Organic LETTERS

Letter

pubs.acs.org/OrgLett

Metal-Free Oxidative Annulation of 2-Naphthols with Terminal Alkynes Affording 2-Arylnaphtho[2,1-*b*]furans

Long Liu, Xuyu Ji, Jianyu Dong,* Yongbo Zhou,* and Shuang-Feng Yin

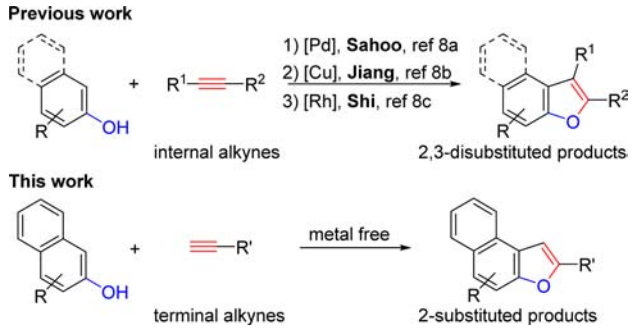
State Key Laboratory of Chemo/Biosensing and Chemometrics, College of Chemistry and Chemical Engineering, Hunan University, Changsha 410082, China

Supporting Information

ABSTRACT: For the first time, the selective oxidative transformation of 2-naphthols with terminal alkynes is disclosed, which enables the straightforward synthesis of 2-arylnaphtho[2,1-*b*]furans in satisfactory yields under metal-free conditions. Mechanistic study suggests that the reaction proceeds via free-radical-mediated sp^2-C−H bond activation, C−C coupling, and C−O cyclization.

Furan derivatives, especially for arene ring-fused furans, are an important class of structural motifs in a large number of natural products,[1] synthetic drugs, and biologically active compounds,[2] as well as organic materials.[3] These compounds are commonly prepared by transition-metal-catalyzed annulation of alkynyl-substituted phenols[4] or tandem reaction of *o*-halophenols with terminal alkynes[5] via cross-coupling and subsequent annulation.[6,7] Recently, direct oxidative functionalization of phenols with alkynes has attracted significant interest because of the employment of simple and accessible phenols for straightforward synthesis of these compounds, and some notable advances have been made (Scheme 1).[8] Sahoo and co-workers[8a]

Scheme 1. Direct Annulation of Free Phenols with Alkynes



explored a Pd-catalyzed oxidative annulation of phenols with internal alkynes to give 2,3-diarylbenzo[*b*]furans. Subsequently, the Cu-[8b] and Rh-catalyzed[8c] systems were also successfully developed by Jiang and Shi, respectively.

However, despite these achievements,[8] these protocols are not compatible with terminal alkynes because the homocoupling of terminal alkynes is favored, and it cannot be suppressed under transition-metal-catalyzed oxidative conditions.[8a,9] Furthermore, facile oxidation of phenols to C−C coupling products and *ortho*-quinones, together with further decomposition, also makes it very difficult to control the chemoselectivity under such conditions.[10] Thus, the synthesis of these compounds direct from terminal alkynes with phenols still remains a significant challenge. Moreover, transition metals are not environmentally benign and must be carefully removed from the products due to their toxicity, especially for the drug industry.

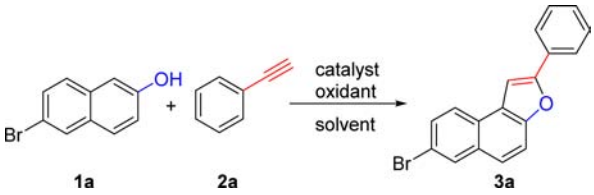
Herein, we describe a metal-free strategy for the synthesis of 2-arylnaphtho[2,1-*b*]furan via acid-catalyzed selective oxidative radical annulation between 2-naphthols and terminal alkynes, in which terminal alkynes are first successfully employed as substrates, and the homocoupling of alkynes is completely suppressed. Naphthofurans represent unique scaffolds in a number of pharmacologically and biologically active compounds,[2g,11] and thus the development of new methods to construct such frameworks is highly relevant for drug discovery.

We commenced our investigation with the treatment of 6-bromonaphthalen-2-ol (**1a**) with phenylacetylene (**2a**, 4.0 equiv) in the presence of $BF_3{\cdot}Et_2O$ (5 mol %) and DDQ (1.2 equiv) in toluene at 80 °C, and annulation product 7-bromo-2-phenylnaphtho[2,1-*b*]furan (**3a**) was observed in a 54% GC yield (Table 1, entry 1). Based on this finding, a variety of Lewis acid catalysts, such as $FeCl_3$, $AlCl_3$, $Zn(OTf)_2$, and $In(OTf)_3$, were examined, and BF_3 was found to be the best choice (Table 1, entries 2−5). The acid catalyst was crucial for this reaction; only a trace amount of the desired product was detected in its absence (Table 1, entry 6), whereas greater catalyst loading did not increase the reaction performance (Table 1, entry 7). DDQ also showed a unique effect on this reaction, and other chemical oxidants such as BQ (1,4-benzoquinone), oxygen, $Na_2S_2O_8$, and DTBP (di-*tert*-butylperoxide) were found to be ineffective (Table 1, entries 8−11). These results show that BF_3 and DDQ were essential ingredients for the reaction, and their interaction probably favored the selective oxidative transformation (vide infra).[12] Solvent also played an important role in the reaction. When *p*-xylene, PhCl, and $CHCl_3$ were used as

Received: May 9, 2016
Published: June 15, 2016

DOI: 10.1021/acs.orglett.6b01352
Org. Lett. 2016, 18, 3138−3141

Table 1. Optimization of the Reaction Conditions[a]



1a 2a 3a

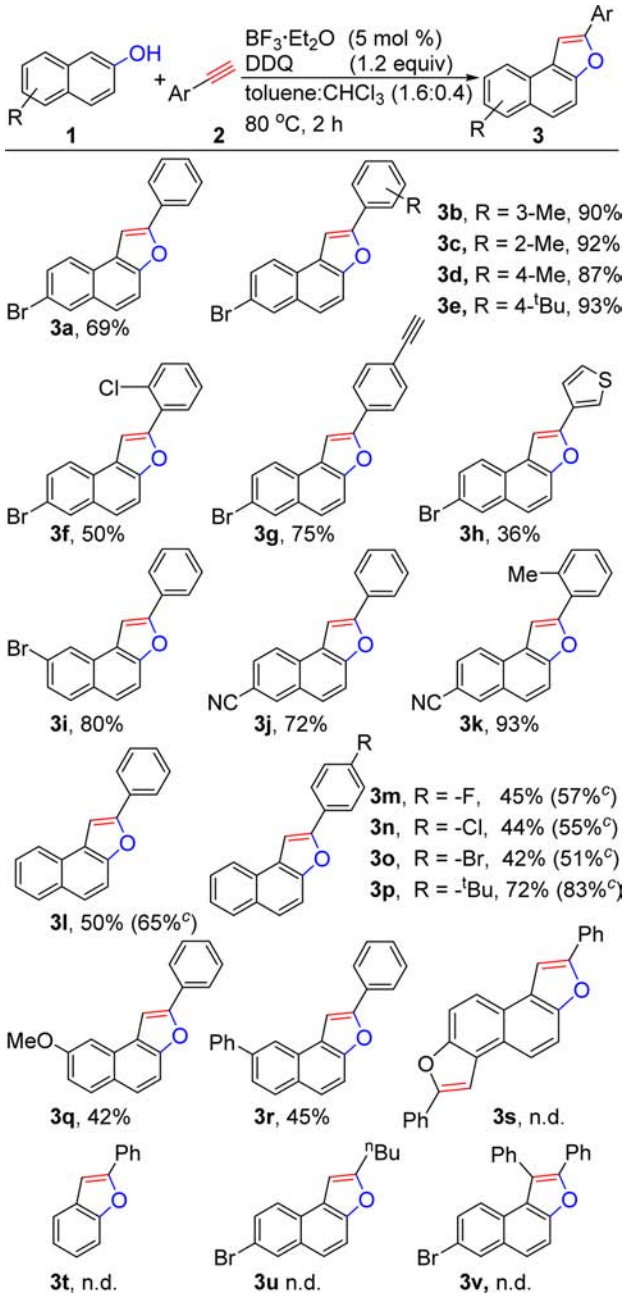
entry	catalyst	oxidant	solvent	yield (%)[b]
1	$BF_3{\cdot}Et_2O$	DDQ	toluene	54
2	$FeCl_3$	DDQ	toluene	12
3	$AlCl_3$	DDQ	toluene	18
4	$Zn(OTf)_2$	DDQ	toluene	7
5	$In(OTf)_3$	DDQ	toluene	32
6		DDQ	toluene	trace
7[c]	$BF_3{\cdot}Et_2O$	DDQ	toluene	53
8	$BF_3{\cdot}Et_2O$	BQ	toluene	nd
9	$BF_3{\cdot}Et_2O$	O_2	toluene	nd
10	$BF_3{\cdot}Et_2O$	$Na_2S_2O_8$	toluene	nd
11	$BF_3{\cdot}Et_2O$	DTBP	toluene	nd
12	$BF_3{\cdot}Et_2O$	DDQ	*p*-xylene	40
13	$BF_3{\cdot}Et_2O$	DDQ	PhCl	58
14	$BF_3{\cdot}Et_2O$	DDQ	$CHCl_3$	35
15[d]	$BF_3{\cdot}Et_2O$	DDQ	PhCl/$CHCl_3$	55
16[d]	$BF_3{\cdot}Et_2O$	DDQ	*p*-xylene/$CHCl_3$	45
17[d]	$BF_3{\cdot}Et_2O$	DDQ	toluene/$CHCl_3$	72
18[d,e]	BF_3 Et_2O	DDQ	toluene/$CHCl_3$	52
19[d,f]	$BF_3{\cdot}Et_2O$	DDQ	toluene/$CHCl_3$	71
20[d,g]	$BF_3{\cdot}Et_2O$	DDQ	toluene/$CHCl_3$	45
21[d,h]	$BF_3{\cdot}Et_2O$	DDQ	toluene/$CHCl_3$	80

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.8 mmol, 4.0 equiv), catalyst (5 mol %), oxidant (0.24 mmol, 1.2 equiv), solvent (2 mL), N_2, 80 °C, 2 h. [b]GC yield using dodecane as an internal standard. [c]With 10 mol % of $BF_3{\cdot}Et_2O$. [d]Ratio of mixed solvent is 4:1 (v/v). [e]60 °C. [f]100 °C. [g]**2a** (0.4 mmol, 2.0 equiv). [h]**2a** (1.6 mmol, 8.0 equiv).

solvents, desired product **3a** was obtained in 40, 58, and 35% yields, respectively (Table 1, entries 12−14). The yield of **3a** was significantly improved by the use of the mixed toluene and $CHCl_3$ (72%, Table 1, entry 17). The reaction temperature was also examined. When the reaction temperature was reduced to 60 °C, only a 52% yield of **3a** was obtained (Table 1, entry 18). No promotion was observed by increasing the temperature to 100 °C (Table 1, entry 19). Notably, excess phenylacetylene could suppress the undesired oxidation of **1a** and accelerate the selective transformation of **1a** to the desired product (Table 1, entries 20 and 21). When the 8.0 molar equiv of **2a** was loaded, 80% yield of **3a** was obtained. Redundant **2a** could survive in the oxidative system and was well recovered (97%).

Next, the scope and generality of this reaction were investigated. Reaction of **1a** and 4.0 equiv of **2a** gave **3a** in a 69% isolated yield. For terminal alkynes, electron-donating groups such as methyl and *t*-butyl, regardless of their positions on the phenyl ring, resulted in excellent yields of the desired products (87−93%, Scheme 2, **3b−e**). The excellent reactivity is probably attributed to the high stability of the vinyl radical intermediate (vide infra). The electron-withdrawing group remarkably lowered the catalytic efficiency, and **3f** was produced in only 50% yield (Scheme 2, **3f**). 1,4-Diethynylbenzene worked well for this transformation, and desired product **3g** was produced in a 75% yield with one alkynyl group untouched. The heteroaromatic alkyne containing thiophene also reacted with **1a** to produce the corresponding product **3h** in a 36% yield

Scheme 2. Substrate Scope[a,b]



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.8 mmol, 4.0 equiv), $BF_3{\cdot}Et_2O$ (5 mol %), DDQ (0.24 mmol, 1.2 equiv), toluene (1.6 mL), $CHCl_3$ (0.4 mL), N_2, 80 °C, 2 h. [b]Isolated yields. [c]**2** (1.6 mmol, 8.0 equiv).

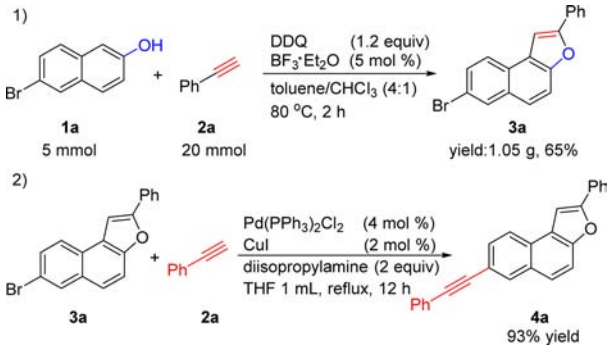
(Scheme 2, **3h**). The diminished reactivity is probably due to the detrimental interaction between sulfur and BF_3. In contrast, electron-withdrawing groups in 2-naphthols facilitated the reaction, and the corresponding naphthofurans were obtained in 72−93% yields (Scheme 2, **3i−k**). Despite relatively low efficiency for 2-naphthol, satisfactory yields could be achieved using excess alkynes (51−83%, Scheme 2, **3l−p**). Electron-donating groups such as CH_3O- and Ph− in naphthols gave moderate yields of the corresponding products (Scheme 2, **3q,r**). The reaction showed high regioselectivity, and 1-naphthol was not applicable for the annulation reaction. Unfortunately, the reaction proceeded sluggishly using phenol and biphenol (2,6-

DOI: 10.1021/acs.orglett.6b01352
Org. Lett. 2016, 18, 3138−3141

dihydroxynaphthalene) as substrates (Scheme 2, **3s**,**t**), and the desired products were not observed nor was 1-hexyne because an alkyl group could not stabilize the reactive vinyl radical intermediate (Scheme 2, **3u**).[13] Compared with terminal alkynes, the internal alkyne did not show any reactivity under the reaction conditions (Scheme 2, **3v**). Therefore, the procedure offers a complementary alternative to current methodologies.[8]

To investigate the potential utility of this transformation, a scale-up reaction was conducted (Scheme 3, eq 1). Gram-scale

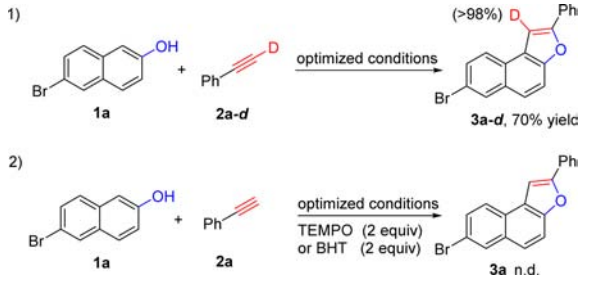
Scheme 3. Synthetic Utility



synthesis was successfully achieved (1.05 g, 65% yield) by treatment of **1a** (5 mmol) with **2a** (20 mmol) under similar conditions. Halo-heteroarenes are important organic intermediates for the synthesis of complex compounds through the transition-metal-catalyzed cross-coupling. For example, reaction of **3a** with phenylacetylene could give a more functionalized compound **4a** in 93% yield (Scheme 3, eq 2) under Pd-catalyzed coupling conditions. The above results verify that this convenient method is practical for the synthesis of complex organic intermediates (see Supporting Information for details).[8]

To gain insight into the mechanism of the reaction, control experiments were conducted. At first, reaction of a deuterium-labeled phenylacetylene **2a**-***d*** with **1a** under the optimized conditions produced corresponding product **3a**-***d*** in 70% yield with deuterium incorporated quantitatively (D content: >98%), revealing that the dehydrogenation of phenylacetylene is not involved in the reaction, but the addition reaction between the alkyne and 2-naphthol takes place (Scheme 4, eq 1). Radical

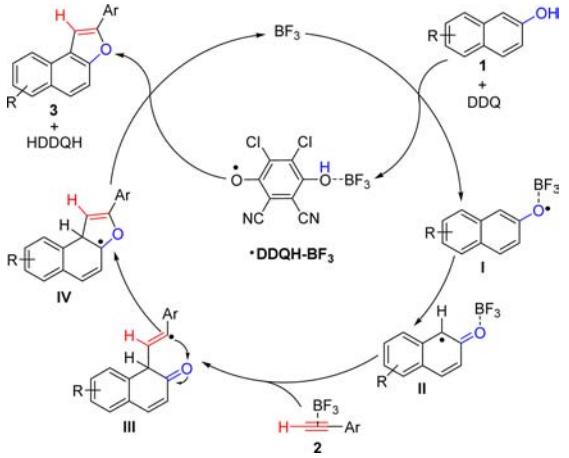
Scheme 4. Control Experiments



inhibitors such as TEMPO and BHT (butylated hydroxyl toluene) could thoroughly block the reaction, and no desired product was detected (Scheme 4, eq 2). Therefore, the reaction probably proceeds via a vinyl radical pathway, which is consistent with the electron effect of the substituent of alkynes.

On the basis of above results and literature reports,[6g,12−14] a possible mechanism is proposed (Scheme 5). Initially, 2-

Scheme 5. Possible Reaction Mechanism



naphthol **1** is oxidized by DDQ under the oxophile Lewis acid BF_3 to form naphthol radical **I** with concomitant generation of a radical DDQH−BF_3 complex.[12] Naphthol radical **I** tautomerizes to C-radical **II**. Then intermediate **II** undergoes a radical addition to the terminal alkyne **2** that could also be activated by BF_3 to generate vinyl radical **III**.[13,14] Vinyl radical **III** is highly reactive, and it attacks the oxygen atom to form intermediate **IV**.[6g] Finally, the desired product naphthofuran **3** is produced by the dehydrogenation of **IV** under the radial DDQH−BF_3 complex, and the release of BF_3 closes the catalytic cycle.

In summary, we have developed for the first time a metal-free selective oxidative transformation of naphthols with terminal alkynes to 2-arylnaphtho[2,1-*b*]furans. Other than the reported reaction mechanisms of the annulation of phenols with internal alkynes, the reaction probably proceeds via free radical C−C coupling and C−O cyclization, initiated by selective oxidative activation of an *ortho*-C−H bond of naphthols. This efficient and metal-free synthesis can be easily scaled up and is practical for the preparation of synthetically useful organic intermediates.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01352.

Experimental procedures, full spectroscopic data, and copies of ^{1}H, ^{19}F, and ^{13}C spectra (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: djyustc@hotmail.com.

*E-mail: zhouyb@hnu.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Financial support by the National NSF of China (Grant Nos. 21573065, 21172062, and 21273066) and the NSF of Hunan Province (Grant No. 2016JJ1017) is appreciated. We also thank Prof. Li-Biao Han (AIST of Japan) for his kind help.

■ REFERENCES

(1) (a) Boto, A.; Alvarez, L. Furan and Its Derivatives. *Heterocycles in Natural Product Synthesis*; Wiley-VCH: Weinheim, Germany, 2011; pp

DOI: 10.1021/acs.orglett.6b01352
Org. Lett. 2016, 18, 3138−3141

97−152. (b) Kratochvil, J. F.; Burris, R. H.; Seikel, M. K.; Harkin, J. M. *Phytochemistry* **1971**, *10*, 2529. (c) Lin, Y.-L.; Tsai, Y.-L.; Kuo, Y.-H.; Liu, Y.-H.; Shiao, M.-S. *J. Nat. Prod.* **1999**, *62*, 1500. (d) Cagniant, P.; Cagniant, D. *Adv. Heterocycl. Chem.* **1975**, *18*, 337. (e) Tatum, J. H.; Baker, R. A.; Berry, R. E. *Phytochemistry* **1987**, *26*, 2499. (f) Quin, L. D.; Tyrell, J. A. *Fundamentals of Heterocyclic Chemistry: Importance in Nature and in the Synthesis of Pharmaceuticals*; Wiley: Hoboken, NJ, 2007; p 196. (g) La Clair, J. J.; Rheingold, A. L.; Burkart, M. D. *J. Nat. Prod.* **2011**, *74*, 2045.

(2) (a) Brown, E. V.; Coleman, R. L. *J. Med. Chem.* **1973**, *16*, 717. (b) Mechoulam, R.; Breuer, A.; Järbe, T. U. C.; Hiltunen, A. J.; Glaser, R. *J. Med. Chem.* **1990**, *33*, 1037. (c) Ecker, G.; Chiba, P.; Hitzler, M.; Schmid, D.; Visser, K.; Cordes, H. P.; Csöllei, J.; Seydel, J. K.; Schaper, K. *J. Med. Chem.* **1996**, *39*, 4767. (d) Day, S.-H.; Chiu, N.-Y.; Tsao, L.-T.; Wang, J.-P.; Lin, C.-N. *J. Nat. Prod.* **2000**, *63*, 1560. (e) Carlsson, B.; Singh, B. N.; Temciuc, M.; Nilsson, S.; Li, Y.; Mellin, C.; Malm, J. *J. Med. Chem.* **2002**, *45*, 623. (f) Bowyer, P. W.; Tate, E. W.; Leatherbarrow, R. J.; Holder, A. A.; Smith, D. F.; Brown, K. A. *ChemMedChem* **2008**, *3*, 402. (g) Le Guével, R.; Oger, F.; Lecorgne, A.; Dudasova, Z.; Chevance, S.; Bondon, A.; Barath, P.; Simonneaux, G.; Salbert, G. *Bioorg. Med. Chem.* **2009**, *17*, 7021.

(3) (a) Ziegert, R. E.; Toräng, J.; Knepper, K.; Bräse, S. *J. Comb. Chem.* **2005**, *7*, 147. (b) Piloto, A. M.; Costa, S. P. G.; Gonçalves, M. S. T. *Tetrahedron Lett.* **2005**, *46*, 4757. (c) Tsuji, H.; Mitsui, C.; Ilies, L.; Sato, Y.; Nakamura, E. *J. Am. Chem. Soc.* **2007**, *129*, 11902. (d) Walker, B.; Tamayo, A. B.; Dang, X. D.; Zalar, P.; Seo, J. H.; Garcia, A.; Tantiwiwat, M.; Nguyen, T. Q. *Adv. Funct. Mater.* **2009**, *19*, 3063. (e) Aiken, S.; Allsopp, B.; Booth, K.; Gabbutt, C. D.; Heron, B. M.; Rice, C. R. *Tetrahedron* **2014**, *70*, 9352.

(4) For selected examples, see: (a) Fürstner, A.; Davies, P. W. *J. Am. Chem. Soc.* **2005**, *127*, 15024. (b) Youn, S. W.; Eom, J. I. *Org. Lett.* **2005**, *7*, 3355. (c) Liang, Y.; Tang, S.; Zhang, X.-D.; Mao, L.-Q.; Xie, Y.-X.; Li, J.-H. *Org. Lett.* **2006**, *8*, 3017. (d) Martinez, C.; Alvarez, R.; Aurrecoechea, J. M. *Org. Lett.* **2009**, *11*, 1083. (e) Ye, Y.; Fan, R. *Chem. Commun.* **2011**, *47*, 5626. (f) Li, C.; Zhang, Y.; Li, P.; Wang, L. *J. Org. Chem.* **2011**, *76*, 4692. (g) Matsuda, N.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2012**, *77*, 617. (h) Li, J.; Zhu, Z.; Yang, S.; Zhang, Z.; Wu, W.; Jiang, H. *J. Org. Chem.* **2015**, *80*, 3870.

(5) For selected examples, see: (a) Arcadi, A.; Cacchi, S.; Del Rosario, M.; Fabrizi, G.; Marinelli, F. *J. Org. Chem.* **1996**, *61*, 9280. (b) Bates, C. G.; Saejueng, P.; Murphy, J. M.; Venkataraman, D. *Org. Lett.* **2002**, *4*, 4727. (c) Jaseer, E. A.; Prasad, D. J. C.; Sekar, G. *Tetrahedron* **2010**, *66*, 2077. (d) Wang, J.-R.; Manabe, K. *J. Org. Chem.* **2010**, *75*, 5340. (e) Wang, R.; Mo, S.; Lu, Y.; Shen, Z. *Adv. Synth. Catal.* **2011**, *353*, 713. (f) Byers, P. M.; Rashid, J. I.; Mohamed, R. K.; Alabugin, I. V. *Org. Lett.* **2012**, *14*, 6032. (g) Moure, M. J.; SanMartin, R.; Domínguez, E. *Adv. Synth. Catal.* **2014**, *356*, 2070. (h) Zhou, R.; Wang, W.; Jiang, Z.; Wang, K.; Zheng, X.; Fu, H.; Chen, H.; Li, R. *Chem. Commun.* **2014**, *50*, 6023.

(6) Metal-catalyzed methods from other functionalized substrates have been well developed. From prefunctionalized alkynes or phenols, see: (a) Wang, S.; Li, P.; Yu, L.; Wang, L. *Org. Lett.* **2011**, *13*, 5968. (b) Zhou, W.; Zhang, Y.; Li, P.; Wang, L. *Org. Biomol. Chem.* **2012**, *10*, 7184. (c) Larock, R. C.; Yum, E. K.; Doty, M. J.; Sham, K. K. C. *J. Org. Chem.* **1995**, *60*, 3270. (d) Oonishi, Y.; Gómez-Suárez, A.; Martin, A. R.; Makida, Y.; Slawin, A. M. Z.; Nolan, S. P. *Chem. - Eur. J.* **2014**, *20*, 13507. (e) Wan, J.-P.; Wang, H.; Liu, Y.; Ding, H. *Org. Lett.* **2014**, *16*, 5160. (f) Rao, V. K.; Shelke, G. M.; Tiwari, R.; Parang, K.; Kumar, A. *Org. Lett.* **2013**, *15*, 2190. From free phenols and olefins, see: (g) Huang, Z.; Jin, L.; Feng, Y.; Peng, P.; Yi, H.; Lei, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 7151. (h) Kshirsagar, U. A.; Regev, C.; Parnes, R.; Pappo, D. *Org. Lett.* **2013**, *15*, 3174. (i) Blum, T. R.; Zhu, Y.; Nordeen, S. A.; Yoon, T. P. *Angew. Chem., Int. Ed.* **2014**, *53*, 11056. (j) Sharma, U.; Naveen, T.; Maji, A.; Manna, S.; Maiti, D. *Angew. Chem., Int. Ed.* **2013**, *52*, 12669. (k) Agasti, S.; Sharma, U.; Naveen, T.; Maiti, D. *Chem. Commun.* **2015**, *51*, 5375. (l) Agasti, S.; Maity, S.; Szabo, K. J.; Maiti, D. *Adv. Synth. Catal.* **2015**, *357*, 2331. (m) Rao, M. L. N.; Dasgupta, P. *RSC Adv.* **2015**, *5*, 65462.

(7) Metal-free methods from specially prefunctionalized substrates: (a) Kobatake, T.; Fujino, D.; Yoshida, S.; Yorimitsu, H.; Oshima, K. *J. Am. Chem. Soc.* **2010**, *132*, 11838. (b) Akai, S.; Morita, N.; Iio, K.; Nakamura, Y.; Kita, Y. *Org. Lett.* **2000**, *2*, 2279. (c) Schevenels, F.; Markó, I. E. *Org. Lett.* **2012**, *14*, 1298. (d) Zhang, F.; Li, C.; Wang, C.; Qi, C. *Org. Biomol. Chem.* **2015**, *13*, 5022. (e) Kanazawa, C.; Goto, K.; Terada, M. *Chem. Commun.* **2009**, *35*, 5248.

(8) (a) Kuram, M. R.; Bhanuchandra, M.; Sahoo, A. K. *Angew. Chem., Int. Ed.* **2013**, *52*, 4607. (b) Zeng, W.; Wu, W.; Jiang, H.; Huang, L.; Sun, Y.; Chen, Z.; Li, X. *Chem. Commun.* **2013**, *49*, 6611. (c) Zhu, R.; Wei, J.; Shi, Z. *Chem. Sci.* **2013**, *4*, 3706.

(9) Stuart, D. R.; Alsabeh, P.; Kuhn, M.; Fagnou, K. *J. Am. Chem. Soc.* **2010**, *132*, 18326.

(10) (a) Xiao, B.; Gong, T.-J.; Liu, Z.-J.; Liu, J.-H.; Luo, D.-F.; Xu, J.; Liu, L. *J. Am. Chem. Soc.* **2011**, *133*, 9250. (b) Li, X.; Hewgley, J. B.; Mulrooney, C. A.; Yang, J.; Kozlowski, M. C. *J. Org. Chem.* **2003**, *68*, 5500. (c) Smrčina, M.; Poláková, J.; Vyskočil, Š.; Kočovský, P. *J. Org. Chem.* **1993**, *58*, 4534. (d) Hay, A. S.; Blanchard, H. S.; Endres, G. F.; Eustance, J. W. *J. Am. Chem. Soc.* **1959**, *81*, 6335. (e) Wang, A.; Jiang, H.; Xu, Q. *Synlett* **2009**, *2009*, 929. (f) Rappoport, Z., Ed. *The Chemistry of Phenols*; John Wiley & Sons, Ltd.: West Sussex, U.K., 2003; p 1153. (g) Allen, S. E.; Walvoord, R. R.; Padilla-Salinas, R.; Kozlowski, M. C. *Chem. Rev.* **2013**, *113*, 6234. (h) Ling, K.-Q.; Lee, Y.; Macikenas, D.; Protasiewicz, J. D.; Sayre, L. M. *J. Org. Chem.* **2003**, *68*, 1358. (i) Esguerra, K. V. N.; Fall, Y.; Petitjean, L.; Lumb, J.-P. *J. Am. Chem. Soc.* **2014**, *136*, 7662. (j) Esguerra, K. V. N.; Fall, Y.; Lumb, J.-P. *Angew. Chem., Int. Ed.* **2014**, *53*, 5877.

(11) (a) Ishiguro, K.; Ohira, Y.; Oku, H. *J. Nat. Prod.* **1998**, *61*, 1126. (b) Lumb, J.-P.; Trauner, D. *J. Am. Chem. Soc.* **2005**, *127*, 2870. (c) Kotoku, N.; Higashimoto, K.; Kurioka, M.; Arai, M.; Fukuda, A.; Sumii, Y.; Sowa, Y.; Sakai, T.; Kobayashi, M. *Bioorg. Med. Chem. Lett.* **2014**, *24*, 3389. (d) Gupta, P. P.; Srimal, R. C.; Verma, N.; Tandon, J. S. *Pharm. Biol.* **1999**, *37*, 46. (e) Goldfarb, D. S. U.S. Patent Appl. US 20090163545A1 20090625, 2009. (f) Paul, N. M.; Kumar, R.; Deschamps, J. R.; Luedtke, R. R.; Newman, A. H. *J. Med. Chem.* **2008**, *51*, 6095. (g) Srivastava, V.; Negi, A. S.; Kumar, J. K.; Faridi, U.; Sisodia, B. S.; Darokar, M. P.; Luqman, S.; Khanuja, S. P. S. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 911. (h) Lee, K.-H.; Huang, B.-R. *Eur. J. Med. Chem.* **2002**, *37*, 333. (i) Ribeiro-Rodrigues, R.; dos Santos, W. G.; Oliveira, A. B.; Snieckus, V.; Zani, C. L.; Romanha, A. J. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 1509. (j) Doe, M.; Shibue, T.; Haraguchi, H.; Morimoto, Y. *Org. Lett.* **2005**, *7*, 1765. (k) Gan, C.-S.; Nan, D.-D.; Qiao, J.-P.; Wang, C.-W.; Zhou, J.-N. *J. Nucl. Med.* **2012**, *53*, 1620.

(12) (a) Ma, Y.; Zhang, D.; Yan, Z.; Wang, M.; Bian, C.; Gao, X.; Bunel, E. E.; Lei, A. *Org. Lett.* **2015**, *17*, 2174. (b) Shi, J.-L.; Zhang, J.-C.; Wang, B.-Q.; Hu, P.; Zhao, K.-Q.; Shi, Z.-J. *Org. Lett.* **2016**, *18*, 1238. (c) Jang, S. S.; Youn, S. W. *Org. Biomol. Chem.* **2016**, *15*, 2200.

(13) Lu, Q.; Zhang, J.; Zhao, G.; Qi, Y.; Wang, H.; Lei, A. *J. Am. Chem. Soc.* **2013**, *135*, 11481.

(14) Yan, H.; Rong, G.; Liu, D.; Zheng, Y.; Chen, J.; Mao, J. *Org. Lett.* **2014**, *16*, 6306.

DOI: 10.1021/acs.orglett.6b01352
Org. Lett. 2016, 18, 3138−3141