termined by the Mosher ester technique (500 MHz). Critical ^1H NMR resonances used in this determination are as follows. Partial data for the (*R*)-MTPA derivative of (*S*)-17: δ 3.57 (q, J = 1.2 Hz, 3 H, OMe), 0.92 (t, J = 7.4 Hz, 3 H, CH_3), and 0.88 (t, J = 7.1 Hz, 3 H, CH_3); partial data for the (*S*)-MTPA derivative of (*S*)-17: δ 3.56 (q, J =1.2 Hz, 3 H, OMe), 0.88 (t, J = 7.1 Hz, 3 H, CH_3), and 0.85 (t, J = 7.4 Hz, 3 H, CH_3). By this method it was determined that the absolute configurations of 17 deriving from (*R*)-**5c** and (*S*)-**5e** are the same (*S*).

Acknowledgment. This research was supported by grants from the National Institute of General Medical Sciences (GM 26782 and GM 38436). We thank Richard Sciotti for his assistance with the characterization of new compounds.

Asymmetric Synthesis Using Tartrate Ester Modified Allylboronates. 2. Single and Double Asymmetric Reactions with Alkoxy-Substituted Aldehydes

William R. Roush,*[1] Lee K. Hoong, Michelle A. J. Palmer, Julie A. Straub, and Alan D. Palkowitz

Department of Chemistry, Indiana University, Bloomington, Indiana 47405, and Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139

Received October 23, 1989

The reactions of tartrate allylboronates **1a** and **1b** with a series of chiral and achiral alkoxy-substituted aldehydes are described. It is shown that conformationally unrestricted α- and β-alkoxy aldehyde substituents have a significant, negative impact on the stereoselectivity of the asymmetric allylborations. For example, α-alkoxy aldehydes **25–27** and β-alkoxy aldehydes **28–30** undergo asymmetric allylborations with **1** in only 56–59% and 63–66% ee, respectively, while the reactions of **1** and aliphatic aldehydes such as decanal or cyclohexanecarboxaldehyde proceed in 86–87% ee under the same conditions. Evidence of reduced stereoselection is also apparent in the double diastereoselectivity data reported in Table I and Scheme I for the asymmetric allylborations of chiral β-alkoxy aldehydes **16** and **19** and chiral α-alkoxy aldehyde **22**. In contrast, chiral aldehydes containing alkoxy groups that are conformationally constrained by incorporation in rings, as in glyceraldehyde acetonide **4**, 4-deoxythreose ketal **7**, and α,β-epoxy aldehydes **10** and **13**, are excellent allylboration substrates, with diastereoselection in the cases of **4** and **7** being significantly greater than that obtained with simpler achiral substrates. A model that rationalizes this "alkoxy effect" is presented. Specifically, it is inferred that the observed trends in stereoselection are not steric in origin, but rather that unfavorable lone pair/lone pair interactions occur between the tartrate ester carbonyl and alkoxy substituents particularly of conformationally unconstrained aldehyde substrates (e.g., **16**, **19**, **22**, **25–30**) that results in diminished reaction stereoselection (see transition structures **58** and **61**). For substrates with conformationally constrained alkoxy substituents, e.g., **4** and **7**, favorable lone pair/dipole interactions between the tartrate ester carbonyl and the backside of the β-alkoxy C–O bond leads to increased stabilization of the favored transition state (see transition structures **59** and **60**) and hence to increased reaction diastereoselection. A simple method for the analysis of the *average diastereofacial selectivity* of a chiral reagent in a pair of double asymmetric reactions is also presented. This analysis, which is independent of the intrinsic diastereofacial bias of the chiral aldehyde, enables one to make direct comparisons of the relative diastereoselectivities of a range of chiral substrates with a given chiral reagent (or vice versa). In this way, double diastereoselectivity data are easily analyzed to determine if the chiral reagent/chiral substrate pair is "well behaved" compared to typical achiral substrate reference systems, thereby providing insight into the structural features that influence reaction stereoselectivity.

The reactions of allyl- and crotylmetal reagents with chiral carbonyl compounds are of considerable interest in the context of acyclic diastereoselective synthesis.[2] Many reagents are now available that permit high levels of simple diastereoselection (that is, the stereochemistry associated with the C–C bond formation) to be achieved in reactions with aldehydes. Like the aldol reaction, however, double asymmetric synthesis using chiral allylmetal reagents is often necessary to achieve synthetically useful levels of diastereofacial selectivity in reactions with chiral aldehydes.[2-4]

In previous papers we have shown that the tartrate allyl- and crotylboronates **1–3** are a family of readily accessible and synthetically convenient allylmetal reagents that exhibit good to excellent enantioselectivity and excellent simple diastereoselectivity in reactions with achiral aldehydes.[5] We have also shown that they function as highly diastereofacially selective chiral acetate and pro-

(1) Current address: Indiana University.

(2) (a) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555. (b) Yamamoto, Y.; Maruyama, K. *Heterocycles* **1982**, *18*, 357. (c) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 489. (d) Roush, W. R. In *Comprehensive Organic Synthesis*, Heathcock, C. H., Ed.; Pergamon Press: Oxford, 1990, Vol. 2, in press.

(3) For a review of double asymmetric synthesis, see: Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.

(4) Leading references to highly enantioselective classes of chiral allyl- and crotylmetal reagents are provided in ref 5c, the preceding paper in this issue.

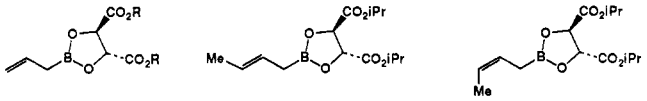
(5) (a) Roush, W. R.; Walts, A. E.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8186. (b) Roush, W. R.; Ando, K.; Powers, D. B.; Halterman, R. L.; Palkowitz, A. D. *Tetrahedron Lett.* **1988**, *29*, 5579. (c) Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Park, J. C. *J. Org. Chem.*, preceding paper in this issue.

Table I. Diastereoselectivity Data for the Reactions of Chiral Alkoxy-Substituted Aldehydes and 1

RCHO	intrinsic diastereofacial selectivity[a]	intrinsically favored diastereomer[b]	$\Sigma\Delta\Delta G^{\ddagger}$, kcal/mol	$\Delta\Delta\bar{G}_R^{\ddagger}$ (average % de)[d]
4	80:20	5	2.5	92
7	90:10	8	2.6	93
10	60:40	11	1.9	84
13	nd	14[e]	2.0	86
16	58:42	17	1.5	75
19a	52:48	20a	1.4	71
19b	54:46	20b	1.1	62
19c	54:46	20c	1.2	67
22	55:45	23	1.0	58

[a] Measured by reactions of the chiral aldehydes with achiral pinacol allylboronate. [b] The major diastereomer from the reaction with pinacol allylboronate. This diastereomer will be the major product of the matched double asymmetric reactions with 1. [c] Total free energy swing of pair of double asymmetric reactions reported in Scheme I; see eq 1 in text. [d] See eq 6 in text. [e] We infer that 14 is the intrinsically favored diastereomer in the allylborations of 13 in view of the double diastereoselection data presented in Scheme I.

pionate enolate equivalents especially in matched double asymmetric reactions with chiral aldehydes.[6]



(R,R)-1a, R = i-Pr
(R,R)-1b, R = Et

(R,R)-2

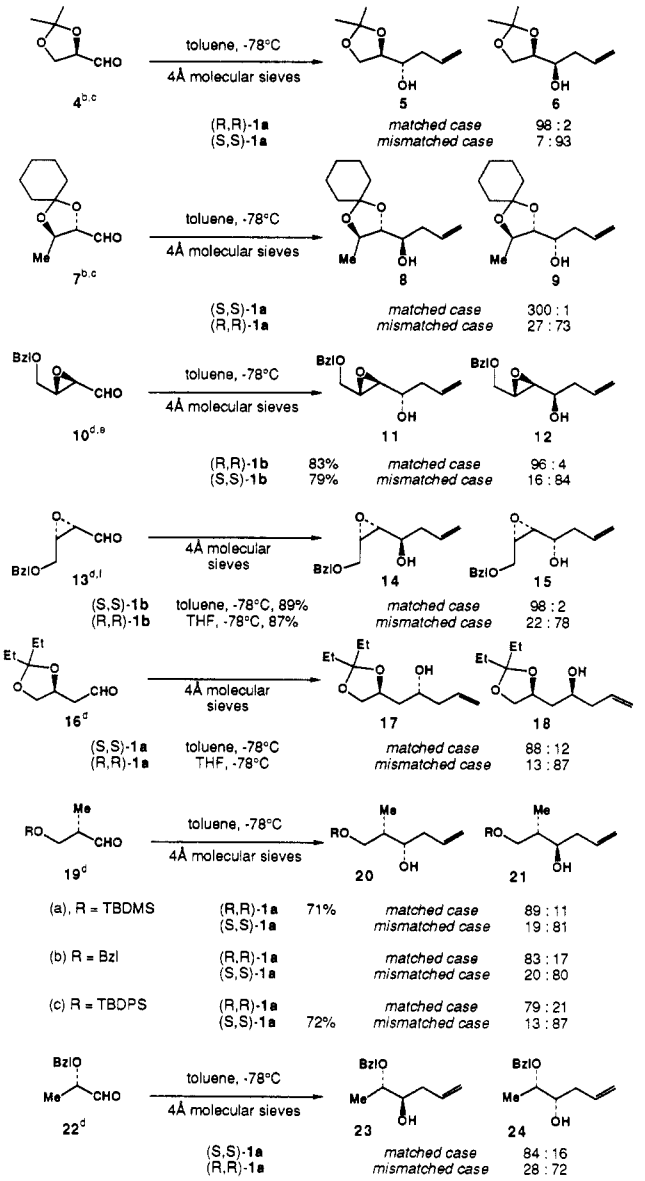
(R,R)-3

We report herein the results of a detailed study of the double asymmetric reactions of 1 and chiral, alkoxy-substituted aldehydes. We have discovered that *conformationally unrestricted* α- and β-alkoxy aldehyde substituents have a significant, negative impact on the diastereoselectivity of these reactions, while in cases where the alkoxy groups are conformationally constrained by incorporation in a ring, as in the example of glyceraldehyde acetonide (4), stereoselectivity is in fact enhanced relative to simpler achiral systems. A model that rationalizes this "alkoxy effect" is presented. We also introduce a simple method for the analysis of the *average diastereofacial selectivity* of a chiral reagent in a pair of double asymmetric reactions. This analysis, which is independent of the intrinsic diastereofacial bias of the chiral aldehyde, enables one to make direct comparisons of the relative diastereoselectivities of a range of chiral substrates with a given chiral reagent. In this way, double diastereoselectivity data are easily analyzed to determine if the chiral reagent/chiral substrate pair is "well behaved", thereby providing insight into the structural features that influence reaction stereoselectivity.

Results and Discussion

Results of the reactions of 1 with a range of chiral, alkoxy-substituted aldehydes are summarized in Scheme I. It is apparent upon inspection of these data that some aldehydes (4, 7, 10, and 13) appear to be good to excellent substrates for the asymmetric allylboration reaction, while others (16, 19, and 22) are not. Thus, the maximum diastereoselectivity obtained in the allylborations of 16, 19, and 22 is 89:11, while with 4, 7, 10, and 13 the diastereoselectivity for at least one of the reaction products (5, 8, 11, and 14, respectively, from matched double asymmetric reactions) is in excess of 96:4. Of course, it is dangerous to make direct comparisons of such diastereoselectivity data since (i) product ratios do not correlate linearly with the free energy difference between competing transition states (e.g., $\Delta\Delta G^{\ddagger}$) and (ii) the intrinsic diast-

Scheme I



[a] All reactions were performed under fully optimized conditions (ref 5c). Solvent dependencies were examined in all cases except 22, and the conditions resulting in maximum diastereoselectivity are reported here. [b] Identical diastereoselectivities were obtained by using the diethyl tartrate containing reagent 1b in place of 1a. [c] Diastereomer ratios were determined by GC as previously described (ref 5a). [d] Diastereomer ratios were determined by HPLC or GC (see the Experimental Section). [e] The enantiomeric purity of epoxy aldehyde 10 was 95% ee. Distereoselectivities in this case are uncorrected for the enantiomeric purity of 10. [f] The enantiomeric purity of epoxy aldehyde 13 was 90% ee. The diastereoselectivity reported for the experiment with (*S,S*)-1b is for a reaction that was stopped well short of completion, reflecting kinetic product formation from the major epoxy aldehyde enantiomer. The diastereoselectivity data for the mismatched double asymmetric reaction with (*R,R*)-1b are corrected for the enantiomeric purity of the isolated products, 14 in particular, with products deriving from the minor enantiomer of 13 having been deleted from the analysis. The diastereoselectivities reported in these cases thus reflect values that would be obtained if 13 were enantiomerically pure.

(6) (a) Roush, W. R.; Halterman, R. L. *J. Am. Chem. Soc.* **1986**, *108*, 294. (b) Roush, W. R.; Palkowitz, A. D.; Palmer, M. A. J. *J. Org. Chem.* **1987**, *52*, 316. (c) Roush, W. R.; Palkowitz, A. D. *J. Am. Chem. Soc.* **1987**, *109*, 953. (d) Roush, W. R.; Brown, B. B.; Drozda, S. E. *Tetrahedron Lett.* **1988**, *29*, 3541. (e) Coe, J. W.; Roush, W. R. *J. Org. Chem.* **1989**, *54*, 915. (f) Roush, W. R.; Palkowitz, A. D. *J. Org. Chem.* **1989**, *54*, 3009. (g) Roush, W. R.; Palkowitz, A. D.; Ando, K. *J. Am. Chem. Soc.*, in press.

ereofacial selectivities of the aldehydic substrates are different (refer to Table I). It stands to reason that aldehydes with greater diastereofacial preferences (e.g., **4**, **7**) will tend to give higher diastereoselectivity ratios in matched double asymmetric reactions than will aldehydes with only moderate diastereofacial preferences (e.g., **16**, **19**, **22**).[3] Consequently, it was of interest to develop a method for comparing diastereoselectivity data that is independent of the intrinsic diastereofacial bias of the substrates.

Double diastereoselectivity data are easily and unambiguously compared if first converted into $\Delta\Delta G^{\ddagger}$ values.[7] Thus, we find it convenient to calculate and compare $\Sigma\Delta\Delta G^{\ddagger}$ values, *defined as the total free energy swing for the pair of matched and mismatched double asymmetric reactions*, for sets of double asymmetric reactions (cf. Table I, column 4). The $\Sigma\Delta\Delta G^{\ddagger}$ values are obtained as indicated in eq 1 simply by adding $\Delta\Delta G_M^{\ddagger}$ and $\Delta\Delta G_{MM}^{\ddagger}$ determined from the diastereoselectivity data for the matched and mismatched double asymmetric reactions, respectively.[7] It is easily shown that $\Sigma\Delta\Delta G^{\ddagger}$ is related to the enantioselectivity (or diastereofacial selectivity) of the chiral reagent, and only of the chiral reagent, as follows.[8]

Masamune has shown that the stereoselectivity of double asymmetric reactions can be expressed in energetic terms ($\Delta\Delta G_M^{\ddagger}$ and $\Delta\Delta G_{MM}^{\ddagger}$) as indicated in eqs 2 and 3, where $\Delta\Delta G_R^{\ddagger}$ and $\Delta\Delta G_S^{\ddagger}$ describe the intrinsic diastereofacial selectivity bias of the chiral reagent and chiral substrate, respectively, while $\Delta G_{RS}^{\ddagger}$ and $\Delta G'_{RS}{}^{\ddagger}$ are correction terms added to compensate for differences (geometric, electronic, or otherwise) that may occur in the double asymmetric transition states relative to the single asymmetric models that give rise to the $\Delta\Delta G_R^{\ddagger}$ and $\Delta\Delta G_S^{\ddagger}$ terms.[3] Adding eqs 2 and 3 gives eq 4 that relates the total free energy swing ($\Sigma\Delta\Delta G^{\ddagger}$) to two times the intrinsic enantioselectivity of the chiral reagent ($2 \times \Delta\Delta G_R^{\ddagger}$) plus the aforementioned $\Delta G_{RS}^{\ddagger}$ and $\Delta G'_{RS}{}^{\ddagger}$ correction terms. It is generally assumed that if suitable single asymmetric models are chosen, then $\Delta G_{RS}^{\ddagger}$ and $\Delta G'_{RS}{}^{\ddagger}$ will be small and can be ignored.[3] Equation 5 results if this assumption is valid, indicating then that $\Sigma\Delta\Delta G^{\ddagger}$ is independent of the intrinsic diastereofacial selectivity of the chiral substrate and depends only on the intrinsic enantioselectivity of the chiral reagent ($\Delta\Delta G_R^{\ddagger}$).

Equations 2 and 3 have been recommended (the "multiplicativity rule") as a means of *predicting* the outcome of double asymmetric experiments.[3] Reliable predictions are possible, of course, only if suitable achiral substrate models are chosen such that the $\Delta G_{RS}^{\ddagger}$ and $\Delta G'_{RS}{}^{\ddagger}$ correction terms are insignificant.

For *analytical* purposes we favor the use of *average diastereofacial selectivity* data, $\Delta\Delta G^{\ddagger}_{R(av)}$, obtained simply by dividing the experimentally determined $\Sigma\Delta\Delta G^{\ddagger}$ by 2 as indicated in eq 6. This term, or the average % de values that are easily calculated from $\Delta\Delta G^{\ddagger}_{R(av)}$, defines the *average diastereofacial selectivity* exerted by the chiral reagent in each of the pair of double asymmetric reactions. Average diastereofacial selectivity $[\Delta\Delta G^{\ddagger}_{R(av)}]$ values so obtained are functionally equivalent to and may be compared with $\Delta\Delta G_R^{\ddagger}$ values determined from single asymmetric induction experiments of the chiral reagent with an achiral substrate.[9]

eq. 1 $\boxed{\Sigma\Delta\Delta G^{\ddagger} = \text{FREE ENERGY SWING} = \Delta\Delta G_M^{\ddagger} + \Delta\Delta G_{MM}^{\ddagger}}$

eq. 2 $\Delta\Delta G_M^{\ddagger} = \Delta\Delta G_R^{\ddagger} + \Delta\Delta G_S^{\ddagger} + \Delta G_{RS}^{\ddagger}$

eq. 3 $\Delta\Delta G_{MM}^{\ddagger} = \Delta\Delta G_R^{\ddagger} - \Delta\Delta G_S^{\ddagger} + \Delta G'_{RS}{}^{\ddagger}$

eq. 4 $\Sigma\Delta\Delta G^{\ddagger} = \Delta\Delta G_M^{\ddagger} + \Delta\Delta G_{MM}^{\ddagger} = 2\,\Delta\Delta G_R^{\ddagger} + \Delta G_{RS}^{\ddagger} + \Delta G'_{RS}{}^{\ddagger}$

eq. 5 $\Sigma\Delta\Delta G^{\ddagger} \approx 2\,\Delta\Delta G_R^{\ddagger}$ (if $\Delta G_{RS}^{\ddagger}$ and $\Delta G'_{RS}{}^{\ddagger}$ can be ignored)

eq. 6 $\boxed{\frac{\Sigma\Delta\Delta G^{\ddagger}}{2} = \Delta\Delta\bar{G}_R^{\ddagger} = \text{average diastereofacial selectivity of chiral reagent in pair of double asymmetric experiments}}$

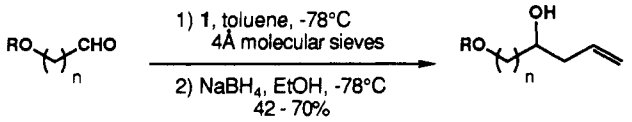
Equations 1 and 6 thus define the total free energy swing and the average diastereofacial selectivity of the chiral reagent in a pair of double asymmetric reactions. These free energy definitions of double diastereoselectivity are independent of achiral models used to determine intrinsic diastereofacial selectivity of the substrate ($\Delta\Delta G_S^{\ddagger}$) and reagent ($\Delta\Delta G_R^{\ddagger}$), and enable one to make direct comparisons of the relative diastereoselectivities of a series of chiral substrates with a given chiral reagent (as we have done in the last column of Table I for the reactions summarized in Scheme I). This is extremely useful especially when the intrinsic diastereofacial selectivities of the substrates are very different. More importantly, double diastereoselectivity data may be analyzed in this way to determine if the chiral reagent/chiral substrate pair is "well behaved", thereby providing insight into the structural

(7) As long as the reactions under consideration are kinetically controlled, then the ratio of reaction products defines $\Delta\Delta G^{\ddagger}$ for the competing transition states. This criterion applies to all of the allylborations discussed in this paper.

(8) It is intuitively obvious that the total free energy swing ($\Sigma\Delta\Delta G^{\ddagger}$) is related only to the enantioselectivity of the chiral reagent. Consider, by analogy, the reaction of an achiral aldehyde with both enantiomers of the chiral reagent. The *R* reagent will provide a predominance of one product enantiomer, while the *S* reagent will give the other enantiomer preferentially. The "total free energy swing" for this pair of single asymmetric induction experiments is then exactly equal to $2 \times \Delta\Delta G_R^{\ddagger}$, assuming of course that the % ee's for the two experiments are identical (which they must be if the two reagents are enantiomerically pure!). Thus, the definition of *average diastereofacial selectivity* in eq 6 applies both to pairs of heterochirally related single or double asymmetric experiments.

(9) (a) Double diastereoselectivity data may also be analyzed by using eq 5. Thus, the total free energy swing $[\Sigma\Delta\Delta G^{\ddagger}]$ for a pair of double asymmetric reactions may be compared to $[2 \times \Delta\Delta G_R^{\ddagger}]'$ values calculated from % ee data for the reaction of the chiral reagent and a "suitable" achiral substrate. If good agreement is found, then one can conclude that the $\Delta G_{RS}^{\ddagger}$ and $\Delta G'_{RS}{}^{\ddagger}$ correction terms of eqs 2–4 are indeed insignificant in the set of double asymmetric reactions at hand; such chiral reagent/chiral substrate pairs may be considered to be "well behaved". If the agreement is poor, however, then the chiral reagent/chiral substrate pair is regarded as problematic or not well behaved. In such cases one must conclude either that the $\Delta G_{RS}^{\ddagger}$ and $\Delta G'_{RS}{}^{\ddagger}$ terms cannot be ignored, or that the achiral substrate chosen for the determination of the reference $[2 \times \Delta\Delta G_R^{\ddagger}]'$ value was not a reasonable reference case. In either event, insight into variables or structural features that influence reaction diastereoselectivity is gained. Such comparisons are of course implicit if double diastereoselectivity data are first converted into average diastereofacial selectivity $[\Delta\Delta G^{\ddagger}_{R(av)}]$ values according to eq 6. (b) As is shown in this paper and elsewhere (refs 16, 18), the asymmetric allylboration reactions of allylboronates 1–3 are particularly sensitive to subtle electronic or dipole effects that appear in the reaction transition states. These effects essentially constitute the $\Delta G_{RS}^{\ddagger}$ and $\Delta G'_{RS}{}^{\ddagger}$ "correction" terms of eqs 2 and 3 and cannot be ignored in analyzing the double asymmetric reactions of 1–3. Many other chiral reagents, including chiral allylboron reagents, however, do not appear to be sensitive in this respect. For example, the chiral diisopinocampheylallylboranes [$(Ipc)_2$B-allyl] studied extensively by Brown and co-workers give consistently similar results (typically 88–92% ee; see ref 5c for leading references) in reactions with the same range of achiral aldehydes (aromatic, α,β-unsaturated, saturated, alkoxy-substituted) that we have studied. Calculation of the average diastereofacial selectivity according to eqs 1 and 6 for the double asymmetric reactions of $(Ipc)_2$B-allyl and related reagents provides $\Delta\Delta G^{\ddagger}_{R(av)}$ values again consistently centered about the 90% $de_{(av)}$ level. Brown's $(Ipc)_2$B-allyl reagents thus appear to be consistently well behaved with a range of chiral aldehydes. Nevertheless, we feel that it is important to analyze all double diastereoselection data according to eqs 1 and 6 since one can never be certain a priori that a suitable achiral reference model has been chosen for the prediction (eqs 2, 3) or the analysis (ref 9a) of double diastereoselectivity.

Table II. Asymmetric Allylborations of Alkoxy-Substituted Aldehydes[a]



entry	aldehyde	n	R	reagent	product[b]	% ee[c]
1	**25**	1	TBDMS	(*R*,*R*)-**1**	(*S*)-**34**	59
2	**26**	1	Bzl	(*S*,*S*)-**1**	(*R*)-**35**	59
3	**27**	1	TBDPS	(*S*,*S*)-**1**	(*R*)-**36**	56
4	**28**	2	TBDMS	(*R*,*R*)-**1**	(*S*)-**37**	66
5	**29**	2	Bzl	(*S*,*S*)-**1**	(*R*)-**38**	66
6	**30**	2	TBDPS	(*S*,*S*)-**1**	(*R*)-**39**	63
7	**31**	3	TBDMS	(*R*,*R*)-**1**	(*R*)-**40**	77
8	**32**	3	Bzl	(*R*,*R*)-**1**	(*R*)-**41**	78
9	**33**	3	TBDPS	(*R*,*R*)-**1**	(*R*)-**42**	74

[a] All reactions were performed under optimized experimental conditions (ref 5c). [b] Absolute configurations assigned by analogy to the cases discussed in text. [c] Enantiomeric excesses were determined by ^1H or ^{19}F NMR analysis of the corresponding (*R*)-MTPA ester derivatives (ref 11).

features that influence reaction stereoselectivity.[9]

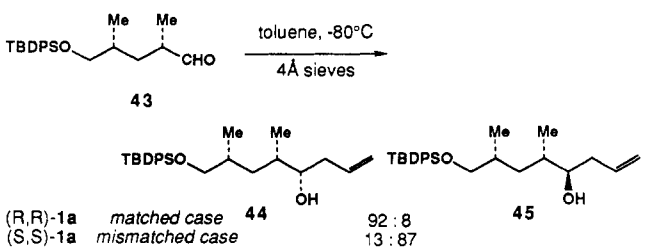
Returning now to Scheme I and Table I, it is clear that α,β-dialkoxy aldehydes **4** and **7** are considerably better than normal substrates ($\Sigma\Delta\Delta G^{\ddagger}$ = 2.5–2.6 kcal mol^{-1}, corresponding to an average diastereoselectivity of 92–93% de), while epoxy aldehydes **10** and **14** are more or less normal in behavior ($\Sigma\Delta\Delta G^{\ddagger}$ = 1.9–2.0 kcal mol^{-1}, corresponding to average stereoselectivities of 84–86% de).[10] By way of comparison, the reactions of **1** and achiral aliphatic aldehydes such as cyclohexanecarboxaldehyde and decanal proceed with 86–87% ee at −78 °C,[5c] for which $\Delta\Delta G_R^{\ddagger}$ is roughly 1.0 kcal mol^{-1}, and hence $\Sigma\Delta\Delta G^{\ddagger}$ values of ca. 2 kcal mol^{-1} are considered "normal". The significantly reduced $\Sigma\Delta\Delta G^{\ddagger}$ values realized with β-alkoxy aldehydes **16** and **19** ($\Sigma\Delta\Delta G^{\ddagger}$ = 1.2–1.5 kcal mol^{-1}) and α-alkoxy aldehyde **22** ($\Sigma\Delta\Delta G^{\ddagger}$ = 1.0 kcal mol^{-1}), however, imply that tartrate allylboronate **1** has performed at an average stereoselectivity corresponding to only 58–75% de in these cases.

As is discussed in more detail in a subsequent section, we believe that the poor performance of **16**, **19**, and **22** as substrates for the asymmetric allylboration reaction is a function of an electronic or dipole effect associated with the conformationally unconstrained alkoxy substituents at the α- and β-positions. Although steric effects cannot be ruled out entirely, since the data for **19** indicates that double diastereoselection in these cases is dependent on the protecting group—greatest selectivity for the syn diastereomer **20** occurs in matched double asymmetric reactions with the TBDMS protected aldehyde **19a**, while the TBDPS protected **19c** gave the best selectivity for the anti diastereomer **21** in the mismatched double asymmetric combination—we suspected at the outset that steric effects are not primarily responsible for the observed trends. For example, the enantioselectivity of the reactions of allylboronate **1** and decanal, cyclohexanecarboxaldehyde, and pivalaldehyde are insensitive to the steric requirements of the aldehyde: each proceeds in 86–87% ee in toluene at −78 °C.[5c]

In order to more fully assess the influence of alkoxy substituents on the enantioselectivity of the aldehyde addition reactions of tartrate allylboronate **1**, we examined the asymmetric allylborations of achiral alkoxy substituted aldehydes **25–33** (Table II). These results show clearly aldehydes possessing *conformationally unrestricted* alkoxy substituents at the α- or β-position are very poor allylboration substrates: α-alkoxy aldehydes **25–27** provide homoallylic alcohols **34–36** with only 56–59% ee, while β-alkoxy aldehydes **28–30** are only slightly better substrates, 63–66% ee for **37–39**. The enantioselectivity with γ-alkoxy aldehydes **31–33**, 74–78% ee, is further improved and closer to "normal", but is still somewhat lower ($\Delta\Delta G_R^{\ddagger}$ = 0.73–0.80 kcal mol^{-1}) than that realized in reactions with unsubstituted aliphatic aldehydes (86–87% ee, vide supra). Interestingly, the % ee data for γ-alkoxy aldehydes **31–33** are similar to that obtained for the reaction of $C_6H_{11}CHO$ in THF (78% ee).[5c]

The data in Table II show that, in contrast to the results with chiral aldehydes **19a–c**, the alcohol protecting group does not have a significant influence on the outcome of these single asymmetric induction experiments. It is also significant that the range of enantioselectivity (56–59% ee) obtained with α-alkoxy aldehydes **25–27** is essentially identical to the "average de" of 58% determined for the double asymmetric reactions of the somewhat more sterically crowded α-(benzyloxy)propionaldehyde **22**. Similarly, the % ee's obtained with β-alkoxy aldehydes **28–30** (63–66% ee) reasonably parallel the "average % de's" determined above for the reactions of **1** and chiral aldehydes **16** (75% de_{av}) and especially **19** (62–71% de_{av}). Thus, the negative "alkoxy effect" experienced by these substrates does not appear to be primarily steric in origin.

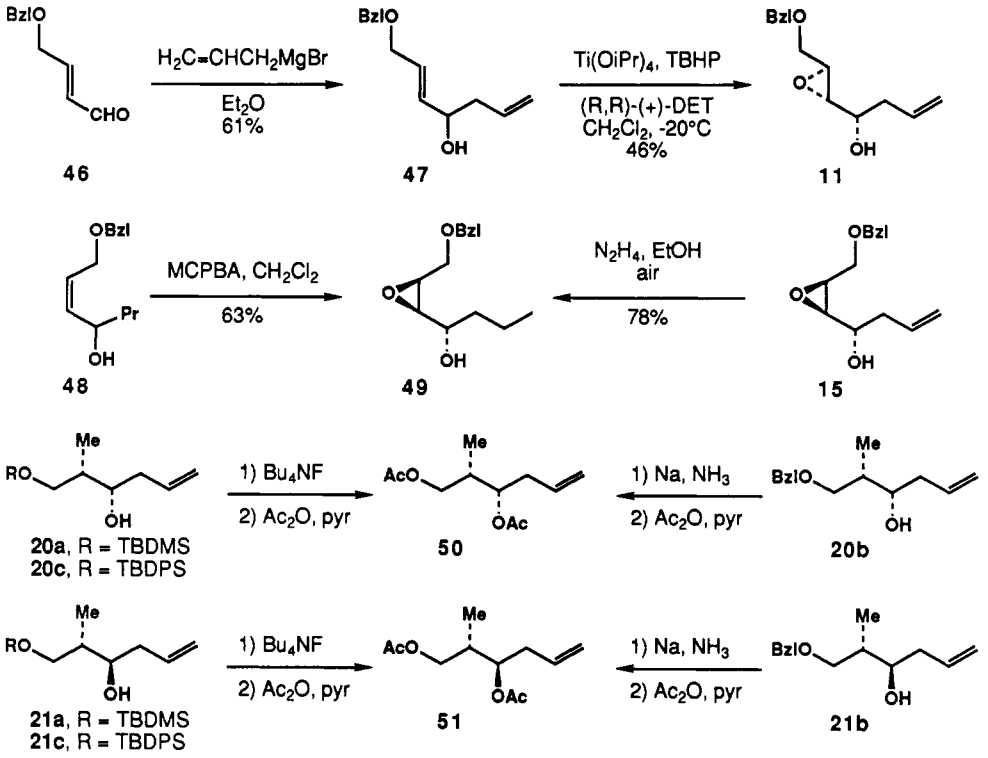
We have also studied the asymmetric allylboration of chiral aldehyde **43** in which the alkoxy group has been moved a considerable distance from the aldehydic center (cf. **31–33**).[6g] The results summarized below show that **43**, unlike **19**, is a good allylboration substrate ($\Sigma\Delta\Delta G^{\ddagger}$ = 1.7 kcal mol^{-1}, corresponding to % de_{av} of 80%). Full details for these experiments will be provided in our full paper concerning the double asymmetric reactions of **1**, **2**, and **3** and α-Me branched chiral aldehydes.[6g]



(10) For previous studies of the diastereoselective addition of carbon nucleophiles to α,β-epoxy aldehydes: (a) Takeda, Y.; Matsumoto, T.; Sato, F. *J. Org. Chem.* **1986**, *51*, 4728. (b) Molander, G. A.; Shubert, D. C. *J. Am. Chem. Soc.* **1987**, *109*, 576. (c) Howe, G. P.; Wang, S.; Proctor, G. *Tetrahedron Lett.* **1987**, *28*, 2629. (d) Iio, H.; Mizobuchi, T.; Tokoroyama, T. *Ibid.* **1987**, *28*, 2379. (e) For diastereoface selective reactions of α,β-epoxy imines: Evans, D. A.; Williams, J. M. *Ibid.* **1988**, *29*, 5065.

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

Scheme II



It is clear from the data summarized above that the α- and β-alkoxy substituents of **16**, **19**, **22**, and **25–30** exert a significant, negative influence on these asymmetric allylborations. It is also apparent that the effect is not primarily steric in origin, and that the negative influence on reaction stereoselectivity diminishes as the alkoxy group is moved out of proximity to the reactive aldehydic center (trienes **31–33**, **43**). It is curious, however, that the alkoxy substituents do not hamper the reactions of α,β-dialkoxy aldehydes **4** and **7** or those of epoxy aldehydes **10** and **13**, which, unlike the problematic substrates discussed above, have alkoxy substituents constrained within rings. This point will be addressed further in a subsequent section (Origin of Asymmetry and the Alkoxy Effect).

Absolute Stereostructural Assignments. Homoallylic alcohols **5**, **6**, **8**, **9**, **20b**, **21b**, **23**, and **24** are known compounds and have been previously fully described in the literature.[5a,12] Absolute stereochemical assignments for the epoxy aldehyde allylboration products **11**, **12**, **14**, and **15** are based on the chemistry summarized in Scheme II. Thus, an authentic sample of **11** was prepared by the Sharpless kinetic resolution–asymmetric epoxidation of racemic allylic alcohol **47**.[13] Since this kinetic resolution procedure is known to provide the erythro epoxy alcohol preferentially, the major product (**11**) of the matched double asymmetric allylboration of **10** must have the 4,5-erythro stereochemistry. Epoxy aldehyde **15**, the major product of the mismatched double asymmetric reaction of **13** and (*R*,*R*)-**1b**, was assigned the 4,5-erythro stereochemistry by diimide reduction[14] to give optically active **49** that was otherwise identical with a sample of the racemate prepared by the MCPBA epoxidation of cis-allylic alcohol **48**.[15]

Homoallylic alcohols **20a,c** and **21a,c** were correlated with the known[12a,b] benzyl ether derivatives **20b** and **21b**, respectively, by deprotection and hydrogenation of each to the corresponding *syn*- or *anti*-1,3-diacetoxy-2-methylhexanes, **50** and **51**.

The sense of asymmetric induction in each of these rigorously established examples is consistent with the stereochemical analysis presented previously, namely that the reactions of the (*R*,*R*)-tartrate derived allylboronates proceed by way of transition state A, providing an (*S*)-alcohol preferentially assuming that the "R" substituent of the aldehydic substrate takes priority over the allyl group that is transferred.[5,6] This outcome is assumed for all other asymmetric allylborations described in this paper.

Origin of Asymmetry and the Alkoxy Effect. We have suggested a stereoelectronic model for the origin of asymmetry of the tartrate allylboronates.[5a,16] We have assumed that A is favored over C as a result of n/n repulsive interactions between the aldehydic oxygen atom and the β-face ester group that destabilizes C relative to A. This requires, of course, that the ester carbonyls eclipse the adjacent C–O bonds, a conformation that is frequently favored in α-heteroatom substituted carbonyl systems.[17] For this mechanism to be correct, it is also necessary that the dioxaborolane adopt the conformation indicated in B with the two CO_2iPr groups in pseudoaxial positions. With any other conformation about the C–CO_2iPr bond or other conformations in the dioxaborolane system, the two oxygen

(12) (a) Heathcock, C. H.; Kiyooka, S.; Blumenkopf, T. A. *J. Org. Chem.* **1984**, *49*, 4214. (b) Keck, G. E.; Abbott, D. E. *Tetrahedron Lett.* **1984**, *25*, 1883. (c) Hoffmann, R. W.; Metternich, R.; Lanz, J. W. *Justus Liebigs Ann. Chem.* **1987**, 881. (d) Brown, H. C.; Bhat, K. S.; Randad, R. S. *J. Org. Chem.* **1989**, *54*, 1570.

(13) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237.

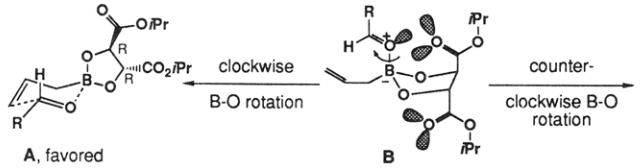
(14) Corey, E. J.; Mock, W. L.; Pasto, D. J. *Tetrahedron Lett.* **1961**, 347.

(15) MCPBA epoxidations of cis allylic alcohols provide the threo diastereomer with high selectivity: (a) Narula, A. S. *Tetrahedron Lett.* **1981**, *22*, 2017. (b) Rossiter, B. E.; Verhoeven, T. R.; Sharpless, K. B. *Ibid.* **1979**, 4733.

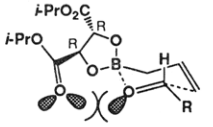
(16) Roush, W. R.; Banfi, L. *J. Am. Chem. Soc.* **1988**, *110*, 3979.

(17) (a) Karabatsos, G. J.; Fenoglio, D. J. *Top. Stereochem.* **1970**, *5*, 167. (b) Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christig, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. P. *J. Org. Chem.* **1986**, *51*, 2370. (c) Siegel, C.; Thornton, E. R. *Tetrahedron Lett.* **1988**, *29*, 5225.

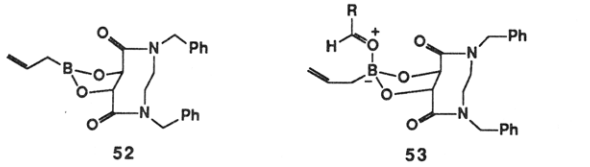
atoms are too far removed to interact. It is noted further that reasonable transition states for C–C bond formation are inaccessible if the aldehyde is symmetrically disposed with respect to the dioxaborolane system, as drawn in B. The favored transition state A is related to B in a formal sense by the indicated clockwise rotation about the B–O bond that moves the aldehyde nonbonding lone pair away from the proximate ester carbonyl. The aldehyde to boron complexation step could of course proceed directly to A, and so it is not necessary to invoke B as an intermediate. Nevertheless, this formalism is useful in that it indicates that the favored (A) and disfavored (C) transition states can be related by conformational interconversion with a common intermediate such as B.



A, favored B



C, disfavored

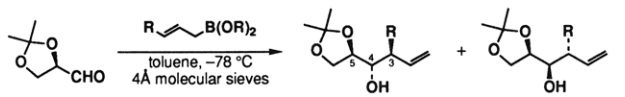


52 53

While we focused initially on lone pair/lone pair repulsive interactions that destabilize C, it is also conceivable that the favored transition state A is stabilized by a favorable charge–charge interaction between the ester carbonyl (δ^-) and the aldehydic carbonyl carbon (δ^+), owing to the proximity of these groups in A (see conformational representation in B). In support of this model, we have synthesized allylboronate **52** containing a conformationally rigid tartramide auxiliary and shown that the allylborations via **53** proceed with substantially improved enantioselectivity relative to **1**.[16] It would seem, therefore, that the lower levels of enantioselection realized with **1** and the related crotylboronates **2** and **3** compared to **52** is due to conformational heterogeneity that gives rise to competitive transition states with the same relative stereochemistry as C but with, for example, the tartrate carbalkoxyl groups in pseudoequatorial rather than pseudoaxial positions, or with the ester carbonyl groups rotated out of the plane containing the adjacent C–O bond. Such transition structures would not suffer from the destabilizing interactions indicated in C, and consequently would be expected to be closer in energy to A.

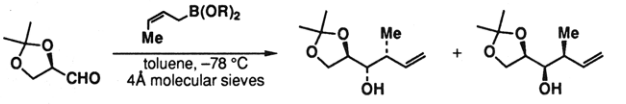
The erosion of enantioselectivity that occurs in the reactions of **1–3** with aromatic, α,β-unsaturated,[5,18] and some, but not all, alkoxyl-substituted aldehydes is curious, particularly since most other asymmetric allylboration methods do not appear to suffer in this respect.[4] We believe it is possible to rationalize the effect of alkoxy substituents in view of the origin of asymmetry model presented above. Clues that point to the involvement of subtle stereoelectronic effects are found in a detailed

Scheme III



4 **5**, R = H; **54**, R = Me **6**, R = H; **55**, R = Me

Entry	Reagent	5 : 6	$\Delta\Delta G^{\ddagger}_{reaction}$ [a] (kcal/mol)	$\Delta\Delta G^{\ddagger}_{reagent}$ [a,b] (kcal/mol)
1	(R,R)-**1**	98 : 2	1.50^{M}	0.96^{M}
2	pinacol allylboronate	80 : 20	0.54	1.54^{MM}
3	(S,S)-**1**	7 : 93	-1.00^{MM}	
		54 : 55		
4	(R,R)-**2**	91 : 9	0.88^{M}	0.80^{M}
5	pinacol (E)-crotylboronate	55 : 45	0.08	1.58^{MM}
6	(S,S)-**2**	2 : 98	-1.50^{MM}	



7 **56** **57**

		56 : 57	$\Delta\Delta G^{\ddagger}_{reaction}$ (kcal/mol)	$\Delta\Delta G^{\ddagger}_{reagent}$ (kcal/mol)
7	(R,R)-**3**	>99.8 :<0.2	$>2.40^{M}$	$>1.06^{M}$
8	pinacol (Z)-crotylboronate	97 : 3	1.34	0.70^{MM}
9	(S,S)-**3**	84 : 16	0.64^{MM}	

[a] The superscripts "M" and "MM" refer to the matched and mismatched double asymmetric reactions, respectively. [b] These values define the free energy contribution of the chiral reagents to the diastereoselection of the matched and mismatched double asymmetric reactions, respectively.

analysis of the reactions of **1–3** with glyceraldehyde acetonide **4** (Scheme III).[6a,19]

Assuming that the data cited for the reactions of **4** with the pinacol allyl- and crotylboronates provide a reasonable estimate of the intrinsic diastereofacial preference of **4** in reactions with achiral allylboronates,[20] it is apparent then that the mismatched double asymmetric reactions of **4** and the tartrate ester modified allyl- (**1**) and (*E*)-crotylboronates (**2**) proceed with much greater diastereoselectivity ($\Delta\Delta G^{\ddagger}_{reagent}$ values of 1.5–1.6 kcal/mol) than would be expected based on the reactions of **1** or **2** with achiral aldehydes such as cyclohexanecarboxaldehyde, for which $\Delta\Delta G^{\ddagger}_{reagent}$ is ca. 1 kcal mol^{-1} (vide supra).[5b,c] The contribution of the chiral reagents to the matched double diastereoselective processes ($\Delta\Delta G^{\ddagger}_{reagent}$ = 0.8–0.9 kcal mol^{-1}), however, is somewhat lower than expected based on this single asymmetric induction model. Suprisingly, the situation is exactly reversed in the reactions of **4** and the chiral (*Z*)-crotylboronate **3**: the contribution of the reagent to the matched double asymmetric process is certainly comparable to if not better than normal ($\Delta\Delta G^{\ddagger}_{reagent}$ = ≥1.1 kcal mol^{-1}; the limits of our analytical methods prevent a more accurate determination in this case), while the reagent contribution to the mismatched double asymmetric reaction ($\Delta\Delta G^{\ddagger}_{reagent}$ = 0.7 kcal mol^{-1}) is considerably lower than "normal". Data similarly generated, but not shown here, for the reactions of **1–3** and the 4-deoxythreose-derived aldehyde **7** are in excellent agreement with these conclusions.

Examination of molecular models of reasonable transition states suggests that the relative orientations of the tartrate ester carbonyl and the glyceraldehyde C(2) and

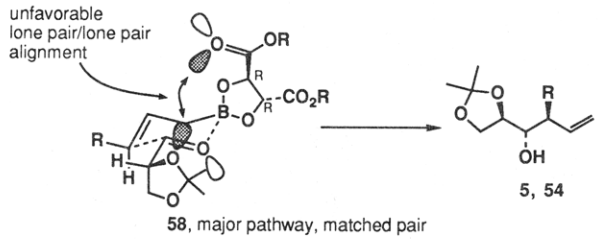
(18) Improved enantioselectivity with unsaturated aldehydes has been achieved by using metal carbonyl complexes as substrate surrogates: Roush, W. R.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 1143. These results have been interpreted in terms of a favorable dipole–dipole interaction that stabilizes transition state A.

(19) The double asymmetric reactions of **4** and **7** with the chiral (*Z*)-crotylboronate **3** were performed by Dr. R. L. Halterman (1986–87) and have not been previously published. The behavior of **7** and **3** closely parallels the data reported in Scheme III for the reactions of **4** and **3**.

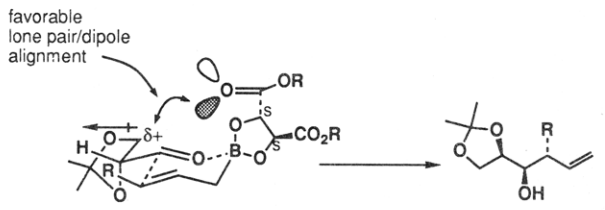
(20) For a discussion of diastereofacial selectivity of the reactions of *achiral* allylboronates and chiral aldehydes, see: (a) Hoffmann, R. W.; Weidmann, U. *Chem. Ber.* **1985**, *118*, 3966. (b) Roush, W. R.; Adam, M. A.; Walts, A. E.; Harris, D. J. *J. Am. Chem. Soc.* **1986**, *108*, 3422.

Scheme IV

Transition States for Reactions of 4 with 1 and 2:

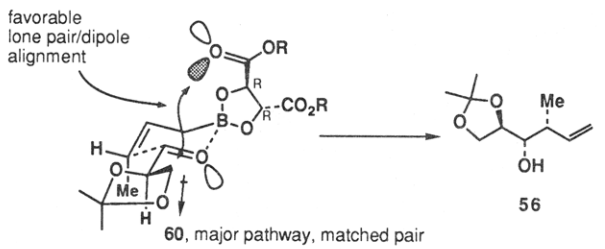


58, major pathway, matched pair 5, 54

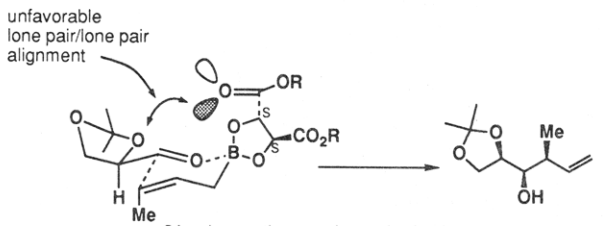


59, major pathway, mismatched pair 6, 55

Transition States for Reactions of 4 and 3:



60, major pathway, matched pair 56



61, minor pathway, mismatched pair 57

C(3) oxygen substituents may be a factor that contributes to the observed trends in diastereoselection (Scheme IV). *The conformations of the chiral aldehyde in these transition states are those that we have previously deduced for the reactions of 4 with the achiral pinacol allyl- and crotylboronates.*[20b] It is readily apparent that the ester carbonyl comes relatively close to the glyceraldehyde C(2) oxygen substituent in **58**, the major pathway of the matched double asymmetric reactions of **4** with **1** and **2**, and also in **61**, the minor pathway in the mismatched double asymmetric reaction of **4** and **3** (the intrinsic diastereofacial preference of **4** is too great for **3** to effect a complete reversal of diastereoselectivity; Scheme III, entry 8). The proximity of these groups presumably results in an unfavorable lone pair/lone pair interaction that detracts from this otherwise energetically favored arrangement ($\Delta\Delta G^{\ddagger}_{reagent}$ is only ca. 0.7–0.9 kcal mol^{-1} in these cases). As a result, transition state A (cf. **58**, **61**) is no longer as highly favored compared to C as it is in cases where this unfavorable lone pair/lone pair interaction is absent.

The situation is much different in transition states **59** and **60**, in which the ester carbonyl is positioned relatively near the backside of the glyceraldehyde C(3)–O bond. The possibility exists that **59** and **60** are additionally stabilized ($\Delta\Delta G^{\ddagger}_{reagent}$ = 1.5–1.6 kcal mol^{-1} in **59**) by a favorable lone pair/dipole interaction as indicated in Scheme IV, thereby stabilizing transition state A and increasing the energy difference between A and C.

These interactions—the dipole–dipole stabilization of transition states **59** and **60**, and the lone pair/lone pair repulsion in **58** and **61**–are essentially examples of the $\Delta G^{\ddagger}_{RS}$ and $\Delta G'^{\ddagger}_{RS}$ terms that appear in Masamune's eqs 2 and 3. They clearly are significant and cannot be ignored in any analysis of the double asymmetric reactions of **4** and the tartrate allylboronates.

We suggest that stereoelectronic effects such as those indicated in **58** and **61** are probably responsible for the drop in diastereo- or enantioselectivity in the reactions of the tartrate allylboronate **1** and alkoxy-substituted aldehydes **16**, **19**, **22**, and **25–30**. Because the alkoxy substituents of these substrates are not conformationally constrained, as they are in **4** and **7**, the possibility exists that these compounds can adopt transition-state conformations in which lone pair/lone pair interactions occur with the tartrate ester carbonyl (cf. **58**, **61**) with a corresponding decrease in the reaction diastereo- or enantioselectivity. While remote steric effects involving the alkoxyl protecting groups cannot be fully discounted, the data do not support the thesis that steric effects are primarily responsible for the observed trends—either for the good (**4**, **7**) or problematic (**16**, **19**, **22**, and **25–30**) substrates. Unfortunately, we have as yet been unable to devise definitive experiments to test this hypothesis. For the time being, therefore, this model remains our best working hypothesis for the rationalization of a surprising body of data.

Concluding Remarks

We have demonstrated that the tartrate ester modified allyl- and crotylboronates **1–3** are useful reagents for the asymmetric diastereoselective synthesis of a range of optically active, acyclic systems.[5,6] While enantio- and diastereoselectivity are excellent with many substrates, the present work demonstrates that aldehydes possessing conformationally unconstrained alkoxy substituents at the α- and β-positions (e.g. **16**, **19**, **22**, and **25–30**) constitute a subset that gives substandard levels of stereoselectivity in reactions with **1**. This poses obvious limitations of this methodology especially in mismatched double asymmetric reactions. While the enantioselectivity and reactivity characteristics of crotylboronates **2** and **3** are very similar to those of allylboronate **1**, it is fortunate for many applications in total synthesis that the detrimental "alkoxy effect" is least problematic with the (*E*)-crotyl reagent **2**.[5b] This point will be addressed further in a subsequent full paper dealing with the double asymmetric reactions of **2** and α-methyl chiral aldehydes.[6g] It is of course also possible to improve the diastereoselectivity of the asymmetric allylborations of the "problematic" alkoxy-substituted aldehydes by using more highly enantioselective reagents, e.g., **52**, which to this date remains one of the most highly enantioselective allylborating reagents yet reported.[4,16] Additional studies along these lines will be reported in due course.

Experimental Section[21]

Enantioselective Allylborations of Aldehydes. The general procedure described in our initial publication was followed,[5a] with the exception that reaction times were typically 2–3 h. Analytical-scale reactions were terminated by adding an excess of $NaBH_4$ in EtOH (precooled to the reaction temperature), while most preparative-scale reactions were directly diluted with aqueous

(21) For general comments about experimental and analytical procedures, see the accompanying paper (ref 5c).

NaOH to hydrolyze the tartrate ester. This two-phase mixture was stirred for 1–3 h, and then the product homoallylic alcohols were isolated by a standard extraction sequence and were purified chromatographically. In cases where the product homoallylic alcohols are sensitive to and do not survive the alkaline hydrolysis step (e.g., **11**–**15**), the tartrate ester was removed either by H_5IO_6 cleavage or by chromatography. Compounds **5**–**6**,[5a] **12**–**13**,[5a] **20b**–**21b**,[12a] **23**–**24**,[12a,c,d] and **35**,[22] **38**,[23] and **39**[24] are previously known compounds.

***lyxo*-(4*S*,5*S*,6*S*)-7-(Benzyloxy)-5,6-epoxyhept-1-en-4-ol (11).** Diethyl tartrate derived allylboronate (*R*,*R*)-**1b** (2.0 g of a crude preparation, estimated to be 50% pure, theoretically 4.0 mmol) was added to a −78 °C solution of epoxy aldehyde **10** (410 mg, 2.13 mmol; 95% ee) and 4-Å molecular sieves (200 mg) in 20 mL of toluene. The reaction was stirred at −78 °C for 1 h and then stored in a −78 °C freezer overnight. The mixture was then allowed to warm to 25 °C. The sieves were filtered off, saturated aqueous $NaHCO_3$ (20 mL) was added, and the solution stirred at 25 °C for 30 min. The organic layer was separated, and the aqueous phase was extracted with ether. The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated in vacuo. To this material was added 40 mL of THF and 20 mL of ether. The solution was cooled to 0 °C, and H_5IO_4 (2.29 g, 11.2 mmol) was added. The reaction was stirred at 0 °C for 50 min and then at 25 °C for 10 min. Saturated aqueous $NaHCO_3$ was added until solid stopped precipitating from solution. The solid was removed by filtration, the organic layer was separated, and the aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. By HPLC analysis (9:1 $CHCl_3$–CH_3CN, 4.6 × 250 mm ChemcoPak column packed with 3μ Chemcosorb silica gel, 0.9 mL/min) the ratio of *lyxo* (**11**) to *xylo* (**12**) diastereomers was 96:4 (**11**, R_f 13.5 min; **12**, R_f 15.1 min). The crude material was chromatographed (flash silica, 20:1 CH_2Cl_2–ether) giving 412 mg (83% yield) of **11** as a colorless liquid: $[\alpha]^{23}_D$ = −9.7° (*c* = 0.7, CH_2Cl_2); ^1H NMR ($CDCl_3$, 250 MHz) δ 7.33 (m, 5 H), 5.84 (m, 1 H), 5.18–5.11 (m, 2 H), 4.59 (d, A of AB, *J* = 12.3 Hz, 1 H), 4.54 (d, B of AB, *J* = 12.3 Hz, 1 H), 3.85 (br m, 1 H), 3.78 (dd, *J* = 3.1, 11.8 Hz, 1H), 3.48 (dd, *J* = 5.2, 11.9 Hz, 1 H), 3.27 (ddd, *J* = 3.2, 3.2, 5.6 Hz, 1 H), 2.97 (dd, *J* = 3.4, 3.4 Hz, 1 H), 2.40 (ddd, *J* = 7.8, 7.8, 14.2 Hz, 1 H), 2.30 (ddd, *J* = 7.5, 7.5, 14.2 Hz, 1 H), 1.89 (d, *J* = 2.6 Hz, 1 H, OH); IR ($CHCl_3$) 3640–3260 (OH), 3070, 3010, 2765, 1643, 1497, 1455, 1363, 1240, 1100, 910, 699 cm^{-1}; mass spectrum, *m*/*e* 243 (parent ion). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.49; H, 7.71.

***xylo*-(4*R*,5*S*,6*S*)-7-(Benzyloxy)-5,6-epoxyhept-1-en-4-ol (12).** Epoxy aldehyde **10** (382 mg, 1.98 mmol; 95% ee) was treated with excess (*S*,*S*)-**1b** in 10 mL of THF according to the procedure described for the synthesis of **11**. Analysis of the crude product by HPLC revealed that the ratio of **12** to **11** was 81:19. Chromatography of the crude product mixture (flash silica, 20:1 CH_2Cl_2–ether) afforded 315 mg of **12** (68% yield, R_f = 0.35) and 53 mg of **11** (11% yield, R_f = 0.31). The ratio of **12** to **11** was somewhat improved (84:16) by using toluene as solvent. Data for **12**: $[\alpha]^{23}_D$ = −12.3° (*c* = 0.52, CH_2Cl_2); ^1H NMR ($CDCl_3$, 250 MHz) δ 7.33 (m, 5 H), 5.81 (m, 1 H), 5.18–5.11 (m, 2 H), 4.59 (d, A of AB, *J* = 12.4 Hz, 1 H), 4.54 (d, B of AB, *J* = 12.4 Hz, 1 H), 3.76 (dd, *J* = 3.0, 11.9 Hz, 1 H), 3.62 (m, 1 H), 3.48 (dd, *J* = 5.3, 11.9 Hz, 1 H), 3.20 (ddd, *J* = 3.1, 3.1, 5.4 Hz, 1 H), 2.96 (dd, *J* = 2.6, 4.5 Hz, 1 H), 2.38 (dd, *J* = 7.2, 7.2 Hz, 2 H), 1.87 (d, *J* = 6.3 Hz, 1 H, OH); IR ($CHCl_3$) 3680, 3010, 2860, 1642, 1497, 1453, 1363, 1238, 1100, 909 cm^{-1}; mass spectrum, *m*/*e* 234 (parent ion). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.46; H, 7.73.

***ribo*-(4*R*,5*R*,6*S*)-7-(Benzyloxy)-5,6-epoxyhept-1-en-4-ol (14).** Epoxy aldehyde **13** (536 mg, 2.79 mmol; 90% ee) was treated with excess (*S*,*S*)-**1b** in toluene (40 mL) according to the procedure described for **11**. The crude material consisted of a 92:8 mixture of epoxides **14** and **15** as determined by HPLC analysis (9:1 $CHCl_3$–CH_3CN, Chemcopak column (see procedure for **11**), 0.9 mL/min flow rate, **14**, R_f = 9.9 min; **15**, R_f = 15.4 min). Chromatographic purification provided **14** in 85% yield: $[\alpha]^{23}_D$ = +28.9° (*c* = 0.87, CH_2Cl_2); ^1H NMR ($CDCl_3$, 250 MHz) δ 7.33 (m, 5 H), 5.87 (m, 1 H), 5.21–5.11 (m, 2 H), 4.61 (d, A of AB, *J* = 11.7 Hz, 1 H), 4.54 (d, B of AB, *J* = 11.7 Hz, 1 H), 3.83 (dd, *J* = 6.6, 10.6 Hz, 1 H), 3.64 (dd, *J* = 5.9, 10.7 Hz, 1 H), 3.49 (m, 1 H), 3.26 (ddd, *J* = 6, 6, 7 Hz, 1 H), 2.96 (dd, *J* = 4.5, 7.7 Hz, 1 H), 2.49 (d overlapping with m, J_d = 2.4 Hz, 2 H, OH), 2.37 (ddd, *J* = 7, 7, 14 Hz, 1 H); IR ($CHCl_3$) 3640–3300 (OH), 3005, 2915, 1642, 1497, 1454, 1215, 1080, 924, 750, 668 cm^{-1}; mass spectrum, *m*/*e* 234 (parent ion). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.75; H, 7.80.

The ratio of **14** to **15** was 98:2 from an analytical-scale reaction that was stopped short of completion. This reflects kinetic product formation from the major enantiomer of **13** (used as 90% ee).

***arabino*-(4*S*,5*R*,6*S*)-7-(Benzyloxy)-5,6-epoxyhept-1-en-4-ol (15).** Epoxy aldehyde **13** (440 mg, 2.29 mmol; 90% ee) was treated with excess (*R*,*R*)-**1b** in 20 mL of THF according to the procedure used to prepare **11**, giving a 75:25 mixture of **15** and **14** (HPLC analysis). Separation of the diastereomers by chromatography (silica, 20:1 CH_2Cl_2–ether) gave 331 mg of **15** (62% yield, 98% ee by Mosher ester analysis, R_f = 0.33) and 136 mg of **14** (25% yield, 55% ee by Mosher ester analysis, R_f = 0.47). The kinetic reaction diastereoselection, correcting for the enantiomeric purity of the reaction products, is therefore 78:22. Compound **15** was obtained as a colorless liquid: $[\alpha]^{23}_D$ = −12.1° (*c* = 0.53, CH_2Cl_2); ^1H NMR ($CDCl_3$, 250 MHz) δ 7.35 (m, 5 H), 5.80 (m, 1 H), 5.18–5.11 (m, 2 H), 4.64 (d, A of AB, *J* = 11.7 Hz, 1 H), 4.53 (d, B of AB, *J* = 11.7 Hz, 1 H), 3.72 (dd, *J* = 3.8, 11.2 Hz, 1 H), 3.60 (dd, *J* = 6.3, 11.0 Hz, 1 H), 3.55 (m, 1 H),3.31 (ddd, *J* = 4.3, 4.3, 7.3 Hz, 1 H), 3.02 (dd, *J* = 4.3, 7.3 Hz, 1 H), 2.36 (dd, *J* = 6.2, 6.2 Hz, 2 H), 2.07 (d, *J* = 3.3 Hz, 1 H, OH); IR ($CHCl_3$) 3590, 3010, 1642, 1453, 1230, 1090, 928, 820-700, 668 cm^{-1}; mass spectrum, *m*/*e* 234 (parent ion). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.91; H, 7.83.

(2*S*,4*R*)-Hept-6-ene-1,2,4-triol 1,2-(3-Pentylidene) Ketals (17 and 18). The asymmetric allylborations of **16**[25] were performed only on analytical scales. Diastereomeric mixtures were analyzed by GC (0.25 in. × 10 ft, 4.1% Carbowax/Chrom. G. column, 80 °C/2 min, then 5 °C/min to 180 °C; R_t (**18**) = 20.3 min; R_t (**17**) = 21.0 min). The two isomers only partially separated by TLC, and the data reported below were therefore obtained on diastereomeric mixtures. Stereochemical assignments rest on the well established enantioselectivity of **1**.[5,6] Interestingly, the asymmetric allylborations of the acetonide corresponding to **16** using Brown's $Ipc_2BCH_2CH{=}CH_2$ reagent have been described, with a diastereoselectivity of 9:1 being observed for the matched double asymmetric reaction leading to the diastereomer corresponding to **17**.[26]

Data for **17**: $[\alpha]^{27}_D$ −6.7° (*c* = 0.4, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 5.85–5.71 (m, 1 H), 5.15–5.06 (m, 2 H), 4.32–4.24 (m, 1 H), 4.11–4.04 (m, 1 H), 3.87–3.86 (m, 1 H), 3.54–3.44 (m, 1 H), 2.32–2.18 (m, 2 H), 1.79–1.66 (m, 2 H), 1.61 (q, *J* = 6 Hz, 4 H), 0.87 (t, *J* = 6 Hz, 6 H); IR (CCl_4) 3620, 3540, 3080, 2980, 2940, 2880, 1465, 1355, 1170, 1080, 920 cm^{-1}; mass spectrum, *m*/*e* 185 (M^+ − 28). Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 66.93; H, 10.46.

Data for **18**: $[\alpha]^{27}_D$ +5.5° (*c* = 0.9, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 5.90–5.72 (m, 1 H), 5.13–5.06 (m, 2 H), 4.35–4.15 (m, 1 H), 4.11–4.04 (m, 1 H), 3.91–3.84 (m, 1 H), 3.54–3.46 (m, 1 H), 3.19 (br s, 1 H), 2.34–2.16 (m, 2 H), 1.77–1.56 (m, 2 H), 1.64–1.57 (m, 4 H), 0.94–0.84 (m, 6 H); IR (CCl_4) 3610, 3530, 3080, 2970, 2930, 2880, 1450, 1170, 1070, 920 cm^{-1}; mass spectrum, *m*/*e* 185 (M^+ − 28). Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 66.90; H, 10.35.

(2*S*,3*S*)- and (2*S*,3*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-methylhex-5-en-3-ol (20a and 21a). Mixtures of **20a** and **21a**

(22) Takano, S.; Sekiguchi, Y.; Sato, N.; Ogasawara, K. *Synthesis* **1987**, 139.

(23) (a) Majewski, M.; Clive, D. L. J.; Anderson, P. C. *Tetrahedon Lett.* **1984**, *25*, 2101. (b) Nicolaou, K. C.; Ahn, K. H. *Tetrahedron Lett.* **1989**, *30*, 1217. This paper describes the synthesis of 74% ee **38** by using Brown's $(Ipc)_2B$-allyl reagent.

(24) Clive, D. L. J.; Murthy, K. S. K.; Wee, A. G. H.; Prasad, J. S.; da Silva, G. V. J.; Majewski, M.; Anderson, P. C.; Haugen, R. D.; Heerze, L. D. *J. Am. Chem. Soc.* **1988**, *110*, 6914.

(25) Aldehyde **16** was prepared according to the procedure of: Masamune, S.; Ma, P.; Okumoto, H.; Ellingboe, J. W.; Ito, Y. *J. Org. Chem.* **1984**, *49*, 2834.

(26) Merifield, E.; Steel, P. G.; Thomas, E. J. *J. Chem. Soc., Chem. Commun.* **1987**, 1826.

were inseparable by TLC, and small samples were separated by HPLC for spectroscopic analysis. HPLC conditions (see procedure for 11): 3% EtOAc in hexane, flow rate 1.1 mL/min, 4.6 × 250 mm Chemcopak column; t_R (**20a**) = 11.4 min; t_R (**21a**) = 10.0 min.

Data for **20a**: $[\alpha]^{25}_D$ −6.4° (*c* = 0.33, $CDCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 5.81 (ddt, *J* = 17, 11, 8 Hz, 1 H), 5.09 (m, 2 H), 3.83 (m, 1 H), 3.6–3.75 (ABX, m, 2 H), 3.05 (d, *J* = 5 Hz, 1 H), 2.21 (m, 2 H), 1.70 (m, 1 H), 0.92 (d, *J* = 7 Hz, 3 H), 0.89 (s, 9 H), 0.10 (s, 6 H); IR ($CHCl_3$) 3540, 3010, 2970, 2910, 1500 cm^{-1}; high-resolution mass spectrum for $C_{10}H_{23}O_2Si$ ($M^+ - C_3H_5$), calcd for 203.1467, found 203.1468 ± 0.0006. Anal. Calcd for $C_{13}H_{28}O_2Si$: C, 63.88; H, 11.54. Found: C, 63.69; H, 11.71.

Data for **21a**: $[\alpha]^{23}_D$ +9.5° (*c* = 1.2, $CDCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.92 (ddt, *J* = 18, 11, 7 Hz, 1 H), 5.12 (m, 2 H), 3.78 (m, 2 H), 3.62 (d, *J* = 8 Hz, 1 H), 3.60 (m, 1 H), 2.36 (m, 1 H), 2.22 (m, 1 H), 1.75 (m, 1 H), 0.93 (s, 9 H), 0.87 (d, *J* = 7 Hz, 3 H), 0.11 (s, 6 H); IR ($CDCl_3$) 3530, 3010, 2980, 2910, 1475 cm^{-1}; high-resolution mass spectrom for $C_{10}H_{23}O_2Si$ ($M^+ - C_3H_5$), calcd for 203.1467, found 203.1468 ± 0.0002. Anal. Calcd for $C_{13}H_{28}O_2Si$: C, 63.88; H, 11.54. Found: C, 63.56; H, 11.85.

(2*S*,3*S*)- and (2*S*,3*R*)-1-(Benzyloxy)-2-methylhept-5-en-3-ol (20b and 21b). These compounds have previously been reported in the literature.[12] Mixtures were separated by HPLC to generate the samples used in the correlation studies subsequently described (5% EtOAc in hexane, 1.1 mL/min, 4.6 × 250 mm Chemcopak column, 3μ Chemcosorb silica gel; t_R (**20b**) = 30.6 min; t_R (**21b**) = 29.3 min).

(2*S*,3*S*)- and (2*S*,3*R*)-1-[(*tert*-Butyldiphenylsilyl)oxy]-2-methylhex-5-en-3-ol (20c and 21c). Mixtures of **20c** and **21c** were separated by HPLC to provide small samples for spectroscopic analysis (3% EtOAc in hexane, 1.1 min/min, 4.6 × 250 mm Chemcopak column; t_R (**20c**) = 15.7 min; t_R (**21c**) = 13.2 min).

Data for **20c**: $[\alpha]^{25}_D$ = −2.3° (*c* = 0.90, $CHCl_3$); ^1H NMR ($CDCl_3$, 250 MHz) δ 7.65 (m, 4 H), 7.40 (m, 6 H), 5.83 (ddt, *J* = 15, 10, 7 Hz, 1 H), 5.10 (m, 2 H), 3.92 (m, 1 H), 3.75 (A of ABX, *J* = 4.5, 9.5 Hz, 1 H), 3.68 (B of ABX, *J* = 6.0, 9.5 Hz, 1 H), 2.80 (d, *J* = 5 Hz, 1 H), 2.24 (m, 2 H), 1.76 (m, 1 H), 1.06 (s, 9 H), 0.93 (d, *J* = 7 Hz, 3 H); IR ($CHCl_3$) 3590, 3080, 3030, 3000, 2925, 1400, 1125 cm^{-1}; high-resolution mass spectrum for $C_{19}H_{23}O_2Si$ (M^+ − *t*-Bu) 311.1467, found 311.1464 ± 0.0006. Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75. Found: C, 74.57; H, 8.75.

Data for **21c**: $[\alpha]^{25}_D$ +4.1° (*c* = 1.3, CCl_4); ^1H NMR ($CDCl_3$, 250 MHz) δ 7.65 (m, 4 H), 7.41 (m, 6 H), 5.92 (m, 1 H), 5.12 (m, 2 H), 3.80–3.60 (m, 3 H), 3.51 (d, *J* = 2.8 Hz, 1 H, OH), 2.36 (m, 1 H), 2.20 (m, 1 H), 1.80 (m, 1 H), 1.04 (s, 9 H), 0.83 (d, *J* = 7 Hz, 3 H); IR ($CDCl_3$) 3540, 3110, 3040, 3000, 2970, 2890, 1500, 1450, 1420, 1120 cm^{-1}; high-resolution mass spectrum for $C_{19}H_{23}O_2Si$ (M^+ − *t*-Bu) 311.1467, found 311.1464 ± 0.0006. Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75. Found: C, 74.91; H, 8.83.

(2*S*,3*R*)- and (2*S*,3*S*)-2-(Benzyloxy)hex-5-en-3-ol (23 and 24). These compounds have previously been reported in the literature.[12a,c,d] Mixtures were separated by TLC for ^1H NMR analysis. The stereochemical correlation described by Heathcock was repeated to confirm the structural assignments.[12a]

(*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-2-hydroxypent-4-ene (34): $[\alpha]^{20}_D$ +1.7° (*c* = 0.24, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.91–5.76 (m, 1 H), 5.14–5.05 (m, 2 H), 3.80–3.65 (m, 1 H), 3.63 (dd, *J* = 10.8, 4.0 Hz, 1 H), 3.44 (dd, *J* = 10.8, 6.0 Hz, 1 H), 2.42 (d, *J* = 3 Hz, 1 H, OH), 2.24 (t, *J* = 7.2 Hz, 2 H), 0.90 (s, 9 H), 0.07 (s, 6 H); IR (neat) 3450 (br), 2960, 2930, 2860, 1730, 1642, 1470, 1465, 1255, 1110, 910, 835, 775, 735 cm^{-1}; high-resolution mass spectrum [CI] for $C_{11}H_{25}O_2Si$ (M^+ + 1) 217.1624, found 217.1623. Anal. Calcd for $C_{11}H_{24}O_2Si$: C, 61.03; H, 11.18. Found: C, 60.70; H, 11.21.

(*R*)-1-(Benzyloxy)-2-hydroxypent-4-ene (35). A previously known compound:[22] $[\alpha]^{20}_D$ +1.7°, $[\alpha]^{20}_{546}$ +1.8° (*c* = 2.27, $CHCl_3$) [lit.[22] $[\alpha]^{29}_D$ −3.1° (*c* = 2.03, $CHCl_3$)] for >95% ee (*R*)-**35**; ^1H NMR ($CDCl_3$, 300 MHz) δ 7.37–7.32 (m, 5 H), 5.90–5.77 (m, 1 H), 5.16–5.08 (m, 2 H), 4.56 (s, 2 H), 3.94–3.85 (m, 1 H), 3.55–3.51 (dd, *J* = 10, 3.7 Hz, 1 H), 3.41–3.36 (dd, *J* = 9.3, 7.4 Hz, 1 H), 2.37 (d, *J* = 3.52 Hz, 1 H), 2.28 (t, *J* = 6.6 Hz, 2 H); IR (neat) 3435 (br), 3060, 3025, 2910, 2855, 1640, 1495, 1451, 1271, 1110, 915, 735, 697 cm^{-1}; high-resolution mass spectrum [CI] for $C_{12}H_{16}O_2$ 192.1150, found 192.1153.

(*R*)-1-(*tert*-Butyldiphenylsiloxy)-2-hydroxypent-4-ene (36): $[\alpha]^{20}_D$ +0.8°, $[\alpha]^{20}_{436}$ +2.7°, $[\alpha]^{20}_{365}$ +6.8° (*c* = 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.74–7.66 (m, 4 H), 7.45–7.37 (m, 6 H), 5.87–5.74 (m, 1 H), 5.12–5.05 (m, 2 H), 3.82–3.77 (br m, 1 H), 3.70–3.66 (dd, *J* = 10.8, 3 Hz, 1 H), 3.59–3.53 (dd, *J* = 10.8, 7 Hz, 1 H), 2.48 (d, *J* = 2.6 Hz, 1 H), 2.25 (t, *J* = 6.51 Hz, 2 H), 1.08 (s, 9 H); IR (neat) 3565, 3430 (br), 3070, 3045, 2960, 2855, 1640, 1589, 1110 cm^{-1}; high-resolution mass spectrum [CI] for $C_{21}H_{27}OSi$ (M^+ − 17) 323.1831, found 323.1808. Anal. Calcd for $C_{21}H_{28}O_2Si$: C, 74.07; H, 8.29. Found: C, 73.74; H, 8.01.

(*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-hydroxyhex-5-ene (37): $[\alpha]^{20}_D$ −4.8°, $[\alpha]^{20}_{436}$ −9.3°, $[\alpha]^{20}_{365}$ −14.5° (*c* = 0.91, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.92–5.78 (m, 1 H), 5.14–5.08 (m, 2 H), 3.94–3.78 (m, 3 H), 3.40 (br s, 1 H), 2.31–2.20 (m, 2 H), 1.70–1.64 (m, 2 H), 0.90 (s, 9 H), 0.08 (s, 6 H); IR (neat) 3420 (br), 3068, 2950, 2925, 2850, 1638, 1468, 1250, 1085, 998, 908, 830, 770 cm^{-1}; high-resolution mass spectrum [CI] for $C_{12}H_{27}O_2Si$ (M^+ + 1) 231.1780, found 231.1773. Anal. Calcd for $C_{12}H_{26}O_2Si$: C, 62.55; H, 11.37. Found: C, 62.19; H, 11.47.

(*R*)-1-(Benzyloxy)-3-hydroxyhex-5-ene (38). A previously known compound:[23] $[\alpha]^{20}_D$ +1.5°, $[\alpha]^{20}_{436}$ +3.8°, $[\alpha]^{20}_{365}$ +7.8° (*c* = 1.12, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.38–7.28 (m, 5 H), 5.91–5.78 (m, 1 H), 5.14–5.08 (m, 2 H), 4.53 (s, 2 H), 3.92–3.84 (m, 1 H), 3.76–3.61 (m, 2 H), 2.89 (br s, 1 H), 2.25 (t, *J* = 7.2 Hz, 2 H), 1.82 (m, 2 H); IR (neat) 3440 (br), 3065, 3030, 2920, 2860, 1745, 1640, 1496, 1454, 1364, 1100, 1026, 995, 910, 732, 698 cm^{-1}; high-resolution mass spectrum [CI] for $C_{13}H_{18}O_2$ 206.1307, found 206.1282.

(*R*)-1-(*tert*-Butyldiphenylsiloxy)-3-hydroxyhex-5-ene (39). A previously known compound:[24] $[\alpha]^{20}_D$ +2.2°, $[\alpha]^{20}_{436}$ +5.3°, $[\alpha]^{20}_{365}$ +8.8° (*c* = 0.49, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.68 (d, *J* = 7.2 Hz, 4 H), 7.47–7.37 (m, 6 H), 5.92–5.78 (m, 1 H), 5.13–5.08 (m, 2 H), 4.0–3.92 (br, m, 1 H), 3.92–3.79 (m, 2 H), 3.25 (br s, 1 H), 2.28 (t, *J* = 6 Hz, 2 H), 1.77–1.64 (m, 2 H), 1.05 (s, 9 H); IR (neat) 3470 (br), 3070, 2930, 2860, 1640, 1590, 1472, 1430, 1110, 910, 820, 735, 700 cm^{-1}; high-resolution mass spectrum [CI] for $C_{22}H_{30}O_2Si$ (M^+ − 17) 337.1987, found 337.1983.

(*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-4-hydroxyhept-6-ene (40): $[\alpha]^{20}_D$ +5.1° (*c* = 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.91–5.77 (m, 1 H), 5.15–5.08 (m, 2 H), 3.68–3.60 (m, 3 H), 2.64 (br s, 1 H), 2.32–2.14 (m, 2 H), 1.69–1.41 (m, 4 H), 0.90 (s, 9 H), 0.08–0.04 (m, 6 H); IR (neat) 3380 (br), 2930, 2860, 1645, 1475, 1255, 1095, 1005, 910, 835, 775 cm^{-1}; high-resolution mass spectrum [CI] for $C_{13}H_{29}O_2Si$ (M^+ + 1) 245.1937, found 245.1935. Anal. Calcd for $C_{13}H_{28}O_2Si$: C, 63.87; H, 11.55. Found: C, 63.92; H, 11.78.

(*R*)-1-(Benzyloxy)-4-hydroxyhept-6-ene (41): $[\alpha]^{20}_D$ +5.2°, $[\alpha]^{20}_{436}$ +9.6°, $[\alpha]^{20}_{365}$ +13.9° (*c* = 1.05, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.38–7.27 (m, 5 H), 5.91–5.77 (m, 1 H), 5.16–5.09 (m, 2 H), 4.52 (s, 2 H), 3.71–3.63 (m, 1 H), 3.52 (dd, *J* = 5.8 Hz, *J* = 6.5 Hz, 2 H), 2.40–2.14 (m, 3 H), 1.80–1.40 (m, 4 H); IR (neat) 3420 (br), 3070, 3030, 2930, 2860, 1640, 1495, 1455, 1360, 1205, 1100, 1025, 995, 913, 735, 695 cm^{-1}; high-resolution mass spectrum [CI] for $C_{14}H_{21}O_2$ (M^+ + 1) 221.1542, found 221.1545. Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 75.98; H, 9.14.

(*R*)-1-(*tert*-Butyldiphenylsiloxy)-4-hydroxyhept-6-ene (42): $[\alpha]^{20}_D$ +1.6°, $[\alpha]^{20}_{546}$ +2.0° (*c* = 0.76, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 7.67 (dd, *J* = 7.4 Hz, *J* = 1.5 Hz, 4 H), 7.47–7.36 (m, 6 H), 5.92–5.77 (m, 1 H), 5.16–5.11 (m, 2 H), 3.71 (m, 3 H), 2.34–2.14 (m, 3 H), 1.74–1.45 (m, 4 H), 1.06 (s, 9 H); IR (neat) 3400 (br), 3068, 2930, 2855, 1640, 1590, 1472, 1429, 1110, 910, 820, 735, 700 cm^{-1}; high-resolution mass spectrum [CI] for $C_{23}H_{33}O_2Si$ (M^+ + 1) 369.2250, found 369.2295. Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75. Found: C, 74.67; H, 8.83.

Synthesis of (−)-*lyxo*-(4*S*,5*S*,6*S*)-7-(Benzyloxy)-5,6-epoxyhept-1-en-4-ol (11) via Asymmetric Epoxidation of 47. Allylmagnesium bromide (2.6 mL, 1 M in ether, 2.6 mmol) was added dropwise to a 0 °C solution of *trans*-4-(benzyloxy)-2-butenal **46** (446 mg, 2.53 mmol) in ether (2.6 mL). The reaction was stirred at 0 °C for 45 min, and then hydrolyzed with saturated aqueous NH_4Cl. The organic layer was separated, and the aqueous layer was extracted with ether. The combined organic extracts were washed with brine, and the brine layers were back extracted with ether. The combined organic phases were dried with $MgSO_4$, filtered, and concentrated in vacuo. The crude product was chromatographed (silica, 20:1 CH_2Cl_2–ether), yielding 339 mg of **47** (61% yield) that was sufficiently pure for use directly in the following experiment: ^1H NMR ($CDCl_3$, 250 MHz) δ 7.33 (m, 5

H), 5.80 (m, 3 H), 5.14 (d, J = 16.5 Hz, 1 H), 5.13 (d, J = 11.8 Hz, 1 H), 4.51 (s, 2 H), 4.19 (m, 1 H), 4.02 (dd, J = 2.0, 4.5 Hz, 2 H), 2.30 (m, 2 H), 1.67 (d, J = 3.9 Hz, 1 H, OH); IR ($CHCl_3$) 3610, 3460, 3015, 2865, 1644, 1469, 1363, 1210, 1090, 970, 692 cm^{-1}; mass spectrum, m/e 218 (parent ion); high-resolution mass spectrum for $C_{14}H_{18}O_2$ calcd 218.1307, found 218.1308.

Allylic alcohol **47** (48 mg, 0.22 mmol) in 0.5 mL of CH_2Cl_2 was added to a −20 °C solution of $Ti(OiPr)_4$ (0.24 mL, 0.08 mmol) and (+)-DET (18 mg, 0.09 mmol) in 0.5 mL of CH_2Cl_2. The mixture was stirred at −20 °C for 30 min, and then TBHP (0.026 mL, 4.26 M in CH_2Cl_2, 0.11 mmol) was added, and the reaction stored at −20 °C for 17 h. The reaction mixture was diluted with ether and washed with 1 N NaOH. The aqueous layer was extracted with ether. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting material was chromatographed (silica gel preparative TLC, 1:1 ether–hexane), affording 24 mg of **11** (93% based on TBHP, 46% based on **41**) and 24 mg of recovered **41**. Epoxy alcohol **11** prepared by this epoxidation method, which is known to give the erythro epoxide,[13] was identical to **11** prepared by the addition of (*R,R*)-**1b** to epoxy aldehyde **10**.

***cis*-1-(Benzyloxy)hept-2-en-4-ol (48).** *n*-BuLi (0.24 mL, 2.7 M in hexane, 0.65 mmol) was added dropwise to propargyl benzyl ether (94 mg, 0.65 mmol) in 8 mL of ether at −78 °C, and the reaction was stirred at −78 °C for 2.5 h. Butyraldehyde (0.06 mL, 0.68 mmol) was added, and the solution stirred at −78 °C for 1 h. The reaction was allowed to warm to 25 °C over 30 min and was then quenched with saturated aqueous NH_4Cl. The ether layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. The resulting liquid was chromatographed (0.5 mm silica gel preparative TLC plate, 1:1 ether–hexane) giving 98 mg of the propargyl alcohol (70%) as a colorless liquid: ^1H NMR ($CDCl_3$, 250 MHz) δ 7.32 (m, 5 H), 4.56 (s, 2 H), 4.41 (m, 1 H), 4.18 (s, 2 H), 1.80–1.30 (complex m, 5 H), 0.93 (t, J = 7.3 Hz, 3 H); IR ($CHCl_3$) 3600, 2980, 1455, 1200, 1065, 708 cm^{-1}.

The above propargyl alcohol (61 mg, 0.028 mmol) was hydrogenated (1 atm H_2) over 10% Pd/Pb on carbon catalyst (5 mg) in 2 mL of MeOH for 9.5 h. The solution was filtered and concentrated in vacuo. Chromatography (silica gel preparative TLC, 1:1 ether–hexane) of the crude product afforded 45 mg (73% yield, R_f = 0.34) of allylic alcohol **48** along with 6 mg of the saturated alcohol that is the product of overreduction (R_f = 0.43). Compound **48** was obtained as a colorless liquid: ^1H NMR ($CDCl_3$, 250 MHz) δ 7.32 (m, 5 H), 5.68 (ddd, J = 7, 7, 12 Hz, 1 H), 5.60 (dd, J = 8, 12 Hz, 1 H), 4.50 (s, 2 H), 4.35 (m, 1 H), 4.14 (m, 1 H), 4.02 (ddd, J = 2.1, 5.3, 11.7 Hz, 1 H), 1.9–1.2 (complex m, 5 H), 0.89 (t, J = 6.5 Hz, 3 H); IR ($CHCl_3$) 3600, 2965, 2875, 1455, 1202, 1065, 1000, 687 cm^{-1}; mass spectrum, m/e 220 (parent ion). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.41; H, 9.31.

(±)-*arabino*-7-(Benzyloxy)-5,6-epoxy-4-heptanol [(±)-49]. A solution of allylic alcohol **48** (25 mg, 0.11 mmol) and MCPBA (25 mg, 0.14 mmol) in 1 mL of CH_2Cl_2 was stored at 0 °C for 19 h. The reaction was diluted with CH_2Cl_2 and washed with saturated aqueous $NaHSO_3$ and saturated aqueous $NaHCO_3$. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. Chromatography (0.5 mm silica gel PTLC plate, 20:1 CH_2Cl_2–ether) of the crude product yielded 17 mg of *arabino* epoxide **49** (63% yield, R_f = 0.20):[15] ^1H NMR ($CDCl_3$, 250 MHz) δ 7.34 (m, 5 H), 4.61 (d, A of AB, J = 12.6 Hz, 1 H), 4.54 (d, B of AB, J = 12.6 Hz, 1 H), 3.72 (dd, J = 5.8, 9.9 Hz, 1 H), 3.61 (dd, J = 6.4, 10.7 Hz, 1 H), 3.48 (m, 1 H), 3.33 (ddd, J = 6, 6, 5 Hz, 1 H), 2.98 (dd, J = 4.5, 7.8 Hz, 1 H), 2.00 (d, J = 3.4 Hz, 1 H, OH), 1.7–1.3 (complex m, 4 H), 0.94 (t, J = 7.3 Hz, 3 H); IR (CH_2Cl_2) 3600, 2930, 2865, 1455, 1250, 1075, 675 cm^{-1}; mass spectrum, m/e 236 (parent ion); high-resolution mass spectrum for $C_{14}H_{20}O_3$ calcd 236.1412, found 236.1412.

(4*S*,5*S*,6*S*)-*arabino*-7-(Benzyloxy)-5,6-epoxy-4-heptanol [(−)-49]. A solution of epoxy alcohol **15** (9 mg, 0.04 mmol) in 1 mL of EtOH was treated with $N_2H_4 \cdot H_2O$ (0.02 mL, 0.41 mmol).[14] The reaction mixture was stirred vigorously at 25 °C for 22 h while open to the air. Ether was added, and the solution was washed with brine. The aqueous layer was back extracted with ether. The combined organic layers were dried over $MgSO_4$, filtered, and concentrated in vacuo. Chromatography (0.25 mm silica gel PTLC plate, 20:1 CH_2Cl_2–ether) afforded 7 mg (78%) of (−)-**49** [$[\alpha]^{23}_D$ = −5.0° (c = 0.70, CH_2Cl_2)], the ^1H NMR spectrum and analytical TLC profile of which were identical with those of (±)-**49** prepared through the MCPBA epoxidation of **48**.

(2*S*,3*S*)-1,3-Diacetoxy-2-methylhex-5-ene (50). A. From 20a and 20c. Alcohols **20a** and **20c** (ca. 8–10 mg each; separate experiments) were dissolved in 1 mL of dry THF. Bu_4NF (1.5 equiv) was then added, and the mixture was stirred at 23 °C for 1 h. The solution was diluted with aqueous $NaHCO_3$ and extracted with Et_2O (3 × 2 mL). The extracts were dried ($MgSO_4$), filtered, and concentrated to give the crude diol that was treated with 0.025 mL of acetic anhydride in 0.3 mL of pyridine. The acylation was worked up in the usual way to provide **50** following chromatographic purification.

B. From 20b. To a three-neck flask equipped with a dry ice condensor containing 10 mL of liquid NH_3 at −78 °C was added **20b** (30 mg, 0.14 mmol) in 1 mL of dry ether and Na (21 mg, 0.61 mmol). The cooling bath was removed, and the solution was allowed to reflux for 1 h. Saturated aqueous NH_4Cl was then added, and the NH_3 was allowed to evaporate. The crude diol was isolated by extraction and then acylated as described above to provide **50**: $[\alpha]^{23}_D$ +3.3° (c = 0.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.79–5.66 (m, 1 H), 5.15–4.97 (m, 3 H), 4.03–3.84 (m, 2 H), 2.43–2.24 (m, 2 H), 2.14–1.98 (m, 1 H), 2.06 (s, 3 H), 2.03 (m, 3 H), 0.97 (d, J = 7 Hz, 3 H); IR ($CHCl_3$) 2980, 1730, 1370, 1245, 1030, 1020, 980, 915, 750 cm^{-1}; high-resolution mass spectrum (CI) for $C_{11}H_{19}O_4$ (M^+ + 1) calcd 215.1283, found 215.1295. Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.88 ; H, 8.45.

(2*S*,3*R*)-1,3-Diacetoxy-2-methylhex-5-ene (51). Silyl ethers **21a** and **21c** and benzyl ether **21b** were converted to anti-diacetate **51** by using the procedures described for the synthesis of **50**: $[\alpha]^{23}_D$ +7.6° (c = 0.5, $CHCl_3$) (rotation obtained on a ca. 3:1 mixture of diastereomers); ^1H NMR ($CDCl_3$, 300 MHz) δ 5.82–5.65 (m, 1 H), 5.15–5.03 (m, 2 H), 4.97–4.87 (m, 1 H), 4.10–3.96 (m, 2 H), 2.47–2.22 (m, 2 H), 2.06 (s, 3 H), 2.04 (m, 3 H), 2.14–1.98 (m, 1 H), 0.97 (d, J = 7 Hz, 3 H); IR ($CHCl_3$) 2980, 1730, 1370, 1245, 1030, 1020, 980, 750 cm^{-1}; high-resolution mass spectrum (CI) for $C_{11}H_{19}O_4$ (M^+ + 1) calcd 215.1283, found 215.1282. Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.94; H, 8.32.

Acknowledgment. This research was supported by grants from the National Institute of General Medical Sciences (GM 38436 and GM 26782).