Organic LETTERS
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Copper-Catalyzed Oxidative C(sp^3)−H Functionalization for Facile Synthesis of 1,2,4-Triazoles and 1,3,5-Triazines from Amidines

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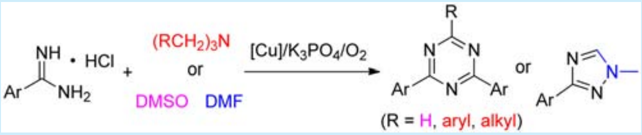
Supporting Information

ABSTRACT: A facile and versatile catalytic system involving copper catalyst, K_3PO_4 as the base, and O_2 as the oxidant has been developed to enable efficient synthesis of 2,4,6-trisubstituted and 2,6-disubstituted 1,3,5-triazines and 1,3-disubstituted 1,2,4-triazoles from amidines with trialkylamines, DMSO, and DMF as the reaction partners, respectively. This protocol features inexpensive metal catalyst, green oxidant, good functional group tolerance, and high regioselectivity, providing an efficient entry to those products that are challenging to prepare by traditional methods. A single-electron-transfer (SET) mechanism is proposed for these transformations.



Nitrogen-containing heterocycles are privileged compounds in natural products and pharmaceutical chemistry. In particular, heterocycles containing three nitrogen atoms such as 1,2,4-triazoles[1] and 1,3,5-triazines[2] feature broad-spectrum biological activities. For example, fluconazole and voriconazole are two triazole drugs that are the most frequently used antifungals in clinical settings.[1a] Triazine CH5015765 has also been determined to exhibit nice biological, physicochemical, and pharmacokinetic profiles (Figure 1).[2b]

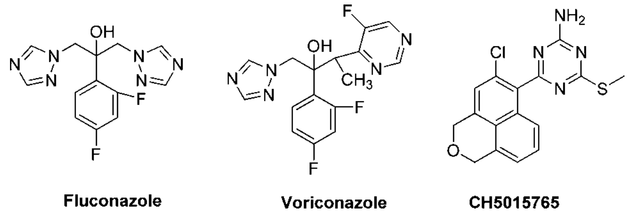
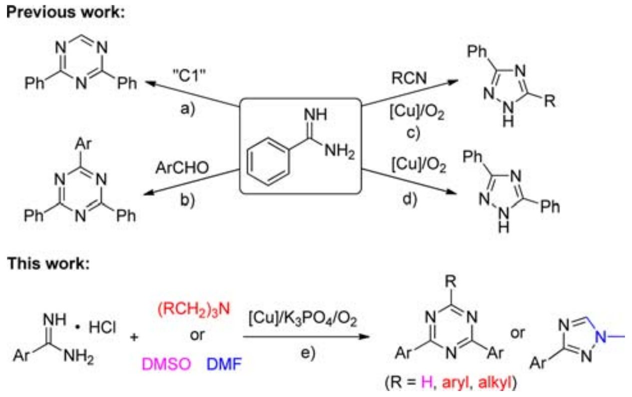


Figure 1. Representative drugs with three nitrogen-containing heterocycle frameworks.

While there exist various synthetic methods for the two heterocycles from cyclic or acyclic precursors,[3,4] amidines are frequently used to prepare multiple-nitrogen-containing heterocycles because of their innate structural advantage. We can summarize four types of reactions for these transformations according to the different substituted heterocycle products: (i) condensation or oxidative condensation of two molecular amidines with a C1 source such as diimino salt, 1,1-diethoxy-*N*,*N*-dimethylmethanamine, and DMF[5] (Scheme 1a); (ii) oxidative condensation of two molecular amidines with aryl aldehydes or aryl methanols[6] (Scheme 1b); (iii) oxidative cyclization with nitriles or acylhydrazines to form 3,5-disubstitued 1,2,4-triazoles[7] (Scheme 1c); and (iv) oxidative dimerization to form 3,5-diaryl-1,2,4-triazoles[8] (Scheme 1d). Despite the synthetic efficiency of these reactions, problems related to substituent diversity of the products are evident. For example, the yield of 2-alkyl-4,6-diaryl-1,3,5-triazines was rather low with the oxidative condensation of amidine and alkyl aldehyde.[9] In the case of 1,2,4-triazoles, the products obtained are usually restricted to 1*H*-3,5-disubstitued products, while 1,3-disubstituted or 1,3,5-trisubstitued 1,2,4-triazoles could not be achieved from the existing methods. It is therefore highly desirable to develop more general and efficient methods for the synthesis of these two kinds of heterocycles.

Scheme 1. Synthesis of 1,2,4-Triazoles and 1,3,5-Triazines from Amidines



Received: April 6, 2015
Published: May 29, 2015

DOI: 10.1021/acs.orglett.5b00995
Org. Lett. 2015, 17, 2894−2897

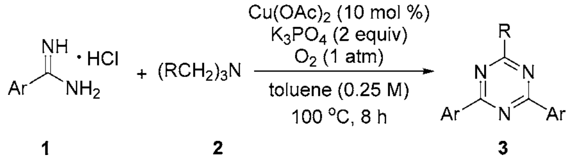
In recent years, copper-catalyzed oxidative transformation has received much attention in organic synthesis because it allows construction of C−X (X = C, N, O, etc.) bonds directly from the C−H bond and notably provides synthetic convergence and flexibility.[10] Copper-catalyzed oxidative functionalization of C(sp^3)−H adjacent to a nitrogen atom has been intensively investigated for direct cross dehydrogenative coupling (CDC)[11] or heterocyclization.[12] Among these reactions, although organic radical oxidants, such as TBHP, TEMPO, and NBS, were often used, molecular oxygen (O_2) has gradually became a hot topic of research in recent years.[10d,f] The obvious advantages of the reactions with O_2 are the low cost, high atom economy, and innocuous reaction byproduct (i.e., water). As part of our continued interest in copper-catalyzed aerobic transformations[13] and aza-heterocycle synthesis[12g−i] via oxidative functionalization of C(sp^3)−H adjacent to a nitrogen atom, we herein describe a facile synthesis of 1,2,4-triazoles and 1,3,5-triazines via an aerobic oxidative cyclization of amidines with amines, catalyzed by Cu with O_2 as the terminal oxidant (Scheme 1e). This protocol is an efficient complement to the previous synthesis, which provides highly efficient access to diverse three-nitrogen-containing heterocycles.

Considering that the alkylamines could serve as carbon sources to construct heterocycles under an oxidative system,[12i] we initially chose benzamidine hydrochloride (**1a**) and triethylamine (TEA, **2a**) as the model substrates and toluene as the reaction media under 1 atm of oxygen atmosphere to optimize the reaction conditions (Table S1, Supporting Information). Both the copper catalyst and the base were found to be critical. Non-halide copper(II) catalysts showed high levels of catalytic activity (Table S1, entries 1−7), of which $Cu(OAc)_2$ gave the best results in the presence of K_3PO_4 as the base (entry 7). Interestingly, carbonates such as K_2CO_3 and Cs_2CO_3 inhibited this cyclization completely (Table S1, entries 8 and 9). Other inorganic or organic bases screened did not enhance the yield of the target product (Table S1, entries 10 and 11). While the reaction performed under air decreased the reaction efficiency to 70% yield (Table S1, entry 12), N_2 atmosphere delivered only a trace amount of **3aa** (Table S1, entry 13). Then 2 equiv of K_3PO_4 was found to be beneficial since the yield decreased with a reduction of the amount of base (Table S1, entries 14 and 15). Finally, when acetaldehyde or ethylamine (3 equiv) instead of triethylamine was subjected to this $Cu(OAc)_2/O_2$ catalytic system, a moderate yield of **3aa** was obtained (Table S1, entries 16 and 17), which might be due to the higher levels of reactivity of the iminium ion intermediate in situ generated by the copper-initiated single-electron oxidation of **2a**.

Having identified the optimized reaction conditions in hand, we next probed the reaction generality and the scope of the substrates (Table 1). Generally, arylamidines bearing either electron-donating or electron-withdrawing groups (**1b**−**e**) are all efficient substrates, reacting with TEA to provide the desired products in good yields (Table 1, entries 1−5). Pyridinylamidines **1f** (entry 6) and **1g** (entry 7) were also effective, although they gave moderate yields (52% and 61%, respectively). Gratifyingly, when arylamidines were treated with tribenzylamines **2b** and **2c** under the present catalytic $Cu(OAc)_2/O_2$ system, triaryl-substituted 1,3,5-triazines were smoothly obtained in moderate to good yields (Table 1, entries 8−12).

The highlight of this triazine synthesis lies in the capability to prepare various trisubstituted triazines in one step. To our satisfaction, an arbitrary combination of two different arylamidines and trialkylamines under the optimized reaction conditions could afford the cross-cyclized triazines as the major product, albeit with some homocyclized heterocycles. However, the problem related to isolation is evident. Fortunately, by using two different amidines with high polarity difference, a range of cross-cyclized triazines (**3aaa**−**aaf**) have been isolated in moderate yields (Scheme 2).

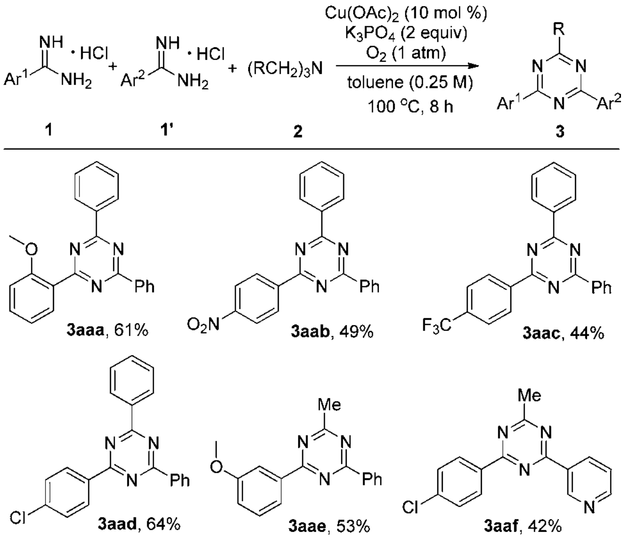
Table 1. Synthesis of Trisubstituted 1,3,5-Triazines[a]



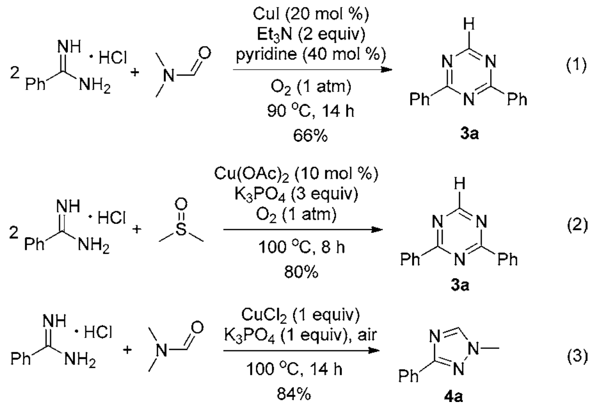
entry	**1** (Ar)	**2** (R)	**3**	yield[b] (%)
1	**1a** (Ph)	**2a** (Me)	**3aa**	85
2	**1b** (4-MeC_6H_4)	**2a** (Me)	**3ba**	81
3	**1c** (4-ClC_6H_4)	**2a** (Me)	**3ca**	62
4	**1d** (4-$CF_3C_6H_4$)	**2a** (Me)	**3da**	65
5	**1e** (3-$OMeC_6H_4$)	**2a** (Me)	**3ea**	69
6	**1f** (pyridin-3-yl)	**2a** (Me)	**3fa**	52
7	**1g** (pyridin-4-yl)	**2a** (Me)	**3ga**	61
8	**1a** (Ph)	**2b** (Ph)	**3ab**	73
9	**1a** (Ph)	**2c** (4-MeC_6H_4)	**3ac**	68
10	**1c** (4-ClC_6H_4)	**2b** (Ph)	**3cb**	46
11	**1d** (4-$CF_3C_6H_4$)	**2b** (Ph)	**3db**	54
12	**1e** (3-$OMeC_6H_4$)	**2b** (Ph)	**3eb**	71

[a] The reaction was performed with **1** (0.25 mmol), **2** (0.25 mmol), $Cu(OAc)_2$ (10 mol %), and K_3PO_4 (2 equiv) in toluene (1 mL) at 100 °C for 8 h. [b] Isolated yields based on **1a**.

Scheme 2. Synthesis of Cross-Cyclized Triazines



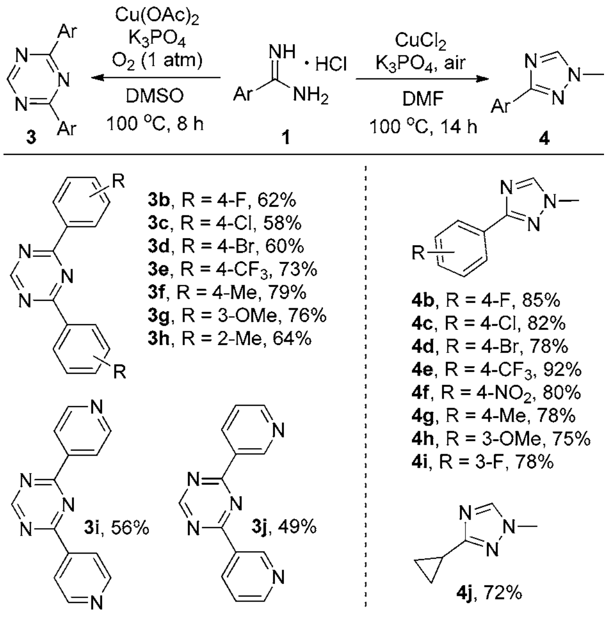
In our previous work, copper-catalyzed aerobic cyclization of amidines using DMF as one carbon source provided novel access to 2,6-diaryl-1,3,5-triazine (**3a**) in moderate to good yields[5e] (eq 1). However, in the present $Cu(OAc)_2/O_2$ system, using DMF as the reaction media did not afford this product; instead, 1-methyl-3-aryl-1,2,4-triazole (**4a**) was isolated as the main product. Interestingly, 2,6-diphenyl-1,3,5-triazine (**3a**) was formed efficiently when DMSO was used as the solvent in the catalytic $Cu(OAc)_2/O_2$ system (eq 2), where DMSO served as an efficient one-carbon source. Moreover, the reaction conditions



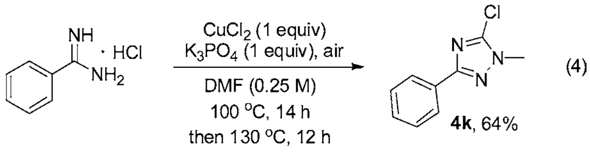
for 1,2,4-triazole synthesis were further modified by changing the catalytic amount of $Cu(OAc)_2$ into stoichiometric $CuCl_2$, which could generate the desired triazole product **4a** in 84% yield (eq 3).

To probe the reaction generality for the synthesis of 2,6-disubstituted 1,3,5-triazines (**3**) and 1,3-disubstituted 1,2,4-triazoles (**4**), a serious of arylamidines were subjected to the DMSO- and DMF-based systems, respectively (Scheme 3). It was found that various functional groups on the benzene ring, such as methyl, fluoro, chloro, bromo, trifluoromethyl, and methoxy, were well tolerated in both systems. The desired three-nitrogen heterocycles were prepared in moderate to good yields. Notably, pyridinylamidines reacted smoothly with DMSO to afford pyridinyltriazines (**3i** and **3j**) in moderate yields, whereas the same substrates could not generate triazole products. In the case of cyclopropylamidine, the corresponding cyclopropyltriazole (**4j**) was formed efficiently.[14]

Scheme 3. Reactions of Amidines with DMSO or DMF

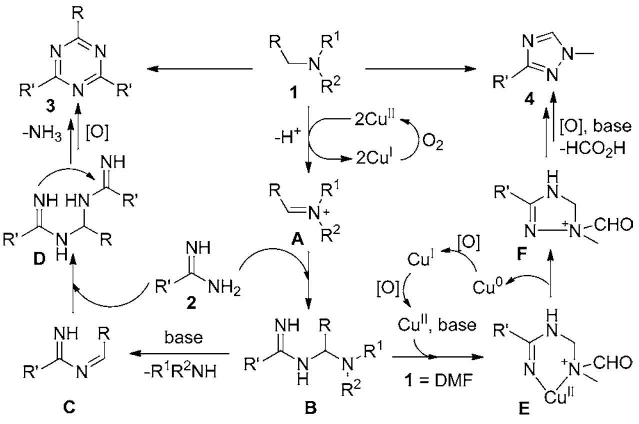


Direct C−H halogenation of the electron-rich aromatic ring under a Cu/O_2 system has been well established. Thus, we hypothesize that the resultant 1,3-disubstituted triazoles could undergo further C5 halogenation in a one-pot manner. While the standard operation led to a trace amount of halogenated product, prolonging the reaction time at an elevated temperature was found optimal to furnish the desired C5 chlorination product **4k** (eq 4). This conveniently provides synthetic flexibility for a further transformation of the resultant heterocycles.



The reaction mechanism of the copper-catalyzed aerobic cyclization of amidines and amines was proposed on the basis of the experimental observation and related work in literature. As shown in Scheme 4, copper-catalyzed $C(sp^3)$−H activation of the amine **1** to form imine-type intermediate **A** via a single-electron-transfer (SET) process would be the first step of these transformations.[10a,e] Subsequently, nucleophilic attack of an imine-type intermediate by the amidine resulted in the formation of intermediate **B**. In the case of tertiary amine, the amine moiety was released to give imine intermediate **C**. The second nucleophilic attack of **C** by another molecular amidine afforded **D**, with an intramolecular nucleophilic cyclization and subsequent oxidation to yield the final 1,3,5-triazine products **3**. When DMF[15] was used as the reaction medium in the catalytic system, copper(II) coordinated with intermediate **B** to form intermediate **E**, which was rather different from the previously reported formation of triazines. Reductive elimination of **E** delivered cyclic product **F**, which underwent hydrolysis and subsequent oxidation to form the final 1,2,4-triazole products. The speculation that the dimethylamine moiety of DMF was integrated into the final triazoles has been demonstrated since benzamidine **1a** could be converted into **4a** when DMA was used as the solvent or treated with tetramethylethylenediamine (TMEDA) in toluene.[16] The copper(0) or copper(I) species generated would be oxidized by oxygen to catalytically active copper(II).[7a] In the DMSO-based system, an analogous SET/nucleophilic attack based reaction sequence would rationalize the generation of 2,6-disubstituted 1,3,5-triazines.

Scheme 4. Possible Reaction Mechanism



As to the special role of base, previous works in the literature revealed that a catalytic system containing K_3PO_4 as base seems to feature very high efficiency for C−heteroatom bond formation, especially for copper-catalyzed C−N bond formation.[17] We hypothesize that K_3PO_4 serves as not only a base but also a phase freshener since normal organic solvents hardly dissolve phosphates. In our system, the reaction mixture behaved as an obvious liquid−solid two-phase system throughout the whole reaction process, so that the crude product could be obtained simply by filtration or centrifugal separation.

In summary, a highly efficient catalytic [Cu]/O_2 system has been developed for the assembly of 1,2,4-triazoles and 1,3,5-triazines from amidines through a catalytic C(sp^3)−H oxidative functionalization. A wide range of the two three-nitrogen-containing heterocycles can be readily accessed by using three different reaction partners: trialkylamines, DMSO, and DMF. The method significantly provides synthetic divergence and flexibility for the synthesis of multinitrogen heterocycles from amidines. These all make the protocol attractive and fascinating. The mechanistic investigation and further application of this method in the synthesis of more complex compounds are currently underway in our laboratory.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

General experimental procedure and characterization data of the products. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b00995.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the National Basic Research Program of China (973 Program) (2011CB808600), the National Natural Science Foundation of China (21172076 and 21420102003), the China Postdoctoral Science Foundation Funded Project (2014M562165), Guangdong Natural Science Foundation (10351064101000000), and Jiangxi Natural Science Foundation (20141BBG70070 and 20151BAB203011).

■ REFERENCES

(1) (a) Sahoo, S.; Veliyath, S. K.; Kumar, M. C. B. *Int. J. Res. Pharm. Sci.* **2012**, *3*, 326. (b) Kathiravan, M. K.; Salake, A. B.; Chothe, A. S.; Dudhe, P. B.; Watode, R. P.; Mukta, M. S.; Gadhwe, S. *Bioorg. Med. Chem.* **2012**, *20*, 5678. (c) Plech, T.; Luszczki, J. J.; Wujec, M.; Flieger, J.; Pizoń, M. *Eur. J. Med. Chem.* **2013**, *60*, 208.

(2) (a) Klenke, B.; Stewart, M.; Barrett, M. P.; Brun, R.; Gilbert, I. H. *J. Med. Chem.* **2001**, *44*, 3440. (b) Iino, Y.; Karakida, T.; Sugamata, N.; Andoh, T.; Takei, H.; Takahashi, M.; Yaguchi, S.; Matsuno, T.; Takehara, M.; Sakato, M.; Kawashima, S.; Morishita, Y. *Anticancer Res.* **1998**, *18*, 171. (c) Suda, A.; Kawasaki, K.; Komiyama, S.; Isshiki, Y.; Yoon, D.-O.; Kim, S. J.; Na, Y.-J.; Hasegawa, K.; Fukami, T. A.; Sato, S. *Bioorg. Med. Chem.* **2014**, *22*, 892.

(3) For 1,2,4-triazole synthesis, see: (a) Moulin, A.; Bibian, M.; Blayo, A.-L.; Habnouni, S. E.; Martinez, J.; Fehrentz, J.-A. *Chem. Rev.* **2010**, *110*, 1809. (b) Holm, S. C.; Straub, B. F. *Org. Prep. Proced. Int.* **2011**, *43*, 319. (c) Tam, A.; Armstrong, I. S.; La Cruz, T. E. *Org. Lett.* **2013**, *15*, 3586. (d) Guru, M. M.; Punniyamurthy, T. *J. Org. Chem.* **2012**, *77*, 5063 and references cited therein.

(4) For 1,3,5-triazine synthesis, see: (a) Diaz-Ortiz, A.; de la Hoz, A.; Moreno, A.; Sanchez-Migallon, A.; Valiente, G. *Green Chem.* **2002**, *4*, 339. (b) Tanaka, H.; Shizu, K.; Miyazaki, H.; Adachi, C. *Chem. Commun.* **2012**, *48*, 11392. (c) Achelle, S.; Ramondenc, Y.; Marsais, F.; Plé, N. *Eur. J. Org. Chem.* **2008**, *14*, 3129. (d) Liu, J.; Wang, K.; Xu, F.; Tang, Z.; Zheng, W.; Zhang, J.; Li, C.; Yu, T.; You, X. *Tetrahedron Lett.* **2011**, *52*, 6492.

(5) (a) Gold, H. *Angew. Chem.* **1960**, *72*, 956. (b) Bredereck, H.; Effenberger, F.; Hofmann, A. *Chem. Ber.* **1963**, *96*, 3265. (c) Huffman, K. R.; Schaefer, F. C. *J. Org. Chem.* **1963**, *28*, 1812. (d) Wessig, P.; Schwarz, J. *Monatsh. Chem.* **1995**, *126*, 99. (e) Xu, X.; Zhang, M.; Jiang, H.; Zheng, J.; Li, Y. *Org. Lett.* **2014**, *16*, 3540.

(6) (a) Biswas, S.; Batra, S. *Eur. J. Org. Chem.* **2012**, *18*, 3492. (b) Xie, F.; Chen, M.-M.; Wang, X.-T.; Jiang, H.-F.; Zhang, M. *Org. Biomol. Chem.* **2014**, *12*, 2761.

(7) (a) Ueda, S.; Nagasawa, H. *J. Am. Chem. Soc.* **2009**, *131*, 15080. (b) Francis, J. E.; Gorczyca, L. A.; Mazzenga, G. C.; Meckler, H. *Tetrahedron Lett.* **1987**, *28*, 5133. (c) Castanedo, G. M.; Seng, P. S.; Blaquiere, N.; Trapp, S.; Staben, S. T. *J. Org. Chem.* **2011**, *76*, 1177. (d) Staben, S. T.; Blaquiere, N. *Angew. Chem., Int. Ed.* **2010**, *49*, 325.

(8) (a) Sudheendran, K.; Schmidt, D.; Frey, W.; Conrad, J.; Beifuss, U. *Tetrahedron* **2014**, *70*, 1635. (b) Xu, H.; Jiang, Y.; Fu, H. *Synlett* **2013**, *24*, 125.

(9) Brough, P.; Gambarelli, S.; Jacquot, J.-F.; Grand, A.; Pcaut, J.; Rey, P. *Chem.—Eur. J.* **2011**, *17*, 11250.

(10) (a) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335. (b) Allen, S. E.; Walvoord, R. R.; Padilla-Salinas, R.; Kozlowski, M. C. *Chem. Rev.* **2013**, *113*, 6234. (c) Lewis, E. A.; Tolman, W. B. *Chem. Rev.* **2004**, *104*, 1047. (d) Wu, W.; Jiang, H. *Acc. Chem. Res.* **2012**, *45*, 1736. (e) Zhang, C.; Tang, C.; Jiao, N. *Chem. Soc. Rev.* **2012**, *41*, 3464. (f) Wendlandt, A. E.; Suess, A. M.; Stahl, S. S. *Angew. Chem., Int. Ed.* **2011**, *50*, 11062. (g) Wu, W.; Jiang, H. *Acc. Chem. Res.* **2014**, *47*, 2483. (h) Zhang, Z.; Ouyang, L.; Wu, W.; Li, J.; Zhang, Z.; Jiang, H. *J. Org. Chem.* **2014**, *79*, 10734.

(11) For representative examples, see: (a) Li, Z.; Li, C.-J. *J. Am. Chem. Soc.* **2004**, *126*, 11810. (b) Li, Z.; Li, C.-J. *J. Am. Chem. Soc.* **2005**, *127*, 3672. (c) Zhao, L.; Li, C.-J. *Angew. Chem., Int. Ed.* **2008**, *47*, 7075. (d) Zhang, G.; Zhang, Y.; Wang, R. *Angew. Chem., Int. Ed.* **2011**, *50*, 10429. (e) Boess, E.; Sureshkumar, D.; Sud, A.; Wirtz, C.; Farès, C.; Klussmann, M. *J. Am. Chem. Soc.* **2011**, *133*, 8106.

(12) (a) Wan, C. F.; Zhang, J. T.; Wang, S. J.; Fan, J. M.; Wang, Z. Y. *Org. Lett.* **2010**, *12*, 2338. (b) Wan, C. F.; Gao, L. F.; Wang, Q.; Zhang, J. T.; Wang, Z. Y. *Org. Lett.* **2010**, *12*, 3902. (c) Zeng, L. Y.; Yi, W. B.; Cai, C. *Eur. J. Org. Chem.* **2012**, *2012*, 559. (d) Han, B.; Yang, X. L.; Wang, C.; Bai, Y. W.; Pan, T. C.; Chen, X.; Yu, W. *J. Org. Chem.* **2011**, *77*, 1136. (e) Han, B.; Wang, C.; Han, R. F.; Yu, W.; Duan, X. Y.; Fang, R.; Yang, X. L. *Chem. Commun.* **2011**, *47*, 7818. (f) Yan, Y. Z.; Wang, Z. Y. *Chem. Commun.* **2011**, *47*, 9513. (g) Jiang, H.; Huang, H.; Cao, H.; Qi, C. *Org. Lett.* **2010**, *12*, 5561. (h) Huang, H.; Ji, X.; Wu, W.; Jiang, H. *Adv. Synth. Catal.* **2013**, *355*, 170. (i) Huang, H.; Ji, X.; Wu, W.; Huang, L.; Jiang, H. *J. Org. Chem.* **2013**, *78*, 3774.

(13) (a) Jiang, H.; Li, X.; Pan, X.; Zhou, P. *Pure. Appl. Chem.* **2012**, *84*, 553. (b) Li, X.; He, L.; Chen, H.; Wu, W.; Jiang, H. *J. Org. Chem.* **2013**, *78*, 3636. (c) Li, X.; Huang, L.; Chen, H.; Wu, W.; Huang, H.; Jiang, H. *Chem. Sci.* **2012**, *3*, 3463. (d) Huang, H.; Ji, X.; Tang, X.; Zhang, M.; Li, X.; Jiang, H. *Org. Lett.* **2013**, *15*, 6254. (e) Huang, L.; Jiang, H.; Qi, C.; Liu, X. *J. Am. Chem. Soc.* **2010**, *132*, 17652.

(14) GC yield of **4j** was given. No product could be obtained after flash column chromatography, which was probably due to the instability or the volatility of this compound.

(15) Ding, S.; Jiao, N. *Angew. Chem., Int. Ed.* **2012**, *51*, 9226.

(16) See the Supporting Information for details.

(17) (a) Klapars, A.; Huang, X.; Buchwald, S. L. *J. Am. Chem. Soc.* **2002**, *124*, 7421. (b) Fukudome, Y.; Naito, H.; Hata, T.; Urabe, H. *J. Am. Chem. Soc.* **2008**, *130*, 1820. (c) Rao, H.; Fu, H.; Jiang, Y.; Zhao, Y. *J. Org. Chem.* **2005**, *70*, 8107. (d) Altman, R. A.; Anderson, K. W.; Buchwald, S. L. *J. Org. Chem.* **2008**, *73*, 5167. (e) Cacchi, S.; Fabrizi, G.; Parisi, L. M. *Org. Lett.* **2003**, *5*, 3843. (f) Sanjaya, S.; Chiba, S. *Org. Lett.* **2012**, *14*, 5342. (g) Chen, H.; Sanjaya, S.; Wang, Y.-F.; Chiba, S. *Org. Lett.* **2013**, *15*, 212. (h) Chiba, S.; Zhang, L.; Lee, J.-Y. *J. Am. Chem. Soc.* **2010**, *132*, 7266. (i) Wang, H.; Wang; Liang, Y. D.; Liu, L.; Zhang, J.; Zhu, Q. *Angew. Chem., Int. Ed.* **2011**, *50*, 5678.