# **Supplementary Data**

# 1. General experimental procedures :

All glass apparatus were oven-dried prior to use. HRESIMS spectra were obtained using a Thermo Fisher LTQ-orbitrap instrument. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded using a Bruker spectrometer (operating at 400 MHz for <sup>1</sup>H NMR; 100 MHz, for <sup>13</sup>C NMR, respectively; or 600 MHz for <sup>1</sup>H; 150 MHz for <sup>13</sup>C, respectively) using CDCl<sub>3</sub> as solvent. Tetramethylsilane ( $\delta$  0.00 ppm) served as an internal standard in <sup>1</sup>H NMR and <sup>13</sup>C NMR unless stated otherwise. Chemical shift ( $\delta$  0.00 ppm) values are reported in parts per million and coupling constants in Hertz (Hz). Splitting patterns are described as singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). Reactions were monitored by TLC (GF254 nm). TLC plates were visualized in UV light (254 nm) and by staining with spray reagent, vanillin or iodine. Flash column chromatography was performed with silica gel (Qingdao Haiyang Chemical Co., Ltd, 200-300 mesh). Andrographolide was purchased from Guanghan Bencao Company. Other chemicals and reagents were obtained from Sigma-Aldrich (USA) or Chengdu Best-Reagent in reagent grade and were used without further purification.

# 2. Synthesis of compound a

Andrographolide (4 g) was dissolved in 100 ml acetone, then 13 ml 2,2dimethoxypropane was added in one portion. The mixture was stirred for 5 minutes, then 0.14 g pyridinium p-toluenesulfonate was added, the resulting mixture was stirred in room temperature for 2 hours. After the reaction, the solvent was removed under vacuum, the residue was dissolved in 80 ml CH<sub>2</sub>Cl<sub>2</sub>, washed with 50 ml sodium hydrogen carbonate solution, 50 ml H<sub>2</sub>O, 50 ml saturated NaCl solution, respectively. The organic layer was dried with anhydrous Na<sub>2</sub>SO<sub>4</sub> and evaporated to dryness under vacuum, the residue was purified by chromatography using ethyl acetate-hexane (3:7) to give **a** as a white solid (4.3 g, 94%). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  6.98 (t, *J*=8.00Hz, 1H), 5.04 (d, *J*=4.00Hz, 1H), 4.92(s, 1H), 4.62 (s, 1H), 4.45-4.44 (q, d, *J*=4.00Hz, 1H), 4.28 (d, *J*=10.00Hz, 1H), 3.95 (d, *J*=10.00Hz, 1H), 3.50 (dd, *JI*=4.00Hz, *J2*=8.00Hz, 1H), 3.18 (d, *J*=10.00Hz, 1H), 2.57-2.55(m, 3H), 2.43 (d, *J*=12.00Hz, 1H), 2.00-1.91(m, 2H), 1.81-1.77 (m,6H), 1.42 (s,3H), 1.37 (s,3H), 1.25 (s,3H), 0.97 (s,3H).

#### 3. Synthesis of 2-(tosyloxy)acetic acid

Ethyl 2-hydroxyacetate (5 g) and 4-methylbenzenesulfonyl chloride (9.2 g) were added in anhydrous ether (40 ml). The solution was cooled to 0 °C, and triethylamine (13.4 ml) was then added dropwise. The mixture was stirred at 0 °C for 2 hours. After the reaction, the solution was washed with water (40 ml×2), saturated NaCl solution (40 ml). The organic layer was dried with anhydrous Na<sub>2</sub>SO<sub>4</sub> and evaporated to dryness under vacuum, the residue was purified by chromatography using ethyl acetate-hexane (1:5) to afford a white solid (9.3 g). The solid was added into a mixed solution of ethanol (20 ml) and 5 % sodium hydroxide (16 ml ), and stirred at 20 °C for 5 hours. After the reaction, the solution was distilled under vacuum until no ethanol, the residue was added to 100 ml ice-water, then the pH was adjusted to 2, the white precipitate was filtered, and crystallized to afforded the 2-(tosyloxy)acetic acid as a white solid (7.6 g, 69%). <sup>1</sup>H NMR (400MHz, CDCl<sub>3</sub>)  $\delta$  7.84 (d, *J*=8.00Hz, 2H), 7.37(d, *J*=8.00Hz, 2H), 4.64 (s, 2H), 2.46 (s, 3H).

## 4. Synthesis of compound b

2-(tosyloxy)acetic acid (1.7 g) and sulfurous dichloride (6 ml) were added to 50 ml flask , refluxed under N<sub>2</sub> for 2 h. After that, the excessive sulfurous dichloride was distilled under vacuum, and then the residue was dissolved in anhydrous  $CH_2Cl_2$  (15 ml). In another flask, **a** (1.8 g), triethylamine (1.2 ml), and anhydrous  $CH_2Cl_2$  (20 ml) were added, stirred, and then cooled to 0 °C. After that, the former prepared acyl chloride was added dropwise, and then stirred at room temperature for 1 h. After the reaction, the mixture was washed with water (50 ml), saturated NaCl solution (50 ml), then the organic layer was dried with anhydrous Na<sub>2</sub>SO4, and evaporated to give the crude oil, which was subjected to chromatography to afford compound **b** as an oil. (2 g, 73%).

### 5. General procedure for the synthesis of compound 1-9

To a flask was added the aromatic (or heteroaromatic) thiol, sodium methanolate, methanol, stirred for 20 min, then the mixture was cooled to 0 °C. Then a solution of **b** in acetone was added into the mixture dropwise, the result solution was stirred at room temperature for 1 hour, and then heated and refluxed for 15 min. After the reaction, the organic solvents were removed under vacuum, and the residue was dissolved in  $CH_2Cl_2$ , washed with  $H_2O$ , saturated NaCl solution. The separated organic layer was dried with anhydrous  $Na_2SO_4$  and evaporated to give the crude product. The crude product was then purified by column chromatography to afford compound **1-9**.

**5.1.** compound **1**: white solid, yield 80%. HR-ESI-MS (*m/z*): 497.273 [M+H]<sup>+</sup>, calcd for C<sub>30</sub>H<sub>41</sub>O<sub>4</sub>S<sub>•</sub> <sup>1</sup>H NMR (400 MHz, CDCl3), δ 7.16 (d, *J*=8.00Hz, 2H), 7.10 (s, 1H), 7.06 (d, *J*=8.00Hz, 2H), 4.91 (s, 1H), 4.75 (s, 1H), 4.71 (s, 2H), 3.97-3.95 (m, 2H), 3.53 (dd, *J*<sub>1</sub>=4.12Hz, *J*<sub>2</sub>=8.00Hz,1H), 3.17 (d, *J*=10.00Hz, 1H), 2.39 (d, *J*=4.00Hz,1H), 2.32 (d, *J*=4.00Hz,1H), 2.30 (s, 3H), 2.04-1.90 (m, 3H), 1.85 (m, 3H), 1.72 (d, *J*=12.00Hz, 2H), 1.41 (s, 3H), 1.37 (s, 3H), 1.26 (m, 3H), 1.21 (s, 3H), 0.97 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 172.41, 147.16, 145.56, 137.45, 135.93, 132.31, 130.71, 129.70, 108.06, 99.09, 76.03, 69.95, 63.98, 53.46, 52.20, 43.57, 38.45, 37.96, 34.20, 29.06, 27.09, 26.10, 25.30, 24.98, 23.42, 21.06, 16.60.

**5.2.** Compound **2**: white solid, yield 79%. HR-ESI-MS (*m/z*): 483.257 [M+H]<sup>+</sup>, calcd for C<sub>29</sub>H<sub>39</sub>O<sub>4</sub>S。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.27-7.16 (m, 6H), 4.93 (s, 1H), 4.80 (s, 1H), 4.72 (s, 2H), 4.07 (d, *J*=12.00Hz, 1H), 3.96 (d, *J*=12.00Hz, 1H), 3.53-3.50 (dd, *J*<sub>1</sub>=4.00Hz, *J*<sub>2</sub>=8.00Hz,1H), 3.16 (d, *J*=10.00Hz, 1H), 2.38 (d, *J*=4.00Hz, 2H), 2.28 (d, *J*=4.00Hz,1H), 1.99- 1.90 (m, 3H), 1.85-1.71 (m, 4H), 1.41(s, 3H), 1.37(s, 3H), 1.26 (m, 3H), 1.20 (s, 3H), 0.97 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 172.40, 147.09, 145.73, 135.98, 134.70, 131.63, 131.34, 128.96, 127.07, 108.14, 99.12, 76.30, 69.99, 63.99, 53.46, 52.16, 43.07, 38.44, 37.97, 34.18, 29.25, 27.05, 26.09, 25.29 24.95, 23.41, 16.61.

**5.3.** Compound **3**: yellow solid, yield 76%. HR-ESI-MS (*m/z*): 528.242 [M+H]<sup>+</sup>,

calcd for C<sub>29</sub>H<sub>38</sub>NO<sub>6</sub>S<sub>•</sub> <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  8.09 (d, *J*=8.00Hz, 2H), 7.37 (s, 1H), 7.30-7.28 (m, 2H), 4.99 (s, 1H), 4.92 (s, 1H), 4.81 (s, 2H), 4.29 (d, *J*=6.00Hz, 2H), 3.94 (d, *J*=12.00Hz, 1H), 3.53-3.50 (dd, *J<sub>I</sub>*=4.00Hz, *J<sub>2</sub>*=8.00Hz, 1H), 3.16 (d, *J*=8.00Hz, 1H), 2.42 (d, *J*=12.00Hz, 1H), 2.16 (d, *J*=12.00Hz, 1H), 1.99-1.90 (m, 2H), 1.83-1.69 (m, 5H), 1.41(s, 3H), 1.37(s, 3H), 1.26 (m, 3H), 1.18 (s, 3H), 0.97 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  172.18, 146.34, 146.22, 145.65, 135.58, 127.83, 124.07, 108.42, 99.12, 80.42, 70.23, 64.11, 55.24, 53.44, 42.93, 41.34, 38.96, 38.05, 36.83, 29.21, 28.19, 23.85, 22.68, 15.49.

**5.4.** Compound **4**: white solid, yield 80%. ESI-MS (*m*/*z*): 501.5 [M+H]<sup>+</sup> $_{\circ}$  <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  7.28 (t, *J*=4.12Hz, 2H), 7.10 (s, 1H), 6.96 (t, *J*=4.00Hz, 2H), 4.91 (s, 1H), 4.73 (s, 2H), 4.69 (s, 1H), 3.96 (d, *J*=12.00Hz, 2H), 3.53-3.52 (dd, *J*<sub>1</sub>=4.00Hz, *J*<sub>2</sub>=8.00Hz,1H), 3.18 (d, *J*=12.00Hz, 1H), 2.41 (d, *J*=12.00Hz, 1H), 2.27 (d, *J*=12.00Hz, 1H), 1.97-1.94 (m, 2H), 1.86-1.73 (m, 5H), 1.41 (s, 3H), 1.37 (s, 3H), 1.28 (d, *J*=16.00Hz, 3H), 1.21 (s, 3H), 0.97 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  172.28, 172.22, 163.62, 161.15, 147.10, 146.73, 145.43, 135.81, 134.62, 134.54, 129.55, 129.52, 116.20, 115.98, 108.04, 99.14, 80.49, 76.23, 69.96, 63.98, 55.29, 53.50, 44.19, 42.95, 38.47, 37.97, 36.85, 29.09, 27.02, 26.11, 25.30, 23.42, 16.62.

5.5. Compound 5: white solid, yield 78%. ESI-MS (*m/z*): 513.3 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.24 (d, *J*=8.00Hz, 2H), 6.98 (s, 1H), 6.80 (d, *J*=12.00Hz, 2H), 4.89 (s, 1H), 4.70 (s, 2H), 4.64 (s, 1H), 3.97 (d, *J*=12.00Hz, 1H), 3.78 (d, *J*=4.00Hz, 1H), 3.46-3.43 (dd, *J*<sub>1</sub>=4.00Hz, *J*<sub>2</sub>=8.00Hz, 1H), 3.17 (d, *J*=12.00Hz, 1H), 2.39 (d, *J*=12.00Hz, 1H), 2.30 (d, *J*=12.00Hz, 1H), 2.02-1.88 (m, 2H), δ1.86-1.72 (m, 5H),

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1.41(s, 3H), 1.37(s, 3H), 1.28 (m, 3H), 1.22 (s, 3H), 0.97 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  172.40, 172.36, 159.76, 159.69, 147.24, 145.30, 135.72, 135.69, 135.42, 124.33, 114.46, 107.94, 99.08, 80.50, 69.94, 63.97, 53.47, 52.24, 44.41, 38.48, 37.98, 37.94, 34.27, 28.76, 27.15, 26.12, 25.32, 25.03, 23.42, 16.62.

**5.6.** Compound **6a and 6b**: after the reaction, compound **6a** and **6b** were separated by silica gel (PE:EA = 10:1). 6a, white solid, yield 76%. ESI-MS (m/z): 489.5 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>), δ 7.37 (s, 1H), 6.96 (s, 1H), 6.91 (s, 1H), 6.81 (s, 1H), 4.81 (s, 1H), 4.64 (q, J=12.00Hz, 2H), 4.42 (s, 1H), 3.90 (d, J=12.00Hz, 1H), 3.72 (d, J=12.00Hz, 1H), 3.48 (s, 1H), 3.12 (d, J=12.00Hz, 1H), 2.36 (d, J=12.00Hz, 1H), 2.23 (d, J=12.00Hz, 1H), 1.96-1.68 (m, 6H), 1.35 (s, 3H), 1.31 (s, 3H), 1.25 (m, 2H), 1.21 (s, 3H), 0.85 (s, 3H). <sup>13</sup>C NMR (150 MHz, CDCl<sub>3</sub>)  $\delta$  171.15, 146.26, 144.39, 135.37, 133.59, 130.07, 129.84, 126.59, 106.78, 98.09, 75.29, 69.01, 62.96, 52.46, 51.12, 44.54, 37.49, 36.93, 33.39, 26.99, 26.08, 25.10, 24.30, 23.97, 22.39, 15.61. **6b**, white solid, yield 7.5 %. ESI-MS (*m/z*): 489.5 [M+H]<sup>+</sup> <sup>1</sup>H NMR (600 MHz, CDCl<sub>3</sub>),  $\delta$  7.32 (d, J = 6.00 Hz, 1H), 7.00 (d, J = 6.00 Hz, 1H), 6.93 (q, J = 6.00 Hz, 1H), 6.75 (s, 1H), 4.82 (s, 1H), 4.67 (s, 2H), 4.49 (s, 1H), 3.88 (d, J=12.00Hz, 1H), 3.82 (d, J=12.00Hz, 1H), 3.35 (dd, J=12.00 Hz, 6 Hz, 1H), 3.10 (d, J=12.00Hz, 1H), 1.34 (s, 3H), 1.29 (s, 3H), 1.19 (s, 3H), 0.83 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>) δ 171.12, 145.73, 145.06, 135.61, 131.86, 130.36, 130.17, 126.71, 106.92, 97.92, 75.67, 68.91, 62.74, 53.00, 51.51, 43.81, 37.72, 36.87, 36.72, 33.46, 27.38, 26.48, 25.12, 24.37, 24.21, 22.34, 15.03..

**5.7.** Compound 7: white solid, yield 77%. ESI-MS (m/z): 484.3 [M+H]<sup>+</sup>° <sup>1</sup>H NMR

(400 MHz, CDCl<sub>3</sub>),  $\delta$  8.40 (d, J=4.00Hz, 1H), 7.46 (t, J=4.00Hz, 1H), 7.33 (s, 1H), 7.13 (d, J=8.00Hz, 1H), 6.98 (t, J=4.00Hz, 1H), 4.96 (s, 1H), 4.88 (s, 1H), 4.74 (d, J=8.00Hz, 2H), 3.96 (d, J=12.00Hz, 1H), 3.53-3.47 (dd, J<sub>I</sub>=4.00Hz, J<sub>2</sub>=8.00Hz,1H), 3.17 (d, J=12.00Hz, 1H), 2.45-2.38 (m, 2H), 2.06-1.88 (m, 3H), 1.77-1.62 (m, 4H), 1.41 (s, 3H), 1.36 (s, 3H), 1.26 (m, 2H), 1.19 (s, 3H), 0.97 (s, 3H). <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>)  $\delta$  172.40, 157.73, 149.28, 146.80, 146.77, 136.13, 134.05, 122.75, 119.80, 108.26, 98.89, 80.50, 69.87, 63.78, 54.15 53.43, 52.71, 38.72, 38.07, 38.00, 37.76, 34.37, 28.01, 27.55, 26.15, 25.40, 25.27, 23.46, 16.62.

**5.8.** Compound **8**: white solid, yield 73%. ESI-MS (*m/z*): 485.3 [M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 8.50 (d, *J*=4.00Hz, 1H), 8.47 (d, *J*=4.00Hz, 1H), 7.41 (d, *J*=12.00Hz, 1H), 6.97 (d, *J*=4.00Hz, 1H), 4.95 (s, 1H), 4.86 (m, 1H), 4.77 (s, 2H), 3.96-3.93 (m, 1H), 3.49 (m, 2H), 3.18-3.17 (m, 1H), 2.40-2.38 (m, 2H), 2.06- 1.88 (m, 4H), 1.77-1.62 (m, 4H), 1.40 (s, 3H), 1.36 (s, 3H), 1.26 (m, 2H), 1.19 (s, 3H), 0.91 (s, 3H).

5.9. Compound 9: white solid, yield 71%. ESI-MS (*m/z*): 490.3 [M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.68 (d, *J*=4.00Hz, 1H), 7.34 (s, 1H), 7.25 (d, *J*=4.00Hz, 1H), 4.93 (s, 1H), 4.77 (s, 2H), 4.75 (s, 1H), 4.45-4.4.42 (m, 1H), 3.95 (d, *J*=12.00Hz, 1H), 3.56-3.53 (m, 2H), 3.16 (d, *J*=8.00Hz, 1H), 2.42 (d, *J*=12.00Hz, 1H), 2.07- 1.91 (m, 4H), 1.86-1.70 (m, 4H), 1.40 (s, 3H), 1.36 (s, 3H), 1.26 (d, *J*=4.00Hz, 2H), 1.19 (s, 3H), 0.91 (s, 3H).

#### 6. General procedure for the synthesis of compound 10-18

The corresponding 3,19-dihydroxy group protected compound and 70% acetic acid

was added in the flask, and stirred for 45 min. After the reaction, H<sub>2</sub>O was added, the pH was adjusted to 7 by using sodium hydrogen carbonate. The mixture was extracted with CH<sub>2</sub>Cl<sub>2</sub> for three times. The organic layers were combined, and dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, then evaporated to give the crude product, which was subject to chromatography to afford the product.

6.1. Compound 10: white solid, yield 60%. ESI-MS (*m/z*): 457.4 [M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.16 (d, *J*=8.00Hz, 2H), 7.06 (d, *J*=8.00Hz, 2H), 7.05 (s, 1H), 4.90 (s, 1H), 4.70 (s, 3H), 4.17 (d, *J*=12.00Hz,1H), 3.97 (d, *J*=12.00Hz,1H), 3.53 (t, *J*2=8.00Hz,1H), 3.32 (d, *J*=4.00Hz,1H), 2.40 (d, *J*=4.00Hz,1H), 2.30 (s, 3H), 2.28 (d, *J*=4.00Hz,1H), 1.95-1.74 (m, 8H), 1.29 (m, 3H), 1.26 (s, 3H), 0.63 (s, 3H).

6.2. Compound 11: yellow solid, yield 59%. ESI- MS (*m/z*): 443.5 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), 7.25 (m, 5H), 7.10 (s, 1H), 4.93 (s, 1H), 4.74 (s, 1H), 4.71 (s, 2H), 4.17 (d, *J*=12.00Hz, 1H), 4.07 (d, *J*=12.00Hz, 1H), 3.52 (t, *J*=8.00Hz, 1H), 3.32 (d, *J*=10.00Hz, 1H), 2.39 (d, *J*=4.00Hz, 1H), 2.25 (d, *J*=4.00Hz, 1H), 1.94-1.92 (m, 2H), 1.83-1.81 (m, 5H), 1.28 (m, 3H), 1.25 (s, 3H), 0.64 (s, 3H).

**6.3.** Compound **12**: white solid, yield 61%. ESI-MS (*m/z*): 460.3 [M+H]<sup>+</sup>° <sup>-1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.27 (t, *J*=4Hz, 2H), 7.03 (s, 1H), 6.97 (t, *J*=4Hz, 2H), 4.89 (s, 1H), 4.72 (s, 2H), 4.64 (s, 1H), 4.18 (d, *J*=6.00Hz, 1H), 3.95 (t, *J*=4.00Hz, 1H), 3.52 (t, *J*=4.00Hz, 1H), 3.32 (d, *J*=10.00Hz, 1H), 2.91 (s, 2H), 2.42 (d, *J*=12.00Hz, 1H), 2.24(m, 1H), 1.94-1.92 (m, 2H), 1.83-1.81 (m, 5H), 1.28 (m, 3H), 1.26 (s, 3H), 0.64 (s, 3H)°

**6.4.** Compound **13**: white solid, yield 61%. ESI-MS (m/z): 460.3 [M+H]<sup>+</sup>. <sup>1</sup>H NMR

(400 MHz, CDCl<sub>3</sub>), δ 7.27 (t, J=4.00Hz, 2H), 7.03 (s, 1H), 6.97 (t, J=4.00Hz, 2H),
4.89 (s, 1H), 4.72 (s, 2H), 4.64 (s, 1H), 4.18 (d, J=6.00Hz, 1H), 3.95 (t, J=4.00Hz,
1H), 3.52 (t, J=4.00Hz, 1H), 3.32 (d, J=10.00Hz, 1H), 2.91 (s, 2H), 2.42 (d,
J=12.00Hz, 1H), 2.24(m, 1H), 1.94-1.92 (m, 2H), 1.83-1.81 (m, 5H), 1.28 (m, 3H),
1.26 (s, 3H), 0.64 (s, 3H).

**6.5.** Compound **14**: white solid, yield 59%. ESI-MS (m/z): 473.4 [M+H]+。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.23 (d, *J*=8.00Hz, 2H), 6.91 (s, 1H), 6.80 (d, *J*=12.00Hz, 2H), 4.88 (s, 1H), 4.69 (s, 2H), 4.59(s, 1H), 4.19(d, *J*=12.00Hz, 1H), 3.85 (d, *J*=8.00Hz, 1H), 3.78 (s, 3H), 3.34-3.32 (m, 1H), 3.19-3.16 (m, 1H), 2.40 (d, *J*=12.00Hz, 1H), 2.26 (d, *J*=12.00Hz, 1H), 1.94-1.88 (m, 2H), 1.85-1.72 (m, 5H), 1.31 (m, 3H), 1.26 (s, 3H), 0.64 (s, 3H).

**6.6.** Compound **15**: white solid, yield 56%. ESI- MS (*m/z*): 448.3 [M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.38 (d, *J*=4.00Hz, 1H), 7.01- 6.99 (m, 2H), 6.83 (s, 1H), 4.87 (s, 1H), 4.70 (d, *J*=8.00Hz, 2H), 4.46 (s, 1H), 4.19 (d, *J*=12.00Hz, 1H), 3.80 (d, *J*=12.00Hz, 1H), 3.56 (t, *J*=4.00Hz, 1H), 3.34 (d, *J*=12.00Hz, 1H), 2.43 (d, *J*=12.00Hz, 1H), 2.28 (d, *J*=12.00Hz, 1H), 2.02-1.91 (m, 2H), 1.86-1.76 (m, 5H), 1.28 (m, 3H), 1.26 (s, 3H), 0.65 (s, 3H).

6.7. Compound 16: white solid, yield 56%. ESI-MS (*m/z*): 444.5 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), 8.36 (d, *J*=8.00Hz, 1H), 7.47 (t, *J*=4.00Hz, 1H), 7.37 (s, 1H), 7.13 (d, *J*=8.00Hz, 1H), 6.98 (t, *J*=4.00Hz, 1H), 4.93 (s, 1H), 4.84 (s, 1H), 4.74 (s, 2H), 4.18 (d, *J*=12.00Hz, 1H), 3.49 (t, *J*=4.00Hz, 1H), 3.30 (d, *J*=12.00Hz, 1H), 2.40 (d, *J*=12.00Hz, 2H), 2.02-1.88 (m, 3H), 1.82-1.62 (m, 5H), 1.26 (m, 3H), 1.22 (s, 3H),

0.64 (s, 3H).

**6.8.** Compound **17**: white solid, yield 73%. ESI-MS (*m/z*): 485.3 [M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 8.50 (d, *J*=4.00Hz, 1H), 8.47 (d, *J*=4.00Hz, 1H), 7.41 (d, *J*=12.00Hz, 1H), 6.97 (d, *J*=4.00Hz, 1H), 4.95 (s, 1H), 4.86 (m, 1H), 4.77 (s, 2H), 3.96-3.93 (m, 1H), 3.49 (m, 2H), 3.18-3.17 (m, 1H), 2.40-2.38 (m, 2H), 2.06- 1.88 (m, 4H), 1.77-1.62 (m, 4H), 1.40 (s, 3H), 1.36 (s, 3H), 1.26 (m, 2H), 1.19 (s, 3H), 0.91 (s, 3H).

6.9. Compound 18: white solid, yield 71%. ESI-MS (*m/z*): 490.3 [M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.68 (d, *J*=4.00Hz, 1H), 7.34 (s, 1H), 7.25 (d, *J*=4.00Hz, 1H), 4.93 (s, 1H), 4.77 (s, 2H), 4.75 (s, 1H), 4.45-4.4.42 (m, 1H), 3.95 (d, *J*=12.00Hz, 1H), 3.56-3.53 (m, 2H), 3.16 (d, *J*=8.00Hz, 1H), 2.42 (d, *J*=12.00Hz, 1H), 2.07- 1.91 (m, 4H), 1.86-1.70 (m, 4H), 1.40 (s, 3H), 1.36 (s, 3H), 1.26 (d, *J*=4.00Hz, 2H), 1.19 (s, 3H), 0.91 (s, 3H).

# 7. synthesis of 2-((4-methylphenyl)thio)acetic acid

To a 50 ml flask was added 4-methylbenzenethiol (0.7 g), sodium methanolate (0.3 g), methanol (15 ml), the mixture was stirred at room temperature for 20 min, then the resulting solution was cooled to 0°C. A solution of ethyl 2-(tosyloxy)acetate (1.5 g) in methanol (10 ml) was added dropwise into the mixture, after that, the solution was stirred at room temperature for 1 hour, then refluxed for 15 min. After the reaction, the solvent was removed under the vacuum, and then  $CH_2Cl_2$  (60 ml) was added to resolve the residue, the solution was washed by  $H_2O$  (60 ml) and saturated NaCl solution (60 ml), respectively. The organic layer was dried with anhydrous Na<sub>2</sub>SO<sub>4</sub>, then evaporated to afford a brown oil. The oil was added to ethanol (10 ml) and 5% NaOH (8 ml), then reacted at 40°C for 1 h. After the reaction, the ethanol was distilled under vacuum, then water (100 ml) was added to the residue, the pH was adjusted to 1. The precipitated solid was filtered and purified by column chromatography to give a white solid (0.8 g, 75%). ESI-MS (m/z): 185.0 [M-H]<sup>-</sup>° <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  7.26 (d, *J*=8.00Hz, 2H), 7.02 (d, *J*=8.00Hz, 2H), 3.96 (s, 2H), 2.32 (s, 3H).

# 8. General procedure for the synthesis of compound 19-22

The corresponding substituted acetic acid and sulfurous dichloride were added to a dry flask , and refluxed under  $N_2$  for 2 h. After that, the excessive sulfurous dichloride was distilled under vacuum, and then the residue was dissolved in anhydrous  $CH_2Cl_2$ . In another flask, **a**, triethylamine, and anhydrous  $CH_2Cl_2$  were added, stirred, and then cooled to 0 °C. After that, the former prepared acyl chloride was added dropwise, and then stirred at room temperature for 1 h. After the reaction, the mixture was washed by  $H_2O$ , saturated NaCl solution, successively. The organic layer was dried with anhydrous  $Na_2SO_4$  and evaporated to get the crude product, which was purified by column chromatography to afford the product.

8.1. Compound 19: oil, yield 57%. ESI-MS (*m/z*): 515.3 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 8.17 (d, *J*=8.00Hz, 2H), 7.45 (d, *J*=8.00Hz, 2H), 7.06 (t, *J*=8.00Hz, 1H), 5.99 (d, *J*=4.00Hz, 1H), 4.88 (s, 1H), 4.54 (q, *J*=4.00Hz, 1H), 4.46 (s, 1H), 4.23 (d, *J*=12.00Hz, 1H), 3.91 (d, *J*=8.00Hz, 1H), 3.81 (s, 2H), 3.47 (dd, *J<sub>I</sub>*=4.00Hz, *J<sub>2</sub>*= 8.00Hz, 1H), 3.17 (d, *J*=12.00Hz, 1H), 2.39 (d, *J*=8.00Hz, 2H), 1.95-1.92 (m, 2H), 1.80-1.72 (m, 5H), 1.40 (s, 3H), 1.36 (s, 3H), 1.26 (m, 3H), 1.17 (s, 3H), 0.85 (s, 3H)

3H).

8.2. Compound 20: oil, yield 71%. ESI-MS (*m/z*): 556.5 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.32 (d, *J*=8.00Hz, 2H), 7.14 (d, *J*=8.00Hz, 2H), 7.03 (t, *J*=8.00Hz, 1H), 5.92 (d, *J*=4.00Hz, 1H), 4.89 (s, 1H), 4.50 (m,2H), 4.11 (d, *J*=12.00Hz, 1H), 3.95 (d, *J*=8.00Hz, 1H), 3.61 (s, 2H), 3.48 (dd, *J<sub>I</sub>*=4.00Hz, *J<sub>2</sub>*= 8.00Hz, 1H), 3.18 (d, *J*=12.00Hz, 1H), 2.40 (d, *J*=8.00Hz, 3H), 2.33 (s, 3H), 1.96 (m,2H), 1.87-1.70 (m, 4H), 1.41 (s, 3H), 1.37 (s, 3H), 1.25 (m, 3H), 1.19 (s, 3H), 0.89 (s, 3H).

8.3. Compound 21: oil, yield 74%. ESI-MS (*m/z*): 559.4 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.43 (t, *J*=4.00Hz, 2H), 7.04 (t, *J*=4.00Hz, 3H), 5.92 (d, *J*=4.00Hz, 1H), 4.88 (s, 1H), 4.53 (q, *J*=4.00Hz, 1H), 4.49 (s, 1H), 4.14 (d, *J*=12.00Hz, 1H), 3.95 (d, *J*=12.00Hz, 1H), 3.60 (s, 2H), 3.48 (dd, *JI*=4.00Hz,*J2*= 8.00Hz,1H), 3.18 (d, *J*=12.00Hz, 1H), 2.39 (d, *J*=8.00Hz, 2H), 1.96 (m,2H), 1.80-1.72 (m, 5H), 1.41 (s, 3H), 1.37 (s, 3H), 1.25 (m, 3H), 1.20 (s, 3H), 0.89 (s, 3H).

8.4. Compound 22: oil, yield 58%. ESI-MS (*m/z*): 547.4 [M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.41 (d, *J*=8.00Hz, 1H), 7.21 (d, *J*=4.00Hz, 1H), 7.05 (t, *J*=8.00Hz, 1H), 7.01 (d, *J*=4.00Hz, 1H), 5.94 (d, *J*=4.00Hz, 1H), 4.89 (s, 1H), 4.52 (m, 2H), 4.18 (d, *J*=8.00Hz, 1H), 3.96 (d, *J*=12.00Hz, 1H), 3.52-3.51 (m, 3H), 3.18 (d, *J*=8.00Hz, 1H), 2.45-2.43 (m, 3H), 1.99-1.92 (m,2H), 1.82-1.71 (m, 5H), 1.41 (s, 3H), 1.37 (s, 3H), 1.26 (m, 3H), 1.20 (s, 3H), 0.93 (s, 3H).

### 9. General procedure for the synthesis of compound 23-26

The corresponding compound (19-22) and 70% acetic acid were added in the flask, and stirred for 45 min. After the reaction,  $H_2O$  was added, then the pH was adjusted to 7 by using sodium hydrogen carbonate. The mixture was extracted with  $CH_2Cl_2$  for three times. The organic layers were combined, and dried with anhydrous  $Na_2SO_4$ , then evaporated to give the crude product, which was subject to chromatography to afford the product.

9.1. Compound 23: white solid, yield 84%. ESI-MS (*m/z*): 546.6 [M+H]<sup>+</sup>. <sup>1</sup>H NMR
(400 MHz, CDCl<sub>3</sub>), δ 8.17 (d, *J*=8.00Hz, 2H), 7.45 (d, *J*=8.00Hz, 2H), 7.08 (t, *J*=8.00Hz, 1H), 5.98 (d, *J*=12.00Hz, 1H), 4.87 (s, 1H), 4.54 (q, *J*=4.00Hz, 1H), 4.47 (s, 1H), 4.17 (d, *J*=8.00Hz, 1H), 4.14 (d, *J*=12.00Hz, 1H), 3.60 (s, 2H), 3.47 (t, *J*=8.00Hz, 1H), 3.28 (d, *J*=8.00Hz, 2H), 2.42 (d, *J*=8.00Hz, 3H), 2.32 (s, 3H), 1.84 (m, 2H), 1.82-1.68 (m, 4H), 1.24 (m, 3H), 1.22 (s, 3H), 0.68 (s, 3H).

9.2. Compound 24: white solid, yield 58%. ESI-MS (*m/z*): 515.3[M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.30 (d, *J*=12.00Hz, 2H), 7.12 (d, *J*=12.00Hz, 2H), 7.02 (t, *J*=8.00Hz, 1H), 5.90 (d, *J*=12.00Hz, 1H), 4.87 (s, 1H), 4.51 (q, *J*=4.00Hz, 1H), 4.47 (s, 1H), 4.17 (d, *J*=8.00Hz, 1H), 4.14 (d, *J*=12.00Hz, 1H), 3.60 (s, 2H), 3.47 (t, *J*=8.00Hz, 1H), 3.32 (d, *J*=8.00Hz, 2H), 2.39 (d, *J*=8.00Hz, 3H), 2.33 (s, 3H), 1.96 (m, 2H), 1.87-1.70 (m, 4H), 1.26 (m, 3H), 1.24 (s, 3H), 0.62 (s, 3H).

**9.3.** Compound **25**: white solid, yield 60%. ESI-MS (*m/z*): 519.3 [M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.43 (t, *J*=4.00Hz, 2H), 7.04-7.01 (m, 3H), 5.91 (d, *J*=8.00Hz, 1H), 4.87 (s, 1H), 4.50 (m, 2H), 4.45 (q, *J*=4.00Hz, 1H), 4.17 (d, *J*=8.00Hz, 1H), 4.14 (d, *J*=8.00Hz, 1H), 3.60 (s, 2H), 3.47 (t, *J*=8.00Hz, 1H), 3.32 (d, *J*=8.00Hz, 1H), 2.40 (d, *J*=8.00Hz, 2H), 1.96 (m, 1H), 1.80-1.72 (m, 5H), 1.28 (s, 3H), 1.23 (m, 3H), 0.63 (s, 3H)<sub>°</sub>

9.4. Compound 26: white solid, yield 57 %. ESI-MS (*m/z*): 507.4 [M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.41 (d, *J*=8.00Hz, 1H), 7.21 (d, *J*=4.00Hz, 1H), 7.05 (t, *J*=8.00Hz, 1H), 7.08-7.02 (m, 3H), 5.94 (d, *J*=8.00Hz, 1H), 4.88 (s, 1H), 4.56 (m, 2H), 4.48 (q, *J*=4.00Hz, 1H), 4.14 (d, *J*=8.00Hz, 1H), 4.12 (d, *J*=8.00Hz, 1H), 3.48 (s, 2H), 3.44 (t, *J*=8.00Hz, 1H), 3.30 (d, *J*=8.00Hz, 1H), 2.42 (d, *J*=8.00Hz, 2H), 1.94 (m, 1H), 1.82-1.70 (m, 5H), 1.24 (s, 3H), 1.26 (m, 3H), 0.68 (s, 3H).

## 10. General procedure for the synthesis of compound 27-32

The corresponding substituted butyric acid and sulfurous dichloride were added to a dry flask , refluxed under  $N_2$  for 2 h. After that, the excessive sulfurous dichloride was distilled under vacuum, and then the residue was dissolved in anhydrous  $CH_2Cl_2$ . In another flask, **a**, triethylamine, and anhydrous  $CH_2Cl_2$  were added, stirred, and then cooled to 0 °C. After that, the former prepared acyl chloride was added dropwise, and then stirred at room temperature for 1 h. After the reaction, the mixture was washed by  $H_2O$ , saturated NaCl solution. The organic layer was dried with anhydrous  $Na_2SO_4$  and evaporated to get the crude product, which was purified by column chromatography to afford the product.

10.1 Compound 27: oil, yield 77%. ESI-MS (*m/z*): 599.4 [M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.34 (d, *J*=8.00Hz, 2H), 7.02 (t, *J*=8.00Hz, 1H), 6.85 (d, *J*=4.00Hz, 2H), 5.94 (d, *J*=4.00Hz, 1H), 4.88 (s, 1H), 4.54 (q, *J*=4.00Hz, 1H), 4.51 (s, 1H), 4.22 (d, *J*=8.00Hz, 1H), 3.96 (d, *J*=12.00Hz, 1H), 3.80 (s, 3H), 3.50 (dd, *J<sub>I</sub>*=4.00Hz, *J<sub>Z</sub>*= 8.00Hz, 1H), 3.18 (d, *J*=12.00Hz, 1H), 2.85 (t, *J*=4.00Hz, 2H), 2.50 (t, *J*=4.00Hz, 2H), 2.43 (d, *J*=8.00Hz, 2H), 2.03 -1.71 (m, 7H), 1.90 (t, *J*=4.00Hz, 2H), 1.41 (s, 3H), 1.37

(s, 3H), 1.26 (m, 3H), 1.18 (s, 3H), 0.91 (s, 3H).

**10.2.** Compound **28**: oil, yield 68%. ESI-MS (*m/z*): 614.5 [M+H]+. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 8.15 (d, *J*=12.00Hz, 2H), 7.36 (d, *J*=8.00Hz, 2H), 7.03 (t, *J*=8.00Hz, 1H), 5.96 (d, *J*=8.00Hz, 1H), 4.86 (s, 1H), 4.55 (q, *J*=4.00Hz, 1H), 4.49 (s, 1H), 4.25 (d, *J*=12.00Hz, 1H), 3.93 (d, *J*=12.00Hz, 1H), 3.50 (dd, *JI*=4.00Hz,*J2*=8.00Hz,1H), 3.18 (d, *J*=12.00 Hz, 1H), 3.10 (t, *J*=4.00Hz, 2H), 2.57 (t, *J*=4.00Hz, 2H), 2.41 (t, *J*=6.00Hz, 3H), 2.07 (t, *J*=4.00Hz, 2H), 1.96-1.94 (m, 2H), 1.86-1.71 (m, 4H), 1.39 (s, 3H), 1.36 (s, 3H), 1.26 (m, 3H), 1.19 (s, 1H), 0.91 (s, 3H).

10.3. Compound 29: oil, yield 75%. ESI-MS (*m/z*): 582.5 [M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.26 (d, *J*=8.00Hz, 2H), 7.11 (d, *J*=4.00Hz, 2H), 7.02 (t, *J*=8.00Hz, 1H), 5.94 (d, *J*=4.00Hz, 1H), 4.88 (s, 1H), 4.52 (q, *J*=4.00Hz, 1H), 4.51 (s, 1H), 4.21(d, *J*=12.00Hz, 1H), 3.95 (d, *J*=8.00Hz, 1H), 3.50 (dd, *J<sub>I</sub>*=4.00Hz, *J<sub>2</sub>*=8.00Hz,1H), 3.18 (d, *J*=12.00Hz, 1H), 2.92 (t, *J*=4.00Hz, 2H), 2.51 (t, *J*=4.00Hz, 2H), 2.42 (t, *J*=6.00Hz, 3H), 1.94 (t, *J*=4.00Hz, 2H), 1.96-1.71 (m, 6H), 1.41 (s, 3H), 1.37 (s, 3H), 1.26 (m, 3H), 1.19(s, 3H), 0.91 (s, 3H).

10.4. Compound 30: oil, yield 73%. ESI-MS (*m/z*): 589.4 [M+H]<sup>+</sup>。 <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.36 (d, *J*=4.00Hz, 2H), 7.03-7.01 (d, *J*=8.00Hz, 2H), 7.01 (t, *J*=12.00Hz, 1H), 5.94 (d, *J*=4.00Hz, 1H), 4.87 (s, 1H), 5.54 (q, *J*=4.00Hz, 1H), 4.50 s, 1H), 4.22 (d, *J*=12.00Hz, 1H), 3.95 (d, *J*=12.00Hz, 1H), 3.49 (dd, *J<sub>I</sub>*=4.00Hz, *J<sub>2</sub>*=8.00Hz,1H), 3.18 (d, *J*=12.00Hz, 1H), 2.90 (t, *J*=4.00Hz, 2H), 2.51 (t, *J*=4.00Hz, 2H), 2.43 (d, *J*=8.00Hz, 2H), 2.05-1.93 (m, 3H), 1.94 (t, *J*=4.00Hz, 2H), 1.86-1.65 (m, 4H), 1.41 (s, 3H), 1.37 (s, 3H), 1.26 (m, 3H), 1.20 (s, 3H), 0.91 (s, 3H).

**10.5.** Compound **31**: oil, yield 73%. ESI-MS (*m/z*): 575.3 [M+H]<sup>+</sup>° <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  7.36 (d, *J*=4.00Hz, 1H), 7.13 (d, *J*=4.00Hz, 1H), 7.03 (t, *J*=8.00Hz, 1H), 6.98 (d, *J*=4.00Hz, 1H), 5.94 (d, *J*=8.00Hz, 1H), 4.89 (s, 1H), 4.54 (q, *J*=4.00Hz, 1H), 4.52 (s, 1H), 4.21 (d, *J*=8.00Hz, 1H), 3.96 (d, *J*=12.00Hz, 1H), 3.50 (dd, *J*=4.00Hz, *J*<sub>2</sub>=8.00Hz, 1H), 3.18 (d, *J*=8.00Hz, 1H), 2.82 (t, *J*=4.00Hz, 2H), 2.52 (t, *J*=4.00Hz, 2H), 2.41 (d, *J*=8.00Hz, 3H), 1.94 (t, *J*=4.00Hz, 2H), 1.96-1.72 (m, 6H), 1.41 (s, 3H), 1.37 (s, 3H), 1.26 (m, 3H), 1.18 (s, 3H), 0.91 (s, 3H).

**10.6.** Compound **32**: oil, yield 69%. ESI-MS (*m/z*): 570.4  $[M+H]^+$ ° <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>),  $\delta$  8.41 (d, *J*=8.00Hz, 1H), 7.48 (t, *J*=8.00Hz, 1H), 7.17 (d, *J*=8.00Hz, 1H), 7.02-6.98 (m, 2H), 5.95 (d, *J*=4.00Hz, 1H), 4.86 (s, 1H), 4.54 (q, *J*=4.00Hz, 1H), 4.45 (s, 1H), 4.25 (d, *J*=8.00Hz, 1H), 3.95 (d, *J*=12.00Hz, 1H), 3.49 (dd, *J<sub>I</sub>*=4.00Hz, *J<sub>2</sub>*= 8.00Hz, 1H), 3.24 (dd, *J<sub>I</sub>*=4.00Hz, *J<sub>2</sub>*= 8.00Hz, 2.00H), 3.18 (d, *J*=10.00Hz, 1H), 2.54 (t, *J*=4.00Hz, 2H), 2.43 (m, 2H), 2.05 (t, *J*=4.00Hz, 2H), 1.96-1.94 (m, 2H), 1.86-1.71 (m, 5H), 1.41 (s, 3H), 1.37 (s, 3H), 1.26 (m, 3H), 1.20 (s, 3H), 0.65 (s, 3H).

### 11. General procedure for the synthesis of compound 33-38

The corresponding compound (**27-32**) and 70% acetic acid were added in the flask, and stirred for 45 min. After the reaction,  $H_2O$  was added, then the pH was adjusted to 7 by using sodium hydrogen carbonate. The mixture was extracted with  $CH_2Cl_2$  for three times. The organic layers were combined, and dried with anhydrous  $Na_2SO_4$ , then evaporated to give the crude product, which was subject to chromatography to afford the product.

11.1. Compound 33: white solid, yield 58%. ESI-MS (*m/z*): 558.5 [M+H]<sup>+</sup>. <sup>1</sup>H NMR

(400 MHz, CDCl<sub>3</sub>), δ 7.34 (d, J=8.00Hz, 2H), 7.02 (t, J=8.00Hz, 1H), 6.85 (d, J=8.00Hz, 2H), 5.93 (d, J=4.00Hz, 1H), 4.86 (s, 1H), 4.51 (q, J=4.00Hz, 1H), 4.45 (s, 1H), 4.18 (t, J=12.00Hz, 2H), 3.80 (s, 3H), 3.47 (dd, J<sub>I</sub>=4.00Hz, J<sub>2</sub>=8.00Hz, 1H), 3.18 (d, J=10.00Hz, 1H), 2.85 (t, J=4.00Hz, 2H), 2.51 (t, J=4.00Hz, 2H), 2.43 (m, 2H), 1.94-1.71 (m,7H), 1.89 (t, J=4.00Hz, 2H), 1.25 (s, 3H), 1.20 (m, 3H), 0.64 (s, 3H).

**11.2.** Compound **34**: white solid, yield 56%. ESI- MS (*m/z*): 574.3 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 8.15 (d, *J*=12.00Hz, 2H), 7.36 (d, *J*=8.00Hz, 2H), 7.01 (t, *J*=8.00Hz, 1H) , 5.96 (d, *J*=4.00Hz, 1H), 4.84 (s, 1H), 4.54 (q, *J*=4.00Hz, 1H), 4.45 (s,1H), 4.25 (d, *J*=12.00Hz, 1H), 4.16 (d, *J*=12.00Hz, 1H), 3.48 (t, *J*=8.00Hz, 1H), 3.33 (d, *J*=8.00Hz, 1H), 3.09 (t, *J*=8.00Hz, 2H), 2.56 (t, *J*=8.00Hz, 2H), 2.41 (d, *J*=6.00Hz, 3H), 2.07 (t, *J*=4.00Hz, 2H), 2.04-1.94 (m, 1H), 1.85-1.71 (m, 6H), 1.26 (m, 3H), 1.20 (s, 3H), 0.63 (s, 3H).

**11.3.** Compound **35**: white solid, yield 60%. ESI-MS (*m/z*): 543.4 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl3), δ 7.25 (d, *J*=8.00Hz, 2H), 7.11 (d, *J*=8.00Hz, 2H), 7.00 (t, *J*=8.00Hz, 1H) , 5.92 (d, *J*=8.00Hz, 1H), 4.86 (s, 1H), 4.54 (q, *J*=4.00Hz, 1H), 4.47 (s, 1H), 4.18 (t, *J*=8.00Hz, 2H), 3.48 (t, *J*=6.00Hz, 1H), 3.32 (d, *J*=12.00Hz, 1H), 2.92 (t, *J*=4.00Hz, 2H), 2.50 (t, *J*=4.00Hz, 2H), 2.42 (d, *J*=8.00Hz, 2H), 2.32 (s, 3H), 1.93 (t, *J*=4.00Hz, 2H), 1.96-1.71 (m, 7H), 1.25 (s, 3H), 1.23 (m, 3H), 0.63 (s, 3H).

11.4. Compound 36: white solid, yield 62%. ESI-MS (*m/z*): 547.3 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.35 (t, *J*=4.00Hz, 2H), 7.01 (t, *J*=8.00Hz, 3H), 5.93 (d, *J*=4.00Hz, 1H), 4.85 (s, 1H), 4.53 (q, *J*=4.00Hz, 1H), 4.46 (s, 1H), 4.23 (d, *J*=4.00Hz, 1H), 4.15 (d, *J*=4.00Hz, 1H), 3.48 (t, *J*=6.00Hz, 1H), 3.33 (d, *J*=12.00Hz, 1H), 2.91 (t, *J*=4.00Hz, 1H), 2.91 (t, *J*=4.00Hz, 1H), 3.48 (t, *J*=6.00Hz, 1H), 3.33 (d, *J*=12.00Hz, 1H), 2.91 (t, *J*=4.00Hz, 1H), 4.15 (d, *J*=4.00Hz, 1H), 3.48 (t, *J*=6.00Hz, 1H), 3.33 (d, *J*=12.00Hz, 1H), 2.91 (t, *J*=4.00Hz, 1H), 3.48 (t, *J*=6.00Hz, 1H), 3.33 (d, *J*=12.00Hz, 1H), 2.91 (t, *J*=4.00Hz, 1H), 3.33 (d, *J*=12.00Hz, 1H), 3.91 (t, *J*=4.00Hz, 1H), 3.91 (t, J=4.00Hz, 1H), 3

*J*=4.00Hz, 2H), 2.51 (t, *J*=4.00Hz, 2H), 2.36 (d, *J*=8.00Hz, 2H), 1.96-1.73 (m, 7H), 1.92 (t, *J*=4.00Hz, 2H), 1.25 (s, 3H), 1.24 (m, 3H), 0.64 (s, 3H).

**11.5.** Compound **37**: white solid, yield 53%. ESI-MS (*m/z*): 534.5 [M+H]<sup>+</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>), δ 7.36 (d, *J*=4.00Hz, 1H), 7.12 (d, *J*=4.00Hz, 1H), 6.99-6.98 (m, 2H), 5.93 (d, *J*=8.00Hz, 1H), 4.88 (s, 1H), 4.54 (q, *J*=4.00Hz, 1H), 4.48 (s, 1H), 4.19 (t, *J*=12.00Hz, 2H), 3.49 (dd, *JI*=4.00Hz,*J2*= 8.00Hz,1H), 3.33 (d, *J*=12.00Hz, 1H), 2.82 (t, *J*=4.00Hz, 2H), 2.51 (t, *J*=12.00Hz, 2H), 2.43-2.39 (m, 3H), 1.94 (t, *J*=4.00Hz,2H), 1.96-1.70 (m, 6H), 1.25 (s, 3H), 1.18 (m, 3H), 0.65 (s, 3H).

11.6. Compound 38: white solid, yield 55%. ESI-MS (*m/z*): 530.5 [M+H]<sup>+</sup>. <sup>1</sup>H NMR
(400 MHz, CDCl<sub>3</sub>), δ 8.42 (d, *J*=8.00Hz, 1H), 7.50-7.48 (m, 2H), 7.19 (d, *J*=8.00Hz,
1H), 7.00 (t, *J*=4.00Hz, 1H) , 5.93 (d, *J*=4.00Hz, 1H), 4.73 (s, 1H), 4.55 (q, *J*=4.00Hz,
1H), 4.48 (s, 1H), 4.26 (d, *J*=8.00Hz, 1H), 4.16 (d, *J*=8.00Hz, 1H), 3.47 (t, *J*=4.00Hz,
1H), 3.30 (d, *J*=8.00Hz, 1H), 3.25 (t, *J*=4.00Hz, 2H), 2.54 (t, *J*=4.00Hz, 2H), 2.422.40 (m, 3H), 2.07 (t, *J*=4.00Hz, 2H), 1.96-1.94 (m, 2H), 1.81-1.71 (m, 4H), 1.26 (m,
3H), 1.22 (s, 3H), 0.68 (s, 3H).

**12.** MTT assay: Cancer cells were cultured in RPMI-1640 (GIBCO) medium with 10% fetal bovine serum (GIBCO) at 5% CO<sub>2</sub> and 37 °C. 100  $\mu$ l cells were planted in 96-well plate at 3×10<sup>4</sup> cells/ml concentration. Proper concentration of compounds were prepared previously and added to each well (four times repeat wells for each concentration of compounds) while refresh the culture medium (volume racial of the culture medium vs. compound was 90  $\mu$ l:10  $\mu$ l) in the next day. 48 hours later,

refreshing the culture liquid with 90  $\mu$ l RPMI-1640 medium and 10  $\mu$ l 5 mg/ml MTT to avoid the interference from compounds and serum. Incubate the plates at former conditions for four hours, then carefully remove medium and add 150  $\mu$ l DMSO into each well to dissolve crystals at room temperature for 10 minutes. Finally transfer the 96-well plates to the reader and measure absorbance at 490nm. IC<sub>50</sub> value was calculated by GraphPad Prism 5 software.



13. <sup>1</sup>H-NMR spectrum of compound **6a** 



14. <sup>13</sup>C-NMR spectrum of compound **6a** 



15. <sup>1</sup>H-NMR spectrum of compound **6b** 



16. <sup>13</sup>C-NMR spectrum of compound **6b** 



17. H-H-COSY spectrum of compound **6b** 

























29. <sup>1</sup>H-NMR spectrum of compound **13** 















35. <sup>1</sup>H-NMR spectrum of compound **20** 





37. <sup>1</sup>H-NMR spectrum of compound **22** 



























