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Directed C3-Alkoxymethylation of Indole via Three-Component Cascade Reaction

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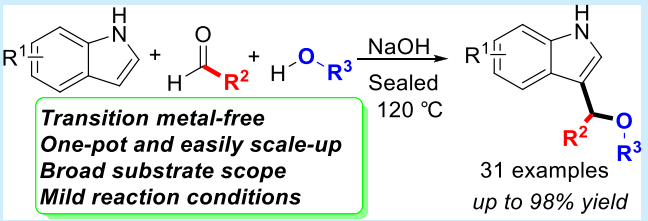
Supporting Information

ABSTRACT: An efficient and regioselective C3-alkoxymethylation of indoles has been developed with aldehydes and alcohols via three-component cascade reaction under transition-metal free conditions. This method allows for rapid access to a variety of C3-alkoxymethylaed free (N−H) indole in up to 98% yield with excellent regioselectivity. The titled products are useful building blocks in organic synthesis.



Indole is a privileged scaffold, acting as an important building block in the synthesis of natural products, pharmaceuticals, and functional materias.[1] Especially, the 3-substituted indole is widely found in biologically active molecules,[2] such as anticancer, anti-inflammatory, antidepressant, anti-Alzheimer, and antihypertensive, as exemplified in Figure 1. Consequently, developing simple and efficient access to build such a motif is of great significance.

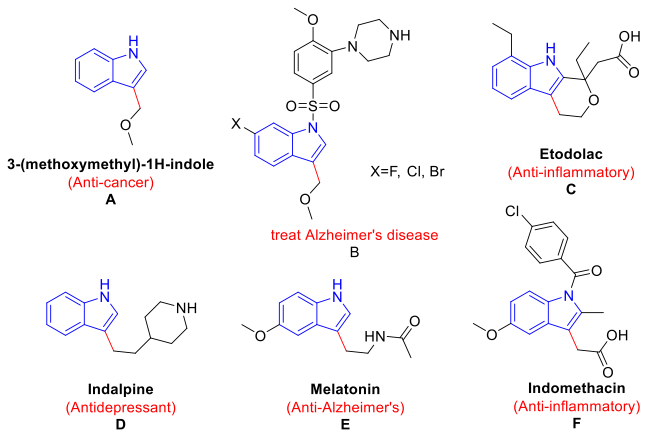
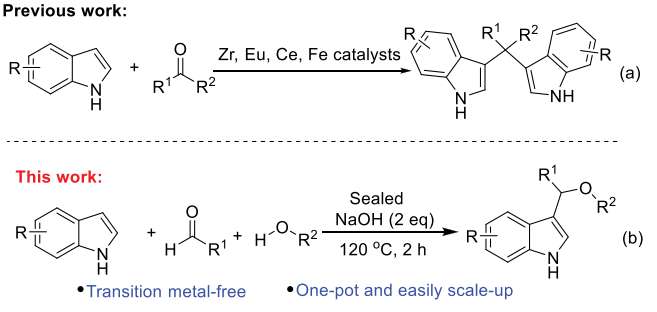


Figure 1. Examples illustrating the importance of 3-substituted indoles of interest.

Traditional methods based on the cyclization are the choice for the synthesis of 3-substituted indoles.[3] However, these protocols suffer from tedious procedures, low atom economy, and relatively harsh reaction conditions. In contrast, the direct C3−H functionalization of commercially available indoles has emerged as an increasingly viable strategy due to its convenience, atomic economy, step economy, and high efficiency.[4] Although various transition-metal catalyzed strategies have been developed,[5] some problems still exist, such as requirement of transition metals as catalysts, which may cause potential contamination of the products, particularly significant in the pharmaceutical industry and advanced functional materials. Moreover, functionalization at the C3 of free (N−H) indoles is still challenging because competing reactions exist at N1 and C2 due to the inherent reactivity of the aromatic system.[5a−d,6] Furthermore, the side reactions such as polymerization and dimerization are difficult to avoid for the electron-rich indoles.[7] Therefore, a general, straightforward, and metal-free strategy to highly regioselective access C3-functionlization starting from free (N−H) indoles remains highly desirable.[8]

The reactions at indole C3 position have been successfully performed employing aldehydes or ketones in the presence of catalyst, and the final products obtained are generally diindolylmethane derivatives (Scheme 1a).[9] However, to the best of our knowledge, highly regioselective C3 alkoxymethylation of indoles with aldehydes has not been developed. Based

Scheme 1. C3-Functional Alkylation Strategies of Indoles



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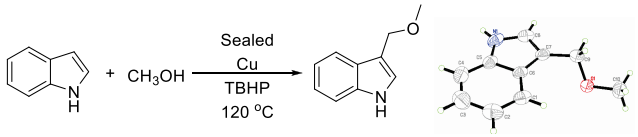
on these important precedents and our continuing effort to develop green C−H functionalization,[10] we have developed a base-promoted direct C3-alkoxymethylation of indoles under transition-metal free conditions via electrophilic aromatic substitution reaction ($S_{Ar}E$) (Scheme 1b). This protocol features rapid access to a variety of useful building blocks with excellent yields and regioselectivity.

We initiated our investigation on the model reaction of indole (**1a**) and methanol to optimize various reaction parameters (Table 1). Initially, a 54% yield of the desired

Table 1. Optimization of the Reaction Conditions[a]



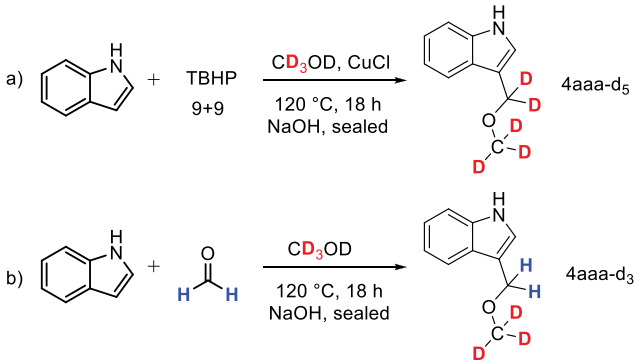
1a **3a** **4aaa**

entry	cat (10% mol)	TBHP (equiv)	time (h)	yield[b]
1	CuCl	1	18	54
2	$Cu(OAc)_2$	1	18	32
3	$CuCl_2$	1	18	47
4	CuBr	1	18	42
5	$CuBr_2$	1	18	45
6	CuI	1	18	53
7	CuCl	2	18	59
8	CuCl	2	18	21[c]
9	CuCl	2	9 + 9	89[d]
10	CuCl	1	1*10	89[e]

[a]Reaction conditions: **1a** (0.10 mmol), methanol (1 mL), NaOH (1 equiv) under air and sealed, 120 °C. [b]Isolated yield. [c]Open in the air. [d]TBHP (2 equiv) was dissolved in 1 mL of methanol and 0.5 mL of the solution was added every 9 h. [e]TBHP (1 equiv) was dissolved in 1 mL of methanol and 0.1 mL of the solution was added every 1 h.

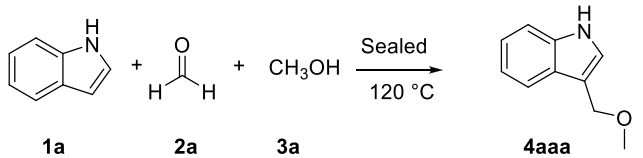
dehydrogenative coupling product **4aaa** was obtained in the presence of CuCl (10 mol %) and TBHP (*tert*-butyl hydroperoxide) in methanol at 120 °C under air for 18 h (Table 1, entry 1). The molecular structure of product **4aaa** was confirmed by NMR spectra and single crystal X-ray diffraction analysis (SI, Figure S1). Among the copper salts examined (CuCl, $Cu(OAc)_2$, $CuCl_2$, CuBr, $CuBr_2$, and CuI), CuCl was the best (Table 1, entry 1 vs entries 2−6). Slightly lower yields were obtained when the loading of NaOH was reduced to 0.5 or 0.3 equiv. The higher yield was obtained by increasing the amount of TBHP to 2 equiv (Table 1, entry 7 vs entry 1). The yield decreased significantly under air atmosphere (Table 1, entry 8). The yield of 89% was obtained by adding TBHP (2 equiv) two times, or adding TBHP (1 equiv) ten times (Table 1, entries 9−10). In order to verify the source of the methyl and methylene in product **4aaa**, the isotope labeled experiments were carried out (Scheme 2). Deuterated methanol was used as the solvent under the condition of entry 9 (Table 1). Based on ^{1}H NMR (SI, **4aaa**-d_5), there is no signal found in the aliphatic area, suggesting that TBHP as methyl source was ruled out. Then, indole and formaldehyde were soluble in deuterated methanol. Only the signal at 4.67 ppm (s, 2H) was observed, and the methyl signal disappeared from the ^{1}H NMR spectrum (SI, **4aaa**-d_3), which implied that the $-CH_2-$ is derived from formaldehyde and the $-CH_3$ is from methanol. On the basis of these results, the reaction conditions were optimized in the absence of copper salt and any oxidants. Additionally, the reaction could also

Scheme 2. Isotope Tracer Experiments



proceed, but slowly without base (Table 2, entry 8). After screening various bases and loading of starting materials (Table

Table 2. Optimization of the Reaction Conditions[a]



1a **2a** **3a** **4aaa**

entry	**2a** (equiv)	bases	time (h)	yield[b]
1	1	NaOH	18	85
2	1	KOH	18	80
3	1	K_2CO_3	18	82
4	1	Et_3N	18	81
5	1	pyridine	18	76
6	2	NaOH	2	62
7	2	NaOH	2	89[c]
8	2	--	18	54

[a]Reaction conditions: **1a** (0.10 mmol), methanol (1 mL), NaOH (1 equiv) under air and sealed, 120 °C. [b]Isolated yield. [c]NaOH (2 equiv).

2), the optimal reaction conditions were assigned as follows: indole (**1a**), paraformaldehyde (**2a**), methanol (1 mL), NaOH (2 equiv) under air and sealed, 120 °C for 2 h (Table 2, entry 7).

With the optimized conditions in hand, the scope of substrates was investigated (Scheme 3). A range of indoles was first investigated to react with paraformaldehyde (**2a**) and methanol (**3a**) under the optimized reaction conditions. Generally, various indoles bearing either electron-donating or -withdrawing groups were well-tolerated and converted into the corresponding products in good to excellent yields (**4aaa** to **4qaa**). Among them, 5-nitro and 6-$COOCH_3$ indoles gave the corresponding products **4iaa** and **4maa** in moderate yields. In addition, 7-nitroindole could give the product **4qaa** in 92% yield prolonging the reaction time to 24 h. In general, the reaction rate of indoles with electron-donating groups is faster than those with electron-withdrawing groups, and the reaction could proceed well for substrates bearing a steric substituent (**4baa**, **4eaa**, and **4faa**). Moreover, the substrates with halogen groups produced the target products (**4caa-4daa**, **4jaa-4laa**, **4naa-4paa**) with high yields, which provide the possibility to build complicated molecules through further chemical transformations. Then, a range of aldehydes were tested with indole (**1a**) and methanol (**3a**). Aromatic aldehydes gave the desired products in good to excellent yields (**4aba-4ama**). Benzalde-

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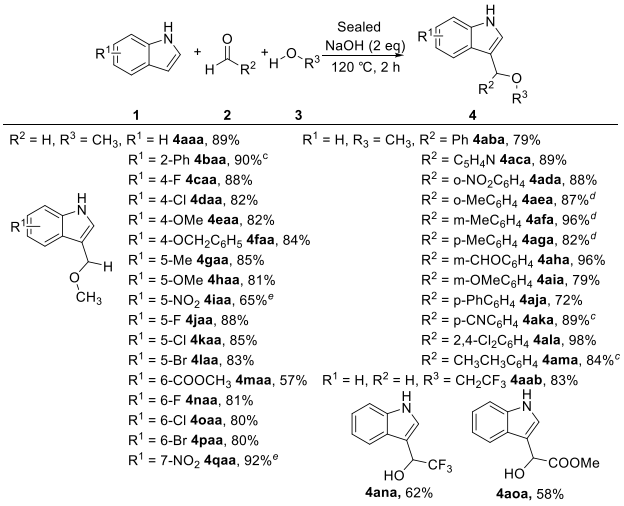
Scheme 3. Substrate Scope of Indoles with Aldehydes and Alcohols[a,b]



[a]Reaction conditions: **1** (0.1 mmol), **2** (0.2 mmol), **3** (1.0 mL), 120 °C, 2 h, air and sealed. [b]Isolated yield. [c]6 h. [d]8 h. [e]24 h.

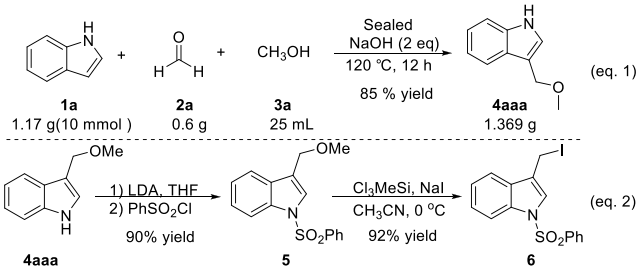
hyde (**2b**) and donating substituted benzaldehydes result in relatively low yields (**4aga** vs **4afa** and **4aea**). The *p*-withdrawing substituted benzaldehydes can give better results (**4aka** and **4ala**). No reaction was observed for pyrroles, thiofuran, furan, benzofuran, 3-mehtyl indole, and benzothiophene under standard reaction conditions. However, the trifluoroacetaldehyde and ethyl glyoxalate obtained the unexpected product in 62% yield (**4ana**) and 58% yields (**4aoa**), respectively. The molecular structure of product **4ana** was confirmed by NMR and single crystal X-ray diffraction analysis (SI, Figure S2). It might be caused by the presence of strong electron-withdrawing groups which inhibit the departure of hydroxyl groups. Other alkylaldehydes, such as acetaldehyde, pivaldehyde, and valeraldehyde, were not beneficial for this transformation and no desired products were detected.

In addition, some alkyl alcohols (such as ethanol, trifluoroethanol, *tert*-butanol, *n*-butanol, *tert*-amyl alcohol, isoamyl alchol, 1-amyl alcohol, and benzyl alcohol) had been examined. Unfortunately, only 2,2,2-trifluoroethanol proceeded smoothly, giving the target product **4aab** in 83% yield.

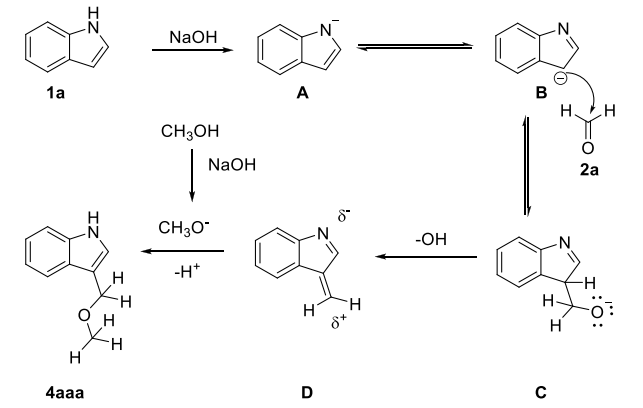
To demonstrate the synthetic potential application of the present method, the 3-(methoxymethyl)-1*H*-indole is an important molecule. A gram scale reaction of indole (**1a**) and paraformaldehyde (**2a**) was carried out in methanol (**3a**) under 120 °C for 12 h. The product (3-(methoxymethyl)-1*H*-indole (**4aaa**) was obtained in 85% yield (eq 1, Scheme 4). In comparison with traditional methods, the current reaction provided an easier, more direct, and step-economic method to various C3-alkoxymethylaed free (N−H) indole derivatives with important biological.[2] Compound **6** that is easy to convert could be synthesized by N-protection and substitution of C3-alkoxymethylated indole obtained from our methodology, providing 83% yield in all (eq 2, Scheme 4).

On the basis of the above discussion and previous literature,[11] a plausible reaction mechanism is illustrated (Scheme 5). Initially, the hydrogen positive ion was removed from indole (**1a**) to form compound **A** by aid of NaOH. Then compound **A** could convert to the indolium intermediate (**B**) through charge transfer in the conjugated system. Intermediate

Scheme 4. Gram-Scale Reaction and Transformation of C3-Alkoxymethylaed Product



Scheme 5. Proposed Mechanism



B reacts with formaldehyde easily and forms intermediate **C** via a nucleophilic addition reaction. Then the hydroxide was removed from **C** by the electron transport process to form **D**. Finally, compound **D** reacted with CH_3O^- which comes from methanol by an addition reaction to give product **4aaa**.

In summary, we have developed a novel, simple, and efficient protocol for the base-promoted direct C3-alkoxymethylation of indoles with aldehydes and alcohols. In this approach, a broad range of 3-(alkoxymethyl)-1*H*-indole were conveniently obtained in moderate to excellent yields with good functional group tolerance under air and metal-free conditions, thus providing an environmentally benign alkoxymethylation process. The present protocol is anticipated to be an important approach to indoles, which would be useful to build multitudinous biologically active molecules.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b00357.

Experimental procedures and characterization data for all new compounds (PDF)

Accession Codes

CCDC 1520906 and 1527983 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.

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#C. P. and X. Y. contributed equally.

Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Gribble, G. W. *Comprehensive Heterocyclic Chemistry II*, Katritzky, A. R. C.; Rees, W. E.; Scriven, F. V.; Bird, C. W., Eds.; Pergamon Press: Oxford (UK), 1996; Vol. 2, p 207. (b) Sundberg, R. J. *Comprehensive Heterocyclic Chemistry II*, Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V.; Bird, C. W., Eds.; Pergamon Press: Oxford (UK), 1996, Vol. 2, p 119. (c) Somei, M.; Yamada, F. *Nat. Prod. Rep.* **2005**, *22*, 73. (d) Walker, S. R.; Carter, E. J.; Huff, B. C.; Morris, J. C. *Chem. Rev.* **2009**, *109*, 3080. (e) Melander, R. J.; J, M.; Melander, C. *Tetrahedron* **2014**, *70*, 6363. (f) Netz, N.; Opatz, T. *Mar. Drugs* **2015**, *13*, 4814. (g) Stempel, E.; Gaich, T. *Acc. Chem. Res.* **2016**, *49*, 2390.

(2) (a) Gueremy, C.; Audiau, F.; Champseix, A.; Uzan, A.; Le Fur, G.; Rataud, J. *J. Med. Chem.* **1980**, *23*, 1306. (b) Brenna, E.; Fuganti, C.; Fuganti, D.; Grasselli, P.; Malpezzi, L.; Pedrocchi-Fantoni, G. *Tetrahedron* **1997**, *53*, 17769. (c) Stork, G. P.; Tang, C.; Casey, M.; Goodman, B.; Toyota, M. *J. Am. Chem. Soc.* **2005**, *127*, 16255. (d) Jump, S. M.; Kung, J.; Staub, R.; Kinseth, M. A.; Cram, E. J.; Yudina, L. N.; Preobrazhenskaya, M. N.; Bjeldanes, L. F.; Firestone, G. L. *Biochem. Pharmacol.* **2008**, *75*, 713. (e) Arisawa, M.; Kasaya, Y.; Obata, T.; Sasaki, T.; Ito, M.; Abe, H.; Ito, Y.; Yamano, A.; Shuto, S. *ACS Med. Chem. Lett.* **2011**, *2*, 353. (f) Wu, S.; Wang, L.; Guo, W.; Liu, X.; Liu, J.; Wei, X.; Fang, B. *J. Med. Chem.* **2011**, *54*, 2668. (g) Gore, S.; Baskaran, S.; Konig, B. *Org. Lett.* **2012**, *14*, 4568. (h) Righi, M.; Topi, F.; Bartolucci, S.; Bedini, A.; Piersanti, G.; Spadoni, G. *J. Org. Chem.* **2012**, *77*, 6351. (i) Zhu, C.; Ma, S. *Org. Lett.* **2013**, *15*, 2782. (j) Samuel, T.; Yehualaeshet, T.; Serbessa, T.; Fadlalla, K. U.S. Patent Application US20150164860A1, 2015. (k) Zapata Hernandez, J. M.; Perez Chacon, G. Spanish Patent ES2532436A2, 2015. (l) Zhang, Y.; Jin, C.; Zhong, W.; Zhang, J.; Gao, L.; Chen, K. Chinese Patent CN104725295A, 2015.

(3) (a) Fischer, E.; Jourdan, F. *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 2241. (b) Robinson, B. *Chem. Rev.* **1963**, *63*, 373. (c) Taber, D. F.; Tirunahari, P. K. *Tetrahedron* **2011**, *67*, 7195.

(4) (a) Asay, M.; Jones, C.; Driess, M. *Chem. Rev.* **2011**, *111*, 354. (b) Kuhl, N.; Hopkinson, M. N.; Wencel-Delord, J.; Glorius, F. *Angew. Chem., Int. Ed.* **2012**, *51*, 10236. (c) Nishino, M.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 4457. (d) Rouquet, G.; Chatani, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 11726. (e) Huang, C. Y.; Doyle, A. G. *Chem. Rev.* **2014**, *114*, 8153. (f) Zhang, N.; Samanta, S. R.; Rosen, B. M.; Percec, V. *Chem. Rev.* **2014**, *114*, 5848. (g) Marek, I.; Masarwa, A.; Delaye, P. O.; Leibeling, M. *Angew. Chem., Int. Ed.* **2015**, *54*, 414. (h) Gulías, M.; Mascarenas, L. *Angew. Chem., Int. Ed.* **2016**, *55*, 11000.

(5) (a) Lane, B. S.; Brown, M. A.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 8050. (b) Bhuvaneswari, S.; Jeganmohan, M.; Cheng, C. H. *Chem. - Eur. J.* **2007**, *13*, 8285. (c) Stuart, D. R.; Fagnou, K. *Science* **2007**, *316*, 1172. (d) Stuart, D. R.; Villemure, E.; Fagnou, K. *J. Am. Chem. Soc.* **2007**, *129*, 12072. (e) Bellina, F.; Benelli, F.; Rossi, R. *J. Org. Chem.* **2008**, *73*, 5529. (f) Kagawa, N.; Malerich, J. P.; Rawal, V. H. *Org. Lett.* **2008**, *10*, 2381. (g) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172. (h) Joucla, L.; Djakovitch, L. *Adv. Synth. Catal.* **2009**, *351*, 673. (i) Joucla, L.; Batail, N.; Djakovitch, L. *Adv. Synth. Catal.* **2010**, *352*, 2929. (j) Liu, Q.; Li, G.; Yi, H.; Wu, P.; Liu, J.; Lei, A. *Chem. - Eur. J.* **2011**, *17*, 2353. (k) Chen, W. L.; Gao, Y. R.; Mao, S.; Zhang, Y. L.; Wang, Y. F.; Wang, Y. Q. *Org. Lett.* **2012**, *14*, 5920. (l) Jiang, T. S.; Wang, G. W. *Org. Lett.* **2013**, *15*, 788. (m) Chen, S. J.; Lu, G. P.; Cai, C. *RSC Adv.* **2015**, *5*, 70329. (n) Jin, L. K.; Wan, L.; Feng, J.; Cai, C. *Org. Lett.* **2015**, *17*, 4726. (o) Yang, Y.; Li, W.; Xia, C.; Ying, B.; Shen, C.; Zhang, P. *ChemCatChem* **2016**, *8*, 304. (p) Pi, C.; Cui, X.; Liu, X.; Guo, M.; Zhang, H.; Wu, Y. *Org. Lett.* **2014**, *16*, 5164. (q) Zheng, Y.; Li, R.-J.; Zhan, Z.; Zhou, Y.; Hai, L.; Wu, Y. *Chin. Chem. Lett.* **2016**, *27*, 41.

(6) (a) Zhang, Z. W.; Xue, H.; Li, H.; Kang, H.; Feng, J.; Lin, A.; Liu, S. *Org. Lett.* **2016**, *18*, 3918. (b) Espejo, V. R.; Rainier, J. D. *J. Am. Chem. Soc.* **2008**, *130*, 12894. (c) Hu, X.; Chen, F.; Deng, Y.; Jiang, H.; Zeng, W. *Org. Lett.* **2018**, *20*, 6140. (d) Fang, X.; Li, Q.; Shi, R.; Yao, H.; Lin, A. *Org. Lett.* **2018**, *20*, 6084. (e) Cruz, F. A.; Zhu, Y.; Tercenio, Q. D.; Shen, Z.; Dong, V. M. *J. Am. Chem. Soc.* **2017**, *139*, 10641.

(7) (a) Ottoni, O.; Neder, A. V. F.; Dias, A. K. B.; Cruz, R. P. A.; Aquino, L. B. *Org. Lett.* **2001**, *3*, 1005. (b) Yeung, K.-S.; Farkas, M. E.; Qiu, Z.; Yang, Z. *Tetrahedron Lett.* **2002**, *43*, 5793.

(8) (a) Li, X.; Gu, X.; Li, Y.; Li, P. *ACS Catal.* **2014**, *4*, 1897. (b) Wang, D.-C.; Song, H.; Xu, C.-Y.; Dong, H.; Liu, J. *Chin. Chem. Lett.* **2015**, *26*, 1050. (c) Li, C.; Zhang, H. H.; Fan, T.; Shen, Y.; Wu, Q.; Shi, F. *Org. Biomol. Chem.* **2016**, *14*, 6932. (d) Shi, Q.; Li, P.; Zhu, X.; Wang, L. *Green Chem.* **2016**, *18*, 4916. (e) Chen, J.; Wu, J. *Angew. Chem., Int. Ed.* **2017**, *56*, 3951.

(9) (a) Yadav, J. S.; Reddy, B. V. S.; Sunitha, S. *Adv. Synth. Catal.* **2003**, *345*, 349. (b) Ma, Z.-H.; Han, H.-B.; Zhou, Z.-B.; Nie, J. *J. Mol. Catal. A: Chem.* **2009**, *311*, 46. (c) Kubczyk, T. M.; Williams, S. M.; Kean, J. R.; Davies, T. E.; Taylor, S. H.; Graham, A. E. *Green Chem.* **2011**, *13*, 2320. (d) Beltra, J.; Gimeno, M. C.; Herrera, R. P. *Beilstein J. Org. Chem.* **2014**, *10*, 2206. (e) Tran, P. H.; Nguyen, X.-T.; Chau, D.-K. *Asian J. Org. Chem.* **2018**, *7*, 232.

(10) (a) Cheng, G.; Zeng, X.; Shen, J.; Wang, X.; Cui, X. *Angew. Chem., Int. Ed.* **2013**, *52*, 13265. (b) Chen, X.; Cui, X.; Yang, F.; Wu, Y. *Org. Lett.* **2015**, *17*, 1445. (c) Gao, M.; Li, Y.; Xie, L.; Chauvin, R.; Cui, X. *Chem. Commun.* **2016**, *52*, 2846. (d) Shen, J.; Wang, X.; Lin, X.; Yang, Z.; Cheng, G.; Cui, X. *Org. Lett.* **2016**, *18*, 1378.

(11) (a) Hix, S.; Morais Mda, S.; Augusto, O. *Free Radical Biol. Med.* **1995**, *19*, 293. (b) Kathing, C.; Tumtin, S.; Singh, N. G.; Rani, J. W.; Phucho, I. T.; Nongpiur, A.; Nongrum, R.; Nongkhlaw, R. L. *Org. Chem. Ind. J.* **2013**, *9*, 257. (c) Li, P.; Zhao, J.; Lang, R.; Xia, C.; Li, F. *Tetrahedron Lett.* **2014**, *55*, 390. (d) Yang, Y.; Bao, Y. J.; Guan, Q. Q.; Sun, Q.; Zha, Z. G.; Wang, Z. Y. *Green Chem.* **2017**, *19*, 112. (e) Chu, P.; Kuhl, G. H. *Ind. Eng. Chem. Res.* **1987**, *26*, 365. (f) Karakaya, I.; Primer, D. N.; Molander, G. A. *Org. Lett.* **2015**, *17*, 3294.

DOI: 10.1021/acs.orglett.9b00357
Org. Lett. XXXX, XXX, XXX−XXX