

GRAM-SCALE SYNTHESIS OF (+)-DISCODERMOLIDE (SUPPORTING INFORMATION)

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Aldehyde (–)-8: Colorless plates (hexanes): mp 45–46 °C; $[\alpha]_{\text{D}}^{23}$ –65.0° (c 1.38, CHCl₃); IR (CHCl₃) 1750, 1720 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 9.68 (d, J = 1.6 Hz, 1 H), 4.22 (dd, J = 8.9, 2.6 Hz, 1 H), 3.68 (s, 3 H), 3.10 (apparent s, 4 H), 2.46 (qdd, J = 7.1, 2.6, 1.5 Hz, 1 H), 1.16 (d, J = 6.9 Hz, 3 H), 1.10 (d, J = 7.0 Hz, 3 H), 0.88 (s, 9 H), 0.092 (s, 3 H), 0.088 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 203.2, 175.6, 75.1, 61.5, 52.1, 39.6, 32.1, 25.9, 18.2, 15.4, 10.2, -4.07, -4.11; high resolution mass spectrum (CI, NH₃) m/z 318.2096 [(M+H)⁺; calcd for C₁₅H₃₂NO₄Si: 318.2100].

Enone (–)-10: white solid: mp 53-55 °C; $[\alpha]_{\text{D}}^{23}$ –10.6° (c 0.88, CHCl₃); IR (CHCl₃) 1728, 1719, 1695 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.09 (m, 1 H), 4.78 (ddd, J = 10.0, 6.6, 4.3 Hz, 1 H), 3.65 (t, J = 2.8 Hz, 1 H), 2.72 (dd, J = 15.8, 4.3 Hz, 1 H), 2.66 (dd, J = 15.8, 6.7 Hz, 1 H), 2.62 (qd, J = 7.6, 3.2 Hz, 1 H), 2.13 (d, J = 1.1 Hz, 3 H), 2.07 (dq, J = 10.0, 6.8, 2.4 Hz, 1 H), 1.87 (d, J = 1.2 Hz, 3 H), 1.25 (d, J = 7.6 Hz, 3 H), 0.97 (d, J = 6.8 Hz, 3 H), 0.87 (s, 9 H), 0.05 (s, 3 H), 0.04 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 196.9, 173.6, 156.8, 124.1, 77.8, 74.3, 47.0, 43.9, 33.6, 27.7, 25.7, 20.9, 18.0, 16.1, 13.8, -4.5, -4.7; high resolution mass spectrum (ES) m/z 377.2127 [(M+Na)⁺; calcd for C₁₉H₃₄O₄SiNa: 377.2124]

Aldehyde (–)-C: White, waxy solid (from hexanes): mp 58-60 °C; $[\alpha]_{\text{D}}^{23}$ –55.5° (c 1.46, CHCl₃); IR (CHCl₃) 1730 (br) cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 9.67 (br s, 1 H), 4.52 (td, J = 10.5, 2.1 Hz, 1 H), 4.46 (dd, J = 10.5, 3.5 Hz, 1 H), 3.67 (t, J = 2.3 Hz, 1 H), 2.66 (qd, J = 7.6, 2.6 Hz, 1 H), 1.95-1.84 (m, 3 H), 1.77 (ddd, J = 14.1, 10.5, 2.1 Hz, 1 H), 1.27 (d, J = 7.6 Hz, 3 H), 0.99 (d, J = 6.7 Hz, 3 H), 0.92 (s, 9 H),

0.89 (s, 9 H), 0.13 (s, 3 H), 0.11 (s, 3 H), 0.08 (s, 3 H), 0.07 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 203.2, 173.1, 76.0, 74.7, 73.7, 44.2, 36.2, 34.1, 25.72, 25.66, 18.1, 17.9, 16.5, 14.0, -4.6 (2), -4.9, -5.2; high resolution mass spectrum (CI) m/z 445.2793 [(M+H) $^+$]; calcd for $\text{C}_{22}\text{H}_{45}\text{O}_5\text{Si}_2$: 445.2806]

Trityl Ether (+)-13: White, microcrystalline solid: mp 54-59 °C; $[\alpha]_{\text{D}}^{23}$ +16.7° (c 0.30, CHCl_3); IR (CHCl_3) 2980, 2880, 1620, 1255 cm^{-1} ; ^1H NMR (500 MHz, C_6D_6) δ 7.62 (d, J = 8.7 Hz, 2 H), 7.60 (m, 6 H), 7.15 (dd, J = 8.8, 6.6 Hz, 6 H), 7.04 (apparent t, J = 7.4 Hz, 3 H), 6.84 (d, J = 8.7, 2 H), 5.43 (s, 1 H), 5.06 (d, J = 9.9 Hz, 1 H), 3.95 (dd, J = 11.0, 4.6 Hz, 1 H), 3.77 (d, J = 7.1 Hz, 1 H), 3.53 (m, 3 H), 3.48 (dd, J = 8.6, 5.2 Hz, 1 H), 3.24 (s, 3 H), 3.00 (apparent t, J = 8.9 Hz, 1 H), 2.72 (m, 1 H), 2.49 (apparent t, J = 12.3 Hz, 1 H), 2.41 (m, 1 H), 2.19 (m, 1 H), 1.98 (m, 2 H), 1.75 (apparent d, J = 12.1 Hz, 1 H), 1.61 (s, 3 H), 1.23 (d, J = 6.8 Hz, 3 H), 1.16 (d, J = 7.0 Hz, 3 H), 1.14 (d, J = 6.7 Hz, 3 H), 1.04 (s, 9 H), 0.98 (d, J = 6.8 Hz, 3 H), 0.95 (s, 9 H), 0.42 (d, J = 6.6 Hz, 3 H), 0.01 (s, 3 H), 0.08 (s, 3 H), 0.07 (s, 3 H), 0.03 (s, 3 H); ^{13}C NMR (125 MHz, C_6D_6) δ 160.4, 145.2, 132.4, 131.2, 129.2, 128.3, 128.0, 127.9, 127.1, 113.8, 101.8, 86.9, 83.5, 79.1 (2), 73.3, 66.6, 54.7, 40.7, 38.7, 37.9, 36.3, 33.9, 31.0, 26.5, 26.4, 23.2, 18.7, 18.5, 18.3, 14.5, 12.9, 11.9, 11.3, -3.3, -3.5, -3.6, -3.8; high resolution mass spectrum (FAB, NBA) m/z 959.6040 [(M+Na) $^+$]; calcd for $\text{C}_{58}\text{H}_{86}\text{O}_6\text{Si}_2\text{Na}$: 959.6017].

Triene 14: White, amorphous solid; IR (CHCl_3) 3500, 2950, 1620, 1250 cm^{-1} ; ^1H NMR (500 MHz, CDCl_3 , major diastereomer) δ 7.27 (d, J = 8.6 Hz, 2 H), 6.87 (d, J = 8.6 Hz, 2 H), 6.61 (ddd, J = 16.8, 10.6, 10.6, 1 H), 6.05 (apparent t, J = 11.0 Hz, 1 H), 5.58 (apparent t, J = 10.6 Hz, 1 H), 5.23 (d, J = 16.8 Hz, 1 H), 5.12 (d, J = 10.3 Hz, 1 H), 4.98 (d, J = 10.2 Hz, 1 H), 4.57 (d, J = 10.6 Hz, 1 H), 4.45 (d, J = 10.5 Hz, 1 H), 3.80 (s, 3 H), 3.66 (ddd, J = 10.8, 4.8, 4.5, 1 H), 3.51 (ddd, J = 11.0, 5.7, 5.6 Hz, 1 H), 3.45 (dd, J = 4.7, 3.9 Hz, 1 H), 3.40 (dd, J = 6.9, 3.8 Hz, 1 H), .26 (dd, J = 7.3, 3.7 Hz, 1 H), 3.0 (m, 1 H), 2.56 (m, 1 H), 2.29 (apparent t, J = 5.5 Hz, 1 H), 2.06 (apparent t, J = 12.4 Hz, 1 H), 1.81 (m, 3 H), 1.65 (apparent d, J = 11.2 Hz, 1 H), 1.59 (s, 3 H), 1.11 (d, J = 6.8 Hz, 3 H), 1.01 (d, J = 7.0 Hz, 3 H), 0.99 (d, J = 7.2 Hz, 3 H), 0.95 (s, 9 H), 0.92 (m, 12 H), 0.72 (d, J = 6.7 Hz, 3 H), 0.11 (s, 9 H), 0.08 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3 , major diastereomer) δ 159.1, 134.5, 132.8, 132.3, 131.2, 130.5, 129.2, 129.0, 117.5, 113.7, 84.6, 81.7, 77.1, 75.0, 65.3, 55.3, 40.1, 38.5, 36.8, 36.1, 35.4, 35.3, 26.3, 26.2, 23.0, 18.7, 18.6, 18.3,

17.6, 15.8, 14.6, 10.6, -3.2, -3.4, -3.6, -3.9; high resolution mass spectrum (FAB, NBA) m/z 739.5129 [(M+Na)⁺; calcd for C₄₂H₇₆O₅Si₂Na: 739.5156].

Phosphonium Salt AB: light-yellow amorphous solid; IR (CHCl₃) 2940, 1610, 1580, 1250 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, major diastereomer) δ 7.75 (m, 15 H) 7.27 (d, J = 8.6 Hz, 2 H) 6.86 (d, J = 8.6 Hz, 2 H), 6.54 (ddd, J = 16.8, 10.6, 10.6 Hz, 1 H), 5.89 (apparent t, J = 11.0 Hz, 1 H), 5.50 (apparent t, J = 10.5 Hz, 1 H), 5.30 (d, J = 10.6 Hz, 1 H), 5.12 (d, J = 16.8 Hz, 1 H), 5.08 (d, J = 10.2 Hz, 1 H), 4.56 (d, J = 10.4 Hz, 1 H), 4.45 (d, J = 10.4 Hz, 1 H), 3.78 (s, 3 H), 3.70 (m, 1 H), 3.69 (dd, J = 6.7, 4.6 Hz, 1 H), 3.42 (dd, J = 5.3, 3.1 Hz, 1 H), 3.23 (dd, J = 7.9, 3.2 Hz, 1 H), 3.19 (m, 1 H), 2.97 (m, 1 H), 2.41 (m, 1 H), 2.03 (m, 1 H), 1.94 (apparent t, J = 12.2 Hz, 1 H), 1.75 (m, 2 H), 1.57 (br d, J = 11.9 Hz, 1 H), 1.54 (s, 3 H), 1.10 (d, J = 6.8 Hz, 3 H), 0.96 (d, J = 6.8 Hz, 3 H),) 0.89 (m, 21 H), 0.69 (d, J = 6.9 Hz, 3 H), 0.66 (d, J = 6.7 Hz, 3 H), 0.095 (s, 3 H), 0.08 (s, 3 H), 0.04 (s, 3 H), - 0.05 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃, major diastereomer) δ 159.1, 135.3, 135.2, 134.2, 133.5, 133.4, 132.6, 132.3, 131.0, 130.9, 130.7, 130.6, 130.4, 129.1, 128.8, 128.2, 118.6, 118.0, 117.6, 113.7, 84.6, 80.0, 79.9, 76.8, 75.1, 55.3, 39.8, 35.8, 35.5, 35.3, 35.2, 26.2, 26.1 (2), 26.0, 22.6, 18.6, 18.5, 18.2, 17.4, 16.9, 15.0, 10.5, -3.3, -3.4 (2), -4.0; high resolution mass spectrum (FAB, NBA) m/z 961.6134 [(M-I)⁺; calcd for C₆₀H₉₀O₄PSi₂: 961.6115].

Tetraene 15: white foam: IR (CHCl₃) 1725 cm⁻¹; ¹H NMR (500 MHz, CDCl₃, major diastereomer) δ 7.25 (d, J = 9.0 Hz, 2 H), 6.84 (d, J = 8.7 Hz, 2 H), 6.57 (ddd, J = 16.7, 10.6, 10.6 Hz, 1 H), 6.00 (apparent t, J = 11.0 Hz, 1 H), 5.55 (apparent t, J = 10.5 Hz, 1 H), 5.26 (dd, J = 11.1, 7.9 Hz, 1 H), 5.19 (dd, J = 15.4, 1.4 Hz, 1 H), 5.18 (apparent t J = 10.1 Hz, 1 H), 5.10 (d, J = 10.2 Hz, 1 H), 5.01 (d, J = 10.0 Hz, 1 H), 4.75 (apparent t, J = 9.2 Hz, 1 H), 4.50 (ddd, J = 10.5, 1.3, 1.3 Hz, 1 H), 4.50 (ABq, J_{AB} = 10.6 Hz, Δ_vAB = 53.2 Hz, 2 H), 3.78 (s, 3 H), 3.60 (apparent t, J = 2.4 Hz, 1 H), 3.42 (dd, J = 5.1, 3.7 Hz, 1 H), 3.23 (dd, J = 7.5, 3.7 Hz, 1 H), 3.20 (apparent t, J = 5.4 Hz, 1 H), 3.01-2.94 (m, 1 H), 2.60 (qd, J = 7.7, 2.6 Hz, 1 H), 2.62-2.55 (m, 1 H), 2.45-2.38 (m, 1 H), 1.98 (apparent t, J = 12.3 Hz, 1 H), 1.84-1.67 (m, 3 H), 1.63 (br d, J = 13.2 Hz, 1 H), 1.52 (s, 3 H), 1.55-1.48 (m, 1 H), 1.20 (d, J = 7.6 Hz, 3 H), 1.09 (d, J = 6.8 Hz, 3 H), 0.98 (d, J = 6.8 Hz, 3 H), 0.93 (apparent d, J = 6.7 Hz, 6 H), 0.93 (s, 9 H), 0.89 (s, 9 H), 0.86 (s, 9 H), 0.85 (s, 9 H), 0.84 (d, J = 6.8 Hz, 3 H), 0.69 (d, J = 6.7 Hz, 3 H), 0.085 (s, 3 H), 0.079 (s, 3 H), 0.051 (s, 3 H), 0.046 (s, 3 H), 0.042 (s, 3 H), 0.029 (s, 3 H), 0.028 (s, 3 H), -0.02 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃,

major diastereomer) δ 173.2, 159.1, 134.4, 133.4, 132.4, 132.2, 131.9, 131.3, 131.2, 129.11, 129.09, 117.6, 113.7, 84.6, 80.5, 76.9, 75.0, 74.9, 64.6, 55.3, 44.1, 42.7, 40.1, 37.5, 36.0, 35.4, 35.4, 35.2, 34.2, 26.3 (2), 25.9, 25.7, 23.0, 18.7, 18.6, 18.4, 18.1, 18.0, 17.1, 16.5, 16.4, 14.9, 14.1, 10.5, -3.0, -3.2, -3.3, -4.3, -4.4, -4.5, -4.8, -4.9; high resolution mass spectrum (FAB, NBA) m/z 1149.7836 [(M+Na)⁺; calcd for C₆₄H₁₁₈O₈Si₄Na: 1149.7802].

Alcohol (+)-16: White foam: $[\alpha]_D^{23}$ +21.6° (c 0.34, CHCl₃); IR (film, NaCl) 3500 (br), 1740cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 6.61 (ddd, J = 16.8, 10.9, 10.9 Hz, 1 H), 6.13 (apparent t, J = 11.0 Hz, 1 H), 5.32 (apparent t, J = 10.5 Hz, 1 H), 5.28 (dd, J = 11.1, 7.9 Hz, 1 H), 5.24-5.21 (m, 1 H), 5.19 (apparent t, J = 10.3 Hz, 1 H), 5.14 (d, J = 10.2 Hz, 1 H), 5.06 (d, J = 10.0 Hz, 1 H), 4.76 (apparent t, J = 9.3 Hz, 1 H), 4.50 (apparent t, J = 9.9 Hz, 1 H), 3.62 (apparent t, J = 2.4 Hz, 1 H), 3.60 (dd, J = 5.5, 3.4 Hz, 1 H), 3.32 (br d, J = 5.3 Hz, 1 H), 3.24 (apparent t, J = 5.1 Hz, 1 H), 2.79 (ddq, J = 9.9, 6.7, 6.7 Hz, 1 H), 2.60 (qd, J = 7.6, 2.7 Hz, 1 H), 2.63-2.57 (m, 1 H), 2.50-2.45 (m, 1 H), 2.16 (apparent t, J = 12.3 Hz, 1 H), 1.90-1.77 (m, 3 H), 1.75-1.69 (m, 2 H), 1.57 (s, 3 H), 1.60-1.50 (m, 1 H), 1.20 (d, J = 7.6 Hz, 3 H), 0.96 (d, J = 6.8 Hz, 3 H), 0.95 (d, J = 6.6 Hz, 3 H), 0.94 (m, 6 H), 0.91 (s, 9 H), 0.89 (s, 9 H), 0.87 (m, 3 H), 0.87 (s, 9 H), 0.85 (s, 9 H), 0.73 (d, J = 6.8 Hz, 3 H), 0.07 (apparent s, 6 H), 0.052 (s, 3 H), 0.051 (s, 3 H), 0.04 (apparent s, 6 H), 0.03 (s, 3 H), -0.01 (s, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 173.3, 134.7, 133.5, 132.5, 132.1, 132.0, 131.5, 131.0, 118.4, 80.5, 78.8, 76.4, 74.9, 64.7, 44.1, 42.7, 38.0, 37.4, 36.3, 36.1, 35.2, 35.1, 34.2, 26.3, 26.2, 25.9, 25.7, 23.2, 18.5, 18.1, 18.0, 17.3, 17.2, 16.4, 16.1, 14.1, 13.7, 9.4, -3.0, -3.3, -3.6, -4.34, -4.36, -4.5, -4.8; high resolution mass spectrum (FAB, NBA) m/z 1029.7273 [(M+Na)⁺; calcd for C₅₆H₁₁₀O₇Si₄Na: 1029.7226];

(+)-Discodermolide [1]. White solid: mp 117–120 °C (acetonitrile); $[\alpha]_D^{23}$ +18° (c 1.0, MeOH); IR (CHCl₃) 3690, 3620, 3540, 3430, 1740 cm⁻¹; ¹H NMR (500 MHz, CD₃CN) δ 6.69 (dddd, J = 16.7, 10.7, 10.7, 0.9 Hz, 1 H), 6.10 (apparent t, J = 11.1 Hz, 1 H), 5.56 (ddd, J = 10.4, 10.2, 0.7 Hz), 5.42 (m, 2 H), 5.26 (dd, J = 16.7, 2.0 Hz, 1 H), 5.16 (d, J = 10.1 Hz, 1 H), 5.07 (bs, 2 H), 5.01 (d, J = 10.1 Hz, 1 H), 4.74 (dd, J = 7.8, 4.3 Hz, 1 H), 4.49 (ddd, J = 10.5, 10.5, 1.9 Hz, 1 H), 4.47 (m, 1 H), 3.65 (apparent q, J = 4.2 Hz, 1 H), 3.28 (d, J = 4.5 Hz, 1 H), 3.16 (ddd, J = 10.3, 6.8, 6.8 Hz, 1 H), 3.09 (m, 2 H), 2.77 (d, J = 5.3 Hz, 1 H), 2.65 (d, J = 5.3 Hz, 1 H), 2.63 (m, 1 H), 2.59 (d, J = 6.4 Hz, 1 H), 2.56 (dq, J = 7.4, 4.7 Hz, 1 H), 2.32

(m, 1 H), 1.87 (m, 1 H), 1.76 (m, 4 H), 1.66 (bd, J = 12.5 Hz, 1 H), 1.60 (s, 3 H), 1.51 (ddd, J = 13.5, 10.9, 1.8 Hz, 1 H), 1.27 (d, J = 7.3 Hz, 3 H), 1.09 (d, J = 6.8 Hz, 3 H), 1.07 (d, J = 6.8 Hz, 3 H), 1.03 (d, J = 6.8 Hz, 3 H), 0.97 (d, J = 6.6 Hz, 3 H), 0.90 (d, J = 6.8 Hz, 3 H), 0.82 (d, J = 6.2 Hz, 3 H); ^{13}C NMR (125 MHz, CD_3CN) δ 174.7, 158.3, 134.2, 133.8 (2), 133.2, 131.1, 130.5, 118.5, 79.8, 79.3, 77.5, 76.0, 73.2, 63.5, 44.0, 42.2, 38.4, 37.0, 36.5, 36.3, 36.2, 34.7, 34.3, 23.3, 19.6, 18.2, 17.4, 15.8, 15.5, 13.1, 9.2;

^1H NMR (500 MHz, CDCl_3) δ 6.60 (dddd, J = 16.8, 8.4, 8.4, 0.8 Hz, 1 H), 6.02 (apparent t, J = 11.1 Hz, 1 H), 5.51 (dd, J = 11.2, 7.9 Hz, 1 H), 5.42 (ddd, J = 10.6, 10.6, 0.6 Hz, 1 H), 5.34 (apparent t, J = 10.4 Hz, 1 H), 5.20 (dd, J = 16.9, 1.9 Hz, 1 H), 5.16 (d, J = 10.0 Hz, 1 H), 5.11 (d, J = 10.1 Hz, 1 H), 4.75 (m, 1 H), 4.70 (dd, J = 7.3, 4.2 Hz, 1 H), 4.60 (ddd, J = 10.0, 10.0, 2.4 Hz, 1 H), 4.56 (br s, 2 H), 3.73 (m, 1 H), 3.28 (m, 1 H), 3.18 (dd, J = 6.8, 4.8 Hz, 1 H), 2.98 (ddq, J = 10.1, 6.9, 6.9 Hz, 1 H), 2.78 (ddq, J = 9.8, 6.8, 6.8 Hz, 1 H), 2.66 (qd, J = 7.3, 4.6 Hz, 1 H), 2.57 (m, 1 H), 1.95 (m, 10 H), 1.69 (ddd, J = 14.4, 10.3, 3.1 Hz, 1 H), 1.64 (d, J = 1.3 Hz, 3 H), 1.30 (d, J = 7.4 Hz, 3 H), 1.06 (d, J = 6.9 Hz, 3 H), 1.00 (d, J = 6.8 Hz, 3 H), 0.99 (d, J = 6.7 Hz, 3 H), 0.97 (d, J = 6.8 Hz, 3 H), 0.94 (d, J = 6.8 Hz, 3 H), 0.82 (d, J = 6.3 Hz, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 173.6, 157.0, 134.4, 133.7, 133.4, 132.9, 132.2, 129.9, 129.8, 117.9, 79.1, 78.9, 77.2, 75.7, 73.2, 64.4, 43.1, 41.0, 37.4, 36.1, 36.0, 35.8, 35.3, 34.8, 33.1, 23.3, 18.4, 17.4, 15.6, 15.5, 13.7, 12.5, 9.0; high resolution mass spectrum (FAB, NBA) m/z 616.3840 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{33}\text{H}_{55}\text{NO}_8\text{Na}$: 616.3826].