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Supporting Information

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Synthesis of (−)-Okilactomycin by a Prins-Type Fragment-Assembly Strategy**

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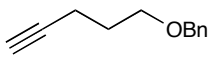
Supporting Information

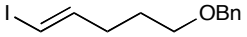
General Information

All reactions were carried out under a nitrogen atmosphere in flame dried glassware with magnetic stirring. Dichloromethane, tetrahydrofuran, benzene, toluene, acetonitrile, ether, and methanol were purified by passage though a bed of activated alumina.[1] Reagents were purified following the guidelines of Armarego and Chai prior to use unless otherwise stated.[2] Purification of reaction products was carried out by flash chromatography using EM Reagent silica gel 60 (230-400 mesh). Preparative HPLC was carried out on an Agilent 1200 Series LC with an Agilent 6130 Quadropole Mass Anaylizer (ESI Source) and a LEAP CTC PAL Fraction Collector. Analytical thin layer chromatography (TLC) was performed on EM Reagent 0.25 mm silica gel 60-F plates. Visualization was accomplished with UV light or ceric ammonium molybdate stain followed by heating. Infrared spectra were recorded on a Bruker Tensor 37 FT-IR spectrometer. ^{1}H NMR spectra were recorded on an INOVA 500 (500 MHz) or an AVANCE III 500 MHz w/ direct cryoprobe (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 7.26 ppm). Data are reported as (ap = apparent, s = singlet, d = doublet, t = apparent triplet, q = quartet, m = multiplet, b = broad; coupling constant(s) in Hz; integration.) Proton-decoupled ^{13}C NMR spectra were recorded on an AVANCE III 500 MHz w/ direct cryoprobe (125 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$ at 77.0 ppm). Optical rotations were measured on a Perkin Elmer Model 341 Polarimeter with a sodium lamp. Mass spectra were obtained on a Thermo Finnegan LCQ (ESI) or an Agilent 1100 series LC/MSD. High resolution mass spectra were obtained on a Agilent 6210 LC-TOF (ESI, APCI, APPI).

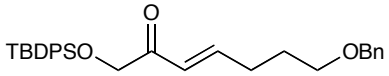
Synthesis of α-Silyloxy Aldehyde 21



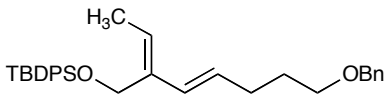
((pent-4-ynyloxy)methyl)benzene (**5**). To a flame-dried, round-bottom flask with stir bar containing sodium hydride (3.1 g, 129 mmol) and THF (180 mL) was added neat 4-pentyn-1-ol (5.0 mL, 54 mmol) dropwise by syringe. The reaction mixture was stirred at room temperature for 1 h. Benzyl chloride (6.2 mL, 54 mmol) and tetrabutylammonium iodide (0.9 g, 2.4 mmol) were added in one portion, respectively. The flask was fitted with a reflux condensor and heated to 70 °C for 18 h. The reaction mixture was cooled to room temperature and diluted with EtOAc (100 mL). The organic layer was washed with water (2 x 100 mL) and brine (100 mL). The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (5% EtOAc/hexanes) to afford alkyne **5** (8.1 g, 86%) as a colorless oil. Analytical data: ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.35-7.34 (m, 4H), 7.30-7.27 (m, 1H), 4.52 (s, 2H), 3.58 (t, J = 6.2 Hz, 2H), 2.33 (td, J = 7.1, 2.7 Hz, 2H), 1.94 (t, J = 2.7 Hz, 1H), 1.84 (tt, J = 7.1, 6.2 Hz, 2H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.4, 128.3, 127.59, 127.54, 83.9, 73.0, 68.61, 68.43, 28.6, 15.3; HRMS (ESI): Mass calcd for $C_{12}H_{15}O$ $[M+H]^+$, 175.1117. Found $[M+H]^+$, 175.1110.



(*E*)-((5-iodopent-4-enyloxy)methyl)benzene (6). To a flame-dried, round-bottom flask with stir bar wrapped in aluminum foil was added $Cp_2Zr(H)Cl$ (3.1 g, 12.1 mmol) and THF (36 mL). The flask was placed in a room temperature water bath and alkyne **5** (2.0 g, 11.5 mmol) was added dropwise by syringe. The flask was removed from the bath and the reaction mixture was stirred for 30 min. The flask was placed in the water bath again and *N*-iodosuccinimide (2.7 g, 12.1 mmol) was added in one portion. The reaction mixture was stirred for 15 min and then diluted with hexanes. The mixture was filtered through Celite and concentrated. The residue was re-dissolved in hexanes and filtered through Florisil and concentrated to afford vinyl iodide **6** (2.9 g, 84%) as a pale yellow oil which was used without further purification. Analytical data: ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.37-7.28 (m, 5H), 6.51 (dt, *J* = 14.4, 7.2 Hz, 1H), 5.99 (dt, *J* = 14.3, 1.4 Hz, 1H), 4.49 (s, 2H), 3.47 (t, *J* = 6.3 Hz, 2H), 2.17 (ddd, *J* = 14.7, 6.8, 1.4 Hz, 2H), 1.73-1.68 (m, 2H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 145.9, 138.4, 128.4, 127.64, 127.59, 75.0, 72.9, 69.0, 32.7, 28.4.

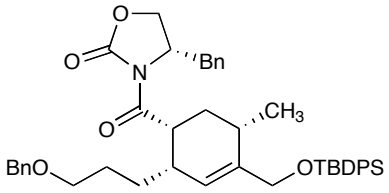


(*E*)-7-(benzyloxy)-1-(*tert*-butyldiphenylsilyloxy)hept-3-en-2-one (S1). To a flame-dried, round-bottom flask with stir bar containing a –78 °C solution of vinyl iodide **6** (11.0 g, 36.4 mmol) in THF (360 mL) was added *n*-BuLi (25 mL, 40 mmol, 1.61 M in hexanes) dropwise by syringe. In a separate flame-dried, round-bottom flask 2-(*tert*-butyldiphenylsilyloxy)-*N*-methoxy-*N*-methylacetamide (**7**) (14.5 g, 40.6 mmol) was dissolved in THF (57 mL). The amide solution was added to the vinyl iodide solution dropwise by canula over 30 min. The reaction mixture was stirred at –78 °C for 3 h. The reaction mixture was quenched with 0.1 N HCl and warmed to room temperature. The mixture was diluted with 1:1 Et_2O:hexanes and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (5% to 10% EtOAc/hexanes) to afford enone **S1** (11.1 g, 65%) as a colorless oil. Analytical data: IR (film) 3071, 2931, 2856, 1695, 1625, 1427, 1110, 823, 739, 700 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.66 (dt, *J* = 7.4, 1.0 Hz, 4H), 7.45-7.27 (m, 12H), 6.94 (dt, *J* = 15.7, 6.9 Hz, 1H), 6.46-6.42 (m, 1H), 4.49 (s, 2H), 4.31 (s, 2H), 3.48 (t, *J* = 6.2 Hz, 2H), 2.35-2.30 (m, 2H), 1.77 (quintet, *J* = 7.0 Hz, 2H), 1.10 (s, 9H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 197.9, 147.7, 138.3, 135.5, 134.8, 132.7, 129.9, 129.6, 128.4, 127.80, 127.70, 127.63, 127.61, 125.5, 73.0, 69.2, 69.0, 29.4, 28.1, 26.7, 19.3; LRMS (ESI): Mass calcd for $C_{30}H_{36}NaO_2Si$ $[2M+Na]^+$, 967.48. Found $[2M+Na]^+$, 967.09.



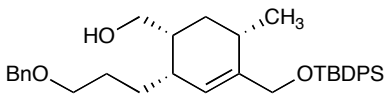
((2*Z*,3*E*)-7-(benzyloxy)-2-ethylidenehept-3-enyloxy)(*tert*-butyl)diphenylsilane (8). To a flame-dried, round-bottom flask with stir bar containing a –78 °C solution of ethyltriphenylphosphonium bromide (23.5 g, 63.3 mmol) in THF (165 mL) was added potassium bis(trimethylsilyl)amide (118 mL, 59 mmol, 0.5 M in toluene) dropwise by cannula over 30 min. The reaction mixture was warmed to 0 °C for 40 min, and then re-

cooled to –78 °C. To the reaction mixture was added a solution of enone **S1** (11.1 g, 23.5 mmol) in THF (65 mL) dropwise by cannula over 45 min. The reaction mixture was warmed to 0 °C and stirred for 3 h. The mixture was poured into 0.1 N HCl (250 mL) and 1:1 Et_2O:hexanes (250 mL). The aqueous layer was extracted with EtOAc (3x), dried with Na_2SO_4, and concentrated to afford a white slurry. The slurry was taken up in 1:1 Et_2O:hexanes and filtered through a plug of SiO_2, eluting with Et_2O in order to remove the solid triphenylphosphine oxide. The resulting oil was purified by flash column chromatography (8% Et_2O/hexanes) to afford diene **8** (9.5 g, 84%) as a colorless oil. Analytical data: IR (film) 3070, 3031, 2930, 2855, 1427, 1109, 1072, 1027, 964, 824 cm $^{-1}$; ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.71 (dt, *J* = 6.6, 1.4 Hz, 4H), 7.44-7.35 (m, 10H), 7.31-7.28 (m, 1H), 5.99 (d, *J* = 15.7 Hz, 1H), 5.81 (dt, *J* = 15.2, 7.4 Hz, 1H), 5.51 (q, *J* = 7.1 Hz, 1H), 4.51 (s, 2H), 4.35 (s, 2H), 3.51 (td, *J* = 6.6, 1.2 Hz, 2H), 2.20 (q, *J* = 7.2 Hz, 2H), 1.77-1.71 (m, 2H), 1.52 (d, *J* = 7.1 Hz, 3H), 1.05 (m, 9H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 138.6, 137.3, 135.7, 133.8, 132.3, 129.5, 128.33, 128.14, 127.62, 127.56, 127.45, 126.8, 72.9, 69.8, 58.6, 29.72, 29.64, 26.8, 19.2, 13.5; LRMS (ESI): Mass calcd for $C_{32}H_{40}NaO_2Si$ $[M+Na]^+$, 507.27. Found $[M+Na]^+$, 507.65.

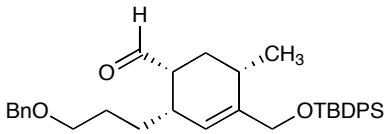


(*S*)-4-benzyl-3-((1*R*,2*S*,5*S*)-2-(3-(benzyloxy)propyl)-4-((*tert*-butyldiphenylsilyloxy)methyl)-5-methylcyclohex-3-enecarbonyl)oxazolidin-2-one (10). To a flame-dried scintillation vial with stir bar wrapped in foil was added diene **8** (1.0 g, 2.1 mmol), silver hexafluorophosphate (0.52 g, 2.1 mmol), and CH_2Cl_2 (4.0 mL), respectively. The reaction mixture was cooled to –78 °C. To the solution was added Et_2AlCl (1.26 mL, 2.3 mmol, 1.8 M in toluene) dropwise by syringe. A –78 °C solution of (*S*)-3-acryloyl-4-benzyloxazolidin-2-one (**9**) (0.51 g, 2.2 mmol) in CH_2Cl_2 (3 mL) was added dropwise by cannula. The reaction mixture was stirred at –78 °C for 1 h, and then poured into saturated aqueous $NaHCO_3$ and diluted with EtOAc. The mixture was filtered through Celite and concentrated. The residue was diluted with CH_2Cl_2, filtered through a Biotage ISOLUTE® phase separator, and the organic filtrate was concentrated. The resulting residue was purified by flash column chromatography (15% EtOAc/hexanes) to afford cyclohexene **10** (1.27 g, 86%) in a >20:1 ratio of diastereomers as a white solid. Analytical data: IR (film) 2931, 2857, 1781, 1697, 1385, 1212, 1110, 823, 701cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.70-7.67 (m, 4H), 7.42-7.37 (m, 6H), 7.31 (q, *J* = 8.6 Hz, 3H), 7.24-7.16 (m, 7H), 5.83 (d, *J* = 5.6 Hz, 1H), 4.70 (ddt, *J* = 10.8, 7.5, 3.5 Hz, 1H), 4.43 (s, 2H), 4.20-4.14 (m, 2H), 4.11-4.07 (m, 2H), 3.84 (ddd, *J* = 12.8, 5.4, 2.5 Hz, 1H), 3.46 (dt, *J* = 9.2, 6.3 Hz, 1H), 3.43-3.37 (m, 2H), 2.85-2.82 (m, 1H), 2.50 (dd, *J* = 13.0, 10.6 Hz, 1H), 2.34-2.29 (m, 1H), 1.81 (ddd, *J* = 13.3, 5.7, 2.2 Hz, 1H), 1.78-1.72 (m, 1H), 1.72-1.65 (m, 1H), 1.61-1.56 (m, 1H), 1.39-1.34 (m, 2H), 1.05 (s, 9H), 1.00 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 175.3, 153.1, 140.4, 138.5, 135.59, 135.55, 133.80, 133.67, 129.6, 129.4, 129.0, 128.3, 127.68, 127.66, 127.62, 127.44, 127.28, 123.9, 73.0, 70.3, 66.3, 65.7, 55.3, 43.1, 38.3, 34.7, 30.9, 29.8, 28.7, 27.4,

26.9, 19.3, 19.1; LRMS (ESI): Mass calcd for $C_{45}H_{57}N_2O_5Si$ $[M+NH_4]^+$, 733.40. Found $[M+NH_4]^+$, 733.25; $[\alpha]_D^{20}$ +81.9 ($CHCl_3$, *c* 0.87).

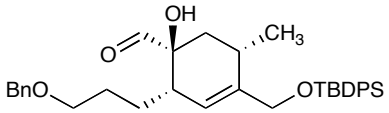


((1*R*,2*S*,5*S*)-2-(3-(benzyloxy)propyl)-4-((*tert*-butyldiphenylsilyloxy)methyl)-5-methylcyclohex-3-enyl)methanol (S2). To a flame-dried, round-bottom flask with stir bar containing a 0 °C solution of cyclohexene **10** (2.7 g, 3.8 mmol), Et_2O (13 mL), and MeOH (0.25 mL) was added $LiBH_4$ (96 mg, 4.4 mmol) in one portion. The reaction mixture was stirred at 0 °C for 3.5 h and then carefully quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (15% to 20% EtOAc/hexanes) to afford primary alcohol **S2** (1.7 g, 83%) as a colorless oil. Analytical data: IR (film) 3401, 2929, 2857, 1428, 1362, 1111, 739, 701 cm^{-1}; ^{1}H-NMR (500 MHz; $CDCl_3$): δ 7.69-7.66 (m, 4H), 7.42-7.33 (m, 10H), 7.29-7.27 (m, 1H), 5.82-5.81 (m, 1H), 4.49 (s, 2H), 4.21 (dd, *J* = 13.0, 1.1 Hz, 1H), 4.08 (d, *J* = 13.0 Hz, 1H), 3.62 (ddd, *J* = 10.6, 7.9, 5.2 Hz, 1H), 3.53 (ddd, *J* = 10.6, 6.9, 5.9 Hz, 1H), 3.47 (td, *J* = 6.5, 1.2 Hz, 2H), 2.35-2.30 (m, 1H), 2.25 (dt, *J* = 10.3, 5.2 Hz, 1H), 1.91 (ttd, *J* = 10.3, 5.3, 2.5 Hz, 1H), 1.78-1.71 (m, 1H), 1.64 (ddd, *J* = 12.9, 6.0, 1.9 Hz, 1H), 1.57 (ddd, *J* = 13.3, 10.2, 6.0 Hz, 1H), 1.53-1.45 (m, 1H), 1.39-1.37 (m, 1H), 1.18-1.13 (m, 1H), 1.05 (s, 9H), 0.95 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 140.5, 138.5, 135.53, 135.50, 133.90, 133.79, 129.53, 129.52, 128.3, 127.66, 127.58, 127.52, 127.51, 125.6, 72.8, 70.5, 66.0, 65.2, 40.1, 34.7, 31.6, 30.9, 27.4, 26.81, 26.67, 19.34, 19.28; LRMS (ESI): Mass calcd for $C_{35}H_{50}NO_3Si$ $[M+NH_4]^+$, 560.36. Found $[M+NH_4]^+$, 560.58; $[\alpha]_D^{20}$ +60.7 (MeOH, *c* 0.83).

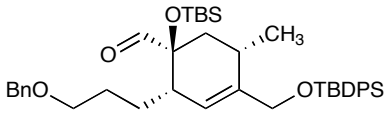


(1*R*,2*S*,5*S*)-2-(3-(benzyloxy)propyl)-4-((*tert*-butyldiphenylsilyloxy)methyl)-5-methylcyclohex-3-enecarbaldehyde (11). To a flame-dried, round-bottom flask with stir bar containing alcohol **S2** (1.9 g, 3.5 mmol) and CH_2Cl_2 (100 mL) was added Dess-Martin periodinane (3.1 g, 7.3 mmol) and a few drops of water. The mixture was stirred at room temperature for 45 min and quenched with saturated aqueous $NaHCO_3$ (60 mL) and ½ saturated aqueous $Na_2S_2O_3$ (60 mL). The mixture was stirred until both layers were clear, filtered through a Biotage ISOLUTE® phase separator, and the organic filtrate was concentrated. The residue was purified by flash column chromatography (5% EtOAc/hexanes) to afford aldehyde **11** (1.7 g, 90%) as a colorless oil. Analytical data: IR (film) 2931, 2857, 2710, 1723, 1428, 1361, 1111, 823, 739, 701 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.77 (s, 1H), 7.66 (tt, *J* = 6.1, 1.7 Hz, 4H), 7.43-7.27 (m, 11H), 5.84 (dd, *J* = 5.3, 1.4 Hz, 1H), 4.47 (s, 2H), 4.19 (dd, *J* = 13.2, 0.9 Hz, 1H), 4.09 (d, *J* = 13.2 Hz, 1H), 3.42 (t, *J* = 6.5 Hz, 2H), 2.63 (dq, *J* = 10.0, 4.9 Hz, 1H), 2.57 (ddd, *J* = 12.1, 5.0, 2.8 Hz, 1H), 2.30 (dq, *J* = 15.6, 7.6 Hz, 1H), 2.00 (ddd, *J* = 13.5, 6.1, 2.5 Hz, 1H), 1.75-

1.67 (m, 1H), 1.63-1.56 (m, 1H), 1.43-1.35 (m, 2H), 1.28 (dtd, *J* = 12.9, 10.4, 5.0 Hz, 1H), 1.06 (s, 9H), 0.98 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 204.9, 141.2, 138.4, 135.51, 135.49, 133.67, 133.63, 129.62, 129.60, 128.3, 127.64, 127.62, 127.57, 127.52, 124.0, 72.9, 70.2, 65.7, 50.9, 34.4, 30.7, 29.1, 27.7, 27.4, 26.8, 19.3; LRMS (ESI): Mass calcd for $C_{35}H_{48}NO_3Si$ $[M+NH_4]^+$, 558.34. Found $[M+NH_4]^+$, 558.75; $[\alpha]_D^{20}$ = +61.8° (MeOH, c 1.57).



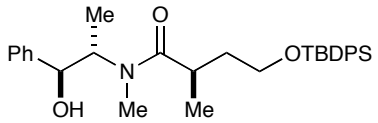
(1*S*,2*S*,5*S*)-2-(3-(benzyloxy)propyl)-4-((*tert*-butyldiphenylsilyloxy)methyl)-1-hydroxy-5-methylcyclohex-3-enecarbaldehyde (3). To a flame-dried, round-bottom flask with stir bar containing aldehyde **11** (1.6 g, 3.0 mmol) and CH_2Cl_2 (7 mL) was added triethylamine (6.0 mL), followed by *t*-butyldimethylsilyltriflate (7.2 mL 31 mmol) dropwise by syringe. The solution was stirred for 1 h at room temperature, then cooled to 0 °C and diluted with hexanes followed by saturated aqueous $Na_2S_2O_3$. The aqueous layer was extracted with hexanes (3x) and the combined organic layers were dried over Na_2SO_4 and concentrated. The resulting yellow oil was added to a round-bottom flask, dissolved in CH_2Cl_2 (64 mL), and cooled to 0 °C. To the solution was added a cold solution of dimethyldioxirane (53.8 mL 3.8 mmol, 0.07 M in acetone) dropwise by syringe. The reaction mixture was concentrated in vacuo after 5 min (bath >25 °C). The residue was redissolved in EtOAc (100 mL) and re-cooled to 0 °C. To the solution was added 0.1 N HCl (50 mL). The mixture was stirred at 0 °C for 30 min and then at room temperature for 30 min. The reaction mixture was extracted with EtOAc (3x), and the combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (10% to 20% EtOAc/hexanes) to afford α-hydroxy aldehyde **3** (1.45 g, 88% over two steps) in a 13:1 ratio of diastereomers as a colorless oil. Analytical data: IR (film) 3431, 2955, 2857, 1724, 1454, 1111, 438 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$): δ 9.64 (s, 1H), 7.67 (ddd, *J* = 7.9, 4.0, 1.5 Hz, 4H), 7.43-7.27 (m, 11H), 5.71 (dd, *J* = 3.2, 1.5 Hz, 1H), 4.47 (s, 2H), 4.20 (q, *J* = 13.9 Hz, 2H), 3.47-3.39 (m, 2H), 3.21 (s, 1H), 2.55 (q, *J* = 6.7 Hz, 1H), 2.26 (d, *J* = 9.4 Hz, 1H), 1.93 (dd, *J* = 13.6, 6.8 Hz, 1H), 1.81-1.73 (m, 1H), 1.62-1.52 (m, 3H), 1.19-1.12 (m, 1H), 1.07 (s, 9H), 0.97 (d, *J* = 7.2 Hz, 3H); ^{13}C NMR (126 MHz; $CDCl_3$): δ 204.7, 140.3, 138.4, 135.56, 135.54, 133.5, 129.71, 129.69, 128.4, 127.67, 127.63, 127.54, 121.3, 78.6, 72.9, 69.9, 65.4, 43.6, 38.4, 28.2, 27.67, 27.63, 26.8, 19.7, 19.2; LRMS (ESI): Mass calcd for $C_{35}H_{48}NO_4Si$ $[M+NH_4]^+$, 574.34. Found $[M+NH_4]^+$, 574.50; $[\alpha]_D^{20}$ +60.9 (MeOH, *c* 0.77).



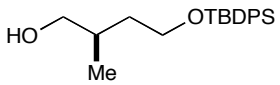
(1*S*,2*S*,5*S*)-2-(3-(benzyloxy)propyl)-1-(*tert*-butyldimethylsilyloxy)-4-((*tert*-butyldiphenylsilyloxy)methyl)-5-methylcyclohex-3-enecarbaldehyde (21). To a flame-dried, round-bottom flask with stir bar containing α-hydroxy aldehyde **3** (3.7 g 6.6

mmol), 2,6-lutidine (4.6 mL, 40 mmol) and CH_2Cl_2 (67 mL) was added *t*-butyldimethylsilyltriflate (4.6 mL, 20 mmol) dropwise by syringe. The reaction mixture was stirred for 40 min, quenched with saturated aqueous $NaHCO_3$ (70 mL), and filtered through a Biotage ISOLUTE® phase separator. The organic filtrate was concentrated and the residue was purified by flash column chromatography (2% to 4% EtOAc/hexanes) to afford α-silyloxy aldehyde **21** (3.9 g, 88%) as a pale yellow oil. Analytical data: IR (film) 2954, 2930, 2857, 2737, 2709, 1734, 1472, 1253, 1112, 837, 777, 739, 702 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$): δ 9.60 (s, 1H), 7.69-7.66 (m, 4H), 7.42-7.27 (m, 11H), 5.73 (dt, *J* = 3.0, 1.5 Hz, 1H), 4.46 (s, 2H), 4.17 (dd, *J* = 12.9, 1.0 Hz, 1H), 4.09 (d, *J* = 12.9 Hz, 1H), 3.41 (td, *J* = 6.4, 1.2 Hz, 2H), 2.53 (d, *J* = 7.6 Hz, 1H), 2.30-2.28 (m, 1H), 1.79 (ddd, *J* = 13.8, 6.3, 1.2 Hz, 1H), 1.75-1.70 (m, 1H), 1.58 (dd, *J* = 13.8, 9.3 Hz, 1H), 1.53-1.45 (m, 2H), 1.12-1.08 (m, 1H), 1.05 (s, 9H), 0.99 (d, *J* = 7.1 Hz, 3H), 0.87 (s, 9H), 0.11 (s, 3H), 0.09 (s, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 202.9, 139.8, 138.4, 135.54, 135.52, 133.61, 133.59, 129.62, 129.55, 128.3, 127.63, 127.59, 127.52, 121.7, 81.1, 72.9, 70.1, 65.7, 43.1, 35.7, 31.6, 29.1, 27.63, 27.56, 26.8, 25.8, 19.2, 19.0, 18.4, 14.1, –2.2, –2.5; LRMS (ESI): Mass calcd for $C_{41}H_{58}O_4Si_2Na$ $[M+Na]^+$, 693.38. Found $[M+Na]^+$, 693.53; $[\alpha]_D^{20}$ +62.1 ($CHCl_3$, *c* 1.02).

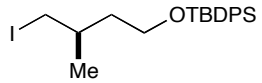
Synthesis of β-Hydroxy Dioxinone 4



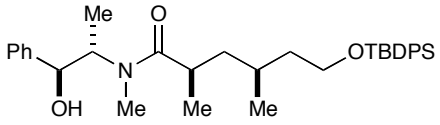
(*R*)-4-(*tert*-butyldiphenylsilyloxy)-*N*-((1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl)-*N*,2-dimethylbutanamide (S3). To a –78 °C suspension of LiCl (21.8 g, 514 mmol) and diisopropylamine (25.7 mL, 183 mmol) in THF (123 mL) was added *n*-BuLi (82 mL, 172 mmol, 2.1 M solution in hexanes) via cannula. The resulting suspension was warmed to 0 °C briefly and then was cooled to –78 °C. An ice-cooled solution of (1*S,2S)*-pseudoephedrine propionamide (20.2 g, 91.5 mmol) in THF (300 mL) was added via cannula. The mixture was stirred at –78 °C for 1 h, at 0 °C for 15 min, and at 23 °C for 5 min. The mixture was cooled to 0 °C and a solution of TBDPS iodoethanol (23.5 g, 57.2 mmol) in THF (27 mL) was added via cannula. The mixture stirred for 18 hours in a water bath before being quenched by the addition of saturated NH_4Cl (300 mL). The organic layer was removed and the remaining aqueous layer was extracted with EtOAc (4 x 100 mL). The combined organic layers were combined and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 75% Et_2O/hexanes) to afford amide **S3** (30.4 g, 98%) as a viscous oil (dr 20:1). Analytical data: IR (film) 3379, 3062, 1959, 1890, 1824, 1770, 1618, 1107 cm^{-1}; ^1H NMR (3:1 rotamer ratio, only major rotamer reported, 500 MHz, C_6D_6) δ 7.69-7.65 (m, 5H), 7.4-7.0 (m, 10H), 4.56-4.53 (m,1H), 3.58-3.52 (m, 2H), 2,80-2.76 (m, 1H) 2.49 (s, 3H), 1.94-1.90 (m, 1H), 1.49-1.45 (m, 1H), 1.21-1.19 (m, 1H), 1.09 (s, 9H), 0.97-0.96 (d, *J* = 5.5 Hz, 3H), 0.96-0.95 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 177.6, 143.6, 135.9, 135.8, 135.7, 134.1, 129.9, 129.8, 128.2, 126.7, 76.1, 61.8, 37.0, 32.6, 27.1, 27.0, 19.3, 17.1, 14.2; LRMS (ESI): Mass calcd for $C_{31}H_{42}NO_3Si$ $[M+H]^+$, 504.75. Found 504.70; $[\alpha]_D^{20}$ +36.4 (CH_2Cl_2, *c* 1.0).



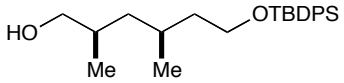
(*R*)-4-(*tert*-butyldiphenylsilyloxy)-2-methylbutan-1-ol (S4). To a –78 °C solution of diisopropylamine (33.1 mL, 234 mmol) in THF (233 mL) was added *n*-BuLi (103 mL, 217 mmol, 2.1 M solution in hexanes) via cannula. The resulting solution was stirred at –78 °C for 10 min, then warmed to 0 °C and held at that temperature for 10 min. Borane-ammonia complex (90%, 6.9 g, 223 mmol) was added in one portion , and the suspension was stirred at 0 °C for 15 min and then armed to 23 °C. After 15 min, the suspension was cooled to 0 °C and a solution of **S3** (30.4 g, 55.7 mmol) in THF (140 mL) was added via cannula. The reaction mixture was warmed to 23 °C, held at this temperature for 2 h, and then cooled to 0 °C where excess hydride was quenched by the addition of 0.01 M aqueous HCl (500 mL). The mixture was stirred for 30 min at 0 °C and then extracted with EtOAc (4 x 150 mL). The combined organic extracts were washed with 0.1 m aqueous HCl (60 mL), 1 M NaOH (2 x 60 mL), and brine (50 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography (SiO_2, 60% Et_2O/hexanes) to afford **S4** (18.3 g, 96%) as a viscous oil. Analytical data: IR (film) 3351, 2931, 1959, 1890, 1824, 1773, 1465, 1427 cm^{-1}; ^1H NMR, (500 MHz, $CDCl_3$) δ 7.69−7.68 (m, 4H), 7.46−7.39 (m, 6H), 3.78−3.74 (m, 1H), 3.73-3.70 (m, 1H), 3.54-3.48 (m, 2H), 2.60 (br s, 1H), 1.88-1.85 (m, 1H), 1.64-1.62 (m, 1H), 1.57-1.49 (m, 1H), 1.06 (s, 9H), 0.92-0.91 (d, J = 7.02 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.8, 133.6, 129.9, 127.6, 68.4, 62.7, 37.0, 34.1, 27.0, 19.3, 17.4; LRMS (ESI): Mass calcd for $C_{21}H_{30}O_2SiNa$ $[M+Na]^+$, 365.5. Found 365.2; $[\alpha]_D^{20}$ +6.3 (CH_2Cl_2, *c* 1.05).



(*R*)-*tert*-butyl(4-iodo-3-methylbutoxy)diphenylsilane (S5).To a solution of Ph_3P (16.8 g, 64.1 mmol) in CH_2Cl_2 (200 mL) was added imidazole (5.45 g, 80 mmol) and iodine (18.4 g, 72.1 mmol) at 23 °C. A solution of **S4** in CH_2Cl_2 (24 mL) was added to this suspension via cannula. After 2 h, CH_2Cl_2 was removed *in vacuo*. The solid residue was purified by flash column chromatography (SiO_2, 10% EtOAc/hexanes) to afford **S5** (20.2 g, 84%) as a colorless oil. Analytical data: IR (film) 3066, 2930, 1959, 1889, 1824, 1771, 1550 cm^{-1}; ^1H NMR, (500 MHz, $CDCl_3$) δ 7.68−7.66 (m, 4H), 7.44−7.38 (m, 6H),), 3.71-3.69 (t, J = 6.23 Hz, 2H), 3.27-3.24 (dd, J = 9.7, 4.5 Hz, 1H), 3.18-3.15 (dd, J = 9.7, 4.5 Hz 1H), 1.76-1.71 (m, 1H), 1.70-1.63 (m, 1H), 1.48-1.43 (m, 1H), 1.07 (s, 9H), 0.98-0.96 (d, J = 6.58 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.8, 134.0, 129.9, 127.9, 61.8, 39.2, 31.6, 27.2, 20.9, 19.5, 18.4; LRMS (ESI): Mass calculated for $C_{21}H_{29}OSi$ $[M–I]^+$, 325.5. Found 325.2; $[\alpha]_D^{20}$ +1.2 (CH_2Cl_2 *c* 1.2).

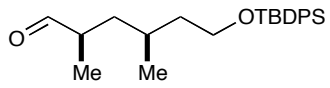


(2*R*,4*S*)-6-(*tert*-butyldiphenylsilyloxy)-*N*-((1*S*,2*S*)-1-hydroxy-1-phenylpropan-2-yl)-*N*,2,4-trimethylhexanamide (S6). To a –78 °C suspension of LiCl (22.7 g, 535 mmol) and diisopropylamine (26.8 mL, 192 mmol) in THF (77 mL) was added *n*-BuLi (87 mL, 178 mmol, 2.05 M solution in hexanes) via cannula. The resulting suspension was warmed to 0 °C briefly and then was cooled to –78 °C. An ice-cooled solution of (1*S,2S)*-pseudoephedrine propionamide (20.8 g, 93.8 mmol) in THF (144 mL) was added via cannula. The mixture was stirred at –78 °C for 1 h, at 0 °C for 15 min, and at 23 °C for 5 min. The mixture was cooled to 0 °C and a solution of **S5** (20.2 g, 44.6 mmol) in THF (10 mL) was added via cannula. The mixture stirred for 18 hours at 23 °C before being quenched by the addition of saturated/½ saturated NH_4Cl (300 mL). The organic layer was removed and the remaining aqueous layer was extracted with EtOAc (4 x 100 mL). The combined organic layers were combined and dried over Na_2SO_4, filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography (SiO_2, 50% EtOAc/hexanes) to afford amide **S6** (22.5 g, 93%) as a viscous oil (dr 20:1). Analytical data: IR (film) 3374, 2931, 1617, 1612, 1107 cm^{-1}; ^1H NMR (3:1 rotamer ratio, only major rotamer reported, 500 MHz, C_6D_6) δ 7.79-7.77 (m, 5H), 7.26-7.00 (m, 10H), 4.5-4.40 (m, 1H), 3.78-3.70 (m, 2H), 2.40-2.35 (m, 1H), 2.25 (s, 3H), 1.82-1.80 (m, 1H), 1.61-1.59 (m, 1H), 1.25-1.20 (m, 1H), 1.15 (s, 9H), 1.05-1.02 (m, 1H), 0.96-0.94 (d, *J* = 8.4 Hz, 3H), 0.94-0.93 (d, J = 6.7 Hz, 3H), 0.90 (m, 1H), 0.85 (m, 1H), 0.65-0.64 (d, *J* = 6.2 Hz, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 178.2, 143.7, 135.9, 135.8, 134.3, 129.8, 128.5, 127.2, 126.5, 76.3, 62.2, 41.7, 40.1, 34.1, 27.5, 27.0, 26.3, 23.6, 19.8, 19.3, 17.9, 14.2; LRMS (ESI): Mass calcd for $C_{34}H_{48}NO_3Si$ $[M+H]^+$, 546.8. Found 546.6; $[\alpha]_D^{20}$ +45.7 (*c* 0.9, CH_2Cl_2).

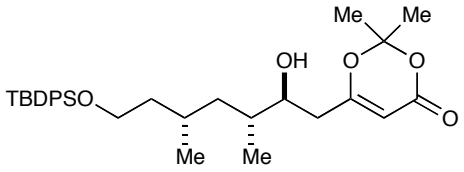


(2*R*,4*S*)-6-(*tert*-butyldiphenylsilyloxy)-2,4-dimethylhexan-1-ol (S7).To a –78 °C solution of diisopropylamine (24.5 mL, 173 mmol) in THF (170 mL) was added *n*-BuLi (80 mL, 160 mmol, 2.0 M solution in hexanes) via cannula. The resulting solution was stirred at –78 °C for 10 min, then warmed to 0 °C and held at that temperature for 10 min. Borane-ammonia complex (90%, 5.1 g, 165 mmol) was added in one portion, and the suspension was stirred at 0 °C for 15 min and then warmed to 23 °C. After 15 min, the suspension was cooled to 0 °C and a solution of amide **S6** (22.5 g, 41.2 mmol) in THF (103 mL) was added via cannula. The reaction mixture was warmed to 23 °C, held at this temperature for 2 h, and then cooled to 0 °C where excess hydride was quenched by the addition of 0.01 M aqueous HCl (500 mL). The mixture was stirred for 30 min at 0 °C and then extracted with EtOAc (4 x 150 mL). The combined organic extracts were washed with 0.1 m aqueous HCl (50 mL), 1 M NaOH (2 x 50 mL), and brine (40 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated. The residue was purified by flash column chromatography (SiO_2, 40% Et_2O/hexanes) to afford **S7** (14.3 g, 91%) as a colorless, viscous oil. Analytical data for II-62: IR (film) 3338, 2929, 1889,

1825, 1427, 1107 cm^{-1}; ^1H NMR, (500 MHz, $CDCl_3$) δ 7.69−7.68 (m, 4H), 7.45−7.38 (m, 6H), 3.74−3.68 (m, 2H),), 3.51-3.48 (m, 1H), 3.40-3.35 (m, 1H), 1.73-1.69 (m, 2H), 1.68-1.63 (m, 2H), 1.32-1.26 (m, 2H), 1.06 (s, 9H), 0.93-0.91 (d, *J* = 6.7Hz, 3H), 0.86-0.84 (d, *J* = 6.71 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.8, 134.3, 129.7, 127.8, 68.6, 62.2, 41.2, 39.3, 33.3, 27.1, 26.9, 20.6, 19.4, 17.3; LRMS (ESI): Mass calcd for $C_{24}H_{36}O_2SiNa$ $[M+Na]^+$, 407.63. Found 407.26; $[\alpha]_D^{20}$ +9.5 (CH_2Cl_2, *c* 0.95).

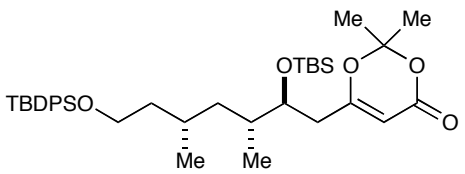


(2*R*,4*S*)-6-(*tert*-butyldiphenylsilyloxy)-2,4-dimethylhexanal (13). To a suspension of powdered 4Å molecular sieves (8.4 g) and **S7** (3.8 g, 9.89 mmol) in CH_2Cl_2 (68 mL) was added NMO (1.85 g, 15.8 mmol) followed by TPAP (172 mg, 0.49 mmol). After 45 min the green reaction mixture was filtered through Celite (eluting with CH_2Cl_2) and concentrated *in vacuo* to approximately 15 mL. The resulting material was filtered through SiO_2 (eluting with 40% Et_2O/hexanes, 300 mL). Removal of the solvent *in vacuo* afforded aldehyde **13** (3.45 g, 92%) as a colorless oil. Aldehyde **13** was used directly in the next step.

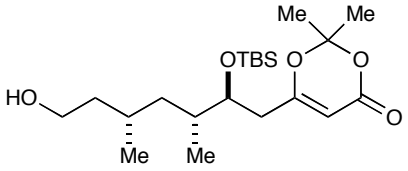


6-((2*S*,3*R*,5*S*)-7-(*tert*-butyldiphenylsilyloxy)-2-hydroxy-3,5-dimethylheptyl)-2,2-dimethyl-4*H*-1,3-dioxin-4-one (15). A mixture of $Cu(OTf)_2$ (651 mg, 1.8 mmol) and (*R*)-Tol-BINAP (1.5 g, 2.25 mmol) in THF (58 mL) was stirred at room temperature under N_2 for 15 minutes to yield a clear yellow solution. A solution of $Bu_4NPh_3SiF_2$ (1.5 g, 2.7 mmol) in THF (16 mL) was added via cannula and the resulting solution was stirred for 15 minutes. The mixture was cooled to –78 °C and enol silane **14** (2.5 g, 11.7 mmol) was added dropwise followed immediately by a solution of **13** (3.45 g, 9.0 mmol) in THF (6.4 mL). The mixture was warmed to –50 °C and allowed to stir for 24 h. Trifluroacetic acid (3.6 mL) was added at –78 °C and the solution was allowed to warm to 23 °C. Stirring was continued for 1 h. The reaction mixture was diluted with EtOAc (90 mL) and saturated $NaHCO_3$ was added dropwise until gas evolution ceased. The organic layer was washed with brine (30 mL), dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (65% Et_2O/hexanes) to afford β-hydroxy-dioxinone **15** (2.90 g, 61%) as an inseperable mixture of diastereomers (dr 7:1). Analytical data: IR (film) 3453, 2930, 1718, 1631, 1384 cm^{-1}; ^1H NMR, (500 MHz, $CDCl_3$) δ 7.69−7.67 (m, 4H), 7.46−7.38 (m, 6H), 5.34 (s, 1H), 3.76-3.67 (m, 3H), 2.36-2.33 (dd, *J* = 14.3, 3.0 Hz, 1H), 2.28-2.23 (dd, *J* = 14.6, 9.7 Hz, 1H), 1.76-1.72 (m, 2H), 1.70 (s, 6H), 1.67-1.62 (m, 2H), 1.33-1.32 (m, 1H), 1.23-1.20 (m,1H), 1.06 (s, 9H), 0.93-0.92 (d, *J* = 6.7 Hz, 3H), 0.88-0.87 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 161.3, 135.8, 134.2, 129.8, 127.8, 106.8, 95.2, 73.0, 62.1, 40.0, 38.7, 38.0, 36.6,

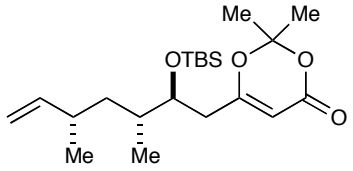
27.1, 25.6, 24.9, 20.9, 19.4, 15.5, 13.6; LRMS (ESI): Mass calculated for $C_{31}H_{48}NO_5Si$ $[M+NH_4]^+$, 542.33. Found 542.51; $[\alpha]_D^{20}$ –1.7 (CH_2Cl_2, *c* 1.0).



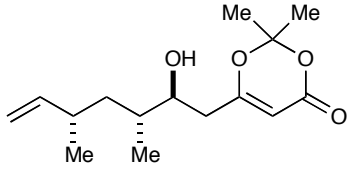
6-((2*S*,3*R*,5*S*)-2-(*tert*-butyldimethylsilyloxy)-7-(*tert*-butyldiphenylsilyloxy)-3,5-dimethylheptyl)-2,2-dimethyl-4*H*-1,3-dioxin-4-one (S8). To a 0 °C solution of **15** (2.90 g, 5.49 mmol) in CH_2Cl_2 (58 mL) was added 2,6-lutidine (1.9 mL, 16.5 mmol) and TBSOTf (1.3 mL, 6.0 mmol). The resulting solution was stirred at 0 °C for 90 minutes and quenched by the addition of saturated $NaHCO_3$ (120 ml). The aqueous layer was extracted with EtOAc (3x 15 ml). The combined organic layers were dried over Na_2SO_4, filtered and concentrated. The resulting residue was purified by flash column chromatography (40% Et_2O/hexanes) to afford bis silyl ether **S8** (3.3 g, 92%) as a clear oil. Analytical data: IR (film) 1736, 1636, 1461, 1384 cm^{-1}; ^1H NMR, (500 MHz, $CDCl_3$) δ 7.68-7.67 (m, 4H), 7.45-7.37 (m, 6H), 5.27 (s, 1H), 3.87-3.84 (ddd, *J* = 8.8, 6.7, 5.1 Hz, 1H), 3.75-3.66 (m, 2H), 2.24-2.22 (dd, *J* = 6.7, 1.5 Hz, 1H), 1.81-1.79 (m, 1H), 1.68 (s, 3H), 1.66 (s, 3H), 1.21-1.18 (dd, *J* = 13.4, 6.1, 1H), 1.06 (s, 9H), 1.02-0.97 (m, 1H), 0.89 (s, 9H), 0.87-0.86 (d, *J* = 6.7, 3H), 0.86-0.82 (m, 4H), 0.79-0.78 (d, *J* = 6.4 Hz, 3H), 0.06 (s, 3H), 0.03 (s, 3H) ; ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.5, 161.3, 135.7, 134.2, 129.8, 127.8, 106.5, 95.4, 72.9, 62.1, 40.9, 39.2, 37.5, 36.3, 27.1, 26.1, 26.0, 24.4, 20.7, 19.4, 18.2, 14.5, –4.1, –4.5; LRMS (ESI): Mass calculated for $C_{74}H_{120}NO_{10}Si_4$ $[2M+NH_4]^+$, 1294.8. Found 1294.03; $[\alpha]_D^{20}$–9.9 (CH_2Cl_2, *c* 1.0).



6-((2*S*,3*R*,5*S*)-2-(*tert*-butyldimethylsilyloxy)-7-hydroxy-3,5-dimethylheptyl)-2,2-dimethyl-4*H*-1,3-dioxin-4-one (S9). To a 23 °C solution of bis silyl ether **S8** (3.3 g, 5.05 mmol) in MeOH (106 mL) was added NH_4F (18.7 g, 505 mmol). The resulting mixture was warmed to 40 °C for 24 h. The solvent was removed *in vacuo* and the resulting residue was purified by flash column chromatography (75% Et_2O/hexanes) to afford **S9** (1.9 g, 92%) as a clear oil. Analytical data: IR (film) 3444, 2931, 1715, 1635, 1461, 1384 cm^{-1}; ^1H NMR, (500 MHz, $CDCl_3$) δ 5.27 (s, 1H), 3.88-3.85 (ddd, *J* = 11.2, 7.6, 3.9 Hz, 1H), 3.72-3.64 (m, 2H), 2.25-2.24 (dd, J = 3.6, 1.2, Hz, 1H), 1.75 (m, 1H), 1.70 (s, 3H), 1.68 (s, 3H), 1.64-1.62 (m, 2H), 1.41 (br s. 1H), 1.30-1.29 (m, 1H), 1.28-1.25 (m, 1H), 1.05-1.00 (m, 1H), 0.95-0.94 (d, *J* = 6.4 Hz, 3H), 0.90-0.88 (d, *J* = 7.0 Hz, 3H), 0.87 (s, 9H), 0.05 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.4, 161.3, 106.5, 95.4, 72.7, 61.0, 40.6, 39.4, 37.5, 36.3, 27.1, 26.0, 24.5, 20.8, 18.2, 14.7, –4.1, –4.5; LRMS (ESI): Mass calculated for $C_{42}H_{80}NaO_{10}Si_2$ $[2M+Na]^+$, 823.52. Found 823.62; $[\alpha]_D^{25}$ –22.7 (CH_2Cl_2, *c* 1.0).



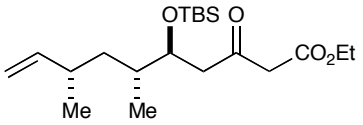
6-((2*S*,3*R*,5*S*)-2-(*tert*-butyldimethylsilyloxy)-3,5-dimethylhept-6-enyl)-2,2-dimethyl-4*H*-1,3-dioxin-4-one (16). To a 23 °C solution of **S9** (1.9 g, 4.64 mmol) in THF (22.5 mL) was added 2-nitrophenylselenocyanide (1.7 g, 7.42 mmol) and *n*-Bu_3P (1.8 mL, 7.42 mmol). The resulting solution stirred at 23 °C for 30 min. The mixture was than passed through a short plug of SiO_2 (eluting with 60% Et_2O/ hexanes) and concentrated. The resulting residue was purified by flash column chromatography (40% Et_2O/hexanes) to afford the intermediate organoselenide as a yellow oil. This oil was dissolved in THF (39 ml) and cooled to 0 °C. Hydrogen peroxide (30%, 8.1 mL) was added slowly. The resulting mixture was allowed to stir for 12 h at 0 °C. The reaction was quenched by the slow addition of saturated Na_2SO_3 (50 mL) at 0 °C. The aqueous layer was extracted with EtOAc (3 x 15 ml) and the combined organic layers were dried over Na_2SO_4, filtered and concentrated. The resulting residue was purified by flash column chromatography (40% Et_2O/hexanes) to afford **16** oil (1.35 g, 76%) as a yellow oil. Analytical data: IR (film) 2962, 1735, 1636, 1265 cm^{-1}; ^1H NMR, (500 MHz, $CDCl_3$) δ 5.58-5.51 (ddd, J = 17.1, 10.0, 8.8 Hz, 1H), 5.25 (s, 1H), 4.98-4.94 (d, *J* = 17.1 Hz, 1H), 4.94-4.93 (d, *J* = 10.0 Hz, 1H), 3.82-3.79 (ddd, *J* = 9.8, 6.4, 5.8 Hz, 1H), 2.26-2.25 (d, *J* = 6.1 Hz, 1H), 2.23-2.21 (m, 1H), 1.69 (s, 3H), 1.67 (s, 3H), 1.27-1.21 (m, 2H), 1.09-1.04 (m, 2H), 1.02-1.01 (d, *J* = 6.7 Hz, 3H), 0.87 (s, 9H), 0.84-0.83 (d, *J* = 7.0 Hz, 3H), 0.03 (s, 3H), 0.02 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 161.3, 144.2, 113.6, 106.5, 95.4, 73.5, 39.7, 37.9, 36.3, 36.1, 26.0, 24.5, 22.0, 18.2, 14.2, –4.1, –4.5; LRMS (ESI): Mass calcd for $C_{42}H_{76}NaO_8Si_2$ $[2M+Na]^+$, 787.5. Found 787.7; $[a]_D^{20}$ –22.1 (CH_2Cl_2, *c* 1.0).



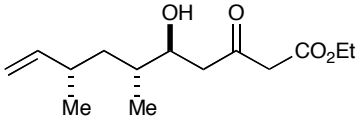
6-((2*S*,3*R*,5*S*)-2-hydroxy-3,5-dimethylhept-6-enyl)-2,2-dimethyl-4*H*-1,3-dioxin-4-one (4). To a plastic bottle with stir bar containing a 0 °C solution of silyl ether **16** (3.0 g, 7.8 mmol) in THF (165 mL) was added HF·pyr (14 mL, 161 mmol) dropwise by plastic syringe. The solution was stirred at room temperature, additional HF·pyr (3 mL) was added every 24 hours and the reaction was monitored by TLC until complete consumption of starting material was observed. The solution was re-cooled to 0 °C and carefully quenched with saturated aqueous $NaHCO_3$. The aqueous layer was extracted with EtOAc (3x) and the combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (30% EtOAc/hexanes) to afford β-hydroxy dioxinone **4** (2.0 g, 93%) as a colorless oil. Analytical data: IR (film) 3459, 2962, 1716, 1635, 1392, 1276, 1205, 1015, 907, 805 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$): δ 5.55 (ddd, *J* = 17.2, 10.1, 8.6 Hz, 1H), 5.33 (s, 1H),

4.99-4.92 (m, 2H), 3.73 (dtd, *J* = 9.5, 4.8, 3.3 Hz, 1H), 2.37 (dd, *J* = 14.6, 3.1 Hz, 1H), 2.28 (dd, *J* = 14.6, 9.5 Hz, 1H), 2.22 (dtd, *J* = 10.7, 7.5, 3.2 Hz, 1H), 1.70 (s, 6H), 1.63 (d, *J* = 5.1 Hz, 1H), 1.38 (ddd, *J* = 13.5, 10.7, 3.0 Hz, 1H), 1.10 (ddd, *J* = 13.7, 10.3, 3.7 Hz, 1H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 169.8, 161.0, 143.7, 113.7, 106.6, 95.0, 73.1, 38.7, 38.1, 36.5, 35.8, 25.4, 24.7, 21.9, 14.9; LRMS (ESI): Mass calcd for $C_{15}H_{25}O_4$ $[M+H]^+$, 269.17. Found $[M+H]^+$, 269.14; $[\alpha]_D^{20}$ –24.8 ($CHCl_3$, *c* 0.52).

Synthesis of δ-Hydroxy β-Ketoester 17



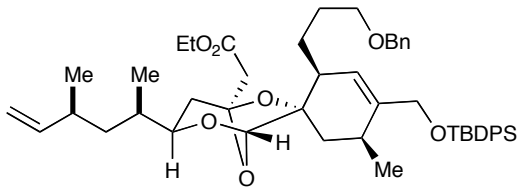
(5*S*,6*R*,8*S*)-ethyl 5-(*tert*-butyldimethylsilyloxy)-6,8-dimethyl-3-oxodec-9-enoate (S10). To a flame-dried, round-bottom flask with stir bar containing a 0 °C solution of β-silyloxy dioxinone **16** (2.25 g, 5.9 mmol) in CH_2Cl_2 (30 mL) was added KOEt (2.1 g, 24 mmol) in one portion. The solution was stirred for 30 min at 0 °C, warmed to room temperature for 4 h, and quenched with brine. The mixture was diluted with water and the aqueous layer was extracted with CH_2Cl_2 (3x). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (5% EtOAc/hexanes) to afford δ-silyloxy β-ketoester **S10** (1.91 g, 88%) as a colorless oil. Analytical data: IR (film) 2958, 2930, 1749, 1721, 1642, 1463, 1252, 1076, 836, 776 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$): δ 5.54 (ddd, *J* = 17.2, 10.2, 8.3 Hz, 1H), 4.99-4.91 (m, 2H), 4.22-4.16 (m, 3H), 4.07 (dt, *J* = 8.9, 3.5 Hz, 1H), 3.50-3.42 (m, 2H), 2.67 (dd, *J* = 15.3, 8.9 Hz, 1H), 2.38 (dd, *J* = 15.3, 3.2 Hz, 1H), 2.20-2.15 (m, 1H), 1.70-1.64 (m, 1H), 1.27 (t, *J* = 7.1 Hz, 3H), 1.18 (ddd, *J* = 13.5, 10.0, 3.6 Hz, 1H), 0.99 (d, *J* = 6.7 Hz, 3H), 0.86 (d, *J* = 6.5 Hz, 3H), 0.85 (s, 9H), 0.03 (s, 3H), –0.01 (s, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 202.6, 167.1, 144.0, 113.3, 72.8, 61.2, 51.1, 45.3, 40.0, 36.4, 35.8, 25.84, 25.80, 21.6, 18.0, 14.1, 13.5, -4.6, -4.9; LRMS (ESI): Mass calcd for $C_{20}H_{38}O_4SiNa$ $[M+Na]^+$, 393.24. Found $[M+Na]^+$, 393.32; $[\alpha]_D^{20}$ –41.6 (MeOH, *c* 1.02).



(5*S*,6*R*,8*S*)-ethyl 5-hydroxy-6,8-dimethyl-3-oxodec-9-enoate (17). To a plastic vial with stir bar containing a 0 °C solution of silyl ether **S10** (52 mg, 0.14 mmol) in THF (2.7 mL) was added HF•pyr (0.25 mL, 2.9 mmol) dropwise by plastic syringe. After the solution was stirred at 0 °C for 24 h and then at room temperature for 24 h, it was carefully quenched with saturated aqueous $NaHCO_3$. The mixture was diluted with CH_2Cl_2 (10 mL), filtered through a Biotage ISOLUTE® phase separator, and the organic filtrate was concentrated. The residue was purified by flash column chromatography (25% EtOAc/hexanes) to afford δ-hydroxy β-ketoester **17** (32.6 mg, 94%) as a colorless oil. Analytical data: IR (film) 3524, 2964, 1743, 1713, 1643, 1461, 1412, 1318, 1031, 912 cm^{-1}; ^{1}H-NMR (500 MHz; CDCl3): δ 5.56 (ddd, *J* = 17.2, 10.1, 8.5 Hz, 1H), 4.98-

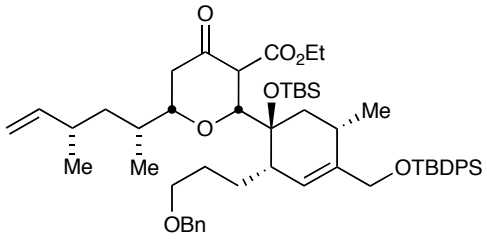
4.91 (m, 2H), 4.20 (q, *J* = 7.1 Hz, 2H), 3.92 (dq, *J* = 8.5, 4.3 Hz, 1H), 3.48 (d, *J* = 1.6 Hz, 2H), 2.66 (m, 3H), 2.21 (dtd, *J* = 14.4, 7.2, 3.7 Hz, 1H), 1.64-1.57 (m, 1H), 1.39 (ddd, *J* = 13.5, 10.5, 3.2 Hz, 1H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.07 (ddd, *J* = 13.7, 10.1, 3.9 Hz, 1H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.88 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 204.2, 166.9, 143.9, 113.4, 71.5, 61.5, 50.0, 46.2, 39.1, 35.71, 35.62, 21.8, 14.8, 14.1; LRMS (ESI): Mass calcd for $C_{14}H_{28}NO_4$ $[M+NH_4]^+$, 274.20. Found $[M+NH_4]^+$, 274.12; $[\alpha]_D^{20}$ –22.2 ($CHCl_3$, *c* 0.32).

Synthesis of Trioxabicyclooctane 18

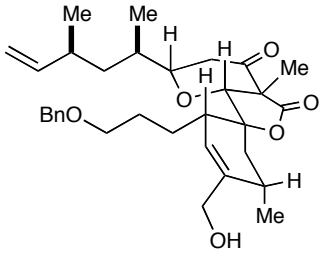


Ethyl 2-((1*S*,1'*S*,2'*S*,3*R*,5*R*,5'*S*)-2'-(3-(benzyloxy)propyl)-4'-((*tert*-butyldiphenylsilyloxy)methyl)-5'-methyl-3-((2*R*,4*S*)-4-methylhex-5-en-2-yl)-2,6,8-trioxaspiro[bicyclo[3.2.1]octane-7,1'-cyclohex[3]ene]-5-yl)acetate (18). To a flame-dried 1-dram vial containing a 0 °C solution of α-hydroxy aldehyde **3** (27 mg, 0.048 mmol), δ-hydroxy-β-ketoester **17** (12.2 mg, 0.048 mmol), and 4Å molecular sieves (27 mg) in CH_2Cl_2 (0.4 mL) was added BF_3•OEt_2 (18 μL, 0.14 mmol) dropwise by syringe. The reaction mixture was stirred at 0 °C for 4 h and warmed to room temperature for 12 h. The reaction mixture was quenched with 1.0 M pH 7 phosphate buffer, diluted with CH_2Cl_2, filtered through a Biotage ISOLUTE® phase separator and concentrated. The residue was purified by flash column chromatography (4%-15% EtOAc/hexanes, gradient) to afford trioxabicyclooctane **18** (13.4 mg, 35%) as a colorless oil. Analytical data: IR (film) 2929, 2856, 1736, 1719, 1471, 1462, 1427, 1112, 821, 701 cm^{-1}; ^{1}H NMR (500 MHz; $CDCl_3$): δ 7.72-7.67 (m, 4H), 7.42-7.31 (m, 11H), 5.90 (d, *J* = 3.7 Hz, 1H), 5.57 (ddd, *J* = 17.2, 10.0, 8.4 Hz, 1H), 5.08 (s, 1H), 4.98-4.89 (m, 2H), 4.48 (d, *J* = 4.2 Hz, 2H), 4.21-4.08 (m, 5H), 3.52-3.43 (m, 2H), 2.79 (s, 2H), 2.58-2.50 (m, 2H), 2.25-2.19 (m, 1H), 1.94-1.79 (m, 4H), 1.63 (tdd, *J* = 15.0, 7.4, 3.7 Hz, 3H), 1.52 (ddd, *J* = 13.5, 10.5, 3.0 Hz, 1H), 1.34 (t, *J* = 12.1 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H and m, 1H), 1.05 (s, 9H), 1.05-1.00 (m, 1H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.85 (d, *J* = 6.7 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 168.6, 144.2, 140.1, 138.6, 135.62, 135.59, 135.1, 134.8, 133.90, 133.74, 129.70, 129.58, 129.55, 128.4, 127.76, 127.65, 127.57, 127.52, 122.1, 113.2, 106.1, 101.3, 86.6, 75.4, 72.8, 70.6, 65.3, 60.8, 44.4, 39.03, 38.95, 37.31, 37.12, 35.69, 35.66, 31.2, 27.8, 27.6, 26.8, 26.6, 21.9, 19.3, 18.6, 14.42, 14.23; LRMS (ESI): Mass calcd for $C_{49}H_{70}NO_7Si$ $[M+NH_4]^+$, 812.49. Found $[M+NH_4]^+$, 812.44; $[\alpha]_D^{20}$ +23.9 ($CHCl_3$, *c* 0.62).

Synthesis of (–)-Okilactomycin 1

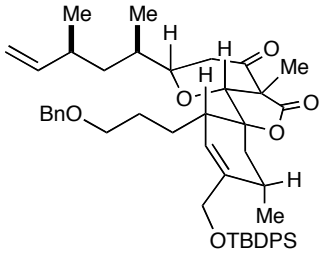


(2*R*,6*S*)-ethyl 2-((1*S*,2*S*,5*S*)-2-(3-(benzyloxy)propyl)-1-(*tert*-butyldimethylsilyloxy)-4-((*tert*-butyldiphenylsilyloxy)methyl)-5-methylcyclohex-3-enyl)-6-((2*R*,4*S*)-4-methylhex-5-en-2-yl)-4-oxotetrahydro-2*H*-pyran-3-carboxylate (22). To a flame-dried, round-bottom flask with stir bar containing a –78 °C solution of a-silyloxy aldehyde **21** (1.4 g, 2.1 mmol), δ-hydroxy-β-ketoester **17** (0.59 g, 2.3 mmol), 4Å molecular sieves (1.4 g), and CH_2Cl_2 (17.5 mL) was added trimethylsilyltriflate (0.38 mL, 2.1 mmol) dropwise by syringe. The reaction was warmed to –40 °C, stirred for 45 min, re-cooled to –78 °C and quenched with 1.0 M pH 7 phosphate buffer. The mixture was filtered through a Biotage ISOLUTE® phase separator and the organic filtrate was concentrated. The residue was purified by flash column chromatography (2% to 6% EtOAc/hexanes, gradient) to afford tetrahydropyranone **22** (1.15 g, 60%) in a 13:1 ratio of diastereomers as a colorless oil. Analytical data: IR (film) 3071, 2929, 1746, 1713, 1472, 1369, 1250, 1111, 834, 774, 740, 701 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$): δ 7.67 (td, *J* = 7.2, 1.4 Hz, 4H), 7.42-7.30 (m, 11H), 5.86 (d, *J* = 4.6 Hz, 1H), 5.55 (ddd, *J* = 17.2, 10.1, 8.4 Hz, 1H), 4.99-4.92 (m, 2H), 4.46 (d, *J* = 2.0 Hz, 2H), 4.18 (m, 3H), 4.11 (d, *J* = 13.1 Hz, 1H), 4.05 (d, *J* = 13.2 Hz, 1H), 3.69 (d, *J* = 9.3 Hz, 1H), 3.59 (ddd, *J* = 11.3, 5.6, 3.2 Hz, 1H), 3.42 (t, *J* = 6.3 Hz, 2H), 2.47-2.39 (m, 2H), 2.27 (dd, *J* = 16.0, 11.4 Hz, 1H), 2.22-2.16 (m, 2H), 1.84-1.71 (m, 3H), 1.48-1.42 (m, 2H), 1.31-1.24 (m, 2H and t, *J* = 7.1 Hz, 3H), 1.08 (q, *J* = 5.1 Hz, 1H), 1.05 (s, 9H and m, 1H), 1.00 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 7.0 Hz, 3H), 0.88 (d, *J* = 6.7 Hz, 3H), 0.82 (s, 9H), 0.10 (s, 3H), 0.04 (s, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 204.0, 169.3, 143.8, 138.6, 138.2, 135.61, 135.49, 133.71, 133.66, 129.56, 129.48, 128.3, 127.68, 127.60, 127.57, 127.46, 123.3, 113.5, 79.9, 78.9, 72.8, 70.7, 65.5, 61.5, 43.3, 42.1, 39.4, 36.3, 35.59, 35.40, 31.6, 28.5, 27.7, 26.8, 26.1, 21.7, 19.3, 18.9, 14.0, –1.9, –2.7; LRMS (ESI): Mass calcd for $C_{55}H_{84}NO_7Si_2$ $[M+NH_4]^+$, 926.58. Found $[M+NH_4]^+$, 926.45; $[\alpha]_D^{20}$ +26.5° ($CHCl_3$, *c* 0.68).



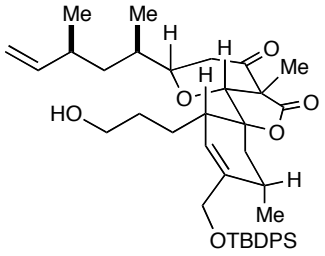
(1*S*,2*S*,2'*S*,4a'*R*,5*S*,7a'*R*)-2-(3-(benzyloxy)propyl)-4-(hydroxymethyl)-4a',5-dimethyl-2'-((2*R*,4*S*)-4-methylhex-5-en-2-yl)-2',3'-dihydrospiro[cyclohex[3]ene-1,7'-furo[3,4-*b*]pyran]-4',5'(4a'*H*,7a'*H*)-dione (23). To a plastic vial with stir bar containing

tetrahydropyranone **22** (0.10 g, 0.11 mmol) in CH_3CN (11 mL) was added aqueous HF (2.9 mL, 48% in water). The solution was stirred at room temperature for 18 h and carefully poured into a flask containing saturated aqueous $NaHCO_3$ (50 mL). $NaHCO_{3(s)}$ was added until the pH > 7. The mixture was diluted with EtOAc and the aqueous layer was extracted with EtOAc (3x). The combined organic layers were washed with saturated aqueous $NaHCO_3$ (2x) and brine (1x), dried over Na_2SO_4, and concentrated. The residue was dissolved in THF (5.5 mL) in a scintillation vial. To the solution was added KO*t*-Bu (12.3 mg, 0.11 mmol) in one portion. The solution was stirred for 15 min and quenched with saturated aqueous NH_4Cl. The mixture was diluted with water and CH_2Cl_2, filtered through a Biotage ISOLUTE® phase separator and the organic filtrate was concentrated. The residue was dissolved in CH_3CN (2.2 mL) in a scintillation vial. To the solution was added K_2CO_3 (63 mg, 0.46 mmol) and MeI (70 μL, 1.1 mmol). The reaction mixture was heated to 70 °C for 2 h, re-cooled to room temperature and quenched with saturated aqueous NH_4Cl. The mixture was diluted with CH_2Cl_2 and filtered through a Biotage ISOLUTE® phase separator and the organic filtrate was concentrated. The residue was purified by flash column chromatography (20% to 30% to 35% EtOAc/hexanes) to afford lactone **23** (35 mg, 61%) as a colorless oil. Analytical data: IR (film) 3420, 2956, 2926, 2869, 1778, 1717, 1455, 1210, 1099, cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$): δ 7.36-7.28 (m, 5H), 5.71 (dd, *J* = 5.2, 1.3 Hz, 1H), 5.55 (ddd, *J* = 17.2, 10.2, 8.3 Hz, 1H), 5.00-4.93 (m, 2H), 4.50 (d, *J* = 2.1 Hz, 2H), 4.28 (s, 1H), 4.15-4.12 (m, 1H), 4.07 (d, *J* = 13.6 Hz, 1H), 3.65 (ddd, *J* = 11.2, 6.3, 3.6 Hz, 1H), 3.54-3.46 (m, 2H), 2.59 (dd, *J* = 17.4, 3.5 Hz, 1H), 2.54-2.49 (m, 1H), 2.40 (dd, *J* = 17.4, 11.3 Hz, 1H), 2.25-2.17 (m, 2H), 1.93-1.82 (m, 3H), 1.72 (dtd, *J* = 9.9, 6.6, 3.3 Hz, 1H), 1.63 (td, *J* = 8.7, 4.1 Hz, 1H), 1.58 (s, 3H), 1.48-1.43 (m, 2H), 1.28-1.23 (m, 1H), 1.06 (m, 4H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 202.0, 171.9, 143.7, 141.3, 138.3, 128.4, 127.6, 121.9, 113.6, 88.3, 84.0, 78.0, 73.0, 69.8, 64.7, 55.6, 43.3, 41.5, 39.2, 35.6, 33.2, 30.0, 28.3, 27.1, 21.88, 21.86, 18.6, 14.5; LRMS (ESI): Mass calcd for $C_{32}H_{45}O_6$ $[M+H]^+$, 525.32. Found $[M+H]^+$, 525.30; $[\alpha]_D^{20}$ +32.8 ($CHCl_3$, *c* 0.09).



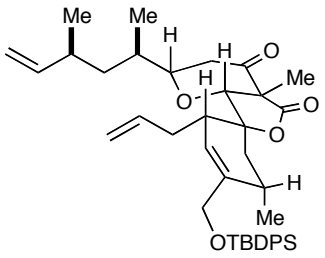
(1*S*,2*S*,2'*S*,4a'*R*,5*S*,7a'*R*)-2-(3-(benzyloxy)propyl)-4-((*tert*-butyldiphenylsilyloxy)methyl)-4a',5-dimethyl-2'-((2*R*,4*S*)-4-methylhex-5-en-2-yl)-2',3'-dihydrospiro[cyclohex[3]ene-1,7'-furo[3,4-*b*]pyran]-4',5'(4a'*H*,7a'*H*)-dione (S11). To a flame-dried, round-bottom flask with stir bar containing a 0 °C solution of allylic alcohol **23** (210 mg, 0.40 mmol) in CH_2Cl_2 (20 mL) was added imidazole (85 mg, 1.25 mmol) followed by *t*-butyldiphenylchlorosilane (0.23 mL, 0.89 mmol). The solution was stirred at room temperature for 3 h and quenched with saturated aqueous $NaHCO_3$. The mixture was filtered through a Biotage ISOLUTE® phase separator and the organic filtrate was concentrated. The residue was purified by flash column chromatography (5%

to 20% EtOAc/hexanes) to afford silyl ether **S11** (280 mg, 92%) as a colorless oil. Analytical data: IR (film) 3071, 2930, 2857, 1780, 1719, 1455, 1206, 1112, 702 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$): δ 7.69 (td, *J* = 4.7, 2.7 Hz, 4H), 7.43-7.36 (m, 6H), 7.35-7.28 (m, 5H), 5.81 (dd, *J* = 5.2, 1.4 Hz, 1H), 5.56 (ddd, *J* = 17.2, 10.1, 8.3 Hz, 1H), 5.01-4.94 (m, 2H), 4.50 (d, *J* = 2.6 Hz, 2H), 4.30 (s, 1H), 4.16 (s, 2H), 3.65 (ddd, *J* = 11.1, 6.3, 3.5 Hz, 1H), 3.53-3.47 (m, 2H), 2.59 (dd, *J* = 17.3, 3.4 Hz, 1H), 2.47 (dt, *J* = 11.1, 5.8 Hz, 1H), 2.41 (dd, *J* = 17.3, 11.3 Hz, 1H), 2.26-2.20 (m, 2H), 1.92 (ddd, *J* = 14.4, 6.0, 1.5 Hz, 1H), 1.89-1.80 (m, 2H), 1.72 (dtd, *J* = 9.8, 6.6, 3.3 Hz, 1H), 1.64 (dd, *J* = 11.6, 5.8 Hz, 1H), 1.60 (s, 3H), 1.49-1.42 (m, 2H), 1.29-1.22 (m, 1H), 1.08 (dd, *J* = 5.5, 3.7 Hz, 1H), 1.05 (s, 9H), 1.02 (d, *J* = 6.7 Hz, 3H), 0.96 (d, *J* = 7.0 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 202.1, 171.8, 143.7, 140.1, 138.3, 135.47, 135.42, 133.62, 133.57, 129.58, 129.53, 128.4, 127.67, 127.60, 120.4, 113.5, 88.4, 84.0, 78.0, 72.9, 69.8, 65.1, 55.7, 43.1, 41.6, 39.1, 35.6, 33.3, 30.1, 28.4, 27.0, 26.7, 21.83, 21.74, 19.2, 18.7, 14.5; LRMS (ESI): Mass calcd for $C_{48}H_{66}NO_6Si$ $[M+NH_4]^+$, 780.47. Found $[M+NH_4]^+$, 780.47; $[\alpha]_D^{20}$ +27.7 ($CHCl_3$, *c* 0.94).

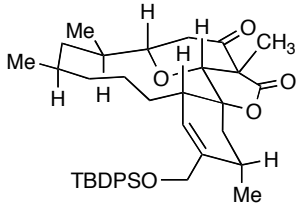


(1*S*,2*S*,2'*S*,4a'*R*,5*S*,7a'*R*)-4-((*tert*-butyldiphenylsilyloxy)methyl)-2-(3-hydroxypropyl)-4a',5-dimethyl-2'-((2*R*,4*S*)-4-methylhex-5-en-2-yl)-2',3'-dihydrospiro[cyclohex[3]ene-1,7'-furo[3,4-*b*]pyran]-4',5'(4a'*H*,7a'*H*)-dione (S12). To a round-bottom flask containing a solution of benzyl alcohol **S11** (0.26 g, 0.34 mmol) in water (0.35 mL) and CH_2Cl_2 (17.5 mL) was added DDQ (2.4 g, 10.5 mmol) in one portion. The reaction mixture was stirred for 22 h and quenched with saturated aqueous $NaHCO_3$ (100 mL) and water (100 mL). The aqueous layer was extracted with CH_2Cl_2 (3x) and the combined organic layers were dried with Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (25% to 35% EtOAc/hexanes) to afford primary alcohol **S12** (0.14 g, 62%) as a white foam. Analytical data: IR (film) 3449, 3071, 2930, 2858, 1774, 1718, 1458, 1383, 1112, 1060 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$): δ 7.68 (ddd, *J* = 7.6, 4.2, 1.9 Hz, 4H), 7.43-7.38 (m, 6H), 5.80 (dd, *J* = 5.3, 1.6 Hz, 1H), 5.57 (ddd, *J* = 17.2, 10.2, 8.3 Hz, 1H), 5.01-4.94 (m, 2H), 4.31 (s, 1H), 4.15 (s, 2H), 3.70-3.65 (m, 3H), 2.60 (dd, *J* = 17.3, 3.4 Hz, 1H), 2.49-2.46 (m, 1H), 2.41 (dd, *J* = 17.4, 11.3 Hz, 1H), 2.25-2.19 (m, 2H), 1.91 (ddd, *J* = 14.5, 6.0, 1.7 Hz, 1H), 1.88-1.83 (m, 1H), 1.80-1.69 (m, 2H), 1.64 (s, 3H), 1.60-1.53 (m, 2H), 1.50-1.42 (m, 2H), 1.27-1.20 (m, 2H), 1.08 (dd, *J* = 9.8, 4.1 Hz, 1H), 1.04 (s, 9H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 202.1, 171.8, 143.8, 140.3, 135.51, 135.46, 133.67, 133.58, 129.63, 129.57, 127.69, 127.62, 120.3, 113.5, 88.4, 84.1, 78.1, 65.1, 62.7, 55.7, 43.3, 41.7, 39.3, 35.66, 35.61, 33.3, 29.96, 29.87, 28.4, 26.8, 21.85, 21.83, 19.3, 18.7, 14.5; LRMS (ESI): Mass calcd for

$C_{41}H_{60}NO_6Si$ $[M+NH_4]^+$, 690.42. Found $[M+NH_4]^+$, 690.63; $[\alpha]_D^{20}$ +24.1 ($CHCl_3$, *c* 0.22).

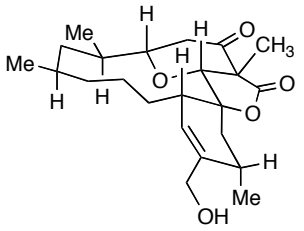


(1*S*,2*S*,2'*S*,4a'*R*,5*S*,7a'*R*)-2-allyl-4-((*tert*-butyldiphenylsilyloxy)methyl)-4a',5-dimethyl-2'-((2*R*,4*S*)-4-methylhex-5-en-2-yl)-2',3'-dihydrospiro[cyclohex[3]ene-1,7'-furo[3,4-*b*]pyran]-4',5'(4a'*H*,7a'*H*)-dione (24). To a flame-dried scintillation vial with stir bar containing a solution of alcohol **S12** (130 mg, 0.19 mmol) in THF (2 mL) was added 2-nitrophenyl selenocyanate (80 mg, 0.35 mmol) followed by P(*n*-Bu)$_3$ (88 μL, 0.35 mmol). The reaction mixture was stirred for 1 h, filtered through SiO_2 (eluting with 60% Et_2O/hexanes) and concentrated. The residue was purified by flash column chromatography (20% to 40% EtOAc/hexanes) to afford an orange oil. The oil was added to a scintillation vial and dissolved in THF (1.5 mL). The solution was cooled to 0 °C and charged with hydrogen peroxide (0.33 mL, 30% in water). The solution was stirred at room temperature for 18 h, re-cooled to 0 °C and carefully quenched with ½ saturated $Na_2S_2O_3$. The mixture was diluted with CH_2Cl_2, filtered through a Biotage BIOTAGE ISOLUTE®® phase separator and the organic filtrate was concentrated. The residue was purified by flash column chromatography to afford diene **24** (75 mg, 60%) as a yellow oil. Analytical data: IR (film) 3071, 2929, 1779, 1719, 1382, 1112, 1060 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$): δ 7.70-7.67 (m, 4H), 7.43-7.37 (m, 6H), 5.85-5.78 (m, 1H), 5.76 (dt, *J* = 5.1, 1.6 Hz, 1H), 5.56 (ddd, *J* = 17.2, 10.2, 8.4 Hz, 1H), 5.11-5.06 (m, 2H), 5.01-4.94 (m, 2H), 4.35 (s, 1H), 4.14 (s, 2H), 3.69 (ddd, *J* = 11.3, 6.2, 3.5 Hz, 1H), 2.60 (dd, *J* = 17.4, 3.4 Hz, 1H), 2.51-2.46 (m, 2H), 2.42 (dd, *J* = 17.4, 11.3 Hz, 1H), 2.32-2.29 (m, 1H), 2.26-2.20 (m, 1H), 2.04-1.98 (m, 1H), 1.90 (ddd, *J* = 14.5, 6.0, 1.8 Hz, 1H), 1.73 (dtd, *J* = 9.8, 6.6, 3.3 Hz, 1H), 1.65 (s, 3H), 1.48-1.42 (m, 2H), 1.08 (dt, *J* = 9.2, 4.4 Hz, 1H), 1.04 (s, 9H), 1.01 (d, *J* = 6.7 Hz, 3H), 0.95 (d, *J* = 7.0 Hz, 3H), 0.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 202.1, 171.7, 143.7, 140.0, 135.50, 135.45, 135.39, 133.64, 133.61, 129.59, 129.54, 128.3, 127.67, 127.59, 120.6, 116.9, 113.6, 88.1, 84.0, 78.1, 64.9, 55.7, 43.6, 41.5, 39.2, 37.8, 35.66, 35.58, 33.5, 28.2, 26.7, 21.86, 21.82, 19.3, 18.7, 14.5; LRMS (ESI): Mass calcd for $C_{41}H_{58}NO_5Si$ $[M+NH_4]^+$, 672.41. Found $[M+NH_4]^+$, 672.55; $[\alpha]_D^{20}$ +37.6 ($CHCl_3$, *c* 0.21).

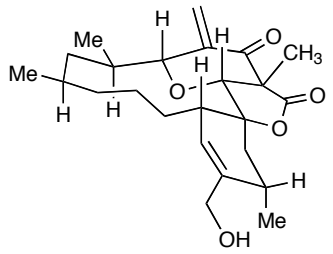


Tetracycle 25. To a flame-dried, 3-liter, 2-neck round-bottom flask fitted with a reflux condensor and a stir bar containing a solution of diene **24** (69 mg, 0.11 mmol) in CH_2Cl_2

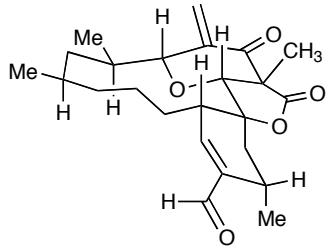
(1.6 L) was added a freshly prepared solution of Grubbs 2nd Generation catalyst (39 mg, 45 μmol) in CH_2Cl_2 (5 mL) by cannula. The solution was heated at reflux for 24 h, cooled to room temperature, stirred while exposed to air for 24 h and concentrated (bath <25 °C). The residue was filtered through SiO_2 (eluting with 60% EtOAc/hexanes), concentrated in a flame-dried, round-bottom flask and dissolved in EtOAc (12 mL). The solution was charged with PtO_2 (70 mg, 0.30 mmol) and the flask was fitted with a balloon filled with H_2 gas. The reaction mixture was stirred vigorously for 1.5 h, filtered through Celite and concentrated. The residue was purified with 10% EtOAc/hexanes to afford tetracycle **25** (43 mg, 65%) as a colorless oil. Analytical data: IR (film) 2958, 1785, 1742, 1718, 1458, 1373, 1273, 1254, 1112, 704 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$): δ 7.67 (ddd, *J* = 7.7, 4.1, 1.8 Hz, 4H), 7.42-7.36 (m, 6H), 5.66 (dd, *J* = 5.4, 1.6 Hz, 1H), 4.36 (s, 1H), 4.08 (s, 2H), 3.58 (ddd, *J* = 10.9, 9.7, 3.8 Hz, 1H), 2.80 (dd, *J* = 18.2, 3.9 Hz, 1H), 2.46-2.39 (m, 2H), 2.23-2.20 (m, 1H), 1.84 (dt, *J* = 12.1, 6.4 Hz, 1H), 1.74-1.71 (m, 1H), 1.69 (s, 3H), 1.64-1.50 (m, 6H), 1.40-1.35 (m, 1H), 1.31-1.22 (m, 3H), 1.04 (s, 9H), 0.91 (d, *J* = 7.0 Hz, 3H), 0.89 (s, 3H), 0.87 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 203.0, 171.9, 138.4, 135.54, 135.46, 133.72, 133.63, 129.57, 129.51, 127.67, 127.59, 123.2, 86.1, 84.8, 82.5, 64.9, 54.1, 45.4, 43.2, 41.9, 38.6, 37.9, 34.18, 34.04, 30.6, 28.3, 26.8, 24.6, 24.1, 23.6, 19.3, 18.8, 18.0; LRMS (ESI): Mass calcd for $C_{39}H_{56}NO_5Si$ $[M+NH_4]^+$, 646.39. Found $[M+NH_4]^+$, 646.56; $[\alpha]_D^{20}$ +13.3 ($CHCl_3$, *c* 0.22).



Allylic alcohol S13. To a plastic vial with stir bar containing a solution of silyl ether **25** (47 mg, 0.075 mmol) in THF (10 mL) was added HF·pyr (0.26 mL, 3.0 mmol). The solution was stirred for 48 h and carefully quenched with saturated aqueous $NaHCO_3$ (50 mL). The aqueous layer was extracted with EtOAc (3x). The combined organic layers were dried over Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (20% to 40% EtOAc/hexanes) to afford allylic alcohol **S13** (30 mg, >99%) as a colorless oil. Analytical data: 3412, 2954, 1782, 1719, 1457, 1234, 1110, 756 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$): δ 5.59 (dd, *J* = 5.2, 1.5 Hz, 1H), 4.35 (s, 1H), 4.10 (dd, *J* = 13.4, 1.0 Hz, 1H), 4.01 (d, *J* = 13.4 Hz, 1H), 3.57 (ddd, *J* = 10.9, 9.7, 3.8 Hz, 1H), 2.80 (dd, *J* = 18.2, 3.9 Hz, 1H), 2.52-2.47 (m, 1H), 2.43 (dd, *J* = 18.2, 11.1 Hz, 1H), 2.20 (dd, *J* = 10.3, 5.4 Hz, 1H), 1.85-1.80 (m, 1H), 1.72 (dd, *J* = 14.3, 11.0 Hz, 1H), 1.68 (s, 3H), 1.65-1.49 (m, 5H), 1.39-1.19 (m, 5H), 1.03 (d, *J* = 7.1 Hz, 3H), 0.88 (d, *J* = 7.0 Hz, 3H), 0.87 (d, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 202.8, 171.9, 139.6, 124.7, 86.0, 84.7, 82.6, 64.7, 54.0, 45.3, 43.2, 42.0, 38.5, 37.9, 34.00, 33.92, 30.6, 28.1, 24.5, 24.0, 23.6, 18.6, 17.9; LRMS (ESI): Mass calcd for $C_{23}H_{38}NO_5$ $[M+NH_4]^+$, 408.27. Found $[M+NH_4]^+$, 408.50; $[\alpha]_D^{20}$ –1.7 ($CHCl_3$, *c* 0.38).

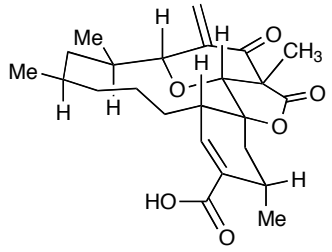


Enone S14. To a flame-dried 1 dram vial containing a –78 °C solution of allylic alcohol **S13** (8.3 mg, 0.021 mmol) in THF (1.0 mL) was added a freshly prepared solution of lithium bis(trimethylsilyl)amide (0.13 mL, 0.065 mmol, 0.5 M in THF) dropwise by syringe. The solution was stirred at –78 °C for 1 h and then charged with dimethylmethylideneammonium iodide (130 mg, 0.7 mmol) in one portion. The reaction mixture was warmed to 0 °C for 10 min and then stirred at room temperature for 3.5 h. The reaction mixture was quenched with EtOAc (1 mL) and saturated aqueous NH_4Cl (1 mL). The mixture was diluted with water and CH_2Cl_2, filtered through a Biotage ISOLUTE® phase separator and the organic filtrate was concentrated. The residue was purified by flash column chromatography (20% to 30% EtOAc/hexanes) to afford enone **S14** (8.0 mg, 95%) as a colorless oil. Analytical data: IR (film) 3399, 2953, 1782, 1708, 1627, 1457, 1261, 1130, 1027, 965 cm^{-1}; ^1H NMR (500 MHz; $CDCl_3$): δ 6.43 (s, 1H), 5.66 (d, *J* = 1.4 Hz, 1H), 5.59 (d, *J* = 4.7 Hz, 1H), 4.43 (s, 1H), 4.08 (d, *J* = 13.3 Hz, 1H), 4.00 (d, *J* = 13.3 Hz, 1H), 3.90 (d, *J* = 9.5 Hz, 1H), 2.48 (dt, *J* = 11.2, 5.9 Hz, 1H), 2.19 (dd, *J* = 10.0, 5.4 Hz, 1H), 2.00-1.94 (m, 1H), 1.80 (dt, *J* = 12.1, 6.3 Hz, 1H), 1.70 (s, 3 H and dd, *J* = 14.5, 10.9 Hz, 1H), 1.61-1.51 (m, 4H), 1.27-1.17 (m, 5H), 1.07 (d, *J* = 6.6 Hz, 3H), 1.00 (d, *J* = 7.0 Hz, 3H), 0.96 (dd, *J* = 14.2, 7.6 Hz, 1H), 0.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 192.3, 171.8, 142.1, 139.5, 124.8, 121.5, 86.0, 84.2, 82.4, 64.7, 52.2, 45.1, 41.8, 37.8, 34.6, 34.01, 33.95, 30.1, 28.2, 25.9, 23.7, 23.4, 20.6, 18.7; LRMS (ESI): Mass calcd for $C_{24}H_{38}NO_5$ $[M+NH_4]^+$, 420.28. Found $[M+NH_4]^+$, 420.42; $[\alpha]_D^{20}$ –37.6 ($CHCl_3$, *c* 0.55).



Aldehyde 26. To a 1-dram vial containing a solution of enone **S14** (5 mg, 0.012 mmol) in CH_2Cl_2 (1.2 mL) was added $NaHCO_3$ (10 mg, 0.11 mmol) followed by Dess-Martin periodinane (10.6 mg, 0.025 mmol). The reaction mixture was stirred at room temperature for 1 h and quenched with saturated aqueous $NaHCO_3$ (1 mL) and saturated aqueous $Na_2S_2O_3$ (1 mL) and stirred until the two layers were clear. The mixture was filtered through a Biotage ISOLUTE® phase separator and the organic filtrate was concentrated. The residue was purified by flash column chromatography (10% to 20% EtOAc/hexanes) to afford aldehyde **26** (4 mg, 83%) as a white solid. Analytical data: IR (film) 2951, 2918, 2720, 1786, 1686, 1628, 1457, 1375, 1252, 1128, 1027, 974 cm^{-1}; ^1H

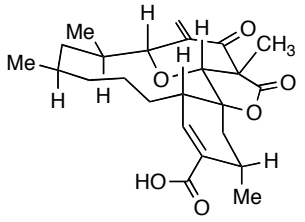
NMR (500 MHz; $CDCl_3$): δ 9.35 (s, 1H), 6.58 (dd, *J* = 5.8, 1.5 Hz, 1H), 6.46 (s, 1H), 5.68 (d, *J* = 1.1 Hz, 1H), 4.46 (s, 1H), 3.93 (d, *J* = 9.5 Hz, 1H), 2.73-2.68 (m, 1H), 2.48-2.44 (m, 1H), 2.02-1.97 (m, 1H), 1.79 (dt, *J* = 12.2, 6.3 Hz, 1H), 1.74-1.66 (m, 2H and s, 3H), 1.55 (dd, *J* = 14.1, 9.5 Hz, 1H), 1.38 (ddd, *J* = 15.1, 6.4, 1.8 Hz, 1H), 1.33-1.22 (m, 5H), 1.14 (d, *J* = 6.9 Hz, 3H), 1.08 (d, *J* = 6.6 Hz, 3H), 0.99 (dd, *J* = 14.2, 7.7 Hz, 1H), 0.91 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz; $CDCl_3$): δ 193.3, 191.8, 171.2, 150.6, 143.2, 141.8, 121.8, 84.9, 83.8, 82.4, 52.2, 45.0, 42.8, 37.6, 34.6, 33.6, 32.3, 30.2, 25.97, 25.77, 23.59, 23.49, 20.5, 19.2; LRMS (ESI): Mass calcd for $C_{24}H_{36}NO_5$ $[M+NH_4]^+$, 418.26. Found $[M+NH_4]^+$, 418.45; $[\alpha]_D^{20}$ – 26.3 ($CHCl_3$, *c* 0.4).



(–)-Okilactomycin (1). To a 1-dram vial containing enone **26** (4 mg, 0.01 mmol) in THF (0.5 mL) was added 2-methyl-2-butene (42 μL, 0.4 mmol), and *t*-butanol (0.5 mL). To the reaction mixture was added a freshly prepared solution of NaH_2PO_4 (11.8 mg, 0.085 mmol) and $NaClO_2$ (6.9 mg, 0.075 mmol) in water (0.17 mL). The reaction mixture was stirred at room temperature for 1 h, quenched with 1 N HCl, and diluted with CH_2Cl_2. The mixture was filtered through a Biotage ISOLUTE® phase separator and the organic filtrate was concentrated. The residue was purified by preparative HPLC (Phenomenex Gemini NX 5 μm C-18 110A 10 mm x 250 mm column, 42% to 77% CH_3CN w/ 0.5% formic acid/water w/ 0.5% formic acid at 8 mL/min over 14 min) to afford (–)-okilactomycin **1** (2 mg, 50%) as a white solid. Analytical data: IR (film) 2925, 2862, 1781, 1709, 1625, 1458, 1262, 1187, 974 cm^{-1}; ^1H NMR (500 MHz; acetone-d6): δ 6.76 (dd, *J* = 6.0, 2.0 Hz, 1H), 6.31 (d, *J* = 0.8 Hz, 1H), 5.76 (d, *J* = 1.4 Hz, 1H), 4.75 (s, 1H), 4.23 (d, *J* = 9.5 Hz, 1H), 2.65-2.59 (m, 1H), 2.44-2.41 (m, 1H), 2.01 (ddd, *J* = 12.9, 6.4, 3.1 Hz, 1H), 1.93-1.78 (m, 3H), 1.72 (dd, *J* = 13.8, 9.3 Hz, 1H), 1.69 (s, 3H), 1.67-1.61 (m, 2H), 1.38-1.28 (m, 2H), 1.25-1.19 (m, 1H), 1.11-1.09 (m, 6H), 1.06-1.04 (m, 1H), 0.93 (dd, *J* = 14.0, 7.6 Hz, 1H), 0.89 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR (125 MHz; acetone-d_6): δ 193.4, 171.8, 168.1, 144.0, 140.2, 134.4, 121.0, 85.5, 83.8, 82.7, 53.2, 45.6, 42.7, 38.6, 35.5, 34.6, 33.3, 31.0, 28.4, 25.5, 24.01, 23.88, 20.70, 20.50; HRMS (ESI): Mass calcd for $C_{24}H_{31}O_6$ $[M-H]^-$, 415.2126. Found $[M-H]^-$, 415.2122; $[\alpha]_D^{20}$ –20 (*c* 0.04, MeOH). Literature value for (+)-okilactomycin: $[\alpha]_D^{20}$ (+34, *c* 1.0, MeOH.[4]

Spectral Comparisons

^{1}H NMR spectroscopy chemical shifts of okilactomycin[3]



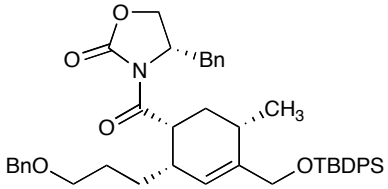
Natural (+)-Okilactomycin δ (ppm in acetone-d6)	**Synthetic (–)-Okilactomycin δ (ppm in acetone-d6)**
6.76 (dd, *J* = 6.0, 1.9 Hz, 1H)	6.76 (dd, *J* = 6.0, 2.0 Hz, 1H)
6.32 (d, *J* = 0.5 Hz, 1H)	6.31 (d, *J* = 0.8 Hz, 1H)
5.76 (d, *J* = 1.3 Hz, 1H)	5.76 (d, *J* = 1.4 Hz, 1H)
4.75 (s, 1H)	4.75 (s, 1H)
4.23 (d, *J* = 9.5 Hz, 1H)	4.23 (d, *J* = 9.5 Hz, 1H)
2.65-2.60 (m, 1H)	2.65-2.59 (m, 1H)
2.44-2.41 (m, 1H)	2.44-2.41 (m, 1H)
2.01 (ddd, *J* = 12.9, 6.5, 3.2 Hz, 1H)	2.01 (ddd, *J* = 12.9, 6.4, 3.1 Hz, 1H)
1.91-1.78 (m, 3H)	1.93-1.78 (m, 3H)
1.72 (dd, *J* = 14.1, 9.6 Hz, 1H)	1.72 (dd, *J* = 13.8, 9.3 Hz, 1H)
1.69 (s, 3H)	1.69 (s, 3H)
1.67-1.62 (m, 2H)	1.67-1.61 (m, 2H)
1.39-1.30 (m, 2H)	1.38-1.28 (m, 2H)
1.25-1.19 (m, 1H)	1.25-1.19 (m, 1H)
1.11-1.09 (m, 6H)	1.11-1.09 (m, 6H)
1.06-1.04 (m, 1H)	1.06-1.04 (m, 1H)
0.93 (dd, *J* = 14.1, 7.6 Hz, 1H)	0.93 (dd, *J* = 14.0, 7.6 Hz, 1H)
0.89 (d, *J* = 6.8 Hz, 3H)	0.89 (d, *J* = 6.8 Hz, 3H)

^{13}C NMR spectroscopy chemical shifts of okilactomycin

Natural (+)-Okilactomycin δ (ppm in acetone-d6)	Synthetic (–)-Okilactomycin δ (ppm in acetone-d6)
193.4	193.4
171.8	171.8
168.1	168.1
144.0	144.0
140.1	140.2
134.4	134.4
121.0	121.0
85.5	85.5
83.8	83.8
82.7	82.7
53.2	53.2
45.7	45.6
42.8	42.7
38.6	38.6
35.6	35.5
34.6	34.6
33.3	33.3
31.0	31.0
28.4	28.4
25.5	25.5
24.05	24.01
23.89	23.88
20.71	20.70
20.53	20.50

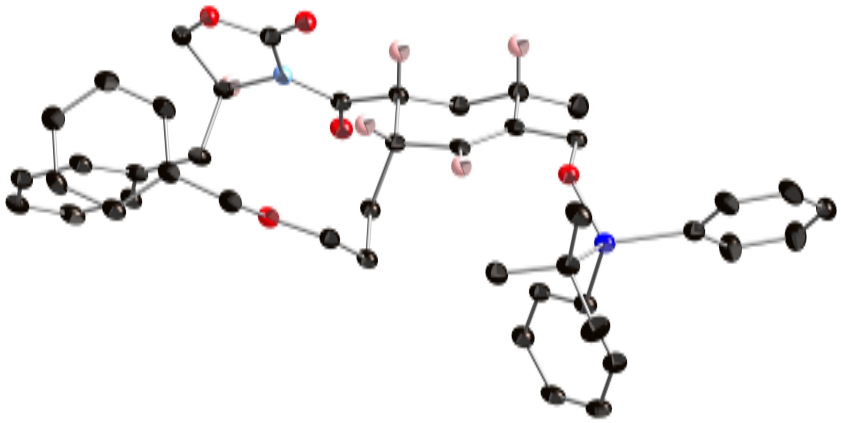
Stereochemical Determination of 10

The relative stereochemistry of the major diastereomer of **10** was determined by the X-ray diffraction. Recrystallized from slow cooling in hot methanol.



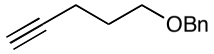
X-ray crystal structure of (*S*)-4-benzyl-3-((1*R*,2*S*,5*S*)-2-(3-(benzyloxy)propyl)-4-((*tert*-butyldiphenylsilyloxy)methyl)-5-methylcyclohex-3-enecarbonyl)oxazolidin-2-one (**10**).

X-ray diffraction was performed at –173 ºC and raw frame data were processed using SAINT. Molecular structure was solved using direct methods and refined by F2 by full-matrix least-squares techniques. The GOF = 0.973 for 473 variables refined to R1 = 0.0637 for 5034 reflections with I>2σ(I). A multi-scan absorption correction (SADABS, Bruker) was applied. Minimum and maximum transmission factors were 0.5801 and 0.9558, respectively. The Flack parameter was refined to 0.01(5). Further information is contained in the CIF file (CCDC 816131).



References

(1) Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518-1520.
(2) Armarego, W. L. F.; Chai, C. L. L. *Purification of Laboratory Chemicals*; 6th ed.; Butterworth-Heinemann, 2009.
(3) Spectra of authentic (+)-okilactomycin was provided by Dr. Margaret Biddle and Dr. Hironori Harada, Astellas Pharmaceuticals, Private Communication.
(4) H. S. Imai, K. I. Suzuki, M. Morioka, Y. Numasaki, S. Kadota, K. Nagai, T. Sato, M. Iwanami, T. Saito, *J. Antibiot*. **1987**, *40*, 1475-1482.



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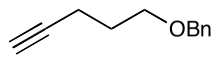

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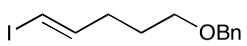

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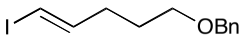

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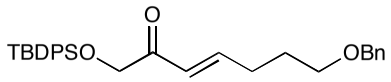

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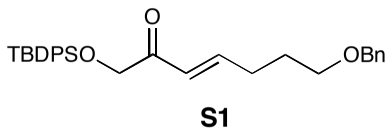
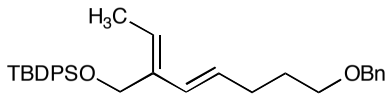


S1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OBn

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3
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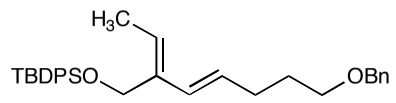

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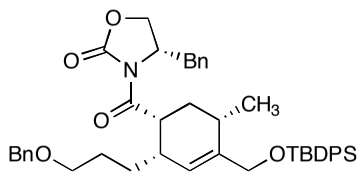
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Bn
O
CH3
BnO
OTBDPS

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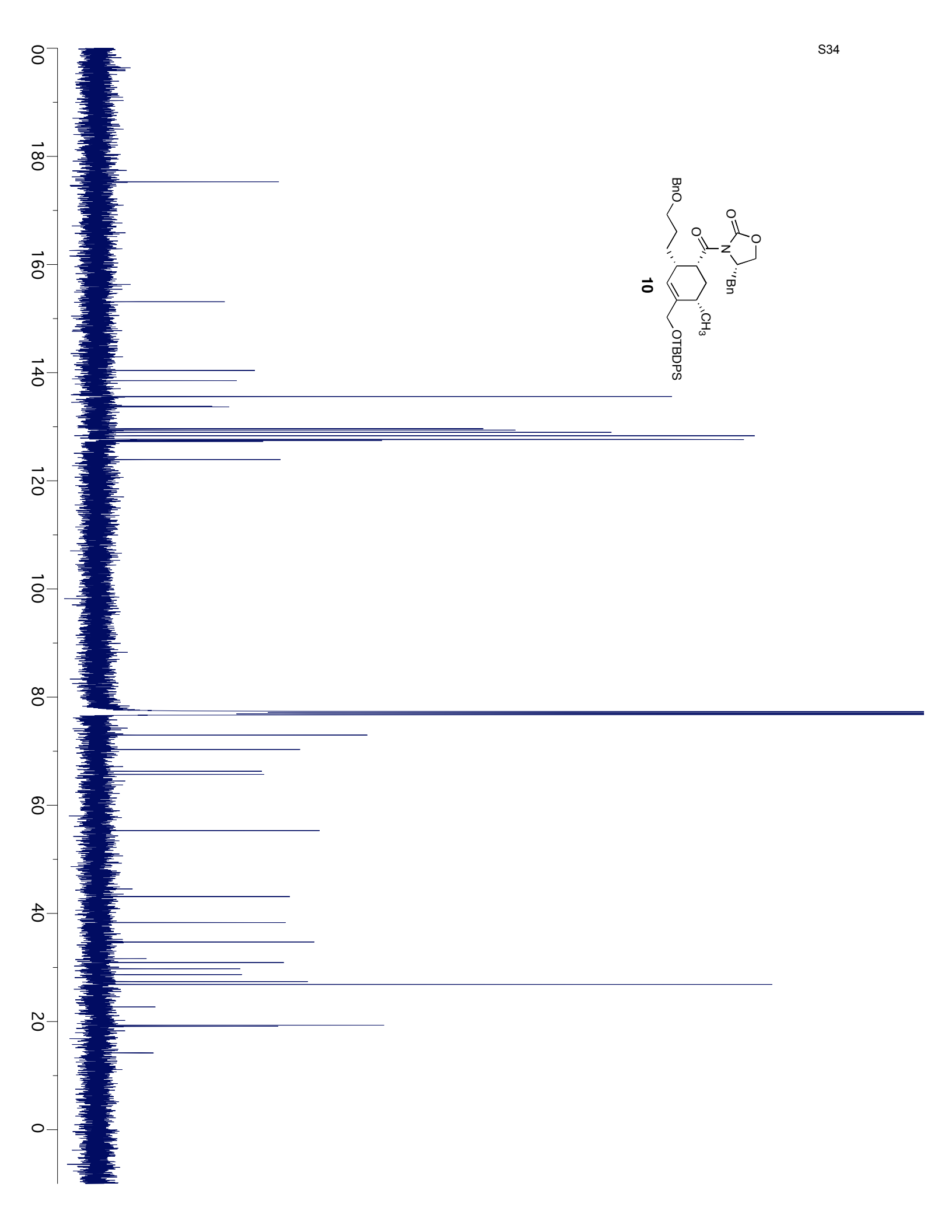
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OTBDPS
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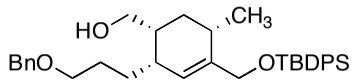
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CH3
BnO
OTBDPS

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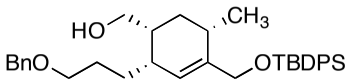

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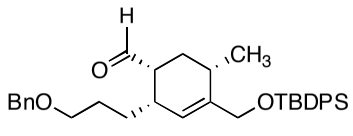
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O
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BnO
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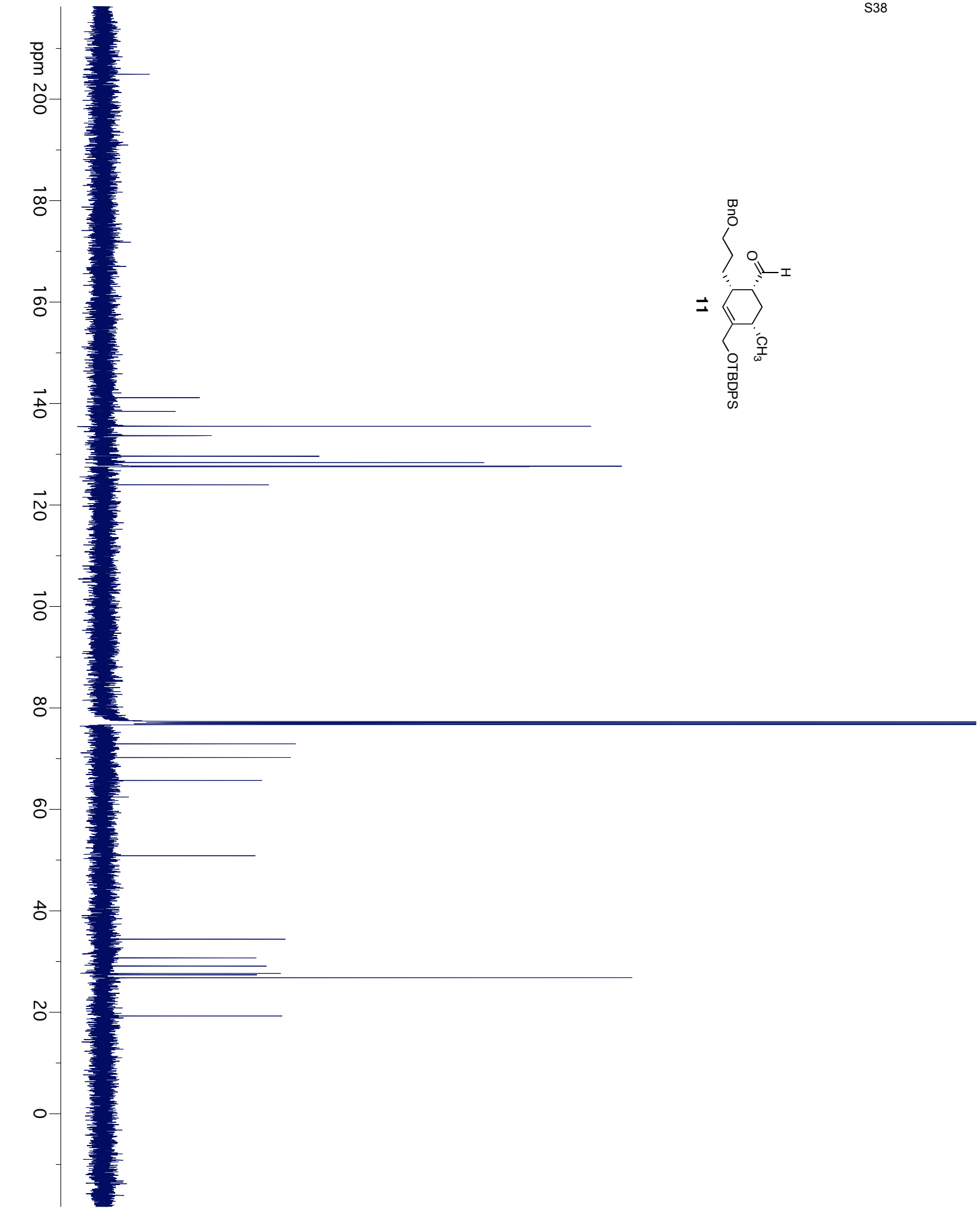
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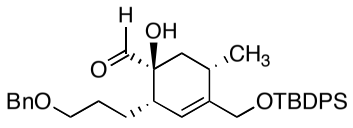
BnO
O
H
CH3
OTBDPS
11



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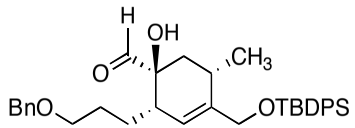

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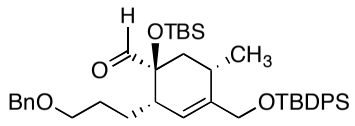
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CH3
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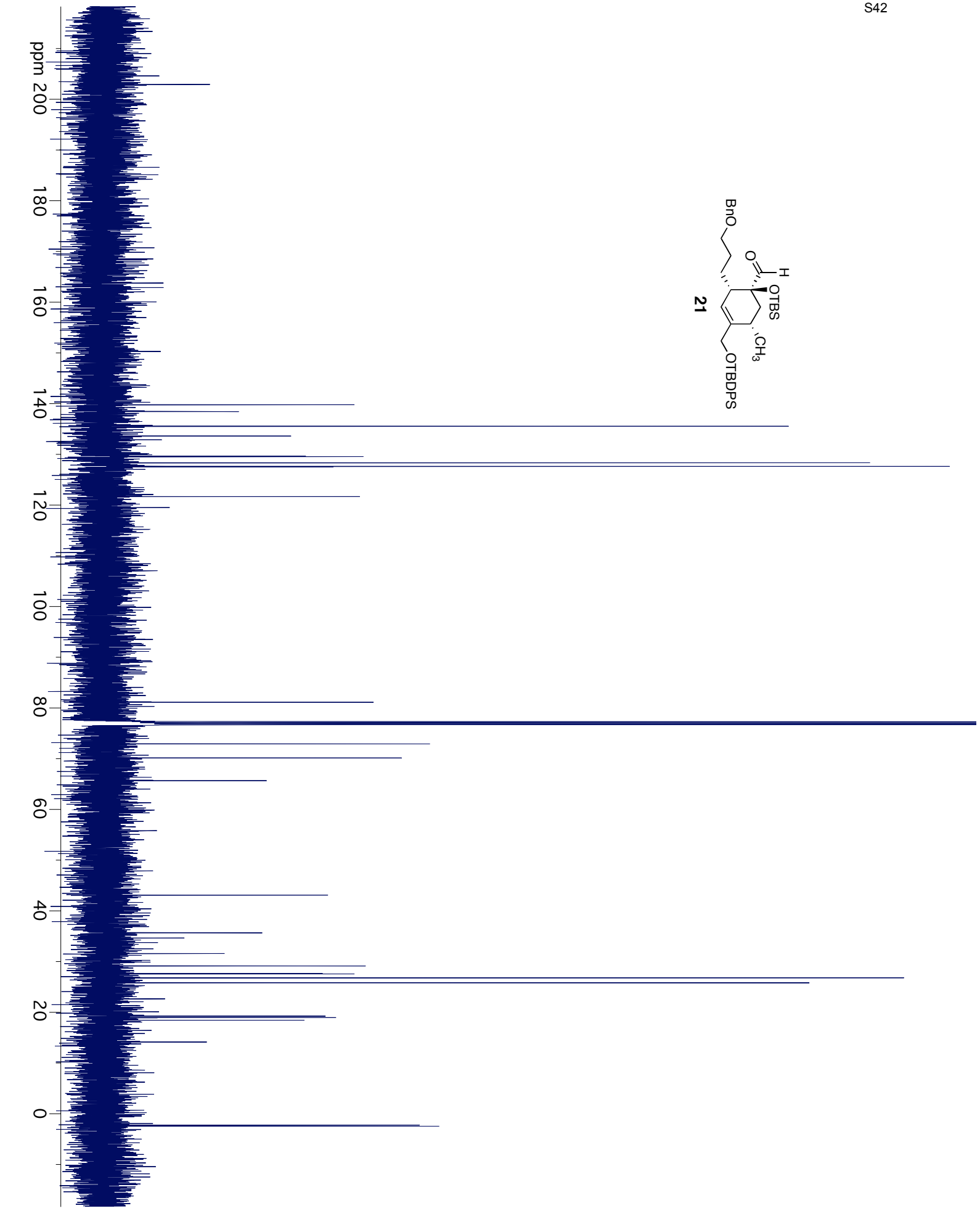
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OTBDPS
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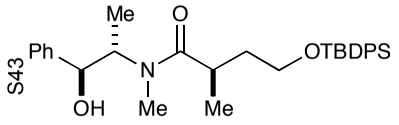
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Me
Me

S43

S3

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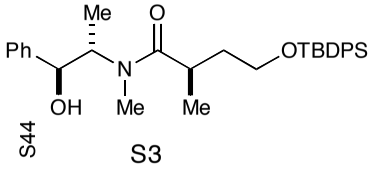
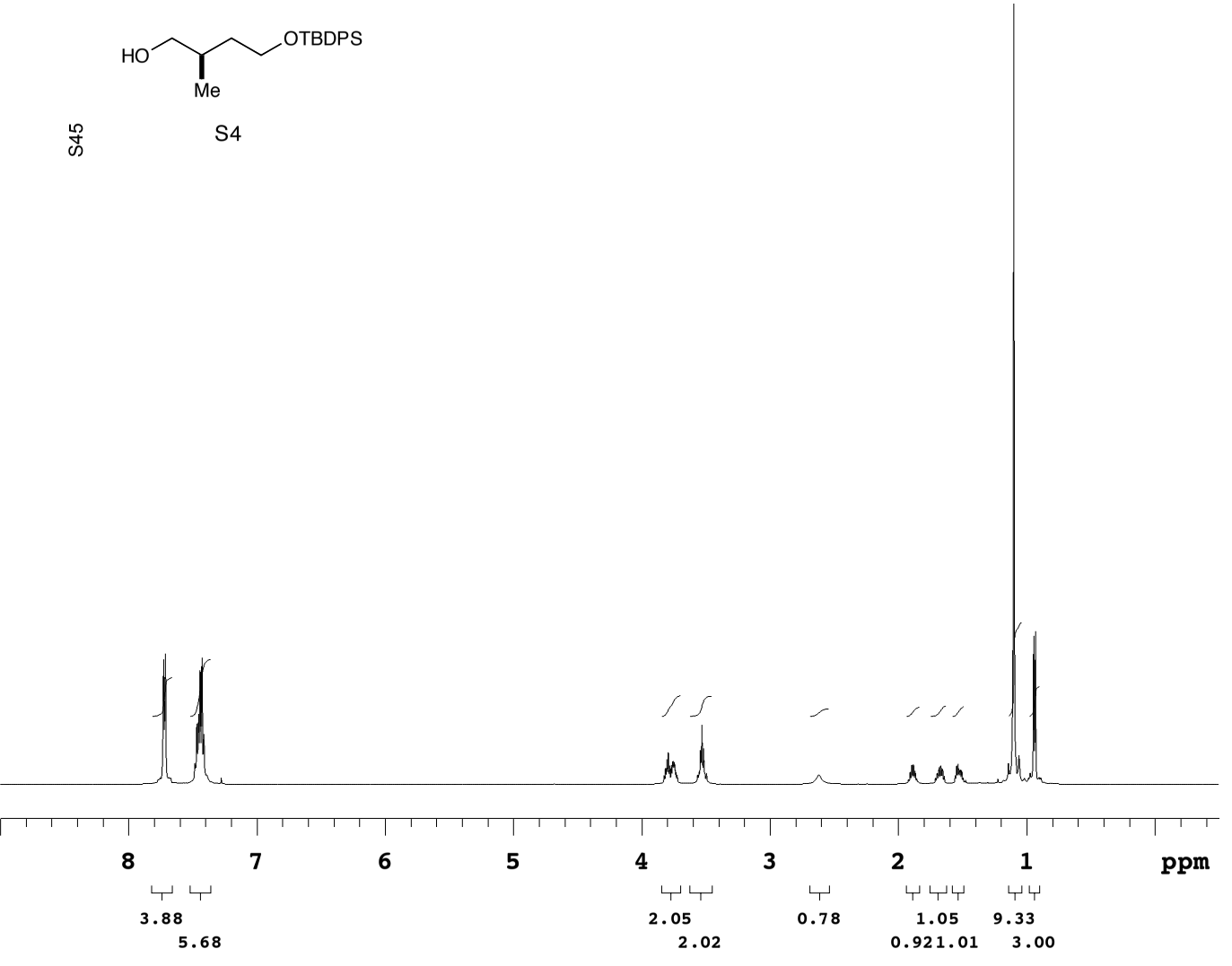


S44

S3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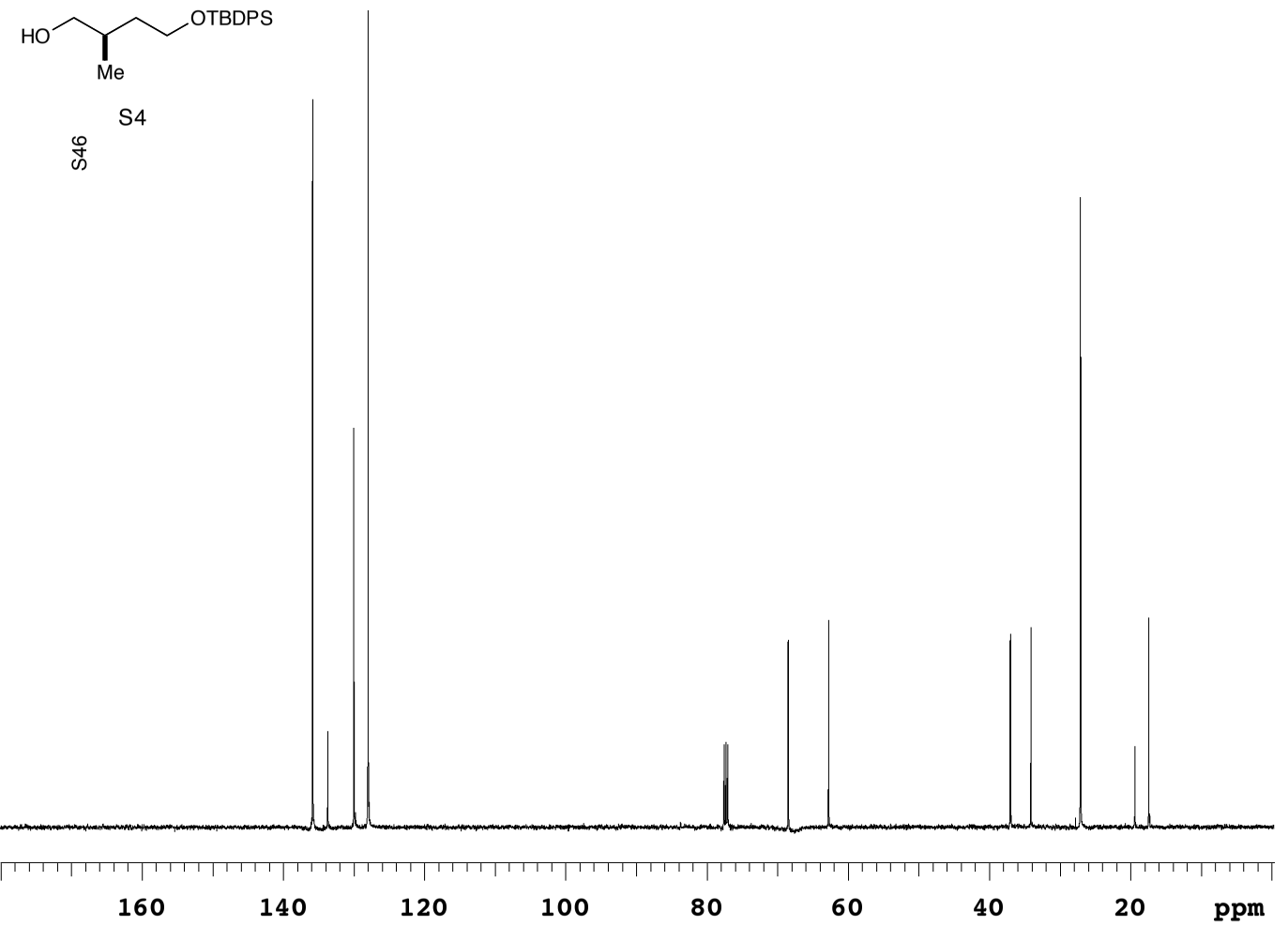
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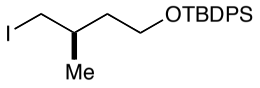
I
OTBDPS
Me

S5

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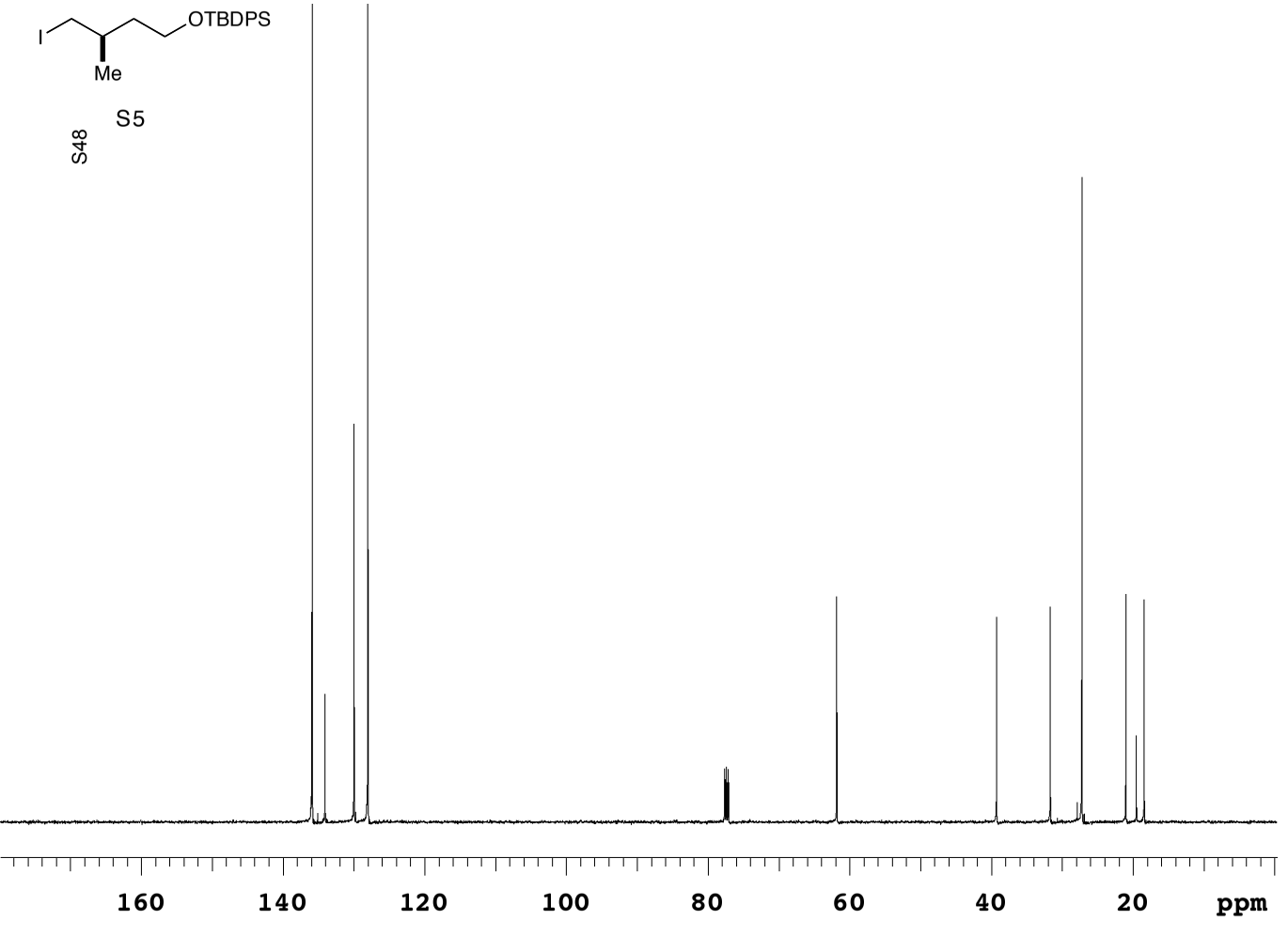
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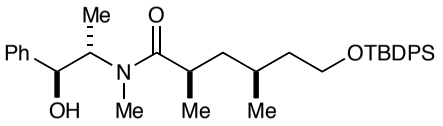
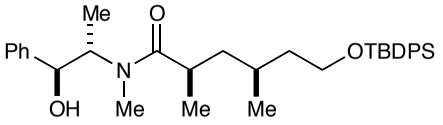
S5
S48
160
140
120
100
80
60
40
20
ppm


Me
O
Ph
N
OTBDPS
OH
Me
Me
Me

S49

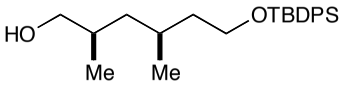
S6

8
7
6
5
4
3
2
1
ppm
0.48
2.00
0.12
0.04
0.24
0.09
0.31
0.18
0.29
1.39
0.05



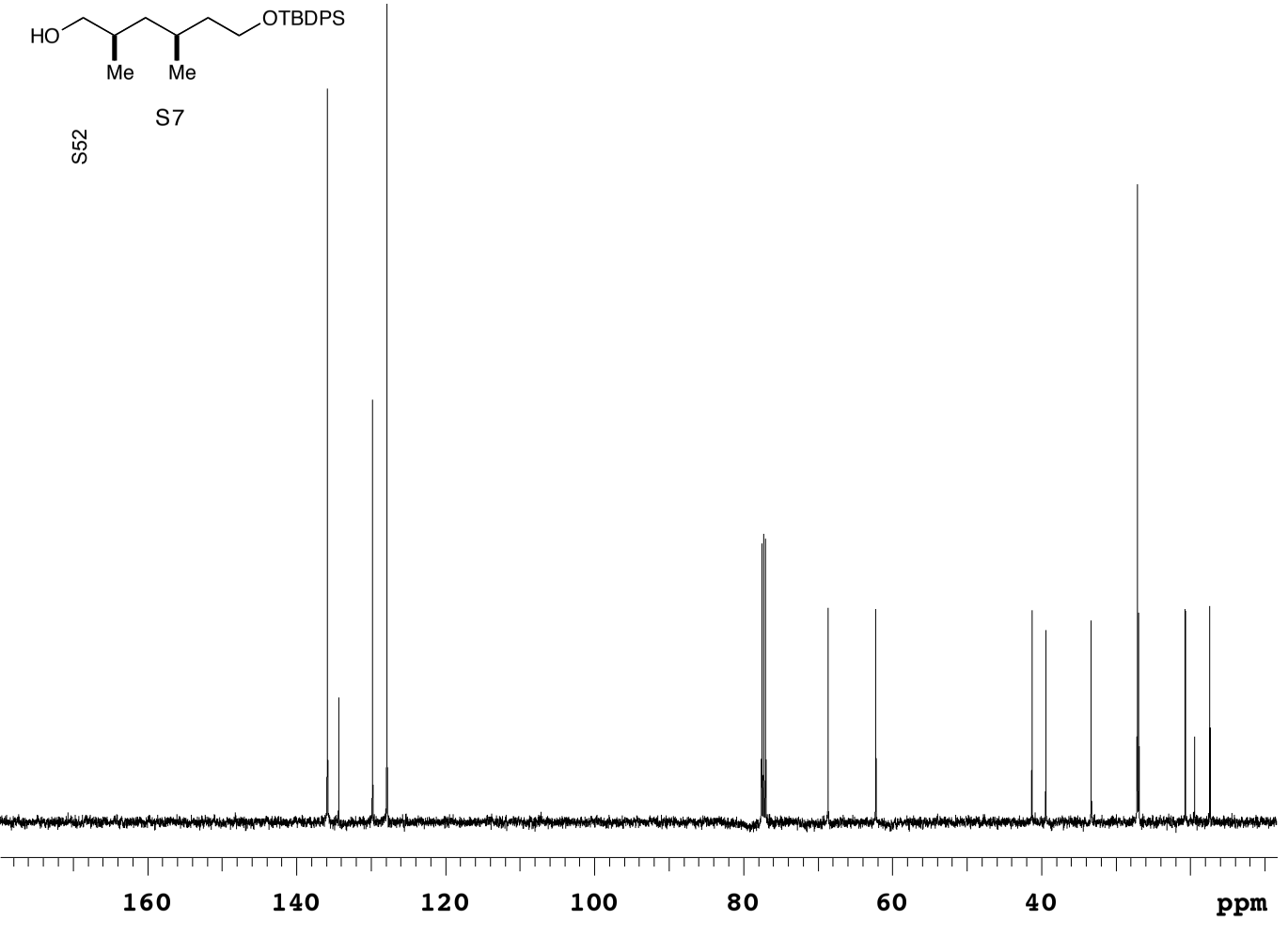
S50

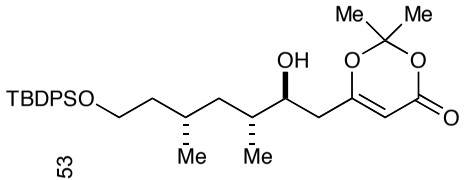
S6



S7

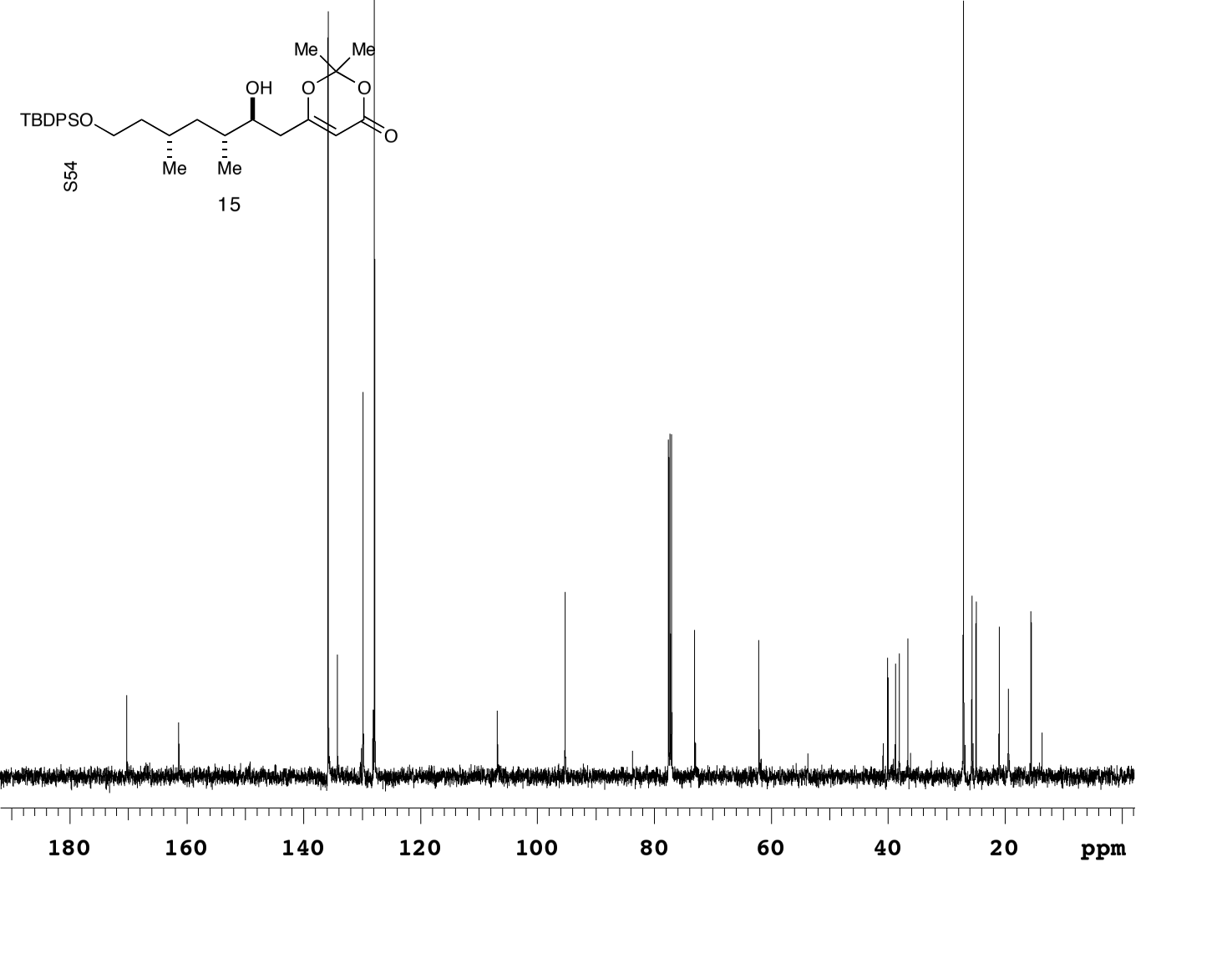
S51

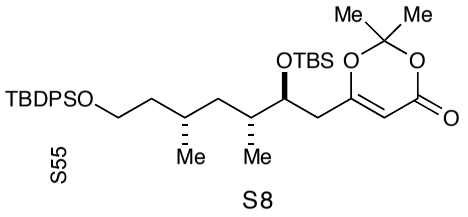

HO
OTBDPS
Me
Me
S7
S52
160
140
120
100
80
60
40
ppm


Me
Me
OH
O
O
TBDPSO
O
Me
Me

15

8
7
6
5
4
3
2
1
ppm
4.31
6.56
1.00
3.34
1.24
0.97
11.64
1.22
6.63
1.41
11.55

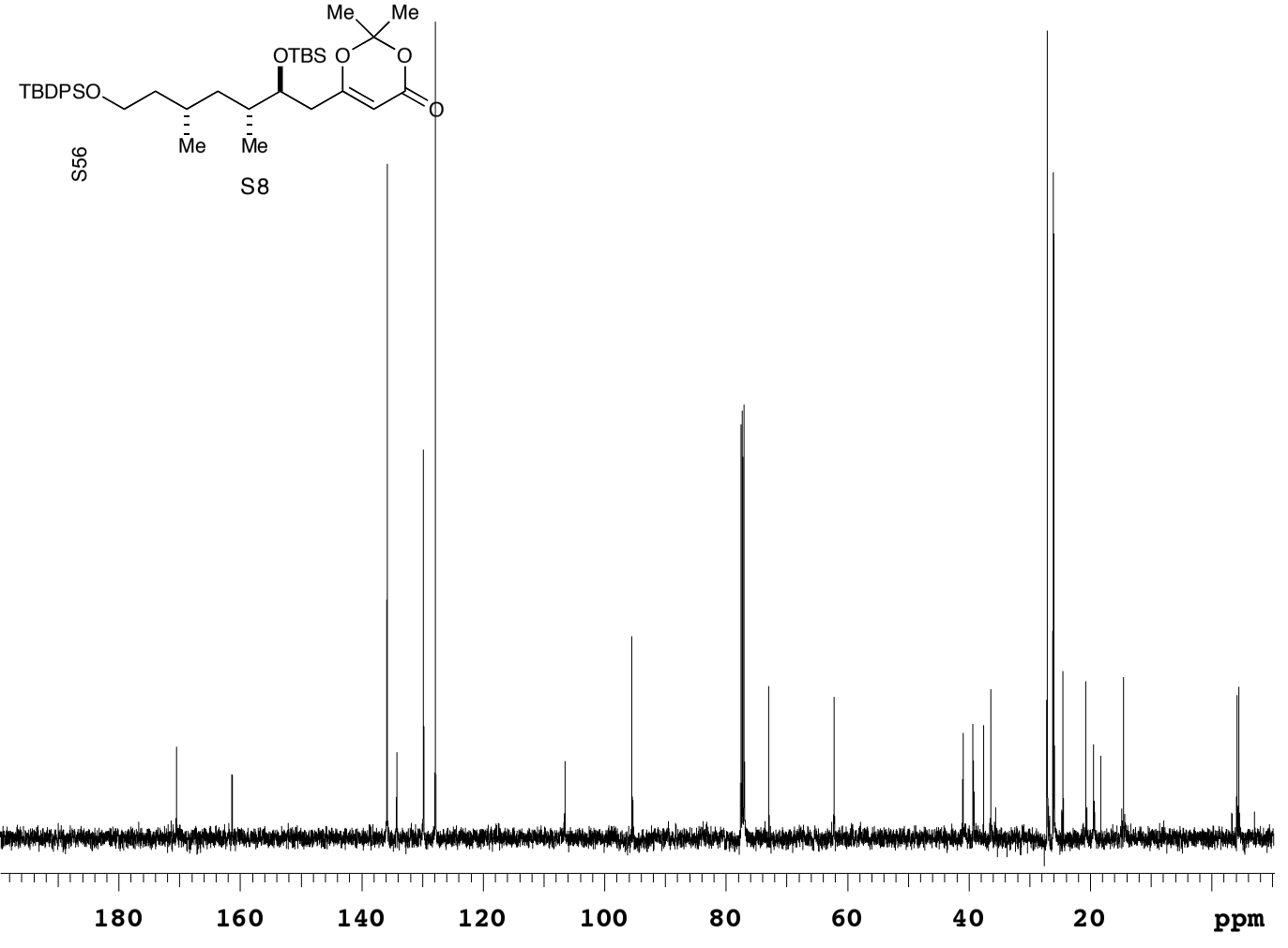

Me
Me
OH
O
O
TBDPSO
O
Me
Me
S54
15
180
160
140
120
100
80
60
40
20
ppm

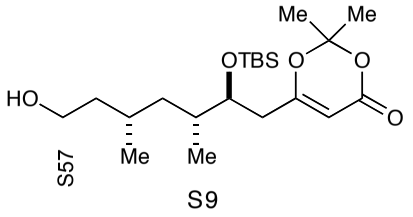

Me
Me
OTBS
O
O
TBDPSO
O
Me
Me

S55

S8

8
7
6
5
4
3
2
1
ppm
4.45
6.85
1.00
2.70
1.10
2.00
0.99
9.88
2.27
11.11
0.51
7.63

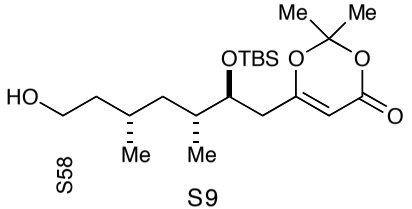

Me
Me
OTBS
O
O
TBDPSO
O
Me
Me
S56
S8
180
160
140
120
100
80
60
40
20
ppm


Me
Me
OTBS
O
O
HO
O
Me
Me

S57

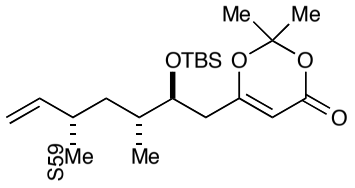
S9

8
7
6
5
4
3
2
1
ppm
1.00
2.55
1.17
2.22
1.30
10.88
2.56
0.66
19.57
7.18



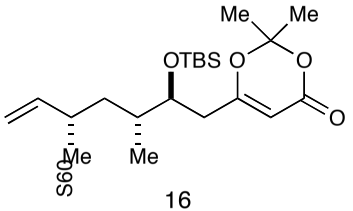
S58

S9

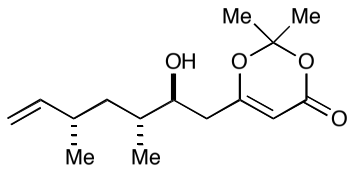

Me
Me
OTBS
O
O
O
Me
Me

16

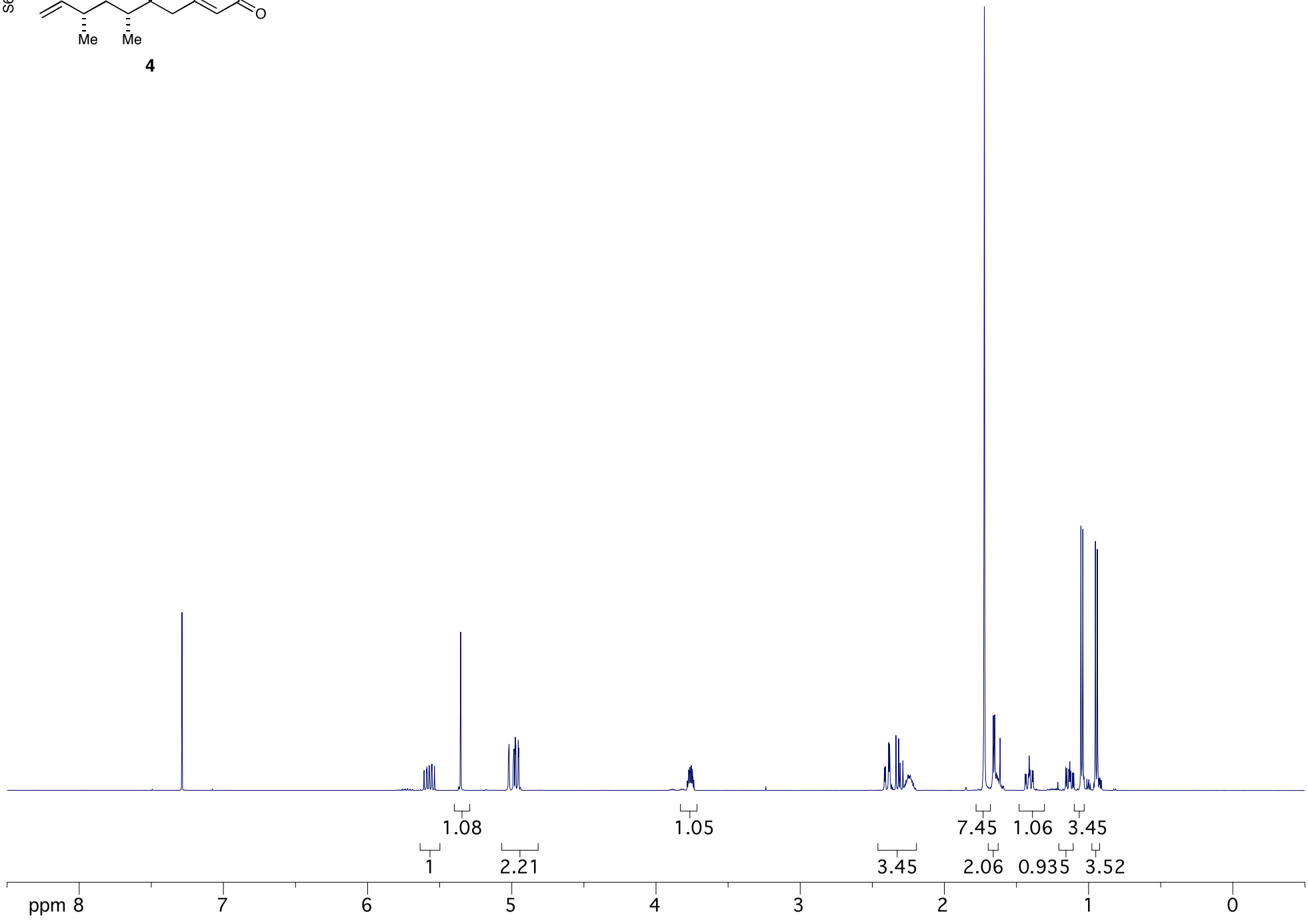
8
7
6
5
4
3
2
1
ppm
1.03
2.36
1.00
1.12
2.16
9.25
1.37
1.15
5.66
7.19

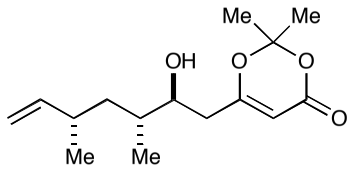


16


Me
Me
OH
O
O
O
Me
Me

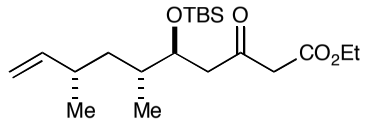
4


1.08
1.05
7.45
1.06
3.45
1
2.21
3.45
2.06
0.935
3.52
ppm 8
7
6
5
4
3
2
1
0



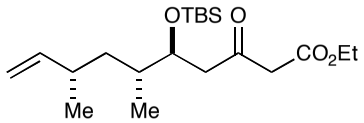
4

S63

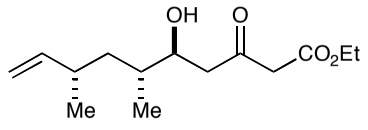

OTBS O
CO2Et
Me
Me

S10

1.71
3.57
1.26
2.61
5.19
9.33
3.7
3
3.68
4.23
2.58
1.24
1.25
1.48
10.1
3.23
ppm 12
11
10
9
8
7
6
5
4
3
2
1
0

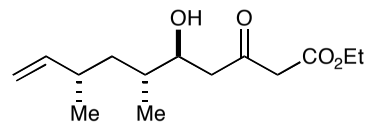


S10

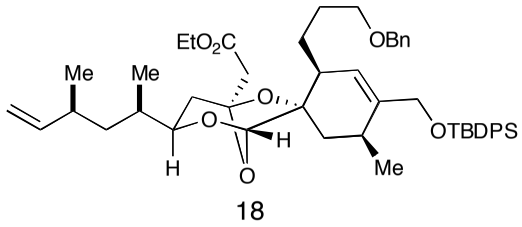

OH
O
CO2Et
Me
Me

17

2.23
0.941
3.06
1.22
3.5
3.4
1
2.24
2.05
1.09
1.06
1.04
3.29
ppm 12
11
10
9
8
7
6
5
4
3
2
1
0

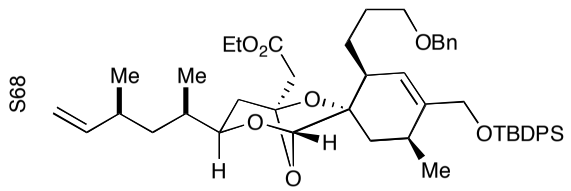


17


EtO2C
OBn
Me
Me
O
O
H
H
O
OTBDPS
Me

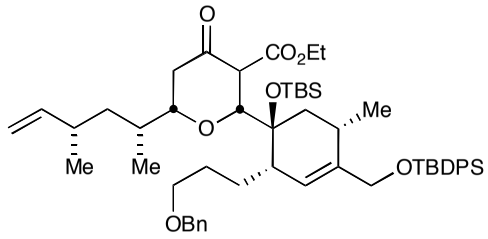
18

12.2
1.01
2.19
5.09
1.98
0.972
2.96
1.01
9.49
3.35
5.08
1
0.992
2.1
2.15
2.06
4
0.927
4.61
3.39
3.2
ppm 8
7
6
5
4
3
2
1
0


EtO2C
OBn
Me
Me
O
O
H
H
O
OTBDPS
Me

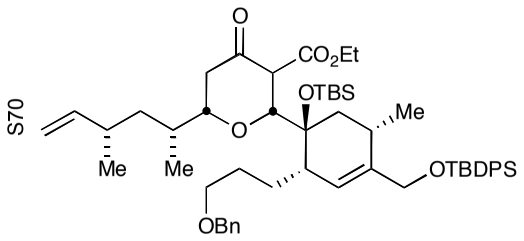
18

ppm 200
180
160
140
120
100
80
60
40
20
0


O
CO2Et
OTBS
Me
O
Me
Me
OTBDPS
OBn

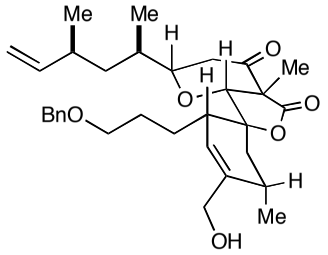
22

11.7
0.795
1.78
1.11
0.795
1.87
0.898
2.64
4.27
0.8
4.4
9.39
2.87
4.46
0.868
1.96
2.96
0.922
0.769
1.58
1.67
1.56
0.90
41
3.07
3
ppm 8
7
6
5
4
3
2
1
0


O
CO2Et
OTBS
Me
O
Me
Me
OTBDPS
OBn

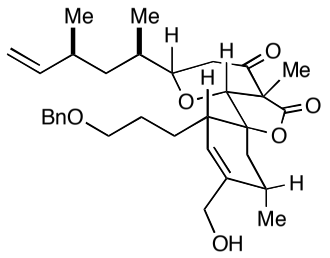
22

20
200
180
160
140
120
100
80
60
40
20
0


Me
Me
H
H
O
Me
H
O
O
BnO
O
H
Me
OH

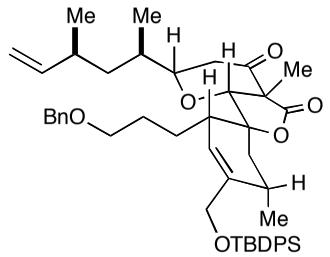
23

1
2.04
0.89
0.922
2.05
0.901
1.92
0.993
1.42
1.33
3.29
5.28
0.826
2.1
1.05
0.798
0.888
2.98
1.03
3.79
3.11
ppm 8
7
6
5
4
3
2
1
0


Me
Me
H
H
O
Me
H
O
O
BnO
O
H
Me
OH

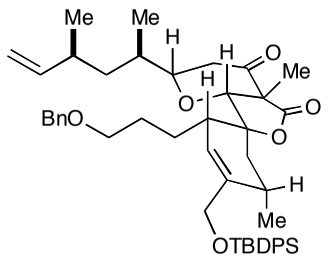
23

ppm 200
180
160
140
120
100
80
60
40
20
0


Me
Me
H
H
O
Me
H
O
O
BnO
O
H
Me
OTBDPS

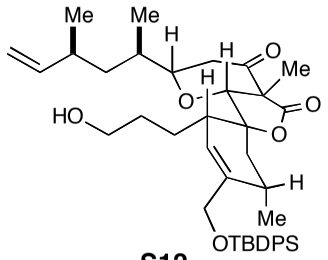
S11

13.5
0.693
2.17
2.22
2.17
0.805
2.01
1.04
3.83
3.59
4.85
1
1.92
0.939
0.941
1.02
1.19
3.29
1.02
2.17
12.7
3.97
ppm 8
7
6
5
4
3
2
1
0


Me
Me
H
H
O
Me
H
O
O
BnO
O
H
Me
OTBDPS

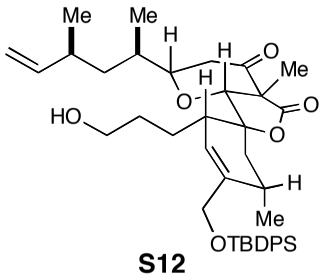
S11

ppm 200
180
160
140
120
100
80
60
40
20
0


Me
Me
H
H
O
Me
H
O
HO
O
O
H
Me
OTBDPS

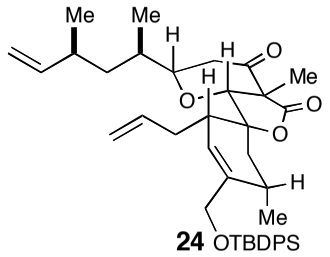
S12

6.44
0.747
0.995
3.01
0.731
1.88
1.92
7.63
1.85
10
3.22
4.35
1
1.81
2.03
0.82
1.03
1.91
3.13
3.06
ppm 8
7
6
5
4
3
2
1
0


Me
Me
H
H
O
Me
H
O
O
HO
O
H
Me
OTBDPS

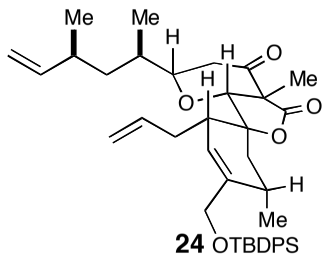
S12

ppm 200
180
160
140
120
100
80
60
40
20
0

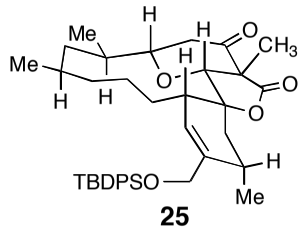

Me
Me
H
H
O
Me
H
O
O
O
H
Me

24 OTBDPS

6.39
1.17
2.2
1.06
1.08
1.85
5.13
1.1
1.08
2.24
9.54
3.24
4.38
1
1.06
2.25
2.14
3.34
3.24
ppm 8
7
6
5
4
3
2
1
0

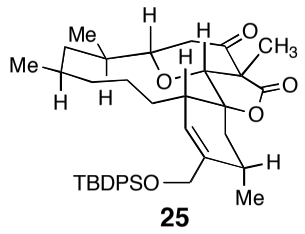


24 OTBDPS


Me
H
H
O
CH3
Me
H
O
H
O
O
H
H
TBDPSO
Me

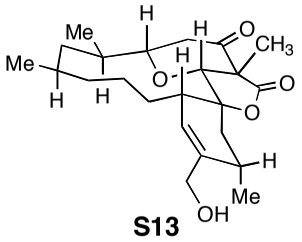
25

6.29
0.972
0.993
2.1
0.96
2.93
1.12
10.4
3.05
4.14
1
1.89
1.02
0.979
0.89
6.28
3.78
3
3.08
ppm 8
7
6
5
4
3
2
1
0


Me
H
H
O
CH3
Me
H
O
H
O
O
H
H
TBDPSO
H
Me

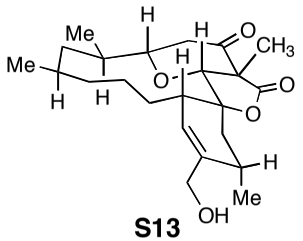
25

ppm 200
180
160
140
120
100
80
60
40
20
0


Me
H
H
O
CH3
Me
H
O
O
H
H
O
H
Me
OH

S13

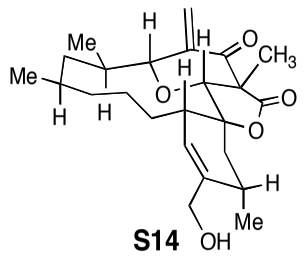
0.166
1.07
0.987
1.15
0.887
0.624
4.82
4.22
3.63
1
0.971
1.01
0.985
1.09
0.743
2.75
5.92
2.42
ppm 8
7
6
5
4
3
2
1
0


Me
H
H
O
CH3
Me
O-
H
O
H
H
O
H
Me
OH

S13

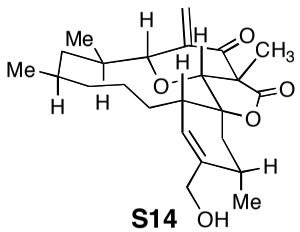
ppm 200
180
160
140
120
100
80
60
40
20
0

S83


Me
H
H
O
CH3
Me
H
O-
O
H
H
O
H
Me
OH

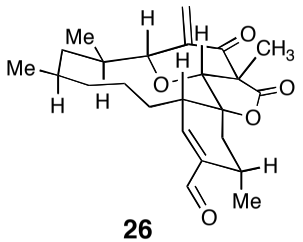
S14

1
0.977
1.05
1
1.07
4.18
5.98
3.95
3.91
0.96
1
1.04
1.06
1.01
1.02
5.6
3.21
1.34
ppm 8
7
6
5
4
3
2
1
0


Me
H
H
O
CH3
Me
H
O
H
H
O
O
H
Me
OH

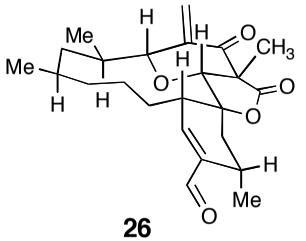
S14

ppm 200
180
160
140
120
100
80
60
40
20
0


Me
H
H
O
CH3
Me
O-
H
O
H
H
O
H
Me
O

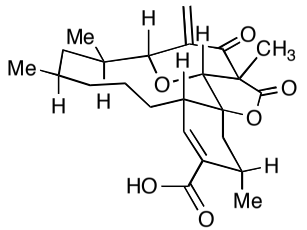
26

0.952
0.973
0.961
0.924
0.967
7.76
5.26
6.52
3.29
1
0.954
0.961
0.952
0.989
6.71
1.39
2.91
1.35
ppm 9
8
7
6
5
4
3
2
1
0


Me
H
H
O
CH3
Me
O
H
O
H
H
O
H
Me
O

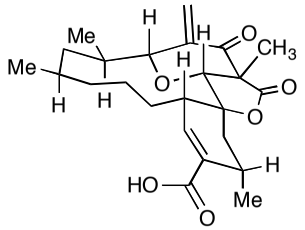
26

ppm 200
180
160
140
120
100
80
60
40
20
0



(–)-okilactomycin (1)
synthetic

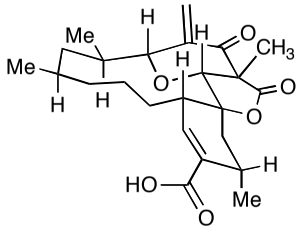
S88



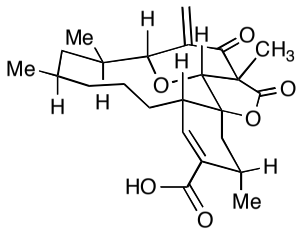
(–)-okilactomycin (1)
synthetic

1

ppm 200 180 160 140 120 100 80 60 40 20 0



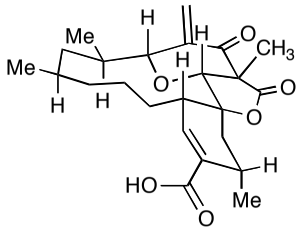
(+)-okilactomycin (1)
natural



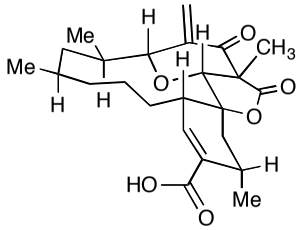
(+)-okilactomycin (1)
natural

S90

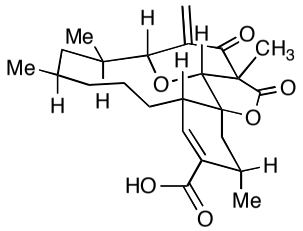
ppm 200 180 160 140 120 100 80 60 40 20 0



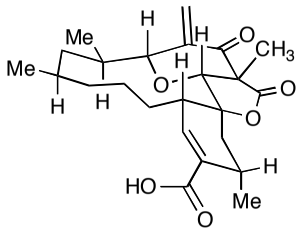
(+)-okilactomycin (1)
natural



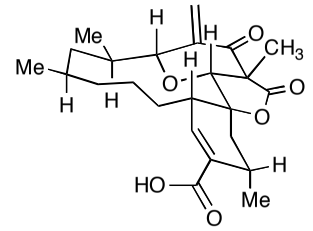
(–)-okilactomycin (1)
synthetic



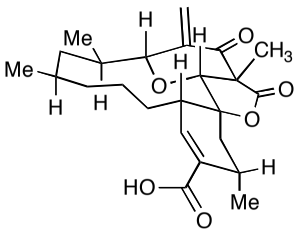
(+)-okilactomycin (1)
natural



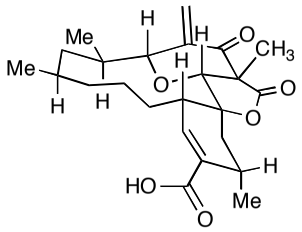
(–)-okilactomycin (1)
synthetic



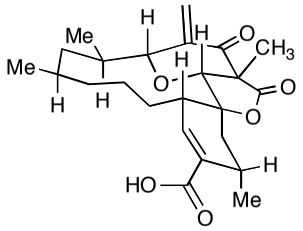
(+)-okilactomycin (1)
natural



(–)-okilactomycin (1)
synthetic

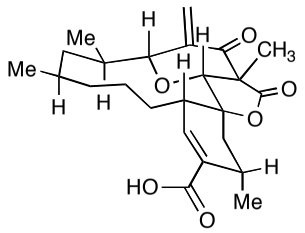


(+)-okilactomycin (1)
natural

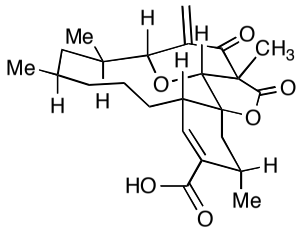


(–)-okilactomycin (1)
synthetic

S95



(+)-okilactomycin (1)
natural



(–)-okilactomycin (1)
synthetic

checkCIF/PLATON report

No syntax errors found. **CIF dictionary** **Interpreting this report**

Datablock: c__users_scheidt_desktop_work_n0565_0m

Bond precision: C-C = 0.0071 A Wavelength=1.54178

Cell: **a=9.2888(8)** **b=15.3271(12)** **c=14.2532(11)**
alpha=90 **beta=100.633(6)** **gamma=90**
Temperature: **100 K**

	Calculated	Reported
Volume	1994.4(3)	1994.4(3)
Space group	P 21	P2(1)
Hall group	P 2yb	P 2yb
Moiety formula	C45 H53 N O5 Si	C45 H53 N O5 Si
Sum formula	C45 H53 N O5 Si	C45 H53 N O5 Si
Mr	715.97	715.97
Dx,g cm-3	1.192	1.192
Z	2	2
Mu (mm-1)	0.877	0.877
F000	768.0	768.0
F000’	770.59	
h,k,lmax	11,18,17	11,18,16
Nref	3719[7146]	6565
Tmin,Tmax	0.915,0.955	0.580,0.956
Tmin’	0.543	

Correction method= MULTI-SCAN

Data completeness= 1.77/0.92 **Theta(max)= 67.240**

R(reflections)= 0.0637(5034) **wR2(reflections)= 0.1866(6565)**

S = 0.973 **Npar= 473**

The following ALERTS were generated. Each ALERT has the format
test-name_ALERT_alert-type_alert-level.
Click on the hyperlinks for more details of the test.

Alert level C
PLAT029_ALERT_3_C _diffrn_measured_fraction_theta_full Low 0.97
PLAT340_ALERT_3_C Low Bond Precision on C-C Bonds (x 1000) Ang .. 7

Alert level G
REFLT03_ALERT_4_G Please check that the estimate of the number of Friedel pairs is

```
           correct. If it is not, please give the correct count in the
           _publ_section_exptl_refinement section of the submitted CIF.
          From the CIF: _diffrn_reflns_theta_max           67.24
          From the CIF: _reflns_number_total               6565
          Count of symmetry unique reflns         3719
          Completeness (_total/calc)           176.53%
          TEST3: Check Friedels for noncentro structure
          Estimate of Friedel pairs measured      2846
          Fraction of Friedel pairs measured     0.765
          Are heavy atom types Z>Si present        yes
PLAT063_ALERT_4_G Crystal Size Likely too Large for Beam Size ....       0.70 mm
PLAT072_ALERT_2_G SHELXL First  Parameter in WGHT Unusually Large.       0.13
PLAT791_ALERT_4_G Note: The Model has Chirality at C20    (Verify)          S
PLAT791_ALERT_4_G Note: The Model has Chirality at C21    (Verify)          R
PLAT791_ALERT_4_G Note: The Model has Chirality at C23    (Verify)          S
PLAT791_ALERT_4_G Note: The Model has Chirality at C28    (Verify)          S
```

```
   0 ALERT level A = Most likely a serious problem - resolve or explain
   0 ALERT level B = A potentially serious problem, consider carefully
   2 ALERT level C = Check. Ensure it is not caused by an omission or oversight
   7 ALERT level G = General information/check it is not something unexpected

   0 ALERT type 1 CIF construction/syntax error, inconsistent or missing data
   1 ALERT type 2 Indicator that the structure model may be wrong or deficient
   2 ALERT type 3 Indicator that the structure quality may be low
   6 ALERT type 4 Improvement, methodology, query or suggestion
   0 ALERT type 5 Informative message, check
```

It is advisable to attempt to resolve as many as possible of the alerts in all categories. Often the minor alerts point to easily fixed oversights, errors and omissions in your CIF or refinement strategy, so attention to these fine details can be worthwhile. In order to resolve some of the more serious problems it may be necessary to carry out additional measurements or structure refinements. However, the purpose of your study may justify the reported deviations and the more serious of these should normally be commented upon in the discussion or experimental section of a paper or in the "special_details" fields of the CIF. checkCIF was carefully designed to identify outliers and unusual parameters, but every test has its limitations and alerts that are not important in a particular case may appear. Conversely, the absence of alerts does not guarantee there are no aspects of the results needing attention. It is up to the individual to critically assess their own results and, if necessary, seek expert advice.

Publication of your CIF in IUCr journals

A basic structural check has been run on your CIF. These basic checks will be run on all CIFs submitted for publication in IUCr journals (*Acta Crystallographica, Journal of Applied Crystallography, Journal of Synchrotron Radiation*); however, if you intend to submit to *Acta Crystallographica Section C* or *E*, you should make sure that full publication checks are run on the final version of your CIF prior to submission.

Publication of your CIF in other journals

Please refer to the *Notes for Authors* of the relevant journal for any special instructions relating to CIF submission.

PLATON version of 16/02/2011; check.def file version of 16/02/2011

Datablock c__users_scheidt_desktop_work_n0565_0m - ellipsoid plot