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ARTICLE

# Copper Mediated C–H Amination with Oximes: En Route to Primary Anilines

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Here we report an efficient Cu(I)-mediated C–H amination reaction with oximes as amino donor to introduce $NH_2$ group directly. Various strongly coordinating heterocycles including quinoline, pyrimidine, pyrazine, pyrazole and triazole were well tolerated. The potential utility was further demonstrated in a late-stage modification of Telmisartan (an antagonist for the angiotensin II receptor).

## Introduction

Primary anilines are important structural motif present in many natural and pharmaceutical compounds (Figure 1).[1] For example, Retigabine is an anticonvulsant used as an adjunctive treatment for partial epilepsies in treatment-experienced adult patients.[2] Anileridine as a member of the piperidine class of analgesic agents is used be analgesic drug.[3] Mesalazine is an aminosalicylate anti-inflammatory drug for treating inflammatory bowel disease,[4] and lenalidomide is a tumour necrosis factor (TNF) inhibitors and can be used to treat multiple myeloma.[5] The development of efficient and practical approaches to access this type of compounds is highly in demand and remains a challenge in organic synthesis.[6]

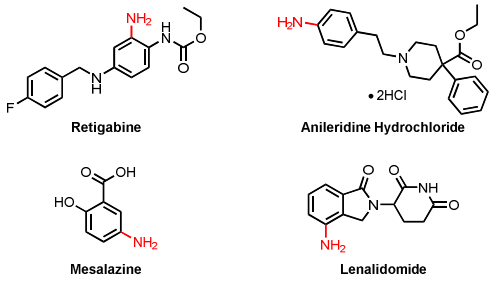
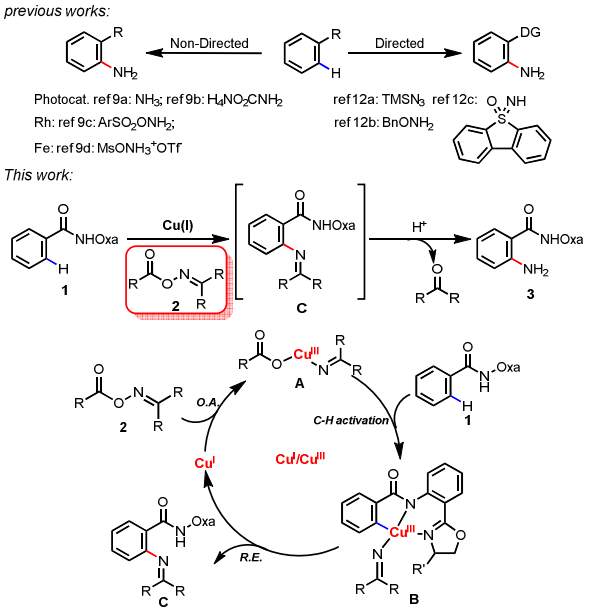



**Fig. 1** Selected drug molecules containing primary anilines.

Recently, C–H amination via transition-metal catalyzed C–H activation process has attracted considerable attention and has been proved to be a useful method to prepare amine molecules.[7] Among these C–H amination reactions, only a few examples were able to directly introduce an unprotected amino group to form primary anilines.[8] These reactions can be classified into two approaches: nondirected and directed (Scheme 1). The former exploits the innate reactivity of the substrates. For examples, nondirected amination of arenes involving photocatalysis were realized by the Tung[9a] and Nicewicz[9b] groups independently.




**Scheme 1** The direct synthesis of primary anilines by C–H amination

Transition metal-catalyzed C–H aminations of arenes were also reported by two groups of Falck[9c] and Morandi[9d]. However, controlling the positional selectivity effectively remains to be a great challenge in these reactions. In recent years, the use of directing group has become a reliable approach to realize selective C–H functionalization.[10] However,

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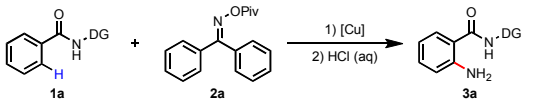
few examples on C–H amination to prepare the primary anilines are known. The use of chacogenide amine donors are largely limited to alkyl amines[11]. In 2014, Zhu group reported an example on employing the $TMSN_3$ as a nitrogen source to form primary anilines[12a]. Uchiyama and co-workers developed another aminated protocol which using $BnONH_2$ as aminated agent and involving the deprotonative cupration with a stoichiometric amount of $(TMP)_2Cu(CN)Li_2$[12b]. More recently, the Bolm and coworkers developed a new reagent dibenzothiophene sulfoximine as the $NH_3$ surrogate to synthesize primary anilines.[12c] However, site selective C–H amination in late-stage heterocycle drug discovery is always a thorny problem, because that heterocycles competed with directing groups for coordination to a metal catalyst, and may result in the poisoning of a catalyst or the functionalization of an undesired C–H bond. Herein, we first reported a facile Cu(I)-mediated $C_{sp2}$–H amination using the oximes derivatives as an aminated agent, in which the free amine products can be easily obtained upon in-situ hydrolysis. The potential use of this method in late-stage diversification for drug discovery was exemplified in the directed amination of Telmisartan.

Oximes derivatives as a class of versatile building blocks has been applied in a number of transition metal-catalyzed C–H functionalization.[13] Due to the weaker N–O σ bond (~57 kcal mol−1) than normal σ C–X (X = C, N, O) bonds, oximes derivatives could not only act as amino source but also as oxidants. Based on our previous works[14] and oximes chemistry reported by other groups,[13] we proposed a Cu(I) to Cu(III) catalytic cycle (Scheme 1): the first step is oxidative insertion of Cu(I) species into the N-O bond to give the Cu(III) intermediate **A**. After coordination of bidentate directing group oxazoline-amide to Cu(III) complex **A**, C–H activation occurs to generate the intermediate **B**. Subsequent reductive elimination affords imines compound **C** and regenerates Cu(I). Finally, imines compound **C** can be hydrolyzed to form primary amine **3** and ketone.

## Results and discussion

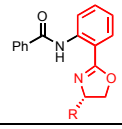
Based on this hypothesis, we initiated studies by investigating the C–H amination of N-arylbenzamide substrate **1a** with oxime **2a**. Encouragingly, we found that C–H amination of **1a-A** with 1.5 equiv of **2a** occurred in the presence of 20 mol % CuOAc in DMSO at 100 °C for 8 h, and the desired aminated product **3a-A** was obtained in 28% yield after acid hydrolysis. The structure of the product **3a-A** was confirmed by X-ray crystallography (Table 1). Other copper catalysts were also investigated (Table 1, entries 1-4), and CuOAc was still the optimal one. Subsequently, we investigated the influence of the directing groups (DG) (Table 1, entries 5-9) on the efficiency of the amination reaction. We found that the use of substrate **1a-B** containing the methyl-substituted oxazoline **DG B** afforded aminated product **3a-B** in 35% yield. Interestingly, the use of Daugulis's 8-aminoquinoline DG under the same conditions did not provide any desired product (entry 9). This result is consistent with our early observation.[14] The yield was improved to 40% by further increasing the amount of CuOAc to 30 mol %. After screening a series of bases (see SI), a higher yield of 49% was obtained using 1 equiv of $K_2HPO_4$ as a base. Considering that the product binds to the catalyst better than the starting material, increasing the amount of copper may be beneficial to the reaction. Indeed, we found that when 1.5 equiv of CuOAc was used, the yield could be increased to 58% with full conversion of substrate **1a** (Table 1, entry 13), which implied that the substrate was decomposed partially at this temperature. Finally, we screened the temperature (Table 1, entries 14-16), and found that a satisfactory yield of 78% could be obtained at 90 °C (entry 14).

**Table 1** Optimization of reaction conditions[a]

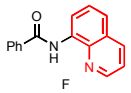



**1a** **2a** **3a**

| entry | DG | [Cu] (equiv) | base | temp, °C | yield, %[b] |
|---|---|---|---|---|---|
| 1 | A | CuOAc (0.2) | - | 100 | 28 |
| 2 | A | CuBr (0.2) | - | 100 | 24 |
| 3 | A | CuCl (0.2) | - | 100 | 25 |
| 4 | A | $Cu(OAc)_2$(0.2) | - | 100 | 21 |
| 5 | B | CuOAc (0.2) | - | 100 | 35 |
| 6 | C | CuOAc (0.2) | - | 100 | 20 |
| 7 | D | CuOAc (0.2) | - | 100 | 20 |
| 8 | E | CuOAc (0.2) | - | 100 | 21 |
| 9 | F | CuOAc (0.2) | - | 100 | n.d. |
| 10 | B | CuOAc (0.3) | - | 100 | 40 |
| 11 | B | CuOAc (0.3) | $K_2HPO_4$ | 100 | 49 |
| 12 | B | CuOAc (1.0) | $K_2HPO_4$ | 100 | 52 |
| 13 | B | CuOAc (1.5) | $K_2HPO_4$ | 100 | 58 |
| ***14*** | ***B*** | ***CuOAc (1.5)*** | ***$K_2HPO_4$*** | ***90*** | ***78 (73)[c]*** |
| 15 | B | CuOAc (1.5) | $K_2HPO_4$ | 80 | 66 |
| 16 | B | CuOAc (1.5) | $K_2HPO_4$ | 70 | 59 |

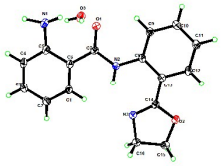



A: R = H
B: R = Me
C: R = *i*-Pr
D: R = *t*-Bu
E: R = Ph




F

[a] Reaction Conditions: 1) **1a** (0.1 mmol), **2a** (0.15 mmol), [Cu], base (0.1 mmol), DMSO (1 mL), $N_2$, 8 h; 2) 2 M HCl (2 mL), rt. 20 mins. [b] Yield determined by $^1$H NMR analysis of crude reaction product using $CH_2Br_2$ as internal standard. [c] Isolated yield is given in parentheses.



**3a-A**

After the optimal reaction condition was found, we proceeded to examine the substrate scope. As shown in Table 2, a wide variety of substituted benzamides were reactive. 2-Methyl substituted substrates **1b** gave the aminated product in a moderated yield of 54%. Various electron-donating and -withdrawing substituents including methyl **1c**, *t*-butyl **1d**, methoxyl **1e**, fluoro **1f**, chloro **1g**, bromo **1h**, acetyl **1i**, trifluoromethyl **1j** and phenyl **1k** , vinyl **1l** at 4-position on benzamides were compatible in the reaction, affording the desired products in moderate to good yields. When the 3-positions of on benzamides were substituted with methyl, methoxyl or fluoro, the C–H activation took place at both 2- and 6-positions to give two regioisomeric products, with the less hindered 6-position-aminated product as a major. In the case of the benzamide bearing 3-$CF_3$ (**3p**), only 6-position-aminated product was obtained. Gratifyingly, this copper-mediated C–H amination protocol was compatible with a wide variety of heterocycles, including pyridines, quinoline, and benzothiphene-derived substrates

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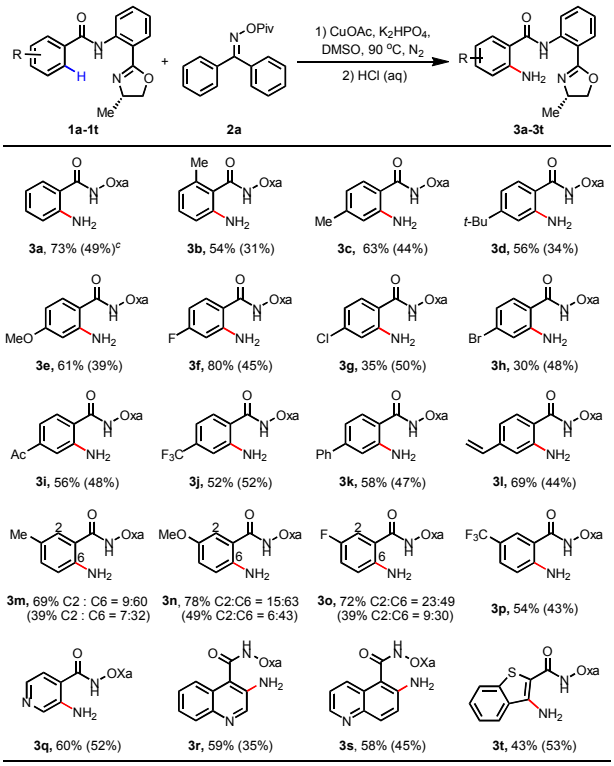
(**3q-t**). Notably, 0.3 equiv of CuOAc was sufficient go enable the amination reaction (the yields were also shown in the parentheses), and the yields were even higher than those obtained in the reactions using 1.5 equiv of CuOAc in some cases (**3g**, **3h** and **3t**).

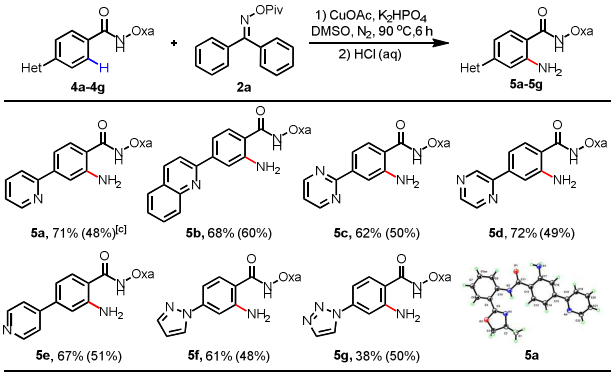
**Table 2** The scope of C–H amination[a, b]




[a] Reaction Conditions: 1) **1a-1t** (0.1 mmol), **2a** (0.15 mmol), CuOAc (0.15 mmol), $K_2HPO_4$ (0.1 mmol), DMSO (1 mL), $N_2$, 90 °C, 8 h; 2) 2 M HCl (2 mL), rt. 20 mins. [b] Isolated yield. [c] 0.3 equiv of CuOAc was used in parentheses.

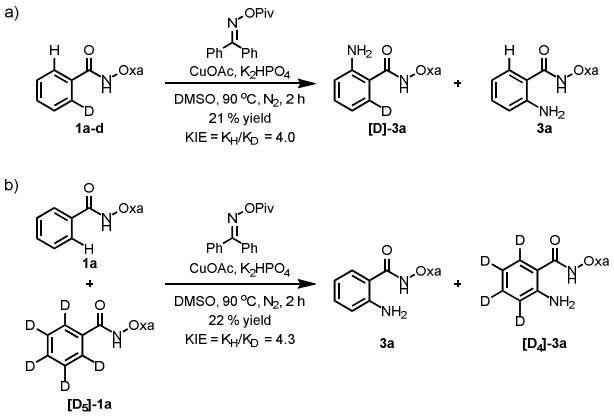
Inspired by previous examples on overcoming the positional selectivity with substrates containing strongly coordinating heterocycles,[15] we subsequently examined whether the C–H amination system could override the heterocycle-directed cyclometalation (Table 3). We chose para-(2-pyridyl)benzamide as a test substrate. Under the

**Table 3** Overcoming the limitation of heterocycles in C–H amination[a, b]



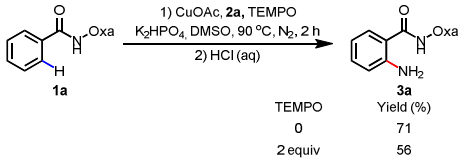

[a] Reaction Conditions: 1) **4a-4g** (0.1 mmol), **2a** (0.15 mmol), CuOAc ( 0.15 mmol), $K_2HPO_4$ (0.1 mmol), DMSO (1 mL), 90 °C, 6 h, $N_2$. 2) 2 M HCl (2 mL), rt. 20 mins. [b] Isolated yield. [c] 0.3 equiv of CuOAc was used in parentheses.

standard conditions, C–H amination proceeded exclusively at the position *ortho* to the amide group, providing the desired product in 71% isolated yield. The structure of **5a** was confirmed by X-ray crystallography. Furthermore, when the pyridine was replaced with other medicinally important heterocycles, including a quinoline, pyrimidine, pyrazine, pyrazole and triazole, the amide group was still an effective directing group, and the desired aminated products were formed in moderate to good yields (38-72%). Furthermore, the reactions using 0.3 equiv of CuOAc as the catalyst were also examined (the yields were also shown in the parentheses).




**Scheme 2** a) Intramolecular kinetic isotope effect (KIE); b) Intermolecular KIE

To probe the reaction mechanism, we measured intra- and intermolecular kinetic isotope effects. Significant isotope effects were observed in both cases (Scheme 2). In addition, the addition of radical scavenger 2,2,6,6-tetramethylpiperidine-N-oxyl (TEMPO) did not affect the reaction efficiency under optimized conditions, which indicates that a radical pathway is unlikely (Scheme 3). These combined data support a mechanism which involves a copper-mediated C–H cleavage step rather than an electrophilic aromatic substitution (SEAr) or radical pathway. Therefore, we proposed a Cu(I) to Cu(III) mechanism as shown in Scheme 1.




**Scheme 3** The effect of TEMPO.

We also conducted the reaction on a gram scale under 0.3 and 1.5 equiv of CuOAc, **3a** was obtained in 45% and 62% yield respectively, and most of benzophenone was recovered (see SI). Removal of this amide-oxazoline DG was demonstrated by treating product **3a** with 2 N KOH/EtOH at 80 °C to release the corresponding carboxylic acid and oxazolyamide DG in good yields (Scheme 4). Interestingly, when the aminated products were treated with concentrated HCl at 190 °C, a series of different substituted primary anilines were obtained with complete removal of the amide-oxazoline part (Table 4).[16] Especially

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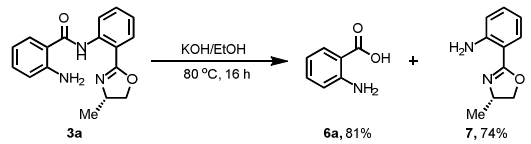
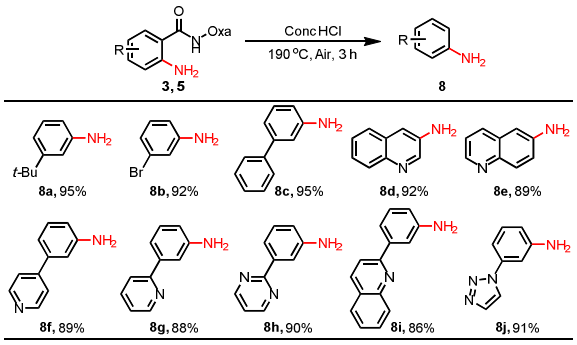
primary anilines containing heterocycles are accessible via this approach, a good complement to early reported nondirected C–H aminations.[9]



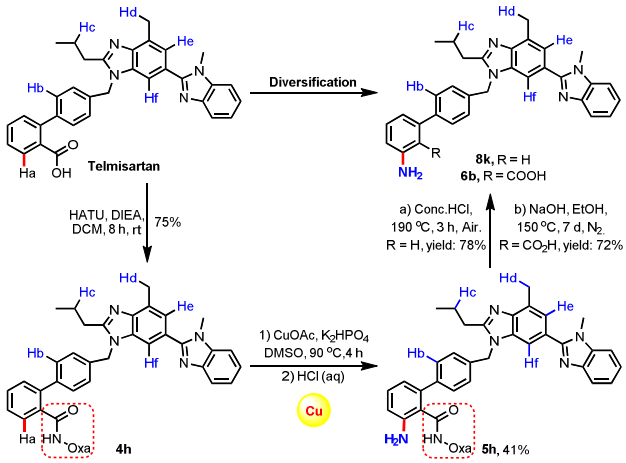

**Scheme 4** Removal of the directing group

**Table 4** The transformation of aminated product[a, b]




[a] Reaction Conditions: **3, 5** (0.03 mmol), Conc HCl (0.5 ml), 190 °C, 3 h, Air, [b] Isolated yield.

To further demonstrate the viability of the C–H amination reactions for late-stage diversification in drug discovery, we chose Telmisartan, an antagonist for the angiotensin II receptor, for functionalization (Scheme 5). As we mentioned earlier,[15f] there are multiple reactive C–H bond in this molecule, which significantly enhance the difficulty of selective functionalization of the target C–H bond. By installing the directing group amide oxazoline into the molecule, we were pleased to find that C–H amination occurred exclusively at the amide-directed position, while other C–H functionalization products were not observed. Furthermore, the resulted aminated product were treated under acidic or alkaline conditions respectively to afford two derivatives **8k** and **6b**.




**Scheme 5** Late-stage diversification of Telmisartan

## Conclusions

In summary, we have developed a Cu(I)-mediated C–H amination reaction for the synthesis of primary anilines. A catalytic cycle involving Cu(I) to Cu(III) was proposed, and the oximes derivatives not only act as the amino source but also as oxidant. This practical reaction is compatible with various functional groups as well as diverse strongly coordinating heterocycles. The potential utility of this method was demonstrated by the late-stage diversification of the drug molecule Telmisartan.

## Conflicts of interest

The authors declare no conflict of interest.

## Acknowledgements

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## References

1 (a)Amines: Synthesis Properties and Applications (Eds.: S. A. Lawrence), Cambridge University Press, Cambridge, **2004**; (b) The Chemistry of Anilines, Parts 1 and 2 (Eds.: Z. Rappoport), John Wiley & Sons, New York, **2007**; (c) Alkaloids. Secrets of Life (Eds.: T. Aniszewski), Elsevier Science, Amsterdam, **2007**; (d) Amino Group Chemistry: From Synthesis to the Life Sciences (Eds.: A. Ricci), Wiley-VCH, Weinheim, **2008**.

2 R. J. Porter, V. Nohria and C. Rundfeldt, *Neurotherapeutics*. **2007**, *4*, 149.

3 J. Weijlard, P. D. Orahoyats, A. P. S. Jr, G. Purdue, F. K. Heath and K. Pfister, *J. Am. Chem. Soc.* **1956**, *78*, 2342.

4 L. P. Yang and P. L. Mccormack, *Drugs*. **2011**, *71*, 221.

5 J. B. Bartlett, K. Dredge and A. G. Dalgleish, *Nature Reviews Cancer*. **2004**, *4*, 314.

6 (a) Q. Shen and J. F. Hartwig, *J. Am. Chem. Soc.* **2006**, *128*, 10028; (b) H. Rao, H. Fu, Y. Jiang and Y. Zhao, *Angew. Chem., Int. Ed.* **2009**, *48*, 1114; (c) N. Xia and M. Taillefer, *Angew. Chem., Int. Ed.* **2009**, *48*, 337; (d) S. N. Mlynarski, A. S. Karns and J. P. Morken, *J. Am. Chem. Soc.* **2012**, *134*, 16449; (e) C. Zhu, G. Li, D. H. Ess, J. R. Falck and L. Kürti, *J. Am. Chem. Soc.* **2012**, *134*, 18253; (f) A. Borzenko, N. L. Rotta-Loria, P. M. MacQueen, C. M. Lavoie, R. McDonald and M. Stradiotto, *Angew. Chem., Int. Ed.* **2015**, *54*, 3773; (g) H. Yue, L. Guo, H.-H. Liao, Y. Cai, C. Zhu and M. Rueping, *Angew. Chem. Int. Ed.* **2017**, *56*, 4282.

7 (a) P. Subramanian, G. C. Rudolf and K. P. Kaliappan, *Chem. Asian J.* **2016**, *11*, 168; (b) D. Hazelard, P.-A. Nocquet and P. Compain, *Org. Chem. Front.* **2017**, *4*, 2500; (c) M. C. Henry, M. A. B. Mostafa and A. Sutherland, *Synthesis* **2017**, *49*, 4586; (d) Y. Park, Y. Kim and S. Chang, *Chem. Rev.* **2017**, *117*, 9247.

8 L. Legnani, B. N.Bhawal and B. Morandi, *Synthesis* **2017**, *49*, 776.

9 (a) Y.-W. Zheng, B. Chen, P. Ye, K. Feng, W. Wang, Q.-Y. Meng, L.-Z. Wu and C.-H. Tung, *J. Am. Chem. Soc.* **2016**, *138*, 10080; (b) N. A. Romero, K. A. Margrey, N. E. Tay and D. A. Nicewicz, *Science* (Washington, D. C.) **2015**, *349*, 1326; (c) M. P. Paudyal, A. M.

View Article Online
DOI: 10.1039/C8SC01256C


Adebesin, S. R. Burt, D. H. Ess, Z. Ma, L. Kürti and J. R. Falck, *Science* (Washington, D. C.) **2016**, *353*, 1144; (d) L. Legnani, G. Prina Cerai and B. Morandi, *ACS Catal.* **2016**, *6*, 8162; (e) L. Legnani and B. Morandi, *Angew. Chem. Int. Ed.* **2016**, *55*, 2248.

10 (a) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879; (b) C.-H. Jun, J.-B. Hong and D.-Y. Lee, *Synlett*, **1999**, *1*, 1; (c) D. A. Colby, R. G. Bergman and J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624; (d) O. Daugulis, H.-Q. Do and D. Shabashov, *Acc. Chem. Res.* **2009**, *42*, 1074; (e) T. W. Lyons and M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147; (f) C. S. Yeung and V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215; (g) K. M. Engle, T. –S. Mei, M. Wasa and J.-Q. Yu, *Acc. Chem. Res.* **2012**, *45*, 788; (h) D. Leow, G. Li, T.-S. Mei and J.-Q.Yu, *Nature* **2012**, *486*, 518.

11 (a) Y.-H. Tan and J. F. Hartwig, *J. Am. Chem. Soc,* **2010**, *132*, 3676; (b) K.-H. Ng, A. S. C. Chan and W.-Y. Yu, *J. Am. Chem. Soc.* **2010**, *132*, 12862; (c) E. J. Yoo, S. Ma, T.-S. Mei, K. S. L. Chan and J.-Q. Yu, *J. Am. Chem. Soc.* **2011**, *133*, 7652; (d) M. Shang, S.-H. Zeng, S.-Z. Sun, H.-X. Dai and J.-Q. Yu, *Org. Lett.* **2013**, *15*, 5286; (e) K. Foo, E. Sella, I. Thomé, M. D. Eastgate and P. S. Baran, *J. Am. Chem. Soc.* **2014**, *136*, 5279; (f) D. Zhu, G. Yang, J. He, L. Chu, G. Chen, W. Gong, M. D. Eastgate and J.-Q. Yu, *Angew. Chem. Int. Ed.* **2015**, *54*, 2497; (g) J. He, T. Shigenari and J.-Q. Yu, *Angew. Chem., Int. Ed.* **2015**, *54*, 6545; (h) P. Wang, G. C. Li, P. Jain, M. E. Farmer, J. He, P.-X. Shen, and J.-Q. Yu, *J. Am. Chem. Soc.* **2016**, *138*, 14092.

12 (a) J. Peng, M. Chen, Z. Xie, S. Luo and Q. Zhu, *Org. Chem. Front.* **2014**, *1*, 777; (b) N. Tezuka, K. Shimojo, K. Hrano, S. Komagawa, K. Yoshida, C. Wang, K. Miyamoto, T. Saito, R. Takita and M. Uchiyama, *J. Am. Chem. Soc.* **2016**, *138*, 9166; (c) Z. Li, H. Yu and C. Bolm, *Angew. Chem. Int. Ed.* **2017**, *56*, 9532.

13 (a) M. Kitamura and K. Narasaka, *The Chemical Record,* **2002**, *2*, 268; (b) H. Huang, X. Ji, W. Wu and H. Jiang, *Chem. Soc. Rev.,* **2015**, *44*, 1155; (c) H. Huang, J. Cai and G.-J. Deng, *Org. Biomol. Chem.,* **2016**, *14*, 1519.

14 (a) M. Shang, S.-Z. Sun, H.-X. Dai and J.-Q. Yu, *J. Am. Chem. Soc.* **2014**, *136*, 3354; (b) M. Shang, H.-L. Wang, S.-Z. Sun, H.-X. Dai and J.-Q. Yu, *J. Am. Chem. Soc.* **2014**, *136*, 11590; (c) M. Shang, S.-Z. Sun, H.-L. Wang, B. N. Laforteza, H.-X. Dai and J.-Q. Yu, *Angew. Chem. Int. Ed.* **2014**, *53*, 10439; (d) M. Shang, S.-Z. Sun, H.-X. Dai and J.-Q. Yu, *Org. Lett.* **2014**, *16*, 5666; (e) H.-L. Wang, M. Shang, S.-Z. Sun, Z.-L. Zhou, B. N. Laforteza, H.-X. Dai and J.-Q. Yu, *Org. Lett.* **2015**, *17*, 1228; (f) S.-Z. Sun, M. Shang, H.-L. Wang, H.-X. Lin, H.-X. Dai and J.-Q. Yu, *J. Org. Chem.* **2015**, *80*, 8843.

15 (a) H. A. Malik, B. L. Taylor, J. R. Kerrigan, J. E. Grob, K. Houk, J. Du Bois, L. G. Hamann and A. W. Patterson, *Chem. Sci.* **2014**, *5*, 2352; (b) Y.-J. Liu, H. Xu, W.-J. Kong, M. Shang, H.-X. Dai and J.-Q. Yu, *Nature* **2014**, *515*, 389; (c) W.-J. Kong, Y.-J. Liu, H. Xu, Y.-Q. Chen; H.-X. Dai and J.-Q. Yu, *J. Am. Chem. Soc.* **2016**, *138*, 2146; (d) H. Wang, M. M. Lorion and L. Ackermann, *Angew. Chem., Int. Ed.* **2016**, *55*, 10386; (e) W.-J. Kong, X. Chen, M. Wang, H.-X. Dai and J.-Q. Yu, *Org. Lett.* **2018**, *20*, 284; (f) M. Shang, M.-M. Wang, T. G. Saint-Denis, M.-H. Li, H.-X. Dai and J.-Q. Yu, *Angew. Chem. Int. Ed.* **2017**, *56*, 5317.

16 (a) J. Sinnreich, *Synthesis*. **1980**, 578; (b) Advanced Organic Chemistry: Reactions, Mechanisms, and Structure 5th ed. (Eds.: M. B. Smith, J. March), Wiley-Interscience: New York, **2001**; (c) D. Baruah, D. Konwar, *Catalysis Communications*. **2015**, *69*, 68.



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