varies from compound to compound); the mixture was stirred at that temperature for 1.0–1.5 h. The excess zinc was removed by filtration through a bed of Celite, which was then washed with methylene chloride, and the combined filtrates were concentrated under reduced pressure. The sticky orange mass was redissolved in methylene chloride and washed three times with water. The aqueous extracts were combined, saturated with sodium chloride, and reextracted with methylene chloride. The organic layers were combined, washed two times with cold water followed by brine, dried, and concentrated to give a light yellow to orange sticky foam, which was purified over a short silica column with ethyl acetate–hexane as eluant.

The following compounds were made by this procedure.

Methyl 6,6-dihydropenicillanate 1,1-dioxide (3v): mp 118–120 °C; IR (KBr) 1809, 1758 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (s, 3 H, CH_3), 1.63 (s, 3 H, CH_3), 3.45 (dd, 1 H, J = 2, 16 Hz, 6β-H), 3.58 (dd, 1 H, J = 4.5, 16 Hz, 6α-H), 4.44 (s, 1 H, 3-H), 4.72 (dd, 1 H, J = 2, 4.5 Hz, 5α-H). Anal. Calcd for $C_9H_{13}NO_5S$: C, 43.72; H, 5.26; N, 5.67; S, 12.95. Found: C, 43.54; H, 5.22; N, 5.57; S, 12.95.

Methyl 6,6-dihydropenicillanate 1α-oxide (3u): mp 142–145 °C dec; IR (KBr) 1782, 1757 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.38 (s, 3 H, CH_3), 1.62 (s, 3 H, CH_3), 3.42 (dd, 1 H, J = 2, 16 Hz, 6β-H), 3.65 (dd, 1 H, J = 4.5, 16 Hz, 6α-H), 4.44 (s, 1 H, 3-H), 4.65 (dd, 1 H, J = 2, 4.5 Hz, 5α-H). Anal. Calcd for $C_9H_{13}NO_4S$: C, 46.75; H, 5.62; N, 6.06; S, 13.85. Found: C, 46.69; H, 5.73; N, 6.19; S, 13.78.

Methyl 6,6-dihydropenicillanate 1β-oxide (3t): mp 75–77 °C; IR (KBr) 1781, 1748 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (s, 3 H, CH_3), 1.72 (s, 3 H, CH_3), 3.38 (d, 2 H, J = 4 Hz, 6α-H + 6β-H), 4.52 (s, 1 H, 3-H), 5.03 (t, 1 H, J = 4 Hz, 5α-H). Anal. Calcd for $C_9H_{13}NO_4S$: C, 46.75; H, 5.62; N, 6.06; S, 13.85. Found: C, 46.81; H, 5.63; N, 6.11; S, 13.81.

Benzhydryl 6,6-Dihydropenicillanate 1β-Oxide (3x). To a stirred solution of benzhydryl 6-diazopenicillanate 1β-oxide (**8c**) (4.407 g, 0.01076 mol) in 200 mL of ethyl acetate at 0 °C was added dropwise a solution of hydrogen bromide in ethyl acetate (6.3 mL, 0.95 g, 0.01183 mol). The mixture was stirred at 0 °C for 30 min. Excess hydrogen bromide was removed at reduced pressure. The mixture was again cooled to 10 °C; to this was added glacial acetic acid (6 mL). Zinc dust (1.75 g, 0.0267 mol) was added portionwise with stirring over 10 min. Stirring was continued for an additional 1.5 h. Filtration (through a bed of Celite) and evaporation gave a light brown oil, which was redissolved in 150 mL of ethyl acetate, washed with cold water, sodium bicarbonate solution, and finally with brine, dried (Na_2SO_4), and evaporated to give **3x** as a pale yellow foam, 3.89 g (94%). Purification by column chromatography eluted with hexane–ethyl acetate provided **3x** in 88% yield: mp 145–148 °C; IR (KBr) 1797, 1759 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.9 (s, 3 H, CH_3), 1.65 (s, 3 H, CH_3), 3.32 (d, 2 H, J = 4 Hz, 6α-H + 6β-H), 4.6 (s, 1 H, 3-H), 4.9 (t, 1 H, J = 4 Hz, 5α-H). Anal. Calcd for $C_{21}H_{21}NO_4S$: C, 65.79; H, 5.48; N, 3.65; S, 8.35. Found: C, 65.83; H, 5.53; N, 3.74; S, 8.29.

Acknowledgment. We thank Taiho Pharmaceutical Co., Tokyo, Japan, for their generous support of this work.

Registry No. **3** (R_1 = NH_2, R_2 = R_3 = H, X = S), 551-16-6; **3** (R_1 = R_2 = Br, R_3 = H, X = S), 24158-88-1; **3a**, 24138-27-0; **3b**, 25663-91-6; **3c**, 24138-29-2; **3d**, 61657-19-0; **3e**, 100298-36-0; **3f**, 34800-34-5; **3g**, 52354-06-0; **3h**, 75527-84-3; **3i**, 76517-35-6; **3j**, 100298-37-1; **3k**, 100298-38-2; **3l**, 74189-25-6; **3m**, 100349-41-5; **3n**, 100298-39-3; **3o**, 62263-89-2; **3p**, 100239-31-4; **3q**, 100298-40-6; **3r**, 100298-41-7; **3s**, 4027-61-6; **3t**, 61657-21-4; **3u**, 61657-20-3; **3v**, 65039-72-7; **3w**, 73968-83-9; **3x**, 100349-42-6; **3y**, 62263-72-3; **4** (R = Br), 100298-44-0; **7a**, 24652-72-0; **7a** (n = 0), 653-89-4; **7c**, 37591-56-3; **8a**, 100298-42-8; **8c**, 100298-43-9; **8d**, 51056-24-7.

Supplementary Material Available: ^1H NMR spectral data for compounds **3e–3n**, **3q**, **3r**, and **3w** (1 page). Ordering information is given on any current masthead page.

Synthesis of 7(8)-Desoxyasperdiol. A Precursor of the Cembranoid Asperdiol

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Received July 31, 1985

A convergent and highly stereoselective synthesis of 7(8)-desoxyasperdiol, a 14-membered synthetic precursor of the cembranoid asperdiol, is described starting from geraniol and the epoxide of *cis*-2-butene-1,4-diol acetonide (A1). The route from the geranyl fragment B2 proceeds in approximately 6% overall yield. Key transformations include a highly *E*-selective Wittig coupling of aldehyde A10 with the α-triphenylphosphorylidene ester B8 and macrocyclization of the iodo sulfone B14, possibly as the dianion. Desulfonylation and bis-debenzylation of the macrocycle B15 were achieved in one step with sodium in liquid NH_3–THF in 71% yield.

Asperdiol, a cembranoid antitumor agent derived from Caribbean gorgonians of the *Eunicea* genus, was isolated by Weinheimer and Matson and elucidated through single-crystal X-ray structure analysis.[1] Kato reported the first synthesis of this unusual cembranoid by a route involving Friedel–Crafts macrocyclization of a homologated farnesol and subsequent elaboration of key structural features through a fascinating series of selective transformations of macrocyclic intermediates.[2] Shortly thereafter, Still and Mobilio described a convergent synthesis in which the crucial C-1/C-14 hydroxyl–isopropenyl relationship was introduced in the context of a novel intramolecular allylchromium–enal macrocyclization step.[3] For several years now we have been exploring potential routes to asperdiol and related structures from readily available precursors. Our efforts have resulted in a straightforward and completely stereoselective synthesis of 7(8)-desoxyasperdiol B16 (II, Y = H), a key intermediate in the Kato synthesis of racemic asperdiol[2] (see Figure 1).

Central to our plan was the stereocontrolled assemblage of a protected erythro α-hydroxy aldehyde V and its ste-

(1) Weinheimer, A. J.; Matson, J.; van der Helm, D.; Poling, M. *Tetrahedron Lett.* **1977**, 1295.

(2) Aoki, M.; Tooyama, Y.; Uyehara, T.; Kato, T. *Tetrahedron Lett.* **1983**, *24*, 2267.

(3) Still, W. C.; Mobilio, D. *J. Org. Chem.* **1983**, *48*, 4786.

(4) The convention suggested by Heathcock et al. is employed wherein the isomer with adjacent syn substituents when the major chain is presented in a zig-zag conformation is defined as erythro. Heathcock, C. H. et al. *J. Org. Chem.* **1980**, *45*, 1066.

0022-3263/86/1951-0858$01.50/0

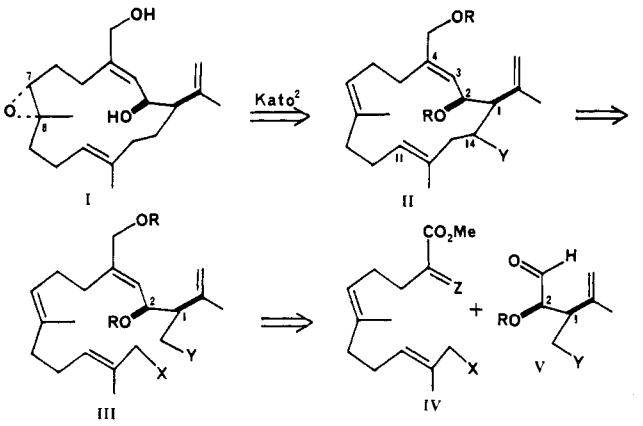
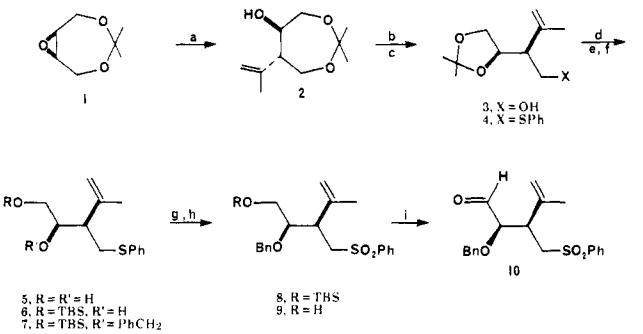


Figure 1. Retrosynthetic analysis of asperdiol (I).

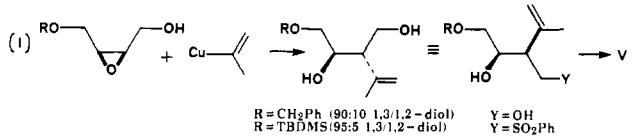
Scheme I.[a,b] **A Series**



[a] (a) CH_2=$C(CH_3)MgBr$, CuI, THF, −45 to 25 °C (89%); (b) *p*-TsOH, Me_2CO, 25 °C (90%); (c) PhSSPh, Bu_3P, THF, 0–25 °C; (d) H^+ resin, MeOH, 25 °C (89%); (e) TBSCl, Et_3N, *p*-$Me_2NC_5H_4N$, CH_2Cl_2, 0–25 °C; (f) *t*-BuLi, $(Me_2N)_3PO$, THF, $PhCH_2Br$, −78 to 25 °C (91%); (g) *m*-$ClC_6H_4CO_3H$, CH_2Cl_2, 0 °C; (h) Bu_4NF, THF, 0–25 °C (83%); (i) $(C_5H_5NH)_2CrO_4$. [b] TBS = *t*-$BuSiMe_2$, Bn = $PhCH_2$.

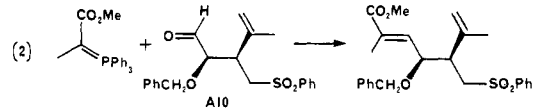
reoselective Wittig coupling with a geraniol-derived, stabilized ylide IV followed by reduction to an intermediate III with all requisite structural features save the macrocyclic ring. Cyclization would be effected via sulfonyl stabilized anion displacement of an allylic halide. This variant of the cyclization strategy offered an advantage over previously reported cases employing allylic sulfones in that the desulfonylation step (II, Y = SO_2Ph → II, Y = H) would not be complicated by attendant double bond isomerization commonly observed with allylic sulfones,[5] sulfides,[6] and selenides.[3]

Our earliest routes to aldehydes such as V were based upon selective cleavage of monoprotected *cis*-2-butene-1,4-diol epoxides with isopropenylcopper reagents (equation 1).[7,8] These reactions were found to proceed with high



regioselectivity and complete stereospecificity to give the desired erythro[4] products. We eventually settled on the route depicted in Scheme I as the most convenient of several examined for producing large quantities of the sulfone aldehyde A10. Accordingly, the known epoxy acetonide A1[9] was treated with isopropenylmagnesium bromide–copper(I) iodide in THF to afford the *trans*-isopropenyl alcohol A2 as the sole product. Rearrangement of this acetonide, along lines reported for the methyl analog,[9] gave the alcohol A3 in 90% yield. As an aside, attempted S_N2 displacements on the unstable bromide or iodide derivatives of A3 (X = Br or X = I) with carbon nucleophiles proved difficult.[10] Sulfide A4, however, could be prepared directly from alcohol A3 via treatment with diphenyl disulfide and tri-*n*-butylphosphine.[11] Protection of the secondary alcohol function of the resulting crystalline diol A5 was achieved via selective silylation of the primary alcohol followed by benzylation. Sulfide A7 was oxidized to the sulfone A8 which was then desilylated with tetra-*n*-butylammonium fluoride and oxidized to the unstable aldehyde A10. This aldehyde decomposed upon storage and was best used immediately after preparation.

Having devised an efficient route to aldehyde A10, we turned our attention to possible olefination protocols with ester-substituted phosphorous reagents. Phosphonopropionates have been well studied as coupling partners for various aldehydes.[12] Their general ease of preparation and the possibility of *E,Z* stereocontrol through variation of the alkoxy substituents made them a logical first choice for our olefination studies. Unfortunately these studies were short-lived as the anion of even the simplest and least basic member, methyl (dimethylphosphinyl)acetate, caused extensive decomposition of aldehyde A10 under a variety of conditions.[13] In contrast, the less basic methyl α-(triphenylphosphorylidene)propionate condensed smoothly with aldehyde A10 affording the *E*-conjugated ester as the



sole product in 76% yield (equation 2). In light of this highly encouraging result, we directed our efforts toward the synthesis of phosphonium salt B7, a likely precursor of phosphorane B8.

The known TBS ether B2[14] of oxidized geraniol (prepared via SeO_2 oxidation of geranyl acetate followed by silylation to B1 and basic methanolysis) was converted to the chloride B3 which smoothly coupled with vinylmagnesium bromide–copper(I) iodide to give the triene B4. Selective hydroboration–oxidation led to the alcohol B5 which was transformed via the Corey iodination procedure to the iodide B6.[15] Conversion to the crystalline phosphonium iodide B7 was effected in nearly quantitative yield.

(5) *Cf.* Takayanagi, H.; Uyehara, T.; Kato, T. *J. Chem. Soc., Chem. Commun.* **1978**, 359.

(6) Cf. Shimada, K.; Kodama, M.; Itô, S. *Tetrahedron Lett.* **1981**, *22*, 4275.

(7) The TBS-protected epoxy alcohol gave a 95:5 mixture of 1,3 and 1,2-diols in 92% yield upon cleavage with the isopropenylcopper reagent. Cleary, D. G. Research Report, August 15, 1981.

(8) Subsequent to these studies a paper by Tius described similar findings on the benzyl protected diol epoxide and a variety of organocopper reagents. Tius, M.; Fauq, A. H. *J. Org. Chem.* **1983**, *48*, 4131. See also: Sharpless, K. B. et al. *Pure and Applied Chem.* **1983**, *55*, 589.

(9) Elliot, W. J.; Fried, J. *J. Org. Chem.* **1976**, *41*, 2471.

(10) Attempts at displacement of the iodide with acetoacetate dianion or dilithioacetate gave no useful product after prolonged reaction time. Diethyl sodiomalonate afforded the expected alkylated malonate in 42% yield after 22 h at room temperature. Cleary, D. G., unpublished observations.

(11) Hanessian, S.; Taylor, P. C.; Demailly, G.; Chapleur, Y. *J. Am. Chem. Soc.* **1981**, *103*, 6243.

(12) Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873. Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405. Kinstle, T. *J. Chem. Soc., Chem., Commun.* **1968**, 1699.

(13) For details see Cleary, D. G., Ph.D. Dissertation, "The Synthesis of 7(8)-Desoxyasperdiol and Related Studies", the University of South Carolina, August, 1985.

(14) Corey, E. J.; Tius, M. A.; Das, J. *J. Am. Chem. Soc.* **1980**, *102*, 1742.

(15) Corey, E. J.; Pyne, S. G.; Su, W. *Tetrahedron Lett.* **1983**, *24*, 4883.

Table I. Cyclizations of Halo Sulfones B13 and B14 to Sulfone B15 with KHMDS in THF[a,b]

run	halo sulfone	KHMDS equiv[a]	additive	temp, °C	yield, %[c]
1	B13	5	18-crown-6	25	41
2	B14	4	18-crown-6	25	42
3	B14	3	18-crown-6	25	44
4	B14	2.2	18-crown-6	0	53
5	B14	2.0		0	37

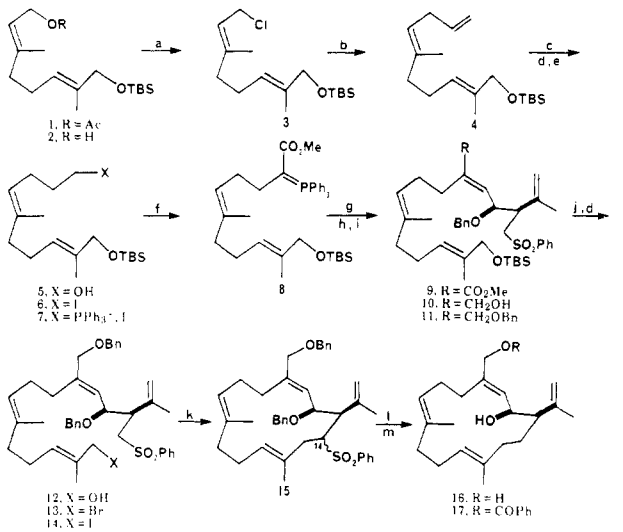
[a] KHMDS = potassium hexamethyldisilazide. [b] Reactions were carried out by slow (~10 h) additions of the halo sulfone in THF to 0.01–0.03 M solutions of the base in THF–toluene followed by prolonged (~10 h) stirring. [c] Chromatographed mixture of sulfone diastereoisomers.

The preparation of carboxyalkylidenephosphoranes by acylation of alkylidenephosphoranes was pioneered by Bestmann.[16a] Best results are obtained with "salt-free ylides" and acyl halides, but the reaction requires 2 molar equiv of the ylide. It is important to avoid excess acyl halide as the acylphosphorane products are succeptable to further acylation. Hoping to avoid the inconvenience of preparing salt-free ylides and the inefficiency of using a two-fold excess of the ylide derived from B7, we employed a more convenient preparation of phosphorane B8 through treatment of phosphonium salt B7 with 2 equiv of potassium hexamethyldisilazide (KHMDS)[16b] followed by 1 equiv of methyl chloroformate.[16c] The crude phosphorane was directly treated with freshly prepared aldehyde A10 whereupon the conjugated ester B9 was secured as a single *E* stereoisomer in 41% yield. The characteristic doublet of the β-vinylic proton at 6.5 ppm in the high field ^{1}H NMR spectrum left no doubt as to the stereochemical integrity of this ester.[17]

Reduction of ester B9 with DIBAH followed by benzylation and desilylation led uneventfully to alcohol B12. We were now in a position to examine the critical cyclization step of our planned synthesis. Alcohol B12 could be converted to the unstable bromide B13 or the unstable iodide B14, the latter by the facile Corey procedure.[15] The iodide was preparatively more convenient and appeared to cyclize faster than the bromide. Slow addition of iodo sulfone B14 to excess KHMDS in THF/18-crown-6 at 0 °C effected cyclization to sulfone B15 in 53% yield (see Scheme II). Under comparable conditions, but without 18-crown-6, the cyclization took place in 37% yield with formation of several by products (Table I, entry 5). Cyclizations at room temperature with 4 to 5 equiv of base proceeded in 41–44% yield (Table I, entries 1–3). The sulfone product B15 was formed as an approximately 3:1 mixture of sulfone (C-14) diastereoisomers as judged by high field ^{1}H NMR analysis. Although this point was not pursued, it is possible that the cyclization proceeds via a dianion intermediate.[18]

Hydrogenolysis of the sulfonyl grouping could be effected selectively with sodium amalgam in methanol,[19] but a more efficient procedure entailed concurrent desulfonylation and debenzylation with sodium in ammonia–THF to give the crystalline diol B16, mp 97–98.5 °C, directly in 71% yield. The identity of this material follows unambiguously from the synthetic sequence and from high-field ^{1}H NMR analysis of B16 and its precursors. Additional support for the structure was provided by direct comparison of the ^{1}H NMR spectrum and mixture melting point with a sample of Professor Kato's diol.

Scheme II.[a,b] B Series



[a] (a) MsCl, LiCl, DMF, 2,6-lutidine, 0 °C (87%); (b) CH_2=CH-MgBr, CuI, THF, −23 °C (79%); (c) disiamylborane, THF, −10 °C; 30% H_2O_2, NaOH (83%); (d) I_2, Ph_3P, imidazole, CH_3CN, Et_2O, 0 °C; (e) Ph_3P, C_6H_6, reflux (94%); (f) $(Me_3Si)_2NK$ (2×), THF, MeOCOCl, −78 to 25 °C; (g) A10, THF, 25 °C (41%); (h) *i*-Bu_2AlH, CH_2Cl_2, −78 °C (94%); (i) *tert*-BuLi, $(Me_2N)_3PO$, $PhCH_2Br$, THF, −78 to 25 °C; (j) Bu_4NF, THF, 25 °C (83%); (k) $(TMS)_2NK$ (2.5×), THF, 18-crown-6 (53%); (l) Na, NH_3, THF, −33 °C (71%); (m) PhCOCl, Et_3N, $Me_2NC_5H_4N$, CH_2Cl_2 (67%). [b] TBS = *t*-BuSiMe_2, Bn = $PhCH_2$.

Selective monobenzoylation of diol B16 afforded the benzoate B17 in 67% yield. Since benzoate B17 has been converted to asperdiol by Kato and co-workers, its preparation constitutes a formal total synthesis of racemic asperdiol.[2] It should be noted that the route described here is admirably suited to the preparation of natural asperdiol.[20]

Experimental Section

The apparatus and methods described by G. W. Kramer, M. M. Midland, and A. B. Levy were used to maintain an argon or nitrogen atmosphere in the reaction flask.[22] Infrared absorption maxima are reported in wavenumbers (cm^{-1}) and are standardized by reference to the 1601-cm^{-1} peak of polystyrene. Proton magnetic resonance spectra were recorded on Varian EM-390 and Bruker WH-400 spectrometers. Chemical shifts (δ) are reported downfield from tetramethylsilane (Me_4Si), in parts per million (ppm) of the applied field. Peak multiplicities are abbreviated: singlet, s; doublet, d; triplet, t; quartet, q; envelope, e; multiplet, m. Combustion microanalyses were performed by Atlantic Laboratories, Atlanta, GA. Column chromatography was performed on E. Merck silica gel 60 (230–400 ASTM mesh) according to the procedure of W. C. Still, M. Kahn, and A. Mitra.[23]

***rel*-(5*R*,6*S*)-2,2-Dimethyl-5-hydroxy-6-isopropenyl-1,3-dioxepane (A2).** The procedure of Hunyh et al. was modified.[24]

(16) (a) Cf. Bestmann, H. J. *Angew. Chem., Int. Ed. Engl.* **1965**, *4*, 645. (b) Bestmann, H. J.; Stransky, W.; Vostrowsky, O. *Chem. Ber.* **1976**, *109*, 1694. (c) For a recent improvement in alkylidenephosphorane formylation methodology see: Schlessinger, R. H.; Poss, M. A.; Richardson, S.; Lin, P. *Tetrahedron Lett.* **1985**, *20*, 2391.

(17) The corresponding proton of the *Z* isomer appears near 5.8 ppm. This region was completely flat in the high-field spectrum of ester B9.

(18) Kondo, K.; Tunemoto, D. *Tetrahedron Lett.* **1975**, 1397.

(19) Cf. Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verhoeven, T. R. *Tetrahedron Lett.* **1976**, 3477.

(20) Starting with optically active epoxy alcohol, prepared via Sharpless epoxidation,[21] we have prepared optically active acetonide A3 of the indicated configuration via the sequence described in eq 1.[13]

(21) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974. Behrens, C. H.; Sharpless, K. B. *Aldrichimica Acta* **1983**, *16*, 67.

(22) Brown, H. C. "Organic Syntheses via Boranes"; Wiley: New York, 1975; pp 191–202.

(23) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2933.

(24) Huynh, C.; Derguini-Boumechal, F.; Linstrumelle, G. *Tetrahedron Lett.* **1979**, *20*, 1503.

To a stirred, cooled (−45 °C) suspension of 3.4 g (18 mmol) of copper(I) iodide in 300 mL of THF was added via an addition funnel over 30 min, 208 mL of 0.72 M isopropenylmagnesium bromide in THF. The orange-yellow slurry was stirred for 45 min, and 7.6 g (52.9 mmol) of 4,4-dimethyl-3,5,8-trioxabicyclo[5.1.0]-octane (A1)[9] in 5 mL of THF was added. The resulting mixture was allowed to stir and warm overnight whereupon 300 mL of ether was added. The black slurry was treated with saturated aqueous NH_4Cl until precipitation occurred, the organic layer was decanted, and the granular salts were washed once with ether. The combined extracts were washed twice with 3% aqueous NH_4OH followed by water and saturated aqueous NaCl. The pale yellow solution was dried over $MgSO_4$, the solvent was removed under reduced pressure, and the crude product was purified by column chromatography on silica gel (1:9 ether–hexane) to afford 8.75 g (89%) of A2 as a colorless oil: ^1H NMR (90 MHz) δ 1.30, 1.32 (acetonide CH_3's), 1.73 (s, isopropenyl CH_3), 3.67 (d, J = 2.8 Hz, $-CH_2O-$), 4.90 (m, vinyl H); IR (film) 3425, 3075, 1235, 1105, 1060 cm^{-1}. Anal. Calcd for $C_{10}H_{10}O_3$: C, 64.49; H, 9.74. Found: C, 64.60; H, 9.76.

***rel*-(2*R*,3*R*)-3-Isopropenyl-4-(phenylthio)-1,2-butanediol Acetonide (A4).** To a stirred, cooled (0 °C) solution of 3.7 g (19.8 mmol) of alcohol A3 and 4.35 g (20 mmol) of diphenyl disulfide in 25 mL of THF was added 6.6 mL (20 mmol) of freshly distilled tri-*n*-butylphosphine. After 18 h, the solution was diluted with 300 mL of ether and washed twice with 10% aqueous NaOH followed by two water washings. The organic layer was dried briefly over $MgSO_4$ and filtered, and the solvent was removed under reduced pressure to give a foul smelling pale yellow oil. The crude product was purified by column chromatography on silica gel (hexane) to afford 4.0 g (87%) of sulfide A4 as a pale yellow oil: ^1H NMR (400 MHz) δ 1.32, 1.38 (s, acetonide CH_3's), 1.78 (s, isopropenyl CH_3), 2.49 (q, J = 6.9 Hz, C-3 H), 3.00 (m, C-4 H), 3.84 (AB of ABX, $\Delta\nu$ = 161.4 Hz, J_{AB} = 12.7 Hz, J_{AX} = 9.8 Hz, J_{BX} = 11.6 Hz, C-1 H's), 4.20 (q, J = 6.8 Hz, C-2 H), 4.81 (s, vinyl H), 4.97 (t, J = 1.6 Hz, vinyl H), 7.12–7.34 (br m, aromatic H's). Anal. Calcd for $C_{16}H_{22}O_2S$: C, 69.02; H, 7.96. Found: C, 68.90; H, 8.00.

***rel*-(2*R*,3*R*)-3-Isopropenyl-4-(phenylthio)-1,2-butanediol (A5).** To a stirred suspension of 6.0 g of Bio-Rad 50W-X8 cation exchange resin (200–400 mesh: 5.1 mequiv/g) in 35 mL of methanol was added 6.96 g (25 mmol) of acetonide A4. The suspension was vigorously stirred for 18 h whereupon the reaction mixture was filtered, diluted with 500 mL of anhydrous benzene, and concentrated under reduced pressure to give a yellow oil. The crude product was purified by column chromatography on silica gel (1:1 ether–hexane) to afford 4.92 g (89%) of diol A5 as a pale yellow oil: ^1H NMR (90 MHz) δ 1.76 (s, isopropenyl CH_3), 2.41 (dd, J = 6.9, 10.8 Hz, C-3 H), 4.78 (s, vinyl H), 4.94 (m, vinyl H), 7.28 (br s, aromatic H's). Anal. Calcd for $C_{13}H_{18}O_2S$: C, 65.51; H, 7.61. Found: C, 65.40; H, 7.64.

***rel*-(2*R*,3*R*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-isopropenyl-4-(phenylthio)-2-butanol (A6).** To a stirred solution of 3.95 g (16.6 mmol) of diol A5, 500 mg of 4-(*N*,*N*-dimethylamino)pyridine, and 2.4 mL (17 mmol) of triethylamine in 150 mL of CH_2Cl_2 was added 2.5 g (16.7 mmol) of *tert*-butyldimethylsilyl chloride. The resulting solution was stirred for 18 h, diluted with 300 mL of CH_2Cl_2, washed sequentially with water, saturated aqueous $CuSO_4$, and saturated aqueous NaCl, dried ($MgSO_4$), and filtered. The solvent was removed under reduced pressure to give a clear oil. This oil was filtered through a small plug of silica gel to give 5.68 g (97%) of alcohol A6 as a clear oil: ^1H NMR (400 MHz) δ 0.07 (s, $-Si(CH_3)_2-$), 0.89 (s, $-SiC(CH_3)_3$), 1.80 (s, isopropenyl CH_3), 2.34 (d, J = 3.83 Hz, −OH), 2.49 (dt, J_t = 14.91 Hz, J_d = 5.99 Hz, C-2 H), 3.12 (AB of ABX, $\Delta\nu$ = 66.48 Hz, J_{AB} = 12.7 Hz, J_{AX} = 6.19 Hz, J_{BX} = 8.95 Hz, C-1 H's), 3.59 (AB of ABX, $\Delta\nu$ = 33.72, J_{AB} = 10.2 Hz, J_{AX} = 3.98 Hz, J_{BX} = 6.94 Hz, C-4 H's), 3.81 (m, C-3 H), 4.80 (br s, vinyl H), 4.98 (m, vinyl H), 7.16 (m, aromatic H, 1 H), 7.27 (m, aromatic H, 2 H), d, J = 8.37 Hz, aromatic H, 2 H); IR (film) 3465, 3070, 2930, 2850, 1640, 1585, 1475, 1440, 1260, 1120, 840 cm^{-1}. Anal. Calcd for $C_{19}H_{32}O_2SSi$: C, 64.72; H, 9.15. Found: C, 64.84; H, 9.18.

***rel*-(2*R*,3*R*)-4-[(*tert*-Butyldimethylsilyl)oxy]-3-(benzyloxy)-2-isopropenylbutyl Phenyl Sulfide (A7).** To a stirred, cooled (−78 °C) solution of 2.2 g (6.23 mmol) of alcohol A6 in 3.6 mL of THF was slowly added 3.5 mL of 1.8 M *tert*-butyllithium in hexane. After 10 min, 2.2 mL (12.5 mmol) of HMPA was slowly added (resulting in a blood red solution) followed immediately by the addition of 750 μl (6.3 mmol) of benzyl bromide. After 30 min the cooling bath was removed and the solution was allowed to stir and warm over a 75-min period whereupon the color faded to pale yellow. The reaction mixture was diluted with 100 mL of ether, washed three times with water, dried over $MgSO_4$, and filtered, and the solvent was removed under reduced pressure to give a yellow oil. The crude product was filtered through a small plug of silica gel to give 2.5 g (91%) of sulfide A7 as a clear oil: ^1H NMR (400 MHz) δ 0.08 (s, $-Si(CH_3)_2-$), 0.87 (s, $-C(CH_3)_3$), 1.77 (s, isopropenyl CH_3), 2.62 (dt, J_d = 5.5 Hz, J_t = 10.9 Hz, C-2 H), 3.08 (AB of ABX, $\Delta\nu$ = 42.08, J_{AB} = 11.4 Hz, J_{AX} = 6.0 Hz, J_{BX} = 5.4 Hz, C-1 H's), 3.63 (AB of ABX, $\Delta\nu$ = 40.52 Hz, J_{AB} = 10.9 Hz, J_{AX} = 6.0 Hz, J_{BX} = 5.8 Hz, C-4 Hs), 3.75 (m, C-3 H), 4.63 (ABq, $\Delta\nu$ = 91.3 Hz, J_{AB} = 11.4 Hz, $PhCH_2O-$), 4.79 (s, vinyl H), 4.92 (t, J = 1.7 Hz, vinyl H), 7.12–7.36 (br m, aromatic H's). Anal. Calcd for $C_{26}H_{38}O_2SSi$: C, 70.53; H, 8.65. Found: C, 70.61; H, 8.66.

***rel*-(2*R*,3*R*)-4-[(*tert*-Butyldimethylsilyl)oxy]-3-(benzyloxy)-2-isopropenylbutyl Phenyl Sulfone (A8).** To a stirred, cooled (0 °C) solution of 5.08 g (25 mmol) of 85% *m*-chloroperoxybenzoic acid in 125 mL of CH_2Cl_2 was added 5.3 g (12 mmol) of sulfide A7 in 5 mL of CH_2Cl_2. The resulting solution was stirred for 1 h, and the white suspension was diluted with 300 mL of CH_2Cl_2, washed with aqueous $Na_2S_2O_3$, $NaHCO_3$, water, and brine, and dried briefly over $MgSO_4$. The solvent was removed under reduced pressure to give 4.73 g (83%) of sulfone A8 as a pale yellow viscous oil: ^1H NMR (400 MHz) δ 0.04 (s, $-Si(CH_3)_2-$), 0.87 (s, $-SiC(CH_3)_3$), 1.69 (s, isopropenyl CH_3), 2.98 (m, C-2 H), 3.69 (m, C-3 H), 4.59 (ABq, $\Delta\nu$ = 74.16 Hz, J_{AB} = 12.4 Hz, $PhCH_2O-$), 4.74 (s, vinyl H), 4.83 (t, J = 1.6 Hz, vinyl H), 7.3 (br m, $PhCH_2-$aromatic H), 7.52 (t, J = 8.9 Hz, $PhSO_2-$aromatic H), 7.63, 7.88 (m, $PhSO_2-$aromatic H). Anal. Calcd for $C_{26}H_{38}O_4SSi$: C, 65.78; H, 8.07. Found: C, 65.78; H, 8.14.

***rel*-(2*R*,3*R*)-2-(Benzyloxy)-3-isopropenyl-4-(phenylsulfonyl)-1-butanol (A9).** To a stirred solution of 2.85 g (6.00 mmol) of silyl ether A8 in 50 mL of THF was added 12 mL of 1.0 M tetrabutylammonium fluoride in THF. After 3 h, the solution was diluted with 250 mL of ether and washed 3 times with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with ether, the combined organic layers were washed with water and dried over $MgSO_4$, and the solvent was removed under reduced pressure to give 1.8 g (83%) of alcohol A9 as a white solid, mp 117–119 °C: ^1H NMR (400 MHz) δ 1.70 (s, isopropenyl CH_3), 1.83 (t, J = 7.2 Hz, −OH), 2.12 (m, C-3 H), 3.41 (AB of ABX, $\Delta\nu$ = 59.42 Hz, J_{AB} = 13.8 Hz, J_{AX} = 5.4 Hz, J_{BX} = 10.5 Hz, C-4 Hs), 3.58 (br m, C-1 H's), 3.78 (m, C-2 H), 4.57 (s, $PhCH_2O-$), 4.77, 4.88 (s, vinyl H's), 7.33 (br m, $PhCH_2-$aromatic H), 7.55 (t, J = 8.4 Hz, $PhSO_2-$aromatic H, 2 H), 7.63 (t, J = 8.4 Hz, $PhSO_2-$aromatic H, 1 H), 7.88 (d, J = 8.4 Hz, $PhSO_2-$aromatic H, 2 H); ^{13}C NMR (20 MHz) δ 21.36; 42.27, 55.25, 62.01, 72.22, 79.93, 115.06, 127.57, 127.90, 128.27, 129.00, 133.48, 137.85, 139.50, 141.62. Anal. Calcd for $C_{20}H_{24}O_4S$: C, 66.64; H, 6.71. Found: C, 66.71; H, 6.72.

***rel*-(2*R*,3*R*)-2-(Benzyloxy)-3-isopropenyl-4-(phenylsulfonyl)butanal (A10).** The procedure of Herscovici and Antonakis[25] was modified. To a stirred, cooled (0 °C) suspension of 190 mg (0.50 mmol) of pyridinium dichromate, and 250 mg of 3-Å molecular sieves in 2 mL of CH_2Cl_2 was added 100 mg (0.27 mmol) of alcohol A9. The resulting suspension was allowed to stir for 2 h whereupon 25 mL of ether was added. The black suspension was filtered through a pad of Florisil, the filtrate was exhaustively washed with ether, the organic solution was diluted with an equal volume of benzene, and the solvent was removed under reduced pressure to give 76 mg (79%) of aldehyde A10 as a pale yellow, sweet-smelling oil. This oil was used immediately without further purification: ^1H NMR (400 MHz) δ 1.64 (s, isopropenyl CH_3), 3.26 (m, C-2 allylic H), 3.34 (AB of ABX, $\Delta\nu$ = 143.72 Hz, J_{AB} = 14.13 Hz, J_{AX} = 7.69 Hz, J_{BX} = 5.08 Hz, $-CH_2SO_2Ph$), 4.22 (d, J = 4.33 Hz, C-2 H), 4.62 (ABq, $\Delta\nu$ = 91.96 Hz, J_{AB} = 11.42 Hz, $PhCH_2O-$), 4.83 (m, vinyl H), 7.35 (br s, $PhCH_2-$aromatic H), 7.5 (t, J = 7.24 Hz, $PhSO_2-$aromatic H, 2 H's), 7.66 (t, J = 7.20 Hz, $PhSO_2-$aromatic H, 1 H), 7.87 (d, J

(25) Herscovici, J.; Antonakis, K. *J. Chem. Soc., Chem. Commun.* **1980**, 561.

= 8.31 Hz, $PhSO_2$–aromatic H, 2 H), 9.57 (s, aldehyde H).

(2*E*,6*E*)-2,6-Dimethyl-8-chloro-2,6-octadienyl *tert*-Butyldimethylsilyl Ether (B3). The procedure of Collington and Meyers was employed.[26] To a vigorously stirred, cooled (0 °C) solution of 1.48 g (35 mmol) of anhydrous lithium chloride in 15 mL of DMF was slowly added a solution of 9.5 g (33.4 mmol) of 8-[(*tert*-butyldimethylsilyl)oxy]geraniol (B2)[14] in 4 mL of freshly distilled 2,6-lutidine. After 30 min, the formation of a thick white slurry was noted, and 2.7 mL (35 mmol) of methanesulfonyl chloride was added. The reaction was allowed to stir for 6 h whereupon it was quenched with 100 mL of water and diluted with 300 mL of ether. The organic layer was sequentially washed with water, saturated aqueous $CuSO_4$, and saturated aqueous NaCl, dried ($MgSO_4$), filtered, and concentrated under reduced pressure to afford 9.6 g (95%) of chloride B3 as a pale yellow oil: ^{1}H NMR (90 MHz) δ 0.04 (s, $-Si(CH_3)_2-$), 0.90 (s, $-Si(CH_3)_3$), 1.59 (, C-2 CH_3), 1.73 (s, C-6 CH_3), 2.10 (br s, C-4 and C-5 allyl H's), 3.98 (s, C-3 H), 4.06 (d, *J* = 8.9 Hz, C-8 H), 5.11–5.50 (br m, C-3 and C-7 vinyl H's).

(2*E*,6*E*)-2,6-Dimethyl-2,6,9-decatrienyl *tert*-Butyldimethylsilyl Ether (B4). To a stirred, cooled (−78 °C) suspension of 3.8 g (20 mmol) of copper(I) iodide in 100 mL of THF was slowly added 108 mL of 0.7 M vinylmagnesium bromide in THF. The yellow tan slurry was allowed to stir for 20 min and was subsequently transferred to a −23 °C bath and vigorously stirred for 35 min whereupon the gradual formation of a dark olive green color was noted. A solution of 9.5 g (33.4 mmol) of chloride B3 in 3 mL of THF was added dropwise, and the resulting solution was allowed to stir for 6 h whereupon it was diluted with 400 mL of ether, sequentially washed with water, 3% aqueous NH_4OH, saturated aqueous $CuSO_4$, and saturated aqueous NaCl, dried briefly over $MgSO_4$, filtered, concentrated, and purified by column chromatography on silica gel (hexane) to afford 7.6 g (77%) of triene B4 as a yellow oil: ^{1}H NMR (90 MHz) δ 0.07 (s, $-Si(CH_3)_2-$), 0.93 (s, $SiC(CH_3)_3$), 1.62 (s, C-2 and C-6 CH_3's), 2.07 (br s, C-4 and C-5 allylic H's), 2.76 (t, *J* = 7.6 Hz, C-8 H), 4.00 (s, C-1 H), 4.76–5.42 (br m, C-3, C-7, C-10 vinyl H's), 4.59–5.97 (br m, C-9 vinyl H).

(4*E*,8*E*)-5,9-Dimethyl-10-[(*tert*-butyldimethylsilyl)oxy]-4,8-decadien-1-ol (B5). The procedure of Brown was modified.[27] To a stirred, cooled, (−10 °C) freshly prepared solution of 46 mL of 1.2 M disiamylborane in THF was slowly added 7.80 g (26.45 mmol) of triene B4 in 6 mL of THF. The resulting yellow solution was vigorously stirred for 5.5 h and was carefully quenched by the sequential addition of 18 mL of water, 18 mL of 3 M aqueous NaOH, and 18 mL of 30% aqueous hydrogen peroxide. The biphasic solution was stirred for 18 h, diluted with 500 mL of ether, washed three times with water, dried briefly over $MgSO_4$, filtered, concentrated, and purified by column chromatography on silica gel (5:95 ether–hexane) to afford 6.83 g (83%) of alcohol B5 as a clear oil: ^{1}H NMR (90 MHz) δ 0.04 (s, $-Si(CH_3)_2-$), 0.89 (s, $SiC(CH_3)_3$), 1.60 (s, C-5 and C-9 vinyl CH_3's), 2.07 (m, C-3, C-7 allylic H's), 3.62 (t, *J* = 7.6 Hz, C-1 H), 3.99 (s, C-10 H), 5.13 (t, *J* = 7.5 Hz, C-4 vinyl H), 5.37 (m, C-8 vinyl H); IR (film) 3340, 2940, 2910, 2845, 1475, 1460, 1260, 1115, 1070, 840, 775 cm^{-1}. Anal. Calcd for $C_{18}H_{36}O_2Si$: C, 69.17; H, 11.63. Found: C, 69.26; H, 11.69.

(2*E*,6*E*)-2,6-Dimethyl-10-iodo-2,6-decadienyl *tert*-Butyldimethylsilyl Ether (B6). The procedure of Corey was modified.[15] To a stirred, cooled (0 °C) solution of 4.80 g (15.35 mmol) of alcohol A5, 5.25 g (20 mmol) of recrystallized triphenylphosphine, and 1.45 g (21 mmol) of imidazole in 15 mL of acetonitrile and 25 mL of ether was slowly added 5.6 g (22 mmol) of iodine resulting in a pale yellow suspension. After being stirred for 45 min, the reaction mixture was diluted with 300 mL of ether and sequentially washed with saturated aqueous $Na_2S_2O_3$, saturated aqueous $CuSO_4$, and water. The organic layer was dried briefly over $MgSO_4$, filtered, and concentrated to give 5.9 g (91%) of iodide B6 as a yellow oil which was used immediately without further purification: ^{1}H NMR (90 MHz) δ 0.04 (s, $-Si(CH_3)_2-$), 0.87 (s, $-SiC(CH_3)_3$), 1.63 (s, C-2 and C-6 CH_3s), 2.05 (m, C-4, C-5, and C-8 allylic H's), 3.56 (t, *J* = 7.5 Hz, C-10 H), 4.00 (s, C-1 H), 5.12–5.26 (br m, C-3 and C-7 vinyl H's); IR (film) 2930, 2845, 1665, 1475, 1460, 1390, 1360, 1260, 1110, 1065, 840, 780 cm^{-1}.

[(4*E*,8*E*)-5,9-Dimethyl-10-[(*tert*-butyldimethylsilyl)oxy]-4,8-decadienyl]triphenylphosphonium Iodide (B7). To a stirred solution of 1.0 g (2.35 mmol) of crude iodide B6 in 3 mL of benzene was added 685 mg (2.60 mmol) of freshly recrystallized triphenylphosphine. The resulting solution was heated at reflux for 24 h whereupon the contents of the flask solidified. The crude solid was dissolved in CH_2Cl_2 and transferred to a 50-mL round-bottom flask, and the solvents were removed under reduced pressure. The resulting semisolid was carefully treated with anhydrous ether until precipitation occurred, and the crystals were collected by vacuum filtration on a sintered glass funnel affording 1.5 g (94%) of phosphonium salt as a white hygroscopic solid: ^{1}H NMR (400 MHz) δ 0.04 (s, $-Si(CH_3)_2-$), 0.88 (s, $-SiC(CH_3)_3$), 1.56, 1.58 (s, vinyl CH_3's), 1.68 (m, C-2 H); 1.97 (t, *J* = 7.0 Hz, C-6 H), 2.03 (m, C-3 allylic H), 2.34 (q, *J* = 7.0 Hz, C-7 H); 3.63 (m, C-1 H), 3.95 (s, C-10 H), 5.00 (t, *J* = 7.0 Hz, vinyl H), 5.31 (t, *J* = 7.0 Hz, vinyl H); 7.66–7.87 (m, aromatic H's).

***rel*-(2*S*,3*R*)-(4*E*,8*E*,12*E*)-2-Isopropenyl-3-(benzyloxy)-5-carbomethoxy-9,13-dimethyl-14-[(*tert*-butyldimethylsilyl)oxy]-4,8,12-tetradecatrienyl Phenyl Sulfone (B9).** To a stirred, cooled (−78 °C) solution of 2.1 g (3.0 mmol) of phosphonium salt B7 in 10 mL of THF was slowly added 9.2 mL of 0.65 M potassium hexamethyldisilazide in toluene. The resulting red-orange solution was allowed to stir for 1.5 h whereupon 240 μl (3.2 mmol) of methyl chloroformate was added. After 30 min, the cooling bath was removed and the solution was allowed to stir for an additional 1.5 h. To this yellow-orange solution was added 698 mg (ca. 1.95 mmol) of freshly prepared crude aldehyde A10 in 2 mL of THF. The resulting mixture was allowed to stir for 32 h, diluted with ether, and washed sequentially with a saturated solution of NH_4Cl followed by water. The organic layer was dried over $MgSO_4$, filtered, concentrated, and purified by column chromatography on silica gel (1:9 ether–hexane) to give 542 mg (41%) of ester B9 as a colorless oil: ^{1}H NMR (400 MHz) δ 0.07 (s, $-Si(CH_3)_2-$), 0.91 (s, $-SiC(CH_3)_3$), 1.615 (s, C-9 CH_3), 1.617 (s, C-13 CH_3), 1.68 (s, isopropenyl CH_3), 2.02 (m, C-10 allylic H), 2.10 (br m, C-7 and C-11 allylic H's), 2.32 (t, *J* = 7.8 Hz, C-6 allylic H), 2.90 (m, C-2 allylic H), 3.45 (AB of ABX, Δν = 131.8 Hz, J_{AB} = 13.4 Hz, J_{AX} = 7.3 Hz, J_{BX} = 8.6 Hz, C-1 H's), 3.76 (s, CH_3CO_2-), 4.01 (s, C-14 H), 4.36 (ABq, Δν = 103.7 Hz, J_{AB} = 12.2 Hz, $PhCH_2O-$), 4.42 (dd, *J* = 6.0, 1.0 Hz, C-3 H), 4.74, 4.86 (s, isopropenyl vinyl H's), 5.16 (t, *J* = 7.9 Hz, C-8 H), 5.38 (t, *J* = 7.9 Hz, C-12 H), 6.49 (d, *J* = 10.7 Hz, C-4 H), 7.22–7.36 (br m, $PhCH_2O-$), 7.55 (t, *J* = 7.4 Hz, $PhSO_2-$), 7.63 (t, *J* = 6.2 Hz, $PhSO_2-$), 7.88 (d, *J* = 9.8 Hz, $PhSO_2-$). Anal. Calcd for $C_{40}H_{58}O_6SSi$: C, 69.12; H, 8.41; S, 4.61. Found: C, 69.21; H, 8.43; S, 4.66.

***rel*-(2*S*,3*R*)-(4*E*,8*E*,12*E*)-2-Isopropenyl-3-(benzyloxy)-5-(hydroxymethyl)-9,13-dimethyl-14-[(*tert*-butyldimethylsilyl)oxy]-4,8,12-tetradecatrienyl Phenyl Sulfone (B10).** To a stirred, cooled (−78 °C) solution of 102 mg (0.14 mmol) of ester B9 in 700 μl of THF was slowly added 280 μL of 1.0 M DIBAH in CH_2Cl_2. The resulting solution was allowed to stir for 40 min, diluted with ether, and quenched with a saturated solution of sodium potassium tartrate. The organic layer was separated and the aqueous layer was extracted once with ether. The combined organic layers were dried briefly over $MgSO_4$, filtered, concentrated, and passed through a small plug of silica gel with ether to give 91 mg (94%) of a viscous colorless oil: ^{1}H NMR (400 MHz) δ 0.04 (s, $-Si(CH_3)_2-$), 0.89 (s, $-SiC(CH_3)_3$), 1.60 (s, C-9 and C-13 vinyl CH_3s), 1.64 (s, isopropenyl CH_3), 2.01–2.17 (br m, C-6, C-10, C-11 allylic H's), 2.86 (m, C-2 H); 3.41 (AB of ABX, Δν = 89.6 Hz, J_{AB} = 13.2 Hz, J_{AX} = 6.0 Hz, J_{BX} = 7.2 Hz, C-1 Hs); 4.01 (s, C-14 H), 4.07 (s, $-CH_2OH$), 4.33 (ABq, Δν = 101.3 Hz, J_{AB} = 12.0 Hz, $PhCH_2O-$), 4.26 (dd, *J* = 6.0, 10.8 Hz, C-3 H), 4.71, 4.82 (s, isopropenyl vinyl H's), 5.11 (br m, C-8 vinyl H), 5.29 (d, *J* = 10.8 Hz, C-4 vinyl H), 5.37 (t, *J* = 6.7 Hz, C-12 vinyl H), 7.20–7.32 (br m, $PhCH_2O-$), 7.53 (t, *J* = 6.0 Hz, $PhSO_2-$), 7.64 (m, $PhSO_2-$), 7.87 (d, *J* = 7.2 Hz, $PhSO_2-$). Anal. Calcd for $C_{39}H_{58}O_5SSi$: C, 70.22; H, 8.76; S, 4.80. Found: C, 70.07; H, 8.82; S, 4.72.

***rel*-(12*R*,13*S*)-(2*E*,6*E*,10*E*)-2,6-Dimethyl-10-[(benzyloxy)methyl]-12-(benzyloxy)-13-isopropenyl-14-(phenylsulfonyl)-2,6,10-tetradecatrien-1-ol (B12).** To a stirred, cooled (−78 °C) solution of 770 mg (1.15 mmol) of alcohol B10 and 3 mg

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of 1,10-phenanthroline in 3 mL of THF was slowly added 670 μL of 1.78 M *n*-butyllithium in hexane resulting in a red-brown solution. This mixture was treated with 435 μL (2.5 mmol) of HMPA followed by 155 μL (1.3 mmol) of benzyl bromide, the bath was removed, and the mixture was allowed to warm to room temperature whereupon the deep red solution faded to pale yellow. This solution was stirred for 1 h and subsequently treated with 3.5 mL of 1.0 M tetra-*n*-butylammonium fluoride in THF. This mixture was stirred for 2 h and partitioned between ether and water. The organic layer was washed with water, dried ($MgSO_4$), filtered, and concentrated under reduced pressure, and purified by column chromatography on silica gel affording 657 mg (89%) of alcohol B12 as a viscous clear oil: ^1H NMR (400 MHz) δ 1.56, 1.63 (s, vinyl CH_3s), 1.67 (s, isopropenyl CH_3), 2.01 (t, J = 9.0 Hz, allylic H's), 2.11 (br s, allylic H's), 2.85 (q, J = 9.8 Hz, C-13 H), 3.40 (AB of ABX, $\Delta\nu$ = 116.4 Hz, J_{AB} = 16.3 Hz, J_{AX} = 6.3 Hz, J_{BX} = 9.0 Hz, C-14 H's), 3.95 (s, C-1 H), 4.32 (dd, J = 6.2, 11.2 Hz, C-12 H), 4.34 (ABq, $\Delta\nu$ = 118.7 Hz, J_{AB} = 11.8 Hz, C-12 $PhCH_2O$–), 4.44 (s, $-CH_2OCH_2Ph$), 4.74, 4.83 (s, isopropenyl vinyl H's), 5.11 (m, vinyl H), 5.31 (d, J = 10.1 Hz, C-11 H), 5.36 (t, J = 6.2 Hz, vinyl H); 7.21–7.37 (br m, $PhCH_2O$–), 7.48 (t, J = 6.2 Hz, $PhSO_2$–), 7.59 (m, $PhSO_2$–), 7.86 (d, J = 6.8 Hz, $PhSO_2$–). Anal. Calcd for $C_{40}H_{50}O_5S$: C, 74.73; H, 7.84; S, 4.99. Found: C, 74.54; H, 7.86; S, 4.91.

***rel*-(1*R*,2*S*)-(3*E*,7*E*,11*E*)-1-Isopropenyl-2-(benzyloxy)-4-[(benzyloxy)methyl]-8,12-dimethyl-14-(phenylsulfonyl)-3,7,11-cyclotetradecatriene (B15).** To a stirred, cooled (0 °C) solution of 152 mg (0.23 mmol) of alcohol B12, 120 mg (0.45 mmol) of freshly recrystallized triphenylphosphine and 35 mg (0.51 mol) of freshly recrystallized imidazole in 0.4 mL of acetonitrile and 0.6 mL of ether was added in a portionwise fashion 140 mg (0.55 mol) of iodine resulting in a brown-black slurry. This mixture was stirred for 30 min, diluted with ether, and sequentially washed with saturated aqueous $Na_2S_2O_3$, saturated aqueous $CuSO_4$, and water. The organic layer was briefly dried over $MgSO_4$, filtered, and carefully concentrated under reduced pressure affording a mixture of crystalline triphenylphosphine oxide and iodide B14 as a pale yellow oil. The entire crude mixture was taken up in 6.8 mL of THF and added over 9.3 h via syringe pump to a stirred, cooled (0 °C) solution of 60 mg (0.23 mol) of 18-crown-6, and 0.78 mL of 0.65 M potassium hexamethyldisilyazide in toluene diluted to 12 mL with THF. The solution was stirred for 10 h following this addition and partitioned between ether and water. The organic layer was dried ($MgSO_4$), filtered, concentrated, and purified via column chromatography on silica gel (1:9 ether–hexane) affording 78 mg (53%) of cyclotetradecatriene B15 as a viscous pale yellow oil: ^1H NMR (400 MHz) δ 1.49, 1.60 (s, vinyl CH_3's), 1.81 (s, isopropenyl CH_3), 2.04–2.12, 2.51–2.64 (m, allylic H's), 4.84, 5.06 (s, isopropenyl vinyl H's), 7.20–7.61 (br m, aromatic H's), 7.83 (m, $PhSO_2$–).

***rel*-(1*R*,2*S*)-(3*R*,7*E*,11*E*)-1-Isopropenyl-4-(hydroxymethyl)-8,12-dimethyl-3,7,11-cyclotetradecatrien-2-ol (7-(8)-Desoxyasperdiol) (B16).** To a stirred solution of 68 mg (0.10 mmol) of sulfone B15 in ca. 8 mL of refluxing ammonia and 300 μL of THF was added 13 mg (0.6 mg-atom) of sodium. The solution immediately became dark blue and was subsequently stirred for 1 h. The reaction was quenched via the addition of solid NH_4Cl, and the ammonia was allowed to evaporate giving a slurry which was diluted with ether and partitioned between ether and water. The organic layer was dried briefly over $MgSO_4$, filtered, concentrated under reduced pressure and purified via column chromatography on silica gel (1:1 ether–hexane) to afford 22 mg (71%) of diol B16 as a viscous clear oil which crystallized on standing, mp 97–98.5 °C: ^1H NMR (400 MHz) δ 1.55 (s, C-8 CH_3), 1.62 (s, C-12 CH_3), 1.65 (m, C-14 H), 1.78 (s, isopropenyl CH_3), 1.84–2.39 (br m, allylic Hs), 4.10 (ABq, $\Delta\nu$ = 29.2 Hz, J_{AB} = 13.0 Hz, CH_2OH), 4.36 (dd, J = 3.8, 8.7 Hz, C-3 H), 4.75, 4.96 (br s, isopropenyl vinyl H's), 5.03 (br m, C-7 and C-11 vinyl H's), 5.54 (d, J = 8.7 Hz, C-3 H). Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 78.79; H, 10.66.

A mixture of the above sample and an authentic sample, mp 96.5–98 °C, provided by Professor Kato exhibited mp 96.5–97.5 °C.

***rel*-(1*R*,2*S*)-(3*E*,7*E*,11*E*)-1-Isopropenyl-4-[(benzoyloxy)methyl]-8,12-dimethyl-3,7,11-cyclotetradecatrien-2-ol (B17).** To a stirred solution of 10 mg (0.033 mmol) of diol B16, 5 mg of 4-(*N*,*N*-dimethylamino)pyridine, and 5 μL (0.04 mmol) of triethylamine in 300 μL of CH_2Cl_2 was added 4 μL (0.033 mmol) of benzoyl chloride. The resulting solution was stirred for 6 h, and the crude product was purified by column chromatography on silica gel (1:5 ether–hexane) to afford 9 mg (67%) of benzoate B17 as a clear oil: ^1H NMR (200 MHz) δ 1.56 (s, C-8 CH_3), 1.62 (s, C-12 CH_3), 1.67 (m, C-14 H), 1.79 (s, isopropenyl CH_3), 1.86–2.41 (br m, allylic H's), 4.40 (m, C-2 H), 4.76 (br s, isopropenyl vinyl H), 4.79 (ABq, $\Delta\nu$ = 35.30 Hz, J_{AB} = 14.28 Hz, $-CH_2OCOPh$), 4.95 (br s, isopropenyl vinyl H), 5.06 (m, C-7 and C-11 vinyl H's), 5.66 (d, J = 9.4 Hz, C-2 H), 7.4 (t, J = 6.7 Hz, $PhCO_2$–), 7.54 (m, $PhCO_2$–), 8.02 (d, J = 9.6 Hz, $PhCO_2$–).

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The Synthesis of Cembranolide Precursors via Addition of Allylstannanes to Conjugated Aldehydes

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The Lewis acid promoted addition of functionalized allylstannanes **A9**, **C10**, and **C11** to a variety of conjugated aldehydes was examined as a possible route to acyclic precursors of macrocyclic diterpenoids. Additions to crotonaldehyde proceeded as expected, giving the erythro adduct **1** with BF_3 catalysis and the threo adduct **2** with a premixed $TiCl_4$–stannane complex at −78 °C. Attempted additions of allylstannanes to the β-substituted crotonaldehydes **B5** and geranial (**B6**), on the other hand, failed completely, giving either recovered starting material at low temperature (−78 to −30 °C) or extensive decomposition at higher temperatures. The acetylenic aldehyde **A3** and the β-iodo-substituted crotonaldehyde **A7**, however, showed normal reactivity with allylstannanes affording adducts **3**–**14**. The steric course of these reactions was confirmed through conversion of the adducts **D3** and **D4** to the δ-lactones **D9** and **D10** via rhodium-catalyzed carbonylation and oxidation. These lactones showed ^1H NMR coupling patterns consistent with the assigned stereochemistry.

The coupling of allylstannanes with aldehydes has received considerable attention recently, much of which has focused on stereochemical and mechanistic aspects of the reaction.[1] Yamamoto's pioneering work showed that the

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