were dried over anhydrous sodium sulfate, and the solvent was evaporated to obtain a mixture of acetates **4b** and **4c** (48 mg), which was separated by silica gel column, petroleum ether/diethyl ether (4:1) as eluent, to obtain acetate **4b** (29 mg, 60% yield) and acetate **4c** (18 mg, 37% yield).

Acetate 4b: mp 141–144 °C (from MeOH); $[\alpha]_D \pm 0°$ ($CHCl_3$, *c* 0.35); UV λ_{max} (MeOH) 204 (ϵ 7300); IR ($CHCl_3$) 1780, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.11 (d, 1 H, *J* = 4.4 Hz), 0.5 (d, 1 H, *J* = 4.4 Hz), 0.71 (ddd, 1 H, *J* = 15.5, 12.5, and 2.8 Hz), 0.94 (d, 3 H, *J* = 7.0 Hz), 0.95 (s, 3 H), 1.03 (s, 3 H) 2.16 (s, 3 H), 4.18 (br s, 2 H), 4.33 (ddd, 1 H, *J* = 10.3, 4.3, and 1.5 Hz), 5.53 (br d, 1 H, *J* = 3.7 Hz), 6.16 (br s, 1 H), 6.94 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 169.25 (s, $COCH_3$), 166.3 (s, C-19), 159.6 (s, C-17), 138.81 (s, C-13), 118.08 (d, C-18), 115.6 (d, C-14), 92.37 (d, C-25), 69.59 (d, C-16), 68.42 (t, C-24), 41.12 (d, C-10), 39.21 (s, C-9), 36.95 (t, C-11), 35.69 (d, C-8), 32.21 (t, C-3), 29.66 (t, C-15), 28.01 (t, C-6), 27.8 (t, C-7), 26.45 (s, C-5), 26.18 (t, C-12), 24.6 (t, C-20), 23.23 (t, C-2), 22.36 (q, C-21), 20.6 (q, $COCH_3$), 20.0 (q, C-23), 19.97 (t, C-1), 17.43 (s, C-4), and 14.22 (q, C-22); MS, *m/z* (relative intensity) 442 $[M]^+$ (5), 440 (2), 382 $[M - HAc]^+$ (10), 205 (20), 192 (100), 191 (83), 189 (83), 177 (44).

Acetate 4c: oil; $[\alpha]_D$ +17° ($CHCl_3$, *c* 0.3); UV λ_{max} (MeOH) 204 (ϵ 7100); IR ($CHCl_3$) 1780, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.11 (d, 1 H, *J* = 4.4 Hz), 0.5 (d, 1 H, *J* = 4.4 Hz), 0.71 (ddd, 1 H, *J* = 15.5, 12.5, and 2.8 Hz), 0.92 (d, 3 H, *J* = 7.0 Hz), 0.96 (s, 3 H), 1.04 (s, 3 H), 2.18 (s, 3 H), 4.13 (br s, 2 H), 4.31 (m, 1 H), 5.55 (br d, 1 H, *J* = 3.7 Hz), 6.09 (br s, 1 H), 7.04 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 169.5 (s), 166.1 (s), 159.3 (s), 138.5 (s), 118.9 (d), 115.5 (d), 92.9 (d), 68.6 (d), 68.5 (t), 41.1 (d), 39.1 (s), 36.9 (t), 35.6 (d), 32.2 (t), 30.4 (t), 28.0 (t), 27.7 (t), 26.4 (s), 26.2 (t), 24.6 (t), 23.3 (t), 22.4 (q), 20.7 (q), 19.9 (q), 19.9 (t), 17.4 (s), and 14.1 (q); MS, *m/z* (relative intensity), 442 $[M]^+$ (5), 382 $([M - HAc]^+$ (14), 205 (21), 192 (100), 191 (86), 189 (86), and 177 (43).

Acknowledgment. This work is a part of an Italian–Yugoslav program on mutual researches of the Adriatic Sea and has been done with the financial support of CNR Roma and SIZ III S. R. Croatia, Zagreb. We thank C. Iodice for the technical assistance. Mass spectral data were provided by "Servizio di Spettrometria di Massa del CNR e dell'Università di Napoli", and the assistance of the staff is gratefully acknowledged. We are grateful to Dr. A. De Giulio for bioassays and to Prof. G. Sodano for helpful discussions.

Registry No. **4a**, 116079-49-3; **4a** (acetate 1), 116079-50-6; **4a** (acetate 2), 116179-72-7.

Application of Allylboronates to the Synthesis of Carbomycin B

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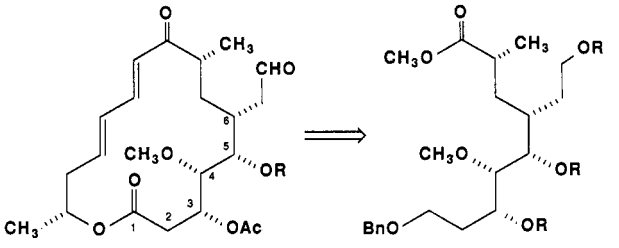
Received February 16, 1988

A formal synthesis of carbomycin B, a representative of the macrolide antibiotics, was achieved. The key steps of the sequence utilized allylboronates to secure the four contiguous stereogenic centers from C3 to C6. Condensation of a (*Z*)-(3-methoxyallyl)boronate with 3-(benzyloxy)propanal secures the centers at C3 and C6. Protection of the hydroxyl and oxidative cleavage of the olefin affords an aldehyde, which is coupled with (2′*E*)-[5′-(*tert*-butyldimethylsiloxy)pent-2′-enyl]-4,4,5,5-tetramethyl-2-bora-1,3-dioxolane to afford the C1–C8 portion of carbomycin B with the correct stereochemistry at the four contiguous stereogenic centers. A hydroformylation introduces C9. A series of straightforward functional group manipulations affords an intermediate identical with that prepared previously by K. C. Nicolaou. This synthesis demonstrates that the factors controlling α-asymmetric induction in simple allylboronates do not necessarily hold true with more complex highly functionalized boronates and aldehydes.

Carbomycin B (**1**) is a representative of the 16-membered ring macrolide antibiotics.[2] The groups of Nicolaou,[3] Tatsuta,[4] and Ziegler[5] have successfully accomplished total or partial syntheses of carbomycin B. All three approaches are based on modifications of the glucose framework as a means to securing chirality as well as the relative stereochemistry at positions 3–5 of the macrolide.

As an alternative to the carbohydrate approach to macrolide synthesis, we have explored the application of allylboronate methodology for securing each of the four contiguous chiral centers of carbomycin B. With the right half of the molecule **2** as an initial target structure, our design was to employ two successive allylboronate condensations to secure relative stereochemistry. On the basis of our work[6] and that of Hoffmann,[7] the relationship at

Scheme I



1a R=(Isovaleryl- α -L-mycarosyl)-D-mycaminose

1b R=H

2

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(2) (a) Hochstein, F. A.; Muri, K. *J. Am. Chem. Soc.* **1954**, *76*, 5080. (b) Freiberg, L. A.; Egan, R. S.; Washburn, W. H. *J. Org. Chem.* **1974**, *39*, 2474. (c) Woodward, R. B. *Angew. Chem.* **1957**, *69*, 50. (d) Woodward, R. B.; Weiler, L. S.; Dutta, P. C. *J. Am. Chem. Soc.* **1965**, *87*, 4662. (e) Kuehne, M.; Benson, B. W. *J. Am. Chem. Soc.* **1965**, *87*, 4660.

(3) Nicolaou, K. C.; Pavia, M. R.; Seitz, S. P. *Tetrahedron Lett.* **1979**, 2327. Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R.; Petasis, N. A. *J. Org. Chem.* **1979**, *44*, 4011. Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R. *J. Am. Chem. Soc.* **1981**, *103*, 1222, 1224.

(4) Tatsuta, K.; Tanaka, A.; Fjujimoto, K.; Kinoshita, M.; Umezawa, S. *J. Am. Chem. Soc.* **1977**, *99*, 5827. Tatsuta, K.; Yamauchi, T.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 3035. Tatsuta, K.; Ameniya, Y.; Maniwa, S.; Kinoshita, M. *Tetrahedron Lett.* **1980**, *21*, 2837.

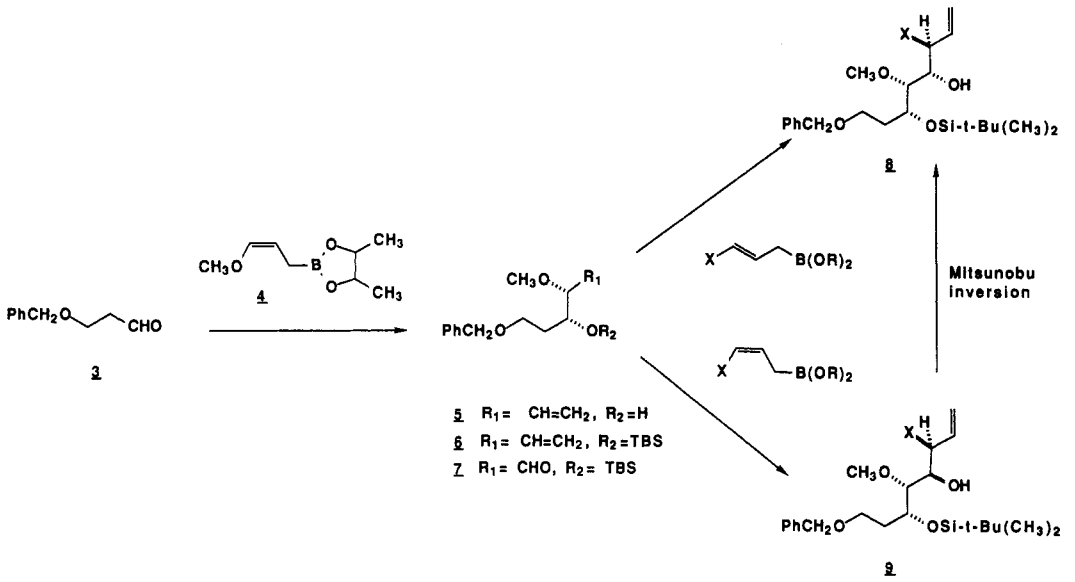
(5) Ziegler, F. E.; Gilligan, P. J. *J. Org. Chem.* **1981**, *46*, 3874. Ziegler, F. E.; Gilligan, P. J. *Tetrahedron Lett.* **1979**, 3371. Ziegler, F. E.; Chakraborty, U. R.; Weisenfeld, R. B. *Tetrahedron* **1981**, *37*, 4035.

(6) Wuts, P. G. M.; Bigelow, S. S. *J. Org. Chem.* **1982**, *47*, 2498.

(7) Hoffmann, R. W.; Kemper, B.; Metternich, R.; Lehmeier, T. *Justus Liebigs Ann. Chem.* **1985**, 2246 and references cited therein.

0022-3263/88/1953-5023$01.50/0

Scheme II

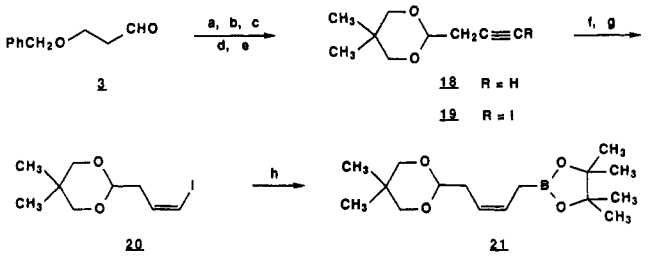


C3 and C4 could readily be obtained by the condensation of a (*Z*)-(γ-methoxyallyl)boronate **4** with a suitable aldehyde **3**. Introduction of the center at C5 would be critically dependent on the α-asymmetric induction in the second condensation with the derived aldehyde **7**. At the outset of this work, little data was available that would allow a prediction.[8] As a result a strategy was developed that would accommodate either result. We felt that if the reaction proceeded to give the anti-Cram addition product **9**, the center at C5 could be inverted via the Mitsunobu reaction[9] to give **8**, which would secure the four contiguous chiral centers. A Cram addition product would give the correct adduct **8** directly. The stereochemistry at C6 follows from the boronate geometry.[10] An anti-Cram adduct would require a (*Z*)-boronate while a Cram adduct would necessitate an (*E*)-boronate to secure the desired stereochemistry at C6.

Aldehyde **3** was chosen as a starting material and treated with (*Z*)-(γ-methoxyallyl)boronate **4** affording olefin **5** in 46% yield (Scheme II).[11] The low yield was due to loss of benzyl alcohol during the condensation, which was confirmed by isolation. Silylation gave ether **6**, which was oxidatively cleaved (OsO_4, NMO, acetone, water, 85%; $NaIO_4$, acetone, water, 100%),[12] giving aldehyde **7**.

In the framework of our initial analysis and since the addition of nucleophiles to α-alkoxy aldehydes generally proceeds to give anti products when chelation is not a controlling factor,[13] we chose to use (*Z*)-boronate **21** in our initial studies. Boronate **21** was prepared as outlined in Scheme III. Aldehyde **3** was converted by a series of

Scheme III[a]



[a] (a) 2,2-Dimethylpropanediol, H^+, 89%; (b) Na/NH_3, 92%; (c) DMSO, $COCl_2$, TEA; (d) CBr_4, PPh_3, 60%; (e) Hg/Li, 85%; (f) *n*-BuLi, I_2, 92%; (g) HN=NH, 62%; (h) Mg, THF, pinacolchloromethylboronate, 65%.

straightforward manipulations to acetylene **18**, which was converted to iodide **19** and reduced with diimide to the (*Z*)-vinyl iodide **20**. Conversion of the iodide to the Grignard reagent and treatment with pinacol chloromethylboronate[14] afforded (*Z*)-boronate **21** in 65% yield.[15] We had envisioned a more direct approach to acetylene **18** through the oxidation of the commercially available 1-butyn-4-ol, but we were unable to perform this oxidation without allene formation.[16] Condensation of aldehyde **7** and (*Z*)-boronate **21** gave a mixture of isomers **10b**, **11b**, **12b**, and **13b** in a ratio of 5.4:1:7.2:14.7 in 86% yield (Scheme IV). The poor product ratio and an inability to separate the major diastereomers **12b** and **13b** led us to examine the course of the reaction with (*E*)-crotylboronate. Surprisingly, in this case the reaction proved to be essentially stereospecific for diastereomer **11a** with <1% of two other diastereomers being formed. Not only was the stereoselectivity surprising in view of the outcome with the (*Z*)-boronate **21**, but the α-asymmetric induction was contrary to expectation and the Felkin–Ahn model,[17] which

(8) For recent examples of related condensations, see: Hoffmann, R. W.; Endesfelder, A.; Zeiss, H.-J. *Carbohydr. Res.* **1983**, *123*, 320. Roush, W. R.; Halterman, R. L. *J. Am. Chem. Soc.* **1986**, *108*, 294. Roush, W. R.; Adam, M. A.; Harris, D. J. *J. Org. Chem.* **1985**, *50*, 2003.

(9) Mitsunobu, O.; Masahiko, E. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 3427. Review: Mitsumobu, O. *Synthesis* **1981**, 1.

(10) For a review on the addition of allylmetal reagents to aldehydes, see: Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555.

(11) When most of this work was complete H. C. Brown published a procedure for the preparation of chiral diol derivatives: Brown, H. C.; Prabhakar, K. J. *J. Am. Chem. Soc.* **1983**, *105*, 2092. Application of this methodology to aldehyde **3** gave chiral **5** in 67% yield and 85% enantiomeric excess ($[\alpha]_D$ −10.79°).

(12) The more direct direct ozonolysis resulted in considerable overoxidation with resultant loss of the benzyl group.

(13) For a review on chelation and none chelation controlled additions to α-alkoxy aldehydes, see: Reetz, M. T. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 556.

(14) Wuts, P. G. M.; Thompson, P. A. *J. Organomet. Chem.* **1982**, *234*, 137.

(15) Wuts, P. G. M.; Thompson, P. A.; Callen, G. R. *J. Org. Chem.* **1983**, *48*, 5400.

(16) All attempts to oxidize 1-butyne-4-ol led to the allene i.

$$\underset{\text{i}}{\text{CH=C=CCHO}}$$

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

Scheme IV

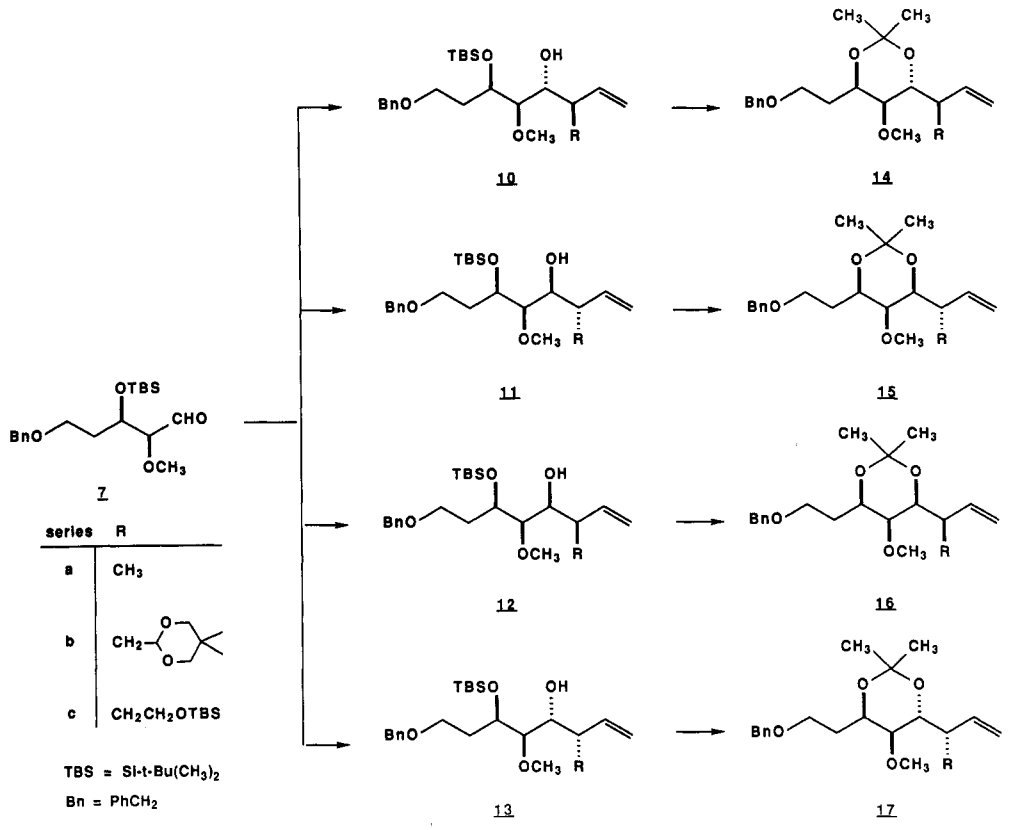


Table I. Ratios of Isomers and C4 Methine Coupling Constants

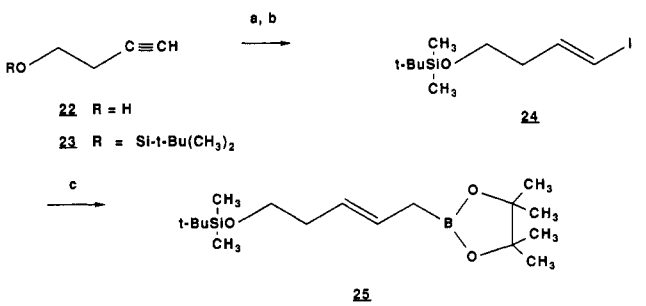
	a		b		c	
compound	J (m[c])	ratio	J (m)	ratio	J (m)	ratio
14	*a*	0	*b*	5.4[d]	3.8, 6.2 (dd)	3.4
15	1.5 (t)	100[d]	*b*	1[d]	1.2 (t)	18
16	*a*	0	2.9, 6.8 (dd)	7.2	1.4 (t)	1.4
17	*a*	0	1.2 (t)	14.7	4.3, 5.8 (dd)	1.0

[a] These isomers were not formed in the reaction. [b] These acetonides were not prepared. [c] m = multiplicity. [d] These assignments are not certain.

generally predicts the diastereoselectivity observed in the addition of nucleophiles to unchelated α-alkoxy aldehydes. As a result of the high selectivity, (*E*)-boronate **25** was prepared from (*E*)-vinyl iodide **24** (Scheme V). The iodide was obtained from silyl ether **23** by hydrozirconation and iodination.[18] Condensation of **25** with aldehyde **7** afforded a mixture of **10c**, **11c**, **12c**, and **13c** in a ratio of 3.4:18:1.4:1 in 85% yield. Again, the 3,4-syn,4,5-syn isomer predominated but this time all four isomers were chromatographically separable.

Structure proofs of the various addition products were based on the following: In each case the condensation products were converted to their respective acetonides **14**–**17** after desilylation and subjected to 360-MHz NMR analysis. The differentiating attribute that distinguished the anti-Cram product from its Cram isomer was the C4 methine (carbomycin numbering), appearing either as a small triplet or a doublet of doublets. Examination of the two possible configurational isomers **26** and **27** shows that in the 3,4-syn,4,5-syn isomer the C3 and C5 methines are symmetrically disposed about the C4 methine. As a consequence the C4 methine in isomer **26** would be expected to appear as a triplet due to the equivalency of $J_{3,4}$ and $J_{4,5}$. In contrast, the less symmetrical 3,4-syn,4,5-anti isomers **27** are expected to have nonequivalent coupling constants, which should result in a doublet of doublets for the C4 methine. Table I summarizes these results.

Scheme V[a]



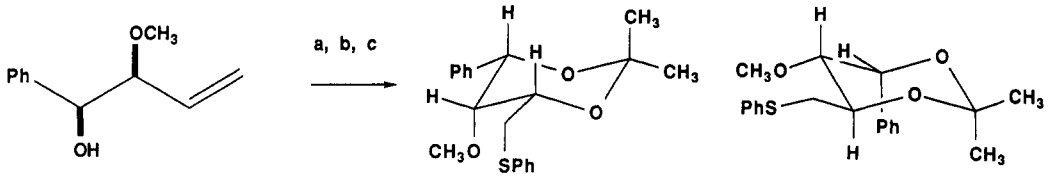
[a] (a) *tert*-Butyldimethylchlorosilane, pyr; (b) $ZrCp_2ClH$, I_2; (c) Mg, pinacol chloromethylboronate.

A lack of absolute veracity in the assignments led us to convert alkene **28** to acetonides **29** and **30** as outlined in Scheme VI. The crystalline all syn isomer **29**, displaying a small triplet (J = 1.5 Hz)[19] for the C3 methine was examined by X-ray crystallography,[20] which confirmed the

(18) Hart, D. W.; Blackburn, T. F.; Schwartz, J. *J. Am. Chem. Soc.* **1981**, *103*, 1222.

(19) Isomer **30** displayed a doublet of doublets (J = 3.9, 7.2 Hz), which was consistent with our predictions.

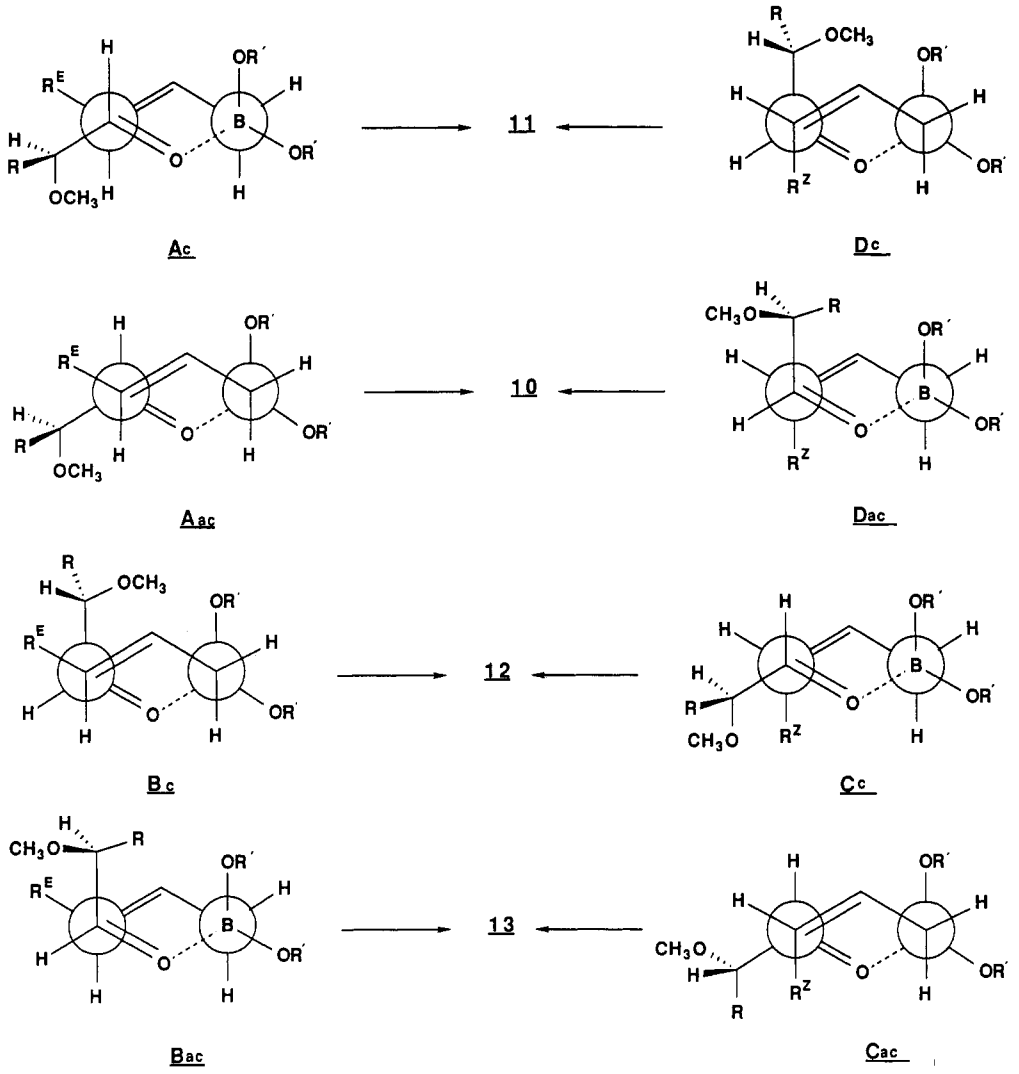
Scheme VI[a]



28 29 30

[a] (a) mCPBA; (b) PhSNa, EtOH; (c) Dimethoxypropane, H^+.

Scheme VII



Ac 11 Dc

Aac 10 Dac

Bc 12 Cc

Bac 13 Cac

all syn assignment. This result then established stereochemical parity for the major diastereomers in each of the boronate condensations and confirms our initial assignments.

The levels of minor isomers **10b** and **11b** for the (*Z*)-boronate and **12c** and **13c** for the (*E*)-boronate are above expectation based on the >95% stereochemical purity of the allylboronates. This divergence in stereochemistry may be explained as follows: of the 16 possible transition states for each boronate isomer, those in Scheme VII represent the ones that give rise to the Cram and anti-Cram products and account for the stereochemistry at the C5–C6 bond. The eight possible boat transition states are not illustrated because we feel that they are on the order of 2–3 kcal higher in energy than the chain forms. This assumption is based on studies of the Claisen rearrangement, which proceeds via similar transition states.[21]

From our results in the *E* series it is clear that as the size of R^E is increased from methyl to CH_2CH_2OTBS there is considerable erosion of both the Cram selectivity (**11c**/**10c** = 5/1, **12c**/**13c** = 1/1.4) as well as the diastereoselectivity at the C5–C6 bond ((**10c** + **11c**)/(**12c** + **13c**) = 9/1). The reduced C5–C6 diastereoselectivity over that obtained from the (*E*)-crotylboronate may be rationalized by invoking an increase in the population of transition states B_c and B_{ac}.[22] In the case where R^E = CH_3, the

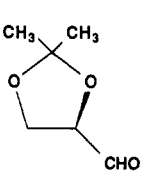
(20) We would like to thank W. Butler for performing the X-ray analysis on compound **29**.

(21) Vittorelli, P.; Hansen, H.-J.; Schmid, H. *Helv. Chim. Acta.* **1975**, *58*, 1293.

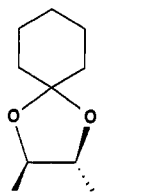
energy difference between transition states A and B is >2 kcal but as R^E increases in size the added steric interactions between R^E and the aldehyde, primarily its side-chain components, are increased to such an extent that now transition state B wherein the aldehyde is placed axially becomes significantly populated even though there now exists a 1-3 diaxial like interaction. Examination of models reveals that in transition state B the interaction between R^E and the axial substituent is much reduced compared to transition state A. The reduced interaction thus serves to compensate for the increase in energy resulting from the axial substituent. Also, since the incipient B–O bond is expected to be much longer than a normal B–O bond the energy associated with the 1-3 interaction is reduced compared to a normal cyclohexane especially when one considers the usual "6/12" potential for van der Waals interactions. The amount of this reduction will, of course, depend on the location of the transition state on the reaction coordinate: The 1-3 interaction in a product like TS will be more significant than in a reactant like TS. The increased interaction between R^E and the chiral center of the aldehyde is also consistent with the increased Cram selectivity observed for material that proceeds through transition state A where 5.3:1 selectivity is observed versus 1.4:1 for material derived from B. The interactions responsible for the overall reduced Cram selectivity for the larger boronate are difficult to evaluate due to the flexible nature of aldehyde **7** and the boronate **25** but probably have their origins in the remote interactions between the boronate and the additional chirality present in the aldehyde.

The (*Z*)-boronate **21** gives a 3.4:1 ((**12b** + **13b**)/(**10b** + **11b**)) ratio for C5–C6 bond formation, which represents an energy different of <0.7 kcal between transition states C and D. Again, the poor selectivity may be attributed to the reduced interaction between the bulky R^Z and the equatorial aldehyde on going from C to D even though there is now an additional axial substituents in D. Alternatively and more likely the D transition structure may actually be a boat or twist-boat, where the energy required to achieve a boat form is compensated for by the pseudoequatorial nature of the aldehyde side chain and R^Z. In fact, this would bring the aldehyde side chain chiral center closer to R^Z. The increased interaction would then explain the 5.4:1 Cram/anti-Cram ratio. It thus appears that when the transition structure contains an axial–equatorial relationship the Cram/anti-Cram selectivity is reduced over transition structures, which contain equatorial–equatorial relationships. It should also be noted that when one compares the results of Hoffmann on the reactions of (*Z*)- and (*E*)-crotylboronates that the selectivity obtained from the (*Z*)-boronate is also reduced from its *E* counterpart by nearly a factor of two.[23]

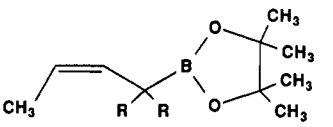
The reactions of the (*E*)-boronates with aldehyde **7** proceed to give primarily 4,5-syn selectivity, which is counter to predictions based on the Felkin–Ahn model where stereoelectronic interactions between σ_{C2-OR}^* and the developing C–C bond are expected to control the facial selectivity in the condensation. Roush has made a similar observation in the reactions of aldehyde **31** and **32** with boronate **36** where syn selectivity is also favored (1.2:1–1.5:1), but in contrast, he found that in the reactions of aldehydes **31** and **32** with boronates **33–35** anti selectivity was predominant. These results tend to suggest that remote steric effects strongly influence the reactions of



31

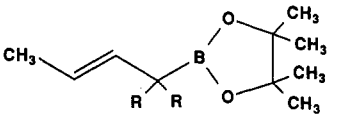


32



33 R=H

34 R=CH_3



35 R=H

36 R=CH_3

allylic boronates with aldehydes and that the guiding principles of the Felkin–Ahn model may not be as important in these reactions.[24] Also, the differences in steric environments associated with the ketide protecting group may account for the reversal in selectivity between the two systems, but these differences are currently impossible to delineate. In our case it is clear from an examination of Dreiding models that the Felkin–Ahn transition states, which would lead to 4,5-anti selectivity, impose a severe steric interaction between R^E, R^Z, and R, which is relieved if one assumes a Cram model where the large substituent is R. An important conclusion that emerges from these results is that the basic tenets established in simple systems for predicting the stereochemical outcome in allylboronate condensations may not apply in cases where more complex allylboronates are condensed with highly functionalized aldehydes due to the unpredictable nature of long range interactions.

With confidence in the stereochemical assignments the elaboration of the remaining two carbons of the right half was pursued (Scheme VIII). Hydroformylation[25] of **11c** followed by PCC oxidation gave lactone **37**, which was alkylated with methyl iodide to afford a 2:1 mixture of lactones **38** and **39** with the undesired isomer **39** predominating. These could at best be isomerized to a 1:1 mixture by employing the Grieco[26] methodology. During both the alkylation and isomerization, we obtained ketene acetal **43**, the product of silyl migration.[27] We did not confirm which of the two silyl groups had migrated, but from molecular models it appears that the group at C3 was more proximate to the enolate and is thus most likely to have migrated. The methylated lactones **38** and **39** were chromatographically separated.

Stereochemical confirmation and completion of the synthesis was achieved by conversion of lactone **38** to alcohol **42**. Both silyl groups were removed by treatment with fluoride to afford diol **40**, which was then selectively

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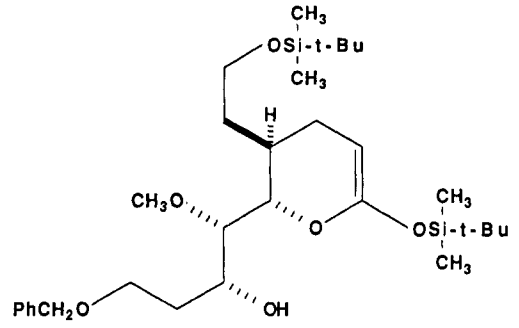

43

protected at the primary hydroxyl with *tert*-butyldiphenylsilyl chloride.[28] Methanolysis followed by acetonide formation gave ester **41** along with its α-methyl isomer (ratio = 5.8:1). Reduction of ester **41** with lithium aluminum hydride afford alcohol **42**. Comparison of the spectra of our material with spectral data kindly provided by Prof. Nicolaou established the identity of our racemic material with their chiral material. Since Nicolaou has previously reported the conversion of **42** to the aglycone of carbomycin B (**1a**) and our ability to prepare olefin **5** in chiral form, a formal synthesis of the natural product was achieved and we succeeded in our goal of demonstrating the use of sequential allylboronate additions for securing the relative stereochemistry in the C1–C9 fragment of carbomycin B. Also, the disparate stereochemical results between the simple crotylboronates, and its more highly substituted counterpart indicates that much more must be learned about the factors that influence diastereoselectivity in allylboronate condensations.

Experimental Section

(4*R,3*R**)-1-(Benzyloxy)-4-methoxy-5-hexen-3-ol (5).** A solution of 25.9 g (360.0 mmol) of allyl methyl ether in 158 mL of dry THF was cooled to −78 °C. To this was added 283 mL (396.0 mmol) of 1.4 M *s*-BuLi in cyclohexane, while the temperature was kept below −50 °C. In a separate three-necked flask, equipped with mechanical stirrer, thermometer, and argon inlet was dissolved 90.2 mL (360.0 mmol) of 2-fluoro-4,5-dimethyl-2-bora-1,3-dioxolane (4.0 M in anhydrous benzene) in 447 mL of ether. The boronate solution was cooled to −90 °C, and the solution of the anion was added dropwise via cannula. The temperature was held below −90 °C during the addition. Stirring was continued for 5 h, while the reaction mixture was allowed to gradually warm to −10 °C. During this time the appearance of the mixture changed from a dark orange slurry to cloudy white. Aldehyde **3** was added, and the mixture was allowed to warm and stir overnight and then poured into 10% NaOH and extracted with ether (3×). The combined extracts were washed with brine, dried over $MgSO_4$, filtered, concentrated, and distilled at 0.1 Torr. Fractions boiling between 80 and 130 °C contained the 33.8 g of product, which contained 5% of the vinyl ether which results from the regioisomeric boronate.[6] Chromatography on 650 g of silica gel, eluting with 25% ethyl acetate in hexane provided 15.1 g of alkene **5** contaminated with 1.6 g of benzyl alcohol. The total yield was 46% based on aldehyde: IR (film) 3460, 3060, 3015, 2905, 1500, 1460, 1100, 740, 700 cm^{-1}; NMR ($CDCl_3$) δ 7.34 (m, 5 H), 5.78 (m, 1 H) 5.29 (m, 2 H), 4.53 (s, 2 H), 3.88 (m, 1 H), 3.67 (m, 2 H), 3.51 (dd, J_1 = 4.8 Hz, J_2 = 8.2 Hz, 1 H), 3.33 (s, 3 H), 2.77 (d, J = 4.3 Hz, 1 H), 1.89–1.64 (m, 2 H). Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.19; H, 8.40.

(4*R*,3*R*)-1-(Benzyloxy)-4-methoxy-5-hexen-3-ol [(−)-5]. (Diisopinocampheyl)methoxyborinate (28.5 g, 0.90 mol) was prepared as described by Brown[11] from (+)-α-pinene, dissolved in 100 mL of dry Et_2O, and cooled to −78 °C. In a separate flask, 7.9 g (0.110 mol) of allyl methyl ether was dissolved in 50 mL of dry THF, and cooled to −78 °C. A solution of *tert*-butyllithium (41 mL, 2.3 M in pentane, 0.095 mol) was added to form the yellow allyl anion, and this solution was added via cannula to the cold borinate solution, while the temperature was kept below −65 °C, to form the (γ-methoxyallyl)borane. The mixture was stirred for 7 h and allowed to slowly warm to −15 °C before recooling to −70 °C and adding 12.3 g (75.0 mmol) of 3-(benzyloxy)propanal **3**. The reaction was allowed to warm to room temperature over a 10-h period. A solution of 3 N NaOH (65 mL) was then added, followed by 27 mL of 30% H_2O_2. The mixture was refluxed for 1 h and cooled, and the layers were separated. The aqueous layer was extracted twice with Et_2O, and the organic layers were combined and washed sequentially with water and brine, dried over $MgSO_4$, concentrated, and bulb-to-bulb distilled. A fraction containing mostly pinanol was obtained (10 Torr, 100 °C), and then the pressure was lowered and a second fraction was obtained (0.1 Torr, 110 °C) of 18.7 g. The analytical sample was prepared by chromatography on silica gel of a sample of this material weighing 204 mg. By elution with 25% EtOAc/hexane, 134 mg of pure material was obtained. On this basis, the total yield of the desired alcohol is 67%. Examination of the 360-MHz NMR spectrum indicated a diastereomeric ratio of 20.7:1, which was not separated: R_f 0.26 (silica, 25% EtOAc/hexane); $[\alpha]^{25}_D$ −11.0° (*c* 4.53, $CHCl_3$). Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.23; H, 8.67. NMR and IR spectra were identical with those of racemic alcohol **5**. The assignment of absolute stereochemistry is based on Brown's work.

(3*R*,4*R*,α*S*)-(−)-6-(Benzyloxy)-3-methoxy-1-hexen-4-yl α-Methoxy-α-(trifluoromethyl)phenylacetate. The method of Mosher was followed.[29] A solution of (−)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (264 mg, 1.04 mmol) in 0.25 mL of CCl_4 and 10 drops of dry pyridine was prepared. To this, a solution of alcohol (−)-**5** (71.4 mg, 0.302 mmol) in 0.75 mL dry CCl_4 was added and the mixture was stirred under an argon atmosphere for 24 h. The reaction mixture was treated with a saturated solution of $NaHCO_3$, extracted into ether, dried, concentrated, and chromatographed on 15 g silica, eluting with 15% EtOAc/hexane, to afford a quantitative yield of the ester. TLC analysis of the crude reaction mixture showed only a single chromatographic component. ^1H NMR analysis showed a 12:1 mixture of diastereomers (OCH_3 peak), representing an optical purity of 85% for alcohol (−)-**5**: (TLC R_f 0.44, silica, 25% EtOAc/hexane); $[\alpha]^{21}_D$ −12.8° (*c* 1.621, $CHCl_3$); IR (film) 3060, 2950, 2860, 1750, 1500, 1460, 1370, 1270, 1180, 1110, 1025, 700 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.58 (m, 2 H, aromatic), 7.36 (m, 8 H, aromatic), 5.55 (m, 1 H, vinylic), 5.37 (m, 1 H), 5.25 (m, 2 H, vinylic), 4.46 (AB q, J = 9.6 Hz, $\Delta\nu$ = 12.0 Hz, 2 H), 3.55 (m, 3 H), 3.50 (d, J = 1.4 Hz, 3 H, OCH_3), 3.18 (s, 3 H, OCH_3), 2.04 (m, 1 H), 1.86 (m, 1 H) ppm. Anal. Calcd for $C_{24}H_{27}O_5F_3$: C, 63.71; H, 6.01; F, 12.60. Found: C, 63.87; H, 6.14; F, 12.89.

(4*R,3*R**)-6-(Benzyloxy)-4-[(*tert*-butyldimethylsilyl)oxy]-3-methoxy-1-hexene (6).** To a solution of 12.0 g (79.8 mmol) of *tert*-butylchlorodimethylsilane and imidazole (10.3 g, 150.0 mmol) in 20.0 mL of freshly distilled DMF was added 14.5 g of a mixture containing 1.6 g benzyl alcohol and 12.9 g (54.6 mmol) of alcohol **5** at 0 °C under an argon atmosphere. The mixture was allowed to warm to room temperature and stirred for 2 days, at which time TLC analysis indicated complete consumption of the starting alcohol. The reaction mixture was poured into 200 mL of H_2O and extracted three times with hexane. The combined extracts were washed sequentially with 50-mL portions of H_2O and brine, dried over $MgSO_4$, filtered, concentrated in vacuo and distilled (0.15 Torr, 110–116 °C) to provide 14.4 g (75.4%) of the desired silyl ether. The benzyl alcohol contaminating the starting material was converted to the corresponding silyl ether and removed as a fraction boiling at 50–63 °C (0.15 Torr). The analytical sample was prepared by chromatography, eluting with 5% ethyl acetate in hexane: IR (film) 3080, 3040, 2940, 2870, 1505, 1480, 1370, 1262, 1105, 842, 784, 740, 704 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.33 (m, 5 H), 5.69 (m, 1 H), 5.26 (m, 2 H), 4.48 (AB q, J = 12.5 Hz, $\Delta\nu$ = 21.1 Hz, 2 H), 3.87 (m, 1 H), 3.56 (dd, J_1 = 5.3 Hz, J_2 = 6.7 Hz, 2 H), 3.46 (br t, J = 6.7 Hz, 1 H), 3.25 (s, 3 H), 1.89 (m, 1 H), 1.58 (m, 1 H), 0.87 (s, 9 H), 0.09

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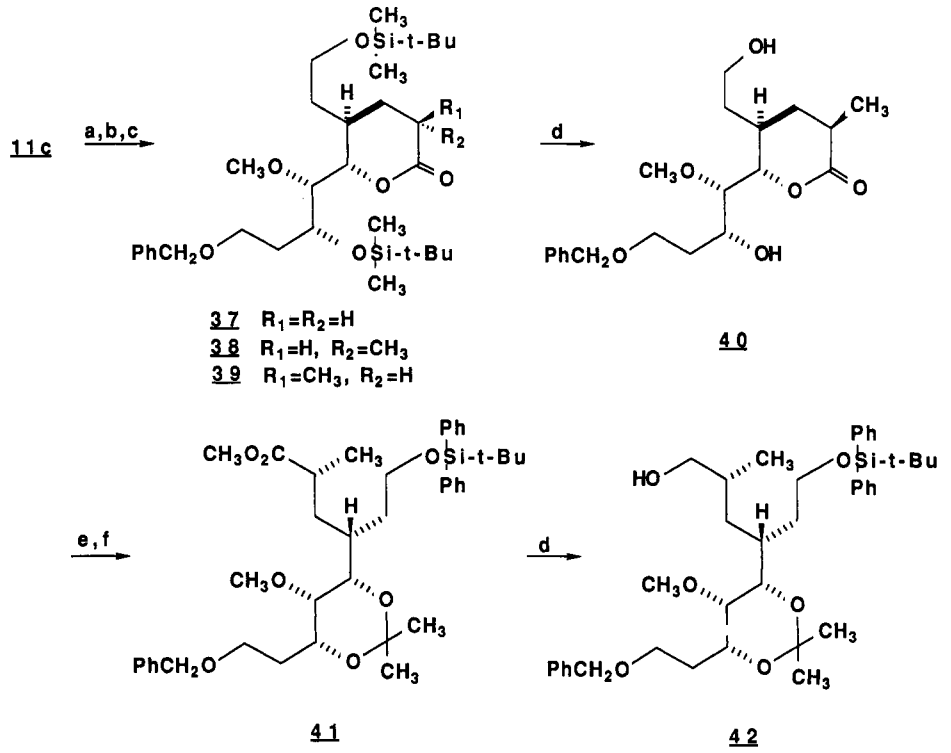
Scheme VIII[a]



[a] (a) $Rh_2(OAc)_4$, H_2, CO, PPh_3, 350 psi, 100 °C, 7 h, 96%; (b) PCC, CH_2Cl_2; (c) LDA, HMPA, CH_3I, THF, 67%; (d) $(n\text{-}Bu)_4NF$, THF, 71%; (e) *tert*-butyldiphenylchlorosilane, pyr, 0 °C, 50%; (f) MeOH, MeONa, dimethoxypropane, acetone, H^+, 64%; (g) LAH, Et_2O, 100%.

(s, 3 H), 0.05 (s, 3 H) ppm. Anal. Calcd for $C_{20}H_{34}O_3Si$: C, 68.52; H, 9.77; Si, 8.01. Found: C, 68.54; H, 9.79; Si, 7.94.

(4*R,3*R**,2*R**)- and (4*R**,3*R**,2*S**)-6-(Benzyloxy)-4-[(*tert*-butyldimethylsilyl)oxy]-3-methoxy-2-hydroxyhexanol.** According to the procedure of VanRheenen[30] a solution of 7.3 g (53.0 mmol) of *N*-methylmorpholine *N*-oxide in 12 mL of acetone and 30 mL of H_2O was combined with 0.3 g of OsO_4 dissolved in 6 mL of *tert*-butyl alcohol. This mixture was added to 14.1 g (40.2 mmol) of alkene **6** and stirred overnight at room temperature, during which time the mixture became black. Workup was accomplished by the addition of 6 g of alumina, and a solution of 0.8 g of $NaHSO_3$ in 29 mL of H_2O, followed by filtration through Celite, washing with Et_2O and a little acetone. The mixture was concentrated in vacuo, and the aqueous residue was extracted three times with CH_2Cl_2. The combined extracts were washed rapidly with 10% HCl, followed immediately with saturated $NaHCO_3$ and brine. The extracts were dried over Na_2SO_4 and concentrated, affording 18.5 g of crude diol. Chromatography on 650 g of silica, eluting with 50–75% ethyl acetate in hexane gradient, provided two fractions. The major material was bulb-to-bulb distilled to provide 11.3 g of diastereomerically pure diol. The minor fraction gave 1.8 g on similar treatment and was identified as the other diastereomeric diol. The combined yield was 13.1 g (85%). No attempt was made to determine which diol was which. Major diastereomer: IR (film) 3450, 2950–2850, 1465, 1370, 1260, 1105, 840, 780, 740, 700 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.34 (m, 5 H), 4.52 (AB q, J = 11.5 Hz, $\Delta\nu$ = 17.8 Hz, 2 H), 4.28 (m, 1 H), 4.08 (br s, 1 H), 3.83–3.53 (m, 5 H), 3.42 (s, 3 H), 3.33 (dd, J_1 = 9.1 Hz, J_2 = 4.3 Hz, 1 H), 2.24 (dd, J_1 = 4.8 Hz, J_2 = 9.1 Hz, 1 H), 2.11 (m, 1 H), 1.78 (m, 1 H), 0.91 (s, 9 H), 0.06 (s, 3 H), 0.02 (s, 3 H) ppm. Anal. Calcd for $C_{20}H_{36}O_5Si$: C, 62.46; H, 9.43; Si, 7.30. Found: C, 62.34; H, 9.43; Si, 7.34. Minor diastereomer: NMR (360 MHz, $CDCl_3$) δ 7.34 (m, 5 H), 4.49 (AB q, J = 11.5 Hz, $\Delta\nu$ = 22.6 Hz, 2 H), 4.15 (m, 1 H), 3.85 (m, 1 H), 3.77–3.50 (m, 5 H), 3.46 (s, 3 H), 3.11 (t, J = 5.3 Hz, 1 H), 2.64 (m, 1 H), 2.00 (m, 1 H), 1.77 (m, 1 H), 0.89 (s, 9 H), 0.11 (s, 3 H), 0.08 (s, 3 H) ppm. Anal. Calcd as above. Found: C, 62.28; H, 9.52; Si, 7.21.

(3*R,2*S**)-5-(Benzyloxy)-3-[(*tert*-butyldimethylsilyl)-oxy]-2-methoxypentanal (7).** A solution of 0.5 g (1.30 mmol) of the above diol in 5 mL of acetone was cooled to 0 °C and treated with 0.31 g (1.43 mmol) of $NaIO_4$ dissolved in 5 mL of H_2O. The mixture was warmed to room temperature and stirred for 8 h, at which time TLC showed complete consumption of the diol. The reaction mixture was left overnight at 0 °C before being extracted three times with CH_2Cl_2. The combined extracts were dried over Na_2SO_4, concentrated in vacuo, and bulb-to-bulb distilled at 0.1 Torr to provide 0.46 g (100%) of the pure aldehyde. The analytical sample was prepared by chromatography on silica, eluting with 15% ethyl acetate in hexane: IR (film) 2985–2870, 1745, 1475, 1370, 1265, 1115, 845, 788, 745, 704 cm^{-1}; NMR ($CDCl_3$) δ 10.03 (d, J = 2.0 Hz, 1 H), 7.51 (m, 5 H), 4.58 (s, 2 H), 4.42–3.60 (m, 4 H), 3.51 (s, 3 H), 2.21–1.42 (m, 2 H), 0.87 (s, 9 H), 0.11 (s, 3 H), 0.02 (s, 3 H). Anal. Calcd for $C_{19}H_{32}O_4Si$: C, 64.73; H, 9.15; Si, 7.97 ppm. Found: C, 64.67; H, 9.17; Si, 7.95.

2-[2-(Benzyloxy)ethyl]-5,5-dimethyl-1,3-dioxane. In a variation of the method of Swern,[31] a solution of 49.6 mL (0.567 mol) of oxalyl chloride in 900 mL of dry methylene chloride was prepared in a 3-L, three-necked flask, equipped with a mechanical stirrer and argon inlet. The temperature of the solution was lowered to −55 °C, and a solution of dimethyl sulfoxide in 180 mL of dry methylene chloride was added dropwise, while the temperature was kept below −45 °C. Two minutes after this addition was complete a solution of 3-(benzyloxy)propanol[32] in 360 mL of dry methylene chloride was added within 5 min. The mixture was stirred for 10 min before the addition of 300 mL of dry triethylamine, during which the temperature remained below −40 °C. The white slurry that formed was stirred for 30 min, warmed to room temperature for 10 min, and then poured into 1 L of water. The layers were separated, and the aqueous layer was extracted three times with methylene chloride. The combined organic phase was washed with 5% HCl and treated with 52.0 g (0.50 mol) of 2,2-dimethyl-1,3-propanediol, and the solvent was removed by distillation, replacing it with benzene. The mixture

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was heated to refux with azeotropic removal of water until the evolution of water ceased. The reaction was cooled, poured into 100 mL of 10% NaOH, extracted three times with benzene, dried over sodium sulfate, concentrated, and distilled (0.08 mm, 118–129 °C) to obtain 100.2 g (88.7%): IR (film) 3040, 2960, 2860, 1460, 1400, 1105 cm^{-1}; NMR ($CDCl_3$) δ 7.14 (s, 5 H), 4.46 (t, J = 2.3 Hz, 1 H), 4.35 (s, 2 H), 3.51 (t, J = 3.0 Hz, 2 H), 3.39 (d, J = 2.3 Hz, 4 H), 1.95 (dd, J = 2.3 Hz, J = 3.0 Hz, 2 H), 1.14 (s, 3 H), 0.65 (s, 3 H). Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.82; H, 8.76.

2-(2-Hydroxyethyl)-5,5-dimethyl-1,3-dioxane. In a 2-L three-necked flask, equipped with a mechanical stirrer and an argon inlet, a solution of 100.2 g (400.0 mmol) of 2-[2-(benzyloxy)ethyl]-5,5-dimethyl-1,3-dioxane in 250 mL of dry THF and 90 mL of *tert*-butyl alcohol was prepared. A dry-ice condensor was used to distill 250 mL of ammonia into the flask. Small pieces of sodium were added until a blue-black color persisted for 15 min. The condensor was removed and 100 g of ammonia chloride was added. The ammonia was allowed to evaporate overnight before the mixture was poured into 1 L of water. The layers were separated, and the aqueous portion was extracted four times with ethyl acetate. The combined organic phases were dried over magnesium sulfate, concentrated, and distilled (0.1 Torr, 55–63 °C), yielding 58.7 g (91.6%): IR (film) 3420, 2940, 2840, 1470, 1395, 1140, 1100, 720, 690 cm^{-1}; NMR ($CDCl_3$) δ 4.55 (t, J = 2.2 Hz, 1 H), 3.67 (t, J = 2.8 Hz, 2 H), 3.44 (d, J = 1.7 Hz, 4 H), 2.95 (s, 1 H), 1.89 (m, 2 H), 1.19 (s, 3 H), 0.65 (s, 3 H). Anal. Calcd for $C_8H_{16}O_3$: C, 59.97; H, 10.06. Found: C, 59.82; H, 9.96.

2-(5,5-Dimethyl-1,3-dioxan-2-yl)ethanal. The alcohol from above (58.7 g, 366.0 mmol) was submitted to the oxidation conditions of Swern as described in the preparation of 2-[2-(benzyloxy)ethyl]-5,5-dimethyl-1,3-dioxane above. The methylene chloride extracts are concentrated, rather than being submitted to an acid wash. The crude oil was poured into water, and the product was extracted three times into ether, dried over sodium sulfate, concentrated, and distilled (10 Torr, 88–95 °C), yielding 39.9 g (69%): IR (film) 2950, 2840, 2730, 1730, 1475, 1395, 1125, 915, 795 cm^{-1}; NMR ($CDCl_3$) δ 9.81 (t, J = 1.1 Hz, 1 H), 4.79 (t, J = 2.1 Hz, 1 H), 3.51 (m, 4 H), 2.61 (dd, J_1 = 1.1 Hz, J_2 = 2.1 Hz, 2 H), 1.19 (s, 3 H), 0.73 (s, 3 H). Anal. Calcd for $C_8H_{14}O_3$: C 60.74; H, 8.92. Found: C, 60.81; H, 8.83.

1,1-Dibromo-3-(5,5-dimethyl-1,3-dioxan-2-yl)-1-propene. To a solution of 82.9 g (250.0 mmol) of carbon tetrabromide in 900 mL of dry methylene chloride was rapidly added a solution of 131.1 g (500.0 mmol) of triphenylphosphine in 100 mL of methylene chloride. A bright orange solution instantly developed. The solution was placed in an ice bath, and 38.2 g (241.0 mmol) of the aldehyde from above was added, causing the color to lighten to a pale yellow. The reaction mixture was passed through 200 g of silica, eluting with hexane. The eluant was concentrated and passed through 50 g of fresh silica. The eluant was again concentrated and distilled (90.1 Torr, 80–82 °C), yielding 45.5 g (60.1%): IR (film) 2950, 2840, 1635, 1470, 1395, 1130, 1020, 855 cm^{-1}; NMR ($CDCl_3$) δ 6.49 (t, J = 3.5 Hz, 1 H), 4.50 (t, J = 2.3 Hz, 1 H), 3.51 (d, J = 2.5 Hz, 4 H), 2.42 (dd, J_1 = 2.3 Hz, J_2 = 3.5 Hz, 2 H), 1.20 (s, 3 H), 0.71 (s, 3 H). Anal. Calcd for $C_9H_{14}Br_2O_2$: C, 34.42; H, 4.49; Br, 50.89. Found: C, 34.54; H, 4.54; Br, 50.85.

3-(5,5-Dimethyl-1,3-dioxan-2-yl)-1-propyne (18). According to the method of Corey,[33] lithium amalgam (474 g, 1.5% w/w) was ground to the consistency of coarse sand and placed in a 2-L, three-necked flask, equipped with a mechanical stirrer and an argon inlet. A solution of 44.2 g (141.0 mmol) of vinylidene bromide from above was introduced, and stirring was continued for 5 h, maintaining the temperature at 25 °C with an ice bath. The reaction mixture was filtered through Celite, concentrated, and distilled (10 Torr, 70–76 °C), yielding 26.4 g (85.2%): IR (film) 3300, 2950, 2850, 2130, 1475, 1395, 1135, 1035, 830 cm^{-1}; NMR ($CDCl_3$) δ 4.52 (t, J = 2.6 Hz, 1 H), 3.49 (d, J = 2.4 Hz, 4 H), 2.51 (dd, J_1 = 1.1 Hz, J_2 = 2.6 Hz, 2 H), 2.02 (t, J = 1.1 Hz, 1 H), 1.09 (s, 3 H), 0.92 (s, 3 H); MS, m/z (relative abundance; 70 ev) 154 (0.09, M^+), 1.53 (0.10, $M^+ - H$), 115 (86.90, $M^+ - C_3H_3$), 69 (51.13), 56 (93.98), 45 (41.14), 41 (base). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.93; H, 9.04.

3-(5,5-Dimethyl-1,3-dioxan-2-yl)-1-iodo-1-propyne (19). A solution of 26.4 g (171.0 mmol) of alkyne **18** in 210 mL of dry THF was cooled to −78 °C, and 88.9 mL (240.0 mmol) of *n*-butyllithium 2.7 M in hexane was added dropwise, while the temperature was kept below −65 °C. Stirring was continued for 1 h before the addition of a solution of 60.9 g (240.0 mmol) of iodine in 98 mL of dry THF, below −55 °C. The mixture was warmed to room temperature and poured into 300 mL of water, the layers were separated, and the aqueous portion was extracted twice with hexane. The organic layers were combined, washed with thiosulfate solution, concentrated over copper wire, and distilled: IR (film) 2950, 2850, 1475, 1395, 1130, 1090, 1030, 825, 665 cm^{-1}; NMR ($CDCl_3$) δ 4.51 (t, J = 2.4 Hz, 1 H), 3.49 (d, J = 2.3 Hz, 4 H), 2.69 (d, J = 2.4 Hz, 2 H), 1.18 (s, 3 H), 0.70 (s, 3 H). Anal. Calcd for $C_9H_{13}IO_2$: C, 38.59; H, 4.68; I, 45.30. Found: C, 38.39; H, 4.64; I, 45.17.

***cis*-3-(5,5-Dimethyl-1,3-dioxan-2-yl)-1-iodo-1-propene (20).** The procedure of Untch[34] was followed. A solution of iodoacetylene **19** (29.8 g, 0.106 mol) in 177 mL of MeOH and 52 mL of dry pyridine was prepared in a flask equipped with mechanical stirrer. To the flask was added freshly prepared dipotassium diazocarboxylate.[35] The reduction was carried out by the slow addition of acetic acid (16 mL) over a 2-h period. After the mixture was stirred for an hour, an additional 21.3-g (130.0-mmol) portion of dipotassium diazocarboxylate was added, followed by the continued slow addition of acetic acid (16 mL). After the mixture was stirred overnight, a third portion of the reactants was added. GC analysis (6 ft OV-17, 150 °C; t_R 5.91 min for the vinyl iodide, 6.63 min for the saturated iodide, 8.51 min for the starting material) indicated that only about 1.4% of the starting material still remained, but 34.9% overreduction had taken place. The reaction was poured into water, extracted five times with hexane, concentrated, and combined with 75 mL (990.0 mmol) of aqueous dimethylamine (40% w/w) in 150 mL of ether. The mixture was stirred overnight, converting the saturated iodide to an amine, which was removed by pouring into 500 mL of water containing 82 mL of 37% HCl and ice. The layers were immediately separated, and the aqueous part was extracted four times with ether. The combined ether layers were washed with sodium bicarbonate solution, dried over magnesium sulfate, concentrated, and distilled from copper wire (0.08 Torr, 58–68 °C), yielding 18.5 g (61.9%) of *cis*-vinyl iodide, contaminated with a small amount of iodoacetylene. No trace of the trans isomer could be detected: IR (film) 2950, 2850, 1620, 1475, 1395, 1135, 1040, 840, 650 cm^{-1}; NMR ($CDCl_3$) δ 6.59 (m, 2 H), 4.71 (t, J = 2.5 Hz, 1 H), 3.63 (d, J = 2.1 Hz, 4 H), 2.59 (t, J = 2.5 Hz, 2 H), 1.24 (s, 3 H), 0.74 (s, 3 H). Anal. Calcd for $C_9H_{15}IO_2$: C, 38.32; H, 5.36; I, 44.98. Found: C, 38.32; H, 5.44; I, 45.03.

2-[4′-(5,5-Dimethyl-1,3-dioxan-2-yl)-2′(*Z*)-butenyl]-4,4,5,5-tetramethyl-2-bora-1,3-dioxolane (21). A three-necked, 250-mL flask was charged with 0.6 g (25.0 mmol) of magnesium turnings, flame-dried, and equipped with a mechanical stirrer and an argon atmosphere. A solution of 5.0 g (17.7 mmol) of *cis*-vinyl iodide **20** in 50 mL of dry THF was prepared, and the reaction mixture was heated to reflux with stirring. The reaction was initiated by the addition of a few drops of dibromoethane. After 4 h, GC analysis indicated complete consumption of the vinyl iodide (6 ft OV-17, 150 °C; t_R 5.83 min). The mixture was cooled to −78 °C, and a solution of pinacol chloromethylboronate (3.75 g, 17.7 mmol) in 25 mL of dry Et_2O was added via cannula. The reaction mixture was stirred, allowed to warm slowly to room temperature over 16 h, and passed through 75 g of basic alumina, eluting with dry Et_2O. The eluant was concentrated and bulb-to-bulb distilled (100 °C, 0.1 Torr), affording 3.4 g (64.8%) of the desired (*Z*)-allylboronate **21**, which was essentially pure by GC analysis (6 ft OV-17, 150 °C; t_R 7.03 min): IR (film) 2980, 2850, 1475, 1360, 1225, 1150, 1030, 975, 855 cm^{-1}; NMR ($CDCl_3$) δ 5.26 (m, 2 H, vinylic), 4.19 (m, 1 H), acetal), 3.31 (AB q, J = 10 Hz, J = 15 Hz, 4 H), 2.4–1.4 (m, 4 H), 1.20 (s, 3 H), 1.18 (s, 12 H), 0.69 (s, 3 H); MS, m/z (relative abundance; 70 ev) 296 (0.28, M^+), 295 (0.46, $M^+ - H$), 281 (0.05, $M^+ - CH_3$), 213 (0.20 ($M^+ - C_6H_{11}$),

(33) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769. Alexander, J.; Krishna Rao, G. S. *J. Chem. Ed.* **1970**, *47*, 277.

(34) Luthy, C.; Konstantin, P.; Untch, K. G. *J. Am. Chem. Soc.* **1978**, *100*, 6211.

(35) Thiele, J. *Justus Liebigs Ann. Chem.* **1842**, 271 127.

180 (4.33, $M^+ - C_6H_{12}O_2$), 115 (base, $C_6H_{11}O_2^+$), 69 (81.45), 41 (62.14).

Isomers 10b, 11b, 12b, and 13b. Aldehyde **7** (0.345 g, 1.00 mmol) and (*Z*)-allylboronate **21** (0.536 g, 1.75 mmol) were combined under an argon atmosphere and stirred at room temperature for 20 h. TLC analysis showed complete consumption of the aldehyde. The mixture was placed on a column of 80 g of silica gel and eluted with 10–35% EtOAc/hexane, providing 425 mg (86%) of a mixture of isomeric homoallylic alcohols. HPLC analysis showed three compounds in the ratio 21.9:1:5.4 (10% EtOAc/hexane; t_R 4.2, 5.26, 6.80 min). The major component was shown by NMR to consist of two inseparable isomers in a ratio of 2:1. Major isomer **13b**: 51.7% of the total mixture; t_R 4.2 min (HPLC, 10% EtOAc/hexane); IR (film, as a mixture of isomers) 3500, 2960, 2870, 1730, 1650, 1480, 1400, 1140, 845, 795 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.34 (m, 5 H, aromatic), 5.89 (m, 1 H, vinylic), 5.10 (m, 2 H, vinylic), 4.49 (AB q, J = 9.6 Hz, $\Delta\nu$ = 14.4 Hz, 2 H, benzylic), 4.43 (m, 1 H), 4.25 (m, 1 H), 3.86 (br s, 1 H), 3.77 (m, 1 H), 3.58 (m, 4 H), 3.42 (m, 1 H), 3.36 (s, 3 H, OCH_3), 3.16 (dd, J_1 = 3.8 Hz, J_2 = 9.1 Hz, 1 H), 2.57 (m, 1 H), 2.35 (m, 1 H), 2.12 (m, 1 H), 1.82 (m, 3 H), 1.19 (s, 3 H, acetal methyl), 0.88 (s, 9 H), *tert*-butyl), 0.71 (s, 3 H, acetal methyl), 0.16 (s, 3 H), 0.08 (s, 3 H) ppm. Anal. Calcd for $C_{29}H_{50}O_6Si$: C, 66.63; H, 9.64; Si, 5.37. Found (as a mixture of isomers): C, 66.76; H, 9.93; Si, 5.59.

12b: t_R 4.2 min (HPLC, 10% EtOAc/hexane); NMR (360 MHz, $CDCl_3$, major peaks) δ 3.34 (s, 3 H, OCH_3), 3.14 (m, 1 H, $CHOCH_3$), 0.14 (s, 3 H, $SiCH_3$) ppm.

11b: t_R 5.26 min (HPLC, 10% EtOAc/hexane); NMR (360 MHz, $CDCl_3$) δ 7.34 (m, 5 H), 5.84 (m, 1 H), 5.08 (m, 2 H), 4.50 (AB q, J = 12.0 Hz, $\Delta\nu$ = 16.8 Hz, 2 H), 4.46 (m, 1 H), 4.23 (m, 1 H), 3.55 (m, 6 H), 3.40 (m, 1 H), 3.39 (s, 3 H), 3.15 (dd, J_1 = 1.9 Hz, J_2 = 8.6 Hz, 1 H), 2.98 (d, J = 4.8 Hz, 1 H), 2.56 (m, 1 H), 1.93 (m, 3 H), 1.75 (m, 1 H), 1.18 (s, 3 H), 0.88 (s, 9 H), 0.71 (s, 3 H), 0.10 (s, 3 H), 0.06 (s, 3 H) ppm.

10b: t_R 6.80 min (HPLC 10% EtOAc/hexane); NMR (360 MHz, $CDCl_3$) δ 7.33 (m, 5 H), 5.81 (m, 1 H), 5.03 (m, 2 H), 4.50 (AB q, J = 12.2 Hz, $\Delta\nu$ = 14.6 Hz, 2 H), 4.15 (m, 1 H), 3.69–3.39 (m, 8 H), 3.47 (s, 3 H), 3.18 (m, 1 H), 2.92 (m, 2 H), 1.89 (m, 2 H), 1.64 (m, 2 H), 1.29 (s, 6 H), 0.90 (s, 9 H), 0.11 (s, 3 H), 0.05 (s, 3 H) ppm.

Acetonides 16b and 17b. A mixture of (*tert*-butyldimethylsilyl)oxy ethers **12b** and **13b** (50.27 mg, 0.961 mmol) was treated with 0.3 mL (1 M in THF) of a solution of $(n\text{-Bu})_4NF$ (0.305 mmol). The solution was stirred at room temperature for 14 h and then poured into water, extracted with ether, dried, and concentrated to provide a quantitative yield of diols. Only the major isomer was characterized after chromatographic isolation: IR (film) 3460, 2950, 2870, 1735, 1650, 1460, 1400, 1110, 1025, 700 cm^{-1}; NMR ($CDCl_3$) δ 7.35 (m, 5 H), 5.67 (m, 1 H), 5.08 (m, 2 H), 4.52 (br s, 2 H), 4.48 (m, 1 H), 4.19 (m, 1 H), 3.89 (m, 1 H), 3.60 (m, 6 H), 3.41 (s, 3 H), 3.12 (m, 1 H), 2.56 (m, 1 H), 2.18–1.50 (m, 6 H), 1.25 (s, 6 H) ppm. Anal. Calcd for $C_{23}H_{36}O_6$: C, 67.62; H, 8.88. Found: C, 67.39; H, 9.02. A mixture of diols from above (50.6 mg, 0.123 mmol) was treated with dimethoxypropane (1.5 mL) and a catalytic amount of *p*-toluenesulfonic acid. After being stirred for 4 h, the reaction mixture was placed on a column of silica gel, eluting with 10–25% EtOAc/hexane, affording 34.5 mg (62.5%) of isomeric acetonides **16b** and **17b** in the ratio of 1:1.7.

Major acetonide **17b**: R_f 0.55 (silica, 25% EtOAc/hexane); IR (film) 2960, 2860, 1650, 1470, 1390, 1240, 1110, 930, 795, 705 cm^{-1}; NMR ($CDCl_3$) δ 7.35 (m, 5 H), 5.71 (m, 1 H), 5.12 (m, 2 H), 4.52 (s, 2 H), 4.45 (dd, J_1 = 4.3 Hz, J_2 = 8.6 Hz, 1 H), 3.98 (dt, J_1 = 2.9 Hz, J_2 = 11.0 Hz, 1 H), 3.60 (m, 4 H), 3.40 (m, 3 H), 3.33 (s, 3 H, OCH_3), 3.14 (dd, J_1 = 2.9 Hz, J_2 = 5.8 Hz, 1 H, $CHOCH_3$), 2.40 (m, 1 H), 2.05 (m, 1 H), 2.89 (m, 2 H), 1.60 (m, 1 H), 1.34 (s, 3 H), 1.26 (s, 3 H), 1.20 (s, 3 H), 0.73 (s, 3 H). Anal. Calcd for $C_{26}H_{40}O_6$: C, 69.61; H, 8.99. Found: C, 69.57; H, 8.52.

Minor acetonide **16b**: R_f 0.30 (silica, 25% EtOAc/hexane); IR (film) 2960, 2860, 1650, 1470, 1385, 1210, 1105, 915, 705 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.34 (m, 5 H, aromatic), 5.78 (m, 1 H, vinylic), 5.04 (m, 2 H, vinylic), 4.52 (AB q, J = 13.0 Hz, $\Delta\nu$ = 15.4 Hz, 2 H, benzylic), 4.46 (dd, J_1 = 2.9 Hz, J_2 = 7.7 Hz, 1 H), 4.00 (dd, J_1 = 3.4 Hz, J_2 = 9.6 Hz, 1 H), 3.67–3.34 (m, 7 H), 3.46 (s, 3 H, OCH_3), 2.94 (br s, 1 H, $CHOCH_3$), 2.67 (m, 1 H), 2.00 (m, 1 H), 1.84 (m, 2 H), 1.64 (m, 1 H), 1.40 (s, 3 H), 1.37 (s, 3 H), 1.18 (s, 3 H), 0.72 (s, 3 H).

(6*R,5*R**,3*S**,4*S**)-8-(Benzyloxy)-6-[(*tert*-butyldimethylsilyl)oxy]-5-methoxy-3-methyl-1-octen-4-ol (11a).** In a flask 0.7 g (3.8 mmol) of *trans*-2-butenyl-4,4,5,5-tetramethyl-2-bora-1,3-dioxolane was dissolved in 2 mL of dry CH_2Cl_2, and the solution was cooled to −78 °C. Aldehyde **7** (0.302 g, 0.857 mmol) was added, and the mixture was allowed to warm and stir overnight, at which time the mixture was poured into 10 mL of 10% NaOH solution, stirred 10 min, and extracted three times with CH_2Cl_2. The combined extracts were dried and concentrated in vacuo to provide 0.57 g of crude material. Chromatography on 80 g of silica gel, eluting with 15% ethyl acetate in hexane, provided 0.239 g (68.3%) of a single stereoisomer, within the limits of detection by 360-MHz NMR. A slower running chromatography fraction contained 1.0 mg (≈1%) of material, which proved to be a 2:1 mixture of diastereomers by NMR: IR (film) 3560, 2970, 2850, 1660, 1475, 1375, 1270, 1110, 850, 790, 745, 710 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.34 (m, 5 H), 5.83 (m, 1 H), 5.06 (m, 2 H), 4.48 (AB q, J = 11.5 Hz, $\Delta\nu$ = 17.8 Hz, 2 H), 4.09 (m, 1 H), 3.64–3.50 (m, 3 H), 3.45 (s, 3 H), 3.15 (dd, J_1 = 2.4 Hz, J_2 = 5.8 Hz, 1 H), 2.32 (quint, J = 7.7 Hz, 1 H), 2.28 (d, J = 8.2 Hz, 1 H), 1.95 (m, 1 H), 1.80 (m, 1 H), 1.04 (d, J = 7.7 Hz, 3 H), 0.88 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H). Anal. Calcd for $C_{23}H_{40}O_4Si$: C, 67.60; H, 9.87; Si, 6.87. Found: C, 67.50; H, 9.73; Si, 6.81.

Acetonide 15a. A flask was charged with 0.221 g (0.54 mmol) of silyl ether **11a** and cooled to 0 °C. A solution of $n\text{-Bu}_4NF$ (1 mL, 1.0 mmol) in THF was added, and the mixture was allowed to warm to room temperature while stirring for 4 h, at which time TLC analysis indicated that the starting material was still present. An additional 0.5 mL (0.05 mmol) of the fluoride solution was added, and the mixture was stirred overnight at room temperature. The entire mixture was then chromatographed on 30 g of silica, eluting with 50% ethyl acetate in hexane to provide 161 mg (100%) of pure diol. An analytical sample was taken from the central fractions: IR (film) 3440, 3060–2860, 1645, 1455, 1370, 1100, 918, 890, 700 cm^{-1}; NMR ($CDCl_3$) δ 7.34 (m, 5 H), 5.84 (m, 1 H), 5.08 (m, 2 H), 4.54 (s, 2 H), 3.98 (m, 1 H), 3.69–3.53 (m, 3 H), 3.55 (s, 3 H), 3.14 (t, J = 4.3 Hz, 1 H), 3.03 (br s, 1 H), 2.41 (m, 2 H), 1.88 (m, 2 H), 1.09 (d, J = 6.7 Hz, 3 H). Anal. Calcd for $C_{17}H_{26}O_4$: C, 69.36; H, 8.90. Found: C, 69.15; H, 8.73. A mixture of Dowex acidic resin, 1 mL (8.1 mmol) of dimethoxypropane, and 149 mg (0.506 mmol) of the above diol was stirred under argon for 24 h. TLC analysis showed only partial reaction, so a small amount of dry camphorsulfonic acid was added. After 2 h, the starting material had been consumed and the reaction mixture was chromatographed on 30 g of silica, eluting with 25% ethyl acetate in hexane to provide 134.6 mg (79.7%) of pure acetonide **15a**: IR (film) 3080–2960, 1745, 1650, 1465, 1390, 1275, 1210, 1105, 750, 710 cm^{-1}; NMR (360 MHz $CDCl_3$) δ 7.34 (m, 5 H), 5.94 (m, 1 H), 5.03 (m, 2 H), 4.53 (AB q, J = 13.4 Hz, $\Delta\nu$ = 14.9 Hz, 2 H), 4.03 (ddd, J_1 = 1.5 Hz, J_2 = 3.9 Hz, J_3 = 9.3 Hz, 1 H, H-4), 3.62 (m, 2 H), 3.54 (s, 3 H), 3.48 (dd, J_1 = 1.5 Hz, J_2 = 9.3 Hz, 1 H, H-6), 2.99 (t, J = 1.5 Hz, 1 H, H-5), 2.61 (m, 1 H), 2.02 (m, 1 H), 1.88 (m, 1 H), 1.41 (s, 3 H), acetonide methyl), 1.38 (s, 3 H, acetonide methyl), 1.04 (d, J = 7.2 Hz, 3 H). Anal. Calcd for $C_{20}H_{30}O_4$: C, 71.82; H, 9.04. Found: C, 71.73; H, 8.98.

4-[(*tert*-Butyldimethylsilyl)oxy]-1-butyne (23). A solution of 4-butyn-1-ol (20.0 g, 0.285 mol) in 46 mL of dry pyridine was cooled to 0 °C under an argon atmosphere. *tert*-Butylchlorodimethylsilane (51.6 g, 0.342 mol) was added, and stirring was continued for 12 h, allowing the mixture to warm to room temperature. The mixture was poured into 300 mL of H_2O and extracted into hexane. The hexane layers were combined and washed rapidly with 10% HCl solution, followed immediately by $NaHCO_3$ and brine. The solution was dried over $MgSO_4$, concentrated, and distilled (10 Torr, 70–74 °C) to give 35.8 g (71.3%) of the desired acetylene: IR (film) 3320, 2940, 2860, 2130, 1475, 1260, 1115, 840, 780, 635 cm^{-1}; NMR ($CDCl_3$) δ 3.78 (t, J = 3.5 Hz, 2 H), 2.38 (dt, J_1 = 1.6 Hz, J_2 = 3.5 Hz, 2 H), 1.92 (t, J = 1.6 Hz, 1 H), 0.84 (s, 9 H), 0.02 (s, 6 H) ppm. Anal. Calcd for $C_{10}H_{20}OSi$: C, 65.15; H, 10.93; Si, 15.23. Found: C, 65.28; H, 10.97; Si, 15.18.

(*E*)-4-[(*tert*-Butyldimethylsilyl)oxy]-1-iodo-1-butene (24). The method of Schwartz[36] was followed. A slurry of Cp_2ZrHCl[37]

(36) Hart, D. W.; Blackburn, T. F.; Schwartz, J. *J. Am. Chem. Soc.* **1975**, *97*, 679.

(41.0 mmol) of 100 mL of dry benzene was prepared, and 7.0 g (37.9 mmol) of alkyne **23** was added, under an argon atmosphere. The mixture was stirred at room temperature for 1.5 h, during which time the white suspension became a dark green solution. A solution of 9.6 g (37.8 mmol) of iodine in 200 mL of CCl_4 was added, and the reaction mixture was filtered and poured into an aqueous solution of sodium thiosulfate. The layers were separated, and the aqueous portion was filtered and extracted four times with CCl_4. The organic layers were combined, dried over $MgSO_4$, concentrated, and distilled (0.1 Torr, 51–55 °C), yielding 8.4 g (70.9%) of the vinyl iodide **24**: IR (film) 2940, 2860, 1610, 1475, 1260, 1110, 840, 780 cm^{-1}; NMR ($CDCl_3$) δ 6.54 (dt, J_1 = 8.6 Hz, J_2 = 14.4 Hz, 1 H, vinylic), 6.07 (dt, J_1 = 1.7 Hz, J_2 = 14.4 Hz, 1 H, vinylic), 3.65 (t, J = 6.7 Hz, 2 H), 2.27 (qd, J_1 = 1.7 Hz, J_2 = 6.7 Hz, 2 H) 0.89 (s, 9 H), 0.06 (s, 6 H). The trans stereochemistry of this material was established by the method of preparation as well as the 14.4-Hz vinylic coupling constant. Anal. Calcd for $C_{10}H_{21}IOSi$: C, 38.46; H, 6.78; I, 40.64; Si, 8.99. Found: C, 38.50; H, 6.67; I, 40.64; Si, 9.04.

(*E*)-Boronate 25. A 500-mL, three-necked flask, equipped with mechanical stirrer and argon inlet was charged with 3.3 g (134.0 mmol) of magnesium turnings and flame-dried. A solution of *trans*-vinyl iodide **24** (8.4 g, 26.9 mmol) in 75 mL of dry THF was then added, and the mixture heated to reflux. The reaction was followed by GC (6 ft OV-17, 80–200 °C, 6 °C/min, t_R 10.78 min for the vinyl iodide). After 4 h, the iodide was consumed, and the mixture was cooled to −100 °C. A solution of 2-(chloromethyl)-4,4,5,5-tetramethyl-2-bora-1,3-dioxalane (5.7 g, 26.9 mmol) in 35 mL of dry Et_2O was added via cannula, and the mixture was allowed to stir and slowly warm to room temperature for 16 h. The crude mixture was then passed through 100 g of basic alumina, eluting with dry Et_2O, and the eluant was concentrated and bulb-to-bulb distilled (0.1 Torr, 120–130 °C), providing 6.1 g (69.4%) of an oil consisting of two boronates. GC analysis indicated that the desired material comprised 47% of the mixture, along with a vinyl boronate, which is derived from methylene extrusion: GC (6 ft OV-17, 80–200 °C, 6 °C/min) t_R = 13.48 min, 16.52 min for the desired (*E*)-allylboronate **25**: GCMS, *m/e* (relative abundance; 70 eV) 311 ($M^+ - CH_3$, 0.03), 269 ($M^+ - C_4H_9$, 3.67), 169 (41), 73 (96), 41 (base); IR (film) 2930, 1475, 1380, 1320, 1145, 1105, 970, 840, 780 cm^{-1}; NMR ($CDCl_3$) δ 5.54 (m, 1 H), 5.38 (m, 1 H), 3.60 (t, J = 7.2 Hz, 2 H), 2.24 (m, 2 H), 1.68 (m, 2 H), 1.22 (s, 12 H), 0.88 (s, 9 H), 0.06 (s, 6 H) ppm.

Isomers 13c, 10c, 12c, and 11c. A solution containing 47% *trans*-allylboronate **25** (6.0 g, 9.0 mmol) in 3 mL of CH_2Cl_2 was cooled to 0 °C, and a solution of aldehyde **7** (2.61 g, 7.6 mmol) in 2 mL of CH_2Cl_2 was added. The solution was allowed to warm to room temperature over several hours and then heated to 40 °C for 4 h. The reaction was conveniently followed by GC, which indicated that the vinylboronate coproduct was inert to the reaction conditions. When the aldehyde was consumed, the mixture was cooled and poured into 10% NaOH solution and extracted three times with Et_2O. The combined extracts were dried over $MgSO_4$, concentrated, and chromatographed on silica, eluting with 10–25% EtOAc/hexane, affording 3.58 g (85.2%) of an isomeric mixture in the ratio 1:3.4:1.4:18 (in order of elution).

13c: R_f 0.30 (silica, 25% EtOAc/hexane); IR (film) 3480, 2930, 2840, 1730, 1465, 1385, 1355, 1250, 1095, 830, 775, 695 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.35 (m, 5 H), 5.85 (m, 1 H), 5.16 (dd, J_1 = 2.9 Hz, J_2 = 9.6 Hz, 1 H), 5.05 (dd, J_1 = 2.9 Hz, J_2 = 16.8 Hz, 1 H), 4.51 (AB q, J = 11.7 Hz, $\Delta\upsilon$ = 13.9 Hz, 2 H, benzylic), 4.26 (dt, J_1 = 2.9 Hz, J_2 = 9.6 Hz, 1 H), 3.63 (m, 5 H), 3.35 (s, 3 H), 3.15 (dd, J_1 = 4.3 Hz, J_2 = 10.1 Hz, 1 H), 2.50 (m, 1 H), 2.27 (m, 2 H), 2.11 (m, 1 H), 1.78 (m, 2 H), 0.88 (s, 18 H), 0.09 (s, 3 H), 0.08 (s, 3 H), 0.05 (s, 6 H) ppm.

10c: R_f 0.23 (silica, 25% EtOAc/hexane); IR (film) 3510, 2950, 2870, 1650, 1480, 1370, 1265, 1110, 840, 785, 705 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.35 (m, 5 H, aromatic), 5.84 (m, 1 H), 5.07 (m, 2 H), 4.50 (AB q, J = 11.3 Hz, $\Delta\upsilon$ = 13.4 Hz, 2 H, benzylic), 4.28 (dt, J_1 = 4.3 Hz, J_2 = 9.1 Hz, 1 H), 3.87 (d, J = 1.9 Hz, 1 H), 3.76 (dt, J_1 = 3.8 Hz, J_2 = 9.1 Hz, 1 H), 3.68 (m, 1 H), 3.57 (AB q, J = 5.3 Hz, $\Delta\upsilon$ = 6.0 Hz, 2 H), 3.37 (s, 3 H), 3.18 (dd, J_1 = 4.3 Hz, J_2 = 9.6 Hz, 1 H), 2.46 (m, 1 H), 2.12 (m, 1 H), 1.81 (m, 2 H), 1.62 (m, 2 H), 0.90 (s, 18 H, *tert*-butyl), 0.18 (s, 3 H), 0.12 (s, 3 H), 0.06 (s, 6 H) ppm. Anal. Calcd for $C_{30}H_{56}O_5Si_2$: C, 65.17; H, 10.21; Si, 10.16. Found (as a mixture of isomers **13c** and **10c**: C, 65.42; H, 10.09; Si, 9.82.

12c: R_f 0.16 (silica, 25% EtOAc/hexane); IR (film) 3490, 2940, 2860, 1650, 1475, 1365, 1260, 1105, 840, 780, 705 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.34 (m, 5 H, aromatic), 5.50 (m, 1 H, vinylic), 5.07 (m, 2 H, vinylic), 4.48 (AB q, J = 11.0 Hz, J = 16.3 Hz, 2 H, $PhOCH_2$), 4.06 (m, 1 H), 3.76 (m, 1 H), 3.56 (m, 4 H), 3.45 (s, 3 H), 3.24 (d, J = 5.8 Hz, 1 H), 2.41 (d, J = 9.1 Hz, 1 H), 2.35 (m, 1 H), 1.95 (m, 2 H), 1.81 (m, 1 H), 1.45 (m, 1 H), 0.88 (s, 18 H, *tert*-butyl), 0.09 (s, 3 H), 0.07 (s, 3 H), 0.05 (s, 6 H) ppm. Anal. Calcd as above. Found: C, 65.26; H, 9.98; Si, 9.88.

11c: the major isomer, comprising 75.6% of the total mixture; R_f 0.14 (silica, 25% EtOAc/hexane); IR (film) 3500, 2940, 2860, 1745, 1475, 1370, 1260, 1105, 840, 780, 705 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.32 (m, 5 H, aromatic), 5.67 (m, 1 H, vinylic), 5.12 (dd, J_1 = 2.1 Hz, J_2 = 10.2 Hz, 1 H, vinylic), 5.05 (dd, J_1 = 2.0 Hz, J_2 = 17.1 Hz, 1 H, vinylic), 3.88 (AB q, J = 11.9 Hz, $\Delta\upsilon$ = 16.8 Hz, 2 H, $PhOCH_2$), 4.07 (m, 1 H), 3.70 (m, 1 H), 3.58 (m, 4 H), 3.42 (s, 3 H), 3.12 (dd, J_1 = 2.2 Hz, J_2 = 5.2 Hz, 1 H), 2.37 (d, J = 7.1 Hz, 1 H), 2.29 (m, 1 H), 1.95 (m, 1 H), 1.78 (m, 2 H), 1.52 (m, 1 H), 0.88 (s, 18 H, *tert*-butyl), 0.08 (s, 3 H), 0.06 (s, 3 H), 0.02 (s, 6 H) ppm. Anal. Calcd as above. Found: C, 65.14; H, 10.00; Si, 10.27.

Acetonide 17c. The acetonide was prepared by following the procedure described for **14c**. From 60 mg (0.109 mmol) of bis(silyl) ether **13c**, 20 mg (38.3%) of desired acetonide was obtained: R_f 0.37 (silica, 25% EtOAc/hexane); IR (film) 2940, 2860, 1740, 1650, 1470, 1390, 1265, 1235, 1110, 840, 785, 705 cm^{-1}; NMR ($CDCl_3$) δ 7.34 (m, 5 H, aromatic), 5.74 (m, 1 H, vinylic), 5.15 (m, 1 H, vinylic), 5.06 (m, 1 H, vinylic), 4.51 (s, 2 H, benzylic), 3.93 (m, 1 H), 3.60 (m, 5 H), 3.37 (s, 3 H, OCH_3), 3.30 (dd, J_1 = 4.3 Hz, J_2 = 5.8 Hz, 1 H, H-5), 2.43 (m, 1 H), 1.85 (m, 2 H), 1.70 (m, 2 H), 1.34 (s, 3 H), 1.25 (s, 3 H), 0.89 (s, 9 H, *tert*-butyl), 0.05 (s, 6 H). Anal. Calcd for $C_{27}H_{46}O_5Si$: C, 67.74; H, 9.68; Si, 5.87. Found: C, 67.56; H, 9.80; Si, 6.13.

Acetonide 14c. Bis(silyl) ether **10c** (240 mg, 0.432 mmol) was dissolved in 5 mL of Et_2O and treated with 2 drops of 10% HCl and 10 drops of water. After the mixture was stirred overnight, TLC analysis indicated complete consumption of the starting material and production of a polar product. Anhydrous magnesium sulfate was added to the mixture, and after 20 min, filtered off. The filtrate was azeotroped several times with benzene on the rotary evaporator, and the residue pumped for several hours at 0.1 Torr. The crude triol was dissolved in 0.5 mL of dry pyridine, cooled to 0 °C, and treated with 78 mg (0.518 mmol) of *tert*-butylchlorodimethylsilane. After 16 h at 0 °C, consumption of the triol was complete, and the mixture was poured into a few milliliters of water, extracted into Et_2O, dried, and concentrated. Residual pyridine was removed azeotropically with toluene by using the rotary evaporator. The remaining material was dissolved in 1 mL of dimethoxypropane, and treated with a catalytic amount of camphorsulfonic acid. After 12 h, the mixture was poured into saturated $NaHCO_3$ and extracted into Et_2O. After drying, filtering, and concentrating, the material was chromatographed on 20 g of silica, eluting with 10% EtOAc/hexane to provide 108 mg (52.4%) of acetonide: R_f 0.47 (silica, 25% EtOAc/hexane); IR (film) 2940, 2850, 1645, 1465, 1380, 1240, 1100, 1000, 840, 775, 700 cm^{-1}; NMR ($CDCl_3$) δ 7.34 (m, 5 H, aromatic); 5.66 (m, 1 H, vinylic), 5.07 (m, 2 H, vinylic), 4.51 (s, 2 H, benzylic), 3.99 (dt, J_1 = 3.8 Hz, J_2 = 10.1 Hz, 1 H), 3.60 (m, 4 H), 3.45 (br t, J = 6.2 Hz, 1 H), 3.33 (s, 3 H, OCH_3), 3.16 (dd, J_1 = 3.8 Hz, J_2 = 6.2 Hz, 1 H, H-5), 2.27 (m, 1 H), 1.88 (m, 3 H), 1.45 (m, 1 H), 1.34 (s, 3 H), 1.26 (s, 3 H), 0.90 (s, 9 H, *tert*-butyl), 0.05 (s, 6 H). Anal. Calcd for $C_{27}H_{46}O_5Si$: C, 67.74; H, 9.68; Si, 5.87. Found: C, 68.01; H, 9.74; Si, 6.07.

Acetonide 16c. Bis(silyl) ether **12c** (160 mg, 0.29 mmol) was treated with *n*-Bu_4NF (1 M in THF, 1.7 mL, 1.7 mmol). The mixture was stirred for 2 h at room temperature and then placed on a column of 5 g of silica, eluting first with hexane, followed by 5% MeOH/EtOAc. The eluant was concentrated, dissolved in 0.5 mL of dry pyridine and treated with 52 mg (0.35 mmol) of *tert*-butylchlorodimethylsilane. After the mixture was stirred for 12 h, TLC showed complete consumption of the triol (TLC, silica, 75% EtOAc/hexane, R_f 0.05). The reaction mixture was

(37) Wailes, P. C.; Weigold, H. *J. Organomet. Chem.* **1970**, *24*, 405.

passed through silica gel, eluting with 50% EtOAc/hexane, and the eluant was concentrated. The residue was treated with dimethoxypropane (1 mL) and a catalytic amount of camphorsulfonic acid. After 16 h, TLC analysis showed complete consumption of the triol and the production of a new compound, which was isolated by passing the mixture through 10 g of silica, eluting with 10% EtOAc/hexane, to afford 29 mg (21%) of pure acetonide: R_f 0.37 (silica, 25% EtOAc/hexane); IR (film) 2940, 2860, 1645, 1475, 1385, 1260, 1205, 1175, 1105, 840, 780, 740, 705, cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.35 (m, 5 H, aromatic), 5.63 (m, 1 H, vinylic), 5.05 (m, 2 H, vinylic), 4.53 (AB q, J = 4.8 Hz, $\Delta\nu$ = 14.2 Hz, 2 H, benzylic), 4.00 (m, 1 H), 3.62 (m, 5 H), 3.50 (s, 3 H), 2.98 (t, J = 1.4 Hz, 1 H, $CHOCH_3$), 2.62 (m, 1 H), 2.00 (m, 1 H), 1.80 (m, 2 H), 1.41 (m, 1 H), 1.38 (s, 3 H), 1.36 (s, 3 H), 0.88 (s, 9 H, *tert*-butyl), 0.06 (s, 6 H). Anal. Calcd for $C_{27}H_{46}O_5Si$: C, 67.74; H, 9.68; Si, 5.87. Found: C, 69.95; H, 9.68; Si, 6.05.

Acetonide 15c. The acetonide was prepared by following the same procedure as described for **14c**. Starting with 97.4 mg (0.176 mmol) of bis(silyl) ether **11c**, 28 mg (33.0%) of the desired acetonide was obtained: R_f 0.37 (silica, 25% EtOAc/hexane); IR (film) 2960, 2860, 1645, 1465, 1365, 1260, 1100, 835, 780, 700 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.34 (m, 5 H, aromatic), 5.55 (m, 1 H, vinylic), 5.14 (m, 2 H, vinylic), 4.52 (AB q, J = 12.0 Hz, $\Delta\nu$ = 17.3 Hz, 2 H, benzylic), 3.98 (br dd, J_1 = 3.4 Hz, J_2 = 10.1 Hz, 1 H), 3.60 (m, 4 H), 3.53 (d, J = 10.1 Hz, 1 H), 3.47 (s, 3 H, OCH_3), 2.89 (t, J = 1.2 Hz, 1 H, H-5), 2.59 (dq, J_1 = 3.4 Hz, J_2 = 9.1 Hz, 1 H), 2.10 (m, 2 H), 1.85 (m, 1 H), 1.41 (s, 3 H), 1.39 (s, 3 H), 1.34 (m, 1 H), 0.89 (s, 9 H, *tert*-butyl), 0.04 (s, 6 H). Anal. Calcd for $C_{27}H_{46}O_5Si$: C, 67.74; H, 9.68; Si, 5.87. Found: C, 67.66; H, 9.64; Si, 6.01.

Lactone 37. Homoallylic alcohol **11c** (221 mg, 0.399 mmol) was dissolved in 10 mL of EtOAc in a steel vessel. Rhodium acetate (50 mg, 0.11 mmol) and triphenylphosphine (900 mg, 3.43 mmol) were added, and the vessel was submitted to 350 psi of CO/H_2 (1:1) at 100 °C for 16 h. The reaction mixture was filtered through Celite, concentrated, and chromatographed on 80 g of silica, eluting with 25% EtOAc/hexane to provide 215 mg (92%) of the desired lactol: R_f 0.17 (silica, 25% EtOAc/hexane); IR (film) 3440, 2940, 2860, 1470, 1265, 1105, 840, 785, 705 cm^{-1}; NMR ($CDCl_3$) δ 7.21 (m, 5 H, aromatic), 5.20 (m, 1 H, anomeric), 4.48 (s, 2 H, benzylic), 4.30–3.18 (m, 6 H), 3.49 (s, 3 H, OCH_3), 2.95 (m, 1 H), 2.00–1.40 (m, 10 H), 0.88 (s, 18 H, *tert*-butyl), 0.04 (s, 12 H) ppm. Anal. Calcd for $C_{31}H_{58}O_6Si_2$: C, 63.87; H, 10.03; Si, 9.63. Found: C, 63.76; H, 9.85; Si, 9.51. In a modification of the method of Corey and Suggs,[38] the lactol from above (89 mg, 0.152 mmol) was dissolved in 1.5 mL of dry CH_2Cl_2 and treated with 81 mg (0.375 mmol) of pyridinium chlorochromate. Oven-dried Celite (100 mg) was added to the reaction mixture. After 4 h, TLC analysis showed complete consumption of the lactol. Dry Et_2O (2 mL) was added to the mixture and filtered through 5 g of silica, eluting with dry Et_2O. The eluant was concentrated and chromatographed on silica, eluting with 25% EtOAc/hexane to provide 59 mg (66.5%) of crystalline lactone: IR (CCl_4) 2940, 2860, 1745, 1475, 1370, 1260, 1110, 840, 780, 700 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.34 (m, 5 H, aromatic), 4.47 (AB q, J = 10.1 Hz, $\Delta\nu$ = 13.4 Hz, 2 H, benzylic), 4.35 (d, J = 7.7 Hz, 1 H), 4.22 (m, 1 H), 3.71 (m, 1 H), 3.61 (m, 2 H), 3.54 (m, 1 H), 3.49 (s, 3 H, OCH_3), 3.30 (d, J = 6.2 Hz, 1 H), 2.54 (dt, J_1 = 5.3 Hz, J_2 = 17.7 Hz, 1 H), 2.41 (dq, J_1 = 4.8 Hz, J_2 = 17.7 Hz, 1 H), 2.14 (m, 1 H), 2.01 (m, 1 H), 1.90 (m, 2 H), 1.65 (m, 1 H), 1.45 (m, 1 H), 1.16 (m, 1 H), 0.88 (s, 18 H, *tert*-butyl), 0.10 (s, 3 H), 0.07 (s, 3 H), 0.05 (s, 6 H) ppm. Anal. Calcd for $C_{31}H_{56}O_6Si_2$: C, 64.09; H, 9.71; Si, 9.67. Found: C, 64.39; H, 9.79; Si, 9.49.

Lactones 38 and 39. A solution of LDA was prepared by the addition of 0.46 mL of *n*-butyllithium (1.6 M in hexane, 0.794 mmol) to a solution of diisopropylamine in 2 mL of dry THF under an argon atmosphere at −78 °C. Freshly distilled, dry HMPA (0.29 mL, 1.7 mmol) was added, followed by addition of lactone **37** (355 mg, 0.611 mmol) dissolved in 1 mL of dry THF. The reaction was stirred for 15 min before the addition of 76 μL (1.2 mmol) of freshly distilled methyl iodide. Stirring was continued for 4 h, after which the cold reaction mixture was treated with excess NH_4Cl solution, extracted into Et_2O, dried over $MgSO_4$, and concentrated. TLC analysis of the crude reaction mixture indicated the presence of three products, two of which were isolable by chromatography (50 g of silica, 15–25% EtOAc/hexane) and proved to be the alkylated lactones. The third product (R_f 0.46, silica, 25% EtOAc/hexane), was extremely labile but was believed to be the result of intramolecular silyl migration in the intermediate enolate, based on NMR and IR evidence. The desired α-methyl lactones were isolated as 251.7 mg (69.2%) of a 2.1:1 epimeric mixture, in favor of the 2S* or undesired isomer **38**. However, treatment of 64 mg (107 mmol) of **38** in 0.5 mL of dry THF at −78 °C with LDA solution, prepared as described above, followed by protonation after 15 min with dry BHT and workup as described above, resulted in the isolation of 43.35 mg (70.8%) of a 1:1 epimeric mixture of methylated lactones. Unfortunately, the previously noted intramolecular silyl transfer evidently also occurred during the epimerization.

38: R_f 0.37 (silica, 25% EtOAc/hexane); IR (film) 2950, 2860, 1740, 1470, 1260, 1105, 840, 780, 700 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.34 (m, 5 H, aromatic), 4.47 (AB q, J = 10.6 Hz, $\Delta\nu$ = 14.2 Hz, 2 H, benzylic), 4.32 (d, J = 10.1 Hz, 1 H), 4.22 (m, 1 H), 3.72 (m, 1 H), 3.61 (m, 2 H), 3.54 (m, 1 H), 3.51 (s, 3 H, OCH_3), 3.28 (d, J = 7.2 Hz, 1 H), 2.45 (m, 1 H), 2.24 (m, 1 H), 2.01 (m, 1 H), 1.90 (m, 2 H), 1.68 (m, 2 H), 1.25 (d, J = 6.2 Hz, 3 H), 1.11 (m, 1 H) 0.88 (s, 18 H, *tert*-butyl), 0.08 (s, 3 H), 0.06 (s, 3 H), 0.04 (s, 6 H) ppm. Anal. Calcd for $C_{32}H_{58}O_6Si_2$: C, 64.60; H, 9.82; Si, 9.44. Found (as a mixture of isomers): C, 64.40; H, 9.79; Si, 9.29.

39: R_f 0.31 (silica, 25% EtOAc/hexane); mp 81.5–82 °C; NMR (360 MHz, $CDCl_3$) δ 7.33 (m, 5 H, aromatic), 4.47 (AB q, J = 10.6 Hz, $\Delta\nu$ = 13.4 Hz, 2 H, benzylic), 4.31 (d, J = 9.1 Hz, 1 H), 4.24 (m, 1 H), 3.69 (m, 1 H), 3.63 (m, 2 H), 3.53 (m, 1 H), 3.50 (s, 3 H, OCH_3), 3.30 (d, J = 6.7 Hz, 1 H), 2.53 (m, 1 H), 2.29 (m, 1 H), 1.90 (m, 1 H), 1.79 (m, 1 H), 1.69 (m, 2 H), 1.63 (m, 1 H), 1.24 (m, 1 H), 1.23 (d, J = 6.7 Hz, 3 H, CH_3), 0.88 (s, 18 H, *tert*-butyl), 0.09 (s, 3 H), 0.06 (s, 3 H), 0.04 (s, 6 H).

Hydroxy Ester 40. Bis(silyl) ether **39** (78.8 mg, 0.132 mmol) was treated at room temperature with 1 mL of a solution of *n*-Bu_4NF in THF (1 M, 1.0 mmol). The solution was stirred overnight and then passed through 3.5 g of silica gel, eluting with EtOAc. Concentration of the eluant provided 34.18 mg (70.6%) of the desired diol–lactone: R_f 0.10 (silica, 75% EtOAc/hexane); IR (film) 3440, 2940, 2880, 1730, 1460, 1380, 1200, 1100, 705 cm^{-1}; NMR ($CDCl_3$) δ 7.34 (m, 5 H, aromatic), 4.53 (s, 2 H, benzylic), 4.36 (dd, J_1 = 2.4 Hz, J_2 = 7.7 Hz, 1 H, H-5), 4.15 (m, 1 H), 3.71 (m, 3 H), 3.56 (s, 3 H), 3.32 (dd, J_1 = 3.4 Hz, J_2 = 5.8 Hz, 1 H), 3.17 (m, 1 H), 2.59 (m, 1 H), 2.34 (m, 1 H), 1.98–1.42 (m, 4 H), 1.75 (dd, J_1 = 7.2 Hz, J_2 = 9.1 Hz, 2 H), 1.61 (br s, 2 H), 1.25 (d, J = 9.1 Hz, 3 H, CH_3).

Acetonide 42. Diol **40** from above (34.18 mg, 0.093 mmol) was dissolved in 0.5 mL of dry pyridine and treated with *tert*-butylchlorodiphenylsilane (36.0 μL, 0.138 mmol). The mixture was stirred for 12 h at room temperature and then chromatographed on 10 g of silica, eluting with 10% EtOAc/hexane–10% MeOH/EtOAc, to provide 25.2 mg of the desired silyl ether and 3.6 mg of recovered diol. The fractions containing silyl ether were combined, concentrated, and dissolved in 0.5 mL of dry MeOH. The solution was treated with 2 μL of a 2 M solution of NaOMe in MeOH (0.005 mmol). After 30 min, TLC showed complete consumption of the lactone (R_f 0.61, silica, 75% EtOAc/hexane). Dimethoxypropane (0.75 mL), camphorsulfonic acid (6 mg, 0.024 mmol), and dry acetone (0.5 mL) were then added to the methanolic solution. After stirring for 4 h, the mixture was passed through 1 g of basic alumina, eluting with dry Et_2O, concentrated, and chromatographed on 4 g of silica, providing 17.89 mg of a 5.8:1 isomeric mixture of acetonide–methyl esters **41** (R_f 0.18 for the major isomer, R_f 0.16 for the minor isomer; silica, 25% EtOAc/hexane). Apparently, lactone cleavage with methoxide was accompanied by epimerization of the α-methyl group; 14.92 mg (0.22 mmol) of the mixture of methyl esters was dissolved in 0.5 mL of dry THF and treated with 22 μL of a 1 M solution of LAH in THF (0.022 mmol). The mixture was stirred for 12 h, and then 1 drop of water, 1 drop of 10% NaOH solution, and $MgSO_4$ were added. The mixture was filtered and concentrated, providing 14.68 mg of acetonide–alcohol **42** and its isomer in the ratio 5.8:1. The isomers were separated by chromatography on silica, eluting with 50% EtOAc/hexane. Overall yield from the diol–lactone **40** was 31%. Acetonide–alcohol: R_f 0.35 (silica, 50% EtOAc/hexane);

(38) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

IR (film, as a mixture of C-2 epimers) 2470, 2940, 2860, 1595, 1470, 1430, 1385, 1205, 1110, 740, 705 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 7.66 (m, 4 H, aromatic), 7.37 (m, 11 H, aromatic), 4.50 (AB q, J = 12.0 Hz, $\Delta\nu$ = 19.7 Hz, 2 H, benzylic), 3.92 (dd, J_1 = 2.4 Hz, J_2 = 9.6 Hz, 1 H), 3.71 (m, 2 H), 3.58 (m, 3 H), 3.55 (m, 1 H), 3.44 (s, 3 H, OCH_3), 3.33 (d, J = 6.0 Hz, 1 H), 2.92 (br s, 1 H, H-5'), 2.00 (m, 1 H), 1.84 (m, 1 H), 1.70 (m, 1 H), 1.65-1.20 (m, 6 H), 1.36 (s, 3 H, acetonide methyl), 1.32 (s, 3 H, acetonide methyl), 1.04 (s, 9 H, *tert*-butyl), 0.81 (d, J = 6.7 Hz, 3 H, CH_3); MS, m/z (relative intensity, 70 eV) 633 (0.01, $M^+ - CH_3$), 409 (0.03, $M^+ - SiPh_2t\text{-}Bu$), 393 (0.43), 393 (0.43), 369 (0.53), 340 (0.31), 339 (1.32), 323 (0.15), 315 (0.30), 285 (0.99), 263 (2.06), 213 (2.07), 200 (1.94), 199 (11.40), 183 (2.42), 135 (6.01), 125 (25.85), 107 (13.32), 91 (base, $PhCH_2$), 71 (41.03), 58 (24.88). Anal. Calcd for $C_{39}H_{56}O_6Si$: C, 72.18; H, 8.70; Si, 4.33. Found (as a mixture of C-2 epimers): C, 72.48; H, 8.80; Si, 4.18. Acetonide-alcohol **42**: R_f 0.26 (silica, 50% EtOAc/hexane); NMR (360 MHz, $CDCl_3$) δ 7.66 (m, 4 H, aromatic), 7.38 (m, 11 H, aromatic), 4.52 (AB q, J = 11.5 Hz, $\Delta\nu$ = 14.6 Hz, 2 H, benzylic), 3.95 (m, 1 H), 3.73 (m, 3 H), 3.60 (m, 3 H), 3.50 (m, 1 H), 3.45 (s, 3 H, OCH_3), 3.32 (dd, J_1 = 4.3 Hz, J_2 = 11.0 Hz, 1 H), 2.97 (br s, 1 H, H-5'), 2.00 (m, 2 H), 1.83 (m, 2 H), 1.57-0.88 (m, 4 H), 1.42 (s, 3 H, acetonide methyl), 1.37 (s, 3 H, acetonide methyl), 1.05 (s, 9 H, *tert*-butyl), 0.81 (d, J = 5.3 Hz, 3 H, CH_3).

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Note Added in Proof. It has recently come to our attention that A. J. Pearson and T. Ray (*Tetrahedron Lett.* **1986**, *27*, 3111) have developed an alternative approach to carbomycin B.

Stereospecific Synthesis of Ether and Thioether Phospholipids. The Use of L-Glyceric Acid as a Chiral Phospholipid Precursor

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A novel stereospecific synthesis of biologically active ether phospholipids is reported. The synthesis is based on (1) the use of L-glyceric acid as the chiral center for the construction of the optically active phospholipid molecule, (2) the introduction of the *sn*-2-short chain alkyl substituent via silver tetrafluoroborate catalyzed alkylation reaction that leaves the neighboring carbomethoxy group unaffected, and then elaboration of the lipophilic alkoxy function at the *sn*-1-position, and (3) the development of the *sn*-3-phosphorylcholine moiety through the 2-chloro-2-oxo-1,3,2-dioxaphospholane-trimethylamine sequence. The entire scheme involves the use of a single protecting group. Through the use of intermediates that became available from the sequence, a scheme for the preparation of antitumor active *sn*-1-thio ether phospholipids has been developed. The synthetic methods have a great deal of flexibility, providing convenient routes to a wide range of ether and thioether phospholipids for physicochemical as well as enzymological studies.

The synthesis of biologically active phospholipid compounds is one of the most timely problems in membrane chemistry today.[1-4] Ether phospholipids occupy a particularly important position in this regard as they have been shown to possess high levels of activity in a wide range of physiologically vital regulatory events.[5,6] Specifically, 1-alkylglycerophosphocholines are potent platelet-activators,[1,7] exhibit strong antihypertensive activity[1,8] and function as effective immunomodulating agents.[9] In addition, recent evidence has established that a series of structural analogues of platelet-activating factor (PAF) show selective tumor cytotoxicity against a number of different human cancer cells.[10] These observations have recently initiated vigorous activity in an attempt to explore the use of alkylphospholipids as potential drugs in antileukemic chemotherapy.[11]

Despite the well-recognized biological importance of these compounds, relatively little progress has been made toward elucidation of their mechanism of action. In order to achieve this goal and to delineate the structural requirements associated with the respective biological activities, synthetic phospholipid derivatives need to be prepared. Furthermore, availability of facile and efficient synthetic procedures leading to the desired compounds represents not only a prerequisite to the establishment of structure-function correlations but also a basis for the

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