soluble in hydrocarbon solvents. ^{13}C NMR in toluene-d_8 charged with 3.0 equiv of THF contained no resonances attributable to the tetramethylpiperidyl residue. ^{13}C NMR spectra of $\mathbf{2}_{\text{solvent-free}}$ with added diisopropylamine were indistinguishable from the spectra derived from the corresponding solvated material **2** prepared as described above.

Acknowledgment. We thank the National Institutes of Health for generous financial support of this work. Acknowledgment is made to the National Science Foundation Instrumentation Program (CHE 7904825 and PCM 8018643) for support of the Cornell Nuclear Magnetic Resonance Facility.

Registry No. Lithium-6, 14258-72-1; lithium 2-carbomethoxycyclohexanone dimethylhydrazone, 101773-94-8; dimeric lithium 2-carbomethoxycyclohexanone dimethylhydrazone, 101773-97-1; dimeric lithiated cyclohexanone phenylimine, 101773-98-2; lithium cyclohexanone phenylimine, 101773-95-9; 2-carbomethoxycyclohexanone dimethylhydrazone, 101773-96-0; cyclohexanone phenylimine, 1132-38-3.

Supplementary Material Available: Fractional coordinates, bond angles, and bond distances for lithiated derivatives **1** and **2** (10 pages). Ordering information is given on any current masthead page.

Stereochemistry of the Reactions of Substituted Allylboronates with Chiral Aldehydes. Factors Influencing Aldehyde Diastereofacial Selectivity[1]

William R. Roush,*[2] Michael A. Adam, Alan E. Walts, and David J. Harris

Contribution from the Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139. *Received August 30, 1985*

Abstract: The stereochemistry of the reactions of substituted allylboronates **5–9** with D-glyceraldehyde acetonide (**4**) and L-4-deoxythreose cyclohexyl ketal (**2**) is described. The reactions involving (*Z*)-crotylboronates **5** and **6** are exceptionally stereoselective, with selectivity for the major 3,4-syn,4,5-anti adducts **19**, **23**, **27**, and **31** approaching the limit defined by the isomeric purity of the reagents. The level of aldehyde diastereofacial selectivity is at least 20:1 with **4** and 90:1 in reactions with **2**. In contrast, the reactions of (*E*)-crotylboronates **7** and **8** afford roughly 1:1 mixtures of anti,anti (**20**, **24**, **28**, **32**) and anti,syn (**21**, **25**, **29**, **33**) adducts differing in the facial sense of reagent addition to the aldehyde. Interestingly, the diastereofacial selectivity of the reactions of allylboronate **9** with these aldehydes is intermediate (4:1 with **4**, 9:1 with **9**). Stereochemical assignments for **19–33** were established by unambiguous chemical correlations with compounds synthesized by stereochemically defined methods. These results clearly show that the substitution pattern at C(3) of the reagent is a significant and previously unappreciated variable in determining diastereofacial selectivity. This effect is a consequence of the nonbonded interactions that the C(3) substituents experience in the competing reaction transition states A–D. These interactions are fundamental in nature and are likely to have a significant influence on the diastereofacial selectivity of other reactions that proceed via cyclic transition states including the aldol reaction and sigmatropic processes such as the Claisen rearrangement. A second variable that influences the extent and direction of diastereofacial selectivity is the electronic structure of the aldehyde. Comparison of the results of reactions of allylic boronates **1**, **5**, **7**, and **9** with glyceraldehyde acetonide (**4**), benzyl lactaldehyde (**78**), and 2-methylbutyraldehyde (**79**) shows (a) that anti diastereofacial selectivity is always greater with **4** than with **78** or **79** (**4** > **78** > **79**) in reactions with each reagent and (b) that for each aldehyde anti diastereofacial selectivity is greater in reactions involving (*Z*)-crotylboronates **1** or **5** than allylboronate **9** or (*E*)-crotylboronate **7** (**1**, **5** > **9** > **7**).

Introduction

The reactions of crotylmetal reagents with chiral carbonyl compounds are of considerable interest in the context of acyclic stereoselective synthesis.[3,4] This transformation, like the aldol reaction,[5] generates two new stereochemical relationships and, potentially, four diastereomeric products (Figure 1). One objective of research in this area, required to support applications in natural products synthesis, is the development of methodology and/or reagents suitable for synthesis of each diastereomeric relationship with exceptional selectivity and control.[6] Although considerable effort has been devoted to the elucidation of the stereochemistry of the reactions of crotylmetal compounds with achiral aldehydes,[3] only recently have studies begun in earnest to probe the factors influencing aldehyde diastereofacial selectivity.[7-9] Consequently, the full potential of allylmetal compounds

(1) Taken in part from the Ph.D. Theses of M. A. Adam and A. E. Walts, Massachusetts Institute of Technology, Cambridge, MA, 1985.
(2) Fellow of the Alfred P. Sloan Foundation, 1982–86.
(3) (a) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555. (b) Yamamoto, Y.; Maruyama, K. *Heterocycles* **1982**, *18*, 357.
(4) (a) Bartlett, P. A. *Tetrahedron* **1980**, *36*, 3; (b) McGarvey, G. J.; Kimura, M.; Oh, T.; Williams, J. M. *J. Carbohydr. Chem.* **1984**, *3*, 125; (c) Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556.
(5) (a) Heathcock, C. H. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, p 111. (b) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. in Stereochem.* **1982**, *13*, 1. (c) Mukaiyama, T. *Org. React. (N.Y.)* **1982**, *28*, 203.
(6) Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.
(7) For recent stereochemical studies, see: (a) Hoffmann, R. W.; Weidmann, U. *Chem. Ber.* **1985**, *118*, 3966. (b) Hoffmann, R. W. *Chem. Scr.* **1985**, *25*, 53. (c) Keck, G. E.; Boden, E. P. *Tetrahedron Lett.* **1984**, *25*, 265, 1879. (d) Keck, G. E.; Abbott, D. E. *Ibid.* **1984**, *25*, 1883. (e) Heathcock, C. H.; Kiyooka, S.-I.; Blumenkopf, T. A. *J. Org. Chem.* **1984**, *49*, 4214. (f) Reetz, M. T.; Kesseler, K.; Jung, A. *Tetrahedron Lett.* **1984**, *25*, 729. (g) Fronza, G.; Fuganti, C.; Graselli, P.; Pedrocchi-Fantoni, G.; Zirotti, C. *Chem. Lett.* **1984**, 335. (h) Yamamoto, Y.; Yatagai, H.; Ishihara, Y.; Maeda, N.; Maruyama, K. *Tetrahedron* **1984**, *40*, 2239. (i) Lewis, M. D.; Kishi, Y. *Tetrahedron Lett.* **1982**, *23*, 2343. (j) Buse, C. T.; Heathcock, C. H. *Ibid.* **1978**, 1685. (k) Yamamoto, Y.; Maruyama, K. *Ibid.* **1981**, *22*, 2895. See also: ref 8a,b and 9b,c.
(8) (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. (c) For recent synthetic applications of these reagents, see: Roush, W. R.; Harris, D. J.; Lesur, B. M. *Ibid.* **1983**, *24*, 2227. (d) Roush, W. R.; Peseckis, S. M.; Walts, A. E. *J. Org. Chem.* **1984**, *49*, 3429. (e) Roush, W. R.; Kageyama, M. *Tetrahedron Lett.* **1985**, *26*, 4327.

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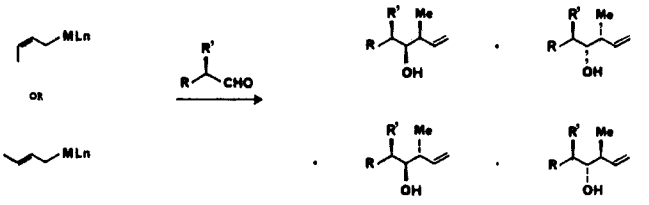
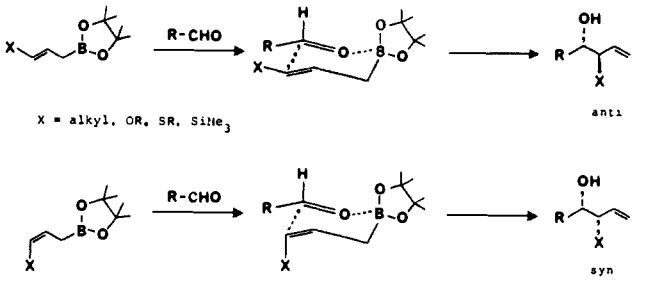


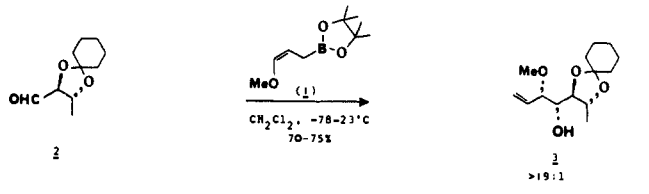
Figure 1.

in acyclic stereoselective synthesis is far from realized.

Of the numerous crotylmetal compounds that have been considered,[3] the crotylboronic esters seem particularly well suited for applications in organic synthesis. First of all, stereochemically defined *Z*- and *E*-substituted allylboronates are readily accessible by several flexible synthetic routes[10] and, unlike the crotylboranes,[11] are configurationally stable at or slightly above room temperature. Second, the stereochemical information present in the reagent is transmitted predictably to a syn or anti relationship in the product via cyclic transition states.[3a] Thus, one of the two stereochemical relationships generated in a reaction with a chiral aldehyde (Figure 1) can be controlled simply by selection of the appropriate olefin geometry of the reagent. These synthetically significant features are not shared by any other group of allylmetal reagents.



At the outset of our studies[8] relatively little information was available regarding the stereochemistry of the reactions of allylboronic esters with chiral aldehydes.[9b] Our observation[8c] that the reaction of γ-methoxyallylboronate (**1**) and L-deoxythreose cyclohexyl ketal (**2**) proceeds with exceptional stereoselectivity



prompted us to examine the reactions of **2** and D-glyceraldehyde acetonide (**4**) with substituted allylboronates **5–9**. α,β-Dialkoxy aldehydes such as **2** and **4** have been used extensively to probe the diastereofacial selectivity of reactions with a range of nu-

Table I[a]

entry	aldehyde	boronate	isomeric purity,[b] %	product ratios[c,d] 19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34
1	4	**5**	98	91	5	1	3												
2	4	**5**	89	80	11	6	3												
3	2	**5**	97					96	2	1	1								
4	2	**5**	89					84	10	6	–								
5	4	**6**	95									90	4	2	4				
6	4	**6**	87									83	6	7	4				
7	2	**6**	93													93	3	3	1
8	4	**7**	98	6	52	42	–												
9	4	**7**	87	14	46	40	–												
10	2	**7**	98					2	51	47	–								
11	2	**7**	89					11	50	39	–								
12	4	**8**	>98									–	44	56	–				
13	4	**8**	93									6	43	51	–				
14	2	**8**	97													1	40	59	–
15	2	**8**	93													4	40	56	–

[a] All reactions were performed as described in text. [b] Isomeric purity of **5–8** was determined by capillary GC (see Experimental Section). [c] Product ratios were determined by GC analysis before chromatographic separation (see Experimental Section). [d] The yield of products isolated by chromatography generally ranged from 75–85%.

(9) For studies on the design of chiral allylmetal compounds which may be useful for controlling aldehyde diastereofacial selectivity, see: (a) Roush, W. R.; Walts, A. E.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8186. (b) Hoffmann, R. W.; Zeiss, H.-J.; Ladner, W.; Tabche, S. *Chem. Ber.* **1982**, *115*, 2357. (c) Hoffmann, R. W.; Endesfelder, A.; Zeiss, H.-J. *Carbohydr. Res.* **1983**, *123*, 320. (d) Brown, H. C.; Jadhav, P. K. *J. Org. Chem.* **1984**, *49*, 4089, and references therein. (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. (h) Hayashi, T.; Konishi, M.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 281. (i) Haruta, R.; Ishiguro, M.; Ikeda, N.; Yamamoto, H. *J. Am. Chem. Soc.* **1982**, *104*, 7667. (j) Midland, M. M.; Preston, S. B. *Ibid.* **1982**, *104*, 2330.

(10) (a) Brown, H. C.; DeLue, N. R.; Yamamoto, Y.; Maruyama, K.; Kasahara, T.; Murahashi, S.-I.; Sonoda, A. *J. Org. Chem.* **1977**, *42*, 4088. (b) Wuts, P. G. M.; Thompson, P. A.; Callen, G. R. *Ibid.* **1983**, *48*, 5398. (c) Hoffmann, R. W.; Zeiss, H.-J. *Ibid.* **1981**, *46*, 1309. (d) Fujita, K.; Schlosser, M. *Helv. Chim. Acta* **1982**, *65*, 1258. (e) Schlosser, M.; Fujita, K. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 309.

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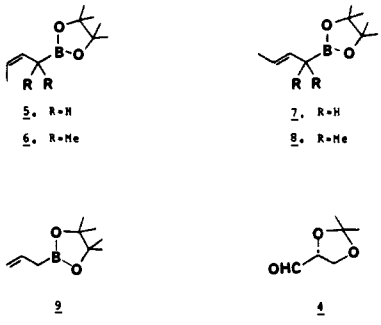
Table II. Temperature Dependence of the Reaction of 7 and 4[a]

entry	reaction temp, °C	product ratio (19:20:21)
1	−78 → 23°[b]	6:52:42
2	23°	5:51:44
3	−20°	3:51:46
4	−78°	−:53:47

[a] All reactions were performed in CH_2Cl_2 (0.1 M) at the indicated temperatures using 1.2–1.3 equiv of 98% isomerically pure 7. The reactions in entries 1 and 2 were complete within 24 h. The experiments in entries 3 and 4, however, were much slower and were not complete when worked up. [b] See Table I for details.

cleophiles, and therefore were regarded as useful model systems.[4b,c,12]

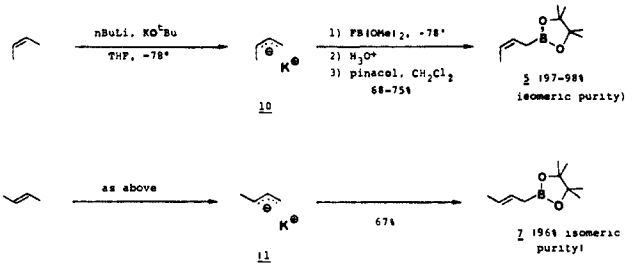
We describe herein the full details of this investigation and show that the substitution pattern at C(3) of **5–9** as well as the electronic



structure of the chiral aldehyde play significant roles in determining the overall stereoselectivity. Preliminary accounts of this work have appeared.[8a,b]

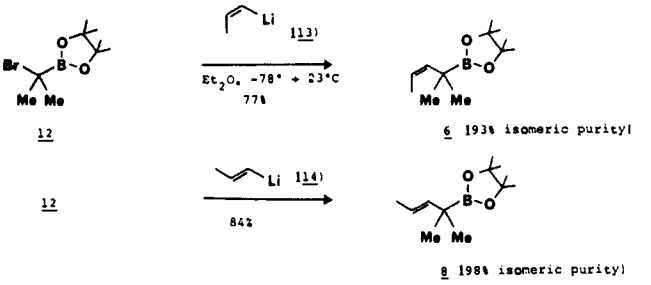
Synthesis of Reagents 5–9

Crotylboronates **5** and **7** were best prepared by using slight modifications of chemistry reported originally by Schlosser for synthesis of crotylboronates via functionalization of crotylpotassium reagents.[10d,e,13] Thus, treatment of (*Z*)-2-butene with 1.0 equiv of the complex base generated from *n*-BuLi and KO-*t*-Bu in THF at −78 °C for 15 h, or at −50 °C for 15 min, followed by treatment of the resulting (*Z*)-crotylpotassium (**10**) with 1.1 equiv of fluorodimethoxyborane at −78 °C for 1 h afforded a solution containing dimethyl (*Z*)-crotylboronate. The reaction mixture was extracted with dilute aqueous HCl and the crude crotylboronic acid was then immediately esterified with pinacol to give **5** in 68–75% yield after vacuum distillation. The isomeric



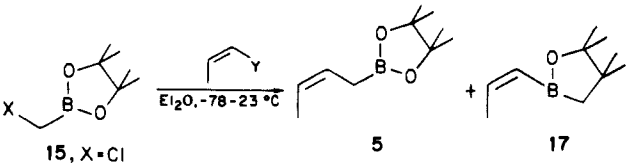
purity of this compound was 97–98% as determined by capillary GC analysis. Similarly, 96% isomerically pure **7** was prepared in comparable yield starting from (*E*)-2-butene. These syntheses are much more convenient and direct than previously reported methods.[10b,c,14]

Reagents **6** and **8** were prepared by adopting the allylboronate synthesis reported originally by Brown.[10a,14] Thus, treatment of 2-bromo-2-propylboronate (**12**)[10a,c] with 1.1 equiv of either (*Z*)- or (*E*)-propenyllithium (**13**, **14**)[15–17] in Et_2O at −78 °C gave **6** and **8**, respectively, in 77–84% yield after distillation.[18] These



compounds, like **5** and **7**, can be handled at room temperature, exposed to atmosphere, and even chromatographed on silica gel without extensive decomposition. They also can be stored at −20 °C under an inert atmosphere for extended periods of time.

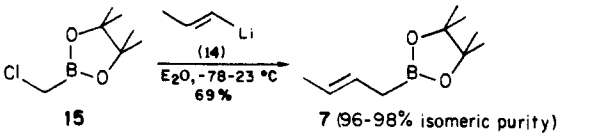
(14) Wuts has reported that the reaction of pinacol α-chloromethylboronate (**15**) with 2 equiv of (*Z*)-propenyllithium (**13**) gives **5** in 47% yield.[10b]



15, X = Cl
16, X = I

substrate	$CH_3CH{=}CHY$ (equiv)	yield	5:17
15	13 (2.0)	50%	20:80
15	13 (1.2)		[a]
15	13 (0.9)	48%	73:27
15	13 (1.2)	48%	72:28
15	18 (1.1)[b]	75–82%	99:1[c]

[a] Reaction failed altogether. [b] Reaction performed in THF. [c] Isomeric purity of **5** was 95%.



In our hands this method afforded **5** (89–90% isomeric purity) in variable yield (0–50%). Moreover, the product contained 20–30%, and sometimes even 80% of propenylboronate **17**. A satisfactory solution to this problem was realized by using (*Z*)-$CH_3CH{=}CHMgBr$ (**18**) in place of **13**. (*Z*)-Crotylboronate **5** prepared in this manner was 95% isomerically pure and contained less than 1% of **17**. Curiously, propenylboronate formation was not a serious problem in the preparations of **6**, **8** (see text), or **7** (see below). For another reaction in which propenylboronate generation was observed, however, see ref 8d.

(15) (*Z*)- and (*E*)-propenyllithium were prepared by lithiation of the corresponding (*Z*)- and (*E*)-propenyl bromides with 1% Na–Li dispersion in ether at 10 °C by using the procedure described by Whitesides.[16] (*Z*)-Propenyl bromide of >98% isomeric purity was obtained by spinning band distillation of the commercial mixture (70:30, *Z*:*E*). (E)-Propenyl bromide was prepared by treating the commercial 70:30 mixture with 0.75 equiv of NaOH in *n*-butyl alcohol at reflux, which selectively eliminates HBr from the (*Z*)-isomer (see: Hayashi, T.; Kabeta, K.; Hamachi, I.; Kumada, M. *Tetrahedron Lett.* **1983**, *24*, 2865). Flash distillation (0 °C, 1 mmHg) of the (*E*)-isomer directly from the reaction mixture gave material of >99% isomeric purity. Both isomers were distilled directly onto K_2CO_3 and were either used immediately or stored under argon at −78 °C to prevent (minimize) olefin isomerization.

(16) (a) Whitesides, G. M.; Casey, C. P.; Krieger, J. K. *J. Am. Chem. Soc.* **1972**, *93*, 1379. (b) Linstrumelle, G.; Krieger, J. K.; Whitesides, G. M. *Org. Synth.* **1976**, *55*, 103.

(17) It is necessary to use propenyl bromides of >98% isomeric purity in order to prepare **5–8** with >97% isomeric purity (see references 14–16). Use of 90–95% isomerically pure propenyl bromides led ultimately to **5–8** of lower purity (87–93%; see entries 2, 4, 6, 7, 9, 11, 13, and 15 of Table I).

(18) For other examples of boron-assisted nucleophilic substitution reactions see: (a) Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.* **1980**, *102*, 7588. (b) Matteson, D. S. *Organometallic Reaction Mechanisms*; Academic Press: New York, 1974; pp 161–171. (c) Matteson, D. S.; Mah, R. W. H. *J. Am. Chem. Soc.* **1963**, *85*, 2599. (d) Pasto, D. J.; Miesel, J. L. *Ibid.* **1963**, *85*, 2118.

(12) (a) Mead, K.; McDonald, T. L. *J. Org. Chem.* **1985**, *50*, 422. (b) Danishefsky, S. J.; Pearson, W. H.; Harvey, D. F.; Maring, C. J.; Springer, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 1256, and references therein. (c) Mulzer, J.; Angermann, A. *Tetrahedron Lett.* **1983**, *24*, 2843.

(13) (a) Rauchschwalbe, G.; Schlosser, M. *Helv. Chim. Acta* **1975**, *58*, 1094. (b) Schlosser, M.; Rauchschwalbe, G. *J. Am. Chem. Soc.* **1978**, *100*, 3258.

Finally, pinacol allylboronate **9** was prepared in 53% yield from CH_2=$CHCH_2MgBr$ by using the general procedure described by Matteson.[19]

Reactions of Aldehydes 2 and 4 with Allylic Boronates 5–9

Table I summarizes the results of reactions of crotylboronates **5–8** with aldehydes **2**[8c] and **4**.[20] Special care was taken to distill each reagent and determine its isomeric purity prior to each experiment. The reactions were performed by addition of a slight excess of aldehyde (also freshly distilled) to a 0.1–1 M solution of crotylboronate in CH_2Cl_2 at −78 °C under an inert atmosphere. They were then allowed to warm to room temperature and stirred until complete (typically 24–48 h). Workup involved dilution with water and extraction with ether; use of triethanolamine to decompose the intermediate borate esters as recommended by Hoffmann is not necessary.[9c,10c,21]

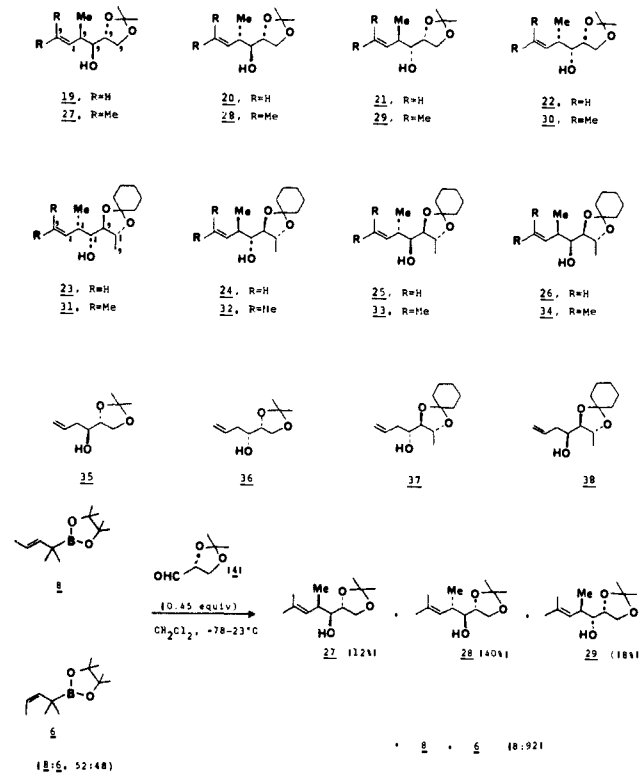
Product mixtures were analyzed by capillary gas chromatography (see Experimental Section) and pure samples of all adducts except **22**, **26**, **30**, and **34** were isolated by chromatography. The presence of **22** and **26** in the experiments summarized in entries 1–4 was confirmed by GC coinjection studies with authentic samples. The stereochemical assignments for **19–29** and **31–33** were established rigorously by correlation with compounds synthesized from epoxides of known configuration. These studies, which included synthesis of authentic samples of **19**, **22**, **23**, and **26**, are described in the following section. Structures **30** and **34** (entries 5–7, Table I) were assigned to minor products detected in the GC analyses.

It is immediately striking that the (*Z*)-crotylboronates **5** and **6** are highly stereoselective in their reactions with **2** and **4** (entries 1–7), with selectivity for the major 3,4-syn,4,5-anti diastereomers (**19**, **23**, **27**, and **31**) approaching the limit defined by the isomeric purity of **5** and **6**.[17] Although four products were detected in these experiments, the minor 3,4-anti,4,5-anti (**20**, **24**, **28**, and **32**) and the 3,4-anti,4,5-syn (**21**, **25**, **29**, and **33**) diastereomers can be attributed primarily to the contaminating (*E*)-crotylboronate isomers **7** and **8** present in **5** and **6**. Of course, these minor anti,anti and anti,syn diastereomers are also possible products from minor reaction pathways wherein the aldehyde carbon chain is oriented in an axial position of the chair-like transition state. The data in entries 1, 3, 5, and 7 for reactions with reagents of highest isomeric purity, however, suggest that less than 4% of such stereochemical crossover occurs.[10c] The last set of products, namely the syn,syn isomers **22**, **26**, **30**, and **34**, serve to define the level of aldehyde facial selectivity in the reactions with **2** and **4**. In the reactions with glyceraldehyde acetonide (**4**) the facial selectivity is at least 20–30:1, whereas in reactions with threonine-derived aldehyde **2** the facial preference is considerably greater (~90:1).

In sharp contrast are the results obtained for the reactions of (*E*)-crotylboronates **7** and **8** with **2** and **4** (entries 8–15). Here the major products are the anti,anti (**20**, **24**, **28**, and **32**) and the anti,syn (**21**, **25**, **29**, and **33**) adducts which derive from different facial approaches of reagent to the aldehyde. Clearly, no significant facial preference exists in these reactions.

We briefly investigated the influence of reaction conditions on the product distribution. As shown in Table II, the ratio of **19**, **20**, and **21** obtained from the reaction of **7** and **4** was not significantly affected whether the reaction was performed at 23 °C, −20 °C, or at −78 °C. However, reactions performed at low temperatures were considerably slower than at 23 °C.

One variable that can influence the product distribution is reaction stoichiometry, since it has been noted that (*E*)-crotylboronates react faster with aldehydes than the corresponding (*Z*)-isomers.[10c,22] To examine this point, a 52:48 mixture of **8** and **6** (0.1 M) was treated with 0.45 equiv of **4**. After all of **4** had been consumed, GC analysis of the unreacted boronate revealed that this material was highly enriched in **6** (92% isomeric purity). The ratio of **27**:**28**:**29** was 12:40:48, confirming that (*E*)-boronate **8** had indeed reacted at a considerably faster rate than **6**. In principle, this difference in reactivity can be used to enrich the isomeric purity of (*Z*)-crotylboronates by selective consumption of contaminating (*E*)-isomers[22] or, as in the case illustrated here, increase the selectivity of reactions involving less than isomerically pure (*E*)-crotylboronates by using the aldehyde as limiting reagent.



The effect of variation of experimental conditions on diastereofacial selectivity was studied in greater detail by using pinacol allylboronate (**9**) as a model substrate (see Table III).[23] Curiously, these data show that the reactions of **9** are more selective than those involving the (*E*)-crotylboronates **7** and **8**, but are considerably less so than with the (*Z*)-crotyl isomers **5** and **6** (compare Tables I and III). Maximal selectivity (80:20) for anti adduct **35** in reactions involving D-glyceraldehyde acetonide **4** was realized in CH_2Cl_2 at −78 °C (entry 1). This reaction was slightly less selective when performed at 23 °C (entry 2). Interestingly, the reactions in toluene and hexane were slightly more selective at room temperature than at −78 °C (entries 3–6) but in no instance did the selectivity exceed 79:21. Although the reaction in ether proved also to be reasonably discriminating (77:23), use of increasingly polar solvents such as THF or DMF resulted in diminished stereoselectivity (compare entries 7–9). This may well reflect a change of mechanism associated with coordination of the boron atom by solvent.[25]

The reactions of **9** and 4-deoxythreose ketal **2** appear to be less solvent dependent than those with **4** (entries 10–13). Identical product ratios were obtained using CH_2Cl_2 or toluene as solvent, with maximal selectivity (90:10) being realized at −78 °C. Selectivity in this case was significantly affected only when an ate complex[25] derived from **9** and *n*-BuLi was used (entry 14). It is

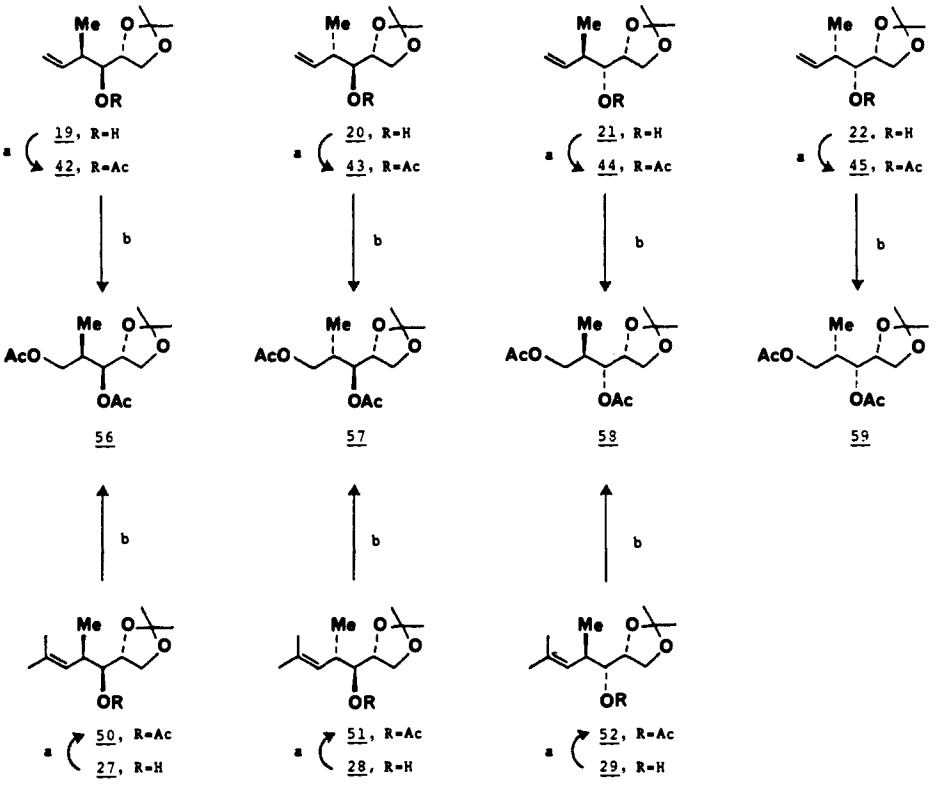
(19) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, *2*, 230.
(20) (a) Baer, E.; Fischer, H. O. *J. Biol. Chem.* **1939**, *128*, 463; (b) Baer, E. *Biochem. Prep.* **1952**, *2*, 31.
(21) Hoffmann, R. W.; Herold, T. *Chem. Ber.* **1981**, *114*, 375.
(22) (a) Moret, E.; Schlosser, M. *Tetrahedron Lett.* **1984**, *25*, 4491. (b) Hoffmann, R. W.; Kemper, B. *Tetrahedron* **1984**, *40*, 2219.
(23) The reaction of **4** with **9** was reported while our studies were in progress (see ref 9c). This publication by Hoffmann also described the reactions of **4** with the (*E*) and (*Z*)-isomers of 2-*exo*,3-*exo*-[(2-butenylborylene)dioxy]*endo*-3-phenylbornane. Our results (Table I) show that this chiral auxiliary has very little effect on the overall stereoselectivity.
(24) Roush, W. R.; Brown, R. J. *J. Org. Chem.* **1983**, *48*, 5093.
(25) The reactions of aldehydes with crotylboron ate complexes have been described: Yamamoto, Y.; Yatagai, H.; Maruyama, K. *J. Am. Chem. Soc.* **1981**, *103*, 1969, 3229.

Table III.[a] Reactions of Pinacol Allylboronate (**9**) with Chiral Aldehydes **2** and **4**

entry	aldehyde	solvent	temp, °C	product ratios[b] 35	36	37	38
1[c]	4	CH_2Cl_2	−78	80	20		
2	4	CH_2Cl_2	23	77	23		
3	4	toluene	−78	71	29		
4	4	toluene	23	73	27		
5	4	hexane	−78	75	25		
6	4	hexane	23	79	21		
7	4	ether	23	77	23		
8	4	THF	23	71	29		
9	4	DMF	0–23	58	42		
10[d]	2	CH_2Cl_2	−78			90	10
11	2	CH_2Cl_2	23			87	13
12	2	toluene	−78			90	10
13	2	toluene	23			87	13
14[e]	2	THF–*n*-BuLi	−78→23			79	21

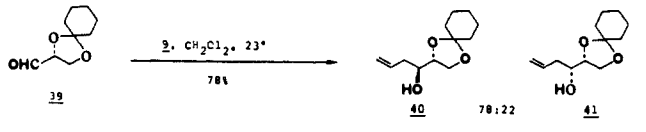
[a] All analytical-scale reactions were performed by addition of 1.5 equiv of aldehyde to a solution of **9** (0.2 M) at the indicated temperature. The reactions were allowed to proceed to completion (generally 12–24 h) and then were worked up by dilution with water and extraction with ether. [b] Product ratios were determined by GC analysis before chromatographic purification (see Experimental Section). [c] The isolated yield of **35** and **36** was 75–79% in preparative-scale experiments (1.0 equiv of **9**, 1.2 equiv of **4**; product purified by chromatography and distillation). [d] The isolated yield of **37** and **38** was 85% in preparative-scale experiments (see *c*). [e] One equivalent of *n*-BuLi in hexane was added to **9** in THF at −78 °C followed by addition of **2**.

Scheme I. Correlations of Crotylboronate Adducts in the Glyceraldehyde Series[a]



[a] (a) AcCl, pyridine, CH_2Cl_2, 23 °C. (b) O_3, CH_2Cl_2, −78 °C; $(CH_3)_2S$, −78–23 °C; $LiAlH_4$, THF, 0 °C; AcCl, pyridine, CH_2Cl_2, 23 °C.

noteworthy, however, that the reactions of **2** and **9** are more erythro selective (9:1) than with **4** (4:1). This trend is also apparent in the reactions of these aldehydes with (*Z*)-crotylboronates **5** and **6** (see Table I). The greater facial selectivity of **2** in these reactions appears to be a function of the C(4)-methyl substituent since the reaction of glyceraldehyde cyclohexyl ketal **39**[26] afforded a mixture of **40** and **41** in a ratio essentially identical with that recorded in entry 2 of Table III.



(26) Sugiyama, T.; Sugawara, H.; Watanabe, M.; Yamashita, K. *Agric. Biol. Chem.* **1984**, *48*, 1841.

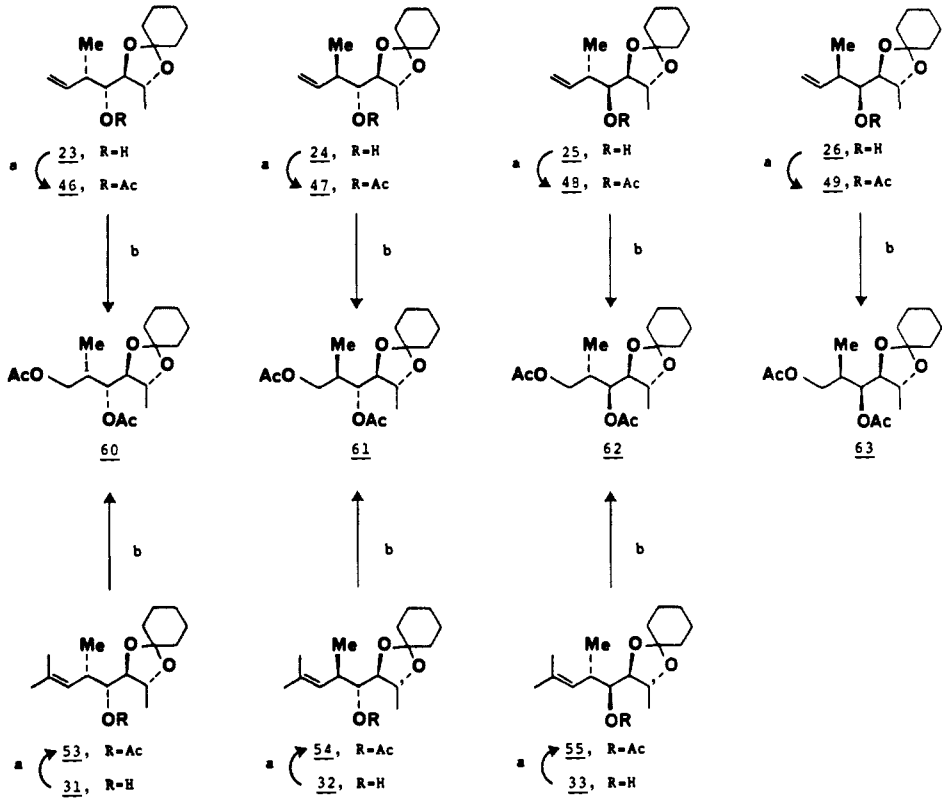
Stereostructural Assignments

A nontrivial aspect of this study was the assignment of stereochemistry to the crotyl addition products **19–34**. Initial attempts to base stereostructural assignments on ^1H coupling constant data were frustrated by the large number of ^3J values that fall in the ambiguous 5–7 Hz range (see Table IV).[27,28] Similarly, it was

(27) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*; Pergamon Press: New York, 1978; p 291.

(28) Numerous examples have been reported in which ^3J(syn) and ^3J(anti) fall outside of the "expected" ranges due to unusual conformational effects: (a) Heng, K. K.; Simpson, J.; Smith, R. A. J.; Robinson, W. T. *J. Org. Chem.* **1981**, 46, 2932. (b) Coxon, J. M.; Simpson, G. W.; Steel, P. J.; Trenerry, V. C. *Tetrahedron Lett.* **1983**, *24*, 1427. (c) Coxon, J. M.; Simpson, G. W.; Steel, P. J.; Trenerry, V. C. *Aust. J. Chem.* **1984**, *37*, 65, and references therein. (d) Kishi, Y. In *Current Trends in Organic Synthesis, Proceedings of the International Conference*, 4th, 1982; Nozaki, H., Ed.; Pergamon Press: Oxford, 1983; p 115. (e) Kurth, M. J.; Yu, C.-M. *J. Org. Chem.* **1985**, *50*, 1840.

Scheme II. Correlations of Crotylboronate Adducts in the Deoxythreose Series[a]



[a] (a) AcCl, pyridine, CH_2Cl_2, 23 °C. (b) O_3, CH_2Cl_2, −78 °C; $(CH_3)_2S$, −78–23 °C; $LiAlH_4$, THF, 0 °C; AcCl, pyridine, CH_2Cl_2, 23 °C.

not possible to make reliable stereochemical assignments by using the ^{13}C method outlined by Heathcock (see Table V).[29] Stereostructural assignments for **19–34**, therefore, were based on unambiguous chemical correlations.

As the first step of these correlations, compounds **19–33** were degraded to the corresponding 1,3-diacetates **56–63** by using the ozonolysis reduction and acylation sequence summarized in Schemes I and II. Selected NMR data for these eight diacetates are provided in Table VI; the diols corresponding to **56–59** have previously been described by Heathcock.[29a]

The stereochemistry of diacetates **56–63**, and therefore also **19–33**, was established by synthesizing each compound by stereochemically defined methods (see Schemes III and IV). Syntheses of **56** and **57** are described here as illustrative cases. Epoxide **65** was prepared from D-glyceraldehyde acetonide **4** by using the methodology described by Sharpless, Masamune, and Kishi.[30] Treatment of **65** with CH_2=$CHMgBr$ and CuBr·S-$(CH_3)_2$ according to the procedure of Tius[31] afforded an 11:1 mixture of **66** and unreacted **65**. After chromatographic separation, pure **66** was monomesylated (MsCl, pyridine, 0 °C) and reduced (LAH, THF, 0 °C) to afford pure **19**. This compound was then degraded to **56** by using the methods described previously (Scheme I). Alternatively, exposure of **65** to Me_2CuLi in Et_2O at −40 °C[32] followed by treatment with $NaIO_4$ in aqueous THF[33] afforded diol **67** which upon acylation (AcCl, pyridine) gave an isomerically pure reference sample of **57**. Similar sequences of reactions with epoxides **68**, **72**, and **75** afforded authentic samples of **22**, **23**, **26** and 1,3-diacetates **58–63**.

The assignment of stereochemistry to compounds **35–38** resulting from reactions of **2** and **4** with pinacol allylboronate (Table III) was more straightforward. Alcohols **35** and **36** are known compounds and are well described in the literature.[9c,12c] Stereochemical assignments for **37** and **38** were established by methanolysis (1:1 MeOH–HOAc, reflux) to the corresponding triols which were compared with authentic samples.[24]

Discussion

On the basis of the excellent selectivity of the reaction of **1** with **2**,[8c] we had anticipated at the outset that all three sets of allylboronates (**5**/**6**, **7**/**8**, and **9**) would display excellent anti (Felkin–Ahn)[34] selectivity in these carbonyl addition reactions. First, reagents such as **5–9** are capable of coordinating with only one ligand (the aldehydic carbonyl group) so α- or β-chelate-controlled pathways would not be possible. Second, aldehydes such as **2** and **4** are highly electrophilic and have a marked tendency to undergo anti nucleophilic addition even with reagents capable of chelation.[4b,12] Although the data for the reactions of (*Z*)-crotylboronates **5** and **6** summarized in Table I are superficially consistent with Felkin–Ahn transition states (e.g. A_Z), the data for **7**, **8**, and **9** suggest that the excellent results with **5** and **6** may be fortuitous and that factors other than conventional acyclic stereochemical considerations must play a major role in these reactions. *Indeed, our results clearly show that the substitution pattern at C(3) of the reagent is a significant and previously unappreciated variable in determining diastereofacial selectivity.*

(29) (a) Heathcock, C. H.; Young, S. D.; Hagen, J. P.; Pirrung, M. C.; White, C. T.; VanDerveer, D. *J. Org. Chem.* **1980**, *45*, 3846. (b) Heathcock, C. H.; Pirrung, M. C.; Sohn, J. E. *Ibid.* **1979**, *44*, 4294. (c) For a recently developed alternative method, see: Hoffmann, R. W.; Weidmann, U. *Chem. Ber.* **1985**, *118*, 3980.

(30) (a) Katsuki, T.; Lee, A. W. M.; Ma, P.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Tuddenham, D.; Walker, F. J. *J. Org. Chem.* **1982**, *47*, 1373. (b) Minami, N.; Ko, S. S.; Kishi, Y. *J. Am. Chem. Soc.* **1982**, *104*, 1109.

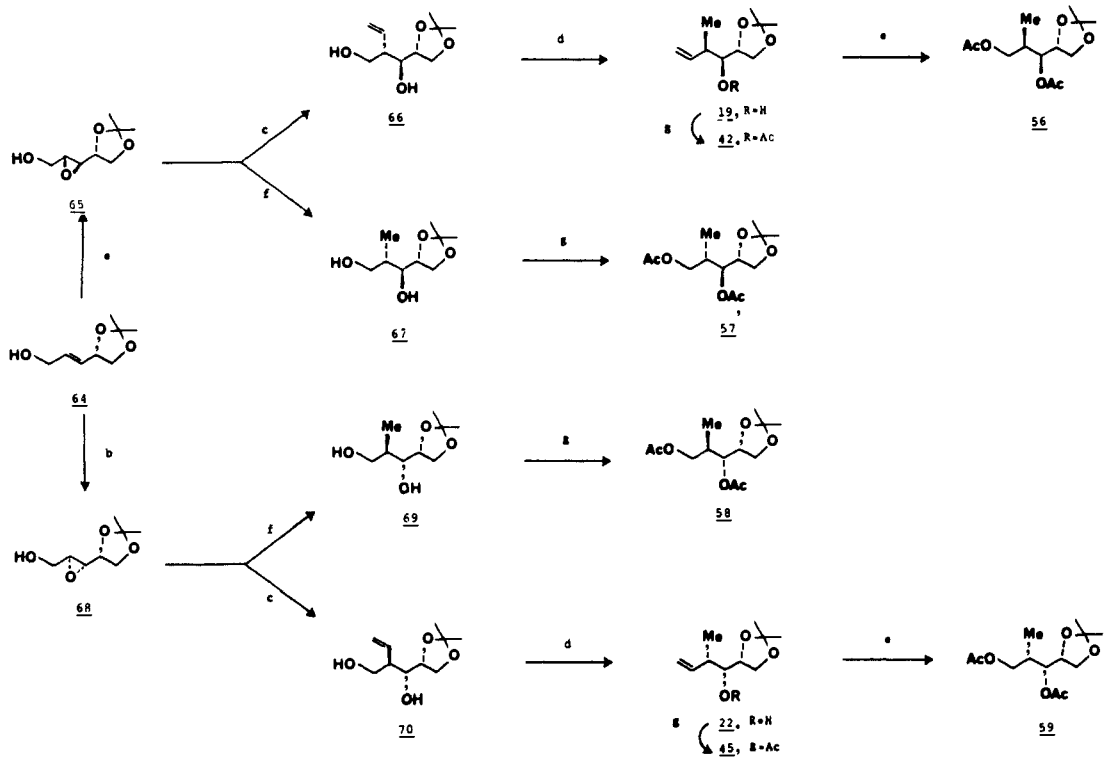
(31) Tius, M. A.; Fauq, A. H. *J. Org. Chem.* **1983**, *48*, 4131.

(32) (a) Johnson, M. R.; Nakata, T.; Kishi, Y. *Tetrahedron Lett.* **1979**, 4343. (b) Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873.

(33) The reactions of **65**, **68**, **72** and **75** with Me_2CuLi afforded the indicated 1,3-diols accompanied by 1–10% of regioisomeric 1,2-diol. Periodate treatment cleaved any 1,2-diol present and simplified the purification of the desired product.

(34) (a) Cherest, M.; Felkin, H.; Prudent, N. *Tetrahedron Lett.* **1968**, 2199. (b) Ahn, N. T.; Eisenstein, O. *Nouv. J. Chim.* **1977**, *1*, 61. (c) Ahn, N. T. *Top. Curr. Chem.* **1980**, *88*, 145.

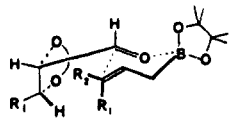
Scheme III. Synthesis of Diacetates **56–59** (Glyceraldehyde Series)[a]



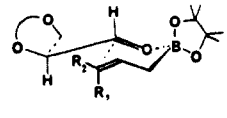
[a] (a) $Ti(OiPr)_4$, (−)-DET, TBHP, CH_2Cl_2, −23 °C. (b) $Ti(OiPr)_4$, (+)-DIPT, TBHP, CH_2Cl_2, −23 °C. (c) CH_2=$CHMgBr$, $CuBr{\cdot}S(CH_3)_2$, Et_2O, −23 °C; (d) MsCl, pyridine, 0 °C; $LiAlH_4$, THF, 0 °C. (e) O_3, CH_2Cl_2, −78 °C; $(CH_3)_2S$, −78–23 °C; $LiAlH_4$, THF, 0 °C; AcCl, pyridine, CH_2Cl_2, 23 °C. (f) $(CH_3)_2CuLi$, Et_2O, −40 °C; $NaIO_4$, THF, H_2O, 23 °C. (g) AcCl, pyridine, CH_2Cl_2, 23 °C.

Consider first the reactions of (*Z*)-crotylboronates **5** and **6**. Although one might have expected that Felkin–Ahn transition state A_Z would be preferred on the basis of favorable stereoelectronic interactions[34] between $\sigma^*_{C(2)-OR}$ and the developing C–C bond, examination of space-filling molecular models reveals that serious steric interactions occur between the axial vinylic methyl group (R_1) and C(3) (and attached substituent R_3) of the aldehydic reactant. These interactions are clearly more severe than in A_E or A_A. After consideration of other possible transition state structures, generated by 120° rotations about the aldehydic C(1)–C(2) bond such that antiperiplanar relationships are maintained with the developing C–C bond[35] and by reversing the face of the carbonyl exposed to the reagent, it is apparent that B_Z contains fewer nonbonded interactions involving R_1, R_2, and the aldehydic C(2) or C(3) substituents than any of the other reasonable alternatives. It is probably this Cornforth-like transition state,[36] and not A_Z, that accounts for formation of the major 3,4-syn,4,5-anti adducts in entries 1–7 of Table I. The level of diastereofacial selectivity is very high in part because the 4,5-syn selective transition states such as C_Z and D_Z are disfavored by nonbonded interactions highlighted here.

4,5-ANTI SELECTIVE:

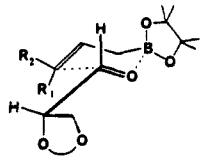


A_Z, R_1 = Me; R_2 = H
A_E, R_1 = H; R_2 = Me
A_A, R_1 = R_2 = H

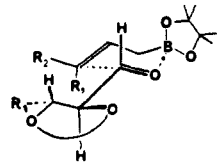


B_Z, R_1 = Me; R_2 = H
B_E, R_1 = H; R_2 = Me
B_A, R_1 = R_2 = H

4,5-SYN SELECTIVE:



C_Z, R_1 = Me; R_2 = H
C_E, R_1 = H; R_2 = Me
C_A, R_1 = R_2 = H



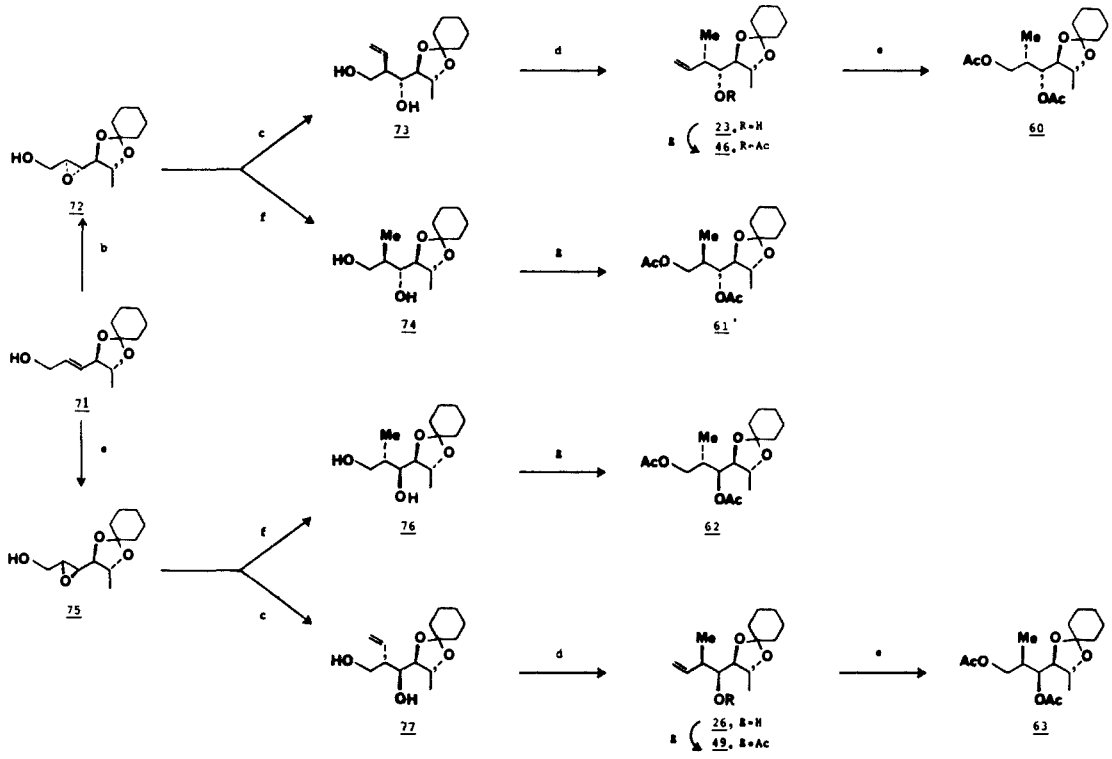
D_Z, R_1 = Me; R_2 = H
D_E, R_1 = H; R_2 = Me
D_A, R_1 = R_2 = H

The lower degree of aldehyde diastereofacial selectivity in reactions of (*E*)-crotylboronates **7** and **8** with **2** and **4** can be rationalized by similar arguments. For example, examination of the 4,5-anti transition states A_E and B_E reveals that the Cornforth-like arrangement B_E is probably the most accessible of these two choices, but considerably less so than B_Z in the (*Z*)-crotylboronate series (note the 1,3-interaction between R_2 and C(2)-OR in B_E). Of the 4,5-syn selective transition states, C_E is analogously less crowded and more accessible than C_Z; transition state D_E is very crowded and is probably insignificant in the reactions of **7** and **8**. Based on this analysis, no great preference would be expected for addition of (*E*)-crotylboronates to either diastereotopic face of aldehydes **2** and **4**.

The observation that allylboronate **9** displays an intermediate level of selectivity relative to the extrema defined by the (*Z*)- and (*E*)-crotylboronates is also consistent with this analysis. The 4,5-anti selective transition states A_A and B_A, from which **35** and **37** are produced, are more accessible in reactions involving **9** (R_1 = R_2 = H) than **7** or **8** (R_1 = H, R_2 = Me) since interactions involving R_2 = H are less serious than when R_2 = Me. On the other hand, transition state C, from which approximately 50% of the product is produced during reactions of **7** and **8**, is less significantly affected by changing R_2 from Me to H. Consequently, the reactions of **9** are somewhat more anti-selective than

(35) Caramella, P.; Rondan, N. G.; Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 2438.
(36) Cornforth, J. W.; Cornforth, R. H.; Mathew, K. K. *J. Chem. Soc.* **1959**, 112.

Scheme IV. Synthesis of Diacetates **60–63** (Deoxythreose Series)[a]



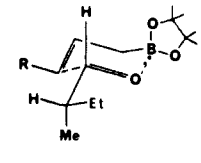
[a] (a) $Ti(OiPr)_4$, (−)-DET, TBHP, CH_2Cl_2, −23 °C. (b) $Ti(OiPr)_4$, (+)-DIPT, TBHP, CH_2Cl_2, −23 °C. (c) CH_2=CHMgBr, CuBr·$S(CH_3)_2$, Et_2O, −23 °C; $NaIO_4$, THF, H_2O, 23 °C. (d) MsCl, pyridine, 0 °C; $LiAlH_4$, THF, 0 °C. (e) O_3, CH_2Cl_2, −78 °C; $(CH_3)_2S$, −78–23 °C; $LiAlH_4$, THF, 0 °C; AcCl, pyridine, CH_2Cl_2, 23 °C. (f) $(CH_3)_2CuLi$, Et_2O, −40 °C; $NaIO_4$, THF, H_2O, 23 °C. (g) AcCl, pyridine, CH_2Cl_2.

those of **7**/**8**. Similarly, comparison of transition states B, C, and D for **9** and (*Z*)-crotylboronate **5**/**6** reveals that syn-selective transition states C and D are considerably more accessible for **9**, consistent with our finding that **9** is less anti-selective than **5**/**6**.

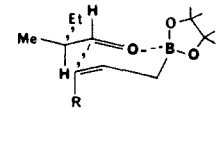
As noted previously, the greater anti-facial preference of **2** relative to **4** in reactions with (*Z*)-crotylboronates **5** and **6** and allylboronate **9** is related to the C(4)-methyl substituent of **2**. The enhanced anti selectivity of these reactions is probably a consequence of enhanced destabilization of syn-selective transition states D_Z and D_A when R_3 = Me (interactions with R_2), leaving only C_Z and C_A to compete with the already favored anti-selective transition states B_Z and B_A. When R_3 = H (e.g., in reactions with **4**), D_Z and D_A are more accessible and the overall anti selectivity is diminished. That a comparable selectivity difference is not seen in reactions of (*E*)-crotylboronates **7** and **8** with these aldehydes is consistent with a lack of involvement of D_E even when R_3 = H (note the serious 1,3-interactions involving R_2 and R_3 in D_E).

The preceding analysis has focused exclusively on nonbonded interactions as a means of rationalizing the *relative* behavior of three classes of substituted allylboronates ((*Z*)-crotyl, (*E*)-crotyl, and allyl) in their reactions with **2** and **4**. From a purely steric viewpoint, however, it is surprising that the reactions of (*E*)-crotylboronates **7** and **8** show as much anti selectivity as they do since C_E appears to be less hindered than B_E. Similarly, nonbonded interactions in C_A and B_A for allylboronate **9** appear to be essentially equivalent, but yet these reactions show appreciable anti selectivity (4–9:1; see Table III). This suggests, therefore, either that Felkin transition states A play a role in spite of the steric interactions noted previously (a reasonable possibility especially in reactions with **9**) or, alternatively, that Cornforth-like transition states B are electronically activated[34] relative to C (Karabatsos-like)[37] and contribute more heavily to the product distribution than expected otherwise. Since the increase in anti selectivity of reactions of (*Z*)-crotylboronates (e.g., **5**) with **2** and **4** relative to **9** (ca. 1.2–1.6 kcal/mol) is greater than for **9** relative to **7** (ca. 0.7–1.1 kcal/mol),[38] we favor the thesis that Cornforth-like transition states B dominate the formation of 4,5-anti diastereomers in each reaction and discount the possibility that Felkin-like transition states A are significantly involved.[39]

It is reasonable to expect, therefore, that the electronic structure of the aldehydic reaction partner may also influence the direction and magnitude of diastereofacial selectivity. The data summarized in Table VII show that this is indeed the case. It is interesting to note, first, that Hoffmann has recently completed a study of the reactions of allylic boronates **5**, **7**, and **9** with a series of α-methyl-branched aldehydes including **79**.[7a,7b,41] The striking difference between Hoffmann's data and ours is that α,β-dialkoxyaldehydes such as **2** and **4** are much more anti-selective than the α-methyl-branched aldehydes (e.g., **79**) in their reactions with allylic boronates. The two examples recorded for benzyl lactaldehyde (**78**) provide additional support to the notion that aldehyde electronic structure influences diastereofacial selectivity. Second, Hoffmann has performed a transition-state analysis essentially identical with the one we have described herein. That is, Hoffmann suggests that transition states E (analogous to C_A and C_E) and F (analogous to B_Z) are responsible for formation



E



F

(37) Karabatsos, G. H. *J. Am. Chem. Soc.* **1967**, *89*, 1367.

(38) The anti selectivity of the reaction of a specific allylic boronate with a chiral aldehyde can be expressed by $\Delta\Delta G^{\ddagger}_X = \Delta G^{\ddagger}_X(\text{anti}) - \Delta G^{\ddagger}_X(\text{syn})$ where X defines the substitution pattern of the reagent (e.g., X = *Z*, *E* or A). The relative anti selectivity of two different reagents with a given aldehyde is $\Delta\Delta G^{\ddagger}_{X_1\text{-}X_2} = \Delta\Delta G^{\ddagger}_{X_1} - \Delta\Delta G^{\ddagger}_{X_2}$.

(39) Recall that steric interactions in the Felkin transition states are most severe for A_Z ($A_Z > A_E > A_A$). Consequently, the large increase in anti-selectivity in reactions of **5**/**6** relative to **9** cannot be attributed to the involvement of transition state A_Z in these reactions.

(40) Wuts, P. G. M.; Bigelow, S. S. *J. Org. Chem.* **1983**, *48*, 3489.

(41) We thank Professor Hoffmann for making these data and his manuscripts (ref 7a,b) available to us prior to publication.

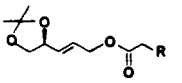
Table IV. Selected ^{1}H NMR Data for **42–55**[a]

primary crotylboronate adduct	acetate derivative	^{1}H chemical shifts[b]								coupling constants[c]	
		$H_{1(E)}$	$H_{1(Z)}$	H_2	H_3	H_4	H_5	$H_{6a,b}$	H_7	C(3)-Me	$^3J_{H(3),H(4)}$	$^3J_{H(4),H(5)}$
19	**42**	5.08	5.01	5.72	2.39	5.06	4.18	3.96, 3.81		1.03	6.6	6.6
20	**43**	5.09	5.01	5.68	2.51	5.03	4.12	3.94, 3.75		1.01	4.5	6.4
21	**44**	5.04	4.98	5.70	2.41	4.85	4.20	3.98, 3.64		1.03	6.1	6.1
22	**45**	5.09	5.04	5.69	2.54	4.79	4.24	3.94, 3.61		1.00	8.0	4.2
23	**46**	5.07	5.01	5.76	2.58	5.02	3.65	4.05	1.25	1.05	6.4	7.4
24	**47**	5.09	5.01	5.72	2.61	4.94	3.58	3.96	1.22	1.01	4.3	7.9
25	**48**	5.05	4.99	5.68	2.58	4.78	3.67	3.78	1.25	1.06	7.6	3.1
26	**49**	5.12	5.07	5.71	2.65	4.74	3.68	3.68	1.22	0.99	9.0	1.6
27	**50**			4.89	2.49	4.94	4.16	3.87		0.92	8.0	4.2
28	**51**			4.97	2.72	5.01	4.06	3.88, 3.75		0.92	4.2	6.1
29	**52**			4.98	2.61	4.80	4.16	3.93, 3.64		0.94	5.9	5.9
31	**53**			4.97	2.66	4.97	3.64	4.05	1.22	0.96	6.3	6.3
32	**54**			4.99	2.82	4.91	3.50	3.95	1.21	0.92	3.9	8.2
33	**55**			4.97	2.78	4.72	3.67	3.80	1.23	0.97	7.5	3.5

[a] Spectra recorded on a Bruker WM 250 instrument (250 MHz) in $CDCl_3$ at 296 K. [b] Chemical Shifts are reported in ppm relative to $CHCl_3$ (7.24). [c] Coupling constants are reported in Hz.

of the major products in reactions of **7**/**9** and **5**, respectively. Third, the increase in anti selectivity[38] of reactions of **7**, **9**, and **5**, in that order, with α-alkoxy-substituted aldehydes such as **4** roughly parallels the increase in anti selectivity of these reagents with **79**. This strongly supports our thesis that favorable electronic activation of Cornforth-like transition states C is responsible for the increased anti selectivity seen in the reactions of alkoxy-substituted aldehydes.[42]

In summary, *diastereofacial selectivity in reactions of allylic boronates with chiral aldehydes is determined both by the substitution pattern of the reagent and the electronic structure of the aldehyde* (cf. Table VII). Conventional models for acyclic 1,2-asymmetric induction,[34-37] which do not take into account long-range nonbonded interactions such as those described here, are not generally useful in predicting the stereochemical outcome of these reactions. These interactions are fundamental in nature and are likely to influence the diastereoselectivity of other reactions that proceed via cyclic transition states. For example, recent data published by Cha[43] on the Ireland–Claisen rearrangements of **80** (~10:1 diastereofacial selectivity via a *Z*(0)-enolate) and **81** (43:57



80, R = OMe
81, R = H

diastereofacial selectivity) can be rationalized by using the transition state analysis described herein. Future studies will address the influence of these nonbonded interactions on the stereochemistry of the aldol reaction.

Experimental Section

General. Proton (^{1}H) NMR spectra were measured in $CDCl_3$ at 250 MHz on a Bruker WM 250 instrument. Chemical shifts are reported in δ units using the 7.24 ppm resonance of residual chloroform as internal reference. Infrared spectra were measured on Perkin-Elmer Model 283B or 237B infrared spectrophotometers calibrated with the 1601-cm^{-1} absorption of polystyrene. IR spectra are reported in wavenumbers (cm^{-1}). Optical rotations were measured on a Perkin-Elmer 144 polarimeter or a Rudolph Autopol III automatic polarimeter using a 1-cm^3 quartz cell (10 cm path length). Mass spectra were measured at 70 eV on a Varian MAT 44 or a Finnegan MAT 8200 instrument. High-resolution mass spectra were measured at 70 eV on the Finnegan MAT 8200. Elemental analyses were performed by Robertson Laboratory, Inc., of Florham Park, NJ.

Capillary GC analyses were performed on a Hewlett-Packard Model 5890 gas chromatograph equipped with a Hewlett-Packard Model 3392A integrator. These analyses were performed on Alltech SE-54 (0.2 mm × 50 m) and Hewlett-Packard dimethylsilicone (0.25 mm × 12 m) fused silica columns using helium as carrier gas (1 mL/min flow rate and 100:1 split ratio). Packed-column GC analyses were performed on a Perkin-Elmer Sigma 3 Model gas chromatograph using a 4.1% Carbowax on Chrom G (80/100) column (0.25 in. × 9 ft) with nitrogen as carrier gas.

All reactions were conducted in oven-dried (125 °C) or flame-dried glassware under atmospheres of dry argon. All solvents were purified before use. Ether, THF, benzene, and toluene were distilled from sodium benzophenone ketyl. Methylene chloride was distilled from CaH_2. Hexane was distilled from NaH.

n-Butyllithium, propenyllithium, propenyl-Grignard, and allyl-Grignard solutions were titrated by using isopropyl alcohol or *sec*-butyl alcohol in benzene or toluene with 1,10-phenanthroline as indicator.[44]

Analytical thin-layer chromatography (TLC) was performed by using 2.5 cm × 10 cm plates coated with a 0.25-mm thickness of silica gel containing PF 254 indicator (Analtech). Preparative thin-layer chromatography (PTLC) was performed by using 20 cm × 20 cm plates coated with 0.25- or 0.5-mm thicknesses of silica gel containing PF 254 indicator (Analtech). Compounds were visualized by charring with either $(NH_4)_2SO_4$ or ethanolic H_2SO_4, or by staining with iodine vapor. Compounds were eluted from the adsorbents with ether or ethyl acetate. Column chromatography was performed using Woelm 230–400 or

(42) Hoffmann has also suggested that Cornforth-like transition states play a significant role in the reactions of benzyl lactaldehyde (**78**) with pinacol (*Z*)- and (*E*)- (methoxyallyl)boronates (see ref 7b).

(43) Cha, J. K.; Lewis, S. C. *Tetrahedron Lett.* **1984**, *25*, 5263.

(44) Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

Table V. Selected ^{13}C NMR Data for **19–33**[a]

crotylboronate adduct	^{13}C chemical shifts							
	C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(3)-Me
19	115.5	140.1	40.5	73.6	77.2	64.5		15.3
20	116.0	139.1	40.0	74.6	77.3	65.4		16.4
21	115.4	139.5	41.3	75.2	77.0	66.1		16.7
23	115.7	140.5	39.7	74.2	81.8	74.7	19.8	14.2
24	116.5	139.1	40.2	74.8	82.3	75.8	19.7	16.2
25	115.4	140.0	42.0	72.6	81.9	73.1	17.8	16.2
27	131.9	126.1	35.3	74.1	77.1	64.1		17.3
28	133.5	125.4	35.4	75.4	77.4	65.2		17.8
29	132.4	125.3	35.2	75.8	77.0	66.1		17.4
31	132.1	126.3	34.8	72.9	82.3	75.6	19.6	16.6
32	134.1	125.3	35.8	74.8	82.7	76.9	19.8	17.8
33	132.8	126.3	37.1	73.1	81.9	73.4	17.9	17.2

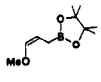
[a] Spectra recorded on a Bruker WM 270 (67.9 MHz) instrument in $CDCl_3$ (77.0 ppm) at 296 K.

Table VI. Selected ^1H NMR Data for **56–63**[a]

diacetate	^1H chemical shifts[b]							coupling constants[c]	
	H_1	H_2	H_3	H_4	$H_{5a,b}$	H_6	C(2)-Me	$^3J_{H(2),H(3)}$	$^3J_{H(3),H(4)}$
56	4.02	2.25	5.08	4.14	3.91, 3.77		0.96	3.2	7.4
57	4.05	2.16	5.02	4.21	3.98, 3.74		0.98	5.0	6.6
58	4.01	2.19	4.90	4.29	3.99, 3.65		1.03	7.6	4.0
59	3.97	2.13	4.99	4.25	3.97, 3.65		0.97	5.1	5.1
60	3.95	2.33	5.07	3.59	3.95	1.22	0.98	3.0	8.4
61	4.06	2.24	5.01	3.66	3.95	1.23	0.99	4.4	7.9
62	4.03	2.29	4.86	3.67	3.67	1.26	1.05	8.3	1.9
63	4.04	2.19	4.95	3.65	3.78	1.26	0.99	5.7	3.1

[a] Spectra recorded on a Bruker WM 250 instrument (250 MHz) in $CDCl_3$ at 296 K. [b] Chemical shifts are reported in ppm relative to $CHCl_3$ (7.24). [c] Coupling constants are reported in Hz.

Table VII. Representative Diastereofacial Selectivities of Reactions of Allylic Boronates and α-Chiral Aldehydes[a]

			
 (5)	97:3[b]		70:30[f,g]
 (1)	>95:5[c]	90:10[d]	
 (9)	80:20[b]	55:45[e]	38:62[g]
 (7)	55:45[b]		17:83[f,g]

[a] Ratios of 4,5-anti to 4,5-syn carbonyl addition products. [b] This study. [c] Roush, W. R.; Michaelides, M. R., unpublished results; see also ref 8c. [d] See ref 40. [e] Roush, W. R.; Palmer, M. A. J., unpublished results. [f] See ref 9b. [g] See ref 7a.

70–230 mesh silica gel (Merck) as described by Still.[45] Radial chromatography was performed on a Harrison Research Chromatotron Model 7924T using 24 cm diameter plates coated with 1 mm thicknesses of silica gel containing PF 254 indicator (Merck). All chromatography solvents were distilled prior to use.

Pinacol (*Z*)-2-Butenylboronate (5). A solution of (*Z*)-2-butene (8.0 mL, 5.0 g, 87 mmol) in 85 mL of THF was treated with KO-*t*-Bu (9.56 g, 85.2 mmol) and *n*-BuLi (55.6 mL of a 1.53 M solution in hexane, 85.1 mmol) at −78 °C for 15 h.[10d,e] The reaction mixture was then treated with $FB(OMe)_2$ (8.22 g, 89.4 mmol) at −78 °C for 1 h. The cold solution was then poured into pH 1 (HCl) 50% saturated aqueous NaCl and extracted with Et_2O (6 × 150 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated to afford 10.2 g of crude crotylboronic acid which was immediately dissolved in CH_2Cl_2 (50 mL) and treated with pinacol (12.1 g, 0.102 mol). The resulting solution was stirred at room temperature overnight. Concentration gave an oil that was distilled through a glass helices packed vigreux column (72–78 °C, >5 mm) to afford 12.1 g (78% from (*Z*)-2-butene) of **5** (97% isomeric purity) as a clear, colorless liquid: R_f 0.66 (4:1 hexane–Et_2O); ^1H NMR δ 5.45 (m, 2 H, H-2, H-3), 1.58 (br d, *J* = 6.6 Hz, 3 H, vinyl CH_3), 1.48 (br d, *J* = 4.2 Hz, 2 H, H-1), 1.22 (s, 12 H, pinacol CH_3's).

Capillary GC analyses of mixtures of **5** and **7** were performed by using a 0.25 mm × 12 m dimethylsilicone on fused silica column with the following temperature program: 70 °C for 4 min then 10°/min to 130 °C, followed by 30°/min to a final temperature of 200 °C. Under these conditions the retention times of **5** and **7** are: **7**, 6.5 min; **5**, 6.6 min.

Pinacol 1-[1,1-Dimethyl-2(*Z*)-butenyl]boronate (6). (*Z*)-Propenyllithium (**13**)[15,16,17] (6.8 mL of a 0.85 M solution in Et_2O, 5.78 mmol) was added dropwise to a solution of **12**[10a,c] (1.18 g, 4.76 mmol) in 48 mL of Et_2O at −78 °C under an argon purge. The resulting solution was stirred at −78 °C for 6 h and then allowed to warm to room temperature overnight. The solvent was removed and the resulting residue was extracted with 50% Et_2O–pentane, filtered through a pad of silica gel, and concentrated to afford 0.91 g (92%) of crude product. This material was distilled (Kugelrohr, 55–60 °C (5 mmHg)) giving 0.77 g (77%) of **6** which was 93% isomerically pure ((*Z*)-propenyllithium (**13**) used in this experiment was prepared from 94% isomerically pure (*Z*)-propenyl bromide[15,17]): R_f 0.73 (4:1 hexane–Et_2O); ^1H NMR δ 5.38 (m, 2 H, H-2, H-3), 1.59 (d, *J* = 5.9 Hz, 3 H, vinyl CH_3), 1.22 (s, 12 H, pinacol CH_3's), 1.09 (s, 6 H, gem-CH_3); IR (CH_2Cl_2) 2970, 2940, 2870, 1480, 1450, 1370, 1120 cm^{-1}; mass spectrum, m/e 210 (parent ion), 195 ($M^+ - CH_3$).

Capillary GC analyses of **6** and **8** were performed by using a 0.25 mm × 12 m dimethylsilicone on fused silica column (70 °C for 4 min, then 10°/min to 130 °C followed by 30°/min to a final temperature of 200 °C). Under these conditions the retention times of **6**, **8** and **17** (see ref 14) are **17**, 4.6 min; **6**, 7.7 min; **8**, 8.2 min.

Pinacol (*E*)-2-Butenylboronate (7). A solution of (*E*)-2-butene (6.0 mL, 3.62 g, 64.6 mmol) in 62 mL of THF was treated with KO-*t*-Bu (6.61 g, 58.9 mmol) and *n*-BuLi (38.5 mL of a 1.53 M solution in hexane, 58.9 mmol) at −78 °C.[10d,e,13] The reaction vessel was transferred to a −50 °C bath for 15 min, and then was recooled to −78 °C.[46] At this point, $FB(OMe)_2$ (6.8 g, 74 mmol) was added; the reaction mixture immediately changed from yellow to colorless. The solution was stirred for 2 h at −78 °C and then was worked up using the procedure described for preparation of **5**. The crude (*E*)-crotylboronic acid (6.2 g) was treated with pinacol (7.9 g, 66.8 mmol) in 50 mL of CH_2Cl_2 overnight at room temperature. The mixture was then concentrated in vacuo and the crude

(45) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

(46) This experiment was performed by Dr. R. L. Halterman. We thank Prof. H. C. Brown for suggesting the conditions (−50 °C, 15 min) for the metallation of (*E*)-2-butene specified here. It should be noted, however, that in our hands this modification of the Schlosser procedure does not lead to any significant improvement in isomeric purity of **7** relative to that obtained when the metallation is performed at −78 °C for 12–15 h (96% isomeric purity).

product distilled through a short vigreaux column (bp 68–76 °C (7 mmHg)) to give 7.2 g (67%) of **7**, the isomeric purity of which was 96%: R_f 0.65 (4:1 hexane–Et_2O); ^1H NMR δ 5.42 (m, 2 H, H-2, H-3), 1.62 (d, J = 6.3 Hz, 3 H, vinyl CH_3), 1.55 (br s, 2 H, H-1), 1.24 (s, 12 H, pinacol CH_3's).

Pinacol 1-[1,1-Dimethyl-2(*E*)-butenyl]boronate (8). (*E*)-Propenyllithium **14** (8.4 mL of a 0.82 M Et_2O solution, 6.87 mmol) was added dropwise over a 45-min period under an argon purge to a solution of **12** (1.54 g, 6.21 mmol) in 60 mL of Et_2O at −78 °C using the procedure described for preparation of **7**. Distillation (Kugelrohr, 68–70 °C (5 mmHg)) of the crude product afforded 1.09 g (84%) of **8** which was 98% isomerically pure and contained 4% of propenylboronate **17** (see ref 14): R_f 0.76 (4:1 hexane–Et_2O): ^1H NMR δ 5.50 (br d, J = 15.4 Hz, 1 H, H-2), 5.33 (dq, J = 15.4, 6.1 Hz, 1 H, H-3), 1.63 (dd, J = 6.1, 1.2 Hz, 3 H, vinyl CH_3), 1.19 (s, 12 H, pinacol CH_3's), 1.00 (s, 6 H, gem-CH_3); IR (neat) 2940, 2850, 1630, 1460, 1380, 1300, 1140 cm^{-1}; mass spectrum, m/e 210 (parent ion), 209 (boron isotope). High-resolution mass spectrum. Calcd for $C_{12}H_{23}{}^{11}BO_2$ requires 210.1791, found 210.2338.

Pinacol Allylboronate (9).[19] Allylmagnesium bromide (182 mL of 1.2 M solution in ether, 0.22 mol) and a solution of freshly distilled trimethyl borate (25 g, 0.24 mol, 1.1 equiv) in 157 mL of ether were added simultaneously, but separately, over a 2.5 h period to 200 mL of ether maintained at −78 °C. The mixture was stirred at −78 °C for 2.5 h (mechanical stirring is required due to the heavy precipitate) and then was warmed to 0 °C at which point 230 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 150 mL portions (4×) of 5:1 ether–CH_2Cl_2. The combined extracts were dried (Na_2SO_4), filtered, and concentrated in vacuo without removal of all of the solvent (anhydrous, concentrated allylboronic acid is unstable).

The solution of allylboronic acid was diluted to 500 mL with anhydrous ether, purged with argon, treated with anhydrous pinacol (19.4 g, 164 mmol, 0.75 equiv), and stirred at room temperature (14 h). Anhydrous Na_2SO_4 was added and the solution was filtered through adsorbent cotton. Distillation (bp 55–60 °C, 30 torr; lit.[19] 50–53 °C (5 torr)) afforded 19.4 g (53% from allylmagnesium bromide) of **9**: R_f 0.6 (23:2 hexane–ether); ^1H NMR δ 5.85 (m, 1 H, H-2), 4.97 (br d, J = 16 Hz, 1 H, H-3a), 4.93 (br m, J = 9 Hz, 1 H, H-3b), 1.72 (d, J = 7.5 Hz, 2 H, H-1), 1.24 (s, 12 H, pinacol CH_3's); IR (neat) 3085, 2985, 2940, 1640, 1350 (br), 1272, 1145 (br), 1114, 992, 970, 900, 878, 847 cm^{-1}; mass spectrum, m/e 168 (M^+).

General Procedure for Reactions of Allylic Boronates 5–9 with Aldehydes 2 and 4. The reaction of **2** with **5** is described as an illustrative case. A solution of (*Z*)-crotylboronate **5** (98% isomeric purity, 0.92 g, 5.07 mmol) in CH_2Cl_2 (50 mL) was treated with aldehyde **2** (1.08 g, 5.85 mmol) at −78 °C. The resulting solution was allowed to warm gradually to room temperature overnight. The progress of the reaction was monitored by TLC until all of **4** was consumed (usually 12–24 h). The reaction mixture was then poured into H_2O (50 mL), extracted with Et_2O (4 × 50 mL), dried over Na_2SO_4, filtered, and concentrated. The crude product (2.23 g) was a 96:2:1:1 mixture of **23**, **24**, **25**, and **26**, respectively, as determined by capillary GC analysis (0.2 mm × 50 m SE-54 on a fused silica column, temperature program 70 °C for 4 min, then 5°/min to a final temperature of 200 °C; retention times were **26**, 32.9 min; **25**, 33.5 min; **24**, 34.0 min; **23**, 34.2 min). Chromatography of the mixture on silica gel (50 × 160 mm column) using 3:1 hexane–Et_2O as eluant gave 0.76 g (63%) of pure **23** and 0.40 g (33%) of a mixture of **23**–**26**. Pure samples of **24**–**26** were obtained by radial chromatography of ca. 100 mg mixtures on silica gel (1 mm plate) using 10:1 hexane–Et_2O as eluant.

Mixtures of **19**–**22** obtained from the reactions of **4** with either **5** or **7** were analyzed by capillary GC (0.2 mm × 50 m SE-54 on a fused silica column, temperature program: 70 °C for 45 min, then 30°/min to a final temperature of 200 °C). The retention times observed are: **22**, 35.1 min; **21**, 37.5 min; **19**, 38.7 min; and **20**, 40.8 min. These adducts were separated by radial chromatography (1 mm silica gel plate) using 10:1 hexane–Et_2O as eluant or by PTLC (3:1 hexane–Et_2O, 2 elutions).

Mixtures of **31**, **32**, and **33** obtained from the reactions of **2** with **6** or **8** were analyzed by GC (0.2 mm × 50 mm SE-54 on a fused silica column, temperature program starting at 70 °C for 4 min, then 10°/min to 200 °C). The retention times of **31**–**33** are **33**, 20.4 min; **32**, 20.6 min; **31**, 21.0 min. A peak with a retention time of 19.9 min was assigned to **34**. Pure samples of **31**–**33** were obtained either by PTLC (3:1 hexane–Et_2O, 2 elutions) or by radial chromatography (1 mm silica gel plate) using 10:1 hexane–Et_2O as eluant.

Mixtures of **27**–**29** obtained from the reactions of **4** with **6** or **8** were analyzed as follows. Mixtures of **28** and **29** were analyzed by packed phase GC (0.25 in. × 9 ft 4.1% Carbowax on Chrom G (80/100) column, temperature program starting at 80 °C for 2 min then 10°/min to a final temperature of 190 °C). The retention times observed for **28** and **29** are **29**, 18.3 min; **28**, 20.8 min. Isomer **27** coelutes with **28** under these conditions. Capillary GC analysis (0.2 mm × 50 m SE-54 on fused silica column, temperature program: 100 °C for 2 min then 3°/min to 130 °C where the rate was increased to 50°/min until a final temperature of 200 °C) resolves **27** from **28** and **29** (which coelute under these conditions); retention times were **28** and **29**, 15.7 min; **27**, 16.0 min. A peak at 14.7 min was assigned to **30**. Pure samples of **27**–**29** were obtained by chromatography using the conditions described for the mixtures of **31**–**33**.

Finally, mixtures of **35** and **36** (from reactions of **4** and **9**) and **37** and **38** (from reactions of **2** and **9**) were easily analyzed by packed-phase GC analysis (0.25 in. × 10 ft 4.1% Carbowax on Chrom. G column). Mixtures of **35** and **36** are not easily separated by silica gel chromatography. Consequently, these mixtures were benzylated as described by Mulzer[12c] and then separated chromatographically. Stereochemical assignments for these benzyl ethers were confirmed by repeating the correlation studies described by Mulzer.[12c] Pure samples of **37** and **38** were obtained by careful PTLC (4:1 hexane ether, multiple elutions). Stereochemical assignments in these cases were confirmed by methanolysis to the corresponding triols which were compared with authentic samples.[24] Complete spectroscopic data for **35**, **36**, **37** and **38** are reported in ref 9a.

Data for 19: R_f 0.39 (3:1 hexane–ether, two elutions); $[\alpha]^{23}_D$ +47.6° (*c* 2.1, CH_2Cl_2); ^1H NMR δ 5.72 (br m, 1 H, H-2), 5.07 (br d, J = 16.6 Hz, 1 H, H-1a), 5.01 (br d, J = 11.4 Hz, 1 H, H-1b), 4.09 (ddd, $J_{5,6}$ = 6.8, 6.8 Hz, $J_{4,5}$ = 4.7 Hz, 1 H, H-5), 3.98–3.84 (m, 2 H, H-6a, H-6b), 3.64 (dd, $J_{3,4}$ = 6.8 Hz, $J_{4,5}$ = 4.7 Hz, 1 H, H-4), 2.26 (m, 1 H, H-3), 2.02 (br s, 1 H, O–H), 1.39 (s, 3 H, acetonide CH_3), 1.32 (s, 3 H, acetonide CH_3), 1.07 (d, J = 6.7 Hz, 3 H, CH_3); IR (neat) 3500, 3100, 3020, 2950, 1450, 1370, 1200, 1050, 910, 850 cm^{-1}; mass spectrum, m/e 171 ($M^+ - CH_3$). The acetate derivative **42** prepared from **19** gave a satisfactory combustion analysis. Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83. Found: C, 63.03; H, 8.90.

Data for 20: R_f 0.30 (3:1 hexane–ether, two elutions); $[\alpha]^{22}_D$ +6.3° (*c* 1.25, CH_2Cl_2); ^1H NMR δ 5.84 (br m, 1 H, H-2), 5.14 (dd, J = 12.9, 1.6 Hz, 1 H, H-1a), 5.08 (dd, J = 16.2, 1.6 Hz, 1 H, H-1b), 4.04 (m, 1 H, H-5), 3.93 (m, 2 H, H-6a, H-6b), 3.59 (dd, $J_{3,4}$ = $J_{4,5}$ = 5.9 Hz, 1 H, H-4), 2.37 (m, 1 H, H-3), 1.40 (s, 3 H, acetonide CH_3), 1.34 (s, 3 H, acetonide CH_3), 1.07 (d, J = 7.2 Hz, 3 H, CH_3); IR (neat) 3480, 2980, 2940, 2900, 1460, 1370, 1250, 1210, 1070, 910, 850 cm^{-1}; mass spectrum, m/e 171 ($M^+ - CH_3$). The acetate derivative **43** prepared from **20** gave a satisfactory combustion analysis. Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83. Found: C, 63.36; H, 9.08.

Data for 21: R_f 0.50 (3:1 hexane–ether, two elutions); $[\alpha]^{23}_D$ +14.5° (*c* 0.95, CH_2Cl_2); ^1H NMR δ 5.86 (br m, 1 H, H-2), 5.07 (dd, J = 17.0, 1.5 Hz, 1 H, H-1a), 5.04 (dd, J = 8.8, 1.5 Hz, 1 H, H-1b), 4.08 (ddd, J = 6.6, 6.6, 6.6 Hz, 1 H, H-5), 3.98 (dd, $J_{6a,6b}$ = 8.2 Hz, $J_{5,6a}$ = 6.6 Hz, 1 H, H-6a), 3.71 (dd, $J_{6a,6b}$ = 8.2 Hz, $J_{5,6b}$ = 6.6 Hz, H-6b), 3.37 (m, 1 H, H-4), 2.25 (br m, 1 H, H-3), 1.40 (s, 3 H, acetonide CH_3), 1.34 (s, 3 H, acetonide CH_3), 1.08 (d, J = 6.9 Hz, 3 H, CH_3); IR (CH_2Cl_2) 3580, 2980, 2880, 1450, 1380, 1370, 1210, 1070, 910, 850 cm^{-1}; mass spectrum, m/e 171 ($M^+ - CH_3$). The acetate derivative **44** gave a correct combustion analysis. Anal. Calcd for $C_{12}H_{20}O_4$: C, 63.14; H, 8.83. Found: C, 63.39; H, 9.07.

Data for 22: R_f 0.37 (2:1 hexane–ether); $[\alpha]^{22}_D$ −11.4° (*c* 0.9, $CHCl_3$); ^1H NMR δ 5.71 (m, 1 H, H-2), 5.08 (br d, J = 16 Hz, 1 H H-1a), 5.03 (br d, J = 10.2 Hz, 1 H, H-1b), 4.13 (ddd, J = 5.0, 6.4, 6.8 Hz, 1 H, H-5), 3.96 (dd, J = 6.4 Hz, 8.1 Hz, 1 H, H-6a), 3.72 (dd, J = 8.1, 6.8 Hz, 1 H, H-6b), 3.29 (ddd, J = 5.0, 6.8, 6.8 Hz, 1 H, H-4), 2.26 (br m, 1 H, H-3), 2.18 (d, J = 6.8 Hz, –OH), 1.41 (s, 3 H, acetonide CH_3), 1.34 (s, 3 H, acetonide CH_3), 1.08 (d, J = 6.8 Hz, 3 H, CH_3); IR (CH_2Cl_2) 3580, 3080, 2980, 2950, 2890, 1450, 1380, 1360, 1200, 1160, 1050, 990, 860 cm^{-1}.

Data for 23: R_f 0.42 (3:1 hexane–ether, two elutions); $[\alpha]^{23}_D$ −12.1° (*c* 1.95, $CHCl_3$); ^1H NMR δ 5.80 (br m, 1 H, H-2), 5.12 (br d, J = 17.7 Hz, 1 H, H-1a), 5.06 (br d, J = 9.9 Hz, 1 H, H-1b), 4.11 (dq, J = 6.3, 6.1 Hz, 1 H, H-6), 3.61 (m, 2 H, H-4, H-5), 2.45 (br m, 1 H, H-3), 1.82 (d, J = 2.1 Hz, 1 H, O–H), 1.43–1.59 (m, 10 H, cyclohexyl), 1.33 (d, J = 6.1 Hz, 3 H, H-7), 1.08 (d, J = 6.8 Hz, 3 H, CH_3); IR (CH_2Cl_2) 3600, 3040, 2960, 2880, 1360, 1100 cm^{-1}; mass spectrum, m/e 240 (parent ion). The acetate derivative **46** gave a correct combustion analysis. Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.06; H, 9.28. Found: C, 68.12; H, 9.29.

Data for 24: R_f 0.30 (1:1 hexane–ethyl ether); $[\alpha]^{24}_D$ +22.5° (*c* 0.7, CH_2Cl_2); ^1H NMR δ 5.86 (br m, 1 H, H-2), 5.17 (br d, J = 17.3 Hz, 1 H, H-1a), 5.10 (br d, J = 10.1 Hz, 1 H, H-1b), 4.09 (dq, J = 6.3, 6.0 Hz, 1 H, H-6), 3.48 (br m, 2 H, H-4, H-5), 2.49 (m, 1 H, H-3), 1.52–1.72 (br m, 10 H, cyclohexyl), 1.33 (d, J = 6.0 Hz, 3 H, H-7), 1.08 (d, J = 7.0 Hz, 3 H, CH_3); IR (CH_2Cl_2) 3600, 3040, 2960, 2860, 1445, 1360, 1160, 1100, 1050, 990, 940, 910, 680 cm^{-1}; mass spectrum, m/e 241 ($M^+ + 1$), 240 (parent ion). The acetate derivative **47** gave a correct

combustion analysis. Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.06; H, 9.28. Found: C, 68.03; H, 9.11.

Data for 25: R_f 0.53 (1:1 hexane–ether); $[\alpha]^{24}_D$ −2.3° (*c* 1.2, CH_2Cl_2); ^1H NMR δ 5.91 (br m, 1 H, H-2), 5.10 (br d, *J* = 17.4 Hz, 1 H, H-1a), 5.04 (br d, *J* = 10.7 Hz, 1 H, H-1b), 4.05 (dq, *J* = 8.2, 6.1 Hz, 1 H, H-6), 3.55 (dd, $J_{4,5}$ = 2.7 Hz, $J_{5,6}$ = 8.2 Hz, 1 H, H-5), 3.29 (m, 1 H, H-4), 2.37 (m, 1 H, H-3), 2.20 (d, *J* = 8.0 Hz, 1 H, O–H), 1.32–1.69 (br m, 10 H, cyclohexyl), 1.25 (d, *J* = 6.1 Hz, 3 H, H-7), 1.07 (d, *J* = 6.8 Hz, 3 H, CH_3); IR (neat) 3520, 2930, 2850, 1440, 1360, 1270, 1220, 1160, 1100, 930, 900 cm^{-1}; mass spectrum, *m/e* 240 (parent ion). The acetate derivative **48** gave a correct combustion analysis. Anal. Calcd for $C_{16}H_{26}O_4$: C, 68.06; H, 9.28. Found: C, 67.94; H, 9.20.

Data for 26: R_f 0.41 (4:1 hexane–ether); $[\alpha]^{22}_D$ +30.1° (*c* 2.8, $CHCl_3$); ^1H NMR δ 5.73 (m, 1 H, H-2), 5.05 (br d, *J* = 16 Hz, 1 H, H-1a), 5.03 (br d, *J* = 10 Hz, H-1b), 4.03 (m, 1 H, H-6), 3.59 (dd, *J* = 8.4, 2.5 Hz, 1 H, H-5), 3.22 (ddd, *J* = 2.5, 5.8, 8.0 Hz, 1 H, H-4), 2.33 (m, 1 H, H-3), 2.13 (d, *J* = 8.0 Hz, 1 H, –OH), 1.33–1.57 (br m, 10 H, cyclohexyl), 1.22 (d, *J* = 6.1 Hz, 3 H, H-7), 1.08 (d, *J* = 6.8 Hz, 3 H, CH_3); IR (CH_2Cl_2) 3530, 2935, 2840, 1445, 1370, 1360, 1325, 1275, 1200, 1160, 1100, 940, 900, 710 cm^{-1}; mass spectrum, *m/e* 240 (parent ion).

Data for 27: R_f 0.48 (3:1 hexane–ether, two elutions); $[\alpha]^{23}_D$ +47.4° (*c* 3.7, CH_2Cl_2); ^1H NMR δ 4.91 (br d, *J* = 9.9 Hz, 1 H, H-2), 4.09 (ddd, $J_{4,5}$ = 3.5 Hz, $J_{5,6}$ = 7.0, 7.0 Hz, 1 H, H-5), 3.87 (m, 2 H, H-6a, H-6b), 3.57 (br d, $J_{3,4}$ = 7.0 Hz, 1 H, H-4), 2.26 (br m, 1 H, H-3), 2.09 (br s, 1 H, O–H), 1.67 (d, *J* = 0.8 Hz, 3 H, vinyl CH_3), 1.58 (d, *J* = 1.0 Hz, 3 H, vinyl CH_3), 1.41 (s, 3 H, acetonide CH_3), 1.35 (s, 3 H, acetonide CH_3), 1.02 (d, *J* = 6.5 Hz, 3 H, CH_3); IR (neat) 3500, 3050, 3000, 2940, 1450, 1375, 1325, 1200, 1150, 1050, 980, 940, 850 cm^{-1}; mass spectrum, *m/e* 214 (parent ion), 199 ($M^+ - CH_3$). The acetate derivative **50** gave a correct combustion analysis. Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44. Found: C, 65.85; H, 9.57.

Data for 28: R_f 0.35 (3:1 hexane–ether, two elutions); $[\alpha]^{23}_D$ −0.5° (*c* 2.2, CH_2Cl_2); ^1H NMR δ 5.02 (br d, *J* = 9.7 Hz, 1 H, H-2), 4.01 (m, 1 H, H-5), 3.91 (m, 2 H, H-6a, H-6b), 3.56 (br dd, *J* = 4.7, 4.7 Hz, 1 H, H-4), 2.54 (br m, 1 H, H-3), 1.87 (br s, 1 H, O–H), 1.70 (d, *J* = 0.9 Hz, 3 H, vinyl CH_3), 1.62 (d, *J* = 1.0 Hz, 3 H, vinyl CH_3), 1.39 (3 H, acetonide CH_3), 1.33 (s, 3 H, acetonide CH_3), 0.98 (d, *J* = 6.8 Hz, 3 H, CH_3); IR (neat) 3500, 2980, 2920, 1450, 1370, 1250, 1210, 1150, 1060, 840 cm^{-1}; mass spectrum, *m/e* 215 (M+1), 214 (parent ion), 199 ($M^+ - CH_3$). The acetate derivative **51** gave a correct combustion analysis. Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44. Found: C, 65.82; H, 9.41.

Data for 29: R_f 0.55 (3:1 hexane–ether, two elutions); $[\alpha]^{23}_D$ +22.5° (*c* 0.8, CH_2Cl_2); ^1H NMR δ 5.10 (br d, *J* = 9.6 Hz, 1 H, H-2), 4.03 (ddd, $J_{4,5}$ = $J_{5,6}$ = 6.3 Hz, 1 H, H-5), 3.94 (dd, *J* = 7.6, 6.3 Hz, 1 H, H-6a), 3.71 (dd, *J* = 7.6, 6.3 Hz, 1 H, H-6b), 3.32 (m, 1 H, H-4), 2.41 (br m, 1 H, H-3), 2.21 (d, *J* = 3.4 Hz, 1 H, O–H), 1.68 (d, *J* = 1.0 Hz, 3 H, vinyl CH_3), 1.58 (d, *J* = 1.1 Hz, 3 H, vinyl CH_3), 1.39 (s, 3 H, acetonide CH_3), 1.33 (s, 3 H, acetonide CH_3), 0.99 (d, *J* = 6.8 Hz, 3 H, CH_3); IR (neat) 3500, 2980, 2920, 2860, 1450, 1370, 1250, 1210, 1150, 1050, 840 cm^{-1}; mass spectrum, *m/e* 214 (parent ion), 199 ($M^+ - CH_3$). The acetate derivative **52** gave a correct combustion analysis. Anal. Calcd for $C_{14}H_{24}O_4$: C, 65.60; H, 9.44. Found: C, 65.47; H, 9.67.

Data for 31: R_f 0.58 (1:1 hexane–ether); $[\alpha]^{23}_D$ −10.5° (*c* 1.2, CH_2Cl_2); ^1H NMR δ 5.01 (br d, *J* = 9.4 Hz, 1 H, H-2), 4.07 (dq, *J* = 6.2, 6.1 Hz, 1 H, H-6), 3.58 (m, 2 H, H-4, H-5), 2.48 (br m, 1 H, H-3), 1.99 (d, *J* = 3.1 Hz, O–H), 1.43–1.79 (m, 16 H, cyclohexyl and both vinyl CH_3), 1.24 (d, *J* = 6.1 Hz, 3 H, H-7), 1.01 (d, *J* = 6.7 Hz, 3 H, CH_3); IR (neat) 3500, 2930, 2860, 1440, 1360, 1320, 1270, 1220, 1160, 1100, 1040, 980, 940, 830 cm^{-1}; mass spectrum, *m/e* 268 (parent ion). The acetate derivative **53** gave a correct combustion analysis. Anal. Calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.65; H, 9.78.

Data for 32: R_f 0.51 (1:1 hexane–ether); $[\alpha]^{24}_D$ +35.6° (*c* 1.0, CH_2Cl_2); ^1H NMR δ 4.97 (br d, *J* = 9.7 Hz, 1 H, H-2), 4.09 (dq, *J* = 6.2, 6.0 Hz, 1 H, H-6), 3.43 (m, 2 H, H-4, H-5), 2.62 (m, 1 H, H-3), 1.56–1.72 (m, 16 H, cyclohexyl and both vinyl CH_3), 1.32 (d, *J* = 6.0 Hz, 3 H, H-7), 1.00 (d, *J* = 7.0 Hz, 3 H, CH_3); IR (neat) 3480, 2920, 2860, 1450, 1360, 1330, 1270, 1250, 1225, 1160, 1050, 980, 940, 900, 840 cm^{-1}; mass spectrum, *m/e* 269 ($M^+ + 1$), 268 (parent ion). The acetate derivative **54** gave a satisfactory high resolution molecular weight determination. Calcd for $C_{18}H_{30}O_4$ requires 310.2144, found 310.2150.

Data for 33: R_f 0.65 (1:1 hexane–ether); $[\alpha]^{23}_D$ +1.8° (*c* 1.9, CH_2Cl_2); ^1H NMR δ 5.07 (br d, *J* = 9.4 Hz, 1 H, H-2), 4.04 (dq, *J* = 8.0, 6.1 Hz, 1 H, H-6), 3.53 (dd, $J_{4,5}$ = 3.0 Hz, $J_{5,6}$ = 8.0 Hz, 1 H, H-5), 3.23 (ddd, $J_{3,4}$ = 6.4 Hz, $J_{4,5}$ = 3.0 Hz, $J_{4,OH}$ = 6.8 Hz, 1 H, H-4), 2.55 (m, 1 H, H-3), 2.19 (d, *J* = 6.8 Hz, 1 H, O–H), 1.36–1.69 (m, 16 H, cyclohexyl and both vinyl CH_3), 1.22 (d, *J* = 6.1 Hz, 3 H, H-7), 0.98 (d, *J* = 6.8 Hz, 3 H, CH_3); IR (neat) 3540, 2940, 2860, 1450, 1370, 1280, 1230, 1170, 1100, 990, 940, 725 cm^{-1}; mass spectrum, *m/e* 269 ($M^+ + 1$), 268 (parent ion). The acetate derivative **55** gave a satisfactory high resolution molecular weight determination. Calcd for $C_{18}H_{30}O_4$ requires 310.2144, found 310.2158.

General Procedure for Degradation of 19–33 to 1,3-Diacetates 56–63 (See Schemes I and II). A mixture of **19** (44 mg, 0.24 mmol), acetyl chloride (86 μL, 95 mg, 1.2 mmol), and pyridine (195 μL, 191 mg, 2.4 mmol) in 2 mL of dry CH_2Cl_2 was stirred overnight at room temperature. The solution was diluted with saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The crude product was purified by preparative TLC (0.5-mm silica gel, 2:1 hexane–ether) giving 47 mg (86%) of pure acetate **42** ($[\alpha]^{20}_D$ +35.1° (*c* 1.1, $CHCl_3$)). Partial ^1H NMR data for acetates **42–55** are summarized in Table IV; complete spectroscopic data and physical constants are reported in the Ph.D. thesis of M.A.A. cited in ref 1.

A solution of **42** (45 mg, 0.19 mmol) in CH_2Cl_2 (10 mL) at −78 °C was treated with a stream of ozone in O_2 for 1.5 min (0.9 mmol/min, 1.4 mmol). The resulting blue solution was then purged with oxygen for 20 min with the temperature maintained at −78 °C. The reaction was quenched by addition of $(CH_3)_2S$ (1 mL) and allowed to warm to room temperature. Solvent was removed in vacuo and the residue dissolved in THF (10 mL) and treated with excess lithium aluminum hydride (110 mg, 2.9 mmol) at 0 °C. Fifteen minutes later, the reaction was quenched by the addition of 0.25 mL of H_2O and 0.75 mL of 1 N NaOH and allowed to warm to room temperature. The resulting slurry was filtered through Celite, dried over Na_2SO_4, filtered, and concentrated to afford 36 mg (96%) of crude diol. This material was dissolved in CH_2Cl_2 (5 mL) and treated with pyridine (0.2 mL, 1.9 mmol) and AcCl (0.07 mL, 0.99 mmol) overnight. The reaction mixture was concentrated in vacuo and the residue chromatographed (1-mm silica gel preparative plate, 2:1 hexane–ether, 2 elutions) to afford 43 mg (80%) of pure **56**. Compound **56** was also prepared by degradation of **27** via **50**: R_f 0.49 (2:1 ether–hexane); $[\alpha]^{23}_D$ +6.2° (*c* 1.1, CH_2Cl_2); partial ^1H NMR data are summarized in Table VI; IR (neat) 2970, 2930, 2860, 1760, 1460, 1375, 1225, 1100, 830 cm^{-1}; mass spectrum, *m/e* 259 ($M^+ - CH_3$). High reslution mass spectrum. Calcd for $C_{12}H_9O_6$ ($M^+ - CH_3$) 259.1181. Found: 259.1179.

Data for 57 (prepared from 20 and 28): R_f 0.35 (1:1 hexane–ether); $[\alpha]^{23}_D$ +6.0° (*c* 0.8, CH_2Cl_2); ^1H NMR, see Table VI; IR (neat) 2980, 2890, 1740, 1370, 1220, 1040, 840 cm^{-1}; mass spectrum, *m/e* 259 ($M^+ - CH_3$). Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 57.01; H, 8.09.

Data for 58 (prepared from 21 and 29): R_f 0.32 (1:1 hexane–ether); $[\alpha]^{23}_D$ +25.4° (*c* 0.7, CH_2Cl_2); ^1H NMR, see Table VI; IR (neat) 2980, 2930, 2880, 1740, 1450, 1370, 1240, 1060, 970, 840 cm^{-1}; mass spectrum, *m/e* 259 ($M^+ - CH_3$). Anal. Calcd for $C_{13}H_{22}O_6$: C, 56.92; H, 8.08. Found: C, 57.25; H, 8.23.

Data for 59 (prepared from 22): R_f 0.56 (2:1 ether–hexane); $[\alpha]^{22}_D$ +18.0° (*c* 0.25, CH_2Cl_2); ^1H NMR, see Table VI; IR (neat) 2940, 1740, 1450, 1370, 1220, 1030 cm^{-1}; mass spectrum, *m/e* 274 (parent ion), 259 ($M^+ - CH_3$).

Data for 60 (prepared from 23 and 31): 0.53 (1:1 hexane–ether); $[\alpha]^{23}_D$ +5.1° (*c* 0.9, CH_2Cl_2); ^1H NMR, see Table VI; IR (neat) 2920, 2880, 2800, 1760, 1500, 1450, 1375, 1225, 1100, 1040, 940 cm^{-1}; mass spectrum, *m/e* 328 (parent ion), 285 ($M^+ - CH_3CO$). Anal. Calcd for $C_{17}H_{28}O_6$: C, 62.18; H, 8.59. Found: C, 61.94; H, 8.87.

Data for 61 (prepared from 24 and 32): 0.56 (1:1 hexane–ether); $[\alpha]^{23}_D$ +9.4° (*c* 2.0, CH_2Cl_2); ^1H NMR, see Table VI; IR (CH_2Cl_2) 2930, 2850, 1770, 1360, 1140, 1090, 1020 cm^{-1}; mass spectrum, *m/e* 328 (parent ion), 285 ($M^+ - CH_3CO$). Anal. Calcd for $C_{17}H_{28}O_6$: C, 62.18; H, 8.59. Found: C, 61.93; H, 8.67.

Data for 62 (prepared from 25 and 33): R_f 0.57 (1:1 hexane–ether); $[\alpha]^{23}_D$ −30.3° (*c* 1.1, CH_2Cl_2); ^1H NMR, see Table VI; IR (CH_2Cl_2) 2930, 2840, 1760, 1420, 1360, 1240, 1090, 1020, 940 cm^{-1}; mass spectrum, *m/e* 328 (parent ion), 285 ($M^+ - CH_3CO$). Anal. Calcd for $C_{17}H_{28}O_6$: C, 62.18; H, 8.59. Found: C, 62.08; H, 8.69.

Data for 63 (prepared from 26): R_f 0.48 (1:1 hexane–ether); $[\alpha]^{22}_D$ +12.0° (*c* 0.5, CH_2Cl_2); ^1H NMR, see Table VI; IR (neat) 2950, 2870, 1740, 1370, 1230, 1100, 1030 cm^{-1}; mass spectrum, *m/e* 329 ($M^+ + 1$), 328 (parent ion), 285 ($M^+ - CH_3CO$).

Preparation of Allylic Alcohol 71. Ethyl diisopropylphosphonoacetate (8.8 g, 34.9 mmol) in 100 mL of THF was treated with KO-*t*-Bu (3.52 g, 31.4 mmol) at 0 °C for 1 h.[32b] The resulting solution was cooled to −78 °C and then **2** (2.14 g, 11.6 mmol) was added. After 2.5 h, the reaction mixture was poured into aqueous NH_4Cl and extracted with CH_2Cl_2. The combined organics were washed with brine, dried over $MgSO_4$, and concentrated. The crude product was chromatographed over silica gel (60 × 160 mm column) eluting with 10% ether–hexane to give 1.93 g (65%) of pure α,β-unsaturated ester: R_f 0.61 (4:1 hexane–ether); ^1H NMR δ 6.88 (dd, *J* = 16.0, 5.0 Hz, 1 H, H-2), 6.12 (dd, *J* = 14.7, 2.1 Hz, 1 H, H-1), 4.20 (q, *J* = 7.6 Hz, 3 H), 4.05 (br t, *J* = 6.3 Hz, 1 H, H-3), 3.82 (br quint, *J* = 5.5 Hz, 1 H, H-5), 1.35–1.68 (m,

10 H, cyclohexyl), 1.32 (t, J = 7.6 Hz, 3 H), 1.28 (d, J = 6.3 Hz, 3 H, H-6).

DIBAL-H (20 mL of a 1.3 M solution in hexane, 25 mmol) was added dropwise to a solution of the above ethyl ester (1.68 g, 6.60 mmol) in 20 mL of Et_2O at 0 °C. After 4 h, saturated Na_2SO_4 (7 mL) was added. The mixture was stirred at room temperature for 2.5 h, and then the resulting slurry was filtered through Celite. The filtrate was washed with aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was Kugelrohr distilled (100–120 °C (2.8 mmHg)) to afford 1.20 g (86%) of pure **71**: R_f 0.10 (1:1 hexane–ether); ^{1}H NMR δ 5.95 (dt, J = 15.2, 4.9 Hz, 1 H, H-2), 5.68 (br dd, J = 15.7, 7.5 Hz, 1 H, H-3), 4.17 (br t, J = 5.3 Hz, 2 H, H-1), 3.92 (t, J = 7.9 Hz, 1 H, H-4), 3.78 (br quint, J = 6 Hz, 1 H, H-5), 1.29–1.71 (m, 11 H, cyclohexyl and –OH), 1.23 (d, J = 6.0 Hz, 3 H, H-6).

Epoxyalcohols 72 and 75. A solution of Ti(O-*i*-Pr)$_4$ (0.85 mL, 1.86 mmol) in 17 mL of CH_2Cl_2 was treated with (+)-diisopropyl tartrate (0.9 g, 3.82 mmol) at –23 °C for 15 min. Allylic alcohol **71** (0.5 g, 2.39 mmol) was then added, followed 15 min later by TBHP (1.97 mL of a 3.64 M solution in toluene, 7.17 mmol).[47] This mixture was stored in a –20 °C freezer overnight and then was treated with $(CH_3)_2S$ (1.0 mL, 14.3 mmol). This solution was stirred at room temperature for 24 h and then saturated aqueous Na_2SO_4 (3 mL) was added. The resulting slurry was filtered through Celite and concentrated, and then the residue was partitioned between Et_2O (50 mL) and brine (50 mL) containing NaOH (4 mL of a 3.75 M solution, 15 mmol). When tartrate was no longer detected by TLC analysis, the mixture was extracted with EtOAc, dried over Na_2SO_4, and concentrated. The crude residue was chromatographed over silica gel (50 × 160 mm column) eluting with 2:1 hexane–ether to afford 0.41 g (75%) of pure **72**: R_f 0.36 (2:1 ether–hexane); $[\alpha]^{22}_D$ –22.5° (c 1.3, $CHCl_3$); ^{1}H NMR δ 4.08 (br quint, J = 5.9 Hz, 1 H, H-5), 4.00 (m, 1 H, H-1a), 3.93 (m, 1 H, H-1b), 3.35 (dd, J = 8.0, 5.6 Hz, 1 H, H-4), 3.13 (m, 1 H, H-2), 3.04 (dd, J = 5.9, 2.1 Hz, 1 H, H-3), 1.54–1.69 (m, 11 H, cyclohexyl and –OH), 1.30 (d, J = 6.1 Hz, 3 H, H-6); IR ($CHCl_3$) 3600, 2950, 2870, 1450, 1370, 1270, 1100, 940, 910 cm^{-1}.

Epoxide **75** was prepared (72% yield) by using an analogous procedure employing (–)-diethyl tartrate as the chiral auxiliary: R_f 0.38 (2:1 ether–hexane); $[\alpha]^{22}_D$ +19.8° (c 1.7, $CHCl_3$); ^{1}H NMR δ 4.04 (br quint, J = 6 Hz, 1 H, H-5), 3.97 (m, 1 H, H-1a), 3.66 (m, 1 H, H-1b), 3.48 (dd, J = 8.3, 4.4 Hz, 1 H, H-4), 3.17 (m, 1 H, H-2), 3.06 (dd, J = 4.5, 2.2 Hz, 1 H, H-3), 1.87 (s, 1 H, O–H), 1.39–1.61 (m, 10 H, cyclohexyl), 1.30 (d, J = 6.0 Hz, 3 H, H-6); IR (CH_2Cl_2) 3680, 2940, 2840, 1440, 1360, 1330, 1090, 930 cm^{-1}.

General Procedure for Reaction of Epoxides 65, 68, 72, and 75 with H_2C=CHMgBr and CuBr·S(CH_3)$_2$ (See Schemes III and IV). A solution of CH_2=CHMgBr in THF (2.9 mL of a 1.38 M solution, 4.04 mmol) was added to a mixture of CuBr·S(CH_3)$_2$ (0.33 g, 1.62 mmol) and 2 mL of $(CH_3)_2S$ in 8 mL of Et_2O at –23 °C.[31] After 10 min, a solution of epoxide **65**[30] (75 mg, 0.43 mmol) in 1 mL of Et_2O was added. The reaction mixture was maintained at –23 °C for 9 h and then was poured into pH 8.5 aqueous NH_4Cl/NH_4OH solution, extracted with EtOAc, dried over Na_2SO_4, filtered, and concentrated. The crude product (85 mg, 97%) was an 11:1 mixture of **66** and **65** (^{1}H NMR analysis). Pure **66** (51 mg, 59%) was obtained by PTLC (0.5-mm plate, 10:1 CH_2Cl_2–ether, 2 elutions): R_f 0.51 (10:1 CH_2Cl_2–ether, 2 elutions); ^{1}H NMR δ 5.68 (m, 1 H, H-2), 5.18 (br d, J = 10.2 Hz, 1 H, H-1a), 5.13 (dd, J = 16.5, 1.4 Hz, 1 H, H-1b), 4.12 (m, 1 H, H-5), 3.94 (br m, 3 H, H-4, H-6a, H-6b), 3.88 (m, 1 H, –CH_2OH), 3.66 (m, 1 H, –CH_2OH), 2.77 (br t, J = 5.4 Hz, 1 H, O–H), 2.71 (d, J = 2.8 Hz, 1 H, O–H), 2.24 (m, 1 H, H-3), 1.40 (s, 3 H, acetonide CH_3), 1.33 (s, 3 H, acetonide CH_3).

Diol **66** (51 mg, 0.25 mmol) was dissolved in 2 mL of pyridine and treated with methanesulfonyl chloride (0.03 mL, 0.35 mmol) at 0 °C for 5 h and then at –10 °C overnight.[32] The reaction mixture was then poured into saturated aqueous $NaHCO_3$, extracted with EtOAc, washed with brine, dried over Na_2SO_4, filtered, and concentrated to give 81 mg of crude monomesylate which was taken on to the next step without purification: R_f 0.44 (2:1 benzene–EtOAc); ^{1}H NMR δ 5.72 (br m, 1 H, H-2), 5.24 (br d, J = 10.1 Hz, 1 H, H-1a), 5.19 (br d, J = 16.8 Hz, 1 H, H-1b), 4.41 (dd, J = 9.6, 6.1 Hz, 1 H, –CH_2OMs), 4.33 (dd, J = 9.6, 3.6 Hz, 1 H, –CH_2OMs), 4.10 (dt, J = 6.5, 3.9 Hz, 1 H, H-5), 3.89 (m, 3 H, H-4, H-6a, H-6b), 2.98 (s, 3 H, CH_3SO_2–), 2.37 (br s, 1 H, O–H), 2.33 (m, 1 H, H-3), 1.39 (s, 3 H, acetonide CH_3), 1.31 (s, 3 H, acetonide CH_3).

A solution of crude monomesylate (81 mg) in 3 mL of THF was treated with lithium aluminum hydride (34 mg, 0.88 mmol) at 0 °C for 3 h. The reaction was then quenched with 4 mL of H_2O and 1 mL of 15% aqueous NaOH. The resulting biphasic mixture was extracted with EtOAc, washed with brine, dried over Na_2SO_4, filtered, and concentrated to afford 36 mg (66% from **66**) of crude **19** which was then purified by PTLC (0.5-mm silica gel plate, 4:1 benzene–EtOAc, R_f 0.39).

Data for 70: R_f 0.12 (10:1 CH_2Cl_2–ether, 3 developments); ^{1}H NMR δ 5.60 (br m, 1 H, H-2), 5.19 (br d, J = 9.0 Hz, 1 H, H-1a), 5.16 (br d, J = 17.6 Hz, 1 H, H-1b), 4.16 (dt, J = 6.7, 4.2 Hz, 1 H, H-5), 3.96 (br t, J = 6.7 Hz, 1 H, H-6a), 3.60–3.82 (br m, 3 H, H-6b, H-4, –CH_2OH), 3.55 (m, 1 H, –CH_2OH), 2.61 (br m, 2 H, OH), 2.45 (m, 1 H, H-3), 1.41 (s, 3 H, acetonide CH_3), 1.33 (s, 3 H, acetonide CH_3).

Data for 73: R_f 0.28 (2:1 hexane–EtOAc); ^{1}H NMR δ 5.74 (m, 1 H, H-2), 5.20 (dd, J = 9.4, 1.9 Hz, 1 H, H-1a), 5.16 (dd, J = 19.7, 1.2 Hz, 1 H, H-1b), 4.13 (br quint, J = 6 Hz, 1 H, H-6), 3.73–3.90 (br m, 3 H, H-4, and –CH_2OH), 3.63 (dd, J = 7.7, 5.1 Hz, 1 H, H-5), 3.05 (br s, 1 H, O–H), 2.86 (br s, 1 H, O–H), 2.42 (m, 1 H, H-3), 1.21–1.73 (m, 10 H, cyclohexyl), 0.92 (d, J = 6.8 Hz, 3 H, H-7).

Data for 77: R_f 0.31 (1:1 hexane–EtOAc); $[\alpha]^{19}_D$ +30.4° (c 1.7, $CHCl_3$); ^{1}H NMR δ 5.66 (br m, 1 H, H-2), 5.21 (br d, J = 10.2 Hz, 1 H, H-1a), 5.17 (br d, J = 17.1 Hz, 1 H, H-1b), 4.07 (br quint, J = 6 Hz, 1 H, H-6), 3.82 (m, 1 H, –CH_2OH), 3.76 (m, 1 H, –CH_2OH), 3.62 (br d, J = 9.1 Hz, 1 H, H-5), 3.51 (br t, J = 9.3 Hz, 1 H, H-4), 2.62 (br t, J = 6.1 Hz, 1 H, O–H), 2.46 (br m, 2 H, H-3, O–H), 1.30–1.59 (br m, 10 H, cyclohexyl), 1.24 (d, J = 6.0 Hz, 3 H, H-7); IR (CH_2Cl_2) 3540, 2930, 2850, 1440, 1360, 1350, 1250, 1100, 1020, 940, 670 cm^{-1}.

General Procedure for Reaction of Epoxides 65, 68, 72, and 75 with Me_2CuLi. MeLi (1.5 mL of a 1.15 M solution in Et_2O, 1.68 mmol) was added dropwise to a slurry of CuI (0.16 g, 0.84 mmol) in 6 mL of Et_2O at 0 °C. After 30 min, the resulting colorless solution was cooled to –40 °C and **72** (80 mg, 0.35 mmol) was added.[32] This mixture, now containing a yellow precipitate, was maintained at –40 °C for 4.5 h and then was poured into aqueous NH_4Cl, extracted with CH_2Cl_2, washed with brine, and dried over Na_2SO_4. Concentration of the filtrate afforded 76 mg (89%) of crude diol. This material was dissolved in 14 mL of 50% aqueous THF and treated with $NaIO_4$ (0.11 g, 0.49 mmol) for 2.5 h.[33] The reaction mixture was then diluted with brine, extracted with CH_2Cl_2, dried over Na_2SO_4, filtered, and concentrated. The resulting crude residue (70 mg) was purified by PTLC (0.5 mm thickness silica gel plate) eluting with 2:1 Et_2O–hexane (R_f 0.30) to afford 48 mg (55%) of pure **74**. Acylation of **74** using the general procedure described above afforded authentic **61** that was identical with the samples obtained by degradation of **24** and **32**.

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