Check for updates

Synthetic Methods

International Edition: DOI: 10.1002/anie.201912703
German Edition: DOI: 10.1002/ange.201912703

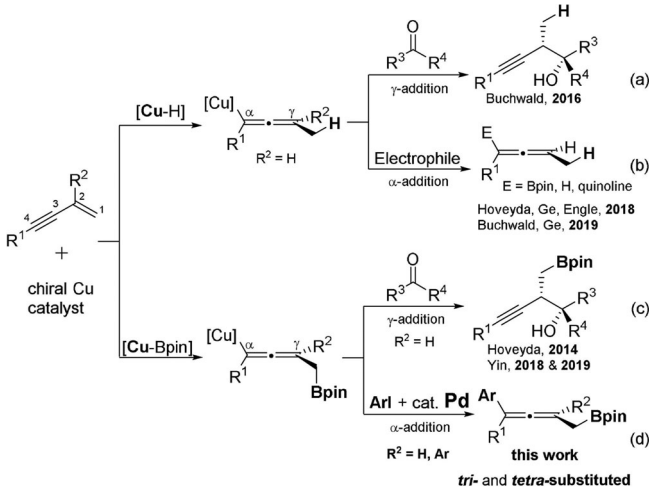
Enantioselective Synthesis of Multisubstituted Allenes by Cooperative Cu/Pd-Catalyzed 1,4-Arylboration of 1,3-Enynes

Yang Liao, Xuemei Yin, Xihong Wang, Wangzhi Yu, Dongmei Fang, Lianrui Hu, Min Wang,* and Jian Liao**

Abstract: *A cooperative Cu/Pd-catalyzed enantioselective synthesis of multisubstituted allenes is established. By employing chiral sulfoxide phosphine (SOP)/Cu and $PdCl_2$(dppf) complexes as catalysts, the 1,4-arylboration of 1,3-enynes provides an efficient approach to trisubstituted chiral allenes with up to 92 % yield and 97:3 er. Furthermore, by using 2-substituted 1,3-enynes as substrates, the tetrasubstituted chiral allenes were successfully generated using this strategy. Finally, theoretical calculations indicate that the transmetallation of the allenylcopper species is the rate-limiting step of this transformation.*

Given their unique structural characteristics (cumulated diene and axial chirality), related biological activities, and physical and chemical properties, chiral allene scaffolds are not only widely present in natural products, pharmaceuticals, and materials, but also frequently employed as an important class of synthetic intermediates in various organic transformations.[1] Allene chemistry has stimulated the interest of organic and medicinal chemists for decades. However, general and efficient enantioselective synthetic method to access axially chiral allenes from prochiral precursors is a long-standing challenge. Many classical methods predominantly rely on central-to-axial chirality transfer[2] or resolution of racemic allenes.[3] Until recently, increasing attention has focused on developing catalytic asymmetric approaches for the synthesis of chiral allenes.[1f,h]

Since the pioneering work of the group of Hayashi,[4] 1,3-enynes have been gradually considered ideal achiral precursors for the construction of highly valuable chiral allenes, and several metal- or organocatalyzed approaches were established in the past few years.[5–7] Among these, enantioselective Cu-catalyzed 1,4-hydrofunctionalization of 1,3-enynes was proven to be an elegant strategy to access nonracemic allenes. Hoveyda and co-workers[6a] first developed Cu-catalyzed 1,4-hydroboration of 1,3-enynes for the synthesis of trisubstituted allenyl-B(pin) compounds with excellent results. Shortly thereafter, the groups of Ge[6b] and Engle[6c] independently disclosed the same protocols (Scheme 1 b). Recently, by employing a proton and quinolone as electrophiles, the groups of Buchwald and Ge reported 1,4-hydroprotonation and 1,4-hydro(hetero)arylation, respectively, of 1,3-enynes. And the corresponding 1,3-disubstituted and quinolinyl-substituted chiral allenes were successfully afforded (Scheme 1 b).[7] The key point of these protocols was the trapping of the chiral allenylcopper species with suitable electrophiles (HBpin, proton, and quinolone), otherwise, for example, when using ketone as an electrophile, the propargylic products were generated exclusively (Scheme 1 a).[8]



Scheme 1. Cu-catalyzed enantioselective 1,2- and 1,4-functionalization of 1,3-enynes.

Similarly, the addition of chiral Cu-Bpin species to 1,3-enynes also enables the generation of chiral allenylcopper intermediates, which were readily captured by aldehydes and ketones to afford the corresponding propargylic products with excellent selectivities (Scheme 1 c).[9] However, the synthesis of chiral allenes by this allenylcopper intermediate still remains challenging. The difficulty can be attributed to the readily racemied allenylcopper species, which could cause low stereoselectivity if an unsuitable electrophile was employed.[1f,6a] Another challenge, as shown in Scheme 1, is access to tetrasubstituted chiral allenes, and this has not been realized via Cu-catalyzed 1,4-bifunctionalization of 2-substituted 1,3-

[*] Y. Liao, X. Yin, X. Wang, W. Yu, D. Fang, Dr. M. Wang, Prof. Dr. J. Liao
Chengdu Institute of Biology, Chinese Academy of Sciences
Chengdu 610041 (China)
and
University of Chinese Academy of Sciences
Beijing 100049 (China)
E-mail: wangmin@cib.ac.cn
jliao@cib.ac.cn
Dr. L. Hu
School of Science and Research Center for Advanced Computation, Xihua University, Chengdu 610039 (China)
E-mail: hulianrui@iccas.ac.cn
Supporting information and the ORCID identification number(s) for the author(s) of this article can be found under: https://doi.org/10.1002/anie.201912703.

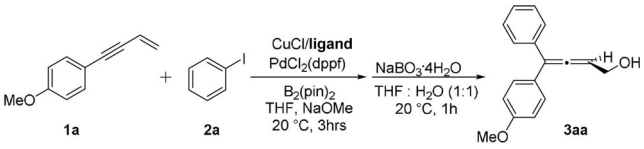
© 2019 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

enynes ($R^2 \neq H$). In fact, to date, asymmetric catalytic methods to access tetrasubstituted chiral allenes have rarely been exploited.[10]

Cooperative Cu/Pd catalysis is an efficient strategy for the enantioselective carbonboration of alkenes.[11,12] We envisioned that a bimetal catalytic system might enable the allenylcopper intermediate to be efficiently trapped by a C electrophile with high stereoselectivity. As a result, nonracemic, multisubstituted allenes could be prepared. The challenge of this strategy is to maintain the highly stereospecific metal-to-metal transfer (allenylcopper to allenylpalladium). Herein, we report the first cooperative Cu/Pd-catalyzed enantioselective synthesis of axially chiral tri- and tetra-substituted ($R^2 = H$, Ar) allenes through 1,4-arylboration of 1,3-enynes (Scheme 1 d).

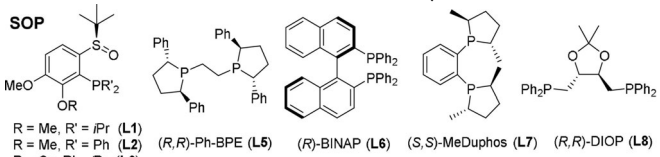
We commenced our study by using the arylsubstituted enyne **1a** as a model substrate, iodobenzene (**2a**) as a C electrophile, and bis(pinacolato)diboron ($B_2(pin)_2$) as a boron source (Table 1). To our delight, the desired product **3aa** was achieved with an excellent yield as determined by NMR spectroscopy and moderate enantioselectivity (90%, 78:22 er; entry 1) under the following reaction conditions: 10 mol% CuCl/sulfoxide phosphine (SOP, **L1**),[11,13] 5 mol% $PdCl_2$(dppf) as catalysts, and 2.5 equivalents NaOMe as base in THF, stirring at 20°C for 3 hours. There are two possible reasons for the unsatisfactory stereoselectivity, one originates from the weak stereocontrol of chiral ligand, and another comes from ineffective Cu-to-Pd stereospecific transfer. We guessed the latter might be caused by a mismatch in the speed of formation between allenylcopper and arylpalladium species.[11b,14] To confirm this hypothesis, the ratio of the Cu and Pd catalyst was carefully tuned (entries 2–6). Encouragingly, an increased er value (93:7) with a satisfactory 86% yield (NMR) was detected when 5 mol% of the Cu catalyst and 15 mol% of the Pd catalyst were used (entry 5). Replacement of CuCl with CuBr can slightly increase the er value (entry 7). Chiral ligand screening showed that the SOPs **L1**–**L4** were the preferred ligands in terms of enantioselectivity, whereas poor er values were achieved when employing commercially available chiral ligands (**L5**–**L8**; entries 8–14). The use of 10 mol% tri(2-furyl)phosphine (TFP) as an additive and replacing NaOMe with NaOEt could further improve the er value slightly (entries 15 and 16). Finally, the best result [94% yield (NMR), 88% yield (isolated) and 96:4 er] was achieved by using a mixed solvent [2:1 THF/2-MeTHF (v/v); entry 17]. It is notable that a 1,2-addition product was not observed in this catalysis, and it could be attributed to the efficient Cu-to-Pd allenylmetal transfer and reductive elimination of allenylpalladium.

Table 1: Optimization of reaction conditions.[a]



Entry	CuCl (*x* mol%)	$PdCl_2$(dppf) (*y* mol%)	Ligand	Yield [%][b]	er[c]
1	10	5	**L1**	90	78:22
2	10	10	**L1**	91	88:12
3	10	15	**L1**	86	91:9
4	10	20	**L1**	70	90:10
5	5	15	**L1**	86	93:7
6	2.5	15	**L1**	72	93:7
7[d]	5	15	**L1**	88	93.5:6.5
8[d]	5	15	**L2**	90	90:10
9[d]	5	15	**L3**	89	93:7
10[d]	5	15	**L4**	76	92:8
11[d]	5	15	**L5**	65	55:45
12[d]	5	15	**L6**	72	52:48
13[d]	5	15	**L7**	80	54:46
14[d]	5	15	**L8**	81	54:46
15[d,e]	5	15	**L1**	90	94.5:5.5
16[d,e,f]	5	15	**L1**	95	95.5:4.5
17[d,e,f,g]	5	15	**L1**	94(88)	96:4

[a] Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $B_2(pin)_2$ (0.4 mmol), CuCl (*x* mol%), $PdCl_2$(dppf) (*y* mol%), and NaOMe (0.5 mmol) in THF (2.0 mL) at 20°C for 3 h. [b] Determined by ^{1}H NMR spectroscopy with dimethyl terephthalate as an internal standard. Yield of the isolated product given within parentheses. [c] Determined by chiral-phase HPLC analysis. [d] CuBr instead of CuCl. [e] 10 mol% TFP was added as additive. [f] NaOEt instead of NaOMe. [g] Mixed solvents: 2.0 mL THF and 1.0 mL 2-MeTHF. THF = tetrahydrofuran.



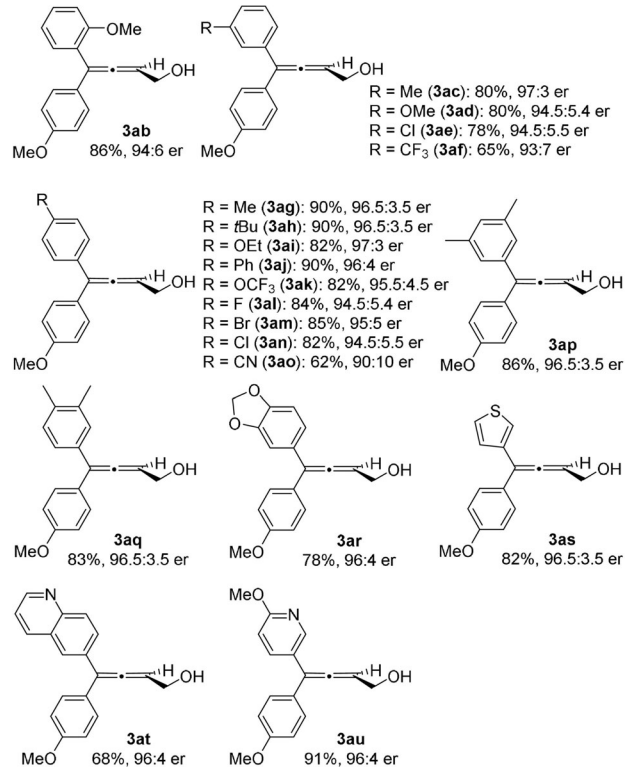
With optimal reaction conditions in hand, we then turned our attention to explore the scope with respect to the aryl iodides for the cooperative Cu/Pd-catalyzed enantioselective 1,4-arylboration of 1,3-enynes (Table 2). We found that various aryl iodides worked well in this reaction. The *ortho*-, *meta*-, and *para*-substituted, as well as disubstituted aryliodides were converted smoothly into the corresponding trisubstituted axially chiral allenes with satisfactory yields and er values (**3ab**–**ar**). Substrates with different functional groups like alkyl (Me, *t*Bu, CF_3), halogens (F, Cl, Br), ether (OMe, OEt, OCF_3), aryl (Ph), and cyanide on the phenyl ring were tolerated in this transformation. It was notable that heteroaromatic iodides (thiophene, quinoline, and pyridine) also worked well and the desired products (**3as**–**au**) were prepared with good yields and excellent enantioselectivities.

Next, we evaluated the scope with respect to the 1,3-enynes. Delightfully, both aromatic and aliphatic substituted 1,3-enynes serve as competent substrates in this process (Table 3). The aromatic 1,3-enynes bearing either electron-donating or electron-withdrawing groups at the *ortho*-, *meta*-, or *para*-positions in the phenyl rings, including alkyl, alkoxy, phenyl, and halogen, were compatible with the reaction conditions, and the corresponding products were afforded in 78–92% yields with 93:7–96.5:3.5 er values (**3bg**–**jg**). In addition, 2-naphthyl (**3kg**) and heteroaromatic 1,3-enynes (**3lg** and **3mg**) did not adversely affect the efficiency and enantioselectivity. Aliphatic 1,3-enynes with different chain lengths and functional groups (phenyl ring and chlorine atom) covert readily into the desired products with moderate yields and good enantioselectivities (**3ng**–**rg**).

 © 2019 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

These are not the final page numbers!

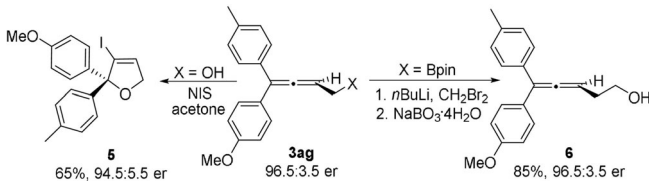
Table 2: Scope with respect to the aryl iodides.[a,b,c]



[a] Reaction conditions: enynes (0.2 mmol, 1.0 equiv), aryl iodides (0.4 mmol, 2.0 equiv), $B_2(pin)_2$ (0.4 mmol, 2.0 equiv), 5 mol% CuBr/SOP **L1**, 15 mol% $PdCl_2$(dppf), NaOEt (0.5 mmol, 2.5 equiv), and 10 mol% TFP in 2:1 THF/2-MeTHF (v/v) at 20°C for 3 h. [b] Yield of isolated product. [c] The er value was determined by chiral-phase HPLC analysis.

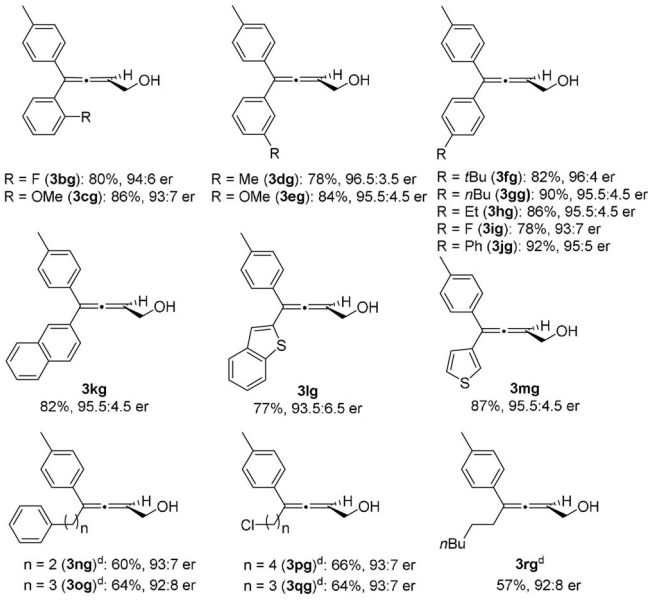
Elegant protocols of transition metal catalyzed 1,4-difunctionalization of 2-substituted 1,3-enynes to afford racemic tetrasubstituted allenes were established recently.[15] To access nonracemic tetrasubstituted allenes with our catalysis, 2-arylsubstituted 1,3-enynes were employed as substrates (Table 4). Under the slightly modified reaction conditions, we were pleased to find that the desired tetrasubstituted chiral allenes were successfully obtained with satisfactory yields and enantioselectivities. In addition, 1,1,3-triaryl tetrasubstituted allene (**4n**) can be prepared with modest yield (48%) and good enantioselectivity (86.5:13.5 er), and the lower er value probably results from a more easily racemization of this conjugated α,γ-diaryl-substituted allenylmetal intermediate.

To demonstrate the synthetic utility of this asymmetric catalysis (Scheme 2), we treated the chiral allene product **3ag**



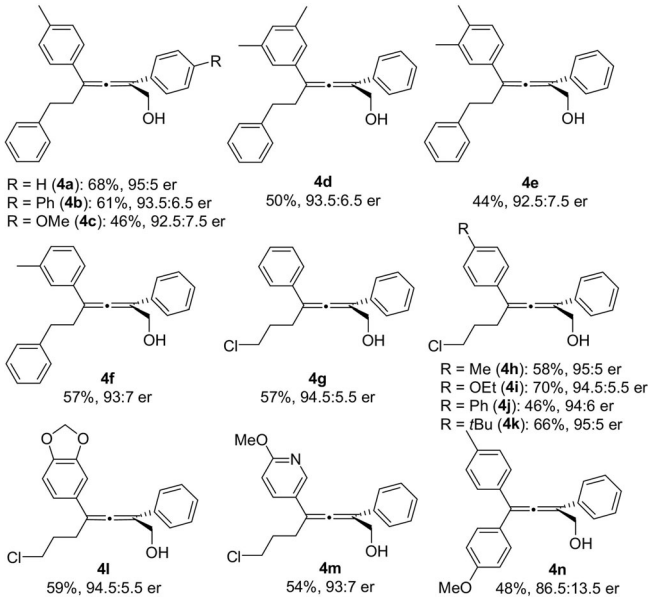
Scheme 2. Transformations of products.

Table 3: Scope with respect to the 1,3-enynes.[a,b,c]



[a] Reaction conditions: enynes (0.2 mmol, 1.0 equiv), aryl iodides (0.4 mmol, 2.0 equiv), $B_2(pin)_2$ (0.4 mmol, 2.0 equiv), 5 mol% CuBr/SOP **L1**, 15 mol% $PdCl_2$(dppf), NaOEt (0.5 mmol, 2.5 equiv), and 10 mol% TFP in 2:1 THF/2-MeTHF (v/v) at 20°C for 3 h. [b] Yield of isolated products. [c] The er value was determined by chiral-phase HPLC analysis. [d] 3 mol% CuBr/SOP, 3.0 mL 2-MeTHF, 0°C, overnight.

Table 4: Synthesis of tetrasubstituted allenes.[a,b,c]



[a] Reaction conditions: enynes (0.2 mmol, 1.0 equiv), aryl iodides (0.4 mmol, 2.0 equiv), $B_2(pin)_2$ (0.4 mmol, 2.0 equiv), 3 mol% CuBr/SOP **L1**, 15 mol% $PdCl_2$(dppf), NaOMe (0.5 mmol, 2.5 equiv), and 5 mol% TFP in 3.0 mL 2-MeTHF at 10°C overnight. [b] Yield of isolated product. [c] The er value was determined by chiral-phase HPLC analysis.

with *N*-iodosuccinimide (NIS) in acetone, and the chiral 2,5-dihydrofuran **5** (a class of important structural motifs presented in various bioactive natural products[16]) bearing a quaternary center was obtained with 65% yield with

© 2019 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

94.5:5.5 er.[17] In addition, a methylene insertion into the C–B bond can be readily realized without loss of enantioselectivity using the standard procedure.[6c,18]

A plausible catalytic pathway is shown in Figure 1. In the copper cycle, (SOP)CuBr reacts with $B_2(pin)_2$ in the presence of NaOEt to produce the chiral Cu-Bpin species **A**. The 1,2-addition of **A** to 1,3-enynes generates the propargylic copper

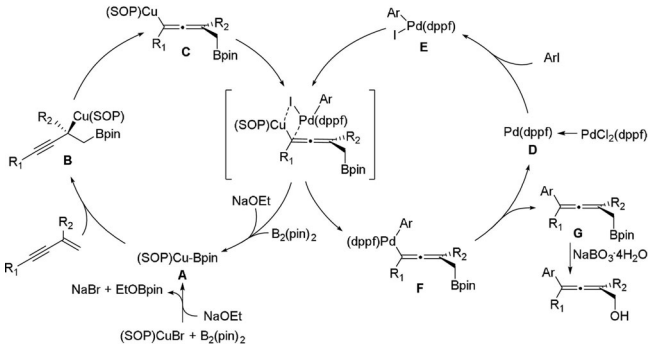


Figure 1. Proposed catalytic pathway.

B, which underwent a stereospecific isomerization to an axially chiral allenylcopper (**C**). The stereospecific metal transformation of **C** with the arylpalladium specie **E** formed the allenylpalladium **F**, which finally afforded the desired axially chiral allene product **G** by reductive elimination. The unstable product **G** was readily oxidized to afford the final product.

In summary, we have developed an efficient approach for the synthesis of multisubstituted chiral allenes with excellent enantioselectivities by cooperative Cu/Pd-catalyzed 1,4-arylboration of 1,3-enynes. By employing this protocol, the prochiral aryl-, alkyl-, and 2-substituted 1,3-enynes were smoothly converted into the corresponding tri- and tetrasubstituted allenes. Theoretical calculations disclosed that the transmetallation of allenylcopper species was the rate-limiting step (for details, see the Supporting Information), which had a much lower energy barrier than both racemization steps, to realize a highly stereospecific 1,4-arylboration of 1,3-enynes.

Acknowledgements

We thank the National Nature Science Foundation of China (No. 21871251, 21572218 and 21472184), the Biological Resources Programme, Chinese Academy of Sciences (KFJ-BRP-008), and Sichuan Sci&Tech Department (2016JZ0022 and 2019YJ0471) for financial support.

Conflict of interest

The authors declare no conflict of interest.

Keywords: allenes · copper · palladium · enantioselectivity · synthetic methods

[1] For selected reviews, see: a) A. Hoffmann-Röder, N. Krause, *Angew. Chem. Int. Ed.* **2004**, *43*, 1196; *Angew. Chem.* **2004**, *116*, 1216; b) S. Ma, *Chem. Rev.* **2005**, *105*, 2829; c) S. Yu, S. Ma, *Chem. Commun.* **2011**, *47*, 5384; d) C. Aubert, L. Fensterbank, P. Garcia, M. Malacria, A. Simonneau, *Chem. Rev.* **2011**, *111*, 1954; e) S. Yu, S. Ma, *Angew. Chem. Int. Ed.* **2012**, *51*, 3074; *Angew. Chem.* **2012**, *124*, 3128; f) J. Ye, S. Ma, *Org. Chem. Front.* **2014**, *1*, 1210; g) J. Ye, S. Ma, *Acc. Chem. Res.* **2014**, *47*, 989; h) W.-D. Chu, Y. Zhang, J. Wang, *Catal. Sci. Technol.* **2017**, *7*, 4570.

[2] For selected examples by chirality transfer, see: a) H. Ohmiya, U. Yokobori, Y. Makaida, M. Sawamura, *Org. Lett.* **2011**, *13*, 6312; b) M. R. Uehling, S. T. Marionni, G. Lalic, *Org. Lett.* **2012**, *14*, 362; c) M. Yang, N. Yokokawa, H. Ohmiya, M. Sawamura, *Org. Lett.* **2012**, *14*, 816; d) X. Huang, T. Cao, Y. Han, X. Jiang, W. Lin, J. Zhang, S. Ma, *Chem. Commun.* **2015**, *51*, 6956; e) S. Wu, X. Huang, W. Wu, P. Li, C. Fu, S. Ma, *Nat. Commun.* **2015**, *6*, 7946; f) J. Ruchti, E.-M. Carreira, *Org. Lett.* **2016**, *18*, 2174.

[3] For selected examples by resolution of racemic allenes, see: a) J. Yu, W. Chen, L. Gong, *Org. Lett.* **2010**, *12*, 4050; b) C. Manzuna Sapu, J.-E. Bäckvall, J. Deska, *Angew. Chem. Int. Ed.* **2011**, *50*, 9731; *Angew. Chem.* **2011**, *123*, 9905; c) T. Inokuma, M. Furukawa, Y. Suzuki, T. Kimachi, Y. Kobayashi, Y. Takemoto, *ChemCatChem* **2012**, *4*, 983; d) W. F. Zheng, W. Zhang, C. Huang, P. Wu, H. Qian, L. Wang, Y. L. Guo, S. Ma, *Nat. Catal.* **2019**, *2*, 997.

[4] a) Y. Matsumoto, M. Naito, Y. Uozumi, T. Hayashi, *J. Chem. Soc. Chem. Commun.* **1993**, 1468; b) J.-M. Han, N. Tokunaga, T. Hayashi, *J. Am. Chem. Soc.* **2001**, *123*, 12915; c) T. Hayashi, N. Tokunaga, K. Inoue, *Org. Lett.* **2004**, *6*, 305; d) T. Nishimura, H. Makino, M. Nagaosa, T. Hayashi, *J. Am. Chem. Soc.* **2010**, *132*, 12865.

[5] a) M. Wang, Z.-L. Liu, X. Zhang, P.-P. Tian, Y.-H. Xu, T.-P. Loh, *J. Am. Chem. Soc.* **2015**, *137*, 14830; b) H. Qian, X. Yu, J. Zhang, J. Sun, *J. Am. Chem. Soc.* **2013**, *135*, 18020; c) W.-D. Chu, L. Zhang, Z. Zhang, Q. Zhou, F. Mo, Y. Zhang, J. Wang, *J. Am. Chem. Soc.* **2016**, *138*, 14588; d) N.-J. Adamson, H. Jeddi, S.-J. Malcolmson, *J. Am. Chem. Soc.* **2019**, *141*, 8574.

[6] a) Y. Huang, J. Pozo, S. Torker, A.-H. Hoveyda, *J. Am. Chem. Soc.* **2018**, *140*, 2643; b) H.-J. Sang, S. Yu, S. Ge, *Org. Chem. Front.* **2018**, *5*, 1284; c) D.-W. Gao, Y. Xiao, M. Liu, M.-K. Karunananda, J.-S. Chen, K.-M. Engle, *ACS Catal.* **2018**, *8*, 3650.

[7] a) S. Yu, H.-L. Sang, S.-Q. Zhang, X. Hong, S. Ge, *Commun. Chem.* **2018**, *1*, 64; b) L. Bayeh-Romero, S.-L. Buchwald, *J. Am. Chem. Soc.* **2019**, *141*, 13788.

[8] Y. Yang, I.-B. Perry, G. Lu, P. Liu, S.-L. Buchwald, *Science* **2016**, *353*, 144.

[9] a) F. Meng, F. Haeffner, A.-H. Hoveyda, *J. Am. Chem. Soc.* **2014**, *136*, 11304; b) X.-C. Gan, L. Yin, *Org. Lett.* **2019**, *21*, 931; c) X.-C. Gan, Q. Zhang, X.-S. Jia, L. Yin, *Org. Lett.* **2018**, *20*, 1070.

[10] a) T. Hashimoto, K. Sakata, F. Tamakuni, M.-J. Dutton, K. Maruoka, *Nat. Chem.* **2013**, *5*, 240; b) D. Qian, L. Wu, Z. Lin, J. Sun, *Nat. Commun.* **2017**, *8*, 567.

[11] a) T. Jia, P. Cao, B. Wang, Y. Lou, X. Yin, M. Wang, J. Liao, *J. Am. Chem. Soc.* **2015**, *137*, 13760; b) B. Chen, P. Cao, X. Yin, Y. Liao, L. Jiang, J. Ye, M. Wang, J. Liao, *ACS Catal.* **2017**, *7*, 2425.

[12] a) K. Semba, Y. Nakao, *J. Am. Chem. Soc.* **2014**, *136*, 7567; b) K.-M. Logan, M.-K. Brown, *Angew. Chem. Int. Ed.* **2017**, *56*, 851; *Angew. Chem.* **2017**, *129*, 869; c) K.-B. Smith, M.-K. Brown, *J. Am. Chem. Soc.* **2017**, *139*, 7721.

[13] a) D. Wang, P. Cao, B. Wang, T. Jia, Y. Lou, M. Wang, J. Liao, *Org. Lett.* **2015**, *17*, 2420; b) Y. Lou, P. Cao, T. Jia, Y. Zhang, M.

 © 2019 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

These are not the final page numbers!

Wang, J. Liao, *Angew. Chem. Int. Ed.* **2015**, *54*, 12134; *Angew. Chem.* **2015**, *127*, 12302; c) T. Jia, P. Cao, D. Wang, Y. Lou, J. Liao, *Chem. Eur. J.* **2015**, *21*, 4918; d) B. Chen, P. Cao, Y. Liao, M. Wang, J. Liao, *Org. Lett.* **2018**, *20*, 1346; e) X. Wang, B. Wang, X. Yin, W. Yu, Y. Liao, J. Ye, M. Wang, L. Hu, J. Liao, *Angew. Chem. Int. Ed.* **2019**, *58*, 12264; *Angew. Chem.* **2019**, *131*, 12392.

[14] S.-D. Michael, M.-T. Pirnot, S.-L. Buchwald, *J. Am. Chem. Soc.* **2016**, *138*, 8372.

[15] For selected recent leading examples, see: a) F. Wang, D. Wang, Y. Zhou, L. Liang, R. Lu, P. Chen, Z. Lin, G. Liu, *Angew. Chem. Int. Ed.* **2018**, *57*, 7140; *Angew. Chem.* **2018**, *130*, 7258; b) X. Zhu, W. Deng, M.-F. Chiou, C. Ye, W. Jian, Y. Zeng, Y. Jiao, L. Ge, Y. Li, X. Zhang, H. Bao, *J. Am. Chem. Soc.* **2019**, *141*, 548; c) K.-F. Zhang, K.-J. Bian, C. Li, J. Sheng, Y. Li, X.-S. Wang, *Angew. Chem. Int. Ed.* **2019**, *58*, 5069; *Angew. Chem.* **2019**, *131*, 5123.

[16] a) W. Chen, X. Fu, L. Lin, X. Yuan, W. Luo, J. Feng, X. Liu, X. Feng, *Chem. Commun.* **2014**, *50*, 11480; b) X. Cheng, Z. Wang, C.-D. Quintanilla, L. Zhang, *J. Am. Chem. Soc.* **2019**, *141*, 3787.

[17] a) C.-J.-T. Hyland, L.-S. Hegedus, *J. Org. Chem.* **2006**, *71*, 8658; b) J. Deska, J.-E. Bäckvall, *Org. Biomol. Chem.* **2009**, *7*, 3379.

[18] S.-P. Thomas, R.-M. French, V. Jheengut, V.-K. Aggarwal, *Chem. Rec.* **2009**, *9*, 24.

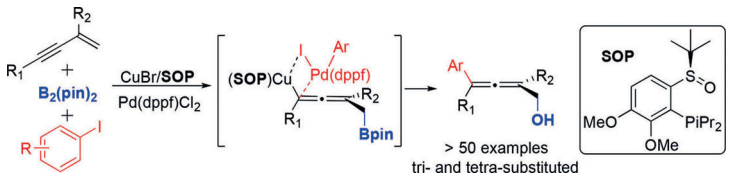
Manuscript received: October 5, 2019
Version of record online: ■■ ■■, ■■■■

 © 2019 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

Communications

Synthetic Methods

Y. Liao, X. Yin, X. Wang, W. Yu, D. Fang, L. Hu,* M. Wang,*
J. Liao* _____ ■■■■–■■■■



Enantioselective Synthesis of Multisubstituted Allenes by Cooperative Cu/Pd-Catalyzed 1,4-Arylboration of 1,3-Enynes

A cooperative Cu/Pd-catalyzed enantioselective 1,4-arylboration of 1,3-enynes was developed with excellent yields and enantioselectivities, and broad substrate scope. By employing this method, tri- and tetrasubstituted axially chiral allenes were prepared. Theoretical calculations indicate that the transmetallation of the allenylcopper species is the rate-limiting step of this transformation.

© 2019 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim

These are not the final page numbers!