Synthesis of Discodermolide Subunits by S_E2' Addition of Nonracemic Allenylstannanes to Aldehydes

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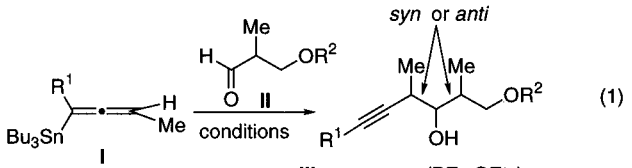
Three subunits, **15**, **29**, and **34**, of the immunosuppressant discodermolide were prepared starting from (*S*)-3-[(*tert*-butyldimethylsilyl)oxy]-2-methylpropanal ((*S*)-**1**) and the enantioenriched allenylstannanes (*P*)-**2a**, (*P*)-**2b**, and (*P*)-**31**. The route to **15** involved BF_3-promoted addition of stannane (*P*)-**2a** to aldehyde (*S*)-**1** which afforded the *syn*,*syn*-homopropargylic alcohol adduct **3** in 97% yield. The derived *p*-methoxybenzylidene acetal **5** was treated with Red-Al to effect cleavage of the pivalate and reduction of the double bond leading to the (*E*)-allylic alcohol **6**. Sharpless epoxidation and subsequent addition of $Me_2CuCNLi_2$ yielded the syn,syn,syn,anti stereopentad, diol **8**. Protection of the secondary alcohol and oxidation of the primary gave aldehyde **12**, which was treated with the α-bromo allylsilane **13** and $CrCl_2$, followed by NaH to effect elimination to the diene **15**. A similar sequence was employed to prepare aldehyde **29**. In this case aldehyde (*S*)-**1** was converted to the *anti*,*syn*-homopropargylic alcohol **20** by treatment with the allenyl indium reagent formed in situ from allenylstannane (*P*)-**2b** and $InBr_3$. Epoxy alcohol **24**, prepared from alcohol **20** by the above-described sequence, was reduced with Red-Al to afford diol **25**. Protection of the secondary alcohol and oxidation of the primary completed the synthesis of **29**. The *anti*,*syn*-homopropargylic alcohol **32** was obtained through addition of the allenic indium reagent, from allenylstannane (*P*)-**31**, to aldehyde (*S*)-**1**. Protection of the derived diol **33** as the *p*-methoxybenzylidene acetal afforded the third subunit, acetylene **34**. Addition of the lithio derivative of **34** to aldehyde **29** gave alcohol **35** with the carbinyl stereochemistry needed for C7 of discodermolide as the major product.

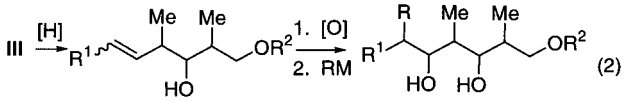
Carbon−carbon bond-forming reactions that create two contiguous stereocenters with predictable and high diastereo- and enantioselectivity have found extensive use in synthetic approaches to polypropionate natural products. Among the most effective are (1) the aldol condensation,[1] (2) additions of chiral allylboronates and boranes to aldehydes,[2] (3) the Ireland−Claisen rearrangement,[3] and (4) the Diels−Alder reaction.[4] We recently described a variant on the second of these in which a chiral allenylstannane, such as **I**, is added to a chiral α-methyl-β-oxygenated aldehyde, such as **II**, in the presence of various Lewis acid promoters to afford any of the four stereotriads **IIIa**−**d** with excellent diastereo- and enantioselectivity, depending upon the reaction conditions (eq 1).[5]



(1)

IIIa syn, syn (BF_3•OEt_2)
IIIb syn, anti ($MgBr_2$)
IIIc anti, anti ($SnCl_4$)
IIId anti, syn ($InBr_3$)

We felt that the foregoing methodology might offer certain advantages over the previous ones, if the alkynyl functionality could be incorporated into the synthetic target as a double bond, as in **IV** or **V**, or for extension of the stereotriad to a stereotetrad, as in **VI**, or a stereopentad, as in **VII** (eq 2). A form of this latter strategy was effectively employed by Kishi in his pioneering studies on polypropionate synthesis.[6]



(2)

IV *(Z)* double bond
V *(E)* double bond
VI R = H
VII R = Me

The goal of the present investigation was to assemble viable subunit precursors of the polypropionate immunosuppresive agent discodermolide.[7] This highly active and extremely scarce natural product has been the target of numerous synthetic studies including several remarkably successful total syntheses.[8−10] The approach of Schreiber et al.[8] utilized chiral boronate additions[2] to prepare key stereotriad segments, that of Smith and co-

(1) Cf. Evans, D. A.; Miller, S. J.; Ennis, M. D.; Ornstien, P. L. *J. Org. Chem.* **1992**, *57*, 1062.
(2) Cf. Roush, W. R.; Koyama, K.; Curtin, M. L.; Moriarity, K. J. *J. Am. Chem. Soc.* **1996**, *118*, 7502.
(3) Cf. Ireland, R. E.; Gleason, J. L.; Gegnas, L. D.; Highsmith, T. K. *J. Org. Chem.* **1996**, *61*, 6856.
(4) Cf. Danishefsky, S. J.; Selnick, H. G.; Zelle, R. E.; DeNinno, M. P. *J. Am. Chem. Soc.* **1988**, *110*, 4368.
(5) (a) Marshall, J. A.; Perkins, J. F.; Wolf, M. A. *J. Org. Chem.* **1995**, *60*, 5556. (b) Marshall, J. A.; Palovich, M. R. *J. Org. Chem.* **1997**, *62*, 6001.
(6) Cf. Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873.
(7) Gunasekera, S. P.; Gunasekera, M.; Longley, R. E. *J. Org. Chem.* **1990**, *55*, 4912: **1991**, *56*, 1346.
(8) Hung, D.; Nerenberg, J. B.; Schreiber, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 11054.
(9) Smith, A. B., III; Qui, Y.; Jones, D. R.; Kobayashi, K. *J. Am. Chem. Soc.* **1995**, *117*, 12011.
(10) Harried, S. S.; Yang, G.; Strawn, M.; Myles, D. C. *J. Org. Chem.* **1997**, *62*, 6098.

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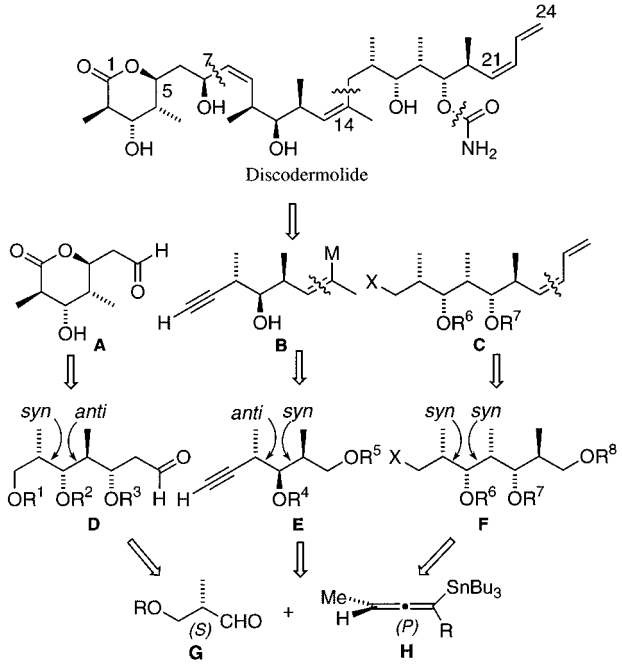
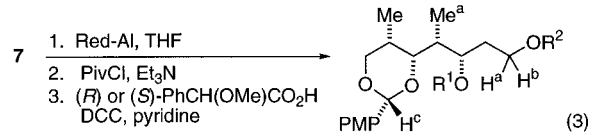


Figure 1. Assemblage of discodermolide subunits.

workers[9] employed Evans chiral oxazolidinone aldol condensations, and Myles et al.[10] effected chelation-controlled alkylation and reduction to install key stereocenters.[1] We hoped to synthesize the three fragments **D**−**F** from aldehyde **G** and the two (*P*)-allenylstannanes **H** (R = CH_2OPiv or CH_2OAc and R = H) to test the feasibility of the chiral allenyltin approach to moderately complex polypropionate (discodermolide) precursors (Figure 1).

Our initial efforts were directed toward subunit **F** which contains a syn,syn stereotriad array. Accordingly we employed the allenylstannane (*P*)-**2a**[11] and the TBS-protected aldehyde (*S*)-**1** in an S_E2' addition promoted by $BF_3{\cdot}OEt_2$. The syn,syn adduct **3** was obtained in 97% yield with less than 5% of other diastereomeric adducts (Scheme 1). Cleavage of the TBS protecting group with TBAF afforded the diol **4** in 94% yield. This was protected as the *p*-methoxybenzylidene acetal in 88% yield by treatment with *p*-anisaldehyde dimethyl acetal in benzene containing (±)-10-camphorsulfonic acid as a catalyst.[12] Extended treatment of the resulting propargylic pivalate acetal **5** with Red-Al in THF effected cleavage of the ester and ensuing reduction of the triple bond to afford the crystalline (*E*)-allylic alcohol **6** in 89% yield.

Asymmetric epoxidation of **6** by the Sharpless protocol with D-(−)-diisopropyl tartrate as the chiral ligand afforded the crystalline epoxide **7** in 85% yield.[13] The epoxide stereochemistry can be assigned on the basis of the Sharpless empirical rule. Additional support was secured by reduction with Red-Al and selective protection of the primary alcohol of the diol product **16** as the pivalate **17** (eq 3). The ^1H NMR spectra of the derived *O*-methylmandelates **18** and **19** confirmed the assumed (*S*) configuration of the carbinyl center.[14]



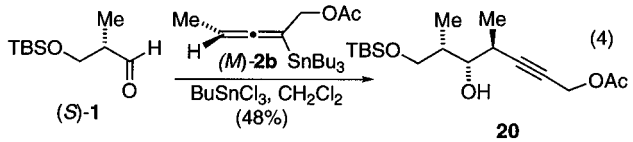
	H^a, H^b	Me^a	H^c, δ (ppm)
18	3.91	1.05	5.22
19	4.05	0.89	4.87

16 $R^1 = R^2 = H$
17 $R^1 = H$, R^2 = Piv
18 R^1 = (*R*)-PhCH(OMe)CO, R^2 = Piv
19 R^1 = (*S*)-PhCH(OMe)CO, R^2 = Piv

Treatment of epoxy alcohol **7** with lithium dimethylcyanocuprate in THF−ether led to the diol **8** in 94% yield. Conversion to the monoprotected alcohol **11** was accomplished by a three-step protection−deprotection sequence involving formation of the primary pivalate **9** (90%), silylation with TBSOTf (99%), and cleavage of pivalate **10** with Red-Al in THF (95%).

Further elaboration of the resulting alcohol **11** to diene **15** (subunit **C**) was achieved through oxidation with the Dess−Martin periodinane reagent[15] and treatment of aldehyde **12** with α-TMS allyl bromide (**13**)[16] and chromous chloride in THF.[17] The resulting mixture of adducts (presumed to be mainly **14**) was treated with NaH in THF to give the diene **15** in 80% overall yield. The stereochemistry of diene **15** was assigned on the basis of the observed 10.5 Hz coupling between the vinylic protons of the (*Z*)-double bond.

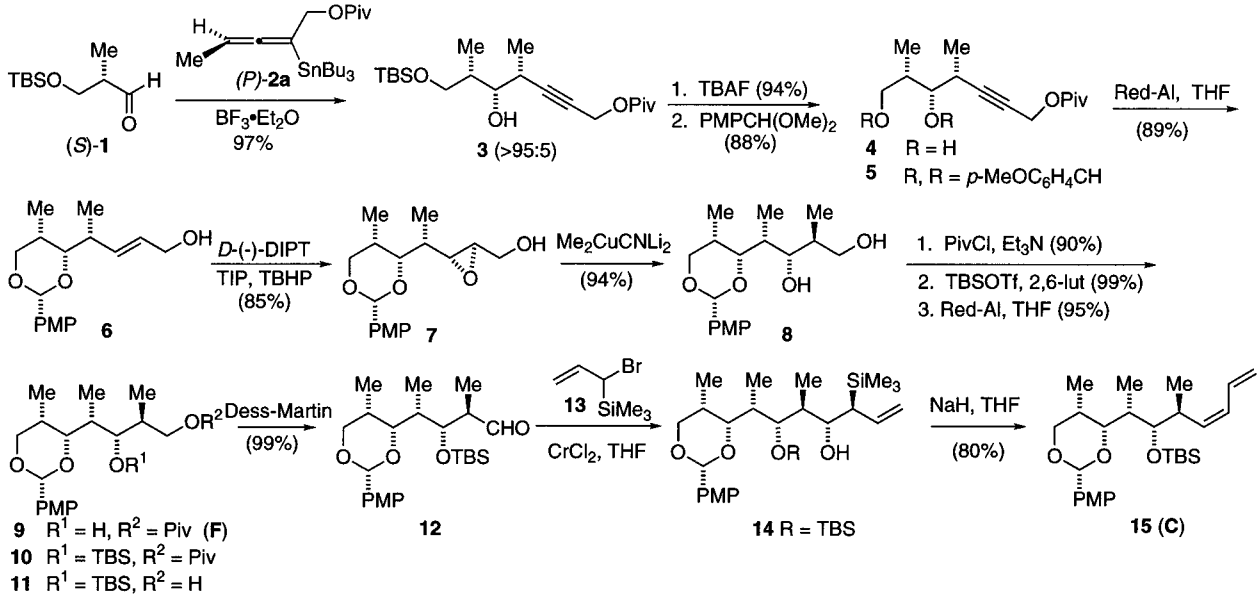
For the synthesis of subunit **D** (Scheme 2, **29**) we required the S_E2' addition of allenylstannane (*M*)-**2b** to aldehyde (*S*)-**1** to occur via a Cram, anti addition pathway. This could be achieved through use of $BuSnCl_3$ in CH_2Cl_2.[5] The adduct **20** was thereby obtained as a single isomer (eq 4). However, the low yield of this reaction, despite several efforts at optimization, prompted our search for a more efficient method.



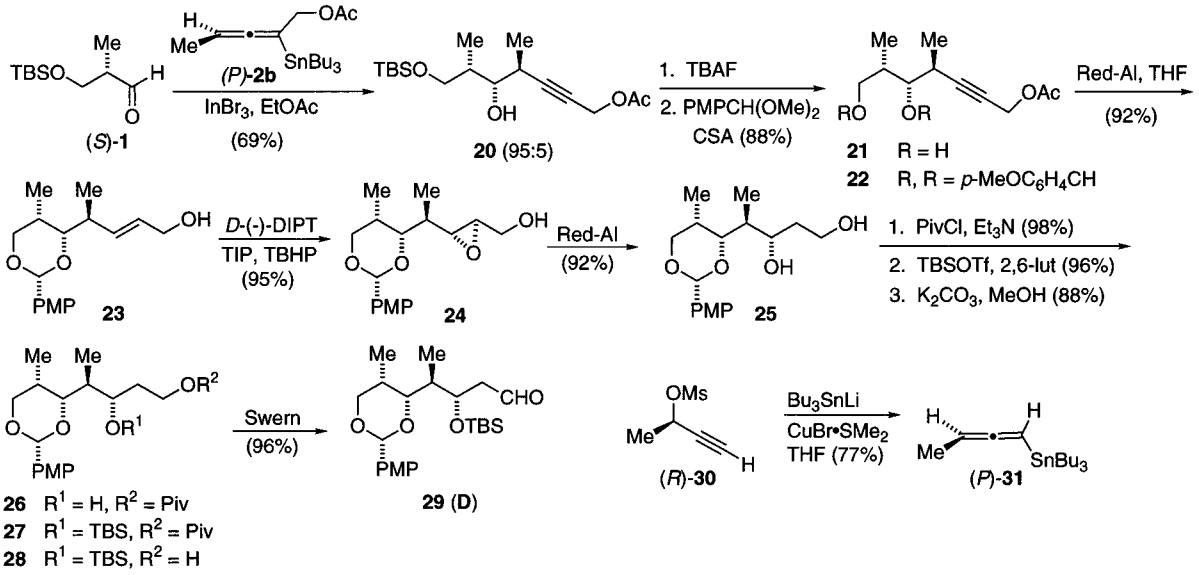
The foregoing addition has been shown to proceed by transmetalation of the stannane, leading to an intermediate propargylic butyldichlorostannane with inversion of configuration.[18] Subsequent isomerization of this intermediate to the corresponding allenyl derivative takes place with retention of stereochemistry (net inversion of allenyl configuration for the two-step process). This allenylstannane adds to aldehydes by a syn pathway to yield the anti adduct. Recently we found that allenylstannanes undergo transmetalation−isomerization

(11) Marshall, J. A.; Xie, S. *J. Org. Chem.* **1995**, *60*, 7230.
(12) The assignment of stereochemistry at the acetal center is based on molecular mechanics calculations. The program Macromodel V4.5 was employed for these calculations. Global minimum multiple conformer searching was achieved with the Monte Carlo subroutine in BATCHMIN through 500-step interations. For a description of the program, see: (a) Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caufield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440. (b) Chang, G.; Guida, W. C.; Still, W. C. *J. Am. Chem. Soc.* **1989**, *111*, 4379.
(13) Cf. Gao, Y.; Hanson, R. M.; Klundu, J. M.; Ko, S. Y.; Masamune, J.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765.
(14) Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. D. *J. Org. Chem.* **1986**, *51*, 2370.
(15) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4156. Ireland, R. E.; Lin, L. *J. Org. Chem.* **1993**, *58*, 2899.
(16) Andringa, H.; Keus-Kloos, Y. A.; Brandsma, L. *J. Organomet. Chem.* **1987**, *336*, C41.
(17) Hodgson, D. M.; Wells, C. *Tetrahedron Lett.* **1992**, *33*, 4761.
(18) Marshall, J. A.; Yu, R. H.; Perkins, J. F. *J. Org. Chem.* **1995**, *60*, 5550.

Scheme 1



Scheme 2



with $InCl_3$, $InBr_3$, or InI_3 by a process that gives an intermediate allenyl indium halide with overall retention of stereochemistry.[5b] Subsequent addition to achiral aldehydes gives rise to anti products enantiomeric to those formed via the allenyl $BuSnCl_2$ intermediate.

In fact, addition of allenylstannane (*P*)-**2b** to aldehyde (*S*)-**1** in the presence of $InBr_3$ afforded the anti,syn adduct **20** in 69% yield with less than 5% contamination by other stereoisomers (Scheme 2). Conversion to the cyclic anisylidene acetal **22**, and reduction as before, yielded the (*E*)-allylic alcohol **23**.[12] This alcohol upon Sharpless epoxidation,[13] as described for alcohol **6**, gave the epoxy alcohol **24** in 95% yield. Subsequent reduction with Red-Al provided diol **25** in 92% yield. The previously described three-step protection−deprotection sequence afforded alcohol **28**, a crystalline solid, in high overall yield. Swern oxidation of this alcohol,[19] with rapid addition of Et_3N to prevent cleavage of the acetal, efficiently produced aldehyde **29** (subunit **D**).

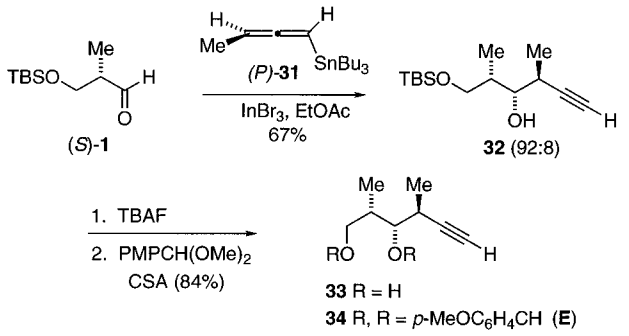
The requisite allenylstannane (*P*)-**31** for subunit **E** was prepared from the mesylate (*R*)-**30** of (*R*)-3-butyn-2-ol (97% ee)[20] by our previously described procedure. Addition of stannane (*P*)-**31** to aldehyde (*S*)-**1** by the $InBr_3$ protocol gave the adduct **32** in 67% yield as a 92:8 mixture of the anti,syn and (presumably) the anti,anti isomers (Scheme 3). Cleavage of the TBS ether with TBAF afforded diol **33** as a crystalline solid in 87% yield. The *p*-anisylidene acetal **34** (fragment **E**) was prepared in 96% yield.

We briefly examined the coupling of acetylene **34** with aldehyde **29** to evaluate the possible utility of these subunits in a projected synthesis of discodermolide. After several trials we found that a 5-fold excess of the acetylene, as its lithio derivative, in THF containing 3 molar equiv of LiBr afforded a 71:24 mixture of alcohol **35** and its epimer in 95% yield (Scheme 4). These epimers could be separated and the unreacted acetylene recovered through column chromatography. The stere-

(19) Omurka, K.; Swern D. *Tetrahedron* **1978**, *34*, 1651.

(20) Purchased from Fine Chemicals Inc., Saddlebrook, N.J.

Scheme 3



ochemistry at the newly formed carbinyl stereocenter of the major product was deduced through Lindlar hydrogenation and analysis of the ^{1}H NMR spectra of the (*R*)- and (*S*)-*O*-methylmandelates **37** and **38**.[14]

Although the final conversion of subunits **15**, **29**, and **34** to discodermolide must await future efforts and is by no means assured, the successful synthesis of these subunits demonstrates the feasibility of utilizing stereotriads derived from chiral allenylstannanes and aldehydes as precursors to stereochemically complex intermediates for the synthesis of polypropionate natural products. The methodology described here compares favorably with previous approaches to similar subunits.[8−10]

Experimental Section

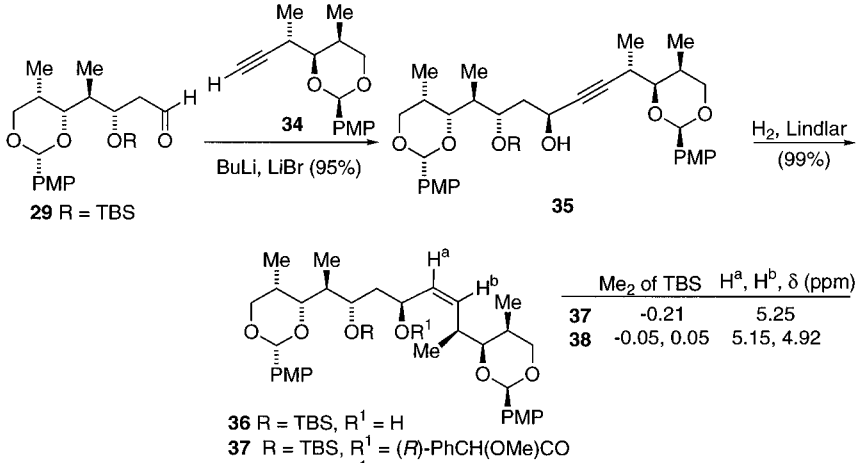
***syn,syn*-Propargylic Pivalate 3.** To a solution of 347 mg (0.76 mmol) of allenylstannane (*P*)-**2a** and 307 mg (1.5 mmol) of aldehyde (*S*)-**1** in 2 mL of CH_2Cl_2 was added 0.23 mL (1.87 mmol) of BF_3·OEt_2 at −78 °C. The resulting mixture was stirred at −78 °C for 5.5 h, quenched with saturated aqueous $NaHCO_3$, and extracted with ether. The extracts were washed with saturated aqueous NH_4Cl and brine. The aqueous layer was extracted with ether, and the combined extracts were dried over Na_2SO_4. Filtration and concentration followed by chromatography on silica gel (10:1 hexanes/EtOAc) provided 272 mg (97%) of alcohol **3** as a clear oil: $[\alpha]_D$ +1.0 (*c* 1.6, $CHCl_3$); IR (neat) 3506, 2930, 2240, 1735, 1139 cm^{-1}; ^{1}H NMR δ 4.62 (d, 2 H, J = 2.4 Hz), 3.84 (dd, 1 H, J = 9.9, 3.0 Hz), 3.71−3.65 (m, 2 H), 3.42 (br, 1 H), 2.52 (m, 1 H), 2.08 (m, 1 H), 1.26 (d, 3 H, J = 7.2 Hz), 1.19 (s, 9 H), 0.97 (d, 3 H, J = 6.9 Hz), 0.89 (s, 9 H), 0.06 (s, 6 H); ^{13}C NMR δ 178.24, 89.15, 78.73, 76.73, 69.83, 53.06, 39.19, 36.89, 30.94, 27.55, 26.32, 18.62, 18.02, 9.9, −5.12, −5.21.

***syn,syn*-*p*-Anisylidene Acetal 5.** To a solution of the alcohol **3** (5.19 g, 14.02 mmol) in THF (60 mL) was added TBAF (21 mL, 1 M in THF, 21.0 mmol) dropwise at 0 °C. After being stirred for 20 min, the mixture was poured into brine, extracted with EtOAc, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed (50% Et_2O−hexanes) to give the diol **4** as a colorless oil (3.40 g, 94%). This sample was dissolved in benzene (100 mL) and *p*-anisaldehyde dimethyl acetal (4.3 g, 23.83 mmol), and a catalytic amount of *dl*-camphorsulfonic acid (ca. 10 mg) was added. The mixture was refluxed with azeotropic removal of methanol for 2 h and then cooled to rt. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (elution with 5% Et_2O−hexane containing 1% Et_3N). Acetal **5** was obtained as a colorless oil (4.60 g, 88%): ^{1}H NMR ($CDCl_3$) 7.40 (d, J = 8.7, 2H), 6.88 (d, J = 8.7, 2H), 5.42 (s, 1H), 4.65 (d, J = 2.1, 2H), 4.05 (m, 2H), 3.80 (s, 3H), 3.66 (dd, J = 10, 2.1, 1H), 2.62 (m, 1H), 1.95 (m, 1H), 1.27 (d, J = 6.9, 3H), 1.22 (s, 9H), 1.18 (d, J = 6.9, 3H); ^{13}C NMR($CDCl_3$) 190.75, 177.71, 131.96, 127.25, 113.57, 101.56, 86.91, 82.68, 76.39, 73.77, 55.27, 52.45, 38.72, 30.57, 28.80, 27.05, 17.49, 11.12. Anal. Calcd for $C_{19}H_{24}O_5$: C, 70.56; H, 8.07. Found: C, 70.64; H, 8.12.

***syn,syn*-Allylic Alcohol 6.** To a solution of acetal **5** (3.2 g, ca. 8.5 mmol, contaminated with anisaldehyde) in THF (100 mL) was added dropwise Red-Al (19 mL, 65 wt % in toluene, 63 mmol) at 0 °C. The mixture was stirred at 0 °C for 24 h and then quenched carefully with saturated aqueous potassium sodium tartrate. After being warmed to rt and stirred for 1 h, the mixture was extracted with EtOAc. The extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was chromatographed on silica gel (elution with 35% Et_2O−hexanes, containing 1% Et_3N) to afford allylic alcohol **6** as a white solid (2.20 g, 89%): mp 78−79 °C; $[\alpha]^{20}_D$ = +11.5 (*c* 0.75, $CHCl_3$); ^{1}H NMR ($CDCl_3$) 7.42 (d, J = 8.7, 2H), 6.89 (d, J = 8.7, 2H), 5.81−5.72 (dt, J = 15.6, 5.7, 1H), 5.57−5.49 (dd, J = 15.6, 9, 1H), 5.44 (s, 1H), 4.13 (dd, J = 8.7, 6.0, 1H), 4.00 (m, 2H), 3.80 (s, 3H), 3.52 (dd, J = 10.2, 2.4, 1H), 2.42 (m, 1H), 1.62 (m, 1H), 1.32 (m, 1H), 1.17 (d, J = 6.9, 3H), 1.11 (d, J = 6.6, 3H); ^{13}C NMR($CDCl_3$) 159.85, 132.93, 131.60, 130.04, 127.27, 113.58, 101.75, 83.47, 74.00, 63.57, 55.30, 38.63, 30.53, 17.43, 11.13. Anal. Calcd for $C_{17}H_{24}O_4$: C, 69.84; H, 8.27. Found: C, 69.73; H, 8.25.

***syn,syn*-Epoxy Alcohol 7.** To the suspension of activated 4 Å MS (ca. 1 g) in dry CH_2Cl_2 (100 mL) was added D-(−)-DIPT (2.42 g, 10.35 mmol), followed by Ti(*i*-PrO)$_4$ (2.56 mL, 8.6 mmol) at −20 °C. The mixture was stirred at −20 °C for 10 min, and TBHP (2.7 mL, 5−6 M in decane, ca. 15 mmol) was added dropwise. The mixture was stirred at −20 °C for 30 min, and then allylic alcohol **6** (2.18 g, 7.47 mmol) in CH_2Cl_2 (10 mL) was added over 3 min. The mixture was stirred at −20 °C for 18 h, quenched with a minimum amount of water, diluted with EtOAc, warmed to rt, and filtered through a short pad of Celite. The filtrate was extracted with EtOAc. The extracts were dried ($MgSO_4$) and concentrated under reduced

Scheme 4



	Me_2 of TBS	H^a, H^b, δ (ppm)
37	-0.21	5.25
38	-0.05, 0.05	5.15, 4.92

pressure. The residue was chromatographed on silica gel (elution with 50% Et_2O−hexanes containing 1% Et_3N) to afford epoxide **7** as white solid (1.95 g, 85%): mp 62−63 °C; $[\alpha]^{20}_D$ +9.4 (*c* 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$) 7.41 (d, *J* = 8.4, 2H), 6.88 (d, *J* = 8.4, 2H), 5.47 (s, 1H), 4.06 (dd, *J* = 11.1, 2.4, 1H), 3.99 (dd, *J* = 11.1, 0.9, 1H), 3.85 (d, *J* = 12.3, 1H), 3.78 (s, 3H), 3.70 (dd, *J* = 10.2, 2.1, 1H), 3.60 (m, 1H), 3.09 (m, 1H), 2.81 (dd, *J* = 6.6, 2.4, 1H), 2.44 (br, 1H), 1.78 (m, 2H), 1.21 (d, *J* = 7.2, 3H), 1.07 (d, *J* = 6.6, 3H); ^{13}C NMR ($CDCl_3$) 159.76, 131.20, 127.14, 113.46, 101.87, 81.66, 73.64, 61.39, 57.66, 56.45, 55.17, 36.15, 30.60, 12.68, 11.65. Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84. Found: C, 66.31; H, 7.85.

***syn,syn,syn,anti*-Diol 8.** To a suspension of CuCN (1.85 g, 20.7 mmol) in THF (30 mL) was added MeLi (29.7 mL, 1.4 M, 41.6 mmol) over 20 min at −78 °C. Upon complete addition, the solution was allowed to warm to 0 °C and stirred for 1 h. The clear homogeneous solution was then cooled to −78 °C, and epoxide **7** (640 mg, 2.1 mmol) in THF (10 mL) was added dropwise over 5 min. This mixture was warmed to 0 °C and stirred for 24 h at which time the reaction was judged complete (TLC). The reaction mixture was quenched by pouring into aqueous NH_4Cl−NH_3·H_20 (9:1) (300 mL) along with 300 mL of Et_2O. The mixture was stirred vigorously at rt for 1 h whereupon the organic layer became clear. The organic layer was separated and washed with brine, and the aqueous layer was extracted with Et_2O. The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure to give the product as a white crystalline solid (631 mg, 94%). This material was used without further purification. Pure diol **8** could obtained as colorless crystals by recrystallization from hexanes−ether or chromatography on silica gel (elution with Et_2O−hexanes 2:1): $[\alpha]^{20}_D$ = +1.4 (*c* 1.85, $CHCl_3$); mp 134−135 °C; ^1H NMR ($CDCl_3$): 7.43 (d, *J* = 8.4, 2H), 6.89 (d, *J* = 8.4, 2H), 5.50 (s, 1H), 4.12 (dd, *J* = 10.8, 2.1, 1H), 4.02 (dd, *J* = 11.1, 1.2, 1H), 3.89 (dd, *J* = 9.6, 1.8, 1H), 3.85−3.75 (m, 1H), 3.80 (s, 3H), 3.75−3.58 (m, 2H), 3.17 (br, 1H), 2.23 (m, 1H), 1.87 (m, 3H), 1.19 (d, *J* = 7.2, 3H), 1.04 (d, *J* = 6.9, 3H), 0.78 (d, *J* = 6.9, 3H); ^{13}C NMR ($CDCl_3$): 159.83, 131.66, 127.26, 113.61, 101.91, 82.10, 76.11, 73.91, 69.45, 55.31, 37.62, 36.59, 29.81, 12.90, 11.63, 8.22.

***syn,syn,syn,anti*-Pivalate 9.** To a solution of diol **8** (625 mg, 1.93 mmol) in CH_2Cl_2 (50 mL) were added successively Et_3N (0.81 mL, 5.8 mmol) and pivaloyl chloride (0.29 mL, 2.3 mmol) at 0 °C. A few crystals of *N*,*N*-(dimethylamino)pyridine (DMAP) were added, and the mixture was stirred at 0 °C for 2 h and then warmed to rt for 14 h. The reaction was quenched with aqueous $NaHCO_3$ solution and extracted with Et_2O. The extracts were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was chromatographed on silica gel (2:1 hexanes:EtOAc, containing 1% Et_3N) to provide pivalate **9** as a clear syrup (713 mg, 90%): $[\alpha]^{20}_D$ = +6.4 (*c* 2.3, $CHCl_3$); IR (neat) 3509, 1724, 1168 cm^{-1}; ^1H NMR ($CDCl_3$): 7.43 (d, *J* = 8.7, 2H), 6.89 (d, *J* = 8.7, 2H), 5.49 (s, 1H), 4.62 (dd, *J* = 11.4, 3.6, 1H), 4.10 (d, *J* = 11.1, 1H), 4.01 (d, *J* = 11.1, 1 H), 3.94 (dd, *J* = 11.4, 3.6, 1 H), 3.89 (dd, *J* = 9.0, 2.1, 1 H), 3.80 (s, 3H), 3.30 (dd, *J* = 9.9, 5.4, 1 H), 2.77 (d, *J* = 5.4, 1 H (OH)), 1.95−1.80 (m, 2H), 1.72 (m, 1H), 1.23 (s, 9H), 1.14 (d, *J* = 6.9, 3H), 1.01 (d, *J* = 6.6, 3H), 0.93 (d, *J* = 7.2, 3H); ^{13}C NMR ($CDCl_3$): 179.67, 159.72, 131.59, 127.15, 113.51, 101.79, 82.12, 73.69, 69.99, 66.91, 55.23, 37.11, 35.52, 29.37, 27.20, 13.48, 11.27, 8.02. Anal. Calcd for $C_{23}H_{36}O_6$: C, 67.62; H, 8.88. Found: C, 67.45; H, 8.89.

***syn,syn,syn,anti*-Pivalate TBS Derivative 10.** To a solution of alcohol **9** (921 mg, 2.26 mmol) in CH_2Cl_2 (25 mL) were added successively 2,6-lutidine (1.04 mL, 8.93 mmol) and TBSOTf (1.3 mL, 5.66 mmol) at 0 °C. After being stirred at 0 °C for 18 h, the reaction mixture was quenched with aqueous $NaHCO_3$ and extracted with Et_2O. The extracts were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was chromatographed on silica gel (9:1 hexanes:EtOAc containing 1% Et_3N) to afford silyl ether **10** as a white solid (1.17 g, 99%). This material could be recrystallized from ether to form colorless rods: mp 86−88 °C; $[\alpha]^{20}_D$ = −21.1 (*c* 2.7, $CHCl_3$); IR (neat) 1730, 1248 cm^{-1}; ^1H NMR ($CDCl_3$): 7.43 (d, *J* = 8.7, 2H), 6.89 (d, *J* = 8.7, 2H), 5.45 (s, 1H), 4.19 (dd, *J* = 10.8, 4.2, 1H), 4.05 (m, 2 H), 3.98 (dd, *J* = 10.8, 6.0, 1H), 3.80 (s, 3H), 3.77 (dd, *J* = 9.9, 1.8, 1 H), 3.71 (d, *J* = 7.8, 1 H), 1.99 (m, 1H), 1.89 (m, 1H), 1.72 (m, 1H), 1.21 (s, 9H), 1.17 (d, *J* = 6.9, 3H), 1.01 (d, *J* = 6.6, 3H), 0.95 (d, *J* = 7.2, 3H), 0.93 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR ($CDCl_3$): 178.38, 159.75, 131.55, 127.18, 113.54, 101.84, 81.26, 73.57, 71.15, 66.54, 55.27, 38.89, 37.89, 36.98, 29.90, 27.24, 26.10, 18.60, 14.20, 11.34, 9.03, −3.26, −4.19. Anal. Calcd for $C_{29}H_{50}O_6Si$: C, 66.63; H, 9.64. Found: C, 66.69; H, 9.64.

***syn,syn,syn,anti*-Alcohol TBS Derivative 11.** To a cold (0 °C) solution of silyl ether **10** (456 mg, 0.87 mmol) in THF (10 mL) was added Red-Al (0.31 mL, 65 wt % in toluene, 1.04 mmol). The resultant solution was stirred at 0 °C for 2 h at which time the reaction was judged complete by the disappearance of starting material (TLC). The mixture was quenched by the dropwise addition of saturated aqueous potassium sodium tartrate. After being warmed to rt and stirred for 1 h, the mixture was diluted with Et_2O, the layers were separated, and the organics were washed with brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. The solvent was removed, and the residue was chromatographed on silica gel (6:1 to 4:1 hexanes:EtOAc containing 1% Et_3N) to give alcohol **11** as a white solid (364 mg, 95%): mp 81−82 °C; $[\alpha]^{20}_D$ = −29.7 (*c* 3.0, $CHCl_3$); IR (neat) 3463, 1248, 1035 cm^{-1}; ^1H NMR ($CDCl_3$): 7.43 (d, *J* = 8.7, 2H), 6.89 (d, *J* = 8.7, 2H), 5.46 (s, 1H), 4.05 (s, 2 H), 3.82 (dd, *J* = 11.4, 1.8, 1 H), 3.80 (s, 3 H), 3.68 (dd, *J* = 6.9, 1.2, 1 H), 3.64−3.56 (m, 2 H), 1.99 (br s, 1 H (OH)), 1.92−1.84 (m, 2 H), 1.74 (m, 1 H), 1.18 (d, *J* = 6.9, 3H), 1.04 (d, *J* = 6.6, 3H), 0.96 (d, *J* = 7.2, 3 H), 0.95 (s, 9H), 0.13 (s, 3H), 0.11 (s, 3H); ^{13}C NMR (CDCl3): 159.71, 131.54, 127.16, 113.48, 101.79, 80.87, 73.69, 73.45, 65.42, 55.21, 39.90, 38.19, 30.32, 26.08, 18.46, 14.80, 11.46, 9.74, −3.59, −4.08. Anal. Calcd for $C_{24}H_{42}O_5Si$: C, 65.71; H, 9.65. Found: C, 65.60; H, 9.57.

***syn,syn,syn,anti*-Aldehyde 12.** To solution of alcohol **11** (399 mg, 0.91 mmol) in CH_2Cl_2 (15 mL) was added the Dess−Martin periodinane (463 mg, 1.09 mmol) at rt. After 1 h another portion (380 mg, 0.89 mmol) of periodinane was added and the mixture was stirred another 1.5 h at which time the reaction was judged complete by TLC. The reaction was quenched by the simultaneous addition of saturated aqueous $NaHCO_3$ (4 mL) and saturated aqueous $Na_2S_2O_3$ (4 mL). Et_2O was added, and the biphasic mixture was stirred vigorously for 40 min. The layers were separated, and the organic extracts were washed sequentially with $Na_2S_2O_3$, $NaHCO_3$, and brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and concentration provided aldehyde **12** (395 mg, 99%) as a clear syrup which was used immediately without further purification: $[\alpha]^{20}_D$ = −37.0 (*c* 2.4, $CHCl_3$); IR (neat) 2710, 1728, 1248 cm^{-1}; ^1H NMR ($CDCl_3$): 9.79 (d, *J* = 2.7, 1 H), 7.43 (d, *J* = 8.7, 2H), 6.89 (d, *J* = 8.7, 2H), 5.44 (s, 1 H), 4.04 (m, 2 H), 3.99 (dd, *J* = 7.5, 1.5, 1 H), 3.85 (dd, *J* = 9.3, 2.4, 1 H), 3.80 (s, 3 H), 2.68 (m, 1 H), 1.86 (m, 1 H), 1.73 (m, 1 H), 1.19 (d, *J* = 6.9, 3 H), 1.05 (d, *J* = 6.3, 3 H), 1.04 (d, *J* = 6.9, 3 H), 0.90 (s, 9 H), 0.10 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR ($CDC1_3$): 204.47, 159.82, 131.44, 127.20, 113.54, 101.84, 80.26, 73.61, 72.39, 55.25, 50.78, 38.31, 30.34, 25.97, 18.44, 12.04, 11.57, 9.37, −3.67, −4.00.

***syn,syn,syn,anti*-Diene 15.** To a solution of aldehyde **12** (395 mg, 0.91 mmol) in degassed THF (15 mL) was added (1-bromoallyl)trimethylsilane (**13**, 879 mg, 4.55 mmol). The mixture was added to a suspension of $CrCl_2$ (929 mg, 7.55 mmol) in degassed THF (10 mL) by canula and stirred at rt for 14 h. The solvent was removed in vacuo, and the brownish residue was taken up in a minimal amount of ether. The chromium salts were precipitated with hexane, and the mixture was filtered through a short pad of Celite. The filtrate was concentrated, and the oily residue was used for the next reaction without further purification. ^1H NMR analysis of this material showed complete conversion to the silyl alcohol adduct as one major diastereomer with only a trace amount of a minor diastereomer.

The foregoing product in THF (25 mL) was cooled to 0 °C, and NaH (218 mg, 95% purity, 9.11 mmol) was added in one portion. The ice bath was removed after 15 min, and the mixture was stirred for 1 h at rt at which time another portion of NaH (218 mg, 95% purity, 9.11 mmol) was added. The resultant suspension was stirred for an additional 2 h, cooled to 0 °C, quenched with H_2O, extracted with Et_2O, washed with brine, dried (Na_2SO_4), and concentrated. The residue was chromatographed on silica gel (12:1 hexanes:EtOAc containing 1% triethylamine) to afford diene **15** as a colorless oil (335 mg, 80% overall yield for three steps from alcohol **11**): $[\alpha]^{20}_D = -7.1$ (*c* 2.0, $CHCl_3$); IR (neat) 1616, 1517, 1249 cm^{-1}; ^1H NMR ($CDCl_3$): 7.43 (d, $J = 8.7$, 2H), 6.89 (d, $J = 8.7$, 2H), 6.60 (dtd, $J = 16.8$, 10.5, 0.9, 1H), 5.99 (td, $J = 10.5$, 0.9, 1H), 5.43 (s, 1H), 5.41 (t, $J = 10.5$, 1H), 5.19 (d, $J = 16.8$, 1H), 5.11 (d, $J = 10.5$, 1H), 4.02 (m, 2 H), 3.80 (s, 3 H), 3.74 (dd, $J = 10.2$, 1.8, 1 H), 3.59 (dd, $J = 6.3$, 1.5, 1 H), 2.86 (m, 1 H), 1.90 (ddtd, $J = 9.9$, 6.6, 6.6, 1.2, 1 H), 1.73 (m, 1 H), 1.15 (d, $J = 6.9$, 3H), 1.03 (d, $J = 6.6$, 3H), 1.00 (d, $J = 6.9$, 3H), 0.91 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); ^{13}C NMR ($CDCl_3$): 159.73, 136.30, 132.34, 131.67, 129.32, 127.21, 117.52, 113.51, 101.83, 81.49, 74.60, 73.64, 55.27, 37.83, 37.65, 30.09, 26.16, 18.48, 18.30, 11.35, 9.99, −3.26, −3.70. Anal. Calcd for $C_{27}H_{44}O_4Si$; C, 70.39; H, 9.63. Found: C, 70.37; H, 9.58.

***syn,anti*-Propargylic Acetate 20. A. $BuSnCl_3$ Procedure.** To a solution of allenylstannane (*M*)-**2b** (7.00 g, 16.86 mmol) in CH_2Cl_2 (25 mL) was added *n*-$BuSnCl_3$ (2.94 mL, 17.62 mmol) at −78 °C. After 10 min, the mixture was warmed to rt and stirred for 5 h. Aldehyde (*S*)-**1** (2.82 g, 13.96 mmol) was added. The mixture was stirred at rt for 20 h and then quenched with saturated aqueous $NaHCO_3$ solution and extracted with Et_2O. The extracts were washed with brine, dried ($MgSO_4$), and treated with Et_3N (1 mL). The white solid was filtered and washed with Et_2O. The filtrate was concentrated and chromatographed on silica gel (elution with 8% Et_2O−hexane) affording alcohol **20** as a colorless oil (2.20 g, 48%).

B. $InBr_3$ Procedure. To a solution of $InBr_3$ (15.0 g, 42.3 mmol) in EtOAc (75 mL) were added aldehyde (*S*)-**1** (8.10 g, 40.1 mmol) and allenylstannane (*P*)-**2b** (28.0 g, 67.4 mmol) in EtOAc (10 mL) at −78 °C. After 15 min, the dry ice bath was removed. The reaction mixture was allowed to warm to 0 °C, stirred for 1 h, and then worked up by addition of brine (20 mL) and Et_2O (150 mL). The ether phase was dried over $MgSO_4$; then Et_3N (15 mL) was added and the mixture was stirred vigorously at rt for 10 min and filtered through a short pad of silica gel to remove a white precipitate. The filtrate was concentrated under reduced pressure and chromatographed (10% Et_2O−hexanes) to afford alcohol **20** as a colorless oil (9.10 g, 69%): $[\alpha]^{20}_D$ −3.3 (*c* 0.36, $CHCl_3$); ^1H NMR ($CDCl_3$): 4.68 (d, $J = 2.1$, 2H), 3.66 (d, $J = 5.1$, 2H), 3.59 (dd, $J = 6.9$, 3.3, 1H), 2.70 (m, 1H), 2.08 (s, 3H), 1.77 (m, 1H), 1.17 (d, $J = 6.9$, 3H), 0.94 (d, $J = 6.9$, 3H), 0.89 (s, 9H), 0.056 (s, 6H).

***syn,anti,anti*-Diol 25.** Sodium bis(2-methoxyethoxy)aluminum hydride (Red-Al) in toluene (4.9 mL, 65 wt %, 16.2 mmol) was added dropwise to a solution of epoxide **24** (1.00 g, 3.24 mmol) in THF (60 mL) at 0 °C. The reaction mixture was stirred at 0 °C for 29 h and quenched carefully with saturated aqueous potassium sodium tartrate. The mixture was stirred at rt for 1 h and extracted with Et_2O. The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated under reduced pressure. The oily residue was chromatographed (elution with 60% Et_2O−hexanes, containing 1% Et_3N) to afford the diol **25** as a white solid (0.92 g, 92%): mp 87−89 °C; $[\alpha]^{20}_D = -31.1$ (*c* 1.7, $CHCl_3$); ^1H NMR ($CDCl_3$): 7.36 (d, $J = 7.8$, 2H), 6.87 (d, $J = 7.8$, 2H), 5.45 (s, 1H), 4.31−3.80 (m, 5H), 3.76 (s, 3H), 3.48 (br, 1H), 1.95−1.55 (m, 4H), 1.19 (d, $J = 6.9$, 3H), 0.77 (d, $J = 6.9$, 3H); ^{13}C NMR ($CDCl_3$): 159.75, 130.53, 127.15, 113.39, 101.39, 84.48, 74.66, 73.62, 60.96, 54.93, 39.61, 34.41, 29.62, 10.59, 10.12. Anal. Calcd for $C_{17}H_{26}O_5$: C, 65.78; H, 8.44. Found: C, 65.70; H, 8.42.

***syn,anti,anti*-Aldehyde 29.** To solution of oxalyl chloride (0.50 mL, 5.73 mmol) in CH_2Cl_2 (50 mL) was added dropwise DMSO (0.60 mL, 8.46 mmol) at −78 °C. After 10 min, a solution of the alcohol **28** (1.10 g, 2.59 mmol) in CH_2Cl_2 (10 mL) was added dropwise, followed by rapid addition of triethylamine (2.0 mL, 14.4 mmol) at −78 °C. The resultant mixture was gradually warmed to ambient temperature within 30 min and poured into ice−brine. The mixture was extracted with Et_2O, the extracts were washed with brine, the solvent was removed, and the residue was chromatographed on deactivated charcoal to give the aldehyde **29** as a colorless oil (1.05 g, 96%): ^1H NMR ($CDCl_3$): 9.70 (s, 1H), $J = 8.7$, 2H), 6.90 (d, $J = 8.7$, 2H), 5.36 (s, 1H), 4.65 (m, 1H), 4.03 (m, 2H), 3.81 (s, 3H), 3.56 (dd, $J = 10.8$, 2.4, 1H), 2.47 (m, 2H), 2.03 (m, 1H), 1.59 (m, 1H), 1.17 (d, $J = 6.9$, 3H), 0.88 (s, 9H), 0.85 (d, $J = 7.5$, 3H), 0.08 (s, 3H), 0.04 (s, 3H); ^{13}C NMR ($CDCl_3$): 202.15, 159.66, 131.17, 127.01, 113.35, 101.12, 80.54, 73.69, 67.01, 55.01, 45.91, 40.06, 29.55, 25.60, 17.81, 10.67, 8.39, −4.64, −4.97. Anal. Calcd for $C_{23}H_{38}O_5Si$: C, 65.36; H, 9.06. Found: C, 65.13; H, 8.98.

Allenylstannane (*P*)-31. To a solution of *i*-Pr_2NH (15.2 mL, 116 mmol) in THF (230 mL) was added *n*-BuLi (42.2 mL, 2.5 M in hexanes, 105.5 mmol) at 0 °C under Ar. After 10 min, *n*-Bu_3SnH (28.3 mL, 105.5 mmol) was added to the mixture, and stirring was continued at 0 °C for another 10 min. The mixture was cooled to −78 °C, and $CuBr{\cdot}Me_2S$ (21.6 g, 105.4 mmol) was added. The mixture was stirred at −78 °C for 40 min; then a solution of mesylate (*R*)-**30** (10.4 g, 70.3 mmol) in THF (20 mL) was added over 5 min. The mixture was stirred virgorously for another 5−10 min and then poured into 1.5 L of a $NH_3{\cdot}H_2O$−NH_4Cl solution (1:8) and diluted with Et_2O (500 mL). The mixture was stirred at rt (12 h) until the organic phase was clear. The organic layer was separated, and the aqueous layer was extracted with Et_2O. The combined extracts were washed with $NH_3{\cdot}H_2O$−NH_4Cl, H_2O, and brine and dried (Na_2SO_4). The solvents were removed under reduced pressure, and the residue was distilled to afford the stannane (*P*)-**31** as a colorless oil (18.4 g, 77%): bp 81−84 °C at 0.05 mmHg; $[\alpha]^{20}_D = +91.4$ (*c* 7.7, $CHCl_3$); ^1H NMR($CDCl_3$): 4.96 (m, 1H), 4.56 (m, 1H), 1.66−1.19 (m, 15H), 1.03−0.78 (m, 15H).

***anti,syn*-Homopropargylic Alcohol 32.** To a solution of $InBr_3$ (6.94 g, 19.55 mmol) in EtOAc (35 mL) was added a solution of aldehyde (*S*)-**1** (3.95 g, 19.5 mmol) in EtOAc (4 mL) and stannane (*P*)-**31** (6.70 g, 19.55 mmol) at −78 °C. After 15 min, the dry ice bath was removed and the mixture was allowed to warm to 0 °C and stirred for another 2 h. The reaction mixture was worked up by addition of H_2O (10 mL) and Et_2O (50 mL). The ether phase was dried over $MgSO_4$; then Et_3N (10 mL) was added and the mixture was stirred vigorously at rt for 10 min and filtered through a short pad of silica gel to remove a white precipitate. The filtrate was concentrated under reduced pressure and chromatographed (10% Et_2O−hexanes) to afford alcohol **32** and a diastereomer (3.35 g, 67%) as a colorless oil, in the ratio of 92:8.

32: $[\alpha]^{20}_D = -3.9$ (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$): 3.68 (d, $J = 5.1$, 2H), 3.60 (m, 1H), 2.66 (m, 1H), 2.13 (d, $J = 2.4$, 1H), 1.79 (m, 1H), 1.19 (d, $J = 7.2$, 3H), 0.96 (d, $J = 6.9$, 3H), 0.89 (s, 9H), 0.056 (s, 6H); ^{13}C NMR ($CDCl_3$): 86.40, 76.16, 70.16, 67.19, 37.42, 30.46, 25.84, 17.58, 10.30, −5.57, −5.60. Diastereomer of **32**: $[\alpha]^{20}_D = +13.5$ (*c* 1.3, $CHCl_3$); ^1H NMR ($CDCl_3$): 3.77 (dd, $J = 13$, 3.6, 1H), 3.63 (dd, $J = 13$, 8.1, 1H), 3.55 (m, 1H), 2.66 (m, 1H), 2.07 (d, $J = 2.4$, 1H), 1.99 (m, 1H), 1.29 (d, $J = 6.9$, 3H), 0.89 (s, 9H), 0.85 (d, $J = 6.9$, 3H), 0.073 (s, 6H).

***syn,anti*-Diol 33.** To a solution of alcohol **32** (6.60 g, 25.78 mmol) in THF (100 mL) was added TBAF (38 mL, 1 M in THF, 38 mmol) at rt. The mixture was stirred for 30 min and then poured into ice−brine (30 mL). The organic layer was separated, and the aqueous layer was saturated with salt and extracted 10 times with EtOAc. The combined organic layers were dried ($MgSO_4$) and concentrated under reduced pressure. The oily residue was chromatographed on silica gel (elution with 50% Et_2O−hexanes to 100% Et_2O) to afford diol **33** as white solid (3.20 g, 87%). The solid containing about 8% of an undesired diastereomer (anti,anti) was recrystallized from Et_2O−hexanes to give colorless crystals: mp 71−73 °C. $[\alpha]^{20}_D = -2.0$ (*c* 1.9, $CHCl_3$); ^1H NMR ($CDCl_3$): 3.64 (d, $J = 4.8$, 2H),

3.57 (m, 1H), 2.62 (m, 1H), 1.81 (m, 1H), 1.15 (d, J = 6.9, 3H), 0.92 (d, J = 6.9, 3H); ^{13}C NMR ($CDCl_3$) 86.03, 75.99, 70.76, 66.39, 37.01, 30.69, 17.32, 9.76.

***syn,anti-p*-Anisylidene Acetal 34.** The diol **33** (3.00 g, 21.1 mmol) in benzene (50 mL), *p*-anisaldehyde dimethyl acetal (5.70 g, 31.3 mmol), and a catalytic amount of *dl*-CSA (ca. 10 mg) was refluxed with azeotropic removal of MeOH for 2 h. After being cooled to rt, the mixture was concentrated under reduced pressure, and the residue was chromatographed on deactivated silica gel (elution with 5% Et_2O−hexanes containing 1% Et_3N) to give acetal **34** as a white solid (5.27 g, 96%). Colorless crystals (mp 72−74 °C) were obtained by recrystallization from hexane: $[\alpha]^{20}_D$ = −98.0 (*c* 3.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$): 7.47 (d, J = 8.7, 2H), 6.89 (d, J = 8.7, 2H), 5.52 (s, 1H), 4.04 (m, 2H), 3.80 (s, 3H), 3.79 (m, 1H), 2.66 (m, 1H), 2.05 (d, J = 2.4, 1H), 1.67 (m, 1H), 1.18 (d, J = 7.2, 3H), 1.15 (d, J = 7.2, 3H); ^{13}C NMR ($CDCl_3$): 159.82, 131.24, 127.27, 113.52, 101.59, 86.75, 82.52, 73.52, 68.81, 55.25, 29.79, 28.56, 15.83, 10.60. Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.82; H, 7.74. Found: C, 73.70; H, 7.81.

Propargylic Alcohol Coupling Product 35. To a solution of the acetylene **34** (3.00 g, 11.53 mmol) in THF (90 mL) and activated 4A MS was added *n*-BuLi (4.20 mL, 2.5 M in hexane, 10.92 mmol) at −50 °C. The mixture was stirred at −50 to −40 °C for 1 h; then a solution of LiBr (1.4 mL, 4.0 M in THF, 5.6 mmol) was added. After 15 min, a precooled (−50 °C) solution of the aldehyde (1.00 g, 2.37 mmol) in THF (10 mL) was added. The mixture was stirred at −45 °C for 30 min and quenched with H_2O. The mixture was warmed to rt and extracted with Et_2O. The extracts were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was chromatographed to afford the adduct **35** (1.14 g, 71%) and its epimer (0.386 g, 24%) as a colorless foam. The excess acetylene was recovered.

35: $[\alpha]^{20}_D$ = −91.9 (*c* 1.48, $CHCl_3$); ^{1}H NMR ($CDCl_3$): 7.46 (dd, J = 8.8, 2.1, 4H), 6.89 (dd, J = 8.8, 2.1, 4H), 5.42 (s, 1H), 5.39 (s, 1H), 4.60 (m, 2H), 4.00 (d, J = 12, 4H), 3.78 (s, 3H), 3.77 (s, 3H), 3.66 (dd, J = 6.9, 1.8, 1H), 3.57 (d, J = 10.8, 1H), 2.81 (d, J = 6.9, 1H), 2.64 (m, 1H), 2.05 (m, 1H), 1.90−1.65 (m, 2H), 1.57 (m, 2H), 1.18 (d, J = 7.2, 3H), 1.13 (d, J = 6.9, 3H), 1.06 (d, J = 6.9, 3H), 0.95 (s, 9H), 0.85 (d, J = 6.9, 3H), 0.14 (s, 6H); ^{13}C NMR ($CDCl_3$): 159.69, 159.63, 131.49, 131.26, 127.21, 127.07, 113.39, 101.42, 100.99, 86.94, 82.47, 82.18, 80.71, 73.87, 73.45, 68.49, 60.02, 55.17, 39.97, 37.97, 29.75, 28.61, 25.85, 17.98, 15.76, 10.74, 10.61, 8.09, −4.45, −4.64. Anal. Calcd for $C_{39}H_{58}O_8Si$: C, 68.59; H, 8.56. Found: C, 68.55; H, 8.60.

***(Z)*-Allylic Alcohol 36.** To a solution of the alcohol **35** (191 mg, 0.28 mmol) in toluene (4 mL) was added a catalytic amount of 5% Pd on $CaCO_3$ (Lindlar catalyst, ca. 100 mg). The flask was fitted with a balloon, flushed with H_2 several times, and stirred under an atmosphere of H_2 for 18 h. The mixture was filtered through a pad of Celite and concentrated under reduced pressure to afford the olefin **36** as a colorless foam (191 mg, 99%): $[\alpha]^{20}_D$ = −20.2 (*c* 3.1, $CHCl_3$); ^{1}H NMR ($CDCl_3$): 7.38 (d, J = 8.7, 4H), 6.87 (d, J = 8.4, 2H), 6.84 (d, J = 8.7, 2H), 5.49 (dd, J = 11.1, 8.1, 1H), 5.37 (s, 1H), 5.25 (d, J = 10.2, 1H), 5.20 (s, 1H), 4.62 (m, 1H), 4.41 (dt, J = 10.5, 3.6, 1H), 4.00 (d, J = 16.2, 4H), 3.80 (s, 3H), 3.77 (s, 3H), 3.52 (dd, J = 9.6, 1.8, 1H), 3.35 (dd, J = 10.8, 1.5, 1H), 2.81 (m, 1H), 2.25 (d, J = 4.2, 1H), 1.95 9m, 1H), 1.74−1.55 (m, 2H), 1.11 (d, J = 7.2, 3H), 0.94 (d, J = 6.3, 3H), 0.91 (s, 9H), 0.68 (d, J = 7.5, 3H), 0.078 (s, 3H), 0.071 (s, 3H); ^{13}C NMR ($CDCl_3$): 158.66, 158.57, 132.62, 132.25, 130.57, 126.37, 126.04, 112.38, 100.55, 99.89, 82.30, 79.77, 72.82, 66.89, 64.68, 54.22, 54.15, 39.07, 36.69, 33.07, 28.76, 24.89, 17.02, 14.87, 10.00, 9.86, 6.89, −5.30, −5.79. Anal. Calcd for $C_{39}H_{60}O_8Si$: C, 68.38; H, 8.83. Found: C, 68.48; H, 8.78.

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Supporting Information Available: ^{1}H NMR spectra for **3**, **8**, **9**, **11**, **12**, **15**, **18**, **19**, **20**, **29**, **32**, *epi*-**32**, **33**, **34**, **37**, and **38**, experimental procedures for **22**−**24** and **26**−**28**, and log files for Monte Carlo minimization of **6** and **23** (25 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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