Asymmetric Synthesis of Serricornin via Boronic Esters

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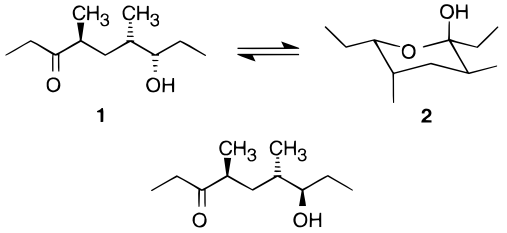
Highly stereoselective boronic ester chemistry has been used for the synthesis of (4*S*,6*S*,7*S*)-7-hydroxy-4,6-dimethylnonanone (**1**), the pheromone of the cigarette beetle. 2-Bromo-1-butene (**8**) was made from 1-butyne via bromoboration and protodeboronation, and was converted to 1-ethylethenylmagnesium bromide. (*R*,*R*)-1,2-Dicyclohexyl-1,2-ethanediol ["(*R*)-DICHED"] methylboronate was treated with (dichloromethyl)lithium to yield (*R*)-DICHED (*S*)-1-chloroethylboronate (**9**), which with 1-ethylethenylmagnesium bromide yielded (*R*)-DICHED (*R*)−(2-ethyl-1-methyl-2-propenyl)boronate (**10**). Further chain extensions with (chloromethyl)lithium, (dichloromethyl)-lithium followed by methylmagnesium bromide, and (dichloromethyl)lithium followed by ethylmagnesium bromide completed assembly of the carbon skeleton. Deboronation with hydrogen peroxide yielded (3*S*,5*S*,6*S*)-2-ethyl-3,5-dimethylocten-6-ol (**14**), which with osmium tetraoxide and sodium periodate yielded **1**.

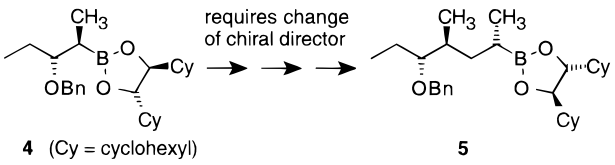
Introduction

The pheromone of the cigarette beetle, *Lasioderma serricorne* F. (Anobiidae), a pest of dried foodstuffs and tobacco, is (4*S*,6*S*,7*S*)-7-hydroxy-4,6-dimethylnonanone (**1**),[1] which exists as an equilibrium mixture with its cyclic hemiacetal tautomer **2**. The attractant activity is inhibited by the (4*S*,6*S*,7*R*)-isomer (**3**) at the 10% level, but the (4*S*,6*R*,7*R*)-isomer and the (4*S*,6*R*,7*S*)-isomer have no apparent effect up to a 1:1 ratio, and it appears that the four enantiomers of these are also inert. Previous stereocontrolled syntheses of **1** have been reported from microbially produced methyl (*R*)-3-hydroxypentanoate[2] and via asymmetric enolate chemistry.[3]



Although the purity requirements for biologically active serricornin are not nearly as stringent as for stegobinone, an anobiid beetle pheromone we have synthesized previously,[4] the three stereocenters offer a worthy synthetic challenge well suited to our asymmetric boronic ester chemistry.[5] Diastereoselections in the 1000:1 range can be achieved by the use of a chiral director that has C_2 symmetry,[6] a level of precise stereocontrol well beyond the minimal requirements for the present synthesis.

We have shown that it is possible to cleave the chiral director (*R*)-(*R**,*R**)-1,2-dicyclohexylethane-1,2-diol [(*R*)-DICHED] from boron and replace it by its (*S*)-enantiomer,[7] but the most efficient synthetic strategy requires use of a single chiral director throughout the synthesis if possible. This requirement rules out the route via (*S*)-DICHED boronic ester **4**, the enantiomer of an intermediate used for the stegobinone synthesis,[4] to (*R*)-DICHED boronic ester **5**, which has to have the opposite chiral director in order to install the second methyl group correctly. What is needed instead is a way to construct the synthetic equivalent of **4** with (*R*)-DICHED as chiral director. The benzyloxy group of **4** and **5** would be a ketone precursor, and stereocontrol at this site is irrelevant.



Results

A carbon−carbon double bond was chosen as the masked carbonyl group to carry through the synthesis of **1**. The strategy to achieve the desired chirality involved reaction of a suitable 1-ethyl-1-metalloalkene with (*R*)-DICHED (*S*)-(1-chloroethyl)boronate (**9**). An obvious way to avoid regioisomer problems would be to use a 3-metallo-3-hexene as the intermediate, but unexpected complications were encountered in the hydroboration of 3-hexyne (see Discussion).

The use of a (2-halo-1-butenyl)magnesium halide was then undertaken. The classical synthesis of 2-chloro-1-butene from 2-butanone[8] yielded a gross mixture and was abandoned in favor of a haloboration strategy. Boron

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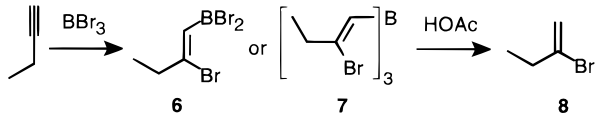
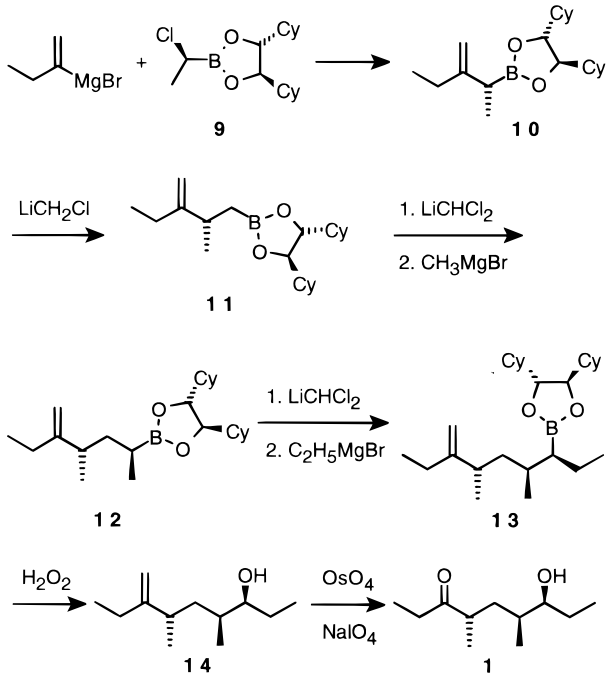
tribromide and 1-butyne react exothermically to produce (2-bromobutenyl)boron dibromide (**6**), which reacts more slowly with the stoichiometric amount of 1-butyne to form tris(2-bromobutenylborane) (**7**). Either **6** or **7** with acetic acid yielded 2-bromo-1-butene (**8**).



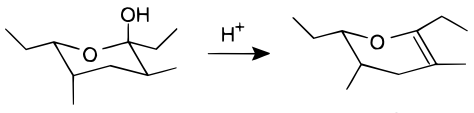
6 **7** **8**

The boronic ester chemistry followed established procedures.[5,6] (*R*,*R*)-1,2-Dicyclohexyl-1,2-ethanediol [(*R*)-DICHED] (*S*)-(1-chloroethyl)boronate (**9**) was prepared from (dichloromethyl)lithium and (*R*)-DICHED methylboronate as previously described.[9] Treatment of **9** with (1-ethylethenyl)magnesium bromide (from **8** and magnesium in THF) yielded (*R*)-(2-ethyl-1-methyl-2-propenyl)boronate **10**, which was converted by (chloromethyl)lithium to (3-ethyl-2-methyl-3-butenyl)boronate **11**.



9 **10** **11** **12** **13** **14** **1**

Chain extension with (dichloromethyl)lithium and methylation with methylmagnesium bromide yielded intermediate **12**, and a final chain extension with (dichloromethyl)lithium and ethylation with ethylmagnesium bromide completed the carbon skeleton, boronic ester **13**. Deboronation of **13** yielded key intermediate alkenol **14**, which was cleaved to serricornin (**1**) by sodium periodate with a catalytic amount of osmium tetraoxide. Purification of **14** was easily accomplished by distillation. Serricornin undergoes dehydration from cyclic tautomer **2** to enol ether **15** if distilled without prior removal of all traces of acid.



2 **15**

Discussion

The overall yield of serricornin from (*R*)-DICHED methylboronate was 59%, calculated as the product of the yields in each step. Although the efficiency of recovery of the chiral director, (*R*)-DICHED, was not measured, it has been shown in previous work that 90% of a similar chiral director can be recovered if the byproduct fractions are kept and included in the recycling.[10] Thus, the synthesis is highly efficient in its use of chiral director.

The overall yield of serricornin based on the achiral precursors 1-butyne and boron tribromide was not measured accurately. The yield of purified 2-bromo-1-butene via the tris(alkenylborane) was 80%, and if it is assumed that the yield of Grignard reagent was 70−80%, the yield of serricornin was 33−39%.

Unsaturated alcohol **14** was the only intermediate in the sequence that was purified by chromatography. Despite the lack of rigorous purification of any of the preceding intermediates in this multistep sequence, the stereoselectivity and yield in each chain-extension step were so high that purified **14** was obtained from its crude predecessor **13** in 89% yield.

The unusually high stereoselection in the rearrangement of (chloroalkyl)borate complexes[6] is a major factor in making this synthesis practical without purification of intermediates at every step. A rational basis for the stereoselectivity has recently been postulated by Corey, Barnes-Seeman, and Lee,[11] and quantum-mechanical calculations by Midland have independently led to a similar conclusion.[12]

The procedures reported here utilized preformed (dichloromethyl)lithium for laboratory convenience, which requires cooling to −100 °C. However, it should be noted that a practical temperature for scale-up, −40 °C, has been used successfully with a number of similar preparations merely by generating the (dichloromethyl)lithium from dichloromethane and lithium diisopropylamide in the presence of the boronic ester.[4,5,13]

At the outset of this work, it was expected that hydroboration of 3-hexyne with catecholborane would produce a single regio- and stereoisomer,[14] which could be converted to a single geometric isomer of 3-bromo-3-hexene,[15] then to 3-lithio-3-hexene, for reaction with (*R*)-DICHED (*S*)-(1-chloroethyl)boronate (**9**) to form the propylidene analogue of (α-methylenealkyl)boronic ester **10**. However, commercial catecholborane with 3-hexyne yielded gross (*E*,*Z*)-mixtures as a result of free radical side reactions, and (*Z*)-3-hexenyl-3-boronic esters isomerize thermally to (*E*,*Z*)-mixtures, reported in detail elsewhere.[16] Such mixtures would have unduly complicated the characterization of a series of intermediates, hence, the use of 2-bromo-1-butene (**8**) instead.

The best alternative synthesis utilizes asymmetric aldol and enolate alkylation processes.[3] The chiral director used for both carbon−carbon bond connections, (*S*-*trans*)-2,5-bis[(methoxymethoxy)methyl]pyrrolidine, re-

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quired a multistep synthesis involving resolution,[3] as did the chiral director for an earlier synthesis of the intermediate (*S,S*)-2-methyl-3-hydroxypentanoic acid.[17] More recent technology could no doubt improve the practicality of this alternative approach.

Experimental Section

General Methods. The usual procedures for handling reactive organometallic reagents were followed, including the use of an inert atmosphere (argon) and THF (tetrahydrofuran) that had been rigorously dried over sodium benzophenone ketyl. Detailed directions for carrying out reactions of boronic esters with (dichloromethyl)lithium have been reported previously.[4−6]

2-Bromo-1-Butene (8). A. Via (2-Bromobutenyl)-(dibromo)borane. 1-Butyne (21.63 g, 31.9 mL, 400 mmol) was condensed in a flask at −78 °C under argon, and boron tribromide (100.2 g, 37.81 mL, 400 mmol) was added dropwise. An exothermic reaction occurred, with the evolution of white fumes. After addition of boron tribromide, the neat reaction mixture was stirred at −78 °C for 0.5 h. Pentane (1 L) was added slowly at −78 °C. The resulting orange homogeneous solution was poured slowly onto excess crushed ice. (CAUTION: Hydrogen bromide evolution occurs.) The pentane solution was separated, the aqueous phase was extracted with pentane, and the combined pentane solution was concentrated to ∼300 mL and then treated with glacial acetic acid (24 mL). The mixture was stirred at 20−25 °C for 24 h or under reflux for 16 h. Excess acetic acid was neutralized with sodium carbonate solution and washed with water. The solution was dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. 2-Bromo-1-butene was distilled under vacuum (1 Torr) from a flask immersed in a bath at <10 °C into a receiver cooled with a −78 °C bath (37.85 g, 70%): 300 MHz ^{1}H NMR ($CDCl_3$) δ 1.11 (t, 3), 2.44 (q, 2), 5.33 (s, 1), 5.52 (d, 1); 75 MHz ^{13}C NMR ($CDCl_3$) δ 13.0, 34.9, 114.9, 136.1; HRMS calcd for C_4H_7Br (M^+) 133.9731, found 133.9713.

B. Via Tris(2-bromobutenyl)borane. Butyne gas (5.9 g, 116 mmol) was condensed at −78 °C in a flask equipped with a dry ice condenser and magnetic stir bar. (The receiver was weighed before and after the introduction of the butyne.) Boron tribromide (9.7 g, 3.6 mL, 38 mmol) was cooled to 0 °C and then added dropwise down the side of the flask over a 5 min period. (Faster addition resulted in loss of butyne due to the exothermic reaction.) The dry ice condenser was kept charged while the mixture was allowed to warm to 25 °C over a period of 4 h. The tris(2-bromobutenyl)borane appeared 95% pure by ^{1}H NMR analysis: 14.5 g (95%); 300 MHz ^{1}H NMR ($CDCl_3$) δ 1.18 (t, 3), 2.61 (dq, 2), 6.78 (t, 1); 75 MHz ^{13}C NMR ($CDCl_3$) δ 13.3, 39.4, 131.2 (br, B−C), 145.2. The tris(2-bromobutenyl)borane was dissolved in pentane (300 mL), and glacial acetic acid (100 mL, 1.4 mol) was added slowly, causing an exothermic reaction. After the mixture was stirred overnight, the acid was neutralized with excess sodium carbonate solution. The pentane phase was separated, dried over anhydrous magnesium sulfate, and filtered. Pentane was distilled at atmospheric pressure at a bath temperature up to 55 °C, and 2-bromo-1-butene was distilled into a dry ice cooled receiver under vacuum, 12.5 g (80%).

[4*R*-(4α,5*β*)]-4,5-Dicyclohexyl-2-methyl-1,3,2-dioxaborolane. This compound was prepared from [(*R*)-(*R**,*R**)]-1,2-dicyclohexyl-1,2-ethanediol and trimethylboroxine by the previously reported method.[18]

[4*R*-[2(*S),4α,5*β*]]-4,5-Dicyclohexyl-2-(1-chloroethyl)-1,3,2-dioxaborolane (9).** The previously described procedure[5a,b] was used for the preparation of (dichloromethyl)-lithium (76 mmol) from a solution of dichloromethane (12.9 g, 150 mmol) in THF (tetrahydrofuran) (200 mL) and butyllithium (47.5 mL of 1.6 M solution in hexane, 76 mmol) at −100 °C. After 5 min, a solution of [4*R*-(4α,5*β*)]-4,5-dicyclohexyl-2-methyl-1,3,2-dioxaborolane (18.0 g, 72 mmol) in THF (100 mL) was added via cannula to the stirred mixture. Anhydrous zinc chloride (7.8 g, 58 mmol) was added. The solution was allowed to warm to 20−25 °C and stirred for 24 h. The solvent was removed under vacuum. Ether was added, and the mixture was washed with saturated ammonium chloride solution. The organic phase was dried over anhydrous magnesium sulfate and filtered. Concentration at reduced pressure yielded [4*R*-[2(*S**),4α,5*β*]]-4,5-dicyclohexyl-2-(1-chloroethyl)-1,3,2-dioxaborolane (**7**) (21.2 g, 98%); 300 MHz ^{1}H NMR ($CDCl_3$) δ 0.88−1.79 (m,22), 1.55 (d, 3), 3.45 (q, J = 7.5 Hz, 1), 3.82−3.96 (m, 2); 75 MHz ^{13}C NMR ($CDCl_3$) δ 20.6, 25.7, 25.9, 26.3, 27.1, 28.0, 37.9, 42.7, 84.0; HRMS calcd for $C_{16}H_{28}BClO_2$ (M^+) 298.1871, found 298.1864. Anal. Calcd for $C_{16}H_{28}BClO_2$: C, 64.35; H, 9.45; B, 3.62; Cl, 11.87. Found: C, 64.63; H, 9.51; B, 3.37; Cl, 11.97.

Bromo(1-ethylethenyl)magnesium (1-Buten-2-ylmagnesium bromide). This Grignard reagent was prepared in the usual manner from magnesium turnings (3.2 g, 113 mmol) in THF (tetrahydrofuran) (250 mL), and a solution of 2-bromo-1-butene (**8**) (13.5 g, 100 mmol) in THF (50 mL) was added slowly. The concentration of Grignard reagent was determined by titration with 2-propanol in THF using 1,10-phenanthroline as an indicator.

[4*R*-[2(*R),4α,5*β*]]-4,5-Dicyclohexyl-2-(2-ethyl-1-methyl-2-propenyl)-1,3,2-dioxaborolane (10).** (1-Buten-2-yl)magnesium bromide (3.25 M in THF, 60 mmol) was added dropwise in 0.5 h to [4*R*-[2(*S**),4α,5*β*]]-4,5-dicyclohexyl-2-(1-chloroethyl)-1,3,2-dioxaborolane (**9**) (17.88 g, 60 mmol) in THF (65 mL) stirred at −78 °C. The bath was allowed to warm to 20−25 °C, and the reaction mixture was stirred for 20 h. The usual workup procedure (see preparation of **9**) yielded colorless liquid **10** (18.13 g, 95%): 300 MHz ^{1}H NMR ($CDCl_3$) δ 0.80−1.77 (m, 22), 1.04 (d, 3), 1.17 (t, 3), 1.90 (q, 1), 2.00 (m, 1), 2.10 (m, 1), 3.83 (d, 2), 4.72 +4.73 (AB, 2); 75 MHz ^{13}C NMR ($CDCl_3$) δ 12.3, 14.8, 25.9, 26.4, 27.3, 28.12, 29.3, 43.0, 83.3, 105.5, 154.0; HRMS calcd for $C_{20}H_{35}BO_2$ (M^+) 318.2730, found 318.2742.

[4*R*-[2(*S),4α,5*β*]]-4,5-Dicyclohexyl-2-(3-ethyl-2-methyl-3-butenyl)-1,3,2-dioxaborolane (11).** Butyllithium (1.6 M in hexane, 40 mL, 64 mmol) was added slowly from a syringe to a stirred solution of chloroiodomethane (21.16 g, 8.73 mL, 120 mmol) and [4*R*-[2(*R**),4α,5*β*]]-4,5-dicyclohexyl-2-(2-ethyl-1-methyl-2-propenyl)-1,3,2-dioxaborolane (**10**) (17.8 g, 56 mmol) in THF (200 mL) cooled with a −78 °C bath.[19] The bath was allowed to warm to 20−25 °C, and the mixture was stirred for 24 h. The solution was concentrated under vacuum, and the residue was worked up in the usual way with ether and saturated aqueous ammonium chloride (see the preparation of **9**). Concentration of the organic phase yielded liquid **11** (17.6 g, 95%): 300 MHz ^{1}H NMR ($CDCl_3$) δ 0.89−1.77 (m, 30), 2.03−2.06 (m, 2), 2.39 (m, 1), 3.80−3.85 (m, 2), 4.63 (d, 1), 4.72 (d, 1); 75 MHz ^{13}C NMR ($CDCl_3$) δ 12.2, 17.9, 22.7, 25.8, 25.9, 26.3, 27.2, 28.3, 35.7, 42.9, 82.1, 105.0, 157.6; HRMS calcd for $C_{21}H_{37}BClO_2$ (M^+) 332.2889, found 332.2881.

[4*R*-[2(*S,*S**),4α,5*β*]]-4,5-Dicyclohexyl-2-(1-chloro-5-ethyl-4-methyl-4-pentenyl)-1,3,2-dioxaborolane.** A solution of [4*R*-[2(*S**),4α,5*β*]]-4,5-dicyclohexyl-2-(3-ethyl-2-methyl-3-butenyl)-1,3,2-dioxaborolane (**11**) (14.9 g, 45 mmol) in THF (50 mL) was added via cannula to (dichloromethyl)lithium (50 mmol) at −100 °C as described for the preparation of **9**. Anhydrous zinc chloride (6.13 g, 45 mmol) was added, the bath was allowed to warm to 20−25 °C, and the mixture was stirred for 24 h. The usual workup procedure yielded liquid [4*R*-[2(*S**,*S**),4α,5*β*]]-4,5-dicyclohexyl-2-(1-chloro-5-ethyl-4-methyl-4-pentenyl)-1,3,2-dioxaborolane (16.5 g, 97%): 300 MHz ^{1}H NMR ($CDCl_3$) δ 0.80−2.09 (m, 32), 2.52−2.55 (m, 1), 3.48 (dd, 1), 3.92 (m, 2), 4.79 (m, 2); 75 MHz ^{13}C NMR ($CDCl_3$) δ 12.2, 20.5, 25.5, 25.8, 25.9, 26.3, 27.2, 28.1, 37.7, 39.5, 42.9, 84.1,

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108.2, 153.8; HRMS calcd for $C_{22}H_{38}BClO_2$ (M^+) 380.2653, found 380.2629.

[4*R*-[2(*S,*S**),4α,5*β*]]-4,5-Dicyclohexyl-2-(4-ethyl-1,3-dimethyl-4-pentenyl)-1,3,2-dioxaborolane (12).** Methylmagnesium bromide (3.0 M in ether, 13.3 mL, 40 mmol) was added to a stirred solution of [4*R*-[2(*S**,*S**),4α,5*β*]]-4,5-dicyclohexyl-2-(1-chloro-5-ethyl-4-methyl-4-pentenyl)-1,3,2-dioxaborolane (15.2 g, 40 mmol) in THF (250 mL) at −78 °C over a period of 20 min. The bath was allowed to warm to 20−25 °C, and the reaction mixture was stirred for 20 h. The usual workup procedure led to liquid **12** (13.8 g, 96%): 300 MHz ^{1}H NMR ($CDCl_3$) δ 0.84−2.27 (m, 37), 3.81 (m, 2), 4.68 and 4.70 (AB, 2); 75 MHz ^{13}C NMR ($CDCl_3$) δ 12.3, 16.2, 20.2, 25.9, 26.0, 26.4, 27.4, 28.28, 28.34, 39.2, 39.5, 43.0, 83.2, 106.7, 156.2); HRMS calcd for $C_{23}H_{41}BO_2$ (M^+) 360.3200, found 360.3199.

[4*R*-[2(*S,*S**,*S**),4α,5*β*]]-4,5-Dicyclohexyl-2-(1-chloro-5-ethyl-2,4-dimethyl-5-hexenyl)-1,3,2-dioxaborolane.** A solution of [4*R*-[2(*S**,*S**),4α,5*β*]]-4,5-dicyclohexyl-2-(4-ethyl-1,3-dimethyl-4-pentenyl)-1,3,2-dioxaborolane (**12**) (13.66 g, 37.94 mmol) in THF (50 mL) was added via cannula to (dichloromethyl)lithium (48 mmol) at −100 °C as described for the preparation of **9**. Anhydrous zinc chloride (5.2 g, 38 mmol) was added, the bath was allowed to warm to 20−25 °C, and the mixture was stirred for 24 h. The usual workup led to liquid [4*R*-[2(*S**,*S**,*S**),4α,5*β*]]-4,5-dicyclohexyl-2-(1-chloro-5-ethyl-2,4-dimethyl-5-hexenyl)-1,3,2-dioxaborolane (15.17 g, 98%): 300 MHz ^{1}H NMR ($CDCl_3$) δ 0.85−2.22 (m, 37), 3.45 (d, 1), 3.93 (m, 2), 4.70 and 4.74 (AB, 2); 75 MHz ^{13}C NMR ($CDCl_3$) δ 12.3, 17.1, 19.7, 25.3, 25.9, 25.9, 26.3, 27.3, 28.2, 34.2, 37.5, 40.3, 42.9, 84.0, 107.1, 156.1; HRMS calcd for $C_{24}H_{42}BClO_2$ (M^+) 408.2966, found 408.2968.

[4*R*-[2(*S,*S**,*S**),4α,5*β*]]-4,5-Dicyclohexyl-2-(1,5-diethyl-2,4-dimethyl-5-hexenyl)-1,3,2-dioxaborolane (13).** Ethylmagnesium bromide (3.0 M in diethyl ether, 35.6 mmol) was added dropwise over 20 min to a stirred solution of [4*R*-[2(*S**,*S**,*S**),4α,5*β*]]-4,5-dicyclohexyl-2-(1-chloro-5-ethyl-2,4-dimethyl-5-hexenyl)-1,3,2-dioxaborolane (14.5 g, 35.6 mmol) in THF (200 mL) cooled with a −78 °C bath. The bath was allowed to warm to 20−25 °C, and the mixture was stirred for 24 h. The usual workup yielded liquid **13** (12.9 g, 90%): 300 MHz ^{1}H NMR ($CDCl_3$) δ 0.87−2.27 (m, 43), 3.81 (m, 2), 4.66 and 4.71 (AB, 2); 75 MHz ^{13}C NMR ($CDCl_3$) δ 12.3, 14.1, 17.6, 19.5, 22.0, 25.8, 25.9, 26.1, 27.1, 27.6, 28.2, 28.5, 31.6, 37.4, 43.1, 83.1, 105.8, 156.8; HRMS calcd for $C_{26}H_{48}BO_2$ [$(M + 1)^+$] 403.3747, found 403.3732.

[*S*-(*R,*R**,*R**)]-2-Ethyl-3,5-dimethyl-1-octen-6-ol (14).** Aqueous 3 M sodium hydroxide (30 mL) and a solution of [4*R*-[2(*S**,*S**,*S**),4α,5*β*]]-4,5-dicyclohexyl-2-(1,5-diethyl-2,4-dimethyl-5-hexenyl)-1,3,2-dioxaborolane (**13**) (4.02 g, 10 mmol) in diethyl ether (200 mL) were stirred and cooled with an ice bath during the portionwise addition of 30% hydrogen peroxide (30 mL) over a period of 1 h. The mixture was stirred for 15 h, more ether (100 mL) was added, and the ether phase was washed with water, dried over magnesium sulfate, and filtered. Concentration at 50 Torr yielded a residue consisting of [*S*-(*R**,*R**,*R**)]-2-ethyl-3,5-dimethyl-1-octen-6-ol (**14**) and [(*R*)-(*R**,*R**)]-1,2-dicyclohexyl-1,2-ethanediol. The latter was recovered by addition of pentane (25 mL) and crystallization at 0 °C. Distillation at 45 °C (0.1 Torr) followed by chromatography on silica with 9:1 pentane/ether yielded pure **14** (1.62 g, 89%): $[\alpha]^{22}_{546}$ −12.5 (c = 2.3, $CHCl_3$); 300 MHz ^{1}H NMR ($CDCl_3$) δ 0.83−2.30 (m, 20), 3.4 (m, 1), 4.75 (d, 2); 75 MHz ^{13}C NMR ($CDCl_3$) δ 10.9, 12.5, 13.4, 20.2, 26.2, 27.8, 35.7, 37.9, 39.9, 75.9, 106.8, 156.6; HRMS calcd for $C_{12}H_{25}O$ ($M + 1$) 185.1905, found (CI) 185.1893. Anal. Calcd for $C_{12}H_{24}O$: C, 78.20; H, 13.12. Found: C, 78.02; H, 12.83.

Serricornin (1 + 2). Osmium tetraoxide (80 mg, 0.3 mmol) was added to a solution of [*S*-(*R**,*R**,*R**)]-2-ethyl-3,5-dimethyl-1-octen-6-ol (**14**) (0.552 g, 3 mmol) in 36 mL of 1,4-dioxane and 12 mL of water at 20−25 °C. After 15 min, finely powdered sodium periodate (10.0 g, 46.8 mmol) was added in several portions over a period of 1 h, in accordance with the literature procedure.[20] The mixture was stirred for 16 h and then extracted with ether. The ether solution was washed with sodium sulfite solution, dried over anhydrous magnesium sulfate, filtered, and concentrated at 50 Torr to yield a residue of serricornin (**1** and **2**) (0.507 g, 91%). The NMR data are consistent with those previously reported:[2] 300 MHz ^{1}H NMR (C_6D_6) (literature data[2] in parentheses) δ 0.8−2.4 (m, 23), 3.2 (lit. 3.17) (m, 0.75, CHO of **2**), 3.75 (lit 3.82) (ddd, 0.25, CHO of **1**); 75 MHz ^{13}C NMR (C_6D_6) assigned to **1**, δ 8.0, 10.7, 14.0, 16.5, 27.0, 33.9, 36.1, 36.8, 43.6, 76.4, 213.4 (8.0, 10.8, 13.7, 16.4, 27.5, 33.9, 35.8, 36.8, 43.8, 76.4, 213.6); assigned to **2**, 7.4, 10.7, 11.7, 16.8, 26.2, 30.2, 31.3, 33.1, 36.1, 72.6, 98.5 (7.4, 10.7, 11.7, 16.7, 26.2, 30.2, 31.3, 33.1, 36.2, 72.7, 98.6); HRMS calcd for $C_{11}H_{20}O$ [$(M - 18)^+$] 168.1514, found 168.1506.

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Supporting Information Available: Copies of the 300 MHz ^{1}H and 75 MHz ^{13}C NMR spectra for compounds **7**−**14**, the (α-chloroalkyl)boronic ester intermediates between **11** and **12** and between **12** and **13**, and the ^{1}H spectrum of **1** (in equilibrium with **2**) (21 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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