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Diels–Alder Reaction of 2,3-Bis-(pinacolatoboryl)-1,3-butadiene: Facile Preparation of 1,2-Bis-(pinacolatoboryl)cyclohexenes and -1,4-cyclohexadiene

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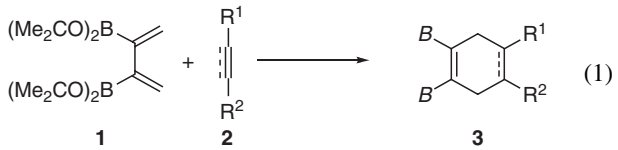
Diels–Alder reaction of 2,3-bis(pinacolato)boryl-1,3-butadiene with electron-deficient alkenes and dimethyl acetylenedicarboxylate proceeded smoothly upon heating, giving rise to the corresponding 1,2-diborylcyclohexenes in good to excellent yields. Conversion of two C–B bonds in the cycloadducts into C–C bonds is also demonstrated.

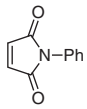
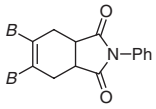
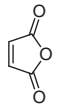
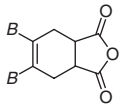
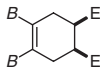
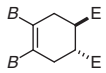
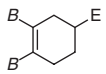
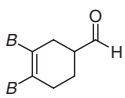
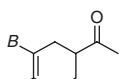
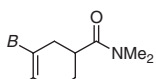
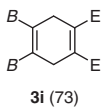
Since a carbon–boron bond of alkenylboron compounds can be converted stereospecifically into a carbon–carbon bond,[1,2] both *gem*- and *vic*-diborylated olefins serve as versatile reagents for concise preparation of multi-substituted olefins.[3] *gem*- and *vic*-Diborylated acyclic olefins are now readily available via diborylation with diborons of alkylidene-type carbenoids and alkynes, respectively.[3] However, such methodologies cannot be applied to preparation of diborylated cycloalkenes. Alternatively, cycloaddition reactions with boron-containing building blocks constitute a promising approach to boryl-substituted cyclic compounds that can serve as useful precursors of polysubstituted cyclic compounds.[4] We report herein that the Diels–Alder reaction of 2,3-bis(pinacolato)-boryl-1,3-butadiene (**1**)[5] provides us with 1,2-diborylcyclohexenes **3** in good to excellent yields (eq 1).



1 **2** **3** (1)

A solution of **1** and a slight excess of dienophile **2** in xylene was heated under the conditions indicated in Table 1. Various electron-deficient olefins were applicable to the cycloaddition. Noteworthy is that dimerization of **1** was not observed at all in view that some 2-boryl-1,3-dienes are reportedly to be highly susceptible to dimerization.[4c,4d] Such cyclic alkenes as *N*-phenylmaleimide (**2a**) and maleic anhydride (**2b**) gave bicyclic products **3a** and **3b** quantitatively (Entries 1 and 2). *cis*- and *trans*-Dimethyl 4,5-diborylcyclohex-4-ene-1,2-dicarboxylates **3c** and **3d** were obtained from dimethyl maleate (**2c**) and fumarate (**2d**), respectively (Entries 3 and 4). Methyl acrylate

Table 1. Diels–Alder Reaction of **1** with Various Dienophiles[a)]

Entry	Dienophile **2**	T/°C (t/h)	Product **3** (Yield/%)
1	 **2a**	130 (1)	 **3a** (95)
2	 **2b**	120 (3)	 **3b** (99)
3[c)]	 **2c**	180 (4)	 **3c** (78)
4[c)]	 **2d**	140 (3)	 **3d** (87)
5[c)]	 **2e**	130 (2)	 **3e** (65)
6	 **2f**	130 (3)	 **3f** (61)
7	 **2g**	130 (23)	 **3g** (78)
8	 **2h**	110 (24)	 **3h** (99)
9[c)]	 **2i**	100 (16)	 **3i** (73)

a) A solution of **1** (0.10 mmol) and **2** (0.11 mmol) in xylene (2 mL) was stirred at the temperature for the hours indicated above. B = (pinacolato)boryl. b) Isolated yield. c) E = CO_2Me.

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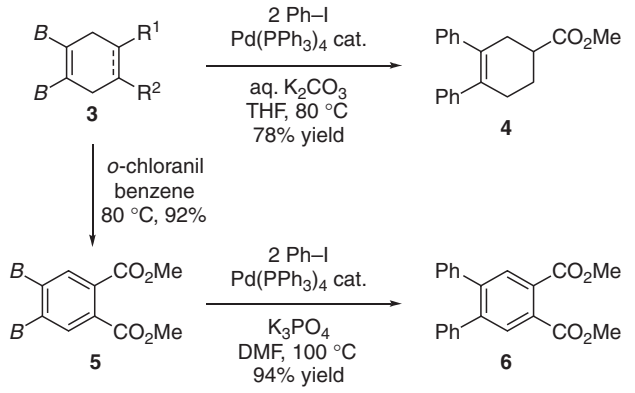

Scheme 1.

(**2e**), acrolein (**2f**), methyl vinyl ketone (**2g**), and dimethyl acrylamide (**2h**) also reacted with **1** to give **3e**–**3h** in moderate to good yields (Entries 5–8). Furthermore, cycloaddition with dimethyl acetylenedicarboxylate (**2i**) gave rise to 1,2-diborylated 1,4-cyclohexadiene **3i** in good yield (Entry 9). When the cycloaddition reaction was monitored by TLC, tailing spots of cycloadducts **3** were often observed. Attempted purification of **3** by preparative TLC resulted in failure due probably to instability of **3** toward silica gel. Hence, all products **3** were purified by gel permeation chromatography.

Two examples of product transformation are shown in Scheme 1. Pd-Catalyzed cross-coupling reaction of **3e** with two molar equivalents of iodobenzene in THF at 80 °C gave 1,2,4-trisubstituted cyclohexene **4** in 78% yield. Meanwhile, cyclohexadiene **3i** was easily oxidized with *o*-chloranil at 80 °C in benzene to give dimethyl 4,5-diborylphthalate **5** in 92% yield, which also coupled with iodobenzene in the presence of a palladium catalyst and a base, giving rise to *o*-terphenyl **6** in excellent yield.

In summary, we have demonstrated that Diels–Alder reaction of 2,3-bis(pinacolatoboryl)-2,3-butadiene constitutes a facile synthetic method for 1,2-bis(pinacolatoboryl)cyclohexenes and the diboryl groups of the cycloadducts are easily transformed into carbonaceous groups to give polysubstituted cyclohexenes and benzenes conveniently.

Experimental

General. NMR spectra (^{1}H and ^{13}C) were measured on a Varian Mercury 200 (200 MHz) spectrometer. Chemical shifts of ^{1}H NMR are expressed in parts per million downfield relative to internal tetramethylsilane (δ 0) or chloroform (δ 7.26). Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; brs, broad singlet. ^{13}C NMR spectra were recorded with tetramethylsilane as an internal standard (δ 0). Infrared spectra (IR) were recorded on a Shimadzu FTIR-8400 spectrometer. GC-MS analyses were obtained with a JEOL JMS-700 spectrometer by electron ionization at 70 eV. Elemental analyses were carried out with a YANAKO MT2 CHN CORDER machine at Kyoto University Elemental Analysis Center. Melting points were determined using a YANAKO MP-500D. Preparative recycling gel permeation chromatography (GPC) was performed with a JAI LC-908 chromatograph equipped with JAIGEL-1H and -2H columns (chloroform as an eluent).

General Procedure for Diels–Alder Reaction of 2,3-Bis-(pinacolatoboryl)-1,3-butadiene (1). A solution of **1** (31 mg, 0.10 mmol) and dienophile **2** (0.11 mmol) in xylene (2 mL) was stirred at the temperature and for the time indicated in Table 1. Removal of xylene under reduced pressure followed by gel permeation chromatography gave **3**.

2-Phenyl-5,6-bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3a,4,7,7a-tetrahydroisoindole-1,3-dione (3a): Yield 99%; a colorless solid; mp 152 °C; R_f 0.10 (hexane/EtOAc 4:1). ^{1}H NMR ($CDCl_3$) δ 1.27 (s, 24H), 2.44–2.69 (m, 4H), 3.02–3.11 (m, 2H), 7.30–7.54 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 24.8, 27.4, 39.2, 83.8, 126.9, 128.4, 128.9, 132.1, 178.7; IR (neat) 2923, 2854, 1701, 1460, 1377, 1340, 1311, 1144, 1115, 1024 cm^{-1}; MS m/z 480 ($M^+ + 1$, 5), 479 (M^+, 17), 338 (100), 297 (51), 83 (47). Anal. Calcd for $C_{26}H_{35}B_2NO_6$: C, 65.17; H, 7.36%. Found: C, 65.10; H, 7.30%.

5,6-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3a,4,7,7a-tetrahydroisobenzofuran-1,3-dione (3b): Yield 99%; colorless oil; R_f 0.53 (hexane/EtOAc 1:1). ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 24H), 2.50–2.53 (m, 4H), 3.15–3.25 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 24.9, 26.6, 39.4, 84.1, 173.6; IR (neat) 1780, 1450, 1344, 1317, 1143, 1110, 1033, 928, 854 cm^{-1}; MS m/z 389 ($M^+ -$ Me, 8.5), 346 (34), 263 (100), 149 (21), 83 (48). Anal. Calcd for $C_{20}H_{30}B_2O_7$: C, 59.45; H, 7.48%. Found: C, 59.33; H, 7.29%.

Dimethyl *cis*-4,5-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohex-4-ene-1,2-dicarboxylate (3c): Yield 94%; colorless oil; R_f 0.21 (hexane/EtOAc 4:1). ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 24H), 2.44–2.93 (m, 4H), 2.94–3.00 (t, $J = 6.5$ Hz, 2H), 3.66 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 24.9, 28.7, 39.1, 51.8, 83.6, 173.6; IR (neat) 2927, 2931, 1731, 1437, 1342, 1305, 1146, 856, 756, 667 cm^{-1}; MS m/z 451 ($M^+ + 1$, 3), 450 (M^+, 9), 449 ($M^+ - 1$, 5), 350 (67), 83 (100). HRMS (FAB) Calcd for $C_{22}H_{36}B_2O_8$: M^+ 450.2596. Found: 450.2600.

Dimethyl *trans*-4,5-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohex-4-ene-1,2-dicarboxylate (3d): Yield 90%; colorless oil; R_f 0.49 (hexane/EtOAc 1:1). ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 24H), 2.14–2.34 (m, 2H), 2.55–2.80 (m, 4H), 3.67 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 24.7, 31.5, 40.9, 51.7, 83.7, 175.5; IR (neat) 1735, 1624, 1458, 1438, 1377, 1344, 1307, 1145, 1114, 1028, 958, 856, 756 cm^{-1}; MS m/z 451 ($M^+ + 1$, 3), 450 (M^+, 9), 449 ($M^+ - 1$, 5), 350 (67), 83 (100). Anal. Calcd for $C_{22}H_{36}B_2O_8$: C, 58.70; H, 8.06%. Found: C, 58.40; H, 7.79%.

Methyl 3,4-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-cyclohex-3-enecarboxylate (3e): Yield: 65%; colorless oil; R_f 0.21 (hexane/EtOAc 4:1). ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 24H), 1.95–3.66 (m, 7H), 3.66 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 24.8, 24.9, 28.3, 30.6, 39.1, 51.1, 83.5, 176.4; IR (neat) 2978, 2932, 2839, 1732, 1622, 1147, 1020, 856, 665 cm^{-1}; MS m/z 393 ($M^+ + 1$, 3), 392 (M^+, 12), 391 ($M^+ - 1$, 8), 292 (100), 83 (92). Anal. Calcd for $C_{20}H_{34}B_2O_6$: C, 61.26; H, 8.74%. Found: C, 61.19; H, 8.44%.

3,4-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-cyclohex-3-enecarbaldehyde (3f): Yield: 61%; colorless oil; R_f 0.35 (hexane/EtOAc 4:1). ^{1}H NMR ($CDCl_3$) δ 1.29 (s, 24H), 1.97–2.02 (m, 1H), 2.19–2.47 (m, 6H), 9.67 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 21.9, 25.0, 27.5, 27.6, 46.0, 83.6, 204.5; IR (neat) 2978, 2925, 2856, 1726, 1620, 1306, 1146, 856, 665 cm^{-1}; MS m/z 364 ($M^+ + 2$, 1), 363 ($M^+ + 1$, 5), 362 (M^+, 21), 262 (100), 221 (71), 83 (83). HRMS (FAB) Calcd for $C_{19}H_{32}B_2O_5$: M^+ 362.2436. Found: m/z 362.2435.

1-[3,4-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohex-3-enyl]ethan-1-one (3g): Yield: 78%; colorless oil; R_f 0.25 (hexane/EtOAc 4:1). ^{1}H NMR ($CDCl_3$) δ 1.28 (s, 24H), 1.35–1.55 (m, 1H), 1.85–2.00 (m, 2H), 2.10–2.20 (s, 3H), 2.20–2.60 (m, 4H); ^{13}C NMR ($CDCl_3$) δ 24.2, 24.9, 28.1, 28.6, 30.1, 47.1, 83.5, 211.8;

IR (neat) 2978, 2928, 1713, 1621, 1305, 1269, 1213, 1147, 1113, 856, 667 cm^{-1}; MS m/z 378 ($M^+ + 2$, 1), 377 ($M^+ + 1$, 4), 376 (M^+, 19), 318 (15), 276 (100), 83 (79). Anal. Calcd for $C_{20}H_{34}B_2O_5$: C, 63.87; H, 9.11%. Found: C, 63.87; H, 8.93%.

***N,N*-Dimethyl 3,4-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohex-3-enecarboxyamide (3h):** Yield: 99%; colorless oil; R_f 0.48 (EtOAc). ^1H NMR ($CDCl_3$) δ 1.27 (s, 24H), 2.24–2.96 (m, 6H), 2.97 (s, 6H); ^{13}C NMR ($CDCl_3$) δ 24.9, 25.1, 28.7, 31.2, 36.4, 83.5, 175.9; IR (neat) 2978, 2929, 1643, 1456, 1342, 1304, 1146, 1014, 854, 663 cm^{-1}; MS m/z 406 ($M^+ + 1$, 23), 405 (M^+, 100), 350 (72), 205 (64), 83 (53). HRMS (FAB) Calcd for $C_{21}H_{37}B_2NO_5$: M^+ 405.2858. Found: m/z 405.2852.

1,2-Bis(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-4,5-bis(methoxycarbonyl)cyclohexa-1,4-diene (3i): Yield 73%; colorless solid; mp 137.9 °C (hexane); R_f 0.20 (hexane/EtOAc 4:1). ^1H NMR (400 MHz, $CDCl_3$) δ 1.29 (s, 24H), 3.08 (s, 4H), 3.75 (d, $J = 0.4$ Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 24.9, 30.3, 52.2, 83.8, 131.9, 168.2; IR (KBr) 2980, 2949, 2359, 2341, 1716, 1672, 1622, 1434, 1346, 1313, 1147, 1099, 1069, 1043, 962, 856, 796 cm^{-1}; MS m/z 448 (M^+, 1), 275 (100). Anal. Calcd for $C_{22}H_{34}B_2O_8$: C, 58.96; H, 7.65%. Found: C, 58.76; H, 7.63%.

Cross-Coupling Reaction of 3e. A solution of **3e** (28 mg, 0.072 mmol), iodobenzene (38 mg, 0.19 mmol), [$Pd(PPh_3)_4$] (6.7 mg, 5.7 μmol, 8 mol %), and 6 M aq K_2CO_3 (72 μL, 0.43 mmol) in THF (2 mL) was stirred at 80 °C for 16 h before quenching with sat. aq NH_4Cl (10 mL). The aqueous layer was extracted with EtOAc (10 mL × 3) and then washed with sat. aq NaCl (10 mL). The organic layer was dried over anhydrous $MgSO_4$ and concentrated in vacuo. Purification of the residue by preparative TLC (hexane/EtOAc 10:1) gave **4** (CAS NO. 62543-95-7, 17 mg, 78% yield) as a colorless solid.

Oxidation of 3i. A solution of **3i** (80 mg, 0.18 mmol) and *o*-chloranil (101 mg, 0.41 mmol) in benzene (4 mL) was stirred at 80 °C for 1 h. Removal of benzene under reduced pressure followed by GPC gave **5** (74 mg, 92% yield) as a colorless solid. Mp 153.9 °C (hexane); R_f 0.20 (hexane/EtOAc 4:1). ^1H NMR (400 MHz, $CDCl_3$) δ 1.38 (s, 24H), 3.90 (s, 6H), 7.98 (d, $J =$ 0.4 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 25.0, 52.5, 84.4, 131.8, 133.3, 167.9; IR (KBr) 2980, 2951, 2359, 1726, 1499, 1435, 1371, 1330, 1292, 1148, 1092, 966, 856, 835, 804, 677, 665 cm^{-1}, MS m/z 446 (M^+, 0.3), 305 (100). Anal. Calcd for $C_{22}H_{32}B_2O_8$: C, 59.23; H, 7.23%. Found: C, 59.04; H, 7.16%.

Cross-Coupling Reaction of 5. A solution of **5** (20 mg, 0.045 mmol), iodobenzene (23 mg, 0.11 mmol), [$Pd(PPh_3)_4$] (4.2 mg, 3.6 μmol, 8 mol %), and K_3PO_4 (38 mg, 0.18 mmol) in DMF (2 mL) was stirred at 100 °C for 6 h before quenching with sat. aq NH_4Cl (10 mL). Workup followed by purification with preparative TLC (hexane/EtOAc 10:1) gave **6** (CAS NO. 7111-79-7, 14 mg, 94% yield) as a colorless solid.

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