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Synthesis of multisubstituted 1,3-butadienes using the ruthenium-catalysed double addition of trimethylsilyldiazomethane to alkynylboronates

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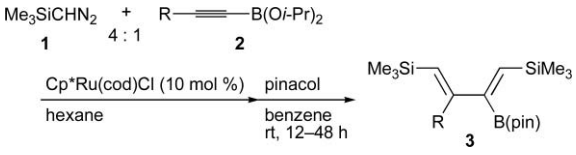
The ruthenium-catalysed double addition of trimethylsilyldiazomethane to alkynes developed by Dixneuf and co-workers was applied to the synthesis of 2-alkyl- or 2-aryl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1,4-bis(trimethylsilyl)-1,3-butadienes by use of alkynylboronates instead of alkynes. Di- and tetrasubstituted 1,3-butadienes were prepared from a 2-boryl-1,4-disilyl-1,3-butadiene, using the Suzuki–Miyaura coupling reaction, iodolysis of the alkenylsilane moieties with *N*-iodosuccinimide and hydrolysis of the carbon–silicon bonds with trifluoroacetic acid. The same compound was converted also to a bicyclic compound, a trisubstituted 1,3-butadiene and a dienone through the Diels–Alder reaction, oxidation of the alkenylboronate moiety and the Mukaiyama aldol reaction.

Introduction

Conjugated dienes are versatile synthetic precursors, which in particular undergo addition reactions in combination with transition metal catalysts.[1] Although much effort has been devoted to development of methods to prepare conjugated dienes,[2] it is still difficult to synthesize multisubstituted ones using readily available compounds.[3,4] Mori and co-workers reported an excellent route to 2,3-disubstituted 1,3-butadienes from readily available internal alkynes and ethenes by ruthenium-catalysed enyne metathesis.[5] Dixneuf and co-workers expanded the strategy that utilizes the reaction of ruthenium–carbene complexes with alkynes by using trimethylsilyldiazomethane (**1**) or ethyl diazoacetate as a carbene source, where double addition of diazoalkanes to alkynes afforded 1,2,3,4-tetrasubsituted 1,3-butadienes.[6] We expected that introduction of a transformable group to the alkyne moiety in addition to conversion of the silyl group derived from **1** to organic groups would enhance the utility of the Dixneuf excellent method. Here we report the ruthenium-catalysed double addition of trimethylsilyldiazomethane to alkynylboronates to give 2-boryl-3-organo-1,4-disilyl-1,3-butadienes, which can be converted into multisubstituted 1,3-butadienes including those having four different organic groups at the 1-, 2-, 3- and 4-positions.

Results and discussion

The Dixneuf reaction conditions can be applied to the double addition of **1** to diisopropyl alkynylboronates (**2**) essentially as they stand but hexane was found to be a better solvent than 1,4-dioxane. Thus, treatment of **1** and diisopropyl 1-octynylboronate (**2a**) with 10 mol% of Cp*Ru(cod)Cl in hexane at 80 °C for 12 h followed by transesterification[7] with pinacol provided 4,4,5,5-tetramethyl-2-[(1*E*,3*E*)-3-hexyl-1,4-bis(trimethylsilyl)buta-1,3-dien-2-yl]-1,3,2-dioxaborolane (**3a**)[8] in 82% yield (eqn. (1) and entry 1 of Table 1). Various alkynylboronates accepted the double addition of the carbene to give 2-boryl-3-organo-1,4-disilyl-1,3-butadienes (Table 1). Chloroalkane and ether moieties were compatible with the addition (entries 2 and 3). An ethynylboronate having an electron-withdrawing group participated in the reaction (entry 4). A phenylethynylboronate, and related compounds having an electron-withdrawing or -donating group underwent the double addition at lower temperature than aliphatic alkynylboronates (entries 5–7).



(1)

The double addition products can be transformed to multisubstituted 1,3-butadienes using the Suzuki–Miyaura coupling protocol (Scheme 1).[3a–c] For example, alkenylboronate **3a** was subjected to the coupling reaction with iodobenzene to give 1,4-disilyl-1,3-butadiene **4**,[9] which underwent selective iodolysis of the Si–C bond on the more electron-rich alkyl-substituted double bond by treatment with 1.0 equiv. of *N*-iodosuccinimide (NIS) at 0 °C.[10] Alkenyl iodide **5** cross-coupled with *p*-tolylboronic acid again using the Suzuki–Miyaura coupling reaction to afford monosilyldiene **6** in 81% yield.[11] Iodolysis of **6** with NIS at room temperature gave alkenyl iodide **7**, which was transformed to 1,3-butadiene **8** having four different organic groups at 1-, 2-, 3- and 4-positions.[11] Alternatively, both of the Si–C bonds in **4** were iodolysed to give diiodide **9**, which reacted with *p*-tolylboronic acid leading to tetrasubstituted 1,3-butadiene **10** with three different organic groups.[11] Disubstituted diene **11** was obtained by hydrolysis of disilyldiene **4** with trifluoroacetic acid.[12]

In addition to the transformation based on the Suzuki–Miyaura coupling reaction, the double addition products are applicable to other carbon–carbon bond forming reactions (Scheme 2). For example, the reaction of **3a** with *N*-phenylmaleimide gave Diels–Alder product **12**, where the boryl group was unaffected.[13] Oxidation of the alkenylboronate moiety of **3a** with hydrogen peroxide–urea complex[14] followed by treatment with trimethylsilyl triflate afforded diene **14**[15] having a silyl enolate moiety through ketone **13**; **14** then underwent the boron trifluoride-catalysed Mukaiyama aldol reaction to give dienone **15**.[16]

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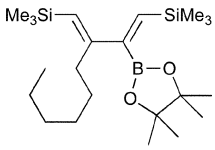
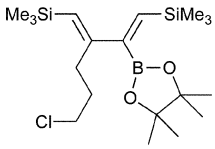
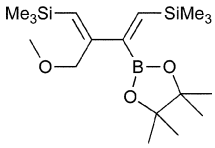
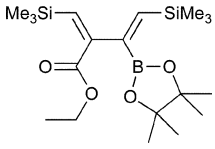
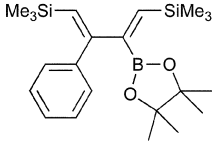
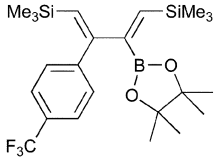
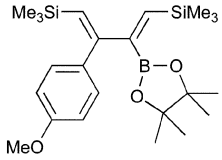
Table 1 Ruthenium-catalysed double addition of trimethylsilyldiazomethane to alkynylboronates[a]

Entry	R	T/°C	t/h	Product	Yield (%)[b]
1	Hex	80	12		82
2	$Cl(CH_2)_3$	80	12		73
3	$MeOCH_2$	80	12		83
4	EtOCO	80	12		64
5	Ph	0	48		77
6[c]	4-CF_3-C_6H_4	0	24		81
7[c]	4-MeO-C_6H_4	0	7		72

[a] The reaction was carried out in hexane (0.2 mL) using trimethylsilyldiazomethane (**1**: 0.4 mL of a 2.0 M solution in hexane, 0.80 mmol), an alkynylboronate (**2**: 0.20 mmol) and Cp*Ru(cod)Cl (20 μmol), which was followed by transesterification with pinacol. [b] Isolated yield based on the alkynylboronate. [c] Transesterification was done in the presence of a catalytic amount of acetic acid.

Conclusion

We have disclosed a convenient method to prepare multisubstituted 1,3-butadienes, utilizing the ruthenium-catalysed double addition of trimethylsilyldiazomethane to alkynylboronates. The combination of the ruthenium-catalysed reaction with the palladium-catalysed Suzuki–Miyaura coupling reaction enables us to prepare highly conjugated systems based on the 1,3-butadiene framework.

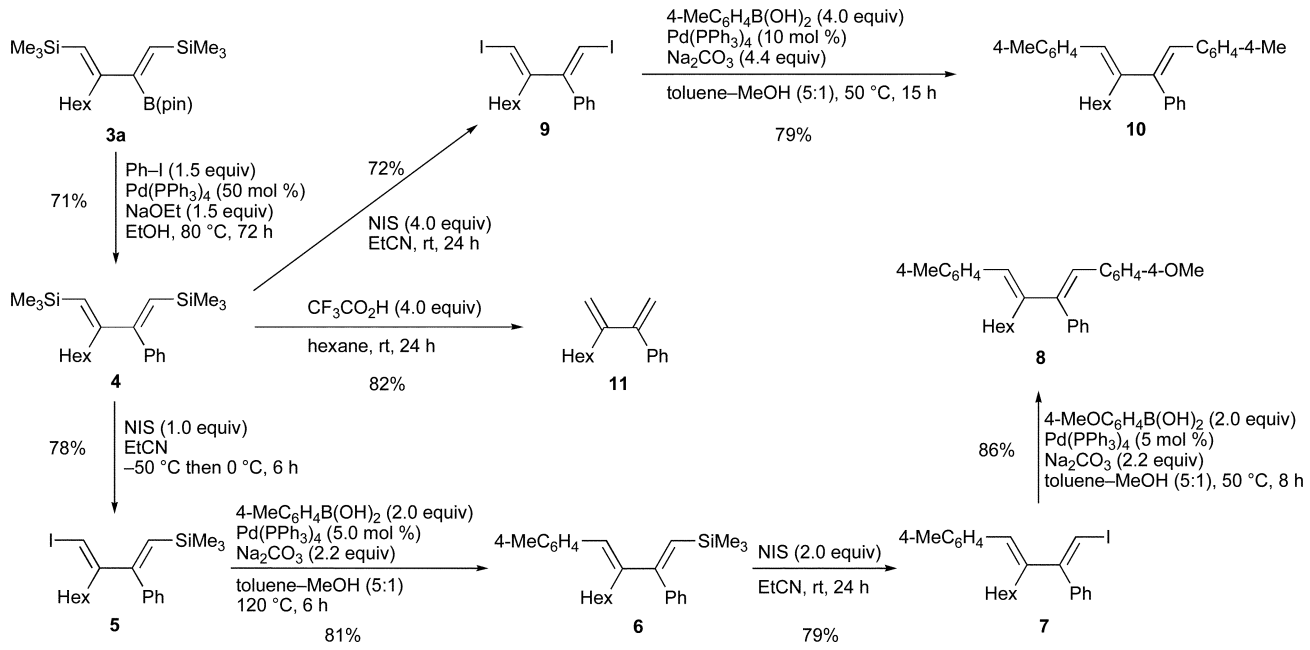
Experimental

General remarks

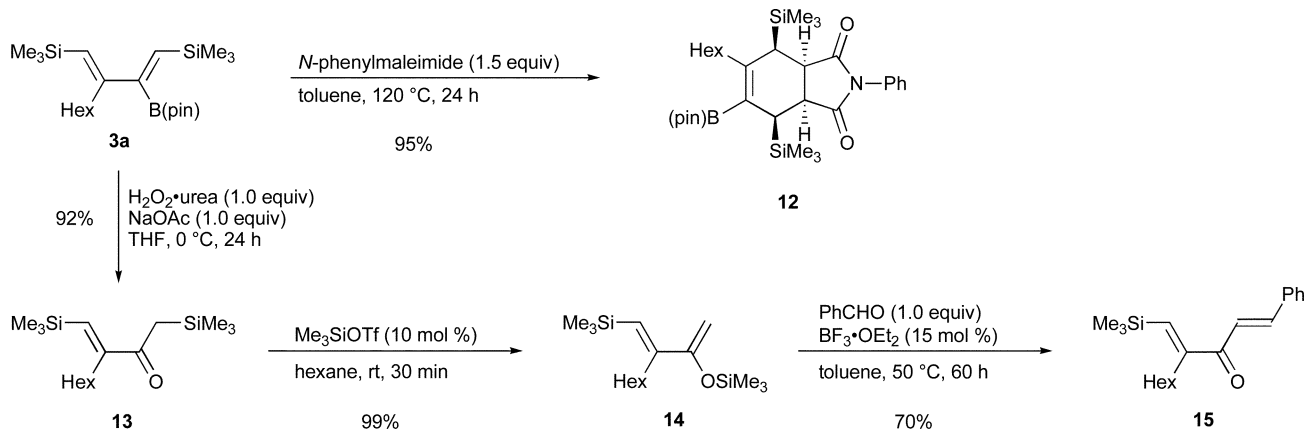
All manipulations of oxygen- and moisture-sensitive materials were conducted with standard Schlenk techniques under a nitrogen atmosphere. Nuclear magnetic resonance spectra were taken on a Varian Gemini 2000 (^{1}H, 300 MHz) or a Varian UNITY 500 plus (^{13}C, 126 MHz) spectrometer. Preparative recycling gel permeation chromatography was performed with a JAI LC-908 equipped with JAIGEL-1H and -2H using chloroform as an eluent. High-resolution mass spectra were obtained with a Bruker Bio APEX 70e (EI) or JEOL JMS-HX110A (FAB+) spectrometer. Unless otherwise noted, reagents were commercially available and used without further purification. Hexane, diethyl ether, THF and toluene were distilled from sodium/benzophenone ketyl. Cp*Ru(cod)Cl was prepared according to the literature procedure.[17]

Preparation of alkynylboronates. A general procedure[18]

To a solution of an alkyne (10 mmol) in diethyl ether (20 mL) was added BuLi (1.56 M in hexane, 6.4 mL, 10 mmol) at −78 °C and the reaction mixture was stirred for 3 h at −78 °C. The resulting mixture was added to a solution of triisopropyl borate (1.88 g, 10 mmol) in diethyl ether (20 mL) and slowly warmed to room temperature over 3 h. The solvent was removed *in vacuo* for



Scheme 1 Transformation of double addition product **3a** to di- and tetrasubstituted 1,3-butadienes.



Scheme 2 Transformation of double addition product **3a** to a bicyclic compound and a dienone.

24 h. Diethyl ether (10 mL) and anhydrous hydrogen chloride (1.5 M diethyl ether solution, 6.6 mL, 10 mmol) were added to the resulting powder at −78 °C and the mixture was slowly warmed to room temperature over 3 h. Filtration of the resulting suspension followed by distillation gave alkynylboronates **2**.[18]

Diisopropyl oct-1-ynylboronate (2a). Bp 70 °C/0.3 mmHg, a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (t, $J = 6.9$ Hz, 3 H), 1.19 (d, $J = 6.0$ Hz, 12 H), 1.24–1.60 (m, 8 H), 2.27 (t, $J = 6.9$ Hz, 2 H), 4.55 (sept, $J = 6.0$ Hz, 2 H).

Diisopropyl 5-chloropent-1-ynylboronate (2b). Bp 60 °C/0.2 mmHg, a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.19 (d, $J = 6.0$ Hz, 12 H), 2.00 (quint, $J = 6.6$ Hz, 2 H), 2.48 (t, $J = 6.6$ Hz, 2 H), 3.66 (t, $J = 6.6$ Hz, 2 H), 4.54 (sept, $J = 6.0$ Hz, 2 H).

Diisopropyl 3-methoxyprop-1-ynylboronate (2c). Bp 60 °C/1.0 mmHg, a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.20 (d, $J = 6.3$ Hz, 12 H), 3.40 (s, 3 H), 4.16 (s, 2 H) 4.57 (sept, $J = 6.3$ Hz, 2 H).

Diisopropyl (ethoxycarbonyl)ethynylboronate (2d). Bp 60 °C/0.1 mmHg, a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.21 (d, $J = 6.3$ Hz, 12 H), 1.31 (t, $J = 7.2$ Hz, 3 H), 4.25 (q, $J = 7.2$ Hz, 2 H), 4.56 (sept, $J = 6.3$ Hz, 2 H).

Diisopropyl phenylethynylboronate (2e). Bp 80 °C/0.3 mmHg, a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (d, $J = 6.0$ Hz, 12 H), 4.65 (sept, $J = 6.0$ Hz, 2 H), 7.28–7.38 (m, 3 H), 7.47–7.55 (m, 2 H).

Diisopropyl 4-(trifluoromethyl)phenylethynylboronate (2f). Bp 70 °C/0.2 mmHg, a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (d, $J = 6.3$ Hz, 12 H), 4.64 (sept, $J = 6.3$ Hz, 2 H), 7.57–7.61 (m, 4 H).

Diisopropyl 4-methoxyphenylethynylboronate (2g). Bp 75 °C/0.2 mmHg, a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.24 (d, $J = 6.3$ Hz, 12 H), 3.81 (s, 3 H), 4.64 (sept, $J = 6.3$ Hz, 2 H), 6.81–6.87 (m, 2 H), 7.42–7.48 (m, 2 H).

Ruthenium-catalysed double addition of trimethylsilyldiazomethane to alkynylborates. A general procedure

A solution (0.2 mL) of an alkynylboronate (0.20 mmol) and Cp*Ru(cod)Cl (7.6 mg, 20 μmol) in hexane (0.2 mL) was degassed by three freeze–thaw cycles. To the solution was added trimethylsilyldiazomethane (2.0 M hexane solution, 0.4 mL, 0.80 mmol), and stirred at 80 or 0 °C. After the time specified in Table 1, the solvent was evaporated, and benzene (1.0 mL) and pinacol (11.8 mg, 1.00 mmol) was added to the resulting mixture [for entries 6 and 7 in Table 1, acetic acid (0.6 mg. 0.01 mmol) also was added]. After stirring at room temperature for 12–48 h, evaporation of the solvent followed by purification

by gel permeation chromatography gave the corresponding 1,3-butadiene. Yields are listed in Table 1.

4,4,5,5-Tetramethyl-2-[(1*E*,3*E*)-3-hexyl-1,4-bis(trimethylsilyl)-buta-1,3-dien-2-yl]-1,3,2-dioxaborolane (3a). A pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.11 (s, 9 H), 0.15 (s, 9 H), 0.88 (t, $J = 6.9$ Hz, 3 H), 1.22–1.38 (m, 8 H), 1.31 (s, 12 H), 2.28–2.37 (m, 2 H), 5.45 (s, 1 H), 6.35 (s, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 0.2, 0.3, 14.0, 22.6, 25.3, 29.5, 29.6, 31.7, 34.0, 83.6, 127.1, 142.7, 163.1; the resonance of *C*–B was not detected due to the low intensity. HRMS (EI): Calcd for $C_{22}H_{45}BO_2Si_2$ $[M]^+$, 408.30486; found, 408.30689.

4,4,5,5-Tetramethyl-2-[(1*E*,3*E*)-3-(3-chloropropyl)-1,4-bis(trimethylsilyl)buta-1,3-dien-2-yl]-1,3,2-dioxaborolane (3b). A pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.13 (s, 9 H), 0.15 (s, 9 H), 1.31 (s, 12 H), 1.75–1.87 (m, 2 H), 2.47–2.55 (m, 2 H), 3.52 (t, $J = 6.6$ Hz, 2 H), 5.51 (s, 1 H), 6.37 (s, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 0.2, 0.3, 25.3, 31.3, 32.4, 45.1, 83.7, 128.5, 143.8, 161.1; the resonance of *C*–B was not detected due to the low intensity. HRMS (EI): Calcd for $C_{19}H_{38}BClO_2Si_2$ $[M]^+$, 400.21897; found, 400.22044.

4,4,5,5-Tetramethyl-2-[(1*E*,3*Z*)-3-methoxymethyl-1,4-bis(trimethylsilyl)buta-1,3-dien-2-yl]-1,3,2-dioxaborolane (3c). A pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.12 (s, 9 H), 0.15 (s, 9 H), 1.30 (s, 12 H), 3.24 (s, 3 H), 4.19 (s, 2 H), 5.74 (s, 1 H), 6.57 (s, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 0.3, 0.4, 25.2, 57.3, 73.2, 83.5, 129.2, 145.8, 159.3; the resonance of *C*–B was not detected due to the low intensity. HRMS (EI): Calcd for $C_{18}H_{37}BO_3Si_2$ $[M–Me]^+$, 353.21375; found, 353.21404.

4,4,5,5-Tetramethyl-2-[(1*E*,3*Z*)-3-ethoxycarbonyl-1,4-bis(trimethylsilyl)buta-1,3-dien-2-yl]-1,3,2-dioxaborolane (3d). A pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.14 (s, 9 H), 0.16 (s, 9 H), 1.28 (s, 12 H), 1.31 (t, $J = 7.2$ Hz, 3 H), 4.20 (q, $J = 7.2$ Hz, 2 H), 6.27 (s, 1 H), 6.53 (s, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ −0.3, 0.2, 14.2, 25.1, 60.6, 83.7, 139.6, 149.2, 153.7, 168.5; the resonance of *C*–B was not detected due to the low intensity. HRMS (EI): Calcd for $C_{19}H_{37}BO_4Si_2$ $[M]^+$, 396.23212; found, 396.23377.

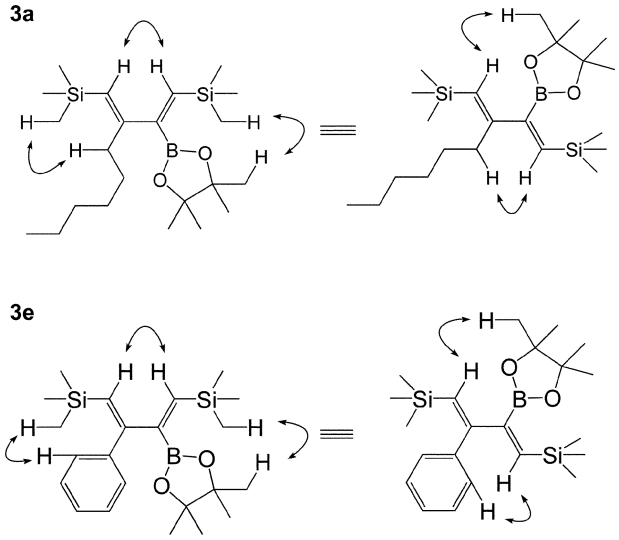
4,4,5,5-Tetramethyl-2-[(1*E*,3*Z*)-3-phenyl-1,4-bis(trimethylsilyl)buta-1,3-dien-2-yl]-1,3,2-dioxaborolane (3e). A pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ −0.22 (s, 9 H), 0.09 (s, 9 H), 1.31 (s, 12 H), 5.95 (s, 1 H), 6.01 (s, 1 H), 7.08–7.14 (m, 2 H), 7.21–7.31 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ −0.4, 0.1, 25.4, 83.9, 126.9, 127.5, 130.0, 131.7, 141.9, 145.2, 161.9; the resonance of *C*–B was not detected due to the low intensity. HRMS (EI): Calcd for $C_{22}H_{37}BO_2Si_2$ $[M]^+$, 400.24230; found, 400.24404.

4,4,5,5-Tetramethyl-2-[(1*E*,3*Z*)-3-{4-(trifluoromethyl)phenyl}-1,4-bis(trimethylsilyl)buta-1,3-dien-2-yl]-1,3,2-dioxaborolane (3f). A pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ −0.21 (s, 9 H), 0.10 (s, 9 H), 1.30 (s, 12 H), 5.95 (s, 1 H), 6.03 (s, 1 H), 7.23–7.25 (m, 2 H), 7.54–7.57 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ −0.2, 0.0, 25.4, 84.0, 124.4 (q, $^1J_{C–F} = 272$ Hz), 124.5 (q, $^3J_{C–F} = 3.8$ Hz), 129.3 (q, $^2J_{C–F} = 32.7$ Hz), 130.2, 132.5, 146.0, 146.4, 160.4; the resonance of *C*–B was not detected due to the low intensity. HRMS (EI): Calcd for $C_{23}H_{36}BF_3O_2Si_2$ $[M]^+$, 468.22968; found, 468.22868.

4,4,5,5-Tetramethyl-2-[(1*E*,3*Z*)-3-(4-methoxyphenyl)-1,4-bis(trimethylsilyl)buta-1,3-dien-2-yl]-1,3,2-dioxaborolane (3g). A pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ −0.20 (s, 9 H), 0.09 (s, 9 H), 1.31 (s, 12 H), 3.82 (s, 3 H), 5.91 (s, 1 H), 6.02 (s, 1 H), 7.00–7.03 (m, 2 H), 7.03–7.06 (m, 2 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ −0.1, 0.0, 25.5, 55.2, 83.8, 112.9, 131.0, 131.3, 134.4, 144.9, 158.8, 161.6; the resonance of *C*–B was not detected due to the low intensity. HRMS (EI): Calcd for $C_{23}H_{39}BO_3Si_2$ $[M]^+$, 430.25285; found, 430.25077.

Determination of configuration of the double addition products with NOESY NMR spectra

Double addition products **3a** and **3e** as the representatives were subjected to NOESY NMR measurement. The cross-peak between the methyl protons of one of the trimethylsilyl groups and R (**3a**: the methylene protons of the allylic position of the hexyl group; **3e**: the *ortho*-protons of the phenyl group) in addition to that between the methyl protons of the other trimethylsilyl group and the methyl protons of the pinacol ester were observed. These results in conjunction with other observed cross-peaks shown below should show that the silyl groups are located *cis* to R or the boronate group.



The coupling reaction of 4,4,5,5-tetramethyl-2-[(1*E*,3*E*)-3-hexyl-1,4-bis-(trimethylsilyl)buta-1,3-dien-2-yl]-1,3,2-dioxaborolane (3a) with iodobenzene[9]

A solution of **3a** (40.9 mg, 0.100 mmol), iodobenzene (30.6 mg, 0.150 mmol), $Pd(PPh_3)_4$ (57.8 mg, 0.050 mmol) and NaOEt (0.5 M ethanol solution, 0.3 mL, 0.150 mmol) in ethanol (1.0 mL) was degassed by three freeze–thaw cycles. After the solution was stirred at 80 °C for 72 h, water (10 mL) was added and the resulting mixture was extracted with diethyl ether (20 mL × 3). The combined organic layer was washed with brine (10 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification by gel permeation chromatography gave (1*E*,3*E*)-3-hexyl-2-phenyl-1,4-bis(trimethylsilyl)buta-1,3-diene (**4**: 25.3 mg, 71%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ −0.21 (s, 9 H), 0.07 (s, 9 H), 0.89 (t, $J = 7.2$ Hz, 3 H), 1.20–1.51 (m, 8 H), 2.30–2.39 (m, 2 H), 5.24 (s, 1 H), 5.89 (s, 1H), 7.05–7.10 (m, 2 H), 7.23–7.31 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ −0.1, 0.2, 14.0, 22.6, 29.5, 29.8, 31.7, 33.6, 126.8, 127.5, 128.2, 129.5, 130.5, 142.8, 159.9, 160.2. HRMS (EI): Calcd for $C_{22}H_{38}Si_2$ $[M]^+$, 358.25100; found, 358.25029.

Partial iodolysis of (1*E*,3*E*)-3-hexyl-2-phenyl-1,4-bis(trimethylsilyl)buta-1,3-diene (4)[10]

N-Iodosuccinimide (9.0 mg, 0.040 mmol) was added to a solution of **4** (14.3 mg, 0.040 mmol) in propionitrile (0.5 mL) at −50 °C. The reaction was slowly warmed to 0 °C over 6 h, at which time a saturated sodium thiosulfate aqueous solution (5.0 mL) was added. The mixture was extracted with diethyl ether (10 mL × 3), then the combined organic layers were washed with brine (10 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification by gel permeation chromatography gave (1*E*,3*E*)-2-hexyl-1-iodo-3-phenyl-4-(trimethylsilyl)buta-1,3-diene (**5**: 12.9 mg, 78%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ −0.20 (s, 9 H), 0.91 (t, $J = 6.6$ Hz, 3 H), 1.24–1.50 (m, 8 H), 2.42–2.52

(m, 2 H), 5.95 (s, 1 H), 6.05 (s, 1 H), 7.04–7.12 (m, 2 H), 7.26–7.33 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ −0.3, 14.0, 22.6, 27.8, 29.1, 31.6, 35.2, 85.1, 127.4, 127.8, 129.4, 130.2, 141.4, 154.1, 155.5. HRMS (EI): Calcd for $C_{19}H_{29}ISi$ $[M]^+$, 412.10817; found, 412.10655.

The coupling reaction of (1*E*,3*E*)-2-hexyl-1-iodo-3-phenyl-4-(trimethylsilyl)buta-1,3-diene (5) with *p*-tolylboronic acid[11]

A mixture of **5** (24.7 mg, 0.060 mmol), *p*-tolylboronic acid (16.3 mg, 0.120 mmol), $Pd(PPh_3)_4$ (3.5 mg, 0.003 mmol), Na_2CO_3 (15.3 mg, 0.144 mmol), toluene (0.5 mL) and methanol (0.1 mL) was degassed by three freeze–thaw cycles. After the solution was stirred at 120 °C for 6 h, water (10 mL) was added and the resulting mixture was extracted with diethyl ether (20 mL × 3). The combined organic layer was washed with brine (10 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification by gel permeation chromatography gave (1*Z*,3*E*)-3-hexyl-2-phenyl-4-(*p*-tolyl)-1-(trimethylsilyl)buta-1,3-diene (**6**: 18.4 mg, 81%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ −0.19 (s, 9 H), 0.89 (t, J = 6.6 Hz, 3 H), 1.24–1.60 (m, 8 H), 2.32 (s, 3 H), 2.41–2.50 (m, 2 H), 5.95 (s, 1 H), 6.05 (s, 1 H) 7.03–7.12 (m, 4 H), 7.14–7.19 (m, 2 H), 7.26–7.34 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ −0.1, 14.0, 21.1, 22.6, 28.2, 29.1, 29.4, 31.5, 126.9, 127.6, 128.4, 128.7, 128.8, 129.7, 131.1, 135.6, 136.1, 142.8, 145.4, 159.0. HRMS (EI): Calcd for $C_{26}H_{36}Si$ $[M]^+$, 376.25844; found, 376.25921.

Iodolysis of (1*Z*,3*E*)-3-hexyl-2-phenyl-4-(*p*-tolyl)-1-(trimethylsilyl)buta-1,3-diene (6)[10]

N-Iodosuccinimide (45.0 mg, 0.200 mmol) was added to a solution of **6** (37.6 mg, 0.100 mmol) in propionitrile (1 mL) at room temperature and the solution was stirred at the temperature for 24 h. The resulting mixture was treated with a saturated sodium thiosulfate aqueous solution (1.0 mL) and extracted with diethyl ether (10 mL × 3). The combined organic layer was washed with brine (10 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification by gel permeation chromatography gave (1*Z*,3*E*)-3-hexyl-1-iodo-2-phenyl-4-(*p*-tolyl)buta-1,3-diene (**7**: 34.0 mg, 79%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.86 (t, J = 6.6 Hz, 3 H), 1.18–1.54 (m, 8 H), 2.28–2.35 (m, 2 H), 2.33 (s, 3 H), 6.39 (s, 1 H), 6.72 (s, 1 H), 7.12 (s, 4 H), 7.21–7.27 (m, 2 H), 7.30–7.44 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.0, 21.2, 22.6, 28.8, 28.9, 29.2, 31.5, 78.9, 127.8, 128.2, 128.7, 128.9, 129.2, 131.4, 134.6, 136.7, 141.4, 143.5, 155.3. HRMS (EI): Calcd for $C_{23}H_{27}I$ $[M]^+$, 430.11561; found, 430.11462.

The coupling reaction of (1*Z*,3*E*)-3-hexyl-1-iodo-2-phenyl-4-(*p*-tolyl)buta-1,3-diene (7) with *p*-methoxyphenylboronic acid[11]

A mixture of **7** (17.2 mg, 0.040 mmol), *p*-methoxyphenylboronic acid (12.2 mg, 0.080 mmol), $Pd(PPh_3)_4$ (2.3 mg, 0.002 mmol), Na_2CO_3 (9.3 mg, 0.088 mmol), toluene (1.0 mL) and methanol (0.2 mL) was degassed by three freeze–thaw cycles. After the solution was stirred at 50 °C for 8 h, water (10 mL) was added and the resulting mixture was extracted with diethyl ether (20 mL × 3). The combined organic layer was washed with brine (10 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification by column chromatography on silica gel (hexane–ethyl acetate = 100 : 1) gave (1*Z*,3*E*)-3-hexyl-1-(*p*-methoxyphenyl)-2-phenyl-4-(*p*-tolyl)buta-1,3-diene (**8**: 14.1 mg, 86%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (t, J = 6.8 Hz, 3 H), 1.20–1.38 (m, 6 H), 1.56–1.65 (m, 2 H), 2.34 (s, 3 H), 2.41–2.47 (m, 2 H), 3.74 (s, 3 H), 6.35 (s, 1 H), 6.61–6.67 (m, 2 H), 6.73 (s, 1 H), 6.81–6.86 (m, 2 H), 7.13 (s, 4 H), 7.18–7.22 (m, 2 H), 7.28–7.34 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.0, 21.1, 22.6, 28.6, 29.1, 29.4, 31.6, 55.2, 113.4, 126.4, 127.0, 128.6, 128.7, 128.8, 129.7, 130.2, 130.3, 130.8, 135.6, 136.0, 140.3, 143.2, 145.3, 158.2. HRMS (FAB+): Calcd for $C_{30}H_{34}O$ $[M]^+$, 410.26079; found, 410.2613.

Iodolysis of (1*E*,3*E*)-3-hexyl-2-phenyl-1,4-bis(trimethylsilyl)-buta-1,3-diene (4)[10]

N-Iodosuccinimide (90.0 mg, 0.400 mmol) was added to a solution of **4** (35.9 mg, 0.100 mmol) in propionitrile (1 mL) at room temperature and the solution was stirred at the temperature for 24 h. The resulting mixture was treated with a saturated sodium thiosulfate aqueous solution (1.0 mL) and extracted with diethyl ether (10 mL × 3). The combined organic layer was washed with brine (10 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification by gel permeation chromatography gave (1*E*,3*E*)-3-hexyl-1,4-diiodo-2-phenylbuta-1,3-diene (**9**: 33.6 mg, 72%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.90 (t, J = 6.6 Hz, 3 H), 1.20–1.48 (m, 8 H), 2.30–2.38 (m, 2 H), 6.28 (s, 1 H), 6.79 (s, 1 H), 7.12–7.18 (m, 2 H), 7.36–7.43 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.0, 22.5, 27.5, 29.0, 31.5, 35.4, 81.0, 84.6, 128.2, 128.4, 128.9, 140.2, 151.9, 152.1. HRMS (EI): Calcd for $C_{16}H_{20}I_2$ $[M]^+$, 465.96534; found, 465.96717.

The coupling reaction of (1*E*,3*E*)-3-hexyl-1,4-diiodo-2-phenyl-buta-1,3-diene (9) with *p*-tolylboronic acid[11]

A mixture of **9** (23.3 mg, 0.050 mmol), *p*-tolylboronic acid (27.2 mg, 0.200 mmol), $Pd(PPh_3)_4$ (5.8 mg, 0.005 mmol), Na_2CO_3 (23.3 mg, 0.220 mmol), toluene (1.0 mL) and methanol (0.2 mL) was degassed by three freeze–thaw cycles. After the solution was stirred at 50 °C for 15 h, water (10 mL) was added and the resulting mixture was extracted with diethyl ether (20 mL × 3). The combined organic layer was washed with brine (10 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification by column chromatography on silica gel (hexane) gave (1*Z*,3*E*)-3-hexyl-2-phenyl-1,4-di(*p*-tolyl)buta-1,3-diene (**10**: 15.5 mg, 79%) as a pale yellow solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.87 (t, J = 6.9 Hz, 3 H), 1.20–1.38 (m, 6 H), 1.52–1.65 (m, 2 H), 2.25 (s, 3 H), 2.34 (s, 3 H), 2.42–2.48 (m, 2 H), 6.37 (s, 1 H), 6.75 (s, 1 H), 6.78–6.82 (m, 2 H), 6.89–6.93 (m, 2 H), 7.13 (s, 4 H), 7.18–7.22 (m, 2 H), 7.28–7.34 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.0, 21.08, 21.14, 22.6, 28.6, 29.0, 29.3, 31.6, 126.9, 127.0, 128.5, 128.6, 128.7, 128.8, 129.5, 130.0, 130.1, 134.8, 135.6, 136.1, 136.2, 140.2, 144.2, 145.3. HRMS (FAB+): Calcd for $C_{30}H_{34}$ $[M]^+$, 394.26588; found, 394.2657.

Hydrolysis of (1*E*,3*E*)-3-hexyl-2-phenyl-1,4-bis(trimethylsilyl)-buta-1,3-diene (4)[12]

A solution of **4** (35.8 mg, 0.100 mmol) and trifluoroacetic acid (45.6 mg, 0.400 mmol) in hexane (2.5 mL) was stirred at room temperature for 24 h. The resulting mixture was treated with a saturated $NaHCO_3$ aqueous solution (5 mL) and extracted with diethyl ether (10 mL × 3). The combined organic layer was washed with brine (10 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification by gel permeation chromatography gave 3-hexyl-2-phenylbuta-1,3-diene (**11**: 17.6 mg, 82%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.88 (t, J = 6.9 Hz, 3 H), 1.20–1.51 (m, 8 H), 2.24 (t, J = 7.5 Hz, 2 H), 4.94 (d, J = 1.1 Hz, 1 H), 5.06 (d, J = 1.1 Hz, 1 H), 5.17 (d, J = 2.1 Hz, 1 H), 5.27 (d, J = 2.1 Hz, 1 H), 7.26–7.35 (m, 5 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 14.0, 22.6, 28.2, 29.0, 31.7, 34.5, 115.1, 113.3, 127.2, 128.0, 128.1, 141.4, 149.4, 150.9. MS (EI) m/z (rel. intensity): 214 (10), 199 (2), 185 (1), 171 (5), 157 (16), 143 (33), 129 (100), 115 (23), 91 (16), 77(13).

The Diels–Alder reaction of 4,4,5,5-tetramethyl-2-[(1*E*,3*E*)-3-hexyl-1,4-bis(trimethylsilyl)buta-1,3-dien-2-yl]-1,3,2-dioxaborolane (3a) with *N*-phenylmaleimide[13]

A solution of **3a** (40.9 mg, 0.100 mmol) and *N*-phenylmaleimide (26.0 mg, 0.15 mmol) in toluene (0.4 mL) was stirred at 120 °C

for 24 h. Evaporation of the solvent followed by purification by gel permeation chromatography gave (±)-(3a*R*,4*S*,7*R*,7a*S*)-5-hexyl-2-phenyl-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,7-bis(trimethylsilyl)-3a,4,7,7a-tetrahydroisoindole-1,3-dione (**12**: 55.1 mg, 95%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.25 (s, 9 H), 0.27 (s, 9 H), 0.79 (t, J = 6.6 Hz, 3 H), 1.06–1.36 (m, 8 H), 1.30 (s, 12 H), 1.41–1.49 (m, 1 H), 1.73–1.78 (m, 1 H), 1.90–2.60 (m, 1 H), 2.46–2.60 (m, 1 H), 3.28 (dd, J = 8.5, 3.8 Hz, 1 H), 3.36 (dd, J = 5.1, 3.8 Hz, 1 H), 7.17–7.24 (m, 2 H), 7.29–7.43 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 0.4, 0.5, 14.0, 22.4, 25.4, 25.5, 29.7, 31.6, 31.8, 33.4, 37.2, 44.0, 44.5, 83.3, 126.8, 128.1, 128.8, 132.5, 158.1, 178.4, 178.8. HRMS (EI): Calcd for $C_{32}H_{52}NO_4Si_2$ $[M]^+$, 581.35246; found, 581.35615.

Oxidation of 4,4,5,5-tetramethyl-2-[(1*E*,3*E*)-3-hexyl-1,4-bis(trimethylsilyl)-buta-1,3-dien-2-yl]-1,3,2-dioxaborolane (3a)[14]

A solution of **3a** (81.7 mg, 0.200 mmol), hydrogen peroxide–urea complex (18.8 mg, 0.200 mmol) and NaOAc (16.4 mg, 0.200 mmol) in THF (1.0 mL) was stirred at 0 °C for 24 h. Filtration of the resulting mixture and evaporation followed by purification by gel permeation chromatography gave (*E*)-3-hexyl-1,4-bis(trimethylsilyl)but-3-en-2-one (**13**: 54.6 mg, 92%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.07 (s, 9 H), 0.18 (s, 9 H), 0.87 (t, J = 7.2 Hz, 3 H), 1.20–1.36 (m, 8 H), 2.27–2.37 (m, 2 H), 2.48 (s, 2 H), 6.43 (s, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ −1.1, −0.4, 13.9, 22.5, 29.7, 30.3, 31.3, 31.6, 32.5, 139.6, 157.7, 201.9. HRMS (EI): Calcd for $C_{16}H_{34}OSi_2$ $[M]^+$, 298.21463; found, 298.21314.

Preparation of (*E*)-2-hexyl-3-trimethylsiloxy-1-(trimethylsilyl)-buta-1,3-diene (14)[15]

To a solution of **13** (35.8 mg, 0.120 mmol) in hexane (1.0 mL) was added TMSOTf (1.7 mg, 0.012 mmol) and the mixture was stirred at room temperature for 30 min. Triethylamine (1.0 mL) and water (10 mL) were added and the resulting mixture was extracted with diethyl ether (20 mL × 3). The combined organic layers were washed with brine (10 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification by gel permeation chromatography gave (*E*)-2-hexyl-3-trimethylsiloxy-1-(trimethylsilyl)buta-1,3-diene (**14**: 35.7 mg, 99%) as a colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.13 (s, 9 H), 0.20 (s, 9 H), 0.89 (t, J = 6.6 Hz, 3 H), 1.20–1.52 (m, 8 H), 2.24–2.32 (m, 2 H), 4.35–4.37 (m, 1 H), 4.56–4.58 (m, 1 H), 5.95 (s, 1 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 0.0, 0.1, 14.0, 22.6, 29.8, 30.7, 31.7, 33.0, 93.0, 126.5, 152.5, 156.5. HRMS (EI): Calcd for $C_{16}H_{34}OSi_2$ $[M]^+$, 298.21463; found, 298.21305.

Aldol reaction of (*E*)-2-hexyl-3-trimethylsiloxy-1-(trimethylsilyl)buta-1,3-diene (14) with benzaldehyde

A solution of **14** (29.8 mg, 0.100 mmol), benzaldehyde (10.6 mg, 0.100 mmol) and boron trifluoride–diethyl ether complex (2.1 mg, 0.015 mmol) in toluene (1.0 mL) was stirred at 50 °C for 60 h. Triethylamine (1.0 mL) and water (10 mL) was added and the resulting mixture was extracted with diethyl ether (20 mL × 3). The combined organic layers were washed with brine (10 mL) and dried over anhydrous magnesium sulfate. Evaporation of the solvent followed by purification by gel permeation chromatography gave (1*E*,4*E*)-2-hexyl-5-phenyl-1-(trimethylsilyl)penta-1,4-dien-3-one (**15**: 21.9 mg, 70%) as a pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.22 (s, 9H), 0.87 (t, J = 6.9 Hz, 3 H), 1.20–1.43 (m, 8 H), 2.48 (t, J = 7.5 Hz, 2 H), 6.51 (s, 1 H), 7.26 (d, J = 15.9 Hz, 1 H), 7.33–7.44 (m, 3 H), 7.52–7.64 (m, 3 H). ^{13}C NMR (126 MHz, $CDCl_3$): δ −0.1, 14.0, 22.6, 29.6, 29.7, 31.7, 31.9, 123.0, 128.3, 128.9, 130.2, 135.2, 138.2, 143.6, 158.1, 193.2. HRMS (EI): Calcd for $C_{20}H_{30}OSi$ $[M]^+$, 304.20643; found, 304.20659.

References

1 J. Tsuji, *Transition Metal Reagents and Catalysts: Innovations in Organic Synthesis*, Wiley, Chichester, 2000, pp. 169–197.

2 R. C. Larock, *Comprehensive Organic Transformations*, 2nd edn., Wiley-VCH, New York, 1999, pp. 463–522.

3 The cross-coupling reaction of alkenylmetals with alkenyl halides, *i.e.*, the Suzuki–Miyaura and the Kosugi–Migita–Stille coupling reactions, should be one of the most effective methods leading to conjugated dienes in a stereospecific way. However, the coupling reaction sometimes can be cumbersome since both substrates, multisubstituted alkenylmetals and alkenyl halides, must be prepared stereoselectively prior to the coupling. For the Suzuki–Miyaura coupling reaction, see: (*a*) N. Miyaura, H. Suginome and A. Suzuki, *Tetrahedron Lett.*, 1981, **22**, 127–130; (*b*) N. Miyaura and A. Suzuki, *Chem. Rev.*, 1995, **95**, 2457–2483; (*c*) N. Miyaura, *Top. Curr. Chem.*, 2002, **219**, 11–59; (*d*) For the Kosugi–Migita–Stille coupling reaction, see: M. Kosugi, K. Sasazawa, Y. Shimizu and T. Migita, *Chem. Lett.*, 1977, 301–302; (*e*) V. Farina, V. Krishnamurthy and W. J. Scott, *Org. React.*, 1997, **50**, 1–652.

4 Although the Mizoroki–Heck reaction may be an alternative for the cross-coupling reaction, low reactivity of multisubstituted alkenes upon the reaction with alkenyl halides may be a major drawback. For recent reviews of the Mizoroki–Heck reaction, see: S. Bröse and A. de Meijere, in *Metal-catalyzed Cross-coupling Reactions*, ed. F. Diederich and P. J. Stang, Wiley-VCH, Weinheim, 1998, ch. 3, pp. 99–166; G. T. Crisp, *Chem. Soc. Rev.*, 1998, **27**, 427–436; I. P. Beletskaya and A. V. Cheprakov, *Chem. Rev.*, 2000, **100**, 3009–3066.

5 A. Kinoshita, N. Sakakibara and M. Mori, *J. Am. Chem. Soc.*, 1997, **119**, 12388–12389.

6 J. Le Paih, S. Dérien, I. Özdemir and P. H. Dixneuf, *J. Am. Chem. Soc.*, 2000, **122**, 7400–7401.

7 Since diisopropyl dienylboronates were found to be unstable to moisture, we transesterified them to pinacol esters. Transesterification was carried out in benzene (1.0 mL) at rt for 12–48 h using 5.0 equiv. of pinacol after evaporation of the reaction mixture of the ruthenium-catalysed reaction. For details, see the Experimental section.

8 Configuration of **3a** and **3e** (R = Ph) was determined by NOESY NMR spectra. For details, see the Experimental section. Although we have not elucidated the stereochemistry of the other products **3**, formation as the single isomer should show that they also have the same configuration.

9 L. Deloux, E. S. Jankun, B. V. Cheesman and M. Srebnik, *J. Am. Chem. Soc.*, 1994, **116**, 10302–10303.

10 N. A. Yakelis and W. R. Roush, *J. Org. Chem.*, 2003, **68**, 3838–3843; D. P. Stamos, A. G. Taulor and Y. Kishi, *Tetrahedron Lett.*, 1996, **37**, 8647–8650.

11 S. Ma, J. Zhang, Y. Cai and L. Lu, *J. Am. Chem. Soc.*, 2003, **125**, 13954–13955.

12 C. Dehnhardt, M. McDonald, S. Lee, H. G. Floss and J. Mulzer, *J. Am. Chem. Soc.*, 1999, **121**, 10848–10849; Z. Xi, X. Liu, J. Lu, F. Bao, H. Fan, Z. Li and T. Takahashi, *J. Org. Chem.*, 2004, **69**, 8547–8549.

13 For the Diels–Alder reaction of 1,3-butadienes having one or two boryl groups, see: A. Kamabuchi, N. Miyaura and A. Suzuki, *Tetrahedron Lett.*, 1993, **34**, 4827–4828; M. Shimizu, T. Kurahashi and T. Hiyama, *Synlett*, 2001, **34**, 1006–1008.

14 N. G. Bhat, A. Tamm and A. Gorena, *Synlett*, 2004, 297–298.

15 Y. Yamamoto, K. Ohdoi, M. Nakatani and K.-Y. Akiba, *Chem. Lett.*, 1984, 1967–1968.

16 For a review, see: T.-H. Chan, in *Comprehensive Organic Synthesis*, ed. B. M. Trost, Pergamon Press, New York, 1991, vol. 2, pp. 595–628.

17 N. Oshima, H. Suzuki and Y. Moro-oka, *Chem. Lett.*, 1984, 1161–1164.

18 H. C. Brown, N. G. Bhat and M. Srebnik, *Tetrahedron Lett.*, 1988, **29**, 2631–2634.