Supporting Information

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Illicium Sesquiterpenes: Divergent Synthetic Strategy and Neurotrophic Activity Studies


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General Procedures

Unless indicated, all commercially available reagents and anhydrous solvents were purchased at the highest commercial quality and were used as received without further purification. All non-aqueous reactions were carried out under argon atmosphere using dry glassware that had been flame-dried under a stream of argon unless otherwise noted. Anhydrous tetrahydrofuran (THF) and dichloromethane (CH$_2$Cl$_2$) were obtained by passing commercially available pre-dried, oxygen-free formulations through activated alumina columns. Flash column chromatography was performed on silica gel (Merck Kieselgel 60, 230-400 mesh) using Hexanes-EtOAc or CH$_2$Cl$_2$-MeOH mixtures of increasing polarity. The progress of all the reactions was monitored by thin-layer chromatography (TLC) using glass plates precoated with silica gel-60 F$_{254}$ to a thickness of 0.5 mm (Merck), and compounds were visualized by irradiation with UV light and/or by treatment with a solution of ninhydrin stain or Seebach’s stain followed by heating. $^{13}$C NMR and $^1$H NMR spectra were recorded on either 500 MHz Varian instrument or 500 MHz JEOL instrument. CDCl$_3$ was treated with flame dried K$_2$CO$_3$, chemical shifts ($\delta$) are quoted in parts per million (ppm) referenced to the appropriate residual solvent peak reference (CDCl$_3$ or CD$_3$OD), with the abbreviations s, br s, d, t, q, m, td, dt and qd denoting singlet, broad singlet, doublet, triplet, quartet, multiplet, quartet of doublets, triplet of doublets, doublet of triplets and quartet of doublets respectively. $J = $ coupling constants given in Hertz (Hz). IR spectras were collected on a Jasco 4100 FTIR. High resolution Mass spectra (HRMS) were recorded on a trisector WG AutoSpecQ spectrometer. Optical rotation data were collected on a Jasco P-1010 polarimeter using HPLC grade anhydrous CHCl$_3$ or anhydrous MeOH.
**11**: Allyl palladium chloride dimer (1.69 g, 4.6 mmol) and 1,2-bis(diphenylphosphino)ethane (9.20 g, 23 mmol) were dissolved in anhydrous THF (1000 ml), then allyl acetate (50.0 ml, 0.46 mol), 1,3-cyclopentadione (10, 45.0 g, 0.46 mol), N,O-bis(trimethylsilyl)acetamide (114 ml, 0.46 mol) and sodium acetate (1.10 g, 13.8 mmol) were added successively. This reaction mixture was refluxed for 40 h before it was cooled to RT and quenched with MeOH (500 ml). The solvents were removed on the rotavap, and the residue was dissolved in hot EtOAc and crystallized to afford the crude product as yellow solid (43.0 g, 70%). A suspension of this yellow solid (43.0 g, 0.31 mol) and methyl vinyl ketone (53.8 ml, 0.62 mol) in a mixture of water (620 ml) and acetic acid (9.20 ml) was refluxed for 4 h. The resulting mixture was cooled down and extracted with EtOAc (3 x 500 ml). The combined organic extracts were washed with saturated NaHCO₃ solution, dried over Na₂SO₄ and concentrated under reduced pressure. Purification of the residue through column chromatography on silica gel (hexanes:EtOAc = 10:1 to 3:1) afforded 11 (60.5 g, 90%, 63% for 2 steps). All the analytical data are in the agreement with the reported data.[1-3]

**9**: To a solution of 11 (36.0 g, 0.17 mol) in dry MeCN (600 mL) was added D-prolinamide (5.92 g, 52.0 mmol) and pyridinium p-toluenesulfonate (PPTS) (13.0 g, 52.0 mmol). This solution was warmed up to 40 °C for 14 days before it was cooled to RT and quenched with
water (300 mL). The mixture was extracted with EtOAc (3 x 500 mL), dried over Na₂SO₄, concentrated and loaded on a short silica pad and washed thoroughly with EtOAc and concentrated under reduced pressure to afford 9 as a yellow oil (22.0 g, 74%) in good purity and was used to next step directly. A pure sample of 9 was purified via silica flash column chromatography (hexanes:EtOAc = 20:1 to 1.5:1) to afford a colorless oil. (ee > 90%); Rᵣ = 0.38 (silica gel, hexanes:EtOAc = 2:1); [α]ᵣ²³ = -288.2 (c 1.0, CHCl₃); All the spectroscopic data are in the agreement with the reported data. [1-3] ¹H NMR (500 MHz, CDCl₃) δ 6.00 (br s, 1H), 5.72 (m, 1H), 5.14 (m, 2H), 2.93 (m, 1H), 2.79 (m, 1H), 2.66 (m, 1H), 2.55-2.36 (m, 5H), 2.23 (m, 1H), 1.76 (m, 1H); ¹³C NMR(125 MHz, CDCl₃) δ 215.8, 198.2, 169.1, 131.8, 124.7, 119.8, 52.7, 39.0, 36.2, 32.6, 27.3, 27.3; HRMS (ESI) m/e 191.1067 [M+H⁺] calcd for C₁₂H₁₅O₂⁺: 191.1068.

12: The enone 9 (21.0 g, 0.11 mol) was dissolved in absolute ethanol (220 mL), NaBH₄ (1.05 g, 27.6 mmol) was added portionwise at 0 °C and the reaction mixture was stirred for 30 min. Then this reaction was carefully quenched with saturated NH₄Cl solution (100 mL) and the solvent was removed under reduced pressure. The mixture was extracted with EtOAc (3 x 200 mL), dried over Na₂SO₄ and concentrated. The crude alcohol was then dissolved in dry DMF (220 mL) and was cooled to 0 °C. To this solution NH₄NO₃ (26.4 g, 0.33 mol) was added followed by TBSCl (33.2 g, 0.22 mol). The reaction mixture was then warmed up to RT for 12 h before it was quenched with saturated NH₄Cl solution (100 mL). The mixture was extracted with EtOAc (3 x 200 mL), dried over Na₂SO₄ and concentrated. The crude product
was then purified by silica flash column chromatography (hexanes:EtOAc = 100:1 to 10:1) to afford the product 12 as light yellow solid (31.1 g, 92% over 2 steps). R_{f} = 0.67 (silica gel, hexanes:EtOAc = 4:1); [\alpha]_{D}^{24} = 72.0 (c 0.76, CHCl_{3}); ^{1}H NMR (500 MHz, CDCl_{3}) \delta 6.01 (m, 1H), 5.82 (br s, 1H), 5.06 (d, J = 14.7 Hz, 1H), 4.99 (d, J = 7.4 Hz, 1H), 3.81 (t, J = 7.8 Hz, 1H), 2.64 (m, 1H), 2.58-2.45 (m, 2H), 2.37 (m, 1H), 2.30-2.21 (m, 3H), 2.00 (m, 1H), 1.84 (m, 1H), 1.69 (m, 1H), 0.91 (s, 9H), 0.06 (s, 6H); ^{13}C NMR (125 MHz, CDCl_{3}) \delta 199.5, 173.6, 136.2, 124.2, 117.0, 82.3, 48.8, 36.4, 33.5, 33.4, 30.0, 27.3, 26.0, 18.1, -4.5, -4.8; HRMS (ESI) m/e 307.2089 [M+H]^+ calcd for C_{18}H_{31}O_{2}Si+: 307.2088.

15: To a solution of 12 (17.0 g, 55.5 mmol) in anhydrous DMF (110 mL) was added magnesium methyl carbonate (111 mL, 0.22 mol, 2.0 M in DMF). This solution was degassed for 5 min under argon, then immersed in an oil bath which was pre-heated to 130 °C and stirred for 3 h. The reaction mixture was cooled to 0 °C and poured in to a mixture of ice/2N HCl (300 mL). Then this mixture was acidified to pH = 2-3 with 2N HCl. Ether (500 mL) was added to form a two-phase clear solution. The aqueous phase was separated and it was re-extracted with ether (2 x 500 mL). The combined organic extracts were dried over Na_{2}SO_{4} and concentrated under reduced pressure at 30 °C. The residue was dried on high-vacuum pump for 1 h to remove the trace of DMF to afford a yellow solid. This solid was dissolved in dry CH_{2}Cl_{2} (100 mL), triethylxonium tetrafluoroborate (50.0 mL, 50.0 mmol, 1 M in CH_{2}Cl_{2}) was added at 0 °C, then DIPEA (13.1 mL, 75.0 mmol) was added dropwise. After 1 minute,
TLC showed completion of this reaction. Then this reaction was quenched with saturated NH₄Cl solution (100 mL), extracted with CH₂Cl₂ (3 x 100 mL), washed with saturated NaHCO₃ solution and brine, dried over Na₂SO₄ and concentrated under reduced pressure. The unstable crude product was passed through a short silica pad (hexanes:EtOAc = 6:1, 2000 mL), concentrated and dried on high-vacuum pump and was used to next step directly. To a solution of this crude ester 13 (20.0 g, ~ 55.5 mmol) in dry CH₂Cl₂ (200 mL) was added 2,6-lutidine (13.1 mL, 111 mmol) at 0 ºC, followed by addition of TMSOTf (13.0 mL, 72.0 mmol) dropwise. After 30 min, the reaction mixture was diluted with hexanes (500 mL), quenched with 5% NaHCO₃ solution (200 mL), extracted with hexanes (3 x 300 mL), the combined organic extracts were dried over Na₂SO₄ and concentrated under reduced pressure. The residue was further dried on high-vacuum pump for 10 min. The unstable crude TMS-enol ether was dissolved in dry THF (200 mL), cooled to -78 ºC, methyl iodide (34.0 mL, 0.55 mol) was added in, followed by addition of TBAF solution dropwise (55.5 mL, 55.5 mmol, 1M in THF). This reaction mixture was then allowed to warm to RT slowly over 30 min, and stirred at RT for extra 2 h before it was quenched with saturated NH₄Cl solution (100 mL). The mixture was extracted with EtOAc (3 x 200 mL), the combined organic phase was washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified via silica flash column chromatography (hexanes:EtOAc = 100:1 to 10:1) to afford 15 as a yellow oil (9.33 g, 43% over 2 steps). Rₜ = 0.70 (silica gel, hexanes:EtOAc = 6:1); [α]D²²³ = -91.3 (c 1.40, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 5.99 (m, 1H), 5.72 (t, J = 2.3 Hz, 1H), 5.02 (d, J = 16.6 Hz, 1H), 4.96 (d, J = 10.3 Hz, 1H), 4.19 (m, 1H), 4.10 (m, 1H), 4.03 (t, J = 8.7 Hz, 1H), 2.81 (m, 1H), 2.44-2.30 (m, 5H), 2.07 (m, 1H), 1.53 (m, 1H), 1.47 (s, 3H), 1.25 (t, J = 12.5 Hz, 3H), 0.90 (s, 9H), 0.04 (s, 3H), 0.04 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 208.0, 172.0, 145.4,
136.4, 125.9, 116.5, 82.9, 61.9, 58.9, 50.8, 39.8, 36.5, 36.2, 34.4, 26.0, 19.8, 18.2, 14.0, -4.4, -4.8; HRMS (ESI) m/e 393.2458 [M+H⁺] calcd for C_{22}H_{37}O_{4}Si⁺: 393.2456.

16: To a solution of 15 (17 g, 43 mmol) in dry THF (200 mL) was added LiAlH₄ solution (165 mL, 0.32 mol, 2M in THF) at 0 ºC. This reaction mixture was stirred for 30 min before it was carefully quenched with 2N NaOH solution (200 mL). The mixture was taken with EtOAc (200 mL) and filtrated through Celite® and washed thoroughly with EtOAc (1000 mL). The organic phase was separated and the aqueous phase was re-extracted with EtOAc (2 x 200 mL). The combined organic extracts were washed with brine, dried over Na₂SO₄ and concentrated under reduced pressure. The crude diol was used to next step directly.

The crude diol was dissolved in CH₂Cl₂ (200 mL) and was cooled to 0 ºC. Imidazole (5.37 g, 80.0 mmol) was added in followed by the adding of TBS-Cl solution (6.78 g, 45.0 mmol) in CH₂Cl₂ (20 mL) slowly. After 30 min, this reaction mixture was quenched with saturated NH₄Cl solution (200 mL), extracted with CH₂Cl₂ (3 x 200 mL), washed with brine and dried over Na₂SO₄, then concentrated under reduced pressure. The crude mono-TBS-ether was used to next step directly.

The crude mono-TBS-ether was dissolved in dry DMSO (200 mL), IBX (33.6 g, 0.12 mol) was added in and this reaction mixture was heated to 80 ºC for 1 h. Upon completion, the reaction mixture was cooled to RT and water (200 mL) was added in and the reaction mixture
was filtered through Celite®, the filtrates were extracted with EtOAc (3 x 200 mL). The combined organic extracts were then washed with brine, dried over Na2SO4 and concentrated under reduced pressure. The obtained residue was purified via silica flash column chromatography (hexanes:EtOAc = 100:1 to 20:1) to afford 16 as a white solid (17.4 g, 85% over 3 steps). Rf = 0.32 (silica gel, hexanes:EtOAc = 20:1); [α]D23 -22.1 (c 0.82, CHCl3); 1H NMR (500 MHz, CDCl3) δ 6.04 (m, 1H), 5.51 (br s, 1H), 5.04 (d, J = 18.4 Hz, 1H), 4.95 (d, J = 10.3 Hz, 1H), 4.01 (t, J = 8.6 Hz, 1H), 3.73 (d, J = 9.7 Hz, 1H), 3.65 (d, J = 9.7 Hz, 1H), 2.58-2.45 (m, 3H), 2.32 (m, 3H), 2.00 (m, 1H), 1.17 (s, 3H), 1.16 (m, 1H), 0.91 (s, 9H), 0.85 (s, 9H), 0.05 (s, 6H), 0.01 (s, 6H); 13C NMR (125 MHz, CDCl3) δ 213.3, 149.0, 136.9, 123.7, 116.3, 83.3, 69.6, 55.1, 50.4, 39.7, 36.4, 35.8, 34.0, 26.0, 25.9, 20.7, 18.5, 18.2, -4.5, -4.7, -5.4, -5.4; HRMS (ESI) m/e 465.3219 [M+H+] calcd for C26H49O3Si2+: 465.321.

8: To a solution of ketone 16 (10.5 g, 22.6 mmol) in dry THF (200 mL) was added in KHMS (226 mL, 113 mmol, 0.5 M in Toluene) dropwise at – 78 ºC and stirred for 30 min. A solution of PhNTf2 (24.2 g, 67.8 mmol) in THF (50 mL) was added in and the reaction mixture was stirred for 30 min at the same temperature before it was warmed up to RT over 30 min. The reaction was quenched by solution with saturated NH4Cl solution (100 mL) and extracted with EtOAc (3 x 200 mL). The combined organic phase was washed with brine and dried over Na2SO4, concentrated under reduced pressure and purified via silica flash column chromatography (hexanes:EtOAc = 100:1) to afford the vinyl triflate 17 as a white solid.
(12.8 g, 95%).

The vinyl triflate 17 obtained above (12.8 g, 21.5 mmol) was dissolved in DMF/MeOH (150 mL/50 mL, 3:1), Pd(PPh3)4 (248 mg, 0.21 mmol) and triethylamine (9.10 mL, 64.3 mmol) was added. This orange solution was degassed under argon atmosphere for 5 min, followed by bubbling in carbon monoxide for 5 min. This solution was then heated to 50 ºC for 2 h under carbon monoxide atmosphere before it was concentrated under reduced pressure. The residue was passed through a short silica pad (hexanes:EtOAc = 50:1, 2000 mL), concentrated and re-dissolved in dry CH2Cl2 (200 mL), TFA (5.9 mL, 77.0 mmol) was added in and this reaction mixture was stirred at RT for 5 h before it was quenched with saturated NaHCO3 solution (50 mL). The mixture was extracted with CH2Cl2 (3 x 100 mL), the combined organic phase was washed with brine and dried over Na2SO4, concentrated under reduced pressure and purified via silica flash column chromatography (hexanes:EtOAc = 100:1 to 10:1) to afford the lactone 8 as a white solid (9.20 g, 80%; 69% over two steps). Rf = 0.20 (silica gel, hexanes:EtOAc = 20:1); [α]D23 – 1.8 (c 0.49, CHCl3); 1H NMR (500 MHz, CDCl3) δ 6.90 (dd, J = 7.9 Hz, 3.0 Hz, 1H), 5.86 (m, 1H), 5.64 (br s, 1H), 4.90 (d, J = 13.2 Hz, 1H), 4.87 (d, J = 19.1 Hz, 1H), 4.13 (d, J = 8.3 Hz, 1H), 4.10 (t, J = 9.8 Hz, 1H), 3.99 (d, J = 8.3 Hz, 1H), 2.56 (dd, J = 15.6 Hz, 7.8 Hz, 1H), 2.47 (m, 1H), 2.36 (m, 1H), 2.19 (m, 2H), 1.95 (dd, J = 16.1 Hz, 3.0 Hz, 1H), 1.32 (s, 3H), 0.92 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H); 13C NMR (125 MHz, CDCl3) δ 169.7, 147.8, 136.6, 135.0, 134.7, 124.3, 116.6, 82.5, 76.3, 54.8, 41.7, 40.1, 37.0, 35.8, 27.5, 25.9, 18.2, -4.4, -4.7; HRMS (ESI) m/e 361.2196 [M+H+] calcd for C21H33O3Si+: 361.2193.
20: To a solution of 8 (4.70 g, 13.0 mmol) in MeOH (100 mL) was added a pre-mixed solution of 3N NaOH (13 mL) and 30% H$_2$O$_2$ (13 mL) dropwise at 0 ºC. This reaction mixture was warmed up to RT and vigorous stirred for 5 h. The mixture was then diluted with water, acidified with 2N HCl to pH = 1, separated with EtOAc/brine (200mL/200mL) and the aqueous phase was extracted with EtOAc (2 x 200 mL). The organic phase was combined, dried over Na$_2$SO$_4$ and concentrate under reduced pressure to afford 20 (4.86 g, 99%) as a white solid. The obtained epoxide 20 was pure enough to use without further purification. $R_f$ = 0.18 (silica hexanes:EtOAc = 20:1); $[\alpha]_D^{22} + 9.0$ (c 0.92, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) δ 5.86 (m, 1H), 5.70 (m, 1H), 5.03 (m, 2H), 4.34 (d, $J$ = 8.8 Hz, 1H), 4.17 (d, $J$ = 9.3 Hz, 1H), 3.94 (t, $J$ = 9.8 Hz, 1H), 3.61 (dd, $J$ = 6.3 Hz, 2.4 Hz, 1H), 2.52-2.40 (m, 3H), 2.28-2.20 (m, 2H), 1.39 (m, 1H), 1.38 (s, 3H), 0.91 (s, 9H), 0.06 (s, 3H), 0.05 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 173.2, 143.3, 135.8, 126.3, 117.7, 82.1, 75.6, 61.4, 58.5, 52.5, 40.6, 39.0, 38.2, 37.5, 26.0, 21.8, 18.2, -4.3, -4.7; HRMS (ESI) m/e 399.1960 [M+Na$^+$] calcd for C$_{21}$H$_{32}$O$_4$SiNa$^+$: 399.1962.

21, 22 and 23: Epoxide 20 (6.25 g, 16.6 mmol) was dissolved in 1,4-dioxane (180 mL) and
water (60 mL). To this solution 2,6-lutidine (3.84 mL, 33.2 mmol), OsO4 (1.05 mL, 4% solution in H2O, 0.166 mmol) was added, then NaIO4 (14.4 g, 66.4 mmol) was added portionwise at 0 ºC. This reaction mixture was then warmed up to RT and stirred for 12 h. The reaction mixture was diluted with water (200 mL) and extracted with CH2Cl2 (3 x 200 mL). The organic phase was dried over Na2SO4 and concentrated under reduced pressure to afford the aldehyde 21 as a white solid, which was clean enough to be used for next reaction.

21: \( R_f = 0.5 \) (silica gel, hexanes:EtOAc = 5:1); \( [\alpha]_D^{23} = +0.05 \) (c 0.5, CHCl3); \(^1\)H NMR (500 MHz, CDCl3) δ 9.85 (dd, \( J = 4.0 \) Hz, 1.2 Hz, 1H), 5.68 (dd, \( J = 2.6 \) Hz, 1.5 Hz, 1H), 4.44 (d, \( J = 9.8 \) Hz, 1H), 4.20 (d, \( J = 9.8 \) Hz, 1H), 4.02 (t, \( J = 8.0 \) Hz, 1H), 3.65 (dd, \( J = 6.3 \) Hz, 2.3 Hz, 1H), 2.67 (dd, \( J = 12.6 \) Hz, 1.1 Hz, 1H), 2.64 (ddd, \( J = 16.6 \) Hz, 8.0 Hz, 3.4 Hz, 1H), 2.57 (dd, \( J = 14.3 \) Hz, 6.3 Hz, 1H), 2.37 (dd, \( J = 12.6 \) Hz, 4.0 Hz, 1H), 2.11 (ddd, \( J = 16.6 \) Hz, 8.6 Hz, 1.7 Hz, 1H), 1.49 (dd, \( J = 14.9 \) Hz, 3.0 Hz, 1H), 1.39 (s, 3H), 0.90 (s, 9H), 0.08 (s, 3H), 0.06 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl3) δ 201.2, 172.7, 142.5, 126.6, 81.1, 75.7, 67.1, 61.2, 57.7, 53.4, 47.3, 40.6, 37.4, 25.8, 21.5, 18.1, -4.4, -4.9; HRMS (ESI) m/e 405.1756 \([\text{M}+\text{Na}^+]\) calcd for C20H30O5SiNa+: 405.1755.

To a solution of the aldehyde 21 obtained above (~ 6.2 g, 16.4 mmol) in acetone (400 mL) was added Jones reagent (37.0 mL, 98.4 mmol, 2.67 M) dropwise at 0 ºC, and this reaction mixture was stirred at 0 ºC for 30 min. Ethanol (50 mL) was carefully dropped in to quench this reaction, followed by dropping the saturated NaHCO3 solution (50 mL). The mixture was stirred for 5 min before it was filtrated through Celite®, and the filter cake was then washed thoroughly with EtOAc (1000 mL). The combined organic extracts were dried over Na2SO4 and concentrated under reduced pressure. The crude residue was purified via column chromatography (hexanes:CH2Cl2 = 1:1 to 1:3 to 100% CH2Cl2, then CH2Cl2:MeOH =200:1 to
50:1) afford the desire lactone 22 as a white solid (4.58 g, 70% over 2 steps), and side product 23 (1.54 g, 20% over 2 steps) as a white solid.

**22:** $R_f = 0.48$ (silica gel, hexanes:EtOAc = 2:1); $[\alpha]_D^{22} = -2.6$ (c 0.58, CHCl$_3$); $^1$H NMR (500 MHz, CDCl$_3$) δ 5.78 (m, 1H), 4.65 (dd, $J = 4.4$ Hz, 1.5 Hz, 1H), 4.06 (t, $J = 7.8$ Hz, 1H), 3.97 (d, $J = 9.8$ Hz, 1H), 3.85 (d, $J = 9.8$ Hz, 1H), 3.02 (d, $J = 19.1$ Hz, 1H), 2.51-2.43 (m, 2H), 2.20 (m, 1H), 2.07 (m, 1H), 1.94 (m, 1H), 1.32 (s, 3H), 0.90 (s, 9H), 0.08 (s, 6H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 177.6, 170.2, 144.1, 126.5, 79.3, 79.3, 76.8, 76.3, 45.4, 42.5, 37.6, 36.7, 29.6, 25.9, 21.6, 18.1, -4.3, -4.7; HRMS (ESI) m/e 395.1886 [M+H$^+$] calcd for C$_{20}$H$_{31}$O$_6$Si$: 395.1884$

**23:** $[\alpha]_D^{22} = -41.8$ (c 0.5, CH$_3$OH); $^1$H NMR (500 MHz, CDCl$_3$) δ 5.79 (m, 1H), 4.76 (dd, $J = 6.0$ Hz, 2.4 Hz, 1H), 4.27 (d, $J = 3.6$ Hz, 2H), 3.73 (dd, $J = 4.8$ Hz, 2.0 Hz, 1H), 2.92 (m, 1H), 2.78 (d, $J = 14.4$ Hz, 1H), 2.69-2.62 (m, 2H), 2.49 (dd, $J = 11.6$ Hz, 1.2 Hz, 1H), 1.73 (dd, $J = 11.6$ Hz, 2.0 Hz, 1H), 1.50 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 174.1, 171.5, 141.1, 128.6, 86.8, 74.5, 62.1, 57.4, 53.8, 39.0, 38.8, 38.2, 36.5, 21.3; HRMS (ESI) m/e 263.0915 [M+H$^+$] calcd for C$_{14}$H$_{15}$O$_5$: 263.0914

**25:** To a solution of 22 (56 mg, 0.14 mmol) in THF/pyridine (900 µl, 2:1, v/v) was added an aqueous solution of OsO$_4$ (902 µl, 4% in H$_2$O, 0.14 mmol). This reaction mixture was stirred for 30 min. An analytical sample of the osmium-pyridine complex 24 was purified via preparative TLC (CH$_2$Cl$_2$:MeOH, 30:1 x 2). The residue obtained above was dissolved in MeOH/H$_2$O (1 ml,
3:1, v/v), sodium bisulfite (400 mg) was added and the mixture was heated at 60 °C for 2 h. The solvent was removed under reduced pressure and the residue was purified via silica flash column chromatography (CH₂Cl₂:MeOH = 100:1 to 20:1) afford the product 25 as a white foam (47 m g, 79%). 24: Rᵣ = 0.52 (silica gel, CH₂Cl₂:MeOH = 10:1); ¹H NMR (500 MHz, CDCl₃) δ 8.74 (m, br, 4 H), 7.83 (m, br, 2H), 7.45 (m, br, 4 H), 4.95 (dd, J = 6.4 Hz, 6.4 Hz, 1H), 4.60 (s, br, 1H), 4.53 (d, J = 10.3 Hz, 1H), 3.95 (d, J = 10.3 Hz, 1H), 3.82 (dd, J = 4.9 Hz, 4.9 Hz, 1H), 3.28 (d, J = 19.1 Hz, 1H), 2.45 (m, 1H), 2.29 (d, J = 19.1 Hz, 1H), 2.27 (m, 1H), 2.03 (dd, J = 14.2 Hz, 4.0 Hz, 2H), 1.61 (s, 3H), 0.85 (s, 9H), 0.07 (s, 3H), 0.04 (s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 176.7, 170.6, 149.2 (br), 140.3 (br), 124.9 (br), 99.1, 93.2, 92.7, 87.8, 73.4, 48.9, 48.5, 37.3, 34.0, 30.7, 26.0, 25.7, 19.0, 17.8, -4.4, -5.3; 25: Rᵣ = 0.50 (silica gel, CH₂Cl₂:MeOH = 10:1); ¹H NMR (500 MHz, CDCl₃) δ 4.18 (d, J = 9.8 Hz, 1H), 4.01 (d, J = 8.6 Hz, 1H), 3.93 (d, J = 8.6 Hz, 1H), 3.74 (m, 1H), 3.62 (dd, J = 13.2 Hz, 8.1 Hz, 1H), 3.55 (d, J = 21.2 Hz, 1H), 2.43 (d, J = 18.9 Hz, 1H), 2.30 (m, 1H), 2.06 (d, J = 12.0 Hz, 1H), 1.84 (m, 1H), 1.70 (m, 1H), 1.43 (s, 3H), 0.88 (s, 9H), 0.08 (s, 6H); HRMS (ESI) m/e 429.1939 [M+H⁺] calcd for C₂₀H₃₃O₈Si⁺: 429.1939.

7: To a solution of 22 (3.95 g, 10.0 mmol) in THF (100 mL) was added TBAF solution (20.0 mL, 20.0 mmol, 1 M in THF) dropwise at RT, then this reaction mixture was stirred at RT for 30 min. pH = 7 buffer solution (20 mL) was added to quench this reaction, and the mixture
was diluted with EtOAc (1000 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified via silica flash column chromatography (CH₂Cl₂:MeOH = 100:1 to 20:1) afford the product 7 as a white foam (2.66 g, 95%). \( R_f = 0.70 \) (silica gel, CH₂Cl₂:MeOH = 5:1); [α]D²³⁳ ~ 38.1 (c 0.67, MeOH); \(^1\)H NMR (500 MHz, CD₃OD) \( \delta \) 5.85 (m, 1H), 4.70 (dd, \( J = 4.6 \text{ Hz, 1.7 Hz, 1H} \)), 4.02 (t, \( J = 7.9 \text{ Hz, 1H} \)), 3.99 (d, \( J = 10.3 \text{ Hz, 1H} \)), 3.72 (d, \( J = 9.7 \text{ Hz, 1H} \)), 2.95 (d, \( J = 18.9 \text{ Hz, 1H} \)), 2.52-2.41 (m, 2H), 2.24-2.14 (m, 2H), 1.91 (m, 1H), 1.29 (s, 3H); \(^{13}\)C NMR (125 MHz, CD₃OD) \( \delta \) 177.4, 171.4, 144.6, 126.1, 79.7, 78.3, 76.6, 75.3, 44.8, 42.2, 36.1, 36.0, 29.0, 20.5; HRMS (ESI) m/e 281.1021 [M+H⁺] calcd for C₁₄H₁₇O₆⁺: 281.1020.

6: To a solution of 7 (870 mg, 3.10 mmol) in THF (30 mL) was added \( m \)CPBA (3.20 g, 13 mmol, ~ 70%) portionwise and warmed up to 50 °C for 3 h. This mixture was then cooled to RT and quenched with saturated NaHCO₃ solution/saturated Na₂S₂O₃ solution (10mL/10mL). Then the mixture was diluted with EtOAc (500 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The afforded crude epoxide 26 was used to next step directly.

26: An analytical sample of the epoxide 26 was purified via preparative TLC (CH₂Cl₂:MeOH, 20:1 x 2). \( R_f = 0.45 \) (silica gel, CH₂Cl₂:MeOH = 10:1); \(^1\)H NMR (500 MHz, CD₃OD) \( \delta \) 4.65 (dd, \( J = 2.9 \text{ Hz, 2.9 Hz, 1H} \)), 4.07 (d, \( J = 10.3 \text{ Hz, 1H} \)), 3.91 (d, \( J = 10.3 \text{ Hz, 1H} \)), 3.74 (d, \( J = 7.5 \text{ Hz, 1H} \)), 3.63 (s, br, 1H), 2.85 (dd, \( J = 19.5 \text{ Hz, 19.5 Hz, 2H} \)), 2.31 (ddd, \( J = 17.2 \text{ Hz, 8.6 Hz, 1.2 Hz, 1H} \)), 2.07 (dd, \( J = 16.1 \text{ Hz, 13.2 Hz, 2H} \)), 1.99 (d, \( J = 15.5 \text{ Hz, 1H} \)), 1.02
(s, 3H); $^{13}$C NMR (125 MHz, CD$_3$OD) $\delta$ 176.4, 170.0, 79.0, 78.2, 76.8, 72.9, 70.1, 61.9, 43.2, 41.7, 33.8, 33.0, 28.9, 18.0; HRMS (ESI) m/e 319.0780 [M+Na$^+$] calcd for C$_{14}$H$_{16}$O$_7$Na$^+$: 319.0788.

Epoxide 26 (~ 3 mmol) was diluted with acetone (30 mL), sonicated for 10 min, and the Dess-Martin periodinane (2.54 g, 6 mmol) was added. This reaction mixture was stirred vigorously (sonication was applied in larger scale) at RT for 2 h and quenched with saturated NaHCO$_3$ solution/saturated Na$_2$S$_2$O$_3$ solution (10mL/10mL). Then the mixture was diluted with EtOAc (500 mL), dried over Na$_2$SO$_4$ and concentrated under reduced pressure to afford the crude product, which was purified via silica flash column chromatography (CH$_2$Cl$_2$:MeOH = 100:1 to 20:1) afford the product 6 as a white solid (346 mg, 38%). $R_f$ = 0.50 (silica gel, CH$_2$Cl$_2$:MeOH = 20:1 x 2 times); $[\alpha]_D^{23}$ – 13.1 (c 0.40, MeOH); $^1$H NMR (500 MHz, CD$_3$OD) $\delta$ 7.96 (d, $J = 5.9$ Hz, 1H), 6.52 (d, $J = 5.9$ Hz, 1H), 4.49 (d, $J = 9.8$ Hz, 1H), 4.02 (d, $J = 9.8$ Hz, 1H), 3.69 (dd, $J = 9.8$ Hz, 3.9 Hz, 1H), 3.21 (d, $J = 19.0$ Hz, 1H), 2.86 (d, $J = 19.1$ Hz, 1H), 2.20 (m, 1H), 2.10 (m, 1H), 1.41 (s, 3H); $^{13}$C NMR (125 MHz, CD$_3$OD) $\delta$ 209.1, 177.5, 174.8, 160.5, 136.2, 93.3, 80.1, 74.9, 72.9, 52.1, 49.5, 39.8, 34.1, 19.4; HRMS (ESI) m/e 317.0634 [M+Na$^+$] calcd for C$_{14}$H$_{14}$O$_7$Na$^+$: 317.0633.

30: A pressure glass reactor was filled with 6 (294 mg, 1.00 mmol), MeOH (5 mL) and palladium (53.0 mg, 5 mol%, 10% on charcoal), then this reactor was loaded on a shaking-hydrogenator and was shaken under hydrogen atmosphere (6 bar) at RT for 24 h. The
pressure was released slowly and the mixture was filtered through a short silica pad. The filter pad was washed with MeOH (5 x 20 mL), and the combined filtrates were concentrated to afford the corresponding reduced ketone, then it was dissolved in THF (5 mL), 2,6-lutidine (463 µL, 4.00 mmol) was added followed by TESOTf (452 µL, 2.00 mmol) at 0 ºC. This reaction mixture was then allowed to warm up to RT and stirred for 30 min before it was quenched with saturated NaHCO₃ solution (5 mL). This mixture was diluted with EtOAc (200 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified via silica flash column chromatography (CH₂Cl₂:MeOH = 200:1 to 50:1) afford the product **30** as a colorless oil (369 mg, 90%). \( R_f = 0.85 \) (silica gel, CH₂Cl₂:MeOH = 20:1); \([\alpha]_D^{23} – 8.5 \) (c 1.32, MeOH);

\( ^1\text{H NMR} (500 \text{ MHz, CD}_3\text{OD}) \delta 4.36 \) (d, \( J = 9.8 \) Hz, 1H), 4.10 (m, 1H), 3.90 (d, \( J = 8.6 \) Hz, 1H), 3.51 (d, \( J = 18.9 \) Hz, 1H), 2.75 (d, \( J = 18.9 \) Hz, 1H), 2.56-2.35 (m, 3H), 2.25 (m, 1H), 1.95 (dd, \( J = 15.5 \) Hz, 3.5 Hz, 1H), 1.81 (dd, \( J = 14.9 \) Hz, 2.9 Hz, 1H), 1.33 (s, 3H), 0.97 (t, \( J = 8.0 \) Hz, 9H), 0.65 (q, \( J = 8.6 \) Hz, 6H); \( ^{13}\text{C NMR} (125 \text{ MHz, CD}_3\text{OD}) \delta 217.9, 177.6, 174.2, 93.1, 79.3, 72.8, 72.2, 53.6, 47.4, 37.4, 32.8, 28.2, 27.3, 17.2, 5.8, 4.1; \) HRMS (ESI) m/e 433.1655 [M+Na⁺] calcd for C₂₀H₃₀O₇SiNa⁺: 433.1653.

**31**: To a solution of **30** (41.0 mg, 0.10 mmol) in dry THF (600 µL) was added KHMDS (150 µL, 0.15 mmol, 1 M in THF) at –78 ºC and stirred for 30 min, then a solution of Comins reagent (N-(5-chloro-2-pyridyl)triflimide, 34.2 mg, 0.11 mmol) in THF (200 µL) was added in dropwise and stirred for another 30 min at –78 ºC before it was warmed up to RT and stirred...
for another 30 min. This reaction mixture was then quenched with saturated NH₄Cl solution (500 µL), diluted with EtOAc (100 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified via silica flash column chromatography (hexanes:EtOAc = 50:1 to 4:1) to afford the corresponding vinyl triflate as light colorless oil (34.7 mg, 64%). This vinyl triflate (34.7 mg, 0.064 mmol) was then dissolved in dry THF (300 µL), Pd(PPh₃)₄ (37.0 mg, 0.032 mmol) was added in, followed by a solution of AlMe₃ (640 µL, 1.28 mmol, 2M in hexanes). This reaction mixture was stirred at RT for 2 h before it was carefully quenched with saturated NaHCO₃ solution (500 µL). This mixture was diluted with EtOAc (100 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified via silica flash column chromatography (hexanes:EtOAc = 50:1 to 4:1) to afford the 31 as light colorless oil (23.3 mg, 89%; 57% over 2 steps). Rᵣ = 0.37 (silica gel, hexanes:EtOAc= 3:1); [α]D²³ + 9.6 (c 1.40, MeOH); ¹H NMR (500 MHz, CD₃OD) δ 5.37 (br s, 1H), 4.38 (d, J = 8.6 Hz, 1H), 3.94 (dd, J = 6.9 Hz, 3.5 Hz, 1H), 3.88 (d, J = 9.2 Hz, 1H), 3.23 (d, J = 18.9 Hz, 1H), 2.74 (m, 1H), 2.70 (d, J = 18.9 Hz, 1H), 2.55 (d, J = 17.8 Hz, 1H), 2.07(dd, J = 14.9 Hz, 6.9 Hz, 1H), 1.78 (dd, J = 14.9 Hz, 3.4 Hz, 1H), 1.69 (br s, 3H), 1.28 (s, 3H), 0.97 (t, J = 8.1 Hz, 9H), 0.64 (q, J = 7.5 Hz, 6H); ¹³C NMR (125 MHz, CD₃OD) δ 177.0, 175.8, 142.6, 121.1, 96.0, 79.6, 73.3, 72.8, 54.3, 47.8, 40.8, 37.4, 32.9, 18.1, 10.7, 5.8, 4.2; HRMS (ESI) m/e 431.1864 [M+Na⁺] calcd for C₂₁H₃₂O₆SiNa⁺: 431.1860.

(−)-2: A high pressure steel autoclave equipped with magnetic stir bar was filled with olefin
31 (20.0 mg, 0.049 mmol), platinum dioxide (2.2 mg, 9.8 µmol) and MeOH (2.0 mL). The autoclave was pressurized to 90 atm with H₂ and the suspension was vigorously stirred at RT for 24 h. The pressure was released slowly and the mixture was filtered through a short silica pad. The filter pad was washed with MeOH (5 x 10 mL), and the combined filtrates were concentrated to afford the crude reduced product 32 with some inseparable impurities. This crude mixture (~ 20 mg, ~ 0.049 mmol) was then dissolved in dry THF (300 µL) and cooled to −78 ºC, to this solution was added NaHMDS (196 µL, 0.196 mmol) dropwise and stirred for 15 min, then a solution of (±)-trans-2-(phenylsulfonyl)-3-phenyloxaziridine (64.0 mg, 0.245 mmol) in THF (100 µL) was added in dropwise and stirred for 30 min before it was warmed up slowly to RT. Then this reaction was quenched with saturated NH₄Cl solution (1 mL) and diluted with EtOAc (200 mL), dried over Na₂SO₄ and concentrated under reduced pressure. Purification via silica flash column chromatography (hexanes:EtOAc = 40:1 to 5:1) afforded the α-hydroxyl lactone 33 (~ 10 mg) with trace of inseparable impurities. This α-hydroxyl lactone (~ 10 mg, ~ 0.024 mmol) was dissolved in acetone (1 mL) then was added Jones reagent (44 µL, 0.120 mmol, 2.67 M) at 0 ºC, stirred for 15 min and carefully quenched with MeOH (100 µL) followed by saturated NaHCO₃ solution (100 µL). This mixture was diluted with EtOAc (100 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified via silica flash column chromatography (CH₂Cl₂:MeOH = 200:1 to 20:1) to afford (–)-jiadifenolide (2) as small white crystals (5.10 mg, 33% over 3 steps). Rₜ = 0.23 (silica gel, CH₂Cl₂:MeOH = 20:1); [α]D₂³ = 73.7 (c 0.38, MeOH), Reported value for natural 2: [α]D₂³ = 56.8 (c 1.14, MeOH). ¹H NMR (500 MHz, CD₃OD) δ 4.61 (d, J = 9.2 Hz, 1H), 4.42 (d, J = 6.3 Hz, 1H), 3.80 (d, J = 9.8 Hz, 1H), 2.47 (dd, J = 13.2 Hz, 5.8 Hz, 1H), 2.22 (m, 1H), 2.09 (d, J = 13.2 Hz, 1H), 2.08 (m, 1H), 2.01 (m, 1H), 1.89 (m, 1H), 1.29 (m, 1H), 1.23 (s, 3H),
1.21 (d, $J = 7.6$ Hz, 3H); $^{13}$C NMR (125 MHz, CD$_3$OD) $\delta$ 178.3, 173.6, 101.9, 97.4, 79.1, 77.6, 74.6, 58.8, 48.1, 41.6, 35.2, 33.0, 32.1, 19.9, 14.7; HRMS (ESI) m/e 333.0942 [M+Na$^+$] calcd for C$_{15}$H$_{18}$O$_7$Na$^+$: 333.0945.

35: To a solution of alcohol 7 (420 mg, 1.5 mmol) in anhydrous THF (20 mL) was added Martin sulfurane (4.0 g, 9.0 mmol) in one portion at RT. This dark brown solution was allowed to stir at the same temperature for 2 h before rotavaped to dryness. The residue was redissolved in MeOH (20 mL), Pd/C (10%, 530 mg, 0.5 mmol) was then loaded under argon atmosphere. This crude diene was then selectively hydrogenated using a double-layer H$_2$-balloon for 30 min. The mixture was passed through a short silica pad and thoroughly rinsed (CH$_2$Cl$_2$:MeOH, 20:1) and the filtrate was concentrated under reduced pressure. The residue was purified via silica flash column chromatography (CH$_2$Cl$_2$:MeOH = 200:1 to 100:1) to afford compound 35 as white foams (284 mg, 72% over 2 steps). $R_f = 0.65$ (silica gel, EtOAc:Hexanes = 2:1); $[\alpha]_D^{23} = -44.6$ (c 1.21, CH$_2$Cl$_2$); $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 5.88, (br s, 1H), 4.69 (dd, $J = 2.7$ Hz, 2.7 Hz, 1H), 3.98 (d, $J = 9.8$ Hz, 1H), 3.85 (d, $J = 9.8$ Hz, 1H), 3.08 (br s, 1H), 2.77 (d, $J = 18.9$ Hz, 1H), 2.62 (d, $J = 18.9$ Hz, 1H), 2.45-2.33 (m, 2H), 1.94 (m, 1H), 1.84 (m, 1H), 1.71-1.60 (m, 2H), 1.36 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 177.6, 169.1, 144.4, 130.5, 79.9, 77.0, 75.9, 43.9, 43.4, 42.4, 40.0, 31.9, 29.1, 22.3; HRMS (ESI): m/e 265.1072 [M+H$^+$] calcd for C$_{14}$H$_{17}$O$_5$: 265.1071.
36: To a solution of compound 35 (140 mg, 0.53 mmol) in anhydrous EtOAc (4 mL) was added tert-butyl hydroperoxide (960 µL, ~ 10 eq., 5~6 M in decane) and 3Å molecular sieves (200 mg). The mixture was stirred for 30 min at RT. Manganese(III) acetate dehydrate (28.4 mg, 0.11 mmol) was added to this mixture in one portion, and this reaction mixture was heated at 40 °C for 16 h. The solution was cooled down, silica gel (2 g) was added in and rotavaped to dryness. The silica-absorbed crude product was then purified via silica flash column chromatography (CH₂Cl₂:MeOH = 100:1 to 20:1) to afford enone 36 as white solid (96 mg, 65%). \( R_f = 0.25 \) (silica gel, CH₂Cl₂:MeOH = 20:1); \( \alpha_D^{24} = 82.3 \) \( (c \ 1.42, \text{MeOH}) \); \(^1\text{H NMR} \) (500 MHz, CD₃OD) δ 6.29, (s, 1H), 4.78 (dd, \( J = 4.6 \text{ Hz}, 1.7 \text{ Hz}, 1 \text{H} \)), 4.14 (d, \( J = 10.3 \text{ Hz}, 1 \text{H} \)), 4.03 (d, \( J = 10.9 \text{ Hz}, 1 \text{H} \)), 3.11 (d, \( J = 18.9 \text{ Hz}, 1 \text{H} \)), 2.87 (dd, \( J = 19.5 \text{ Hz}, 2.7 \text{ Hz}, 1 \text{H} \)), 2.64 (d, \( J = 18.9 \text{ Hz}, 1 \text{H} \)), 2.43 (dd, \( J = 14.3 \text{ Hz}, 4.0 \text{ Hz}, 1 \text{H} \)), 2.40 (d, \( J = 18.9 \text{ Hz}, 1 \text{H} \)), 2.32 (dt, 14.3 Hz, 2.3 Hz, 1H), 1.45 (s, 3H); \(^{13}\text{C NMR} \) (125 MHz, CD₃OD) δ 206.8, 181.1, 177.3, 170.4, 133.9, 80.2, 80.0, 74.4, 51.3, 45.5, 43.2, 42.4, 32.1, 22.4; HRMS (ESI): m/e 277.0719 [M–H]⁻ caleed for C₁₄H₁₃O₆: 277.0718.

37 and 38: To a solution of enone 36 (20 mg, 71.9 µmol) in THF (800 µL) was added freshly
prepared LDA solution (360 µL, 1M in THF) at –78 °C, this solution was slowly warmed up to –15 °C over 1 h and stirred at –15 °C for 30 min. This solution was cooled to –40 °C, MeI (14 µL, 216 µmol) was dropped in slowly. This reaction mixture was slowly warmed up to –10 °C over 1 h and stirred at –10 °C for 30 min before quenched with saturated NH₄Cl solution (1 mL). This mixture was diluted with EtOAc (200 mL) and dried over Na₂SO₄, filtrated and concentrated. The residue was purified via preparative TLC (CH₂Cl₂:MeOH:THF = 80:1:1 x 8 times) to afford compounds 37 and 38 as small white crystals.

37: 11 mg, 50%; Rᵣ = 0.38 (silica gel, CH₂Cl₂:MeOH:THF = 60:1:1 x 2 times); [α]D²² = –286.4 (c 0.16, THF); ¹H NMR (500 MHz, CD₃OD) δ 6.32 (s, 1H), 4.74 (dd, J = 4.6 Hz, 1.2 Hz, 1H), 4.14 (d, J = 10.3 Hz, 1H), 4.09 (d, J = 10.9 Hz, 1H), 2.83 (qd, J = 7.5 Hz, 1.7 Hz, 1H), 2.76 (d, J = 18.4 Hz, 1H), 2.63 (dd, J = 14.9 Hz, 4.6 Hz, 1H), 2.42 (d, J = 18.4 Hz, 1H), 2.16 (dt, 14.9 Hz, 1.8 Hz, 1H), 1.49 (d, J = 7.4 Hz, 3H), 1.46 (s, 3H); ¹³C NMR (125 MHz, CD₃OD) δ 206.8, 182.0, 177.4, 174.9, 134.3, 79.9, 79.6, 74.5, 47.8, 46.5, 45.8, 45.3, 27.7, 23.2, 18.6; HRMS (ESI): m/e 293.1023 [M+H⁺] calcd for C₁₅H₁₇O₆⁺: 293.1020.

38: 6 mg, 25%; Rᵣ = 0.4 (silica gel, CH₂Cl₂:MeOH:THF = 60:1:1 x 2 times); [α]D²³ = –276.6 (c 0.30, THF); ¹H NMR (500 MHz, CD₃OD) δ 6.32 (s, 1H), 4.77 (dd, J = 4.6 Hz, 1.2 Hz, 1H), 4.15 (d, J = 10.3 Hz, 1H), 4.11 (d, J = 10.9 Hz, 1H), 2.77 (qd, J = 7.5 Hz, 1.8 Hz, 1H), 2.58 (q, J = 7.6 Hz, 1H), 2.51 (dd, J = 14.9 Hz, 4.3 Hz, 1H), 2.07 (dt, J = 14.3, 1.8 Hz, 1H), 1.51 (d, J = 7.5 Hz, 3H), 1.45 (s, 3H), 1.14 (d, J = 7.5 Hz, 3H); ¹³C NMR (125 MHz, CD₃OD) δ 210.2, 181.3, 177.4, 175.0, 133.0, 80.1, 79.8, 74.5, 50.0, 49.4, 46.8, 45.5, 23.7, 23.3, 18.2, 12.7; HRMS (ESI): m/e 307.1177 [M+H⁺] calcd for C₁₆H₁₉O₆⁺: 307.1176.
39 and 40: To a solution of enone 36 (20 mg, 71.9 µmol) in THF (500 µL) was added NaHMDS (216 µL, 216 µmol, 1M in THF) dropwise at −78 °C, this solution was stirred for 20 min. Then the Davis oxaziridine ((±)-trans-2-(phenylsulfonyl)-3-phenyloxaziridine, 18.8 mg, 71.9 µmol) in THF (200 µL) was added in dropwise. This solution was stirred at the same temperature for 30 min before quenched with saturated NH₄Cl solution (1 mL). This mixture was diluted with EtOAc (200 mL) and dried over Na₂SO₄, filtrated and concentrated. The residue was purified via silica flash column chromatography (CH₂Cl₂:MeOH = 100:1 to 20:1) to afford compound 39 as small white crystals (13 mg, 61%) and compound 40 as white crystals (3 mg, 19%).

39: Rₜ = 0.4 (silica gel, CH₂Cl₂:MeOH = 20:1 x 2 times); [α]D²⁵ = −136.4 (c 0.83, THF); ¹H NMR (500 MHz, CD₃OD) δ 6.38 (s, 1H), 4.75 (dd, J = 4.6 Hz, 1.2 Hz, 1H), 4.12 (d, J = 10.9 Hz, 1H), 3.94 (d, J = 10.9 Hz, 1H), 4.09 (d, J = 1.2 Hz, 1H), 3.90 (d, J = 10.3 Hz, 1H), 3.00 (d, J = 18.9 Hz, 1H), 2.70 (dd, J = 14.4 Hz, 4.6 Hz, 1H), 2.38 (d, J = 18.9 Hz, 1H), 2.17(dt, J = 14.3, 1.8 Hz, 1H), 1.46 (s, 3H); ¹³C NMR (125 MHz, CD₃OD) δ 207.4, 178.8, 177.4, 171.2, 135.6, 80.2, 79.4, 74.5, 73.2, 49.5, 47.1, 45.3, 26.8, 22.9; HRMS (ESI): m/e 293.0668 [M–H]− calcd for C₁₄H₁₃O₇−: 293.0667.

40: [α]D²² = −38.8 (c 0.4, CH₃OH); ¹H NMR (500 MHz, CD₃OD) δ 6.35 (s, 1H), 4.78 (dd, J = 4.6 Hz, 1.2 Hz, 1H), 4.25 (s, 1H), 4.11 (d, J = 10.9 Hz, 1H), 3.96 (d, J = 1.7 Hz, 1H), 3.87 (d, J = 10.9 Hz, 1H), 2.53 (dd, J = 18.9 Hz, 4.0 Hz, 1H), 2.17(m, 1H), 1.43 (s, 3H); ¹³C NMR (125 MHz, CD₃OD) δ 207.4, 178.8, 177.4, 171.2, 135.6, 80.2, 79.4, 74.5, 73.2, 49.5, 47.1, 45.3, 26.8, 22.9; HRMS (ESI): m/e 293.0668 [M–H]− calcd for C₁₄H₁₃O₇−: 293.0667.
(1R, 10S)-2-oxo-3,4-dehydroxyneomajucin (ODNM, 4) and (–)-Jiadifenin (3): To freshly prepared LDA solution (476 µL, 1M in THF) was added a solution of 39 (28 mg, 95.2 µmol) in THF (1 mL) at –78 °C, this solution was slowly warmed up to –20 °C over 1 h and stirred at –20 °C for 30 min. This solution was cooled to –40 °C, HMPA (19.9 µL, 114 µmol) and MeI (7.1 µL, 114 µmol) was dropped in slowly. This reaction mixture was slowly warmed up to –10 °C over 1 h and stirred at –10 °C for 4 h before quenched with saturated NH₄Cl solution (1 mL). This mixture was diluted with EtOAc (200 mL) and dried over Na₂SO₄, filtrated and concentrated. The residue was purified via preparative TLC (CH₂Cl₂:MeOH = 20:1 x 5 times) to afford ODNM 4 (~ 11 mg, 60% brsm, contaminated with trace of 39) and recovered compound 39 (10 mg). Without intensive purification of 4, to a solution of ODNM 4 (11.0 mg, 35.7 µmol) in acetone (3 mL) was added Jones reagent (2.6 M, 200 µL, 2.67 M) at RT and the resulting mixture was stirred for 20 min. The reaction mixture was quenched with MeOH at RT (1 mL) and stirred for 15 min. The reaction mixture was cooled to 0 °C, quenched with saturated NaHCO₃ (1 mL), diluted with EtOAc (100 mL) and dried over Na₂SO₄, filtrated and concentrated. The residue was purified via preparative TLC (CH₂Cl₂:MeOH = 50:1 x 3 times, then CH₂Cl₂:MeOH = 35:1 x 3 times) to afford (–)-Jiadifenin (3) as white foams (5.4 mg,
45%.

4: \( R_f = 0.4 \) (silica gel, CH\(_2\)Cl\(_2\):MeOH = 20:1); \([\alpha]_D^{22} = -139.3 \) (c 0.1, dioxane); \(^1\)H NMR (500 MHz, pyridine-\(d_5\)-TMS) \( \delta \) 9.71 (d, br, \( J = 4.6 \) Hz, 1H), 9.59 (s, br, 1H), 6.62 (s, 1H), 5.31 (dd, \( J = 4.6 \) Hz, 1.5 Hz, 1H), 4.41 (d, \( J = 1.6 \) Hz, 1H), 4.39 (d, \( J = 10.3 \) Hz, 1H), 4.27 (d, \( J = 10.3 \) Hz, 1H), 3.30 (q, \( J = 7.7 \) Hz, 1H), 2.89 (dd, \( J = 13.7 \) Hz, 4.6 Hz, 1H), 2.47 (d, \( J = 13.8 \) Hz, 1H), 1.66 (s, 3H), 1.32 (d, \( J = 8.1 \) Hz, 3H); \(^13\)C NMR (125 MHz, pyridine-\(d_5\)-TMS) \( \delta \) 208.7, 177.2, 176.2, 170.7, 133.6, 79.8, 79.5, 73.8, 73.5, 51.4, 49.0, 44.9, 23.2, 22.6, 13.3; HRMS (ESI): m/e 331.0782 [M+Na]\(^+\) calcd for C\(_{15}\)H\(_{16}\)O\(_7\)Na\(^+\): 331.0788.

3: \( R_f = 0.3 \) (silica gel, CH\(_2\)Cl\(_2\):MeOH = 20:1 x 2 times); \([\alpha]_D^{24} = -123.8 \) (c 0.17, EtOH); \(^1\)H NMR (500 MHz, pyridine-\(d_5\)-TMS) \( \delta \) 10.94 (major C-10 anomer, br s, 1H), 10.64* (minor C-10 anomer, br s, 1H), 9.14* (br s, 1H), 9.08 (br s, 1H), 6.59 (s, 1H), 6.52* (s, 1H), 5.89 (d, \( J = 8.6 \) Hz, 1H), 5.14* (d, \( J = 6.3 \) Hz, 1H), 5.07 (d, \( J = 6.3 \) Hz, 1H), 4.44* (d, \( J = 9.2 \) Hz, 1H), 4.22 (d, \( J = 8.6 \) Hz, 1H), 4.18* (d, \( J = 9.2 \) Hz, 1H), 3.69 (s, 3H), 3.57* (s, 3H), 3.53* (q, \( J = 7.5 \) Hz, 1H), 3.19* (dd, \( J = 12.0 \), 6.3 Hz, 1 H), 3.04 (dd, \( J = 12.6 \), 6.3 Hz, 1 H), 2.97 (q, \( J = 7.6 \) Hz, 1 H), 2.64* (d, \( J = 12.1 \) Hz, 1 H), 2.54 (d, \( J = 12.6 \) Hz, 1 H), 1.70 (s, 3 H), 1.65* (s, 3 H), 1.39* (d, \( J = 7.4 \) Hz, 3 H), 1.25 (d, \( J = 8.0 \) Hz, 3 H); \(^13\)C NMR (200 MHz, pyridine-\(d_5\)-TMS) \( \delta \) 209.7* (minor C-10 anomer), 208.9 (major C-10 anomer), 180.2, 179.0, 178.7*, 177.4*, 171.6169.2*, 131.3*, 130.7, 106.0, 104.1*, 81.0, 80.6, 80.4*, 79.5*, 76.1, 75.4*, 61.5*, 60.3, 52.7, 52.0*, 45.2, 44.9*, 44.8*, 43.0, 31.6*, 31.4, 23.3, 23.2*, 14.5*, 13.1; HRMS (ESI): m/e 339.1072 [M+H]\(^+\) calcd for C\(_{16}\)H\(_{19}\)O\(_8\)\(^+\): 339.1074.
To a solution of alcohol 7 (100 mg, 0.357 mmol) in DCM (7.2 mL) was added Celite® (0.22 g) followed by PCC (0.154 g, 0.714 mmol). The reaction mixture was allowed to stir at RT for 30 minutes. The reaction mixture was filtered through Celite®, washed thoroughly with EtOAc (200 mL). The filtrate was dried over Na₂SO₄ and the solvent was removed. The crude product was purified via flash column chromatography (silica, hexanes:EtOAc = 50:1 to 4:1) to afford unstable ketone 41 as white solid (65.5 mg, 65%). ¹H NMR (500 MHz, CD₃OD) δ 6.27 (bs, 1H), 4.75 (d, J = 2.9 Hz, 1H), 4.05 (d, J = 10.3 Hz, 1H), 3.90 (d, J = 10.3 Hz, 1H), 3.11 (d, J = 23.5 Hz, 1H), 3.01 (d, J = 23.5 Hz, 1H), 2.82 (d, J = 7.4 Hz, 1H), 2.70 (d, J = 7.4 Hz, 1H), 2.23 (dd, 13.8 Hz, 3.5 Hz, 1H), 1.96 (d, J = 14.3 Hz, 1H), 1.39 (s, 3H).

To a solution of the unstable ketone 41 (20.0 mg, 72 µmol) in anhydrous THF (450 µL) was added 1,5-di-tert-butyl-3-methylpyridine (45.0 mg, 216 µmol) followed by triflate anhydride (25.0 µL, 144 µmol) at 0 °C. Upon complete addition, the reaction mixture was warmed up to RT and left overnight. The solvent was removed and the crude product was purified by flash column chromatography (silica, Hexane:EtOAc = 50:1 to 6:1) to afford triflate as white solid (18.0 mg, 61%). ¹H NMR (500 MHz, CD₃OD) δ 6.46 (d, J = 2.9 Hz, 1H), 6.41 (d, J = 2.9 Hz, 1H), 4.80 (dd, J = 2.9 Hz, 1.7 Hz, 1H), 4.08 (d, J = 10.3 Hz, 1H), 3.94 (d, J = 10.3 Hz, 1H), 3.08 (d, J = 18.9 Hz, 1H), 2.59 (dd, J = 13.8 Hz, 4.6 Hz, 1H), 2.46 (dd, J = 16.1 Hz, 2.3 Hz, 1H), 1.87 (td, J = 15.4 Hz, 2.5 Hz, 1H), 1.40 (s, 3H).

This vinyl triflate (18.0 mg, 44 µmol) was then dissolved in dry THF (300 µL), Pd(PPh₃)₄
(15.0 mg, 13 µmol) was added in, followed by a solution of AlMe₃ (210 µL, 440 µmol, 2M in hexanes). This reaction mixture was stirred at RT for 1 h before it was carefully quenched with saturated NaHCO₃ solution (200 µL). This mixture was diluted with EtOAc (50 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified via silica flash column chromatography (hexanes:EtOAc = 50:1 to 3:1) to afford the 42 as white solid (6.8 mg, 57%). [α]D²³ = −38.7 (c 0.3, CHCl₃); ¹H NMR (500 MHz, CD₃OD) δ 6.37 (d, J = 2.3 Hz, 1H), 6.12 (m, 1H), 4.76 (dd, J = 4.0 Hz, 2.9 Hz, 1H), 4.02 (d, J = 10.3 Hz, 1H), 3.93 (d, J = 10.3 Hz, 1H), 2.99 (d, J = 19.5 Hz, 1H), 2.42 (dd, J = 13.8 Hz, 4.0 Hz, 1H), 2.14 (dd, J = 18.9 Hz, 7.1 Hz, 1H), 1.90 (d, J = 1.4 Hz, 3H), 1.60 (td, J = 13.8 Hz, 2.3 Hz, 1H), 1.37 (s, 3H); ¹³C NMR (125 MHz, CD₃OD) δ 176.9, 169.9, 150.3, 148.8, 129.5, 126.1, 80.4, 79.7, 74.5, 50.2, 43.8, 35.8, 28.8, 20.5, 10.8; HRMS (ESI) m/e 277.1069 [M+H⁺] calcd for C₁₅H₁₇O₅⁺: 277.1071.

43: To a solution of 42 (420 mg, 1.5 mmol) in MeOH (20 mL), Pd/C (10%, 162 mg, 0.15 mmol) was then loaded under argon atmosphere. Diene 42 was then selectively hydrogenated using a double-layer H₂-balloon for 30 min. The mixture was passed through a short silica pad and thoroughly rinsed (CH₂Cl₂:MeOH, 20:1) and the filtrate was concentrated under reduced pressure. The residue was purified via silica flash column chromatography (hexanes:CH₂Cl₂ = 1:1 to 1:3 to 100% CH₂Cl₂, then CH₂Cl₂:MeOH =500:1 to 100:1) to afford compound 43 as white foams (168 mg, 23%, 3 steps). [α]D²² = −20.7 (c 0.3, CHCl₃); ¹H NMR (500 MHz, CD₃OD) δ 5.95 (appeared as t, J = 5.6 Hz, 1H), 4.71 (dd, J = 2.9 Hz, 1.7 Hz, 1H),
3.99 (d, J = 9.8 Hz, 1H), 3.73 (d, J = 10.3 Hz, 1H), 2.69 (d, J = 18.3 Hz, 1H), 2.40 (m, 2H), 2.16 (dd, J = 13.8 Hz, 4.6 Hz, 1H), 2.06 (m, 2H), 1.85 (m, 1H), 1.30 (s, 3H), 1.04 (d, J = 6.9 Hz, 3H);

13C NMR (125 MHz, CDCl3) δ 177.5, 171.3, 146.5, 129.3, 129.1, 79.9, 76.7, 75.3, 44.9, 44.6, 42.0, 37.1, 29.5, 21.2, 12.4; HRMS (ESI) m/e 301.1048 [M+Na+] calcd for C15H18O5Na+: 301.1046.

44: To a solution of lactone 43 (10 mg, 71.9 µmol) in THF (350 µL) was added NaHMDS (180 µL, 180 µmol, 1M in THF) dropwise at −78 °C, this solution was stirred for 20 min. Then the Davis oxaziridine (20.5 mg, 79.1 µmol) in THF (100 µL) was added in dropwise. This solution was stirred at the same temperature for 30 min before quenched with saturated NH4Cl solution (1 mL). This mixture was diluted with EtOAc (200 mL) and dried over Na2SO4, filtrated and concentrated. The residue was purified by pre-plate (elute, DCM:MeOH = 50:1, 8 x) afford compound 44 as white foam (6 mg, 57%). [α]D25 − 9.4 (c 0.3, CHCl3); 1H NMR (500 MHz, CD3OD) δ 6.09 (d, J = 3.8 Hz, 1H), 4.70 (d, J = 4.6 Hz, 1H), 4.15 (s, 1H), 3.97 (d, J = 9.8 Hz, 1H), 3.78 (d, J = 9.8 Hz, 1H), 2.80 (dd, J = 13.7 Hz, 4.6 Hz, 1H), 2.39 (m, 1H), 2.17 (m, 2H), 1.82 (d, J = 13.8 Hz, 1H), 1.32 (s, 3H), 1.24 (d, J = 6.9 Hz, 3H); 13C NMR (125 MHz, CD3OD) δ 177.7, 170.5, 143.6, 133.9, 79.9, 76.8, 75.6, 70.3, 49.2, 47.9, 41.9, 37.3, 29.5, 23.4, 16.1; HRMS (ESI): m/e 293.1034 [M-H]− calcd for C15H17O6−: 293.1031.
45: To a solution of compound 43 (20 mg, 72 µmol) in anhydrous EtOAc (720 µL) was added tert-butyl hydroperoxide (145 µL, ~ 10 eq., 5–6 M in decane) and 3Å molecular sieves. The mixture was stirred for 30 min at RT. Manganese(III) acetate dehydrate (3.5 mg, 14 µmol) was added to this mixture in one portion, and this reaction mixture was left stirred overnight. Upon completion, silica gel (500 mg) was added in and rotavaped to dryness. The silica-absorbed crude product was then purified via silica flash column chromatography (CH₂Cl₂:MeOH = 100:1 to 20:1) to afford enone 45 as white solid (10.9 mg, 60%). [α]D⁰₂₄ – 111.4 (c 0.1, CHCl₃); ¹H NMR (500 MHz, CDCl₃) δ 6.31 (s, 1H), 4.75 (t, J = 2.9 Hz, 1H), 4.12 (d, J = 10.3 Hz, 1H), 4.05 (d, J = 10.3 Hz, 1H), 2.92 (m, 2H), 2.48 (q, J = 7.5 Hz, 1H), 2.29 (m, 2H), 1.48 (s, 3H), 1.15 (d, d, J = 7.4 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 205.3, 176.2, 175.6, 167.3, 132.2, 78.0, 74.3, 53.3, 44.0, 43.6, 39.9, 30.1, 29.7, 22.4, 9.1; HRMS (ESI): m/e 291.9877 [M-H] - calcd for C₁₅H₁₅O₆: 291.0874.

(1R, 10S)-2-oxo-3,4-dehydroxyneomajucin (ODNM, 4, synthesized from 45): To a solution of lactone 45 (4 mg, 13.7 µmol) in THF (50 µL) was added NaHMDS (41.1 µL, 41.1 µmol, 1M in THF) dropwise at –78 °C, this solution was stirred for 20 min. Then the Davis oxaziridine
(3.75 mg, 14.4 μmol) in THF (50 μL) was added in dropwise. This solution was stirred at the same temperature for 30 min before quenched with 1 drop of saturated NH₄Cl solution. This mixture was diluted with EtOAc (100 mL) and dried over Na₂SO₄, filtrated and concentrated. The residue was purified by preparative TLC (DCM:MeOH = 30:1 x 3) afford compound 4 as white foam (6 mg, 57%). The analytical data of 4 were identical to the data of 4 that synthesized from 39 (see SI-22).

46: To a solution of enone 45 (7 mg, 24 μmol) and CeCl₃·7H₂O (27 mg, 72 μmol) in THF (1.3 mL)/MeOH (0.4 mL) was cooled to –78 °C and treated with a solution of NaBH₄ (144 μL, 72 μmol) in 2-methoxyethyl ether (0.5 M). The resulting mixture was stirred at –50 °C for 30 minutes. The reaction mixture was quenched with 1N HCl (60 μL), diluted with brine (10 mL) and extracted with EtOAc (5 x 30 mL). Combined organic extracts were dried over Na₂SO₄, filtered and concentrated under reduced pressure. The crude product was purified via preparative TLC (DCM:MeOH = 30:1 x 4) to afford allylic alcohol 45a as white solid (6.0 mg, 85%). To a solution of 45a (6 mg, 20.0 μmol) in THF (100 μL) was added NaHMDS (50 μL, 50 μmol, 1M in THF) dropwise at –78 °C, this solution was stirred for 20 min. Then the Davis oxaziridine (5.7 mg, 22.0 μmol) in THF (100 μL) was added in dropwise. This solution was stirred at the same temperature for 30 min before quenched with 1 drop of saturated NH₄Cl solution. This mixture was diluted with EtOAc (100 mL) and dried over Na₂SO₄, filtrated and concentrated. The residue was purified by pre-plate (elute, DCM:MeOH = 30:1 x 4) afford
compound 46 as white foam (3 mg, 47%). 45a: $[\alpha]_D^{24} = +10.4$ (c 0.3, EtOH); $^1$H NMR (500 MHz, CD$_3$OD) $\delta$ 5.90 (s, 1H), 4.69 (dd, $J = 4.6$ Hz, 1.2 Hz, 1H), 4.38 (d, $J = 8.6$ Hz, 1H), 3.98 (d, $J = 10.3$ Hz, 1H), 3.74 (d, $J = 9.7$ Hz, 1H), 2.86 (d, $J = 18.4$ Hz, 1H), 2.37 (dd, $J = 18.4$ Hz, 2.9 Hz, 1H), 2.15 (dd, $J = 14.3$ Hz, 4.6 Hz, 1H), 1.94 (m, 1H), 1.81 (m, 1H), 1.33 (s, 3H), 1.09 (d, $J = 7.5$ Hz, 3H); $^{13}$C NMR (125 MHz, CD$_3$OD) $\delta$ 177.2, 170.7, 147.1, 133.9, 80.0, 79.4, 76.8, 74.8, 53.9, 44.7, 41.7, 38.1, 29.5, 21.1, 10.0; HRMS (ESI): m/e 295.1178 [M+H]$^+$ calcd for C$_{15}$H$_{19}$O$_6$: 295.1176. 46: $[\alpha]_D^{24} = -14.1$ (c 0.7, dioxane); $^1$H NMR (500 MHz, pyridine-$d_5$-TMS) $\delta$ 9.09 (s br, 1H), 6.90 (d, $J = 6.3$ Hz, 1H), 6.25 (s, br, 1H), 5.15 (d, $J = 4.6$ Hz, 1H), 4.77 (t, $J = 8.0$ Hz, 1H), 4.16 (d, $J = 9.7$ Hz, 1H), 4.06 (d, $J = 9.2$ Hz, 1H), 2.98 (d, $J = 18.4$ Hz, 1H), 2.62 (d, $J = 20.6$ Hz, 1H), 2.25 (m, 2H), 2.07 (dd, $J = 13.7$ Hz, 4.1 Hz, 1H), 1.53 (s, 3H), 1.20 (d, $J = 6.9$ Hz, 3H); $^{13}$C NMR (125 MHz, pyridine-$d_5$-TMS) $\delta$ 178.7, 171.4, 145.3, 139.6, 80.7, 80.4, 77.5, 76.0, 72.1, 58.0, 51.1, 42.3, 24.7, 24.4, 14.7; HRMS (ESI): m/e 333.0950 [M+Na]$^+$ calcd for C$_{15}$H$_{18}$O$_7$Na$: 333.0945.

47: To a solution of 46 (3.1 mg, 10 µmol) in THF (100 µL) was added Dess-Martin periodinane (8.7 mg, 20 µmol) and stirred for 10 min. The reaction mixture was quenched with 2 drop of saturated Na$_2$S$_2$O$_3$ solution and 2 drop of saturated NaHCO$_3$ solution and stirred for 5 min. The mixture was diluted with EtOAc (50 mL), dried over Na$_2$SO$_4$ and concentrated. Without intensive purification, the crude $\alpha$-keto lactone was dissolved in MeOH (100 µL) and NaBH$_4$ (1.1 mg, 30 µmol) was added in at 0 °C. After 5 min, the reaction mixture was quenched with 2
drops of saturated NH₄Cl solution. This mixture was diluted with EtOAc (100 mL) and dried over Na₂SO₄, filtrated and concentrated. The residue was purified by preparative TLC (DCM:MeOH = 30:1 x 4) afford compound 47 as white foam (1.2 mg, 40%). ¹H NMR (500 MHz, CD₃OD) δ 5.99 (s, 1H), 4.58 (dd, J = 4.6 Hz, 1.7 Hz, 1H), 4.47 (d, J = 8.0 Hz, 1H), 4.21 (s, 1H), 3.89 (d, J = 10.3 Hz, 1H), 3.83 (d, J = 10.3 Hz, 1H), 2.26 (dd, J = 14.3 Hz, 4.6 Hz, 1H), 2.01 (m, 1H), 1.78 (m, 1H), 1.35 (s, 3H), 1.16 (d, J = 7.5 Hz, 3H); HRMS (ESI): m/e 333.0950 [M+Na]⁺ calcd for C₁₅H₁₈O₇Na+: 333.0945.

Biological Assay Protocols: Rat PC-12M pheochromocytoma cells (obtained from the laboratories of Drs. Paul C. Sternweis, Elliott M. Ross and Joseph Goldstein; University of Texas Southwestern Medical Center) were cultured at a density of 2 x 10⁴ cells/well in a 24-well plate in growth medium containing DMEM (Cellgro), 10% normal horse serum (HyClone), 5% fetal calf serum (Gibco), 100 U/mL penicillin G, 100 µg/mL streptomycin sulfate (Cellgro) and incubated at 37°C, 5% CO₂. Four hours after plating, growth medium was replaced with differentiation medium (DMEM; 1% normal horse serum, 0.5% fetal calf serum) containing nerve growth factor (NGF, 50 ng/mL). After 24 hours of incubation, fresh differentiation medium was added containing NGF (50 ng/mL) with and without jiadifenin (0.3 or 0.5 µM, 1% DMSO) and allowed to incubate an additional 48 hours. Triplicate wells were used for controls and experimental agents. Live cell images were obtained using a Leica EL6000 microscope (20X). Five regions with similar cell density from each well were selected for imaging. Cells from each well were photographed and analyzed, and from the data of the triplicate wells, the mean values were obtained. Total neurite outgrowth length was measured by randomly selecting 15 neurons from the images of each treatment. The ratio was calculated by comparing the average neurite length found in the treatment to the NGF with 1% DMSO control. Student T test was performed.

References:
$^1$H NMR (CDCl$_3$, 500 MHz) of compound 9
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 9
$^1$H NMR (CDCl₃, 500 MHz) of compound 12
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 12
$^1$H NMR (CDCl$_3$, 500 MHz) of compound 15
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 15
$^{1}$H NMR (CDCl$_3$, 500 MHz) of compound 16
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 16
$^1$H NMR (CDCl$_3$, 500 MHz) of compound 8
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 8
$^1$H NMR (CDCl$_3$, 500 MHz) of compound 20
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 20
$^1$H NMR (CDCl$_3$, 500 MHz) of compound 21
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 21
$^1$H NMR (CDCl$_3$, 500 MHz) of compound 22
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 22
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 22
$^1$H NMR (CDCl$_3$, 500 MHz) of compound 23
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 23
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 7
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 7
$^1$H NMR (CDCl$_3$, 500 MHz) of compound 24
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 24
$^1$H NMR (CDCl$_3$, 500 MHz) of compound 25
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 26
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 26
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 6
$^{13}\text{C} \text{NMR (CD}_3\text{OD, 125 MHz) of compound 6}$
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 6
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 30
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 30
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 30
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 31
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 31
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 31
$^1$H NMR (CD$_3$OD, 500 MHz) of (-)-jiadifenolide (2)
$^1$H NMR (CD$_3$OD, 500 MHz) of (-)-jiadifenolide (2)
$^{13}$C NMR (CD$_3$OD, 125 MHz) of (-)-jiadifenolide (2)
$^{13}$C NMR (CD$_3$OD, 125 MHz) of (-)-jiadifenolide (2)
$^1$H NMR (CDCl$_3$, 500 MHz) of compound 34
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 34
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 34
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 36
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 36
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 37
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 37
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 37
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 38
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 38
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 38
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 39
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 39
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 39
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 40
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 40
$^1$H NMR (Pyridine-d$_6$-TMS, 500MHz) of (-)-ODNM (4)
$^{13}$C NMR (Pyridine-d$_6$-TMS, 125 MHz) of (-)-ODNM (4)
$^1$H NMR (Pyridine-d$_6$-TMS, 500 MHz) of (-)-jiadifenin (3)
$^{13}$C NMR (Pyridine-d$_6$-TMS, 125 MHz) of (-)-jiadifenin (3)
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 42
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 42
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 43
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 43
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 44
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 44
NOSEY (CD$_3$OD, 500 MHz) of compound 44
$^1$H NMR (CDCl$_3$, 500 MHz) of compound 45
$^{13}$C NMR (CDCl$_3$, 125 MHz) of compound 45
$^1$H NMR (CD$_3$OD, 500 MHz) of compound 45a
$^{13}$C NMR (CD$_3$OD, 125 MHz) of compound 45a
$^1$H NMR (Pyridine-d6-TMS, 500 MHz) of compound 46
$^{13}$C NMR (Pyridine-d$_6$-TMS, 125 MHz) of compound 46
NOSEY (Pyridine-d6-TMS, 500 MHz) of compound 46
$^1$H NMR (Pyridine-d$_6$-TMS, 500 MHz) of compound 47