Supporting Information

The racemic synthesis of an intermediate for the formal synthesis of madindoline A and B

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3-*n*-Butyl-4-methylcyclobut-3-ene-1,2-dione (16). A solution of CH₃Li (1.6 M in Et₂O, 3.4 mL, 5.5 mmol) was added dropwise to a solution of diisopropyl squarate (**17b**) (990 mg, 5.0 mmol) in THF (20 mL) at –78 °C under argon. After 5 min of stirring, a solution of *n*-BuLi (2.4 M in hexane, 2.5 mL, 6.0 mmol) was added dropwise to the system. 10 min later, the reaction was quenched with saturated ammonium chloride solution, and extracted with EtOAc. The organic layer was washed with water, brine, and dried over Na₂SO₄. Removal of the solvent, then a solution of concentrated hydrochloric acid in CH₂Cl₂ was added to a solution of the intermediate in CH₂Cl₂ and controlled pH = 3, stirred at room temperature about 30 min, and then the mixture was dried over Na₂SO₄. Removal of the solvent and flash chromatography of the residue on silica gel (PE/EtOAc = 10/1) afforded the **16** (600 mg, 79 %) brown oil. *R*_f = 0.4 (PE/EtOAc = 4/1). ¹H NMR (400 MHz, CDCl₃): δ 2.74 (t, *J* = 8 Hz, 2H), 2.35 (s, 3H), 1.67-1.75 (m, 2H), 1.37-1.43 (m, 2H), 0.96 (t, *J* = 8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 203.7, 199.7, 199.4, 199.2, 27.9, 26.2, 22.8, 13.6, 11.2. HRMS (ESI⁺) *m/z*: [M + Na]⁺ calcd for C₉H₁₂NaO₂, 175.0730; found, 175.0733.

4-butyl-2-methoxycarbonyl-2,5-dimethylcyclopent-4-ene-1,3-dione (14b). colorless oil. (146 mg, 80% (based on the recovery of 23% of **16**)) *R*_f = 0.6 (PE/EtOAc = 4/1). ¹H NMR (400 MHz, CDCl₃): δ 3.67 (s, 3H), 2.52 (t, *J* = 8 Hz, 3H), 2.09 (s, 3H), 1.48-1.55 (m, 2H), 1.44 (s, 3H), 1.33-1.39 (m, 2H), 0.94 (t, *J* = 8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 199.7, 199.4, 167.1, 159.9, 155.5, 57.4, 53.2, 29.7, 24.1, 22.7, 15.3, 13.9, 9.7. HRMS (ESI⁺) *m/z*: [M + Na]⁺ calcd for C₁₃H₁₈NaO₄, 261.1097; found, 261.1090.

((4-butyl-2-methoxycarbonyl-2,5-dimethylcyclopent-4-ene-1,3-diyl)bis(oxy))bis(*tert*-butyldimethylsilane) (13): **14b** (50 mg, 0.21 mmol) and cerous chloride heptahydrate (16 mg, 0.04 mmol) was dissolved in methanol (5 mL), the mixture was then cooled to 0 °C, and to the solution was

added NaBH₄ (32 mg, 0.84 mmol) slowly. The reaction mixture was warmed up to room temperature. After 3 h, the reaction mixture was quenched with saturated ammonium chloride solution. The aqueous phase was extracted with CH₂Cl₂ (3×20mL). The combined organic layer was washed with saturated brine and dried over Na₂SO₄. The solvent was removed under reduced pressure. Then tert- butyldimethylsilyl trifluoromethanesulfonate (TBSOTf) (172 mg, 1.1 mmol) was added to the solution of the crude residue and triethylamine (213mg, 2.1 mmol) in CH₂Cl₂ (5 mL) at room temperature. After 1h, the reaction was quenched with water. The aqueous phase was extracted with CH₂Cl₂ and the combined organic layers were dried over Na₂SO₄. The solvent was removed under reduced pressure. The crude residue was purified by silica gel chromatography (PE/EtOAc, 100/1) to give **13** (52 mg, 53%) as a colorless oil. *R*_f = 0.8 (PE/EtOAc = 4/1). ¹H NMR (400 MHz, CDCl₃): δ 4.82 (s, 1H), 4.69 (s, 1H), 3.69 (s, 3H), 2.04-2.08 (m, 1H), 1.92-1.95 (m, 1H), 1.57 (s, 3H), 1.30 (m, 4H), 1.01 (s, 3H), 0.89 (s, 21H), 0.04 (s, 6H), -0.06 (s, 6H). ¹³C NMR (100 MHz, CDCl₃): δ 178.4, 137.3, 133.0, 82.2, 81.1, 60.9, 51.8, 31.0, 26.0 (6C), 25.3, 23.1, 18.3, 18.2, 14.2, 11.5, 11.4, -4.4, -4.6, -4.7, -4.8. HRMS (ESI⁺) *m/z*: [M + Na]⁺ calcd for C₂₅H₅₀NaO₄Si₂, 493.3140; found, 493.3120.

14a

yellow oil. (144 mg, 86%) *R*_f = 0.6 (PE/EtOAc = 4/1). ¹H NMR (400 MHz, CDCl₃): δ 4.04-4.09 (m, 2H), 2.42-2.49 (m, 2H), 2.02 (s, 3H), 1.43-1.47 (m, 2H), 1.34 (s, 3H), 1.28-1.31 (m, 2H), 1.09 (t, *J* = 8 Hz, 3H), 0.86 (t, *J* = 8 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ 199.8, 199.5, 166.6, 159.9, 155.4, 62.2, 57.5, 29.6, 24.0, 22.6, 15.0, 13.9, 13.8, 9.7. HRMS (ESI⁺) *m/z*: [M + Na]⁺ calcd for C₁₄H₂₀NaO₄, 275.1254; found, 275.1249.

14c

yellow oil. (282 mg, 77%) R_f = 0.6 (PE/EtOAc = 4/1). ^1H NMR (400 MHz, CDCl_3): δ 3.95-4.01 (m, 2H), 2.41-2.47 (m, 2H), 2.01 (s, 3H), 1.41-1.44 (m, 2H), 1.35 (s, 3H), 1.26-1.31 (m, 2H), 1.16-1.19 (m, 2H), 0.85 (t, J = 8 Hz, 3H), 0.79 (t, J = 8 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 199.8, 199.5, 166.6, 159.8, 155.5, 65.9, 57.6, 30.3, 29.7, 24.0, 22.7, 18.9, 15.0, 13.9, 13.6, 9.6. HRMS (ESI^+) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{24}\text{NaO}_4$, 303.1567; found, 303.1563.

14d

yellow oil. (275 mg, 83%) R_f = 0.6 (PE/EtOAc = 4/1). ^1H NMR (400 MHz, CDCl_3): δ 3.58 (s, 3H), 2.46 (t, J = 8 Hz, 2H), 2.40-2.10 (m, 2H), 2.02 (s, 3H), 1.42-1.47 (m, 2H), 1.26-1.32 (m, 2H), 0.86 (t, J = 8 Hz, 3H), 0.62 (t, J = 8 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 199.7, 199.4, 166.8, 161.2, 156.9, 62.1, 53.1, 29.8, 24.1, 23.5, 22.7, 13.9, 9.6, 8.5. HRMS (ESI^+) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{14}\text{H}_{20}\text{NaO}_4$, 275.1254; found, 275.1258.

14e

yellow oil. (299 mg, 81%) R_f = 0.6 (PE/EtOAc = 4/1). ^1H NMR (400 MHz, CDCl_3): δ 4.01-4.05 (m, 2H), 2.46 (t, J = 8 Hz, 2H), 2.01 (s, 3H), 1.97-2.00 (m, 2H), 1.42-1.46 (m, 2H), 1.26-1.31 (m, 2H), 1.09 (t, J = 8 Hz, 3H), 0.88-0.93 (m, 2H), 0.86 (t, J = 8 Hz, 3H), 0.78 (t, J = 8 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 199.0, 199.6, 166.4, 161.0, 156.6, 62.1, 61.9, 32.0, 29.8, 24.0, 22.7, 17.5, 14.3, 13.9, 13.9, 9.6. HRMS (ESI^+) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{24}\text{NaO}_4$, 303.1567; found, 303.1560.

14f

yellow oil. (286 mg, 78%) R_f = 0.6 (PE/EtOAc = 4/1). ^1H NMR (400 MHz, CDCl_3): δ 2.35-2.53 (m, 2H), 2.00 (s, 3H), 1.41-1.47 (m, 2H), 1.28 (s, 14H), 0.86 (t, J = 8 Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ 200.3, 200.0, 165.5, 159.6, 155.3, 83.0, 58.4, 29.8, 27.7, 24.0, 22.7, 14.7, 13.9, 9.6. HRMS (ESI^+) m/z : $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{16}\text{H}_{24}\text{NaO}_4$, 303.1567; found, 303.1569.

¹H and ¹³C NMR Spectra of Compounds

¹H NMR Spectrum for compound **16**

¹³C NMR Spectrum for compound **16**

^1H NMR Spectrum for compound **14b**

^{13}C NMR Spectrum for compound **14b**

¹H NMR Spectrum for compound **13**

¹³C NMR Spectrum for compound **13**

¹H NMR Spectrum for compound **14a**

¹³C NMR Spectrum for compound **14a**

¹H NMR Spectrum for compound **14c**

¹³C NMR Spectrum for compound **14c**

¹H NMR Spectrum for compound **14d**

¹³C NMR Spectrum for compound **14d**

¹H NMR Spectrum for compound **14e**

¹³C NMR Spectrum for compound **14e**

¹H NMR Spectrum for compound **14f**

¹³C NMR Spectrum for compound **14f**