# Enantioselective Capture and Retroracemization of (1-Bromoalkyl)boronic Esters by an *N*-Propanoyloxazolidinone Enolate and Iodide Ion

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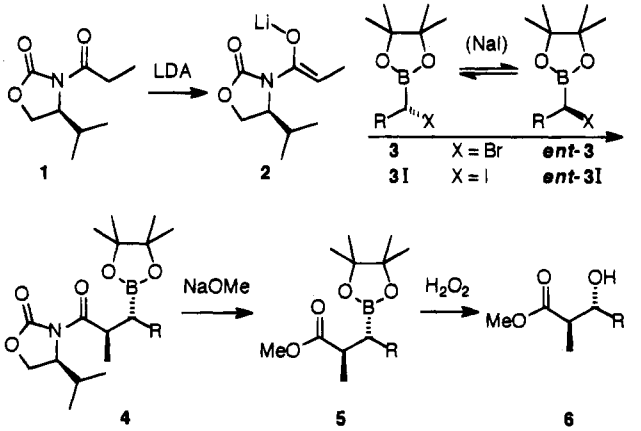
Lithium enolates of *N*-propanoyloxazolidinones react with (1-bromoethyl)boronic esters to form predominantly *threo*-2-methyl-3-borylbutanoic acid derivatives. The reaction of enantiomerically pure oxazolidinone enolate **2** with excess racemic (1-bromoethyl)boronic ester *rac*-**3a** produced a single isolable product **4a** in high diastereomeric and enantiomeric purity. Iodide catalysis resulted in racemization of any excess of *ent*-**3a** back to *rac*-**3a** so that both enantiomers were utilized via **3a** (hence, "retroracemization") in the presence of 1 equiv of **2** to produce **4a**, again in high purity and yield. The (1-bromopentyl)boronic ester *rac*-**3b** underwent similar retroracemization, though less efficiently. (Haloalkyl)boronic esters of much higher or lower reactivity did not undergo useful retroracemization. In an attempt to direct the reaction to produce *erythro* isomer, **2** was paired with (1-bromoethyl)boronic ester **10**, but the predominant product remained the *threo* isomer. The enantiomeric composition of this *threo* product was subsequently called into question by the observation that (1-bromopentyl)boronic ester **13** epimerizes readily to **14** and that both **13** and **14** react equally efficiently with the lithium enolate of *tert*-butyl propanoate. This result contrasts sharply to the previously reported grossly differing behaviors of diastereomeric pairs of (1-chloroalkyl)boronic esters toward Grignard reagents and provides a warning that the previously reported reactions of (1-bromoalkyl)boronic esters with carboxylic ester enolates do not necessarily lead to good enantiomeric purities.

It has been reported previously that the lithium enolate of *tert*-butyl propanoate, which is known to have a *trans* relationship between the lithium alkoxide oxygen and the methyl group,[1] reacts with several (1-bromoalkyl)boronic esters to yield *threo*-2-methyl-3-borylalkanoic esters in good to excellent diastereomeric excess.[2] It was of interest to determine whether the easily generated lithium enolate of an *N*-propanoyloxazolidinone, which has the lithium alkoxide oxygen *cis* to the methyl group,[3] might yield the opposite *erythro*-2-methyl-3-borylalkanoyl derivative.

The present investigation has instead shown that *threo* products predominate. The most important finding is that a chiral oxazolidinone enolate provides excellent asymmetric control, allowing kinetic resolution of α-bromo boronic esters, or in favorable cases, iodide-catalyzed enantiomer equilibration resulting in complete utilization of a racemic boronic ester via one of its enantiomers, in effect a retroracemization, to produce a single product in high diastereomeric and enantiomeric purity.

## Results

For clarity and brevity, the later, more significant results are described first. (*S*)-4-(1-Methylethyl)-3-propanoyl-1,3,2-oxazolidinone (**1**) was converted to its lithium enolate **2** by the literature method.[4] Reaction with 2 equiv of racemic pinacol (1-bromoethyl)boronate [2-(1-bromoethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane] (*rac*-**3a**; = **3a** + *ent*-**3a**) resulted in formation of substituted oxazolidinone **4a**, which has two newly formed chiral centers, in high stereopurity. Clearly, (*S*)-α-bromo boronic ester **3a** reacts much faster than (*R*)-enantiomer *ent*-**3a** with **2**.




The stereochemical relationship was easily proved by acyl cleavage with sodium methoxide[5] to boron-substituted carboxylic ester **5a** (72% based on **1**) followed by deboronation with hydrogen peroxide to form the known (*R*)-(*R**,*R**)-2-methyl-3-hydroxybutanoic acid methyl ester (**6a**),[6] the (*R**,*R**) (*threo*) and (*R**,*S**) (*erythro*) isomers of which are readily distinguishable by $^{13}$C-NMR.[7] The *threo*/*erythro* ratio of **6a** prepared without purification of

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(1) Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066–1081.

(2) Matteson, D. S.; Michnick, T. J. *Organometallics* **1990**, *9*, 3171–3177.

(3) Evans, D. A.; Takacs, J. M.; McGee, L. R.; Ennis, M. D.; Mathre, D. J.; Bartroli, J. *Pure Appl. Chem.* **1981**, *55*, 1109.

(4) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127.

(5) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737.

(6) (a) Tai, A.; Imaida, M. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 1114–1117. (b) Gouzoules, F. H.; Whitney, R. A. *J. Org. Chem.* **1986**, *50*, 2026.

(7) Heathcock, C. H.; Pirrung, M. C.; Sohn, J. E. *J. Org. Chem.* **1979**, *44*, 4294–4299.

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**Table 1. Products from Reaction of α-Halo Boronic Esters *rac*-3 with Oxazolidinone Enolate 2 under Back Racemization Conditions**

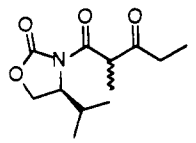
| compd | R | 4, % yield[a] | 5, % yield[a] | 6, *threo*/*erythro*[b] | % ee |
|---|---|---|---|---|---|
| *rac*-**3a** | $CH_3$ | 100[b] | 73[c] | 85:1 | 94[d] |
| *rac*-**3b** | $CH_3(CH_2)_3$ | 73[b] | 53[c] | 46:1 | 96.4[e] |
| *rac*-**3c** | $(CH_3)_2CH$ | 19[c] | | | |
| *rac*-**3cI** | $(CH_3)_2CH$ | 40[c] | | >500:1 | 96.4[e] |
| *rac*-**3d** | $C_6H_5$ | 50–65[f] | | | |

[a] Based on **1**. [b] Estimated by NMR. [c] Isolated yield. [d] By optical rotation of **6**. [e] By $^1H$ NMR with chiral shift reagent. [f] 50% **4d**, 50% diastereomer by NMR, 65:35 by GC.

any intermediates was ~55:1 based on peaks at δ 14.00 and 20.69 typical of the *threo* series and at δ 10.99 and 19.74 for the *erythro* isomer. After purification, the rotation indicated 98% ee (*R*)-(−)-**6a**.

Attempts to use only 1 mol of *rac*-**3a** gave ~50% conversion, and addition of lithium bromide led to unidentified byproducts. However, addition of a catalytic amount of sodium iodide and 18-crown-6 to aid the conversion of *ent*-**3a** to **3a** or iodide **3aI** resulted in a clean reaction, yielding 98% complete formation of **4a** by NMR analysis and 73% of purified methyl ester derivative **5a**. The apparent ee of the derived **6a** was 93–94% after correction for pinacol present in the partially purified small sample.

The high efficiency of the enantioselective capture with retroracemization of boronic ester **3a** prompted a brief investigation of its generality. As is indicated in Table 1, it was found feasible to use this process with the linear (1-bromopentyl)boronic ester **3b**. However, yields were lowered because of competing condensation of the enolate **2** with its precursor **1** to form β-keto amide **7**. The side

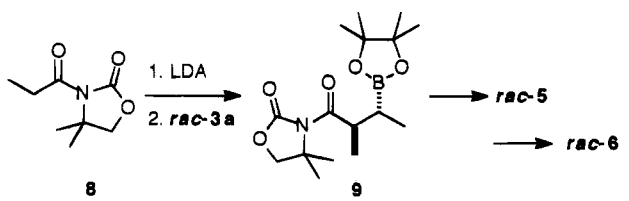


**7** (two diastereomers)

reaction to produce **7** made it impossible to achieve satisfactory yields of **4c** from the less reactive branched chain (1-bromo-2-methylpropyl)boronic ester **3c**. Recovered **3c**/**3cI** showed no optical rotation, as expected. Use of the corresponding iodide **3cI** resulted in a mediocre yield of **4c**, though with excellent stereoselectivity.

Finally, the much more reactive bromobenzylboronic ester **3d** showed little diastereoselectivity and was not investigated further.

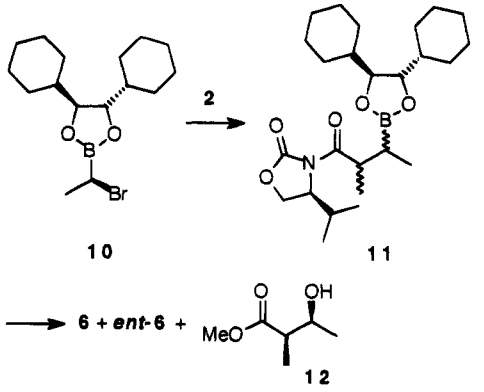
Prior to achieving the foregoing results, various reactions of α-halo boronic esters with oxazolidinone enolates were explored. Attempted reaction of the lithium enolate of unsubstituted *N*-propanoyloxazolidinone with (bromoethyl)boronic ester *rac*-**3a** was unpromising. However, the more sterically hindered enolate from 4,4-dimethyl-3-propanoyl-1,3,2-oxazolidinone (**8**) yielded the *threo* derivative **9**. The stereochemical relationship was easily




**8** **9**

proved by acyl cleavage with sodium methoxide[5] to the ester *rac*-**5a** followed by oxidation of the boronic ester group with hydrogen peroxide to form the known *erythro*- and *threo*-methyl 2-methyl-3-hydroxybutanoates (*threo* = *rac*-**6a**).[6,7] The 22.5-MHz $^{13}C$ NMR spectrum of ester *rac*-**6a** prepared without chromatography of any intermediates showed *threo* isomer peaks at δ 14.00 and 20.69 but no visible *erythro* isomer peaks at δ 10.99 and 19.74.

Although the natural preference for the reaction was thus established to be in favor of the *threo* isomer, the possibility of forcing reversal of the stereochemistry was tested. The enolate (**2**) from 4-(methylethyl)-3-propanoyl-1,3,2-oxazolidinone (**1**) is known to react with alkyl halides preferentially at the bottom face in the orientation illustrated.[5] When paired with {4*S*-[2(*S**),4α,5β]}-2-(1-bromoethyl)-4,5-dicyclohexyl-1,3,2-dioxaborolane (**10**), which must undergo inversion at the point of substitution, it was expected that the paired chiral directors should force formation of the *erythro* or *syn* product, which would ultimately yield hydroxy ester **12**. However,




**10** **11** **12**

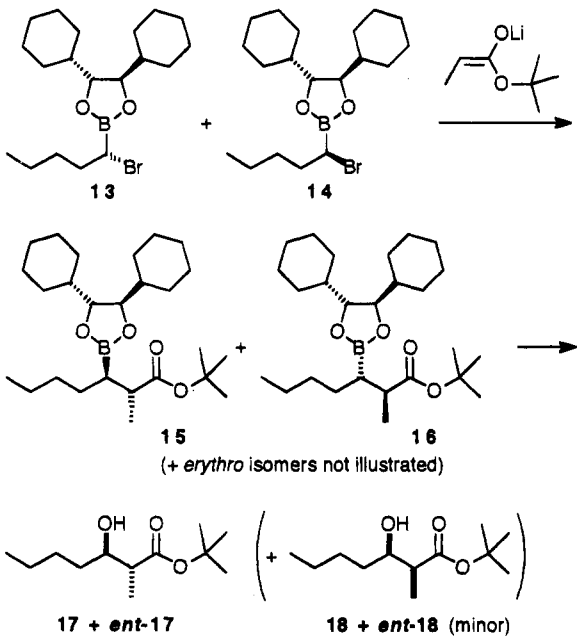
what was actually obtained was a mixture of *threo* isomer (**6a** + *ent*-**6a** in an unknown ratio) in a ~3:1 ratio to (**12** + *ent*-**12**) based on the 500-MHz $^1H$-NMR spectrum. Rotations were not measured in this exploratory work, leaving the absolute configurations of the **6a** and **12** unknown. However, the 125-MHz $^{13}C$-NMR spectrum of **11** showed no peaks above the noise level, ~5%, in excess of the number required by unchanged oxazolidinone **1** plus a single *erythro* and a single *threo* product **11**.

The stereoselectivity of the process was also briefly examined with achiral acyloxazolidinone enolate **8** and the (*S*)-bromoethylboronic ester *ent*-**10**. The results were disappointing, as the *threo*/*erythro* ratio was only 1.6:1 as indicated by the 500-MHz $^1H$-NMR spectrum. Since the diastereomeric ratio was so poor, no further investigation was made.

None of the products from **10** or *ent*-**10** were checked for enantiomeric purity or absolute configuration. During this exploratory phase of the work, it was presumed that the absolute configuration of **10** would determine the result, inasmuch as a number of α-bromo boronic esters of pinanediol were known to yield displacement products in excellent diastereomeric purity.[8,9] Furthermore, diastereomeric α-chloro boronic esters of a diol of $C_2$ symmetry have shown highly differentiated products and consequent sequential double diastereoselection in their reaction with a Grignard reagent.[10]

(8) Matteson, D. S.; Beedle, E. C. *Tetrahedron Lett.* **1987**, *28*, 4499–4502.
(9) Matteson, D. S.; Kandil, A. A.; Soundararajan, R. *J. Am. Chem. Soc.* **1990**, *112*, 3964–3969.
(10) Tripathy, P. B.; Matteson, D. S. *Synthesis* **1990**, 200–206.

The disquieting observation that this chemistry was not so simple was made after the acquisition of higher field NMR spectrometers. It became evident that a freshly prepared sample of {4*R*-[2(*S**),4α,5β]}-2-(1-bromopentyl)-4,5-dicyclohexyl-1,3,2-dioxaborolane was a ~3:1 mixture of 2(*S**)- (**13**) and 2(*R**)-epimers (**14**) and became a ~1:1 mixture after 6 days. The behavior of this 1:1 mixture was tested with the enolate from *tert*-butyl propanoate, which was more conveniently available than amide enolates **2** or **8**. The product was a ~50:50 mixture of two major diastereomers **15** and **16**. The $^1$H NMR spectrum showed two sets of major peaks at δ 2.4–2.6 ppm, one a doublet of quartets and one a pentuplet having equal intensity, and the $^{13}$C NMR also showed several paired peaks, the best separated appearing at δ (15.78 + 16.19) and (83.48 + 83.58). That both were *threo* was proved by peroxidic deboronation to the known (*R**,*R**)-2-methyl-3-hydroxyhexanoic acid *tert*-butyl ester (*threo* isomer) (**17** and *ent*-**17**),[2] which in the present experiment was obtained in a 12:1 ratio to its (*R**,*S**) [or *erythro* ] isomer (**18**). The *erythro* diastereomers of **15** and **16**, not illustrated, are the precursors of **18**.




## Discussion

This investigation has produced three significant discoveries: (1) The (*Z*)-enolates from oxazolidinones such as **1** or **8** react with 2-(1-haloalkyl)-1,3,2-dioxaborolanes (α-halo boronic esters) such as **3** or **10** to form predominantly *threo* (or *anti*) diastereomers **4** or **9**. (2) 2-(1-Halo-*n*-alkyl)-1,3,2-dioxaborolanes (*rac*-**3a,b**) can be equilibrated in the presence of an oxazolidinone enolate **2**, and one enantiomer reacts much faster than the other to yield one major product (**4a,b**) in high enantiomeric and diastereomeric purity. (3) Both diastereomers of a (4α,5β)-4,5-dialkyl-2-haloalkyl-1,3,2-dioxaborolane such as **10** or **13/14** react with enolates with approximately equal facility.

The high diastereofacial selectivity of the chiral oxazolidinone enolate **2** in displacement reactions with alkyl halides has already been well established,[5] and our results are in complete accord with this precedent.

Discovery 2, the interconversion of enantiomers **3a** and *ent*-**3a** in the presence of asymmetric enolate **2** with preferential consumption of **3a** to produce **4a** in high diastereomeric and enantiomeric purity, is synthetically more valuable than mere kinetic resolution, since it utilizes both enantiomers of the racemate to produce a new chiral center with a single absolute configuration. For lack of appropriate established terminology, we describe the process as "enantioselective capture with retroracemization." In a mechanistic sense, "enantioselective capture" is kinetic resolution, but here no net resolution of substrate occurs because the racemization reverses it. "Retroracemization" in one sense is an oxymoron, as racemization can only go one way. However, the net result of the combined process is as if racemization had been reversed, the term has some precedent,[11] and we believe its practical operational meaning is self-evident.[12]

Enantioselective capture with retroracemization has been observed previously in the reaction of a racemic Grignard reagent with an enantiomerically pure 2-alkoxy-1,3,2-dioxaborolane to form a boronic ester in 97% ee,[13] as well as in reactions of α-substituted benzylic lithium reagents with asymmetric carbonyl compounds.[14] Asymmetric catalytic capture of equilibrating Grignard reagents during coupling with alkenyl halides is an earlier example.[15] Hydrogenation of equilibrating enantiomers of β-keto esters over BINAP–ruthenium(II) complexes has yielded some examples of highly stereoselective production of a single stereoisomer.[16] The earliest example of retroracemization that has come to our attention is that of "trithymotide", the trimeric lactone of 2-hydroxy-3-isopropyl-6-methylbenzoic acid. The enantiomeric forms that result from restricted rotation equilibrate rapidly enough that the racemate can be crystallized to a single enantiomer corresponding to the seed crystal introduced.[17] Several processes described as "deracem-

(11) (a) Belokon, Yu. N.; Zel'tser, I. E.; Bakhmutov, V. I.; Saporovskaya, M. B.; Ryzhov, M. G.; Yanovskii, A. I.; Struchkov, Yu. T.; Belikov, V. M. *J. Am. Chem. Soc.* **1983**, *105*, 2010–2017. (b) Belokon, Yu. N.; Zel'tser, I. E.; Loim, N. M.; Tsyryapkin, V. A.; Aleksandrov, G. G.; Kursanov, D. N.; Parnes, Z. N.; Struchkov, Yu. T.; Belikov, V. M. *Tetrahedron* **1980**, *36*, 1089–1097. (c) Belokon, Yu. N.; Zel'tser, I. E.; Loim, N. M.; Tsiryapkin, V. A.; Parnes, Z. N.; Kursanov, D. N.; Belikov, V. M. *J. Chem. Soc., Chem. Commun.* **1979**, 789–790. "Retroracemization" was used in the sense of equilibration of enantiomers in the presence of an asymmetric complexing agent. Enantiomerically enriched material could be recovered from the complexes. The actual mechanism was probably epimerization, but the intent of the terminology was clear.

(12) Although ordinary racemization is the only kind that occurs, the overall direction and significance of the present process are not conveyed by the term. "Retro" is generally defined as a prefix meaning "back" or "backward". "Back racemization" suggests return to racemate, "backward racemization" the net direction of the total process. The precedents most closely related to the present work say only "racemization"[13] or, to avoid implying racemization detrimental to stereoselection, substitute the indefinite "enantiomerization".[14] The first catalytic example was described by "racemization" in context,[15] and the recent one was described as "dynamic kinetic resolution of chirally labile enantiomers", also shortened to "dynamic kinetic resolution", or alternatively, "kinetic resolution utilizing in situ racemization".[16] "Resolution" implies separation of enantiomers, but in all of these processes the racemic substrate remains continuously racemic, while the total process is twice as productive as resolution in quantity of asymmetric product and has an inherent advantage in stereoselectivity because the proportion of the faster reacting isomer does not diminish. The short phrase "dynamic kinetic resolution" implies something better than resolution, but is not self-explanatory.

(13) Stürmer, R *Angew. Chem.* **1990**, *102*, 62; *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 59.

(14) (a) Hoffmann, R. W.; Rühl, T.; Chemla, F.; Zahnheisen, T. *Liebigs Ann. Chem.* **1992**, 719–724. (b) Hoffmann, R. W.; Rühl, T.; Harbach, J. *Liebigs Ann. Chem.* **1992**, 725–730.

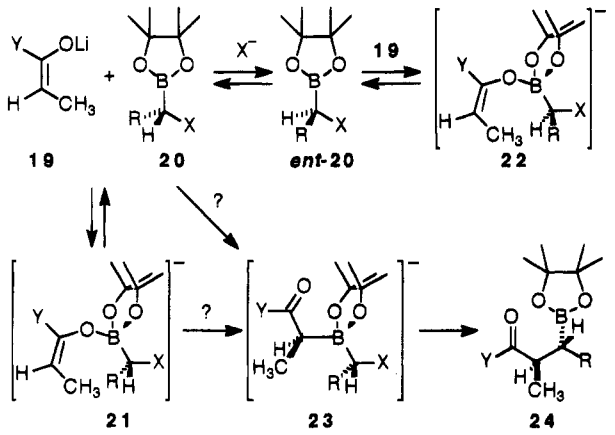
(15) Hayashi, T.; Konishi, M.; Fukushima, M.; Mise, T.; Kagotani, M.; Tajika, M. Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 180–186.

(16) Kitamura, M.; Tokunaga, M.; Noyori, R. *J. Am. Chem. Soc.* **1993**, *115*, 144–152.

ization"[18,19] are more distantly related. There is no systematic way to search for other examples, and it should not be assumed that this literature coverage is complete.[20]

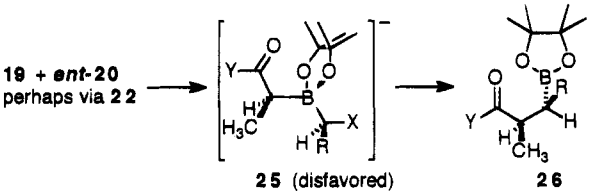
The major limitation on the utility of our retroracemization process is the instability of the enolate **2** under the reaction conditions. Although the concentration of the free amide **1** is presumably low, it is not possible to exclude all possible sources of protons, including possible hydrogen halide elimination from **3**, that might convert some **2** to **1**, and only a catalytic amount of **1** is required. Furthermore, possible borylated intermediates such as **23** may well act as surrogates for **1** in the aldol condensation. Yields of **4** have been optimized by operating at the lowest practical temperatures.

α-Halo boronic esters complex with the oxygen of lithium enolates, as shown by $^{11}$B-NMR.[21] In order for α-halo boronic esters **20** and *ent*-**20** to equilibrate, formation of their respective enol borate complexes **21** and **22** with **19** must be reversible, because the sterically hindered, neopentyl-like haloborate anions **21** and **22** cannot undergo boron assisted $S_N2$ halide exchange, a well-known process.[22-25]




The general mechanism for carbon–carbon bond formation in reactions of α-halo boronic esters involves a B–C bonded intermediate,[23-25] which would be **23** for the major reaction pathway and **25** for the disfavored reaction. Rearrangement of **23** via boron to carbon alkyl migration would yield the major observed product **24**. It is also conceivable that **24** is formed directly from **21** via a five-membered cyclic intermediate, with or without associated carbon–boron bonding and **23**-like character in the transition state, but there is no precedent or evidence for such a mechanism.

If **23** and **25** were formed reversibly and if there were free rotation about the C–C bond adjacent to the carbonyl group, the (*Z*)- and (*E*)-enolates would equilibrate. It seems unlikely that (*Z*)-enolate **2** and its (*E*)-isomer would both strongly favor the same stereoisomers of the products **4**, and the high stereopurities of **4** thus imply no *Z*/*E* equilibration. The generally high **24**/**26** product ratios are easier to understand on the basis of two competing transition states rather than four. The similarity of preference for **24** over **26** by both (*Z*)- and (*E*)-enolates remains unexplained, but suggests that the size of the carbonyl functionality rather than its orientation might be the governing factor. The generally high sensitivity of $S_N2$-type transition states to steric influences is a likely factor in the stereoselectivity, just as it probably is in the asymmetric synthesis of α-halo boronic esters via rearrangement of (dihalomethyl)borate anions.[23,24]




The unanticipated facile epimerization of **13** requires that the useful reaction of carboxylic ester enolates with α-bromo boronic esters[2] needs to be monitored carefully for this side reaction. Pinanediol α-bromo boronic esters do not usually epimerize readily, though some loss of diastereomeric purity in the presence of bromide ion has been encountered with unhindered examples in earlier work.[8] α-Chloro boronic esters would epimerize more slowly, but do not give good yields with carboxylic ester enolates.[2]

The failure of the reaction of *tert*-butyl propanoate enolate with diastereomeric α-bromo boronic esters **13** and **14** to show useful diastereodifferentiation contrasts sharply with the reactions of analogous α-chloro boronic esters with a Grignard reagent,[10] in which the minor diastereomer was destroyed by an expansion of the dioxaborolane ring. The reason for the difference is not obvious.

It has not been proved whether the slightly lower ee (93–94%) achieved with **6a** derived from equilibration of 1 equiv of **3a**, **3aI**, *ent*-**3a**, and *ent*-**3aI** compared with that (98%) from 2 mol of *rac*-**3a** is real or merely experimental error, though NMR data showed no evidence of an extra diastereomer at the 3% level in **4a** that could lead to that much *ent*-**6a**. It is clear that we have achieved a potentially useful highly stereoselective asymmetric synthesis of the β-hydroxy esters **6a** and **6b** and that the possibility of enantioselective capture with retroracemization merits consideration in the design of future synthetic processes.

## Experimental Section

**General.** Reactive carbanionic intermediates were protected from air and moisture, and tetrahydrofuran (THF) and zinc chloride were dried as described previously.[2,23] Lithium diisopropylamide (LDA) (1.8–2 M in cyclohexane as THF complex) and (*S*)-4-(methylethyl)-3-propanoyl-1,3,2-oxazolidinone (**1**) were purchased from Aldrich Chemical Co. (*R*,*R*)-1,2-Dicyclohexyl-1,2-ethanediol was prepared as described

(17) (a) Baker, W.; Gilbert, B.; Ollis, W. D. *J. Chem. Soc.* **1952**, 1443–1446. (b) Powell, H. M. *Nature* **1952**, *170*, 155.

(18) Naruse, Y.; Watanabe, H.; Inagaki, S. *Tetrahedron: Asymmetry* **1992**, *3*, 603–606. The reaction described is analogous to the original "retroracemization".[11]

(19) "Deracemization" describes processes in which a racemic compound is converted to an achiral intermediate, which is converted enantioselectively back to the original compound. For example, see: Duhamel, L.; Ravard, A.; Plaquevent, J. C.; Ple, G.; Davoust, D. *Bull. Soc. Chim. Fr.* **1990**, 787–797. Duhamel, L.; Plaquevent, J. C. *Tetrahedron Lett.* **1977**, 2285–2288.

(20) For information and suggestions for finding references, we thank Professors J. F. Bunnett (ref 17), E. Negishi (ref 15), B. K. Carpenter (ref 16), and M. P. Cooke (refs 11, 18, and 19).

(21) Whiting, A. *Tetrahedron Lett.* **1991**, *32*, 1503–1506.

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

(23) Matteson, D. S.; Sadhu, K. M.; Peterson, M. L. *J. Am. Chem. Soc.* **1986**, *108*, 812–819.

(24) Matteson, D. S. *Chem. Rev.* **1989**, *89*, 1535–1551.

(25) Matteson, D. S.; Mah, R. W. H. *J. Am. Chem. Soc.* **1963**, *85*, 2599–2603.

previously.[26] A Bruker 300 MHz NMR spectrometer was used to obtain 300-MHz $^1$H and 75-MHz $^{13}$C NMR spectra. Microanalyses were by Desert Analytics, Tucson, AZ.

**2-Alkyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolanes.** In a typical procedure, the known[23] 2,4,4,5,5-pentamethyl-1,3,2-dioxaborolane was prepared from pinacol (5 g, 43 mmol) and trimethylboroxine (1.8 g, 14.3 mmol) in ether (20 mL) stirred at room temperature for 18 h. More ether (100 mL) and water (50 mL) were added. The ether phase was washed with water (3 × 50 mL), dried over magnesium sulfate, and concentrated to yield a residue of the dioxaborolane (5.7 g, 95%), which was used without further purification: 300-MHz $^1$H-NMR ($CDCl_3$) $\delta$ 0.25 (br s, 3), 1.26 (s, 12); 75-MHz $^{13}$C-NMR ($CDCl_3$) $\delta$ 24.81, 82.94. Other known 2-alkyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolanes were similarly prepared from the corresponding boronic acids or their isopropyl esters with pinacol.[27]

**[*R*-(4α,5β)]-2-Methyl-4,5-dicyclohexyl-1,3,2-dioxaborolane.** A mixture of (*R*,*R*)-1,2-dicyclohexyl-1,2-ethanediol (5 g, 22 mmol) and trimethylboroxine (0.93 g, 7.4 mmol) in ether (20 mL) was stirred at room temperature for 18 h. To the mixture was added ether (100 mL) and water (50 mL). The organic layer was washed with water (3 × 50 mL) and dried over magnesium sulfate. Removal of solvent and vacuum distillation gave [*R*-(4α,5β)]-2-methyl-4,5-dicyclohexyl-1,3,2-dioxaborolane: 5.1 g, 93%; bp 93–95 °C (0.1 Torr); 200-MHz $^1$H-NMR ($CDCl_3$) $\delta$ 0.3 (s), 1.0–1.9 (m, 22), 3.8–4.0 (m, 2); 25-MHz $^{13}$C-NMR ($CDCl_3$) $\delta$ 26.2, 26.3, 26.8, 27.6, 28.7, 43.3, 83.6.

**[*S*-(4α,5β)]-2-Methyl-4,5-dicyclohexyl-1,3,2-dioxaborolane** was prepared from (*S*,*S*)-1,2-dicyclohexyl-1,2-ethanediol in the same manner as the *R*-isomer, same yield and NMR data.

**[*R*-(4α,5β)]-2-Butyl-4,5-dicyclohexyl-1,3,2-dioxaborolane.** A mixture of diisopropyl butylboronate (3.5 g, 17.3 mmol) and (1*R*,2*R*)-dicyclohexylethanediol (3.9 g, 17.2 mmol) in ether (100 mL) was stirred for 24 h. The solvent was removed under vacuum. Isolation by flash chromatography (silica gel, pentane) gave [*R*-(4α,5β)]-2-butyl-4,5-dicyclohexyl-1,3,2-dioxaborolane (4.93 g, 98%): 300-MHz $^1$H-NMR ($CDCl_3$) $\delta$ 0.81 (br t, $J$ = 7.4 Hz, 2), 0.89 (t, $J$ = 7.1 Hz, 3), 0.90–1.45, 1.55–1.82 (m, 26), 3.80–3.85 (m, 2); 75-MHz $^{13}$C-NMR (APT) ($CDCl_3$) $\delta$ 13.88 ($CH_3$), 25.46 ($CH_2$), 25.90 ($CH_2$), 26.03 ($CH_2$), 26.38 ($CH_2$), 26.46 ($CH_2$), 27.34 ($CH_2$), 28.31 ($CH_2$), 43.02 (CH), 83.17 (CH). Anal. Calcd for $C_{18}H_{33}BO_2$: C, 73.97; H, 11.38; B, 3.70. Found: C, 74.23; H, 11.32; B, 3.57.

**2-(1-Bromoethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (*rac*-3a). General Procedure for Formation of 3.** To a solution of 2,4,4,5,5-pentamethyl-1,3,2-dioxaborolane (5 g, 35.2 mmol) and dibromomethane (7.3 g, 42 mmol) in THF (200 mL) was added LDA (40 mmol) at −78 °C under argon followed by addition of anhydrous zinc chloride (9.57 g, 69.3 mmol). The solution was allowed to warm to room temperature overnight. The solvent was removed under vacuum. To the crude mixture was added pentane (300 mL) and aqueous saturated ammonium chloride (200 mL). The organic layer was washed with brine (100 mL), dried over magnesium sulfate, decolorized with charcoal, and filtered through a short pad of magnesium sulfate. Removal of solvent and vacuum distillation gave *rac*-**3a** (with 23 mol % of ethyl benzene, which is from the LDA): 7.65 g, 82%; bp 45 °C (1 Torr); 300-MHz $^1$H-NMR ($CDCl_3$) $\delta$ 1.28 (s, 12), 1.70 (d, $J$ = 7.5 Hz, 3), 3.44 (q, $J$ = 7.5 Hz, 1); 75-MHz $^{13}$C-NMR ($CDCl_3$) $\delta$ 20.52, 24.40, 24.46, 84.20.

**2-(1-Bromopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (*rac*-3b).** This compound was prepared by the general procedure described for preparation of *rac*-**3a** from 2-butyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (3.4 g, 18.5 mmol), LDA (22.1 mmol), dibromomethane (4.2 g, 24.2 mmol), and THF (50 mL), but without zinc chloride. After the usual workup, *rac*-**3b** was distilled: 4.4 g, 86%; bp 90 °C (2 Torr); 300-MHz $^1$H-NMR ($CDCl_3$) $\delta$ 0.91 (t, $J$ = 7.35 Hz, 3), 1.20–1.50 (m, 4), 1.28 (s, 12), 1.86–1.93 (m, 2), 3.31 (t, $J$ = 7.9 Hz, 1), in agreement with 200-MHz NMR data.[2]

**2-(1-Bromo-2-methyl-propyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (*rac*-3c).** This compound was prepared by the general procedure described for preparation of *rac*-**3a** from 2-(methylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5.18 g, 27.2 mmol), LDA (32 mmol), dibromomethane (8.04 g, 46.2 mmol), and THF (130 mL) but without zinc chloride to yield crude *rac*-**3c**. After workup and vacuum distillation, *rac*-**3a** was obtained: 6 g, 84%; bp 85 °C (2 Torr); 300-MHz $^1$H-NMR ($CDCl_3$) $\delta$ 1.03 (d, $J$ = 6.7 Hz, 3), 1.09 (d, $J$ = 6.6 Hz, 3), 1.28 (s, 12), 1.98–2.13 (m, 1), 3.14 (d, $J$ = 8.2 Hz, 1); 75-MHz $^{13}$C-NMR ($CDCl_3$) $\delta$ 21.05, 21.47, 24.34, 24.48, 31.51, 42 (br), 84.05; HRMS calcd for $C_{10}H_{20}BrBO_2$ ($M^+$) 262.0740, found 262.0757.

**{4*S*-[3(α*S**,β*S**),4α]}-3-(α,β,4,4,5,5-Hexamethyl-1,3,2-dioxaborolanepropanoyl)-4-(1-methylethyl)-1,3,2-oxazolidinone (4a). Method A: with 2 Equiv of *rac*-3a.** To a solution of LDA (4.9 mL, 2 M, 9.8 mmol) in THF (30 mL) was added a solution of (*S*)-4-(methylethyl)-3-propanoyl-1,3,2-oxazolidinone (**1**) (1.65 g, 8.9 mmol) in THF (5 mL) at −78 °C via cannula. After 40 min, crude 2-(1-bromoethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (*rac*-**3a**) (4.2 g, 17.8 mmol) in THF (5 mL) was added. After 2 h, the solution was moved to an ice–salt bath (−10 to −20 °C) and kept for 9 h. To the solution was added ether (250 mL) and saturated ammonium chloride (100 mL). The aqueous layer was extracted with ether (250 mL). The combined ether layer was washed with brine (100 mL) and dried over magnesium sulfate. Unchanged bromo boronic ester **3a** was distilled, bp 45 °C (1 Torr), followed by 3.19 g of a 1:10 mixture of **1** with **4a**, bp 130–150 °C (1 Torr) (100% based on **1**). The **4a** appeared to be a single isomer based on $^1$H and 75-MHz $^{13}$C-NMR. In order to determine the *threo*/*erythro* ratio, this material was used in the next step without further purification: 300-MHz $^1$H-NMR ($CDCl_3$) $\delta$ 0.89 (d, $J$ = 7.1 Hz, 3), 0.91 (d, $J$ = 7.2 Hz, 3), 0.96 (d, $J$ = 7.6 Hz, 3), 1.18 (d, $J$ = 7.0 Hz, 3), 1.22 (1s + 1m, 13), 2.40 (d of sept, $J = 3.7_d, 7.0_{sept}$ Hz, 1), 3.74 (p, $J$ = 7.0 Hz, 1), 4.17–4.28 (m, 2), 4.42 (dt, $J = 3.3_t, 8.0_d$ Hz, 1); 75-MHz $^{13}$C-NMR ($CDCl_3$) $\delta$ 11.96, 13.83, 15.77, 17.80, 20.2 (br), 24.41, 24.77, 28.04, 40.46, 58.50, 62.74, 82.92, 153.46, 177.55; HRMS calcd for $C_{17}H_{30}BO_5N$ ($M^+$) 339.2217, found 339.2213. **Method B: with 1 Equiv of *rac*-3a.** Method A was modified to include oxazolidinone **1** (0.69 g, 3.75 mmol) in THF (2 mL), LDA (4 mmol) in THF (15 mL), and *rac*-**3a** (crude, 880 mg, 3.75 mmol) in THF (2 mL), followed by sodium iodide (56 mg, 0.38 mmol) and 18-crown-6 (50 mg, 0.19 mmol). After similar conditions and workup, **4a** (1.33 g, 100% crude, containing 2% unchanged **1**) was isolated and used without further purification; 75 MHz $^{13}$C-NMR same as previous sample, signal to noise >400, single isomer, impurity peaks ≤2%.

**[α*R*-(α*R**,β*R**)]-α,β,4,4,5,5-Hexamethyl-1,3,2-dioxaborolane-2-propanoic Acid, Methyl Ester (5a). General Procedure for Reaction of Oxazolidinones with Sodium Methoxide.** A mixture of {4*S*-[3(α*S**,β*S**),4α]}-3-(α,β,4,4,5,5-hexamethyl-1,3,2-dioxaborolanepropanoyl)-4-(1-methylethyl)-1,3,2-oxazolidinone (**4a**) (crude, 3.29 g, 8.9 mmol) and sodium methoxide (1.44 g, 27 mmol) in methanol (36 mL) was stirred for 10 min at 0 °C. To the solution was added ether (50 mL), saturated ammonium chloride (25 mL), and sufficient hydrochloric acid (12 M) to bring the pH to 3. The aqueous layer was extracted with ether (3 × 50 mL). The combined ether layer was washed with brine (25 mL) and dried over magnesium sulfate. After flash chromatography (silica gel with 5%–10% ether/pentane), **5a** was isolated: from **2** and *rac*-**3a** 1:2 (scale 8.9 mmol) 1.55 g of (**5a**), 72% based on **1**, $[\alpha]^{23}_D$ −7.98°, $[\alpha]^{23}_{577}$, −8.27° (*c* 1.04, $CHCl_3$); from **2** and *rac*-**3a** 1:1 (scale 3.75 mmol) 0.66 g of (**5a**), 73% based on *rac*-**3a** or **1**, $[\alpha]^{23}_D$ −9.18°, $[\alpha]^{23}_{577}$ −9.5° (*c* 1.10, $CHCl_3$); 300-MHz $^1$H-NMR ($CDCl_3$) $\delta$ 0.95 (d, $J$ = 7.5 Hz, 3), 1.18 (d, $J$ = 7.1 Hz, 3), 1.23–1.32 (2s + m, 13), 2.55 (p, $J$ = 7.1 Hz, 1), 3.66 (s, 3). 75-MHz $^{13}$C-NMR ($CDCl_3$) $\delta$ 12.34, 15.29, 20 (br), 24.64, 24.66, 41.63, 51.39, 82.98, 177.32; HRMS calcd for $C_{12}H_{23}BO_4$ ($M^+$) 242.1689,

(26) The preparation of (*R*,*R*)-1,2-dicyclohexylethane-1,2-diol and some of its boronic esters is described in: Matteson, D. S.; Man, H.-W. *J. Org. Chem.* **1993**, *58*, 6545–6547. Preparation of α-bromo boronic esters is described in ref 2.

(27) (a) 2-Butyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: Matteson, D. S.; Mendoza, A. *J. Org. Chem.* **1979**, *44*, 1352–1354. (b) 2-(1-Methylethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: Hoffmann, R. W.; Zeiss, H. J. *J. Org. Chem.* **1981**, *46*, 1309–1314. (c) 2-Phenyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane: Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, *2*, 1529–1535.

found 242.1661. The $^1$H-NMR spectrum indicated 0.9% (12 mol %) water impurity, as did analysis. Anal. Calcd for $C_{12}H_{23}BO_4$: C, 59.53; H, 9.57. [Calcd for $C_{12}H_{23}BO_4 \cdot 0.12H_2O$: C, 59.00; H, 9.59.] Found: C, 58.75; H, 9.66.

**[*R*-(2*R**,3*R**]-(Methyl 2-Methyl-3-hydroxybutanoate) (6a) from 5a. General Procedure for Deboronation.** To a solution of (*R*)-(α*R**,β*R**)-α,β,4,4,5,5-hexamethyl-1,3,2-dioxaborolane-2-propanoic acid methyl ester (**5a**) (1.51 g, 6.24 mmol), which had been prepared from 2 equiv of bromide *rac*-**3a**, in ether (20 mL), sodium bicarbonate (0.53 g), and 0.1 M borate buffer at pH 8.6 (20 mL), was added hydrogen peroxide (30%, 2 mL) dropwise at 0 °C. The solution was stirred at room temperature overnight. To the solution was added ether (100 mL), sodium iodide (10 mg), and sodium thiosulfate (2 g). The aqueous layer was extracted with ether (4 × 100 mL). The combined organic layers were washed with brine (20 mL) and dried over magnesium sulfate. Removal of solvent and vacuum distillation yielded a mixture of (*R*)-(2*R**,3*R**)-methyl 2-methyl-3-hydroxybutanoate (**6a**) and pinacol, mol ratio 1:0.52 (68.3% **6a** by weight) by 300-MHz $^1$H NMR analysis (1.13 g, 91%), bp 75 °C (17 Torr), *threo/erythro* ratio ~55:1 based on the heights of diagnostic $^{13}$C peaks at δ 14.00 and 20.69; 10.99 and 19.74 (signal to noise 100:1); $[\alpha]^{23}_D$ −35.93° (*c* 3.48, methanol, corrected for pinacol content) [lit.[6a] (*S*)-(2*R**,3*R**)-isomer (*threo*) $[\alpha]_D$ +36.80°, (*S*)-(2*R**,3*S**)-isomer (*erythro*) $[\alpha]_D$ +14.32° (*c* 5, methanol)]. Flash chromatography of 1.10 g of this material on silica gel with 1:1 ether/pentane yielded 0.73 g (89% from **5a**) of pure **6a**, $[\alpha]^{23}_D$ −36.06° (ee 98%), $[\alpha]^{23}_{577}$ −37.50°, $[\alpha]^{23}_{546}$ −40.40° (*c* 5.01, methanol). For **6a** from 1 equiv of *rac*-**3a** (not chromatographed, corrected for pinacol content) $[\alpha]^{23}_D$ −34.49°, $[\alpha]^{23}_{577}$ −35.65° (*c* 2.54, methanol); *threo/erythro* ratio by NMR, 85:1.

**{4*S*-[3(α*S**,β*S**),4α]}-3-(β-butyl-α,4,4,5,5-pentamethyl-1,3,2-dioxaborolanepropanoyl)-4-(1-methylethyl)-1,3,2-oxazolidinone (4b).** The general procedure described for the preparation of **4a** (method B) was modified to include conversion of oxazolidinone **1** (0.59 g, 3.2 mmol) in THF (2 mL) to the enolate **2** by treatment with LDA (3.8 mmol) in THF (10 mL), followed by treatment with 2-(1-bromopentyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (*rac*-**3b**) (0.88 g, 3.2 mmol) in THF (2 mL) followed by sodium iodide (124 mg, 0.82 mmol) and 18-crown-6 (42 mg, 0.16 mmol). Workup gave a mixture of **4b** (1.13 g, NMR yield 73%) and side products, including unchanged **1**, *rac*-**3b** + **3bI** (no optical rotation after flash chromatography), (4*S*)-3-(2′-methyl-3′-oxopentanoyl)-4-(1-methylethyl)-1,3,2-oxazolidinone (**7**) (two diastereomers), and pinacol. In order to determine the ee and *threo*/*erythro* ratio, the sample was used in the next step without further purification: 300-MHz $^1$H-NMR ($CDCl_3$) δ 0.89 (d, *J* = 6.9 Hz, 3), 0.91 (d, *J* = 7.1 Hz, 3), 0.85−0.93 (m, 3), 1.19 (d, *J* = 7.0 Hz, 3), 1.219 + 1.222 (2s, 12), 1.20−1.50 (m, 7), 2.41 (m, 1), 3.81 (quintet, *J* = 7.0 Hz), 4.17−4.27 (m, 2), 4.39−4.43 (m, 1); 75-MHz $^{13}$C-NMR ($CDCl_3$) δ 13.99, 14.47, 16.64, 18.00, 23.04, 24.42, 24.98, 27.46, 28.07, 31.02, 39.13, 58.60, 62.70, 82.86, 153.50, 177.80; HRMS calcd for $C_{20}H_{36}BNO_5$ ($M^+$) 381.2686, found 381.2677.

**[α*R*-(α*R**,β*R**)]-(β-Butyl-α,4,4,5,5-pentamethyl-1,3,2-dioxaborolane)propanoic Acid, Methyl Ester (5b).** A mixture of {4*S*-[3(α*S**,β*S**),4α]}-3-(β-butyl-α,4,4,5,5-pentamethyl-1,3,2-dioxaborolanepropanoyl)-4-(1-methylethyl)-1,3,2-oxazolidinone (**4b**) (crude, 1.13 g) and sodium methoxide (0.51 g, 9.4 mmol) in methanol (15 mL) was stirred for 10 min at 0 °C. To the solution was added ether (50 mL), saturated ammonium chloride (25 mL), and sufficient hydrochloric acid (12 M) to bring the pH to 3. The aqueous layer was extracted with ether (3 × 50 mL). The combined ether layer was washed with brine (25 mL) and dried over magnesium sulfate. After flash chromatography (silica gel with 5%−10% ether/pentane), **5b** was isolated: 0.49 g, 53% based on **1**; 300-MHz $^1$H-NMR ($CDCl_3$) δ 0.85−0.90 (m, 3), 1.19 (d, *J* = 7.1 Hz, 3), 1.23 + 1.24 (2s, 12), 1.10−1.42 (m, 7), 2.57 (quintet, *J* = 7.3 Hz, 1), 3.65 (s, 2); 75-MHz $^{13}$C-NMR δ 14.00, 16.14, 22.89, 24.73, 24.82, 27.96, 31.15, 40.62, 51.39, 82.99, 177.50; HRMS calcd for $C_{15}H_{29}BO_4$ ($M^+$) 284.2159, found 284.2172. Anal. Calcd for $C_{15}H_{29}BO_4$: C, 63.39; H, 10.29; B 3.80. Found: C, 63.14; H, 10.03; B 3.81.

**[*R*-(2*R**,3*R**]-(Methyl 2-methyl-3-hydroxyheptanoate) (6b).** A mixture of [α*R*-(α*R**,β*R**)]-(β-butyl-α,4,4,5,5-pentamethyl-1,3,2-dioxaborolane)propanoic acid, methyl ester (**5b**) (0.4 g, 1.4 mmol), buffer made from 0.1 M potassium dihydrogen phosphate and 0.1 M sodium hydroxide in the ratio 54:46 (pH 8) (30 mL), sodium carbonate (120 mg, 1.4 mmol), ether (30 mL), and hydrogen peroxide (0.5 mL) at 0 °C. The solution was stirred at room temperature overnight. After the usual workup a mixture of pinacol (20 mol %) and **6b** (80 mol %) was obtained (0.22 g, 78% yield of **6b** contained). The *threo*/*erythro* ratio was 46:1 based on the heights of diagnostic $^{13}$C peaks at δ 13.84, 45.19, 73.10 (*threo*) and 10.60, 44.25, 71.63 (*erythro*).[2] The enantiomeric excess was determined by $^1$H-NMR with chiral shift reagent. The crude mixture (10 mg) and tris[3-(heptafluoropropyl)hydroxymethylene]-*d*-camphoratoeuropium (10 mg) was dissolved in $CDCl_3$ (0.4 mL). The OMe singlet was observed as separate signals at δ 3.86 (major) and 3.94 (minor). The $^{13}$C satellite of major enantiomer (δ 4.10, $J_{C,H}$ = 146 Hz) was also observed. By comparing the peak heights among those signals, the ratio was 98.2:1.8 (96.4% ee): 300-MHz $^1$H-NMR ($CDCl_3$) δ 0.88−0.95 (m, 3), 1.22 (d, *J* = 7.2 Hz, 3), 1.28−1.60 (m, 6), 2.1−2.3 (brs, 1), 2.54 (dq, $J = 6.4_d\ 7.2_q$ Hz, 1), 3.63-3.70 (m, 1), 3.72 (s, 3); 75-MHz $^{13}$C-NMR ($CDCl_3$) δ 13.84, 13.99, 22.46, 27.52, 34.13, 45.19, 51.51, 73.10, 176.33.

**{4*S*-[3(α*S**,β*S**),4α]}-3-[β-(1-Methylethyl)-α,4,4,5,5-pentamethyl-1,3,2-dioxaborolanepropanoyl]-4-(1-methylethyl)-1,3,2-oxazolidinone (4c). Method A**: with 2 equiv of *rac*-**3c**. Conversion of **1** (0.35 g, 1.9 mmol) to enolate **2** and treatment with (*rac*-**3c**) (1 g, 3.8 mmol) was carried out according to the general procedure (Method A) described for conversion of **1** and *rac*-**3a** to **4a**. The usual workup and flash chromatography (silica gel with 1:2 ether/hexanes) yielded 0.15 g (22%) of **4c**: mp 84−85.5 °C; 300-MHz $^1$H-NMR ($CDCl_3$) δ 0.90 (d, *J* = 6.8 Hz, 3), 0.91 (d, *J* = 6.8 Hz, 3), 0.92 (d, *J* = 7.0 Hz, 3), 1.03 (d, *J* = 6.9 Hz, 3), 1.19 (d, *J* = 7.0 Hz, 3), 1.20 + 1.22 (2s, 12), 1.15−1.25 (m, 1), 1.80−1.95 (m, 1), 2.35−2.50 (m, 1), 3.85 (dq, $J = 9.5_d, 7.0_q$), 4.18−4.28 (m, 2), 4.36−4.40 (m, 1); 75-MHz $^{13}$C-NMR ($CDCl_3$) δ 14.39, 18.00, 18.04, 20.21, 23.35, 24.38, 25.22, 26.21, 27.95, 37.92, 58.78, 62.54, 82.80, 153.49, 178.24; HRMS calcd for $C_{19}H_{34}BNO_5$ ($M^+$) 367.2530, found 367.2535. Anal. Calcd for $C_{19}H_{34}BNO_5$: C, 62.13; H, 9.33; N, 3.81; B 2.94. Found: C, 61.83; H, 9.17; N, 4.01; B 2.77. **Method B.** The route to **4a** described as Method B was modified to include oxazolidinone **1** (0.37 g, 2.0 mmol) in THF (2 mL), LDA (2.16 mmol) in THF (10 mL), and *rac*-**3c** (crude, 0.54 g, 2.0 mmol) in THF (2 mL), followed by sodium iodide (66 mg, 0.44 mmol) and 18-crown-6 (34 mg, 0.12 mmol). After similar conditions, workup, and flash chromatography (silica gel with 1:2 ether/pentane), **4c** (0.14 g, 19%) was isolated. The side products included unchanged **1**, halo boronic esters **3c**/**3cI** (0.2 g), $[\alpha]^{23}_{546}$ 0.00° (*c* 2.4, $CHCl_3$), (4*S*)-3-(2′-methyl-3′-oxopentanoyl)-4-(1-methylethyl)-1,3,2-oxazolidinone (**7**) (two isomers), and pinacol. **Method B with *rac*-3cI.** 2-(1-Iodo-2-methylpropyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (*rac*-**3cI**) was prepared from *rac*-**3c** (1 g, 3.8 mmol) by treatment with sodium iodide (1 g, 6.6 mmol) in acetone (20 mL) at 25 °C overnight, followed by workup with pentane (100 mL) and water (2 × 50 mL), drying over magnesium sulfate, and concentration: 1.1 g (93%); 300-MHz $^1$H-NMR ($CDCl_3$) δ 1.03 (d, *J* = 6.3 Hz, 3), 1.10 (d, *J* = 6.5 Hz, 3), 1.27 + 1.28 (2s, 12), 1.78−1.90 (m, 1), 3.08 (d, *J* = 8.8 Hz); 75-MHz $^{13}$C-NMR δ 21.68, 24.06, 24.15, 24.37, 31.39, 83.80. HRMS calcd for $C_{10}H_{20}BO_2I$ ($M^+$) 310.0603, found 310.0594. Conversion of **1** (0.60 g, 3.24 mmol) in THF (2 mL) with LDA (3.5 mmol) in THF (10 mL) to enolate **2** was followed by addition of *rac*-**3cI** (crude, 1 g, 3.23 mmol) in THF (2 mL), followed by sodium iodide (97 mg, 0.65 mmol) and 15-crown-5 (71 mg, 0.32 mmol). After similar conditions, workup, and flash chromatography (silica gel with 1:2 ether/pentane), **4c** (0.48 g, 40.5%) was isolated. The side products seen in the reaction of *rac*-**3c** were also present.

**[*R*-(2*R**,3*R**]-2,4-Dimethyl-3-hydroxypentanoic Acid, Methyl Ester (6c).** A mixture of **4c** (crude from *rac*-**3c** via Method B, 700 mg) and sodium methoxide (400 mg) in methanol (5 mL) was stirred at 0 °C for 30 min. To the

mixture was added phosphate buffer (see **6b**) (30 mL, pH of solution is ca. 9), ether (30 mL), and hydrogen peroxide (0.5 mL) at 0 °C. The solution was stirred at room temperature for 3 h. After workup and flash chromatography (silica gel with 1:1 ether/hexanes), **6c** (0.080 g, 0.5 mmol) was isolated. 75 MHz $^{13}$C-NMR showed no *erythro* isomer, signal to noise >500:1.[7] The enantiomeric excess was determined by $^{1}$H-NMR with chiral shift reagent. Ester **6c** (10 mg) and tris[3-(heptafluoropropyl)hydroxymethylene]-*d*-camphoratoeuropium (10 mg) was dissolved in $CDCl_3$ (0.4 mL). The OMe singlet was observed as separate signals at $\delta$ 3.92 (major) and 3.99 (minor) [lit.[28] $\delta$ 4.08 (2*R*,3*R*); 4.13 (2*S*,3*R*)]. The $^{13}$C satellite of the major enantiomer ($\delta$ 4.16, $J_{C,H}$ = 144 Hz) was also observed. By comparing the peak heights among those signals, the ratio was 98.2:1.8 (96.4% ee). The absolute configuration was assigned as (2*R*,3*R*) according to Meyers and Yamamoto:[28] 300-MHz $^{1}$H-NMR ($CDCl_3$) $\delta$ 0.93 (d, $J$ = 6.7 Hz, 3), 0.97 (d, $J$ = 6.8 Hz, 3), 1.21 (d, $J$ = 7.2 Hz, 3), 1.60−1.80 (m, 1), 2.56 (d, $J$ = 7.3 Hz, 1), 2.67 (dq $J$ = $6.5_d$, $7.2_q$), 3.36−3.42 (m, 1), 3.72 (s, 3); 75-MHz $^{13}$C-NMR ($CDCl_3$) $\delta$ 14.74, 16.28, 19.73, 30.93, 42.51, 51.71, 78.15, 176.85.

**[(±)-3(α*R**,β*R**)]-4,4-Dimethyl-3-(α,β,4,4,5,5-hexamethyl-1,3,2-dioxaborolanepropanoyl)-1,3,2-oxazolidinone (9).** By a modification of the general procedure used to convert **1** and *rac*-**3a** to **4a**, 4,4-dimethyl-3-propanoyl-1,3,2-oxazolidinone (**8**) (2.9 g, 17 mmol) was converted to enolate and treated with *rac*-**3a** (3.8 g, 16.5 mmol). After the usual aqueous workup, the solution of **9** was concentrated under vacuum to an oil, which appeared to be a single isomer by NMR analysis. The oil crystallized from pentane (1.61 g, 30%; some **9** remained in solution): mp 100−101 °C; 300-MHz $^{1}$H-NMR ($CDCl_3$) $\delta$ 0.97 (d, $J$ = 7.5 Hz, 3), 1.19 (d, $J$ = 7.0 Hz, 3), 1.215 and 1.217 (2s + m, 13), 1.54 (s, 3), 1.57 (s, 3), 3.63 (p, $J$ = 7.4 Hz, 1), 3.99 (s, 2); 125-MHz $^{13}$C-NMR ($CDCl_3$) $\delta$ 12.61, 16.49, 20 (br), 24.57, 24.81, 24.85, 24.94, 42.18, 60.38, 75.02, 82.89, 154, 179; HRMS calcd for $C_{16}H_{28}BO_5N$ ($M^+$) 325.2060, found 325.2045. Anal. Calcd for $C_{16}H_{28}BO_5N$: C, 59.09; H, 8.68; B, 3.32; N ,4.31. Found: C, 59.44; H, 8.68; B, 3.37; N, 4.30.

**(±)-(α*R**,β*R**)-α,β,4,4,5,5-Hexamethyl-1,3,2-dioxaborolane-2-propanoic acid Methyl Ester (*rac*-5).** This was prepared from **9** (1.3 mmol) by the general procedure described for preparation of **5a** from **4a**. Concentration of the ether extract without chromatography yielded crude *rac*-**5a** (0.25 g, 79%), which was not purified further: 300-MHz $^{1}$H-NMR, 75-MHz $^{13}$C-NMR, same as **5a**.

**{4*S*-[2(*S**),4α,5β]}-2-(1-bromoethyl)-4,5-dicyclohexyl-1,3,2-dioxaborolane (10).** This compound was prepared by the general procedure described for preparation of *rac*-**3a** from [*S*-(4α,5β)]-2-methyl-4,5-dicyclohexyl-1,3,2-dioxaborolane (1.84 g, 7.4 mmol), LDA (7.6 mmol), dibromomethane (5.1 g, 28.7 mmol), THF (100 mL), and anhydrous zinc chloride (2 g, 14.6 mmol) to yield crude **10**, 1.9 g, which was used without further purification: 200-MHz $^{1}$H-NMR ($CDCl_3$) $\delta$ 0.85−1.90 (m, 22), 1.72 (d, $J$ = 7.5 Hz, 3), 3.48 (q, $J$ = 7.5 Hz, 1), 3.8−4.0 (m, 2).

**{4*S*-[3[2(α*RS**,β*RS**),4β,5α],4α]}-3-(α,β-Dimethyl-4,5-dicyclohexyl-1,3,2-dioxaborolanepropanoyl)-4-(1-methylethyl)-1,3,2-oxazolidinone (11).** This mixture was prepared in the manner described above for **4a** from {4*S*-[2(*S**),4α,5β]}-2-(1-bromoethyl)-4,5-dicyclohexyl-1,3,2-dioxaborolane (**10**) (crude, 0.64 g,1.87 mmol) in THF (1 mL), oxazolidinone **1** (0.35 g, 1.89 mmol) in THF (1 mL), and LDA (2 mmol) in THF (10 mL). After the usual workup and flash chromatography (silica gel with 1:2 ether/hexanes), 0.37 g of **11** (44%) was isolated as a mixture of *threo* and *erythro* isomers. In order to determine the *threo/erythro* ratio, the crude material was used in the next step without chromatography: 500-MHz $^{1}$H-NMR ($CDCl_3$) [*erythro*] $\delta$ 0.86 (d, $J$ = 7.5 Hz, 3), 0.88 (d, $J$ = 7.5 Hz, 3), 0.94 (d, $J$ = 7 Hz, 3), [1.01 (d $J$ = 7 Hz, 3)], [1.14 (d $J$ = 7 Hz, 3)], 1.16 (d, $J$ = 7 Hz, 3), 0.90−1.80 (m, 23), 2.24−2.41 (2m, 1), 3.76−3.82 (m, 3), 4.15−4.17 (m,1), 4.19−4.25 (m, 1), 4.40−4.46 (m, 1); 125-MHz $^{13}$C-NMR ($CDCl_3$) [*erythro*] $\delta$ [12.07], [14.46, 14.54], 14.57, 15,27, 16.16, [16.19], 18.00, [25.95], 26.01, [26.46], 26.48, [27.41], 27.59, 28.17, [28.41], 40.17, [40.48], 42.89 [42.99], 58.56 [58.59], [62.82], 62.95, 83.34, 153.5, 177. HRMS calcd for $C_{25}H_{42}BO_5N$ ($M^+$) 447.3156, found 447.3148.

**{4*S*-[3[2(α*RS**,β*RS**),4β,5α],4α]}-3-(4,5-Dicyclohexyl-α,β-dimethyl-1,3,2-dioxaborolanepropanoyl)-4,4-dimethyl-1,3,2-oxazolidinones.** This mixture was prepared in the manner described above for **4a** from {4*R*-[2(*S**),4α,5β]}-2-(1-bromoethyl)-4,5-dicyclohexyl-1,3,2-dioxaborolane (*ent*-**10**) (crude, 3.43 g, 10 mmol) in THF (10 mL), oxazolidinone **8** (1.71 g, 10 mmol) in THF (10 mL), and LDA (8.2 mL, 1.34 M, 11 mmol) in THF (90 mL). The usual workup and flash chromatography (silica gel with 1:2 ether/hexanes) yielded 1.6 g of {4*S*-[3-[2(α*RS**,β*RS**),4β,5α],4α]}-3-(4,5-dicyclohexyl-α,β-dimethyl-1,3,2-dioxaborolanepropanoyl)-4,4-dimethyl-1,3,2-oxazolidinones in a (α*R**,β*R**)/(α*R**,β*S**) ratio of 1.6:1 by $^{13}$C NMR: 500-MHz $^{1}$H-NMR ($CDCl_3$) [*erythro*] $\delta$ [0.949 (d, $J$ = 7.0 Hz)], 0.954 (d, $J$ = 8.0 Hz, 3), [1.15 (d, $J$ = 6.5 Hz)], 1.21 (d $J$ = 7 Hz, 3), 1.50 (br s, 3).1.52 (s, 3), [1.53 (s)], 0.80−1.78 (m, 23), 3.66 (p, $J$ = 6.5 Hz), 3.69 (p, $J$ = 6.5 Hz) (unassigned to isomers, these two pentuplets have similar peak heights), 3.76−3.78 (m, 2), 3.95 (s, 2); 125-MHz $^{13}$C-NMR ($CDCl_3$) [*erythro*] $\delta$ [12.69], 13.41, [16.11], 16.58, 20.05 (br), [24.70], 24.81, [24.93], 25.89, 26.00, 26.46, [27.59], 27.65, [28.29], 28.48, [42.78], 42.91, 60.39, 74.99, 83.41, 153.58, [178.84], 178.87; HRMS calcd for $C_{24}H_{40}BO_5N$ ($M^+$) 433.2999, found 433.3000.

**{4*S*-[2(α*RS**,β*RS**),4α,5β]}-α,β-Dimethyl-4,5-dicyclohexyl-1,3,2-dioxaborolane-2-propanoic Acids, Methyl Esters.** By the procedure described above for **5a**, this mixture was prepared from {4*S*-[3-[2(α*RS**,β*RS**),4β,5α],4α]}-3-(α,β-dimethyl-4,5-dicyclohexyl-1,3,2-dioxaborolanepropanoyl)-4-(1-methylethyl)-1,3,2-oxazolidinone (**11**) (crude, 360 mg, 0.8 mmol) in methanol (4 mL), and sodium methoxide (130 m g, 2.4 mmol). After the usual workup, 286 mg of a mixture of {4*S*-[2(α*RS**,β*RS**),4α,5β]}-α,β-dimethyl-4,5-dicyclohexyl-1,3,2-dioxaborolane-2-propanoic acid methyl esters (94%) was isolated, *threo/erythro* ratio 3:1 by $^{1}$H NMR, used without further purification: 300-MHz $^{1}$H-NMR ($CDCl_3$) [*erythro* peaks in brackets] $\delta$ [0.96 (d, $J$ = 7.2 Hz)], 0.98 (d, $J$ = 7.5 Hz, 3), 1.17 (d, $J$ = 7.2 Hz, 3), [1.18 (d $J$ = 7.1 Hz)], 0.82−1.82 (m, 23), 2.57 (p, $J$ = 7.2 Hz, 1), [2.65 (p, $J$ = 7.2 Hz)], 3.65 (s, 3), 3.80−3.86 (m, 2); HRMS calcd for $C_{20}H_{35}BO_4$ ($M^+$) 350.2628, found 350.2606.

**[(±)-(2*R**,3*R**)]-2-Methyl-3-hydroxybutanoic Acid, Methyl Ester (*rac*-6a).** To a mixture of crude (α*R**,β*R**)-α,β,4,4,5,5-hexamethyl-1,3,2-dioxaborolane-2-propanoic acid methyl ester (*rac*-**5a**) (0.66 g, 2.75 mmol), which had been prepared from **9**, in THF (60 mL), sodium hydroxide (1 mL, 3 M), and 0.1 M borate buffer at pH 8.6 (30 mL) was added hydrogen peroxide (30%, 3 mL) dropwise at 0 °C. The solution was stirred at room temperature overnight. To the solution was added ether (100 mL). The aqueous layer was extracted with ether (2 × 100 mL). The combined organic layers were washed with brine (20 mL) and dried over magnesium sulfate. Removal of solvent gave [(±)-(2*R**,3*R**)]-**6a** (350 mg, 96%) with no detectable (2*R**,3*S**)-isomer by $^{13}$C NMR (signal to noise ~50:1, diagnostic peaks at $\delta$ 14.00 and 20.69 present, 10.99 and 19.74 absent). The remainder of the $^{13}$C NMR spectrum corresponded to that listed below for **6a** in a mixture with **12**.

**(2*R**,3*R**)- (6a) and (2*R**,3*S**)-2-Methyl-3-hydroxybutanoic Acid Methyl Ester (12).** Deboronation of a mixture of {4*S*-[2(α*RS**,β*RS**),4α,5β]}-α,β-dimethyl-4,5-dicyclohexyl-1,3,2-dioxaborolane-2-propanoic acid, methyl esters (crude, 286 mg, 0.75 mmol) in THF (10 mL), sodium hydroxide (1 mL, 3 M), 0.1 M borate buffer at pH 8.6 (7 mL), and hydrogen peroxide (1 mL, 30%) was carried out in the manner described above. A mixture of **6a** and **12** (100 mg, 100%) was isolated, ratio 3.3:1 by $^{1}$H NMR, 3:1 ($\delta$ 14.00 vs 10.99) or 2.2:1 ($\delta$ 20.69 vs 19.74) by $^{13}$C NMR: 500-MHz $^{1}$H-NMR ($CDCl_3$) [(2*R**,3*S**)-isomer peaks in brackets] $\delta$ 1.18 (d, $J$ = 7 Hz, 3), 1.19 (d, $J$ = 7 Hz, 3), [1.22 (d, $J$ = 6.5 Hz, 3)], 2.45 (p, $J$ = 7 Hz, 1), [2.51 (dq, $J$ = $4_d$, $6.5_q$)], 2.5−3.0 (br, 1), 3.71 (s, 3), 3.87 (p, $J$ = 7 Hz, 1), [4.05 (dq, $J$ = $4_d$, $6.5_q$)]; 75-MHz $^{13}$C-NMR ($CDCl_3$) [*erythro*] $\delta$ [10.99], 14.00, [19.74], 20.69, [45.42], 46.84, 51.70, [67.97], 69.4, 176.32.

**{4*R*-[2(*S**),4α,5β]}-2-(1-Bromopentyl)-4,5-dicyclohexyl-1,3,2-dioxaborolane (13) and Its 2(*R**)-Epimer (14).** Lithium diisopropylamide (10.2 mL, 2.0 M, 20.4 mmol) was

(28) Meyers, A. I.; Yamamoto, Y. *Tetrahedron* **1984**, *40*, 2309−2315.

added dropwise to a solution of [*R*-(4α,5β)]-2-butyl-4,5-dicyclohexyl-1,3,2-dioxaborolane (4.93 g, 16.9 mmol) and dibromomethane (3.6 mL, 51 mmol) in THF (30 mL) stirred at −78 °C under argon. After the addition was complete, powdered fused zinc chloride (5.06 g, 37 mmol) was added. The solution was allowed to warm to room temperature and kept for 18 h and then concentrated. Pentane (300 mL) and saturated aqueous ammonium chloride (150 mL) were added. The organic layer was dried over magnesium sulfate and filtered through a short pad of magnesium sulfate. Removal of solvent in a rotary evaporator yielded [4*R*-[2(*S**),4α,5β]]-2-(1-bromopentyl)-4,5-dicyclohexyl-1,3,2-dioxaborolane (**13**) and its 2(*R**)-epimer (**14**) in a ratio of 3:1 based on $^1$H and $^{13}$C NMR (5.54 g, 85%). The bromide had epimerized to a 50:50 mixture of **13** and **14** after 6 days at room temperature: 300-MHz $^1$H-NMR ($CDCl_3$) [**14** in brackets where distinguishable] δ 0.85−2.0 (m, 26), 0.91 (t, $J$ = 7.3 Hz, 3), 1.90 (br q, $J$ = 7.3 Hz, 2), [3.36 (t, $J$ = 7.9 Hz)], 3.37 (t, $J$ = 7.7 Hz, 1), 3.94−3.98 (m, 2); 75-MHz $^{13}$C-NMR ($CDCl_3$) δ 13.94, 22.11, [22.14], 25.85, 25.95, 26.40, 27.27, [27.29], 28.16, [28.24], 30.90, [30.93], 33.93, [34.08], 42.86, [42.89], 83.90, [83.96]; HRMS calcd for $C_{19}H_{34}BBrO_2$ ($M^+$) 384.1835, found 384.1830.

**(*R**,*R**)-2-Methyl-3-hydroxyhexanoic Acid, 1,1-Dimethylethyl Ester (17 and *ent*-17).** A solution of *tert*-butyl propanoate (0.37 g, 2.8 mmol) in THF (10 mL) which was cooled to −78 °C was added via cannula to a solution of LDA (1.56 mL, 2 M, 3.1 mmol) in THF (30 mL) at −78 °C under argon. After 30 min at −78 °C, a solution of a ~50:50 mixture of **13** and **14** (1 g, 2.6 mmol) in THF (10 mL) was added. The solution was allowed to warm to room temperature overnight, and the solvent was removed under vacuum. The residue was dissolved in ether/pentane (10%, 150 mL) and saturated aqueous ammonium chloride (150 mL). The organic layer was separated, washed with brine, and dried over magnesium sulfate. Concentration in a rotary evaporator yielded a crude mixture of [(4*R*-[2(α*R**,β*R**),4α,5β]- and [(4*R*-[2(α*S**,β*S**),4α,5β]-4,5-dicyclohexyl-β-butyl-α-methyl-1,3,2-dioxaborolane-2-propanoic acid, 1,1-dimethylethyl esters (**15** and **16**) (1 g): 300-MHz $^1$H-NMR ($CDCl_3$) δ 0.85−1.8 (m), (1.13 + 1.17) (2 d's, $J$ = 7.2 Hz), (1.425 + 1.4275) (2 s's), 2.4−2.6 (p + dq), 3.78−3.85 (m); 75-MHz $^{13}$C-NMR ($CDCl_3$) δ 14.06, (15.77 + 16.19), 22.99, 25.89, 26.02, 26.52, (27.84 + 27.89), (28.07 + 28.10), (28.59 + 28.64), (31.33 + 31.60), 41.08, 41.97, 42.99, (83.48 + 83.58). The mixture of crude **15** and **16** (0.7 g) in THF (15 mL) was treated with sodium hydroxide (0.6 mL, 3 M, 1.8 mmol) and borate buffer (10 mL, pH 8.6) followed by hydrogen peroxide (1 mL, 30%) at 0 °C. The mixture was stirred at room temperature for 18 h and then extracted with ether (50 mL). The aqueous phase was washed with ether (3 × 20 mL). The combined organic phase was dried over magnesium sulfate. Removal of solvent gave a mixture of (*R*,*R*)-1,2-dicyclohexyl-1,2-ethanediol, its boric acid ester, (*R**,*R**)-2-methyl-3-hydroxyhexanoic acid, 1,1-dimethylethyl ester (**17** and *ent*-**17**), and (*R**,*S**)-2-methyl-3-hydroxyhexanoic acid, 1,1-dimethylethyl ester (**18**) (0.7 g). The diastereomeric ratio **17**/**18** was estimated to be 12:1 by 75-MHz $^{13}$C-NMR, based on the relative peak heights of the *threo* isomer (**17**) peaks at δ 14.04, 45.84, 73.53 and the *erythro* isomer (**18**) peaks at δ 10.85, 45.06, 71.87. The $^1$H- and $^{13}$C-NMR spectra agreed with those reported previously.[2]

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**Supplementary Material Available:** Copies of 300-MHz $^1$H and 75-MHz $^{13}$C NMR spectra of 2,4,4,5,5-pentamethyl-1,3,2-dioxaborolane, [*R*-(4α,5β)]-2-methyl-4,5-dicyclohexyl-1,3,2-dioxaborolane, *rac*-**3a**, *rac*-**3c**, *rac*-**3cI**, **4a**−**c**, **5a**−**c**, **6a**,**c**, **9**, **10** (200 MHz $^1$H only), **11**, **13**/**14**, and **15**/**16** (36 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.