Organic LETTERS

Letter

pubs.acs.org/OrgLett

Palladium/Copper Co-catalyzed Oxidative C−H/C−H Carbonylation of Diphenylamines: A Way To Access Acridones

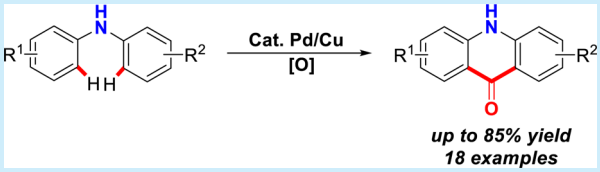
Jiangwei Wen,[†] Shan Tang,[†] Fan Zhang,[†] Renyi Shi,[†] and Aiwen Lei*[,†,‡]

[†]The Institute for Advanced Studies (IAS), College of Chemistry and Molecular Sciences, Wuhan University, Wuhan 430072, Hubei, China

[‡]Conducted and State Key Laboratory for Oxo Synthesis and Selective Oxidation, Lanzhou Institute of Chemical Physics, Chinese Academy of Sciences, Lanzhou 730000, China

Supporting Information

ABSTRACT: An efficient palladium/copper co-catalyzed oxidative double C(sp^2)−H functionalization/carbonylation of diphenylamines for synthesis of acridones has been developed. This method utilizes readily available starting materials and mild reaction conditions. The protocol provides a simple, efficient, and atom-economic way to access acridones. Notably, the present protocol has excellent functional group tolerance and application value.



As one of the most important heterocyclic compounds, acridones have been thought as privileged structures in dyestuffs, pharmaceuticals, and biomaterials.[1] Moreover, the acridones were considered ideal building blocks for the synthesis of nitrogen-containing compounds, which widely exist in antileishmanial, antifungal, and DNA-intercalating anticancer drugs[1h] and as fluorescent labels.[2] For example, 10-CMA, a known antiviral agent which is the most potent inducer of interferons forms leukocytes and macrophages (Figure 1, **A**).[3] In particular, acridone as the framework

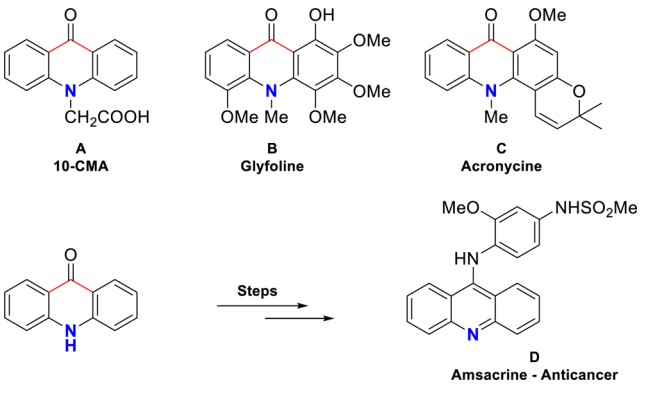


Figure 1. Representative acridone-based natural products and anticancer drugs.

(antitumor drugs, Figure 1, **B**, **C**)[4] gives very important structural motifs. Acridones are especially revealed to be essential precursors for the synthesis of biologically active drugs (present as the central core of antitumor agents, Figure 1, D).[5] Consequently, substantial efforts have been devoted to the synthesis of acridones.

In general, classical routes to construct this scaffold are mainly based on the acid-promoted cyclization of *N*-phenylanthranilic acids or intramolecular nucleophilic substitution of 2-amino-2′-halobenzophenones.[6] Moreover, Larock, Greaney, and Jiang have described novel approaches to acridones through nucleophilic addition coupling of benzamides or benzoates with arynes generated from silylaryl triflate precursors.[6c,7] However, most of these methods suffer from some limitations, such as low atom economy, tedious workup procedures, unreadily available starting materials, and/or harsh reaction conditions. It is still a challenging but attractive task to develop a simple, efficient reaction system to afford a variety of important and structurally diverse functional acridones. Here, we report a simple and direct oxidative carbonylation of diphenylamines toward acridones by Pd/Cu co-catalysis.

Transition-metal-catalyzed C−H carbonylation has emerged as one of the most efficient methods for constructing carbonyl compounds and has received more attention over the past decade.[8] Among these transformations, oxidative C−H/C−H carbonylation of hydrocarbons represents an ideal way to access ketones.[9] Though transition-metal-catalyzed oxidative C−H/C−H cross-coupling has undergone tremendous development in recent years, methods for developing oxidative C−H/C−H carbonylation are rare.[10] This might be due to the facile direct C−H/C−H cross-coupling in the attempts at oxidative C−H/C−H carbonylation reactions.[11] In recent years, the oxidative C−H/C−H carbonylation access to carbonyl compounds has seen preliminary development. Consequently, we report a simple and efficient method for the construction of acridones through the double C−H oxidative carbonylation strategy.

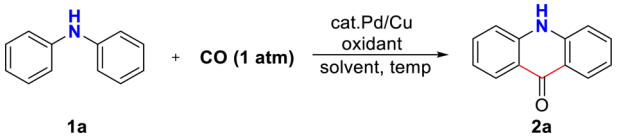
Initially, diphenylamine (**1a**) was chosen as the model substrate to optimize the reaction conditions. To our delight, the desired product **2a** was obtained in 40% yield when the reaction was carried out by utilizing $PdCl_2$ and $Cu(OPiv)_2$ in a

Received: November 11, 2016

DOI: 10.1021/acs.orglett.6b03356
Org. Lett. XXXX, XXX, XXX−XXX

mixed solvent of toluene/DMSO at 100 °C under 1 atm of CO using O_2 as the terminal oxidant (Table 1, entry 1). Further

Table 1. Condition Optimization of the Palladium-/Copper-Catalyzed Oxidative C−H/C−H Functionalization/Carbonylation for the Synthesis of Acridones[a]



1a 2a

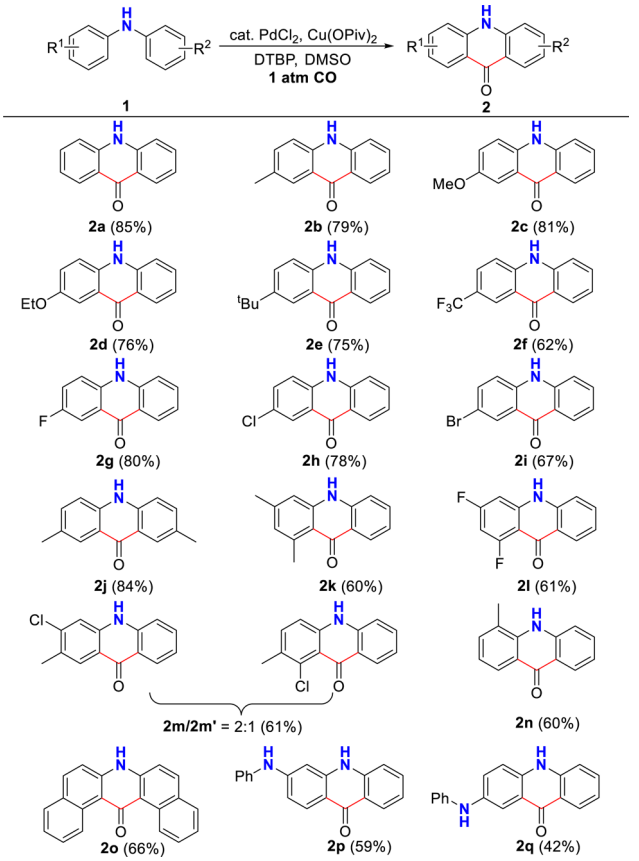
entry	cat. [Pd]	oxidant	solvent	yield[b] (%)
1	$PdCl_2$	O_2	Tol/DMSO	40
2	$PdCl_2$	O_2	DMF	38
3	$PdCl_2$	O_2	Tol	15
4	$PdCl_2$	O_2	dioxane	50
5	$PdCl_2$	O_2	AcOH	48
6	$PdCl_2$	O_2	PhCl	27
7	$PdCl_2$	O_2	DMA	25
8	$PdCl_2$	O_2	DMSO	82
9		O_2	DMSO	n.d.
10	$Pd(OAc)_2$	O_2	DMSO	39
11	$Pd(PPh_3)_4$	O_2	DMSO	41
12	$PdCl_2(PPh_3)_2$	O_2	DMSO	63
13	$PdCl_2$(dppb)	O_2	DMSO	46
14	$Pd(OPiv)_2$	O_2	DMSO	20
15	$PdCl_2$	TBHP	DMSO	nd
16	$PdCl_2$	$PhI(OAc)_2$	DMSO	nd
17	$PdCl_2$	$K_2S_2O_8$	DMSO	nd
18	$PdCl_2$	DCP	DMSO	66
19	$PdCl_2$	DTBP	DMSO	72[c]
20	$PdCl_2$	DTBP	DMSO	85[d]
21	$PdCl_2$		DMSO	20[e]
22	$PdCl_2$	DTBP	DMSO	67[f]
23	$PdCl_2$	DTBP	DMSO	51[g]

[a]Reaction conditions: **1a** (0.25 mmol), $PdCl_2$ (10 mol %), $Cu(OPiv)_2$ (20 mol %), CO/O_2 = 1:7, DMSO (3.0 mL), 100 °C, 24 h. TBHP: *tert*-butyl hydroperoxide, 65% solution in water. DTBP:di-*tert*-butyl peroxide. DCP: dicumyl peroxide. [b]Isolated yields. [c]DTBP (2 equiv). [d]DTBP (3 equiv). [e]$Cu(OPiv)_2$ (1.0 eqiuv). [f]80 °C. [g]120 °C.

optimization of solvents demonstrated that DMSO was the optimized reaction medium for the formation of product **2a** (Table 1, entries 1−8). Replacing $PdCl_2$ with other catalysts such as $Pd(OAc)_2$, $Pd(PPh_3)_4$, $PdCl_2(PPh_3)_2$, $PdCl_2$(dppb), and $Pd(OPiv)_2$ did not improve the reaction efficiency (Table 1, entries 9−14). Subsequently, the effects of oxidants such as CuCl, CuBr, CuI, CuCN, CuO, $Cu(OAc)_2$, and $Cu(OPiv)_2$ were separately examined. Among the above oxidants tested, $Cu(OPiv)_2$ stood out to be the best choice, while others including CuCl, CuBr, CuI, CuCN, CuO, and $Cu(OAc)_2$ were less effective (see Table S1). However, no conversion was observed when the reaction was performed separately in $Cu(OTf)_2$ and $Cu(acac)_2$ (see Table S1). In particular, when $Cu(OAc)_2{\cdot}H_2O$ was utilized as the oxidant and trimethylacetic acid as the additive, the desired product could be obtained in 30% yield (see Table S1, entry 10). However, no desired product was generated when $PdCl_2$ was replaced with $Pd(OPiv)_2$ (see Table S1, entry 11). Form the above experimental results, consequently, the $Cu(OPiv)_2$ may have two different roles; one is oxidation of Pd^0 to Pd^{II}, and the other is the exchange of $PdCl_2$ with the anion. Moreover, other terminal oxidants also have been separately investigatied, such as TBHP, $K_2S_2O_8$, $PhI(OAc)_2$, DCP, and DTBP. Better results were obtained when the terminal oxidant O_2 was replaced by DTBP (Table 1, entries 15−20). Notably, the desired product was obtained 20% yield when DTBP was removed and stoichiometric $Cu(OPiv)_2$ was used as the oxidant (Table 1, entry 21). In addition, the best yield of **2a** was obtained when the reaction was performed at 100 °C (Table 1, entries 22 and 23). After extensive screening of the reaction parameters, the optimized conditions was obtained by employing $PdCl_2$ (10 mol %), $Cu(OPiv)_2$ (20 mol %), and DTBP (3.0 equiv) in DMSO at 100 °C under 1 atm of carbon monoxide in 24 h.

With the optimized conditions established, the substrate scope of this oxidative carbonylation reaction was explored, with some results summarized in Scheme 1. Gratifyingly,

Scheme 1. Pd-Catalyzed Oxidative Double C−H Carbonylation of Different Diphenylamines[a,b]

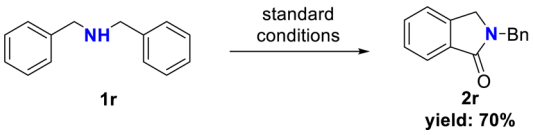


[a]Reaction conditions: **1a** (0.25 mmol), $PdCl_2$ (10 mol %), $Cu(OPiv)_2$ (20 mol %), DTBP (3 equiv), CO (1 atm) in DMSO (3.0 mL) at 100 °C for 24 h. [b]Isolated yields.

reaction of diphenylamine with electron-donating substituents (such as Me, OMe, OEt, and *t*-Bu) proceeded under the optimized reaction conditions in high yields (**2a−e**), while the electron-withdrawing group on the aromatic ring also furnished the desired products **2f**, but the yield was slightly lower. Moreover, the halogen substituent can be effectively compatible, and it is very important for further functionalization of acridones (**2g−i**). Subsequently, we investigated if oxidative carbonylation of symmetrical diphenylamines could form the corresponding desired product **2j**. Furthermore, the 3,5-dimethyl-*N*-phenylanilines and 3,5-difluoro-*N*-phenylanilines

DOI: 10.1021/acs.orglett.6b03356
Org. Lett. XXXX, XXX, XXX−XXX

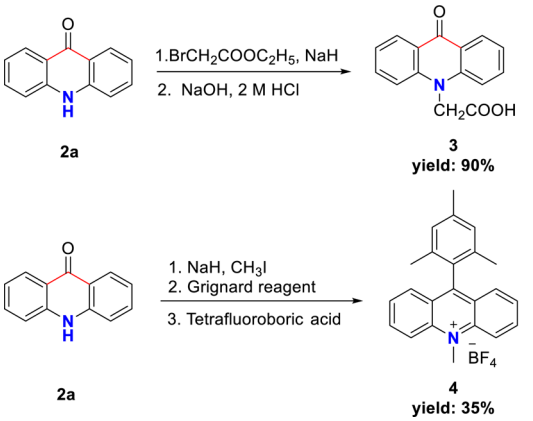
were suitable for this reaction, with the desired products obtained in excellent yields (**2k**,**l**). In addition, substitution on the *ortho*- or *meta*-position of the diphenylamines could also lead to the desired product in good yield (**2m**−**o**). To our delight, the reaction also worked well with di(naphthalen-2-yl)amines, leading to the corresponding product **2o** in 66% yield. Finally, the N_1,N_4-diphenylbenzene-1,3-diamines or 1,4-diamines that were used as substrates could also obtain the corresponding acridones **2p** and **2q** in 59% and 42% yields, respectively. It is worth noting that dibenzylamines did not generate the desired product. However, the 2-benzylisoindolin-1-one **2r** was obtained in satisfactory yield under the standard conditions (eq 1).[12]



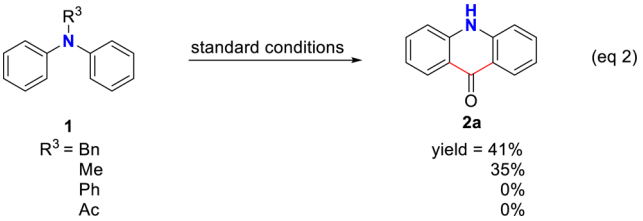
(eq 1)

Acridone having a keto group and a nitrogen atom at positions 9 and 10, respectively, resulted in a planar structure. This typical chemical structure scaffold is well reported to describe a wide range of biological potentials including anticancer, antimalarial, and fluorescence.[1h,3c,13] We demonstrate herein the postsynthetic transformations of nitro-containing acridones as shown in Scheme 2. As one of the most potent low molecular weight antiviral agents, the traditional synthetic methods leading to 10-CMA often require tedious steps.[14] However, only two steps are needed to obtain this product in 90% yield (Scheme 2a). Moreover, the photocatalyst **4** was also easily prepared in 35% yield in three steps by initial treatment of the corresponding acridones **2a** (Scheme 2b).[15]

Scheme 2. Some of Synthetic Application of the Acridones



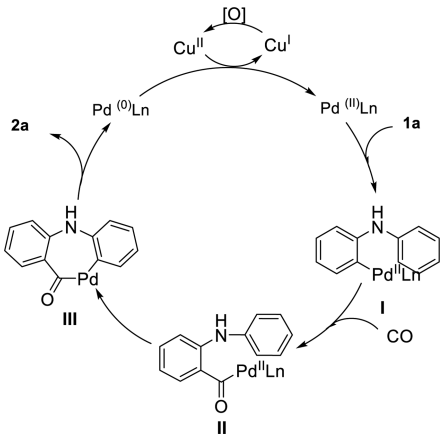
Interestingly, changing the N-H group to N-Bn or N-Me could give the corresponding acridone **2a** in 41% and 35% yield by releasing the C−N bond.[16] However, changing the N-H group to N-Ph or N-Ac failed to yield the desired product (eq 2).



(eq 2)

Although the mechanism is not completely clear yet, based on our previous experiment results and the literature,[8j,9c,17] a postulated reaction pathway is proposed as shown in Scheme 3. Initially, the electrophilic palladation of **1a** with Pd^{II} affords the arylpalladium species **I**, which further reacts with CO to produce the intermediate **II**. The subsequent intramolecular C−H functionalization and reductive elimination of **III** gives the acridone **2a** and generates Pd^0 species. Pd^{II} is then regenerated by oxidation of Cu^{II}. Finally, the Cu^{II} regenerated by oxidation of DTBP.

Scheme 3. Postulated Reaction Pathway



In conclusion, we have disclosed a palladium/copper-co-catalyzed oxidative C−H/C−H carbonylation of diphenylamines. This method provides an efficient and atom-economic way to access synthetically useful acridones. Various acridones were synthesized in good to high yields with excellent functional group tolerance. The acridone was also used in the synthesis of some useful materials. Application of oxidative C−H/C−H carbonylation in the synthesis of other cyclic compounds is underway in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b03356.

Experimental procedures, optimization of reaction conditions, characterization data, and NMR spectra of the products (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: aiwenlei@whu.edu.cn.

ORCID

Aiwen Lei: 0000-0001-8417-3061

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by the National Natural Science Foundation of China (21390400, 21520102003, 21272180, 21302148), the Hubei Province Natural Science Foundation of China (2013CFA081), the Research Fund for the Doctoral

DOI: 10.1021/acs.orglett.6b03356
Org. Lett. XXXX, XXX, XXX−XXX

Program of Higher Education of China (20120141130002), and the Ministry of Science and Technology of China (2012YQ120060). The Program of Introducing Talents of Discipline to Universities of China (111 Program) is also appreciated.

REFERENCES

(1) (a) Taraporewala, I. B.; Cessac, J. W.; Chanh, T. C.; Delgado, A. V.; Schinazi, R. F. *J. Med. Chem.* **1992**, *35*, 2744. (b) Itoigawa, M.; Ito, C.; Wu, T.-S.; Enjo, F.; Tokuda, H.; Nishino, H.; Furukawa, H. *Cancer Lett.* **2003**, *193*, 133. (c) Harrison, R. J.; Reszka, A. P.; Haider, S. M.; Romagnoli, B.; Morrell, J.; Read, M. A.; Gowan, S. M.; Incles, C. M.; Kelland, L. R.; Neidle, S. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5845. (d) Kuzovkina, I.; Al'terman, I.; Schneider, B. *Phytochemistry* **2004**, *65*, 1095. (e) MacNeil, S. L.; Wilson, B. J.; Snieckus, V. *Org. Lett.* **2006**, *8*, 1133. (f) Tabarrini, O.; Manfroni, G.; Fravolini, A.; Cecchetti, V.; Sabatini, S.; De Clercq, E.; Rozenski, J.; Canard, B.; Dutartre, H.; Paeshuyse, J. *J. Med. Chem.* **2006**, *49*, 2621. (g) Chukaew, A.; Ponglimanont, C.; Karalai, C.; Tewtrakul, S. *Phytochemistry* **2008**, *69*, 2616. (h) Kelly, J. X.; Smilkstein, M. J.; Brun, R.; Wittlin, S.; Cooper, R. A.; Lane, K. D.; Janowsky, A.; Johnson, R. A.; Dodean, R. A.; Winter, R. *Nature* **2009**, *459*, 270. (i) Zhang, S.; Li, Y.; You, J.; Wang, H.; Zheng, Y.; Suo, Y. *J. Agric. Food Chem.* **2012**, *60*, 10985.

(2) (a) Bahr, N.; Tierney, E.; Reymond, J.-L. *Tetrahedron Lett.* **1997**, *38*, 1489. (b) Games, D. *Chem. Commun.* **1997**, 1529.

(3) (a) Storch, E.; Kirchner, H. *Eur. J. Immunol.* **1982**, *12*, 793. (b) Storch, E.; Kirchner, H.; Brehm, G.; Hüller, K.; Marcucci, F. *Scand. J. Immunol.* **1986**, *23*, 195. (c) Kumar, R.; Bahia, M. S.; Silakari, O. *Med. Chem. Res.* **2015**, *24*, 921.

(4) Woo Chun, M.; Olmstead, K. K.; Choi, Y. S.; Lee, C. O.; Lee, C.-K.; Kim, J. H.; Lee, J. *Bioorg. Med. Chem. Lett.* **1997**, *7*, 789.

(5) (a) Belmont, P.; Bosson, J.; Godet, T.; Tiano, M. *Anti-Cancer Agents Med. Chem.* **2007**, *7*, 139. (b) Singh, P.; Kaur, P.; Kaur, S. *Bioorg. Med. Chem.* **2009**, *17*, 2423.

(6) (a) Gorvin, J. H.; Whalley, D. P. *J. Chem. Soc., Perkin Trans. 1* **1979**, *1*, 1364. (b) Nishio, R.; Wessely, S.; Sugiura, M.; Kobayashi, S. *J. Comb. Chem.* **2006**, *8*, 459. (c) Pintori, D. G.; Greaney, M. F. *Org. Lett.* **2010**, *12*, 168. (d) Stankiewicz-Drogon, A.; Dörner, B.; Erker, T.; Boguszewska-Chachulska, A. M. *J. Med. Chem.* **2010**, *53*, 3117. (e) Woydziak, Z. R.; Fu, L.; Peterson, B. R. *J. Org. Chem.* **2012**, *77*, 473. (f) Zhou, W.; Liu, Y.; Yang, Y.; Deng, G. J. *Chem. Commun. (Cambridge, U. K.)* **2012**, *48*, 10678. (g) Huang, P. C.; Parthasarathy, K.; Cheng, C. H. *Chem. - Eur. J.* **2013**, *19*, 460. (h) Yu, J.; Yang, H.; Jiang, Y.; Fu, H. *Chem. - Eur. J.* **2013**, *19*, 4271. (i) Zhou, W.; Yang, Y.; Liu, Y.; Deng, G.-J. *Green Chem.* **2013**, *15*, 76.

(7) (a) Zhao, J.; Larock, R. C. *J. Org. Chem.* **2007**, *72*, 583. (b) Dubrovskiy, A. V.; Larock, R. C. *Org. Lett.* **2011**, *13*, 4136. (c) Fang, Y.; Rogness, D. C.; Larock, R. C.; Shi, F. *J. Org. Chem.* **2012**, *77*, 6262. (d) Feng, M.; Tang, B.; Wang, N.; Xu, H. X.; Jiang, X. *Angew. Chem., Int. Ed.* **2015**, *54*, 14960.

(8) (a) Lu, W.; Yamaoka, Y.; Taniguchi, Y.; Kitamura, T.; Takaki, K.; Fujiwara, Y. *J. Organomet. Chem.* **1999**, *580*, 290. (b) Kalinovskii, I.; Pogorelov, V.; Gelbshtein, A.; Akhmetov, N. *Russ. J. Gen. Chem.* **2001**, *71*, 1457. (c) Orito, K.; Horibata, A.; Nakamura, T.; Ushito, H.; Nagasaki, H.; Yuguchi, M.; Yamashita, S.; Tokuda, M. *J. Am. Chem. Soc.* **2004**, *126*, 14342. (d) Ohashi, S.; Sakaguchi, S.; Ishii, Y. *Chem. Commun.* **2005**, 486. (e) Giri, R.; Yu, J.-Q. *J. Am. Chem. Soc.* **2008**, *130*, 14082. (f) Giri, R.; Lam, J. K.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 686. (g) Houlden, C. E.; Hutchby, M.; Bailey, C. D.; Ford, J. G.; Tyler, S. N.; Gagné, M. R.; Lloyd-Jones, G. C.; Booker-Milburn, K. I. *Angew. Chem., Int. Ed.* **2009**, *48*, 1830. (h) Li, H.; Cai, G.-X.; Shi, Z.-J. *Dalton Trans.* **2010**, *39*, 10442. (i) Haffemayer, B.; Gulias, M.; Gaunt, M. J. *Chem. Sci.* **2011**, *2*, 312. (j) Liu, Q.; Zhang, H.; Lei, A. *Angew. Chem., Int. Ed.* **2011**, *50*, 10788. (k) López, B.; Rodriguez, A.; Santos, D.; Albert, J.; Ariza, X.; Garcia, J.; Granell, J. *Chem. Commun.* **2011**, *47*, 1054. (l) Guan, Z.-H.; Chen, M.; Ren, Z.-H. *J. Am. Chem. Soc.* **2012**, *134*, 17490. (m) Chen, M.; Ren, Z.-H.; Wang, Y.-Y.; Guan, Z.-H. *J. Org. Chem.* **2015**, *80*, 1258.

(9) (a) Kulka, M. *J. Am. Chem. Soc.* **1954**, *76*, 5469. (b) Dharshwar, G.; Hosangadi, B. *Chem. Informationsdienst* **1978**, *9*, 9. (c) Zhang, H.; Shi, R.; Gan, P.; Liu, C.; Ding, A.; Wang, Q.; Lei, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 5204. (d) Sarkar, S.; Tadigoppula, N. *RSC Adv.* **2014**, *4*, 40964. (e) Xu, Y.; Zhou, J.; Zhang, C.; Chen, K.; Zhang, T.; Du, Z. *Tetrahedron Lett.* **2014**, *55*, 6432. (f) Motiwala, H. F.; Vekariya, R. H.; Aubé, J. *Org. Lett.* **2015**, *17*, 5484. (g) Jadhav, S. N.; Kumbhar, A. S.; Rode, C. V.; Salunkhe, R. S. *Green Chem.* **2016**, *18*, 1898. (h) Liu, C.; Achtenhagen, M.; Szostak, M. *Org. Lett.* **2016**, *18*, 2375. (i) Mondal, M.; Bora, U. *New J. Chem.* **2016**, *40*, 3119. (j) Weires, N. A.; Baker, E. L.; Garg, N. K. *Nat. Chem.* **2015**, *8*, 75. (k) Zawartka, W.; Pośpiech, P.; Cypryk, M.; Trzeciak, A. M. *J. Mol. Catal. A: Chem.* **2016**, *417*, 76.

(10) (a) Li, Z.; Bohle, D. S.; Li, C.-J. *Proc. Natl. Acad. Sci. U. S. A.* **2006**, *103*, 8928. (b) Li, C.-J. *Acc. Chem. Res.* **2009**, *42*, 335. (c) Yin, W.; He, C.; Chen, M.; Zhang, H.; Lei, A. *Org. Lett.* **2009**, *11*, 709. (d) Yeung, C. S.; Zhao, X.; Borduas, N.; Dong, V. M. *Chem. Sci.* **2010**, *1*, 331. (e) Zhao, X.; Yeung, C. S.; Dong, V. M. *J. Am. Chem. Soc.* **2010**, *132*, 5837. (f) Liu, C.; Zhang, H.; Shi, W.; Lei, A. *Chem. Rev.* **2011**, *111*, 1780. (g) He, C.; Guo, S.; Ke, J.; Hao, J.; Xu, H.; Chen, H.; Lei, A. *J. Am. Chem. Soc.* **2012**, *134*, 5766. (h) Girard, S. A.; Knauber, T.; Li, C. J. *Angew. Chem., Int. Ed.* **2014**, *53*, 74. (i) Liu, D.; Liu, C.; Li, H.; Lei, A. *Chem. Commun.* **2014**, *50*, 3623. (j) Gong, H.; Zeng, H.; Zhou, F.; Li, C. J. *Angew. Chem., Int. Ed.* **2015**, *54*, 5718.

(11) (a) Dwight, T. A.; Rue, N. R.; Charyk, D.; Josselyn, R.; DeBoef, B. *Org. Lett.* **2007**, *9*, 3137. (b) Liégault, B.; Lee, D.; Huestis, M. P.; Stuart, D. R.; Fagnou, K. *J. Org. Chem.* **2008**, *73*, 5022. (c) Kandukuri, S. R.; Oestreich, M. *J. Org. Chem.* **2012**, *77*, 8750. (d) Laha, J. K.; Dayal, N.; Jethava, K. P.; Prajapati, D. V. *Org. Lett.* **2015**, *17*, 1296.

(12) (a) Wada, Y.; Nagasaki, H.; Tokuda, M.; Orito, K. *J. Org. Chem.* **2007**, *72*, 2008. (b) Gross, U.; Koos, P.; O'Brien, M.; Polyzos, A.; Ley, S. V. *Eur. J. Org. Chem.* **2014**, *2014*, 6418.

(13) (a) Singh, P.; Kaur, J.; Yadav, B.; Komath, S. S. *Bioorg. Med. Chem.* **2010**, *18*, 4212. (b) Cholewiński, G.; Dzierzbicka, K.; Kołodziejczyk, A. M. *Pharmacol. Rep.* **2011**, *63*, 305.

(14) Girdhar, A.; Jain, S.; Jain, N.; Girdhar, S. *Acta Poloniae Pharmaceutica – Drug Research* **2010**, *67*, 211.

(15) Wilger, D. J.; Grandjean, J.-M. M.; Lammert, T. R.; Nicewicz, D. A. *Nat. Chem.* **2014**, *6*, 720.

(16) (a) Shi, R.; Lu, L.; Zhang, H.; Chen, B.; Sha, Y.; Liu, C.; Lei, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 10582. (b) Shi, R.; Zhang, H.; Lu, L.; Gan, P.; Sha, Y.; Zhang, H.; Liu, Q.; Beller, M.; Lei, A. *Chem. Commun.* **2015**, *51*, 3247.

(17) (a) Izawa, Y.; Shimizu, I.; Yamamoto, A. *Bull. Chem. Soc. Jpn.* **2004**, *77*, 2033. (b) Hu, Y.; Liu, J.; Lü, Z.; Luo, X.; Zhang, H.; Lan, Y.; Lei, A. *J. Am. Chem. Soc.* **2010**, *132*, 3153. (c) Li, W.; Duan, Z.; Jiang, R.; Lei, A. *Org. Lett.* **2015**, *17*, 1397.

DOI: 10.1021/acs.orglett.6b03356
Org. Lett. XXXX, XXX, XXX–XXX