EXPERIMENTAL SECTION

Chemistry

Melting points (mp) were obtained with an MPA 100 OptiMelt automated melting point system (Stanford Research Systems, California, USA). ^{1}H NMR and ^{13}C NMR spectral analyses were performed on a Varian Inova 400 MHz spectrometer (Varian, San Francisco, CA,USA) or a BrukerAvance III 400 spectrometer, respectively, in $CDCl_3$,or DMSO-d_6 with Me_4Si as the internal standard. ESI high-resolution mass spectrometry (HRMS) was performed on an AutospecUltimaTOF mass spectrometer (Micromass UK Ltd, Manchester, UK). Flash chromatography was performed on a CombiflashRf 200 system (Teledyne, Nebraska, USA), with a particle size of 0.038 mm.

General procedures for 12-*N*-substituted (*E*)-$\Delta^{\beta\gamma}$-sophocarpinicacids (11a-b), Methyl 12-*N*-substituted (*E*)-$\Delta^{\beta\gamma}$-sophocarpinate (12a-c) and 12-*N*-substituted (*E*)-$\Delta^{\alpha\beta}$-sophocarpinic acids (13a-c)

Compound **1** (5.0 g, 20 mmol, 1 equiv) was added to 5 N NaOH (30 mL), and the reaction mixture was heated at reflux for 9 h, cooled with an ice–water bath and then acidified with HCl (2 N) to pH 6–7. The solvent was removed *in vacuo*, and the residue was dissolved in methanol to give mixture **6**. A solution of diphenylmethanonehydrazone (5.8 g, 30 mmol,1.5 equiv) in methanol was added to the solution of **6** in methanol, and the mixture was then stirred overnight at room temperature. Extraction with EtOAc, washing of the organic phases with brine, drying with Na_2SO_4 and evaporation afforded the crude product **7**, which was used in the

next reaction without further purification. Anhydrous K_2CO_3 (3.5 equiv) and sulfonyl chloride (1 equiv) were added to solution of **7** in dichloromethane (30 mL), and the reaction mixture was then stirred at room temperature until TLC analysis showed completion of the reaction. The reaction mixture was filtered and the filtrate was evaporated to afford mixture **8**. Separation of compounds **9** and **10** were achieved by flash column chromatography on silica gel with ethyl acetate and hexamethylene as the eluents. Compound **9** was then dissolved in m-cresol (10 mL), and the reaction mixture was stirred at 80 °C for 8–9 h. It was then cooled, and methylisobutylketone (15 mL) was added. The resulting solution was extracted with H_2O (20 mL×3), and the combined extracts were evaporated to afford the crude compound, which was purified by flash columnchromatography on silica gel with dichloromethane and methanol as the eluents to afford **11a-b** in 60–80% yields. Compounds **13a-c** were obtained from compound **10** with the same method. Compounds **11a-b** were dissolved in 2 N MeOH/HCl and the reaction solution were refluxed for 2 h. Compounds **12a-c** were obtained after a sequence of extraction, drying, filtration and flash purification.

(*E*)-12-*N*-(*o*-Cyanobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinic acid (11a).White solid (420 mg, 5%). mp: 119–121 °C. MS-ESI$[M+H]^+$ m/s: 430.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ12.16 (s, 1H), 8.05 (t, J = 7.8 Hz, 1H), 7.94 (t, J = 9.0 Hz, 1H), 7.87–7.77 (m, 2H), 5.51–5.37 (m, 1H), 5.15 (dd, J = 15.1, 10.1 Hz, 1H), 3.91 (t, J = 10.3 Hz, 1H), 3.83–3.77 (m, 1H), 3.45 (t, J = 12.3 Hz, 1H), 2.73 (d, J = 9.8 Hz, 3H), 2.58 (dd, J = 17.1, 6.4 Hz, 1H), 2.15 (s, 1H), 1.92–1.84 (m, 3H), 1.73 (d, J = 10.2 Hz, 1H), 1.64–1.50 (m, 4H), 1.40–1.33 (m, 2H), 1.22 (t, J = 13.7 Hz, 2H); ^{13}C NMR (400 MHz,

DMSO-d_6) δ 172.4, 144.1, 136.1, 133.8, 133.4, 130.3, 130.2, 129.5, 116.5, 109.7, 62.6, 60.0, 56.9, 56.8, 49.1, 47.7, 37.6, 36.1, 28.0, 26.4, 21.1, 20.1; HRMS: calcd for $C_{22}H_{28}O_4N_3S$ $[M+H]^+$: 430.1795, found: 430.1792.

(*E*)-12-*N*-(*o*-Trifluoromethybenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinic acid (11b). White solid (560 mg, 6%). mp: 114–116 °C. MS-ESI$^+$ m/s: 473.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.98 (d, *J* = 7.6 Hz, 1H), 7.86 (d, *J* = 7.2 Hz, 1H), 7.81–7.72 (m, 2H), 5.39–5.32 (m, 1H), 5.09 (dd, *J* = 15.3, 10.0 Hz, 1H), 3.98 (t, *J* = 10.4 Hz, 1H), 3.63 (dd, *J* = 12.8, 3.9 Hz, 1H), 3.45 (t, *J* = 12.4 Hz, 1H), 2.70 (d, *J* = 10.9 Hz, 2H), 2.55 (dd, *J* = 17.3, 7.2 Hz, 1H), 2.31 (dd, *J* = 16.6, 6.0 Hz, 1H), 2.13 (s, 2H), 1.86–1.77 (m, 3H), 1.71 (d, *J* = 10.9 Hz, 1H), 1.57 (s, 4H), 1.38–1.24 (m, 2H), 1.23–1.09 (m, 2H); HRMS: calcd for $C_{22}H_{28}O_4N_2F_3S$ $[M+H]^+$: 473.1716, found: 473.1711.

(*E*)-12-*N*-(*o*-Cyanobenzenesulfonyl) $\Delta^{\alpha\beta}$-sophocarpinic acid (13a). White solid (850 mg, 10%). mp: 121–123 °C. MS-ESI$^+$ m/s: 430.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.16 (s, 1H), 8.08 (d, *J* = 7.9Hz, 1H), 8.01 (d, *J* = 7.6 Hz, 1H), 7.87 (d, *J* = 7.8Hz, 1H), 7.76 (d, *J* = 7.6 Hz, 1H), 6.39 (dt, *J* = 15.7, 6.4 Hz, 1H), 5.47 (d, *J* = 15.7 Hz, 1H), 3.93 (d, *J* = 8.8 Hz, 1H), 3.69 (dd, *J* = 13.3, 5.5 Hz, 1H), 3.55–3.48 (m, 1H), 2.65–2.58 (m, 3H), 2.52 (dd, *J* = 8.1 Hz, 8.4 Hz, 1H), 2.09 (s, 1H), 1.97–1.91 (m, 2H), 1.81 (t, *J* = 9.3 Hz, 2H), 1.73 (d, *J* = 8.7 Hz, 1H), 1.57–1.45 (m, 3H), 1.37–1.26 (m, 4H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 166.9, 144.9, 143.8, 136.2, 134.1, 133.5, 129.5, 123.5, 116.6, 109.8, 63.0, 57.5, 56.7(2), 48.9, 35.7(2), 32.3, 27.9, 27.6, 20.7, 20.4. HRMS: calcd for $C_{22}H_{28}O_4N_3S$ $[M+H]^+$: 430.17950, found: 430.17904.

(*E*)-12-*N*-(*p*-Cyanobenzenesulfonyl) $\Delta^{\alpha\beta}$-sophocarpinic acid (13b). White solid

(680 mg, 8%). mp: 122–124 °C. MS-ESI$^+$ m/s: 430.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.17 (s, 1H), 8.05 (d, J = 8.6 Hz, 2H), 7.99 (d, J = 8.6 Hz, 2H), 6.78–6.70 (m, 1H), 5.72 (d, J = 15.7 Hz, 1H), 3.68 (dd, J = 14.2, 6.2 Hz, 1H), 3.45 (dd, J = 12.7, 6.5 Hz, 1H), 3.25 (dd, J = 12.6, 10.3 Hz, 1H), 2.71 (dt, J = 15.3, 5.3 Hz, 1H), 2.58–2.52 (m, 1H), 2.52–2.51 (m, 1H), 2.48–2.44 (m, 1H), 1.94 (s, 1H), 1.88 (s, 1H), 1.74–1.65 (m, 4H), 1.50 (d, J = 9.3 Hz, 1H), 1.39–1.23 (m, 6H); HRMS: calcd for $C_{22}H_{28}O_4N_3S$ $[M+H]^+$: 430.17950, found: 430.17960.

(*E*)-12-*N*-(*o*-Trifluoromethybenzenesulfonyl) $\Delta^{\alpha\beta}$-sophocarpinic acid (13c). White solid (480 mg, 5%). mp: 218–220 °C. MS-ESI$^+$ m/s: 473.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.97 (s, 1H), 8.08 (d, J = 7.7 Hz, 1H), 7.90 (d, J = 6.8 Hz, 1H), 7.81 (d, J = 7.1 Hz, 2H), 6.38 (dt, J = 15.7, 6.1 Hz, 1H), 5.50 (d, J = 15.8 Hz, 1H), 4.82–4.74 (m, 1H), 4.12 (t, J = 13.5 Hz, 1H), 3.75 (dd, J = 14.1, 4.2 Hz, 1H), 3.69 (d, J = 9.9 Hz, 1H), 3.21 (d, J = 11.1 Hz, 2H), 2.95 (d, J = 9.5 Hz, 2H), 2.59 (d, J = 6.3 Hz, 1H), 2.36 (d, J = 11.0 Hz, 1H), 2.25 (d, J = 12.0 Hz, 1H), 1.90 (d, J = 12.9 Hz, 2H), 1.70–1.49 (m, 7H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 166.8, 144.7, 141.0, 133.8, 133.7, 130.3, 130.2, 129.1, 126.0, 123.5, 63.5, 57.5, 55.1, 55.0, 49.5, 49.0, 35.9, 30.8, 25.2, 24.5, 18.8, 18.4; HRMS: calcd for $C_{22}H_{28}O_4N_2F_3S$ $[M+H]^+$: 473.17164, found: 473.17152.

Methyl (*E*)-12-*N*-(*m*-cyanobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinate hydrochloride (12a). White solid (350 mg, 85%). mp: 134–136 °C. MS-ESI$^+$ m/s: 444.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.77 (s, 1H), 8.22–8.12 (m, 2H), 8.04 (d, J = 7.7 Hz, 1H), 7.77 (t, J = 7.6 Hz, 1H), 5.65–5.46 (m, 1H), 5.28 (dt, J = 15.0, 6.8 Hz, 1H), 4.24 (t, J = 10.3 Hz, 1H), 3.84 (dd, J = 12.6, 3.8 Hz, 1H), 3.72–3.65 (m, 2H), 3.61 (s, 3H), 3.54

(d, J = 9.0 Hz, 1H), 3.13 (d, J = 6.0 Hz, 1H), 3.07 (dd, J = 17.2, 7.2 Hz, 1H), 2.87 (d, J = 9.2 Hz, 1H), 2.22 (d, J = 11.6 Hz, 1H), 2.00 (d, J = 9.9 Hz, 1H), 1.86 (s, 2H), 1.73–1.60 (m, 6H), 1.46 (s, 2H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 171.5, 140.9, 136.9, 132.4, 131.4, 131.2, 130.9, 127.1, 118.1, 112.9, 61.9, 59.0, 54.9, 54.8, 52.1, 47.3, 38.9, 36.8, 34.6, 25.4, 24.2, 18.9, 17.9; HRMS: calcd for $C_{23}H_{30}O_4N_3S$·HCl [M–HCl+H]$^+$: 444.1952, found: 444.1950.

Methyl (*E*)-12-*N*-(*o*-cyanobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinate hydrochloride (12b). White solid (370 mg, 83%). mp: 136–138 °C. MS-ESI$^+$ m/s: 444.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.90 (s, 1H), 8.07–7.96 (m, 2H), 7.85–7.81 (m, 2H), 5.47–5.40 (m, 1H), 5.34 (dd, J = 15.6, 9.4 Hz, 1H), 4.65–4.57 (m, 1H), 3.98–3.95 (m, 2H), 3.62 (d, J = 7.2 Hz, 2H), 3.54 (s, 3H), 3.21 (s, 2H), 2.97–2.85 (m, 2H), 2.81–2.73 (m, 1H), 2.22–2.13 (m, 2H), 1.92–1.86 (m, 1H), 1.79–1.65 (m, 5H), 1.48 (d, J = 11.6 Hz, 2H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 171.1, 144.1, 136.2, 133.8, 133.5, 130.0, 129.9, 129.6, 116.4, 109.7, 62.2, 58.9, 55.0, 54.8, 52.0, 47.1, 38.4, 36.8, 34.9, 25.5, 24.1, 18.8, 17.8; HRMS: calcd for $C_{23}H_{30}O_4N_3S$·HCl [M–HCl+H]$^+$: 444.1952, found: 444.1948.

Methyl (*E*)-12-*N*-(*o*-trifluoromethybenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinate hydrochloride (12c). White solid (420 mg, 86%). mp: 141–143 °C. MS-ESI$^+$ m/s: 487.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.87 (s, 1H), 8.15 (d, J = 6.1 Hz, 1H), 7.87 (d, J = 6.5 Hz, 1H), 7.78 (s, 2H), 5.42–5.30 (m, 1H), 5.18 (dt, J = 16.9, 8.2 Hz, 1H), 4.67 (t, J = 10.4 Hz, 1H), 4.01 (t, J = 13.0 Hz, 1H), 3.84 (d, J = 11.6 Hz, 1H), 3.63–3.56 (m, 1H), 3.50–3.44 (m, 1H), 3.42 (s, 3H), 3.25–3.14 (m, 2H), 2.93–2.77 (m,

2H), 2.54–2.49 (m, 1H), 2.20–2.01 (m, 2H), 1.96–1.81 (m, 1H), 1.73–1.55 (m, 5H), 1.50–1.37 (m, 2H); HRMS: calcd for $C_{23}H_{30}O_4N_2F_3S \cdot HCl$ $[M–HCl+H]^+$: 487.1873, found: 487.1869.

(*Z*)-$\Delta^{\beta\gamma}$-Sophocarpinic acid hydrochloride (15). Compound **5** (3.0 g, 12.2 mmol, 1 equiv) was added to a solution of 5 N HCl (30 mL). The reaction mixture was heated at reflux for 9 h. The solvent was then removed in vacuo, and the residue was recrystallized by methanol and ethyl acetate to afford the compound **15** (2.5 g, 60%). mp:191–193 °C. MS-ESI$^+$ m/s: 265.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.39 (s, 1H), 11.21 (d, J = 8.0 Hz, 1H), 10.27 (d, J = 9.3 Hz, 1H), 9.30 (d, J = 9.0 Hz, 1H), 6.01 (dt, J = 10.8, 7.3 Hz, 1H), 5.49 (t, J = 10.4 Hz, 1H), 4.98 (q, J = 10.4 Hz, 1H), 3.86 (dd, J = 24.2, 12.3 Hz, 1H), 3.65 (d, J = 10.1 Hz, 1H), 3.44–3.33 (m, 2H), 3.25–3.20 (m, 2H), 3.10 (dd, J = 12.2, 3.2 Hz, 1H), 2.97–2.89 (m, 2H), 2.53 (d, J = 12.2 Hz, 1H), 2.33 (dd, J = 11.8, 2.7 Hz, 1H), 1.89–1.56 (m, 8H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 172.4, 132.4, 125.7, 60.4, 54.8, 54.7, 49.8, 41.5, 35.5, 33.8, 30.8, 24.6, 23.6, 18.5(2); HRMS: calcd for $C_{15}H_{25}N_2O_2 \cdot 2HCl$ $[M–2HCl+H]^+$: 265.1911, found: 265.1909.

General procedures for methyl (*Z*)-12-*N*-substituted $\Delta^{\beta\gamma}$-sophocarpinate (17a-i) and (*Z*)-12-*N*-substituted $\Delta^{\beta\gamma}$-sophocarpinic acids (18a-h). Compound **15** (1.0 g, 3.0 mmol) was dissolved in 2 N MeOH/HCl (30 mL). The reaction mixture was refluxed for 2 h. Compound **16** was obtained by evaporation and used in the next reaction without further purification. Anhydrous K_2CO_3 (3.5 equiv) and sulfonyl chloride (1.5 equiv) were added to a solution of compound **16** in dichloromethane (30

mL), and the reaction solution was then stirred at room temperature until TLC analysis showed completion of the reaction. The reaction mixture was filtered, and the filtrate was washed by water and brine, dried with anhydrous Na_2SO_4, filtrated, and concentrated to afford crude compound **17**. The title compounds **17a**–**i** were obtained by purifying with flash column chromatographyon silica gel with dichloromethane and methanol as the eluents.

Compounds **17** (0.76 mmol) were then dissolved in 3 N HCl (15 mL), and the mixture was heated at reflux for 3 h. The pH of the reaction solution was then adjusted to 7–8 by ammonium hydroxide. The solvent was removed under reduced pressure, and the residue was dissolved in MeOH, filtered and evaporated. The title compounds **18a**–**h** were gained by flash column chromatography on silica gel with dichloromethane and methanol as the eluents in 70–80% yields.

Methyl (*Z*)-12-*N*-(*o*-cyanobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinate (17a). White solid (1.02 g, 71%). mp: 121–123 °C. MS-ESI$^+$ m/s: 444.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ8.07–7.96 (m, 2H), 7.88–7.77 (m, 2H), 5.47 (dt, J = 10.2, 7.2 Hz, 1H), 5.23 (t, J = 10.2 Hz, 1H), 4.92 (t, J = 10.5 Hz, 1H), 4.12–3.95 (m, 2H), 3.63 (d, J = 10.0 Hz, 1H), 3.54 (s, 3H), 3.27–3.19 (m, 3H), 2.96–2.86 (m, 2H), 2.73 (dd, J = 18.4, 6.4 Hz, 1H), 2.25–2.14 (m, 2H), 1.93–1.87 (m, 1H), 1.81–1.48 (m, 7H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 171.2, 144.2, 136.0, 133.8, 133.5, 130.0(2), 127.8, 116.3, 109.6, 62.2, 54.9(2), 53.3, 52.0, 46.9, 38.6, 34.8, 33.0, 25.5, 24.1, 18.9, 18.4; HRMS: calcd for $C_{23}H_{30}O_4N_3S$ $[M+H]^+$: 444.1952, found:444.1947.

Methyl (*Z*)-12-*N*-(*m*-cyanobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinate (17b). White solid

(840 mg, 63%). mp:115–116 °C. MS-ESI$^+$ m/s: 444.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.13 (m, 2H), 8.04–7.94 (m, 1H), 7.77 (t, J = 8.1 Hz, 1H), 5.57 (m, 1H), 5.45 (t, J = 10.7 Hz, 1H), 3.88 (t, J = 10.3 Hz, 1H), 3.71 (dd, J = 12.0, 4.0 Hz, 1H), 3.59 (s, 3H), 3.38 (t, J = 12.0 Hz, 1H), 2.84 (m, 1H), 2.73–2.59 (m, 3H), 2.53–2.47 (m, 1H), 2.12 (s, 1H), 1.95–1.77 (m, 3H), 1.72–1.48 (m, 5H), 1.36 (d, J = 13.0 Hz, 1H), 1.20 (t, J = 6.6 Hz, 2H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 171.2, 141.6, 136.7, 132.0, 131.1, 131.0, 130.9, 125.4, 118.0, 112.9, 62.5, 56.9, 56.8, 54.1, 52.1, 48.2, 40.9, 36.4, 32.8, 28.1, 26.4, 21.2, 20.9; HRMS: calcd for $C_{23}H_{30}O_4N_3S[M+H]^+$: 444.1952, found:444.1954.

Methyl (*Z*)-12-*N*-(*p*-cyanobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinate (17c). White solid (770 mg, 58%). mp: 175–177 °C. MS-ESI$^+$ m/s: 444.2; ^{1}H NMR (400 MHz, DMSO) δ 8.05 (s, 1H), 8.03 (s, 1H), 7.87 (s, 1H), 7.84 (s, 1H), 5.57 (dt, J = 11.2, 7.2 Hz, 1H), 5.46 (t, J = 10.7 Hz, 1H), 3.82 (t, J = 10.3 Hz, 1H), 3.71 (dd, J = 11.8, 4.0 Hz, 1H), 3.64–3.61 (m, 1H), 3.60 (s, 3H), 3.40–3.30 (m, 2H), 2.82-2.76 (m, 1H), 2.70–2.56 (m, 3H), 2.12 (s, 1H), 1.95–1.17 (m, 10H); ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.2, 144.1, 133.7(2), 130.9, 128.4(2), 125.3, 118.2, 115.5, 62.5, 56.9, 56.8, 54.2, 52.1, 48.4, 40.9, 36.4, 32.9, 28.1, 26.4, 21.2, 20.9; HRMS: calcd for $C_{23}H_{30}O_4N_3S$ $[M+H]^+$: 444.1952, found: 444.1956.

Methyl (*Z*)-12-*N*-(*m*-trifluoromethybenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinate (17d). White solid (904 mg, 62%). mp: 107–109 °C. MS-ESI$^+$ m/s: 487.2; ^{1}HNMR (400 MHz, DMSO-d_6) δ 8.04 (dd, J = 13.5, 7.8 Hz, 2H), 7.91 (s, 1H), 7.83 (t, J = 7.8 Hz, 1H), 5.56 (dt, J = 11.0, 7.2 Hz, 1H), 5.43 (t, J = 10.6 Hz, 1H), 3.91 (t, J = 9.9 Hz, 1H). 3.73 (dd, J = 8.0, 4.0 Hz, 1H), 3.56 (s, 3H), 3.38–3.32 (m, 3H), 2.83 (dd, J = 17.8, 7.7

Hz, 1H), 2.67 (t, *J* = 10.8Hz, 2H), 2.56 (dd, *J* = 17.8, 6.8 Hz, 1H), 2.12 (s, 1H), 1.91–1.78 (m, 3H), 1.69–1.50 (m, 5H), 2.38–1.26 (m, 2H); HRMS: calcd for $C_{23}H_{30}F_3N_2O_4S$ $[M+H]^+$: 487.1873, found: 487.1879.

Methyl (*Z*)-12-*N*-(*p*-trifluoromethybenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinate (17e). White solid (920 mg，59%). mp: 82–84 °C. MS-ESI$^+$ m/s: 487.2; ^{1}HNMR (400 MHz, DMSO-d_6) δ7.88 (m, 4H), 5.60–5.55 (m, 1H), 5.47 (t, *J* = 10.6 Hz, 1H), 4.59–4.50 (m, 1H), 3.89 (d, *J* = 8.1 Hz, 1H), 3.54 (d, *J* = 7.7 Hz, 1H), 3.49 (s, 3H), 3.23–3.09 (m, 2H), 2.99–2.80 (m, 3H), 2.41 (d, *J* = 6.5 Hz, 1H), 2.20 (s, 1H), 2.01 (d, *J* = 10.3 Hz, 1H), 1.82 (s, 1H), 1.75–1.37 (m, 8H); HRMS: calcd for $C_{23}H_{30}F_3N_2O_4S$ $[M+H]^+$: 487.1873, found: 487.1874.

Methyl (*Z*)-12-*N*-(*o*-nitrobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinate (17f). White solid (910 mg, 61%). mp: 115–117 °C. MS-ESI$^+$ m/s: 464.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ8.05 (d, *J* = 7.7Hz, 1H), 7.92 (d, *J* = 7.8Hz, 1H), 7.87–7.77 (m, 2H), 5.52–5.45 (m, 1H), 5.28 (t, *J* = 10.4 Hz, 1H), 4.88 (t, *J* = 10.7 Hz, 1H), 4.03 (t, *J* = 13.2 Hz, 1H), 3.82 (dd, *J* = 13.5, 4.5 Hz, 1H), 3.71–3.59 (m, 1H), 3.53 (s, 3H), 3.29–3.18 (m, 3H), 2.97–2.86 (m, 2H), 2.64–2.57 (m, 1H), 2.17 (d, *J* = 12.6 Hz, 1H), 2.09 (d, *J* = 11.0 Hz, 1H), 1.90 (d, *J* = 8.5 Hz, 1H), 1.76–1.49 (m, 7H); HRMS: calcd for $C_{22}H_{30}N_3O_6S$ $[M+H]^+$: 464.1850, found: 464.1847.

Methyl (*Z*)-12-*N*-(*m*-nitrobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinate (17g). White solid (1.0 g, 72%). mp: 116–118 °C. MS-ESI$^+$ m/s: 464.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (t, *J* = 1.9 Hz, 1H), 8.42–8.39 (m, 1H), 8.13–8.10 (m, 1H), 7.70 (t, *J* = 8.0 Hz, 1H), 5.76–5.69 (m, 1H), 5.56 (t, *J* = 10.7 Hz, 1H), 4.12 (t, *J* = 10.4 Hz, 1H), 3.90 (dd,

J = 11.9, 4.0 Hz, 1H), 3.68 (s, 3H), 3.49 (t, *J* = 12.0 Hz, 1H), 2.97–2.91 (m, 1H), 2.81–2.75 (m, 3H), 2.24 (t, *J* = 2.9 Hz, 1H), 2.09–1.92 (m, 3H), 1.84–1.62 (m, 6H), 1.52–1.49 (m, 1H), 1.36–1.34 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.1, 148.1, 143.1, 133.2, 130.8, 130.0, 126.6, 125.9, 122.7, 62.8, 57.1, 57.0, 54.4, 51.9, 47.9, 40.9, 36.5, 33.0, 28.0, 26.4, 21.2, 21.1; HRMS: calcd for $C_{22}H_{30}O_6N_3S[M+H]^+$: 464.1850, found: 464.1872.

Methyl (*Z*)-12-*N*-(*p*-nitrobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinate (17h). White solid (820 mg, 59%). mp: 164–166 °C. MS-ESI$^+$ m/s: 464.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 8.8 Hz, 2H), 7.96 (d, *J* = 8.8 Hz, 2H), 5.77–5.71 (m, 1H), 5.58 (t, *J* = 10.7 Hz, 1H), 4.06 (t, *J* = 10.4 Hz, 1H), 3.89 (dd, *J* = 11.8, 4.1 Hz, 1H), 3.70 (s, 3H), 3.46 (t, *J* = 12.0 Hz, 1H), 2.95–2.88 (m, 1H), 2.80–2.71 (m, 3H), 2.23 (t, *J* = 2.8 Hz, 1H), 2.07–1.92 (m, 3H), 1.82–1.62 (m, 6H), 1.52–1.49 (m, 1H), 1.35–1.34 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 171.2, 149.7, 146.7, 130.8, 128.8(2), 125.8, 124.0(2), 62.8, 57.1, 57.0, 54.4, 52.0, 48.0, 40.9, 36.5, 33.0, 28.0, 26.4, 21.2, 21.1; HRMS: calcd for $C_{22}H_{30}N_3O_6S$ $[M+H]^+$: 464.1850, found: 464.1866.

Methyl (*Z*)-12-*N*-(4,5-dibromothiophene-2-sulfonyl) $\Delta^{\beta\gamma}$-sophocarpinate (17i). White solid (950 mg, 55%). mp: 164–166 °C. MS-ESI$^+$ m/s: 582.9; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.63 (s, 1H), 5.68 (dt, *J* = 11.3, 7.2 Hz, 1H), 5.55 (t, *J* = 10.8 Hz, 1H), 3.91 (t, *J* = 10.4 Hz, 1H), 3.63 (s, 3H), 3.57 (dd, *J* = 11.7, 4.0 Hz, 1H), 3.32 (t, *J* = 5.9 Hz, 1H), 2.99–2.82 (m , 2H), 2.69 (d, *J* = 11.2 Hz, 2H), 2.12 (s, 1H), 1.85 (dt, *J* = 14.6, 11.8 Hz, 3H), 1.70–1.44 (m, 5H), 1.40–1.15 (m, 4H). ^{13}C NMR (400 MHz, DMSO) δ 171.3, 140.7, 134.2, 130.9, 124.7, 118.9, 115.3, 62.3, 56.9(2), 54.8, 52.2,

48.4, 41.0, 36.0, 33.1, 28.1, 26.5, 21.1, 21.1; HRMS: calcd for $C_{20}H_{27}O_4N_2Br_2S_2$ $[M+H]^+$: 582.9753, found: 582.9762.

(*Z*)-12-*N*-(*o*-Cyanobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinic acid hydrochloride(18a). White solid (290 mg, 82%). mp: 140–142 °C. MS-ESI$^+$ m/s: 430.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.20 (s, 1H), 10.79 (d, J = 6.3 Hz, 1H), 8.05 (dd, J = 7.4, 1.5 Hz, 1H), 7.97 (dd, J = 7.8, 1.3 Hz, 1H), 7.87–7.78 (m, 2H), 5.50–5.44 (m, 1H), 5.17 (t, J = 10.3 Hz, 1H), 4.84 (t, J = 10.6 Hz, 1H), 4.04–3.94 (m, 2H), 3.63 (d, J = 10.3 Hz, 1H), 3.28–3.13 (m, 3H), 2.97–2.86 (m, 2H), 2.60–2.54 (m, 1H), 2.25 (s, 1H), 2.14 (d, J = 11.0 Hz, 1H), 1.95–1.85 (m, 1H), 1.82–1.57 (m, 5H), 1.53–1.46 (m, 2H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 172.3, 144.2, 136.0, 133.8, 133.6, 130.9, 130.1, 127.3, 116.4, 109.6, 62.2, 54.9, 54.9, 53.2, 46.7, 38.6, 34.8, 33.3, 25.5, 24.1, 18.9, 18.5; HRMS: calcd for $C_{22}H_{28}O_4N_3S{\cdot}HCl$ $[M–HCl+H]^+$: 430.1795, found: 430.1792.

(*Z*)-12-*N*-(*m*-Cyanobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinic acid hydrochloride(18b). White solid (270 mg, 76%). mp: 182–184 °C. MS-ESI$^+$ m/s: 430.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.24 (s, 1H), 10.71 (s, 1H), 8.28–8.06 (m, 2H), 8.01 (d, J = 8.0 Hz, 1H), 7.74 (t, J = 7.9 Hz, 1H), 5.70–5.52 (m, 1H), 5.45 (t, J = 10.5 Hz, 1H), 4.55 (t, J = 10.1 Hz, 1H), 3.96–3.77 (m, 2H), 3.56 (d, J = 9.7 Hz, 1H), 3.26–3.13 (m, 2H), 2.90 (m, 3H), 2.49–2.37 (m, 1H), 2.22 (s, 1H), 2.22 (s, 1H), 2.07–1.94 (m, 1H), 1.86 (s, 1H), 1.79–1.37 (m, 6H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 172.4, 141.5, 136.7, 132.1, 131.3, 130.9, 128.9, 128.0, 118.1, 113.0, 62.1, 54.9, 54.8, 53.6, 47.3, 39.3, 34.8, 33.2, 25.5, 24.2, 19.0, 18.8; HRMS: calcd for $C_{22}H_{28}O_4N_3S{\cdot}HCl$ $[M–HCl+H]^+$: 430.1795, found: 430.1796.

(*Z*)-12-*N*-(*p*-Cyanobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinic acid hydrochloride(18c). White solid (250 mg, 71%). mp: 186–188 °C. MS-ESI$^+$ m/s: 430.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.25 (s, 1H), 10.74 (s, 1H), 8.00 (d, J = 8.4 Hz, 2H), 7.89 (d, J = 8.5 Hz, 2H), 5.62 (dt, J = 11.1, 7.2 Hz, 1H), 5.47 (t, J = 10.5 Hz, 1H), 4.55 (t, J = 10.5 Hz, 1H), 3.95–3.77 (m, 2H), 3.57 (d, J = 10.3 Hz, 1H), 3.26–3.13 (m, 2H), 2.97–2.83 (m, 3H), 2.46 (d, J = 6.8 Hz, 1H), 2.31–2.17 (m, 1H), 2.02 (d, J = 10.6 Hz, 1H), 1.85–1.41 (m, 8H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 172.5, 144.2, 133.7(2), 128.7, 128.4(2), 128.1, 118.3, 115.5, 62.1, 54.9, 54.8, 53.7, 47.4, 39.4, 34.8, 33.2, 25.5, 24.2, 18.9, 18.8; HRMS: calcd for $C_{22}H_{28}O_4N_3S\cdot HCl$ $[M–HCl+H]^+$: 430.1795, found: 430.1795.

(*Z*)-12-*N*-(*p*-Trifluoromethybenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinic acid (18d). White solid (323 mg, 83%). mp: 134–136 °C. MS-ESI$^+$ m/s: 473.2; ^{1}HNMR(400MHz, DMSO-d_6): δ 10.68 (s, 1H), 7.96–7.90 (m, 4H), 5.64–5.59 (m, 1H), 5.48 (t, J = 10.8 Hz, 1H), 4.51 (d, J = 9.2 Hz, 1H), 3.93–3.82 (m, 2H), 3.59–3.17 (m, 2H), 2.95–2.86 (m, 3H), 2.54–2.34 (m, 1H), 2.25 (d, J = 8.4 Hz, 1H),1.91–1.43(m, 10H); HRMS: calcd for $C_{22}H_{28}F_3N_2O_4S$ $[M+H]^+$: 473.1716, found: 473.1738.

(*Z*)-12-*N*-(*o*-Nitrobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinic acid(18e). White solid (310 mg, 84%). mp: 143–145 °C. MS-ESI$^+$ m/s: 450.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.63 (s, 1H), 8.04 (dd, J = 7.6, 1.6 Hz, 1H), 7.92 (dd, J = 7.6, 1.6 Hz, 1H), 7.87–7.80 (m, 2H), 5.52–5.45 (m, 1H), 5.21 (d, J = 10.6 Hz, 1H), 4.79 (t, J = 10.6 Hz, 1H), 3.95 (d, J = 13.1 Hz, 1H), 3.80 (dd, J = 13.5, 4.5 Hz, 1H), 3.64–3.60 (m, 1H), 3.30–3.23 (m, 2H), 3.17–3.10 (m, 1H), 3.00–2.87 (m, 2H), 2.48–2.42 (m, 1H), 2.20–2.12 (m,

1H), 2.07 (d, *J* = 11.0 Hz, 1H), 1.97–1.80 (m, 1H), 1.79–1.35 (m, 7H); HRMS: calcd for $C_{21}H_{28}O_6N_3S$ $[M+H]^+$: 450.1693, found: 450.1698.

(*Z*)-12-*N*-(*m*-Nitrobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinic acid (18f). White solid (280 mg, 82%). mp: 124–126 °C. MS-ESI$^+$ m/s: 450.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.43 (d, *J* = 8.2 Hz, 1H), 8.15 (d, *J* = 7.3 Hz, 1H), 7.76 (t, *J* = 8.0 Hz, 1H), 5.78–5.71 (m, 1H), 5.59 (t, *J* = 10.2 Hz, 1H), 4.70 (t, *J* = 10.4 Hz, 1H), 4.09 (dd, *J* = 13.5, 4.1 Hz, 1H), 3.82 (t, *J* = 12.5 Hz, 1H), 3.61 (d, *J* = 8.9 Hz, 1H), 3.45 (d, *J* = 11.4 Hz, 1H), 3.18–3.11 (m, 1H), 3.03 (s, 1H), 2.49–2.20 (m, 5H), 2.01–1.87 (m, 3H), 1.79–1.67 (m, 2H), 1.45–1.34 (m, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 174.7, 147.9, 144.2, 132.9, 131.9, 130.2, 126.8, 126.2, 122.4, 64.2, 55.6, 55.5, 53.5, 47.8, 39.6, 36.3, 33.8, 26.5, 25.2, 19.5, 19.0; HRMS: calcd for $C_{21}H_{28}O_6N_3S$ $[M+H]^+$: 450.1693, found: 450.1704.

(*Z*)-12-*N*-(*p*-Nitrobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinic acid (18g). White solid (260 mg, 76%). mp: 175–177 °C. MS-ESI$^+$ m/s: 450.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.37 (d, *J* = 6.1 Hz, 2H), 7.96 (d, *J* = 6.0 Hz, 2H), 5.62 (s, 1H), 5.43 (s, 1H), 3.81 (t, *J* = 8.5 Hz, 1H), 3.70 (d, *J* = 9.0 Hz, 1H), 3.29 (t, *J* = 11.1 Hz, 1H), 2.65 (s, 3H), 2.52 (s, 1H), 2.13 (s, 1H), 1.90–1.82 (m, 3H), 1.72–1.43 (m, 5H), 1.36 (d, *J* = 6.5 Hz, 1H), 1.20 (s, 3H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 172.6, 150.1, 145.1, 129.8, 129.2(2), 126.7, 124.9(2), 62.5, 56.8(2), 54.5, 48.4, 40.9, 36.3, 34.1, 28.0, 26.4, 21.1, 21.0; HRMS: calcd for $C_{21}H_{28}O_6N_3S$ $[M+H]^+$: 450.1693, found: 450.1698.

(*Z*)-12-*N*-(4,5-Dibromothiophene-2-sulfonyl) $\Delta^{\beta\gamma}$-sophocarpinic acid hydrochloride (18h). White solid (330 mg, 73%). mp: 175–177 °C. MS-ESI$^+$ m/s:

568.9; ^{1}H NMR (400 MHz, DMSO) δ 12.34 (d, *J* = 19.8 Hz, 1H), 10.24 (s, 1H), 7.68 (s, 1H), 5.77-5.68 (m, 1H), 5.50 (t, *J* = 10.0 Hz,1H), 4.70–4.42 (m, 1H), 3.84–3.61 (m, 2H), 3.56 (d, *J* = 10.0 Hz, 1H), 3.30–3.13 (m, 2H), 3.12–2.97 (m, 1H), 2.91 (s, 2H), 2.77-2.70 (m, 1H), 2.30–2.17 (m, 1H), 2.06–1.95 (m, 1H), 1.93–1.78 (m, 1H), 1.74-1.70 (m, 3H), 1.67-1.56 (m, 2H), 1.48 (d, *J* = 13.7 Hz, 2H); ^{13}C NMR (101 MHz, DMSO) δ 172.4, 140.7, 134.2, 128.8, 127.6, 119.1, 115.2, 61.9, 54.9, 54.8, 54.2, 47.4, 39.4, 34.4, 33.5, 25.5, 24.2, 18.9(2); HRMS: calcd for $C_{19}H_{25}O_4N_2Br_2S_2 \cdot HCl$ $[M–HCl+H]^+$: 568.9596, found: 568.9607.

General procedures for (*Z*)-12-*N*-substituted $\Delta^{\beta\gamma}$-sophocarpinnols (24a-e)

The compound **15** (1.0 g, 4.0mmol) was dissolved in 2 N HCl/MeOH (30 mL). The reaction mixture was refluxed for 2 h, then anhydrous K_2CO_3 (3.5 equiv) and Boc_2O (1.5 equiv) were added to the reaction solution, and the mixture solution was stirred at room temperature until TLC analysis showed completion of the reaction. The reaction mixture was filtered, and the filtrate was washed by water and brine, dried with anhydrous Na_2SO_4, filtrated and concentrated to afford the crude compound **19**.

A solution of the $LiAlH_4$ in THF (2.4 N, 1.2 equiv) was added to the solution of compound **19** in anhydrous THF in ice-bath, then the mixture solution was stirred at room temperature for 30 min, the reaction was then quenched with acetone, 2 ml saturated ammonium chloride solution was added and stirred for 30 min, and the precipitation was filtrated off. The filtrate was concentrated, and the residue of compound **20** was dissolved in ethyl acetate, and washed with water and brine, dried with anhydrous Na_2SO_4, filtrated and concentrated. The residue was stirred in 2 N

HCl/Et_2O (20 ml) to remove the Boc protection group, then the mixute was filtrated to give the crude **21**.

The crude **21** (1.0 equiv), TBSCl (1.2 equiv) and imidazole (1.5 equiv) were used to synthesize compound **22** in CH_2Cl_2, after reaction was complete, benzenesulfonyl chloride (3.0equiv) and TEA (3.0equiv) were added to the reaction solution, which was stirred at room temperature until TLC analysis showed completion of the reaction. The reaction solution was washed by water and brine, dried over anhydrous Na_2SO_4, filtrated and concentrated to afford the crude compound **23**.

The crude **23** was dissolved in 2 N HCl (15 mL), and the mixture was stirred until TLC analysis showed completion of the reaction. The pH of the reaction solution was then adjusted to 7-8 by addition of ammonium hydroxide. The solvent was removed under reduced pressure, and the residue was dissolved in MeOH and filtered to remove the organic salts. The solution was concentrated, and the residue was purified by flash column chromatography on silica gel with dichloromethane and methanol as the eluents to afford compounds **24a-e**.

(*Z*)-12-*N*-(*m*-Cyanobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinnol hydrochloride(24a). White solid (370 mg, 26%). mp: 158–160 °C. MS-ESI$^+$ m/s: 416.2;^{1}H NMR (400 MHz, DMSO-d_6) δ 10.66 (d, J = 6.2 Hz, 1H), 8.14–8.11 (m, 2H), 8.05 (dd, J = 8.1, 1.3 Hz, 1H), 7.77 (t, J = 7.9 Hz, 1H), 5.54–5.48 (m, 1H), 5.37 (t, J = 10.3 Hz, 1H), 4.60 (t, J = 10.4 Hz, 1H), 4.47 (s, 1H), 3.96–3.84 (m, 2H), 3.59 (dd, J = 7.2, 3.1 Hz, 1H), 3.25–3.11 (m, 4H), 2.95–2.86 (m, 2H), 2.23 (dd, J = 7.3, 3.4 Hz, 1H), 2.08–1.99 (m, 2H), 1.88 (dd, J = 7.0, 3.3 Hz, 1H), 1.76–1.45 (m, 8H); ^{13}C NMR (400 MHz,

DMSO-d_6) δ 142.3, 136.5, 133.1, 132.1, 131.1, 130.9, 127.5, 118.1, 112.8, 62.3, 60.4, 54.9(2), 53.7, 47.4, 39.2, 35.2, 31.6, 25.5, 24.2, 19.0, 18.7; HRMS: calcd for $C_{22}H_{30}O_3N_3S$·HCl [M–HCl+H]$^+$: 416.2002, found: 416.1997.

(*Z*)-12-*N*-(*m*-Trifluoromethybenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinnol hydrochloride (24b). White solid (500 mg, 32%). mp: 91–93 °C. MS-ESI$^+$ m/s: 459.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.67 (s, 1H), 8.09 (d, *J* = 8.0 Hz, 1H), 8.03 (d, *J* = 7.8 Hz, 1H), 7.90 (s, 1H), 7.82 (t, *J* = 7.9 Hz, 1H), 5.49–5.42 (m, 1H), 5.37 (t, *J* = 10.4 Hz, 1H), 4.66 (d, *J* = 9.7 Hz, 1H), 3.99–3.89 (m, 2H), 3.63–3.59 (m, 1H), 3.25–3.14 (m, 3H), 3.10–3.04 (m, 1H), 2.97–2.86 (m, 2H), 2.25–2.20 (m, 1H), 2.12–2.00 (m, 2H), 1.96–1.81 (m, 1H), 1.76–1.63 (m, 6H), 1.52–1.39 (m, 3H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 142.3, 133.2, 131.0, 130.7, 129.6, 129.3, 129.2, 126.6, 123.5, 62.0, 59.8, 54.5, 54.4, 53.2, 46.9, 38.7, 34.9, 31.0, 25.0, 23.7, 18.5, 18.1; HRMS: calcd for $C_{22}H_{30}O_3N_2F_3S$·HCl [M–HCl+H]$^+$: 459.1924, found: 459.1924.

(*Z*)-12-*N*-(*p*-Trifluoromethybenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinnol hydrochloride (24c). White solid (460 mg，29%). mp: 87–89 °C. MS-ESI$^+$ m/s: 459.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.48 (s, 1H), 7.91 (q, 4H), 5.48–5.39 (m, 1H), 5.33 (t, *J* = 11.2 Hz, 1H), 4.52 (t, *J* = 10.4 Hz, 1H), 3.92–3.78 (m, 3H), 3.57–3.53 (m, 1H), 3.22–3.11 (m, 3H), 3.07–3.02 (m, 1H), 2.92–2.84 (m, 2H), 2.20 (d, *J* = 11.8 Hz, 1H), 2.02 (d, *J* = 11.0 Hz, 1H), 1.98–1.86 (m, 1H), 1.81 (s, 1H), 1.76–1.37 (m, 8H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 145.0, 133.3, 132.8, 132.5, 128.6(2), 127.4, 126.7, 122.7, 62.4, 60.3, 55.0(2), 53.8, 47.5, 39.3, 35.2, 31.5, 25.6, 24.3, 19.0, 18.8.HRMS: calcd for $C_{22}H_{30}F_3N_2O_3S$·HCl [M–HCl+H]$^+$: 459.1924, found: 459.1930.

(*Z*)-12-*N*-(*o*-Nitrobenzenesulfonyl)$\Delta^{\beta\gamma}$-sophocarpinnol hydrochloride (24d). White solid (400 mg, 27%). mp: 147–149 °C. MS-ESI$^+$ m/s: 436.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.70 (s, 1H), 8.06 (dd, *J* = 7.6, 1.6 Hz, 1H), 7.92 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.86–7.78 (m, 2H), 5.43–5.36 (m, 1H), 5.20 (t, *J* = 10.3 Hz, 1H), 4.84 (t, *J* = 10.5 Hz, 1H), 4.03 (t, *J* = 13.3 Hz, 1H), 3.82 (dd, *J* = 13.7, 4.4 Hz, 1H), 3.65–3.61 (m, 1H), 3.29–3.22 (m, 2H), 3.17–3.13 (m, 1H), 3.08–3.02 (m, 1H), 2.98–2.87 (m, 2H), 2.22–2.08 (m, 3H), 1.99–1.86 (m, 1H), 1.76–1.66 (m, 6H), 1.57–1.49 (m, 3H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 147.2, 134.6, 134.1(2), 132.4, 129.6, 125.2, 124.3, 62.0, 59.9, 54.6, 54.5, 53.2, 46.9, 38.9, 35.0, 31.0, 25.0, 23.7, 18.5, 18.0; HRMS: calcd for $C_{21}H_{30}O_5N_3S{\cdot}HCl$ $[M–HCl+H]^+$: 436.1901, found: 436.1909.

(*Z*)-12-*N*-(*p*-Nitrobenzenesulfonyl) $\Delta^{\beta\gamma}$-sophocarpinnol hydrochloride (24e). White solid (420 mg, 28%). mp: 148–150 °C. MS-ESI$^+$ m/s: 436.2;^{1}H NMR (400 MHz, $CDCl_3$) δ10.50 (s, 1H),8.33 (d, *J* = 8.9 Hz, 2H), 7.99 (d, *J* = 8.9 Hz, 2H), 5.54–5.41 (m, 2H), 4.27 (t, *J* = 10.1 Hz, 1H), 3.87 (dd, *J* = 12.1, 4.0 Hz, 1H), 3.63–3.55 (m, 2H), 3.50 (t, *J* = 12.2 Hz, 1H), 2.81–2.77 (m, 2H), 2.24 (s, 1H), 2.21–2.14 (m, 1H), 2.08–1.93 (m, 4H), 1.84–1.61 (m, 6H), 1.51–1.26 (m, 4H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 149.6, 147.5, 131.1, 130.1, 128.8(2), 123.9(2), 62.9, 61.8, 57.1(2), 54.6, 47.8, 40.9, 36.6, 31.4, 28.0, 26.5, 21.2, 21.1; HRMS: calcd for $C_{21}H_{30}O_5N_3S{\cdot}HCl$ $[M–HCl+H]^+$:436.1901, found: 436.1911.

General procedures for methyl 12-*N*-substituted matrinate (28a-e) and 12-*N*-substituted matrinic acids (29a-c).

Compound **25** (1.0 g, 4 mmol, 1 equiv) was added to 5 N NaOH (20 mL), and the

reaction mixture was heated at reflux for 9 h, cooled with an ice–water bath and then acidified with HCl (6 N) to pH < 5. The solvent was removed *in vacuo*, and the residue was dissolved in methanol. Then the solution was filtered to remove inorganic salt and the solvent was removed *in vacuo*. The crude product **26** was obtained to use the next reaction without further purification. Compound **26** was dissolved in 2 N HCl/MeOH (20 mL) and the mixture was refluxed for 2 h. Compound **27** was obtained by evaporation and used in the next reaction without further purification. Anhydrous K_2CO_3 (3.5 equiv) and sulfonyl chloride (1.5 equiv) were added to a solution of compound **27** in dichloromethane (20 mL), and the reaction solution was then stirred at room temperature until TLC analysis showed completion of the reaction. The reaction mixture was filtered, and the filtrate was washed by water and brine, dried with anhydrous Na_2SO_4, filtrated, and concentrated to afford crude compound **28**. The title compounds **28a**–**e** were obtained by purifying with flash column chromatographyon silica gel with dichloromethane and methanol as the eluents.

Compounds **28a**–**c** (1.04 mmol) were then dissolved in 3 N HCl (15 mL), and the mixture was heated at reflux for 3 h. The pH of the reaction solution was then adjusted to 7–8 by ammonium hydroxide. The solvent was removed under reduced pressure, and the residue was dissolved in MeOH, filtered and evaporated. The title compounds **29a**–**c** were gained by flash column chromatography on silica gel with dichloromethane and methanol as the eluents in 78–83% yields.

Methyl 12-*N*-(*m*-Cyanobenzenesulfonyl) matrinate hydrochloride (28a). White

solid (1.02 g, 53%). mp: 103–105 °C. MS-ESI m/s: 446.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.61 (s, 1H), 8.33 (s, 1H), 8.16 (d, J = 7.8 Hz, 2H), 7.81 (t, J = 7.9 Hz, 1H), 4.14–4.08 (m, 1H), 3.81–3.78 (m, 2H), 3.61–3.55 (m, 1H), 3.53 (s, 3H), 3.20 (d, J = 11.6 Hz, 2H), 2.93–2.85 (m, 2H), 2.31–2.21 (m, 3H), 2.12–2.04 (m, 1H), 1.91–1.85 (m, 2H), 1.75–1.56 (m, 8H), 1.38–1.27 (m, 1H), 1.20–1.08 (m, 1H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 173.4, 142.9, 136.9, 131.6, 131.3, 130.7, 118.0, 113.2, 63.4, 58.0, 55.0, 54.9, 51.6, 49.0, 38.5, 35.1, 33.3, 27.5, 25.3, 24.8, 21.3, 18.8, 18.5; HRMS: calcd for $C_{23}H_{32}O_4N_3S$·HCl [M–HCl+H]+: 446.21080, found: 446.21005.

Methyl 12-*N*-(*p*-Trifluoromethybenzenesulfonyl) matrinate hydrochloride (28b). White solid (1.12 g, 53%). mp: 127–129 °C. MS-ESI m/s: 489.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.82 (d, J = 7.9 Hz, 1H), 8.07 (d, J = 8.3 Hz, 2H), 7.97 (d, J = 8.4 Hz, 2H), 4.22–4.17 (m, 1H), 3.92–3.79 (m, 2H), 3.59 (d, J = 10.2 Hz, 1H), 3.49 (s, 3H), 3.19 (d, J = 11.5 Hz, 2H), 2.93–2.85 (m, 2H), 2.29–2.18 (m, 3H), 2.04–1.95 (m, 1H), 1.90 (d, J = 13.1 Hz, 2H), 1.77–1.52 (m, 8H), 1.36–1.24 (m, 1H), 1.11–1.00 (m, 1H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 173.3, 145.9, 132.9, 128.0 (2), 127.1, 127.0, 123.9, 63.4, 58.2, 55.1, 55.0, 51.5, 49.3, 38.6, 35.4, 33.2, 27.4, 25.3, 24.7, 21.6, 18.8, 18.5; HRMS: calcd for $C_{23}H_{32}O_4N_2F_3S$·HCl [M–HCl+H]+: 489.20294, found: 489.20295.

Methyl 12-*N*-(*o*-Nitrobenzenesulfonyl) matrinate hydrochloride (28c). White solid (1.2 g, 60%). mp: 199–201 °C. MS-ESI m/s: 466.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.76 (d, J = 7.2 Hz, 1H), 8.11 (dd, J = 7.7, 1.4 Hz, 1H), 8.00 (dd, J = 7.7, 1.4 Hz, 1H), 7.93–7.84 (m, 2H), 4.30–4.25 (m, 1H), 3.93 (t, J = 13.5 Hz, 1H), 3.69 (dd, J = 14.0, 4.5 Hz, 1H), 3.60 (d, J = 10.2 Hz, 1H), 3.49 (s, 3H), 3.23 (d, J = 11.5 Hz, 2H),

2.99–2.84 (m, 2H), 2.32 (d, *J* = 10.4 Hz, 1H), 2.21–2.13 (m, 2H), 2.06–1.98 (m, 1H), 1.91 (d, *J* = 12.2 Hz, 2H), 1.74–1.53 (m, 8H), 1.34–1.22 (m, 1H), 1.14–1.03 (m, 1H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 173.2, 147.5, 135.1, 134.3, 133.2, 129.7, 125.1, 63.5, 58.8, 55.1, 55.0, 51.6, 49.5, 38.9, 35.8, 33.1, 27.3, 25.3, 24.7, 21.9, 18.8, 18.5; HRMS: calcd for $C_{22}H_{32}O_6N_3S$·HCl $[M–HCl+H]^+$: 466.20063, found: 466.19983.

Methyl 12-*N*-(*m*-Nitrobenzenesulfonyl) matrinate (28d). White solid (0.95 g, 51%). mp: 72–74 °C. MS-ESI m/s: 466.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (t, *J* = 1.9 Hz, 1H), 8.44–8.41 (m, 1H), 8.26–8.24 (m, 1H), 7.72 (t, *J* = 8.0 Hz, 1H), 3.74–3.70 (m, 1H), 3.69 (s, 3H), 3.54 (dd, *J* = 12.8, 7.4 Hz, 1H), 3.28 (dd, *J* = 12.8, 9.7 Hz, 1H), 2.56–2.53 (m, 1H), 2.44 (d, *J* = 11.2 Hz, 1H), 2.38–2.29 (m, 2H), 2.02–2.00 (m, 2H), 1.85–1.65 (m, 8H), 1.52–1.41 (m, 5H), 1.35–1.28 (m, 2H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 173.7, 148.0, 142.6, 133.3, 129.6, 126.5, 123.0, 62.3, 57.1, 56.4, 56.3, 51.5, 45.6, 39.6, 33.8, 33.7, 33.2, 28.8, 27.9, 21.3, 20.8, 20.4; HRMS: calcd for $C_{22}H_{32}O_6N_3S$ $[M+H]^+$: 466.20063, found: 466.19957.

Methyl 12-*N*-(*m*-Trifluoromethybenzenesulfonyl) matrinate hydrochloride (28e). White solid (1.17 g, 56%). mp: 99–101 °C. MS-ESI m/s: 489.2; ^{1}H NMR (600 MHz, DMSO-d_6) δ 10.83 (d, *J* = 7.0 Hz, 1H), 8.15 (d, *J* = 7.7 Hz, 1H), 7.98 (d, *J* = 7.3 Hz, 1H), 7.86 (dt, *J* = 14.8, 7.1 Hz, 2H), 4.33–4.29 (m, 1H), 3.96 (t, *J* = 13.5 Hz, 1H), 3.74 (dd, *J* = 14.1, 4.3 Hz, 1H), 3.60 (d, *J* = 10.3 Hz, 1H), 3.43 (s, 3H), 3.21 (d, *J* = 10.9 Hz, 2H), 2.93–2.86 (m, 2H), 2.34 (d, *J* = 10.8 Hz, 1H), 2.20 (dd, *J* = 8.8, 3.7 Hz, 1H), 2.11–2.06 (m, 1H), 1.91–1.86 (m, 3H), 1.71–1.52 (m, 8H), 1.22–1.17 (m, 1H), 0.98–0.95 (m, 1H); ^{13}C NMR (400 MHz, $CDCl_3$) δ 177.9, 146.1, 138.8, 138.6, 134.0,

130.8, 129.4, 126.6, 68.4, 63.2, 59.9, 59.8, 56.3, 54.2, 43.8, 40.7, 37.8, 32.3, 30.0, 29.5, 26.7, 23.6, 23.3; HRMS: calcd for $C_{23}H_{32}O_4N_2F_3S\cdot HCl$ $[M–HCl+H]^+$: 489.20294, found: 489.20328.

12-*N*-(*m*-Cyanobenzenesulfonyl) matrinic acid hydrochloride (29a). White solid (380 mg, 78%). mp: 206–208 °C. MS-ESI m/s: 432.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.92 (s, 1H), 10.59 (d, J = 6.7 Hz, 1H), 8.33 (s, 1H), 8.15 (dd, J = 9.2, 8.1 Hz, 2H), 7.81 (t, J = 7.9 Hz, 1H), 4.09 (dt, J = 11.1, 5.8 Hz, 1H), 3.87–3.72 (m, 1H), 3.56 (d, J = 10.2 Hz, 1H), 3.45–3.36 (m, 1H), 3.20 (d, J = 11.6 Hz, 2H), 2.93–2.85 (m, 2H), 2.26–2.24 (m, 2H), 2.19–2.11 (m, 1H), 2.02–1.95 (m, 1H), 1.91–1.85 (m, 2H), 1.74–1.52 (m, 8H), 1.37–1.24 (m, 1H), 1.11 (dt, J = 14.0, 7.0 Hz, 1H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 174.5, 142.8, 136.9, 131.6, 131.3, 130.8, 118.0, 113.2, 63.3, 58.0, 55.0, 54.9, 49.0, 38.5, 35.0, 33.7, 27.6, 25.3, 24.8, 21.3, 18. 8, 18.5; HRMS: calcd for $C_{22}H_{30}O_4N_3S\cdot HCl$ $[M–HCl+H]^+$: 432.19515, found: 432.19499.

12-*N*-(*p*-Trifluoromethybenzenesulfonyl) matrinic acid hydrochloride (29b). White solid (430 mg, 81%). mp: 212–214 °C. MS-ESI m/s: 475.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.89 (s, 1H), 10.63 (s, 1H), 8.07 (d, J = 8.3 Hz, 2H), 7.97 (d, J = 8.4 Hz, 2H), 4.15–4.09 (m, 1H), 3.82 (d, J = 5.6 Hz, 1H), 3.58 (d, J = 10.2 Hz, 1H), 3.34 (s, 1H), 3.20 (d, J = 11.4 Hz, 2H), 2.90 (dd, J = 21.1, 11.7 Hz, 2H), 2.26 (d, J = 9.4 Hz, 2H), 2.14–2.07 (m, 1H), 1.98–1.85 (m, 3H), 1.73–1.52 (m, 8H), 1.37–1.26 (m, 1H), 1.14–1.03 (m, 1H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 174.5, 145.5, 133.0, 128.1(2), 127.1, 127.0, 123.9, 63.4, 58.1, 55.1, 55.0, 49.9, 38.5, 35.2, 33. 7, 27.6, 25.3, 24.8, 21.4, 18.8, 18.5; HRMS: calcd for $C_{22}H_{30}O_4N_2F_3S\cdot HCl$ $[M–HCl+H]^+$:

475.18729, found: 475.18719.

12-*N*-(*o*-Nitrobenzenesulfonyl) matrinic acid hydrochloride (29c). White solid (420 mg, 83%). mp: 218–220 °C. MS-ESI m/s: 452.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 11.89 (s, 1H), 10.72 (d, J = 7.5 Hz, 1H), 8.11 (dd, J = 7.6, 1.6 Hz, 1H), 8.00 (dd, J = 7.6, 1.5 Hz, 1H), 7.92–7.84 (m, 2H), 4.28–4.23 (m, 1H), 3.92 (t, J = 13.4 Hz, 1H), 3.68 (dd, J = 14.1, 4.4 Hz, 1H), 3.60 (d, J = 10.2 Hz, 1H), 3.23 (d, J = 11.4 Hz, 2H), 2.94–2.87 (m, 2H), 2.32 (d, J = 10.6 Hz, 1H), 2.19 (dd, J = 8.8, 3.3 Hz, 1H), 2.08–2.00 (m, 1H), 1.97–1.84 (m, 3H), 1.75–1.54 (m, 8H), 1.32–1.21 (m, 1H), 1.12–1.01 (m, 1H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 174.4, 147.5, 135.1, 134.3, 133.2, 129.8, 125.1, 63.5, 58.9, 55.1, 55.0, 49.4, 38.9, 35.8, 33.5, 27.5, 25.3, 24.7, 22.0, 18.8, 18.5; HRMS: calcd for $C_{21}H_{30}O_6N_3S$·HCl $[M–HCl+H]^+$: 452.18498, found: 452.18497.

12-*N*-(*p*-Trifluoromethybenzenesulfonyl) matrinol hydrochloride (34b). A solution of the $LiAlH_4$ in THF (2.4 N, 1.2 equiv) was added to the solution of compound **28b** (500 mg, 1.02 mmol) in anhydrous THF in ice-bath, then the mixture solution was stirred at room temperature for 30 min, the reaction was then quenched with acetone, 2 ml saturated ammonium chloride solution was added and stirred for 30 min, and the precipitation was filtrated off. The filtrate was concentrated, and the residue of compound **34b** was dissolved in ethyl acetate, and washed with water and brine, dried with anhydrous Na_2SO_4, filtrated and concentrated. The title compounds **34b** were gained by flash column chromatography on silica gel with dichloromethane and methanol as the eluents in 79% yields. White solid (400 mg, 79%). mp:

183–185 °C. MS-ESI m/s: 461.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.57 (d, J = 6.8 Hz, 1H), 8.06 (d, J = 8.3 Hz, 2H), 7.98 (d, J = 8.4 Hz, 2H), 4.14–4.01 (m, 3H), 3.83–3.75 (m, 2H), 3.58 (d, J = 10.3 Hz, 1H), 3.21 (d, J = 10.5 Hz, 2H), 3.13 (d, J = 5.9 Hz, 1H), 2.94–2.85 (m, 2H), 2.26 (d, J = 8.9 Hz, 2H), 1.94–1.88 (m, 2H), 1.69–1.52 (m, 8H), 1.30–1.22 (m, 1H), 1.11–1.05 (m, 2H), 0.90–0.79 (m, 1H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 145.9, 132.9, 128.1(2), 127.0, 127.0, 123.9, 63.4, 60.9, 58.6, 55.1, 55.0, 49.0, 38.7, 35.2, 32.6, 28.3, 25.3, 24.9, 22.7, 18.8, 18.6; HRMS: calcd for $C_{22}H_{32}O_3N_2F_3S$·HCl $[M–HCl+H]^+$: 461.20802, found: 461.20797.

General procedures for 12-*N*-substituted matrinol (34a, 34c)

Compound **25** (1.0 g, 4 mmol, 1 equiv) was added to 5 N NaOH (20 mL), and the reaction mixture was heated at reflux for 9 h, cooled with an ice–water bath and then acidified with HCl (6 N) to pH < 5. The solvent was removed *in vacuo*, and the residue was dissolved in methanol. Then the solution was filtered and evaporated *in vacuo* to obtain the crude product **26**. Compound **26** was dissolved in 2 N HCl/MeOH (20 mL), and the mixture was refluxed for 2 h. Compound **27** was obtained by evaporation and used in the next reaction without further purification. Then anhydrous K_2CO_3 (3.5 equiv) and Boc_2O (1.5 equiv) were added to the reaction solution of **27** in methanol, and the mixture solution was stirred at room temperature until TLC analysis showed completion of the reaction. The reaction mixture was filtered, and the filtrate was washed by water and brine, dried with anhydrous Na_2SO_4, filtrated and concentrated to afford the crude compound **30**.

A solution of the $LiAlH_4$ in THF (2.4 N, 1.2 equiv) was added to the solution of

compound **30** in anhydrous THF in ice-bath, then the mixture solution was stirred at room temperature for 30 min, the reaction was then quenched with acetone, 2 ml saturated ammonium chloride solution was added and stirred for 30 min, and the precipitation was filtrated off. The filtrate was concentrated, and the residue of compound **31** was dissolved in ethyl acetate, and washed with water and brine, dried with anhydrous Na_2SO_4, filtrated and concentrated. The residue was stirred in 2 N HCl/Et_2O (20 ml) to remove the Boc protection group, and the mixute was filtrated. The filter cake, TBSCl (1.2 equiv) and imidazole (1.5 equiv) were used to synthesize compound **32** in CH_2Cl_2, after reaction was complete, benzenesulfonyl chloride (3.0 equiv) and TEA (3.0 equiv) were added to the reaction solution, which was stirred at room temperature until TLC analysis showed completion of the reaction. The reaction solution was washed by water and brine, dried over anhydrous Na_2SO_4, filtrated and concentrated to afford the crude compound **33**.

The crude **33** was dissolved in 2 N HCl (15 mL), and the mixture was stirred until TLC analysis showed completion of the reaction. The pH of the reaction solution was then adjusted to 7-8 by addition of ammonium hydroxide. The solvent was removed under reduced pressure, and the residue was dissolved in MeOH and filtered to remove the organic salts. The solution was concentrated, and the residue was purified by flash column chromatography on silica gel with dichloromethane and methanol as the eluents to afford compounds **34a** and **34c**.

12-*N*-(*m*-Cyanobenzenesulfonyl) matrinol hydrochloride (34a). White solid (370 mg, 20%). mp: 97–99 °C. MS-ESI m/s: 418.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ

10.75 (d, *J* = 7.4 Hz, 1H), 8.30 (t, *J* = 1.5 Hz, 1H), 8.15 (dd, *J* = 7.9, 1.7 Hz, 2H), 7.82 (t, *J* = 7.9 Hz, 1H), 4.17–4.11 (m, 1H), 3.87–3.78 (m, 2H), 3.58 (d, *J* = 10.3 Hz, 1H), 3.20–3.15 (m, 4H), 2.93–2.85 (m, 2H), 2.27–2.24 (m, 2H), 1.89 (d, *J* = 13.2 Hz, 2H), 1.74–1.51 (m, 8H), 1.29 (m, 1H), 1.16–1.04 (m, 2H), 0.93–0.77 (m, 1H); HRMS: calcd for $C_{22}H_{32}O_3N_3S{\cdot}HCl$ $[M–HCl+H]^+$: 418.21589, found: 418.21564.

12-*N*-(*o*-Nitrobenzenesulfonyl) matrinol hydrochloride (34c). White solid (460 mg, 24%). mp: 208–210 °C. MS-ESI m/s: 438.2; ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.68 (s, 1H), 8.09 (dd, *J* = 7.5, 1.6 Hz, 1H), 8.00 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.93–7.85 (m, 2H), 4.25–4.19 (m, 1H), 4.02 (s, 1H), 3.90 (t, *J* = 13.4 Hz, 1H), 3.68 (dd, *J* = 14.2, 4.3 Hz, 1H), 3.60 (d, *J* = 10.2 Hz, 1H), 3.23 (d, *J* = 11.5 Hz, 2H), 3.08 (t, *J* = 6.1 Hz, 2H), 2.98–2.86 (m, 2H), 2.31 (d, *J* = 10.1 Hz, 1H), 2.19 (dd, *J* = 8.7, 3.2 Hz, 1H), 1.90 (s, 2H), 1.70–1.53 (m, 8H), 1.24–1.16 (m, 1H), 1.12–1.00 (m, 2H), 0.87–0.77 (m, 1H); ^{13}C NMR (400 MHz, DMSO-d_6) δ 147.5, 135.0, 134.6, 133.2, 129.8, 125.1, 63.5, 60.8, 59.3, 55.2, 55.0, 49.5, 39.1, 35.9, 32. 5, 28.2, 25.3, 24.8, 23.3, 18.8, 18.6; HRMS: calcd for $C_{21}H_{32}O_5N_3S{\cdot}HCl$ $[M–HCl+H]^+$: 438.20572, found: 438.20778.

Biological methods

Virus resources

Madin-Darby Canine Kidney (MDCK) cells and Coxsackie viruses B (CVB1, CVB 2, CVB3, CVB5 and CVB6 Nancy strain) were purchased from ATCC. Influenza A strains (H1N1) were all obtained from the Institute of Virology, Chinese Academy of Preventive Medicine.

Anti-CVB assays:

Confluent Vero cells grown in 96-well microplates were infected with 100 median tissue culture infective doses of CVB. After 1 h of adsorption at 37 °C, the monolayers were washed with phosphate-buffered saline (PBS) and incubated at 37 °C in the maintenance medium (minimum essential medium (MEM) plus 2% fetal bovine serum (FBS) with or without test compounds. The viral cytopathic effect was observed when the viral control group reached 4+, and the antiviral activity of the tested compounds was determined by the Reed and Muench analyses.

Cytotoxicity assay:

The cytotoxicity of the compounds in the presence of Vero cells was monitored by a CPE assay. Vero cells (3×10^4 in each well) were plated into a 96-well plate. After 24 h, the monolayer cells were incubated in the presence of various concentrations of test compounds. After 48 h of culture at 37 °C and 5% CO_2 in a carbon dioxide incubator, the cells were monitored with the CPE assay. The median TC_{50} value was calculated by Reed and Muench analyses.