Organic Letters
Letter
pubs.acs.org/OrgLett

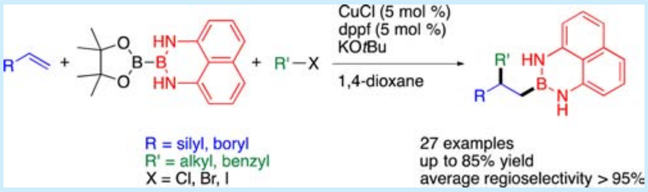
Copper-Catalyzed B(dan)-Installing Carboboration of Alkenes

Ikuo Kageyuki, Itaru Osaka, Ken Takaki, and Hiroto Yoshida*

Department of Applied Chemistry, Graduate School of Engineering, Hiroshima University, Higashi-Hiroshima 739-8527, Japan

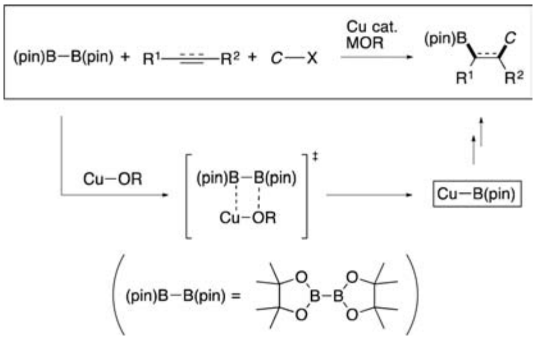
Supporting Information

ABSTRACT: Carboboration of alkenes was found to occur readily with an unsymmetrical diboron [(pin)B−B(dan)] and alkyl halides under copper catalysis, leading to the direct formation of protected alkylboron compounds via synchronous C−C and C−B bond-forming processes. The B(dan) moiety was solely installed into the organic frameworks with the regioselective attachment to a terminal carbon of alkenes employed.



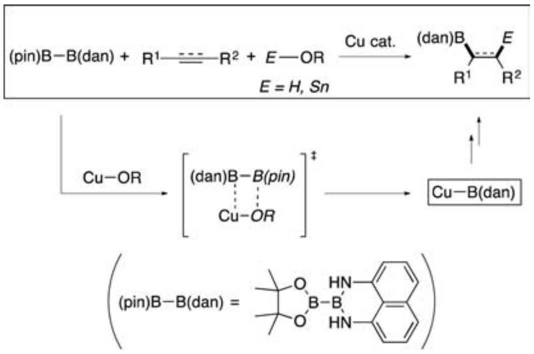
Carboboration of unsaturated carbon−carbon bonds, which enables carbon−carbon and carbon−boron bonds to be constructed synchronously, has certainly been an invaluable method for synthesizing organoboron compounds of multifarious structures.[1] The organoboron compounds thus generated are facilely transformable into synthetically significant compounds by a variety of established carbon−carbon[2] and carbon−heteroatom[3] bond-forming reactions, and hence development of new carboboration reactions endowed with high regio- and stereoselectivities has been a central subject in modern synthetic organic chemistry. Recently, considerable attention has been concentrated on unique copper catalysis toward the carboboration of alkynes,[4] allenes,[5] and alkenes[6] depending upon three-component coupling using bis(pinacolato)diboron and carbon electrophiles, in which a borylcopper(I) species, Cu−B(pin),[7] arising from σ-bond metathesis between a copper(I) complex and the diboron acts as a key intermediate (Scheme 1).

Scheme 1. Cu-Catalyzed B(pin)-Installing Carboboration



We have just disclosed that 1,8-diaminonaphthalene-substituted borylcopper species, Cu−B(dan), can be formed by use of an unsymmetrical diboron, (pin)B−B(dan),[8] through selective Lewis acid [(*pin*)*B*−B(dan)]−base (Cu−*OR*) interaction in the σ-bond metathesis step, and that this species exhibits apparent affinity for unsaturated carbon−carbon bonds, leading to three-component hydroboration[9] and borylstannylation[10] (Scheme 2). Herein we report that Cu−B(dan) also serves as a key catalytic intermediate in the first B(dan)-installing carboboration, which enables a protected boryl moiety to be installed into organic frameworks.[11,12] The reaction provides a direct way of synthesizing diverse alkyl−B(dan) compounds of structural complexity, thus contributing to further progress in a boron-masking strategy.[13]

Scheme 2. Cu-Catalyzed B(dan)-Installing Hydroboration and Borylstannylation

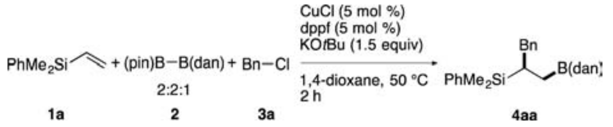


First, we carried out the reaction of dimethyl(phenyl)vinylsilane (**1a**) with (pin)B−B(dan) (**2**) and benzyl chloride (**3a**) in 1,4-dioxane in the presence of potassium *tert*-butoxide (KO*t*Bu) and cuprous chloride (CuCl) and found that the carboboration smoothly occurred to give an alkylborane (**4aa**) in 85% yield by using dppf as a supporting ligand (entry 1, Table 1). The protected boryl moiety, B(dan), was solely transferred to the carbon−carbon double bond with the regioselective attachment to the terminal carbon, and a carboboration product having a B(pin) moiety[6] was not generated at all. Such bidentate ligands as BINAP and dppp

Received: December 22, 2016
Published: February 3, 2017

DOI: 10.1021/acs.orglett.6b03820
Org. Lett. 2017, 19, 830−833

Table 1. Optimization of Reaction Conditions[a]



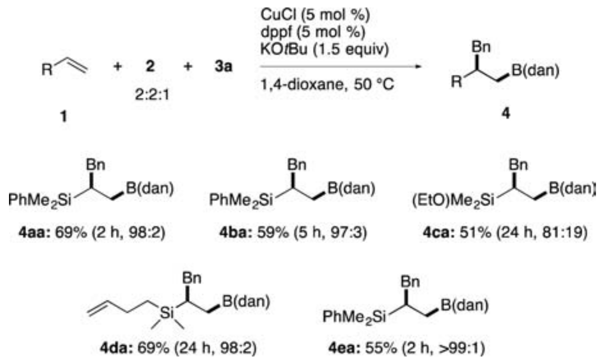
entry	change from standard conditions	yield (%)[b]
1	none	85
2	*rac*-BINAP instead of dppf	83
3	dppp instead of dppf	77
4	**1a** (1 equiv), **2** (1.3 equiv), **3a** (3 equiv)	65

[a] Conditions: **1a** (0.60 mmol), **2** (0.60 mmol), **3a** (0.30 mmol), KO*t*Bu (0.45 mmol), CuCl (0.015 mmol), dppf (0.015 mmol), 1,4-dioxane (1 mL), 50 °C, 2 h. [b] Determined by ^{1}H NMR (average of two runs).

have also proven to be effective for the carboboration (entries 2 and 3);[14] however, a change in molar ratio of the substrates led to a lowering of the yield because of the generation of a hydroboration byproduct (entry 4).[15]

With the optimized reaction conditions in hand, we next investigated the carboboration of various alkenes (Scheme 3).

Scheme 3. Scope of Alkenes[a]

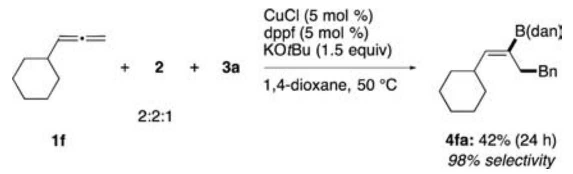


[a] Isolated yield. Conditions: **1** (0.60 mmol), **2** (0.60 mmol), **3a** (0.30 mmol), KO*t*Bu (0.45 mmol), CuCl (0.015 mmol), dppf (0.015 mmol), 1,4-dioxane (1 mL), 50 °C. Regioisomeric ratio is in parentheses.

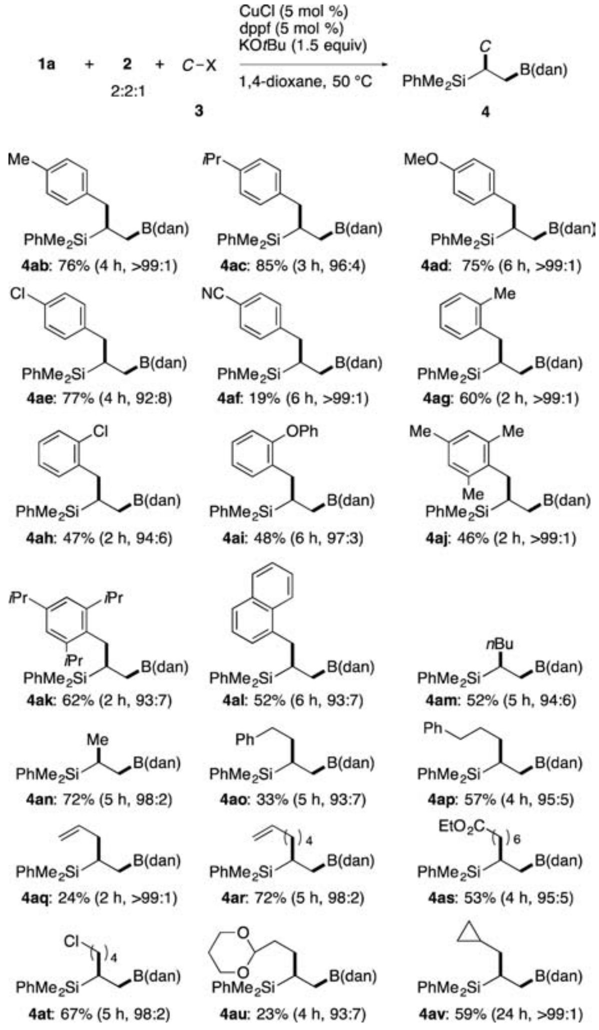
Thus, treatment of trimethyl(vinyl)silane (**1b**) or ethoxy(dimethyl)vinylsilane (**1c**) with **2** and **3a** provided the corresponding products regioselectively in 59% or 51% yield (**4ba** and **4ca**), whose Si−OEt bond remained undamaged in the latter case regardless of its relative lability. A carbon−carbon double bond attached to a silicon atom exhibited superior reactivity toward the carboboration: a vinyl group of homoallyl(vinyl)silane (**1d**) exclusively underwent the reaction, demonstrating the high chemoselectivity of the carboboration (**4da**). In addition to vinylsilanes, a vinylborane (**1e**) participated in the carboboration with perfect regioselectivity, giving a 1,2-diborylalkane bearing protected [B(dan)] and reactive [B(pin)] boryl moieties (**4ea**). Furthermore, the reaction was also found to be applicable to an allene (**1f**) to afford an alkenylborane in a regio- and stereoselective manner (Scheme 4), whereas the reaction of an alkyne (diphenylacetylene) or other alkenes including allyl(trimethyl)silane, styrene, and 1-octene did not furnish desired carboboration products.[16]

The synthetic versatility of the carboboration could further be expanded by employing other carbon electrophiles (Scheme 5). Thus, a variety of *para*- or *ortho*-substituted benzyl chlorides were readily coupled with **1a** and **2** under copper catalysis to offer the respective products with over 92% regioselectivity (**4ab**−**4ai**). As shown in the case of **4ae** and **4ah**, the C(benzyl)−Cl moiety solely served as an electrophilic carbon center, and the C(aryl)−Cl bond remained unchanged. Such sterically congested carbon electrophiles as 2,4,6-triisopropyl/2,4,6-trimethyl benzyl chloride and 1-(chloromethyl)-naphthalene were also convertible into the carboboration products (**4aj**−**4al**), and moreover primary alkyl halides (I for **4an**, Br for the others) and an allyl chloride could act as a carbon electrophile (**4am**−**4aq**). Functionalized alkyl bromides

Scheme 4. Carboboration of an Allene



Scheme 5. Scope of Organic Halides[a]

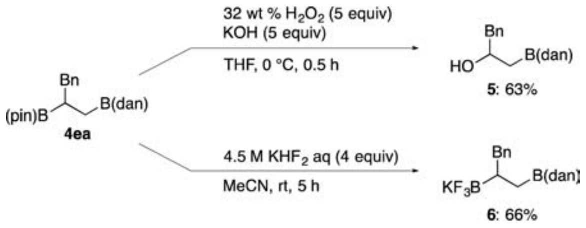


[a] Isolated yield. Conditions: **1** (0.60 mmol), **2** (0.60 mmol), **3a** (0.30 mmol), KO*t*Bu (0.45 mmol), CuCl (0.015 mmol), dppf (0.015 mmol), 1,4-dioxane (1 mL), 50 °C. Regioisomeric ratio is in parentheses.

with a carbon−carbon double bond (**4ar**), a carbon−chloride bond (**4as**), ester (**4at**), or acetal (**4au**) similarly furnished the respective products with these functional groups remaining intact, demonstrating the high functional group compatibility of the reaction. It should be noted that the radical clock reaction[17] using cyclopropylmethyl bromide (**4av**) proceeded without ring opening, which indicates that a radical pathway should not be operative in the carboboration, and the result is in marked contrast to those of the copper-catalyzed direct borylation of alkyl halides.[18,19]

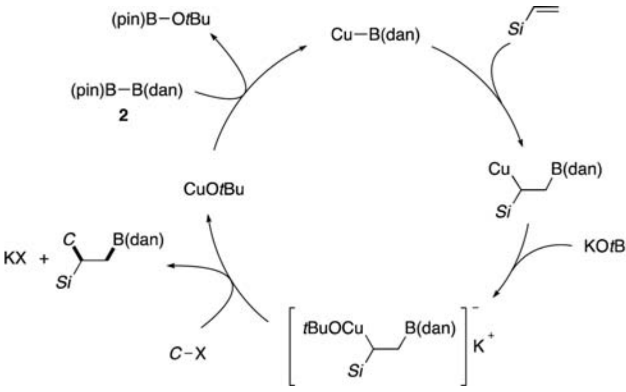
The difference in reactivity between the B(dan) and the B(pin) of 1,2-diborylalkane (**4ea**) obtained in the present reaction allowed chemoselective transformation: oxidation[20] of the sterically hindered position became feasible to give a B(dan)-substituted secondary alcohol (**5**) in 63% yield (Scheme 6). Furthermore, the B(pin) moiety was also transformable into potassium trifluoroborate (**6**) by treatment with KHF_2[21] without damaging the B(dan) moiety.

Scheme 6. Chemoselective Transformation of 4ea



As depicted in Scheme 7, selective *σ*-bond metathesis between a copper(I) alkoxide and an unsymmetrical diboron (**2**), which provides Cu−B(dan),[9,10] would trigger the carboboration. Subsequent insertion of an alkene into the Cu−B bond followed by coordination of an alkoxide to the resulting alkylcopper species generates an alkylcuprate species.[6,22] The cuprate is finally captured by a carbon electrophile[23,24] to give a carboboration product with regeneration of a copper alkoxide. Although a borylcopper species may accept coordination of an alkoxide to give a borylcuprate species as was the case in the direct borylation of alkyl halides,[18e] this pathway should be ruled out, because the borylcuprate serves as a strong one-electron reductant for generating alkyl radicals from alkyl halides, being in sharp contrast to the above result (**4au**, Scheme 5).

Scheme 7. A Plausible Catalytic Cycle



In conclusion, we have disclosed that the first B(dan)-installing carboboration becomes feasible by use of an unsymmetrical diboron [(pin)B−B(dan)] under CuCl−dppf catalysis. The present carboboration provides a direct and regioselective method for synthesizing diverse protected alkylboron compounds, which are otherwise difficult to obtain. Further studies on the copper-catalyzed three-component carboboration of unsaturated carbon linkages as well as on details of the reaction mechanism are in progress.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b03820.

Experimental procedures and compound characterization data for all new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: yhiroto@hiroshima-u.ac.jp.

ORCID

Hiroto Yoshida: 0000-0001-6890-4397

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This paper is dedicated to Prof. Tamejiro Hiyama (Chuo University, Japan) on the occasion of his 70th birthday. This work was financially supported by JSPS KAKENHI Grant Number JP16H01031 in Precisely Designed Catalysts with Customized Scaffolding.

■ REFERENCES

(1) (a) Suginome, M.; Yamamoto, A.; Murakami, M. *J. Am. Chem. Soc.* **2003**, *125*, 6358−6359. (b) Suginome, M.; Yamamoto, A.; Murakami, M. *Angew. Chem., Int. Ed.* **2005**, *44*, 2380−2382. (c) Suginome, M.; Yamamoto, A.; Murakami, M. *J. Organomet. Chem.* **2005**, *690*, 5300−5308. (d) Yamamoto, A.; Suginome, M. *J. Am. Chem. Soc.* **2005**, *127*, 15706−15707. (e) Suginome, M.; Shirakura, M.; Yamamoto, A. *J. Am. Chem. Soc.* **2006**, *128*, 14438−14439. (f) Suginome, M.; Yamamoto, A.; Sasaki, T.; Murakami, M. *Organometallics* **2006**, *25*, 2911−2913. (g) Daini, M.; Yamamoto, A.; Suginome, M. *J. Am. Chem. Soc.* **2008**, *130*, 2918−2919. (h) Daini, M.; Suginome, M. *Chem. Commun.* **2008**, 5224−5226. (i) Suginome, M. *Chem. Rec.* **2010**, *10*, 348−358. (j) Daini, M.; Yamamoto, A.; Suginome, M. *Asian J. Org. Chem.* **2013**, *2*, 968−976. (k) Nakagawa, N.; Hatakeyama, T.; Nakamura, M. *Chem. - Eur. J.* **2015**, *21*, 4257−4261.

(2) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483. (b) Miyaura, N. *Top. Curr. Chem.* **2002**, *219*, 11−59. (c) Candeias, N. R.; Montalbano, F.; Cal, P. M. S. D.; Gois, P. M. P. *Chem. Rev.* **2010**, *110*, 6169−6193. (d) Hayashi, T. *Synlett* **2001**, *2001*, 879−887. (e) Hayashi, T.; Yamasaki, K. *Chem. Rev.* **2003**, *103*, 2829−2844.

(3) Ley, S. V.; Thomas, A. W. *Angew. Chem., Int. Ed.* **2003**, *42*, 5400−5449.

(4) (a) Alfaro, R.; Parra, A.; Aleman, J.; Ruano, J. L. G.; Tortosa, M. *J. Am. Chem. Soc.* **2012**, *134*, 15165−15168. (b) Yoshida, H.; Kageyuki, I.; Takaki, K. *Org. Lett.* **2013**, *15*, 952−955. (c) Liu, P.; Fukui, Y.; Tian, P.; He, Z.-T.; Sun, C.-Y.; Wu, N.-Y.; Lin, G.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 11700−11703. (d) Bidal, Y. D.; Lazreg, F.; Cazin, C. S. J. *ACS Catal.* **2014**, *4*, 1564−1569. (e) Zhou, Y.; You, W.; Smith, B. K.; Brown, M. K. *Angew. Chem., Int. Ed.* **2014**, *53*, 3475−3479. (f) Bin, H.-Y.; Wei, X.; Zi, J.; Zuo, Y.-J.; Wang, T.-C.; Zhong, C.-M. *ACS Catal.* **2015**, *5*, 6670−6679. (g) Kubota, K.; Iwamoto, H.; Yamamoto, E.; Ito,

H. *Org. Lett.* **2015**, *17*, 620−623. (h) Itoh, T.; Shimizu, Y.; Kanai, M. *J. Am. Chem. Soc.* **2016**, *138*, 7528−7531. (i) Su, W.; Gong, T.-J.; Zhang, Q.; Zhang, Q.; Xiao, B.; Fu, Y. *ACS Catal.* **2016**, *6*, 6417−6421.

(5) (a) Meng, F.; Jang, H.; Jung, B.; Hoveyda, A. H. *Angew. Chem., Int. Ed.* **2013**, *52*, 5046−5051. (b) Semba, K.; Bessho, N.; Fujihara, T.; Terao, J.; Tsuji, Y. *Angew. Chem., Int. Ed.* **2014**, *53*, 9007−9011.

(6) (a) Ito, H.; Kosaka, H.; Nonoyama, K.; Sasaki, Y.; Sawamura, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 7424−7427. (b) Ito, H.; Toyoda, T.; Sawamura, M. *J. Am. Chem. Soc.* **2010**, *132*, 5990−5992. (c) Zhong, C.; Kunii, S.; Kosaka, Y.; Sawamura, M.; Ito, H. *J. Am. Chem. Soc.* **2010**, *132*, 11440−11442. (d) Kubota, K.; Yamamoto, E.; Ito, H. *J. Am. Chem. Soc.* **2013**, *135*, 2635−2640. (e) Kageyuki, I.; Yoshida, H.; Takaki, K. *Synthesis* **2014**, *46*, 1924−1932. (f) Meng, F.; McGrath, K. P.; Hoveyda, A. H. *Nature* **2014**, *513*, 367−374. (g) Semba, K.; Nakao, Y. *J. Am. Chem. Soc.* **2014**, *136*, 7567−7570. (h) Su, W.; Gong, T.-J.; Lu, X.; Yu, C.-G.; Xu, Z.-Y.; Yu, H.-Z.; Xiao, B.; Fu, Y. *Angew. Chem., Int. Ed.* **2015**, *54*, 12957−12961. (i) Semba, K.; Ohtagaki, Y.; Nakao, Y. *Org. Lett.* **2016**, *18*, 3956−3959.

(7) (a) Laitar, D. S.; Müller, P.; Sadighi, J. P. *J. Am. Chem. Soc.* **2005**, *127*, 17196−17197. (b) Segawa, Y.; Yamashita, M.; Nozaki, K. *Angew. Chem., Int. Ed.* **2007**, *46*, 6710−6713. (c) Kleeberg, C.; Dang, L.; Lin, Z.; Marder, T. B. *Angew. Chem., Int. Ed.* **2009**, *48*, 5350−5354. (d) Semba, K.; Shinomiya, M.; Fujihara, T.; Terao, J.; Tsuji, Y. *Chem. - Eur. J.* **2013**, *19*, 7125−7132.

(8) (a) Iwadate, N.; Suginome, M. *J. Am. Chem. Soc.* **2010**, *132*, 2548−2549. (b) Miralles, J.; Cid, J.; Cuenca, A. B.; Carbó, J. J.; Fernández, A. B. *Chem. Commun.* **2015**, *51*, 1693−1696. (c) Xu, L.; Li, P. *Chem. Commun.* **2015**, *51*, 5656−5659.

(9) (a) Yoshida, H.; Takemoto, Y.; Takaki, K. *Chem. Commun.* **2014**, *50*, 8299−9302. (b) Yoshida, H.; Takemoto, Y.; Takaki, K. *Asian J. Org. Chem.* **2014**, *3*, 1204−1209.

(10) Yoshida, H.; Takemoto, Y.; Takaki, K. *Chem. Commun.* **2015**, *51*, 6297−6300.

(11) For reviews on copper-catalyzed borylations, see: (a) Yun, J. *Asian J. Org. Chem.* **2013**, *2*, 1016−1025. (b) Fujihara, T.; Semba, K.; Terao, J.; Tsuji, Y. *Catal. Sci. Technol.* **2014**, *4*, 1699−1709. (c) Semba, K.; Fujihara, T.; Terao, J.; Tsuji, Y. *Tetrahedron* **2015**, *71*, 2183−2197. (d) Yoshida, H. *ACS Catal.* **2016**, *6*, 1799−1811.

(12) For our reports on the copper-catalyzed metalation reactions for synthesizing main group organometallics containing boron, tin, or silicon, see: (a) Yoshida, H.; Kawashima, S.; Takemoto, Y.; Okada, K.; Ohshita, J.; Takaki, K. *Angew. Chem., Int. Ed.* **2012**, *51*, 235−238. (b) Takemoto, Y.; Yoshida, H.; Takaki, K. *Chem. - Eur. J.* **2012**, *18*, 14841−14844. (c) Yoshida, H.; Shinke, A.; Takaki, K. *Chem. Commun.* **2013**, *49*, 11671−11673. (d) Takemoto, Y.; Yoshida, H.; Takaki, K. *Synthesis* **2014**, *46*, 3024−3032. (e) Yoshida, H.; Hayashi, Y.; Ito, Y.; Takaki, K. *Chem. Commun.* **2015**, *51*, 9440−9442. (f) Yoshida, H.; Shinke, A.; Kawano, Y.; Takaki, K. *Chem. Commun.* **2015**, *51*, 10616−10619. (g) Yoshida, H. *Chem. Rec.* **2016**, *16*, 419−434.

(13) For a boron-masking strategy, see: (a) Noguchi, H.; Hojo, K.; Suginome, M. *J. Am. Chem. Soc.* **2007**, *129*, 758−759. (b) Noguchi, H.; Shioda, T.; Chou, C.-M.; Suginome, M. *Org. Lett.* **2008**, *10*, 377−380. (c) Iwadate, N.; Suginome, M. *Org. Lett.* **2009**, *11*, 1899−1902. (d) Iwadate, N.; Suginome, M. *Chem. Lett.* **2010**, *39*, 558−560.

(14) For detailed optimization of reaction conditions, see Supporting Information.

(15) A hydroboration product ($PhMe_2SiCH_2CH_2B(dan)$) and BnB(dan) were generated as byproducts in each entry. For example, a 17% yield (based on **1a**) of a hydroboration product and a 6% yield (based on **3a**) of BnB(dan) were obtained in entry 1.

(16) These reactions mainly gave BnB(dan) instead of a carboboration product, which may be ascribable to low reactivity of Cu−B(dan) toward these unsaturated compounds employed.

(17) For a review on radical clock reactions, see: Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317−323.

(18) (a) Yang, C.-T.; Zhang, Z.-Q.; Tajuddin, H.; Wu, C.-C.; Liang, J.; Liu, J.-H.; Fu, Y.; Czyzewska, M.; Steel, P. G.; Marder, T. B.; Liu, L. *Angew. Chem., Int. Ed.* **2012**, *51*, 528−532. (b) Ito, H.; Kubota, K. *Org. Lett.* **2012**, *14*, 890−893. (c) Iwamoto, H.; Kubota, K.; Ito, H. *Chem. Commun.* **2015**, *51*, 9655−9658. (d) Bose, S. K.; Brand, S.; Omoregie, H. O.; Haehnel, M.; Maier, J.; Bringmann, G.; Marder, T. B. *ACS Catal.* **2016**, *6*, 8332−8335. (e) Kubota, K.; Iwamoto, H.; Ito, H. *Org. Biomol. Chem.* **2017**, *15*, 285−300.

(19) A hydroboration product was usually formed as a major byproduct in the reactions with the lower yields.

(20) Corberán, R.; Mszar, W. N.; Hoveyda, H. A. *Angew. Chem., Int. Ed.* **2011**, *50*, 7079−7082.

(21) Churches, I. Q.; Hooper, F. J.; Hutton, C. A. *J. Org. Chem.* **2015**, *80*, 5428−5435.

(22) For examples on mixed cuprate(I) species, see: (a) Posner, G. H.; Sterling, J. J. *J. Am. Chem. Soc.* **1973**, *95*, 3076−3077. (b) Posner, G. H.; Whitten, C. E. *Tetrahedron Lett.* **1973**, *14*, 1815−1818. (c) Posner, G. H.; Whitten, C. E.; Sterling, J. J. *J. Am. Chem. Soc.* **1973**, *95*, 7788−7800.

(23) Mixed cuprate(I) species of this type were reported to be coupled with organic halides. See ref 22.

(24) A detailed mechanism for the reaction of a dppf-coordinated alkylcuprate (18-electron) with an alkyl halide is unclear at present. A referee suggested that dppf may serve as a hemilabile ligand in this step and that a neutral dppf-coordinated alkylcopper may interact with an alkyl halide.