Supporting Information
Total Synthesis of (-)-Apicularen A
Qibin Su and James S. Panek

Department of Chemistry and Center for Chemical Methodology and Library Design,
Metcalf Center for Science and Engineering, 590 Commonwealth Avenue, Boston University, Boston,
Massachusetts 02215

General Information: ^1H - and ^{13}C -NMR were recorded in CDCl_3 at 400 MHz and 75.0 MHz respectively unless specified otherwise. Chemical shifts are reported in parts per million using the solvent resonance internal standard chloroform (7.24 and 77.0 ppm, unless specified otherwise). Data are reported as follows: chemical shift, integration, multiplicity (app = apparent, par obsc = partially obscured, ovrlp = overlapping, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad, abq = ab quartet) and coupling constant. Ratios of diastereomers (dr) were determined by ^1H -NMR (400 MHz) operating at a signal/noise ratio of >200:1. Infrared Resonance (IR) spectra were recorded on a Nicolet Impact 400 FT-IR spectrometer. Optical rotations were recorded on an AUTOPOL III digital polarimeter at 589 nm, and are reported as $[\alpha]_D$ (concentration in grams/100 mL solvent). Tetrahydrofuran (THF), ethyl ether (Et_2O), methylene chloride (CH_2Cl_2), benzene and toluene were dried using a solvent drying system (Al_2O_3). All other reagents were used as supplied from commercial sources. All reactions were carried out in oven-dried glassware under argon or N_2 atmosphere unless otherwise noted. Analytical thin layer chromatography was performed using Whatman Reagent silica gel 60-A plates. Flash chromatography was performed using E. Merck silica gel (230-400 mesh).

Silylepoxide methyl ether (11). A solution of hydroxy epoxide **10**^{SI1} (10 g, 48 mmol) in Et_2O (20 mL) was treated with NaOH aqueous solution (22.4 mL 50%) and Me_2SO_4 (10 mL, 105 mmol). The mixture was stirred for 8 h at room temperature before water (50 mL) was added. The mixture was extracted with Et_2O (3 x 100 mL). The combined organic layers were dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 20% EtOAc in hexane) afforded the methyl ether **11** as pale yellow oil (9.71 g, 91%). ^1H NMR (400 MHz, CDCl_3) δ 7.52 (2H, m), 7.36 (3H, m), 3.71 (1H, dd, $J = 2.6$ Hz, 11.5 Hz); 3.37 (3H, s), 3.28 (1H, dd, $J = 5.9$ Hz, 11.5 Hz), 2.99 (1H, m), 2.25 (1H, d, $J = 3.7$ Hz), 0.34 (3H, s), 0.30 (3H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 135.9, 134.1, 129.8, 128.1, 74.7, 59.3, 54.7, 47.4, -4.9, -5.1; 3069, 2958, 2821, 1452, 1427, 1250, 1115; $[\alpha]_D^{23} = -11.2^\circ$ ($c = 1.7$, CH_2Cl_2); CIHRMS $[\text{M}]^+$ calculated for $\text{C}_{12}\text{H}_{18}\text{O}_2\text{Si}$ 222.1076, found: 222.1061.

^{SI1} Chauret, D.C.; Chong, J. M.; Ye, Q.; *Tetrahedron: Asym.* **1999**, 10, 3601.

Allylsilane. To a suspension of CuI (1.06 g, 5.5 mmol) in Et₂O (87 mL) at -30 °C was slowly added vinyl magnesium bromide (1M in THF, 111.4 mL, 111.4 mmol). The resulting dark red solution was stirred for 10 min. To this was added a solution of epoxide **11** (11.7 g, 52.7 mmol) in Et₂O (80 mL). The reaction mixture was stirred for 45 min. before a saturated aqueous solution of NH₄Cl (300 mL) was added. The mixture was extracted with Et₂O (3 x 200 mL). The combined organic layers were dried over MgSO₄. Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 25% EtOAc in hexane) afforded the allyl silane as a pale yellow oil (12.5 g, 95%). ¹H NMR (400 MHz, CDCl₃) δ 7.53 (2H, m), 7.31 (3H, m), 5.54 (1H, m), 4.89 (1H, dd, *J* = 10 Hz, 1.2 Hz), 4.83 (1H, d, *J* = 17.2 Hz), 3.81 (1H, m), 3.98 (1H, dd, *J* = 9.6 Hz, 2.4 Hz), 3.28 (3H, s), 3.14 (1H, dd, *J* = 8 Hz, *J* = 9.2 Hz), 2.28 (1H, d, *J* = 4 Hz), 2.00 (1H, dd, *J* = 8.8 Hz, 10 Hz), 0.36 (3H, s), 0.32 (3H, s); ¹³C NMR (75 MHz, CDCl₃) δ 138.1, 136.1, 134.4, 129.0, 127.7, 114.6, 76.9, 71.1, 58.9, 39.6, -2.6, -2.9; IR (neat) ν_{max}: 3460, 3070, 2894, 1627, 1427, 1247, 1113; [α]_D²³ = -1.32° (c = 4.0, CH₂Cl₂); CIHRMS [M+1]⁺ calculated for C₁₄H₂₂O₂Si 251.1468, found 251.1484.

Allylsilane (7a). To a solution of allyl silane **11** (12.5 g, 50 mmol) in THF (140 mL) was added pyridine (13.5 mL, 167 mmol) at 0 °C and followed by TMSCl (14 mL, 110 mL). The reaction mixture was stirred for 12h and slowly warm up to room temperature before water (100 mL) was added. The mixture was extracted with Et₂O (3 x 100 mL). The combined organic layers were dried over MgSO₄. Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 5 % EtOAc in hexane) afforded the silyl ether **7a** as a pale yellow oil (16 g, 100%). ¹H NMR (400 MHz, CDCl₃) δ 7.50 (2H, m), 7.30 (3H, m), 5.67 (1H, m), 4.87 (1H, dd, *J* = 1.6 Hz, 10.4 Hz), 4.80 (1H, dd, *J* = 1.6 Hz, 16 Hz), 3.89 (1H, m), 3.24 (1H, dd, *J* = 3.6 Hz, 10 Hz), 3.18 (3H, s), 3.10 (1H, dd, *J* = 6.4 Hz, 10 Hz), 2.06 (1H, dd, *J* = 7.2 Hz, 8.4 Hz), 0.30 (3H, s), 0.29 (3H, s), 0.02 (9H, s); ¹³C NMR (75 MHz, CDCl₃) δ 138.9, 137.3, 134.4, 128.9, 127.6, 114.2, 77.0, 73.9, 58.6, 40.6, 0.7, -2.1, -2.7; IR (neat) ν_{max}: 2956, 2893, 1626, 1427, 1249, 1113; [α]_D²³ = -7.53° (c = 4.8, CH₂Cl₂); EIHRS [M]⁺ calculated for C₁₇H₃₀O₂Si₂ 322.5899, found 322.5890.

General experimental procedure for Table1:

To a solution of an aldehyde (1 mmol) and the allyl silane (1 mmol) in CH₂Cl₂ (5 mL) at -50 °C was slowly added TMSOTf (0.182 mL, 1 mmol). The reaction mixture was stirred for 2.5 h at -50 °C before a saturated solution of NaHCO₃ (10 mL) was added. The mixture was extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were washed with brine and dried over MgSO₄. Removal of solvent under reduced pressure and

purification by flash chromatography afforded the pyran **6** as pale yellow oil in the yield and diastereo ratio (dr) as indicated in Table 1.

6c (entry 2, Table 1). *Cis* dihydropyran: ^1H NMR (300 MHz, CDCl_3) δ 7.35-7.19 (5H, m), 5.86 (1H, m), 5.57 (1H, dd, $J = 0.9$ Hz, 7.8 Hz), 4.35 (1H, m), 4.11 (2H, d, $J = 3.9$ Hz), 3.87 (1H, m), 3.01 (1H, dd, $J = 4.8$ Hz, 10.2 Hz), 2.69 (1H, dd, $J = 4.8$ Hz, 10.2 Hz), 2.07 (3H, s), 2.01 (1H, m), 1.87 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 171.1, 138.3, 129.4, 128.2, 127.0, 126.2, 125.7, 74.6, 73.1, 66.3, 42.1, 30.4, 20.8; IR (neat) ν_{max} 3029, 1740, 1469, 1454, 1368, 1232; $[\alpha]_D^{23} = 33.6^\circ$ ($c = 0.7$, CH_2Cl_2), CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{15}\text{H}_{18}\text{O}_3$ 247.1335, found 247.1330. *Trans* dihydropyran: ^1H NMR (300 MHz, CDCl_3) δ 7.39-7.14 (5H, m), 5.94 (1H, m), 5.63 (1H, dd, $J = 2.1$ Hz, 10.5 Hz), 4.42 (1H, m), 4.28 (1H, dd, $J = 8.7$ Hz, 11.7 Hz), 3.96 (1H, m), 3.92 (1H, dd, $J = 3.3$ Hz, 11.7 Hz), 2.93 (1H, dd, $J = 4.5$ Hz, 10.5 Hz), 2.70 (1H, dd, $J = 6.6$ Hz, 10.5 Hz), 2.01 (3H, s), 1.98 (2H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 171.1, 138.4, 129.3, 128.3, 127.2, 126.2, 124.7, 71.1, 69.1, 64.1, 41.6, 29.8, 20.7; $[\alpha]_D^{23} = 45^\circ$ ($c = 0.22$, CH_2Cl_2), IR (neat) ν_{max} 2952, 2249, 1759, 1454, 1366, 1120; CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{15}\text{H}_{18}\text{O}_3$ 247.1335, found 247.1333.

rac-**6d** (entry 3, Table 1). *Cis* dihydropyran: ^1H NMR (300 MHz, CDCl_3) δ 7.29-7.17 (5H, m), 5.89 (1H, m), 5.79 (1H, dd, $J = 1.2$ Hz, 7.8 Hz), 4.82 (1H, m), 3.82 (1H, m), 3.77 (3H, s), 3.12 (1H, dd, $J = 7.8$ Hz, 10.5 Hz), 2.77 (1H, dd, $J = 5.4$ Hz, 10.5 Hz), 2.12 (1H, m), 1.90 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 170.6, 140.0, 134.3, 129.5, 128.4, 127.2, 126.4, 124.3, 75.1, 74.9, 52.3, 42.0, 29.8; IR (neat) ν_{max} 2952, 2249, 1759, 1495, 1120; CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{14}\text{H}_{16}\text{O}_3$ 233.1178, found 233.1175. *Trans* dihydropyran: ^1H NMR (300 MHz, CDCl_3) δ 7.30-7.16 (5H, m), 5.93 (1H, m), 5.86 (1H, m), 4.78 (1H, m), 4.19 (1H, m), 3.70 (3H, s), 3.04 (1H, dd, $J = 4.8$ Hz, 10.5 Hz), 2.77 (1H, dd, $J = 5.1$ Hz, 10.2 Hz), 2.01 (1, m), 1.90 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 171.7, 137.9, 129.5, 128.3, 126.9, 126.3, 123.4, 72.8, 71.2, 51.8, 41.9, 29.4; IR (neat) ν_{max} 3029, 1740, 1469, 1454, 1368, 1232; $[\alpha]_D^{23} = 45.3^\circ$ ($c = 0.22$, CH_2Cl_2), CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{14}\text{H}_{16}\text{O}_3$ 233.1178, found 233.1174.

rac-**6e** (entry 4, Table 1). *Cis* dihydropyran: ^1H NMR (300 MHz, CDCl_3) δ 5.95 (1H, m), 5.80 (1H, m), 5.46 (1H, t, $J = 5.1$ Hz), 4.86 (1H, m), 3.96 (1H, dd, $J = 2.4$ Hz, 8.1 Hz), 3.74 (3H, s), 2.29 (1H, m), 2.07-1.92 (3H, m), 1.67 (3H, s), .94 (3H, t, $J = 5.7$ Hz); ^{13}C NMR (75 MHz, CDCl_3) δ 170.7, 133.7, 128.9, 127.6, 124.2, 78.5, 75.2, 52.2, 28.8, 20.7, 13.7, 12.0; IR (neat) ν_{max} 2962, 1763, 1739, 1437, 1180, 1119; CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{12}\text{H}_{18}\text{O}_3$ 210.1256, found 210.1251.

rac-**6f** (entry 5, Table 1). *Cis* dihydropyran: ^1H NMR (300 MHz, CDCl_3) δ 7.41 (2H, d, $J = 5.7$ Hz), 7.34 (2H, m), 7.26 (1H, m), 6.05 (1H, m), 5.91 (1H, m), 5.01 (1H, m), 4.66 (1H, dd, $J = 2.4$ Hz, 8.1 Hz), 3.78 (3H, s), 2.41 (1H, m), 2.26 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 170.5, 141.6, 128.5, 127.8, 127.4, 126.0, 124.4, 75.6, 75.5, 52.3, 32.3; IR (neat) ν_{max} 2962, 1763, 1739, 1437, 1180, 1119; CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{13}\text{H}_{14}\text{O}_3$ 218.0943, found 218.0947.

6g (entry 2, Table 2) To a solution of aldehyde (1 mmol) and allylsilane (322 mg, 1 mmol) in CH₂Cl₂ (5 mL) at –50 °C was slowly added TMSOTf (0.182 mL, 1 mmol). The reaction mixture was stirred for 2.5 h at –50 °C before a saturated solution of NaHCO₃ (10 mL) was added. The mixture was extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were washed with brine and dried over MgSO₄. Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 10% EtOAc in hexane) afforded the pyran **6e** as pale yellow oil (0.16 g, 91%). ¹H NMR (400 MHz, CDCl₃) δ= 5.91 (1H, m), 5.66 (1H, m), 4.35 (1H, m), 3.51 (1H, dd, *J* = 7.2 Hz, 10.4 Hz), 3.38 (3H, s), 3.36 (2H, m), 1.97 (2H, m), 1.70 (1H, m), 0.96 (3H, d, *J* = 6.8 Hz), 0.88 (3H, d, *J* = 7.2 Hz); ¹³C DCI δ 126.4, 126.1, 73.9, 73.5, 72.4, 59.0, 32.1, 27.3, 18.6, 18.0; IR (neat) ν_{max} 2958, 2892, 1470, 1189, 1128, 1076; [α]_D²³ = 143.8° (c = 0.6, CH₂Cl₂), CIHRMS [M+1]⁺ calculated for C₁₀H₁₈O₂ 171.1381, found 171.1413.

6h (entry 3, Table 2). To a solution of aldehyde (112 mg, 1 mmol) and allylsilane (322 mg, 1 mmol) in CH₂Cl₂ (5 mL) at –50 °C was slowly added TMSOTf (0.182 mL, 1 mmol). The reaction mixture was stirred for 2.5 h at –50 °C before a saturated solution of NaHCO₃ (10 mL) was added. The mixture was extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were washed with brine and dried over MgSO₄. Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 35% EtOAc in hexane) afforded the pyran **6h** as pale yellow oil (0.2 g, 95%). ¹H NMR (400 MHz, CDCl₃) δ 5.91 (1H, m), 5.65 (1H, m), 4.34 (1H, m), 3.51 (1H, dd, *J* = 7.2 Hz, 10.4 Hz), 3.38 (3H, s), 3.25 (2H, m), 1.98 (2H, m), 1.65 (2H, m), 1.40 (1H, m), 1.20 (5H, m), 0.99 (3H, m); ¹³C NMR (75 MHz, CDCl₃) δ 126.4, 126.1, 73.9, 72.6, 72.3, 59.0, 41.8, 29.1, 28.3, 27.4, 26.4, 25.9, 25.8; IR (neat) ν_{max} 2923, 2851, 1449, 1187, 1128, 1803; [α]_D²³ = 123.7° (c = 2.75, CH₂Cl₂), CIHRMS [M+1]⁺ calculated for C₁₃H₂₂O₂ 211.1694, found 211.1702.

6b (entry 4, Table 2). To a solution of aldehyde (120 mg, 1 mmol) and allyl silane (322 mg, 1 mmol) in CH₂Cl₂ (5 mL) at –50 °C was slowly added TMSOTf (0.182 mL, 1 mmol). The reaction mixture was stirred for 2.5 h at –50 °C before a saturated solution of NaHCO₃ (10 mL) was added. The mixture was extracted with CH₂Cl₂ (3 x 10 mL). The combined organic layers were washed with brine and dried over MgSO₄. Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 10% EtOAc in hexane) afforded the pyran **6b** as pale yellow oil (0.2 g, 90%). ¹H NMR (400 MHz, CDCl₃) δ 7.23 (5H, m), 5.88 (1H, m), 5.66 (1H, m), 4.39 (1H, m), 4.01 (1H, m), 3.48 (1H, dd, *J* = 7.2 Hz, 10.4 Hz), 3.44 (1H, dd, *J* = 7.2 Hz, 12.4 Hz), 3.32 (3H, s), 2.98 (1H, dd, *J* = 6.8 Hz, 14.4 Hz), 2.74 (1H, dd, 6.8 Hz, 10.4 Hz), 1.97 (2H, m); ¹³C DCI δ 138.7, 129.3, 128.3, 126.1, 126.0, 125.9, 74.0, 72.1, 69.8, 59.0, 41.3, 29.4; IR (neat) ν_{max} 3029, 2891, 1495, 1453, 1126; [α]_D²³ = 87.8° (c = 1.0, CH₂Cl₂), CIHRMS [M+1]⁺ calculated for C₁₄H₁₈O₂ 219.1381, found 219.1413. Enantiomeric excess of the resulting dihydropyran was determined using HPLC analysis with chiral column (CHIRALCEL OD), hexane : *i*PrOH = 95 : 5, flow rate 1 mL/min. Racemic dihydropyran: retention time: 4.73 min and 13.71 min. Chiral pyran: retention time 13.71 min, ee = 96%.

Determine the relative and the absolute stereochemistry of dihydropyran **6b**:

To a solution of dihydropyran **6b** (100 mg, 0.46 mmol) in CCl_4 (4.12 mL) at 0 °C was added *m*-CPBA (1.18 g, 60%, 4.8 mmol). The reaction was stirred for 48 h at 0 °C before a saturated solution of NaHCO_3 (20 mL) and NaS_2O_3 (20 mL) were added. The mixture was extracted with EtOAc (20 mL). The organic layer was dried over MgSO_4 . Removal of solvent under reduce pressure and purification by flash chromatography (silica gel, 50% EtOAc in hexane) afforded the epoxide as a pale yellow oil (91 mg, 90%). ^1H NMR (400 MHz, CDCl_3) δ 7.27-7.15 (5H, m), 4.30 (1H, m), 3.84 (1H, m), 3.57 (1H, m), 3.47 (1H, dd, $J = 7.6$ Hz, 6.4 Hz), 3.36 (1H, m), 3.29 (3H, s), 3.26 (1H, m), 2.81 (1H, dd, $J = 7.2$ Hz, 14.4 Hz), 2.60 (1H, dd, $J = 6.4$ Hz, 14.4 Hz), 1.93 (1H, m), 1.69 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) 138.1, 129.3, 128.3, 126.3, 70.4, 70.3, 66.8, 59.2, 51.5, 50.7, 41.6, 30.3; IR (neat) ν_{max} : 2952, 1496, 1454, 1429, 1266, 1118, 1073; $[\alpha]_D^{23} = +15.9^\circ$ ($c = 1.0$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{14}\text{H}_{18}\text{O}_3$ 235.1330, found 235.1343.

To a solution of epoxide (90 mg, 8.5 mmol) in CH_2Cl_2 (70 mL) at -78 °C was added DIBAL-H (0.58 mL, 1.0 M in CH_2Cl_2). The reaction was stirred for 40 min at -78 °C before a solution of sodium, potassium tartrate (200 mL) was added. The mixture was extracted with EtOAc (20 mL). The organic layer was dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 50% EtOAc in hexane) afforded the alcohol as a colorless oil (63 mg, 60%). ^1H NMR (400 MHz, CDCl_3) δ 7.28-7.23 (5H, m), 4.28 (1H, m), 4.09 (1H, m), 3.96 (1H, m), 3.46 (2H, m), 3.36 (3H, s), 2.95 (1H, dd, $J = 6.4$ Hz, 9.6 Hz), 2.75 (1H, dd, $J = 8$ Hz, 14.4 Hz), 1.98 (1H, m), 1.75 (1H, m), 1.53 (1H, m), 1.41 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) 138.6, 129.2, 128.4, 126.3, 76.1, 72.7, 68.9, 63.5, 59.2, 39.1, 36.6, 36.1; IR (neat) ν_{max} : 3422, 2926, 1652, 1087; $[\alpha]_D^{23} = -52.7^\circ$ ($c = 0.6$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{14}\text{H}_{20}\text{O}_3$ 237.1486, found 237.1474.

The relative stereochemistry of resulting pyran was determined by NOE measurement. A strong NOE between H1, H6 and H4 and NOE between H1 and H7 were observed.

The absolute chemistry was determined by Mosher ester analysis.^{SI2} The secondary alcohol on pyran was individually esterified with (*R*)-(+)- α -methoxy- α -(trifluoromethyl)-phenylacetic acid and (*S*)-(-)- α -methoxy- α -(trifluoromethyl)-phenylacetic acid to afford two esters. Comparison of ^1H NMR of the individual Mosher's esters established the absolute configuration at carbinol center to be *S*, which in turn to determine the absolute configuration of **6b** to be (2*S*, 6*R*).

^{SI2} (a) Dale, J. A.; Mosher, H S. *J. Am. Chem. Soc.* **1973**, 95, 512; (b) Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, 113, 4092.

^1H NMR (400 MHz, CDCl_3)

^1H NMR (400 MHz, CDCl_3)

^1H NMR (400 MHz, CDCl_3) NOE

^1H NMR (400 MHz, CDCl_3) NOE

Aryl methyl ester. To a solution of aryl carboxylic acid^{SI3} (8.5 g, 47.7 mmol) in CH₃CN (113 mL) at 0 °C was added DBU (12.4 mL, 83 mmol) and followed by MeI (5.6 mL, 89 mmol). The resulting solution was covered by aluminum foil and stirred for 24 h at room temperature before water (200 mL) was added. The mixture was extracted with EtOAc (3 x 200 mL). The combined organic layers were dried over MgSO₄. Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 30% EtOAc in hexane) afforded the methyl ester as a pale yellow oil (7.8 g, 85%). ¹H NMR (400 MHz, CDCl₃) δ 11.08 (1H, s), 7.31 (1H, dd, *J* = 8 Hz, 7.6 Hz), 6.86 (1H, d, *J* = 8 Hz), 6.73 (1H, d, 7.6 Hz), 5.94 (1H, m), 5.00 (1H, dd, *J* = 9.6 Hz, 1.2 Hz), 4.95 (1H, *J* = 6.4 Hz, 1.2 Hz), 3.93 (1H, s), 3.66 (2H, d, *J* = 6.4 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 171.9, 162.2, 142.9, 137.7, 134.6, 122.6, 116.4, 115.6, 52.4, 40.6; IR (neat) ν_{max}: 3077, 2954, 1665, 1449, 1315, 1249, 1221, 1118; CIHRMS [M]⁺ calculated for C₁₁H₁₂O₃ 192.0786, found 192.0766.

^{SI3} Fürsterner, A.; Konetski, I. *Tetrahedron* **1996**, 52, 15071.

To a solution of phenol (9.3 g, 48.7 mmol) in CH_2Cl_2 (100 mL) at 0 °C was added pyridine (11.8 mL, 146 mmol) and followed by Ac_2O (9.18 mL, 97.3 mmol). The resulted solution was stirred at room temperature for 16 h before water (200 mL) was added. The mixture was extracted with ethyl ether (3 x 200 mL). The combined organic layers were dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 5% EtOAc in hexane) afforded the acetate as a pale yellow oil (10.2 g, 90%). ^1H NMR (400 MHz, CDCl_3) δ 7.35 (1H, t, J = 8 Hz), 7.11 (1H, d, J = 8 Hz), 6.98 (1H, J = 8 Hz), 5.88 (1H, m), 5.04 (1H, m), 5.00 (1H, dd, J = 8.4 Hz, 2 Hz), 3.83 (3H, s), 3.46 (2H, d, J = 6.8 Hz), 2.24 (3H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 169.2, 166.9, 148.5, 140.2, 136.3, 131.0, 127.6, 121.1, 116.7, 52.3, 38.1, 20.9; IR (neat) ν_{max} : 3079, 2952, 1772, 1731, 1459, 1432, 1280, 1199, 1112, 1020; CIHRMS $[\text{M}]^+$ calculated for $\text{C}_{13}\text{H}_{14}\text{O}_4$ 234.0892, found 234.0872.

Salicylate aldehyde (8a). To a solution of olefine (9.4 g, 40.1 mmol) in CH_2Cl_2 (385 mL) at -78 °C was bubbled in O_3 for 20 min until the reaction mixture turned pale blue. The reaction was quenched by addition of Me_2S (100 mL) and the reaction mixture was slowly warmed up to room temperature. The resulting mixture was concentrated *in vacuo*. Purification by flash chromatography (silica gel, 50% EtOAc in hexane) afforded the aldehyde **8a** as a pale yellow glue (7.5 g, 80%). ^1H NMR (400 MHz, CDCl_3) δ 9.71 (1H, d, J = 1.2 Hz), 7.46 (1H, t, J = 7.6 Hz), 7.13 (1H, d, J = 8 Hz), 7.08 (1H, d, J = 8 Hz), 3.84 (3H, s), 3.81 (2H, s), 2.27 (3H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 198.9, 169.8, 166.6, 150.1, 134.3, 132.5, 129.8, 126.6, 123.4, 53.0, 49.4, 21.4; IR (neat) ν_{max} : 2955, 2836, 1753, 1724, 1603, 1578, 1472, 1298, 1208; CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{12}\text{H}_{12}\text{O}_5$ 237.0764, found 237.0793.

Trans-dihydropyran (6a). A solution of aldehyde **8a** (7g, 29.7 mmol) and allyl silane **7a** (10.59 g, 32.8 mmol) in CH_2Cl_2 (200 mL) was cooled to -50 °C. To this solution was slowly added TMSOTf (5.44 mL, 29.8 mmol) at -50 °C. The reaction mixture was stirred for 2.5 h at -50 °C before a saturated solution of NaHCO_3 (200 mL) was added. The mixture was extracted with CH_2Cl_2 (3 x 200 mL). The combined organic layers were dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 35% EtOAc in hexane) afforded the pyran **6a** as a pale yellow oil (8.93 g, 90%). ^1H NMR (400 MHz, CDCl_3) δ 7.35 (1H, t, J = 8 Hz), 7.23 (1H, d, J = 8 Hz), 6.98 (1H, d, J = 8 Hz), 5.86 (1H, m), 5.64 (1H, m), 4.33 (1H, m), 3.96 (1H,

m), 3.86 (3H, s), 3.41 (1H, dd, $J = 7.2$ Hz, 10.8 Hz), 3.32 (1H, dd, $J = 4$ Hz, 10.6 Hz), 3.25 (3H, s), 3.01 (1H, dd, $J = 6.8$ Hz, 13.6 Hz), 2.85 (1H, dd, $J = 6.4$ Hz, 14 Hz), 2.42 (1H, s), 1.95 (2H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 169.6, 167.5, 148.8, 139.2, 131.1, 128.9, 127.2, 126.5, 126.4, 121.5, 74.4, 73.1, 69.8, 59.7, 52.8, 39.6, 30.3, 21.4; IR (neat) ν_{max} : 2893, 1771, 1730, 1458, 1369, 1281, 1200, 1111; $[\alpha]_D^{23} = +53.8^\circ$ ($c = 1.85$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{18}\text{H}_{22}\text{O}_6$ 335.1486, found 335.1483.

To a solution of acetate **6a** (8.4 g, 25 mmol) in MeOH (200 mL) was added K_2CO_3 (1.4 g, 1.3 mmol). The reaction was stirred for 1 h at room temperature before water (200 mL) was added. The mixture was extracted with EtOAc (3 x 200 mL). The combined organic layers were dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 35% EtOAc in hexane) afforded the phenol as a pale yellow oil (6.7 g, 93%). ^1H NMR (400 MHz, CDCl_3) δ 11.09 (1H, s), 7.29 (1H, t, $J = 8$ Hz), 6.86 (1H, d, $J = 8$ Hz), 6.77 (1H, $J = 8$ Hz), 5.88 (1H, m); 5.65 (1H, m), 4.37 (1H, m), 3.96 (3H, s), 3.90 (1H, m), 3.43 (1H, dd, $J = 6.8$ Hz, 10 Hz), 3.33 (2H, m), 3.27 (3H, s), 3.00 (1H, dd, $J = 6.4$ Hz, 13.2 Hz), 1.98 (1H, m), 1.87 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 171.9, 162.7, 141.2, 134.1, 126.1, 126.0, 123.7, 116.4, 112.3, 73.9, 72.4, 69.5, 59.0, 52.2, 41.9, 29.9; IR (neat) ν_{max} : 3583, 3035, 2893, 1663, 1608, 1449, 1250, 1210; $[\alpha]_D^{23} = +53.3^\circ$ ($c = 2.0$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{32}\text{H}_{38}\text{O}_5\text{Si}$ 293.1390, found 293.1407.

Trans-dihydropyran (12). To a solution of phenol (6.7 g, 23 mmol) and imidazole (3.16 g, 46 mmol) in DMF (46 mL) was added TBDPSCl (6.3 mL, 24 mmol). The reaction was stirred at room temperature for 16 h before water (50 mL) was added. The mixture was extracted with EtOAc (200 mL). The organic layers were washed with water (5 x 50 mL) and dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 10% EtOAc in CH_2Cl_2) afforded the TBDPS ether **12** as a thick glue (11.5 g, 94%). ^1H NMR (400 MHz, CDCl_3) δ 7.70 (4H, m), 7.42-7.32 (6H, m), 6.81 (2H, m), 6.22 (1H, d, $J = 8$ Hz), 5.88 (1H, m), 5.63 (1H, m), 4.38 (1H, m), 4.02 (1H, m), 3.92 (3H, s), 3.48 (1H, dd, $J = 7.2$ Hz, 10.4 Hz), 3.37 (1H, dd, 3.6 Hz, 10.4 Hz), 3.30 (3H, s), 2.95 (1H, dd, $J = 6$ Hz, 13.6 Hz), 2.71 (1H, $J = 7.2$ Hz, 14 Hz), 1.96 (2H, m), 1.02 (9H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 169.1, 152.2, 136.9, 135.4, 132.14, 132.11, 130.0, 129.5, 127.9, 126.0, 125.8, 122.6, 116.9, 73.8, 72.4, 69.1, 59.1, 52.0, 38.7,

29.5, 25.9, 19.1; IR (neat) ν_{max} : 2931, 1732, 1582, 1464, 1280, 1112; $[\alpha]_{\text{D}}^{23} = +29.4^\circ$ ($c = 1.0$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{16}\text{H}_{20}\text{O}_5$ 531.2568, found 531.2509.

Epoxide (13). To a solution of olefin **12** (11.55 g, 21.7 mmol) in CCl_4 (412 mL) at 0°C was added *m*-CPBA (11.8 g, 60%, 48 mmol). The reaction was stirred for 48 h at 0°C before a saturated solution (200 mL) of NaHCO_3 and a saturated solution of NaS_2O_3 (200 mL) were added. The mixture was extracted with EtOAc (200 mL). The combined organic layers were dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 50% EtOAc in hexane) afforded the epoxide **13** (unseparable diastereomers $\alpha:\beta = 7.5:1$) as a thick glue (10.11 g, 85%). ^1H NMR (400 MHz, CDCl_3) δ 7.71 (4H, m), 7.42-7.32 (6H, m), 6.81 (1H, t, $J = 8.0$ Hz), 6.73 (1H, d, $J = 8.0$ Hz), 6.25 (1H, 8.0 Hz), 4.29 (1H, m), 3.92 (3H, s), 3.84 (1H, m), 3.59 (1H, dd, $J = 5.6$ Hz, 10.4 Hz), 3.51 (1H, dd, $J = 8$ Hz, 10 Hz), 3.37 (1H, m), 3.31 (3H, s), 3.26 (1H, t, $J = 4.4$ Hz), 2.81 (1H, dd, $J = 6.8$ Hz, 14 Hz), 2.61 (1H, dd, $J = 6.8$ Hz, 14 Hz), 1.94 (1H, d, $J = 10.4$ Hz), 1.69 (1H, dd, $J = 10.4$ Hz, 14.4 Hz), 1.02 (9H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 168.7, 151.9, 136.3, 135.1, 131.8, 129.8, 129.2, 127.6, 126.0, 122.4, 116.8, 70.2, 70.0, 65.9, 58.8, 51.7, 51.1, 50.3, 38.0, 30.0, 25.7, 18.8; IR (neat) ν_{max} : 2932, 1731, 1583, 1464, 1429, 1282, 1112, 1073; $[\alpha]_{\text{D}}^{23} = +9.8^\circ$ ($c = 1.8$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{32}\text{H}_{32}\text{O}_8\text{Si}$ 547.2517, found 547.2490.

Alcohol (14). To a solution of epoxide **13** (4.7 g, 8.5 mmol) in CH_2Cl_2 (70 mL) at -78°C was added DIBAL-H (12.28 mL, 1.0 M in CH_2Cl_2). The reaction was stirred for 40 min at -78°C before a solution of sodium, potassium tartrate (200 mL) was added. The mixture was extracted with EtOAc (2 x 200 mL). The combined organic layers were dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 50% EtOAc in hexane) afforded the alcohol **14** as a thick glue (3.5 g, 74%). ^1H NMR (400 MHz, CDCl_3) δ 7.70 (4H, m), 7.42-7.33 (6H, m), 6.83 (1H, t, $J = 8\text{Hz}$), 6.75 (1H, d, $J = 8$ Hz), 6.25 (1H, d, $J = 5$ Hz), 4.323 (1H, m), 4.06 (1H, m), 3.47 (2H, m), 3.37 (3H, s), 2.92 (1H, dd, $J = 6$ Hz, 13.6 Hz), 2.75 (1H, dd, $J = 8$ Hz, 13.6 Hz), 2.11 (1H, d, br, $J = 5.2$ Hz), 1.98 (1H, dt, $J = 3.2$ Hz, 10 Hz), 1.76 (1H, dt, 10Hz, 3.2 Hz), 1.51 (1H, m), 1.42 (1H, m), 1.01 (9H, s); ^{13}C NMR (75 MHz, CDCl_3)

8169.2, 152.2, 137.0, 135.4, 132.0, 131.9, 130.0, 129.7, 127.8, 126.2, 122.3, 116.9, 75.8, 72.3, 69.1, 63.5, 59.1, 52.1, 36.6, 36.2, 36.0, 25.9, 19.0; IR (neat) ν_{max} : 3430, 2932, 2859, 1730, 1582, 1464, 1282, 1113; $[\alpha]_{\text{D}}^{23} = -22.8^\circ$ ($c = 0.75$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{32}\text{H}_{40}\text{O}_6\text{Si}$ 549.2937, found 549.2640.

Chloroacetate (15). A solution of alcohol **14** (3.2 g, 5.8 mmol), PPh_3 (2.92 g, 11.1 mmol) and chloroacetic acid (1.15 g, 12.2 mmol) in toluene (55 mL) was cooled to 0°C . To this cold solution was slowly added DIAD (2.2 mL, 11.6 mmol). The reaction was stirred for 16h and slowly warmed up to room temperature. Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 35% EtOAc in hexane) afforded the ester **15** as a thick white glue (2.6 g, 70%). ^1H NMR (400 MHz, CDCl_3) δ 7.70 (1H, m), 7.42-7.32 (6H, m), 6.83 (1H, t, $J = 8$ Hz), 6.75 (1H, d, $J = 8$ Hz), 6.26 (1H, d, $J = 8$ Hz), 5.18 (1H, m), 4.18 (1H, m), 4.06 (1H, m), 4.04 (2H, s), 3.92 (3H, s), 3.55 (1H, dd, $J = 6.4$ Hz, 10.4 Hz), 3.43 (1H, dd, $J = 5.2$ Hz, 10.4 Hz), 3.34 (3H, s), 3.49 (1H, dd, $J = 7.2$ Hz, 14 Hz), 2.66 (1H, dd, $J = 6.4$ Hz, 14 Hz), 1.95 (2H, m), 1.75 (1H, m), 1.45 (1H, m), 1.02 (9H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 169.1, 166.8, 152.3, 136.5, 135.5, 132.2, 132.0, 130.1, 129.6, 127.9, 122.6, 117.2, 73.4, 70.6, 69.9, 69.8, 59.2, 52.1, 40.9, 38.9, 34.9, 31.4, 26.0, 19.1; IR (neat) ν_{max} : 2932, 1732, 1463, 1284, 1112; $[\alpha]_{\text{D}}^{23} = -10.3^\circ$ ($c = 0.5$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{34}\text{H}_{41}\text{O}_7\text{ClSi}$ 625.2388, found 625.2430.

To a solution of methyl ether **15** (2.6 g, 4.1 mmol) in CH_2Cl_2 (21 mL) at -30°C was added 15-crown-5 / NaI saturated solution (63 mL, 0.3 M in CH_2Cl_2) and followed by BBr_3 solution (1 M in CH_2Cl_2). The reaction was stirred for 1 h at -30°C before a saturated solution of NaHCO_3 (100 mL) was added. The mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 70% EtOAc in hexane) afforded the alcohol as a thick glue (2.2 g, 88%). ^1H NMR (400 MHz, CDCl_3) δ 7.70 (4H, m), 7.38 (6H, m), 6.32 (1H, t, $J = 8$ Hz), 6.72 (1H, d, $J = 8$ Hz), 6.28 (1H, d, $J = 8$ Hz), 5.11 (1H, m), 4.13 (1H, m), 4.04 (2H, s), 3.98 (1H, m), 3.93 (3H, s), 3.78 (1H, dd, $J = 11.6$ Hz, 9.2 Hz), 3.46 (1H, dd, $J = 3.2$ Hz, 11.6 Hz), 3.04 (1H, dd, $J =$

7.2 Hz, 14 Hz), 2.68 (1H, dd, $J = 5.6$ Hz, 14 Hz), 2.26 (1H, br), 2.04 (1H, m), 1.79 (2H, m), 1.53 (1H, m), 1.02 (9H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 169.2, 166.7, 136.9, 135.4, 132.1, 130.1, 129.8, 127.9, 125.9, 122.6, 117.4, 71.0, 70.0, 69.6, 62.3, 52.2, 40.8, 39.1, 35.1, 30.6, 26.0, 19.1; IR (neat) ν_{max} : 3583, 2932, 2858, 1731, 1464, 1282, 1113; ; $[\alpha]_{\text{D}}^{23} = -12.1^\circ$ ($c = 0.9$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{33}\text{H}_{39}\text{O}_7\text{ClSi}$ 611.2232, found 611.2227.

TBS ether of primary alcohol. To a solution of alcohol (2.04 g, 3.3 mmol) in CH_2Cl_2 (66 mL) at -78°C was added 2,6 lutidine (1.16 mL, 9.9 mmol) and followed by TBSOTf (1.53 mL, 6.6 mmol). The reaction was stirred for 4 h and slowly warm up to room temperature before water (100 mL) was added. The mixture was extracted with CH_2Cl_2 (3 x 50 mL). The combined organic layers were dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 20% EtOAc in hexane) afforded the alcohol **16** as a thick glue (2.3 g, 95%). ^1H NMR (400 MHz, CDCl_3) δ 7.72 (4H, m), 7.39 (m, 6H), 6.82 (2H, m), 6.28 (1H, d, $J = 8$ Hz), 5.26 (1H, m), 4.09 (2H, m), 4.05 (2H, s), 3.93 (3H, s), 3.73 (2H, m), 3.02 (1H, dd, 6.8 Hz, 14 Hz), 2.67 (1H, dd, $J = 5.6$ Hz, 14 Hz), 1.98 (2H, br), 1.76 (1H, m), 1.46 (1H, m), 1.30 (1H, m), 1.04 (9H, s), 0.89 (9H, s), 0.55 (6H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 169.0, 166.6, 136.7, 135.4, 132.1, 130.0, 129.6, 127.8, 126.3, 122.4, 117.0, 71.6, 71.0, 69.9, 64.6, 51.9, 40.9, 30.0, 35.2, 31.0, 25.9, 25.7, 19.1, 18.0, -5.6, -5.7; IR (neat) ν_{max} : 2953, 2931, 2858, 1733, 1464, 1284, 1113; $[\alpha]_{\text{D}}^{23} = -11^\circ$ ($c = 1.0$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{39}\text{H}_{53}\text{O}_7\text{ClSi}_2$ 725.3096, found 725.3066.

Alcohol 16. To a solution of chloroacetate (2.3 g, 3.2 mmol) in MeOH (60 mL) was added K_2CO_3 (44 mg, 0.32 mmol). The reaction was stirred for 10 min at room temperature before water (100 mL) was added. The mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine and dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 50% EtOAc in hexane) afforded the alcohol **16** as a thick glue (2.2 g, 95%). ^1H NMR (400 MHz, CDCl_3) δ 7.71 (4H, m), 7.38 (6H, m), 6.80 (2H, m), 6.26 (1H, d, $J = 8.8$

Hz), 4.05 (2H, m), 3.92 (3H, s), 3.91 (1H, m), 3.70 (1H, dd, $J = 5.6$ Hz, 10 Hz), 3.64 (1H, dd, $J = 6.4$ Hz, 10 Hz), 2.96 (1H, dd, $J = 6$ Hz, 14 Hz), 2.74 (dd, $J = 6.8$ Hz, 14 Hz), 1.94 (1H, m), 1.87 (1H, m), 1.71 (1H, br), 1.57 (1H, m), 1.26 (1H, m), 1.03 (9H, s), 0.87 (9H, s), 0.03 (6H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 169.4, 152.2, 131.9, 135.5, 132.2, 132.1, 130.0, 129.6, 127.9, 126.3, 122.7, 116.9, 72.1, 71.4, 64.5, 64.0, 52.1, 39.5, 38.9, 34.6, 26.0, 25.8, 19.1, 18.1, -5.5, -5.6; IR (neat) ν_{max} : 3443, 2931, 2857, 1732, 1582, 1464, 1429, 1282, 1113; $[\alpha]^{23}_{\text{D}} = -5^\circ$ ($c = 0.9$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{37}\text{H}_{52}\text{O}_6\text{Si}_2$ 649.3380, found 649.3354.

To a solution of alcohol (1.7 g, 2.6 mmol) and $\text{BnOC}(\text{NH})\text{CCl}_3$ (0.99 g, 3.9 mmol) in Et_2O (26 mL) at 0°C was treated with TfOH (11.5 μL , 0.13 mmol). The reaction was stirred for 1 h at room temperature and another 23 μL of TfOH was added. The reaction was stirred for another 3 h before a saturated solution of NaHCO_3 (100 mL) was added. The mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine and dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 10% EtOAc in hexane) afforded the alcohol as a thick glue (1.8 g, 93%). ^1H NMR (400 MHz, CDCl_3) δ 7.74 (4H, m), 7.49-7.24 (11H, m), 6.83 (2H, m), 6.29 (1H, d, $J = 8$ Hz), 4.55 (2H, s), 4.09 (1H, m), 3.97 (1H, m), 3.93 (3H, s), 3.80 (1H, m), 3.71 (1H, dd, $J = 5.6$ Hz, 10.4 Hz), 3.66 (1H, dd, $J = 6.4$ Hz, 10.4 Hz), 3.05 (1H, dd, $J = 6.8$ Hz, 14 Hz), 2.72 (1H, dd, $J = 14$ Hz, 5.6 Hz), 2.04 (2H, m), 1.71 (1H, m), 1.41 (1H, m), 1.06 (9H, s), 0.90 (9H, s), 0.42 (6H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 169.1, 152.1, 138.7, 137.2, 135.5, 132.2, 132.1, 130.0, 129.5, 128.4, 128.2, 127.8, 127.5, 126.3, 122.8, 116.9, 71.9, 71.3, 69.7, 64.1, 52.0, 39.4, 36.3, 31.6, 26.0, 25.8, 19.1, 18.1, -5.5, -5.6; IR (neat) ν_{max} : 2930, 2857, 1733, 1463, 1283, 1113; $[\alpha]^{23}_{\text{D}} = -5.5^\circ$ ($c = 0.8$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{44}\text{H}_{58}\text{O}_6\text{Si}_2$ 739.3850, found 739.3817.

Alcohol (17). To a solution of TBSEther (1.8 g, 2.4 mmol) in MeOH (10 mL) was added HCl/MeOH (48 mL, 2%). The reaction was stirred for 10 min at room temperature before a solution of NaHCO_3 (100 mL) was added. The mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine and dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography

(silica gel, 10% EtOAc in hexane) afforded the alcohol **17** as a thick glue (1.46 g, 95%). ^1H NMR (400 MHz, CDCl_3) δ 7.70 (4H, m), 7.41-7.24 (11H, m), 6.83 (1H, t, $J = 8$ Hz), 6.73 (1H, d, $J = 8$ Hz), 6.26 (1H, d, $J = 8$ Hz), 4.51 (2H, s), 4.16 (1H, m), 3.90 (3H, s), 3.73 (1H, m), 3.67 (1H, m), 3.39 (1H, m), 3.05 (1H, dd, $J = 7.6$ Hz, 14 Hz), 2.70 (1H, dd, $J = 5.2$ Hz, 14 Hz), 2.07 (1H, m), 2.04 (1H, m), 1.75 (1H, m), 1.47 (1H, m), 1.01 (9H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 169.3, 152.4, 138.5, 137.4, 135.4, 132.1, 131.9, 130.0, 129.7, 128.4, 127.9, 127.6, 127.5, 125.9, 122.8, 117.2, 71.3, 70.3, 69.8, 62.3, 52.1, 39.4, 36.0, 31.4, 25.9, 19.1; IR (neat) ν_{max} : 3454, 2932, 1731, 1464, 1282, 1113; $[\alpha]^{23}_{\text{D}} = -2^\circ$ ($c = 0.6$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{44}\text{H}_{58}\text{O}_6\text{Si}_2$ 625.2925, found 625.2925.

To a solution of alcohol (1.5 g, 2.4 mmol) in CH_2Cl_2 (47 mL) was added molecular sieves (4 Å, 2.4 g) and followed by PCC (1.53 g, 0.72 mmol). The reaction was stirred for 4 h. The resulted reaction mixture was filter through a short path of silica gel. Removal of solvent under reduced pressure afforded the aldehyde as a thick glue (1.4 g, 93%). ^1H NMR (400 MHz, CDCl_3) δ 9.71 (1H, s), 7.70 (4H, m), 7.41-7.24 (11H, m), 6.84 (1H, t, $J = 8$ Hz), 6.75 (1H, d, $J = 8$ Hz), 6.29 (1H, d, $J = 8$ Hz), 4.50 (2H, abq, $J = 11.2$ Hz), 4.34 (1H, m), 3.91 (3H, s), 3.74 (1H, m), 3.40 (1H, m), 3.01 (1H, dd, $J = 6.4$ Hz, 14 Hz), 2.72 (1H, dd, $J = 6.4$ Hz, 14 Hz), 2.51 (1H, m), 1.98 (1H, m), 1.64 (1H, m), 1.31 (1H, m), 1.02 (9H, s); ^{13}C NMR (75 MHz, CDCl_3) δ 204.6, 169.0, 152.4, 138.3, 136.2, 135.5, 132.1, 132.0, 129.7, 128.4, 127.9, 127.7, 126.2, 122.9, 117.4, 78.7, 74.0, 71.4, 69.9, 52.1, 39.9, 36.9, 30.0, 26.0, 19.1; IR (neat) ν_{max} : 2952, 2858, 1732, 1583, 1464, 1429, 1284, 1113; $[\alpha]^{23}_{\text{D}} = -17^\circ$ ($c = 1.7$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{38}\text{H}_{42}\text{O}_6\text{Si}_2$ 623.2829, found 623.2771.

Aldehyde (5). To a solution of $\text{PPh}_3\text{CH}_2\text{OMeCl}$ in THF (30 mL) at -78°C was treated with LHMDS (6.27 mL, 1.0 M in THF). The reaction mixture was slowly warm up to room temperature. After 0.5 h, the deep brown reaction mixture was recooled to -78°C . A solution of aldehyde (1.3 g, 2.09 mmol) in THF (12 mL) was slowly added to the resulting cold reaction flask. The reaction mixture was stirred for 18h and slowly warmed up to room temperature before water (100 mL) was added. The mixture was extracted

with EtOAc (3 x 50 mL). The combined organic layers were washed with brine and dried over MgSO₄. Removal of solvent under reduced pressure afforded the crude enol ether that was used directly in next step. The crude enol ether was dissolved in THF (21 mL) and water (10 mL). Hg(OAc)₂ (1.23 g, 3.8 mmol) was added. The resulted mixture was stirred for 15 min before KI aqueous solution (8%, 83 mL) was added. A black precipitate formed. The reaction mixture was stirred for 0.5 h before water (200 mL) was added. The mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine and dried over MgSO₄. Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 35% EtOAc in hexane) afforded the aldehyde **5** as a thick glue (1.19 g, 84% 2 steps). ¹H NMR (400 MHz, CDCl₃) δ 9.61 (1H, d, *J* = 2.4 Hz), 7.70 (4H, m), 7.41-7.24 (6H, m), 6.81 (1H, t, *J* = 8 Hz), 6.68 (1H, d, *J* = 8 Hz), 6.25 (1H, d, *J* = 8 Hz), 4.67 (1H, m), 3.88 (3H, s), 3.71 (1H, m), 3.03 (1H, dd, *J* = 6.8 Hz, 14 Hz), 2.72 (2H, m), 2.39 (1H, ddd, *J* = 3.6 Hz, 5.6 Hz, 16 Hz), 2.00 (1H, m), 1.80 (2H, m), 1.44 (1H, m), 1.01 (9H, s); ¹³C NMR (75 MHz, CDCl₃) δ 200.9, 169.0, 152.2, 138.3, 136.8, 135.3, 132.0, 131.9, 129.9, 129.5, 128.3, 127.8, 127.5, 127.4, 126.2, 122.7, 116.9, 70.9, 76.6, 70.8, 70.4, 69.8, 65.9, 52.0, 46.3, 38.9, 35.6, 34.7, 25.9, 19.0; IR (neat) ν_{max}: 2932, 2858, 1728, 1464, 1282, 1113; [α]_D²³ = -8.2° (c = 0.8, CH₂Cl₂); CIHRMS [M+1]⁺ calculated for C₃₉H₄₄O₆Si 637.2907 found 637.2925.

Alcohol (18). Generating (+)Icp₂Ballyl: To a solution of (-)-DIP chlorideTM (888 mg, 2.77 mmol) at -78 °C in Et₂O (5.63 mL) was added allyl magnesium bromide (2.77 mL, 1 M in Et₂O). The resulted reaction mixture was stirred for 1 h at -78 °C and was slowly warmed up to room temperature. After the reaction was stirred for 2 h at room temperature, the stirring was stopped.

To a solution of aldehyde **5** (0.4 g, 0.63 mmol) in Et₂O (15 mL) at -78 °C was added (+)-IcpBallyl solution (5.5 mL, 0.33 M in Et₂O). The reaction was stirred at -78 °C for 4 h before NaHCO₃ saturated solution (35 mL) and H₂O₂ solution (30%, 20 mL) was added. After stirred for 1.5 h, the reaction mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine and dried over MgSO₄. Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 25%- 35% EtOAc in hexane) afforded the alcohol **18** as thick glue (318 mg, 75%). ¹H NMR (400 MHz, CDCl₃) δ 7.23 (4H, m), 7.42 – 7.38 (11H, m), 6.86 (1H, t, *J* = 8 Hz), 6.77 (1H, d, *J* = 8 Hz), 6.31 (1H, d, *J* = 8 Hz), 5.80 (1H, m), 5.08 (1H, d, *J* = 9.2 Hz), 5.05 (1H, d, *J* = 1.5 Hz), 5.54 (2H, abq, *J* = 12 Hz), 4.32 (1H, m), 4.06 (1H, m), 3.91 (3H, s), 3.76 (2H, m), 3.12 (1H, dd, *J* = 7.6 Hz, 14 Hz), 3.06 (1H, br), 2.80 (1H, dd, *J* = 6.4 Hz, 14 Hz), 2.21 (2H, m), 2.01 (1H, m), 1.79 (3H, m), 1.51 (1H, m), 1.43 (1H, m), 1.06 (9H, s); ¹³C NMR (75 MHz, CDCl₃) δ 169.1, 152.3, 138.5, 136.9, 135.4, 135.0, 132.2, 132.0, 129.9, 129.6, 128.4, 127.8, 127.5, 127.4, 126.2, 122.7, 117.2, 117.1, 71.1, 70.7,

70.5, 70.3, 69.9, 52.1, 41.4, 38.9, 38.6, 35.8, 35.2, 25.9, 19.1; ; IR (neat) ν_{max} 3502, 2932, 2858, 1732, 1582, 1464, 1283, 1114; $[\alpha]^{23}_{\text{D}} = -16.6^\circ$ ($c = 0.35$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{42}\text{H}_{50}\text{O}_6\text{Si}$ 679.3377 found 679.3369.

Hydroxy acid (19). To a solution of ester **18** (520 mg, 0.766 mmol) in MeOH (20 mL), H_2O (20 mL) and THF (80 mL) was added $\text{LiOH}\cdot\text{H}_2\text{O}$ (3.1g, 74 mmol). The reaction mixture was stirred for 6 h at reflux. The mixture was cooled to room temperature and water (50 mL) was added. After the mixture was extracted with hexane (50 mL), the aqueous layer was acidified to $\text{pH}=1$ with concentrated HCl. The acidic aqueous layer was extracted with EtOAc (3 x 50 mL). The combined organic layers were concentrated at 70°C under reduced pressure. The pure acid **19** (310 mg 95%) was obtained as a thick oil and was used directly in next step. ^1H NMR (400 MHz, CDCl_3) δ 7.28 (6H, m); 6.87 (1H, d, $J = 8.4$ Hz), 6.70 (1H, d, $J = 7.2$ Hz), 5.76 (1H, m), 5.09 (1H, d, $J = 6.8$ Hz), 5.05 (1H, s), 4.52 (2H, s), 4.36 (1H, m), 4.04 (1H, m), 3.95 (1H, m), 3.72 (1H, m), 3.55 (1H, dd, $J = 4$ Hz, 12 Hz), 3.11 (1H, $J = 8$ Hz, 12 Hz), 2.43 (2H, m), 1.90 (2H, m), 1.79 (2H, m), 1.52 (1H, m), 1.44 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 173.1, 163.2, 141.0, 138.3, 134.2, 134.0, 128.2, 127.6, 127.4, 123.8, 117.9, 116.8, 112.4, 71.9, 71.6, 71.3, 71.0, 70.0, 41.8, 40.9, 37.5, 35.7, 34.8; IR (neat) ν_{max} 3349, 2925, 1660, 1452, 1224; $[\alpha]^{23}_{\text{D}} = +4.8^\circ$ ($c = 0.25$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{25}\text{H}_{30}\text{O}_6$ 427.2120, found 427.2113.

To a solution of acid **19** (550 mg, 1.29 mmol) in acetone (11 mL) was treated with Et_3N (0.52 mL, 3.8 mmol) and followed by chloroacetonitrile (0.23 mL, 3.8 mL). The reaction mixture was stirred for 48 h at 52°C . The mixture was cooled to room temperature. Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 45% EtOAc in hexane) afforded the ester as a thick oil (512 mg, 80%). ^1H NMR (400 MHz, CDCl_3) δ 10.59 (1H, s), 7.30 (6H, s), 6.92 (1H, d, $J = 8$ Hz), 6.75 (1H, d, $J = 7.2$ Hz), 5.75 (1H, m), 5.06 (4H, m), 4.98 (2H, abq, $J = 12$ Hz), 4.31 (1H, m), 3.90 (1H, m), 3.70 (2H, m), 3.43 (1H, dd, $J = 6.8$ Hz, 13.2 Hz), 3.30 (1H, s), 2.96 (1H, dd, $J = 6.8$ Hz, 13.2 Hz), 2.18 (2H, m), 1.89 (1H, m), 1.79m (3H, m), 1.41 (1H, m), 1.35 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 169.9, 163.3, 140.5, 138.5, 135.4, 134.8, 128.5, 127.7, 127.6, 124.5, 117.5, 117.1, 114.3, 110.8, 72.4, 71.6, 71.1, 70.2, 70.1, 49.0, 42.0, 41.4,

37.6, 36.1, 35.9; IR (neat) ν_{max} 3454, 2924, 1740, 1670, 1450, 1109, 1071; $[\alpha]_{\text{D}}^{23} = +0.5^{\circ}$ ($c = 0.95$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{27}\text{H}_{31}\text{NO}_6$ 466.2229, found 466.2269.

Hydroxy cyanomethyl ester (4). To a solution of phenol (267 mg, 0.57 mmol) and Bu_4NI (396 mg, 1.07 mmol) in CH_2Cl_2 (13 mL) and aqueous NaOH solution (1N, 6.4 mL) was treated with MOMCl (0.21 mL, 2.7 mmol). The reaction mixture was stirred at room temperature for 3 h before water (20 mL) was added. The mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine and dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 50% EtOAc in hexane) afforded the alcohol **4** as a thick oil (263 mg, 90%). ^1H NMR (400 MHz, CDCl_3) δ 7.32 (6H, m), 7.03 (1H, d, $J = 8.4$ Hz), 6.90 (1H, d, $J = 7.6$ Hz), 5.74 (1H, m), 5.16 (2H, abq, 6 Hz), 5.05 (1H, m), 5.02 (1H, s), 4.50 (2H, abq, 12 Hz), 4.26 (1H, m), 3.96 (1H, m), 3.71 (1H, m), 3.67 (1H, m), 3.44 (3H, s), 3.07 (1H, dd, $J = 8$ Hz, 14 Hz), 2.85 (1H, br.), 2.77 (1H, dd, $J = 5.6$ Hz, 14 Hz), 2.13 (2H, m), 1.99 (1H, m), 1.74 (3H, m), 1.48 (1H, m), 1.36 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 166.6, 154.6, 138.5, 137.6, 134.9, 131.4, 128.5, 127.7, 127.6, 123.9, 122.5, 117.3, 114.5, 112.9, 94.6, 71.07, 70.9, 70.8, 70.2, 70.1, 56.2, 48.6, 41.4, 38.7, 38.4, 35.8, 35.4; IR (neat) ν_{max} 3466, 2926, 1747, 1256, 1070; $[\alpha]_{\text{D}}^{23} = -17^{\circ}$ ($c = 1.2$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{29}\text{H}_{35}\text{NO}_7$ 510.2493, found 510.2507.

Macrolide (20). To a solution of hydroxy ester **4** (240 mg, 0.47 mmol) in THF (240 mL) was treated with NaH (580 mg, 60%, 14.5 mmol). The reaction mixture was stirred for 2 h at reflux. Another portion of NaH (290 mg, 60%, 7.25 mmol) was added. The reaction mixture was stirred for another 2 h at reflux. The reaction mixture turned to purple. A saturated solution of NH_4Cl (100 mL) was slowly added. The mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine and dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 20% EtOAc in hexane) afforded **20** as a thick oil (130 mg, 63%). ^1H NMR (400 MHz, CDCl_3) δ 7.35- 7.25 (6H, m), 7.19 (1H, dt, $J = 7.6$ Hz, 8 Hz),

6.99 (1H, d, $J = 8$ Hz), 6.79 (1H, d, $J = 7.6$ Hz), 5.85 (1H, m), 5.59 (1H, m), 5.16-5.08 (4H, m), 4.52 (2H, abq, $J = 12$ Hz), 4.33 (1H, m), 3.95 (1H, m), 3.75 (1H, m), 3.47 (1H, dd, $J = 10.4$ Hz, 14.4 Hz), 3.43 (3H, s), 2.43 (2H, m), 2.32 (1H, m), 2.02 (1H, m), 1.85-1.63 (4H, m), 1.57 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 169.4153.5, 138.7, 138.6, 133.7, 130.0, 128.5, 127.6, 127.5, 124.0, 123.9, 117.6, 112.9, 94.6, 73.5, 72.8, 71.7, 70.1, 66.4, 56.0, 39.2, 38.9, 38.8, 36.3, 34.6; IR (neat) ν_{max} 2922, 1717, 1652, 1463, 1254, 1070; $[\alpha]_{\text{D}}^{23} = -11.3^\circ$ ($c = 0.6$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{27}\text{H}_{32}\text{O}_6$ 452.2199, found 452.2189.

Vinyl iodide (22). To a solution of macrolide (130 mg, 0.30 mmol) and NMO (67.3 mg) in acetone (2.40 mL) and water (0.6 mL) was treated with OsO_4 (0.144 mL, 0.2 M in toluene). The reaction mixture was stirred at room temperature for 4 h before a saturated solution of NaS_2O_3 (10 mL) was slowly added. The mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine and dried over MgSO_4 . Removal of solvent under reduced pressure afforded crude diol that is used directly in next step. To a solution of crude diol in THF (1.5 mL) and water (1.5 mL) was added NaIO_4 (123 mg, 0.57 mmol). The reaction mixture was stirred at room temperature for 2 h before NaS_2O_3 saturated solution (10 mL) was slowly added. The mixture was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine and dried over MgSO_4 . Removal of solvent under reduced pressure afforded aldehyde that is used directly in next step.

To a slurry of a flame-dried CrCl_2 (527 mg, 4.28 mmol) in THF (0.8 mL) was added a solution of aldehyde and HCl_3 (787 mg, 2 mmol) in dioxane (4.9 mL) at 0°C . The resulted brown reaction mixture was stirred for 24 h before a saturated solution of NaHCO_3 (20 mL) was added. The mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine and dried over MgSO_4 . Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 5-35% EtOAc in hexane) afforded the vinyl iodide **22** (E: Z = 6:1) as a oil (120 mg, 70% over 3 steps). ^1H NMR (400 MHz, CDCl_3) δ 7.32- 7.24 (5H, m), 7.20 (1H, t, $J = 8$ Hz), 7.02 (1H, d, $J = 8$ Hz), 6.79 (1H, d, $J = 8$ Hz), 6.60 (1H, m), 6.18 (1H, d, $J = 14.4$ Hz), 5.60 (1H, m), 5.20 (2H, abq, $J = 7.2$ Hz), 4.53 (2H, abq, 13.6 Hz), 4.32 (1H, m), 3.95 (1H, m), 3.75 (1H, m), 3.47 (3H, s), 3.47 (1H, dd, $J = 9.2$ Hz, 8.8 Hz), 2.38 (3H, m), 2.02 (1H, m), 1.83-1.62 (4H, m), 1.55 (1H, m); ^{13}C NMR (75 MHz, CDCl_3) δ 169.4, 153.6, 141.5, 138.7, 138.6, 130.1, 128.5, 127.6, 127.5, 126.2, 123.8, 112.8, 94.6, 77.6, 73.7, 71.65, 71.61, 70.1, 65.9, 56.0, 40.8, 39.2, 38.7, 36.2, 34.4; IR (neat) ν_{max} 2922, 1707, 1652, 1463, 1290, 1118; $[\alpha]_{\text{D}}^{23} = -17.3$ ($c = 1.0$, CH_2Cl_2); CIHRMS $[\text{M}+1]^+$ calculated for $\text{C}_{27}\text{H}_{31}\text{IO}_6$ 579.1244, found 579.1258.

Vinyl iodide (2). To a solution of ether **22** (112 mg, 0.193 mmol) in CH₂Cl₂ (10 mL) was treated with BCl₃ (2.9 mL, 1.0 M in hexane) at -78 °C. The reaction was stirred for 8 h at -78 °C before MeOH (10 mL) was added and followed by a saturated solution of NaHCO₃ (20 mL). The mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine and dried over MgSO₄. Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 75% EtOAc in hexane) afforded the alcohol **2** as a solid (79 mg, 81%). ¹H NMR (400 MHz, acetone-*d*₆) δ 8.56 (1H, s), 7.11 (1H, t, *J* = 8 Hz), 6.79 (1H, d, *J* = 8 Hz), 6.69 (1H, d, *J* = 8 Hz), 6.64 (1H, m), 6.32 (1H, d, *J* = 14.4 Hz), 5.48 (1H, m), 4.26 (1H, m), 3.99 (1H, m), 3.87 (2H, m br), 3.32 (1H, dd, *J* = 10 Hz, 14.4 Hz), 2.44 (1H, d, 14 Hz), 2.37 (2H, m), 1.92 (1H, m), 1.84 (1H, m), 1.67 (1H, m), 1.56 (1H, m), 1.47 (2H, m); ¹³C NMR (75 MHz, Acetone-*d*₆) δ 169.6, 154.6, 143.2, 140.4, 138.6, 130.6, 122.6, 114.6, 78.5, 73.7, 72.7, 68.2, 65.0, 41.7, 40.4, 39.9, 39.8, 39.0; IR (neat) ν_{max} 2922, 1707, 1652, 1463, 1290, 1118; [α]_D²³ = -46 (c = 0.75, Acetone); CIHRMS [M+1]⁺ calculated for C₁₈H₂₁IO₅ 444.0434, found 444.0433.

Apicularen A (1). To a solution of amide **3** (28 mg, 0.22 mmol), Rb₂CO₃ (55.2 mg, 0.24 mmol), CuTC (28.5 mg, 0.15 mmol) and 1,10-phenanthroline (0.3 mmol) in DMA (0.25 mL) was added vinyl iodide **2** (30 mg, 0.067 mmol). The reaction mixture was degassed on high vacuum for 5 min. The deep red reaction mixture was stirred at 58 °C for 8 h before PH 7 buffer solution (10 mL) was added. The mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers were washed with brine and dried over MgSO₄. Removal of solvent under reduced pressure and purification by flash chromatography (silica gel, 50%-75%-100% EtOAc in hexane) afforded apicularen A, **1** as a white solid (12 mg, 40%). ¹H NMR (400 MHz, acetone-*d*₆) δ 9.11 (1H, d, *J* = 10 Hz), 8.43 (1H, s), 7.52 (1H, dd, *J* = 12 Hz, 10.8 Hz), 7.10 (1H, t, *J* = 8 Hz), 6.87 (1H, m), 6.77 (1H, d, *J* = 8 Hz), 6.69 (1H, d, *J* = 8 Hz), 5.80 (1H, m), 5.74 (1H, d, *J* = 12.4 Hz), 5.42 (1H, m), 5.25 (1H, m), 4.26 (1H, m), 3.99 (1H, m), 3.87 (1H, m), 3.81 (1H, d, *J* = 4 Hz), 3.34 (1H, dd, *J* = 10 Hz, 14.4 Hz), 2.43 (1H, d, *J* = 14.4 Hz), 2.32 (2H, m), 2.27 (2H, m), 1.92 (1H, m), 1.82 (1H, m), 1.68 (1H, m), 1.58 (1H, m), 1.48 (2H, m), 1.00 (3H, t, 7.2 Hz); ¹³C NMR (75 MHz, Acetone-*d*₆) δ 169.5, 163.8, 154.4, 141.6, 140.3, 136.9, 130.3, 126.3, 125.5, 122.3, 120.9, 114.4, 108.1, 74.2, 73.6, 68.0, 64.8, 40.2, 39.8, 39.5, 38.7, 36.3, 20.9, 14.2; IR (neat) ν_{max} 3275, 2924, 2852, 1716, 1683, 1652, 1583, 1524;

$[\alpha]^{23}_{\text{D}} = -34^{\circ}$ ($c = 0.4$, CH_3CN); $R_f = 0.39$ ($\text{CH}_2\text{Cl}_2 : \text{MeOH} = 9:1$), $R_f = 0.21$ ($\text{EtOAc} : \text{Hexane} = 3:1$), $R_f = 0.28$ ($\text{EtOAc} : \text{CH}_2\text{Cl}_2 = 4:1$); CIHRMS $[\text{M}]^+$ calculated for $\text{C}_{25}\text{H}_{31}\text{NO}_6$ 441.2151, found 441.2135.

¹H NMR (400 MHz, Acetone-d₆)
of natural Apicularen A

¹H NMR (400 MHz, Acetone-d₆)
of synthetic Apicularen A