Supporting Information

A Practical Improvement, Enhancing the Large-Scale Synthesis of (+)-Discodermolide:

A Third-Generation Approach

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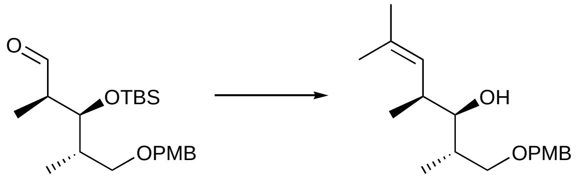
Materials and Methods. Reactions were carried out in oven or flame-dried glassware under an argon atmosphere, unless otherwise noted. All solvents were reagent grade. Diethyl ether (Et_2O) and tetrahydrofuran (THF) were freshly distilled from sodium/benzophenone under argon. *n*-Butyllithium and *t*-butyllithium were purchased from Aldrich. Reactions were magnetically stirred and monitored by thin layer chromotography (TLC) with 0.25 mm E. Merck pre-coated silica gel plates. Flash chromatography was performed with silica gel 60 (particle size 0.040 – 0.062 mm) supplied by Silicycle and Sorbent Technologies. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated. Infrared spectra were recorded on a Jasco Model FT/IR-480 Plus spectrometer. Proton and carbon-13 NMR spectra were recorded on a Bruker AMX-500 spectrometer. Chemical shifts are reported relative to either chloroform (d7.26) or benzene (d7.15) for ^{1}H-NMR and either chloroform (d77.0) or benzene (d128.0) for ^{13}C NMR. Optical rotations were measured on a Perkin-Elmer model 241 polarimeter. High resolution mass spectra were measured at the University of Pennsylvania Mass Spectrometry Service Center.

Model System

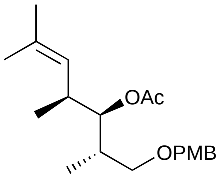


(-)-17 **(-)-19**

Alcohol (-)-19 Under argon, a solution of isopropyltriphenylphosphonium iodide (4.41 g, 10.2 mmol), in toluene (40 mL), was treated with 0.6 M NaHMDS in toluene (16.5 mL, 9.93 mmol) over 10 min. at room temperature. After an additional 15 min., the mixture was cooled to –78 ˚C. A solution of known aldehyde (-)-**17** (2.62 g, 6.89 mmol) in toluene (29 mL) was added dropwise via cannula to the ylide solution at –78 ˚C. After 5 min., the resulting solution was warmed to room temperature and stirred for 25 min. further. The reaction was quenched with MeOH (2 mL), filtered, and concentrated to afford the crude trisubstituted olefin **18** (not shown), which was taken on without purification.

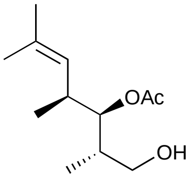
To a solution of the crude olefin **18** in MeOH (138 mL) was added 3 N HCl aq. solution (27.6 mL) over 4 h at room temperature. The mixture was stirred for 9 h, whereupon the reaction mixture was neutralized with solid $NaHCO_3$. MeOH was removed *in vacuo*, and the remaining mixture was diluted with Et_2O (50 mL), washed with H_2O, dried over Na_2SO_4, filtered, and concentrated . Flash chromatography (hexanes/EtOAc = 50/1Æ3/1) afforded alcohol (-)-**19** (1.10 g, 55%) as a colorless oil: $[a]_D^{20}$ –2.5 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3495 (brs), 2962 (s), 2930 (s), 2867 (s), 1613 (s), 1586 (m), 1514 (s), 1456 (s), 1363 (m), 1302 (m), 1249 (s), 1173 (m), 1084 (s), 1037 (s), 986 (m), 821 (m) cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.24 (d, *J* = 8.4 Hz, 2H), 6.87 (d, *J* = 8.4 Hz, 2H), 5.06 (d, *J* = 9.5 Hz, 1H), 4.45 (d, *J* = 11.5 Hz, 1H), 4.41 (d, *J* = 11.5 Hz, 1H), 3.80 (s, 3H), 3.58 (dd, *J* = 9.3, 4.0 Hz, 1H), 3.41 (dd, *J* = 9.3, 5.5 Hz, 1H), 3.28

(apparent t, *J* = 6.0 Hz, 1H), 3.12 (bs, 1H), 2.45 (m, 1H), 1.88 (m, 1H), 1.68 (s, 3H), 1.56 (s, 3H), 0.99 (d, *J* = 7.1 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 159.3, 130.3, 129.9, 129.3 (2C), 128.3, 113.8 (2C), 80.1, 74.1, 73.2, 55.2, 36.1, 35.6, 25.8, 17.8, 15.4, 14.9; high resolution mass spectrum (ES$^+$) *m/z* 315.1945 [(M+Na)$^+$; calcd for $C_{18}H_{28}O_3Na$: 315.1936].



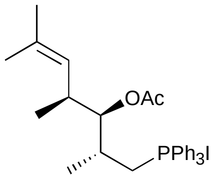
20

Acetate ester 20. To a solution of alcohol (-)-**19** (89.5 mg, 0.307 mmol) and DMAP (3.7 mg, 0.0307 mmol) in pyridine (0.77 mL) was added acetyl chloride (54.7 mL, 0.766 mmol) at room temperature. The mixture was stirred for 1.5 h, then diluted with a hexanes•EtOAc (2:1) solution (10 mL), and washed with saturated NH_4Cl aq. and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated. Preparative TLC (hexanes/EtOAc = 4/1) afforded acetate **20** (83.2 mg, 81%) as a colorless oil: ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.24 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.89 (ddd, *J* = 9.6, 1.3, 1.3 Hz, 1H), 4.76 (dd, *J* = 7.8, 4.8 Hz, 1H), 4.39 (s, 2H), 3.80 (s, 3H), 3.49 (dd, *J* = 9.2, 4.5 Hz, 1H), 3.19 (apparent t, *J* = 9.2 Hz, 1H), 2.67 (m, 1H), 2.08 (m, 1H), 2.03 (s, 3H), 1.66 (d, *J* = 1.3 Hz, 3H), 1.57 (d, *J* = 1.3 Hz, 3H), 0.96 (d, *J* = 6.9 Hz, 3H), 0.87 (d, *J* = 6.7 Hz, 3H).



21

Alcohol 21. At 0 ˚C, a solution of **20** (82.2 mg, 0.246 mmol) in CH_2Cl_2 (2.46 mL) was treated with H_2O (0.098 mL) and DDQ (61.5 mg, 0.271 mmol) and stirred for 1 h 20 min. The reaction was quenched with saturated $NaHCO_3$ aq. (4 mL) and the layers separated. The aqueous layer was then extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (hexanes/EtOAc = 20/1Æ1/1) provided primary alcohol **21** (52.2 mg, 99%) as a colorless oil): (Acyl migration precluded ^{1}H-NMR on this substrate).

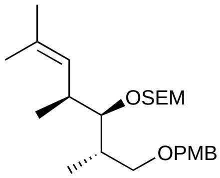


10a

Wittig salt 10a. A solution of **21** (50.5 mg, 0.236 mmol), PPh_3 (92.8 mg, 0.354 mmol) and imidazole (24.1 mg, 0.354 mmol) in benzene•Et_2O (1:2) (2.6 mL) was cooled to 0 ˚C and treated with iodine (89.8 mg, 0.354 mmol). The reaction mixture was warmed to room temperature and stirred for 3.5 h. The reaction was then quenched with saturated $NaHCO_3$ aq. (5 mL). The layers were separated, and the aqueous layer was extracted with Et_2O (3 x 10 mL). The combined organics were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (hexanes/EtOAc = 30/1) provided a mixture of the desired alkyl iodide **9a** and PPh_3, which was taken onto the next step without further purification.

To the neat alkyl iodide **9a** (mixed with PPh_3) was added additional PPh_3 (619 mg, 2.36 mmol) and *i*-Pr_2NEt (0.37 mL) at room temperature. The mixture was warmed to 100 ˚C and stirred for 17 h. The reaction mixture was cooled to room temperature and diluted with CH_2Cl_2 (0.5 mL). The resulting solution was directly purified via flash chromatography (CH_2Cl_2/CH_3CN = 5/1Æ2/1) to provide Wittig salt **10a** (80.9 mg, 59% for 2 steps) and the mixture of cyclopentane byproducts (18.9 mg, 41% for 2 steps).

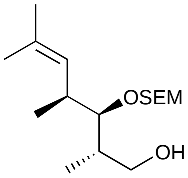
Wittig salt (**10a**); light yellow oil; ^{1}H-NMR (500 MHz, C_6D_6) d 7.84 (m, 6H), 7.07 (m, 9H), 5.38 (m, 1H), 4.95 (d, *J* = 9.4 Hz, 1H), 4.62 (d, *J* = 9.8 Hz, 1H), 3.26 (apparent t, *J* = 15.3 Hz, 1H), 2.74 (m, 1H), 2.48 (s, 3H), 1.88 (m, 1H), 1.32 (s, 3H), 1.26 (s, 3H), 0.98 (d, *J* = 7.0 Hz, 3H), 0.95 (d, *J* = 6.5 Hz, 3H); high resolution mass spectrum (ES^+) *m/z* 459.2437 $[(M–I)^+$; calcd for $C_{30}H_{36}O_2P$: 459.2453].



22

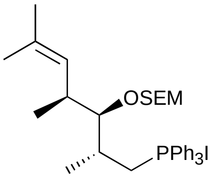
SEM ether 22. To a solution of alcohol (-)-**19** (87.3 mg, 0.300 mmol) and *i*-Pr_2NEt (260 mL, 1.49 mmol) in CH_2Cl_2 (1.0 mL) was added SEMCl (159 mL, 0.897 mmol) at room temperature. After stirring for 19.5 h, the reaction was quenched with saturated NH_4Cl aq. (5 mL) and extracted with $CHCl_3$ (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Preparative TLC (hexanes/EtOAc = 6/1) provided SEM ether **22** (112.5 mg, 89%) as a colorless oil: ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.24 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 4.97 (ddd, *J* = 9.6, 1.3, 1.3 Hz, 1H), 4.69 (d, *J*

= 6.7 Hz, 1H), 4.65 (d, *J* = 6.7 Hz, 1H), 4.40 (s, 2H), 3.80 (s, 3H), 3.65 (apparent t, *J* = 8.5 Hz, 1H), 3.63 (apparent t, *J* = 8.5 Hz, 1H), 3.54 (dd, *J* = 9.1, 4.3 Hz, 1H), 3.29 (dd, *J* = 9.1, 8.0 Hz, 1H), 3.24 (dd, *J* = 6.5, 5.0 Hz, 1H), 2.59 (m, 1H), 2.02 (m, 1H), 1.66 (d, *J* = 1.3 Hz, 3H), 1.57 (d, *J* = 1.3 Hz, 3H), 1.01 (d, *J* = 6.9 Hz, 3H), 0.94 (apparent t, *J* = 8.5 Hz, 2H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.02 (s, 9H).



23

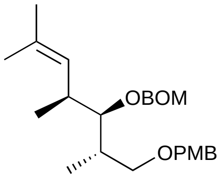
Alcohol 23. At 0 ˚C, a solution of **22** (110.2 mg, 0.261 mmol) in CH_2Cl_2 (2.75 mL) was treated with H_2O (0.10 mL) and DDQ (65.2 mg, 0.287 mmol), and stirred for 1 h 20 min. The reaction was quenched with saturated $NaHCO_3$ aq. (4 mL) and the layers separated. The aqueous layer was then extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (hexanes/EtOAc = 20/1Æ1/1) provided primary alcohol **23** (71.6 mg, 91%) as a colorless oil): ^{1}H-NMR (500 MHz, $CDCl_3$) d 5.00 (ddd, *J* = 9.5, 1.3, 1.3 Hz, 1H), 4.72 (d, *J* = 6.7 Hz, 1H), 4.68 (d, *J* = 6.7 Hz, 1H), 3.84 (dd, *J* = 11.2, 3.5 Hz, 1H), 3.75 (dt, *J* = 9.7, 8.2 Hz, 1H), 3.57 (dt, *J* = 9.7, 8.2 Hz, 1H), 3.48 (dd, *J* = 11.2, 4.0 Hz, 1H), 3.31 (dd, *J* = 7.1, 4.9 Hz, 1H), 2.63 (m, 1H), 1.79 (m, 1H), 1.69 (d, *J* = 1.3 Hz, 3H), 1.62 (d, *J* = 1.3 Hz, 3H), 1.03 (d, *J* = 7.1 Hz, 3H), 0.96 (dd, *J* = 8.2, 8.2 Hz, 2H), 0.95 (d, *J* = 6.8 Hz, 3H), 0.02 (s, 9H).



10b

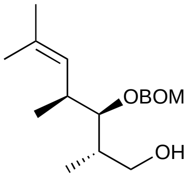
Wittig salt 10b. A solution of **23** (71.6 mg, 0.237 mmol), PPh_3 (93.3 mg, 0.356 mmol) and imidazole (24.2 mg, 0.356 mmol) in benzene•Et_2O (1:2) (2.4 mL) was cooled to 0 ˚C, and treated with iodine (90.3 mg, 0.356 mmol). The reaction mixture was warmed to room temperature and stirred for 3.5 h. The reaction was then quenched with saturated $NaHCO_3$ aq. (5 mL). The mixture was extracted with Et_2O (3 x 10 mL), and the combined organics were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (hexanes/EtOAc = 30/1) provided a mixture of the desired alkyl iodide **9b** and PPh_3, which was taken onto the next step without further purification.

To the neat alkyl iodide **9b** (mixed with PPh_3) was added additional PPh_3 (622 mg, 2.37 mmol) and *i*-Pr_2NEt (0.34 mL) at room temperature. The mixture was warmed to 100 ˚C and stirred for 17 h. The reaction mixture was cooled to room temperature and diluted with CH_2Cl_2 (0.5 mL). The resulting solution was directly purified *via* flash chromatography (CH_2Cl_2/CH_3CN = 5/1Æ2/1) to give Wittig salt **10b** (100.0 mg, 63% for 2 steps) and the mixture of cyclopentane byproducts (23 mg, 34% for 2 steps). Wittig salt **10b**, light yellow oil; ^{1}H-NMR (500 MHz, C_6D_6) d 7.91 (m, 6H), 7.12 (m, 9H), 5.39 (d, *J* = 9.1 Hz, 1H), 5.19 (m, 1H), 4.98 (d, *J* = 6.0 Hz, 1H), 4.94 (d, *J* = 6.0 Hz, 1H), 4.30 (apparent t, *J* = 15.0 Hz, 1H), 4.07 (dd, *J* = 6.4, 4.9 Hz, 1H), 3.79 (m, 1H), 3.71 (m, 1H), 2.74 (m, 1H), 2.14 (m, 1H), 1.67 (s, 3H), 1.61 (s, 3H), 1.03 (m, 1H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H), 0.76 (m, 1H), –0.01 (s, 9H); high resolution mass spectrum (ES^+) *m/z* 547.3141 [$(M–I)^+$; calcd for $C_{34}H_{48}O_2PSi$: 547.3161].



24

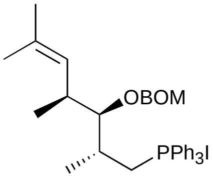
BOM ether 24. To a solution of alcohol (-)- **19** (97.7 mg, 0.335 mmol) and *i*-Pr_2NEt (291 mL, 1.67 mmol) in CH_2Cl_2 (1.1 mL) was added BOMCl (139 mL, 1.00 mmol) at room temperature. After stirring for 38 h, the reaction was quenched with saturated NH_4Cl aq. (6 mL) and extracted with $CHCl_3$ (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Preparative TLC (hexanes/EtOAc = 4/1) provided BOM ether **24** (138 mg, 100%) as a colorless oil: ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.33 (m, 5H), 7.23 (d, *J* = 8.6 Hz, 2H), 6.85 (d, *J* = 8.6 Hz, 2H), 4.99 (ddd, *J* = 11.0, 1.3, 1.3 Hz, 1H), 4.79 (d, *J* = 6.7 Hz, 1H), 4.74 (d, *J* = 6.7 Hz, 1H), 4.64 (d, *J* = 11.6 Hz, 1H), 4.61 (d, *J* = 11.6 Hz, 1H), 4.39 (s, 2H), 3.79 (s, 3H), 3.56 (dd, *J* = 9.1, 4.4 Hz, 1H), 3.32 (dd, *J* = 9.1, 3.3 Hz, 1H), 3.31 (dd, *J* = 7.8, 6.9 Hz, 1H), 2.62 (m, 1H), 2.05 (m, 1H), 1.64 (d, *J* = 1.3 Hz, 3H), 1.58 (d, *J* = 1.3 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H), 0.97 (d, *J* = 6.7 Hz, 3H).



25

Alcohol 25. At 0 ˚C, a solution of **24** (140 mg, 0.340 mmol) in CH_2Cl_2 (2.75 mL) was treated with H_2O (0.14 mL) and DDQ (84.9 mg, 0.374 mmol), and stirred for 1 h 20 min. The reaction was quenched with saturated $NaHCO_3$ aq. (4 mL) and the layers separated. The aqueous layer was then extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (hexanes/EtOAc = 20/1Æ1/1) provided primary alcohol **25** (85.4 mg, 86%) as a colorless oil: ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.34 (m, 5H), 4.98 (ddd, *J* = 9.5, 1.1, 0.9 Hz, 1H), 4.82 (d, *J* =

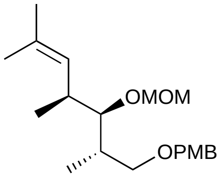
6.6 Hz, 1H), 4.77 (d, *J* = 6.6 Hz, 1H), 4.73 (d, *J* = 11.9 Hz, 1H), 4.60 (d, *J* = 11.9 Hz, 1H), 3.85 (dd, *J* = 11.2, 3.7 Hz, 1H), 3.54 (dd, *J* = 11.2, 4.4 Hz, 1H), 3.37 (dd, *J* = 6.3, 5.6 Hz, 1H), 2.65 (m, 1H), 1.85 (m, 1H), 1.67 (d, *J* = 0.9 Hz, 3H), 1.62 (d, *J* = 1.1 Hz, 3H), 1.60 (br s, 1H), 1.05 (d, *J* = 7.1 Hz, 3H), 0.98 (d, *J* = 6.8 Hz, 3H).



10c

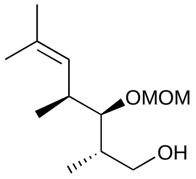
Wittig salt 10c. A solution of **25** (83.2 mg, 0.275 mmol), PPh_3 (108.4 mg, 0.413 mmol) and imidazole (28.1 mg, 0.413 mmol) in benzene•Et_2O (1:2) (2.75 mL) was cooled to 0 ˚C, and treated with iodine (104.9 mg, 0.413 mmol). The reaction mixture was warmed to room temperature and stirred for 3.5 h. The reaction was then quenched with saturated $NaHCO_3$ aq. (5 mL) and the layers separated. The aqueous layer was extracted with Et_2O (3 x 10 mL), and the combined organics were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (hexanes/EtOAc = 30/1) provided a mixture of the desired alkyl iodide **9c** and PPh_3, which was taken onto the next step without further purification.

To the neat alkyl iodide **9c** (mixed with PPh_3) was added additional PPh_3 (722.6 mg, 2.75 mmol) and *i*-Pr_2NEt (0.39 mL) at room temperature. The mixture was warmed to 100 ˚C and stirred for 17 h. The reaction mixture was cooled to room temperature and diluted with CH_2Cl_2 (0.5 mL). The resulting solution was loaded onto flash chromatography (CH_2Cl_2/CH_3CN = 5/1Æ2/1) to give Wittig salt **10c** (129.5 mg, 69% for 2 steps) and the mixture of cyclopentane byproducts (24 mg, 30% for 2 steps). Wittig salt (**10c**); light yellow oil; ^{1}H-NMR (500 MHz, C_6D_6) d 7.85 (m, 6H), 7.41 (m, 2H), 7.10 (m, 12H), 5.40 (d, *J* = 8.5 Hz, 1H), 5.02 (d, *J* = 6.1 Hz, 1H), 4.95 (d, *J* = 6.1 Hz, 1H), 4.87 (m, 1H), 4.74 (d, *J* = 12.2 Hz, 1H), 4.65 (d, *J* = 12.2 Hz, 1H), 4.34 (apparent t, *J* = 14.9 Hz, 1H), 4.15 (dd, *J* = 6.0, 5.2 Hz, 1H), 2.75 (m, 1H), 2.15 (m, 1H), 1.64 (s, 3H), 1.60 (s, 3H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 6.8 Hz, 3H); high resolution mass spectrum (ES^+) *m/z* 537.2921 [$(M–I)^+$; calcd for $C_{36}H_{42}O_2P$: 537.2922].



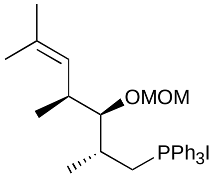
26

MOM ether 26. To a solution of alcohol (-)-**19** (85.0 mg, 0.291 mmol) and *i*-Pr_2NEt (304 mL, 1.75 mmol) in CH_2Cl_2 (0.97 mL) was added MOMCl (88.4 mL, 1.16 mmol) at room temperature. After stirring for 21 h, the reaction was quenched with saturated NH_4Cl aq. (4 mL), and extracted with $CHCl_3$ (3 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (hexanes/EtOAc = 15/1) afforded MOM ether **26** (98.0 mg, 100%) as a colorless oil: ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.25 (d, *J* = 8.5 Hz, 2H), 6.87 (d, *J* = 8.5 Hz, 2H), 4.97 (d, *J* = 9.5 Hz, 1H), 4.64 (d, *J* = 6.6 Hz, 1H), 4.61 (d, *J* = 6.6 Hz, 1H), 4.41 (s, 2H), 3.80 (s, 3H), 3.53 (dd, *J* = 9.1, 4.4 Hz, 1H), 3.38 (s, 3H), 3.29 (apparent t, *J* = 8.4 Hz, 1H), 3.23 (apparent t, *J* = 6.2 Hz, 1H), 2.59 (m, 1H), 2.02 (m, 1H), 1.66 (s, 3H), 1.58 (s, 3H), 1.02 (d, *J* = 7.0 Hz, 3H), 0.95 (d, *J* = 6.7 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 159.3, 131.0, 130.5, 129.2 (2C), 128.4, 113.7 (2C), 98.2, 85.7, 72.7, 72.3, 56.0, 55.3, 36.6, 35.1, 25.8, 17.9, 16.6, 15.1.



27

Alcohol 27. A solution of **26** (92.3 mg, 0.275 mmol) in CH_2Cl_2 (2.75 mL) was cooled to 0 ˚C, treated with H_2O (0.11 mL), DDQ (68.6 mg, 0.302 mmol) and stirred for 1 h 20 min. The reaction was quenched with saturated $NaHCO_3$ aq. (4 mL) and the layers separated. The aqueous layer was then extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (hexanes/EtOAc = 20/1Æ1/1) provided primary alcohol **27** (60.2 mg, 100%) as a colorless oil: ^{1}H-NMR (500 MHz, $CDCl_3$) d 4.99 (d, *J* = 9.5 Hz, 1H), 4.68 (d, *J* = 6.5 Hz, 1H), 4.65 (d, *J* = 6.5 Hz, 1H), 3.83 (dd, *J* = 11.2, 3.6 Hz, 1H), 3.51 (dd, *J* = 11.2, 4.2 Hz, 1H), 3.43 (s, 3H), 3.30 (dd, *J* = 6.5, 5.4 Hz, 1H), 2.63 (m, 1H), 1.82 (m, 1H), 1.69 (s, 3H), 1.62 (s, 3H), 1.55 (br s, 1H), 1.04 (d, *J* = 7.1 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H).

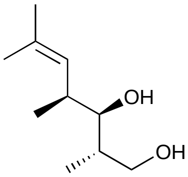


10d

Wittig salt 10d. A solution of **27** (56.0 mg, 0.259 mmol), PPh_3 (102.0 mg, 0.389 mmol) and imidazole (26.5 mg, 0.389 mmol) in benzene•Et_2O (1:2) (2.6 mL) was cooled to 0 ˚C and treated with iodine (98.7 mg, 0.389 mmol). The reaction mixture was warmed to room temperature and stirred for 3.5 h. The reaction was then quenched with saturated aq. $NaHCO_3$ (5 mL). The mixture was extracted with Et_2O (3 x 10 mL) and the combined organics were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (hexanes/EtOAc = 30/1) provided a mixture of the desired alkyl iodide **9d** and PPh_3, which was taken onto the next step without further purification.

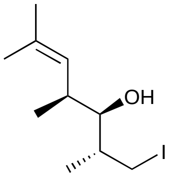
To the neat alkyl iodide **9d** (mixed with PPh_3) was added additional PPh_3 (679 mg, 2.59 mmol) and *i*-Pr_2NEt (0.37 mL) at room temperature. The mixture was warmed to 100 ˚C and stirred for 17 h. The reaction mixture was cooled to room temperature and diluted with CH_2Cl_2 (0.5 mL). The resulting solution was directly purified *via* flash chromatography (CH_2Cl_2/CH_3CN = 5/1Æ2/1) to give the Wittig salt **10d** (104.5 mg, 69% for 2 steps) and the mixture of cyclopentane byproducts (12.2 mg, 24% for 2 steps).

Wittig salt (**10d**); light yellow oil; ^{1}H-NMR (500 MHz, C_6D_6) d 7.86 (m, 6H), 7.15 (m, 9H), 5.39 (d, *J* = 9.3 Hz, 1H), 5.08 (m, 1H), 4.88 (d, *J* = 5.9 Hz, 1H), 4.79 (d, *J* = 5.9 Hz, 1H), 4.32 (apparent t, *J* = 15.0 Hz, 1H), 4.10 (apparent t, *J* = 5.4 Hz, 1H), 3.28 (s, 3H), 2.73 (m, 1H), 2.11 (m, 1H), 1.66 (s, 3H), 1.60 (s, 3H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H); high resolution mass spectrum (ES^+) *m/z* 461.2607 $[(M–I)^+$; calcd for $C_{30}H_{38}O_2P$: 461.2609].



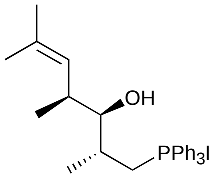
28

Diol 28. At 0 ˚C, a solution of (-)-**19** (96.5 mg, 0.330 mmol) in $CH_3CN•H_2O$ (20:1) (3.3 mL) was treated with DDQ (82.5 mg, 0.364 mmol), stirred for 10 min., warmed to room temperature, and then stirred for 2 h. The reaction was then quenched with saturated $NaHCO_3$ aq. (10 mL) and the layers separated. The aqueous layer was then extracted with Et_2O (2 x 10 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (hexanes/EtOAc = 10/1Æ1/1) provided the diol **28** (38.4 mg, 68%) as a colorless oil: ^{1}H-NMR (500 MHz, $CDCl_3$) d 5.03 (ddd, *J* = 9.3, 1.4, 1.4 Hz, 1H), 3.77 (dd, *J* = 10.8, 3.5 Hz, 1H), 3.62 (dd, *J* = 10.8, 6.5 Hz, 1H), 3.40 (dd, *J* = 6.7, 5.4 Hz, 1H), 2.59 (m, 1H), 2.07 (br s, 2H), 1.82 (m, 1H), 1.71 (d, *J* = 1.4 Hz, 3H), 1.64 (d, *J* = 1.4 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H), 0.97 (d, *J* = 7.1 Hz, 3H).



9e

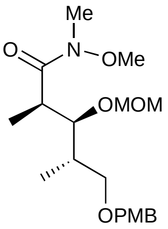
Iodide 9e. A solution of **28** (38.2 mg, 0.222 mmol), PPh_3 (87.4 mg, 0.333 mmol) and imidazole (22.7 mg, 0.333) in benzene•Et_2O (1:2) (2.2 mL) was cooled to 0 ˚C, and treated with iodine (84.6 mg, 0.333 mmol). The mixture was warmed to room temperature and stirred for 25 min. The reaction was then quenched with saturated $NaHCO_3$ aq. (3 mL). The layers were separated and the aqueous layer was extracted with Et_2O (2 x 10 mL). The combined organic extracts were dried over Na_2SO_4, filtered, and concentrated . Flash chromatography (hexanes/EtOAc = 40/1Æ20/1) provided alkyl iodide **9e** (21.9 mg, 33%) as a colorless oil: ^{1}H-NMR (500 MHz, $CDCl_3$) d 5.04 (ddd, *J* = 9.2, 1.3, 1.3 Hz, 1H), 3.41 (dd, *J* = 9.6, 3.0 Hz, 1H), 3.33 (dd, *J* = 9.6, 6.9 Hz, 1H), 3.27 (dd, *J* = 7.0, 4.9 Hz, 1H), 2.57 (m, 1H), 1.72 (d, *J* = 1.3 Hz, 3H), 1.65 (d, *J* = 1.3 Hz, 3H), 1.57 (m, 1H), 1.03 (d, *J* = 6.7 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H).



10e

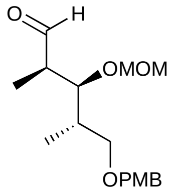
Wittig salt 10e. To the neat alkyl iodide **9e** (21.4 mg, 0.0718 mmol) was added PPh_3 (188.4 mg, 0.718 mmol) and *i*-Pr_2NEt (0.10 mL) at room temperature. The resulting solution was warmed to 100 ˚C and after 16 h, the reaction mixture was cooled to room temperature and diluted with CH_2Cl_2 (0.5 mL). The solution was directly purified *via* flash chromatography (CH_2Cl_2/CH_3CN = 5/1Æ3/1) to provide the Wittig salt **10e** (24.8 mg, 62%) as a light yellow solid and the mixture of cyclized byproducts (4.6 mg, 38%): Wittig salt (**10e)**: ^{1}H-NMR (500 MHz, CD_3OD) d 7.89-7.72 (m, 15H), 4.90 (d, *J* = 8.5 Hz, 1H), 3.67 (m, 3H), 2.52 (m, 1H), 2.08 (m, 1H), 1.53 (s, 3H), 1.46 (s, 3H), 0.88 (d, *J* = 6.7 Hz, 3H), 0.82 (d, *J* = 6.8 Hz, 3H); high resolution mass spectrum (ES$^+$) *m/z* 417.2362 [(M–I)$^+$; calcd for $C_{28}H_{34}OP$: 417.2347].

(+)-Discodermolide System (Beginning from (-)-Common Precursor):



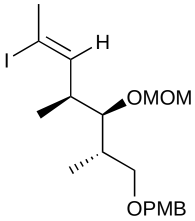
(-)-29

MOM Ether (–)-29. A solution of common precursor (–)-**CP** (7.0 g, 21.6 mmol) and *i*-Pr_2NEt (7.5 mL, 43.2 mmol) in CH_2Cl_2 (210 mL) was cooled to 0 °C and MOMCl (2.42 mL, 32.0 mmol) was added. The mixture was stirred for 2 h, at which time another portion of MOMCl was added (this was repeated until no SM remained). The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (50 mL). The aqueous layer was extracted (3 x 100 mL of Et_2O), and the combined organic layers were washed with water, saturated $NaHCO_3$ (2 x 50 mL), and brine. The organic layer was dried over $MgSO_4$, filtered, and concentrated to yield (–)-**29** (7.5 g, 95%) as a clear, colorless oil. The product was purified via flash chromatography (15% ethyl acetate/hexanes): $[a]^{23}_{D}$ –20.8° (*c* 4.8, $CHCl_3$); IR (NaCl) 2937, 1662, 1612, 1513, 1464, 1379, 1248, 1090, 1034 cm^{-1}; ^1H-NMR (500 MHz, $CDCl_3$) d 7.23 (d, *J* = 8.7 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 4.61 (ABq, J_{AB} = 6.54 Hz, Dn_{AB} = 17.3 Hz, 2H), 4.39 (s, 2H), 3.78 (s, 3H), 3.76 (dd, *J* = 6.1, 4.8 Hz, 1H), 3.58 (s, 3H), 3.56 (d, *J* = 4.8 Hz, 1H), 3.34 (s, 3H), 3.27 (dd, *J* = 9.1, 7.1 Hz, 1H), 3.13 (m, 1H), 3.12 (s, 3H), 1.97-1.91 (m, 1H), 1.15 (d, *J* = 6.9 Hz, 3H), 1.03 (d, *J* = 6.9 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 176.8, 159.0, 130.7, 129.1, 113.4, 98.3, 82.3, 72.7, 71.8, 61.0, 56.1, 55.1, 38.4, 37.1, 32.2, 15.2, 12.9; high resolution mass spectrum (ES^+) *m/z* 392.20554 [$(M+Na)^+$; calcd for $C_{19}H_{31}NO_6$: 392.204908].



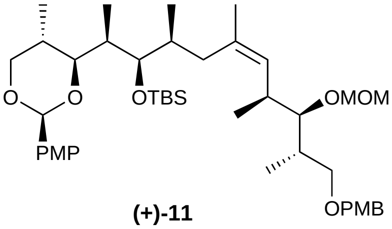
(-)-30

Aldehyde (–)-30. At –10 °C, a solution of amide (–)-**29** (3.9 g, 10.5 mmol) in THF (105 mL) was treated with DIBAL-H (1.0 M in toluene, 12.7 mL) via drop-wise addition down the side of the flask (10 min. addition time). The reaction was stirred for an additional 3 h and quenched with MeOH (1 mL). The –10 °C reaction mixture was poured into saturated aqueous Rochelle's salt (100 mL), diluted with Et_2O (150 mL), and stirred at room temperature for 30 min. The mixture was then poured into a separatory funnel and vigorously shaken (emulsion). The layers were separated, and the organic layer was washed with saturated aqueous Rochelle's salt, water, saturated $NaHCO_3$, and brine (1 x 100 mL each). The organic layer was dried over $MgSO_4$, filtered, and concentrated to give (–)-**30** (3.2 g, 99%) as a clear, colorless oil, which was taken onto the next step without further purification. An analytical sample was obtained via flash chromatography (15% EtOAc/hexanes): $[a]^{23}_{D}$ –30.1° (*c* 6.5, $CHCl_3$); IR ($CHCl_3$) 2938, 2901, 1513, 1248, 1726 cm^{-1}; ^1H-NMR (500 MHz, $CDCl_3$) d 9.70 (s, 1H), 7.24 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 4.60 (d, *J* = 6.8 Hz, 1H), 4.49 (d, *J* = 6.8 Hz, 1H), 4.41 (s, 2H), 4.06 (dd, *J* = 8.5, 3.0 Hz, 1H), 3.80 (s, 3H), 3.49 (dd, *J* = 8.9, 5.0 Hz, 1H), 3.44 (dd, *J* = 8.9, 4.1 Hz, 1H), 3.23 (s, 3H), 2.50 (ddd, *J* = 14.0, 6.8, 2.6 Hz, 1H), 2.03-1.95 (m, 1H), 1.11 (d, *J* = 7.0 Hz, 3H), 1.00 (d, *J* = 7.0 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 203.9, 159.1, 130.4, 129.1, 113.7, 97.7, 78.9, 72.7, 71.4, 55.6, 55.2, 48.6, 36.6, 14.5, 6.9; high resolution mass spectrum (FAB, NBA) *m/z* 333.1665 [$(M+Na)^+$; calcd for $C_{17}H_{26}O_5Na$: 333.16775].



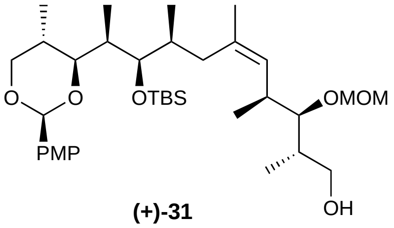
(+)-B

(+) - **Fragment B.** At 0 °C, a suspension of $EtPh_3PI$ (1.34 g, 3.06 mmol, dried at 70 °C / 0.2 Torr for 2 h) in THF (11 mL, dried over 4 Å MS, sparged with argon) was treated with *n*-BuLi (2.4 M in hexanes, 1.27 mL, 3.06 mmol) over 30 min. to form a dark red solution. After an additional 10 min., the red ylide was added over 10 min. via cannula to a cooled (–78 °C) solution of I_2 (774 mg, 3.06 mmol) in THF (27 mL solution, prepared by adding I_2 to degassed THF at rt and vigorously stirring for 40 min. before cooling) such that the internal temperature did not exceed –70 °C. The resultant yellow slurry was stirred at –75 °C (internal) for 5 min. and warmed to –23 °C (internal). NaHMDS (1.0 M in THF, 2.75 mL) was added via cannula over 30 min., and the resulting orange suspension was stirred 15 min. further and cooled to –33 °C (internal). A solution of the crude aldehyde (-)-**30** (475 mg, 1.53 mmol) in THF (5 mL) was introduced via cannula over 15 min., and the reaction mixture was stirred at –30 °C for an additional 45 min., warmed to 7 °C over 1 h, and quenched with MeOH (2 mL). The mixture was then suction filtered through a 6 to 8" silica plug (100% Et_2O, 20 mL sintered glass frit), the filtrate was washed with saturated aqueous $Na_2S_2O_3$ and brine, dried over $MgSO_4$, filtered, and concentrated. Flash chromatography (15% CH_2Cl_2/hexanes; then gradient elution 2% ethyl acetate/hexanes Æ 5% ethyl acetate/hexanes) furnished (+)-**B** (190 mg, 40% yield for two steps, 9:1 *Z/E*) as a clear, colorless oil. An analytical sample of the *Z* isomer was obtained by flash chromatography (2% ethyl acetate/hexanes): $[a]^{23}_{D}$ +9.2° (*c* 2.5, $CHCl_3$); IR 2965, 2929, 2849, 1612, 1512, 1456, 1247, 1090, 1034 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.25 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.35 (dd, *J* = 8.9, 1.5 Hz, 1H), 4.61 (d, *J* = 6.6 Hz, 1H), 4.58 (d, *J* = 6.6 Hz, 1H), 4.42 (s, 2H), 3.80 (s, 3H), 3.52 (dd, *J* = 9.1, 4.3 Hz, 1H), 3.38 (apparent t, *J* = 5.7 Hz, 1H), 3.37 (s, 3H), 3.35 (dd, *J* = 9.1, 2.0 Hz, 1H), 2.60-2.56 (m, 1H), 2.46 (d, *J* = 1.5 Hz, 3H), 1.99 (ddd, *J* = 10.4, 6.8, 4.3 Hz, 1H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.99 (d, *J* = 6.8 Hz, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 159.0, 138.5, 130.7, 129.1, 113.6, 99.5, 98.1, 83.7, 72.6, 72.0, 55.9, 55.2, 43.6, 36.7, 33.5, 14.8, 14.2; high resolution mass spectrum (FAB, NBA) *m/z* 471.099989 [$(M+Na)^+$; calcd for $C_{19}H_{29}IO_4Na$: 471.100831].



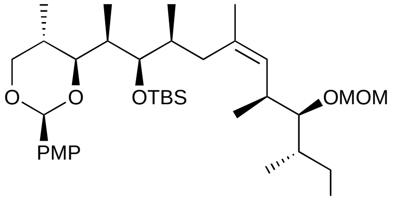
(+)-11

(+)-11 (Modified Negishi Coupling). A 1.0 M solution of anhydrous $ZnCl_2$ (11.91 mL, 1.92 mmol) was added via syringe to a solution of alkyl iodide (+)-**A** (1.05 g, 1.9 mmol) in dry Et_2O (8 mL), and the resulting solution was cooled to –78 °C and degassed by briefly pumping and backfilling with argon. *t*-BuLi (1.7 M in pentane, 13.8 mL, 5.7 mmol) was added via syringe over 12 min. The resulting solution was stirred 5 min. further, evacuated (1 x 0.1 torr) and again back-filled with argon. The –78 °C bath was then removed, and the reaction was stirred at ambient temperature for 1 h. The resulting cloudy suspension was transferred by cannula into an intimate mixture of vinyl iodide (+)-**B** (0.750 g, 1.67 mmol; 9:1 *Z/E*) and $Pd(PPh_3)_4$ (0.140g, 0.13 mmol). The reaction mixture was stirred overnight in the absence of light, and quenched via slow addition of the reaction mixture to water (20 mL). The mixture was diluted with Et_2O, and the layers were separated. The aqueous layer was extracted (3 x Et_2O), and the combined organic layers were washed (saturated aqueous $NaHCO_3$, brine), dried ($MgSO_4$), filtered and concentrated. Flash chromatography (gradient elution: 2% EtOAc/hexanesÆ5%EtOAc/hexanes) provided (+)-**11** as a light orange oil (0.997 g, 80% yield, 90% based on purity of vinyl iodide): [a]$^{23}_{D}$ +30.0° (*c* 0.5, $CHCl_3$); IR (NaCl) 2958, 2931, 2872, 2854, 1615, 1516, 1461, 1388, 1249, 1035 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.37 (d, *J* = 8.7 Hz, 2H), 7.24 (d, *J* = 8.6 Hz, 2H), 6.86 (apparent t, *J* = 8.2 Hz, 4H), 5.39 (s, 1H), 5.05 (d, *J* = 9.7 Hz, 1H), 4.61 (ABq, J_{AB} = 6.3 Hz, Dn_{AB} = 14.9 Hz, 2H), 4.39 (ABq, J_{AB} = 11.5 Hz, Dn_{AB} = 17.1 Hz, 2H), 4.09 (dd, *J* = 11.2, 4.5 Hz, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 3.63 (dd, *J* = 7.1, 1.9 Hz, 1H), 3.51 (m, 2H), 3.48 (apparent t, *J* = 8.9 Hz, 1H), 3.37 (s, 3H), 3.30 (dd, *J* = 8.9, 7.8 Hz, 1H), 3.22 (apparent t, *J* = 5.9 Hz, 1H), 2.61 (ddd, *J* = 10.1, 6.7, 6.7 Hz, 1H), 2.31 (apparent t, *J* = 12.3 Hz, 1H), 2.1-1.9 (m, 3H), 1.89 (ddd, *J* = 7.1, 7.1, 1.8 Hz, 1H), 1.71 (br d, *J* = 12.3 Hz, 1H), 1.57 (s, 3H), 1.01 (d, *J* = 7.1 Hz, 3H), 0.99 (d, *J* = 7.1 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.91 (s, 9H), 0.75 (d, *J* = 7.1 Hz, 3H), 0.74 (s, 3H), 0.09 (s, 3H), 0.42 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 159.7, 159.0, 132.8, 131.5, 130.9, 130.3, 129.0, 127.2, 113.7, 113.4, 101.0, 98.2, 85.3, 83.3, 78.4, 73.2, 72.5, 72.3, 56.0, 55.2, 38.1, 37.6, 36.7, 34.5, 33.7, 30.7, 26.1, 26.2, 18.4, 16.3, 14.8, 12.6, 12.1, 10.8, -3.5, -3.9; high resolution mass spectrum (ES+) *m/z* 765.4767 [(M+Na)$^+$; calcd for $C_{43}H_{70}O_8SiNa$: 765.4738].



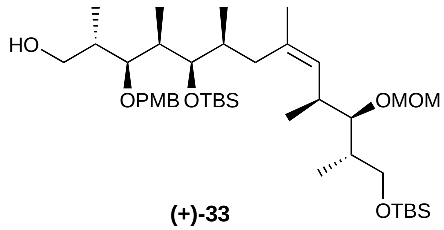
(+)-31

Alcohol (+)-31 (Chemoselective Hydrolysis of PMB Ether). At 0 ^{o}C, a solution of PMB ether (+)-**11** (850 mg, 1.14 mmol) in CH_2Cl_2 (10.5 mL) was treated with H_2O (0.5 mL), DDQ (312 mg, 1.37 mmol) and stirred for 3 h. The mixture was quenched with 2 mL of saturated $NaHCO_3$, washed with H_2O (2 x 10 mL) and the layers were separated. The aqueous layer was then extracted with CH_2Cl_2 (2 x 10 mL). The combined organic extracts were dried ($MgSO_4$), filtered, concentrated and chromatographed (10% EtOAc/hexanes) to provided 630 mg (+)-**31** (93%); mp: 65-68 °C; $[a]^{23}_{D}$ +18.6° (*c* 6.8, $CHCl_3$); IR ($CHCl_3$) 3509, 2923, 1739, 1615, 1518, 1461, 1388, 1302, 1253 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.37 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.38 (s, 1H), 5.05 (d, *J* = 10.0 Hz, 1H), 4.66 (d, *J* = 6.5 Hz, 1H), 4.64 (d, *J* = 6.5 Hz, 1H), 4.09 (dd, *J* = 11.2, 4.7 Hz, 1H), 3.84-3.80 (m, 1H), 3.80 (s, 3H), 3.63 (dd, *J* = 7.1, 1.8 Hz, 1H), 3.51 (dd, *J* = 9.9, 1.7 Hz, 1H), 3.50-3.46 (m, 2H), 3.42 (s, 3H), 3.26 (dd, *J* = 7.0, 5.1 Hz, 1H), 2.69 (dd, *J* = 7.6, 5.2 Hz, 1H), 2.64 (dd, *J* = 6.3, 1.6 Hz, 1H), 2.30 (apparent t, *J* = 12.2 Hz, 1H), 2.09-2.03 (m, 1H), 2.03-1.95 (m, 1H), 1.89 (ddd, *J* = 7.0, 7.0, 1.7 Hz, 1H), 1.79 (dddd, *J* = 17.6, 7.1, 7.1, 3.3 Hz, 1H), 1.74 (br d, *J* = 12.7 Hz, 1H), 1.60 (s, 3H), 1.02 (d, *J* = 7.2 Hz, 3H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.7 Hz, 3H), 0.91 (s, 9H), 0.76 (d, *J* = 6.9 Hz, 3H), 0.74 (d, *J* = 6.7 Hz, 3H), 0.05 (s, 3H), 0.01 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 159.7, 133.3, 131.4, 130.0, 127.2, 113.3, 100.9, 99.0, 87.2, 83.3, 73.2, 65.0, 56.2, 55.1, 38.1, 37.6, 37.3, 34.6, 33.8, 30.7, 26.1, 23.2, 18.3, 15.2, 15.0, 12.5, 12.0, 10.7, –3.5, –3.8; high resolution mass spectrum (CI, NH_3) *m/z* 645.417132 $[(M+Na)^+$; calcd for $C_{35}H_{62}O_7SiNa$: 645.416253.



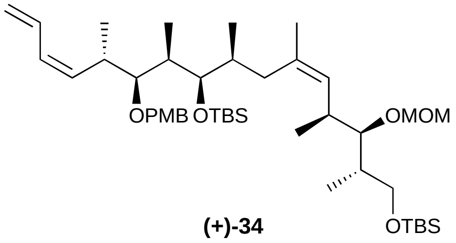
(+)-32

Silyl protected anisylidene acetal (+)-32. To a solution of alcohol (+)-**31** (624 mg, 1.00 mmol) in CH_2Cl_2 (10 mL) was added imidazole (137.8 mg, 2.02 mmol) and TBS-Cl (227.9 mg, 1.52 mmol). The mixture was stirred for 1 h at ambient temperature. The reaction was then quenched with a brine solution, extracted with CH_2Cl_2 (3 x 10 mL), and washed with H_2O (10 mL). The organic layers were separated, dried ($MgSO_4$), filtered, and concentrated *in vacuo*. Flash chromatography (10% EtOAc/hexanes) provided (+)-**32** (723 mg, 98%); $[a]^{23}_{D}$ +28.2° (*c* 3.5, $CHCl_3$) IR ($CHCl_3$) 2964, 2931, 2861, 1618, 1520, 1466, 1390, 1248 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.37 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.38 (s, 1H), 5.10 (d, *J* = 9.9 Hz, 1H), 4.64 (d, *J* = 6.4 Hz, 1H), 4.61 (d, *J* = 6.5 Hz, 1H), 4.10 (dd, *J* = 11.2, 4.7 Hz, 1H), 3.80 (s, 3H), 3.65-3.63 (m, 2H), 3.54-3.44 (m, 3H), 3.40 (s, 3H), 3.21 (apparent t, *J* = 5.9 Hz, 1H), 2.58 (ddd, *J* = 16.2, 12.2, 6.0 Hz, 1H), 2.32 (apparent t, *J* = 12.2 Hz, 1H) 2.10-2.04 (m, 1H), 2.04-1.94 (m, 1H), 1.92-1.85 (m, 1H), 1.83 (br ddd *J* = 13.9, 6.9, 4.2 Hz, 1H), 1.75 (apparent d, *J* = 12.0 Hz, 1H), 1.60 (s, 3H), 1.01 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 6.6 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.88 (s, 9H), 0.76 (d, *J* = 6.9 Hz, 3H), 0.74 (d, *J* = 6.7 Hz, 3H), 0.04 (s, 3H), 0.02 (app s, 6H), 0.01 (s, 3H); ^{13}C-NMR (125 MHz, $CHCl_3$) d 159.7, 132.5, 131.4, 130.5, 127.8, 113.3, 101.0, 98.1, 84.7, 83.4, 78.3, 73.2, 64.8, 56.0, 55.1, 38.9, 38.0, 37.4, 34.1, 33.7, 30.7, 26.1, 25.8, 23.1, 18.3, 18.2, 14.1, 12.6, 12.0, 10.7, –3.4, –3.9; high resolution mass spectrum (ES$^+$) *m/z* 759.506365 [(M+Na)$^+$; calcd for $C_{40}H_{76}O_7SiNa$: 759.502732].



(+)-33

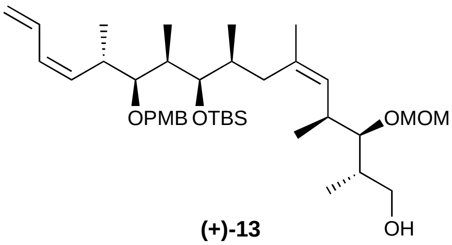
Silyl protected alcohol (+)-33. To a –50 °C solution of silyl ether (+)-**32** (724 mg, 0.98 mmol) in CH_2Cl_2 (10 mL) was added DIBAL-H (1 M in toluene, 3.9 mL, 3.9 mmol). The resulting solution was stirred for 24 h, quenched via dropwise addition of pH 7.0 buffer (20 mL), and then diluted with CH_2Cl_2 (20 mL). The mixture was then added to 50 mL of saturated sodium potassium tartrate solution, extracted with CH_2Cl_2 (4 x 30 mL), and the layers separated. The organic layer was washed with H_2O (50 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (20% EtOAc/hexanes) provided 615 mg (+)-**33** (85 %) as a white foam: $[a]^{23}_{D}$ + 3.8 (*c* 2.6, $CHCl_3$); IR ($CHCl_3$) 3474, 2957, 2929, 2856, 1612, 1514, 1472, 1387, 1250, 1089, 1036 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.26 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 5.12 (d, *J* = 10.0 Hz, 1H), 4.65 (d, *J* = 6.4 Hz, 1H), 4.61 (d, *J* = 6.5 Hz, 1H), 4.53 (d, *J* = 10.5 Hz, 1H), 4.49 (d, *J* = 10.4 Hz, 1H), 3.80 (s, 3H), 3.75 (ddd, *J* = 11.0, 5.2, 3.5 Hz, 1H), 3.63 (dd, *J* = 9.7, 4.2 Hz, 1H), 3.58 (dt, *J* = 11.0, 5.5 Hz, 1H), 3.54 (dd, *J* = 5.1, 3.6 Hz, 1H), 3.48 (dd, *J* = 9.8, 7.4 Hz, 1H), 3.40 (s, 3H), 3.35 (apparent t, *J* = 5.5 Hz, 1H), 3.21 (apparent t, *J* = 5.8 Hz, 1H), 2.73 (apparent t, *J* = 5.6 Hz, 1H), 2.57 (dq, *J* = 12.8, 6.4 Hz, 1H), 2.24 (apparent t, *J* = 12.3 Hz, 1H), 2.00-1.88 (m, 3H), 1.86-1.80 (m, 2H), 1.64 (s, 3H), 1.05 (d, *J* = 7.2 Hz, 3H), 1.03 (d, *J* = 7.1 Hz, 3H), 0.96 –0.92(m, 6H) 0.94 (s, 9H), 0.88 (s, 9H), 0.75 (d, *J* = 6.7 Hz, 3H), 0.08 (s, 6H), 0.02 (br s, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 159.2, 132.1, 130.9, 130.2, 129.3, 113.8, 98.1, 86.3, 84.7, 77.3, 75.2, 65.2, 64.8, 56.0, 55.2, 39.7, 38.4, 37.3, 36.5, 35.2, 34.2, 26.1, 25.8, 23.1, 18.4, 18.2, 16.0, 15.6, 14.1, 13.6, 11.4, –3.2, -3.5, -5.4 (2); high resolution mass spectrum (ES$^+$) *m/z* 761.516364 [(M+Na)$^+$; calcd for $C_{41}H_{78}O_7Si_2Na$: 761.518382].



(+)-34

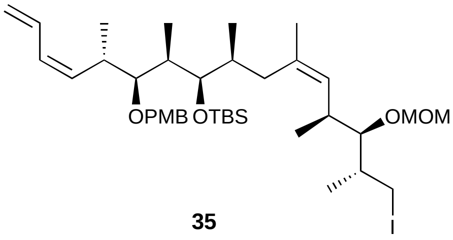
Silyl Protected Triene 34. To a 0 °C solution of alcohol (+)-**33** (160 mg, 0.21 mmol) in CH_2Cl_2 (2.1 mL) was added Dess-Martin periodinane (87.4 mg, 0.23 mmol) and $NaHCO_3$ (47.4 mg, 0.63 mmol). The resulting solution was stirred for 2.5 h and quenched with saturated NaS_2O_3 solution (2 mL) and saturated $NaHCO_3$ solution (2 mL). The mixture was then extracted with Et_2O (3 x 10 mL) and the layers were separated. The organic layer was then washed with H_2O, dried ($MgSO_4$), filtered, and concentrated. The resulting white foam **12** was used without further purification. An analytical sample was obtained *via* flash chromatography (3% EtOAc / hexanes): **Aldehyde 12**: IR ($CHCl_3$) 2953, 2926, 2861, 1716, 1515, 1460, 1253 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) d 9.80 (d, *J* = 2.5 Hz, 1H), 7.22 (d, *J* = 8.6 Hz, 2H), 6.80 (d, *J* = 8.6 Hz, 2H), 5.13 (d, *J* = 9.8 Hz, 1H), 4.65 (d, *J* = 6.5 Hz, 1H), 4.61 (d, *J* = 6.5 Hz, 1H), 4.47 (s, 2H), 3.79 (s, 3H), 3.64 (dd, *J* = 9.9, 4.3 Hz, 1H), 3.60 (dd, *J* = 5.3, 3.2 Hz, 1H), 3.57 (apparent t, *J* = 5.4 Hz, 1H), 3.49 (dd, *J* = 9.3, 7.1 Hz, 1H), 3.41 (s, 3H), 3.22 (apparent t, *J* = 5.8 Hz, 1H), 2.74 (ddd, *J* = 15.2, 7.0, 2.6 Hz, 1H), 2.57 (ddd, *J* = 16.8, 13.1, 6.5 Hz, 1H), 2.25 (apparent t, *J* = 12.5 Hz, 1H), 2.00-1.88 (m, 2H), 1.98-1.81 (m, 1H), 1.78 (bd, *J* = 13.1 Hz, 1H), 1.63 (s, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 1.04 (d, *J* = 6.9 Hz, 3H), 0.96-0.93 (m, 6H), 0.93 (s, 9H), 0.89 (s, 9H), 0.76 (d, *J* = 6.7 Hz, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.03 (s, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 204.4, 159.2, 131.9, 131.0, 130.2, 129.0, 113.7, 98.1, 84.7, 82.6, 77.0, 76.6, 74.3, 64.8, 56.0, 55.1, 49.4, 40.1, 38.8, 36.5, 35.0, 34.2, 26.1, 25.8, 23.1, 18.4, 18.2, 16.0, 14.1, 13.4, 12.1, 11.3, –3.2, –3.6, –5.4; high resolution mass spectrum (ES^+) *m/z* 759.506140 [$(M+Na)^+$; calcd for $C_{41}H_{76}O_7Si_2Na$: 759.502732].

To a –78 °C solution of freshly distilled allyldiphenylphosphine (95 mL, 0.44 mmol) in THF (2.1 mL, degassed) was added 270 mL of *t*-butyllithium (1.7 M in pentane, 0.44 mmol) and the solution was stirred for 5 min. The solution was warmed to 0 °C, stirred for 30 min. and cooled to –78 °C. The solution was then treated with freshly distilled Ti(O*i*-Pr)$_4$ (131 mL, 0.44 mmol) and stirred for 30 min. A precooled (–78 °C) solution of aldehyde **12** (160 mg, 0.217 mmol) in THF (2 mL) was added via cannula (rinse 1 x 2 mL), stirred for 1 h, and then warmed to 0 °C. Iodomethane (0.13 mL, 2.17 mmol) was added, and the solution was warmed to ambient temperature and stirred for 16 h. The solution was quenched with pH 7.0 buffer (2 mL) and extracted with CH_2Cl_2 (3 x 10 mL) and Et_2O (3 x 10 mL). The combined organic layers were washed with brine, dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (2% EtOAc/hexanes) provided (+)-**34** (102 mg, 66% from (+)-**33**, 14:1 mixture of Z:E isomers) as a white foam: $[a]^{23}_{D}$ + 30.0 (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 3060, 2940, 1600, 1450 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$, Z isomer) d 7.28 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 6.56 (ddd, *J* = 16.8, 10.6, 10.6 Hz, 1H), 6.02 (apparent t, *J* = 11.0 Hz, 1H), 5.58 (apparent t, *J* = 10.5 Hz, 1H), 5.20 (dd, *J* = 16.8, 1.3 Hz, 1H), 5.10 (m, 2H), 4.65 (d, *J* = 6.5 Hz, 1H), 4.62 (d, *J* = 6.5 Hz, 1H), 4.57 (d, *J* = 10.6 Hz, 1H), 4.47 (d, *J* = 10.6 Hz, 1H), 3.80 (s, 3H), 3.64 (dd, *J* = 9.6, 4.3 Hz, 1H), 3.52-3.46 (m, 2H), 3.41 (s, 3H), 3.25 (dd, *J* = 7.1, 3.9 Hz, 1H), 3.21 (apparent t, *J* = 5.8 Hz, 1H), 3.04-2.96 (m, 1H), 2.58-2.52 (m, 1H), 2.09 (apparent t, *J* = 12.2 Hz, 1H), 1.88-1.79 (m, 3H), 1.75 (br d, *J* = 13.0 Hz, 1H), 1.60 (s, 3H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.02 (d, *J* = 6.8 Hz, 3H), 0.96 (s, 9H), 0.94 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.5 Hz, 3H), 0.90 (s, 9H), 0.74 (d, *J* = 6.7 Hz, 3H), 0.11 (s, 3H), 0.10 (s, 3H), 0.04 (s, 3H), 0.04 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$, Z isomer) d 159.0, 134.5, 132.3, 132.2, 131.1, 130.6, 129.0, 128.9, 117.4, 113.6, 98.0, 84.7, 84.5, 77.0, 74.8, 64.9, 55.9, 55.1, 40.0, 38.9, 36.1, 35.4, 35.3, 34.1, 26.2, 25.9, 23.0, 18.6, 18.2, 18.1, 16.0, 14.3, 14.0, 10.7, –3.2, – 3.4, –5.4 (2); high resolution mass spectrum (ES^+) *m/z* 783.5400 [$(M+Na)^+$; calcd for $C_{44}H_{80}O_6Si_2Na$: 783.5391].



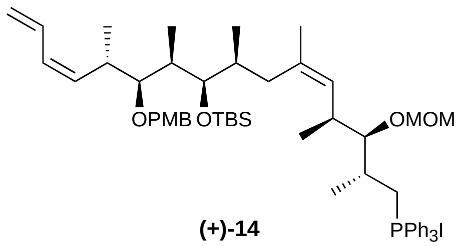
(+)-13

MOM ether (+)-13. Bis-TBS alcohol (+)-**34** (211.1 mg, 0.278 mmol) was dissolved in a 1.0% conc. HCl/EtOH solution (9.3 mL) (37% HCl solution:EtOH = 1:99) and stirred for 25 min. at room temperature. The mixture was then neutralized with saturated $NaHCO_3$ aq., extracted with $CHCl_3$ (3 x 50 mL), and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated . Flash chromatography (10% Æ 30% EtOAc/hexanes) provided MOM-ether (+)-**13** (175.6 mg, 98%) as a colorless oil: $[a]_D^{23}$ +16.0 ° (*c* 2.0, $CHCl_3$); IR ($CHCl_3$) 3502 (br), 2960 (s), 2932 (s), 2880 (m), 2856 (m), 1616 (w), 1514 (m), 1456 (m), 1374 (w), 1302 (w), 1250 (s), 1145 (w), 1091 (s), 1038 (s), 956 (m), 905 (w), 835 (s), 772 (m) cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.27 (d, *J* = 8.7 Hz, 2H), 6.87 (d, *J* = 8.7 Hz, 2H), 6.60 (ddd, *J* = 16.7, 10.7, 10.5 Hz, 1H), 6.03 (apparent t, *J* = 10.9 Hz, 1H), 5.58 (apparent t, *J* = 10.5 Hz, 1H), 5.21 (d, *J* = 16.7 Hz, 1H), 5.12 (d, *J* = 10.3 Hz, 1H), 5.02 (d, *J* = 10.1 Hz, 1H), 4.65 (s, 2H), 4.57 (d, *J* = 10.6 Hz, 1H), 4.46 (d, *J* = 10.6 Hz, 1H), 3.81 (dd, *J* = 10.8, 3.6 Hz, 1H), 3.80 (s, 3H), 3.46 (m, 2H), 3.43 (s, 3H), 3.23 (m, 2H), 3.00 (m, 1H), 2.59 (m, 1H), 2.04 (apparent t, *J* = 12.2 Hz, 1H), 1.79 (m, 3H), 1.71 (apparent d, *J* = 13.2 Hz, 1H), 1.59 (s, 3H), 1.50 (br s, 1H), 1.10 (d, *J* = 6.8 Hz, 3H), 1.01 (d, *J* = 7.1 Hz, 6H), 0.95 (s, 9H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.72 (d, *J* = 6.7 Hz, 3H), 0.10 (s, 3H), 0.09 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 159.1, 134.5, 133.3, 132.3, 131.2, 130.1, 129.1, 129.0, 117.5, 113.7, 99.1, 87.6, 84.6, 77.0, 74.9, 65.0, 56.3, 55.3, 40.2, 37.4, 36.2, 35.6, 35.4, 34.8, 26.3, 23.2, 18.7, 18.6, 15.5, 15.2, 14.5, 10.7, –3.3, –3.3; high resolution mass spectrum (FAB, NBA) *m/z* 669.4520 [$(M+Na)^+$; calcd for $C_{38}H_{66}O_6SiNa$: 669.4526].



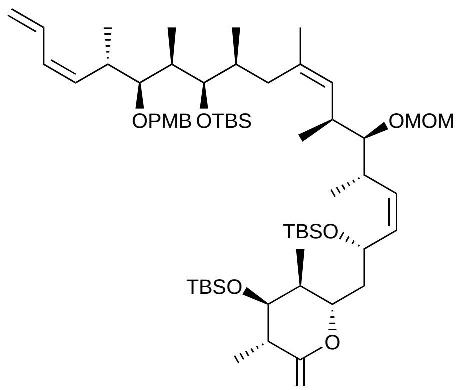
35

Iodide 35. A solution of (+)-**13** (47.9 mg, 0.0741 mmol), PPh_3 (29.2 mg, 0.111 mmol) and imidazole (7.6 mg, 0.111 mmol) in benzene•Et_2O (1:2) (1.06 mL) was cooled to 0 ˚C, and treated with iodine (28.2 mg, 0.111 mmol). The reaction mixture was warmed to room temperature and stirred for 12 min. The reaction was then quenched with saturated $NaHCO_3$ aq. (5 mL). The mixture was extracted with Et_2O (3 x 15 mL), and the combined organics were dried over Na_2SO_4, filtered, and concentrated. Flash chromatography (15% EtOAc/hexanes) provided a mixture of the desired alkyl iodide **35** and PPh_3, which was taken onto the next step without further purification.



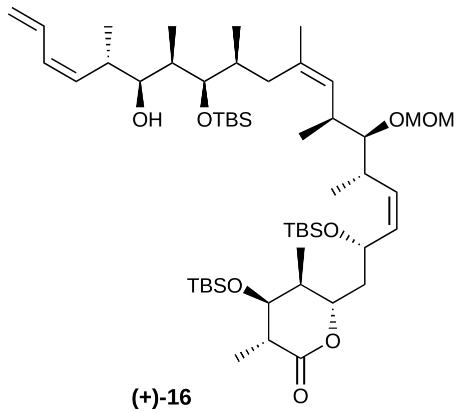
(+)-14

Wittig Salt (+)14. To the neat alkyl iodide **35** (mixed with PPh_3) was added additional PPh_3 (194 mg, 0.741 mmol) and *i*-Pr_2NEt (0.37 mL) at room temperature under argon. The mixture was warmed to 100 ˚C and stirred. After 18 h, the reaction mixture was cooled to room temperature and diluted with CH_2Cl_2 (0.5 mL). The resulting solution was directly purified *via* flash chromatography (20% EtOAc/hexane, then 15% Æ 50% CH_3CN/CH_2Cl_2) to give Wittig salt (+)-**14** as a colorless oil (52.2 mg, 70% for 2 steps) and the mixture of cyclized byproducts (13.1 mg, 28% for 2 steps): **Wittig Salt** (+)-**14:** $[a]^{23}_{D}$ +17.8 ˚ (*c* 1.0, $CHCl_3$); IR ($CHCl_3$) 2962 (s), 2931 (s), 2854 (m), 1612 (w), 1587 (w),1514 (m), 1456 (m), 1438 (w), 1249 (s), 1035 (s), 835 (s), 750 (s) cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.74 (m, 15H), 7.26 (d, *J* = 8.6 Hz, 2H), 6.86 (d, *J* = 8.6 Hz, 2H), 6.55 (ddd, *J* = 16.8, 10.7, 10.5 Hz, 1H), 5.94 (apparent t, *J* = 11.0 Hz, 1H), 5.53 (apparent t, *J* = 10.5 Hz, 1H), 5.13 (d, *J* = 16.8 Hz, 1H), 5.08 (d, *J* = 10.1 Hz, 1H), 5.05 (d, *J* = 10.1 Hz, 1H), 4.70 (d, *J* = 6.1 Hz, 1H), 4.66 (d, *J* = 6.1 Hz, 1H), 4.55 (d, *J* = 10.5 Hz, 1H), 4.44 (d, *J* = 10.5 Hz, 1H), 3.78 (s, 3H), 3.72 (apparent t, *J* = 16.8 Hz, 1H), 3.42 (dd, *J* = 4.8, 3.5 Hz, 1H), 3.34 (s, 3H), 3.31 (apparent t, *J* = 5.8 Hz, 1H), 3.22 (m, 2H), 2.96 (m, 1H), 2.50 (m, 1H), 2.14 (m, 1H), 1.92 (apparent t, *J* = 12.2 Hz, 1H), 1.73 (m, 2H), 1.59 (m, 1H), 1.50 (s, 3H), 1.09 (d, *J* = 6.9 Hz, 3H), 0.94 (d, *J* = 6.9 Hz, 3H), 0.90 (s, 9H), 0.83 (d, *J* = 6.6 Hz, 3H), 0.76 (d, *J* = 6.8 Hz, 3H), 0.65 (d, *J* = 6.7 Hz, 3H), 0.08 (s, 3H), 0.04 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 159.1, 135.3, 135.3, 134.3, 133.8, 133.5, 132.1, 131.0, 130.7, 130.6, 129.1, 128.9, 118.8, 118.1, 117.6, 113.7, 99.3, 88.1, 88.0, 84.5, 75.0, 56.2, 55.3, 54.8, 39.9, 35.7, 35.5, 35.3, 34.2, 31.7, 26.2, 22.9, 18.7, 18.5, 17.9, 15.6, 14.8, 10.7, –3.3, –3.4; high resolution mass spectrum (ES^+) *m/z* 891.5537 $[(M–I)]^+$; calcd for $C_{56}H_{80}O_5PSi$: 891.5513]. **Cyclized byproducts**; high resolution mass spectrum (ES^+) *m/z* 651.4414 $[(M+Na)]^+$; calcd for $C_{38}H_{64}O_5SiNa$: 651.4421].



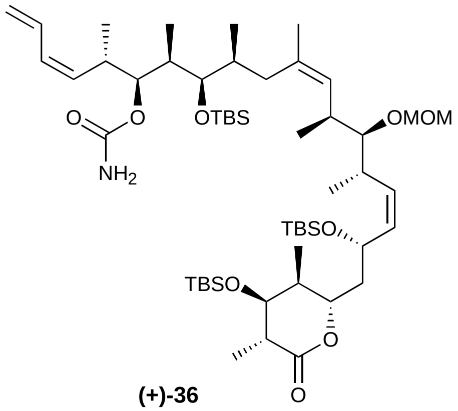
(+)-15

Tetraene (+)-15 (Wittig Coupling). Phosphonium salt (+)-**14** (330 mg, 0.324 mmol; 14:1 ratio of diene isomers), was azeotropically dried with benzene (3 x 0.5 mL) using a double manifold and further dried by heating to 50 °C under vacuum (0.2 torr) for 24 h. The flask was back-filled with argon, dissolved in 1.5 mL of freshly distilled THF and cooled to –78 °C. The resultant solution was treated with methyllithium-lithium bromide complex (2.2 M in pentane, 0.147 mL), warmed to 0 °C, stirred for 30 min., and then recooled to –78 °C. To this orange/red solution was transferred dropwise via syringe a solution of aldehyde (–)-**C** (128 mg, 0.287 mmol) in THF (1.0 mL + 1 x 0.5 mL rinse) over 45 min. The resulting orange solution was stirred for a further 30 min. at –78 °C, and then warmed to –10 °C and allowed to stir for 3 hrs. The resulting light yellow solution was quenched with saturated NH_4Cl and diluted (Et_2O/H_2O). The layers were separated, and the aqueous layer was extracted (3 x Et_2O). The combined organic layers were dried ($MgSO_4$), concentrated, and chromatographed (gradient elution: 3% EtOAc/hexanes Æ 50% EtOAc/hexanes; then 40% CH_3CN/CH_2Cl_2) to afford *cis* isomer (+)-**15** (164 mg, 48%; clear oil, 14:1 ratio of diene isomers), *trans* isomer (11.5 mg, 3.4%; clear oil; 14:1 ratio of diene isomers), and phosphonium salt (+)-**14** (132 mg, 39%; 14:1 ratio of diene isomers): **Cis olefin (+)-15:** $[a]_D^{23}$ +32.0° (*c* 0.3 $CHCl_3$); IR (NaCl) 2958, 2929, 2884, 2857, 1734, 1472, 1253, 1045, 836 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) d 7.25 (d, *J* = 8.1 Hz, 2H), 6.84 (d, *J* = 8.9 Hz, 2H), 6.57 (ddd, *J* = 17.1, 10.8, 10.8 Hz, 1H), 6.00 (apparent t, *J* = 10.8 Hz, 1H), 5.55 (apparent t, *J* = 10.8 Hz, 1H), 5.31 (dd, *J* = 10.8, 7.8 Hz, 1H), 5.24-5.16 (m, 2H), 5.10 (d, *J* = 10.4 Hz, 1H), 4.99 (d, *J* = 10.0 Hz, 1H), 4.80 (apparent t, *J* = 8.9 Hz, 1H), 4.59 (ABq, J_{AB} = 6.7 Hz, Dn_{AB} = 26.4 Hz, 2H), 4.54 (d, *J* = 10.4 Hz, 2H), 4.19 (apparent t, *J* = 10.8 Hz, 1H), 3.77 (s, 3H), 3.61 (apparent t, *J* = 2.6 Hz, 1H), 3.43 (apparent t, *J* = 4.1 Hz, 1H), 3.24 (s, 3H), 3.23 (dd, *J* = 7.4, 3.7 Hz, 1H), 3.04 (apparent t, *J* = 5.6 Hz, 1H), 2.98 (ddd, *J* = 10.0, 6.7, 3.3 Hz, 1H), 2.73-2.65 (m, 1H), 2.60 (ddd, *J* = 15.3, 7.4, 3.0 Hz, 1H), 2.49 (ddd, *J* = 16.8, 13.0, 6.3 Hz, 1H), 2.02 (apparent t, *J* = 12.3 Hz, 1H), 1.85-1.61 (m, 4H), 1.60-1.54 (m, 2H), 1.54 (s, 3H), 1.22 (d, *J* = 7.4 Hz, 3H), 1.08 (d, *J* = 6.7 Hz, 3H), 0.99 (d, *J* = 7.1 Hz, 3H), 0.96-0.91 (m, 6H), 0.93 (s, 9H), 0.90 (d, *J* = 6.7 Hz, 3H), 0.87 (s, 9H), 0.85 (s, 9H), 0.70 (d, *J* = 7.1 Hz, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.03 (br s, 6H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 173.3, 158.9, 134.4, 133.6, 132.4, 132.1, 131.9, 131.2, 130.8, 129.1, 129.0, 117.6, 113.6, 97.4, 86.3, 84.5, 77.0, 74.9, 74.69, 74.68, 64.6, 55.9, 55.2, 43.9, 42.3, 40.1, 36.2, 35.5, 35.3 (2), 34.2, 34.1, 26.2, 25.8, 25.6, 23.0, 18.6, 18.5, 18.0, 17.8, 16.63, 16.61, 16.2, 14.7, 13.9, 10.5, –3.29, –3.32, –4.4, -4.6, -4.9 (2); high resolution mass spectrum (ES+) *m/z* 1079.7214 $[(M+Na)^+$; calcd for $C_{60}H_{108}O_9Si_3Na$: 1079.7199]..



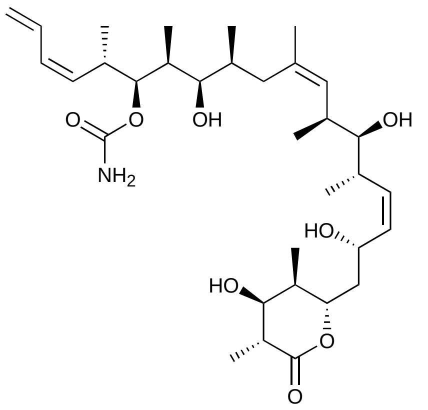
(+)-16

Alcohol (+)-16. At 0 °C, a solution of PMB ether (+)-**15** (124 mg, 0.117 mmol, 14:1 mixture of *cis/trans* diene isomers) in CH_2Cl_2 (6 mL) was treated with H_2O (100 mL) and DDQ (40 mg, 0.160 mmol). The mixture was stirred for 50 min. at 0 °C, warmed to rt and stirred an additional 15 min. The mixture was quenched with 7.0 mL saturated $NaHCO_3$, and diluted with CH_2Cl_2 (25 mL) and H_2O (30 mL). The layers were separated and the aqueous layer was extracted with 3 x 25 mL CH_2Cl_2. The combined organic layers were washed with brine (10 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography (gradient elution; 5% EtOAc Æ 20% EtOAc/hexanes) provided **(+)-16** (101 mg, 92%) as a colorless oil: $[a]^{23}_{D}$ +35.6° (*c* 1.0, $CDCl_3$)]; IR (NaCl) 3510, 2957, 2929, 2884, 2857, 1734, 1472, 1252, 1097, 1044 cm^{-1}; ^1H-NMR (500 MHz, $CDCl_3$) d 6.61 (ddd, *J* = 17.1, 10.9, 10.8 Hz, 1H), 6.12 (apparent t, *J* = 11.1 Hz, 1H), 5.34-5.28 (m, 2H), 5.25-5.19 (m, 1H), 5.23 (d, *J* = 10.1 Hz, 1H), 5.13 (d, *J* = 10.1 Hz, 1H), 5.02 (d, *J* = 10.1 Hz, 1H), 4.80 (apparent t, *J* = 8.6 Hz, 1H), 4.59 (ABq, J_{AB} = 6.7 Hz, Dn_{AB} = 18.9 Hz, 2H), 4.49, (apparent t, *J* = 10.1 Hz, 1H), 3.63 (apparent t, *J* = 2.6 Hz, 1H), 3.60 (dd, *J* = 5.6, 3.4 Hz, 1H), 3.34 (s, 3H), 3.34-3.30 (m, 1H), 3.08 (apparent t, *J* = 5.6 Hz, 1H), 2.79 (ddd, *J* = 16.7, 14.1, 6.7 Hz, 1H), 2.69 (ddd, *J* = 16.0, 12.6, 6.3 Hz, 1H), 2.60 (ddd, *J* = 14.9, 7.4, 2.6 Hz, 1H), 2.54 (ddd, *J* = 16.4, 12.6, 6.3 Hz, 1H), 2.18 (apparent t, *J* = 12.3 Hz, 1H), 1.90-1.75 (m, 4H), 1.73-1.69 (m, 2H), 1.59 (s, 3H), 1.55 (m, 1H), 1.22 (d, *J* = 7.4 Hz, 3H), 0.97-0.92 (m, 15H), 0.91 (s, 9H), 0.87 (s, 9H), 0.85 (s, 9H), 0.74 (d, *J* = 6.7 Hz, 3H), 0.07 (apparent s, 6H), 0.06 (s, 3H), 0.05 (s, 3H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C-NMR (125 MHz, $CDCl_3$) d 173.4, 134.6, 133.7, 132.3, 132.0, 131.9, 130.9, 130.7, 118.3, 97.5, 86.3, 78.9, 77.0, 76.2, 74.7, 64.7, 55.9, 43.9, 42.3, 38.0, 36.5, 36.3, 35.5, 34.9, 34.3, 34.2, 26.2, 25.8, 25.7, 23.24, 18.4, 18.0, 17.9, 17.1, 16.8, 16.5, 16.2, 13.9, 13.6, 9.4, –3.3, –3.8, –4.4, -4.6, -4.9 (2); high resolution mass spectrum (ES+) *m/z* 959.6625 [(M+Na)$^+$; calcd for $C_{52}H_{100}O_8Si_3Na$: 959.6624].



(+)-36

Carbamate (+)-36. A solution of alcohol (+)-**16** (10 mg, 0.011 mmol) in CH_2Cl_2 (1.0 mL) was treated with a 1 M solution of $Cl_3CCON{=}C{=}O$ in toluene (16 mL, 0.016 mmol) at room temperature for 30 min. Neutral Al_2O_3 (1 g) was added, followed by 2 mL CH_2Cl_2. After 4 h, the material was transferred to a cotton-plugged chromatography column and flushed from the Al_2O_3 (EtOAc, 50 mL). Concentration and purification by preparatory TLC (250 mm plate, 20% ethyl acetate/hexanes) provided 6.0 mg (+)-**36** (60%) as a colorless oil and 3.5 mg (35%) of recovered (+)-**16**. **Carbamate** (+)-**36:** $[a]^{23}_{D}$ +46.2° (*c* 0.5, $CHCl_3$); IR (NaCl) 3510, 3360, 2957, 2936, 2884, 2849, 1732, 1594, 1253, 1033 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) d 6.58 (ddd, *J* = 17.1, 10.8, 10.8 Hz, 1H), 6.01 (apparent t, *J* = 11.1 Hz, 1H), 5.35 (apparent t, *J* = 10.4 Hz, 1H), 5.33-5.27 (m , 1H), 5.25-5.18 (m, 2H), 5.12 (d, *J* = 10.0 Hz, 1H), 5.01 (d, *J* = 10.0 Hz, 1H), 4.80 (apparent t, *J* = 8.9 Hz, 1H), 4.71 (apparent t, *J* = 6.0 Hz, 1H), 4.60 (ABq, J_{AB} = 6.7 Hz, Dn_{AB} = 26.4 Hz, 2H), 4.50 (apparent t, *J* = 10.4 Hz, 1H), 4.44 (br s, 2H), 3.64 (apparent t, *J* = 2.4 Hz, 1H), 3.43 (apparent t, *J* = 4.1 Hz, 1H), 3.34 (s, 3H), 3.06 (apparent t, *J* = 5.6 Hz, 1H), 3.02-2.94 (m, 1H), 2.75-2.66 (m, 1H), 2.65-2.57 (m, 1H), 2.57-2.47 (m, 1H), 2.12 (apparent t, *J* = 12.4 Hz, 1H), 1.93-1.79 (m, 3H), 1.74-1.66 (m, 2H), 1.58 (apparent s, 3H), 1.55-1.50 (m, 1H), 1.23 (d, *J* = 7.4 Hz, 3H), 0.98 (d, *J* = 7.4 Hz, 3H), 0.96 (d, *J* = 6.7 Hz, 3H), 0.94 (d, *J* = 5.4 Hz, 3H), 0.94-0.92 (m, 6H), 0.91 (s, 9H), 0.87 (s, 9H), 0.85 (s, 9H), 0.71 (d, *J* = 6.7 Hz, 3H), 0.08 (s, 3H), 0.06 (apparent s, 9H), 0.04 (s, 3H), 0.03 (s, 3H); ^{13}C-NMR (125 MHz, MeOH –d6) d 174.9, 158.7, 133.5, 132.9, 131.9, 131.8, 131.6, 130.5, 129.5, 117.1, 97.3, 86.5, 77.8, 76.7, 74.4, 64.5, 55.0, 44.3, 42.0, 38.4, 36.4, 35.6, 34.9, 34.3, 34.2, 33.4, 25.4, 24.9, 18.0, 17.5, 17.4, 16.6, 16.1, 15.7, 15.2, 13.2, 13.1, 9.3, –4.4, –4.5, –5.4, –5.9 (2), –6.2; high resolution mass spectrum (ES+) *m/z* 1002.6638 [(M+Na)$^+$; calcd for $C_{53}H_{101}NO_9Si_3Na$: 1002.6682].



(+)-Discodermolide

(+)-Discodermolide (1). Carbamate (+)-**36** (6.0 mg, 0.006 mmol) was dissolved in MeOH (1.5 mL) and stirred for 15 min. at room temperature. Aqueous hydrochloric acid (4 N, 1.5 mL) was added in small portions over 4 hours at a rate which minimized precipitation (ca. 10 to 15 min. intervals). After 4 h, an additional 1 mL of 4 N aq HCl was added in one portion, and the resulting solution was stirred for 2 h at rt, diluted with 10 mL of water and poured into 15 mL of EtOAc. The resulting mixture was quenched *via* careful portionwise addition of $NaHCO_3$ until CO_2 evolution ceased. The layers were separated, the aqueous layer was saturated with NaCl and extracted (3 x EtOAc). The combined organic layers were washed with brine (1 x 10 mL), dried ($MgSO_4$), filtered, and concentrated. Flash chromatography using washed SiO_2 (10% MeOH/CH_2Cl_2 then 55% EtOAc/hexanes) *via* gradient elution (55% EtOAc/hexanes then 10% MeOH/CH_2Cl_2) provided (+)-discodermolide (3.1 mg, 87% yield) as a white amorphous solid, whose spectral data (^{1}H-NMR, HRMS) matched that previously reported for the natural product.