A Highly Enantioselective and Diastereoselective Synthesis of Cyclobutanes via Boronic Esters

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Supplementary Data

2-(3-Bromopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (2). An equimolar mixture of allyl bromide and triethylsilane was added to boron trichloride under the conditions described previously to provide (3-bromopropyl)dichloroborane (**1**).[3] Treatment of **1** with pinacol in ether yielded **2**, which was distilled. Complete separation of triethylsilyl chloride from **2** was difficult, and crude material was generally used. 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.92 (br.t, J = 7.6 Hz, 2, CH_2B), 1.25 (s, 12, CH_3CO), 1.92-2.02 (m, 2, CH_2CH_2B), 3.42 (t, J = 6.9 Hz, CH_2Br); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 24.8, 27.5, 36.2, 83.2; HRMS: calcd for $C_9H_{18}BO_2Br$ (M^+) 248.0583, found 248.0599. Anal. Calcd for $C_9H_{18}BO_2Br$: C, 43.42; H, 7.29; B, 4.34, Found: C, 43.38; H, 7.20; B, 4.34.

4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-butanenitrile (3a). A mixture of 2-(3-bromopropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**2**) (9 g, 36 mmol) and sodium cyanide (2.0 g, 40 mmol) in DMSO (10 mL) was heated at 50 °C for 12 h. Ethyl acetate (100 mL), brine (100 mL), and few mL of hydrochloric acid (to pH 1-2) were added. The organic layer was washed with brine (3×100 mL) and dried over magnesium sulfate. Nitrile **3a** was isolated by flash chromatography (Silica gel, dichloromethane/pentane 0%–50%), 5.9 g (91%), or by distillation, bp 145 °C (2 torr); 85 °C (0.5 torr); 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.94 (t, = 7.9 Hz, 2), 1.25 (s, 12), 1.78 (m, J = 7.5 Hz, 2), 2.37 (t, J = 7.2 Hz, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 19.1, 20.3, 24.8, 83.3, 119.8. HRMS calcd for $C_9H_{15}BO_2N$ (M^+–15) 180.1196, found 180.1190. Anal. Calcd for $C_{10}H_{18}BNO_2$: C, 61.57; H, 9.30; B, 5.54. Found: C, 61.75; H, 9.46; B, 5.97.

(4*R*,5*R*)-4,5-Dicyclohexyl-1,3,2-dioxaborolane-2-butanenitrile (4a). A mixture of 1*R*,2*R*-dicyclohexylethane-1,2-diol (5 g, 22.1 mmol) and 4,4,5,5-tetramethyl-1,3,2-dioxaborolane-2-butanenitrile (**3a**) (3.91 g, 20 mmol) in ether (100 mL) was stirred at room temperature overnight. The solvent was distilled, pentane (100 mL) was added, the solid was filtered, and the organic layer was washed with water (3×100 mL) and dried over magnesium sulfate. Concentration and flash chromatography (silica gel, dichloromethane/pentane 0%-50%) yielded **4a**, 5.8 g (95%); 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.96-1.85 (m, 26), 2.39 (t, *J* = 7.2 Hz, 2), 3.84-3.86 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 10 (br), 19.13, 20.5, 25.8, 25.9, 26.4, 27.3 28.3, 42.9, 83.5, 119.9. HRMS calcd for $C_{18}H_{30}BO_2N$ (M^+) 303.2369, found 303.2363. Anal. Calcd for $C_{18}H_{30}BO_2N$: C, 71.29; H, 9.97; B, 3.56, Found: C, 71.66; H, 10.03; B, 3.92.

(1*R*,2*R*)-2-[(4*R*,5*R*)-4,5-Dicyclohexyl-1,3,2-dioxaborolan-2-yl]cyclobutanecarbonitrile (7a). Dichloromethane (3 eq) was treated with butyllithium (1.3 eq) at –100 °C in THF in the previously described manner to form (dichloro-methyl)lithium.[2a] (4*R*,5*R*)-4,5-Dicyclohexyl-1,3,2-dioxa-borolane-2-butanenitrile (**4a**) (1 eq) was added, followed by zinc chloride (1.8 eq) and warming to 25 °C for 18 h. After aqueous work up, concentration of the organic phase yielded (δ*S*,4*R*,5*R*)-δ-chloro-4,5-dicyclohexyl-1,3,2-dioxa-borolane-2-pentanenitrile (**5a**) (96%); 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.80-1.45, 1.52-2.2 (m, 26), 2.40 (t, *J* = 6.7 Hz, 2),3.45-3.49 (m, 1), 3.85-3.95 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 16.7, 23.2, 25.8, 25.9, 26.3, 27.2, 28.2, 32.8, 42.8, 84.3 HRMS calcd for $C_{19}H_{31}BClO_2N$ (M^+) 351.2136, found 351.2117. Lithium diisopropylamide (either commercial[5] or freshly prepared from butyllithium and diisopropylamine in THF) (11.25 mmol) was added dropwise to a solution of **5a** (4.12 g, 12 mmol) in THF (100 mL) stirred at –78 °C under argon. Stirring at –78 °C was continued for 20 min. Magnesium bromide (~12 mmol), which had been prepared from magnesium metal and 1,2-dibromoethane in THF, was added slowly. The mixture was kept at 20-25 °C for 48 h, when monitoring of aliquots by ^{1}H NMR indicated reaction was complete. The mixture was filtered through a short pad of silica gel, which was then washed with ether (2×200 mL). The combined organic phase was concentrated to an oil (3.62 g), by ^{1}H NMR analysis 5%

unchanged (4*R*,5*R*)-4,5-dicyclohexyl-1,3,2-dioxaborolane-2-butanenitrile and 95% **7a**, contained yield 93%; 300 MHz ^{1}H NMR ($CDCl_3$) δ 0.85-1.82 (m, 22, C_6H_{11}), 2.04 (dq, J = 8.9_q, 11.0_d Hz, 1, C*H*H), 2.12-2.52 (m, 4, CH_2CHH, C*H*B), 3.15 (dq, J = 8.2_q, 0.75_d, 1, C*H*CN), 3.87-3.91 (m, 2, C*H*-O); 75 MHz ^{13}C NMR ($CDCl_3$) δ 21.8, 23.1, 25.8, 25.9, 27.1, 27.2, 28.3, 42.9, 83.8, 122.7; HRMS calcd for $C_{19}H_{30}BO_2N$ (M^+) 315.2369, found 315.2346. Anal. Calcd. for $C_{19}H_{30}BO_2N$: C, 72.39; H, 9.59; B, 3.43, Found: C, 72.35; H, 9.59; B, 3.42. Connectivity was confirmed by COSY and HETCORR. When magnesium bromide was not added to the reaction mixture, additional ^{1}H-NMR peaks attributed to the *cis* isomer were noted at δ 3.27 (q, J = 8.2 Hz); additional ^{13}C at δ 21.6, 23.6, 26.8, 27.4, 28.4, 42.8, 84.1, 121.8.

α,4,4,5,5-Pentamethyl-1,3,2-dioxaborolane-2-butanenitrile (3b). 4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-butanenitrile (**3a**) (2.9 g, 15 mmol) in THF (10 mL) was added to LDA (8.3 mL, 2.0 M, 16.6 mmol) in THF (50 mL) at –78 °C. After 30 min at –78 °C, methyl iodide (6.1 g, 43 mmol) was added. The solution was allowed to warm slowly to 20-25 °C and kept for 18 h. After the usual work up with saturated ammonium chloride and ether, concentration yielded crude methylation product **3b** (2.8 g); 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.85-1.05 (m, 2), 1.25 (s, 12), 1.30 (d, J = 7.1 Hz), 1.60-1.80 (m, 2), 2.55-2.68 (m, 1); 75-MHz ^{13}C-NMR ($CDCl_3$) [ATP]: δ 9 (br) [CB], 17.7[CH_3], 24.74 [CH_3], 24.77 [CH_3], 27.5 [CH], 28.6 [CH_2], 83.1 [C], 123.0 [CN]. HRMS: calcd for $C_{11}H_{20}BNO_2$ (M^+) 209.1587, found 209.1590.

(4*R*,5*R*)-4,5-Dicyclohexyl-α-methyl-1,3,2-dioxaboro-lane-2-butanenitrile (4b). A mixture of crude **3b** (2.8 g) and (1*R*,2*R*)-1,2-dicyclohexyl-1,2-ethanediol (3.8 g, 16.8 mmol) in ether/methanol (50 mL, 1:1) was stirred 16 h. Concentration and chromatography (Silica, 5% ether in pentane) yielded **4b** (3.65 g, 77% from **3a**); 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.82-1.85 (m, 26), 1.31 (d, J = 7.1 Hz, 3), 2.57-2.69 (m, 1), 3.82-3.87 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 8 (br), 17.7, 25.8, 25.95, 26.37, 27.3 27.47, 27.49, 28.31, 28.33, 28.8, 42.9, 83.5, 123.1. HRMS calcd for $C_{19}H_{32}BNO_2$ (M^+) 317.2526, found 317.2504. Anal. Calcd for

$C_{19}H_{32}BNO_2$: C, 71.93; H, 10.17; N, 4.41; B 3.41. Found: C, 72.06; H, 10.10; N, 4.46; B 3.57.

(δ*S*,4*R*,5*R*)-δ-Chloro-4,5-dicyclohexyl-α-methyl-1,3,2-dioxaborolane-2-pentanenitrile (5b). Prepared in the usual manner from **4b** (3.2 g, 10.1 mmol) and (dichloromethyl)lithium (from 13.9 mmol of butyllithium) followed by zinc chloride (12.2 mmol); 3.8 g; used without purification; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.85-2.20 (m, 26), 1.349 + 1.350 (overlapping d's due to diastereomers, J = 7.1 Hz, 3), 2.58-2.75 (m, 1), 3.45-3.55 (m, 1), 3.95-4.00 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 18.0, 24.9, 25.4, 25.8, 25.9, 26.3, 27.2, 28.1, 31.1, 31.44, 31.49, 32.0, 42.8, 84.2, 122.5, 122.7.

(1*R*,2*R*)-2-[(4*R*,5*R*)-4,5-Dicyclohexyl-1,3,2-dioxaborolan-2-yl]-1-methylcyclobutanecarbonitrile (7b). Lithium diisopropylamide (5.5 mL, 2M in heptane/THF/PhEt, stabilized with magnesium diisopropylamide, 11 mmol) was added to a solution of (δ*S*,4*R*,5*R*)-δ-chloro-4,5-dicyclohexyl-α-methyl-1,3,2-dioxaborolane-2-pentanenitrile (**5b**) (3.8 g, crude) in THF (100 mL) at –78 °C. The solution was allowed to warm to 20-25 °C and kept for 3 days. Ether (200 mL) and saturated ammonium chloride (100 mL) were added. The organic phase was dried over magnesium sulfate and concentrated under vacuum to yield crude **7b**, B-CN *trans*/*cis* ratio of 8:1 based on GC and GCMS, which also showed that the two components are isomers. Flash chromatography (Silica gel, ether/pentane 5%) yielded **7b**, 2.0 g (60%); recrystallized from pentane (no *cis* isomer in GC); 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.9-1.40, 1.52-1.80 (m, 22), 1.51 (s, 3), 2.0-2.22 (m, 2), 2.45-2.52 (m, 1), 2.58-2.70 (m, 1), 3.85-3.89 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 18.5, 23.0, 25.8, 26.0, 26.4, 27.5, 28.5, 34.1, 43.0, 83.9, 125.9. HRMS calcd for $C_{20}H_{32}BNO_2$ (M^+) 329.2526, found 329.2525. Anal. Calcd for $C_{20}H_{32}BNO_2$: C, 72.95; H, 9.80; B, 3.28; N, 4.25. Found: C, 73.02; H, 9.99; B, 3.00; N, 4.19.

1-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-2-iodo-ethane. Lithium diisopropylamide (1.5 M THF complex in cyclohexane, 108 mL, 0.162 mol) was added dropwise over 45 min to a solution of 2-iodoethanol (25.4 g, 0.147 mol) and *tert*-butyldimethylsilyl chloride (22.2 g, 0.147 mol) in THF (250 mL) stirred at –78 °C under argon. After 15 h at 20-25 °C, saturated ammonium chloride was added. After extraction with 1:1 pentane/ether (400 mL) and washing with saturated ammonium chloride (3×150 mL), the residue (41.9 g, 99.5%) was distilled, bp 65 °C (5 torr) (32.0 g, 76%); 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.64 (s, 6), 0.88 (s, 9), 3.17 (t, 2), 3.81 (t, 2).

(4*R*,5*R*)-4,5-Dicyclohexyl-α-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethyl]-1,3,2-dioxaborolane-2-butanenitrile (4c). Lithium diisopropylamide (56.5 mL, 1.5 M in cyclohexane, 0.0847 mol) was added by syringe to (4*R*,5*R*)-4,5-dicyclohexyl-1,3,2-dioxaborolane-2-butanenitrile (**3b**) (23.3 g, 0.0768 mol) in THF (250 mL) stirred at –78 °C under argon. The mixture was stirred at –78 °C for 40 min. 1-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]-2-iodoethane (22.1 g, 0.077 mol) in THF (40 mL) in a separate flask was cooled to –78 °C and transferred to the reaction flask by cannula. The mixture was stirred for 15 h at 20-25 °C, then worked up with saturated ammonium chloride and 3:1 pentane/diethyl ether. Concentration and removal of unchanged silyl ether by distillation yielded a liquid residue of **4c** (34.4 g, 97%) as a mixture of C-α diastereomers; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.064 (s, 3), 0.071 (s, 3), 0.89 (s, 9), 0.90-1.82 (m, 28), 2.81 (m, *J* = 7.3 Hz, 1), 3.76 (t, *J* = 5.8 Hz), 3.82-3.86 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$): δ -5.47, 9 (br), 18.2, 25.85, 25.88, 25.99, 26.4, 26.93 & 26.95, 27.3, 28.4, 30.2, 34.94 & 35.00, 42.9, 59.98 & 60.00, 83.5, 122.1; HRMS calcd for $C_{26}H_{48}BNO_3Si$ (M^+) 461.3496, found 461.3490.

Alternative route to 4c: **3a** was alkylated directly to form 4,4,5,5-tetramethyl-α-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethyl]-1,3,2-dioxaborolane-2-butanenitrile; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.062 (s, 3), 0.071 (s, 3), 0.89 (s, 9), 0.85-1.15 (m, 2), 1.25 (s, 12), 1.63-1.90 (m, 4), 2.81 (p, *J* = 7.4 Hz, 1), 3.76 (t, *J* = 5.9 Hz, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ -5.5, 9 (br),

24.78, 24.81, 25.9, 26.8, 30.1, 35.0, 60.0, 83.4, 122.1; HRMS calcd for $C_{18}H_{36}BNO_3Si$ (M^+ – 1) 352.2480, found 352.2473. Transesterification with (1*R*,2*R*)-1,2-dicyclohexyl-1,2-ethanediol in the usual manner yielded **4c**.

(δ*S*,4*R*,5*R*)-δ-Chloro-4,5-dicyclohexyl-α-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethyl]-1,3,2-dioxaborolane-2-pentanenitrile (5c). A solution of (4*R*,5*R*)-4,5-dicyclohexyl-α-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethyl]-1,3,2-dioxaborolane-2-butanenitrile (**4c**) (14.06 g, 0.0305 mol) in THF (100 mL) was added to (dichloromethyl)lithium that had been prepared at –100 °C from dichloromethane (4 mL) in THF (250 mL) treated with butyllithium (0.0352 mol) in the manner previously described.[2a] The mixture was allowed to warm to –78 °C over 45 min. Anhydrous zinc chloride (7.5 g, 0.055 mol, dried with thionyl chloride) was added to the reaction flask in one portion. The mixture was stirred 18 h at 20-25 °C, quenched with saturated ammonium chloride, and worked up in the usual manner. The product was dissolved in pentane (200 mL), passed through a short silica column with the aid of more pentane, and concentrated to an oil (14.2 g, 91%); 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.070 (s, 3), 0.077 (s, 3), 0.90 (s, 12), 0.90-2.20 (m, 28), 2.75-2.90 (m, 1), 3.45-3.51 (m, 1), 3.73-3.80 (m, 2), 3.96-3.98 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$): δ -5.51, -5.49, 18.19, 25.78, 25.83, 25.91, 26.34, 27.23, 27.30 & 27.79, 28.19, 29.51&30.02, 31.26 & 31.61, 42.83, 59.71, 84.23 & 84.24, 121.59 & 121.72; HRMS calcd for $C_{23}H_{40}BClNO_3Si$ (M^+ – 57) 452.2559, found 452.2546.

(1*R*,2*R*)-2-[(4*R*,5*R*)-4,5-Dicyclohexyl-1,3,2-dioxaborolan-2-yl]-1-[2-[[(1,1-dimethylethyl)dimethylsilyl]oxy]ethyl]cyclobutanecarbonitrile (7c). A solution of the product **5c** from the previous step (14.2 g, 0.0278 mol) in THF (200 mL) was stirred at –78 °C during the dropwise addition of LDA (Aldrich LDA·THF in cyclohexane, 20.4 mL, 0.0306 mol, containing no magnesium bis(diisopropylamide)) and for an additional 30 min. Magnesium bromide in THF (140 mL, ~0.2 M, from magnesium metal and 1,2-dibromoethane) was added slowly to the cold solution. The mixture was stirred for three days at 20-25 °C. The reaction

mixture was worked up in the usual manner with saturated ammonium chloride and 3:1 pentane/ether. Aqueous work up followed by chromatography on a short silica column with 10% ethyl acetate in pentane yielded **7c**, Rf ~0.9, as an oil (12.36 g, ~95% **7c** with ~5% unchanged precursor, probably **4c**, by ^{1}H NMR, 89% yield of **7c** contained); 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.03 (s, 6), 0.85 (s, 9), 0.85-1.74 (m, 23), 1.97 (t, 2), 2.28 (m, 2), 2.4 (m, 2), [2.8 **5c** impurity] 3.73 (m, 2), 3.83 (m, 2), [3.95 **5c**]; 75-MHz ^{13}C-NMR (DEPT) ($CDCl_3$) δ –5.5 (*C*H_3), 18.2 (w, *C*Si?), 19.4 (*C*H_2), 25.75 (*C*H_3), 25.82 (*C*H_2), 25.90 (*C*H_2), 26.3 (*C*H_2), 27.3 (*C*H_2), 27.5 (*C*H_2), 32.8 (*C*H_2), 35.4 (w, *C*CN?), 38.4 (*C*H_2), 42.9 (*C*H), 60.1 (*C*H_2), 84.0 (*C*H), 125.0 (*C*N); *C*B (br) not observed. [An earlier sample prepared without the aid of added magnesium bromide yielded ~20% of a ~3:1 ratio of **7c** with its *cis* diastereomer; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.06 (s, 6), 0.89 (s, 12), 0.90-1.8 (m, 22), 1.8-2.55 (m, 7), 3.70-3.82 (m, 2), 3.85-3.95 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ –5.50 + –5.46, 18.17, 19.35 + 19.46, 25.7, 25.8, 25.9, 26.36 + 26.41, 27.50 + 27.57, 28.42 + 28.51, 32.9, 33.9, 35.5, 36.9, 38.5, 42.0, 42.86 + 42.97, 59.96 + 60.15, 83.89 + 84.02, 123.6 + 125.1.] HRMS calcd for $C_{27}H_{48}BNO_3SiN$ (MH+) 474.3574, found 474.3565. The analytical sample was further purified by chromatography. Anal. calcd. for $C_{27}H_{48}BNO_3SiN$: C, 68.48; H, 10.22; B, 2.28; N, 2.96; Si, 5.93, Found: C, 68.36; H, 10.17; B, 1.84; N, 2.82; Si, 5.84.

(1*R*,2*S*)-1-[2-[[(1,1-Dimethylethyl)dimethylsilyl]oxy]ethyl]-2-(1-methylethenyl)cyclobutanecarbonitrile (8c). 2-Propenylmagnesium bromide (22 mL, 0.5 M, 11.0 mmol, from 2-bromopropene and magnesium in THF) was added slowly by syringe to a solution of cyclobutylboronic ester **7c** (4.76 g, 10.1 mmol) in THF (200 mL) stirred at –78 °C. The mixture was allowed to warm to 0 °C, then cooled again to –78 °C. Iodine (2.7 g, 10.6 mmol) in methanol (250 mL) at –78 °C in a separate flask was transferred to the reaction flask by cannula under argon pressure while simultaneously adding sodium methoxide in methanol (30 mL, 1 M slurry, ~30 mmol). The stirring mixture was allowed to warm to 20-25 °C during 1.5 h. Sodium thiosulfate (25 mL saturated solution in distilled water) was added to quench excess iodine. The mixture was poured into pentane (400 mL) and washed with water (3×250 mL). The product was

distilled, bp 110 °C (0.5 torr) (1.80 g, 6.45 mmol, 65%). 300-MHz ^{1}H NMR ($CDCl_3$) δ 0.04 (s, 6), 0.87 (s, 9), 1.51-1.65 (m, 2), 1.71 (s, 3), 1.72-2.01 (m, 2), 2.07-2.23 (m, 2), 2.31-2.45 (m, 1), 2.28 (t, 1), 3.79 (m, 2), 4.73 (s, 1), 4.98 (s, 1); 125-MHz ^{13}C NMR ($CDCl_3$) δ –5.5, 18.2, 20.4, 21.7, 25.9, 27.8, 32.4, 35.4, 49.6, 60.0, 112.8, 124.0, 141.6; HRMS calcd for $C_{12}H_{20}NOSi$ (M – 57), 222.1314, found 222.1320.

4,4,5,5-Tetramethyl-1,3,2-dioxaborolane-2-propanenitrile (10a). Acetonitrile (3.25 g, 79.2 mmol) was added to a solution of LDA (50 mL, 1.74 M, 87 mmol) in THF (100 mL) stirred at –78 °C. After 30 min, 2-bromomethyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (**9**) (17.5 g, 79.2 mmol) was added to the solution at –78 °C. The solution was allowed to warm to room temperature and kept for 18 h. Saturated ammonium chloride (500 mL), hydrochloric acid (12 M, 8 mL) and ethyl acetate (750 mL) were added. The aqueous layer was extracted with ethyl acetate (2×500 mL), then saturated by sodium chloride and extracted with more ethyl acetate to obtain more of the water-soluble **10a**. Vacuum distillation yielded **10a** in a 4.5:1 mixture (NMR anal.) with pinacol, bp 130 °C (20 torr), 10.84 g, (66%); 300-MHz ^{1}H-NMR δ 1.16-1.21 (m, 2), 1.26 (s, 12), 2.41 (dd, J = 7.7, 8.7 Hz, 2); HRMS calcd for $C_9H_{16}BO_2N$ (M^+) 181.1274, found 181.1254. (Note: The proton coupling pattern at δ 1.18 and 2.41 attributed the B-CH_2CH_2-CN group is unusual in showing two different vicinal coupling constants.)

(4*R*,5*R*)-4,5-Dicyclohexyl-1,3,2-dioxaborolane-2-propanenitrile (11a). A mixture of **10a** (4.07 g, 22.5 mmol) and (1*R*,2*R*)-1,2-dicyclohexyl-1,2-ethanediol (6.5 g, 28.8 mmol) in ether/methanol (50 mL, 1:1) was stirred overnight. Removal of solvent and flash chromatography (Silica gel, 5% ether/pentane) yielded (4*R*,5*R*)-4,5-dicyclohexyl-1,3,2-dioxaborolane-2-propanenitrile (**11a**) (6.5 g, 99%); 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.85-1.80 (m, 24), 2.40-2.45 (m, 2), 3.86-3.90 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 7 (br), 12.0, 25.76, 25.93, 26.3, 27.2, 28.3, 42.9, 83.9, 121.0. HRMS calcd for $C_{17}H_{28}BNO_2$ (M^+) 289.2213, found 289.2187. Anal. Calcd for $C_{17}H_{28}BNO_2$: C, 70.60; H, 9.76; B 3.74; N, 4.84, Found: C, 70.75; H, 9.86; B, 3.99; N, 4.56.

(γ*S*,4*R*,5*R*)-γ-Chloro-4,5-dicyclohexyl-1,3,2-dioxaborolane-2-butanenitrile (12a). (4*R*,5*R*)-4,5-Dicyclohexyl-1,3,2-dioxaborolane-2-propanenitrile (**11a**) (3.59 g, 12.4 mmol) in THF (5 mL) was added to (dichloromethyl)lithium (13.8 mmol) prepared in THF (25 mL) at –100 °C. Zinc chloride (2.2 g, 16.2 mmol) was added. Aqueous work-up yielded (γ*S*,4*R*,5*R*)-γ-chloro-4,5-dicyclohexyl-1,3,2-dioxaborolane-2-butanenitrile (**12a**) (3.73 g, 89%), used without further purification; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.86-1.82 (m, 22), 2.06-2.30 (m, 2), 2.62 (dd, *J* = 6.7, 7.7 Hz, 2), 3.57 (dd, *J* = 4.4, 9.8 Hz), 3.95-4.00 (m, 2); 75-MHz ^{13}C-NMR (CDCl3) δ 15.1, 25.74, 25.88, 26.3, 27.2, 28.2, 29.9, 42.8, 84.4, 118.9. HRMS calcd for $C_{18}H_{29}BClNO_2$ (M^+) 337.1980, found 337.1971. Anal. Calcd for $C_{18}H_{29}BClNO_2$: C, 64.02; H, 8.66; B 3.20; N, 4.15, Found: C, 64.67; H, 8.61; B 3.00, N, 4.15.

(γ*S*,4*R*,5*R*)-4,5-Dicyclohexyl-γ-methyl-1,3,2-dioxaborolane-2-butanenitrile (13a). Methylmagnesium chloride (4 mL, 2.8 M, 11.2 mmol in ether) was added to a solution of (γ*S*,4*R*,5*R*)-γ-chloro-4,5-dicyclohexyl-1,3,2-dioxaborolane-2-butanenitrile (**12a**) (3.73 g, crude) in THF (20 mL) stirred at –78 °C. The solution was allowed to warm to room temperature overnight. Work-up with pentane/ether (4:1, 150 mL) and saturated ammonium chloride (100 mL) followed by flash chromatography (Silica gel, 30-50% dichloromethane in pentane) yielded **13a** (3.06 g, 74% based on (4*R*,5*R*)-4,5-dicyclohexyl-1,3,2-dioxaborolane-2-propanenitrile (**11a**)), mp 54-55 °C; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.85-1.90 (m, 25); 1.04 (d, *J* = 7.4 Hz, 3), 2.42 (t, *J* = 7.4 Hz, 2), 3.83-3.87 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 15.3, 16.2, 25.82, 25.95, 26.4, 27.3, 28.3, 28.9, 42.9, 83.5, 120.1. HRMS calcd for $C_{19}H_{32}BNO_2$ (M^+) 317.2526, found 317.2500. Anal. Calcd for $C_{19}H_{32}BNO_2$: C, 71.93; H, 10.17; B 3.41; N, 4.41. Found: C, 72.04; H, 9.92; B 2.97; N, 4.49.

(γ*S*,δ*S*,4*R*,5*R*)-δ-Chloro-4,5-dicyclohexyl-γ-methyl-1,3,2-dioxaborolane-2-pentanenitrile (14a). A solution of **13a** (2.17 g, 6.5 mmol) in THF (5 mL) was added to (dichloromethyl)lithium (7.54 mmol) prepared at –100 °C in the usual manner, then treated with zinc chloride (1.1 g, 8.1 mmol). The usual work-up yielded (γ*S*, δ*S*,4*R*,5*R*)-δ-chloro-4,5-

dicyclohexyl-γ-methyl-1,3,2-dioxaborolane-2-pentanenitrile (**14a**) (2.2 g, 89%), used in the next step without further purification; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.85-2.0 (m, 24), 1.07 (d, *J* = 6.7 Hz, 3), 2.09-2.20 (m, 1), 2.37-2.42 (m, 2), 3.51 (d, *J* = 4.1 Hz, 1), 3.85-3.98 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 15.1, 16.4, 25.77, 25.89, 26.3, 27.4, 28.3, 29.7, 35.4, 42.9, 84.3, 119.4. HRMS calcd for $C_{20}H_{33}BClNO_2$ (M^+) 365.2293, found 365.2314.

(1*R*,2*R*,3*S*)-2-[(4*R*,5*R*)-4,5-Dicyclohexyl-1,3,2-dioxaborolan-2-yl]-3-methylcyclobutanecarbonitrile (15a) and its (1*S*,2*R*,3*S*)-isomer (16a). LDA (3.7 mL, 1.8 M, 6.7 mmol) was added to a solution of (γ*S*, δ*S*,4*R*,5*R*)-δ-chloro-4,5-dicyclohexyl-γ-methyl-1,3,2-dioxaborolane-2-pentanenitrile (**14a**) (2.2 g, crude) in THF (50 mL) stirred at –78 °C, then kept at 20-25 °C for 3 days. After work-up with ether (100 mL) and aqueous ammonium chloride (100 mL) followed by concentration of the organic phase, a residue of (1*R*,2*R*,3*S*)-isomer **15a** in a 94:6 mixture with its (1*S*,2*R*,3*S*)-diastereomer **16a** based on 300-MHz ^{1}H-NMR analysis [δ 2.96 (**15a**) and 3.20 **16a**] was obtained. Recrystallization from pentane yielded pure **15a** (0.46 g), mp 73.5-74 °C. Chromatography of the mother liquor (Silica, dichloromethane/pentane 1:3-2:1) yielded **15a** (0.72 g) and a mixture of **16a**/**15a** (0.099 g, ~2:1); total yield of **16a** 62%, **15a** 3%; 300-MHz ^{1}H-NMR ($CDCl_3$) [*cis* isomer peaks in brackets] δ 0.85-1.82 (m, 22, C_6H_{11}), [1.14 (d, *J* = 6.7 Hz, CH_3)], 1.15 (d, *J* = 6.5 Hz, 3, CH_3), 1.89 (t, *J* =9.8 Hz, 1, C*H*B), [2.04 (dddd, *J* = 0.96, 7.2, 9.0, 11.3, C$H^{4\beta}$)], 2.06 (dt, *J* = 9.3_t, 10.7_d Hz, 1, C$H^{4\beta}$H), 2.30-2.45 (m, 1, C$H^{3\alpha}CH_3$), [2.50 (dddd, *J* = 0.72, 5.3, 8.2, 11.3, C$H^{4\alpha}$)], 2.52 (ddt, *J* = 0.63_d, 7.7_t, 10.7_d, 1, C$H^{4\alpha}$H), [2.62-2.78 (m, C$H^{3\alpha}CH_3$)], 2.96 (dt, *J* = 7.9_d, 9.8_t Hz, 1, C$H^{1\alpha}$CN), [3.20 (dddd, *J* = 1.2, 5.1, 9.1, 9.7, C$H^{1\beta}$CN)], 3.85-3.90 (m, 2, C*H*OB), [3.90-3.95 (m, C*H*OB)]; 75-MHz ^{13}C-NMR ($CDCl_3$) [*cis* isomer]: δ 19.3, [21.2], [21.7], 22.4, 25.8, 26.0, 26.4, 27.2, [27.4], 28.2, [28.4], [30.9], 31.4, [34.1], 35.3, 42.9, 83.7, [84.0], 122.7. HRMS calcd for $C_{20}H_{32}BNO_2$ (M^+) 329.2526, found 329.2516. Anal. Calcd for $C_{20}H_{32}BNO_2$: C, 72.95; H, 9.8; B 3.28; N, 4.25, Found: C, 73.07; H, 9.91; B 3.15; N, 4.09.

Coupling constants and NOE data for 15a and 16a. Coupling constants calculated with an MMX program (PCModel) are correlated with observed data in Tables 1 and 2. NOE data are listed in Tables 3 and 4. In **15a**, no NOE was observed between methyl and $H^{1\alpha}$, so they must be *trans* to each other, but the methyl group has an NOE enhancement with $H^{1\beta}$ in **16a**, indicating that they are *cis.* NMR and NOE spectra of a mixture of ~2:1 **16a** and **15a** are illustrated in Figure 1. The NOESY spectrum of **15a** is summarized in Table 5.

Table 1. The coupling constants of **15a**: experimental, (MMX); and [calculated dihedral angle].

	$H^{1\alpha}$	$H^{4\beta}$	$H^{4\alpha}$	$H^{3\alpha}$
$H^{2\beta}$	9.8 (12)	-	-	9.8 (12)
$H^{1\alpha}$	-	9.3 (11) [156°]	7.9 (8.6) [25°]	-
$H^{4\beta}$	-	-	-	9.3 (11)
$H^{4\alpha}$	-	-	-	7.9 (8.4)

Table 2. The coupling constants of **16a**: experimental, (MMX); and [calculated dihedral angle].

	$H^{1\beta}$	$H^{4\beta}$	$H^{4\alpha}$	$H^{3\alpha}$
$H^{2\beta}$	9.7 (9.5)	-	-	? (12)
$H^{1\beta}$	-	9.1 (8.6) [24°]	5.1 (2.1) [104°]	1.2
$H^{4\beta}$	-	-	-	7.2 (11)
$H^{4\alpha}$	-	-	-	8.2 (8.3)

Table 3. One dimensional NOE data for **15a**, shown as percentages.

irradiated H (below)	$H^{2\beta}$	$H^{1\alpha}$	$H^{4\beta}$	$H^{4\alpha}$	$H^{3\alpha}$	$CH_3{}^{3\beta}$
$H^{2\beta}$	-	4.2	*	*	2.74	4.8
$H^{1\alpha}$	1.8	-	1.3	2.8		0
$H^{4\beta}$	*	1.3	-	16	-	5.5
$H^{4\alpha}$	0	4.8	22	-	*	1.5
$CH_3{}^{3\beta}$	3.1	0	2.5	0	3.8	-

* Either the NOE is negative or the chemical shift is too close to the irradiation peak.

Table 4. One dimensional NOE data for **16a**, shown as s (strong),m (medium), or w (weak).

irradiated H (below)	$H^{1\beta}$	$H^{4\beta}$	$H^{4\alpha}$	$H^{3\alpha}$
$CH_3{}^{3\beta}$	m	w	s	s

Figure 1. Top curve: 300-MHz ^{1}H-NMR spectrum of a ~2:1 mixture of (1*S*,2*R*,3*S*)- (**16a**) and (1*R*,2*R*,3*S*)-2-[(4*R*,5*R*)-4,5-dicyclohexyl-1,3,2-dioxaborolan-2-yl]-3-methylcyclobutane-carbonitrile (**15a**). Bottom curve: NOE spectrum of the same mixture, with irradiation of the 3β-CH_3 group protons at δ 1.14-1.15.

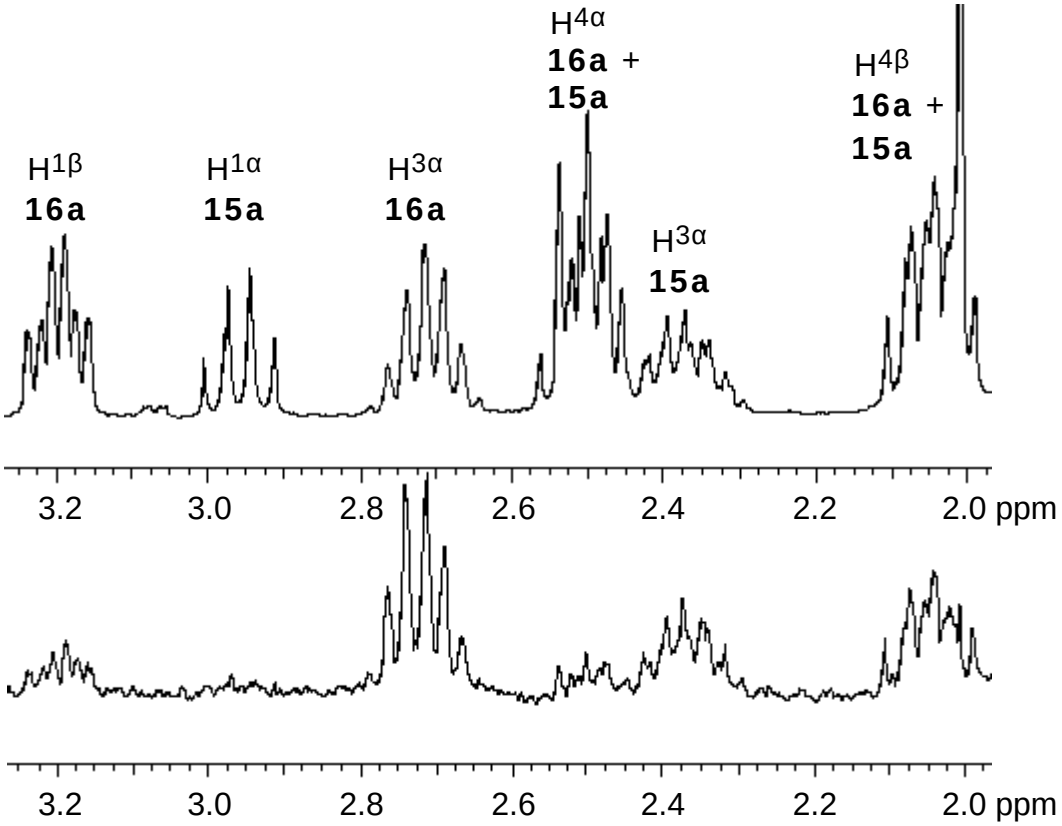

Table 5. 2D-NOESY of **15a** (2.5 s delay, 1.5 s mixing time): cross peak intensity: (s) strong (m) medium (w) weak:

	$H^{1\alpha}$	$H^{4\beta}$	$H^{4\alpha}$	$H^{3\alpha}$	CH_3^{β}
$H^{2\beta}$	yes (w)	yes (m)	no	yes (m)	yes (s)
$H^{1\alpha}$	-	yes (m)	yes (s)	yes (w)	no
$H^{4\beta}$	-	-	yes (s)	yes (m)	yes (s)
$H^{4\alpha}$	-	-	-	yes (s)	yes (w)
$H^{3\alpha}$	-	-	-	-	yes (s)

α,4,4,5,5-Pentamethyl-1,3,2-dioxaborolane-2-propanenitrile (10b).

Propanenitrile was used in place of acetonitrile in a similar procedure to that used for **10a**.

Distillation yielded an oil, bp 85 °C (2-3 torr), 74%; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 1.10 (dd, *J* = 8.1, 16.2 Hz, 1), 1.19-1.30 (dd + 1.26 s, 13), 1.34 (d, *J* = 7.1 Hz, 3), 2.81 (m, 1); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 15.49, 18 (br), 20.91, 24.63, 24.66, 83.72, 123.95. HRMS calcd for $C_{10}H_{18}BO_2N$ (M^+) 195.1431, found 195.1424.

(4*R*,5*R*)-4,5-Dicyclohexyl-α-methyl-1,3,2-dioxaborolane-2-propanenitrile (11b) was made (as a diastereomeric pair at C-α) from **10b** by the procedure used for **11a**; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.80-1.80 (m, 24), 1.35 + 1.36 (2d, *J* = 7.1 Hz, 3), 2.75-2.87 (m, 1), 3.86-3.90 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 16 (br), 20.09 + 20.21, 21.00 + 21.02, 25.76, 25.92, 26.3, 27.23 + 27.29, 28.34 + 28.38, 42.9, 83.8, 124.06 + 124.08 HRMS calcd for $C_{18}H_{30}BO_2N$ (M^+) 303.2369, found 303.2370 Anal. Calcd for $C_{18}H_{30}BO_2N$: C, 71.29; H, 9.97; B, 3.56, Found: C, 71.38; H, 10.07; B, 3.43.

(γ*S*,4*R*,5*R*)-γ-Chloro-4,5-dicyclohexyl-α-methyl-1,3,2-dioxaborolane-2-butanenitrile (12b) (diastereomeric mixture at C-α) was made from **11b** and (dichloromethyl)lithium in the usual manner and used in the next step without purification; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.85-1.82 (m, 22), 1.35 + 1.38 (2 d's, *J* = 7.1 Hz, 3), 1.9-2.15 (m) + 2.27 (ddd, *J* = 6.1, 8.2, 14.2 Hz, 2), 2.90-3.01 + 3.05-3.20 (m, 1), 3.53 + 3.68 (2dd's, *J* = 5.7, 10.2 + 3.1, 12.1 Hz, 1), 3.96-3.99 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 16.5 + 18.0, 22.6 + 23.8, 25.75, 25.89, 26.3, 27.2, 28.17 + 28.19, 37.7 + 38.3, 42.75 + 42.78, 84.37 + 84.46, 121.9 + 122.6; HRMS calcd for $C_{19}H_{31}BClO_2N$ (M^+) 351.2136, found 351.2131.

(γ*S*,4*R*,5*R*)-γ-Butyl-4,5-dicyclohexyl-α-methyl-1,3,2-dioxaborolane-2-butanenitrile (13b) was made from the preceding chloro compound **12b** by treatment with butyllithium in the usual manner[2] and chromatographed, leading to an umequal mixture of C-α diastereomers, 59%; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.85-1.90 (m, 34), 1.299 + 1.305 (2d, *J* = 7.0 Hz, 3), 2.65-2.80 (m, 1), 3.81-3.85 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 14.0, [lesser isomer 18.0] + 18.5, 20.5 (br), 22.9 + [24.3], 25.4, 25.8, 26.0, 26.4, 27.5, 28.5 + [29.9],

[30.87] + 30.93, [35.1] + 36.0, 43.0, 83.51 + [83.57], [123.2] + 123.5; HRMS calcd for $C_{23}H_{40}BNO_2$ (M^+) 373.3152, found 373.3141. Anal. Calcd for $C_{23}H_{40}BNO_2$: C, 73.99; H, 10.8; B, 2.9, Found: C, 73.97; H, 10.54; B, 3.11.

(γ*S*,δ*S*,4*R*,5*R*)-γ-Butyl-δ-chloro-4,5-dicyclohexyl-α-methyl-1,3,2-dioxaborolane-2-pentanenitrile (14b). This compound was prepared in the usual manner from (dichloromethyl)lithium (1.8 mmol) and **13b** (1.37 mmol) followed by zinc chloride (2.5 mmol), 0.5 g crude (87%), used without purification; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.82-2.15 (m, 32), 1.34 + 1.35 (2d, *J* = 7.0 Hz, 3), 2.65-2.80 (m, 1), 3.62 + 3.65 (2d, *J* = 4.2 + 3.5 Hz, 1), 3.94-3.96 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$), δ 13.98 + [minor isomer 14.02], [18.3] + 18.6, 22.9 + [23.0], [23.5] + 23.6, 25.8, 25.9, 26.3, 27.5, 28.3, 29.3, [31.7] + 32.3, 35.9 + [36.4], 39.6, 42.9+ [43.0], [84.36] + 84.44, 122.8. HRMS calcd for $C_{24}H_{41}BClO_2N$ (M^+) 421.2919, found 421.2919.

(1*R*,2*R*,3*S*)-2-[(4*R*,5*R*)-4,5-Dicyclohexyl-1,3,2-dioxaborolan-2-yl]-3-butyl-1-methylcyclobutanecarbonitrile (15b). The chloro boronic ester **14b** (0.5 g, 1.2 mmol) in THF (10 mL) was treated with LDA (0.65 mL, 2 M, 1.3 mmol) at –78 °C. After 48 h at 20-25 °C, the reaction mixture was worked up with ether and saturated ammonium chloride in the usual way. Concentration yielded an oily mixture of **15b** and its (1*S*,2*R*,3*S*)-isomer **16b** in a ratio of 12:1 based on ^{13}C NMR ($CDCl_3$). The GC retention times were **15b**, 18.76 min and **16b**, 19.68 min (DB-5, 25 m, 60 °C/2min/20 °C/min/310 °C). Flash chromatography (Silica gel, 4% ether/pentane) gave a **15b**/**16b** ratio of 15:1 (0.23 g, 50%) based on ^{13}C NMR; 300-MHz ^{1}H-NMR ($CDCl_3$) δ 0.87 (t, *J* = 7.3 Hz, 3), 0.9-1.82 (m, 28), 1.51 (s, 3), 2.03 (d, *J* = 9.8 Hz, 1), 2.13 (ddd, *J* = 0.6, 7.9, 11.0 Hz, 1), 2.25 (dd, *J* = 8.9, 11.1 Hz, 1), 2.33-2.44 (m, 1), 3.82-3.87 (m, 2); 75-MHz ^{13}C-NMR ($CDCl_3$), δ 14.06, 22.57, 22.98, 25.95, 26.39, 27.38, 27.46, 28.52, (29.05) + 29.15, (32.29) + 32.38, (37.40) + 37.25, 40.52, (42.89), 43.04, 83.82 + (83.93), (125.35) + 125.70 HRMS calcd for $C_{24}H_{40}BO_2N$(M^+) 385.3152, found 385.3154. Anal. Calcd for $C_{24}H_{40}BO_2N$: C, 74.80; H, 10.46; B, 2.81, Found: C, 74.79; H, 10.54; B, 3.02.

(γ*R*,4*R*,5*R*)-4,5-Dicyclohexyl-γ-phenylmethoxy-α-methyl-1,3,2-dioxaborolane-2-butanenitrile (13c) (diastereomer mixture at C-α). (γ*S*,4*R*,5*R*)-γ-Chloro-4,5-dicyclohexyl-α-methyl-1,3,2-dioxaborolane-2-butanenitrile (**12b**) (5.7 mmol, prepared as described above) was treated with lithium benzyl oxide (5.7 mmol) in THF (20 mL) at –78 °C. After 10 min, dimethyl sulfoxide (3 mL) was added. The solution was allowed to warm to room temperature and kept overnight. The solution was concentrated and worked up with pentane and saturated ammonium chloride in the usual way. Flash chromatography (Silica gel, ether/pentane 5%) yielded **13c**, 1.8 g (74%); 300-MHz ^{1}H-NMR ($CDCl_3$) [lesser diastereomer in brackets] δ 0.90-1.95 (m, 22), [1.21 (d, *J* = 7.1 Hz)], 1.31 (d, *J* = 7.2 Hz, 3), 2.15 (dd, *J* = 5.8, 10.1 Hz, 1), 2.20 (dd, *J* = 5.9, 10.1 Hz), [2.80-2.95 (m)], 2.98-3.12 (m, 1), [3.40 (dd, *J* = 4.7, 10.1 Hz)], 3.59 (dd, *J* = 4.2, 10.8 Hz, 1), [4.41 (AB, *J* = 11.5 Hz)], 4.46 (AB, *J* = 11.0 Hz, 1), [4.67 (AB, *J* = 11.4 Hz)], 4.69 (AB, *J* = 10.9 Hz, 1), 7.25-7.40 (m, 5); 75-MHz ^{13}C-NMR ($CDCl_3$) δ [16.9], 18.2, [21.8], 23.0, 25.8, 25.9, 26.3, 27.2, [27.3], 28.3, [35.7], 36.6, [42.77], 42.82, [72.5], 73.3, 83.9, [84.0], 122.8, [123.5], 127.7, 128.1, 128.2, 128.3, [138.32],138.37. HRMS calcd for $C_{26}H_{38}BNO_3$ (M^+) 423.2945, found 423.2930.

(γ*S*,δ*S*,4*R*,5*R*)-δ-Chloro-4,5-dicyclohexyl-γ-phenylmethoxy-α-methyl-1,3,2-dioxaborolane-2-pentanenitrile (14c). Reaction of **13c** (1.9 mmol) with (dichloromethyl)lithium (2.1 mmol) at –100 °C followed by treatment with zinc chloride (3.5 mmol) according to the usual procedure[2a] yielded (γ*S*,δ*S*,4*R*,5*R*)-δ-chloro-4,5-dicyclohexyl-γ-phenylmethoxy-α-methyl-1,3,2-dioxaborolane-2-pentanenitrile (**14c**), 0.9 g, used in the next step without further purification; 300-MHz ^{1}H-NMR ($CDCl_3$) [lesser C-α diastereomer in brackets] δ 0.85-1.80 (m, 22), [1.24 (d, *J* = 7.1 Hz)], 1.33 (d, *J* = 7.1 Hz, 3), 1.85-2.10 (m, 2), [2.66-2.80 (m)], 2.80-2.96 (m, 1), 3.70 (d, *J* = 5.8 Hz, 1), [3.71 (d, *J* = 5.5 Hz)], [3.81-3.87(m)], 3.95-3.98 (m, 2), 4.01-4.07 (m, 1), [4.55 + 4.74 (2 AB's, *J* = 11.4 Hz)], 4.57 + 4.81 (2 AB's, *J* = 10.8 Hz, 2), 7.25-7.40 (m, 5); 75-MHz ^{13}C-NMR ($CDCl_3$) δ [17.5],18.3,[22.0], 22.4, 25.75, 25.86, 26.3, 27.3, 28.1, [35.8], 37.0, 42.8, [72.3], 73.6, 78.5, 84.2, [84.3], 122.5, 127.8,

[127.8], [127.92], 127.96, [128.40], 128.44, 137.7. HRMS calcd for $C_{27}H_{39}BClNO_3$ (M^+) 471.2711, found 471.2688.

(1*R*,2*S*,3*S*)-2-[(4*R*,5*R*)-4,5-Dicyclohexyl-1,3,2-dioxaborolan-2-yl]-1-methyl-3-(phenylmethoxy)cyclobutanecarbonitrile (15c) and its (1*S*,2*S*,3*S*)-isomer (16c). LDA (2 mmol) was added to a solution of crude (γ*S*,δ*S*,4*R*,5*R*)-δ-chloro-4,5-dicyclohexyl-γ-phenylmethoxy-α-methyl-1,3,2-dioxaborolane-2-pentanenitrile (**14c**) (0.9 g) in THF (20 mL) at –78 °C. After 6 days at 20-25 °C, the usual work-up yielded a 9:1 mixture of **15c** (0.81 g) and its (1*S*,2*S*,3*S*)-isomer **16c** based on integrals of peaks at δ 4.15 (**15c**) and 4.27 (**16c**) in the 300 MHz ^{1}H-NMR; recrystallized from 95% ethanol, isomer ratio 50:1 by ^{1}H NMR, mp 86-87 °C; 300-MHz ^{1}H-NMR ($CDCl_3$) [**16c** peaks in brackets]: δ 0.93-1.82 (m, 22, C_6H_{11}), 1.47 (s, 3, CH_3), [1.65 (s, CH_3)], [1.93 (d, *J* = 8.0 Hz, C*H*B)], [2.12 (dd, *J* = 7.7, 11.7 Hz, C*H*$^{4\beta}$H)], 2.38 (ddd, *J* = 0.48, 6.9, 11.7 Hz, 1, C*H*$^{4\alpha}$H), 2.46 (d, *J* = 7.9 Hz, 1, C*H*B), 2.68 (dd, *J* = 7.3, 11.7 Hz, 1, C*H*$^{4\beta}$H), [2.80 (ddd, *J* = 0.39, 6.5, 11.2 Hz, C*H*$^{4\alpha}$H)], 4.15 (q, *J* = 7.6 Hz, 1, C*H*OBn), [4.27 (q, *J* = 7.4 Hz, C*H*OBn)], 4.408 (AB, *J* = 11.9 Hz, 1, C*H*HPh), [4.44 (AB, *J* = 11.9 Hz, C*H*HPh)], 4.52 (AB, *J* = 11.9 Hz, 1, C*H*HPh), [4.53 (AB, *J* = 11.9 Hz, C*H*HPh)], 7.28-7.40 (m, 5, C_6H_5); 75-MHz ^{13}C-NMR ($CDCl_3$) δ 23.8, 25.8, 25.95, 26.39, 27.5, 28.6, 42.6, 43.0, 70.3, 84.2, 127.61, 127.67, 128.4. HRMS calcd for $C_{27}H_{38}BNO_3$ (M^+) 435.2945, found 435.2951. Anal. Calcd for $C_{27}H_{38}BNO_3$: C, 74.48; H, 8.8; N, 3.22. Found: C, 74.02; H, 8.54; N, 3.20.

NOE Data for 15c and 16c. The stereochemistry was determined by 1D-NOE, as shown in Tables 6 and 7. The assignments of $H^{4\beta}$ in both isomers are based on the presence of small coupling with $H^{2\beta}$. Moreover, the 2D-NOESY showed that $CH_3{}^{1\alpha}$, $H^{4\alpha}$ and $H^{3\alpha}$ are on the same side of the cyclobutane ring in **15c**. When the CH_3 in **15c** was irradiated there were NOE for $H^{2\beta}$, $H^{4\alpha}$, and $H^{3\alpha}$ at δ 2.46, 2.38 and 4.15, respectively, but no NOE was observed for $H^{4\beta}$ (δ 2.68). Therefore, $H^{4\beta}$ must be *trans* to CH_3. While the $H^{3\alpha}$ was irradiated, $CH_3{}^{1\alpha}$ (δ 1.47), $H^{4\alpha}$ and $H^{2\beta}$ had a measurable NOE, but not the $H^{4\beta}$, so $H^{3\alpha}$ is *cis* to $CH_3{}^{1\alpha}$. Although $H^{2\beta}$ is

trans to $CH_3^{1\alpha}$ and $H^{3\alpha}$, they have small NOE's among each other. A 2D-NOESY was also performed to confirm the assignment. Strong cross peaks were observed between $CH_3^{1\alpha}$-$H^{3\alpha}$, $CH_3^{1\alpha}$-$H^{4\alpha}$, $H^{2\beta}$-$H^{3\alpha}$, $H^{2\beta}$-$H^{4\beta}$, $H^{3\alpha}$-$H^{4\alpha}$, $H^{4\beta}$-$H^{4\alpha}$, $OCH_2^{3\beta}$-$H^{2\beta}$, $OCH_2^{3\beta}$-$H^{3\alpha}$, $OCH_2^{3\beta}$-$H^{4\beta}$, and there was a very weak cross peak between $CH_3^{1\alpha}$ and $H^{2\beta}$. For **16c**, no NOE was observed between $H^{3\alpha}$ and $CH_3^{1\beta}$. The 2D-NOESY showed cross peaks between $CH_3^{1\beta}$-$H^{2\beta}$, $CH_3^{1\beta}$-$H^{4\beta}$, $H^{4\beta}$-$H^{4\alpha}$, $H^{2\beta}$-$H^{4\beta}$.

Table 6. NOE data for **15c**.

irradiated H (below)	$H^{2\beta}$	$H^{3\alpha}$	$H^{4\beta}$	$H^{4\alpha}$	$CH_3^{1\alpha}$
$H^{2\beta}$ δ 2.46	--	4.9%	*	*	0.8%
$H^{3\alpha}$ δ 4.15	2.4%	--	0	4.7%	1.9%
$H^{4\beta}$ δ 2.68	0	0	--	24%	0
$H^{4\alpha}$ δ 2.38	*	6.6%	24%	--	2.1%
$CH_3^{1\alpha}$ δ 1.47	0.8%	3.1%	0	3.4%	--

* The chemical shift is too close to the irradiation peak, so the NOE is not reliable.

Table 7. NOE data for **16c**.

irradiated H (below)	$H^{2\beta}$	$H^{3\alpha}$	$H^{4\beta}$	$H^{4\alpha}$	$CH_3^{1\beta}$
$H^{3\alpha}$ δ 1.93	1.6%	--	0	5.7%	0
$H^{4\beta}$ δ 2.12	*	0	--	25%	0
$H^{4\alpha}$ δ 2.80	0	5.8%	20%	--	0
$CH_3^{1\beta}$ δ 1.65	1.0%	0	2.1%	0	--