The Total Synthesis of (±)-Jiadifenin A Non-Peptidyl Neurotrophic Modulator.

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Analytical Equipment: ^1H and ^{13}C NMR spectra were recorded on a Bruker AMX-400 MHz or a Bruker Advance DRX-500 MHz spectrometer in CDCl_3 [referenced to 7.26 ppm (δ) for ^1H NMR and 77.0 ppm for ^{13}C NMR], CD_3COCD_3 [referenced to 2.05 ppm (δ) for ^1H NMR and 20.83 ppm for ^{13}C NMR], CD_3OD [referenced to 3.30 ppm (δ) for ^1H NMR and 49.05 ppm for ^{13}C NMR], and $\text{C}_5\text{D}_5\text{N-TMS}$ [referenced to 0 ppm (δ) for ^1H NMR and 123.44 ppm for ^{13}C NMR]. Low resolution mass spectra (ionspray, a variation of electrospray) were acquired on a Perkin-Elmer Sciex API 100 spectrometer. High resolution mass spectra (fast atom bombardment, FAB) were acquired on a Micromass 70-SE-4F spectrometer. Infrared spectra were obtained on a Perkin-Elmer 1600 FT-IR spectrophotometer with a NaCl plate.

TBS ether 7. To a cooled ($-78\text{ }^\circ\text{C}$) solution of LHMDs (1.0 M in THF, 89.5 mL, 1.0 equiv) in THF (250 mL) was added a solution of ketone **6** (13.90 g, 89.00 mmol) in THF (40 mL) slowly over 15 min and the resulting mixture was stirred at $-78\text{ }^\circ\text{C}$ for 34 min. Iodomethane (6.5 mL, 1.2 equiv) was added to the reaction mixture and the resulting solution was stirred at $-78\text{ }^\circ\text{C}$ for 20 min and at room temperature for 2 h. The reaction mixture was quenched by addition of saturated NH_4Cl (250 mL) and extracted with ether (3 X 250 mL). Combined extracts were dried (MgSO_4), filtered, and concentrated *in vacuo*. Flash chromatography (pentane-ether 4:1 $\rightarrow$ 3:1 $\rightarrow$ 2:1) afforded α -methylcyclohexanone (11.16 g, 74% yield). The spectroscopic data of the product were in accord with the published data (Pfau, M.; Jabin, I.; Revial, G. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1935).

To a cooled ($0\text{ }^\circ\text{C}$) yellow solution of α -methylcyclohexanone (1.871 g, 10.67 mmol) in 10% KOH in MeOH (10 g) was added a solution of 37% aqueous formaldehyde (0.80 mL, 1.0 equiv) in MeOH (0.80 mL) dropwise over 31 min. The reaction mixture was stirred at $0\text{ }^\circ\text{C}$ for 15 min. The reaction mixture was quenched by addition of 1 N aqueous HCl (18 mL), diluted with saturated NH_4Cl (20 mL), and extracted with CH_2Cl_2 (4 X 100 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-ether 1.5:1 $\rightarrow$ 1:1 $\rightarrow$ 1:2 $\rightarrow$ 1:3) gave alcohol (1.508 g, 71% yield, 89% based on recovered starting material): IR (neat) 3475 (m, br), 2959 (m), 2933 (m), 2883 (m), 1706 (s), 1457 (w), 1432 (w), 1362 (w), 1308 (w), 1275 (w), 1151 (w), 1113 (m), 1078 (m), 1038 (m), 995 (w), 948 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 4.07-3.93 (m, 4 H), 3.58 (dd, J = 7.4, 11.3 Hz, 1 H), 3.37 (dd, J = 6.6, 11.4 Hz, 1 H), 2.75 (ddd, J = 6.1, 11.1, 15.0 Hz, 1 H), 2.59 (t, J = 7.0 Hz, 1 H), 2.40 (td, J = 5.5, 15.0 Hz,

1 H), 2.16 (d, $J = 14.1$ Hz, 1 H), 2.06-1.93 (m, 2 H), 1.74 (dd, $J = 2.6, 14.1$ Hz, 1 H), 1.55 (s, 1 H), 1.20 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 215.1, 107.3, 68.5, 64.4, 64.1, 49.4, 42.1, 36.2, 34.0, 21.4; high resolution mass spectrum m/z 223.0943 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{10}\text{H}_{16}\text{O}_4\text{Na}$: 223.0946].

A solution of alcohol (2.800 g, 14 mmol) in CH_2Cl_2 (150 mL) was cooled to 0 °C, treated with 2,6-lutidine (4.0 mL, 2.5 equiv) and TBSOTf (3.7 mL, 1.1 equiv) and stirred at 0 °C for 15 min. The reaction mixture was quenched with saturated NH_4Cl (175 mL) and extracted with CH_2Cl_2 (3 X 150 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-ether 4:1 $\rightarrow$ 3:1 $\rightarrow$ 2:1) gave TBS ether **7** (4.726 g, 97% yield): IR (neat) 2955 (s), 2930 (s), 2884 (s), 2859 (s), 1716 (s), 1472 (m), 1463 (m), 1433 (w), 1387 (w), 1361 (m), 1307 (w), 1255 (m), 1101 (m, br), 1035 (w), 1005 (w), 949 (w), 837 (m, br) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 3.98 (m, 4 H), 3.73 (d, $J = 9.4$ Hz, 1 H), 3.46 (d, $J = 9.4$ Hz, 1 H), 2.52 (tdd, $J = 6.8, 15.6, 37.8$ Hz, 2 H), 2.25 (d, $J = 14.2$ Hz, 1 H), 1.97 (t, $J = 7.1$ Hz, 2 H), 1.72 (d, $J = 14.0$ Hz, 1 H), 1.10 (s, 3 H), 0.84 (s, 9 H), 0.01 (s, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 213.2, 107.9, 68.3, 64.4, 64.3, 49.9, 41.6, 36.3, 33.9, 25.8, 21.8, 18.2, -5.58, -5.59; high resolution mass spectrum m/z 337.1808 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{16}\text{H}_{30}\text{O}_4\text{NaSi}$: 337.1811].

Esters 8 and 9. To a cooled (-78 °C) solution of TBS ether **7** (1.389 g, 4.42 mmol) in THF (45 mL) was added LHMDs (1.0 M in THF, 4.40 mL, 1.0 equiv) dropwise and the resulting mixture was stirred at -78 °C for 23 min. The reaction mixture was treated with allyl bromide (0.57 mL, 1.5 equiv) and warmed to room temperature over 4 h. The reaction mixture was quenched with saturated NH_4Cl (100 mL) and extracted with ether (3 X 100 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-ether 10:1 $\rightarrow$ 3:1) afforded a mixture (less polar compound:more polar compound = 1:1.3) of α -allylcyclohexanone (1.147 g, 73% yield, 99% based on recovered starting material); IR (neat) 2954 (s), 2929 (s), 2884 (s), 2857 (s), 1716 (s), 1641 (w), 1472 (m), 1463 (m), 1387 (w), 1361 (m), 1297 (w), 1257 (m), 1202 (w), 1177 (w), 1095 (s, br), 1031 (w), 1006 (w), 948 (w), 913 (w), 836 (m, br) cm^{-1} ; **less polar compound** ^1H NMR (500 MHz, CDCl_3) δ 5.73 (m, 1 H), 5.01 (m, 2 H), 4.05 (m, 2 H), 3.96 (m, 2 H), 3.80 (d, $J = 9.5$ Hz, 1 H), 3.27 (d, $J = 9.5$ Hz, 1 H), 2.83 (m, 1 H), 2.51 (td, $J = 6.2, 14.4$ Hz, 1 H), 2.24 (d, $J = 14.1$ Hz, 1 H), 2.08-1.98 (m, 2 H), 1.81 (dd, $J = 3.6, 14.1$ Hz, 1 H), 1.65 (t, $J = 13.6$ Hz, 1 H), 1.19 (s, 3 H), 0.86 (s, 9 H), 0.03 (s, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 213.5, 136.1, 116.6, 107.9, 68.3, 64.7, 64.0, 49.6, 43.1, 41.8, 39.3, 33.2, 25.8, 22.5, 18.2, -5.5, -5.6; **more polar compound** ^1H NMR (500 MHz, CDCl_3) δ 5.76

(m, 1 H), 5.00 (m, 2 H), 4.02 (m, 2 H), 3.92 (t, $J = 6.2$ Hz, 2 H), 3.89 (d, $J = 9.4$ Hz, 1 H), 3.61 (d, $J = 9.5$ Hz, 1 H), 2.81 (m, 1 H), 2.51 (td, $J = 6.1, 14.1$ Hz, 1 H), 2.21 (dd, $J = 2.8, 14.4$ Hz, 1 H), 2.13 (ddd, $J = 3.0, 5.4, 13.6$ Hz, 1 H), 1.96 (td, $J = 7.3, 14.4$ Hz, 1 H), 1.68 (d, $J = 14.3$ Hz, 1 H), 1.65 (t, $J = 13.7$ Hz, 1 H), 1.06 (s, 3 H), 0.85 (s, 9 H), 0.01 (s, 6 H); ^{13}C NMR (125 MHz, CDCl_3) δ 213.3, 136.2, 116.5, 107.6, 68.8, 64.6, 64.1, 50.0, 43.6, 42.7, 40.5, 33.4, 25.7, 21.0, 18.1, -5.61, -5.64; high resolution mass spectrum m/z 377.2113 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{19}\text{H}_{34}\text{O}_4\text{NaSi}$: 377.2124].

To a cooled (-78°C) solution of LDA (1.1 equiv) in THF (30 mL) was added a solution of α -allylcyclohexanone (3.036 g, 8.562 mmol) in THF (6 mL) dropwise and the resulting mixture was warmed to -20°C over 2 h. The reaction mixture was cooled to -78°C and treated with a mixture of ethyl bromoacetate (2.0 mL, 2.1 equiv) and HMPA (1.5 mL, 1.1 equiv). The resultant mixture was stirred at -78°C for 21 h. The reaction mixture was quenched with saturated NH_4Cl (200 mL) and extracted with ether (3 X 250 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-ether 10:1 $\rightarrow$ 6:1 $\rightarrow$ 3:1) afforded esters **8** (2.754 g, 73% yield) and **9** (0.905 g, 24% yield).

8: IR (neat) 2955 (s), 2929 (s), 2883 (s), 2857 (s), 1733 (s), 1710 (s), 1638 (w), 1472 (m), 1463 (m), 1407 (m), 1388 (m), 1370 (m), 1344 (m), 1254 (m), 1190 (m), 1155 (m), 1098 (m, br), 1033 (m), 984 (m), 947 (m), 917 (m), 839 (m, br) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.65 (m, 1 H), 5.06 (m, 2 H), 4.04 (q, $J = 7.2$ Hz, 2 H), 4.00-3.88 (m, 4 H), 3.96 (d, $J = 8.9$ Hz, 1 H), 3.13 (d, $J = 9.1$ Hz, 1 H), 2.89 (d, $J = 16.6$ Hz, 1 H), 2.58 (d, $J = 14.6$ Hz, 1 H), 2.45 (dd, $J = 7.5, 13.8$ Hz, 1 H), 2.43 (d, $J = 14.4$ Hz, 1 H), 2.20 (d, $J = 16.7$ Hz, 1 H), 2.16 (dd, $J = 7.3, 13.8$ Hz, 1 H), 1.95 (d, $J = 14.5$ Hz, 1 H), 1.81 (d, $J = 15.4$ Hz, 1 H), 1.19 (t, $J = 7.1$ Hz, 3 H), 1.13 (s, 3 H), 0.84 (s, 9 H), 0.00 (s, 3H), -0.01 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 214.9, 171.5, 133.0, 119.2, 107.8, 68.4, 64.0, 63.8, 60.3, 49.5, 48.3, 41.2, 40.6, 39.6, 39.4, 25.8, 22.8, 18.2, 14.2, -5.6, -5.7; high resolution mass spectrum m/z 463.2478 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{23}\text{H}_{40}\text{O}_6\text{NaSi}$: 463.2492].

9: IR (neat) 2929 (s, br), 2883 (s), 2858 (s), 1732 (s), 1698 (s), 1638 (m), 1474 (m), 1408 (w), 1389 (w), 1370 (m), 1341 (m), 1304 (w), 1252 (m), 1187 (m), 1152 (m), 1094 (m), 1033 (m), 1013 (m), 972 (m), 948 (m), 918 (m), 836 (m, br) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.61 (m, 1 H), 5.06 (m, 2 H), 4.03 (q, $J = 7.1$ Hz, 2 H), 4.01-3.95 (m, 2 H), 3.90 (m, 2 H), 3.71 (d, $J = 9.3$ Hz, 1 H), 3.47 (d, $J = 9.3$ Hz, 1 H), 2.82 (d, $J = 16.7$ Hz, 1 H), 2.55 (dd, $J = 7.6, 13.8$

Hz, 1 H), 2.38 (dd, $J = 7.2, 13.8$ Hz, 1 H), 2.29 (d, $J = 14.4$ Hz, 1 H), 2.22 (d, $J = 14.2$ Hz, 1 H), 2.21 (d, $J = 16.7$ Hz, 1 H), 1.97 (dd, $J = 2.6, 14.2$ Hz, 1 H), 1.85 (dd, $J = 2.6, 14.4$ Hz, 1 H), 1.193 (s, 3 H), 1.185 (t, $J = 7.1$ Hz, 3 H), 0.85 (s, 9 H), 0.004 (s, 3 H), -0.002 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 215.9, 171.8, 133.7, 119.6, 108.2, 69.8, 65.0, 63.8, 60.7, 49.6, 49.5, 42.3, 41.6, 40.8, 39.9, 26.3, 23.4, 18.7, 14.6, -5.1, -5.2; high resolution mass spectrum m/z 463.2487 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{23}\text{H}_{40}\text{O}_6\text{NaSi}$: 463.2492].

Alcohol 10. IR (neat) 3501 (s, br), 3076 (m), 2934 (s, br), 1843 (w), 1699 (s), 1636 (m), 1456 (s), 1362 (m), 1262 (m), 1150 (m), 1079 (m), 920 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.60 (m, 2 H), 5.05 (m, 4 H), 3.95 (m, 4 H), 3.63 (dd, $J = 7.6, 11.1$ Hz, 1 H), 3.29 (dd, $J = 6.0, 11.1$ Hz, 1 H), 2.44 (m, 3 H), 2.27 (dd, $J = 7.8, 13.9$ Hz, 1 H), 2.23 (d, $J = 14.6$ Hz, 1 H), 2.14 (dd, $J = 8.1, 13.9$ Hz, 1 H), 2.02 (m, 2 H), 1.81 (d, $J = 14.7$ Hz, 1 H), 1.15 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 218.2, 133.5, 133.4, 119.0, 118.9, 107.6, 69.5, 64.3, 63.8, 50.6, 48.7, 41.4, 41.1, 40.9, 39.6, 21.9; high resolution mass spectrum 281.1739 (M^+ ; calcd for $\text{C}_{16}\text{H}_{25}\text{O}_4$: 281.1753).

Bromoether 11. The alcohol **10** (22.6 mg, 0.0806 mmol) was azeotroped with anhydrous toluene (3 X 10 mL) and placed under high vacuum for 1 h. Then **10** was dissolved in THF (3 mL), cooled to -45°C , and treated with *N*-bromosuccinimide (34.6 mg, 2.4 equiv) in one portion. The resulting mixture was stirred at $-40 \sim -45^\circ\text{C}$ for 20 min. The reaction mixture was quenched by addition of saturated NaHCO_3 (30 mL) and extracted with ether (3 X 40 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-ether 3:1 $\rightarrow$ 1:1 $\rightarrow$ 1:2 $\rightarrow$ 1:4 $\rightarrow$ ether) afforded bromoether **11** (24.3 mg, 66% yield) and a mixture of other isomers (8.8 mg, 24% yield). The structure of **11** was deduced from the 2D NMR studies. **11**: IR (neat) 3543 (m, br), 2962 (s), 2879 (s), 1709 (m), 1458 (m), 1419 (m), 1361 (m), 1317 (w), 1223 (m), 1096 (s), 1017 (s), 880 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 4.38 (m, 2 H), 3.90-3.83 (m, 4 H), 3.58 (dd, $J = 5.0, 11.7$ Hz, 1 H), 3.49-3.43 (m, 4 H), 3.37 (dd, $J = 6.2, 10.4$ Hz, 1 H), 2.60 (t, $J = 6.7$ Hz, 1 H), 2.18-2.02 (m, 5 H), 1.96 (m, 1 H), 1.92 (d, $J = 15.0$ Hz, 1 H), 1.64 (d, $J = 15.1$ Hz, 1 H), 1.06 (s, 3 H); ^{13}C NMR (125 MHz, CDCl_3) δ 119.2, 108.7, 77.4, 77.1, 68.1, 63.9, 63.8, 52.7, 46.1, 45.3, 44.0, 41.9, 40.2, 34.4, 34.3, 20.1; high resolution mass spectrum 455.0073 (M^+ ; calcd for $\text{C}_{16}\text{H}_{25}\text{O}_5\text{Br}_2$: 455.0069).

Determination of Stereochemistry of 11. The analysis of 2D NOESY NMR experiment is shown below.

Ha — Hb	Hb — Hc	Hc — He	Hd — He	He — Hf	Hf — Hb
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Alcohol 12. To a cooled ($-78\text{ }^{\circ}\text{C}$) solution of dimethyl methylphosphonate (0.51 mL, 20 equiv) in THF (3.0 mL) was added a solution of *n*BuLi (1.6 M in hexanes, 2.80 mL, 19 equiv) dropwise and the resulting cloudy mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 22 min. A solution of ester **8** (104 mg, 0.237 mmol) in THF (1.0 mL) was added dropwise to the reaction mixture and the resulting mixture was stirred at $-78\text{ }^{\circ}\text{C}$ for 1 h. The reaction mixture was quenched by water (40 mL) and extracted with EtOAc (3 X 45 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-EtOAc 3:1 $\rightarrow$ 1:1) gave phosphonate (100 mg, 81% yield, 99% based on recovered starting material): IR (neat) 2954 (s), 2929 (s), 2856 (m), 1709 (s), 1462 (m), 1389 (w), 1361 (m), 1257 (s), 1182 (w), 1099 (m), 1030 (s), 983 (w), 948 (w), 917 (w), 838 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 5.64 (m, 1 H), 5.07 (m, 2 H), 4.02-3.84 (m, 5 H), 3.733 (d, $J = 11.3\text{ Hz}$, 3 H), 3.726 (d, $J = 11.3\text{ Hz}$, 3 H), 3.15 (m, 2 H), 3.09 (dd, $J = 13.8, 22.4\text{ Hz}$, 1 H), 2.89 (dd, $J = 13.8, 22.7\text{ Hz}$, 1 H), 2.56 (d, $J = 18.6\text{ Hz}$, 1 H), 2.54 (d, $J = 14.6\text{ Hz}$, 1 H), 2.41 (dd, $J = 7.9, 13.9\text{ Hz}$, 1 H), 2.35 (d, $J = 14.5\text{ Hz}$, 1 H), 2.16 (dd, $J = 7.2, 13.9\text{ Hz}$, 1 H), 1.87 (d, $J = 14.5\text{ Hz}$, 1 H), 1.81 (d, $J = 14.7\text{ Hz}$, 1 H), 1.15 (s, 3 H), 0.83 (s, 9 H), -0.01 (s, 3 H), -0.02 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 215.2, 199.6 (d, $J = 6.1\text{ Hz}$), 133.0, 119.2, 107.7, 68.0, 64.1, 63.6, 53.1 (d, $J = 6.8\text{ Hz}$), 52.9 (d, $J = 6.1\text{ Hz}$), 51.1, 49.6, 48.2, 42.2, 40.9, 40.4, 39.2 (d, $J = 16.5\text{ Hz}$), 25.8, 23.0, 18.2, -5.6 , -5.7 ; high resolution mass spectrum m/z 541.2355 $[(\text{M}+\text{Na})^+]$; calcd for $\text{C}_{24}\text{H}_{43}\text{O}_8\text{NaSiP}$: 541.2363].

To a solution of phosphonate (71.4 mg, 0.136 mmol) in THF (12 mL) was added NaH (60%, 28.7 mg, 5.2 equiv) in one portion and the resulting mixture was stirred at room temperature for 5 min until gas evolution ceased. The reaction mixture was heated at $60\text{ }^{\circ}\text{C}$ for 2 h. The reaction mixture was quenched with saturated NH_4Cl (55 mL) and extracted with ether (3 X 65 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-EtOAc 1:1) afforded cyclopentenone (48.9 mg, 91% yield): IR (neat) 2955 (s), 2928 (s), 2884 (s), 2856 (s), 1733 (m), 1716 (s), 1699 (s), 1604 (m), 1471 (m), 1418 (w), 1388 (w), 1361 (m), 1257 (m), 1202

(w), 1158 (w), 1098 (m, br), 1057 (w), 1026 (w), 1006 (w), 989 (w), 946 (w), 916 (w), 838 (m, br) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.00 (s, 1 H), 5.63 (m, 1 H), 5.01 (m, 2 H), 3.99 (m, 2 H), 3.89 (d, J = 9.6 Hz, 1 H), 3.85 (m, 2 H), 3.62 (d, J = 9.6 Hz, 1 H), 2.64 (dd, J = 6.0, 14.0 Hz, 1 H), 2.48 (d, J = 17.7 Hz, 1 H), 2.47 (dd, J = 6.6, 14.0 Hz, 1 H), 2.15 (dd, J = 2.3, 13.8 Hz, 1 H), 2.06 (d, J = 17.9 Hz, 1 H), 2.00 (dd, J = 2.3, 14.3 Hz, 1 H), 1.67 (d, J = 13.8 Hz, 1 H), 1.51 (d, J = 14.3 Hz, 1 H), 1.20 (s, 3 H), 0.85 (s, 9 H), 0.01 (s, 3 H), -0.005 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 206.9, 186.5, 134.3, 131.5, 118.7, 107.9, 67.6, 65.0, 63.3, 51.7, 47.5, 44.9, 43.0, 42.8, 42.5, 26.7, 25.7, 18.1, -5.6, -5.7; high resolution mass spectrum m/z 393.2469 ($\text{M}+\text{H}^+$; calcd for $\text{C}_{22}\text{H}_{37}\text{O}_4\text{Si}$: 393.2461).

A mixture of cyclopentenone (1.87 g, 4.77 mmol) and 2 N aqueous HCl (13 mL) in THF (20 mL) was stirred at room temperature for 3 d. The reaction mixture was poured into ice (60 mL)-saturated NaHCO_3 (100 mL) and extracted with EtOAc (3 X 200 mL, 2 X 130 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo* to give alcohol **12** (1.05 g, 95% yield): IR (neat) 3413 (m, br), 2969 (m), 2925 (m), 2873 (m), 1687 (s), 1602 (m), 1455 (w), 1414 (m), 1385 (w), 1315 (w), 1279 (m), 1212 (m), 1176 (w), 1058 (m), 1008 (w), 934 (m) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.21 (s, 1 H), 5.69-5.58 (m, 1 H), 5.18-5.10 (m, 2 H), 3.71 (dd, J = 5.8, 11.8 Hz, 1 H), 3.64 (dd, J = 5.7, 10.8 Hz, 1 H), 2.88 (d, J = 16.6 Hz, 1 H), 2.80 (d, J = 16.3 Hz, 1 H), 2.63 (d, J = 18.0 Hz, 1 H), 2.45 (d, J = 16.2 Hz, 1 H), 2.49-2.43 (m, 1 H), 2.40-2.35 (m, 1 H), 2.34 (d, J = 16.5 Hz, 1 H), 2.28 (d, J = 18.0 Hz, 1 H), 1.61 (t, J = 5.8 Hz, 1 H), 1.30 (s, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 207.9, 205.6, 184.4, 132.5, 131.1, 120.3, 69.5, 53.4, 50.9, 50.0, 48.1, 47.5, 43.1, 27.6; high resolution mass spectrum m/z 257.1140 [$(\text{M}+\text{Na})^+$; calcd for $\text{C}_{14}\text{H}_{18}\text{O}_3\text{Na}$: 257.1154].

Lactone 13. To a cooled (0 $^\circ\text{C}$) solution of alcohol **12** (1.05 g, 4.50 mmol) in CH_2Cl_2 (90 mL) were added DMAP (11 mg, 0.02 equiv), pyridine (8.5 mL, 23 equiv) and ethyl chloroformate (5.2 mL, 12 equiv) and the resulting mixture was stirred at room temperature for 21 h. Another 2.6 mL of ethyl chloroformate was added and the reaction mixture was stirred for an additional 15 min. The reaction mixture was quenched with 2N aqueous HCl (200 mL) and extracted with EtOAc (3 X 200 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-EtOAc 2:1 $\rightarrow$ 1:1 $\rightarrow$ 1:2 $\rightarrow$ 1:5) gave ethyl carbonate **12a** (1.32 g, 93% yield): IR (neat) 2979 (m), 2937 (w), 1746 (s), 1712 (s), 1606 (w), 1466 (w), 1399 (w), 1375 (m), 1255 (s), 1206 (m), 1180 (w), 1090 (w), 1007 (m), 962 (w), 927 (w), 873 (w) cm^{-1} ; ^1H NMR (400 MHz, CDCl_3) δ 6.21 (s, 1 H), 5.58 (m, 1 H), 5.13

(m, 2 H), 4.22 (d, J = 10.9 Hz, 1 H), 4.18 (q, J = 7.1 Hz, 2 H), 4.07 (d, J = 10.9 Hz, 1 H), 2.87 (d, J = 16.8 Hz, 1 H), 2.81 (d, J = 16.9 Hz, 1 H), 2.60 (d, J = 18.0 Hz, 1 H), 2.40 (dd, J = 6.9, 14.3 Hz, 1 H), 2.38 (t, J = 16.3 Hz, 2 H), 2.32 (dd, J = 6.3, 14.4 Hz, 1 H), 2.21 (d, J = 17.9 Hz, 1 H), 1.32 (s, 3 H), 1.28 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 206.7, 205.2, 182.7, 154.7, 131.8, 131.2, 120.6, 72.5, 64.4, 49.6, 49.3, 47.8, 47.1, 43.0, 40.3, 28.1, 14.1; high resolution mass spectrum m/z 329.1362 [(M+Na) $^+$; calcd for $\text{C}_{17}\text{H}_{22}\text{O}_5\text{Na}$: 329.1365].

To a solution of ethyl carbonate **12a** (1.29 g, 4.20 mmol) in THF (250 mL) was added NaH (60%, 1.99 g, 12 equiv) in one portion and the resulting mixture was heated to reflux for 12 h. The reaction mixture was quenched with saturated NH_4Cl (150 mL) and 4N aqueous HCl (75 mL), and after separation, further extracted with EtOAc (3 X 250 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-EtOAc 2:1 $\rightarrow$ 1:1 $\rightarrow$ 1:3 $\rightarrow$ CH_2Cl_2 -MeOH 20:1 $\rightarrow$ 10:1) gave lactone **13** (1.02 g, 94% yield): IR (neat) 2976 (m), 2917 (m), 1791 (s), 1716 (s, br), 1609 (m), 1455 (m), 1418 (m), 1391 (m), 1365 (m), 1337 (w), 1264 (m), 1164 (m), 1101 (w), 1024 (m), 992 (w), 929 (w), 889 (w), 862 (w) cm^{-1} ; ^1H NMR (500 MHz, CD_3COCD_3) δ 6.40 (s, 1 H), 5.57 (m, 1 H), 5.13 (m, 2 H), 4.45 (d, J = 9.5 Hz, 1 H), 4.25 (d, J = 9.5 Hz, 1 H), 3.63 (s, 1 H), 2.96 (d, J = 14.3 Hz, 1 H), 2.78 (d, J = 14.3 Hz, 1 H), 2.54 (d, J = 17.9 Hz, 1 H), 2.413 (d, J = 18.0 Hz, 1 H), 2.410 (dd, J = 7.4, 14.5 Hz, 1 H), 2.29 (dd, J = 6.5, 14.4 Hz, 1 H), 1.68 (s, 3 H); ^{13}C NMR (125 MHz, CD_3COCD_3) δ 204.9, 200.3, 179.7, 171.3, 133.9, 133.4, 121.0, 76.6, 61.5, 51.5, 50.4, 49.9, 46.0, 43.5, 27.9; high resolution mass spectrum m/z 283.0935 [(M+Na) $^+$; calcd for $\text{C}_{15}\text{H}_{16}\text{O}_4\text{Na}$: 283.0946].

Diol 14. To a solution of lactone **13** (78.1 mg, 0.300 mmol) in CH_2Cl_2 (10 mL) was added mCPBA (~100%, 51.0 mg, 0.99 equiv) and the resulting mixture was stirred at room temperature for 15 min. The reaction mixture was quenched with a mixture of saturated $\text{Na}_2\text{S}_2\text{O}_3$ (35mL)-water (35 mL)-saturated NaHCO_3 (35 mL) and extracted with EtOAc (3 X 150 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-EtOAc 1:1) afforded α -hydroxy lactone **13a** (74.4 mg, 90% yield): IR (film) 3340 (m, br), 2976 (w), 2923 (w), 1793 (s), 1715 (s), 1688 (s), 1604 (w), 1392 (w), 1364 (w), 1291 (w), 1250 (w), 1206 (w), 1159 (m), 1108 (m), 1021 (w), 1001 (m), 934 (w) cm^{-1} ; ^1H NMR (400 MHz, CD_3OD) δ 6.39 (s, 1 H), 5.47 (m, 1 H), 5.13 (m, 2 H), 4.42 (d, J = 9.9 Hz, 1 H), 4.16 (d, J = 10.0 Hz, 1 H), 3.36 (d, J = 12.3 Hz, 1 H), 2.62 (d, J = 12.3 Hz, 1 H), 2.56 (d, J = 3.1 Hz, 2 H), 2.43 (d, J = 7.2 Hz, 2 H), 1.47 (s, 3 H); ^{13}C NMR (100 MHz, CD_3OD) δ 207.1, 205.1, 178.1,

174.2, 136.3, 132.9, 121.0, 85.3, 72.5, 51.82, 51.75, 51.73, 48.2, 43.7, 19.9; high resolution mass spectrum m/z 299.0891 $[(M+Na)^+]$; calcd for $C_{15}H_{16}O_5Na$: 299.0895].

To a cooled ($-78\text{ }^{\circ}\text{C}$) solution α -hydroxy lactone **13a** (1.16 g, 4.20 mmol) in THF (90 mL)-MeOH (90 mL) was added NaBH_4 (179 mg, 1.1 equiv) in one portion and the resulting mixture was stirred for 1 min. The reaction mixture was quenched with brine (175 mL) and extracted with EtOAc (3 X 300 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-EtOAc 2:1) gave diol **14** (1.08 g, 93 % yield): IR (film) 3342 (m, br), 2919 (w), 1754 (s), 1678 (s), 1590 (w), 1449 (w), 1408 (w), 1361 (w), 1261 (w), 1226 (w), 1161 (m), 1114 (m), 1079 (m), 1020 (m), 991 (m) cm^{-1} ; ^1H NMR (400 MHz, CD_3OD) δ 6.23 (s, 1 H), 5.58 (m, 1 H), 5.06 (m, 2 H), 4.87 (d, $J = 8.5\text{ Hz}$, 1 H), 3.99 (d, $J = 8.4\text{ Hz}$, 1 H), 3.32 (m, 1 H), 3.12 (dd, $J = 7.0, 14.1\text{ Hz}$, 1 H), 2.67 (dd, $J = 7.8, 14.1\text{ Hz}$, 1 H), 2.53 (d, $J = 18.0\text{ Hz}$, 1 H), 2.23 (dd, $J = 2.8, 14.4\text{ Hz}$, 1 H), 2.21 (d, $J = 18.0\text{ Hz}$, 1 H), 1.97 (dd, $J = 3.0, 14.5\text{ Hz}$, 1 H), 1.39 (s, 3 H); ^{13}C NMR (100 MHz, CD_3OD) δ 209.2, 183.8, 179.5, 135.2, 134.9, 119.5, 83.7, 73.7, 72.8, 53.8, 48.3, 47.7, 45.5, 39.9, 22.0; high resolution mass spectrum m/z 279.1232 ($M+H^+$; calcd for $C_{15}H_{19}O_5$: 279.1232).

Lactone 15. To a cooled ($-45\text{ }^{\circ}\text{C}$) solution of LDA (3.5 equiv) in THF (20 mL) was added a solution of diol **14** (153 mg, 0.548 mmol) in THF (2.5 mL) and the resulting mixture was warmed to $-15\text{ }^{\circ}\text{C}$ over 55 min. The reaction mixture was cooled to $-40\text{ }^{\circ}\text{C}$, treated with a mixture of iodomethane (40 μL , 1.2 equiv) and HMPA (90 μL , 1.0 equiv), and stirred at $-35\text{ }^{\circ}\text{C}$ for 18 h. The reaction mixture was quenched with saturated NH_4Cl (125 mL) and extracted with EtOAc (3 X 150 mL). Combined extracts were dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-EtOAc 2:1 $\rightarrow$ 1:1 $\rightarrow$ CH_2Cl_2 -MeOH 10:1) gave cyclopentenone (103 mg, 64% yield, 77% based on recovered starting material): IR (film) 3382 (m, br), 3265 (m, br), 1762 (s), 1686 (s), 1600 (m), 1456 (w), 1401 (w), 1371 (w), 1260 (w), 1164 (m), 1115 (m), 1056 (w), 1023 (w), 989 (m) cm^{-1} ; ^1H NMR (400 MHz, CD_3OD) δ 6.18 (s, 1 H), 5.62 (m, 1 H), 5.06 (m, 2 H), 4.87 (d, $J = 8.5\text{ Hz}$, 1 H), 4.12 (t, $J = 3.0\text{ Hz}$, 1 H), 4.00 (d, $J = 8.4\text{ Hz}$, 1 H), 2.99 (dd, $J = 6.9, 14.0\text{ Hz}$, 1 H), 2.80 (dd, $J = 7.8, 14.0\text{ Hz}$, 1 H), 2.42 (q, $J = 7.6\text{ Hz}$, 1 H), 1.96 (dq, $J = 3.0, 14.0\text{ Hz}$, 2 H), 1.39 (s, 3 H), 1.01 (d, $J = 7.7\text{ Hz}$, 3 H); ^{13}C NMR (100 MHz, CDCl_3) δ 213.5, 183.5, 179.6, 135.3, 132.7, 119.7, 83.7, 73.9, 73.0, 54.1, 50.1, 48.3, 46.7, 33.5, 22.0, 13.9; high resolution mass spectrum m/z 293.1395 ($M+H^+$; calcd for $C_{16}H_{21}O_5$: 293.1389).

A red solution of cyclopentenone (10 mg, 0.034 mmol) and Sudan Red 7B (trace) in CH₂Cl₂ (1.8 mL)-EtOH (1.8 mL) was cooled to -78 °C and a stream of ozone was bubbled through the solution until a red color turned into a yellow/orange. Argon was bubbled through the reaction mixture for 10 min. The mixture was treated with Me₂S (0.02 mL), warmed to room temperature, and concentrated *in vacuo* to give a mixture of lactols. The residue was diluted with acetone (1.7 mL), cooled to 0 °C, and treated with Jones reagent (2.6 M, 0.25 mL, 19 equiv). The reaction mixture was stirred at 0 °C for 7 min and quenched by addition of EtOH (1.5 mL). The resulting green mixture was diluted with EtOAc (20 mL) and washed with saturated NaHCO₃ (20 mL). The aqueous phase was combined with green solid residue and further extracted with EtOAc (3 X 20 mL). Combined extracts were dried (MgSO₄), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-EtOAc 2:1 → 1:1 → 1:3) afforded lactone **15** (9 mg, 90% yield): IR (film) 3334 (m, br), 2975 (m), 2877 (m), 1784 (s), 1748 (s), 1710 (s), 1609 (m), 1491 (w), 1456 (m), 1367 (m), 1348 (w), 1327 (w), 1286 (w), 1251 (m), 1200 (m), 1159 (m), 1119 (m), 1063 (m), 1027 (m), 996 (m), 976 (w), 948 (w), 888 (w) cm⁻¹; ¹H NMR (400 MHz, CD₃OD) δ 6.27 (s, 1 H), 4.79 (dd, *J* = 1.8, 4.1 Hz, 1 H), 4.14 (d, *J* = 10.5 Hz, 1 H), 4.05 (d, *J* = 10.6 Hz, 1 H), 3.10 (d, *J* = 19.1 Hz, 1 H), 2.81 (dd, *J* = 2.7, 19.1 Hz, 1 H), 2.30 (dd, *J* = 4.1, 14.0 Hz, 1 H), 2.25 (q, *J* = 7.7 Hz, 1 H), 2.19 (td, *J* = 2.3, 14.4 Hz, 1 H), 1.44 (s, 3 H), 1.13 (d, *J* = 7.7 Hz, 3 H); ¹³C NMR (100 MHz, CDCl₃) δ 207.3, 176.7, 175.9, 167.6, 131.9, 78.7, 78.4, 73.7, 52.4, 44.3, 43.2, 42.6, 27.7, 22.1, 11.6; high resolution mass spectrum *m/z* 293.1013 (M+H⁺; calcd for C₁₅H₁₇O₆: 293.1025).

α-Hydroxy Lactone 16. A solution of lactone **15** (40 mg, 0.0137 mmol) and CeCl₃•7H₂O (153 mg, 3.0 equiv) in THF (8.2 mL)-MeOH (2.8 mL) was cooled to -60 °C and treated with a solution of NaBH₄ (0.82 mL, 3.0 equiv) in 2-methoxyethyl ether (0.5 M). The resulting mixture was stirred at -55~50 °C for 35 min. The reaction mixture was quenched with 1N aqueous HCl (0.23 mL), diluted with brine (50 mL), and extracted with EtOAc (5 X 100 mL). Combined extracts were dried (MgSO₄), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-EtOAc 1:1 → CH₂Cl₂-MeOH 40:1) gave alcohol (35 mg, 88% yield). The configuration of the newly generated stereocenter was determined by NOE studies: IR (neat) 3384 (s, br), 2972 (s), 2935 (s), 2876 (m), 1784 (s), 1749 (s), 1456 (m), 1368 (m), 1325 (w), 1226 (m), 1162 (m), 1117 (m), 1087 (m), 1064 (m), 1028 (m), 999 (m), 969 (w), 913 (w), 888 (w) cm⁻¹; ¹H NMR (400 MHz, CD₃OD) δ 5.80 (d, *J* = 1.3 Hz, 1 H), 4.89 (dd, *J* = 1.3, 6.6 Hz, 1H), 4.72 (dd, *J* = 1.3, 4.3 Hz, 1 H), 4.00 (d, *J* = 10.1 Hz, 1 H), 3.80 (d, *J* = 10.1 Hz, 1 H), 2.85 (d, *J* = 18.8 Hz, 1 H), 2.67 (dd, *J* = 2.6, 18.9 Hz, 1

H), 2.17 (m, 2 H), 1.93 (dd, $J = 4.4, 14.0$ Hz, 1 H), 1.35 (s, 3 H), 0.92 (d, $J = 7.3$ Hz, 3 H); ^{13}C NMR (100 MHz, CD_3OD) δ 178.6, 172.0, 147.5, 133.6, 81.4, 78.7, 76.6, 76.0, 50.3, 48.0, 44.4, 43.7, 28.3, 22.5, 9.1; high resolution mass spectrum m/z 295.1184 ($\text{M}+\text{H}^+$; calcd for $\text{C}_{15}\text{H}_{19}\text{O}_6$: 295.1182).

The alcohol (69.5 mg, 0.236 mmol) was azeotroped with anhydrous benzene (3 X 80 mL) and placed under high vacuum for 1 h. Then the alcohol was dissolved in THF (80 mL), cooled to -78°C , and treated with a solution of NaHMDS (0.93 mL, 3.9 equiv) in THF (1.0 M). The resultant mixture was stirred at -78°C for 6 min. A solution of 3-phenyl-2-(phenylsulfonyl)-1,2-oxaziridine (248 mg, 4.0 equiv) in THF (1.0 mL) was added to the reaction mixture and the resulting mixture was stirred at -78°C for 3 min. The reaction mixture was quenched with saturated NH_4Cl (5.0 mL), diluted with EtOAc (500 mL), dried (MgSO_4), filtered and concentrated *in vacuo*. Flash chromatography (hexanes-EtOAc 1:1 $\rightarrow$ CH_2Cl_2 -MeOH 30:1 $\rightarrow$ 20:1 $\rightarrow$ 10:1) gave the unreacted alcohol starting material (51.2 mg, 73% recovered) and α -hydroxy lactone **16** [19.1 mg, 26% yield, 99% based on recovered starting material, 6:1 at C(10)]. Recovered starting material (51.2 mg, 0.174 mmol) was engaged in a second hydroxylation reaction followed by flash chromatography to provide the unreacted starting material (28.3 mg, 56% recovered, total recovery: 41%) and α -hydroxy lactone **16** (11.3 mg, 21% yield, 42% overall yield): IR (neat) 3337 (m, br), 2975 (m), 2877 (m), 1783 (s), 1456 (m), 1369 (m), 1343 (w), 1228 (m), 1171 (m), 1111 (m), 1085 (m), 1051 (m), 1024 (m), 997 (m), 966 (w), 890 (w) cm^{-1} ; ^1H NMR (400 MHz, CD_3OD) δ 5.89 (s, 1 H), 5.00* [dd, $J = 1.6, 7.1$ Hz, 1 H, minor diastereomer at C(10)], 4.94 (dd, $J = 1.3, 6.6$ Hz, 1 H), 4.70 (dd, $J = 1.2, 4.7$ Hz, 1 H), 4.62* (dd, $J = 1.7, 4.2$ Hz, 1 H), 3.99 (d, $J = 10.0$ Hz, 1 H), 3.79 (d, $J = 1.6$ Hz, 1 H), 3.64 (d, $J = 10.1$ Hz, 1 H), 2.91 (quintet, $J = 7.1$ Hz, 1 H), 2.49* (quintet, $J = 7.3$ Hz, 1 H), 2.23 (dd, $J = 4.7, 14.1$ Hz, 1 H), 2.03 (td, $J = 1.4, 14.0$ Hz, 1 H), 1.36* (s, 3 H), 1.35 (s, 3 H), 0.91* (d, $J = 7.5$ Hz, 3 H), 0.85 (d, $J = 7.3$ Hz, 3 H); ^{13}C NMR (100 MHz, CD_3OD) δ 178.8, 172.4, 144.3, 136.0, 81.3, 77.5, 76.6, 76.5, 73.3, 54.2, 44.6, 42.8, 23.2, 21.4, 9.5; high resolution mass spectrum m/z 333.0953 [$(\text{M}+\text{Na})^+$; calcd for $\text{C}_{15}\text{H}_{18}\text{O}_7\text{Na}$: 333.0950].

(1*R,10*S**)-2-Oxo-3,4-dehydroneomajucin 17 and Jiadifenin 1.** To a solution of α -hydroxy lactone **16** (19.1 mg, 0.0615 mmol) in acetone (8.0 mL) was added Jones reagent (2.6 M, 1.0 mL, 42 equiv) and the resulting mixture was stirred at room temperature for 19 min. The reaction mixture was treated with MeOH (3.5 mL) and stirred at room temperature for 10 min. The reaction mixture was placed into an ice bath, quenched with saturated NaHCO_3 (7 mL),

diluted with EtOAc (450 mL), dried (MgSO₄), filtered and concentrated *in vacuo*. Preparative TLC (250 μ m X 20 cm X 20 cm, CH₂Cl₂-MeOH 25:1) afforded (1*R**,10*S**)-2-oxo-3,4-dehydroneomajucin **17** (5.6 mg, 29% yield) and jiadifenin **1** (8.5 mg, 40% yield).

(1*R,10*S**)-2-Oxo-3,4-dehydroneomajucin 17**: IR (film) 3392 (m, br), 2933 (m), 1785 (s), 1751 (s), 1710 (s), 1608 (w), 1558 (w), 1456 (w), 1368 (w), 1289 (w), 1226 (w), 1158 (w), 1114 (m), 1065 (m), 996 (m), 967 (w), 853 (w) cm⁻¹; ¹H NMR (500 MHz, C₅D₅N-TMS) δ 6.57 (s, 1 H), 5.29 (m, 1 H), 4.40 (brs, 1 H), 4.38 (d, *J* = 10.5 Hz, 1 H), 4.26 (d, *J* = 10.5 Hz, 1 H), 3.28 (q, *J* = 7.7 Hz, 1 H), 2.88 (dd, *J* = 4.3, 14.0 Hz, 1 H), 2.46 (d, *J* = 14.0 Hz, 1 H), 1.65 (brs, 3 H), 1.31 (d, *J* = 7.7 Hz, 3 H); ¹³C NMR (125 MHz, C₅D₅N-TMS) δ 208.6, 177.1, 176.1, 170.6, 133.6, 79.8, 79.4, 73.7, 73.4, 51.3, 49.0, 44.8, 23.0, 22.6, 13.1; high resolution mass spectrum *m/z* 331.0784 [(M+Na)⁺; calcd for C₁₅H₁₆O₇Na: 331.0794].

Jiadifenin 1: IR (film) 3402 (m, br), 2957 (m), 2876 (w), 1778 (s), 1746 (s), 1710 (s), 1610 (w), 1456 (w), 1398 (w), 1374 (w), 1257 (m), 1224 (w), 1192 (m), 1165 (w), 1104 (w), 1052 (m), 1036 (m), 998 (w), 938 (w), 895 (w) cm⁻¹; ¹H NMR (500 MHz, C₅D₅N-TMS) δ 6.57 (s, 1 H), 6.50* [s, 1 H, minor diastereomer at C(10)], 5.87 (d, *J* = 8.5 Hz, 1 H), 5.12* (d, *J* = 6.2 Hz, 1 H), 5.05 (d, *J* = 6.2 Hz, 1 H), 4.43* (d, *J* = 9.0 Hz, 1 H), 4.20 (d, *J* = 8.4 Hz, 1 H), 4.16* (d, *J* = 9.0 Hz, 1 H), 3.68 (s, 3 H), 3.56* (s, 3 H), 3.51* (q, *J* = 7.7 Hz, 1 H), 3.17* (dd, *J* = 6.3, 11.8 Hz, 1 H), 3.03 (dd, *J* = 6.2, 12.4 Hz, 1 H), 2.95 (q, *J* = 7.6 Hz, 1 H), 2.62* (d, *J* = 11.8 Hz, 1 H), 2.53 (d, *J* = 12.4 Hz, 1 H), 1.69 (s, 3 H), 1.64* (s, 3 H), 1.38* (d, *J* = 7.7 Hz, 3 H), 1.24 (d, *J* = 7.7 Hz, 3 H); ¹³C NMR (125 MHz, C₅D₅N-TMS) δ 209.6*, 208.7, 180.0, 178.8, 178.6*, 177.2*, 171.4, 169.0*, 131.1*, 130.5, 105.8, 103.9*, 80.8, 80.4, 80.2*, 79.3*, 75.9, 75.2*, 61.3*, 60.1, 52.6, 51.9*, 45.1, 44.7*, 44.6*, 42.8, 31.5*, 31.3, 23.1, 23.0*, 14.4*, 12.9; high resolution mass spectrum *m/z* 339.1072 (M⁺; calcd for C₁₆H₁₉O₈: 339.1080).

Assay Protocols: Rat pheochromocytoma cells (PC12, Greene, L. A.; Tischler, A. S. *P. Natl. Acad. Sci. U.S.A.* **1976**, *73*, 2424) were cultured in a 96 well collagen coated plate in F-12K medium supplemented with 0.5 % fetal calf serum and 50 ng/ml of NGF (2.5 S) with or without each compound at 0.3 μ M in DMSO solution for 48 h. Fresh medium with the same supplements was placed on the cell for an additional 48 h. After overall 96 hours of

treatment, the PC12 cells were fixed by using 4% paraformaldehyde incubating for 30 minutes at room temperature. Five regions with similar cell density for each treatment were selected for photographing by ECLIPSE TE2000-S Nikon microscope. For each treatment, 15 neurons were randomly selected to measure the length of neurites. Student T test was used to check the P value.

Table 1. Effect of **1** and **17** on the NGF-induced neurite outgrowth of PC12 cells

Treatment ^a	DMSO	17**	1*
Average neurite length (mean $\pm$ SE, arbitrary unit)	10.1 $\pm$ 1.6	18.6 $\pm$ 1.9	16.2 $\pm$ 2.1

^a duplicate ^b Compounds **17** and **1** were dissolved in DMSO at 0.3 μ M concentration.

** P= 0.002, * P= 0.028