C–H Functionalization

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Stereoselective Synthesis of *cis*-β-Methyl- and Phenyl-Substituted Alkenylboronates by Platinum-Catalyzed Dehydrogenative Borylation**

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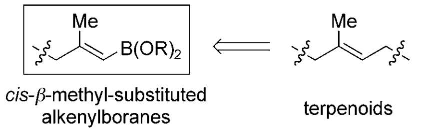
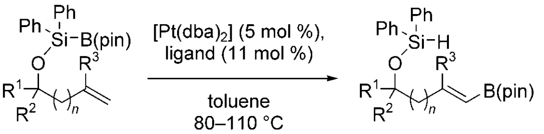
Increasing attention is being paid to the development of efficient methods for the synthesis of alkenylboron compounds, which serve as versatile building blocks in organic synthesis.[1] For example, a variety of alkenylboronates that are difficult to obtain by classical hydroboration have been synthesized with high regio- and stereoselectivity by the transition-metal-catalyzed addition of B–R bonds (R = H,[2] S,[3] B,[4] Si,[5] Sn,[6] CN,[7] alkynyl[8]) to alkynes. Transition-metal-mediated C–C bond formation with 1-alkynylboronates[9] and vinylboronates[10] is an alternative route to stereodefined alkenylboronates. However, stereoselective synthesis of alkenylboranes bearing a β-methyl group *cis* to the boryl group is still limited,[11] although such alkenylboranes are attractive for construction of the terpenoid unit widely found in natural products (Scheme 1).



Scheme 1. A potential synthetic intermediate of terpenoids.

In our recent study on platinum-catalyzed intramolecular silaboration of alkenes,[12] we have found that dehydrogenative borylation was the major side reaction under certain conditions. Because dehydrogenative borylation of alkenes is an attractive route to alkenylboranes,[13] our interest was then focused on the efficiency and selectivity of this process. In this paper, we describe a new platinum-catalyzed transformation of geminally disubstituted alkenes, which results in the stereoselective functionalization of alkenyl C–H bonds [Eq. (1); dba = dibenzylideneacetone, B(pin) = 4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl].



1 (*n* = 1)
3 (*n* = 0)

2 (*n* = 1)
4 (*n* = 0)

(1)

A toluene solution of **1a** ($R^1,R^2 = Et$), prepared easily from the corresponding homoallylic alcohols with $ClPh_2SiB(pin)$,[14] was stirred at 110°C in the presence of $[Pt(dba)_2]$ (5 mol%) and PPh_3 (11 mol%; entry 1, Table 1). The starting **1a** was completely consumed after 21 h with no intramolecular silaboration products in the reaction mixture. We found that alkenylboronate **2a** was formed by dehydrogenative borylation in 84% yield with high stereoselectivity (> 98:2). The configuration of the double bond in the product was determined to be *E* by NOE. Compounds **1b–d** derived from homoallylic alcohols were subjected to the same reaction conditions (entries 2–4, Table 1). Dehydroborylation took place efficiently for both tertiary-alcohol-derived **1b** and secondary-alcohol-derived **1c** (entries 2 and 3, Table 1). The silyl group was readily removed by treatment with 1N HCl aq. to give the corresponding alcohol **2c′** (entry 3, Table 1). Stereoselective formation of the β,β-disubstituted alkenylboronate was also achieved in the reaction of (−)-isopulegol derivative **1d**, affording **2d** in 87% yield (entry 4, Table 1).

The reaction of the allylic substrate **3a**[14] was then examined (entry 5, Table 1). After optimizing the reaction conditions,[15] we found that a platinum complex bearing the electron-deficient phosphine ligand $P(4\text{-}CF_3C_6H_4)_3$ catalyzed the reaction of **3a** effectively even at 80°C, giving **4a** in high yield. The reaction produced small amounts of side products, one of which might be the stereoisomer. After hydrolysis of the Si–O bond in **4a**, the corresponding alcohol was obtained as the isomerically pure form in 57% yield. Various allylic substrates **3b–e** were then reacted under the same reaction conditions (entries 6–9, Table 1). Silylboronates **3b–d** derived from secondary and tertiary alcohols bearing sterically bulky substituents reacted well under these conditions, giving the corresponding alkenylboronates **4b–d** in 73–86% yield (entries 6–8, Table 1). Substrate **3e**, which has a phenyl group on the double bond, also reacted under the same conditions to give **4e** in 59% yield (entry 9, Table 1). In contrast, reaction of the sterically less hindered 2-methyl-1-hepten-3-ol derivative ($R^1 = n$Bu, $R^2 = H$, $R^3 = Me$, $n = O$) suffered from a slow reaction rate and provided the desired product in low yield (< 10%). In addition, no reaction took

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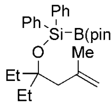
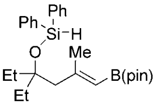
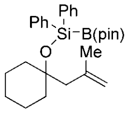
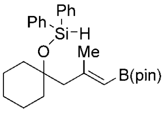
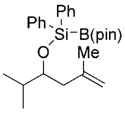
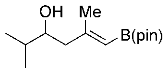
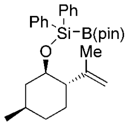
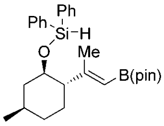
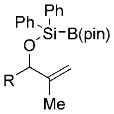
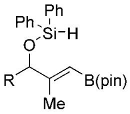
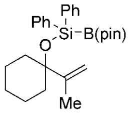
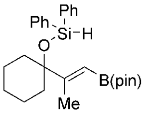
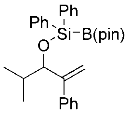
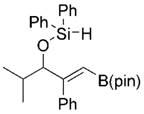
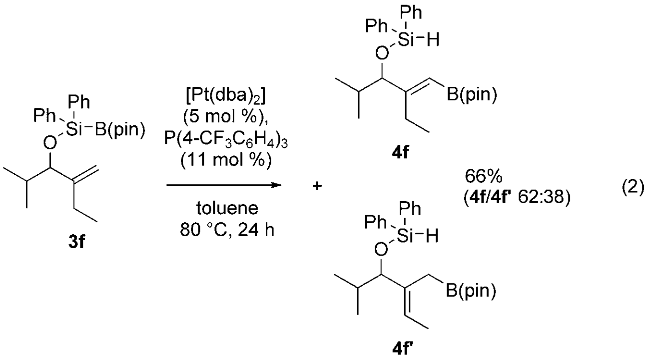
Table 1: Pt-catalyzed dehydrogenative borylation of **1** and **3**.

Entry	Substrate		Conditions,[a] time	Product		Yield [%][b]
1		**1a**	A, 21 h		**2a**	84
2		**1b**	A, 6 h		**2b**	85
3[c]		**1c**	A, 6 h		**2c′**[c]	58[d]
4		**1d**	A, 6 h		**2d**	87
5		**3a** (R = *i*Pr)	B, 3 h		**4a**	87[e,f] (57)[g]
6		**3b** (R = Cy)	B, 6 h		**4b**	73
7		**3c** (R = *t*Bu)	B, 6 h		**4c**	86
8		**3d**	B, 24 h		**4d**	81
9		**3e**	B, 6 h		**4e**	59

[a] Reaction conditions A: A mixture of $[Pt(dba)_2]$ (5 mol%), PPh_3 (11 mol%), **1** (100 mg), and toluene (0.7 mL) was stirred at 110°C. Reaction conditions B: A mixture of $[Pt(dba)_2]$ (5 mol%), $P(4\text{-}CF_3C_6H_4)_3$ (11 mol%), **3** (100 mg), and toluene (0.7 mL) was stirred at 80°C. [b] Yield of isolated product. [c] After the reaction, the product **2c** was treated with 1 N HCl aq. in EtOH at RT for 1 h. [d] Overall yield for two steps. [e] Yield determined by GC; internal standard: nonane. [f] Although **4a** was purified by silica gel chromatography, a small amount of side products could not be removed. [g] Yield of the isolated corresponding allylic alcohol after desilylation. Cy = cyclohexyl.

place with a methallyl alcohol derivative ($R^1 = R^2 = H$, $R^3 =$ Me, $n = 0$).

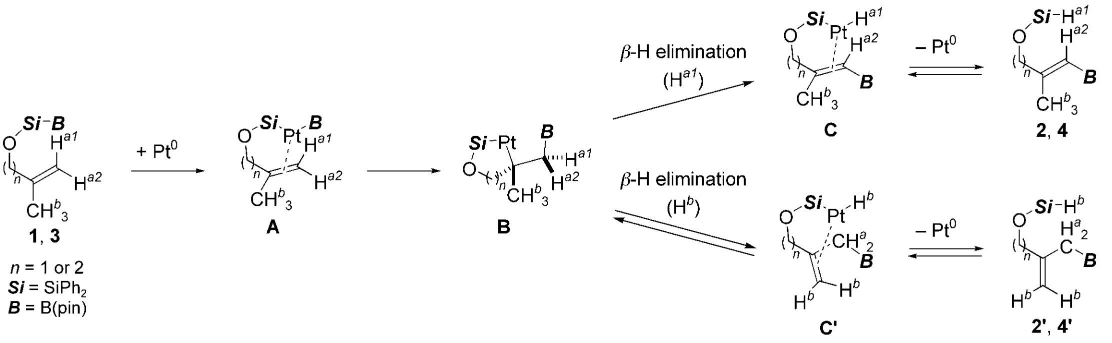
The reaction of **3f**, which has an ethyl group on the double bond, afforded a mixture of alkenylboronate **4f** and allylboronate **4f′** (62:38) in 66% total yield [Eq. (2)]. The isomer ratio did not change on prolonged reaction.



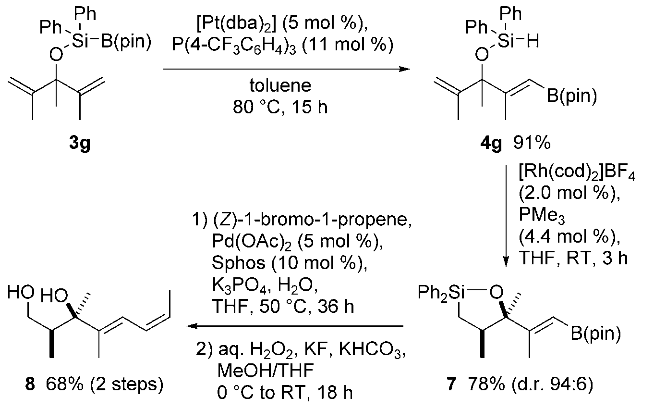
(2)

We propose that the borylation reaction occurs by the mechanism shown in Scheme 2. Oxidative addition of the Si–B bond of the silylboronate (**1** or **3**) to Pt^0 affords intermediate **A**, and subsequent insertion of the C=C bond into the Pt–B bond gives metallacycle **B**. β-Hydride elimination of H^a yields **C**, from which alkenylboronate **2** or **4** is formed by reductive elimination of the Si–H bond. Alternatively, the β-hydride elimination would proceed with H^b, giving allylboronate **2′** or **4′** through the formation of intermediate **C′**. It should be pointed out that intermediate **B** and allylboronates **2′** and **4′** could be in equilibrium through the intramolecular hydroplatination/β-hydride-elimination sequence. Because the hydroplatination is highly dependent on the substitution pattern of the C=C bond, the formation of alkenylboronates (**2** and **4**) could be irreversible, leading to the major formation of **C** through **B** by elimination of H^a. Selective formation of *E* alkenylboronates indicates that the β-hydride elimination proceeds by elimination of H^{a1} rather than the diastereomeric hydrogen H^{a2}.

A synthetic application of the dehydrogenative borylation is depicted in Scheme 3. Dehydrogenative borylation of **3g** took place in the presence of the platinum catalyst to give dienylboronate **4g** in 91% yield. Because the product has a reactive hydrosilane moiety, intramolecular hydrosilylation of **4g** was then carried out in the presence of $[Rh(cod)_2]BF_4$



Scheme 2. Possible reaction mechanism.



Scheme 3. Transformation of **3g** by dehydrogenative borylation. cod = 1,5-cyclooctadiene, Sphos = 2-dicyclohexylphosphino-2′,6′-dimethoxy-1,1′-biphenyl.

(2.0 mol%) and PMe_3 (4.4 mol%) to afford cyclic silyl ether **7** with high diastereoselectivity (78% yield, d.r. 94:6).[16] Suzuki–Miyaura coupling of **7** with (*Z*)-1-bromo-1-propene[17] followed by Tamao–Fleming oxidation[18] gave diol **8** in 68% yield from **7**.

In conclusion, we have established a novel borylation of homoallylic and allylic silyl ethers containing geminally disubstituted C=C double bonds. The reaction gave β,β-disubstitituted alkenylboronates, including synthetically useful *cis*-β-methyl alkenylboronates, with efficient stereoselectivities.

Experimental Section

General procedure for the preparation of **1** and **3**: A solution of (chlorodiphenylsilyl)pinacolborane[14] (3.45 g, 10 mmol) and pyridine (0.97 mL, 12 mmol) in CH_2Cl_2 was treated with an alcohol (10 mmol) at 0°C. The pyridinium salt precipitated immediately. After the mixture had been stirred at room temperature for 12 h, the volatiles were removed by evaporation and the residue was diluted with pentane. The salt was removed by filtration through a Celite pad under nitrogen. The filtrate was concentrated to give a borylsilanyl ether, which can be used in the Pt-catalyzed dehydrogenative borylation without further purification. The compound can be purified by bulb-to-bulb distillation or silica gel column chromatography in a drybox, if necessary.

General procedure for dehydrogenative borylation of **1** (reaction conditions A): A glass tube having a polytetrafluoroethylene (PTFE, J. Young) stopcock was charged with PPh_3 (6.3 mg, 0.024 mmol), $[Pt(dba)_2]$ (7.3 mg, 0.011 mmol), toluene (0.70 mL), and **1** (0.22 mmol). The tube was sealed by the stopcock, and the mixture was heated at 110°C with stirring. The reaction was monitored by GC. After the reaction was complete (6–21 h), the volatile materials were removed by evaporation. The product was purified by silica gel column chromatography or by HPLC.

General procedure for dehydrogenative borylation of **3** (reaction conditions B): A glass tube having PTFE (J. Young) stopcock was charged with $P(4\text{-}CF_3C_6H_4)_3$ (12 mg, 0.026 mmol), $[Pt(dba)_2]$ (8.0 mg, 0.012 mmol), toluene (0.7 mL), and **3** (0.24 mmol). The tube was sealed by the stopcock, and the mixture was heated at 80°C with stirring. The reaction was monitored by GC. After the reaction was complete (3–24 h), the volatile materials were removed by evaporation. The product was purified by silica gel column chromatography or by HPLC.

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Keywords: boranes · cross-coupling · dehydrogenative borylation · platinum · stereoselective synthesis

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[14] Substrates **1** and **3** were prepared by the reaction of $ClPh_2Si{-}B(pin)$ with homoallylic and allylic alcohols in the presence of pyridine. T. Ohmura, K. Masuda, H. Furukawa, M. Suginome, *Organometallics* **2007**, *26*, 1291.

[15] Reaction yields with various ligands (GC yield after 3 h at 80 °C): PPh_3 (57 %), $P(4\text{-}MeC_6H_4)_3$ (22 %), $P(4\text{-}MeOC_6H_4)_3$ (35 %), $P(4\text{-}ClC_6H_4)_3$ (62 %), $P(4\text{-}FC_6H_4)_3$ (76 %), $P(4\text{-}CF_3C_6H_4)_3$ (87 %), $P(2\text{-}MeC_6H_4)_3$ (no reaction), 1,2-bis(diphenylphosphanyl)ethane (dppe, no reaction).

[16] This is the first example of a diastereoselective intramolecular hydrosilylation of a substrate derived from a tertiary allylic alcohol. For Rh-catalyzed intramolecular hydrosilylation, see: a) K. Tamao, T. Tohma, N. Inui, O. Nakayama, Y. Ito, *Tetrahedron Lett.* **1990**, *31*, 7333; b) S. H. Bergens, P. Noheda, J. Whelan, B. Bosnich, *J. Am. Chem. Soc.* **1992**, *114*, 2121.

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