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# Enantioselective Synthesis of the Elaiophylin Aglycone

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# Supporting Information

General Information: Melting points are uncorrected. Optical rotations were measured on a Jasco DIP-0181 digital polarimeter with a mercury lamp and reported as follows:  $[\alpha]^{t^{\circ}C}\lambda$  (c g/100 ml, solvent). Infrared spectra were recorded on a Perkin Elmer model 1600 FT-IR spectrometer. <sup>1</sup>H NMR spectra were recorded on Bruker AM-500 (500 MHz) or AM-400 (400 MHz) spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as the internal standard (deuterochloroform:  $\delta$  7.26 ppm, benzene:  $\delta$  7.15 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, br = broad, m = multiplet), coupling constants (Hz), integration, and assignment. Elaiophylin numbering<sup>1</sup> is used for proton assignments of all intermediates. <sup>13</sup>C NMR spectra were recorded on Bruker AM-500 (125 MHz) or AM-400 (100 MHz) spectrometers with complete proton decoupling. Chemical shifts are reported in ppm from tetramethylsilane with the solvent as the internal standard (deuterochloroform:  $\delta$  77.07 ppm, benzene:  $\delta$  128.0 ppm). Mass spectra were obtained on a JEOL AX-505 or SX-102 high resolution magnetic sector mass spectrometer by the Harvard University Mass Spectrometry Laboratory. Combustion analyses were performed by Atlantic Microlab (Norcross, GA). Analytical thin layer chromatography was performed on EM Reagent 0.25 mm silica gel 60-F plates. Flash chromatography was performed using EM silica gel 60 (230-240 mesh). Solvents for extraction and chromatography were HPLC grade. Unless otherwise noted, all reactions were conducted in oven (80 °C) or flamedried glassware with magnetic stirring under an inert atmosphere of dry nitrogen. When necessary, solvents and reagents were dried prior to use. Deuterochloroform was stored over 4 Å molecular sieves. Tetrahydrofuran (THF) and diethyl ether were distilled from potassium metal/benzophenone ketyl. Methanol was distilled from magnesium methoxide. Dichloromethane (CH<sub>2</sub>Cl<sub>2</sub>), 2,6-lutidine, N,N-diisopropylethylamine, triethylamine, diisopropylamine, and 1,1,1,3,3,3-hexamethyldisilazane were distilled from calcium hydride. Dimethylsulfoxide (DMSO) was distilled under reduced pressure from calcium hydride and stored over 4 Å molecular sieves. Dichlorophenylborane, methacrolein, and oxalyl chloride were distilled prior to use. All other commercially obtained reagents were used as received.

Methyl (2*R*,3*R*)-2-ethyl-3-tert-butyldimethylsilyloxybutanoate. To a solution of methyl (2*R*,3*R*)-2-ethyl-3hydroxybutanoate (458 mg, 3.13 mmol) in 6 ml of CH<sub>2</sub>Cl<sub>2</sub> at 0 °C was added tert-butyldimethylsilyl trifluoromethanesulfonate (755  $\mu$ l, 3.29 mmol), followed by 2,6-lutidine (438  $\mu$ l, 3.76 mmol). After stirring for 1 h at 0 °C, the reaction was quenched by the addition of 0.5 N HCl (10 ml) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (3 x 10 ml). The combined organic layers were washed with brine (10 ml), dried over MgSO4, filtered, and concentrated *in vacuo*. Purification *via* flash chromatography (5% EtOAc/hexanes) afforded 800 mg (98%) of methyl (2*R*,3*R*)-2-ethyl-3-tert-butyldimethylsilyloxybutanoate as a clear, colorless oil. TLC  $R_f = 0.71$  (10% EtOAc/hexanes); [ $\alpha$ ]<sub>365</sub> -82.6 ° (*c* 1.0, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 2954, 2931, 2884, 2857, 1740, 1473, 1463, 1446, 1434, 1378, 1256, 1195, 1172, 1118, 1079, 1001, 977, 832, 776 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  3.96 (dq, 1H, *J* = 7.8, 6.2 Hz, C<sub>15</sub>-*H*), 3.66 (s, 3H, OCH<sub>3</sub>), 2.31 (ddd, 1H, *J* = 10.0, 7.9, 4.9 Hz, C<sub>14</sub>-*H*), 1.52 (m, 2H, C<sub>14</sub>-*CH*<sub>2</sub>CH<sub>3</sub>), 1.14 (d, 3H, *J* = 6.2 Hz, C<sub>15</sub>-*CH*<sub>3</sub>), 0.87 (t, 3H, *J* = 7.4 Hz, C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 0.85 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub>), 0.04 (s, 3H, one of Si(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  175.1, 69.9, 56.6, 51.2, 25.7, 21.5, 21.4, 17.9, 12.1, -4.2, -5.1; Exact mass calcd. for C<sub>13</sub>H<sub>29</sub>O<sub>3</sub>Si[(M+H)<sup>+</sup>]: 261.1886; found: 261.1888 (CI).

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<sup>OH</sup> butyldimethylsilyloxybutanoate (1.7 g, 6.53 mmol) in 10 ml of CH<sub>2</sub>Cl<sub>2</sub> at -78 °C was added DIBAI-H (18.9 ml, 1 M in CH<sub>2</sub>Cl<sub>2</sub>, 18.9 mmol) dropwise *via* syringe. After stirring for 1 h at -78 °C, the reaction was warmed to -40 °C and stirred for an additional 0.5 h. The solution was then recooled to -78 °C and transferred via cannula to a solution of 1:1 CH<sub>2</sub>Cl<sub>2</sub>/saturated Na/K tartrate (50 ml) at 0 °C. The mixture was warmed to ambient temperature and stirred for 0.5 h. Separation of the layers was followed by extraction with Et<sub>2</sub>O (2 x 10 ml) The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo. Purification via flash chromatography (20% EtOAc/hexanes) afforded 1.51 g (quant.) of (2S,3R)-2-ethyl-3tert-butyldimethylsilyloxy-1-butanol as a clear, colorless oil. TLC  $R_f = 0.37$  (10% EtOAc/hexanes);  $[\alpha]_{365}^{23}$  -47.2 ° (c 1.0, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 3443, 2957, 2930, 2884, 2858, 1472, 1463, 1376, 1361, 1255, 1154, 1108, 1079, 1032, 1005, 962, 938, 836, 775, 665 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  3.98 (dd, 1H, J = 8.6, 5.9 Hz, one of C<sub>13</sub>-H<sub>2</sub>), 3.95 (dd, 1H, J = 5.9, 3.1 Hz, one of C<sub>13</sub>-H<sub>2</sub>), 3.60 (dq, 1H, J = 6.3, 4.7 Hz, C<sub>15</sub>-H), 3.09 (br. s, 1H, OH), 1.56 (dq, 1H, J = 20.7, 7.6 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.43 (dq, 1H, J = 20.7, 7.6 Hz, one of C14-CH2CH3), 1.25 (d, 3H, J = 6.3 Hz, C15-CH3), 1.21 (m, 1H, C14-H), 0.95 (t, 3H, J = 7.6 Hz, C14-CH2CH3), 0.89 (s, 9H, SiC(CH<sub>3</sub>)<sub>3</sub>), 0.09 (s, 6H, Si(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 72.9, 62.4, 48.0, 25.8, 22.5, 22.0, 17.9, 12.0, -4.2, -5.0; Exact mass calcd. for C12H29O2Sil(M+H)<sup>+</sup>]: 233.1937; found: 233.1933 (FAB).

(2S,3R)-2-ethyl-3-tert-butyldimethylsilyloxy-1-butanol. To a solution of methyl (2R,3R)-2-ethyl-3-tert-

(2R,3R)-2-ethyl-3-tert-butyldimethylsilyloxy-1-butanal (5). To a solution of oxalyl chloride (30 µl, 0.34 mmol) in 3 <sub>H</sub> ml of CH<sub>2</sub>Cl<sub>2</sub> at -78 °C was added dimethyl sulfoxide (50 μl, 0.71 mmol) dropwise via syringe. After stirring for 10 min at -78 °C, a solution of (2S,3R)-2-ethyl-3-tert-butyldimethylsilyloxy-1-butanol (50 mg, 0.21 mmol) in 2 ml of 5 CH<sub>2</sub>Cl<sub>2</sub> was added dropwise via cannula. The solution was then stirred for 20 min at -78 °C, followed by the addition of triethylamine (200 µl, 1.44 mmol). After stirring for 1 h at -78 °C, the reaction mixture was poured into a solution of sat. NH4Cl (10 ml) and stirred for 10 min at ambient temperature. The layers were separated and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x 5 ml). The combined organic layers were washed with brine, dried over MgSO4, filtered, and concentrated in vacuo. Purification via flash chromatography (10% EtOAc/hexanes) afforded 49.5 mg (quant.) of 5 as a clear, colorless oil. TLC  $R_f = 0.61$  (10% EtOAc/hexanes);  $[\alpha]_{365}^{353}$  -63.8 ° (*c* 1.0, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 2958, 2930, 2884, 2857, 1710, 1472, 1463, 1377, 1256, 1120, 986, 835, 775 cm<sup>-1</sup>; <sup>1</sup>H NMR  $(400 \text{ MHz}, \text{CDCl}_3) \delta 9.68 \text{ (d, 1H, } J = 3.9 \text{ Hz}, \text{Cl}_3-H), 4.06 \text{ (dq, 1H, } J = 6.3, 4.8 \text{ Hz}, \text{Cl}_5-H), 2.08 \text{ (dt, 1H, } J = 13.2, 4.8 \text{ Hz}, \text{Cl}_4-H),$ 1.72 (ddq, 1H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.53 (ddq, 1H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.20 (d, 3H, J = 13.2, 7.5, 5.0 Hz, one of C<sub>14</sub>-CH<sub>2</sub>C = 6.3 Hz, C15-CH3), 0.90 (t, 3H, J = 7.5 Hz, C14-CH2CH3), 0.86 (s, 9H, SiC(CH3)3), 0.06 (s, 3H, one of Si(CH3)2), 0.05 (s, 3H, one of Si(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 205.7, 68.9, 61.1, 25.8, 22.3, 19.6, 18.0, 11.9, -4.1, -5.0.

(4R, 5S, 6R)-2,5-diethyl-4-hydroxy-6-tert-butyldimethylsilyloxyheptene (7). Aldehyde 5 (175 mg, 0.76 Me mmol) and ethallylstannane 6 (682 mg, 1.9 mmol) were combined in 10 ml of CH<sub>2</sub>Cl<sub>2</sub> and cooled to -78 C. Boron trifluoride diethyl etherate (96 µl, 0.84 mmol) was added dropwise via syringe, and the mixture was stirred for 45 min at -78 °C. The reaction was quenched by the addition of sat. NaHCO3 (10 ml) and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x 10 ml). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo. GLC analysis

of the unpurified reaction mixture (DB-1701 column, 50 - 130 °C @ 1.5 °C/ min, 15 psi) revealed a 92:8 ratio of the desired Felkin isomer ( $t_r = 62.42 \text{ min}$ ) to anti-Felkin isomer ( $t_r = 60.53 \text{ min}$ ). Purification via flash chromatography (1% EtOAc/hexanes) afforded 203 mg (89%) of the major diastereomer as a clear, colorless oil. TLC  $R_f = 0.75$  (10% EtOAc/hexanes);  $[\alpha]_{365}^{23}$  -22.0 ° (c 0.8, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 3521, 3076, 2959, 2932, 2885, 2858, 1645, 1463, 1377, 1362, 1254, 1107, 1035, 964, 899, 835, 776 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.80 (s, 1H, one of C<sub>11</sub>-CH<sub>2</sub>), 4.79 (s, 1H, one of C<sub>11</sub>-CH<sub>2</sub>), 4.32 (t, 1H, J = 7.0 Hz, C<sub>13</sub>-H), 4.18 (dq, 1H, J = 6.4, 2.0 Hz, C<sub>15</sub>-H), 3.65 (s, 1H, OH), 2.34 (dd, 1H, J = 13.9, 7.2 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 6.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 7.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 7.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.13 (dd, 1H, J = 13.9, 7.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 3.14 (dd, 1H, J = 13.9, 7.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 3.14 (dd, 1H, J = 13.9, 7.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 3.14 (dd, 1H, J = 13.9, 7.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 3.14 (dd, 1H, J = 13.9, 7.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 3.14 (dd, 1H, J = 13.9, 7.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 3.14 (dd, 1H, J = 13.9, 7.9 Hz, one of C<sub>12</sub>-H<sub>2</sub> C12-H2), 2.05 (q, 2H, J = 7.4 Hz, C10-H2), 1.61-1.42 (m, 2H, C14-CH2CH3), 1.25 (d, 3H, J = 6.4 Hz, C15-CH3), 1.04 (t, 3H, J = 7.4 Hz, C10-CH3), 0.93 (t, 3H, J = 7.5 Hz, C14-CH2CH3), 0.88 (s, 10H, SiC(CH3)3 and C14-H), 0.10 (s, 3H, one of Si(CH3)2), 0.09 (s, 3H, one of Si(CH<sub>3</sub>)<sub>2</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 148.7, 110.2, 70.1, 68.4, 49.0, 41.3, 28.9, 25.9, 22.3, 17.9, 16.9, 12.6, 12.4, -4.1, -5.1; Exact mass calcd. for C17H37O2Si[(M+H)<sup>+</sup>]: 301.2563; found: 301.2565 (CI).



(4R, 5R, 6R)-2,5-diethyl-4,6-dihydroxyheptene. To a solution of 7 (72.5 mg, 0.24 mmol) in 1 ml of THF at ambient temperature was added tetrabutylammonium fluoride (480 µl, 1 M solution in THF, 0.48 mmol). After stirring for 10 min, the reaction mixture was diluted with 10 ml of CH<sub>2</sub>Cl<sub>2</sub> and quenched with 1 N HCl (10 ml). Separation of the layers was followed by extraction with CH<sub>2</sub>Cl<sub>2</sub> (2 x 10 ml). The combined organic

layers were dried over MgSO4, filtered, and concentrated in vacuo. Purification via flash chromatography (50% EtOAc/hexanes) afforded 43 mg (96%) of (4*R*, 5*R*, 6*R*)-2,5-diethyl-4,6-dihydroxyheptene as a clear, colorless oil. TLC  $R_f = 0.61$  (50% EtOAc/hexanes); [ $\alpha$ ]<sup>23</sup><sub>365</sub> -8.36° (*c* 1.0, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 3346, 3077, 2968, 2932, 2873, 1646, 1458, 1428, 1370, 1326, 1246, 1101, 1065, 1021, 890 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.86 (q, 1H, J = 1.5 Hz, one of C<sub>11</sub>-CH<sub>2</sub>), 4.82 (d, 1H, J = 0.6 Hz, one of C<sub>11</sub>-CH<sub>2</sub>) CH<sub>2</sub>), 4.14 (ddd, 1H, J = 9.4, 4.1, 2.0 Hz, C<sub>13</sub>-H), 3.98 (dq, 1H, J = 6.4, 5.4 Hz, C<sub>15</sub>-H), 3.13 (br. s, 2H, both OH), 2.29 (dd, 1H, J =

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13.8, 9.4 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.16 (dd, 1H, J = 13.8, 4.1 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.11-1.98 (m, 2H, C<sub>10</sub>-H<sub>2</sub>), 1.54-1.42 (m, 1H, C<sub>14</sub>-H), 1.38-1.29 (m, 2H, C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.22 (d, 3H, J = 6.4 Hz, C<sub>15</sub>-CH<sub>3</sub>), 1.02 (t, 3H, J = 7.4 Hz, C<sub>10</sub>-CH<sub>3</sub>), 0.94 (t, 3H, J = 7.3 Hz, C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  148.3, 111.0, 69.4, 68.8, 49.3, 40.3, 28.6, 22.2, 18.7, 12.6, 12.3; Exact mass calcd. for C<sub>11</sub>H<sub>23</sub>O<sub>2</sub>[(M+H)<sup>+</sup>]: 187.1698; found: 187.1698 (EI).



(4R, 5R, 6R)-2,2-di-tert-butyl-5-ethyl-6-(2-ethylallyl)-4-methyl-1,3-dioxa-2-silacyclohexane. To a solution of (4R, 5R, 6R)-2,5-diethyl-4,6-dihydroxyheptene (600 mg, 3.22 mmol) in 30 ml of CH<sub>2</sub>Cl<sub>2</sub> at 0 °C was added
2,6-lutidine (1.1 ml, 9.66 mmol). After stirring for 2 min, di-tert-butylsilyl bis(trifluoromethanesulfonate) (1.5 ml, 4.19 mmol) was added dropwise via syringe. The mixture was stirred for 1 h at 0 °C, followed by quenching with sat. NaHCO<sub>3</sub> (20 ml). Separation of the layers was followed by extraction with CH<sub>2</sub>Cl<sub>2</sub> (2 x

20 ml). The combined organic layers were dried over MgSO4, filtered, and concentrated *in vacuo*. Purification *via* flash chromatography (5% EtOAc/hexanes) afforded 957 mg (91%) of (4R, 5R, 6R)-2,2-di-*tert*-butyl-5-ethyl-6-(2-ethylallyl)-4-methyl-1,3-dioxa-2-silacyclohexane as a clear, colorless oil. TLC  $R_f = 0.89$  (5% EtOAc/hexanes); [ $\alpha$ ]  $_{365}^{365}$  +193.0 ° (*c* 1.0, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 3083, 2967, 2934, 2890, 2859, 1646, 1475, 1461, 1376, 1363, 1211, 1138, 1120, 1077, 1052, 984, 961, 888, 825, 781, 735, 646 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  4.87 (s, 1H, one of C<sub>11</sub>-CH<sub>2</sub>), 4.83 (s, 1H, one of C<sub>11</sub>-CH<sub>2</sub>), 4.34 (ddd, 1H, J = 10.2, 4.6, 3.0 Hz, C<sub>13</sub>-H), 4.08 (dq, 1H, J = 8.1, 6.2 Hz, C<sub>15</sub>-H), 2.28 (dd, 1H, J = 14.8, 10.2 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.17 (dd, 1H, J = 14.8, 3.0 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.11 (m, 2H, C<sub>10</sub>-H<sub>2</sub>), 1.75 (m, 1H, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.47 (m, 1H, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.21 (d, 3H, J = 6.2 Hz, C<sub>15</sub>-CH<sub>3</sub>), 1.13 (m, 1H, C<sub>14</sub>-H), 1.06 (t, 3H, J = 7.4 Hz, C<sub>10</sub>-CH<sub>3</sub>), 1.00 (s, 9H, one of SiC(CH<sub>3</sub>)<sub>3</sub>), 0.99 (s, 9H, one of SiC(CH<sub>3</sub>)<sub>3</sub>), 0.91 (t, 3H, J = 7.4 Hz, C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  149.0, 109.9, 72.3, 70.0, 50.0, 37.9, 28.8, 27.9, 27.4, 23.3, 21.3, 21.1, 20.8, 12.5, 12.3; Exact mass calcd. for C<sub>19</sub>H<sub>38</sub>O<sub>2</sub>Si: 326.2641; found: 326.2633 (EI).



1-[(4R, 5R, 6R)-2,2-di-tert-butyl-5-ethyl-4-methyl-1,3-dioxa-2-silacyclohex-6-yl]-2-butanone (8). To a solution of (4R, 5R, 6R)-2,2-di-tert-butyl-5-ethyl-6-(2-ethylallyl)-4-methyl-1,3-dioxa-2-silacyclohexane (110 mg, 0.337 mmol) in 3.5 ml of CH<sub>2</sub>Cl<sub>2</sub> and 1.5 ml of methanol at -78  $^{\circ}$ C was added a drop of pyridine and 5 mg Sudan III. Ozone was bubbled through the reaction mixture for 5 min turning the indicator from red to yellow. The flask was then purged with nitrogen and dimethyl sulfide (250 µl, 3.37 mmol) was added. The

mixture was warmed to ambient temperature and stirred for 3 h, followed by concentration *in vacuo*. Purification *via* flash chromatography (5% EtOAc/hexanes) afforded 99.8 mg (90%) of **8** as a clear, colorless oil. TLC  $R_f = 0.58$  (10% EtOAc/hexanes); [ $\alpha$ ]  $_{365}^{23} + 180.1^{\circ}$  (*c* 1.0, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 2969, 2935, 2891, 2859, 1717, 1475, 1461, 1377, 1364, 1218, 1137, 1076, 1039, 980, 825, 786, 646 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.72 (ddd, 1H, J = 10.9, 4.9, 2.6 Hz, C<sub>13</sub>-H), 4.01 (dq, 1H, J = 8.5, 6.2 Hz, C<sub>15</sub>-H), 2.73 (dd, 1H, J = 14.8, 10.9 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 2.58 (dq, 1H, J = 17.9, 7.3 Hz, one of C<sub>10</sub>-H<sub>2</sub>), 2.53 (dq, 1H, J = 17.9, 7.3 Hz, one of C<sub>10</sub>-H<sub>2</sub>), 2.33 (dd, 1H, J = 14.8, 2.6 Hz, one of C<sub>12</sub>-H<sub>2</sub>), 1.79 (m, 1H, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.47 (m, 1H, one of C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.21 (d, 3H, J = 6.2 Hz, C<sub>15</sub>-CH<sub>3</sub>), 1.07 (t, 3H, J = 7.3 Hz, C<sub>10</sub>-CH<sub>3</sub>), 1.02 (m, 1H, C<sub>14</sub>-H), 0.98 (s, 9H, one of SiC(CH<sub>3</sub>)<sub>3</sub>), 0.97 (s, 9H, one of SiC(CH<sub>3</sub>)<sub>3</sub>), 0.92 (t, 3H, J = 7.1 Hz, C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  210.4, 71.3, 69.8, 49.5, 45.0, 36.2, 27.7, 27.4, 23.1, 21.3, 21.2, 20.7, 12.1, 7.7; Exact mass calcd. for C<sub>18</sub>H<sub>37</sub>O<sub>3</sub>Si[(M+H)<sup>+</sup>]: 329.2512; found: 329.2526 (CI).

Bn OH (4)

(4*R*)-4-benzyl-3-[(2*R*, 3*S*)-3-hydroxy-2,4-dimethyl-4-pentenoyl]-2-oxazolidinone. To a solution of imide 9<sup>4</sup> (16 g, 68.6 mmol) in 150 ml of CH<sub>2</sub>Cl<sub>2</sub> at 0 °C was added di-*n*-butylboron triflate<sup>5</sup> (20.5 ml, 82.3 mmol) dropwise *via* syringe followed by *N*,*N*-diisopropylethylamine (15.5 ml, 89.2 mmol). The reaction mixture was cooled to -78 °C, and methacrolein (12.8 ml, 154.7 mmol) was added dropwise from an addition funnel. The solution was stirred at -78 °C for 20 min followed by warming to 0 °C and stirring for 1 h. The reaction was

quenched by the addition of 100 ml of pH 7 phosphate buffer followed by 150 ml of methanol. After 5 min, 100 ml of 30% aqueous hydrogen peroxide in 200 ml of methanol was added dropwise in order to maintain a temperature < 10 °C (*caution*: initial reaction is highly exothermic). After stirring for 1 h at 0 °C, the reaction mixture was concentrated *in vacuo*. The resulting mixture was extracted with Et<sub>2</sub>O (3 x 200 ml). The combined organic layers were washed with brine, dried over MgSO4, filtered, and concentrated *in vacuo*. Purification *via* flash chromatography (20% EtOAc/hexanes) afforded 17.98 g (86%) of (4*R*)-4-benzyl-3-[(2*R*, 3*S*)-3-hydroxy-2,4-dimethyl-4-pentenoyl]-2-oxazolidinone as a clear, colorless oil. TLC  $R_f = 0.23$  (30% EtOAc/hexanes); [ $\alpha$ ]  $_{365}^{223}$ -214.4 °(*c* 1.0, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 3513, 3028, 2977, 2938, 1779, 1698, 1453, 1385, 1209, 1108, 986, 904, 762, 746, 702 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.36-7.20 (m, 5H, PhH<sub>5</sub>), 5.13 (d, 1H, *J* = 0.8 Hz, one of C6-CH<sub>2</sub>), 4.98 (dd, 1H, *J* = 3.0, 1.5 Hz, one of C6-CH<sub>2</sub>), 4.71 (dddd, 1H, *J* = 16.6, 9.5, 3.3, 3.1 Hz, CHN), 4.42 (br. s, 1H, C7-H), 4.22 (dd, 1H, *J* = 16.6, 9.1 Hz, one of CH<sub>2</sub>O), 3.97 (dq, 1H, *J* = 7.0, 3.1 Hz, C8-H), 3.27 (dd, 1H, *J* = 13.4, 3.3 Hz, one of PhCH<sub>2</sub>), 2.94 (d, 1H, *J* = 3.2 Hz, OH), 2.80 (dd, 1H, *J* = 13.4, 9.5 Hz, one of PhCH<sub>2</sub>), 1.73 (s, 3H, C6-CH<sub>3</sub>), 1.19 (d, 3H, *J* = 7.0 Hz, C8-CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  177.1, 153.0, 143.7, 135.1, 129.5, 129.0, 127.5, 111.9, 73.9, 66.3, 55.3, 40.1, 37.8, 19.5, 10.0; Exact mass calcd. for C<sub>17</sub>H<sub>21</sub>NO<sub>4</sub>: 303.1471; found: 303.1457 (EI).



(4R)-4-benzyl-3-[(2R, 3S)-2,4-dimethyl-3-(triethylsilyloxy)-4-pentenoyl]-2-oxazolidinone. To a solution of (4R)-4-benzyl-3-[(2R, 3S)-3-hydroxy-2,4-dimethyl-4-pentenoyl]-2-oxazolidinone (17.88 g, 58.9 mmol) in 150 ml of CH<sub>2</sub>Cl<sub>2</sub> at 0 °C was added 2,6-lutidine (8.2 ml, 70.7 mmol) followed by triethylsilyl trifluoromethanesulfonate (14 ml, 61.9 mmol). The reaction mixture was stirred for 0.5 h at 0 °C and then quenched by the addition of 30 ml of methanol. The solution was concentrated *in vacuo* and then taken up in

Et<sub>2</sub>O (200 ml). The resulting mixture was washed with sat. NH<sub>4</sub>Cl, which was then extracted with additional Et<sub>2</sub>O (2 x 100 ml). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. Purification *via* flash chromatography (10% EtOAc/hexanes) afforded 22.65 g (92%) of (4*R*)-4-benzyl-3-[(2*R*, 3*S*)-2,4-dimethyl-3-(triethylsilyloxy)-4-pentenoyl]-2-oxazolidinone as a clear, colorless oil. TLC  $R_f$  = 0.66 (20% EtOAc/hexanes); [ $\alpha$ ]<sup>23</sup><sub>655</sub> -182.8 ° (*c* 1.0, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 2955, 2912, 2877, 1782, 1701, 1454, 1380, 1209, 1105, 1088, 1011, 975, 902, 856, 835, 743, 726., 702 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  7.35-7.21 (m, 5H, PhH<sub>5</sub>), 4.94 (d, 1H, *J* = 0.8 Hz, one of C<sub>6</sub>-CH<sub>2</sub>), 4.83 (s, 1H, one of C<sub>6</sub>-CH<sub>2</sub>), 4.58 (dddd, 1H, *J* = 16.3, 9.7, 3.2, 2.5 Hz, CHN), 4.38 (d, 1H, *J* = 6.8 Hz, C7-H), 4.16 (dd, 1H, *J* = 9.0, 2.5 Hz, one of CH<sub>2</sub>O), 4.13 (dd, 1H, *J* = 16.3, 9.0 Hz, one of CH<sub>2</sub>O), 4.04 (dq, 1H, *J* = 6.8, 6.8 Hz, C8-H), 3.28 (dd, 1H, *J* = 13.3, 3.2 Hz, one of PhCH<sub>2</sub>), 2.76 (dd, 1H, *J* = 13.3, 9.7 Hz, one of PhCH<sub>2</sub>), 1.72 (s, 3H, C6-CH<sub>3</sub>), 1.23 (d, 3H, *J* = 6.8 Hz, C8-CH<sub>3</sub>), 0.95 (t, 9H, *J* = 8.0 Hz, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.58 (m, 6H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  175.0, 153.1, 146.0, 135.4, 129.5, 129.0, 127.4, 112.5, 77.2, 66.1, 55.7, 42.5, 37.8, 17.7, 12.7, 6.9, 4.8; Exact mass calcd. for C<sub>23</sub>H<sub>36</sub>NO<sub>4</sub>Si[(M+H)<sup>+</sup>]: 418.2414; found: 418.2400 (CI).

(2S, 3R)-2,4-dimethyl-3-(triethylsilyloxy)-4-penten-1-ol. To a solution of (4R)-4-benzyl-3-[(2R, 3S)-2,4-dimethyl-3-(triethylsilyloxy)-4-pentenoyl]-2-oxazolidinone (22.0 g, 52.68 mmol) in 250 ml of Et<sub>2</sub>O and 1.04 ml of water (57.7 mmol) at ambient temperature was added lithium borohydride (29.0 ml, 2 M in THF, 58 mmol)*via*syringe (gas evolution). After stirring for 3 h, the cloudy, white solution was quenched by the addition of saturated Na<sup>+</sup>/K<sup>+</sup> tartrate solution (150 ml). The mixture was then stirred for 20 min before the layers were separated and extracted with Et<sub>2</sub>O (2 x 100 ml). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated*in vacuo*. Purification*via* $flash chromatography (30% Et<sub>2</sub>O/pentane) afforded 11.2 g (87%) of (2S, 3R)-2,4-dimethyl-3-(triethylsilyloxy)-4-penten-1-ol as a clear, colorless oil, along with 8.1 g (87%) recovered oxazolidinone. TLC <math>R_f = 0.65$  (30% Et<sub>2</sub>O/pentane);  $[\alpha]_{365}^{325} + 52.6^{\circ}$  (*c* 1.0, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 3350, 2955, 2913, 2877, 1652, 1457, 1414, 1379, 1239, 1117, 1078, 1027, 1010, 973, 900, 831, 740, 725 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  4.93 (d, 1H, J = 1.1 Hz, one of C<sub>6</sub>-CH<sub>2</sub>), 4.88 (d, 1H, J = 1.1 Hz, one of C<sub>6</sub>-CH<sub>2</sub>), 4.08 (d, 1H, J = 4.3 Hz, C<sub>7</sub>-H), 3.58 (ddd, 1H, J = 9.0, 5.4, 4.4 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.48 (ddd, 1H, J = 9.0, 8.3, 4.4 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 2.05 (t, 1H, J = 4.4 Hz, OH), 1.86 (dddq, 1H, J = 8.3, 5.7, 5.4, 4.3 Hz, C<sub>8</sub>-H), 1.72 (s, 3H, C<sub>6</sub>-CH<sub>3</sub>), 0.95 (t, 9H, J = 6.3 Hz, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.87 (d, 3H, J = 5.7 Hz, C<sub>8</sub>-CH<sub>3</sub>), 0.60 (q, 6H, J = 6.3 Hz, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  146.5, 112.0, 78.6, 66.1, 39.4, 18.7, 12.1, 6.9, 4.9; Exact mass calcd. for C<sub>13</sub>H<sub>28</sub>O<sub>2</sub>Si: 244.1859; found: 244.1862 (EI).

(3*R*, 4*S*)-2,4-dimethyl-3-(triethylsilyloxy)-5-(triphenylmethoxy)-pentene (10). To a solution of (2*S*, 3*R*)-2,4dimethyl-3-(triethylsilyloxy)-4-penten-1-ol (1.2 g, 4.91 mmol) in 7 ml of CH<sub>2</sub>Cl<sub>2</sub> at ambient temperature was added triethylamine (1.23 ml, 8.84 mmol) followed by triphenylmethyl chloride (1.64 g, 5.89 mmol) and 4dimethylaminopyridine (30 mg, 0.25 mmol). After stirring for 6 h, the solution was diluted with hexanes (25 ml), filtered through a plug of celite, and concentrated *in vacuo*. Purification *via* flash chromatography (2% EtOAc/hexanes) afforded 2.2 g (92%) of 10 as a clear, colorless oil. TLC  $R_f = 0.90$  (4% EtOAc/hexanes); [ $\alpha$ ]  $_{365}^{365} + 19.4$  ° (*c* 1.0, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 3086, 3059, 3022, 2955, 2935, 2912, 2875, 1650, 1597, 1490, 1448, 1413, 1373, 1238, 1125, 1059, 1004, 898, 831, 743, 704, 632 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.49-7.23 (m, 15H, (PhH<sub>5</sub>)<sub>3</sub>), 4.83 (s, 1H, one of C<sub>6</sub>-CH<sub>2</sub>), 4.74 (s, 1H, one of C<sub>6</sub>-CH<sub>2</sub>), 4.09 (d, 1H, *J* = 5.5 Hz, C<sub>7</sub>-H), 3.08 (dd, 1H, *J* = 9.0, 5.7 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 2.94 (dd, 1H, *J* = 9.0, 6.8 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 1.87 (dq, 1H, *J* = 6.8, 5.7 Hz, C<sub>8</sub>-H), 1.62 (s, 3H, C<sub>6</sub>-CH<sub>3</sub>), 0.99 (d, 3H, *J* = 6.8 Hz, C<sub>8</sub>-CH<sub>3</sub>), 0.91 (t, 9H, *J* = 7.9 Hz, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.60-0.45 (m, 6H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  146.4, 144.6, 128.8, 127.7, 126.8, 111.5, 86.4, 77.2, 66.2, 37.9, 18.2, 12.3, 7.0, 4.9; Exact mass calcd. for C<sub>32</sub>H<sub>42</sub>O<sub>2</sub>Si: 486.2954; found: 486.2966 (EI).

Tro 9 (25, 35, 45)-2,4-dimethyl-3-(triethylsilyloxy)--5-(triphenylmethoxy)-pentanol. To a solution of 10 (113 mg, 0.23 mmol) in 3 ml of THF at 0 °C was added a solution of 9-BBN dimer (91 mg, 0.37 mmol) in 1 ml THF via cannula. After stirring for 3 h at 0 °C, the reaction was quenched by the addition of 0.5 ml of ethanol and 0.5 ml pH 7 phosphate buffer. 0.5 ml of 30% aqueous hydrogen peroxide solution was added slowly, and the mixture was added. The layers were separated and extracted with Et<sub>2</sub>O (3 x 10 ml). The combined organic layers were dried over MgSO4, filtered, and concentrated *in vacuo*. <sup>1</sup>H NMR analysis of the unpurified reaction mixture (400 MHz) revealed only one detectable diastereomer. Purification via flash chromatography (5% EtOAc/hexanes) afforded 104 mg (89%) of (2S, 3S, 4S)-2,4-dimethyl-3-

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(triethylsilyloxy)--5-(triphenylmethoxy)-pentanol as a clear, colorless oil. TLC  $R_f = 0.52$  (20% EtOAc/hexanes); [ $\alpha$ ]  $^{23}_{365}$  -35.6 ° (c 1.0, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 3442, 3086, 3058, 3022, 2956, 2934, 2911, 2875, 1597, 1490, 1448, 1414, 1380, 1239, 1222, 1088, 1064, 1033, 1007, 763, 743, 706, 632 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.45-7.22 (m, 15H, (PhH<sub>5</sub>)<sub>3</sub>), 3.78 (dd, 1H, J = 6.3, 3.3 Hz, C7-H), 3.56 (t, 2H, J = 5.0 Hz, C5-H<sub>2</sub>), 3.03 (dd, 1H, J = 9.0, 6.6 Hz, one of C9-H<sub>2</sub>), 2.99 (dd, 1H, J = 9.0, 6.7 Hz, one of C9-H<sub>2</sub>), 2.51 (t, 1H, J = 5.0 Hz, OH), 1.98 (dq, 1H, J = 6.8, 3.3 Hz, C8-H), 1.73 (m, 1H, C6-H), 0.96 (d, 3H, J = 6.9 Hz, C8-CH<sub>3</sub>), 0.95 (d, 3H, J = 7.0 Hz, C6-CH<sub>3</sub>), 0.87 (t, 9H, J = 7.8 Hz, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.54-0.38 (m, 6H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  144.3, 128.8, 127.8, 127.0, 86.6, 78.1, 66.4, 66.2, 38.7, 38.2, 15.5, 12.2, 7.0, 5.2; Exact mass calcd. for C<sub>32</sub>H<sub>44</sub>O<sub>3</sub>SiNa[(M+Na)<sup>+</sup>]: 527.2957; found: 527.2962 (FAB, *m*-nitrobenzyl alcohol, added NaI).



(25, 35, 45)-2,4-dimethyl-3-(triethylsilyloxy)--5-(triphenylmethoxy)-pentanal (11). To a solution of oxalyl <sub>H</sub> chloride (2.25 ml, 25.65 mmol) in 100 ml of CH<sub>2</sub>Cl<sub>2</sub> at -78 °C was added dimethyl sulfoxide (3.75 ml, 52.9 mmol) dropwise *via* syringe. After stirring for 10 min at -78 °C, a solution of (2S, 3S, 4S)-2,4-dimethyl-3-(triethylsilyloxy)--5-(triphenylmethoxy)-pentanol (8.09 g, 16.0 mmol) in 25 ml of CH<sub>2</sub>Cl<sub>2</sub> was added dropwise

(intentivisity loxy)--2-(dipinently intentioxy)-peritation (6.09 g, 10.0 minut) in 25 mi of CH2CH2 was added dropwise via cannula. The solution was then stirred for 20 min at -78 °C, followed by the addition of triethylamine (15.0 ml, 107.4 mmol). After stirring for 1 h at -78 °C, the reaction mixture was poured into a solution of sat. NH4Cl (100 ml) and stirred for 10 min at ambient temperature. The layers were separated and extracted with CH2Cl2 (2 x 50 ml). The combined organic layers were washed with brine, dried over MgSO4, filtered, and concentrated *in vacuo*. Purification via flash chromatography (5% EtOAc/hexanes) afforded 7.9 g (98%) of **11** as a clear, colorless oil. TLC  $R_f$  = 0.75 (10% EtOAc/hexanes); [α<sup>23</sup><sub>655</sub> -136.6 ° (c 1.0, CH2Cl2); IR (neat) 3086, 3058, 3023, 2956, 2935, 2911, 2876, 2730, 2707, 1727, 1597, 1490, 1456, 1448, 1152, 1115, 1087, 1067, 1036, 1009, 763, 744, 707, 632 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl3) δ 9.66 (d, 1H, *J* = 2.3 Hz, C5-*H*), 7.41-7.18 (m, 15H, (PhH5)3), 4.01 (dd, 1H, *J* = 6.3, 3.1 Hz, C7-*H*), 3.03 (dd, 1H, *J* = 9.1, 6.7 Hz, one of C9-*H*2), 3.00 (dd, 1H, *J* = 9.1, 6.9 Hz, one of C9-*H*2), 2.46 (ddq, 1H, *J* = 7.0, 3.1, 2.3 Hz, C6-*H*), 1.91 (dq, 1H, *J* = 6.8, 3.3 Hz, C8-*H*), 1.00 (d, 3H, *J* = 7.0 Hz, C6-CH3), 0.91 (d, 3H, *J* = 6.8 Hz, C8-CH3), 0.80 (t, 9H, *J* = 8.0 Hz, Si(CH2CH3)3), 0.45-0.33 (m, 6H, Si(CH2CH3)3); <sup>13</sup>C NMR (125 MHz, CDCl3) δ 204.9, 144.2, 128.8, 127.8, 127.0, 86.7, 74.8, 66.2, 50.5, 38.0, 11.8, 6.9, 5.2; Anal. calcd. for C32H42O3Si: C, 76.45; H, 8.42; found: C, 76.40; H, 8.47.

Ethyl (2E, 4E, 6S, 7S,8S )-6,8-dimethyl-7-(triethylsilyloxy)-9-(triphenylmethoxy)-2,4- $C_{2E}$  nonadienoate. To a solution of 1,1,1,3,3,3-hexamethyldisilazane (3,33 ml, 15.8 mmol) in 75 ml of THF at -78 °C was added *n*-butyllithium (6.3 ml, 2.5 M in hexanes, 15.75 mmol) dropwise via syringe. Me After stirring for 15 min at -78 °C, triethyl 4-phosphonocrotonate (3.5 ml, 15.8 mmol) was added dropwise via syringe. The reaction mixture was then stirred for 20 min at -78 °C, followed by the dropwise cannula addition of a solution of 11 (7.8 g, 15.5 mmol) in 50 ml of THF. The reaction mixture was stirred for 11 h allowing the bath to warm from -78 °C to ambient temperature. The reaction was quenched by the addition of sat. NH4Cl (100 ml) and extracted with Et<sub>2</sub>O (2 x 50 ml). The combined organic layers were washed with brine, dried over MgSO4, filtered, and concentrated in vacuo. <sup>1</sup>H NMR analysis of the unpurified reaction mixture (500 MHz, CDCl3) revealed a 92:8 ratio of E,E:Z,E isomers. Purification via flash chromatography (5% EtOAc/hexanes) afforded 7.875 g (85%) of the major diastereomer as a clear, colorless oil. TLC  $R_f = 0.72$  (20% EtOAc/hexanes); [ $\alpha$ ] <sup>23</sup><sub>365</sub> -148.4 ° (c 1.0, CH<sub>2</sub>Cl<sub>2</sub>); IR (neat) 3086, 3058, 3023, 2958, 2931, 2910, 2875, 1714, 1641, 1616, 1490, 1448, 1366, 1300, 1260, 1239, 1224, 1140, 1095, 1062, 1034, 1002, 744, 707, 632 cm<sup>-1</sup>; <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 7.43-7.22 (m, 15H, (PhH<sub>5</sub>)<sub>3</sub>), 7.20  $(dd, 1H, J = 15.3, 10.9 Hz, C_3-H), 6.06 (dd, 1H, J = 15.3, 8.4 Hz, C_5-H), 5.93 (dd, 1H, J = 15.3, 10.9 Hz, C_4-H), 5.72 (d, 1H, J = 15.3, 10.9 Hz, C_4-H), 5.72 (d, 1H, J = 15.3, 10.9 Hz, C_4-H), 5.73 (d, 1H, J = 15.3, 10.9 Hz, C_4-H), 5.73 (d, 1H, J = 15.3, 10.9 Hz, C_4-H), 5.73 (d, 1H, J = 15.3, 10.9 Hz, C_4-H), 5.74 (d$ Hz, C<sub>2</sub>-H), 4.21 (q, 2H, J = 7.1 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 3.67 (t, 1H, J = 4.5 Hz, C<sub>7</sub>-H), 3.01 (dd, 1H, J = 8.9, 5.8 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 2.91 (dd, 1H, J = 8.9, 6.7 Hz, one of C9-H2), 2.27 (m, 1H, C6-H), 1.86 (m, 1H, C8-H), 1.30 (t, 3H, J = 7.1 Hz, OCH2CH3), 0.99 (d, 3H, J = 7.1 Hz, OCH2CH3), 0 = 6.9 Hz, C<sub>6</sub>-CH<sub>3</sub>), 0.97 (d, 3H, J = 6.9 Hz, C<sub>8</sub>-CH<sub>3</sub>), 0.86 (t, 9H, J = 8.0 Hz, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>), 0.49-0.40 (m, 6H, Si(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>) & 167.3, 147.2, 145.2, 144.4, 128.8, 128.0, 127.7, 126.9, 119.4, 86.4, 77.2, 66.3, 60.2, 41.8, 38.2, 17.8, 14.4, 13.0, 7.1, 5.4; Exact mass calcd. for C<sub>38</sub>H<sub>50</sub>O<sub>4</sub>SiNa[(M+Na)<sup>+</sup>]: 621.3376; found: 621.3360 (FAB, *m*-nitrobenzyl alcohol, added NaI).



Ethyl (2E, 4E, 6S, 7S, 8S)-7-hydroxy-6,8-dimethyl-9-(triphenylmethoxy)-2,4-nonadienoate (12). To a solution of Ethyl (2E, 4E, 6S, 7S, 8S)-6,8-dimethyl-7-(triethylsilyloxy)-9-(triphenylmethoxy)-2,4-nonadienoate (950 mg, 1.59 mmol) in 20 ml of THF at 0  $^{\circ}$ C in a Nalgene tube was added 3.0 ml of pyridinium hydrofluoride. After stirring for 4 h at 0  $^{\circ}$ C, the reaction was quenched by the addition of

sat. NaHCO3 (30 ml) and extracted with Et<sub>2</sub>O (2 x 20 ml). The combined organic layers were washed with brine, dried over MgSO4, filtered, and concentrated *in vacuo*. Purification *via* flash chromatography (10% EtOAc/hexanes) afforded 715 mg (93%) of **12** as a white foam. TLC  $R_f = 0.36$  (20% EtOAc/hexanes);  $[\alpha_{165}^{23} - 146.9^{\circ} (c \ 1.0, CH_2Cl_2);$  IR (neat) 3504, 3086, 3056, 3022, 2973, 2929, 2873, 1710, 1639, 1616, 1490, 1448, 1367, 1302, 1261, 1223, 1140, 1033, 1002, 764, 746, 706, 648, 632 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl\_3)  $\delta$  7.39-7.16 (m, 16H, (PhH<sub>5</sub>)3 and C<sub>3</sub>-H), 6.06 (m, 2H, C<sub>5</sub>-H and C<sub>4</sub>-H), 5.72 (d, 1H, J = 15.3 Hz, C<sub>2</sub>-H), 4.13 (q, 2H, J =

7.1 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 3.48 (ddd, 1H, J = 6.2, 4.7, 3.0 Hz, C<sub>7</sub>-H), 3.21 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd, 1H, J = 9.1, 5.3 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.05 (dd 4.3 Hz, one of C9-H2), 2.34 (d, 1H, J = 3.0 Hz, OH), 2.27 (m, 1H, C6-H), 1.79 (m, 1H, C8-H), 1.23 (t, 3H, J = 7.1 Hz, OCH2CH3), 1.00 (d, 3H, J = 7.0 Hz, C<sub>6</sub>-CH<sub>3</sub>), 0.90 (d, 3H, J = 6.8 Hz, C<sub>8</sub>-CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  167.2, 146.8, 144.9, 143.9, 128.7, 128.6, 127.9, 127.1, 119.9, 86.9, 76.9, 67.4, 60.2, 40.7, 35.8, 16.9, 14.4, 10.8; Exact mass calcd. for C32H36O4Na[(M+Na)<sup>+</sup>]; 507.2511; found: 507.2505 (FAB, m-nitrobenzyl alcohol, added NaI).



(2E, 4E, 6S, 7S, 8S)-7-hydroxy-6,8-dimethyl-9-(triphenylmethoxy)-2,4-nonadienoic acid (13).  $^{O_2H}$  The hydrolysis of ester 12 was performed according to the method of Seebach and co-workers.<sup>6</sup> Purification via flash chromatography (50% EtOAc/hexanes) afforded a 98% yield of 13 as a white foam. TLC  $R_f = 0.30$  (60% EtOAc/hexanes); The following spectral data are consistent with previously reported values: <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  7.44-7.21 (m, 16H, (PhH5)<sub>3</sub> and C<sub>3</sub>-H), 6.16 (m, 2H, C<sub>5</sub>-H and C<sub>4</sub>-H), 5.77 (d, 1H, J = 15.3 Hz, C<sub>2</sub>-H), 3.55 (dd, 1H, J = 7.8, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 9.1, 5.2 Hz, one of C<sub>9</sub>-H<sub>2</sub>), 3.12 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.55 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.55 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.55 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.12 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.12 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.12 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.27 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.12 (dd, 1H, J = 1.5, 3.2 Hz, C<sub>7</sub>-H), 3.2 Hz, C<sub>7</sub> 9.1, 4.2 Hz, one of C9-H2), 2.34 (dq, 1H, J = 7.4, 7.0 Hz, C6-H), 2.05 (s, 1H, C7-OH), 1.85 (m, 1H, C8-H), 1.06 (d, 3H, J = 7.0 Hz, C6-CH<sub>3</sub>), 0.97 (d, 3H, J = 6.8 Hz, C8-CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  171.9, 148.3, 147.3, 143.9, 128.7, 128.4, 128.0, 127.1, 118.9, 86.9, 77.3, 67.4, 40.8, 35.8, 16.9, 10.8; Exact mass calcd. for C30H32O4Na[(M+Na)<sup>+</sup>]: 479.2198; found: 479.2189 (FAB, mnitrobenzyl alcohol, added NaI).



(3E, 5E, 7S, 8S, 11E, 13E, 15S, 16S,)-8,16-bis[(1S)-1-triphenylmethoxymethylethyl]-7,15dimethyl-1,9-dioxacyclohexadeca-3,5,11,13-tetraene-2,10-dione (14). To a solution of 13 (995 mg, 2.18 mmol) in 50 ml of toluene at ambient temperature was added triethylamine (910 μl, 6.54 mmol). After stirring for 2 min, 2,4,6-trichlorobenzoyl chloride (360 μl, 2.29 mmol) was added dropwise via syringe. The solution was stirred for 1 h at ambient temperature, followed by the addition of 4-dimethylaminopyridine (27 mg, 0.22 mmol). After stirring for 45 min, the reaction was quenched by the addition of 1 M sodium bisulfate solution (50 ml) and

extracted with Et<sub>2</sub>O (3 x 50 ml). The combined organic layers were washed with sat. NaHCO<sub>3</sub>, dried over MgSO<sub>4</sub>, filtered, and concentrated in vacuo. Purification via flash chromatography (10% EtOAc/hexanes) afforded 595 mg (62%) of 14 as a white, crystalline solid. TLC  $R_f = 0.63$  (20% EtOAc/hexanes); The following spectral data are consistent with previously reported values: <sup>1</sup>H NMR (500 MHz,  $CDCl_3$ )  $\delta$  7.46-7.20 (m, 30H, (PhH5)3), 6.91 (dd, 2H, J = 15.3, 11.2 Hz, C3-H), 5.95 (dd, 2H, J = 15.0, 11.2 Hz, C4-H), 5.64 (dd, 2H, J = 15.0, 9.9 Hz, C5-H), 5.49 (d, 2H, J = 15.3 Hz, C2-H), 5.01 (dd, 2H, J = 10.3, 1.4 Hz, C7-H), 3.08 (dd, 2H, J = 9.2, 7.7 Hz, one of each C9-H<sub>2</sub>), 3.00 (dd, 2H, J = 9.2, 6.5 Hz, one of each C9-H<sub>2</sub>), 2.41 (m, 2H, C<sub>6</sub>-H), 1.98 (br. q, 2H, J = 6.6 Hz, C<sub>8</sub>-H), 1.02 (d, 6H, J = 6.6 Hz, C<sub>6</sub>-CH<sub>3</sub>), 0.89 (d, 6H, J = 6.9 Hz, C<sub>8</sub>-CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  167.4, 145.2, 144.5, 144.3, 128.9, 128.0, 127.8, 126.9, 121.4, 86.6, 76.4, 66.0, 41.9, 34.0, 15.8, 10.3; Exact mass calcd. for C60H60O6Na[(M+Na)<sup>+</sup>]: 899.4288; found: 899.4281 (FAB, m-nitrobenzyl alcohol, added NaI).



(3E, 5E, 7S, 8S, 11E, 13E, 15S, 16S,)-8,16-bis[(1S)-1-hydroxymethylethyl]-7,15-dimethyl-1,9-dioxacyclohexadeca-3,5,11,13-tetraene-2,10-dione (15). The tritlyl deprotection of 14 was performed according to the method of Seebach and co-workers.<sup>6</sup> Purification via flash chromatography (50% EtOAc/hexanes) afforded a 65% yield of 15 as a white, crystalline solid. TLC  $R_f = 0.27$  (60% EtOAc/hexanes); The following spectral data are consistent with previously reported values: <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>)  $\delta$  6.96 (dd, 2H, J = 15.3, 11.2 Hz, C<sub>3</sub>-H), 6.10 (dd, 2H, J = 15.0, 11.2 Hz, C<sub>4</sub>-H), 5.67 (d, 2H, J = 15.3 Hz, C<sub>2</sub>-H), 5.63 (dd, 2H, J = 15.0, 9.7

Hz, C5-H), 4.80 (dd, 2H, J = 10.3, 2.0 Hz, C7-H), 3.47 (br. s, 2H, one of each C9-H2), 3.34 (t, 2H, J = 10.9 Hz, one of each C9-H2), 2.78 (br. s, 2H, OH), 2.52 (ddq, 2H, J = 10.3, 9.7, 6.7 Hz, C<sub>6</sub>-H), 2.13 (ddq, 2H, J = 7.3, 6.9, 2.0 Hz, C<sub>8</sub>-H), 1.04 (d, 6H, J = 6.7 Hz, C<sub>8</sub>-H), 2.52 (ddq, 2H, J = 10.3, 9.7, 6.7 Hz, C<sub>6</sub>-H), 2.13 (ddq, 2H, J = 7.3, 6.9, 2.0 Hz, C<sub>8</sub>-H), 1.04 (d, 6H, J = 6.7 Hz, C<sub>8</sub>-H), 2.52 (ddq, 2H, J = 10.3, 9.7, 6.7 Hz, C<sub>6</sub>-H), 2.13 (ddq, 2H, J = 7.3, 6.9, 2.0 Hz, C<sub>8</sub>-H), 1.04 (d, 6H, J = 6.7 Hz, C<sub>8</sub>-H), 2.52 (ddq, 2H, J = 10.3, 9.7, 6.7 Hz, C<sub>6</sub>-H), 2.13 (ddq, 2H, J = 7.3, 6.9, 2.0 Hz, C<sub>8</sub>-H), 1.04 (d, 6H, J = 6.7 Hz, C<sub>8</sub>-H), 1.04 (d, 6H, JC6-CH<sub>3</sub>), 0.85 (d, 6H, J = 6.9 Hz, C8-CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  169.1, 144.9, 144.3, 131.8, 121.3, 76.8, 64.7, 41.0, 35.5, 15.2, 9.1; Exact mass calcd. for C22H32O6Na[(M+Na)<sup>+</sup>]: 415.2097; found: 415.2091 (FAB, m-nitrobenzyl alcohol, added NaI).



(3E, 5E, 7S, 8S, 11E, 13E, 15S, 16S,)-8,16-bis[(1R)-1-formylethyl]-7,15-dimethyl-1,9dioxacyclohexadeca-3,5,11,13-tetraene-2,10-dione (16). The Swern oxidation of diol 15 was performed according to the method of Seebach and co-workers.<sup>3</sup> Purification via flash chromatography (40% EtOAc/hexanes) afforded a 96% yield of 16 as a white, crystalline solid. TLC  $R_f = 0.33$  (40% EtOAc/hexanes); The following spectral data are consistent with previously reported values: <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>) δ 9.67 (s, 2H, C9-H), 6.96 (dd, 2H, J = 15.4, 11.2 Hz, C<sub>3</sub>-H), 6.05 (dd, 2H, J = 15.0, 11.2 Hz, C<sub>4</sub>-H), 5.65 (dd, 2H, J = 15.0, 9.9 Hz, C<sub>5</sub>-H), 5.57 (d,

2H, J = 15.4 Hz, C<sub>2</sub>-H), 5.40 (dd, 2H, J = 10.3, 2.3 Hz, C<sub>7</sub>-H), 2.72 (dq, 2H, J = 7.0, 2.3 Hz, C<sub>8</sub>-H), 2.52 (ddq, 2H, J = 10.3, 9.9, 6.7 Hz, C<sub>6</sub>-H), 1.19 (d, 6H, J = 7.0 Hz, C<sub>8</sub>-CH<sub>3</sub>), 1.10 (d, 6H, J = 6.7 Hz, C<sub>6</sub>-CH<sub>3</sub>); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>)  $\delta$  202.0, 167.1, 145.5, 143.2, 131.9, 121.2, 74.2, 46.9, 41.8, 15.5, 6.7; Exact mass calcd. for C<sub>22</sub>H<sub>28</sub>O<sub>6</sub>Na[(M+Na)<sup>+</sup>]: 411.1784; found: 411.1791 (FAB, *m*-nitrobenzyl alcohol, added NaI).



(3E, 5E, 7S, 8S, 11E, 13E, 15S, 16S,)-8,16-bis[(1S,2R,3S)-5-[(4R,5R,6R)-2,2-di-*tert*-butyl-5-ethyl-6-methyl-1,3-dioxa-2silacyclohex-4-yl]-2-hydroxy-1,3-dimethyl-4-oxopentyl]-7,15dimethyl-1,9-dioxacyclohexadeca-3,5,11,13-tetraene-2,10dione (17). To a solution of ketone 8 (228 mg, 0.69 mmol) in 3 ml of CH<sub>2</sub>Cl<sub>2</sub> at -78 °C was added a solution of

dichlorophenylborane (195 µl, 1.5 mmol) in 1.5 ml of CH<sub>2</sub>Cl<sub>2</sub>

dropwise via cannula. After stirring for 20 min at -78 °C, N,N-diisopropylethylamine (343 µl, 1.97 mmol) was added dropwise via syringe. The reaction mixture was stirred at -78 °C for 0.5 h, followed by warming to 0 °C and stirring for 0.5 h. The solution was recooled to -78 °C and dialdehyde 16 (90 mg, 0.23 mmol) was added as a solution in 1.5 ml of CH2Cl2 dropwise via cannula. After stirring for 1 h at -78 °C, the reaction was quenched by the addition of 1:1 methanol/pH 7 phosphate buffer (10 ml) and warmed to 0 C. After 5 min, a solution of 1:1 methanol/30% aqueous hydrogen peroxide (15 ml) was added dropwise. After stirring for 0.5 h at 0 °C, the reaction mixture was diluted CH<sub>2</sub>Cl<sub>2</sub>, washed with sat. NaHCO<sub>3</sub> (20 ml), and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x 20 ml). The combined organic layers were dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. <sup>1</sup>H NMR analysis of the unpurified reaction mixture (500 MHz) revealed only one detectable aldol diastereomer. Purification via flash chromatography (20% EtOAc/hexanes) afforded 160 mg (66%) of 17 as a white, crystalline solid. TLC  $R_f = 0.46$  (40% EtOAc/hexanes); m.p. 176-177 °C;  $[\alpha]_{365}^{23} + 454.1$  ° (c 1.0, CH2Cl2); IR (CDCl3) 3488, 3154, 2974, 2935, 2901, 2860, 2253, 1816, 1793, 1710, 1639, 1473, 1381, 1095, 1000, 964, 914, 738, 651 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  6.96 (dd, 2H, J = 15.3, 11.2 Hz, C<sub>3</sub>-H), 6.05 (dd, 2H, J = 15.0, 11.2 Hz, C<sub>4</sub>-H), 5.66  $(dd, 2H, J = 15.0, 9.7 Hz, C_5-H), 5.60 (d, 2H, J = 15.3 Hz, C_2-H), 5.10 (dd, 2H, J = 10.3, 1.5 Hz, C_7-H), 4.75 (ddd, 2H, J = 10.7, 7.3, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-H), 5.60 (d, 2H, J = 10.7, 1.5 Hz, C_7-Hz, C_7-H), 5.60 (d, 2H, J$ 2.6 Hz, C13-H), 4.02 (dq, 2H, J = 7.4, 6.3 Hz, C15-H), 3.76 (ddd, 2H, J = 8.9, 3.3, 1.9 Hz, C9-H), 3.39 (d, 2H, J = 3.3 Hz, OH), 2.85  $(dq, 2H, J = 7.1, 1.9 Hz, C_{10}-H), 2.80 (dd, 2H, J = 15.0, 10.7 Hz, one of each C_{12}-H_2), 2.49 (ddq, 2H, J = 10.3, 9.7, 6.7 Hz, C_6-H),$ 2.37 (dd, 2H, J = 15.0, 2.6 Hz, one of each C<sub>12</sub>-H<sub>2</sub>), 1.92 (ddq, 2H, J = 8.9, 7.0, 1.5 Hz, C<sub>8</sub>-H), 1.73 (m, 2H, one of each C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.48 (m, 2H, one of each C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.22 (d, 6H, J = 6.3 Hz, C<sub>15</sub>-CH<sub>3</sub>), 1.14 (d, 6H, J = 7.1 Hz, C<sub>10</sub>-CH<sub>3</sub>), 1.04 (d, 6H, J = 6.7 Hz, C6-CH3), 1.08-1.03 (m, 2H, C14-H), 0.96 (s, 18H, one of each SiC(CH3)3), 0.94 (s, 18H, one of each SiC(CH3)3), 0.93 (t, 6H, J = 7.5 Hz, C14-CH2CH3), 0.88 (d, 6H, J = 7.0 Hz, C8-CH3); <sup>13</sup>C NMR (100 MHz, CDCl3)  $\delta$  213.5, 168.4, 145.2, 144.6, 131.4, 121.2, 76.5, 71.5, 70.8, 69.9, 49.5, 47.3, 43.5, 41.6, 35.9, 27.7, 27.3, 23.2, 21.3, 21.0, 20.8, 15.2, 12.3, 9.2, 8.1; Unit mass calcd. for C58H100O12SiNa[(M+Na)<sup>+</sup>]: 1067; found: 1067 (FAB, m-nitrobenzyl alcohol, added NaI).



(3*E*, 5*E*, 7*S*, 8*S*, 11*E*, 13*E*, 15*S*, 16*S*,)-8,16-bis[(1*S*,2*R*,3*S*)-3-[(2*R*,4*R*,5*S*,6*R*)-5-ethyl-3,4,5,6-tetrahydro-2,4-dihydroxy-6-methyl-2H-pyran-2-yl]-2-hydroxy-1-methylbutyl]-7,15-dimethyl-1,9-

dioxacyclohexadeca-3,5,11,13-tetraene-2,10-dione (2). To a solution of 17 (90 mg, 0.086 mmol) in 5 ml of THF at ambient temperature in a Nalgene tube was added 0.5 ml of a buffered solution of pyridinium hydrofluoride (stock solution prepared from 1 g of Aldrich pyridinium

hydrofluoride, 1.5 ml of pyridine, and 6.5 ml of THF) and 1 drop of water. After stirring for 3 h, the reaction was diluted with CH<sub>2</sub>Cl<sub>2</sub> (15 ml), quenched by the addition of sat. NaHCO<sub>3</sub> (20 ml), and extracted with CH<sub>2</sub>Cl<sub>2</sub> (2 x 15 ml). The combined organic layers were washed with brine, dried over MgSO<sub>4</sub>, filtered, and concentrated *in vacuo*. Purification *via* flash chromatography (60% EtOAc/hexanes) afforded 60 mg (91%) of **2** as a white, crystalline solid. TLC  $R_f = 0.33$  (80% EtOAc/hexanes); m.p. 170-171 °C; [ $\alpha$ ]  $_{27}^{29} + 27.8$  ° (*c* 0.3, CHCl<sub>3</sub>); IR (neat) 3487, 2970, 2939, 2881, 1700, 1639, 1615, 1463, 1383, 1348, 1306, 1282, 1223, 1182, 1147, 1080, 1065, 999, 876 cm<sup>-1</sup>; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>)  $\delta$  6.97 (dd, 2H, *J* = 15.4, 11.1 Hz, C<sub>3</sub>-H), 6.12 (dd, 2H, *J* = 15.0, 11.1 Hz, C<sub>4</sub>-H), 5.68 (d, 2H, *J* = 15.4 Hz, C<sub>2</sub>-H), 5.62 (dd, 2H, *J* = 15.0, 9.5 Hz, C<sub>5</sub>-H), 5.32 (d, 2H, *J* = 1.8 Hz, C<sub>11</sub>-OH), 4.72 (dd, 2H, *J* = 10.1, 1.4 Hz, C<sub>7</sub>-H), 4.16 (d, 2H, *J* = 10.1, 9.5, 6.8 Hz, C<sub>6</sub>-H), 2.28 (dd, 2H, *J* = 11.9, 4.7 Hz, C<sub>12</sub>-H<sub>eq</sub>), 1.95 (ddq, 2H, *J* = 10.0, 6.9, 1.4 Hz, C<sub>8</sub>-H), 1.71 (q, 2H, *J* = 7.1 Hz, C<sub>10</sub>-H), 1.66 (s, 2H, C<sub>13</sub>-OH), 1.62 (m, 2H, one of each C<sub>14</sub>-CH<sub>2</sub>CH<sub>3</sub>), 1.16 (dt, 2H, *J* = 11.7, 2.0 Hz, C<sub>10</sub>-CH<sub>3</sub>), 0.89 (t, 6H, *J* = 6.2 Hz, C<sub>15</sub>-CH<sub>3</sub>), 0.80 (d, 6H, *J* = 6.9 Hz, C<sub>8</sub>-CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  170.1, 145.1, 144.4, 132.1, 121.0, 99.2, 77.9, 70.6, 67.0, 66.9, 50.9, 43.5, 41.5, 40.8, 35.9, 19.4, 19.3, 15.0, 9.8, 8.8, 7.0; Exact mass calcd. for C4<sub>2</sub>H<sub>68</sub>O<sub>12</sub>Na[(M+Na)<sup>+</sup>]: 787.4608; found: 787.4592 (FAB, *m*-nitrobenzyl alcohol, added NaI).

## **Footnotes and References:**

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