

Copper(I)-Catalyzed Substitution of Propargylic Carbonates with Diboron:  
Selective Synthesis of Multisubstituted Allenylboronates

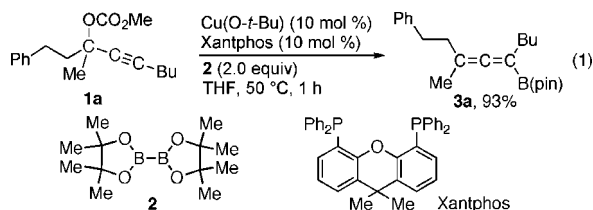
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Allenylboron compounds are potentially general synthetic reagents that could be used for various transformations; however, their availability is limited as compared to the other corresponding allenylmetal reagents such as allenyltins and allenylsilanes.<sup>1–4</sup> Multisubstituted allenylboronates with different alkyl groups on the  $\alpha$ - and  $\gamma$ -carbons as well as those bearing functional groups or axial chirality are still difficult to prepare. We report here a versatile synthetic method for the preparation of the allenylboronates, Cu(I)-catalyzed reaction of propargylic carbonates with a diboron derivative. A Cu(O-*t*-Bu)–Xantphos catalyst system<sup>5,6</sup> appeared to be effective for the preparation of various allenylboronates with different substitution patterns, including  $\alpha,\gamma,\gamma$ -trisubstituted,<sup>7</sup>  $\alpha,\gamma$ -disubstituted, and  $\alpha$ -monosubstituted derivatives. Moreover, the allenylboron synthesis tolerated functional groups such as ester, carbamate, and silyl ether. The reaction with an optically active propargylic alcohol derivative proceeded with complete chirality transfer, giving an axially chiral allenylboronate with high enantiomeric purity.<sup>8</sup> The Lewis acid promoted aldehyde addition forming homopropargylic alcohols showed the usefulness of the new allenylboronates.<sup>9</sup>

The reaction of propargylic carbonate **1a** with bis(pinacolato)diboron (**2**, 2.0 equiv) in the presence of Cu(O-*t*-Bu)/Xantphos catalyst (10 mol %) at 50 °C in THF completed in 1 h to give trisubstituted allenylboronate **3a**, having three different alkyl groups on the allene moiety, in 93% GC yield (eq 1). This is a “formal S<sub>N</sub>2’ substitution” of a propargylic system with a boryl nucleophile. No “S<sub>N</sub>2-type product (propargylic boronate)” was detected in the reaction mixture. Reactions with other phosphine ligands resulted in lower yields under otherwise identical conditions (PPh<sub>3</sub>: 58%, dppe: 25%, dppp: 43%, dppf: 66%, no ligand: trace).<sup>10</sup>



This Cu(I)-catalysis showed a broad substrate scope toward synthesis of various allenylboron compounds (Table 1). Trialkyl-substituted allenylboronates **3b,c** were also formed in high yields (97% and 90%, entries 1 and 2, respectively). The carbonates involving six- and five-membered rings (**1d,e**) were converted into allenylboronates containing allenylidenecyclohexane (**3d**) and allenylidenecyclopentane (**3e**) structures, respectively (entries 3 and 4). Allenylboronate **3f** with a phenyl group at the  $\alpha$ -position of the boryl group was, however, obtained in only a low yield (22% yield, entry 5).<sup>11</sup>

Although  $\alpha,\gamma$ -disubstituted (**3g,h**) and  $\alpha$ -monosubstituted allenylboronates (**3j**) were also obtained in good and moderate yields (Table 1, entries 6, 7, and 9),<sup>12</sup>  $\gamma,\gamma$ -disubstituted compound **3i** could not be prepared (entry 8). The latter is probably due to the high reactivity of the C–H bond at the alkyne terminus of **1i**. This

allenylboron synthesis tolerated functional groups such as ester (**3k**), carbamate (**3l**), and silyl ether (**3m**) (Table 1, entries 10–12). Accordingly, this method should be useful for the synthesis of complex molecules.

Combined with Lewis acid promoted addition of the allenylboronates to aldehydes, the present Cu(I)-catalysis offers a general route to homopropargylic alcohols (Scheme 1).<sup>13</sup> Conversion of propargylic carbonate **1n** ( $R^1 = c\text{-Hex}$ ,  $R^2 = \text{H}$ ,  $R^3 = \text{Bu}$ ) to the corresponding  $\alpha,\gamma$ -disubstituted allenylboronates<sup>14</sup> and subsequent

Table 1. Reaction of Propargylic Carbonates **1** and Diboron **2**<sup>a</sup>

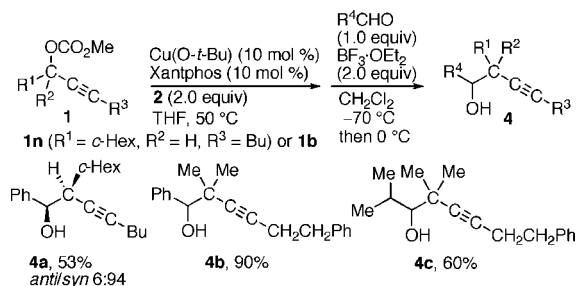
entry	carbonate	product	time (h)	yield <sup>b</sup> (%)
1			1.5	97 (87)
2			3	90 (82)
3			2.5	98 (85)
4			2.5	82 (53)
5 <sup>c</sup>			44	22
6			3	80 (62)
7			5	75
8			2	trace
9			5	57 (46)
10			5	(82)
11			2.5	70 (55)
12			1.5	88 (53)

<sup>a</sup> Conditions: **1** (0.5 mmol); **2**, (1.0 mmol); Cu(O-*t*-Bu) (10 mol %), 0.05 mmol; Xantphos (10 mol %, 0.05 mmol); THF (0.5 mL). <sup>b</sup> <sup>1</sup>H NMR yield of the crude mixture. Isolated yield is shown in parentheses.

<sup>c</sup> The reaction was carried out at 70 °C.

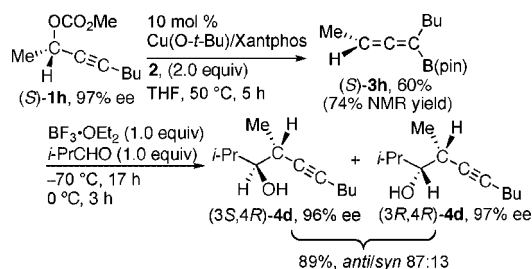
addition reaction with benzaldehyde in the presence of  $\text{BF}_3 \cdot \text{OEt}_2$  furnished *syn*-homopropargylic alcohol **4a** with a high diastereoselectivity (*anti/syn* 6:94, 53%).<sup>9,15–17</sup> Reaction of the  $\alpha,\gamma,\gamma$ -trisubstituted allenylboronate, which was prepared from carbonate **1b** ( $\text{R}^1 = \text{R}^2 = \text{Me}$ ,  $\text{R}^3 = \text{PhCH}_2\text{CH}_2$ ), with benzaldehyde and isobutyraldehyde gave the corresponding homopropargylic alcohols (**4b**: 90%, **4c**: 60%) involving a sterically congested alcohol moiety with an adjacent quaternary carbon center.

**Scheme 1.** Synthesis of Homopropargylic Alcohols **4** via Lewis Acid Catalyzed Reaction of Allenylboronates **3** and Aldehydes



Optically active carbonate (*S*)-**1h** (97% ee) was converted to chiral allenylboronate [(*S*)-**3h**]. A subsequent  $\text{BF}_3$ -promoted addition reaction of (*S*)-**3h** with isobutyraldehyde afforded homopropargylic alcohols *anti*-(3*S*,4*R*)-**4d** and *syn*-(3*R*,4*R*)-**4d** in 89% yield with good diastereoselectivity (*anti/syn* 87:13)<sup>15–17</sup> with retention of the enantiomeric purity (>96% ee) (Scheme 2). The stereochemical outcome suggests that the allenylboronate [(*S*)-**3h**]<sup>18</sup> was produced with complete 1,3-chirality transfer with *anti*-stereochemistry and that the propargylation of the aldehyde took place through a cyclic transition state with complete *Re*-face selectivity with respect to the allenylboronate reagent.<sup>17</sup>

**Scheme 2.** Synthesis and Lewis Acid Promoted Addition of Chiral Allenylboronate (*S*)-**3h**



In summary, the  $\text{Cu}(\text{O}-t\text{-Bu})/\text{Xantphos}$  system was identified to be a catalyst for the regio- and stereoselective substitution of propargylic carbonates with bis(pinacolato)diboron. Having tolerance toward different substitution patterns and functional groups, the  $\text{Cu}$ -catalyzed reaction would serve as a useful method for the synthesis of various allenylboronates. An axially chiral allenylboronate with unprecedented high enantiomeric purity was prepared from an optically active propargylic carbonate. Synthetic utilities of the allenylboronates have been demonstrated in their stereoselective addition to aldehydes.

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**Supporting Information Available:** Experimental procedures and compound characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (10) The reaction of substrates that have acetoxy or methoxy leaving groups instead of the carbonate resulted in lower yields even after longer reaction times (acetoxy: 88%, 24 h; methoxy: 53%, 48 h).
- (11) Directing effect of the phenyl group may have caused formation of a  $\beta$ -borylation intermediate. See ref 6f.
- (12) Low yields were due to the low reactivity of the di- and monosubstituted substrates. Unreacted starting materials were recovered.
- (13) For the synthesis of homopropargylic alcohols with allenyltin, allenylzinc, and allenylsilane reagents, see ref 1.
- (14) Crude allenylboronates that were obtained by short-pass silica gel chromatography were used.
- (15) In the absence of the external Lewis acid ( $\text{BF}_3$ ), the reaction of **1n** with benzaldehyde resulted in a lower yield of the product (**4a**) with a *syn*-selectivity (0 °C, 44 h, 44%, *anti/syn* 16:84). The reaction of (*S*)-**1h** with isobutyraldehyde without the Lewis acid catalyst afforded the product ((3*S*,4*R*)-**4d**) in a moderate yield (0 °C, 44 h, 61%) with a high enantiomeric purity (97% ee for *anti* product) and a slightly lower *anti*-selectivity (*anti/syn* 86:14) than that of the Lewis acid promoted reaction.
- (16) In the case of **4a** and **4d**, methanol (5.0 equiv) was added in the aldehyde addition. This slightly improved the *syn/anti* selectivities.
- (17) The carbonyl additions of allenylmetal reagents bearing a Lewis acidic metal group tend to favor production of *anti*-propargylic alcohols through cyclic transition states. However, anomalous *syn*-preference in the addition of allenyltitanium and allenylzinc reagents to benzaldehyde have been reported. See: (a) Furuta, K.; Ishiguro, M.; Haruta, R.; Ikeda, N.; Yamamoto, H. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 2768–2776. (b) Harada, T.; Katsuhira, T.; Osada, A.; Iwazaki, K.; Maejima, K.; Oku, A. *J. Am. Chem. Soc.* **1996**, *118*, 11377–11390.
- (18) Direct measurement of the enantiomeric purity of (*S*)-**3h** was unsuccessful because of its instability.

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