Title	Palladium-catalyzed cross-coupling reaction of bis(pinacolato)diboron with vinyl triflates α -substituted by a carbonyl group: efficient synthesis of α -boryl- α , β -unsaturated carbonyl compounds and their synthetic utility
Author(s)	Ishiyama, Tatsuo; Takagi, Jun; Kamon, Akihiro; Miyaura, Norio
Citation	Journal of Organometallic Chemistry, 687(2), 284-290 https://doi.org/10.1016/S0022-328X(03)00611-9
Issue Date	2003-12-07
Doc URL	http://hdl.handle.net/2115/56318
Type	article (author version)
File Information	(39) B-B + X-Enone (Full).pdf

[Instructions for use](#)

Palladium-catalyzed cross-coupling reaction of bis(pinacolato)diboron with vinyl triflates β -substituted by a carbonyl group: Efficient synthesis of β -boryl- α,β -unsaturated carbonyl compounds and their synthetic utility

Tatsuo Ishiyama*, Jun Takagi, Akihiro Kamon, Norio Miyauchi*

Division of Molecular Chemistry, Graduate School of Engineering, Hokkaido University, Sapporo 060-8628, Japan

Dedicated to Professor J. P. Genêt in recognition of his significant contributions to the art of organic synthesis (on the occasion of his 60th birthday)

Abstract

Cross-coupling reaction of bis(pinacolato)diboron with β -(trifluoromethanesulfonyloxy)- α,β -unsaturated carbonyl compounds was carried out in the presence of $\text{PdCl}_2(\text{PPh}_3)_2$ - 2PPh_3 (3 mol%) and KOPh in toluene or K_2CO_3 in dioxane for the synthesis of cyclic and acyclic β -boryl- α,β -unsaturated esters, amides, and ketones in high yields. The vinylboronates thus obtained readily participated in carbon-carbon bond formation, such as cross-coupling with vinyl triflates and

1,4-addition to α,β -unsaturated ketones.

Keywords: Bis(pinacolato)diboron; Vinyl triflate; Palladium catalyst; Vinylboronate;
Cross-coupling

* Corresponding author. Fax: +81-11-7066562.

E-mail address: ishiyama@org-mc.eng.hokudai.ac.jp (T. Ishiyama).

1. Introduction

β -Boryl- α,β -unsaturated carbonyl compounds are attractive synthetic intermediates which allow inter- or intramolecular Diels-Alder reaction [1], asymmetric dipolar cycloaddition or 1,4-addition [2], cyclopropanation [3], and radical addition [4]. Although β -borylacrylates are available *via* hydroboration of propiolic acid esters [1,5], preparation of the corresponding ketone and aldehyde derivatives requires a multi-step procedure [1,6] and there are few reports for cyclic or polysubstituted derivatives [7]. In connection with our interest in the synthesis of organoboron compounds *via* the cross-coupling reaction of diborons with organic electrophiles [8] including aryl [8,9], vinyl [8,10], allyl [8,11], and benzyl [8,12] halides or triflates, we wish to disclose here a palladium-catalyzed cross-coupling reaction of bis(pinacolato)diboron [13] (pin_2B_2 , $\text{pin} = \text{Me}_4\text{C}_2\text{O}_2$) **1** with vinyl triflates [14] **2** to yield the corresponding

β -boryl- α,β -unsaturated carbonyl compounds **3** (Scheme 1) [15].

<<Scheme 1>>

2. Results and discussion

2.1. Cross-coupling of diboron with vinyl triflates

The effects of bases and solvents on the reaction are shown in Table 1. The conditions previously reported for the coupling of pin_2B_2 **1** with vinyl halides or triflates ($\text{PdCl}_2(\text{PPh}_3)_2\text{-2PPh}_3/\text{KOPh}/\text{toluene}/50\text{ }^\circ\text{C}$) [10] gave borylated products **3** in high yields for most of the vinyl triflates **2**, but the reaction often resulted in very low yields due to a competitive base-induced side-reaction. For example, the reaction of **1** (1.1 mmol) with ethyl 2-(trifluoromethanesulfonyloxy)-1-cyclopentenecarboxylate (1.0 mmol) in the presence of $\text{PdCl}_2(\text{PPh}_3)_2\text{-2PPh}_3$ (0.03 mmol) and KOPh (1.5 mmol) in toluene (6 ml) at 50 $^\circ\text{C}$ resulted in 9% yield (Entry 1). Analysis of the reaction mixture revealed the formation of phenyl triflate (90%) resulted by ester-exchange between the triflate and KOPh [16]. A sterically more hindered 2-MeC₆H₄OK base, which is expected to inhibit the ester-exchange, also produced the corresponding triflate in 69% yield (Entry 2). Alternatively, use of a K₂CO₃ base in dioxane was found to be effective for such substrates sensitive to the phenoxy anion to promote the desired coupling in 67% yield (Entry 3). Although K₂CO₃ was prone to induce further coupling of **3** with **2** giving a dimer of **2** (ca. 30%), stronger bases such as K₃PO₄ further enhanced the dimerization (Entry 4) and weaker bases such as KOAc did not promote the coupling (Entry 5). Use of less-polar solvents such as toluene resulted in low conversion (Entry 6). Although the

reactions using K₂CO₃ took longer times at 50 °C, the same reactions were completed at 80 °C within 5 h in dioxane and 24 h in toluene, respectively (Entries 7 and 8).

<<Table 1>>

The palladium-catalyzed cross-coupling of pin₂B₂ **1** with the representative vinyl triflates **2** in the presence of KOPh in toluene at 50 °C (Method A) or K₂CO₃ in dioxane at 80 °C (Method B) is summarized in Table 2. All **2** including cyclic or acyclic ester, amide, and ketone derivatives were converted into the corresponding β-boryl-α,β-unsaturated carbonyl compounds **3** in high yields by either Method A or B. The reactions were faster under the conditions of Method A than those of Method B; however, the yields highly depended upon the substrates. Method A resulted in low yields due to the formation of phenyl triflate (30-90%) for substrates sensitive to the phenoxy anion, including five-membered ester (Entry 1), six-membered amide (Entry 5), five-membered ketone (Entry 6), and less-hindered six-membered ketone having no substituent at the α carbon (Entry 8). On the other hand, Method A was a better choice for seven- and eight-membered esters (Entries 3 and 4), and acyclic ester (Entry 10), because Method B resulted in the formation of symmetrical 1,3-dienes (15-30%) arising from dimerization of **2**. The borylation of acyclic ester and amide derivatives of **2** having *E* stereochemistry retained completely the configuration of the double bond to give isomerically pure (*Z*)-**3** in high yields (Entries 10 and 11).

<<Table 2>>

In general, *E* or *Z* configuration of vinyl halides or triflates can be retained completely in the cross-coupling of organoboron compounds [17]; however, the amide derivative of triflate (*Z*)-**4** unexpectedly provided the borylated product (*Z*)-**5** by Method A and a mixture of (*Z*)-**5** and (*E*)-**5** (64:36) by Method B (Scheme 2). Monitoring of a

benzene-*d*₆ solution of the (*Z*)-**4** or (*E*)-**5** in the presence of Pd(PPh₃)₄ and KOPh by ¹H NMR and GC at 50 °C resulted in no conversion into (*E*)-**4** or (*Z*)-**5**, suggesting the isomerization during the catalytic process. It remains unclear which step is responsible for such isomerization; however, a vinylpalladium(II) species generated by oxidative addition of a vinyl halide or triflate to a palladium(0) complex often undergoes *E-Z* isomerization [18].

<<Scheme 2>>

2.2. One-pot synthesis of 1,3-dienes via borylation-coupling sequence

The direct preparation of β-boryl-α,β-unsaturated carbonyl compounds **3** from pin₂B₂ **1** and the corresponding vinyl triflates **2** now allows a one-pot, two-step procedure for the synthesis of ketone or ester derivatives of unsymmetrical 1,3-dienes **7** (Table 3). The stereoselective synthesis of three dienes **7** were easily achieved in 76%, 76%, and 77% yields when the borylation of **2** (1.1 mmol) with **1** (1.1 mmol) was directly followed by the coupling with another vinyl triflate **6** (1.0 mmol). A combination of PdCl₂(dppf) (0.03 mmol) and K₃PO₄ (3.0 mmol) in dioxane at 80 °C was recognized to be the best conditions for the second coupling [17].

<<Table 3>>

2.3. 1,4-Addition of vinylboronates to α,β-unsaturated ketones

Although we examined one-pot synthesis *via* borylation-addition sequence at first, all attempts at the reactions of *in situ* generated vinylboroates **3** with α,β-unsaturated

ketones **8** by using a rhodium catalyst were unsuccessful. On the other hand, it was found that isolated **3** readily underwent the expected 1,4-addition. The addition did not occur in the presence of a catalytic amount of both a rhodium complex and $\text{PdCl}_2(\text{PPh}_3)_2\text{-2PPh}_3$, indicating that the palladium catalyst used at the borylation step inhibited the addition step. Representative results of the 1,4-addition of **3** (1.0 mmol) to **8** (1.1 mmol) catalyzed by a rhodium complex (3 mol%) are summarized in Table 4. Acyclic-acyclic (Entries 1 and 3), acyclic-cyclic (Entries 2 and 4), cyclic-acyclic (Entry 5), and cyclic-cyclic (Entry 6) combinations all produced the corresponding ϵ -oxo- α,β -unsaturated ester, amide, and ketone derivatives **9** in high yields. The reactions of acyclic ester and amide derivatives of **3** having *Z* stereochemistry retained completely the configuration of the double bond (Entries 1-4). In the case of the cyclic-cyclic reaction, use of 1.1 mmol of **8** resulted in a moderate yield (42%); however, the yield was improved to 65% when using 2.0 mmol of **8** (Entry 6). Although reaction conditions were not fully optimized, the addition smoothly proceeded in the presence of a $[\text{Rh}(\text{COD})_2]\text{BF}_4$ catalyst in aqueous dioxane at 90 °C [19].

<<Table 4>>

3. Experimental

3.1. Materials and reagents

Bis(pinacolato)diboron [13], vinyl triflates [14], potassium phenoxide [20], and potassium 2-methylphenoxide [21] were prepared by the reported procedures. Solvents were purified by distillation from appropriate drying agents. All of other compounds

were used as received.

3.2. General procedure for cross-coupling of bis(pinacolato)diboron with vinyl triflates (Table 2 and Scheme 2)

A 25 ml flask assembled a magnetic stirring bar, a septum inlet, and a condenser was charged with $\text{PdCl}_2(\text{PPh}_3)_2$ (0.03 mmol), PPh_3 (0.06 mmol), bis(pinacolato)diboron **1** (1.1 mmol), and KOPh or K_2CO_3 (1.5 mmol) and then flushed with nitrogen. Dry toluene or dioxane (6 ml) and a vinyl triflate **2** or **4** (1.0 mmol) were added and the mixture was stirred at 50 °C or 80 °C for the period shown in Table 2 or Scheme 2. The product was extracted with benzene, washed with brine, and dried over MgSO_4 . Column chromatography over silica gel followed by Kugelrohr distillation gave an analytically pure vinylboronate **3** or **5**.

3.2.1. Ethyl

2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-cyclopentene-1-carboxylate

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.28 (t, 3 H, $J = 7.1$ Hz), 1.34 (s, 12 H), 1.89-1.97 (m, 2 H), 2.60 (t, 4 H, $J = 7.7$ Hz), 4.21 (q, 2 H, $J = 7.2$ Hz); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 14.39, 24.09, 24.74, 33.50, 37.52, 60.19, 83.86, 142.90, 165.81; MS (EI) m/e 121 (28), 179 (81), 208 (100), 266 ($[\text{M}^+]$, 5); exact mass Found: 266.1682; $\text{C}_{14}\text{H}_{23}\text{BO}_4$ Calc.: 266.1689.

3.2.2. Ethyl

2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-cyclohexene-1-carboxylate

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.27 (t, 3 H, $J = 7.2$ Hz), 1.33 (s, 12 H), 1.54-1.66 (m, 4 H), 2.22 (br s, 4 H), 4.21 (q, 2 H, $J = 7.2$ Hz); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 14.25, 21.42, 21.85, 24.12, 24.77, 27.93, 60.70, 83.34, 134.24, 169.19; MS (EI) m/e 79 (40), 108 (37), 153 (41), 193 (55), 222 (100), 280 ($[\text{M}^+]$, 4); exact mass Found: 280.1846; $\text{C}_{15}\text{H}_{25}\text{BO}_4$ Calc.: 280.1846.

3.2.3.

Ethyl

2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-cycloheptene-1-carboxylate

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.29 (t, 3 H, $J = 7.1$ Hz), 1.32 (s, 12 H), 1.48-1.52 (m, 2 H), 1.55-1.59 (m, 2 H), 1.76-1.78 (m, 2 H), 2.32-2.34 (m, 2 H), 2.46-2.49 (m, 2 H), 4.24 (q, 2 H, $J = 7.1$ Hz); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 14.19, 24.82, 25.86, 25.90, 27.09, 30.99, 32.20, 61.90, 82.67, 139.52, 171.45; MS (EI) m/e 83 (29), 93 (24), 122 (34), 167 (34), 236 (100), 294 ($[\text{M}^+]$, 5); exact mass Found: 294.1992; $\text{C}_{16}\text{H}_{27}\text{BO}_4$ Calc.: 294.2002.

3.2.4.

Ethyl

2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-cyclooctene-1-carboxylate

$^1\text{H-NMR}$ (400 MHz, CDCl_3) δ 1.28 (t, 3 H, $J = 7.2$ Hz), 1.32 (s, 12 H), 1.45-1.46 (m, 4 H), 1.50-1.60 (m, 2 H), 1.60-1.70 (m, 2 H), 2.33-2.36 (m, 2 H), 2.42-2.45 (m, 2 H), 4.23 (q, 2 H, $J = 7.2$ Hz); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ 14.25, 24.68, 24.72, 26.19, 26.27, 28.75, 28.99, 29.62, 61.16, 82.93, 137.01, 170.16; MS (EI) m/e 83 (33), 107 (22), 136 (33), 181 (21), 250 (100), 308 ($[\text{M}^+]$, 5); exact mass Found: 308.2134; $\text{C}_{17}\text{H}_{29}\text{BO}_4$ Calc.: 308.2159.

3.2.5.

N,N-Diethyl

2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-cyclohexene-1-carboxamide

¹H-NMR (400 MHz, CDCl₃) δ 1.23 (s, 12 H), 1.25 (t, 6 H, *J* = 6.8 Hz), 1.54-1.59 (m, 2 H), 1.63-1.68 (m, 2 H), 2.28-2.31 (m, 2 H), 2.40-2.43 (m, 2 H), 3.50-3.60 (m, 4 H); ¹³C-NMR (100 MHz, CDCl₃) δ 12.51, 14.73, 21.28, 23.06, 25.24, 25.84, 26.85, 42.42, 44.66, 79.70, 129.25, 173.76; MS (EI) *m/e* 83 (57), 207 (23), 249 (100), 292 (22), 307 ([M⁺], 37); exact mass Found: 307.2319; C₁₇H₃₀BNO₃ Calc.: 307.2319.

3.2.6. 2-Methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclopenten-1-one

¹H-NMR (400 MHz, CDCl₃) δ 1.33 (s, 12 H), 1.94 (t, 3 H, *J* = 2.2 Hz), 2.33-2.35 (m, 2 H), 2.61-2.64 (m, 2 H); ¹³C-NMR (100 MHz, CDCl₃) δ 10.52, 24.85, 28.77, 34.19, 83.94, 151.92, 212.11; MS (EI) *m/e* 83 (51), 122 (74), 136 (71), 165 (82), 207 (93), 222 ([M⁺], 100); exact mass Found: 222.1429; C₁₂H₁₉BO₃ Calc.: 222.1427.

3.2.7. 2-Methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclohexen-1-one

¹H-NMR (400 MHz, CDCl₃) δ 1.31 (s, 12 H), 1.92-1.99 (m, 2 H), 1.96 (t, 3 H, *J* = 2.0 Hz), 2.38-2.44 (m, 4 H); ¹³C-NMR (100 MHz, CDCl₃) δ 14.86, 23.43, 24.76, 28.62, 38.50, 83.98, 143.39, 199.82; MS (EI) *m/e* 83 (100), 137 (44), 179 (76), 236 ([M⁺], 53); exact mass Found: 236.1586; C₁₃H₂₁BO₃ Calc.: 236.1584.

3.2.8. 5,5-Dimethyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclohexen-1-one

¹H-NMR (400 MHz, CDCl₃) δ 1.02 (s, 6 H), 1.30 (s, 12 H), 2.25 (s, 2 H), 2.32 (d,

2 H, $J = 2.0$ Hz), 6.54 (s, 1 H); ^{13}C -NMR (100 MHz, CDCl_3) δ 24.77, 28.22, 33.96, 41.11, 51.73, 84.31, 137.66, 200.19; MS (EI) m/e 83 (100), 194 (17), 235 (20), 250 ($[\text{M}^+]$, 14); exact mass Found: 250.1741; $\text{C}_{14}\text{H}_{23}\text{BO}_3$ Calc.: 250.1740.

3.2.9. 2-Methyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-cyclohepten-1-one

^1H -NMR (400 MHz, CDCl_3) δ 1.31 (s, 12 H), 1.60-1.80 (m, 4 H), 2.01 (s, 3 H), 2.39 (t, 2 H, $J = 5.6$ Hz), 2.50 (t, 2 H, $J = 6.1$ Hz); ^{13}C -NMR (100 MHz, CDCl_3) δ 17.86, 20.93, 24.54, 24.73, 28.66, 41.25, 83.75, 148.21, 208.40; MS (EI) m/e 101 (25), 165 (100), 250 ($[\text{M}^+]$, 9); exact mass Found: 250.1741; $\text{C}_{14}\text{H}_{23}\text{BO}_3$ Calc.: 250.1740.

3.2.10. Ethyl (Z)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-butenolate

^1H -NMR (400 MHz, CDCl_3) δ 1.28 (s, 12 H), 1.28 (t, 3 H, $J = 7.1$ Hz), 2.17 (d, 3 H, $J = 1.7$ Hz), 4.17 (q, 2 H, $J = 7.2$ Hz), 6.45 (d, 1 H, $J = 1.7$ Hz) [the irradiation of the vinylic proton at 6.45 ppm resulted in no enhancement of the allylic methyl signal at 2.17 ppm]; ^{13}C -NMR (100 MHz, CDCl_3) δ 14.24, 16.29, 24.74, 59.75, 84.11, 130.56, 166.21; MS (EI) m/e 112 (75), 140 (100), 195 (32), 240 ($[\text{M}^+]$, 4); exact mass Found: 240.1534; $\text{C}_{12}\text{H}_{21}\text{BO}_4$ Calc.: 240.1533.

3.2.11. N,N-Diethyl (Z)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-butenamide

^1H -NMR (400 MHz, CDCl_3) δ 1.15 (t, 6 H, $J = 7.1$ Hz), 1.27 (s, 12 H), 1.85 (d, 3 H, $J = 1.7$ Hz), 3.25-3.50 (m, 4 H), 6.68 (d, 1 H, $J = 1.5$ Hz) [the irradiation of the vinylic proton at 6.68 ppm resulted in no enhancement of the allylic methyl signal at 1.85 ppm]; ^{13}C -NMR (100 MHz, CDCl_3) δ 13.04, 14.29, 16.18, 24.77, 38.70, 42.21,

83.74, 136.03, 168.06; MS (EI) m/e 167 (100), 252 (21), 267 ($[M^+]$, 43); exact mass Found: 267.2013; $C_{14}H_{26}BNO_3$ Calc.: 267.2006.

3.2.12. N,N-Diethyl (E)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-butenamide

1H -NMR (400 MHz, $CDCl_3$) δ 1.16 (t, 3 H, $J = 7.3$ Hz), 1.17 (t, 3 H, $J = 7.6$ Hz), 1.19 (s, 12 H), 2.01 (d, 3 H, $J = 1.5$ Hz), 3.37 (q, 2 H, $J = 7.3$ Hz), 3.48 (q, 2 H, $J = 7.2$ Hz), 6.06 (s, 1 H) [the irradiation of the vinylic proton at 6.06 ppm resulted in an 3.2% enhancement of the allylic methyl signal at 2.01 ppm]; ^{13}C -NMR (100 MHz, $CDCl_3$) δ 12.75, 14.25, 18.12, 25.15, 42.82, 42.86, 80.23, 117.68, 173.54; MS (EI) m/e 83 (37), 167 (39), 209 (100), 252 (31), 267 ($[M^+]$, 2); exact mass Found: 267.2019; $C_{14}H_{26}BNO_3$ Calc.: 267.2006.

3.3. NMR studies on isomerization of N,N-diethyl (Z)-3-(trifluoromethanesulfonyloxy)-2-butenamide and N,N-diethyl (E)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2-butenamide

In an NMR tube, a mixture of $Pd(PPh_3)_4$ (0.003 mmol), $KOPh$ (0.15 mmol), the vinyl triflate or the vinylboronate (0.1 mmol), and benzene- d_6 (0.6 ml) was heated at 50 °C for 1 h. 1H NMR and GC analyses indicated no isomerization of the vinyl triflate or the vinylboronate.

3.4. General procedure for one-pot synthesis of 1,3-dienes via borylation–coupling sequence (Table 3)

To a solution of a vinylboronate **3** resulted by the reaction of bis(pinacolato)diboron **1** (1.1 mmol) with a vinyl triflate **2** (1.1 mmol) in toluene or dioxane (4 ml) were added a second vinyl triflate **6** (1.0 mmol), PdCl₂(dppf) (0.03 mmol), K₃PO₄ (3.0 mmol), and dioxane (4 ml), and the mixture was stirred at 80 °C for 16 h. The product was extracted with benzene, washed with water, and dried over MgSO₄. Column chromatography over silica gel provided an analytically pure 1,3-diene **7**.

3.4.1. Ethyl 2-[(*E*)-3-ethoxycarbonyl-2-propen-2-yl]-1-cyclohexene-1-carboxylate

¹H-NMR (400 MHz, CDCl₃) δ 1.22 (t, 3 H, *J* = 7.1 Hz), 1.26 (t, 3 H, *J* = 7.2 Hz), 1.60-1.70 (m, 4 H), 2.15-2.20 (m, 2 H), 2.28 (d, 3 H, *J* = 1.5 Hz), 2.30-2.35 (m, 2 H), 4.11 (q, 2 H, *J* = 7.1 Hz), 4.14 (q, 2 H, *J* = 7.1 Hz), 5.51 (d, 1 H, *J* = 1.2 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ 13.87, 14.28, 18.25, 21.85, 21.94, 25.56, 30.19, 59.59, 60.31, 114.94, 125.24, 149.60, 160.61, 166.61, 168.27; MS (EI) *m/e* 165 (62), 193 (100), 266 ([M⁺], 1); exact mass Found: 266.1519; C₁₅H₂₂O₄ Calc.: 266.1518.

3.4.2. Ethyl (*E*)-3-(2-methyl-3-oxo-1-cyclohexenyl)-2-butenolate

¹H-NMR (400 MHz, CDCl₃) δ 1.30 (t, 3 H, *J* = 7.2 Hz), 1.73 (s, 3 H), 1.98-2.06 (m, 2 H), 2.29 (d, 3 H, *J* = 1.2 Hz), 2.36-2.42 (m, 2 H), 2.45 (t, 2 H, *J* = 6.7 Hz), 4.19 (q, 2 H, *J* = 7.2 Hz), 5.62 (d, 1 H, *J* = 1.5 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ 12.19, 14.24, 17.44, 22.78, 29.89, 37.70, 60.06, 117.21, 129.70, 156.37, 158.00, 166.23, 199.44; MS (EI) *m/e* 137 (37), 149 (100), 166 (37), 179 (44), 194 (38), 222 ([M⁺], 70); exact mass Found: 222.1263; C₁₃H₁₈O₃ Calc.: 222.1256.

3.4.3. Ethyl 2-(2-methyl-3-oxo-1-cyclopentenyl)-1-cyclohexene-1-carboxylate

^1H -NMR (400 MHz, CDCl_3) δ 1.17 (t, 3 H, $J = 7.2$ Hz), 1.58 (t, 3 H, $J = 2.0$ Hz), 1.68-1.74 (m, 4 H), 2.12-2.22 (m, 2 H), 2.36-2.50 (m, 4 H), 2.60-2.70 (m, 2 H), 4.07 (q, 2 H, $J = 7.2$ Hz); ^{13}C -NMR (100 MHz, CDCl_3) δ 8.19, 13.92, 21.67, 21.84, 25.47, 28.99, 29.31, 34.10, 60.33, 126.58, 134.33, 144.77, 167.22, 173.62, 209.29; MS (EI) m/e 163 (31), 177 (25), 191 (47), 220 (100), 248 ($[\text{M}^+]$, 2); exact mass Found: 248.1412; $\text{C}_{15}\text{H}_{20}\text{O}_3$ Calc.: 248.1412.

3.5. General procedure for 1,4-addition of vinylboronates to α,β -unsaturated ketones (Table 4)

A 25 ml flask charged with $[\text{Rh}(\text{COD})_2]\text{BF}_4$ (0.03 mmol) was flushed with nitrogen. Aqueous dioxane (dioxane:water = 6:1, 6 ml), a vinylboronate **3** (1.0 mmol), and an α,β -unsaturated carbonyl compound **8** (1.1 mmol) were then added. The resulting mixture was stirred at 90 °C for 6 h. The product was extracted with benzene, washed with water, and dried over MgSO_4 . Column chromatography over silica gel gave an analytically pure 1,4-adduct **9**.

3.5.1. Ethyl (E)-3-methyl-6-oxo-2-heptenoate

^1H -NMR (400 MHz, CDCl_3) δ 1.28 (t, 3 H, $J = 7.1$ Hz), 2.16 (d, 3 H, $J = 1.2$ Hz), 2.18 (s, 3 H), 2.42 (t, 2 H, $J = 7.8$ Hz), 2.62 (t, 2 H, $J = 7.7$ Hz), 4.14 (q, 2 H, $J = 7.2$ Hz), 5.63-5.66 (m, 1 H); ^{13}C -NMR (100 MHz, CDCl_3) δ 14.27, 18.83, 29.97, 34.20,

41.11, 59.59, 115.91, 157.94, 166.57, 207.09; MS (EI) m/e 43 (100), 58 (33), 95 (48), 113 (25), 138 (36), 184 ($[M^+]$, 9); exact mass Found: 184.1097; $C_{10}H_{16}O_3$ Calc.: 184.1099.

3.5.2. Ethyl (E)-3-(3-oxocyclohexyl)-2-butenate

1H -NMR (400 MHz, $CDCl_3$) δ 1.29 (t, 3 H, $J = 7.2$ Hz), 1.50-1.70 (m, 2 H), 1.80-1.95 (m, 1 H), 2.00-2.10 (m, 1 H), 2.15-2.45 (m, 5 H), 2.17 (s, 3 H), 4.16 (q, 2 H, $J = 7.1$ Hz), 5.69 (d, 1 H, $J = 1.0$ Hz); ^{13}C -NMR (100 MHz, $CDCl_3$) δ 14.25, 16.84, 25.08, 29.58, 41.09, 45.87, 48.34, 59.75, 115.56, 159.96, 166.70, 210.18; MS (EI) m/e 95 (41), 137 (50), 164 (100), 181 (37), 210 ($[M^+]$, 37); exact mass Found: 210.1246; $C_{12}H_{18}O_3$ Calc.: 210.1256.

3.5.3. N,N-Diethyl (E)-3-methyl-6-oxo-2-heptenamide

1H -NMR (400 MHz, $CDCl_3$) δ 1.14 (t, 6 H, $J = 7.2$ Hz), 1.90 (s, 3 H), 2.18 (s, 3 H), 2.38 (t, 2 H, $J = 7.4$ Hz), 2.63 (t, 2 H, $J = 7.6$ Hz), 3.36 (br s, 4 H), 5.80 (s, 1 H); ^{13}C -NMR (100 MHz, $CDCl_3$) δ 13.48, 14.35, 18.54, 30.00, 33.24, 40.00, 41.32, 43.04, 118.43, 147.05, 167.74, 207.72; MS (EI) m/e 43 (100), 111 (78), 115 (66), 168 (79), 211 ($[M^+]$, 11); exact mass Found: 211.1583; $C_{12}H_{21}NO_2$ Calc.: 211.1572.

3.5.4. N,N-Diethyl (E)-3-(3-oxocyclohexyl)-2-butenamide

1H -NMR (400 MHz, $CDCl_3$) δ 1.15 (t, 6 H, $J = 7.1$ Hz), 1.60-1.80 (m, 2 H), 1.90-2.00 (m, 1 H), 1.92 (s, 3 H), 2.00-2.20 (m, 1 H), 2.20-2.60 (m, 5 H), 3.20-3.50 (m, 4 H), 5.83 (s, 1 H); ^{13}C -NMR (100 MHz, $CDCl_3$) δ 13.23, 14.27, 16.36, 25.03, 29.54,

39.66, 41.23, 42.56, 46.27, 47.27, 118.26, 149.26, 167.58, 210.86; MS (EI) m/e 72 (93), 100 (64), 137 (100), 165 (61), 237 ($[M^+]$, 82); exact mass Found: 237.1738; $C_{14}H_{23}NO_2$ Calc.: 237.1729.

3.5.5. 2-Methyl-3-(3-oxobutyl)-2-cyclohepten-1-one

1H -NMR (400 MHz, $CDCl_3$) δ 1.65-1.75 (m, 4 H), 1.81 (s, 3 H), 2.19 (s, 3 H), 2.35 (t, 2 H, $J = 5.5$ Hz), 2.45-2.60 (m, 6 H); ^{13}C -NMR (100 MHz, $CDCl_3$) δ 14.23, 20.96, 24.39, 29.93, 30.85, 32.14, 40.99, 41.37, 134.44, 150.95, 207.04, 207.45; MS (EI) m/e 95 (62), 123 (50), 133 (52), 151 (100), 194 ($[M^+]$, 17); exact mass Found: 194.1296; $C_{12}H_{18}O_2$ Calc.: 194.1307.

3.5.6. 2-Methyl-3-(3-oxocyclohexyl)-2-cyclohepten-1-one

1H -NMR (400 MHz, $CDCl_3$) δ 1.60-1.80 (m, 8 H), 1.82 (s, 3 H), 2.10-2.55 (m, 8 H), 3.00-3.15 (m, 1 H); ^{13}C -NMR (100 MHz, $CDCl_3$) δ 13.76, 20.56, 24.46, 25.55, 25.75, 28.33, 41.09, 41.19, 43.22, 44.52, 133.77, 149.66, 208.55, 210.33; MS (EI) m/e 95 (74), 123 (100), 202 (38), 220 ($[M^+]$, 12); exact mass Found: 220.1451; $C_{14}H_{20}O_2$ Calc.: 220.1463.

Acknowledgments

This work was partially supported by Grant-in-Aid for Scientific Research on Priority Areas (No. 14078101, "Reaction Control of Dynamic Complexes") from Ministry of Education, Culture, Sports, Science and Technology, Japan. T.I. thanks Itoh

Science Foundation for support of a part of his work.

References

- [1] A recent review, see: M. Vaultier, G. Lorvelec, B. Plunian, O. Paulus, P. Bouju, J. Mortier, in: M.G. Davidson, A.K. Hughes, T.B. Marder, K. Wade (Eds.), *Contemporary Boron Chemistry*, The Royal Society of Chemistry, Cambridge, 2000, p. 464.
- [2] (a) C.D. Davies, S.P. Marsden, E.S.E. Stokes, *Tetrahedron Lett.* 39 (1998) 8513;
(b) C.D. Davies, S.P. Marsden, E.S.E. Stokes, *Tetrahedron Lett.* 41 (2000) 4229;
(c) C.N. Farthing, S.P. Marsden, *Tetrahedron Lett.* 41 (2000) 4235.
- [3] P. Fontani, B. Carboni, M. Vaultier, G. Maas, *Synthesis* (1991) 605.
- [4] N. Guennouni, F. Lhermitte, S. Cochard, B. Carboni, *Tetrahedron* 51 (1995) 6999.
- [5] E.-i. Negishi, T. Yoshida, *J. Am. Chem. Soc.* 95 (1973) 6837.
- [6] E. Jehanno, M. Vaultier, *Tetrahedron Lett.* 36 (1995) 4439.
- [7] (a) S.M. Marcuccio, M. Rodopoulos, H. Weigold, WO 9858935 A1, 1998;
(b) S.M. Marcuccio, M. Rodopoulos, H. Weigold, 10th International Conference on Boron Chemistry, England, Durham, July 1999, PB-35.
- [8] A recent review, see: T. Ishiyama, N. Miyaura, *J. Organomet. Chem.* 611 (2000) 392;
- [9] (a) T. Ishiyama, M. Murata, N. Miyaura, *J. Org. Chem.* 60 (1995) 7508;
(b) T. Ishiyama, Y. Itoh, T. Kitano, N. Miyaura, *Tetrahedron Lett.* 38 (1997) 3447;

- (c) T. Ishiyama, K. Ishida, N. Miyaura, *Tetrahedron* 57 (2001) 9813.
- [10] (a) K. Takahashi, J. Takagi, T. Ishiyama, N. Miyaura, *Chem. Lett.* (2000) 126;
 (b) J. Takagi, K. Takahashi, T. Ishiyama, N. Miyaura, *J. Am. Chem. Soc.* 124 (2002) 8001.
- [11] (a) T. Ishiyama, T.-a. Ahiko, N. Miyaura, *Tetrahedron Lett.* 37 (1996) 6889;
 (b) T.-a. Ahiko, T. Ishiyama, N. Miyaura, *Chem. Lett.* (1997) 811.
- [12] T. Ishiyama, Z. Oohashi, T.-a. Ahiko, N. Miyaura, *Chem. Lett.* (2002) 780.
- [13] (a) H. Nöth, *Z. Naturforsch.* 39b (1984) 1463;
 (b) T. Ishiyama, M. Murata, T.-a. Ahiko, N. Miyaura, *Org. Synth.* 77 (2000) 176.
- [14] Reviews, see: (a) P.J. Stang, M. Hanack, L.R. Subramanian, *Synthesis* (1982) 85;
 (b) K. Ritter, *Synthesis* (1993) 735.
- [15] Preliminary results were discussed in: J. Takagi, A. Kamon, T. Ishiyama, N. Miyaura, *Synlett* (2002) 1880.
- [16] L.R. Subramanian, M. Hanack, L.W.K. Chang, M.A. Imhoff, P.v.R. Schleyer, F. Effenberger, W. Kurtz, P.J. Stang, T.E. Dueber, *J. Org. Chem.* 41 (1976) 4099.
- [17] Recent reviews, see: (a) N. Miyaura, A. Suzuki, *Chem. Rev.* 95 (1995) 2457;
 (b) A. Suzuki, in: F. Diederich, P.J. Stang (Eds.), *Metal-Catalyzed Cross-Coupling Reactions*, Wiley-VCH, Weinheim, 1998, p. 49;
 (c) N. Miyaura, *Top. Curr. Chem.* 219 (2002) 11.
- [18] (a) D. Zargarian, H. Alper, *Organometallics* 10 (1991) 2914;
 (b) A. Arcadi, S. Cacchi, G. Fabrizi, L. Moro, *Eur. J. Org. Chem.* (1999) 1137.
- [19] Recent reviews, see: (a) N. Miyaura, in: P.V. Ramachandran, H.C. Brown (Eds.),

ACS Symposium Series 783: Organoboranes for Syntheses (Chapter 7),
American Chemical Society, Washington DC, 2001;

(b) T. Hayashi, Synlett (2001) 879.

[20] N. Kornblum, A.P. Lurie, J. Am. Chem. Soc. 81 (1959) 2705.

[21] G. Sartori, G. Casnati, F. Bigi, G. Predieri, J. Org. Chem. 55 (1990) 4371.

Scheme 1.

KOPh/toluene/50 °C/1 h: 88% (Z > 99%)

K₂CO₃/dioxane/80 °C/5 h: 91% (Z = 64%)

Scheme 2.

Table 1
Effects of bases and solvents ^a

Entry	Base/Solvent	Temp/°C	Time/h	Yield/%
^b				
1	KOPh/toluene	50	2	9 ^c
2	2-MeC ₆ H ₄ OK/toluene	50	2	4 ^d
3	K ₂ CO ₃ /dioxane	50	16	67 ^e
4	K ₃ PO ₄ /dioxane	50	16	58 ^e
5	KOAc/dioxane	50	16	4
6	K ₂ CO ₃ /toluene	50	16	1
7	K ₂ CO ₃ /dioxane	80	5	67 ^e
8	K ₂ CO ₃ /toluene	80	24	65 ^e

^a The coupling reaction of diboron **1** (1.1 mmol) with ethyl 2-(trifluoromethanesulfonyloxy)-1-cyclopentenecarboxylate (1.0 mmol) was carried out in the presence of PdCl₂(PPh₃)₂ (0.03 mmol), PPh₃ (0.06 mmol), and base (1.5 mmol) in 6 ml of solvent.

^b GC yields based on the triflate.

^c The reaction accompanied PhOTf (90%).

^d The reaction produced 2-MeC₆H₄OTf (69%)

^e The reactions gave a dimer of the triflate (30-40%).

Table 2
 Synthesis of vinylboronates **3** (Scheme 1) ^a

Entry	Triflate 2	Yield/% ^b	
		Method A ^c	Method B ^d
1		9 (2 h)	67 (5 h)
2		78 (1 h)	91 (6 h)
3		76 (1 h)	74 (3 h)
4		72 (1 h)	60 (5 h)
5		60 (6 h)	98 (3 h)
6		21 (1 h)	78 (2 h)

Table 2 (continued)

7		81 (2 h)	91 (5 h)
8		25 (2 h)	78 (2 h)
9		72 (1 h)	77 (3 h)
10	<i>E</i> > 99%	93 ^e (1 h)	72 ^e (3 h)
11	<i>E</i> > 99%	75 ^e (1 h)	76 ^e (2 h)

^a All reactions were conducted by using diboron **1** (1.1 mmol), triflate **2** (1.0 mmol), PdCl₂(PPh₃)₂ (0.03 mmol), PPh₃ (0.06 mmol), base (1.5 mmol), and solvent (6 ml).

^b GC yields based on triflates **2**.

^c Method A: KOPh/toluene/50 °C.

^d Method B: K₂CO₃/dioxane/80 °C.

^e (*Z*)-**3** were obtained with isomeric purities over 99%.

Table 3

One-pot synthesis of 1,3-dienes **7**^a

Entry	1,3-Diene 7 ^b	Yield/% ^c
1		76 ^d
2		76
3		77

^a To a solution of vinylboronate **3** resulted by the reaction of diboron **1** (1.1 mmol) with triflate **2** (1.1 mmol) in toluene or dioxane (4 ml) were added second triflate **6** (1.0 mmol), PdCl₂(dppf) (0.03 mmol), K₃PO₄ (3.0 mmol), and dioxane (4 ml), and the mixture was stirred at 80 °C for 16 h.

^b Left part of dotted line comes from **2** and right part from **6**.

^c Isolated yields based on triflates **6**.

^d GC yield after 5 h.

Table 4

1,4-Addition of **3** to α,β -unsaturated ketones **8**^a

Entry	Adduct 9 ^b	Yield/% ^c
1		77
2		71
3		80
4		83
5		93
6		65 ^d

^a A mixture of vinylboronate **3** (1.0 mmol), α,β -unsaturated ketone **8** (1.1 mmol), $[\text{Rh}(\text{COD})_2]\text{BF}_4$ (0.03 mmol), and aqueous dioxane (dioxane:H₂O = 6:1, 6 ml) was stirred at 90 °C for 6 h.

^b Left part of dotted line comes from **3** and right part from **8**.

^c Isolated yields based on vinylboronates **3**.

^d 2.0 mmol of 2-cyclohexen-1-one was used.

Graphical Abstract (60% reduction)

Cross-coupling reaction of bis(pinacolato)diboron with vinyl triflates β -substituted by a carbonyl group smoothly proceeded in the presence of $\text{PdCl}_2(\text{PPh}_3)_2$ - 2PPh_3 (3 mol%) and KOPh in toluene or K_2CO_3 in dioxane to produce cyclic and acyclic β -boryl- α,β -unsaturated esters, amides, and ketones in high yields.