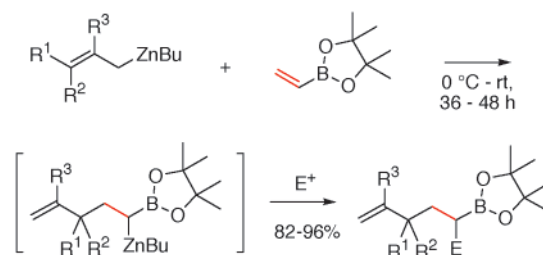


Regioselective Allylzincation of  
AlkenylboronateMasaharu Nakamura, Kenji Hara,<sup>†</sup> Takuji Hatakeyama, and Eiichi Nakamura\*Department of Chemistry, The University of Tokyo, Hongo, Bunkyo-ku,  
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## ABSTRACT



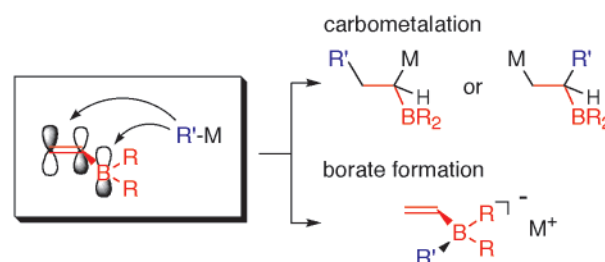
Boryl substitution on an olefin activates the olefinic double bond toward addition of an organozinc reagent. Addition of an allylic zinc reagent to an alkenylboronate thus takes place smoothly to afford a variety of *gem*-zincio/boryl species. Theoretical studies with density functional calculations on the reaction pathway revealed that the reaction proceeds via a zincio-ene reaction rather than a bora-Claisen rearrangement.

Among various examples of activation of an alkene toward organometallic addition across the olefinic double bond, replacement of the alkenyl hydrogen atom with a metal or a metalloid atom has been used as an effective protocol and has provided a unique route to synthesis of a variety of  $sp^3$ -geminal organodimetallics.<sup>1,2</sup> While a Group 14 metal substituent on an olefin has long been known to electrophilically activate the olefin toward organometallic addition,<sup>3</sup> few examples have been reported about the effect of Group

13 element substitution on the carbometalation reaction.<sup>4</sup> Here we report that an alkenylboronate **1** can serve as a versatile substrate for carbometalation reaction, in which an allylic zinc reagent reacts with the olefin to afford synthetically useful geminal Zn/B organometallic species.<sup>5,6</sup>

Scheme 1 depicts two possible reaction pathways in the

**Scheme 1.** Organometallic Addition to Vinylboron Compound



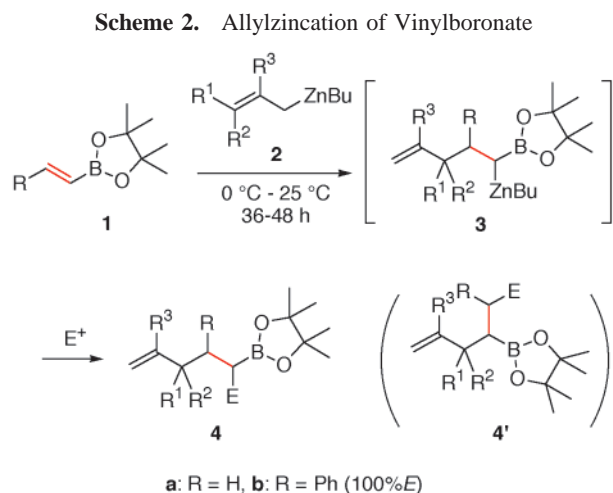
addition of a nucleophilic organometallic reagent to a vinylboronate. Our strategy to employ an allylic zinc reagent

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to achieve selective carbometalation was inspired by our recent theoretical studies, by which the pathways of the addition of allylic zinc reagents to various vinylmetal species were proved for the first time.<sup>7</sup> We expected that the propensity of the zinc atom to assist the carbometalation reaction<sup>8</sup> would direct the allylic zinc reagent to the C=C double bond rather than to the boron atom.

The addition of an allylic zinc reagent **2** to the alkenylboronate (**1a** and **b**) was found to take place smoothly to afford an organoboronate **4** under mild conditions. Upon electrophilic trapping of an intermediary Zn/B organometallic species **3**, a variety of organoboronates were obtained in fair to excellent yield (Scheme 2). The product



**4'**, which is a regioisomer of **4**, did not form at all. The addition of allylmagnesium bromide and allyllithium to **1** did not give the allylation product at all under the same conditions.<sup>9</sup> None of the desired carbometalation product was obtained even in the reaction of **2**, when the pinacol borane moiety was replaced with a dibutoxy boryl group.

Table 1 summarizes the results of the reaction between a variety of allylic zinc reagents and alkenylboronates. The

(4) There is only one report on the carbometalation of alkenylborane, in which the carbolithiation reaction of 1-(dimesityl)boryl-1-silylalkenes was examined: Cooke, M. P., Jr.; Widener, R. K. *J. Am. Chem. Soc.* **1987**, *109*, 931–933. Boryl substitution activates the carbon–carbon triple bond as well as the olefinic double bond toward intramolecular carbolithiation reaction: Cooke, M. P., Jr. *J. Org. Chem.* **1994**, *59*, 2930–2931.

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(9) The reaction with allylmagnesium bromide and allyllithium resulted largely in the loss of the material with some recovery of the vinylboronate (8% and 30%, respectively).

**Table 1.** Addition of Allylic Zinc Reagents to Alkenylboronate **1**

entry	allylic zinc reagent	equiv	product	yield (%)
1		1.0		47
2		1.2		82
3		1.2		87
4		1.2		96
5		1.2		90
6		1.2		69 <sup>b</sup>
7		1.2		90
8		1.2		89
9 <sup>c</sup>		1.2		95
10		1.2		21 (41% ee) <sup>d</sup>

<sup>a</sup> All reactions were performed in THF/hexane at 0–25 °C for 36–48 h using 1.0–1.2 equiv of an allylic zinc reagent. <sup>b</sup> SE regioisomer was obtained in 11% yield. <sup>c</sup> (*E*)-Styrylboronate **1b** was used. <sup>d</sup> The enantiomeric excess was determined by chiral capillary gas chromatography after oxidative conversion to the corresponding alcohol.

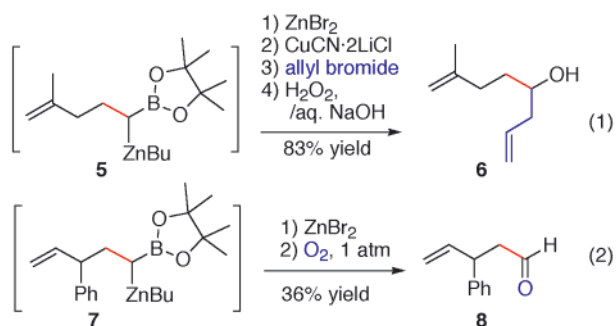
reaction was carried out simply by mixing a slight excess amount of the allylic zinc reagent **2** with vinylboronate **1a** at 0–25 °C for 36–48 h. The addition reaction is much faster with allylbutylzinc than with allylzinc bromide (entries 1 and 2). The allylbutylzinc reagent **2** was prepared by treatment of an allylic zinc bromide with a stoichiometric amount of butyllithium.<sup>10</sup> Butylmethallylzinc also added to vinylboronate **1** to give the allylzincation product in 87% yield (entry 3). Note that the butyl group on the zinc atom is essential to

(10) **Typical Procedure.** To a solution of allylic zinc bromide (0.902 M in THF, 1.33 mL, 1.2 mmol) was added BuLi (1.60 M in hexane, 0.750 mL, 1.2 mmol) at 0 °C, 2-vinyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (0.174 mL, 1.0 mmol) was added at 0 °C, and the mixture was gradually warmed to room temperature. After 36 h, aqueous hydrochloric acid (6 M, 1.0 mL) was added at 0 °C, and the mixture was warmed to 25 °C. The aqueous layer was extracted three times with Et<sub>2</sub>O. The combined organic extracts were washed with a 30% aqueous potassium sodium tartrate and

achieve smooth conversion as we previously reported for the related carbozincation reactions.<sup>2</sup>

The addition of a  $\gamma$ -substituted allylic zinc reagent (entries 4–6), as well as  $\gamma,\gamma$ - and  $\beta,\gamma$ -disubstituted allylic zinc reagents (entries 7 and 8) to the vinylboronate **1** proceeded smoothly under the same conditions. The C–C bond formation took place exclusively at the  $\gamma$ -position of the allylic zinc reagents in 69–96% yield.<sup>11</sup> The reaction of styrylborane **1b** with butylmethylallylzinc gave the regioisomer **4** as an exclusive product.<sup>12</sup> As shown in entry 10, installation of chiral bis-oxazoline ligand in place of the butyl group resulted in chirality induction (44% ee). Further experimentation is clearly necessary to obtain acceptable selectivity and reactivity.

Through suitable functional group manipulations, the geminal Zn/B moiety in intermediates **3** can be transformed to useful functional groups. The alkenylboronate molecule, hence, serves as a useful acceptor synthon of a functionalized two-carbon unit. Thus, intermediary zinc compound **5** could be trapped with a carbon electrophile, and the resulting boronate product afforded the secondary alcohol **6** upon oxidation with basic hydrogen peroxide in 83% yield (eq 1). Oxidation with molecular oxygen after the addition of 1 equiv of zinc bromide to the intermediate **7** allows direct transformation to aldehyde **8** (eq 2).<sup>13</sup>



Density functional theoretical studies on the reaction pathway of the allylzincation at the B3LYP/631A level<sup>14,15</sup>

then with a saturated sodium chloride solution, dried over sodium sulfate, and concentrated. The residual colorless oil was pure by TLC or NMR (0.161 g, 82%,  $R_f = 0.24$ , 5% EtOAc in hexane). Further purification was, if necessary, carried out by silica gel chromatography.

(11) Compare: Kubota, K.; Mori, S.; Nakamura, M.; Nakamura, E. *J. Am. Chem. Soc.* **1998**, *120*, 13334–13341.

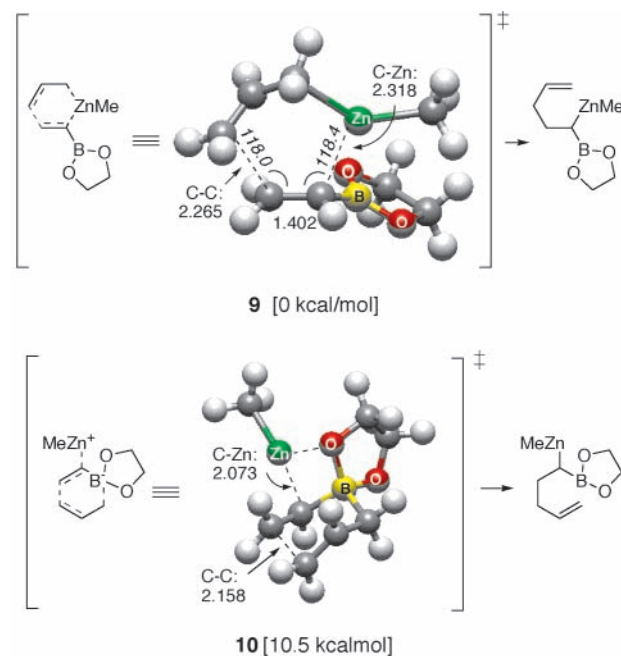
(12) In the reaction of 1-boryl-1-propene, the regioselectivity as to the allylic zinc reagent eroded and gave a nearly 1:1 mixture of  $\alpha$ - and  $\gamma$ -regioisomers. The diastereoselectivity as to the newly formed C–C bond was also very low.

(13) The oxidation was performed according to Knochel's procedure with slight modification: Knochel, P. *Tetrahedron Lett.* **1988**, *29*, 6697–6700. See also ref 2a.

(14) The DFT study was conducted with a model system that consists of allylmethylzinc and vinylboronate ethylene glycol ester. All theoretical calculations were carried out with the Gaussian 98 program.<sup>15</sup> Geometry optimization was performed with the hybrid B3LYP density functional by using Ahlrichs' SVP basis set for Zn and 6-31+G(d) basis set for the rest (denoted as B3LYP/631A). The basis sets are implemented in the program.

(15) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick,

showed that the Zn/B product can form via two independent pathways, carbometalation (zincio-ene reaction) and borate paths (followed by bora-Claisen rearrangement) (Scheme 1). Transmetalation of the allyl group from zinc to boron was found to give the borate complex, which is 9.6 kcal/mol higher in energy than the starting material, a complex between vinylboronate and allylmethylzinc. The transition structures of the two paths are shown in Figure 1. The zincio-



**Figure 1.** Transition structures of allylzincation of vinylboronate (B3LYP/631A).

ene transition state (**9**) is of lower energy than the bora-Claisen rearrangement TS (**10**) by ca. 10.5 kcal/mol. Molecular orbital analysis indicated that the zincio-ene transition state is stabilized by the interaction between the forming C–Zn  $\sigma$  bond and the boron's vacant p orbital.<sup>16</sup>

In summary, the present study revealed that the boryl substituent activates an olefin toward carbozincation reaction and provides an efficient method for the synthesis of a variety of geminal Zn/B organodimetallic species. Experiments and theory suggested that the formation of a stable borate complex can be avoided by the combined use of an allylic zinc reagent and the bulky pinacol borane substituent.

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(16) Theoretical details including discussion on the electronic properties of the transition structures will be reported in a full paper.

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**Supporting Information Available:** Experimental procedures and physical properties of new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.  
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