The Enantioselective Total Synthesis of the Antitumor Macrolide Rhizoxin D

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Supporting Information (Part 1 of 2)

Table of Contents:

General Experimental Procedures	S2
Experimental Procedures	S2-S21

General Experimental Procedures. All reactions with air- and/or moisture-sensitive compounds were performed under a nitrogen atmosphere in a flame-dried or oven-dried reaction flask, and reagents were added *via* syringe or cannula. Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. The following solvents were distilled under nitrogen immediately prior to use: Et₂O and THF were distilled from sodium benzophenone ketyl, CH₂Cl₂, benzene, CH₃CN, and toluene were distilled from CaH₂, and diisopropylamine was distilled from KOH. The concentration of commercially available solutions of butyllithium in hexanes was periodically checked by titration with diphenylacetic acid. Brine refers to satd. aq. NaCl. Unless otherwise noted, all ¹H NMR spectra were recorded at 500 MHz, and ¹³C NMR spectra were recorded at 125 MHz in CDCl₃.

Ethyl (2*E*, 5*S*, 7*R*, 8*S*)-8-methyl-7-benzyloxy-5-[2-(benzyloxy)ethyl]-9-[(2'-benzothiazoyl)sulfonyl]-2-nonenoate (6). In a round-bottomed flask equipped with a condenser, 2-mercaptobenzothiazole (123 mg, 0.737 mmol) was dissolved in DMF (0.7 mL) and cooled to 0 °C. NaH (60 % dispersion in oil, 29.5 mg, 0.737 mmol) then was added to the solution in one portion, and the resulting mixture was stirred for 20 min. Mesylate **26** (85.3 mg, 0.246 mmol) in 0.10 mL of DMF was then added to the anion *via* syringe, and the cloudy mixture was heated to 55 to 60 °C for 12 h. The reaction was then judged complete by TLC analysis, and was quenched with satd. aq. NaHCO₃ and extracted with Et₂O. The combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo*. The resulting crude material was purified by column chromatography to afford the sulfide as a mixture with 2-mercaptobenzothiazole; this mixture was carried directly into the following oxidation.

Ammonium molybdate (43.3 mg, 0.034 mmol) was added to 30 % H₂O₂ (54.7 mL, 0.53 mmol) at 0 °C to give a bright yellow solution. In a separate flask, the thioether formed above was dissolved in 0.81 mL of absolute EtOH and 0.1 mL of THF and cooled to 0 °C. The molybdate solution was then added by syringe to the thioether, resulting in a cloudy yellow mixture which was stirred for 48 h. The solution was concentrated *in vacuo*, diluted with Et₂O, and extracted with satd. aq. NaHCO₃ solution. The aqueous phase was then extracted with THF and EtOAc, and the combined organic extracts were then dried over MgSO₄, filtered, and concentrated. The resulting crude material was purified by column chromatography (19:1 to 9:1 hexanes/EtOAc) to give 69.4 mg (80% over two steps) of **6** as a clear oil: [α]_D²³ + 15.2 (c

1.03, CH₂Cl₂); IR (thin film): 2932, 1713, 1651, 1472, 1324 cm⁻¹; ¹H NMR: 1.12 (d, 3H, *J* = 6.9 Hz), 1.29 (t, 3H, *J* = 7.1 Hz), 1.30 (m, 1H), 1.40 (m, 1H), 1.59 (m, 2H), 1.87 (m, 1H), 2.1 (m, 2H), 2.81 (m, 1H), 3.25 (dd, 1H, *J* = 9.4, 14.2 Hz), 3.46 (t, 2H, *J* = 6.5 Hz), 3.51 (dt, 1H, *J* = 3.7, 9.0 Hz), 3.84 (dd, 1H, *J* = 2.8, 14.2 Hz), 4.18 (q, 2H, *J* = 7.1 Hz), 4.32 (d, 1H, *J* = 11.4 Hz), 4.45 (d, 1H, *J* = 11.4 Hz), 4.46 (s, 2H), 5.76 (d, 1H, *J* = 15.6 Hz), 6.81 (dt, 1H, *J* = 7.7, 15.6 Hz), 7.21-7.34 (m, 10H), 7.59 (dt, 1H, *J* = 1.4, 7.2 Hz), 7.62 (dt, 1H, *J* = 1.4, 7.2 Hz), 8.00 (d, 1H, *J* = 7.3 Hz), 8.18 (d, 1H, *J* = 7.5 Hz); ¹³C NMR: 5.6, 29.9, 31.1, 33.6, 33.9, 36.0, 56.5, 60.2, 67.9, 70.9, 72.9, 78.4, 122.3, 123.2, 125.4, 127.5, 127.56, 127.64, 127.7, 127.9, 128.0, 128.29, 128.33, 136.7, 137.9, 138.4, 146.7, 152.7, 166.2. Anal. Calcd. for C₃₅H₄₁NO₆S₂: C, 66.12; H, 6.50; N, 2.20. Found: C, 66.09; H, 6.44; N, 2.47.

(3S-Hydroxymethyl-1-(benzyloxy))-5-hexene (7). To a solution of ketoimide **11** (0.693 g, 1.76 mmol) in 30 mL of THF at 0 °C was added MeOH (0.289 mL, 7.07 mmol) and LiBH₄ (2.0 M in THF, 4.42 mL, 8.83 mmol) sequentially. The mixture was stirred for 4 h at rt, and then quenched by the addition of 0.5 M aq. Rochelle's salt (75 mL). The resulting mixture was diluted with Et₂O (50 mL) and stirred vigorously for 2 h. The mixture was then extracted with Et₂O and brine, and the combined organic extracts were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. The crude product was filtered through a plug of silica to afford 0.300 g (1.36 mmol, 76 %) of the alcohol product, **7**. [_D²³] -75.5 (*c* 0.6, CHCl₃); IR (thin film) 3407, 3056, 3030, 2921, 2864, 1640, 1454 cm⁻¹; ¹H NMR: 1.55 (m, 3H), 1.95 (m, 2H), 3.00 (t, 1H, *J* = 6.0 Hz), 3.40 (m, 4H), 4.40 (s, 2H), 4.94 (m, 2H), 5.67 (m, 1H), 7.20 (m, 5H); ¹³C NMR: 31.3, 35.9, 38.6, 65.2, 68.5, 72.9, 116.1, 127.5, 127.6, 128.2, 136.6, 137.8. Anal. Calcd for C₁₄H₂₀O₂: C, 76.33; H, 9.15. Found: C, 76.16; H, 9.40.

4-Benzzyloxy-1-butanoic Acid (8). In a three-necked round bottomed flask, a mixture of benzyl bromide (83.0 mL, 0.700 mol) and γ -butyrolactone (15.0 mL, 0.195 mol) in dry toluene (300 mL) was mechanically stirred at rt and crushed potassium hydroxide (50.4 g, 0.884 mol) was added. The mixture was heated to reflux for 3 d, then was cooled to rt and allowed to stand for 1 d. The mixture was treated with Et₂O (300 mL) and water (200 mL) and was shaken and separated. The aqueous phase was extracted with Et₂O, and the combined organic extracts were used as described below. The aqueous phase was cooled to 0 °C and

slowly acidified with 6 N sulfuric acid. The acidic wash was extracted with Et₂O, and the combined organic extracts were dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a colorless oil.

To the initial organic phase from above was added water (80 mL) and KOH (28.8 g, 0.500 mol), and the mixture was heated to reflux for 1 d. The resulting solution was diluted with water and extracted with Et₂O. The aqueous phase was cooled and acidified as above and extracted with Et₂O. The organic extracts were combined, dried over Na₂SO₄, filtered, and concentrated *in vacuo* to give a yellow oil. This oil was combined with that obtained above, and the material was purified by Kugelrohr distillation (125 °C/1.0 mm Hg) to give 36.7 g (0.189 mol, 97 %) of carboxylic acid **8**. IR (thin film) 2867 (broad), 1708, 1454, 737 cm⁻¹; ¹H NMR: 1.96 (dd, 2H, *J* = 6.2, 7.3 Hz), 2.51 (t, 2H, *J* = 7.3 Hz), 3.53 (t, 2H, *J* = 6.2 Hz), 4.51 (s, 2H), 7.31 (m, 5H); ¹³C NMR: 24.8, 31.0, 69.0, 72.9, 127.5, 127.6, 128.4, 138.3, 179.8.

[4S]-4-Benzyl-3-(4-benzyloxy-1-butanoyl)-2-oxazolidinone (10). In a three-necked flask equipped with a mechanical stirrer, carboxylic acid **8** (10.2 g, 52.6 mmol) was dissolved in dry Et₂O (500 mL). Triethylamine (7.33 mL, 52.6 mmol) was added, and the mixture was stirred at rt for 15 min. This solution was cooled to 0 °C, and ethyl chloroformate (5.03 mL, 52.6 mmol) was added. A thick white precipitate immediately formed. This solution was warmed to rt and stirred for an additional 1 h. In a separate flask, (4S)-benzyl oxazolidinone (9.32 g, 52.6 mmol) was dissolved in 75 mL of THF and cooled to 78 °C, and *n*-butyllithium (1.5 M in hexanes, 33.9 mL, 52.6 mmol) was added dropwise to this solution. The oxazolidinone solution was transferred *via* cannula into the solution containing the anhydride, the mixture was stirred for 30 min at -78 °C, and then was warmed to 0 °C for an additional 30 min. The solution was quenched with satd. aq. NH₄Cl and extracted with Et₂O. The combined organic extracts were washed with brine, dried over Na₂SO₄, filtered, and concentrated *in vacuo*. Purification by column chromatography (9:1 hexanes/EtOAc) afforded 15.2 g (46.3 mmol, 88 %) of the product as a pale yellow oil: [α]_D²³ + 44.8 (*c* 1.0, CHCl₃); IR (thin film) 3029, 2929, 2860, 1780, 1699 cm⁻¹; ¹H NMR: 1.93 (dt, 2H, *J* = 6.2, 7.2 Hz), 2.61 (dd, 1H, *J* = 9.6, 13.4 Hz), 2.98 (t, 2H, *J* = 7.2 Hz), 3.16 (dd, 1H, *J* = 3.3, 13.4 Hz), 3.49 (t, 2H, *J* = 6.2 Hz), 4.01 (m, 2H), 4.42 (s, 2H), 4.51 (m, 1H), 7.08-7.25 (m, 10H); ¹³C NMR: 24.4, 32.4, 37.7,

55.0, 68.0, 69.1, 72.8, 127.2, 127.5, 127.6, 128.2, 128.8, 129.3, 135.3, 138.3, 153.4, 172.9; Anal. Calcd. for C₂₁H₂₃NO₄: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.54; H, 6.48; N, 4.15.

[4S, 3(2S)]-4-Benzyl-3-(4-benzyloxy-2-allyl-1-butanoyl)-2-oxazolidinone (11). In a three-necked flask equipped with an internal thermometer, NaHMDS (1 M in THF, 14.6 mL, 14.6 mmol) was cooled to -78 °C, and a solution of ketoimide **10** (4.00 g, 12.2 mmol) in 10 mL of THF was added dropwise *via* syringe at a rate such that the internal temperature was maintained below -70 °C. This mixture was stirred for 30 min, after which allyl bromide (1.58 mL, 18.3 mmol) in 15 mL of THF was added dropwise. The reaction mixture was warmed to -50 °C and stirred for an additional 18 h at this temperature. The solution was then quenched with satd. aq. NH₄Cl and was extracted with Et₂O. The combined organic extracts were washed with brine, dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography (9:1 hexanes/EtOAc) to afford 3.50 g (8.90 mmol, 73 %) of the alkylated product as a clear oil: [α]_D²³ +54.8 (*c* 1.0, CHCl₃); IR (thin film) 2920, 2860, 1778, 1697, 1387 cm⁻¹; ¹H NMR:

1.73 (m, 1H), 2.10 (m, 1H), 2.19 (m, 1H), 2.40 (m, 1H), 2.49 (dd, 1H, *J* = 10.0, 13.4 Hz), 3.15 (dd, 1H, *J* = 3.3, 13.4 Hz), 3.49 (m, 3H), 3.81 (dd, 1H, *J* = 2.8, 9.0 Hz), 4.04 (m, 1H), 4.29 (m, 3H), 4.99 (m, 2H), 5.74 (m, 1H), 7.06-7.26 (m, 10H); ¹³C NMR: 31.9, 37.5, 38.2, 39.9, 55.3, 65.6, 68.9, 72.8, 171.4, 127.1, 127.4, 127.6, 128.2, 128.8, 129.3, 135.1, 135.6, 138.3, 153.4, 176.1; Anal. Calcd for C₂₄H₂₇NO₄: C, 73.26; H, 6.92; N, 3.56. Found: C, 72.95; H, 6.85; N, 3.42.

[(3S-(*p*-Toluenesulfonate)-methyl)-1-benzyloxy]-5-hexene (12). A solution of alcohol **7** (0.230 g, 1.04 mmol) in CH₂Cl₂ (2 mL) was cooled to 0 °C, and tosyl chloride (0.219 g, 1.14 mmol), triethylamine (0.174 mL, 1.25 mmol), and DMAP (12.2 mg, 0.104 mmol) were added sequentially. The solution was warmed to rt, stirred for 18 h, and quenched by the addition of satd. aq. NH₄Cl. The mixture was extracted with CH₂Cl₂, and the combined organic extracts were dried over Na₂SO₄, filtered, and concentrated *in vacuo*. Purification by column chromatography (9:1 hexanes/EtOAc) afforded 0.377 g (1.01 mmol, 97 %) of **12** as a clear oil: [α]_D²² + 8.9 (*c* 0.3, CHCl₃); IR (thin film) 3065, 2923, 1640, 1598, 1495, 1454 cm⁻¹; ¹H NMR: 1.53 (m, 2H), 1.85 (m, 1H), 2.00 (m, 2H), 2.35 (s, 3H), 3.35 (t, 2H, *J* = 6.2 Hz), 3.88 (m, 2H), 4.35 (s, 2H), 4.88 (m, 2H), 5.55 (m, 1H), 7.21 (m, 7H), 7.68 (d, 2H, *J* = 8.1 Hz); ¹³C NMR: 21.6, 30.2,

34.7, 34.9, 67.5, 72.0, 72.8, 117.4, 127.5, 127.9, 128.0, 128.3, 129.7, 132.9, 135.1, 138.2, 144.9. Anal. Calcd for C₂₁H₂₆O₄S: C, 67.35; H, 7.00. Found: C, 67.12; H, 7.19.

(3S-Iodomethyl-1-benzyloxy)-5-hexene (13).ⁱ Alcohol **7** (0.350 g, 1.59 mmol) was dissolved in a 3:1 mixture of Et₂O: CH₃CN (7.5 mL total). To this solution was added triphenylphosphine (0.417 g, 1.59 mmol) and imidazole (0.119 g, 1.75 mmol); the mixture was stirred for 10 min at rt, and then cooled to 0 °C. A solution of iodine (0.444 g, 1.59 mmol) in 1:1 CH₃CN: THF (3 mL total) was added dropwise *via* syringe, and the resulting pale yellow solution was stirred for an additional 15 min at 0 °C. The reaction mixture was quenched with satd. aq. Na₂S₂O₃ and diluted with Et₂O. The phases were shaken and separated, and the organic extracts were washed with satd. aq. CuSO₄, dried briefly over MgSO₄, filtered, and concentrated *in vacuo*. The crude product was purified by column chromatography (pet. ether 19:1 pet. ether/EtOAc) to give 0.368 g (1.11 mmol, 70 %) of iodide **13** as a clear liquid: [α]_D²³ +7.7 (*c* 0.54, CHCl₃); IR (thin film): 3072, 2919, 2857, 1640, 1453 cm⁻¹; ¹H NMR: 1.39 - 1.67 (m, 3H), 2.00 (m, 2H), 3.21 (m, 2H), 3.43 (t, 2H, *J* = 6.1 Hz), 4.43 (s, 2H), 5.03 (m, 2H), 5.61 (m, 1H), 7.18 - 7.31 (m, 5H); ¹³C NMR (acetone-d₆): 16.6, 34.7, 36.3, 39.3, 68.1, 73.3, 117.4, 128.1, 128.3, 129.0, 136.6, 139.8; Anal. Calcd for C₁₄H₁₉IO: C, 50.92; H, 5.80. Found: C, 50.91; H, 5.90.

2S-[2-(Benzyloxy)ethyl]-4-pentenal (16). Alcohol **7** (2.47 g, 11.2 mmol) was dissolved in CH₂Cl₂ (56 mL) and cooled to 0 °C. Dess-Martin periodinane (6.65 g, 15.7 mmol) was then added in one portion. The solution was warmed to rt, stirred for 30 min, and then quenched with 25 g of sodium thiosulfate in 100 mL of satd. aq. NaHCO₃. The resulting solution was stirred for 5 min, then extracted with Et₂O. The organic layers were combined and dried over MgSO₄, and the solution was filtered and concentrated *in vacuo*. The crude material was then purified by column chromatography (49:1 to 19:1 hexanes/EtOAc) to afford 2.44 g (100 %) of aldehyde **16** as a colorless oil. [α]_D²³ +3.9 (*c* 0.6, CDCl₃); IR (thin film) 2859, 1727, 1364, 1101 cm⁻¹; ¹H NMR: 1.80 (m, 1H), 1.99 (m, 1H), 2.24 (m, 1H), 2.42 (m, 1H), 2.54 (m, 1H), 3.51 (m, 2H), 4.47 (s, 2H), 5.07 (m, 2H), 5.73 (m, 1H), 7.31 (m, 5H), 9.65 (d, 1H, *J* = 2.1 Hz); ¹³C NMR: 28.8, 33.0, 48.6, 67.5, 73.0, 117.4, 127.66, 127.68, 128.4, 134.8, 138.2, 204.2.

(2R, 3R, 5S)-2-Methyl-5-[2-(benzyloxy)ethyl]-7-octene-1,3-diol (20). A solution of aldol adduct **19** (5.30 g, 11.3 mmol) in THF (106 mL) was cooled to 0 °C. MeOH (1.12 mL, 25.0 mmol) and LiBH₄ (2 M in THF, 17.0 mL, 34.0 mmol) were added to the solution sequentially, and the mixture was stirred overnight. The reaction was then quenched by the addition of 0.5 M aq. Rochelle's salt solution (200 mL), diluted with Et₂O, and stirred vigorously for 2 h. The aqueous phase was then extracted with Et₂O, and the combined organic extracts were dried over K₂CO₃, filtered, and concentrated *in vacuo*. Purification by column chromatography (6:1 to 5:2 hexanes/EtOAc) provided 3.26 g (99 %) of diol **20**. [α]_D²³ + 8.3 (c 0.66, CHCl₃); IR (thin film) 3391, 2928, 1453, 1070, 1028 cm⁻¹; ¹H NMR: 0.82 (d, 3H, *J* = 7.0 Hz), 1.37 (ddd, 1H, *J* = 3.3, 6.9, 14.1 Hz), 1.48 (dd, 1H, *J* = 5.4, 9.3 Hz), 1.54 (m, 1H), 1.73 (m, 3H), 2.08 (m, 2H), 2.34 (br s, 1H), 2.65 (br s, 1H), 3.54 (m, 3H), 3.67 (d, 1H, *J* = 4.9 Hz), 3.91 (d, 1H, *J* = 9.1 Hz), 4.49 (s, 2H), 5.01 (m, 2H), 5.73 (m, 1H), 7.33 (m, 5H); ¹³C NMR: 10.2, 31.6, 33.6, 37.6, 38.1, 39.4, 66.5, 68.2, 72.1, 72.8, 116.4, 127.5, 127.6, 128.2, 136.4, 138.1. Anal. Calcd for C₁₈H₂₈O₃: C, 73.93; H, 9.65. Found: C, 73.90; H, 9.54.

(2R, 3R, 5S)-1-[[*t*-Butyldiphenylsilyl]-oxy]-2-methyl-5-[2-(benzyloxy)ethyl]-7-octene-3-ol (21). Diol **20** (293 mg, 1.00 mmol) was dissolved in CH₂Cl₂ (2.0 mL) and cooled to 0 °C. To this solution was added Et₃N (0.167 mL, 1.20 mmol), DMAP (12.2 mg, 0.100 mmol), and *t*-butyldiphenylsilyl chloride (0.287 mL, 1.10 mmol) sequentially. This mixture was stirred for 12 h, and then quenched with satd. aq. NH₄Cl. The aqueous phase was extracted with Et₂O, and the combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo*. The resulting crude material was purified by column chromatography to afford silyl ether **21** (514 mg, 97 %) as a colorless oil. [α]_D²³ + 6.04 (c 2.4, CHCl₃); IR (thin film) 3484, 2929, 2857, 1112 cm⁻¹; ¹H NMR: 0.78 (d, 3H, *J* = 6.2 Hz), 0.98 (s, 9H), 1.24 (ddd, 1H, *J* = 2.9, 6.5, 9.6 Hz), 1.42 (ddd, 1H, *J* = 4.1, 7.2, 10.7 Hz), 1.50 - 1.76 (m, 4H), 2.03 (m, 2H), 2.63 (d, 1H, *J* = 4.2 Hz), 3.45 (t, 2H, *J* = 6.5 Hz), 3.57 (dd, a of ab quartet, 1H, *J* = 6.5, 10.1 Hz), 3.63 (dd, b of ab quartet, 1H, *J* = 4.5, 10.1 Hz), 3.87 (br s, 1H), 4.51 (s, 2H), 5.05 (m, 2H), 5.79 (m, 1H), 7.29 - 7.46 (m, 11H), 7.69 (m, 4H); ¹³C NMR: 10.4, 19.2, 26.9, 31.5, 34.0, 37.9, 38.2, 39.7, 68.3, 68.6, 71.5, 72.9, 116.5, 127.5, 127.6,

127.8, 128.3, 128.9, 129.8, 135.6,

Anal. Calcd for C₃₄H₄₆O₃Si: C, 75.93; H, 8.54. Found:

C, 75.79; H, 8.34.

Ethyl (2*E*, 5*S*, 7*R*, 8*R*)-9-Hydroxy-8-methyl-7-benzyloxy-5-[2-(benzyloxy)ethyl]-2-nonenoate (25).

Silyl ether **24** (63.0 mg, 0.091 mmol) was dissolved in a solution of 19:1 CH₃CN:HF (40 % aq.) (0.91 mL total) and the resulting mixture was stirred at rt for 3 h. The reaction was then quenched by the addition of 20 % KOH and extracted with Et₂O. The combined organic extracts were dried over K₂CO₃, filtered, and concentrated. The crude material was purified by column chromatography to afford 41 mg (100 %) of alcohol **25**. IR (thin film) 3437, 2935, 1718, 1036 cm⁻¹; ¹H NMR: 0.84 (d, 3H, *J* = 7.1 Hz), 1.27 (t, 3H, *J* = 7.1 Hz), 1.36 (ddd, 1H, *J* = 4.2, 8.1, 14.2 Hz), 1.64 (m, 3H), 1.87 (m, 1H), 2.13 (m, 3H), 2.51 (br s, 1H), 3.49 (t, 2H, *J* = 6.5 Hz), 3.59 (dt, 1H, *J* = 3.8, 6.2 Hz), 3.67 (dd, 1H, *J* = 8.3, 10.5 Hz), 4.17 (q, 2H, *J* = 7.1 Hz), 4.45 (d, 1H, *J* = 11.4 Hz), 4.46 (s, 2H), 4.60 (d, 1H, *J* = 11.4 Hz), 5.77 (d, 1H, *J* = 15.6 Hz), 6.85 (dt, 1H, *J* = 7.6, 15.6 Hz), 7.24-7.34 (m, 10H); ¹³C NMR: 12.0, 14.1, 31.1, 33.9, 34.0, 36.3, 36.6, 60.0, 65.4, 67.9, 71.4, 72.8, 79.2, 123.0, 127.4, 127.5, 127.6, 127.9, 128.2, 128.3, 138.1, 138.3, 146.9, 166.2.

Ethyl (2*E*, 5*S*, 7*R*, 8*S*)-8-methyl-7-benzyloxy-5-[2-(benzyloxy)ethyl]-9-(methanesulfonyl)-2-nonenoate (26). A solution of alcohol **25** (49 mg, 0.11 mmol) in CH₂Cl₂ (0.43 mL) was cooled to 0 °C, and Et₃N (30

L, 0.22 mmol), DMAP (1.3 mg, 0.011 mmol), and methanesulfonyl chloride (9.2 L, 0.12 mmol) were added sequentially. The resulting cloudy mixture was stirred for 15 min, and was then quenched by the addition of satd. aq. NaHCO₃. The aqueous phase was extracted with Et₂O, and the combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo* to afford 55 mg (96 %) of the desired

26. [²³D + 3.13 (*c* 0.67, CH₂Cl₂); IR (thin film) 2935, 2359, 1715, 1357, 1175 cm⁻¹; ¹H NMR: 0.96 (d, 3H, *J* = 7.0 Hz), 1.28 (t, 3H, *J* = 7.1 Hz), 1.38 (m, 1H), 1.58 (m, 4H), 1.83 (m, 1H, *J* = 6.4 Hz), 2.15 (dd, 2H, *J* = 6.3, 7.4 Hz), 2.19 (dq, 1H, *J* = 3.0, 6.8 Hz), 2.91 (s, 3H), 3.45-3.49 (m, 2H), 3.55 (m, 1H), 4.05 (dd, 1H, *J* = 7.2, 9.5 Hz), 4.17 (q, 2H, *J* = 7.1 Hz), 4.26 (dd, 1H, *J* = 6.5, 9.5 Hz), 4.47 (s, 1H), 4.49 (s, 2H), 5.79 (d, 1H, *J* = 15.6 Hz), 6.84 (dt, 1H, *J* = 7.5, 15.6 Hz), 7.23-7.35 (m, 10H); ¹³C NMR: 11.3, 14.2, 31.2, 33.7, 34.7, 35.7, 36.4, 37.1, 60.1, 67.8, 71.6, 71.7, 72.9, 76.5, 123.2, 127.47, 127.53, 127.6, 127.7, 128.29, 128.32, 138.3, 146.7, 166.2. Anal. Calcd for C₂₉H₄₀O₇S: C, 65.39; H, 7.57. Found: C, 65.35; H, 7.37.

Oxazoline 31. To a stirred suspension of ethylacetimidate hydrochloride (61.8 g, 0.500 mol) and DL-serine methyl ester hydrochloride (77.8 g, 0.500 mol) in CH₂Cl₂ (1 L) was added dropwise over 45 min a solution of triethylamine (150 mL, 1.08 mol) in CH₂Cl₂ (350 mL). After 18 h the solids were removed by filtration and washed with ether. The filtrate was concentrated and the resulting solid residue was washed several times with ether. The combined organic extracts were concentrated to give a yellow oil. Purification by Kugelrohr distillation gave **31** (57.2 g, 80 %) as a colorless oil. IR (thin film) 2955, 1742 (s), 1667 (s), 1439 cm⁻¹; ¹H NMR: 2.03 (d, 3 H, *J* = 1.3), 3.79 (s, 3 H), 4.41 (t, 1 H, *J* = 9.7), 4.49 (t, 1 H, *J* = 8.3), 4.74 (dt, 1 H, *J* = 1.3, 5.3); ¹³C NMR: 13.7, 52.5, 68.1, 69.2, 167.6, 175.1; bp 85-100 °C/15 torr.

Oxazole 32. Hexamethylenetetramine (2.45 g, 17.5 mmol) and DBU (2.61 mL, 17.4 mmol) were added to a stirred suspension of copper (II) bromide (3.90 g, 17.4 mmol) at 0 °C. After 20 min, oxazoline **31** (1.00 g, 6.99 mmol) was added and the reaction mixture was stirred at rt for 2 h. The solvent was removed *in vacuo* and the residue was partitioned between ethyl acetate and 1:1/satd. aq. NH₄Cl: satd. aq. NH₄OH. The aqueous layer was extracted with ethyl acetate and the combined organic layers were washed with 1:1/NH₄Cl:NH₄OH, 10% citric acid, satd. aq. NaHCO₃, and brine, then dried, filtered, and concentrated to give **32** (0.837 g, 85 %) as a white solid. IR (thin film): 3007, 1735 (s), 1593, 1439, 1326 cm⁻¹; ¹H NMR: 2.52 (s, 3 H), 3.91 (s, 3 H), 8.14 (s, 1 H); ¹³C NMR: 13.8, 52.1, 133.2, 143.8, 161.7, 162.4.

(2-Methyl-oxazol-4-yl)-methanol (33). Lithium aluminum hydride (30.0 mL, 1.0 M in THF, 30.0 mmol) was added to a solution of oxazole **32** (2.86 g, 20.2 mmol) in ether (200 mL) at -78 °C. After 3 h, a satd. aq. solution of sodium potassium tartrate (100 mL) was added and the mixture was extracted with ether. The combined organic layers were dried, filtered, and concentrated. Purification by flash chromatography (ether) provided **33** (1.49 g, 65%) as a white solid. IR (thin film) 3300 (b), 3002, 1582 cm⁻¹; ¹H NMR: 2.45 (s, 3 H), 4.49 (s, 1 H), 4.54 (s, 2 H), 7.48 (s, 1 H); ¹³C NMR: 13.7, 55.8, 134.8, 140.2, 162.2.

Alkene 37. A solution of 2-butene-1,4-diol (5.00 g, 56.7 mmol) in dry CH₂Cl₂ (70 mL) was cooled to 0 °C with stirring under nitrogen and a solution of *tert*-butyltrimethylsilyl chloride (17.1 g, 113 mmol) and 4-

dimethylaminopyridine (0.548 g, 4.48 mmol) in dry CH₂Cl₂ (45 mL) at 0 °C was added via cannula. The reaction mixture was allowed to warm to rt and was stirred for 18 h. Water (125 mL) was added and the mixture was extracted with CH₂Cl₂, dried, filtered, and concentrated. Purification by flash chromatography gave **37** (17.9 g, 100 %) as a colorless oil. IR (thin film): 2955, 2857, 1472, 1405, 1389 cm⁻¹; ¹H NMR: 0.07 (s, 12 H), 0.90 (s, 18 H), 5.23 (d, 4 H, *J* = 3.5), 5.55 (t, 2 H, *J* = 3.5); ¹³C NMR: 5.2, 18.3, 25.9, 59.6, 130.2; bp 96-106 °C/0.075 torr.

Benzyl ether 41. A suspension of sodium hydride (2.08 g, 60% oil dispersion, 51.9 mmol) in dry THF (175 mL) was stirred at rt and a solution of alcohol **40** (10.0 g, 39.2 mmol) in dry THF (30 mL) was added dropwise. The reaction mixture was stirred for 45 min followed by the addition of tetrabutylammonium iodide (0.147 g, 0.398 mmol), 18-crown-6 (0.229 g, 0.867 mmol), and benzyl bromide (5.80 mL, 48.8 mmol). The reaction mixture was stirred at rt for 2 d. Water (150 mL) was added and the mixture was extracted with ether. The combined organic layers were dried, filtered, and concentrated. Purification by flash chromatography afforded **41** (13.1 g, 96 %). ²⁵D -28.8 (*c* 1.02) IR (thin film) 2929, 2857, 1642, 1462, 1386, 1254 cm⁻¹; ¹H NMR: 0.15 (s, 6 H), 0.98 (s, 9 H), 1.66 (d, 3 H, *J* = 0.7), 2.32 (m, 1 H), 2.49 (m, 1 H), 3.78 (t, 1 H, *J* = 6.9), 4.31 (d, 1 H, *J* = 11.9), 4.32 (m, 3 H), 4.54 (d, 1 H, *J* = 11.9), 5.09 (m, 2 H), 5.59 (t, 1 H, *J* = 5.9), 5.80 (m, 1 H), 7.36 (m, 5 H); ¹³C NMR: -5.13, -5.12, 11.0, 18.3, 25.9, 38.3, 59.8, 69.7, 84.0, 116.3, 127.3, 127.7, 128.2, 129.2, 134.8, 135.0, 138.6; Anal. calcd. for C₂₁H₃₄O₂Si: C, 72.78; H, 9.89. Found: C, 72.64; H, 9.87.

Methyl (4*E*, 3*S*)-6-[(*t*-butyldimethylsilyl)oxy]-4-methyl-3-[(triisopropylsilyl)oxy]-4-hexenoate (45). Alcohol **43** (446 mg, 1.62 mmol) was dissolved in CH₂Cl₂ (3.2 mL) and cooled to 0 °C. To this solution was added 2,6-lutidine (0.283 mL, 2.43 mmol) and triisopropylsilyl trifluoromethane sulfonate (0.566 mL, 2.11 mmol) sequentially. After 5 min, the reaction was quenched by the addition of satd. aq. NH₄Cl, and the resulting mixture was extracted with Et₂O. The combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude material was purified by column chromatography (hexanes to 19:1 hexanes/EtOAc) to afford **45** (689 mg, 99 %). IR (thin film) 2945, 2866, 1745, 1464, 1065 cm⁻¹; ¹H NMR: 0.03 (s, 6H), 0.86 (s, 9H), 1.03 (m, 21H), 1.60 (s, 3H), 2.45 (dd, 1H, *J* = 5.0, 15.0 Hz), 2.58

(dd, 1H, $J = 5.0, 10.0$ Hz), 3.61 (s, 3H), 4.16 (m, 2H), 4.61 (t, 1H, $J = 6.5$ Hz), 5.50 (t, 1H, $J = 6.0$ Hz);

^{13}C NMR: -5.33, -5.30, 10.9, 12.3, 17.6, 17.9, 18.2, 25.8, 42.5, 51.4, 59.7, 75.1, 126.7, Anal. Calcd for $\text{C}_{23}\text{H}_{48}\text{O}_4\text{Si}_2$: C, 62.11; H, 10.88. Found: C, 62.32; H, 10.62.

Methyl ether 51. To a solution of diol **50** (0.9814 g, 2.27 mmol) in THF (20 mL) at rt was added NaH (0.101 g, 60% oil dispersion, 2.53 mmol) followed by cooling to -78°C . Methyl iodide (0.155 mL, 2.49 mmol) was added and the mixture was allowed to warm slowly to rt and was stirred for 15 h. Water (15 mL) was added and the mixture was extracted with ether. The combined extracts were dried, filtered, and concentrated. The crude residue was purified by flash chromatography to produce **51** (0.838 g, 83 %).

$^{25}\text{D} +1.20$ (c 1.08); IR (thin film) 3525 (b), 3306, 2929, 2857, 2245 (w), 1463, 1388, 1255 cm^{-1} ; ^1H NMR: 0.090 (s, 3 H), 0.092 (s, 3 H), 0.92 (s, 9 H), 1.03 (d, 3 H, $J = 7.0$), 1.53 (ddd, 1 H, $J = 2.7, 4.2, 14.3$), 1.63 (s, 3 H), 1.71 (m, 1 H), 1.92 (dt, 1 H, $J = 7.2, 9.4$), 2.48 (d, 1 H, $J = 2.0$), 3.41 (s, 3 H), 3.96 (dd, 1 H, $J = 4.2, 9.2$), 4.00 (dd, 1 H, $J = 2.1, 6.2$), 4.06 (dt, 1 H, $J = 9.5, 2.8$), 4.27 (d, 1 H, $J = 11.7$), 4.28 (m, 2 H), 4.47 (d, 1 H, $J = 11.5$), 5.59 (t, 1 H, $J = 5.3$), 7.30 (m, 5 H); ^{13}C NMR: -5.1, 8.8, 11.1, 18.3, 25.9, 38.5, 43.4, 56.7, 59.8, 70.0, 71.8, 74.2, 74.6, 81.8, 84.7, 127.6, 127.9, 128.4, 129.3, 134.7, 138.0; Anal. calcd. for $\text{C}_{26}\text{H}_{42}\text{O}_4\text{Si}$: C, 69.91; H, 9.48. Found: C, 69.71; H, 9.64.

(1'E,3'E)-2-Methyl-4-(2'-methyl-5'-oxo-1',3'-pentadienyl)-oxazole (53).ⁱⁱ To a solution of alcohol **56** (42.9 mg, 0.239 mmol) in CH_2Cl_2 (1.19 mL) was added Dess-Martin periodinane (122 mg, 0.287 mmol) at 0°C . The resulting cloudy solution was stirred for 15 min, and was then quenched by the addition of 1 N NaOH. The mixture was extracted with Et_2O , and the combined organic extracts were dried over MgSO_4 , filtered, and concentrated *in vacuo*. Purification by column chromatography gave aldehyde **53** as a white solid (32.0 mg, 75 %). mp: $96.8\text{--}96.9^\circ\text{C}$; IR (thin film) 2359, 1665, 1604, 1137, 1109 cm^{-1} ; ^1H NMR: 2.21 (d, 3H, $J = 0.9$ Hz), 2.50 (s, 3H), 6.28 (dd, 1H, $J = 7.7, 15.5$ Hz), 6.66 (s, 1H), 7.24 (d, 1H, $J = 15.5$ Hz), 7.70 (s, 1H), 9.64 (d, 1H, $J = 7.8$ Hz) ^{13}C NMR: 13.8, 14.1, 128.1, 128.3, 134.8, 138.0, 138.4, 156.7, 161.5, 193.7. Anal. Calcd for $\text{C}_{10}\text{H}_{11}\text{NO}_2$: C, 67.78; H, 6.26; N, 7.90. Found: C, 67.89; H, 6.49; N, 7.92.

(1'E,3'E)-4-(5'-Hydroxy-2'-methyl-1',3'-pentadienyl)-2-methyloxazole (56). Ester **55** (478 mg, 2.16 mmol) was dissolved in toluene (10.8 mL) and cooled to 0 °C. To this solution was added DIBAL-H (1.0 M in hexanes, 5.25 mL, 5.25 mmol) dropwise, and the resulting mixture was stirred for 5 min, and then quenched by the addition of 0.5 M aq. Rochelle's salt solution. The material was diluted with Et₂O, and the biphasic mixture was stirred vigorously overnight. The reaction was then extracted with Et₂O (2 x) and EtOAc (1 x), and the combined organic extracts were dried over MgSO₄, filtered, and concentrated to give a yellow oil. This crude material was purified by column chromatography (19:1 to 2:1 hexanes/EtOAc) to afford 375 mg (97 %) of alcohol **56** as a colorless oil. This material, which was found to be extremely unstable and turned black upon standing, was used immediately in the oxidation to aldehyde **53**. IR (thin film) 3360, 2921, 2863, 1581, 1099 cm⁻¹; ¹H NMR: 1.98 (s, 3H), 2.39 (s, 3H), 3.48 (br s, 1H), 4.19 (d, 2H, *J* = 5.5 Hz), 5.88 (dt, 1H, *J* = 5.5, 15.5 Hz), 6.16 (s, 1H), 6.34 (d, 1H, *J* = 15.5 Hz), 7.46 (s, 1H) ¹³C NMR: 13.6, 14.4, 63.0, 120.0, 128.9, 135.0, 135.7, 136.2, 138.2, 160.9.

Weinreb amide 57. To a solution of alcohol **48** (61.2 mg, 0.131 mmol) and trimethylsilyl chloride (50.0 mL, 0.394 mmol) in CH₂Cl₂ (1.5 mL) was added triethylamine (100 mL, 0.717 mmol). After heating to reflux for 15 h the mixture was cooled and then treated with saturated aqueous sodium bicarbonate (2 mL) and extracted with CH₂Cl₂. The combined extracts were dried, filtered, and concentrated. Purification by flash chromatography provided **57** (70.8 mg, 100 %) as a colorless oil. ²⁵D -1.7 (*c* 1.35); IR (thin film) 2956, 2932, 2857, 1661 (s), 1462 cm⁻¹; ¹H NMR: 0.088 (s, 15 H), 0.91 (s, 9 H), 1.12 (d, 3 H, *J* = 6.8), 1.57 (s, 3 H), 1.80 (m, 2 H), 3.00 (s, 1 H), 3.11 (s, 3 H), 3.55 (s, 3 H), 3.87 (m, 2 H), 4.26 (m, 3 H), 4.43 (d, 1 H, *J* = 11.7), 5.54 (t, 1 H, *J* = 5.7), 7.28 (m, 5 H); ¹³C NMR: -5.1, 0.6, 10.8, 14.3, 18.3, 25.9, 32.0, 40.0, 41.9, 59.9, 61.2, 69.7, 71.5, 81.4, 127.3, 127.9, 128.2, 129.8, 134.9, 138.8, 164.0; Anal. calcd. for C₂₈H₅₁NO₅Si₂: C, 62.52; H, 9.56; N, 2.60. Found: C, 62.24; H, 9.68; N, 2.60.

Methyl ether 62. NaH (24.0 mg, 60% oil dispersion, 0.600 mmol) was added to a solution of diol **61** (0.201 g, 0.337 mmol) in THF (5 mL) followed by cooling of the solution to -78 °C. After 15 min, methyl iodide (24.0 mL, 0.386 mmol) was added and the mixture was warmed to room temperature over 2 h and then stirred for an additional 15 h. Water (5 mL) was added and the aqueous layer was extracted with

ether. The combined organic layers were dried, filtered, and concentrated. The crude residue was purified by flash chromatography to produce **62** (0.129 g, 63 %) as a yellow oil. ^{25}D -22.0 (*c* 0.83); IR (thin film) 3496 (b), 2928, 2857, 1581 cm^{-1} ; ^1H NMR: 0.85 (s, 6 H), 0.91 (s, 9 H), 0.95 (d, 3 H, *J* = 6.8), 1.44 (d, 1 H, *J* = 14.4), 1.62 (s, 3 H), 1.71 (s, 3 H), 1.75 (m, 1 H), 1.94 (dt, 1 H, *J* = 14.3, 9.6), 2.17 (s, 3 H), 2.46 (s, 3 H), 3.21 (s, 3 H), 3.39 (s, 1 H), 3.57 (d, 1 H, *J* = 7.1), 3.73 (d, 1 H, *J* = 15.0), 3.90 (dd, 1 H, *J* = 2.0, 5.1), 4.26 (m, 3 H), 4.47 (d, 1 H, *J* = 11.6), 5.56 (t, 1 H, *J* = 5.1), 6.19 (d, 1 H, *J* = 11.0), 6.27 (s, 1 H), 6.41 (d, 1 H, *J* = 15.1), 6.60 (dd, 1 H, *J* = 11.0, 15.1), 7.28 (m, 5 H), 7.54 (s, 1 H); ^{13}C NMR: -5.1, 8.5, 11.1, 12.7, 13.8, 14.3, 18.3, 25.9, 38.9, 41.2, 56.5, 59.8, 69.8, 71.7, 84.7, 89.2, 120.1, 124.4, 127.6, 127.8, 128.3, 128.4, 129.2, 134.9, 135.8, 136.4, 136.9, 138.0, 138.8, 138.8, 160.8.

Triene 63. To a solution of alcohol **62** (0.129 g, 0.211 mmol) in pyridine (2 mL) was added *p*-nitrobenzoyl chloride (77.9 mg, 0.420 mmol) and DMAP (1.0 mg, 0.008 mmol). After 7 h, water was added and the mixture was extracted with ether. The combined organic layers were washed with satd. aq. NaHCO_3 and then dried, filtered, and concentrated. Purification by flash chromatography yielded **63** (0.126 g, 82 %) as a yellow oil. ^{25}D -33.0 (*c* 0.64); IR (thin film) 2930, 2856, 1725 (s), 1607, 1581, 1529 cm^{-1} ; ^1H NMR: 0.068 (s, 6 H), 0.90 (s, 9 H), 1.12 (d, 3 H, *J* = 6.7), 1.61 (s, 3 H), 1.62 (s, 3 H), 1.79 (dt, 1 H, *J* = 14.2, 5.7), 2.02 (m, 1 H), 2.11 (s, 3 H), 2.20 (dt, 1 H, *J* = 14.2, 7.2), 2.47 (s, 3 H), 3.13 (s, 3 H), 3.42 (d, 1 H, *J* = 7.1), 3.86 (dd, 1 H, *J* = 4.6, 7.9), 4.10 (d, 1 H, *J* = 11.4), 4.21 (dq, 2 H, *J* = 5.5, 16.9), 4.38 (d, 1 H, *J* = 11.4), 5.20 (m, 1 H), 5.53 (t, 1 H, *J* = 5.5), 5.90 (d, 1 H, *J* = 5.5), 6.16 (d, 1 H, *J* = 14.9), 6.19 (s, 1 H), 6.48 (dd, 1 H, *J* = 11.0, 14.9), 7.18 (m, 5 H), 7.54 (s, 1 H), 8.07 (d, 2 H, *J* = 8.7), 8.21 (d, 2 H, *J* = 8.7); ^{13}C NMR: -5.1, 10.4, 10.9, 12.3, 13.8, 14.3, 18.3, 25.9, 35.9, 39.1, 65.4, 59.8, 69.9, 74.8, 82.2, 88.7, 120.5, 123.4, 124.0, 127.2, 127.6, 128.1, 129.2, 129.6, 130.5, 134.6, 135.4, 135.9, 136.2, 136.9, 137.3, 138.3, 138.7, 150.3, 160.9, 163.8

Alcohol 64. To a solution of silyl ether **63** (51.3 mg, 0.0702 mmol) in THF (0.7 mL) at 0 °C was added tetrabutylammonium fluoride (0.800 mL, 1.0 M in THF, 0.800 mmol). The reaction mixture was stirred at 0 °C for 3 h and then at rt for 10 min. satd. aq. NH_4Cl was added and the aqueous layer was extracted with ether. The combined organic layers were washed with satd. aq. NaHCO_3 and then dried, filtered, and

concentrated. Purification by flash chromatography yielded **64** (39.2 mg, 87 %) as a yellow oil. ^{25}D - 52.7 (c 0.99); IR (thin film) 3416 (b), 2930, 2860, 1722 (s), 1607, 1579, 1527, 1454 cm^{-1} ; ^1H NMR: 1.10 (d, 3 H, J = 6.8), 1.25 (s, 1 H), 1.64 (s, 3 H), 1.66 (s, 3 H), 1.86 (dt, 1 H, J = 14.4, 6.0), 1.98 (m, 1 H), 2.12 (s, 3 H), 2.24 (dt, 1 H, J = 14.5, 8.1), 2.47 (s, 3 H), 3.13 (s, 3 H), 3.46 (d, 1 H, J = 6.9), 3.86 (t, 1 H, J = 6.8), 4.14 (d, 1 H, J = 11.5), 4.20 (m, 2 H), 4.39 (d, 1 H, J = 11.5), 5.20 (m, 1 H), 5.55 (t, 1 H, J = 6.3), 5.95 (d, 1 H, J = 11.0), 6.21 (s, 1 H), 6.22 (d, 1 H, J = 15.0), 6.49 (dd, 1 H, J = 11.0, 15.0), 7.20 (m, 5 H), 7.54 (s, 1 H), 8.08 (d, 2 H, J = 8.8), 8.22 (d, 2 H, J = 8.8); ^{13}C NMR: 10.3, 10.8, 12.6, 13.8, 14.4, 35.8, 39.7, 56.4, 58.9, 70.1, 74.7, 82.2, 88.3, 120.5, 123.5, 124.0, 127.3, 127.6, 128.2, 128.6, 129.0, 130.6, 135.4, 135.9, 136.0, 136.8, 136.9, 137.4, 138.2, 138.7, 150.4, 160.9, 164.1.

Silyl Ether 73. Aldol adduct **72** (710 mg, 0.790 mmol) was stirred at 0 °C in CH_2Cl_2 (3.0 mL). Imidazole (177 mg, 2.60 mmol) and trimethylsilyl chloride (0.302 mL, 2.38 mmol) were then added to the solution sequentially, and the resulting mixture was stirred for 5 min. The reaction was then quenched by the addition of satd. aq. NH_4Cl and was extracted with Et_2O . The combined organic extracts were dried over MgSO_4 , filtered, and concentrated *in vacuo*. The resulting crude oil was purified by column chromatography (hexanes to 40:1 hexanes/ EtOAc) to give the fully protected product **73** (658 mg, 86 %).

[^{23}D -1.26 (c 1.6, CDCl_3); IR (thin film) 2944, 1738, 1461, 1329 cm^{-1} ; ^1H NMR: 0.05 (s, 9H), 0.88 (s, 9H), 0.93 (m, 21H), 1.06 (d, 3H, J = 7.0 Hz), 1.17 (d, 3H, J = 7.0 Hz), 1.55 (s, 3H), 1.58 (m, 1H), 1.78 (m, 1H), 2.28 (s, 3H), 2.48 (s, 7H), 3.71 (m, 1H), 4.08 (m, 1H), 4.17 (m, 2H), 4.54 (d, 1H, J = 16.5 Hz), 4.79 (d, 1H, J = 16.5 Hz), 5.40 (t, 1H, J = 5.0 Hz), 5.81 (d, 1H, J = 5.0 Hz), 6.87 (m, 4H), 7.22 (m, 9H) ^{13}C NMR: -5.3, 0.5, 11.0, 12.3, 13.4, 13.7, 18.0, 18.3, 20.8, 22.9, 25.8, 41.4, 45.0, 48.1, 56.9, 72.0, 75.4, 78.0, 126.4, 126.5, 127.0, 127.6, 128.1, 128.3, 132.1, 133.3, 138.0, 138.46, 138.53, 140.2, 142.4, 171.7. Anal. Calcd for $\text{C}_{53}\text{H}_{87}\text{NO}_7\text{SSi}_3$: C, 65.86; H, 9.07; N, 1.45. Found: C, 65.68; H, 8.94; N, 1.48.

(6E, 2R, 3S, 5S)-8-[(*t*-Butyldimethylsilyl)oxy]-2,6-dimethyl-5-[(triisopropylsilyl)oxy]-3-[(trimethylsilyl)oxy]-6-octen-1-ol (74). Ester **73** (223 mg, 0.23 mmol) was dissolved in CH_2Cl_2 (2.3 mL) and cooled to 0 °C. DIBAL-H (1 M in toluene, 0.508 mL) was added dropwise to the solution, the mixture was stirred for 5 min and then quenched with 0.5 M aq. Rochelle's salt solution (10 mL). The solution was

diluted with Et₂O and stirred vigorously for 2 h. The mixture was then extracted with Et₂O, and the combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo*. The resulting crude material was purified by column chromatography (hexanes to 19:1 hexanes/EtOAc) to give 107 mg (100 %) of alcohol **74**. [δ]_D²³ + 2.24 (c 1.5, CH₂Cl₂); IR (thin film) 3468, 2955, 2865, 1462, 1251, 1063 cm⁻¹; ¹H NMR: 0.05 (s, 3H), 0.10 (s, 6H), 0.88 (s, 9H), 1.02 (s, 21H), 1.04 (d, 3H, *J* = 7.2 Hz), 1.61 (s, 3H), 1.66 (m, 1H), 1.77 (ddd, 1H, *J* = 4.2, 9.4, 13.9 Hz), 2.00 (ddd, 1H, *J* = 5.1, 9.7, 13.9 Hz), 2.88 (dd, 1H, *J* = 2.1, 8.6 Hz), 3.50 (ddd, 1H, *J* = 4.0, 8.8, 10.9 Hz), 3.57 (ddd, 1H, *J* = 2.0, 4.0, 9.8 Hz), 4.00 (dt, 1H, *J* = 2.6, 11.1 Hz), 4.06 (dd, 1H, *J* = 5.2, 9.4 Hz), 4.18 (d, 2H, *J* = 6.0 Hz), 5.36 (t, 1H, *J* = 5.8 Hz) ¹³C NMR: -5.0, 0.5, 11.0, 12.6, 15.5, 18.30, 18.34, 18.6, 26.36, 41.7, 59.9, 64.4, 75.4, 75.8, 127.2, 137.8. Anal. Calcd for C₂₈H₆₂O₄Si₃: C, 61.48; H, 11.42. Found: C, 61.52; H, 11.27.

(6E, 2R, 3S, 5S)-8-[(*t*-Butyldimethylsilyl)oxy]-2,6-dimethyl-5-[(triisopropylsilyl)oxy]-3-[(trimethylsilyl)oxy]-6-octenal (75). Alcohol **74** (75.8 mg, 0.138 mmol) was dissolved in CH₂Cl₂ (1.38 mL) and cooled to 0 °C. Dess-Martin periodinane (117 mg, 0.277 mmol) was then added in one portion. The solution was warmed to rt, stirred for 1 h, and then quenched with 1 N NaOH. The resulting solution was extracted with Et₂O, and the organic layers were combined and dried over MgSO₄. The solution was filtered and concentrated *in vacuo*. The crude material was purified by column chromatography to afford 68.0 mg (90 %) of aldehyde **75**. [δ]_D²³ + 22.5 (c 0.9, CH₂Cl₂); IR (thin film) 2952, 1726, 1463, 1252, 1078 cm⁻¹; ¹H NMR: 0.06 (s, 3H), 0.10 (s, 6H), 0.89 (s, 9H), 1.03 (m, 21H), 1.08 (d, 3H, *J* = 6.5 Hz), 1.61 (s, 3H), 1.79 (ddd, 1H, *J* = 5.0, 8.0, 14.0 Hz), 1.91 (ddd, 1H, *J* = 5.5, 8.0, 14.0 Hz), 2.45 (m, 1H), 3.78 (m, 1H), 4.18 (dd, 2H, *J* = 1.0, 6.0 Hz), 4.21 (dd, 1H, *J* = 5.5, 8.0 Hz), 5.43 (t, 1H, *J* = 5.5 Hz), 9.77 (d, 1H, *J* = 5.0 Hz) ¹³C NMR: -5.3, 0.4, 10.9, 11.3, 12.4, 18.0, 18.1, 18.2, 25.8, 42.1, 50.2, 59.6, 71.7, 75.2, 126.9, 137.7, 204.9. Anal. Calcd for C₂₈H₆₀O₄Si₃: C, 61.70; H, 11.10. Found: C, 61.80; H, 10.86.

(2E, 4S, 6S, 7S, 8R, 9E, 11E, 13E)-3,7,9,13-Tetramethyl-8-methoxy-14-(2'-methyl-4'-oxazolyl)-6-(*p*-nitrobenzoate)-4-[(triisopropylsilyl)oxy]-2,9,11,13-tetradecatetraen-1-ol (85). Silyl ether **84** (262 mg, 0.318 mmol) was dissolved in a solution containing CH₃CN (4 mL), *t*-butanol (1 mL), and fluorosilicic acid (25 % in water, 0.13 mL). The resulting mixture was stirred at 0 °C for 21 h, and was then quenched

by the addition of satd. aq. NaHCO₃ and extracted with Et₂O. The combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude oil was purified by column chromatography (6:1 to 4:1 hexanes/EtOAc) to give 212 mg (94 %) of product **85** as a foamy yellow solid. [α]_D²³ + 51.8 (c 0.90, CH₂Cl₂); IR (thin film) 3422, 2943, 2865, 1720, 1277, 1104 cm⁻¹; ¹H NMR: 0.98 (m, 21H), 1.07 (d, 3H, *J* = 3.9 Hz), 1.52 (s, 3H), 1.56 (br s, 1H), 1.87 (s, 3H), 1.88 (m, 1H), 2.00 (m, 1H), 2.14 (s, 3H), 2.16 (m, 1H), 2.47 (s, 3H), 3.18 (s, 3H), 3.27 (d, 1H, *J* = 8.5 Hz), 3.77 (dd, 1H, *J* = 7.0, 12.8 Hz), 3.89 (dd, 1H, *J* = 6.2, 12.8 Hz), 4.13 (t, 1H, *J* = 7.0 Hz), 5.03 (dd, 1H, *J* = 4.0, 8.5 Hz), 5.41 (t, 1H, *J* = 6.2 Hz), 6.10 (d, 1H, *J* = 11.0 Hz), 6.25 (s, 1H), 6.36 (d, 1H, *J* = 15.5 Hz), 6.60 (dd, 1H, *J* = 11.0, 15.0 Hz), 7.55 (s, 1H), 8.16 (d, 2H, *J* = 9.0 Hz), 8.28 (d, 2H, *J* = 9.0 Hz); ¹³C NMR: 10.5, 11.1, 11.8, 12.2, 13.8, 14.3, 17.9, 18.0, 35.4, 39.5, 56.2, 58.7, 74.2, 76.6, 89.0, 120.7, 123.6, 123.9, 125.8, 129.4, 130.4, 135.7, 135.9, 136.0, 136.8, 137.7, 138.6, 139.6, 150.5, 160.8, 164.0. Anal. Calcd for C₃₉H₅₈N₂O₈Si: C, 65.88; H, 8.22; N, 3.94. Found: C, 65.55; H, 8.38; N, 3.88.

(2E, 4S, 6S, 7S, 8R, 9E, 11E, 13E)-3,7,9,13-Tetramethyl-8-methoxy-14-(2'-methyl-4'-oxazolyl)-6-(p-nitrobenzoate)-4-[(triisopropylsilyl)oxy]-2,9,11,13-tetradecatetraen-1-al (86). Alcohol **85** (192 mg, 0.270 mmol) was dissolved in CH₂Cl₂ (2.7 mL) and cooled to 0 °C. Dess-Martin periodinane (171 mg, 0.405 mmol) was added in one portion, and the reaction mixture was stirred for 30 min, warmed to rt, and stirred for an additional 10 min. The reaction was quenched with 1 N NaOH and extracted with Et₂O, and the combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude material was then purified by column chromatography (hexanes to 6:1 hexanes/EtOAc) to give aldehyde **86** (156.5 mg, 82 %). [α]_D²³ + 40.5 (c 0.38, CH₂Cl₂); IR (thin film) 2942, 1723, 1677, 1529, 1276, 1103 cm⁻¹; ¹H NMR: 0.96 (m, 21H), 1.05 (d, 3H, *J* = 7.0 Hz), 1.55 (s, 3H), 1.87 (s, 3H), 1.91 (m, 1H), 2.07 (m, 1H), 2.09 (s, 3H), 2.24 (m, 1H), 2.47 (s, 3H), 3.18 (s, 3H), 3.29 (d, 1H, *J* = 8.0 Hz), 4.27 (t, 1H, *J* = 6.2 Hz), 5.09 (dd, 1H, *J* = 3.8, 9.3 Hz), 5.87 (d, 1H, *J* = 7.8 Hz), 6.09 (d, 1H, *J* = 10.4 Hz), 6.26 (s, 1H), 6.36 (d, 1H, *J* = 15.2 Hz), 6.59 (dd, 1H, *J* = 10.8, 15.1 Hz), 7.55 (s, 1H), 8.11 (dt, 2H, *J* = 2.0, 8.9 Hz), 8.28 (dt, 2H, *J* = 2.0, 8.9 Hz), 9.68 (d, 1H, *J* = 7.8 Hz); ¹³C NMR: 10.2, 12.2, 12.5, 13.8, 14.3, 17.87, 17.92, 22.6, 31.5, 35.6, 39.1, 56.2, 73.7, 75.7, 88.6, 120.7, 123.6, 123.9, 126.4, 129.2, 130.3, 135.7, 135.9,

136.7, 137.7, 138.6, 150.5, 160.8, 162.8, 163.6, 190.7 Anal. Calcd for C₃₉H₅₆N₂O₈Si: C, 66.07; H, 7.96; N, 3.95. Found: C, 65.74; H, 8.33; N, 3.67.

(2R, 3R, 5S)-1-[(Triisopropylsilyl)-oxy]-2-methyl-5-[2-(benzyloxy)ethyl]-7-octene-3-ol (87). A solution of diol **20** (184 mg, 0.632 mmol) in CH₂Cl₂ (1.26 mL) was cooled to 0 °C, and Et₃N (105 L, 0.758 mmol), DMAP (7.7 mg, 0.063 mmol), and triisopropylsilyl chloride (182 L, 0.943 mmol) were added sequentially. The resulting mixture was stirred for 48 h, and was then quenched by the addition of satd. aq. NH₄Cl. The aqueous phase was extracted with Et₂O, and the combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo*. Purification by column chromatography (hexanes to 9:1 hexanes/EtOAc) afforded 268 mg (95 %) of the desired silyl ether **87**. [²³D + 7.31 (*c* 1.34, CH₂Cl₂); IR (thin film): 3477, 1463, 1099, 882 cm⁻¹; ¹H NMR: 0.90 (d, 3H, *J* = 7.2 Hz), 1.05 - 1.14 (m, 21H), 1.34 (ddd, 1H, *J* = 3.9, 8.3, 13.9 Hz), 1.49 (ddd, 1H, *J* = 5.3, 9.7, 13.9 Hz), 1.49 - 1.84 (m, 4H), 2.11 (m, 2H), 3.54 (t, 2H, *J* = 6.9 Hz), 3.76 (dd, 1H, *J* = 6.0, 9.7 Hz), 3.82 (dd, 1H, *J* = 4.1, 9.7 Hz), 3.93 (ddd, 1H, *J* = 2.4, 5.0, 10.5 Hz), 4.50 (s, 2H), 5.0 (m, 2H), 5.77 (m, 1H), 7.25 - 7.34 (m, 5H); ¹³C NMR: 10.5, 11.7, 17.6, 17.9, 31.2, 33.9, 37.76, 37.79, 39.3, 68.47, 68.54, 72.2, 72.8, 116.3, 127.4, 127.5, 128.2, 136.5, 138.5. Anal. Calcd. for C₂₇H₄₈O₃Si: C, 72.26; H, 10.78. Found: C, 72.17; H, 10.95.

[4R, 6R, 6(1R)]-4-Allyl-6-[(1-methyl-2-hydroxy)ethyl]-4H-pyran-2-one (94). Silyl ether **89** (374 mg, 1.05 mmol) was dissolved in a solution of 19:1 CH₃CN:HF (40 % aq.) (10.5 mL total) and the resulting mixture was stirred at rt for 30 min. The reaction was then quenched by the addition of satd. aq. NaHCO₃ and extracted with Et₂O, and the combined organic extracts were dried over MgSO₄, filtered, and concentrated. The crude material was purified by column chromatography (9:1 to 1:1 hexanes/EtOAc) to afford 199 mg (95 %) of alcohol **94**. [²³D -19.5 (*c* 0.81, CDCl₃); IR (thin film): 3402, 2924, 2359, 1724, 1250; ¹H NMR: 0.95 (d, 3H, *J* = 7.0 Hz), 1.38 (m, 1H), 1.74 (br s, 1H), 1.87 (m, 2H), 2.06 (m, 4H), 2.68 (ddd, 1H, *J* = 2.0, 5.0, 17.0 Hz), 3.61 (dd, 1H, *J* = 5.0, 10.5 Hz), 3.71 (dd, 1H, *J* = 8.0, 10.5 Hz), 4.52 (dt, 1H, *J* = 3.0, 12.0 Hz), 5.08 (m, 2H), 5.72 (m, 1H); ¹³C NMR: 10.5, 31.4, 31.9, 36.0, 39.7, 40.4, 64.3, 80.3, 117.7, 134.5, 171.5. Anal. Calcd. for C₁₁H₁₈O₃: C, 66.64; H, 9.15. Found: C, 66.46; H, 8.96.

[4R, 6R, 6(1R)]-4-Allyl-6-[1-methyl-2-(methanesulfonyl) ethyl]-4H-pyran-2-one (95). A solution of alcohol **94** (190 mg, 0.960 mmol) in CH₂Cl₂ (3.8 mL) was cooled to 0 °C, and Et₃N (268 L, 1.93 mmol), DMAP (11.7 mg, 0.096 mmol), and methanesulfonyl chloride (81.9 L, 1.05 mmol) were added sequentially. The resulting cloudy mixture was stirred for 5 min, and was then quenched by the addition of satd. aq. NaHCO₃. The aqueous phase was extracted with Et₂O, and the combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo*. The crude material was purified by column chromatography (Et₂O) to afford 255 mg (96 %) of the desired **95**. [α]_D²³ -28.1 (*c* 0.47, CH₂Cl₂); IR (thin film): 2939, 1731, 1352, 1174; ¹H NMR: 1.03 (d, 3H, *J* = 7.0 Hz), 1.36 (m, 1H), 1.86 (d, 1H, *J* = 16.0 Hz), 2.09-2.18 (m, 5H), 2.72 (m, 1H), 3.03 (s, 3H), 4.20 (dd, 1H, *J* = 5.5, 10.0 Hz), 4.25 (dd, 1H, *J* = 8.5, 10.0 Hz), 4.48 (dt, 1H, *J* = 3.0, 12.0 Hz), 5.11 (m, 2H), 5.71 (m, 1H); ¹³C NMR: 10.1, 31.1, 31.3, 35.8, 37.0, 37.3, 40.1, 70.7, 78.7, 117.7, 134.4, 170.8. Anal. Calcd. for C₁₂H₂₀O₅S: C, 52.16; H, 7.29. Found: C, 52.37; H, 7.25.

Hemiacetal 97. Lactone **96** (162 mg, 0.427 mmol) was dissolved in CH₂Cl₂ and cooled to -78 °C. DIBAL-H (1.5 M in toluene, 0.284 mL, 0.428 mmol) was then added to the solution dropwise, and the reaction mixture was stirred for 10 min. The reaction was then quenched by the addition of 1 mL of MeOH, and was then diluted with 0.5 M aq. Rochelle's salt and Et₂O. The mixture was stirred vigorously for 2 h, then extracted with Et₂O. The combined organic extracts were dried over MgSO₄, filtered, and concentrated, and the crude material was purified by column chromatography (hexanes to 6:1 hexanes/EtOAc) to give 129 mg (80 %) of hemiacetal **97**, as well as 5 mg (3 %) of recovered lactone. IR (thin film): 3544, 2917, 1319, 1147; ¹³C NMR: 14.3, 14.5, 28.7, 32.6, 32.7, 32.9, 33.4, 33.9, 36.2, 39.0, 40.7, 41.1, 57.7, 57.8, 69.6, 76.4, 92.2, 116.4, 116.7, 122.3, 125.4, 127.6, 128.0, 128.2, 129.0, 135.7, 135.9, 136.7, 152.6, 166.7. Anal. Calcd. for C₁₈H₂₃NO₄S₂: C, 56.67; H, 6.08; N, 3.67. Found: C, 56.78; H, 6.21; N, 3.73. See supplemental material section for ¹H NMR spectrum of the 2 isomers.

Sulfone 98. Hemiacetal **97** (48.0 mg, 0.125 mmol) was dissolved in CH₂Cl₂ and cooled to 0 °C. Imidazole (11.1 mg, 0.163 mmol) and *t*-butyldimethylsilyl chloride (22.7 mg, 0.150 mmol) were added to the solution sequentially, and the mixture was stirred for 30 min at rt. The reaction was quenched by the

addition of satd. aq. NH_4Cl ; the aqueous phase was extracted with Et_2O , and the combined organic extracts were dried over MgSO_4 , filtered, and concentrated. The crude material was purified by column chromatography (hexanes to 9:1 hexanes/ EtOAc) to give 53.0 mg (85 %) of silyl ether **98** as one isomer.

$[\alpha]_D^{23} + 2.98$ (c 1.4, CH_2Cl_2); IR (thin film): 2937, 1332, 1148; ^1H NMR: 0.07 (s, 6H), 0.87 (s, 9H), 0.96 (m, 2H), 1.15 (d, 3H, $J = 7.0$ Hz), 1.46 (m, 1H), 1.76 (m, 1H), 1.77 (d, 1H, $J = 12.8$ Hz), 1.99 (t, 2H, $J = 6.6$ Hz), 2.46 (m, 1H), 3.41 (dd, 1H, $J = 7.2, 14.4$ Hz), 3.54 (d, 1H, $J = 12.9$ Hz), 3.79 (dd, 1H, $J = 5.1, 14.4$ Hz), 4.69 (dd, 1H, $J = 2.1, 9.2$ Hz), 5.00 (m, 2H), 5.74 (m, 1H), 7.59 (ddd, 1H, $J = 1.4, 7.3, 7.5$ Hz), 7.64 (ddd, 1H, $J = 1.5, 7.3, 7.7$ Hz), 8.01 (m, 1H), 8.21 (m, 1H); ^{13}C NMR: -5.0-3.8, 14.7, 18.0, 25.8, 32.9, 33.1, 34.0, 40.2, 40.8, 58.1, 76.5, 97.1, 116.6, 122.4, 125.5, 127.6, 128.0, 136.0, 136.9, 152.7, 166.0. Anal. Calcd. for $\text{C}_{24}\text{H}_{37}\text{NO}_4\text{S}_2\text{Si}$: C, 58.15; H, 7.52; N, 2.83. Found: C, 58.39; H, 7.64; N, 2.85.

Sulfone 106. A solution of alcohol **105** (115 mg, 0.229 mmol) in CH_2Cl_2 (1.15 mL) was cooled to 0 °C, and Et_3N (64.0 μL , 0.459 mmol), DMAP (2.8 mg, 0.023 mmol), and triethylsilyl chloride (42.4 μL , 0.252 mmol) were added sequentially. The resulting cloudy mixture was stirred for 5 min, and was then quenched by the addition of satd. aq. NH_4Cl . The aqueous phase was extracted with Et_2O , and the combined organic extracts were dried over MgSO_4 , filtered, and concentrated *in vacuo*. The crude material was purified by column chromatography (hexanes to 9:1 hexanes/ EtOAc) to afford 135 mg (96 %) of the desired silyl ether **106**. $[\alpha]_D^{23} + 3.68$ (c 0.38, CH_2Cl_2); IR (thin film): 2953, 1472, 1330, 1150; ^1H NMR: 0.06 (s, 6H), 0.58 (q, 6H, $J = 7.9$ Hz), 0.87 (s, 9H), 0.94 (t, 9H, $J = 7.9$ Hz), 0.90-1.04 (m, 2H), 1.15 (d, 3H, $J = 7.0$ Hz), 1.46 (m, 3H), 1.76 (m, 1H), 1.79 (d, 1H, $J = 14.0$ Hz), 2.46 (m, 1H), 3.40 (dd, 1H, $J = 7.5, 14.4$ Hz), 3.54 (d, 1H, $J = 12.7$ Hz), 3.63 (t, 2H, $J = 6.5$ Hz), 3.79 (dd, 1H, $J = 4.9, 14.4$ Hz), 4.69 (dd, 1H, $J = 2.0, 9.0$ Hz), 7.59 (dt, 1H, $J = 1.2, 7.2$ Hz), 7.64 (dt, 1H, $J = 1.2, 7.2$ Hz), 8.01 (d, 1H, $J = 7.7$ Hz), 8.20 (d, 1H, $J = 7.7$ Hz); ^{13}C NMR: -5.1, -3.9, 4.3, 6.7, 14.7, 18.0, 25.7, 30.7, 32.8, 33.3, 39.3, 40.4, 58.1, 59.9, 76.6, 97.0, 122.3, 125.4, 127.6, 127.9, 136.7, 152.7, 166.4. Anal. Calcd. for $\text{C}_{29}\text{H}_{51}\text{NO}_5\text{S}_2\text{Si}_2$: C, 56.73; H, 8.37; N, 2.28. Found: C, 56.80; H, 8.32; N, 2.13.

Oxazole 108. To a solution of ester **107** (167 mg, 0.151 mmol) in CH_2Cl_2 at -78 °C was added DIBAL-H (1.5 M in toluene, 0.400 mL, 0.600 mmol) dropwise. The resulting solution was stirred for 5 min, and was

then quenched by the addition of 0.5 M aq. Rochelle's salt solution. The mixture was diluted with Et₂O, and the biphasic solution was stirred vigorously for 2 h and then extracted with Et₂O; the combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo*. The resulting crude material was purified by column chromatography (hexanes to 14:1 hexanes/EtOAc) to give 130 mg (90 %) of alcohol **108**. [α]²³_D + 46.6 (*c* 0.5, CH₂Cl₂); IR (thin film): 3433, 2936, 1459, 1086 ; ¹H NMR: 0.10 (s, 3H), 0.12 (s, 3H), 0.57 (q, 6H, *J* = 7.9 Hz), 0.90 (s, 9H), 0.94 (t, 9H, *J* = 7.9 Hz), 1.05 (m, 26H), 1.45 (m, 3H), 1.51 (d, 1H, *J* = 12.6 Hz), 1.65 - 1.79 (m, 7H), 1.65 (s, 3H), 1.73 (s, 3H), 2.12 (s, 3H), 2.30 (m, 1H), 2.47 (s, 3H), 3.10 (ddd, 1H, *J* = 1.6, 8.0, 9.3 Hz), 3.21 (s, 3H), 3.54 (d, 1H, *J* = 5.7 Hz), 3.57 (d, 1H, *J* = 2.3 Hz), 3.61 (t, 2H, *J* = 6.6 Hz), 3.75 (br s, 1H), 4.44 (t, 1H, *J* = 4.4 Hz), 4.65 (dd, 1H, *J* = 2.0, 9.2 Hz), 5.50 (dd, 1H, *J* = 8.6, 13.6 Hz), 6.04 (d, 1H, *J* = 11.2 Hz), 6.13 (s, 1H), 6.17 (m, 1H), 6.25 (s, 1H), 6.35 (d, 1H, *J* = 15.2 Hz), 6.54 (dd, 1H, *J* = 10.9, 15.1 Hz), 7.53 (s, 1H); ¹³C NMR: -5.3, -4.0, 4.3, 6.7, 10.4, 12.2, 13.3, 13.77, 13.80, 14.3, 16.9, 17.95, 17.99, 18.03, 25.8, 30.6, 35.3, 37.8, 39.4, 40.4, 41.3, 42.7, 56.6, 60.0, 69.9, 76.2, 78.9, 87.6, 97.1, 120.1, 124.3, 125.1, 125.7, 127.2, 135.7, 136.4, 136.5, 136.6, 136.8, 137.0, 138.7, 160.8 Anal. Calcd. for C₅₄H₉₉NO₇Si₃: C, 67.66; H, 10.41; N, 1.46. Found: C, 67.66; H, 10.74; N, 1.63.

Phosphonate 110. A solution of silyl ether **109** (127 mg, 0.111 mmol) in 2-propanol (2 mL) was cooled to -45 °C (CH₃CN/dry ice bath), and fluorosilicic acid (25 % in water, 100 μL) was added dropwise. The resulting mixture was stirred for 30 min, and was then quenched by the addition of satd. aq. NaHCO₃ and extracted with Et₂O. The combined organic extracts were dried over MgSO₄, filtered, and concentrated *in vacuo*. Purification of the crude material by column chromatography (6:1 hexanes/EtOAc to EtOAc) gave 101 mg (88 %) of alcohol **110**. [α]²³_D + 61.3 (*c* 0.15, CH₂Cl₂); IR (thin film): 3420, 1733, 1652, 1457, 1073 ; ¹H NMR: 0.09 (s, 3H), 0.11 (s, 3H), 0.81 (m, 1H), 0.88 (s, 9H), 0.97 (m, 23H), 1.06 (d, 3H, *J* = 6.6 Hz), 1.33 (q, 6H, *J* = 7.0 Hz), 1.51 (m, 2H), 1.58 - 1.68 (m, 4H), 1.68 (s, 3H), 1.75 - 1.85 (m, 2H), 1.81 (s, 3H), 2.03 (s, 3H), 2.13 (s, 3H), 2.23 (m, 1H), 2.47 (s, 3H), 2.67 (dd, 1H, *J*_{H-H} = 14.2 Hz, *J*_{P-H} = 22.0 Hz), 2.78 (dd, 1H, *J*_{H-H} = 14.2 Hz, *J*_{P-H} = 22.0 Hz), 3.02 (t, 1H, *J* = 9.4 Hz), 3.15 (s, 3H), 3.23 (d, 1H, *J* = 8.5 Hz), 3.64 (t, 2H, *J* = 5.7 Hz), 4.00 (dd, 1H, *J* = 5.4, 8.4 Hz), 4.11 (m, 4H), 4.63 (dd, 1H, *J* = 2.0, 8.9 Hz), 4.74 (dd, 1H, *J* = 3.5, 10.0 Hz), 5.40 (dd, 1H, *J* = 8.9, 15.1 Hz), 5.73 (d, 1H, *J* = 10.8 Hz), 6.05 (d, 1H, *J* =

10.9 Hz), 6.12 (dd, 1H, $J = 10.9, 14.6$ Hz), 6.24 (s, 1H), 6.33 (d, 1H, $J = 15.3$ Hz), 6.59 (dd, 1H, $J = 11.2, 15.3$ Hz), 7.54 (s, 1H); ^{13}C NMR: -5.3, -4.0, 10.1, 11.3, 11.9, 12.4, 13.8, 14.4, 16.31 (d, $J_{\text{C-P}} = 5.6$ Hz), 16.35 (d, $J_{\text{C-P}} = 5.6$ Hz), 17.5, 18.0, 18.09, 18.13, 25.8, 30.7, 34.6 (d, $J_{\text{C-P}} = 133.3$ Hz), 35.0, 35.9, 39.1, 39.5, 40.5, 43.3, 56.2, 60.0, 62.6 (d, $J_{\text{C-P}} = 6.3$ Hz), 62.8 (d, $J_{\text{C-P}} = 6.3$ Hz), 73.8, 77.3, 78.7, 88.8, 97.1, 120.4, 124.3, 125.7, 125.9, 129.1, 135.8, 136.3, 136.9, 137.0, 137.4, 138.1, 138.6, 160.9, 164.6.

Aldehyde 111. Alcohol **110** (71.0 mg, 68.0 μmol) was dissolved in CH_2Cl_2 and cooled to 0 $^\circ\text{C}$. Dess-Martin periodinane (31.7 mg, 75.0 μmol) was then added in one portion, and the resulting cloudy solution was warmed to rt and stirred for 20 min. The reaction was then quenched by the addition of 1 N NaOH, diluted with Et_2O , and stirred vigorously for 5 min. The mixture was then extracted with Et_2O , and the combined organic extracts were dried over MgSO_4 , filtered, and concentrated *in vacuo*. The resulting crude material was purified by column chromatography (hexanes to 1:1 hexanes/ EtOAc) to afford 55.0 mg (78 %) of aldehyde **111**. $[\alpha]_{\text{D}}^{23} + 46.8$ (c 0.59, CH_2Cl_2); IR (thin film): 2933, 1732, 1458, 1162, 1080 ; ^1H NMR: 0.09 (s, 3H), 0.12 (s, 3H), 0.89 (s, 9H), 0.97 (m, 27H), 1.07 (d, 3H, $J = 6.7$ Hz), 1.08 (m, 1H), 1.32 (dt, 6H, $J_{\text{H-H}} = 7.1$ Hz, $J_{\text{P-H}} = 2.9$ Hz), 1.55 - 1.69 (m, 2H), 1.69 (s, 3H), 1.78 - 1.83 (m, 2H), 1.82 (s, 3H), 2.12 (s, 3H), 2.29 (m, 1H), 2.36 (dd, 1H, $J = 1.7, 7.1$ Hz), 2.39 (dd, 1H, $J = 1.4, 6.6$ Hz), 2.46 (s, 3H), 2.71 (dd, 1H, $J_{\text{H-H}} = 14.1$ Hz, $J_{\text{P-H}} = 21.7$ Hz), 2.85 (dd, 1H, $J_{\text{H-H}} = 14.1$ Hz, $J_{\text{P-H}} = 21.7$ Hz), 3.16 (m, 1H), 3.16 (s, 3H), 3.21 (d, 1H, $J = 8.2$ Hz), 4.07 (m, 1H), 4.11 (dq, 2H, $J_{\text{H-H}} = 7.1$ Hz, $J_{\text{P-H}} = 2.0$ Hz), 4.16 (dq, 2H, $J_{\text{H-H}} = 7.1$ Hz, $J_{\text{P-H}} = 2.0$ Hz), 4.68 (dd, 1H, $J = 2.0, 9.2$ Hz), 4.79 (dd, 1H, $J = 3.6, 9.2$ Hz), 5.40 (dd, 1H, $J = 8.1, 15.0$ Hz), 5.79 (d, 1H, $J = 10.1$ Hz), 6.05 (d, 1H, $J = 10.6$ Hz), 6.14 (dd, 1H, $J = 10.9, 15.0$ Hz), 6.24 (s, 1H), 6.33 (d, 1H, $J = 15.2$ Hz), 6.58 (dd, 1H, $J = 10.9, 15.2$ Hz), 7.54 (s, 1H), 9.75 (t, 1H, $J = 1.5$ Hz); ^{13}C NMR: -5.3, -3.9, 10.0, 11.7, 12.0, 12.4, 13.8, 14.4, 16.3 (d, $J_{\text{C-P}} = 6.3$ Hz), 16.4 (d, $J_{\text{C-P}} = 6.3$ Hz), 16.8, 18.0, 18.06, 18.13, 25.8, 28.8, 34.5 (d, $J_{\text{C-P}} = 132.5$ Hz), 35.0, 35.3, 38.7, 40.2, 42.4, 50.3, 56.2, 62.4 (d, $J_{\text{C-P}} = 6.4$ Hz), 62.5 (d, $J_{\text{C-P}} = 6.4$ Hz), 73.9, 76.4, 78.7, 88.8, 96.7, 120.4, 124.4, 125.5, 125.9, 129.0, 135.8, 136.3, 136.4, 137.0, 137.3, 138.5, 138.7, 160.9, 164.7, 201.4.

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- ⁱ A modified procedure of the following was employed: Marshall, J. A.; Cleary, D. G. *J. Org. Chem.* **1986**, *51*, 858.
- ⁱⁱ Nakada, M. *J. Syn. Org. Chem. Jpn.* **1995**, *53*, 54.