Elimination of 17 with Bu_3SnH. (*E*)-18 and (*Z*)-18 were prepared by the same procedures as in the elimination from **6**. The results are summarized in Table V.

(*E*)-**18a**: NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 8 Hz), 1.76 (s, 3 H), 2.10 (m, 2 H), 4.76 (s, 2 H), 5.58 (t, 1 H, J = 7 Hz), 7.36–7.54 (m, 3 H), 8.0–8.1 (d, 2 H, J = 8 Hz); MS, m/e (M^+) calcd for $C_{13}H_{16}O_2$ 204.1150, found 204.1190.

(*Z*)-**18a**: NMR ($CDCl_3$) δ 1.00 (t, 3 H, J = 8 Hz), 1.84 (s, 3 H), 2.10 (m, 2 H), 4.80 (s, 2 H), 5.40 (t, 1 H, J = 7 Hz), 7.36–7.54 (m, 3 H), 8.0–8.1 (d, 2 H); MS, m/e (M^+) found 204.1181.

(*E*)-**18b**: NMR ($CDCl_3$) δ 0.88 (t, 3 H, J = 8 Hz), 1.20–1.45 (m, 6 H), 1.74 (s, 3 H), 2.03 (m, 2 H), 4.76 (s, 2 H), 5.60 (t, 1 H, J = 8 Hz), 7.4–7.5 (m, 3 H), 8.0–8.1 (m, 2 H); MS, m/e (M^+) calcd for $C_{16}H_{22}O_2$ 246.1619, found 246.1618.

(*Z*)-**18b**: NMR ($CDCl_3$) δ 0.88 (t, 3 H, J = 8 Hz), 1.20–1.45 (m, 6 H), 1.84 (s, 3 H), 2.12 (m, 2 H), 4.84 (s, 2 H), 5.44 (t, 1 H, J = 8 Hz), 7.38–7.50 (m, 3 H), 7.96–8.08 (m, 2 H); MS, m/e (M^+) found 246.1620.

(*E*)-**18c**: NMR ($CDCl_3$) δ 0.90–1.80 (m, 10 H), 1.74 (s, 3 H), 2.10–2.40 (m, 1 H), 4.70 (s, 2 H), 5.37 (d, 1 H, J = 8 Hz), 7.30–7.50 (m, 3 H), 7.92–8.05 (m, 2 H); MS, m/e (M^+) calcd for $C_{17}H_{22}O_2$ 258.1620, found 258.1669.

(*Z*)-**18c**: NMR ($CDCl_3$) δ 1.0–1.8 (m, 10 H), 1.84 (s, 3 H), 2.1–2.5 (m, 1 H), 4.88 (s, 2 H), 5.30 (d, 1 H, J = 8 Hz), 7.4–7.6 (m, 3 H), 7.98–8.10 (m, 2 H); MS, m/e (M^+) found 258.1608.

Isomerization of Olefins. A mixture of (*E*)-**9** or (*Z*)-**9** (1 mmol) and 2,3-dimethyl-2,3-dinitrobutane (1 mmol) in 3 mL of dimethylformamide was stirred at room temperature for 3 h. After the usual workup, the product was analyzed by GLC. (*E*)-**9** or (*Z*)-**9** was recovered, respectively. No isomerization took place under the reaction conditions. The reaction of **6a** or **6b** with Bu_3SnH was carried out under various conditions. The E/Z ratio was determined by GLC using pentadecane as an internal standard. No isomerization was observed at 80 °C, and very slow isomerization took place at 140 °C.

Registry No. **3a**, 79424-86-5; **3b**, 79424-87-6; **4a**, 110511-65-4; **4b**, 110511-66-5; **5a**, 110511-67-6; **5b**, 110511-68-7; **6a**, 94421-38-2; **6b**, 94421-18-8; **7a**, 94482-12-9; **7b**, 94421-13-3; **8a**, 110511-69-8; **8b**, 110511-70-1; (*E*)-**9**, 67275-05-2; (*Z*)-**9**, 67275-06-3; (*E*)-**10**, 110511-73-4; (*Z*)-**10**, 110511-74-5; (*E*)-**11**, 94421-26-8; (*Z*)-**11**, 94421-27-9; *u*-**17a**, 110511-71-2; *l*-**17a**, 110529-54-9; *u*-**17b**, 110529-55-0; *l*-**17b**, 110529-56-1; *u*-**17c**, 110511-72-3; *l*-**17c**, 110529-57-2; (*E*)-**18a**, 94421-24-6; (*Z*)-**18a**, 94421-25-7; (*E*)-**18b**, 110511-75-6; (*Z*)-**18b**, 110511-76-7; (*E*)-**18c**, 110511-77-8; (*Z*)-**18c**, 110511-78-9; *m*-DNB, 99-65-0; Bu_3Sn^*, 20763-88-6; PhSH, 108-98-5; Bu_3SnH, 688-73-3; Na_2S, 1313-82-2; NaTeH, 65312-92-7; 4-methyl-2-nitro-2-pentene, 33972-68-8; 2,3-dimethyl-2,3-dinitrobutane, 3964-18-9.

Supplementary Material Available: X-ray structure (Figure 1) and tables of bond distances and angles and crystal data (Tables I and II) for compound **3a** (3 pages). Ordering information is given on any current masthead page.

Synthesis of L-(+)-Ribose via (*s*)-Pinanediol (αS)-α-Bromo Boronic Esters

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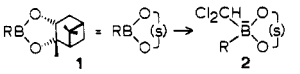
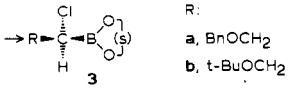
(Dibromomethyl)lithium has been tested for the chirally controlled homologation of benzyloxy-substituted boronic esters to α-halo boronic esters and found to give better yields and diastereomeric ratios than (dichloromethyl)lithium. Displacement by benzyl oxide is also more efficient with the bromides than the chlorides. (*s*)-Pinanediol [(benzyloxy)methyl]boronate (**1a**) has been converted to L-(+)-ribose (**16**) in 13% overall yield via repeated homologations and replacement of the α-bromine by benzyl oxide. The directed chiral assembly of the first four carbons is highly efficient. The low yield during connection of the fifth carbon is accompanied by boron–oxygen β-elimination and is attributed to steric hindrance.

The reaction of an (*s*)-pinanediol[1] alkylboronate **1** with (dichloromethyl)lithium inserts a carbon atom into the carbon–boron bond to form a (1*S*)-(1-chloroalkyl)boronate **3**.[2] With zinc chloride catalysis, less than 1% of the (1*R*)





isomer is formed in most cases.[3] This nearly stereospecific chiral synthesis has proved successful in the presence of ether and other functionalities and has been used for the synthesis of the insect pheromones brevicomin and eldanolide.[3] (*r*)-Pinanediol derived from (−)-α-pinene, the costlier enantiomer, was required for these pheromone syntheses.

One of the obvious applications of this chemistry would be the synthesis of carbohydrates by repetitive homologation, with replacement of the α-chlorine by benzyl oxide at each step, provided certain potential pitfalls could be avoided. Alkoxy substituents slow the rearrangement of the intermediate borate complex **2** to the point that (*s*)-pinanediol [(benzyloxy)methyl]boronate (**1a**) failed to undergo homologation to the (1*S*)-[2-(benzyloxy)-1-chloroethyl]boronate **3a** until after the discovery of the zinc chloride catalysis.[2-4] β-Elimination of boron and oxygen from β-alkoxy boronic esters should be thermodynamically highly favorable, and although it proved not to be a serious problem in the series of model compounds studied,[3] it remained a potential threat to multistep synthesis.

(1) (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) (*s*)-Pinanediol is derived from (+)-α-pinene. The "*s*" signifies "(*S*)-directing" as discussed in ref 3.

(2) Matteson, D. S.; Ray, R.; Rocks, R. R.; Tsai, D. J. *Organometallics* **1983**, *2*, 1536–1543.

(3) Matteson, D. S.; Sadhu, K. M.; Peterson, M. L. *J. Am. Chem. Soc.* **1986**, *108*, 810–819.

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

0022-3263/87/1952-5116$01.50/0

Results

Zinc Chloride Ratio. We had previously found that the rearrangement of borate complexes **2** derived from functionalized boronic esters can be relatively sluggish and in two examples added an extra 1 mol of zinc chloride with good results.[3] However, caution in using a large excess was indicated by the previous finding that epimerization of α-chloro boronic esters can be greatly accelerated by a mixture of zinc chloride and lithium trichlorozincate, there being a term in the rate law that is first order in each species.[5]

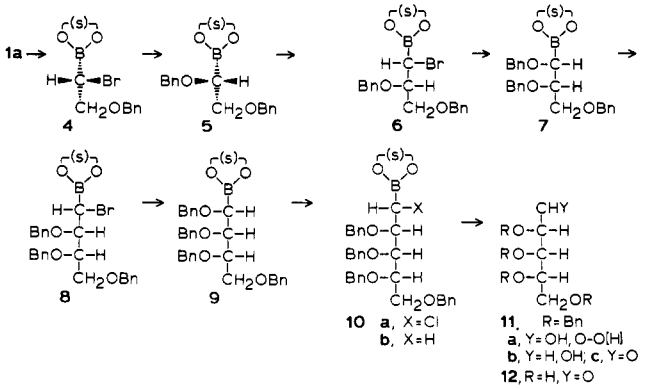
The first evidence that excess zinc chloride might be beneficial with highly oxygenated substrates was obtained in a separate investigation of the homologation of diacetone mannitol butylboronate, which had yielded (1*S*)-(1-chloropentyl)boronate of only 36% de without zinc chloride.[2] The de was not improved by the usual 0.6 mol of zinc chloride but rose to 80–87% with 2.7 mol of zinc chloride.[6] These results suggested that unproductive preferential complexation with the oxygen functionality made the excess zinc chloride unavailable for catalysis.

A brief study of the homologation of (*s*)-pinanediol [(benzyloxy)methyl]boronate (**1a**) showed that 1.7 mol of zinc chloride yielded about 10% more **3a** than 0.7 mol and that the time required was less. Larger amounts of zinc chloride had no apparent effect. The (1*S*) to (1*R*) diastereomer ratio was also unaffected. We then adopted the rule of thumb that 1 mol of zinc chloride would be added for each benzyloxy group, plus 0.7 mol for catalysis of the rearrangement of **2** to **3**.

α-Chloro Boronic Esters. Previous work had not revealed the diastereoselectivity in the conversion of (*s*)-pinanediol [(benzyloxy)methyl]boronate (**1a**) to (*s*)-pinanediol (1*S*)-[2-(benzyloxy)-1-chloroethyl]boronate (**3a**), because the (1*R*) epimer shows insufficient difference at any point in the 200-MHz ^{1}H NMR spectrum.[4] Preparation of an epimer mixture by treatment of **3a** with lithium chloride in THF/water turned out to require several days in order to get enough (1*R*) epimer to detect unequivocally, even though these conditions would epimerize an unsubstituted (α-chloroalkyl)boronic ester to equilibrium. The ^{13}C NMR spectrum then showed a pair of peaks near δ 87.0 distinctly separated by δ 0.07, the upfield peak corresponding to the (1*R*) epimer. This is assigned to the methyl-substituted diol carbon of the pinanediol group. The diastereomer ratio turned out to be a disappointing 9:1.

Originally, **1a** was tedious to make because there was no easy route to its precursor, an (iodomethyl)boronic ester[7] or (chloromethyl)boronic ester.[8] We explored the use of (*s*)-pinanediol (*tert*-butoxymethyl)boronate (**1b**) instead, since the precursor (*tert*-butoxymethyl)lithium is easily prepared.[9] Yields of **1b** proved low but usable. The diastereomer ratio of **3b** was easily determined from either the ^{1}H or ^{13}C NMR spectrum to be in the range 8:1–11:1.

Parallel studies were carried out on the further homologation of the benzyloxy (a series) and *tert*-butoxy (b series) boronic esters. In each case, the alkoxy boronic ester was added to performed (dichloromethyl)lithium at −100 °C, then treated with zinc chloride, and warmed to room temperature over 24–48 h, according to the general procedure described previously.[3] The resulting α-chloro boronic ester was purified and then treated with lithium benzyl oxide to form the α-benzyloxy boronic ester. In the a series, yields for each step were as follows: **3a**, 70–83%; [1,2-bis(benzyloxy)ethyl]boronate **5**, 68%; Cl analogue of **6**, 43%; [1,2,3-tris(benzyloxy)propyl]boronate **7**, 40%; overall conversion of **1a** to **7**, 10%. In the b series, yields



were as follows: **3b**, 83–88%; 1-(benzyloxy)-2-*tert*-butoxy analogue of **5**, 62%, analogue of **6**, 59%, analogue of **7**, 46%; overall 15%. In the latter case, there was enough material for one further homologation to the 1-chloro-4-*tert*-butoxy analogue of **8**, but only 15% was obtained. Compounds **3a**, **3b**, **5**, and **7** were fully characterized. The remainder were supported by good 200-MHz ^{1}H and 22.6-MHz ^{13}C NMR data[10] but were not analyzed and are not described in experimental detail in view of their similarity to fully described compounds and our finding of a much better synthetic route.

It was clear at this point that our synthetic target, ribose, could not be reached without some fundamental improvements in the process.

The first improvement was the separate discovery of an efficient route to diisopropyl (chloromethyl)boronate,[11] which led to an adequate supply of **1a**.

α-Bromo Boronic Esters. Major improvements in the yields were achieved by the use of (dibromomethyl)lithium in place of (dichloromethyl)lithium. (Dibromomethyl)-lithium cannot be generated from dibromomethane with butyllithium but requires (dichloromethyl)lithium or lithium diisopropylamide (LDA) as the base.[12] We chose in situ generation from dibromomethane and LDA in the presence of the boronic ester substrate, an approach that had previously been reported for ketone substrates.[13] We had used analogous in situ generation of (dichloromethyl)lithium to homologate achiral boronic esters[14] and pinanediol butylboronate[15] and to convert triisopropyl borate to diisopropyl (dichloromethyl)boronate.[16]

Since the diisopropylamine generated by the use of LDA complexes with zinc chloride, in order to have free zinc chloride for catalysis of the rearrangement of **2** to **3**, it is

(5) Matteson, D. S.; Erdik, E. *Organometallics* **1983**, *2*, 1083–1088.
(6) Unpublished work with James G. Patterson. The diacetone mannitol (1-chloropentyl)boronate was transesterified to the pinanediol ester, and the (1*S*) to (1*R*) ratio was determined by ^{1}H NMR as described in ref 3.
(7) Matteson, D. S.; Majumdar, D. *J. Organomet. Chem.* **1979**, *170*, 259–264.
(8) Wuts, P. G. M.; Thompson, P. A. *J. Organomet. Chem.* **1982**, *234*, 137–141.
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(10) Peterson, M. L. Ph.D. Thesis, Washington State University, 1987.
(11) Sadhu, K. M.; Matteson, D. S. *Organometallics* **1985**, *4*, 1687–1689.
(12) (a) Köbrich, G.; Fischer, R. H. *Chem. Ber.* **1968**, *101*, 3208–3218. (b) Villieras, J.; Bacquet, C.; Masure, D.; Normant, J. F. *J. Organomet. Chem.* **1973**, *50*, C7–C11.
(13) Taguchi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 3010–3011.
(14) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, *2*, 1529–1535.
(15) Matteson, D. S.; Sadhu, K. M. U.S. Patent 4 525 309, June 25, 1985.
(16) Matteson, D. S.; Hurst, G. D. *Organometallics* **1986**, *5*, 1465–1467.

necessary to add extra zinc chloride or to remove the amine. We chose the latter approach. The intermediate (dibromomethyl)borate complex (analogous to **2**) is stable below 0 °C, and the diisopropylamine was removed by vacuum distillation before the zinc chloride was added.

The (1*S*) to (1*R*) diastereomer ratio was improved to 35:1 when (*s*)-pinanediol [(benzyloxy)methyl]boronate (**1a**) was homologated with (dibromomethyl)lithium to form (*s*)-pinanediol (1*S*)-[2-(benzyloxy)-1-bromoethyl]boronate (**4**). The mixture of (1*S*) and (1*R*) epimers of **4** for comparison was made by homologation of pinacol [(benzyloxy)-methyl]boronate with (dibromomethyl)lithium followed by transesterification with pinanediol. There were readily apparent differences between the two epimers in the ^1H as well as the ^{13}C NMR spectra.

The displacement of bromide from **4** by benzyl oxide to yield (*s*)-pinanediol (1*R*)-[1,2-bis(benzyloxy)ethyl]boronate (**5**) was faster and more efficient than the displacement of chloride from **3a**. From a parallel displacement on the (1*R*)/(1*S*) epimer mixture, it was found that **5** was readily distinguishable from its epimer in the ^1H and ^{13}C NMR spectra and that the major (1*R*) epimer moved faster than the (1*S*) epimer and was thus purified by chromatography.

Two repetitions of the chain extension and displacement reactions led to (*s*)-pinanediol (1*R*,2*R*,3*S*)-[tetrakis(benzyloxy)butyl]boronate (**9**) in a net overall yield from **1a** of 37%.

The diastereomeric purity of the higher homologues **6–9** was not proved, but in view of the good selectivity seen in the first homologation and the precedent of high diastereomeric ratios with other [α-(benzyloxy)alkyl]boronic esters,[3] as well as the clean NMR spectra observed, it is unlikely that any substantial amount of diastereomer was formed. In the following paper, the controlled synthesis of the (1*S*,2*R*,3*S*) epimer of (1*R*,2*R*,2*S*)-[tetrakis(benzyloxy)butyl]boronic ester **9** is described, with evidence that neither epimer is contaminated with the other at the limit of detectability by 200-MHz ^1H NMR.[17] The ultimate proof of the configuration of **9** is the conversion to crystalline L-(+)-ribose (**12**).

L-(+)-Ribose. Having come this far, it might be expected that one more homologation to add the fifth carbon of ribose would be straightforward. Instead, reaction of (dibromomethyl)lithium with **9** gave an intractable mixture that failed to yield any 2,3,4,5-tetrabenzylribose on peroxidic oxidation. (Dichloromethyl)lithium also yielded a gross mixture, but some of the α-chloro boronic ester **10a** must have been present, since treatment with hydrogen peroxide yielded a polar compound **11a** showing all of the expected features of tetrabenzylribose except the aldehyde in the ^1H NMR spectrum. Instead, there was an appropriate multiplet at δ 5.3, which is characteristic of the hydrogen peroxide adducts of aldehydes sometimes obtained from such oxidations of boronic esters.[18] Although **11a** is represented as a hydroperoxide for simplicity, the OH band was not clearly identified, and a 2:1 adduct of aldehyde to peroxide would follow precedent.[18] Hydrogenation of **11a** over palladium yielded ribose **12** (14% from **9**).

Since steric hindrance seemed the most likely cause of the difficulties, homologation of **9** with (chloromethyl)-lithium was tried. Zinc chloride has facilitated other difficult alkylations of α-chloro boronic esters, but in this case, the only products were those of B–O elimination, (3*S*)-1,3,4-tris(benzyloxy)-1-butene [$BnOCH_2CH(OBn)$-$CH{=}CHOBn$, **13**] and pinanediol [(benzyloxy)methyl]-boronate (**1a**). The NMR spectrum of **13** suggested the presence of only one geometric isomer. If the elimination is anti, it is the *Z* isomer. This is consistent with, though not proved by, the coupling constant of the vinylic protons, J = 12.8 Hz. The boronic ester product should be pinanediol chloromethylboronate, but reaction of this with the benzyl oxide formed in the elimination would produce **1a**.

Modest (36%) success was achieved with (chloromethyl)lithium and **9** without zinc chloride. The boronic ester **10b** was not purified but oxidized to 2,3,4,5-tetrabenzyl-L-ribitol (**11b**) with hydrogen peroxide and then to 2,3,4,5-tetrabenzyl-L-ribose (**11c**) by Swern's method[19] and finally hydrogenated over palladium to L-(+)-ribose (**12**). The conversion of **10b** to **12** was essentially quantitative.

Discussion

New carbohydrate syntheses can serve the following functions: (1) preparing specifically labeled sugars for testing biosynthetic pathways; (2) providing structure proofs and perhaps useful samples of new discovered exotic sugars; (3) demonstrating the general versatility of new methods of chiral synthesis.

The synthesis of L-ribose is a severe test of the method of chiral synthesis via boronic esters and appears to have pushed the sequential assembly of (benzyloxy)methylene groups to the limit. There is no apparent reason except cumulative steric bulk for the difficulty of introducing the fifth carbon in the sequence. The bulk is no doubt increased by the complexation of the zinc chloride catalyst to the benzyloxy groups. The β-elimination of boron and oxygen, which is not a significant side reaction with the lower homologues, suddenly becomes an overwhelming side reaction at the introduction of the fifth carbon.

Our synthesis of ribose has bypassed easier targets such as glyceraldehyde, erythrose, or deoxyribose. Our results suggest that the synthetic method is likely to provide efficient syntheses of such compounds, which could be useful for preparing samples labeled with carbon isotopes in any desired combination of specific positions. In this regard, the use of dihalomethanes as the source of each carbon is a useful feature.

Although the 13% overall yield of ribose from **1a** is disappointing, good total syntheses of carbohydrates are not common. The Masamune–Sharpless method produced arabinitol pentaacetate in 49% yield from glyceraldehyde acetonide,[20] but this starting material was derived from mannitol. For certain isotopic label patterns, our synthesis might provide a labeled segment such as the glyceraldehyde, and the Masamune–Sharpless method could be used to elaborate this to a more complex sugar.

Experimental Section

General Data. Reactions involving air-sensitive reagents were run under argon. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl. Zinc chloride was vacuum dried at 100 °C (0.1 Torr). Dimethyl sulfoxide was either Aldrich Gold Label or was dried over calcium hydride and distilled. (*s*)-Pinanediol[1-3] was prepared from (+)-α-pinene of 99% ee purchased from Aldrich Chemical Co., or purified potassium pinanediol borate[3] was used. If not otherwise noted, techniques were similar to those described previously.[3] Instruments used included a Nicolet NT-200 high-field NMR spectrometer, a JEOL FX-90Q NMR spectrometer, a VG Instruments 7070 EHF mass spectrometer, and a Jasco DIP-181 digital polarimeter. Rotations at

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(20) Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373–1378.

25 °C were thermostated to 25.0 ± 0.1 °C; others were at room temperature. Melting points were taken in capillary tubes in a Thomas-Hoover apparatus and are uncorrected. Microanalyses were by Galbraith Laboratories, Knoxville, TN.

(*s*)-Pinanediol (Chloromethyl)boronate. A solution of 48.3 g of diisopropyl (chloromethyl)boronate[11] and 46.1 g of (*s*)-pinanediol[1,3] in 200 mL of ether was stirred overnight. After concentration, the product was chromatographed on a short column and distilled: bp 95–100 °C (0.2 Torr); 95%; 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.849 (s, 3, pinyl CH_3), 1.157 (d, 1, J = 10.9 Hz, pinyl C*H*), 1.299 (s, 3, pinyl CH_3), 1.432 (s, 3, pinyl CH_3), 1.69–2.36 (m, 5, pinyl C*H*), 3.013 (s, 2, BCH_2Cl), 4.379 (dd, 1, J = 1.8, 8.6 Hz, pinyl C*H*OB); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 23.0 (br, B*C*), 23.95, 26.36, 26.99, 28.42, 35.16, 38.18, 39.34, 51.10, 78.66, 87.03; $[\alpha]^{25}_{546}$ +49.23° (*c* 1.7, toluene). Anal. Calcd for $C_{11}H_{18}BClO_2$: C, 57.81; H, 7.94; B, 4.73; Cl, 15.51. Found: C, 57.41; H, 7.97; B, 4.60; Cl, 16.01.

(*s*)-Pinanediol [(Benzyloxy)methyl]boronate (1a). A solution of 90 mmol of lithium benzyl oxide was prepared from 9.2 mL of benzyl alcohol in 100 mL of THF at −78 °C by addition of 56 mL of 1.6 M butyllithium in hexane, and 7 g (90 mmol) of DMSO[3] was added. This solution was added to 16.38 g (71.7 mmol) of (*s*)-pinanediol (chloromethyl)boronate in 60 mL of THF stirred at −78 °C. The mixture was allowed to warm to room temperature and then heated at 45–50 °C for 3 h, at which time TLC indicated that the reaction was complete. The mixture was worked up with aqueous 0.5 M hydrochloric acid, and the product was extracted into ether. The ether, dimethyl sulfoxide, and benzyl alcohol were removed by vacuum distillation, and the residue was charomatographed on silica with 10% ethyl acetate in hexane. The (*s*)-pinanediol [(benzyloxy)methyl]boronate (**1a**) was distilled: bp 158–162 °C (0.2 Torr) [lit.[4] 138–140 °C (0.2 Torr)]; 19.77 g (92%), solidified on cooling mp 25–27 °C; 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.83 (s, 3, CCH_3), 1.15 (d, 1, J = 10.8 Hz, pinyl C*H*), 1.28 (s, 3, CCH_3), 1.41 (s, 3, CCH_3), 1.87–2.33 (m, 5, pinyl C*H*), 3.34 (s, 2, OCH_2B), 4.43 (dd, 1, J = 1.8, 8.6 Hz, pinyl C*H*OB), 4.52 (AB, 2, PhCH_2O), 7.25–7.37 (m, 5, C_6H_5); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 23.96, 26.45, 27.03, 28.50, 35.15, 38.06, 39.40, 51.11, 57.0 (br, B*C*), 75.80, 78.14, 86.35, 127.50, 128.14, 128.21, 138.09; $[\alpha]^{25}_{546}$ +36.5° (*c* 1.7, toluene). Anal. Calcd for $C_{18}H_{25}BO_3$: C, 72.02; H, 8.39; B, 3.60. Found: C, 72.17; H, 8.07; B, 3.79.

(*s*)-Pinanediol (*tert*-Butoxymethyl)boronate (1b). (*tert*-Butoxymethyl)lithium was prepared in methyl *tert*-butyl ether by the method of Corey and Eckrich.[9] Trimethyl borate (1 equiv) was added dropwise at −78 °C. The mixture was acidified and extracted with ether and 1-butanol to make dibutyl (*tert*-butoxymethyl)boronate: bp 63–66 °C (0.1 Torr); 15–30%. The butyl ester was mixed with 1 equiv of (*s*)-pinanediol and the product **1b** was chromatographed with 15% ether in hexane on silica; bp 92–98 °C (0.25 Torr); mp 38–40 °C; 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.83 (s, 3), 1.19 (s, 9), 1.29 (s, 3), 1.41 (s, 3) (CCH_3's), 1.14 (d, 1, partially obscured), 1.90–2.38 (m, 5) (pinyl C*H*'s), 3.26 (s, 2, OCH_2B), 4.34 (dd, J = 1.9, 9.1 Hz, 1, C*H*OB); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 23.99, 26.42, 26.97 (C(CH_3)$_3$), 27.05, 28.52, 35.15, 38.10, 39.42, 47.5 (br, B*C*), 51.18, 73.29, 78.08, 86.13; $[\alpha]^{25}_{546}$ +41.1° (*c* 1.5, toluene). Anal. Calcd for $C_{15}H_{27}BO_3$: C, 67.68; H, 10.22; B, 4.06. Found: C, 67.79; H, 9.93; B, 3.90.

(*s*)-Pinanediol (1*S*)-(2-*tert*-Butoxy-1-chloroethyl)boronate (3b). This compound was prepared by addition of **1b** to (dichloromethyl)lithium according to the previously described procedure,[3] except that 1.8 equiv of zinc chloride was used as catalyst; after chromatography: 83–88%; 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.84 (s, 3), 1.20 (s, 9), 1.29 (s, 3), 1.43 (s, 3) (CCH_3's), 1.284 (d, J = 10.8 Hz, 1, pinyl C*H*) [(1*R*) epimer, 1.299 (d, J = 10.8 Hz)], 1.86–2.42 (m, 5, pinyl C*H*), 3.540 (dd, J = 5.6, 7.0 Hz, 1, C*H*Cl) [(1*R*) epimer, 3.522 (dd, J = 5.8, 7.2 Hz, C*H*Cl)], 3.69 (m, 2, OCH_2CHCl), 4.36 (dd, J = 2.0, 8.8 Hz, 1, C*H*OB); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 23.93, 26.25 [(1*R*) epimer shifted, +0.04], 26.99, 27.46 (C(CH_3)$_3$), 28.41, 35.19, 38.10, 39.25, 51.06, 64.18 [(1*R*), −0.03], 73.19 [(1*R*), +0.07], 78.46 [(1*R*), −0.07], 86.66 [(1*R*), +0.12]; $[\alpha]^{25}_{546}$ +30.4° (*c* 1.5, toluene). Based on the ^{1}H NMR multiplets centered at δ 3.54 and 3.52, the (1*S*) to (1*R*) diastereomer ratio was 10:1, and from the ^{13}C NMR data at δ 86.7 and 86.8, the ratio was 8:1. Epimerization required 14 days with lithium chloride in aqueous THF to achieve a 2:1 (1*S*) to (1*R*) ratio. Anal. Calcd for $C_{16}H_{28}BClO_3$: C, 61.07; H, 8.97; B, 3.44; Cl, 11.27. Found: C, 61.27; H, 9.03; B, 3.64; Cl, 11.95.

(*s*)-Pinanediol (1*S*)-[2-(Benzyloxy)-1-chloroethyl]boronate (3b). This compound was prepared by the method reported previously,[4] but with 1.7 equiv of zinc chloride as rearrangement catalyst: 70–83%; ^{1}H NMR as reported;[4] 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 23.90, 26.17, 26.94, 28.34, 35.08, 38.09, 39.21, 41.5 (br, B*C*), 51.01, 71.91, 73.05, 78.56, 86.88 [(1*R*) epimer, +0.07], 127.51, 128.06, 128.21, 137.86; $[\alpha]^{25}_{546}$ +12.9° (*c* 1.1, toluene). The (1*S*)/(1*R*) diastereomer ratio was 9:1 as shown by the pair of peaks at δ 86.9–87.0 in the ^{13}C NMR, the only well-separated pair in the NMR spectra. The epimer mixture was prepared by treating **3b** with lithium chloride in aqueous THF for several days.

General Procedure for Reaction of (Dibromomethyl)-lithium with Benzyloxy Boronic Esters. A solution of 12 mmol of LDA was prepared by addition of 12 mmol of 1.6 M butyllithium in hexane to 15 mmol of diisopropylamine in approximately 15 mL of THF at 0 °C and then chilled to −78 °C. A solution of 10 mmol of the benzyloxy boronic ester and 60–100 mmol (10–17 g) of dibromomethane in 20 mL of THF was stirred at −78 °C during the dropwise addition of the LDA solution via cannula. The mixture darkened to orange-brown as a result of decomposition of some of the (dibromomethyl)lithium. The mixture was kept at −78 °C for 1 h. The solvent was distilled under high vacuum below 0 °C, leaving a solid residue of boronate salt. The flask was returned to a −78 °C bath. An 0.5–0.7 M solution of anhydrous zinc chloride in THF was added from a syringe. The quantity used depended on the number of benzyloxy groups in the boronic ester, 10 mmol for each benzyloxy group plus 6–8 mmol more for the 10-mmol scale described. The mixture was stirred and allowed to warm to room temperature overnight, during which time the solid borate salt dissolved. The mixture was worked up by addition of an equal volume of light petroleum ether (bp 30–60 °C) followed by 100 mL of saturated aqueous ammonium chloride. After separation, the aqueous phase was extracted with two portions of 20% diethyl ether in light petroleum ether, the combined organic phase was filtered through a 5-cm column of magnesium sulfate with the aid of additional solvent, and the solution was concentrated. If stable on silica, the α-bromo boronic ester was purified by flash chromatography, but if not, it was used directly in the next step.

General Procedure for Reaction of Lithium Benzyl Oxide with α-Bromo Boronic Esters. A solution of 13 mmol of benzyl alcohol in 10–15 mL of THF with a crystal of 1,10-phenanthroline as indicator was cooled to −78 °C, and a solution of 1.6 M butyllithium in hexane was added to the endpoint. A drop of benzyl alcohol was added to fade the indicator, followed by 10 mmol of anhydrous dimethyl sulfoxide,[3] which solidifed. A solution of 10 mmol of the α-bromo boronic ester in 10 mL of THF was added from a syringe. After the mixture warmed to room temperature overnight, it was stirred for 1–2 h at 40–45 °C and checked for completion by TLC. The mixture was worked up with 0.5 M hydrochloric acid and ether extraction. The solvents were removed under vacuum, and for runs on a scale of 30 mmol or more, the residue was heated with a 40–50 °C bath under vacuum to remove the DMSO and residual benzyl alcohol. The benzyloxy boronic ester product was purified by flash chromatography on silica.

(*s*)-Pinanediol (1*S*)-[2-(Benzyloxy)-1-bromoethyl]boronate (4). The general procedure was followed with 10.91 g (36.3 mmol) of (*s*)-pinanediol [(benzyloxy)methyl]boronate (**1a**). The solution of product **4** was passed through a 25-cm column of magnesium sulfate, and the crude product, which contained 6% of starting material **1a** by NMR analysis, was used directly in the next step. An analytical sample was chromatographed with considerable loss. **4**: 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.84 (s, 3, CH_3), 1.26 (d, 1, partly obscured, pinyl C*H*), 1.29 (s, 3, CH_3), 1.41 (s, 3, CH_3), 1.83–2.43 (m, 5, pinyl C*H*), [3.519, (1*R*) epimer, t, J = 7.3 Hz, 0.03, OCH$_2$C*H*Br], 3.528 (m, J = 6.7, 7.7 Hz, 1, OCH$_2$C*H*Br), 3.836 (m, 2, OCH_2CHBr), 4.36 (dd, J = 1.9, 8.7 Hz, 1, C*H*OB), 4.60 (s, 2, PhCH_2O), 7.26–7.36 (m, 5, C_6H_5); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 23.94, 26.19, 26.98, 28.33, 29.5 (br, B*C*), 35.17, 38.24, 39.26, 51.18, 71.44, 73.03, 78.53, 86.71, [86.79, 1(*R*) epimer], 127.58, 128.28, 137.94; $[\alpha]^{25}_{546}$ +41.1° (*c* 2.7, toluene). The 1-(*S*)/1(*R*) epimer ratio calculated from the ^{13}C NMR data was 35:1, confirmed by measurement in the presence of chromium(III) acetylacetonate to remove any T_1 or NOE differences. Anal. Calcd for $C_{19}H_{26}BBrO_3$: C, 58.05; H, 6.67; B, 2.75; Br, 20.33. Found:

C, 57.97; H, 6.74; B, 2.75; Br, 20.39.

Mixed (1*S*),(1*R*) Epimers of (*s*)-Pinanediol [2-(Benzyloxy)-1-bromoethyl]boronate (4 and Epimer). Pinacol [(benzyloxy)methyl]boronate was treated with dibromomethane and LDA according to the general procedure, and the resulting pinacol ester was transesterified with pinanediol[3] to yield the epimer mixture. The 200-MHz ^{1}H NMR spectrum was similar to that of the (1*S*) isomer 4 except for the additional triplet at δ 3.519, J = 7.3 Hz, and an additional multiplet in the δ 3.84 region, with an incompletely resolved additional doublet near δ 1.26. The ^{13}C NMR showed pairs of peaks at δ 35.16–35.18, 71.41–71.46, 78.45–78.52, 86.72–86.80, and 137.90–137.92 and was otherwise similar to that of the (1*S*) epimer.

(*s*)-Pinanediol (1*R*)-[1,2-Bis(benzyloxy)ethyl]boronate (5). The crude (*s*)-pinanediol (1*S*)-[1-(benzyloxy)-2-bromoethyl]boronate (4; 36 mmol) was treated with 48 mmol of lithium benzyl oxide according to the general procedure. Flash chromatography with 7% ethyl acetate/hexane yielded 12.4 g of 5 containing 6% (benzyloxy)methylboronate (1a), yield corrected for impurity, 82%. The analytical sample was rechromatographed, and the (1*S*) epimer was depleted in the earlier fractions of 5: 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.83 (s, 3, CH_3), 1.23 (d, 1, pinyl CH), 1.28 (s, 3, CH_3), 1.39 (s, 3, CH_3), 1.86–2.42 (m, 5, pinyl CH), 3.596 (dd, J = 3.2, 5.2 Hz, 1, OCH$_2$CHB), [(1*S*) epimer, 3.579, dd, J = 3.3, 5.0 Hz, not detected], 3.77 (m, 2, OCH_2CHB), 4.33 (dd, 1, CHOB), 4.57 (m, 2, PhCH_2O), 4.66 (s, 2, PhCH_2O), 7.24–7.39 (m, 10, Ph); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 23.94, 26.22, 27.00, 28.57, 35.14, 38.02, 39.36, 51.07, 68.5 (br, B*C*), 71.33, [(1*S*) epimer, 71.50, not detected], 72.44, 73.07, 78.18, 86.40, 127.20, 127.46, 127.71, 128.09, 138.45, 138.86; $[\alpha]^{25}_{546}$ +12.4° (*c* 0.7, toluene). Anal. Calcd for $C_{26}H_{33}BO_4$: C, 74.29; H, 7.91; B, 2.57. Found: C, 74.09; H, 7.91; B, 2.55.

Mixed Epimers, (*s*)-Pinanediol (1*R*)/(1*S*)-[1,2-Bis(benzyloxy)ethyl]boronate (5 and Epimer). The epimer mixture of (*s*)-pinanediol (1*S*)/(1*R*)-[2-(benzyloxy)-1-bromoethyl]boronate was treated with lithium benzyl oxide in the usual manner. The mixture showed additional peaks in the ^{1}H NMR at δ 3.579 (dd, J = 3.3, 5.0 Hz, 1, OCH$_2$CHB), 4.57 (second AB pattern superimposed), 4.66 (br s); in the ^{13}C NMR, well-separated additional peaks at δ 26.40, 35.28, 71.50, slightly separated at 28.55, 37.99, 39.35, 51.01, 72.53, 73.12, 78.14, 86.46, 127.21, 127.48, 127.57, 127.73, 128.10, 138.45, 138.87, coincident at 23.95, 27.01.

(*s*)-Pinanediol (1*S*,2*S*)-[2,3-Bis(benzyloxy)-1-bromopropyl]boronate (6). Reaction of 10.93 g (24.4 mmol contained) of 94% (*s*)-pinanediol (1*R*)-[1,2-bis(benzyloxy)ethyl]boronate (5 containing 6% 1a) with dibromomethane and LDA by the general procedure followed by flash chromatography with 5% ethyl acetate/hexane yielded 11.06 g (88%) of 6 (free from 4, which appears unstable to chromatography): 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.81 (s, 3), 1.27 (s, 3), 1.29 (s, 3) (pinyl CH_3's), 1.30 (d, half obscured, pinyl CH), 1.82–2.33 (m, 5, pinyl CH), 3.59 (m, 3, CHOC, CHBr), 3.96 (m, 1, CHOC), 4.29 (dd, J = 1.8, 8.7 Hz, 1, CHOB), 4.51 (m, 2, PhCH_2O), 4.70 (m, 2, PhCH_2O), 7.23–7.40 (m, 10, C_6H_5); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 23.96, 26.06, 26.98, 28.13, 35.15, 38.28, 39.25, 51.24, 70.80, 73.72, 73.31, 78.68, 86.47, 127.60, 127.84, 128.21, 128.30, 137.78, 138.18; $[\alpha]^{25}_{546}$ +20.9° (*c* 2.1, $CHCl_3$). Anal. Calcd for $C_{27}H_{34}BBrO_4$: C, 63.18; H, 6.68; B, 2.11; Br, 15.57. Found: C, 63.42; H, 6.86; B, 2.25; Br, 15.25.

(*s*)-Pinanediol (1*R*,2*S*)-[1,2,3-Tris(benzyloxy)propyl]boronate (7). Treatment of 3.61 g (7.06 mmol) of (*s*)-pinanediol (1*S*,2*S*)-[2,3-bis(benzyloxy)-1-bromopropyl]boronate (6) with 8.0 mmol of lithium benzyl oxide according to the general procedure followed by flash chromatography with 10% diethyl ether in light petroleum ether yielded 3.38 g (89%) of 7: 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.81 (s, 3, CH_3), 1.22 (d, J = 10.3 Hz, 1, pinyl CH), 1.26 (s, 3, CH_3), 1.31 (s, 3, CH_3), 1.77–2.4 (m, 5, pinyl CH), 3.68 (m, 3, CHOC), 3.98 (dt, J = 2.8, 6.0 Hz, 1, CHOC), 4.28 (dd, J = 1.85, 8.7 Hz, 1, CHOB), 4.53 (s, 2, PhCH_2O), 4.66 (s, 2, PhCH_2O), 4.69 (m, PhCH_2O), 7.23–7.37 (m, 15, C_6H_5); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 23.99, 26.22, 27.03, 28.47, 35.22, 38.07, 39.42, 51.10, 69.82, 71.98, 72.80, 73.12, 78.11, 80.03, 86.30, 127.16, 127.19, 127.35, 127.48, 127.54, 127.71, 128.06, 128.12, 128.19, 138.37, 138.81, 138.94; $[\alpha]^{25}_{546}$ +16.2° (*c* 1.1, $CHCl_3$). Anal. Calcd for $C_{34}H_{41}BO_5$: C, 75.55; H, 7.65; B, 2.00. Found: C, 75.43; H, 7.58; B, 1.91.

(*s*)-Pinanediol (1*S*,2*S*,3*S*)-[1-Bromo-2,3,4-tris(benzyloxy)butyl]boronate (8). Reaction of 5.65 g (10.45 mmol) of (*s*)-pinanediol (1*R*,2*S*)-[1,2,3-tris(benzyloxy)propyl]boronate (7) with dibromomethane and LDA followed the general procedure, except that the mixture was heated to 35 °C for 1 h before workup. Repeated flash chromatography with 6% ethyl acetate/hexane yielded 0.43 g (7%) of unchanged 7 and 4.68 g (70%) of 8: 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.81 (s, 3), 1.27 (s, 3), 1.29 (s, 3) (pinyl CH_3's), 1.37 (d, J = 10.8 Hz, 1, pinyl CH), 1.79–2.40 (m, 5, pinyl CH), 3.67 (m, 3, CHOC), 3.73 (d, J = 8.0 Hz, 1, CHBr), 4.04 (dd, J = 6.35, 8.0 Hz, 1, CHOC), 4.31 (dd, J = 1.9, 8.7 Hz, 1, CHOB), 4.50 (m, 2, PhCH_2O), 4.67 (m, 2, PhCH_2O), 4.71 (m, 2, PhCH_2O), 7.23–7.39 (m, 15, C_6H_5); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 23.93, 26.01, 26.95, 28.09, 35.07, 38.25, 39.20, 51.23, 68.58, 71.94, 73.16, 74.38, 78.16, 79.09, 79.28, 86.37, 127.48, 127.61, 127.67, 127.83, 128.08, 128.14, 128.24, 128.45, 128.59, 128.65, 128.90, 137.80, 138.04, 138.22; $[\alpha]^{25}_{546}$ +15.2° (*c* 0.2, toluene). Analytical results were unsatisfactory. Anal. Calcd for $C_{35}H_{42}BBrO_5$: C, 66.37; H, 6.68; B, 1.71; Br, 12.62. Found (single sample): C, 67.11, 65.20; H, 7.10, 6.97; B, 2.75; Br, 11.78.

(*s*)-Pinanediol (1*R*,2*R*,3*S*)-[1,2,3,4-Tetrakis(benzyloxy)butyl]boronate (9). Treatment of 5.18 g (8.18 mmol) of (*s*)-pinanediol (1*S*,2*S*,3*S*)-[1-bromo-2,3,4-tris(benzyloxy)butyl]boronate (8) with lithium benzyl oxide according to the general procedure followed by flash chromatography with 9% diethyl ether/light petroleum ether yielded 4.49 g (83%) of 9: 200-MHz ^{1}H NMR ($CDCl_3$) δ 0.79 (s, 3), 1.25 (s, 3), 1.27 (s, 3) (pinyl CH_3'), 1.23 (d, partially obscured, pinyl CH), 1.59–2.38 (m, 5, pinyl CH), 3.67–4.02 (m, 5, CHOC), 4.25 (dd, J = 1.8, 9.1, CHOB), 4.49 (m, 2), 4.66 (m, 2), 4.68 (s, 2), 4.69 (s, 2) (4 PhCH_2O's), 7.21–7.35 (m, 20, C_6H_5); 50.3-MHz ^{13}C NMR ($CDCl_3$) δ 23.99, 26.13, 27.05, 28.43, 35.15, 38.08, 39.43, 51.18, 68.7 (br, B*C*), 70.12, 72.42, 72.58, 72.61, 73.23, 78.02, 80.61, 86.21, 127.11, 127.16, 127.31, 127.60, 127.66, 127.69, 127.82, 128.01, 128.04, 128.13, 128.18, 138.55, 138.70, 138.86, 139.07; $[\alpha]^{25}_{546}$ −5.2° (*c* 0.7, toluene). Although the 200-MHz NMR spectrum showed no evidence of impurity, the analysis was unsatisfactory. Anal. Calcd for $C_{42}H_{49}BO_6$: C, 76.36; H, 7.48; B, 1.64. Found: C, 73.90; H, 7.60; B, 1.92.

L-(+)-Ribose (12). A. Via (Dichloromethyl)lithium. Addition of 1.17 g (1.78 mmol) of (1*R*,2*R*,3*S*)-[1,2,3,4-tetrakis(benzyloxy)butyl]boronate (9) to 2.4 mmol of (dichloromethyl)lithium in the usual manner[3] was followed by addition of 8.5 mmol of zinc chloride as a 1 M solution in diethyl ether. After 24 h at room temperature, the mixture was worked up with saturated ammonium chloride and light petroleum ether. After concentration, the residue (1.22 g) was oxidized with excess hydrogen peroxide in borate-buffered aqueous THF. Chromatography on a silica plate with 30% ethyl acetate in hexane yielded two major fractions, R_f 0.46, from which the NMR spectrum appeared to contain the pinanediol unit, and R_f 0.26, which lacked pinyl absorptions: IR 3420 cm^{-1} (OH); 200-MHz ^{1}H NMR ($CDCl_3$) δ 3.455 (m) 3.5–3.9 (m's), 3.97 (m), 4.2–4.6 (m's), 4.634 (s), 4.637 (m, AB), 4.644 (s), 5.31 (m, 1, OCHOH?), 7.29 (m, 20, C_6H_5), apparently a hydrogen peroxide adduct[18] of 2,3,4,5-tetrabenzylribose (11a). This impure material was hydrogenated over 100 mg of 10% palladium on charcoal in 10 mL of 95% ethanol for 24 h. Filtration and concentration yielded 55 mg of crude ribose (12): mp 85–91 °C, recrystallized from ethanol, 38 mg (14% from 9), mp 86–87 °C, mixture up (with authentic sample purchased from Aldrich) 85–87 °C; $[\alpha]^{25}_D$ +18.3° (*c* 1.8, H_2O) (lit.[21] and Aldrich data, +19°); 200-MHz ^{1}H NMR (D_2O) identical with that of purchased sample.

B. Via (Chloromethyl)lithium. A solution of 0.75 g (1.14 mmol) of 9 and 1 mL of chloroiodomethane in 30 mL of THF was treated with 1.6 mmol of butyllithium at −78 °C in the usual manner.[11] The product was a complex mixture and was oxidized with hydrogen peroxide in borate-buffered aqueous THF. Flash chromatography yielded 0.21 g (36%) of slightly impure oily 2,3,4,5-tetrabenzylribitol (11b): 200-MHz ^{1}H NMR ($CDCl_3$) δ 1.26 (1–2, impurity), 2.37 (br s, 1, OH), 3.65–3.75 (m, 5, CHO), 3.8–4.0 (m, 2, CHO), 4.486 (s, 2), 4.554 (s, 2), [4.63 (s, 0.3, impurity)] 4.67 and 4.68 (AB m's, 4) (4 PhCH_2O's)8 7.29 (m, 20, C_6H_5). An 80-mg portion of this material was oxidized under Swern conditions[19] to produce 2,3,4,5-tetrabenzylribose (11c), which was not purified: 200-MHz ^{1}H NMR (C_6D_6) δ 3.5–4.2 (m, 5, CHOC), 4.2–4.8 (m,

(21) Buckingham, J., Ed. *Dictionary of Organic Compounds*, 5th ed.; Chapman and Hall: New York, 1982; Vol. 5, p 4921.

8, PhCH_2O), 7.0-7.37 (m, 20, C_6H_5), 9.61 (d, J = 0.8 Hz, 1, CHO), with impurities at δ 1-2, 5.07; 22.6 MHz ^{13}C NMR (C_6D_6) δ 69.8, 72.8, 72.9, 73.2, 73.5, 77.6, 81.2, 83.1, 126.9, 127.7, 127.8, 128.1, 128.5, 129.1, 138.3, 138.6, 138.9, 139.0, 200.2; IR 1726 cm^{-1} (C=O). Hydrogenation of this material over 100 mg of 10% palladium on charcoal in ethanol for 24 h, filtration, concentration, and recrystallization from ethanol yielded 28 mg (97% based on **11b**) of L-ribose (**12**): mp and mixture mp (with sample purchased from Aldrich) 85-86 °C; $[\alpha]^{23}_D$ +18.6° (c 0.6, H_2O) (lit.[21] +18.8° for L, -19.5° for D); 200-MHz ^{1}H NMR (D_2O) δ 3.5-4.2 (m), identical with that of an Aldrich sample.

(3*R*)-1,3,4-Tris(benzyloxy)-1-butene (13). Reaction of 1.61 g (2.44 mmol) of (*s*)-pinanediol (1*R*,2*R*,3*S*)-[1,2,3,4-tetrakis(benzyloxy)butyl]boronate (**9**) with chloroiodomethane and butyllithium in the usual manner[11] was followed 3.5 h later by addition of 6.1 mmol of zinc chloride in diethyl ether. After overnight at room temperature and workup with saturated ammonium chloride and ether, the mixture of products (1.59 g) was separated by flash chromatography with 10% diethyl ether in light petroleum ether; TLC with 20% diethyl ether/light petroleum ether; R_f 0.42 and R_f 0.28. The latter was identified as pinanediol [(benzyloxy)methyl]boronate (**1a**) by ^{1}H NMR. The more mobile fraction, 0.76 g (83%), was **13**: mp 28-30 °C; 200-MHz ^{1}H NMR ($CDCl_3$) δ 3.56 (m, 2, COCH_2CH), 3.93 (m, 1, CH_2CHOC), 4.56 (m, 2, PhCH_2O), 4.57 (m, 2, PhCH_2O), 4.75 (s, 2, PhCH_2O), 4.82 (dd, J = 9.1, 12.8 Hz, 1, CCH=CHOC), 6.53 (d, J = 12.8 Hz, 1, CH=CHOC), 7.19-7.48 (m, 15, C_6H_5); 22.6-MHz ^{13}C NMR ($CDCl_3$) δ 69.4, 71.1, 73.2, 73.8, 76.3, 102.0, 127.3, 127.5, 127.6, 127.9, 128.2, 128.4, 136.6, 138.4, 138.7, 150.0. Analytical purity was not achieved. Anal. Calcd for $C_{25}H_{26}O_3$: C, 80.18; H, 7.00. Found: C, 78.93; H, 6.94.

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Conversion of α-Halo Boronic Esters to Inverted α-(Methylsulfonyl)oxy Boronic Esters

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The conversion of a pinanediol (α*S*)-α-halo boronic ester (**1**) via an (α*R*)-α-(methoxybenzyl)oxy boronic ester (**2a,b**) to an (α*R*)-α-hydroxy boronic ester (**3**) and then to the (α*R*)-methanesulfonate (**4**) followed by displacement of the methanesulfonate by lithium benzyl oxide yields the (α*S*)-α-benzyloxy boronic ester (**5**), the product of two inversions at the α-carbon atom. This work establishes that methoxylated benzyl groups can be deprotected oxidatively in the presence of the boronic ester function. The double inversion allows assembly of adjacent chiral centers, with one of them having its absolute configuration opposite to that directed by the pinanediol boronic ester group. These results also provide unequivocal direct proof of inversion in nucleophilic displacement at the α-carbon of a boronic ester.

The first demonstration of the potential utility of chiral synthesis with α-chloro boronic esters featured the controlled construction of (2*S*,3*S*)-3-phenyl-2-butanol and its diastereomer (2*S*,3*R*)-3-phenyl-2-butanol.[1] The first diastereomer was the natural result of two sequential homologations of (*s*)-pinanediol phenylboronate with subsequent simple manipulations. The second diastereomer was reached by cleaving the (*s*)-pinanediol after the first homologation and replacing it by its enantiomer (*r*)-pinanediol to direct the second homologation in the opposite sense. Unfortunately, the conditions required for the pinanediol cleavage, treatment with boron trichloride, are incompatible with any sensitive functionality.

Where only pairs of chiral centers are involved, it is often possible to choose the sequence of introduction of groups and the chirality of the pinanediol at the outset so that the ultimate product will be any desired one of the four possibilities.[2] Alternatively, (*R*,*R*)-2,3-butanediol has been shown to be a good chiral directing group that can be cleaved rapidly by water at room temperature,[3] though it has not actually been used to assemble two chiral centers.

None of the foregoing approaches can be used with [(benzyloxy)alkyl]boronic esters. Boron trichloride cleaves benzyloxy groups under the required conditions,[4] the chloromethylene group cannot be inserted into a carbon-oxygen bond,[5] and (*R*,*R*)-2,3-butanediol has failed to produce a useful diastereomeric excess in the reaction of its [(benzyloxy)methyl]boronate ester with (dichloromethyl)lithium.[6]

The recent report that (methoxybenzyl)oxy protecting groups can be cleaved with dichlorodicyanoquinone (DDQ) to yield alcohols, even in the presence of benzyloxy groups,[7] led us to investigate the compatibility of this differential hydroxyl protection system with boronic ester chemistry. One reason for choosing this system was that the reactions of pinanediol α-halo boronic esters with lithium benzyl oxide were already well established to occur without significant side reactions.[2,8] Displacement of the α-halide involves formation of an intermediate tetrahedral borate complex, and there is always a chance that competing oxide migrations will yield a mixture of products.[9]

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