Supporting Information for

New Silicon-Mediated, Sequential Ring Expansions of n-sized 2-

Cycloalkenones into Hydroxyolefinic n+m+p Medium-Sized Lactones:

Short Synthesis of (-)-Phoracantholide-J

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Experimental Section

Unless otherwise noted, all reactions were performed in oven dried glassware and were stirred under an atmosphere of ultra high purity Argon. The tetrahydrofuran used was distilled from sodium/benzophenone, and the dichloromethane was distilled from calcium hydride. All other reagents were used as received from commercial suppliers, unless otherwise noted. Analytical TLC analysis was conducted on precoated glass-backed silica gel plates (Merck Kieselgel 60 F₂₅₄, 250 μ thickness) and visualized with *p*-anisaldehyde or KMnO₄ stains. Column chromatography was performed using flash silica gel (particle size 230-400 mesh). Yields reported are for pure products (>95% based on their chromatographic and spectroscopic homogeneity), and are unoptimized. NMR spectra were obtained on a Varian XL-400 spectrometer, operating at 400 MHz for ¹H and 100 MHz for ¹³C, or a Bruker 400 spectrometer operating at the same frequencies. Chemical shifts are reported in ppm (δ) and are referenced to CDCl₃ (7.26 and 77.0 ppm).

4-tert-butyltrimethylsiloxy-1,2-epoxybutane. Prepared following the

known procedure from Ficini, J.; Barbara, C.; Desmale, D.; Ouerfelli,

O. *Heterocycles*. **1987**, 25, 329.

5-tert-butyltrimethylsiloxy-1,2-epoxypentane. Prepared following

the known procedure from Yang, L.; Weber, A.E.; Greenlee, W.J.;

Patchett, A.A. *Tetrahedron Lett.* **1993**, 34, 7035.

Gem-dimethyl epoxide. 2,2-Dimethyl-4-penten-1-ol (2.0 g, 17.8 mmol, Aldrich) was placed in a 50 mL flask and dissolved in methanol (20 mL). To this was added NaBH₄ (1.36 g, 35.6 mmol) in 3 portions over 15 minutes at 0 °C. This mixture was allowed to warm up to room temperature over the course of 1 hour. After starting material had been consumed, the reaction was quenched by the slow addition of H₂O (4 mL) and concentrated to remove the methanol. The water layer was then poured into a separatory funnel and extracted with Et₂O (2x 25 mL). The ether fractions were washed with brine (1x 50mL), dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (70 % hexanes, 30% ethyl acetate) to give the desired alcohol (1.6 g, 80 %) as a colorless oil.

This alcohol (1.6 g, 14.3 mmol) was then placed in a 250 mL flask and dissolved in CH₂Cl₂ (60 mL). To this was added imidazole (2.86 g, 42.9 mmol) and TBSCl (3.2 g, 21.5 mmol) and the reaction mixture was allowed to stir overnight. After it was evident that all starting material had been consumed, the contents of the flask were poured into a separatory funnel and extracted from H₂O (2x 50 mL). The combined organics were dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (80 % hexanes, 20% ethyl acetate) to give the desired olefinic protected alcohol **5** (2.46 g, 66 %) as a colorless oil.

The olefinic silyl protected alcohol (2.5g, 11.5 mmol) was placed in a 100 mL flask, dissolved in CH₂Cl₂ (30 mL), and cooled to 0 °C. A separate flask was charged with *m*-CPBA (3.86 g, 22.4 mmol, 77 %) and Et₂O (20 mL). The residual water collected at the bottom of the flask and was not cannulated into the reaction flask. The reaction was warmed to room temperature and stirred overnight. The next day, the mixture was

quenched with sodium bisulfite and extracted with CH₂Cl₂. The organic fractions were washed with saturated NaHCO₃ and H₂O, dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (80% hexanes, 20% ethyl acetate) to give the desired epoxide (1.52 g, 58 %) as a colorless oil. ¹H NMR (CDCl₃) δ 3.31 (dd, *J*=9.6, 27.2, 2H), 3.01-2.94 (m, 1H), 2.75-2.71 (m, 1H), 2.41-2.40 (m, 1H), 1.45 (d, *J*=6.0, 2H), 0.938 (s, 6H), 0.88 (s, 9H), 0.02 (s, 6H); ¹³C NMR (CDCl₃) δ 71.73, 49.55, 46.99, 41.64, 35.55, 25.86, 24.63, 24.25, 18.24, -5.58; IR (neat, cm⁻¹) 2955, 2919, 2861, 2884, 1467, 1249, 1102, 838, 773; HRMS (EI) *m/z* (*M*⁺) calcd. 244.1858 for C₁₃H₂₈O₂Si⁺, found 244.1832.

(4-*R*)-4-*tert*-butyldimethylsiloxy-1,2-epoxypentane. Prepared following the known procedure from Goldberg, A.O.; Balzarini, J.; Gilbert, I.H.

Bioorg. Med. Chem. Lett. **1988**, 8, 1211.

Oxetane, p=2. Prepared following the known procedure from Kwon, D.W., Kim, Y.H. *Journal of Organic Chemistry.* **2002**, 67, 9488.

Lactone 4a. Silyl enol-ether **1a** (0.228g, 1.0 mmol) and THF (1.5 mL) were added to a 25 mL flask. The flask was cooled to 0 °C and MeLi (0.64 mL, 1.0 mmol, 1.6 M in Et₂O) was added dropwise and stirred for 5 minutes. The flask was then cooled to -78 °C before a solution of trimethylene oxide (0.029 g, 0.499 mmol) in THF (1.5 mL) was cannulated into the reaction. The reaction stirred for 5 minutes before BF₃·Et₂O (0.064 mL, 0.499 mmol, neat) was added very slowly (1drop / 4 sec), using a

100 μ L syringe, while cooling the needle with a piece of dry ice. After 30 minutes, the reaction was quenched with phosphate buffer (3.0 mL, pH 7.0) and warmed to room temperature. The mixture was extracted with Et₂O (3x 25 mL), and the combined organics were dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (90% hexanes, 10% ethyl acetate, ~1% TEA) to give the desired hemiketal **3a** (0.072 g, 67%) as a colorless oil.

Hemiketal **3a** (0.072 g, 0.336 mmol) was placed in a 25 mL flask and dissolved in a 1:1 mixture of acetonitrile (2 mL) and H₂O (2 mL), and to this was added ceric ammonium nitrate (0.736 g, 1.34 mmol). The reaction immediately turned a yellow color indicating the completion of the reaction (less than 1 minute). The reaction was quenched with H₂O (3 mL), and extracted with ether (3x 25 mL). The combined ether fractions were washed once with NaHCO₃ (1x 25 mL), dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (90% hexanes, 10% ethyl acetate) to give the desired lactone **4a** (0.037 g, 80%) as a colorless oil. ¹H NMR (CDCl₃) δ 5.54-5.37 (m, 2H), 4.55-4.49 (m, 1H), 4.05-3.99 (m, 1H), 2.34-2.14 (m, 6H), 1.19-1.69 (m, 2H); ¹³C NMR (CDCl₃) δ 174.47, 133.97, 126.17, 66.31, 35.21, 33.63, 29.28, 27.74; IR (neat, cm⁻¹) 2944, 2859, 1734, 1444, 1230, 1149, 980; HRMS (CI) *m/z* (M+O₂+Na) calcd. 195.0628 for C₈H₁₂O₄Na⁺, found 195.0626.

Lactone 4b. Prepared in the same manner as lactone **3a**, using **1b** instead of **1a**. ¹H NMR (CDCl₃) δ 5.546-5.475 (m, 1H), 5.290-5.216 (m, 1H), 5.024-4.961 (m, 1H), 3.721-3.677 (m, 1H), 2.304-2.085 (m, 3H), 2.080-1.713 (m, 6H), 1.628-1.671 (m, 1H); ¹³C NMR (CDCl₃) δ 176.13, 133.50, 128.23, 64.03, 34.74, 33.83,

31.91, 27.60, 26.09; IR (neat, cm^{-1}) 2931, 2837, 1725, 1431, 1343, 1220, 1179, 1155, 1108, 1038, 967; HRMS (EI) m/z (M^+) calcd. 154.0993 for $\text{C}_9\text{H}_{14}\text{O}_2^+$, found 154.0965.

***E*-Lactone 6a.** Prepared in the same manner as lactone **3a**. ^1H NMR (CDCl_3) δ 5.63-5.55 (m, 1H), 5.36-5.28 (m, 1H), 4.78-4.71 (m, 1H), 3.58-3.57 (m, 2H), 3.30-3.28 (m, 1H), 2.47-2.27 (m, 5H), 2.10-2.04 (m, 1H), 1.86-1.58 (m, 4H); ^{13}C NMR (CDCl_3) δ 177.30, 138.89, 123.41, 57.58, 38.01, 35.54, 34.78, 32.81, 23.16; IR (neat, cm^{-1}) 3430, 2952, 1729; HRMS (CI) m/z (M^+Na) calcd. 207.0992 for $\text{C}_{10}\text{H}_{16}\text{O}_3\text{Na}^+$, found 209.0992.

Lactone 7a. Lactone **6a** (0.017 g, 0.092 mmol) was placed into a 5 mL flask. To this was added methanol (2 mL) and palladium on carbon (0.002 g, 10%). The flask was then covered with a rubber septa before evacuating and placing it under a hydrogen atmosphere. After 2 hours, the reaction was quickly passed over celite to remove the palladium, and washed several times with ether. The ether was washed with H_2O , extracted, and the combined organics were dried over MgSO_4 and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (70% hexanes, 30% ethyl acetate) to give the desired saturated lactone **6a** (0.010 g, 60%) colorless oil.

Lactone **6a** was dissolved in CH_2Cl_2 (4 mL) and *p*-toluenesulfonic acid (catalytic amount) was added and allowed to stir at room temperature for 24 hr. The reaction was quenched with water (3.0 mL) and was extracted with CH_2Cl_2 (3x 25 mL), and the combined organics were dried over MgSO_4 and concentrated *in vacuo*. The crude product

was purified by silica gel chromatography (70% hexanes, 30% ethyl acetate) to give the desired lactone **7a** (0.008g, 80%) as a colorless oil. ^1H NMR (CDCl_3) δ 4.34-4.29 (m, 1H), 4.19-4.14 (m, 1H), 3.95-3.90 (m, 1H), 2.35-2.31 (m, 2H), 2.09-1.93 (m, 2H), 1.75-1.32 (m, 10H); ^{13}C NMR (CDCl_3) δ 173.52, 70.02, 60.53, 35.46, 33.32, 33.24, 25.99, 24.53, 21.19, 19.44; IR (neat, cm^{-1}) 3409, 2949, 2868, 1730, 1251, 1040; HRMS (CI) m/z (M^+Na) calcd. 209.1148 for $\text{C}_{10}\text{H}_{18}\text{O}_3\text{Na}^+$, found 209.1153.

Lactone 9, n=5, p=1. Silylenol-ether **1a**⁴ (2.50 g, 10.9 mmol) and THF (20.0 mL) were added to a flame dried 100 mL flask and was then cooled to 0 °C. MeLi (7.01 mL, 11.3 mmol, 1.6 M in Et_2O) was

added dropwise turning the solution bright yellow. After 5 minutes, the flask was removed from the ice bath, and cooled to -78 °C before a solution of *t*-butyldimethylsilyl glycidol ether (1.04 g, 5.50 mmol) in THF (5.0 mL) was cannulated into the reaction. This stirred for 5 minutes before $\text{BF}_3 \cdot \text{Et}_2\text{O}$ (0.693 mL, 5.50 mmol, neat) was added very slowly (1drop/4sec) while cooling the needle with a piece of dry ice. The reaction was quenched after 30 minutes of stirring with phosphate buffer (15.0 mL, pH 7.0) and warmed to room temperature. The mixture was extracted with Et_2O (3x 50 mL), and the combined organics were dried over MgSO_4 and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (90% hexanes, 10% ethyl acetate, ~1% TEA) to give the desired hemiketal (1.39 g, 73%) as a colorless oil.

Hemiketal **8, n = 5, p = 1** (1.39 g, 4.04 mmol) was placed in a 250 mL flask with CH_2Cl_2 (100.0 mL) and cooled to 0 °C. $\text{PhI}(\text{OAc})_2$ (1.43 g, 4.44 mmol) and then I_2 (1.02 g, 4.04 mmol, crystals) were added. The reaction immediately turned a dark purple color.

The reaction was stirred for 5 hrs at 0 °C before quenching with a saturated solution of sodium thiosulfate. The mixture was extracted with CH₂Cl₂ (3x 50 mL), and the combined organics were dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (90 % hexanes, 10% ethyl acetate) to give lactone (0.73 g, 67 %) as a colorless oil. ¹H NMR (CDCl₃) δ 5.81-5.73 (m, 2H), 4.64 - 4.58 (m, 1H), 3.73 (dq, *J* = 10.4, 4.8 Hz, 2H), 2.89-2.72 (m, 2H), 2.55-2.47 (m, 1H), 2.38-2.30 (m, 1H), 2.20-2.90 (m, 2H), 0.901 (s, 9H), 0.073 (d, *J* = 4.4Hz, 6H); ¹³C NMR (CDCl₃) δ 176.76, 132.67, 128.13, 77.84, 64.88, 37.94, 30.59, 25.87, 18,30, -5.32, -5.35; IR (neat, cm⁻¹) 3025, 2955, 2931, 2849, 1755, 1467, 1249, 1208, 1149, 1055, 832, 779. HRMS (CI) *m/z* (M⁺Na) calcd. 293.1543 for C₁₄H₂₆O₃SiNa⁺, found 293.1532.

Lactone 9, n=5, p=2. Prepared in the same manner as lactone 9, n=5, p=1. ¹H NMR (CDCl₃) δ 5.83–5.72 (m, 2H), 4.77-4.71 (m, 1H), 3.70 (dd, *J* = 7.2, 5.2 Hz, 2H), 2.8 -2.68 (m, 2H), 2.5-2.42 (m, 1H), 2.36-2.29 (m, 1H), 2.17-2.10 (m, 2H), 1.89-1.73 (m, 2H), 0.894 (s, 9H), 0.055 (d, *J* = 3.2 Hz, 6H); ¹³C NMR (CDCl₃) δ 177.04, 132.50, 128.33, 75.24, 59.50, 37.80, 37.76, 34.54, 25.91, 24.30, 18.28, –5.38, –5.45; IR (neat, cm⁻¹) 3014, 2954, 2856, 1751, 1471, 1216, 1103, 836; HRMS (CI) *m/z* (M+Na) caclcd. 307.1699 for C₁₅H₂₈O₃SiNa⁺, found 307.1689.

Lactone 9, n=5, p=3. Prepared in the same manner as lactone 9, n=5, p=1. ¹H NMR (CDCl₃) δ 5.82-5.72 (m, 2H), 4.6-4.59 (m, 1H), 3.70-3.59 (m, 2H), 2.90-2.70 (m, 2H), 2.50-2.42 (m, 1H), 2.35-2.27 (m, 1H), 2.13-2.03 (m, 2H), 1.70-1.59 (m, 2H), 0.891 (s, 9H), 0.047 (s, 6H); ¹³C NMR (CDCl₃) δ

177.38, 132.63, 128.41, 78.21, 62.57, 37.81, 34.48, 31.02, 28.98, 25.95, 24.37, 18.33, -
5.311; IR (neat, cm^{-1}) 2929, 2856, 1749, 1462, 1253, 1214, 1100, 1057, 836, 776. HRMS
(CI) m/z ($\text{M}+\text{Na}$) calcd. 321.1856 for $\text{C}_{16}\text{H}_{30}\text{O}_3\text{SiNa}^+$, found 321.1862.

Lactone 9, n=6, p=1. Prepared in the same manner as lactone **9, n=5, p=1**, except using **1b** instead of **1a**. ^1H NMR (CDCl_3) δ 5.54-5.44 (m, 2H), 4.84-4.78 (m, 1H), 3.77-3.67 (m, 2H), 2.52-2.22 (m, 4H), 2.12-2.01 (m, 3H), 1.83-1.73 (m, 1H), 0.90 (s, 9H), 0.07 (s, 3H), 0.06 (s, 3H); ^{13}C NMR (CDCl_3) δ 174.10, 134.62, 124.60, 73.33, 64.74, 33.49, 30.25, 26.49, 25.81, 25.26, 18.29, -5.32; IR (neat, cm^{-1}) 2954, 2930, 2857, 1746, 1472, 1360, 1255, 1132, 1097, 837, 778; HRMS (FAB) m/z (M^+) calcd. 284.1807 for $\text{C}_{15}\text{H}_{28}\text{O}_3\text{Si}^+$, found 284.1818.

Lactone 9, n=6, p=2. Prepared in the same manner as lactone **9, n=5, p=1**, except using **1b** instead of **1a**. ^1H NMR (CDCl_3) δ 5.83-5.71 (m, 2H), 4.77-4.70 (m, 1H), 3.70 (dd, $J = 7.2, 5.2$ Hz, 2H), 2.85-2.68 (m, 2H), 2.50-2.42 (m, 1H), 2.36-2.29 (m, 1H), 2.17-2.10 (m, 2H), 1.89-1.73 (m, 2H), 0.89 (s, 9H), 0.05 (d, $J = 3.2, 6\text{H}$); ^{13}C NMR (CDCl_3) δ 177.04, 132.50, 128.33, 75.24, 59.50, 37.80, 37.76, 34.53, 25.91, 24.30, 18.2, -5.38, -5.45; IR (neat, cm^{-1}) 3014, 2954, 2856, 1751, 1471, 1216, 1103, 836; HRMS (CI) m/z (M^+Na) calcd. 307.1699 for $\text{C}_{15}\text{H}_{28}\text{O}_3\text{SiNa}^+$, found 307.1689.

Lactone 9, n=6, p=3. Prepared in the same manner as lactone **9, n=5, p=1**, except using **1b** instead of **1a**. ^1H NMR (CDCl_3) δ 5.49-

5.44 (m, 2H), 4.80-4.74 (m, 1H), 3.65-3.61 (m, 2H), 2.52-2.42 (m, 1H), 2.38-2.22 (m, 3H), 2.09-1.99 (m, 3H), 1.80-1.76 (m, 1H), 1.68-1.56 (m, 4H), 0.89 (s, 9H), 0.04 (s, 6H); ^{13}C NMR (CDCl_3) δ 174.57, 134.41, 124.88, 73.15, 62.62, 34.12, 33.64, 30.78, 28.93, 26.55, 25.93, 25.27, 18.32, -5.33; IR (neat, cm^{-1}) 2928.2, 2856.5, 1730.7, 1471.8, 1361.7, 1253.5, 1097.1, 835.8, 775.7; HRMS (EI), m/z (M^+Na) calcd. 335.2012 for $\text{C}_{17}\text{H}_{32}\text{O}_3\text{SiNa}^+$, found 335.2021.

Lactone 10; n=5, p=1. A 10 mL flask was charged with lactone **9**; n=5, p=1 (0.025 g, 0.0924 mmol) and THF (2.5 mL). To this mixture, TBAF (0.23 mL, 0.231 mmol, 1.0 M in THF) was added at room temperature.

After 2 hours of stirring, the reaction was quenched by the addition of H_2O (3 mL), and extracted with Et_2O (2x 25 mL). The ether fractions were washed with brine (1x 50mL), dried over MgSO_4 and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (70 % hexanes, 30% ethyl acetate) to give the desired lactone (0.010g, 89%) as a colorless oil. ^1H NMR (CDCl_3) δ 5.68-5.61 (m, 2H), 4.59 - 4.55 (m, 1H), 4.14-4.04 (m, 2H), 2.64-2.54 (m, 2H), 2.36-2.43 (m, 1H), 2.34-2.02 (m, 3H), 1.98 (s, 1H); ^{13}C NMR (CDCl_3) δ 174.66, 129.21, 128.11, 70.47, 68.62, 33.87, 32.12, 30.28, 29.67, 24.12; IR (neat, cm^{-1}) 3410, 2925, 2854, 1741, 1458, 1235, 1089, 730; HRMS (EI), m/z ($2\text{M}^+\text{Na}$) calcd. 335.1465 for $\text{C}_{16}\text{H}_{24}\text{O}_6\text{Na}^+$, found 335.1443.

Lactone 10; n=5, p=2. Prepared in the same manner as lactone **10**, n=5, p=1. ^1H NMR (CDCl_3) δ 5.53-5.49 (m, 2H), 4.09-4.03 (m, 1H), 2.50-1.52 (m, 10H); ^{13}C NMR (CDCl_3) δ 172.19, 128.41, 125.49, 33.98, 30.28, 29.67,

22.73; IR (neat, cm^{-1}) 3411, 2920, 1734, 1455, 1331, 1244, 1077; HRMS (CI) m/z (M^+) calcd. 170.0937 for $\text{C}_9\text{H}_{14}\text{O}_3^+$, found 170.0939.

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Lactone 10; n=5, p=3. Prepared in the same manner as lactone **10, n=5, p=1**. Evidenced as a 2:1 mixture of rings in favor of the 8

membered ring lactone. ^1H NMR (CDCl_3) δ 5.81-5.72 (m, 2H, 8 membered ring), 5.48-5.45 (m, 1H, 11 membered ring), 4.6-4.58 (m, 1H, 8 membered ring), 4.24-4.18 (m, 0.5H, 11 membered ring); ^{13}C NMR (CDCl_3) δ 177.48, 132.70, 128.30, 78.21, 71.14, 64.17, 62.33, 37.78, 34.99, 34.53, 30.94, 30.16, 29.68, 28.85, 24.35, 23.44. IR (neat, cm^{-1}) 3401.8, 2924.7, 2854.5, 1733.4, 1456.3, 1217.5, 1055.0, 729.4. HRMS (CI) m/z ($\text{M}+\text{Na}$) calcd. 207.0992 for $\text{C}_{10}\text{H}_{16}\text{O}_3\text{Na}^+$, found 207.0988.

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Lactone 10; n=6, p=1. Prepared in the same manner as lactone **10, n=5, p=1**, using **1b** instead of **1a**. Evidenced as a 10:1 mixture of rings in favor of the 10 membered ring

lactone. ^1H NMR (CDCl_3) δ 5.45-5.30 (m, 2H), 4.51-4.54 (m, 1H), 4.13-4.03 (m, 1H), 3.97-3.86 (m, 1H), 2.63-1.47 (m, 8H); ^{13}C NMR (CDCl_3) δ 174.30, 132.44, 123.96, 68.53, 67.10, 35.14, 32.06, 26.44, 25.29; IR (neat, cm^{-1}) 3411, 2920, 1734, 1455, 1331, 1244, 1077; HRMS (EI) m/z (M^+) calcd. 170.0942 for $\text{C}_9\text{H}_{14}\text{O}_3^+$, found 170.0940.

Lactone 10; n=6, p=2. Prepared in the same manner as lactone **10, n=5, p=1**, using **1b** instead of **1a**. ^1H NMR (CDCl_3) δ 5.52-5.46 (m, 2H),

4.95-4.89 (m, 1H), 3.74-3.71 (m, 2H), 2.80-2.40 (m, 2H), 2.33-2.25 (m, 2H), 2.10-2.01 (m, 2H), 1.89-1.68 (m, 4H); ^{13}C NMR (CDCl_3) δ 175.04, 134.49, 124.65, 70.98, 58.97, 37.08, 34.00, 33.59, 25.52, 25.23. IR (neat, cm^{-1}) 3416, 2949, 2360, 1736, 1448, 1356, 1264, 1217, 1139, 1051. HRMS (EI), m/z (M^+) calcd. 207.0992 for $\text{C}_{10}\text{H}_{16}\text{O}_3\text{Na}^+$, found 207.1002.

Lactone 10; n=6, p=2. Evidenced as a 8:1 mixture of rings in favor of the 11 membered ring lactone. To a solution of lactone **10; n=6, p=2** in CH_2Cl_2 , p-

toluenesulfonic acid was added and allowed to stir at room temperature for 24 hr. The reaction was quenched with water (3.0 mL) and was extracted with CH_2Cl_2 (3x 25 mL). The combined organics were dried over MgSO_4 and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (70% hexanes, 30% ethyl acetate) to give the desired lactone as a colorless oil (80%). ^1H NMR (CDCl_3) δ 5.41-5.29 (m, 2H), 4.27-4.22 (m, 1H), 4.11-3.99 (m, 2H), 2.26-1.73 (m, 10H); ^{13}C NMR (CDCl_3) δ 173.86, 131.15, 125.07, 70.65, 60.41, 35.42, 34.51, 33.17, 26.67, 24.83; IR (neat, cm^{-1}) 3416, 3003, 2950, 2855, 1732, 1449, 1352, 1217, 1148, 1048; HRMS (EI), m/z (M^+) calcd. 207.0992 for $\text{C}_{10}\text{H}_{16}\text{O}_3\text{Na}^+$, found 207.1002.

Lactone 10; n=6, p=3. Prepared in the same manner as lactone **10, n=5, p=1**, using **1b** instead of **1a**. Evidenced as a 15:1 mixture of products in favor of the 9

membered ring lactone. ^1H NMR (CDCl_3) δ 5.50-5.47 (m, 2H, 2H, 9 membered ring),

5.63-5.55 (m, 0.06H, 12 membered ring), 4.83-4.77 (m, 1H, 9 membered ring), 4.48-4.44 (m, 0.06H, 12 membered ring). ^{13}C NMR (CDCl_3) δ 174.68 134.51, 124.78, 73.12, 62.42, 34.15, 33.64, 30.73, 28.81, 26.54, 25.28. IR (neat, cm^{-1}) 3425, 2919, 1737, 1720, 1443, 1267, 1292, 1132, 1055; HRMS (EI), m/z (M^+Na) calcd. 221.1148 for $\text{C}_{11}\text{H}_{18}\text{O}_3\text{Na}^+$, found 221.1134.

Lactone 9a. Prepared in the same manner as lactone **9**, $n=5$,

$p=1$. ^1H NMR (CDCl_3) δ 5.79-5.70 (m, 2H), 4.77-4.71 (m, 1H),

3.29 (dd, $J=9.6, 39.2$, 2H), 2.86-2.79 (m, 1H), 2.73-2.68 (m, 1H), 2.52-2.46 (m, 1H),

2.32-2.25 (m, 1H), 2.10-2.07 (m, 1H), 2.00-1.95 (m, 1H), 1.66-1.60 (m, 1H), 1.47-1.43

(m, 1H), 0.94-0.89 (m, 15H), 0.02 (s, 6H); ^{13}C NMR (CDCl_3) δ 176.96, 132.67, 128.44,

76.01, 71.45, 42.36, 37.94, 36.14, 35.10, 25.88, 24.79, 24.46, 24.09, 18.27, -5.53, -5.55;

IR (neat, cm^{-1}) 2954, 2929, 1748, 1472, 1218, 1098, 1056, 837; HRMS (EI), m/z ($\text{M}+\text{Na}$)

calcd. 349.2169 for $\text{C}_{18}\text{H}_{34}\text{O}_3\text{SiNa}^+$, found 349.2161.

Lactone 10a. Following the procedure as described above for lactone **10**

in 89% yield. ^1H NMR (CDCl_3) δ 5.70-5.65 (m, 1H), 5.55-5.45 (m, 1H),

4.03-3.98 (m, 1H), 3.75 (q, $J=10.8$, 2H), 2.50-2.20 (m, 6H), 1.87-1.81 (m,

1H), 1.36-1.32 (m, 1H), 1.05 (s, 3H), 1.03 (s, 3H); ^{13}C NMR (CDCl_3) δ 173.20, 129.28,

127.58, 73.41, 69.61, 46.09, 35.04, 34.52, 32.79, 28.34, 24.92, 23.45; IR (neat, cm^{-1})

3408, 2956, 1731, 1224, 1150; HRMS (EI), m/z (M^+) calcd. 235.1304 for $\text{C}_{12}\text{H}_{20}\text{O}_3\text{Na}^+$,

found 235.1309.

Lactone 9b. Prepared in the same manner as lactone **9**, **n=5**, **p=1**. ^1H

NMR (CDCl_3) δ 7.376-7.260 (m, 5H), 5.539-5.458 (m, 2H), 5.024-4.966

(m, 1H), 4.631-4.546 (q, $J = 12.4$ Hz, 2H), 3.649-3.547 (m, 2H), 2.540-

2.238 (m, 4H), 2.105-2.020 (m, 2H), 1.856-1.736 (m, 1H); ^{13}C NMR (CDCl_3) δ 174.07,

137.87, 134.72, 128.31, 127.62, 127.58, 124.25, 73.09, 71.58, 71.28, 33.44, 30.52, 26.42,

25.21; IR (neat, cm^{-1}) 2935, 1740, 1454, 1378, 1248, 1090, 1026, 836, 697; HRMS (EI),

m/z (M^+Na) calcd. 283.1304 for $\text{C}_{16}\text{H}_{20}\text{O}_3\text{Na}^+$, found 283.1303.

+

Lactone10b, n=6, p=1. Evidenced as a 9:1 mixture of rings

in favor of the 9 membered ring lactone. A 100 mL flask

was charged with the benzyl lactone (0.220 g, 0.85 mmol)

and dissolved in CH_2Cl_2 (15 mL) and pH buffer ($\text{pH} = 7$, 1.5 mL). To this was added

DDQ (0.768 g, 3.38 mmol) turning the solution a rust color. The next day, and additional

4 equivalents of DDQ was added, and the reaction was monitored. After 5 days of stirring,

the reaction was quenched with H_2O , extracted with CH_2Cl_2 (2x 25 mL), and the

combined organics were washed with NaHCO_3 (1x 50 mL) before being dried over

MgSO_4 and concentrated *in vacuo*. The crude product was purified by silica gel

chromatography (90% hexanes, 10% ethyl acetate) to give the desired lactone **18** (0.114 g,

79 %) as a colorless oil. ^1H NMR (CDCl_3) δ 5.52-5.45 (m, 2H), 5.40-5.31 (m, 0.26H),

4.90-4.85 (m, 1H), 4.50-4.43 (m, 0.11H), 4.08-4.02 (m, 0.12H), 3.93-3.88 (m, 0.12H),

3.79-3.69 (m, 2H), 2.52-2.25 (m, 5H), 2.11-1.74 (m, 7H); ^{13}C NMR (CDCl_3) δ 174.53,

134.66, 124.18, 73.94, 64.45, 33.46, 29.92, 26.41, 25.17; IR (neat, cm^{-1}) 3424, 3010,

2948, 2861, 1740, 1449, 1357, 1263, 1220, 1142, 1054; HRMS (EI) m/z (M^+) calcd.

170.0942 for $C_9H_{14}O_3^+$, found 170.0940.

Lactone10b, n=6, p=1. Evidenced as an 11:1 mixture of rings in favor of the 11 membered ring lactone. To a

solution of lactone **18** (0.018 g, 0.129 mmol) in THF (2 mL),

trimethyl amine (0.020 mL, 0.271 mmol) and TBAF (0.258 mL, 0.259 mmol) was added

and allowed to stir at room temperature for 18 hr. The reaction was quenched with water

(3.0 mL) and was extracted with ether (3x 25 mL), and the combined organics were dried

over $MgSO_4$ and concentrated *in vacuo*. The crude product was purified by silica gel

chromatography (70% hexanes, 30% ethyl acetate) to give the lactone mixture (0.016 g,

88%) as a colorless oil. 1H NMR ($CDCl_3$) δ 5.45-5.30 (m, 2H), 4.51-4.54 (m, 1H), 4.13-

4.03 (m, 1H), 3.97-3.86 (m, 1H), 2.63-1.47 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 174.30, 132.44,

123.96, 68.53, 67.10, 35.14, 32.06, 26.44, 25.29.; IR (neat, cm^{-1}) 3411, 2920, 1734, 1455,

1331, 1244, 1077; HRMS (EI) m/z (M^+) calcd. 170.0942 for $C_9H_{14}O_3^+$, found 170.0940.

Hemi-ketal 12. To 50 mL flask was added silyl enol-ether **1a**

(1.375 g, 5.983 mmol) and THF (7.0 mL). The solution was cooled

to 0°C and MeLi (3.899 mL, 6.234 mmol, 1.6 M in Et_2O) was

added dropwise. After 5 min, the solution was cooled to -78°C. A separate flask

containing a solution of epoxide **11** (0.613 g, 2.836 mmol) in THF (3.0 mL, anhydrous)

was then cannulated into the reaction at -78°C. The reaction was stirred for another 2-3

min at -78°C and $BF_3 \cdot Et_2O$ (0.360 mL, 2.836 mmol, neat) was added very slowly (1

drop/ 4 sec) while cooling the needle with a piece of dry ice. The reaction was quenched after 30 min of stirring with phosphate buffer (3 mL, pH 7.0) and warmed to rt. The mixture was extracted with Et₂O (3 x 25 mL), the organics were combined, dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (80% hexanes, 20% ethyl acetate, ~Et₃N 3%) to give desired product **12** (0.831 g, 78%) as a colorless oil. ¹H NMR (CDCl₃) and ¹³C NMR (CDCl₃) is a complex mixture of diastereomers and equilibrium structural isomers.

Lactone 13. Hemi-ketal **12** (0.831 g, 2.23 mmol) was placed in a 200 mL flask with CH₂Cl₂ (80 mL, anhydrous) and cooled to 0°C. To this was added PhI(OAc)₂ (0.790 g, 2.45 mmol) and then I₂ (0.566 g, 2.23 mmol, crystals). The reaction immediately turned a dark purple color. The reaction was stirred for 8.5 hrs at 0°C. The organics were washed with sodium thiosulfate (sat. solution, 2x 20 mL), H₂O, dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (97% hexanes, 3% ethyl acetate) to give the desired lactone **13** (0.458 g, 69%) as a mixture of easily separable diastereomers. **Major diastereomer:** $[\alpha]^{24}_{\text{D}} -29.67^\circ$ (c = 3.45, CHCl₃); ¹H NMR (CDCl₃) δ 5.83-5.71 (m, 2H), 4.77-4.71 (m, 1H), 3.97-3.90 (m, 1H), 2.83-2.75 (m, 1H), 2.73-2.66 (m, 1H), 2.44-2.37 (m, 1H), 2.31 (ddd, *J* = 15.6, 10.8, 4.4 Hz, 1H), 2.17-2.09 (m, 2H), 1.69 (ddd, *J* = 14.4, 9.6, 3.2 Hz, 1H), 1.58 (ddd, *J* = 14.4, 8.8, 2.8 Hz, 1H), 1.14 (d, *J* = 4 Hz, 3H), 0.88 (s, 9H), 0.67 (d, *J* = 15.2 Hz, 6H); ¹³C NMR (CDCl₃) δ 176.93, 132.45, 128.29, 75.25, 65.34, 45.04, 37.88, 34.85, 25.93, 24.53, 24.35, 17.99, -4.22, -4.80; IR (neat, cm⁻¹) 2956, 2930, 2856, 1751, 1254, 1217, 1054, 837; HRMS (CI) *m/z* (*M*⁺) calcd. 298.1958 for C₁₆H₃₀O₃Si⁺, found

298.1980. **Minor diastereomer:** ^1H NMR (CDCl_3) δ 5.83-5.71 (m, 2H), 4.68-4.61 (m, 1H), 3.96-3.88 (m, 1H), 2.88-2.78 (m, 1H), 2.72 (ddd, $J = 13.6, 6, 3.2$ Hz, 1H), 2.48-2.40 (m, 1H), 2.31 (ddd, $J = 16.4, 11.6, 4.8$ Hz, 1H), 2.14-2.07 (m, 2H), 1.92 (ddd, $J = 14.0, 9.2, 5.6$ Hz, 1H), 1.56 (ddd, $J = 14.0, 7.6, 4.8$ Hz, 1H), 1.20 (d, $J = 6.0$ Hz, 3H), 0.88 (s, 9H), 0.53 (s, 6H); ^{13}C NMR (CDCl_3) δ 177.04, 132.72, 128.26, 75.73, 65.68, 44.36, 37.78, 34.62, 25.83, 24.33, 23.09, 18.05, -4.45, -4.81; IR (neat, cm^{-1}) 2956, 2930, 2856, 1751, 1254, 1217, 1054, 837; HRMS (CI) m/z (M^+) calcd. 298.1958 for $\text{C}_{16}\text{H}_{30}\text{O}_3\text{Si}^+$, found 298.1961.

Lactone 14. Lactone **13** (0.350 g, 1.173 mmol) was placed in a 25 mL flask with THF (8 mL) and then TBAF (5.865 mL, 5.865 mmol, 1.0 M in THF) was added at rt. The reaction stirred at rt. for 8 hours and then was quenched with H_2O . The organics were extracted with Et_2O (3 x 30 mL), dried over MgSO_4 and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (60% hexanes, 40% ethyl acetate) to give the desired lactone **14** (0.173 g, 80%) as a colorless oil. **Major diastereomer:** $[\alpha]^{23}_{\text{D}} -47.67^\circ$ ($c = 2.0$, CHCl_3); ^1H NMR (CDCl_3) δ 5.55-5.43 (m, 2H), 4.94-4.88 (m, 1H), 3.89-3.81 (m, 1H), 2.97-2.42 (broad m, 3H), 2.28-1.79 (m, 6H), 1.33 (d, $J = 9.2$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 172.13, 128.59, 127.60, 71.09 (broad), 69.46, 41.23 (broad), 36.07 (broad), 35.05, 22.82, 20.92; IR (neat, cm^{-1}) 3439, 2934, 1731, 1250, 1095; HRMS (CI) m/z (M^+) calcd. 184.1093 for $\text{C}_{10}\text{H}_{16}\text{O}_3^+$, found 184.1103.

(-)-phoracantholide-J 15. Lactone **14** (0.126 g, 0.684 mmol) was placed in a 25 mL flask with CH_2Cl_2 (5 mL) and then pyridine (0.249 mL,

3.077 mmol) and chloro thionoformate (0.189, 1.367 mmol) were added via syringe over 2-3 min at rt. The reaction stirred at rt. for 3 hours and then was quenched with H₂O. The organics were extracted with E₂O (3 x 25 mL), dried over MgSO₄ and concentrated *in vacuo*. The crude product was purified by silica gel chromatography (95% hexanes, 5% ethyl acetate) to give the desired product (0.208 g, 95%) as a viscous yellow oil.

This xanthate product (0.208 g, 0.649 mmol) was placed in a 25 mL flask with benzene (6 mL, anhydrous). To this solution was added Bu₃SnH (0.262 mL, 0.974 mmol) and then AIBN (0.010 g, 0.065 mmol). The reaction was heated to a reflux for 1.5 hrs and then cooled to rt. The benzene solution was placed directly onto a silica gel column and eluted with hexanes (100%) followed by a hexane/ethyl acetate mixture (90/10) to give the desired product **15** (0.098 g, 90%) as a colorless oil. $[\alpha]^{23}_{-40.31^\circ}$ (c = 2.4, CHCl₃); ¹H NMR (CDCl₃) δ 5.49-5.40 (m, 1H), 5.38-5.30 (m, 1H), 5.11-5.03 (m, 1H), 2.81-2.60 (m, 2H), 2.51 (dt, *J* = 19.6, 6.4 Hz, 1H), 2.21 (ddd, *J* = 19.6, 17.6, 6.0 Hz, 1H), 1.96-1.81 (m, 4H), 1.48-1.30 (m, 2H), 1.24 (d, *J* = 8.8 Hz, 3H); ¹³C NMR (CDCl₃) δ 171.92, 132.12, 127.00, 70.82, 34.79, 29.48 (broad), 25.54, 22.35, 22.24 (broad), 17.30 (broad); IR (neat, cm⁻¹) 3003, 2979, 2941, 2858, 1731, 1455, 1326, 1248, 1144, 1061, 968; HRMS (CI) *m/z* (M⁺) calcd. 168.1150 for C₁₀H₁₆O₂⁺, found 168.1165.

9, n=6, p=3

10, n=5, p=1

10, n=5, p=1

10, n=5, p=2

10, n=5, p=3

10, n=5, p=3

10, n=6, p=1

10, n=6, p=1

10, n=6, p=2

10, n=6, p=2

10, n=6, p=2
(after TsOH)

10, n=6, p=2
(after TsOH)

n=6, p=1 from benzyl ether

n=6, p=1 from benzyl ether

n=6, p=1 from benzyl ether
(after TsOH)

13, Major

13, Major

13, Minor