CHEMISTRY
A European Journal

A Journal of
ChemPubSoc Europe

## Accepted Article

**Title:** Copper-Catalyzed Trifunctionalization of Alkynes: Rapid Assembly of Oxindoles Bearing Geminal Diboron

**Authors:** Tao He, Bin Li, Li-Chuan Liu, Jing Wang, Wenpeng Ma, Guang-Yu Li, Qing-Wei Zhang, and Wei He



**To be cited as:** *Chem. Eur. J.* 10.1002/chem.201804480

**Link to VoR:** http://dx.doi.org/10.1002/chem.201804480

Supported by
ACES

WILEY-VCH

10.1002/chem.201804480

WILEY-VCH

COMMUNICATION

# Copper-Catalyzed Trifunctionalization of Alkynes: Rapid Assembly of Oxindoles Bearing Geminal Diboron

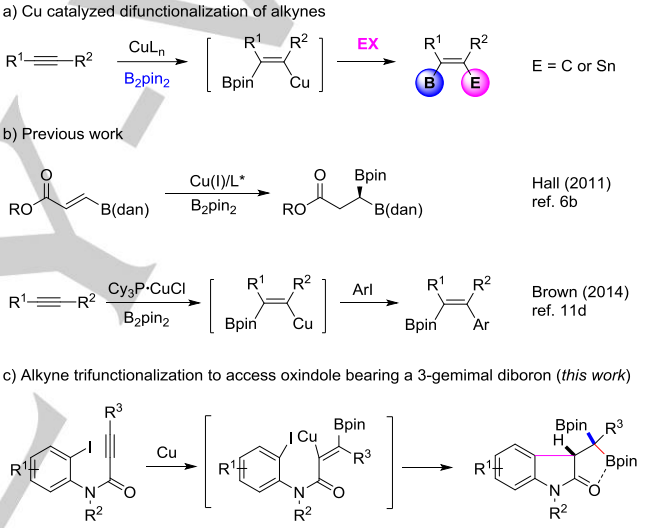
Tao He[a], Bin Li[a], Li-Chuan Liu[a], Jing Wang[a], Wen-Peng Ma[a], Guang-Yu Li[c], Qing-Wei Zhang*[b] and Wei He*[a]

Dedication ((optional))

**Abstract:** We report a copper catalyzed trifunctionalization of alkynes that provides rapid entry to oxindoles bearing a geminal bis(boronates) side chain, highlighted by the simultaneous formation of one C-C bond and two C-B bonds. This new reaction features simple reaction conditions (ligand free catalysis), a general substrate scope, as well as excellent chemoselectivity. Mechanistic study revealed a reaction sequence in the order of borylation/intramolecular cross coupling/hydroboration, which has been rarely documented.

Since the ground-breaking discovery of Suzuki and Miyaura[1] in 1993, transition metal catalyzed addition of stable diboron reagents (e.g. bis(pinacolato)diboron,$B_2Pin_2$) to alkynes[2] has emerged as a powerful means to prepare pivotal organoboron building blocks.[3] In the past two decades, the field has witnessed significant progresses with regard to catalyst systems and reaction complexity. In terms of catalysts, the current toolbox has expanded to homogeneous metal complex (Pt,[1,4] Ir,[5] and Cu[6]), heterogeneous metal composites (Pt nanoparticles,[7] nanoporous Au,[8] and Au nanoparticles[9]) as well as organocatalysts.[10] In terms of reaction complexity, the focus has moved beyond the relatively simple *cis*-diborylation (forming two C-B bonds), which now encompasses the simultaneous formation of a C-B bond and another C-X bond. The latter design was accomplished by intercepting the reactive M-C($sp^2$) intermediate with an electrophile or a cross coupling partner (Scheme 1a). Along this line, Cu catalyzed carboborylation[11] and borylstannylation[12] have met with encouraging successes. On an important note, with no exception these reactions afforded substituted alkenes as the desired products.

We took great inspiration from the remarkable work of Hall[6b] and Brown[11d] (Scheme 1b), when pursuing a drug lead that features an oxindole[13] bearing a functionalized side chain on the 3 position. We envisioned that the Cu catalyzed intermolecular cross coupling invented by Brown would lead to the ring formation. A subsequent addition resembling the Hall's report in a stereo-controlled manner would ultimately install the 3-geminal bis(boronates) functionality[14] (Scheme 1c). Given the versatile reactivity of the C-B bonds,[15] the obtained products will be amenable to late stage derivatizations in lead optimization efforts, which will also serve as a useful starting point for the syntheses of other bioactive oxindoles as they are privileged scaffolds in numerous marketed drugs and investigational compounds.[16]




**Scheme 1.** Overall reaction design.

Herein we disclose a simple, ligand free Cu(I) catalyzed trifunctionalization of 2-ynamide that provides rapid entry to oxindoles bearing a geminal bis(boronates) moiety on the side chain. It is worthy to mention that the reported examples[17] of alkyne trifunctionalization are still limited and our products are of the highest molecule complexity to date.

We commenced our study using 2-ynamide **1a** and Bis(pinacolato)diboron ($B_2pin_2$) (2.1 equiv.) as the model substrates, with CuCl (20 mol%) as the catalyst and NaO*t*Bu (2.1 equiv.) as the base. The reactions were monitored by $^1$H NMR using 1-(4-nitrophenyl)ethanone as the internal standard. The initial trial gave the desired product **2a** at room temperature, albeit in a 33% yield (entry 1, Table 1). Other reaction parameters were then extensively screened to identify the optimized condition. First, various $Cu^I$ catalysts were screened (entries 2-7), which showed distinct impacts on the reaction yields. For example, CuI has the best performance compared with CuCl and CuBr (entry 3 vs entries 1 and 2). Moderate yields were observed with CuOAc (entry 4), CuOTf (entry 5) and CuTC (entry 6). $Cu_2O$ was not a competent catalyst (entry 7) and no product was observed in the

[a] T. He, B. Li, L.-C. Liu, J. Wang, W.-P. Ma, Prof. Dr. W. He
MOE Key Laboratory of Bioorganic Phosphorus Chemistry & Chemical Biology and School of Pharmaceutical Sciences
Tsinghua University, Beijing, P. R. China, 100084
E-mail: whe@tsinghua.edu.cn
[b] Prof. Dr. Q.-W. Zhang
Department of Chemistry
University of Science and Technology of China, Hefei, China, 230026
E-mail: qingweiz@ustc.edu.cn
[c] G.-Y. Li
Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Ling Ling Road, Shanghai, 200032, China

Supporting information for this article is given via a link at the end of the document.

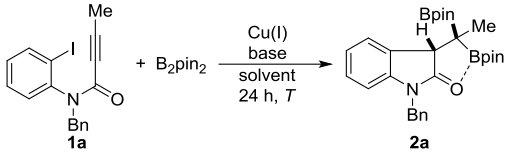
10.1002/chem.201804480

WILEY-VCH

COMMUNICATION

absence of a copper catalyst (entry 8). Gratifyingly, decreasing the catalyst loading to 5 mol% did not compromise the reaction, as a comparable yield (75%) was obtained (entry 9 vs entry 3). The choice of the base was important (entries 9-14): NaO*t*Bu was the best while other bases such as NaOEt, LiO*t*Bu, DMAP, $Et_3N$ and KOH gave diminished yields (entry 9 vs 10-14). No desired product was observed in the absence of a base (entry 15). A lower yield was observed when only 1.0 equiv. of NaO*t*Bu was used (entry 16). Increasing the reaction temperature to 60 °C or 80 °C also resulted in diminished yield (entries 17 and 18). Other solvents, such as THF, DCE or DMF, gave unsatisfactory yields (entries 19-21).

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

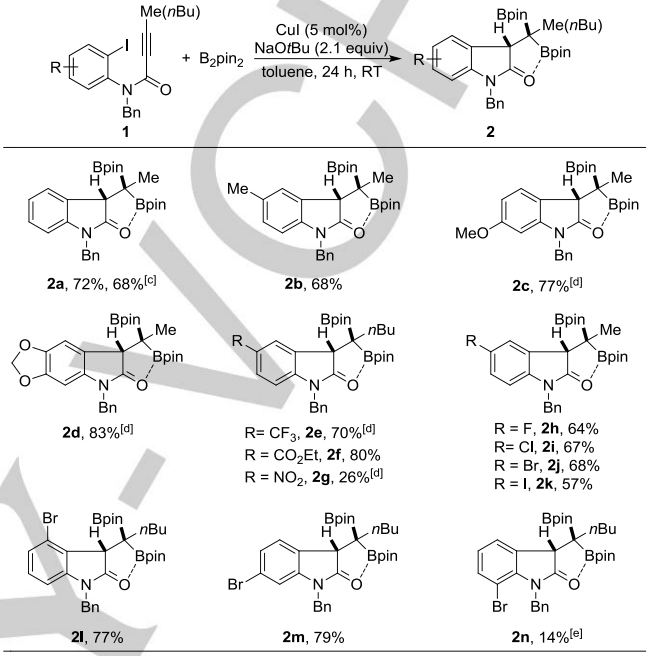



| Entry | Cat.[mol%] | Base | Solvent | *T*[°C] | Yield[%][b] |
|---|---|---|---|---|---|
| 1 | CuCl [20] | NaO*t*Bu | toluene | RT | 33 |
| 2 | CuBr [20] | NaO*t*Bu | toluene | RT | 51 |
| 3 | CuI [20] | NaO*t*Bu | toluene | RT | 74 |
| 4 | CuOAc [20] | NaO*t*Bu | toluene | RT | 68 |
| 5 | CuOTf [20] | NaO*t*Bu | toluene | RT | 45 |
| 6 | CuTC[c] [20] | NaO*t*Bu | toluene | RT | 45 |
| 7 | $Cu_2O$ [20] | NaO*t*Bu | toluene | RT | <5 |
| 8 | none | NaO*t*Bu | toluene | RT | 0 |
| **9** | **CuI [5]** | **NaO*t*Bu** | **toluene** | **RT** | **75** |
| 10 | CuI [5] | NaOEt | toluene | RT | 35 |
| 11 | CuI [5] | LiO*t*Bu | toluene | RT | 37 |
| 12 | CuI [5] | KOH | toluene | RT | 15 |
| 13 | CuI [5] | DMAP | toluene | RT | trace |
| 14 | CuI [5] | $Et_3N$ | toluene | RT | trace |
| 15 | CuI [5] | none | toluene | RT | 0 |
| 16[d] | CuI [5] | NaO*t*Bu | toluene | RT | 25 |
| 17 | CuI [5] | NaO*t*Bu | toluene | 60 | 49 |
| 18 | CuI [5] | NaO*t*Bu | toluene | 80 | 53 |
| 19 | CuI [5] | NaO*t*Bu | THF | RT | 45 |
| 20 | CuI [5] | NaO*t*Bu | DCE | RT | 12 |
| 21 | CuI [5] | NaO*t*Bu | DMF | RT | <5 |

[a] Reaction conditions: 2-ynamide **1a** (0.10 mmol), $B_2pin_2$ (0.21 mmol, 2.1 equiv.), base (0.21 mmol, 2.1 equiv.) and catalyst under argon in the indicated solvent (2.0 mL). [b] NMR yields using 1-(4-nitrophenyl)ethanone (0.10 mmol) as the internal standard. [c] TC = thiophene-2-carboxylate. [d] 1.0 equiv. base was used.

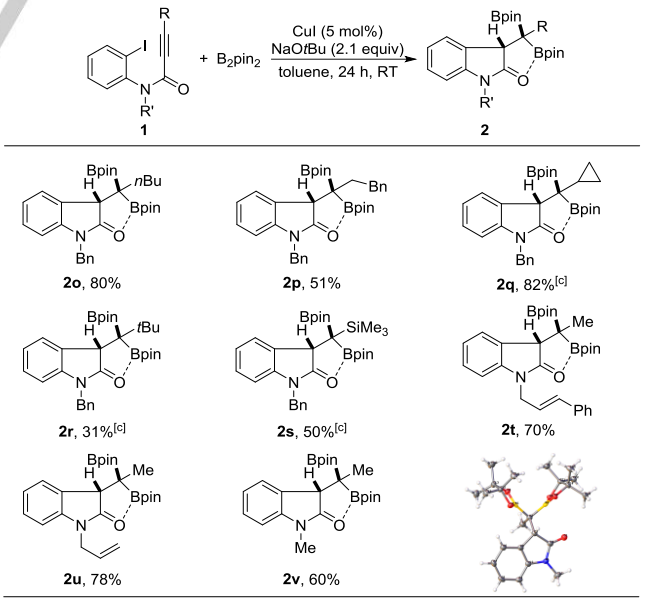
We then demonstrated the substrate scope under the optimized conditions (Table 2). Different substitutions on the aryl group ($R^1$) were first tested. With 2-ynamide **1a**, the desired product **2a** was isolated in a 72% yield for a 0.1 mmol scale reaction. The reaction is amenable to scale up, as the 8.26 mmol reaction (80 fold scale up) gave a 68% yield. Substrates bearing electron-donating methyl (**2b**), methoxyl (**2c**), piperonyl (**2d**) groups reacted smoothly, furnishing the desired product in 68%, 77% and 83% yield, respectively. Substrates with electron-withdrawing groups gave higher yields, as seen in the cases of $CF_3$ (**2e**) and $CO_2Et$ (**2f**). However, substrate **1g** containing a nitro group suffered from a low 26% yield (**2g**). Aryl halides ranging from fluoride (**2h**), chloride (**2i**), bromide (**2j**, **2l** and **2m**) to iodide (**2n**) are compatible with the reaction. It is remarkable that in the reaction of diiodide **1k**, only the *ortho*-iodine participated the arylation reaction while the other one remained intact. The excellent chemoselectivity among these halides (**1h**, **1i**, **1j**, **1l**, **1m** and **1n**) provide ample opportunity to further elaborate the aryl ring by either $S_NAr$ reactions or cross-coupling reactions, as long as the desired halogen atom is properly installed beforehand. However, for reasons that we have yet to understand, the substrate containing *ortho*-bromine to amide (**1n**) gave a complex mixture that defied silica gel purification and the NMR yield was low (14%).

**Table 2**. Substrate scope of aryls.[a,b]




[a] Reaction conditions: 2-ynamide **1** (0.10 mmol), $B_2pin_2$ (0.21 mmol, 2.1 equiv.), NaO*t*Bu (0.21 mmol, 2.1 equiv) and CuI (5 mol%, 1.0 mg) under Ar in toluene (2.0 mL) at room temperature. [b] Yield of the isolated product after silica gel column chromatography. [c] On 8.26 mmol scale. [d] At 60 °C. [e] NMR yield using 4-nitroacetophenone as the internal standard.

**Table 3**. Substrate scope of alkynes and protecting groups on N-atom.[a,b]



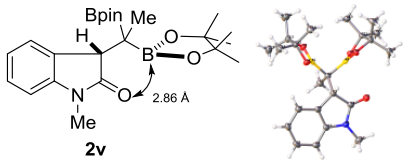

[a] Reaction conditions: 2-ynamide **1** (0.10 mmol), $B_2pin_2$ (0.21 mmol, 2.1 equiv), NaO*t*Bu (0.21 mmol, 2.1 equiv) and CuI (5 mol%, 1.0 mg) under argon in toluene (2.0 mL) at room temperature. [b] Yield of the isolated product after silica gel column chromatography. [c] At 60 °C.

10.1002/chem.201804480



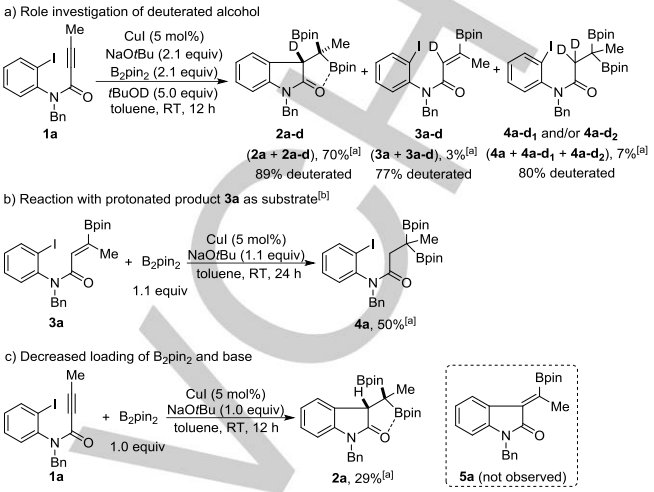
# COMMUNICATION

The substituents on the alkyne (R) as well as the protecting groups (R') on the N-atom were then examined (Table 3). Substrates containing *n*-butyl (**1o**), ethylphenyl (**1p**) and cyclopropyl (**1q**) groups are compatible with the reaction, resulting in moderate to good yields. Increasing the steric hindrance of the $R^2$ groups decreased the reactivity of the substrates, such that a high reaction temperature was demanded and the reaction yields dropped. For examples, substrate **1r** containing a *tert*-butyl group gave a 31% yield. Interestingly, the even bulkier trimethylsilyl substrate **1s** gave a higher yield of 50%. We want to point out that the C-Si bond in product **2s** would allow functionalization orthogonal to that of the C-B bonds. Electron-donating protecting groups such as allyl (**1t**, **1u**) and alkyl (**1v**) were compatible with the reaction, giving satisfactory yields. The structure of the compound **2v** were unequivocally determined by single crystal X-ray crystallography,[18] which indicates the benzylic hydrogen is *trans* to the terminal methyl group. Besides, the distance between the carbonyl oxygen and the B was measured to be 2.858 Å in the X-ray structure, which is shorter than the Bondi's van der Waals radii sum (3.65 Å) of B and O.[19] This indicates that a nonbonding interaction existed between the B and O atoms in the product.



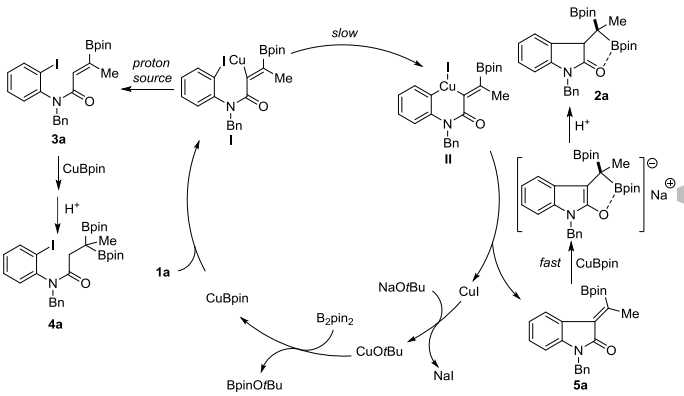

**Scheme 2.** Illustration for interaction between O and B.

A number of experiments were carried out to probe the reaction mechanism (Scheme 3, also see the supporting information). When water was deliberately added to the reaction, the acyclic products **3a** and **4a** were isolated in a combined 68% yield. When *t*BuOD was used to quench the reaction, besides the desired product **2a-d** (89% deuterium incorporation), a small amount of both **3a-d** and **4a-d** (**4a-d$_1$** and/or **4a-d$_2$**) were observed (Scheme 3a). The formation of the acyclic product **3** and **4**, as well as the deuterium incorporation at the α position of the amide substantiated the existence of a Cu-C intermediate. The protonation/deuteration of such a Cu-C intermediate (leading to product **3** and **4**) is a pathway competing with the C-C bond formation pathway (leading to product **2**). The remaining question is whether the C-C bond formation is by virtue of a Cu-C($sp^2$) intermediate (the precursor to product **3**) or a Cu-C($sp^3$) intermediate (the precursor to product **4**). To distinguish these two possible scenarios, we prepared **3a** using an independent method (see supporting information) and subjected it to the reaction conditions (Scheme 3b). Compound **4a** was observed in a 50% NMR yield while **2a** was not detected, therefore ruling out the second scenario. This is consistent with the report of Brown[11d] and confirms our initial reaction design. If such a mechanism is operative, compound **5a** might be detected in the reaction mixture, especially when the second equiv. of $B_2pin_2$ is deprived. To this end, we performed the reaction with 1.0 equiv. of $B_2pin_2$ and NaO*t*Bu under otherwise identical conditions (Scheme 3c). However, the product **2a** was observed in a 29% yield while **5a** was not observed. These observations indicated that the addition of Cu-Bpin to **5a** is much faster than the formation of **5a**. We believe that relief of the ring strain in **5a** serves as a major driving force for this fast addition, as the similar addition to acyclic enons[14] were reported to be slow. In other words, the successful geminal bisborylation could not be assumed despite the traits reported by Hoveyda[20] and Yun.[14]




**Scheme 3.** Mechanism exploration. [a] NMR yields using 1-(4-nitrophenyl)ethanone as internal standard. [b] See supporting information for the preparation and identification of **3a** and **4a**.

A possible catalytic cycle was proposed as shown in Scheme 4 using **1a** as the example. The reaction begins with the addition of Cu-BPin species[21] to 2-ynamide **1a**, forming the Cu-C($sp^2$) species **I**. As a side reaction, intermediate **I** could be protonated by a proton source in the reaction mixture to give acyclic byproduct **3a**. A second borylation of **3a** followed by protonation would afford byproduct **4a**. Alternatively, a productive intramolecular oxidative insertion of intermediate **I** would form the putative Cu(III) intermediate **II**. Reductive elimination would form the C-C bond, [11d] affording the 3-ylidene 2-oxindole **5a**. This C-C bond formation step is likely the rate limiting step. A consequential borylcupration of C=C bond would proceed rapidly to form the second C-B bond in the form of sodium enolates, which upon workup would give the final product **2a**.




**Scheme 4.** Proposed catalytic cycle.

In summary, we have developed a ligand free, copper catalyzed trifunctionalization of alkynes, with the simultaneous construction of one C-C bond and two C-B bonds. The reaction shows a wide substrate scope, good efficiency and excellent chemoselectivity. The reaction products feature a unique oxindole skeleton bearing a geminal diboron functionality, which could be easily elaborated into interesting drug-like lead compounds. Efforts to trap the Cu-C($sp^2$) in an enantioselective manner are undergoing in our labs.

## Acknowledgements

We gratefully acknowldege financial support form the National Key R&D Program of China (No. 2017YFA0505200) and NSFC (21625104, 21521091).

**Keywords:** trifunctionalization • oxindole • alkyne • bis-borylation • copper

[1] a) T. Ishiyama, N. Matsuda, N. Miyaura, A. Suzuki, *J. Am. Chem. Soc.* **1993**, *115*, 11018-11019; b) T. Ishiyama, N. Matsuda, M. Murata, F. Ozawa, A. Suzuki, N. Miyaura, *Organometallics* **1996**, *15*, 713-720;

[2] For selected reviews, see: a) J. Takaya, N. Iwasawa, *Acs Catal.* **2012**, *2*, 1993-2006; b) J. Yun, Asian. *J. Org. Chem.* **2013**, *2*, 1016-1025; c) R. Barbeyron, E. Benedetti, J. Cossy, J. J. Vasseur, S. Arseniyadis, M. Smietana, *Tetrahedron* **2014**, *70*, 8431-8452; d) H. Yoshida, *ACS Catal.* **2016**, *6*, 1799-1811.

[3] For selected reviews, see: a) D. E. Kaufmann, D. S. Matteson, *Science of Synthesis,Boron Compounds*, Thieme, Stuttgart, **2005**; b) H. C. Brown, *Angew. Chem.* **1980**, *92*, 675-683; c) H. Y. Cho, J. P. Morken, *Chem. Soc. Rev.*, **2014**, *43*, 4368-4380.

[4] a) R. L. Thomas, F. E. S. Souza, T. B. Marder, *J. Chem. Soc., Dalton Trans.,* **2001**, 1650-1656; b) V. Lillo, J. Mata, J. Ramirez, E. Peris, E. Fernandez, *Organometallics* **2006**, *25*, 5829-5831.

[5] N. Iwadate, M. Suginome, *J. Am. Chem. Soc.* **2010**, *132*, 2548-2549;

[6] a) V. Lillo, M. R. Fructos, J. Ramirez, A. A. C. Braga, F. Maseras, M. M. Diaz-Requejo, P. J. Perez, E. Fernandez, *Chem. Eur. J.* **2007**, *13*, 2614-2621; b) J. C. H. Lee, R. McDonald, D. G. Hall, *Nat. Chem.* **2011**, *3*, 894-899. c) H. Yoshida, S. Kawashima, Y. Takemoto, K. Okada, J. Ohshita, K. Takaki, *Angew. Chem. Int. Ed.* **2012**, *51*, 235-238; *Angew. Chem.* **2012**, *124*, 239-242.

[7] a) A. Grirrane, A. Corma, H. Garcia, *Chem. Eur. J.* **2011**, *17*, 2467-2478; b) F. Alonso, Y. Moglie, L. Pastor-Perez, A. Sepulveda-Escribano, *Chemcatchem* **2014**, *6*, 857-865.

[8] Q. Chen, J. Zhao, Y. Ishikawa, N. Asao, Y. Yamamoto, T. N. Jin, *Org. Lett.* **2013**, *15*, 5766-5769.

[9] M. Kidonakis, M. Stratakis, *Eur. J. Org. Chem.* **2017**, 4265-4271.

[10] a) A. Yoshimura, Y. Takamachi, L. B. Han, A. Ogawa, *Chem. Eur. J.* **2015**, *21*, 13930-13933; b) K. Nagao, H. Ohmiya, M. Sawamura, *Org. Lett.* **2015**, *17*, 1304-1307; c) A. Yoshimura, Y. Takamachi, K. Mihara, T. Saeki, S. I. Kawaguchi, L. B. Han, A. Nomoto, A. Ogawa, *Tetrahedron* **2016**, *72*, 7832-7838;

[11] a) L. Zhang, J. H. Cheng, B. Carry, Z. M. Hou, *J. Am. Chem. Soc.* **2012**, *134*, 14314-14317; b) R. Alfaro, A. Parra, J. Aleman, J. L. G. Ruano, M. Tortosa, *J. Am. Chem. Soc.* **2012**, *134*, 15165-15168; c) H. Yoshida, I. Kageyuki, K. Takaki, *Org. Lett.* **2013**, *15*, 952-955; d) Y. Q. Zhou, W. You, K. B. Smith, M. K. Brown, *Angew. Chem. Int. Ed.* **2014**, *53*, 3475-3479; *Angew. Chem.* **2014**, *126*, 3543-3547; e) N. Nakagawa, T. Hatakeyama, M. Nakamura, *Chem. Eur. J.* **2015**, *21*, 4257-4261; e) W. Su, T. J. Gong, Q. Zhang, Q. Zhang, B. Xiao, Y. Fu, *Acs Catal.* **2016**, *6*, 6417-6421.

[12] a) Y. Takemoto, H. Yoshida, K. Takaki, *Chem. Eur. J.* **2012**, *18*, 14841-14844; b) H. Yoshida, Y. Takemoto, K. Takaki, *Chem. Commun.* **2015**, *51*, 6297-6300; c) H. Yoshida, *Chem. Rec.* **2016**, *16*, 419-434; d) H. Yoshida, M. Kimura, I. Osaka, K. Takaki, *Organometallics* **2017**, *36*, 1345-1351.

[13] C. Liu, Q. Zhang, H. B. Li, S. X. Guo, B. Xiao, W. Deng, L. Liu, W. He, *Chem. Eur. J.* **2016**, *22*, 6208-6212.

[14] *Gem*-diboron was observed as a minor product in the $B_2pin_2$ addition to ethyl 2-butynoate, see: H. Y. Jung, X. Feng, H. Kim, J. Yun, *Tetrahedron* **2012**, *68*, 3444-3449.

[15] For Selected examples on carbonation of geminal bis(boronates), see: a) R. P. Sonawane, V. Jheengut, C. Rabalakos, R. Larouche-Gauthier, H. K. Scott, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2011**, *50*, 3760-3763; *Angew. Chem.* **2011**, *123*, 3844-3847; b) K. Hong, X. Liu, J. P. Morken, *J. Am. Chem. Soc.* **2014**, *136*, 10581-10584; For oxidation, see: c) M. J. Hesse, S. Essafi, C. G. Watson, J. N. Harvey, D. Hirst, C. L. Willis, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2014**, *53*, 6145-6149; *Angew. Chem.* **2014**, *126*, 6259-6263; For amination, see: d) V. Bagutski, T. G. Elford, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2011**, *50*, 1080-1083; *Angew. Chem.* **2011**, *123*, 1112-1115; For alkynylation, see: e) Y. H. Wang, A. Noble, E. L. Myers, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2016**, *55*, 4270-4274; *Angew. Chem.* **2016**, *128*, 4342-4346.

[16] a) C. Marti, E. M. Carreira, *Eur. J. Org. Chem.* **2003**, 2209-2219; b) H. Lin, S. J. Danishefsky, *Angew. Chem. Int. Ed.* **2003**, *42*, 36-51; *Angew. Chem.* **2003**, *115*, 38-53; c) C. V. Galliford, K. A. Scheidt, *Angew. Chem. Int. Ed.* **2007**, *46*, 8748-8758; *Angew. Chem.* **2007**, *119*, 8902-8912; d) A. Millemaggi, R. J. K. Taylor, *Eur. J. Org. Chem.* **2010**, 4527-4547.

[17] a) L. Hu, C. Che, Z. Tan, G. G. Zhu, *Chem. Commun.* **2015**, *51*, 16641-16644; b) Y. Y. Li, D. C. Qiu, R. R. Gu, J. L. Wang, J. R. Shi, Y. Li, *J. Am. Chem. Soc.* **2016**, *138*, 10814-10817; c) S. Y. Ni, W. X. Sha, L. J. Zhang, C. Xie, H. B. Mei, J. L. Han, Y. Pan, *Org. Lett.* **2016**, *18*, 712-715; d) J. Chen, S. X. Su, D. C. Hu, F. H. Cui, Y. L. Xu, Y. Y. Chen, X. L. Ma, Y. M. Pan, Y. Liang, *Asian. J. Org. Chem.* **2018**, *7*, 892-896; e) C. J. Lv, C. W. Wan, S. Liu, Y. Lan, Y. Li, *Org. Lett.* **2018**, *20*, 1919-1923; f) Y. Nagashima, K. Hirano, R. Takita, M. Uchiyama, *J. Am. Chem. Soc.* **2014**, *136*, 8532-8535; g) C. I. Lee, W. C. Shih, J. Zhou, J. H. Reibenspies, O. V. Ozerov, *Angew. Chem. Int. Ed.* **2015**, *54*, 14003-14007; *Angew. Chem.* **2015**, *127*, 14209-14213; h) Q. Feng, K. Yang, Q. L. Song, *Chem. Commun.* **2015**, *51*, 15394-15397; i) G. L. Gao, J. X. Yan, K. Yang, F. E. Chen, Q. L. Song, *Green Chem.* **2017**, *19*, 3997-4001.

[18] CCDC 1828748 **2v** contain the crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre.

[19] A. Bondi. *J. Phys. Chem.* **1964**, *68*, 441.

[20] Y. Lee, H. Jang, A. H. Hoveyda, *J. Am. Chem. Soc.* **2009**, *131*, 18234-18235.

[21] K. Takahashi, T. Ishiyama, N. Miyaura, *J. Organomet. Chem.* **2001**, 625, 47-53.

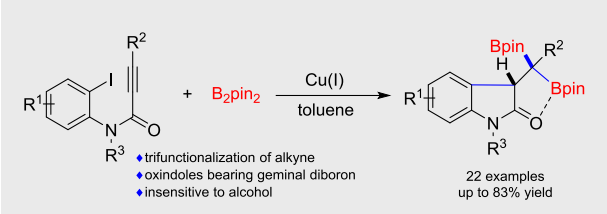
10.1002/chem.201804480

WILEY-VCH



**Entry for the Table of Contents** (Please choose one layout)

## COMMUNICATION




A ligand free Cu(I) catalyzed trifunctionalization of 2-ynamide is developed, which provides rapid entry to oxindoles bearing a geminal bis(boronates) substitution on the side chain. The new reaction features simple reaction conditions, a general substrate scope and excellent chemoselectivity.

*Tao He, Bin Li, Li-Chuan Liu, Jing Wang, Wen-Peng Ma, Guang-Yu Li, Qing-Wei Zhang* and Wei He**

***Page No. – Page No.***

**Copper-Catalyzed Trifunctionalization of Alkynes: Rapid Assembly of Oxindoles Bearing Geminal Diboron**