1075, 1025, 970, and 950 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.69 (s, 1 H), 5.20–5.25 (m, 1 H), 5.20 (s, 2 H), 3.77 (s, 3 H), 3.60 (t, 2 H, J = 6.2 Hz), 3.40 (d, 2 H, J = 6.8 Hz), 2.15 (s, 3 H), 2.07 (t, 2 H, J = 7.4 Hz), 1.81 (br s, 3 H), and 1.64–1.73 (m, 2 H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 172.8, 163.6, 153.6, 143.9, 135.5, 122.3, 116.7, 106.3, 69.9, 62.7, 60.9, 36.0, 30.6, 22.6, 16.0, and 11.5; UV max (isooctane) 249 nm (ϵ 6200) and 305 (3700); MS, m/e 306 (M^+), 288, 273, 260, 247, 229, 219, 207, 159, and 85. Anal. Calcd for $C_{17}H_{22}O_5$: C, 66.65; H, 7.24. Found: C, 66.39; H, 7.30.

(*E*)-6-(1,3-Dihydro-4-hydroxy-6-methoxy-7-methyl-3-oxo-5-isobenzofuranyl)-4-methyl-4-hexenoic Acid (1). A 50-mL recovery flask equipped with a Claisen head, rubber septum, and nitrogen inlet adapter was charged with a solution of the alcohol **11** (0.086 g, 0.28 mmol) in 25 mL of acetone and then cooled to −30 °C with a dry ice–bromobenzene bath. Jones reagent[24] (0.20 mL, 1.4 equiv) was then added dropwise by syringe over 3 min, and the resulting brown mixture was stirred at −30 °C for 5 h. Isopropyl alcohol (55 mg, 0.070 mL, 0.92 mmol) was then added, and the resulting mixture was filtered through a pad of Celite with the aid of two 5-mL portions of acetone and then concentrated to afford a brown oil. Column chromatography on silica gel (elution with dichloromethane–ethyl acetate) provided 0.056 g (61%) of mycophenolic acid (**1**) as colorless crystals: mp 139–141 °C (ethanol–water [lit.[2a] mp 141 °C]); IR (CCl_4) 3430, 3300–2900, 2935, 1740, 1710, 1410, 1130, 1075, 1025, 905 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 7.68 (br s, 1 H), 5.20–5.30 (m, 1 H), 5.20 (s, 2 H), 3.76 (s, 3 H), 3.39 (d, 2 H, J = 6.9 Hz), 2.41–2.48 (m, 2 H), 2.28–2.34 (m, 2 H), 2.15 (s, 3 H), and 1.90 (s, 3 H); ^{13}C NMR (67.9 MHz, $CDCl_3$) δ 179.1, 172.8, 163.5, 153.5, 144.0, 133.8, 122.8, 122.0, 116.6, 106.2, 70.0, 60.9, 34.1, 32.6, 22.5, 16.0 and 11.4; UV max (ethanol) 305 nm (ϵ 5300) and 249 (10 300); MS, m/e 320 (M^+), 302, 261, 260, 247, 245, 229, 219, 207, 159, 152, and 149. Anal. Calcd for $C_{17}H_{20}O_6$: C, 63.74; H, 6.29. Found: C, 63.82; H, 6.31.

Acknowledgment. We thank the National Institutes of Health, Firmenich SA, and Eli Lilly and Co. for generous financial support. J.J.P. was supported by PHS Grant IF32CA 07584 awarded by the National Cancer Institute.

(24) See Djerassi, C.; Engle, R. R.; Bowers, A. *J. Org. Chem.* **1956**, *21*, 1547 and references cited therein.

99% Chirally Selective Syntheses via Pinanediol Boronic Esters: Insect Pheromones, Diols, and an Amino Alcohol

Donald S. Matteson,* Kizhakethil Mathew Sadhu, and Mark L. Peterson

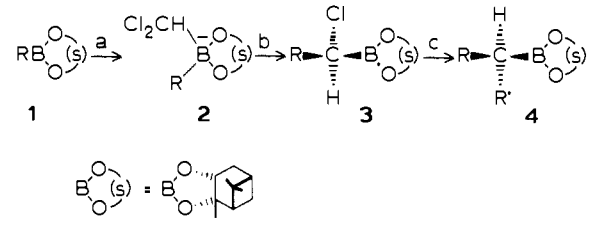
Contribution from the Department of Chemistry, Washington State University, Pullman, Washington 99164-4630. *Received September 16, 1985*

Abstract: Chiral selectivities generally exceed 99% in the homologation of (+)-pinanediol alkylboronates (**1**) to (1*S*)-(1-chloroalkyl)boronates (**3**) by reaction of **1** with (dichloromethyl)lithium at −100 °C followed by zinc chloride catalyzed rearrangement of the resulting borate complexes (**2**) at 0–25 °C. Diastereoselectivity falls to 95.7% with the methylboronate. (−)-Pinanediol leads to the 1*R* isomers. Nucleophilic displacements on (1-chloroalkyl)boronic esters yield new chiral boronic esters which can be homologated further. Compatible substituents include α- or β-benzyloxy, δ- or ϵ-ethylene ketal, β-carbo-*tert*-butoxy, α-azido, and β-hexylthio. Three insect pheromones each containing two chiral centers have been synthesized: (3*S*,4*S*)-4-methyl-3-heptanol (**5**) (elm bark beetle), *exo*-brevicomin (**12**) (western pine beetle), and eldanolide (**18**) (African sugar cane borer). Synthetic utility is further illustrated by stereocontrolled syntheses of a chiral *vic*-diol (**22**), an alcohol having three adjacent chiral centers (**24a**), a chiral α,γ-diol (**24b**), and a chiral *vic*-amino alcohol (**28b**).

Directed chiral synthesis is based on the reaction of chiral boronic esters (**1**, Scheme I) with (dichloromethyl)lithium gives the chemist absolute choice of the chirality of the carbon atom introduced and provides a unique means for systematic construction of a series of chiral centers.[1-3] The starting materials are easily obtained and the laboratory procedures are relatively simple. In the present work, we show that zinc chloride catalysis of the rearrangement of the intermediate borate complexes (**2**) results in very high diastereoselection (typically >99%) and high yields (usually 85–90%) of (1-chloroalkyl)boronic esters (**3**). Enantiomerically pure (+)- or (−)-pinanediol is used as the chiral directing group.

The present work establishes the compatibility of this process with various functional groups. Remote ketal and carboxylic ester groups do not interfere, and the utility of the process has been demonstrated with the synthesis of three insect pheromones, each of which contains two adjacent chiral centers. More crucial is the question of β-elimination of boron and nucleofugic substituents. The promise of the new process is therefore illustrated by the successful homologation of boronic esters bearing α- or β-benzyloxy, α-azido, or β-alkylthio substituents, and several subsidiary problems created by such substituents have been solved. Also illustrated are syntheses of a chiral *vic*-diol, the assembly of three adjacent chiral centers, a chiral α,γ-diol, and a chiral *vic*-amino alcohol.

Scheme I[a,b]



[a] Conditions: (a) $LiCHCl_2$, −100 °C; (b) $ZnCl_2$, 20 °C; (c) R'MgX or R'Li at −78 °C, then 20 °C. [b] **a**, R = CH_3; **b**, R = $CH_3CH_2CH_2$; **c**, R = $CH_3(CH_2)_3$; **d**, R = $(CH_3)_2CHCH_2$; **e**, R = $C_6H_5CH_2$; **f**, R = $CH_3CH_2CH_2CH(CH_3)$ (see Scheme II for configuration); **g**, R = *n*-$C_6H_{13}SCH_2CH_2$.

(1) Preliminary communication: Matteson, D. S.; Sadhu, K. M. *J. Am. Chem. Soc.* **1983**, *105*, 2077–2078; correction, 6195 (identification of tabulated compounds).

(2) (a) Matteson, D. S.; Ray, R.; Rocks, R. R.; Tsai, D. J. *Organometallics* **1983**, *2*, 1536–1543. (b) Matteson, D. S.; Ray, R. *J. Am. Chem. Soc.* **1980**, *102*, 7590–7591.

(3) Sadhu, K. M.; Matteson, D. S.; Hurst, G. D.; Kurosky, J. M. *Organometallics* **1984**, *3*, 804–806.

0002-7863/86/1508-0810$01.50/0

Table I. Diastereoselectivities and Isolated Yields in Conversions of $RBO_2C_{10}H_{16}$ (**1**) to (αS)-$RCHClBO_2C_{10}H_{16}$ (**3**) with and without Zinc Chloride

		without $ZnCl_2$		with $ZnCl_2$		
compd	R	% (αS)	yield, %	% (αS)	yield, %	anal.[a]
1a	CH_3	74[b]	57[b]	93.3–95.7	83	A, B,[c] C
1b	$CH_3(CH_2)_2$			99.1	87[d]	B
1c	$CH_3(CH_2)_3$	90[b]	61[b]	98.5	86	A, B
1d	$(CH_3)_2CHCH_2$	88[e]	~30[e]	99.5	89	C
1e	$C_6H_5CH_2$	92.5[f]	75	99.5	99	A

[a] (A) 200-MHz NMR analysis of **3**. (B) Rotation of derived alcohol prepared as in ref 2. (C) 200-MHz NMR analysis of acetamido derivative; see ref 6–8. [b] Reference 2. [c] Lowest value, possibly due to impurity in derived alcohol. [d] **3b** not isolated; yield is of **1f** obtained after treatment with methylmagnesium bromide. [e] Reference 6. [f] Reference 8.

Results

Pinanediols. An efficient preparation of pinanediol has been described.[4] For enantiomeric purification, we previously used sodium bis[pinanediol]borate,[2] but the potassium salt crystallizes more efficiently and is described in the present Experimental Section. This salt is the form in which pinanediol may be recovered after peroxidic cleavage of the boronic esters.

The trivial name "(+)-pinanediol" previously used for the isomer derived from (+)-α-pinene[2,4] suffers from inherent ambiguity and will be supplanted by the mnemonic "(s)-pinanediol", which reflects the fact that this isomer directs all homologations to form (1*S*)-(1-chloroalkyl)boronic esters and also that three of its four chiral centers are *S*.[5] Similarly, "(−)-pinanediol" is renamed "(r)-pinanediol".

Conditions. Zinc chloride catalysis was discovered in response to the unexpected difficulty of homologating (s)-pinanediol (2-methylpropyl)boronate (**1d**) to the (1*S*)-(1-chloro-3-methylbutyl)boronate (**3d**),[6] which appeared to be caused by slow and inefficient rearrangement of the intermediate borate complex **2d**. An attempt to bypass the problem by reacting isobutylmagnesium chloride with pinanediol (dichloromethyl)boronate resulted in a good yield but a useless 1:2 diastereomeric ratio.[7]

Addition of 0.5–0.7 mol of anhydrous zinc chloride improved the results dramatically. Not only did the conversion of **1d** to **3d** rise to 89%, with recovery of 10% unconverted **1d**, but the ratio of **3d** to its 1*R* diastereomer, previously 9:1,[7] rose to 200:1. The first analytical method involved conversion to the 1-acetamido derivative[8] and measurement of the NH peaks by 200-MHz NMR.

It was then found that (s)-pinanediol (1*S*)-(1-chloroalkyl)-boronates (**3**) can usually be analyzed directly for 1*R* epimer as a result of the different chemical shift of the single pinanyl proton that appears as a doublet near δ 1.1–1.2 (J = 11 Hz),[9,10] though the peak separation is not normally as great as in the (α-chlorobenzyl)boronate where it was first observed. An example typical of the alkyl series, estimated diastereomeric purity ~99.5%, is shown in Figure 1. Functionalized boronic esters sometimes showed better separations in other peaks as in Figures 2 and 3.

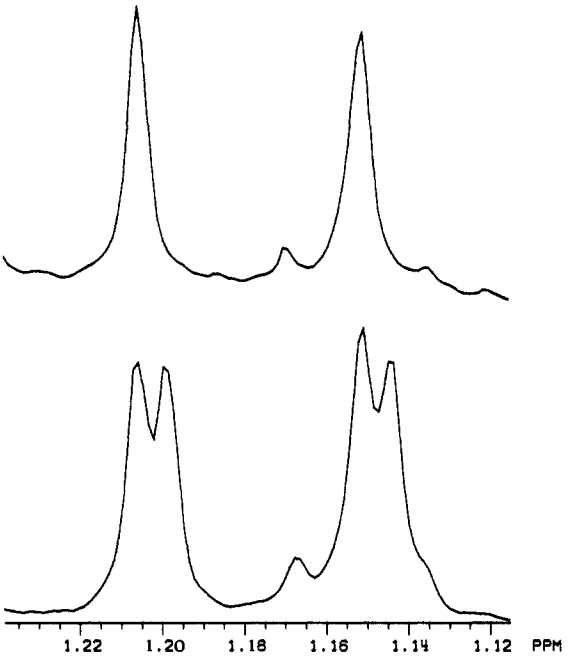
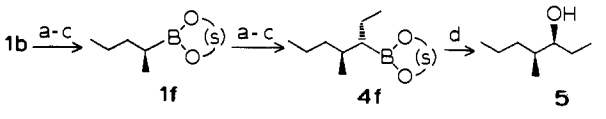


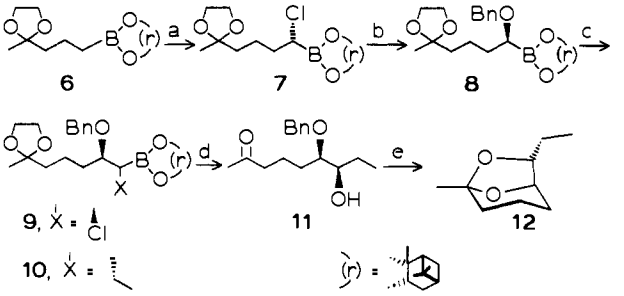
Figure 1. Top curve: 200-MHz ^1H NMR spectrum of the differentiated pinanyl proton of 2-methyl-2-[(4*R*)-4-[(r)-(pinanediyldioxy)boryl]-4-chlorobutyl]dioxolane (**7**) as obtained from homologation of **6**. The estimated diastereomeric purity is ~99.5%. Bottom curve: Spectrum of mixture of (enantiomer of) **7** and diastereomer from homologation of 2-methyl-2-[3-(1,3,2-dioxaborolyl)propyl]-1,3-dioxolane (ethylene glycol ester analogue of **6**) with (dichloromethyl)lithium followed by transesterification with (s)-pinanediol.

Scheme II[a]



[a] (a–c) See Scheme I; (d) OH^-, H_2O_2.

Scheme III[a]



[a] (a) $LiCHCl_2$, −100 °C; $ZnCl_2$; 20 °C; (b) $C_6H_5CH_2OLi$; (c) step a, then C_2H_5MgBr, −78 °C; 20 °C; (d) OH^-, H_2O_2; H_2SO_4/SiO_2; (e) H_2/Pd (ref 16).

Diastereomeric mixtures of (1-chloroalkyl)boronic esters for comparison and positive identification of the minor isomer were generated either by epimerization with lithium chloride[9] or by

(4) (a) Ray, R.; Matteson, D. S. *Tetrahedron Lett.* **1980**, *21*, 449–450. (b) Ray, R.; Matteson, D. S. *J. Indian Chem. Soc.* **1982**, *59*, 119–123. (c) Overheating this preparation causes overoxidation to keto alcohol. The internal temperature should not exceed 70 °C. We thank A. Kandil for this observation.

(5) The systematic name for (+)- or (s)-pinanediol is (1*S*,2*S*,3*R*,5*S*)-2,6,6-trimethylbicyclo[3.1.1]heptane-2,3-diol.

(6) Matteson, D. S.; Jesthi, P. K.; Sadhu, K. M. *Organometallics* **1984**, *3*, 1284–1288.

(7) Tsai, D. J. S.; Jesthi, P. K.; Matteson, D. S. *Organometallics* **1983**, *2*, 1543–1545.

(8) (a) Matteson, D. S.; Sadhu, K. M.; Lienhard, G. E. *J. Am. Chem. Soc.* **1981**, *103*, 5241–5242. (b) Matteson, D. S.; Sadhu, K. M. *Organometallics* **1984**, *3*, 614–618.

(9) Matteson, D. S.; Erdik, E. *Organometallics* **1983**, *2*, 1083–1088.

(10) (a) The J reported[9] for this indicator proton of the (α-chlorobenzyl)boronic esters was erroneous; it should have been 11 Hz. (b) We assign this signal to the endo C-7 (four-membered ring) proton, dihedral angle ~90° to its C-1 and C-5 neighbors. In the coupled ^{13}C NMR spectrum of (s)-pinanediol phenylboronate, the cyclobutyl CH_2 carbon is a triplet at δ 26.3, which collapses to a doublet on irradiation of the indicator proton. Similar proton assignments have been made for myrtenal and α-pinene: Kaplan, F.; Schulz, C. O.; Weisleder, D.; Klopfenstein, C. *J. Org. Chem.* **1968**, *33*, 1728–1730. Bates, R. B.; Thalacker, V. P. *J. Org. Chem.* **1968**, *33*, 1730–1732.

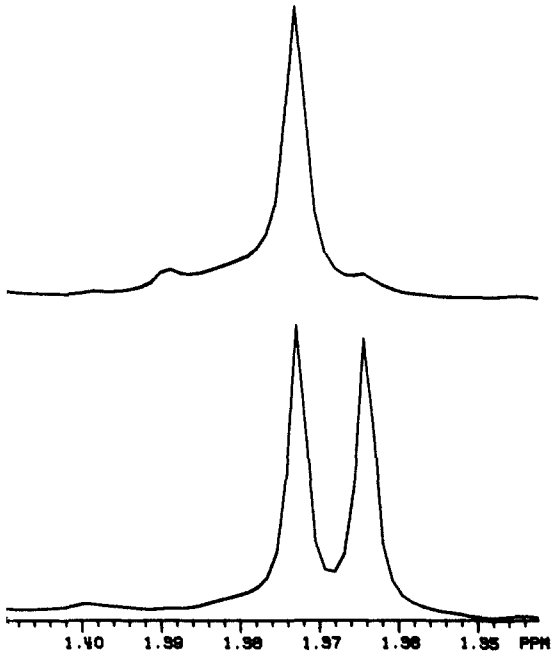


Figure 2. Top curve: 200-MHz ^{1}H NMR spectrum of the differentiated pinanyl methyl group of *tert*-butyl (3*S*)-3-[(r)-(pinanediyldioxy)boryl]-butanoate (**14**) after one recrystallization of material containing ~5% diastereomeric impurity. The estimated diastereomeric purity is ~98.0–98.5%. Bottom curve: Spectrum of mixture of (enantiomer of) **14** and diastereomer from homologation of pinacol methylboronate with (dichloromethyl)lithium followed by reaction with *tert*-butyl lithioacetate and transesterification with (s)-pinanediol.

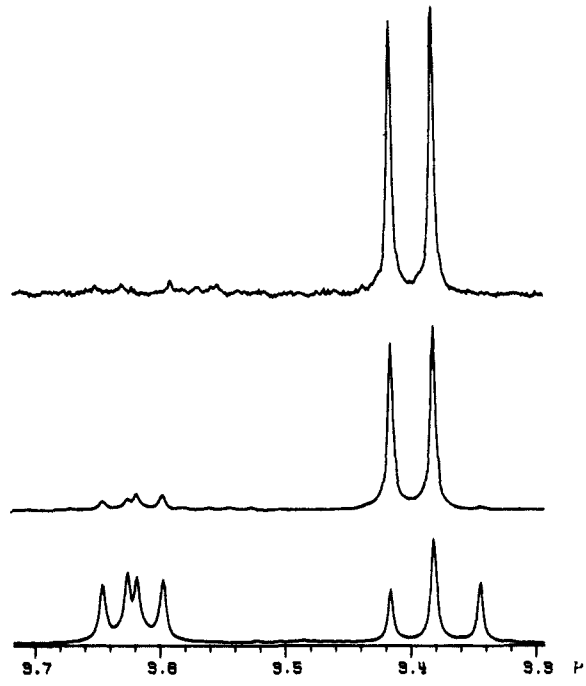


Figure 3. Top curve: 200-MHz ^{1}H NMR spectrum of the CHCl proton of *tert*-butyl (3*S*,4*R*)-4-chloro-3-methyl-4-[(r)-(pinanediyldioxy)boryl]-butanoate (**15**), δ 3.40, d, J = 7.0 Hz. This sample was obtained by treatment of the sample of **14** whose spectrum is illustrated in Figure 2 with (dichloromethyl)lithium and was not purified beyond evaporation of the solvent. The estimated 1.5–2% of (3*R*,4*R*)-isomer derived from the diastereomeric impurity in **14** is clearly visible, δ 3.64, d, J = 4.0 Hz. The (3*S*,4*S*)-isomer derived from imperfect diastereoselectivity in the homologation of **14** to **15** is not distinguishable from the noise level of the instrument, δ 3.61, J = 4.2 Hz. (The impurity peak at δ 3.59 is ~1 Hz upfield from the upfield peak of the doublet.) The doubly incorrect (3*R*,4*S*)-isomer, δ 3.36, J = 7.4 Hz, is absent as required by theory. Center curve: Spectrum of a sample of **15** which initially contained ~7% of the (3*R*,4*R*)-isomer after treatment with lithium chloride in moist THF (protected from acidity with calcium carbonate) for several days. The peaks of the (3*S*,4*S*)-isomer grew in gradually during the very slow epimerization. Bottom curve: Spectrum of a sample of (the enantiomer of) **15** and all of its diastereomers prepared by starting with pinacol methylboronate in place of pinanediol methylboronate and carrying the synthesis through both homologations, then transesterifying with (s)-pinanediol.

homologation of an ethylene glycol or pinacol boronic ester[11] followed by transesterification with pinanediol. Comparison of yields and diastereomeric ratios with and without the use of zinc chloride catalysis is shown in Table I.

Several other Lewis acid catalysts were tested. In the "uncatalyzed" process, yields were significantly higher when (1-chloroalkyl)boronic esters were not isolated but treated in situ with Grignard reagents,[2] suggesting the possibility of magnesium salt catalysis. However, magnesium bromide failed to improve the conversion of **1d** to **3d**. Mercuric chloride also proved ineffective.[6]. Cuprous triflate was insoluble in THF (tetrahydrofuran) and inactive, and stannic chloride forms an insoluble precipitate with THF. Ferric chloride (1.1 mol) increased the yield of **3d** to 55%, with recovery of 45% of the **1d**, in a single experiment.

Elm Bark Beetle Pheromone (5). (3*S*,4*S*)-4-Methyl-3-heptanol (**5**), a component of the aggregation pheromone of the European elm bark beetle, *Scolytus multistriatus*,[12] was synthesized from (s)-pinanediol propylboronate (**1b**) as outlined in Scheme II in an overall yield of 58–63%. An attempt to detect the expected ~1% of diastereomeric impurity in **5** by 200-MHz NMR analysis of the MTPA ester[13] with Eu–fod shift reagent[12c] failed.

***exo*-Brevicomin (12).** This component of the aggregation pheromone of the western pine beetle, *Dendroctonus brevicomis*,[14] has been synthesized a number of ways as the racemate[14,15] or the pure enantiomer.[16,17] Our synthesis began with conversion of the ethylene ketal of 5-chloro-2-pentanone to the corresponding (r)-pinanediol boronic ester **6** and continued as outlined in Scheme III.

The first homologation to α-chloro boronic ester **7** appeared to be ~99.5% diastereoselective (Figure 1), but similar NMR analysis of benzyloxy derivative **8** showed ~2% epimer, evidently the result of epimerization of **7** by the lithium chloride[9] liberated during the rather slow reaction with benzyloxide. Conversion of **8** to the next α-chloro boronic ester **9** was accomplished without measurable change in the epimer content, as shown by NMR analysis of **9**. The derived **12** contained ~3% epimer by NMR analysis, ~2% by gas chromatography. The partially deprotected intermediate **11** was obtained previously as an oil by Sherk and Fraser-Reid,[16] but our material was a low melting solid, from which the 2–3% diastereomeric impurity could be removed by recrystallization. Thus, in principle our synthesis is capable of yielding diastereomerically and enantiomerically pure brevicomin (**12**).

(11) (a) Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.* **1980**, *102*, 7588–7590. (b) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, *2*, 1529–1535.

(12) (a) Pearce, G. T.; Grove, W. E.; Silverstein, R. M. Peacock, J. W.; Cuthbert, R. A.; Lanier, G. N.; Simeone, J. B. *J. Chem. Ecol.* **1975**, *1*, 115. (b) Mori, K. *Tetrahedron* **1977**, *33*, 289–294. (c) Mori, K.; Isawa, H. *Tetrahedron* **1980**, *36*, 2209–2213.

(13) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549.

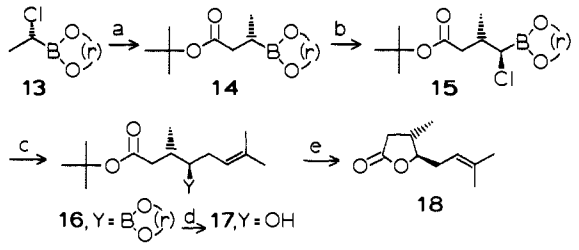
(14) (a) Silverstein, R. M.; Brownlee, R. G.; Bellas, T. E.; Wood, D. L.; Browne, L. E. *Science* **1968**, *159*, 889–891. (b) Bellas, T. E.; Brownlee, R. G.; Silverstein, R. M. *Tetrahedron* **1969**, *25*, 5149–5153.

(15) (a) Wasserman, H. H.; Barber, E. H. *J. Am. Chem. Soc.* **1969**, *91*, 3674–3675. (b) Hoffmann, R. W.; Kemper, B. *Tetrahedron Lett.* **1982**, *23*, 845–848. (c) Yamamoto, Y.; Saito, Y.; Maruyama, K. *Tetrahedron Lett.* **1982**, *23*, 4959–4962. (d) Wuts, P. G. M.; Bigelow, S. S. *Synth. Commun.* **1982**, *12*, 779–785.

(16) Sherk, A. E.; Fraser-Reid, B. *J. Org. Chem.* **1982**, *47*, 932–935. We thank Professor Fraser-Reid for a copy of the 60-MHz NMR spectrum of brevicomin.

(17) (a) Mori, K. *Tetrahedron* **1974**, *30*, 4223–4227. (b) Johnston, B. D.; Oehlschlager, A. C. *J. Org. Chem.* **1982**, *47*, 5384–5386. (c) Masaki, Y.; Nagata, K.; Serizawa, Y.; Kaji, K. *Tetrahedron Lett.* **1982**, *23*, 5553–5554 and references cited therein. (d) Wuts, P. G. M.; Bigelow, S. *J. Chem. Soc., Chem. Commun.* **1984**, 736–737.

Scheme IV[a]



[a] (a) *t*-BuO_2CCH_2Li; (b) $LiCHCl_2$, $ZnCl_2$; (c) $(CH_3)_2C{=}CHCH_2MgCl$; (d) OH^-, H_2O_2; (e) CF_3CO_2H, CH_2Cl_2.

Care had to be taken to avoid premature hydrolysis of the ethylene ketal during the synthesis, and the homologations were slower in the presence of this functionality than in its absence. Our route was chosen in order to test the compatibility of the ketal function with the homologation, not for maximum efficiency, which might have been achieved by starting from (r)-pinanediol ethylboronate and introducing the group containing the ketal function as the last carbon connection.

Eldanolide (18). This compound is the long range sex attractant isolated from the wing glands of the male African sugar cane borer moth, *Eldana saccharina*.[18] Syntheses based on incorporation of chiral carbons have been reported.[19,20] Our synthesis, outlined in Scheme IV, illustrates the compatibility of the homologation process with the presence of an ester function and also the regioselective incorporation of the allylic "prenyl" (3-methyl-2-buten-1-yl) group.

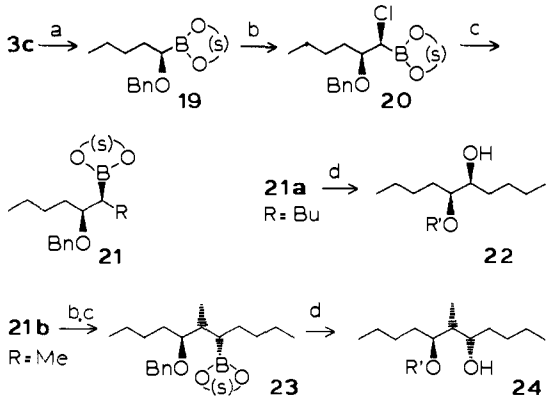
At the outset, formation of (r)-pinanediol (1*R*)-(1-chloroethyl)boronate (**13**) from (r)-pinanediol methylboronate is only 95% diastereoselective. However, **13** with *tert*-butyl lithioacetate yielded the displacement product **14**, a low melting solid purifiable by recrystallization with some effort. We used singly recrystallized 98–98.5% pure **14** (Figure 2) for our synthesis.

Homologation of **14** to **15** proved very sluggish, but increasing the amount of zinc chloride to 1.1 equiv improved the rate and yield. The 3*S*,4*S* diastereomeric impurity introduced into the derived **15** during this homologation is not clearly detectable against the background noise level of the NMR spectrum, but could be as much as ~0.5% (Figure 3). This isomer was positively identified by its generation from **15** by epimerization with lithium chloride,[9] which proved to be very slow (Figure 3). The spectrum of **15** clearly shows the 1.5–2% 3*R*,4*R* impurity that arose from the diastereomer of **14** that was not removed by recrystallization. This diastereomer was positively identified as part of a mixture made by starting from pinacol methylboronate for the first homologation, then transesterifying with (s)-pinanediol before carrying out the second homologation (not illustrated). By a similar procedure, except that the transesterification with (s)-pinanediol was delayed until after the second homologation, a mixture of all four of the possible diastereomers was obtained (Figure 3).

Prenylmagnesium chloride was checked first with a model, (s)-pinanediol (1-chloro-2-phenylethyl)boronate (**3e**), and the NMR spectrum indicated a single product, (s)-pinanediol (1*S*)-(1-prenyl-2-phenylethyl)boronate. Reaction of prenylmagnesium chloride with **15** yielded **16** slowly but efficiently. Cuprous iodide, an additive which has been found to prevent formation of allylic rearrangement products in reactions of prenylmagnesium chloride with other types of substrates,[21] was not only unnecessary with these boronic esters but was found to be detrimental to the yields.

The boronic ester **16** with basic hydrogen peroxide yielded the alcohol **17**, which could not be purified because it underwent spontaneous lactonization on silica or under very mildly acidic conditions to eliminate *tert*-butyl alcohol (confirmed by NMR) and form eldanolide (**18**).

Scheme V[a]



[a] (a) LiOBn (= $LiOCH_2C_6H_5$); (b) $LiCHCl_2$, −100 °C; 1.7 $ZnCl_2$, −78 °C to +25 °C; (c) RMgX; (d) H_2O_2 yields **a**, R′ = Bn; then H_2/Pd yields b, R′ = H.

β-Substituents

It is known that β-halo boronic esters undergo boron/halide elimination with such ease that water is a sufficient base to catalyze the reaction.[22] β-Alkoxy boronic esters are much more stable, though they do suffer thermal decomposition at ~100 °C.[11] Thus, an inherent limitation on our chiral synthesis will be the β-elimination of labile nucleofugic groups together with boron. The studies which follow show that a variety of β-substituted boronic esters have sufficient stability to permit broad applicability of our synthesis.

***vic*-Diol Synthesis.** The homologation of **8** to **9** in the synthesis of brevicomin (**12**) provides an example of utilization of a pinanediol (α-alkoxyalkyl)boronate to make a (β-alkoxyalkyl)-boronate. As a model reaction prior to this synthesis, we demonstrated the conversion of (s)-pinanediol (1*R*)-(1-(benzyloxy)-pentyl)boronate (**19**) to the (1*S*,2*S*)-(2-(benzyloxy)-1-chlorohexyl)boronate (**20**) (Scheme V). More recently, we have obtained better yields and shorter reaction times by increasing the amount of zinc chloride to 1.7 equiv for this step.

The conversion of **20** to (s)-pinanediol (1-butyl-2-benzyloxy)-hexylboronate (**21a**) with butylmagnesium chloride was straightforward, indicating that the β-benzyloxy *B*-butylborate intermediate is not prone to elimination. Hydrogen peroxide oxidation of **21a** readily yielded (5*S*,6*S*)-6-(benzyloxy)-5-decanol (**22a**), and debenzylation (H_2/Pd) gave (5*S*,6*S*)-5,6-decanediol (**22b**), which contained ~1.5% of the meso isomer by ^{13}C NMR analysis. This demonstrates the utility of this process as a route to chiral *vic*-diols and verifies the stereoselectivity. Enantiomerically pure **23** was obtained after a single recrystallization. Only the racemate of **23** has been reported previously.[23] The meso isomer was synthesized by epoxidation of (*E*)-5-decene[23] for purposes of identification in the NMR spectrum.

Three Chiral Centers. To demonstrate the potential for appending additional chiral centers, the (2-(benzyloxy)-1-chlorohexyl)boronic ester **20** was treated with methylmagnesium bromide to form the (2-(benzyloxy)-1-methylhexyl)boronic ester **21b**. Rearrangement of the intermediate borate complex was slow, and zinc chloride (1.6 equiv) was found to help. The next homologation step was the most likely point for β-elimination, since the (di-

(18) Kunesch, G.; Zagatti, P.; Lallemand, J. Y.; Debal, A.; Vigneron, J. P. *Tetrahedron Lett.* **1981**, *22*, 5271–5274.

(19) Vigneron, J. P.; Mĕric, R.; Larchevêque, M.; Debal, A.; Kunesh, G.; Zagatti, P.; Gallois, M. *Tetrahedron Lett.* **1982**, *23*, 5051–5054.

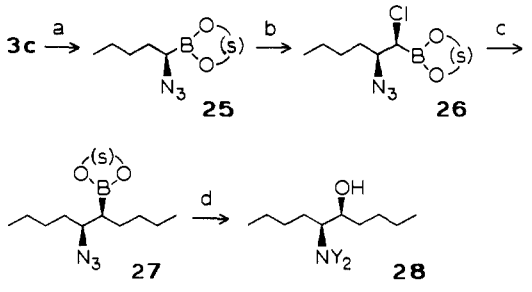
(20) (a) Uematsu, T.; Umemura, T.; Mori, K. *Agric. Biol. Chem.* **1983**, *47*, 597–601. We thank Professor Mori for a copy of the 60-MHz NMR spectrum of eldanolide. (b) Yokoyama, Y.; Yunokihara, M. *Chem. Lett.* **1983**, 1245. (c) Suzuki, K.; Ohkuma, T.; Tsuchihashi, G. *Tetrahedron Lett.* **1985**, *26*, 861–864.

(21) Derguini-Boumechal, F.; Lorne, R.; Linstrumelle, G. *Tetrahedron Lett.* **1977**, 1181–1184.

(22) (a) Matteson, D. S.; Liedtke, J. D. *J. Org. Chem.* **1963**, *28*, 1924–1925. (b) Matteson, D. S.; Liedtke, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 1526–1531. (c) Matteson, D. S. *Acc. Chem. Res.* **1970**, *3*, 186–193.

(23) Levy, G. C.; Pehk, T.; Lipmaa, E. *Org. Mag. Res.* **1980**, *14*, 214–219.

Scheme VI[a]



[a](a) NaN_3, Bu_4N^+, H_2O/CH_2Cl_2; (b) $LiCHCl_2$, −100 °C; 0.7 $ZnCl_2$, −100 °C to +25 °C; (c) BuMgCl, −78 °C; 4 $ZnCl_2$, −78 °C to +25 °C; (d) H_2O_2 at pH 7–8 yields **28a**, Y = N; then $LiAlH_4$ yields **28b**, Y = H.

chloromethyl)boronate complexes **2** rearrange more slowly than (monochloroalkyl)boronates, but formation of **23** proceeded smoothly in the presence of 1.7 equiv of zinc chloride. Butylation of **23** and oxidation to (5*S*,6*R*,7*S*)-7-(benzyloxy)-6-methyl-5-undecanol (**24a**) proceeded normally. Debenzylation with hydrogen over palladium yielded (5*S*,7*S*)-6-methyl-5,7-undecanediol (**24b**), in which the 6-position has become achiral because of symmetry. (C_2 rotation interchanges the two possible orientations of the methyl group. However, the two 1-hydroxypentyl side chains retain their diastereotopic identities.) The racemate of **24b** has been reported previously by Still as part of development of a route to rifamycin S.[24]

There are two possible meso isomers of **24b**, syn,syn and anti,anti, and in order to detect the presence of either of these in the **24b**, a mixture of all isomers was prepared by methylation of the thallium enolate of 5,7-undecanedione followed by borohydride reduction.[25] Although the first α-chloro boronic ester intermediate, **3c**, contained 1–2% of the 1*R* epimer according to NMR analysis, none of either meso isomer could be detected at the 0.5% level by ^{13}C NMR analysis of the **24b**. It appears likely that chromatographic purification of one of the intermediates between **19** and **21b**, in which the margins of the fractions were trimmed, resulted in removal of the diastereomeric impurity. The conversion of **21b** to **24b** was carried out in a manner that would not have removed any diastereomer, and the purity of the **24b** indicates that this final homologation is essentially stereospecific.

***vic*-Amino Alcohol Synthesis.** Azido boronic esters provide several opportunities for β-elimination and other problems, some of which materialized and had to be overcome by modification of the reaction conditions. Remarkably, α-azido boronic esters are stable, and we have so far been unable to provoke N_2N–CHR–$B(OR')_2$ into β-elimination to N_2 and $RCH{=}NB(OR')_2$ or related products. The major problem in the preparation of (s)-pinanediol (1*R*)-(1-azidopentyl)boronate (**25**) is that the azide ion is not much more nucleophilic than the chloride ion liberated in the reaction, and considerable epimerization[9] of the chloro compound **3c** results under ordinary displacement conditions. The slow addition of **3c** to a tenfold excess of sodium azide with tetrabutylammonium ion as phase-transfer catalyst between dichloromethane and water resulted in ~99% diastereoselective displacement.

Homologation of the α-azido boronic ester **25** with (dichloromethyl)lithium to form the (1-chloro-2-azidohexyl)boronic ester **26** did not require more than the usual 0.7 equiv of zinc chloride. However, treatment of **26** with butylmagnesium chloride resulted in β-elimination, leading to (s)-pinanediol butylboronate as the major isolated product and NMR evidence that the volatile material contained unsaturation. The yield of (s)-pinanediol (1*S*,2*S*)-(1-butyl-2-azidohexyl)boronate (**27**) improved with increasing amounts of zinc chloride up to ~4 equiv, which gave satisfactory results. Peroxidic oxidation of **27** under basic conditions appeared to result in mostly elimination to form decene, but at pH 7.6 a nearly quantitative yield of (5*S*,6*S*)-6-azido-5-decanol (**28a**) was produced. Reduction of **28a** with lithium aluminum hydride[26] provided (5*S*,6*S*)-6-amino-5-decanol (**28b**). Both racemic isomers, (5*R**,6*R**)- and (5*R**,6*S**)-6-amino-5-decanol, have been reported,[27] and we prepared the latter for identification purposes by opening of *trans*-5,6-epoxydecane with sodium azide[28] followed by reduction.[26]

A β-Alkylthio Boronic Ester. Another test of resistance to β-elimination was provided by the successful homologation of (s)-pinanediol (2-(hexylthio)ethyl)boronate (**1g**) to the (1*S*)-(1-chloro-3-(hexylthio)propyl)boronate (**3g**), with no evidence of boron/sulfur β-elimination. None of the 1*R* diastereomer could be detected, but as much as 5–10% might have been invisible because of the small separation of the relevant NMR peaks.

Discussion

Scope. The new chemistry described here provides an efficient general synthesis of chiral acyclic secondary alcohols of high enantiomeric purity. This has been extended to provide a practically enantiospecific synthesis of alcohols having paired chiral centers, $R^1R^2C^*H$–$C^*H(OH)R^3$.[29] Extension to three chiral centers has been demonstrated, and further extension is clearly possible, the only limit being the loss of material inherent in any linear synthetic scheme. A potential method for insertion of a methylene group between chiral centers has recently been described.[30]

The absolute configuration of each chiral center is chosen independently by the chemist, since chirality is totally predictable based on the order of connection of the groups R^1 and R^2 and the isomer of pinanediol used. There are a few groups (R^1) that are accessible through $R^1B(OR)_2$ via hydroboration but not obtainable as R^1MgX or R^1Li and other groups (R^2) available as anions but not as boronic esters. Examples of the latter include t-BuO_2CCH_2 and $PhCH_2O$. In such instances, R^1 and R^2 must be introduced in a fixed order, and only one diastereomer is accessible without removing the first chiral directing group and replacing it by its enantiomer[2] or pursuing other routes as yet untested. The use of 2,3-butanediol[3] in place of pinanediol promises easy removal of the first chiral directing group for this purpose, though further development work will be needed for this alternative chiral director.

The functional groups shown to be tolerated, with some specific restrictions on proximity, include ether, ketal, ester, azido, and alkylthio. These are among the most useful groups for general synthetic purposes. Assembly of three adjacent chiral centers has been demonstrated, and extension to additional chiral centers is clearly possible. The synthesis could be terminated to products other than alcohols.

Precautions. The laboratory procedures described must be strictly followed in order to achieve the stated diastereoselectivities and yields. The most likely cause of poor diastereoselection would be accidental epimerization of the α-chloro boronic ester product **3**.[9] One operator encountered repeated contamination of (s)-pinanediol (1*S*)-(1-chloropentyl)boronate (**3c**) by ~10% epimer, until a slight alteration of the workup procedure was corrected. At the point where saturated aqueous ammonium chloride was added to the crude product still containing zinc chloride, a nuisance precipitate was encountered, and this had been prevented by a prior extraction with a small amount of water, which caused the

(24) Still, W. C.; Barrish, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 2487–2489.
(25) (a) Undecane-5,7-dione modeled on nonane-4,6-dione: Morgan, G. T.; Thompson, R. W. *J. Chem. Soc.* **1924**, *125*, 754–759. (b) Thallium enolate methylation: Taylor, E. C.; Hawkes, III, G. H.; McKillop, A. *J. Am. Chem. Soc.* **1968**, *90*, 2421–2422. (c) Borohydride reduction: Dale, J. *J. Chem. Soc.* **1961**, 910–922.
(26) Boyer, J. H. *J. Am. Chem. Soc.* **1951**, *73*, 5865–5866.
(27) Pankova, M.; Sicher, J. *Collect. Czech. Chem. Commun.* **1965**, *30*, 388–412.
(28) (a) Epoxidation conditions: McMurry, J. E.; Fleming, M. P.; Kees, K. L.; Krepski, L. R. *J. Org. Chem.* **1978**, *43*, 3255–3266. (b) Opening by azide: VanderWerf, C. A.; Heisler, R. Y.; McEwen, W. E. *J. Am. Chem. Soc.* **1954**, *76*, 1231–1235.
(29) If the diastereoselectivity is 99% in each of two steps, the diastereomeric impurity overall is (0.01 + 0.01) or 2%, but the enantiomeric impurity is (0.01 × 0.01) or ~0.01%, and the residual enantiomer in the pinanediol becomes the actual limiting factor.
(30) Sadhu, K. M.; Matteson, D. S. *Organometallics* **1985**, *4*, 1687–1689.

problem. Even though workup with a very large amount of plain cold water does no harm, it would appear that the combination of a small amount of water with the zinc salts, in which some THF remains bound even after extended vacuum treatment, results in formation of a phase in which the α-chloro boronic ester **3c**, zinc chloride, and water are mutually soluble to some degree. Extrapolation from previous kinetic studies suggests that epimerization might be extremely rapid under such conditions.[9] Omitting the water extraction returned the diastereoselectivity to 98.5%, the reproducible standard for this particular compound.

In one instance, poor diastereoselection followed the use of a strongly discolored batch of (dichloromethyl)lithium. The darkening had resulted from an accidental surge of the rate of injection of the butyllithium.

Substituents. The compatibility of the homologation process with functional substituents is particularly significant. Although we had previously shown that homologations of ethylene glycol or pinacol boronic esters are tolerant of ether, ketal, or ester substituents,[11] these reactions were slower than normal and required unusually vigorous conditions, and an attempt to homologate pinanediol ((benzyloxy)methyl)boronate without zinc chloride had failed.[2]

The carboxylic ester substituent in **14** greatly slowed the homologation and required the use of more than the usual amount of zinc chloride in order to obtain satisfactory yields. In view of the data, which indicate that $ZnCl_2$ in the presence of $LiZnCl_3$ at high concentrations is a potent catalyst for epimerization of α-chloro boronic esters,[9] we were concerned about possible loss of stereoselectivity in the formation of **15**, but no such loss was observed in this case.

Other homologations of functionalized boronic esters have been reported elsewhere without proof of diastereoselectivity.[6] These include pinanediol (3-halopropyl)- and (3-(benzyloxy)propyl)-boronates as well as the ((benzyloxy)methyl)boronate.

Limitations on the functional group compatibility include the failure of attempted homologation of pinacol ((phenylthio)-methyl)boronate without catalyst[11] and failure of the pinanediol ester in the presence of zinc chloride. Cleavage of $PhSCH_2^-$ rather than β-elimination appears to be the problem. The extreme ease of base-catalyzed dehaloboronation[22] makes it appear most unlikely that a β-halogen substituent could be tolerated in any starting material or product.

Alternatives. The enantioselectivity of our secondary alcohol synthesis is comparable to the best of chiral hydroborations,[31,32] and the range of accessible structures is much greater. Hydroborations lack regioselectivity with unsymmetrical alkenes, and no such limitation applies to our new route. On the other hand, hydroboration is applicable to certain cyclic systems, which are inaccessible by our chemistry.

Other highly enantioselective syntheses which utilize chiral auxiliary groups to direct the introduction of two adjacent chiral centers include chiral aldol condensations[33,34] and chiral epoxidation of allylic alcohols.[35,36] The Sharpless epoxidation[35] has the advantage of utilizing inexpensive reagents, and for those structures that can be reached unambiguously and fairly directly from epoxy alcohols it will remain the method of choice.

The unique feature of our boronic ester homologation is the possibility of immediate repetition of the cycle to introduce additional chiral centers without limit, except for the attrition of material inherent in the best of linear multistep syntheses. Even though all of the alternatives can introduce two chiral centers simultaneously,[31-36] they require a prior synthetic operation in order to establish olefinic geometry. Repetition of aldol condensations requires prior removal of the first chiral directing group and introduction of another,[33,34] and repetition of epoxidation requires intervening stereoselective olefin condstruction.[36] Hydroboration cannot be repeated, though chiral boronic esters derived from hydroboration products[37] might serve as substrates for our synthesis. Even though our approach adds only one chiral center at a time, the actual number of laboratory manipulations required in order to reach a particular target is often less than with any of the alternatives.

Major advantages of our boron chemistry are its conceptual simplicity and the ease of designing and executing straightforward, unambiguous routes to a wide variety of complex structures.

Experimental Section

General Data. Reactions involving carbanions were carried out under argon. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl. Butyllithium (1.6 M in hexane) was titrated against 2-propanol to the 1,10-phenanthroline end point. Boronic acids were prepared from the corresponding Grignard reagents and trimethyl borate[38] unless otherwise noted. Butylboronic acid was purchased from Aldrich Chemical Co. ^1H (200-MHz) and ^{13}C (50.3-MHz) NMR spectra were taken with a Nicolet NT-200 instrument, other NMR spectra with a JEOL FX90Q. IR spectra were recorded on a Nicolet 5MX Fourier transform instrument. Optical rotation data were taken with a Jasco DIP-181 digital polarimeter. Microanalyses were done by Galbraith Laboratories, Knoxville, TN.

Enantiomerically Pure Potassium Bis(pinanediol)borate Monohydrate. (s)-Pinanediol[4,5] 92% enantiomeric excess (ee) (341 g, 2 mol) in ether (500 mL) and light petroleum ether (500 mL) was stirred with boric acid (62.5 g, 1 mol), and a solution of potassium hydroxide (65 g of 85%, 1 mol) in water (~150 mL) was added in small portions, resulting in an exothermic reaction and formation of a voluminous white precipitate, which was collected, washed with ether, and dried. This material was recrystallized from ~2 L of acetone containing 5–10% water,[39] recovery ~55%, and the mother liquors were partially concentrated by evaporation in a beaker at room temperature to yield a second crop of crystals. The two crops were combined and the recrystallization repeated. Measurement of the enantiomeric excess by conversion to (s)-pinanediol phenylboronate[2] indicated 100% ee at this point. After a third recrystallization, the total yield was 55%, with 65% recoverable by more reworking of mother liquors. Rotations were somewhat variable as a result of potassium borate impurity, a typical value being $[\alpha]^{24.8}546$ −16.2° (*c* 3, methanol). Anal. Calcd for $C_{20}H_{34}BKO_5$: C, 59.40; H, 8.47; B, 2.67; K, 9.67. Found: C, 59.71; H, 8.24; B, 2.68; K, 9.61. (r)-Pinanediol required one extra recrystallization in order to bring the ee from 85% up to ~95%; fully purified salt, $[\alpha]^{23}546$ +17.0°, $[\alpha]^{23}365$ +53.3° (*c* 5, methanol).

[(s)-Pinanediol]methoxyborane. Treatment of potassium bis(pinanediol) borate with aqueous hydrochloric acid (methyl orange end point) and extraction with ether yielded a 1:1 mixture of pinanediol and pinanediol borate, which was satisfactory for transesterifying boronic esters.[2] This mixture (50 mmol) with trimethyl borate (7 mL) and 2,2-dimethoxypropane (7 mL) refluxed 2 h and distilled yielded 81% [(s)-pinanediyldioxy]methoxyborane; redistilled, bp 86 °C (1.7 torr), mp 60–62 °C; $[\alpha]^{25.0}589$ +36.6°, $[\alpha]^{25.0}546$ +43.6°, $[\alpha]^{25.0}365$ +116.3° (*c* 1.2, toluene). Anal. Calcd for $C_{11}H_{19}BO_3$: C, 62.89; H, 9.12; B, 5.15. Found: C, 63.09; H, 9.01; B, 5.35.

Enantiomerically Pure (s)-Pinanediol. Treatment of the pinanediol/pinanediol borate mixture from the preceding paragraph with excess methanol and slow distillation through an efficient packed column for 3 days removed only a small fraction of the boron as the methanol–tri-

(31) (a) Mandal, A. K.; Jadhav, P. K.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 3543–3544. (b) Enantioselectivity enhanced by crystallization of product: Brown, H. C.; Singaram, B. *J. Am. Chem. Soc.* **1984**, *106*, 1797–1800.

(32) Masamune, S.; Kim, B. M.; Petersen, J. S.; Sato, T.; Veenstra, S. J.; Imai, T. *J. Am. Chem. Soc.* **1985**, *107*, 4549–4551.

(33) (a) Evans, D. A.; Vogel, E.; Nelson, J. V.; Taber, T. R. *J. Am. Chem. Soc.* **1981**, *103*, 3099–3111. (b) Review: Evans, D. A.; Nelson, J. V.; Taber, T. R. "Topics in Stereochemistry"; Allinger, N. L.; Eliel, E. L.; Wilen, S. H., Eds.; Wiley: New York, 1982; Vol. 13, pp 1–116.

(34) (a) Masamune, S.; Kaiho, T.; Garvey, D. S. *J. Am. Chem. Soc.* **1982**, *104*, 5521–5523. (b) Masamune, S.; Lu, L. D.-L.; Jackson, W. P.; Kaiho, T.; Toyoda, T. *J. Am. Chem. Soc.* **1982**, *104*, 5523–5526.

(35) (a) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. (b) Review: Sharpless, K. B.; Behrens, C. H.; Katsuki, T.; Lee, A. W. M.; Martin, V. S.; Takatani, M.; Viti, S. M.; Walker, F. J.; Woodard, S. S. *Pure Appl. Chem.* **1983**, *55*, 589–604.

(36) Ko, S. Y.; Lee, A. W. M.; Masamune, S.; Reed, L. A.; III; Sharpless, K. B.; Walker, F. J. *Science*, **1983**, *220*, 949–951.

(37) (a) Brown, H. C.; Jadhav, P. K.; Desai, M. C. *J. Am. Chem. Soc.* **1982**, *104*, 4303–4304. (b) Use in a related homologation not involving chiral selection: Brown, H. C.; Imai, T.; Desai, M. C.; Singaram, B. *J. Am. Chem. Soc.* **1985**, *107*, 4980–4983.

(38) (a) Washburn, R. M.; Levens, E.; Albright, C. F.; Billig, F. A. "Organic Syntheses"; Wiley: New York, 1963; Collect Vol. 4, 68–72. (b) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, *2*, 230–236.

(39) Alternatively, the salt was dissolved in 2–3 mL/g of hot ~50% aqueous acetone, then diluted with acetone to ~10% water content to crystallize the product, with similar results.

methyl borate azeotrope. Pure (s)-pinanediol (39%) was recovered from the residue by distillation below 130 °C (0.1 torr), sublimed at 67 °C (0.01 torr); mp 53–59 °C; $[\alpha]^{25.0}546$ −2.56°, $[\alpha]^{25.0}365$ −12.26° (*c* 7, methanol); $[\alpha]^{25.0}546$ +11.40°, $[\alpha]^{25.0}365$ +25.05° (*c* 6.6, toluene).

(r)-Pinanediol Methylboronate (Enantiomer of 1a). To a solution of 23 g of potassium bis[(r)-pinanediol]borate in ~75 mL of ice-cold water was added ~150 mL of 1:1 ether/petroleum ether followed by 65 mL of ice-cold 2 M hydrochloric acid in small portions with stirring. After the cloudiness in the aqueous phase had disappeared, the phases were separated and the aqueous phase was saturated with sodium chloride and extracted with 50 mL of ether. The combined organic phases were treated with 16.3 g (113 mmol) of diisopropyl methylboronate[40,41] and kept at 25 °C for 30 min, then dried over magnesium sulfate and distilled, 19.7 g (90%), bp 85–87 °C (5 torr), crystallized in freezer, mp 13–15 °C, $[\alpha]^{23}546$ −45.2° (*c* 3.1, $CHCl_3$). The NMR and analytical data of the (+)-enantiomer have been reported.[2]

(s)-Pinanediol Butylboronate (1c). The procedure described for the enantiomer of **1a**, preceding paragraph, was followed with potassium bis[(s)-pinanediol]borate in place of the r isomer and butylboronic acid in place of diisopropyl methylboronate, $[\alpha]^{25.0}546$ +49.0° (*c* 3.4, toluene); other properties were reported previously.[2] Other pinanediol boronic esters were similarly prepared. Small amounts of unreacted pinanediol or boronic acid were generally removed by chromatography on a short silica column before distillation.

(s)-Pinanediol (2-(Hexylthio)ethyl)boronate (1g). Dibutyl (2-(hexylthio)ethyl)boronate[42] was converted to the (s)-pinanediol ester **1g** in the usual manner; bp 135 °C (0.05 torr). Anal. Calcd for $C_{18}H_{33}BO_2S$: C, 66.66; H, 10.26; B, 3.33; S, 9.89. Found: C, 66.96; H, 10.28; B, 3.45; S, 10.04.

(s)-Pinanediol (1-Chloroalkyl)boronates (3). (Dichloromethyl)lithium was prepared by adding butyllithium dropwise down the side of the flask to excess dichloromethane stirred in THF at −100 °C as described in detail previously[11] on a 5–100-mmol scale. For 28 mmol, 25 mmol of the (s)-pinanediol alkylboronate (**1**) in ~15 mL of anhydrous ether was injected. A 14–18-mmol (1.9–2.4-g) portion of rigorously anhydrous powdered zinc chloride[43] was added to the cold mixture, briefly removing the cap from the argon-filled flask and flushing with argon afterward. The mixture and cooling bath were allowed to warm slowly to 20–25 °C and stirred overnight. The mixture was concentrated on a rotary evaporator with the heating bath below 30 °C, and the thick residue was stirred with ~100 mL of light petroleum ether, then stirred with 25 mL of saturated aqueous ammonium chloride. The phases were separated, the aqueous phase was washed with petroleum ether (2 × 50 mL), and the combined organic phase was filtered through a bed of anhydrous magnesium sulfate. (In an alternative procedure, the aqueous treatment was omitted, the gummy phase which separates on addition of the petroleum ether was washed repeatedly with petroleum ether, and the petroleum ether solution was passed through a short column of silica, which was well washed with more solvent.) Concentration yielded a residue of **3** containing **1** (often ~10%) as the only major impurity. The **3** was usually purified by chromatography on silica with 5–10% ethyl acetate in light petroleum (bp 40–60 °C) or hexane.

(s)-Pinanediol (1*S*)-(1-Chloroethyl)boronate (3a). Preparation and NMR data were similar to those of the enantiomer (**13**, below).[44] The diastereomeric purity was 95.7% based on conversion to the acetamido derivative,[6] 200-MHz NMR δ 9.8 and 9.2 (N*H*), ratio 23:1. Treatment of **3a**, 92% ee, with phenylmagnesium bromide followed by oxidation and acetylation[2] yielded 1-phenylethyl acetate, $[\alpha]^{22}589$ +99.2° (benzene) [lit.[45] $[\alpha]589$ −124.5° for enantiomer], which corresponds to 93.3% diastereoselection.

(s)-Pinanediol (1*S*)-(1-Chloropentyl)boronate (3c). This was prepared by the standard procedure from 9.98 g (42 mmol) of **1c** (100% ee), 51 mmol of (dichloromethyl)lithium, and 3.8 g (28 mmol) of zinc chloride. The **3c** was chromatographed on silica with 4% ethyl acetate/hexane, then distilled,[46] 0.82 g (8%) of forerunner **1c**; 10.3 g (86%) of 3c; bp 113–115 °C (0.2 torr); $[\alpha]^{22}546$ +56.5° (*c* 1.3, toluene); 200-MHz ^1H NMR ($CDCl_3$) δ 0.85 (s, 3), 91 (t, 3), 1.184 (d, *J* = 11.0 Hz, 1), 1.175 (d, 1*R* epimer, 1.5 (±0.5)% of 1), 1.30 (s, 3), 1.42 (s, 3), 1.29–2.29 (m, 11), 3.47 (t, *J* = 7.2 Hz, 1, BC*H*Cl), 4.37 (dd, *J* = 1.9 and 8.7 Hz, 1, C*H*OB); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 13.97, 22.21, 23.96, 26.32, 26.99, 28.44, 29.49, 33.88, 35.26, 38.20, 39.31, 43.4 (broad, B*C*), 51.10, 78.44, 86.64. Anal. Calcd for $C_{15}H_{26}BClO_2$: C, 63.30; H, 9.21; B, 3.80; Cl, 12.46. Found: C, 63.27; H, 9.04; B, 3.97; Cl, 12.43. The position of the epimer peak was verified by treatment of **3c** with lithium chloride for several days in THF.[9] The diastereoselectivity was further verified by treatment of a sample of **3c**, 92% ee, with methylmagnesium bromide followed by peroxidic oxidation of the pinanediol (1-methylpentyl)boronate to (*S*)-2-hexanol,[2] bp 133 °C, $[\alpha]^{24}589$ +9.72° (*c* 3.5, EtOH) [lit.[47] + 10.9°], which corresponds to 98.5% diastereoselection.

(s)-Pinanediol (1*S*)-(1-Chloro-3-methylbutyl)boronate (3d). This was not purified but converted directly to the acetamido derivative;[6-8] 200-MHz NMR ($CDCl_3$) δ 9.0, 8.3 (N*H*, ratio 200:1). Addition of the epimer[7] increased the absorption at δ 8.3.

(s)-Pinanediol (1*S*)-(1-Chloro-2-phenylethyl)boronate (3e). The usual procedure with **1e**, 100% ee, yielded 99.2% **3e** as a crystalline residue on evaporation of the solvent; 200-MHz NMR ($CDCl_3$) δ 0.82 (s, 3), 1.062 (d, *J* = 10.9 Hz, 1), (0.973, epimer, not detected), 1.27 (s, 3), 1.33 (s, 3), 1.80–2.40 (m, 5), 3.15 (m, 2, CH_2Ph), 3.652 (m, *J* = ~8 Hz, C*H*Cl), (epimer, 3.634, <0.5%), 4.33 (dd, 1, C*H*OB), 7.16–7.33 (m, 5, C_6H_5).[44] Anal. Calcd for $C_{18}H_{24}BClO_2$: C, 67.84; H, 7.59; B, 3.39; Cl, 11.13. Found: C, 68.03; H, 7.55; B, 3.42; Cl, 10.91. Treatment of **3e** with lithium chloride in THF[9] led to 45% 1*R* epimer, additional NMR peaks at δ 0.973 (d, *J* = 10.8 Hz, 1) and 3.634 (t, *J* = 8.3 Hz, 1, C*H*Cl).

(s)-Pinanediol (1-Chloro-3-(hexylthio)propyl)boronate (3g). A 1.63-g (5-mmol) sample of **1g** was added to (dichloromethyl)lithium in the usual manner for preparation of **3** and 0.38 g (2.8 mmol) of zinc chloride was added. After 16 h at 25 °C, the mixture was treated with petroleum ether and saturated aqueous ammonium chloride, and the **3g** was chromatographed on silica with 2:2:1 dichloromethane/hexane/1,2-dichloroethane. This material showed a doublet, *J* = 11 Hz, at δ 1.173 in the 200-MHz NMR spectrum, and an epimer mixture prepared by way of the pinacol ester showed distinct broadening indicative of an additional doublet at δ ~1.175. No evidence of epimer was seen in the sample of **3g**, but as much as 5–10% might have escaped detection. The remainder of the NMR spectra ($CDCl_3$) were identical: δ 0.85 (s, 3, pinanyl CH_3), 0.89 (t, 3, CH_3CH$_2$), 1.25–2.8 (m, aliphatic and pinanyl, with CH_3's at 1.30 and 1.43), 3.65 (t, 1, C*H*ClB), 4.36 (dd, 1, C*H*OB). Anal. Calcd for $C_{19}H_{34}BClO_2S$: C, 61.21; H, 9.19; B, 2.90; Cl, 9.51; S, 8.60. Found: C, 61.35; H, 9.33; B, 2.94; Cl, 9.74; S, 8.62.

(3*S*,4*S*)-4-Methyl-3-heptanol (5). All of the steps involve procedures described elsewhere in this article or previously.[2] Properties of intermediates: **(s)-Pinanediol propylboronate (1b)**: bp 104–106 °C (4 torr); 200-MHz NMR ($CDCl_3$) δ 0.81 (t, 2, CH_2B), 0.85 (s, 3, CH_3), 0.94 (t, 3, CH_3), 1.13 (d, 1, *J* = 10.7 Hz), 1.29 (s, 3, CH_3), 1.38 (s, 3, CH_3), 1.37–1.69 (m, 2, CH_2), 1.79–2.40 (m, 5), 4.25 (dd, 1, C*H*OB); $[\alpha]^{24}589$ +44.2° (c 2.7, toluene; ee 100%). Anal. Calcd for $C_{13}H_{23}BO_2$: C, 70.29; H, 10.44; B, 4.87. Found: C, 70.51; H, 10.12; B, 4.79. **(s)-Pinanediol (1-methylbutyl)boronate (1f)**: $[\alpha]^{25}546$ +52.3° (*c* 2.7, toluene); 200-MHz NMR ($CDCl_3$) δ 0.84–2.41 (m, 26), 4.25 (dd, 1, C*H*OB). Anal. Calcd for $C_{15}H_{27}BO_2$: C, 72.01; H, 10.88; B, 4.32. Found: C, 72.27; H, 10.76; B, 4.57. The chiral purity was checked by oxidation with alkaline hydrogen peroxide to (*S*)-2-pentanol, bp 114–116 °C, $[\alpha]^{25}589$ +12.86° (*c* 1.5, EtOH) [lit.[48] +13.1° (*c* 0.55, EtOH)], ee 98.2%. **(s)-Pinanediol (1-ethyl-2-methylpentyl)boronate (4f)**: Purified by chromatography on silica with 20% ethyl acetate in hexane, then Kugelrohr distillation, 200-MHz NMR ($CDCl_3$) δ 0.84–1.02 (m, 13), 1.11–1.63 (m, 14), 1.78–2.43 (m, 5), 4.27 (dd, 1, C*HOB*). Anal. Calcd for $C_{18}H_{33}BO_2$: C, 73.97; H, 11.38; B, 3.70. Found: C, 73.79; H, 11.20; B, 3.88.

2-Methyl-2-[3-((r)-(pinanediyldioxy)boryl)propyl]-1,3-dioxolane (6). This compound was prepared from 2-methyl-2-(3-chloropropyl)-1,3-dioxolane via the Grignard reagent[49] and methyl borate in the usual manner[38] followed by transesterification with potassium bis[(r)-pinanediol]borate in 68% yield, bp 123–124 °C (0.05 torr); $[\alpha]^{21}546$ −17.0° (*c*

(40) Brown, H. C.; Cole, T. E. *Organometallics* **1983**, *2*, 1316–1319.

(41) Omitted from the reported preparation[40] is the need for a fractionating column to separate the diisopropyl methylboronate, bp 106–107 °C, cleanly from 2-propanol. *CAUTION*: Increased concentrations in a scale-up of the Brown–Cole procedure led to stirring difficulties and *spontaneously flammable byproduct* (trimethylborane?) at the inert gas exist during distillation. The specified concentrations have proved safe, and this is much superior to our previously reported methylboronic ester preparation: (a) Matteson, D. S. *J. Org. Chem.* **1964**, *29*, 3399–3400. (b) Hazard noted: Matteson, D. S.; Moody, R. J. *Organometallics* **1982**, *1*, 20–28.

(42) Matteson, D. S. *J. Am. Chem. Soc.* **1960**, *82*, 4228–4233.

(43) The sample of reagent grade crystalline anhydrous zinc chloride was heated to ~100 °C under vacuum in a narrow-neck (volumetric) flask with magnetic stirring for a few hours, final pressure 0.01–0.02 torr, which yielded finely powdered material, and argon was admitted to the flask.

(44) Portion of spectral curve filed as Supplementary Material to ref 1.

(45) Huisgen, R.; Ruchardt, C. *Justus Liebigs Ann. Chem.* **1956**, *601*, 21–34.

(46) The NMR spectrum showed the epimer content to be the same before and after distillation. We did not normally distill α-chloro boronic esters out of concern that accidental chloride might cause epimerization.

(47) Levene, P. A.; Haller, H. L. *J. Biol. Chem.* **1929**, *83*, 591–600.

(48) Williams, H. J.; Silverstein, R. M.; Burkholder, W. E.; Khorramshahi, A. *J. Chem. Ecol.* **1981**, *7*, 759–780.

(49) Prepared with special Grignard grade magnesium from Reade Manufacturing Company, Lakehurst, NJ.

10, $CHCl_3$) (ee 100%); 200-MHz NMR ($CDCl_3$) δ 0.79–0.86 (m, 5), 1.11 (d, J = 10.7 Hz, 1), 1.29 (s, 3, CH_3), 1.31 (s, 3, CH_3), 1.37 (s, 3, CH_3), 1.38–1.46 (m, 9), 3.92 (m, 4, OCH_2CH_2O), 4.25 (dd, 1, CHOB). Anal. Calcd for $C_{17}H_{29}BO_4$: C, 66.24; H, 9.48; B, 3.51. Found: C, 66.36; H, 9.51; B, 3.70.

2-Methyl-2-[(4*R*)-4-[(*r*)-(pinanediyldioxy)boryl]-4-chlorobutyl]dioxolane (7). This compound was prepared in the standard manner for **6** and (dichloromethyl)lithium. The crude material obtained after workup with aqueous ammonium chloride and concentration of the organic phase was used directly in the next step. 200-MHz NMR ($CDCl_3$) δ 0.847 (s, 3, CH_3), 1.180 (d, J = 10.9 Hz, 1), 1.170 (d due to epimer, <0.005, see Figure 1), 1.296 (s, 3, CH_3), 1.314 (s, 3, CH_3), 1.418 (s, 3, CH_3), 1.5–2.43 (m, 11), 3.47 (t, 1, CHCl), 3.93 (m, 4, $-OCH_2CH_2O-$), 4.366 (dd, 1, CHOB). A mixture containing 50% epimer was prepared from the ethylene glycol ester analogue of **6** followed by transesterification with (s)-pinanediol.

2-Methyl-2-[(4*S*)-4-[(r)-(pinanediyldioxy)boryl-4-(benzyloxy)butyl]dioxolane (8). Crude **7** (24 mmol) in THF (~25 mL) at −78 °C was treated with lithium benzyl oxide (25 mmol, ~1 M in THF, from benzyl alcohol and butyllithium) and stirred overnight at 25 °C. The mixture was treated with saturated ammonium chloride and extracted with ether, and the organic phase was concentrated and chromatographed on a short column of silica with 20% ethyl acetate/hexane, R_f 0.47. Kugelrohr distillation (170 °C, 0.05 torr) yielded 94% (based on **6**). NMR analysis showed an extract peak at δ 4.545 corresponding to the 4*R* epimer (prepared from the epimeric mixture of **7**, see Diastereoselectivities) in the amount of 2%. There appeared to be a small amount of unsaturated byproduct in the NMR spectrum at δ 5–6, and prolonged exposure to silica was found to cause partial hydrolysis of the ethylene ketal. The analytical sample was prepared by flash chromatography; 200-MHz NMR ($CDCl_3$) δ 0.84 (s, 3, CH_3), 1.16 (d, J = 10.8 Hz, 1), 1.286 (s, 3, CH_3), 1.298 (s, 3, CH_3), 1.39 (s, 3, CH_3), 1.52–2.28 (m, 11), 3.36 (t, 1, BCHO), 3.89 (m, 4, OCH_2CH_2O), 4.31 (dd, 1, CHOB), 4.50–4.59 (AB pattern, 2, $PhCH_2O$), 7.22–7.39 (m, 5, C_6H_5). Anal. Calcd for $C_{25}H_{37}BO_5$: C, 70.09; H, 8.71; B, 2.52. Found: C, 69.84; H, 8.65; B, 2.54.

2-Methyl-2-[(4*R*,5*R*)-4-(benzyloxy)-5-chloro-5-((r)-(pinanediyldioxy)boryl)pentyl]-1,3-dioxolane (9). This compound was prepared according to the general procedure for **3**. After concentration of the ethereal extract, the residue of **9** was used directly in the next step. 200-MHz NMR ($CDCl_3$) δ 0.83 (s, 3, CH_3), 1.19 (d, J = 10.8 Hz, 1), 1.28 (s, 3, CH_3), 1.29 (s, 3 CH_3), 1.39 (s, 3, CH_3), 1.4–1.95 (m, 11), 3.65 (d, J = 6.3 Hz, CHCl), 3.74 (m, 1, $CHOCH_2Ph$), 3.90 (m, 4, $(OCH_2)_2$), 4.36 (dd, 1, CHOB), 4.65 (AB multiplet, 2, OCH_2Ph), 7.24–7.40 (m, 5, C_6H_5).

2-Methyl-2-[(4*S*,5*R*)-4-(benzyloxy)-5-((r)-(pinanediyldioxy)boryl)heptyl]-1,3-dioxolane (10). A sample of crude **9** from 20 mmol of **8** was dissolved in 40 mL of THF, cooled to −78 °C, treated with 23 mmol of ethylmagnesium bromide, and kept at 20–25 °C for 36 h. (A lower yield was obtained after 16 h). After the usual workup with aqueous ammonium chloride, the **10** was chromatographed on silica with 20% ethyl acetate in hexane and, after solvent evaporation, found to be pure by TLC, NMR, and elemental analysis, 7.7 g (82%), $[\alpha]^{23}$546 −2.09° (*c* 5, $CHCl_3$); 200-MHz NMR ($CDCl_3$) δ 0.82 (s, 3, CH_3), 0.84–0.98 (m, 4), 1.170 (d, J = 10.2 Hz, 1), 1.255 (s, 3, CH_3), 1.294 (s, 3, CH_3), 1.327 (s, 3, CH_3), 1.35–2.4 (m, 13), 3.52–3.65 (m, 1, $CHOCH_2Ph$), 3.90 (m, 4, OCH_2CH_2O), 4.25 (dd, 1), 4.51 (AB pattern, 2, OCH_2Ph), 7.21–7.37 (m, 5, C_6H_5). Anal. Calcd for $C_{28}H_{43}BO_5$: C, 71.48; H, 9.21; B, 2.30. Found: C, 71.48; H, 9.13; B, 2.22.

(3*R*,4*R*)-4-(Benzyloxy)-8-oxo-3-nonanol (11). A 2.57-g sample of **10** was oxidized with alkaline hydrogen peroxide[50] and the product was treated with 5 g of silica (60–200 mesh) containing 0.5 g of 7% sulfuric acid.[51] After 3 h the product was extracted with dichloromethane and purified by chromatography on silica with 1:1 ethyl acetate/hexane, 1.12 g (79%), matched lit.[16] IR, mass spectral, and 60-MHz NMR data. Though reported as an oil,[16] ours solidified, recrystallized from ether/pentane (which removed the 2–3% diastereomer), mp 30–31 °C; $[\alpha]^{23}$589 −13.4° (*c* 3.4, $CHCl_3$); 200-MHz NMR ($CDCl_3$) δ 0.97 (t, 3, CH_2CH_3), 1.38–1.80 (m, 6), 2.12 (s, 3, CH_3CO), 2.28 (d, 1, OH), 2.45 (m, 2, CH_2CO), 3.30 (m, 1, $CHOCH_2Ph$), 3.48 (m, 1, CHOH), 4.51–4.65 (AB pattern, OCH_2Ph), 7.34 (m, 5, C_6H_5). Anal. Calcd for $C_{16}H_{24}O_3$: C, 72.69; H, 9.15. Found: C, 72.79; H, 9.14.

***exo*-Brevicomin (12).** Hydrogenolysis of 97–98% **11** by the reported procedure[16] yielded **12**; 200-MHz NMR in accord with published data,[14a] with t at δ 0.97[14b] indicting ~3% of the epimer, *endo*-brevicomin, which by GC analysis[14b] was ~2%; $[\alpha]^{23}$589 +81.1° (*c* 1.4, ether) (lit. $[\alpha]^{25}$D +84.1°,[17a] +81.5°[16]).

(r)-Pinanediol (*R*)-(1-Chloroethyl)boronate (13). This was prepared from (r)-pinanediol methylboronate by the general procedure described for **3** (25-mmol scale). The NMR spectrum indicated the presence of 12 ± 2% unchanged pinanediol methylboronate, 0.63 g (10%) recoverable by distillation. Yields of **13** were 4.8–5.27 g (80–87%), bp 80–82 °C (0.2 torr); 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.85 (s, 3, pinanyl CH_3), 1.17 (d, J = 11 Hz, 1, pinanyl), 1.16 (d, J = 11 Hz, 5% of 1, diastereomer), 1.30 (s, 3, pinanyl CH_3), 1.42 (s, 3, pinanyl CH_3), 1.57 (d, 3, CH_3CHClB), 1.85–2.43 (m, 5, pinanyl), 3.57 (q, J = 7.54 Hz, 1, CHClB), 4.37 (dd, 1, pinanyl CHOB). Anal. [(αS)-Enantiomer] Calcd for $C_{12}H_{20}BClO_2$: C, 59.42; H, 8.31; B, 4.46; Cl, 14.62. Found: C, 59.21; H, 8.23; B, 4.33; Cl, 14.76.

***tert*-Butyl (3*S*)-3-[(r)-(Pinanediyldioxy)boryl]butanoate (14).** *tert*-Butyl lithioacetate was generated from 8.0 mL (58 mmol) of *tert*-butyl acetate and 50 mmol of LDA in THF at −78 °C.[11,52] After 30 min, 11.31 g (46.6 mmol) of (r)-pinanediol (1*R*)-(1-chloroethyl)boronate (**13**) was added. The mixture was allowed to warm to 20 °C and kept 17 h. The mixture was concentrated on a rotary evaporator and 100 mL of light petroleum (bp 40–60 °C) was added, followed by 30 mL of saturated aqueous ammonium chloride. The aqueous phase was washed with two 50-mL portions of petroleum ether, and the combined organic extracts were dried over magnesium sulfate and concentrated. The **14** was chromatographed on silica with 1:1 dichloromethane/hexane, 11.86 g (79%), or distilled, bp 130–135 °C (0.5 torr). Recrystallization of 3.46 g of **14** from ~5 mL of ether in the freezer yielded 2.80 g (81%) of 98% (1*R*) **14**. A second recrystallization yielded material having $[\alpha]^{20}$546 −39.31° (*c* 1.3, toluene), unchanged on further recrystallization; mp 13–16 °C; 200-MHz NMR ($CDCl_3$) δ 0.84 (s, 3, CH_3), 1.02 (d, J = 7.4 Hz, 3, CH_3CH), 1.19 (d, J = 10.8 Hz, 1, pinanyl), 1.28 (s, 3, CH_3), 1.37 (s, 3, CH_3), 1.44 (s, 9, $C(CH_3)_3$), 2.33 (m, 2, CH_2CO), 1.5–2.41 (m, 6), 4.27 (dd, 1, CHOB). Anal. Calcd for $C_{18}H_{31}BO_4$: C, 67.09; H, 9.70; B, 3.35. Found: C, 67.29; H, 9.80; B, 3.50.

***tert*-Butyl (3*S*,4*R*)-4-Chloro-3-methyl-4-[(r)-(pinanediyldioxy)boryl]butanoate (15).** (Dichloromethyl)lithium was generated from 12.8 mmol of butyllithium and 1.1 mL of dichloromethane in 20 mL of THF at −100 °C, then treated with 3.59 g (11.1 mmol) of **14** in 5 mL of ether followed by 1.77 g (12.9 mmol) of powdered anhydrous zinc chloride.[43] After warming to 20 °C and keeping 12 h the mixture was concentrated on a rotary evaporator, keeping the bath below 30 °C, and the residue was treated with ~30 mL of light petroleum (bp 40–60 °C) followed by ~10 mL of saturated aqueous ammonium chloride. Further washing of the aqueous phase with light petroleum followed by concentration of the combined organic phase yielded 4.12 g of crude **15**, which showed no evidence of unconverted **14** in the 200-MHz NMR spectrum at δ 4.27 (dd, CHOB). 200-MHz NMR ($CDCl_3$) δ 0.85 (s, 3, pinanyl CH_3), 1.09 (d, J = 6.6, 3, CH_3CH), 1.19 (d, J = 10.9, 1, pinanyl), 1.30 (s, 3, pinanyl CH_3), 1.42 (s, 3, pinanyl CH_3), 1.45 (s, 9, $C(CH_3)_3$), 1.55–2.55 (m, 6), 2.63 (dd, J = 4.3 and 14.9 Hz, CH_2CO), 3.40 (d, J = 6.8 Hz, 1, CHCl), 4.37 (dd, 1, pinanyl CHOB). Anal. Calcd for $C_{19}H_{32}BClO_4$: C, 61.55; H, 8.70; B, 2.92; Cl, 9.57. Found: C, 61.67; H, 8.93; B, 2.91; Cl, 9.68.

***tert*-Butyl (3*S*,4*R*)-3,7-Dimethyl-4-[(r)-(pinanediyldioxy)boryl]oct-6-enoate (16).** To a solution of 3.98 g (10.7 mmol) of **15** in ~15 mL of THF at −78 °C was added 12 mL (14.4 mmol) of 1.2 M (3-methylbut-2-en-1-yl)magnesium chloride in ether. The mixture was stirred 38 h at 20–25 °C. At this point, TLC analysis indicated little unreacted **15** remained, and NMR indicated 6%. Workup with saturated ammonium chloride and light petroleum in the usual manner followed by column chromatography on silica with dichloromethane as eluant yielded 3.63 g (84%) of **16** as an oil; 200-MHz NMR ($CDCl_3$) δ 0.84 (s, 3, pinanyl CH_3), 0.99 (d, J = 6.4, 3, CH_3CH), 1.13 (d, 1, pinanyl), 1.28 (s, 3, pinanyl CH_3), 1.35 (s, 3, pinanyl CH_3), 1.44 (s, 9, $C(CH_3)_3$), 1.60 and 1.66 (2s, 3 + 3, $(CH_3)_2C{=}C$), 1.70–2.45 (m, 11), 4.53 (dd, 1, pinanyl CHOB), 5.13 (t, 1, $C{=}CH$). Anal. Calcd for $C_{24}H_{41}BO_4$: C, 71.28; H, 10.22; B, 2.67. Found: C, 71.38; H, 10.12; B, 2.70.

Pinacol (1-Chloroethyl)boronate. This compound was obtained from homologation of pinacol methylboronate with (dichloromethyl)lithium by the usual zinc chloride catalyzed procedure, 94%, bp 94–95 °C (10 torr); 90-MHz NMR ($CDCl_3$) δ 1.29 (s, 12, CCH_3), 1.54 (d, 3, J = 7.6 Hz, $CHClCH_3$), 3.51 (q, 1, CHCl). Anal. Calcd for $C_8H_{16}BClO_2$: C, 50.44; H, 8.47; B, 5.68; Cl, 18.62. Found: C, 50.65; H, 8.28; B, 6.07; Cl, 18.95.

***tert*-Butyl (3*R*)- and (3*S*)-3-[(s)-(Pinanediyldioxy)boryl]butanoate.** This diastereomer mixture was prepared by treatment of pinacol (1-chloroethyl)boronate with *tert*-butyl lithioacetate as in the preparation of **14**, then by transesterification with (s)-pinanediol; 200-MHz NMR

(50) Brown, H. C. "Boranes in Organic Chemistry"; Cornell University Press: Ithaca, N.Y., 1972; 321–325.

(51) Huet, F.; Lechevallier, A.; Pellet, M.; Conia, J. M. *Synthesis* **1978**, 63–65.

(52) Rathke, M. W.; Sullivan, D. F. *J. Am. Chem. Soc.* **1973**, *95*, 3050–3051.

($CDCl_3$) same as **14**, except that the singlet (CH_3) at δ 1.372 was paired with another at δ 1.364, and the doublet (J = 10.8 Hz) at δ 1.189 was paired with another at δ 1.199. Anal. Calcd for $C_{18}H_{31}BO_4$: C, 67.09; H, 9.70; B, 3.35. Found: C, 67.14; H, 9.82; B, 3.51.

***tert*-Butyl (3*R*,4*S*)- and (3*S*,4*S*)-4-Chloro-3-methyl-4-[(s)-(pinanediyldioxy)boryl]butanoate (enantiomer + diastereomer of 15).** The mixture of diastereomeric pinanediol esters from the preceding paragraph was homologated in the usual manner; 200 MHz NMR ($CDCl_3$) same as for **15**, except that the doublet at δ 3.401 (J = 6.8 Hz) was diminished in intensity and paired with a similar doublet at δ 3.642 (J = 4.0 Hz). Anal. Calcd for $C_{19}H_{32}BClO_4$: C, 61.55; H, 8.70; B, 2.92; Cl, 9.57. Found: C, 61.75; H, 8.90; B, 2.99; Cl, 9.87.

(s)-Pinanediol (1-Phenyl-5-methylhex-4-en-2-yl)boronate. This compound was prepared by adding 2 mmol of (s)-pinanediol (1-chloro-2-phenylethyl)boronate (**3e**) in ~3 mL of THF to 2 mmol of (3-methylbut-2-en-1-yl)magnesium chloride in ~7 mL of THF at −78 °C followed by 48 h at 20 °C and chromatography on silica with 7% ethyl acetate in light petroleum; $[\alpha]^{22}546$ +23.87° (*c* 1.4, $CHCl_3$); 200-MHz NMR ($CDCl_3$) δ 0.75–2.38 (m, 24, with CH_3's at 0.797, 1.241, 1.248, pinanyl; 1.574, 1.673, C=C(CH_3)$_2$), 2.71 (d, J = 8.2 Hz, 2, PhCH_2), 4.17 (dd, 1, C*H*OB), 5.17 (t, 1, C=C*H*CH$_2$), 7.16–7.26 (m, 5, C_6H_5). Anal. Calcd for $C_{23}H_{33}BO_2$: C, 78.41; H, 9.44; B, 3.07. Found: C, 78.49; H, 9.49; B, 3.23.

Eldanolide (18). A solution of 3.04 g (7.5 mmol) of the boronic ester **16** in 25 mL of THF was cooled in an ice bath and treated with ~10 mL of 2.2 M aqueous sodium hydroxide followed by dropwise addition of 2 mL (~20 mmol) of 30% hydrogen peroxide. The mixture was warmed to 45 °C for 0.5 h, cooled, and concentrated on a rotary evaporator. The residue was extracted with ether (3 × 100 mL), concentrated, and chromatographed on silica with 5% ethyl acetate in hexane, 1.43 g (78%) of *tert*-butyl (3*S*,4*R*)-3,7-dimethyl-4-hydroxy-6-octenoate (17), which appeared from the NMR spectrum to have suffered some cleavage of the *tert*-butyl ester to the acid. This impure **17** dissolved in 100 mL of dichloromethane was treated with a few drops of trifluoroacetic acid at 25 °C for 1 h to hydrolyze the ester.[53] NMR analysis indicated that the products consisted of **18** and *tert*-butyl alcohol, confirmed by adding *tert*-butyl alcohol to the mixture. The **18** was isolated by chromatography on silica with dichloromethane, and ^{1}H NMR and mass spectra were in accord with reported data.[18,20a]

(s)-Pinanediol (1*R*)-(1-(Benzyloxy)pentyl)boronate (19). A solution of 39 mmol of benzyl alcohol in ~50 mL of THF was treated with an equivalent amount of butyllithium at −78 °C, followed by 40 mmol of dimethyl sulfoxide.[54] After the solids had dissolved, 10.14 g (36 mmol) of (s)-pinanediol (1*S*)-(1-chloropentyl)boronate (**3c**) was transferred via cannula into the reaction mixture, which was then allowed to warm to 25 °C overnight. Treatment with water and ether, drying the ether phase over magnesium sulfate, and distillation yielded 11.30 g (89%) of **19**, bp 132–134 °C (0.3 torr); 200-MHz NMR ($CDCl_3$) δ 0.83 (s, 3), 0.89 (t, J= 7.0 Hz, 3), 1.16 (d, J = 10.7 Hz, 1), 1.35–2.39 (m, 11), 1.28 (s, 3); 1.39 (s, 3), 3.35 (t, J = 6.5 Hz, 1, BC*H*OCH$_2$Ph), 4.31 (dd, J = 1.9, 8.7 Hz), 4.54 (m, 2, OCH_2Ph), 7.30 (m, 5, C_6H_5). The 1*R* epimer at δ 1.14, J = 11 Hz, was estimated to be 1.5%. The peak position was verified by preparing an epimer mixture by transesterification of the racemic pinacol ester with pinanediol. Anal. Calcd for $C_{22}H_{33}BO_3$: C, 74.16; H, 9.34; B, 3.03. Found: C, 74.39; H, 9.20; B, 2.92.

(s)-Pinanediol (1*S*,2*S*)-(1-Chloro-2-(benzyloxy)hexyl)boronate (20). A 7.0-g (19.6-mmol) portion of (s)-pinanediol (1*R*)-(1-(benzyloxy)-pentyl)boronate (**19**) was added to (dichloromethyl)lithium at −100 °C in the usual manner and then treated with 31 mmol (1.6 equiv) of zinc chloride. The mixture was stirred 36 h at 25 °C, then treated with water and ether, and concentrated. No evidence of unchanged **19** was seen in the NMR spectrum of the crude **20**. The residual oil was chromatographed on silica with 15% ether/hexane to yield 7.1 g (89%) of **20**: 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.83 (s, 3), 0.89 (t, 3), 1.20 (d, 1), 1.28 (s, 3), 1.39 (s, 3), 1.27–2.18 (m, 11), 3.65 (d, 1, C*H*Cl), 3.77 (q, 1, C*H*OCH$_2$Ph), 4.37 (dd, 1), 4.65 (m, 2, OCH_2Ph), 7.32 (m, 5, C_6H_5); 50.3-MHz ^{13}C NMR δ 13.99, 22.69, 23.97, 26.31, 26.99, 27.63, 28.39, 31.74, 35.19, 38.20, 39.31, 46.2 (broad, B*C*), 51.09, 72.51, 78.51, 80.38, 86.65, 127.44, 127.75, 128.19, 138.48. Anal. Calcd for $C_{23}H_{34}BO_3Cl$: C, 68.25; H, 8.47; B, 2.67; B, 2.67; Cl, 8.76. Found: C, 68.16; H, 8.42; B, 2.59; Cl, 8.80.

(s)-Pinanediol (1*S*,2*S*)-(1-Butyl-2-(benzyloxy)hexyl)boronate (21a). A solution of 17.5 mmol of **20** in 40 mL of THF at −78 °C was treated with *n*-butylmagnesium chloride (12 ml, 23 mmol, of 1.9 M solution in THF). After a night at 25 °C, the mixture was treated with wet ether followed by the usual water/ether extraction. The ether phase was dried over magnesium sulfate, and the residual oil was chromatographed on silica with 10% ether/hexane to yield 6.57 g (78%) of pure **21a**: 200-MHz NMR ($CDCl_3$) δ 0.84 (s, 3), 0.89 (m, 6), 1.13 (d, 1), 1.25 (s, 3), 1.38 (s, 3), 1.20–2.40 (m, 18), 3.55 (m, 1, C*H*OCH$_2$Ph), 4.24 (dd, 1), 4.51 (s, 2, OCH_2Ph), 7.30 (m, 5, C_6H_5). Anal. Calcd for $C_{27}H_{43}BO_3$: C, 76.05; H, 10.16; B, 2.53. Found: C, 75.69; H, 9.85; B, 2.80.

(5*S*,6*S*)-6-(Benzyloxy)-5-decanol (22a). Treatment of 2.2 mmol of **21a** in ~10 mL of THF with 2.6 mmol of aqueous hydrogen peroxide and ~3 mmol of sodium hydroxide at 0 °C for 3 h was followed by addition of 25 mL of saturated ammonium chloride solution. The aqueous phase was extracted with ether, the ether phase was dried over potassium carbonate, and the product was freed from a polar impurity by chromatography on silica (25% ether/hexane). Kugelrohr distillation of the residue at 100 °C (0.1 torr) yielded 0.49 g (85%) of 22a: $[\alpha]^{22}546$ +13.35° (*c* 1.7, $CHCl_3$); 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.91 (m, 6, CH_3), 1.22–1.68 (m, 12), 3.26 (q, 1, J = 5.5 Hz, C*H*OCH$_2$Ph), 3.53 (m, 1, C*H*OH), 4.57 (m, 2, CH_2Ph), 7.33 (m, 5, C_6H_5); 22.6-MHz ^{13}C NMR ($CDCl_3$) δ 14.1 (2), 22.8, 23.1, 27.4, 28.0, 30.2, 33.3, 72.5, 72.8, 82.5, 127.8, 128.5, 138.6. Anal. Calcd for $C_{17}H_{28}O_2$: C, 77.22; H, 10.67. Found: C, 77.33; H, 10.58.

(−)-(5*S*,6*S*)-5,6-Decanediol (22b). To a suspension of 250 mg of 10% palladium on charcoal in 10 mL of ethanol under hydrogen was injected a solution of 0.45 g (1.7 mmol) of **22a** in 5 mL of ethanol. The mixture was stirred 1 h under hydrogen at 1 atm. The mixture was filtered through Celite with thorough washing with ethanol and concentrated under vacuum to yield a yellow solid, which was sublimed under vacuum to yield 0.32 g (97%) of crude **22b** as a white powder, mp 42–44 °C. The diastereomeric purity of this material was proved by comparison of its NMR spectra with those of the meso isomer prepared from *E*-5-decene according to the literature procedure[23] (sublimed, mp 133–135 °C). The C*H*OH protons of the (*S*,*S*)-isomer appeared at δ 3.40, the meso isomer at δ 3.60. In the ^{13}C NMR, the C*H*OH peak of the (*S*,*S*)-isomer appeared at 73.11 ppm, the meso isomer at 73.77 ppm in Me_2SO-d_6, and the meso peak in the (*S*,*S*)-isomer spectrum was unambiguously identified by spiking the sample with meso compound. From the data obtained, the meso content of the crude (*S*,*S*)-decanediol was estimated to be 1.5% (±0.5%). After two recrystallizations from ethanol, no evidence of any remaining *meso*-5,6-decanediol could be seen in the proton NMR spectrum of the (*S*,*S*)-5,6-decanediol, mp 43.5–44 °C; $[\alpha]^{23.0}546$ −40.2° (*c* 0.4, absolute EtOH); 200-MHz ^{1}H NMR (Me_2SO-d_6) δ 0.92 (m, 6, CH_3), 1.20–1.60 (m, 12, CH_2), 2.22 (broad s, CHO*H*, 2), 3.40 (m, C*H*OH, 2). Anal. Calcd for $C_{10}H_{22}O_2$: C, 68.92; H, 12.72. Found: C, 69.08; H, 12.60.

(s)-Pinanediol (1*S*,2*S*)-(2-(Benzyloxy)-1-methylhexyl)boronate (21b). A solution of 1.52 g (3.8 mmol) of (s)-pinanediol (1*S*,2*S*)-(2-(benzyloxy)-1-chlorohexyl)boronate (**20**) in 25 mL of THF at −78 °C was treated with 1.80 mL of 2.65 M methylmagnesium bromide in ether, followed by 0.56 g (4.1 mmol) of zinc chloride.[43] After the usual procedure, flash chromatography on silica with 5% ethyl acetate/hexane yielded 1.33 g of **21b** was an oil; $[\alpha]^{23}546$ +13.94° (*c* 4.3, toluene); 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.83 (s, 3), 0.88 (t, 3), 0.99 (d, J = 7.4 Hz, 3, CHCH_3), 1.13 (d, J = 10.6 Hz, 1), 1.27 (s, 3), 1.34 (s, 3), 1.26–2.32 (m, 12), 3.56 (m, 1, C*H*OCH$_2$Ph), 4.25 (dd, 1, C*H*OB), 4.50 (m, 2, OCH_2Ph), 7.30 (m, 5, C_6H_5); 22.6-MHz ^{13}C NMR ($CDCl_3$) δ 10.5, 14.1, 22.9, 24.0, 26.4, 27.2, 27.8, 28.7, 30.1, 32.1, 35.6, 38.2, 39.6, 51.4, 70.9, 81.8, 85.4, 127.1, 127.6, 128.1, 139.6, B*C* peak not observed. Anal. Calcd for $C_{24}H_{37}BO_3$: C, 75.00, H, 9.70; B, 2.81. Found: C, 74.89; H, 9.67; B, 2.62.

(s)-Pinanediol (1*S*,2*R*,3*S*)-(3-(Benzyloxy)-1-butyl-2-methylheptyl)-boronate (23). The product from the preceding paragraph, **21b**, 0.64 g (1.7 mmol), was homologated with (dichloromethyl)lithium followed by 0.38 g (2.8 mmol) of zinc chloride according to the standard procedure. The oily (s)-pinanediol (1*S*,2*S*,3*S*)-(3-(benzyloxy)-1-chloro-2-methylheptyl)boronate was chromatographed on silica with 7% ethyl acetate/hexane but was not fully purified; 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.83 (s, 3), 0.90 (t, 3), 1.21 (d, 1), 1.28 (s, 3), 1.36 (s, 3), 1.24–2.40 (m, 12), 3.40 (m, 1, C*H*OCH$_2$Ph), 3.95 (d, J = 5.1 Hz, 1, C*H*Cl), 4.32 (dd, 1), 4.55 (s, 2, OCH_2Ph), 7.33 (m, 5, C_6H_5). Anal. Calcd for $C_{25}H_{38}BClO_3$: C, 69.37; H, 8.85; B, 2.50; Cl; 8.19. Found: C, 69.92; H, 8.73; B, 2.13; Cl, 7.20. An entire batch (0.57 g) of this crude α-chloro boronic ester at −78 °C was treated with 1.6 mmol of butylmagnesium chloride in the usual manner, then with 0.17 g (1.2 mmol) of zinc chloride. After stirring overnight at 25 °C and chromatography with 5% ethyl acetate/hexane, 0.53 g of **23** was isolated as an oil; 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.83 (s, 3), 0.88 (t, 3); 0.91 (t, 3), 1.25 (s, 3). 1.32 (s, 3), 1.09–2.35 (m, 23), 3.39 (q, J = 4.6 Hz, 1, C*H*OCH$_2$Ph), 4.22 (dd, 1), 4.50 (m, 2, OCH_2Ph), 7.35 (m, 5, C_6H_5); 22.6-MHz ^{13}C NMR ($CDCl_3$) δ 13.9, 14.1,

(53) Bryan, D. B.; Hall, R. F.; Holden, K. G.; Huffman, W. F.; Gleason, J. G. *J. Am. Chem. Soc.* **1977**, *99*, 2353–2355.

(54) The Me_2SO accelerated the reaction and may have reduced the epimerization of **3c**, which was too small to measure (<0.5% in this step).

(55) Phase-transfer catalyst for azide: Reeves, W. P.; Bahr, M. L. *Synthesis* **1976**, 823.

14.4, 23.0, 24.1, 25.4, 26.4, 26.6, 27.2, 28.0, 28.8, 31.8, 35.6, 35.8, 36.9, 38.3, 39.7, 51.5, 71.4, 77.6, 82.0, 85.2, 127.2, 127.9, 128.2, 139.6.

(5*S*,6*R*,7*S*)-(Benzyloxy)-6-methyl-5-undecanol (24a). The oily **23**, 0.53 g, in 10 mL of THF was treated with 1 mL of 30% hydrogen peroxide and 1.0 mL of 5 M sodium hydroxide at 0 °C for 3 h, then refluxed 0.5 h and cooled. Workup with saturated ammonium chloride and ether followed by flash chromatography on silica with 15% ethyl acetate/hexane and kugelrohr distillation at 120 °C (0.1 torr) yielded 0.28 g of **24a**, 57% based on **21b**; $[\alpha]^{21}546$ −3.16° (*c* 1.5, absolute EtOH); 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.90 (t, 3), 0.92 (t, 3), 0.98 (d, J = 7.1 Hz, 3, $CHCH_3$), 1.24–1.73 (m, 13), 3.16 (broad s, 1, O*H*), 3.47 (q, J = 6, 1, $CHOCH_2Ph$), 3.92 (m, 1, $CHOH$), 4.53 (m, 2, OCH_2Ph), 7.29 (m, 5, C_6H_5); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 11.49, 14.10, 22.82, 22.94, 27.50, 28.50, (29.71 impurity), 30.95, 34.08, 39.22, 70.93, 72.47, 84.42, 127.66, 127.70, 128.38, 138.21. Anal. Calcd for $C_{18}H_{32}O_2$: C, 78.03; H, 11.03. Found: C, 78.30; H, 10.86.

(5*S*,7*S*)-6-Methyl-5,7-undecanediol (24b). Hydrogenolysis of 120 mg of **24a** was carried out in 95% ethanol (10 mL) with 1 atm of hydrogen over 20 mg of 10% palladium on charcoal for 24 h. The product was sublimed at 120 °C (0.05 torr), 83 mg (99%) of **24b**; recrystallized from dichloromethane/pentane, mp 45–47 °C; $[\alpha]^{22}546$ −26.15° (*c* 0.9, $CHCl_3$); 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.91 (t, J = 6.6 Hz, 6, CH_2CH_3), 0.95 (d, J = 7.1 Hz, 3, $CHCH_3$), 1.20–1.66 (m, 13), 2.78 (broad s, 2, O*H*), 3.63 (q, J = 6 Hz, 1, $CHOH$), 3.93 (m, 1, $CHOH'$); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 11.45, 14.08 (2), 22.76 (2), 27.99, 28.50, 33.78, 35.28, 41.09, 72.54, 76.18. Anal. Calcd for $C_{12}H_{26}O_2$: C, 71.23; H, 12.95. Found: C, 71.34; H, 12.84. None of the meso isomers could be detected in the crude **24b** by NMR spectroscopy (0.5% detection limit).

Mixed 6-Methyl-5,7-undecanediols. Methyl pentanoate and methyl butyl ketone with sodium methoxide yielded 5,7-undecanedione, which was purified through the copper salt, converted to the thallium enolate, and methylated with methyl iodide to form 6-methyl-5,7-undecanedione, which was reduced with sodium borohydride;[25] 200-MHz ^{1}H NMR ($CDCl_3$) δ 3.57 (m, meso + chiral isomer $CHOH$), 3.82 (m, other meso isomer $CHOH$), 3.93 (chiral isomer $CHOH'$), 4.1 (O*H*, concentration dependent), CH_2 and CH_3 regions similar to chiral isomer but more complex, with one of the meso CH_3's at δ 0.79 (d, J = 6.9 Hz); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ [4.18, 13.24, 11.54] (meso, meso′, chiral $CHCH_3$), 14.13 (CH_2CH_3), [22.83, 22.86, 22.93] (CH_2CH_3), [27.22, 28.33, (28.11 + 28.60)] (meso, meso′, chiral CH_2Et), [34.67, 34.96, (33.66 + 35.28)] (CH_2Pr), [39.81, 43.34, 40.96] (central *C*), [76.496, 77.345, (72.48 + 75.81)] (*C*OH). Slight shifts in the chiral isomer peaks are attributed to the higher sample concentration. Anal. $C_{12}H_{26}O_2$: Found, C, 70.95; H, 12.84.

(s)-Pinanediol (1*R*)-(1-Azidopentyl)boronate (25). A solution of 2.81 g (9.9 mmol) of (s)-pinanediol (1*S*)-(1-chloropentyl)boronate (3c) in 35 mL of dichloromethane was placed in a dropping funnel equipped with a needle valve and added very slowly, <0.5 mL/min, to a vigorously stirred mixture of 6.5 g (100 mmol) of sodium azide and 160 mg (0.5 mmol) of tetrabutylammonium bromide[55] in 50 mL of water and 200 mL of dichloromethane at 25 °C. After stirring overnight the mixture was treated with saturated ammonium chloride solution to aid in separation of the phases, and the aqueous phase was extracted with 3 × 150 mL of dichloromethane. The dichloromethane solution was dried over magnesium sulfate, concentrated, chromatographed on a short column of silica with 5% ethyl acetate/hexane to remove the phase-transfer catalyst, and distilled, 2.75 g (96%) of (s)-pinanediol (1*R*)-(1-azidopentyl)boronate (**25**): bp 98–100 °C (0.05 torr); $[\alpha]^{25}546$ +9.58° (*c* 1.6, toluene); IR (neat) 2100 cm^{-1} (N_3); 200-MHz NMR ($CDCl_3$) δ 0.85 (s, 3), 0.91 (t, 3), 1.10 (d, J = 11 Hz, 1), 1.30 (s, 3), 1.42 (s, 3), 1.24–2.44 (m, 11), 3.115 (t, J = 6.9 Hz, 1, $BCHN_3$), 3.124 (t, ~2% of 1, $BCHN_3$ of epimer), 4.35 (dd, J = 1.8 and 8.7 Hz, 1, C*H*OB); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 13.97, 22.48, 23.97, 26.46, 27.00, 28.54, 29.43, 30.33, 35.27, 38.11, 39.41, 48.3 (broad, B*C*), 57.04, 78.41, 86.76. Anal. Calcd for $C_{15}H_{26}BN_3O_2$: C, 61.87; H, 9.00; B, 3.71; N, 14.43. Found: C, 62.10; H, 8.79; B, 3.88; N, 14.65. The (1*S*)-epimer was a major byproduct from reaction of **3c** with sodium azide in THF.

(s)-Pinanediol (1*S*,2*S*)-(1-Chloro-2-azidohexyl)boronate (26). Treatment of 23 mmol of (dichloromethyl)lithium with 5.50 g (18.9 mmol) of (s)-pinanediol (1*R*)-(1-azidopentyl)boronate (**25**) followed by 1.78 g (13.1 mmol) of zinc chloride according to the usual procedure, then flash chromatography on silica with 3% ethyl acetate/hexane yielded 5.87 g (92%) of **26**: $[\alpha]^{23}546$ +32.4° (*c* 4, $CHCl_3$); IR 2101 cm^{-1} (N_3); 200-MHz NMR ($CDCl_3$) δ 0.85 (s, 3), 0.93 (t, 3), 1.21 (d, J = 11, 1), 1.30 (s, 3), 1.42 (s, 3), 1.27–2.38 (m, 11), 3.54 (d, J = 6.1, 1, $CHCl$), 3.66 (m, 1, CHN_3), 4.40 (dd, 1, C*H*OB). Anal. Calcd for $C_{16}H_{27}BClN_3O_2$: C, 56.58; H, 8.01; B, 3.18; Cl, 10.44; N, 12.37. Found: C, 56.83; H, 7.96; B, 3.24; Cl, 10.60; N, 12.05.

(s)-Pinanediol (1*S*,2*S*)-(2-Azido-1-butylhexyl)boronate (27). Butylmagnesium chloride (1.5 M in ether, 5.7 mL) was added dropwise down the side of the flask to 2.55 g (7.5 mmol) of **26** in 75 mL of THF at −78 °C. After 30 min, 5.13 g (38 mmol) of powdered anhydrous zinc chloride[43] was added from a powder addition funnel, slowly enough to avoid clumping or overheating. The mixture was stirred 16 h at 25 °C, then extracted with 100 mL of saturated ammonium chloride. The ammonium chloride phase was extracted with ether, and the combined organic phase was dried over magnesium sulfate, concentrated, and partially purified by flash chromatography to yield 2.12 g of **27** contaminated with ~5% (s)-pinanediol butylboronate according to NMR analysis; IR 2095 cm^{-1} (N_3); $[\alpha]^{21}546$ +16.2° (*c* 2, toluene); 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.85 (s, 3), 0.90 (m, 6), 1.20 (d, J = 10.7 Hz, 1), 1.29 (s, 3), 1.39 (s, 3), 1.25–2.42 (m, 18), 3.42 (m, 1, CHN_3), 4.31 (dd, C*H*OB); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 14.0 (2), 22.5, 22.9, 24.1, 26.4, 27.1, 28.0, 28.6, 28.8, 30.0 (broad, B*C*), 31.3, 33.5, 35.6, 38.2, 39.5, 51.1, 65.7, 77.7, 85.7. Anal. Calcd for $C_{20}H_{36}BN_3O_2$: C, 66.48; H, 10.04; B, 2.99; N, 11.63. Found: C, 67.01; H, 10.35; B, 3.11; N, 11.13.

(5*S*,6*S*)-6-Azido-5-decanol (28a). The crude **27** (2.12 g, preceding paragraph) in 20 mL of THF was added dropwise to a mixture of 5 mL of 30% hydrogen peroxide, 20 mL of water buffered with sodium hydrogen and dihydrogen phosphate to pH 7.6, and 20 mL of THF at 0 °C, then stirred 16 h at 25 °C and refluxed 30 min. Workup with aqueous ammonium chloride and ether followed by flash chromatography on silica with 5% ethyl acetate/hexane and then kugelrohr distillation at 90 °C (0.3 torr) yielded 1.07 g (71% based on **26**) of **28a**: $[\alpha]^{25.0}546$ +4.09° (*c* 2, chloroform); Gc (3.8-m phenylmethylsilicone capillary column, 100 °C) 22.3 min with 2.25% (5*R**,6*S**) epimer at 23.2 min; IR (cm^{-1}) 3424 (OH), 2099 (N_3); 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.93 (m, 6, CH_3), 1.2–1.7 (m, 12, CH_2), 1.92 (d, 1, O*H*), 3.21 (m, CHN_3), 3.53 (m, C*H*OH); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 13.98, 14.02, 22.58, 22.66, 27.80, 28.41, 30.65, 34.00, 67.19, 73.51. Anal. Calcd for $C_{10}H_{21}N_3O$: C, 60.27; H, 10.62; N, 21.08. Found: C, 60.32; H, 10.70; N, 20.78.

(5*S*,6*S*)-6-Amino-5-decanol (28b). A solution of 0.48 g (2.4 mmol) of the azido alcohol **28a** in 10 mL of ether was added dropwise to a stirred suspension of 0.34 g (8.9 mmol) of lithium aluminum hydride in 30 mL of ether, then refluxed 3 h.[26] After destruction of the excess hydride with wet ether, the mixture was treated with 15 mL of water and the aluminum salts filtered. The filtrate was extracted with ether (3 × 50 mL), dried over magnesium sulfate, and concentrated to white solid **28b**, sublimed at 95 °C (0.25 torr), 0.34 g (83%); $[\alpha]^{25.0}546$ −35.3° (*c* 0.8, chloroform); mp 37–38 °C (lit.[27] mp of racemate 38–40 °C); 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.91 (t, 6, CH_3), 1.17–1.59 (m, 12), 1.98 (broad s, 3, N*H* + O*H*), 2.54 (m, 1, $CHNH_2$), 3.25 (m, 1, C*H*OH); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 14.09 (2), 22.76, 22.86, 28.09, 28.49, 34.11, 34.29, 55.42, 73.79. Anal. Calcd for $C_{10}H_{23}NO$: C, 69.31; H, 13.38; N, 8.08. Found: C, 69.00; H, 13.40; N, 7.96. The diastereomer content estimated from the NMR spectra was ~2%.

(5*R,6*S**)-6-Amino-5-decanol.** This diastereomer was made for comparison purposes from the corresponding racemic azido alcohol[28] by reduction as described for **28b**; mp 45–47 °C (lit[27] mp 49–50 °C); 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.91 (t, 6), 1.19–1.55 (m, 12), 1.82 (broad s, 3, O*H* + N*H*), 2.75 (m, 1, $CHNH_2$), 3.47 (m, 1, C*H*OH); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 14.07 (2), 22.83 (2), 28.42, 28.86, 31.11, 31.89, 55.35, 74.31. Anal. Calcd for $C_{10}H_{23}NO$: see **28b**. Found: C, 69.29; H, 13.13; N, 7.95.

Acknowledgment. We thank the National Science Foundation for Grants CHE8025229 and CHE8400715 and the Boeing Corporation for a grant in support of departmental purchase of the Nicolet NT-200 NMR instrument.