Electronic Supplementary Information

Building a quadruple stimuli-responsive supramolecular gel based on a supra-amphiphilic metallogelator

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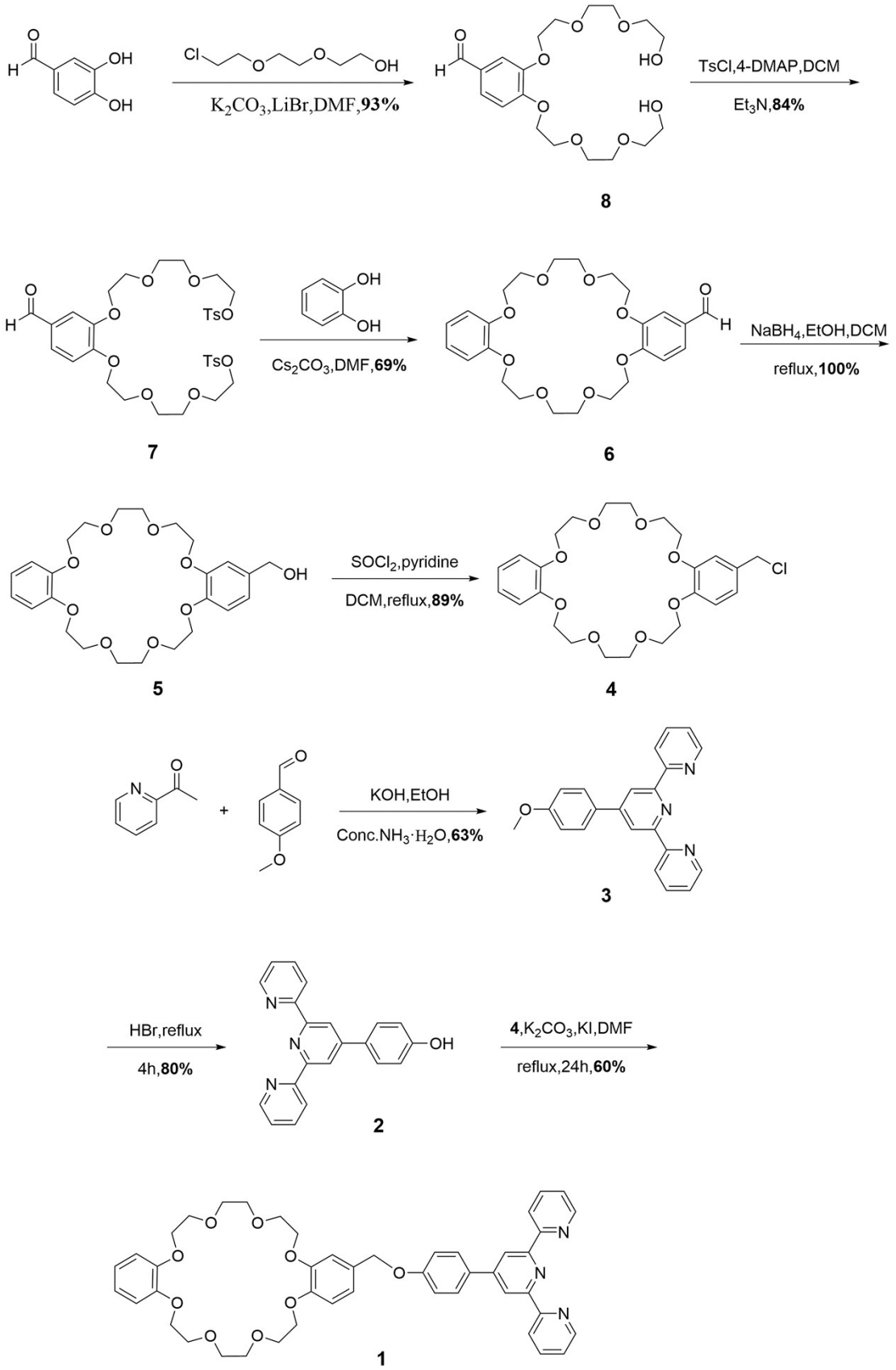

Scheme S1. Synthetic routes to the targeted monomer **1**

Compounds **8**[1], **7**[1], **6**[1], **5**[2], **4**[2], **3**[3], **2**[4] and **1**[5] were synthesized according to the previously reported procedures.

Synthesis of compound 8

3,4-dihydroxy benzaldehyde (0.50 g, 0.36 mmol), K_2CO_3 (1.24 g, 0.90 mmol) and LiBr (0.32 g, 0.36 mmol) was added to a three-neck flask with 25 mL dry DMF. 2-chloroethoxy-2-ethoxy diethanol (1.35 g, 0.80 mmol) was dissolved in 10 mL dry DMF and placed in a constant pressure drop funnel. It was added drop by drop to a flask under stirring conditions within one hour and stirred at 100℃ for 3 days under nitrogen atmosphere. The reaction mixture was filtered to remove the inorganic salts, and the residue after drying the filtrate was dissolved in CH_2Cl_2 (10 mL) and 10% K_2CO_3 (10 mL) solutions. The organic phase was washed with 10% K_2CO_3 solution (3×10 mL), and then dried, filtered and concentrated with in vacuum. The crude product was purified by flash column chromatography (SiO_2, CH_2Cl_2/MeOH=96/4) to give compound **1** as yellowish oil (1.40 g, 93%). ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ (ppm): 9.82 (s, 1H), 7.44-7.42 (m, 2H), 6.98 (d, *J*=8.6 Hz, 1H), 4.25-4.22 (m, 4H), 3.93-3.89 (m, 4H), 3.76-3.67 (m, 16H), 3.60(m, 4H), 2.98(s, 3H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K) δ (ppm): 190.81, 154.12, 149.02, 130.27, 126.79, 112.30, 111.56, 72.67, 71.95, 70.87, 70.32, 69.47, 69.32, 68.59, 61.67.

Synthesis of compound 7

Compound **8** (1.89 g, 4.7 mmol), triethylamine (4.76 g, 47.0 mmol) and catalytic amount of DMAP were dissolved in CH_2Cl_2 (28 mL) and cooled to 0-5℃.The *p*-methylbenzene sulfonyl chloride (4.48 g, 23.5 mmol) was dissolved in CH_2Cl_2 (15 mL), the reaction temperature was maintained below 5℃ and the mixture was stirred for 4h. The reaction mixture was washed with brine (2×15 mL) and 2 M HCl solution (15 mL). The organic layer was dried over Na_2SO_4, filtered and concentrated in vacuum. The crude product was purified by flash column chromatography (SiO_2, ethyl acetate/petroleum ether=3/1) affording compound **7** as yellowish oil (2.77 g, 84%). ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ (ppm): 9.83 (s, 1H), 7.78 (d, *J*=8.2 Hz, 4H), 7.45-7.42 (m, 2H), 7.32 (d, *J*=8.2 Hz, 4H), 6.99 (d, *J*=8.2 Hz, 1H), 4.24-4.13 (m, 8H), 3.86 (m, 4H), 3.70-3.60 (m, 12H), 2.42 (s, 6H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K): δ (ppm): 190.82, 154.29, 149.13, 144.80, 132.96, 130.26, 129.81, 127.93,

126.73, 112.50, 111.81, 70.85, 70.82, 70.80, 69.58, 69.45, 69.27, 69.23, 68.71, 68.64, 21.60.

Synthesis of compound 6

Catechol (155 mg, 1.41 mmol) and cesium carbonate (2.29 g, 7.03 mmol) were added into anhydrous DMF (10 mL) solution under the protection of nitrogen. Compound **7** (1.00 g, 1.41 mmol) was dissolved in anhydrous DMF (10 mL), placed in a drop funnel, and added dropwise to the reaction flask. The mixture was heated and stirred at 100℃ for 1 day. The solvent was removed, toluene (30 mL) and 10% K_2CO_3 (30 mL) solution were added. The aqueous phase was extracted with toluene (3×25 mL) and the organic phase was rewashed with 10% K_2CO_3 (30 mL) and dried over Na_2SO_4. The organic solvent was removed in vacuum and the crude product was purified by flash column chromatography (SiO_2, ethyl acetate/methanol =99/1) affording compound **6** as white solid (460 mg, 69%). m.p.: 87-88 ℃; ^{1}H NMR (600 MHz, $CDCl_3$, 298K) δ (ppm): 9.81 (s, 1H), 7.41 (d, *J*=8.0 Hz, 1H), 7.37 (s, 1H), 6.94 (d, *J*=8.2 Hz, 1H), 6.89-6.86 (m, 4H), 4.22-4.18 (m, 8H), 3.96-3.90 (m, 8H), 3.84-3.82 (m, 8H); ^{13}C NMR (151 MHz, $CDCl_3$, 298K): δ (ppm): 190.94, 154.39, 149.27, 148.99, 130.28, 126.89, 121.51, 114.06, 111.97, 111.15, 71.64, 71.53, 71.41, 70.04, 69.78, 69.62, 69.55, 69.51, 69.42.

Synthesis of compound 5

Compound **6** (0.05 g, 1.05 mmol) was dissolved in a mixture of ethanol (15 mL) and CH_2Cl_2 (15 mL) and cooled to 0℃ in an ice bath. Then $NaBH_4$ (0.12 g, 3.14 mmol) was slowly added and returned to room temperature for 6 h. After the reaction was completed, the reaction mixture was acidified with 1M HCl solution (3×10 mL) and then extracted with CH_2Cl_2. The organic phase was successively washed with 1M $NaHCO_3$ (3×10 mL) and water (2×10 mL), and then dried over Na_2SO_4. The organic solvent was removed in vacuum and the crude product was purified by flash column chromatography (SiO_2, ethyl acetate/methanol=70/1) affording compound **5** as white solid (0.58 g, 100%). m.p.: 94-95℃. ^{1}H NMR (400 MHz, $CDCl_3$, 298K) δ (ppm):

6.86 (m, 7H), 4.57 (s, 2H), 4.15 (m, 8H), 3.95-3.86 (m, 8H), 3.82 (s, 8H). ^{13}C NMR (151 MHz, $CDCl_3$, 298K): δ (ppm): 149.00, 148.90, 148.38, 134.20, 121.40, 119.90, 114.06, 113.88, 112.99, 71.23, 69.88, 69.52, 69.35, 65.16.

Synthesis of compound 4

$SOCl_2$ (0.2 mL, 4.83 mmol) and pyridine (0.41 mL, 5.06 mmol) were dissolved in anhydrous CH_2Cl_2 (10 mL) and placed in a drop funnel. This solution was added dropwise into a solution of compound **5** (0.5 g, 1.04 mmol) in CH_2Cl_2 (10 mL) at 0℃ under nitrogen atmosphere and then stirring at room temperature for 4 h. After the reaction was completed, 20 mL cold water was added to the reaction mixture, the liquid was separated and the aqueous phase was extracted with CH_2Cl_2 (2×20 mL). The organic phase was combined and washed with water (2×20 mL), 1M $NaHCO_3$ (2×20 mL) and brine (2×20 mL) successively. The organic phase was dried over Na_2SO_4 and the solvent was removed in vacuum. The crude product was purified by flash column chromatography (SiO_2, ethyl acetate/petroleum ether=10/1) affording compound **4** as white solid (0.45 g, 89%). m.p.: 88-89℃. ^{1}H NMR (400 MHz, $CDCl_3$, 298K) δ (ppm): 6.91-6.79 (m, 7H), 4.52 (s, 2H), 4.21-4.11 (m, 8H), 3.96-3.88 (m, 8H), 3.83 (d, *J*=0.7 Hz, 8H). ^{13}C NMR (151 MHz, $CDCl_3$, 298K): δ (ppm): 149.07, 148.93, 148.90, 130.44, 121.63, 121.39, 114.28, 114.03, 113.51, 71.29, 71.25, 69.91, 69.81, 69.79, 69.45, 69.36, 46.52.

Synthesis of compound 3

2-acetylpyridine (0.45 g, 3.675 mmol) and p-methoxybenzaldehyde (0.25 g, 1.838 mmol) were dissolved in 10 mL ethanol with the addition of KOH (0.32 g, 5.75 mmol) and $NH_3 \cdot H_2O$ (6 mL, 28%). The reaction mixture was stirred at 34℃ for 16h, then the solution was gradually cooled to 20℃, and the light green solid was filtered. The solid was washed with glacial ethanol (10 mL), and then recrystallized with hot ethanol to obtain compound **3** as white crystal (0.40 g, 63%). m.p.: 153-154℃. ^{1}H NMR (400 MHz, $CDCl_3$, 298K) δ (ppm): 8.77-8.69 (m, 4H), 8.67 (d, *J*=7.9 Hz, 2H), 7.88 (t, *J*=7.3 Hz, 4H), 7.40-7.31 (m, 2H), 7.03 (d, *J*=7.7 Hz, 2H), 3.89 (s, 3H). ^{13}C

NMR (151 MHz, $CDCl_3$, 298K): δ (ppm): 160.52, 156.23, 155.67, 149.80, 148.95, 136.98, 130.66, 128.53, 123.78, 121.42, 118.36, 114.31, 55.37.

Synthesis of compound 2

Under the protection of nitrogen, compound **3** was dissolved in 6.89 mL HBr (48%) in a 50 mL round-bottom flask. The mixture was refluxed at 120℃ for 4 h and then cooled down to room temperature, treated with $NaHCO_3$ solution. The compound **2** (0.36 g, 80%) was recrystallized with hot ethanol. The compound was used directly for the next step reaction without further purification due to its unstability.

Synthesis of compound 1

A mixture of compound **2** (65 mg, 0.2 mmol), compound **4** (100 mg, 0.2 mmol) K_2CO_3 (55.2 mg, 0.4 mmol) and KI (3.3 mg, 0.02 mmol) in anhydrous DMF (20 mL) was refluxed at 150℃ for 8 h under the nitrogen atmosphere. The solvent was removed in vacuum and then the residue was partitioned with CH_2Cl_2 (50 mL) and H_2O (50 mL). The aqueous phase was washed with CH_2Cl_2 (3×50 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed in vacuum. The crude product was purified by flash column chromatography (SiO_2, ethyl acetate) to obtain compound **1** as white solid (0.48 g, 60%). m.p.: 151-152℃. ^{1}H NMR (400 MHz, $CDCl_3$, 298K) δ (ppm): 8.72 (s, 4H), 8.66 (d, *J*=7.9 Hz, 2H), 7.91 (t, *J*=7.8 Hz, 4H), 7.42-7.35 (m, 2H), 7.09 (d, *J*=8.7 Hz, 2H), 6.98 (s, 2H), 6.89 (d, *J*=7.4 Hz, 5H), 5.03 (s, 2H), 4.22-4.11 (m, 8H), 3.92 (d, *J*=8.0, 4.1 Hz, 8H), 3.84 (d, *J*=1.5 Hz, 8H); ^{13}C NMR (100 MHz, $CDCl_3$, 298K) δ (ppm): 159.84, 156.44, 155.91, 149.87, 149.22, 149.17, 149.10, 148.98, 137.04, 131.06, 129.86, 128.67, 123.91, 121.55, 121.52, 120.95, 118.46, 115.39, 114.24, 113.99, 113.72, 71.43, 71.42, 70.19, 70.07, 70.01, 69.69, 69.61, 69.54. ESI-MS calcd. for $C_{46}H_{47}N_3O_9$ 785.33 ($M+H^+$), found 786.32.

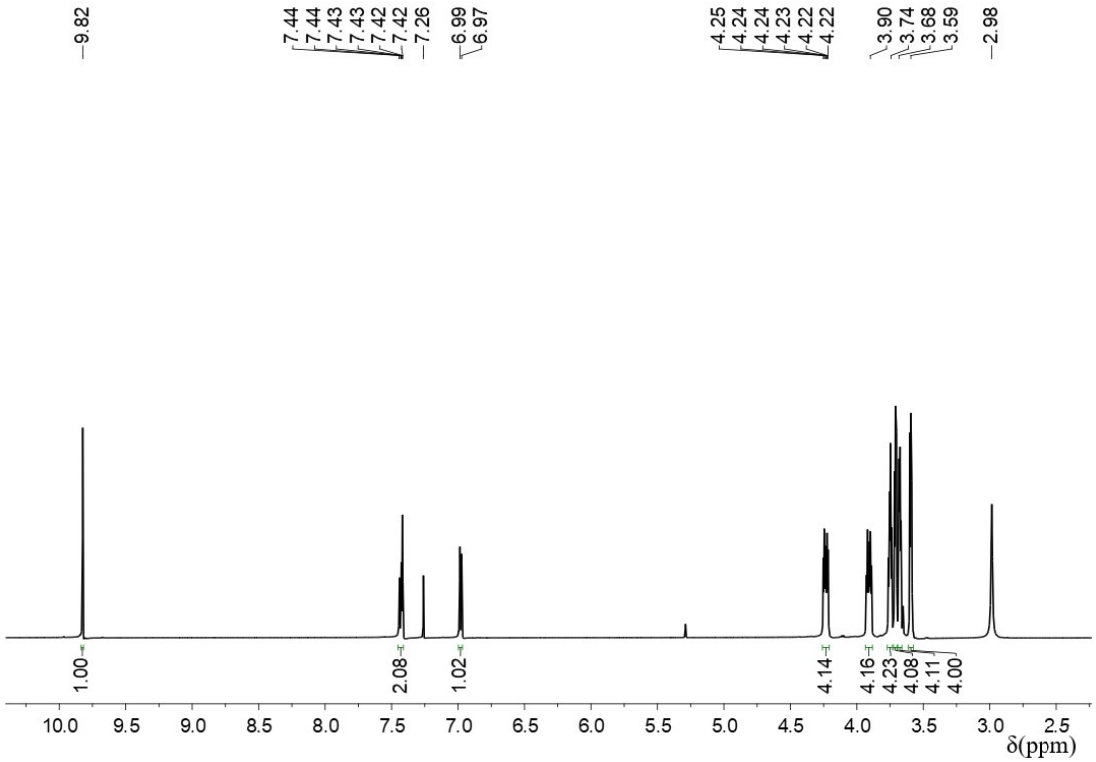

Fig. S1. ^{1}H NMR spectrum of compound **8** in $CDCl_3$ (600 MHz, 298K).

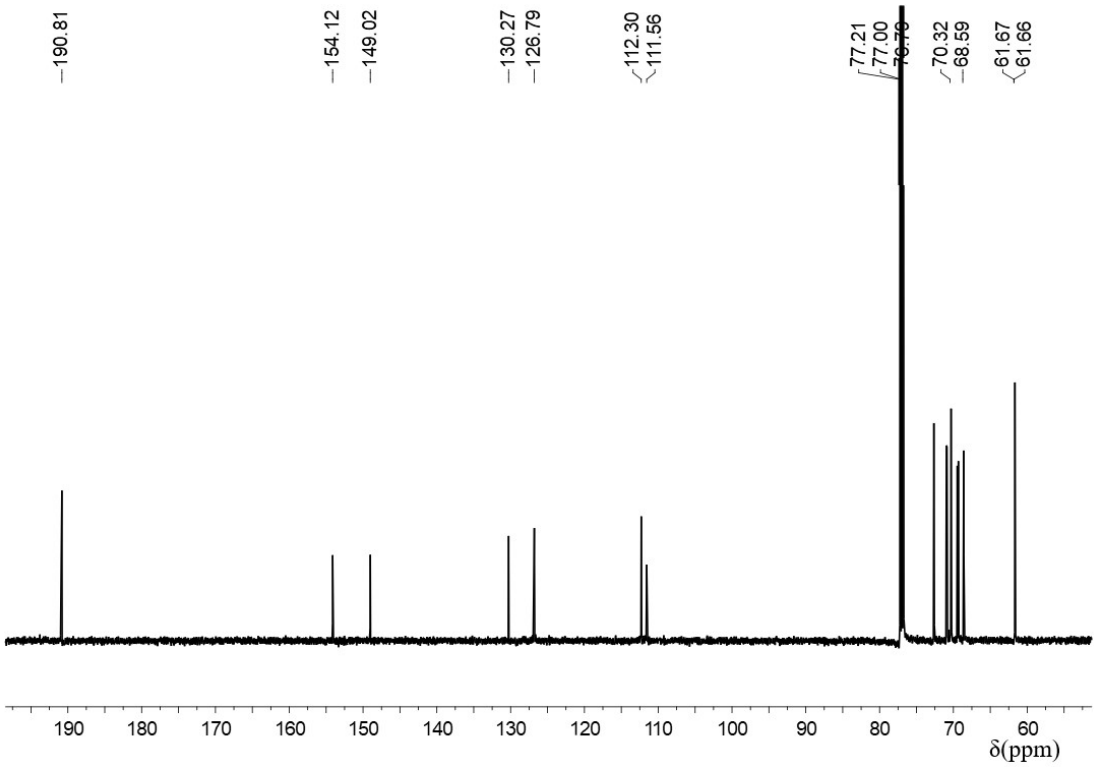

Fig. S2. ^{13}C NMR spectrum of compound **8** in $CDCl_3$ (151 MHz, 298K).

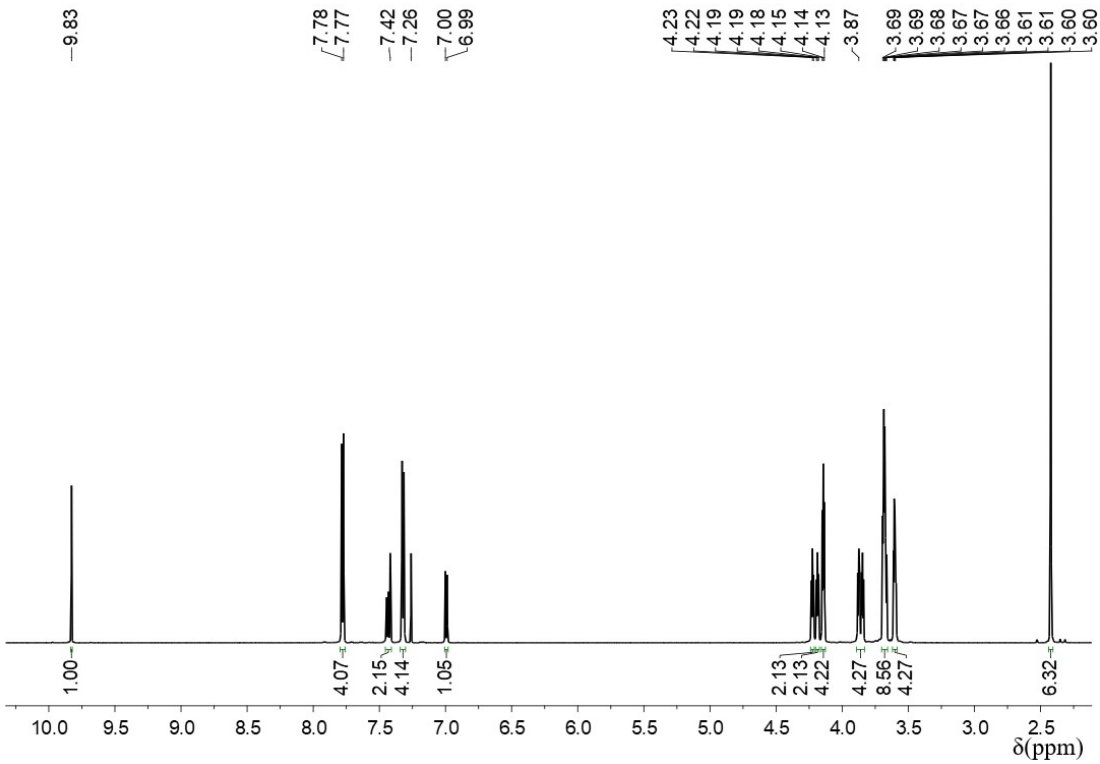

Fig. S3. ^{1}H NMR spectrum of compound **7** in $CDCl_3$ (600 MHz, 298K).

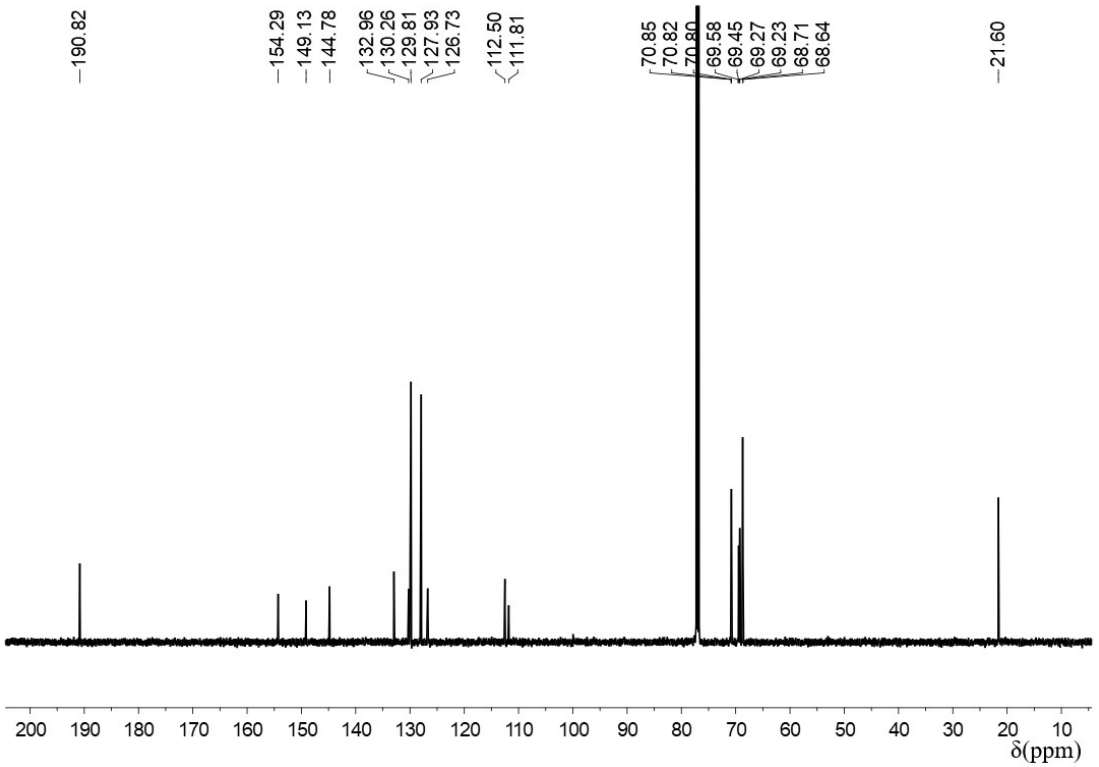

Fig. S4. ^{13}C NMR spectrum of compound **7** in $CDCl_3$ (151 MHz, 298K).

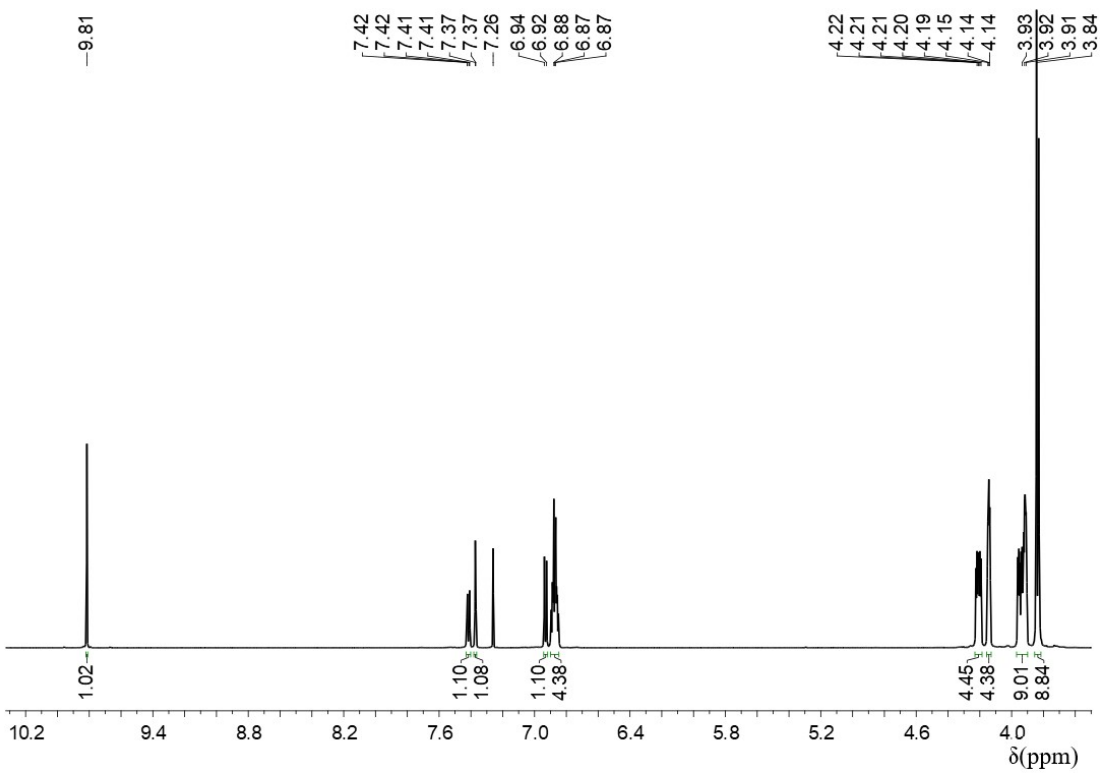

Fig. S5. ^{1}H NMR spectrum of compound **6** in $CDCl_3$ (600 MHz, 298K).

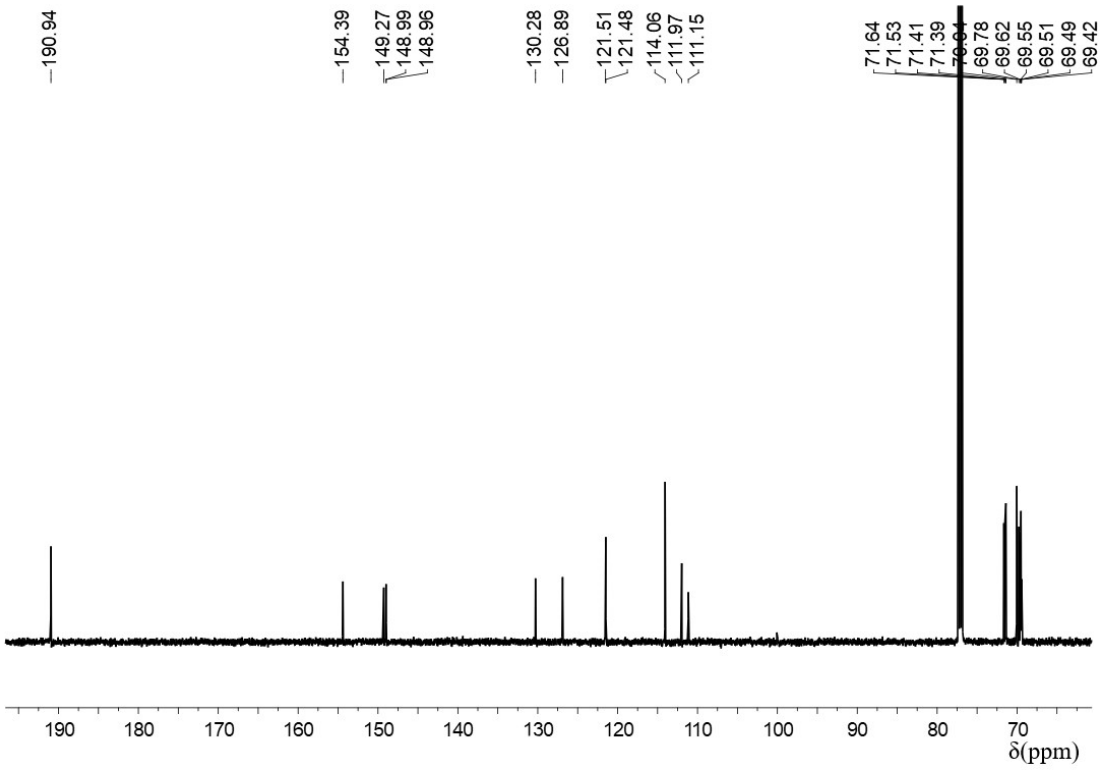

Fig. S6. ^{13}C NMR spectrum of compound **6** in $CDCl_3$ (151 MHz, 298K).

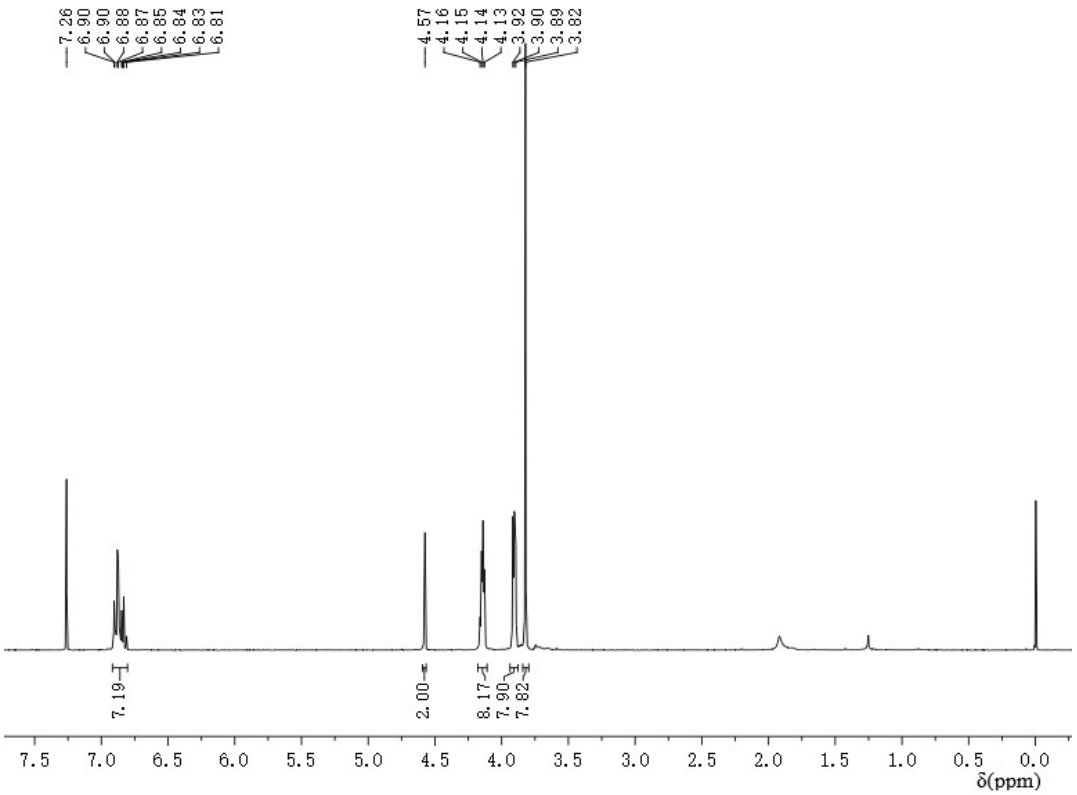

Fig. S7. ^{1}H NMR spectrum of compound **5** in $CDCl_3$ (400 MHz, 298K).

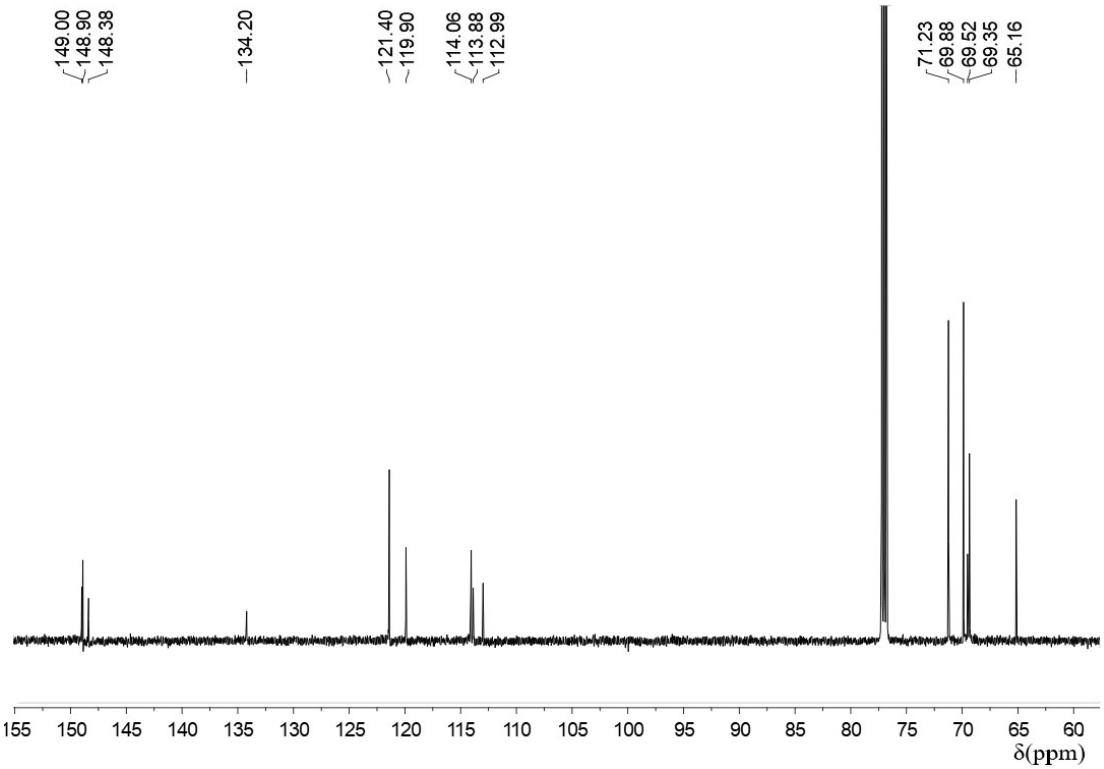

Fig. S8. ^{13}C NMR spectrum of compound **5** in $CDCl_3$ (151 MHz, 298K).

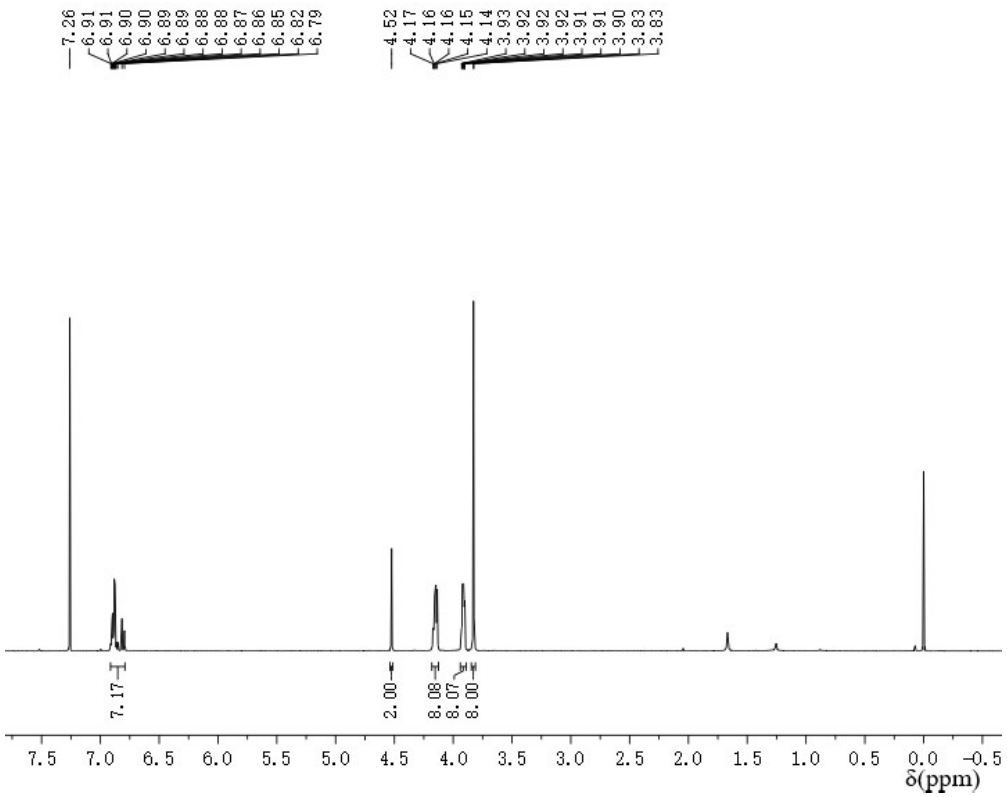

Fig. S9. ^{1}H NMR spectrum of compound **4** in $CDCl_3$ (400 MHz, 298K).

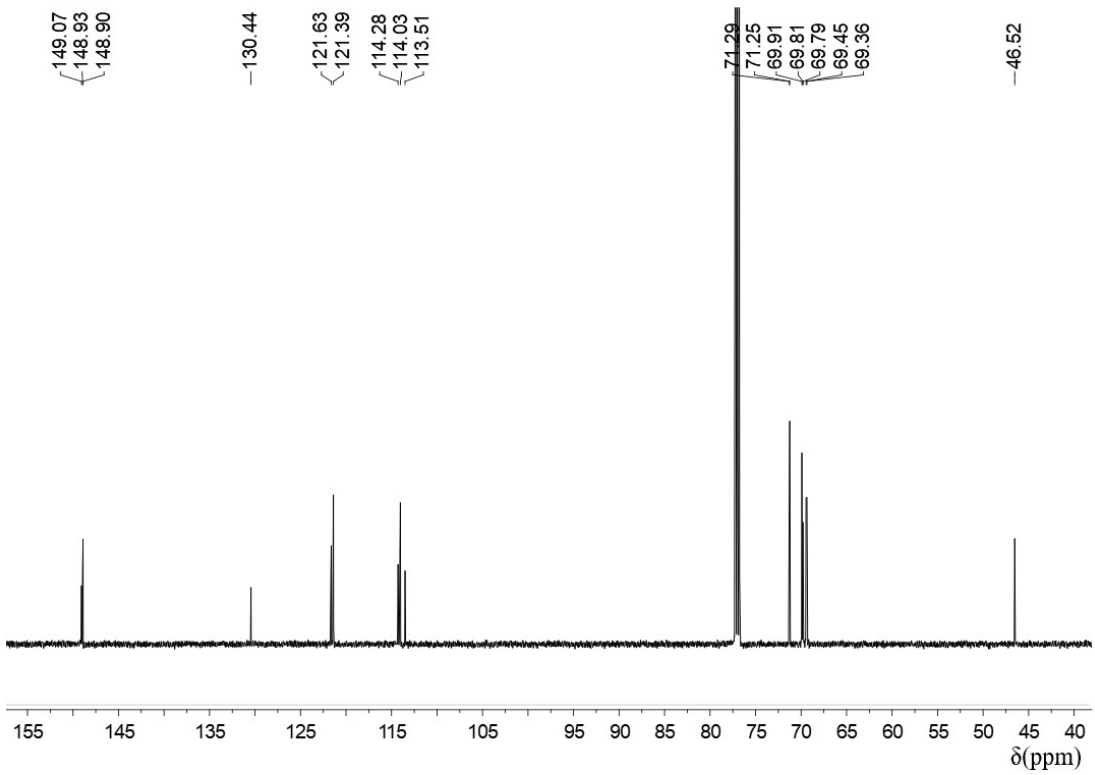

Fig. S10. ^{13}C NMR spectrum of compound **4** in $CDCl_3$ (151 MHz, 298K).

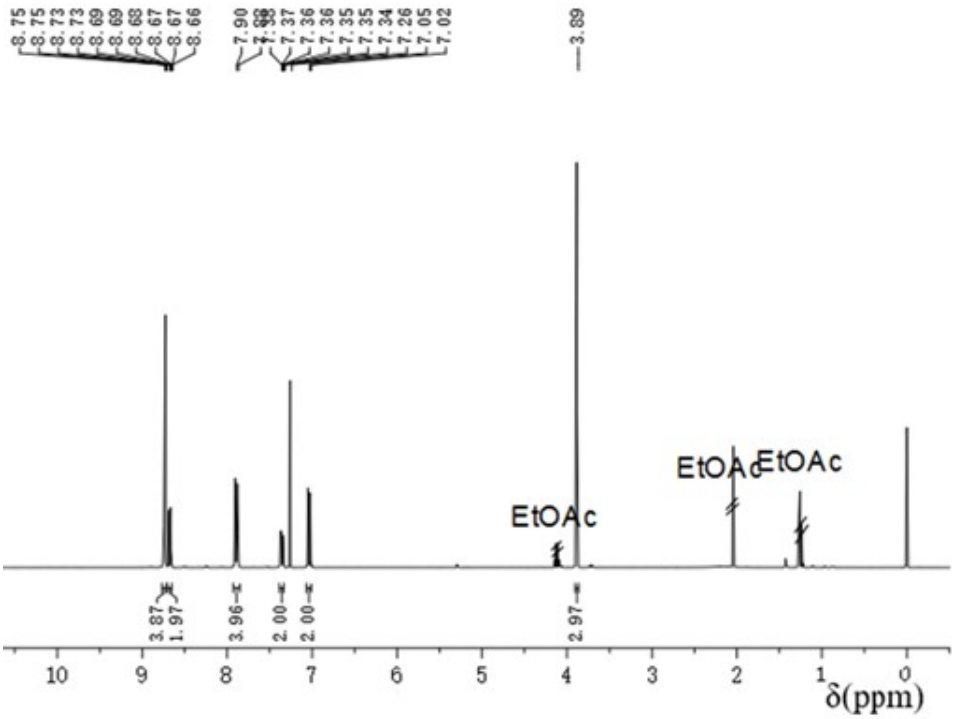

Fig. S11. ^{1}H NMR spectrum of compound **3** in $CDCl_3$ (400 MHz, 298K).

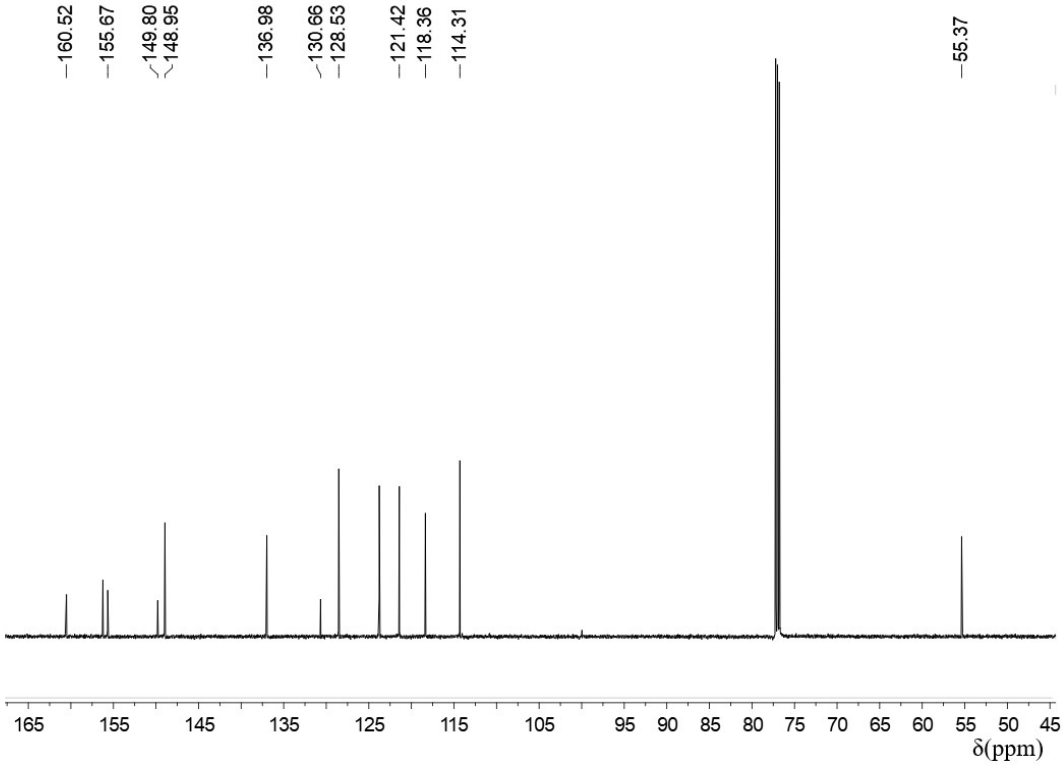

Fig. S12. ^{13}C NMR spectrum of compound **3** in $CDCl_3$ (151 MHz, 298K).

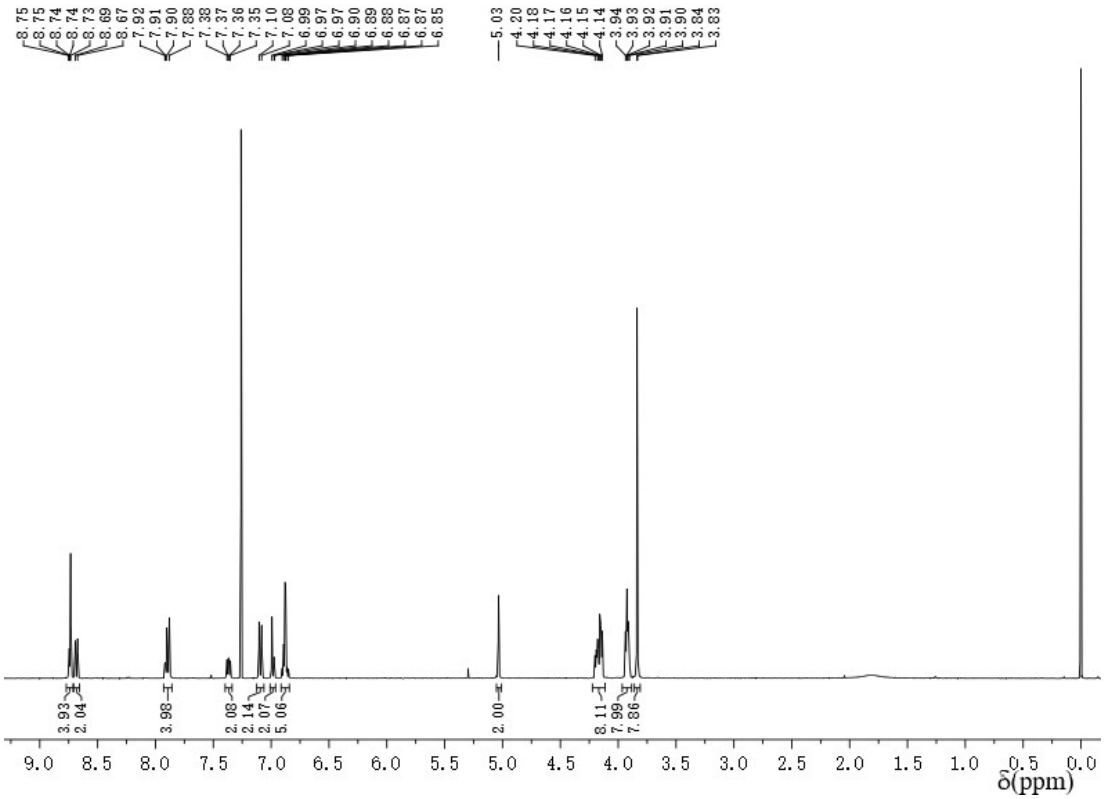

Fig. S13. ^{1}H NMR spectrum of compound **1** in $CDCl_3$ (400 MHz, 298K).

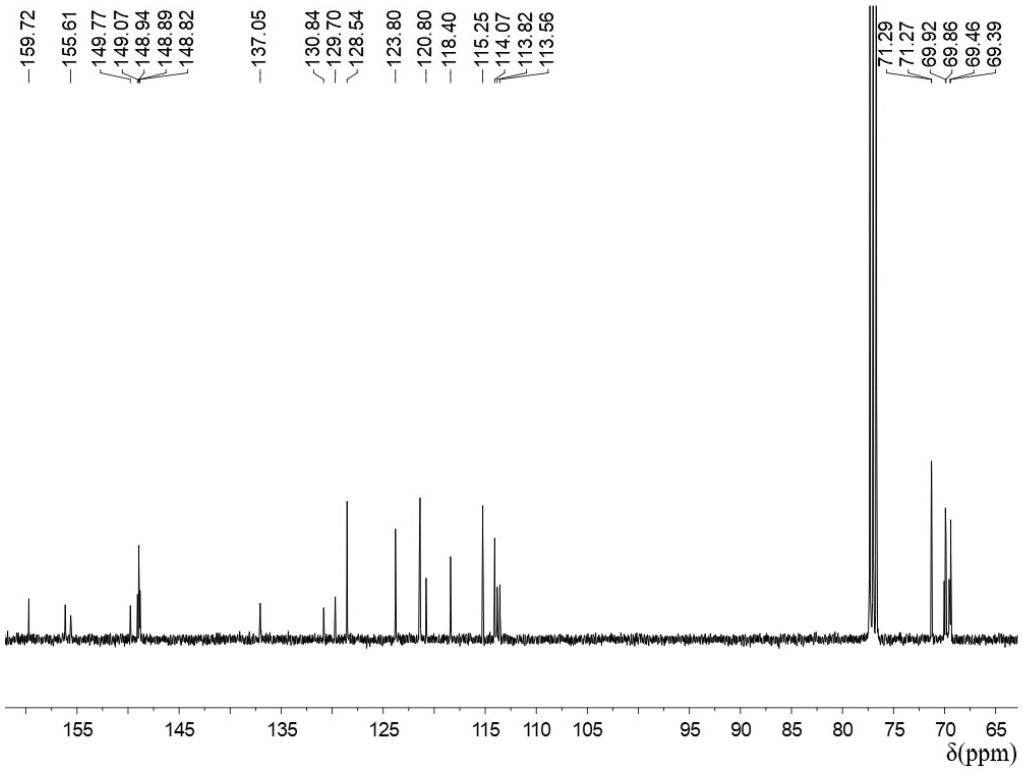

Fig. S14. ^{13}C NMR spectrum of compound **1** in $CDCl_3$ (100 MHz, 298K).

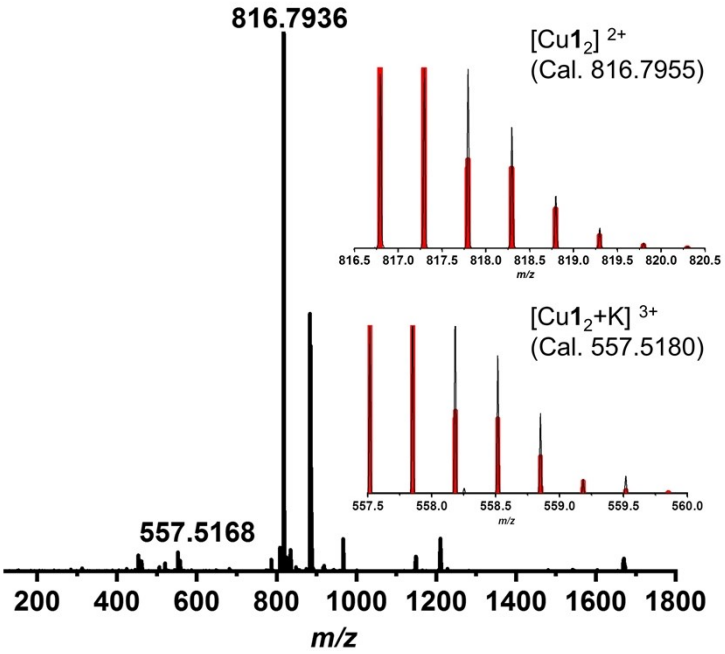

Fig. S15. Mass spectrum of $[Cu\mathbf{1}_2](OTf)_2$.

The molecular formula of $[Cu\mathbf{1}_2](OTf)_2$ is $C_{94}H_{96}N_6O_{24}F_6S_2Cu$ (M=1934.35). Therefore, under the positive mode on the ESI-MS spectrum, $[Cu\mathbf{1}_2](OTf)_2$ will show the fragment of $(Cu\mathbf{1}_2)^{2+}$, giving the signal m/z at (M-2OTf$^-$)/2=816.7955; also it can show the fragment of $(Cu\mathbf{1}_2+K)^{3+}$, giving the signal m/z at (M-2 OTf$^-$+K)/3=557.5180.

2. Preparation of gel

After compound **1** is coordinated with the metal, the complex is added into different solvents (or mixed solvents), and the concentration of gelator is controlled in 1%-10% (w/w) with a concentration gradient of 0.5%. Heating the mixture in a closed glass vial until the desolvation of the complex, and then cooling down naturally to room temperature. The formation of the gel was validated by the "inverted" method.. The solvents screened were toluene, MeCN, THF, Acetone, MeOH, EtOH, Hexane, DMF, DMAc. The metals used were copper sulfate ($CuSO_4$), copper acetate ($C_6H_4Cu_2O_7$), copper citrate ($Cu(CH_3COO)_2$), copper chloride ($CuCl_2$), copper nitrate ($Cu(NO_3)_2$), copper bromide ($CuBr_2$), copper perchlorate ($Cu(ClO_4)_2$), copper trifluoromethanesulfonic acid ($Cu(CF_3SO_3)_2$), copper hexafluorophosphate ($Cu(PF_6)_2$), copper fluoroborate ($Cu(BF_4)_2$). Copper hexafluorophosphate and copper fluoroborate are obtained by anion exchange of copper chloride with sodium hexafluorophosphate and sodium fluoroborate, respectively.

3. Stimuli-responsive test

3.1 Thermal responsiveness

[Cu**1**$_2$](OTf)$_2$ gel was heated to 60℃ and a solution was obtained. The gel was reformed upon cooling the solution to room temperature.

3.2 K^+/B18C6 responsiveness

When 1.2 equivalent KPF_6 was added to the gel and heated to 60℃ and then cooled, no gel could be formed. B18C16 was added to the solution, heated and cooled to regain the gel.

3.3 pH responsiveness

The [Cu**1**$_2$](OTf)$_2$ gel was exposed to TFA vapor, and the gel was turned into a solution gradually. The solution was then exposed to TEA vapor, and the gel was reformed.

3.4 Ultrasound responsiveness

After the gel was exposed to ultrasonic waves for 20 minutes, all the gel turned into a solution. Then the solution was heated to 60℃, cooling down to room temperature and the gel was reformed.

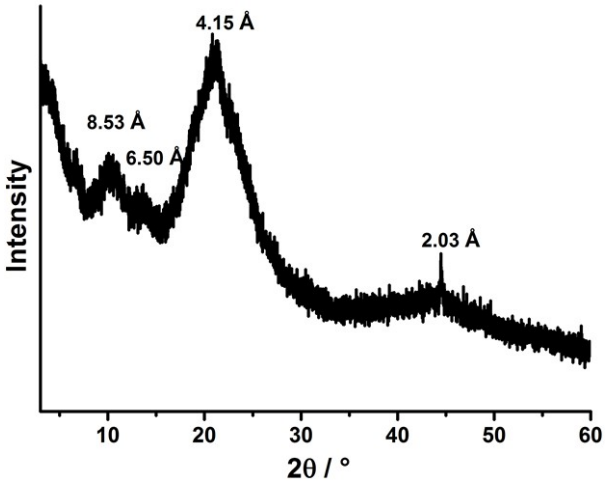

Fig. S16. Powder X-ray diffraction pattern of [Cu**1**$_2$](OTf)$_2$

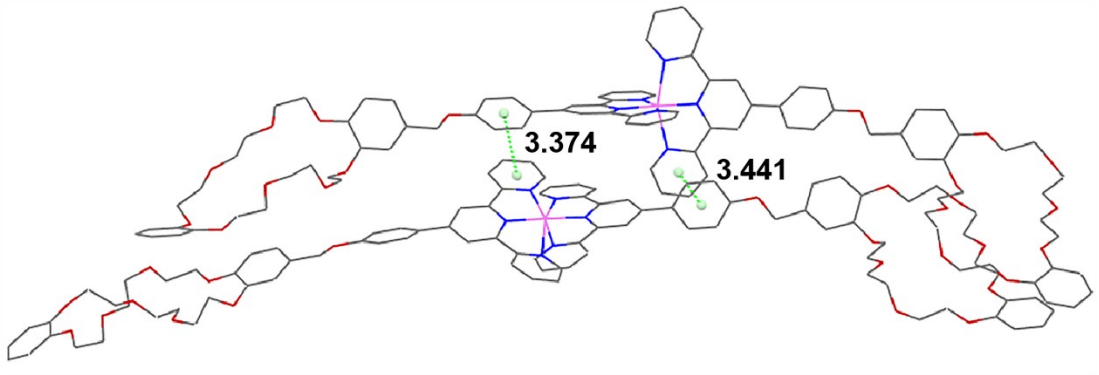

Fig. S17. Optimized conformation of a dimer of $[Cu\mathbf{1}_2](OTf)_2$ by GFN2-xTB method. The color for the atoms is marked as: C, gray; O, red; N, blue; Cu, violet. All the hydrogens and the anion OTf^- were omitted for clarity. The centroid from each π unit was labeled as light green, and the distance was measured as 3.374 and 4.441 Å.

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