Total Synthesis of Formamycin

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Part II

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I. GENERAL INFORMATION.

General Methods: All reaction solvents were purified before use. Tetrahydrofuran, dichloromethane, diethyl ether, and toluene were purified by passage through a solvent column composed of activated A-1 alumina.¹ Unless otherwise indicated, all commercial reagents were used as received without further purification.

Physical Properties and Spectroscopic Measurements: Proton nuclear magnetic resonance (¹H NMR) spectra and carbon-13 (¹³C) NMR spectra were recorded on a Varian VXR-400 spectrometer at 400 MHz and 100 MHz respectively, or on a Varian Inova-500 spectrometer at 500 MHz and 125 MHz respectively. The proton signal of residual, non-deuterated solvent (δ 7.26 ppm for CHCl₃; δ 7.16 ppm for C₆D₅H) or tetramethylsilane (δ 0 ppm, CDCl₃) was used as an internal reference for ¹H spectra. For ¹³C spectra, chemical shifts are reported relative to the δ 77.23 ppm resonance of CDCl₃ or the δ 128.39 ppm resonance of C₆D₆. Coupling constants are reported in Hz. Infrared (IR) spectra were recorded as thin films on a Perkin-Elmer Spectrum 1000 FTIR. Optical rotations were measured on a Rudolph Autopol III polarimeter using a quartz cell with 1 mL capacity and a 10 cm path length. Mass spectra were recorded on a VG 70-250-S spectrometer manufactured by Micromass Corp. (Manchester UK).

Analytical thin layer chromatography (TLC) was performed on Kieselgel 60 F₂₅₄ glass plates precoated with a 0.25 mm thickness of silica gel. The TLC plates were visualized with UV light and/or by staining with Hanessian stain (a mixture of ceric sulfate and ammonium molybdate in aqueous sulfuric acid), KMnO₄, or *p*-anisaldehyde solutions. Column chromatography was generally performed using Kieselgel 60 (230-400 mesh) silica gel. Unless noted otherwise, all compounds isolated by chromatography were sufficiently pure by ¹H NMR analysis for use in subsequent reactions. High resolution mass spectra were measured on a VG 70-250-S Micromass spectrometer at the University of Michigan Mass Spectrometry Laboratory. Elemental analyses were performed by the University of Michigan CHN Laboratory.

HPLC purifications were performed by using a HPLC system composed of two Rainin HPXL pumps connected to various Dynamax[®] axial compression columns packed with Rainin 60 Å irregular silica gel. Samples were loaded into the system with a 2 mL Rheodyne 7125 injector and were detected using either a Rainin Dynamax[®] UV-C detector or a Rainin

Dynamax[®] RI-1 detector. Integration of the various signals was performed using the reprocessing program within the Dynamax[®] HPLC Method Manager.

II. EXPERIMENTAL PROCEDURES.

A. First Generation Synthesis of Fragment 7.

1-Trimethylsilyl-1-acetoxy-2-methyl-2-propene (13).^{2,3} A 250-mL three-necked round bottom flask fitted with a pressure-equalizing funnel, N_2 inlet, and rubber septum was charged with 80 mL of THF and 4.00 mL (47.5 mmol) of 2-methyl-2-propen-1-ol (**12**). After the solution was cooled to $-78\text{ }^{\circ}\text{C}$ in a dry ice/acetone bath, 22.3 mL (52.3 mmol, 2.35 M in hexanes) of $n\text{-BuLi}$ was added dropwise and the solution was stirred at $-78\text{ }^{\circ}\text{C}$ for 30 min. A solution of TMSCl (6.65 mL, 52.3 mmol) in 5 mL of THF was added dropwise to the reaction mixture through the addition funnel, rinsed with 5 mL of THF. The resulting light yellow solution was stirred at $-78\text{ }^{\circ}\text{C}$ for 30 min. A solution of $t\text{-BuLi}$ (38.0 mL, 57.0 mmol, 1.5 M in pentane) was added through the addition funnel over a 15 min period. The resulting dark yellow slurry was stirred at $-78\text{ }^{\circ}\text{C}$ for 10 min, then warmed to $-40\text{ }^{\circ}\text{C}$ (dry ice/ CH_3CN), and the dark yellow solution was maintained at -40 to $-30\text{ }^{\circ}\text{C}$ for 3 h. A solution of Ac_2O (6.3 mL, 67 mmol) in 5 mL of THF was added rapidly through the addition funnel, rinsing with 5 mL of THF, and the resulting slurry was allowed to warm to room temperature. The mixture was carefully quenched by the addition of H_2O , then the mixture was diluted with 100 mL of Et_2O . The organic layer was washed with H_2O , saturated aqueous NaHCO_3 , and saturated NaCl solution, dried over MgSO_4 , and concentrated to afford crude **13**^{2,3} as a reddish yellow oil. This material was used in

the next step without further purification: ^1H NMR (500 MHz, CDCl_3) δ 5.02 (s, 1 H), 4.73 (d, J = 1.5 Hz, 1 H), 4.70 (d, J = 1.5 Hz, 1 H), 2.08 (s, 3 H), 1.71 (s, 3 H), 0.07 (s, 9 H).

***t*-Butyldimethylsilyl (*E*)-4-methyl-5-trimethylsilyl-4-pentenoate (79).** A solution of α -acetoxysilane **13** (the crude product from the preceding step) in 95 mL of dry CH_2Cl_2 was flushed with N_2 and cooled in an ice bath. To this solution was added $i\text{-Pr}_2\text{NEt}$ (16.6 mL, 95.1 mmol), followed by 14.2 mL (61.8 mmol) of TBSOTf. The ice bath was removed, and the red solution was stirred at room temperature for 72 h. The mixture was then cooled in an ice bath and diluted with saturated aqueous NaHCO_3 and extracted with 150 mL of CH_2Cl_2 . The organic layer was washed with 1 *N* KHSO_4 (x2) and saturated NaCl solution, dried over Na_2SO_4 , and concentrated to give 23.4 g of crude **79** as a red oily solid which was used in the next step without further purification: ^1H NMR (500 MHz, CDCl_3) δ 5.19 (s, 1 H), 2.47 (m, 2 H), 2.35 (m, 2 H), 1.79 (s, 3 H), 0.93 (s, 9 H), 0.25 (s, 6 H), 0.08 (s, 9 H).

(*R*)-4-Benzyl-3-[4-methyl-5-(trimethylsilyl)-pent-4-enoyl]-oxazolidin-2-one (15). Ester **79** (30 g, 97.0 mmol, the crude product from the preceding step) was dissolved in $\text{MeOH}/\text{H}_2\text{O}$ 1 : 1 (200 mL) and cooled to 0 °C. To this solution was added $\text{LiOH}\cdot\text{H}_2\text{O}$ (16.4 g, 391 mmol) and the resulting mixture allowed to warm to 23 °C. After 3 h, the reaction mixture was extracted with diethyl ether (x3). CH_2Cl_2 was added to the aqueous phase followed by slow

addition of HCl (1N) until the pH of the aqueous phase was ~ 2. The layers were separated and the aqueous phase was extracted with CH₂Cl₂ (x4). All of the CH₂Cl₂ extracts were combined, washed with saturated NaCl solution, dried over Na₂SO₄, filtered, and concentrated to give **14** (12.7 g, 70% from **12**) as a red/orange oil. This material was used without further purification in the next step.

Acid **14** (12.7 g, 68.2 mmol, 1.3 equiv) was placed in a 500 mL three-neck round-bottom flask, dissolved in dry ether (230 mL) under nitrogen, and cooled to 0 °C. To the cooled solution was added Et₃N (11 mL, 78.9 mmol, 1.5 equiv) followed by pivaloyl chloride (8.4 mL, 68.2 mmol, 1.3 equiv). The ice bath was removed and the reaction mixture warmed to 23 °C and stirred for 1 h. The resulting solution was then cooled to 0 °C. One of the necks of the flask was equipped with a filter frit (Schlenk apparatus) and the reaction mixture filtered under nitrogen into a second dry 1000 mL round-bottom flask, with washing of the filtered solid (ether, 30 mL x 2). The filtering apparatus was removed and the orange filtrate was cooled to –78 °C and then diluted with dry THF (130 mL).

A separate 250-mL round bottom flask, under nitrogen, was charged with 9.44 g (53.3 mmol, 1 equiv) of (*R*)-4-(phenylmethyl)-2-oxazolidinone, a few crystals of 1,10-phenanthroline, and 100 mL of THF (100 mL) and cooled to –78 °C in a dry ice/acetone bath. A solution of *n*-BuLi (2.35 M in hexanes) was added dropwise until the red color persisted for 10 min. The lithiated oxazolidinone solution was then added to the chilled mixed anhydride solution via cannula over 40 min. The resulting solution was stirred at –78 °C for 30 min, then poured into saturated aqueous NH₄Cl solution (400 mL). The layers were separated and the aqueous layer was extracted with CH₂Cl₂ (x3). The combined organic layers were washed with saturated NaCl solution, dried over Na₂SO₄, and concentrated in vacuo. Purification of the crude product by flash chromatography (SiO₂, 10% EtOAc/hexanes) gave 14.9 g of **15** (81% from **14**) as a viscous orange oil: $[\alpha]_D^{26} -53.0^\circ$ ($c = 0.39$, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 7.34 (tt, $J = 7.2, 1.3$ Hz, 2 H), 7.28 (tt, $J = 7.3, 1.2$ Hz, 1 H), 7.21 (dd, $J = 7.6, 1.5$ Hz, 2 H), 5.25 (s, 1 H), 4.67 (dddd, $J = 10.7, 6.6, 3.3, 3.3$ Hz, 1 H), 4.19 (A of ABX, $J_{AB} = 16.4$ Hz, $J_{AX} = 9.0$ Hz, 1 H), 4.17 (B of

ABX, $J_{AB} = 9.3$ Hz, $J_{BX} = 3.1$ Hz, 1 H), 3.29 (dd, $J = 13.4, 3.4$ Hz, 1 H), 3.15 (ddd, $J = 16.6, 9.3, 6.4$ Hz, 1 H), 3.03 (ddd, $J = 16.6, 9.3, 6.4$ Hz, 1 H), 2.75 (dd, $J = 13.4, 9.5$ Hz, 1 H), 2.45 (m, 2 H), 1.84 (s, 3 H), 0.10 (s, 9 H); ^{13}C NMR (125 MHz, CDCl_3) δ 172.8, 153.4, 152.9, 135.2, 129.4 (2), 128.9 (2), 127.3, 123.9, 66.1, 55.1, 34.9, 36.4, 34.0, 21.7, 0.0 (3); FT-IR (thin film) 3064, 3029, 2955, 1785, 1701, 1619, 1498, 1481, 1454, 1444, 1387, 1353, 1248, 1212, 1109, 1076, 1051, 1016, 840, 762, 747, 702 cm^{-1} ; HRMS (CI/ NH_3) calcd for $[\text{C}_{19}\text{H}_{27}\text{NO}_3\text{Si}+\text{H}]^+$ 346.1838, found 346.1826 m/z .

(4R)-4-Benzyl-3-[(2R,3S)-2-(2-methyl-3-trimethylsilyl-E-2-propen-1-yl)-3-hydroxy-octanoyl]-oxazolidin-2-one (16). A 250-mL round bottom flask was charged with 3.24 g (9.37 mmol) of oxazolidinone **15** and 20 mL of CH_2Cl_2 . The solution was cooled in an ice bath, then 2.83 mL (11.3 mmol) of Bu_2BOTf was added dropwise, followed by 1.70 mL (12.2 mmol) of Et_3N . The resulting light yellow solution was stirred at 0 °C for 10 min. The ice bath was replaced with a dry ice/acetone bath (-78 °C) and 1.35 mL (11.3 mmol) of hexanal (freshly distilled) was added by syringe over a 5 min period. The reaction mixture was stirred at -78 °C for 1 h, warmed to 0 °C for 2 h, and quenched by addition of 15 mL of pH 7 buffer and 15 mL of MeOH. Ten mL of 2:1 MeOH/30% aqueous H_2O_2 solution was added dropwise and the biphasic mixture was stirred vigorously at room temperature for 1 h. The mixture was diluted with 100 mL of H_2O and the layers were separated. The aqueous layer was washed with CH_2Cl_2 (2 $\times$) and the combined organic layers were washed with saturated aqueous NaHCO_3 , dried over MgSO_4 , and concentrated. Purification of the crude product by flash chromatography (SiO_2 , 15% EtOAc/hexanes) gave 3.62 g (97%) of **16** as a pale yellow oil: $[\alpha]_D^{24} -35.8^\circ$ ($c = 0.65$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.34 (t, $J = 7.1$ Hz, 2 H), 7.28 (t, $J = 7.1$ Hz, 1 H), 7.21 (d, $J = 7.1$ Hz, 2 H), 5.29 (s, 1 H), 4.69 (dddd, $J = 10.5, 6.5, 3.1, 3.1$ Hz, 1 H), 4.38 (ddd, $J = 10.5, 4.0, 4.0$

Hz, 1 H), 4.17 (A of ABX, $J_{AB} = 17.1$ Hz, $J_{AX} = 7.8$ Hz, 1 H), 4.12 (B of ABX, $J_{AB} = 9.0$ Hz, $J_{BX} = 2.9$ Hz, 1 H), 3.87 (m, 1 H), 3.34 (dd, $J = 13.2, 2.9$ Hz, 1 H), 2.63 (dd, $J = 13.9, 10.5$ Hz, 1 H), 2.52 (dd, $J = 13.2, 10.7$ Hz, 1 H), 2.48 (d, $J = 3.2$ Hz, 1 H), 2.41 (dd, $J = 13.9, 10.5$ Hz, 1 H), 1.86 (s, 3 H), 1.57-1.50 (m, 3 H), 1.34-1.24 (m, 5 H), 0.89 (t, $J = 6.8$ Hz, 3 H), 0.07 (s, 9 H); ^{13}C NMR (125 MHz, CDCl_3) δ 175.5, 153.5, 152.4, 135.3, 129.2 (2), 129.0 (2), 127.3, 125.8, 72.7, 65.9, 55.6, 45.9, 10.1, 38.2, 33.7, 31.7, 25.7, 22.6, 22.0, 14.0, 0.0 (3); FT-IR (thin film) 3502, 3030, 2955, 2931, 2860, 1783, 1697, 1616, 1383, 1350, 1247, 1195, 1107, 1051, 1016, 838, 700 cm^{-1} ; HRMS (CI/ NH_3) calcd for $[\text{C}_{25}\text{H}_{39}\text{NO}_4\text{Si}+\text{H}]^+$ 446.2726, found 446.2716 m/z .

(1E,4R,5S)-5-Hydroxy-2-methyl-4-hydroxymethyl-1-trimethylsilyl-1 decene (81).

To a 0 °C solution of aldol **16** (1.67 g, 3.75 mmol) in 32 mL of THF was added dropwise a solution of 0.567 g (15.0 mmol) of NaBH_4 in 8 mL of deionized H_2O . Once addition was complete, the ice bath was removed and the biphasic mixture was stirred vigorously at room temperature for 8 h. The mixture was then recooled in an ice bath and 50 mL of 1 *N* HCl was added carefully to quench the excess hydride reagent. The aqueous layer was extracted with 50 mL of Et_2O (3 $\times$). The combined organic layers were washed with saturated NaCl solution, dried over MgSO_4 , and concentrated. Purification of the crude product by flash chromatography (SiO_2 , 25% EtOAc /hexanes then 30% EtOAc /hexanes) gave 0.801 g (78%) of the diol as a yellowish white solid: $[\alpha]_{\text{D}}^{25} +3.5^\circ$ ($c = 1.38$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 5.26 (d, $J = 1.0$ Hz, 1 H), 3.83 (m, 1 H), 3.75 (m, 1 H), 3.68 (m, 1 H), 2.44 (bs, 1 H), 2.30 (bs, 1 H), 2.10 (d, $J = 8.1$ Hz, 2 H), 1.93 (m, 1 H), 1.79 (d, $J = 1.0$ Hz, 3 H), 1.54-1.42 (m, 3 H), 1.34-1.25 (m, 5 H), 0.89 (t, $J = 7.0$ Hz, 3 H), 0.09 (s, 9 H); ^{13}C NMR (125 MHz, CDCl_3) δ 153.1, 126.0, 74.8, 64.8, 42.1, 39.2, 33.1, 31.8, 25.9, 22.6, 21.3, 14.0, 0.0 (3); FT-IR (thin film) 3291, 2953, 2931, 2859,

1616, 1441, 1377, 1248, 1028, 859, 836, 690 cm^{-1} ; HRMS (CI/ NH_3) calcd for $[\text{C}_{15}\text{H}_{32}\text{O}_2\text{Si}+\text{H}]^+$ 273.2250, found 273.2258 m/z .

(2*R*,4*S*,5*S*)-5-(2-methyl-3-trimethylsilyl-*E*-prop-2-en-1-yl)-2-(4-methoxyphenyl)-4-pentyl-1,3-dioxane (82). A solution of diol **81** from the preceding experiment (319 mg, 1.17 mmol) in 6 mL of dry CH_2Cl_2 was treated with anisaldehyde dimethyl acetal (640 mg, 3.51 mmol) and PPTS (15 mg). The resulting solution was stirred at room temperature for 3 h. The reaction mixture was diluted with 50 mL of Et_2O , washed with 1 *N* KHSO_4 , saturated aqueous NaHCO_3 , and saturated NaCl solution, dried over MgSO_4 , and concentrated. Purification of the crude product by flash chromatography (SiO_2 , 5% EtOAc /hexanes) gave 434 mg (95%) of the *p*-methoxybenzylidene acetal **82** as a clear oil. This material was used immediately in the next step: ^1H NMR (500 MHz, CDCl_3) δ 7.42 (d, J = 8.8 Hz, 2 H), 6.89 (d, J = 8.6 Hz, 2 H), 5.47 (s, 1 H), 5.34 (s, 1 H), 4.14 (d, J = 11.0 Hz, 1 H), 3.96 (m, 1 H), 3.86 (d, J = 10.5 Hz, 1 H), 3.80 (s, 3 H), 2.54 (dd, J = 13.9, 11.2 Hz, 1 H), 2.26 (d, J = 13.9 Hz, 1 H), 1.78 (s, 3 H), 1.65 (m, 1 H), 1.56 (m, 1 H), 1.51-1.44 (m, 2 H), 1.31-1.25 (m, 5 H), 0.89 (t, J = 6.7 Hz, 3 H), 0.10 (s, 9 H).

(1*E*,4*R*,5*S*) 4-Hydroxymethyl-5- *p*-methoxybenzyloxy-2-methyl-1-trimethylsilyl-1-decene (17). A solution of the *p*-methoxybenzylidene acetal **82** (434 mg) in 20 mL of dry toluene was cooled to -10°C in an ice/acetone bath. DIBAL-H (2.3 mL, 2.22 mmol, 1.0 M in hexane) was added dropwise via syringe, and the yellowish solution was allowed to warm to

room temperature and stirred for 32 h. The reaction mixture was carefully quenched with saturated aqueous potassium sodium tartrate solution and stirred vigorously for 1 h to dissolve the aluminum salts. The biphasic mixture was diluted with Et₂O, and the organic layer was washed with saturated aqueous potassium sodium tartrate solution. The aqueous layer was washed with Et₂O (3×), and the combined organic layers were washed with saturated NaCl solution, dried over MgSO₄, and concentrated. Purification of the crude product by flash chromatography (SiO₂, 15% EtOAc/hexanes then 20% EtOAc/hexanes) gave 396 mg (91%) of **17** as a yellowish oil: $[\alpha]_D^{25}$ -6.1° (*c* = 1.62, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.27 (d, *J* = 8.8 Hz, 2 H), 6.89 (d, *J* = 8.8 Hz, 2 H), 5.24 (s, 1 H), 4.56 (A of AB, *J*_{AB} = 11.0 Hz, 1 H), 4.43 (B of AB, *J*_{AB} = 11.2 Hz, 1 H), 3.81 (s, 3 H), 3.72 (ddd, *J* = 11.4, 8.6, 3.3 Hz, 1 H), 3.55 (ddd, *J* = 11.2, 7.1, 4.4 Hz, 1 H), 3.48 (ddd, *J* = 9.0, 3.2, 3.2 Hz, 1 H), 2.96 (dd, *J* = 7.3, 3.4 Hz, 1 H), 2.28 (m, 1 H), 2.02 (A of ABX, *J*_{AB} = 13.4 Hz, *J*_{BX} = 7.4 Hz, 1 H), 1.97 (B of ABX, *J*_{AB} = 13.4 Hz, *J*_{BX} = 6.7 Hz, 1 H), 1.79 (d, *J* = 1.0 Hz, 3 H), 1.51 (m, 1 H), 1.49-1.41 (m, 2 H), 1.33-1.20 (m, 5 H), 0.89 (t, *J* = 7.2 Hz, 3 H), 0.10 (s, 9 H); ¹³C NMR (125 MHz, CDCl₃) δ 159.3, 152.6, 130.3, 129.6 (2), 126.1, 113.8 (2), 81.1, 71.4, 64.3, 55.2, 41.2, 39.0, 31.8, 29.1, 25.8, 22.6, 21.2, 14.0, 0.0 (3); FT-IR (thin film) 3436, 2954, 2860, 1614, 1514, 1466, 1303, 1248, 1174, 1038, 862, 837, 734, 690 cm⁻¹; HRMS (CI/NH₃) calcd for [C₂₃H₄₀O₃Si+H]⁺ 393.2825, found 393.2826 *m/z*.

(2*R*,3*S*)-2-(2-methyl-3-trimethylsilyl-*E*-prop-2-en-1-yl)-3-(*p*-methoxy-benzyloxy)-octanal (9**).** A 25-mL round bottom flask was charged with 106 μL (1.49 mmol) of anhydrous DMSO and 6 mL of dry CH₂Cl₂ and cooled to -78 °C in a dry ice/acetone bath. Oxalyl chloride (130 μL, 1.49 mmol) was added, and the solution was stirred at -78 °C for 10 min. A solution of 451 mg (1.15 mmol) of **17** in 1.5 mL of CH₂Cl₂ was added to the reaction mixture via cannula, rinsing with 1.5 mL of CH₂Cl₂. The resulting solution was stirred for an additional 10 min. Et₃N

(416 μ L, 2.99 mmol) was added dropwise, the cold bath was removed, and the reaction mixture was warmed to 0 °C and stirred for 10 min. The resulting cloudy suspension was diluted with H₂O and the layers were separated. The aqueous layer was washed with CH₂Cl₂ (3 $\times$). The combined organic layers were washed with saturated NaCl solution, dried over MgSO₄, and concentrated to a yellow oil (**9**) that was used immediately in the following reaction without further purification: ¹H NMR (500 MHz, CDCl₃) δ 9.76 (d, J = 2.2 Hz, 1 H), 7.24 (d, J = 8.4 Hz, 2 H), 6.87 (d, J = 8.8 Hz, 2 H), 5.20 (s, 1 H), 4.87 (A of AB, J_{AB} = 11.0 Hz, 1 H), 4.43 (B of AB, J_{AB} = 11.0 Hz, 1 H), 3.80 (s, 3 H), 3.67 (ddd, J = 8.8, 4.4, 4.4 Hz, 1 H), 2.74 (dddd, J = 10.4, 4.4, 4.4, 2.2 Hz, 1 H), 2.56 (ddd, J = 15.0, 8.4, 0.7 Hz, 1 H), 2.25 (ddd, J = 15.0, 6.2, 1.1 Hz, 1 H), 1.76 (s, 3 H), 1.55-1.20 (m, 8 H), 0.87 (t, J = 7.1 Hz, 3 H).

2',6'-Di-*t*-butyl-4'-methylphenyl (2*R*,3*S*,4*R*,5*S*)-3-Hydroxy-5-*p*-methoxybenzyloxy-2-methoxy-methyleneoxy-2-methyl-4-(*E*-2'-methyl-3-trimethylsilylprop-2-enyl)decanoate

(**18**). A solution of 807 μ L (5.70 mmol) of diisopropylamine in 10 mL of dry THF was cooled in to –30 °C and treated with 2.40 mL (5.7 mmol, 2.4 M in hexanes) of *n*-BuLi. The cold bath was removed and the solution was warmed to 0 °C for 30 min and then re-cooled to –78 °C. A solution of lactate ester **8**⁴ in THF (3.0 mL) and was added dropwise to the LDA solution via syringe, rinsing with an additional 1.0 mL of THF. The resulting bright yellow solution was warmed to –50 °C and stirred at for 10 min, then re-cooled to –95 °C. A solution of the crude aldehyde **9** in THF (2.5 mL) was added dropwise to the enolate solution via syringe while maintaining the internal temperature below –92 °C, rinsing with an additional 0.5 mL of THF. The solution was slowly warmed to –78 °C over 1 h and stirred at –78 ° for 1 h. The reaction was quenched by addition of saturated aqueous NH₄Cl, warmed to room temperature, and diluted

with 100 mL of Et₂O. The organic layer was washed with 1 N KHSO₄, saturated aqueous NaHCO₃, dried over MgSO₄, and concentrated. Purification of the crude product by flash chromatography (SiO₂, 6% to 12% EtOAc/hexanes) gave 2.20 g (78%) of an inseparable >11 : 1 mixture (as judged by ¹H-NMR) of **18** and the minor aldol isomer **19** as a yellow oil.

Characterization data for **18**: ¹H NMR (500 MHz, CDCl₃) δ 7.22 (d, *J* = 8.6 Hz, 2 H), 7.14 (s, 1 H), 7.13 (s, 1 H), 6.83 (d, *J* = 8.6 Hz, 2 H), 5.28 (s, 1 H), 5.15 (A of AB, *J*_{AB} = 7.6 Hz, 1 H), 4.88 (B of AB, *J*_{AB} = 7.6 Hz, 1 H), 4.51 (A of AB, *J*_{AB} = 11.2 Hz, 1 H), 4.45 (d, *J* = 8.3 Hz, 1 H), 4.27 (B of AB, *J*_{AB} = 11.5 Hz, 1 H), 3.79 (s, 3 H), 3.45 (s, 3H), 3.35 (bd, *J* = 9.8 Hz, 1 H), 2.82 (d, *J* = 8.1 Hz, 1 H), 2.60 (m, 2 H), 2.32 (s, 3 H), 2.17 (m, 1 H), 1.81 (s, 3 H), 1.77 (s, 3 H), 1.54-1.43 (m, 2 H), 1.35 (3, 9 H), 1.34 (s, 9 H), 1.33-1.20 (m, 3 H), 1.19-1.12 (m, 3 H), 0.84 (t, *J* = 7.3 Hz, 3H), 0.10 (s, 9 H); ¹³C NMR (125 MHz, CDCl₃) δ 173.0, 165.8, 159.0, 153.0, 146.5, 142.6, 142.2, 134.8, 131.0, 129.5 (2), 127.2, 127.1, 125.4, 113.6 (2), 93.3, 84.6, 79.0, 72.2, 70.7, 56.5, 55.2, 38.3, 36.4, 35.3, 32.2, 31.6, 31.5 (3), 31.4 (3), 29.6, 26.3, 22.8, 21.8, 21.4, 20.0, 14.0, 0.0 (3); FT-IR (thin film) 3571, 2955, 1756, 1614, 1514, 1464, 1417, 1395, 1365, 1302, 1247, 1173, 1145, 1063, 838, 758, 690 cm⁻¹; HRMS (FAB) calcd for [C₄₃H₇₀O₇Si+Na]⁺ 749.4789, found 749.4778 *m/z*.

DDQ oxidation of PMB ether **18** gave the p-methoxybenzylidene (PMP) acetal **83**. Key ¹H NOE enhancements were observed between the C(7), C(25), and the acetal methine protons,

clearly indicating the *syn*-1,3-diol relationship. Further, ^1H NOE enhancements between the C(8)-H and C(6)-Me as well as between the acetal methine and the aryl ring dicte that C(6) has (*R*)-configuration, as shown.

(2*S*,3*S*,4*R*,5*S*)-3-Hydroxy-5-*p*-methoxybenzyloxy-2-methoxymethyleneoxy-2-methyl-4-(*E*-2'-methyl-3'-trimethylsilylprop-2'-enyl)decan-1-ol (20). A 35 mL round bottom flask was charged with 3.0 mL (2.0 mmol) of a 0.67 M solution of LiAlH_4 in THF. A solution of 600 mg (0.82 mmol) of esters **18** and **19** (>11 : 1) in 2 mL of THF was added dropwise followed by rinsing (0.5 mL of THF). The resulting solution was stirred at room temperature for 13 h. The excess hydride was quenched by the careful addition of EtOAc (300 μL). The resulting solution was diluted with Et_2O then saturated aqueous Rochelle's salt and the biphasic mixture was stirred vigorously for 8 h. The organic layer was separated and the aqueous was washed with Et_2O (3 $\times$). The combined organic layers were washed with saturated NaCl solution, dried over MgSO_4 , and concentrated. Purification of the crude product by flash chromatography (SiO_2 , gradient 20% to 50% EtOAc/hexanes) gave 363 mg (93%) of diol **20** as a yellow oil and 27 mg (6.4%) of the diastereomeric diol **21**. Data for **20**: $[\alpha]_D^{26} -16.8^\circ$ ($c = 1.71$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.23 (d, $J = 8.8$ Hz, 2 H), 6.86 (d, $J = 8.6$ Hz, 2 H), 5.23 (s, 1 H), 4.90 (A of AB, $J_{AB} = 7.6$ Hz, 1 H), 4.75 (B of AB, $J_{AB} = 7.3$ Hz, 1 H), 4.43 (A of AB, $J_{AB} = 11.5$ Hz, 1 H), 4.30 (B of AB, $J_{AB} = 11.5$ Hz, 1 H), 3.97 (d, $J = 3.7$ Hz, 1 H), 3.79 (s, 3 H), 3.70 (dd, $J = 12.5, 4.4$ Hz, 1 H), 3.62 (dd, $J = 12.7, 9.3$ Hz, 1 H), 3.55 (dd, $J = 9.3, 4.6$ Hz, 1 H), 3.43 (s, 3H), 3.35 (ddd, $J = 9.0, 3.2, 3.2$ Hz, 1 H), 2.82 (d, $J = 3.9$ Hz, 1 H), 2.82 (d, $J = 3.9$ Hz, 1 H), 2.43 (d, $J = 13.9$ Hz, 1 H), 2.18 (ddd, $J = 11.5, 2.7, 2.7$ Hz, 1 H), 2.09 (dd, $J = 14.2, 11.5$ Hz, 1 H), 1.75 (s, 3 H), 1.57-

1.51 (m, 2 H), 1.43 (m, 1 H), 1.29-1.20 (m, 2 H), 1.19-1.12 (m, 3 H), 1.16 (s, 3 H), 0.85 (t, $J = 7.2$ Hz, 3H), 0.10 (s, 9 H); ^{13}C NMR (125 MHz, CDCl_3) δ 159.3, 153.1, 130.2, 129.9 (2), 125.8, 113.8 (2), 91.2, 82.4, 79.6, 72.5, 71.1, 67.0, 55.7, 55.2, 38.6, 37.6, 31.7, 29.3, 26.2, 22.7, 21.4, 16.2, 14.1, 0.0 (3); FT-IR (thin film) 3437, 2954, 2858, 1613, 1514, 1466, 1302, 1248, 1173, 1142, 1115, 1037, 870, 837 cm^{-1} ; HRMS (FAB) calcd for $[\text{C}_{28}\text{H}_{50}\text{O}_6\text{Si}+\text{Na}]^+$ 533.3274, found 533.3257 m/z .

(2*S*,3*S*,4*R*,5*S*)-2,5-*O*-Methylidene-2-methyl-4-(prop-2'-en-1'-yl)-3-

[(triethylsilyl)oxy]-1-trimethylacetoxyl-decane (25).⁴ A flame-dried 25-mL round bottom flask was charged with 224 mg (0.441 mmol) of pivalate **22**⁴ and 7.5 mL of CH_2Cl_2 . The solution was treated sequentially with 410 μL (3.52 mmol) of 2,6-lutidine and 398 μL (1.76 mmol) of TESOTf, and the resulting mixture stirred at 23 °C for 4 h. Saturated aqueous NaHCO_3 was added, then the layers were separated and the aqueous layer was washed with CH_2Cl_2 (3 $\times$). The combined organic layers were washed with 1 *N* KHSO_4 and saturated aqueous NaHCO_3 , dried over MgSO_4 , and concentrated. Purification of the crude product by flash chromatography (SiO_2 , 4% EtOAc/hexanes then 5% EtOAc/hexanes) gave 161 mg (78%) of acetal **25** as a colorless oil: $[\alpha]_D^{25} +16.7^\circ$ ($c = 0.91$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 5.82 (ddd, $J = 18.7$, 10.3, 8.6, 5.9 Hz, 1 H), 5.08 (m, 2 H), 4.85 (A of AB, $J_{AB} = 5.9$ Hz, 1 H), 4.78 (B of AB, $J_{AB} = 5.8$ Hz, 1 H), 4.35 (A of AB, $J_{AB} = 11.2$ Hz, 1 H), 4.18 (dd, $J = 9.5$, 2.5 Hz, 1 H), 3.90 (B of AB, $J_{AB} = 11.2$ Hz, 1 H), 3.88 (d, $J = 3.2$ Hz, 1 H), 2.47 (m, 1 H), 2.28 (ddd, $J = 14.9$, 9.3, 9.3 Hz, 1 H), 1.78 (m, 1 H), 1.68 (m, 1 H), 1.43 (m, 1 H), 1.38 (s, 3 H), 1.33-1.25 (m, 6 H), 1.21 (s, 9 H), 0.96 (t, $J = 7.9$ Hz, 9 H), 0.88 (t, $J = 6.9$ Hz, 3 H), 0.61 (q, $J = 8.3$ Hz, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 178.2, 137.9, 116.4, 90.2, 80.8, 75.3, 73.7, 67.8, 52.3, 38.9, 33.5, 31.7, 30.9, 27.2 (3), 26.2, 22.6, 19.4, 14.0, 7.0 (3), 5.1 (3); FT-IR (thin film) 3078, 2957, 2878, 1736, 1459, 1414,

1378, 1283, 1238, 1147, 1073, 1004, 837, 741 cm^{-1} ; HRMS (CI/ NH_3) calcd for $[\text{C}_{26}\text{H}_{50}\text{O}_5\text{Si}+\text{H}]^+$ 471.3514, found 471.3506 m/z ; Anal. calcd for $\text{C}_{26}\text{H}_{50}\text{O}_5\text{Si}$: C, 66.34; H, 10.71; found C, 66.40; H, 10.85.

(2*S*,3*S*,4*R*,5*S*)-1-Trimethylacetoxy-3-hydroxy-5-*p*-methoxybenzyloxy-2-methoxymethyleneoxy-2-methyl-4-(*E*-2'-methyl-3'-trimethylsilylprop-2'-enyl)decane (28).

A solution of 1.16 g (2.30 mmol) of diol **20** in 10 mL of CH_2Cl_2 and 3 mL of dry pyridine was treated with 560 μL (4.60 mmol) of pivaloyl chloride. The solution was stirred at room temperature for 7 h. The reaction mixture was diluted with 100 mL of Et_2O , washed with 1 *N* KHSO_4 (4 x 15 mL) NaHCO_3 (1 x 25 mL), dried over MgSO_4 , and concentrated. Purification of the crude product by flash chromatography (25 g SiO_2 , 10% EtOAc /hexanes) gave 1.30 g (96%) of pivalate **28** as a yellow oil: $[\alpha]_{\text{D}}^{24} -33.7^\circ$ ($c = 1.34$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.22 (d, $J = 8.6$ Hz, 2 H), 6.84 (d, $J = 8.6$ Hz, 2 H), 5.24 (s, 1 H), 4.81 (A of AB, $J_{\text{AB}} = 7.1$ Hz, 1 H), 4.75 (B of AB, $J_{\text{AB}} = 7.1$ Hz, 1 H), 4.45 (A of AB, $J_{\text{AB}} = 11.2$ Hz, 1 H), 4.27 (A of AB, $J_{\text{AB}} = 11.5$ Hz, 1 H), 4.24 (B of AB, $J_{\text{AB}} = 11.2$ Hz, 1 H), 4.16 (B of AB, $J_{\text{AB}} = 11.5$ Hz, 1 H), 3.87 (d, $J = 6.6$ Hz, 1 H), 3.79 (s, 3 H), 3.38 (s, 3 H), 3.31 (ddd, $J = 9.8, 2.7, 2.6$ Hz, 1 H), 2.62 (d, $J = 6.6$ Hz, 1 H), 2.45 (A of ABX, $J_{\text{AB}} = 14.4$, $J_{\text{AX}} = 2.0$ Hz, 1 H), 2.29 (ddd, $J = 11.2, 3.2, 2.9$ Hz, 1 H), 2.11 (B of ABX, $J_{\text{AB}} = 14.2$, $J_{\text{BX}} = 11.2$ Hz, 1 H), 1.80 (s, 3 H), 1.60 – 1.52 (m, 1H), 1.51 – 1.38 (m, 2 H), 1.28 (s, 3 H), 1.28 – 1.20 (m, 2 H), 1.20 (s, 9H), 1.16 – 1.10 (m, 3 H), 0.84 (t, $J = 7.1$ Hz, 3H), 0.09 (s, 9 H); ^{13}C NMR (125 MHz, CDCl_3) δ 178.1, 159.1, 153.1, 130.8, 129.6, 125.7, 113.7, 91.6, 80.9, 79.3, 72.0, 70.7, 66.9, 55.7, 55.3, 38.8, 38.4, 36.6, 31.6, 29.4, 27.2, 26.2, 22.8, 21.6, 17.6, 14.1, 0.03; FT-IR (neat) 3520, 2956, 1732, 1614, 1514, 1481, 1464, 1398, 1284,

1248, 1148, 1080, 1036, 921, 870, 837 cm^{-1} ; HRMS (FAB) calcd for $[\text{C}_{33}\text{H}_{58}\text{O}_7\text{Si}+\text{Na}]^+$ 617.3849, found 617.3853 m/z .

(2*S*,3*S*,4*R*,5*S*)-2,5-*O*-Methylidene-2-methyl-4-(*E*-2'-methyl-3'-trimethylsilylprop-2'-enyl)-3-[(triethylsilyl)oxy]-1-trimethylacetoxy-decane (29). A 50 mL round-bottom flask with septum was charged with 815 mg (1.37 mmol) of pivaloate ester **28** and 16 mL of CH_2Cl_2 . The solution was treated sequentially with 1.28 mL (12.6 mmol) of 2,6-lutidine and 1.24 mL (5.50 mmol) of TESOTf, and stirred at room temperature for 4 h. After quenching the reaction with saturated aqueous NaHCO_3 and separation of the layers, the aqueous layer was washed with Et_2O . The combined organic layers were washed with 1 *N* KHSO_4 and saturated aqueous NaHCO_3 , dried over MgSO_4 , and concentrated. Purification of the crude product by flash chromatography (30 g of SiO_2 , gradient 0.5% to 4% EtOAc /hexanes) gave 620 mg (84%) of acetal **29** as a colorless oil which contained about 10% of an impurity that was carried through the next reaction: $[\alpha]_D^{24} +11.6^\circ$ ($c = 1.17$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 5.29 (s, 1 H), 4.84 (A of AB, $J_{AB} = 6.1$ Hz, 1 H), 4.77 (B of AB, $J_{AB} = 6.1$ Hz, 1 H), 4.36 (A of AB, $J_{AB} = 11.5$ Hz, 1 H), 4.19 (dd, $J = 9.5, 2.4$ Hz, 1 H), 3.90 (B of AB, $J_{AB} = 11.2$ Hz, 1 H), 3.89 (d, $J = 3.2$ Hz, 1 H), 2.38 (A of ABX, $J_{AB} = 15.4$, $J_{AX} = 4.0$ Hz, 1 H), 2.28 (B of ABX, $J_{AB} = 15.4$, $J_{BX} = 9.0$ Hz, 1 H), 1.92 – 1.87 (m, 1 H), 1.81 (s, 3 H), 1.72 – 1.63 (m, 1 H), 1.48 – 1.36 (m, 1 H), 1.37 (s, 3 H), 1.35–1.20 (m, 6 H), 1.20 (s, 3 H), 0.96 (t, $J = 8.1$ Hz, 9 H), 0.87 (t, $J = 6.8$ Hz, 3H), 0.65 – 0.58 (m, 6 H), 0.10 (s, 9 H); ^{13}C NMR (125 MHz, CDCl_3) δ 178.2, 153.5, 125.3, 90.2, 80.9, 75.5, 74.2, 67.7, 49.9, 38.9, 38.7, 33.4, 31.8, 27.2, 26.3, 22.6, 22.1, 20.5, 14.0, 6.95, 5.09, -0.07; FT-IR (thin film) 2957, 1732, 1614, 1480, 1463, 1378, 1283, 1128, 1065, 838, 769, 743 cm^{-1} ; HRMS (FAB) calcd for $[\text{C}_{30}\text{H}_{60}\text{O}_5\text{Si}_2+\text{Na}]^+$ 579.3877, found 579.3888 m/z .

Synthesis of (2*S*,3*S*,4*R*,5*S*)-2,5-*O*-Methylidene-2-methyl-4-(*E*-2'-methyl-3'-trimethylsilylprop-2'-enyl)-3-[(triethylsilyl)oxy]-1-(2',6'-Di-*t*-butyl-4'-methylphenylcarboxy)-decane (32). A flame-dried 1 mL Wheaton vial was charged with a solution 23 mg (0.032 mmol) of ester **18** and 300 μ L of CH_2Cl_2 . The solution was treated sequentially with 38 μ L (0.32 mmol) of 2,6-lutidine and 64 μ L (0.28 mmol) of TESOTf, and heated to reflux for 24 h. After quenching the reaction with saturated aqueous NaHCO_3 and separation of the layers, the aqueous layer was washed with Et_2O . The combined organic layers were washed with 1 *N* KHSO_4 and saturated aqueous NaHCO_3 , dried over MgSO_4 , and concentrated. Purification of the crude product by prep-plate chromatography (250 μ m, 5% EtOAc /hexanes) gave 12.3 mg (58%) of acetal **32**, and 4.9 mg of acetal **33** (23%):

Data for 32: ^1H NMR (500 MHz, CDCl_3) δ 7.10 (s, 2H), 5.33, (s, 1H), 5.09, (A of AB, $J_{AB} = 6.1$ Hz, 1 H), 5.02, (A of AB, $J_{AB} = 5.1$ Hz, 1 H), 4.25, (d, $J = 3.4$, 1H), 4.21, (d, $J = 9.3$ Hz, 1H) 2.42- 2.36, (m, 1H), 2.34 – 2.26, (m, 1H), 2.31 (s, 3H), 1.70 – 1.60, (m, 1H), 1.52 – 1.42, (m, 1H), 1.36, (s, 9H), 1.36 – 1.24, (m, 6H), 1.33 (s, 9H), 0.92, (app. q, $J = 8.1$ Hz, 9H), 0.70 – 0.50, (m, 6H), 0.10 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 171.2, 153.4, 146.9, 142.9, 142.1, 134.1, 126.9, 126.8, 125.5, 90.2, 84.7, 76.6, 74.5, 40.0, 35.33, 35.32, 31.8, 31.5, 31.4, 26.3, 22.6, 22.0, 21.7, 21.4, 14.0, 7.1, 5.2, –0.08; HRMS (FAB) calcd for $[\text{C}_{40}\text{H}_{72}\text{O}_5\text{Si}_2+\text{Na}]^+$ 711.4816, found 711.4830 m/z .

Data for 33: ^1H NMR (500 MHz, CDCl_3) δ 7.19, (d, $J = 8.4$ Hz, 2H), 7.12, (s, 1H), 6.81, (d, $J = 8.8$ Hz, 2H), 5.25, (s, 1H), 5.22, (dd, $J = 6.6$, 1.1 Hz, 2H), 4.82, (s, 1H), 4.42, (A of AB, $J_{AB} = 11.7$ Hz, 1 H) 4.37 (B of AB, $J_{AB} = 11.7$ Hz, 1 H), 3.78, (s, 3H), 3.33 (app.dt, $J = 9.5$, 2.6 Hz, 1H), 2.42- 2.33, (m, 1H), 2.33, (s, 3H), 2.24 – 2.15, (m, 1H), 1.75, (s, 3H), 1.68, (s, 3H), 1.60

– 1.40 , (m, 3H), 1.32 (s, 9H), 1.30 (s, 9H), 1.30 – 1.20, (m, 2H), 1.20 – 1.12, (m, 3H), 0.85, (t, $J = 7.3$ Hz, 3H), 0.10 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 173.1, 159.0, 152.1, 146.4, 142.5, 141.9, 134.7, 131.1, 129.5, 127.1, 127.0, 126.2, 113.6, 95.5, 83.5, 78.1, 78.0, 70.7, 55.2, 38.7, 37.5, 35.3, 31.7, 31.4, 30.0, 26.2, 22.8, 21.4, 20.1, 14.1, -0.01; FT-IR (thin film) 2956, 1748, 1615, 1514, 1456, 1418, 1366, 1249, 1180, 1098, 838, 736, 699 cm^{-1} ; HRMS (FAB) calcd for $[\text{C}_{42}\text{H}_{66}\text{O}_6\text{Si}+\text{Na}]^+$ 717.4526, found 717.4529 m/z .

(2*S*,3*S*,4*R*,5*S*)-2,5-*O*-Methylidene-2-methyl-4-(*E*-2'-methyl-3'-iodoprop-2'-enyl)-3-[(triethylsilyl)oxy]-1-trimethylacetoxyl-decane (84**).** A 100 mL round bottom flask was charged with a solution of 600 mg (1.11 mmol) of vinylsilane **29** in dry CH_3CN (30 mL) and cooled in an ice bath. *N*-iodosuccinimide (374 mg, 1.66 mmol) was added in a single portion and the solution was stirred at room temperature for 1 h. An additional 115 mg (0.50 mmol) of *N*-iodosuccinimide was added and the reaction was stirred for 4 h until complete. The reaction mixture was diluted with 100 mL of Et_2O and washed with $\text{Na}_2\text{S}_2\text{O}_3$ (1 x 20 mL). The aqueous layer was washed with 10 mL of Et_2O . The combined organic layers were washed with saturated NaCl solution, dried over MgSO_4 , and concentrated. The crude oily solid was suspended in hexanes and filtered to remove the solid succinimide and the filtrate concentrated to provide 675 mg (99%) of vinyl iodide **84** as a clear oil that was sufficiently pure for the next reaction: ^1H NMR (500 MHz, CDCl_3) δ 5.98 (s, 1 H), 4.84 (A of AB, $J_{AB} = 5.9$ Hz, 1 H), 4.76 (B of AB, $J_{AB} = 5.9$ Hz, 1 H), 4.35 (A of AB, $J_{AB} = 11.2$ Hz, 1 H), 4.20 (dd, $J = 8.8, 1.8$ Hz, 1 H), 3.92 (B of AB, $J_{AB} = 11.2$ Hz, 1 H), 3.78 (d, $J = 2.9$ Hz, 1 H), 2.55 – 2.42, (m, 2H), 1.88 (s, 3 H), 1.84, (m, 1 H), 1.68 (m, 1 H), 1.46 – 1.38 (m, 1 H), 1.39 (s, 3 H), 1.36 – 1.22 (m, 6 H), 1.20 (s, 9 H), 1.10 – 0.94, (m, 9H), 0.88 (t, $J = 6.8$ Hz, 3H), 0.65 – 0.58 (m, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ

178.1, 146.4, 90.2, 80.8, 76.5, 75.3, 73.7, 67.6, 50.0, 38.9, 36.4, 33.4, 31.7, 27.2, 26.2, 24.2, 22.6, 20.2, 14.0, 7.0, 5.1; FT-IR (neat) 3449(br), 2957, 2878, 1732, 1480, 1462, 1378, 1282, 1128, 1063, 1009, 838, 743, 685 cm^{-1} ; HRMS (FAB) calcd for $[\text{C}_{27}\text{H}_{51}\text{IO}_5\text{Si}_2+\text{Na}]^+$ 633.2448, found 633.2457 m/z .

(2*S*,3*S*,4*R*,5*S*)-2,5-*O*-Methylidene-2-methyl-4-(*E*-2'-methyl-3'-iodoprop-2'-enyl)-3-[(triethylsilyl)oxy]-decan-1-ol (85**).** A solution of 660 mg (0.067 mmol) of the pivalate ester **84** in 20 mL of dry CH₂Cl₂ was cooled in a dry ice/acetone bath and treated dropwise with 2.78 mL (2.78 mmol, 1 M in hexanes) of DIBAL-H. The reaction mixture was stirred at -78 °C for 45 min and then quenched with saturated aqueous potassium sodium tartrate solution (15 mL) and diluted with Et₂O (50 mL). The biphasic mixture was stirred for 12 h, the layers separated, the aqueous reextracted with Et₂O (2 × 15 mL). The combined organic layers were washed saturated NaCl solution, dried over MgSO₄, and concentrated. Purification of the crude product by flash chromatography (30 g of SiO₂, 20% to 25% EtOAc/hexanes) gave 518 mg (91%) slightly impure alcohol. HPLC purification (21 mm column; 30% EtOAc/hexanes) of this material furnished 480 mg (85%) of pure neopentyl alcohol **85** as a light yellow oil: $[\alpha]_D^{25} +14.2^\circ$ ($c = 0.77$, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 5.99 (s, 1 H), 4.89 (A of AB, $J_{AB} = 5.9$ Hz, 1 H), 4.87 (B of AB, $J_{AB} = 6.1$ Hz, 1 H), 4.18 (dd, $J = 9.8, 2.4$ Hz, 1 H), 3.86 (dd, $J = 11.2, 2.2$ Hz, 1 H), 3.77 (d, $J = 2.9$ Hz, 1 H), 3.37 (dd, $J = 10.5, 10.5$ Hz, 1 H), 2.51 (dd, $J = 14.8, 4.3$ Hz, 1 H), 2.45 (dd, $J = 14.9, 8.8$ Hz, 1 H), 1.95 (dd, $J = 9.9, 2.8$ Hz, 1 H), 1.87 (s, 3 H), 1.84 (m, 1 H), 1.67 (m, 1H), 1.41 (m, 1 H), 1.38 (s, 3 H), 1.32-1.24 (m, 6 H), 0.96 (t, $J = 8.0$ Hz, 9 H), 0.88 (t, $J = 6.8$ Hz, 3H), 0.60 (q, $J = 7.7$ Hz, 3 H), 0.59 (q, $J = 8.1$ Hz, 3 H); ¹³C NMR (125 MHz,

CDCl₃) δ 146.5, 90.3, 81.9, 76.7, 76.6, 73.8, 68.3, 50.0, 36.5, 33.3, 31.7, 26.2, 24.3, 22.3, 19.9, 14.0, 6.9 (3), 5.0 (3); FT-IR (thin film) 3468, 3054, 2955, 2932, 2876, 1459, 1413, 1377, 1271, 1237, 1125, 1066, 836, 737, 725 cm⁻¹; HRMS (FAB) calcd for [C₂₂H₄₃IO₄Si+Na]⁺ 549.1875, found 549.1895 *m/z*.

(2*S*,3*S*,4*R*,5*S*)-2,5-*O*-Methylidene-2-methyl-4-(*E*-2'-methyl-3'-iodoprop-2'-enyl)-3-[(triethylsilyl)oxy]-decan-1-al (34**).** A solution of 60 μ L (0.84 mmol) of anhydrous DMSO in 4.0 mL of CH₂Cl₂ was cooled in a dry ice/acetone bath, treated with 55 μ L (0.63 mmol) of oxalyl chloride, and stirred for 15 min. A solution of 222 mg (0.42 mmol) of the neopentyl alcohol **85** in 0.5 mL of CH₂Cl₂ was added dropwise to the reaction mixture followed by 0.5 mL rinse, and the resulting solution was stirred at -78 °C for 20 min. Et₃N (55 μ L, 0.388 mmol) was added, the cold bath was removed, and the cloudy suspension was allowed to warm to 0 °C. After dilution of the mixture with pentanes (30 mL), the reaction was filtered to remove the Et₃N salts and the filtrate was washed with H₂O (2 $\times$ 5 mL). The combined organics were washed with saturated aqueous NaHCO₃, dried over MgSO₄, and concentrated. The crude material was passed through a short pad of SiO₂ with 30% EtOAc/hexanes to provide 215 mg (97%) of aldehyde **34** as a yellow oil: ¹H NMR (500 MHz, CDCl₃) δ 9.52 (s, 1 H), 6.01 (s, 1 H), 5.00 (A of AB, *J*_{AB} = 5.8 Hz, 1 H), 4.94 (B of AB, *J*_{AB} = 5.8 Hz, 1 H), 4.25 (dd, *J* = 9.6, 2.6 Hz, 1 H), 4.07 (d, *J* = 2.8 Hz, 1 H), 2.51 (dd, *J* = 14.5, 3.8 Hz, 1 H), 2.36 (dd, *J* = 14.9, 9.5 Hz, 1 H), 1.87 (s, 3 H), 1.80 (m, 1H), 1.69 (m, 1 H), 1.43 (m, 1 H), 1.37 (s, 3 H), 1.31-1.25 (m, 6 H), 0.92 (t, *J* = 7.9 Hz, 9 H), 0.89 (t, *J* = 7.0 Hz, 3H), 0.55 (q, *J* = 7.6 Hz, 3 H), 0.54 (q, *J* = 8.2 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 203.0, 145.9, 90.7, 86.5, 76.9, 76.6, 73.6, 49.9, 35.9, 33.2, 31.7, 26.4, 24.2, 22.6, 17.6, 14.0, 6.8

(3), 5.0 (3); FT-IR (thin film) 2955, 2933, 2877, 1740, 1458, 1413, 1375, 1271, 1138, 1126, 1062, 1008, 726 cm^{-1} ; HRMS (FAB) calcd for $[\text{C}_{22}\text{H}_{41}\text{IO}_4\text{Si}+\text{Na}]^+$ 547.1717, found 547.1716 m/z .

Ethyl-(4*S*,5*S*,6*R*,7*S*)-2,4-dimethyl-4,7-*O*-methylidene-6-(*E*-2'-methyl-3'-iodoprop-2'-enyl)-5-[(triethylsilyl)oxy]-dodec-2-enoate (86). A 25 mL round bottom flask fitted with a cold-finger condensor was charged with 215 mg (0.41 mmol) of aldehyde **34** [pre-dried by coevaporation from PhH (2×)] and 10 mL of toluene. Carbethoxyethylidenetriphenylphosphorane (148 mg, 3.70 mmol) was added in a single portion, and the resulting yellow suspension was heated to vigorous reflux for 18 h. After being cooled to room temperature, the reaction was diluted with hexanes, filtered and concentrated to remove Ph_3PO and unreacted carbethoxyethylidenetriphenylphosphorane. The filtrate was concentrated and the preceding process repeated two more times to remove the majority of Ph_3PO and unreacted carbethoxyethylidenetriphenylphosphorane. The residue was purified by flash chromatography (15 g of SiO_2 , 5% EtOAc/hexanes) to give 245 mg (99%) of **86** as a 10:1 mixture of *E*:*Z* olefin isomers. Spectral data for the *E* olefin isomer: $[\alpha]_D^{26} +1.3^\circ$ ($c = 1.50$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.01 (d, $J = 1.5$ Hz, 1 H), 6.00 (s, 1 H), 4.91 (A of AB, $J_{AB} = 6.6$ Hz, 1 H), 4.74 (B of AB, $J_{AB} = 6.4$ Hz, 1 H), 4.19 (q, $J = 7.1$ Hz, 2 H), 4.08 (dd, $J = 9.5, 2.9$ Hz, 1 H), 3.79 (d, $J = 3.4$ Hz, 1 H), 2.49 (m, 2 H), 1.96 (d, $J = 1.2$ Hz, 3 H), 1.87 (d, $J = 1.0$ Hz, 3 H), 1.86 (m, 1 H), 1.66 (m, 1H), 1.48 (s, 3 H), 1.42 (m, 1 H), 1.32-1.25 (m, 6 H), 1.30 (t, $J = 7.2$ Hz, 3 H), 0.95 (t, $J = 8.0$ Hz, 9 H), 0.89 (t, $J = 6.8$ Hz, 3H), 0.61 (q, $J = 7.7$ Hz, 3 H), 0.60 (q, $J = 8.0$ Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 168.6, 146.5, 13.8, 128.3, 90.3, 83.4, 78.5, 76.5, 74.3, 60.7, 49.4, 37.1, 33.2, 31.7, 26.2, 24.2, 24.1, 22.6, 14.2, 14.0, 13.1, 7.0 (3), 5.1 (3); FT-IR (thin film) 3054,

2955, 2933, 2876, 1712, 1458, 1376, 1250, 1168, 1061, 828, 744 cm^{-1} ; HRMS (FAB) calcd for $[\text{C}_{27}\text{H}_{49}\text{IO}_5\text{Si}+\text{Na}]^+$ 631.2292, found 631.2320.

(4*S*,5*S*,6*R*,7*S*)-2,4-Dimethyl-4,7-*O*-methylidene-6-(*E*-2'-methyl-3'-iodoprop-2'-enyl)-5-[(triethylsilyl)oxy]-dodec-2-en-1-ol (87). A solution of 245 mg (0.40 mmol) of the ester **86** in 3.0 mL of dry CH_2Cl_2 was cooled in a dry ice/acetone bath, treated dropwise with 1.0 mL (1.0 mmol, 1.0 M in hexanes) of DIBAL-H, and stirred at -78°C for 30 min. After carefully quenching the reaction mixture with saturated aqueous potassium sodium tartrate solution and diluting with Et_2O (25 mL), the biphasic mixture was stirred vigorously at room temperature for 1 h. The aqueous layer was separated and washed with Et_2O (3×10 mL). The combined organic layers were washed with H_2O and saturated NaCl solution, dried over MgSO_4 , and concentrated. Purification of the crude product by flash chromatography (12 g of SiO_2 , 10 % to 20% EtOAc /hexanes) gave 205 mg (90%) of the allylic alcohol **87** as a slightly yellow oil: $[\alpha]_D^{25} -14.1^\circ$ ($c = 1.18$, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 5.98 (d, $J = 1.0$ Hz, 1 H), 5.79 (d, $J = 1.3$ Hz, 1 H), 4.88 (A of AB, $J_{AB} = 6.4$ Hz, 1 H), 4.78 (B of AB, $J_{AB} = 6.4$ Hz, 1 H), 4.01 (m, 3 H), 3.69 (d, $J = 3.7$ Hz, 1 H), 2.52 (A of ABX, $J_{AB} = 14.7$ Hz, $J_{AX} = 8.1$ Hz, 1 H), 2.44 (B of ABX, $J_{AB} = 14.7$ Hz, $J_{BX} = 4.4$ Hz, 1 H), 1.87 (m, 1 H), 1.86 (d, $J = 1.2$ Hz, 3 H), 1.77 (d, $J = 1.2$ Hz, 3 H), 1.65 (m, 1 H), 1.47 (s, 3 H), 1.38 (m, 1 H), 1.34-1.25 (m, 6 H), 0.96 (t, $J = 8.0$ Hz, 9 H), 0.89 (t, $J = 6.9$ Hz, 3H), 0.60 (q, $J = 8.1$ Hz, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 146.7, 136.4, 128.0, 89.8, 82.8, 78.9, 76.4, 74.3, 69.6, 49.1, 37.6, 32.8, 31.7, 26.2, 25.8, 24.0, 22.6, 14.5, 14.0, 7.0 (3), 5.2 (3); FT-IR (thin film) 3401, 3054, 2954, 2931, 2875, 1458, 1376, 1270, 1235,

1077, 1037, 1011, 815, 726 cm^{-1} ; HRMS (FAB) calcd for $[\text{C}_{25}\text{H}_{47}\text{IO}_4\text{Si}+\text{Na}]^+$ 589.2186, found 589.2200 m/z .

(4*S*,5*S*,6*R*,7*S*)-2,4-dimethyl-4,7-*O*-methylenedioxy-6-(*E*-2'-methyl-3'-iodoprop-2'-enyl)-5-[(triethylsilyl)oxy]-dodec-2-en-1-al (35**).** A solution of 51 μL (0.72 mmol) of anhydrous DMSO in 3.0 mL of CH_2Cl_2 was cooled in a dry ice/acetone bath, treated with 47 μL (0.54 mmol) of oxalyl chloride, and stirred for 15 min. A solution of 205 mg (0.36 mmol) of the allylic alcohol **87** in 300 μL of CH_2Cl_2 was added dropwise to the reaction mixture, followed by CH_2Cl_2 rinse (0.30 mL). The solution was stirred for 30 min. Et_3N (151 μL , 1.08 mmol) was added, and the cloudy reaction mixture was allowed to warm to $0\text{ }^\circ\text{C}$ over 30 min and stirred at $0\text{ }^\circ\text{C}$ for an additional 10 min. The white suspension was diluted with pentanes (30 mL), and the reaction was filtered to remove the majority of the Et_3N salts. The filtrate was washed with H_2O (2×5 mL). The combined organics were washed with saturated aqueous NaHCO_3 , dried over MgSO_4 , and concentrated to give 211 mg ($>99\%$) of aldehyde **35** as a clear oil: ^1H NMR (500 MHz, CDCl_3) δ 9.40 (s, 1 H), 6.69 (d, $J = 1.4$ Hz, 1 H), 6.02 (d, $J = 0.8$ Hz, 1 H), 4.93 (A of AB, $J_{AB} = 6.3$ Hz, 1 H), 4.72 (B of AB, $J_{AB} = 6.6$ Hz, 1 H), 4.07 (dd, $J = 9.3, 2.3$ Hz, 1 H), 3.86 (d, $J = 3.3$ Hz, 1 H), 2.51 (m, 2 H), 1.90 (m, 1 H), 1.88 (d, $J = 1.1$ Hz, 3 H), 1.87 (d, $J = 1.4$ Hz, 3 H), 1.67 (m, 1 H), 1.53 (s, 3 H), 1.43 (m, 1 H), 1.33-1.25 (m, 6 H), 0.95 (t, $J = 7.8$ Hz, 9 H), 0.89 (t, $J = 6.9$ Hz, 3 H), 0.59 (q, $J = 7.8$ Hz, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 195.7, 156.8, 146.3, 138.5, 90.4, 83.7, 78.2, 76.7, 74.4, 48.5, 37.0, 33.0, 31.7, 26.2, 24.1, 23.9, 22.6, 14.0, 9.9, 7.0 (3), 5.2 (3); FT-IR (thin film) 3054, 2955, 2932, 2876, 2703, 1693, 1458, 1411, 1376, 1271, 1233, 1199,

1120, 1062, 1017, 818, 725 cm^{-1} ; HRMS (FAB) calcd for $[\text{C}_{25}\text{H}_{45}\text{IO}_4\text{Si}+\text{Na}]^+$ 587.2030, found 587.2049 m/z .

Synthesis of Methyl-(6*S*,7*S*,8*R*,9*S*)-4,6-dimethyl-6,9-*O*-methylidene-8-(*E*-2'-methyl-3'-iodoprop-2'-enyl)-7-[(triethylsilyl)oxy]-dodeca-2,4-dienoate (7). A 5 mL round bottom flask fitted with a cold-finger condensor was charged with 211 mg (0.36 mmol) of aldehyde **35** [pre-dried by coevaporation from PhH (2 $\times$)] and 2 mL of benzene. Methyl triphenylphosphorylideneacetate (361 mg, 1.08 mmol) was added in a single portion, and the resulting suspension was heated to 65 – 70 $^{\circ}\text{C}$ for 13 h. After being cooled to room temperature, the reaction was diluted with hexanes, filtered and concentrated to remove Ph_3PO and unreacted methyl triphenylphosphorylideneacetate. The filtrate was concentrated and the preceding process repeated two more times to remove the majority of Ph_3PO and unreacted methyl triphenylphosphorylideneacetate. The residue was flushed through 5 g of SiO_2 , (15% EtOAc/hexanes) followed by purification by HPLC to give 189 mg (85%) of pure **7**: $[\alpha]_{\text{D}}^{24}$ - 9.2 $^{\circ}$ (c = 0.34, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.32 (d, J = 15.7 Hz, 1 H), 6.25 (s, 1 H), 6.00 (s, 1 H), 5.87 (d, J = 15.7 Hz, 1 H), 4.87 (A of AB, J_{AB} = 6.6 Hz, 1 H), 4.72 (B of AB, J_{AB} = 6.6 Hz, 1 H), 3.95 (m, 1 H), 3.76 (s, 3 H), 3.73 (d, J = 3.6 Hz, 1 H), 2.52 (A of ABX, J_{AB} = 14.6 Hz, J_{AX} = 8.6 Hz, 1 H), 2.42 (B of ABX, J_{AB} = 14.6 Hz, J_{BX} = 5.2 Hz, 1 H), 1.91 (s, 3 H), 1.88 (m H), 1.86 (s, 3 H), 1.64 (m H), 1.48 (s, 3 H), 1.42 (m, 1 H), 1.32-1.25 (m, 6 H), 0.95 (t, J = 8.0 Hz, 9 H), 0.89 (t, J = 6.9 Hz, 3H), 0.59 (q, J = 8.0 Hz, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 167.8, 150.5, 146.5, 142.6, 133.9, 116.1, 90.0, 83.2, 78.9, 76.6, 74.9, 51.5, 49.0, 37.9, 32.7, 31.7, 26.2, 26.1, 24.0, 22.6, 14.0, 13.0, 7.0 (3), 5.2 (3); FT-IR (thin film) 3059, 2954, 2932, 2876, 1722,

1623, 1458, 1433, 1377, 1298, 1270, 1170, 1121, 1074, 1019, 841, 726 cm^{-1} ; HRMS (FAB) calcd for $[\text{C}_{28}\text{H}_{49}\text{IO}_5\text{Si}+\text{Na}]^+$ 643.2292, found 643.2295 m/z .

B. Second Generation Synthesis of Fragment 7.

(4R) 4 - B e n z y l - 3 - [2 - (1 ' S , 2 R , 4 E) - (1 ' - m e t h o x y m e t h o x y - h e x y l) - 4 - m e t h y l - 5 - (t r i m e t h y l s i l a n y l) - p e n t - 4 - e n o y l] - o x a z o l i d i n - 2 - o n e (8 8). To a solution of **16** (15.7 g, 35.3 mmol) and *i*-Pr₂NEt (18.5 mL, 105.8 mmol, 3 eq) in CH₂Cl₂ (7.5 mL) at 0 °C was added MOMCl (7.7 mL, 101.0 mmol, 2.9 eq) dropwise. After 1.5 h at 0 °C, the reaction mixture was diluted with saturated NaCl solution and the aqueous layer extracted with CH₂Cl₂. The combined organic layers were dried over MgSO₄, filtered and concentrated. The crude residue was dissolved in cold hexanes (0 °C), filtered through a pad of Celite® and rinsed thoroughly with hexanes. After concentration, **88** was obtained as a yellow oil which was used directly in the next step. Purification of an aliquot of **88** by flash chromatography on silica gel (hexanes / ethyl acetate = 85/15) afforded an analytical sample as a colorless oil having the following properties: $[\alpha]_D^{24} = -81.3$ (*c* 1.55, CHCl₃) ¹H NMR (500 MHz, CDCl₃) δ 7.35-7.32 (2H), 7.29-7.26 (1H), 7.22 (d, *J* = 6.8 Hz, 2H), 5.27 (s, 1H), 4.71 (dd, *J* = 7.1 Hz, 1H), 4.65 (ddd, *J* = 10.0, 6.6 and 2.9 Hz, 1H), 4.54 (d, *J* = 7.1 Hz, 1H), 4.50 (dt, *J* = 8.8 and 4.4 Hz, 1H), 4.09-4.03 (2H), 3.76 (ddd, *J* = 8.3, 4.1 and 4.1 Hz, 1H), 3.37 (s, 3H), 3.32 (dd, *J* = 13.8 and 3.0 Hz, 1H), 2.65 (dd, *J* = 14.3 and 10.4 Hz, 1H), 2.57 (dd, *J* = 13.2 and 10.4 Hz, 1H), 2.32 (dd, *J* = 13.8 and 3.8 Hz, 1H), 1.86 (s, 3H), 1.64-1.47 (3H), 1.33-1.26 (5H), 0.89 (t, *J* = 6.8 Hz, 3H), 0.1 (s, 9H); ¹³C NMR (100 MHz,

(1'S,3S,4R,6E) 2-Ethoxy-4-(1'-methoxymethoxy-hexyl)-6-methyl-7-(trimethylsilyl)-hepta-1,6-dien-3-ol (89): To a solution of oxalyl chloride (2.2 mL, 25.2 mmol, 2 eq) in CH_2Cl_2 (100 mL) at -70°C was added dropwise dry DMSO (2.6 mL, 36.6 mmol, 3 eq). After 15 min at -70°C , a solution of **36** (3.90 g, 12.3 mmol) in CH_2Cl_2 (20 mL) was added slowly via canula. The reaction mixture was stirred for another 15 min at -70°C before addition of Et_3N (7.0 mL, 50.2 mmol, 4 eq). The reaction mixture was allowed to warm to 0°C over a 35 min period and then stirred at 0°C for 15 min. Cold hexanes (150 mL) were then added and the resulting suspension was filtered through Celite®, the filter cake was rinsed thoroughly with cold hexanes, and the filtrate was concentrated. The residue was dissolved in hexanes and washed with water (x3). The aqueous washes were combined and extracted with ether (x3). The organic layers were combined, washed with saturated NaCl solution, dried over MgSO_4 , filtered and concentrated to give a slightly yellow oil which was used directly in the next step without any purification.

To a solution of ethylvinyl ether (10.6 mL, 111 mmol) in THF (15 mL) at -78°C was added *t*-BuLi (1.7 M in pentane, 85.0 mmol, 50 mL) dropwise such that $T < -60^\circ\text{C}$. The reaction mixture was then warmed to 0°C , stirred at that temperature for 30 min, cooled to -78°C and diluted with THF (30 mL). The solution of α -ethoxyvinyl lithium was then further cooled to -118°C (internal temperature, pentane/ $\text{N}_{2(l)}$ bath) and a solution of the crude aldehyde in THF (20 mL) was then slowly added such that the internal reaction temperature was $< -115^\circ\text{C}$. After 20 min at -118°C , the reaction mixture was quenched by slow addition of MeOH (5 mL) followed by an aqueous saturated solution of NaHCO_3 (5 mL) and the resulting mixture was allowed to warm to 0°C . The reaction mixture was diluted with water. The aqueous layer was separated and extracted with CH_2Cl_2 (x4). The organic layers were combined, washed with saturated NaCl

solution, dried over K_2CO_3 , filtered, and concentrated to give a slightly yellow oil (4.9 g). This material was used directly in the next reaction. Purification of a small aliquot by flash chromatography on silica gel (hexanes / ethyl acetate = 95/5) gave an analytical sample of **89** as a colorless oil. $[\alpha]_D^{25} = -3.3$ (c 1.04, $CHCl_3$); 1H NMR (500 MHz, $CDCl_3$) δ 5.28 (s, 1H), 4.65 (s, 2H), 4.27 (t, $J = 3.7$ Hz, 1H), 4.22 (d, $J = 1.7$ Hz, 1H), 4.01 (d, $J = 1.7$ Hz, 1H), 3.78-3.68 (2H), 3.63 (dt, $J = 6.7$ and 2.7 Hz, 1H), 3.38 (s, 3H), 2.70 (d, $J = 4.2$ Hz, 1H), 2.31 (dd, $J = 13.9$ and 7.6 Hz, 1H), 2.25 (m, 1H), 2.18 (dd, $J = 13.9$ and 7.6 Hz, 1H), 1.75 (s, 3H), 1.62-1.53 (2H), 1.35-1.17 (9H including 1.27 (t, $J = 7.1$ Hz, 3H)), 0.87 (t, $J = 7.1$ Hz, 3H), 0.07 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.7, 154.9, 124.7, 95.8, 81.7, 81.0, 74.3, 62.7, 55.7, 40.9, 37.0, 31.8, 31.3, 26.0, 22.7, 21.2, 14.4, 14.0, -0.1; IR (thin film) 3468 (br), 2955, 2361, 1662, 1616, 1247, 1100, 1040, 870, 840 cm^{-1} ; HRMS (CI, NH_3) for $C_{21}H_{42}O_4Si$ $[M+H]^+$ calcd. 387.2931, found 387, 2985 m/z .

(1'S,3S,4R,6E) 2-Ethoxy-3-*p*-methoxybenzyloxy-4-(1'-methoxymethoxy-hexyl)-6-methyl-7-(trimethylsilyl)-hepta-1,6-diene (90). To a 0 °C solution of **89** (4.9 g, used crude from the previous reaction) in THF (120 mL) was added Et_3N (5.2 mL, 75.0 mmol, 3 eq), PMB-Br (3.5 mL, 24.3 mmol, 2 eq) followed by KHMDS (0.5 M in toluene, 30 mL, 15 mmol, 1 eq). After 1.5 h at 0 °C, the reaction was complete by TLC analysis. The crude reaction mixture was used directly in the next reaction. An analytical sample of **90** was obtained by removal of a small aliquot of the crude reaction mixture and quenching with an aqueous saturated solution of $NaHCO_3$. The aqueous layer was extracted with ethyl acetate and the combined organic layers washed with saturated $NaCl$ solution, dried over $MgSO_4$, filtered and concentrated. Purification of the crude material by flash chromatography on silica gel (hexanes / ethyl acetate = 100 / 3 +

1% NEt₃) afforded **90** as a colorless oil. $[\alpha]_D^{25} = -73.7$ (*c* 1.38, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.27 (d, *J* = 8.7 Hz, 2H), 6.88 (d, *J* = 8.7 Hz, 2H), 5.25 (s, 1H), 4.70 (d, *J* = 6.8 Hz, 1H), 4.59 (d, *J* = 6.8 Hz, 1H), 4.55 (d, *J* = 11.0 Hz, 1H), 4.30 (d, *J* = 11.0 Hz, 1H), 4.20 (d, *J* = 1.8 Hz, 1H), 4.13 (d, *J* = 1.8 Hz, 1H), 3.95 (d, *J* = 3.9 Hz, 1H), 3.82 (s, 3H), 3.81-3.76 (2H), 3.52 (dt, *J* = 8.8 and 3.4 Hz, 1H), 3.39 (s, 3H), 2.45 (dd, *J* = 13.9 and 3.4 Hz, 1H), 2.29 (m, 1H), 2.14 (dd, *J* = 13.9 and 10.6 Hz, 1H), 1.77 (s, 3H), 1.66 (m, 1H), 1.50-1.41 (2H), 1.35-1.20 (8H including 1.32 (t, *J* = 7.0 Hz, 3H)), 0.91 (t, *J* = 7.1 Hz, 3H), 0.10 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 160.5, 158.9, 154.3, 130.9, 129.2, 125.1, 113.5, 96.1, 82.7, 78.7, 78.5, 70.3, 62.7, 55.5, 55.2, 41.1, 38.9, 31.7, 30.8, 26.3, 22.7, 21.0, 14.4, 14.1, 0.0; IR (thin film) 2954, 1615, 1515, 1248, 1098, 1038, 869, 837 cm⁻¹; HRMS (FAB) for C₂₉H₅₀O₅SiNa [M+Na]⁺ calcd. 529.3325, found 529.3322 *m/z*.

Stereochemical assignment of **89** was made as follows: Aldol **16** was converted to the β -methoxymethoxy Weinreb amide **91** in 2 steps (73%). Displacement of the amide moiety by α -ethoxyvinyl lithium in THF to give **92**, followed by non-selective reduction of the ketone function afforded a 1/1 mixture of **89-syn** and **89-anti**. Formation of the cyclic acetal **93** was effected by treatment with Me₂BBr and 2,6-DTBP. NOE experiments on the acetal derived from **89-syn** were not conclusive. However, NOE enhancements were observed for **93** (derived from

89-anti) between the vinylic and acetal protons, C(8)-H and C(25)-H, and C(25)-H and the acetal proton. This indicates an *anti* relationship between C(7)-H and (C8)-H and a *syn* relationship between C(8)-H and C(25)-H. Therefore, by deduction, compound **89-syn** must possess a *syn,syn* relationship between the C(7)-C(8) and C(8)-C(25) stereocenters.

(1'S,3S,4R,6E) 3-*p*-Methoxybenzyloxy-4-(1'-methoxymethoxy-hexyl)-6-methyl-7-(trimethylsilyl)-hept-6-en-2-one (11). To the crude reaction mixture containing PMB ether **90** (from the previous experiment) at 0°C was slowly added dropwise HCl (1N, 10 mL). After 10 min, additional HCl solution (90 mL) was added. The reaction was slowly warmed to 23 °C and stirred for 30 min. The crude reaction was then poured into a separatory funnel and the aqueous layer was separated. The aqueous layer was extracted with CH₂Cl₂ (x4). The organic layers were then combined and washed successively with an aqueous saturated solution of NaHCO₃ (x2) and saturated NaCl solution, dried over Na₂SO₄, filtered and concentrated. Purification of the crude mixture by flash chromatography (95 : 5 → 90 : 10 hexanes/EtOAc) provided **11** as a yellow oil (4.66 g, 79% from **36**): $[\alpha]_D^{25} = -83.0$ (*c* 0.43, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.21 (d, *J* = 8.8 Hz, 2H), 6.84 (d, *J* = 8.8 Hz, 2H), 5.20 (s, 1H), 4.62 (d, *J* = 6.6 Hz, 1H), 4.50 (d, *J* = 6.6 Hz, 1H), 4.42 (d, *J* = 11.0 Hz, 1H), 4.27 (d, *J* = 11.0 Hz, 1H), 3.86 (d, *J* = 4.4 Hz, 1H), 3.76 (s, 3H), 3.46 (dt, *J* = 9.2 and 2.9 Hz, 1H), 3.33 (s, 3H), 2.38-2.28 (2H), 2.12 (s, 3H), 2.03 (dd, *J* = 13.4 and 9.0 Hz, 1H), 1.69 (s, 3H), 1.54-1.36 (3H), 1.27-1.14 (5H), 0.84 (t, *J* = 7.0 Hz, 3H), 0.03 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 211.3, 159.3, 152.3, 129.7, 129.4, 129.6, 113.7, 96.2, 84.3, 78.0, 72.1, 55.8, 42.4, 39.8, 31.6, 30.0, 26.5, 26.2, 22.6, 21.0, 14.0, -0.1; IR (thin film) 2954, 1715, 1614, 1515, 1249, 1035, 838 cm⁻¹; HRMS (ES) for C₂₇H₄₆O₅SiNa [M+Na]⁺ calcd. 501.3012, found 501.3020 *m/z*.

(1'*S*,4*S*,5*S*,6*R*,8*E*) 5- *p*-Methoxybenzyloxy-6-(1'-methoxymethoxy-hexyl)-4,8-dimethyl-9-(trimethylsilyl)-non-8-en-2-yn-4-ol (37): To a solution of 11 (4.3 g, 9.0 mmol) in THF (80 mL) at $-45\text{ }^{\circ}\text{C}$ was added 1-propynylmagnesium bromide (0.5 M in THF, 25 mmol, 50 mL, 2.8 eq). After 12 h at $-45\text{ }^{\circ}\text{C}$, the reaction mixture was allowed to warm to $-30\text{ }^{\circ}\text{C}$ and stirred 3 h at that temperature. The reaction was then poured into an aqueous saturated solution of NH_4Cl and the aqueous layer extracted with CH_2Cl_2 . The combined organic layers were dried over MgSO_4 , filtered and concentrated. Purification of the crude material by flash chromatography on silica gel (hexanes / ethyl acetate = 85/15 to 70/30) afforded 4.36 g (94%) of 37 as a colorless oil: $[\alpha]_{\text{D}}^{25} = -87.9$ (*c* 0.33, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.27 (d, $J = 8.8$ Hz, 2H), 6.87 (d, $J = 8.8$ Hz, 2H), 5.24 (s, 1H), 4.73 (d, $J = 6.8$ Hz, 1H), 4.70 (d, $J = 10.7$ Hz, 1H), 4.57 (d, $J = 6.8$ Hz, 1H), 4.54 (d, $J = 10.7$ Hz, 1H), 4.30 (s, 1H), 3.80 (s, 3H), 3.66 (m, 1H), 3.45 (d, $J = 5.1$ Hz, 1H), 3.39 (s, 3H), 2.68 (dd, $J = 13.7$ and 3.8 Hz, 1H), 2.56 (m, 1H), 2.00 (dd, $J = 13.7$ and 11.8 Hz, 1H), 1.83 (s, 3H), 1.79 (s, 3H), 1.62-1.47 (5H including 1.52 (s, 3H)), 1.32-1.23 (6H), 0.90 (t, $J = 7.1$ Hz, 3H), 0.10 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 159.1, 153.5, 130.6, 129.3, 129.5, 113.7, 95.2, 83.6, 82.5, 80.2, 77.6, 74.4, 71.6, 55.9, 55.2, 41.1, 40.4, 31.6, 29.6, 27.3, 26.4, 22.7, 20.8, 14.1, 3.8, -0.1; IR (thin film) 3409 (br), 2954, 2252, 1614, 1515, 1456, 1249, 1095, 1036, 869, 840 cm^{-1} ; HRMS (ES) for $\text{C}_{30}\text{H}_{50}\text{O}_5\text{SiNa}$ $[\text{M}+\text{Na}]^+$ calcd. 541.3325, found 541.3315 *m/z*.

The stereochemistry of **37** was assigned as follows: DDQ oxidation of PMB ether **37** gave the *p*-methoxylidene (PMP) acetal **94**. Semi-hydrogenation of the triple bond with H₂ and Lindlar's catalyst afforded **95**. Key ¹H NOE enhancements were observed between C(5)-H, C(7)-H, and the acetal methine proton, indicating a *syn* relationship for the C(6)-C(7) hydroxyl functions in **37**.

(1'S,2E,4S,5S,6R,8E) 2-[(Tributyl)stannyl]-4,8-dimethyl-5-*p*-methoxybenzyloxy-6-(1'-methoxymethoxy-hexyl)-9-(trimethylsilyl)-nona-2,8-dien-4-ol (38): A round-bottom flask equipped with an argon balloon was charged with **37** (3.47 g, 6.69 mmol), (*o*-Tol₃P)₂PdCl₂ (530 mg, 0.67 mmol, 0.1 equiv), and THF (12 mL). The resulting heterogeneous mixture was stirred for 20 min at 23 °C. Bu₃SnH (17 mL, 63.2 mmol, 10 eq) was then added via a syringe pump over 2 h. The resulting mixture was then stirred for an additional 10 min and then diluted with hexanes and filtered through Celite[®]. The filtrate was concentrated and the residue purified

by flash chromatography on silica gel (hexanes / ethyl acetate = 95/5 to 90 /10) to provide 4.83 g of **38** (89 %) as a light yellow oil: $[\alpha]_D^{25} = -27.6$ (*c* 0.54, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ 7.25 (d, *J* = 8.6 Hz, 2H), 6.87 (d, *J* = 8.6 Hz, 2H), 5.73 (d, *J* = 1.8 Hz, *J*_{Sn-H} = 79.7 Hz, 1H), 5.22 (s, 1H), 4.65 (d, *J* = 11.0 Hz, 1H), 4.64 (d, *J* = 6.6 Hz, 1H), 4.51 (2H), 3.81 (s, 1H), 3.80 (s, 3H), 3.59 (m, 1H), 3.50 (d, *J* = 4.8 Hz, 1H), 3.37 (s, 3H), 2.65 (dd, *J* = 13.8 and 3.7 Hz, 1H), 2.35 (m, 1H), 2.16 (s, *J*_{Sn-H} = 24.5 Hz, 3H), 2.02 (dd, *J* = 13.8 and 11.7 Hz, 1H), 1.77 (s, 3H), 1.59-1.39 (11H), 1.34-1.23 (12H), 0.93-0.80 (18H), 0.09 (s, 9H); ¹³C NMR (100 MHz, CDCl₃) δ 158.9, 153.7, 144.5, 140.7, 131.0, 128.5, 126.2, 113.6, 95.3, 84.1, 78.7, 78.0, 74.0, 55.8, 55.2, 41.0, 40.2, 31.7, 29.8, 29.2 (*J*_{Sn-C} = 19.1 Hz), 27.4 (*J*_{Sn-C} = 54.2 Hz), 26.5, 22.7, 20.9, 20.7, 14.1, 13.7, 9.2 (*J*_{Sn-C} = 309.8 Hz), -0.1; IR (thin film) 3414, 2955, 1614, 1514, 1250, 1090, 1040, 868, 840 cm⁻¹; HRMS (ES) for C₄₂H₇₈O₅SiSnNa [M+Na]⁺ calcd. 833.4538, found 833.4570 *m/z*.

(1'S,2E,4S,5S,6R)-2-[(Tributyl)stannyl]-4-methyl-4,7-O-methylidene-5-p-methoxybenzyloxy-6-(E-2'-methyl-3'-trimethylsilanyl-2'-enyl) dodec-2-ene (39): To a solution of **38** (4.83 g, 5.96 mmol) and 2,6-di-*t*-butyl-4-methylpyridine (2,6-DTBMP) (4.82 g, 23.5 mmol, 4 equiv) in CH₂Cl₂ (120 mL) at -78 °C was added Me₂BBr (1.7 mL, 17.4 mmol, 3 equiv) dropwise. After 30 min, the reaction mixture was slowly warmed to -50 °C over a period of 15 min. The reaction was stirred at -50 °C for 15 min, at which point TLC analysis indicated complete consumption of **38**. The reaction mixture was then poured into an aqueous saturated solution of NaHCO₃, and the aqueous layer was extracted with CH₂Cl₂ (x4). The organic layers were then combined, washed with saturated NaCl solution, dried over Na₂SO₄, filtered, and concentrated. Purification of the crude material by flash chromatography on silica gel (hexanes / ethyl acetate = 97/3 to 95/5) afforded 4.53 g (98%) of **39** as a light yellow oil: $[\alpha]_D^{25} = -39.5^\circ$ (*c*

0.20, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.24 (d, *J* = 8.7 Hz, 2H), 6.86 (d, *J* = 8.7 Hz, 2H), 5.81 (d, *J* = 1.7 Hz, *J*_{Sn-H} = 77.4 Hz, 1H), 5.33 (s, 1H), 4.92 (d, *J* = 6.5 Hz, 1H), 4.87 (d, *J* = 6.5 Hz, 1H), 4.46 (d, *J* = 11.3 Hz, 1H), 4.43 (d, *J* = 11.3 Hz, 1H), 4.06 (m, 1H), 3.81 (s, 3H), 3.41 (d, *J* = 3.9 Hz, 1H), 2.39 (dd, *J* = 13.9 and 9.0 Hz, 1H), 2.32 (dd, *J* = 13.9 and 5.9 Hz, 1H), 2.17 (m, 1H), 2.00 (d, *J* = 2.0 Hz, *J*_{Sn-H} = 49 Hz, 3H), 1.75 (s, 3H), 1.65-1.24 (23H), 0.96-0.79 (18H), 0.12 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 159.0, 153.5, 141.8, 140.8, 1309.9, 128.9, 126.4, 113.6, 89.3, 85.5, 83.7, 75.0, 72.9, 55.2, 45.0, 41.1, 32.4, 31.8, 29.2 (*J*_{Sn-C} = 19.7 Hz), 27.4 (*J*_{Sn-C} = 54.0 Hz), 26.3, 25.0, 22.6, 21.2, 20.8, 14.1, 13.7, 9.3 (*J*_{Sn-C} = 318.6 Hz), 0.0; IR (thin film) 2926, 1614, 1514, 1464, 1248, 1040, 865, 840 cm⁻¹; HRMS (ES) for C₄₁H₇₄O₅SiSnNa [M+Na]⁺ calcd. 801.4276, found 801.4299 *m/z*.

Methyl-(2*E*,4*E*,6*S*,7*S*,8*R*,9*S*)-4,6-dimethyl-6,9-*O*-methylidene-8-(*E*-2'-methyl-3'-trimethylsilyl-2'-enyl)-7-*p*-methoxybenzyloxy-tetradeca-2,4-dienoate (47). A three-neck round-bottom flask fitted with three rubber septa was charged with **12** (2.26 g, 2.91 mmol), tetrabutylammonium diphenylphosphinate⁵ (1.52 g, 3.31 mmol, 1.1 eq), and dry NMP (16 mL) under a nitrogen atmosphere. In a separate round-bottom flask, (*E*)-ethyl β-iodoacrylate⁶ (1.19 g, 5.61 mmol, 1.9 eq) was dissolved in dry NMP (11 mL) and this solution was drawn up into a dry syringe. The total volume of the iodoacrylate solution was ~12 mL. To the flask containing **39** was then added 2 mL of the iodoacrylate solution. The syringe with the remaining solution of the iodoacrylate was placed in a syringe pump apparatus. To the flask containing **39** was then quickly added CuTc⁷ (1.11 g, 5.82 mmol) in a single portion, under positive nitrogen pressure (to exclude oxygen and moisture). Immediately, the syringe pump with the syringe containing the iodoacrylate solution was activated and the remaining iodoacrylate solution was

added at a steady rate to the heterogeneous reaction mixture over 18 min. The resulting mixture was stirred for an additional 10 min and then diluted with ether. The mixture was then filtered through a pad of neutral alumina with washing. The filtrate was then washed with water (x2), saturated NaCl solution, dried over MgSO_4 , filtered, and concentrated. Purification of the crude material by flash chromatography (hexanes/EtOAc = 95/5) gave 1.43 g (85%) of **47** as a yellow oil: $[\alpha]_D^{25} = -63.8$ (c 0.50, CHCl_3). ^1H NMR (500 MHz, CDCl_3) δ 7.23 (d, $J = 8.7$ Hz, 2H), 7.19 (d, $J = 15.8$ Hz, 1H), 6.90 (d, $J = 8.7$ Hz, 2H), 5.82 (d, $J = 15.8$ Hz, 1H), 5.74 (s, 1H), 5.33 (s, 1H), 4.94 (d, $J = 5.9$ Hz, 1H), 4.81 (d, $J = 5.9$ Hz, 1H), 4.56 (d, $J = 11.7$ Hz, 1H), 4.29 (d, $J = 11.7$ Hz, 1H), 4.10 (m, 1H), 3.85 (s, 3H), 3.77 (s, 3H), 3.34 (d, $J = 3.7$ Hz, 1H), 2.40-2.32 (2H), 2.17 (m, 1H), 1.86 (s, 3H), 1.85 (s, 3H), 1.68 (m, 1H), 1.51 (s, 3H), 1.48-1.27 (7H), 0.91 (t, $J = 6.8$ Hz, 3H), 0.15 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3) δ 167.8, 159.4, 153.1, 150.8, 144.9, 133.0, 130.1, 129.8, 126.7, 115.6, 113.8, 89.4, 83.5, 82.3, 74.4, 71.8, 55.3, 51.4, 44.4, 40.3, 32.2, 21.7, 26.2, 22.8, 22.6, 21.4, 14.0, 12.8, 0.0; IR (thin film) 2953, 1721, 1619, 1515, 1301, 1249, 1060, 1040, 840 cm^{-1} ; HRMS (ES) for $\text{C}_{33}\text{H}_{52}\text{O}_5\text{SiNa}$ $[\text{M}+\text{Na}]^+$ calcd. 595.3431, found 595.3435 m/z .

Methyl-(2*E*,4*E*,6*S*,7*S*,8*R*,9*S*)-4,6-dimethyl-6,9-*O*-methylidene-8-(*E*-2'-methyl-3'-trimethylsilylanyl-2'-enyl)-7-[(triethylsilyl)oxy]-tetradeca-2,4-dienoate (96). To a solution of **47** (29 mg, 0.05 mmol) in $\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}$ (1 mL/ 0.1 mL) at 0 °C was added DDQ (17.2 mg, 0.08 mmol, 1.5 eq). After 1 h at 0 °C and 1 h at 23 °C, the reaction mixture was diluted with an aqueous saturated solution of NaHCO_3 . The aqueous layer was extracted with CH_2Cl_2 , the combined organic layers were washed with saturated NaCl solution, dried over MgSO_4 , filtered and concentrated. The crude material was dissolved in CH_2Cl_2 (0.5 mL) and cooled to 0 °C. 2,6-

Lutidine (18 μ L, 0.15 mmol, 3 eq) was then added, followed by TESOTf (23 μ L, 0.10 mmol, 2 eq). After 30 min at 0 $^{\circ}$ C, the reaction mixture was quenched by addition of an aqueous saturated solution of NaHCO₃. The aqueous layer was extracted with CH₂Cl₂, the combined organic layers were washed with saturated NaCl solution, dried over MgSO₄, filtered and concentrated. Filtration of this material through a pad of silica gel (hexanes / ethyl acetate = 80/20) followed by HPLC purification (hexanes / ethyl acetate = 85/15) afforded 22.2 mg (77% from **47**) of **96** as a colorless oil: $[\alpha]_D^{25} = -20.4$ (*c* 0.93, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 7.33 (d, *J* = 15.5 Hz, 1H), 6.20 (s, 1H), 5.87 (d, *J* = 15.5 Hz, 1H), 5.31 (s, 1H), 4.89 (d, *J* = 6.6 Hz, 1H), 4.74 (d, *J* = 6.6 Hz, 1H), 4.02 (m, 1H), 3.82 (d, *J* = 4.2 Hz, 1H), 3.77 (s, 3H), 2.38 (dd, *J* = 14.9 and 8.6 Hz, 1H), 2.30 (dd, *J* = 14.9 and 5.6 Hz, 1H), 1.98 (m, 1H), 1.93 (s, 3H), 1.82 (s, 3H), 1.65 (m, 1H), 1.49 (s, 3H), 1.45-1.41 (2H), 1.36-1.24 (5H), 0.97 (t, *J* = 8.0 Hz, 9H), 0.89 (t, *J* = 7.0 Hz, 3H), 0.62 (q, *J* = 8.0 Hz, 6H), 0.12 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 167.9, 153.4, 150.8, 144.0, 133.2, 125.8, 115.8, 89.9, 83.1, 78.8, 75.0, 51.5, 48.6, 40.2, 32.5, 31.8, 26.3, 25.3, 22.6, 21.8, 14.0, 12.9, 7.0, 5.2, 0.0; IR (thin film) 2955, 1724, 1622, 1300, 1250, 1170, 1070, 1020, 840 cm⁻¹; HRMS (ES) for C₃₁H₅₈O₅Si₂Na [M+Na]⁺ calcd. 589.3721, found 589.3727 *m/z*.

Methyl-(2*E*,4*E*,6*S*,7*S*,8*R*,9*S*)-4,6-dimethyl-6,9-*O*-methylidene-8-(*E*-2'-methyl-3'-iodoprop-2'-enyl)-7-[(triethylsilyl)oxy]-tetradeca-2,4-dienoate (7). To a solution of **96** (1.12 g, 1.98 mmol) in CH₃CN (20 mL) at 0 °C was added NIS (1.17 g, 5.20 mmol, 2.6 eq) in one portion. After 4.5 h at 0 °C, the reaction mixture was diluted ether and washed with 10% Na₂S₂O₃ solution (x3). The organic phase was then washed with saturated NaCl solution, dried over Na₂SO₄, filtered, and concentrated to give pure **7** (1.18 g, 96%) as a yellow oil.

C. Synthesis of Formamycinone (2).

Methyl-(6*S*,7*S*,8*R*,9*S*)-4,6-dimethyl-6,9-*O*-methylidene-8-[(1'*E*-3'*E*,5'*S*,6'*R*,7'*R*,8'*R*,9'*R*,10'*R*)-8'-[(*tert*-butyldimethylsilyl)oxy]-10'-[(triethylsilyl)oxy-)]-6'-(hydroxy)-[1',7',9'-trimethyl]-5'-(methoxy)-undeca-1',3'-diene]-7-[(triethylsilyl)oxy]-icosa-2,4,10,12-tetraenoate (48**):** The vinyl boronic acid **6**^{8,9} (291 mg, 0.577 mmol) and vinyl iodide **7** (233 mg, 0.375 mmol) were combined in 3.6 mL of degassed THF/ H_2O (3 : 1 v/v). The reaction was treated sequentially with $\text{Pd(PPh}_3)_4$ (73 mg, 0.063 mmol), and Ti_2CO_3 (581 mg, 1.24 mmol) and the mixture stirred at 23 °C. After 3 h, additional $\text{Pd(PPh}_3)_4$ (30 mg, 0.026 mmol), and Ti_2CO_3 (110 mg, 0.24 mmol) were added and the reaction stirred for 1.5 h, at which time TLC analysis indicated the reaction was complete. The reaction mixture was diluted with Et_2O /hexanes (1 : 1), filtered through Celite[®] to remove salts, and the residue concentrated. Purification of this crude product by column chromatography (5 : 95 EtOAc/hexanes) provided 315 mg (88%) of **48**: $[\alpha]_D^{26} -21.2$ (*c* 0.92, CHCl_3); ^1H NMR (CDCl_3 , 500 MHz) δ 7.26 (d, *J* = 14.3 Hz, 1H), 6.45 (dd, *J* = 15.1, 10.7 Hz, 1H), 6.21 (s, 1H), 5.99 (d, *J* = 10.7 Hz, 1H), 5.83 (d, *J* = 15.6 Hz, 1H), 5.56 (dd, *J* = 15.1, 8.1 Hz, 1H), 4.91 (A of AB, *J* = 6.5 Hz, 1H), 4.76 (B of AB, *J* = 6.5 Hz, 1H), 4.00 (dd, *J* = 9.2, 2.00 Hz, 1H), 3.92 (d, *J* = 8.1 Hz, 1H), 3.82 to 3.72 (m, 3H), 3.75 (s, 3H), 3.49, (app. t, *J* = 8.1 Hz, 1H), 3.35 (s, 1H), 3.25 (s, 3H), 2.34 (dd, *J* = 14.4, 8.8 Hz, 1H), 2.24 (dd, *J* = 14.4, 4.6 Hz, 1H), 2.01 to 1.95 (m, 1H), 1.93 to 1.80 (m, 2H), 1.91 (s, 3H), 1.79 (s, 3H), 1.70 to 1.60 (m, 1H), 1.51 (s, 3H), 1.48 to 1.38 (m, 1H), 1.38 to 1.20 (m, 6H), 1.05 (d, *J* = 6.1 Hz, 3H), 1.01 (d, *J* = 7.1 Hz, 3H), 0.99 to 0.85 (m, 18H), 0.89 (s, 12H), 0.88 (t, *J* =

3.2 Hz, 3H), 0.64 to 0.55 (m, 12H), 0.10 (s, 3H), 0.08 (s, 3H); ^{13}C NMR (CDCl_3 , 125 MHz) δ 167.9, 150.7, 143.7, 137.1, 133.4, 130.6, 129.8, 126.7, 115.8, 89.9, 83.2, 82.3, 79.5, 78.8, 77.2, 74.9, 73.5, 70.1, 55.9, 51.5, 49.1, 44.3, 37.6, 37.6, 32.8, 31.7, 26.2, 25.5, 22.6, 19.9, 18.3, 16.9, 14.0, 12.9, 11.7, 11.6, 7.0, 6.9, 5.2, -3.5, -3.7; IR (neat) 2956, 2878, 1724, 1623, 1463, 1298, 1253, 1170, 1075, 1017, 837, 774, 742 cm^{-1} ; HRMS (FAB+) for $\text{C}_{52}\text{H}_{100}\text{O}_9\text{NaSi}_3$ $[\text{M}+\text{Na}]^+$ calcd. 975.6573, found 975.6527 m/z .

(1*S*,2*E*,4*E*,8*R*,9*S*,10*E*,12*E*,15*R*,16*S*,20*S*)-8-[(1'*R*,2'*R*,3'*S*,6'*R*,7'*S*,8'*R*)-2',7'-[di(*tert*-Butyldimethylsilyl)oxy]-4'-[(triethylsilyl)oxy]-(1',3',dimethyl)-pentyl]-20-[(triethylsilyl)oxy]-9-methoxy-1,3,13-trimethyl-16-pentyl-7,17,19-trioxabicyclo[13.4.1]eicosa-2,4,10,12-tetraene-6-one (49).

Deprotection of the methyl ester: To a solution of ester **48** (130 mg, 0.14 mmol) in $\text{Et}_2\text{O}/\text{THF}$ (5.5 mL, 10 : 1) was added $\text{KOSi}(\text{Me})_3$ (39 mg, 0.30 mmol) and this mixture was stirred for 24 h at 23 °C. The reaction was diluted with EtOAc (25 mL) and H_2O (5 mL), and the biphasic mixture stirred vigorously for 5 min. The organic layer was separated and the aqueous was made acidic by the addition of 1N HCl (500 μL), and further extracted with EtOAc . The combined organic solution was washed with saturated NaCl solution, dried over Na_2SO_4 , filtered and concentrated *in vacuo* to provide 126 mg of the crude acid which was used in the next step without further purification.

Macrolactonization procedure A: The crude acid (126 mg, 0.14 mmol) was azeotropically dried by concentration from benzene (3x) on a rotary evaporator. The residue was dissolved in 3 mL of THF and treated sequentially with *i*- Pr_2NEt (356 μL , 2.1 mmol) and 2,4,6-trichlorobenzoyl chloride (TCBC) (174 μL , 1.1 mmol), and the reaction stirred at 23 °C for 2 h.

The reaction mixture was concentrated *in vacuo* and the residue was dissolved in 1.5 mL of toluene, and added to a solution of 4-dimethylaminopyridine (DMAP) (166 mg 1.36 mmol), followed by 2 mL of toluene rinse. The reaction was heated to reflux for 13 h, cooled to 23 °C and filtered. The filtrate was diluted with Et₂O and washed with H₂O, saturated NaCl solution, dried over Na₂SO₄, filtered and concentrated *in vacuo*. The residue was purified by column chromatography (10 g of Davisil, 2% - 5% EtOAc/hexanes) followed by HPLC (21 mm column, 5% EtOAc/hexanes) to provide 78 mg (62%) of **49**.

Macrolactonization procedure B: To the crude acid (0.0357 mmol) in dry toluene (16 mL) under nitrogen was added DMAP (69 mg, 0.566 mmol) followed by TCBC (56 µL, 0.358 mmol). A white precipitate formed immediately. The heterogeneous mixture was heated to 110 °C for 12 h. The reaction mixture was cooled to ambient temperature, diluted with ether, and washed with water followed by saturated NaCl solution. The solution was dried over Na₂SO₄, filtered and concentrated. Purification of the crude product by preparative TLC (5% EtOAc/hexanes) provided **49** as a clear oil (17 mg, 52%): $[\alpha]_D^{26} -2.3$ (*c* 0.78, CHCl₃), ¹H NMR (CDCl₃, 500 MHz) δ 7.10 (d, *J* = 15.6 Hz, 1H), 6.49 (dd, *J* = 14.9, 10.7 Hz, 1H), 5.8 (d, *J* = 10.7 Hz, 1H), 5.70 (d, *J* = 15.8 Hz, 1H) 5.65 (s, 1H), 5.22 (dd, *J* = 14.9, 8.6 Hz, 1H), 5.02 (dd, *J* = 7.6, 4.6 Hz, 1H), 4.76 (d, *J* = 8.8 Hz, 1H), 4.68 (d, *J* = 8.8 Hz, 1H), 3.96 (app. t, *J* = 3.4 Hz, 1H), 3.88 (app. t, *J* = 8.1 Hz, 1H), 3.83 (app t, *J* = 6.4 Hz, 1H), 3.79 (d, *J* = 7.3 Hz, 1H), 3.64 to 3.58 (m, 1H), 3.24 (s, 3H), 2.67 (dd, *J* = 7.3, 6.9 Hz, 1H), 2.09 to 2.02 (m, 1H), 1.99 (dd, *J* = 9.0, 4.9 Hz, 1H), 1.96 (s, 3H), 1.95 (d, *J* = 8.3, 1H), 1.92 to 1.85 (m, 1H), 1.86 (s, 3H), 1.65 to 1.55 (m, 1H), 1.40 to 1.20 (m, 7H), 1.39 (s, 3H), 1.10 (d, *J* = 6.4 Hz, 3H), 1.02 (t, *J* = 8.1 Hz, 12H), 0.95 (t, *J* = 7.8 Hz, 9H), 0.88 (t, *J* = 3.4 Hz, 3H), 0.88 (s, 12H), 0.81 to 0.69 (m, 6H), 0.61 (q, *J* = 7.8 Hz, 6H), 0.09 (s, 3H), 0.07 (s, 3H); ¹³C NMR (CDCl₃, 125 MHz) δ 166.7, 150.8, 142.2, 141.2, 134.4, 131.6, 128.2, 125.1, 116.5, 86.4, 85.4, 81.2, 78.6, 75.5, 74.9, 73.2, 70.3, 55.7, 47.4, 43.1, 42.6, 34.2, 31.9, 30.2, 26.1, 25.9, 25.5, 22.6, 20.1, 20.0, 18.5, 14.1, 12.0, 11.5, 10.2, 7.3, 7.1, 5.7, 5.3, -3.6, -4.1; IR (neat) 2957, 2878, 1713, 1461, 1373, 1253, 1089, 1018,

967, 869, 835, 773, 736, 674 cm^{-1} ; HRMS (FAB+) for $\text{C}_{51}\text{H}_{58}\text{O}_4\text{NaSi}_3$ $[\text{M}+\text{Na}]^+$ calcd. 943.6310, found 943.6318 m/z .

(1*S*,2*E*,4*E*,8*R*,9*S*,10*E*,12*E*,15*R*,16*S*,20*S*)-8-[(1'*R*,2'*R*,3'*S*,6'*R*,7'*S*,8'*R*)-2',7'-di(*tert*-Butyldimethylsilyl)oxy-(1',3'-dimethyl)-pent-4'-one]-20-[(trimethylsilyl)oxy]-9-methoxy-1,3,13-trimethyl-16-pentyl-7,17,19-trioxabicyclo[13.4.1]eicosa-2,4,10,12-tetraene-6-one (50**).**

A solution of the macrolactone **49** (78 mg, 0.085 mmol) in THF (2.5 mL) was cooled to 0 °C and a solution of TFA (212 μL , 4.0M in H₂O) was added. The reaction was stirred for 150 min until complete by TLC analysis (20% ethyl acetate/hexanes). The reaction was diluted with 15 mL of Et₂O and washed with NaHCO₃ (3 x 2 mL), dried over MgSO₄, filtered, and concentrated on the rotary evaporator followed by high vacuum to give 72 mg (>99%) of crude alcohol which was >95% pure by ¹H-NMR.

A solution of the crude alcohol (72 mg, 0.085 mmol) in CH₂Cl₂ (3.0 mL) at 0 °C was treated with pyridine (34 μL , 0.42 mmol), followed by Dess-Martin periodinane (72 mg, 0.17 mmol). The reaction stirred at 0 °C for 2 h. TLC analysis (20% ethyl acetate/hexanes) at this point showed the reaction to be approximately 70% complete. Additional pyridine (68 μL , 0.84 mmol) and Dess-Martin periodinane (72 mg, 0.17 mmol) were added and the reaction stirred until complete by TLC analysis (4 h). The reaction mixture was diluted with Et₂O (20 mL) and washed (3 x 2 mL) with a 1:1 (v:v) mixture of satd. Na₂S₂O₃ and satd. NaHCO₃, dried over MgSO₄, filtered, and concentrated on the rotary evaporator. The crude residue was purified on a Davisil® column (5.0 g) eluted with a gradient of ethyl acetate/hexanes (5–20%) to yield 61 mg (90% from macrolactone **49**) of the methyl ketone **50**: $[\alpha]_D^{23} +13.4$ (c 1.65, CHCl₃) ¹H NMR (CDCl₃, 500 MHz) δ 7.13 (d, J = 15.9 Hz, 1H), 6.48 (dd, J = 15.1, 11.0 Hz, 1H), 5.78 (d, J =

11.0 Hz, 1H), 5.72 (d, $J = 15.9$ Hz, 1H), 5.66 (s, 1H), 5.14 (dd, $J = 15.1, 9.5$ Hz, 1H), 4.91 (dd, $J = 7.8, 5.6$ Hz, 1H), 4.77 (d, $J = 8.5$ Hz, 1H), 4.70 (d, $J = 8.5$ Hz, 1H), 4.30 (app. t, $J = 3.7$ Hz, 1H), 3.80 (d, $J = 7.3$ Hz, 1H), 3.70 (d, $J = 8.8$ Hz, 1H) 3.61 (app. t, $J = 7.6$ Hz, 1H), 3.19 (s, 3H), 2.95 (ddd, $J = 11.0, 10.3, 3.2$ Hz, 1H), 2.75 to 2.64 (m, 1H), 2.18, (s, 3H), 2.04 to 1.90 (m, 2H), 1.98 (s, 3H), 1.88 (s, 3H), 1.64 to 1.56 (m, 1H), 1.38 (s, 3H), 1.38 to 1.22 (m, 8H), 1.13 (d, $J = 7.1$ Hz, 3H), 1.02 (d, $J = 7.8$ Hz, 3H), 1.00 (t, $J = 5.6$ Hz, 9H), 0.89 (t, $J = 6.8$ Hz, 3H), 0.88 (s, 9H), 0.81 to 0.70 (m, 6H), 0.15 (s, 3H), 0.09 (s, 3H) δ 211.8, 166.9, 151.2, 142.7, 141.8, 134.3, 132.1, 127.8, 125.0, 116.1, 86.4, 81.2, 78.6, 75.5, 74.7, 71.8, 55.6, 48.7, 47.4, 43.8, 34.2, 31.9, 30.2, 29.7, 29.1, 26.0, 25.8, 25.5, 22.6, 20.2, 18.3, 14.1, 12.5, 12.0, 11.0, 7.3, 5.7, -4.2, -4.3; IR (thin film, CHCl_3) 2956, 2930, 2878, 2857, 1709, 1462, 1369, 1359, 1252, 1173, 1089, 1024, 869, 829, 774, 738 cm^{-1} ; HRMS (ES) for $\text{C}_{45}\text{H}_{80}\text{O}_8\text{Si}_2\text{Na}$ $[\text{M}+\text{Na}]^+$ calcd. 827.5289, found 827.5301 m/z .

(2*S*,3*R*)-3-(*tert*-Butyl-dimethyl-silanyloxy)-2-methyl-butylaldehyde (5): To a solution of alcohol **97**¹⁰ (0.5 g, 2.29 mmol) in CH_2Cl_2 (15 mL) and pyridine (0.26 mL, 3.2 mmol) at 23 °C was added the Dess-Martin periodinane reagent (1.16 g, 2.75 mmol). A solution of wet CH_2Cl_2 (8 mL of dry CH_2Cl_2 and 30 μL of H_2O) was then added dropwise over 30 min. The resulting solution was concentrated to ~2 mL and Et_2O (10 mL) was added. The organic layer was washed successively with a saturated aqueous solution of $\text{Na}_2\text{S}_2\text{O}_3$ (3 mL), a saturated aqueous solution of NaHCO_3 (3 mL) and water (10 mL). The combined aqueous layers were back-extracted with Et_2O , washed with saturated NaCl solution, dried over MgSO_4 , filtered and concentrated under reduced pressure. The crude oil was dissolved in pentane and filtered through a plug of Celite®. After evaporation of the solvent, the aldehyde **5** was obtained as a slightly yellow oil and was used in the next step without purification.

(1*S*,2*E*,4*E*,8*R*,9*S*,10*E*,12*E*,15*R*,16*S*,20*S*)-8-[(1'*R*,2'*R*,3'*S*,6'*R*,7'*S*,8'*R*)-2',7'-di(*tert*-Butyldimethylsilyl)oxy-(1',3',7'-trimethyl)-non-4'-one]-20-[(trimethylsilyl)oxy]-9-methoxy-1,3,13-trimethyl-16-pentyl-7,17,19-trioxabicyclo[13.4.1]eicosa-2,4,10,12-tetraene-6-one (4):

A solution of the methyl ketone **50** (80 mg, 0.099 mmol) in THF (1 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ and treated with a 1:1 (v:v) mixture of Et_3N and TMS-Cl (200 μL , premixed under nitrogen and aged for 10 min), stirred for 10 min and then treated with LiHMDS (1.0M in THF, 320 μL , 0.320 mmol). The solution was stirred for 30 min and then quenched by the addition of cold pH 7 buffer (300 μL) and diluted with 1:1 Et_2O /pentane. The layers were separated and the aqueous phase extracted with 1:1 Et_2O /pentane (x 2). The organic extracts were combined, dried over Na_2SO_4 , filtered and concentrated. The residue was diluted with benzene and re-concentrated two times to give the crude enol silane.

To this material was added a solution of aldehyde **5**¹⁰ (200 mg, 0.924 mmol) in dry benzene and the resulting mixture was concentrated on the rotary evaporator. The mixture was then dried under high vacuum ($< 0.7\text{ mm of Hg}$) for 30 sec (Note: aldehyde **5** is volatile). The residue was then dissolved in dry CH_2Cl_2 (450 μL) under nitrogen atmosphere. To the solution were then added 4 Å MS (powdered and freshly activated by heating under vacuum) and the resulting mixture was stirred at $23\text{ }^{\circ}\text{C}$ for 10 min. The heterogeneous mixture was cooled to $-78\text{ }^{\circ}\text{C}$ and $\text{BF}_3\cdot\text{OEt}_2$ (95 μL , 1.0 M in CH_2Cl_2 , 0.095 mmol) was added such that the solution was cooled by running down the side of the flask. After 80 min, the reaction was quenched with saturated NaHCO_3 solution and warmed to ambient temperature. The layers were separated and the aqueous phase was extracted with Et_2O . The organic phases were combined, dried over

Na₂SO₄, filtered, and concentrated on the rotary evaporator. ¹H NMR analysis of the crude reaction mixture showed the diastereoselectivity to be >95 : 5. The residue was purified by column chromatography (DavisilTM pH = 7 SiO₂, 5% to 10 % EtOAc/hexanes) to provide 88 mg of the desired Felkin aldol **4** (86%): [α]_D²⁶ +18.8 (*c* 0.98, benzene); ¹H NMR (C₆H₆, 500 MHz) δ 7.40, (d, *J* = 16.7 Hz, 1H), 6.64, (dd, *J* = 14.9, 10.7 Hz, 1H), 5.92, (d, *J* = 16.7 Hz, 1H), 5.80, (d, *J* = 10.7 Hz, 1H), 5.77, (s, 1H), 5.43, (dd, *J* = 15.1, 9.3 Hz, 1H), 5.42, (dd, *J* = 8.3, 8.0 Hz, 1H), 4.81, (ddd, *J* = 9.3, 5.1, 2.4 Hz, 1H), 4.73, (d, *J* = 8.5 Hz, 1H), 4.68 (dd, *J* = 4.6, 3.2 Hz, 1H), 4.42 (A of AB, *J*_{AB} = 8.6 Hz, 1H), 3.95, (B of AB, *J*_{AB} = 8.6 Hz, 1H), 3.90 – 3.82, (M, 2H), 3.54, (dd, *J* = 9.0, 6.6 Hz, 1H), 3.32, (d, *J* = 2.2 Hz, 1H), 3.21, (s, 3H), 3.18 – 3.10, (m, 1H), 2.84, (A of ABX, *J*_{AB} = 17.1 Hz, *J*_{AX} = 9.5 Hz, 1H), 2.66, (app. q, *J* = 7.3 Hz, 1H), 2.56, (B of ABX, *J*_{AB} = 17.1 Hz, *J*_{BX} = 2.9 Hz, 1H), 2.34 – 2.26, (m, 1H), 1.99, (s, 3H), 1.92 – 1.80, (m, 3H), 1.72, (s, 3H), 1.60 – 1.50, (m, 1H), 1.46 (s, 3H), 1.42 – 1.30, (m, 7H), 1.24 (d, *J* = 7.3 Hz, 3H), 1.18, (d, *J* = 7.1 Hz, 3H), 1.16, (d, *J* = 6.1 Hz, 3H), 1.08, (s, 9H), 0.99, (d, *J* = 7.1 Hz, 3H), 0.96, (s, 9H), 0.92, (s, 9H), 0.92, (t, *J* = 8.1 Hz, 3H), 0.70 – 0.58, (m, 6H), 0.34 (s, 3H), 0.29, (s, 3H), 0.12, (s, 3H), 0.04, (s, 3H); ¹³C NMR (C₆H₆, 125 MHz) δ 213.5, 166.8, 151.0, 142.5, 141.7, 134.7, 132.3, 129.0, 125.8, 116.9, 86.9, 86.6, 81.2, 78.5, 75.8, 75.1, 72.5, 71.9, 66.5, 55.7, 49.2, 47.8, 47.0, 44.9, 44.2, 34.5, 32.2, 30.6, 26.4, 26.2, 26.0, 25.8, 23.0, 21.9, 20.3, 18.7, 18.1, 14.3, 12.6, 12.0, 11.1, 10.5, 7.4, 6.0, -3.8, -4.0, -4.3, -4.9; IR (thin film, benzene) 2965, 1710, 1460, 1376, 1254, 1087, 1022, 836, 775, 737, cm⁻¹; HRMS (ES) for C₅₆H₁₀₄O₁₀Si₃Na [M+Na]⁺ calcd. 1043.6835, found 1043.6838 *m/z*.

(1*S*,2*E*,4*E*,8*R*,9*S*,10*E*,12*E*,15*R*,16*S*,20*S*)-8-[(1'*R*,2'*R*,3'*S*,6'*R*,7'*S*,8'*R*)-3'-(2''*R*,4''*R*,5''*R*,6''*S*)-(2''-dihydroxy-5'',6''-dimethyl-tetrahydropyran-2''-yl)-2'-hydroxy-1'-methylbutyl]-20-hydroxy-9-methoxy-1,3,13-trimethyl-16-pentyl-7,17,19-trioxabicyclo[13.4.1]eicosa-2,4,10,12-tetraene-6-one (Formamicin Aglycon) (2). A solution of TAS-F (9.7mg, 0.035 mmol,) and H₂O (1.4 μL, 0.078 mmol,) in DMF (100 μL) was added to a solution of **4** (3.6 mg, 0.0035 mmol) in DMF (50 μL). The reaction stirred for two hours until only one lower R_f spot (R_f = 0.25) was present by TLC analysis (50% ethyl acetate/hexanes). The reaction was concentrated to approx. 50 μL and then loaded directly onto a Davisil® column (3.0 g) and eluted with a gradient of ethyl acetate/hexanes (25–50%). In this way, 2.4 mg of a crude white solid was obtained which was further purified by HPLC (10 mm column, 60% EA/hex) to furnish 1.9 mg (80%) of the formamicin aglycon **2** as a white solid: $[\alpha]_D^{26} +12.1$ (*c* 0.19, benzene); ¹H NMR (4 : 1 CDCl₃/C₆H₆, 500 MHz) δ 7.22, (d, *J* = 15.6 Hz, 1H), 6.48, (dd, *J* = 14.9, 10.7 Hz, 1H) 5.71 (d, *J* = 11.0 Hz, 1H), 5.68 (s, 1H), 5.65, (d, *J* = 15.9 Hz, 1H), 5.64, (d, *J* = 1.2 Hz, 1H), 5.15 (dd, *J* = 14.9, 9.5 Hz, 1H), 4.91, (d, *J* = 9.0 Hz, 1H), 4.78, (d, *J* = 4.1 Hz, 1H), 4.68, (A of AB, *J*_{AB} = 8.7 Hz, 1H), 4.58, (B of AB, *J*_{AB} = 8.7 Hz, 1H), 4.14, (m, *J* = 10.7, 2.7 Hz, 1H), 3.86, (app. t, *J* = 9.0 Hz, 1H), 3.70, (m, *J* = 12.5, 10.0, 6.1 Hz, 1H), 3.63, (m, 1H), 3.56, (app. t, *J* = 7.3 Hz, 1H), 3.51, (dd, *J* = 8.3, 5.6 Hz, 1H), 3.18, (s, 3H), 2.60, (app. q, *J* = 9.3 Hz, 1H), 2.24, (dd, *J* = 12.0, 4.6 Hz, 1H), 2.14, (ddd, *J* = 13.9, 10.7, 7.1 Hz, 1H), 1.92, (d, *J* = 14.1 Hz, 1H), 1.88, (s, 3H), 1.80 – 1.73 (m, 1H), 1.77, (s, 3H), 1.69, (app. q, *J* = 7.1 Hz), 1.62 – 1.52, (m, 1H), 1.44, (d, *J* = 5.6 Hz, 1H), 1.30 – 1.18 (m, 8H), 1.28, (s, 3H), 1.09, (d, *J* = 6.4 Hz, 1H), 1.07, (m, 1H), 1.01, (d, *J* = 7.1, Hz, 1H), 0.89, (d, *J* = 6.6 Hz, 1H), 0.86, (d, *J* = 6.8 Hz, 1H), 0.78 (d, *J* = 6.8 Hz, 1H); ¹³C NMR (4 : 1 CDCl₃/C₆H₆, 125 MHz) δ 169.5, 153.6, 143.2, 142.5, 134.6, 132.7, 127.4, 125.3, 114.9, 99.3, 86.4, 82.2, 80.0, 77.8, 75.8, 74.8, 70.4, 70.3, 69.2, 55.6, 47.1, 45.9, 43.4, 41.7, 37.2, 34.7, 32.0, 30.1, 25.7, 24.9, 22.7, 20.1, 19.3, 14.1, 12.9, 11.6, 9.7, 7.1; IR (thin film, benzene) 3419, 2929, 1682, 1455, 1260, 1150, 1087, 1037, 968, 899, 847, 808, 678 cm⁻¹; HRMS (FAB) for C₃₈H₆₂O₁₀Na [M+Na]⁺ calcd. 701.4241, found 701.4244 *m/z*.

Table 1: ¹H-NMR and ¹³C-NMR Data of formamycin and formamycin aglycon.

Position	Formamycin	¹³ C-NMR Formamycin aglycon	Difference	Formamycin	¹ H-NMR Formamycin Aglycon	Difference
1	169.6	169.5	0.1			0.00
2	115.0	114.9	0.1	5.69	5.65	0.04
3	153.8	153.6	0.2	7.27	7.22	0.05
4	134.6	134.6	0.0			0.00
5	142.6	142.5	0.1	5.71	5.68	0.03
6	80.0	80.0	0.0			0.00
7	74.8	74.8	0.0	3.56	3.51	0.05
				1.66	1.58	0.08
8	47.2	47.1	0.1	2.65	2.60	0.05
9	34.8	34.7	0.1	1.83	1.78	0.05
				1.97	1.92	0.05
10	143.4	143.2	0.2			0.00
11	125.3	125.3	0.0	5.76	5.71	0.05
12	132.9	132.7	0.2	6.53	6.48	0.05
13	127.8	127.4	0.4	5.20	5.15	0.05
14	82.3	82.2	0.1	3.91	3.86	0.05
15	75.8	75.8	0.0	4.96	4.91	0.05
16	37.3	37.2	0.1	2.19	2.14	0.05
17	70.5	70.4	0.1	4.20	4.14	0.06
			0.0	4.87	4.78	0.09
18	41.9	41.7	0.2	1.76	1.69	0.07
19	99.4	99.3	0.1	5.71	5.64	0.07
20	40.2	45.9	-5.7	1.17	1.07	0.10
				2.34	2.24	0.10
21	76.2	69.2	7.0	3.81	3.63	0.18
			0.0		1.44	21(OH)
22 ^a	43.7	43.4	0.3	1.20-1.35	1.18-1.30	0.04
23	69.8	70.3	-0.5	3.78	3.70	0.08
24	19.5	19.3	0.2	1.15	1.09	0.06
25	78.0	77.8	0.2	3.61	3.56	0.05
26 ^a	30.2	30.1	0.1	1.20-1.35	1.18-1.30	0.04
27 ^a	25.8	25.7	0.1	1.20-1.35	1.18-1.30	0.04
28 ^a	32.0	32.0	0.0	1.20-1.35	1.18-1.30	0.04
29 ^a	22.8	22.7	0.1	1.20-1.35	1.18-1.30	0.04
30	14.2	14.1	0.1	0.91	0.86	0.05
31	11.7	11.6	0.1	1.83	1.77	0.06
32	24.9	24.9	0.0	1.33	1.28	0.05
33	86.5	86.4	0.1	4.63	4.58	0.05
34	20.2	20.1	0.1	1.93	1.88	0.05
35	55.7	55.6	0.1	3.23	3.18	0.05
36	9.7	9.7	0.0	0.83	0.78	0.05
37	7.3	7.1	0.2	1.08	1.01	0.07
38	13.3	12.9	0.4	0.99	0.89	0.10

^a The proton resonances overlapped and could not be resolved.

D. Glycosidation Studies.

(5S, 6S, 7R)-6-Methyl-7-[(*tert*-butyldimethyl)silyloxy]-octan-5-ol-3-one (58). To a solution of LiHMDS (1M in THF, 7 mL, 7 mmol) in THF (8 mL) at $-78\text{ }^{\circ}\text{C}$ was slowly added neat isopropyl methyl ketone (0.73 mL, 6.80 mmol). The mixture was stirred at $-75\text{ }^{\circ}\text{C}$ for 40 min, then a solution of aldehyde **5** (0.5 g, 2.29 mmol) in THF (2 mL) was added dropwise over 15 min. The reaction mixture was stirred for 1.75 h and quenched by inverse addition into a biphasic mixture of Et_2O and a saturated aqueous solution of NH_4Cl . The aqueous layer was extracted with CH_2Cl_2 , dried over MgSO_4 , filtered and concentrated under reduced pressure. The ratio of diastereomeric products was determined by ^1H NMR (500 MHz) to be 45/55 (Felkin : anti-Felkin). The crude yellow oil was filtrated on silica gel (hexanes - ethyl acetate = 90:10). HPLC purification (hexanes/ethyl acetate = 92/8) gave 175 mg (26%) of the Felkin diastereomer **58** as a colorless oil: $[\alpha]_{\text{D}}^{25} = -5.0$ (c 1.3, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 4.53 (m, 1H), 3.86 (dq, $J = 6.3$ and 2.9 Hz, 1H), 3.45 (s, 1H), 2.68 (dd, $J = 16.6$ and 8.8 Hz, 1H), 2.57 (septet, $J = 6.8$ Hz, 1H), 2.38 (dd, $J = 16.6$ and 4.9 Hz, 1H), 1.37 (m, 1H), 1.22 (d, $J = 6.3$ Hz, 3H), 1.05 (d, $J = 7.1$ Hz, 3H), 1.04 (d, $J = 6.8$ Hz, 3H), 0.91 (d, $J = 7.1$ Hz, 3H), 0.83 (s, 9H), 0.03 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 214.0, 73.4, 66.3, 45.0, 42.6, 41.3, 25.7, 21.8, 18.0, 17.8, -4.5 , -5.2 ; IR (thin film) 3508, 2960m, 1711, 1464, 1383, 1112, 1079, 1006, 838, 776 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{16}\text{H}_{34}\text{O}_3\text{NaSi}$ $[\text{M}+\text{Na}]^+$: 325.2175 m/z , observed 325.2173 m/z .

6-Bromo-3,4-bis-*O*-(*tert*-butyldimethyl)silyl-2,6-deoxy-2-iodo- β -D-glucopyranosyl Fluoride (3). To a solution of 6-bromo-3,4-bis-*O*-(*tert*-butyldimethyl)silyl-2,6-deoxy-2-iodo- β -D-glucopyranosyl acetate **51**¹¹ (885 mg, 1.42 mmol) in $\text{MeOH}/\text{Et}_2\text{O}$ (2/1, 15 mL) at $0\text{ }^{\circ}\text{C}$ was

added hydrazine (11M in H₂O, 220 μ L, 2.4 mmol). After 1.5 h at 0 °C, the reaction mixture was quenched by the addition of H₂O (5 mL) and extracted with Et₂O. The combined organic layers were washed with saturated NaCl solution, dried over MgSO₄, filtered and concentrated under reduced pressure. The crude colorless oil was dissolved in CH₂Cl₂, and DAST (260 μ L, 2.13 mmol) was added dropwise at 0 °C. After 30 min at 0 °C, the reaction was poured into a saturated aqueous solution of NaHCO₃ (3 mL). The aqueous layer was extracted with CH₂Cl₂, washed with saturated NaCl solution, dried over MgSO₄, filtered and concentrated under reduced pressure. The crude oil was purified by flash chromatography on silica gel (hexanes - ethyl acetate = 100 : 1) to give 710 mg of **3** (86% from **51**) as a colorless oil. Further purification by HPLC (hexanes - ethyl acetate = 97 : 3) gave 646 mg of **3** (78% from **51**) as a colorless oil (When high quality DAST was used in the reaction, HPLC purification was not necessary): $[\alpha]_D^{25} = +20.3$ (*c* 1.1, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 6.02 (dd, *J* = 1.8 Hz, ¹*J*_{H-F} = 53.1 Hz, 1H), 4.30 (bs, 1H), 4.19 (d, *J* = 3.3 Hz, 1H), 4.16 (dd, *J* = 10.6 and 6.2 Hz, 1H), 4.03-3.97 (2H), 3.58 (dd, *J* = 9.7 and 4.9 Hz, 1H), 0.96 (s, 9H), 0.91 (s, 9H), 0.14 (s, 2x3H), 0.13 (2x3H); ¹³C NMR (125 MHz, CDCl₃) 108.8 (¹*J*_{C-F} = 222.8 Hz), 78.3, 74.0, 67.9, 32.5, 25.9, 25.6, 18.9, 18.6, 17.9 (²*J*_{C-F} = 29 Hz), -4.5, -4.6, -4.8, -5.1; IR (thin film) 2930, 1472, 1259, 1170, 1109, 938, 871, 835, 777 cm⁻¹; HRMS (ES) calcd for C₁₈H₃₇BrFO₃NaSi₂ [M+Na]⁺: 605.0391 *m/z*, observed: 605.0397 *m/z*.

(5S, 6S, 7R)-5-O-[2-Deoxy-2-iodo-3,4-bis-O-(*tert*-butyldimethyl)silyl-6-bromo- β -D-glucopyranosyl]-6-methyl-7-[(*tert*-butyldimethyl)silyloxy]-octan-3-one (59**).**

Representative Glycosidation Procedure: A solution of the acceptor **58** (20 mg, 0.066 mmol) in Et₂O (0.8 mL) and flame-dried powdered 4Å molecular sieves was stirred at 23 °C for 45 min. The suspension was then cooled to -20 °C, SnCl₂ (124 mg, 0.65 mmol) and AgClO₄ (136 mg, 0.65 mmol) were added successively followed by a slow addition of a solution of the donor **3** (115 mg, 0.2 mmol) in Et₂O (0.5 mL). The mixture was stirred for 1.5 h at -20 °C, then the

bright yellow suspension was filtered through cotton and washed with pH 7 buffer. The aqueous layer was extracted with Et₂O, washed with saturated NaCl solution, dried over MgSO₄, filtered and concentrated under reduced pressure. The crude oil was purified by two successive preparative TLC runs (hexanes - ethyl acetate = 95:5) to give 37 mg (65%) of **59** as a colorless oil: $[\alpha]_D^{26} = +4.5$ (*c* 1.1, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 5.19 (d, *J* = 8.3 Hz, 1H), 4.43 (dd, *J* = 5.9 and 3.2 Hz, 1H), 4.40 (m, 1H), 4.06 (dt, *J* = 5.6 and 2.9 Hz, 1H), 3.97 (d, *J* = 4.2 Hz, 1H), 3.88 (p, *J* = 6.1 Hz, 1H), 3.71 (dd, *J* = 8.5 Hz, 1H), 3.65 (dd, *J* = 10.0 and 9.4 Hz, 1H), 3.46 (dd, *J* = 10.0 and 5.4 Hz, 1H), 2.92 (dd, *J* = 17.0 and 6.2 Hz, 1H), 2.67-2.60 (2H), 1.6 (m, 1H), 1.14-1.11 (9H including 1.13 (d, *J* = 7.1 Hz, 3H) and 1.12 (d, *J* = 6.8 Hz, 3H)), 0.96 (s, 9H), 0.92 (s, 9H), 0.90 (s, 9H), 0.87 (d, *J* = 7.1 Hz, 3H), 0.17 (s, 3H), 0.16 (s, 2x3H), 0.13 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) 212.2, 99.2, 81.0, 80.7, 74.0, 71.9, 70.0, 45.3, 43.8, 41.2, 32.5, 32.0, 25.9 (2C), 25.8, 20.7, 18.3, 18.1, 18.0 (2C), 17.9, 9.5, -4.1, -4.2 (2C), -4.3, -4.6 (2C); IR (thin film) 2930, 1716, 1472, 1362, 1257, 1093, 1037, 1006, 868 cm⁻¹; HRMS (ES) calcd for C₃₄H₇₀BrIO₆NaSi₃ [M+Na]⁺: 887.2606 *m/z*, observed: 887.2616 *m/z*.

Methyl 4-*O*-[2-Deoxy-2-iodo-3,4-bis-*O*-(*tert*-butyldimethyl)silyl-6-bromo- β -D-glucopyranosyl]-2,3,6-tri-*O*-benzyl- α -D-glucopyranoside (61**).** Following the representative procedure described for the preparation of **59**, the acceptor **60**¹² (20 mg, 0.04 mmol) in Et₂O (0.5 mL) was treated with SnCl₂ (73 mg, 0.38 mmol) and AgClO₄ (80 mg, 0.38 mmol) followed by a slow addition of a solution of the donor **3** (75 mg, 0.13 mmol) in Et₂O (0.5 mL). After 20 min at -15 °C, the reaction was worked up and the crude yellow oil was purified by preparative TLC (hexanes - ethyl acetate = 85 : 15) to give 39 mg (89%) of **61**.¹³ The β/α ratio was >98 : 2 according to the ¹H NMR analysis (500 MHz).

filtered, and concentrated to give the benzoate as a yellow oil. This material was used directly in the next reaction.

The crude benzoate from the previous reaction was dissolved in THF (0.9 mL) and AcOH (0.9 mL) was added followed by water (0.15 mL). After 16 h, the reaction was diluted with ether and washed with water (x1), saturated NaHCO₃ (x3), saturated NaCl solution, dried over Na₂SO₄, filtered, and concentrated to give 137 mg of a yellow oil which was used directly in the next reaction.

The crude alcohol from the previous reaction was dissolved in 0.5 mL of dry CH₂Cl₂ and treated with pyridine (38 μ L, 0.47 mmol) and Dess-Martin periodinane¹⁵ (144 mg, 0.340 mmol). To this solution was then added “wet” CH₂Cl₂ (1.5 mL, prepared from vigorously mixing 10 mL CH₂Cl₂ and 10 μ L of water)¹⁶ dropwise. After 40 min, an additional portion of Dess-Martin periodinane (32 mg) was added and the reaction was stirred for an additional 10 min. The reaction was then diluted with ether, washed with 10% Na₂S₂O₃ solution (x2), saturated NaCl solution, dried over Na₂SO₄, filtered, and concentrated. The residue was purified by flash chromatography (90 : 10 hexanes/Et₂O) to give **65** as a clear oil (105 mg, 96% from **64**): $[\alpha]_D^{25} = +5.3$ ($c = 0.4$, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.07 (m, 2H), 7.55 (m, 1H), 7.43 (m, 2H), 5.31 (dd, $J = 5.5, 4.5$ Hz, 1H), 4.28 (d, $J = 5.0$ Hz, 1H), 3.37 (s, 3H), 2.82 (m, 1H), 2.23 (m, 1H), 2.22 (s, 3H), 1.15 (d, $J = 7.5$ Hz, 3H), 1.09 (d, $J = 7.5$ Hz, 3H), 0.85 (s, 9H), .12 (s, 9H), 0.09 (s, 3H), 0.02 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) 211.8, 166.0, 133.1, 130.7, 130.1, 128.5, 101.3, 93.1, 74.1, 73.7, 73.3, 57.3, 50.3, 40.01, 29.8, 26.2, 18.5, 13.2, 12.1, -0.1, -3.9, -4.1; IR (thin film) 1723 cm⁻¹; HRMS (ES) calcd for C₂₈H₄₆O₅NaSi₂ [M+Na]⁺: 541.2782 m/z , observed: 541.2781 m/z .

(2R, 3S, 4R, 7S, 8R, 9R, 10R, 11S)-2,8-Di-
 -[(*tert*-butyldimethyl)silyloxy]-3,7,9-
 trimethyl-10-[(benzoyl)oxy]-11-methoxy-13-trimethylsilyl-tridec-4-ol-12-yn-6 one (**68**). To
 a solution of **65** (80 mg, 0.15 mmol) in THF (1.5 mL) at -78 °C was added 0.2 mL of a 1:1

solution of TMSCl and Et₃N (0.4 mL). LiHMDS (1 M solution in THF, 0.50 mL, 0.50 mmol) was added dropwise. The mixture was stirred for 1 h at –78 °C, then pH 7 buffer (5 mL) and pentane (5 mL) were added and the solution was allowed to warm to 23 °C. The aqueous layer was extracted with pentane, dried over MgSO₄, filtered and concentrated under reduced pressure. The crude oil was used in the next step without any further purification.

To a solution of the crude enol ether and aldehyde **5** (70 mg, 0.32 mmol) in CH₂Cl₂ (0.8 mL) at –78 °C was added BF₃•OEt₂ (40 µL, 0.504 mmol). After 1 h at –78 °C, the reaction mixture was quenched by pH 7 buffer and diluted with ether. The layers were separated and the aqueous layer was extracted with ether. The organic phases were combined, dried over Na₂SO₄, filtered, and concentrated under reduced pressure. The diastereomeric ratio was determined by ¹H NMR analysis (500 MHz) to be > 96/4 in favor of the desired Felkin aldol product **67**. The crude yellow oil was purified by flash chromatography (hexanes - ethyl acetate = 95:5) to give 75 mg (66%) of **67** as a clear oil: [α]_D²³ = +42.0° (c 0.64, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.05-8.03 (2H), 7.52 (m, 1H), 7.42-7.38 (2H), 5.24 (dd, *J* = 5.7 and 4.6 Hz, 1H), 4.57 (m, 1H), 4.23 (d, *J* = 4.6 Hz, 1H), 4.09 (dd, *J* = 5.7 and 4.6 Hz, 1H), 3.88 (dq, *J* = 6.2 and 3.7 Hz, 1H), 3.42 (d, *J* = 1.1 Hz, 1H), 3.33 (s, 3H), 2.86-2.76 (2H), 2.48 (dd, *J* = 17.2 and 4.0 Hz, 1H), 2.20 (m, 1H), 1.41 (m, 1H), 1.24 (d, *J* = 6.2 Hz, 3H), 1.12 (d, *J* = 7.0 Hz, 3H), 1.05 (d, *J* = 7.0 Hz, 3H), 0.94 (d, *J* = 7.0 Hz, 3H), 0.85 (s, 9H), 0.81 (s, 9H), 0.08 (s, 9H), 0.05 (s, 9H), 0.00 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) 212.7, 165.7, 132.8, 130.5, 129.9, 128.2, 101.1, 92.7, 73.8, 73.5, 73.3, 73.0, 66.1, 57.0, 50.0, 47.1, 42.8, 39.9, 26.0, 25.8, 21.9, 18.2, 17.9, 13.1, 11.6, 11.2, –4.0, –4.3, –4.4, –5.0; IR (thin film) 3501, 2956, 1728, 1463, 1378, 1252, 1108, 1027, 839, 776, 709 cm^{–1}; HRMS (ES) calcd for C₃₆H₇₀O₇NaSi₂ [M+Na]⁺: 757.4327 *m/z*, observed: 757.4330 *m/z*.

(2R, 3S, 4R, 7S, 8R, 9R, 10R, 11S)-2,8-Bis-[(*tert*-butyldimethyl)silyloxy]-3,7,9-trimethyl-4-*O*-[2-deoxy-2-iodo-3,4-bis-*O*-(*tert*-butyldimethyl)silyl-6-bromo-β-D-

glucopyranosyl)]-10-[(benzoyl)oxy]-11-methoxy-13-trimethylsilyl-tridec-4-ol-12-yn-6-one (70). Following the representative procedure described for the preparation of **59**, the acceptor **68** (12.8 mg, 0.017 mmol) in Et₂O (0.9 mL) was treated with SnCl₂ (29 mg, 0.15 mmol) and AgClO₄ (32.2 mg, 0.15 mmol) followed by a slow addition of a solution of the 14 (30.5 mg, 0.05 mmol) in Et₂O (0.5 mL). The mixture was stirred for 30 min at -15 °C, the reaction was worked up and ¹H NMR analysis of the crude product indicated that 8% of the starting aldol **68** were still present. The crude yellow oil was filtered through silica gel (hexanes - ethyl acetate = 100:1 to 95:5). HPLC purification (hexanes - ethyl acetate = 97:3) gave 19 mg (84%) of **70**: [α]_D²³ = +24.4 (*c* 0.73, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.06 (d, *J* = 7.1 Hz, 2H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 2H), 5.32 (t, *J* = 4.9 Hz, 1H), 5.15 (d, *J* = 8.3 Hz, 1H), 4.43 (m, 1H), 4.36 (m, 1H), 4.25 (d, *J* = 5.1 Hz, 1H), 4.11 (t, *J* = 5.1 Hz, 1H), 4.01 (br t, *J* = 7.1 Hz, 1H), 3.94-3.89 (2H), 3.66 (dd, *J* = 7.1 and 2.1 Hz, 1H), 3.62 (dd, *J* = 10.0 and 8.6 Hz, 1H), 3.44 (dd, *J* = 10.0 and 5.6 Hz, 1H), 3.36 (s, 3H), 2.96 (dd, *J* = 18.0 and 6.7 Hz, 1H), 2.83 (m, 1H), 2.67 (dd, *J* = 18.0 and 4.6 Hz, 1H), 2.19 (m, 1H), 1.67 (m, 1H), 1.18 (d, *J* = 7.3 Hz, 3H), 1.08 (d, *J* = 6.3 Hz, 6H), 0.95 (s, 9H), 0.90 (s, 9H), 0.87 (s, 9H), 0.86 (d, *J* = 7.1 Hz, 3H), 0.84 (s, 9H), 0.15 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H), 0.11 (s, 3H), 0.10 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H), 0.05 (s, 3H), 0.00 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) 210.6, 165.6, 132.8, 130.6, 129.9, 128.2, 101.1, 99.6, 92.8, 80.8, 80.6, 73.6, 73.5 (2C), 73.0, 72.0, 69.9, 57.0, 50.0, 45.6, 45.4, 39.6, 32.7, 32.0, 26.1, 25.9 (2C), 25.8, 20.5, 18.3, 18.0 (2C), 17.9, 13.0, 11.9, 9.3, -0.3, -4.0 (2C), -4.1, -4.2 (2C), -4.3, -4.6, -4.7; IR (thin film) 2955, 1723, 1472, 1361, 1252, 1097, 1005, 835, 776, 708 cm⁻¹; HRMS (ES) calcd for C₅₇H₁₀₆BrIO₁₀NaSi₅ [M+Na]⁺: 1319.4758 *m/z*, observed: 1319.4774 *m/z*.

E. Deprotection Studies.

(2R, 3S, 4R, 7S, 8R, 9R, 10R, 11S)-2,8-Bis-[(*tert*-butyldimethyl)silyloxy]-3,7,9-trimethyl-4-*O*-[2,6-deoxy-3,4-bis-*O*-(*tert*-butyldimethyl)silyl- β -D-glucopyranosyl]-10-[(benzoyl)oxy]-11-methoxy-13-trimethylsilyl-tridec-4-ol-12-yn-6-one (72**).** A solution of **70** (50 mg, 0.04 mmol) in toluene (0.7 mL) at 23 °C was treated with Bu₃SnH (110 μ L, 0.39 mmol) and triethylborane (1M solution in hexanes, 13 μ L, 0.013 mmol). After 12 h at 23 °C, the reaction mixture was quenched by addition of saturated NaCl solution and diluted with ether. The layers were separated and the organic phase dried over Na₂SO₄, filtered and concentrated. The reaction mixture was filtered through silica gel (hexanes - ethyl acetate = 100:0 to 100:1). HPLC purification (hexanes - ethyl acetate = 97:3) of this material gave 38 mg (90%) of pure **72** as a colorless oil: $[\alpha]_D^{23} = +15.7$ (*c* 0.51, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 8.07 (d, *J* = 7.8 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.44 (d, *J* = 7.8 Hz, 2H), 5.32 (t, *J* = 5.1 Hz, 1H), 4.51 (dd, *J* = 9.8 and 1.7 Hz, 1H), 4.35 (td, *J* = 9.0 and 3.2 Hz, 1H), 4.23 (d, *J* = 5.1 Hz, 1H), 4.08 (dd, *J* = 6.1 and 4.2 Hz, 1H), 3.94 (p, *J* = 6.1 Hz, 1H), 3.58 (m, 1H), 3.37 (s, 3H), 3.17 (dd, *J* = 8.8 and 6.4 Hz, 1H), 3.08 (dd apt t, *J* = 8.4 Hz, 1H), 2.93 (dd, *J* = 17.2 and 9.3 Hz, 1H), 2.86 (p, *J* = 6.8 Hz, 1H), 2.50 (dd, *J* = 17.2 and 3.2 Hz, 1H), 2.19 (m, 1H), 1.93 (ddd, *J* = 12.2, 4.9 and 1.7 Hz, 1H), 1.44 (m, 1H), 1.37 (m, 1H), 1.23 (d, *J* = 6.1 Hz, 3H), 1.11 (d, *J* = 7.1 Hz, 3H), 1.09 (d, *J* = 7.6 Hz, 3H), 1.09 (d, *J* = 5.9 Hz, 3H), 0.90 (s, 9H), 0.89 (s, 9H), 0.88 (s, 9H), 0.86 (d, *J* = 7.1 Hz, 3H), 0.84 (s, 9H), 0.10 (s, 9H), 0.09 (s, 3H), 0.08 (s, 9H), 0.07 (s, 6H), 0.03 (s, 3H), 0.01 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) 211.9, 165.5, 132.8, 130.5, 129.9, 128.2, 101.1, 99.7, 92.8, 78.0, 75.8, 73.8, 73.4, 73.1, 72.9, 72.4, 69.8, 57.0, 50.3, 47.2, 45.6, 41.5, 39.6, 26.3, 26.1, 26.0, 25.9, 20.8, 18.8, 18.3, 18.2, 18.1, 18.0, 12.9, 12.0, 10.3, 0.0, -0.3, -2.7, -3.0, -3.9 (2C), -4.1 (2C), -4.6; IR (thin film) 2930, 1728, 1472, 1463, 1380, 1361, 1252, 1102, 1006, 910, 889, 837, 776, 735, 709, 674 cm⁻¹; HRMS (ES) calcd for C₅₇H₁₀₈O₁₀NaSi₅ [M+Na]⁺: 1115.6687 *m/z*, observed: 1115.6691 *m/z*.

(3*S*,4*R*,5*R*,6*R*,7*S*)-4-(Benzoyloxy)-6-hydroxy-7-[(2'*S*,4'*R*,5'*S*,6'*S*)-4'-*O*-(2'',6'')-dideoxy- β -D-glucopyranosyl)-2-hydroxy-5,6-dimethyl-tetrahydropyranyl-2-yl]-3-methoxy-5-methyl-oct-1-yne (74). To glycoside **72** (13 mg, 0.12 mmol) in a dry round-bottom flask under nitrogen atmosphere was added a solution of Et₃N·3HF (40 μ L, 0.25 mmol) and Et₃N (9 μ L, 0.65 mmol) in acetonitrile (0.5 mL) which had been aged for 1 h. After 7 h, no reaction was observed by mass spectrometry (ES/Na⁺) analysis of the reaction mixture. More Et₃N·3HF (100 μ L) and Et₃N (20 μ L) were added and the reaction was allowed to stir for 60 h. Mass spectrometry analysis still indicated the presence of starting material. Additional Et₃N·3HF (100 μ L) and Et₃N (20 μ L) were added and the reaction was allowed to stir for an additional 48 h. The reaction was diluted with EtOAc, washed with pH 7.0 buffer (x2) followed by saturated NaCl solution, dried over MgSO₄, filtered, and concentrated. The residue was purified by preparative TLC (10% MeOH/CH₂Cl₂) to provide 3.8 mg of **73** as a clear oil (47% from **72**, 75/25 mixture of diastereomeric ketals) and 2.6 mg of **74** as a film (39% from **72**).

Data for **74**: $[\alpha]_D^{23} = -11.0$ (c 0.2, CH₂Cl₂); ¹H NMR (500 MHz, CDCl₃) δ 8.06 (m, 2H), 7.60 (m, 1H), 7.46 (m, 2H), 5.48 (dd, *J* = 1.5, 8.5 Hz, 1H), 5.37 (d, *J* = 2.50 Hz, 1H), 4.55 (dd, *J* = 2.0, 9.5 Hz, 1H), 4.30 (dd, *J* = 2.0, 8.5 Hz, 1H), 4.09-4.07 (m, 2H), 3.74-3.64 (m, 2H), 3.60 (m, 1H), 3.48 (s, 3H), 3.26-3.20 (m, 1H), 3.09 (at, *J* = 9.0 Hz, 1H), 2.39 (d, *J* = 2.0 Hz, 1H), 2.27 (dd, *J* = 5.0, 12.0 Hz, 1H), 2.22 (m, 1H), 2.12 (dd, *J* = 2.0, 5.0 Hz, 1H), 2.10 (dd, *J* = 2.0, 4.50 Hz, 1H), 1.70 (m, 1H), 1.60 (dd, *J* = 9.5, 11.5 Hz, 1H), 1.29 (d, *J* = 6.0 Hz, 3H), 1.03 (d, *J* = 7.0 Hz, 3H), 0.93 (d, *J* = 6.0 Hz, 3H), 0.92 (d, *J* = 6.5 Hz, 3H), 0.86 (d, *J* = 7.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 168.1, 133.8, 130.2, 129.4, 128.7, 99.4, 96.8, 95.0, 80.2, 76.2, 75.5, 74.7, 72.2, 71.5, 70.3 (2C), 69.9, 56.8, 43.6, 41.7, 40.1, 39.8, 37.0, 29.9, 19.3, 17.8, 13.3, 9.4, 7.1, 1.2; IR (thin film) 3401, 17.02 cm⁻¹; HRMS (ES) calcd for C₃₀H₄₄O₁₀Na [M+Na]⁺: 587.2832 *m/z*, observed: 587.2834 *m/z*.

Partial data for **73** (major diastereomer): ^1H NMR (500 MHz, CDCl_3) δ 8.09 (d, $J = 7.0$ Hz, 2H), 7.57 (m, 1H), 7.45 (at, 7.5 Hz, 2H), 5.25 (dd, 3.0, 8.5 Hz, 1H), 4.75 (d, $J = 5.0$ Hz, 1H), 4.55 (dd, $J = 1.5$, 9.5 Hz, 1H), 3.72, (m, 1H), 3.60 (m, 1H), 3.47 (d, $J = 1.5$ Hz, 1H), 3.38 (s, 3H), 3.24 (m, 1H), 3.10 (t, $J = 9.0$ Hz, 1H), 2.54 (d, $J = 2.0$ Hz, 1H), 2.21 (dd, $J = 5.0$, 12.0 Hz, 1H), 2.18 (m, 1H), 2.13 (dd, $J = 5.0$, 12.0 Hz, 1H), 1.72 (q, $J = 7.5$ Hz, 1H), 1.30 (d, $J = 6.5$ Hz, 3H), 1.21 (d, $J = 6.5$ Hz, 3H), 1.08 (d, 7.0 Hz, 3H), 1.05 (d, $J = 7.0$ Hz, 3H), 0.97 (d, $J = 6.0$ Hz, 3H), 0.92 (s, 9H), 0.18 (s, 3H), 0.16 (s, 3H).

F. Synthesis of Formamycin.

Glycoside 76. To a solution of acceptor **4** (9.5 mg, 0.0093 mmol) in dry ether (0.15 mL), under a nitrogen atmosphere, was added freshly activated 4 Å MS. The resulting mixture was stirred for 5 min and then cooled to -10°C . To the cooled suspension were added sequentially AgClO_4 (24 mg, 0.12 mmol) and SnCl_2 (18 mg, 0.95 mmol) and the resulting mixture was stirred for 10 min. To the reaction was then added dropwise a solution of donor **3** (26 mg, 0.446 mmol) in ether (0.1 mL) followed by an ether rinse (0.3 mL). After 40 min, the reaction mixture was filtered through a pipette fitted with a cotton plug into pH = 7 buffer solution. The diluted with ether. The aqueous layer was discarded and the organic phase was washed with pH = 7 buffer solution (x3). The aqueous washes were then combined and extracted with ether (x3). The organic extracts were then combined, washed with saturated NaCl solution, dried over Na_2SO_4 , filtered, and concentrated. The residue was purified by preparative TLC (90 : 10 hexanes/ EtOAc) to give glycoside **76** as a clear oil (10 mg, 68%). $[\alpha]_{\text{D}}^{23} = +15.1^\circ$ (c 0.4, CH_2Cl_2); ^1H NMR (500 MHz, CDCl_3) δ 7.10 (d, $J = 15.5$ Hz, 1H), 6.47 (dd, $J = 15.0$, 11.0 Hz, 1H), 5.78 (d, $J = 10.5$ Hz, 1H), 5.72 (d, $J = 16.0$ Hz, 1H), 5.65 (s, 1H), 5.15 (dd, $J = 9.5$, 15.5 Hz, 1H), 5.12 (d, $J = 8.0$ Hz, 1H), 4.94 (dd, $J = 8.5$, 15.0 Hz, 1H), 4.76 (d, $J = 8.5$ Hz, 1H), 4.46 (m, 1H), 4.35 (dd, $J = 4.0$, 2.5 Hz, 1H), 4.20 (t, $J = 4.0$ Hz, 1H), 4.01 (m, 1H), 3.93 (m, 2H), 3.80 (d, $J = 7.5$ Hz, 1H), 3.70-3.60 (m,

4H), 3.46 (dd, $J = 5.5, 10.0$ Hz, 1H), 3.13 (s, 3H), 3.00-2.95 (m, 2H), 2.71 (m, 1H), 2.67 (dd, $J = 5.0, 18.0$ Hz, 1H), 1.98 (s, 3H), 1.96 (m, 2H), 1.87 (s, 3H), 1.69-1.40 (m, 2H), 1.39 (s, 3H), 1.38-1.26 (m, 9H), 1.25 (s, 3H), 1.17 (d, $J = 7.0$ Hz, 3H), 1.09 (d, $J = 6.0$ Hz, 3H), 1.02 (t, $J = 9.0$ Hz, 9H), 0.99 (d, $J = 7.0$ Hz, 3H), 0.95 (s, 9H), 0.90 (s, 9H), 0.88 (s, 18H), 0.85 (d, $J = 7.0$ Hz, 3H), 0.79-0.74 (m, 6H), 0.16 (s, 3H), 0.15 (s, 3H), 0.14 (s, 3H), 0.13 (s, 3H), 0.12 (s, 3H), 0.08 (s, 3H), 0.07 (s, 3H), 0.05 (3H); ^{13}C NMR (125 MHz, CDCl_3) δ 211.2, 167.0, 151.2, 142.9, 141.8, 134.6, 132.3, 128.2, 125.3, 116.6, 99.8, 86.7, 86.4, 81.4, 80.8, 80.7, 78.9, 77.4, 75.7, 74.6, 73.7, 72.8, 72.3, 70.2, 55.9, 49.1, 47.7, 45.7, 43.2, 34.4, 33.0, 32.4, 32.1, 30.4, 29.9, 26.3, 26.2, 26.1, 25.7, 22.8, 20.8, 20.5, 18.6, 18.3 (2C), 18.1, 14.3, 13.6, 12.3, 11.5, 9.3, 7.5, 5.9, 1.2, 0.2 –3.6, –3.7, –3.8, –3.9, –4.0 (2C), –4.3, –4.4; IR (thin film) 1707, 16.54 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{74}\text{H}_{142}\text{O}_{13}\text{Si}_5\text{Na}$ $[\text{M}+\text{Na}]^+$: 1605.7266 m/z , observed: 1605.7279 m/z .

Glycoside 77. Glycoside **76** (11 mg, 0.0069 mmol) was dissolved in dry toluene (0.7 mL). To this solution were added sequentially Bu_3SnH (20 μL , 0.074 mmol) and Et_3B (0.7 μL , 1 M in hexanes, 0.0007 mmol). Air (1 mL) was then sparged through the solution with a syringe and the reaction was stirred for 30 min. The reaction was then diluted with ether and quenched with saturated NaCl solution. The organic layer was separated and dried over Na_2SO_4 , filtered, and concentrated. The residue was purified by preparative TLC (90 : 10 hexanes/ EtOAc) to provide glycoside **77** (9 mg, 94%) as a clear oil. $[\alpha]_{\text{D}}^{27} = -12.4^\circ$ (c 0.25, CHCl_3); ^1H NMR (500 MHz, CDCl_3) δ 7.10 (d, $J = 15.5$ Hz, 1H), 6.47 (dd, $J = 11.0, 15.0$ Hz, 1H), 5.77 (d, $J = 10.0, 11.0$ Hz, 1H), 5.71 (d, $J = 15.5$ Hz, 1H), 5.65 (s, 1H), 5.13 (dd, $J = 9.0, 15.0$ Hz, 1H), 4.93 (dd, $J = 5.5, 8.0$ Hz, 1H), 4.76 (d, $J = 8.5$ Hz, 1H), 4.69 (d, 8.5 Hz, 1H), 4.50 (dd, $J = 2.0, 10.0$ Hz, 1H), 4.35 (dt, $J = 3.0, 8.0$ Hz, 1H), 4.20 (t, $J = 4.5$ Hz, 1H), 3.93 (m, 1H), 3.80 (d, $J = 9.0$ Hz, 1H), 3.68 (t, $J = 8.5$ Hz, 1H), 3.61 (m, 1H), 3.56 (ddd, $J = 4.5, 8.0, 12.5$ Hz, 1H), 3.17-3.13 (m, 1H), 3.10 (s, 3H), 3.07 (t, $J = 8.5$ Hz, 1H), 2.99 (m, 1H), 2.92 (dd, $J = 9.0, 17.5$ Hz, 1H), 2.71 (m, 1H), 2.45

(dd, $J = 3.0, 17.5$ Hz, 1H), 1.98 (s, 3H), 1.95-1.90 (m, 4H), 1.87 (s, 3H), 1.60 (m, 2H), 1.44 (m, 2H), 1.56 (s, 3H), 1.36-1.24 (m, 13H), 1.22 (d, $J = 6.0$ Hz, 3H), 1.08 (m, 6H), 1.04-1.00 (m, 11H), 0.92-0.84 (m, 36H), 0.79-0.69 (m, 6H), 0.12 (s, 3H), 0.09 (s, 6H), 0.07 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 212.5, 167.0, 151.2, 143.0, 141.8, 134.5, 132.4, 127.9, 125.3, 116.5, 99.6, 86.6, 81.41, 78.9, 78.3, 75.8, 75.7, 74.4, 73.4, 72.8, 72.6, 70.0, 55.8, 49.2, 47.8, 47.2, 45.9, 43.3, 41.8, 34.5, 32.1, 30.6, 30.4, 26.6, 26.4, 26.3, 26.2, 26.1, 25.7, 22.9, 20.5, 19.1, 18.6, 18.5, 18.3 (2C), 14.3, 12.9, 12.3, 11.5, 10.4, 7.5, 7.4, 6.0, 5.5, -2.4, -2.8, -3.6, -3.7, -3.8, -3.9, -4.3; IR (thin film) 1716, 1494, 1264 cm^{-1} ; HRMS (ES) calcd for $\text{C}_{74}\text{H}_{142}\text{O}_{13}\text{Si}_5\text{Na}$ $[\text{M}+\text{Na}]^+$: 1401.9195 m/z , observed: 1401.9175 m/z .

Formamycin (1). Glycoside **77** (4.3 mg, 0.0031 mmol) was dissolved in dry THF (0.7 mL) under a nitrogen atmosphere. To this solution was added dry CH_3CN (0.7 mL). The resulting solution was then treated with $\text{Et}_3\text{N}\cdot 3\text{HF}$ (0.8 mL, 4.9 mmol, Aldrich) dropwise. During this addition the solution became slightly cloudy. To this mixture was then added Et_3N (0.14 mL, 1.0 mmol) slowly via syringe. The resulting mixture was stirred at ambient temperature for 72 h. The reaction mixture was then diluted with ether (50 mL) and washed with pH = 7 buffer solution (30 mL x 4) and saturated NaCl solution. The organic phase was dried over Na_2SO_4 (15 g) and KHCO_3 (10 g)¹⁷ for 1.5 h, filtered, and the volume of the reaction mixture was concentrated to ~ 10 mL. Na_2SO_4 was added to remove residual water and the solution was again filtered and then concentrated to dryness to give ~4.6 mg of a film. This material (a mixture of mono TBS ether ketals) was used without further purification in the next step.

The residue from the previous reaction was dissolved in dry CH_3CN (0.8 mL) under a nitrogen atmosphere. The resulting solution was then treated with $\text{Et}_3\text{N}\cdot 3\text{HF}$ (0.8 mL, 4.9 mmol) dropwise. To this mixture was then added Et_3N (0.15 mL, 1.1 mmol) slowly via syringe. The resulting mixture was stirred at ambient temperature for 11 days. The reaction mixture was then

diluted with ether (50 mL) and washed with pH = 7 buffer solution (30 mL x 4), saturated NaCl solution, dried over Na₂SO₄ (10 g) and KHCO₃ (10 g) for 1.5 h, filtered, and the volume of the reaction mixture was concentrated to ~ 10 mL. Na₂SO₄ was added to remove residual water and the solution was again filtered and then concentrated to dryness. The residue was purified by preparative TLC (4 : 1 EtOAc/CHCl₃) to give **1** (1.5 mg, 60% from **77**) as a yellow oil. This material had a slight amount of an impurity that appeared as a broad multiplet at 5.38-5.28 ppm in the ¹H NMR spectrum. This material could not be removed under a variety of flash chromatography, normal-phase HPLC, or reverse-phase HPLC conditions. However, dissolution of the slightly impure material in acetonitrile and washing with hexanes (x8) provided an analytical sample of **1** (0.4 mg, 16% from **77**).

Analytical Data for Synthetic Formamicin

Comparison of synthetic **1** to a sample of natural **1** supplied by Igarashi et al^{18,19} showed synthetic **1** to be identical to natural **1**. Tabulated spectroscopic data, ¹H NMR spectra of synthetic and natural **1**, as well as ¹³C NMR spectra of synthetic **1** are provided on the following pages.

Figure 1. Formamicin Numbering System.

Table 1. ¹H NMR Data for Synthetic and Natural Formamycin (**1**).

Natural Formamycin				Synthetic Formamycin			
Position	¹ H (500 MHz) δ	Multiplicity (J in Hz)	#H	¹ H (500 MHz) δ	Multiplicity (J in Hz)	#H	Difference (Δ δ)
3	7.22	d (16.0)	1	7.22	d (16.0)	1	0
12	6.49	dd (11.0, 15.0)	1	6.49	dd (10.5, 15.0)	1	0
11	5.71	d (11.0)	1	5.71	d (10.0)	1	0
19-OH	5.68	s	1	5.67	s	1	0.01
5	5.67	d (2.0) ^a	1	5.67	s	1	0
2	5.65	d (15.5)	1	5.65	d (16.0)	1	0
13	5.15	dd (9.5, 15.0)	1	5.15	dd (9.5, 15.0)	1	0
15	4.91	d (9.0)	1	4.91	d (9.0)	1	0
17-OH	4.80	d (4.0)	1	4.80	d (4.0)	1	0
33	4.69	d (8.5)	1	4.68	d (8.5)	1	0.01
33	4.58	d (8.5)	1	4.58	d(8.5)	1	0
1'	4.48	dd (1.5, 9.5)	1	4.48	dd (1.5, 9.5)	1	0
17	4.15	ddd (1.5, 3.5, 11.0)	1	4.15	ddd (1.5, 4.0, 10.0)	1	0
14	3.86	t (9.5)	1	3.86	t (9.5)	1	0
21	3.78 - 3.70	m	1	3.77 - 3.71	m	1	—
23	3.78 - 3.70	m	1	3.77 - 3.71	m	1	—
25	3.56	m	1	3.57	m	1	-0.01
7	3.51	dd (5.0, 8.0)	1	3.51	dd (5.5, 8.5)	1	0
3'	3.39	m	1	3.39	m	1	0
35	3.18	s	3	3.18	s	3	0
5'	3.10	m	1	3.10	m	1	0
4'	2.91	t (9.0)	1	2.91	t (8.0)	1	0
8	2.60	m	1	2.60	m	1	0
20	2.29	dd (4.5, 11.5)	1	2.29	dd (4.5, 11.5)	1	0
16	2.26 - 2.18	m	1	2.27 - 2.18	m	1	—
3'-OH	2.15	m	1	2.15	ddd (8.0, 14.5, 17.0)	1	0
4'-OH	2.00	ddd (2.0, 3.5, 12.0)	1	2.01	ddd (2.0, 4.5, 12.0)	1	-0.01
2'	1.97	m	1	1.97	m	1	0
9	1.92	d (14.5)	1	1.92	d (13.5)	1	0
34	1.89	s	3	1.89	s	3	0
9	1.78	s	3	1.77	d (7.5)	3	0.01
31	1.76 - 1.70	m	1	1.76 - 1.71	m	1	—
18	1.76 - 1.70	m	1	1.76 - 1.71	m	1	—
7-OH	1.58	m	1	1.58	m	1	0
2'	1.56 - 1.49	m	1	1.55 - 1.49	m	1	—
32	1.42	d (5.0)	1	1.42	d (5.5)	1	0
28	1.28	s	3	1.28	s	3	0
29	1.27 - 1.18	m	2	1.27 - 1.19	m	2	—
27	1.27 - 1.18	m	2	1.27 - 1.19	m	2	—
26	1.27 - 1.18	m	2	1.27 - 1.19	m	2	—
22	1.27 - 1.18	m	2	1.27 - 1.19	m	2	—
6'	1.20	d (6.5)	3	1.19	d (6.5)	3	0.01
20	1.14 ^b	m	1	1.13 ^b	m	1	—
24	1.10	d (6.5)	3	1.10	d (6.5)	3	0
37	1.03	d (7.5)	3	1.03	d (7.0)	3	0
38	0.94	d (7.5)	3	0.94	d (6.5)	3	0
30	0.86	t (7.0)	3	0.86	t (7.5)	3	0
36	0.78	d (7.0)	3	0.78	d (6.5)	3	0
Total number of H = 72				Total number of H = 72			

^aIgarashi et al report this resonance at 5.71 ppm (s, 1H) (see ref. 19). We also observed that this peak would overlap with C(19)-OH in certain samples. ^bObscured by H₂O.

Table 2. ^{13}C NMR Data for Synthetic and Natural Formamycin (**1**).

Position	Natural Formamycin ^a ^{13}C (125 MHz) δ	Synthetic Formamycin ^b ^{13}C (125 MHz) δ	Difference ($\Delta \delta$)
1	169.6	169.7	-0.1
3	153.8	153.9	-0.1
10	143.4	143.5	-0.1
5	142.6	142.7	-0.1
4	134.6	134.8	-0.2
12	132.9	133	-0.1
13	127.8	128	-0.2
11	125.3	125.5	-0.2
2	115.0	115.2	-0.2
19	99.4	99.6	-0.2
1'	96.8	96.9	-0.1
33	86.5	86.7	-0.2
14	82.3	82.4	-0.1
6	80.1	80.2	-0.1
25	78.0	78.1	-0.1
4'	77.9	78	-0.1
21	76.2	76.3	-0.1
15	75.8	76	-0.2
7	74.8	75	-0.2
3'	72.0	72.2	-0.2
5'	71.4	71.5	-0.1
17	70.5	70.6	-0.1
23	69.8	69.9	-0.1
35	55.7	55.8	-0.1
8	47.2	47.3	-0.1
22	43.7	43.8	-0.1
18	41.9	42	-0.1
20	40.2	40.4	-0.2
2'	39.7	39.9	-0.2
16	37.3	37.5	-0.2
9	34.8	34.9	-0.1
28	32.0	32.2	-0.2
26	30.2	30.3	-0.1
27	25.8	26	-0.2
32	24.9	25.1	-0.2
29	22.8	22.9	-0.1
34	20.2	20.3	-0.1
24	19.5	19.7	-0.2
6'	17.7	17.8	-0.1
30	14.2	14.3	-0.1
38	13.3	13.5	-0.2
31	11.7	11.9	-0.2
36	9.7	9.9	-0.2
37	7.3	7.4	-0.1

^aPublished data from Igarashi et al are shown here (see ref. 19).^bA broad peak was observed at 30.0 ppm. We believe this resonance corresponds to "hydrocarbon grease." Gottlieb et al have observed this impurity at 29.8 ppm in CDCl_3 , and 30.2 ppm in C_6D_6 .²⁰

Table 3. Other Analytical Data for Synthetic and Natural Formamycin (**1**).

Method	Natural Formamycin	Synthetic Formamycin
Optical Rotation	$[\alpha]_D^{27} = -31^\circ$ (<i>c</i> 0.08, CHCl ₃) $[\alpha]_D^{27} = -36^\circ$ (<i>c</i> 0.1, CHCl ₃)	
HRMS ^a	HRMS (FAB) calcd for C ₄₄ H ₇₂ O ₁₃ Na [M+Na] ⁺ : 831.4871 <i>m/z</i> , observed: 831.4859 <i>m/z</i>	HRMS (ES) calcd for C ₄₄ H ₇₂ O ₁₃ Na [M+Na] ⁺ : 831.4871 <i>m/z</i> , observed: 831.4891 <i>m/z</i>
IR ^a	cm ⁻¹ (KBr)	cm ⁻¹ (thin film)
	3423	3419
	2933	2924
	1685	1683
	1452	1455

^aPublished data from Igarashi et al are reported here. See reference 19.

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^1H AND ^{13}C NMR Spectra for Synthetic and Natural Formamycin.

STANDARD PROTON PARAMETERS

Pulse Sequence: s2pu1
 Solvent: CDCl3
 Ambient temperature
 INOVA-500
 PULSE SEQUENCE
 Pulse width 1.000 sec
 Pulse delay 44.6 degrees
 Acq. time 2.500 sec
 Width 8000.0 Hz
 68 repetitions
 99.9042329 MHz
 DATA PROCESSING
 FT size 65536
 Total time 97 hr, 28 min, 2 sec

^1H NMR (500 MHz, 4 : 1 $\text{CDCl}_3/\text{C}_6\text{D}_6$) of Synthetic **1**.

¹H NMR (500 MHz, 4 : 1 CDCl₃/C₆D₆) of Synthetic 1.

STANDARD PROTON PARAMETERS

Pulse Sequence: s2pul
 Solvent: CDCl3
 Acquisition
 FT size 65536
 INOVA-500 "Kr"
 PULSE SEQUENCE
 Relax delay 1.000 sec
 Pulse 44.6 degrees
 Acq. time 2.500 sec
 Width 8000.0 Hz
 88 repetitions
 OBSERVED F1
 DATA PROCESSING
 FT size 65536
 Total time 97 hr, 28 min, 2 sec

¹H NMR (500 MHz, 4 : 1 CDCl₃/C₆D₆) of Synthetic **1**.

STANDARD PROTON PARAMETERS

Pulse Sequence: s2pu1
 Solvent: CDCl3
 Ambient temperature
 File: T80-III-121-1H_GREAT
 INOVA-500 -K1-
 PULSE SEQUENCE
 Relax. delay 1.000 sec
 Acq. time 2.560 sec
 Width 8000.0 Hz
 68 repetitions
 OBSERVE H1: 499.9042329 MHz
 P1 12.00000000
 P1 delay 6.5536
 Total time 37 hr, 28 min, 2 sec

¹H NMR (500 MHz, 4 : 1 CDCl₃/C₆D₆) of Synthetic **1**.

¹H NMR (500 MHz, 4 : 1 CDCl₃/C₆D₆) of Synthetic **1**.

Pulse Sequence: s2pu1

Solvent: CDC13
Ambient temperature
File: TBD-III-Nat_formamycin-1H_clean
Inova 500 1H-2

INNOVA 300 KI
PULSE SEQUENCE

Relax. delay 1.000 sec

Pulse 44.6 degrees
Acq. time 2,500 sec

Width 8000.0 Hz
96 repetitions

96 repetitions
OBSERVE H1, 499.9042329 MHZ

DATA PROCESSING
FT size 65536

Total time 97 hr, 28 min, 2 sec

¹H NMR (500 MHz, 4 : 1 CDCl₃/C₆D₆) of Natural **1**.

```
Pulse Sequence: s2pul  
Solvent: CDCl3  
Ambient Temperature  
P1: 0.00 sec  
INNOVA-500 MHz  
NUC1: 1H  
PULSE SEQUENCE  
Ref1: delay 1.000 sec  
P1: 0.00 sec  
Pulse 44.6 degrees  
P2: 0.00 sec  
Acq. time 2.500 sec  
Width 8000.0 Hz  
FID size 65536  
DATA PROCESSING  
Spectrum  
FT size 65536  
Total time 97 hr, 28 min, 2 sec
```

¹H NMR (500 MHz, 4 : 1 CDCl₃/C₆D₆) of Natural **1**.

STANDARD PROTON PARAMETERS
Pulse Sequence: s2pul
Solvent: CDCl₃
Acquisition temperature: 300 K
File: T80-II-Nat_formamycin-1H_clean
INOVA-500 "K"r"
PULSE SEQUENCE
Relax delay 1.000 sec
Pulse 44.6 degrees
Acq. time 2.500 sec
Width 8000.0 Hz
96 repetitions
OBSERVE H1, 499.9042329 MHz
DATA PROCESSING
P1 12.000000 sec
Total time 97 hr, 28 min, 2 sec

¹H NMR (500 MHz, 4 : 1 CDCl₃/C₆D₆) of Natural 1.


```
Pulse Sequence: s2pul
Solvent: CDCl3
Amplitude: 10.00 V
Temperature: 300.2 K
Acq. time: 2.500 sec
NUC1: 1H
NUC2: 13C
PULSE SEQUENCE
Relax delay: 1.000 sec
Pulse 44: 90 degrees
Pulse 45: 90 degrees
Acq. time: 2.500 sec
Width: 8000.0 Hz
Sweep range: 60000.0 Hz
Number of acquisitions: 1
FID processing parameters
Data file name: g3g_9042323.MHZ
FT size: 65536
Total time: 97 hr, 28 min, 2 sec
```

¹H NMR (500 MHz, 4 : 1 CDCl₃/C₆D₆) of Natural **1**.

¹H NMR (500 MHz, 4 : 1 CDCl₃/C₆D₆) of Natural 1.

STANDARD CARBON PARAMETERS

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 Date: 11/11/02
 File: T80-111-148-13C_sat_10AM
 INOVA-500 "Kr"
 PULSE SEQUENCE
 Relax. delay 0.700 sec
 Pulse 45.0 degrees
 Acq. time 1.300 sec
 Width 30018.8 Hz
 F2 RESERVE C13, 125.7005937 MHz
 DECOUPLE H1, 499.9067532 MHz
 Power 39 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 F2 RESERVE C13, 125.7005937 MHz
 FI size 131072
 Total time 557895 hr, 36 min, 32 sec

¹³C NMR (125 MHz, 4 : 1 CDCl₃/C₆D₆) of Synthetic **1**.

STANDARD CARBON PARAMETERS

Pulse Sequence: s2pu1
 Solvent: CDCl3
 Name: 1
 User: jmg
 File: T60-111-148-13C_set_10AM
 INOVA-500 "Kr"
 PULSE SEQUENCE
 Relax. delay 0.700 sec
 Pulse 45.0 degrees
 Acq. time 1.300 sec
 Width 30018.8 Hz
 Frequency 125.760 MHz
 OBSERVE C13, 125.7009937 MHz
 DECOUPLE H1, 499.9067532 MHz
 Power 39 dB
 continuously on
 WALTZ-16 modulated
 WALTZ-16 modulated
 Line broadening 2.0 Hz
 FT size 131072
 Total time 557895 hr, 96 min, 32 sec

^{13}C NMR (125 MHz, 4 : 1 $\text{CDCl}_3/\text{C}_6\text{D}_6$) of Synthetic **1**.

STANDARD CARBON PARAMETERS

Pulse Sequence: s2pul
 Solvent: CDCl3
 Ambient temperature
 F1: T80-112/148-13C_sat_10AM
 INOVA-500 "Krf"
 PULSE SEQUENCE
 Relax delay 0.700 sec
 Pulse 45.0 degrees
 Acq. time 1.300 sec
 Width 30018.8 Hz
 Q3884 repetitions
 DECOUPLE C41, 499.9067532 MHz
 Power 39 dB
 continuously on
 WALTZ-16 modulated
 DATA PROCESSING
 F1: 125.000 MHz
 F2: 330.000 MHz
 Total time 557895 hr, 36 min, 32 sec

¹³C NMR (125 MHz, 4 : 1 CDCl₃/C₆D₆) of Synthetic **1**.

STANDARD CARBON PARAMETERS

Pulse Sequence: s2pu1
 Solvent: CDCl3
 User: j1487
 File: T8D-III-148-13C_sat_10AM
 INOVA-500 "Kr"
 PULSE SEQUENCE
 Relax. delay 0.700 sec
 Pulse 45.0 degrees
 Acq. time 1.300 sec
 21685
 OBSERVE C13, 125.7009337 MHZ
 DECOUPLE H1, 499.9067532 MHZ
 Power 39 dB
 continuously on
 WALTZ16 modulated
 45.0 degrees
 FT size 131072
 Total time 557895 hr, 36 min, 32 sec

¹³C NMR (125 MHz, 4 : 1 CDCl₃/C₆D₆) of Synthetic 1.