

A water-soluble biphen[3]arene: synthesis, host–guest complexation, and application in controllable self-assembly and controlled release

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Electronic Supplementary Information (19 pages)

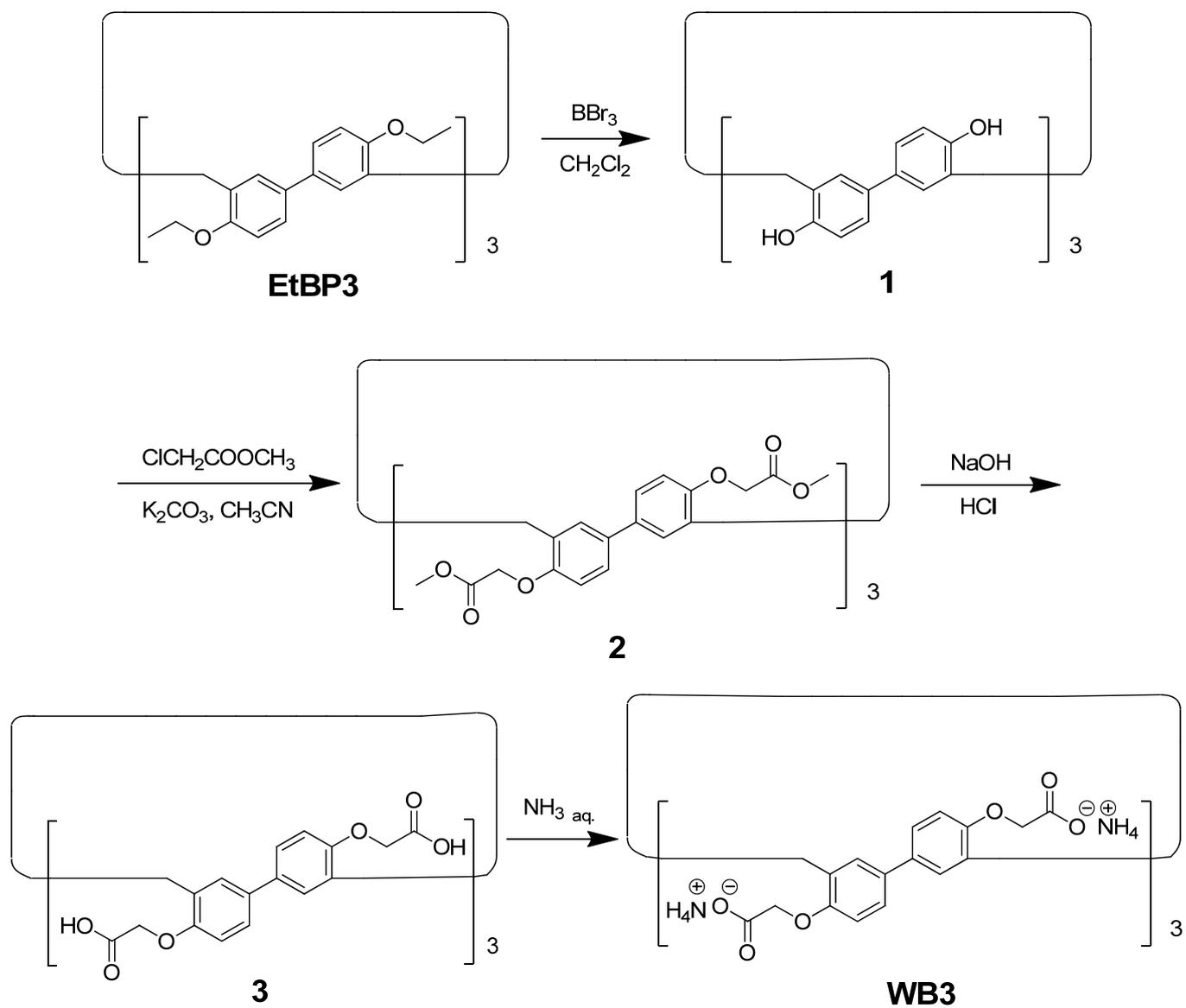
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1. Materials and methods

All reagents were commercially available and used as supplied without further purification. Solvents were either employed as purchased or dried according to procedures described in the literature. Compounds **EtBP3**^{S1} and **G**^{S2} were synthesized according to published literature procedures. NMR spectra were recorded with a Bruker Avance DMX 400 spectrophotometer or a Bruker Avance DMX 500 spectrophotometer with the deuterated solvent as the lock and the residual solvent or TMS as the internal reference. Low-resolution electrospray ionization mass spectra (LRESI-MS) were obtained on a Bruker Esquire 3000 Plus spectrometer (Bruker-Franzen Analytik GmbH Bremen, Germany) equipped with an ESI interface and an ion trap analyzer. High-resolution electrospray ionization mass spectra (HRESI-MS) were obtained on a Bruker 7-Tesla FT-ICR mass spectrometer equipped with an electrospray source (Billerica, MA, USA). The melting points were collected on a SHPSIC WRS-2 automatic melting point apparatus. The fluorescence experiments were conducted on a RF-5301 spectrofluorophotometer (Shimadzu Corporation, Japan). The ITC experiment was performed on a VP-ITC micro-calorimeter (Microcal, USA). The critical aggregation concentration (CAC) values of **G** and **WB3G** were determined on a DDS-307 instrument. Transmission electron microscopy (TEM) investigations were carried out on a JEM-1200EX instrument. Dynamic light scattering measurements were performed on a goniometer ALV/CGS-3 using a UNIPHASE He-Ne laser operating at 632.8 nm.

2. Synthesis of water-soluble biphen[3]arene **WB3**

Scheme S1. Synthetic route to water-soluble biphen[3]arene **WB3**.



2.1. Synthesis of compound 2

Synthesis of **2**: To a solution of **EtBP3** (760 mg, 1.00 mmol) in dried dichloromethane (50 mL) was added boron tribromide (6.01 g, 24.0 mmol). The mixture was stirred at room temperature for 24 h. Then the mixture was added into water. The resulting precipitated product **1** was collected by filtration, washed with water and dried completely under vacuum (0.580 g, 98%). To a solution of **1** (0.580 g, 0.980 mmol) in CH₃CN (60 mL) was added methyl chloroacetate (2.59 g, 24.0 mmol) and K₂CO₃ (3.31 g, 24.0 mmol). The mixture was heated in a flask at 80 °C under nitrogen gas protection for 2 d. Then the reaction mixture was cooled to room temperature and filtered. The filter cake was washed with dichloromethane (2 × 60 mL). Then the filtrate was concentrated under vacuum, and then the residue was purified by column chromatography on silica gel with dichloromethane/ethyl acetate (10:1 v/v) as the eluent to get product **2** as a white solid (400 mg, 40%), mp: 188.2–189.5 °C. The ¹H NMR spectrum of **2** is shown in Figure S1. ¹H NMR (500 MHz, dichloromethane-*d*₂, 293 K) δ (ppm): 7.20 (d, *J* = 10 Hz, 6H), 7.00 (s, 6H), 6.68 (d, *J* = 10 Hz, 6H), 4.56 (s, 12H), 4.00 (s, 6H), 3.65 (s, 18H). The ¹³C NMR spectrum of **2** is shown in Figure S2. ¹³C NMR (125 MHz, dichloromethane-*d*₂, 293 K) δ (ppm): 169.89, 155.42, 134.70, 130.32, 129.41, 125.92, 112.39, 66.25, 52.37 and 29.32. LRESIMS is shown in Figure S3: *m/z* 1049.3 [M + Na]⁺. HRESIMS: *m/z* calcd for [M + Na]⁺ C₅₇H₅₄O₁₈Na⁺, 1049.3208; found 1049.3259; error –5 ppm.

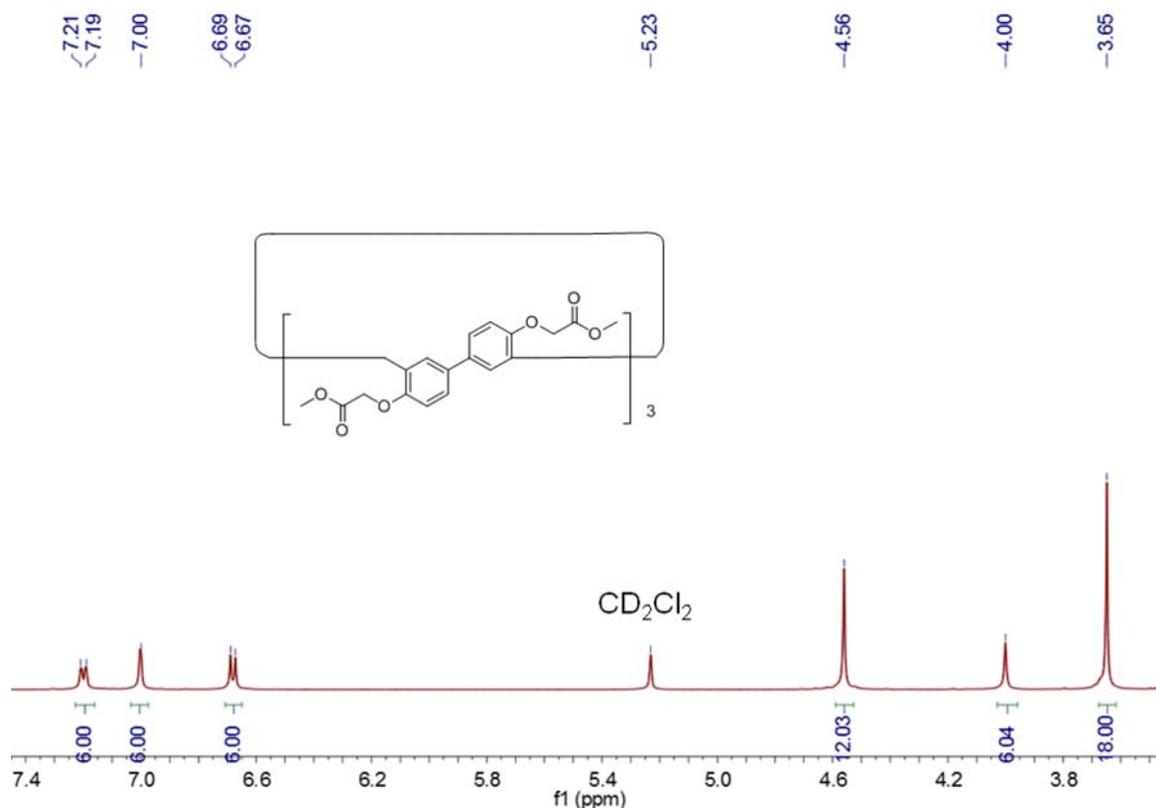


Figure S1. ¹H NMR spectrum (500 MHz, dichloromethane-*d*₂, 293K) of **2**.

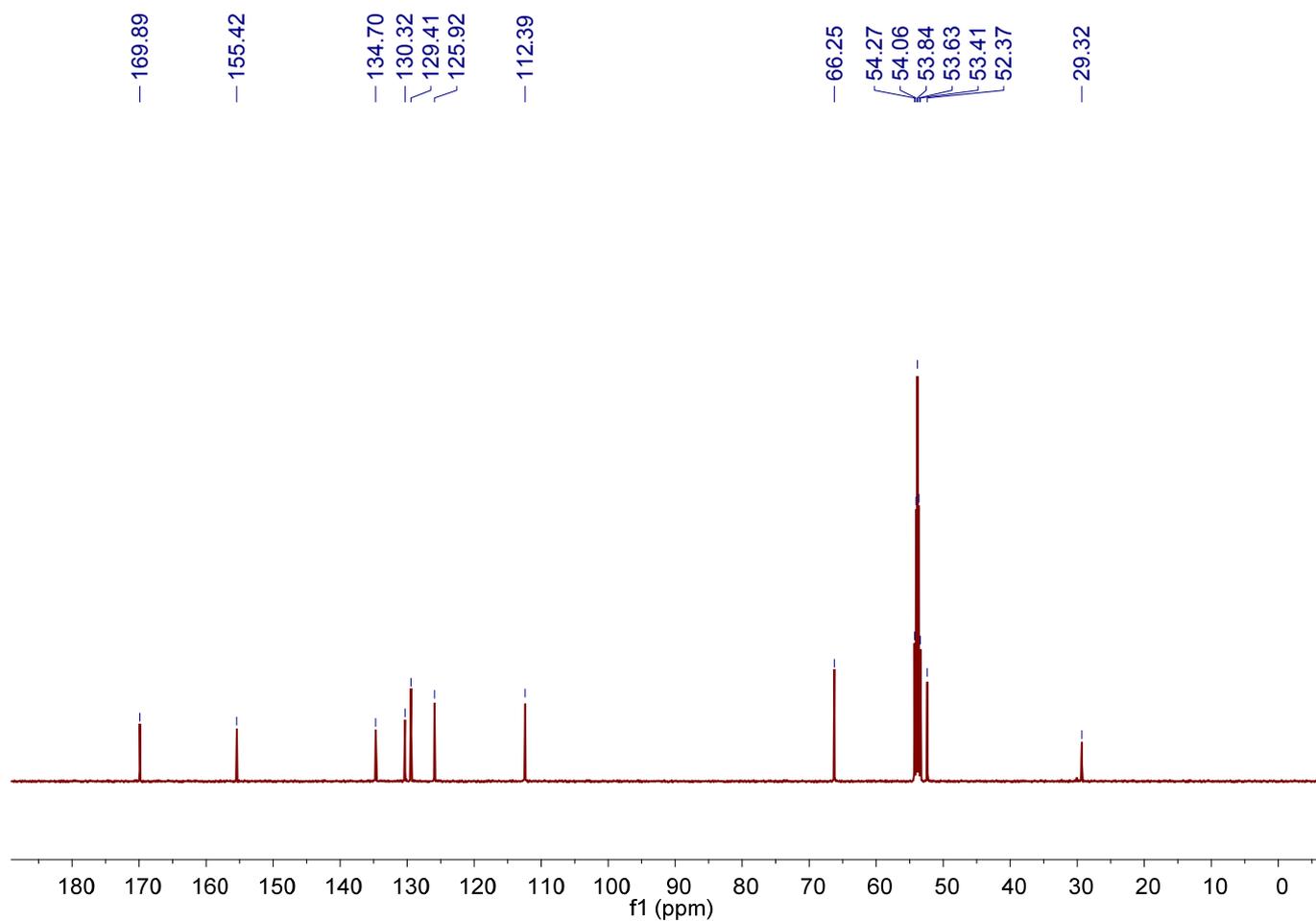


Figure S2. ^{13}C NMR spectrum (125 MHz, dichloromethane- d_2 , 293K) of **2**.

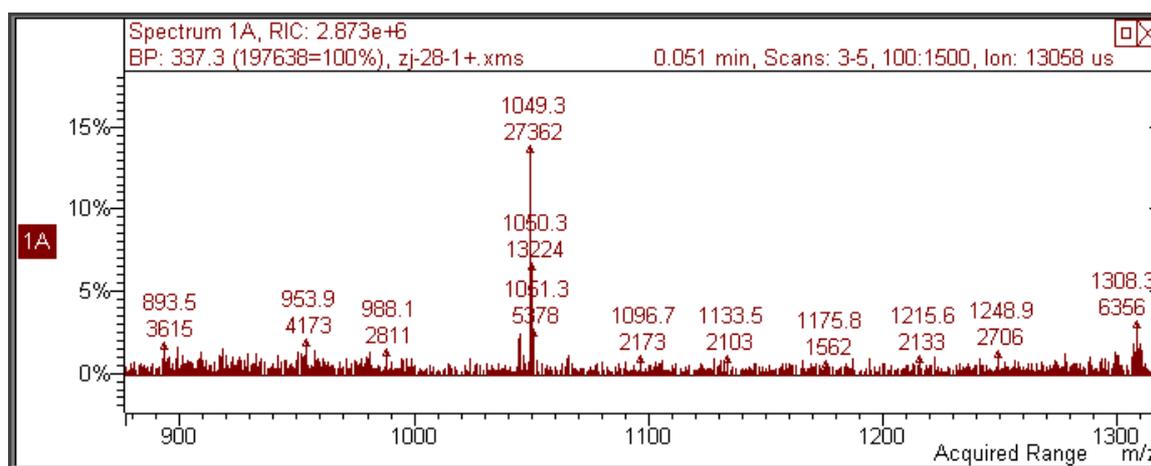


Figure S3. Electrospray ionization mass spectrum of **2**. Assignment of the main peak: m/z 1049.3 $[\text{M} + \text{Na}]^+$.

2.2. Synthesis of compound 3

Synthesis of **3**: A solution of **2** (205 mg, 0.200 mmol) in anhydrous ethyl alcohol (15 mL) was treated with 40% aqueous sodium hydroxide (15 mL) at 80 °C for 12 h. Then the reaction mixture was evaporated under vacuum, diluted with water (15 mL) and acidified with aqueous HCl solution. The resulting precipitate was filtered, washed with water and dried to afford product **3** (140 mg, 74%) as a white powder, mp: > 300 °C. The ¹H NMR spectrum of **3** is shown in Figure S4. ¹H NMR (400 MHz, DMSO-*d*₆, 293 K) δ (ppm): 7.23 (d, *J* = 8 Hz, 6H), 6.89 (s, 6H), 6.84 (d, *J* = 8 Hz, 8H), 4.69 (s, 12H), 3.97 (s, 6H). The ¹³C NMR spectrum of **3** is shown in Figure S5. ¹³C NMR (100 MHz, DMSO-*d*₆, 293 K) δ (ppm): 170.32, 154.76, 133.23, 129.06, 128.24, 125.25, 112.02 and 64.98. LRESIMS is shown in Figure S6: *m/z* 965.2 [M + Na]⁺. HRESIMS: *m/z* calcd for [M + Na]⁺ C₅₁H₄₂O₁₈Na⁺, 965.2269; found 965.2299; error -3 ppm.

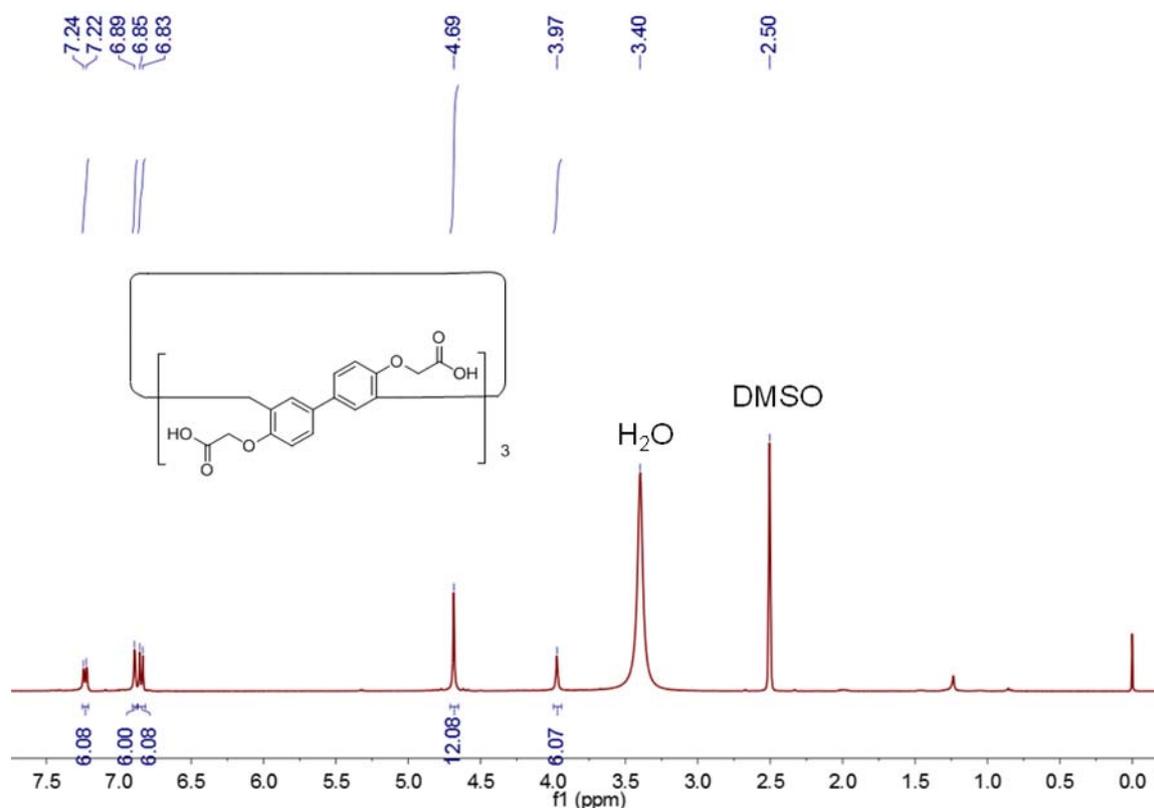


Figure S4. ¹H NMR spectrum (400 MHz, DMSO-*d*₆, 293K) of **3**.

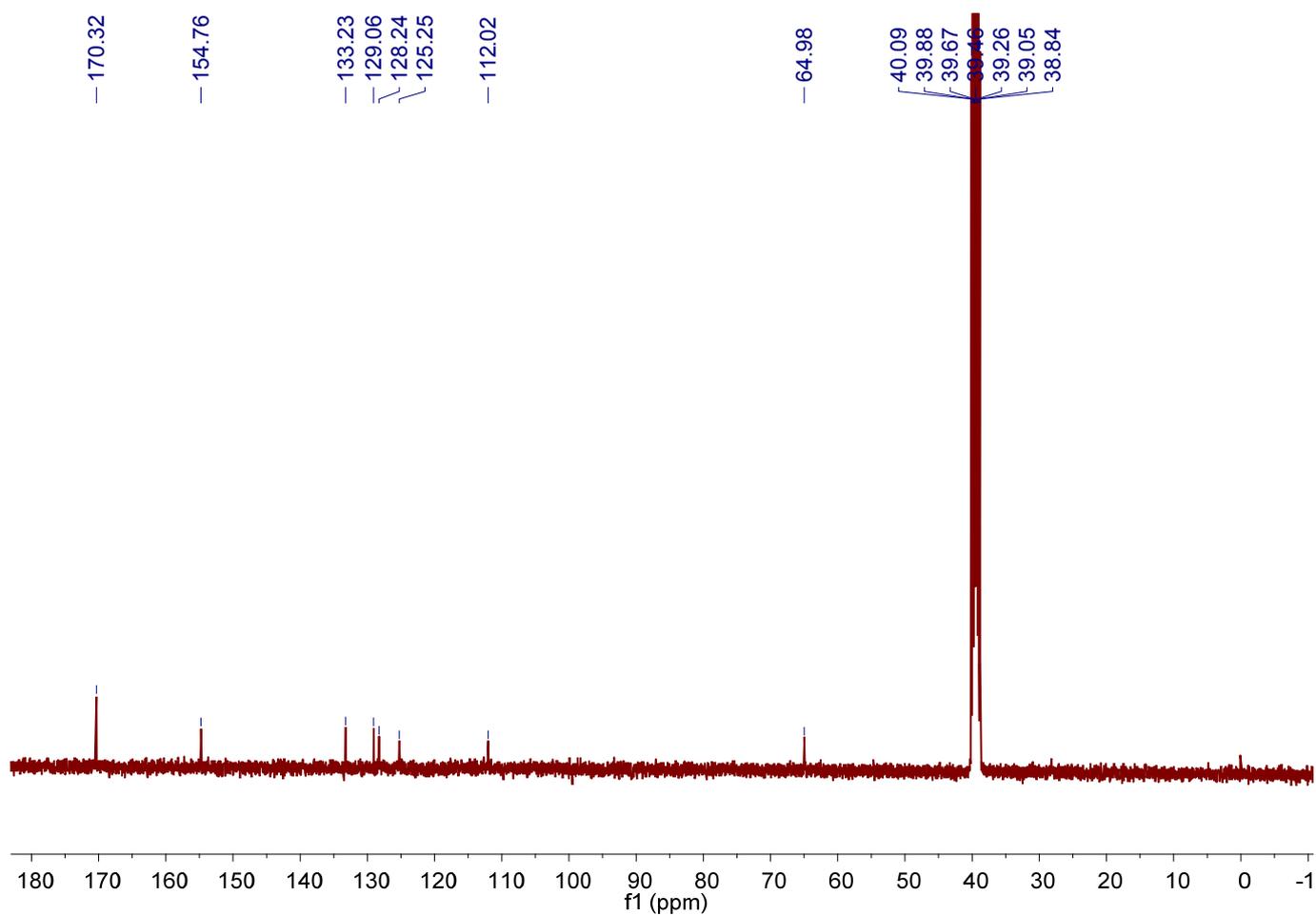


Figure S5. ^{13}C NMR spectrum (100 MHz, $\text{DMSO-}d_6$, 293K) of **3**.

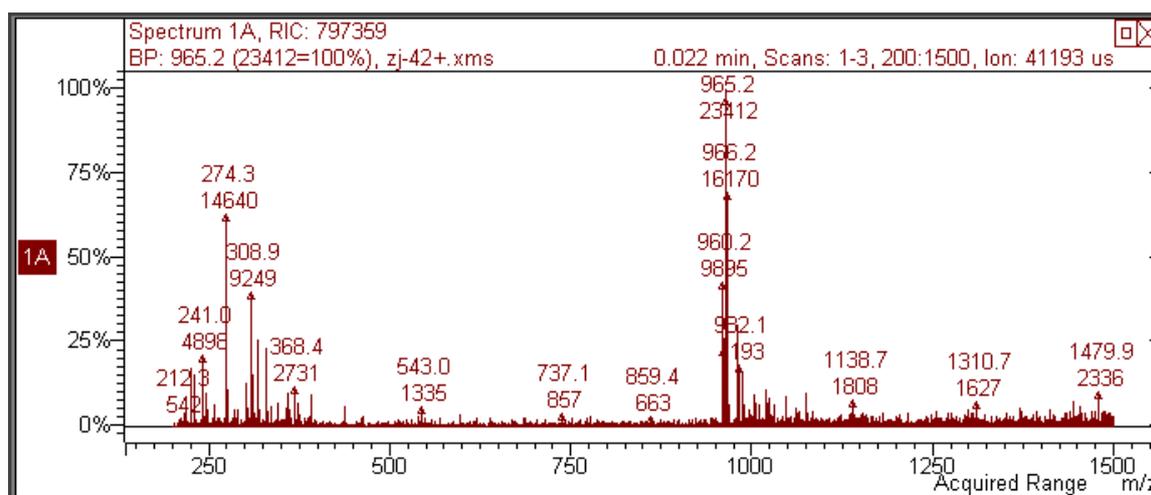


Figure S6. Electrospray ionization mass spectrum of **3**. Assignment of the main peak: m/z 965.2 $[\text{M} + \text{Na}]^+$.

2.3. Synthesis of water-soluble biphen[3]arene **WB3**

Synthesis of **WB3**: Compound **3** (100 mg, 0.106 mmol) and ammonium hydroxide solution (25–28 %, 25 mL) were stirred at room temperature for 2 h. Water was then removed by rotary evaporation to gain **WB3** as a white powder (110 mg, 100%), mp: > 300 °C. The ^1H NMR spectrum of **WB3** is shown in Figure S7. ^1H NMR (400 MHz, D_2O , 293 K) δ (ppm): 7.41 (d, $J = 8$ Hz, 6H), 7.18 (s, 6H), 6.89 (d, $J = 8$ Hz, 6H), 4.44 (s, 36H), 3.92 (s, 12H), 4.10 (s, 6H). The ^{13}C NMR spectrum of **WB3** is shown in Figure S8. ^{13}C NMR (100 MHz, D_2O , 293 K) δ (ppm): 187.23, 165.23, 161.83, 160.18, 157.65, 144.81, 99.42, 60.65 and 29.18. LRESIMS is shown in Figure S9: m/z 941.5 $[\text{M} - 6\text{NH}_4 + 5\text{H}]^-$. HRESIMS: m/z calcd for $[\text{M} - 6\text{NH}_4 + 5\text{H}]^-$ $\text{C}_{51}\text{H}_{41}\text{O}_{18}^-$, 941.2293; found 941.2246; error 5 ppm.

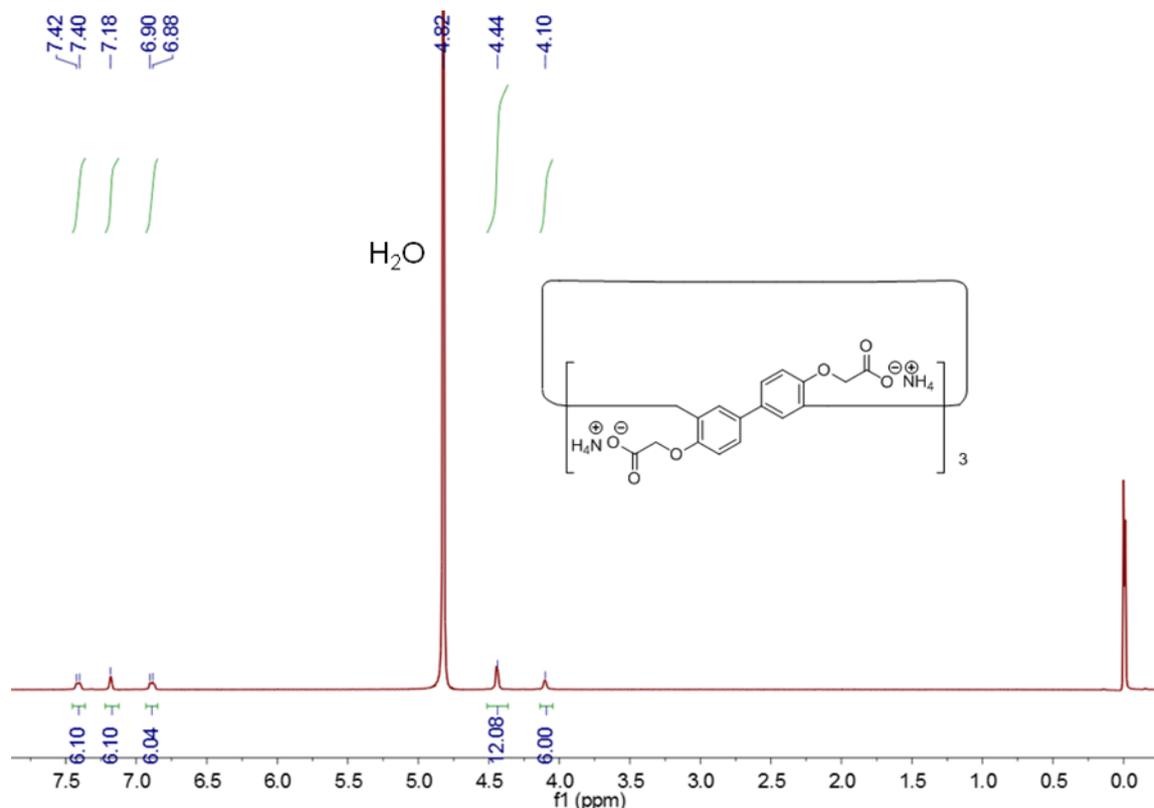


Figure S7. ^1H NMR spectrum (400 MHz, D_2O , 293K) of **WB3**.

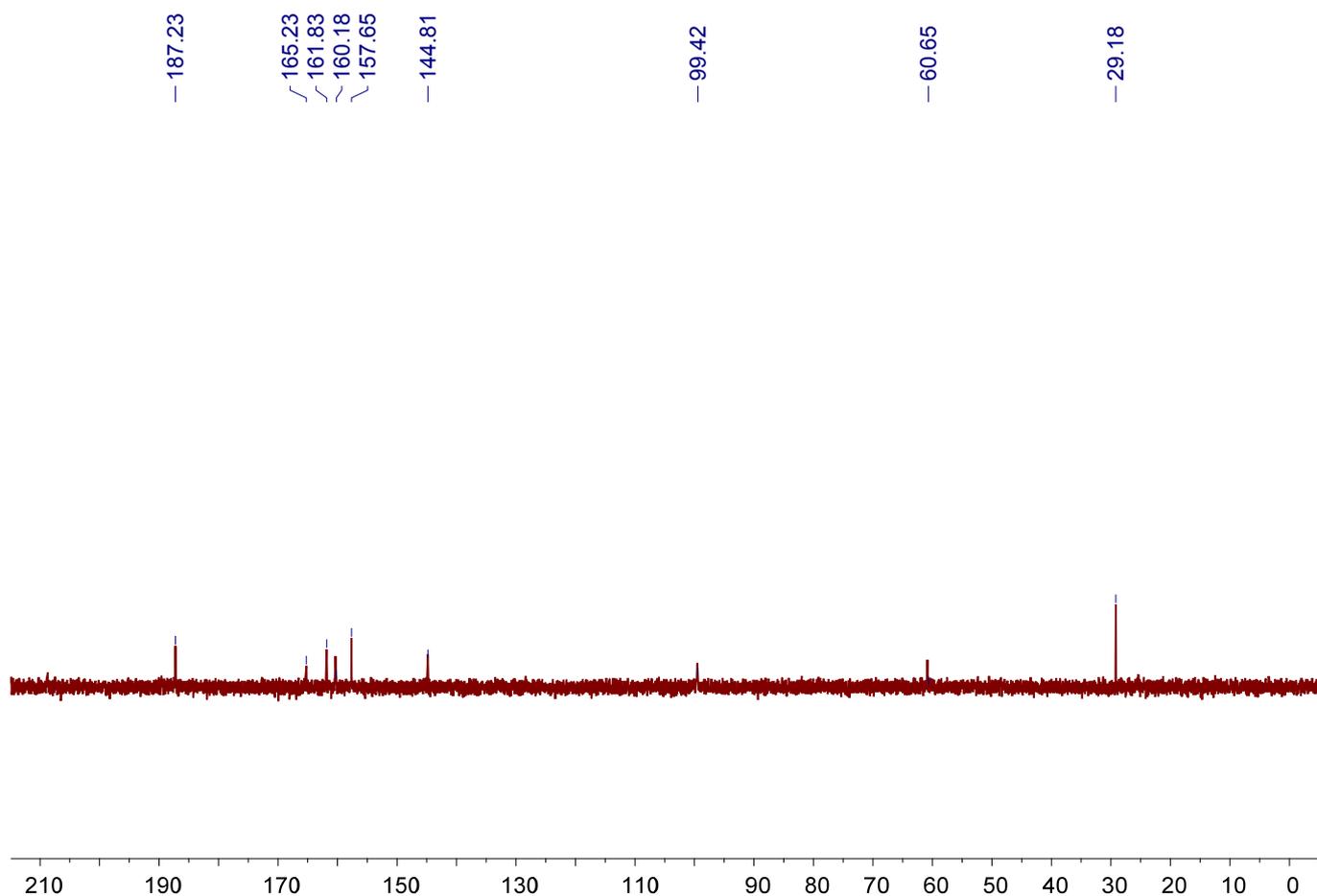


Figure S8. ^{13}C NMR spectrum (125 MHz, D_2O , 293K) of **WB3**.

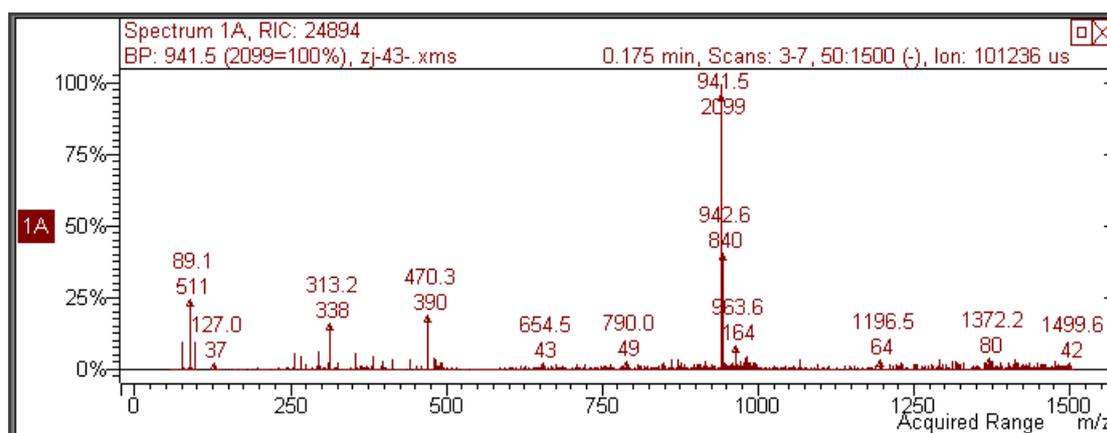


Figure S9. Electrospray ionization mass spectrum of **WB3**. Assignment of the main peak: m/z 941.5 [$\text{M} - 6\text{NH}_4 + 5\text{H}$].

3. Investigation of the interactions between model compound **G'** and **WB3**

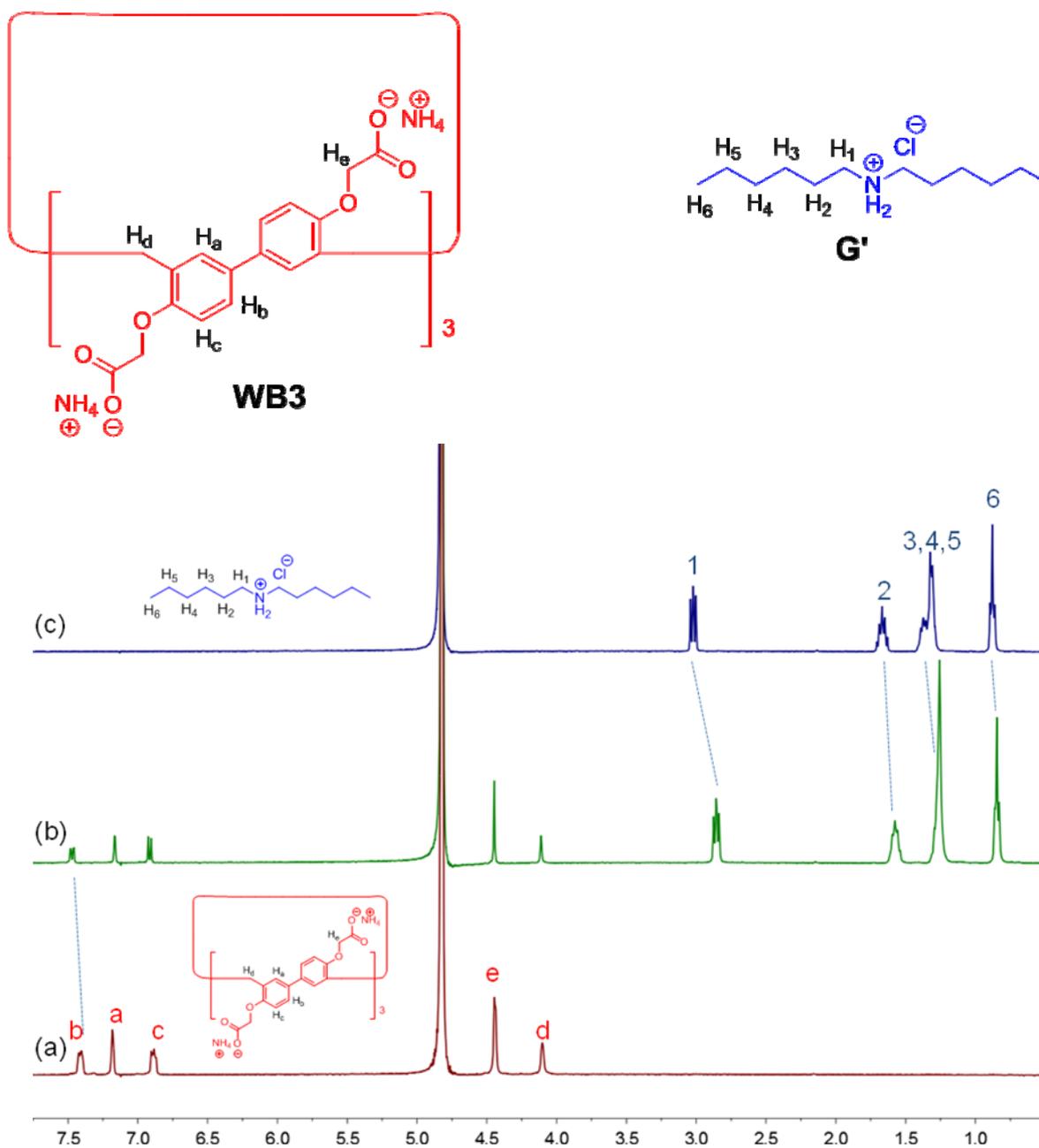


Figure S10. Partial ¹H NMR spectra (400 MHz, D₂O, room temperature): (a) **WB3** (1.00 mM); (b) **WB3** (1.00 mM) and model compound **G'** (5.00 mM); (c) model compound **G'** (1.00 mM).

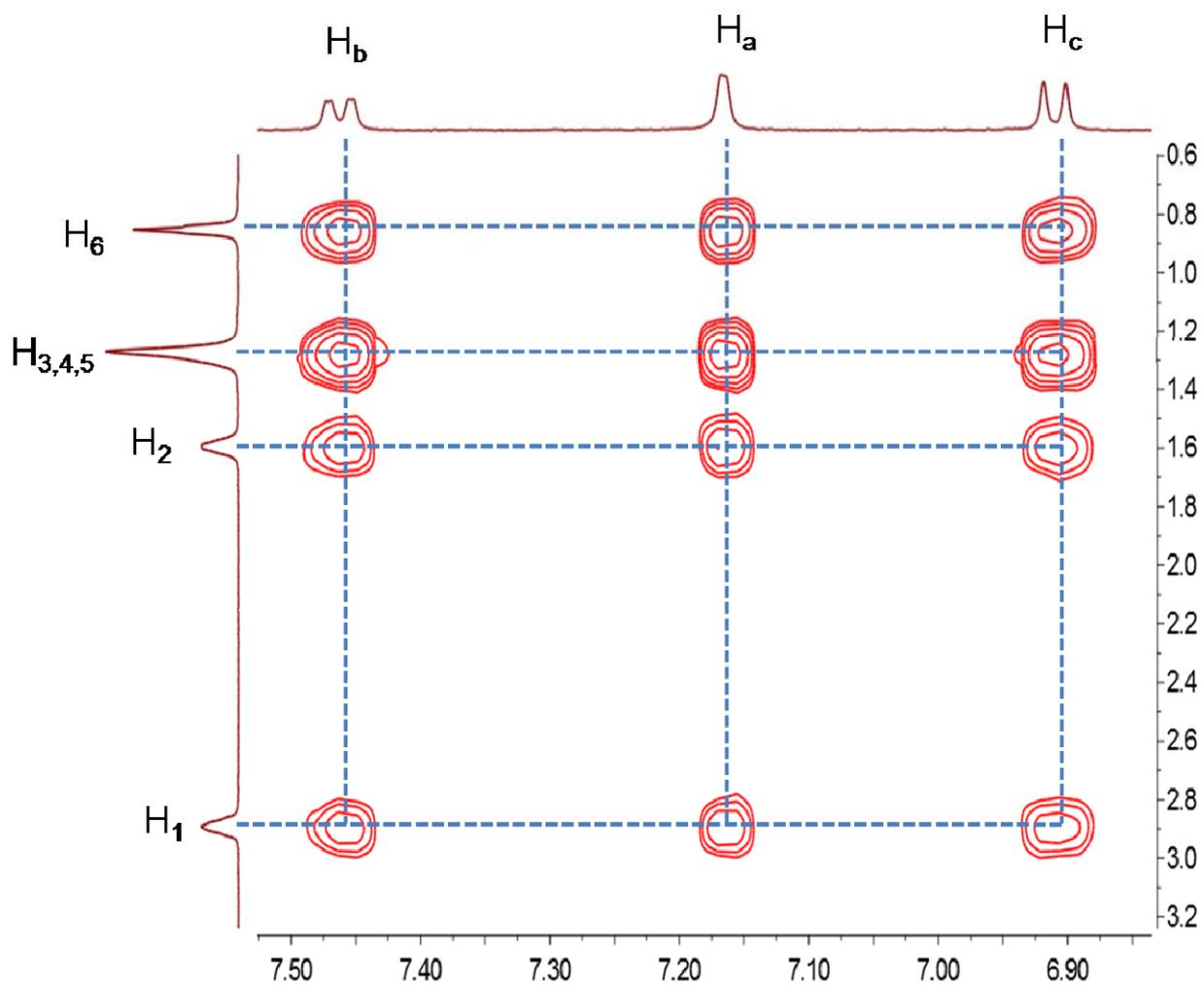


Figure S11. Partial NOESY NMR spectrum (500 MHz, D₂O, room temperature) of **WB3** (5.00 mM) and model compound **G'** (25.0 mM).

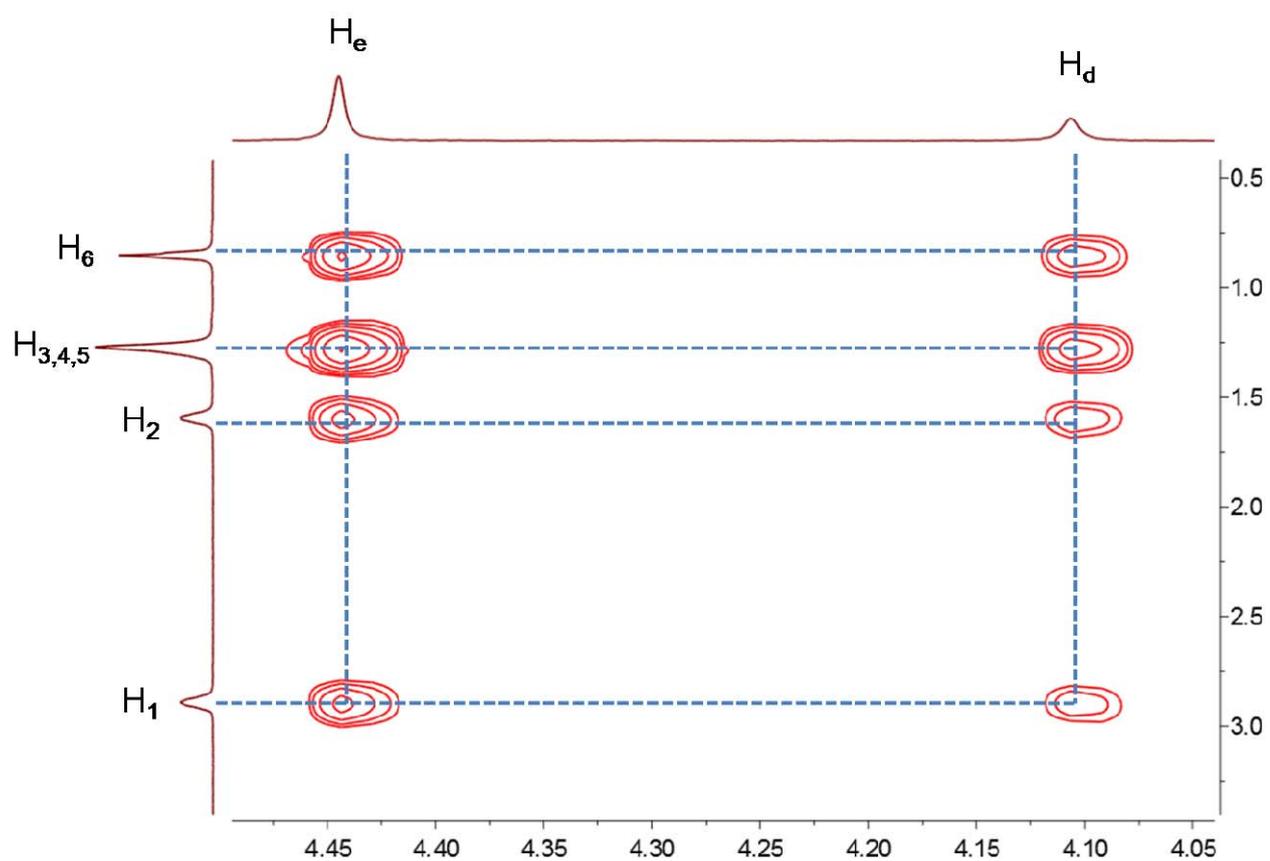


Figure S12. Partial NOESY NMR spectrum (500 MHz, D₂O, room temperature) of **WB3** (5.00 mM) and model compound **G'** (25.0 mM).

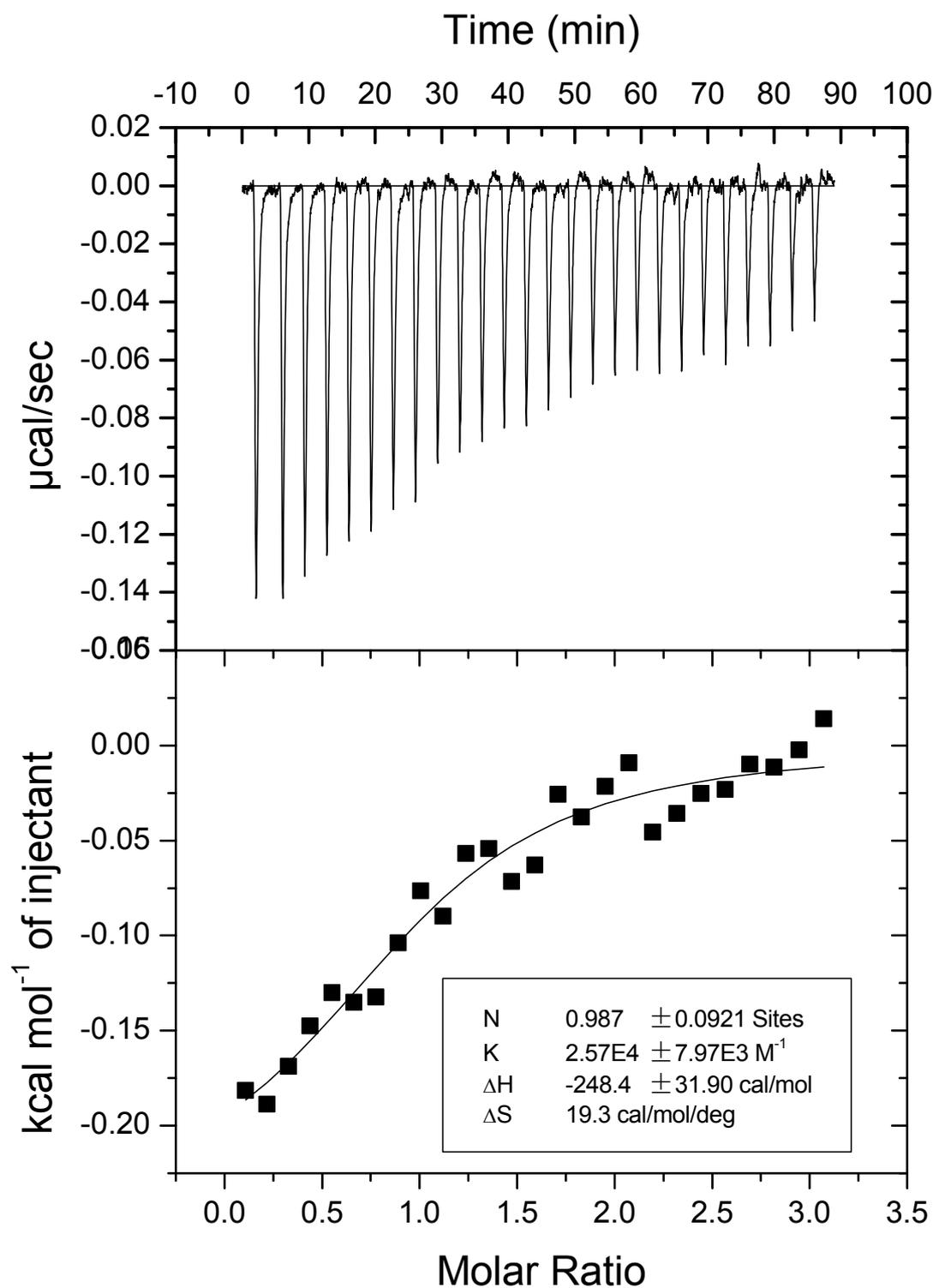


Figure S13. Microcalorimetric titration of **WB3** with **G'** in water at 298.15 K. (Top) Raw ITC data for 26 sequential injections (10 μ L per injection) of a **G'** solution (2.00 mM) into a **WB3** solution (0.100 mM). (Bottom) Net reaction heat obtained from the integration of the calorimetric traces.

4. pH-responsiveness of water-soluble biphen[3]arene **WB3**

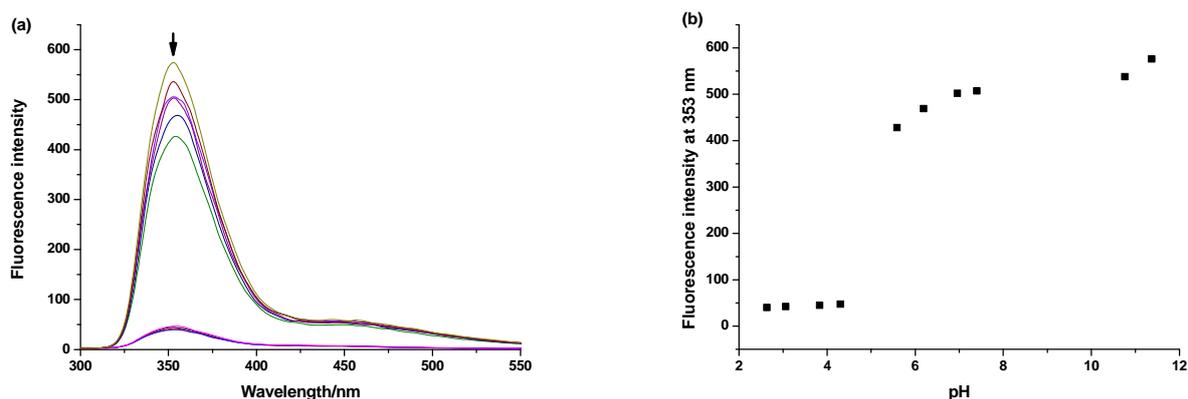


Figure S14. (a) Fluorescence emission spectra of **WB3** (2.00×10^{-5} M) with different pH values; (b) fluorescence intensity at 353 nm decreased gradually when the pH value of the solution changed from 11.37 to 2.63.

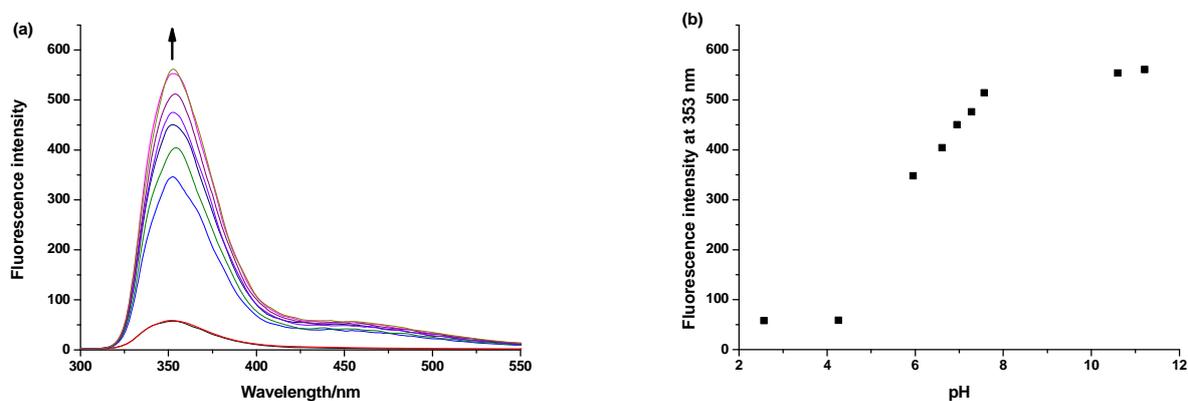


Figure S15. (a) Fluorescence emission spectra of **WB3** (2.00×10^{-5} M) with different pH values; (b) fluorescence intensity at 353 nm increased gradually when the pH value of the solution changed from 2.57 to 11.21.

5. Fluorescence spectroscopy studies of the aggregation behaviors

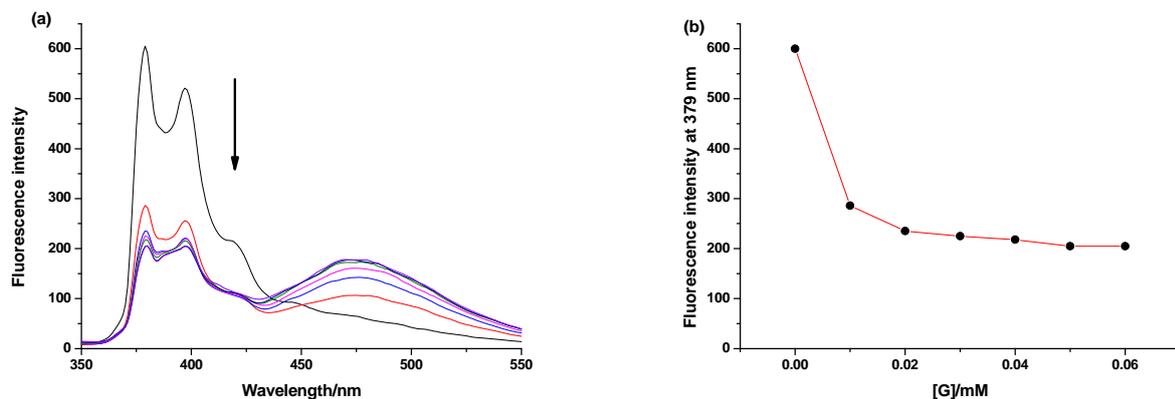


Figure S16. (a) Fluorescence emission spectra of pyrene in aqueous solutions at different concentrations of **G** in the presence of 10.0 μM **WB3** at room temperature. (b) Dependence of the relative fluorescence intensity of pyrene on the **G** concentration in the presence of 10.0 μM **WB3**. [pyrene] = 1.00 μM .

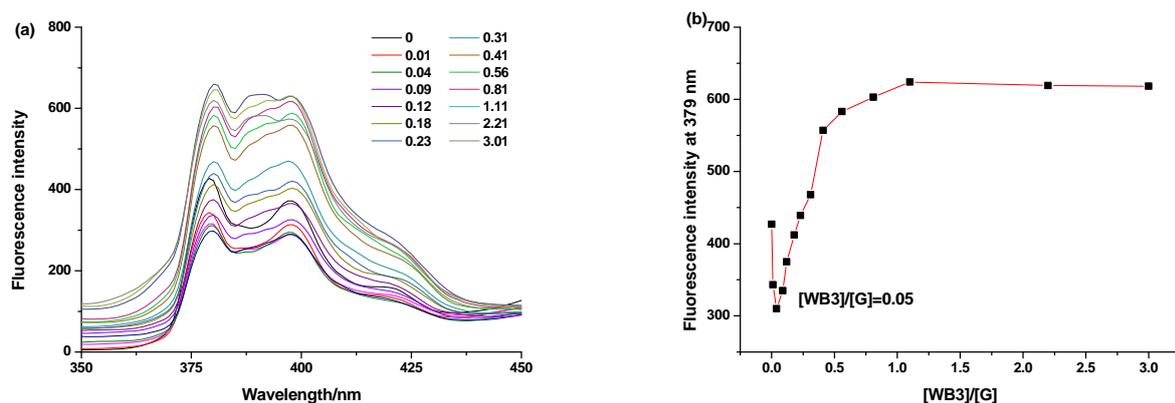


Figure S17. (a) Fluorescence emission spectra of pyrene in aqueous solutions of **G** (80.0 μM) by increasing the concentration of **WB3** from 0 to 240 μM (0~3 equiv) at room temperature. (b) Dependence of the relative fluorescence intensity of pyrene on **WB3** concentration with a fixed concentration of **G** (80.0 μM) at room temperature. [pyrene] = 1.00 μM .

6. Critical aggregation concentration (CAC) determination of **G** and **WB3**⊃**G**

Some parameters such as the conductivity, fluorescence intensity, osmotic pressure and surface tension of the solution change sharply around the critical aggregation concentration. The dependence of the solution conductivity on the solution concentration is used to determine the critical aggregation concentration. Typically, the slope of conductivity versus the concentration below CAC is steeper than the slope above the CAC. Therefore, the junction of the conductivity-concentration plot represents the CAC value. To measure the CAC values of **G** and **WB3**⊃**G**, the conductivities of the solutions at different concentrations (from 0 to 0.180 mM) were determined. By plotting the conductivity versus the concentration, we estimated the CAC values of **G** and **WB3**⊃**G**.

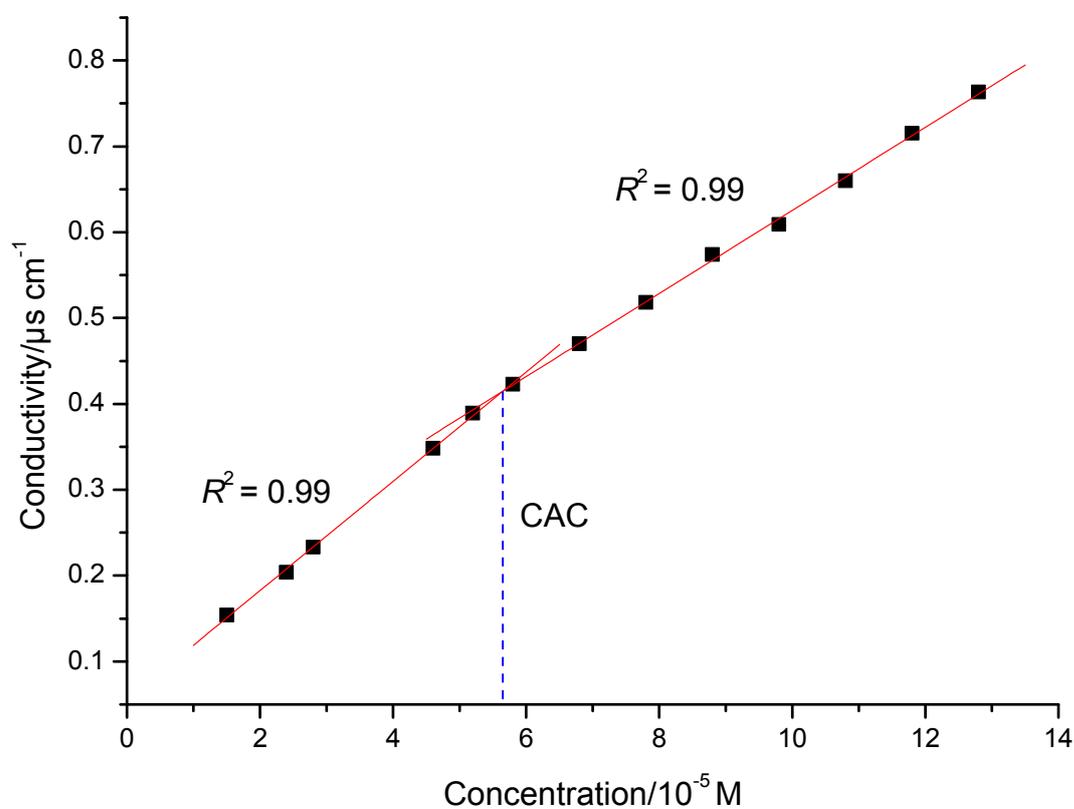


Figure S18. The concentration-dependent conductivity of **G**. The critical aggregation concentration was determined to be 5.65×10^{-5} M.

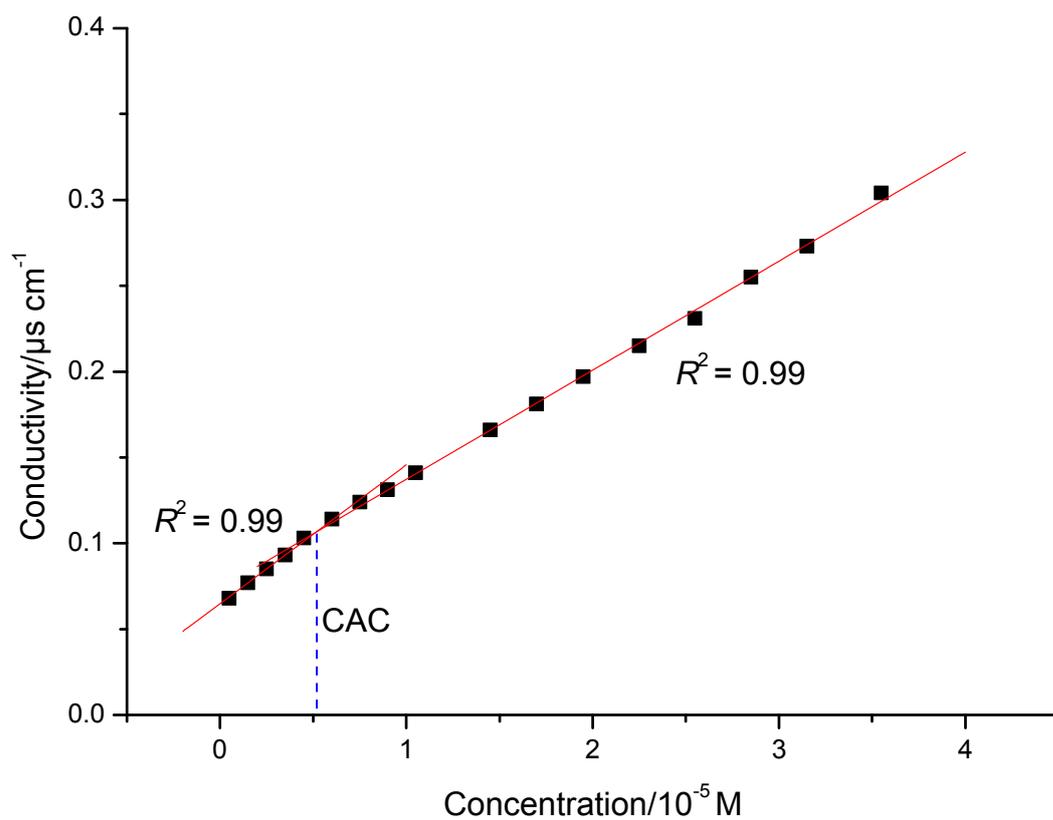


Figure S19. The concentration-dependent conductivity of **WB3D-G**. The critical aggregation concentration (CAC) was determined to be 5.20×10^{-6} M.

7. Self-assembly of **G** in water

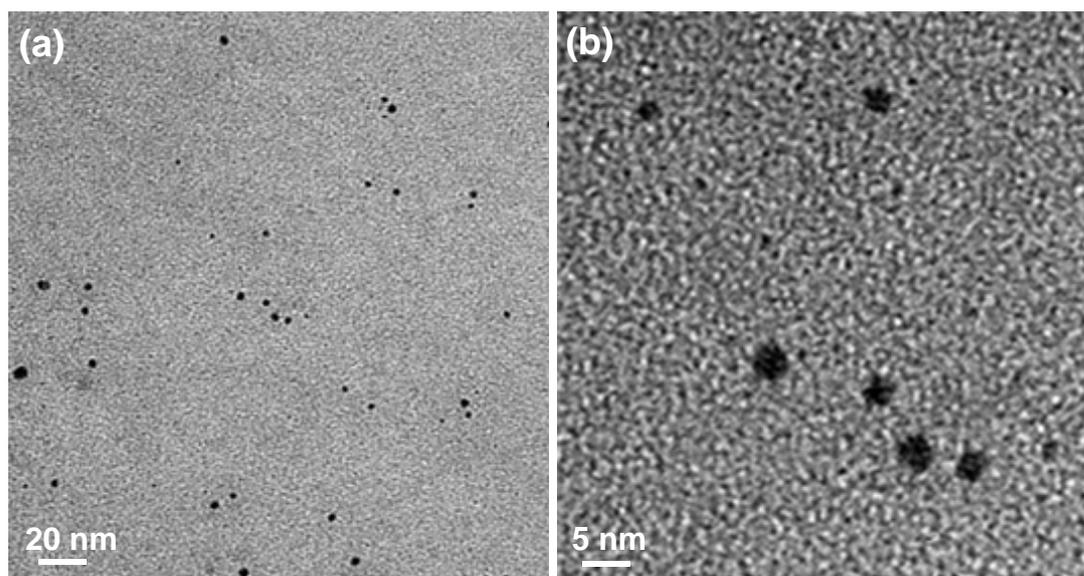


Figure S20. TEM images: (a) **G**; (b) enlarged image of (a).

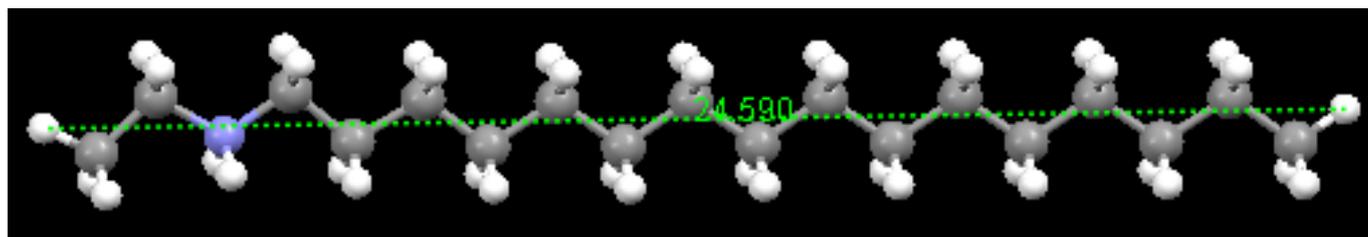


Figure S21. The energy-minimized structure of **G** obtained from ChemBio 3D Ultra 12.0 and Mercury 1.4.1. Chloride anion was omitted for clarity. The length of **G** molecule was calculated to be about 2.46 nm.

8. Controlled release of pyrene molecules

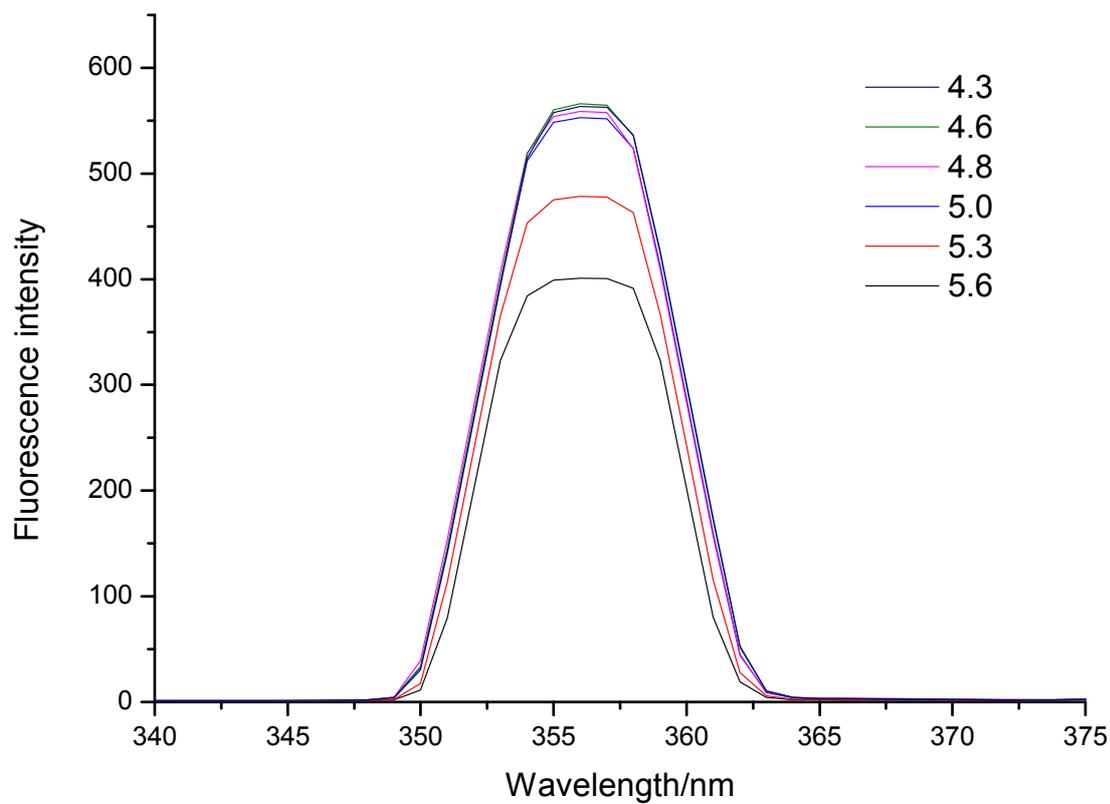


Figure S22. Fluorescence emission spectra of pyrene ($\lambda_{\text{ex}} = 350$ nm) encapsulated in a solution of **WB3** (0.100 mM) and **G** (2.00 mM) at different pH values.

References:

- S1. H. Chen, J. Fan, X. Hu, J. Ma, S. Wang, J. Li, Y. Yu, X. Jia and C. Li, *Chem. Sci.*, 2015, **6**, 197–202.
- S2. E. T. Borrows, B. M. C. Hargreaves, J. E. Page, J. C. L. Resuggan and F. A. Robinson, *J. Chem. Soc.*, 1947, 197–202.