ACS Catalysis

Subscriber access provided by LUNDS UNIV

Letter

Selective Dehydrogenative Mono- or Diborylation of Styrenes by Supported Copper Catalysts

Daichi Yoshii, Xiongjie Jin, Noritaka Mizuno, and Kazuya Yamaguchi

ACS Catal., **Just Accepted Manuscript** • DOI: 10.1021/acscatal.9b00761 • Publication Date (Web): 06 Mar 2019

Downloaded from http://pubs.acs.org on March 6, 2019

Just Accepted

"Just Accepted" manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides "Just Accepted" as a service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. "Just Accepted" manuscripts appear in full in PDF format accompanied by an HTML abstract. "Just Accepted" manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are citable by the Digital Object Identifier (DOI®). "Just Accepted" is an optional service offered to authors. Therefore, the "Just Accepted" Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the "Just Accepted" Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these "Just Accepted" manuscripts.

ACS Publications

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Published by American Chemical Society. Copyright © American Chemical Society. However, no copyright claim is made to original U.S. Government works, or works produced by employees of any Commonwealth realm Crown government in the course of their duties.

Selective Dehydrogenative Mono- or Diborylation of Styrenes by Supported Copper Catalysts

Daichi Yoshii,[†] Xiongjie Jin,[*,‡] Noritaka Mizuno,[†] and Kazuya Yamaguchi[*,†]

[†]Department of Applied Chemistry, School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

[‡]Department of Chemistry and Biotechnology, School of Engineering, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

---

ABSTRACT: The selective dehydrogenative borylation of alkenes is an attractive method for synthesizing useful borylalkenes. However, very few catalytic systems have been reported far that fulfill this objective. All the reported examples are homogeneous catalysts with special ligands requiring the usage of bases. This study describes the heterogeneously catalyzed dehydrogenative borylation by supported copper hydroxide catalysts ($Cu(OH)_x$/support). In the presence of $Cu(OH)_x$/support and suitable ketones, the dehydrogenative borylation of styrenes with bis(pinacolato)diboron efficiently proceeded to selectively afford the corresponding β-monoboryl- or β,β-diborylstyrenes. The observed catalysis was truly heterogeneous, and the catalysts could be reused several times though their catalytic performance gradually declined.

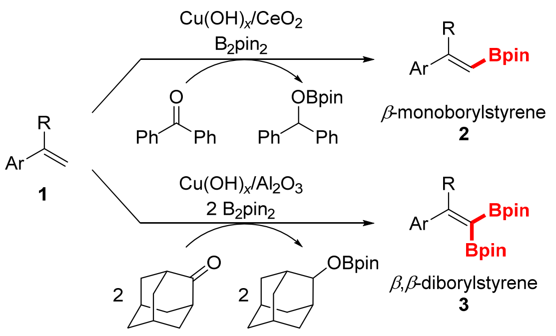
KEYWORDS: Copper • Dehydrogenative borylation • Heterogeneous catalysis • Selectivity control • Styrenes

---

The development of heterogeneous catalysts for liquid-phase organic functional group transformations, which are used in the production of fine chemicals and pharmaceuticals, is becoming increasingly important because of the easy recovery/reuse of catalysts and minimization of metal contamination in the synthesized products.[1] Moreover, there has been an upsurge in the need to develop heterogeneous catalysts for use in continuous flow systems for the on-demand synthesis of valuable chemicals.[2] However, highly regio- and stereoselective reactions have traditionally been accomplished using homogeneous catalysts with well-designed ligands. Recent advances in homogeneous copper-catalyzed C–B bond formation reactions using *N*-heterocyclic carbenes or phosphines as the ligands have allowed to synthesize a range of valuable organoboron compounds.[3,4] However, heterogeneously copper-catalyzed borylation reactions are very rare.[5] Due to the importance of the use of organoboron compounds as key building blocks in several organic synthesis reactions, the development of new efficient heterogeneous copper-based catalysts for selective borylation reactions is highly desirable from economic and environmental viewpoints.

Here, we report that the copper hydroxide species on suitable metal oxide supports ($Cu(OH)_x$/support) can act as an efficient heterogeneous catalyst for the dehydrogenative borylation of styrene and its derivatives with bis(pinacolato)diboron (B_2pin_2) to selectively produce β-monoboryl- or β,β-diborylstyrenes (Scheme 1). Both monoboryl- and diborylalkenes are useful compounds for serving as building blocks to selectively synthesize a range of multisubstituted alkenes *via* C–C and C–heteroatom bond-forming reactions.[6] Monoborylalkenes have been prepared *via* the hydroboration of alkynes,[7] the borylation of alkenyl halides,[8] alkene cross-metathesis,[9] the boryl–Heck reaction using electrophilic boron reagents,[10] or *via* the dehydrogenative borylation of alkenes.[11] Dehydrogenative borylation can be used to directly convert readily available alkenes into the corresponding vinyl boronic esters, providing simple access to a wide range of compounds, including β,β-disubstituted vinyl boronic esters, which cannot be synthesized *via* the hydroboration of alkynes. Recently, rhodium-,[12] iron-,[13] and copper-based[14] homogeneous catalysts are reported to be effective in the dehydrogenative borylation of alkenes to monoborylalkenes using alkenes or ketones as the sacrificial oxidants. Furthermore, the homogeneous palladium-[15] and cobalt-catalyzed[16] dehydrogenative diborylation of terminal alkenes has been recently reported.

Scheme 1. The dehydrogenative monoborylation and diborylation of styrenes using $Cu(OH)_x$/support



In this work, $Cu(OH)_x/CeO_2$ was found to efficiently promote the dehydrogenative borylation of styrene and its derivatives using benzophenone as the HBpin acceptor, to selectively afford β-monoborylstyrenes in moderate to high yields with high regioselectivities (Scheme 1). Furthermore, dehydrogenative diborylation was used to produce β,β-

diborylstyrenes through a simple modifcation of the reaction conditions, *e.g.*, increasing the amounts of B_2pin_2, the HBpin acceptor 2-adamantanone, and the $Cu(OH)_x/Al_2O_3$ catalyst (Scheme 1). In the proposed $Cu(OH)_x$/support-catalyzed dehydrogenative borylation reaction, additives, such as special ligands and bases, which were found to be necessary in the previously reported homogeneously catalyzed systems,[12–16] were not required. To the best of our knowledge, the present work is the first report on dehydrogenative borylation using heterogeneous catalysts.

With reference to the previously reported homogeneous copper-catalyzed C–B bond formation reactions,[14] heterogeneous copper-based catalysts were initially examined for the borylation of styrene (**1a**) with B_2pin_2 on the assumption of the mechanism shown in Scheme 2a. Surprisingly, out of all of the catalysts examined for the borylation of **1a** under the conditions described in Table 1 (entries 1–11, without HBpin acceptors), significant amounts of **2a** were only afforded in the presence of supported copper-hydroxide catalysts ($Cu(OH)_x$/support,[17,18] Figure S1), and it was observed that the use of $Cu(OH)_x/CeO_2$ gave **2a** in 31% yield (Table 1, entry 1). No reactions were observed to proceed in air, even in the presence of $Cu(OH)_x/CeO_2$ (Table 1, entry 2). The borylation reaction did not proceed in the presence of $CuCl_2$ or $Cu(OAc)_2$ (OAc = acetate) supported on CeO_2 (Table 1, entries 3 and 4), or in the absence of catalysts or the presence of a CeO_2 support alone (Table 1, entry 11). Other simple Cu^{I} and Cu^{II} salts, such as CuCl, $CuCl_2$, and $Cu(OAc)_2$, were not effective in the catalysis of the borylation reaction (Table 1, entries 8–10). The borylation reaction barely proceeded in the presence of bulk copper hydroxide $Cu(OH)_2$ or copper oxides (Table 1, entries 5–7). Therefore, it was concluded that the use of a highly dispersed copper hydroxide species is crucial for the borylation reaction to proceed.

Scheme 2. The assumed mechanism of the copper-catalyzed dehydrogenative borylation of styrenes

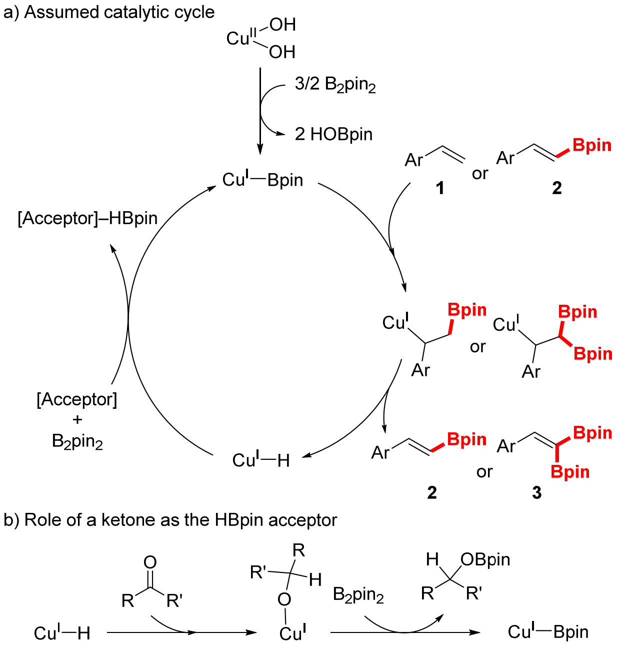
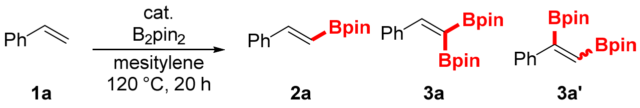


Table 1. Optimization of the reaction conditions of the dehydrogenative borylation of styrene (1a) to *β*-monoborylstyrene (2a) and *β*,*β*-diborylstyrene (3a)



Entry	Catalyst	Acceptor	Yield (%)		
			2a	3a	3a'
1[a,b]	$Cu(OH)_x/CeO_2$	—	31	5	2
2[a,c]	$Cu(OH)_x/CeO_2$	—	<1	<1	<1
3[a]	$CuCl_2/CeO_2$	—	<1	<1	<1
4[a]	$Cu(OAc)_2/CeO_2$	—	<1	<1	<1
5[a]	$Cu(OH)_2$	—	4	<1	<1
6[a]	CuO	—	<1	<1	<1
7[a]	Cu_2O	—	<1	<1	<1
8[a]	$CuCl_2$	—	4	<1	<1
9[a]	CuCl	—	<1	<1	<1
10[a]	$Cu(OAc)_2$	—	2	<1	<1
11[a,d]	CeO_2	—	<1	<1	<1
12[a,e]	$Cu(OH)_x/CeO_2$	benzophenone	87	8	2
13[a,e]	$Cu(OH)_x/CeO_2$	2-adamantanone	75	7	3
14[a,e]	$Cu(OH)_x/Al_2O_3$	benzophenone	64	10	1
15[f]	$Cu(OH)_x/CeO_2$	benzophenone	14	58	15
16[f]	$Cu(OH)_x/CeO_2$	2-adamantanone	<1	59	5
17[f]	$Cu(OH)_x/Al_2O_3$	benzophenone	55	31	4
18[f]	$Cu(OH)_x/Al_2O_3$	2-adamantanone	5	84	<1

[a] Reaction conditions: **1a** (0.5 mmol), B_2pin_2 (1.25 mmol), catalyst (Cu: 4 mol%), acceptor (0.75 mmol), mesitylene (2 mL), 120 °C, Ar (1 atm), 20 h. Yields were determined by GC analysis using *n*-hexadecane as an internal standard. [b] The hydroborated products and ethylbenzene were also significantly produced in 29% (α/β = 2.6:1) and 26% yields, respectively. [c] Under an air atmosphere. [d] CeO_2 (80 mg). [e] *p*-Xylene was used as a solvent instead of mesitylene. [f] Reaction conditions: **1a** (0.2 mmol), B_2pin_2 (1.0 mmol), catalyst (Cu: 8 mol%), acceptor (0.6 mmol), *p*-xylene (2 mL), 120 °C, Ar (1 atm), 20 h. See also Tables S1 and S2.

The Cu K-edge x-ray absorption near edge structure (XANES) spectrum and its first-derivative spectrum of freshly prepared $Cu(OH)_x/CeO_2$ were recorded to be quite similar to those of $Cu(OH)_2$ (Figure S2), indicating that $Cu(OH)_x/CeO_2$ possesses Cu^{II} hydroxide species dispersed on CeO_2 support. After the catalyst was used in the reaction of **1a** or treated with B_2pin_2 under an Ar atmosphere, the Cu^{II} species in $Cu(OH)_x/CeO_2$ was reduced to Cu^{I} and Cu^{0} species (Figure S2). In a separate experiment, we prepared Cu^{0}/CeO_2 by the treatment of $Cu(OH)_x/CeO_2$ with H_2 (1 atm) at 200 °C for 1 h,[19] and the borylation of **1a** was performed with the catalyst; however, no reaction proceeded. Thus, the *in situ* formed Cu^{I} species is likely the true active species in the borylation reaction. We treated $Cu(OH)_x/CeO_2$ (100 mg) with B_2pin_2 (30 mg) in benzene-d_6 at 120 °C for 10 min, and the catalyst was removed by the filtration. ^{11}B NMR (Figure S3) and GC-MS analyses of the filtrate revealed that HOBpin was produced during the pre-catalyst reduction step. It is possibly that B_2pin_2 and surface hydroxy species and/or trace amounts of water contained in the catalyst (and/or solvent) act as reductants to form the reduced copper species according to the first step in Scheme 2a, although the detailed reduction mechanism remains unclear.[20] Further, we have reported that $Cu(OH)_2$ can be easily reduced than other Cu^{II} species, such as $CuCl_2 \cdot 2H_2O$ and $Cu(OAc)_2 \cdot H_2O$.[19] Therefore, $Cu(OH)_x/CeO_2$ can be used to easily generate the active reduced copper species and thus exhibit high catalytic activity in the borylation reaction.

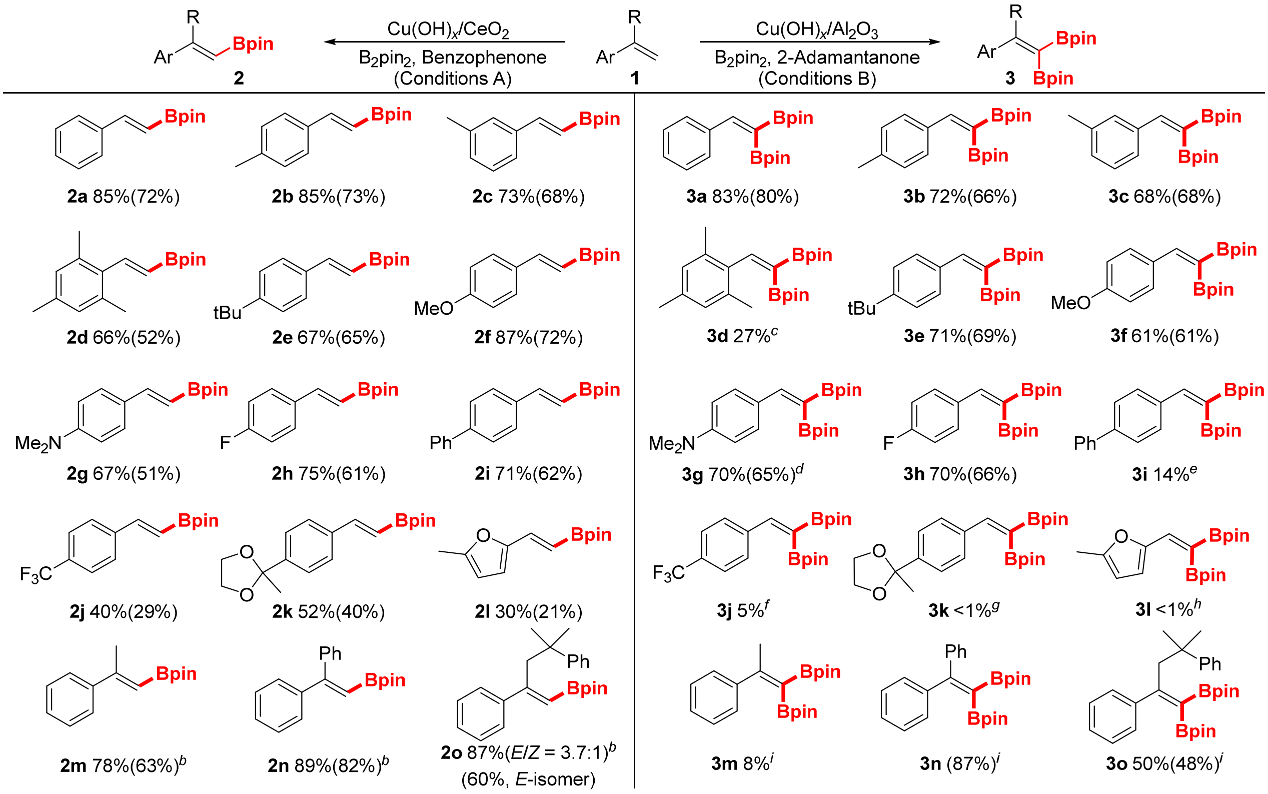
Under the proposed $Cu(OH)_x$/support-catalyzed system, the Cu^I–Bpin species is likely to form readily. The Cu^I–Bpin species is involved in an insertion reaction with **1a**, followed by *β*-hydride elimination to produce *β*-monoborylstyrene (**2a**) and a Cu^I–H species (Scheme 2a). To complete the catalytic cycle, an appropriate HBpin acceptor is required to regenerate the Cu^I–Bpin from Cu^I–H (Scheme 2a). Although $Cu(OH)_x/CeO_2$ is an excellent catalyst for the borylation of **1a**, the yield of **2a** was only 31%, even in the quantitative conversion of **1a** without the use of a HBpin acceptor (Table 1, entry 1). The reason the yield of **2a** cannot theoretically exceed 50% is that in the absence of a HBpin acceptor, **1a** itself acts as the HBpin (or hydride) acceptor. As can be seen in Table 1, entry 1, the hydroboration products and ethylbenzene were also produced in 29% and 26% yields, respectively. Therefore, the search began for an optimal HBpin acceptor for use in the $Cu(OH)_x/CeO_2$-catalyzed borylation of **1a** (Table S1, entries 1–5). Fortunately, several ketones, such as benzophenone and 2-adamantanone, were found to be effective (Table 1, entries 12 and 13), and benzophenone was found to give the best result, with the desired compound **2a** being obtained in 87% yield (Table 1, entry 12). Among various supprorted copper-hydroxide catalysts examined, such as $Cu(OH)_x/CeO_2$, $Cu(OH)_x/Al_2O_3$,[21] $Cu(OH)_x/TiO_2$, and $Cu(OH)_x/ZrO_2$, $Cu(OH)_x/CeO_2$ showed the best catalyitic performance (Table 1, entries 12 and 14, see also Table S1). In the presence of benzophenone, the hydroboration and hydrogenation of styrene barely proceeded. ^1H NMR analysis was used to confirm that the hydroboration product of benzophenone was also produced during the reaction. Furthermore, when using *β*,*β*-dideuteriostyrene (**1a-D$_2$**) as the substrate, the deuterium content at the *α*-position of the hydroborated benzophenone was 64%.[22] Thus, the hydrogen at the *β*-position of styrene is mostly transferred to benzophenone through a *β*-elimination process (Scheme 2a) and hydride addition sequence (Scheme 2b).

Under the conditions described in Table 1, entry 12, the main product was the monoborylated compound **2a** alongside a small amount of the diborylated compounds **3a** and **3a'**. Next, the reaction was attempted using an increased amount of B_2pin_2 (five equivalents with respect to **1a**) to selectively obtain the *β*,*β*-diborylated product **3a**. Although the reaction using $Cu(OH)_x/CeO_2$ and benzophenone preferentially resulted in the formation of the *β*,*β*-diborylated compound **3a** in 58% yield, the *α*,*β*-diborylated product **3a'** was also concomitantly produced in 15% yield (Table 1, entry 15). After the various reaction-condition optimization experiments, the target product **3a** could be selectively obtained in 84% yield using $Cu(OH)_x/Al_2O_3$ as the catalyst and 2-adamantanone as the HBpin acceptor (Table 1, entries 15–18, Figure S4).[23] Several control experiments were conducted using **2a** as the starting material and revealed that 2-adamantanone was more able to promote the second dehydrogenative borylation than benzophenone (Figure S5).[24]

To establish whether the observed catalysis for the borylation of **1a** occurred heterogeneously on $Cu(OH)_x/CeO_2$ or was a result of the presence of leached Cu species in the solution, the catalyst was removed by hot filtration (at 55% yield of **2a**) under the conditions described in Figure S6, and the reaction was restarted with the filtrate under the same conditions. The production of **2a** immediately ceased upon the removal of the catalyst (Figure S6). Additionally, after the reaction, the filtrate was analyzed using inductively coupled plasma-atomic emission spectroscopy (ICP-AES), and it was observed that the Cu species was barely detectable (Cu: <0.01%). Thus, the observed catalysis for the present dehydrogenative borylation was determined to be truly heterogeneous.[25] Furthermore, $Cu(OH)_x/CeO_2$ was retrieved from the reaction mixture by simple filtration under an Ar atmosphere, and repeated reuse experiments were carried out using the retrieved $Cu(OH)_x/CeO_2$. Although the catalsyt could be reused several times, its catalytic performance gradually declined during the repeated reuse experiments.[26]

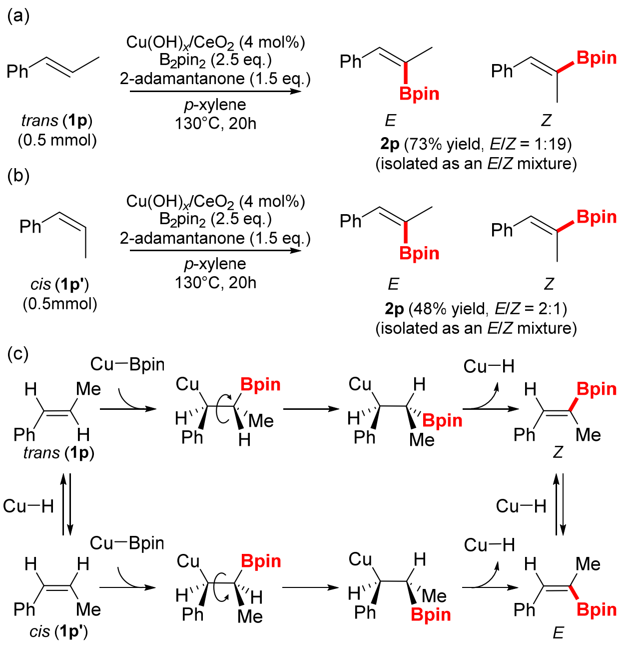
With the optimized reaction conditions, the substrate scope for the proposed $Cu(OH)_x/CeO_2$-catalyzed dehydrogenative monoborylation reaction was investigated in the presence of benzophenone as the HBpin acceptor (Figure S7). As shown in the left of Table 2, various styrene derivatives could be converted into the corresponding *β*-monoborylstyrenes in an *E*-selective fashion. When styrenes substituted with a methyl group at the *ortho*-, *meta*-, or *para*-position (**1b**, **1c**, and **1d**) were used as the substrates, the borylation reaction proceeded efficiently to give the corresponding *β*-monoborylstyrenes in moderate to high yields, indicating that the influence of the steric hindrance of the benzene-ring substituents is not considered significant. Styrenes with a range of electronically diverse substituents at the *para*-position, including methyl (**1b**), *tert*-butyl (**1e**), methoxy (**1f**), dimethylamino (**1g**), fluoro (**1h**), phenyl (**1i**), trifluoromethyl (**1j**), and acetal (**1k**) groups, were applicable to this proposed system. In addition, the reaction of vinylfuran (**1l**) afforded the corresponding borylated product, but vinylpyridine did not undergo this transformation. Unfortunately, the reaction of styrenes with chloro, nitro, cyano, phosphine, and hydroxyl group at *para*-position generated unidentified byproducts, and the corresponding *β*-monoborylstyrenes were hardly obtained. The $Cu(OH)_x/CeO_2$-catalyzed monoborylation of *α*-substituted styrenes (**1m**, **1n**, and **1o**) was also explored to produce *α*-substituted *β*-monoborylstyrene, which cannot be synthesized *via* the hydroboration of alkynes. However, the desired monoborylation products were obtained in low yields (<40%) under the standard reaction conditions using benzophenone. For these *α*-substituted styrenes, the yields of the target products could be enhanced using 2-adamantanone as the HBpin acceptor and by increasing the reaction temperature from 120 °C to 130 °C. The reaction of **1m** or **1n** gave the corresponding *α*-substituted *β*-monoborylstyrene in a high yield with an *E*-selective fashion. For the reaction of **1o**, a mixture of *E*- and *Z*-isomers was obtained, with the preferential formation of the *E*-isomer (*E*/*Z* = 3.7:1). In addition, the reaction of *trans*-*β*-methylstyrene (**1p**) gave the corresponding *β*-monoborylated product (**2p**) in 73% isolated yield with high *Z*-selectivity (*E*/*Z* = 1:19) (Scheme 3a). In contrast, when *cis*-*β*-methylstyrene (**1p'**) was subjected to the same conditions, the yield was relatively low (48%), and the *E*-isomer was mainly obtained (*E*/*Z* = 2:1) (Scheme 3b). These results are consistent with the assumed reaction mechanism shown in Scheme 2 including sequential migratory insertion and *β*-hydride elimination (Scheme 3c). When alkyl alkenes,

Table 2. Substrate scope of the dehydrogenative monoborylation and diborylation reactions[a]



[a]Set of reaction conditions A (monoborylation): **1** (0.5 mmol), B_2pin_2 (1.25 mmol), $Cu(OH)_x/CeO_2$, (Cu: 4 mol%), benzophenone (0.75 mmol), *p*-xylene (2 mL), 120 °C, Ar (1 atm), 20 h. Set of reaction conditions B (diborylation): **1** (0.2 mmol), B_2pin_2 (1.0 mmol), $Cu(OH)_x/Al_2O_3$, (Cu: 8 mol%), 2-adamantanone (0.6 mmol), *p*-xylene (2 mL), 120 °C, Ar (1 atm), 20 h. Yields were determined by ^1H NMR and the values in parentheses are the isolated yields. [b]2-Adamantanone was added instead of benzophenone and the reaction was carried out at 130 °C. [c]**2d** was also obtained in 38% yield. [d]$Cu(OH)_x/CeO_2$ was used instead of $Cu(OH)_x/Al_2O_3$. [e]**2i** was also obtained in 49% yield. [f]**2j** was also obtained in 41% yield. [g]**2k** was obtained 70% yield. [h]**2l** was obtained 30 % yield. [i]2-Adamantanone (0.8 mmol) was added and the reaction was carried out at 130 °C for 64 h.

Scheme 3. Dehydrogenative monoborylation of (a) *trans-β*-methylstyrene and (b) *cis-β*-methylstyrene, and (c) the assumed reaction mechanism



such as 4-phenyl-1-butene, were examined, multiple indistinguishable mixtures of monoborylated products were unfortunately obtained.

Next, we attempted to synthesize *β*,*β*-diborylstyrenes using the $Cu(OH)_x/Al_2O_3$-catalyzed dehydrogenative diborylation reaction. Several styrenes containing a range of electronically diverse aryl groups were selectively converted into the corresponding *β*,*β*-diborylstyrenes in moderate to high yields with high regioselectivities (right of Table 2). However, **3d**, **3i**, **3j**, **3k**, and **3l** were obtained in low yields because a significant amount of the monoborylated intermediates (**2d**, **2i**, **2j**, **2k**, and **2l**) remained unreacted. Further, the reaction of **1m** gave the diborylated product **3m** in only 8% yield, even though complete conversion of **1m** and **2m** was achieved. This is because the double bond isomerization and borylation of **2m** and **3m** may occur at the *α*-methyl substituent. In contrast, the diborylation products **3n** and **3o** could be obtained using the present $Cu(OH)_x/Al_2O_3$-catalyzed system.

In conclusion, for the first time, a heterogeneous catalytic system was developed using $Cu(OH)_x$/support for the dehydrogenative borylation of styrene and its derivatives with B_2pin_2 under ligand- and base-free conditions. The desired reaction was tested using suitable ketones as HBpin acceptors. Various types of β-monoborylstyrenes were synthesized in moderate to high yields and high regioselectivities. Moreover, dehydrogenative diborylation was also realized by simply modifying the reaction conditions, leading to selective synthesis of β,β-diborylstyrenes. It is believed that this study highlights the considerable potential of heterogeneous catalysts for various functional group transformations.

ASSOCIATED CONTENT

Supporting Information

The supporting information is available free of charge on the ACS Publication website: experimental details, additional experimental results, characterization data, and NMR spectra (PDF).

AUTHOR INFORMATION

Corresponding Author

*E-mail: kyama@appchem.t.u-tokyo.ac.jp, t-jin@mail.ecc.u-tokyo.ac.jp

Notes

The authors declare no competing financial interests.

ACKNOWLEDGMENT

This work was financially supported by JSPS KAKENHI Grant No. 15H05797 in Precisely Designed Catalysts with Customized Scaffolding. D. Y. was supported by the JSPS through the Research Fellowship for Young Scientists (Grant No. 18J21337).

REFERENCES

(1) (a) *Fine Chemicals through Heterogeneous Catalysis;* Sheldon, R. A., van Bekkum, H., Eds.; Wiley-VCH: Weinheim, **2001**. (b) Climent, M. J.; Corma, A.; Iborra, S. Heterogeneous Catalysts for the One-Pot Synthesis of Chemicals and Fine Chemicals. *Chem. Rev.* **2011**, *111*, 1072–1133.

(2) (a) Paste, J. C.; Browne, D. L.; Ley, S. V. Flow chemistry syntheses of natural products. *Chem. Soc. Rev.* **2013**, *42*, 8849–8869. (b) Kobayashi, S. Flow "Fine" Synthesis: High Yielding and Selective Organic Synthesis by Flow Methods. *Chem. Asian. J.* **2016**, *11*, 425–436. (c) Porta, R.; Benaglia, M.; Puglisi, A. Flow Chemistry: Recent Developments in the Synthesis of Pharmaceutical Products. *Org. Process. Res. Dev.* **2016**, *20*, 2–25.

(3) (a) Yun, J. Copper(I)-Catalyzed Boron Addition Reactions of Alkynes with Diboron Reagents. *Asian. J. Org. Chem.* **2013**, *2*, 1016–1025. (b) Tsuji, Y.; Fujihara, T. Copper-Catalyzed Transformations Using Cu–H, Cu–B, and Cu–Si as Active Catalyst Species. *Chem. Rec.* **2016**, *16*, 2294–2313. (c) Semba, K.; Fujihara, T.; Terao, J.; Tsuji, Y. Copper-catalyzed borylative transformations of non-polar carbon–carbon unsaturated compounds employing borylcopper as an active catalyst species. *Tetrahedron* **2015**, *71*, 2183–2197. (d) Collins, B. S. L.; Wilson, C. M.; Myers, E. L.; Aggarwal, V. K. Asymmetric Synthesis of Secondary and Tertiary Boronic Esters. *Angew. Chem. Int. Ed.* **2017**, *56*, 11700–11733.

(4) Recently, dehydrogenative borylation of alkynes using first row transition metal catalysis has been reported: (a) Wei, D.; Carboni, B; Sortais, J.-B.; Darcel, C. Iron-Catalyzed Dehydrogenative Borylation of Terminal Alkynes. *Adv. Synth. Catal.* **2018**, *360*, 3649–3654. (b) Romero, E.-A.; Jazzar, R.; Bertrand, G. (CAAC)CuX-catalyzed hydroboration of terminal alkynes with pinacolborane directed by the X-ligand. *J. Organomet. Chem.* **2017**, *829*, 11–13. (c) Romero, E.-A.; Jazzar, R.; Bertrand, G. Copper-catalyzed dehydrogenative borylation of terminal alkynes with pinacolborane. *Chem. Sci.* **2017**, *8*, 165–168.

(5) (a) Grirrane, A.; Corma, A.; Garcia, H. Stereoselective Single (Copper) or Double (Platinum) Boronation of Alkynes Catalyzed by Magnesia-Supported Copper Oxide or Platinum Nanoparticles. *Chem. Eur. J.* **2011**, *17*, 2467–2478. (b) Zhou, X.-F.; Wu, Y.-D.; Dai, J.-J.; Li, Y.-J.; Huang, Y.; Xu, H.-J. Borylation of primary and secondary alkyl bromides catalyzed by Cu_2O nanoparticles. *RSC Adv.* **2015**, *5*, 46672–46676. (c) Zhou, X.-F.; Sun, Y.-Y.; Wu, Y.-D.; Dai, J.-J.; Xu, J.; Huang, Y.; Xu, H.-J. Borylation and selective reduction of α,β-unsaturated ketones under mild conditions catalyzed by Cu nanoparticles. *Tetrahedron* **2016**, *72*, 5691–5698.

(6) (a) Miyaura, N.; Suzuki, A. Palladium-Catalyzed Cross-Coupling Reactions of Organoboron Compounds. *Chem. Rev.* **1995**, *95*, 2457–2483. (b) Kohta, S.; Lahiri, K.; Kashinath, D. Recent applications of the Suzuki–Miyaura cross-coupling reaction in organic synthesis. *Tetrahedron* **2002**, *58*, 9633–9695. (c) Matteson, D. S. Boronic Esters in Stereodirected Synthesis. *Tetrahedron* **1989**, *45*, 1859–1885.

(7) (a) Trost, B. M.; Ball, Z. T. Addition of Metalloid Hydrides to Alkynes: Hydrometallation with Boron, Silicon, and Tin. *Synthesis* **2005**, 853–887. (b) Barbeyron, R.; Benedetti, E.; Cossy, J.; Vasseur, J.-J.; Arseniyadis, S.; Smietana, M. Recent developments in alkyne borylations. *Tetrahedron* **2014**, *70*, 8431–8452. (c) Yoshida, H. Borylation of Alkynes under Base/Coinage Metal Catalysis: Some Recent Developments. *ACS Catal.* **2016**, *6*, 1799–1811.

(8) Takagi, J.; Takahashi, K.; Ishiyama, T.; Miyaura, N. Palladium-Catalyzed Cross-Coupling Reaction of Bis(pinacolato)diboron with 1-Alkenyl Halides or Triflates: Convenient Synthesis of Unsymmetrical 1,3-Dienes via the Borylation-Coupling Sequence. *J. Am. Chem. Soc.* **2002**, *124*, 8001–8006.

(9) Morrill, C.; Funk, T. W.; Grubbs, R. H. Synthesis of tri-substituted vinyl boronates via ruthenium-catalyzed olefin cross-metathesis. *Tetrahedron Lett.* **2004**, *45*, 7733–7736.

(10) Reid, W. B.; Spillane, J. J.; Krause, S. B.; Watson, D. A. Direct Synthesis of Alkenyl Boronic Esters from Unfunctionalized Alkenes: A Boryl-Heck Reaction. *J. Am. Chem. Soc.* **2016**, *138*, 5539–5542.

(11) Geier, S. J.; Westcott, S. A. Dehydrogenative borylation: the dark horse in metal-catalyzed hydroborations and diborations? *Rev. Inorg. Chem.* **2015**, *35*, 69–79.

(12) Morimoto, M.; Miura, T.; Murakami, M. Rhodium-Catalyzed Dehydrogenative Borylation of Aliphatic Terminal Alkenes with Pinacolborane. *Angew. Chem. Int. Ed.* **2015**, *54*, 12659–12663.

(13) (a) Wang, C.; Wu, C.; Ge, S. Iron-Catalyzed *E*-Selective Dehydrogenative Borylation of Vinylarenes with Pinacolborane. *ACS Catal.* **2016**, *6*, 7585–7589. (b) Jiang, S.; Quintero-Duque, S.; Roisnel, T.; Dorcet, V.; Grellier, M.; Sabo-Etienne, S.; Darcel, C.; Sortais, J.-B. Direct synthesis of dicarbonyl PCP-iron hydride complexes and catalytic dehydrogenative borylation of styrene. *Dalton Trans.* **2016**, *45*, 11101–11108.

(14) Mazzacano, T. J.; Mankad, N. P. Dehydrogenative Borylation and Silylation of Styrenes Catalyzed by Copper-Carbenes. *ACS Catal.* **2017**, *7*, 146–149.

(15) (a) Takaya, J.; Kirai, N.; Iwasawa, N. Efficient Synthesis of Diborylalkenes from Alkenes and Diboron by a New PSiP-Pincer Palladium-Catalyzed Dehydrogenative Borylation. *J. Am. Chem. Soc.* **2011**, *133*, 12980–12983. (b) Kirai, N.; Iguchi, S.; Ito, T.; Takaya, J.; Iwasawa, N. PSiP-Pincer Type Palladium-Catalyzed Dehydrogenative Borylation of Alkenes and 1,3-Dienes. *Bull. Chem. Soc. Jpn.* **2013**, *86*, 784–799.

(16) Wen, H.; Zhang, L.; Zhu, S.; Liu, G.; Huang, Z. Stereoselective Synthesis of Trisubstituted Alkenes via Cobalt-Catalyzed Double Dehydrogenative Borylations of 1-Alkenes. *ACS Catal.* **2017**, *7*, 6419–6425.

(17) Supported copper hydroxide catalysts were prepared according to our previous reports: (a) Oishi, T.; Katayama, T.; Yamaguchi, K.; Mizuno, N.; Heterogeneously Catalyzed Efficient Alkyne–Alkyne Homocoupling by Supported Copper Hydroxide on Titanium Oxide. *Chem. Eur. J.* **2009**, *15*, 7539–7542. (b) Yamaguchi, K.; Oishi, T.; Katayama, T.; Mizuno, N. A Supported Copper Hydroxide on Titanium Oxide as an Efficient Reusable Heterogeneous Catalyst for 1,3-Dipolar Cycloaddition of Organic Azides to Terminal Alkynes. *Chem. Eur. J.* **2009**, *15*, 10464–10472. (c) Oishi, T.; Yamaguchi, K.; Mizuno, N. Conceptual Design of Heterogeneous Oxidation Catalyst: Copper Hydroxide on Manganese Oxide-Based Octahedral Molecular Sieve for Aerobic Oxidative Alkyne Homocoupling. *ACS Catal.* **2011**, *1*, 1351–1354.

(18) The XRD patterns of freshly prepared $Cu(OH)_x/CeO_2$ and $Cu(OH)_x/Al_2O_3$ were the same as those of the parent CeO_2 and Al_2O_3 support, respectively; no signals due to copper metal (clusters) and copper oxides were observed (Figure S1).

(19) Kim, I.; Itagaki, S.; Jin, X.; Yamaguchi, K.; Mizuno, N. Heterogeneously catalyzed self-condensation of primary amines to

secondary amines by supported copper catalysts. *Catal. Sci. Technol.* **2013**, *3*, 2397–2403.

(20) Recently, reduction of alkenes, alkynes, and heterocycles using diboron compounds and water as reducing agents has been reported. For the examples, see: (a) Cummings, S. P.; Le, T.-N.; Fernandez, G. E.; Quiambao, L. G. B.; Stokes, J. Tetrahydroxydiboron-Mediated Palladium-Catalyzed Transfer Hydrogenation and Deuteriation of Alkenes and Alkynes Using Water as the Stoichiometric H or D Atom Donor. *J. Am. Chem. Soc.* **2016**, *138*, 6107–6110. (b) Xuan, Q.; Song, Q. Diboron-Assisted Palladium-Catalyzed Transfer Hydrogenation of *N*-Heteroaromatics with Water as Hydrogen Donor and Solvent. *Org. Lett.* **2016**, *18*, 4250–4253. (c) Ojha, D. P.; Gadde, K.; Prabhu, K. R. Generation of Hydrogen from Water: A Pd-Catalyzed Reduction of Water Using Diboron Reagent at Ambient Conditions. *Org. Lett.* **2016**, *18*, 5062–5065. (d) Rao, S.; Prabhu, K. R. Stereodivergent Alkyne Reduction by using Water as the Hydrogen Source. *Chem. Eur. J.* **2018**, *24*, 13954–13962.

(21) We confirmed by XANES analysis that all Cu^{II} species in $Cu(OH)_x/Al_2O_3$ were reduced to mainly Cu^{I} species after the catalyst was utilized for the reaction of **1a** or treated with B_2pin_2 (Figure S2). The reaction profiles revealed that $Cu(OH)_x/Al_2O_3$ showed the higher initial rate than $Cu(OH)_x/CeO_2$, and $Cu(OH)_x/Al_2O_3$ gave **2a** in 80% yield after 6 h (Figure S8). However, when prolonging the reaction time for the $Cu(OH)_x/Al_2O_3$-catalyzed reaction, the yield of **2a** and the mass balance gradually decreased. In contrast, the yield of **2a** gradually increased and the mass balance was preserved when prolonging the reaction time for the $Cu(OH)_x/CeO_2$-catalyzed reaction. When **2a** was treated with Al_2O_3 in *p*-xylene at 120 °C, the mass balance of **2a** significantly decreased (Figure S9). In the case of CeO_2, the mass balance was almost preserved (Figure S9). Therefore, $Cu(OH)_x/CeO_2$ gave the better yield of **2a** after 20 h than $Cu(OH)_x/Al_2O_3$ in the monoborylation.

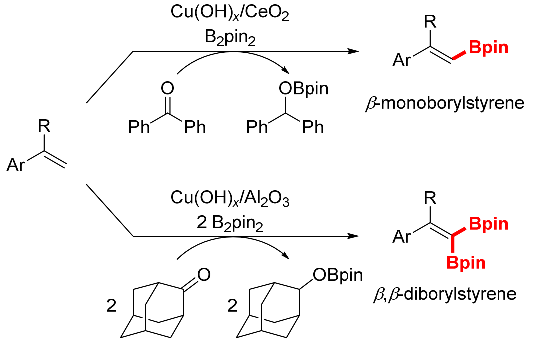
(22) After the borylation, the reaction mixture was treated with water, and benzhydrol (hydrolysis product of the hydroborylated benzophenone) was isolated by silica gel column chromatography. Then, the deuterium content at the α-position was determined by ^1H NMR analysis (see the Supporting Information).

(23) Several control experiments using **2a** as the starting material revealed that $Cu(OH)_x/Al_2O_3$ promoted the second step of the dehydrogenative diborylation (from **2a** to **3a**) with high β-selectivity. The difference in the regioselectivity was caused by the choice of supports, not ketones (Figure S5). We supposed that **3a** and **3a’** were produced by the insertion of **2a** into the Cu–B bond followed by the β-hydride elimination and that the regioselectivity depended on the electronic state of Cu species and/or the steric hinderance around Cu species; therefore, the choice of the supports possibly gave a difference in the regioselectivity.

(24) We speculated that **1a** was most easily adsorbed onto the catalyst, followed in order by benzophenone, **2a**, 2-adamantanone; therefore, we consider that benzophenone decreased the reaction rate of the borylation of **2a** to **3a**.

(25) Sheldon, R. A.; Wallau, M.; Arends, I. W. C. E.; Schuchardt, U. Heterogeneous Catalysts for Liquid-Phase Oxidations: Philosophers' Stones or Trojan Horses? *Acc. Chem. Res.* **1998**, *31*, 485–493.

(26) The reaction profiles and the final yields of the repeated reuse experiments for the $Cu(OH)_x/CeO_2$-catalyzed monoborylation of **1a** are summarized in Figure S10. In addition, the details of the reuse experiments for the $Cu(OH)_x/Al_2O_3$-catalyzed diborylation of **1a** are also summarized in Figure S11.


Cu(OH)x/CeO2
B2pin2
Ar
R
Bpin
β-monoborylstyrene
O
Ph
Ph
OBpin
Ph
Ph
Cu(OH)x/Al2O3
2 B2pin2
Bpin
Bpin
β,β-diborylstyrene
2
O
2
OBpin