Total Synthesis of (+)-Discodermolide

James A. Marshall* and Brian A. Johns

Department of Chemistry, University of Virginia, Charlottesville, Virginia 22901

Received June 15, 1998

The total synthesis of (+)-discodermolide is described. The approach involves assemblage of three key stereotriad subunits through addition of nonracemic allenyltin, -indium, and -zinc reagents to (*S*)-3-silyloxy-2-methylpropanal derivatives, followed by reduction of the resulting *anti*,*syn*- or *syn*,*syn*-homopropargylic alcohol adducts to the (*E*)-homoallylic alcohols and subsequent Sharpless epoxidation. Addition of methyl cuprate reagents or Red-Al to the resultant epoxy alcohols yielded the key precursors, alkyne **4**, aldehyde **9**, and alcohol **24**. Addition of alkyne **4** (as the lithio species **10**) to aldehyde **9** afforded the propargylic alcohol **11** as the major stereoisomer. Lindlar hydrogenation and installation of appropriate protecting groups led to aldehyde **17**. This was converted to the (*Z*)-vinylic iodide **18** upon treatment with α-iodoethylidene triphenylphosphorane. Suzuki coupling of this vinylic iodide with a boranate derived from iodide **25** led to the coupled product **27** with the complete carbon backbone of (+)-discodermolide and the correct stereochemistry. The synthesis was completed by cleavage of the cyclic PMP acetal at C1 with *i*-Bu_2AlH and three-step oxidation−esterification to the ester **31**. Cleavage of the C19 Et_3Si ether and C19 carbamate formation followed by cleavage of the remaining alcohol protecting groups, first with DDQ and then aqueous HCl, afforded (+)-discodermolide (**36**).

The polyketide marine natural product discodermolide, by virtue of its potent immunosuppressant and potential antitumor activity and in view of its limited availability,[1] has stimulated significant interest as a target for total synthesis.[2] To date, three syntheses of the enantiomer[2a−c] and one of the natural material[2a] have been described. These synthetic efforts were initiated before the absolute configuration had been established. In fact, Schreiber and co-workers prepared both enantiomers of the natural product, thereby establishing the correct absolute configuration.[2a]

We viewed the synthesis of (+)-discodermolide as a test of our allenylmetal−homoaldol approach to stereotriads and their further elaboration to polypropionate subunits.[3,4] The previous routes to discodermolide and various subunits have utilized chiral allyl boronate additions, Evans oxazolidinone-mediated aldol condensations and alkylations, and substrate-directed alkylations and aldol condensations for the introduction of various stereocenters.[2] We have developed an approach, outlined in Figure 1, in which key stereocenters are introduced through additions of chiral allenylmetal reagents **K** to the readily available aldehyde (*S*)-2-methyl-3-silyloxypropanal **J**.[5] Subsequent reduction of the triple bond in

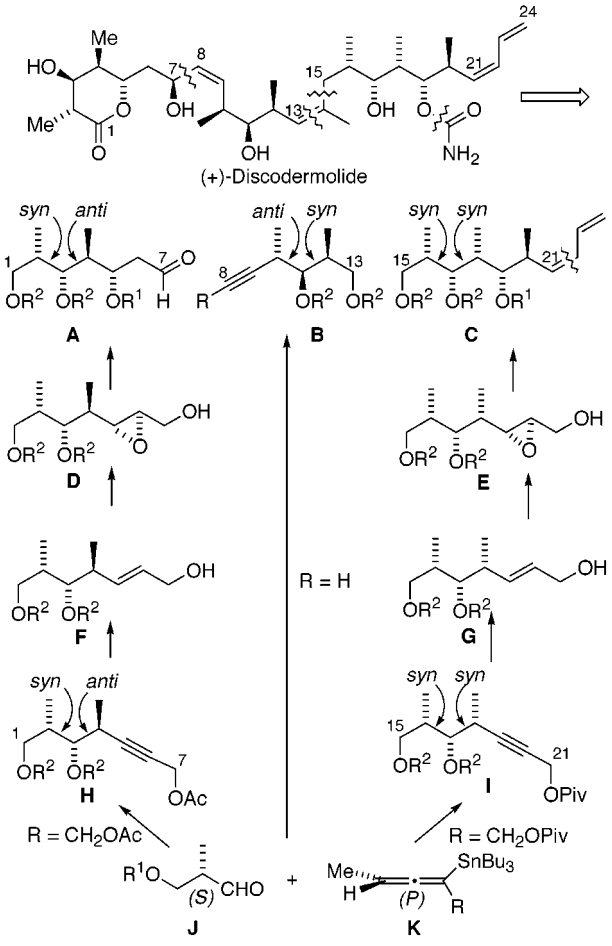


Figure 1. Synthetic plan for (+)-discodermolide (R^1 = TBS; R^2 = PMP).

adducts **H** and **I** leads to allylic alcohols **F** and **G**, which are subjected to asymmetric epoxidation followed by

(1) For information about isolation of this compound, see: Gunasekera, S. P.; Gunasekera, M.; Longley, R. E. *J. Org. Chem.* **1990**, *55*, 4912; **1991**, *56*, 1346.

(2) (a) Hung, D. T.; Nerenberg, J. B.; Schreiber, S. L. *J. Am. Chem. Soc.* **1996**, *118*, 11054. (b) Smith, A. B., III; Qui, Y.; Jones, D. R.; Kobayashi, K. *J. Am. Chem. Soc.* **1995**, *117*, 12011. (c) Harried, S. S.; Yang, G.; Strawn, M. A.; Myles, D. C. *J. Org. Chem.* **1997**, *62*, 6098. (d) Paterson, I.; Schlapbach, A. *Synlett* **1995**, 498. (e) Clark, D. L.; Heathcock, C. H. *J. Org. Chem.* **1993**, *58*, 5878. (f) Golec, J. M. C.; Jones, S. D. *Tetrahedron Lett.* **1993**, *34*, 8159 and two accompanying papers.

(3) Marshall, J. A.; Perkins, J. F.; Wolf, M. A. *J. Org. Chem.* **1995**, *60*, 5556.

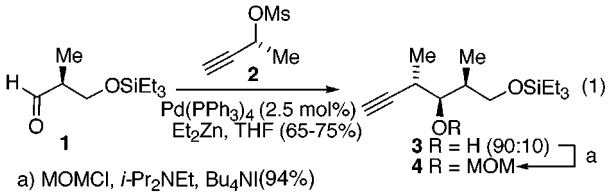
(4) Marshall, J. A.; Lu, Z.-H.; Johns, B. A. *J. Org. Chem.* **1998**, *63*, 817.

(5) Roush, W. R.; Palkowitz, A. D.; Ando, K. *J. Am. Chem. Soc.* **1990**, *112*, 6348.

10.1021/jo9811423 CCC: $15.00
Published on Web 10/09/1998

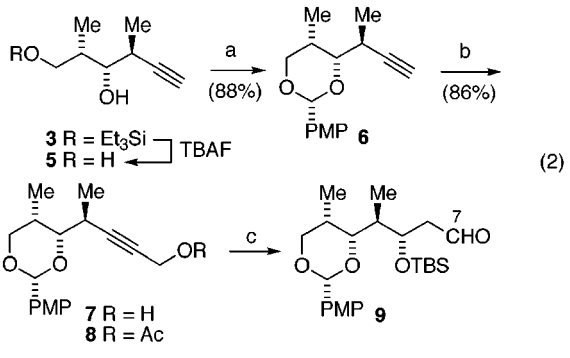
regioselective epoxide cleavage with hydride or a methyl cuprate to provide subunits **A** and the precursor to **C**.[6] The sequential allenylstannane addition, reduction, epoxidation, and methyl cuprate reaction protocol represents an efficient assemblage of stereopentad arrays common to various polypropionate natural products.[7] In the present report, we describe an improved synthesis of the anti,syn subunits **A** and **B** and delineate our successful merging of these with subunit **C**, which results in a total synthesis of (+)-discodermolide.

In an earlier effort we prepared subunit **B** through condensation of aldehyde **J** (R^1 = TBS) with the allenylindium reagent derived from allenylstannane **K** (R = H).[4] This addition afforded the anti,syn product in 67% yield as a 92:8 mixture of inseparable diastereomers. In the interim, we developed an alternative method for the equivalent conversion through use of chiral allenylzinc reagents, prepared in situ by treatment of propargylic mesylates with catalytic $Pd(PPh_3)_4$ and excess Et_2Zn.[8] Application of this methodology to aldehyde **1**[9] led to the adduct **3** as a 90:10 mixture of separable diastereomers in 65−75% yield (eq 1). Conversion to the MOM derivative was effected with MOMCl and *i*-Pr_2NEt in the presence of Bu_4NI. In the present work, it was found that triethylsilyl ethers are preferable to the previously employed TBS ethers because of their more facile cleavage.



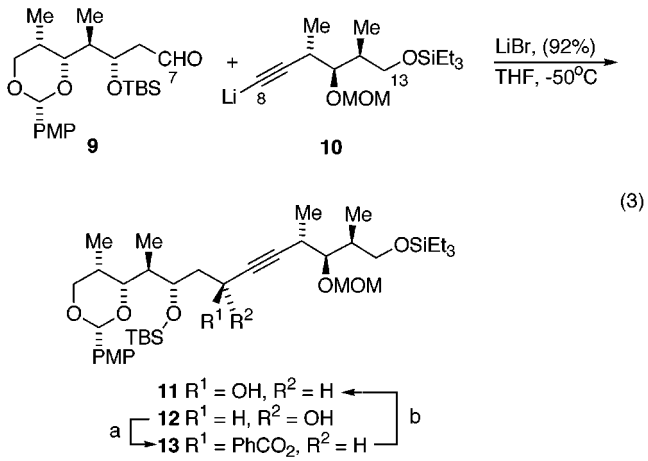
(1)

The next phase of the synthesis called for coupling of the lithiated derivative of alkyne **4** with aldehyde **9** (eq 3). Our previous synthesis of aldehyde **9** entailed addition of the allenylindium reagent derived from stannane **K** (R = CH_2OAc) to aldehyde **J** (R^1 = TBS) followed by TBS cleavage and acetal formation leading to **8** in 58% overall yield.[4] A more expeditious synthesis of the precursor **7** to aldehyde **9** employs the acetal **6**, prepared from the alcohol **3** via diol **5** (eq 2). Lithiation and addition of formaldehyde affords the propargylic alcohol **7**, which is subsequently reduced to allylic alcohol **F** (R^2 = *p*-$MeOC_6H_4CH$) with Red-Al.[4] Elaboration of subunit **F** to aldehyde **9** was accomplished as previously described in six steps and 70% overall yield.



(2)

Treatment of aldehyde **9**[10] with lithiated alkyne **10** afforded a separable 85:15 mixture of alcohols **11** and **12** in 92% yield. The minor diastereomer **12** was efficiently inverted by Mitsunobu displacement with benzoic acid[11] and subsequent reduction of the benzoate **13** with *i*-Bu_2-AlH (eq 3).



(3)

The propargylic alcohol **11** was converted to the (*Z*)-allylic alcohol **14** by hydrogenation over the Lindlar catalyst,[12] thus completing assemblage of the C1−C13 backbone of (+)-discodermolide (Scheme 1). The next sequence of reactions involved further homologation of **14** to the (*Z*)-vinyl iodide **18**, an intermediate that was deemed suitable for coupling to an appropriate C15−C24 fragment (**C** in Figure 1). To that end, protection as the MOM ether **15** followed by selective cleavage of the triethylsilyl ether with HF−pyridine led to alcohol **16**. Oxidation with the Dess−Martin periodinane reagent[13] afforded aldehyde **17** in near-quantitative yield. Conversion to the vinyl iodide **18** was effected by condensation with α-iodoethylidene triphenylphosphorane.[14]

This reaction was the most challenging of the entire sequence. Yields were typically in the 40% range, although on several occasions we obtained ca. 20% of the desired product. The principal byproduct was a conjugated aldehyde, presumed to arise by deprotonation of aldehyde **17** and subsequent loss of the *β*-OMOM grouping. The (*Z*)-vinyl iodide was the major product of the

(6) Elaboration of the terminal diene unit of **C** was effected as described by Paterson and Schlapbach.[2d]

(7) The epoxidation−cuprate addition sequence was first developed by Kishi and co-workers. See: Nagoaka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873.

(8) Marshall, J. A.; Adams, N. D. *J. Org. Chem.* **1998**, *63*, 3812.

(9) Barrett, A. G. M.; Edmunds, J. J.; Hendrix, J. A.; Horita, K.; Parkinson, C. J. *J. Chem. Soc., Chem. Commun.* **1992**, 1238.

(10) The synthesis of aldehyde **9** was completed as previously described,[4] except for the final oxidation step which was effected in essentially quantitative yield with the Dess−Martin periodinane reagent.[13]

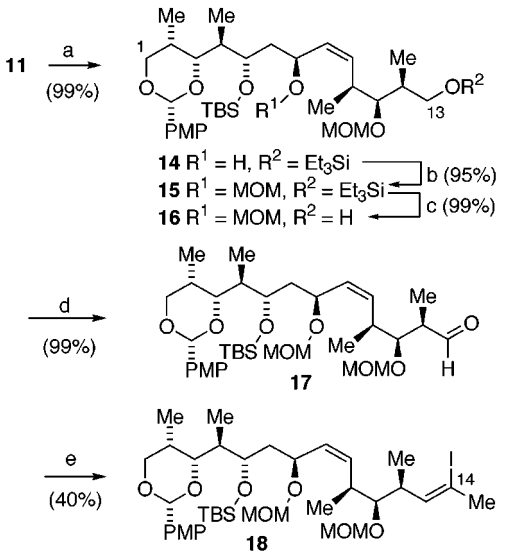
(11) Mitsunobu, O. *Synthesis* **1981**, 1. Hsu, C.-T.; Wang, N.-Y.; Latimer, L. H.; Sih, C. J. *J. Am. Chem. Soc.* **1983**, *105*, 593.

(12) The catalyst, Pd−$CaCO_3$ poisoned with lead, was purchased from Aldrich Chemical Co., Milwaukee, WI.

(13) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155. Meyer, S. D.; Schreiber, S. L. *J. Org. Chem.* **1994**, *59*, 7549.

(14) Chen, J.; Wang, T.; Zhao, K. *Tetrahedron Lett.* **1994**, *35*, 2827. Smith and co-workers identified an epoxide as a significant byproduct in an analogous condensation. We found none of a related epoxide in any of our reaction mixtures. See: Arimoto, H.; Kaufman, M. D.; Kobayashi, K.; Qiu, Y.; Smith, A. B., III. *Synlett* **1998**, 765.

Scheme 1[a]



[a] Key: (a) H_2, Pd/Pb−$CaCO_3$ (99%); (b) MOMCl, *i*-Pr_2NEt, Bu_4NI (95%); (c) HF−py, THF (99%); (d) Dess−Martin periodinane (99%); (e) $Ph_3P{=}C(Me)I$ (40%).

condensation. Generally an 85:15 inseparable mixture of (*Z*) and (*E*) isomers was obtained, although ratios as low as 70:30 and as high as 90:10 were realized from several experiments. In addition, small amounts of protonolysis product arising from the noniodinated ylide were also formed. The most favorable isomer ratios and the highest yields were obtained from experiments in which the condensation was conducted at −78 °C for a prolonged period. Although the protonolysis byproduct could eventually be separated, products arising from the (*E*) isomer of vinylic iodide **18** could not. Thus, intermediates following the coupling step contain small amounts (5−10%) of the 13*E* isomer.

We now reached a crucial point in these synthetic studies: the coupling of subunits **18** and **24** to form the C14−C15 carbon−carbon bond. An analogous connection was employed by Smith and co-workers, who joined a C9−C14 vinyl iodide with a C15−C21 iodozinc reagent in a $Pd(Ph_3P)_4$-catalyzed coupling reaction which proceeded in 66% yield (Figure 2).[2b] Both Schreiber[2a] and Myles[2c] utilized Nozaki−Kishi addition of a C8 acetylenic or (*Z*)-vinylic chromium species to a C7 aldehyde as a major coupling event. The diastereoselectivity of these additions was 2:1 and 2.5:1, respectively. The C13−C15 segment of precursors to the foregoing additions was fashioned through a (*Z*)-selective Still−Horner−Emmons condensation.[15]

After several unpromising attempts to couple truncated C14 vinyl cuprates and C15 iodides, we turned to the use of a Suzuki coupling approach employing (*Z*)-vinyl iodide and alkyl boranate prototypes.[16] These studies proved sufficiently promising to warrant examination of the actual subunits **24** and **18**. Accordingly, alcohol **24** was converted to the iodide **25**,[17] a precursor of the requisite boranate.

Our initial coupling experiments were conducted with diene **22** derived from the syn,syn adduct **21** of aldehyde

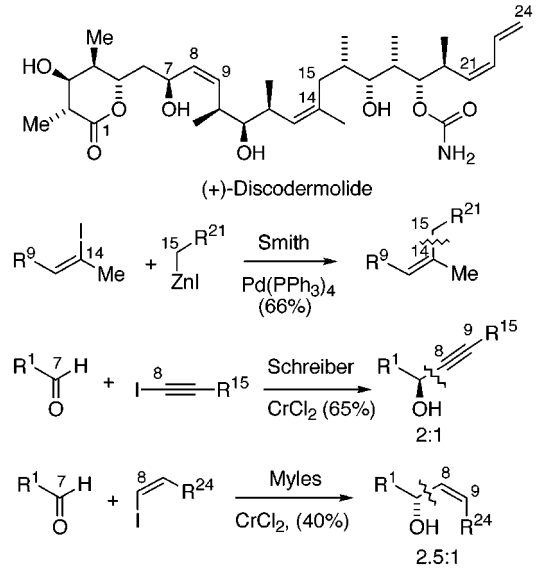
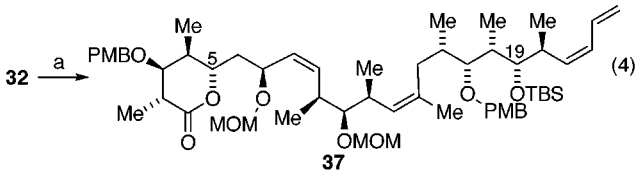


Figure 2. Coupling strategies for the assemblage of major segments of discodermolide.

19 and allenylstannane **20**.[4] However, problems with the ultimate deprotection of the C19 TBS ether **22** forced us to abandon this intermediate in favor of the triethylsilyl analogue **23** (Scheme 2). Selective cleavage of the PMP acetal with *i*-Bu_2AlH[18] gave the primary alcohol **24** exclusively. The derived iodide **25** was converted to the trialkyl boranate **26** by lithiation and subsequent addition of *B*-methoxy-9-BBN. Suzuki coupling with vinyl iodide **18** in the presence of the $PdCl_2$(dppf) catalyst[16] afforded the coupled product **27** in 74% yield, thus completing all requisite carbon−carbon bond-forming reactions for the discodermolide skeleton.

The final steps of the synthesis are summarized in Scheme 3. Selective cleavage of the PMP acetal of **27** with *i*-Bu_2AlH again proved successful, affording the primary alcohol **28** in 79% yield. Alcohol **28** was oxidized in two stages, first with the Dess−Martin periodinane reagent[13] to aldehyde **29**, which then yielded acid **30** upon treatment with buffered $NaClO_2$.[19] The methyl ester **31** was prepared with $TMSCHN_2$.[20]

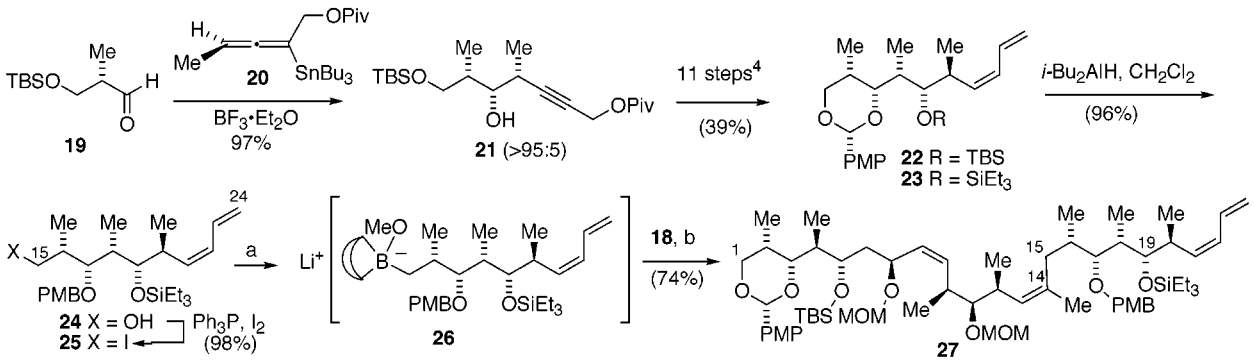
As noted above, the foregoing sequence was initially carried out on the TBS ether **22**. However, cleavage of this ether in the coupled product **32** could not be achieved. Treatment with TBAF was ineffective and afford starting material or decomposition, depending on conditions. Prolonged acid treatment (*p*-TsOH in MeOH at 0 °C over 7 days) led to the δ-lactone **37** in 40% yield (eq 4). Only a small amount of more polar material,



(4)

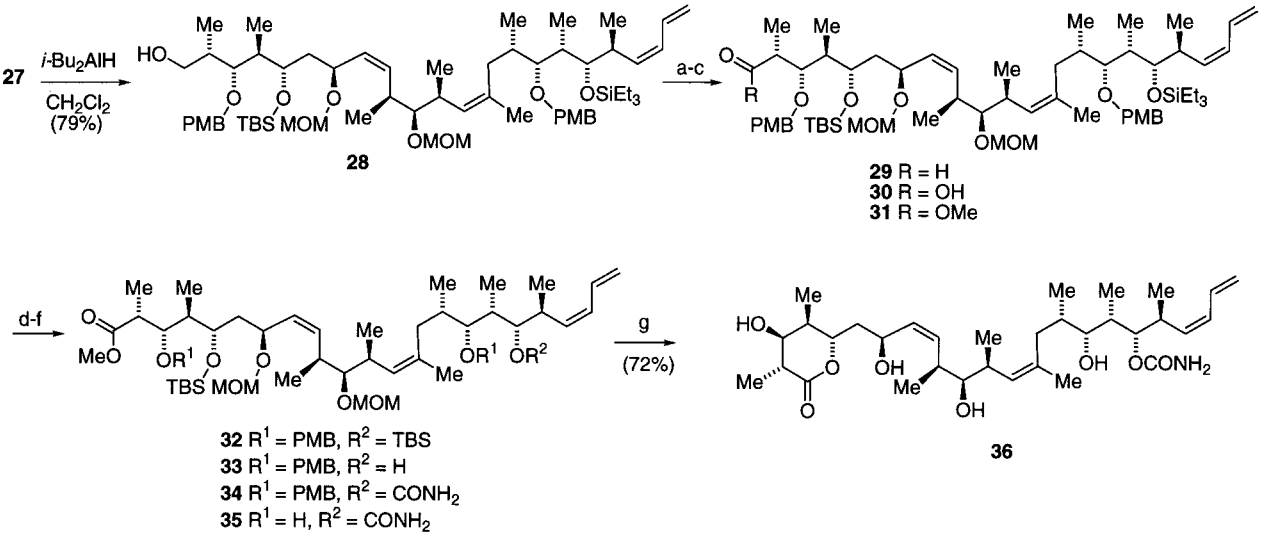
(15) Still, W. C.; Gennari, C. *Tetrahedron Lett.* **1983**, *24*, 4405.
(16) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
(17) Garegg, P. J.; Samuelson, B. *J. Chem. Soc., Chem. Commun.* **1979**, 978.
(18) Takano, S.; Akiyama, M.; Sato, S.; Ogasawara, K. *Chem. Lett.* **1983**, 1593.
(19) Bal, B. S.; Childers, W. E.; Pinnick, H. W. *Tetrahedron* **1983**, *37*, 2091.
(20) Hashimoto, N.; Aoyama, T.; Shioiri, T. *Chem. Pharm. Bull.* **1981**, *29*, 1475.

Scheme 2[a]



[a] Key: (a) *t*-BuLi, Et_2O, −78 °C; 9-BBNOMe, THF, −78 °C to rt; (b) $PdCl_2$(dppf), K_3PO_4, DMF.

Scheme 3[a]



[a] Key: (a) Dess−Martin periodinane (99%); (b) $NaClO_2$, NaH_2PO_4, isobutylene, *t*-BuOH (98%); (c) $TMSCHN_2$ (82%); (d) *p*-TsOH, MeOH, 0 °C (72%); (e) $Cl_3CC(O)NCO$, CH_2Cl_2; K_2CO_3, MeOH (93%); (f) DDQ (85%); (g) 4 N HCl, THF at room temperature (72%).

judged to be the result of C19 TBS cleavage, was produced in this reaction.

Attempted acidic cleavage of the TBS ethers at room temperature led to complete decomposition within 6 h. In view of these unpromising results, we turned to the triethylsilyl ether **31**. This modification proved successful. Exposure of **31** to *p*-TsOH in methanol afforded the C19 alcohol **33** selectively in 72% yield.

The carbamate derivative **34** was obtained through addition of trichloroacetyl isocyanate[21] and in situ cleavage of the derived trichloroacetyl derivative with methanolic K_2CO_3. Next the PMB protecting groups were removed through oxidative cleavage with DDQ in aqueous CH_2Cl_2.[22] Prolonged exposure of the resulting diol **35** to 4 N HCl in THF effected cleavage of the MOM protecting groups and lactonization to yield discodermolide (**36**) as a white amorphous solid. The optical rotation of our sample was of magnitude comparable to the reported values (+17 compared with +14,[2a] −14,[2c] and −16[2b]). Furthermore, the ^1H and ^{13}C NMR spectra matched those of the previously synthesized samples of both (+)- and (−)-discodermolide. However, several small extraneous peaks were present, indicative of an impurity (~5%) presumed to be the C13 (*E*) isomer from the minor (*E*)-vinylic iodide produced in the Wittig condensation leading to **18**.

The present synthesis of discodermolide illustrates the potential of chiral allenylmetal reagents for the synthesis of polypropionate natural products. These reagents are readily prepared in situ from easily available nonracemic propargylic alcohols. Among the benefits to be gained by this strategy are excellent stereocontrol in the addition reactions and a range of options for further elaboration of the alkynyl group in the homopropargylic alcohol adducts.

Experimental Section

(2*S*,3*S*,4*S*)-1-(Triethylsilyl)oxy-5-hexyn-3-ol (3). To a cold (0 °C) solution of tetrakis-triphenylphosphine palladium-(0) (287 mg, 0.25 mmol) in THF (225 mL) was added propargyl mesylate **2**[4] (2.66 g, 19.9 mmol) in THF (10 mL) and then aldehyde **1** (2.01 g, 10.0 mmol) in THF (10 mL). Diethylzinc (28.9 mL, 1 M in hexane, 28.9 mmol) was added dropwise over 20 min. The resultant solution was stirred for 18 h at 0 °C, allowed to warm to room temperature over 3 h, and stirred an additional 2 h. The reaction mixture was cooled to 0 °C and quenched by the dropwise addition of saturated aqueous NH_4Cl (***Caution: vigorous evolution of gaseous ethane***). Upon warming, Et_2O was added, and the organic layer was washed with brine. The aqueous layer was extracted with

(21) Kocovsky, P. *Tetrahedron Lett.* **1986**, *27*, 5521.
(22) Oikawa, Y.; Yoshioka, T.; Yonemitsu, O. *Tetrahedron Lett.* **1982**, *23*, 885.

Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and concentration followed by flash chromatography (14:1 to 8:1 hexanes−EtOAc) provided homopropargyl alcohol **3** (1.58 g, 62%) as a clear oil: R_f 0.65 (4:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −4.3 (*c* 1.4, $CHCl_3$); IR (film) 3488 (br), 3312 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.67 (d, J = 4.8 Hz, 2H), 3.61 (ddd, J = 7.2, 3.9, 3.9 Hz, 1 H), 2.77 (d, J = 3.9 Hz, 1 H), 2.64 (qdd, J = 6.9, 6.9, 2.4 Hz, 1 H), 2.12 (d, J = 2.4 Hz, 1 H), 1.84−1.74 (m, 1 H), 1.18 (d, J = 6.9 Hz, 3 H), 0.95 (t, J = 7.8 Hz, 9 H), 0.95 (d, J = 6.6 Hz, 3 H), 0.59 (q, J = 7.8 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 86.48, 76.13, 70.08, 66.99, 37.27, 30.53, 17.52, 10.11, 6.69, 4.22. Anal. Calcd for $C_{14}H_{28}O_2Si$: C, 65.57; H, 11.00. Found: C, 65.72; H, 11.03.

(2*S*,3*S*,4*S*)-3-(Methoxymethyl)oxy-1-(triethylsilyl)oxy-5-hexyne (4). To a cold (0 °C) solution of alcohol **3** (1.58 g, 6.2 mmol) in CH_2Cl_2 (50 mL) were added *N*,*N*-diisopropylethylamine (21.5 mL, 123.2 mmol), chloromethyl methyl ether (4.7 mL, 61.6 mmol), and tetrabutylammonium iodide (227 mg, 0.62 mmol). The reaction mixture was immediately allowed to warm to room temperature and protected from light. After 18 h, saturated aqueous $NaHCO_3$ was added along with Et_2O. The organic layer was washed with brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and concentration followed by flash chromatography (16:1 hexanes−EtOAc) provided alkyne **4** (1.73 g, 94%) as a clear oil: R_f 0.51 (4:1 hexanes−EtOAc); $[\alpha]^{20}_D$ +19.5 (*c* 1.4, $CHCl_3$); IR (film) 3310, 1092, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.77 (d, J = 6.9 Hz, 1 H), 4.72 (d, J = 6.9 Hz, 1 H), 3.60 (dd, J = 9.9, 6.0 Hz, 1 H), 3.52 (dd, J = 9.9, 6.9 Hz, 1 H), 3.51 (dd, J = 5.7, 4.2 Hz, 1 H), 3.41 (s, 3 H), 2.81−2.71 (m, 1 H), 2.07 (d, J = 2.4 Hz, 1 H), 1.99−1.87 (m, 1 H), 1.22 (d, J = 6.9 Hz, 3 H), 0.95 (t, J = 8.1 Hz, 9 H), 0.95 (d, J = 6.9 Hz, 3 H), 0.58 (q, J = 8.1 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 98.22, 86.72, 81.99, 69.56, 65.37, 56.12, 38.61, 29.74, 18.04, 11.81, 6.79, 4.37. Anal. Calcd for $C_{16}H_{32}O_3Si$: C, 63.95; H, 10.73. Found: C, 63.97; H, 10.61.

(2*S*,3*S*,4*S*)-1,3-(4-Methoxybenzylidene)dioxy-5-heptyn-7-ol (7). To a cold (−78 °C) solution of alkyne **6**[4] (598 mg, 2.3 mmol) in THF (15 mL) was added BuLi (1.58 mL, 1.6 M in hexane, 2.5 mmol) dropwise. The solution was allowed to warm to −40 °C, stirred for 1 h, and recooled to −78 °C. Solid paraformaldehyde (140 mg, 4.6 mmol) was then added in one portion, and the resultant cloudy solution was stirred for 10 min before being allowed to warm to room temperature. The solution cleared within 1.5 h and was stirred for an additional 16 h. The mixture was quenched with water, and Et_2O was added. The organic layer was washed with brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and concentration followed by flash chromatography (3:2 hexanes−EtOAc with 1% triethylamine) provided alcohol **7** (575 mg, 86%) as a viscous syrup: R_f 0.26 (2:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −88.9 (*c* 2.6, $CHCl_3$); IR (film) 3421 (br), 2240 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.43 (d, J = 9.0 Hz, 2 H), 6.87 (d, J = 9.0 Hz, 2 H), 5.48 (s, 1 H), 4.13 (m, 2 H), 4.01 (m, 2 H), 3.77 (s, 3 H), 3.74 (dd, J = 9.9, 2.4 Hz, 1H), 2.66 (m, 1 H), 2.25 (br, 1 H), 1.64 (m, 1 H), 1.14 (d, J = 6.6 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 159.73, 131.08, 127.28, 113.46, 101.61, 88.07, 82.53, 79.16, 73.44, 55.15, 51.04, 29.66, 28.62, 15.79, 10.51.

(2*S*,3*R*,4*S*,5*S*,7*S*,10*S*,11*S*,12*S*)-5-(*tert*-Butyldimethylsilyl)oxy-1,3-(4-methoxybenzylidene)dioxy-11-(methoxymethyl)oxy-13-(triethylsilyl)oxy-8-tridecyn-7-ol (11) and (2*S*,3*R*,4*S*,5*S*,7*R*,10*S*,11*S*,12*S*)-5-(*tert*-Butyldimethylsilyl)oxy-1,3-(4-methoxybenzylidene)dioxy-11-(methoxymethyl)oxy-13-(triethylsilyl)oxy-8-tridecyn-7-ol (12). To a cold (−50 °C) solution of alkyne **4** (1.4 g, 4.7 mmol) and 4 Å molecular sieves (2 g) in THF (40 mL) was added BuLi (1.9 mL, 2.5 M in hexane, 4.7 mmol) dropwise. The solution was allowed to warm to −40 °C over 1 h. Lithium bromide (0.68 mL, 4.0 M in THF, 2.7 mmol) was added, and the resultant solution was stirred for 15 min. The solution was cooled to −78 °C, a precooled (−78 °C) solution of aldehyde **9**[4,10] (500 mg, 1.18 mmol) in THF (10 mL) was added dropwise, and the resultant solution was placed in a −50 °C bath and allowed to warm to −40 °C over 1 h. After being stirred for 1.5 h at −40 °C, the reaction was quenched by the dropwise addition of H_2O and allowed to warm to room temperature. Et_2O was added, and the mixture was filtered through Celite. The organic layer was washed with brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and concentration followed by flash chromatography (8:1 to 4:1 to 2:1 hexanes−EtOAc with 1% triethylamine) provided alcohol **11** (650 mg, 76%) as a clear syrup. Further elution provided the minor diastereomer **12** (135 mg, 16%) as a clear syrup. Excess alkyne **4** eluted from the column first and was recovered (1.06 g, 99% recovery).

11: R_f 0.63 (2:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −35.5 (*c* 1.9, $CHCl_3$); IR (film) 3471 (br) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.40 (d, J = 8.7 Hz, 2 H), 6.86 (d, J = 8.7 Hz, 2 H), 5.39 (s, 1 H), 4.74 (d, J = 6.6 Hz, 1 H), 4.68 (d, J = 6.6 Hz, 1 H), 4.53 (dt, J = 10.2, 3.0 Hz, 1 H), 4.54−4.49 (m, 1 H), 4.08−3.98 (m, 2 H), 3.79 (s, 3 H), 3.61−3.54 (m, 2 H), 3.48−3.44 (m, 2 H), 3.37 (s, 3 H), 2.71 (m, 1 H), 2.51 (d, J = 6.9 Hz, 1 H), 2.01 (m, 1 H), 1.91−1.81 (m, 1 H), 1.78−1.65 (m, 2 H), 1.58 (m, 1 H), 1.15 (d, J = 6.9 Hz, 3 H), 1.04 (d, J = 6.9 Hz, 3 H), 0.95 (t, J = 8.1 Hz, 9 H), 0.90 (s, 9 H), 0.89 (d, J = 6.9 Hz, 3 H), 0.83 (d, J = 7.2 Hz, 3 H), 0.58 (q, J = 8.1 Hz, 6 H), 0.11 (s, 3 H), 0.10 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.67, 131.48, 127.08, 113.42, 101.12, 98.15, 87.15, 82.92, 81.87, 80.70, 73.93, 68.36, 65.50, 59.91, 56.02, 55.22, 40.04, 38.18, 29.88, 29.81, 25.88, 18.03, 17.67, 11.35, 10.78, 8.16, 6.80, 4.37, −4.39, −4.66. Anal. Calcd for $C_{39}H_{70}O_8Si_2$: C, 64.78; H, 9.76. Found: C, 64.67; H, 9.83.

12: R_f 0.46 (2:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −38.0 (*c* 1.2, $CHCl_3$); IR (film) 3602−3226 (br) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.38 (d, J = 8.7 Hz, 2 H), 6.86 (d, J = 8.7 Hz, 2 H), 5.39 (s, 1 H), 4.73 (d, J = 6.6 Hz, 1 H), 4.66 (d, J = 6.6 Hz, 1 H), 4.48 (td, J = 6.3, 1.5 Hz, 1 H), 4.36 (dt, J = 10.8, 3.0 Hz, 1 H), 4.04 (dd, J = 11.1, 2.1 Hz, 1 H), 3.98 (dd, J = 11.1, 1.2 Hz, 1 H), 3.78 (s, 3 H), 3.58 (dd, J = 9.9, 1.5 Hz, 1 H), 3.54 (dd, J = 9.9, 6.3 Hz, 1 H), 3.47−3.36 (m, 2 H), 3.36 (s, 3 H), 3.13 (br, 1 H), 2.65−2.50 (m, 1 H), 1.98 (m, 1 H), 1.91−1.78 (m, 2 H), 1.67 (ddd, J = 13.2, 6.3, 3.0 Hz, 1 H), 1.61−1.56 (m, 1 H), 1.15 (d, J = 6.9 Hz, 3 H), 0.94 (t, J = 7.8 Hz, 9 H), 0.94 (d, J = 6.9 Hz, 3 H), 0.89 (s, 9 H), 0.86 (d, J = 6.9 Hz, 3 H), 0.82 (d, J = 6.9 Hz, 3 H), 0.58 (q, J = 7.8 Hz, 6 H), 0.10 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.74, 131.42, 127.16, 113.42, 101.21, 98.13, 87.66, 82.09, 81.79, 80.54, 73.86, 70.51, 65.50, 61.75, 55.95, 55.18, 40.32, 38.25, 37.99, 29.81, 29.70, 25.79, 17.91, 17.54, 11.03, 10.67, 8.00, 6.76, 4.33, −4.35, −4.81.

Mitsunobu Inversion of Propargylic Alcohol 12. (2*S*,3*R*,4*S*,5*S*,7*S*,10*S*,11*S*,12*S*)-7-Benzoyloxy-5-(*tert*-butyldimethylsilyl)oxy-1,3-(4-methoxybenzylidene)dioxy-11-(methoxymethyl)oxy-13-(triethylsilyl)oxy-8-tridecyne (13). A solution of alcohol **12** (135 mg, 0.19 mmol) in THF (8 mL) was treated with triphenylphosphine (98 mg, 0.37 mmol), benzoic acid (46 mg, 0.37 mmol), and diisopropyl azodicarboxylate (DIAD) (73 μL, 0.37 mmol). The resultant solution was stirred at room temperature for 21 h, concentrated in vacuo, and subjected to flash chromatography (12:1 to 8:1 to 4:1 hexanes−EtOAc with 1% triethylamine) to provide benzoate **13** (126 mg, 82%) as a clear oil: R_f 0.51 (4:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −47.5 (*c* 2.8, $CHCl_3$); IR (film) 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.77 (d, J = 8.7 Hz, 2 H), 7.41 (m, 1 H), 7.37 (d, J = 8.7 Hz, 2 H), 7.10 (t, J = 7.8 Hz, 2 H), 6.79 (d, J = 8.7 Hz, 2 H), 5.52 (m, 1 H), 5.50 (s, 1 H), 4.75 (d, J = 6.6 Hz, 1 H), 4.63 (d, J = 6.6 Hz, 1 H), 4.36 (dt, J = 11.4, 3.0 Hz, 1 H), 4.10 (dd, J = 11.1, 2.1 Hz, 1 H), 4.03 (d, J = 11.1 Hz, 1 H), 3.77 (s, 3 H), 3.69 (dd, J = 10.5, 2.1 Hz, 1 H), 3.58 (dd, J = 9.9, 6.3 Hz, 1 H), 3.49 (dd, J = 7.2, 3.6 Hz, 1 H), 3.45 (dd, J = 9.9, 6.6 Hz, 1 H), 3.22 (s, 3 H), 2.75 (m, 1 H), 2.17−1.99 (m, 2 H), 1.92−1.83 (m, 2 H), 1.62 (m, 1 H), 1.16 (d, J = 6.6 Hz, 3 H), 1.15 (d, J = 6.9 Hz, 3 H), 0.93 (t, J = 8.1 Hz, 9 H), 0.87 (d, J = 6.9 Hz, 3 H), 0.87 (s, 9 H), 0.86 (d, J = 6.9 Hz, 3 H), 0.56 (q, J = 8.1 Hz, 6 H), −0.02 (s, 3 H), −0.13 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.36, 159.61, 132.50, 131.43, 130.05, 129.37, 128.12, 127.09, 113.51, 101.16, 98.17, 87.75, 81.78, 80.73, 79.79, 73.94, 66.54, 65.54, 62.02, 55.87, 55.17, 39.88, 38.05, 36.74, 30.01, 29.79, 25.83, 17.94, 17.50, 11.06, 10.70, 7.83, 6.76, 4.33, −4.50, −5.03.

Debenzoylation of the Mitsunobu Inversion Product 13 (Alcohol 11). To a cold (−78 °C) solution of benzoate **13**

(110 mg, 0.13 mmol) in CH_2Cl_2 (10 mL) was added diisobutylaluminum hydride (0.28 mL, 1 M in hexane, 0.28 mmol) dropwise. After 30 min, saturated aqueous sodium potassium tartrate (Rochelle's salt) was added dropwise ***(Caution: vigorous evolution of H_2 may result)***, and the mixture was allowed to warm to room temperature. Et_2O and H_2O were added, and the biphasic mixture was stirred vigorously for 2 h. The layers were separated, and the organic solution was washed with brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and concentration followed by flash chromatography (2:1 hexanes−EtOAc with 1% triethylamine) provided alcohol **11** (90 mg, 94%) as a clear syrup. This material was identical to authentic alcohol **11** (major diastereomer) from the acetylide/aldehyde addition step previously described.

(2*S*,3*R*,4*S*,5*S*,7*S*,8*Z*,10*S*,11*S*,12*S*)-5-(*tert*-Butyldimethylsilyl)oxy-1,3-(4-methoxybenzylidene)dioxy-11-(methoxymethyl)oxy-13-(triethylsilyl)oxy-8-tridecen-7-ol (14). A solution of propargyl alcohol **11** (338 mg, 0.47 mmol) in toluene (6 mL) was treated with $Pd/CaCO_3$ poisoned with Pb (5% Pd, 75 mg). Hydrogen was bubbled through the reaction mixture for 20 min, and the resultant suspension was stirred vigorously for 24 h under a balloon atmosphere of H_2. After filtration through Celite with Et_2O, the solvents were removed in vacuo to provide allylic alcohol **14** as a viscous syrup which did not require any further purification: $[\alpha]^{20}_D$ −14.3 (*c* 1.7, $CHCl_3$); IR (film) 3570−3337 (br) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.41 (d, *J* = 9.0 Hz, 2 H), 6.87 (d, *J* = 9.0 Hz, 2 H), 5.46−5.34 (m, 2 H), 5.40 (s, 1 H), 4.63−4.52 (m, 1 H), 4.59 (d, *J* = 6.6 Hz, 1 H), 4.55 (d, *J* = 6.6 Hz, 1 H), 4.42 (dt, *J* = 8.7, 3.0 Hz, 1 H), 4.08−3.99 (m, 2 H), 3.80 (s, 3 H), 3.64 (d, *J* = 10.8, 2.1 Hz, 1 H), 3.53 (dd, *J* = 9.9, 6.9 Hz, 1 H), 3.46 (dd, *J* = 9.9, 6.9 Hz, 1 H), 3.43−3.37 (m, 1 H), 3.33 (s, 3 H), 2.80 (m, 1 H), 2.17 (d, *J* = 3.9 Hz, 1 H), 2.04 (m, 1 H), 1.82 (m, 1 H), 1.66−1.48 (m, 3 H), 1.16 (d, *J* = 6.9 Hz, 3 H), 0.95 (t, *J* = 8.1 Hz, 9 H), 0.95 (d, *J* = 6.9 Hz, 3 H), 0.91 (s, 9 H), 0.86 (d, *J* = 6.6 Hz, 3 H), 0.84 (d, *J* = 6.9 Hz, 3 H), 0.58 (q, *J* = 8.1 Hz, 6 H), 0.10 (s, 3 H), 0.09 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.67, 134.46, 132.61, 131.50, 127.06, 113.47, 101.10, 98.02, 82.73, 80.89, 73.99, 68.24, 65.62, 65.33, 55.98, 55.23, 40.13, 38.39, 38.26, 35.58, 29.88, 25.90, 18.48, 18.04, 10.87, 10.65, 8.40, 6.81, 4.42, −4.46, −4.74. Anal. Calcd for $C_{39}H_{72}O_8Si_2$: C, 64.60; H, 10.01. Found: C, 64.53; H, 9.92. On occasion, analysis of the crude reaction mixture by ^1H NMR revealed the presence of starting alkyne (starting material and product are indistinguishable by TLC). This material could be resubjected to the above conditions (typically decreasing the catalyst loading by 50%) until complete formation of the desired (*Z*)-allylic alcohol was realized without any loss in yield or purity.

(2*S*,3*R*,4*S*,5*S*,7*S*,8*Z*,10*S*,11*S*,12*S*)-5-(*tert*-Butyldimethylsilyl)oxy-7,11-di(methoxymethyl)oxy-1,3-(4-methoxybenzylidene)dioxy-13-(triethylsilyl)oxy-8-tridecene (15). To a cold (0 °C) solution of alcohol **14** (402 mg, 0.56 mmol) in CH_2Cl_2 (15 mL) were added *N*,*N*-diisopropylethylamine (1.9 mL, 11.1 mmol), chloromethyl methyl ether (0.42 mL, 5.6 mmol), and tetrabutylammonium iodide (21 mg, 0.06 mmol). The reaction was immediately allowed to warm to room temperature and protected from light. After 19 h, saturated aqueous $NaHCO_3$ was added along with Et_2O. The organic layer was washed with brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and concentration followed by flash chromatography (8:1 to 4:1 hexanes−EtOAc with 1% triethylamine) provided allylic ether **15** (408 mg, 95%) as a clear oil: R_f 0.40 (4:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −28.5 (*c* 0.85, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 7.43 (d, *J* = 8.7 Hz, 2 H), 6.84 (d, *J* = 8.7 Hz, 2 H), 5.51 (t, *J* = 10.8 Hz, 1 H), 5.43 (s, 1 H), 5.26 (dd, *J* = 10.8, 9.3 Hz, 1 H), 4.61 (d, *J* = 6.6 Hz, 1 H), 4.59 (d, *J* = 6.6 Hz, 1 H), 4.57 (d, *J* = 6.6 Hz, 1 H), 4.51−4.39 (m, 2 H), 4.38 (d, *J* = 6.6 Hz, 1 H), 4.06 (dd, *J* = 11.4, 2.1 Hz, 1 H), 4.01 (dd, *J* = 11.4, 1.2 Hz, 1 H), 3.79 (s, 3 H), 3.60 (dd, *J* = 10.5, 1.8 Hz, 1 H), 3.54 (dd, *J* = 9.6, 7.2 Hz, 1 H), 3.44−3.39 (m, 2 H), 3.34 (s, 3 H), 3.11 (s, 3 H), 2.67 (m, 1 H), 1.97 (m, 1 H), 1.89−1.78 (m, 1 H), 1.69−1.57 (m, 2 H), 1.42 (ddd, *J* = 13.8, 9.6, 1.5 Hz, 1 H), 1.16 (d, *J* = 6.9 Hz, 3 H), 0.95 (d, *J* = 6.9 Hz, 3 H), 0.95 (t, *J* = 8.1 Hz, 9 H), 0.90 (s, 9 H), 0.87 (d, *J* = 6.9 Hz, 3 H), 0.79 (d, *J* = 7.2 Hz, 3 H), 0.58 (q, *J* = 8.1 Hz, 6 H), 0.09 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.58, 135.73, 131.76, 130.27, 127.22, 113.22, 101.26, 97.83, 94.08, 82.74, 80.87, 74.02, 69.56, 67.77, 65.62, 55.89, 55.51, 55.23, 40.54, 38.61, 38.06, 35.56, 29.85, 25.90, 18.47, 18.04, 10.89, 7.65, 6.80, 4.42, −4.52. Anal. Calcd for $C_{41}H_{76}O_9Si_2$: C, 64.02; H, 9.96. Found: C, 64.24; H, 9.85.

(2*S*,3*R*,4*S*,5*S*,7*S*,8*Z*,10*S*,11*S*,12*S*)-5-(*tert*-Butyldimethylsilyl)oxy-7,11-di(methoxymethyl)oxy-1,3(4-methoxybenzylidene)dioxy-8-tridecen-13-ol (16). A polypropylene reaction vessel was charged with silyl ether **15** (313 mg, 0.41 mmol) and THF (20 mL). To this solution was added 3 mL of a stock solution of HF−pyridine complex in pyridine and THF. (The stock solution was prepared by adding 1.25 mL of HF−pyridine complex and 5 mL of pyridine to 12.5 mL of THF in a 30 mL polypropylene screw top vial. This solution was stored at 5 °C and used over several months without any loss in reactivity.) The resultant solution was stirred for 3.5 h, at which time the reaction was judged complete by TLC. The mixture was quenched by the careful dropwise addition of saturated aqueous $NaHCO_3$ until bubbling ceased. Et_2O was added, and the organic solution was washed with brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and concentration followed by flash chromatography (1:1 hexanes−EtOAc with 1% triethylamine) provided alcohol **16** (266 mg, 99%) as a viscous syrup: R_f 0.69 (1:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −6.0 (*c* 1.9, $CHCl_3$); IR (film) 3599−3263 (br) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.42 (d, *J* = 8.7 Hz, 2 H), 6.84 (d, *J* = 8.7 Hz, 2 H), 5.43 (s, 1 H), 5.42 (t, *J* = 10.8 Hz, 1 H), 5.28 (dd, *J* = 10.8, 9.0 Hz, 1 H), 4.63 (d, *J* = 6.6 Hz, 1 H), 4.57 (d, *J* = 6.6 Hz, 1 H), 4.51 (d, *J* = 6.6 Hz, 1 H), 4.50−4.42 (m, 2 H), 4.37 (d, *J* = 6.6 Hz, 1 H), 4.06 (dd, *J* = 11.1, 2.1 Hz, 1 H), 4.00 (dd, *J* = 11.1, 1.2 Hz, 1 H), 3.79 (s, 3 H), 3.61 (dd, *J* = 10.5, 2.1 Hz, 1 H), 3.51−3.42 (m, 3 H), 3.38 (s, 3 H), 3.13−3.09 (m, 1 H), 3.10 (s, 3 H), 2.81−2.68 (m, 1 H), 2.01−1.88 (m, 2 H), 1.71−1.57 (m, 2 H), 1.38 (dd, *J* = 12.6, 9.6 Hz, 1 H), 1.16 (d, *J* = 6.6 Hz, 3 H), 0.92 (d, *J* = 6.9 Hz, 3 H), 0.90 (s, 9 H), 0.81 (d, *J* = 7.2 Hz, 3 H), 0.79 (d, *J* = 7.5 Hz, 3 H), 0.09 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.58, 135.62, 131.74, 130.71, 127.22, 113.22, 101.28, 98.62, 93.95, 82.77, 80.83, 74.01, 69.14, 67.75, 64.77, 56.12, 55.50, 55.25, 40.62, 38.19, 36.98, 35.64, 29.85, 25.91, 18.04, 17.76, 10.89, 10.04, 7.68, −4.45, −4.58. Anal. Calcd for $C_{35}H_{62}O_9Si$: C, 64.18; H, 9.54. Found: C, 64.19; H, 9.43.

Aldehyde 17. To a solution of alcohol **16** (273 mg, 0.42 mmol) in CH_2Cl_2 (10 mL) was added the Dess−Martin periodinane reagent (213 mg, 0.50 mmol). The resultant solution was stirred for 35 min and quenched by the simultaneous addition of saturated aqueous $Na_2S_2O_3$ (3 mL) and saturated aqueous $NaHCO_3$ (3 mL). Et_2O was added, and the solution was stirred vigorously for 20 min. The organic solution was washed with brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and removal of the solvent in vacuo provided aldehyde **17** (273 mg, 99%) as a clear oil, and this material was used immediately without further purification: R_f 0.63 (3:2 hexanes−EtOAc); $[\alpha]^{20}_D$ −43.2 (*c* 1.8, $CHCl_3$); IR (film) 1728, 1616 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.76 (s, 1 H), 7.43 (d, *J* = 8.7 Hz, 2 H), 6.83 (d, *J* = 8.7 Hz, 2 H), 5.47 (t, *J* = 10.8 Hz, 1 H), 5.43 (s, 1 H), 5.33 (dd, *J* = 10.8, 9.3 Hz, 1 H), 4.65 (d, *J* = 7.2 Hz, 1 H), 4.56 (d, *J* = 6.6 Hz, 1 H), 4.54 (d, *J* = 7.2 Hz, 1 H), 4.49−4.39 (m, 2 H), 4.38 (d, *J* = 6.6 Hz, 1 H), 4.06 (dd, *J* = 11.1, 2.1 Hz, 1 H), 4.00 (dd, *J* = 11.1, 1.2 Hz, 1 H), 3.83 (dd, *J* = 6.0, 3.3 Hz, 1 H), 3.79 (s, 3 H), 3.60 (dd, *J* = 10.8, 2.1 Hz, 1 H), 3.27 (s, 3 H), 3.11 (s, 3 H), 2.75 (dq, *J* = 16.8, 6.6 Hz, 1 H), 2.52 (qd, *J* = 6.9, 3.3 Hz, 1 H), 1.97 (m, 1 H), 1.70−1.56 (m, 2 H), 1.36 (ddd, *J* = 11.1, 9.9, 1.2 Hz, 1 H), 1.16 (d, *J* = 6.9 Hz, 3 H), 1.12 (d, *J* = 7.2 Hz, 3 H), 1.01 (d, *J* = 6.9 Hz, 3 H), 0.89 (s, 9 H), 0.80 (d, *J* = 6.9 Hz, 3 H), 0.08 (s, 6 H); ^{13}C NMR ($CDCl_3$) δ 203.89, 159.58, 133.28, 131.94, 131.73, 127.21, 113.22, 101.24, 97.52, 94.11, 81.60, 80.88, 74.02, 69.33, 67.71, 55.84, 55.53, 55.24, 49.55, 40.53, 37.47, 35.32, 29.81, 25.88, 18.47, 18.05, 10.88, 8.07, 7.60, −4.48, −4.59.

Vinyl Iodide 18. A suspension of ethyl triphenylphosphonium bromide (310 mg, 0.84 mmol) in THF (8 mL) was treated with BuLi (0.33 mL, 2.5 M in hexane, 0.84 mmol) at room temperature. The resultant red solution was transferred by cannula to a cold (−78 °C) solution of iodine (212 mg, 0.84 mmol) and 4 Å molecular sieves (300 mg) in THF (20 mL). After 10 min, the orange suspension was warmed to −20 °C for 10 min. Sodium bis(trimethylsilyl)amide (0.75 mL, 1 M in THF, 0.75 mmol) was added, and the resultant ylide was stirred for 2 min at −20 °C and then cooled to −78 °C. A solution of aldehyde **17** (273 mg, 0.42 mmol) in THF (3 mL) was added by cannula, and the mixture was allowed to warm to room temperature after 5 min. The solution was stirred for 2.5 h and quenched with CH_3OH. The solvent was removed in vacuo, the residue was dissolved in a minimal amount of CH_2Cl_2, and Et_2O was added. The insoluble material was removed by filtration through a plug of silica. Concentration followed by flash chromatography (6:1 hexanes−EtOAc) provided vinyl iodide **18** (132 mg, 40%, 6:1 *Z*/*E*) as a viscous syrup: R_f 0.38 (4:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −9.6 (*c* 0.7, $CHCl_3$); IR (film) 1615, 1249, 1033 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.43 (d, *J* = 9.0 Hz, 2 H), 6.84 (d, *J* = 9.0 Hz, 2 H), 5.54 (t, *J* = 10.5 Hz, 1 H), 5.44 (s, 1 H), 5.37 (dd, *J* = 8.7, 1.2 Hz, 1 H), 5.28 (m, 1 H), 4.62−4.58 (m, 3 H), 4.45−4.40 (m, 2 H), 4.39 (d, *J* = 6.6 Hz, 1 H), 4.09−4.00 (m, 2 H), 3.79 (s, 3 H), 3.61 (dd, *J* = 10.8, 1.5 Hz, 1 H), 3.37 (s, 3 H), 3.29 (t, *J* = 5.1 Hz, 1 H), 3.11 (s, 3 H), 2.75−2.63 (m, 1 H), 2.60−2.53 (m, 1 H), 2.49 (d, *J* = 0.9 Hz, 3 H), 1.97 (m, 1 H), 1.62−1.57 (m, 2 H), 1.42 (dd, *J* = 12.9, 9.6 Hz, 1 H), 1.16 (d, *J* = 6.6 Hz, 3 H), 1.04 (d, *J* = 6.9 Hz, 3 H), 0.99 (d, *J* = 6.9 Hz, 3 H), 0.90 (s, 9 H), 0.80 (d, *J* = 6.9 Hz, 3 H), 0.09 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.63, 138.43, 134.62, 130.82, 127.25, 113.26, 101.30, 97.83, 94.09, 85.23, 80.90, 77.20, 74.05, 69.56, 67.84, 56.03, 55.54, 55.26, 44.03, 40.62, 38.02, 35.23, 33.64, 29.89, 25.96, 18.48, 18.08, 14.32, 10.90, 7.85, −4.40, −4.60.

Suzuki Adduct 27. To a cold (−78 °C) solution of alkyl iodide **25** (210 mg, 0.35 mmol) in Et_2O (5 mL) was added rapidly *t*-BuLi (0.44 mL, 1.7 M in pentane, 0.75 mmol). After 3 min, 9-methoxy-9-borabicyclo[3.3.1]nonane (0.82 mL, 1 M in hexanes, 0.82 mmol) was added followed by THF (5 mL). The solution was stirred for 10 min at −78 °C and then allowed to warm to room temperature for 1.25 h. Aqueous 3 M K_3PO_4 (0.27 mL, 0.80 mmol) was added followed by the addition of vinyl iodide **18** (126 mg, 0.16 mmol) in DMF (5 mL). $PdCl_2$(dppf) (13 mg, 0.016 mmol) was added, and the resultant dark solution was stirred for 16 h. Et_2O was added, and the organic solution was washed with H_2O and then brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and concentration followed by flash chromatography (6:1 to 4:1 hexanes−EtOAc with 1% triethylamine) provided coupled product **27** (131 mg, 74%) as a clear oil: R_f 0.55 (2:1 hexanes−EtOAc); ^1H NMR ($CDCl_3$) δ 7.43 (d, *J* = 8.7 Hz, 2 H), 7.27 (d, *J* = 8.7 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 6.84 (d, *J* = 8.7 Hz, 2 H), 6.58 (dt, *J* = 17.1, 10.5 Hz, 1 H), 6.02 (t, *J* = 11.1 Hz, 1 H), 5.58−5.46 (m, 2 H), 5.43 (s, 1 H), 5.26−5.19 (m, 2 H), 5.13 (d, *J* = 10.2 Hz, 1 H), 5.07 (d, *J* = 10.2 Hz, 1 H), 4.62−4.54 (m, 4 H), 4.46−4.36 (m, 4 H), 4.09−3.98 (m, 2 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.60−3.56 (m, 2 H), 3.38 (s, 3 H), 3.15 (m, 1 H), 3.10 (m, 1 H), 3.09 (s, 3 H), 2.86 (m, 1 H), 2.68−2.53 (m, 2 H), 2.17 (t, *J* = 12.3 Hz, 1 H), 1.96−1.72 (m, 4 H), 1.64 (s, 3 H), 1.59−1.51 (m, 2 H), 1.34 (m, 1 H), 1.16 (d, *J* = 6.6 Hz, 3 H), 1.01−0.93 (m, 12 H), 0.98 (t, *J* = 7.8 Hz, 9 H), 0.91 (s, 9 H), 0.82 (d, *J* = 6.6 Hz, 3 H), 0.78 (d, *J* = 6.6 Hz, 3 H), 0.63 (q, *J* = 7.8 Hz, 6 H), 0.09 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.58, 159.06, 134.85, 134.77, 132.35, 131.75, 131.14, 130.56, 130.40, 129.03, 127.24, 117.41, 113.72, 113.22, 101.28, 97.99, 93.88, 87.04, 84.89, 80.85, 77.69, 74.70, 74.01, 69.54, 67.81, 56.05, 55.50, 55.23, 40.57, 39.94, 37.94, 36.18, 35.99, 34.76, 33.92, 29.86, 25.90, 23.27, 18.76, 18.38, 18.03, 16.51, 14.14, 10.87, 10.63, 7.83, 7.20, 5.69, −4.39, −4.65. Anal. Calcd for $C_{64}H_{108}O_{11}Si_2$: C, 69.27; H, 9.81. Found: C, 69.05; H, 9.65.

Alcohol 28. A cold (−78 °C) solution of acetal **27** (131 mg, 0.12 mmol) in CH_2Cl_2 (5 mL) was treated with diisobutylaluminum hydride (1.16 mL, 1 M in hexane, 1.16 mmol). The reaction mixture was allowed to warm to −50 °C over several hours and stirred for 18 h. Excess hydride was quenched by the dropwise addition of saturated aqueous sodium potassium tartrate ***(Caution: vigorous evolution of H_2 may result)***, and the mixture was allowed to warm to room temperature. After being stirred vigorously for 1 h, the organic solution was washed with brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and concentration followed by flash chromatography (2:1 hexanes−EtOAc with 1% triethylamine) provided alcohol **28** (103 mg, 79%) as a clear oil: R_f 0.46 (2:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −3.2 (*c* 2.8, $CHCl_3$); IR (film) 3479, 1614 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.29 (d, *J* = 8.4 Hz, 2 H), 7.27 (d, *J* = 8.7 Hz, 2 H), 6.87 (d, *J* = 8.4 Hz, 2 H), 6.85 (d, *J* = 8.7 Hz, 2 H), 6.58 (dt, *J* = 17.1, 10.8 Hz, 1 H), 6.02 (t, *J* = 11.1 Hz, 1 H), 5.59−5.46 (m, 2 H), 5.28−5.09 (m, 4 H), 4.79 (d, *J* = 10.8 Hz, 1 H), 4.65−4.40 (m, 9 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.61−3.55 (m, 3 H), 3.39 (m, 1 H), 3.37 (s, 3 H), 3.18 (s, 3 H), 3.18−3.10 (m, 2 H), 2.86 (m, 1 H), 2.71−2.55 (m, 2 H), 2.20 (t, *J* = 12.3 Hz, 1 H), 2.10−1.67 (m, 6 H), 1.64 (s, 3 H), 1.43 (m, 1 H), 1.01−0.93 (m, 12 H), 0.98 (t, *J* = 7.8 Hz, 9 H), 0.91 (s, 9 H), 0.88 (d, *J* = 7.2 Hz, 3 H), 0.84 (d, *J* = 6.3 Hz, 3 H), 0.78 (d, *J* = 6.9 Hz, 3 H), 0.63 (q, *J* = 7.8 Hz, 6 H), 0.10 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 159.05, 158.78, 135.16, 134.97, 132.38, 131.59, 131.16, 130.44, 129.04, 128.60, 117.36, 113.74, 113.51, 97.82, 94.11, 86.82, 84.84, 80.21, 77.68, 74.66, 73.33, 69.66, 68.33, 66.09, 56.05, 55.67, 55.21, 42.76, 39.97, 38.17, 37.62, 36.19, 36.07, 34.80, 34.47, 33.92, 25.90, 23.31, 18.75, 18.24, 16.17, 13.97, 10.69, 9.80, 9.51, 7.19, 5.69, −4.22, −4.63. Anal. Calcd for $C_{64}H_{110}O_{11}Si_2$: C, 69.14; H, 9.97. Found: C, 69.44; H, 10.02.

Methyl Ester 31. To a solution of alcohol **28** (103 mg, 0.092 mmol) in CH_2Cl_2 (4 mL) was added the Dess−Martin periodinane reagent (47 mg, 0.11 mmol). The resultant solution was stirred for 1 h and quenched by the simultaneous addition of saturated aqueous $Na_2S_2O_3$ (2 mL) and saturated aqueous $NaHCO_3$ (2 mL). Et_2O was added, and the solution was stirred vigorously for 20 min. The organic solution was washed with saturated aqueous $Na_2S_2O_3$, saturated aqueous $NaHCO_3$, and brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and removal of the solvent in vacuo provided aldehyde **29** (102 mg, 99%) as a clear oil. This material was used immediately without further purification.

An aqueous solution of $NaClO_2$ (14 mg, ∼80% pure, 0.12 mmol) and $NaH_2PO_4 \cdot H_2O$ (16 mg, 0.12 mmol) was added dropwise to a solution of aldehyde **29** (102 mg, 0.092 mmol) in *t*-BuOH (6 mL) and 2-methyl-2-butene (3 mL). The resultant mixture was stirred at room temperature for 1 h, and then an additional 1 equiv of $NaClO_2/NaH_2PO_4 \cdot H_2O$ was added. After an additional 1 h, the solvents were removed in vacuo, and the residue was taken up in Et_2O. The solution was acidified by the dropwise addition of 10% aqueous HCl. The organic solution was washed with brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and concentration provide carboxylic acid **30** (102 mg, 98%) as an oil. This material was used immediately without further purification.

To a solution of carboxylic acid **30** (102 mg, 0.091 mmol) in benzene (3.5 mL) and methanol (1 mL) was added dropwise (trimethylsilyl)diazomethane (2 M in hexanes) until a yellow tint persisted. After 15 min, the solvents were removed in vacuo, and the residue was subjected to flash chromatography (4:1 hexanes−EtOAc) to provide methyl ester **31** (84 mg, 82%) as a clear oil: R_f 0.73 (2:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −8.5 (*c* 1.4, $CHCl_3$); IR (film) 1739, 1616, 1035 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.27 (d, *J* = 8.7 Hz, 2 H), 7.25 (d, *J* = 8.7 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 6.82 (d, *J* = 8.7 Hz, 2 H), 6.58 (dt, *J* = 16.8, 10.8 Hz, 1 H), 6.02 (t, *J* = 11.1 Hz, 1 H), 5.56 (d, *J* = 11.1 Hz, 1 H), 5.48 (d, *J* = 11.1 Hz, 1 H), 5.33−5.10 (m, 4 H), 4.67−4.41 (m, 9 H), 4.31 (d, *J* = 10.2 Hz, 1 H), 3.80 (s, 3 H), 3.79 (s, 3 H), 3.74 (dd, *J* = 10.2, 2.4 Hz, 1 H), 3.68 (s, 3 H), 3.58 (t, *J* = 5.4 Hz, 1 H), 3.37 (s, 3 H), 3.22 (s, 3 H), 3.14 (m, 2 H), 2.86 (m, 1 H), 2.71−2.55 (m, 3 H), 2.20 (t, *J* = 12.0 Hz, 1 H), 1.95−1.91 (m, 2 H), 1.85−1.67 (m, 3 H), 1.64 (s, 3 H), 1.43 (m, 1 H), 1.17 (d, *J* = 6.9 Hz, 3 H), 0.94 (m, 21 H), 0.89 (s, 9 H), 0.82 (d,

J = 6.6 Hz, 3 H), 0.81 (d, J = 6.9 Hz, 3 H), 0.62 (q, J = 7.8 Hz, 6 H), 0.08 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 175.97, 159.06, 158.75, 135.19, 135.01, 132.39, 131.30, 131.14, 130.52, 130.40, 129.03, 128.75, 117.34, 113.72, 113.39, 97.79, 94.16, 86.76, 84.87, 81.19, 77.65, 74.72, 73.03, 69.59, 68.11, 56.05, 55.70, 55.21, 51.62, 42.85, 41.37, 39.98, 38.14, 36.23, 36.07, 34.82, 34.40, 33.95, 25.88, 23.33, 18.75, 18.23, 18.06, 16.09, 13.94, 10.65, 9.79, 8.83, 7.19, 5.69, −4.30, −4.67. Anal. Calcd for $C_{65}H_{110}O_{12}Si_2$: C, 68.50; H, 9.73. Found: C, 68.66; H, 9.76.

Alcohol 33. To a cold (0 °C) solution of triethylsilyl ether **31** (40 mg, 0.035 mmol) in methanol (5 mL) was added *p*-TsOH·H_2O (∼2 mg, 0.010 mmol). The resultant mixture was stirred for 1 h at 0 °C. Triethylamine (2 mL) was added, and the mixture was concentrated under reduced pressure. The residue was purified by flash chromatography (4:1 to 2:1 hexanes−EtOAc) to provide alcohol **33** (26 mg, 72%) as a clear oil: R_f 0.58 (2:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −12.2 (*c* 1.05, $CHCl_3$); IR (film) 3551 (br), 1740, 1033 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.28 (d, J = 8.7 Hz, 2 H), 7.25 (d, J = 9.0 Hz, 2 H), 6.86 (d, J = 9.0 Hz, 2 H), 6.81 (d, J = 8.7 Hz, 2 H), 6.65 (dt, J = 17.1, 10.5 Hz, 1 H), 6.15 (t, J = 10.8 Hz, 1 H), 5.55 (t, J = 10.5 Hz, 1 H), 5.39−5.08 (m, 5 H), 4.66−4.47 (m, 8 H), 4.47−4.40 (m, 2 H), 4.30 (d, J = 10.5 Hz, 1 H), 3.79 (s, 3 H), 3.78 (s, 3 H), 3.73 (dd, J = 10.5, 2.4 Hz, 1 H), 3.68 (s, 3 H), 3.39 (m, 1 H), 3.37 (s, 3 H), 3.21 (s, 3 H), 3.14 (t, J = 5.4 Hz, 1 H), 2.81 (m, 1 H), 2.71−2.58 (m, 3 H), 2.27 (t, J = 12.0 Hz, 1 H), 2.04 (m, 1 H), 1.96−1.89 (m, 3 H), 1.70 (m, 1 H), 1.67 (s, 3 H), 1.44 (dd, J = 13.5, 10.8 Hz, 1 H), 1.17 (d, J = 7.2 Hz, 3 H), 1.04 (d, J = 6.9 Hz, 3 H), 0.99 (d, J = 6.6 Hz, 3 H), 0.97 (d, J = 6.3 Hz, 3 H), 0.94 (d, J = 6.9 Hz, 3 H), 0.89 (s, 9 H), 0.86 (d, J = 6.9 Hz, 3 H), 0.80 (d, J = 6.9 Hz, 3 H), 0.07 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 176.01, 159.16, 158.77, 135.17, 132.46, 132.15, 131.29, 130.72, 130.54, 130.48, 129.15, 128.76, 118.26, 113.79, 113.40, 97.90, 94.16, 87.38, 86.78, 81.21, 77.08, 74.37, 73.03, 69.59, 68.09, 56.08, 55.70, 55.23, 51.66, 42.91, 41.45, 38.10, 36.93, 36.45, 36.19, 34.87, 34.64, 33.51, 25.87, 23.44, 18.27, 18.06, 17.06, 16.11, 13.89, 9.79, 8.96, 8.18, −4.28, −4.69.

Carbamate 34. A solution of alcohol **33** (41 mg, 0.040 mmol) in CH_2Cl_2 (3 mL) was treated with trichloroacetyl isocyanate (5 μL, 0.042 mmol) at room temperature. After 10 min, the solution was concentrated under reduced pressure, and the residue was taken up in methanol (4 mL). To this solution was added K_2CO_3 (30 mg), and the mixture was stirred for 1.25 h. The reaction mixture was concentrated under reduced pressure, and the residue was taken up in Et_2O. The organic solution was washed with H_2O and brine. The aqueous layer was extracted with Et_2O, and the combined extracts were dried over Na_2SO_4. Filtration and concentration followed by flash chromatography (2:1 hexanes−EtOAc) provided carbamate **34** (39 mg, 93%) as a foam: R_f 0.37 (2:1 hexanes−EtOAc); $[\alpha]^{20}_D$ −3.7 (*c* 1.1, $CHCl_3$); IR (film) 3498, 3365, 1730, 1612 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (d, J = 8.5 Hz, 2 H), 7.24 (d, J = 8.5 Hz, 2 H), 6.88 (d, J = 8.5 Hz, 2 H), 6.82 (d, J = 8.5 Hz, 2 H), 6.61 (dt, J = 16.5, 11.0 Hz, 1 H), 6.04 (t, J = 11.0 Hz, 1 H), 5.57 (t, J = 10.0 Hz, 1 H), 5.38 (t, J = 11.0 Hz, 1 H), 5.26−5.20 (m, 2 H), 5.14 (d, J = 10.0 Hz, 1 H), 5.06 (d, J = 9.5 Hz, 1 H), 4.75 (m, 1 H), 4.65−4.41 (m, 11 H), 4.30 (d, J = 10.5, 1 H), 3.80 (s, 3 H), 3.78 (s, 3 H), 3.71 (dd, J = 10.0, 2.5 Hz, 1 H), 3.68 (s, 3 H), 3.38 (s, 3 H), 3.20 (s, 3 H), 3.12 (m, 2 H), 2.97 (m, 1 H), 2.66−2.56 (m, 3 H), 2.24 (t, J = 12.0 Hz, 1 H), 2.07−1.99 (m, 2 H), 1.93 (m, 1 H), 1.77 (m, 1 H), 1.69 (dd, J = 13.5, 11.0 Hz, 1 H), 1.64 (s, 3 H), 1.41 (dd, J = 12.0, 10.5 Hz, 1 H), 1.17 (d, J = 7.0 Hz, 3 H), 1.04 (d, J = 7.0 Hz, 3 H), 0.98 (d, J = 6.5 Hz, 3 H), 0.96 (d, J = 6.5 Hz, 3 H), 0.95 (d, J = 6.5 Hz, 3 H), 0.89 (s, 9 H), 0.82 (d, J = 6.5 Hz, 3 H), 0.81 (d, J = 7.0 Hz, 3 H), 0.07 (s, 3 H), 0.04 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 176.22, 159.09, 158.78, 156.91, 134.92, 133.69, 132.62, 132.14, 131.28, 131.02, 130.59, 130.23, 129.83, 129.07, 128.73, 117.88, 113.78, 113.42, 98.00, 94.15, 87.02, 84.79, 81.35, 78.51, 74.61, 73.07, 69.64, 68.08, 56.09, 55.71, 55.26, 55.23, 51.74, 42.90, 41.61, 38.09, 37.58, 36.57, 34.79, 34.47, 33.56, 29.69, 25.87, 23.12, 18.28, 18.04, 17.40, 16.45, 13.56, 9.80, 8.98, −4.23, −4.71. Anal. Calcd for $C_{60}H_{97}NO_{13}Si$: C, 67.44; H, 9.15; N, 1.31. Found: C, 67.19; H, 9.39; N, 1.49.

(+)-Discodermolide (36). To a solution of methyl ester **34** (32 mg, 0.030 mmol) in CH_2Cl_2−H_2O (18:1, 4 mL) was added solid $NaHCO_3$ (160 mg) followed by the dropwise addition of a freshly prepared stock solution of DDQ (0.72 mL, 0.088 M in CH_2Cl_2, 0.063 mmol). The resultant green solution was stirred for 1 h, and then an additional 0.5 mL (0.044 mmol) of the stock solution of DDQ was added. After being stirred for 1 h, the solvents were removed in vacuo, and the residue was purified by flash chromatography (1:1 to 1:2 hexanes−EtOAc) to provide diol **35** as a clear oil (21 mg, 85%).

To a solution of diol **35** (16 mg, 0.020 mmol) in THF (2 mL) was added an aqueous solution of 4 N HCl (2 mL). The flask was fitted with a glass stopper, and the resultant solution was stirred at room temperature for 65 h. Saturated aqueous $NaHCO_3$ was added dropwise followed by EtOAc. The organic solution was washed with brine. The aqueous layer was extracted with EtOAc, and the combined extracts were dried over Na_2SO_4. Filtration and concentration followed by flash chromatography (10% CH_3OH−CH_2Cl_2) provided (+)-discodermolide **(36)** (8.1 mg, 72%) as a white amorphous solid: R_f 0.25 (10% CH_3OH−CH_2Cl_2); $[\alpha]^{20}_D$ +17.0 (*c* 0.41, CH_3OH); ^{1}H NMR ($CDCl_3$) δ 6.61 (dt, J = 16.8, 10.5 Hz, 1 H), 6.02 (t, J = 11.1 Hz, 1 H), 5.52 (dd, J = 11.1, 7.8 Hz, 1 H), 5.44 (t, J = 10.5 Hz, 1 H), 5.35 (t, J = 10.5 Hz, 1 H), 5.21 (d, J = 16.8 Hz, 1 H), 5.16 (d, J = 10.0 Hz, 1 H), 5.12 (d, J = 10.8 Hz, 1 H), 4.77−4.67 (m, 4 H), 4.62 (td, J = 9.9, 2.1 Hz, 1 H), 3.74 (t, J = 3.9 Hz, 1 H), 3.28 (m, 1 H), 3.19 (dd, J = 6.9, 4.8 Hz, 1 H), 2.99 (m, 1 H), 2.77 (m, 1 H), 2.69 (qd, J = 7.2, 4.5 Hz, 1 H), 2.60 (m, 1 H), 2.60−1.90 (m, 10 H), 1.67 (ddd, J = 13.8, 10.2, 3.0 Hz, 1 H), 1.64 (d, J = 0.9 Hz, 3 H), 1.31 (d, J = 7.5 Hz, 3 H), 1.07 (d, J = 6.9 Hz, 3 H), 1.02 (d, J = 6.3 Hz, 3 H), 0.99 (d, J = 6.3 Hz, 3 H), 0.98 (d, J = 6.9 Hz, 3 H), 0.94 (d, J = 6.9 Hz, 3 H), 0.83 (d, J = 6.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 174.00, 157.14, 134.29, 133.65, 133.35, 132.83, 132.11, 129.91, 129.71, 117.96, 79.00, 78.79, 75.66, 73.17, 64.30, 43.12, 40.93, 37.30, 36.10, 35.95, 35.63, 35.31, 34.75, 33.03, 23.28, 18.36, 17.46, 15.71, 15.60, 13.69, 12.60, 8.98.

Acknowledgments. This investigation was supported by Research Grant R01-AI37422 from the National Institute of Allergy and Infectious Diseases. B.J. is the recipient of an NIH postdoctoral fellowship (GM19366) from the National Institutes of General Medical Sciences. We thank Professor David Evans for helpful insight regarding the use of Et_3Si protection for α,α′-branched secondary alcohols. The ^{1}H and ^{13}C NMR spectra of (−)-discodermolide in $CDCl_3$ were provided by Professor Amos B. Smith, III, to whom we are grateful.

Supporting Information Available: Experimental procedures for **1**, **23**, **24**, **25**, and intermediates leading to **23**. ^{1}H NMR spectra for **12**, **13**, **17**, **18**, **27**, **28**, **33**, **34**, and **36** and comparison spectra for **36** (22 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.

JO9811423