Supporting Information for *Angew. Chem. Int. Ed.* Z18907

A Cascade Cycloaddition Strategy Leading to the Total Synthesis of (-)-FR182877.

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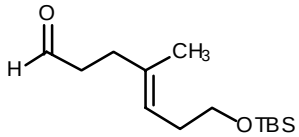
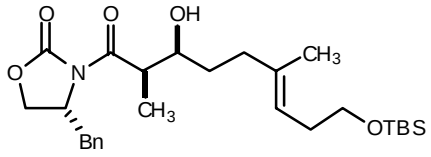
General Information. All reactions were carried out under an atmosphere of argon in flame-dried glassware. The reaction solvents: THF, Et_2O, CH_2Cl_2 were purified by passage over activated alumina.[1] Reagents were used as received from the manufacturer unless otherwise stated. Flash chromatography was carried out using EM reagent silica gel 60 (230-400 mesh). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. All TLC plates were visualized by UV fluorescence quenching and were stained with either p-anisaldehyde or ceric ammonium molybdate (CAM). Optical rotations were measured on a Jasco DIP-0181 digital polarimeter with a sodium lamp and are reported as follows: $[\alpha]_\lambda^{T\ ^\circ C}$ (c=g/100 mL solvent). Infrared spectra were recorded on a Perkin-Elmer 1600 series FT-IR spectrometer. ^{1}H-NMR spectra were recorded on a Varian Inova-500 (500 MHz) spectrometer and are reported in ppm using solvent as an internal standard ($CDCl_3$=7.26 ppm). Data are reported as: [δ shift]([s= singlet, d=doublet, t=triplet, q=quartet, m=multiplet, b=broad], [integration], and [*J*=coupling constant in Hz]). Proton decoupled ^{13}C-NMR spectra were recorded on a Varian Mercury 400 (100 MHz) spectrometer and are reported in ppm using solvent as internal standard ($CDCl_3$=77.0 ppm). Low and high resolution mass spectra were obtained at the Harvard University Mass Spectrometry Laboratory.



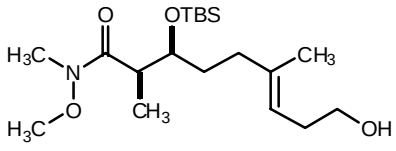
(4E)-4-methyl-7-(1,1,2,2-tetramethyl-1-silapropoxy) hept-4-enal (**4**) To a solution of TBSCl (24.0g, 159 mmol) in 100 mL DMF at 0 °C under argon was added imidazole (17.3g, 254 mmol) followed by 3-butenol (10.3g, 143 mmol). The reaction was warmed to RT and stirred for 24h during which time the product, 1-*tert*-butyldimethylsilyloxy-3-butene, formed an immiscible layer on top of the reaction. The top layer was collected and the DMF layer was poured onto 300 mL water and extracted 3 x 100 mL pentane. The combined organic layers were washed 1 x 50 mL 10% aq. $CuSO_4$, 3 x 100 mL water, 1 x 100 mL brine then dried over Na_2SO_4. Concentration *in vacuo* yielded 24.0g (90%) of 1-*tert*-butyldimethylsilyloxy-3-butene as a colorless oil that was used without purification. Into a solution of 1-*tert*-butyldimethylsilyloxy-3-butene (24.0g, 129 mmol) in 200 mL CH_2Cl_2 and 50 mL MeOH at –78 °C was passed a dilute stream of O_3 in O_2 until the reaction achieved a persistent blue color. Triphenylphosphine (33.8g, 129 mmol) was then added and the reaction was warmed to RT under argon and stirred 6h. The mixture was then concentrated *in vacuo* to give a slurry of white precipitate and oil which was resuspended in 300 mL hexanes and filtered. The filter cake was washed 3 x 50 mL hexanes and the combined filtrates were concentrated *in vacuo*. The resulting oil was distilled (23 torr, 90-95 °C) to give 19.9g

(83%) of pure 3-*tert*-butyldimethylsilyloxy-propanal. To a solution of isopropenylmagnesium bromide (80 mL, 1.0 M, 80 mmol) at 0 °C under argon was added 3-*tert*-butyldimethylsilyloxy-propanal (8.28g, 43.9 mmol) dropwise. The reaction was immediately poured onto 100 mL sat. aq. NH_4Cl and extraced 3 x 100 mL Et_2O. The combined organic layers were washed 1 x 100 mL brine then dried over Na_2SO_4. Solvent removal *in vacuo* gave a quantitative return of unpurified (+/-)-5-*tert*-butyldimethylsilyloxy-2-methyl-1-penten-3-ol as a colorless oil. This oil was dissolved in 50 mL freshly distilled triethylorthoacetate and propionic acid (0.02 mL) was added. The solution was heated to reflux for 1h then the solvent was directly distilled off the reaction under vacuum (50 torr). The residue was purified by silica gel chromatography (20:1 hexanes / EtOAc) to give 9.86g (75% 2 steps) of ethyl 7-*tert*-butyldimethylsilyloxy-4-methyl-*trans*-4-heptenoate as a colorless oil. To a solution of ethyl 7-*tert*-butyldimethylsilyloxy-4-methyl-*trans*-4-heptenoate (8.88g, 29.5 mmol) in 50 mL CH_2Cl_2 at –78 °C under argon was added DIBAL (29.5 mL, 1.0 M in CH_2Cl_2, 29.5 mmol) dropwise while maintaining the internal temperature at <-65 °C. The reaction was quenched by the addition of 0.1 mL EtOAc then 50 mL of sat. aq. Na/K tartrate was added and the slurry was stirred vigorously at RT for 12h. The resulting clear biphase was extracted 3 x 100 mL CH_2Cl_2 and the combined organic layers were washed 1 x 100 mL brine then dried over Na_2SO_4. Concentration *in vacuo* yielded a colorless oil that was purified by silica gel chromatography (20:1 pentane / Et_2O) to give 7.37g (97%) of aldehyde **4** as a colorless pungent oil. **R_f:** 0.25 (9:1 hexanes / Et_2O) **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 9.76 (s, 1H), 5.18 (t, 1H, *J*=7.6 Hz), 3.57 (t, 2H, *J*=7.3 Hz), 2.52 (t, 2H, *J*=7.3 Hz), 2.33 (t, 2H, *J*=7.3 Hz), 2.22 (q, 2H, *J*=6.8 Hz), 1.64 (s, 3H), 0.89 (s, 9H), 0.05 (s, 6H) **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 202.38, 134.79, 121.53, 62.75, 42.01, 31.74, 31.66, 25.86, 18.25, 16.15, -5.35 **FTIR** ν 2929, 2858, 1727, 1472, 1255, 1096, 938, 835, 775 **HRMS** (FAB) Calc'd for $C_{14}H_{28}O_2Si$ [M + Na]: 274.2202; found 274.2197

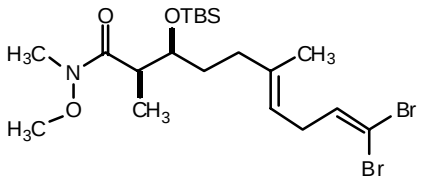


(6E)-1-[(4R)-2-oxo-4-benzyl (1,3-oxazolidin-3-yl)] (3S, 2R)-3-hydroxy-2, 6-dimethyl-9-(1,1,2,2-tetra-methyl-1-silapropoxy)non-6-en-1-one (**5**) To a solution of (R)-4-benzyl-N-propionyl-2-oxazolidinone (5.74g, 24.6 mmol) in 60 mL CH_2Cl_2 at 0 °C under Ar was added Bu_2BOTf (8.00 mL, 31.7 mmol) followed by TEA (6.0 mL, 43.0 mmol). The reaction was cooled to –78 °C and aldehyde **4** (7.35g, 28.6 mmol) was added in one portion. The reaction was stirred for 30 minutes then warmed to 0 °C and stirred for 2h. The reaction was quenched by the addition of 40 mL of pH=7 phosphate buffer followed by addition of 60 mL MeOH. To the resulting slurry was then added slowly 60 mL of a 2:1 v/v mixture of MeOH / 30% aq. H_2O_2 and the mixture was stirred vigorously for 1h. The reaction was then extracted 3 x 100 mL Et_2O and the combined organic layers were washed 1 x 100 mL water, 1 x 50 mL sat. aq. $NaHCO_3$, 1 x 100 mL brine, and dried over $MgSO_4$. Evaporation *in vacuo* yielded an oil that was purified by silica gel chromatography (grad. 4:1 – 2:1 hexanes/EtOAc) to give 10.52g (88%) of **5** as a colorless oil. **R_f:** 0.5 (2:1 hexanes / EtOAc) $[\alpha]_D^{25}$ = –45.8° (c=0.60, CH_2Cl_2) **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 7.4-7.3 (m, 3H), 7.20 (d, 2H, *J*=7.3 Hz), 5.17 (t, 1H, *J*=7.3 Hz), 4.71 (m, 1H), 4.22 (m, 2H), 3.93 (m, 1H), 3.76 (qd, 1H, *J*=6.8, 2.9 Hz), 3.57 (t, 2H, *J*=7.4 Hz), 3.24 (dd, 1H, *J*=13.7, 3.3 Hz), 2.86 (bm, 1H), 2.76 (dd, 1H, *J*=13.7, 9.3 Hz), 2.25-2.15

(m, 3H), 2.05 (m, 1H), 1.63 (m, 1H), 1.62 (s, 3H), 1.53 (m, 1H), 1.26 (d, 3H, *J*=6.8 Hz), 0.89 (s, 9H), 0.05 (s, 6H) **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 177.38, 152.97, 136.55, 134.97, 129.39, 128.94, 127.40, 120.83, 71.14, 66.11, 62.99, 55.06, 42.15, 37.73, 36.04, 31.96, 31.79, 25.93, 18.34, 16.10, 10.53, -5.27 **FTIR** (film) ν 3500, 2930, 1782, 1698, 1455, 1385, 1211, 1098, 836, 764, 702 **HRMS** (ES) Calc'd for $C_{27}H_{43}NO_5Si$ [M+H]: 490.2989; found 490.2982

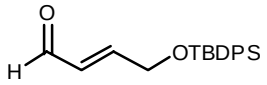


(6E) (3S,2R)-9-hydroxy-N-methoxy-2, 6-dimethyl-N-methyl-3-(1,1,2,2-tetramethyl-1-silapropoxy) non-6-enamide (**6**) To a suspension of MeNHOMe hydrochloride (2.19g, 22.5 mmol) in 25 mL THF at 0 °C under Ar was added neat Me_3Al (2.20 mL, 22.9 mmol) dropwise. Gas evolution was noted. The solution was cooled to –78 °C and a solution of **5** (3.60g, 7.35 mmol) in 15 mL THF was added *via* cannula. The reaction was then warmed to 0 °C, stirred for 1h, then poured onto sat. aq. 200 mL NH_4Cl, acidified with 200 mL 1N HCl and extracted 3 x 100 mL Et_2O. The combined organic layers were washed 1 x 100 mL 1N HCl, 1 x 50 mL sat. aq. $NaHCO_3$, 1 x 100 mL brine then dried over Na_2SO_4. Solvent removal *in vacuo* gave a colorless oil that was triturated by slow addition of 20 mL 10:1 hexanes/Et_2O and gentle agitation until the formation of copious white solid appeared to cease. The slurry was then filtered and the filter cake was washed 3 x 100 mL hexanes. The combined filtrates were evaporated *in vacuo* to yield 2.66g pure Weinreb amide (96%) as a colorless oil. Instead of trituration smaller runs were purified by silica gel chromatography (grad. 5:2 – 3:2 hexanes/EtOAc). To a solution of Weinreb amide (2.66g, 7.11 mmol), and imidazole (2.91g, 42.7 mmol) in 10 mL DMF was added TBSCl (2.42g, 16.1 mmol) and the reaction was stirred under Ar for 24h. The reaction was then poured onto 500 mL water and extracted 3 x 100 mL Et_2O. The combined organics were washed 1 x 50 mL 10% aq. $CuSO_4$, 3 x 100 mL water, 1 x 100 mL brine then dried over Na_2SO_4. Evaporation *in vacuo* gave 3.33g (96%) of the silylated product as a colorless oil. To a solution of the bis-silylated product (1.50g, 3.07 mmol) in 30 mL MeOH at 0 °C under argon was added tetrabutylammonium hydrogensulfate (0.117g, 0.345 mmol) followed by p-toluenesulfonic acid (0.025g, 0.13 mmol). The reaction was stirred for 1 h then 10 mL sat. aq. $NaHCO_3$ was added and the mixture was poured onto 100 mL water. The aqueous mixture was extracted 3 x 50 mL Et_2O and the combined organic layers were washed 1 x 50 mL water, 1 x 50 mL brine and dried over $MgSO_4$. Evaporation *in vacuo* gave a colorless oil that was purified by silica gel chromatography (grad. 1:1 – 0:1 hexanes / Et_2O) to give 1.025g (89%) of alcohol **6** as a colorless oil. **R_f:** 0.33 (1:1 hexanes / EtOAc) $[\alpha]_D^{25}$ = +2.5° (c=1.34, CH_2Cl_2) **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 5.12 (t, 1H, *J*=7.4 Hz), 3.93 (ddd, 1H, *J*= 7.8, 4.9, 4.9), 3.69 (s, 3H), 3.61 (m, 2H), 3.17 (s, 3H), 3.00 (bm, 1H), 2.26 (q, 2H, *J*=6.7 Hz), 2.06 (t, 2H, *J*=8.3 Hz), 1.61 (s, 3H), 1.6-1.5 (m, 2H), 1.15 (d, 3H, *J*=6.8 Hz), 0.91 (s, 9H), 0.07 (s, 6H) **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 138.99, 119.67, 73.31, 62.44, 61.47, 40.53, 34.37, 34.32, 31.51, 25.94, 18.14, 16.30, 14.86, -4.10, -4.39 **FTIR** (film) ν 3448, 2933, 2857, 1661, 1462, 1382, 1255, 1046, 995, 835, 774, 668 **HRMS** (ES) Calc'd for $C_{19}H_{39}NO_4Si$ [M+H]: 374.2726; found 374.2719

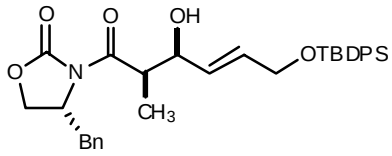


(3S,2R) (9Z,6E)-10,10-dibromo-N-methoxy-2, 6-dimethyl-N-methyl-3-(1,1,2,2-tetramethyl-1-silapro-

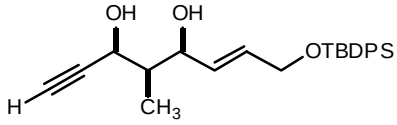
poxy) deca-6,9-dienamide (**7**) To a solution of alcohol **6** (1.49g, 3.98 mmol) in 30 mL CH_2Cl_2 at 0 °C under argon was added $NaHCO_3$ (0.503g) followed by Dess-Martin periodinane (2.32g, 5.47 mmol). The reaction was stirred vigorously for 3 h then poured onto water and extracted 3 x 50 mL Et_2O. The combined organic layers were washed 2 x 50 mL sat. aq. $NaHCO_3$ then dried over Na_2SO_4. Evaporation *in vacuo* yielded 1.39g of the unstable aldehyde product as a colorless resin. To a solution of CBr_4 (2.94g, 8.86 mmol) in 20 mL CH_2Cl_2 at 0 °C under argon was added PPh_3 (4.65g, 17.7 mmol) portionwise over 10 min. The resulting orange/red solution was stirred for 30 min then cooled to –78 °C and the aldehyde (1.15g, 3.09 mmol) was added *via* cannula as a solution in 7 mL CH_2Cl_2. The reaction was warmed to 0 °C and stirred for 30 min then it was directly poured onto a silica gel column. Chromatography (grad. 6:1 – 4:1 hexanes / EtOAc) gave 1.20g (74%) of the desired dibromide **7**. **R_f:** 0.74 (1:1 hexanes / EtOAc) $[\alpha]_D^{25}$ =+5.3° (c=1.4, CH_2Cl_2) **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 6.33 (t, 1H, *J*=6.8 Hz), 5.09 (t, 1H, *J*=7.3 Hz), 3.93 (dt, 1H, *J*=7.8, 4.8 Hz), 3.69 (s, 3H), 3.18 (s, 3H), 3.00 (bm, 1H), 2.76 (t, 2H, *J*=7.3 Hz), 2.04 (t, 2H, *J*=8.3 Hz), 1.60 (s, 3H), 1.6-1.5 (m, 2H), 1.15 (d, 3H, *J*=6.9 Hz), 0.91 (s, 9H), 0.07 (s, 6H) **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 138.37, 137.36, 118.30, 88.52, 73.37, 61.48, 40.43, 34.15, 34.06, 32.09, 25.94, 18.14, 16.33, 14.85, -4.12, -4.43 **FTIR** (film) 2932, 2856, 1660, 1461, 1383, 1253, 1174, 1105, 1059, 997, 835, 774 **HRMS** (ES) Calc'd for $C_{20}H_{37}Br_2NO_3Si$ [M+H]: 526.0987; found 526.0988



(2E)-4-(2,2-dimethyl-1,1-diphenyl-1-silaprop-oxy)but-2-enal (**8**) To a solution of *cis*-2-butene-1,4-diol (9.48g, 107 mmol) in 300 mL THF at 0 °C under argon was added nBuLi (41.0 mL, 2.60 M, 107 mmol) dropwise. The resulting thick milky suspension was stirred vigorously while TBDPSCl (26.2 mL, 101 mmol) was added dropwise. After 1.5h, the reaction was quenched with pH=7 buffer and extracted 3 x 300 mL Et_2O. The combined organic layers were washed 1 x 200 mL brine then dried over Na_2SO_4. Evaporation *in vacuo* yielded 33.1g (94%) of 1-*tert*-butyldiphenylsilyloxy-*cis*-2-butene-4-ol as a colorless oil that was used without purification. To a solution of 1-*tert*-butyldiphenylsilyloxy-*cis*-2-butene-4-ol (10.2g, 31.2 mmol), TEA (18.0 mL, 129 mmol), and DMSO (20 mL) in 200 mL CH_2Cl_2 at 0 °C was added SO_3-pyridine complex (9.75g, 61.3 mmol). The reaction was warmed to RT, stirred for 2h then poured onto 200 mL water and extracted 3 x 200 mL Et_2O. The combined organic layers were washed 1 x 100 mL sat. aq. NH_4Cl, 1 x 50 mL 10% aq. $CuSO_4$, 3 x 100 mL water, 1 x 100 mL brine then dried over Na_2SO_4. Concentration *in vacuo* gave an orange oil. ^{1}H-NMR analysis of the unpurified mixture showed a 2:1 mixture of the *cis* and *trans* isomeric aldehydes. The orange oil was allowed to stand at RT under HIVAC (<1 torr) for 24 h whereupon complete isomerization to the *trans* aldehyde was observed by TLC. The oil was then subjected to silica gel chromatography (20:1 hexanes / EtOAc) to give 6.35g (63%) of aldehyde **8** as a colorless solid. **R_f:** 0.35 (4:1 hexanes/ EtOAc) **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 9.61 (d, 1H, *J*=8.3 Hz), 7.66 (d, 2H, *J*=5.8 Hz), 7.4 (m, 3H), 6.84 (dt, 1H, *J*=15.1, 1.0 Hz), 6.57 (dd, 1H, *J*=15.1, 8.3 Hz), 4.45 (d, 2H, *J*=1.0 Hz), 1.08 (s, 9H) **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 193.38, 155.94, 135.37, 132.66, 130.52, 129.94, 127.83, 62.91, 26.67, 19.18 **FTIR** (film) ν 3071, 2931, 2857, 1688, 1472, 1427, 1362, 1113, 965, 823, 741, 702 **HRMS** (FAB) Calc'd for $C_{20}H_{24}O_2Si$ [M + Na]: 342.1890; found 342.1890

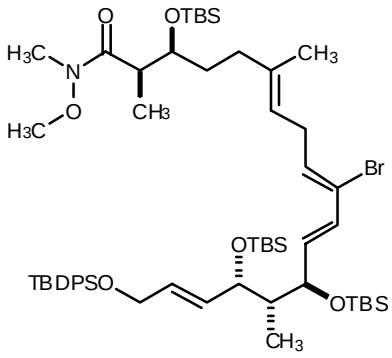


(4E)-1-[(4R)-2-oxo-4-benzyl (1,3-oxazolidin-3-yl)] (3S, 2R)-6-(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)-3-hydroxy-2-methylhex-4-en-1-one (**9**) To a solution of (R)-4-benzyl-N-propionyl-2-oxazolidinone (3.81g, 16.3 mmol) in 70 mL CH_2Cl_2 at 0 °C under Ar was added Bu_2BOTf (5.00 mL, 19.8 mmol) followed by TEA (3.50 mL, 25.1 mmol). The reaction was cooled to –78 °C and *trans*-4-*tert*-butyldiphenylsilyloxy-2-butenal (6.00g, 18.5 mmol) was added in one portion. The reaction was stirred for 30 minutes then warmed to 0 °C and stirred for 2h. The reaction was quenched by the addition of 40 mL of pH=7 phosphate buffer followed by addition of 60 mL MeOH. To the resulting slurry was then added slowly 60 mL of a 2:1 v/v mixture of MeOH / 30% aq. H_2O_2 and the mixture was stirred vigorously for 1h. The reaction was then extracted 3 x 100 mL Et_2O and the combined organic layers were washed 1 x 100 mL water, 1 x sat. aq. $NaHCO_3$, 1 x 100 mL brine, and dried over $MgSO_4$. Evaporation *in vacuo* yielded an oil that was purified by silica gel chromatography (grad. 4:1 – 2:1 hexanes/EtOAc) to give 8.14g (89%) of **9** as a colorless oil. **R_f:** 0.62 (1:1 hexanes / EtOAc). $[\alpha]_D^{25}$ = –45.9° (c=1.0, CH_2Cl_2) **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 7.68 (d, 2H, *J*= Hz), 7.44-7.28 (m, 6H), 7.22 (d, 2H, *J*= 7 Hz), 5.87 (m, 1H), 5.79 (dd, 1H, *J*= 15, 4.8 Hz), 4.68 (m, 1H), 4.53 (bs, 1H), 4.23 (bs, 2H), 4.17 (d, 2H, *J*=4.8 Hz), 3.85 (m, 1H), 3.24 (d, 1H, *J*= 13.5 Hz), 2.79 (dd, 2H, *J*= 13.5, 9.2 Hz), 1.25 (d, 3H, *J*=7.0 Hz), 1.06 (s, 9H) **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 176.66, 153.04, 135.49, 135.00, 133.59, 133.55, 131.18, 129.65, 129.41, 128.96, 128.69, 127.66, 127.42, 71.99, 66.16, 63.70, 55.15, 42.77, 37.76, 26.79, 19.21, 11.07 **FTIR** (film) ν 3500, 2931, 1781, 1698, 1428, 1388, 1210, 1112, 822, 702 **HRMS** (CI) Calc'd for $C_{33}H_{39}NO_5Si$ [M +NH_4]: 575.2941; found 575.2932



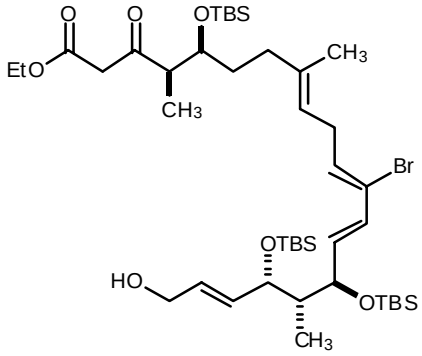
(6E) (3S, 5S, 4R)-8-(2, 2-dimethyl-1, 1-diphenyl-1-silapropoxy)-4-methyloct-6-en-1-yne-3, 5-diol (**10**) To a suspension of MeNHOMe hydrochloride (1.55g, 15.9 mmol) in 20 mL THF at 0 °C under Ar was added neat Me_3Al (1.50 mL, 15.6 mmol) dropwise. Gas evolution was noted. The solution was cooled to –78 °C and a solution of **9** (3.01g, 5.39 mmol) in 10 mL THF was added *via* cannula. The reaction was then warmed to 0 °C, stirred for 1h, then poured onto sat. aq. 200 mL NH_4Cl, acidified with 200 mL 1N HCl and extracted 3 x 100 mL Et_2O. The combined organic layers were washed 1 x 100 mL 1N HCl, 1 x 50 mL sat. aq. $NaHCO_3$, 1 x 100 mL brine then dried over $MgSO_4$. Solvent removal *in vacuo* gave a colorless oil that was triturated by slow addition of 20 mL 10:1 hexanes/Et_2O and gentle agitation until the formation of copious white solid appeared to cease. The slurry was then filtered and the filter cake was washed 3 x 100 mL hexanes. The combined filtrates were evaporated *in vacuo* to yield 2.28g pure Weinreb amide (97%) as a colorless oil. Instead of trituration smaller runs were purified by silica gel chromatography (grad. 5:2 – 3:2 hexanes/EtOAc). To a solution of Weinreb amide (1.42g, 3.21 mmol) in 5 mL THF at 0 °C under argon was added ethynylmagnesium bromide (25 mL, 0.5 M, 12.5 mmol). The reaction was stirred 3h then poured onto 50 mL sat. aq. NH_4Cl and extracted 3 x 50 mL Et_2O. The combined organic layers were washed 1 x 50 mL brine and dried over

Na_2SO_4. Evaporation *in vacuo* yielded a yellow oil that was purified by silica gel chromatography (4:1 hexanes / EtOAc) to give 1.00g (77%) of the desired ynone as a slightly yellow oil. To a solution of ynone (0.893g, 2.20 mmol) in 15 mL THF at –78 °C under argon was added DIBAL (4.40 mL, 1 M in CH_2Cl_2, 4.40 mmol) dropwise. After 30 min the reaction was quenched by the addition of 0.1 mL EtOAc and 15 mL sat. aq. Na/K tartrate and the slurry was warmed to RT with vigorous stirring for 12h. The resulting clear biphase was extracted 3 x 30 mL Et_2O and the combined organic layers were washed 1 x 30 mL brine then dried over Na_2SO_4. Evaporation *in vacuo* gave a pale yellow oil that was purified by silica gel chromatography (2:1 hexanes / EtOAc) to give 0.880g (98%) of diol **10**. **R_f:** 0.4 (2:1 hexanes / EtOAc) $[\alpha]_D^{25}$ = –5.2° (c=1.5, CH_2Cl_2) **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 7.69 (d, 2H, *J*=7.0 Hz), 7.5-7.35 (m, 3H), 5.89-5.79 (m, 2H), 4.62 (s, 1H), 4.49 (s, 1H), 4.25 (m, 2H), 2.60 (bs, 1H), 2.53 (s, 1H), 2.15 (bs, 1H), 1.88 (m, 1H), 1.10 (d, 3H, *J*=6.5 Hz), 1.08 (s, 9H) **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 135.49, 133.56, 130.48, 130.44, 129.68, 127.66, 83.70, 74.67, 73.79, 65.98, 63.66, 60.41, 43.68, 26.78, 21.04, 19.20, 14.16, 7.46 **FTIR** (film) ν 3288, 2933, 2856, 1466, 1427, 1379, 1256, 1112, 968, 823, 742, 702 **HRMS** (FAB) Calc'd for $C_{25}H_{32}O_3Si$ [M+Na]: 431.2019; found 431.2010



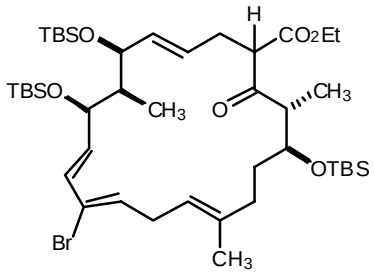
(3S, 15S, 2R, 13R, 14R) (9Z, 6E, 11E, 16E)-18-(2,2-dimethyl-1, 1-diphenyl-1-silapropoxy)-10-bromo-N-methoxy-2, 6, 14-trimethyl-N-methyl-3, 13, 15-tris (1,1,2,2-tetramethyl-1-silapropoxy)octadeca-6,9,11,16-tetraenamide (**12**) To a solution of diol **10** (0.810g, 1.98 mmol) and imidazole (0.572g, 8.40 mmol) in 6 mL DMF at RT under argon was added TBSCl (0.719g, 4.77 mmol). The reaction was stirred 36h then poured onto 50 mL water and extracted 3 x 50 mL pentane. The combined organic layers were dried over Na_2SO_4 then concentrated *in vacuo* to reveal a colorless oil. Chromatography on silica gel (20:1 hexanes / EtOAc) gave 1.19g (94%) of the desired bis-silylated product. To a solution of bis silylated alkyne (0.914g, 1.43 mmol) in 3 mL THF at RT under argon was added freshly distilled catechol borane (0.20 mL, 1.9 mmol) followed by freshly prepared dicyclohexylborane (0.70 mL, 0.20 M in THF, 0.14 mmol). After 2 h the reaction was poured into 100 mL Et_2O and washed 10 x 20 mL 1 N NaOH (until aqueous layers were no longer colored), 1 x 50 mL brine then dried over $MgSO_4$. The yellow solution gradually decolorized as the remaining colored contaminants in the organic phase were adsorbed onto the $MgSO_4$ surface. The solution was filtered and solvent removal *in vacuo* gave 0.952g (97% unpur.) of the desired boronic acid **11** as a colorless resin that was used immediately. To a degassed (4 x freeze/pump/thaw under N_2) solution of dibromide **7** (1.00g, 1.89 mmol) and boronic acid **11** (1.67g, 2.44 mmol) in 30 mL THF and 10 mL water was added $Pd(PPh_3)_4$ (0.187g, 0.162 mmol) followed by Tl_2CO_3 (1.73g, 3.70 mmol). A yellow precipitate rapidly formed. After 5h the reaction was poured onto 100 mL Et_2O and washed 1 x 100 mL 1 M $NaHSO_4$ (gas evolution!). The resulting precipitate was removed by filtration through celite and the aqueous layer was discarded. The remaining organic layer was then washed 2 x 50 mL water, 1 x 50 mL brine then dried over Na_2SO_4. Evaporation *in vacuo* gave an orange oil. Chromatography on silica

gel (grad. 10:1 – 6:1 hexanes / EtOAc) gave 1.73g (84%) of the desired coupled product **12** as a slightly yellow oil. **R_f:** 0.34 (9:1 hexanes / EtOAc) $[\alpha]_D^{23}$ =+0.66° (c=0.90, CH_2Cl_2) **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 7.67 (d, 2H, *J*=7.8 Hz), 7.42-7.35 (m, 3H), 6.15-6.00 (m, 2H), 5.80 (t, 1H, *J*=6.7 Hz), 5.75 (dd, 1H, *J*=15.7, 7.4 Hz), 5.68 (dt, 1H, *J*=15.7, 4.8 Hz), 5.15 (t, 1H, 6.8 Hz), 4.22 (t, 1H, *J*=5.4 Hz), 4.18 (d, 2H, *J*=4.4 Hz), 4.12 (t, 1H, *J*=6.3), 3.93 (dt, 1H, *J*=8.8, 4.4 Hz), 3.68 (s, 3H), 3.17 (s, 3H), 2.97 (bm, 1H + t, 2H, *J*=6.8 Hz), 2.05 (t, 2H, *J*=7.3 Hz), 1.60-1.45 (m, 2H + s, 3H), 1.16 (d, 3H, *J*=6.9 Hz), 1.05 (s, 9H), 0.95 (d, 3H, *J*=6.9 Hz), 0.90 (s, 9H), 0.89 (s, 18H), 0.066 (s, 6H), 0.034 (s, 3H), 0.010 (s, 6H), -0.016 (s, 3H) **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 137.43, 136.61, 135.48, 133.69, 132.74, 132.19, 129.74, 129.60, 129.07, 127.64, 124.50, 119.88, 73.85, 73.37, 73.34, 63.87, 61.44, 47.51, 40.40, 34.21, 34.10, 31.57, 30.77, 26.77, 25.93, 25.63, 22.64, 19.21, 18.21, 18.19, 18.13, 16.33, 14.78, 14.13, 9.72, -3.65, -3.73, -4.13, -4.45, -4.75 **FTIR** (film) ν 2930, 2857, 1712, 1633, 1471, 1254, 1112, 836, 776, 702

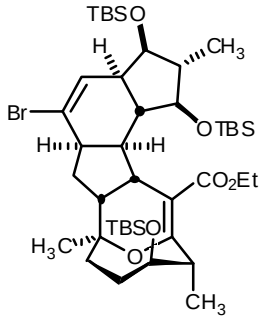


ethyl (5S,17S,4R,15R,16R) (11Z,8E,13E,18E)-12-bromo-20-hydroxy-4, 8, 16-trimethyl-3-oxo-5, 15, 17-tris (1, 1, 2, 2-tetramethyl-1-silapropoxy) icosa-8,11,13,18-tetraenoate (**13**) To a solution of amide **12** (1.14g, 1.05 mmol) in 10 mL THF at –78 °C under argon was added DIBAL (0.22 mL, 1.23 mmol) dropwise. The reaction was stirred 3 h then quenched by the addition of 0.5 mL EtOAc followed by 10 mL sat. aq. Na/K tartrate. The resulting slurry was warmed to RT and stirred vigorously for 12 h then extracted 3 x 50 mL Et_2O. The combined organic layers were washed 1 x 50 mL brine and dried over Na_2SO_4. Evaporation *in vacuo* yielded a colorless oil that was immediately redissolved in 8 mL CH_2Cl_2 at RT under argon. In a separate flask, $SnCl_2$ (0.230g, 0.880 mmol) was suspended in 2 mL CH_2Cl_2 at RT and EDA (1.25g, 8.00 mmol) was added (gas evolution!). To this opaque yellow mixture was then added the aldehyde solution and the reaction was stirred vigorously for 2 h. The reaction was then poured onto 50 mL brine and extracted 3 x 50 mL Et_2O. The combined organic layers were dried over Na_2SO_4 and solvent removal *in vacuo* gave a yellow oil. The oil was placed under HIVAC (<1 torr) for 24h to remove the bulk of residual EDA then chromatography on silica gel (grad. 50:1-20:1 hexanes / EtOAc) gave 0.818g (70%) of the β-keto ester as a colorless oil. To a stirring solution of TBAF trihydrate (0.0569g, 0.181 mmol) and AcOH (0.0109g, 0.182 mmol) in 1 mL DMF in a plastic vial was added the β-keto-ester (0.145g, 0.130 mmol) as a solution in 1 mL DMF. After 3 h the reaction was poured onto 20 mL water and extracted 3 x 20 mL Et_2O. The combined organic layers were washed 1 x 30 mL water, 1 x 30 mL sat. aq. $NaHCO_3$, 1 x 30 mL brine then dried over Na_2SO_4. Evaporation *in vacuo* yielded a yellow oil that was purified by silica gel chromatography (6:1 hexanes / EtOAc) to give 0.105g (92%) of the desired alcohol **13** as a colorless oil. **R_f:** 0.39 (4:1 hexanes / EtOAc) $[\alpha]_D^{23}$ = –15.8° (c=1.1, CH_2Cl_2) **^{1}H-NMR** (500 MHz, $CDCl_3$, 1:1 keto/enol) δ 12.14 (s, 0.5H, enol-OH), 6.09 (d, 1H, *J*=14.6 Hz), 6.03 (dd, 1H, *J*=14.6, 6.3 Hz), 5.83 (t, 1H, *J*=6.9 Hz), 5.72 (m, 2H), 5.16 (bm, 1H), 5.01 (s, 0.5H, enol), 4.23 (t, 1H, *J*=5.4 Hz), 4.18 (q, 2H, *J*=7.3 Hz), 4.16-4.10 (m, 3H), 3.92 (q, 0.5H, *J*=5.8 Hz, keto), 3.84 (dt, 0.5H, *J*=6.8, 4.9 Hz, enol), 3.60 (d,

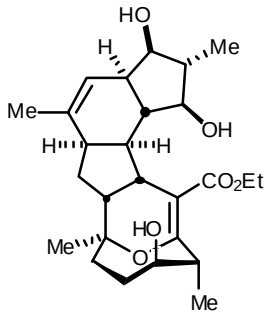
0.5H, *J*=15.6 Hz, keto), 3.53 (d, 0.5H, *J*=15.6 Hz, keto), 3.00 (t, 2H, *J*=6.8 Hz), 2.84 (m, 0.5H, enol), 2.36 (m, 0.5H, keto), 2.1-2.0 (m, 1.5H, keto + enol), 1.91 (m, 0.5H, enol), 1.64 (s, 3H), 1.6-1.5 (m, 2.5H, keto + enol), 1.41 (m, 0.5H, enol), 1.28 (m, 3H), 1.09 (d, 1.5H, *J*=6.8 Hz, keto), 1.06 (d, 1.5H, *J*=6.9 Hz, enol), 0.94 (d, 3H, *J*=6.8 Hz), 0.89 (s, 18H), 0.87 (s, 9H), 0.077 (s, 3H), 0.073 (s, 3H), 0.030 (s, 3H), 0.021 (s, 3H), -0.006 (s, 3H), -0.011 (s, 3H) **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 205.26, 180.66, 172.80, 167.48, 137.00, 136.54, 136.48, 136.35, 134.76, 134.35, 132.27, 132.03, 129.69, 129.67, 129.59, 129.25, 129.17, 127.67, 124.57, 124.42, 120.42, 120.18, 89.64, 73.78, 73.57, 73.25, 73.21, 72.74, 63.21, 61.16, 59.92, 51.68, 49.45, 47.36, 43.88, 35.69, 34.74, 33.58, 32.32, 30.76, 30.73, 26.53, 25.91, 25.89, 25.84, 18.98, 18.16, 18.08, 18.02, 16.33, 16.31, 14.27, 14.08, 12.20, 11.66, 9.84, -3.61, -3.73, -4.28, -4.41, -4.77 **FTIR** (film) ν 3445, 2954, 2939, 2886, 1747, 1715, 1651, 1472, 1361, 1255, 1225, 1094, 1030, 957, 835, 774, 672 **HRMS** (FAB) Calc'd for $C_{43}H_{81}BrO_7Si_3$ [M+Na]: 895.4371; found 895.4379



ethyl (5S, 17S, 6R, 7R, 18R)-10-bromo-6, 14, 18-trimethyl-19-oxo-5, 7, 17-tris (1, 1, 2, 2-tetramethyl-1-silapropoxy) cyclononadeca-3, 8, 10, 13-tetraene carboxylate (**14**) To a solution of alcohol **13** (0.020g, 0.0230 mmol) in 1 mL CH_2Cl_2 at 0 °C under argon was added a premixed solution of PPh_3 (0.0125g, 0.0477 mmol), imidazole (0.0110g, 0.162 mmol), and iodine (0.0159g, 0.0626 mmol) in 1 mL CH_2Cl_2. After 5 min the reaction was diluted to 10 mL with hexane (precipitate formed) and the orange heterogeneous mixture was passed through a short plug of silica. The silica plug was washed 3 x 2 mL 10:1 hexanes / EtOAc and the combined filtrates were concentrated *in vacuo* to give a quantitative yield of the allylic iodide as a colorless resin. The iodide was immediately redissolved in 5 mL THF and Cs_2CO_3 (0.0110g, 0.034 mmol) was added. After 5 h of vigorous stirring the reaction was quenched with 1 mL 1 N HCl (gas evolution!), diluted with 20 mL EtOAc and washed 2 x 20 mL water, 1 x 20 mL sat. aq. $NaHCO_3$, 1 x 20 mL brine then dried over Na_2SO_4. Solvent removal *in vacuo* revealed a colorless film that was purified by silica gel chromatography (50:1 hexane / EtOAc) to give 0.0151g (77%) of the desired macrocycle **14** as a 1:1 mixture of diastereomers. A portion of the more polar isomer eluted free of its epimer and was characterized. In practice, the mixture was used in the subsequent step without being separated. **R_f:** 0.65 (20:1 hexanes / EtOAc) $[\alpha]_D^{23}$ = –120.5° (c=0.66, CH_2Cl_2) **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 5.92 (m, 2H), 5.80 (t, 1H, *J*=7.4 Hz), 5.53 (dd, 1H, *J*=15.1, 6.8 Hz), 5.24 (t, 1H, *J*=7.4 Hz), 5.09 (dt, 1H, *J*=15.1, 7.3 Hz), 4.17 (q, 2H, *J*=6.8 Hz), 3.91 (dd, 1H, *J*=8.3, 6.3 Hz), 3.85 (m, 1H), 3.76 (m, 1H), 3.71 (t, 1H, *J*=7.2 Hz), 2.94 (t, 2H, *J*=7.8 Hz), 2. 92 (m, 1H), 2.50 (t, 2H, *J*=6.9 Hz), 2.09 (m, 1H), 1.94 (m, 1H), 1.67 (s, 3H), 1.64 (m, 2H), 1.25 (m, 3H), 1.03 (d, 3H, *J*=7.3 Hz), 1.01 (d, 3H, *J*=7.3 Hz), 0.89 (s, 9H), 0.88 (s, 9H), 0.87 (s, 9H), 0.04 (s, 3H), 0.016 (s, 3H), 0.014 (s, 3H), 0.003 (s, 6H), -0.007 (s, 3H) **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 205.62, 169.14, 136.45, 135.36, 132.85, 130.87, 130.12, 127.86, 123.80, 120.94, 75.92, 75.20, 72.73, 70.01, 61.35, 58.36, 50.69, 47.31, 36.04, 33.58, 29.99, 25.91, 25.87, 25.84, 18.23, 18.20, 18.05, 15.92, 14.13, 13.57, 11.95, -3.83, -4.01, -4.27, -4.72, -5.01 **FTIR** (film) ν 2929, 2856, 1738, 1715, 1471, 1364, 1255, 1112, 1057, 835, 774 **HRMS** (FAB) Calc'd for $C_{43}H_{79}BrO_6Si_3$ [M+Na]: 877.4266; found 877.4273

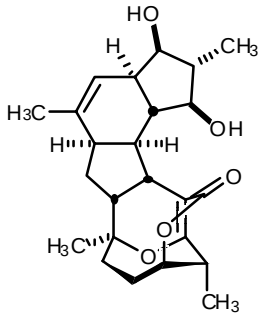


ethyl (1S, 10S, 17S, 8R, 9R, 16R)-5-bromo-1, 9, 16-trimethyl-20-oxa-8, 10, 17-tris (1, 1, 2, 2-tetramethyl-1-silapropoxy) pentacyclo[13.4.1.0<2,13>.0<4,12>.0<7,11>]icosa-5,14-diene-14-carboxylate (**16**) To a suspension of $Ph_2Se_2O_3$ (0.0492g, 0.137 mmol) and SO_3 pyridine complex (0.0229g, 0.144 mmol) in 1 mL THF at RT under argon was added TEA (0.050 mL, 0.36 mmol) and the mixture was stirred vigorously for 15 min to form an "oxidant solution." To a solution of macrocycle **14** (0.0580g, 0.0677 mmol) in 1 mL THF at RT under argon was added TEA (0.050 mL, 0.36 mmol) followed by the oxidant solution and the reaction was stirred for 2 h. Hexane (10 mL) was then added (a precipitate formed). The resulting opaque mixture was filtered through a short plug of silica and the bright yellow filtrate was heated to 50 °C for 6 h. Concentration *in vacuo* gave a yellow oil that was purified by silica gel chromatography (4:1 hexane / benzene) to give 0.036g (63%) of the desired Diels-Alder adduct **16** as a colorless film. **R_f:** 0.69 (20:1 hexanes/ EtOAc) $[\alpha]_D^{\leftrightarrow}$ = –44.4° (c=0.15, CH_2Cl_2) **^{1}H-NMR** (500 MHz, $CDCl_3$) δ 5.89 (s, 1H), 4.23 (m, 1H), 4.02 (m, 1H), 3.70 (m, 1H), 3.67 (q, 1H, *J*=6.8 Hz), 3.63 (d, 1H, *J*=3.4 Hz), 3.59 (bs, 1H), 2.78 (q, 1H, *J*=5.9 Hz), 2.46 (m, 1H), 2.38 (m, 1H), 2.22 (td, 1H, *J*=12.2, 7.8 Hz), 2.1-2.0 (m, 3H), 1.85 (m, 1H), 1.73 (m, 2H), 1.54 (s, 3H), 1.46 (m, 1H), 1.28 (t, 3H, *J*=7.3 Hz), 1.24 (s, 3H), 1.07 (d, 3H, *J*=7.3 Hz), 1.01 (d, 3H, *J*=7.8 Hz), 0.88 (s, 9H), 0.86 (s, 9H), 0.84 (s, 9H), 0.14 (s, 3H), 0.10 (s, 3H), 0.04 (s, 6H), -0.005 (s, 6H) **^{13}C-NMR** (100 MHz, $CDCl_3$) δ 168.21, 165.79, 128.40, 127.72, 117.95, 82.55, 79.47, 78.60, 73.78, 59.49, 53.06, 50.71, 48.65, 47.86, 46.21, 46.08, 42.73, 42.65, 34.06, 27.92, 27.82, 25.98, 25.88, 25.80, 25.69, 23.99, 19.01, 18.11, 17.93, 17.69, 14.55, 13.17, -3.44, -4.35, -4.43, -4.86, -4.95, -5.18 **FTIR** (film) ν 2928, 2854, 1698, 1627, 1465, 1359, 1258, 1055, 836, 767 **HRMS** (FAB) Calc'd for $C_{43}H_{77}BrO_6Si_3$ [M+H]: 853.4289; found 853.4296



ethyl (1S, 9S, 10S, 17S, 8R, 16R)-8, 10, 17-trihydroxy-1, 5, 9, 16-tetramethyl-20-oxapentacyclo [13.4.1.0 <2,13>.0 <4,12>.0 <7,11>] icosa-5, 14-diene-14-carboxylate (**20**) Diels-Alder adduct **16** (0.036g, 0.042 mmol) was dissolved in HF-CH_3CN (95:5:1 CH_3CN/48% aq. HF/water, 10 mL) in a plastic vial at RT under argon. After 4 h the reaction was poured onto 50 mL sat. aq. $NaHCO_3$ (gas evolution!) and extracted 3 x 20 mL EtOAc. The combined organic layers were washed 1 x 20 mL brine and dried over Na_2SO_4. Evaporation *in vacuo* yielded a colorless oil that was purified by silica gel chromatography (100% EtOAc) to give the desire product as an oil. Azeotropic removal of residual EtOAc with hexane (3 x 10 mL) gave 0.0186g (89%) of a colorless amorphous solid. **R_f:** 0.29 (100% EtOAc) $[\alpha]_D^{\leftrightarrow}$ = –0.66° (c=0.75, CH_2Cl_2) To a portion of the desilylated product (0.010g, 0.019 mmol) in 1.0 mL DMF was added $Pd(dppf)Cl_2$ – CH_2Cl_2 (0.0021g, 0.0026 mmol) followed by a premixed solution of Cs_2CO_3 (0.573g, 1.75 mmol) and trimethylboroxine (0.048g, 0.38 mmol) in 0.75 mL water. The reaction was heated to 80 °C under argon, stirred vigorously for 2 h, then was then cooled to RT, poured onto 10 mL water, and extracted 3 x 5 mL Et_2O. The combined ethereal extracts were dried over Na_2SO_4. Evaporation *in vacuo* gave a yellow

film that was purified by silica gel chromatography (100% EtOAc) to give 0.0064g (71%) of the desired methyl adduct **20**. A small amount (~5%) of the saponified Suzuki product (FR182877 seco-acid) could be recovered from the combined aqueous layers after acidification (1 N HCl) and extraction with CH_2Cl_2. **R_f:** 0.34 (100% EtOAc) $[\alpha]_D^{23}$ = -18.3 (c=0.13, CH_2Cl_2) **^{1}H-NMR** (500 MHz, C_6D_6) δ 5.31 (s, 1H), 4.48 (bd, 1H, *J*=4.4 Hz), 4.03 (m, 1H), 3.91-3.83 (m, 3H), 3.52 (s, 2H), 3.48 (d, 1H, *J*=4.8 Hz), 2.55 (m, 1H), 2.21 (m, 1H), 2.15 (dd, 1H, *J*=13.2, 6.9 Hz), 2.06 (ddd, 1H, *J*=12.2, 12.2, 9.3 Hz), 1.91 (m, 3H), 1.78 (m, 1H), 1.61 (s, 3H), 1.55 (dd, 1H, *J*=13.7, 13.7), 1.42 (m, 2H), 1.12 (d, 3H, *J*= 7.3 Hz), 1.01 (m, 6H), 0.95 (t, 3H, *J*=7.3 Hz) **^{13}C-NMR** (100 MHz, C_6D_6) δ 169.94, 166.64, 139.45, 121.55, 120.71, 84.02, 81.39, 77.33, 72.99, 70.10, 61.03, 53.48, 52.49, 47.11, 46.99, 46.80, 46.09, 44.52, 40.64, 34.55, 30.32, 27.22, 22.66, 18.75, 14.18, 13.69 **FTIR** (film) ν 3394, 2924, 1669, 1558, 1457, 1375, 1328, 1284, 1162, 1085, 1046 **HRMS**(ES) Calc'd for $C_{26}H_{38}O_6$ [M+H]: 447.2746; found 447.2742



FR182877 (**1**) To a solution of ethyl ester **20** (0.0030g, 0.0067 mmol) in 1 mL THF at RT was added TMSOK (0.0048g, 0.037 mmol) and the resulting solution was stirred for 12 h. The reaction was then diluted to 5 mL with 0.1 M $NaHCO_3$ and extracted 2 x 2 mL Et_2O and the organic layers were discarded. The aqueous layer was then acidified by the addition of 5 mL 1 N HCl and extracted 3 x 3 mL CH_2Cl_2. The combined organic layers were then dried over Na_2SO_4. Evaporation *in vacuo* yielded a quantitative return of the FR182877 seco-acid as a colorless amorphous solid. To a suspension of the FR182877 seco-acid (0.0010g, 0.0025 mmol) in 2 mL CH_2Cl_2 was added powdered $NaHCO_3$ (0.0491g) and the mixture was degassed by 3 cycles of "freeze-pump-thaw." To the reaction was added Mukaiyama's reagent (0.010g, 0.039 mmol) and the yellow hetereogeneous mixture was vigorously stirred for 24 h then transferred directly to a silica gel column and purified by chromatography (100:1 EtOAc/MeOH) to give 0.00061g (62%) of FR182877 as a white solid. **R_f:** 0.26 (100:1 EtOAc/MeOH) $[\alpha]_D^{23}$ = -5° (c=0.15, MeOH) **^{1}H-NMR** (500 MHz, D_3COD) δ 5.41 (s, 1H), 4.43 (s, 1H), 3.61 d, 1H, *J*=3.9 Hz), 3.46 (m, 2H), 2.77 (m, 1H), 2.65 (t, 1H, *J*=8.3 Hz), 2.44 (m, 1H), 2.28 (dd, 1H, *J*=13.2, 8.3 Hz), 2.04 (dd, 1H, *J*=11.7, 6.9 Hz), 1.85 (bd, 1H, *J*=9.8 Hz), 1.83-1.73 (m, 4H), 1.71 (s, 3H), 1.66 (d, 1H, *J*=3.9 Hz), 1.62-1.55 (m, 2H), 1.40 (s, 3H), 1.12 (d, 3H, *J*=7.4 Hz), 1.10 (d, 3H, *J*=6.9 Hz) **^{13}C-NMR** (100 MHz, D_3COD) δ 172.9, 168.7, 140.5, 121.2, 115.9, 88.6, 84.5, 79.3, 78.4, 54.6, 53.1, 52.4, 47.4, 46.9, 46.1, 43.4, 42.5, 36.2, 33.7, 25.2, 24.1, 22.9, 18.6, 9.4 **FTIR** (film) ν 3420, 2925, 1704, 1624, 1457, 1366, 1269, 1212, 1018 **HRMS**(FAB) Calc'd for $C_{24}H_{32}O_5$ [M + H]: 401.2328; found 401.2329

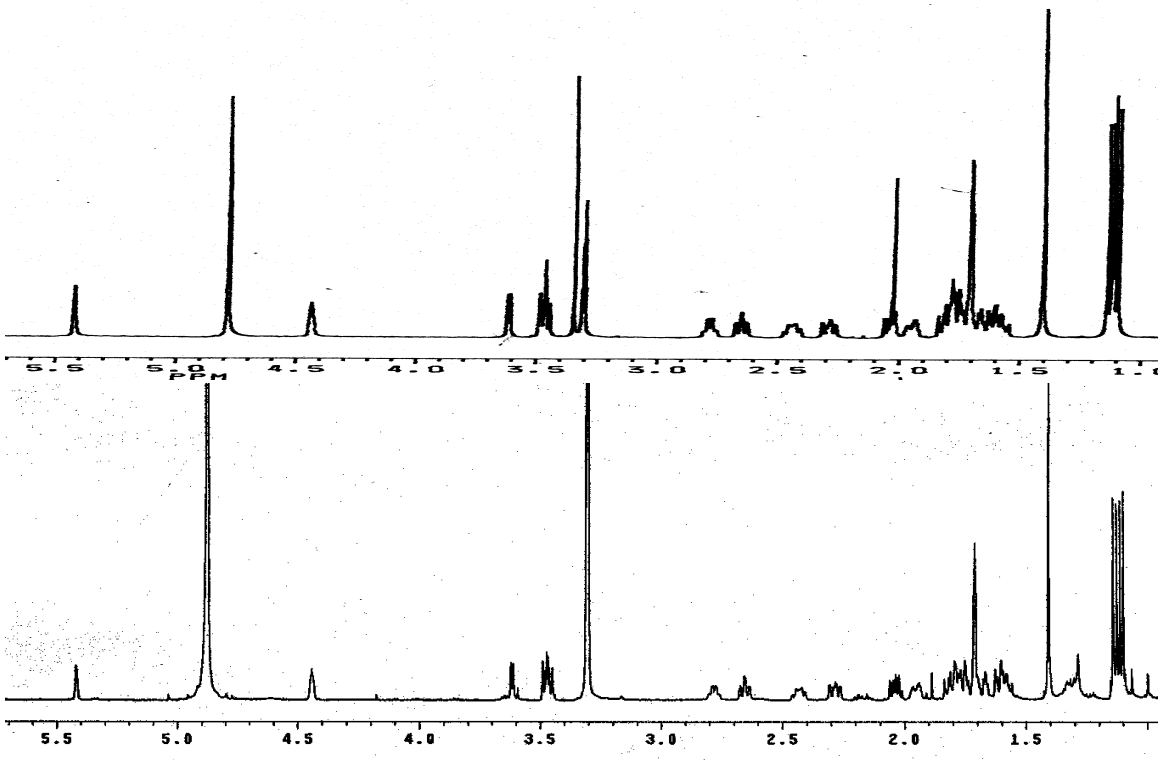


Figure 1. ^{1}H-NMR comparison of natural FR182877 (top, 400 MHz; D_3COD) and synthetic FR182877 (bottom, 500 MHz; D_3COD). Additional singlets at 3.3 and 2.0 ppm in the spectrum of natural **1** are not recorded as part of the natural product structure by the authors of the original report.[2]

Table 1. Tabular comparison of ^{13}C-NMR data for natural and synthetic FR182877.

Carbon Number	δ Natural (125 MHz; D_3COD)	δ Synth. (100 MHz; D_3COD)
1	172.9	172.9
2	115.9	115.9
3	43.4	43.4
4	53.2	53.1
5	46.2	46.1
6	84.6	84.5
7	54.6	54.6
7-Me	18.6	18.6
8	78.4	79.3
9	46.9	47.4
10	121.2	121.2
11	140.5	140.5
11-Me	22.7	22.9
12	46.5	46.9
13	33.3	33.7
14	52.5	52.4
15	87.7	88.6
15-Me	23.9	24.1
17	167.7	168.7
18	41.5	42.5
18-Me	9.3	9.4
19	77.8	78.4
20	24.4	25.2
21	36.0	36.2

References and Notes

[1] Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518.

[2] Yoshimura, S.; Sato, B.; Kinoshita, T.; Takase, S.; Terano, H. *J. Antibiotics* **2000**, *53*, 615.