

## SUPPLEMENTARY MATERIAL

### Design, synthesis and biological evaluation of chrysin benzimidazole derivatives as potential anticancer agents

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**Abstract:** A series of chrysin benzimidazole derivatives were firstly synthesised and evaluated on their anticancer activity in the search for potential anticancer agents. Among them, compound **18** displayed the most potent antiproliferative activity against MFC cells with IC<sub>50</sub> values of 25.72 ± 3.95 μM. The flow cytometry results displayed that compound **18** induced apoptosis of MFC cells in a dose-dependent manner and caused the cell cycle to be arrested in the G0/G1 phase. Furthermore, the preliminary anticancer activity in vivo was also studied in tumour-bearing mice, and the compound **18** exerted good inhibition effect for tumour growth. These results

suggested that compound **18** had good anticancer activity, which could be a potential anticancer agent to further optimization and evaluation.

**Keywords:** Chrysin; benzimidazole; synthesis; anticancer

## Experimental data

### *The <sup>1</sup>H NMR and ESI-MS data of compounds 2a-2c, 3-23*

#### *7-(2-bromoethoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (2a)*

Light yellow powder, yield: 92%. Mp:114-116 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.75 (s, 1H, 5-OH), 7.83 (t, 2H, 2',6'-H), 7.54 (d, 3H, 3',4',5'-H), 6.68 (s, 1H, 3-H), 6.52 (s, 1H, 8-H), 6.38 (s, 1H, 6-H), 4.36 (d, 2H, 10-CH<sub>2</sub>), 3.67 (t, 2H, 11-CH<sub>2</sub>). MS (ESI):360.0 ([M+H<sup>+</sup>]).

#### *7-(3-bromopropoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (2b)*

Light yellow powder, yield: 88%. Mp:123-125 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.72 (s, 1H, 5-OH), 7.89 (d, 2H, 2',6'-H), 7.54 (d, 3H, 3',4',5'-H), 6.67 (s, 1H, 3-H), 6.52 (s, 1H, 8-H), 6.38 (s, 1H, 6-H), 4.19 (d, 2H, 10-CH<sub>2</sub>), 3.62 (t, 2H, 12-CH<sub>2</sub>), 2.47-2.25 (m, 2H, 11-CH<sub>2</sub>). MS (ESI):374.1 ([M+H<sup>+</sup>]).

#### *7-(4-bromobutoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (2c)*

Light yellow powder, yield: 90%. Mp:141-143 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.71 (s, 1H, 5-OH), 7.84 (t, 2H, 2',6'-H), 7.53 (d, 3H, 3',4',5'-H), 6.65 (s, 1H, 3-H), 6.48 (s, 1H, 8-H), 6.36 (d, 1H, 6-H), 4.09 (dd, 2H, 10-CH<sub>2</sub>), 3.49 (dd, 2H, 13-CH<sub>2</sub>), 2.14-1.91 (m, 4H, 11,12-CH<sub>2</sub>CH<sub>2</sub>). MS (ESI):388.1 ([M+H<sup>+</sup>]).

*7-(2-(1H-benzo[d]imidazol-1-yl)ethoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (3)*

White powder, yield: 45%. Mp:218-220 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.74 (s, 1H, 5-OH), 8.03 (s, 1H, 13-H), 7.85 (d, 3H, H<sub>arom</sub>), 7.59-7.43 (m, 4H, H<sub>arom</sub>), 7.41-7.28 (m, 2H, H<sub>arom</sub>), 6.65 (s, 1H, 3-H), 6.42 (s, 1H, 8-H), 6.31 (s, 1H, 6-H), 4.62 (s, 2H, 10-CH<sub>2</sub>), 4.38 (s, 2H, 11-CH<sub>2</sub>). MS (ESI):398.1 ([M+H<sup>+</sup>]).

*5-hydroxy-7-(2-(2-methyl-1H-benzo[d]imidazol-1-yl)ethoxy)-2-phenyl-4H-chromen-4-one (4)*

White powder, yield: 52%. Mp:219-220 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.73 (s, 1H, 5-OH), 7.85 (d, 2H, H<sub>arom</sub>), 7.71 (d, 1H, H<sub>arom</sub>), 7.53 (d, 3H, H<sub>arom</sub>), 7.37 (d, 1H, H<sub>arom</sub>), 7.27 (s, 2H, H<sub>arom</sub>), 6.66 (s, 1H, 3-H), 6.38 (s, 1H, 8-H), 6.30 (s, 1H, 6-H), 4.58 (s, 2H, 10-CH<sub>2</sub>), 4.37 (s, 2H, 11-CH<sub>2</sub>), 2.73 (s, 3H, 13-CH<sub>3</sub>). MS (ESI):412.1 ([M+H<sup>+</sup>]).

*7-(2-(2-chloro-1H-benzo[d]imidazol-1-yl)ethoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (5)*

White powder, yield: 40%. Mp:201-203 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.71 (s, 1H, 5-OH), 7.84 (dd, 2H, H<sub>arom</sub>), 7.69 (d, 1H, H<sub>arom</sub>), 7.55-7.47 (m, 3H, H<sub>arom</sub>), 7.44 (d, 1H, H<sub>arom</sub>), 7.37-7.26 (m, 2H, H<sub>arom</sub>), 6.64 (s, 1H, 3-H), 6.39 (d, 1H, 8-H), 6.28 (d, 1H, 6-H), 4.64 (t, 2H, 10-CH<sub>2</sub>), 4.37 (t, 2H, 11-CH<sub>2</sub>). MS (ESI):432.1 ([M+H<sup>+</sup>]).

*5-hydroxy-7-(2-(6-nitro-1H-benzo[d]imidazol-1-yl)ethoxy)-2-phenyl-4H-chromen-4-one (6)*

Light yellow powder, yield: 53%. Mp: 216-218 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.75 (d, 1H, 5-OH), 8.74 (s, 1H, 1H, 13-H), 8.52 (s, 1H, H<sub>arom</sub>), 8.33-8.18 (m, 2H,

H<sub>arom</sub>), 7.86 (dd, 2H, H<sub>arom</sub>), 7.58 (d, 1H, H<sub>arom</sub>), 7.52 (t, 2H, H<sub>arom</sub>), 6.65 (s, 1H, 3-H), 6.43 (dd, 1H, 8-H), 6.30 (s, 1H, 6-H), 4.74-4.64 (m, 2H, 10-CH<sub>2</sub>), 4.41 (dd, 2H, 11-CH<sub>2</sub>). MS (ESI):443.1 ([M+H<sup>+</sup>]).

*7-(2-(5,6-dimethyl-1H-benzo[d]imidazol-1-yl)ethoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (7)*

Light yellow powder, yield: 42%. Mp: 214-216 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.73 (s, 1H, 5-OH), 7.91 (s, 1H, 13-H), 7.86 (d, 2H, H<sub>arom</sub>), 7.61-7.49 (m, 4H, H<sub>arom</sub>), 7.24 (s, 1H, H<sub>arom</sub>), 6.66 (s, 1H, 3-H), 6.43 (s, 1H, 8-H), 6.32 (s, 1H, 6-H), 4.57 (s, 2H, 10-CH<sub>2</sub>), 4.36 (s, 2H, 11-CH<sub>2</sub>), 2.40 (d, 6H, 16,17-CH<sub>3</sub>). MS (ESI):426.2 ([M+H<sup>+</sup>]).

*5-hydroxy-7-(2-(5-methyl-1H-benzo[d]imidazol-1-yl)ethoxy)-2-phenyl-4H-chromen-4-one (8)*

White powder, yield: 38%. Mp: 194-197 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.74 (s, 1H, 5-OH), 7.97 (d, 1H, 13-H), 7.86 (d, 2H, H<sub>arom</sub>), 7.70 (d, 1H, H<sub>arom</sub>), 7.56 (t, 3H, H<sub>arom</sub>), 7.37 (d, 1H, H<sub>arom</sub>), 7.16 (dd, 1H, H<sub>arom</sub>), 6.66 (s, 1H, 3-H), 6.43 (s, 1H, 8-H), 6.32 (s, 1H, 6-H), 4.59 (s, 2H, 10-CH<sub>2</sub>), 4.37 (s, 2H, 11-CH<sub>2</sub>), 2.51 (d, 3H, 16-CH<sub>3</sub>). MS (ESI):412.1 ([M+H<sup>+</sup>]).

*5-hydroxy-7-(2-(5-methoxy-1H-benzo[d]imidazol-1-yl)ethoxy)-2-phenyl-4H-chromen-4-one (9)*

White powder, yield: 44%. Mp: 293-295 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.74 (s, 1H, 5-OH), 7.95 (d, 1H, 13-H), 7.86 (d, 2H, H<sub>arom</sub>), 7.70 (d, 1H, H<sub>arom</sub>), 7.53 (d, 3H, H<sub>arom</sub>), 7.33 (dd, 1H, H<sub>arom</sub>), 6.94 (d, 1H, H<sub>arom</sub>), 6.66 (s, 1H, 3-H), 6.43 (d, 1H, 8-H), 6.33 (s, 1H, 6-H), 4.58 (s, 1H, 10-CH<sub>2</sub>), 4.38 (s, 2H, 11-CH<sub>2</sub>), 3.89 (d, 3H, OCH<sub>3</sub>). MS (ESI):428.1 ([M+H<sup>+</sup>]).

*7-(3-(1H-benzo[d]imidazol-1-yl)propoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one*  
(10)

Light yellow powder, yield: 54%. Mp: 207-208 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.75 (d, 1H, 5-OH), 8.73 (d, 1H, 14-H), 8.41 (d, 1H, H<sub>arom</sub>), 8.22 (dd, 1H, H<sub>arom</sub>), 8.10 (d, 1H, H<sub>arom</sub>), 7.93-7.79 (m, 2H, H<sub>arom</sub>), 7.51 (dt, 3H, H<sub>arom</sub>), 6.67 (d, 1H, H<sub>arom</sub>), 6.47 (d, 1H, 3-H), 6.41 (d, 1H, 8-H), 6.37-6.31 (m, 1H, 6-H), 4.62-4.41 (m, 2H, 10-CH<sub>2</sub>), 4.00 (dd, 2H, 12-CH<sub>2</sub>), 2.42 (dd, 2H, 11-CH<sub>2</sub>). MS (ESI):412.1 ([M+H<sup>+</sup>]).

*5-hydroxy-7-(3-(2-methyl-1H-benzo[d]imidazol-1-yl)propoxy)-2-phenyl-4H-chromen-4-one* (11)

White powder, yield: 55%. Mp: 183-185 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.73 (s, 1H, 5-OH), 7.94-7.81 (m, 2H, H<sub>arom</sub>), 7.68 (d, 1H, H<sub>arom</sub>), 7.57-7.45 (m, 3H, H<sub>arom</sub>), 7.32-7.27 (m, 1H, H<sub>arom</sub>), 7.22-7.18 (m, 2H, H<sub>arom</sub>), 6.67 (s, 1H, 3-H), 6.43 (d, 1H, 8-H), 6.36 (d, 1H, 6-H), 4.37 (t, 2H, 10-CH<sub>2</sub>), 3.96 (t, 2H, 12-CH<sub>2</sub>), 2.58 (s, 3H, 14-CH<sub>3</sub>), 2.38-2.28 (m, 2H, 11-CH<sub>2</sub>). MS (ESI):426.2 ([M+H<sup>+</sup>]).

*7-(3-(2-chloro-1H-benzo[d]imidazol-1-yl)propoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one* (12)

Light yellow powder, yield: 47%. Mp: 162-166 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.73 (s, 1H, 5-OH), 7.86 (dd, 2H, H<sub>arom</sub>), 7.72-7.65 (m, 1H, H<sub>arom</sub>), 7.52 (t, 3H, H<sub>arom</sub>), 7.33-7.28 (m, 1H, H<sub>arom</sub>), 7.25 (d, 1H, H<sub>arom</sub>), 7.23 (s, 1H, H<sub>arom</sub>), 6.67 (s, 1H, 3-H), 6.42 (d, 1H, 8-H), 6.35 (d, 1H, 6-H), 4.45 (t, 2H, 10-CH<sub>2</sub>), 4.00 (t, 2H, 12-CH<sub>2</sub>), 2.47-2.26 (m, 2H, 11-CH<sub>2</sub>). MS (ESI):446.1 ([M+H<sup>+</sup>]).

*5-hydroxy-7-(3-(6-nitro-1H-benzo[d]imidazol-1-yl)propoxy)-2-phenyl-4H-chromen-4-one (13)*

Yellow powder, yield: 61%. Mp: 209-210 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.75 (d, 1H, 5-OH), 8.73 (d, 1H, 14-H), 8.41 (d, 1H, H<sub>arom</sub>), 8.22 (dd, 1H, H<sub>arom</sub>), 8.10 (d, 1H, H<sub>arom</sub>), 7.89-7.83 (m, 2H, H<sub>arom</sub>), 7.52 (dd, 2H, H<sub>arom</sub>), 6.67 (d, 1H, H<sub>arom</sub>), 6.47 (d, 1H, 3-H), 6.41 (d, 1H, 3-H), 6.36- 6.32 (m, 1H, 3-H), 4.57-4.48 (m, 2H, 10-CH<sub>2</sub>), 4.00 (dd, 2H, 12-CH<sub>2</sub>), 2.42 (dd, 2H, 11-CH<sub>2</sub>). MS (ESI):457.2 ([M+H<sup>+</sup>]).

*7-(3-(5,6-dimethyl-1H-benzo[d]imidazol-1-yl)propoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (14)*

White powder, yield: 58%. Mp: 182-184 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.72 (s, 1H, 5-OH), 7.92-7.82 (m, 2H, 14-H, H<sub>arom</sub>), 7.76 (s, 1H, 13-H), 7.52 (dd, 4H, H<sub>arom</sub>), 7.14 (s, 1H, H<sub>arom</sub>), 6.67 (s, 1H, 3-H), 6.43 (d, 1H, 8-H), 6.36 (d, 1H, 6-H), 4.39 (t, 2H, 10-CH<sub>2</sub>), 3.95 (t, 2H, 12-CH<sub>2</sub>), 2.36 (d, 2H, 11-CH<sub>2</sub>), 2.33 (d, 6H, 17,18-CH<sub>3</sub>). MS (ESI):440.1 ([M+H<sup>+</sup>]).

*5-hydroxy-7-(3-(5-methyl-1H-benzo[d]imidazol-1-yl)propoxy)-2-phenyl-4H-chromen-4-one (15)*

Light yellow powder, yield: 63%. Mp: 181-183 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.74 (s, 1H, 5-OH), 7.86 (dd, 2H, 14-H, H<sub>arom</sub>), 7.56 (t, 3H, H<sub>arom</sub>), 7.35-7.23 (m, 2H, H<sub>arom</sub>), 7.11 (t, 1H, H<sub>arom</sub>), 6.69 (s, 1H, 3-H), 6.45 (s, 1H, 8-H), 6.38 (s, 1H, 6-H), 4.43 (s, 2H, 10-CH<sub>2</sub>), 3.97 (s, 2H, 12-CH<sub>2</sub>), 2.46 (d, 3H, 17-CH<sub>3</sub>), 2.42-2.32 (m, 2H, 11-CH<sub>2</sub>). MS (ESI):426.1 ([M+H<sup>+</sup>]).

*5-hydroxy-7-(3-(5-methoxy-1H-benzo[d]imidazol-1-yl)propoxy)-2-phenyl-4H-chromen-4-one (16)*

Light yellow powder, yield: 56%. Mp: 160-162 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.75 (s, 1H, 5-OH), 7.85 (dd, 3H, 14-H, H<sub>arom</sub>), 7.68 (d, 1H, H<sub>arom</sub>), 7.54 (d, 2H, H<sub>arom</sub>), 7.28 (s, 1H, H<sub>arom</sub>), 6.99-6.86 (m, 1H, H<sub>arom</sub>), 6.84 (s, 1H, H<sub>arom</sub>), 6.69 (s, 1H, 3-H), 6.45 (s, 1H, 8-H), 6.38 (d, 1H, 6-H), 4.42 (d, 2H, 10-CH<sub>2</sub>), 3.98 (d, 2H, 12-CH<sub>2</sub>), 3.83 (d, 3H, OCH<sub>3</sub>), 2.38 (s, 2H, 11-CH<sub>2</sub>). MS (ESI):442.1 ([M+H<sup>+</sup>]).

*7-(4-(1H-benzo[d]imidazol-1-yl)butoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (17)*

Light yellow powder, yield: 54%. Mp: 172-173 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.71 (s, 1H, 5-OH), 7.92 (s, 1H, 15-H), 7.89-7.83 (m, 2H, H<sub>arom</sub>), 7.81 (d, 1H, H<sub>arom</sub>), 7.55-7.47 (m, 3H, H<sub>arom</sub>), 7.41 (d, 1H, H<sub>arom</sub>), 7.34-7.25 (m, 3H, H<sub>arom</sub>), 6.65 (s, 1H, 3-H), 6.44 (d, 1H, 8-H), 6.33 (d, 1H, 6-H), 4.28 (t, 2H, 10-CH<sub>2</sub>), 4.03 (t, 2H, 13-CH<sub>2</sub>), 2.11 (dt, 2H, 11-CH<sub>2</sub>), 1.85 (dd, 2H, 12-CH<sub>2</sub>). MS (ESI):426.2 ([M+H<sup>+</sup>]).

*5-hydroxy-7-(4-(2-methyl-1H-benzo[d]imidazol-1-yl)butoxy)-2-phenyl-4H-chromen-4-one (18)*

Light yellow powder, yield: 60%. Mp: 156-158 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.72 (s, 1H, 5-OH), 7.89-7.84 (m, 2H, H<sub>arom</sub>), 7.72-7.65 (m, 1H, H<sub>arom</sub>), 7.52 (t, 3H, H<sub>arom</sub>), 7.33-7.27 (m, 1H, H<sub>arom</sub>), 7.24-7.18 (m, 2H, H<sub>arom</sub>), 6.65 (s, 1H, 3-H), 6.44 (d, 1H, 8-H), 6.33 (d, 1H, 6-H), 4.21 (t, 2H, 10-CH<sub>2</sub>), 4.03 (t, 2H, 13-CH<sub>2</sub>), 2.63 (s, 3H, 15-CH<sub>3</sub>), 2.02 (dd, 2H, 11-CH<sub>2</sub>), 1.88 (dd, 2H, 12-CH<sub>2</sub>). MS (ESI):440.1 ([M+H<sup>+</sup>]).

*7-(4-(2-chloro-1H-benzo[d]imidazol-1-yl)butoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (19)*

Yellow powder, yield: 53%. Mp: 140-142 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.73 (s, 1H, 5-OH), 7.88 (s, 2H, H<sub>arom</sub>), 7.71 (d, 1H, H<sub>arom</sub>), 7.54 (s, 3H, H<sub>arom</sub>), 7.42-7.26 (m, 3H, H<sub>arom</sub>), 6.67 (s, 1H, 3-H), 6.46 (s, 1H, 8-H), 6.34 (s, 1H, 6-H), 4.31 (s, 2H, 10-CH<sub>2</sub>), 4.06 (s, 2H, 13-CH<sub>2</sub>), 2.12 (d, 2H, 11-CH<sub>2</sub>), 1.90 (s, 2H, 12-CH<sub>2</sub>). MS (ESI):460.1 ([M+H<sup>+</sup>]).

*5-hydroxy-7-(4-(6-nitro-1H-benzo[d]imidazol-1-yl)butoxy)-2-phenyl-4H-chromen-4-one (20)*

White powder, yield: 60%. Mp: 163-166 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.74 (s, 1H, 5-OH), 8.74 (s, 1H, 15-H), 8.42 (s, 1H, H<sub>arom</sub>), 8.35-8.08 (m, 2H, H<sub>arom</sub>), 7.88 (d, 2H, H<sub>arom</sub>), 7.68-7.43 (m, 3H, H<sub>arom</sub>), 6.67 (s, 1H, 3-H), 6.46 (d, 1H, 8-H), 6.33 (s, 1H, 6-H), 4.45-4.29 (m, 2H, 10-CH<sub>2</sub>), 4.09 (d, 2H, 13-CH<sub>2</sub>), 2.27-2.09 (m, 2H, 11-CH<sub>2</sub>), 1.90 (d, 2H, 12-CH<sub>2</sub>). MS (ESI):471.2 ([M+H<sup>+</sup>]).

*7-(4-(5,6-dimethyl-1H-benzo[d]imidazol-1-yl)butoxy)-5-hydroxy-2-phenyl-4H-chromen-4-one (21)*

Light yellow powder, yield: 65%. Mp: 112-115 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.71 (s, 1H, 5-OH), 7.87 (dd, 2H, 15-H, H<sub>arom</sub>), 7.80 (s, 1H, H<sub>arom</sub>), 7.58-7.49 (m, 4H, H<sub>arom</sub>), 7.16 (s, 1H, H<sub>arom</sub>), 6.66 (s, 1H, 3-H), 6.43 (d, 1H, 8-H), 6.32 (d, 1H, 6-H), 4.22 (t, 2H, 10-CH<sub>2</sub>), 4.01 (t, 2H, 13-CH<sub>2</sub>), 2.37 (d, 6H, 18,19-CH<sub>3</sub>), 2.07 (dd, 2H, 11-CH<sub>2</sub>), 1.93-1.71 (m, 2H, 12-CH<sub>2</sub>). MS (ESI):454.2 ([M+H<sup>+</sup>]).



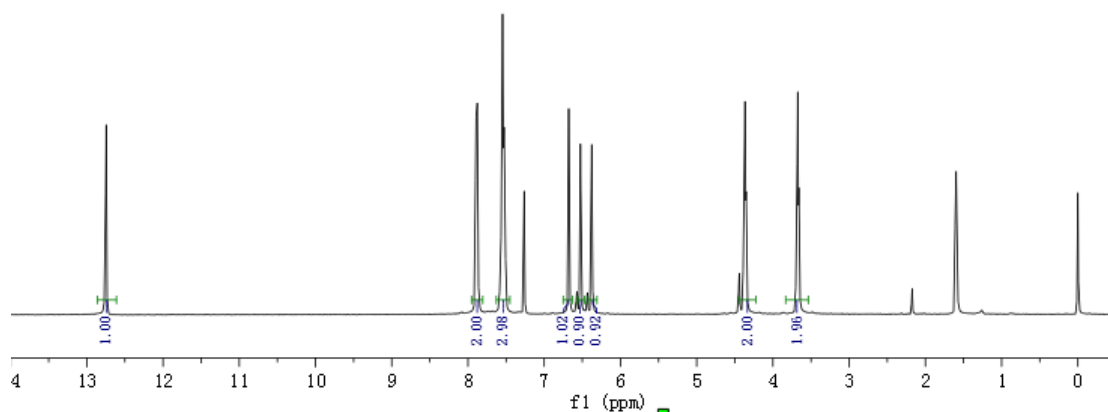
*5-hydroxy-7-(4-(5-methyl-1H-benzo[d]imidazol-1-yl)butoxy)-2-phenyl-4H-chromen-4-one (22)*

Yellow powder, yield: 56%. Mp: 138-140 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.73 (s, 1H, 5-OH), 7.88 (d, 3H, 15-H, H<sub>arom</sub>), 7.69 (d, 1H, H<sub>arom</sub>), 7.53 (d, 3H, H<sub>arom</sub>), 7.33-7.24 (m, 1H, H<sub>arom</sub>), 7.17-7.07 (m, 1H, H<sub>arom</sub>), 6.67 (s, 1H, 3-H), 6.47 (d, 1H, 8-H), 6.33 (s, 1H, 6-H), 4.25 (s, 2H, 10-CH<sub>2</sub>), 4.00 (t, 2H, 13-CH<sub>2</sub>), 2.52 (t, 3H, 18-CH<sub>3</sub>), 2.15-2.06 (m, 2H, 11-CH<sub>2</sub>), 1.83 (s, 2H, 12-CH<sub>2</sub>). MS (ESI):440.2 ([M+H<sup>+</sup>]).

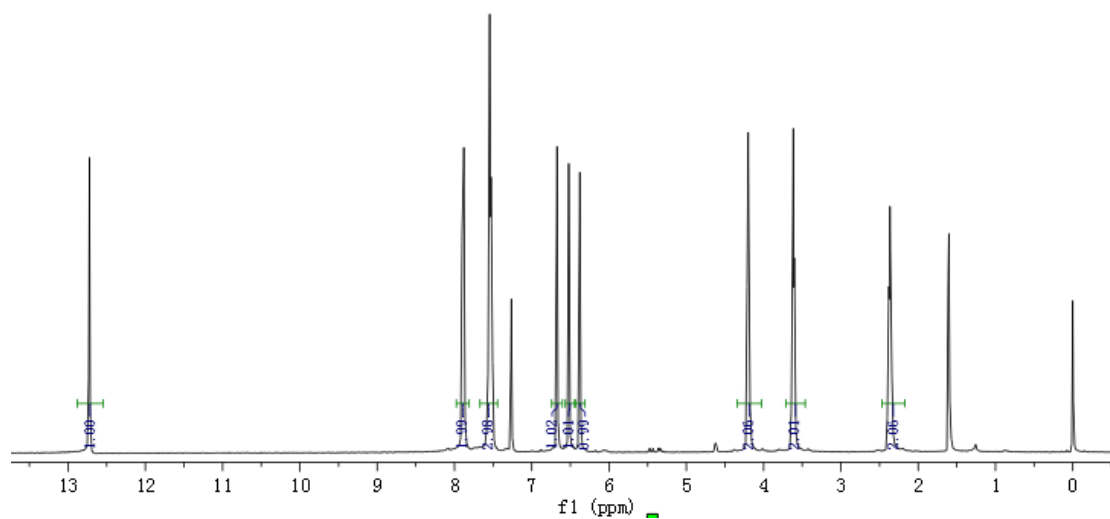
*5-hydroxy-7-(4-(5-methoxy-1H-benzo[d]imidazol-1-yl)butoxy)-2-phenyl-4H-chromen-4-one (23)*

White powder, yield: 60%. Mp: 114-117 °C; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) δ 12.73 (s, 1H, 5-OH), 7.86 (d, 3H, 15-H, H<sub>arom</sub>), 7.69 (d, 1H, H<sub>arom</sub>), 7.54 (s, 3H, H<sub>arom</sub>), 7.01-6.81 (m, 2H, H<sub>arom</sub>), 6.67 (s, 1H, 3-H), 6.45 (s, 1H, 8-H), 6.33 (s, 1H, 6-H), 4.25 (d, 2H, 10-CH<sub>2</sub>), 4.04 (d, 2H, 13-CH<sub>2</sub>), 3.87 (d, 3H, OCH<sub>3</sub>), 2.11 (s, 2H, 11-CH<sub>2</sub>), 1.85 (s, 2H, 12-CH<sub>2</sub>). MS (ESI):456.1 ([M+H<sup>+</sup>]).

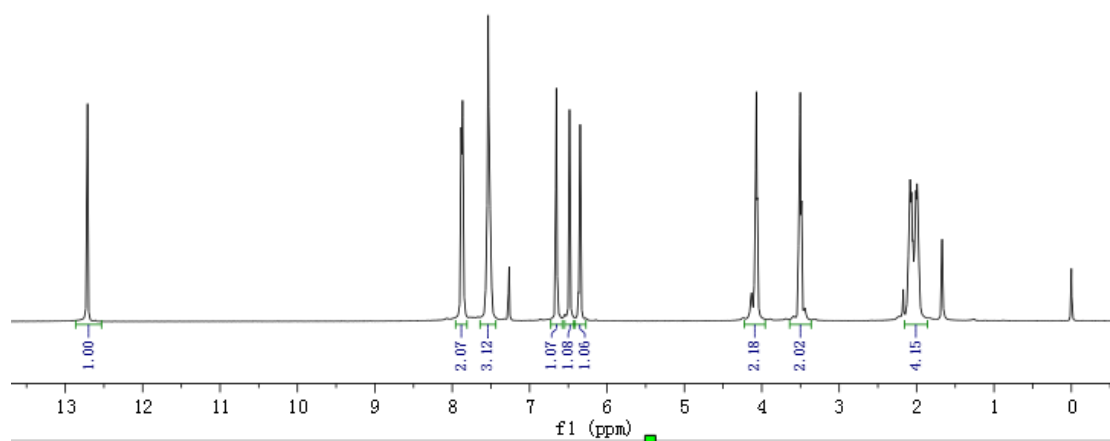
***<sup>1</sup>H NMR spectral data of 2a-2c, 3-23***



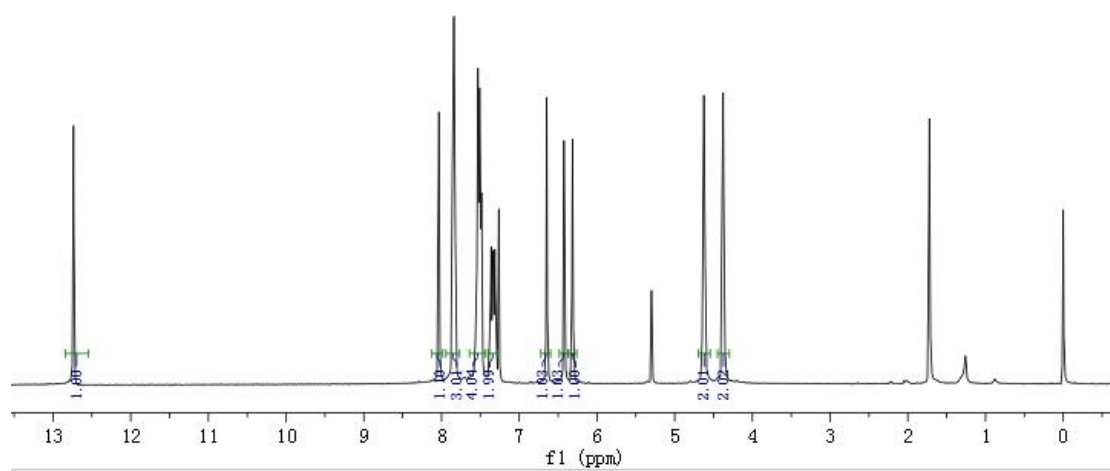
**Figure S1.** <sup>1</sup>H NMR of compound **2a**.



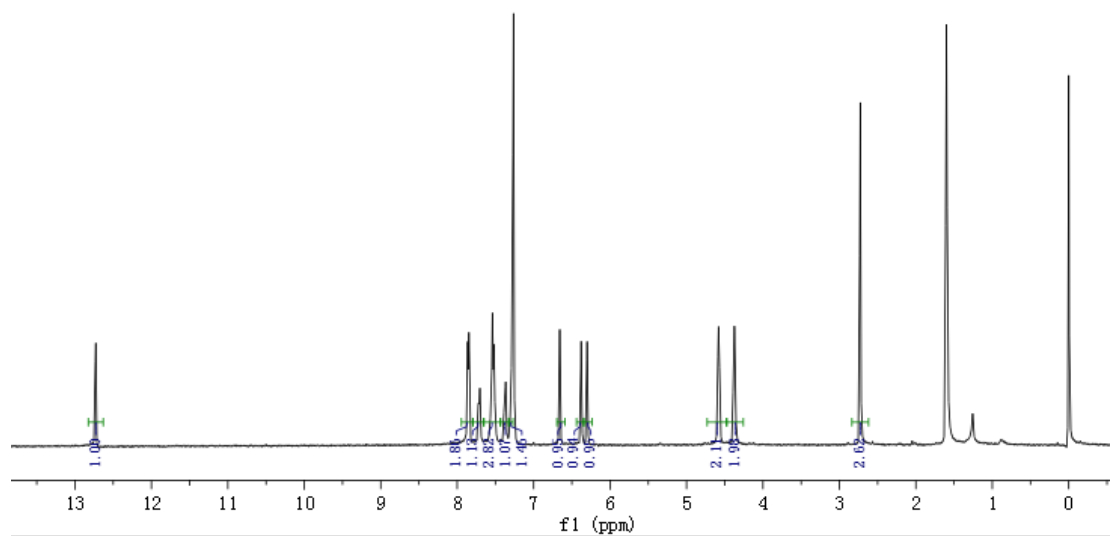
**Figure S2.** <sup>1</sup>H NMR of compound **2b**.



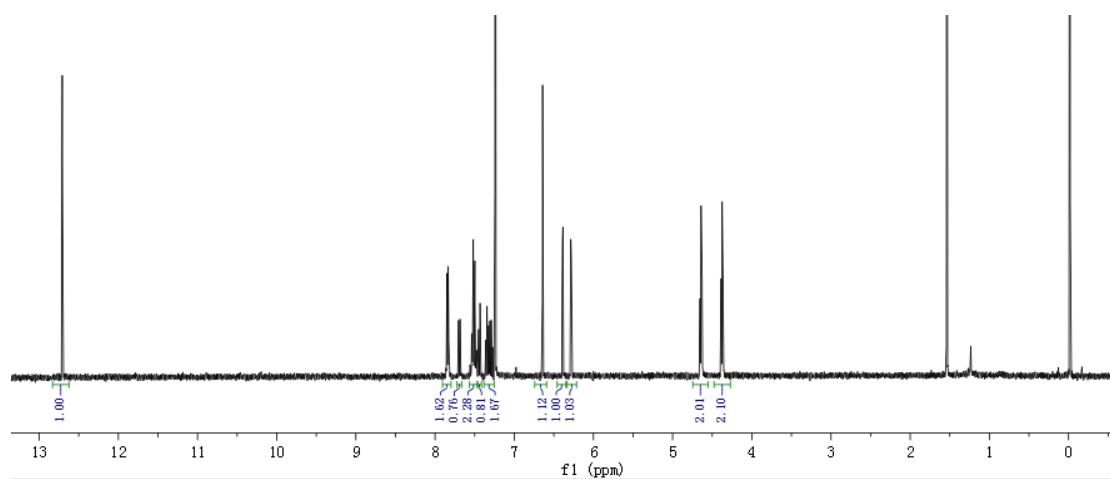
**Figure S3.** <sup>1</sup>H NMR of compound **2c**.



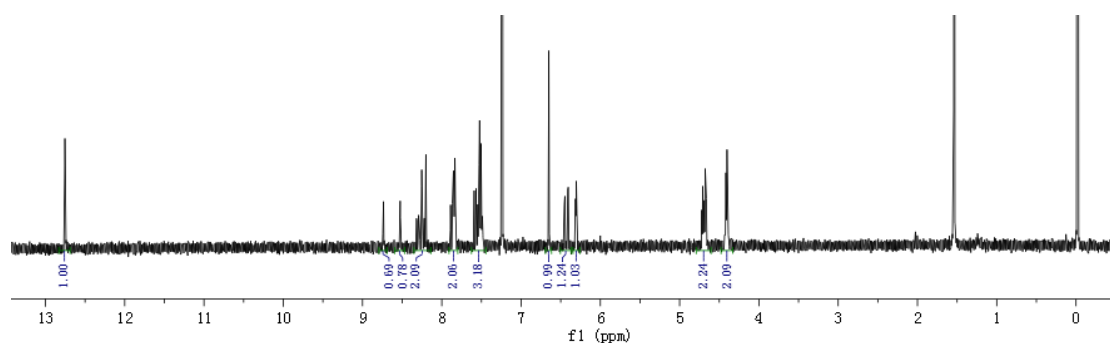
**Figure S4.** <sup>1</sup>H NMR of compound **3**.



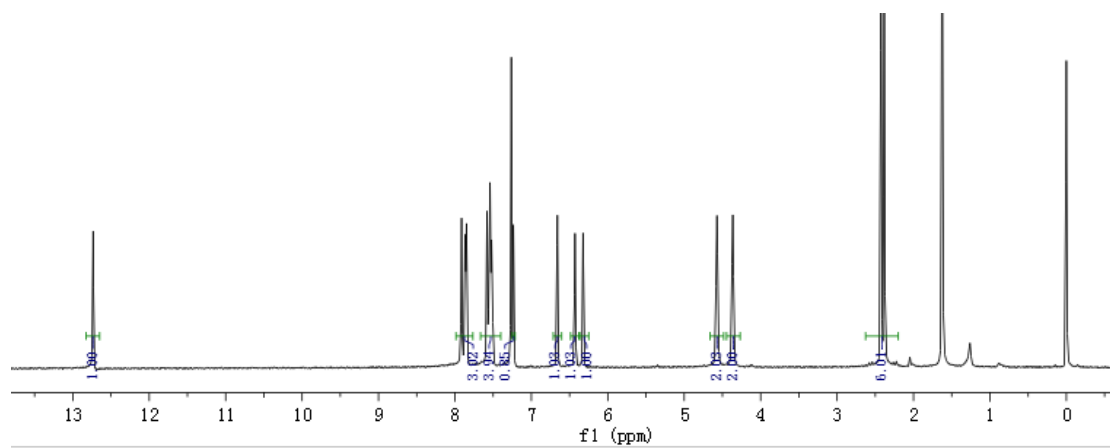
**Figure S5.**  $^1\text{H}$  NMR of compound **4**.



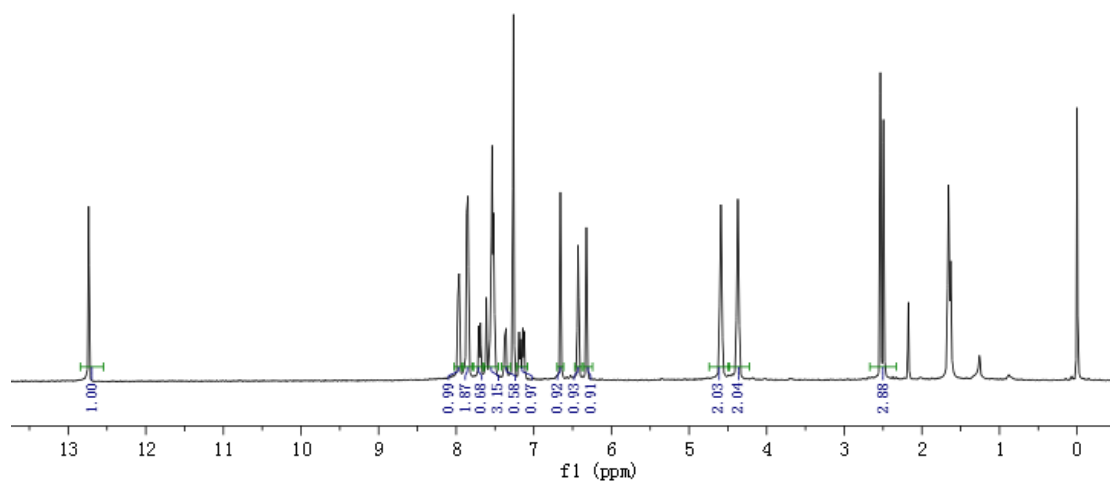
**Figure S6.**  $^1\text{H}$  NMR of compound **5**.



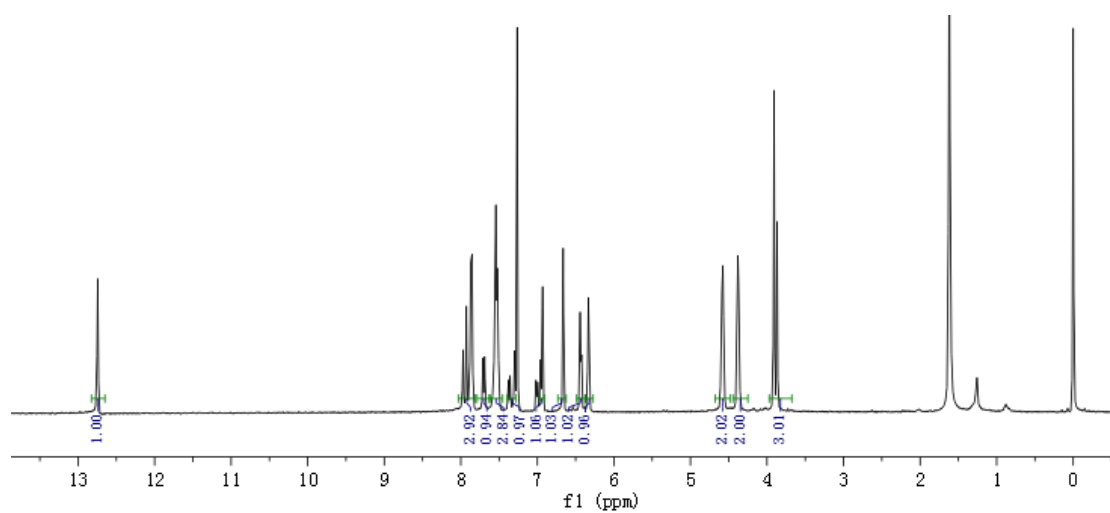
**Figure S7.**  $^1\text{H}$  NMR of compound **6**.



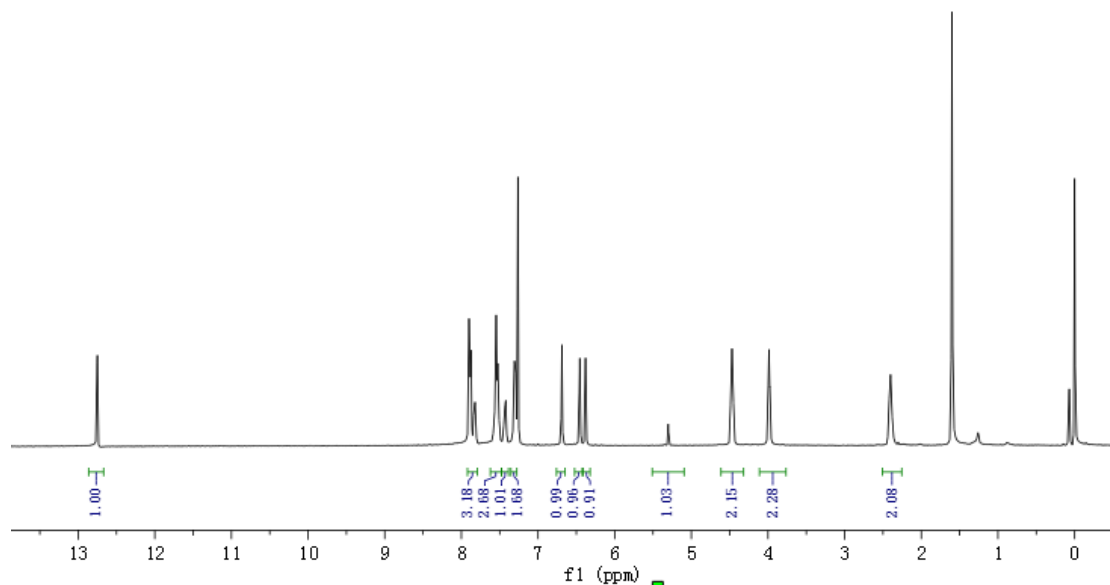
**Figure S8.**  $^1\text{H}$  NMR of compound **7**.



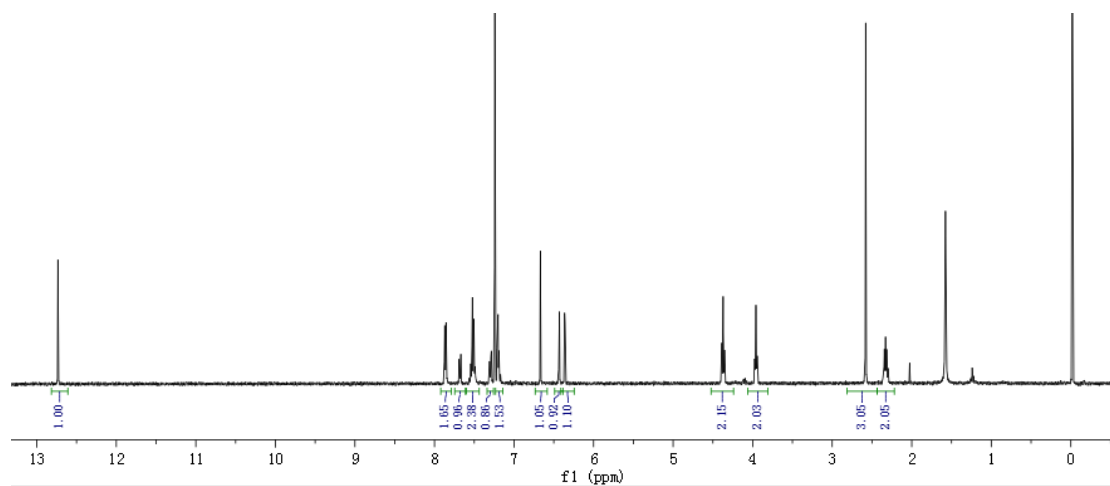
**Figure S9.**  $^1\text{H}$  NMR of compound **8**.



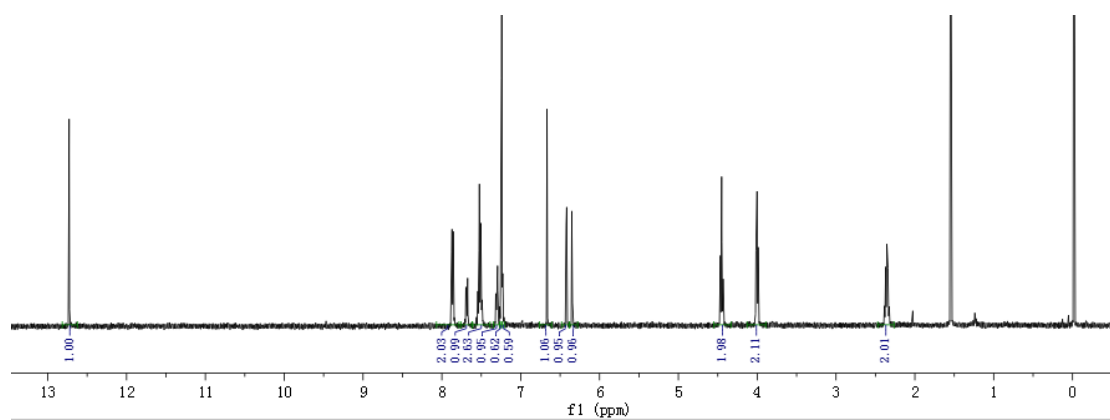
**Figure S10.**  $^1\text{H}$  NMR of compound **9**.



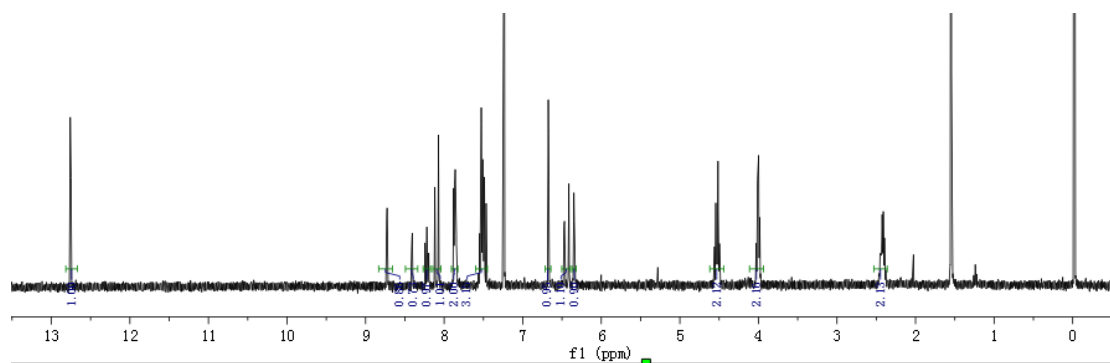
**Figure S11.**  $^1\text{H}$  NMR of compound **10**.



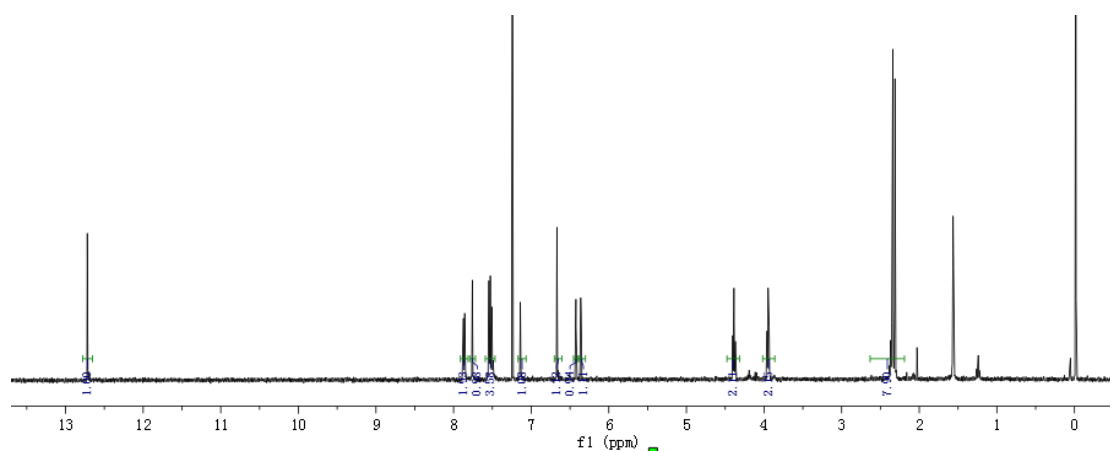
**Figure S12.**  $^1\text{H}$  NMR of compound **11**.



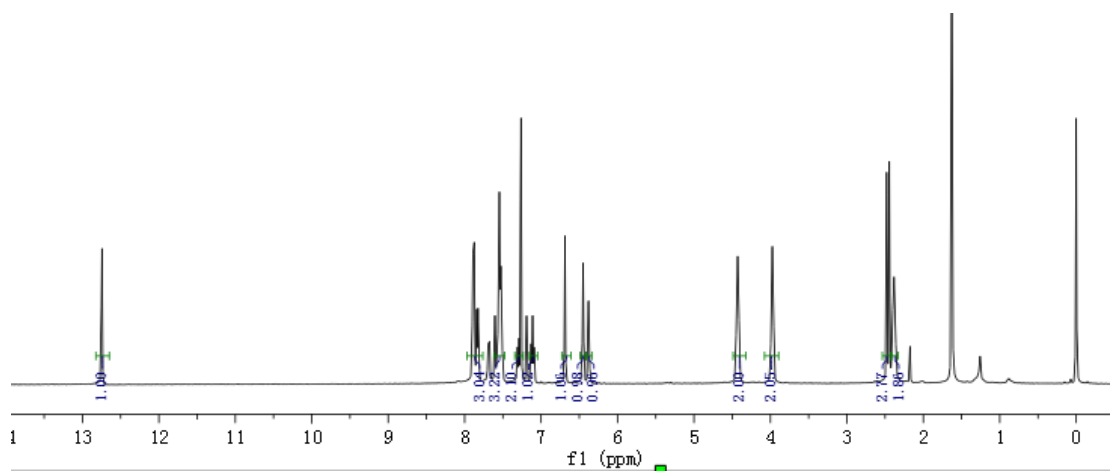
**Figure S13.**  $^1\text{H}$  NMR of compound **12**.



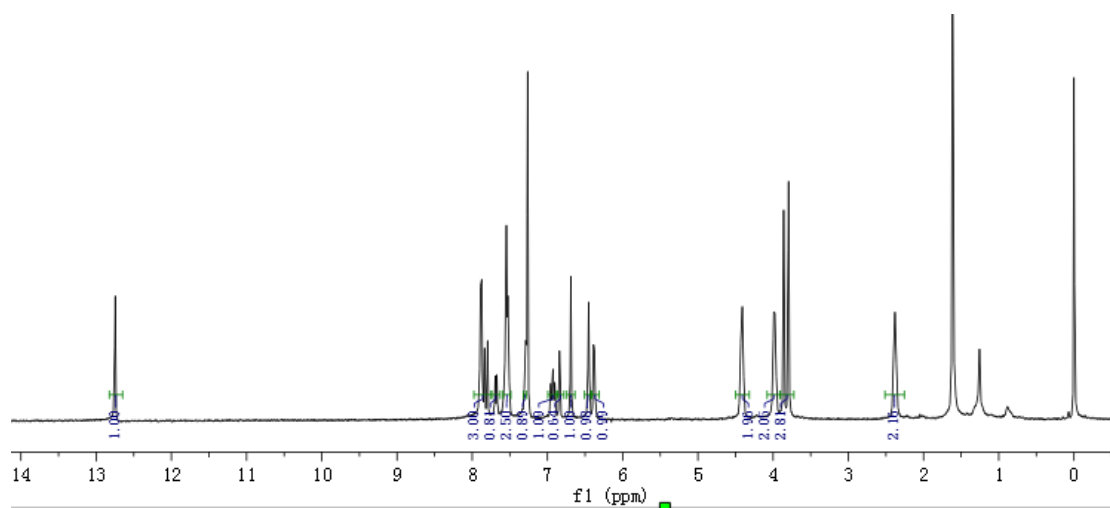
**Figure S14.**  $^1\text{H}$  NMR of compound **13**.



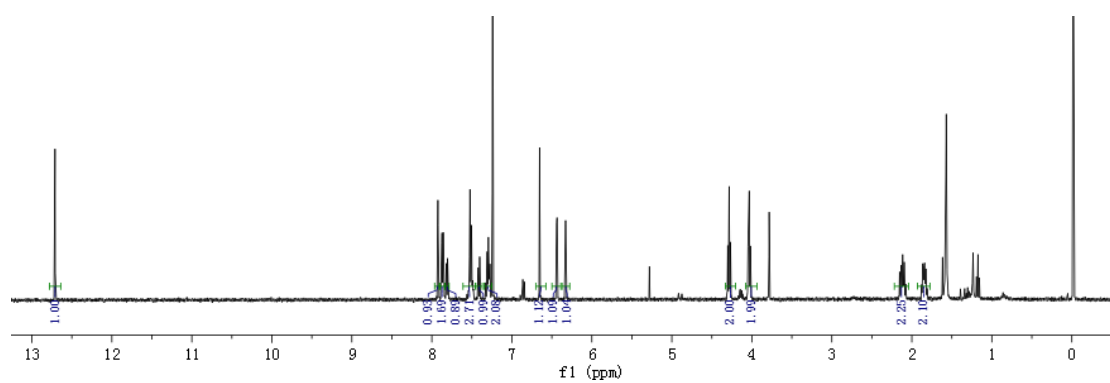
**Figure S15.**  $^1\text{H}$  NMR of compound **14**.



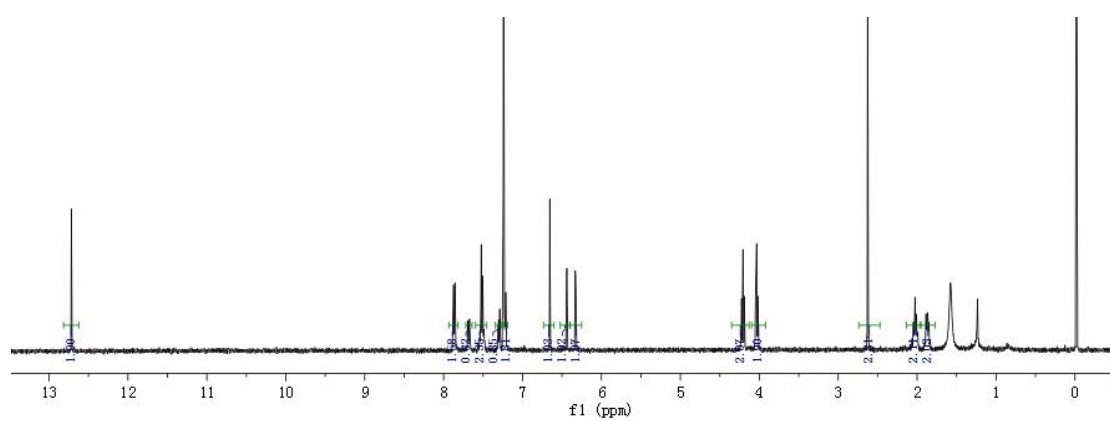
**Figure S16.**  $^1\text{H}$  NMR of compound **15**.



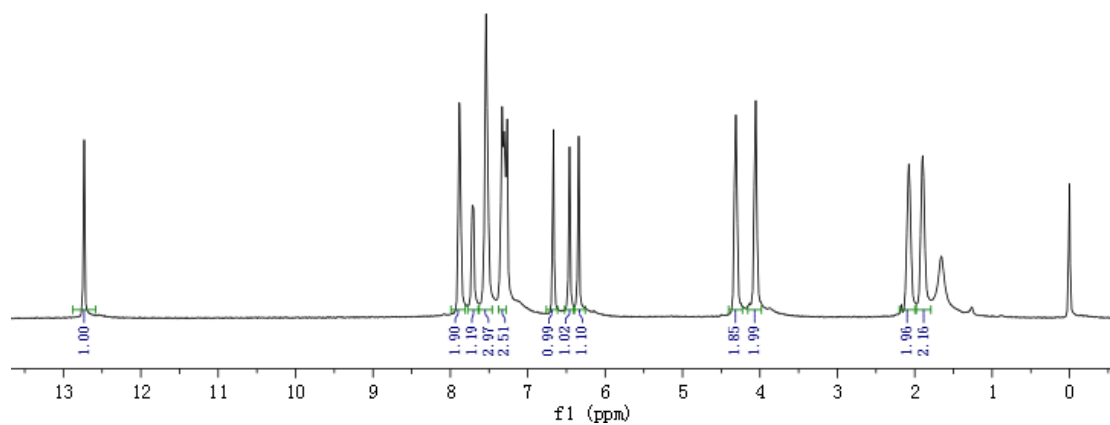
**Figure S17.**  $^1\text{H}$  NMR of compound **16**.



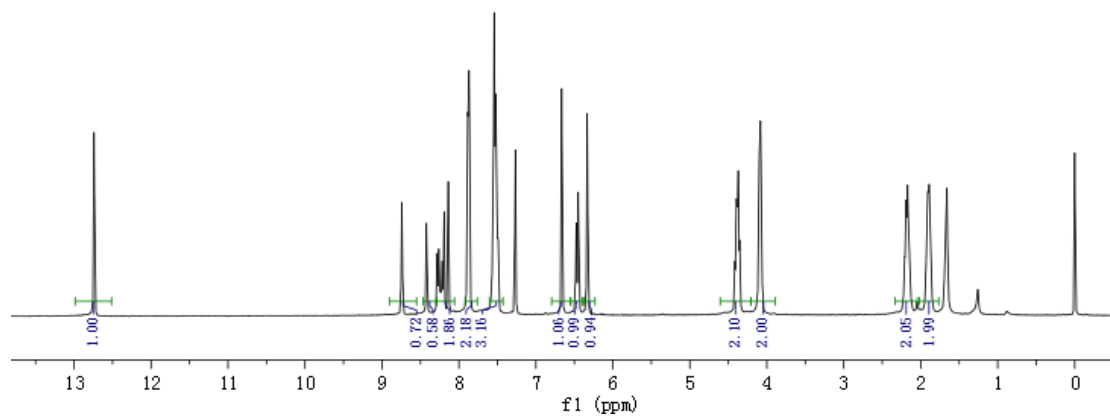
**Figure S18.**  $^1\text{H}$  NMR of compound **17**.



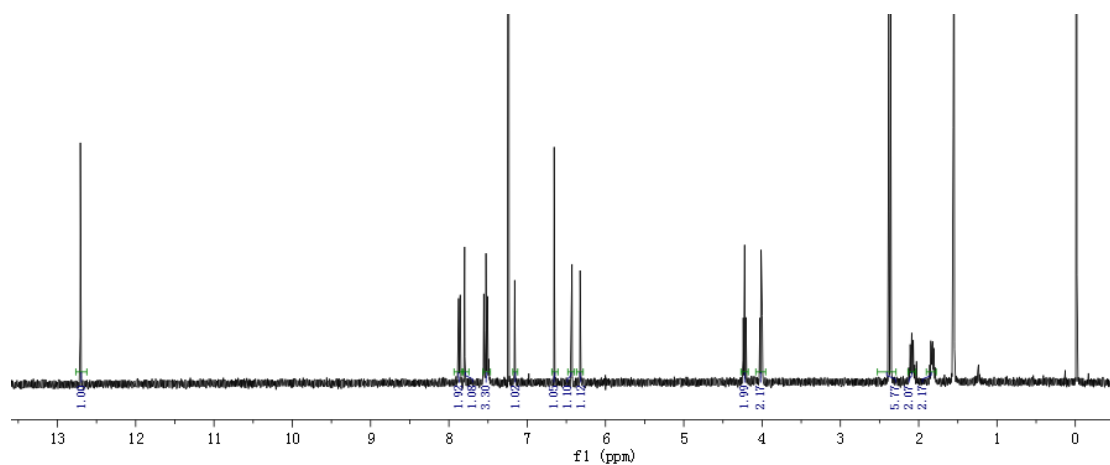
**Figure S19.**  $^1\text{H}$  NMR of compound **18**.



**Figure S20.**  $^1\text{H}$  NMR of compound **19**.

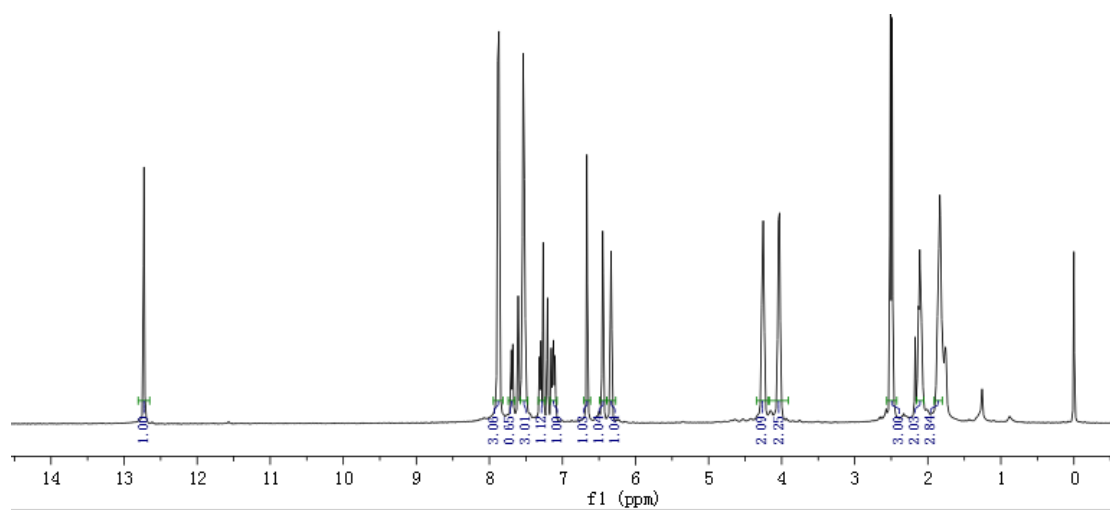


**Figure S21.**  $^1\text{H}$  NMR of compound **20**.

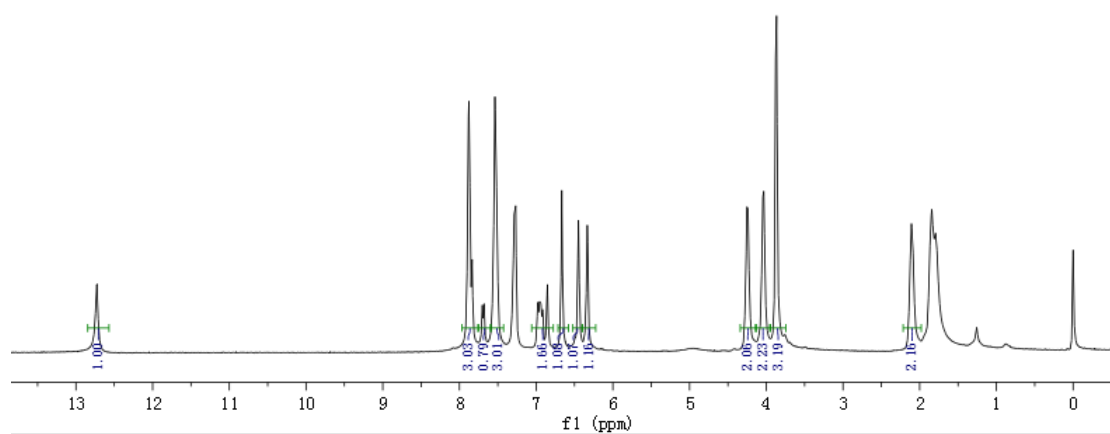


**Figure S22.**  $^1\text{H}$  NMR of compound **21**.





**Figure S23.**  $^1\text{H}$  NMR of compound **22**.



**Figure S24.**  $^1\text{H}$  NMR of compound **23**.