Organic LETTERS

Letter

pubs.acs.org/OrgLett

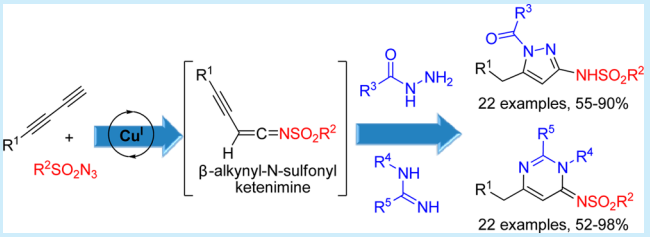
# Copper-Catalyzed Three-Component Synthesis of 3-Aminopyrazoles and 4-Iminopyrimidines via β-Alkynyl-*N*-sulfonyl Ketenimine Intermediates

Yanpeng Xing, Binyu Cheng, Jing Wang, Ping Lu,* and Yanguang Wang*

Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. China

Supporting Information

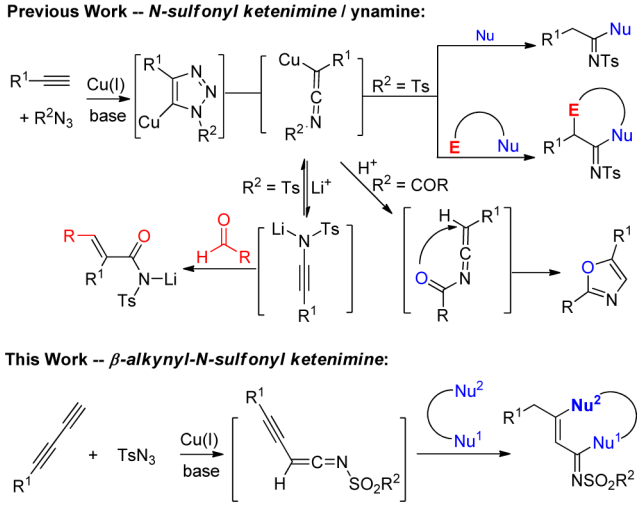
**ABSTRACT:** 3-Aminopyrazoles and 4-iminopyrimidines were efficiently prepared via copper-catalyzed three-component reactions of butadiynes, sulfonylazides, and hydrazides or imidamides. The reactions were regioselectively approached via the formation of a β-alkynyl-*N*-sulfonyl ketenimine intermediate which represented a new and effective 1,3-dielectrophilic equivalent in organic synthesis.



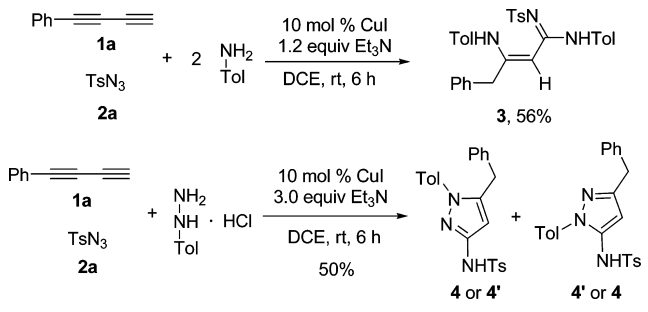

Copper catalyzed alkyne azide cycloaddition (CuAAC) has become a powerful and reliable tool for the construction of 1,4-disubstituted-1,2,3-triazole since Sharpless and Meldal published their pioneer works.[1] It represents one of the most important click reactions and has been widely applied in bioconjugation,[2] drug discovery,[3] and material science.[4] Meanwhile, the CuAAC mechanism was well demonstrated by Fokin's research group.[5] Nevertheless, the ring of the 1,2,3-triazole is fragile when the N1-position of the triazole is occupied by the electron-withdrawing group such as sulfonyl and phosphoryl.[6] For this reason, the 4-substituted-1-sulfonyl-1,2,3-triazole ring would open to form ketenimine or ynamine intermediates with the exclusion of nitrogen gas after the CuAAC process (Scheme 1).[7] In these cases, ketenimine or ynamine intermediates could be inter-[8] or intramolecularly[9] trapped by various nucleophiles,[8,9] electrophiles,[10] or readily available reagents containing both nucleo- and electrophilic centers.[11] Additionally, [2 + 2] and [4 + 2] cycloadditions[12] as well as sigmatropic rearrangement[13] of ketenimines generated through CuAAC have also been explored. Thus, a number of amidines, amidates, carbocycles, and heterocycles were feasibly assembled via these copper catalyzed tandem reactions. We would like to report a new reaction model based on the β-alkynyl-*N*-sulfonyl ketenimine intermediate and its trapping by reagents with two nucleophilic centers.

Initially, *p*-toluidine (2 equiv) was applied to trap the β-alkynyl-*N*-sulfonyl ketenimine intermediate in situ generated from 1-phenyl-1,3-butadiyne (**1a**) and tosyl azide (**2a**) in the presence of CuI (10 mol %) and triethylamine (1.2 equiv) (Scheme 2). To our delight, imidamide **3** was obtained in 56% yield. Stimulated by this result and attracted by the importance of heterocycles, we tried to use the reagents with two nucleophilic centers to trap the ketenimine intermediate. Thus, *p*-tolylhydrazine hydrochloride was preliminarily consid-

**Scheme 1. Previous Works and Our Design**




**Scheme 2. Formation of β-Alkynyl-*N*-sulfonyl Ketenimine and Its Trapping with *p*-Toluidine or Hydrazine**




**Received:** August 3, 2014

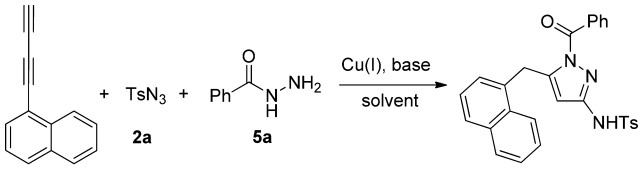




dx.doi.org/10.1021/ol502302w | *Org. Lett.* XXXX, XXX, XXX−XXX

ered. After the mixture of **1a**, **2a**, *p*-tolylhydrazine hydrochloride, CuI (10 mol %), and $Et_3N$ in dichloroethane (DCE) was stirred at room temperature for 6 h, pyrazole **4** and its isomer **4′** were isolated in 50% total yield. Pyrazole is a significant heterocycle in a series of bioactive compounds, and many conventional approaches for the preparation of pyrazoles have been disclosed.[14] Although the pyrazole ring was ideally constructed via this three-component strategy, the outcome lacks the regioselectivity. We have expended much effort to obtain better regioselectivity, but we failed. Therefore, we changed the trapping reagent from *p*-tolylhydrazine to benzohydrazide (**5a**). In this case, **5a** reacted with 1-(naphthalene-1-yl)-1,3-butadiyne (**1b**) and **2a** to give 3-aminopyrazole **6a** in 77% yield (Table 1, entry 1).

**Table 1. Screening of Reaction Conditions for the Formation of 6a[a]**



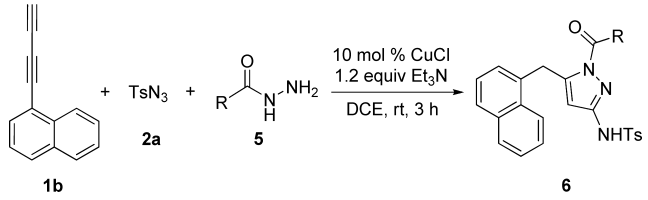

| entry | catalyst | base | solvent | yield (%)[b] |
|---|---|---|---|---|
| 1 | CuI | $Et_3N$ | DCE | 77 |
| 2 | CuI | $Et_3N$ | DCM | 74 |
| 3 | CuI | $Et_3N$ | $CHCl_3$ | 69 |
| 4 | CuI | $Et_3N$ | $CH_3CN$ | 70 |
| 5 | CuI | $Et_3N$ | THF | 23 |
| 6 | CuI | $Et_3N$ | toluene | 59 |
| 7 | CuI | $Et_3N$ | DMF | 53 |
| 8 | CuBr | $Et_3N$ | DCE | 70 |
| 9 | CuCl | $Et_3N$ | DCE | 83 |
| 10 | CuTc | $Et_3N$ | DCE | 71 |
| 11 | $CuBr(SMe_2)$ | $Et_3N$ | DCE | 75 |
| 12 | CuCl | DABCO | DCE | 35 |
| 13 | CuCl | 2,6-lutidine | DCE | ND |
| 14 | CuCl | pyridine | DCE | ND |
| 15 | CuCl | $K_2CO_3$ | DCE | ND |

[a]Reaction conditions: **1b** (0.24 mmol), **2a** (0.24 mmol), **5a** (0.2 mmol), base (0.24 mmol), Cu(I) (0.02 mmol), solvent (1 mL), rt, 3 h. [b]Isolated yield based on **5a**.

Encouraged by this result, we optimized the reaction conditions for the formation of **6a** (Table 1). The yield of **6a** largely depended on the solvent. DCE was selected to be optimal among dichloromethane (DCM), chloroform, acetonitrile, THF, toluene, and DMF (Table 1, entries 1–7). Among the various tested copper catalysts, such as CuBr, CuCl, CuTc, and $CuBr(Me_2S)$, CuCl gave the best yield (Table 1, entries 8–11). DABCO worked for the reaction, but with a lower yield (Table 1, entry 12). When 2,6-lutidine, pyridine, or potassium bicarbonate was used as the base additive, **6a** was not detected with the recovery of **5a** (Table 1, entries 13–15). Thus, the optimal reaction conditions were established (Table 1, entry 9).

With the optimized reaction conditions in hand, we tested the substrate diversity. A series of monosubstituted benzohydrazides (**5a–g** in Table 2) were tested first. The corresponding products (**6a–g**) were obtained in yields between 63% and 83%. No apparent substituent effect could be concluded. Without any substitution, the benzohydrazide

**Table 2. Substrate Scope for the Synthesis of 3-Aminopyrazoles 6a–l[a]**



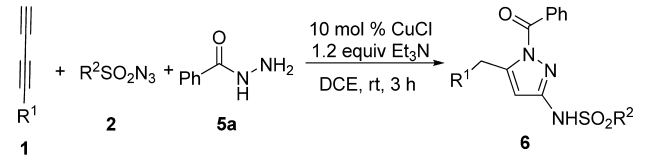

| entry | **5** (R) | **6**/yield (%) |
|---|---|---|
| 1 | **5a** ($C_6H_5$) | **6a**/83 |
| 2 | **5b** (*p*-$MeOC_6H_4$) | **6b**/80 |
| 3 | **5c** (*o*-$MeC_6H_4$) | **6c**/68 |
| 4 | **5d** (*m*-$MeC_6H_4$) | **6d**/82 |
| 5 | **5e** (*o*-$FC_6H_4$) | **6e**/73 |
| 6 | **5f** (*m*-$FC_6H_4$) | **6f**/76 |
| 7 | **5g** (*p*-$FC_6H_4$) | **6g**/63 |
| 8 | **5h** (2-furyl) | **6h**/62 |
| 9 | **5i** (2-thienyl) | **6i**/77 |
| 10 | **5j** (Me) | **6j**/72 |
| 11 | **5k** ($Me_3CO$) | **6k**/66 |
| 12 | **5l** ($C_6H_5CH_2O$) | **6l**/60 |

[a]Reaction conditions: **1b** (0.24 mmol), **2a** (0.24 mmol), **5** (0.2 mmol), $Et_3N$ (0.24 mmol), CuCl (0.02 mmol), DCE (1 mL), rt, 3 h. [b]Isolated yield based on **5**.

(**5a**) gave the best yield. Furan-2-carbohydrazide (**5h**) and thiophen-2-carbohydrazide (**5i**) furnished **6h** and **6i** in yields of 62% and 77%, respectively. It was noticeable that acetohydrazide (**5j**) worked for the reaction and produced **6j** in 72% yield. Finally, hydrazine carboxylates (**5k**, **5l**) were tested for the reaction. **6k** and **6l**, with Boc and CBz protected on pyrazoles, were obtained in 66% and 60% yields, respectively.

Various substituted benzenesulfonyl azides **2b–g** (Table 3) worked for the reaction and produced corresponding **6m–6r** in yields varying from 60% to 90%. A moderate electron-donating group on benzenesulfonyl azide, such as 2,4,6-trimethylbenzenesulfonyl azide (**2g**), furnished **6r** in the highest yield

**Table 3. Substrate Scope for the Synthesis of 3-Aminopyrazoles 6m–v[a]**




| entry | **1** ($R^1$) | **2** ($R^2$) | **6**/yield (%) |
|---|---|---|---|
| 1 | **1b** (1-naphthalenyl) | **2b** ($C_6H_5$) | **6m**/71 |
| 2 | **1b** | **2c** (*p*-$MeOC_6H_4$) | **6n**/72 |
| 3 | **1b** | **2d** (*p*-$ClC_6H_4$) | **6o**/74 |
| 4 | **1b** | **2e** (*p*-$CF_3C_6H_4$) | **6p**/70 |
| 5 | **1b** | **2f** (*p*-$NO_2C_6H_4$) | **6q**/60 |
| 6 | **1b** | **2g** (2,4,6-$Me_3C_6H_2$) | **6r**/90 |
| 7 | **1b** | **2h** (Me) | **6s**/72 |
| 8 | **1c** (*p*-$ClC_6H_4$) | **2a** | **6t**/80 |
| 9 | **1d** (*p*-$MeOC_6H_4$) | **2a** | **6u**/64 |
| 10 | **1e** (*n*-$C_6H_{13}$) | **2a** | **6v**/55 |

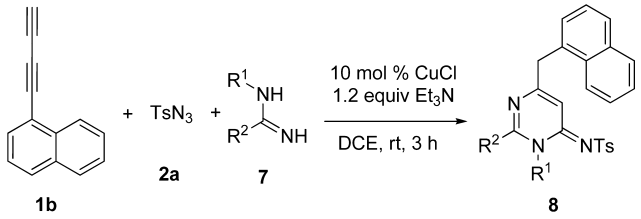
[a]Reaction conditions: **1** (0.24 mmol), **2** (0.24 mmol), **5a** (0.2 mmol), $Et_3N$ (0.24 mmol), CuCl (0.02 mmol), DCE (1 mL), rt, 3 h. [b]Isolated yield based on **5a**.


dx.doi.org/10.1021/ol502302w | *Org. Lett.* XXXX, XXX, XXX–XXX

(Table 3, entry 6). Besides arenesulfonyl azides, methanesulfonyl azide (**2h**) also worked for the reaction and provided **6s** in 72% yield. From investigation of the substituent effect of 1-aryl-1,3-butadiynes, it is evident that the electron-withdrawing group (Cl) benefitted the reaction and gave a better yield (**6t**, 80%) than the electron-donating group (MeO) did (**6u**, 64%). Deca-1,3-diyne (**1e**) reacted smoothly and prepared **6v** in 55% yield.

When *N*-phenylbenzimidamide (**7a**) was used as the trapping reagent under the reaction conditions established for the pyrazole formation, 4-iminopyrimine (**8a**) was isolated in 74% yield (Table 4, entry 1). Due to the importance of

**Table 4. Substrate Scope for the Synthesis of 4-Iminopyrimines 8a–m[a]**




| entry | 7 ($R^1$, $R^2$) | 8/yield (%) |
|---|---|---|
| 1 | **7a** ($C_6H_5$, $C_6H_5$) | **8a**/74 |
| 2 | **7b** (*p*-$MeC_6H_4$, $C_6H_5$) | **8b**/88 |
| 3 | **7c** (*p*-$MeOC_6H_4$, $C_6H_5$) | **8c**/70 |
| 4 | **7d** (*p*-$BrC_6H_4$, $C_6H_5$) | **8d**/83 |
| 5 | **7e** (*o*-$BrC_6H_4$, $C_6H_5$) | **8e**/97 |
| 6 | **7f** (*m*-$BrC_6H_4$, $C_6H_5$) | **8f**/98 |
| 7 | **7g** ($C_6H_5$, *o*-$FC_6H_4$) | **8g**/98 |
| 8 | **7h** ($C_6H_5$, *p*-$MeC_6H_4$) | **8h**/72 |
| 9 | **7i** ($C_6H_5$, *p*-$MeOC_6H_4$) | **8i**/71 |
| 10 | **7j** ($C_6H_5$, *n*-$C_4H_9$) | **8j**/65 |
| 11 | **7k** ($C_6H_5$, *o*-$ClC_6H_4$) | **8k**/62 |
| 12 | **7l** ($C_6H_5$, *p*-$ClC_6H_4$) | **8l**/91 |
| 13 | **7m** ($C_6H_5$, *m*-$ClC_6H_4$) | **8m**/86 |

[a]Reaction conditions: **1b** (0.24 mmol), **2a** (0.24 mmol), **7** (0.2 mmol), $Et_3N$ (0.24 mmol), CuCl (0.02 mmol), DCE (1 mL), rt, 3 h. [b]Isolated yield based on **7**.

pyrimidine base pairs in genomics and other utilities of pyrimidine in pharmaceutics,[15] we investigated the substrate scope for the formation of 4-iminopyrimidines. The reaction tolerated a variety of substituents on imidamides (**7a–m**) and afforded corresponding 4-iminopyrimidines (**8a-m**) in yields varied from 62% to 98% without the apparent substitution effect. It was noticeable that pentanimidamide (**7j**) afforded **8j** in 65% yield.

Imidamide hydrochlorides **7n** and **7o** could be directly used as the starting materials without pretreatment. They could work well and afforded **8n** and **8o** in 52% and 61% yields, respectively. In these cases, 3 equiv of triethylamine should be applied to consume hydrochloride (Scheme 3).

The substituent effect on benzenesulfonyl azides was also investigated. 4-Chlorobenzenesulfonyl azide (**2d**) and 4-methoxybenzenesulfonyl azide (**2c**) provided the corresponding 4-iminopyrimidines **8p** and **8q** in 72% and 65% yields, respectively (Table 5). To our surprise, methanesulfonyl azide (**2h**) gave the best yield in comparison with other arenesulfonyl azides. This is different from the result obtained for the aforementioned synthesis of 3-aminopyrazoles. By changing the

**Scheme 3. Preparation of 4-Iminopyrimidines 8n and 8o**

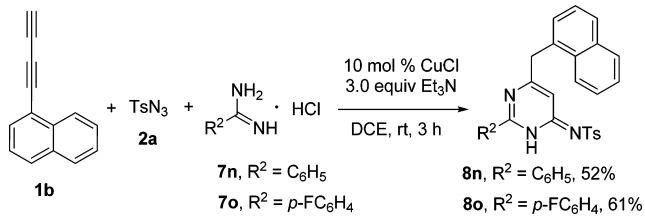
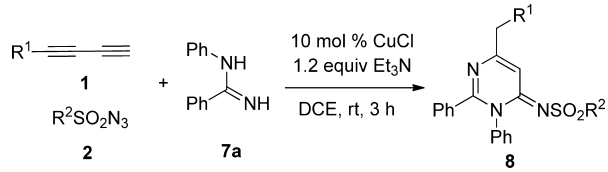



**Table 5. Substrate Scope for the Synthesis of 4-Iminopyrimidines 8p–u[a]**



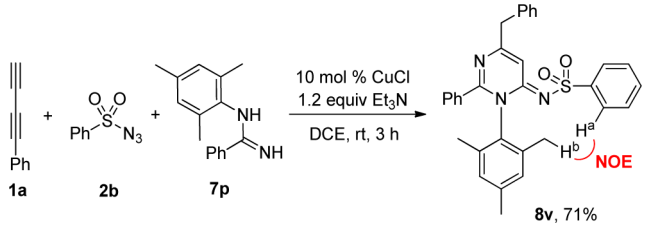

| entry | 1 ($R^1$) | 2 ($R^2$) | 8/yield (%) |
|---|---|---|---|
| 1 | **1b** (1-naphthalenyl) | **2d** (*p*-$ClC_6H_4$) | **8p**/72 |
| 2 | **1b** | **2c** (*p*-$MeOC_6H_4$) | **8q**/65 |
| 3 | **1b** | **2h** (Me) | **8r**/95 |
| 4 | **1c** (*p*-$ClC_6H_4$) | **2a** (Ts) | **8s**/69 |
| 5 | **1d** (*p*-$MeOC_6H_4$) | **2a** | **8t**/77 |
| 6 | **1e** (*n*-$C_6H_{13}$) | **2a** | **8u**/55 |

[a]Reaction conditions: **1** (0.24 mmol), **2** (0.24 mmol), **7a** (0.2 mmol), $Et_3N$ (0.24 mmol), CuCl (0.02 mmol), DCE (1 mL), room temperature, 3 h. [b]Isolated yield based on **7a**.

substituent on 1-aryl-1,3-butadiynes, **1c** and **1d** reacted smoothly and produced **8s** and **8t** in 69% and 77% yields, respectively. Furthermore, deca-1,3-diyne (**1e**) could furnish **8u** in 55% yield.

The regioselectivity of this reaction was determined by the NOE technique. The NOE between $H^a$ and $H^b$ in the molecule of **8v** clearly indicated that the reaction was highly regioselective (Scheme 4).

**Scheme 4. Determination of Regioselectivity of Reaction**

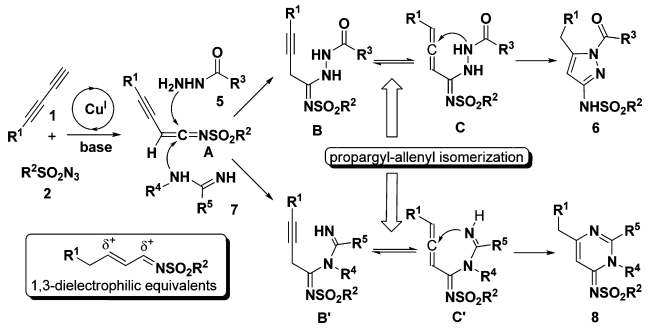



We postulated a working mechanism for the formation of 3-aminopyrazoles **6** and 4-iminopyrimidines **8** (Scheme 5). First, butadiyne **1** reacts with sulfonyl azide **2** in the presence of CuI and $Et_3N$ to form ketenimine intermediate **A** through a cascade CuAAC/intramolecular rearrangement. Second, **A** is trapped by **5** and **7** to form **B** and **B′**, respectively. Finally, **B** and **B′** undergo a propargyl-allenyl isomerization,[16] followed by cyclization to afford **6** and **8**, respectively. It is noteworthy that *β*-alkynyl-*N*-sulfonyl ketenimine **A** functions as a 1,3-dielectrophilic equivalent in this process.

In conclusion, we have developed a facile and efficient synthesis of 3-aminopyrazoles and 4-iminopyrimidines via a copper-catalyzed three-component reaction of butadiynes, sulfonylazides, and hydrazides or imidamides. The reaction


dx.doi.org/10.1021/ol502302w | *Org. Lett.* XXXX, XXX, XXX–XXX

**Scheme 5. Proposed Mechanism**




involved a $\beta$-alkynyl-*N*-sulfonyl ketenimine intermediate as a 1,3-dielectrophilic equivalent and furnished 3-aminopyrazoles and 4-iminopyrimidines in moderate to good yields with high regioselectivity. Furthermore, the starting materials are readily available. Work on the preparation of other heterocycles using this strategy is underway in our laboratory.

## ■ ASSOCIATED CONTENT

### Supporting Information

Experimental procedures and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION

### Corresponding Authors

*E-mail: pinglu@zju.edu.cn.
*E-mail: orgwyg@zju.edu.cn.

### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS

The authors thank the financial support from the National Natural Science Foundation of China (Nos. 21032005, 21272204, and J1210042).

## ■ REFERENCES

(1) (a) Rostovtsev, V. V.; Green, L. G.; Fokin, V. V.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 2596. (b) Tornóe, C. W.; Christensen, C.; Meldal, M. *J. Org. Chem.* **2002**, *67*, 3057.

(2) (a) Wang, Q.; Chan, T. R.; Hilgraf, R.; Fokin, V. V.; Sharpless, K. B.; Finn, M. G. *J. Am. Chem. Soc.* **2003**, *125*, 3192. (b) Sun, X.-L.; Stabler, C. L.; Cazalis, C. S.; Chaikof, E. L. *Bioconjugate Chem.* **2006**, *17*, 52.

(3) (a) Lewis, W. G.; Green, L. G.; Grynszpan, F.; Radic, Z.; Carlier, P. R.; Taylor, P.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2002**, *41*, 1053. (b) Moorhouse, A. D.; Santos, A. M.; Gunaratnam, M.; Moore, M.; Neidle, S.; Moses, J. E. *J. Am. Chem. Soc.* **2006**, *128*, 15972. (c) Ferreira, S. B.; Sodero, A. C. R.; Cardoso, M. F. C.; Lima, E. S.; Kaiser, C. R.; Silva, F. P., Jr.; Ferreira, V. F. *J. Med. Chem.* **2010**, *53*, 2364. (d) Wilkinson, B. L.; Innocenti, A.; Vullo, D.; Supuran, C. T.; Poulsen, S.-A. *J. Med. Chem.* **2008**, *51*, 1945.

(4) (a) Wu, P.; Feldman, A. K.; Nugent, A. K.; Hawker, C. J.; Scheel, A.; Voit, B.; Pyun, J.; Frechet, J. M. J.; Sharpless, K. B.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2004**, *43*, 3928. (b) Wu, P.; Malkoch, M.; Hunt, J. N.; Vestberg, R.; Kaltgrad, E.; Finn, M. G.; Fokin, V. V.; Sharpless, K. B.; Hawker, C. J. *Chem. Commun.* **2005**, 5775. (c) Laurent, B. A.; Grayson, S. M. *J. Am. Chem. Soc.* **2006**, *128*, 4238.

(5) (a) Hein, J. E.; Fokin, V. V. *Chem. Soc. Rev.* **2010**, *39*, 1302. (b) Worrell, B. T.; Malik, J. A.; Fokin, V. V. *Science* **2013**, *340*, 457.

(6) (a) Hermes, M. E.; Marsh, F. D. *J. Am. Chem. Soc.* **1967**, *89*, 4760. (b) Harmon, R. E.; Stanley, F.; Gupta, S. K.; Johnson, J. *J. Org. Chem.* **1970**, *35*, 3444.

(7) (a) Lu, P.; Wang, Y. G. *Synlett* **2010**, *2*, 165. (b) Kim, S. H.; Park, S. H.; Choi, J. H.; Chang, S. *Chem.—Asian J.* **2011**, *6*, 2618. (c) Lu, P.; Wang, Y. G. *Chem. Soc. Rev.* **2012**, *41*, 5687.

(8) (a) Bae, I.; Han, H.; Chang, S. *J. Am. Chem. Soc.* **2005**, *127*, 2038. (b) Yoo, E. J.; Bae, I.; Cho, S. H.; Han, H.; Chang, S. *Org. Lett.* **2006**, *8*, 1347. (c) Cho, S. H.; Yoo, E. J.; Bae, I.; Chang, S. *J. Am. Chem. Soc.* **2005**, *127*, 16046. (d) Cassidy, M. P.; Raushel, J.; Fokin, V. V. *Angew. Chem., Int. Ed.* **2006**, *45*, 3154.

(9) Cano, I.; Álvarez, E.; Nicasio, M. C.; Pérez, P. J. *J. Am. Chem. Soc.* **2011**, *133*, 191.

(10) Cheng, D.; Ling, F.; Li, Z. X.; Yao, W. J.; Ma, C. *Org. Lett.* **2012**, *14*, 3146.

(11) (a) Cui, S. L.; Lin, X.-F.; Wang, Y. G. *Org. Lett.* **2006**, *8*, 4517. (b) Cui, S. L.; Wang, J.; Wang, Y. G. *Org. Lett.* **2007**, *9*, 5023. (c) Shen, Y.; Cui, S. L.; Wang, J.; Chen, X. P.; Lu, P.; Wang, Y. G. *Adv. Synth. Catal.* **2010**, *352*, 1139. (d) Namitharan, K.; Pitchumani, K. *Org. Lett.* **2011**, *13*, 5728. (e) Li, S. Y.; Luo, Y.; Wu, J. *Org. Lett.* **2011**, *13*, 4312.

(12) (a) Li, B.; Yang, B.; Wang, S.; Zhang, Y.; Cao, X.; Tu, Y. *Chem. Sci.* **2012**, *3*, 1975. (b) Xing, Y.; Zhao, H.; Shang, Q.; Wang, J.; Lu, P.; Wang, Y. *Org. Lett.* **2013**, *15*, 2668. (c) Whiting, M.; Fokin, V. V. *Angew. Chem.* **2006**, *118*, 3229. (d) Lu, W.; Song, W.; Hong, D.; Lu, P.; Wang, Y. *Adv. Synth. Catal.* **2009**, *351*, 1768.

(13) Sun, L.; Zhu, Y.; Lu, P.; Wang, Y. *Org. Lett.* **2013**, *15*, 5894.

(14) (a) Fustero, S.; Sanchez-Rosello, M.; Barrio, P.; Simon-Fuentes, A. *Chem. Rev.* **2011**, *111*, 6984. (b) Mohamed Ahmed, M. S.; Kobayashi, K.; Mori, A. *Org. Lett.* **2005**, *7*, 4487. (c) Willy, B.; Mueller, T. J. J. *Org. Lett.* **2011**, *13*, 2082. (d) Gers, C. F.; Rosellen, J.; Merkul, E.; Müller, T. J. J. *Beilstein J. Org. Chem.* **2011**, *7*, 1173. (e) Boersch, C.; Merkul, E.; Müller, T. J. J. *Angew. Chem., Int. Ed.* **2011**, *50*, 10448. (f) Willy, B.; Müller, T. J. J. *Eur. J. Org. Chem.* **2008**, 4157.

(15) Ono, A.; Torigoe, H.; Tanaka, Y.; Okamoto, I. *Chem. Soc. Rev.* **2011**, *40*, 5855.

(16) (a) Xing, Y.; Wei, Y. X.; Zhou, H. *Curr. Org. Chem.* **2012**, *16*, 1594. (b) Müller, T. J. J. *Synthesis* **2012**, *44*, 159.


dx.doi.org/10.1021/ol502302w | *Org. Lett.* XXXX, XXX, XXX−XXX