Acknowledgment. The authors thank F. Gaudemer for preliminary experiments and Dr. S. K. Kan for kindly allowing them to use his 400-MHz NMR spectrometer. Grant support from the Research Corporation and the National Institutes of Health (Grant GM 34676) is gratefully acknowledged.

Supplementary Material Available: Tables of Δ^i_{LP} for all NMR experiments, results for the ionic strength and temperature dependences of K_1 and Δ^i_{LP}, and the conditions for the temperature-jump experiments (6 pages). Ordering information is given on any current masthead page.

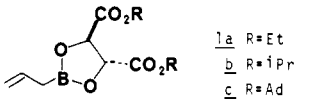
Diastereo- and Enantioselective Aldehyde Addition Reactions of 2-Allyl-1,3,2-dioxaborolane-4,5-dicarboxylic Esters, a Useful Class of Tartrate Ester Modified Allylboronates[1]

William R. Roush,*[2] Alan E. Walts, and Lee K. Hoong

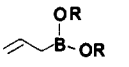
Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139. *Received May 17, 1985*

Abstract: The preparation and aldehyde addition reactions of the title compounds (**1a–c**) are described. These tartrate ester based reagents are the most highly enantioselective group of allylboronate esters reported to date. Reagent **1b** prepared from diisopropyl tartrate reacts with achiral aldehydes to give homoallylic alcohols in good yield and high enantioselectivity (71–87% ee). Interestingly, the greatest selectivity is obtained with α-branched aldehydes such as pivaldehyde (82% ee) and cyclohexanecarboxaldehyde (87% ee). These reagents also exhibit useful levels of matched and mismatched diastereoselection in reactions with chiral aldehydes. For example, the reaction of glyceraldehyde acetonide (**4**) and **1b** is selective either for erythro alcohol **6** (96:4) or the threo diastereomer **7** (92:8) depending on the chirality of **1b** and the reaction solvent. The asymmetric induction in these reactions appears to originate from a novel stereoelectronic effect involving n/n repulsive interactions between the aldehydic oxygen atom and an ester carbonyl in the disfavored transition state B.

The reactions of allyl and crotylmetal compounds with aldehydes have been extensively investigated in recent years.[3] Although excellent stereochemical control has been achieved in the additions of several classes of reagents (e.g., B, Sn, Si, Cr, Ti, etc.) to achiral aldehydes,[3a] a general solution to the problem of controlling facial selectivity in reactions with chiral aldehydes has not been found.[3,4] As an extension of our studies of allylic boronate aldehyde addition reactions,[5] we have turned to double-asymmetric synthesis[6] as a possible solution to this problem.[7] We are pleased therefore to report the preparation of a new class of tartrate ester based allylboronates (**1a–c**) that exhibit useful levels of matched and mismatched diastereoselection in reactions with chiral aldehydes.[8,9] In addition, reagent **1b** reacts with achiral



1a R=Et
b R=iPr
c R=Ad



2 R=H
3 R=iPr

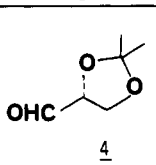
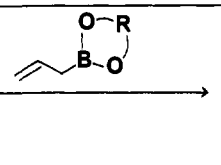
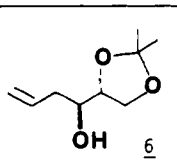
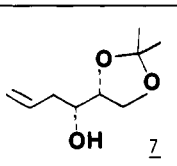
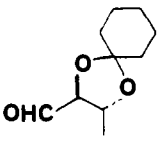
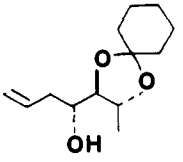
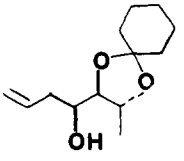
aldehydes to give homoallylic alcohols in good yield and with high enantioselectivity (71–87% ee). This compound is the most highly enantioselective allylboronate reported to date, is very easily prepared in either enantiomeric series, and consequently is well-suited for use as a reagent in organic synthesis.

The preferred method (A) for synthesis of **1a–c** involves esterification of allylboronic acid (**2**)[10] with the appropriate tartrate ester.[11] Although crude **1a–c** can be used directly in aldehyde addition reactions (the only significant impurity is residual tartrate ester, typically 0.3–0.5 equiv), we have found that tartrate-free reagents generally give superior results especially in reactions with achiral aldehydes and therefore recommend that the crude boronic ester be purified by distillation. By using this procedure, ≥97% pure **1b** has been prepared in 78% yield from DIPT (54% yield based on the allylmagnesium bromide used to prepare **2**). This reagent is sensitive to moisture but can be stored under an inert

(1) Portions of this work are described in: Walts, A. E. Ph.D. Thesis, Massachusetts Institute of Technology, Cambridge, 1985.
(2) Fellow of the Alfred P. Sloan Foundation, 1982–1986.
(3) (a) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555. (b) Reetz, M. T. *Ibid.* **1984**, *23*, 556. (c) McGarvey, G. J.; Kimura, M.; Oh, T.; Williams, J. M. *J. Carbohydr. Chem.* **1984**, *3*, 125.
(4) For recent stereochemical studies, see: (a) Hoffmann, R. W.; Weidmann, U. *Chem. Ber.* **1985**, *118*, 3966. (b) Keck, G. E.; Boden, E. P. *Tetrahedron Lett.* **1984**, *25*, 265, 1879. (c) Keck, G. E.; Abbott, D. E. *Ibid.* **1984**, *25*, 1883. (d) Heathcock, C. H.; Kiyooka, S.-I.; Blumenkopf, T. A. *J. Org. Chem.* **1984**, *49*, 4214. (e) Reetz, M. T.; Kesseler, K.; Jung, A. *Tetrahedron Lett.* **1984**, *25*, 729. (f) Yamamoto, Y.; Yatagai, H.; Ishihara, Y.; Maeda, N.; Maruyama, K. *Tetrahedron* **1984**, *40*, 2239. (g) Lewis, M. D.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2343. (h) Buse, C. T.; Heathcock, C. H. *Tetrahedron Lett.* **1978**, 1685.
(5) (a) Roush, W. R.; Adam, M. A.; Harris, D. J. *J. Org. Chem.* **1985**, *50*, 2000. (b) Roush, W. R.; Walts, A. E. *Tetrahedron Lett.* **1985**, *26*, 3427.
(6) Masamune, S.; Choy, W.; Peterson, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.
(7) Reactions of chiral aldehydes with allylic boronates prepared from *endo*-3-phenyl-*exo*-2,3-bornanediol have been studied by Hoffman and coworkers: (a) Hoffmann, R. W.; Zeiss, H.-J.; Ladner, W.; Tabche, S. *Chem. Ber.* **1982**, *115*, 2357. (b) Hoffmann, R. W.; Endesfelder, A.; Zeiss, H.-J. *Carbohydr. Res.* **1983**, *123*, 320. For reactions of these reagents with achiral aldehydes, see: (c) Herold, T.; Schrott, U.; Hoffmann, R. W.; Schnelle, G.; Ladner, W.; Steinbach, K. *Chem. Ber.* **1981**, *114*, 359. (d) Hoffmann, R. W.; Herold, T. *Chem. Ber.* **1981**, *114*, 375.
(8) Use of tartrate esters as chiral auxiliaries in the asymmetric reactions of allenyl boronic acid has been reported: Haruta, R.; Ishiguro, M.; Ikeda, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1982**, *104*, 7667.
(9) For leading references to several other classes of chiral allylmetal compounds, see: (a) Midland, M. M.; Preston, S. B. *J. Am. Chem. Soc.* **1982**, *104*, 2330. (b) Brown, H. C.; Jadhav, P. K. *Ibid.* **1983**, *105*, 2092. (c) Brown, H. C.; Jadhav, P. K. *J. Org.* Chem. **1984**, *49*, 4089. (d) Hayashi, T.; Konishi, M.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 281. (e) Jephcote, V. J.; Pratt, A. J.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1984**, 800. (f) Hoffmann, R. W.; Landmann, B. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 437. (g) Roder, H.; Helmchen, G.; Peters, E.-M.; Peters, K.; von Schnering, H.-G. *Ibid.* **1984**, *23*, 898.
(10) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, *2*, 230.
(11) L-(+)-Diethyl tartrate, and L-(+)- and D-(−)-diisopropyl tartrate were obtained from Aldrich Chemical Co. L-(+)-Diadamantyl tartrate was synthesized from tartaric acid by using methods developed by Prof. K. B. Sharpless.

0002-7863/85/1507-8186$01.50/0

Table I. Reactions of Chiral Allylic Boronic Esters **1** with Chiral Aldehydes **4** and **5**[a]

entry	reagent	diol[b]	method[c]	conditions	product ratio[d] (yield)
	 **4**		 **6**	 **7**	
1	(−)-**1b**	(+)-DIPT	A–C	CH_2Cl_2, −78 °C	96:4 (91%)[e]
2	(−)-**1b**	(+)-DIPT	B	toluene, −78 °C	93:7 (86%)[e]
3	**10**	pinacol	A	CH_2Cl_2, −78 °C	80:20 (75%)[f]
4	**10**	pinacol	A	toluene, −78 °C	71:29[f]
5	(+)-**1b**	(−)-DIPT	B	CH_2Cl_2, −78 °C	39:61
6	(+)-**1b**	(−)-DIPT	C[g]	toluene, −78 °C	8:92
7	(+)-**1b**	(−)-DIPT	B	toluene, −78 °C	10:90 (79%)[h]
8[i]	(+)-**1b**	(−)-DIPT	B	toluene, −78 °C	15:85 (93%)[e]
9	**11**	(−)-2,3-butanediol	A	CH_2Cl_2, 23 °C	81:19
10	**11**	(−)-2,3-butanediol	A	toluene, −78 °C	76:24
11	**12**	(−)-2,4-pentanediol	A	CH_2Cl_2, −78 °C	68:32
	 **5**		 **8**	 **9**	
12	(+)-**1b**	(−)-DIPT	B	CH_2Cl_2, −78 °C	98:2 (94%)[e]
13	**10**	pinacol	A	CH_2Cl_2, −78 °C	90:10 (85%)[f]
14	**10**	pinacol	A	toluene, −78 °C	90:10[f]
15	(−)-**1b**	(+)-DIPT	A	CH_2Cl_2, −78 °C	71:29
16	(−)-**1b**	(+)-DIPT	B	toluene, −78 °C	36:64
17	(−)-**1a**	(+)-DET	B	toluene, −78 °C	32:68 (63%)
18	(−)-**1c**	(+)-DAT	B	toluene, −78 °C	40:60
19	**11**	(−)-2,3-butanediol	A	CH_2Cl_2, 23 °C	86:14

[a] Analytical scale reactions were performed by addition of 1.5 equiv of aldehyde to an anhydrous 0.25 M solution of allylboronic ester at −78 °C. Reaction times were typically 24–48 h (see ref 22). Workup involved dilution with water and extraction with ether. [b] Diol used in preparation of boronate ester. [c] Method used for reagent preparation (see text). Tartrate allylboronates **1a–c** prepared via method B were used without purification (see Experimental Section). [d] Ratios of **6/7** and **8/9** were determined by gas chromatography (0.25 in. × 10 ft 4.1% Carbowax/Chrom G column). [e] Yields are for preparative scale experiments and are based on aldehyde as the limiting reagent. [f] See ref 5b. [g] See ref 14. [h] Yield based on boronate as the limiting reagent. [i] This experiment was performed with **4** as the limiting reagent (excess **1b**).

atmosphere at −10 °C without apparent decomposition.

Reagents **1a–c** have also been prepared by two other synthetic procedures. Method B involves the transesterification of diisopropyl allylboronate (**3**) with the appropriate chiral diol. This method was used in preliminary exploratory studies since allylboronic acid (method A) is unstable, especially when neat, necessitating that fresh **2** be prepared for each series of experiments with a new chiral diol. Since boronic esters are usually less sensitive than the corresponding acids, we hoped that a transesterification method would simplify the task of screening a range of chiral auxiliaries. Although the reaction of **3** with tartrate esters proceeds smoothly, method B suffers from the low yield and unsatisfactory purity of **3** which resulted in a lower purity of **1a–c** than that obtained via method A (see Experimental Section). In spite of this problem, however, crude **1a–c** prepared by methods A and B gave essentially identical results in aldehyde addition reactions. The third method (C) used for preparation of these reagents involves the reaction of triallylborane[12] with the appropriate tartrate ester. Although this procedure provides a very pure reagent that does not need to be distilled, it suffers from the difficulty of preparation and handling of triallylborane which is pyrophoric.

Table I summarizes the results of the reactions of **1** with α,β-dialkoxyaldehydes **4** and **5**. These aldehydes have been used extensively as probes of diastereofacial selectivity in reactions with a range of nucleophiles.[3c,5,13] It is noteworthy therefore that the tartrate ester residue effectively enhances or overrides the intrinsic facial selectivity of **4** and **5**, as measured in reactions with achiral pinacol allylboronate (**10**),[5b] thereby making possible the most selective preparations of **6–8** yet reported.[3c] Thus, whereas glyceraldehyde acetonide displays only moderate facial preference in reactions with **10** (80:20 or 71:29, depending on solvent; entries 3 and 4), selectivity for erythro alcohol **6** is enhanced to 96:4 by using reagent (−)-**1b** prepared from (+)-DIPT. With pure (+)-**1b** prepared from the antipodal (−)-DIPT, however, 92:8 selectivity for the threo adduct **7** has been achieved (compare entries 1, 4, and 6). Interestingly, the selectivity for **7** decreases somewhat when less pure reagent is used[14] (90:10, entry 7) and more significantly when **1b** is used in excess (85:15, entry 8). The 90:10 preference for **8** realized in the reaction of **5** and **10** (entries 13 and 14) is enhanced to 98:2 by using (−)-DIPT-derived (+)-**1b** (entry 12), whereas with the antipodal reagent prepared from (+)-DET the selectivity for threo adduct **9** reaches a maximal value of 68:32 (entry 17).

These examples include the most powerful cases of mismatched double asymmetric induction reported to date for reactions involving a chiral allylic organometallic reagent.[6,7] The tartrate auxiliary exerts a 1.1–1.2 kcal mol^{-1} facial bias in the mismatched reactions with both **4** (71:29 → 8:92; entries 4 and 6) and **5** (90:10 → 32:68; entries 14 and 17). That a comparably large swing in relative transition-state energies is not seen in the matched reaction (ca. 0.7 kcal/mol^{-1} for both **4** and **5**) may well reflect the optical purity of these aldehydes, especially **4**, which defines the maximal

(12) Schröder, S.; Thiele, K.-H. *Z. Anorg. Allg. Chem.* **1977**, *428*, 225.
(13) (a) Mulzer, J.; Angermann, A. *Tetrahedron Lett.* **1983**, *24*, 2843. (b) Mead, K.; Macdonald, T. L. *J. Org. Chem.* **1985**, *50*, 422.

(14) The 92:8 selectivity for **7** has been obtained with (+)-**1b** containing 0–0.2 equiv of excess (−)-DIPT. The selectivity decreases to 90:10 in the presence of 0.4 equiv of excess tartrate, to 88:12 with 1.2 equiv of excess tartrate, and to 85:15 with 2.5 equiv of excess tartrate. These experiments were performed by using pure (+)-**1b** prepared via method C to which measured quantitites of (−)-DIPT were added.

Table II. Reactions of Chiral Allylboronates with Achiral Aldehydes[a]

entry	aldehyde	reagent	diol	method[b]	reaction conditions	yield[c]	% ee[d] (config)[e]
1	2,2-dimethylpropionaldehyde	(−)-**1b**	(+)-DIPT	A	toluene, −78 °C, 4-Å sieves		82(*S*)
2	2,2-dimethylpropionaldehyde	(−)-**1b**	(+)-DIPT	B	toluene, −78 °C		78(*S*)
3	cyclohexanecarboxaldehyde	(+)-**1b**	(−)-DIPT	C	toluene, −78 °C	72%	87(*R*)
4	cyclohexanecarboxaldehyde	(−)-**1b**	(+)-DIPT	A[f]	toluene, −78 °C	77%	78(*S*)
5	cyclohexanecarboxaldehyde	(+)-**1b**	(−)-DIPT	B	toluene, −78 °C	70%	82(*R*)
6	benzaldehyde	(−)-**1b**	(+)-DIPT	A	toluene, −78 °C, 4-Å sieves	78%	71(*S*)
7	benzaldehyde	(−)-**1b**	(+)-DIPT	A	toluene, −78 °C	60%	61(*S*)
8	benzaldehyde	(−)-**1b**	(+)-DIPT	A[f]	CH_2Cl_2, −78 °C	55%	54(*S*)
9	benzaldehyde	(−)-**1b**	(+)-DIPT	A[g]	CH_2Cl_2, 23 °C	61%	30(*S*)
10	benzaldehyde	**11**	(−)-2,3-butanediol	A	CH_2Cl_2, −78 → 23°C	66%	17(*S*)
11	benzaldehyde	**12**	(−)-2,4-pentanediol	A	toluene, −78 °C	48%	~0
12	decanal	(−)-**1b**	(+)-DIPT	A	toluene, −78 °C, 4-Å sieves	86%	79(*R*)[h]
13	decanal	(−)-**1b**	(+)-DIPT	A	toluene, −78 °C	86%	69(*R*)
14	decanal	(−)-**1b**	(+)-DIPT	B	toluene, −78 °C	95%	58(*R*)
15	decanal	(−)-**1b**	(+)-DIPT	B	CH_2Cl_2, −78 °C	95%	26(*R*)

[a] Reactions were performed as described in Table I. Reaction times were typically 20–24 h (see ref 22). [b] Method used to prepare **1b** (see text). Unless noted otherwise, pure **1b** was used in cases specified by methods A and C. Reagents prepared by method B contained 0.2–0.7 equiv of excess DIPT and were used without purification. [c] Yield of chromatographically purified product. The yields in entries 1 and 2 were not determined owing to the volatility of the product. [d] Optical purities were determined by ^1H NMR analysis of the Mosher ester derivatives: Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543. [e] Absolute configurations for all products except entires 12–15 were assigned by comparison of the optical rotations with those reported in the literature (ref 9b and 15a). [f] Reagent **1b** was unpurified and contained 1.0 equiv of free DIPT. [g] Reagent **1b** was unpurified and contained 0.25 equiv of free DIPT. [h] Absolute configuration assigned by analogy to the other examples. The product in this case (79% ee) had $[\alpha]_D^{20}$ +5.8° (*c* 1.8, $CHCl_3$).

selectivity possible in these cases. The dramatic effect of solvent on stereoselectivity, however, must not be overlooked. Methylene chloride seems to favor formation of the erythro alcohols **6** and **8** in matched cases (entries 1 and 2), whereas toluene strongly influences selectivity for threo alcohols **7** and **9** in the mismatched series (entries 5–8, 15, and 16). Interestingly, the bulkiness of the tartrate residue seems to have a relatively minor effect on the reaction stereoselectivity (entries 16–18). Finally, it is noteworthy that homochiral diols such as 2,3-butanediol and 2,4-pentanediol are ineffective chiral auxiliaries for these reactions (entries 9–11, and 19).[15]

Results of reactions of **1b** with several representative achiral aldehydes are summarized in Table II. The best results have been consistently realized by using pure reagents in toluene at −78 °C in the presence of 4-Å molecular sieves. Under these conditions, homoallylic alcohols are obtained from pivaldehyde in 82% ee (entry 1), from cyclohexanecarboxaldehyde in 87% ee (entry 3), from decanal in 79% ee (entry 12), and from benzaldehyde in 71% ee (entry 6). These results clearly show that **1b** is more highly enantioselective than Hoffman's 3-phenyl-*exo*-2,3-bornanediol derivatives.[7] Moreover, it is also noteworthy that our results with pivaldehyde (82% ee) and cyclohexanecarboxaldehyde (87% ee) are competitive with those reported by Brown for reactions of pivaldehyde (83% ee) and isobutyraldehyde (90% ee) with *B*-allyl-diisopinocampheylborane.[9b]

The molecular sieves presumably help maximize the enantioselectivity of these reactions by maintaining a rigorously anhydrous reaction medium, thereby preventing adventitious hydrolysis of **1b** to achiral allylboronic acid.[16] Comparison of entries 6 and 7 and 12 and 13 shows that the enantioselectivity is somewhat lower when sieves are omitted. It is also clear that use of pure reagents even without sieves gives better results than experiments performed with tartrate ester contaminated reagents (compare entries 3–5 and 13 and 14). Entries 14 and 15 show that toluene is superior to CH_2Cl_2 as the solvent, while entries 8 and 9 reveal that low reaction temperatures are necessary to maximize enantioselectivity. Finally, it is of mechanistic interest that reagents prepared from (+)-DIPT and (−)-2,3-butanediol, which have *opposite* absolute configurations, induce *identical* absolute configurations in reactions with benzaldehyde (Table II, entries 6–9 and 10), glyceraldehyde acetonide **4**, and deoxythreose ketal **5** (see Table I).

The asymmetric induction realized with **1a–c** is consistent with major product formation occurring via transition state A.[17] The origin of asymmetry, however, cannot be explained by simple steric interactions (e.g., conventional nonbonded interactions) since the

A (favored) B (disfavored)

aldehydic R^2 substituent is too far removed to interact strongly with the tartrate ester functionality and also because the alkyl group present in the tartrate ligand seems to have a relatively minor effect on the overall reaction stereoselectivity.[18] In this respect, the tartrate auxiliary would appear to play a substantially different role than in the reactions of chiral allenylboronates described by Yamamoto.[8]

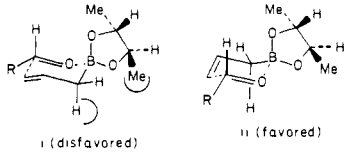
A more likely explanation is that transition state A is favored as a consequence of *n*/*n* electronic repulsive interactions involving the aldehydic oxygen atom and the β-face ester group that destabilizes B relative to A. These electronic interactions are possible since a favored conformation of the α-hetereoatom-substituted carbonyl systems is one in which the heteroatom and carbonyl are syn-coplanar.[19] Toluene, in fact, appears to be particularly effective among nonpolar solvents in stabilizing this type of conformation.[20] Although an ester carbonyl can come reasonably

(15) For several applications of these chiral diols in asymmetric synthesis, see: (a) Bartlett, P. A.; Johnson, W. S.; Elliott, J. D. *J. Am. Chem. Soc.* **1983**, *105*, 2088. (b) Sadhu, K. M.; Matteson, D. S.; Hurst, G. D.; Kurosky, J. M. *Organometallics* **1984**, *3*, 804.

(16) The observation that addition of molecular sieves improves the enantioselectivity of these reactions was first made in our laboratory by Dr. R. L. Halterman in studies of aldehyde addition reactions of tartrate ester modified (*E*)-crotylboronates (unpublished research).

(17) Stereochemical studies of crotylboronate–aldehyde addition reactions strongly suggests that R of RCHO occupies an equatorial position of a cyclic transition state (ref 3a).

(18) The selectivity predicted on steric grounds is opposite to that observed with the tartrate-based reagents but consistent with results obtained with boronate **11** prepared from (−)-2,3-butanediol. Nonbonded interactions of the ester methyl substituent and the axial allylic hydrogen presumably favors ii over i.



i (disfavored) ii (favored)

(19) (a) Kroon, J. In "Molecular Structure and Biological Activity"; Griffin, J. F., Duax, W. L., Eds.; Elsevier Biomedical: New York, 1982; p 151. (b) Karabatsos, G. J.; Fenoglio, D. J. *Top. Stereochem.* **1970**, *5*, 167.

close to the aldehydic oxygen in either A or B, the nonbonded electron pair of the aldehydic carbonyl, which is nonsymmetrically disposed relative to the dioxaborolane system, must interact more strongly with the cis ester group in B than in A. That is, we suggest that the origin of asymmetry in these reactions involves a novel and previously undocumented stereoelectronic effect.

In summary, tartrate modified allylic boronates **1a–c** offer an experimentally simple, highly attractive approach to the control of facial selectivity in reactions with chiral and achiral aldehydes. Reagent **1b** is the most highly enantioselective chiral allylboronate ester reported to date and is also a very competitive alternative to *B*-allyldiisopinocamphenylborane,[9b,c] especially for additions to substituted, α-branched aldehydes. Since the origin of asymmetry in reactions of **1b** appears to be primarily stereoelectronic in nature, an important conclusion of this study is that the design of highly effective asymmetric reagents need not depend primarily or exclusively on conventional nonbonded interactions between bulky substituents. Extensions of this strategy to other classes of reactions, including the development of efficient chiral crotylboronic esters, are in progress and will be reported in due course.

Experimental Section

General. ^{1}H NMR spectra were measured at 250 or 270 MHz on a Bruker WH-250 or WM-270 instrument. Chemical shifts are reported in δ units relative to internal $CHCl_3$ (7.24 ppm). ^{13}C NMR spectra were measured at 69 MHz on a Bruker 270 using the 77.0 ppm resonance of $CDCl_3$ as the internal standard. ^{11}B NMR spectra were measured at 28.7 MHz on a JEOL FX-90Q instrument and are reported in δ units relative to external BF_3–OEt_2. Infrared spectra were measured on a Perkin-Elmer Model 237B infrared spectrophotometer and were calibrated with the 1601-cm^{-1} absorption of polystyrene. Low- and high-resolution mass spectra were measured at 70 eV on a Finnigan MAT 8200 instrument. Optical rotations were measured on a Rudolph Autopol III polarimeter using a 1-cm^3-capacity quartz cell (10-cm path length). Elemental analyses were performed by Robertson Laboratories, Inc., Florham Park, NJ.

All reactions were conducted in oven-dried (120 °C) glassware under atmospheres of dry argon or nitrogen. All solvents were freshly distilled before use: THF, Et_2O, and toluene were distilled from sodium benzophenone ketyl; CH_2Cl_2 was distilled from CaH_2.

Analytical thin-layer chromatography (TLC) was performed by using 2.5 cm × 10 cm plates coated with a 0.25-mm layer of silica gel containing PF254 indicator (Analtech). Preparative thin-layer chromatography was performed on 20 × 20 cm plates coated with 0.25- or 0.5-mm thicknesses of silica gel containing PF 254 indicator (Analtech). Compounds were eluted from the adsorbents with diethyl ether. All chromatography solvents were distilled prior to use.

Preparation of 2-Allyl-1,3,2-dioxaborolane-4,5-dicarboxylic Acid Bis-(1′-methylethyl) Ester (1b). Method A. Allylmagnesium bromide (29.5 mL of freshly prepared 0.84 M solution in ether, 24.8 mmol, 0.9 equiv) and a solution of freshly distilled trimethyl borate (2.84 g, 27.3 mmol) in 25 mL of ether were added simultaneously, but separately, over a 30-min period to 25 mL of ether maintained at −78 °C. The mixture was stirred at −78 °C for 3 h (mechanical stirring is required due to the heavy precipitate) and then was warmed to 0 °C at which point 27 mL of cold (0 °C) 2 M aqueous HCl was added. The two-phase mixture was stirred at room temperature for 1 h and then the aqueous layer was extracted with 25-mL portions (4 times) of 5:1 Et_2O–CH_2Cl_2. The combined extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo without removal of all the solvent (anhydrous, concentrated allylboronic acid is unstable). TLC analysis (2:1 EtOAc–hexane, I_2 visualization) showed a single spot at R_f 0.57.

The crude allylboronic acid was dissolved in 45 mL of dry ether and treated with L-(+)-diisopropyl tartrate (4.01 g, 17.1 mmol, 0.7 equiv based on allylmagnesium bromide used in the previous step). The solution was stirred overnight (14 h) at 23 °C, and then anhydrous $MgSO_4$ (ca. 1 g) was added. Twenty minutes later, the solution was filtered under Ar and concentrated in vacuo. Distillation of the crude product (115–120 °C, 0.15 mm Hg) through a short path column then afforded 3.77 g of 97% pure (−)-**1b**. The yield of **1b** was 77% based on DIPT and 54% based on CH_2=$CHCH_2MgBr$. The purity of **1b** is easily determined by capillary GC analysis (0.25 mm × 12 m dimethylsilicone on fused silica column, 70 °C for 4 min and then the temperature increased at 10 °C/min to a final temperature of 200 °C). Under these conditions, DIPT elutes at 11.7 min, **1b** at 13.7 min, and an unknown minor (3%) impurity at 13.2 min. Reagent **1b** prepared in this manner has been stored at −10 °C under argon for 4–6 weeks without apparent decomposition. Hydrolysis readily occurs, however, upon exposure to moist air, wet solvents (including commercial NMR solvents), or TLC analysis. Data for (−)-**1b**: $[\alpha]^{20}_D$ +47.9 (*c* 1.96, CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 270 MHz) δ 5.91–5.78 (m, 1 H), 5.15–4.93 (overlapping m's, 4 H), 4.74 (s, 2 H), 1.98 (d, J = 7.3 Hz, 2 H), 1.26 (d, J = 6.2 Hz, 12 H); ^{1}H NMR (toluene-d_8, 250 MHz) δ 6.03–5.86 (m, 1 H), 5.06 (dd, J = 1.5, 17 Hz, 1 H), 4.96 (br d, J = 11.4 Hz, 1 H), 4.85 (quint, J = 6.2 Hz, overlapping s at 4.81, 4 H total), 1.86 (d, J = 7.2 Hz, 2 H), 0.93 (d, J = 6.6 Hz, 12 H); ^{13}C NMR ($CDCl_3$, 69 MHz) δ 168.8, 132.6, 115.8, 77.7, 70.0, 21.5; ^{11}B NMR ($CDCl_3$, 28.7 MHz) δ 35 (br; sample contained 17% of (+)-DIPT); IR (CH_2Cl_2) 3065, 2980, 2940, 2880, 1750, 1640, 1535, 1490, 1470, 1375 (br), 1280 (br), 1220 (br), 1145, 1100, 985, 960, 910, 820 cm^{-1}.

Method B. Allylboronic acid was prepared from 162 mmol of allylmagnesium bromide and 135 mmol of trimethylborate using the procedure described in method A. A solution of the crude acid in 300 mL of reagent-grade benzene was treated with 200 mmol of 2-propanol (2 equiv assuming a 75% yield of allylboronic acid) and heated to reflux until evolution of H_2O was completed (Dean-Stark trap). The solution was then fractionally distilled to give 7.5 g (bp 62–64 °C, 40 mmHg) of a 3:1 mixture of diisopropyl allylboronate (**3**) and triisopropyl borate (NMR analysis). Such mixtures could not be separated efficiently, and we were uniformly unsuccessful in attempts to suppress formation of triisopropyl borate. Consequently, material prepared in this manner was used directly in the next step. Data for a mixture of **3** and triisopropyl borate: ^{1}H NMR ($CDCl_3$, 250 MHz) δ 5.98–5.80 (m, 1 H), 4.92 (br d, J = 17.0 Hz, 1 H), 4.88 (br d, J = 12.1 Hz, 1 H), 4.45–4.28 (m of 18 lines, –OC*H*$(CH_3)_2$ of **3** and triisopropyl borate, 3 H total), 1.69 (d, J = 8.3 Hz, 2 H), 1.3–1.08 (series of d, CH(CH_3)$_2$ of **3** and triisopropyl borate, 22 H total).

To a solution of diisopropyl allylboronate (**3**) [2.83 g of a 3:1 mixture containing triisopropyl borate, thus 2.1 g (12.1 mmol) of **3**] in 15 mL of dry THF was added 4.18 g (17.9 mmol, 1.1 equiv per boron present) of (−)-DIPT. The solution was stirred at 23 °C for 24 h and then all volatiles were removed in vacuo [rotary evaporation followed by exposure to vacuum (1–2 mmHg) at 100 °C, 30 min]. NMR analysis of the colorless oil thus obtained (5.6 g) indicated a 53:33:14 mixture of **1b**, (−)-DIPT, and a minor tartrate-containing impurity presumably deriving from triisopropyl borate. This mixture, therefore, contained roughly 3.1 g of **1b** (90% yield based on available allylboronate **3**). Tartrate-modified allylboronates prepared in this manner were typically 50–65% pure, containing 25–35% free tartrate ester and 10–15% triisopropyl borate derived impurity. In all cases, they were used without further purification.

Method C. To a solution of 238 mg (1.78 mmol) of triallylborane[12] in 2.4 mL of dry THF under argon was added 354 mg (1.51 mmol, 0.85 equiv) of D-(−)-diisopropyl tartrate. This mixture was stirred at room temperature for 2 h and then was heated at reflux for 1 h. The solution was cooled, and all volatile components (including excess triallylborane) were removed in vacuo (1 mmHg, 23 °C) to give pure (+)-**1b** in quantitative yield.

***erythro*-1,2-*O*-Isopropylidenehex-5-ene-1,2,3-triol (6).** Reagent (−)-**1b** was prepared from 913 mg (6.81 mmol) of triallylborane and 1.92 g (8.18 mmol, 1.2 equiv) of (+)-DIPT in 9 mL of THF using the procedure described in method C. This gave 2.24 g (97%) of a 4.8:1 mixture of **1b** and (+)-DIPT (NMR analysis). A slight excess of DIPT was used in this experiment in order to suppress adventitious hydrolysis during the reaction with **4** described below.

To a solution of 1.64 g of this reagent [containing 1.40 g (4.9 mmol) of (−)-**1b**] in 10 mL of dry CH_2Cl_2 at −78 °C was added dropwise a solution of 0.53 g (4.1 mmol) of freshly distilled D-glyceraldehyde acetonide (**4**) in 6.4 mL of dry CH_2Cl_2. The resulting mixture was kept at −78 °C until reaction was judged complete by TLC analysis and then was worked up by pouring the cold reaction mixture into water and extracted with ether (80 mL). The aqueous phase was washed with additional portions of ether (3 × 20 mL). The combined extracts were dried (Na_2SO_4) and filtered and then the solvent was removed in vacuo.

The residue was dissolved in ether (50 mL), treated with aqueous 1 M KOH (50 mL), and stirred vigorously at 23 °C for 25 h. The aqueous phase was separated and extracted with ether (4 × 20 mL). The combined extracts were washed with saturated aqueous $NaHCO_3$ (40 mL), dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude product was then distilled (Kugelrohr, 90 °C, 1 mmHg) to give 596 mg (85%) of a 95.3:4.7 mixture of **6**/**7** (GC analysis, 0.25 in. × 10 ft 4.1% Carbowax on Chrom G column). Stereochemical assignments for these known compounds[5b,7b,13] were confirmed by repeating the correlation studies described by Mulzer.[13a]

(20) (a) Karabatsos, G. J.; Fenoglio, D. J.; Lande, S. S. *J. Am. Chem. Soc.* **1969**, *91*, 3572. (b) Karabatsos, G. J.; Taller, R. A. *Tetrahedron* **1968**, *24*, 3923.

A preparative-scale experiment (480 mg of **4**) using (−)-**1b** prepared via method B (ratio of **1b** to free (+)-DIPT to impurity = 2.8:1:1) afforded 578 mg (91%) of a 96:4 mixture of **6**/**7**. The same result in analytical-scale experiments was obtained by using the reagent prepared via method A.

Data for **6** (96% isomeric purity): $[\alpha]^{20}_D$ +16.0° (*c* 1.80, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 5.92–5.75 (m, 1 H), 5.15 (d, *J* = 16 Hz, 1 H), 5.13 (d, *J* = 10.5 Hz, 1 H), 4.05–3.87 (m, 3 H), 3.77 (d, q, *J* = 8.8, 4.4 Hz, 1 H), 2.43–2.10 (m, 2 H), 2.0 (d, *J* = 3.4 Hz, 1 H), 1.43 (s, 3 H), 1.37 (s, 3 H); IR (neat) 3470 (br), 3070, 2980, 2915, 2890, 1660, 1360, 1240, 1205, 1150, 1060, 980, 910, 855 cm^{-1}; mass spectrum, *m*/*z* 157 (M^+ − 15).

***threo*-1,2-*O*-Isopropylidenehex-5-ene-1,2,3-triol (7).** To a solution of 1.32 g of reagent (+)-**1b** prepared from (−)-DIPT as described in procedure B [a 6.4:2.6:1 mixture of (+)-**1b**, (−)-DIPT, and impurity containing, therefore, 0.87 g (3.1 mmol) of (+)-**1b**] in 13.4 mL of dry toluene at −78 °C was added dropwise a solution of freshly distilled glyceraldehyde acetonide (0.598 g, 4.60 mmol) in 4.5 mL of toluene. The solution was kept at −78 °C until reaction was judged complete by TLC analysis and then was worked up by using the procedure described for the preparation of **6**. Distillation of the crude product (Kugelrohr, 80–90 °C, 1 mmHg) afforded 420 mg (79%) of a 90:10 mixture of **7**/**6** (GC analysis). This mixture is not easily separated by chromatography (R_f 0.40, 1:1 ether–hexane). Separation of the diastereomers, however, is easily accomplished after benzylation according to Mulzer's procedure.[13a]

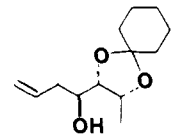
Data for **7** (90% isomeric purity): $[\alpha]^{20}_D$ +10.2° (*c* 1.82, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 5.93–5.76 (m, 1 H), 5.12 (d, *J* = 17 Hz, 1 H), 5.11 (d, *J* = 10.5 Hz, 1 H), 4.07–3.95 (m, 2 H), 3.78–3.67 (m, 1 H), 3.58 (quint, *J* = 6.3 Hz, 1 H), 3.27–2.19 (m, 3 H), 1.43 (s, 3 H), 1.36 (s, 3 H); IR (neat) 3480 (br), 3080, 2980, 2930, 2890, 1645, 1375, 1260, 1215, 1160, 1060, 915, 860 cm^{-1}.

***lyxo*-5,6-*O*-Cyclohexylidenehept-1-ene-4,5,6-triol (8).** To a solution of 1.97 g of (+)-**1b** prepared from (−)-DIPT according to method B [a 3.8:2.3:1 mixture of **1b**, DIPT, and impurity containing, therefore, 1.1 g (3.8 mmol) of **1b**] in 7.7 mL of dry CH_2Cl_2 at −78 °C was added dropwise a solution of freshly distilled **5** (584 mg, 3.18 mmol) in CH_2Cl_2 (5 mL). The mixture was maintained at −78 °C until reaction was judged complete by TLC analysis and then was worked up by using the procedure described for preparation of **6**. The crude product was distilled (Kugelrohr, 120 °C, 2 mmHg) to give 680 mg (94%) of a 98:2 mixture of **8** and **9** (GC analysis).

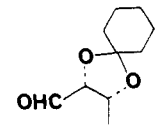
Data for **8** (98% isomeric purity): $[\alpha]^{19}_D$ +9.7° (*c* 2.03, $CHCl_3$); R_f 0.35 (2:1 hexane–ether); ^1H NMR ($CDCl_3$, 250 MHz) δ 5.92–5.76 (m, 1 H), 5.17 (br d, *J* = 16.3 Hz, 1 H), 5.14 (br d, *J* = 11.5 Hz, 1 H), 4.09 (d q, *J* = 7.7, 6.1 Hz, 1 H), 3.79–3.71 (br m, 1 H), 3.49 (d d, *J* = 5.5, 7.8 Hz, 1 H), 2.43–2.32 (m, 1 H), 2.26–2.14 (m, 1 H), 1.97 (d, *J* = 3.0 Hz, 1 H), 1.70–1.50 (m, 9 H), 1.48–1.3 (m and overlapping d, *J* = 6.0 Hz, 5 H); IR (neat) 3450 (br), 3080, 2940, 2870, 1642 cm^{-1}; mass spectrum, *m*/*e* 226 (M^+). Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.72; H, 9.80.

Diastereomer **9** could be purified by careful preparative TLC (4:1 hexane–ether, multiple elutions) of **8**/**9** mixtures: $[\alpha]^{19}_D$ +7.9° (*c* 0.19, $CHCl_3$); R_f 0.38 (2:1 hexane–ether); ^1H NMR ($CDCl_3$, 250 MHz) δ 5.91–5.78 (m, 1 H), 5.12 (br d, *J* = 17.7 Hz, 1 H), 5.10 (br d, *J* = 9.9 Hz, 1 H), 4.04 (d q, *J* = 7.9, 6.1 Hz, 1 H), 3.60–3.45 (series of m, 2 H), 2.30 (br t, *J* = 7.1 Hz, 2 H), 2.12 (d, *J* = 7.7 Hz, 1 H), 1.7–1.5 (m, 8 H), 1.48–1.3 (m, 2 H), 1.27 (d, *J* = 6.0 Hz, 3 H); high-resolution mass spectrum, obsd 226.1568 (±0.002), $C_{13}H_{22}O_3$ requires 226.1569.

In some experiments a small amount (0–5%) of a third diastereomer **13** was produced. This compound derives from erythro aldehyde **14**, small amounts of which (<5%) are present in the various batches of **5** used in this study. Data for **13**: ^1H NMR ($CDCl_3$, 250 MHz) δ



13



14

5.93–5.76 (m, 1 H), 5.19 (br d, *J* = 11.7 Hz, 1 H), 5.18 (br d, *J* = 15.0 Hz, 1 H), 4.34 (d q, *J* = 5.7, 6.5 Hz, 1 H), 3.79 (d d, *J* = 6.6, 8.8 Hz, 1 H), 3.75–3.65 (m, 1 H), 2.68–2.55 (m, 1 H), 2.26–2.14 (5 lines, 1 H), 1.68–1.50 (br m, 8 H), 1.45–1.30 (br m, 2 H), 1.28 (d, *J* = 6.4 Hz, 3 H).

Stereochemical assignments for **8**, **9** and **13** were confirmed by methanolysis (1:1 MeOH–HOAc, reflux) to the corresponding triols which were compared with authentic samples.[21]

Representative Procedure for Reactions of (−)-1b with Achiral Aldehydes. A solution of 97% pure (−)-**1b** (75 mg, 0.265 mmol, prepared via method A) and powdered 4-Å molecular sieves (50 mg) in 1.0 mL of dry toluene was cooled to −78 °C and stirred under an atmosphere of dry N_2. Cyclohexanecarboxaldehyde (45 mg, 0.4 mmol, 50 μL) was then added dropwise via syringe. The reaction vessel was immersed in a dewar containing acetone/dry ice and stored overnight in a −78 °C freezer.[22] After a total reaction time of 20 h, the mixture was quenched with an excess of ethanolic $NaBH_4$ to destroy the unreacted aldehyde and then was diluted with 10 mL of 1 N NaOH and 10 mL of ether. The two-phase mixture was stirred for 30 min at 23 °C to hydrolyze DIPT and then was extracted with Et_2O (3 × 10 mL). The combined extracts were dried (Na_2SO_4), filtered, and concentrated and then the crude product mixture was separated by PTLC (0.5-mm silica gel preparative plate, 2:1 hexane–Et_2O). The band centered at R_f 0.4 was isolated to give 39 mg (95% yield based on **1b**) of (*S*)-1-cyclohexylbut-3-en-1-ol ($[\alpha]^{22}_D$ −8.7° (*c* 0.54, EtOH) [lit.[15a] $[\alpha]_D$ −7°] for a sample of (*S*)-alcohol reported to be 64% ee). The optical purity of this material was determined to be 87% ee by the Mosher ester technique.

Acknowledgment. This research was generously supported by grants from the National Institutes of Health (GM 26782 and AI 20779). We would also like to thank Prof. K. B. Sharpless and M. G. Finn for helpful discussions throughout the course of these investigations.

(21) Roush, W. R.; Brown, R. J. *J. Org. Chem.* **1983**, *48*, 5093.

(22) **Note Added in Proof**: We have recently discovered that **1b** is much more reactive than originally presumed. For example, the reaction of **1b** (2 equiv) and cyclohexanecarboxaldehyde (0.1 M, toluene) is complete within 1 h at −78 °C. Similarly, the reactions of (+)- and (−)-**1b** with glyceraldehyde acetonide (0.2 M, toluene) are ca. 80% complete within 1 h at −78 °C but, surprisingly, require at least 24 h to reach completion. Product inhibition is suspected in these cases (Roush, W. R.; Palmer, M. A. J., unpublished research results). Details of these and related observations will be reported separately.