Enantioselective Total Synthesis of (+)-Jasplakinolide

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General

¹H NMR and ¹³C NMR spectra were recorded on Bruker Avance DRX-400 spectrometers. IR spectra were recorded on a Matteson Genesis II FT-IR spectrometer. Optical rotations were recorded on a Perkin Elmer 341 polarimeter. Anhydrous solvents were obtained as follows: THF and diethyl ether by distillation from sodium and benzophenone; dichloromethane from CaH₂. All other solvents were reagent grade. All moisture sensitive reactions were carried out in flame dried flask under nitrogen atmosphere. Column chromatography was performed with Whatman 240-400 mesh silica gel. TLC was carried out with E. Merck silica gel 60-F-254 plates.

Experimental Section

To a stirred solution of oxazolidinone **5** (13.5 g, 57.9 mmol) in CH₂Cl₂ (200 mL) was added Bu₂BOTf (69.5 mL, 69.5 mmol) and diisopropylethylamine (14 mL, 81 mmol) at 0 °C. After stirring for 50 min, distilled methacrolein (12 mL, 144.7 mmol) was added to the enolate

reaction mixture at -78°C . The reaction mixture was stirred for 20 min and then was warmed to 0°C . After additional 1 h, pH 7 buffer solution (10 mL) followed by MeOH (20 mL) was added to the reaction mixture at 0°C and continuously added H_2O_2 (20 mL), MeOH (20 mL) at the same temperature. After stirring for 1 h at 0°C , a volatile solvent was removed and then H_2O was added to the reaction mixture. The mixture was extracted with EtOAc. The combined extracts were dried over anhydrous MgSO_4 , filtered, and concentrated *in vacuo*. The organic residue was purified by column chromatography on silica gel (25% ethyl acetate in hexane) to afford 16.5 g (54.4 mmol, 94%) of **6**. ^1H NMR (400 MHz, CDCl_3) δ 7.34-7.30(m, 2 H), 7.27-7.24(m, 1 H), 7.19-7.18(m, 2 H), 5.10(s, 1 H), 4.96(s, 1 H), 4.71-4.67(m, 1 H), 4.40(s, 1 H), 4.24-4.16(m, 2 H), 3.96-3.92(m, 1 H), 3.25(dd, $J = 13.4$ Hz, 3.3 Hz, 1 H) 2.77(dd, $J = 13.4$ Hz, 9.4 Hz, 1 H), 2.68(bs, 1 H), 1.71(s, 3 H), 1.17(d, $J = 7.1$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 177.1, 152.9, 143.7, 135.0, 129.4, 128.9, 127.4, 111.8, 73.9, 66.2, 55.2, 40.1, 37.7, 19.4, 9.99

To a solution of aldol adduct **6** (8 g, 26.4 mmol) was added propionic acid (0.4 mL, 5.28 mmol) and triethylorthopropionate (50 mL). The reaction mixture was stirred for 1 h at 140°C . The reaction mixture was cooled to room temperature and was purified directly by column chromatography on silica gel (10% ethyl acetate in hexane) to afforded 9.5 g (24.6 mmol, 93%) of **8**, $[\alpha]_{\text{D}}^{23} = +104$, c 1.0, CHCl_3 ; IR (neat) 1782, 1730, 1699; ^1H NMR (400 MHz, CDCl_3) δ 7.33-7.29(m, 2 H), 7.27-7.25(m, 1 H), 7.20-7.18(m, 2 H), 5.28(d, $J = 8.5$ Hz, 1 H), 4.64-4.60(m, 2 H), 4.16-4.12(m, 2 H), 4.11-4.07(m, 2 H), 3.26(dd, $J = 13.4$ Hz, 3.2 Hz, 1 H), 2.75(dd, $J = 13.4$ Hz, 9.7 Hz, 1 H), 2.63-2.57(m, 1 H), 2.39-2.34(m, 1 H), 2.08-2.05(m, 1 H), 1.65(d, $J = 1.2$ Hz, 3 H), 1.26-1.21(m, 6 H), 1.07(d, $J = 6.9$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 176.2, 175.7, 152.9, 135.3, 135.2, 129.4, 128.9, 127.3, 125.6, 65.9, 60.1, 55.5, 43.7, 37.9, 37.8, 37.2, 18.2, 16.5, 16.2, 14.2; LRMS(ESI) m/z $[\text{M}+\text{Na}]^+$ 410.11, HRMS(ESI) $[\text{M}+\text{Na}]^+$: calculated for $\text{C}_{22}\text{H}_{29}\text{NO}_5$: 410.1943, Found: 410.1942.

To a solution of Claisen adduct **8** (8.5 g, 22 mmol) in Et₂O (70 mL) was added EtOH (1.3 mL, 22 mmol) and LiBH₄ (10.5 mL, 21 mmol : 2 M in THF) at 0 °C. After stirring for 20 min. sodium-potassium tartrate (sat.) was added to the reaction mixture and then was extracted with EtOAc. The organic layer was dried over anhydrous MgSO₄, filtered, and concentrated *in vacuo*, the residue was purified by column chromatography (20% ethyl acetate in hexane) to afford 3.9 g (18.2 mmol, 83%) of the corresponding alcohol.

To the solution of alcohol (30 mg, 0.14 mmol) in THF (2 mL) was added triphenylphosphine (73 mg, 0.28 mmol) and diisopropylazodicarboxylate (55 µL, 0.28 mmol) dropwise at 0 °C. After stirring for 10 min at ice bath, acetone cyanohydrin (20 µL, 0.21 mmol) was added to the reaction mixture. The resulting mixture was allowed to warm to reflux and then stirred for 6 h. The reaction mixture was poured into H₂O. The resulting solution was extracted with EtOAc and the combined organic extracts were dried over anhydrous MgSO₄, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography (10% ethyl acetate in hexane) to afford 24 mg (0.11 mmol, 79%) of **9**, [α]_D²³ = + 6.1, *c* 3.0, CHCl₃; IR (neat) 2246, 1732 ; ¹H NMR (400 MHz, CDCl₃) δ 4.97(d, *J* = 9.6 Hz, 1 H), 4.09-4.02(m, 2 H), 2.77-2.71(m, 1 H), 2.58-2.53(m, 1 H), 2.35-2.30(m, 1 H), 2.23-2.20(m, 2 H), 2.03-1.97(m, 1 H), 1.61(d, *J* = 1.0 Hz, 3 H), 1.19(t, 3 H), 1.07(d, *J* = 6.8 Hz, 3 H), 1.02(d, *J* = 6.8 Hz, 3 H) ; ¹³C NMR (100 MHz, CDCl₃) δ 176.1, 134.4, 129.1, 118.6, 60.1, 43.6, 37.7, 29.7, 24.8, 20.3, 16.5, 15.9, 14.1; LRMS(ESI) *m/z* [M+Na]⁺ 245.88, HRMS(ESI) [M+Na]⁺: calculated for C₁₃H₂₁NO₂ : 246.1470, Found : 246.1468.

To a solution of nitrile **9** (38 mg, 0.17 mmol) in pyridine / AcOH / H₂O (0.4 mL / 0.2 mL / 0.2 mL) was added hydrated sodium hypophosphite NaH₂PO₃·H₂O (90 mg, 0.85 mmol) and 50 mg of Raney-Ni (50% slurry in water). The reaction mixture was stirred for 3 h at 50 °C, 50 mg of Raney-Ni was added, and the mixture was stirred for additional 3 h. The mixture was filtered and then the catalyst was washed with water. The mixture was extracted with Et₂O, dried over anhydrous MgSO₄, filtered and the resulting solution was concentrated *in vacuo*. The organic residue was purified by column chromatography on silica gel (7% ethyl acetate in hexane) to afford 31 mg (0.14 mmol, 81%) of aldehyde.

A solution of aldehyde (31 mg, 0.14 mmol) in THF (1 mL) was treated with MeMgBr (53 µL, 0.16 mmol, 3 M in THF) at 0 °C and was stirred for 30 min. The reaction mixture was poured into NH₄Cl(sat.) and the aqueous layer was extracted with EtOAc. The combined organic extracts were dried over anhydrous MgSO₄, concentrated *in vacuo* and purified by the flash chromatography on silica gel (15% ethyl acetate in hexane) to produce 30 mg (0.12 mmol, 90%) of alcohol **10**, **11** ; **10**, ¹H NMR (400 MHz, CDCl₃) δ 4.88(d, *J* = 9.8 Hz, 1 H), 4.10-4.04(m, 2 H), 3.71-3.67(m, 1 H), 2.60-2.55(m, 2 H), 2.32(dd, *J* = 13.7 Hz, 7.5 Hz, 1 H), 2.00(dd, *J* = 13.7 Hz, 7.5 Hz, 1 H), 1.61(d, *J* = 0.9 Hz, 3 H), 1.53(bs, 1 H), 1.40-1.37(m, 1 H), 1.28-1.24(m, 1 H), 1.22(t, 3 H) 1.13(d, *J* = 6.2 Hz, 3 H), 1.07(d, *J* = 6.9 Hz, 3 H), 0.88(d, *J* = 6.8 Hz, 3 H) ; ¹³C NMR (100 MHz, CDCl₃) δ 176.6, 133.0, 131.6, 66.3, 60.1, 47.0, 43.9, 38.0, 29.1, 24.1, 21.6, 16.7, 15.9, 14.2

11, [α]_D²³ = - 27.9, *c* 1.3, CHCl₃ ; IR (neat) 3446, 1734 ; ¹H NMR (400 MHz, CDCl₃) δ 4.98(d, *J* = 9.6 Hz, 1 H), 4.10-4.04(m, 2 H), 3.79-3.74(m, 1 H), 2.60-2.55(m, 1 H), 2.49-2.41(m, 1 H), 2.34-2.29(m, 1 H), 2.02-1.97(m, 1 H), 1.66(bs, 1 H), 1.60(d, *J* = 1.1 Hz, 3 H), 1.41-1.36(m, 2 H), 1.22(t, 3 H), 1.12(d, *J* = 6.2 Hz, 3 H), 1.07(d, *J* = 6.9 Hz, 3 H), 0.89(d, *J* = 6.8 Hz, 3 H) ; ¹³C NMR (100 MHz, CDCl₃) δ 176.4, 133.4, 131.4, 67.1, 60.1, 47.0, 43.9, 38.0, 30.2, 23.4, 21.3, 16.7, 15.9, 14.2 ; LRMS(ESI) *m/z* [M+Na]⁺ 242.82, HRMS(ESI) [M+Na]⁺ : calculated for C₁₄H₂₆O₃ : 243.1960, Found : 243.1959.

To a solution of (R)-alcohol **10** (10 mg, 0.04 mmol) in Et₂O (3 mL) was added Ph₃P (108 mg, 0.4 mmol), *p*-nitrobenzoic acid (69 mg, 0.4 mmol) and then diisopropylazodi carboxylate (40 μ L, 0.2 mmol) dropwise at room temperature. After stirring for 10 h, the reaction mixture was filtered and concentrated *in vacuo*.

To the solution of crude compound in EtOH was added potassium carbonate at room temperature. After stirring for 5 h, the reaction mixture was quenched with NH₄Cl(sat) and extracted with EtOAc. The organic extracts were dried over anhydrous MgSO₄, filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (15% ethyl acetate in hexane) produced 7.8 mg (0.03 mmol, 78%) of (S)-**11**.

To a solution of alcohol **11** (475 mg, 1.96 mmol) in CH₂Cl₂ (6 mL) was added Et₃N (0.41 mL, 2.94 mmol) and TBSOTf (0.54 mL, 2.35 mmol) at room temperature. After stirring for 3 h, the reaction mixture was quenched with NH₄Cl(sat) and extracted with EtOAc. The organic extracts were dried over anhydrous MgSO₄, filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (3% ethyl acetate in hexane) produced 685 mg (1.92 mmol, 98%) of **11a**, [α]_D²³ = -7.3, *c* 2.0, CHCl₃; IR (neat) 1737; ¹H NMR (400 MHz, CDCl₃) δ 4.92(d, *J* = 9.6 Hz, 1 H), 4.10-4.05(m, 2 H), 3.75-3.70(m, 1 H), 2.59-2.53(m, 1 H), 2.44-2.38(m, 1 H), 2.35-2.30(m, 1 H), 2.01-1.95(m, 1 H), 1.56(d, *J* = 1.1 Hz, 3 H), 1.42-1.36(m, 1 H), 1.29-1.24(m, 1 H),

1.22(t, 3 H), 1.07-1.05(m, 6 H), 0.87-0.86(m, 12 H), 0.02(s, 6 H) ; ^{13}C NMR (100 MHz, CDCl_3) δ 176.6, 133.9, 130.2, 66.6, 60.1, 47.5, 44.1, 37.8, 29.0, 25.8, 23.6, 20.8, 18.1, 16.4, 15.5, 14.2, -4.37, -4.77 ; LRMS(ESI) m/z $[\text{M}+\text{Na}]^+$ 378.87, HRMS(ESI) $[\text{M}+\text{Na}]^+$: Calculated for $\text{C}_{20}\text{H}_{40}\text{O}_3\text{Si}$: 379.2644, Found : 379.2648.

To a solution of **11a** (685 mg, 1.92 mmol) in THF / H₂O / MeOH (3 mL / 1 mL / 1 mL) was added LiOH (242 mg, 5.76 mmol) at room temperature. After stirring for 6 h, the reaction mixture was quenched with 1N HCl(aq) until pH 3 and extracted with EtOAc. The organic extracts were dried over anhydrous MgSO₄, filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (10% ethyl acetate in hexane) produced 599 mg (1.82 mmol, 95%) of **3** ; ¹H NMR (400 MHz, CDCl₃) δ 4.95(d, *J* = 9.4 Hz, 1 H), 3.75-3.70(m, 1 H), 2.62-2.57 (m, 1 H), 2.43-2.34(m, 2 H), 2.03-1.98(m, 1 H), 1.57(d, *J* = 0.8 Hz, 3 H), 1.41-1.39(m, 1 H), 1.29-1.25(m, 1 H), 1.08(t, 6 H), 0.89-0.86(m, 12 H), 0.02(s, 6 H) ; ¹³C NMR (100 MHz, CDCl₃) δ 182.9, 134.3, 129.8, 66.7, 47.5, 43.7, 37.7, 29.0, 25.8, 23.6, 20.8, 18.1, 16.1, 15.5, -4.38, -4.77

To a stirred solution of **12** (1.7 g, 6 mmol) in CH₂Cl₂ (20 mL) was added (*S*)-*p*-toluene sulfinamide (950 mg, 6 mmol) and Ti(OEt)₄ (6.4 mL, 30 mmol) at 0 °C. The reaction mixture was stirred at 40 °C for 5 h. The reaction mixture was cooled to 0 °C and was poured into H₂O

and was filtered with celite. The reaction mixture was washed with H₂O and aqueous layer was extracted with CH₂Cl₂ and the combined organic extracts were dried over anhydrous MgSO₄, filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (5% ethyl acetate in hexane) afforded 2.2 g (5.3 mmol, 87%) of **13** ; ¹H NMR (400 MHz, CDCl₃) δ 8.64(s, 1 H), 7.71(d, *J* = 11.2 Hz, 1 H), 7.60(d, *J* = 8.2 Hz, 1 H), 7.28(d, *J* = 8.1 Hz, 1 H), 6.89(d, *J* = 8.7 Hz, 1 H), 2.37(s, 3 H), 1.27-1.21(m, 3 H), 1.09-1.03(m, 18 H)

To a stirred solution of distilled methylacetate (1 mL, 12.5 mmol) in Et₂O (10 mL) was added NaHMDS (12.5 mL, 12.5 mmol) at -78 °C. The reaction mixture was stirred for 40 min. Compound **13** (1.3 g, 3.1 mmol) was added to the enolate mixture at the same temperature. The resulting mixture was stirred for 1 h. The reaction mixture was poured into NH₄Cl (sat) and the aqueous layer was extracted with EtOAc and the combined organic extracts were dried over anhydrous MgSO₄, filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (35% ethyl acetate in hexane) afforded 1.2 g (2.5 mmol, 78%) of **13a**, [α]_D²³ = + 37.5, *c* 1.0, CHCl₃; IR (neat) 3181, 1739, 1607, 1265, 1169 ; ¹H NMR (400 MHz, CDCl₃) δ 7.56(d, *J* = 8.2 Hz, 1 H), 7.28-7.22(m, 4 H), 6.85(d, *J* = 8.4 Hz, 1 H), 4.88-4.82(m, 2 H), 3.56(s, 3 H), 2.78(d, *J* = 6.3 Hz, 2 H), 2.39(s, 3 H), 1.27-1.20 (m, 3 H), 1.12-1.06(m, 18 H) ; ¹³C NMR (100 MHz, CDCl₃) δ 171.3, 155.8, 142.3, 141.2, 132.3, 129.4, 128.3, 125.2, 120.0 54.2, 51.7, 42.0, 21.2, 17.8, 12.5 ; LRMS (ESI) *m/z* [M+Na]⁺ 512.05, HRMS (ESI) [M+Na]⁺: Calculated for C₂₆H₃₉NO₄SSi: 512.2267, Found : 512.2261.

To a stirred solution of **13a** (1.1 g, 2.3 mmol) in MeOH (5 mL) was added Trifluoroacetic acid (0.34 mL 4.6 mmol) at 0°C. The reaction mixture was stirred for 1 h. The reaction mixture was poured into NaHCO₃(sat) and pH adjusted to 7-8 and aqueous layer was extracted with CH₂Cl₂ and the combined organic extracts were dried over anhydrous MgSO₄, filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (5% methanol in dichloromethane) afforded 653 mg (1.9 mmol, 83%) of **14**, [α]_D²³ = + 7.1, *c* 2.4, CHCl₃ ; IR (neat) 1737, 1607, 1510, 1265 ; ¹H NMR (400 MHz, CDCl₃) δ 7.16(d, *J* = 8.4 Hz, 1 H), 6.81(d, *J* = 8.6 Hz, 1 H), 4.33(t, 1 H), 3.64(s, 3 H), 2.60(d, *J* = 6.9 Hz, 2 H), 1.24-1.18(m, 3 H), 1.07-1.05(m, 18 H) ; ¹³C NMR (100 MHz, CDCl₃) δ 172.5, 155.1, 136.9, 126.9, 119.8, 51.9, 51.5, 44.0, 17.8, 12.5 ; LRMS(ESI) *m/z* [M+Na]⁺ 373.67, HRMS(ESI) [M+Na]⁺: Calculated for C₂₆H₃₉NO₄SSi : 374.2127, Found : 374.2126.

To a stirred solution of acid **15** (49 mg, 0.1 mmol) in THF (2 mL) was added amine **14** (36 mg, 0.1 mmol) and DCC (23 mg, 0.11 mmol) at 0 °C. The reaction mixture was stirred for 12 h. The reaction mixture was filtered and concentrated *in vacuo*. Flash chromatography on silica gel (35% ethyl acetate in hexane) afforded 66 mg (0.083 mmol, 83%) of **4a**, $[\alpha]_{\text{D}}^{23} = +20.3$, *c* 2.0, CHCl₃ ; IR (neat) 3323, 1652, 1511, 1451, 1267 ; ¹H NMR (400 MHz, CDCl₃) δ 8.15(s, 1 H), 7.50(d, *J* = 7.7 Hz, 1 H), 7.19(d, *J* = 7.8 Hz, 1 H), 7.12-7.03(m, 4 H), 6.84(d, *J* =

8.3 Hz, 1 H), 6.76(d, J = 8.5 Hz, 2 H), 5.67-5.63(m, 1 H), 5.40-5.35(m, 1 H), 5.08(d, J = 6.8 Hz, 1 H), 4.30-4.24(m, 1 H), 3.57(s, 3 H), 3.36(dd, J = 15.3 Hz, 5.4 Hz, 1 H), 3.19(dd, J = 15.2 Hz, 11.0 Hz, 1 H), 2.94(s, 3 H), 2.84(dd, J = 15.2 Hz, 7.5 Hz, 1 H), 2.73(dd, J = 15.2 Hz, 5.8 Hz, 1 H), 1.34(s, 9 H), 1.25-1.18(m, 3 H), 1.07-1.04(m, 18 H), 0.63(d, J = 6.8 Hz, 3 H) ; ^{13}C NMR (100 MHz, CDCl_3) δ 174.1, 171.1, 169.1, 155.5, 136.0, 132.8, 127.4, 127.3, 122.4, 120.1, 119.9, 118.3, 110.8, 110.3, 108.9, 79.6, 56.0, 51.7, 49.4, 46.4, 40.6, 31.5, 28.3, 23.3, 17.9, 16.8, 12.6 ; LRMS(ESI) m/z $[\text{M}+\text{Na}]^+$ 823.0, HRMS(ESI) $[\text{M}+\text{Na}]^+$: Calculated for $\text{C}_{26}\text{H}_{39}\text{NO}_4\text{SSi}$: 823.3078, Found : 823.3086.

To a stirred solution of **4a** (121 mg, 0.15 mmol) in CH_2Cl_2 (1 mL) was trifluoroacetic acid (0.5 mL) at 0 °C. The reaction mixture was stirred for 1 h. The reaction mixture was poured into $\text{NaHCO}_3(\text{sat})$ and pH adjusted to 7-8 and aqueous layer was extracted with CH_2Cl_2 . The combined organic extracts were dried over anhydrous MgSO_4 , filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (5% methanol in dichloromethane) afforded 100 mg (0.14 mmol, 94%) of **4**.

To a stirred solution of amine **4** (50 mg, 0.07 mmol) in THF (2 mL) was added acid **3** (22.4 mg, 0.07 mmol), DCC (15 mg, 0.074 mmol) and HOBT (9.2 mg, 0.07 mmol) at -20 °C. The reaction mixture was warmed to 0 °C and was stirred for 12 h. The reaction was stirred at room temperature for additional 12 h. The reaction mixture was filtered and concentrated *in*

vacuo. Flash chromatography on silica gel (35% ethyl acetate in hexane) afforded 55.3 mg (0.056 mmol, 80%) of **16**, $[\alpha]_{\text{D}}^{23} = +18.3$, c 1.0, CHCl_3 ; IR (neat) 3303, 1742, 1641, 1511, 1451, 1267; ^1H NMR (400 MHz, CDCl_3) δ 8.59(s, 1 H), 7.50(d, $J = 7.6$ Hz, 1 H), 7.20(d, $J = 7.8$ Hz, 1 H), 7.12-7.04(m, 4 H), 6.98(d, $J = 8.5$ Hz, 1 H), 6.76(d, $J = 8.4$ Hz, 2 H), 6.11(d, $J = 5.7$ Hz, 1 H), 5.63-5.59(m, 1 H), 5.40-5.34(m, 1 H), 4.91(d, $J = 9.3$ Hz, 1 H), 4.50-4.45(m, 1 H), 3.74-3.69(m, 1 H), 3.56(s, 3 H), 3.39(dd, $J = 15.4$ Hz, 5.5 Hz, 1 H), 3.18(dd, $J = 15.4$ Hz, 10.9 Hz, 1 H), 2.97(s, 3 H), 2.89(dd, $J = 15.4$ Hz, 7.8 Hz, 1 H), 2.75(dd, $J = 15.4$ Hz, 5.8 Hz, 1 H), 2.43-2.38(m, 1 H), 2.33-2.24(m, 2 H), 1.94-1.89(m, 1 H), 1.51(d, $J = 1.0$ Hz, 3 H), 1.26-1.18(m, 5 H), 1.07-1.05(m, 21 H), 0.98(d, $J = 6.8$ Hz, 3 H), 0.85-0.84(m, 12 H), 0.69(d, $J = 6.8$ Hz, 3 H), 0.064(s, 6 H); ^{13}C NMR (100 MHz, CDCl_3) δ 176.1, 173.7, 171.2, 168.7, 155.3, 135.9, 134.2, 132.8, 129.9, 127.4, 122.3, 120.1, 119.8, 118.2, 110.8, 110.2, 108.8, 66.6, 56.2, 51.6, 49.4, 47.5, 45.4, 43.8, 40.6, 38.3, 33.9, 28.9, 25.8, 24.9, 23.6, 20.7, 18.0, 17.8, 16.5, 16.2, 15.4, 12.5, -4.43, -4.85; LRMS(ESI) m/z $[\text{M}+\text{Na}]^+$ 1033.42, HRMS(ESI) $[\text{M}+\text{Na}]^+$: Calculated for $\text{C}_{52}\text{H}_{83}\text{BrN}_4\text{O}_7\text{Si}_2$: 1033.4881, Found: 1033.4885.

To a solution of **16** (51 mg, 0.05 mmol) in THF / H₂O / MeOH (3 mL / 1 mL / 1 mL) was added LiOH (6.3 mg, 0.15 mmol) at room temperature. After stirring for 2 h, the reaction mixture was quenched with 1N HCl(aq) until pH 3 and extracted with EtOAc. The organic

extracts were dried over anhydrous MgSO_4 , filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (65% ethyl acetate in hexane) produced 40 mg (0.048 mmol, 96%) of free phenol-acid compound.

To a solution of free phenol-acid compound (12 mg, 0.014 mmol) in CH_2Cl_2 (1 mL) was added 2,6-lutidine (7 μL , 0.056 mmol) and TIPSOTf (12 μL , 0.042 mmol) at room temperature. After stirring for 1 h, the reaction mixture was quenched with H_2O and extracted with CH_2Cl_2 . The organic extracts were dried over anhydrous MgSO_4 , filtered, and concentrated *in vacuo*.

To a solution of above crude compound in THF / H_2O / MeOH (0.4 mL / 0.2 mL / 0.2 mL) was added K_2CO_3 (4 mg, 0.03 mmol) at room temperature. After stirring for 30 min, 2 N HCl(aq) was added to the reaction mixture and was stirred for 1 h. The reaction mixture was extracted with EtOAc. The organic extracts were dried over anhydrous MgSO_4 , filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (5% methanol in dichloromethane) produced 10 mg (0.0112 mmol, 80%) of seco acid **2**, $[\alpha]_{\text{D}}^{23} = +32$, c 0.8, CHCl_3 ; IR (neat) 3295, 2475, 1717, 1640, 1511, 1449, 1267; ^1H NMR (400 MHz, CD_3OD) δ 7.48(d, $J = 7.8$ Hz, 1 H), 7.22(d, $J = 7.1$ Hz, 3 H), 7.05(t, 1 H), 6.97(t, 1 H), 6.76(d, $J = 8.6$ Hz, 2 H), 5.69-5.65(m, 1 H), 5.46-5.42(m, 1 H), 4.93(d, $J = 9.6$ Hz, 1 H), 4.40-4.35(m, 1 H), 3.69-3.64(m, 1 H), 3.46(dd, $J = 15.2$ Hz, 4.5 Hz, 1 H), 3.13(dd, $J = 15.2$ Hz, 11.8 Hz, 1 H), 3.07(s, 3 H), 2.92(dd, $J = 15.8$ Hz, 8.8 Hz, 1 H), 2.77(dd, $J = 15.8$ Hz, 5.1 Hz, 1 H), 2.48-2.42(m, 2 H), 2.27-2.23(m, 1 H), 1.92-1.87(m, 1 H), 1.56(s, 3 H), 1.45-1.39(m, 1 H), 1.28-1.20(m, 4 H), 1.10-1.06(m, 21 H), 0.97(d, $J = 6.8$ Hz, 3 H), 0.90(d, $J = 6.5$ Hz, 3 H), 0.62(d, $J = 6.9$ Hz, 3 H); ^{13}C NMR (100 MHz, CD_3OD) δ 179.2, 176.2, 174.7, 171.2, 156.6, 137.9, 135.5, 134.8, 131.9, 128.9, 128.7, 122.7, 120.8, 120.4, 119.0, 111.5, 110.7, 110.3, 66.6, 57.9, 51.1, 46.9, 44.9, 41.8, 38.9, 32.8, 30.8, 30.4, 24.4, 23.4, 21.4, 18.4, 16.9, 16.0, 15.6, 13.9; LRMS(ESI) m/z $[\text{M}+\text{Na}]^+$ 905.29, HRMS(ESI) $[\text{M}+\text{Na}]^+$: Calculated for $\text{C}_{45}\text{H}_{67}\text{BrN}_4\text{O}_7\text{Si}$: 905.3860, Found: 905.3872.

To a solution of seco acid **2** (10 mg, 0.011 mmol) in THF (2 mL) was added DIPEA (20 μ L, 0.11 mmol) and 2,4,6-trichlorobenzoyl chloride (9 μ L, 0.055 mmol) at room temperature. After stirring for 2.5 h, the reaction mixture was concentrated *in vacuo*. The reaction mixture was diluted with dry benzene (100 mL). To a solution of the resulting mixture was slowly added DMAP (7 mg, 0.055 mmol) in benzene (10 mL) over a period of 8 h. The reaction mixture was concentrated *in vacuo* and then was directly purified by column chromatography on silica gel (35% ethyl acetate in hexane) to give 8 mg (0.009 mmol, 82%) of **2a**, $[\alpha]_D^{23} = +58$, c 0.7, CHCl_3 ; IR (neat) 3305, 1641, 1510, 1455, 1266; ^1H NMR (400 MHz, CDCl_3) δ 8.42(s, 1 H), 7.53(d, $J = 7.1$ Hz, 1H), 7.48(d, $J = 9.1$ Hz, 1 H), 7.21(d, $J = 8.4$ Hz, 1 H), 7.12-7.02(m, 2 H), 7.01(d, $J = 8.6$ Hz, 2 H), 6.77(d, $J = 8.6$ Hz, 2 H), 6.60(d, $J = 6.5$ Hz, 1 H), 5.84-5.80(m, 1 H), 5.31-5.26(m, 1 H), 4.71-4.65(m, 2 H), 4.59-4.54(m, 1 H), 3.31(dd, $J = 15.2$ Hz, 6.2 Hz, 1 H), 3.23(dd, $J = 15.2$ Hz, 10.6 Hz, 1 H), 2.93(s, 3 H), 2.65(dd, $J = 14.8$ Hz, 4.8 Hz, 1 H), 2.58(dd, $J = 14.8$ Hz, 4.9 Hz, 1 H), 2.49-2.34(m, 2 H), 2.23-2.19(m, 1 H), 1.84(d, $J = 15.6$ Hz, 1 H), 1.54(s, 3 H), 1.26-1.19(m, 4 H), 1.10-1.04(m, 22 H), 1.02(d, $J = 6.3$ Hz, 3 H), 0.78(d, $J = 6.5$ Hz, 3 H), 0.66(d, $J = 6.7$ Hz, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 174.7, 174.3, 170.7, 168.8, 155.4, 136.1, 133.6, 132.1, 127.3, 127.1, 122.4, 120.1, 119.8, 118.2, 110.4, 108.9, 70.5, 55.1, 48.7, 45.9, 43.4, 40.5, 39.9, 39.2, 30.7, 29.1, 23.0, 21.9, 20.4, 18.9, 18.5, 17.9, 17.6, 12.6; LRMS(ESI) m/z $[\text{M}+\text{Na}]^+$ 887.31, HRMS(ESI) $[\text{M}+\text{Na}]^+$: calculated for $\text{C}_{45}\text{H}_{65}\text{BrN}_4\text{O}_6\text{Si}$: 887.3754, Found: 887.3760.

To a stirred solution of **2a** (3 mg, 3.5 μ mol) in THF (1 mL) was added TBAF (0.1 M solution, 35 μ L, 3.5 μ mol) at 0 °C. The reaction mixture was stirred for 10 min. The reaction mixture was poured into NH₄Cl(sat) and the aqueous layer was extracted with EtOAc and the combined organic extracts were dried over anhydrous MgSO₄, filtered, and concentrated *in vacuo*. Flash chromatography on silica gel (50% ethyl acetate in hexane) produced (+)-Jasplakinolide (**1**) (2.2 mg, 90%), $[\alpha]_D^{23} = +67.7$, c 0.2, CH₂Cl₂; IR (neat) 3305, 1715, 1684, 1675, 1640, 1515, 1450; ¹H NMR (400 MHz, CDCl₃) δ 8.36(s, 1 H), 7.59(d, J = 8.8 Hz, 1 H), 7.57(d, J = 7.7 Hz, 1 H), 7.25(d, J = 8.2 Hz, 1 H), 7.17-7.09(m, 2 H), 6.97(d, J = 8.4 Hz, 2 H), 6.68(d, J = 8.4 Hz, 2 H), 6.61(d, J = 6.6 Hz, 1 H), 6.19(bs, 1 H), 5.87-5.83(m, 1 H), 5.29-5.25(m, 1 H), 4.76-4.70(m, 2 H), 4.64-4.59(m, 1 H), 3.39(dd, J = 15.3 Hz, 6.3 Hz, 1 H), 3.24(dd, J = 15.3 Hz, 10.4 Hz, 1 H), 2.98(s, 3 H), 2.68(dd, J = 15.8 Hz, 4.6 Hz, 1 H), 2.61(dd, J = 15.8 Hz, 5.6 Hz, 1 H), 2.52-2.46(m, 1 H), 2.42-2.35(m, 1 H), 2.27-2.19 (m, 1 H), 1.89(d, J = 15.7 Hz, 1 H), 1.57(s, 3 H), 1.35-1.28(m, 1 H), 1.12(d, J = 6.8 Hz, 3 H), 1.06(d, J = 6.3 Hz, 3 H), 0.81(d, J = 6.6 Hz, 3 H), 0.72(d, J = 6.7 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 175.0, 174.4, 170.8, 168.9, 155.4, 136.1, 133.6, 131.6, 127.6, 127.2, 122.5, 120.2, 118.1, 115.5, 110.5, 110.3, 108.9, 70.7, 55.4, 48.9, 45.9, 43.3, 40.7, 40.0, 39.6, 30.8, 29.2, 23.2, 21.9, 20.4, 19.0, 18.5, 17.7; LRMS(ESI) m/z [M+Na]⁺ 731.20, HRMS(ESI) [M+Na]⁺: Calculated for C₃₆H₄₅BrN₄O₆: 731.2420, Found: 731.2419.