

NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  4.93 (d,  $J$  = 3.7 Hz, 1 H), 4.79 (dd,  $J$  = 9.9, 1.8 Hz, 1 H), 4.04 (bd,  $J$  = 7.7 Hz, 1 H), 3.84 (dt,  $J$  = 9.2, 2.6 Hz, 1 H), 3.82–3.69 (m, 4 H), 3.52–3.50 (m, 2 H), 3.49 (s, 3 H), 3.46–3.41 (m, 2 H), 3.40 (s, 3 H), 3.34 (s, 3 H), 3.27 (s, 3 H), 3.21–3.11 (m, 2 H), 3.00–2.94 (m, 1 H), 2.73 (d,  $J$  = 5.1 Hz, 1 H), 2.56 (bs, 1 H), 2.44 (bs, 1 H), 2.34–2.28 (m, 4 H), 2.04 (dd,  $J$  = 10.6, 6.6 Hz, 1 H), 1.96–1.80 (m, 5 H), 1.77 (t,  $J$  = 2.4 Hz, 3 H), 1.76–1.66 (m, 4 H), 1.38 (s, 3 H), 1.33 (d,  $J$  = 6.2 Hz, 3 H), 1.26 (d,  $J$  = 6.2 Hz, 3 H), 1.11 (d,  $J$  = 6.6 Hz, 3 H), 0.89 (d,  $J$  = 7.0 Hz, 3 H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  102.2, 99.9, 97.1, 84.1, 81.7, 80.8, 78.6, 76.1, 75.5, 75.2, 74.8, 74.6, 72.5, 71.5, 71.7, 68.9, 68.1, 67.6, 66.5, 59.2, 59.1, 56.4, 48.3, 43.7, 38.5, 35.9, 35.5, 35.5, 34.6, 31.9, 23.3, 20.2, 18.4, 17.8, 15.4, 11.5, 5.1; HRMS (MALDI-FTMS) for  $\text{C}_{37}\text{H}_{66}\text{NaO}_{15}$  [ $\text{M} + \text{Na}^+$ ] calcd 773.4294, found 773.4281.

**Vinyl iodide methyl ether 65.** Acetylenic alcohol **63** (290 mg, 0.60 mmol) was added to a suspension of NaH (60% dispersion in mineral oil, 42 mg, 1.80 mmol) in DMF (6 mL) at room temperature. The reaction mixture was stirred for 30 min. MeI (0.12 mL, 1.80 mmol) and tetrabutylammonium iodide (111 mg, 0.30 mmol) were added and the reaction mixture was stirred for an additional 12 h at room temperature. The reaction mixture was treated with saturated aqueous  $\text{NH}_4\text{Cl}$  (10 mL). The mixture were extracted with ether ( $3 \times 15$  mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered, concentrated and purified by column chromatography (silica gel, hexanes:EtOAc, 7:1) to afford methyl ether **64** (290 mg, 98%) which was dissolved in THF (3 mL) and  $\text{Cp}_2\text{ZrHCl}$  (313 mg, 1.2 mmol, dried under vacuum for 2 h) was added in one portion under argon. The reaction mixture was heated to 65 °C with stirring for 3 h and then was cooled to –25 °C. To this blood-red solution was added  $\text{I}_2$  (300 mg, 1.2 mmol) in THF (2 mL) dropwise and the resulting mixture was stirred at that temperature for 2 min before quenching with saturated aqueous  $\text{Na}_2\text{S}_2\text{O}_3$  (10 mL). The aqueous layer was extrated with EtOAc ( $3 \times 20$  mL) and the combined organic layer was washed with brine (15 mL) and dried over  $\text{Na}_2\text{SO}_4$ . The crude product was purified by flash chromatography (hexanes:EtOAc, 6:1) to afford vinyl iodide

methoxy ether **65** (330 mg, 85%) as a mixture (ca 10:1 ratio of regioisomers). *Note:* The mixture of regioisomers in **65** was used in the next step without additional purifications. **65**:  $R_f = 0.30$  (silica gel, hexanes:EtOAc, 4:1);  $[\alpha]_D = -24.0$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ); IR (film)  $\nu_{\text{max}}$  2932, 1722, 1465, 1385, 1253, 1160, 1098, 1066, 1012, 969, 906, 757  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  6.94–6.86 (m, 2 H), 6.82 (d,  $J = 8.1$  Hz, 1 H), 6.15 (td,  $J = 7.3, 1.5$  Hz, 1 H), 4.66 (d,  $J = 11.4$  Hz, 1 H), 3.88 (s, 3 H), 3.87 (s, 3 H), 3.77–3.69 (m, 2 H), 3.46 (d,  $J = 5.1$  Hz, 2 H), 3.37 (s, 3 H), 3.34–3.28 (m, 1 H), 3.26 (s, 3 H), 2.35 (s, 3 H), 2.22–2.13 (m, 1 H), 1.98–1.91 (m, 1 H), 1.76–1.69 (m, 1 H), 1.61–1.53 (m, 2 H), 1.44–1.32 (m, 2 H), 0.87 (s, 9 H), 0.05 (s, 3 H), 0.05 (s, 3 H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  148.7, 148.3, 140.9, 131.4, 120.3, 111.2, 110.7, 93.5, 79.9, 75.8, 71.8, 70.9, 59.0, 58.0, 55.8, 55.6, 31.8, 30.5, 27.3, 27.2, 25.8, 25.7, 17.9, –4.3, –4.8; HRMS (MALDI-FTMS) for  $\text{C}_{27}\text{H}_{47}\text{INaO}_6\text{Si}$   $[\text{M} + \text{Na}^+]$  calcd 645.2079, found 645.2084.

**Vinyl iodide acetate 67.** Vinyl iodide DMB ether **65** (535 mg, 0.86 mmol) was dissolved in a mixture of  $\text{CH}_2\text{Cl}_2$ : $\text{H}_2\text{O}$  (18:1, 19 mL) and 2,3-dichloro-5,6-dicyano-benzoquinone (DDQ, 293 mg, 1.29 mmol) was added at 0 °C and the reaction mixture was stirred at that temperature for 2 h. The reaction mixture was filtered and the filtrate was washed with saturated aqueous  $\text{NaHCO}_3$  ( $3 \times 10$  mL). The organic phase was separated and the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  ( $3 \times 15$  mL) and the combined organic layer was washed with brine (20 mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated. The crude product was purified by flash chromatography (silica gel, hexanes:EtOAc, 3:1) to afford vinyl iodide hydroxy compound **66** (380 mg, 90%) which was dissolved in  $\text{CH}_2\text{Cl}_2$  (5 mL).  $\text{Ac}_2\text{O}$  (0.41 mL, 4.3 mmol),  $\text{Et}_3\text{N}$  (0.60 mL, 4.3 mmol) and 4-DMAP (61 mg, 0.43 mmol) were added and the reaction was stirred at room temperature for 12 h. The reaction mixture was filtered and the filtrate was washed with saturated aqueous  $\text{NaHCO}_3$  (3 mL). The organic phase was separated and the aqueous layer was extracted with  $\text{CH}_2\text{Cl}_2$  ( $2 \times 15$  mL) and the combined organic layer was washed with water (10 mL) and brine (10 mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated. The crude product was purified by flash

chromatography (hexanes:EtOAc, 6:1) to afford vinyl iodide acetate **67** (365 mg, 85%) as a clear, colorless, viscous oil. **67**:  $R_f$  = 0.40 (silica gel, hexanes:EtOAc, 4:1);  $[\alpha]_D = -12.0$  ( $c = 1.0$ ,  $\text{CHCl}_3$ ); IR (film)  $\nu_{\text{max}}$  2952, 2928, 2856, 1740, 1462, 1373, 1240, 1198, 1105, 1053, 971, 837, 775  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  6.15 (d,  $J = 6.6$  Hz, 1 H), 5.28–5.23 (m, 1 H), 3.78 (ddd,  $J = 9.6, 3.7, 3.5$  Hz, 1 H), 3.44 (d,  $J = 4.8$  Hz, 1 H), 3.36 (s, 3 H), 3.35 (s, 3 H), 3.10 (dd,  $J = 10.3, 3.7$  Hz, 1 H), 2.36 (s, 3 H), 2.23–2.17 (m, 1 H), 2.07 (s, 3 H), 1.98–1.92 (m, 1 H), 1.84 (dd,  $J = 14.9, 10.1$  Hz, 1 H), 1.64–1.57 (m, 3 H), 1.46 (ddd,  $J = 14.5, 11.2, 2.6$  Hz, 1 H), 1.36–1.28 (m, 1 H), 0.90 (s, 9 H), 0.07 (s, 3 H), 0.06 (s, 3 H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  170.7, 140.9, 93.7, 80.2, 80.2, 74.6, 70.4, 69.8, 59.1, 58.5, 35.4, 30.5, 30.2, 27.5, 25.8, 21.2, 18.0, –4.4, –4.6; HRMS (MALDI-FTMS) for  $\text{C}_{20}\text{H}_{39}\text{INaO}_5\text{Si}$  [ $\text{M} + \text{Na}^+$ ] calcd 537.1504, found 537.1504.

**Stille coupling of vinyl stannane 2 and vinyl iodide 67. Hydroxy diene 68.** Vinyl stannane **2** (606 mg, 1.1 mmol) and vinyl iodide **67** (364 mg, 0.73 mmol) were combined and azeotroped three times with toluene. After dried under high vacuum for 30 min, the mixture was dissolved in DMF (15 mL) and the solution was degassed thoroughly by using the FTP (freeze-thaw-process) three times.  $\text{PdCl}_2(\text{MeCN})_2$  (9.5 mg, 0.04 mmol) was added at room temperature and the resulting mixture was stirred for 15 h. The reaction mixture was quenched with  $\text{H}_2\text{O}$  (10 mL) and the aqueous layer was extracted with ether ( $3 \times 15$  mL). The combined organic layer was washed with brine (20 mL), dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The crude product was purified by flash chromatography (hexanes:EtOAc, 4:1) to afford hydroxy diene **68** (294 mg, 66%) as colorless, viscous oil. **68**:  $R_f$  = 0.60 (silica gel, hexanes:EtOAc, 1:1);  $[\alpha]_D = +28.5$  ( $c = 2.50$ ,  $\text{CHCl}_3$ ); IR (film)  $\nu_{\text{max}}$  3468, 2954, 2856, 1740, 1712, 1461, 1375, 1255, 1114, 964, 837, 775  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.15 (s, 1 H), 6.22 (d,  $J = 15.8$  Hz, 1 H), 6.01 (s, 1 H), 5.57 (dd,  $J = 15.6, 7.1$  Hz, 1 H), 5.46 (bt,  $J = 7.0$  Hz, 1 H), 5.29–5.20 (m, 3 H), 4.07–4.02 (m, 1 H), 3.82–3.78 (m, 1 H), 3.75 (d,  $J = 10.6$  Hz, 1 H), 3.75 (s, 3 H), 3.43 (d,  $J = 5.1$  Hz, 2 H), 3.35 (s, 3 H), 3.34 (s, 3 H), 3.13–3.08 (m, 1 H), 2.69 (dd,  $J = 9.9, 6.4$  Hz, 1 H), 2.32–2.25 (m, 1 H), 2.06

(s, 3 H), 2.03 (d,  $J = 1.5$  Hz, 3 H), 1.96 (d,  $J = 1.1$  Hz, 3 H), 1.87–1.81 (m, 1 H), 1.79 (d,  $J = 1.1$  Hz, 3 H), 1.71 (s, 3 H), 1.65–1.55 (m, 2 H), 1.50–1.34 (m, 1 H), 1.05 (d,  $J = 6.6$  Hz, 3 H), 0.90 (s, 9 H), 0.07 (s, 6 H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  170.7, 170.0, 143.9, 139.1, 136.2, 133.9, 133.0, 132.7, 131.7, 127.1, 125.4, 80.2, 77.0, 74.5, 71.5, 70.6, 69.7, 59.0, 58.4, 51.8, 39.4, 30.7, 27.8, 25.8, 25.0, 21.1, 18.2, 17.9, 17.5, 17.2, 16.6, 14.1, 13.5, 12.4, –4.5, –4.6; HRMS (MALDI-FTMS) for  $\text{C}_{36}\text{H}_{62}\text{NaO}_8\text{Si}$  [ $\text{M} + \text{Na}^+$ ] calcd 673.4106, found 673.4098.

**Glycoside lactone 73.** Sulfoxide **70** (514 mg, 1.0 mmol) was dissolved in ether (33 mL). 4 Å MS (460 mg) were added and the resulting suspension was cooled to  $-90$  °C. To this mixture was added DTBMP (205 mg, 1.0 mmol) in ether (2 mL) followed by  $\text{Ti}_2\text{O}$  (0.042 mL, 0.25 mmol) dropwise and stirring was continued at  $-90$  °C for 3 h. Allylic alcohol (hydroxyl diene) **68** (65 mg, 0.10 mmol) in ether (1 mL) was then added dropwise and after stirring at  $-90$  °C for 1.5 h, the reaction was quenched with saturated aqueous  $\text{NaHCO}_3$  (10 mL) at that temperature. The aqueous layer was extracted with ether ( $3 \times 15$  mL) and the combined organic layer was washed with brine (20 mL), dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The crude product was purified by flash chromatography (hexanes:EtOAc, 6:1) to afford glycoside (65 mg, 63%) which was dissolved in dioxane (7 mL). KOH (2 M in  $\text{H}_2\text{O}$ , 0.67 mL, 1.35 mmol) was added and the mixture was heated to  $75$  °C for 18 h. After cooling to room temperature, the reaction was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  (5 mL). The aqueous layer was extracted with EtOAc ( $3 \times 10$  mL) and the combined organic layer was washed with brine (10 mL), dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The crude hydroxy acid (**72**) so obtained was taken to the next step without purification.

Crude seco dihydroxy acid **72** (25 mg, 0.025 mmol) was dissolved in THF (2 mL) and cooled to  $0$  °C.  $\text{Et}_3\text{N}$  (0.14 mL, 1.0 mmol) and 2,4,6-trichlorobenzoyl chloride (0.079 mL, 0.5 mmol) was added and the resulting mixture was stirred at room temperature for 2 h and then the cloudy suspension was added dropwise via cannula to a solution of 4-DMAP (244 mg, 2.0

mmol) in toluene (90 mL) at room temperature over 10 min. The white suspension was heated to 70 °C and stirred for 2 h. The reaction was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  (30 mL) and the aqueous layer was extracted with EtOAc ( $3 \times 50$  mL). The combined organic layer was washed with brine (30 mL), dried over  $\text{Na}_2\text{SO}_4$ , and concentrated. The crude product was purified by flash chromatography (hexanes:EtOAc, 8:1) to afford glycoside lactone **73** (15 mg, 65%) as a clear, colorless, viscous oil. **73**:  $R_f = 0.30$  (silica gel, hexanes:EtOAc, 4:1);  $[\alpha]_D = -30.3$  ( $c = 0.30$ ,  $\text{CHCl}_3$ ); IR (film)  $\nu_{\text{max}}$  2929, 2842, 1704, 1462, 1377, 1355, 1250, 1106, 1029, 864, 838, 775  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.16 (s, 1 H), 6.09 (d,  $J = 15.8$  Hz, 1 H), 6.07 (s, 1 H), 5.47 (dd,  $J = 7.9, 7.0$  Hz, 1 H), 5.17 (dt,  $J = 10.7, 4.2$  Hz, 1 H), 5.10 (dd,  $J = 15.6, 9.0$  Hz, 1 H), 5.07 (d,  $J = 10.1$  Hz, 1 H), 4.78 (d,  $J = 3.1$  Hz, 1 H), 3.82 (dd,  $J = 8.8, 8.8$  Hz, 1 H), 3.74 (dd,  $J = 9.2, 9.2$  Hz, 1 H), 3.71 (dd,  $J = 9.4, 6.4$  Hz, 1 H), 3.56 (dd,  $J = 10.5, 3.9$  Hz, 1 H), 3.51 (dd,  $J = 9.2, 3.5$  Hz, 1 H), 3.49 (s, 3 H), 3.47 (dd,  $J = 6.8, 3.7$  Hz, 1 H), 3.39 (s, 3 H), 3.36 (s, 3 H), 2.82 (dd,  $J = 9.4, 8.1$  Hz, 1 H), 2.68–2.60 (m, 2 H), 2.44–2.36 (m, 1 H), 2.10 (s, 3 H), 2.08 (s, 3 H), 2.06–1.86 (m, 5 H), 1.83 (s, 3 H), 1.59 (s, 3 H), 1.30 (d,  $J = 6.6$  Hz, 3 H), 1.12 (d,  $J = 6.6$  Hz, 3 H), 0.93 (s, 9 H), 0.92 (s, 9 H), 0.92 (s, 9 H), 0.13 (s, 3 H), 0.12 (s, 3 H), 0.10 (s, 3 H), 0.07 (s, 3 H), 0.07 (s, 3 H), 0.07 (s, 3 H), 0.01 (s, 3 H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  168.8, 145.1, 145.1, 140.6, 140.1, 140.0, 133.1, 132.1, 132.0, 131.7, 125.2, 123.3, 95.1, 87.6, 82.3, 81.4, 75.5, 74.4, 74.2, 73.7, 70.4, 67.1, 61.2, 61.2, 59.4, 53.5, 37.9, 36.7, 35.7, 35.6, 26.5, 26.4, 26.2, 26.1, 25.8, 24.7, 18.5, 18.3, 18.3, 18.1, 17.4, 16.4, 13.8, 11.9, –3.0, –3.7, –3.9, –4.1, –4.3; HRMS (MALDI-FTMS) for  $\text{C}_{52}\text{H}_{96}\text{NaO}_{10}\text{Si}_3$  [ $\text{M} + \text{Na}^+$ ] calcd 987.6203, found 987.6212.

**Compound 74.** Glycoside lactone **73** (11 mg, 0.011 mmol) was dissolved in THF (2 mL) and cooled to –30 °C.  $\text{HF} \cdot \text{py}$  (0.5 mL) was added dropwise and then the reaction mixture was kept at 0 °C for 48 h. Pyridine (2 mL) was added to the reaction mixture at –30 °C and then the mixture was poured to a pre-cooled (at 0 °C) mixture of saturated aqueous  $\text{NaHCO}_3$  (10 mL) and EtOAc (10 mL). The mixture was stirred at 0 °C for 30 min. The aqueous layer was extracted

with EtOAc ( $5 \times 10$  mL) and the combined organic layer was washed with brine (20 mL), dried over  $\text{Na}_2\text{SO}_4$ , and concentrated. The crude product was purified by flash chromatography (silica gel,  $\text{CHCl}_3:\text{MeOH}:\text{H}_2\text{O}$ , 15:3:1) to afford compound **74** (5 mg, 70%) as a clear, colorless, viscous oil. **74**:  $R_f = 0.25$  (silica gel,  $\text{CHCl}_3:\text{MeOH}$ , 95:5);  $[\alpha]_D = -90.0$  ( $c = 0.32$ ,  $\text{CHCl}_3$ ); IR (film)  $\nu_{\text{max}}$  3448, 2965, 2930, 1700, 1654, 1458, 1449, 1388, 1385, 1247, 1111, 1084, 1056, 1017, 966, 754  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.16 (s, 1 H), 6.11 (d,  $J = 15.3$  Hz, 1 H), 6.05 (s, 1 H), 5.58 (dd,  $J = 9.9, 6.4$  Hz, 1 H), 5.18 (dt,  $J = 9.6, 4.7$  Hz, 1 H), 5.09 (dd,  $J = 15.6, 9.0$  Hz, 1 H), 4.91 (d,  $J = 4.4$  Hz, 1 H), 3.82 (dd,  $J = 9.2, 9.2$  Hz, 1 H), 3.74–3.67 (m, 2 H), 3.58 (s, 3 H), 3.58–3.54 (m, 1 H), 3.52–3.45 (m, 3 H), 3.41 (s, 3 H), 3.35 (s, 3 H), 3.37–3.33 (m, 1 H), 2.85 (dd,  $J = 8.3, 6.1$  Hz, 1 H), 2.78 (dd,  $J = 9.2, 9.2$  Hz, 1 H), 2.61–2.54 (m, 1 H), 2.53–2.46 (m, 1 H), 2.28 (bd,  $J = 3.9$  Hz, 1 H), 2.09 (s, 3 H), 2.06 (s, 3 H), 1.98–1.85 (m, 2 H), 1.83 (s, 3 H), 1.79–1.72 (m, 3 H), 1.65 (s, 3 H), 1.49–1.44 (m, 1 H), 1.40–1.33 (m, 1 H), 1.29 (d,  $J = 6.1$  Hz, 3 H), 1.09 (d,  $J = 6.6$  Hz, 3 H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  170.3, 147.2, 146.2, 142.0, 141.0, 134.8, 134.4, 133.7, 133.5, 125.7, 124.9, 95.6, 86.6, 84.6, 83.5, 76.5, 75.7, 75.2, 74.1, 72.4, 68.7, 62.3, 61.9, 60.8, 39.3, 36.9, 36.0, 26.0, 19.5, 19.3, 18.7, 17.8, 15.2, 13.5; HRMS (MALDI-FTMS) for  $\text{C}_{34}\text{H}_{54}\text{NaO}_{10}$  [ $\text{M} + \text{Na}^+$ ] calcd 645.3609, found 645.3613.

**Lactone 75.** Hydroxy diene **68** (68 mg, 0.10 mmol) was dissolved in DMF (1 mL) and cooled to 0 °C. Imidazole (68 mg, 1.0 mmol) was added, followed by TBSCl (121 mg, 0.8 mmol) and the reaction mixture was warmed to room temperature and stirred for 15 h. The reaction mixture was quenched with saturated aqueous  $\text{NaHCO}_3$  (5 mL), warmed to room temperature and diluted with water (5 mL), extracted with ether ( $3 \times 10$  mL). The combined organic layer was washed with brine (10 mL), dried over  $\text{Na}_2\text{SO}_4$ , filtered and concentrated. The crude product was purified by flash chromatography (hexanes:EtOAc, 4:1) to afford diene TBS ether (61 mg, 81%) which was dissolved in dioxane (7 mL). KOH (2 M in  $\text{H}_2\text{O}$ , 0.71 mL, 1.42 mmol) was added and the mixture was heated to 75 °C for 18 h. After cooling to room

temperature, the reaction was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  (5 mL). The aqueous layer was extracted with EtOAc ( $3 \times 10$  mL) and the combined organic layer was washed with brine (10 mL), dried over  $\text{Na}_2\text{SO}_4$  and concentrated. The crude hydroxy acid (**69**) so obtained was taken to the next step without purification.

Crude seco dihydroxy acid **69** (32 mg, 0.045 mmol) was dissolved in THF (4 mL) and cooled to 0 °C.  $\text{Et}_3\text{N}$  (0.25 mL, 1.8 mmol) and 2,4,6-trichlorobenzoyl chloride (0.14 mL, 0.9 mmol) was added and the resulting mixture was stirred at room temperature for 2 h and then the cloudy suspension was added dropwise via cannula to a solution of 4-DMAP (440 mg, 3.6 mmol) in toluene (160 mL) at room temperature over 15 min. The white suspension was heated to 65 °C and stirred for 5 h. The reaction was quenched with saturated aqueous  $\text{NH}_4\text{Cl}$  (30 mL) and the aqueous layer was extracted with EtOAc ( $3 \times 60$  mL). The combined organic layer was washed with brine (30 mL), dried over  $\text{Na}_2\text{SO}_4$ , and concentrated. The crude product was purified by flash chromatography (hexanes:EtOAc, 6:1) to afford lactone **75** (20 mg, 70%) as a clear, colorless, viscous oil. **75**:  $R_f$  = 0.45 (silica gel, hexanes:EtOAc, 4:1);  $[\alpha]_D^{25} = +21.0$  ( $c$  = 0.80,  $\text{CHCl}_3$ ); IR (film)  $\nu_{\text{max}}$  2928, 2856, 1704, 1602, 1462, 1386, 1360, 1249, 1113, 965, 836, 775  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (500 MHz,  $\text{CDCl}_3$ )  $\delta$  7.17 (s, 1 H), 6.08 (s, 1 H), 5.94 (d,  $J$  = 15.8 Hz, 1 H), 5.45 (dd,  $J$  = 7.3, 7.3 Hz, 1 H), 5.26 (dd,  $J$  = 15.8, 8.8 Hz, 1 H), 5.20–5.14 (m, 1 H), 5.07 (d,  $J$  = 10.3 Hz, 1 H), 3.77 (dd,  $J$  = 8.6, 8.6 Hz, 1 H), 3.58 (dd,  $J$  = 10.6, 3.7 Hz, 1 H), 3.52–3.45 (m, 1 H), 3.40 (s, 3 H), 3.38–3.34 (m, 1 H), 3.36 (s, 3 H), 2.84 (dd,  $J$  = 8.8, 8.1 Hz, 1 H), 2.47–2.36 (m, 2 H), 2.19–2.14 (m, 1 H), 2.11 (s, 3 H), 2.09 (s, 3 H), 1.98–1.86 (m, 2 H), 1.82 (s, 3 H), 1.67–1.60 (m, 1 H), 1.63 (s, 3 H), 1.34–1.24 (m, 1 H), 1.08 (d,  $J$  = 6.6 Hz, 3 H), 0.93 (s, 9 H), 0.89 (s, 9 H), 0.11 (s, 3 H), 0.07 (s, 3 H), 0.07 (s, 3 H), 0.03 (s, 3 H);  $^{13}\text{C}$  NMR (125 MHz,  $\text{CDCl}_3$ )  $\delta$  168.8, 145.5, 145.3, 140.8, 135.9, 133.4, 131.8, 131.5, 129.2, 123.2, 119.8, 81.4, 81.1, 75.6, 74.4, 70.4, 61.2, 59.4, 40.6, 35.8, 35.7, 26.2, 25.9, 24.7, 18.3, 17.7, 17.4, 16.5, 13.8, 12.0, –

3.8, -3.9, -4.4, -4.7; HRMS (MALDI-FTMS) for  $C_{39}H_{70}NaO_6Si_2$   $[M + Na^+]$  calcd 713.4603, found 713.4597.

**Compound 76.** Lactone **75** (15 mg, 0.022 mmol) was dissolved in THF (1.6 mL) and cooled to  $-30\text{ }^{\circ}\text{C}$ . HF•py (0.4 mL) was added dropwise and then the reaction mixture was kept at  $0\text{ }^{\circ}\text{C}$  for 48 h. Pyridine (2 mL) was added to the reaction mixture at  $-30\text{ }^{\circ}\text{C}$  and then the mixture was poured to a pre-cooled (at  $0\text{ }^{\circ}\text{C}$ ) mixture of saturated aqueous  $NaHCO_3$  (10 mL) and EtOAc (10 mL). The mixture was stirred at  $0\text{ }^{\circ}\text{C}$  for 30 min. The aqueous layer was extracted with EtOAc ( $5 \times 10\text{ mL}$ ) and the combined organic layer was washed with brine (20 mL), dried over  $Na_2SO_4$ , and concentrated. The crude product was purified by flash chromatography (silica gel,  $CHCl_3$ :MeOH:H $_2$ O, 15:3:1) to afford compound **76** (8 mg, 80%) as a clear, colorless, viscous oil. **76**:  $R_f = 0.20$  (silica gel, hexanes:EtOAc, 1:1);  $[\alpha]_D = -9.5$  ( $c = 0.20$ ,  $CHCl_3$ ); IR (film)  $\nu_{max}$  3446, 2929, 2846, 1700, 1458, 1388, 1251, 1106, 1031, 970, 867, 838, 777, 746  $cm^{-1}$ ;  $^1H$  NMR (600 MHz,  $CDCl_3$ )  $\delta$  7.19 (s, 1 H), 6.09 (s, 1 H), 6.08 (d,  $J = 15.4\text{ Hz}$ , 1 H), 5.57 (dd,  $J = 7.9, 7.9\text{ Hz}$ , 1 H), 5.36 (dd,  $J = 15.8, 8.3\text{ Hz}$ , 1 H), 5.23–5.17 (m, 1 H), 5.14 (d,  $J = 10.1\text{ Hz}$ , 1 H), 4.12 (dd,  $J = 14.0, 7.0\text{ Hz}$ , 1 H), 3.90 (d,  $J = 8.3\text{ Hz}$ , 1 H), 3.54–3.46 (m, 3 H), 3.43 (s, 3 H), 3.40–3.33 (m, 2 H), 3.37 (s, 3 H), 2.88 (dd,  $J = 8.1, 5.9\text{ Hz}$ , 1 H), 2.55–2.45 (m, 1 H), 2.13 (s, 3 H), 2.08 (s, 3 H), 1.94–1.88 (m, 1 H), 1.87 (s, 3 H), 1.81–1.76 (m, 1 H), 1.69 (s, 3 H), 1.51–1.38 (m, 1 H), 1.27–1.24 (m, 2 H), 1.14 (d,  $J = 7.0\text{ Hz}$ , 3 H);  $^{13}C$  NMR (125 MHz,  $CDCl_3$ )  $\delta$  168.8, 146.0, 145.2, 140.6, 137.2, 133.5, 132.5, 132.3, 131.8, 127.6, 123.2, 82.1, 79.8, 74.3, 73.8, 71.0, 60.5, 59.4, 39.6, 35.5, 34.7, 24.5, 17.6, 17.2, 16.3, 13.8, 12.0; HRMS (MALDI-FTMS) for  $C_{27}H_{42}NaO_6$   $[M + Na^+]$  calcd 485.2873, found 485.2866.

**Compound 77.** Macrolactone **41** (14 mg, 0.010 mmol) was dissolved in THF (2.0 mL) and cooled to  $-30\text{ }^{\circ}\text{C}$ . HF•py (0.5 mL) was added dropwise and then the reaction mixture was kept at  $-25\text{ }^{\circ}\text{C}$  for 24 h and then stirred at  $0\text{ }^{\circ}\text{C}$  for 48 h. Pyridine (2 mL) was added to the reaction mixture at  $-30\text{ }^{\circ}\text{C}$  and then the mixture was poured to a pre-cooled (at  $0\text{ }^{\circ}\text{C}$ ) mixture of



saturated aqueous  $\text{NaHCO}_3$  (10 mL) and EtOAc (10 mL). The mixture was stirred at 0 °C for 30 min. The aqueous layer was extracted with EtOAc ( $5 \times 10$  mL) and the combined organic layer was washed with brine (20 mL), dried over  $\text{Na}_2\text{SO}_4$ , and concentrated. The crude product was purified by flash chromatography (silica gel,  $\text{CHCl}_3$ :MeOH:H<sub>2</sub>O, 15:3:1) to afford compound **77** (8 mg, 4:1 ratio of regioisomers, 80%) as a clear, colorless, viscous oil. **77** [reported as a mixture (4:1 ratio of regioisomer) suffering from the facile lactone migration]:  $R_f = 0.50$  (silica gel,  $\text{CHCl}_3$ :MeOH, 10:1);  $[\alpha]_D = -22.0$  ( $c = 0.35$ ,  $\text{CHCl}_3$ ); IR (film)  $\nu_{\text{max}}$  3448, 2928, 1695, 1670, 1448, 1384, 1252, 1111, 1079, 1026, 967, 908, 732  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR (600 MHz,  $\text{CDCl}_3$ )  $\delta$  7.27 (s, 1 H), 6.15 (d,  $J = 15.8$  Hz, 1 H), 6.14 (s, 1 H), 5.62 (dd,  $J = 9.9, 5.9$  Hz, 1 H), 5.24 (d,  $J = 11.0$  Hz, 1 H), 5.16 (d,  $J = 9.6$  Hz, 1 H), 5.07 (dd,  $J = 15.8, 9.2$  Hz, 1 H), 5.05 (d,  $J = 16.0, 9.0$  Hz, 1 H), 4.92 (d,  $J = 3.5$  Hz, 1 H), 4.19 (ddd,  $J = 9.2, 3.1, 2.6$  Hz, 1 H), 4.01–3.97 (m, 1 H), 3.87–3.83 (m, 3 H), 3.76–3.69 (m, 4 H), 3.59 (s, 3 H), 3.56–3.49 (m, 2 H), 3.42–3.37 (m, 2 H), 3.35 (s, 3 H), 3.30 (s, 3 H), 3.21 (dd,  $J = 9.4, 3.3$  Hz, 1 H), 3.10 (dd,  $J = 9.4, 7.7$  Hz, 1 H), 2.79–2.77 (m, 1 H), 2.72 (dd,  $J = 9.4, 5.7$  Hz, 1 H), 2.62–2.44 (m, 3 H), 2.14 (s, 3 H), 2.09 (s, 3 H), 2.01–1.95 (m, 3 H), 1.88 (s, 3 H), 1.65 (s, 3 H), 1.49–1.36 (m, 4 H), 1.29 (d,  $J = 6.1$  Hz, 3 H), 1.10 (d,  $J = 6.6$  Hz, 3 H), 1.04 (d,  $J = 6.6$  Hz, 3 H), 0.84 (d,  $J = 7.0$  Hz, 3 H);  $^{13}\text{C}$  NMR (150 MHz,  $\text{CDCl}_3$ )  $\delta$  168.0, 148.0, 146.4, 143.7, 141.2, 140.7, 133.4, 133.1, 133.0, 132.2, 124.5, 124.0, 99.7, 94.1, 85.2, 83.2, 82.2, 81.8, 76.3, 75.0, 74.3, 74.0, 73.4, 72.7, 71.3, 70.6, 69.1, 67.3, 66.6, 60.9, 60.8, 59.3, 59.1, 37.9, 36.9, 35.8, 31.9, 29.7, 28.5, 26.4, 17.9, 17.6, 14.1, 12.0, 4.8; HRMS (MALDI-FTMS) for  $\text{C}_{44}\text{H}_{72}\text{NaO}_{15}$  [ $\text{M} + \text{Na}^+$ ] calcd 863.4763, found 863.4766.