

Design and Synthesis of coumarin-based amphoteric antimicrobials with the biofilm interference and immunoregulation effects

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General procedure for preparation of target compound 2

2 Properly substituted resorcinol (100 mmol) was dissolved in dioxane (100 ml) and ethylpropiolate (100 mmol), and dried zinc chloride (100 mmol) was added. The mixture was refluxed for 24 h. After cooling to room temperature, 100 ml of 5% HCl was added slowly. After addition, the mixture was concentrated to half volume and kept at 4°C. The precipitate was filtered and dried at room temperature. The product (**2**) was recrystallised from ethanol.

General procedure for preparation of target compound 10

To a stirred mixture of **9** (1.15 mmol) and sodium hydride (138 mg, 5.75 mmol) in 5 ml dry toluene, a solution of the diethyl carbonate (1.15 mmol) in dry toluene was dropped. The mixture was reacted at 0°C for 30 min, then heated to reflux and reacted for another 4 h. The reaction mixture was quenched with water (20 mL) at ice bath and neutralized to pH 7 with 2 N HCl. The precipitate was filtered, washed with cold water and dried to get **10**.

General procedure for preparation of target compound 3-5 and 11-13

The appropriate dibromoalkane (1.5 mmol) was added to a solution of hydroxycoumarin (1.5 mmol) and potassium carbonate (3 mmol) in acetone (50 mL) with stirring. The mixture was heated at refluxed and the reaction was monitored by TLC. After cooling, the mixture was separated and the solvent was evaporated. The crude product was Purification by column chromatography to yield compounds **3-5** and **11-13**.

General procedure for preparation of target compound 6-8 and 14-16

The appropriate Amino group (1.5 mmol) was added to a solution of coumarin derivatives (1.5 mmol) and potassium carbonate (3 mmol) in acetone (50 mL) with stirring. The mixture was heated at refluxed and the

reaction was monitored by TLC. After cooling, the mixture was separated and the solvent was evaporated. The crude product was Purification by column chromatography to yield compounds **6-8** and **14-16**.

7-hydroxy-2H-chromen-2-one (2)

¹H NMR (400 MHz, DMSO-d₆) δ = 10.54 (s, 1H), 7.91 (d, *J* = 9.5 Hz, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 6.78 (dd, *J* = 8.5, 2.3 Hz, 1H), 6.71 (d, *J* = 2.2 Hz, 1H), 6.19 (d, *J* = 9.5 Hz, 1H).

7-(4-bromobutoxy)-2H-chromen-2-one (3)

¹H NMR (400 MHz, DMSO) δ = 7.98 – 7.95 (d, *J* = 12 Hz, 1H), 7.61 – 7.59 (d, 1H), 6.96 – 6.91 (m, 2H), 6.28 – 6.25 (d, *J* = 12 Hz, 1H), 4.12 – 4.08 (t, *J* = 8 Hz, 2H), 3.62 – 3.59 (t, *J* = 6 Hz, 2H), 2.00 – 1.82 (m, 4H). ¹³C NMR (100 MHz, DMSO) δ = 161.63, 160.17, 155.31, 144.18, 129.36, 112.60, 112.34, 101.08, 67.36, 34.58, 28.90, 27.08. TOF-MS, *m/z*: [M+H⁺] calculated for C₁₃H₁₃BrO₃, 296.0048, found: 297.0148.

7-((8-bromooctyl)oxy)-2H-chromen-2-one (4)

¹H NMR (400 MHz, DMSO) δ = 7.99 – 7.97 (d, *J* = 8 Hz, 1H), 7.62 – 7.60 (d, 1H), 6.96 – 6.91 (m, 2H), 6.28 – 6.26 (d, *J* = 8 Hz, 1H), 4.08 – 4.04 (t, *J* = 8 Hz, 2H), 3.53 – 3.50 (t, *J* = 6 Hz, 2H), 1.81 – 1.71 (m, 4H), 1.40 – 1.27 (m, 8H). ¹³C NMR (100 MHz, DMSO) δ = 161.83, 160.23, 155.37, 144.26, 129.39, 112.64, 112.30, 101.06, 68.22, 35.11, 32.16, 28.48, 28.33, 27.98, 27.89, 27.41, 27.37, 25.27. TOF-MS, *m/z*: [M+H⁺] calculated for C₁₇H₂₁BrO₃, 352.0674, found: 353.0975.

7-((12-bromododecyl)oxy)-2H-chromen-2-one (5)

¹H NMR (400 MHz, CDCl₃) δ = 7.63 – 7.60 (d, *J* = 6 Hz, 1H), 7.35 – 7.33 (d, 1H), 6.83 – 6.78 (m, 2H), 6.23 – 6.21 (d, *J* = 8 Hz, 1H), 4.01 – 3.98 (t, *J* = 8 Hz, 2H), 3.41 – 3.37 (t, *J* = 8 Hz, 2H), 1.87 – 1.76 (m, 4H), 1.47 – 1.28 (m, 16H). ¹³C NMR (100 MHz, DMSO) δ = 162.40, 161.18, 155.89, 144.18, 128.63, 112.93, 112.33, 101.32, 68.63, 33.93, 32.79, 29.44, 29.36, 29.25, 28.93, 28.70, 28.12, 25.89. TOF-MS, *m/z*: [M+H⁺] calculated for C₂₁H₂₉BrO₃, 408.1300, found: 409.1377.

7-(4-(dimethylamino)butoxy)-2H-chromen-2-one (6a)

¹H NMR (400 MHz, DMSO) δ 7.98 (d, *J* = 9.4 Hz, 1H), 7.61 (d, *J* = 8.6 Hz, 1H), 6.99

– 6.90 (m, 2H), 6.27 (dd, $J = 9.5, 1.3$ Hz, 1H), 4.08 (t, $J = 6.5$ Hz, 2H), 1.74 (p, $J = 6.7$ Hz, 2H), 1.57 (q, $J = 7.6$ Hz, 2H), 1.42 (d, $J = 7.6$ Hz, 2H), 0.83 (t, $J = 7.3$ Hz, 6H). ^{13}C NMR (101 MHz, DMSO) δ 162.28, 160.74, 155.87, 144.79, 129.92, 113.16, 112.83, 112.71, 101.57, 68.61, 26.66, 12.09.

7-(4-(diethylamino)butoxy)-2H-chromen-2-one (6b)

^1H NMR (400 MHz, DMSO) δ 8.00 (d, $J = 9.5$ Hz, 1H), 7.64 (d, $J = 8.6$ Hz, 1H), 7.06 – 6.90 (m, 2H), 6.29 (d, $J = 9.5$ Hz, 1H), 4.12 (d, $J = 5.5$ Hz, 2H), 3.10 (q, $J = 6.9$ Hz, 5H), 1.90 – 1.69 (m, 4H), 1.20 (t, $J = 7.2$ Hz, 5H). ^{13}C NMR (101 MHz, DMSO) δ 162.13, 160.73, 155.88, 144.80, 130.00, 113.19, 112.96, 112.86, 101.70, 68.15, 50.96, 46.81, 26.06, 20.65, 9.13.

7-(4-(dipropylamino)butoxy)-2H-chromen-2-one (6c)

^1H NMR (400 MHz, DMSO) δ 7.69 – 7.53 (m, 2H), 6.99 (d, $J = 15.5$ Hz, 1H), 6.50 – 6.39 (m, 2H), 3.96 (t, $J = 5.7$ Hz, 2H), 3.09 (d, $J = 8.0$ Hz, 4H), 2.90 (q, $J = 6.3, 4.8$ Hz, 3H), 2.76 (s, 5H), 2.53 (d, $J = 1.1$ Hz, 2H), 1.76 (dq, $J = 13.1, 7.3, 6.7$ Hz, 4H), 1.18 (t, $J = 7.2$ Hz, 1H). ^{13}C NMR (101 MHz, DMSO) δ 166.79, 160.98, 158.05, 136.92, 129.94, 115.60, 115.06, 106.58, 102.15, 67.16, 56.76, 42.62, 34.69, 26.13, 21.20.

7-(4-(dibutylamino)butoxy)-2H-chromen-2-one (6d)

^1H NMR (400 MHz, CDCl_3) δ 7.51 (t, $J = 9.5$ Hz, 1H), 7.25 – 7.19 (m, 1H), 6.75 – 6.58 (m, 2H), 6.13 – 6.02 (m, 1H), 3.91 (dt, $J = 9.4, 6.2$ Hz, 2H), 2.44 – 2.17 (m, 7H), 1.71 (ddt, $J = 15.2, 8.8, 6.5$ Hz, 2H), 1.49 (qd, $J = 9.2, 8.8, 6.4$ Hz, 3H), 1.36 – 1.24 (m, 4H), 1.23 – 1.00 (m, 7H), 0.79 (dt, $J = 9.6, 7.3$ Hz, 7H). ^{13}C NMR (101 MHz, CDCl_3) δ 162.25, 155.76, 143.32, 128.63, 112.71, 112.69, 112.67, 112.65, 112.25, 101.19, 68.41, 53.68, 53.57, 29.12, 26.88, 23.51, 20.58, 13.96.

7-((8-(dimethylamino)octyl)oxy)-2H-chromen-2-one (7a)

^1H NMR (400 MHz, DMSO) δ 7.99 (d, $J = 9.5$ Hz, 1H), 7.62 (d, $J = 8.5$ Hz, 1H), 7.04

– 6.85 (m, 2H), 6.27 (dd, $J = 9.4, 1.0$ Hz, 1H), 4.06 (t, $J = 6.5$ Hz, 2H), 2.97 (dd, $J = 9.6, 6.6$ Hz, 2H), 2.70 (d, $J = 1.4$ Hz, 4H), 1.77 – 1.55 (m, 3H), 1.47 – 1.19 (m, 7H). ^{13}C NMR (101 MHz, DMSO) δ 162.34, 160.77, 155.89, 144.82, 129.97, 113.17, 112.84, 112.72, 101.58, 68.75, 57.19, 42.75, 42.72, 28.93, 28.89, 28.84, 26.33, 25.78, 24.29.

7-((8-(diethylamino)octyl)oxy)-2H-chromen-2-one (7b)

^1H NMR (400 MHz, DMSO) δ 7.99 (d, $J = 9.5$ Hz, 1H), 7.62 (d, $J = 8.5$ Hz, 1H), 7.03 – 6.88 (m, 2H), 6.27 (d, $J = 9.5$ Hz, 1H), 4.06 (t, $J = 6.5$ Hz, 2H), 3.08 (q, $J = 7.2$ Hz, 3H), 3.01 – 2.89 (m, 2H), 1.73 (p, $J = 6.7$ Hz, 1H), 1.60 (dq, $J = 11.6, 6.5, 5.6$ Hz, 1H), 1.41 – 1.11 (m, 11H). ^{13}C NMR (101 MHz, DMSO) δ 162.34, 160.77, 155.88, 144.83, 129.97, 113.17, 112.83, 112.72, 101.57, 68.75, 51.26, 46.68, 41.81, 28.95, 28.91, 28.84, 26.48, 25.78, 23.61, 11.44, 9.07.

7-((8-(dipropylamino)octyl)oxy)-2H-chromen-2-one (7c)

^1H NMR (400 MHz, DMSO) δ 7.97 (d, $J = 9.5$ Hz, 1H), 7.60 (d, $J = 8.6$ Hz, 1H), 7.03 – 6.83 (m, 2H), 6.27 (d, $J = 9.5$ Hz, 1H), 4.05 (t, $J = 6.5$ Hz, 2H), 2.30 (dt, $J = 14.2, 7.1$ Hz, 5H), 1.71 (q, $J = 6.9$ Hz, 2H), 1.37 (dq, $J = 14.5, 7.0$ Hz, 6H), 1.32 – 1.18 (m, 5H), 0.81 (t, $J = 7.3$ Hz, 5H). ^{13}C NMR (101 MHz, DMSO) δ 162.36, 160.75, 155.90, 144.79, 129.91, 113.15, 112.82, 112.70, 101.56, 68.73, 56.00, 53.95, 29.35, 29.19, 28.86, 27.25, 27.09, 25.84, 20.36, 12.24.

7-((8-(dibutylamino)octyl)oxy)-2H-chromen-2-one (7d)

^1H NMR (400 MHz, DMSO) δ 7.96 (d, $J = 9.5$ Hz, 1H), 7.58 (d, $J = 8.5$ Hz, 1H), 7.00 – 6.82 (m, 2H), 6.25 (d, $J = 9.5$ Hz, 1H), 4.03 (t, $J = 6.5$ Hz, 2H), 2.28 (t, $J = 7.0$ Hz, 5H), 1.70 (p, $J = 6.7$ Hz, 2H), 1.38 (dd, $J = 10.9, 4.9$ Hz, 2H), 1.35 – 1.17 (m, 13H), 0.83 (t, $J = 7.1$ Hz, 5H). ^{13}C NMR (101 MHz, DMSO) δ 162.33, 144.71, 129.85, 113.05, 112.80, 112.68, 101.49, 68.69, 53.92, 53.63, 29.41, 29.37, 29.23, 28.90, 27.26, 27.13, 25.86, 20.49, 14.32.

7-((12-(dimethylamino)dodecyl)oxy)-2H-chromen-2-one (8a)

¹H NMR (400 MHz, DMSO) δ 7.65 (d, *J* = 15.5 Hz, 1H), 7.55 (d, *J* = 8.4 Hz, 1H), 6.98 (d, *J* = 15.4 Hz, 1H), 6.47 – 6.34 (m, 2H), 3.91 (t, *J* = 6.5 Hz, 3H), 3.10 (s, 3H), 2.90 (s, 3H), 2.74 – 2.67 (m, 2H), 2.54 (s, 4H), 1.67 (q, *J* = 6.9 Hz, 2H), 1.25 (s, 12H).
¹³C NMR (101 MHz, DMSO) δ 166.81, 161.23, 158.04, 136.96, 129.90, 115.42, 114.94, 106.66, 102.01, 67.84, 57.96, 43.64, 34.80, 29.43, 29.40, 29.33, 29.20, 29.11, 29.04, 26.66, 25.93, 25.29.

7-((12-(diethylamino)dodecyl)oxy)-2H-chromen-2-one (8b)

¹H NMR (400 MHz, DMSO) δ 7.99 (d, *J* = 9.5 Hz, 1H), 7.62 (d, *J* = 8.6 Hz, 1H), 7.00 – 6.86 (m, 2H), 6.28 (d, *J* = 9.5 Hz, 1H), 4.06 (t, *J* = 6.5 Hz, 2H), 3.01 (dq, *J* = 51.3, 11.5, 9.4 Hz, 5H), 1.72 (p, *J* = 6.7 Hz, 2H), 1.57 (t, *J* = 7.7 Hz, 2H), 1.43 – 1.11 (m, 19H). ¹³C NMR (101 MHz, DMSO) δ 162.33, 160.75, 144.81, 129.94, 113.16, 112.82, 112.70, 101.57, 68.74, 51.31, 46.69, 29.42, 29.40, 29.37, 29.30, 29.15, 29.01, 28.87, 26.53, 25.87.

7-((12-(dipropylamino)dodecyl)oxy)-2H-chromen-2-one (8c)

¹H NMR (400 MHz, DMSO) δ 7.99 (d, *J* = 9.5 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.05 – 6.82 (m, 2H), 6.28 (d, *J* = 9.5 Hz, 1H), 4.06 (t, *J* = 6.5 Hz, 2H), 3.34 (s, 3H), 2.97 (t, *J* = 8.5 Hz, 4H), 1.81 – 1.52 (m, 6H), 1.40 (t, *J* = 7.6 Hz, 2H), 1.35 – 1.17 (m, 11H), 0.89 (t, *J* = 7.3 Hz, 5H). ¹³C NMR (101 MHz, DMSO) δ 162.33, 160.75, 155.87, 144.81, 129.94, 113.15, 112.82, 112.70, 101.57, 68.74, 53.95, 52.51, 29.43, 29.40, 29.37, 29.30, 29.16, 28.99, 28.88, 26.51, 25.87, 11.33.

7-((12-(dibutylamino)dodecyl)oxy)-2H-chromen-2-one (8d)

¹H NMR (400 MHz, DMSO) δ 7.97 (d, *J* = 9.5 Hz, 1H), 7.60 (d, *J* = 8.6 Hz, 1H), 7.02 – 6.83 (m, 2H), 6.27 (d, *J* = 9.5 Hz, 1H), 4.04 (t, *J* = 6.5 Hz, 2H), 2.38 (s, 4H), 1.71 (p, *J* = 6.7 Hz, 2H), 1.44 – 1.15 (m, 19H), 0.85 (t, *J* = 7.2 Hz, 5H). ¹³C NMR (101 MHz, DMSO) δ 162.33, 155.88, 144.76, 129.89, 113.11, 112.81, 112.68, 101.54, 68.71, 55.35, 29.44, 29.42, 29.40, 29.30, 29.16, 28.89, 27.14, 25.87, 20.40, 14.30.

4-hydroxy-2H-chromen-2-one (10)

¹H NMR (400 MHz, DMSO-d₆) δ = 12.49 (s, 1H), 7.81 (d, *J* = 7.8 Hz, 1H), 7.62 (t, *J* = 8.4 Hz, 1H), 7.41 – 7.21 (m, 2H), 5.60 (s, 1H).

4-(4-bromobutoxy)-2H-chromen-2-one (11)

¹H NMR (400 MHz, CDCl₃) δ = 7.82 – 7.80 (d, *J* = 8 Hz, 1H), 7.58 – 7.55 (t, 1H), 7.32 – 7.26 (m, 2H), 5.68 (s, 1H), 4.20 – 4.17 (t, *J* = 6 Hz, 2H), 3.54 – 3.51 (t, *J* = 6 Hz, 2H), 2.12 – 2.11 (m, 4H). ¹³C NMR (100 MHz, DMSO) δ = 165.42, 162.76, 153.22, 132.35, 123.84, 122.84, 116.69, 115.54, 90.46, 68.35, 32.78, 29.17, 27.10. TOF-MS, *m/z*: [M+H⁺] calculated for C₁₃H₁₃BrO₃, 296.0048, found: 297.0098.

4-((8-bromooctyl)oxy)-2H-chromen-2-one (12)

¹H NMR (400 MHz, CDCl₃) δ = 7.82 – 7.80 (d, *J* = 8 Hz, 1H), 7.58 – 7.55 (t, 1H), 7.32 – 7.26 (m, 2H), 5.68 (s, 1H), 4.20 – 4.17 (t, *J* = 6 Hz, 2H), 3.54 – 3.51 (t, *J* = 6 Hz, 2H), 2.12 – 2.11 (m, 4H). ¹³C NMR (100 MHz, DMSO) δ = 165.42, 162.76, 153.22, 132.35, 123.84, 122.84, 116.69, 115.54, 90.46, 68.35, 32.78, 29.17, 27.10. TOF-MS, *m/z*: [M+H⁺] calculated for C₁₃H₁₃BrO₃, 296.0048, found: 297.0098.

4-((12-bromododecyl)oxy)-2H-chromen-2-one (13)

¹H NMR (400 MHz, CDCl₃) δ = 7.84 – 7.82 (d, *J* = 8 Hz, 1H), 7.57 – 7.53 (t, 1H), 7.33 – 7.26 (m, 2H), 5.67 (s, 1H), 4.15 – 4.12 (t, *J* = 6 Hz, 2H), 3.43 – 3.40 (t, *J* = 6 Hz, 2H), 1.93 – 1.82 (m, 4H), 1.55 – 1.30 (m, 16H). ¹³C NMR (100 MHz, DMSO) δ = 165.68, 162.99, 153.31, 132.26, 123.77, 122.97, 116.72, 115.80, 90.33, 69.39, 34.02, 32.77, 29.44, 29.42, 29.37, 29.18, 28.71, 28.43, 28.12, 25.90. TOF-MS, *m/z*: [M+H⁺] calculated for C₂₁H₂₉BrO₃, 408.1300, found: 409.1328.

4-(4-(dimethylamino)butoxy)-2H-chromen-2-one (14a)

¹H NMR (400 MHz, CDCl₃) δ 7.81 (d, *J* = 7.8 Hz, 1H), 7.54 (t, *J* = 7.9 Hz, 1H), 7.34 – 7.26 (m, 2H), 5.69 (s, 1H), 4.20 (t, *J* = 5.8 Hz, 2H), 3.47 (d, *J* = 14.2 Hz, 1H), 3.25 – 3.09 (m, 2H), 2.85 (d, *J* = 2.6 Hz, 6H), 2.11 (dt, *J* = 44.1, 7.9 Hz, 4H). ¹³C NMR (101

MHz, CDCl₃) δ 165.37, 162.83, 153.25, 132.57, 124.12, 122.98, 116.78, 115.42, 90.74, 68.13, 57.62, 43.19, 43.16, 25.88, 21.47.

4-(4-(diethylamino)butoxy)-2H-chromen-2-one (14b)

¹H NMR (400 MHz, CDCl₃) δ 7.74 (dd, J = 8.2, 1.6 Hz, 1H), 7.46 (ddd, J = 8.7, 7.3, 1.6 Hz, 1H), 7.24 – 7.16 (m, 2H), 5.63 (s, 1H), 4.15 (t, J = 6.0 Hz, 2H), 3.44 (q, J = 7.2 Hz, 1H), 3.13 (p, J = 7.3 Hz, 5H), 2.14 – 1.89 (m, 4H), 1.37 (dt, J = 18.5, 7.3 Hz, 7H). ¹³C NMR (101 MHz, CDCl₃) δ 165.50, 162.92, 153.11, 132.46, 124.08, 123.06, 123.02, 116.57, 115.42, 90.55, 68.45, 51.52, 46.85, 26.01, 20.81, 8.88.

4-(4-(dipropylamino)butoxy)-2H-chromen-2-one (14c)

¹H NMR (400 MHz, CDCl₃) δ 7.77 (dd, J = 7.9, 1.6 Hz, 1H), 7.48 (ddd, J = 8.6, 7.2, 1.6 Hz, 1H), 7.27 – 7.17 (m, 2H), 5.61 (s, 1H), 4.10 (t, J = 6.4 Hz, 2H), 2.49 – 2.39 (m, 2H), 2.38 – 2.28 (m, 4H), 1.88 (dq, J = 8.5, 6.5 Hz, 2H), 1.66 – 1.53 (m, 2H), 1.46 – 1.33 (m, 4H), 0.82 (t, J = 7.4 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 165.65, 162.92, 132.23, 123.75, 122.97, 116.63, 90.30, 69.34, 56.16, 53.64, 26.51, 23.74, 20.18, 11.90.

4-(4-(dibutylamino)butoxy)-2H-chromen-2-one (14d)

¹H NMR (400 MHz, CDCl₃) δ 7.83 (dd, J = 7.9, 1.6 Hz, 1H), 7.55 (ddd, J = 8.6, 7.1, 1.6 Hz, 1H), 7.38 – 7.24 (m, 2H), 5.70 (s, 1H), 4.19 (t, J = 5.8 Hz, 2H), 3.46 (d, J = 1.6 Hz, 2H), 2.99 – 2.93 (m, 2H), 2.87 (d, J = 5.4 Hz, 2H), 2.77 (t, J = 8.1 Hz, 3H), 2.02 – 1.85 (m, 4H), 1.62 (ddd, J = 12.3, 9.8, 6.3 Hz, 3H), 1.37 (dq, J = 14.9, 7.5 Hz, 4H), 0.94 (dd, J = 8.0, 6.8 Hz, 6H). ¹³C NMR (101 MHz, CDCl₃) δ 165.58, 163.00, 153.24, 132.46, 123.99, 123.01, 116.71, 115.58, 90.50, 68.76, 53.04, 52.99, 47.70, 27.83, 26.26, 20.39, 20.09, 13.78, 13.49.

4-((8-(dimethylamino)octyl)oxy)-2H-chromen-2-one (15a)

¹H NMR (400 MHz, CDCl₃) δ 7.79 (dd, J = 7.9, 1.6 Hz, 1H), 7.52 (ddd, J = 8.6, 7.1, 1.6 Hz, 1H), 7.35 – 7.17 (m, 2H), 5.63 (s, 1H), 4.10 (t, J = 6.4 Hz, 2H), 2.71 – 2.57

(m, 2H), 1.87 (m, $J = 6.7$ Hz, 2H), 1.67 (m, $J = 7.3$ Hz, 2H), 1.53 – 1.42 (m, 2H), 1.36 (h, $J = 5.9, 5.0$ Hz, 6H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.70, 153.32, 132.32, 123.85, 123.01, 116.74, 90.35, 69.32, 58.88, 44.07, 29.13, 29.03, 28.41, 26.93, 25.84.

4-((8-(diethylamino)octyl)oxy)-2H-chromen-2-one (15b)

^1H NMR (400 MHz, CDCl_3) δ 7.80 (dd, $J = 7.9, 1.7$ Hz, 1H), 7.53 (ddd, $J = 8.6, 7.2, 1.6$ Hz, 1H), 7.35 – 7.20 (m, 2H), 5.64 (s, 1H), 4.11 (t, $J = 6.4$ Hz, 2H), 3.13 (q, $J = 7.3$ Hz, 4H), 3.03 – 2.92 (m, 2H), 1.86 (dp, $J = 14.8, 6.8$ Hz, 4H), 1.57 – 1.32 (m, 14H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.69, 153.30, 132.35, 123.89, 123.01, 116.71, 115.76, 90.35, 69.25, 51.41, 46.62, 28.95, 28.88, 28.36, 26.78, 25.78, 23.28.

4-((8-(dipropylamino)octyl)oxy)-2H-chromen-2-one (15c)

^1H NMR (400 MHz, CDCl_3) δ 7.79 (dd, $J = 8.0, 1.6$ Hz, 1H), 7.51 (ddd, $J = 8.7, 7.3, 1.6$ Hz, 1H), 7.37 – 7.18 (m, 2H), 5.63 (s, 1H), 4.09 (t, $J = 6.4$ Hz, 2H), 2.46 – 2.27 (m, 7H), 1.98 – 1.80 (m, 2H), 1.60 – 1.21 (m, 17H), 0.84 (t, $J = 7.4$ Hz, 7H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.67, 132.24, 123.77, 122.97, 116.69, 115.80, 90.31, 69.39, 56.22, 54.19, 29.43, 29.21, 28.44, 27.49, 27.01, 25.89, 20.12, 20.10, 11.97.

4-((8-(dibutylamino)octyl)oxy)-2H-chromen-2-one (15d)

^1H NMR (400 MHz, CDCl_3) δ 7.77 (dd, $J = 7.9, 1.6$ Hz, 1H), 7.49 (ddd, $J = 8.7, 7.3, 1.6$ Hz, 1H), 7.31 – 7.16 (m, 2H), 5.62 (s, 1H), 4.08 (t, $J = 6.4$ Hz, 2H), 2.46 – 2.29 (m, 5H), 1.95 – 1.79 (m, 2H), 1.54 – 1.17 (m, 15H), 0.87 (t, $J = 7.3$ Hz, 5H). ^{13}C NMR (101 MHz, CDCl_3) δ 165.66, 162.93, 132.23, 123.76, 122.97, 116.66, 90.29, 69.38, 54.11, 53.83, 29.42, 29.20, 29.04, 28.43, 27.48, 26.92, 25.88, 20.74, 14.06.

4-((12-(dimethylamino)dodecyl)oxy)-2H-chromen-2-one (16a)

^1H NMR (400 MHz, DMSO) δ 7.65 (d, $J = 15.5$ Hz, 1H), 7.55 (d, $J = 8.4$ Hz, 1H), 6.98 (d, $J = 15.4$ Hz, 1H), 6.42 (t, $J = 1.9$ Hz, 2H), 3.91 (t, $J = 6.5$ Hz, 3H), 3.10 (s, 3H), 2.90 (s, 3H), 2.71 (s, 2H), 2.54 (s, 4H), 1.68 (m, $J = 6.7$ Hz, 2H), 1.26 (d, $J = 8.5$ Hz, 12H). ^{13}C NMR (101 MHz, DMSO) δ 166.81, 161.23, 158.04, 136.96, 129.90,

115.42, 114.94, 106.66, 102.01, 67.84, 57.96, 43.64, 34.80, 29.43, 29.40, 29.33, 29.20, 29.11, 29.04, 26.66, 25.93, 25.29.

4-((12-(diethylamino)dodecyl)oxy)-2H-chromen-2-one (16b)

¹H NMR (400 MHz, DMSO) δ 7.99 (d, *J* = 9.5 Hz, 1H), 7.62 (d, *J* = 8.6 Hz, 1H), 7.00 – 6.86 (m, 2H), 6.28 (d, *J* = 9.5 Hz, 1H), 4.06 (t, *J* = 6.5 Hz, 2H), 3.01 (dq, *J* = 51.3, 11.5, 9.4 Hz, 5H), 1.71 (q, *J* = 6.9 Hz, 2H), 1.57 (t, *J* = 7.7 Hz, 2H), 1.43 – 1.11 (m, 19H). ¹³C NMR (101 MHz, DMSO) δ 162.33, 160.75, 144.81, 129.94, 113.16, 112.82, 112.70, 101.57, 68.74, 51.31, 46.69, 29.42, 29.40, 29.37, 29.30, 29.15, 29.01, 28.87, 26.53, 25.87.

4-((12-(dipropylamino)dodecyl)oxy)-2H-chromen-2-one (16c)

¹H NMR (400 MHz, DMSO) δ 7.99 (d, *J* = 9.5 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.05 – 6.82 (m, 2H), 6.28 (d, *J* = 9.5 Hz, 1H), 4.06 (t, *J* = 6.5 Hz, 2H), 3.34 (s, 3H), 2.96 (t, *J* = 8.6 Hz, 4H), 1.81 – 1.52 (m, 6H), 1.45 – 1.19 (m, 13H), 0.89 (t, *J* = 7.3 Hz, 5H). ¹³C NMR (101 MHz, DMSO) δ 162.33, 160.75, 155.87, 144.81, 129.94, 113.15, 112.82, 112.70, 101.57, 68.74, 53.95, 52.51, 29.43, 29.40, 29.37, 29.30, 29.16, 28.99, 28.88, 26.51, 25.87, 11.33.

4-((12-(dibutylamino)dodecyl)oxy)-2H-chromen-2-one (16d)

¹H NMR (400 MHz, DMSO) δ 7.97 (d, *J* = 9.5 Hz, 1H), 7.60 (d, *J* = 8.6 Hz, 1H), 7.02 – 6.83 (m, 2H), 6.27 (d, *J* = 9.5 Hz, 1H), 4.04 (t, *J* = 6.5 Hz, 2H), 2.38 (s, 4H), 1.71 (m, *J* = 6.7 Hz, 2H), 1.52 – 1.16 (m, 20H), 0.85 (t, *J* = 7.2 Hz, 5H). ¹³C NMR (101 MHz, DMSO) δ 162.33, 160.72, 155.88, 144.76, 129.89, 113.11, 112.81, 112.68, 101.54, 68.71, 55.35, 29.44, 29.42, 29.40, 29.30, 29.16, 28.89, 25.87, 20.40, 14.30.

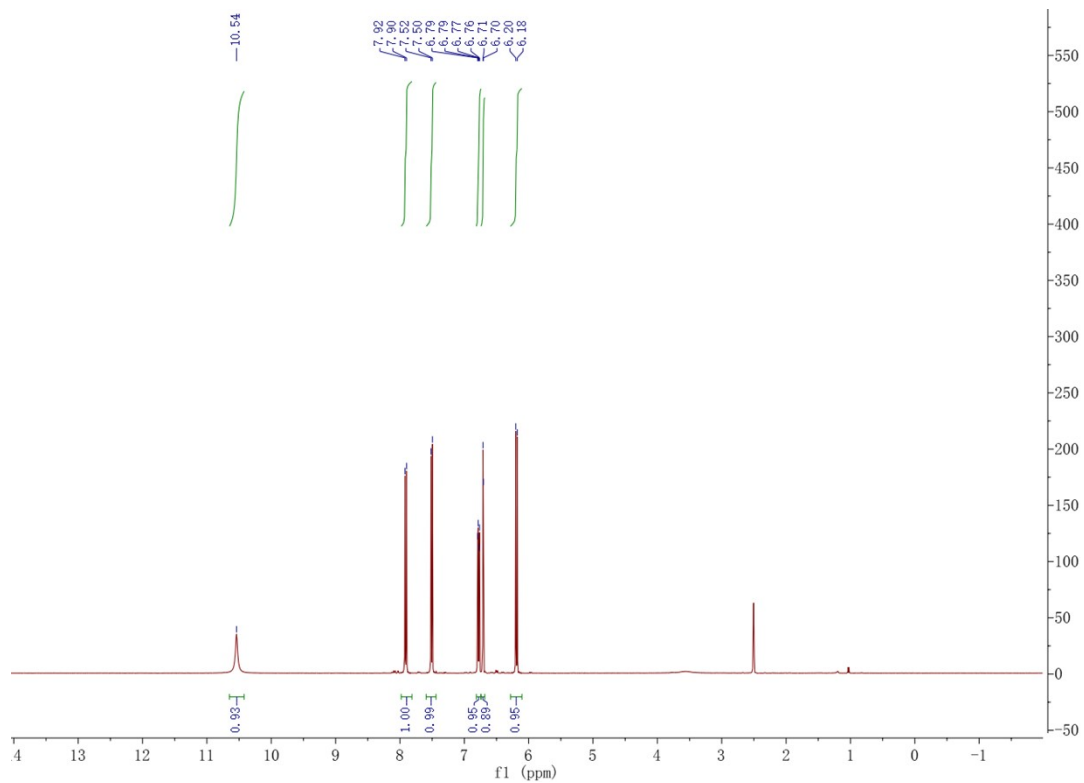


Fig.S1 ^1H NMR of **2** (400 MHz, DMSO)

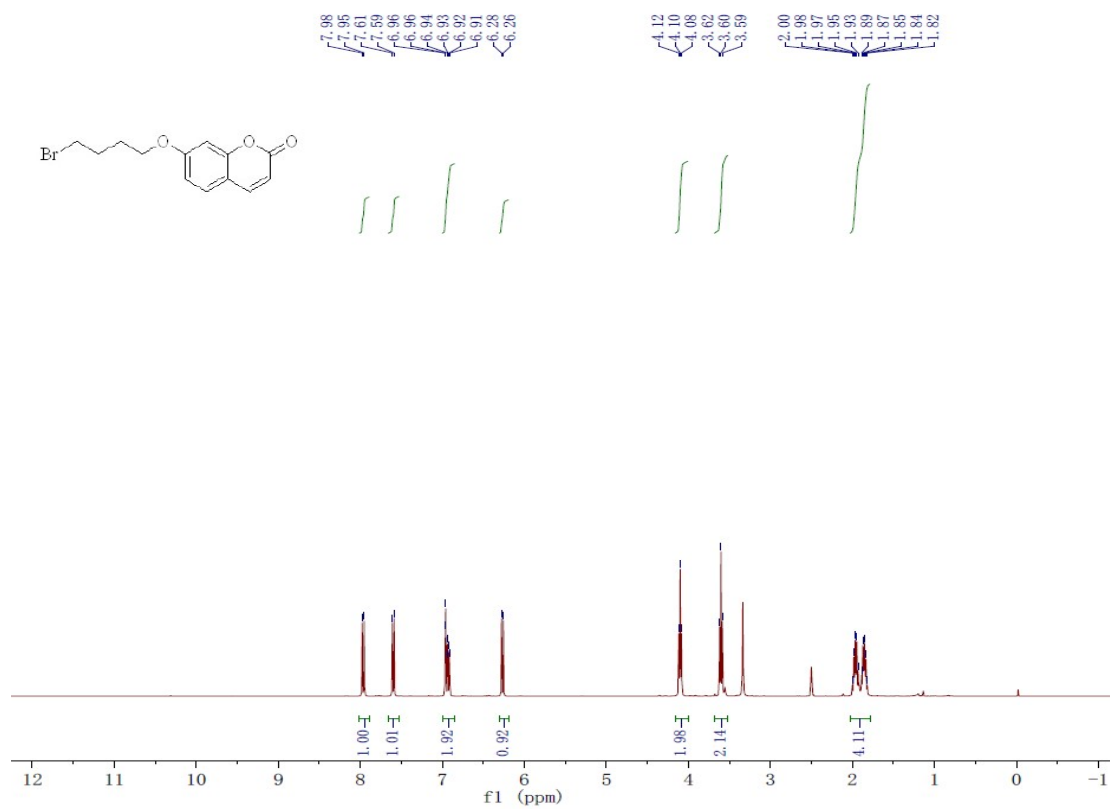


Fig.S2 ^1H NMR of **3** (400 MHz, DMSO)

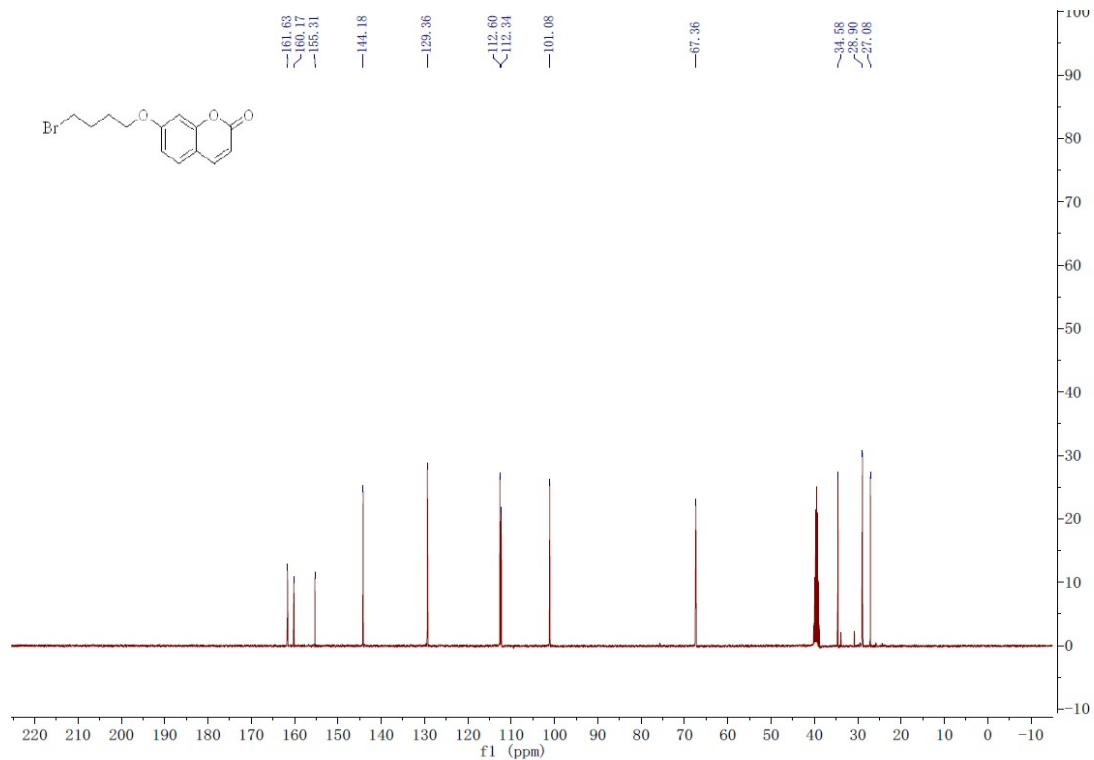


Fig.S3 ^{13}C NMR of **3** (100 MHz, DMSO)

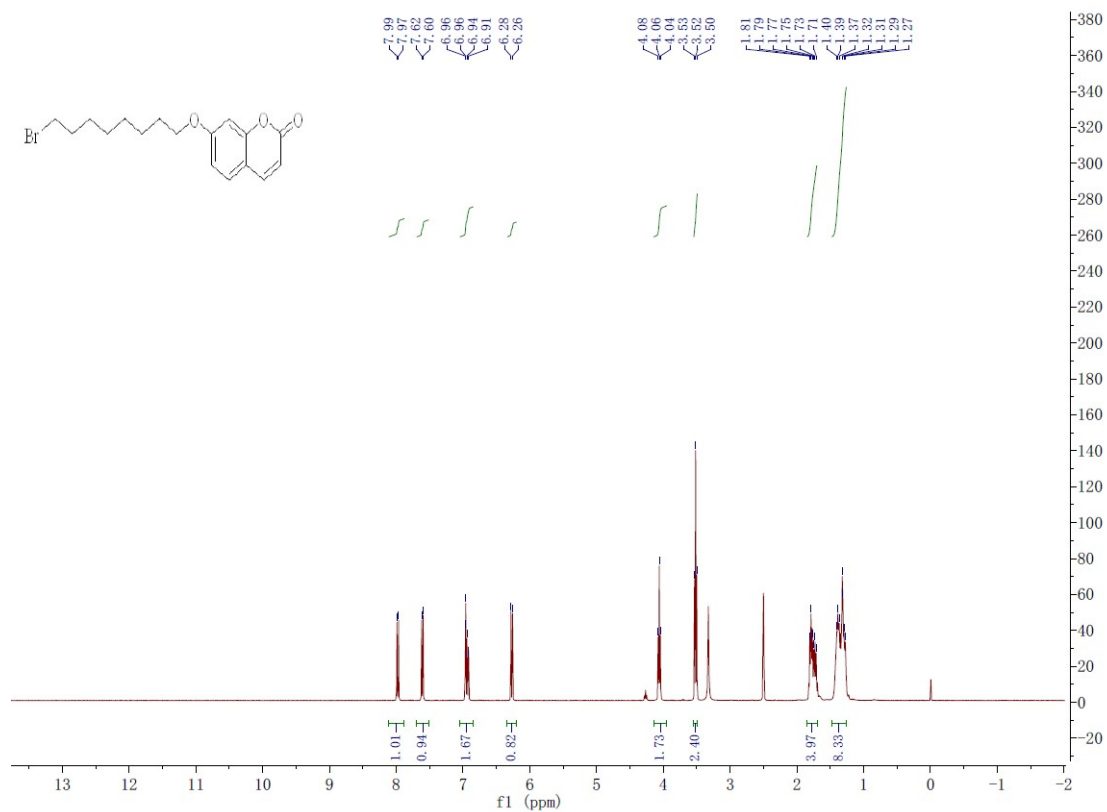


Fig.S4 ^1H NMR of **4** (400 MHz, DMSO)

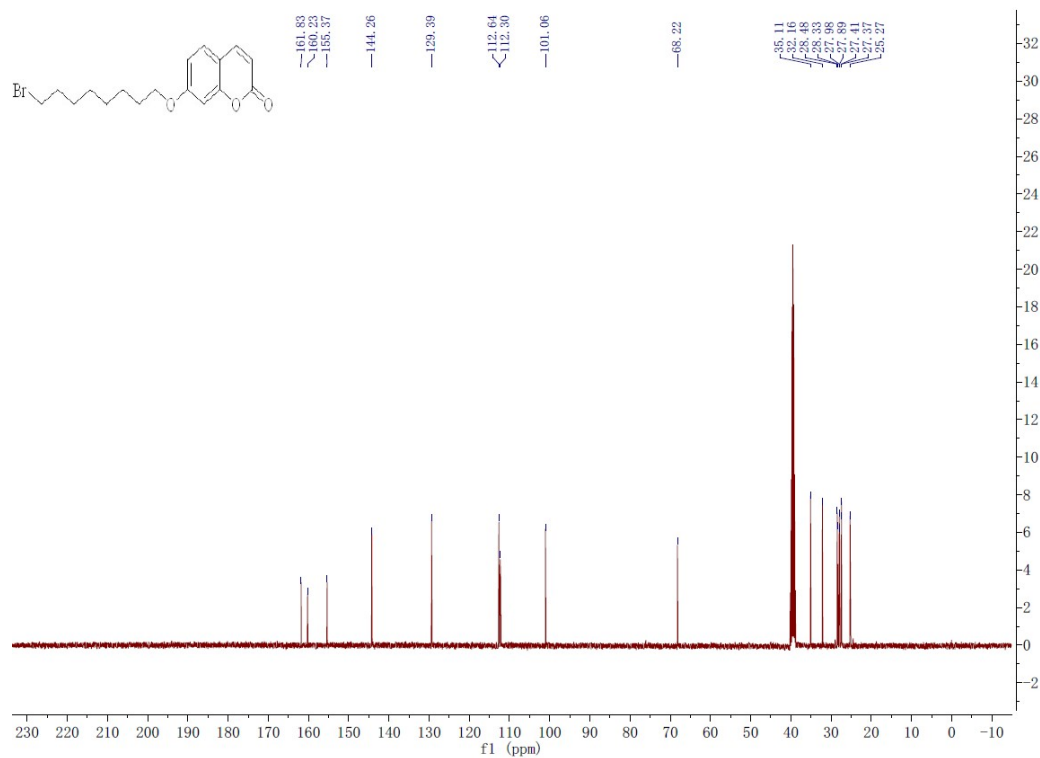


Fig.S5 ^{13}C NMR of 4 (100 MHz, DMSO)

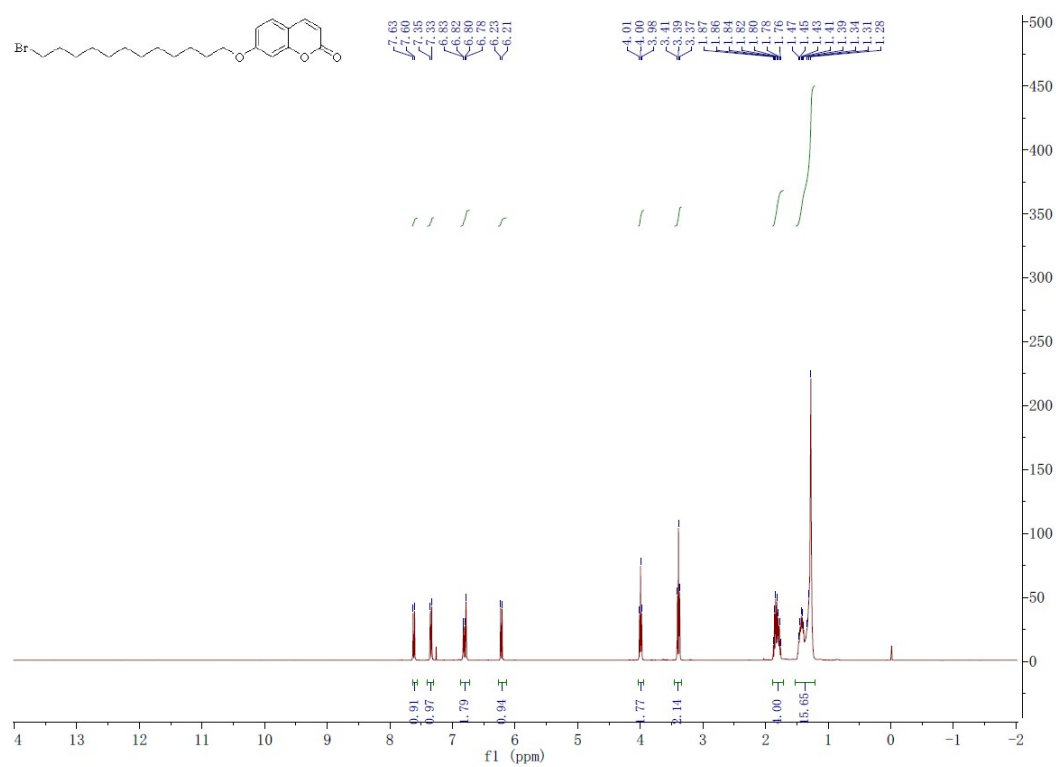


Fig.S6 ^1H NMR of 5 (400 MHz, CDCl_3)

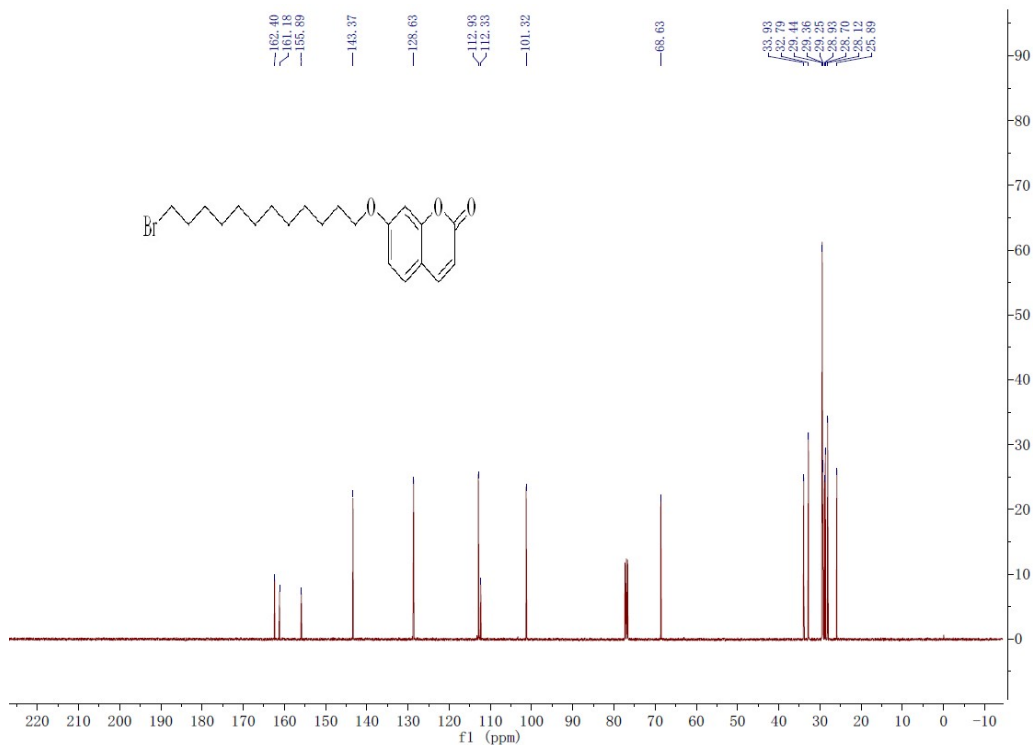


Fig.S7 ^{13}C NMR of **5** (100 MHz, CDCl_3)

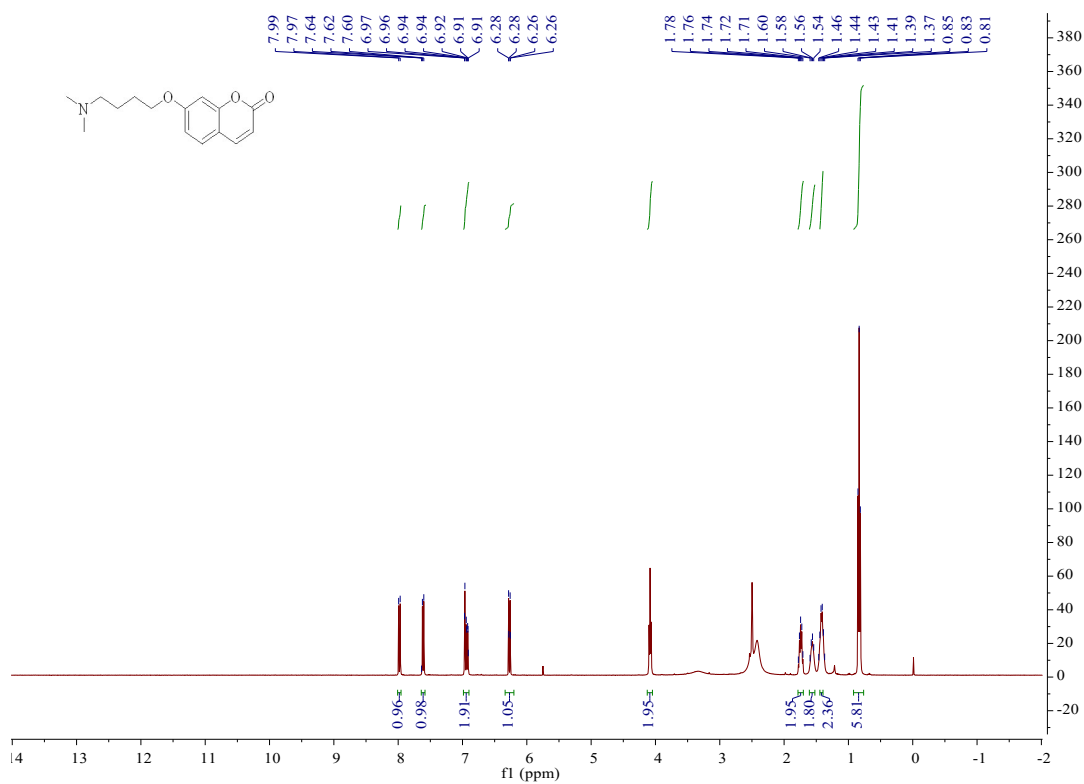


Fig.S8 ^1H NMR of **6a** (400 MHz, DMSO)

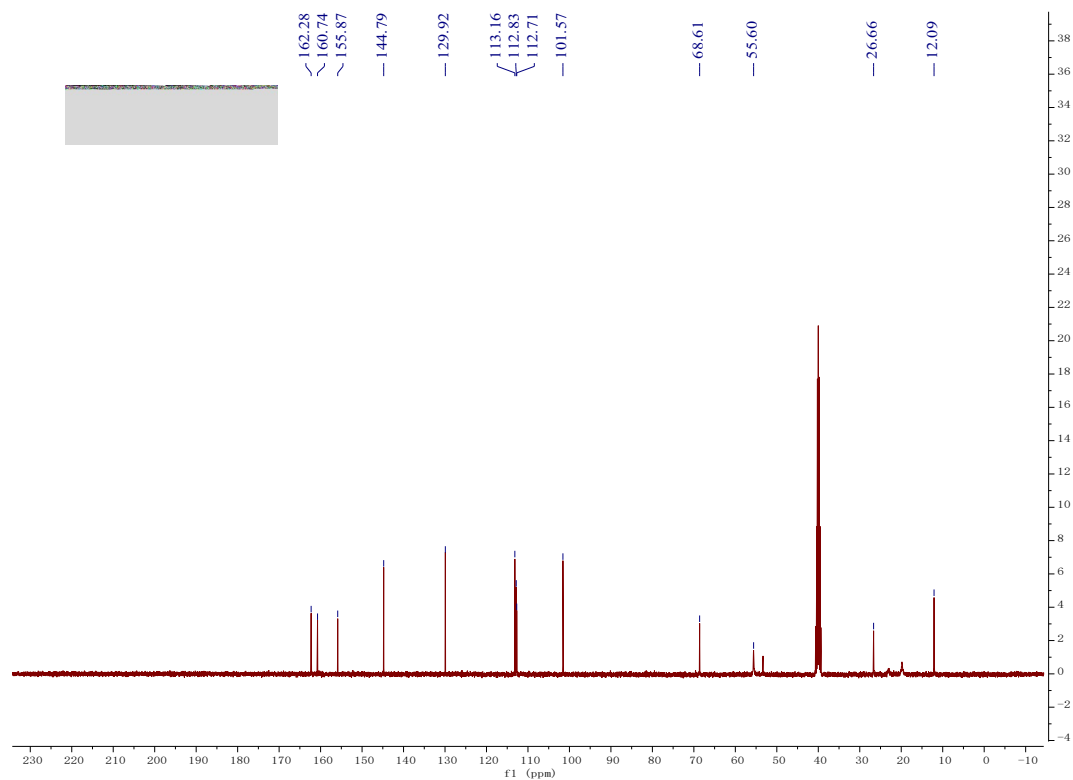


Fig.S9 ^{13}C NMR of **6a** (100 MHz, DMSO)

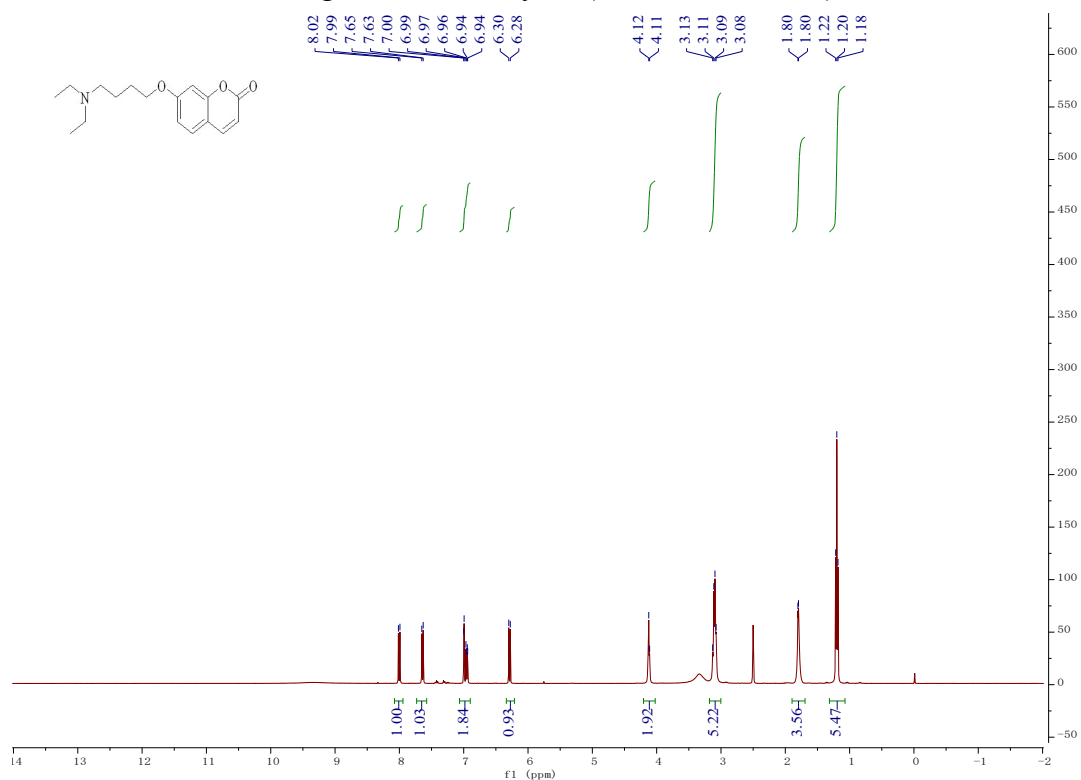


Fig.S10 ^1H NMR of **6b** (400 MHz, DMSO)

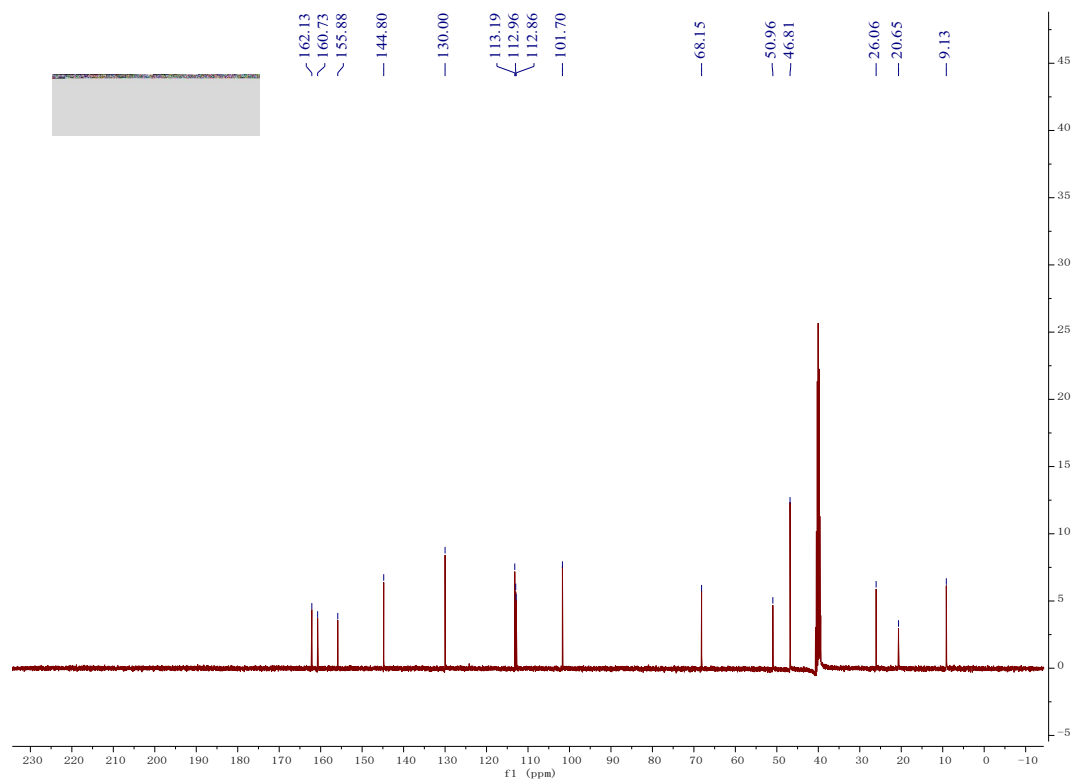


Fig.S11 ^{13}C NMR of **6b** (100 MHz, DMSO)

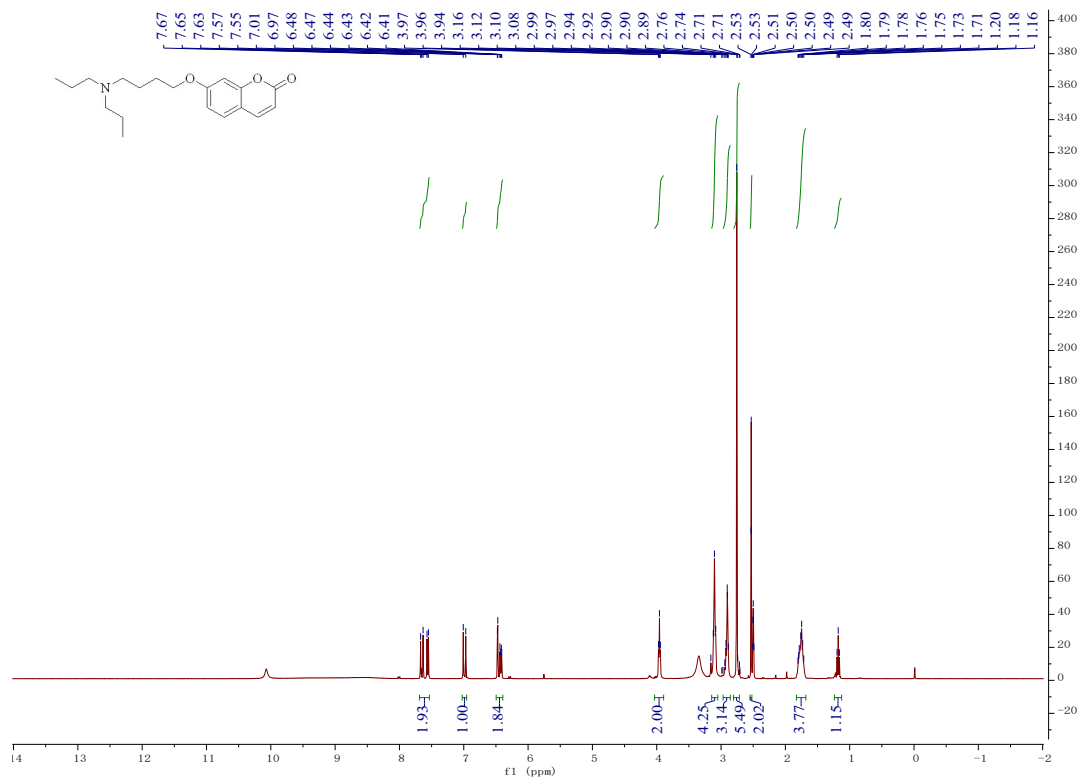


Fig.S12 ^1H NMR of **6c** (400 MHz, DMSO)

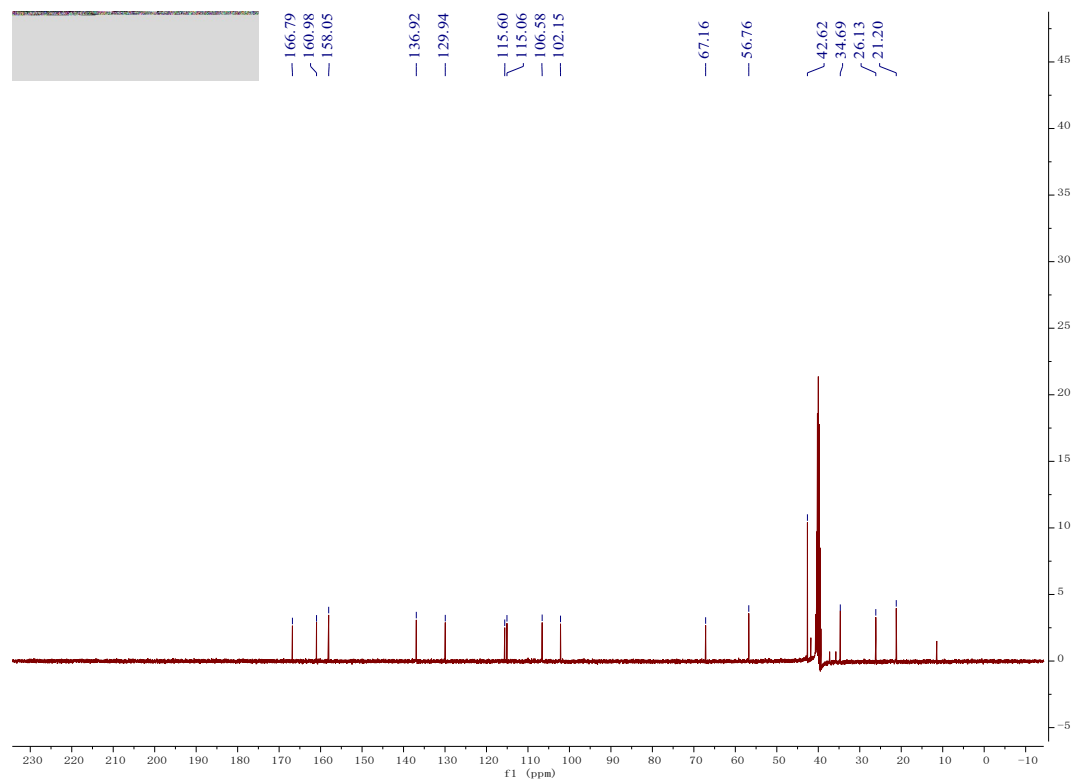


Fig.S13 ^{13}C NMR of **6c** (400 MHz, DMSO)

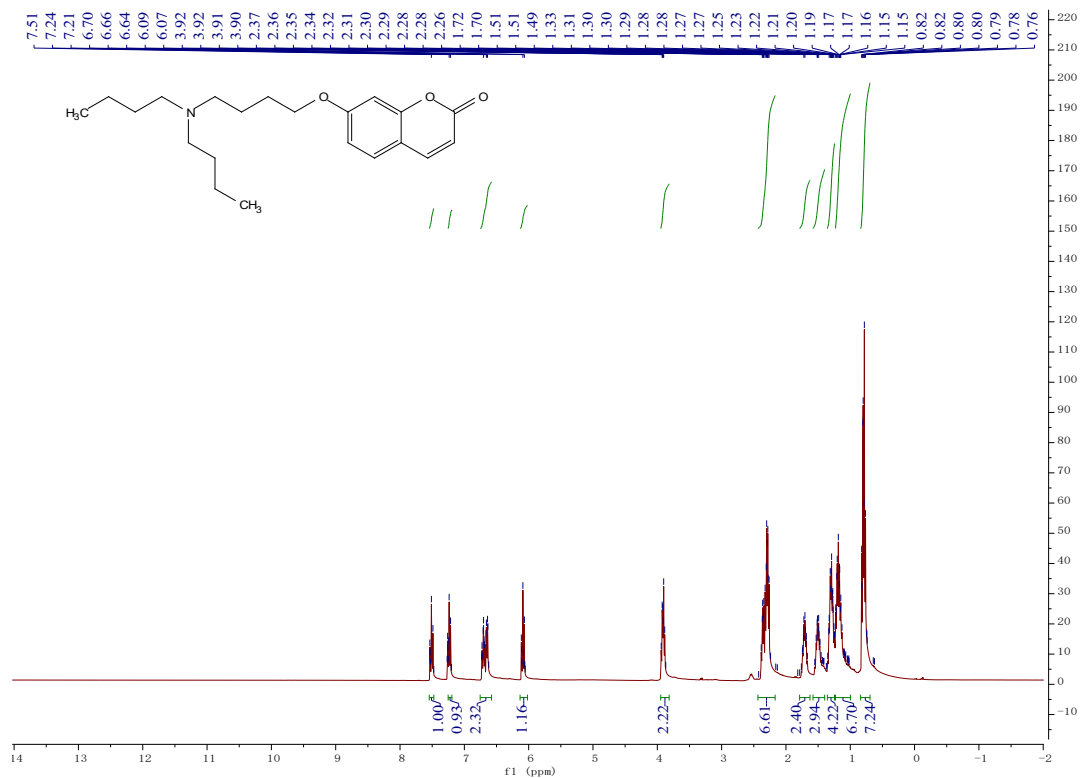


Fig.S14 ^1H NMR of **6d** (400 MHz, CDCl_3)

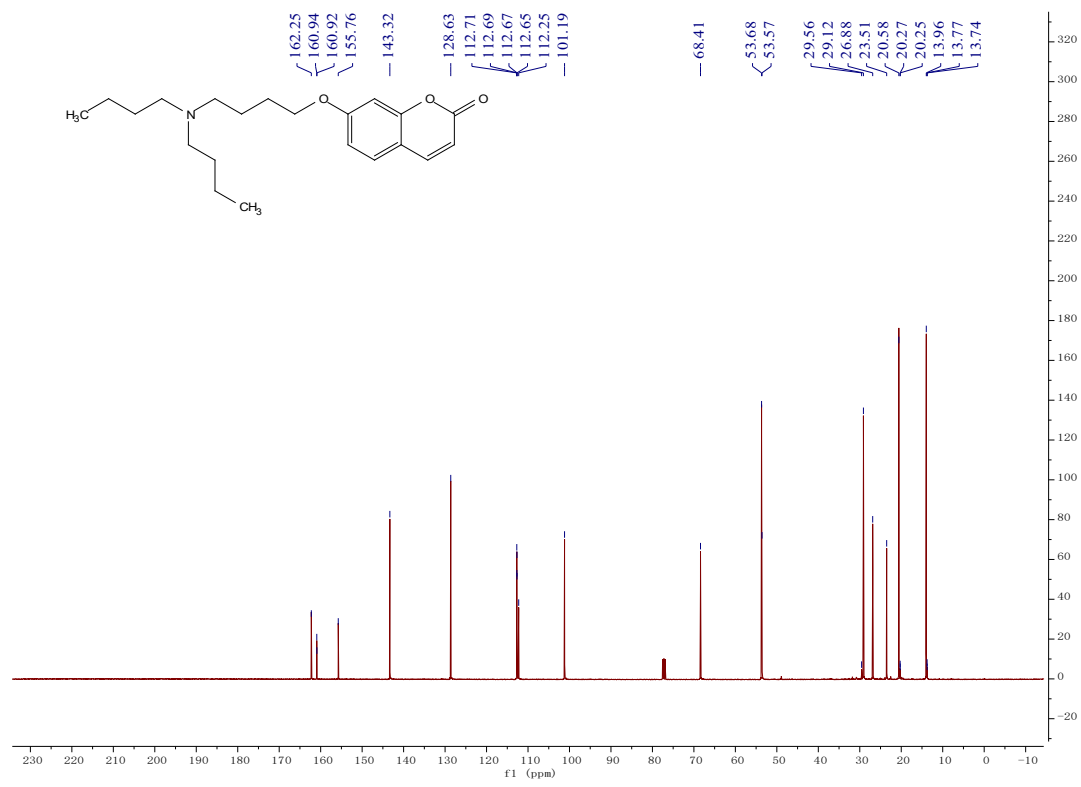


Fig.S15 ^{13}C NMR of **6d** (400 MHz, CDCl_3)

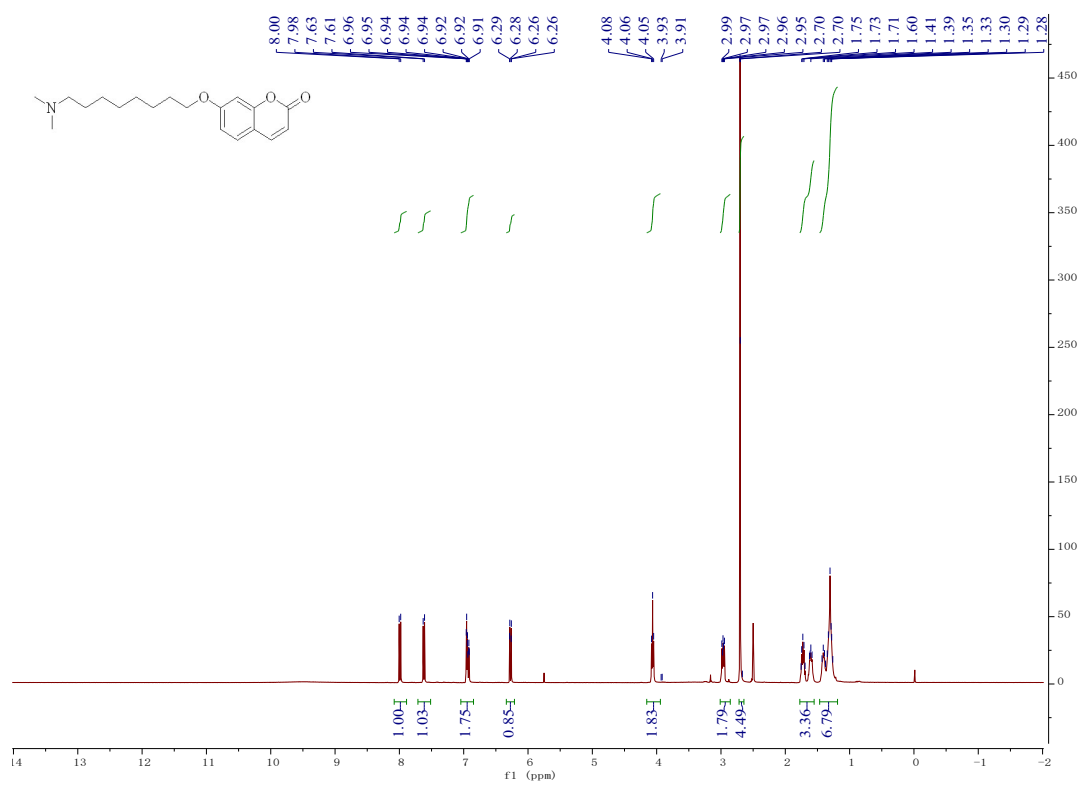


Fig.S16 ^1H NMR of **7a** (400 MHz, DMSO)

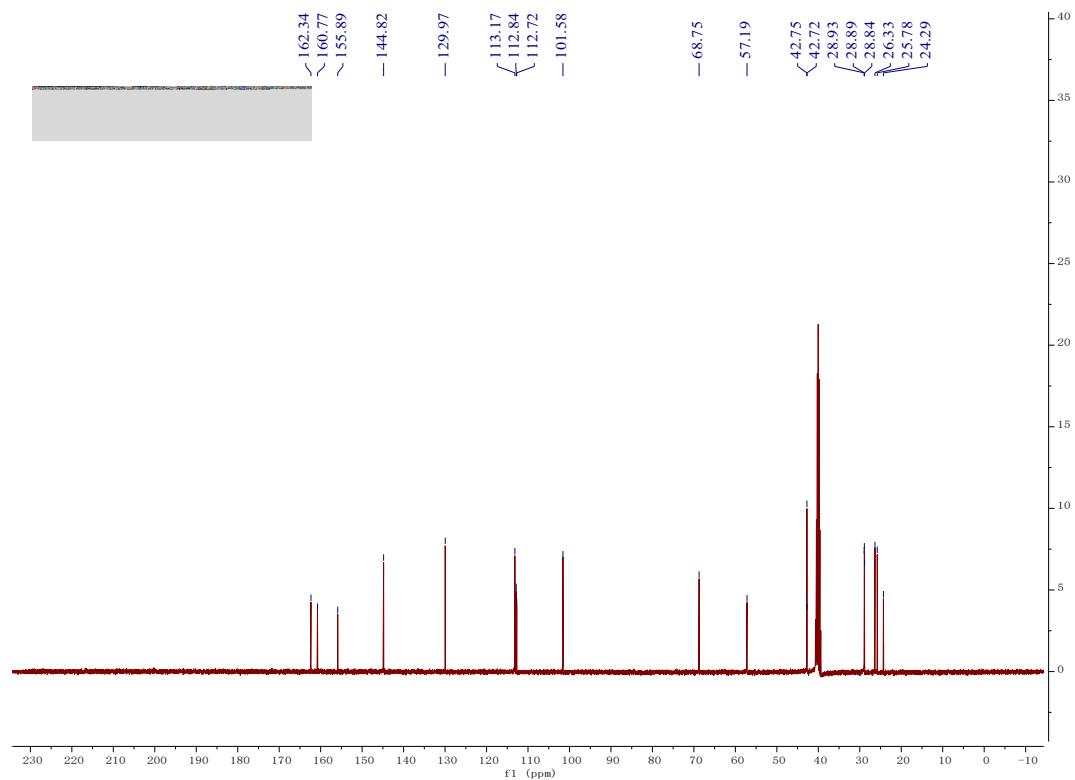


Fig.S17 ^{13}C NMR of **7a** (400 MHz, DMSO)

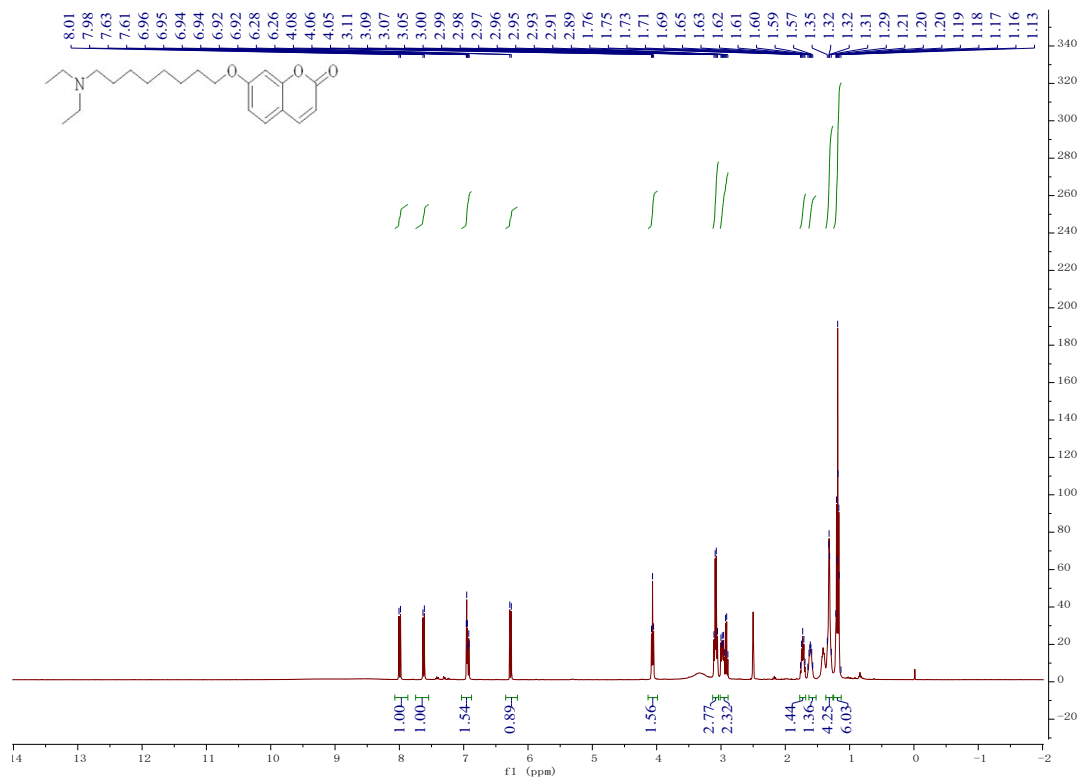


Fig.S18 ^1H NMR of **7b** (400 MHz, DMSO)

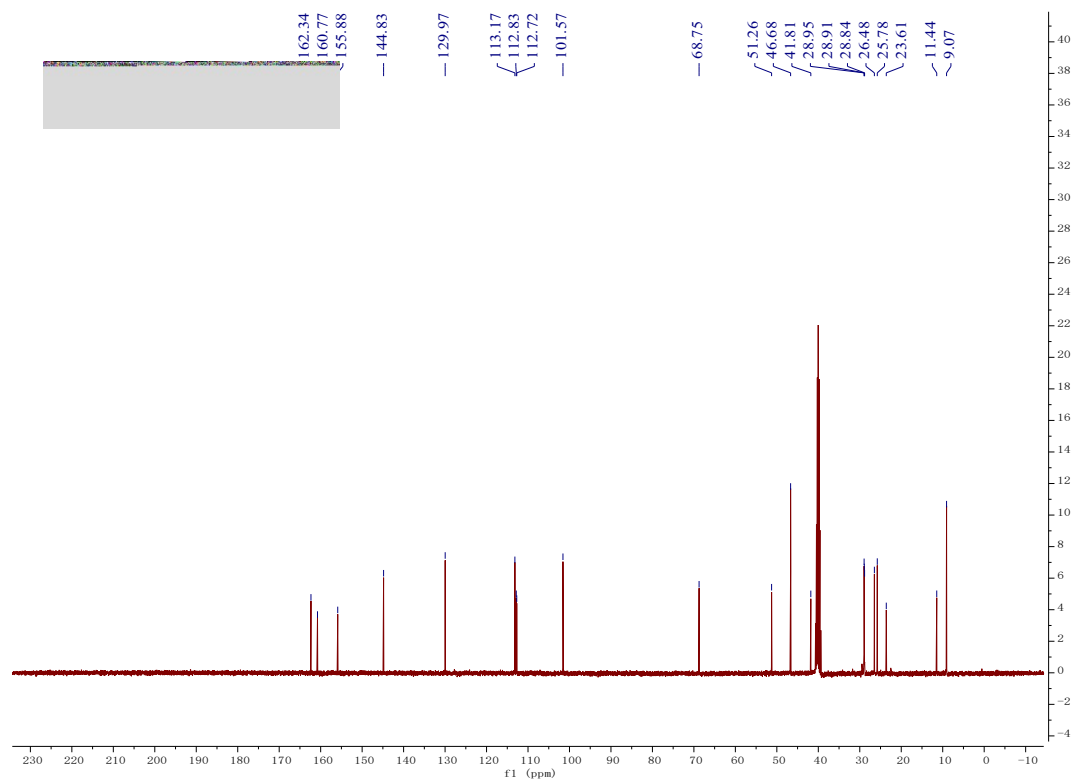


Fig.S19 ^{13}C NMR of **7b** (400 MHz, DMSO)

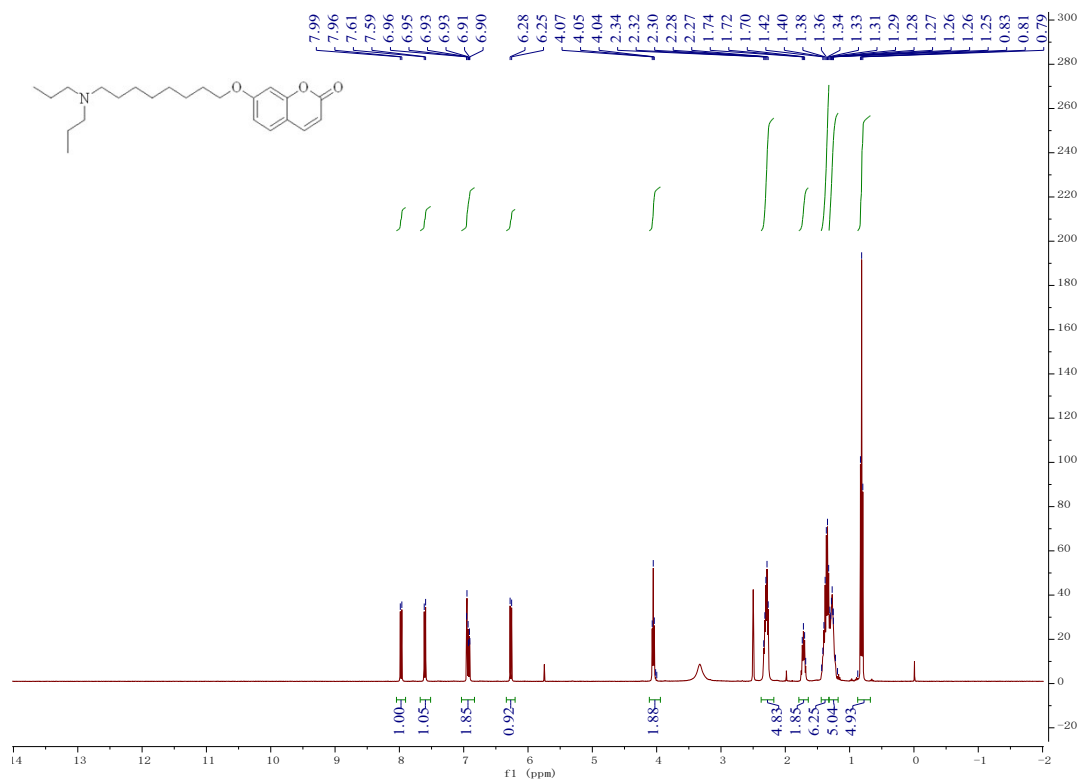


Fig.S20 ^1H NMR of **7c** (400 MHz, DMSO)

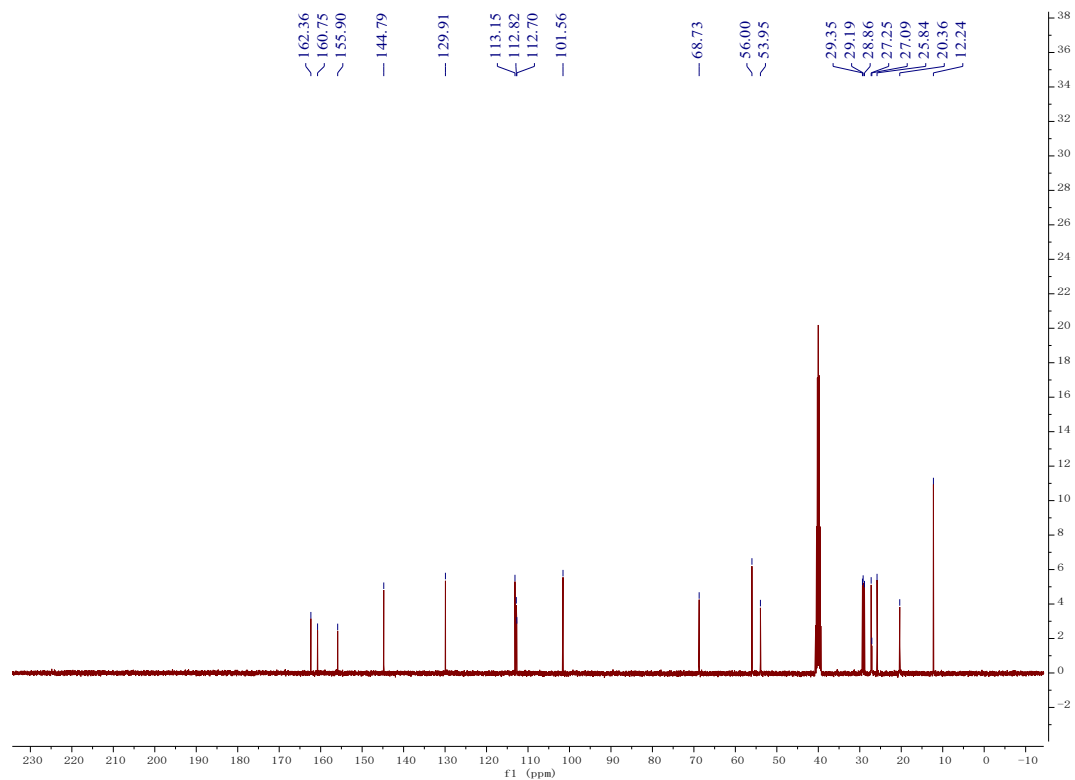


Fig.S21 ^{13}C NMR of **7c** (400 MHz, DMSO)

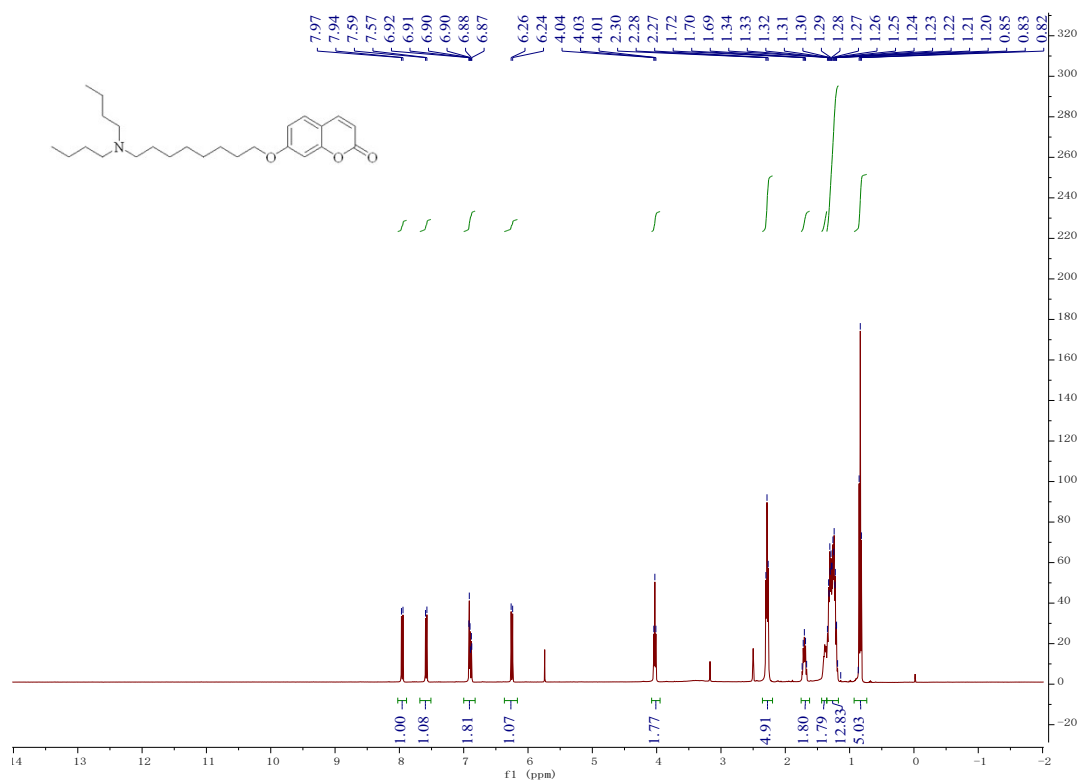


Fig.S22 ^1H NMR of **7d** (400 MHz, DMSO)

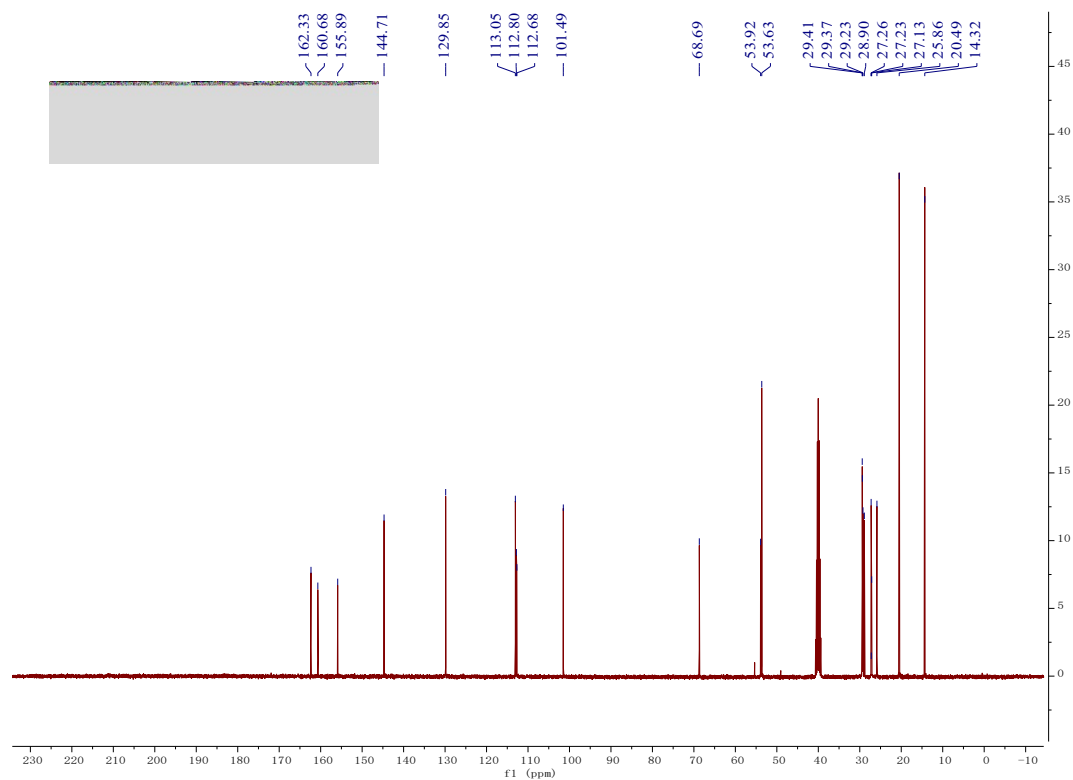


Fig.S23 ^{13}C NMR of **7d** (400 MHz, DMSO)

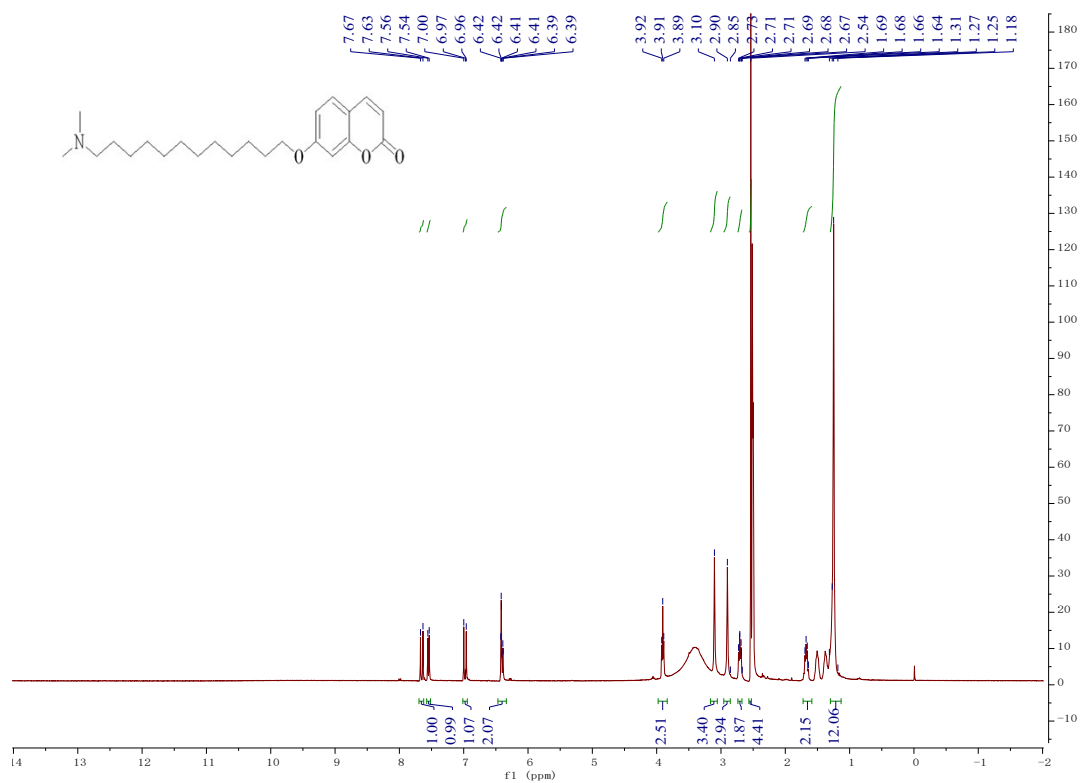


Fig.S24 ^1H NMR of **8a** (400 MHz, DMSO)

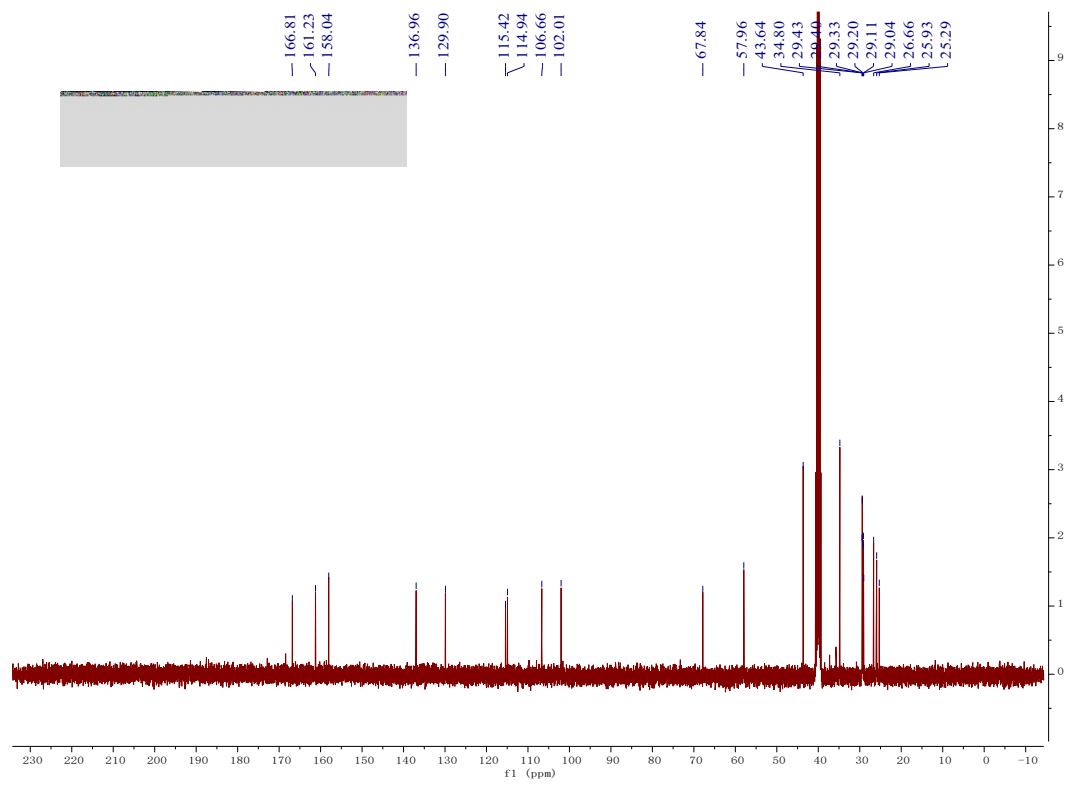


Fig.S25 ^{13}C NMR of **8a** (400 MHz, DMSO)

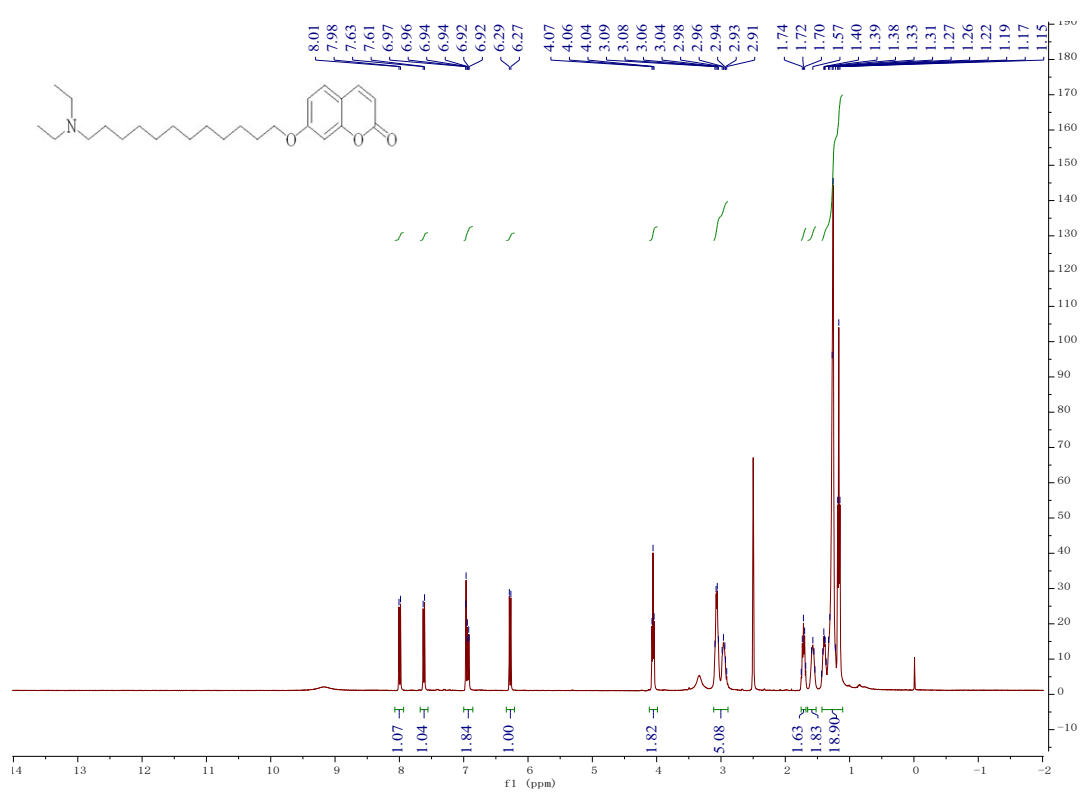


Fig.S26 ^1H NMR of **8b** (400 MHz, DMSO)

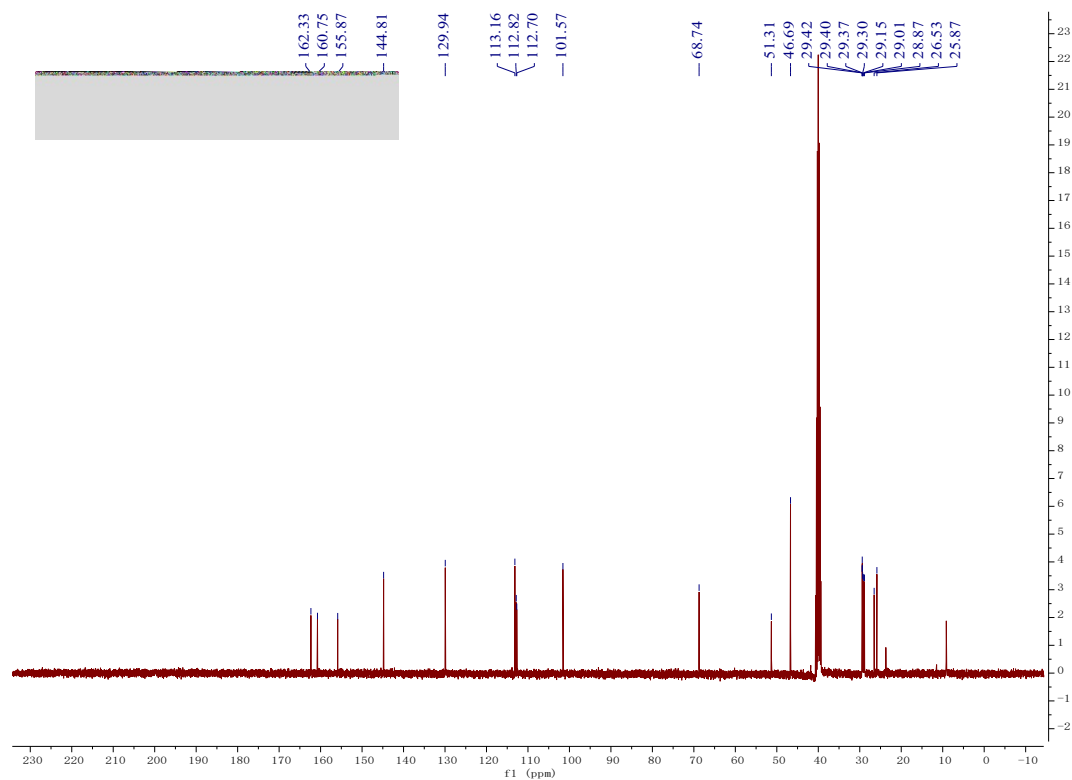


Fig.S27 ^{13}C NMR of **8b** (400 MHz, DMSO)

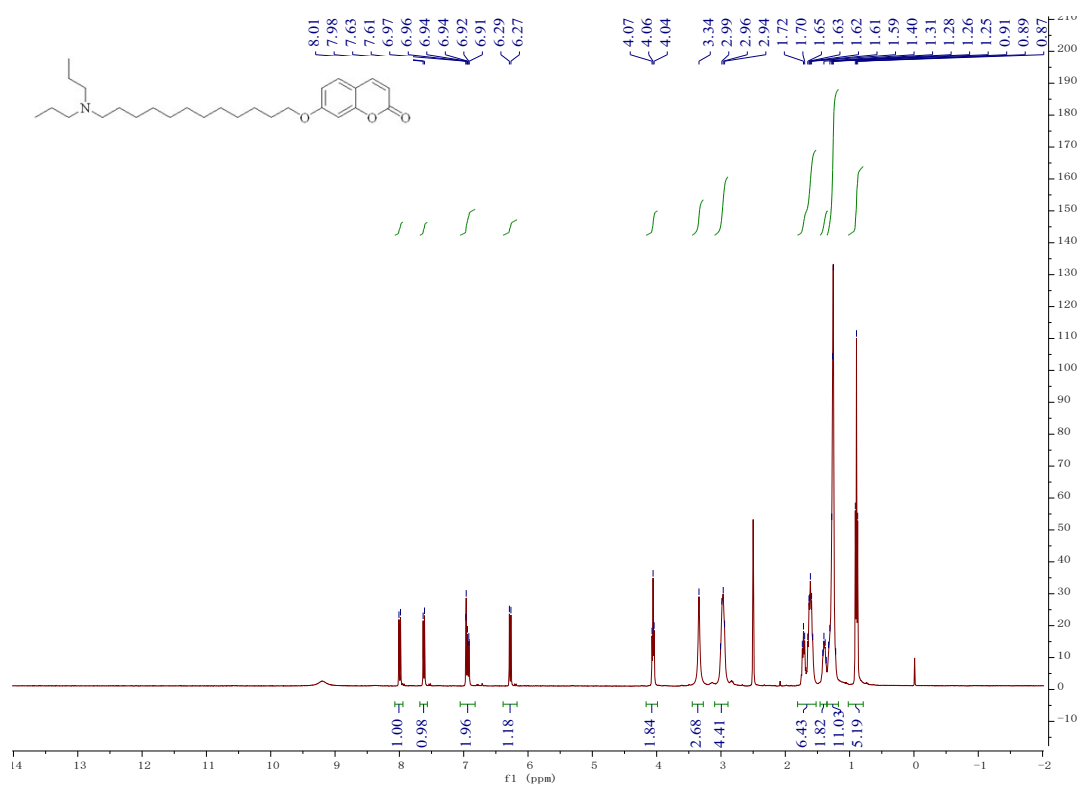


Fig.S28 ^1H NMR of **8c** (400 MHz, DMSO)

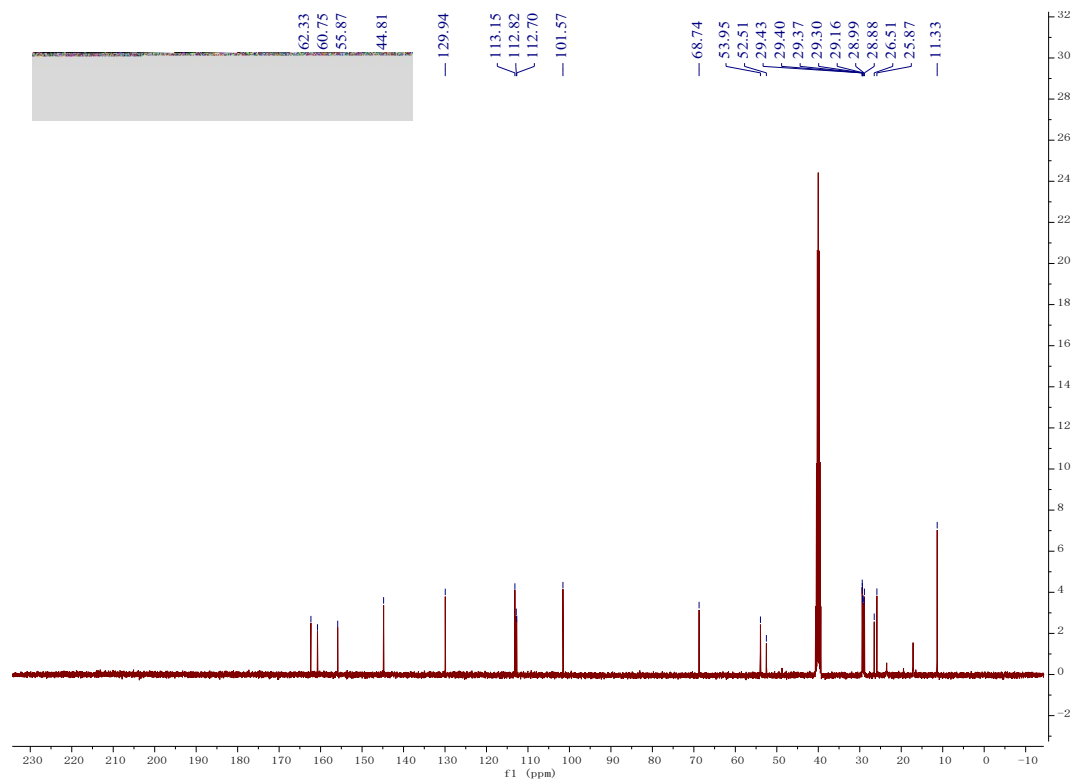


Fig.S29 ^{13}C NMR of **8c** (400 MHz, DMSO)

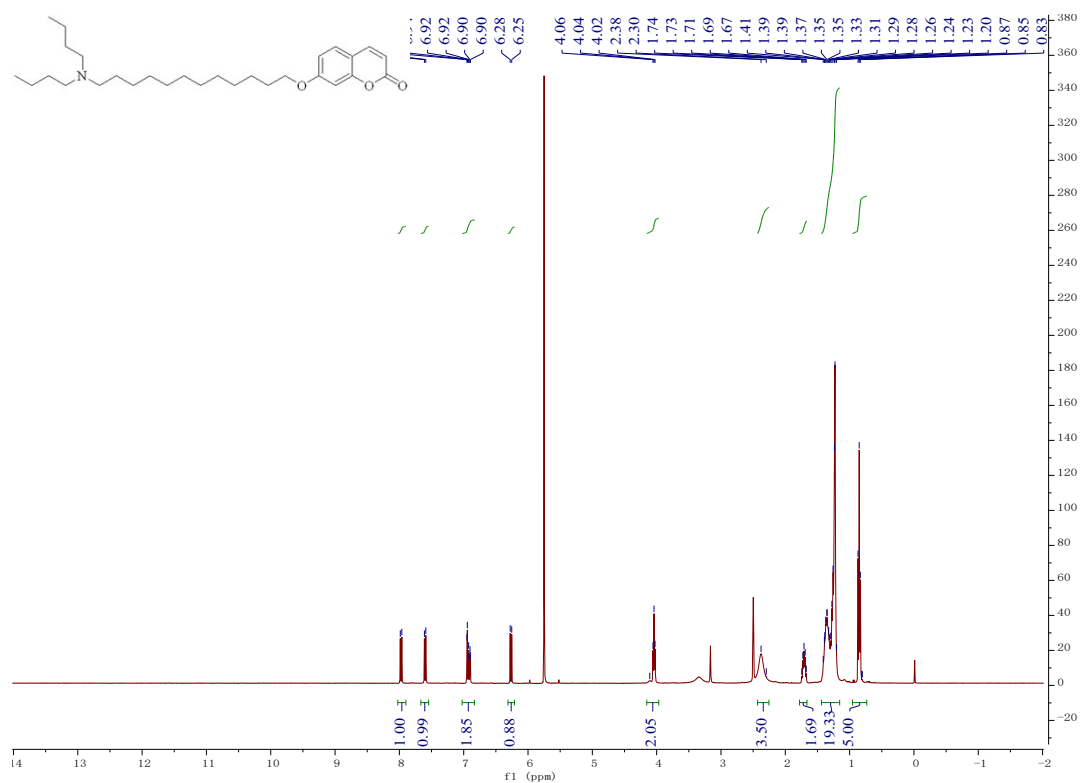


Fig.S30 ^1H NMR of **8d** (400 MHz, DMSO)

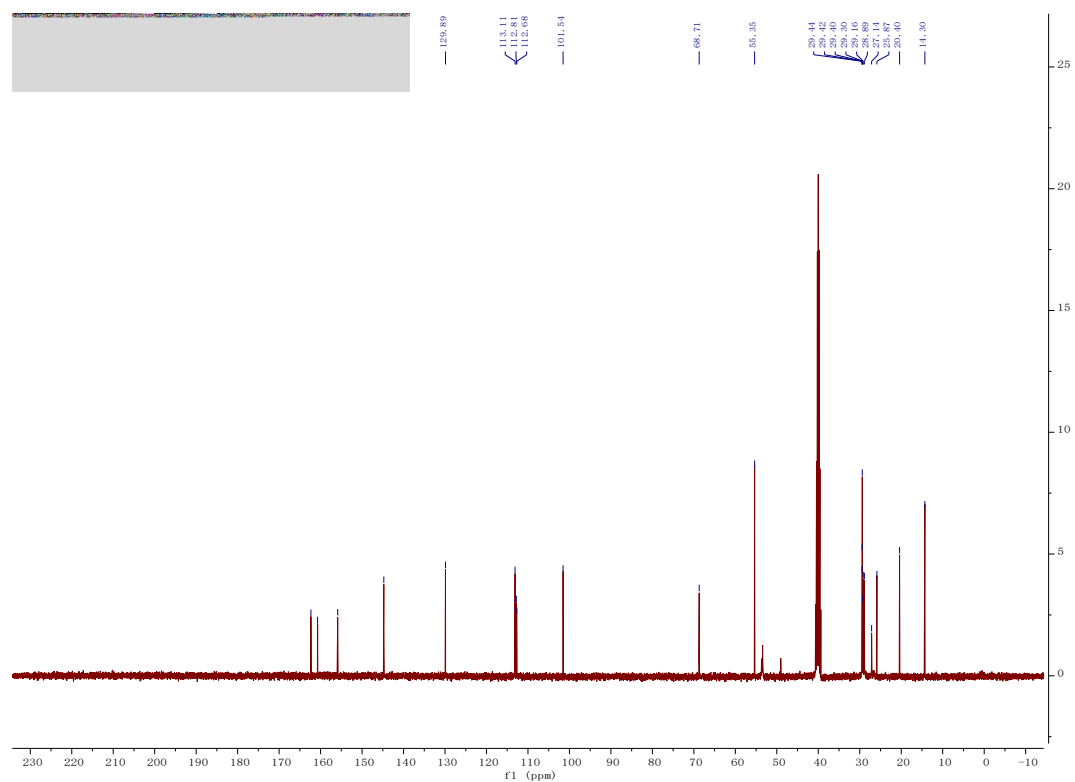


Fig.S31 ¹³C NMR of **8d** (400 MHz, DMSO)

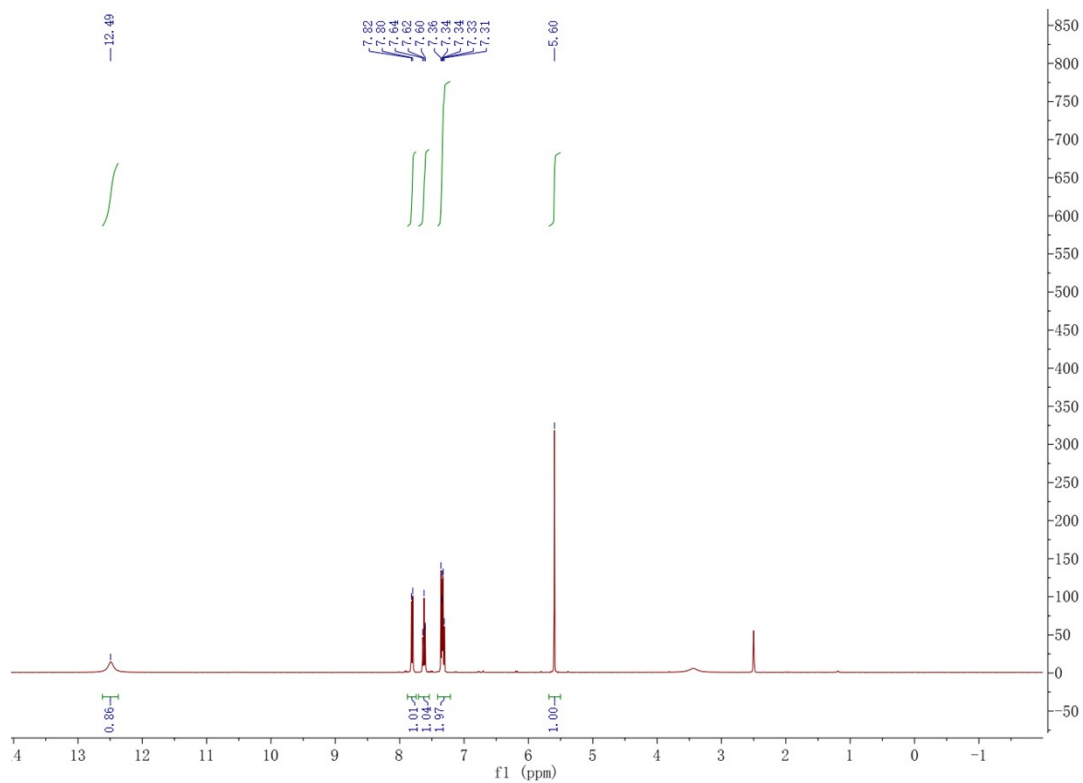


Fig.S32 ¹H NMR of **10** (400 MHz, DMSO)

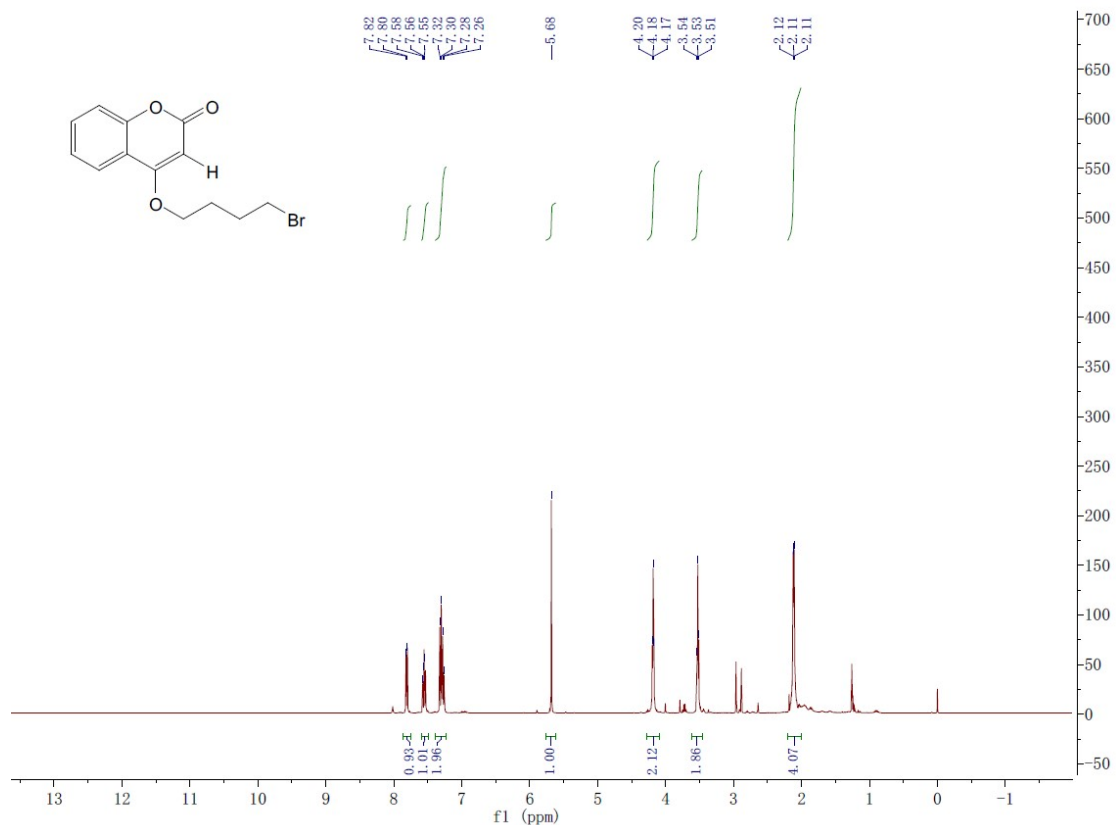


Fig.S33 $^1\text{H NMR}$ of **11** (400 MHz, CDCl_3)

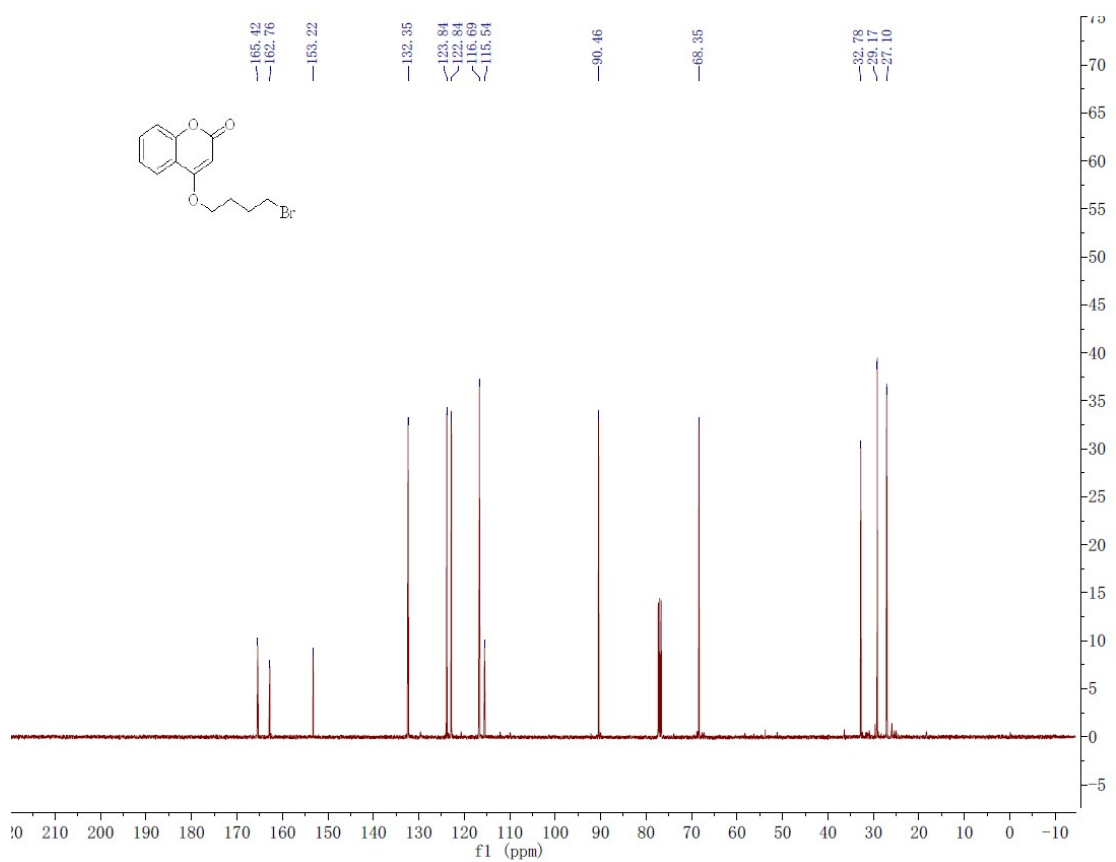


Fig.S34 $^{13}\text{C NMR}$ of **11** (100 MHz, CDCl_3)

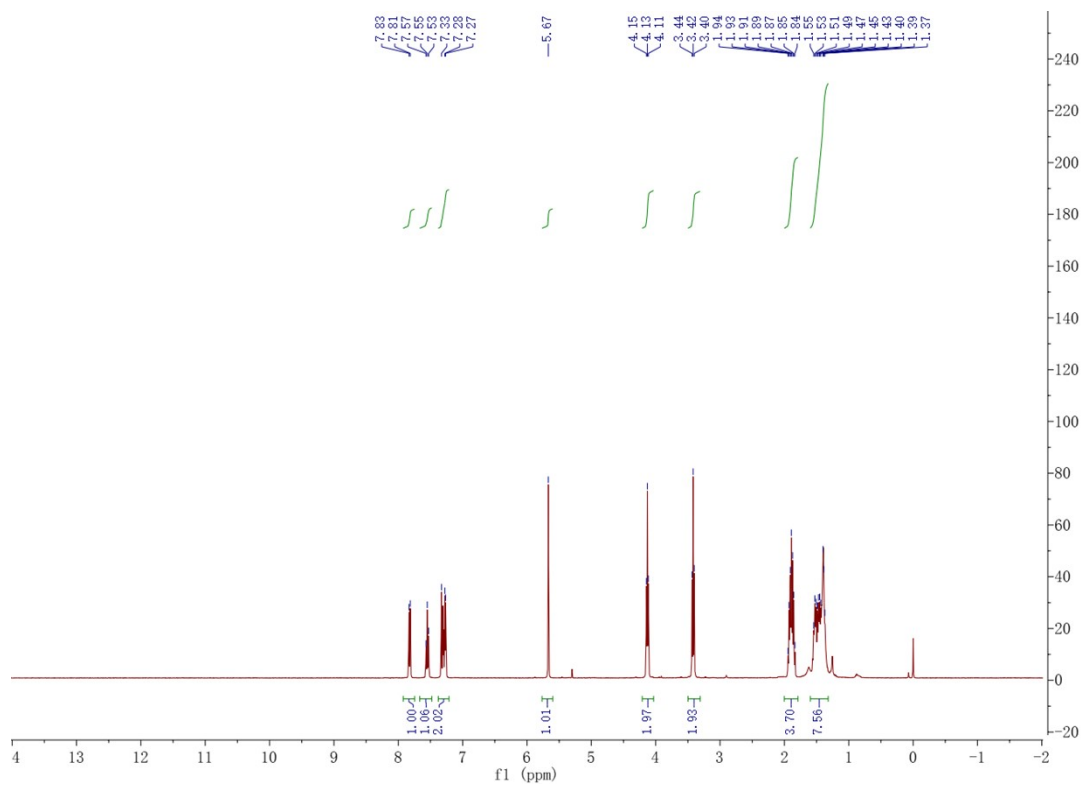


Fig.S35 ^1H NMR of **12** (400 MHz, CDCl_3)

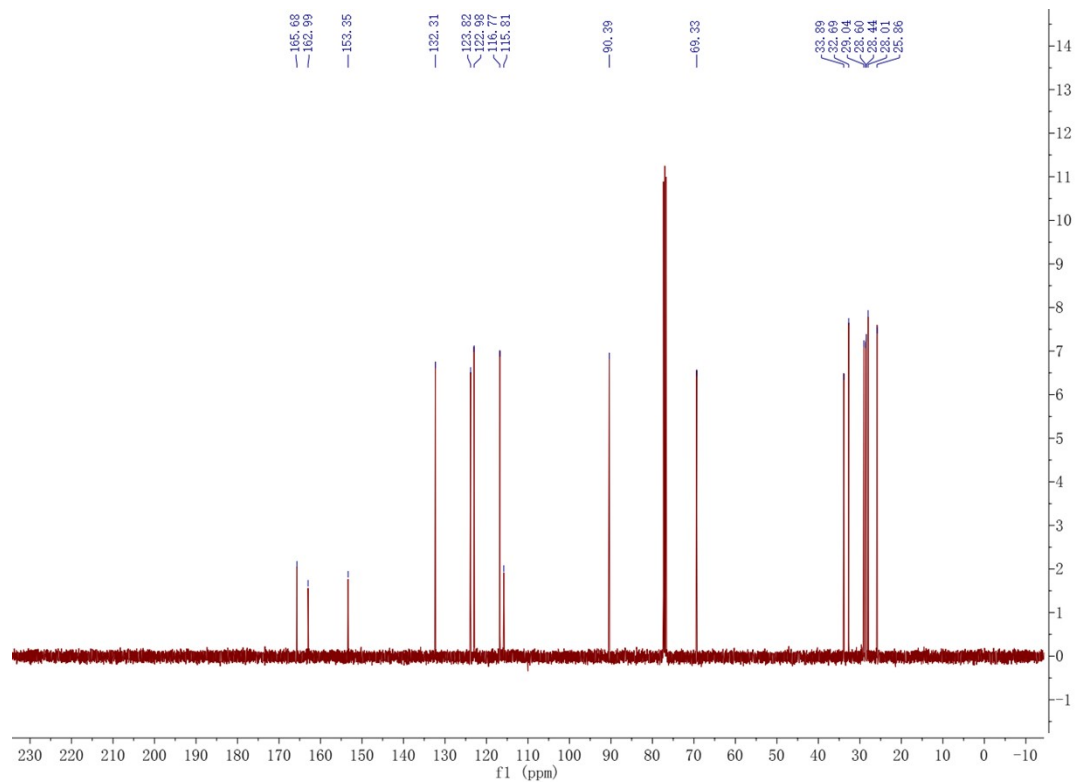


Fig.S36 ^{13}C NMR of **12** (100 MHz, CDCl_3)

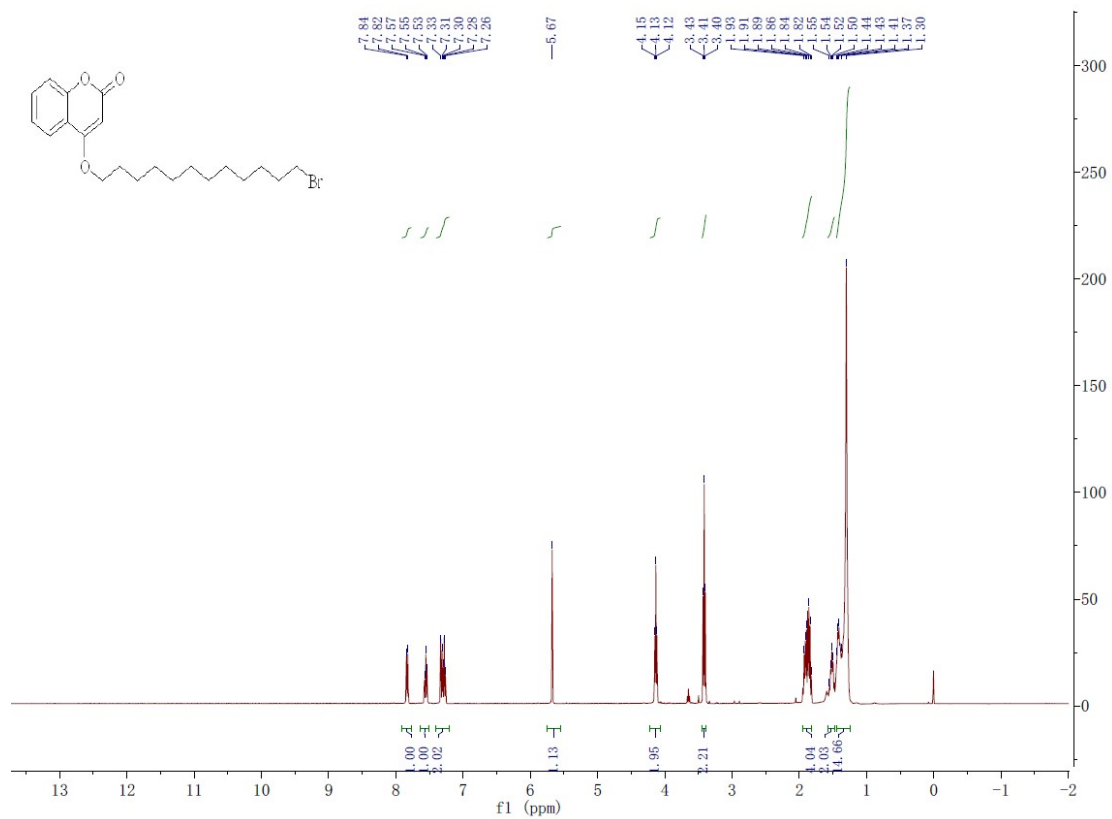


Fig.S37 ¹H NMR of 13 (400 MHz, CDCl₃)

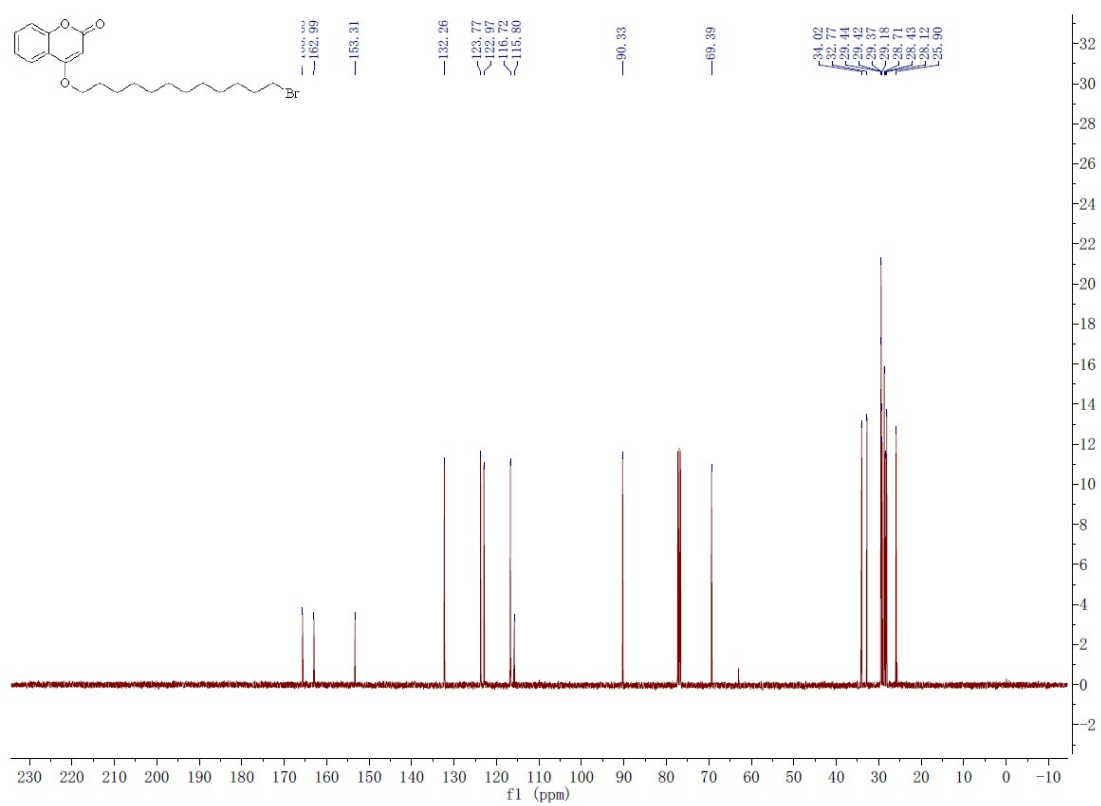


Fig.S38 ¹³C NMR of 13 (100 MHz, CDCl₃)

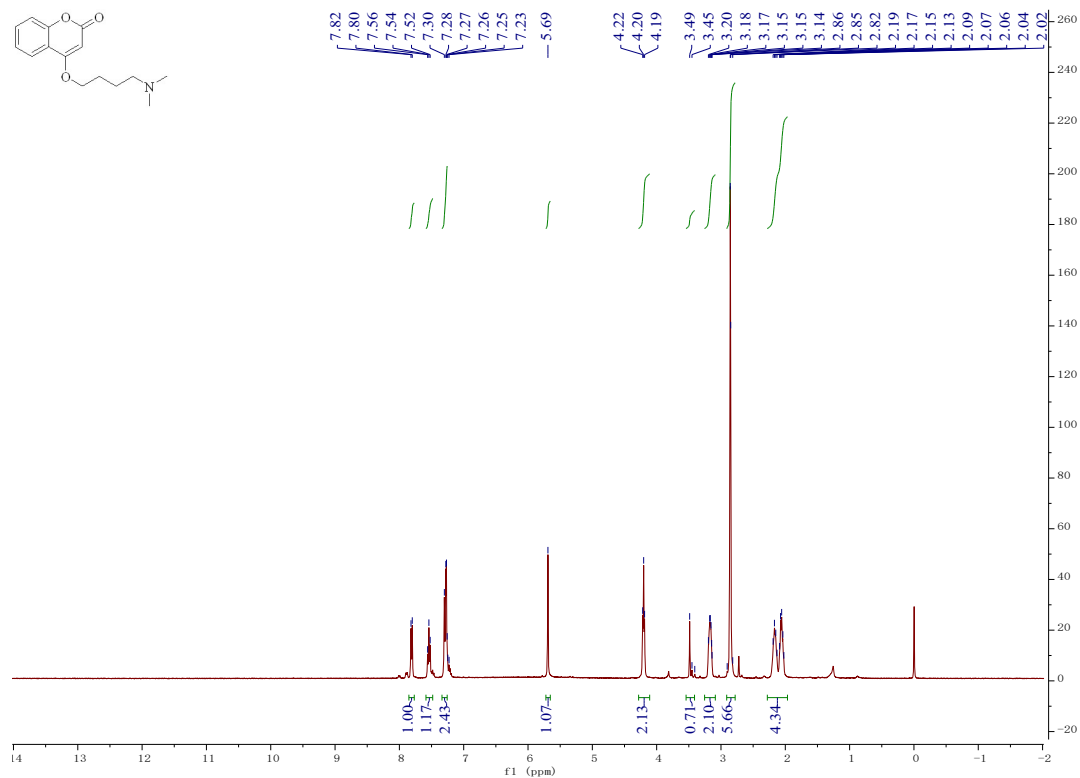


Fig.S39 $^1\text{H NMR}$ of 14a (400 MHz, CDCl_3)

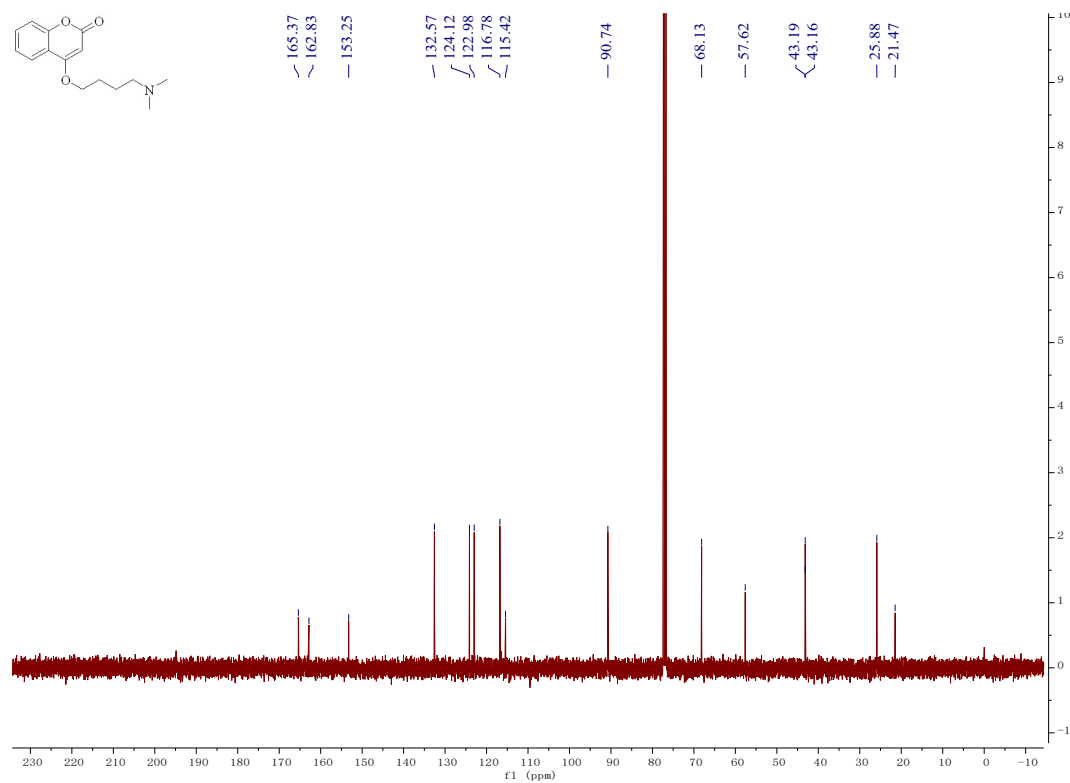


Fig.S40 $^{13}\text{C NMR}$ of 14a (100 MHz, CDCl_3)

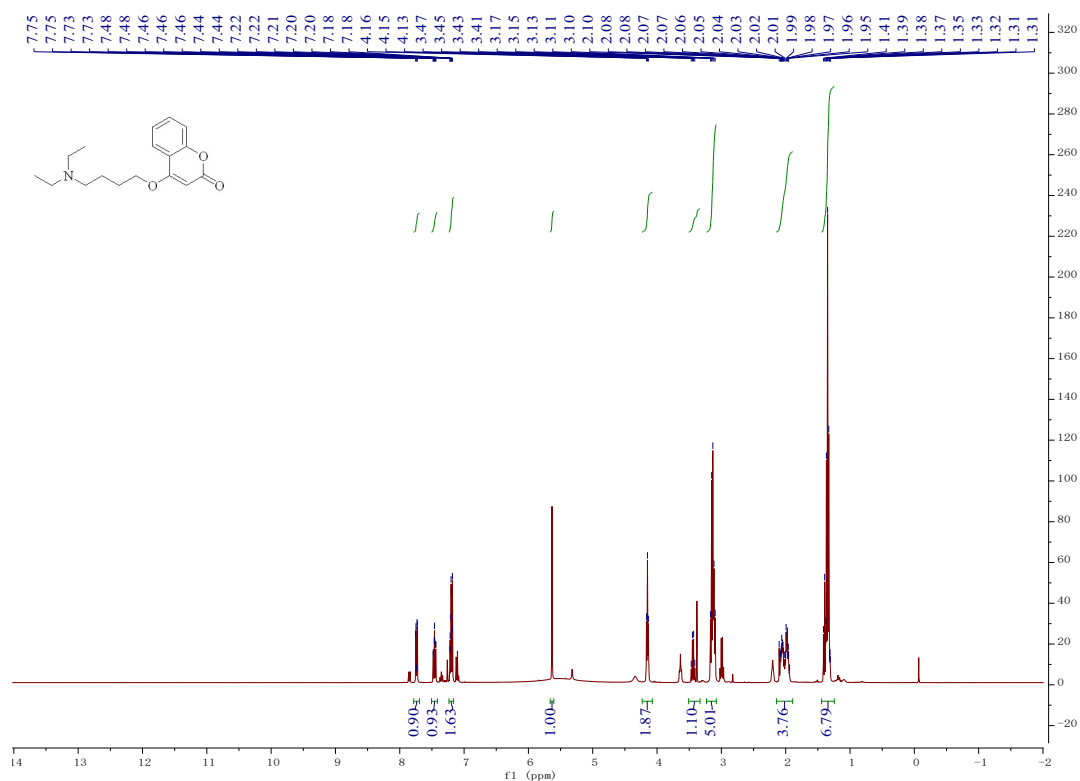


Fig.S41 ^1H NMR of **14b** (400 MHz, CDCl_3)

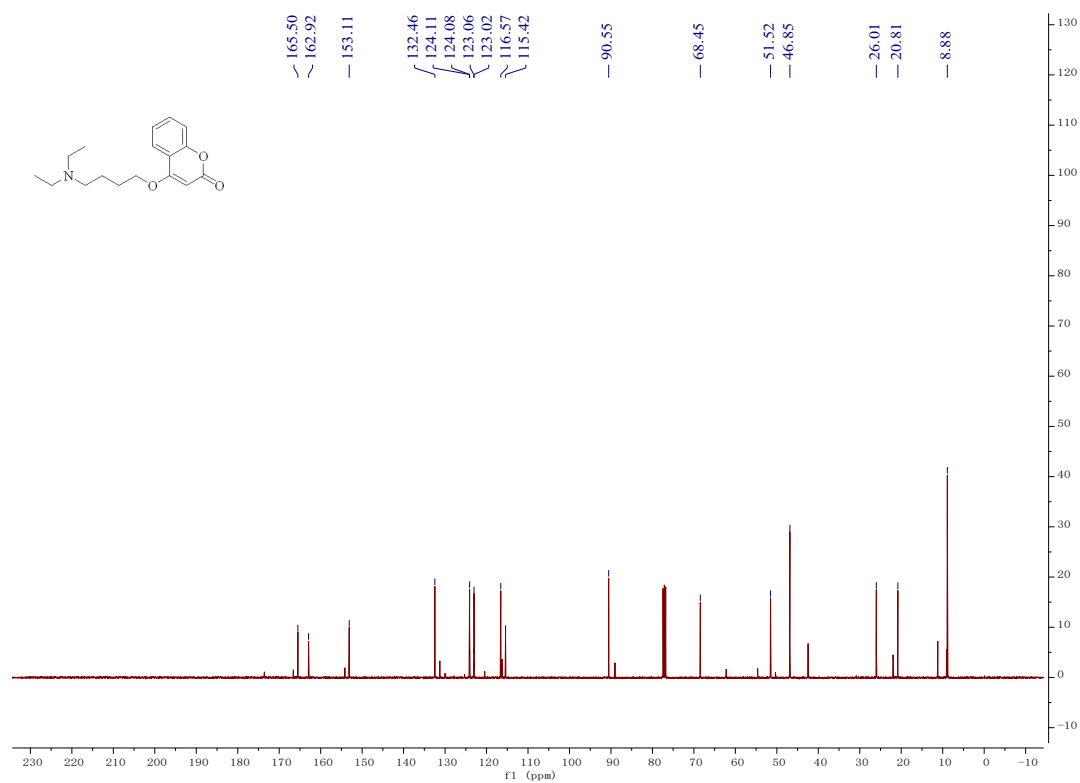


Fig.S42 ^{13}C NMR of **14b** (100 MHz, CDCl_3)

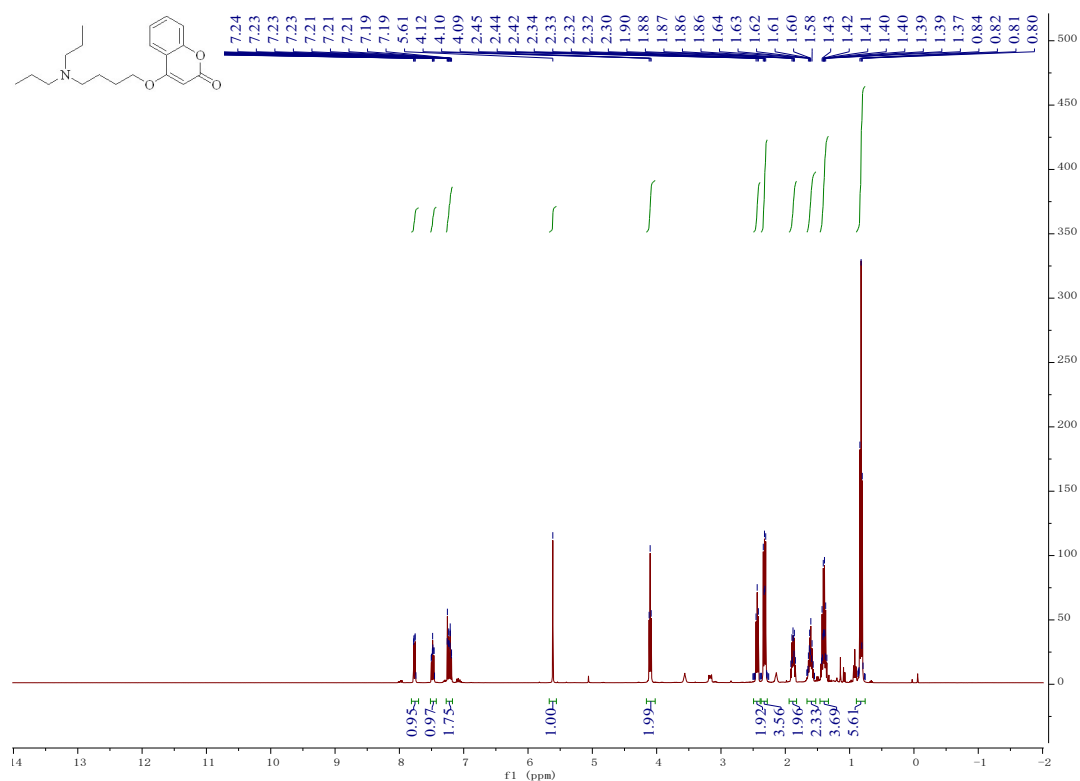


Fig.S43 ^1H NMR of 14c (400 MHz, CDCl_3)

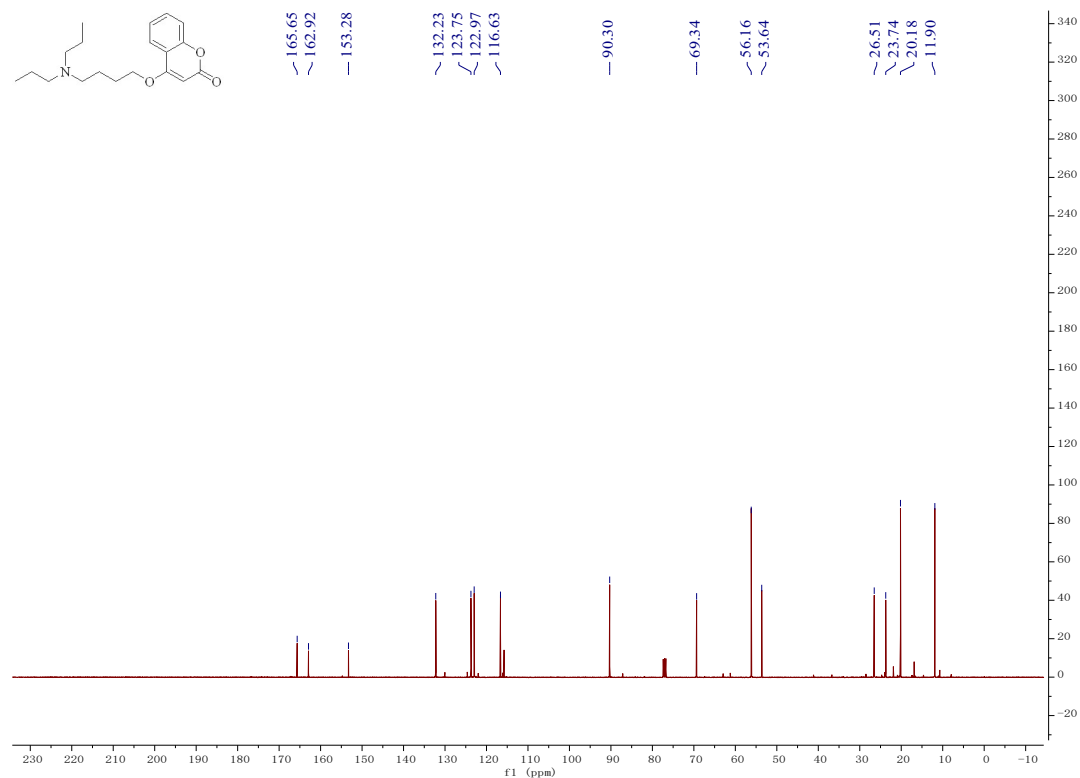


Fig.S44 ^{13}C NMR of 14c (100 MHz, CDCl_3)

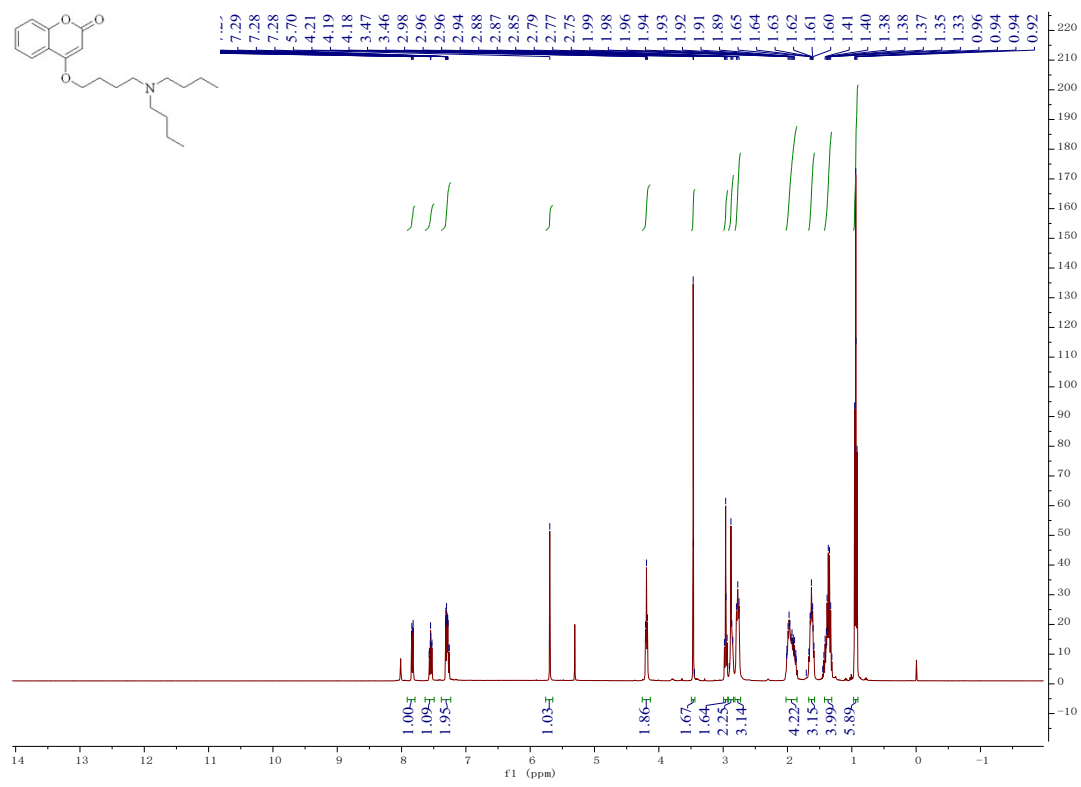


Fig.S45 ¹H NMR of 14d (400 MHz, CDCl₃)

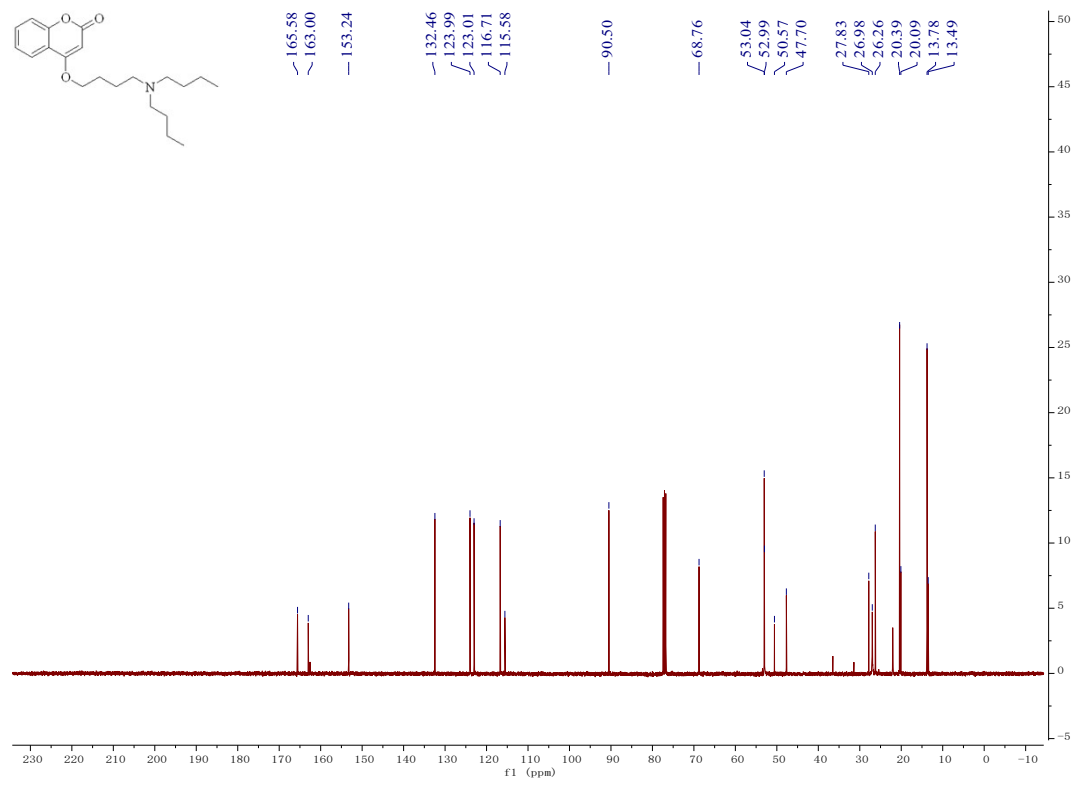


Fig.S46 ¹³C NMR of 14d (100 MHz, CDCl₃)

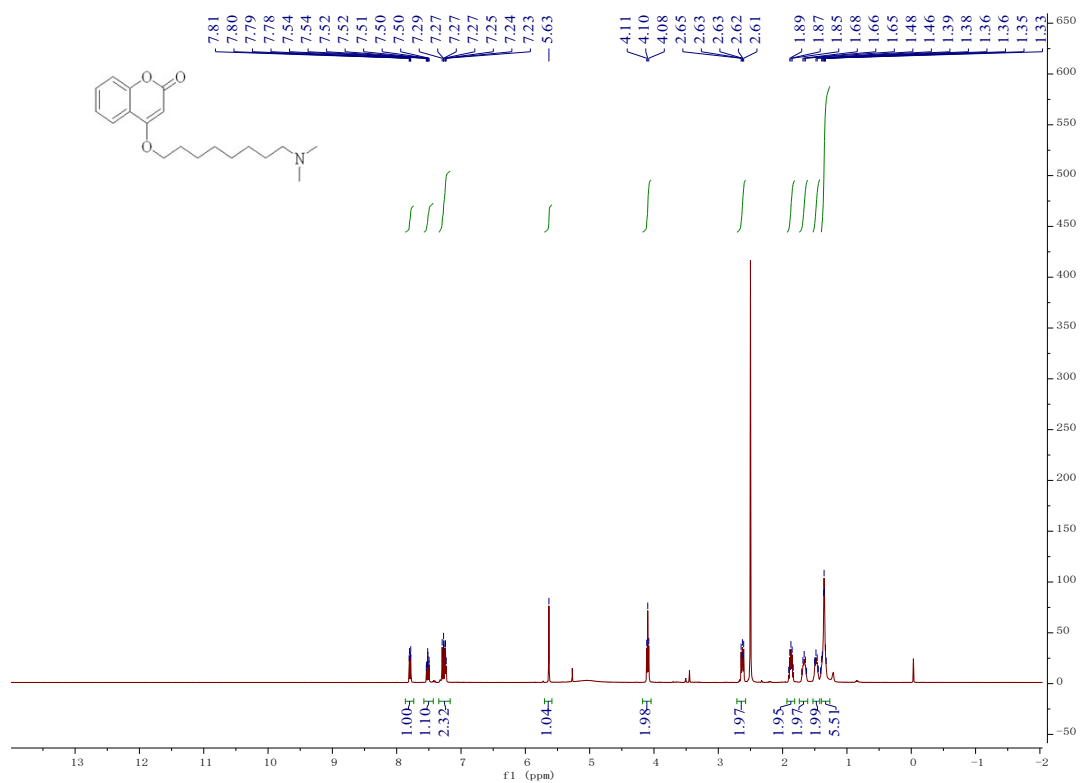


Fig.S47 ^1H NMR of 15a (400 MHz, CDCl_3)

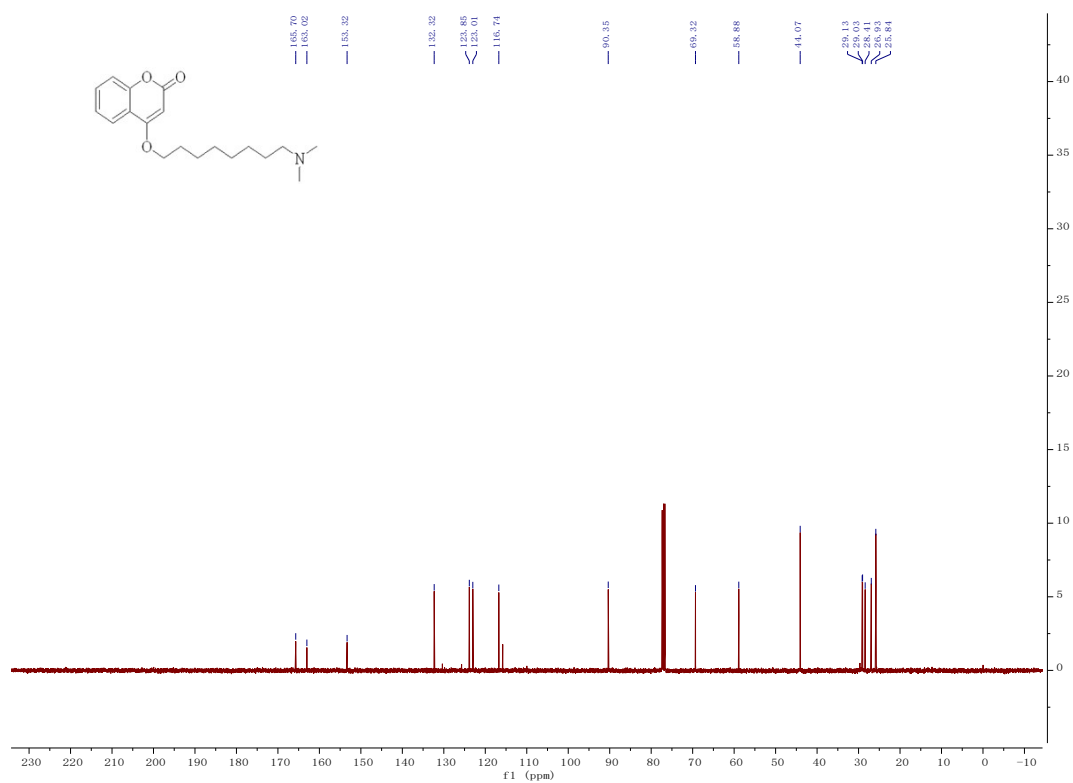


Fig.S48 ^{13}C NMR of 15a (100 MHz, CDCl_3)

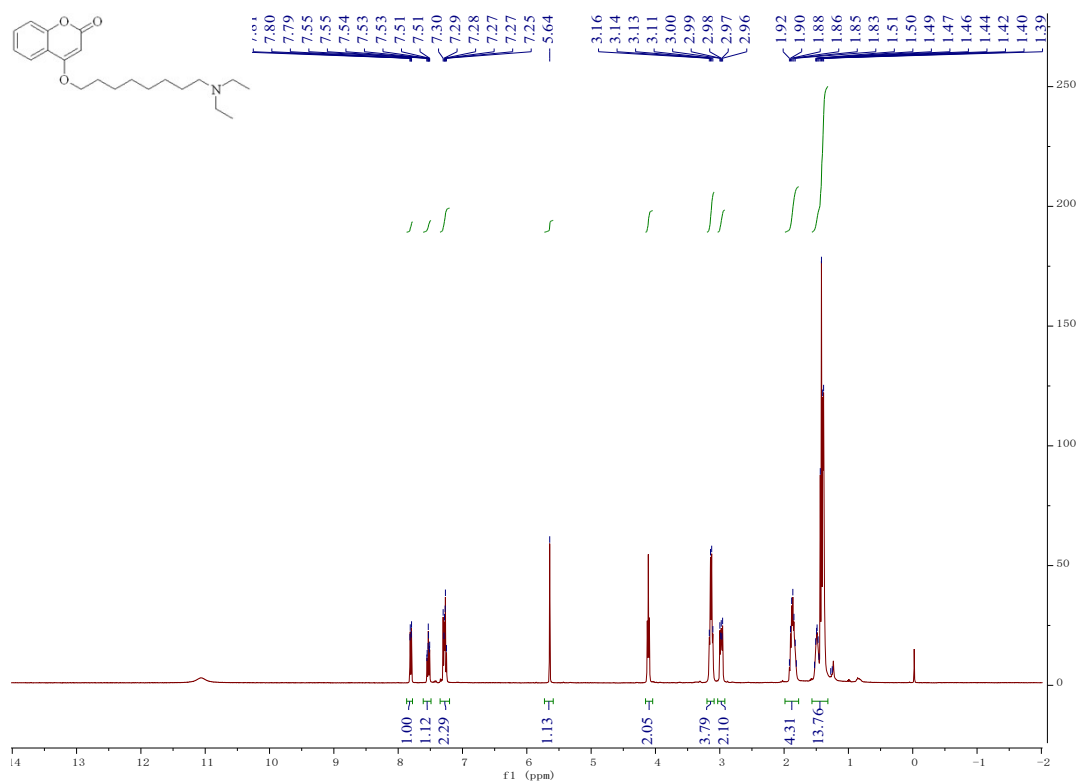


Fig.S49 ^1H NMR of **15b** (400 MHz, CDCl_3)

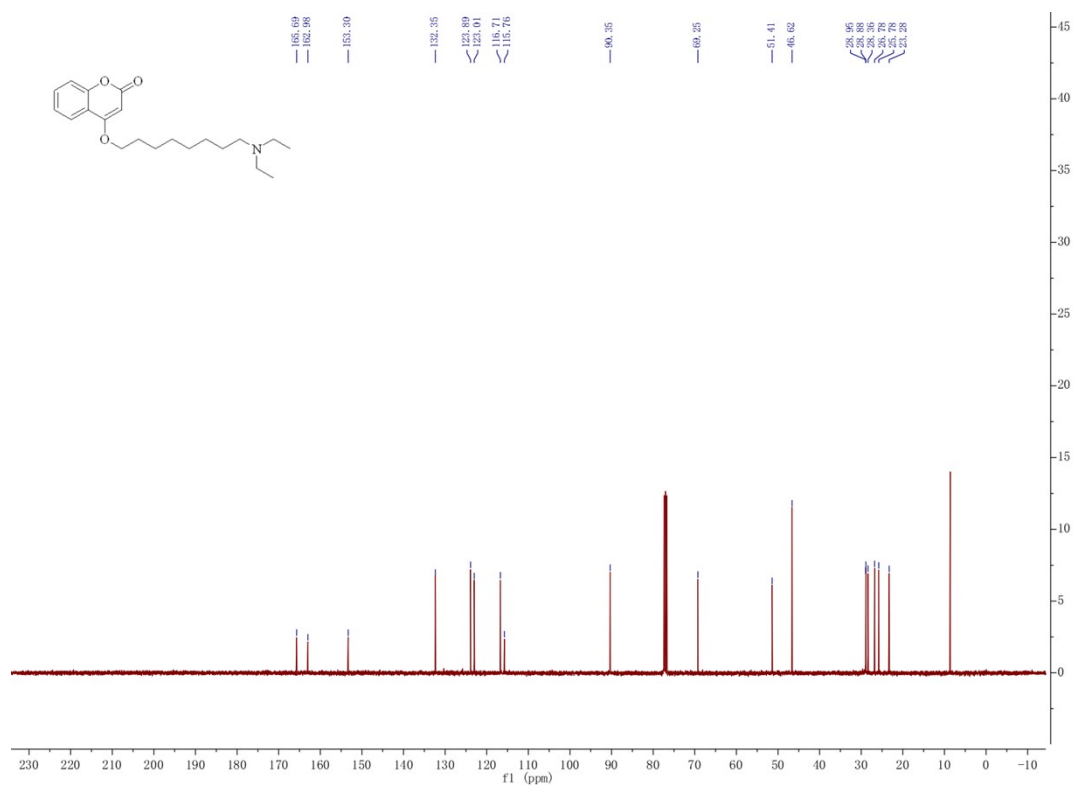


Fig.S50 ^{13}C NMR of **15b** (100 MHz, CDCl_3)

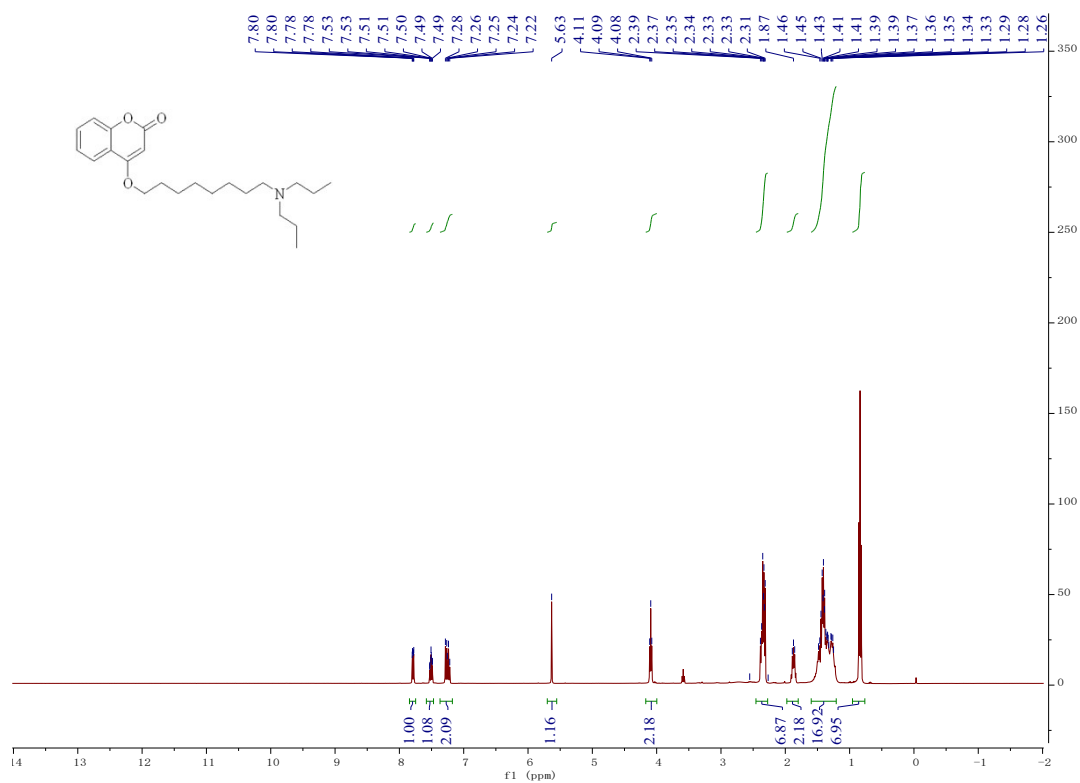


Fig.S51 ^1H NMR of 15c (400 MHz, CDCl_3)

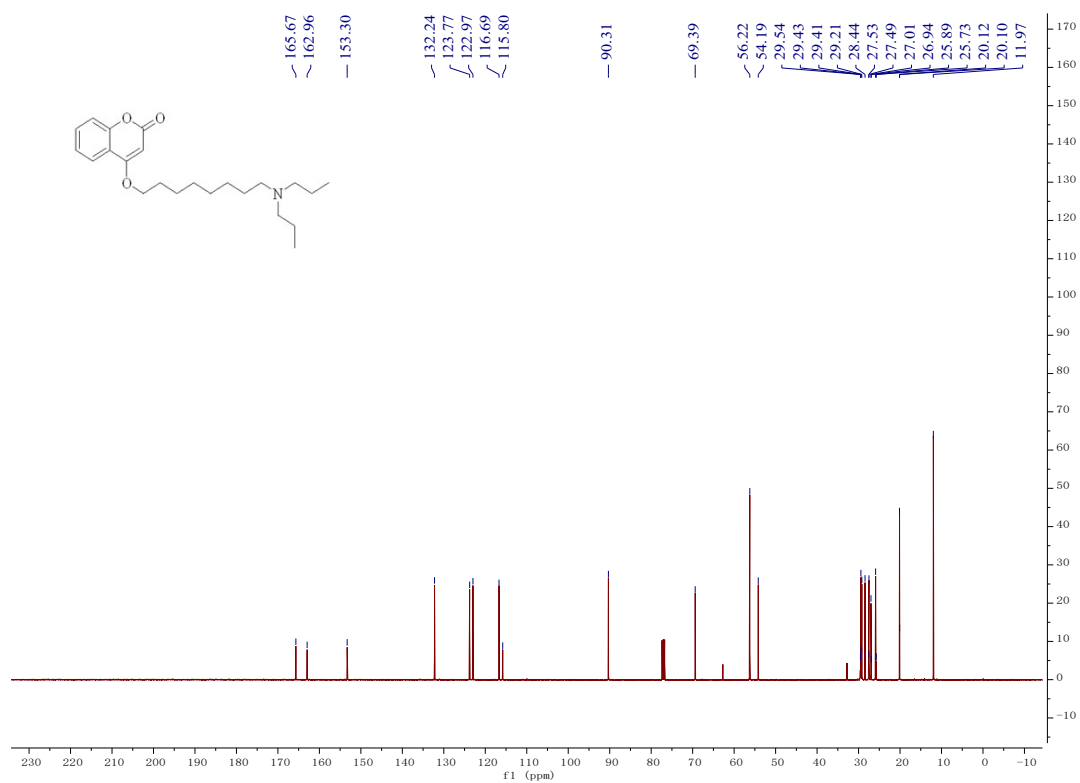


Fig.S52 ^{13}C NMR of 15c (400 MHz, CDCl_3)

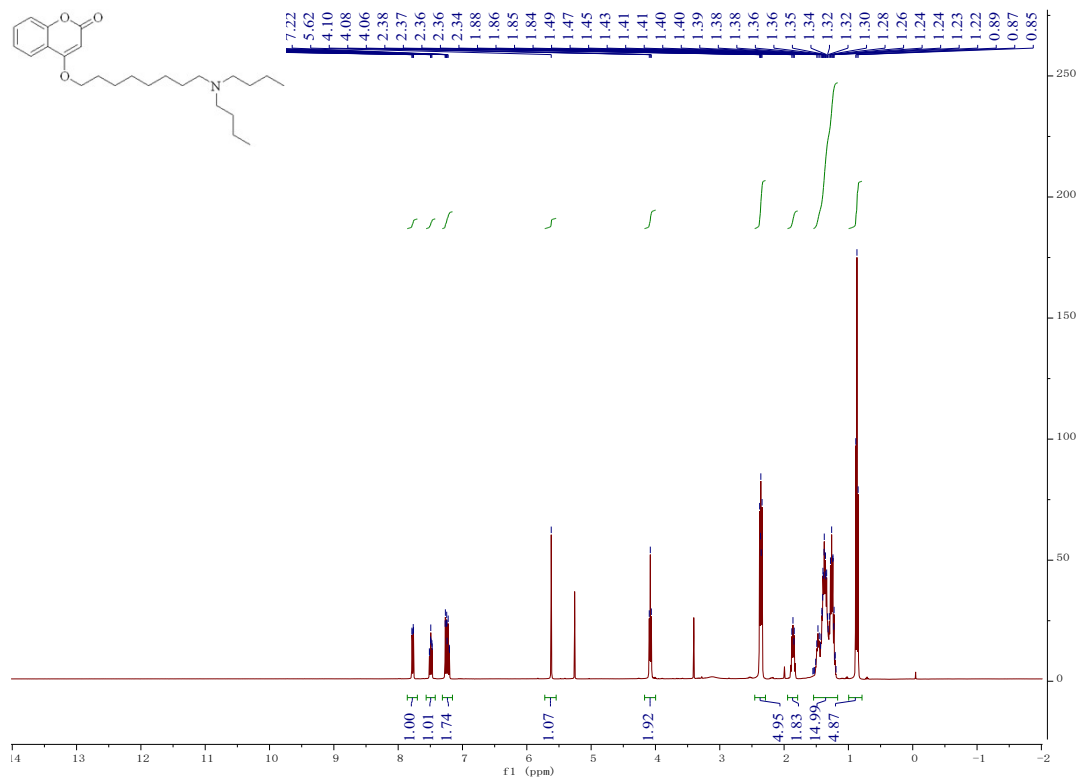


Fig.S53 $^1\text{H NMR}$ of 15d (400 MHz, CDCl_3)

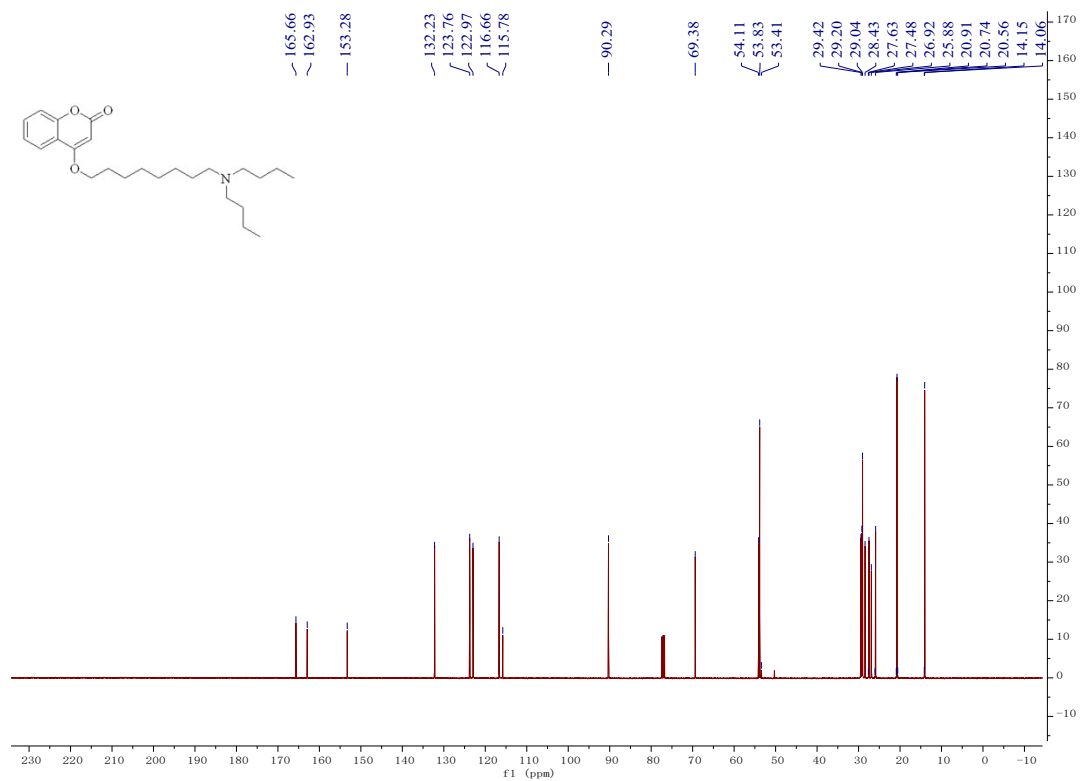


Fig.S54 $^{13}\text{C NMR}$ of 15d (400 MHz, CDCl_3)

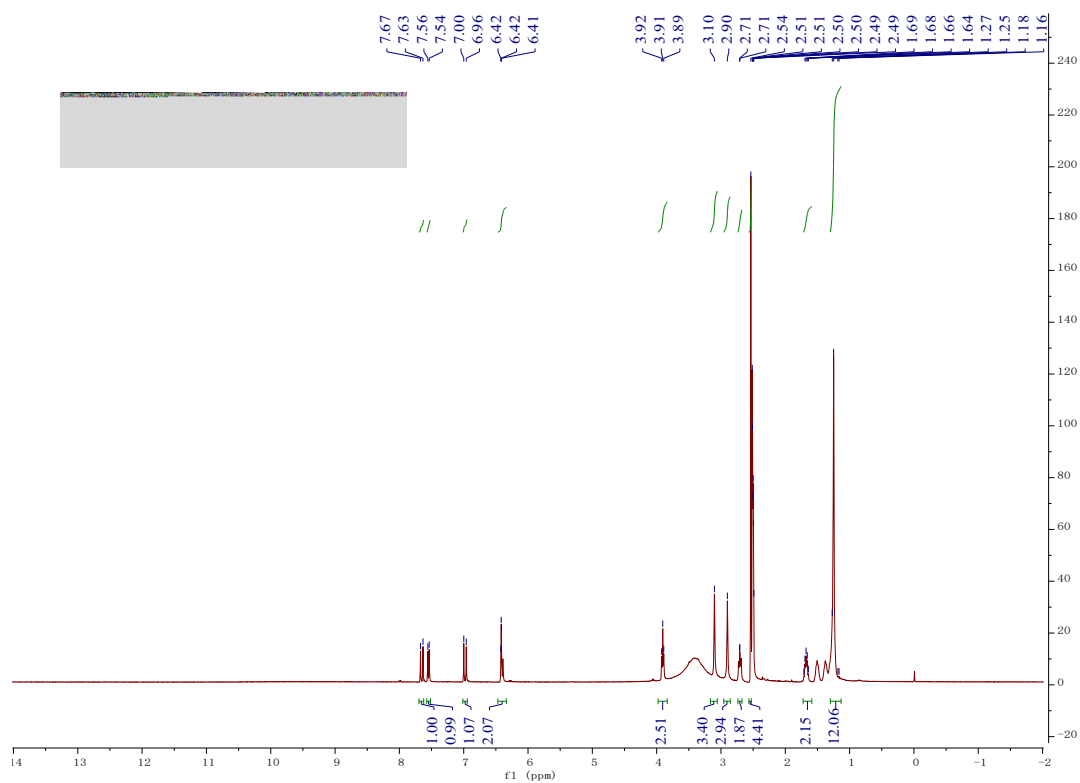


Fig.S55 ^1H NMR of 16a (400 MHz, DMSO)

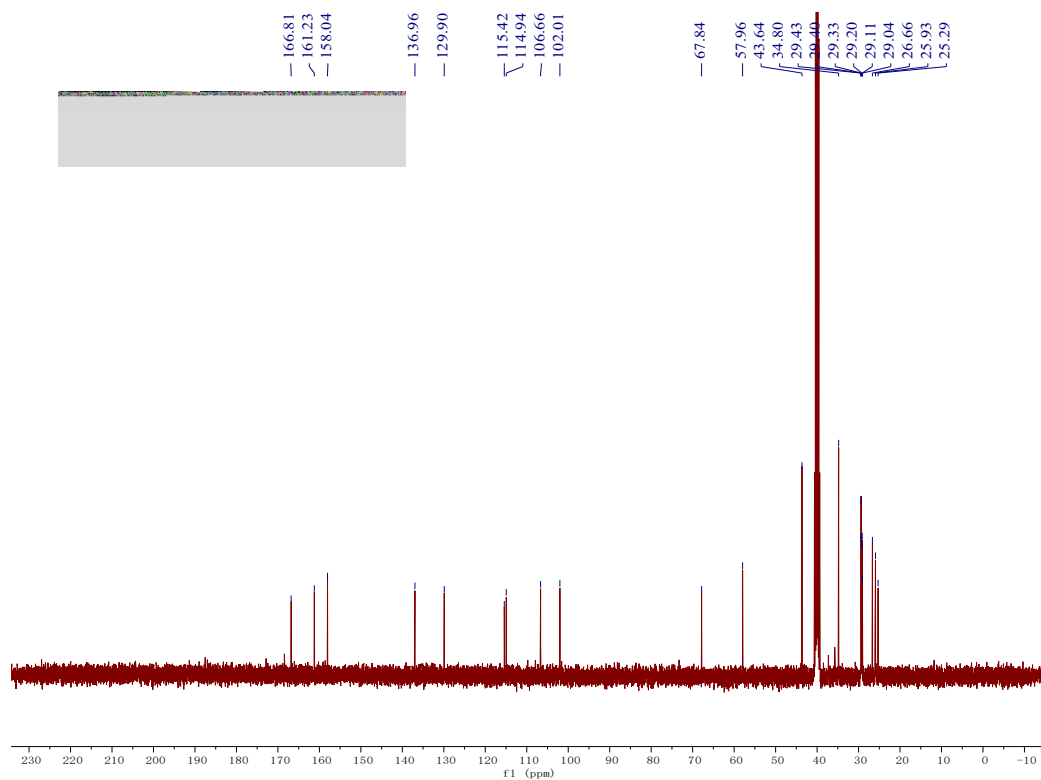


Fig.S56 ^{13}C NMR of 16a (400 MHz, DMSO)

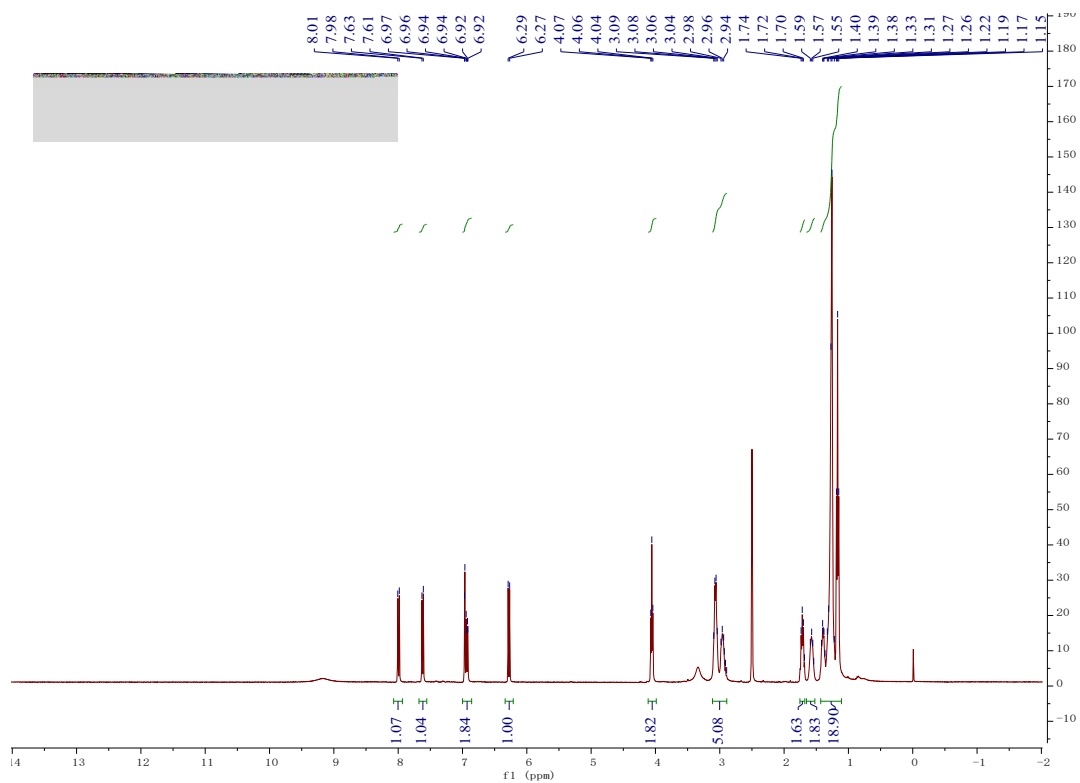


Fig.S57 ^1H NMR of **16b** (400 MHz, DMSO)

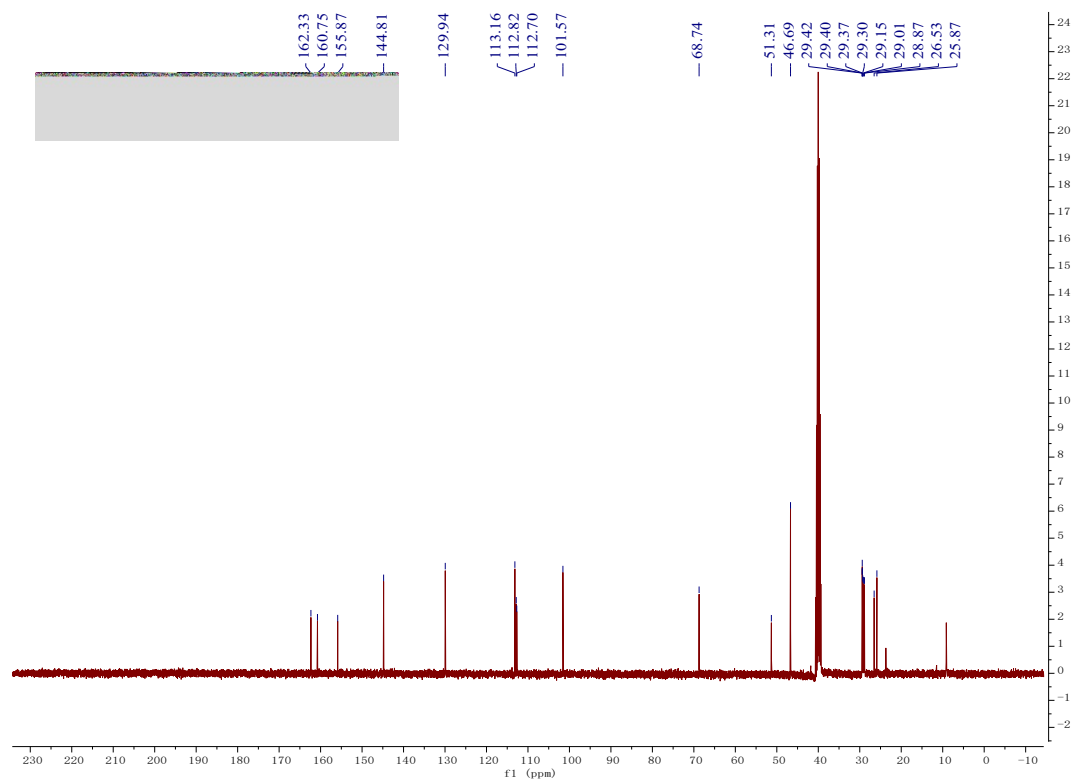


Fig.S58 ^{13}C NMR of **16b** (400 MHz, DMSO)

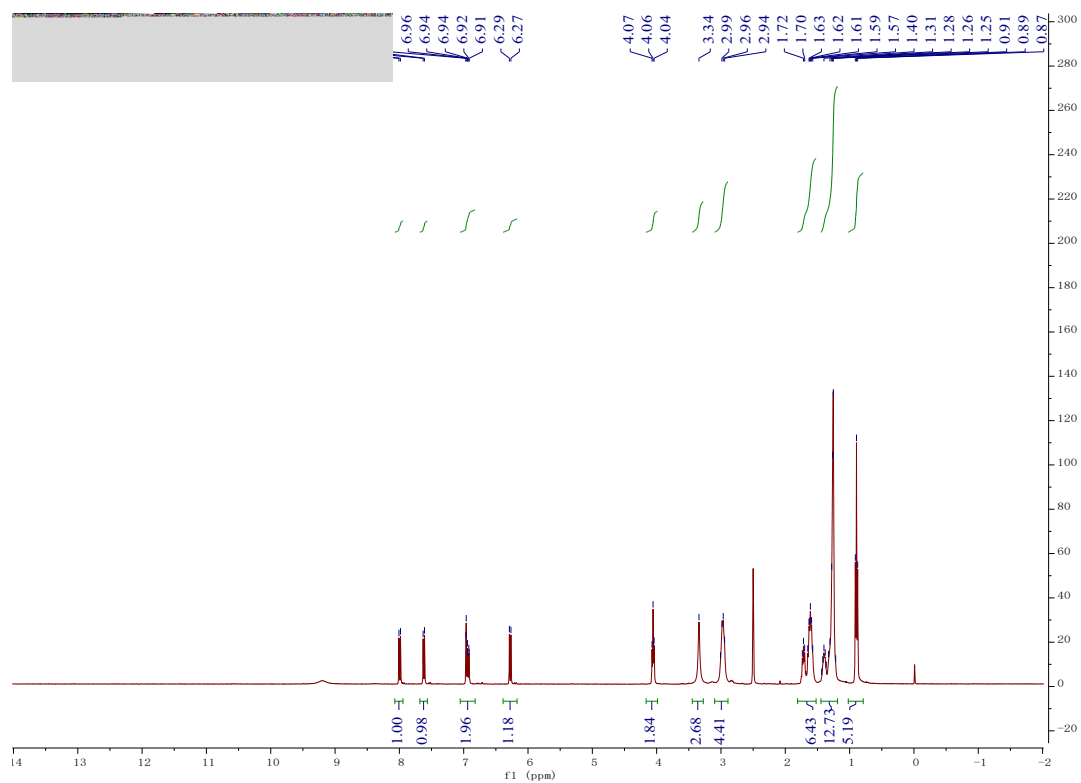


Fig.S59 ^1H NMR of 16c (400 MHz, DMSO)

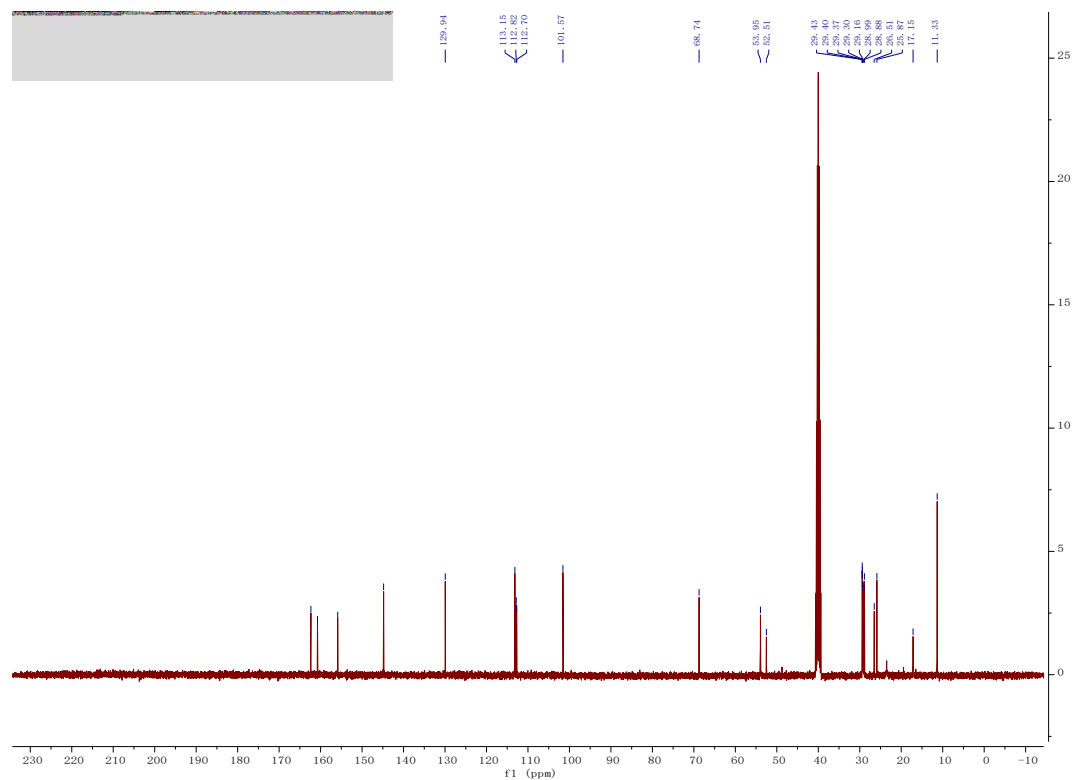


Fig.S60 ^{13}C NMR of 16c (400 MHz, DMSO)

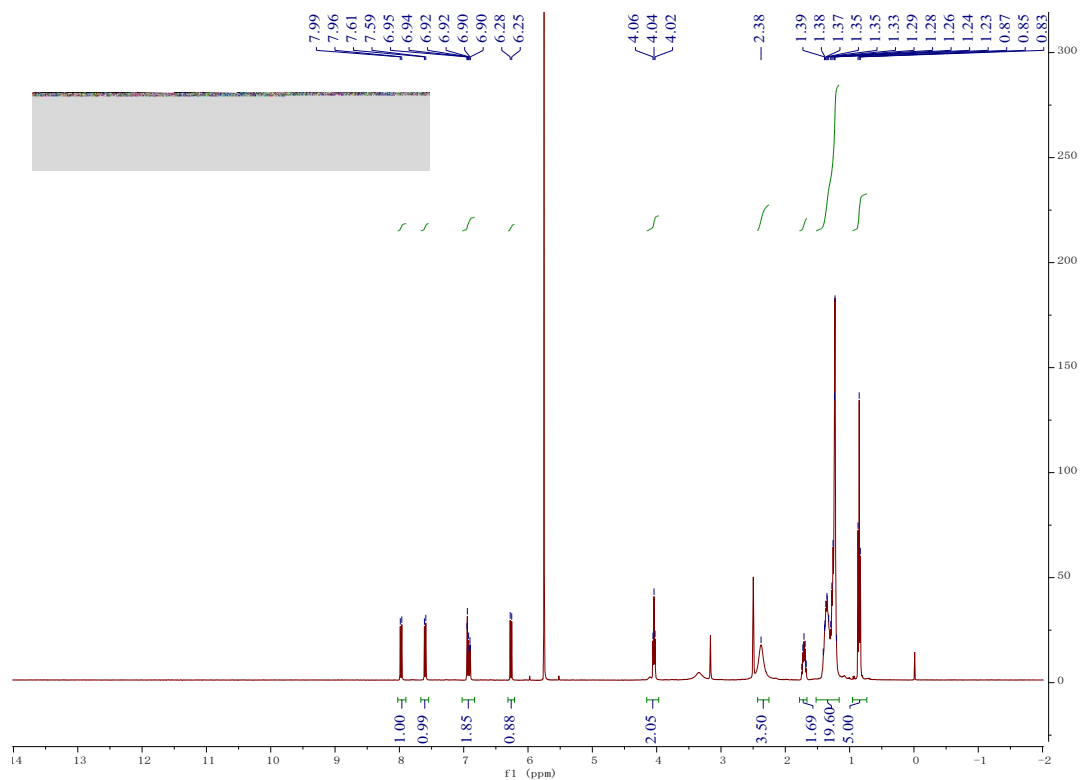


Fig.S61 ^1H NMR of **16d** (400 MHz, DMSO)

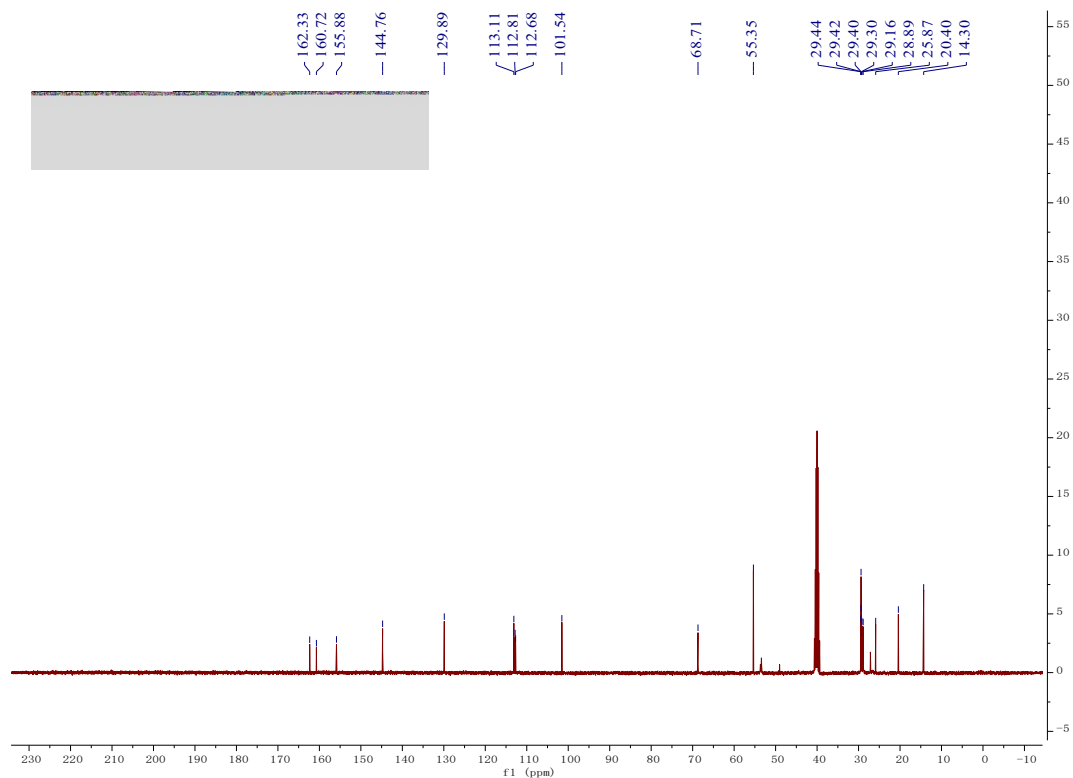


Fig.S62 ^{13}C NMR of **16d** (400 MHz, DMSO)