org. Lett. XXXX, XXX, XXX−XXX

Scheme 2. Cu-Catalyzed Denitrogenative Ring-Opening of 3-Aminoindazoles

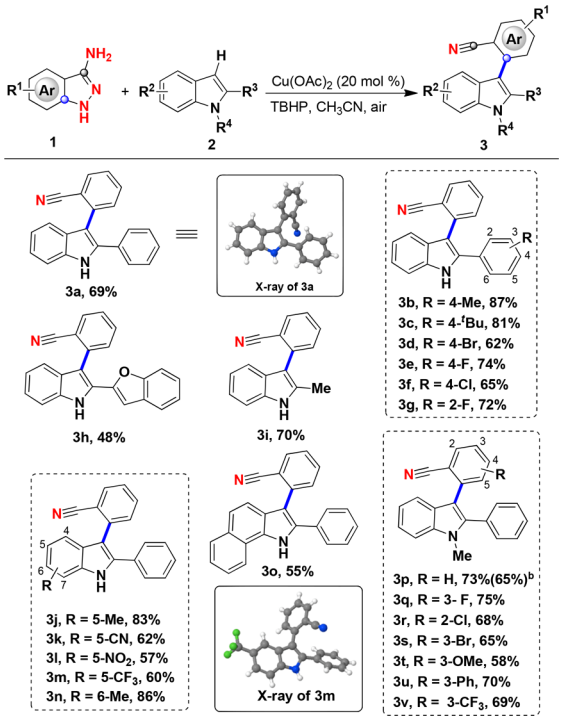


phenyl-16H-indol-3-yl)benzonitrile (**3a**) could be obtained in 69% yield when the reaction was performed in the presence of $Cu(OAc)_2$ (20 mol %) using *tert*-butyl hydroperoxide (TBHP) as oxidant in CH_3CN at 60 °C.[15]

Having established the optimal reaction conditions, the scope of this Cu-catalyzed denitrogenative ring-opening of 3-aminoindazoles to afford benzonitrile-containing indole derivatives was assessed. A variety of 2-phenylindoles bearing different substituents on the benzene ring of C2 position were inspected initially. As shown in Scheme 3, the desired 2-(2-phenyl-1*H*-indol-3-yl)benzonitriles (**3a**–**g**) were obtained in 62–87% yields. The structure of **3a** was unambiguously confirmed by X-ray crystallographic analysis.[16] In addition to C2-phenyl-substituted indoles, 2-(benzofuran-2-yl)-1*H*-indole **2h**, and 2-methyl-1*H*-indole **2i** were amenable to this reaction as well, delivering the targeted products **3h** and **3i** in modest yields. Unfortunately, the polar functional groups such as free OH and NH_2 were not compatible in this transformation. When 2-methyl-1*H*-indol-5-ol or 2-methyl-1*H*-indol-5-amine was used as substrate, the reaction was deteriorated. We also screened a suite of 2-phenylindoles (**2j**–**n**) having different groups on the indole ring, and it turned out that they were good candidates in this oxidative C–H functionalization to render the corresponding products (**3j**–**n**) in decent isolated yields (57–83%). 2-Phenyl-1*H*-benzo[*g*]indole **2o** was also found to proceed smoothly, enabling the production of **3o** in 55% yield. Subsequently, we focused on the scope with respect to various 3-aminoindazoles. A series of substituted 3-aminoindazoles were good donors for generating benzonitrile-containing indole derivatives in this denitrogenative reaction. The expected products **3p**–**v** could be isolated in 58–75% yields under the standard conditions. Of note, the reaction was amenable to scale-up without loss of its efficiency, and product **3p** could be obtained in 65% yield when the reaction was performed in 5 mmol scale.

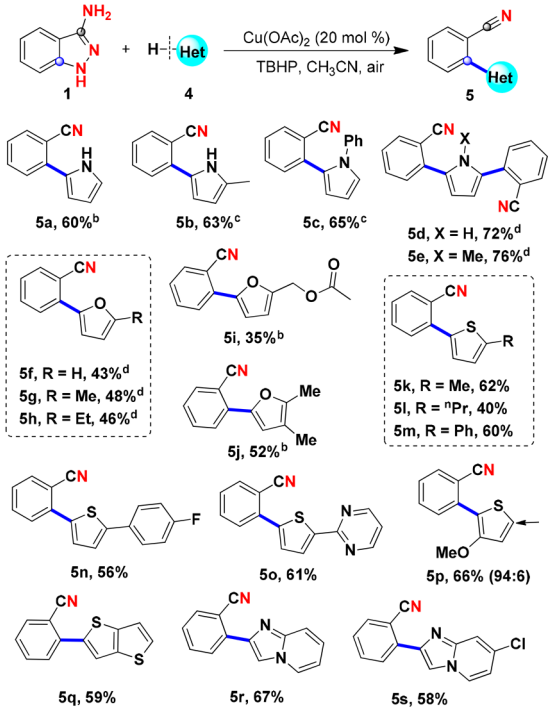
Intrigued by the novel reactivity of 3-aminoindazoles to provide benzonitrile-containing indole derivatives, we extended the transformation to other heterocycles underlying this Cu-catalyzed denitrogenation of 3-aminoindazoles. As described in Scheme 4, pyrroles **4a**–**c** were also good substrates for C–H functionalization, affording the desired 2-(1*H*-pyrrol-2-yl)-benzonitriles **5a**–**c** in good yields. When an excess amount of 3-aminoindazole (**1a**) was added, double arylation of pyrroles took place, furnishing products **5d** and **5e** in 72 and

Scheme 3. Substrate Scope for Synthesis of Benzonitrile-Containing Indole Derivatives[a]



[a]All reactions unless otherwise stated were carried out with **1** (0.3 mmol), **2** (0.02 mmol), $Cu(OA_c)_2$ (20 mol %), and TBHP (2 equiv) in MeCN (1.0 mL) heated at 60 °C for 18 h. All isolated products are reported. [b]Starting from 5 mmol of **1p**.

Scheme 4. Substrate Scope with Respect to Other Heterocycles[a]



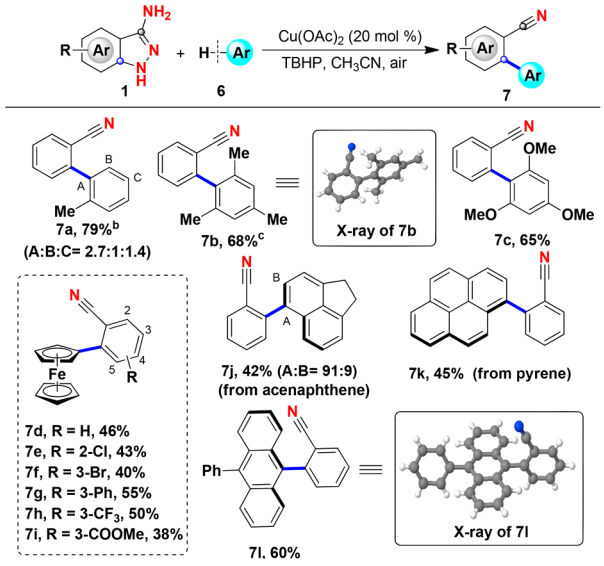
[a]The reactions were carried out with **1** (0.3 mmol), **4** (0.2 mmol), $Cu(OA_c)_2$ (20 mol %), and TBHP (2 equiv) in MeCN (1.0 mL) heated at 60 °C for 18 h. All isolated products are reported. [b]Compounds **1** (0.2 mmol) and **4** (0.6 mmol). [c]Compounds **1** (0.2 mmol) and **4** (0.4 mmol). [d]Compounds **1** (0.5 mmol) and **4** (0.2 mmol) at 50 °C.

DOI: 10.1021/acs.orglett.8b02629
Org. Lett. XXXX, XXX, XXX–XXX

76% yields, respectively. Subsequently, a range of furans were tested. Compared with pyrroles, furans demonstrated relatively conservative reactivity in this Cu-catalyzed C−H arylation of (hetero)arenes, and the desired 2-(furan-2-yl)benzonitriles (**5f−j**) were gained in moderate isolated yields. The current C−H functionalization was also applied to thiophenes. Various thiophenes (**4k−p**) could undergo C−H arylation at the ortho-position to deliver the targeted products **5k−p** in 40−66% yields. Thieno[3,2-*b*]thiophene (**4q**) was also suitable substrates for producing benzonitrile-containing thiophenes **5q** in 59% yield. To our delight, the C−H arylation of imidazo[1,2-*a*]pyridines in this Cu-catalyzed denitrogenation of 3-aminoindazoles was also successful, providing products **5r** and **5s** in 67 and 58% yields, respectively.

For the substrate scale to be broadened, various arenes were also utilized as limiting reagents in this Cu-catalyzed C−N bond activation/C−H arylation of arenes. As described in Scheme 5, toluene, mesitylene, and 1,3,5-trimethoxybenzene

Scheme 5. Scope for Aromatic Rings[a]

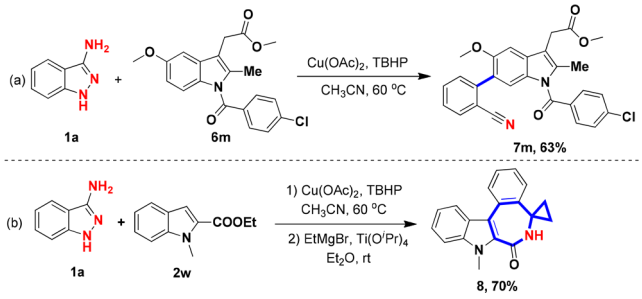


[a]All reactions unless otherwise stated were carried out with **1** (0.2 mmol), **6** (0.4 mmol), $Cu(OAc)_2$ (20 mol %), and TBHP (2 equiv) in MeCN (1.0 mL) heated at 80 °C for 20 h. All isolated products are reported. [b]PhMe:CH_3CN = 1:1 (v/v). [c]Mesitylene:CH_3CN = 1:3 (v/v).

were all arylated under this denitrogenation of 3-aminoindazoles, affording the corresponding products **7a−c** in 79, 68, and 65% yields, respectively. In addition to electron-rich arenes, ferrocene could undergo this C−H functionalization as well. The treatment of ferrocene in conjection with a variety of 3-aminoindazoles gave the targeted benzonitrile-derived ferrocenes **7d−l** in modest isolated yields. Polycyclic aromatic hydrocarbons such as acenaphthene, pyrene, and 9-phenylanthracene, which are important frameworks in material science,[17] could be functionalized smoothly under this transformation as well, furnishing the desired products **7j−l** in 42−60% yields.

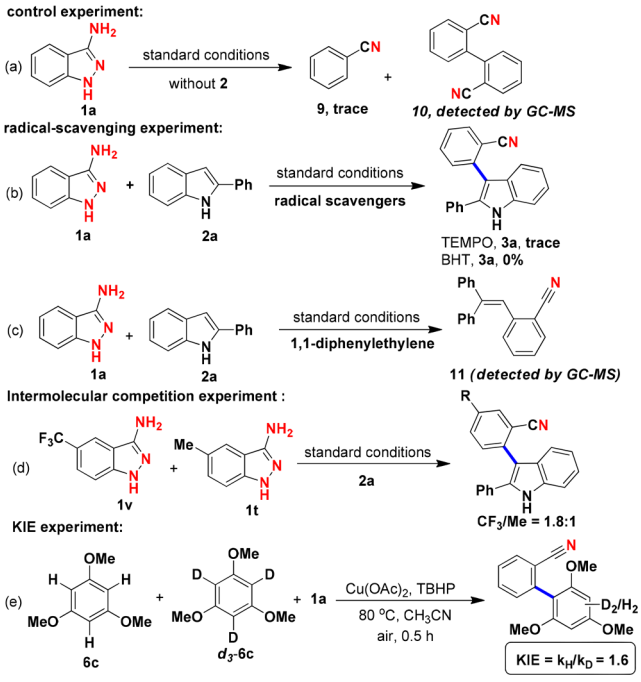
As demonstrated in Scheme 6, the potential application in drug decoration of this method was also showcased by late-stage functionalization of indometacin derivative, delivering the indometacin derivative **7m** in 63% yield. In addition, the product ethyl 3-(2-cyanophenyl)-1-methyl-1*H*-indole-2-carboxylate **3w** could undergo a cyclopropanation-lactamization sequence to produce indole-fused lactam **8** in good yield, which is an analogue of the inhibitors for the treatment of tubulin polymerization.[18]

Scheme 6. Synthetic Applications and Transformations



Because the mechanistic details of this Cu-catalyzed denitrogenation of 3-aminoindazoles are unclear, preliminary mechanistic investigations were carried out. When 3-amino-1*H*-indazole (**1a**) was submitted to the reaction conditions in the absence of 2-phenyl-1*H*-indole, a trace amount of benzonitrile (**9**) and [1,1′-biphenyl]-2,2′-dicarbonitrile (**10**) were detected by GC-MS (Scheme 7a). When 2,2,6,6-

Scheme 7. Primary Mechanism Studies



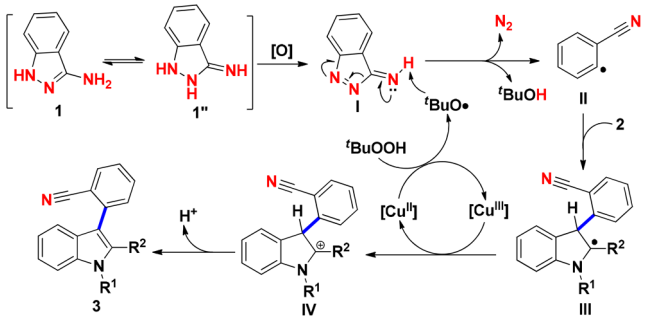
tetramethyl-1-piperidinyloxy (TEMPO) and 2,6-di-*tert*-butyl-4-methylphenol (BHT) were added as radical scavengers under the standard conditions, this reaction was significantly inhibited (Scheme 7b), and compound **11** was detected by GC-MS when 1,1-diphenylethylene served as the additive (Scheme 7c). These results indicate that a radical-type reaction regime might be involved in this denitrogenative ring-opening of 3-aminoindazoles. To gain more insight into this Cu-catalyzed oxidative C−N bond activation/C−H functionalization, we executed several kinetic experiments. The intermolecular competition experiment in Scheme 7d manifested that electron-poor 3-aminoindazoles react preferentially, which can

DOI: 10.1021/acs.orglett.8b02629
Org. Lett. XXXX, XXX, XXX−XXX

be explained by the occurrence of a radical-controlled SOMO-HOMO interaction.[19,9d] An intermolecular kinetic isotope effect (KIE) was also studied to elucidate the step of C−H bond cleavage. When a 1:1 mixture of **6c** and [D_3]-**6c** was treated with 3-aminoindazole **1a**, a KIE of 1.6 from the competition experiment was observed (Scheme 7e), which suggested that C−H functionalization in this transformation is facile.

On the basis of the primary mechanism studies, a plausible mechanism for this ring-opening of 3-aminoindazoles is proposed in Scheme 8. First, compound **I** is formed by the

Scheme 8. Proposed Reaction Mechanism



oxidation of 3-aminoindazole **1** under these oxidative conditions. Simultaneously, the Cu(II) species donates an electron to TBHP to generate the Cu(III) species and the *tert*-butoxyl radical. Then, the ^{t}BuO• abstracts a hydrogen atom from compound **I**, which successively suffers from the extrusion of one molecular nitrogen to produce the radical intermediate **II**. Subsequently, intermediate **II** is attacked by the indole **2** to provide radical intermediate **III**, which undergoes oxidation by the Cu(III) species to deliver carbocation intermediate **IV**. At the same time, the Cu(II) species is regenerated to continue the catalytic cycle. Ultimately, deprotonation of intermediate **IV** affords desired product **3**.

In summary, we have successfully developed a novel method for the streamlined synthesis of aromatic nitrile-containing (hetero)arenes by merging C−N bond activation and C−H arylation of (hetero)arenes, which represents the first example of denitrogenation of 3-aminoindazoles through oxidative cleavage of two C−N bonds. A broad scope of (hetero)arenes were tolerated in this transformation to afford diverse functionalized aromatic nitrile-derived (hetero)arenes. A mechanism study shows that a radical-type reaction is involved in this denitrogenative ring-opening of 3-aminoindazoles. The current protocol can be readily scaled-up without loss of its efficiency. Meanwhile, further synthetic utility as demonstrated in the late-stage functionalization of drug derivatives could lead to valuable bioactive compounds.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.8b02629.

General experimental procedures and spectroscopic data for the corresponding products (PDF)

Accession Codes

CCDC 1568306, 1842362, 1845361, and 1851058 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: qsong@hqu.edu.cn.

ORCID

Yao Zhou: 0000-0002-3500-7355

Qiuling Song: 0000-0002-9836-8860

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support from the Recruitment Program of Global Experts (1000 Talents Plan), the Natural Science Foundation of Fujian Province (2016J01064), Fujian Hundred Talents Plan, Program of Innovative Research Team of Huaqiao University (Z14X0047), and Subsidized Project for Cultivating Postgraduates' Innovative Ability in Scientific Research of Huaqiao University (for Y. Z.) is gratefully acknowledged. We also thank the Instrumental Analysis Center of Huaqiao University for analysis support.

■ REFERENCES

(1) For some reviews, see: (a) Chattopadhyay, B.; Gevorgyan, V. *Angew. Chem., Int. Ed.* **2012**, *51*, 862. (b) Davies, H. M. L.; Alford, J. S. *Chem. Soc. Rev.* **2014**, *43*, 5151. (c) Jiang, Y.; Sun, R.; Tang, X.-Y.; Shi, M. *Chem. - Eur. J.* **2016**, *22*, 17910.

(2) (a) Micó, X. À.; Ziegler, T.; Subramanian, L. R. *Angew. Chem., Int. Ed.* **2004**, *43*, 1400. (b) Nakamura, I.; Nemoto, T.; Shiraiwa, N.; Terada, M. *Org. Lett.* **2009**, *11*, 1055. (c) Battula, S.; Kumar, A.; Gupta, A. P.; Ahmed, Q. N. *Org. Lett.* **2015**, *17*, 5562. (d) Su, Y.; Petersen, J. L.; Gregg, T. L.; Shi, X. *Org. Lett.* **2015**, *17*, 1208. (e) Teders, M.; Gómez-Suárez, A.; Pitzer, L.; Hopkinson, M. N.; Glorius, F. *Angew. Chem., Int. Ed.* **2017**, *56*, 902. (f) Teders, M.; Pitzer, L.; Buss, S.; Glorius, F. *ACS Catal.* **2017**, *7*, 4053. (g) Yin, Z.; Wang, Z.; Wu, X.-F. *Org. Lett.* **2017**, *19*, 6232. (h) Wang, Y.; Wu, Y.; Li, Y.; Tang, Y. *Chem. Sci.* **2017**, *8*, 3852. (i) Wang, Y.; Li, Y.; Fan, Y.; Wang, Z.; Tang, Y. *Chem. Commun.* **2017**, *53*, 11873.

(3) (a) Miura, T.; Yamauchi, M.; Murakami, M. *Org. Lett.* **2008**, *10*, 3085. (b) Yamauchi, M.; Morimoto, M.; Miura, T.; Murakami, M. *J. Am. Chem. Soc.* **2010**, *132*, 54. (c) Miura, T.; Morimoto, M.; Yamauchi, M.; Murakami, M. *J. Org. Chem.* **2010**, *75*, 5359. (d) Miura, T.; Yamauchi, M.; Kosaka, A.; Murakami, M. *Angew. Chem., Int. Ed.* **2010**, *49*, 4955. (e) Fang, Z.-J.; Zheng, S.-C.; Guo, Z.; Guo, J.-Y.; Tan, B.; Liu, X.-Y. *Angew. Chem., Int. Ed.* **2015**, *54*, 9528. (f) Wang, H.; Yu, S. *Org. Lett.* **2015**, *17*, 4272.

(4) (a) Luo, K.; Meng, L.; Zhang, Y.; Zhang, X.; Wang, L. *Adv. Synth. Catal.* **2013**, *355*, 765. (b) Zhang, L.; Zheng, L.; Guo, B.; Hua, R. *J. Org. Chem.* **2014**, *79*, 11541. (c) Nakamuro, T.; Hagiwara, K.; Miura, T.; Murakami, M. *Angew. Chem., Int. Ed.* **2018**, *57*, 5497. (d) Das, S. K.; Roy, S.; Khatua, H.; Chattopadhyay, B. *J. Am. Chem. Soc.* **2018**, *140*, 8429.

(5) (a) Hu, W.; Guo, Z.; Bai, F. C. A.; Yi, X.; Cheng, G.; Li, J. *Bioorg. Med. Chem.* **2003**, *11*, 1153. (b) Zhang, H.-Z.; Drewe, J.; Tseng, B.; Kasibhatla, S.; Cai, S. X. *Bioorg. Med. Chem.* **2004**, *12*, 3649. (c) Gorak, Y. I.; Obushak, N. D.; Matiichuk, V. S.; Lytvyn, R. Z. *Russ. J. Org. Chem.* **2009**, *45*, 541. (d) Yang, Y.; Lan, J.; You, J. *Chem. Rev.*

DOI: 10.1021/acs.orglett.8b02629
Org. Lett. XXXX, XXX, XXX−XXX

2017, *117*, 8787. (e) Simonetti, M.; Cannas, D. M.; Larrosa, I. *Adv. Organomet. Chem.* **2017**, *67*, 299.
(6) For some reviews, see: (a) Seregin, I. V.; Gevorgyan, V. *Chem. Soc. Rev.* **2007**, *36*, 1173. (b) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (c) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. (d) Sharma, A.; Vacchani, D.; Van der Eycken, E. V. d. *Chem. - Eur. J.* **2013**, *19*, 1158. (e) Sandtorv, A. H. *Adv. Synth. Catal.* **2015**, *357*, 2403.
(7) (a) Lane, B. S.; Sames, D. *Org. Lett.* **2004**, *6*, 2897. (b) Wang, X.; Lane, B. S.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 4996. (c) Lane, B. S.; Brown, M. A.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 8050. (d) Yanagisawa, S.; Sudo, T.; Noyori, R.; Itami, K. *J. Am. Chem. Soc.* **2006**, *128*, 11748. (e) Touré, B. B.; Lane, B. S.; Sames, D. *Org. Lett.* **2006**, *8*, 1979. (f) Wang, X.; Gribkov, D. V.; Sames, D. *J. Org. Chem.* **2007**, *72*, 1476. (g) Stuart, D. R.; Villemure, E.; Fagnou, K. *J. Am. Chem. Soc.* **2007**, *129*, 12072. (h) Lebrasseur, N.; Larrosa, I. *J. Am. Chem. Soc.* **2008**, *130*, 2926. (i) Bellina, F.; Benelli, F.; Rossi, R. *J. Org. Chem.* **2008**, *73*, 5529. (j) Join, B.; Yamamoto, T.; Itami, K. *Angew. Chem., Int. Ed.* **2009**, *48*, 3644. (k) Roger, J.; Doucet, H. *Adv. Synth. Catal.* **2009**, *351*, 1977. (l) Ueda, K.; Yanagisawa, S.; Yamaguchi, J.; Itami, K. *Angew. Chem., Int. Ed.* **2010**, *49*, 8946. (m) Joucla, L.; Batail, N.; Djakovitch, L. *Adv. Synth. Catal.* **2010**, *352*, 2929. (n) Ackermann, L.; Lygin, A. V. *Org. Lett.* **2011**, *13*, 3332. (o) Nadres, E. T.; Lazareva, A.; Daugulis, O. *J. Org. Chem.* **2011**, *76*, 471. (p) Cao, H.; Zhan, H.; Lin, Y.; Lin, X.; Du, Z.; Jiang, H. *Org. Lett.* **2012**, *14*, 1688. (q) Yamaguchi, M.; Suzuki, K.; Sato, Y.; Manabe, K. *Org. Lett.* **2017**, *19*, 5388. (r) Pi, J.-J.; Lu, X.-Y.; Liu, J.-H.; Lu, X.; Xiao, B.; Fu, Y.; Guimond, N. *J. Org. Chem.* **2018**, *83*, 5791. (s) Jiang, H.; Bellomo, A.; Zhang, M.; Carroll, P. J.; Manor, B. C.; Jia, T.; Walsh, P. J. *Org. Lett.* **2018**, *20*, 2522.
(8) (a) Deprez, N. R.; Kalyani, D.; Krause, A.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 4972. (b) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172. (c) Ackermann, L.; Dell'Acqua, M.; Fenner, S.; Vicente, R.; Sandmann, R. *Org. Lett.* **2011**, *13*, 2358. (d) Wen, J.; Zhang, R.-Y.; Chen, S.-Y.; Zhang, J.; Yu, X.-Q. *J. Org. Chem.* **2012**, *77*, 766.
(9) (a) Amaya, T.; Hata, D.; Moriuchi, T.; Hirao, T. *Chem. - Eur. J.* **2015**, *21*, 16427. (b) Gemoets, H. P. L.; Kalvet, I.; Nyuchev, A. V.; Erdmann, N.; Hessel, V.; Schoenebeck, F.; Noel, T. *Chem. Sci.* **2017**, *8*, 1046. (c) Ahmed, J.; Sreejyothi, P.; Vijaykumar, G.; Jose, A.; Raj, M.; Mandal, S. K. *Chem. Sci.* **2017**, *8*, 7798. (d) Liang, Y.-F.; Steinbock, R.; Yang, L.; Ackermann, L. *Angew. Chem., Int. Ed.* **2018**, *57*, 10625.
(10) (a) Demir, A. S.; Reis, Ö.; Emrullahoglu, M. *J. Org. Chem.* **2003**, *68*, 578. (b) Yang, S. D.; Sun, C. L.; Fang, Z.; Li, B. J.; Li, Y. Z.; Shi, Z. J. *Angew. Chem., Int. Ed.* **2008**, *47*, 1473. (c) Zhao, J. L.; Zhang, Y. H.; Cheng, K. *J. Org. Chem.* **2008**, *73*, 7428. (d) Kirchberg, S.; Fröhlich, R.; Studer, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 4235. (e) Wen, J.; Qin, S.; Ma, L.-F.; Dong, L.; Zhang, J.; Liu, S.-S.; Duan, Y.-S.; Chen, S.-Y.; Hu, C.-W.; Yu, X.-Q. *Org. Lett.* **2010**, *12*, 2694.
(11) (a) Cornella, J.; Lu, P.; Larrosa, I. *Org. Lett.* **2009**, *11*, 5506. (b) Liang, Z.; Yao, B.; Zhang, Y. *Org. Lett.* **2010**, *12*, 3185. (c) Zhou, J.; Hu, P.; Zhang, M.; Huang, S. J.; Wang, M.; Su, W. P. *Chem. - Eur. J.* **2010**, *16*, 5876. (d) Zhang, M.; Zhang, S.; Liu, M.; Cheng, J. *Chem. Commun.* **2011**, *47*, 11522. (e) Wu, M. Y.; Luo, J. Y.; Xiao, F. H.; Zhang, S. F.; Deng, G. J.; Luo, H. A. *Adv. Synth. Catal.* **2012**, *354*, 335. (f) Chen, S.; Liao, Y.; Zhao, F.; Qi, H.; Liu, S.; Deng, G.-J. *Org. Lett.* **2014**, *16*, 1618. (g) Chen, Y. X.; Guo, S. B.; Li, K. N.; Qu, J. P.; Yuan, H.; Hua, Q. R.; Chen, B. H. *Adv. Synth. Catal.* **2013**, *355*, 711.
(12) (a) Rossi, R.; Lessi, M.; Manzini, C.; Marianetti, G.; Bellina, F. *Adv. Synth. Catal.* **2015**, *357*, 3777. (b) Chen, J.; Wu, J. *Angew. Chem., Int. Ed.* **2017**, *56*, 3951.
(13) (a) Juwaini, N. A. B.; Ng, J. K. P.; Seayad, J. *ACS Catal.* **2012**, *2*, 1787. (b) Cheng, Y.; Li, G.; Liu, Y.; Shi, Y.; Gao, G.; Wu, D.; Lan, J.; You, J. *J. Am. Chem. Soc.* **2016**, *138*, 4730. (c) Tan, G.; He, S.; Huang, X.; Liao, X.; Cheng, Y.; You, J. *Angew. Chem., Int. Ed.* **2016**, *55*, 10414. (d) Cheng, Y.; Wu, Y.; Tan, G.; You, J. *Angew. Chem., Int. Ed.* **2016**, *55*, 12275. (e) Chen, C.; Chen, X.; Zhao, H.; Jiang, H.; Zhang, M. *Org. Lett.* **2017**, *19*, 3390.
(14) (a) Hari, D. P.; Schroll, P.; König, B. *J. Am. Chem. Soc.* **2012**, *134*, 2958. (b) Cheng, Y. N.; Gu, X. Y.; Li, P. X. *Org. Lett.* **2013**, *15*, 2664. (c) Zhang, Y.-P.; Feng, X.-L.; Yang, Y.-S.; Cao, B.-X. *Tetrahedron Lett.* **2016**, *57*, 2298. (d) Yang, F.; Koeller, J.; Ackermann, L. *Angew. Chem., Int. Ed.* **2016**, *55*, 4759. (e) Fürst, M. C. D.; Gans, E.; Böck, M. J.; Heinrich, M. R. *Chem. - Eur. J.* **2017**, *23*, 15312.
(15) See Supporting Information for details.
(16) CCDC 1568306 (**3a**), CCDC 1842362 (**3m**), CCDC 1845361 (**7b**), and CCDC 1851058 (**7l**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.
(17) Iwahara, H.; Kushida, T.; Yamaguchi, S. *Chem. Commun.* **2016**, *52*, 1124.
(18) Singh, A. K.; Raj, V.; Saha, S. *Eur. J. Med. Chem.* **2017**, *142*, 244.
(19) Vaillard, S. E.; Studer, A. In *Encyclopedia of Radicals in Chemistry, Biology and Materials*, Vol. 2; Chatgilialoglu, C., Studer, A., Eds.; Wiley: Chichester, 2012; p 1059.

DOI: 10.1021/acs.orglett.8b02629
Org. Lett. XXXX, XXX, XXX−XXX