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Total Synthesis of Filipin III

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Supporting Information

Full spectral data for compounds **2-14**, **17-27** and filipin III are included.

***E*-2-octene-1-ol (5):** IR (neat) 3314, 2655, 2925, 2857, 1670 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.70-5.57 (m, 2 H), 4.05 (m, 2 H), 2.01 (q, $J = 7.0$ Hz, 2 H), 1.70 (m, 1 H), 1.39-1.21 (m, 6 H), 0.862 (t, $J = 7.0$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ CH, 133.5, 128.8, CH_2 , 63.8, 32.1, 31.4, 28.8, 22.5, CH_3 , 14.0. Anal. calcd for $\text{C}_8\text{H}_{15}\text{O}$: C, 74.94; H, 12.58. Found: C, 74.98; H, 12.60.

(2*R*,3*R*)-3-pentyloxirane-2-methanol (6): Analysis by chiral GC showed the product was 99% ee; mp = 34-36 $^\circ\text{C}$; $[\alpha]_{\text{D}}^{27} = +38.9^\circ$ ($c = 1.11$, CHCl_3); IR (neat) 3254, 3117, 2987, 2931, 2853 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 3.87 (ddd, $J = 2.4, 5.8, 12.5$ Hz, 1 H), 3.57 (ddd, $J = 4.6, 6.9, 12.5$ Hz, 1 H), 2.93-2.88 (m, 2 H), 2.43 (t, $J = 7.1$ Hz, 1 H), 1.58-1.22 (m, 8 H), 0.863 (t, $J = 6.9$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ CH, 58.7, 56.1, CH_2 , 61.8, 31.6, 31.5, 25.6, 22.5, CH_3 , 14.0. Anal. calcd for $\text{C}_8\text{H}_{16}\text{O}_3$: C, 66.63; H, 11.18. Found: C, 66.40; H, 10.98.

(3*S*,4*R*)-3-hydroxymethyl-1-nonen-4-ol (7): $[\alpha]_{\text{D}}^{27} = 22.5^\circ$ ($c = 1.48$, CHCl_3); IR (neat) 3348, 3078, 2955, 2930, 2865, 2860, 1640 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.64 (ddd, $J = 8.8, 11.1, 16.3$ Hz, 1 H), 5.19-5.15 (m, 2 H), 3.82-3.67 (m, 3 H), 2.76 (t, $J = 5.0$ Hz, 1 H), 2.56 (d, $J = 4.3$ Hz, 1 H), 2.30 (m, 1 H), 1.59-1.23 (m, 8 H), 0.880 (t, $J = 7.0$ Hz, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ CH, 136.2, 74.6, 51.4, CH_2 , 117.8, 65.3, 35.4, 31.7, 24.9, 22.6, CH_3 , 14.0. Anal. calcd for $\text{C}_{10}\text{H}_{20}\text{O}$: C, 69.72; H, 11.70. Found: C, 69.88; H, 11.36.

(3*S*,4*R*)-3-*O*-(1,1-dimethylethyl)dimethylsilyl-3-hydroxymethyl-1-nonen-4-ol (8): $[\alpha]_D^{27} = -13.1^\circ$ ($c = 1.45$, CHCl_3); IR (neat) 3414, 3077, 2953, 2932, 2859, 1640 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.79 (ddd, $J = 8.9, 9.7, 14.4$ Hz, 1 H), 5.17-5.12 (m, 2 H), 3.77 (dt, $J = 5.6, 11.2$ Hz, 1 H), 3.74-3.65 (m, 2 H), 2.48 (dd, $J = 4.5, 7.0$ Hz, 1 H), 2.35 (dq, $J = 5.7, 8.9$ Hz, 1 H), 1.52-1.48 (m, 2 H), 1.35-1.19 (m, 6 H), 0.882 (s, 9 H), 0.872 (t, $J = 6.9$ Hz, 3 H), 0.064 (s, 3 H), 0.056 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ C, 18.8 CH, 137.6, 75.2, 49.9, CH_2 , 117.3, 63.5, 35.0, 32.0, 23.8, 22.6, CH_3 , 25.8 (3), 14.0, -4.26, -4.69. Anal. calcd for $\text{C}_{16}\text{H}_{34}\text{O}_2\text{Si}$: C, 67.07; H, 11.96. Found: C, 67.13; H, 11.78.

(4*S*,5*R*)-5-(1,1-dimethylethyl)dimethylsiloxy-4-ethenyl-3-oxodecanoic acid, ethyl ester (9): $[\alpha]_D^{24} = 57.1^\circ$ ($c = 1.20$, CHCl_3); IR (neat) 3083, 2954, 2933, 2860, 1749, 1720, 1642 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.68 (dt, $J = 17.4, 9.7$ Hz, 1 H), 5.20-5.15 (m, 2 H), 4.20-4.11 (m, 2 H), 4.08 (dt, $J = 8.4, 4.2$ Hz, 1 H), 3.54 (d, $J = 15.8$ Hz, 1 H), 3.46 (dd, $J = 9.1, 9.6$ Hz, 1 H), 3.44 (d, $J = 15.8$ Hz, 1 H), 1.48-1.38 (m, 2 H), 1.31-1.17 (m, 2 H), 1.24 (t, $J = 7.0$ Hz, 3 H), 0.845 (s, 9 H), 0.845 (t, $J = 7.0$ Hz, 3 H), 0.034 (s, 3 H), -0.009 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ C, 202.3, 166.9, 18.0, CH, 133.0, 73.1, 62.4, CH_2 , 119.5, 61.1, 50.7, 34.1, 32.0, 22.6, 22.4, CH_3 , 25.8 (3), 14.3, 14.2, -4.53, -4.98. Anal. calcd for $\text{C}_{20}\text{H}_{38}\text{O}_4\text{Si}$: C, 64.82; H, 10.33. Found: C, 64.92; H, 10.55.

(3*S*,4*R*,5*R*)-5-(1,1-dimethylethyl)dimethylsiloxy-4-ethenyl-3-hydroxydecanoic acid, ethyl ester (10): $[\alpha]_D^{25} = -19.1^\circ$ ($c = 1.05$, CHCl_3); IR (neat) 3510, 3078, 2955, 2932, 2858, 1722, 1640 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.52 (dt, $J = 16.9, 10.1$ Hz, 1 H), 5.13-5.07 (m, 2 H), 4.17-4.10 (m, 3 H), 3.91 (dt, $J = 11.3, 5.3$ Hz, 1 H), 3.55 (d, $J = 3.5$ Hz, 1 H), 2.56 (dd, $J = 3.3, 16.1$ Hz, 1 H), 2.35 (ddd, $J = 6.5, 8.3, 10.1$ Hz, 1 H), 2.31 (dd, $J = 9.1, 16.1$ Hz, 1 H), 1.52-1.42 (m, 2 H), 1.38-1.20 (m, 6 H), 1.24 (t, $J = 7.1$ Hz, 3 H), 0.886 (s, 9 H), 0.864 (t, $J = 7.2$ Hz, 3 H), 0.095 (s, 3 H), 0.072 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ C, 172.8, 18.1, CH, 135.4, 74.2, 68.9, 54.8, CH_2 , 118.9, 60.5, 39.9, 34.1, 32.0, 23.7, 22.6, CH_3 , 25.9 (3), 14.2, 14.1, -4.23, -4.59. Anal. calcd for $\text{C}_{20}\text{H}_{40}\text{O}_4\text{Si}$: C, 64.47; H, 10.82. Found: C, 64.13; H, 10.70.

(2*R*,4*S*,5*R*,6*R*) and (2*R*,4*S*,5*R*,6*R*)-2,4-dihydroxy-6-(1,1-dimethylethyl)dimethylsiloxy-5-ethenyl-2,4-*O*-(1-methylethylidene)-

undecanenitrile (4): Trans isomer: $[\alpha]_D^{26} = 36.4^\circ$ ($c = 1.10$, CH_2Cl_2); IR (neat) 3080, 2956, 2932, 2858, 1641, 1465 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.61 (dt, $J = 10.2$, 16.9 Hz, 1 H), 5.16-5.04 (m, 2 H), 4.80 (t, $J = 4.1$ Hz, 1 H), 4.18 (dt, $J = 6.0$, 8.6 Hz, 1 H), 3.89 (dt, $J = 3.7$, 7.5 Hz, 1 H), 4.57 (ddd, $J = 3.7$, 8.6, 10.2 Hz, 1 H), 1.82-1.78 (m, 2 H), 1.63 (s, 3 H), 1.51-1.20 (m, 8 H), 1.34 (s, 3 H), 0.872 (s, 9 H), 0.866 (t, $J = 6.9$ Hz, 3 H), 0.040 (s, 3 H), 0.027 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ C, 119.9, 100.7, 18.1, CH, 134.1, 71.7, 64.8, 59.0, 54.9, CH_2 , 119.1, 33.0, 32.3, 31.9, 25.4, 22.6, CH_3 , 29.7, 25.9 (3), 21.7, 14.0, -4.34, -4.38. Anal. calcd for $\text{C}_{22}\text{H}_{41}\text{NO}_3\text{Si}$: C, 66.79; H, 10.44. Found: C, 67.00; H, 10.32.

Cis isomer: $[\alpha]_D^{26} = 29.9^\circ$ ($c = 1.28$, CH_2Cl_2); IR (neat) 3079, 2994, 2954, 2926, 2857, 1640, 1472, 1463 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.55 (dt, $J = 10.1$, 16.8 Hz, 1 H), 5.16-5.05 (m, 2 H), 4.69 (dd, $J = 3.6$, 11.3 Hz, 1 H), 3.92 (ddd, $J = 3.2$, 8.4, 10.7 Hz, 1 H), 3.86 (m, 1 H), 2.29 (dt, $J = 3.9$, 9.0 Hz, 1 H), 1.82-1.60 (m, 2 H), 1.40 (s, 3 H), 1.39 (s, 3 H), 1.31-1.16 (m, 8 H), 0.863 (s, 9 H), 0.873 (t, $J = 7.0$ Hz, 3 H), 0.031 (s, 3 H), 0.024 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ C, 117.9, 99.8, 18.1, CH, 134.0, 71.7, 67.1, 59.4, 54.7, CH_2 , 119.3, 33.2 (2), 31.9, 25.2, 22.6, CH_3 , 29.5, 25.9 (3), 19.0, 14.0, -4.36 (2). Anal. calcd for $\text{C}_{22}\text{H}_{41}\text{NO}_3\text{Si}$: C, 66.79; H, 10.44. Found: C, 66.65; H, 10.30.

[4*S*,4(1*R*)]-4-(1-benzoyloxyethyl)-2,2-dimethyl-1,3-dioxolane (11): IR (neat) 3067, 2987, 2939, 2885, 1720, 1602, 1584 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.06-8.03 (m, 2 H), 7.56 (tt, $J = 1.3$, 6.9 Hz, 1 H), 7.45-7.26 (m, 2 H), 5.20 (dq, $J = 5.7$, 6.4 Hz, 1 H), 4.24 (ddd, $J = 5.7$, 6.0, 6.6 Hz, 1 H), 4.12 (dd, $J = 6.6$, 8.4 Hz, 1 H), 3.93 (dd, $J = 6.0$, 8.4 Hz, 1 H), 1.40 (s, 3 H), 1.39 (d, $J = 6.4$ Hz, 1 H), 1.38 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ C, 165.8, 130.3, 109.8, CH, 133.0, 129.7 (2), 128.4 (2), 77.5, 71.2, CH_2 , 66.2, CH_3 , 26.5, 25.3, 16.4. Anal. calcd for $\text{C}_{14}\text{H}_{18}\text{O}_4$: C, 67.18; H, 7.25. Found: C, 66.89; H, 7.10.

(2*S*,3*R*)-3-*O*-benzoyl-2-*O*-(1,1-dimethylethyl)dimethylsilyl-butane-1,2,3-triol (12): $[\alpha]_D^{25} = -10.5^\circ$ ($c = 1.18$, CHCl_3); IR (neat) 3466, 2953, 2929, 2885, 2857, 1717, 1603, 1585 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 8.03-8.01 (m, 2 H), 7.55 (tt, $J = 1.2$, 7.4 Hz, 1 H), 7.44-7.41 (m, 2 H), 5.22 (dq, $J = 4.6$, 6.5 Hz, 1 H), 3.92 (q, $J = 4.6$ Hz, 1 H), 3.65 (d, $J = 4.7$ Hz, 1 H), 1.95 (s, 1 H), 1.36 (d, $J = 6.5$ Hz, 1 H), 0.909 (s, 9 H), 0.097 (s, 3 H), 0.094 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ C, 166.0, 130.4, 18.0, CH, 132.9, 129.6 (2), 128.3 (2), 74.6, 71.8, CH_2 , 63.6, CH_3 , 25.8 (3),

15.5, -4.50, -4.64. Anal. calcd for $C_{17}H_{28}O_4Si$: C, 62.93; H, 8.70. Found: C, 62.69; H, 8.57.

(2R,3R)-3-benzoyloxy-2-(1,1-dimethylethyl)dimethylsiloxy-butanal (13):

$[\alpha]_D^{27} = 0.8^\circ$ ($c = 1.54$, CH_2Cl); IR (neat) 3064, 2955, 2931, 2887, 2858, 1738, 1721, 1603, 1585 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 9.66 (d, $J = 1.4$ Hz, 1 H), 8.21-8.00 (m, 2 H), 7.56 (tt, $J = 1.2, 7.5$ Hz, 1 H), 7.45-7.41 (m, 2 H), 5.43 (dq, $J = 3.8, 6.5$ Hz, 1 H), 4.25 (dd, $J = 1.5, 3.8$ Hz, 1 H), 1.35 (d, $J = 6.5$ Hz, 1 H), 0.919 (s, 9 H), 0.068 (s, 3 H), 0.064 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ C, 165.7, 130.0, 18.1, CH, 201.5, 133.1, 129.6 (2), 128.4 (2), 79.3, 71.5, CH_3 , 25.6, 15.0, -4.75, -5.00. Anal. calcd for $C_{17}H_{26}O_4Si$: C, 63.32; H, 8.13. Found: C, 62.98; H, 7.89. HRMS(Cl) calcd for $C_{17}H_{27}O_4Si$: 323.1678. Found: 323.1676 (M+H).

(10S,11R)-11-benzoyloxy-10-(1,1-dimethylethyl)dimethylsiloxy-2,4,6,8-

dodecatetraenal (14): $[\alpha]_D^{24} = -33.9^\circ$ ($c = 1.05$, CH_2Cl_2); IR (neat) 3024, 2952, 2929, 2856, 2712, 1717, 1674, 1640, 1594 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 9.54 (d, $J = 7.9$ Hz, 1 H), 8.02-7.99 (m, 2 H), 7.53 (tt, $J = 1.4, 7.3$ Hz, 1 H), 7.42-7.39 (m, 2 H), 7.10 (dd, $J = 11.3, 15.3$ Hz, 1 H), 6.66 (dd, $J = 11.0, 14.8$ Hz, 1 H), 6.48-6.40 (m, 2 H), 6.37 (ddd, $J = 1.4, 11.0, 15.1$ Hz, 1 H), 6.29 (dd, $J = 11.0, 14.5$ Hz, 1 H), 6.13 (dd, $J = 7.9, 15.1$ Hz, 1 H), 5.87 (dd, $J = 6.0, 15.0$ Hz, 1 H), 5.08 (dq, $J = 3.8, 6.5$ Hz, 1 H), 4.44 (ddd, $J = 1.4, 3.8, 5.3$ Hz, 1 H), 1.29 (d, $J = 6.5$ Hz, 1 H), 0.891 (s, 9 H), 0.005 (s, 3 H), -0.019 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ C, 165.9, 130.4, 18.1, CH, 193.4, 151.6, 142.3, 137.6, 136.6, 132.8, 131.6, 131.1, 130.9, 130.0, 129.5 (2), 128.2 (2), 74.5, 73.9, CH_3 , 25.7 (3), 14.2, -4.51, -4.97. HRMS(Cl) calcd for $C_{18}H_{31}O_3Si$: 427.2306. Found: 427.2317 (M+H).

(10S,11R)-11-hydroxy-10-(1,1-dimethylethyl)dimethylsiloxy-2,4,6,8-

dodecatetraenal (2): $[\alpha]_D^{24} = 4.2^\circ$ ($c = 1.6$, CH_2Cl_2); IR (neat) 3458, 2954, 2929, 2885, 2857, 1659, 1591 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 9.54 (d, $J = 7.9$ Hz, 1 H), 7.11 (dd, $J = 11.3, 15.1$ Hz, 1 H), 6.67 (dd, $J = 11.0, 14.8$ Hz, 1 H), 6.48-6.41 (m, 2 H), 6.32-6.24 (m, 2 H), 6.13 (dd, $J = 7.9, 15.1$ Hz, 1 H), 5.84 (dd, $J = 6.9, 15.0$ Hz, 1 H), 4.07 (ddd, $J = 1.0, 3.8, 7.2$ Hz, 1 H), 3.74 (tq, $J = 4.3, 6.5$ Hz, 1 H), 2.18 (d, $J = 4.3$ Hz, 1 H), 1.07 (d, $J = 6.5$ Hz, 1 H), 0.883 (s, 9 H), 0.052 (s, 3 H), 0.016 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ C, 18.2, CH, 193.5, 151.7, 142.3, 137.7, 136.1,

131.7, 131.6, 131.1, 130.1, 77.1, 70.9, CH₃, 25.8 (3), 17.6, -4.26, -4.85. HRMS(Cl) calcd for C₁₈H₃₁O₃Si: 323.2043. Found: 323.2043 (M+H).

(2S,4S)-1-chloro-4-C-cyano-2:4-O-(1-methylethylidene)-6-O-phenylmethyl-hexane-2,4,6-triol (17): $[\alpha]_D^{23} = 25.0^\circ$ ($c = 1.10$, CHCl₃); IR (neat) 3000, 2940, 2870, 2808, 1457, 1432 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.38-7.28 (m, 5 H), 4.54 (d, $J = 11.8$ Hz, 1 H), 4.51 (d, $J = 11.8$ Hz, 1 H), 4.36 (dddd, $J = 2.1, 5.5, 7.6, 11.3$ Hz, 1 H), 3.78-3.71 (m, 2 H), 3.56 (dd, $J = 5.3, 11.3$ Hz, 1 H), 3.47 (dd, $J = 5.5, 11.3$ Hz, 1 H), 2.19-2.12 (m, 2 H), 2.09 (dd, $J = 2.1, 13.6$ Hz, 1 H), 1.72 (s, 3 H), 1.71 (dd, $J = 11.6, 13.6$ Hz, 1 H), 1.41 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ C, 137.8, 121.2, 101.5, 68.3, CH, 128.4 (2), 127.6 (3), 66.5, CH₂, 73.2, 64.8, 46.2, 41.9, 37.1, CH₃, 30.6, 21.4. Anal. calcd for C₁₇H₂₂NO₃Cl: C, 63.06; H, 6.85. Found: C, 62.86; H, 6.81.

(2S,4S)-4-C-cyano-1-iodo-2:4-O-(1-methylethylidene)-6-O-phenylmethyl-hexane-2,4,6-triol (18): $[\alpha]_D^{26} = 28.9^\circ$ ($c = 1.70$, CHCl₃); IR (neat) 3061, 2999, 2936, 2868, 2806, 1455 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.39-7.29 (m, 5 H), 4.55 (d, $J = 11.8$ Hz, 1 H), 4.52 (d, $J = 11.8$ Hz, 1 H), 4.12 (dtd, $J = 2.0, 5.6, 11.5$ Hz, 1 H), 3.77-3.69 (m, 2 H), 3.18-3.12 (m, 2 H), 2.20-2.05 (m, 3 H), 1.72 (s, 3 H), 1.63 (d, $J = 11.5, 13.6$ Hz, 1 H), 1.42 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ C, 137.9, 121.4, 101.8, 68.5, CH, 128.5 (2), 127.8 (3), 68.5, CH₂, 73.3, 64.9, 41.9, 37.2, 7.64, CH₃, 30.7, 21.5. Anal. calcd for C₁₇H₂₂NO₃I: C, 49.17; H, 5.34. Found: C, 49.30; H, 5.45.

(2S,4S,6S,8S)-1-chloro-4,8-cyano-2:4,6:8-bis-O-(1-methylethylidene)-6-O-phenylmethyl-decane-2,4,6,8,10-pentol (19): $[\alpha]_D^{24} = 48.5^\circ$ ($c = 1.26$, CHCl₃); IR (neat) 2996, 2938, 2868, 1495, 1455 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 7.38-7.29 (m, 5 H), 4.54 (d, $J = 11.7$ Hz, 1 H), 4.52 (m, 1 H), 4.50 (d, $J = 11.7$ Hz, 1 H), 4.37 (dtd, $J = 2.0, 4.9, 11.8$ Hz, 1 H), 3.76-3.69 (m, 2 H), 3.58 (dd, $J = 4.9, 11.4$ Hz, 1 H), 3.54 (dd, $J = 5.0, 11.4$ Hz, 1 H), 2.17-2.06 (m, 4 H), 2.01 (dd, $J = 3.0, 14.6$ Hz, 1 H), 1.91 (dd, $J = 2.0, 13.6$ Hz, 1 H), 1.87 (dd, $J = 2.0, 13.6$ Hz, 1 H), 1.70 (dd, $J = 11.7, 13.6$ Hz, 1 H), 1.73 (s, 6 H), 1.45 (s, 3 H), 1.37 (s, 3 H); ¹³C NMR (75 MHz, CDCl₃, DEPT) δ C, 137.8, 121.6, 121.4, 101.7, 101.1, 68.7, 67.6, CH, 128.5 (2), 127.7 (3), 66.4, CH₂, 73.3, 64.9, 46.6, 46.1, 41.9, 39.5, 35.0, CH₃, 30.8, 30.6, 21.5, 21.3. Anal. calcd for C₂₅H₃₃N₂O₅Cl: C, 62.95; H, 6.97. Found: C, 62.75; H, 6.95.

(2*S*,4*S*,6*S*,8*S*)-bis-*C*-4,8-cyano-1-iodo-2:4,6:8-bis-*O*-(1-

methylethylidene)-6-*O*-phenylmethyl-decane-2,4,6,8,10-pentol (20): $[\alpha]_D^{23} = 43.7^\circ$ ($c = 1.74$, CHCl_3); IR (neat) 3062, 2994, 2935, 2866, 1494, 1455, 1431 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.38-7.28 (m, 5 H), 4.54 (d, $J = 11.8$ Hz, 1 H), 4.52 (m, 1 H), 4.50 (d, $J = 11.8$ Hz, 1 H), 4.04 (dtd, $J = 2.1, 5.2, 11.4$ Hz, 1 H), 3.76-3.69 (m, 2 H), 3.24 (dd, $J = 5.0, 10.5$ Hz, 1 H), 3.21 (dd, $J = 5.2, 10.5$ Hz, 1 H), 2.16-1.99 (m, 5 H), 1.92-1.88 (m, 2 H), 1.75 (s, 3 H), 1.72 (s, 3 H), 1.70 (dd, $J = 11.7, 13.6$ Hz, 1 H), 1.45 (s, 3 H), 1.38 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ C, 137.9, 121.8, 121.4, 101.9, 101.1, 68.7, 67.7, CH, 128.5 (2), 127.8 (3), 65.8, 61.7, CH_2 , 73.3, 64.9, 46.0, 41.9, 39.5, 37.9, 8.7, CH_3 , 30.8, 30.6, 21.7, 21.4. Anal. calcd for $\text{C}_{25}\text{H}_{33}\text{N}_2\text{O}_5\text{I}$: C, 52.82; H, 5.85. Found: C, 52.88; H, 6.04.

(3*S*,5*S*,7*S*,9*S*,11*S*,13*S*,14*R*,15*R*)-1-*O*-phenylmethyl-3,7,11-tris-*C*-cyano-

15-*O*-(1,1-dimethylethyl)dimethylsilyl-14-ethenyl-3:5,7:9,11:13-tris-*O*-(1-methylethylidene)-eicosane-1,3,5,7,9,11,13,15-octol (21): $[\alpha]_D^{26} = 50.7^\circ$ ($c = 2.11$, CHCl_3); IR (neat) 3076, 2994, 2929, 2857, 2255, 1640, 1462, 1433 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 7.36-7.26 (m, 5 H), 5.62 (dt, $J = 16.9, 9.8$ Hz, 1 H), 5.17-5.05 (m, 2H), 4.52 (d, $J = 11.9$ Hz, 1 H), 4.48 (d, $J = 11.9$ Hz, 1 H), 4.47 (m, 2 H), 4.19 (dt, $J = 5.5, 8.3$ Hz, 1 H), 3.91 (dddd, $J = 3.9$ Hz, 1 H), 3.72-3.69 (m, 2H), 2.28 (ddd, $J = 3.9, 8.3, 9.8$ Hz, 1 H), 2.13-1.68 (m, 12 H), 1.70 (s, 3 H), 1.69 (s, 3 H), 1.67 (s, 3 H), 1.38 (s, 3 H), 1.37 (s, 3 H), 1.35 (s, 3 H), 1.48-1.19 (m, 8 H), 0.881 (s, 9 H), 0.872 (t, $J = 7.0$ Hz, 3 H), 0.049 (s, 3 H), 0.037 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ C, 137.8, 122.0, 121.6, 121.3, 101.2, 101.0, 100.9, 68.6, 67.9, 67.8, 18.1, CH, 134.1, 128.4 (2), 127.7, 127.6 (2), 71.4, 65.4, 61.9, 61.7, 55.0, CH_2 , 119.1, 73.2, 64.8, 46.4, 46.2, 41.8, 39.5, 37.7, 36.5, 32.9, 31.8, 25.2, 22.5, CH_3 , 30.7 (3), 25.9 (3), 21.3 (2), 21.2, 14.0, -4.39, -4.45. Anal. calcd for $\text{C}_{47}\text{H}_{73}\text{N}_3\text{O}_8\text{Si}$: C, 67.51; H, 8.80. Found: C, 67.26; H, 8.55.

(3*S*,5*S*,7*S*,9*S*,11*S*,13*S*,14*R*,15*R*)-15-*O*-(1,1-dimethylethyl)dimethylsilyl-

14-ethenyl-3:5,7:9,11:13-tris-*O*-(1-methylethylidene)-eicosane-1,3,5,7,9,11,13,15-octol (22): $[\alpha]_D^{25} = 16.3^\circ$ ($c = 4.00$, CH_2Cl_2); IR (neat) 3467, 3078, 2999, 2943, 2861, 1642, 1464 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.55 (dt, $J = 10.0, 17.1$ Hz, 1 H), 5.09-5.00 (m, 2 H), 4.08 (m, 1 H), 4.04-3.90 (m, 5 H), 3.83 (ddd, $J = 1.9, 8.4, 10.8$ Hz, 1 H), 3.76-3.69 (m, 2 H), 2.55 (dd, $J = 4.3, 6.6$ Hz, 1 H), 2.23

(dd, $J = 4.3, 9.1$ Hz, 1 H), 1.79-1.65 (m, 4 H), 1.46-0.890 (m, 16 H), 1.41 (s, 3 H), 1.37 (s, 3 H), 1.36 (s, 3 H), 1.34 (s, 3 H), 1.32 (s, 3H), 1.31 (s, 3 H), 0.847 (s, 9 H), 0.843 (t, $J = 7.0$ Hz, 3 H), 0.017 (s, 3 H), 0.005 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ C, 98.5, 98.3, 98.1, 18.1, CH, 134.7, 71.3, 69.4, 68.1, 65.4, 65.1 (2), 65.0, 55.7, CH_2 , 118.5, 60.9, 42.6, 42.5, 38.0, 36.4, 36.3, 35.0, 32.5, 31.8, 25.3, 22.6, CH_3 , 30.2 (2), 30.1, 25.9 (3), 19.8 (2), 19.6, 14.1, -4.32, -4.42. Anal. calcd for $\text{C}_{37}\text{H}_{70}\text{O}_8\text{Si}$: C, 66.23; H, 10.51. Found: C, 66.45; H, 10.36. HRMS(FAB) calcd for $\text{C}_{36}\text{H}_{67}\text{O}_8\text{Si}$: 655.4607. Found: 655.4638 ($\text{M}-\text{CH}_3$).

(2*R*,5*R*,7*R*,9*R*,11*S*,13*S*,15*S*,16*R*,17*R*)- and (2*S*,5*R*,7*R*,9*R*,11*S*,13*S*,15*S*,16*R*,17*R*)-2-diethylphosphono-17-*O*-(1,1-dimethylethyl)dimethylsilyl-16-ethenyl-5:7,9:11,13:15-tris-*O*-(1-methylethylidene)-3-oxo-docosane-5,7,9,11,13,15,17-heptol (23): IR (neat) 3077, 2988, 2938, 2857, 1715, 1640, 1462 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 5.55 (dt, $J = 10.1, 17.1$ Hz, 1 H), 5.09-4.99 (m, 2 H), 4.36 (dtd, $J = 2.4, 6.1, 11.8$ Hz, 1 H), 4.30 (dddd, $J = 2.3, 5.1, 7.5, 11.6$ Hz, 1 H), 4.12-3.89 (m, 9 H), 3.82 (ddd, $J = 2.1, 8.6, 11.0$ Hz, 1 H), 3.25 (m, 1 H), 2.82 (m, 1 H), 2.69 (m, 1 H), 2.22 (dt, $J = 4.2, 9.1$ Hz, 1 H), 1.74 (m, 2 H), 1.55-1.01 (m, 43 H), 0.842 (s, 9 H), 0.838 (t, $J = 7.0$ Hz, 3 H), 0.011 (s, 3 H), -0.001 (2, 3 H); ^{13}C NMR (75 MHz, CDCl_3) δ 204.3, 134.7, 118.4, 98.5, 98.3, 98.1, 71.4, 68.1, 66.1, 65.5, 65.4, 65.1, 65.0, 62.5, 55.7, 49.9, 49.0, 48.5, 47.8, 46.8, 46.1, 42.6, 36.4, 36.1, 35.1, 32.6, 31.8, 30.1 (3), 25.9 (3), 25.3, 22.5, 19.7 (2), 19.6, 18.1, 16.4, 16.3, 14.0, 10.7, 10.5, -4.33, -4.44. HRMS(MALDI) calcd for $\text{C}_{43}\text{H}_{81}\text{O}_{11}\text{PSiNa}$: 855.5183. Found: 855.5183 ($\text{M}+\text{Na}$).

[2(1*R*),2*R*,3*S*,5*S*,7*S*,9*R*,11*R*,13*R*,16*R*]- and [2(1*R*),2*R*,3*S*,5*S*,7*S*,9*R*,11*R*,13*R*,16*S*]-16-diethylphosphono-2-(1-(1,1-dimethylethyl)dimethylsiloxy-hexyl)-3,5,7,9,11,13-hexahydroxy-3:5,7:9,11:13-tris-*O*-(1-methylethylidene)-15-oxo-heptadecanoic acid (3): IR (neat) 3700, 2989, 2938, 2857, 1718, 1462 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3) δ 10.2 (broad s, 1 H), 4.38-4.21 (m, 2 H), 4.13-3.91 (m, 9 H), 3.27 (m, 1 H), 2.83 (m, 1 H), 2.68 (m, 1 H), 2.58 (dd, $J = 5.1, 9.2$ Hz, 1 H), 1.94 (d, $J = 12.5$ Hz, 1 H), 1.75 (m, 2 H), 1.55-1.08 (m, 42 H), 0.881 (s, 9 H), 0.846 (t, $J = 7.0$ Hz, 3 H), 0.106 (s, 3 H), 0.089 (s, 3 H); ^{13}C NMR (75 MHz, CDCl_3 , DEPT) δ 204.4, 204.1, 172.6, 98.6 (2), 98.4, 69.9, 66.8, 66.2, 65.5, 65.1, 62.6, 55.9, 49.9, 49.1, 48.5, 47.7, 46.0, 42.5, 36.4, 36.1, 36.0, 32.3, 31.6, 30.1, 30.0, 25.7 (3), 25.1, 22.4, 19.7, 19.6, 17.9, 16.3, 13.9,

10.7, 10.5, -4.60, -4.72. HRMS(MALDI) calcd for $C_{42}H_{79}O_{13}PSiNa$: 873.4941. Found: 873.4925 (M+Na).

[2(1R),2R,3S,5S,7S,9R,11R,13R,16R]- and [2(1R),2R,3S,5S,7S,9R,11R,13R,16S]-16-diethylphosphono-2-(1-((1,1-dimethylethyl)dimethylsiloxy)-hexyl)-3,5,7,9,11,13-hexahydroxy-3:5,7:9,11:13-tris-O-(1-methylethylidene)-15-oxo-heptadecanoic acid, (1R,2S)-1-methyl-2-(1,1-dimethylethyl)dimethylsiloxy-11-oxoundeca-3,5,7,9-tetraenyl ester (24): IR (neat) 2991, 2953, 2930, 2857, 1720, 1678, 1594, 1463 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 9.54 (d, $J = 7.9$ Hz, 1 H), 7.12 (dd, $J = 11.3$, 15.1 Hz, 1 H), 6.66 (dd, $J = 11.0$, 14.6 Hz, 1 H), 6.47-6.40 (m, 2 H), 6.32-6.26 (m, 2 H), 6.13 (dd, $J = 7.9$, 15.1 Hz, 1 H), 5.81 (dd, $J = 5.9$, 15.3 Hz, 1 H), 4.85 (dq, $J = 4.6$, 6.4 Hz, 1 H), 4.38-4.23 (m, 2 H), 4.18-3.89 (m, 10 H), 3.27 (m, 1 H), 2.85 (m, 1 H), 2.74-2.65 (m, 2 H), 1.79-1.71 (m, 2 H), 1.58-1.05 (m, 46 H), 0.886 (s, 9 H), 0.861 (s, 9 H), 0.850 (t, $J = 7.0$ Hz, 3 H), 0.050 (s, 3 H), 0.046 (s, 3 H), 0.020 (s, 3 H), -0.003 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 204.5, 204.2, 193.4, 171.1, 151.6, 142.3, 137.6, 136.8, 131.7, 131.2, 130.9, 130.2, 129.5, 128.2, 98.6, 98.5, 98.3, 74.9, 73.4, 69.8, 67.7, 66.2, 65.5, 65.1 (3), 62.5 (2), 57.0, 49.9, 49.1, 48.6, 47.8, 46.9, 46.1, 42.9, 42.6 (2), 36.4, 36.1, 33.2, 31.8, 30.2 (2), 30.1, 25.9 (3), 25.8 (3), 24.8, 22.6, 19.8, 19.7, 19.6, 18.2, 18.0, 16.4, 16.3, 15.1, 14.0, 10.7, 10.5, -4.34, -4.39, -4.50, -4.74. HRMS(MALDI) calcd for $C_{60}H_{107}O_{15}PSi_2Na$: 1177.6783. Found: 1177.6778 (M+Na).

1',26-bis-O-(1,1-dimethylethyl)dimethylsilyl-15-oxo-3,5:9,11:13,15-tris-O-(1-methylethylidene)filipin III (25): $[\alpha]_D^{23} = -76.7^\circ$ ($c = 1.0$, CH_2Cl_2); IR (neat) 2992, 2942, 2858, 1729, 1651, 1615, 1572, 1461 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 7.11 (d, $J = 11.0$ Hz, 1 H), 6.65 (dd, $J = 9.9$, 14.6 Hz, 1 H), 6.55 (dd, $J = 11.0$, 14.6 Hz, 1 H), 6.41-6.22 (m, 5 H), 5.98 (dd, $J = 5.0$, 14.0 Hz, 1 H), 4.71 (dq, $J = 6.2$, 7.6 Hz, 1 H), 4.18-3.92 (m, 6 H), 3.81-3.72 (m, 2 H), 3.15 (t, $J = 11.0$ Hz, 1 H), 2.66 (t, $J = 7.0$ Hz, 1 H), 2.61 (dd, $J = 3.8$, 11.6 Hz, 1 H), 1.88 (s, 3 H), 1.39 (s, 3 H), 1.36 (s, 3 H), 1.32 (s, 3 H), 1.30 (s, 3 H), 1.24 (d, $J = 6.3$ Hz, 3 H), 1.20 (s, 3 H), 0.894 (s, 9 H), 0.875 (s, 9 H), 0.851 (t, $J = 7.0$ Hz, 1 H), 0.053 (s, 3 H), 0.047 (s, 3 H), 0.041 (s, 3 H), 0.009 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$, DEPT) δ 199.5, 170.6, 141.8, 141.0, 138.0, 136.3, 136.2, 131.2, 130.3, 129.7, 128.5, 127.5, 98.9, 98.6, 98.3, 74.3, 73.7, 69.7, 67.8, 67.7, 66.2, 65.5, 65.3, 65.1, 64.8, 57.3, 45.6, 44.4, 43.2, 42.5, 37.7, 37.5, 34.6, 33.2, 31.8, 30.2, 30.1, 30.0, 25.9 (3), 25.8 (3), 22.6, 19.8, 19.5 (2), 18.2, 18.1,

14.0, 11.7, -4.28, -4.31, -4.46, -4.99. HRMS(FAB) calcd for $C_{56}H_{96}O_{11}Si_2Na$: 1023.6388. Found: 1023.6350 (M+Na).

1',26-bis-*O*-(1,1-dimethylethyl)dimethylsilyl-3,5:7,9:11,13-tris-*O*-(1-methylethylidene)filipin III (26): $[\alpha]_D^{24} = -1.5^\circ$ ($c = 1.6$, CH_2Cl_2); IR (neat) 3466, 2991, 2953, 2933, 2858, 1731, 1471, 1463 cm^{-1} ; 1H NMR (500 MHz, $CDCl_3$) δ 6.41 (dd, $J = 11.4, 13.8$ Hz, 1 H), 6.34-6.12 (m, 6 H), 6.07 (d, $J = 11.4$ Hz, 1 H), 5.82 (dd, $J = 5.8, 14.5$ Hz, 1 H), 4.68 (dq, $J = 8.6, 6.3$ Hz, 1 H), 4.24 (m, 1 H), 4.13-4.84 (m, 6 H), 3.72 (m, 1 H), 3.62 (m, 1 H), 2.66 (t, $J = 7.1$ Hz, 1 H), 2.16 (broad s, 1 H), 1.74 (s, 3 H), 1.51-1.08 (m, 20 H), 1.39 (s, 3 H), 1.38 (s, 3 H), 1.35 (s, 3 H), 1.31 (s, 3 H), 1.30 (s, 3 H), 1.23 (d, $J = 6.3$ Hz, 1 H), 0.885 (s, 9 H), 0.870 (s, 9 H), 0.852 (t, $J = 7.0$ Hz, 1 H), 0.039 (s, 6 H), 0.028 (s, 3 H), 0.001 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.6, 138.5, 134.8, 133.7, 133.6, 133.1, 132.5, 131.9, 130.7, 127.6, 126.5, 98.8, 98.6 (2), 77.2, 74.5, 73.8, 69.8, 68.0, 67.1, 66.3, 65.8, 65.7, 65.0, 56.2, 42.8, 42.5, 38.9, 37.4, 35.2, 33.8, 31.9, 30.4, 30.3, 30.1, 28.9, 25.9 (3), 25.8 (3), 23.9, 22.6, 20.0, 19.9, 19.6, 19.5, 18.1 (2), 14.0, 12.0, -4.15, -4.27, -4.49, -4.98. HRMS(MALDI) calcd for $C_{56}H_{98}O_{11}SiNa$: 1025.6548. Found: 1025.6553 (M+Na).

1',26-bis-*O*-(1,1-dimethylethyl)dimethylsilyl-15-*O*-triisopropylsilyl-3,5:7,9:11,13-tris-*O*-(1-methylethylidene)filipin III (27): 1H NMR (500 MHz, $CDCl_3$) δ 6.43-6.12 (m, 7 H), 5.99 (d, $J = 11.4$ Hz, 1 H), 5.90 (dd, $J = 5.2, 15.6$ Hz, 1 H), 4.76 (dq, $J = 8.8, 6.3$ Hz, 1 H), 4.26 (dd, $J = 4.0, 9.8$ Hz, 1 H), 4.14-3.48 (m, 6 H), 3.71 (m, 1 H), 3.58 (m, 1 H), 2.61 (t, $J = 6.9$ Hz, 1 H), 1.94-1.18 (m, 23 H), 1.74 (s, 3 H), 1.39 (s, 6 H), 1.37 (s, 3 H), 1.35 (s, 6 H), 1.33 (s, 3 H), 1.24 (d, $J = 6.3$ Hz, 3 H), 1.03 (s, 18 H), 0.891 (s, 9 H), 0.875 (s, 9 H), 0.870 (t, $J = 7.0$ Hz, 3 H), 0.049 (s, 3 H), 0.040 (s, 3 H), 0.025 (s, 3 H), -0.002 (s, 3 H); HRMS(MALDI) calcd for $C_{65}H_{118}O_{11}Si_3Na$: 1181.7880. Found: 1181.7826 (M+Na).

filipin III (1): 1H NMR (500 MHz, CD_3OD) δ 6.39 (dd, $J = 13.9, 11.2$, 1 H), 6.33 (dd, $J = 8.9, 14.8$ Hz, 1 H), 6.36-6.18 (m, 6 H), 5.94 (d, $J = 11.2$, 1 H), 5.89 (dd, $J = 5.11, 14.8$, 1 H), 4.72 (q, $J = 6.3$, 1 H, obscured by MeOH), 4.08 (ddd, $J = 3.8, 7.4, 7.1$, 1 H), 4.03 (dd, $J = 4.5, 10.8$, 1 H), 3.97 (dd, $J = 6.3, 5.1$, 1 H), 3.94-3.85 (m, 4 H), 3.75 (ddd, $J = 2.1, 8.4, 8.8$, 1 H), 3.12 (ddd, $J = 3.4, 10.6, 10.5$, 1 H), 2.45 (dd, $J = 7.4, 8.8$, 1 H), 1.79 (ddd, $J = 3.4, 9.4, 10.8$, 1 H), 1.67 (s, 3 H), 1.66-1.58 (m, 3 H), 1.32-1.44 (m, 8 H), 1.16-1.30 (m, 8 H), 1.19 (d, $J = 6.3$, 3 H), 0.816 (t, $J = 7.1$, 3 H).

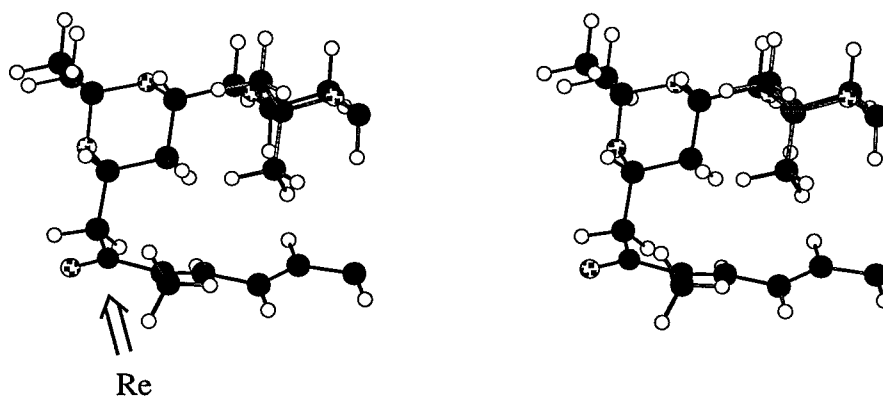


Figure 1. Stereoselective Re-face reduction of ketone **25** was predicted and observed. Ketone **25** was investigated with a 5000 step Monte Carlo search in Macromodel 5.5 using MM2 and CHCl_3 solvation. The C7-C19 segment is illustrated.