Total synthesis of borrelidin

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Table of contents

1. General Information	S4
2. Experimental Procedures and Characterization Data	
Compound 2'	S45
Compound 3	S13
Compound 4	S18
Compound 6a	S4
Compound 6b	S5
Compound 7	S5
Compound 8	S6
Compound 11	S7
Compound 12	S8
Compound 13	S8
Compound 14	S9
Compound 14a	S10
Compound 14b	S11
Compound 15	S11
Compound 16	S12
Compound 19	S14
Compound 21	S15
Compound 25	S16
Compound 26	S16
Compound 27	S17
Compound 28	S18
Compound 29a	S29
Compound 29b	S30
Compound 30	S40
Compound 30a	S41
Compound 31	S42
Compound 31a	S43
Compound 31b	S44
Compound 38 (from 56 , only experimental procedure)	S28

Compound 43	S23
Compound 44	S19
Compound 45	S20
Compound 46	S21
Compound 47	S22
Compound 48	S24
Compound 51	S25
Compound 53	S26
Compound 55	S27
Compound 56	S28
Compound 57	S39
Compound 58a	S37
Compound 58b	S38
Compound 59a	S30
Compound 59b	S31
Compound 60a	S32
Compound 60b	S32
Compound 61a	S33
Compound 61b	S33
Compound 61b'	S35
Compound 62a	S34
Compound 62b	S36
3. NMR spectra	S'1 – S'91

General Information. Commercial reagents were used without further purification unless otherwise indicated. Organic solvents were distilled and dried over molecular sieves 3 Å or 4 Å. Reactions were performed in flame-dried glassware under positive Ar pressure with stirring by a magnetic stirbar unless otherwise indicated. Cold baths were generated as follows: 0 °C, wet ice/water; -78 °C, dry ice/acetone. Flash chromatography was performed on silica gel 60N (spherical, neutral, particle size 40-50 µm). TLC was performed on 0.25 mm E. Merck silica gel 60 F254 plates and visualized by UV (254 nm) and cerium ammonium molybdenate.

(2*S*,4*R*)-5-Hydroxy-2,4-dimethylpentyl acetate (6**)**

This compound was prepared according to Mori's procedure. (Fujita, K.; Mori, K. *Eur. J. Org. Chem.* **2001**, 66, 493-502.)

(2*S*,4*R*)-5-(*tert*-butyldimethylsilyloxy)-2,4-dimethylpentyl acetate (6a**)**

To a solution of **6** (1.01 g, 5.83 mmol) in CH₂Cl₂ (20 ml) were added imidazole (790 mg, 11.6 mmol) and TBSCl (1.30 g, 8.74 mmol) at room temperature. The resulting solution was stirred for 30 min and diluted with water. The aqueous phase was extracted with CH₂Cl₂. The combined organic extracts were dried over anhydrous Na₂SO₄ and concentrated in vacuo. Flash chromatography (30:1 hexanes/EtOAc) afforded **6a** (1.64 g, 98%) as a colorless oil. $[\alpha]_D^{22} +5.6^\circ$ (*c* 0.24, CHCl₃); IR (KBr) 2956, 2931, 2892, 2888, 1743, 1251, 1238 cm⁻¹; ¹H-NMR (270 MHz, CDCl₃) δ 0.01 (s, 6H), 0.87 (s, 9H), 0.88 (d, 3H, *J* = 6.6 Hz), 0.90 (m, 1H), 0.92 (d, 3H, *J* = 6.6 Hz), 1.44 (m, 1H), 1.67 (m, 1H), 1.88 (m, 1H), 2.02 (s, 3H), 3.34 (dd, 1H, *J* = 9.6, 6.3 Hz), 3.41 (dd, 1H, *J* = 9.6, 5.6 Hz), 3.80 (dd, 1H, *J* = 10.9, 6.9 Hz), 3.94 (dd, 1H, *J* = 10.9, 5.3 Hz); ¹³C-NMR (67.5 MHz, CDCl₃) δ -5.4, 17.4, 17.8, 18.2, 20.9, 25.9, 30.0, 33.0, 37.4, 68.0, 69.3, 171.2; HRMS (FAB, *m*-NBA) [M+H]⁺ calcd for C₁₅H₃₃O₃Si 289.2199, found 289.2193.

(2*S*,4*R*)-5-(*tert*-Butyldimethylsilyloxy)-2,4-dimethylpentan-1-ol (6b**)**

To a stirred solution of **6a** (1.64 g, 5.72 mmol) in MeOH (6 ml) was added potassium carbonate (870 mg, 6.29 mmol). The reaction was stirred at room temperature for 2h, and then diluted with water. The aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na₂SO₄ and concentrated in vacuo. Flash chromatography (10:1 hexanes/EtOAc) afforded **6b** (1.47 g, 98%) as a colorless oil. $[\alpha]_D^{22} +0.8^\circ$ (*c* 0.32, CHCl₃); IR (KBr) 3411, 2956, 2929, 2858, 1471, 1255, 1093, 837 cm⁻¹; ¹H-NMR (270 MHz, CDCl₃) δ 0.03 (s, 6H), 0.88 (m, 1H), 0.89 (s, 9H), 0.90 (d, 3H, *J* = 6.6 Hz), 0.93 (d, 3H, *J* = 6.6 Hz), 1.42 (m, 1H), 1.70 (m, 1H), 1.81 (m, 1H), 3.32-3.52 (m, 4H); ¹³C-NMR (67.5 MHz, CDCl₃) δ -5.4, 17.7, 17.8, 18.3, 25.9, 33.2, 33.3, 37.3, 68.1, 68.3; HRMS (FAB, *m*-NBA) [M+H]⁺ calcd for C₁₃H₃₁O₂Si 247.2093, found 247.2079.

(2R,4S)-5-(tert-Butyldiphenylsilyloxy)-2,4-dimethylpentan-1-ol (7)

To a solution of **6b** (3.10 g, 12.6 mmol) in DMF (63 ml) were added imidazole (1.70 g, 25.2 mmol) and TBDPSCl (4.90 ml, 18.9 mmol) at 0 °C. The reaction was allowed to warm to room temperature and stirred for 30 min. After addition of water, the reaction mixture was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na₂SO₄ and concentrated in vacuo. Flash chromatography (50:1 hexanes/EtOAc) afforded the corresponding disilyl ether (5.52 g) including unseparable impurities.

To a solution of the disilyl ether in EtOH (40 ml) was added PPTS (1.43 g, 5.70 mmol), and the mixture was allowed to warm up to 50 °C. After 7h, water was added and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na₂SO₄ and concentrated in vacuo. Flash chromatography (15:1 hexanes/EtOAc) afforded **7** (4.19 g, 97% for 2 steps) as a colorless oil. $[\alpha]_D^{23} +1.8^\circ$ (*c* 0.23, CHCl₃); IR (KBr) 3455, 2931, 2856, 1112, 1091, 702 cm⁻¹; ¹H-NMR (270 MHz, CDCl₃) δ 0.91 (d, 3H, *J* = 6.6 Hz), 0.95 (m, 1H), 0.98 (d, 3H, *J* = 6.6 Hz), 1.08 (s, 9H), 1.49 (m, 1H), 1.65 (m, 1H), 1.76 (m, 1H), 3.36 (dd, 1H, *J* = 10.2, 6.6 Hz), 3.45 (m, 1H), 3.51 (dd, 1H, *J* = 9.6, 5.3 Hz), 3.55 (dd, 1H, *J* = 9.6, 5.3 Hz), 7.35-7.72 (m, 10H); ¹³C-NMR (67.5 MHz, CDCl₃) δ 17.4, 17.9, 19.3, 26.9, 33.1, 37.1, 68.2, 68.7, 127.6, 129.5, 134.0, 135.6; HRMS (FAB, *m*-NBA) [M+H]⁺ calcd for C₂₃H₃₅O₂Si 371.2406, found 371.2415.

(2S,4S)-5-(tert-Butyldiphenylsilyloxy)-2,4-dimethylpentanal (8)

To a solution of **7** (3.13 g, 8.44 mmol) in CH₂Cl₂ (88 ml) were added dried MS4Å (17.5 g), NMO (1.09 g, 9.28 mmol) and TPAP (147 mg, 420 μmol) at room temperature. The

reaction mixture was stirred for 30 min and filtered through a silica pad. After evaporation of the filtrate, the residue was purified by flash chromatography (50:1 hexanes/EtOAc) to afford **8** (2.73 mg, 88%) as a colorless oil. $[\alpha]_D^{23} -6.3^\circ$ (c 0.40, CHCl_3); IR (KBr) 2960, 2931, 2858, 1727, 1427, 1112, 1089 cm^{-1} ; ^1H NMR (270 MHz, CDCl_3) δ 0.94 (d, 3H, $J = 6.6$ Hz), 1.04 (d, 3H, $J = 6.6$ Hz), 1.06 (s, 9H), 1.14 (m, 1H), 1.75 (m, 1H), 1.90 (m, 1H), 2.39 (m, 1H), 3.49 (d, 2H, $J = 5.6$ Hz), 7.34-7.70 (m, 10H), 9.54 (d, 1H, $J = 2.3$ Hz); ^{13}C -NMR (67.5 MHz, CDCl_3) δ 14.1, 17.2, 19.3, 26.9, 33.3, 34.5, 44.1, 68.4, 127.6, 129.6, 133.7, 135.6, 205.2; HRMS (FAB, m -NBA) $[\text{M}]^+$ calcd for $\text{C}_{23}\text{H}_{32}\text{O}_2\text{Si}$ 368.2171, found 368.2142.

(S)-1-[(4,4-Dibromo-2-methylbut-3-enyloxy)methyl]-4-methoxybenzene (9)

This compound was prepared according to the known procedure. (Paquette, L. A.; Guevel, R.; Sakamoto, S.; Kim, I. H.; Crawford, J. *J. Org. Chem.* **2003**, *68*, 6096-6107.)

***tert*-Butyl[(2*S*,4*R*,8*S*)-9-(4-methoxybenzyloxy)-2,4,8-trimethylnon-6-ynyloxy]diphenylsilane (11)**

To a solution of **9** (2.66 g, 7.33 mmol) in THF (22.4 ml) was added *n*-BuLi (1.58 M solution in hexane, 9.28 ml, 14.7 mmol) at $-78\text{ }^{\circ}\text{C}$, and the mixture was allowed to warm up to $-40\text{ }^{\circ}\text{C}$. The reaction was stirred for 1 h, and then treated with a solution of **8** (1.80 g, 4.90 mmol) in THF (22.4 ml). The reaction was continued for 1 h at $-30\text{ }^{\circ}\text{C}$, and methyl chloroformate (2.88 ml, 36.8 mmol) was added at $-20\text{ }^{\circ}\text{C}$. The reaction was quenched with saturated aqueous NH_4Cl solution, and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (30:1 hexanes/EtOAc) afforded the corresponding carbonate **10** (3.23 g) including unseparable impurities.

To a solution of palladium acetylacetonate (73.6 mg, 245 μmol) and tributylphosphine (256 μl , 979 μmol) in toluene (22.4 ml) were added a solution of the crude carbonate **10** in toluene (22.4 ml) and ammonium formate (771 mg, 12.2 mmol). The resulting solution was warmed up to $70\text{ }^{\circ}\text{C}$ and stirred for 1 hr. The reaction mixture was concentrated in vacuo and purified by column chromatography (50:1 hexanes/EtOAc) to afford **11** (2.44 g, 90% for 2 steps) as a colorless oil. $[\alpha]_{\text{D}}^{24} -3.1^{\circ}$ (c 0.29, CHCl_3); IR (KBr) 2910, 2898, 2856, 1513, 1459, 1112, 1106, 1091 cm^{-1} ; ^1H -NMR (270 MHz, CDCl_3) δ 0.95 (d, 6H, $J = 6.6\text{ Hz}$), 0.98 (m, 1H), 1.08 (s, 9H), 1.17 (d, 3H, $J = 6.9\text{ Hz}$), 1.46 (m, 1H), 1.68 (m, 1H), 1.75 (m, 1H), 1.97 (ddd, 1H, $J = 16.2, 7.3, 1.7\text{ Hz}$), 2.15 (ddd, 1H, $J = 16.5, 4.9, 1.7\text{ Hz}$), 2.70 (m, 1H), 3.30 (m, 1H), 3.48 (m, 3H), 3.81 (s, 3H), 4.48 (s, 2H), 6.89 (d, 2H, $J = 8.6\text{ Hz}$), 7.28 (d, 2H, $J = 8.6\text{ Hz}$), 7.37-7.71 (m, 10H); ^{13}C -NMR (67.5 MHz, CDCl_3) δ 17.5, 18.3, 19.3, 20.1, 25.9, 26.7, 26.9, 30.1, 33.2, 40.1, 55.2, 69.0, 72.6, 74.3, 79.7, 83.0, 113.7, 127.5, 129.2, 129.5, 130.5, 134.0, 135.6, 159.1; HRMS (FAB, *m*-NBA) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{36}\text{H}_{48}\text{O}_3\text{Si}$ 556.3372, found 556.3364.

(2*S*,6*R*,8*S*)-9-(*tert*-Butyldiphenylsilyloxy)-2,6,8-trimethylnon-3-yn-1-ol (12)

To a solution of **11** (649 mg, 1.16 mmol) in CH_2Cl_2 (12 ml) and H_2O (1.2 ml) was added DDQ (344 mg, 1.51 mmol) at room temperature. The reaction mixture was stirred for 30 min, and then diluted with water. The aqueous phase was extracted with EtOAc. The

combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (30:1 hexanes/EtOAc) afforded **12** (494 mg, 97%) as a colorless oil. $[\alpha]_D^{24} -11.6^\circ$ (c 0.26, CHCl_3); IR (KBr) 3644, 2964, 2960, 2931, 2325, 1112, 761 cm^{-1} ; $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ 0.96 (d, 6H, $J = 6.6$ Hz), 0.98 (m, 1H), 1.08 (s, 9H), 1.14 (d, 3H, $J = 6.9$ Hz), 1.47 (m, 1H), 1.70 (m, 1H), 1.75 (m, 1H), 1.98 (ddd, 1H, $J = 16.5, 6.9, 1.7$ Hz), 2.17 (ddd, 1H, $J = 16.1, 5.0, 1.7$ Hz), 2.64 (m, 1H), 3.49 (m, 4H), 7.37-7.71 (m, 10H); $^{13}\text{C-NMR}$ (67.5 MHz, CDCl_3) δ 17.3, 17.5, 19.3, 20.2, 25.8, 26.9, 29.5, 30.0, 33.2, 40.1, 67.1, 68.9, 81.1, 82.4, 127.6, 129.5, 134.0, 135.6; HRMS (FAB, m -NBA) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{28}\text{H}_{40}\text{O}_2\text{SiNa}$ 459.2695, found 459.2677.

(2S,6R,8S,Z)-9-(tert-Butyldiphenylsilyloxy)-2,4,6,8-tetramethylnon-3-en-1-ol (13)

To a solution of trimethylaluminum (1.0 M solution in hexanes, 6.20 ml, 6.20 mmol) was added a solution of **12** (673 mg, 1.54 mmol) in CH_2Cl_2 (3 ml) at 0 °C. The mixture was allowed to warm to room temperature, stirred for 20 min, and then cooled to -15°C . The resulting solution was treated with titanium tetrachloride (1.0 M solution in CH_2Cl_2 , 3.10 ml, 3.10 mmol) and continued for 15 min. The reaction was cooled to -40°C and then cautiously quenched with ice-cooled MeOH (3 ml) followed by Celite (10 g) and $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$ (10 g). The mixture was allowed to warm to room temperature and stirred for 2 hr. The mixture was filtered through a pad of Celite and the filtrate was concentrated in vacuo. The residue was purified by flash chromatography (40:1 hexanes/EtOAc) to afford **13** (557 mg, 80%) as a colorless oil. $[\alpha]_D^{24} -9.1^\circ$ (c 0.17, CHCl_3); IR (KBr) 3444, 2960, 2931, 2896, 2869, 1473, 1459, 1450, 1427, 1105 cm^{-1} ; $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ 0.77 (d, 3H, $J = 6.3$ Hz), 0.90 (d, 3H, $J = 6.6$ Hz), 0.95 (d, 3H, $J = 6.6$ Hz), 0.98 (m, 1H), 1.06 (s, 9H), 1.34 (m, 1H), 1.66 (s, 3H), 1.70 (m, 1H), 1.79 (m, 1H), 1.90 (m, 2H), 2.62 (m, 1H), 3.28 (dd, 1H, $J = 10.2, 8.2$ Hz), 3.43 (m, 2H), 3.52 (dd, 1H, $J = 9.8, 5.1$ Hz), 4.93 (d, 1H, $J = 9.6$ Hz), 7.30-7.70 (m, 10H); $^{13}\text{C-NMR}$ (67.5 MHz, CDCl_3) δ 17.1, 17.7, 19.3, 19.7, 23.7, 27.0, 28.3, 33.2, 35.2, 39.5, 41.5, 67.9, 68.9, 127.5, 128.8, 129.5, 134.0, 135.5, 137.0; HRMS (FAB, m -NBA) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{29}\text{H}_{44}\text{O}_2\text{SiNa}$ 475.3008, found: 475.3022.

(2S,4R,6S,8S)-9-(tert-Butyldiphenylsilyloxy)-2,4,6,8-tetramethylnon-1-ol (14)

A solution of **13** (941 mg, 2.08 mmol) and $\text{Rh}[(\text{nbd})\text{dppb}]\text{BF}_4$ (148 mg, 0.208 mmol) in CH_2Cl_2 (4 ml) was stirred under 1 Mpa of H_2 gas for 2 hr. The resulting solution was filtered through a short plug of silica gel and concentrated in vacuo. The residue was purified by flash chromatography (40:1 hexanes/EtOAc) to afford **14** (929 mg, 91%) as a colorless oil. $[\alpha]_D^{25} -16.6^\circ$ (c 0.15, CHCl_3); IR (KBr) 3425, 2958, 2929, 2858, 1461, 1427, 1112, 1081 cm^{-1} ; $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ 0.83 (d, 3H, $J = 6.3$ Hz), 0.84 (d, 3H, $J = 6.6$ Hz), 0.85 (m, 1H), 0.89 (d, 3H, $J = 6.9$ Hz), 0.93 (m, 1H), 0.95 (d, 3H, $J =$

6.6 Hz), 1.03 (m, 2H), 1.07 (s, 9H), 1.12 (m, 1H), 1.33 (m, 1H), 1.52 (m, 1H), 1.57 (m, 1H), 1.70 (m, 2H), 3.36-3.59 (m, 4H), 7.30-7.74 (m, 10H); ^{13}C -NMR (67.5 MHz, CDCl_3) δ 16.0, 18.0, 19.2, 20.2, 20.5, 26.8, 27.0, 27.4, 33.1, 33.2, 39.9, 41.5, 46.1, 68.8, 69.2, 127.5, 129.4, 134.0, 135.5; HRMS (FAB, *m*-NBA) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{29}\text{H}_{46}\text{O}_2\text{SiNa}$ 477.3164, found 477.3266.

***tert*-Butyldiphenyl[(2*S*,4*S*,6*R*,8*S*)-2,4,6,8-tetramethyl-9-(tetrahydro-2*H*-pyran-2-yloxy)nonyloxy]silane (**14a**)**

To a solution of **14** (929 mg, 2.05 mmol) in CH_2Cl_2 (20 ml) were added dihydropyran (1.85 ml, 20.5 mmol) and PPTS (51.0 mg, 0.205 mmol). The resulting solution was stirred at room temperature for 2 hr. The reaction was quenched with saturated aqueous NaHCO_3 solution and the aqueous phase was extracted with CH_2Cl_2 . The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (50:1 hexanes/EtOAc) afforded **14a** (1.10 g, 100%) as a colorless oil. $[\alpha]_{\text{D}}^{25} -10.5^\circ$ (*c* 0.19, CHCl_3); IR (KBr) 3450, 2956, 2929, 2366, 1473, 1461, 1079 cm^{-1} ; ^1H NMR (270 MHz, CDCl_3) δ 0.82 (d, 3H, $J = 6.6$ Hz), 0.83 (d, 3H, $J = 6.6$ Hz), 0.84 (m, 1H), 0.91 (d, 3H, $J = 6.3$ Hz), 0.92 (m, 1H), 0.94 (d, 3H, $J = 6.6$ Hz), 1.03 (m, 2H), 1.07 (s, 9H), 1.09 (m, 1H), 1.29 (m, 1H), 1.47-1.80 (m, 10H), 3.17 (m, 1H), 3.39-3.61 (m, 4H), 3.87 (m, 1H), 4.58 (m, 1H), 7.35-7.71 (m, 10H); ^{13}C -NMR (67.5 MHz, CDCl_3) δ 16.7, 16.8, 17.9, 18.0, 19.3, 19.5, 19.6, 20.3, 20.6, 20.7, 25.6, 26.8, 27.0, 27.1, 27.4, 30.7, 30.8, 30.9, 33.1, 40.6, 41.4, 46.1, 62.0, 62.2, 68.8, 73.8, 74.0, 98.6, 99.0, 127.5, 129.5, 134.1, 135.6; HRMS (FAB, *m*-NBA) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{34}\text{H}_{54}\text{O}_3\text{SiNa}$ 561.3739, found 561.3741.

(2*S*,4*S*,6*R*,8*S*)-2,4,6,8-Tetramethyl-9-(tetrahydro-2*H*-pyran-2-yloxy)nonan-1-ol (14b)

To a stirred solution of **14a** (1.10 g, 2.05 mmol) in THF (20 ml) was added TBAF (1.0 M solution in THF, 5.00 ml, 5.00 mmol). The resulting solution was stirred for 3 hr, diluted with saturated aqueous NH_4Cl solution, and extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (10:1 hexanes/EtOAc) afforded **14b** (590 mg, 96%) as a colorless oil. $[\alpha]_{\text{D}}^{25} -13.7^\circ$ (c 0.29, CHCl_3); IR (KBr) 3422, 2957, 2922, 2871, 2359, 1457, 1377, 1261, 1201, 1118 cm^{-1} ; $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ 0.81 (d, 3H, $J = 6.9$ Hz), 0.84 (d, 3H, $J = 7.3$ Hz), 0.89 (d, 3H, $J = 6.0$ Hz), 0.90 (d, 3H, $J = 6.9$ Hz), 0.92 (m, 2H), 1.01-1.32 (m, 4H), 1.48-1.86 (m, 10H), 3.15 (m, 1H), 3.34 (dd, 1H, $J = 10.2, 6.9$ Hz), 3.41-3.58 (m, 3H), 3.84 (m, 1H), 4.54 (m, 1H); $^{13}\text{C-NMR}$ (67.5 MHz, CDCl_3) 16.7, 16.8, 17.4, 17.5, 19.4, 19.6, 20.3, 20.6, 20.8, 25.5, 27.1, 27.2, 27.4, 30.6, 30.7, 30.8, 33.0, 40.5, 41.3, 45.8, 62.0, 68.1, 68.2, 73.6, 73.9, 98.6, 99.0; HRMS (FAB, m -NBA) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{18}\text{H}_{37}\text{O}_3$ 301.2742, found 301.2746.

(2*R*,4*S*,6*R*,8*S*)-2,4,6,8-Tetramethyl-9-(tetrahydro-2*H*-pyran-2-yloxy)nonanal (15)

To a solution of **14b** (389 mg, 1.30 mmol) in CH_2Cl_2 (13 ml) were added MS4Å (1 g), NMO (321 mg, 2.70 mmol), and TPAP (24.0 mg, 68.5 μmol). The reaction was stirred at room temperature for 30 min, and then filtered through a silica pad. After evaporation of the filtrate, the residue was purified by flash chromatography (40:1 hexanes/EtOAc) to afford **15** (344 mg, 89%) as a colorless oil. $[\alpha]_{\text{D}}^{25} +1.0^\circ$ (c 0.14, CHCl_3); IR (KBr) 2955, 2873, 1734, 1488, 1457, 1261, 1031 cm^{-1} ; $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ 0.81 (d, 3H, $J = 6.3$ Hz), 0.87 (d, 6H, $J = 6.3$ Hz), 1.00-1.07 (m, 5H), 1.16 (d, 3H, $J = 6.9$ Hz), 1.47-1.87 (m, 10H), 2.56 (m, 1H), 3.16 (m, 1H), 3.40-3.58 (m, 2H), 3.85 (m, 1H), 4.56 (m, 1H), 9.57 (d, 1H, $J = 2.3$ Hz); $^{13}\text{C-NMR}$ (67.5 MHz, CDCl_3) δ 16.8, 16.9, 18.0, 19.4, 19.6, 19.8, 20.1, 25.5, 27.0, 27.1, 28.0, 30.6, 30.7, 30.8, 37.2, 40.9, 41.1, 45.9, 62.0, 62.2, 73.6, 73.9, 98.6, 99.0, 182.7; HRMS (FAB, m -NBA) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{18}\text{H}_{34}\text{O}_3\text{Na}$ 321.2405, found 321.2391.

(4*R*)-4-Benzyl-3-[(3*S*,4*S*,6*S*,8*R*,10*S*)-3-hydroxy-4,6,8,10-tetramethyl-11-(tetrahydro-2*H*-pyran-2-yloxy)undecanoyl]oxazolidin-2-one (16)

To a solution of samarium iodide (0.1 M solution in THF, 58.0 ml, 5.80 mmol) was added a solution of **15** (344 mg, 1.15 mmol) and (*R*)-4-benzyl-3-bromoacetyl-2-oxazolidinone (376 mg, 1.26 mmol) in THF (11 ml) at $-78\text{ }^{\circ}\text{C}$. The reaction was stirred for 20 min and then treated with hexane (100 ml) followed by silica gel (50 g). The mixture was allowed to warm to room temperature and stirred for 30 min. The mixture was filtered through a short plug of silica gel and concentrated in vacuo. The residue was purified by flash chromatography (5:1 hexanes/EtOAc) to afford **16** (551 mg, 92%) along with its epimer (40.0 mg, 6.2%). $[\alpha]_{\text{D}}^{26} -43.8^{\circ}$ (*c* 0.25, CHCl_3); IR (KBr) 3566, 2955, 1785, 1698, 1456, 1386, 1199, 1030 cm^{-1} ; ^1H -NMR (270 MHz, CDCl_3) δ 0.85 (d, 3H, $J = 5.9\text{ Hz}$), 0.87 (d, 3H, $J = 5.3\text{ Hz}$), 0.89 (d, 3H, $J = 5.0\text{ Hz}$), 0.93 (d, 3H, $J = 6.3\text{ Hz}$), 0.98-1.14 (m, 3H), 1.25 (m, 2H), 1.42-1.74 (m, 10H), 1.83 (m, 1H), 2.79 (dd, 1H, $J = 13.2, 9.6\text{ Hz}$), 3.07 (d, 2H, $J = 6.3\text{ Hz}$), 3.19 (m, 1H), 3.31 (dd, 1H, $J = 13.2, 2.6\text{ Hz}$), 3.48 (m, 1H), 3.54 (m, 1H), 3.86 (m, 1H), 4.10 (m, 1H), 4.21 (m, 2H), 4.57 (m, 1H), 4.69 (m, 1H), 7.18-7.36 (m, 5H); ^{13}C -NMR (67.5 MHz, CDCl_3) δ 14.5, 16.7, 16.8, 19.4, 19.6, 20.3, 20.7, 25.5, 27.1, 27.2, 30.6, 30.8, 30.9, 35.2, 37.9, 40.4, 40.5, 40.9, 45.6, 55.1, 62.2, 61.9, 66.3, 70.2, 70.3, 73.7, 73.9, 98.6, 99.0, 127.3, 128.9, 129.3, 135.1, 153.4, 173.1; HRMS (FAB, *m*-NBA) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{30}\text{H}_{47}\text{O}_6\text{NNa}$ 540.3301, found 540.3309.

After conversion of **16** into the corresponding methyl ester, absolute configuration of C3 was determined by modified Mosher ester analysis.*

$$\Delta\delta = (\delta_S - \delta_R) \text{ for } (R)\text{- and } (S)\text{-MTPA derivatives}$$

* Ohtani, I.; Kusumi, J.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092.

(3*S*,4*S*,6*S*,8*R*,10*S*)-3-(*tert*-Butyldimethylsilyloxy)-4,6,8,10-tetramethyl-11-(tetrahydro-2*H*-pyran-2-yloxy)undecanoic acid (3**)**

To a solution of **16** (453 mg, 0.876 mmol) in CH_2Cl_2 (9 ml) was added 2,6-lutidine (170 μl , 1.49 mmol) followed by TBSOTf (260 μl , 1.14 mmol) at 0 °C. After 30 min, the reaction was quenched with water and the aqueous phase was extracted with CH_2Cl_2 . The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. This residue was employed in the next reaction without further purification.

The resulting silyl ether was dissolved in THF (6 ml) and H_2O (2 ml) at 0 °C. Lithium hydroxide (72.9 mg, 1.74 mmol) and hydrogen peroxide (30% solution in H_2O , 590 μl , 5.21 mmol) were added to the solution. After 3 hr, the reaction was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution, and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (5:1 hexanes/EtOAc) afforded **3** (347 mg, 84% for 2 steps) as a colorless oil. $[\alpha]_D^{27} -31.5^\circ$ (c 0.24, CHCl_3); IR (KBr) 3444, 2955, 2927, 1789, 1456, 1385, 1350, 1250, 1031 cm^{-1} ; ^1H -NMR (270 MHz, CDCl_3) δ 0.02 (s, 3H), 0.05 (s, 3H), 0.78-0.92 (m, 23H), 0.95-0.92 (m, 3H), 1.33-1.88 (m, 11H), 2.42 (d, 2H, $J = 5.9$ Hz), 3.15 (m, 1H), 3.50 (m, 2), 3.85 (m, 1H), 4.06 (m, 1H), 4.57 (m, 1H); ^{13}C -NMR (67.5 MHz, CDCl_3) δ -4.7, -4.6, 15.2, 16.6, 16.7, 18.0, 19.4, 19.5, 20.6, 20.7, 20.8, 25.5, 25.8, 27.2, 27.3, 27.5, 30.6, 30.8, 30.9, 35.9, 39.3, 40.1, 40.4, 45.7, 61.9, 62.1, 72.5, 73.8, 74.0, 98.6, 99.0, 177.9; HRMS (FAB, m -NBA) $[\text{M}+\text{H}]^+$ calcd for $\text{C}_{26}\text{H}_{52}\text{O}_5\text{SiNa}$ 495.3481, found 495.3489.

(1*R*,2*R*)-Cyclopentane-1,2-diylldimethanol (17**)**

This diol was synthesized according to Yamamoto's procedure. (Misumi, A.; Iwanaga, K.; Furuta, K.; Yamamoto, H. *J. Am. Chem. Soc.* **1985**, *107*, 3343.)

(1*R*,2*R*)-2-[(4-Methoxybenzyloxy)methyl]cyclopentanecarbaldehyde (19**)**

To a solution of **17** (3.63 g, 27.7 mmol) in DMF (277 ml) was added sodium hydride (60% in oil, 1.32 g, 31.0 mmol) at $-20\text{ }^{\circ}\text{C}$. After stirring for 30 min, the resulting suspension was treated with PMBCl (3.96 mL, 33.0 mmol) and then warmed to room temperature. The reaction was quenched with water, and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (7:1 hexanes/EtOAc) afforded the corresponding alcohol **18** including unseparable impurities.

To a solution of the alcohol in CH_2Cl_2 (297 ml) was added Dess-Martin periodinane (18.7 g, 44.2 mmol). After stirring at room temperature for 30 min, the reaction mixture was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution and saturated aqueous NaHCO_3 solution, the aqueous phase was extracted with CH_2Cl_2 . The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (20:1 hexanes/EtOAc) afforded **19** (6.24 g, 89% for 2 steps) as a colorless oil. $[\alpha]_{\text{D}}^{21} -25.9^{\circ}$ (c 0.27, CHCl_3); IR (KBr) 2955, 2854, 1721, 1613, 1513, 1247, 1095, 1034 cm^{-1} ; ^1H -NMR (270 MHz, CDCl_3) δ 1.31 (m, 1H), 1.57 (m, 2H), 1.66-1.86 (m, 3H), 2.33-2.51 (m, 2H), 3.25 (dd, 1H, $J = 8.9, 7.3$ Hz), 3.39 (dd, 1H, $J = 8.9, 5.6$ Hz), 3.72 (s, 3H), 4.36 (s, 2H), 6.79 (d, 2H, $J = 8.6$ Hz), 7.15 (d, 2H, $J = 8.6$ Hz), 9.75 (d, 1H, $J = 2.0$ Hz); ^{13}C -NMR (67.5 MHz, CDCl_3) δ 24.9, 26.5, 29.3, 41.2, 55.2, 55.7, 72.6, 72.9, 113.7, 129.1, 130.4, 159.1, 203.7; HRMS (EI) $[M]^+$ calcd for $\text{C}_{15}\text{H}_{20}\text{O}_3$ 248.1412, found 248.1407.

(S)-1-((1R,2R)-2-[(4-Methoxybenzyloxy)methyl]cyclopentyl)but-3-en-1-ol (21)

To a solution of **19** (112 mg, 0.45 mmol) in CH_2Cl_2 (4.5 ml) were added allyltrimethylsilane (110 μl , 0.67 mmol) and magnesium bromide diethyl etherate (116 mg, 0.45 mmol) at $0\text{ }^{\circ}\text{C}$. The reaction was stirred for 7 hr and then quenched with water. The aqueous phase was extracted with CH_2Cl_2 . The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (25:1 hexanes/EtOAc) afforded **21** (117 mg, 90%) as a colorless oil along with its epimer **22** (6.00 mg, 4.5%). $[\alpha]_{\text{D}}^{21} +6.1^{\circ}$ (c 0.30, CHCl_3); IR (KBr) 3432, 2950, 2865, 1613, 1513, 1248, 1091, 1036 cm^{-1} ; ^1H -NMR (270 MHz, CDCl_3) δ 1.18-1.33 (m, 2H), 1.47 (m, 1H), 1.51-1.63 (m, 2H), 1.72-1.84 (m, 2H), 2.02-2.17 (m, 2H), 2.39 (m, 1H), 3.20 (t, 1H, $J = 8.9$ Hz), 3.41 (m, 1H), 3.53 (dd, 1H, $J = 8.9, 4.6$ Hz), 3.81 (s, 3H), 4.47 (d, 1H, $J = 11.9$ Hz), 4.53 (d, 1H, $J = 11.9$ Hz), 5.10 (m, 2H), 5.98 (m, 1H), 6.89 (d, 2H, $J = 8.6$ Hz), 7.26 (d, 2H, $J = 8.6$ Hz); ^{13}C -NMR (67.5 MHz, CDCl_3) δ 24.5, 29.9, 30.9, 40.4, 43.9, 51.6, 55.2, 72.8, 74.2, 74.9, 113.8, 116.4, 129.4, 129.6, 135.7, 159.2; HRMS (EI) $[M]^+$ calcd for $\text{C}_{18}\text{H}_{26}\text{O}_3$ 290.1882, found 290.1887.

Stereochemical assignment of the newly created asymmetric center was achieved by Mosher's method.

$\Delta\delta = (\delta_S - \delta_R)$ for (*R*)- and (*S*)-MTPA ester of **21**

***tert*-Butyl((*S*)-1-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)but-3-enyloxy)dimethylsilane (**25**)**

To a solution of **21** (1.91 g, 6.61 mmol) in CH_2Cl_2 (66 ml) at 0 °C was added 2,6-lutidine (1.10 ml, 9.92 mmol) followed by TBSOTf (2.00 ml, 8.59 mmol). After 1 hr, the reaction was quenched with water, and the aqueous phase was extracted with CH_2Cl_2 . The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (50:1 hexanes/EtOAc) afforded **25** (2.65 g, 99%) as a colorless oil. $[\alpha]_D^{22} -8.6^\circ$ (c 0.27, CHCl_3); IR (KBr) 2953, 2856, 1471, 1249, 1095 cm^{-1} ; ^1H -NMR (270 MHz, CDCl_3) δ 0.06 (s, 6H), 0.90 (s, 9H), 1.23-1.36 (m, 2H), 1.44-1.74 (m, 5H), 2.15 (m, 1H), 2.26 (m, 2H), 3.18 (t, 1H, $J = 8.6$ Hz), 3.46 (dd, 1H, $J = 8.6, 4.9$ Hz), 3.64 (m, 1H), 3.80 (s, 3H), 4.40 (d, 2H, $J = 11.5$ Hz), 4.46 (d, 2H, $J = 11.5$ Hz), 5.01 (m, 2H), 5.85 (m, 1H), 6.88 (d, 2H, $J = 8.2$ Hz), 7.27 (d, 2H, $J = 8.2$ Hz); ^{13}C -NMR (67.5 MHz, CDCl_3) δ -4.6, -4.2, 18.0, 25.5, 25.9, 29.5, 30.5, 39.8, 41.0, 46.8, 55.2, 72.6, 74.7, 75.5, 113.7, 116.5, 129.1, 130.9, 135.2, 150.0; HRMS (FAB, *m*-NBA) $[\text{M}-\text{H}]^+$ calcd for $\text{C}_{24}\text{H}_{39}\text{O}_3\text{Si}$ 403.2668, found 403.2669.

(*S*)-3-(*tert*-Butyldimethylsilyloxy)-3-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)propanal (26**)**

To a solution of **25** (516 mg, 1.27 mmol) in acetone (12 ml) and H_2O (12 ml) were added osmium tetroxide (32.4 mg, 0.127 mmol) and NMO (600 mg, 5.10 mmol). The reaction was stirred at room temperature for 4 hr. The reaction mixture was quenched with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo to give the corresponding diol as a yellow oil.

The crude diol was dissolved in MeOH (18 ml) and H_2O (6 ml). To the reaction mixture was added sodium metaperiodate (545 mg, 2.55 mmol) at 0 °C. The mixture was stirred for 2 hr, then diluted with saturated aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution. The aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (40:1 hexanes/EtOAc) afforded **26** (533 mg, 100% for 2 steps) as a colorless oil. $[\alpha]_D^{22} -14.4^\circ$ (c 0.36, CHCl_3); IR (KBr) 2954, 2857, 1725, 1614, 1513, 1249, 1093, 1037 cm^{-1} ; ^1H -NMR (270 MHz, CDCl_3) δ 0.03 (s, 3H), 0.06 (s, 3H), 0.86 (s, 9H), 1.32-1.75 (m, 6H), 1.83 (m, 1H), 2.04 (m, 1H), 2.48 (ddd, 1H, $J = 15.8, 5.9, 2.6$ Hz), 2.58 (ddd, 1H, $J = 15.8, 4.9, 1.7$ Hz), 3.31 (m, 2H), 3.80 (s, 3H), 4.20 (m, 1H), 4.41 (m, 2H), 6.87 (d, 2H, $J = 8.6$ Hz), 7.24 (d, 2H, $J = 8.6$ Hz), 9.73 (m, 1H); ^{13}C -NMR (67.5 MHz, CDCl_3) δ -4.6, 17.9, 25.2, 25.8, 28.0, 30.3, 41.0, 48.6, 48.7, 55.2, 70.9, 72.8, 74.5, 113.7, 129.2, 130.6, 159.1, 202.5; HRMS (FAB, *m*-NBA) $[\text{M}-\text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{37}\text{O}_4\text{Si}$ 405.2461, found 405.2451.

(*S,E*)-5-(*tert*-Butyldimethylsilyloxy)-5-[(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl]pent-2-enal (27**)**

To a solution of **26** (20.0 mg, 49.2 μmol) in benzene (1.0 ml) was added triphenylphosphoranylideneacetaldehyde (45.0 mg, 98.5 μmol). The resulting solution was stirred at 80 $^\circ\text{C}$ for 2 days. The solvent was then removed in vacuo and the residue was purified by flash chromatography (30:1 hexanes/EtOAc) to afford **27** (15.5 mg, 73%) as a yellow oil. $[\alpha]_D^{23} +8.3^\circ$ (*c* 0.35, CHCl_3); IR (KBr) 2953, 2857, 1694, 1513, 1249, 1091, 1038 cm^{-1} ; ^1H NMR (270 MHz, CDCl_3) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.88 (s, 9H), 1.28-1.71 (m, 7H), 2.08 (m, 1H), 2.49 (m, 2H), 3.22 (t, 1H, $J = 8.6$ Hz), 3.39 (dd, 1H, $J = 8.6$ Hz), 3.78 (m, 1H), 3.80 (s, 3H), 4.39 (d, 1H, $J = 11.9$ Hz), 4.43 (d, 1H, $J = 11.9$ Hz), 6.10 (dd, 1H, $J = 15.5, 7.9$ Hz), 6.86 (d, 2H, $J = 8.2$ Hz), 6.88 (m, 1H), 7.24 (d, 2H, $J = 8.2$ Hz), 9.47 (d, 1H, $J = 7.9$ Hz); ^{13}C -NMR (67.5 MHz, CDCl_3) δ -4.6, -4.3, 18.0, 25.2, 25.8, 29.2, 30.3, 38.4, 41.4, 47.7, 55.2, 72.7, 74.5, 74.6, 113.7, 129.2, 130.7, 134.7, 155.2, 159.1, 193.9; HRMS (EI) $[M]^+$ calcd for $\text{C}_{25}\text{H}_{40}\text{O}_4\text{Si}$ 432.2696, found 432.2702.

(*S*,2*E*,4*E*)-2-Bromo-7-(*tert*-butyldimethylsilyloxy)-7-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)hepta-2,4-dienenitrile (28**)**

To a solution of **27** (39.8 mg, 92.1 μmol) and diethyl bromo(cyano)methylphosphate (47.0 mg, 184 μmol) in acetonitrile (1 ml) at 0 °C were added DBU (20.0 μl , 138 μmol) and lithium chloride (6.00 mg, 138 μmol). The solution was stirred for 2 hr and then diluted with saturated aqueous NaHCO_3 solution. The aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (60:1 hexanes/EtOAc) afforded **28** (47.3 mg, 96%) as a colorless oil. $[\alpha]_D^{22} +31.0^\circ$ (c 0.47, CHCl_3); IR (KBr) 2952, 2856, 2217, 1614, 1513, 1248, 1078 cm^{-1} ; $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ 0.03 (s, 3H), 0.05 (s, 3H), 0.88 (s, 9H), 1.25-1.71 (m, 7H), 2.07 (m, 1H), 2.36 (m, 2H), 3.20 (t, 1H, $J = 8.6$ Hz), 3.39 (dd, 1H, $J = 8.6, 5.6$ Hz), 3.69 (m, 1H), 3.80 (s, 3H), 4.39 (d, 1H, $J = 11.9$ Hz), 4.44 (d, 1H, $J = 11.9$ Hz), 6.25 (m, 1H), 6.36 (dd, 1H, $J = 15.2, 10.6$ Hz), 6.87 (d, 2H, $J = 8.6$ Hz), 7.10 (d, 1H, $J = 10.6$ Hz), 7.24 (d, 2H, $J = 8.6$ Hz); $^{13}\text{C-NMR}$ (67.5 MHz, CDCl_3) δ -4.6, -4.3, 17.9, 25.2, 25.8, 29.3, 30.3, 38.8, 41.3, 47.4, 55.1, 72.6, 74.5, 74.7, 84.1, 113.6, 114.6, 127.6, 129.1, 130.7, 143.5, 149.7, 159.0; HRMS (FAB, m -NBA) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{27}\text{H}_{40}\text{O}_3\text{NBrSiNa}$ 556.1858, found 556.1855.

(*S*,2*E*,4*E*)-2-Bromo-7-hydroxy-7-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)hepta-2,4-dienenitrile (4**)**

28 (184 mg, 345 μmol) was placed in a solution of HF-pyridine (500 μl) in THF (500 μl) and pyridine (500 μl) and stirred at room temperature for 2 days. The resulting solution was filtered through a short plug of silica gel and concentrated in vacuo. The residue was purified by flash chromatography (7:1 hexanes/EtOAc) to afford **4** (135 mg, 94%) as a colorless oil. $[\alpha]_D^{24} +11.3^\circ$ (c 0.25, CHCl_3); IR (KBr) 3406, 2949, 2222, 2216, 1613, 1513, 1248, 1075, 1035 cm^{-1} ; $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ 1.25 (m, 1H), 1.41-1.67 (m, 5H), 1.77 (m, 1H), 2.04 (m, 1H), 2.24 (m, 1H), 2.47 (m, 1H), 3.14 (dd, 1H, $J = 10.6, 8.6$ Hz), 3.41 (m, 1H), 3.56 (dd, 1H, $J = 8.6, 4.0$ Hz), 3.81 (s, 3H), 4.49 (m, 2H), 6.33-6.48 (m, 2H), 6.88 (d, 2H, $J = 8.6$ Hz), 7.15 (m, 1H), 7.24 (d, 2H, $J = 8.6$ Hz); $^{13}\text{C-NMR}$ (67.5 MHz, CDCl_3) δ 24.3, 29.6, 30.9, 39.6, 44.0, 52.2, 55.1, 72.8, 74.0, 74.5, 83.8, 113.7, 114.6, 127.1, 129.1, 129.4, 144.3, 150.0, 159.2; HRMS (FAB, m -NBA) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{21}\text{H}_{26}\text{O}_3\text{NBrNa}$ 442.0994, found 442.1002.

(*S*,2*Z*,4*E*)-2-Bromo-7-(*tert*-butyldimethylsilyloxy)-7-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)hepta-2,4-dienoate (44**)**

To a solution of **27** (461 mg, 1.07 mmol) in benzene (10.7 ml) was added (allyloxycarbonylbromomethylidene)triphenylphosphorane (1.04 g, 3.20 mmol) at room temperature. The reaction mixture was stirred at 70 °C for 39 h and concentrated in vacuo. The residue was purified by column chromatography (70 : 1 hexanes/EtOAc) to give **44** (531 mg, 84%) as a yellow oil. $[\alpha]_D^{25} +9.4^\circ$ (*c* 0.18, CHCl_3); IR (KBr) 2943, 2860, 2367, 1720, 1622, 1534, 1460, 1363, 1250, 1076, 835, 773 cm^{-1} ; ^1H -NMR (300 MHz, CDCl_3) δ 0.03 (s, 3H), 0.04 (s, 3H), 0.87 (s, 9H), 1.27 (m, 1H), 1.40-1.75 (m, 6H), 2.08 (m, 1H), 2.39 (m, 2H), 3.17 (t, 1H, $J = 8.6$ Hz), 3.40 (dd, 1H, $J = 8.6, 5.3$ Hz), 3.77, (m, 1H), 3.79 (s, 3H), 4.38 (d, 1H, $J = 11.6$ Hz), 4.44 (d, 1H, $J = 11.6$ Hz), 4.67 (ddt, 1H, $J = 13.1, 5.8, 1.3$ Hz), 4.75 (ddt, 1H, $J = 13.1, 5.8, 1.3$ Hz), 5.28 (dd, 1H, $J = 10.3, 1.5$ Hz), 5.39 (dd, 1H, $J = 17.3, 1.5$ Hz), 5.98 (ddt, 1H, $J = 17.3, 10.3, 5.8$ Hz), 6.35 (m, 1H), 6.48 (dd, 1H, $J = 15.3, 10.1$ Hz), 6.86 (d, 2H, $J = 8.7$ Hz), 7.24 (d, 2H, $J = 8.7$ Hz), 7.64 (d, 1H, $J = 10.1$ Hz); ^{13}C -NMR (100 MHz, CDCl_3) δ -4.5, -4.2, 18.1, 25.3, 25.9, 29.4, 30.4, 39.4, 41.4, 47.4, 55.3, 66.8, 72.7, 74.6, 75.1, 111.8, 113.7, 118.7, 129.2, 129.6, 130.8, 131.7, 141.7, 144.5, 159.0, 162.9; HRMS (FAB, *m*-NBA+NaI) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{30}\text{H}_{45}\text{BrO}_5\text{SiNa}$ 615.2117, found 615.2107.

(*S*,2*Z*, 4 *E*) - Allyl 2-bromo-7-hydroxy-7-[(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl]hepta-2,4-dienoate (**45**)

To a solution of **44** (287 mg, 0.484 mmol) in THF (0.9 ml) at room temperature was added a HF·pyridine-THF solution (HF·pyridine : pyridine : THF = 1 : 1 : 1, 3.6 ml). After stirring for 9.5 h at room temperature, the reaction mixture was filtered through a silica gel pad (eluate 60 : 1 CH₂Cl₂/MeOH) and concentrated in vacuo. The residue was purified by column chromatography (8 : 1 hexanes/EtOAc) to give **45** (221 mg, 96%) as a yellow oil. $[\alpha]_D^{25} = +3.2^\circ$ ($c = 0.17$, CHCl₃); IR (KBr) 3433, 2924, 2858, 1724, 1624, 1512, 1456, 1368, 1248, 1167, 1034 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃) δ 1.17 (m, 2H), 1.40-1.84 (m, 5H), 2.03 (m, 1H), 2.28 (m, 1H), 2.52 (m, 1H), 3.14 (dd, 1H, $J = 10.6, 8.7$ Hz), 3.44 (m, 1H), 3.55 (dd, 1H, $J = 8.7, 3.9$ Hz), 3.80 (s, 3H), 4.46 (d, 1H, $J = 11.7$ Hz), 4.51 (d, 1H, $J = 11.7$ Hz), 4.68 (ddt, 1H, $J = 13.1, 5.8, 1.3$ Hz), 4.75 (ddt, 1H, $J = 13.1, 5.8, 1.3$ Hz), 5.27 (dd, 1H, $J = 10.4, 1.4$ Hz), 5.38 (dd, 1H, $J = 17.3, 1.4$ Hz), 5.96 (ddt, 1H, $J = 17.3, 10.4, 5.8$ Hz), 6.51-6.55 (m, 2H), 6.88 (d, 2H, $J = 8.7$ Hz), 7.24 (d, 2H, $J = 8.7$ Hz), 7.70 (d, 1H, $J = 9.7$ Hz); ¹³C-NMR (100 MHz, CDCl₃) δ 24.4, 29.8, 31.1, 40.1, 44.21, 52.3, 55.3, 66.7, 73.0, 74.2, 74.9, 111.7, 113.9, 118.6, 129.1, 129.3, 129.5, 131.7, 142.0, 145.2, 159.4, 162.9; HRMS (FAB, *m*-NBA+NaI) $[M+Na]^+$ calcd for C₂₄H₃₁BrO₅Na 501.1253, found 501.1250.

(3*S*,4*S*,6*S*,8*R*,10*S*)-((*S*,3*E*,5*Z*)-7-(Allyloxy)-6-bromo-1-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)-7-oxohepta-3,5-dienyl) 3-(*tert*-butyldimethylsilyloxy)-4,6,8,10-tetramethyl-11-(tetrahydro-2*H*-pyran-2-yloxy)undecanoate (46**)**

A solution of **3** (229 mg, 0.485 mmol) in benzene (4.7 ml) at room temperature was treated with Et₃N (0.140 ml, 0.970 mmol) and 2,4,6-trichlorobenzoyl chloride (80.0 μ L, 0.533 mmol) under an argon atmosphere. After 1 h, a solution of **45** (301 mg, 0.630 mmol) in benzene (5.0 ml) was added dropwise and DMAP (77.0 mg, 0.630 mmol) was then added. After stirring for 2 h at room temperature, the reaction was quenched with aqueous NaHCO₃ solution and the resulting mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product was purified by column chromatography (25 : 1 hexanes/EtOAc) to give **46** (452 mg, 100%) as a colorless oil. $[\alpha]_D^{24}$ -4.8° (*c* 0.17, CHCl₃); IR (KBr) 2949, 2862, 1728, 1626, 1514, 1460, 1371, 1248, 1171, 1080, 1032, 833, 775 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃) δ 0.02 (s, 3H), 0.05 (s, 3H), 0.79-0.91 (m, 23H), 0.95-1.14 (m, 5H), 1.45-1.92 (m, 16H), 2.04 (m, 1H), 2.31-2.60 (m, 4H), 3.17 (m, 1H), 3.24 (t, 1H, *J* = 8.6 Hz), 3.37 (dd, 1H, *J* = 8.6, 5.6 Hz), 3.44-3.57 (m, 2H), 3.79 (s, 3H), 3.86 (m, 1H), 4.06 (m, 1H), 4.39 (d, 1H, *J* = 11.7 Hz), 4.45 (d, 1H, *J* = 11.7 Hz), 4.56 (m, 1H), 4.68 (ddt, 1H, *J* = 13.1, 5.8, 1.3 Hz), 4.75 (ddt, 1H, *J* = 13.1, 5.8, 1.3 Hz), 4.95 (m, 1H), 5.28 (dd, 1H, *J* = 10.4, 1.3 Hz), 5.75 (dd, 1H, *J* = 17.2, 1.3 Hz), 5.95 (ddt, 1H, *J* = 17.2, 10.4, 5.8 Hz), 6.24 (m, 1H), 6.49 (dd, 1H, *J* = 15.5, 10.4 Hz), 6.86 (d, 2H, *J* = 8.6 Hz), 7.24 (d, 2H, *J* = 8.6 Hz), 7.62 (d, 1H, *J* = 10.4 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ -4.7 , -4.3 , 14.5, 16.0, 16.5, 16.6, 18.1, 19.5, 19.6, 20.5, 20.6, 20.7, 20.7, 25.1, 25.5, 25.9, 27.0, 27.1, 27.1, 27.3, 27.3, 29.7, 29.8, 30.3, 30.7, 30.9, 30.9, 33.3, 35.5, 36.8, 39.6, 39.8, 40.0, 40.9, 41.0, 41.2, 41.6, 41.6, 45.0, 45.8, 45.8, 55.2, 62.0, 62.2, 66.9, 69.3, 71.6, 71.7, 72.7, 73.9, 74.1, 75.9, 98.7, 99.0, 112.8, 113.7, 118.8, 129.0, 130.1, 130.7, 131.6, 141.2, 142.3, 159.1, 162.6, 172.7; HRMS (FAB, *m*-NBA+NaI) $[M+Na]^+$ calcd for C₅₀H₈₁BrO₉SiNa 955.4731, found 955.4759.

(3*S*,4*S*,6*S*,8*R*,10*S*)-((*S*,3*E*,5*Z*)-7-(Allyloxy)-6-bromo-1-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)-7-oxohepta-3,5-dienyl) 3-(*tert*-butyldimethylsilyloxy)-11-hydroxy-4,6,8,10-tetramethylundecanoate (47**)**

To a solution of **46** (156 mg, 0.167 mmol) in EtOH (3.3 ml) at room temperature was

added PPTS (21.0 mg, 84.0 μ mol). After stirring for 16 h at 50 °C, the reaction mixture was diluted with water and extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product was purified by column chromatography (7 : 1 hexanes/EtOAc) to give **47** (136 mg, 96%) as a colorless oil. $[\alpha]_D^{25}$ -11.9° (*c* 0.17, CHCl₃); IR (KBr) 2952, 2862, 1726, 1626, 1514, 1460, 1371, 1248, 1171, 1090, 1134, 833, 777 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃) δ 0.02 (s, 3H), 0.05 (s, 3H), 0.77-1.42 (m, 28H), 1.47-1.78 (m, 9H), 1.86 (m, 1H), 2.05 (m, 1H), 2.30-2.60 (m, 4H), 3.23 (dd, 1H, *J* = 8.8, 7.8 Hz), 3.34-3.46 (m, 3H), 3.78 (s, 3H), 4.05 (m, 1H), 4.39 (d, 1H, *J* = 11.7 Hz), 4.45 (d, 1H, *J* = 11.7 Hz), 4.66 (ddt, 1H, *J* = 13.1, 5.8, 1.3 Hz), 4.75 (ddt, 1H, *J* = 13.1, 5.8, 1.3 Hz), 4.95 (m, 1H), 5.27 (dd, 1H, *J* = 10.4, 1.4 Hz), 5.38 (dd, 1H, *J* = 17.8, 1.4 Hz), 5.96 (ddt, 1H, *J* = 17.8, 10.4, 5.8 Hz), 6.23 (dt, 1H, *J* = 15.1, 7.4 Hz), 6.48 (dd, 1H, *J* = 15.1, 10.5 Hz), 6.86 (d, 2H, *J* = 8.8 Hz), 7.24 (d, 2H, *J* = 8.8 Hz), 7.62 (d, 1H, *J* = 10.5 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ -4.7 , -4.3 , 14.5, 16.0, 18.1, 20.6, 20.7, 25.1, 25.9, 27.1, 27.3, 29.8, 30.3, 33.3, 35.5, 36.8, 39.6, 39.8, 41.2, 41.6, 45.0, 45.8, 55.3, 66.9, 69.3, 71.7, 72.7, 74.1, 76.0, 112.8, 113.7, 118.8, 129.1, 130.1, 130.6, 131.6, 141.2, 142.3, 159.1, 162.7, 171.7; HRMS (FAB, *m*-NBA+NaI) $[M+Na]^+$ calcd for C₄₅H₇₃BrO₈SiNa 871.4156, found 871.4142.

(3*S*,4*S*,6*S*,8*R*,10*S*)-((*S*,3*E*,5*Z*)-7-(Allyloxy)-6-bromo-1-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)-7-oxohepta-3,5-dienyl) 3-(*tert*-butyldimethylsilyloxy)-4,6,8,10-tetramethyl-11-oxoundecanoate (43**)**

To a mixture of dried MS4Å and **47** (110 mg, 0.130 mmol) in CH₂Cl₂ (2.6 ml) were added NMO (30.5 mg, 0.259 mmol) and TPAP (2.30 mg, 7.00 μmol) at room temperature under a nitrogen atmosphere. After stirring for 0.5 h at room temperature, the reaction was quenched with aqueous Na₂S₂O₃ solution and the resulting suspension was then filtered through a pad of Celite. The filtrate was extracted with EtOAc and the combined organic layers were dried over anhydrous Na₂SO₄. The organic solvent was removed in vacuo to give the crude product. Flash chromatography (20 : 1 hexanes/EtOAc) afforded aldehyde **43** (94.2 mg, 86%) as a colorless oil. ¹H-NMR (300 MHz, CDCl₃) δ 0.02 (s, 3H), 0.05 (s, 3H), 0.80-0.99 (m, 20H), 1.06 (d, 3H, *J* = 6.9 Hz), 1.18-1.91 (m, 14H), 2.06 (m, 1H), 2.31-2.59 (m, 5H), 3.24 (dd, 1H, *J* = 8.7, 7.9 Hz), 3.37 (dd, 1H, *J* = 8.7, 5.7 Hz), 3.80 (s, 3H), 4.06 (dt, 1H, *J* = 6.3, 2.4 Hz), 4.39 (d, 1H, *J* = 11.6 Hz), 4.45 (d, 1H, *J* = 11.6 Hz), 4.68 (ddt, 1H, *J* = 13.1, 5.8, 1.3 Hz), 4.76 (ddt, 1H, *J* = 13.1, 5.8, 1.3 Hz), 4.96 (m, 1H), 5.28 (dd, 1H, *J* = 10.4 Hz, 1.3 Hz), 5.40 (dd, 1H, *J* = 17.2, 1.3 Hz), 5.96 (ddt, 1H, *J* = 17.2, 10.4, 5.8 Hz), 6.24 (m, 1H), 6.49 (dd, 1H, *J* = 15.4, 10.5 Hz), 6.86 (d, 2H, *J* = 8.6 Hz), 7.24 (d, 2H, *J* = 8.6 Hz), 7.61 (d, 1H, *J* = 10.5 Hz), 9.60 (d, 1H, *J* = 1.7 Hz); HRMS (FAB, *m*-NBA+NaI) [M+Na]⁺ calcd for C₄₅H₇₁BrO₈SiNa 869.3999, found 869.4013.

**(2*S*,4*E*,6*Z*,9*S*,11*R*,13*S*,15*S*,16*S*)-Allyl 16-(*tert*-butyldimethylsilyloxy)-8-hydroxy-2-
{(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl}-9,11,13,15-tetramethyl-18-
oxooxacyclooctadeca-4,6-diene-7-carboxylate (**48**)**

To a solution of SmI_2 (0.1 M in THF, 16.7 ml, 1.67 mmol) was added dropwise a solution of **43** (70.5 mg, 83.0 μmol) in THF (66 ml) over 1 h at -78°C under an argon atmosphere. After exposure to oxygen gas, the reaction mixture was treated with silica gel (21 g) and hexane (50 ml) and stirred for 30 min at room temperature. The resulting mixture was filtered through a pad of silica gel (eluate EtOAc) and concentrated in vacuo. The residue was purified by column chromatography (20 : 1 hexanes/EtOAc) to give **48** (50.9 mg, 79%, C11 stereochemistry is unknown.) as a yellow oil and the cyclized diastereomixtures (13.1 mg, 21%).

48 : $[\alpha]_D^{26} -28.0^\circ$ (c 0.18, CHCl_3); IR (KBr) 2952, 2864, 2357, 1730, 1624, 1514, 1460, 1373, 1296, 1248, 1173, 1084, 833, 777 cm^{-1} ; ^1H -NMR (300 MHz, CDCl_3) δ 0.09 (s, 3H), 0.14 (s, 3H), 0.64 (m, 1H), 0.73-0.92 (m, 23H), 0.97-1.60 (m, 9H), 1.66-2.08 (m, 6H), 2.14-2.55 (m, 4H), 3.24 (dd, 1H, $J = 9.0, 7.7$ Hz), 3.38 (dd, 1H, $J = 9.0, 5.7$ Hz), 3.79 (s, 3H), 3.95 (m, 1H), 4.39 (d, 1H, $J = 11.7$ Hz), 4.45 (d, 1H, $J = 11.7$ Hz), 4.48 (d, 1H, $J = 2.2$ Hz), 4.65 (ddt, 1H, $J = 13.1, 5.8, 1.3$ Hz), 4.72 (ddt, 1H, $J = 13.1, 5.8, 1.3$ Hz), 5.07 (m, 1H), 5.25 (dd, 1H, $J = 10.4, 1.3$ Hz), 5.34 (dd, 1H, $J = 17.2, 1.3$ Hz), 5.83 (m, 1H), 5.96 (ddt, 1H, $J = 17.2, 10.4, 5.8$ Hz), 6.58 (d, 1H, $J = 11.4$ Hz), 6.86 (d, 2H, $J = 8.5$ Hz), 7.08 (dd, 1H, $J = 15.0, 11.4$ Hz), 7.25 (d, 2H, $J = 8.5$ Hz); ^{13}C -NMR (100 MHz, CDCl_3) δ -4.6, -4.1, 14.8, 17.6, 18.0, 18.4, 20.0, 25.0, 25.8, 25.9, 26.2, 29.1, 30.2, 34.2, 34.7, 35.2, 35.8, 37.8, 41.7, 43.3, 46.4, 48.5, 55.2, 65.0, 72.3, 72.7, 74.3, 75.7, 76.7, 113.7, 118.5, 129.0, 129.4, 130.7, 132.1, 139.0, 139.3, 140.9, 159.0, 166.6, 171.5; HRMS (FAB, *m*-NBA+NaI) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{45}\text{H}_{72}\text{O}_8\text{SiNa}$ 791.4894, found 791.4894.

**(2*S*,4*E*,8*S*,9*S*,11*R*,13*S*,15*S*,16*S*)-Allyl 16-(*tert*-butyldimethylsilyloxy)-8-hydroxy-2-
{(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl}-9,11,13,15-tetramethyl-18-
oxooxacyclooctadeca-4,6-diene-7-carboxylate (**51**)**

To a solution of SmI_2 (0.1 M in THF, 13.3 ml, 1.33 mmol) was added dropwise a solution of **43** (56.3 mg, 66.5 μmol) in THF (53.3 ml) over 1 h at -78°C under an argon atmosphere. After exposure to oxygen gas, the reaction mixture was treated with silica gel (16 g) and hexane (28 ml) and stirred for 30 min at room temperature. The resulting mixture was filtered through a pad of silica gel (eluate EtOAc) and concentrated in

vacuo. The residue was briefly purified by column chromatography (20 : 1 hexanes/EtOAc) to give the cyclized diastereomixtures.

To a solution of the mixture (51.1 mg, 0.067 mmol) in CH₂Cl₂ (1.3 ml) was added Dess-Martin periodinane (70.5 mg, 0.166 mmol) at room temperature. After stirring for 0.5 h, the reaction mixture was quenched with aqueous NaHCO₃ solution and aqueous Na₂S₂O₃ solution and extracted with CH₂Cl₂. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo to afford the crude ketones **49** and **50**.

To a solution of the crude ketones in CH₂Cl₂ (1.3 ml) was added DMAP (12.3 mg, 0.099 mmol). After 7 day, the reaction mixture was diluted with water and extracted with CH₂Cl₂. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo to give the crude ketones **49** and **50**.

To a solution of the mixture in MeOH (1.3 ml) was added CeCl₃·7H₂O (37.2 mg, 0.100 mmol) and NaBH₄ (3.80 mg, 0.100 mmol) at 0 °C. After stirring for 0.5 h, the reaction mixture was treated with water. After MeOH was removed in vacuo, the resulting mixture was extracted with EtOAc. The combined organic layers were dried over anhydrous Na₂SO₄ and removed in vacuo. The residue was purified by column chromatography (25 : 1 hexanes/EtOAc) to give **51** (31.2 mg, 61% for 4 steps) as a yellow oil. $[\alpha]_D^{24} -21.6^\circ$ (c 0.17, CHCl₃); IR (KBr) 2952, 2864, 1738, 1693, 1630, 1417, 1373, 1246, 1171, 1082, 835, 775 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃) δ 0.07 (s, 3H), 0.08 (s, 3H), 0.72-0.90 (m, 22H), 0.92-1.10 (m, 3H), 1.17-1.61 (m, 5H), 1.68-1.77 (m, 4H), 1.83-1.96 (m, 2H), 1.97-2.16 (m, 3H), 2.19-2.47 (m, 4H), 3.24 (dd, 1H, *J* = 8.8, 7.7 Hz), 3.37 (dd, 1H, *J* = 8.8, 5.7 Hz), 3.79 (s, 3H), 3.99 (m, 1H), 4.40 (d, 1H, *J* = 11.8 Hz), 4.45 (d, 1H, *J* = 11.8 Hz), 4.61 (ddt, 1H, *J* = 13.1, 5.8, 1.3 Hz), 4.67 (ddt, 1H, *J* = 13.1, 5.8, 1.30 Hz), 4.67 (m, 1H), 5.02 (m, 1H), 5.26 (dd, 1H, *J* = 10.4, 1.1 Hz), 5.34 (dd, 1H, *J* = 17.4, 1.1 Hz), 5.89-6.03 (m, 2H), 6.57 (m, 1H), 6.86 (d, 2H, *J* = 8.5 Hz), 7.23 (d, 1H, *J* = 11.2 Hz), 7.25 (d, 2H, *J* = 8.5 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ -5.1, -4.0, 13.8, 17.9, 18.8, 19.7, 25.0, 25.8, 26.0, 26.5, 29.5, 29.7, 30.2, 35.8, 36.2, 36.7, 37.8, 41.8, 43.7, 45.8, 48.4, 55.2, 65.5, 72.7, 73.3, 74.3, 74.8, 75.2, 113.7, 119.9, 128.0, 129.1, 130.7, 132.0, 139.3, 141.2, 141.7, 159.0, 169.0, 171.5; HRMS (FAB, *m*-NBA+NaI) [M+Na]⁺ calcd for C₄₅H₇₂O₈SiNa 791.4894, found 791.4914.

(2*S*,4*E*,6*E*,8*S*,9*S*,11*R*,13*S*,15*S*,16*S*)-Allyl 8,16-bis(*tert*-butyldimethylsilyloxy)-2-[(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl]-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-diene-7-carboxylate (53**)**

A solution of **51** (29.8 mg, 0.039 mmol) and 2,6-lutidine (0.010 ml, 0.066 mmol) in CH₂Cl₂ (0.8 ml) was cooled to 0 °C under an nitrogen atmosphere. To the stirring solution was added TBSOTf (0.010 ml, 0.050 mmol). After stirring for 30 min, the mixture was treated with H₂O and extracted with CH₂Cl₂. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated under reduced pressure. The

residue was purified by column chromatography (60 : 1 hexanes/EtOAc) to give **53** (19.1 mg, 85%) as a colorless oil. $[\alpha]_D^{25} -9.2^\circ$ (c 0.17, CHCl_3); IR (KBr) 2947, 2862, 2357, 1736, 1631, 1514, 1458, 1371, 1244, 1169, 1076, 835, 779, 675 cm^{-1} ; $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ -0.09 (s, 3H), 0.04 (s, 3H), 0.05 (s, 3H), 0.05 (s, 3H), 0.71-0.90 (m, 30H), 0.95-1.22 (m, 5H), 1.25-2.03 (m, 13H), 2.27 (d, 2H, $J = 6.5$ Hz), 2.42 (m, 2H), 3.18 (t, 1H, $J = 8.9$ Hz), 3.38 (dd, 1H, $J = 8.9, 4.4$ Hz), 3.78 (s, 3H), 3.93 (m, 1H), 4.41 (s, 2H), 4.63 (ddt, 1H, $J = 13.1, 5.8, 1.3$ Hz), 4.67 (ddt, 1H, $J = 13.1, 5.8, 1.3$ Hz), 4.80 (m, 1H), 4.95 (m, 1H), 5.23 (dd, 1H, $J = 10.4, 1.4$ Hz), 5.32 (dd, $J = 17.2, 1.4$ Hz), 5.89-6.09 (m, 2H), 6.66 (d, 1H, $J = 11.2$ Hz), 6.86 (d, 2H, $J = 8.7$ Hz), 7.08 (m, 1H), 7.24 (d, 2H, $J = 8.7$ Hz); HRMS (FAB, $m\text{-NBA} + \text{NaI}$) $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{51}\text{H}_{86}\text{O}_8\text{Si}_2\text{Na}$ 905.5759, found 905.5740.

(2S,4E,6E,8S,9S,11R,13S,15S,16S)-16-(tert-Butyldimethylsilyloxy)-8-hydroxy-2-[(1R,2R)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl]-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-diene-7-carboxylic acid (55**)**

To a solution of **53** (9.50 mg, 0.011 mmol) in MeOH (0.22 ml) at 0°C were added $\text{Pd}(\text{PPh}_3)_4$ (1.00 mg, 0.001 mmol) and NaBH_4 (1.20 mg, 0.032 mmol). After stirring for 30 min at 0°C , the reaction mixture was diluted with water and MeOH was concentrated under reduced pressure. The resulting mixture was extracted with EtOAc. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The residue was purified by column chromatography (2 : 1 hexanes/EtOAc) to give **55** (6.7 mg, 85%) as a colorless oil. $[\alpha]_D^{27} -34.4^\circ$ (c 0.17, CHCl_3); $^1\text{H-NMR}$ (300MHz, CDCl_3) δ 0.07 (s, 3H), 0.09 (s, 3H), 0.75-1.18 (m, 25H), 1.20-1.77 (m, 9H), 1.87-2.45 (m, 9H), 3.24 (dd, 1H, $J = 9.0, 7.9$ Hz), 3.37 (dd, 1H, $J = 9.0, 5.7$ Hz), 3.79 (s, 3H), 3.99 (m, 1H), 4.40 (d, 1H, $J = 11.7$ Hz), 4.45 (d, 1H, $J = 11.7$ Hz), 4.68 (d, 1H, $J = 3.6$ Hz), 5.02 (m, 1H), 6.02 (m, 1H), 6.59 (m, 1H), 6.86 (d, 2H, $J = 8.6$ Hz), 7.25 (d, 2H, $J = 8.6$ Hz), 7.34 (d, 1H, $J = 11.5$ Hz); $^{13}\text{C-NMR}$ (100 MHz, CDCl_3) δ -5.1, -4.0, 14.1, 17.9, 18.8, 19.6, 21.0, 22.7, 25.0, 25.8, 26.2, 26.5, 29.5, 30.2, 33.6, 35.8, 36.4, 36.7, 41.9, 43.7, 45.7, 48.3, 55.2, 72.7, 73.4, 74.3, 74.6, 75.2, 113.8, 125.8, 128.1, 129.1, 130.7, 142.3, 143.7, 159.1, 171.5, 172.1; LRMS (FAB, $m\text{-NBA} + \text{NaI}$) $[\text{M} - \text{H}]^+$ 727, $[\text{M} + \text{Na}]^+$ 751.

**(2*S*,4*E*,6*E*,8*S*,9*S*,11*R*,13*S*,15*S*,16*S*)-16-(*tert*-Butyldimethylsilyloxy)-8-hydroxy-2-
{(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl}-9,11,13,15-tetramethyl-18-
oxooxacyclooctadeca-4,6-diene-7-carboxamide (**56**)**

To a solution of **55** (20.3 mg, 0.028 mmol) in THF (0.56 ml) at room temperature were added a solution of NH₃ in dioxane (0.5 M, 0.560 ml), Et₃N (0.020 ml, 0.112 mmol) and BOP (24.7 mg, 0.056 mmol). The reaction mixture was stirred for 21.5 h at 23 °C and then treated with a solution of NH₃ in dioxane (0.5 M, 0.560 ml) again. After stirring for 26.5 h (total 48 h), the reaction mixture was quenched with NH₄Cl solution and extracted with EtOAc. The combined organic layers were dried over anhydrous Na₂SO₄ and removed in vacuo. The residue was purified by column chromatography (1 : 1 hexanes/EtOAc) to give **56** (13.9 mg, 69%) as a colorless oil. ¹H-NMR (300MHz, CDCl₃) δ 0.09 (s, 3H), 0.11 (s, 3H), 0.76-0.87 (m, 21H), 0.96-2.14 (m, 18H), 2.22-2.48 (m, 4H), 3.27 (dd, 1H, *J* = 8.5, 7.3 Hz), 3.37 (dd, 1H, *J* = 8.5, 6.4 Hz), 3.80 (s, 3H), 4.04 (m, 1H), 4.40 (d, 1H, *J* = 11.7 Hz), 4.45 (d, 1H, *J* = 11.7 Hz), 4.70 (d, 1H, *J* = 3.0 Hz), 5.00 (m, 1H), 5.86 (m, 1H), 6.44 (dd, 1H, *J* = 14.2, 11.2 Hz), 6.76 (d, 1H, *J* = 11.2 Hz), 6.87 (d, 2H, *J* = 8.6 Hz), 7.25 (d, 2H, *J* = 8.6 Hz)

**(2*S*,4*E*,6*Z*,8*S*,9*S*,11*R*,13*S*,15*S*,16*S*)-16-(*tert*-Butyldimethylsilyloxy)-8-hydroxy-2-
{(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl}-9,11,13,15-tetramethyl-18-
oxooxacyclooctadeca-4,6-diene-7-carbonitrile (**38**)**

To a solution of **56** (13.3 mg, 0.018 mmol) in CH₂Cl₂ (0.4 ml) were added Et₃N (0.020 ml, 0.132 mmol), TFA (0.005 ml, 0.066 mmol), and a solution of 2-chloro-1,3-dimethylimidazolinium chloride (DMC) in CH₂Cl₂ (25%, 0.050 ml, 0.066 mmol) under an argon atmosphere. After stirring for 1.5 h, the reaction mixture was diluted with water and extracted with CH₂Cl₂. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product was purified by column chromatography (15 : 1 hexanes/EtOAc, EtOAc) to give the corresponding C8-trifluoroacetyl compound (4.60 mg, 0.006 mmol, 31%) and **38** (1.30 mg, 0.002 mmol, 10%).

To a solution of the C8-trifluoroacetyl compound in MeOH (0.5 ml) at room temperature was added K₂CO₃ (3.60 mg, 0.026 mmol). After stirring for 1.5 h, the mixture was treated with an additional K₂CO₃ (3.60 mg, 0.026 mmol) and stirred for 2.5 h at room temperature. The reaction mixture was then stirred for 1.0 h at 50 °C and quenched with H₂O. After MeOH was removed in vacuo, the resulting mixture was extracted with EtOAc. The combined organic layers were dried over anhydrous Na₂SO₄

and removed in vacuo. The crude product was purified by column chromatography (5 : 1 hexanes/EtOAc) to give **38** (2.96 mg, 73%, total 4.26 mg, 33% for 2 steps).

(*S*,2*Z*, 4*E*) - Ethyl 2-bromo-7-(*tert*-butyldimethylsilyloxy)-7-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)hepta-2,4-dienoate (29a**)**

A solution of **27** (184 mg, 0.426 mmol) in benzene (4.2 ml) was treated with (ethoxycarbonylbromomethylidene)triphenylphosphorane (544 mg, 1.27 mmol) and refluxed at 80 °C for 12 h. The reaction mixture was concentrated in vacuo and purified by column chromatography (40 : 1 hexanes/EtOAc) to give **29a** (201 mg, 81%) as a colorless oil. ¹H-NMR (270 MHz, CDCl₃) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.88 (s, 9H), 1.26 (m, 1H), 1.34 (t, 3H, *J* = 7.1 Hz), 1.46-1.72 (m, 6H), 2.11 (m, 1H), 2.39 (m, 2H), 3.18 (t, 1H, *J* = 8.6 Hz), 3.41 (dd, 1H, *J* = 8.6, 5.8 Hz), 3.70 (m, 1H), 3.80 (s, 3H), 4.29 (q, 2H, *J* = 7.1 Hz), 4.39 (d, 1H, *J* = 11.9 Hz), 4.45 (d, 1H, *J* = 11.9 Hz), 6.34 (m, 1H), 6.48 (dd, 1H, *J* = 15.5, 10.2 Hz), 6.86 (d, 2H, *J* = 8.6 Hz), 7.24 (d, 2H, *J* = 8.6 Hz), 7.62 (d, 1H, *J* = 10.2 Hz); ¹³C-NMR (67.5 MHz, CDCl₃) δ -4.6, -4.2, 14.2, 18.0, 25.3, 25.9, 29.4, 30.4, 39.3, 41.3, 47.4, 55.2, 62.3, 72.7, 74.6, 75.1, 113.7, 129.1, 129.4, 130.8, 141.2, 144.1, 159.0, 163.1, 190.8; HRMS (FAB, *m*-NBA+NaI) [*M*+Na]⁺ calcd for C₂₉H₄₅O₅BrSiNa 603.2117, found 603.2146.

(*S*,2*Z*,4*E*)-Ethyl 7-(*tert*-butyldimethylsilyloxy)-2-iodo-7-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)hepta-2,4-dienoate (29b**)**

To a solution of **27** (205 mg, 0.572 mmol) in MeOH at room temperature were added (ethoxycarbonyliodomethylidene)triphenylphosphorane (568 mg, 0.944 mmol), TBAB (15.2 mg, 0.047 mmol), and K₂CO₃ (65.3 mg, 0.472 mmol). The reaction mixture was then stirred at 50 °C for 9.5 h and concentrated in vacuo. The crude product was purified by column chromatography (80 : 1 hexanes/EtOAc) to give **29b** (180 mg, 61%) as a colorless oil. [α]_D²⁴ = +19.4° (*c* = 0.50, CHCl₃); IR (KBr) 2945, 2858, 1712, 1622, 1579, 1514, 1462, 1363, 1248, 1180, 1083, 833, 771 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃) δ 0.05 (s, 3H), 0.05 (s, 3H), 0.88 (s, 9H), 1.34 (t, 3H, *J* = 7.2 Hz), 1.41-1.73 (m, 7H), 2.10 (m, 1H), 2.32-2.48 (m, 2H), 3.18 (t, 1H, *J* = 8.7 Hz), 3.42 (dd, 1H, *J* = 8.7, 5.3 Hz), 3.70 (m, 1H), 3.79 (s, 3H), 4.28 (q, 2H, *J* = 7.2 Hz), 4.39 (d, 1H, *J* = 11.6 Hz), 4.45 (d, 1H, *J* = 11.6 Hz), 6.35-6.46 (m, 2H), 6.86 (d, 2H, *J* = 8.5 Hz), 7.25 (d, 2H, *J* = 8.5 Hz), 7.55 (d, 1H, *J* = 9.4 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ -4.6, -4.2, 14.2, 18.0, 25.3, 25.9, 29.4, 30.4, 39.3, 41.3, 47.4, 55.2, 62.6, 72.7, 74.6, 75.1, 90.5, 113.7, 129.2, 130.8, 134.0, 144.8, 147.6, 159.0, 163.6; HRMS (FAB, *m*-NBA+NaI) [*M*+Na]⁺ calcd for C₂₉H₄₅IO₅SiNa 651.1979, found 651.1985.

(*S*,2*Z*,4*E*)-2-Bromo-7-(*tert*-butyldimethylsilyloxy)-7-((1*R*,2*R*)-2-[(4-

methoxybenzyloxy)methyl]cyclopentyl}hepta-2,4-dien-1-ol (59a**)**

To a solution of **29a** (101 mg, 0.171 mmol) in CH_2Cl_2 (1.7 ml) was added dropwise DIBAL (0.94 M in hexane, 0.460 ml, 0.428 mmol) at 0°C . After stirring for 0.5 h, the reaction mixture was quenched with MeOH, diluted with CH_2Cl_2 , and treated with Celite (0.2 g) and $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$ (0.2 g). The resulting mixture was stirred for 2 h at room temperature, filtered through a pad of Celite and concentrated in vacuo. The residue was purified by column chromatography (15 : 1 hexanes/EtOAc) to give **59a** (85.0 mg, 92%) as a colorless oil. $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ 0.04 (s, 3H), 0.07 (s, 3H), 0.88 (s, 9H), 1.23-1.72 (m, 7H), 2.12 (m, 1H), 2.32 (m, 2H), 3.18 (t, 1H, $J = 8.7$ Hz), 3.42 (dd, 1H, $J = 8.7, 5.1$ Hz), 3.64 (m, 1H), 3.80 (s, 3H), 4.29 (s, 2H), 4.39 (d, 1H, $J = 11.5$ Hz), 4.45 (d, 1H, $J = 11.5$ Hz), 5.94 (m, 1H), 6.30 (dd, 1H, $J = 15.2, 9.9$ Hz), 6.51 (d, 1H, $J = 9.9$ Hz), 6.87 (d, 2H, $J = 8.6$ Hz), 7.25 (d, 2H, $J = 8.6$ Hz); LRMS (FAB, $m\text{-NBA} + \text{NaI}$) $[\text{M} + \text{Na}]^+$ 561.

(*S*,2*Z*,4*E*)-7-(*tert*-Butyldimethylsilyloxy)-2-iodo-7-[(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl}hepta-2,4-dien-1-ol (59b**)**

To a solution of **29b** (291 mg, 0.463 mmol) in CH_2Cl_2 (4.6 ml) was added dropwise DIBAL (0.94 M in hexane, 1.20 ml, 1.16 mmol) at 0°C . After stirring for 0.5 h, the reaction mixture was quenched with MeOH, diluted with CH_2Cl_2 , and treated with Celite (0.7 g) and $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$ (0.7 g). The mixture was stirred for 2 h at room temperature, filtered through a pad of Celite, and concentrated in vacuo. The residue was purified by column chromatography (20 : 1 hexanes/EtOAc) to give **59b** (247 mg, 91%). $[\alpha]_D^{24} +22.8^\circ$ (c 0.18, CHCl_3); IR (KBr) 2943, 2858, 1614, 1514, 1462, 1250, 1076, 833, 773 cm^{-1} ; $^1\text{H-NMR}$ (300MHz, CDCl_3) δ 0.03 (s, 6H), 0.87 (s, 9H), 1.45-1.73 (m, 7H), 2.11 (m, 1H), 2.32 (m, 2H), 3.17 (t, 1H, $J = 8.7$ Hz), 3.42 (dd, 1H, $J = 8.7, 5.1$ Hz), 3.65 (m, 1H), 3.79 (s, 3H), 4.29 (bs, 2H), 4.38 (d, 1H, $J = 11.6$ Hz), 4.45 (d, 1H, $J = 11.6$ Hz), 5.99 (m, 1H), 6.17 (dd, 1H, $J = 15.2, 9.8$ Hz), 6.42 (d, 1H, $J = 9.8$ Hz), 6.86 (d, 2H, $J = 8.7$ Hz), 7.24 (d, 2H, $J = 8.7$ Hz); $^{13}\text{C-NMR}$ (75MHz, CDCl_3) δ -4.6, -4.1, 18.1, 25.3, 25.9, 29.5, 30.5, 38.9, 41.1, 47.1, 55.3, 71.7, 72.7, 75.3, 76.6, 105.2, 113.7, 129.2, 130.9, 133.1, 134.0, 136.9, 159.0; HRMS (FAB, $m\text{-NBA} + \text{NaI}$) $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{27}\text{H}_{43}\text{IO}_4\text{SiNa}$ 609.1873, found 609.1854.

(*S*,2*Z*,4*E*)-2-Bromo-7-[(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl]hepta-2,4-diene-1,7-diol (60a**)**

To a solution of **59a** (85.0 mg, 0.158 mmol) in THF (0.3 ml) at room temperature was added a solution of HF·pyridine in THF (HF·pyridine : pyridine : THF = 1 : 1 : 1, 1.3 ml). After stirring for 16.5 h at room temperature, the reaction mixture was filtered through a pad of silica gel (eluate CH₂Cl₂ : MeOH = 60 : 1) and concentrated in vacuo. The residue was purified by column chromatography (2 : 1 hexanes/EtOAc) to give **60a** (60.3 mg, 90%) as a colorless oil. ¹H-NMR (300 MHz, CDCl₃) δ 1.17-1.29 (m, 2H), 1.39-1.65 (m, 3H), 1.69-1.84 (m, 2H), 2.05 (m, 1H), 2.19 (m, 1H), 2.45 (m, 1H), 3.15 (dd, 1H, *J* = 10.3, 8.8 Hz), 3.54 (dd, 1H, *J* = 8.8, 4.1 Hz), 3.80 (s, 3H), 4.73 (s, 2H), 4.48 (s, 2H), 6.11 (m, 1H), 6.37 (dd, 1H, *J* = 15.2, 9.9 Hz), 6.57 (d, 1H, *J* = 9.9 Hz), 6.88 (d, 1H, *J* = 8.6 Hz), 7.24 (d, 1H, *J* = 8.6 Hz); LRMS (FAB, *m*-NBA+NaI) [M+Na]⁺ 447.

(*S*,2*Z*,4*E*)-2-Iodo-7-[(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl]hepta-2,4-diene-1,7-diol (60b**)**

To a solution of **59b** (135 mg, 0.230 mmol) in THF (0.4 ml) at room temperature was added a solution of HF·pyridine in THF (HF·pyridine : pyridine : THF = 1 : 1 : 1, 2.0 ml). After stirring for 19 h at room temperature, the reaction mixture was filtered through a pad of silica gel (eluate CH₂Cl₂ : MeOH = 60 : 1) and concentrated in vacuo. The residue was purified by column chromatography (5 : 1 hexanes/EtOAc) to give **60b** (103 mg, 95%) as a colorless oil. [α]_D²⁵ +22.6° (*c* 0.18, CHCl₃); IR (KBr) 2943, 2862, 2359, 1612, 1514, 1452, 1248, 1080, 1036, 821 cm⁻¹; ¹H-NMR (300MHz, CDCl₃) δ 1.17-1.29 (m, 2H), 1.39-1.64 (m, 3H), 1.69-1.84 (m, 2H), 2.05 (m, 1H), 2.20 (m, 1H), 2.46 (m, 1H), 3.14 (dd, 1H, *J* = 10.4, 8.7 Hz), 3.40 (m, 1H), 3.54 (dd, 1H, *J* = 8.7, 4.1 Hz), 3.80 (s, 3H), 4.29 (s, 2H), 4.48 (s, 2H), 6.12-6.27 (m, 2H), 6.48 (d, 1H, *J* = 8.8 Hz), 6.87 (d, 2H, *J* = 8.6 Hz), 7.24 (d, 2H, *J* = 8.6 Hz); ¹³C-NMR (75MHz, CDCl₃) δ 24.4, 29.8, 31.0, 39.4, 43.9, 51.8, 55.2, 71.5, 72.9, 74.1, 75.0, 113.8, 129.3, 129.5, 132.8, 133.7, 137.0, 159.2; HRMS (FAB, *m*-NBA+NaI) [M+Na]⁺ calcd for C₂₁H₂₉IO₄SiNa 495.1008, found 495.1014.

(*S*,3*E*,5*Z*)-6-Bromo-1-[(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl]-7-(triisopropylsilyloxy)hepta-3,5-dien-1-ol (61a**)**

A solution of **60a** (67.2 mg, 0.158 mmol) in CH₂Cl₂ (1.6 ml) at 0 °C under nitrogen were treated with 2,6-lutidine (24 μL, 0.206 mmol) and TIPSOTf (47 μL, 0.174 mmol).

After stirring for 1 h at 0 °C, 2,6-lutidine (24 μ L, 0.206 mmol) and TIPSOTf (47 μ L, 0.174 mmol) were added again. The reaction mixture was stirred for 0.5 h, diluted with H₂O, and extracted with CH₂Cl₂. The organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product was purified by column chromatography (40 : 1 hexanes/EtOAc) to give **61a** (61.6 mg, 67%) as a colorless oil. ¹H-NMR (300 MHz, CDCl₃) δ 1.04-1.30 (m, 23H), 1.39-1.86 (m, 5H), 2.05 (m, 1H), 2.19 (m, 1H), 2.44 (m, 1H), 3.16 (dd, 1H, *J* = 10.2, 8.7 Hz), 3.40 (m, 1H), 3.52 (dd, 1H, *J* = 8.7, 4.3 Hz), 3.80 (s, 3H), 4.37 (s, 2H), 4.40 (d, 1H, *J* = 11.7 Hz), 4.52 (d, 1H, *J* = 11.7 Hz), 6.07 (m, 1H), 6.41 (dd, 1H, *J* = 15.5, 10.1 Hz), 6.69 (d, 1H, *J* = 10.1 Hz), 6.87 (d, 2H, *J* = 8.6 Hz), 7.24 (d, 2H, *J* = 8.6 Hz); HRMS (FAB, *m*-NBA+NaI) [M+Na]⁺ calcd for C₃₀H₄₉BrO₄SiNa 603.2481, found 603.2462.

(*S*,3*E*,5*Z*)-6-Iodo-1-[(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl]-7-(triisopropylsilyloxy)hepta-3,5-dien-1-ol (61b**)**

A solution of **60b** (16.5 mg, 0.0350 mmol) in CH₂Cl₂ (0.4 ml) at 0 °C were treated with 2,6-lutidine (20 μ L, 0.182 mmol) and TIPSOTf (40 μ L, 0.153 mmol). After stirring for 6 h at 0 °C, the reaction mixture was diluted with H₂O and extracted with EtOAc. The organic phases were dried and concentrated in vacuo. The crude product was purified by column chromatography (30 : 1 hexanes/EtOAc) to give **61b** (16.5 mg, 75%). [α]_D²⁴ +10.7° (*c* 0.50, CHCl₃); IR (KBr) 3427, 2945, 2864, 1614, 1514, 1460, 1248, 1115, 881, 809, 681 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃) δ 1.04-1.11 (m, 21H), 1.25 (m, 1H), 1.39-1.67 (m, 5H), 1.78 (m, 1H), 2.06 (m, 1H), 2.22 (m, 1H), 2.45 (m, 1H), 3.16 (dd, 1H, *J* = 10.2, 8.8 Hz), 3.40 (m, 1H), 3.52 (dd, 1H, *J* = 8.8 Hz, 4.2 Hz), 3.79 (s, 3H), 4.38 (s, 2H), 4.45 (d, 1H, *J* = 11.8 Hz), 4.51 (d, 1H, *J* = 11.8 Hz), 6.11 (m, 1H), 6.28 (dd, 1H, *J* = 15.3, 9.6 Hz), 6.62 (d, 1H, *J* = 9.6 Hz), 6.87 (d, 2H, *J* = 8.7 Hz), 7.24 (d, 2H, *J* = 8.7 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ 12.0, 18.0, 24.5, 29.9, 31.0, 39.6, 44.0, 51.9, 55.2, 71.6, 72.9, 74.2, 75.2, 104.7, 113.8, 129.4, 131.5, 132.9, 135.8, 159.3; HRMS (FAB, *m*-NBA+NaI) [M+Na]⁺ calcd for C₃₀H₄₉IO₄SiNa 651.2342, found 651.2367.

(3*S*,4*S*,6*S*,8*R*,10*S*)-((*S*,3*E*,5*Z*)-6-Bromo-1-[(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl]-7-(triisopropylsilyloxy)hepta-3,5-dienyl) 3-(*tert*-butyldimethylsilyloxy)-11-hydroxy-4,6,8,10-tetramethylundecanoate (62a**)**

A solution of **3** (13.4 mg, 28.4 μ mol) in benzene (0.4 ml) at room temperature was

To a solution of the ester in EtOH (0.9 ml) at room temperature was added PPTS (3.90 mg, 15.5 μ mol). After stirring for 8 h at 50°C, the reaction mixture was diluted with water and extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product was purified by column chromatography (10 : 1 hexanes/EtOAc) to give **62a** (20.9 mg, 77% for 2 steps). ¹H-NMR (300 MHz, CDCl₃) δ 0.02 (s, 3H), 0.05 (s, 3H), 0.80-1.39 (m, 49H), 1.48-1.76 (m, 9H), 1.84 (m, 1H), 2.06 (m, 1H), 2.30-2.48 (m, 4H), 3.21 (t, 1H, *J* = 8.7 Hz), 3.35-3.47 (m, 3H), 3.79 (s, 3H), 4.06 (dt, 1H, *J* = 6.3, 2.5 Hz), 4.36 (s, 2H), 4.39 (d, 1H, *J* = 11.8 Hz), 4.46 (d, 1H, *J* = 11.8 Hz), 4.90 (m, 1H), 5.78 (m, 1H), 6.36 (dd, 1H, *J* = 15.2, 10.1 Hz), 6.62 (d, 1H, *J* = 10.1 Hz), 6.68 (d, 2H, *J* = 8.7 Hz), 7.24 (d, 2H, *J* = 8.7 Hz).

S30

A solution of **3** (44.3 mg, 0.094 mmol) in benzene (0.7 ml) at room temperature was treated with Et₃N (26 μ L, 0.188 mmol) and 2,4,6-trichlorobenzoyl chloride (16 μ L, 0.103 mmol) under an argon atmosphere. After stirring for 1 h, a solution of **61b** (74.2 ml, 0.118 mmol) in benzene (1.2 ml) was added dropwise and DMAP was then added. After stirring for 2 h at room temperature, the resulting mixture was treated with aqueous NaHCO₃ solution and extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product was purified by column chromatography (60 : 1 hexanes/EtOAc) to give a mixture of **61b'** and **61b**.

61b': $[\alpha]_D^{27} -8.4^\circ$ (*c* 0.17, CHCl₃); IR (KBr) 2945, 2862, 2357, 1734, 1460, 1373, 1250, 1116, 1032, 827, 679 cm⁻¹; ¹H-NMR (300MHz, CDCl₃) δ 0.03 (s, 3H), 0.06 (s, 3H), 0.79-0.90 (m, 23H), 0.95-1.41 (m, 26H), 1.49-1.87 (m, 16H), 2.07 (m, 1H), 2.32-2.52 (m, 4H), 3.09-3.27 (m, 2H), 3.36-3.58 (m, 3H), 3.80 (s, 3H), 3.85 (m, 1H), 4.07 (m, 1H), 4.37 (s, 2H), 4.42 (d, 1H, *J* = 11.7 Hz), 4.47 (d, 1H, *J* = 11.7 Hz), 4.57 (m, 1H), 4.92 (m, 1H), 5.83 (m, 1H), 6.24 (dd, 1H, *J* = 15.0, 9.9 Hz), 6.56 (d, 1H, *J* = 9.9 Hz), 6.87 (d, 2H, *J* = 8.8 Hz), 7.25 (d, 2H, *J* = 8.8 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ -4.6, -4.1, 12.1, 12.2, 14.5, 16.6, 16.7, 18.1, 18.2, 19.6, 19.7, 20.6, 20.8, 25.3, 25.7, 26.0, 27.1, 27.2, 27.3, 29.8, 30.5, 31.0, 31.0, 35.5, 36.4, 40.1, 41.6, 44.7, 46.0, 55.3, 62.1, 62.2, 71.6, 71.7, 72.8, 74.0, 74.1, 74.2, 98.7, 99.1, 106.1, 109.3, 113.8, 129.1, 130.8, 131.1, 133.4, 134.2, 159.1, 171.8; HRMS (FAB, *m*-NBA+NaI) $[M+Na]^+$ calcd for C₅₆H₉₉IO₈Si₂Na 1105.5821, found 1105.5821.

(3*S*,4*S*,6*S*,8*R*,10*S*)-((*S*,3*E*,5*Z*)-6-Iodo-1-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)-7-(triisopropylsilyloxy)hepta-3,5-dienyl) 3-(*tert*-butyldimethylsilyloxy)-11-hydroxy-4,6,8,10-tetramethylundecanoate (62b**)**

To a solution of the mixture of **61b'** and **61b** in EtOH (3.5 ml) at room temperature was added PPTS (13.2 mg, 0.052 mmol). After stirring for 12.5 h at 50°C, the reaction mixture was diluted with water and extracted with EtOAc. The combined organic phases were dried over anhydrous Na₂SO₄ and concentrated in vacuo. The crude product was purified by column chromatography (40 : 1 hexanes/EtOAc) to give **62b** (77.4 mg, 83% for 2 steps). $[\alpha]_D^{24} -15.5^\circ$ (*c* 0.17, CHCl₃); IR (KBr) 3464, 2951, 2862, 1732, 1514,

1462, 1375, 1250, 1113, 833, 781, 679 cm^{-1} ; ^1H -NMR (300 MHz, CDCl_3) δ 0.03 (s, 3H), 0.06 (s, 3H), 0.79-1.00 (m, 24H), 1.02-1.40 (m, 25H), 1.49-1.78 (m, 9H), 1.87 (m, 1H), 2.07 (m, 1H), 2.31-2.52 (m, 4H), 3.22 (t, 1H, $J = 8.4$ Hz), 3.41 (dd, 1H, $J = 8.4, 6.4$ Hz), 3.35–3.47 (m, 2H), 3.80 (s, 3H), 4.07 (dt, 1H, $J = 6.4, 2.4$ Hz), 4.37 (s, 2H), 4.40 (d, 1H, $J = 11.8$ Hz), 4.42 (d, 1H, $J = 11.8$ Hz), 4.91 (m, 1H), 5.83 (dt, 1H, $J = 15.0, 7.4$ Hz), 6.24 (dd, 1H, $J = 15.0, 9.8$ Hz), 6.56 (d, 1H, $J = 9.8$ Hz), 6.87 (d, 2H, $J = 8.7$ Hz), 7.25 (d, 2H, $J = 8.7$ Hz); ^{13}C -NMR (100 MHz, CDCl_3) δ -4.7, -4.3, 12.0, 14.4, 16.0, 18.0, 18.1, 20.6, 20.7, 25.2, 25.9, 27.1, 27.3, 29.8, 30.4, 33.3, 35.4, 36.4, 39.6, 40.0, 41.3, 41.5, 44.6, 45.8, 55.2, 69.3, 71.6, 71.7, 72.7, 74.1, 76.4, 106.0, 113.7, 129.0, 130.7, 131.0, 133.3, 134.1, 159.0, 171.7; HRMS (FAB, m -NBA+NaI) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{51}\text{H}_{91}\text{IO}_7\text{Si}_2\text{Na}$ 1021.5246, found 1021.5275.

(3*S*,4*S*,6*S*,8*R*,10*S*)-((*S*,3*E*,5*Z*)-6-Bromo-1-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)-7-(triisopropylsilyloxy)hepta-3,5-dienyl) 3-(*tert*-butyldimethylsilyloxy)-4,6,8,10-tetramethyl-11-oxoundecanoate (58a)

To a mixture of dried MS4Å (10.0 mg) and **62a** (19.9 mg, 20.9 μmol) in CH_2Cl_2 (1.1 ml) were added NMO (4.90 mg, 41.8 μmol) and TPAP (0.40 mg, 1.0 μmol) at room temperature under a argon atmosphere. After stirring for 15 minute at room temperature, additional NMO (4.90 mg, 41.8 μmol) and TPAP (0.40 mg, 1.0 μmol) were added. After 30 minute, the reaction mixture was treated with aqueous $\text{Na}_2\text{S}_2\text{O}_3$ solution, filtered through a pad of Celite, and extracted with EtOAc. The combined organic layers were dried over anhydrous Na_2SO_4 and removed in vacuo. The crude product was purified by column chromatography (30 : 1 hexanes/EtOAc) to give aldehyde **58a** (16.4 mg, 83%). ^1H -NMR (300 MHz, CDCl_3) δ 0.02 (s, 3H), 0.04 (s, 3H), 0.79-0.99 (m, 20H), 1.04-1.41 (m, 30H), 1.46-1.76 (m, 7H), 1.84 (m, 1H), 2.06 (m, 1H), 2.30-2.50 (m, 5H), 3.21 (t, 1H, $J = 8.7$ Hz), 3.39 (dd, 1H, $J = 8.7, 5.1$ Hz), 3.79 (s, 3H), 4.06 (dt, 1H, $J = 6.2, 2.4$ Hz), 4.35 (s, 2H), 4.39 (d, 1H, $J = 11.7$ Hz), 4.45 (d, 1H, $J = 11.7$ Hz), 4.90 (m, 1H), 5.78 (m, 1H), 6.36 (dd, 1H, $J = 15.1, 10.2$ Hz), 6.62 (d, 1H, $J = 10.2$ Hz), 6.68 (d, 1H, $J = 8.6$ Hz), 7.24 (d, 1H, $J = 8.6$ Hz), 9.60 (d, 1H, $J = 1.6$ Hz); HRMS (FAB, m -NBA+NaI) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{51}\text{H}_{89}\text{BrO}_7\text{Si}_2\text{Na}$ 971.5228, found 971.5195.

(3*S*,4*S*,6*S*,8*R*,10*S*)-((*S*,3*E*,5*Z*)-6-Iodo-1-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl)-7-(triisopropylsilyloxy)hepta-3,5-dienyl) 3-(*tert*-butyldimethylsilyloxy)-4,6,8,10-tetramethyl-11-oxoundecanoate (58b)

To a mixture of dried MS4Å (35.0 mg) and **62b** (66.5 mg, 0.070 mmol) in CH₂Cl₂ (3.5 ml) were added NMO (16.5 mg, 0.140 mmol) and TPAP (1.20 mg, 3.5 μmol) at room temperature under a nitrogen atmosphere. After stirring for 15 min at room temperature, the reaction mixture was treated with aqueous Na₂S₂O₃ solution, filtered through a pad of Celite, and extracted with EtOAc. The combined organic layers were dried over anhydrous Na₂SO₄ and removed in vacuo. The crude product was purified by column chromatography (30 : 1 hexanes/EtOAc) to give aldehyde **58b** (54.6 mg, 82%). $[\alpha]_D^{24} +1.1^\circ$ (*c* 0.48, CHCl₃) IR (KBr) 2935, 2862, 1732, 1514, 1462, 1375, 1250, 1113, 833, 679 cm⁻¹; ¹H-NMR (300 MHz, CDCl₃) δ 0.02 (s, 3H), 0.05 (s, 3H), 0.79-1.00 (m, 20H), 1.12-1.90 (m, 38H), 2.06 (m, 1H), 2.30-2.51 (m, 5H), 3.21 (t, 1H, *J* = 8.7 Hz), 3.39 (dd, 1H, *J* = 8.7, 5.4 Hz), 3.79 (s, 3H), 4.06 (m, 1H), 4.36 (s, 2H), 4.39 (d, 1H, *J* = 11.7 Hz), 4.46 (d, 1H, *J* = 11.7 Hz), 4.91 (m, 1H), 5.83 (m, 1H), 6.23 (dd, 1H, *J* = 15.0, 9.7 Hz), 6.55 (d, 1H, *J* = 9.7 Hz), 6.86 (d, 2H, *J* = 8.2 Hz), 7.24 (d, 2H, *J* = 8.2 Hz), 9.60 (d, 1H, *J* = 1.7 Hz); ¹³C-NMR (100 MHz, CDCl₃) δ -4.7, -4.2, 12.0, 12.0, 13.0, 14.4, 18.0, 18.1, 20.4, 20.5, 25.2, 25.9, 27.3, 29.8, 30.4, 35.4, 36.3, 36.4, 39.9, 41.0, 41.5, 44.3, 44.6, 45.4, 55.2, 71.5, 71.6, 72.7, 74.1, 76.4, 106.0, 113.7, 129.0, 130.7, 131.0, 133.3, 134.1, 159.0, 171.6, 205.2; HRMS (FAB, *m*-NBA+NaI) [M+Na]⁺ calcd for C₅₁H₈₉IO₇Si₂Na 1019.5089, found 1019.5070.

**(4*S*,5*S*,7*S*,9*R*,11*S*,13*Z*,15*E*,18*S*)-4-(*tert*-Butyldimethylsilyloxy)-12-hydroxy-18-
 {(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl}-5,7,9,11-tetramethyl-13-
 [(triisopropylsilyloxy)methyl]oxacyclooctadeca-13,15-dien-2-one (**57**)**

To a solution of CrCl_2 (25.1 mg, 0.204 mmol) and NiCl_2 (0.30 mg, 2.30 μmol) in DMF (0.5 ml) at room temperature under argon was added a solution of **58a** (15.5 mg, 16.3 μmol) in DMF (1.1 ml). After stirring for 12 h at room temperature, the reaction mixture was filtered through a pad of Celite and extracted with EtOAc. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography (30 : 1 hexanes/EtOAc) to give the unreacted starting material **58a** (10.0 mg, 68%) and **57** (1.10 mg, 13%).

To a solution of CrCl_2 (61.6 mg, 0.501 mmol) and NiCl_2 (0.60 mg, 4.70 μmol) in DMF (1.9 ml) at room temperature under argon was added a solution of **58b** (44.3 mg, 0.047 mmol) in DMF (2.8 ml). After stirring for 14 h at room temperature, the reaction mixture was filtered through a pad of Celite and extracted with EtOAc. The combined organic phases were dried over anhydrous Na_2SO_4 and concentrated in vacuo. The crude product was purified by column chromatography (40 : 1 hexanes/EtOAc) to give **57** (22.2 mg, 55%).

Major isomer: $[\alpha]_{\text{D}}^{25} = -19.2^\circ$ ($c = 0.20$, CHCl_3); IR (KBr) 2927, 2860, 1734, 1514, 1462, 1375, 1250, 1173, 1082, 833 679 cm^{-1} ; ^1H -NMR (300 MHz, CDCl_3) δ 0.08 (s, 3H), 0.11 (s, 3H), 0.77-1.18 (m, 46H), 1.50-2.46 (m, 16H), 3.15 (t, 1H, $J = 9.0$ Hz), 3.35 (dd, 1H, $J = 9.0, 5.0$ Hz), 3.79 (s, 3H), 4.04 (m, 1H), 4.14 (d, 1H, $J = 10.0$ Hz), 4.17 (d, 1H, $J = 12.1$ Hz), 4.40 (s, 2H), 4.64 (d, 1H, $J = 12.1$ Hz), 4.98 (m, 1H), 5.79 (m, 1H), 6.13 (d, 1H, $J = 10.9$ Hz), 6.28 (dd, 1H, $J = 14.4, 10.9$ Hz), 6.85 (d, 2H, $J = 8.7$ Hz), 7.23 (d, 2H, $J = 8.7$ Hz); ^{13}C -NMR (100 MHz, CDCl_3) δ -5.4, -3.6, 11.8, 11.9, 14.1, 15.4, 17.7, 18.0, 18.6, 19.8, 24.9, 25.9, 26.1, 30.0, 33.5, 34.6, 35.6, 35.7, 36.5, 38.1, 42.7, 43.4, 43.6, 48.3, 55.2, 67.2, 72.4, 73.7, 74.1, 75.7, 76.0, 113.8, 128.4, 128.9, 129.3, 130.0, 130.8; HRMS (FAB, *m*-NBA+NaI) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{51}\text{H}_{91}\text{O}_7\text{Si}_2\text{Na}$ 893.6123, found 893.6139.

(*S*,2*Z*,4*E*)-2-Bromo-7-(*tert*-butyldimethylsilyloxy)-7-[(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl]hepta-2,4-dienal (30**)**

A solution of **27** (2.15 g, 4.97 mmol) in benzene (49.7 ml) was treated with (ethoxycarbonyl(bromomethylidene)triphenylphosphorane (6.35 g, 14.9 mmol) and refluxed at 80 °C for 12 h. The reaction mixture was concentrated in vacuo and roughly purified by column chromatography (30 : 1 hexanes/EtOAc) to give the *E,Z* mixture of **29a** (2.83 g, 98%).

To a solution of the *E,Z* mixture of **29a** (2.83 mg, 4.88 mmol) in CH₂Cl₂ (49 ml) was added dropwise DIBAL (0.95 M in hexane, 12.8 ml, 12.2 mmol) at 0 °C. After stirring for 0.5 h, the reaction was quenched with MeOH, diluted with CH₂Cl₂, and treated with Celite (30 g) and Na₂SO₄·10H₂O (30 g). The resulting mixture was stirred for 2 h at room temperature, filtered through a pad of Celite, and concentrated in vacuo to give the corresponding alcohol.

The crude alcohol was dissolved in CH₂Cl₂ (49 ml) and treated with manganese dioxide (12.7 g, 146 mmol). After stirring for 12 h at room temperature, the resulting mixture was filtered through a pad of Celite and concentrated in vacuo to afford a *E,Z* mixture of the corresponding aldehyde.

To a solution of the crude aldehyde in CH₂Cl₂ (49 ml) was added DMAP (366 mg, 2.99 mmol). The mixture was stirred for 24 h at room temperature, diluted with water, and extracted with CH₂Cl₂. The combined organic extracts were dried over anhydrous Na₂SO₄ and concentrated in vacuo. Flash chromatography (30:1 hexanes/EtOAc) afforded **30** (2.43 g, 93% for 3 steps) as a colorless oil. ¹H-NMR (270 MHz, CDCl₃) δ 0.04 (s, 3H), 0.06 (s, 3H), 0.88 (s, 9H), 1.30 (m, 1H), 1.45-1.75 (m, 6H), 2.09 (m, 1H), 2.45 (m, 2H), 3.22 (t, 1H, *J* = 8.6 Hz), 3.40 (dd, 1H, *J* = 8.6, 5.6 Hz), 3.75 (m, 1H), 3.79 (s, 3H), 4.40 (d, 1H, *J* = 11.9 Hz), 4.44 (d, 1H, *J* = 11.9 Hz), 6.51 (m, 1H), 6.69 (dd, 1H, *J* = 15.2, 10.6 Hz), 6.86 (d, 2H, *J* = 8.2 Hz), 7.24 (d, 2H, *J* = 8.2 Hz), 7.36 (d, 1H, *J* = 10.5 Hz), 9.21 (s, 1H); ¹³C-NMR (67.5 MHz, CDCl₃) δ -4.5, -4.2, 18.0, 25.2, 25.9, 29.3, 30.4, 39.4, 41.3, 47.6, 55.2, 72.8, 74.6, 74.9, 113.7, 123.9, 129.1, 130.8, 147.5, 149.1, 159.0, 186.2; HRMS (FAB, *m*-NBA+NaI) [M+Na]⁺ calcd for C₂₇H₄₁O₄BrSiNa 559.1855, found 559.1857.

(*S,1E,2Z,4E*)-2-Bromo-7-(*tert*-butyldimethylsilyloxy)-7-[(1*R,2R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl]hepta-2,4-dienal oxime (30a**)**

To a solution of **30** (19.7 mg, 36.7 μ mol) in *N*-methyl pyrrolidinone (NMP, 700 μ l) was added hydroxylamine hydrochloride (3.00 mg, 44.1 μ mol). After stirring for 4 h at 50 °C, water was added and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (15:1 hexanes/EtOAc) afforded **30a** (14.7 mg, 73%) as a colorless oil. ^1H -NMR (270 MHz, CDCl_3) δ 0.04 (s, 3H), 0.05 (s, 3H), 0.88 (s, 9H), 1.29 (m, 1H), 1.46-1.71 (m, 6H), 2.09 (m, 1H), 2.40 (m, 2H), 3.20 (t, 1H, J = 8.6 Hz), 3.40 (dd, 1H, J = 8.6, 5.3 Hz), 3.71 (m, 1H), 3.79 (s, 3H), 4.39 (d, 1H, J = 11.9 Hz), 4.45 (d, 1H, J = 11.9 Hz), 6.14 (m, 1H), 6.55 (dd, 1H, J = 14.8, 10.2 Hz), 6.69 (d, 1H, J = 10.2 Hz), 6.86 (d, 2H, J = 8.2 Hz), 7.24 (d, 2H, J = 8.2 Hz), 7.78 (s, 1H); ^{13}C -NMR (67.5 MHz, CDCl_3) δ -4.6, -4.2, 18.0, 25.2, 25.9, 29.4, 30.4, 39.1, 41.2, 47.3, 55.2, 72.7, 74.6, 75.2, 113.7, 115.0, 129.2, 129.3, 130.8, 137.3, 140.0, 149.0, 159.0; HRMS (FAB, *m*-NBA+NaI) $[\text{M}+\text{Na}]^+$ calcd for $\text{C}_{27}\text{H}_{42}\text{O}_4\text{NBrSiNa}$ 574.1964, found 574.1968.

(*S*,2*Z*,4*E*)-2-Bromo-7-(*tert*-butyldimethylsilyloxy)-7-[(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl]hepta-2,4-dienenitrile (31**)**

To a solution of **30a** (14.7 mg, 26.7 μ mol) in CH_2Cl_2 (500 μ l) was added 1,1'-carbonyldiimidazole (8.60 mg, 53.4 μ mol). After stirring for 12 h at room temperature, the mixture was concentrated in vacuo. Flash chromatography (30:1 hexanes/EtOAc) afforded **31** (13.0 mg, 92%) as a colorless oil. ^1H -NMR (270 MHz, CDCl_3) δ 0.03 (s, 3H), 0.05 (s, 3H), 0.88 (s, 9H), 1.25-1.71 (m, 7H), 2.07 (m, 1H), 2.38 (m, 2H), 3.21 (t, 1H, J = 8.6 Hz), 3.39 (dd, 1H, J = 8.6, 5.6 Hz), 3.72 (m, 1H), 3.80 (s, 3H), 4.39 (d, 1H, J = 11.9 Hz), 4.44 (d, 1H, J = 11.9 Hz), 6.33-6.43 (m, 2H), 6.87 (d, 2H, J = 8.6 Hz), 7.14 (m, 1H), 7.24 (d, 2H, J = 8.6 Hz); ^{13}C -NMR (67.5 MHz, CDCl_3) δ -4.6, -4.3, 17.9, 25.2, 25.8, 29.2, 30.3, 39.0, 41.3, 47.6, 55.2, 72.7, 74.5, 74.7, 85.7, 113.6, 116.8, 129.1, 127.9, 130.6, 145.7, 145.8, 159.0; HRMS (FAB, *m*-NBA) $[\text{M}]^+$ calcd for $\text{C}_{27}\text{H}_{40}\text{O}_3\text{NBrSi}$ 533.1960, found 533.1931.

(3*S*,4*S*,6*S*,8*R*,10*S*)-((*S*,3*E*,5*Z*)-6-Bromo-6-cyano-1-{(1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl}hexa-3,5-dienyl) 3-(*tert*-butyldimethylsilyloxy)-4,6,8,10-tetramethyl-11-(tetrahydro-2*H*-pyran-2-yloxy)undecanoate (31a**).**

To a stirred solution of **3** (102 mg, 0.216 mmol) in benzene (3.80 ml) was added triethylamine (60 μ l, 0.432 mmol) followed by 2,4,6-trichlorobenzoyl chloride (37 μ l, 0.238 mmol) at room temperature. The resulting solution was stirred for 1 hr, then treated with a solution of **31** (113 mg, 0.270 mmol) and DMAP (34.0 mg, 0.281 mmol) in benzene (1.5 ml), and stirred for additional 30 min. The reaction was quenched with saturated aqueous NaHCO₃ solution and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na₂SO₄ and concentrated in vacuo. Flash chromatography (25:1 hexanes/EtOAc) afforded **31a** (156 mg, 82%) as a colorless oil. ¹H-NMR (270 MHz, CDCl₃) δ 0.03 (s, 3H), 0.07 (s, 3H), 0.80-0.92 (m, 23H), 0.99-1.42 (m, 5H), 1.46-1.94 (m, 16H), 2.07 (m, 1H), 2.31-2.60 (m, 4H), 3.10-3.39 (m, 3H), 3.45-3.59 (m, 2H), 3.80 (s, 3H), 3.86 (m, 1H), 4.06 (m, 1H), 4.41 (d, 1H, *J* = 11.9 Hz), 4.44 (d, 1H, *J* = 11.9 Hz), 4.57 (m, 1H), 4.96 (m, 1H), 6.24 (m, 1H), 6.38 (dd, 1H, *J* = 15.5, 9.9 Hz), 6.87 (d, 2H, *J* = 8.6 Hz), 7.11 (d, 1H, *J* = 9.9 Hz), 7.24 (d, 2H, *J* = 8.6 Hz); ¹³C-NMR (67.5 MHz, CDCl₃) δ -4.7, -4.4, 14.5, 16.4, 16.5, 18.0, 19.4, 19.5, 20.4, 20.6, 25.0, 25.5, 25.8, 26.9, 27.0, 27.2, 29.6, 30.1, 30.6, 30.8, 30.9, 35.4, 36.6, 39.7, 39.9, 40.8, 40.9, 41.4, 45.0, 45.8, 55.1, 61.9, 62.1, 71.6, 72.7, 73.7, 73.9,

74.0, 75.6, 86.6, 98.6, 98.9, 113.6, 116.5, 128.2, 128.9, 130.5, 143.6, 145.2, 159.0, 171.5; HRMS (FAB, *m*-NBA) $[M+Na]^+$ calcd for $C_{47}H_{76}O_7BrSiNa$ 896.4472, found 896.4467.

(3*S*,4*S*,6*S*,8*R*,10*S*)-((*S*,3*E*,5*Z*)-6-Bromo-6-cyano-1-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl}hexa-3,5-dienyl) 3-(*tert*-butyldimethylsilyloxy)-11-hydroxy-4,6,8,10-tetramethylundecanoate (31b)

To a solution of **31a** (156 mg, 0.179 mmol) in EtOH (5.0 ml) was added PPTS (22.4 mg, 89.4 μmol). The resulting solution was stirred at 50 $^\circ\text{C}$. After 12 hr, the reaction mixture was diluted with water and the aqueous phase was extracted with EtOAc. The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated in vacuo. Flash chromatography (7:1 hexanes/EtOAc) afforded **31b** (129 mg, 91%) as a colorless oil. $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ 0.03 (s, 3H), 0.07 (s, 3H), 0.80-0.91 (m, 24H), 0.94-1.41 (m, 4H), 1.45-1.81 (m, 9H), 1.88 (m, 1H), 2.06 (m, 1H), 2.31-2.60 (m, 4H), 3.24-3.47 (m, 4H), 3.80 (s, 3H), 4.06 (m, 1H), 4.37 (d, 1H, $J = 11.9$ Hz), 4.41 (d, 1H, $J = 11.9$ Hz), 4.93 (m, 1H), 6.21 (m, 1H), 6.34 (dd, 1H, $J = 15.2, 9.9$ Hz), 6.83 (d, 2H, $J = 8.2$ Hz), 7.08 (d, 1H, $J = 9.9$ Hz), 7.24 (d, 2H, $J = 8.2$ Hz); $^{13}\text{C-NMR}$ (67.5 MHz, CDCl_3) δ -4.7, -4.4, 14.4, 16.0, 18.0, 20.5, 20.6, 25.0, 25.8, 27.1, 27.3, 29.7, 30.2, 33.2, 35.5, 36.7, 39.5, 39.7, 41.0, 41.5, 45.0, 45.7, 55.1, 69.1, 71.7, 72.7, 74.0, 75.6, 86.6, 113.7, 116.6, 128.3, 129.0, 130.5, 143.6, 145.3, 159.1, 171.6.

(3*S*,4*S*,6*S*,8*R*,10*S*)-((*S*,3*E*,5*Z*)-6-Bromo-6-cyano-1-((1*R*,2*R*)-2-[(4-methoxybenzyloxy)methyl]cyclopentyl}hexa-3,5-dienyl) 3-(*tert*-butyldimethylsilyloxy)-4,6,8,10-tetramethyl-11-oxoundecanoate (2')

To a solution of **31b** (42.1 mg, 53.4 μmol) in CH_2Cl_2 (1.0 ml) were added dried $\text{MS4}\text{\AA}$ (100 mg), TPAP (1.00 mg, 2.66 μmol) and NMO (12.5 mg, 0.106 mmol) at room temperature. The resulting solution was stirred for 30 min and filtered through a silica pad. After evaporation of the filtrate, the residue was purified by flash chromatography (15:1 hexanes/EtOAc) to afford **2'** (31.9 mg, 76%) as a colorless oil. $^1\text{H-NMR}$ (270 MHz, CDCl_3) δ 0.03 (s, 3H), 0.07 (s, 3H), 0.80-0.91 (m, 21H), 0.93-1.10 (m, 2H), 1.07 (d, 3H, $J = 6.9$ Hz), 1.18-1.43 (m, 2H), 1.47-1.76 (m, 9H), 1.88 (m, 1H), 2.06 (m, 1H), 2.30-2.59 (m, 4H), 3.31 (m, 2H), 3.80 (s, 3H), 4.06 (m, 1H), 4.40 (d, 1H, $J = 11.9$ Hz), 4.44 (d, 1H, $J = 11.9$ Hz), 4.96 (m, 1H), 6.27 (m, 1H), 6.38 (dd, 1H, $J = 15.6, 9.9$ Hz), 6.87 (d, 2H, $J = 8.6$ Hz), 7.11 (d, 1H, $J = 9.9$ Hz), 7.24 (d, 2H, $J = 8.6$ Hz), 9.60 (s, 1H,

CHO); ^{13}C -NMR (67.5 MHz, CDCl_3) δ -4.7, -4.4, 13.0, 14.6, 18.0, 20.4, 20.5, 25.0, 25.8, 27.3, 27.4, 29.7, 30.2, 35.5, 36.4, 36.7, 39.6, 40.8, 41.5, 44.2, 45.0, 45.3, 55.2, 71.6, 72.7, 74.0, 75.6, 86.7, 113.7, 116.6, 128.3, 129.0, 130.5, 143.7, 145.3, 159.1, 171.6, 205.1.