Copper-catalyzed substitution of allylic carbonates with diboron: A new approach to allylboronate synthesis*

Hajime Ito‡, Shinichiro Ito, Yusuke Sasaki, Kou Matsuura, and Masaya Sawamura‡

Department of Chemistry, Faculty of Science, Hokkaido University, Sapporo 060-0810, Japan

Abstract: Copper-catalyzed γ-selective substitution of allylic carbonates with diboron provides a new method for the efficient synthesis of allylboronates. Optically active α-chiral allylboronates were synthesized through the reaction of chiral allylic carbonates with bis(pinacolato)diboron in the presence of achiral Cu(I)-catalyst with highly efficient chirality transfer. Additionally, in the presence of a chiral Cu(I) catalyst, optically active α-chiral allylboronates were obtained with >90 % ee through the reaction of prochiral substrates with the diboron.

Keywords: copper; catalysis; allylboronates; asymmetric; chiral ligands.

INTRODUCTON

Stereoselective addition of allylboronates to carbonyl compounds is a powerful and widely used method for the synthesis of homoallylic alcohols [1,2]. Although many sophisticated synthetic procedures for allylboronates have been developed, there seems to still be room for improvement. Most of the reported procedures for the synthesis of allylboronates depend on the reaction of carbon nucleophiles utilizing electrophilic features of boryl reagents. Accordingly, these methodologies are not generally applicable to the synthesis of allylboronates that have a functional group sensitive to the nucleophiles. Furthermore, although optically active allylboronates that have a chiral center at the α-position of the boron atom are extremely useful reagents due to their high efficiency in chirality transfer upon reaction with carbonyl compounds, synthesis of such compounds usually requires a stoichiometric chiral auxiliary at the boronic ester [3,4].

We developed a novel and versatile method for the synthesis of allylboronates through the γ-selective substitution of allylic carbonates with diboron in the presence of Cu(I)–phosphine catalysts [5,6]. The Cu(I)-catalyzed reaction includes formal nucleophilic reaction of B–Cu intermediates to allylic carbonates. The advantages of this method over the conventional methods are high availability of the starting allylic carbonates and high tolerance to functional groups. Optically active α-chiral allylboronates were synthesized from optically active allylic carbonates that have a leaving group at a chiral carbon with high fidelity of α- to γ-chirality transfer. Additionally, a catalytic enantioselective reaction with a chiral Cu(I) catalyst was also developed. This method would facilitate synthesis of complex

allylboronates containing functional groups and a chiral center at the α-carbon of the boryl group. We wish to describe herein our recent progress in developing the Cu(I)-catalyzed reactions of allylic carbonates with a diboron.

COPPER-CATALYZED REACTION OF ALLYLIC CARBONATES WITH DIBORON

Screening of Cu(I) complexes [5]

During our studies on copper-catalyzed hydrosilane alcoholysis, we found a remarkable rate-acceleration of a chelating phosphine (xantphos) featuring a large natural bite-angle [7]. It was able to be presumed that the ligand with large bite-angle would activate a Cu(I)–OR intermediate for σ-bond metathesis with a H–Si bond of the hydrosilane to form a monomeric, highly active copper hydride, Cu(I)–H. On an analogy between H–Si and B–B, we envisioned that xantphos-ligated Cu–OR would react with a diboron reagent to form a Cu–B species useful as a "formal boryl nucleophile" [8]. Formal S_N2' attack of the Cu–B species on an allylic carbonate would allow γ-selective formation of an allylboron compound along with a copper carbonate that would undergo decarboxylation to regenerate the Cu–OR.

The reaction of allylic carbonate **1a** and bis(pinacolato)diboron **2** in the presence of Cu(O-*t*-Bu)/xantphos catalyst (5 mol %) proceeded at room temperature to give the corresponding allylboronate in a quantitative yield with high regio- (**3a**:**3b** = 99:1) and *E/Z*- (*E*-**3a**:*Z*-**3a** = 97:3) selectivities (Table 1, entry 1). On the other hand, the reaction with dppe (entry 2) afforded the product in a low yield

Table 1 Cu(I)-catalyzed reaction of allylic carbonate **1a** with diboron **2**.[a]
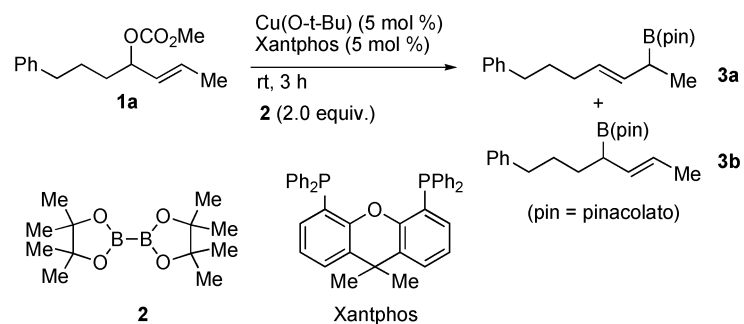
Entry	Catalyst	Solvent	Yield[b] (%)	Selectivity[c] 3a/3b	*E/Z* (3a)[d]
1	Cu(O-*t*-Bu)–xantphos	THF	100	99:1	97:3
2	Cu(O-*t*-Bu)–dppe	THF	11	>99:<1	62:38
3	Cu(O-*t*-Bu)–dppp	THF	44	>99:<1	97:3
4	Cu(O-*t*-Bu)–dppf	THF	37	>99:<1	96:4
5	Cu(O-*t*-Bu)–PPh₃	THF	2	nd	nd
6	CuOTf–PBu₃	DMF	0	nd	nd
7[e,f]	CuCl–KOAc–LiCl	DMF	0	nd	nd
8[f]	Pd(dba)₂	DMSO	96	57:43	98:2

[a]Conditions: catalyst (5 mol %), **1a** (0.25 mmol), **2** (0.5 mmol), and solvent (0.25 mL).
[b]Yield of all allylboronates was determined by GC.
[c]Ratio of regio- and *E/Z*-isomers was determined by GC.
[d]The *Z*-isomer of **3b** was not detected.
[e]110 mol % of catalyst was used.
[f]0.28 mmol of **2** and 1.5 mL of the solvent were used.

(11 %) with a poor *E/Z*-selectivity (62:38). Although the dppp (entry 3) and dppf (entry 4) complexes exhibited high regio- and *E/Z*-selectivities, their activities were still significantly lower than that of the xantphos complex. The PPh$_3$ complex (entry 5) gave poor results. Furthermore, CuOTf–PBu$_3$ (entry 6) and stoichiometric CuCl–KOAc–LiCl system (entry 7), which have been reported to be a catalyst for the borylation of α,β-unsaturated carbonyl compounds and allyl chloride [8a,b], were ineffective for the reaction of **1a**. Palladium complex Pd(dba)$_2$ (entry 8), which also has been reported to be a catalyst for the reaction of allylic esters with diboron, catalyzed the conversion, but afforded a mixture of **3a** and **3b** in a ratio of 57:43. This low regioselectivity is attributable to the loss of regiochemical information of substrate **1a** upon formation of a (π-allyl)palladium(II) complex intermediate [9].

Synthesis of various allylboronates through Cu(I)-catalyzed reaction

By using the Cu(I)–xantphos catalyst, a variety of allylboronates, including functionalized allyl-boronates, were synthesized (Scheme 1). Allylboronate **3b** was almost exclusively obtained from allylic carbonate **1b** through the Cu(I)-catalyzed reaction. High γ-selectivity (γ:α = >97:3) was also observed even when the allylic systems are located at the terminal of the carbon chain. Accordingly, carbonates **1c** and **1d** were converted into the branched (**3c**) and linear (**3d**) allylboronates, respectively. Cyclic allylboronate **3e** was also obtained in a good yield. High functional group compatibility of this reaction allowed one-step preparation of functionalized allylboronates from the corresponding allylic carbon-ates. Allylboronates containing acetal (**3f**), ester (**3g**), and isolated alkene (**3h**) were also obtained in high yields.
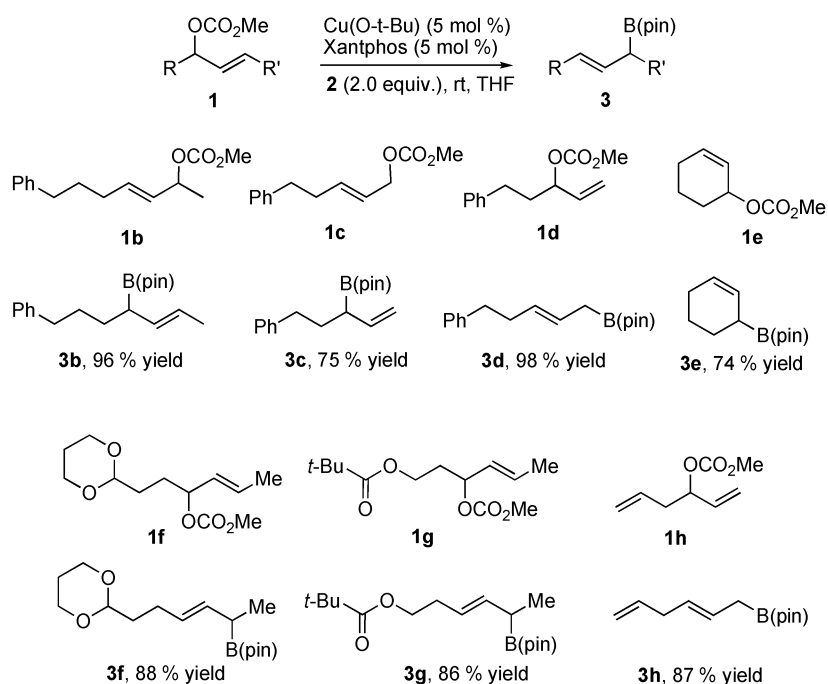

Scheme 1 Cu(I)–xantphos-catalyzed reaction of allylic carbonates **1** with diboron **2**.

Synthesis of optically active allylboronates from chiral allylic carbonates

The present Cu(I)-catalyzed reaction serves as a versatile tool for the synthesis of optically active α-chiral allylboronates, which have a stereogenic carbon with a boryl substituent. The reaction of (*S*)-(*E*)-

1i (98 % ee) with **2** in the presence of Cu(I)–xantphos catalyst (10 mol %) at 0 °C underwent an α-to-γ chirality transfer accompanied by only a slight loss of enantiomeric purity to afford (*S*)-(*E*)-**3i** (96 % ee) along with a small amount of the α-substituted *E*-isomer and γ-*Z*-isomer (Scheme 2). On the other hand, the reaction of (*S*)-(*Z*)-**1i** (97 % ee), the *Z*-isomer with the same configuration at the chiral center as (*S*)-(*E*)-**1i**, gave (*R*)-(*E*)-**3i** (97 % ee), the antipode of the product derived from (*S*)-(*E*)-**1i**, with complete chirality transfer and γ-selectivity. These results show that the two enantiomeric α-chiral allylboronates can be prepared either by changing the *E/Z* stereochemistry of the double bond or by changing the configuration of the allylic carbonate.
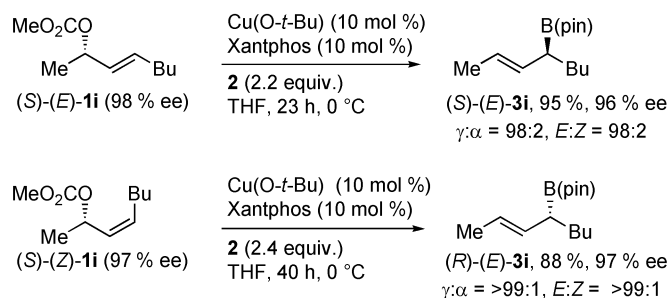
Scheme 2 Synthesis of optically active allylboronates (*S*)-(*E*)-**3i** and (*R*)-(*E*)-**3i** from chiral allylic carbonates (*S*)-(*E*)-**1i** and (*S*)-(*Z*)-**1i**.

The observed stereochemical outcome can be explained by the *anti*-attack of the B–Cu intermediate to an allylic carbonate in a conformation that avoids an allylic 1,3-strain (Scheme 3). The coordination of a carbon–carbon double bond of (*S*)-(*E*)-**1i** to a copper center of the B–Cu intermediate gives a π-complex **A** where the O–C(α) bond and the forming Cu–C(β) bond are in an *anti*-periplanar arrangement that avoids an allylic 1,3-strain between the α-methyl group and the γ-hydrogen atom. Addition of the Cu–B bond across the carbon–carbon double bond gives alkylcopper intermediate **B**, making chiral centers at the β- and γ-positions. Then, subsequent β-elimination of the Cu(I) moiety and the carbonate group from **B** results in the formation of (*S*)-(*E*)-**3i**. In the case of (*S*)-(*Z*)-**1i**, similar π-complex **A'** is allowed to take an *anti*-periplanar arrangement of the carbonate and the copper center. A chiral center at γ-position with an opposite configuration to that of **B** is created upon the B–C bond-forming reaction. Then, (*R*)-(*E*)-**3i**, which is the enantiomer of the product from (*S*)-(*E*)-**1i**, is produced through β-elimination. The substantial allylic 1,3-strain between the methyl group and the butyl group is responsible for the high *E/Z*-selectivity observed in the reaction of (*S*)-(*Z*)-**1i**.
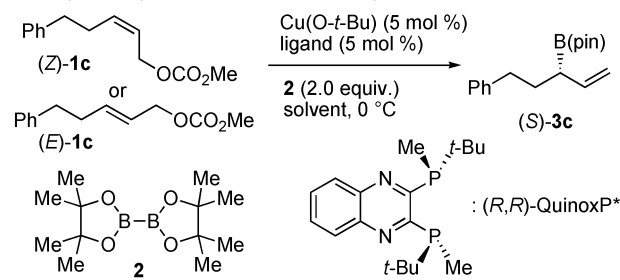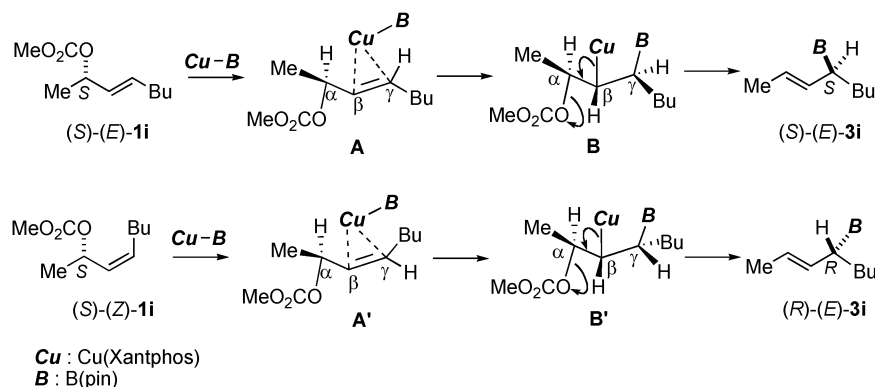

Scheme 3 Reaction mechanism for Cu(I)-catalyzed reaction of chiral allylic carbonates.

ENANTIOSELECTIVE REACTION OF PROCHIRAL ALLYLIC CARBONATE AND DIBORON [6]

Next, we examined an enantioselective version of the Cu(I)-catalyzed allylic substitution with the diboron. A series of Cu(I)–phosphine catalysts were prepared in situ by mixing Cu(O-*t*-Bu) with chiral ligands. Catalytic activity and enantioselectivity of the catalysts were determined using the yields and ee values of allylboronate **3c** (Table 2). Good yields of **3c** with high enantiomeric excesses (94–96 % ee) were obtained for the reactions of (*Z*)-**1c** with the (*R*,*R*)-QuinoxP* chiral ligand, which was recently developed by Imamoto and coworkers [10], in various solvents such as THP, THF, toluene, and DMI (entries 1–4). The reaction using (*R*,*R*)-Me-DuPhos as a ligand showed good activity, but lower ee (80 % ee, entry 5). We envisioned that (*R*,*R*)-*i*-Pr-DuPhos could show a better result since it should have stronger steric effects than that of Me-DuPhos. However, (*R*,*R*)-*i*-Pr-DuPhos did not improve the enantioselectivity (entry 6).

Table 2 Cu(I)-catalyzed asymmetric reaction of allylic carbonate **1c** with diboron **2**.[a]

Entry	Carbonate	Ligand	Solvent	Time (h)	Yield[b] (%)	ee[c] (%)
1	(*Z*)-**1c**	(*R*,*R*)-QuinoxP*	THP	20	77[d]	94
2	(*Z*)-**1c**	(*R*,*R*)-QuinoxP*	THF	20	85	95
3	(*Z*)-**1c**	(*R*,*R*)-QuinoxP*	Toluene	20	78	96
4[e]	(*Z*)-**1c**	(*R*,*R*)-QuinoxP*	DMI	20	65	94
5	(*Z*)-**1c**	(*R*,*R*)-Me-DuPhos	THP	3	97	80
6	(*Z*)-**1c**	(*R*,*R*)-*i*-Pr-DuPhos	Toluene	20	72	79 (*R*)
7	(*Z*)-**1c**	(*R*,*R*)-DIOP	THP	20	59	37
8	(*Z*)-**1c**	(*R*)-SEGPHOS	THP	21	19	20
9	(*Z*)-**1c**	(*R*)-BINAP	THP	20	16	31
10	(*E*)-**1c**	(*R*,*R*)-QuinoxP*	THP	20	94	44 (*R*)

[a]Conditions: Cu(O-*t*-Bu) (0.025 mmol), ligand (0.025 mmol), **1c** (0.5 mmol), **2** (1.0 mmol) at 0 °C in solvent (0.5 mL).
[b]NMR yield.
[c]The ee value of **3c** was determined by chiral GC analysis of the trifluoroacetate of the allylic alcohol derived from H_2O_2/NaOH oxidation of **3c**.
[d]Isolated yield.
[e]The reaction was carried out at rt.

Moderate yield with a low ee value was obtained for the reaction with (*R*)-DIOP (entry 7), whereas poor yields and low selectivities were obtained for axially chiral ligands such as (*R*)-SEGPHOS (entry 8) and (*R*)-BINAP (entry 9). The enantioselectivity and absolute configuration of the product are greatly influenced by the *E*/*Z* configuration of the substrate. The reaction of (*E*)-**1c** in the presence of Cu(I)–QuinoxP* afforded (*R*)-**3c** with only 44 % ee (entry 10).

As shown in Scheme 4, various (*Z*)-allylic carbonates (**1j–p**) were subjected to the reaction with diboron in the presence of the Cu(I)–QuinoxP* catalyst. Optically active allylboronates bearing alkyl substituents [R = CH$_3$ (**3j**), CH$_3$(CH$_2$)$_4$ (**3k**)] were obtained in good yields with high enantioselectivities in the presence of 5 mol % of the catalyst. A higher catalyst loading (10 mol %) is required for the reaction of an allylic carbonate with a β-branched alkyl substituent (*i*-Bu, **1l**) to reach a reasonable conversion. No reaction proceeded with the allylic carbonate (**1m**) substituted with a bulkier isopropyl group even in the presence of 10 mol % of the catalyst. Importantly, our asymmetric reaction was applicable to a wide range of functionalities—allylboronates that have silyloxy (**3n**), benzoate (**3o**), or prenyloxy groups (**3p**)—were obtained with high enantioselectivities [11].
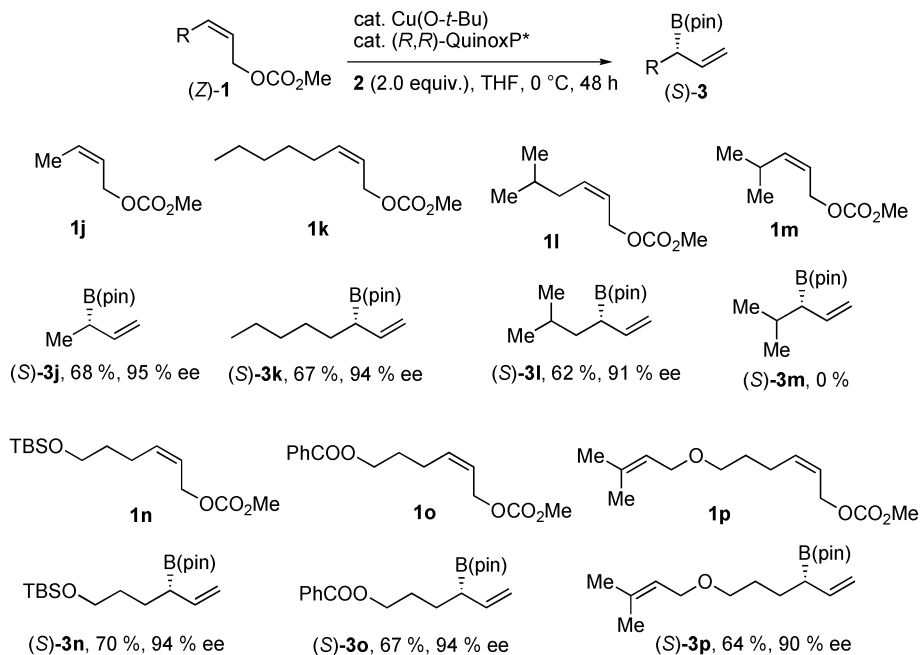
Scheme 4 Synthesis of optically active allylboronates **3** through enantioselective reaction of prochiral allylic carbonates (*Z*)-**1**.

SUMMARY

We developed a versatile method for the synthesis of allylboronates involving optically active and functionalized ones through the reaction of allylic carbonates with diboron in the presence of a Cu(I) catalyst. The features of this method are their high γ-selectivity, tolerance of functional groups, and high fidelity of α- to γ-chirality transfer for the substrates with a chiral carbon at the α-position of the leaving group. Catalytic enantioselective reaction with Cu(O-*t*-Bu)/QuinoxP* complex was also developed as another method for the synthesis of optically active α-chiral allylboronates.

ACKNOWLEDGMENTS

REFERENCES AND NOTES

1. For reviews, see: (a) R. W. Hoffmann. In *Stereocontrolled Organic Synthesis*, B. M. Trost (Ed.), pp. 259–274, Blackwell Scientific, Oxford (1994); (b) D. S. Matteson. *Stereodirected Synthesis with Organoboranes*, Springer, Berlin (1995); (c) D. G. Hall (Ed.). *Boronic Acids*, Wiley-VCH, Weinheim (2000).

2. For Lewis acid-mediated reactions of allylboronates with aldehydes, see: (a) T. Ishiyama, T. Ahiko, N. Miyaura. *J. Am. Chem. Soc.* **124**, 12414 (2002); (b) J. W. J. Kennedy, D. G. Hall. *J. Am. Chem. Soc.* **124**, 11586 (2002).

3. For the selected synthesis of α-chiral allylboronates with chiral auxiliary, see: (a) R. W. Hoffmann. *Pure Appl. Chem.* **60**, 123 (1988); (b) R. W. Hoffmann, G. Niel, A. Schlapbach. *Pure Appl. Chem.* **62**, 1993 (1990); (c) D. S. Matteson. *Tetrahedron* **54**, 10555 (1998); (d) J. Pietruszka, N. Schone. *Angew. Chem., Int. Ed.* **42**, 5638 (2003); (e) G. Fang, V. Aggarwal. *Angew. Chem., Int. Ed.* **46**, 359 (2007).

4. For the synthesis of α-chiral allylboronates through asymmetric catalysis, see: (a) X. Gao, D. G. Hall. *J. Am. Chem. Soc.* **125**, 9308 (2003); (b) N. Pelz, A. Woodward, H. Burks, J. Sieber, J. P. Morken. *J. Am. Chem. Soc.* **126**, 16328 (2004); (c) L. Carosi, D. G. Hall. *Angew. Chem., Int. Ed.* **46**, 5913 (2007); (d) F. Peng, D. G. Hall. *Tetrahedron Lett.* **48**, 3305 (2007).

5. For the synthesis of allylboronates with Cu(I) catalysis, see: H. Ito, C. Kawakami, M. Sawamura. *J. Am. Chem. Soc.* **127**, 16034 (2005).

6. H. Ito, S. Ito, Y. Sasaki, K. Matsuura, M. Sawamura *J. Am. Chem. Soc.* **129**, 14856 (2007).

7. H. Ito, A. Watanabe, M. Sawamura. *Org. Lett.* **7**, 1869 (2005).

8. For studies on reactions of nucleophilic boryl compounds, see: (a) H. Ito, H. Yamanaka, J. Tateiwa, A. Hosomi. *Tetrahedron Lett.* **41**, 6821 (2000); (b) K. Takahashi, T. Ishiyama, N. Miyaura. *Chem. Lett.* 982 (2000); (c) P. V. Ramachandran, D. Pratihar, D. Biswas, A. Srivastava, M. V. R. Reddy. *Org. Lett.* **6**, 481 (2004); (d) D. S. Laitar, E. Y. Tsui, J. P. Sadighi. *J. Am. Chem. Soc.* **128**, 11036 (2006); (e) J. E. Lee, J. Yun. *Angew. Chem., Int. Ed.* **47**, 145 (2008).

9. For Pd-catalyzed reactions of derivatives of allylic alcohols and diborons, see: (a) T. Ishiyama, T. Ahiko, N. Miyaura. *Tetrahedron Lett.* **37**, 6889 (1996); (b) S. Sebelius, V. J. Olsson, K. J. Szabó. *J. Am. Chem. Soc.* **127**, 10478 (2005); (c) V. J. Olsson, S. Sebelius, N. Selander, K. J. Szabó. *J. Am. Chem. Soc.* **128**, 4588 (2006).

10. T. Imamoto, K. Sugita, K. Yoshida. *J. Am. Chem. Soc.* **127**, 11934 (2005).

11. A catalyst loading of 5 mol % was used in the reaction of **1j**, **1k**, **1o**, while the reactions of **1l**, **1m**, **1n**, **1p** were carried out in the presence of 10 mol % of the catalyst.