SUPPORTING INFORMATION

for

Synthetic Studies Aimed at (-)-Cochleamycin A. Evaluation of Late-Stage Macrocyclization Alternatives

by Leo A. Paquette,* Jiyoung Chang, and Zuosheng Liu

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

(125 pages)

- Experimental details pp S2-S46
- Copies of the high field $^1\text{H}/^{13}\text{C}$ NMR spectra of all compounds pp S47-S125

Experimental Details

All reactions were performed in the appropriate flame-dried glass apparatus under a static nitrogen or argon atmosphere. Thin-layer chromatography was performed on precoated silica gel 60 F₂₅₄ analytical plates. The organic extracts were dried over anhydrous magnesium sulfate or sodium sulfate. Solvents were reagent grade and in most cases properly dried before use.

PMB Ether 14. A suspension of **13** (500 mg, 2.69 mmol) and NaH (60%, 538 mg, 13.5 mmol) in dry DMF (38 mL) was stirred for 30 min at 0 °C to rt under N₂, treated with *p*-methoxybenzyl bromide (1.86 mL, 10.7 mmol) at 0 °C, stirred overnight at rt, quenched with water, diluted with hexanes/ethyl acetate (1:1), washed with brine, dried, and concentrated *in vacuo*. Purification of the residue on silica gel (hexanes/ethyl acetate 20:1) gave **14** as a colorless oil (822 mg, 100%); IR (neat, cm⁻¹) 1613, 1514, 1369; ¹H NMR (300 MHz, CDCl₃) δ 7.26 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 5.90-5.76 (m, 1 H), 5.14-5.07 (m, 2 H), 4.57 (d, *J* = 10.9 Hz, 1 H), 4.39 (d, *J* = 10.9 Hz, 1 H), 4.27-4.18 (m, 1 H), 4.02 (dd, *J* = 8.0, 5.8 Hz, 1 H), 3.80 (s, 3 H), 3.71-3.62 (m, 1 H), 3.50 (t, *J* = 7.9 Hz, 1 H), 2.38-2.32 (m, 2 H), 1.82-1.42 (m, 2 H), 1.39 (s, 3 H), 1.35 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 159.4, 134.4, 130.9, 129.6, 117.6, 114.0, 108.5, 75.8, 73.8, 71.3, 70.2, 55.4, 38.9 (2 C), 27.2, 26.0; HRMS ES *m/z* (M + Na)⁺ calcd 329.1729, obsd 329.1730; [α]_D¹⁹ -48.7 (c 3.55, CHCl₃).

Anal. Calcd for C₁₈H₂₆O₄: C, 70.56; H, 8.55. Found: C, 70.58; H, 8.60.

Diol 15. A solution of **14** (4.0 g, 13.1 mmol) in acetic acid: THF:H₂O (1:1:1) (66 mL) was stirred for 8 h at 50-60 °C, freed of solvent *in vacuo*, diluted with CH₂Cl₂, and washed with saturated NaHCO₃ solution. The aqueous layer was re-extracted with CH₂Cl₂, the combined organic layers were washed with brine, dried, and evaporated, and the residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 1:2) to give **15** (3.22 g, 92%) as a colorless oil; IR (neat, cm⁻¹) 3402, 1612, 1514; ¹H NMR (300 MHz, CDCl₃) δ 7.25 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H),

5.86-5.73 (m, 1 H), 5.13-5.07 (m, 2 H), 4.57 (d, $J = 11.1$ Hz, 1 H), 4.42 (d, $J = 11.1$ Hz, 1 H), 3.98-3.91 (m, 1 H), 3.79 (s, 3 H), 3.79-3.72 (m, 1 H), 3.58 (dd, $J = 11.1, 3.0$ Hz, 1 H), 3.41 (dd, $J = 11.1, 6.8$ Hz, 1 H), 2.81 (br s, 2 H), 2.47-2.31 (m, 2 H), 1.73-1.65 (m, 1 H), 1.56 (ddd, $J = 14.6, 8.0, 3.2$ Hz, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.3, 134.2, 130.2, 129.5, 117.6, 113.9, 75.5, 70.9, 69.1, 66.9, 55.2, 38.0, 36.3; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 289.1410, obsd 289.1404; $[\alpha]_{\text{D}}^{20}$ -61.1 (c 1.55, CHCl_3).

Hydroxy Pivalate 16. To a stirred solution of **15** (413 mg, 1.55 mmol) in pyridine (5 mL) and CH_2Cl_2 (10 mL) was added pivaloyl chloride (0.23 mL, 1.86 mmol) at 0 °C under N_2 . The mixture was allowed to warm to rt, stirred overnight, diluted with ethyl acetate, washed with 1N HCl, saturated NaHCO_3 solution, and brine, then dried and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 7:1) to give **16** (496 mg, 91%); IR (neat, cm^{-1}) 3488, 1729, 1613; ^1H NMR (300 MHz, CDCl_3) δ 7.27 (d, $J = 8.6$ Hz, 2 H), 6.88 (d, $J = 8.7$ Hz, 2 H), 5.89-5.73 (m, 1 H), 5.15-5.07 (m, 2 H), 4.59 (d, $J = 11.1$ Hz, 1 H), 4.43 (d, $J = 11.1$ Hz, 1 H), 4.13-3.96 (m, 3 H), 3.80 (s, 3 H), 3.83-3.75 (m, 1 H), 2.71 (br s, 1 H), 2.50-2.29 (m, 2 H), 1.72-1.58 (m, 2 H), 1.21 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 178.4, 159.2, 134.1, 130.2, 129.4, 117.5, 113.8, 75.2, 68.2, 66.8, 55.2, 38.7, 38.1, 36.8, 27.1; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 373.1985, obsd 373.2007; $[\alpha]_{\text{D}}^{19}$ -35.5 (c 1.85, CHCl_3).

Unsaturated Epoxide 17. To a cooled (0 °C), stirred solution of **16** (6.66 g, 19 mmol) in pyridine (7.7 mL) and CH_2Cl_2 (95 mL) were added DMAP (230 mg, 1.9 mmol) and methanesulfonyl chloride (4.4 mL, 57 mmol) under N_2 . The solution was allowed to warm to rt, stirred overnight, diluted with ethyl acetate, washed with 1N HCl and brine, and dried. The solvent was removed and the residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 8:1) to give the mesylate as a colorless oil (7.9 g, 97%); IR (neat, cm^{-1}) 1734, 1515, 1350; ^1H NMR (300 MHz, CDCl_3) δ 7.31 (d, $J = 8.5$ Hz, 2 H), 6.88 (d, $J = 8.6$ Hz, 2 H), 5.88-5.74 (m, 1 H), 5.19-5.09 (m, 3 H), 4.57 (d, $J = 10.4$ Hz, 1 H), 4.45 (d, $J = 10.2$ Hz, 1 H), 4.41 (dd, $J = 12.2, 3.1$ Hz, 1

H), 4.07 (dd, $J = 12.5, 5.6$ Hz, 1 H), 3.79 (s, 3 H), 3.77-3.68 (m, 1 H), 3.01 (s, 3 H), 2.43-2.34 (m, 2 H), 1.91 (ddd, $J = 14.9, 9.4, 2.4$ Hz, 1 H), 1.73 (ddd, $J = 14.8, 10.2, 3.2$ Hz, 1 H), 1.22 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 177.7, 159.1, 133.5, 130.3, 129.6, 117.8, 113.7, 77.3, 73.6, 70.6, 65.4, 55.1, 38.7, 38.6, 37.7, 36.5, 27.0; HRMS ES m/z ($\text{M} + \text{Na}$)⁺ calcd 451.1761, obsd 451.1728; $[\alpha]_{\text{D}}^{19} -26.6$ (c 2.98, CHCl_3).

Anal. Calcd for $\text{C}_{21}\text{H}_{32}\text{O}_7\text{S}$: C, 58.86; H, 7.53. Found: C, 59.04; H, 7.60.

The mesylate (1.0 g, 2.3 mmol) was dissolved in MeOH (117 mL), treated with K_2CO_3 (484 mg, 3.50 mmol) and stirred overnight at rt. The mixture was diluted with ethyl acetate, washed with brine, dried, and freed of solvent. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 7:1) to give epoxide **17** (518 mg, 89%); IR (neat, cm^{-1}) 1613, 1514, 1302; ^1H NMR (300 MHz, CDCl_3) δ 7.27 (d, $J = 8.5$ Hz, 2 H), 6.87 (d, $J = 8.7$ Hz, 2 H), 5.92-5.78 (m, 1 H), 5.15-5.06 (m, 2 H), 4.53 (d, $J = 11.3$ Hz, 1 H), 4.45 (d, $J = 11.3$ Hz, 1 H), 3.80 (s, 3 H), 3.63 (quintet, $J = 5.9$ Hz, 1 H), 3.07-3.01 (m, 1 H), 2.73 (t, $J = 4.5$ Hz, 1 H), 2.46 (dd, $J = 5.1, 2.7$ Hz, 1 H), 2.44-2.38 (m, 2 H), 1.88-1.79 (m, 1 H), 1.76-1.67 (m, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.2, 134.4, 130.6, 129.2, 117.4, 113.8, 76.0, 70.5, 55.2, 49.5, 46.8, 38.3, 36.6; HRMS EI m/z (M^+) calcd 248.1412, obsd 248.1432; $[\alpha]_{\text{D}}^{20} -23.3$ (c 1.39, CHCl_3).

Anal. Calcd for $\text{C}_{15}\text{H}_{20}\text{O}_3$: C, 72.55; H, 8.12. Found: C, 72.51; H, 8.06.

Conversion of 17 to 18. A cold (-78°C), stirred solution of **17** (1.34 g, 5.40 mmol) in ethyl acetate (54 mL) was exposed to a stream of ozone. The completion of reaction was carefully monitored by TLC. After 7 min, Ph_3P (1.42 g, 5.40 mmol) was introduced and the mixture was allowed to warm to rt, stirred overnight, and freed of solvent. The resulting aldehyde was taken up in MeOH (54 mL), cooled to 0°C , and treated with NaBH_4 (408 mg, 10.8 mmol) at 0°C . After 30 min, H_2O was added, methanol was removed *in vacuo*, and the residue was diluted with CH_2Cl_2 , washed with 1N HCl, saturated NaHCO_3 solution, and brine prior to drying and concentration *in vacuo*. The residue was purified by column chromatography on silica gel (hexanes/ethyl

acetate 1:1) to give the alcohol. Since separation from triphenylphosphine oxide was not readily achieved, the mixture of these two compounds was used in the pivaloylation step.

To a stirred solution of crude alcohol in pyridine (4.4 mL) and CH₂Cl₂ (11 mL) was added pivaloyl chloride (1.33 mL, 10.8 mmol) at 0 °C under N₂. The mixture was allowed to warm to rt, stirred for 5 h, diluted with hexanes, and filtered through a short silica gel pad, which was washed with hexanes/ethyl acetate (5:1). The filtrate was concentrated and the residue was purified by silica gel column chromatography (hexanes/ethyl acetate 20:1) to give **18** (980 mg, 54%) and **19** (416 mg, 23%), both as colorless oils.

For **18**: IR (neat, cm⁻¹) 1726, 1612, 1514; ¹H NMR (300 MHz, CDCl₃) δ 7.26 (d, *J* = 8.6 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 4.50 (d, *J* = 11.1 Hz, 1 H), 4.42 (d, *J* = 11.1 Hz, 1 H), 4.19 (t, *J* = 6.4 Hz, 2 H), 3.79 (s, 3 H), 3.73-3.65 (m, 1 H), 3.06-3.00 (m, 1 H), 2.76 (dd, *J* = 4.9, 4.1 Hz, 1 H), 2.47 (dd, *J* = 5.0, 2.7 Hz, 1 H), 1.94 (q, *J* = 6.3 Hz, 2 H), 1.89-1.71 (m, 2 H), 1.17 (s, 9 H); ¹³C NMR (75 MHz, CDCl₃) δ 178.4, 159.3, 130.3, 129.4, 113.6, 73.3, 70.8, 61.0, 55.2, 49.1, 46.7, 38.7, 36.8, 33.4, 27.2; HRMS ES *m/z* (M + Na)⁺ calcd 359.1829, obsd 359.1863; [α]_D²⁰ +39.6 (*c* 2.13, CHCl₃).

For **19**: IR (neat, cm⁻¹) 1725, 1612, 1514; ¹H NMR (300 MHz, CDCl₃) δ 7.25 (d, *J* = 8.6 Hz, 2 H), 6.88 (d, *J* = 8.6 Hz, 2 H), 4.55 (d, *J* = 11.0 Hz, 1 H), 4.42 (d, *J* = 11.0 Hz, 1 H), 4.18 (t, *J* = 6.5 Hz, 2 H), 4.00-3.82 (m, 1 H), 3.80 (s, 3 H), 3.80-3.74 (m, 1 H), 3.48 (d, *J* = 5.4 Hz, 2 H), 2.00-1.91 (m, 2 H), 1.89-1.73 (m, 2 H), 1.20 (s, 9 H); ¹³C NMR (75 MHz, CDCl₃) δ 178.4, 159.4, 129.6, 129.5, 114.0, 75.1, 70.7, 70.4, 60.6, 55.2, 49.3, 38.7, 38.2, 32.7, 27.1; HRMS ES *m/z* (M + Na)⁺ calcd 359.1829, obsd 359.1864; [α]_D²⁰ -18.0 (*c* 1.08, CHCl₃).

Acetylenic Carbinol 20. To a cooled (-78 °C), stirred solution of trimethylsilylacetylene (3.8 mL, 26.77 mmol) in THF (67 mL) was added *n*-BuLi (1.45 M solution in hexane, 14.8 mL, 21.42 mmol) dropwise under N₂. After 30 min at -78 °C,

BF₃•Et₂O (3.9 g, 42.84 mmol) was added to the reaction mixture. The mixture was stirred for 20 min at -78 °C and to this reaction mixture was added a solution of epoxide **18** (3.6g, 10.71 mmol) in THF (40 mL). After 1 h at -78 °C, the mixture was quenched with saturated NH₄Cl solution, extracted with ethyl acetate, washed with brine, and dried over Na₂SO₄. The solvent was removed *in vacuo* and the resulting oil was used for the next step without added purification. In one instance, a small aliquot was chromatographed to allow for characterization; colorless oil; IR (neat, cm⁻¹) 3491, 2175, 1728; ¹H NMR (300 MHz, CDCl₃) δ 7.25 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 4.53 (d, *J* = 10.9 Hz, 1 H), 4.43 (d, *J* = 10.9 Hz, 1 H), 4.22-4.13 (m, 2 H), 3.90-3.85 (m, 1 H), 3.79 (s, 3 H), 3.79-3.73 (m, 1 H), 2.43 (dd, *J* = 16.8, 5.8 Hz, 1 H), 2.35 (dd, *J* = 16.8, 6.6 Hz, 1 H), 1.97-1.85 (m, 2 H), 1.84-1.70 (m, 2 H), 1.19 (s, 9 H), 0.15 (s, 9 H); ¹³C NMR (75 MHz, CDCl₃) δ 178.4, 159.4, 129.8, 129.5, 114.0, 103.2, 87.2, 75.5, 70.7, 69.2, 60.7, 55.2, 39.9, 38.7, 32.8, 28.9, 27.2, 0.1; HRMS ES *m/z* (M + Na)⁺ calcd 457.2381, obsd 457.2346; [α]_D²⁰ -15.9 (*c* 1.30, CHCl₃).

A solution of the unpurified silylacetylene from above and TBAF (1 M solution in THF, 32 mL, 32mmol) in THF (107 mL) was stirred for 1 h at 0 °C. Water was added and the mixture was diluted with ethyl acetate, washed with brine, dried, and evaporated. The residue was purified by silica gel column chromatography (hexanes/ethyl acetate 3:1) to give **20** (3.7 g, 95% for the two steps); IR (neat, cm⁻¹) 3494, 1725, 1613; ¹H NMR (300 MHz, CDCl₃) δ 7.25 (d, *J* = 8.5 Hz, 2 H), 6.87 (d, *J* = 8.6 Hz, 2 H), 4.55 (d, *J* = 10.9 Hz, 1 H), 4.41 (d, *J* = 10.9 Hz, 1 H), 4.17 (t, *J* = 6.5 Hz, 2 H), 4.13-3.80 (m, 1 H), 3.79 (s, 3 H), 3.79-3.74 (m, 1 H), 3.40 (s, 1 H), 2.42-2.26 (m, 2 H), 2.01 (t, *J* = 2.6 Hz, 1 H), 1.98-1.87 (m, 2 H), 1.84-1.71 (m, 2 H), 1.19 (s, 9 H); ¹³C NMR (75 MHz, CDCl₃) δ 178.4, 159.5, 129.6 (2 C), 114.0, 80.8, 76.0, 70.7, 70.5, 69.4, 60.7, 55.3, 40.0, 38.7, 32.7, 27.3, 27.2; HRMS ES *m/z* (M + Na)⁺ calcd 385.1985, obsd 385.1975; [α]_D²⁰ -23.9 (*c* 0.97, CHCl₃).

Acetylenic Acetal 21. A suspension of **20** (20 mg, 0.055 mmol) and molecular sieves (40 mg) in dry CH₂Cl₂ (5 mL) was stirred for 20 min under N₂ prior to the addition of DDQ (19 mg, 0.083 mmol) at rt. The reaction mixture was stirred for 3 h and saturated NaHCO₃ solution was introduced prior to dilution with ethyl acetate, washing with brine, drying, and solvent evaporation. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 10:1) to give **21** (17 mg, 85%) as a colorless oil; IR (neat, cm⁻¹) 1726, 1615, 1518; ¹H NMR (300 MHz, CDCl₃) δ 7.42 (d, *J* = 8.7 Hz, 2 H), 6.88 (d, *J* = 8.8 Hz, 2 H), 5.48 (s, 1 H), 4.23 (t, *J* = 6.5 Hz, 2 H), 4.02-3.89 (m, 2 H), 3.80 (s, 3 H), 2.64 (ddd, *J* = 16.6, 5.2, 2.7 Hz, 1 H), 2.43 (ddd, *J* = 16.6, 8.1, 2.7 Hz, 1 H), 2.03 (t, *J* = 2.5 Hz, 1 H), 2.00-1.85 (m, 3 H), 1.56-1.41 (m, 1 H), 1.20 (s, 9 H); ¹³C NMR (125 MHz, CDCl₃) δ 178.6, 160.1, 131.0, 127.5, 113.7, 100.8, 80.0, 74.9, 73.8, 70.6, 60.8, 55.4, 38.8, 36.1, 35.0, 27.3, 25.8; HRMS ES *m/z* (M + Na)⁺ calcd 383.1829, obsd 383.1820; [α]_D¹⁶ +36.5 (c 0.69, CHCl₃).

Vinylstannane 22. To a stirred solution of **21** (40 mg, 0.11 mmol) in benzene (22 mL) were added *n*-Bu₃SnH (0.3 mL, 1.1 mmol) and AIBN (2 mg, 0.01 mmol) at rt under N₂. The reaction mixture was gently refluxed with stirring for 2 h. The solvent was removed and the residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 50:1) to give **22** (71 mg, 99%) as a colorless oil; IR (neat, cm⁻¹) 1730, 1615, 1518; ¹H NMR (300 MHz, CDCl₃) δ 7.41 (d, *J* = 8.7 Hz, 2 H), 6.87 (d, *J* = 8.7 Hz, 2 H), 6.14-5.93 (m, 2 H), 5.47 (s, 1 H), 4.26-4.19 (m, 2 H), 3.95-3.81 (m, 2 H), 3.80 (s, 3 H), 2.79-2.52 (m, 1 H), 2.41-2.32 (m, 1 H), 2.03-1.83 (m, 2 H), 1.68-1.45 (m, 7 H), 1.42-1.22 (m, 7 H), 1.20 (s, 9 H), 1.03-0.82 (m, 15 H); ¹³C NMR (75 MHz, CDCl₃) δ 178.4, 160.0, 144.0, 131.5, 127.3, 113.5, 100.5, 76.3, 73.6, 60.7, 55.3, 44.4, 38.7, 36.4, 35.0, 29.1, 27.2, 13.7, 9.4; HRMS ES *m/z* (M + Na)⁺ calcd 675.3042, obsd 675.3019; [α]_D¹⁷ +8.0 (c 0.69, CHCl₃).

Vinyl iodide 23. To a cooled (0 °C), stirred solution of **22** (207 mg, 0.318 mmol) in CH₂Cl₂ (11 mL) was added iodine (161 mg, 0.636 mmol). After 10 min at 0 °C, the

reaction mixture was diluted with ethyl acetate, washed with saturated $\text{Na}_2\text{S}_2\text{O}_3$ and 10% KF solutions, and brine. The organic layer was dried, filtered, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 20:1) to give **23** (149 mg, 96%); IR (neat, cm^{-1}) 1725, 1614, 1518, 1249; ^1H NMR (300 MHz, CDCl_3) δ 7.41 (d, $J = 8.7$ Hz, 2 H), 6.89 (d, $J = 8.7$ Hz, 2 H), 6.60 (dt, $J = 14.6, 7.4$ Hz, 1 H), 6.15 (d, $J = 14.5$ Hz, 1 H), 5.46 (s, 1 H), 4.21 (t, $J = 6.5$ Hz, 2 H), 3.95-3.82 (m, 2 H), 3.80 (s, 3 H), 2.48-2.26 (m, 2 H), 2.04-1.84 (m, 2 H), 1.63-1.54 (m, 1 H), 1.44 (q, $J = 11.1$ Hz, 1 H), 1.20 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 178.4, 160.0, 141.6, 130.9, 127.3, 113.6, 100.5, 77.3, 75.1, 73.5, 60.6, 55.3, 42.2, 38.7, 36.2, 34.9, 27.2; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 511.0952, obsd 511.0963; $[\alpha]_{\text{D}}^{19} +3.5$ (c 0.49, CHCl_3).

Lactone 25. To a vigorously stirred suspension of CuI (6.54 g, 34.32 mmol) in dry ether (50 mL) was added MeLi (1.4 M solution in ether, 49 mL, 68.66 mmol) dropwise at -20 °C under N_2 . The resulting solution was stirred for 30 min at -20 °C and **24** (4.03 g, 11.44 mmol) dissolved in THF (20 mL) was introduced at -30 °C. After 35 min at this temperature, the mixture was quenched with saturated NH_4Cl solution, extracted with ethyl acetate, washed with brine, dried, and concentrated. Purification of the residue on silica gel (hexanes/ethyl acetate 6:1) gave **25** (3.74 g, 89%), the enantiomeric form of which has previously been prepared in the same manner;³⁰ $[\alpha]_{\text{D}}^{17} -27.4$ (c 1.2, CHCl_3).

Hydroxy Ester 26. To a stirred solution of **25** (93 mg, 0.38 mmol) in dry CH_2Cl_2 was added Dibal-H (1 M solution in hexane, 0.57 mL, 0.57 mmol) dropwise at -78 °C under N_2 . After 1 h, the reaction mixture was quenched with methanol, allowed to warm to rt, treated with Rochelle's salt solution and stirred until two clear layers were visible. The mixture was extracted with CH_2Cl_2 and the combined organic layers were dried and concentrated. The resulting lactol was dissolved directly in dry benzene (7.6 mL), treated with (methoxycarbonyl-methylene)triphenylphosphorane (367 mg, 1.14

mmol), and stirred for 3 h at 100 °C. The solvent was evaporated and the residue was preadsorbed from CH₂Cl₂ on to silica gel and purified by silica gel column chromatography (hexanes/ethyl acetate 8:1) to give **26** (115 mg, quantitative); IR (neat, cm⁻¹) 3491, 1724, 1428; ¹H NMR (300 MHz, CDCl₃) δ 7.67-7.64 (m, 4 H), 7.48-7.32 (m, 6 H), 6.99-6.89 (m, 1 H), 5.83 (dt, *J* = 15.6, 1.3 Hz, 1 H), 3.73 (s, 3 H), 4.13-3.65 (m, 1 H), 3.55 (dd, *J* = 9.9, 7.5 Hz, 1 H), 3.49-3.41 (m, 1 H), 2.63 (d, *J* = 3.7 Hz, 1 H), 2.55-2.46 (m, 1 H), 2.15-2.04 (m, 1 H), 1.81-1.68 (m, 1 H), 1.07 (s, 9 H), 0.76 (d, *J* = 6.8 Hz, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 166.9, 148.1, 135.5, 132.9, 129.9, 127.8, 122.4, 75.0, 65.9, 51.4, 35.4, 35.2, 26.8, 19.2, 15.4; HRMS ES *m/z* (*M* + Na)⁺ calcd 449.2119, obsd 449.2124; [α]_D¹⁹ -3.8 (c 0.48, CHCl₃).

Allylic Alcohol 28. A solution of **26** (510 mg, 1.20 mmol) and (4-methoxybenzyl)trichloroacetimidate (676 mg, 2.39 mmol) in CH₂Cl₂ (12 mL) was cooled to 0 °C and camphorsulfonic acid (28 mg, 0.12 mmol) was added under N₂. The reaction mixture was stirred at 0 °C for 2 h and at rt overnight, diluted with ethyl acetate, and washed with 1N HCl and brine. The organic layer was dried and evaporated. The residual **27** was used for the next step without further purification.

To a cooled (-78 °C), stirred solution of unpurified **27** in CH₂Cl₂ (26 mL) was added Dibal-H (1M solution in hexane, 5.2 mL, 5.21 mmol) under N₂. After 2 h at -78 °C, the reaction mixture was quenched with MeOH and the temperature of reaction mixture was allowed to 20 °C. Saturated Rochelle's salt solution was added and the resulting mixture was stirred overnight. The aqueous layer was extracted with CH₂Cl₂ and the combined organic layers were washed with brine, dried, and evaporated. Purification was realized on silica gel (hexanes/ethyl acetate 5:1) to afford **28** (386 mg, 60% for 2 steps); IR (neat, cm⁻¹) 3420, 1612; ¹H NMR (500 MHz, CDCl₃) δ 7.76-7.72 (m, 4 H), 7.50-7.46 (m, 2 H), 7.45-7.40 (m, 4 H), 7.30-7.27 (m, 2 H), 6.92-6.89 (m, 2 H), 5.68-5.60 (m, 2 H), 4.68 (d, *J* = 11.2 Hz, 1 H), 4.45 (d, *J* = 11.2 Hz, 1 H), 4.11-4.10 (m, 2 H), 3.85 (s, 3 H), 3.84-3.71 (m, 2 H), 3.33 (ABq, Δv = 9.7 Hz, *J* = 5.3 Hz, 1 H), 2.33-

2.29 (m, 1 H), 1.97-1.91 (m, 2 H), 1.44 br s, 1 H), 1.12 (s, 9 H), 0.92 (d, $J = 6.5$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.0, 135.6, 133.5 (2 C), 131.8, 131.0, 130.3, 129.6, 129.3, 127.6, 113.6, 83.1, 72.2, 64.1, 63.7, 55.2, 35.0, 34.7, 26.8, 19.2, 15.7; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 541.2750, obsd 541.2748; $[\alpha]_{\text{D}}^{19} +13.9$ (c 0.54, CHCl_3).

Acetate 29. To a stirred solution of **28** (74 mg, 0.14 mmol) in CH_2Cl_2 (7 mL) were added pyridine (0.033 mL, 0.41 mmol), DMAP (2.0 mg, 0.014 mmol) and acetic anhydride (0.040 mL, 0.41 mmol) at rt under N_2 . The reaction mixture was stirred for 1 h and diluted with ethyl acetate. The organic layer was washed with brine, dried, filtered, and evaporated. Purification on silica gel (hexanes/ethyl acetate 15:1) gave **29** (76 mg, 97%); IR (neat, cm^{-1}) 1739, 1613, 1514; ^1H NMR (300 MHz, CDCl_3) δ 7.70 (d, $J = 7.0$ Hz, 4 H), 7.47-7.35 (m, 6 H), 7.27-7.23 (m, 2 H), 6.89-6.84 (m, 2 H), 5.73-5.64 (m, 1 H), 5.58-5.48 (m, 1 H), 4.63 (d, $J = 11.2$ Hz, 1 H), 4.50 (d, $J = 6.3$ Hz, 2 H), 4.40 (d, $J = 11.2$ Hz, 1 H), 3.82 (s, 3 H), 3.80-3.72 (m, 2 H), 3.28 (q, $J = 4.9$ Hz, 1 H), 2.32-2.09 (m, 1 H), 2.07 (s, 3 H), 1.95-1.85 (m, 2 H), 1.07 (s, 9 H), 0.86 (d, $J = 6.2$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.9, 159.0, 135.6, 135.1, 133.5 (2 C), 131.0, 129.6, 129.3, 127.7, 125.2, 113.6, 83.1, 72.2, 65.3, 64.1, 55.2, 35.1, 34.5, 26.8, 21.0, 19.2, 15.8; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 583.2850, obsd 583.2875; $[\alpha]_{\text{D}}^{17} +14.4$ (c 0.39, CHCl_3).

Dibromide 30. To a cooled (0 °C), solution of **29** (76 mg, 0.14 mmol) in THF (6.8 mL) was added TBAF (1 M solution in THF, 0.3 mL, 0.27 mmol) under N_2 . After 4 h at 0 °C, the mixture was diluted with ethyl acetate and washed with water and brine. The organic layer was dried, filtered, and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 1:1) to afford the acetoxo alcohol (44 mg, 100%); IR (neat, cm^{-1}) 3449, 1736, 1612; ^1H NMR (300 MHz, CDCl_3) δ 7.29-7.25 (m, 2 H), 6.91-6.87 (m, 2 H), 5.77-5.67 (m, 1 H), 5.63-5.54 (m, 1 H), 4.56-4.47 (m, 4 H), 3.81 (s, 3 H), 3.73 (dd, $J = 11.7, 3.2$ Hz, 1 H), 3.60 (dd, $J = 11.7, 5.8$ Hz, 1 H), 3.31-3.26 (m, 1 H), 2.34-2.26 (m, 1 H), 2.06 (s, 3 H), 1.97-1.89 (m, 3 H), 0.90 (d, $J = 6.5$

Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.8, 159.3, 134.3, 130.4, 129.4, 125.6, 113.9, 82.9, 71.8, 65.0, 61.2, 55.2, 35.6, 33.8, 21.0, 15.0; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 345.1672, obsd 345.1660; $[\alpha]_{\text{D}}^{20}$ +4.6 (c 2.24, CHCl_3).

A mixture of the above compound (52 mg, 0.16 mmol) and IBX (226 mg, 0.81 mmol) in THF/DMSO (9:1, 5.4 mL) was stirred for 4 h at rt, diluted with hexanes, filtered through Celite, and rinsed with hexanes/ethyl acetate (3:1). The filtrate was transferred to a separatory funnel and washed with brine. The organic layer was dried, filtered, and evaporated to leave a residue that was purified by column chromatography on silica gel (hexanes/ethyl acetate 5:1). There was isolated 46 mg (90%) of the aldehyde; IR (neat, cm^{-1}) 1732, 1613, 1514; ^1H NMR (300 MHz, CDCl_3) δ 9.62 (d, J = 2.8 Hz, 1 H), 7.27-7.24 (m, 2 H), 6.90-6.86 (m, 2 H), 5.70-5.52 (m, 2 H), 4.59 (d, J = 11.4 Hz, 1 H), 4.49 (d, J = 5.2 Hz, 2 H), 4.43 (d, J = 11.4 Hz, 1 H), 3.81 (s, 3 H), 3.48 (dd, J = 5.8, 2.8 Hz, 1 H), 2.35-2.24 (m, 1 H), 2.05 (s, 3 H), 2.05-1.97 (m, 2 H), 0.93 (d, J = 6.6 Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 204.3, 170.8, 159.6, 133.3, 129.7, 129.3, 126.5, 113.9, 86.4, 72.6, 64.9, 55.3, 34.9, 34.7, 21.0, 15.5; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 343.1516, obsd 343.1539; $[\alpha]_{\text{D}}^{18}$ +68.3 (c 1.06 CHCl_3).

To a cooled (0 °C), stirred solution of carbon tetrabromide (377 mg, 1.14 mmol) in CH_2Cl_2 (4 mL) was added triphenylphosphine (596 mg, 2.27 mmol) in CH_2Cl_2 (4 mL) under Ar. After 10 min, the reaction mixture was cooled to -78 °C and a solution of the above aldehyde (91 mg, 0.28 mmol) in CH_2Cl_2 (6 mL) was introduced into the yellowish ylide solution. The mixture was stirred for 2 h at -78 °C, quenched with saturated NaHCO_3 solution, and extracted with ethyl acetate. The combined organic layers were washed with brine, dried, and evaporated to leave a residue that was purified by column chromatography on silica gel (hexanes/ethyl acetate 20:1) to afford **30** (132 mg, 98%); IR (neat, cm^{-1}) 1739, 1612, 1514; ^1H NMR (300 MHz, CDCl_3) δ 7.29-7.24 (m, 2 H), 6.90-6.85 (m, 2 H), 6.39 (d, J = 8.9 Hz, 1 H), 5.73-5.60 (m, 1 H), 4.52 (d, J = 11.5 Hz, 1 H), 4.49 (d, J = 6.5 Hz, 2 H), 4.30 (d, J = 11.5 Hz, 1 H), 3.83 (dd, J = 9.0, 7.3 Hz, 1 H),

3.81 (s, 3 H), 2.40-2.32 (m, 1 H), 2.05 (s, 3 H), 1.98-1.88 (m, 1 H), 1.87-1.76 (m, 1 H), 0.88 (d, $J = 6.8$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.8, 159.3, 138.5, 133.9, 130.2, 129.5, 125.9, 113.8, 92.0, 82.1, 70.6, 65.1, 55.3, 37.4, 35.2, 21.0, 14.9; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 498.9913, obsd 498.9902; $[\alpha]_{\text{D}}^{19} +9.1$ (c 0.69, CHCl_3).

Acetylenic Alcohol 10. To a cooled (-78°C), stirred solution of **30** (64 mg, 0.13 mmol) in THF (6.7 mL) was added $n\text{-BuLi}$ (2.5 M solution in hexane, 0.32 mL, 0.80 mmol) dropwise under Ar. After 30 min, the reaction mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate. The organic layer was washed with brine, dried, and evaporated to leave a residue that was purified by column chromatography on silica gel (hexanes/ethyl acetate 5:1) to give **10** (33 mg, 90%); IR (neat, cm^{-1}) 3286, 1613, 1514; ^1H NMR (300 MHz, CDCl_3) δ 7.29-7.26 (m, 2 H), 6.90-6.85 (m, 2 H), 5.85-5.54 (m, 2 H), 4.74 (d, $J = 11.4$ Hz, 1 H), 4.42 (d, $J = 11.4$ Hz, 1 H), 4.05 (d, $J = 4.3$ Hz, 2 H), 3.91 (dd, $J = 5.7, 2.1$ Hz, 1 H), 3.80 (s, 3 H), 2.46 (d, $J = 2.1$ Hz, 1 H), 2.32-2.25 (m, 1 H), 2.03-1.84 (m, 2 H), 1.46 (br s, 1 H), 1.00 (d, $J = 6.6$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.2, 131.0, 130.5, 129.9, 129.6, 113.7, 81.4, 74.8, 72.0, 70.2, 63.6, 55.2, 37.7, 35.4, 15.1; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 297.1461, obsd 297.1465; $[\alpha]_{\text{D}}^{20} +98.7$ (c 0.95, CHCl_3).

Sonagashira Coupling of 10 to 23. To a stirred mixture of $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (8.4 mg, 0.012 mmol) and CuI (4.6 mg, 0.024 mmol) in Et_3N (2 mL) were added solutions of **10** (67 mg, 0.137 mmol) in Et_3N (2 mL) and of **23** (33 mg, 0.120 mmol) in Et_3N (2 mL) under Ar at rt. After 4 h, the reaction mixture was filtered through Celite and the filtrate was concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 3:1) to give **31** (62 mg, 82%) as a yellow syrup; IR (neat, cm^{-1}) 3505, 1726, 1614; ^1H NMR (300 MHz, CDCl_3) δ 7.43 (d, $J = 8.6$ Hz, 2 H), 7.28 (d, $J = 8.6$ Hz, 2 H), 6.90-6.85 (m, 4 H), 6.21 (dt, $J = 15.9, 7.6$ Hz, 1 H), 5.69-5.60 (m, 3 H), 5.48 (s, 1 H), 4.72 (d, $J = 11.5$ Hz, 1 H), 4.42 (d, $J = 11.5$ Hz, 1 H), 4.23 (t, $J = 6.4$ Hz, 2 H), 4.13-4.02 (m, 3 H), 3.96-3.84 (m, 2 H), 3.80 (s, 6 H), 2.57-2.42 (m, 1 H), 2.40-2.27

(m, 2 H), 2.03-1.85 (m, 4 H), 1.66-1.61 (m, 1 H), 1.51-1.41 (m, 1 H), 1.32 (br s, 1 H), 1.20 (s, 9 H), 1.00 (d, $J = 6.5$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 178.4, 159.8, 159.2, 139.5, 131.0, 130.8, 130.7, 130.2, 129.5, 127.3, 113.7, 111.9, 100.5, 86.2, 85.2, 75.6, 73.6, 72.7, 70.2, 63.6, 60.0, 55.2 (2 C), 39.4, 38.7, 38.0, 36.4, 35.5, 34.9, 27.2, 15.3; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 657.3398, obsd 657.3399; $[\alpha]_{\text{D}}^{18} +47.8$ (c 0.25, CHCl_3).

Aldehyde 34. To a solution of **31** (106 mg, 0.167 mmol) in 8 mL of ethyl acetate:pyridine:1-octene (10:1:1) was added Lindlar's catalyst (32 mg). The reaction mixture was stirred for 5.5 h under a balloon of H_2 at rt and filtered through a Celite pad. The filtrate was concentrated and the residue was used for the next step without further purification (triene:over-reduced compounds 1.9:1 by ES MS analysis)

The above mixture and IBX (234 mg, 0.835 mmol) in THF:DMSO (9:1, 8 mL) was stirred for 2 h at rt, diluted with hexanes, filtered through Celite, washed with hexanes/ethyl acetate (2:1), and concentrated. The filtrate was washed with brine, dried, and concentrated. The residue was purified by chromatography on silica gel (hexanes/ethyl acetate 5:1) to afford a mixture of the corresponding aldehydes (102 mg, 96%). This mixture (102 mg, 0.161 mmol) together with BHT (35 mg, 0.161 mmol) and toluene (23 mL) was placed in a sealed tube, degassed with Ar, and heated at 150-160 $^{\circ}\text{C}$ for 24 h. The mixture was cooled to rt, and toluene was removed. The residue was purified by chromatography on silica gel (hexanes/ethyl acetate 10:1) to give **34** (34 mg, 32% for the three steps) as a colorless oil; IR (neat, cm^{-1}) 1724, 1614, 1515, 1249; ^1H NMR (300 MHz, CDCl_3) δ 9.71 (d, $J = 1.8$ Hz, 1 H), 7.40 (d, $J = 8.7$ Hz, 2 H), 7.27 (d, $J = 8.6$ Hz, 2 H), 6.91-6.84 (m, 4 H), 5.91 (dq, $J = 10.1, 2.0$ Hz, 1 H), 5.77 (br d, $J = 9.7$ Hz, 1 H), 5.46 (s, 1 H), 4.46 (s, 2 H), 4.25-4.20 (m, 2 H), 3.94-3.87 (m, 2 H), 3.80 (s, 6 H), 3.48 (t, $J = 4.8$ Hz, 1 H), 2.95-2.90 (m, 1 H), 2.79-2.69 (m, 2 H), 2.44-2.41 (m, 1 H), 2.16-2.10 (m, 1 H), 2.01-1.82 (m, 3 H), 1.77-1.63 (m, 1 H), 1.59-1.41 (m, 4 H), 1.19 (s, 9 H), 1.00 (d, $J = 6.9$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 204.6, 178.5, 159.8, 131.0,

130.8, 130.3, 129.9, 129.0, 128.7, 127.2, 113.7 (2 C), 113.5, 100.4, 86.7, 74.2, 73.5, 70.9, 60.6, 55.3, 55.2, 55.0, 41.8, 38.7, 38.1, 37.4, 36.4, 34.9, 31.1, 28.9, 27.2, 13.8; HRMS ES m/z (M + Na)⁺ calcd 657.3398, obsd 657.3408; $[\alpha]_{\text{D}}^{21}$ -52.5 (c 1.30, CHCl₃).

Carbinol 35. Aldehyde **34** (26 mg, 0.0410 mmol) was dissolved in MeOH (6 mL) and treated with NaBH₄ (8 mg, 0.205 mmol) at 0 °C. After 30 min, the mixture was quenched with saturated NaHCO₃ solution and diluted with ethyl acetate. The organic layer was washed with brine, dried, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 2:1) to give **35** (21.2 mg, 82%) as a colorless oil; IR (neat, cm⁻¹) 3433, 1728, 1614; ¹H NMR (500 MHz, C₆D₆) δ 7.59 (d, J = 8.7 Hz, 2 H), 7.29 (d, J = 8.6 Hz, 2 H), 6.82 (dd, J = 10.0, 8.7 Hz, 4 H), 5.99 (ddd, J = 9.9, 4.9, 2.4 Hz, 1 H), 5.90 (dd, J = 10.0, 2.0 Hz, 1 H), 5.42 (s, 1 H), 4.39 (s, 2 H), 4.33-4.23 (m, 2 H), 3.72 (t, J = 10.3 Hz, 1 H), 3.68-3.65 (m, 1 H), 3.51-3.34 (m, 3 H), 3.32 (s, 3 H), 3.26 (s, 3 H), 2.81 (dd, J = 9.3, 4.6 Hz, 1 H), 2.73 (br s, 2 H), 2.27-2.20 (m, 1 H), 2.09-2.04 (m, 1 H), 1.89-1.79 (m, 2 H), 1.74-1.60 (m, 3 H), 1.43-1.38 (m, 1 H), 1.32-1.22 (m, 3 H), 1.20 (s, 9 H), 1.07 (d, J = 6.9 Hz, 3 H); ¹³C NMR (75 MHz, C₆D₆) δ 177.8, 160.4, 159.7, 132.2, 132.0, 131.7, 129.6, 129.3, 114.1, 113.9, 101.2, 87.1, 75.3, 73.9, 71.2, 63.1, 61.0, 54.8 (2 C), 44.6, 42.4, 38.8, 38.0, 37.3, 36.7, 35.5, 35.3, 32.9, 30.1, 27.4, 14.3; HRMS ES m/z (M + Na)⁺ calcd 659.3554, obsd 659.3537; $[\alpha]_{\text{D}}^{22}$ -89.3 (c 0.94, CHCl₃).

Iodoalkyne 36. To a cooled (0 °C), stirred solution of carbon tetrabromide (133 mg, 0.402 mmol) in CH₂Cl₂ (1 mL) was added a solution of triphenylphosphine (211 mg, 0.804 mmol) in pyridine (0.07 mL, 0.0804 mmol) and CH₂Cl₂ (1.5 mL) under Ar. After 10 min, a solution of **34** (17 mg, 0.027 mmol) in CH₂Cl₂ (1.5 mL) was introduced into the reddish ylide solution. The mixture was stirred for 1.5 h at 0 °C, quenched with saturated NaHCO₃ solution, and extracted with ethyl acetate. The combined organic layers were washed with brine, dried, and evaporated to leave a residue that was purified by column chromatography on silica gel (hexanes/ethyl acetate 10:1) to afford

the homologated dibromide (20.6 mg, 98%) as a white gel; IR (neat, cm^{-1}) 1726, 1614, 1515; ^1H NMR (300 MHz, CDCl_3) δ 7.43 (d, J = 8.7 Hz, 2 H), 7.28 (d, J = 8.6 Hz, 2 H), 6.89 (dd, J = 8.7, 2.0 Hz, 4 H), 6.33 (d, J = 9.7 Hz, 1 H), 5.74 (d, J = 10.8 Hz, 1 H), 5.68 (d, J = 11.3 Hz, 1 H), 5.47 (s, 1 H), 4.51 (d, J = 11.6 Hz, 1 H), 4.43 (d, J = 11.6 Hz, 1 H), 4.24 (t, J = 5.6 Hz, 2 H), 3.94-3.83 (m, 2 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.50 (t, J = 4.2 Hz, 1 H), 2.65 (br s, 2 H), 2.56-2.50 (m, 1 H), 2.47-2.37 (m, 1 H), 2.18-2.07 (m, 1 H), 2.01-1.83 (m, 2 H), 1.75-1.40 (m, 6 H), 1.20 (s, 9 H), 1.00 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 178.5, 159.8, 159.0, 140.3, 131.0, 130.3, 129.6, 128.9, 127.3, 113.7, 113.5, 100.4, 88.6, 86.8, 74.1, 73.5, 70.9, 60.6, 55.3, 46.2, 42.3, 38.7, 38.2, 37.4, 36.5, 35.8, 35.3, 34.9, 29.7 (2 C), 27.2, 14.0; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 813.1795, obsd 813.1835; $[\alpha]_{\text{D}}^{22}$ -26.1 (c 1.70, CHCl_3).

To a cold (-78 $^\circ\text{C}$), stirred solution of the dibromide (30.6 mg, 0.387 mmol) in THF (4 mL) was added *n*-BuLi (2.5 M solution in hexane, 0.14 mL, 0.348 mmol) dropwise under Ar. After 30 min, the reaction mixture was quenched with saturated NH_4Cl solution and extracted with ethyl acetate. The organic layer was washed with brine, dried, and evaporated to leave a residue that was purified by column chromatography on silica gel (hexanes/ethyl acetate 2:1) to give the alkyne (18 mg, 86%) as a white gel; IR (neat, cm^{-1}) 3444, 3286, 1614, 1515; ^1H NMR (300 MHz, C_6D_6) δ 7.58-7.55 (m, 2 H), 7.25-7.23 (m, 2 H), 6.83-6.76 (m, 4 H), 5.88-5.77 (m, 2 H), 5.42 (s, 1 H), 4.39 (d, J = 11.6 Hz, 1 H), 4.29 (d, J = 11.6 Hz, 1 H), 3.80-3.57 (m, 4 H), 3.40 (t, J = 4.6 Hz, 1 H), 3.31 (s, 3 H), 3.25 (s, 3 H), 2.91 (br s, 1 H), 2.75-2.65 (m, 2 H), 2.51-2.47 (m, 1 H), 2.27-2.19 (m, 1 H), 2.06-1.98 (m, 1 H), 1.89 (d, J = 2.3 Hz, 1 H), 1.83-1.31 (m, 7 H), 1.03 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 160.7, 160.0, 132.5, 131.9, 130.8, 129.7, 129.6, 114.4, 114.2, 101.6, 87.0, 86.7, 75.9, 74.9, 71.3, 70.7, 60.2, 55.1 (2 C), 43.4, 39.5, 39.1, 38.0, 37.8, 36.7, 35.9, 35.6, 31.6, 14.8; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 569.2874, obsd 569.2864; $[\alpha]_{\text{D}}^{22}$ -96.8 (c 0.72, CHCl_3).

To a stirred mixture of iodine (29.2 mg, 0.115 mmol) in benzene (2 mL) was added morpholine (0.03 mL, 0.34 mmol) under N₂ at rt. The mixture was stirred for 30 min until the purple color of the solution turned into an orange colored mixture. A solution of the alkyne (14.5 mg, 0.0265 mmol) in benzene (3.5 mL) was introduced. The reaction mixture was stirred overnight at 50-60 °C, cooled to rt, diluted with ethyl acetate, washed with saturated Na₂S₂O₃ solution and brine, dried, and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 2:1) to give **36** (17 mg, 90%) as a white gel; IR (neat, cm⁻¹) 3436, 1614, 1515; ¹H NMR (300 MHz, C₆D₆) δ 7.55 (d, *J* = 8.7 Hz, 2 H), 7.23 (d, *J* = 8.7 Hz, 2 H), 6.88 (dd, *J* = 11.4, 8.7 Hz, 4 H), 6.76-5.72 (m, 2 H), 5.39 (s, 1 H), 4.36 (d, *J* = 11.7 Hz, 1 H), 4.26 (d, *J* = 11.7 Hz, 1 H), 3.91-3.57 (m, 4 H), 3.35 (t, *J* = 4.7 Hz, 1 H), 3.31 (s, 3 H), 3.25 (s, 3 H), 2.86 (br s, 1 H), 2.71-2.57 (m, 3 H), 2.15-2.06 (m, 1 H), 2.03-1.92 (m, 1 H), 1.78-1.66 (m, 2 H), 1.58-1.43 (m, 3 H), 1.36-1.25 (m, 4 H), 1.01 (d, *J* = 6.9 Hz, 3 H); ¹³C NMR (75 MHz, C₆D₆) δ 160.7, 160.0, 132.5, 131.9, 130.6, 129.7, 129.6, 114.4, 114.2, 101.6, 86.9, 76.0, 74.8, 71.3, 60.3, 55.1 (2 C), 43.4, 39.6, 39.1, 38.1, 37.9, 36.6, 35.9, 31.8, 14.7; HRMS ES *m/z* (M + Na)⁺ calcd 695.1840, obsd 695.1868; [α]_D²¹ -70.8 (c 0.85, CHCl₃).

Oxidation of 36. To a stirred solution of **36** (7.2 mg, 0.0107 mmol) in dry CH₂Cl₂ (2 mL) were added 4 Å molecular sieves and sodium acetate (4.4 mg, 0.0535 mmol) under N₂. The mixture was cooled to 0 °C and pyridinium chlorochromate (11.5 mg, 0.0535 mmol) was added. The mixture was stirred for 1 h at 0 °C, diluted with ether, and stirred for 30 min at 0 °C. The mixture was filtered through Florisil and washed with ether. The solvent was removed and the residue was purified by chromatography on silica gel (hexanes/ethyl acetate 5:1) to give **6** (7 mg, 97%) as a colorless oil; IR (neat, cm⁻¹) 1724, 1613, 1515, 1249; ¹H NMR (300 MHz, C₆D₆) δ 9.42 (s, 1 H), 7.54 (d, *J* = 8.3 Hz, 2 H), 7.23 (d, *J* = 8.4 Hz, 2 H), 6.81 (dd, *J* = 7.8, 6.6 Hz, 4 H), 5.82-5.72 (m, 2 H), 5.34 (s, 1 H), 4.35 (d, *J* = 11.7 Hz, 1 H), 4.26 (d, *J* = 11.6 Hz, 1 H), 3.95-3.86 (m, 1

H), 3.68 (br t, $J = 10.1$ Hz, 1 H), 3.35 (t, $J = 4.7$ Hz, 1 H), 3.31 (s, 3 H), 3.25 (s, 1 H), 2.86 (br s, 1 H), 2.65-2.59 (m, 3 H), 2.36-2.30 (m, 1 H), 2.28-1.92 (m, 3 H), 1.76-1.67 (m, 1 H), 1.57-1.43 (m, 2 H), 1.36-1.32 (m, 2 H), 1.01 (d, $J = 6.8$ Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 199.4, 160.8, 160.0, 132.2, 131.9, 130.5, 129.8, 129.6, 114.4, 114.1, 101.5, 97.4, 86.9, 74.6, 72.2, 71.3, 55.1 (2 C), 49.9, 43.4, 39.4, 38.1, 37.9, 37.6, 36.6, 35.9, 31.8, 30.6, 14.7; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 693.1684, obsd 693.1687; $[\alpha]_{\text{D}}^{19}$ -78.0 (c 0.61, CHCl_3).

Dienyl Aldehyde 38. To a cold (-78 °C), stirred suspension of methyltriphenylphosphonium bromide (407 mg, 1.14 mmol) in THF (3 mL) was added *n*-BuLi (2.5 M in hexane, 0.34 mL, 0.855 mmol) under N_2 . The mixture was stirred for 15 min at -78 °C and for 15 min at rt. The ylide (deep yellow color) was cooled to -78 °C and a solution of **34** (36.8 mg, 0.0580 mmol) in THF (4 mL) was added. The mixture was stirred for 50 min at -78 °C, allowed to warm to -15 °C, stirred for 30 min, quenched with saturated NH_4Cl solution, diluted with hexanes, and filtered through silica gel. The column was flushed with hexanes/ethyl acetate (5:1), and the eluate was dried and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 5:1) to give the diene (28.7 mg, 78%) as a colorless oil; IR (neat, cm^{-1}) 1728, 1615, 1515; ^1H NMR (300 MHz, C_6D_6) δ 7.59 (d, $J = 8.7$ Hz, 2 H), 7.28 (d, $J = 8.4$ Hz, 2 H), 6.81 (t, $J = 8.6$ Hz, 4 H), 5.95-5.75 (m, 3 H), 5.44 (s, 1 H), 5.09-5.02 (m, 2 H), 4.42 (d, $J = 11.7$ Hz, 1 H), 4.35 (d, $J = 11.7$ Hz, 1 H), 4.33-4.23 (m, 2 H), 3.82-3.64 (m, 2 H), 3.50 (t, $J = 4.7$ Hz, 1 H), 3.31 (s, 3 H), 3.25 (s, 3 H), 2.81 (br s, 1 H), 2.72 (br s, 1 H), 2.48-2.41 (m, 1 H), 2.21-2.14 (m, 1 H), 2.11-2.04 (m, 1 H), 1.88-1.66 (m, 4 H), 1.60-1.51 (m, 1 H), 1.37-1.22 (m, 2 H), 1.19 (s, 9 H), 1.09 (d, $J = 6.8$ Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 178.1, 160.7, 141.2, 132.5, 132.0, 129.9, 129.6, 116.0, 114.4, 114.1, 101.5, 87.5, 74.9, 74.2, 71.4, 61.4, 55.1 (2 C), 47.7, 42.9, 39.1, 38.2, 37.3, 37.0, 35.8, 32.4, 27.7, 14.8; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 655.3605, obsd 655.3585; $[\alpha]_{\text{D}}^{20}$ -59.3 (c 1.00, CHCl_3).

To a cooled (-78 °C), stirred solution of the above product (20 mg, 0.0321 mmol) in THF (4.6 mL) was added *n*-BuLi (2.5 M solution in hexane, 0.077 mL, 0.193 mmol) dropwise under N₂. After 50 min, the reaction mixture was quenched with saturated NH₄Cl solution and extracted with ethyl acetate. The organic layer was washed with brine, dried, and evaporated to leave a residue that was purified by column chromatography on silica gel (hexanes/ethyl acetate 2:1) to give the carbinol (16.2 mg, 92%) as a white gel; IR (neat, cm⁻¹) 3453, 1614, 1515; ¹H NMR (300 MHz, C₆D₆) δ 7.56 (d, *J* = 8.7 Hz, 2 H), 7.27 (d, *J* = 8.6 Hz, 2 H), 6.80 (dd, *J* = 15.4, 8.7 Hz, 4 H), 5.95-5.74 (m, 3 H), 5.42 (s, 1 H), 5.08-5.01 (m, 2 H), 4.42 (d, *J* = 11.6 Hz, 1 H), 4.35 (d, *J* = 11.6 Hz, 1 H), 3.80-3.60 (m, 4 H), 3.49 (t, *J* = 4.7 Hz, 1 H), 3.31 (s, 3 H), 3.24 (s, 3 H), 2.83-2.80 (m, 1 H), 2.74-2.68 (m, 1 H), 2.46-2.41 (m, 1 H), 2.20-2.04 (m, 2 H), 1.85-1.69 (m, 4 H), 1.59-1.46 (m, 2 H), 1.40-1.28 (m, 2 H), 1.09 (d, *J* = 6.9 Hz, 3 H); ¹³C NMR (75 MHz, C₆D₆) δ 160.7, 160.0, 141.2, 132.5, 132.0 (2 C), 129.9, 129.6, 116.0, 114.4, 114.2, 101.6, 87.5, 75.9, 74.9, 71.4, 60.2, 55.1 (2 C), 47.7, 42.9, 39.1, 39.0, 38.2, 37.4, 36.9, 35.8, 32.2, 14.8; HRMS ES *m/z* (M + Na)⁺ calcd 571.3030, obsd 571.3026; [α]_D²¹ -72.0 (*c* 1.25, CHCl₃).

To a stirred solution of the carbinol (23.4 mg, 0.0426 mmol) in dry CH₂Cl₂ (5 mL) were added 4 Å molecular sieves and sodium acetate (17.5 mg, 0.213 mmol) under N₂. The mixture was cooled to 0 °C and pyridinium chlorochromate (46 mg, 0.21 mmol) was added. The mixture was stirred for 2 h at 0 °C, diluted with ether, and stirred for 30 min at 0 °C. The mixture was filtered through Florisil and washed with ether. The filtrate was evaporated and the resulting **38** (17.7 mg, 76%) was used without further purification; colorless oil; ¹H NMR (300 MHz, C₆D₆) δ 9.44 (t, *J* = 1.7 Hz, 1 H), 7.55 (d, *J* = 8.7 Hz, 2 H), 7.28 (d, *J* = 8.7 Hz, 2 H), 6.81 (dd, *J* = 11.1, 8.7 Hz, 4 H), 5.93-5.74 (m, 3 H), 5.38 (s, 1 H), 5.09-5.01 (m, 2 H), 4.43 (d, *J* = 11.5 Hz, 1 H), 4.36 (d, *J* = 11.6 Hz, 1 H), 3.97-3.89 (m, 1 H), 3.76-3.69 (m, 1 H), 3.50 (t, *J* = 4.7 Hz, 1 H), 3.31 (s, 3 H), 3.24 (s, 3 H), 2.87-2.82 (m, 1 H), 2.73-2.68 (m, 1 H), 2.50-2.39 (m, 1 H), 2.32 (ddd, *J* = 16.7, 7.1, 2.1

Hz, 1 H), 2.21-2.04 (m, 2 H), 1.97 (ddd, $J = 16.7, 5.2, 1.5$ Hz, 1 H), 1.82-1.71 (m, 2 H), 1.60-1.51 (m, 1 H), 1.36-1.15 (m, 3 H), 1.09 (d, $J = 6.9$ Hz, 3 H).

Trienone 40. To a cold (-78 °C), stirred solution of **38** (17.7 mg, 0.0324 mmol) in THF (3 mL) was added vinylmagnesium bromide (1 M in THF, 0.2 mL, 0.162 mmol) under N_2 . After 30 min, the mixture was allowed to warm to 0 °C, stirred for 1 h, quenched with saturated NH_4Cl solution, and diluted with ethyl acetate. The combined organic phases were washed with brine, dried, and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 5:1) to give **39** (17.8 mg, 96% as a 1:1 mixture of diastereomers) as a colorless oil; IR (neat, cm^{-1}) 3488, 1614, 1515; 1H NMR (300 MHz, C_6D_6) δ 7.56 (dd, $J = 10.6, 8.7$ Hz, 2 H), 7.28 (d, $J = 8.6$ Hz, 2 H), 6.84-6.75 (m, 4 H), 5.94-5.75 (m, 4 H), 5.41-5.26 (m, 2 H), 5.08-5.01 (m, 3 H), 4.45-4.33 (m, 1 H), 4.43 (d, $J = 11.6$ Hz, 1 H), 4.35 (d, $J = 11.6$ Hz, 1 H), 4.04-3.97 (m, 0.5 H), 3.82-3.70 (m, 1.5 H), 3.50 (t, $J = 4.6$ Hz, 1 H), 3.31 (s, 3 H), 3.23 (s, 3 H), 2.85-2.80 (m, 1 H), 2.73-2.67 (m, 1 H), 2.61 (br s, 0.5 H), 2.47-2.43 (m, 1 H), 2.21-2.16 (m, 1 H), 2.14-2.04 (m, 1 H), 1.99 (br s, 0.5 H), 1.89-1.70 (m, 3 H), 1.59-1.42 (m, 2 H), 1.40-1.24 (m, 3 H), 1.09 (d, $J = 6.9$ Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 160.8, 160.0, 142.4, 141.8, 141.2 (2 C), 132.5, 132.2, 132.0 (2 C), 131.9, 129.9 (2 C), 129.6, 116.0, 114.4, 114.3, 114.2 (2 C), 113.9, 101.6, 101.5, 87.5, 76.4, 75.0, 74.9, 74.4, 71.9, 71.4, 69.5, 55.1 (2 C), 47.6, 43.7, 42.9, 39.0 (2 C), 38.3, 37.4, 37.3, 36.9, 35.8, 32.2, 14.8; HRMS ES m/z ($M + Na$) $^+$ calcd 597.3187, obsd 597.3198.

To a stirred solution of **39** (16 mg, 0.028 mmol) in dry CH_2Cl_2 (5 mL) were added 4 Å molecular sieves and sodium acetate (11.4 mg, 0.139 mmol) under N_2 . The mixture was cooled to 0 °C and pyridinium chlorochromate (30 mg, 0.139 mmol) was added. The mixture was stirred for 2 h at 0 °C, diluted with ether, and stirred for 30 min at 0 °C. The mixture was filtered through a Florisil pad and washed with ether. The filtrate was evaporated and the residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 5:1) to give **40** (10.9 mg, 69%) as a colorless oil; IR (neat, cm^{-1})

1684, 1614, 1515; ^1H NMR (300 MHz, C_6D_6) δ 7.58 (d, J = 8.7 Hz, 2 H), 7.28 (d, J = 8.6 Hz, 2 H), 6.88 (dd, J = 10.4, 8.7 Hz, 4 H), 6.13 (dd, J = 17.7, 10.5 Hz, 1 H), 5.92-5.74 (m, 4 H), 5.45 (s, 1 H), 5.20 (dd, J = 10.7, 1.0 Hz, 1 H), 5.09-5.01 (m, 2 H), 4.43 (d, J = 11.6 Hz, 1 H), 4.36 (d, J = 11.6 Hz, 1 H), 4.32-4.25 (m, 1 H), 3.83-3.77 (m, 1 H), 3.49 (t, J = 4.7 Hz, 1 H), 3.31 (s, 3 H), 3.24 (s, 3 H), 2.83-2.71 (m, 2 H), 2.78 (dd, J = 16.3, 6.3 Hz, 1 H), 2.49-2.39 (m, 1 H), 2.32 (dd, J = 16.3, 6.2 Hz, 1 H), 2.21-2.17 (m, 1 H), 2.15-2.04 (m, 1 H), 1.85-1.71 (m, 2 H), 1.60-1.51 (m, 1 H), 1.43-1.12 (m, 3 H), 1.09 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, C_6D_6) δ 197.5, 160.7, 160.0, 141.3, 137.5, 132.5, 132.1, 131.9, 129.9, 129.6, 115.9, 114.4, 114.0, 101.5, 87.5, 74.8, 73.5, 71.4, 55.1 (2 C), 47.7, 46.1, 42.9, 39.1, 38.2, 37.4, 36.9, 35.9, 32.2, 14.8; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 595.3030, obsd 595.3002; $[\alpha]_{\text{D}}^{21}$ -89.8 (c 0.54, CHCl_3).

Epoxide 44. A stirred solution of **13** (31 g, 16.7 mmol) in dry CH_2Cl_2 (560 mL) was admixed with diisopropylethylamine (87 mL, 50 mmol), cooled to 0 °C, and treated slowly with MEM chloride (29 mL, 25 mmol). The reaction mixture was stirred for 30 min at 0 °C, allowed to warm to rt, stirred overnight, and diluted with ethyl acetate. The separated organic phase was washed with brine, dried, and freed of solvent. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 10:1) to give the ether (40.4 g, 88%) as a colorless oil; IR (neat, cm^{-1}) 1641, 1455, 1370; ^1H NMR (300 MHz, CDCl_3) δ 5.86-5.74 (m, 1 H), 5.12-5.05 (m, 2 H), 4.78 (dd, J = 14.8, 7.0 Hz, 2 H), 4.25-4.17 (m, 1 H), 4.05 (dd, J = 7.9, 5.9 Hz, 1 H), 3.92-3.84 (m, 1 H), 3.77-3.68 (m, 2 H), 3.57-3.48 (m, 3 H), 3.39 (s, 3 H), 2.36-2.31 (m, 2 H), 1.80-1.60 (m, 2 H), 1.38 (s, 3 H), 1.33 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 134.0, 117.6, 108.5, 94.4, 73.9, 73.1, 71.7, 69.8, 67.0, 59.0, 39.3, 38.6, 27.0, 25.8; HRMS ES m/z ($\text{M} + \text{Na}$) $^+$ calcd 297.1672, obsd 297.1674; $[\alpha]_{\text{D}}^{18}$ -20.4 (c 0.80, CHCl_3).

The above compound (26 g, 95 mmol) in $\text{AcOH}/\text{THF}/\text{H}_2\text{O}$ (1:1:1) (480 mL) was stirred for 12 h at 50 °C, diluted with CH_2Cl_2 , and neutralized with saturated NaHCO_3 solution and solid NaHCO_3 . The separated aqueous layer was extracted with EtOAc

(5x), the combined organic layers were dried and evaporated, and the residue was purified by column chromatography on silica gel (ethyl acetate) to give the diol (18.7 g, 84%) as a colorless oil; IR (neat, cm^{-1}) 3418, 1641, 1454, 1366; ^1H NMR (300 MHz, CDCl_3) δ 5.84-5.70 (m, 1 H), 5.29-5.05 (m, 2 H), 4.82 (d, $J = 7.2$ Hz, 1 H), 4.67 (d, $J = 7.2$ Hz, 1 H), 4.04-3.92 (m, 2 H), 3.92-3.85 (m, 2 H), 3.92-3.85 (m, 2 H), 3.64-3.51 (m, 4 H), 3.40 (s, 3 H), 2.34-2.25 (m, 3 H), 1.61-1.42 (m, 2 H); ^{13}C NMR (75 MHz, CDCl_3) δ 134.0, 117.7, 93.8, 73.0, 71.7, 67.7, 67.1, 66.9, 59.0, 38.9, 37.5; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 257.1359, obsd 257.1365; $[\alpha]_{\text{D}}^{18} -108.7$ (c 1.65, CHCl_3).

This diol (17 g, 72.6 mmol) was dissolved in pyridine (24 mL, 0.29 mol) and CH_2Cl_2 (200 mL), treated with pivaloyl chloride (10.7 mL, 87.1 mmol) at 0 °C under N_2 , allowed to warm to rt, stirred overnight, diluted with ethyl acetate, and washed with brine. The organic phase was dried and concentrated to leave a residue that was purified by column chromatography on silica gel (hexanes/ethyl acetate 5:1) to give the monopivalate (23 g, quantitative) as a colorless oil; IR (neat, cm^{-1}) 3473, 1729, 1285; ^1H NMR (300 MHz, CDCl_3) δ 5.85-5.71 (m, 1 H), 5.12-5.05 (m, 2 H), 4.81 (d, $J = 7.1$ Hz, 1 H), 4.70 (d, $J = 4.7$ Hz, 1 H), 4.10-3.97 (m, 4 H), 3.88-3.81 (m, 1 H), 3.67-3.61 (m, 1 H), 3.60 (t, $J = 2.5$ Hz, 1 H), 3.56 (dd, $J = 5.3, 3.0$ Hz, 1 H), 3.49 (br d, $J = 4.4$ Hz, 1 H), 3.40 (s, 3 H), 2.40-2.25 (m, 2 H), 1.60-1.56 (m, 2 H), 1.21 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 178.4, 134.1, 117.7, 94.2, 73.3, 71.8, 68.4, 67.2, 65.5, 59.0, 39.1, 38.8, 37.9, 27.2; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 341.1935, obsd 341.1939; $[\alpha]_{\text{D}}^{22} -77.1$ (c 0.94, CHCl_3).

To a cooled (0 °C), stirred solution of the above material (4.9 g, 15.4 mmol) in pyridine (6.2 mL, 77.0 mmol) and CH_2Cl_2 (100 mL) were added DMAP (188 mg, 1.54 mmol) and methanesulfonyl chloride (3.6 mL, 46 mmol) under N_2 . The reaction mixture was allowed to warm to rt, stirred overnight, and diluted with ethyl acetate. The separated organic phase was washed with brine, dried, and freed of solvent. The residue was purified by column chromatography (hexanes/ethyl acetate 4:1) on silica

gel to give the mesylate (6.1 g, quantitative) as a colorless oil; IR (neat, cm^{-1}) 1732, 1359, 1284, 1177; ^1H NMR (300 MHz, CDCl_3) δ 5.84-5.70 (m, 1 H), 5.13-5.05 (m, 3 H), 4.82 (dd, $J = 8.7, 7.2$ Hz, 2 H), 4.40 (dd, $J = 12.4, 3.3$ Hz, 1 H), 4.11 (dd, $J = 12.4, 5.7$ Hz, 1 H), 3.85-3.77 (m, 1 H), 3.75-3.72 (m, 2 H), 3.57-3.54 (m, 2 H), 3.38 (s, 3 H), 3.07 (s, 3 H), 2.47-2.30 (m, 2 H), 1.90 (ddd, $J = 15.1, 9.1, 2.6$ Hz, 1 H), 1.73 (ddd, $J = 15.1, 9.8, 3.3$ Hz, 1 H), 1.22 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 178.0, 133.5, 118.1, 95.3, 77.4, 73.7, 71.7, 67.6, 65.5, 59.0, 39.3, 38.9, 38.8, 36.7, 27.1; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 419.1710, obsd 419.1714; $[\alpha]_{\text{D}}^{22} -23.9$ (c 1.45, CHCl_3).

The above mesylate (15g, 38 mmol) was dissolved in MeOH (540 mL), treated with K_2CO_3 (6.3 mg, 45.4 mmol), and stirred overnight at rt. The mixture was freed of solvent, diluted with ethyl acetate, washed with brine, dried, and evaporated. The residue was purified by column chromatography (hexanes/ethyl acetate 5: 1) on silica gel to give epoxide **44** (8.0 g, 98%); IR (neat, cm^{-1}) 1641, 1106; ^1H NMR (300 MHz, CDCl_3) δ 5.88-5.74 (m, 1 H), 5.14-5.05 (m, 2 H), 4.78 (dd, $J = 12.1, 7.2$ Hz, 2 H), 3.87 (quintet, $J = 5.9$ Hz, 1 H), 3.79-3.68 (m, 2 H), 3.55 (t, $J = 4.7$ Hz, 2 H), 3.38 (s, 3 H), 3.06-3.00 (m, 1 H), 2.75 (dd, $J = 5.0, 4.0$ Hz, 1 H), 2.46 (dd, $J = 5.0, 2.7$ Hz, 1 H), 2.38 (tq, $J = 7.1, 1.1$ Hz, 2 H), 1.75 (t, $J = 5.8$ Hz, 2 H); ^{13}C NMR (75 MHz, CDCl_3) δ 134.2, 117.6, 94.2, 74.7, 71.7, 67.1, 59.0, 49.4, 46.6, 38.8, 37.0; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 239.1254, obsd 239.1253; $[\alpha]_{\text{D}}^{17} -3.4$ (c 0.90, CHCl_3).

Enyne 45. To a cold (-78°C), stirred solution of trimethylsilylacetylene (20.6 mL, 146 mmol) in THF (450 mL) was added *n*-butyllithium (2.5 M solution in hexane, 43.9 mL, 110 mmol) dropwise under N_2 . After 30 min at -78°C , $\text{BF}_3\cdot\text{Et}_2\text{O}$ (20.2 mL, 219 mmol) was introduced, and the mixture was stirred for 20 min at -78°C prior to being treated with a solution of **44** (15.8 g, 73.1 mmol) in THF (40 mL), and quenched with saturated NH_4Cl solution after 1.5 h at -78°C . The product was extracted into ethyl acetate, washed with brine, dried, and freed of solvent. The residue was purified by silica gel column chromatography (hexanes/ethyl acetate 5: 1) to give the acetylene

(20.6 g, 90%); IR (neat, cm^{-1}) 3446, 1641, 1414; ^1H NMR (300 MHz, CDCl_3) δ 5.85-5.72 (m, 1 H), 5.42-5.07 (m, 2 H), 4.84 (d, $J = 7.1$ Hz, 1 H), 4.75 (d, $J = 7.1$ Hz, 1 H), 3.94-3.81 (m, 2 H), 3.79-3.66 (m, 2 H), 3.56 (t, $J = 4.5$ Hz, 2 H), 3.39 (s, 3 H), 3.06 (d, $J = 3.1$ Hz, 1 H), 2.44-2.33 (m, 4 H), 1.89 (dt, $J = 14.9, 3.7$ Hz, 1 H), 1.74-1.64 (m, 1 H), 0.15 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 133.7, 117.5, 103.2, 93.8, 86.8, 75.6, 71.5, 68.6, 67.1, 58.7, 39.9, 38.5, 28.5, -0.2; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 337.1806, obsd 337.1805; $[\alpha]_{\text{D}}^{18} -38.0$ (c 1.76, CHCl_3).

A solution of the acetylene (18.8 g, 59.8 mmol) and TBAF (1 M solution in THF, 78 mL, 77.7 mmol) in THF (300 mL) was stirred for 1 h at 0 °C. Water was added to the reaction mixture, which was diluted with ethyl acetate, washed with brine, dried, and evaporated. The residue was purified by silica gel column chromatography (hexanes/ethyl acetate 4: 1) to give the acetylenic alcohol (13.6 g, 94%); IR (neat, cm^{-1}) 3452, 1640, 1432; ^1H NMR (300 MHz, CDCl_3) δ 5.85-5.71 (m, 1 H), 5.41-5.06 (m, 2 H), 4.85 (d, $J = 7.1$ Hz, 1 H), 4.75 (d, $J = 7.1$ Hz, 1 H), 3.98-3.88 (m, 2 H), 3.81-3.65 (m, 2 H), 3.56 (t, $J = 4.5$ Hz, 2 H), 3.39 (s, 3 H), 3.20 (d, $J = 3.0$ Hz, 1 H), 2.40-2.31 (m, 4 H), 2.02 (t, $J = 2.7$ Hz, 1 H), 1.85 (ddd, $J = 14.6, 4.1, 3.4$ Hz, 1 H), 1.78-1.68 (m, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 133.7, 117.8, 94.0, 80.8, 76.1, 71.7, 70.4, 69.0, 67.4, 58.9, 40.0, 38.7, 27.2; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 265.1410, obsd 265.1414; $[\alpha]_{\text{D}}^{16} -59.6$ (c 1.45, CHCl_3).

A mixture of this carbinol (15.8 g, 65.2 mmol), TBSCl (14.7 g, 97.8 mmol), imidazole (13.3 g, 196 mmol), and DMAP (800 mg, 6.52 mmol) in CH_2Cl_2 (325 mL) was stirred for 12 h at rt, diluted with ethyl acetate, washed with brine, dried, and freed of solvent. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 15: 1) to give **45** (23.2 g, 100%); IR (neat, cm^{-1}) 1472, 1255; ^1H NMR (300 MHz, CDCl_3) δ 5.88-5.75 (m, 1 H), 5.12-5.05 (m, 2 H), 4.74 (dd, $J = 11.5, 7.1$ Hz, 2 H), 3.94 (quintet, $J = 5.9$ Hz, 1 H), 3.80 (quintet, $J = 6.0$ Hz, 1 H), 3.72-3.69 (m, 2 H), 3.57-3.53 (m, 2 H), 3.39 (s, 3 H), 2.38 (quintet, $J = 2.9$ Hz, 2 H), 2.35-2.23 (m, 2 H),

1.96 (t, J = 2.7 Hz, 1 H), 1.80 (t, J = 6.3 Hz, 2 H), 0.89 (s, 9 H), 0.09 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 134.4, 117.3, 94.1, 81.4, 73.7, 71.7, 70.1, 68.1, 67.1, 59.0, 41.1, 38.9, 27.2, 25.8, 18.0, -4.5, -4.7; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 379.2275, obsd 379.2271; $[\alpha]_{\text{D}}^{21}$ -6.1 (c 1.42, CHCl_3).

Weinreb Amide 46. A cold (-78 °C), stirred solution of **45** (9.73 g, 27.3 mmol) in CH_2Cl_2 :MeOH (1:1, 90 mL) was exposed to a stream of ozone. Red 23 (0.1% solution of Sudan III in CH_2Cl_2 :MeOH (1:1), 2 mL) was used as an internal indicator.

Triphenylphosphine (8.59 g, 32.7 mmol) was added to the reaction mixture when the pink color had faded. The resulting mixture was stirred overnight at rt and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 5: 1) to give the aldehyde (7.95 g, 81%); IR (neat, cm^{-1}) 1726, 1472, 1256; ^1H NMR (300 MHz, CDCl_3) δ 9.80 (s, 1 H), 4.76 (dd, J = 13.4, 7.2 Hz, 2 H), 4.28 (quintet, J = 6.1 Hz, 1 H), 3.93 (quintet, J = 5.9 Hz, 1 H), 3.73-3.61 (m, 2 H), 3.54 (t, J = 4.6 Hz, 2 H), 3.38 (s, 3 H), 2.67-2.65 (m, 2 H), 2.39 (dd, J = 5.9, 2.6 Hz, 2 H), 2.03-1.94 (m, 2 H), 1.99 (t, J = 2.6 Hz, 1 H), 1.90-1.81 (m, 1 H), 0.89 (s, 9 H), 0.09 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 201.1, 94.6, 80.9, 71.7, 70.5, 70.3, 67.9, 67.3, 59.0, 48.8, 41.4, 27.3, 25.8, 18.0, -4.4, -4.7; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 381.2068, obsd 381.2083; $[\alpha]_{\text{D}}^{23}$ +35.0 (c 1.21, CHCl_3).

To a stirred solution of this aldehyde (6.61 g, 18.4 mmol) in *tert*-butyl alcohol (69 mL) and H_2O (23 mL) were added 2-methyl-2-butene (19 mL, 184 mmol), sodium hydrogen phosphate (7.63 g, 55.3 mmol), and sodium chlorite (5.0 g, 55.3 mmol). The mixture was stirred for 20 min at rt, freed of solvent, diluted with brine, and extracted with ethyl acetate (3x). The combined organic layers were dried and evaporated. The crude acid was dissolved in ether (40 mL) and this solution was treated with an excess of freshly prepared ethereal diazomethane at 0 °C. After 30 min, acetic acid was added, the mixture was concentrated, and the residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 7: 1) to give the methyl ester (6.44

g, 91%); IR (neat, cm^{-1}) 1742, 1256, 1102; ^1H NMR (300 MHz, CDCl_3) δ 4.75 (s, 2 H), 4.18 (quintet, $J = 6.3$ Hz, 1 H), 3.93 (quintet, $J = 5.9$ Hz, 1 H), 3.68 (s, 3 H), 3.70-3.68 (m, 2 H), 3.55 (dd, $J = 5.2, 4.0$ Hz, 2 H), 3.38 (s, 3 H), 2.58 (d, $J = 6.2$ Hz, 2 H), 2.41-2.38 (m, 2 H), 1.98 (t, $J = 2.6$ Hz, 1 H), 1.96-1.82 (m, 2 H), 0.90 (s, 9 H), 0.09 (s, 3 H), 0.08 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.5, 94.6, 81.2, 71.7, 70.2, 68.0, 67.2, 58.9, 51.5, 41.3, 40.2, 27.2, 25.7, 17.9, -4.5, -4.8; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 411.2173, obsd 411.2157; $[\alpha]_{\text{D}}^{21} +20.5$ (c 1.28, CHCl_3).

To a stirred suspension of the above ester (4.08 g, 10.50 mmol) and *N,O*-dimethylhydroxylamine hydrochloride (2.05g, 21.0 mmol) in THF (150 mL) was added isopropylmagnesium bromide (2M solution in THF, 21 mL) dropwise at such a rate that the internal temperature did not exceed $-15\text{ }^\circ\text{C}$. The reaction mixture was stirred for 1 h at $-15\text{ }^\circ\text{C}$, quenched with saturated NaHCO_3 solution, and extracted with ethyl acetate (3x). The combined organic solutions were dried and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 3: 1) to give **46** (5.61 g, 77%); IR (neat, cm^{-1}) 1664, 1472, 1386, 1254; ^1H NMR (300 MHz, CDCl_3) δ 4.76 (dd, $J = 12.9, 6.9$ Hz, 2 H), 4.28-4.20 (m, 1 H), 3.96 (quintet, $J = 5.9$ Hz, 1 H), 3.69 (s, 3 H), 3.71-3.67 (m, 2 H), 3.56-3.53 (m, 2 H), 3.38 (s, 3 H), 3.17 (s, 3 H), 2.83 (dd, $J = 15.4, 7.7$ Hz, 1 H), 2.55 (dd, $J = 15.4, 4.9$ Hz, 1 H), 2.49-2.33 (m, 2 H), 1.97 (t, $J = 2.6$ Hz, 1 H), 1.95-1.82 (m, 2 H), 0.90 (s, 9 H), 0.09 (s, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 172.4, 95.3, 82.0, 72.2 (2C), 70.5, 68.6, 67.6, 61.7, 59.4, 42.3, 38.3, 27.6, 26.3, 18.4, -4.0, -4.2; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 440.2439, obsd 440.2426; $[\alpha]_{\text{D}}^{23} +8.6$ (c 1.12, CHCl_3).

Iodo Weinreb Amide 47. To a stirred solution of **46** (860 mg, 2.06 mmol) in benzene (295 mL) were added tri-*n*-butyltin hydride (2.77 mL, 10.30 mmol) and AIBN (34 mg, 0.21 mmol) at rt under N_2 . The reaction mixture was gently refluxed with stirring for 3.5 h. The solvent was removed and the residue was purified by column chromatography on silica gel (hexane: ethyl acetate = 7: 1) to give the vinyl stannane.

To a cooled (0 °C), stirred solution of this material in CH₂Cl₂ (70 mL) was added a solution of iodine in CH₂Cl₂ until a purple color persisted. After 15 min at 0 °C, saturated Na₂S₂O₃ solution was added until the color faded. The mixture was diluted with ethyl acetate, washed with brine, dried and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 3: 1) to give **47** (0.67 g, 60% over two steps); IR (neat, cm⁻¹) 1666, 1463, 1386, 1255; ¹H NMR (300 MHz, CDCl₃) δ 6.58-6.48 (m, 1 H), 6.08-6.02 (m, 1 H), 4.78 (d, *J* = 6.9 Hz, 1 H), 4.70 (d, *J* = 6.9 Hz, 1 H), 4.19-4.11 (m, 1 H), 3.91-3.83 (m, 1 H), 3.74-3.62 (m, 2 H), 3.69 (s, 3 H), 3.56-3.52 (m, 2 H), 3.39 (s, 3 H), 3.17 (s, 3 H), 2.80 (dd, *J* = 15.3, 7.0 Hz, 1 H), 2.53 (dd, *J* = 15.5, 5.6 Hz, 1 H), 2.40-2.31 (m, 1 H), 2.25-2.15 (m, 1 H), 1.85-1.76 (m, 1 H), 1.71-1.59 (m, 1 H), 0.89 (s, 9 H), 0.06 (s, 3 H), 0.05 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 172.3, 143.6, 95.5, 77.7, 72.5, 72.2, 68.7, 67.8, 67.7, 61.7, 59.5, 43.6, 42.9, 38.4, 26.3, 18.4, -4.0, -4.1; HRMS ES *m/z* (M+Na)⁺ calcd 568.1562, obsd 568.1569; [α]_D²³ -9.6 (c 1.07, CHCl₃).

Coupling of 47 to 10. To a stirred mixture of Pd(PPh₃)₂Cl₂ (397 mg, 0.57 mmol) and CuI (215 mg, 1.13 mmol) in triethylamine (64 mL) were added solutions of **47** (1.6 g, 2.93 mmol) in triethylamine (15 mL) and **10** (776 mg, 2.83 mmol) in triethylamine (15 mL) at rt under Ar. After 1 h, the precipitates were filtered off through a pad of silica gel and washed with ethyl acetate. The filtrate was concentrated and the residue was purified by column chromatography on silica gel (hexanes/acetone 3: 1) to give **48** (1.60 g, 82%); IR (neat, cm⁻¹) 3456, 1661, 1612, 1514; ¹H NMR (300 MHz, CDCl₃) δ 7.29-7.26 (m, 2 H), 6.90-6.85 (m, 2 H), 6.22-6.11 (m, 1 H), 5.64-5.55 (m, 3 H), 4.78 (d, *J* = 7.0 Hz, 1 H), 4.72 (d, *J* = 11.4 Hz, 1 H), 4.72 (d, *J* = 7.0 Hz, 1 H), 4.41 (d, *J* = 11.4 Hz, 1 H), 4.23-4.15 (m, 1 H), 4.06 (br s, 2 H), 4.02 (dd, *J* = 5.7, 1.6 Hz, 1 H), 3.98-3.85 (m, 1 H), 3.80 (s, 3 H), 3.72-3.68 (m, 2 H), 3.69 (s, 3 H), 3.56-3.53 (m, 2 H), 3.38 (s, 3 H), 3.17 (s, 3 H), 2.81 (dd, *J* = 15.4, 7.4 Hz, 1 H), 2.55 (dd, *J* = 15.4, 5.4 Hz, 1 H), 2.47-2.38 (m, 1 H), 2.32-2.23 (m, 3 H), 2.02-1.74 (m, 3 H), 1.73-1.66 (m, 1 H), 0.99

(d, $J = 6.6$ Hz, 3 H), 0.90 (s, 9 H), 0.07 (d, $J = 1.5$ Hz, 6 H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.9, 159.2, 141.3, 130.9, 130.8, 130.2, 129.6, 113.7, 111.6, 95.0, 85.6 (2C), 72.7, 72.0, 71.7, 70.1, 68.9, 67.3, 63.6, 61.2, 59.0, 55.2, 42.6, 40.5, 38.0 (2C), 35.6, 25.9, 18.0, 15.2, -4.5 (2C); HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 714.4008, obsd 714.3985; $[\alpha]_{\text{D}}^{22}$ +47.8 (c 1.21, CHCl_3).

Aldehyde 49. To a stirred suspension of zinc dust (2.36 g) in water (13 mL) was added $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (326 mg) at rt under Ar. After 15 min, AgNO_3 (236 mg) was introduced and the mixture was stirred for 30 min, filtered, and washed sequentially with water (27 mL), methanol (27 mL), acetone (27 mL), and ether (27 mL). The activated zinc was suspended in 50% aqueous methanol (13 mL) and a solution of **48** (232 mg, 0.335 mmol) in methanol (3 mL) was introduced under Ar. The mixture was deoxygenated and stirred overnight at 65 °C, filtered through Celite, and rinsed with methanol. The filtrate was concentrated, diluted with ethyl acetate, washed with brine, dried, and freed of solvent. The residue was purified by column chromatography on silica gel (hexanes/acetone 3: 1) to give the trienol (162 mg, 70%); IR (neat, cm^{-1}) 3456, 1660, 1612, 1514; ^1H NMR (300 MHz, CDCl_3) δ 7.23 (d, $J = 8.6$ Hz, 2 H), 6.86 (d, $J = 8.6$ Hz, 2 H), 6.33-6.21 (m, 2 H), 5.80-5.70 (m, 1 H), 5.64-5.62 (m, 2 H), 5.26-5.20 (m, 1 H), 4.77 (d, $J = 6.9$ Hz, 1 H), 4.71 (d, $J = 6.9$ Hz, 1 H), 4.47 (d, $J = 11.4$ Hz, 1 H), 4.21 (d, $J = 11.4$ Hz, 1 H), 4.25-4.17 (s, 1 H), 4.07 (br s, 2 H), 4.01 (dd, $J = 9.6, 7.1$ Hz, 1 H), 3.93-3.85 (m, 1 H), 3.80 (s, 3 H), 3.68-3.66 (m, 2 H), 3.67 (s, 3 H), 3.55-3.51 (m, 2 H), 3.37 (s, 3 H), 3.15 (s, 3 H), 2.81 (dd, $J = 16.0, 7.6$ Hz, 1 H), 2.54 (dd, $J = 15.6, 5.0$ Hz, 1 H), 2.42-2.29 (m, 3 H), 1.96-1.65 (m, 4 H), 0.89 (s, 9H), 0.84 (d, $J = 6.8$ Hz, 3 H), 0.07 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 172.0, 159.0, 132.9, 132.7, 131.2, 131.0, 130.8, 129.3, 128.6, 127.9, 113.6, 95.0, 77.3, 72.1, 71.7, 69.6, 69.2, 67.2, 63.7, 61.2, 59.0, 58.3, 55.2, 42.5, 40.4, 37.9, 35.6, 25.9, 18.4, 18.0, 15.2, -4.4, -4.5; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 716.4164, obsd 716.4190; $[\alpha]_{\text{D}}^{22}$ -33.9 (c 0.95, CHCl_3).

A mixture of the trienol (124 mg, 0.179 mmol) and IBX (250 mg, 0.893 mmol) in THF/DMSO (9:1, 18 mL) was stirred for 3 h at rt, diluted with hexanes, filtered through Celite, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/acetone 5: 1) to give the aldehyde (120 mg, 97%); IR (neat, cm^{-1}) 1692, 1663, 1613, 1514; ^1H NMR (300 MHz, CDCl_3) δ 9.46 (dd, $J = 7.9, 0.8$ Hz, 1 H), 7.22 (d, $J = 8.4$ Hz, 2 H), 6.87 (d, $J = 8.3$ Hz, 2 H), 6.78 (dd, $J = 18.9, 7.5$ Hz, 1 H), 6.33-6.21 (m, 2 H), 6.10 (dd, $J = 15.7, 8.0$ Hz, 1 H), 5.83-5.74 (m, 1 H), 5.24-5.18 (m, 1 H), 4.77 (d, $J = 6.6$ Hz, 1 H), 4.72 (d, $J = 6.6$ Hz, 1 H), 4.49 (d, $J = 11.3$ Hz, 1 H), 4.20 (d, $J = 11.3$ Hz, 1 H), 4.22-4.18 (m, 1 H), 3.97 (t, $J = 8.6$ Hz, 1 H), 3.90 (t, $J = 5.8$ Hz, 1 H), 3.80 (s, 3 H), 3.69-3.66 (m, 2 H), 3.67 (s, 3 H), 3.54-3.51 (m, 2 H), 3.37 (s, 3 H), 3.15 (s, 3 H), 2.81 (dd, $J = 15.5, 7.0$ Hz, 1 H), 2.72-2.63 (m, 1 H), 2.55 (dd, $J = 15.6, 5.1$ Hz, 1 H), 2.45-2.17 (m, 3 H), 1.91-1.80 (m, 2 H), 1.75-1.66 (m, 1 H), 0.88 (s, 9 H), 0.86 (d, $J = 7.1$ Hz, 3 H), 0.07 (s, 3 H), 0.05 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.5, 171.6, 158.8, 157.5, 133.8, 133.3, 132.9, 130.2, 129.1, 127.9, 127.2, 113.3, 94.6, 77.0, 71.7, 71.4, 69.3, 68.8, 66.8, 60.8, 58.6, 54.8, 42.1, 40.0, 37.5, 37.3, 36.0, 25.5, 17.7, 15.4, -4.7, -4.9; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 714.4008, obsd 714.3993; $[\alpha]_{\text{D}}^{18} +15.9$ (c 0.95, CHCl_3).

A deoxygenated solution of the aldehyde (90.6 mg, 0.131 mmol) and BHT (18 mg, 20% w/w) in toluene (16 mL) was placed in a sealed tube and heated at 155 °C for 24 h. The mixture was cooled to rt, concentrated, and purified by column chromatography on silica gel (hexanes/acetone 8: 1) to give **49** (82.6 mg, 91%); IR (neat, cm^{-1}) 1720, 1662, 1613, 1514; ^1H NMR (500 MHz, CDCl_3) δ 9.74 (d, $J = 2.2$ Hz, 1 H), 7.30 (d, $J = 8.6$ Hz, 2 H), 6.91 (d, $J = 8.6$ Hz, 2 H), 5.87 (d, $J = 10.0$ Hz, 1 H), 5.73 (d, $J = 10.0$ Hz, 1 H), 4.79 (d, $J = 6.9$ Hz, 1 H), 4.74 (d, $J = 6.9$ Hz, 1 H), 4.53 (d, $J = 11.6$ Hz, 1 H), 4.45 (d, $J = 11.6$ Hz, 1 H), 4.16-4.14 (m, 1 H), 4.01-3.98 (m, 1 H), 3.84 (s, 3 H), 3.76-3.70 (m, 2 H), 3.72 (s, 3 H), 3.56 (t, $J = 4.7$ Hz, 2 H), 3.51 (t, $J = 4.1$ Hz, 1 H), 3.40 (s, 3 H), 3.20 (s, 3 H), 2.87-2.78 (m, 4 H), 2.58 (dd, $J = 15.4, 5.7$ Hz, 1 H), 2.40 (br

s, 1 H), 2.11-2.09 (m, 1 H), 1.92-1.86 (m, 2 H), 1.76-1.72 (m, 2 H), 1.55-1.49 (m, 2 H), 1.03 (d, $J = 6.9$ Hz, 3 H), 0.92 (s, 9 H), 0.12 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 205.0, 171.8, 159.0, 130.9, 130.4, 130.2, 128.9, 113.6, 95.1, 86.9, 72.1, 71.7, 70.7, 67.3, 61.1, 58.9, 55.5, 55.2, 43.4, 41.8, 39.3, 38.0, 36.1, 35.3, 32.7, 28.5, 25.8, 17.9, 13.7, -4.1, -4.8; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 714.4008, obsd 714.3968; $[\alpha]_{\text{D}}^{21}$ - 43.6 (c 0.56, CHCl_3).

Borohydride Reduction of 49. Confirmation of Stereochemistry by NOE. To a cooled (0 °C), stirred solution of **49** (52.2 mg, 0.0754 mmol) in methanol (7 mL) was added sodium borohydride (8.6 mg, 0.23 mmol). After 1 h at 0 °C, the mixture was quenched with water and the organic solvent was evaporated. The aqueous layer was extracted with ethyl acetate (3x). The combined organic layers were dried, filtered, and evaporated to leave a residue that was purified by column chromatography on silica gel (hexanes/acetone 7:1) to give the alcohol (40.2 mg, 77%) as a colorless oil; IR (neat, cm^{-1}) 3465, 1660, 1613, 1514; ^1H NMR (500 MHz, CDCl_3) δ 7.28 (d, $J = 8.7$ Hz, 2 H), 6.88 (d, $J = 8.6$ Hz, 2 H), 6.86-5.81 (m, 1 H), 5.76-5.65 (m, 1 H), 4.76 (d, $J = 6.9$ Hz, 1 H), 4.71 (d, $J = 6.9$ Hz, 1 H), 4.46 (dd, $J = 14.1, 11.7$ Hz, 2 H), 4.14-4.11 (m, 1 H), 4.00-3.97 (m, 1 H), 3.81 (s, 3 H), 3.69 (s, 3 H), 3.69-3.68 (m, 2 H), 3.59-3.56 (m, 2 H), 3.55-3.53 (m, 2 H), 3.47 (t, $J = 5.2$ Hz, 1 H), 3.37 (s, 3 H), 3.17 (s, 3 H), 2.83 (dd, $J = 15.4, 6.1$ Hz, 1 H), 2.62-2.55 (m, 3 H), 2.37-2.34 (m, 1 H), 2.15-2.10 (m, 1 H), 1.86-1.81 (m, 1 H), 1.77-1.70 (m, 2 H), 1.66-1.61 (m, 1 H), 1.60-1.52 (m, 1 H), 1.51-1.46 (m, 2 H), 0.98 (d, $J = 6.9$ Hz, 3 H), 0.89 (s, 9 H), 0.09 (s, 3 H), 0.06 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.9, 158.9, 131.9, 131.1, 129.0, 128.7, 113.6, 95.1, 86.9, 72.2, 71.7, 70.9, 67.6, 67.3, 63.0, 59.0, 55.2, 44.8, 43.6, 41.5, 37.9, 37.4, 36.2, 34.9, 32.9, 28.8, 25.9, 18.0, 13.8, -4.2, -4.7; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 716.4164, obsd 716.4162; $[\alpha]_{\text{D}}^{20}$ - 83.5 (c 2.01, CHCl_3).

Bromo Ester 50. To a cooled (-78 °C), stirred solution of methyl bis(trifluoroethyl)phosphonoacetate (1.40 g, 3.53 mmol) in THF (7 mL) was added sodium hexamethyldisilazide (1 M solution in THF, 2.64 mL, 2.64 mmol) under N₂. After 30 min at -78 °C, a solution of **49** (183 mg, 0.26 mmol) in THF (6 mL) was introduced and the reaction mixture was stirred for 2 h at -78 °C, stirred for 25 h at 5 °C, quenched with saturated NH₄Cl solution, and diluted with ethyl acetate. The organic phase was washed with brine, dried, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ether 2: 1) to give **50** (176 mg, 81%); IR (neat, cm⁻¹) 1719, 1664, 1613, 1514; ¹H NMR (300 MHz, CDCl₃) δ 7.28-7.25 (m, 2 H), 6.90-6.85 (m, 2 H), 6.66 (d, *J* = 10.7 Hz, 1 H), 5.65 (br s, 2 H), 4.74 (q_{AB}, Δ*v* = 12.49, *J* = 6.8 Hz, 2 H), 4.52 (d, *J* = 11.7 Hz, 1 H), 4.40 (d, *J* = 11.7 Hz, 1 H), 4.20-4.11 (m, 2 H), 3.94-3.81 (m, 1 H), 3.81 (s, 3 H), 3.80 (s, 3 H), 3.69 (s, 3 H), 3.68-3.66 (m, 2 H), 3.55-3.52 (m, 2 H), 3.48 (t, *J* = 3.5 Hz, 1 H), 3.37 (s, 3 H), 3.27-3.21 (m, 1 H), 3.17 (s, 3 H), 2.81 (dd, *J* = 15.0, 8.0 Hz, 1 H), 2.68-2.65 (m, 1 H), 2.59-2.52 (m, 2 H), 2.49-2.42 (m, 1 H), 2.27-2.02 (m, 1 H), 1.90-1.81 (m, 1 H), 1.79-1.64 (m, 2 H), 1.59-1.50 (m, 1 H), 1.46-1.35 (m, 2 H), 0.98 (d, *J* = 6.9 Hz, 3 H), 0.87 (s, 9 H), 0.05 (s, 3 H), 0.02 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 172.0, 163.1, 159.0, 151.1, 131.1, 130.2, 129.5, 128.9, 113.7, 110.9, 95.2, 87.0, 72.1, 71.8, 70.8, 67.3, 66.8, 61.2, 59.0, 55.2, 52.8, 43.8, 42.9, 41.9, 39.8, 38.6, 38.1, 36.1, 35.5, 30.3, 30.2, 25.8, 17.9, 13.9, -4.2, -4.7; HRMS ES *m/z* (M+Na)⁺ calcd 848.3375, obsd 848.3372; [α]_D¹⁸ -26.4 (c 1.54, CHCl₃).

Selective Deprotection of 50. To a cooled (-78 °C), stirred solution of **50** (75.6 mg, 0.0914 mmol) in CH₂Cl₂ (5 mL) was added 2-chloro-dithioborolan (126.5 mg, 0.914 mmol) under N₂. After being stirred for 45 min at -78 °C, the mixture was quenched

with saturated NaHCO₃ solution and diluted with ethyl acetate. The organic phase was washed with brine, dried, and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 4:1) to give **51** (54.8 mg, 81 %); IR (neat, cm⁻¹) 3455, 1720, 1646, 1514; ¹H NMR (300 MHz, CDCl₃) δ 7.26 (d, *J* = 8.7 Hz, 2 H), 6.89-6.85 (m, 2 H), 6.66 (d, *J* = 10.8 Hz, 1 H), 5.64 (br s, 2 H), 4.53 (d, *J* = 11.7 Hz, 1 H), 4.39 (d, *J* = 11.7 Hz, 1 H), 4.13-3.99 (m, 1 H), 3.80 (s, 6 H), 3.69 (s, 3 H), 3.49-3.46 (m, 1 H), 3.27-3.19 (m, 1 H), 3.19 (s, 3 H), 2.69-2.66 (m, 2 H), 2.56-2.43 (m, 3 H), 2.04-1.97 (m, 1 H), 1.82-1.71 (m, 2 H), 1.68-1.50 (m, 2 H), 1.49-1.41 (m, 1 H), 1.38-1.26 (m, 2 H), 0.98 (d, *J* = 6.8 Hz, 3 H), 0.87 (s, 9 H), 0.06 (s, 3 H), 0.04 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 173.6, 163.2, 159.0, 150.9, 131.1, 130.1, 129.5, 128.9, 113.7, 110.9, 87.0, 70.7, 67.3, 65.2, 61.2, 55.2, 52.8, 44.2, 43.9, 41.9, 39.8, 39.0, 38.8, 36.2, 35.7, 30.3, 29.8, 25.8, 17.9, 13.9, -4.2, -4.6; HRMS ES *m/z* (M+Na)⁺ calcd 760.2851, obsd 760.2852.

Allyl Ester 54. To a cooled (-78 °C), stirred solution of allyl bis(2,2,2-trifluoroethyl)bromophosphonoacetate (**53**, 1.42 g, 3.35 mmol) in THF (5 mL) was added sodium hexamethyldisilazide (1M in THF, 2.3 mL) under N₂. After 30 min of stirring at -78 °C, a solution of **48** (135 mg, 0.195 mmol) was added, and the reaction mixture was stirred for 2 h at -78 °C, allowed to warm to -10 °C, and stirred overnight prior to being quenched with saturated NH₄Cl solution and extracted with ethyl acetate (2x). The combined organic layers were dried and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ether 5:1) to give **54** (131mg, 79%); IR (neat, cm⁻¹) 1720, 1665, 1612, 1514; ¹H NMR (300 MHz, CDCl₃) δ 7.27-7.24 (m, 2H), 6.90-6.85 (m, 2H), 6.66 (d, *J* = 10.7 Hz, 1 H), 6.01-5.86 (m, 1 H), 5.64 (br s, 2 H), 5.42-5.35 (m, 1 H), 5.32-5.23 (m, 1H), 4.76 (d, *J* = 6.8 Hz, 1H), 4.72 (d, *J* = 6.8 Hz, 1H), 4.70-4.63 (m, 2H), 4.51 (d, *J* = 11.7 Hz, 1 H), 4.39 (d, *J* = 11.7 Hz, 1 H), 4.22-4.11 (m, 1 H), 3.93-3.83 (m, 1 H), 3.80 (s, 3 H), 3.69 (s, 3 H), 3.69-3.66 (m, 2 H), 3.55-3.22 (m, 2 H), 3.48-3.46 (m, 1 H), 3.37 (s, 3 H), 3.27-3.21 (m, 1 H), 3.17 (s, 3 H), 2.81 (dd, *J* = 15.4,

7.3 Hz, 1 H), 2.68-2.66 (m, 1 H), 2.55 (dd, $J = 15.4, 5.0$ Hz, 1 H), 2.54-2.44 (m, 2 H), 2.06-1.99 (m, 1 H), 1.93-1.81 (m, 1 H), 1.77-1.62 (m, 2 H), 1.57-1.49 (m, 2 H), 1.46-1.38 (m, 1 H), 0.97 (d, $J = 6.8$ Hz, 3 H), 0.86 (s, 9 H), 0.05 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.9, 162.3, 158.9, 150.8, 131.3, 131.0, 130.1, 129.4 (2C), 128.8, 118.8, 113.6, 111.1, 95.1, 86.9, 72.0, 71.7, 70.7, 67.2, 66.7, 66.4, 61.1, 58.9, 55.1, 43.7, 42.9, 41.8, 40.3, 39.8, 36.1, 35.4, 30.2, 30.1, 25.8, 17.9, 13.8, -4.2, -4.7; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 874.3532, obsd 874.3524.

Selective Deprotection of 54. To a cooled ($-78\text{ }^\circ\text{C}$), stirred solution of **54** (28.3 mg, 0.0328 mmol) in CH_2Cl_2 (3 mL) was added 2-chloro-dithioborolan (46.0 mg, 0.332 mmol) under N_2 . After being stirred for 1.5 h at $-78\text{ }^\circ\text{C}$, the mixture was quenched with saturated NaHCO_3 solution, diluted with ethyl acetate. The organic phase was washed with brine, dried, and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 3:1) to give **55** (18.1 mg, 72 %); IR (neat, cm^{-1}) 3444, 2929, 1722, 1650, 1513, 1249, 1080; ^1H NMR (300 MHz, CDCl_3) δ 7.28-7.24 (m, 2 H), 6.90-6.86 (m, 2 H), 6.67 (d, $J = 10.8$ Hz, 1 H), 6.01-5.90 (m, 1 H), 5.64 (s, 2 H), 5.39 (dd, $J = 17.2, 1.4$ Hz, 1 H), 5.28 (dd, $J = 10.5, 1.3$ Hz, 1 H), 4.71-4.68 (m, 2 H), 4.53 (d, $J = 11.7$ Hz, 1 H), 4.39 (d, $J = 11.7$ Hz, 1 H), 4.13-4.00 (m, 2 H), 3.84 (s, 1 H), 3.81 (s, 3 H), 3.48-3.46 (m, 1 H), 3.27-3.22 (m, 1 H), 3.19 (s, 3 H), 2.70-2.66 (m, 1 H), 2.57-2.42 (m, 3 H), 2.02-2.01 (m, 1 H), 1.82-1.67 (m, 2 H), 1.55-1.42 (m, 4H), 1.38-1.26 (m, 1 H), 0.98 (d, $J = 6.8$ Hz, 3 H), 0.87 (s, 9 H), 0.06 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 173.6, 162.4, 159.0, 150.7, 131.3, 131.1, 130.1, 129.5, 128.8, 118.9, 113.7, 111.1, 87.0, 70.7, 67.2, 66.4, 65.2, 55.2, 44.2, 43.9, 41.8, 39.8, 38.9, 38.8, 36.1, 35.6, 29.8, 25.8, 17.9, 13.8, -4.3, -4.7; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 786.3007, obsd 786.2980.

Deallylation/Macrolactonization of 55. A solution of **55** (15.7 mg, 0.021 mmol), $\text{Pd}(\text{OAc})_2$ (0.5 mg, 0.0021 mmol), triphenylphosphine (8 mg, 0.03 mmol), and dimedone (14.4 mg, 0.103 mmol) in THF (2 mL) was stirred for 2 h at rt. The solvent was removed

and the residue was filtered through a short silica gel pad (hexanes/ethyl acetate 1:1 to ethyl acetate/methanol 5:1). The mixture of hydroxy acid and dimedone was dissolved in THF (2 mL) and triethylamine (0.04 mL, 0.308 mmol) together with 2,4,6-trichlorobenzoyl chloride (0.03 mL, 0.205 mmol) were introduced. After 2 h, the triethylammonium chloride was filtered off through Celite and washed with THF. Anhydrous toluene (4 mL) was added to the combined filtrates. The solution was added dropwise over 1 h to a refluxing solution of DMAP (50 mg, 0.41 mmol) in 6 mL of toluene. The mixture was refluxed for 2 h, cooled to rt, freed of toluene, and diluted with ethyl acetate. The aqueous phase was washed with saturated citric acid solution, water, saturated NaHCO₃ solution, and brine, then dried and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 5:1) to give **56** (10.6 mg, 73%); IR (neat, cm⁻¹) 1741, 1665, 1613, 1514; ¹H NMR (300 MHz, CDCl₃) δ 7.27-7.25 (m, 2 H), 6.90-6.85 (m, 2 H), 6.01 (d, *J* = 9.6 Hz, 1 H), 5.65-5.54 (m, 2 H), 5.40-5.30 (m, 1 H), 4.53 (d, *J* = 11.7 Hz, 1 H), 4.41 (d, *J* = 11.7 Hz, 1 H), 4.28-4.24 (m, 1 H), 3.81 (s, 3 H), 3.72 (s, 3 H), 3.49-3.47 (m, 1 H), 3.19 (s, 3 H), 2.96 (dd, *J* = 15.3, 6.9 Hz, 1 H), 2.79-2.68 (m, 4H), 2.51-2.48 (m, 1 H), 2.35-2.17 (m, 2 H), 2.04-1.93 (m, 1 H), 1.79-1.68 (m, 2 H), 1.60-1.51 (m, 2 H), 0.97 (d, *J* = 6.8 Hz, 3 H), 0.88 (s, 9 H), 0.04 (s, 3 H), 0.03 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 170.2, 163.8, 159.0, 138.7, 134.2, 131.1, 128.9, 128.7, 113.7, 108.9, 87.1, 70.7, 70.5, 67.0, 61.4, 55.2, 45.0, 41.4, 38.7, 38.2, 37.8, 36.0 (2C), 35.1, 32.1, 28.3, 25.8, 18.0, 13.7, -4.8, -4.9; HRMS ES *m/z* (M+Na)⁺ calcd 728.2589, obsd 728.2601; [α]_D¹⁹ -23.8 (c 1.82, CHCl₃).

Reductive Debromination of **56**. A. With Trimethyl(tributylstannyl)silane.

To a stirred solution of **56** (3.5 mg, 4.9 μmol) in dry DMF (1 mL) were added benzyltriethylammonium chloride (4.6 mg, 14.9 μmol) and trimethyl(tributylstannyl)silane (3.0 μL, 9.9 μmol) under Ar. After 11 h at rt, the mixture was quenched with water and diluted with hexanes/ethyl acetate (1:1). The organic phase was washed with brine (2x), dried, and evaporated. The residue was purified by column chromatography on

silica gel (hexanes/ethyl acetate 4:1) to give **57** (3.0 mg, 97%) as a colorless oil; IR (neat, cm^{-1}) 1734, 1664, 1613, 1514; ^1H NMR (300 MHz, CDCl_3) δ 7.28-7.25 (m, 2 H), 6.89-6.86 (m, 2 H), 5.93 (d, J = 12.7 Hz, 1 H), 5.73 (dd, J = 12.0, 8.6 Hz, 1 H), 5.57-5.52 (m, 3 H), 5.47-5.43 (m, 1 H), 4.51 (d, J = 11.6 Hz, 1 H), 4.42 (d, J = 11.6 Hz, 1 H), 4.26-4.22 (m, 1 H), 3.80 (s, 3 H), 3.71 (s, 3 H), 3.48 (t, J = 3.7 Hz, 1 H), 3.19 (s, 3 H), 3.00-2.91 (m, 1 H), 2.87-2.80 (m, 1 H), 2.77-2.64 (m, 2 H), 2.48-2.38 (m, 1 H), 2.35-2.25 (m, 2 H), 2.08-2.04 (m, 1 H), 1.80-1.64 (m, 2 H), 1.58-1.49 (m, 2 H), 0.97 (d, J = 6.9 Hz, 3 H), 0.87 (s, 9 H), 0.04 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.0, 168.3, 159.4, 140.1, 135.2, 131.6, 129.4, 128.7, 122.8, 114.1, 87.8, 71.2, 69.5, 67.8, 61.8, 55.7, 43.9, 41.9, 39.4, 36.6, 36.3, 32.4, 30.1, 28.6, 26.2, 23.1, 18.5, 14.5, 14.2, -4.4 (2C); HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 650.3483, obsd 650.3497; $[\alpha]_{\text{D}}^{19}$ -11.8 (c 0.80, CHCl_3).

B. With Samarium Iodide. To a cooled (0 °C), stirred, and deoxygenated solution of **56** (19.4 mg, 0.0274 mmol) in THF (4 mL) was added HMPA (20 μL , 0.11 mmol) and samarium iodide (0.1 M solution in THF, 0.63 mL, 0.0631 mmol) under Ar. After 10 min, the mixture was quenched with water and extracted with ethyl acetate. The combined organic layers were washed with brine, dried, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 3:1) to give **57** (16 mg, 93%) spectroscopically identical to the material produced in part A. Comparable results were obtained when $\text{Fe}(\text{acac})_3$ was used in place of HMPA.

Desilylation of 56. To a stirred solution of **56** (21 mg, 0.0297 mmol) in THF (2.5 mL) and pyridine (0.5 mL) was added $\text{HF}\cdot\text{pyridine}$ (65-70%, 0.2 mL). The mixture was stirred for 2 d, quenched with saturated NaHCO_3 solution, and extracted with ethyl acetate (2x). The combined organic layers were dried and evaporated. The residue was purified by column chromatography on silica gel (hexanes/acetone 3:1) to give **59** (17.6 mg, quantitative); IR (neat, cm^{-1}) 3470, 1726, 1646, 1613; ^1H NMR (500 MHz, CDCl_3) δ 7.29 (d, J = 8.7 Hz, 2 H), 6.91 (d, J = 8.6 Hz, 2 H), 6.61 (d, J = 6.3 Hz, 1 H),

5.67 (d, $J = 10.1$ Hz, 1 H), 5.55 (d, $J = 9.9$ Hz, 1 H), 5.14 (br s, 1 H), 4.56 (d, $J = 11.7$ Hz, 1 H), 4.42 (d, $J = 11.7$ Hz, 1 H), 4.23 (br s, 1 H), 3.84 (s, 3 H), 3.73 (s, 3 H), 3.49-3.48 (m, 1 H), 3.23 (s, 3 H), 2.77-2.65 (m, 5 H), 2.55 (dd, $J = 16.9, 9.6$ Hz, 1 H), 2.09-2.03 (m, 4 H), 1.84-1.74 (m, 2 H), 1.57-1.52 (m, 1 H), 1.01 (d, $J = 6.8$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 173.9, 166.0, 159.5, 143.5, 132.1, 129.7, 129.4, 125.9, 114.2, 86.7, 71.1, 65.2, 61.8, 55.7, 45.1, 42.4, 42.3, 39.0, 38.2, 36.7, 36.2, 34.6, 32.3, 30.8, 30.1, 21.6, 14.4; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 614.1724, obsd 614.1738; $[\alpha]_{\text{D}}^{20}$ -49.0 (c 1.10, CHCl_3).

Carbinol 61. Epoxide **44** was treated with lithium trimethylsilyl acetylide and desilylated in the predescribed manner. To a stirred solution of the resulting alcohol (6.19 g, 25.5 mmol) in CH_2Cl_2 (250 mL) were added imidazole (5.21 g, 76.5 mmol), DMAP (312 mg, 2.55 mmol), and *tert*-butyldiphenylchlorosilane (9.95 mL, 38.3 mmol) under N_2 . The mixture was stirred overnight, quenched with H_2O , and extracted with ethyl acetate. The combined organic phases were washed with brine, dried, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 20:1) to give the silyl ether (12.26 g, 100%) as a colorless oil; IR (neat, cm^{-1}) 3308, 1641, 1473, 1428; ^1H NMR (300 MHz, CDCl_3) δ 7.72-7.66 (m, 4 H), 7.45-7.34 (m, 6 H), 5.76-5.62 (m, 1 H), 5.01-4.93 (m, 2 H), 4.68 (d, $J = 7.2$ Hz, 1 H), 4.61 (d, $J = 7.2$ Hz, 1 H), 3.97-3.90 (m, 1 H), 3.79-3.71 (m, 1 H), 3.59-3.49 (m, 2 H), 3.46-3.42 (m, 2 H), 3.35 (s, 3 H), 2.41-2.23 (m, 2 H), 2.20-2.04 (m, 2 H), 1.93 (t, $J = 2.6$ Hz, 1 H), 1.88 (t, $J = 6.3$ Hz, 2 H), 1.07 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 135.9, 134.3, 134.1, 133.7, 129.6, 127.6, 127.5, 117.3, 94.1, 73.7, 71.7, 70.4, 68.6, 67.0, 59.0, 40.4, 38.8, 27.0, 26.6, 19.3; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 503.2588, obsd 503.2597; $[\alpha]_{\text{D}}^{20}$ +3.9 (c 0.74, CHCl_3).

A solution of the above product (12.2 g, 25.4 mmol) and carbon tetrabromide (842 mg, 25.4 mmol) in *i*-PrOH (130 mL) was refluxed for 12 h. The mixture was cooled to rt, concentrated, and purified by column chromatography on silica gel (hexanes/ethyl

acetate 20:1) to give the MEM-deprotected product (9.38 g, 94%) as a colorless oil; IR (neat, cm^{-1}) 3456, 3309, 1641, 1473, 1428; ^1H NMR (300 MHz, CDCl_3) δ 7.72-7.67 (m, 4 H), 7.48-7.36 (m, 6 H), 5.83-5.69 (m, 1 H), 5.11-5.04 (m, 2 H), 4.11-4.04 (m, 1 H), 3.91-3.83 (m, 1 H), 2.37-2.17 (m, 2 H), 2.16-2.06 (m, 2 H), 1.94 (t, $J = 2.6$ Hz, 1 H), 1.91-1.72 (m, 3 H), 1.07 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 135.9, 135.8, 134.5, 133.8, 133.3, 129.9, 129.8, 127.8, 127.6, 117.9, 80.8, 70.6, 68.6, 42.4, 42.1, 27.0, 26.9, 19.2; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 415.2064, obsd 415.2087; $[\alpha]_{\text{D}}^{20} +22.3$ (c 1.18, CHCl_3).

To a stirred solution of this alcohol (1.52 g, 3.87 mmol) in CH_2Cl_2 (40 mL) were added pyridine (6.26 mL, 77.40 mmol) and benzoyl chloride (1.34 mL, 11.61 mmol). The mixture was stirred overnight, quenched with saturated NaHCO_3 solution, and extracted with ethyl acetate. The combined organic phases were washed with brine, dried, and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 50:1) to give the benzoate (1.82 g, 95%) as a colorless oil; IR (neat, cm^{-1}) 3306, 1717, 1428; ^1H NMR (300 MHz, CDCl_3) δ 7.92-7.88 (m, 2 H), 7.70-7.66 (m, 4 H), 7.58-7.52 (m, 1 H), 7.45-7.30 (m, 8 H), 5.78-5.65 (m, 1 H), 5.33-5.25 (m, 1 H), 5.04-4.98 (m, 2 H), 3.97-3.89 (m, 1 H), 2.39-2.24 (m, 4 H), 2.10-2.02 (m, 2 H), 1.98 (t, $J = 2.6$ Hz, 1 H), 1.09 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.8, 135.8, 133.7, 133.5, 133.1, 132.8, 130.3, 129.7 (2 C), 129.5, 128.2, 127.6, 127.5, 118.1, 80.6, 70.8, 70.6, 68.2, 39.6, 38.8, 26.9, 26.3, 19.2; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 519.2326, obsd 519.2361; $[\alpha]_{\text{D}}^{20} -4.60$ (c 0.87, CHCl_3).

To a cooled (0 $^\circ\text{C}$), stirred solution of the above intermediate (9.61 g, 19.3 mmol) in THF (100 mL) and pyridine (30 mL) was added HF•pyridine (65-70%, 8 mL). After 2 d of stirring at rt, an additional 8 mL of HF•pyridine was introduced. After 4 d, the mixture was quenched with saturated NaHCO_3 solution, and extracted with ethyl acetate (2x). The combined organic phases were washed with brine, dried, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl

acetate 4:1) to give the product of desilylation (4.79 g, 96%) as a colorless oil; IR (neat, cm^{-1}) 3450, 3301, 1713, 1451; ^1H NMR (300 MHz, CDCl_3) δ 8.05-8.01 (m, 2 H), 7.59-7.54 (m, 1 H), 7.47-7.41 (m, 2 H), 5.91-5.77 (m, 1 H), 5.35-5.27 (m, 1 H), 5.18-5.08 (m, 2 H), 3.98-3.90 (m, 1 H), 2.55-2.36 (m, 4 H), 2.09-1.93 (m, 4 H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.2, 133.0, 130.2, 129.5, 128.4, 118.4, 80.2, 71.8, 71.3, 67.4, 39.9, 38.8, 27.3; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 281.1148, obsd 281.1156; $[\alpha]_{\text{D}}^{20}$ -17.2 (c 0.90, CHCl_3).

To a cooled (0 °C), stirred solution of this material (2.56 g, 9.91 mmol) and *p*-methoxybenzyltrichloroacetimidate (14.0 g, 49.95 mmol) in CH_2Cl_2 (50 mL) was added camphosulfonic acid (460 mg, 1.98 mmol). After being stirred for 1 h at 0 °C, the reaction mixture was allowed to warm to rt and stirred overnight. The solvent was removed *in vacuo*, and the residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 15:1) to give the ether (which was not completely separated from PMB-imidate derived impurities). The mixture of the compounds in methanol (66 mL) was cooled to -78 °C and exposed to a stream of ozone. Red 23 (0.1% solution of Sudan III in MeOH, 2 mL) was used as an internal indicator. Sodium borohydride (1.13 g, 29.73 mmol) was added when the pink color had faded. The resulting mixture was allowed to warm to rt and quenched with saturated NaHCO_3 solution. Methanol was evaporated and the mixture was diluted with ethyl acetate, washed with brine, dried, and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 3:1) to give **61** (2.34 g, 62% for the two steps) as a colorless oil; IR (neat, cm^{-1}) 3469, 3298, 1715, 1514; ^1H NMR (300 MHz, CDCl_3) δ 8.00-7.97 (m, 2 H), 7.59-7.54 (m, 1 H), 7.45-7.40 (m, 2 H), 7.25-7.19 (m, 2 H), 6.83-6.77 (m, 2 H), 5.49-5.41 (m, 1 H), 4.57 (d, J = 11.3 Hz, 1 H), 4.41 (d, J = 11.3 Hz, 1 H), 3.77 (s, 3 H), 3.75-3.63 (m, 2 H), 3.61-3.52 (m, 1 H), 2.58-2.42 (m, 2 H), 2.23-2.05 (m, 3 H), 2.03 (t, J = 2.7 Hz, 1 H), 2.01-1.87 (m, 1 H), 1.85-1.76 (m, 1 H); ^{13}C NMR (75 MHz, CDCl_3) δ 167.0, 133.1, 129.9, 129.7, 129.5, 128.4, 113.7, 80.4, 73.5, 70.7, 69.6, 58.4, 55.2, 38.8, 37.7,

23.5; ^1H NMR (300 MHz, CDCl_3) δ 7.96-7.93 (m, 2 H), 7.67-7.52 (m, 5 H), 7.45-7.31 (m, 6 H), 7.28-7.17 (m, 4 H), 6.81-6.75 (m, 2 H), 5.52-5.44 (m, 1 H), 4.54 (d, J = 11.2 Hz, 1 H), 4.40 (d, J = 11.2 Hz, 1 H), 3.76 (s, 3 H), 3.78-3.72 (m, 2 H), 3.70-3.62 (m, 1 H), 2.59-2.43 (m, 2 H), 2.13-2.08 (m, 2 H), 2.00-1.94 (m, 3 H), 1.02 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.1, 135.5, 133.6, 133.5, 132.7, 130.5, 130.1, 129.6, 129.5, 129.4, 128.2, 127.6, 113.7, 80.6, 73.6, 70.6, 70.5, 69.8, 60.1, 55.2, 38.5, 37.1, 26.8, 23.6, 19.1; ^1H NMR ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 405.1672, obsd 405.1650; $[\alpha]_{\text{D}}^{18}$ +25.7 (c 1.35, CHCl_3).

Vinyl iodide 62. To a stirred solution of **61** (3.73 g, 9.75 mmol) in DMF (100 mL) were added ammonium nitrate (2.34 g, 29.3 mmol) and TBDPSCI (3.8 mL, 14.6 mmol). The mixture was stirred overnight, quenched with H_2O , and diluted with hexanes/ethyl acetate (1:1). The organic layer was washed with brine (2x), dried, and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 15:1) to give the silyl ether (6.06 g, 100%) as a colorless oil; IR (neat, cm^{-1}) 1717, 1514, 1274; ^1H NMR (300 MHz, CDCl_3) δ 7.96-7.93 (m, 2 H), 7.67-7.52 (m, 5 H), 7.45-7.31 (m, 6 H), 7.28-7.17 (m, 4 H), 6.81-6.75 (m, 2 H), 5.52-5.44 (m, 1 H), 4.54 (d, J = 11.2 Hz, 1 H), 4.40 (d, J = 11.2 Hz, 1 H), 3.76 (s, 3 H), 3.78-3.72 (m, 2 H), 3.70-3.62 (m, 1 H), 2.59-2.43 (m, 2 H), 2.13-2.08 (m, 2 H), 2.00-1.94 (m, 3 H), 1.02 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 159.1, 135.5, 133.6, 133.5, 132.7, 130.5, 130.1, 129.6, 129.5, 129.4, 128.2, 127.6, 113.7, 80.6, 73.6, 70.6, 70.5, 69.8, 60.1, 55.2, 38.5, 37.1, 26.8, 23.6, 19.1; ^1H NMR ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 643.2850, obsd 643.2844; $[\alpha]_{\text{D}}^{20}$ +16.3 (c 0.91, CHCl_3).

To a stirred solution of the fully protected alkyne (6.06 g, 9.76 mmol) in $\text{CH}_2\text{Cl}_2:\text{H}_2\text{O}$ (18:1, 133 mL) was added DDQ (3.32 g, 14.64 mmol). After 1 h, the mixture was quenched with saturated NaHCO_3 solution, and diluted with ethyl acetate. The organic phase was washed with brine, dried, and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 7:1) to give the selectively deprotected alcohol (4.47 g, 91%) as a colorless oil; IR (neat, cm^{-1}) 3465, 3302, 1717, 1428; ^1H NMR (300 MHz, CDCl_3) δ 8.00-7.96 (m, 2 H), 7.68-7.53 (m, 5 H), 7.45-7.32 (m, 6 H), 7.29-7.24 (m, 2 H), 5.46 (quintet, J = 6.2 Hz, 1 H), 3.94 (quintet, J = 6.0 Hz, 1 H), 3.78 (t, J = 6.3 Hz, 2 H), 2.52-2.36 (m, 3 H), 2.06-2.00 (m, 5 H), 1.04 (s, 9 H); ^{13}C NMR (75 MHz, CDCl_3) δ 166.2, 135.5, 133.6, 133.4, 132.9, 130.3, 129.6,

128.3, 127.7, 127.6, 80.3, 71.1, 70.3, 67.4, 60.0, 40.8, 37.1, 27.4, 26.8, 19.1;_HRMS ES m/z (M+Na)⁺ calcd 523.2276, obsd 523.2284; $[\alpha]_D^{19}$ +5.4 (c 1.04, CHCl₃).

A mixture of the above alcohol (1.03 g, 2.06 mmol), TBSCl (620 mg, 4.11 mmol), imidazole (560 mg, 8.23 mol), and DMAP (25 mg, 0.21 mmol) in CH₂Cl₂ (21 mL) was stirred overnight. The mixture was diluted with ethyl acetate, and the organic phase was washed with brine, dried, and freed of solvent. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 100:1) to afford the silyl ether (1.21 g, 96%) as a colorless oil; IR (neat, cm⁻¹) 3310, 1719, 1273; ¹H NMR (300 MHz, CDCl₃) δ 8.00-7.97 (m, 2 H), 7.66-7.52 (m, 5 H), 7.44-7.23 (m, 8 H), 5.46-5.38 (m, 1 H), 4.05-3.91 (m, 1 H), 3.75 (t, J = 6.6 Hz, 2 H), 2.41 (dd, J = 5.6, 2.7 Hz, 2 H), 2.06-1.96 (m, 4 H), 1.94 (t, J = 2.6 Hz, 1 H), 1.02 (s, 9 H), 0.89 (s, 9 H), 0.06 (d, J = 1.0 Hz, 6 H); ¹³C NMR (75 MHz, CDCl₃) δ 165.8, 135.5, 132.7, 130.5, 129.6, 129.5, 128.3, 127.6 (2 C), 81.1, 70.4, 69.6, 67.9, 60.1, 41.4, 37.3, 27.1, 26.8, 25.9, 19.1, 18.0, -4.5, -4.7;_HRMS ES m/z (M+Na)⁺ calcd 637.3140, obsd 637.3130; $[\alpha]_D^{20}$ +8.7 (c 1.12, CHCl₃).

To a stirred solution of the above intermediate (620 mg, 1.01 mmol) in benzene (144 mL) were added tri-*n*-butyltin hydride (2.70 mL, 10.08 mmol) and AIBN (16.6 mg, 0.10 mmol) at rt under N₂. The reaction mixture was gently refluxed with stirring for 3.5 h. The solvent was removed and the residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 300:1) to give the vinyl stannane. To a cooled (0 °C), stirred solution of this material in CH₂Cl₂ (95 mL) was added a solution of iodine in CH₂Cl₂ until a purple color persisted. After 10 min at 0 °C, saturated Na₂S₂O₃ solution was added until the color faded. The mixture was diluted with ethyl acetate, washed with brine, dried and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 200:1) to give **62** (705 mg, 94% over two steps) as a colorless oil; IR (neat, cm⁻¹) 1718, 1603, 1272; ¹H NMR (300 MHz, CDCl₃) δ 8.00-7.97 (m, 2 H), 7.67-7.55 (m, 5 H), 7.46-7.32 (m, 6 H), 7.29-7.24 (m, 2 H), 6.51 (qd, J =

7.0, 8.1 Hz, 1 H), 6.02 (d, $J = 14.4$ Hz, 1 H), 5.53-5.39 (m, 1 H), 3.83-3.74 (m, 1 H), 3.72 (t, $J = 6.4$ Hz, 2 H), 2.42-2.34 (m, 1 H), 2.25-2.16 (m, 1 H), 1.99-1.89 (m, 3 H), 1.86-1.77 (m, 1 H), 1.03 (s, 9 H), 0.88 (s, 9 H), 0.02 (d, $J = 4.0$ Hz, 6 H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.9, 142.9, 137.6, 135.5, 133.6, 132.9, 130.3, 129.6, 129.5, 128.3 (2 C), 127.6 (2 C), 84.4, 69.3, 68.2, 60.0, 42.9, 42.1, 37.6, 26.8, 25.8, 19.1, 18.0, -4.5, -4.7; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 765.2263, obsd 765.2227; $[\alpha]_{\text{D}}^{21}$ -8.8 (c 0.94, CHCl_3).

Coupling of 10 to 62. To a stirred mixture of $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (76 mg, 0.11 mmol) and CuI (41 mg, 0.22 mmol) in triethylamine (10 mL) were added solutions of **62** (403 mg, 0.54 mmol) in triethylamine (6 mL) and **10** (201 mg, 0.73 mmol) in triethylamine (6 mL) at rt under Ar. After 2 h, the mixture was concentrated and the residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 3:1) to give **63** (418 mg, 87%) as a yellowish syrup; IR (neat, cm^{-1}) 3482, 1718, 1514, 1273; ^1H NMR (300 MHz, CDCl_3) δ 7.99-7.97 (m, 2 H), 7.66-7.54 (m, 5 H), 7.45-7.23 (m, 10 H), 6.88-6.84 (m, 2 H), 6.21-6.11 (m, 1 H), 5.63-5.53 (m, 3 H), 5.46-5.38 (m, 1 H), 4.71 (d, $J = 11.5$ Hz, 1 H), 4.40 (d, $J = 11.5$ Hz, 1 H), 4.05 (d, $J = 3.9$ Hz, 2 H), 4.01-4.00 (m, 1 H), 3.82-3.78 (m, 1 H), 3.80 (s, 3 H), 3.73 (t, $J = 6.3$ Hz, 2 H), 2.50-2.42 (m, 1 H), 2.31-2.21 (m, 2 H), 2.06-1.79 (m, 6 H), 1.03 (s, 9 H), 0.98 (d, $J = 6.5$ Hz, 3 H), 0.88 (s, 9 H), 0.03 (d, $J = 2.1$ Hz, 6 H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.9, 159.1, 141.2, 135.5, 132.8, 130.9, 130.8, 130.4, 130.2, 129.6 (2 C), 129.5, 128.3, 127.6 (2 C), 113.7, 111.7, 85.6, 72.6, 70.1, 69.4, 68.8, 63.7, 60.0, 55.3, 42.3, 40.3, 38.0, 37.5, 35.6, 26.8, 25.8, 19.1, 18.0, 15.2, 14.2, -4.5, -4.6; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 911.4709, obsd 911.4679; $[\alpha]_{\text{D}}^{21}$ +32.0 (c 0.75, CHCl_3).

Aldehyde 64. To a stirred suspension of zinc dust (7.4 g) in water (44 mL) was added $\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$ (740 mg) at rt under Ar. After 30 min, AgNO_3 (740 mg) was introduced and the mixture was stirred for 30 min and filtered. The filtrate was washed sequentially with water (88 mL), methanol (88 mL), acetone (88 mL), and ether (88 mL).

The activated zinc was suspended in 50% aqueous THF (44 mL) and a solution of **63** (492 mg, 0.553 mmol) in methanol (6 mL) was introduced under Ar. The mixture was deoxygenated and stirred for 1.5 d under reflux, filtered through Celite, and rinsed with methanol. The filtrate was concentrated, diluted with ethyl acetate, washed with brine, dried, and freed of solvent. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 3:1) to give the trienol (430 mg, 87%) as a colorless syrup; IR (neat, cm⁻¹) 3468, 1717, 1514; ¹H NMR (300 MHz, CDCl₃) δ 7.98 (d, *J* = 6.3 Hz, 2 H), 7.67-7.54 (m, 5 H), 7.45-7.32 (m, 6 H), 7.29-7.22 (m, 4 H), 6.87 (d, *J* = 8.5 Hz, 2 H), 6.33-6.20 (m, 2 H), 5.81-5.71 (m, 1 H), 5.62-5.60 (m, 2 H), 5.49-5.40 (m, 1 H), 5.23 (t, *J* = 9.7 Hz, 1 H), 4.48 (d, *J* = 11.3 Hz, 1 H), 4.21 (d, *J* = 11.3 Hz, 1 H), 4.06 (d, *J* = 3.1 Hz, 2 H), 3.98 (t, *J* = 8.5 Hz, 1 H), 3.85 (t, *J* = 5.4 Hz, 1 H), 3.80 (s, 3 H), 3.75 (t, *J* = 6.3 Hz, 2 H), 2.49-2.23 (m, 3 H), 2.08-1.81 (m, 5 H), 1.78-1.70 (m, 1 H), 1.04 (s, 9 H), 0.89 (s, 9 H), 0.81 (d, *J* = 6.8 Hz, 3 H), 0.05 (s, 3 H), 0.03 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃) δ 165.9, 159.0, 135.5, 133.6, 133.4, 132.9, 132.8, 132.7, 131.4, 130.9, 130.6, 130.4, 129.5 (2 C), 129.4, 128.6, 128.3, 127.9, 127.6, 127.5, 113.6, 77.4, 69.7, 69.6, 69.2, 63.7, 60.1, 55.2, 42.2, 40.2, 37.9, 37.4, 35.5, 26.7, 25.8, 19.0, 18.0, 15.2, -4.4, -4.6; HRMS ES *m/z* (M+Na)⁺ calcd 913.4865, obsd 913.4830; [α]_D²⁰ -17.0 (*c* 0.60, CHCl₃).

A mixture of the above trienol (121 mg, 0.136 mmol) and IBX (190 mg, 0.679 mmol) in THF:DMSO (9:1, 10 mL) was stirred for 2 h at rt, diluted with hexanes, filtered through Celite, and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 10:1) to give the aldehyde (112.5 mg, 93%) as a colorless oil; IR (neat, cm⁻¹) 1718, 1693, 1514; ¹H NMR (300 MHz, CDCl₃) δ 9.45 (d, *J* = 7.9 Hz, 1 H), 7.98-7.95 (m, 2 H), 7.66-7.52 (m, 5 H), 7.44-7.31 (m, 6 H), 7.28-7.18 (m, 4 H), 6.88-6.85 (m, 2 H), 6.76 (tt, *J* = 8.6, 6.8 Hz, 1 H), 6.30-6.21 (m, 2 H), 6.08 (dd, *J* = 15.5, 7.9 Hz, 1 H), 5.82-5.73 (m, 1 H), 5.48-5.39 (m, 1 H), 5.20 (t, *J* = 9.6 Hz, 1 H), 4.48 (d, *J* = 11.3 Hz, 1 H), 4.18 (d, *J* = 11.3 Hz, 1 H), 3.95 (t, *J* = 8.6 Hz, 1 H), 3.90-3.79 (m,

1 H), 3.79 (s, 3 H), 3.74 (t, $J = 6.4$ Hz, 2 H), 2.70-2.62 (m, 1 H), 2.49-2.40 (m, 1 H), 2.32-2.12 (m, 2 H), 2.07-1.94 (m, 3 H), 1.91-1.80 (m, 2 H), 1.02 (s, 9 H), 0.88 (s, 9 H), 0.82 (d, $J = 6.9$ Hz, 3 H), 0.04 (s, 3 H), 0.01 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.9, 165.9, 159.2, 158.0, 135.5, 134.1, 133.6 (2 C), 133.5, 133.2, 132.8, 130.6, 130.5, 129.6 (2 C), 129.5 (2 C), 128.4, 128.3, 127.6 (2 C), 113.7, 77.5, 69.8, 69.7, 69.2, 60.1, 55.2, 42.2, 40.2, 37.7, 37.5, 36.4, 26.8, 25.9, 19.1, 18.0, 15.7, -4.4, -4.5; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 911.4709, obsd 911.4670; $[\alpha]_{\text{D}}^{20}$ -9.3 (c 1.51, CHCl_3).

A deoxygenated solution of the above aldehyde (168.5 mg, 0.189 mmol) and BHT (51 mg, 0.23 mmol) in toluene (24 mL) was placed in a sealed tube and heated at 155 °C for 30 h. The mixture was cooled to rt, concentrated, and purified by column chromatography on silica gel (hexanes/ethyl acetate 15:1) to give **64** (71.3 mg, 64%) as a colorless oil; IR (neat, cm^{-1}) 1719, 1514, 1273; ^1H NMR (300 MHz, CDCl_3) δ 9.66 (d, $J = 2.3$ Hz, 1 H), 7.99-7.95 (m, 2 H), 7.66-7.53 (m, 5 H), 7.45-7.31 (m, 6 H), 7.29-7.23 (m, 4 H), 6.90-6.85 (m, 2 H), 5.72-5.65 (m, 1 H), 5.61-5.58 (m, 1 H), 5.40-5.37 (m, 1 H), 4.50 (d, $J = 11.7$ Hz, 1 H), 4.39 (d, $J = 11.7$ Hz, 1 H), 4.01-3.84 (m, 1 H), 3.80 (s, 3 H), 3.72 (t, $J = 5.8$ Hz, 2 H), 3.43 (t, $J = 3.5$ Hz, 1 H), 2.80-2.63 (m, 3 H), 2.30 (br s, 1 H), 2.09-1.92 (m, 4 H), 1.87-1.74 (m, 3 H), 1.47-1.38 (m, 2 H), 1.02 (s, 9 H), 0.98 (d, $J = 6.8$ Hz, 3 H), 0.87 (s, 9 H), 0.05 (s, 3 H), -0.02 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 205.2, 165.7, 159.0, 135.5, 133.6, 133.4, 132.8, 131.0, 130.5, 130.4, 130.0, 129.6, 129.5, 129.0, 128.3, 127.6 (2 C), 113.7, 86.9, 70.6, 69.3, 66.9, 60.0, 55.6, 55.2, 43.2, 41.8, 39.3, 37.8, 36.1, 35.4, 32.9, 28.5, 26.7, 25.8, 19.1, 17.9, 13.7, -4.1, -4.8; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 911.4709, obsd 911.4702; $[\alpha]_{\text{D}}^{21}$ -45.6 (c 0.79, CHCl_3).

Allyl Ester 65. To a cooled (-78 °C), stirred solution of allyl bis(2,2,2-trifluoroethyl)bromophosphonoacetate (1.32 g, 3.113 mmol) in THF (5 mL) was added sodium hexamethyldisilazide (1M in THF, 2.4 mL) under N_2 . After 30 min of stirring at -78 °C, a solution of **64** (98.5 mg, 0.143 mmol) in THF (5 mL) was added, and the reaction mixture was stirred for 1 h at -78 °C, allowed to warm to -15 °C, and stirred

overnight prior to being quenched with saturated NH_4Cl solution and extracted with ethyl acetate (2x). The combined organic layers were dried and concentrated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 20:1) to give **65** (95.8 mg, 64%); IR (neat, cm^{-1}) 1717, 1514, 1272; ^1H NMR (300 MHz, CDCl_3) δ 7.98-7.95 (m, 2 H), 7.66-7.53 (m, 5 H), 7.44-7.31 (m, 6 H), 7.28-7.23 (m, 4 H), 6.87 (d, $J = 8.6$ Hz, 2 H), 6.65 (d, $J = 10.7$ Hz, 0.83 H), 6.44 (d, $J = 10.7$ Hz, 0.17 H), 5.97-5.88 (m, 1 H), 5.55 (br dd, $J = 17.2, 10.4$ Hz, 2 H), 5.44-5.34 (m, 2 H), 5.26 (dd, $J = 10.4, 1.0$ Hz, 1 H), 4.67-4.65 (m, 2 H), 4.51 (d, $J = 11.7$ Hz, 1 H), 4.38 (d, $J = 11.7$ Hz, 1 H), 3.86-3.81 (m, 1 H), 3.81 (s, 3 H), 3.74 (t, $J = 6.4$ Hz, 2 H), 3.43 (t, $J = 3.3$ Hz, 1 H), 3.27-3.18 (m, 1 H), 2.72-2.64 (m, 1 H), 2.54 (br s, 1 H), 2.48-2.39 (m, 1 H), 2.03-1.90 (m, 4 H), 1.81-1.65 (m, 2 H), 1.56-1.46 (m, 2 H), 1.38-1.24 (m, 1 H), 1.03 (s, 9 H), 0.97 (d, $J = 6.8$ Hz, 3 H), 0.87 (s, 9 H), 0.03 (s, 3 H), -0.03 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.7, 151.0, 135.5, 133.7, 133.5, 132.7, 131.4, 131.2, 130.5, 130.0, 129.6 (2 C), 129.5, 128.9, 128.3, 127.6 (2 C), 118.8, 113.7, 111.2, 87.0, 70.7, 69.4, 66.8, 60.1, 55.3, 44.0, 42.8, 41.9, 39.7, 38.8, 37.7, 36.2, 35.6, 26.8, 25.8, 19.1, 18.0, 13.9, 1.0, -4.2, -4.7; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 1071.4233, obsd 1071.4289; $[\alpha]_{\text{D}}^{21}$ -25.4 (c 1.25, CHCl_3).

Bromo Lactone 66. A solution of **65** (65.8 mg, 0.0627 mmol), $\text{Pd}(\text{OAc})_2$ (1.4 mg, 6 μmol), triphenylphosphine (24.6 mg, 0.094 mmol), and dimedone (26.4 mg, 0.188 mmol) in THF (4 mL) was stirred for 2 h at rt. The solvent was removed and the residue was purified by chromatography (hexanes/ethyl acetate 2:1) on silica gel to give the carbocyclic acid (55.4 mg, 88%) as a yellowish oil; IR (neat, cm^{-1}) 1718, 1514, 1272; ^1H NMR (300 MHz, CDCl_3) δ 7.96-7.93 (m, 2 H), 7.65-7.52 (m, 5 H), 7.44-7.22 (m, 10 H), 6.87 (d, $J = 8.6$ Hz, 2 H), 6.75 (d, $J = 10.5$ Hz, 0.86 H), 6.56 (d, $J = 9.6$ Hz, 0.14 H), 5.58-5.49 (m, 2 H), 5.44-5.34 (m, 1 H), 4.56 (d, $J = 11.7$ Hz, 1 H), 4.39 (d, $J = 11.7$ Hz, 1 H), 3.88-3.80 (m, 1 H), 3.80 (s, 3 H), 3.73 (t, $J = 6.6$ Hz, 2 H), 3.44 (br s, 1 H), 3.33-3.26 (m, 1 H), 2.64 (br s, 1 H), 2.58-2.43 (m, 2 H), 2.05-1.94 (m, 4 H), 1.82-1.67 (m, 2

H), 1.56-1.48 (m, 2 H), 1.40-1.28 (m, 1 H), 1.02 (s, 9 H), 0.94 (d, $J = 6.8$ Hz, 3 H), 0.85 (s, 9 H), 0.02 (s, 3 H), -0.04 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 165.8, 159.0, 135.5, 133.6, 133.4, 132.8, 130.9, 130.4, 129.9, 129.6, 129.5, 129.1, 128.3, 127.7, 127.6, 113.7, 86.9, 70.6, 69.4, 66.8, 60.1, 55.3, 44.3, 42.8, 42.0, 39.7, 39.1, 37.7, 36.2, 35.6, 26.8, 25.8, 19.1, 18.0, 13.9, -4.2, -4.7; HRMS ES m/z ($\text{M}+\text{Na}$) $^+$ calcd 1031.3920, obsd 1031.3939; $[\alpha]_{\text{D}}^{19}$ -26.4 (c 1.40, CHCl_3).

To a cooled ($-78\text{ }^\circ\text{C}$), stirred solution of the carboxylic acid (61.9 mg, 0.0613 mmol) in CH_2Cl_2 (8 mL) was added Dibal-H (20% in hexanes, 0.175 mL, 0.245 mmol) under N_2 . After 50 min, the mixture was quenched with saturated Rochelle's salt solution, stirred for 3 h at rt, and extracted with CH_2Cl_2 and ethyl acetate. The combined organic layers were dried and evaporated. The crude hydroxy acid was dissolved in THF (6 mL) and triethylamine (0.069 mL, 0.49 mmol) together with 2,4,6-trichlorobenzoyl chloride (0.048 mL, 0.307 mmol) were introduced. After 2 h, the triethylammonium chloride was filtered off through Celite and rinsed with THF. Anhydrous toluene (10 mL) was added to the combined filtrates. The solution was added dropwise over 1 h to a refluxing solution of DMAP (150 mg, 1.23 mmol) in 10 mL of toluene. The mixture was refluxed for 2 h, cooled to rt, freed of toluene, and diluted with ethyl acetate. The organic phase was washed with saturated citric acid solution, water, saturated NaHCO_3 solution, and brine, then dried and evaporated. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 30:1) to give **66** (29.5 mg, 54 %) as a colorless oil; IR (neat, cm^{-1}) 1741, 1613, 1514; ^1H NMR (300 MHz, CDCl_3) δ 7.68-7.64 (m, 4 H), 7.46-7.36 (m, 6 H), 7.28-7.24 (m, 2 H), 6.91-6.86 (m, 2 H), 5.97 (d, $J = 9.5$ Hz, 0.8 H), 5.80 (d, $J = 9.5$ Hz, 0.2 H), 5.56-5.50 (m, 1 H), 5.47-5.36 (m, 2 H), 4.53 (d, $J = 11.7$ Hz, 1 H), 4.41 (d, $J = 11.7$ Hz, 1 H), 4.23-4.16 (m, 1 H), 3.81 (s, 3 H), 3.75-3.67 (m, 2 H), 3.48 (t, $J = 3.2$ Hz, 1 H), 2.87-2.79 (m, 2 H), 2.69-2.60 (m, 1 H), 2.52-2.44 (m, 1 H), 2.32-2.17 (m, 2 H), 2.05-1.90 (m, 2 H), 1.85-1.68 (m, 2 H), 1.61-1.49 (m, 2 H), 1.35-1.25 (m, 1 H), 1.05 (s, 9 H), 0.97 (d, $J = 6.8$ Hz, 3 H),

0.87 (s, 9 H), 0.07 (s, 3 H), -0.05 (s, 3 H);_HRMS ES m/z (M+Na)⁺ calcd 909.3552, obsd 909.3519; $[\alpha]_D^{21}$ -2.3 (c 0.65, CHCl₃).

Bromo Aldehyde 60. To a stirred solution of acetic acid (3.3 mg, 0.0548 mmol) in DMF (2.5 mL) was added TBAF (1 M solution in THF, 0.055 mL, 0.055 mmol). After 5 min, a solution of **66** (24.3 mg, 0.0274 mmol) was introduced. The mixture was stirred overnight, quenched with saturated NaHCO₃ solution, and extracted with EtOAc. The combined organic layers were dried and evaporated. The residue was purified by chromatography on silica gel (hexanes/ethyl acetate 3:1) to give the bromo alcohol (14.8 mg, 83%) as a colorless oil; IR (neat, cm⁻¹) 3458, 1740, 1612, 1514; ¹H NMR (300 MHz, CDCl₃) δ _7.26 (d, J = 8.4 Hz, 2 H), 6.88 (d, J = 8.4 Hz, 2 H), 6.04 (d, J = 9.6 Hz, 0.8 H), 5.88 (d, J = 9.6 Hz, 0.2 H), 5.56 (d, J = 9.9 Hz, 1 H), 5.36 (br d, J = 8.5 Hz, 2 H), 4.54 (d, J = 11.7 Hz, 1 H), 4.41 (d, J = 11.7 Hz, 1 H), 4.26-4.24 (m, 1 H), 3.81 (d, J = 1.2 Hz, 3 H), 3.76-3.62 (m, 2 H), 3.48 (br s, 1 H), 2.78-2.70 (m, 3 H), 2.52-2.45 (m, 1 H), 2.40-2.31 (m, 1 H), 2.14-1.46 (m, 7 H), 1.32-1.22 (m, 1 H), 0.98 (d, J = 6.8 Hz, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H); ¹³C NMR (75 MHz, CDCl₃) δ _165.4, 159.0, 131.1, 128.9, 113.7, 108.9, 87.1, 70.7, 67.3, 58.6, 55.3, 45.1, 41.5, 36.2, 36.0, 29.7, 25.8, 18.0, 13.8, -4.6, -4.8;_HRMS ES m/z (M+Na)⁺ calcd 671.2374, obsd 671.2390; $[\alpha]_D^{19}$ -9.3 (c 0.74, CHCl₃).

To a stirred solution of the bromo alcohol (7 mg, 0.011 mmol) in dry CH₂Cl₂ (2 mL) were added 4 Å molecular sieves and sodium acetate (4.4 mg, 0.054 mmol) under N₂. The mixture was cooled to 0 °C and pyridinium chlorochromate (12 mg, 0.054 mmol) was added. The mixture was stirred for 2 h at 0 °C and for 30 min at rt, diluted with ether, and stirred for 30 min. The mixture was filtered through a Florisil pad and washed with ether. The residue was purified by column chromatography on silica gel (hexanes/ethyl acetate 5:1) to give **60** (5.1 mg, 73%) as a colorless oil; ¹H NMR (300 MHz, CDCl₃) δ _9.76 (t, J = 1.7 Hz, 1 H), 7.28-7.23 (m, 2 H), 6.89-6.86 (m, 2 H), 6.01 (d, J = 9.5 Hz, 1 H), 5.69-5.62 (m, 1 H), 5.58-5.54 (m, 1 H), 5.39-5.35 (m, 1 H), 4.53 (d, J =

11.7 Hz, 1 H), 4.41 (d, $J = 11.7$ Hz, 1 H), 4.23-4.19 (m, 1 H), 3.81 (s, 3 H), 3.48 (br d, 1 H), 2.92 (ddd, $J = 17.2, 8.1, 2.0$ Hz, 1 H), 2.77-2.66 (m, 4 H), 2.52-2.48 (m, 1 H), 2.32-2.18 (m, 2 H), 2.04-1.98 (m, 1 H), 1.80-1.65 (m, 2 H), 1.55-1.49 (m, 2 H), 0.98 (d, $J = 6.8$ Hz, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H); HRMS ES m/z (M+Na)⁺ calcd 669.2217, obsd 669.2237.

¹H NMR spectrum of **14**

^{13}C NMR spectrum of **14**

¹H NMR spectrum of **15**

¹³C NMR spectrum of **15**

¹H NMR spectrum of **16**

¹³C NMR spectrum of **16**

¹H NMR spectrum of **17**

¹³C NMR spectrum of **17**

^1H NMR spectrum of **18**

¹³C NMR spectrum of **18**

¹H NMR spectrum of **19**

¹³C NMR spectrum of **19**

¹H NMR spectrum of **20**

¹³C NMR spectrum of **20**

¹H NMR spectrum of **21**

¹³C NMR spectrum of **21**

¹H NMR spectrum of **22**

¹³C NMR spectrum of **22**

¹H NMR spectrum of **23**

^{13}C NMR spectrum of **23**

¹³C NMR spectrum of **26**

¹H NMR spectrum of **28**

¹³C NMR spectrum of **28**

¹H NMR spectrum of **29**

¹³C NMR spectrum of **29**

^1H NMR spectrum of **30**

¹³C NMR spectrum of **30**

¹³C NMR spectrum of **10**

^1H NMR spectrum of **31**

^{13}C NMR spectrum of **31**

^1H NMR spectrum of **34**

^{13}C NMR spectrum of **34**

^1H NMR spectrum of **35**

^1H NMR spectrum of **36**

^{13}C NMR spectrum of **36**

^1H NMR spectrum of **6**

^{13}C NMR spectrum of **6**

^1H NMR spectrum of **39**

^{13}C NMR spectrum of **39**

^{13}C NMR spectrum of **40**

¹H NMR spectrum of **44**

S91

¹³C NMR spectrum of **44**

¹H NMR spectrum of **45**

¹³C NMR spectrum of **45**

¹H NMR spectrum of **46**

¹³C NMR spectrum of **46**

¹³C NMR spectrum of **47**

^1H NMR spectrum of **48**

^{13}C NMR spectrum of **48**

¹H NMR spectrum of **49**

¹³C NMR spectrum of **49**

^1H NMR spectrum of 50

S103

^{13}C NMR spectrum of **50**

^1H NMR spectrum of **51**

¹³C NMR spectrum of **51**

^{13}C NMR spectrum of **54**

^{13}C NMR spectrum of **55**

¹³C NMR spectrum of **56**

^1H NMR spectrum of **57**

^1H NMR spectrum of **59**

^{13}C NMR spectrum of **59**

¹H NMR spectrum of **61**

¹³C NMR spectrum of **61**

CCCC[C@H](O[C@@H]1C=CC=C1)[C@H](O[C@@H]2C=CC=C2)CCCCI

¹³C NMR spectrum of **62**

¹³C NMR spectrum of **63**

¹H NMR spectrum of **65**

^{13}C NMR spectrum of **65**

^{13}C NMR spectrum of **66**

^1H NMR spectrum of **60**