Responsive Reverse Giant Vesicles and Gel from Self-Organization of a Bolaamphiphilic Pillar[5]arene

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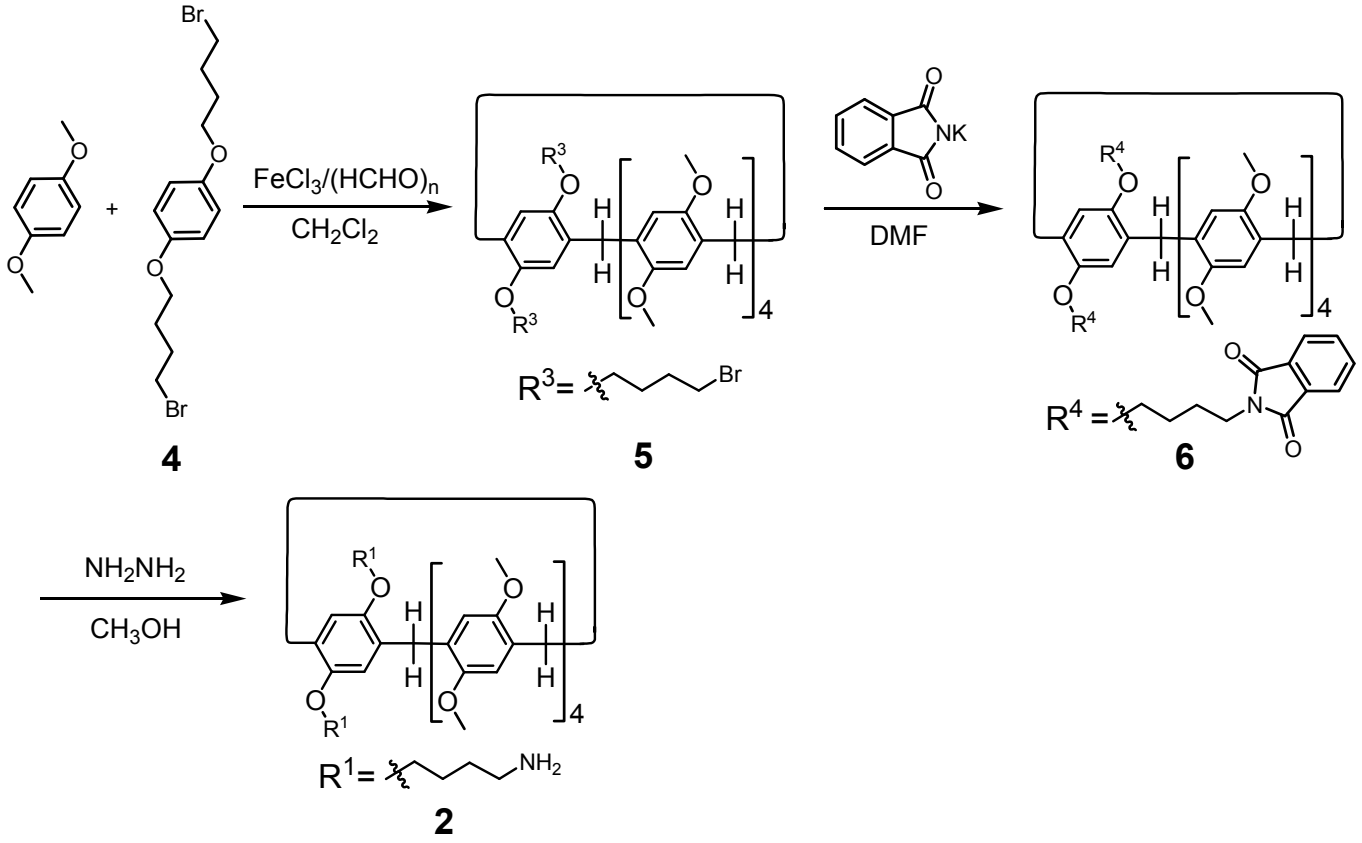
Electronic Supplementary Information (23 pages)

1. Materials and methods

All reagents were commercially available and used as supplied without further purification. Compounds **3**[S1] and 1,4-bis(4'-bromobutoxy)benzene[S2] were prepared according to published procedures. NMR spectra were recorded with a Bruker Avance DMX 500 spectrophotometer or a Bruker Avance DMX 400 spectrophotometer using the deuterated solvent as the lock and the residual solvent or TMS as the internal reference. Low-resolution electrospray ionization mass spectra were recorded with a Bruker Esquire 3000 Plus spectrometer. High-resolution mass spectrometry experiments were performed with IonSpec 4.7 Tesla FTMS. Elemental analysis experiment was performed with Vario MICRO cube. Transmission electron microscopy investigations were carried out on a JEM-1200EX instrument. Scanning electron microscopy investigations were carried out on a JEOL 6390LV instrument and a SIRTON-100 instrument. Dynamic light scattering was carried out on a Malvern Nanosizer S instrument at room temperature. Optical microscopy investigations were carried out on a Nikon ECLIPSE 80i instrument. Fluorescent microscopy investigations were carried out on an Axiovert 200 instrument. XRD patterns were acquired using a Rigaku Ultimate-IV X-ray diffractometer operating at 40 kV/40mA using Cu Kα line (λ = 1.5418 Å). FTIR spectroscopy investigations were carried out on a Thermo Nicoqt 6700 instrument.

*2. Syntheses of compounds **5**, **6**, **2** and **1***



Scheme S1. Synthetic route for **2**.

2.1. Synthesis of compound ***5***

A mixture of 1,4-dimethoxybenzene (2.20 g, 15.8 mmol), 1,4-bis(4-bromobutoxy)benzene (0.500 g, 1.30 mmol), paraformaldehyde (1.50 g, 48.4 mmol) and $FeCl_3$ (0.400 g, 2.47 mmol) was stirred in dichloromethane under nitrogen atmosphere at room temperature for 8 h. The solution was evaporated under vacuo and the residue was purified by flash column chromatography on silica gel (petroleum ether/dichloromethane = 40/1, *v*/*v*) to afford **5** as a light yellow solid (0.50 g, 40%), mp: 189.8–191.0 ºC. The ^{1}H NMR spectrum of compound **5** is shown in Figure S1. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ (ppm): 6.83–6.73 (m, 10H), 3.78 (s, 14H), 3.70–3.65 (m, 24H), 3.09 (s, 4H), 1.67 (s, 8H). The ^{13}C NMR spectrum of **5** is shown in Figure S2. ^{13}C NMR (125 MHz, $CDCl_3$, 298 K) δ (ppm): 150.84, 150.79, 150.75, 150.62, 149.88, 128.44, 128.32, 128.28, 128.22, 128.11, 114.95, 114.19, 113.98, 113.76, 67.34, 55.96, 55.94, 55.79, 55.72. LRESIMS is shown in Figure S3: *m*/*z* 1010.5 $[M + Na]^+$ (100%). HRESIMS: *m*/*z* calcd for $[M]^+$ $C_{51}H_{60}O_{10}Br_2^+$, 990.2551; found 990.2548, error –0.3 ppm.

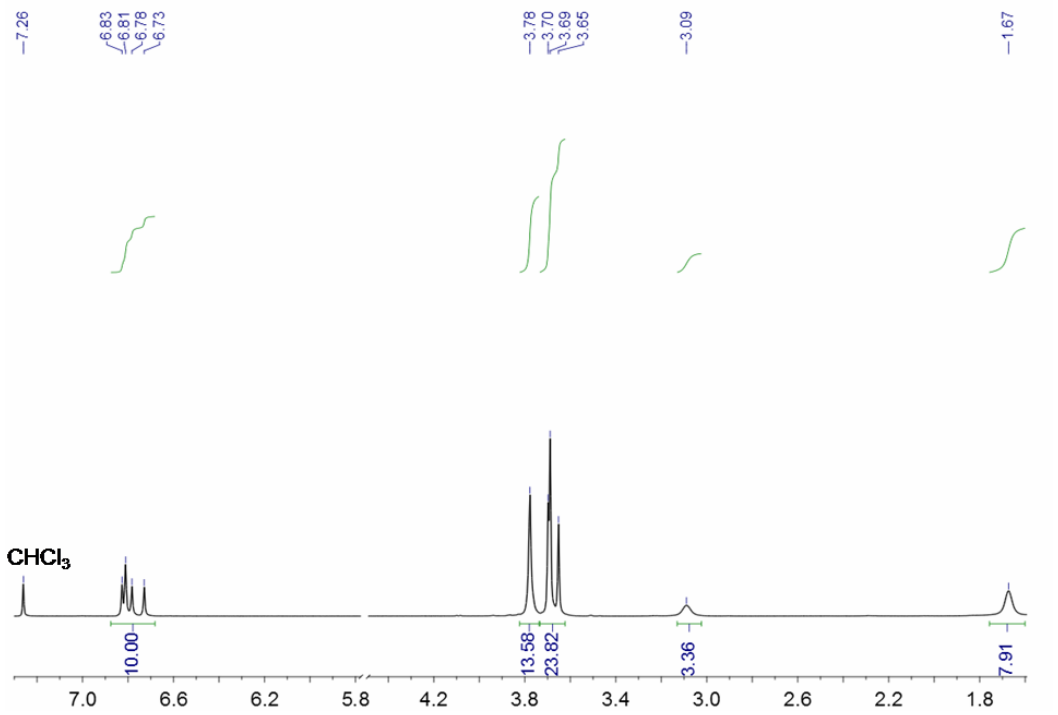


Figure S1. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 298 K) of **5**.

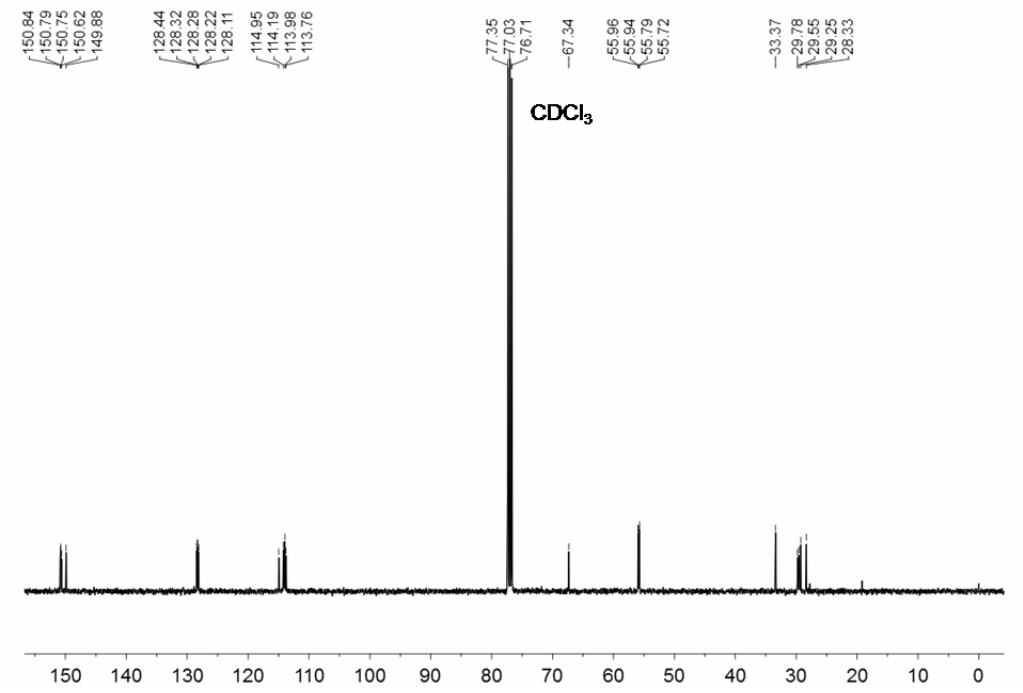


Figure S2. ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of **5**.

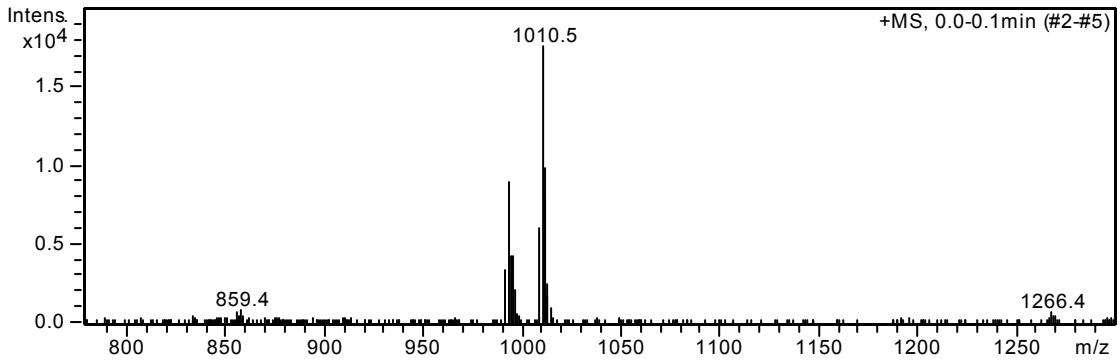


Figure S3. Electrospray ionization mass spectrum of **5.** Main peak: *m*/*z* 1010.5 $[M + Na]^+$ (100%).

2.2. Synthesis of compound ***6***

A mixture of **5** (1.00 g, 1.00 mmol) and potassium phthalimide (1.00 g, 5.00 mmol) was stirred in *N*,*N*-dimethylformamide at 90 ºC for 24 h. The solution was evaporated under vacuo and the residue was purified by flash column chromatography on silica gel (petroleum ether/dichloromethane = 2/1, *v*/*v*) to afford **6** as a yellow solid (1.00 g, 89%), mp: 70.5–72.1 ºC. The ^{1}H NMR spectrum of compound **6** is shown in Figure S4. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ (ppm): 7.84–7.77 (m, 4H), 7.73–7.71 (m, 4H), 6.76–6.71 (m, 10H), 3.85–3.82 (m, 4H), 3.78–3.58 (m, 38H), 1.94–1.92 (m, 4H), 1.86–1.82 (m, 4H). The ^{13}C NMR spectrum of **6** is shown in Figure S5. ^{13}C NMR (125 MHz, $CDCl_3$, 298 K) δ (ppm): 168.41, 166.84, 162.54, 150.84, 150.82, 150.77, 150.75, 149.97, 134.38, 33.97, 132.11, 131.69, 128.07, 123.22, 115.07, 114.24, 114.15, 113.96, 67.82, 55.84, 55.80, 55.77, 55.72. LRESIMS is shown in Figure S6: *m*/*z* 1125.7 $[M + H]^+$ (100%), 1142.8 $[M + H_2O]^+$ (60%). HRESIMS: *m*/*z* calcd for $[M + Na]^+$ $C_{67}H_{68}N_2O_{14}Na^+$, 1147.4563; found 1147.4562, error –0.08 ppm.

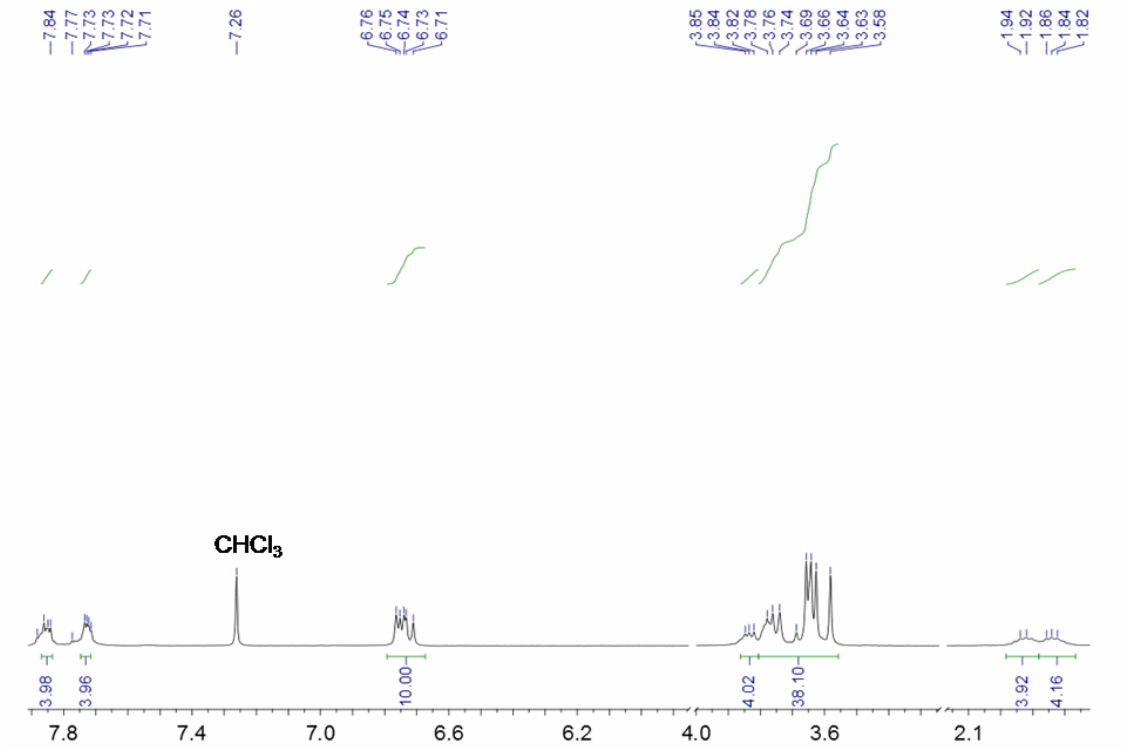


Figure S4. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 298 K) of **6**.

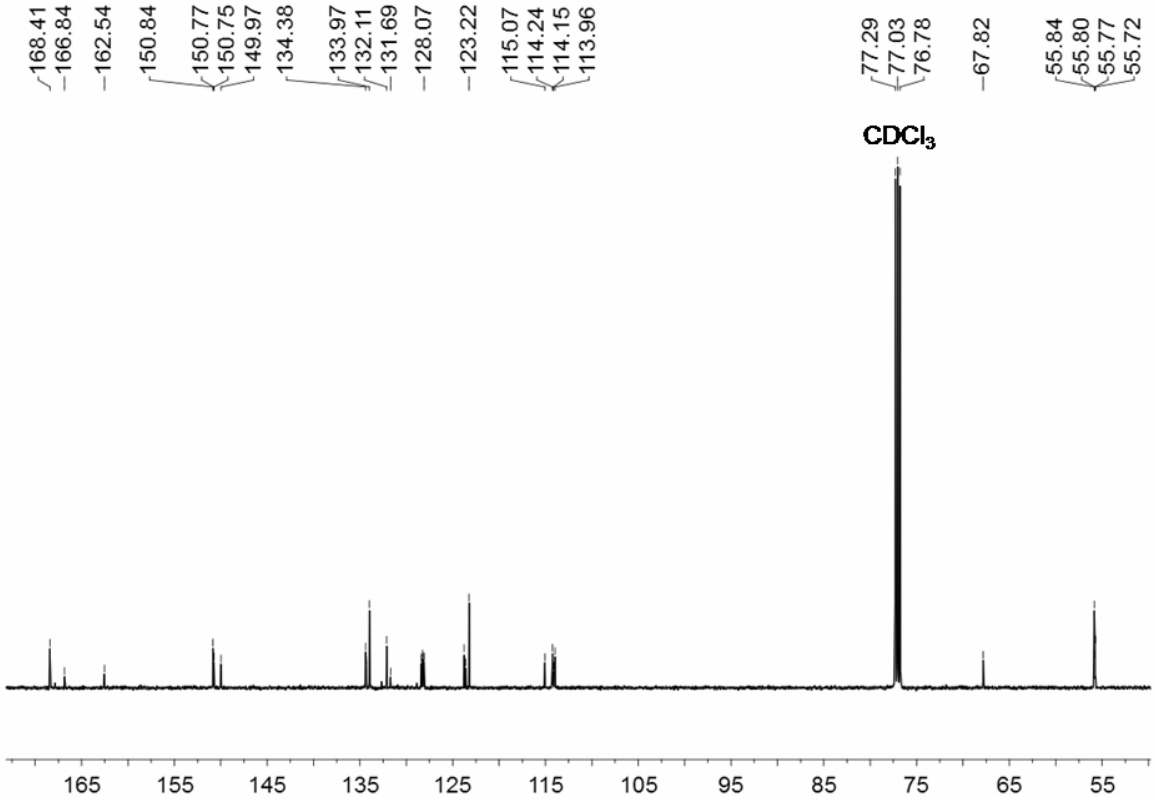


Figure S5. ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of **6**.

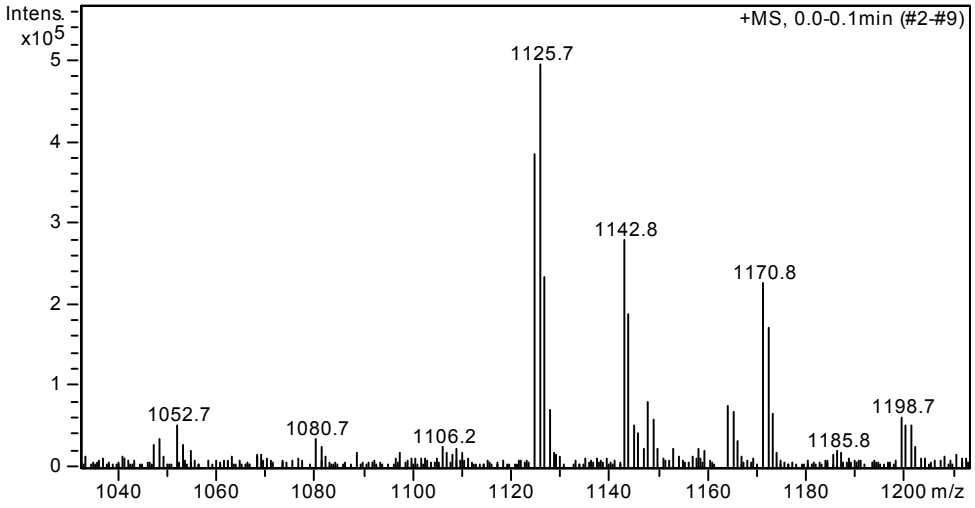


Figure S6. Electrospray ionization mass spectrum of **6.** Main peaks: *m/z* 1125.7 $[M + H]^+$ (100%), 1142.8 $[M + H_2O]^+$ (60%).

*2.3. Synthesis of compound **2***

A mixture of **6** (0.500 g, 0.400 mmol) and NH_2NH_2 (10 mL) was heated at reflux in methanol (10 mL) for 12 h. Then the mixture was filtered and the residue was washed with methanol (10 mL × 2) to give **7** as a white solid (0.20 g, 58%), mp: 163.4–165.1 ºC. The ^{1}H NMR spectrum of compound **2** is shown in Figure S7. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ (ppm): 6.80–6.76 (m, 10H), 3.86–3.83 (m, 4H), 3.77 (s, 10H), 3.68–3.65 (d, 24H), 2.47 (s, 4H), 1.95 (s, 4H), 1.70 (s, 4H), 1.44 (s, 4H). The ^{13}C NMR spectrum of **2** is shown in Figure S8. ^{13}C NMR (125 MHz, $CDCl_3$, 298 K) δ (ppm): 150.81, 150.69, 150.54, 149.81, 128.65, 128.57, 128.37, 128.27, 115.05, 114.58, 114.04, 113.71, 68.54, 56.19, 55.96, 55.90, 55.85, 55.80. LRESIMS is shown in Figure S9: *m/z* 865.6 $[M + H]^+$ (100%). HRESIMS: *m/z* calcd for $[M + H]^+$ $C_{51}H_{65}N_2O_{10}^+$, 865.4633; found 865.4636, error 0.3 ppm.

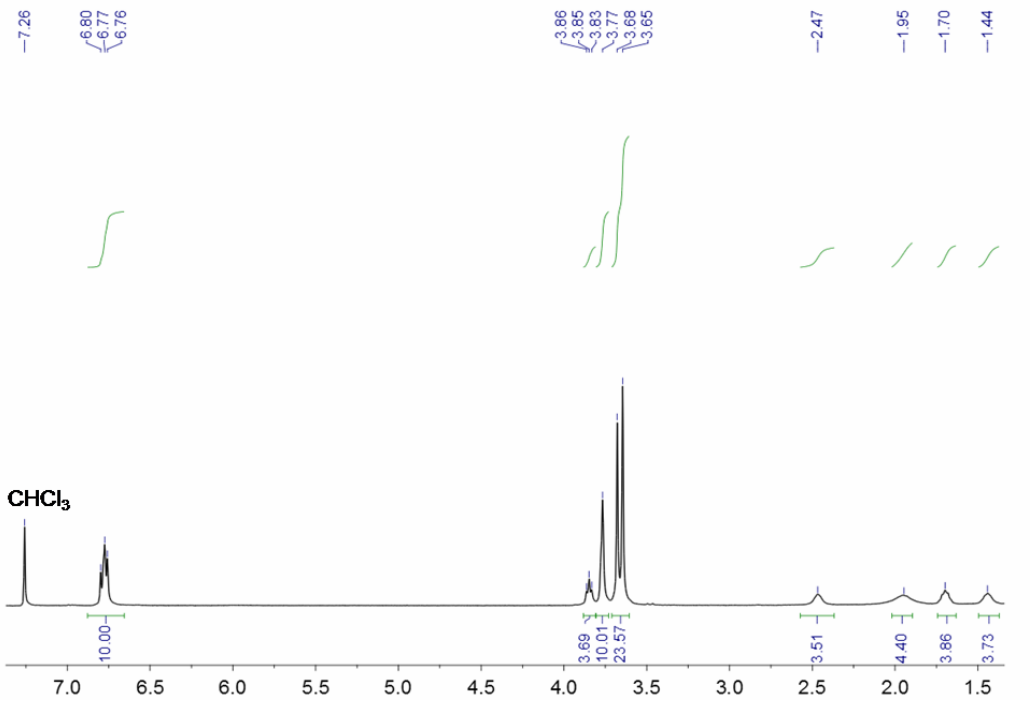


Figure S7. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 298 K) of **2**.

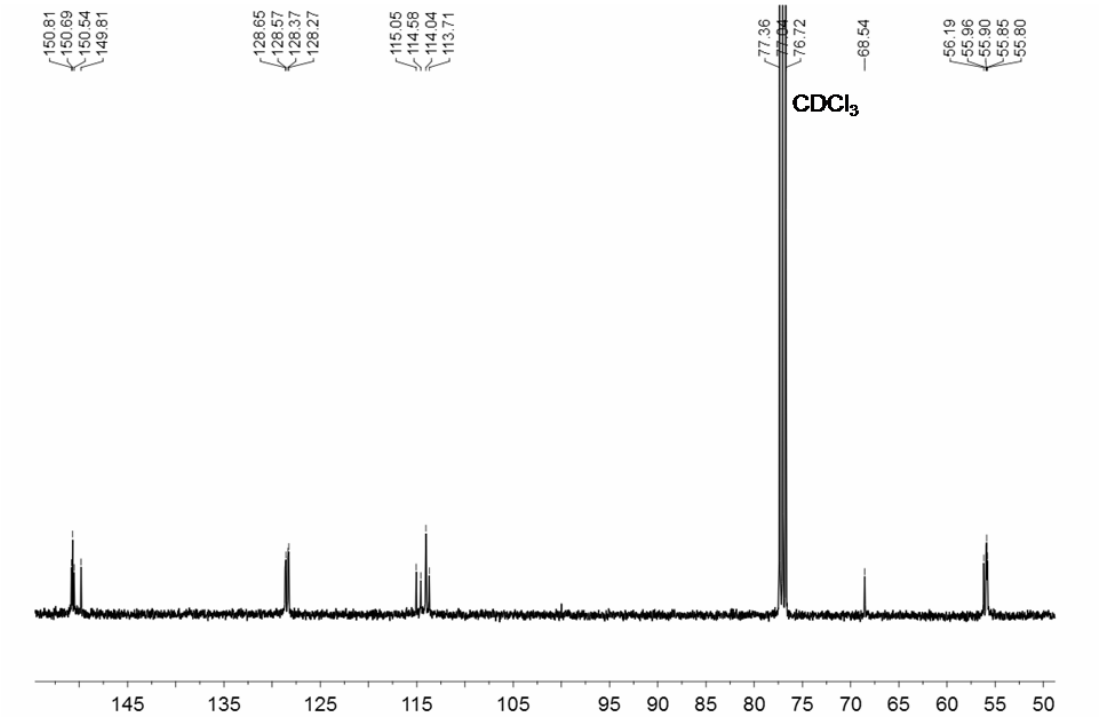


Figure S8. ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of **2**.

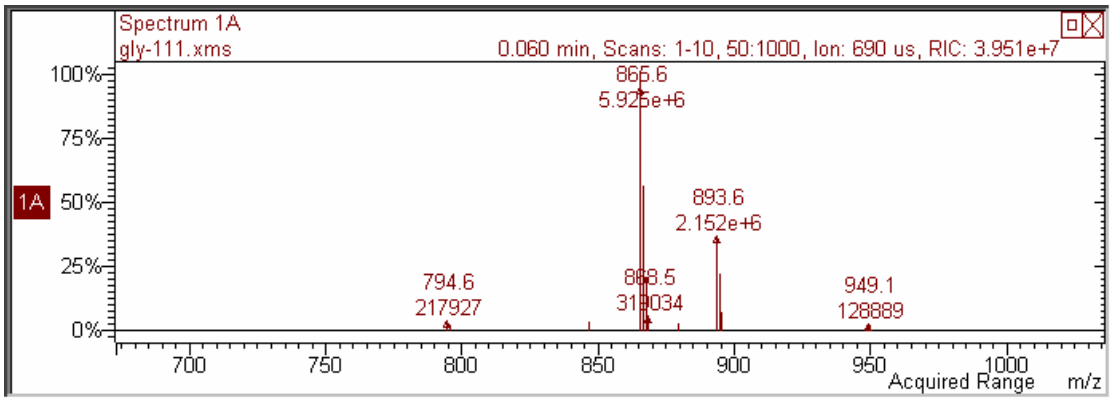


Figure S9. Electrospray ionization mass spectrum of **2.** Main peak: *m*/*z* 865.6 $[M + H]^+$ (100%).

*2.4. Synthesis of compound **1***

A mixture of **2** (0.100 g, 0.100 mmol), **3** (1.03 g, 0.200 mmol), 4-dimethylaminopyridine (DMAP, catalytic amount) and 1-(3'-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC, 1.77 g, 0.800 mmol) were stirred in dichloromethane (50 mL) for 8 h. The solution was evaporated under vacuo and the residue was purified by flash column chromatography on silica gel (dichloromethane/methanol = 10/1, *v*/*v*) to afford **1** as a yellow oil (0.13 g, 76%). The ^{1}H NMR spectrum of compound **1** is shown in Figure S10. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ (ppm): 7.45 (d, J = 1.6 Hz, 2H), 7.29 (dd, J = 8.4, 1.6 Hz, 2H), 6.87 (d, J = 8.4 Hz, 2H), 6.75 (s, 2H), 6.73–6.70 (m, 8H), 6.47–6.44 (m, 2H), 4.21–4.18 (m, 8H), 3.89–3.83 (m, 14H), 3.76–3.72 (m, 16H), 3.66–3.63 (m, 28H), 3.59–3.52 (m, 28H), 3.49–3.46 (m, 4H), 3.37 (s, 3H), 3.35 (s, 3H). The ^{13}C NMR spectrum of **1** is shown in Figure S11. ^{13}C NMR (125 MHz, $CDCl_3$, 298 K) δ (ppm): 167.12, 151.75, 151.12, 151.00, 150.95, 150.88, 150.05, 148.70, 128.54, 128.50, 128.38, 128.35, 128.24, 127.82, 120.37, 115.11, 114.65, 114.47, 114.32, 114.08, 113.82, 113.20,

72.04, 70.99, 70.87, 70.79, 70.76, 70.65, 70.59, 69.82, 69.70, 69.07, 68.77, 67.99, 59.14, 59.10, 56.27, 56.07, 55.96, 55.90. LRESIMS is shown in Figure S12: *m/z* 862.0 $[M + 2H]^{2+}$ (100%). HRESIMS: *m/z* calcd for $[M + Na]^+$ $C_{93}H_{128}N_2O_{28}Na^+$, 1743.8546; found 1743.8545, error –0.05 ppm.

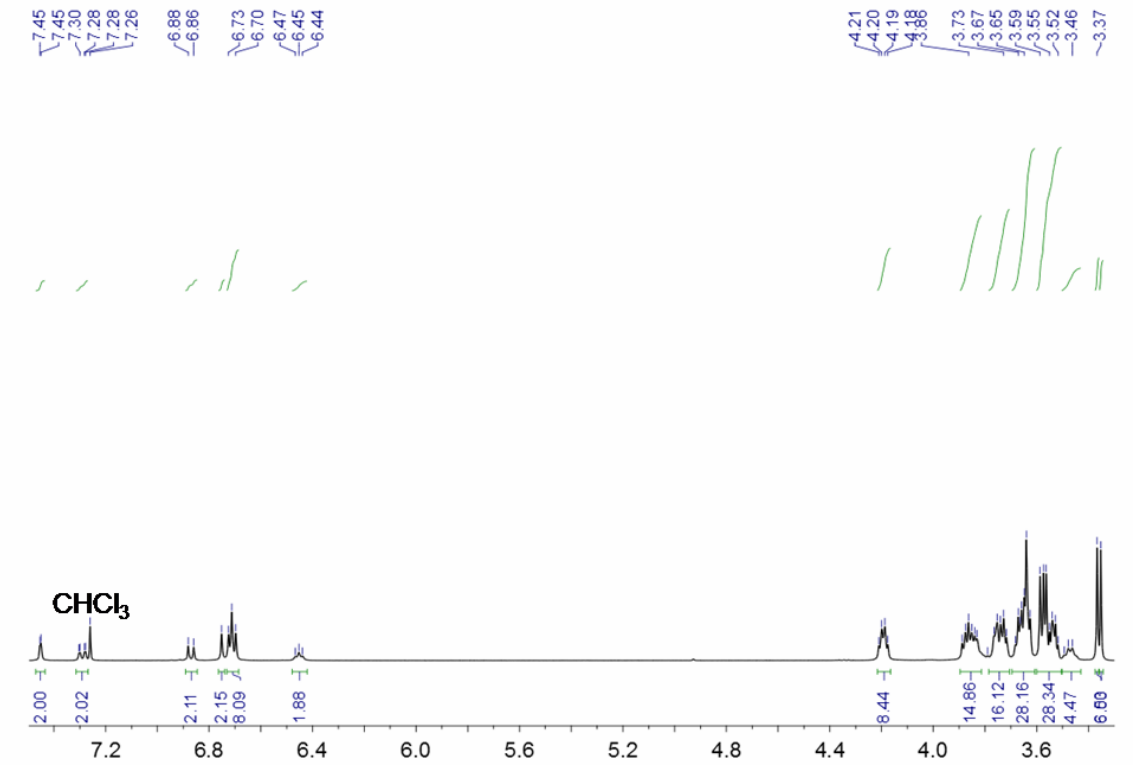


Figure S10. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 298 K) of **1**.

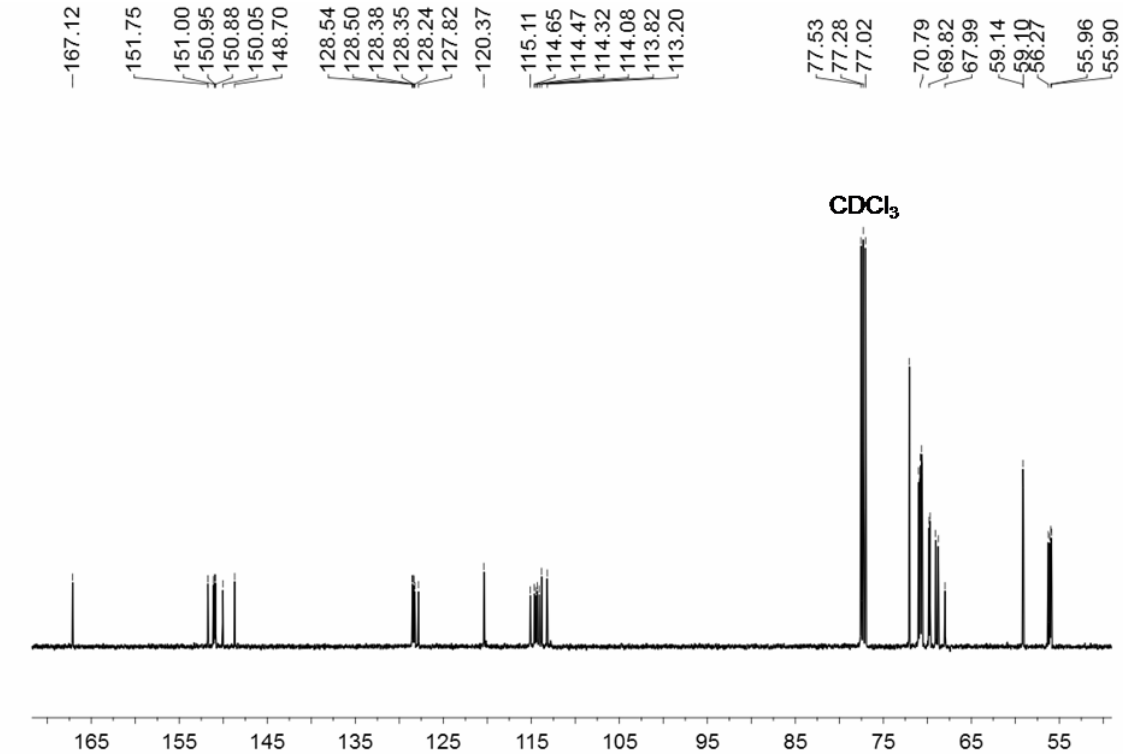


Figure S11. ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of **1**.

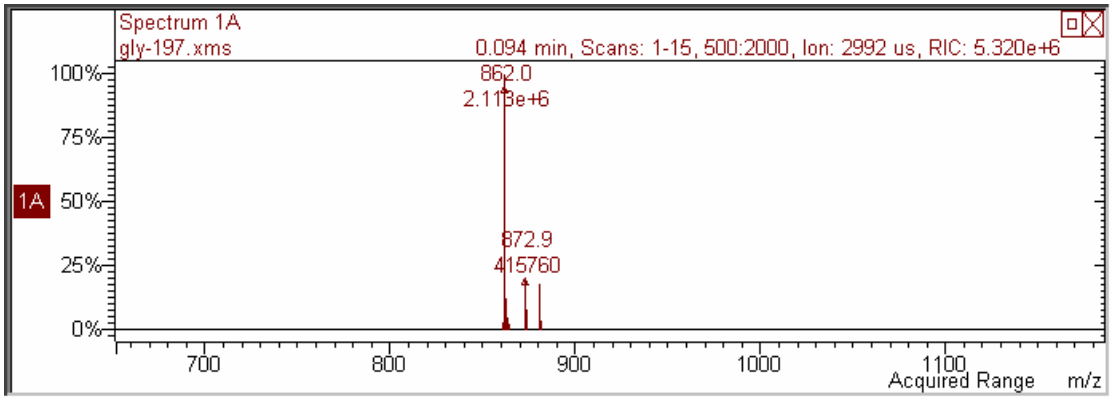
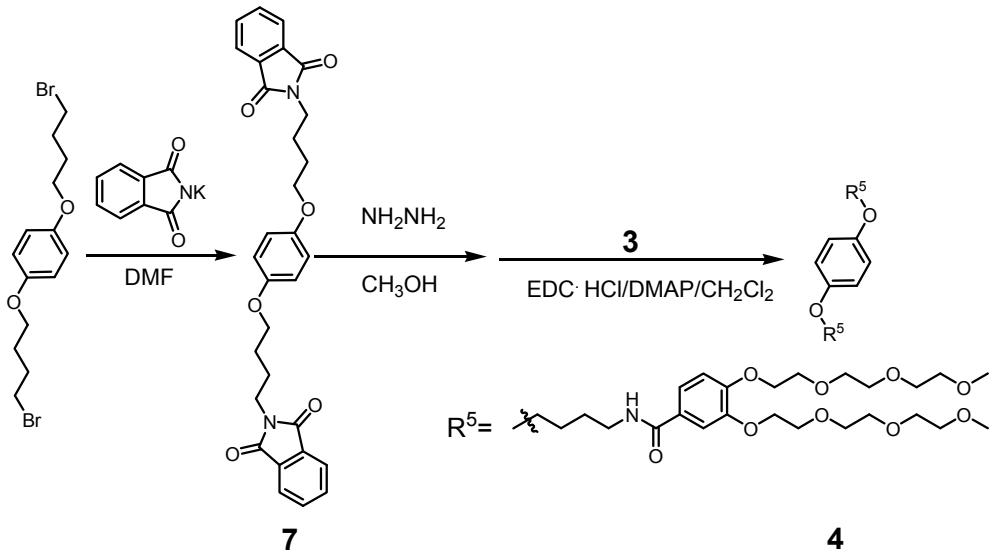


Figure S12. Electrospray ionization mass spectrum of **1.** Main peak: *m*/*z* 862.0 $[M + 2H]^{2+}$ (100%).

*3. Synthesis of model compound **4***



Scheme S2. Synthetic route for **8**.

3.1. Synthesis of compound 7

A mixture of 1,4-bis(4-bromobutoxy)benzene (1.00 g, 2.60 mmol) and potassium phthalimide (2.00 g, 10.0 mmol) was stirred in *N*,*N*-dimethylformamide at 90 ºC for 24 h. The solution was evaporated under vacuo and the residue was purified by flash column chromatography on silica gel (petroleum ether/dichloromethane = 10/1, *v*/*v*) to afford **7** as a yellow solid (1.10 g, 82%), mp: 72.1–74.8 ºC. The ^{1}H NMR spectrum of compound **7** is shown in Figure S13. ^{1}H NMR (400 MHz, DMSO-d_6, 298 K) δ (ppm): 8.06 (dd, J = 5.8, 3.3 Hz, 4H), 7.83 (dd, J = 5.8, 3.3 Hz, 4H), 6.82 (s, 4H), 3.88 (t, J = 6.3 Hz, 4H), 2.66 (t, J = 7.1 Hz, 4H), 1.72–1.68 (m, 4H), 1.56–1.52 (m, 4H). The ^{13}C NMR spectrum of **7** is shown in Figure S14. ^{13}C NMR (125 MHz, $CDCl_3$, 298 K) δ (ppm): 168.47, 153.13, 133.86, 132.15, 123.17, 115.39, 68.49, 68.41, 37.94. LRESIMS is shown in Figure S15: *m*/*z* 568.6 $[M + H_2O + K]^{+}$. HRESIMS: *m*/*z* calcd for $[M + C_4H_8]^{+}$ $C_{34}H_{28}N_2O_6^{+}$, 568.2573; found 568.2569, error –0.7 ppm.

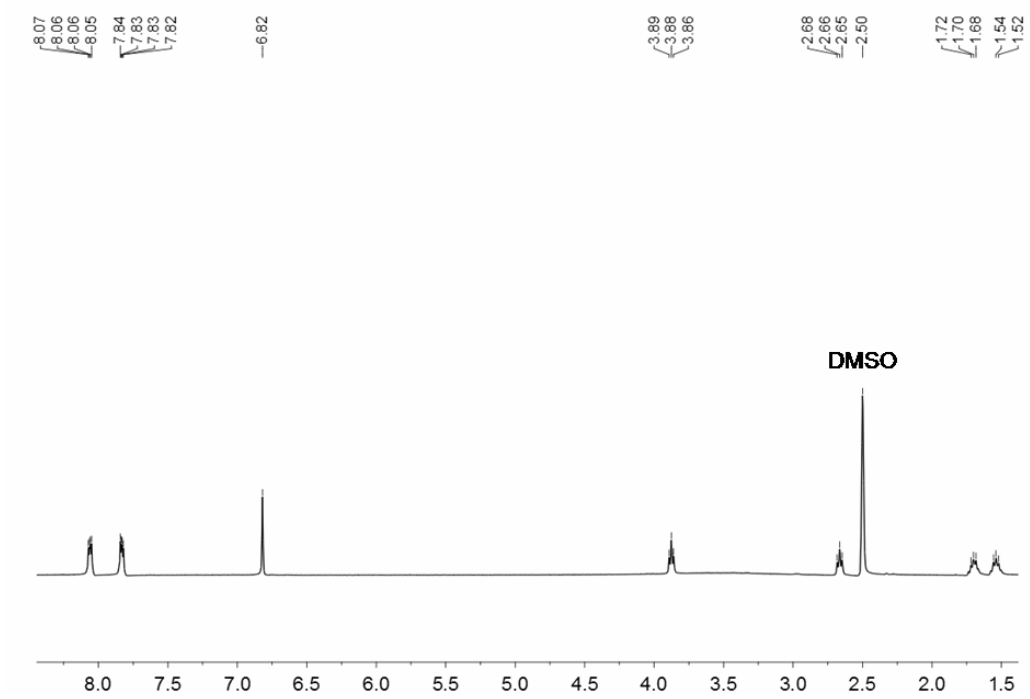


Figure S13. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, 298 K) of **7**.

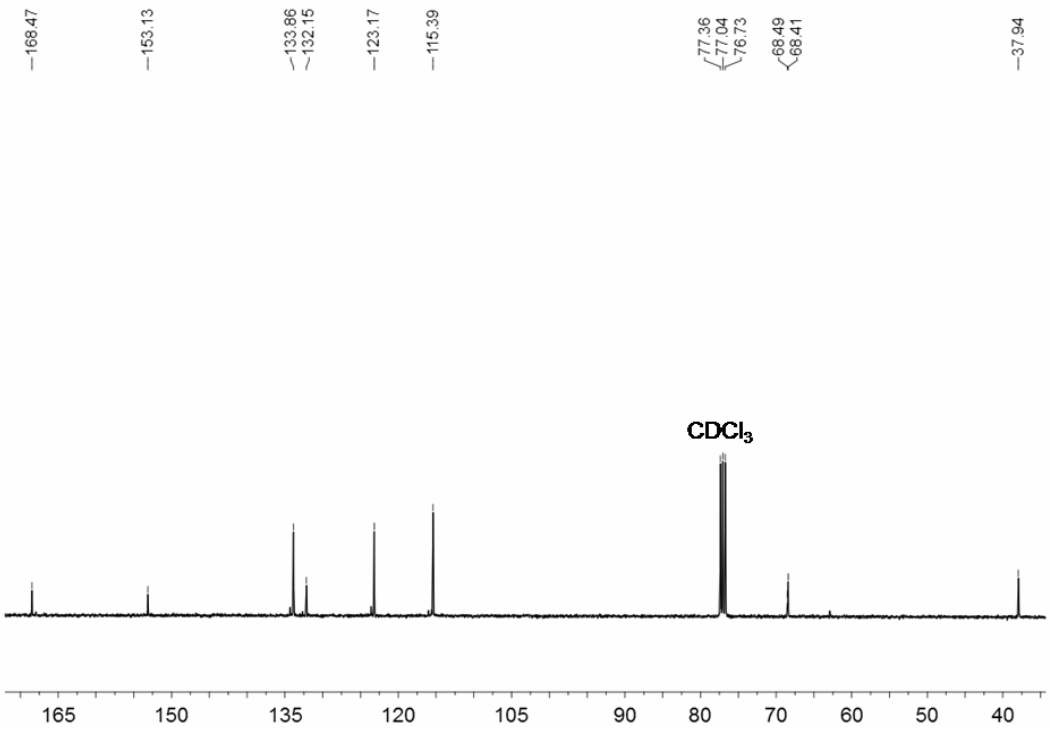


Figure S14. ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of **7**.

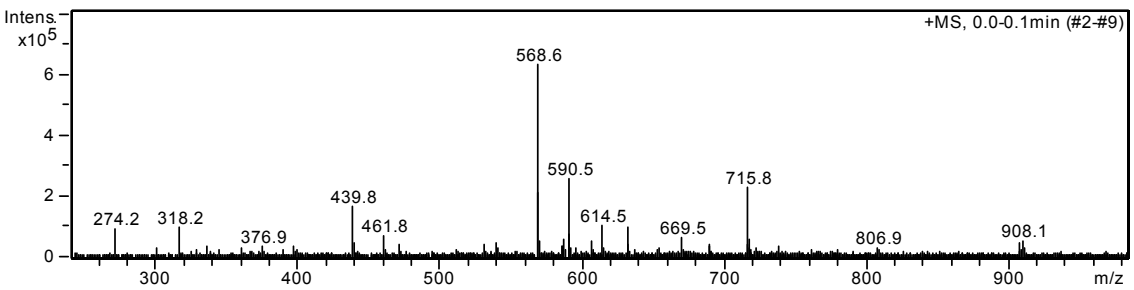


Figure S15. Electrospray ionization mass spectrum of **7**. Main peak: *m*/*z* 568.6 $[M + H_2O+K]^+$ (100%).

*3.2. Synthesis of compound **4***

A mixture of **7** (0.500 g, 0.400 mmol) and NH_2NH_2 (10 mL) was heated at reflux in methanol (10 mL) for 12 h. Then the mixture was filtered and the residue was washed with methanol (10 mL × 2) to get a crude product. Then a mixture of the crude product (0.200 g), **3** (0.350 g, 0.700 mmol), 4-dimethylaminopyridine (DMAP, catalytic amount) and 1-(3'-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC, 0.190 g, 0.900 mmol) were stirred in dichloromethane (30 mL) for 8 h. The solution was evaporated under vacuo and the residue was purified by flash column chromatography on silica gel (dichloromethane/methanol = 40/1, *v*/*v*) to afford **4** as a yellow oil (0.23 g, 60%). The ^{1}H NMR spectrum of compound **4** is shown in Figure S16. ^{1}H NMR (400 MHz, $CDCl_3$, 298 K) δ (ppm): 7.66 (d, J = 8.5 Hz, 2H), 7.57 (s, 2H), 6.91 (d, J = 8.5 Hz, 2H), 6.79 (d, 4H), 4.34 (q, J = 7.1 Hz, 4H), 4.22–4.20 (m, 8H), 3.90–3.88 (m, 12H), 3.71 (s, 8H), 3.68–3.66 (m, 20H), 3.54–3.53 (m, 8H), 3.37 (s, 12H), 1.50–1.48 (m, 4H). The ^{13}C NMR spectrum of **4** is shown in Figure S17. ^{13}C NMR (125 MHz, $CDCl_3$, 298 K) δ (ppm): 166.31, 153.12, 152.86, 148.25, 133.85, 132.16, 123.92, 123.38, 123.16, 115.38, 115.05, 112.73, 71.94, 70.92, 70.88, 70.70, 70.56, 69.64, 69.54, 68.83, 68.58, 68.40, 60.77, 60.77, 59.03, 59.03. LRESIMS is shown in Figure S18: *m*/*z* 981.9 $[M - C_6H_{14}O_4 + Na]^+$ (100%), *m*/*z* 889.9 $[M - C_{10}H_{21}O_6 + NH_4]^+$ (59%). HRESIMS: *m*/*z* calcd for $[M - C_6H_{14}O_4 + Na]^+$ $C_{50}H_{74}N_2NaO_{16}^+$, 981.4936; found 981.4928, error –0.8 ppm.

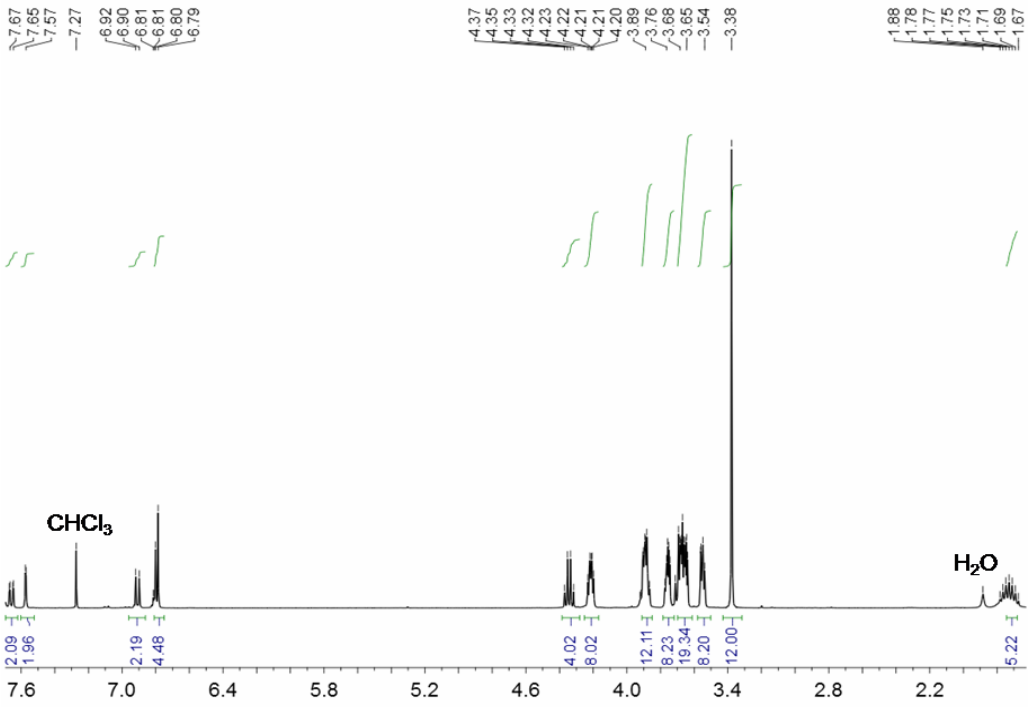


Figure S16. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 298 K) of **4**.

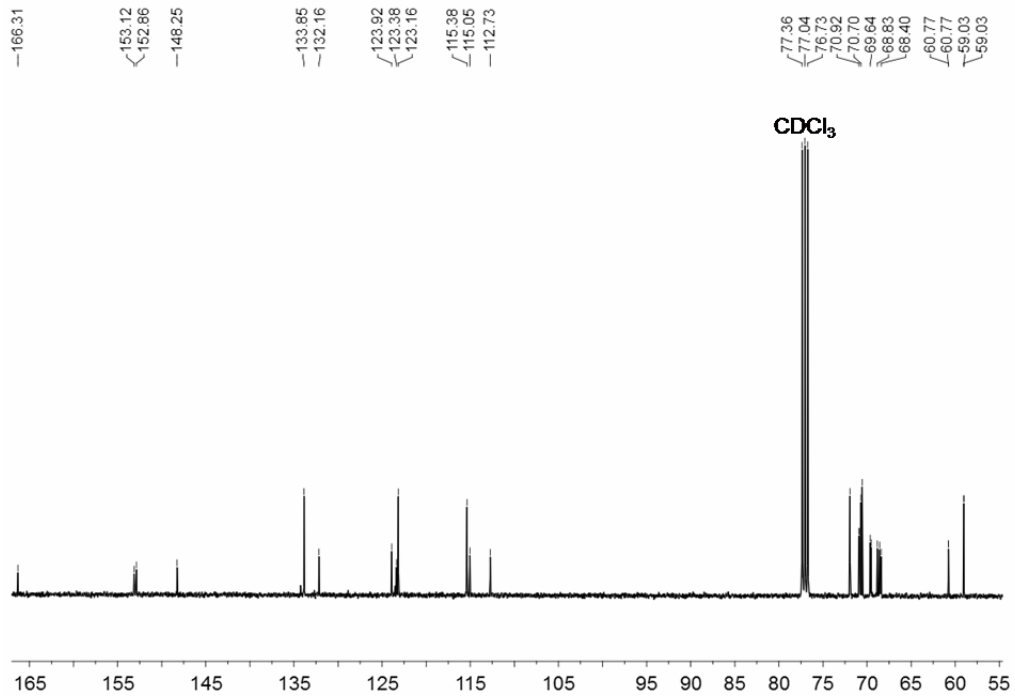


Figure S17. ^{13}C NMR spectrum (125 MHz, $CDCl_3$, 298 K) of **4**.

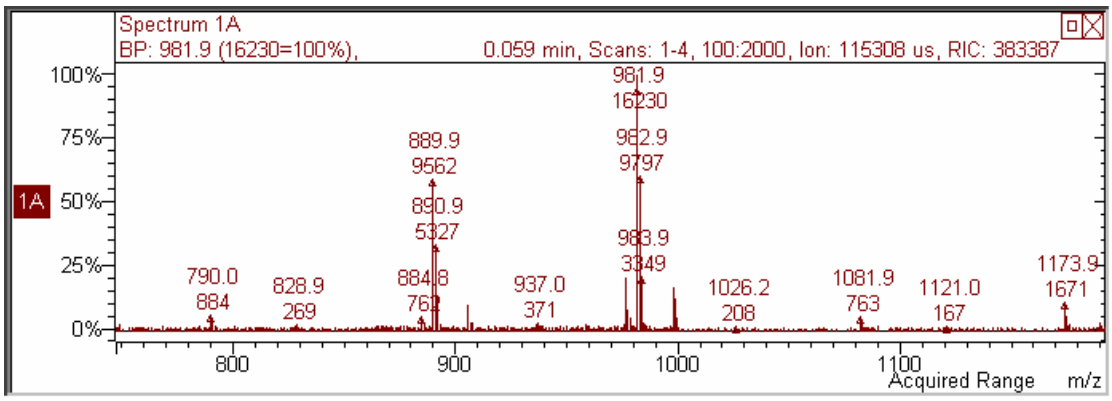


Figure S18. Electrospray ionization mass spectrum of **4.** Main peaks: *m/z* 981.9 $[M - C_6H_{14}O_4 + Na]^+$ (100%), 889.9 $[M - C_{10}H_{21}O_6 + NH_4]^+$ (59%).

*4. Fluorescent microscopy images of Rhodamine B-entrapped vesicles of **1***

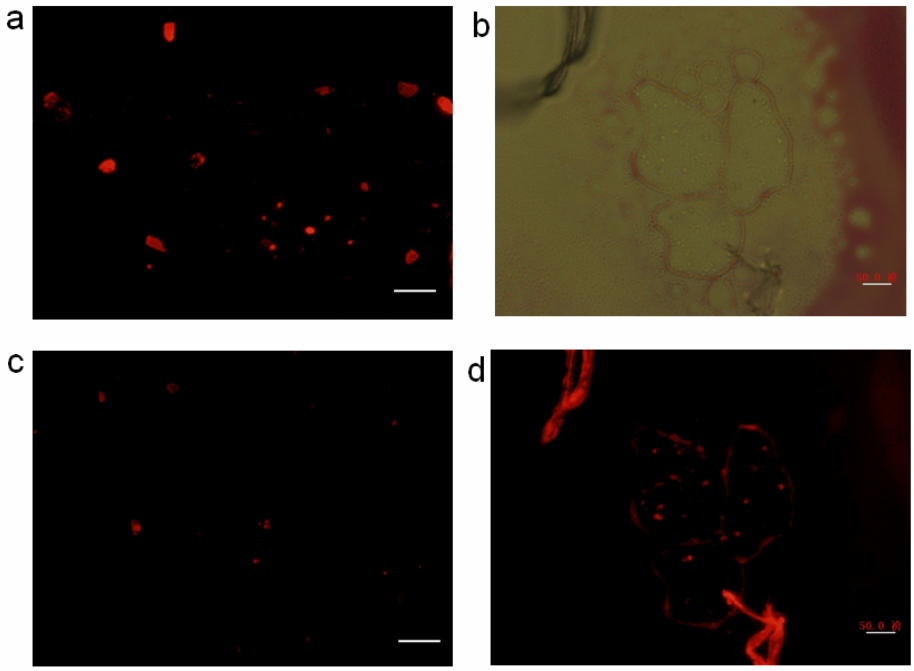


Figure S19. Fluorescence microscopy images (a, c, d) of Rhodamine B-entrapped vesicles of **1** after being purified by dialysis for 3 days and the corresponding optical microscopy image (b) of d. The scale bar is 50 μm.

*5. TEM images and DLS result of compound **4** in chloroform*

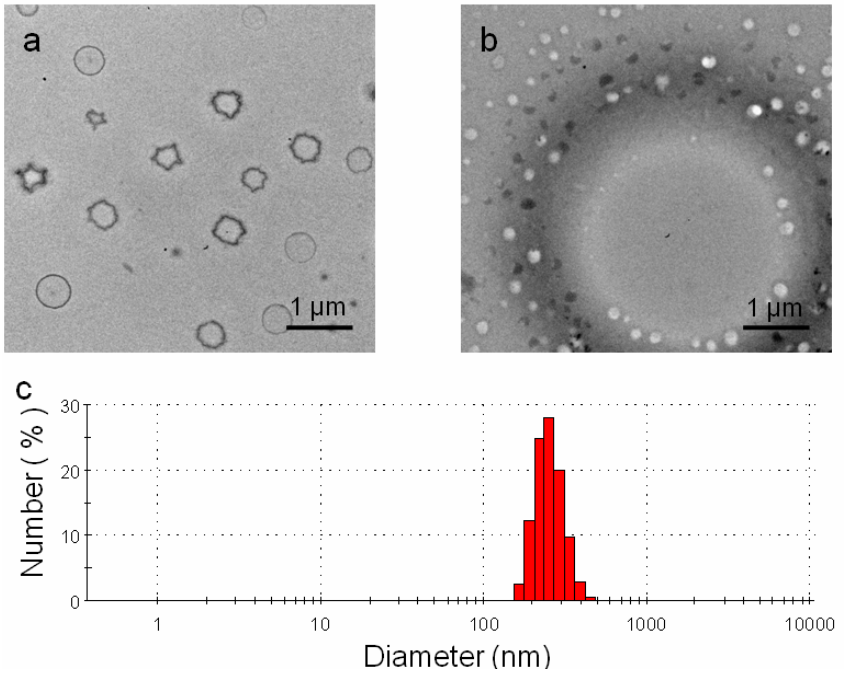


Figure S20. TEM images (a and b) of 1.00 mM **4** in chloroform and DLS result (c) of 1.00 mM **4** in chloroform.

*6. Transformation processes of vesicles of **1** under external physical stimuli*

*6.1. Optical microscopy images of the transformation process of vesicles of **1** under heating*

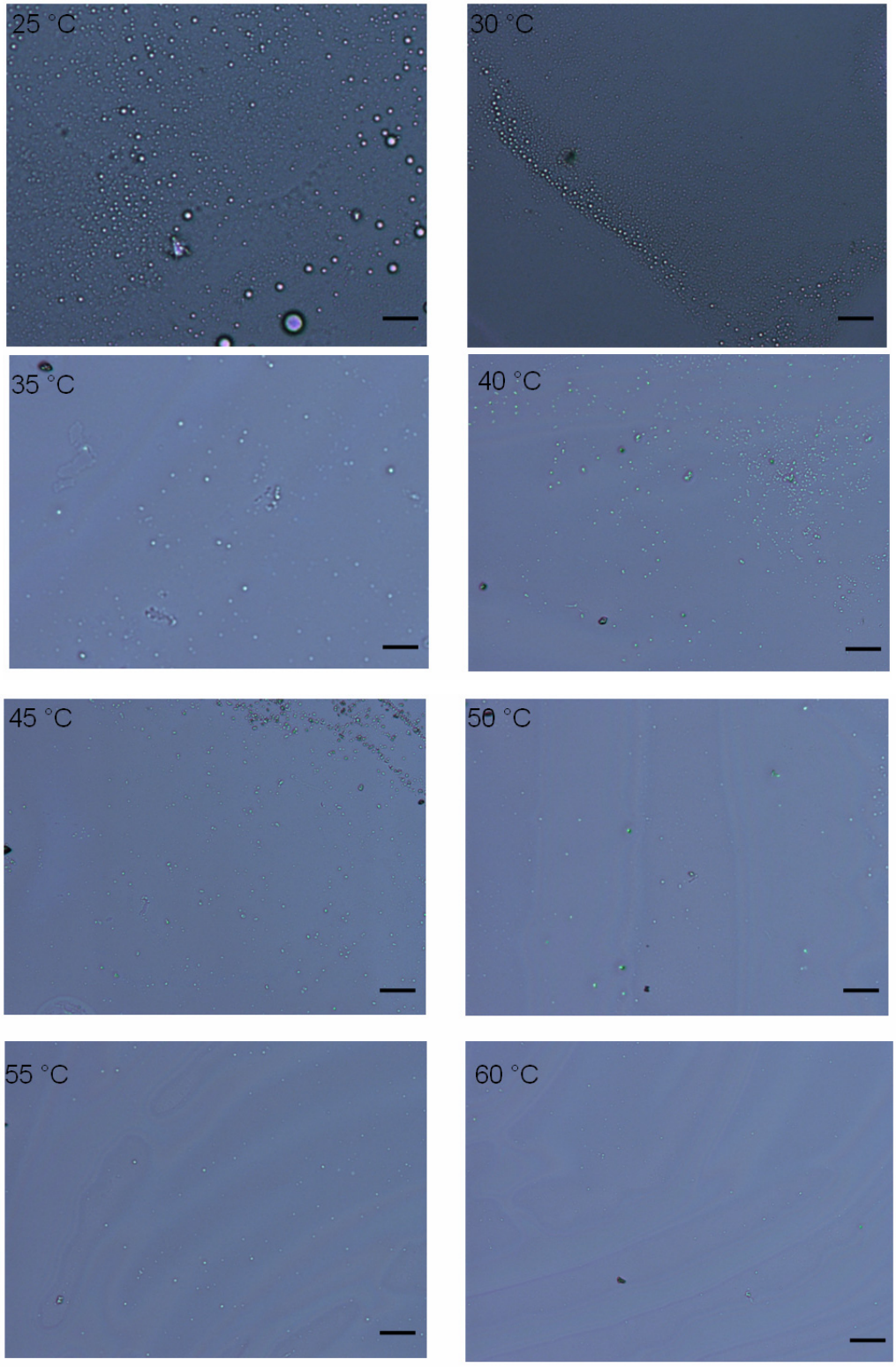


Figure S21. Optical microscopy images of the transformation process of the vesicles formed by **1** in chloroform under heating. The scale bar is 10 μm.

*6.2. Optical microscopy images and DLS results of the disassembly and the re-assembly behaviors of **1** under heating*

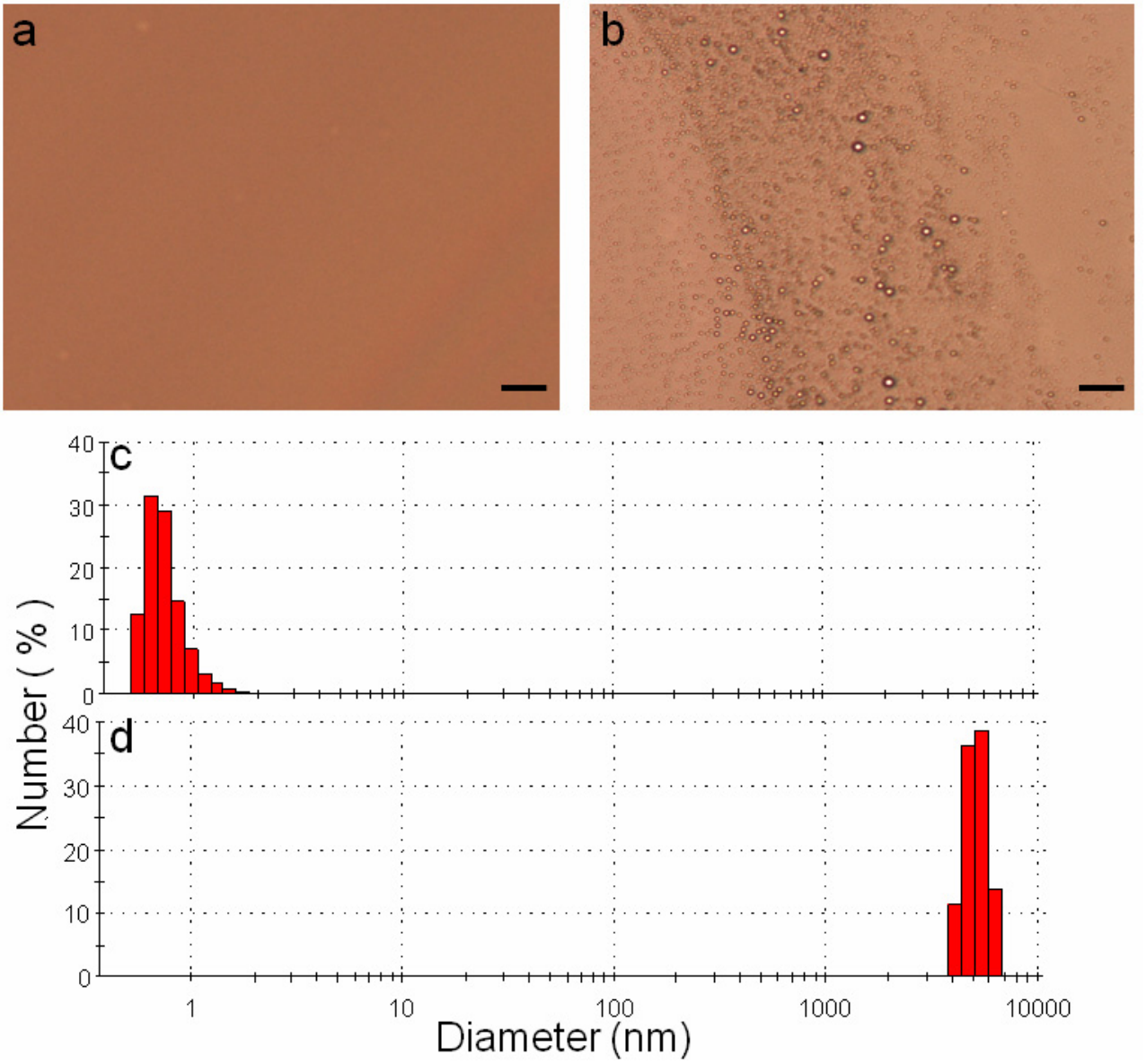


Figure S22. The optical microscopy images and DLS results of the disassembly and re-assembly behaviors of **1** in chloroform under external stimulus of heating to 60 °C: (a) the optical microscopy image of the sample heating up to 60 °C; (b) the optical microscopy image of the heated sample back to room temperature; (c) the DLS result of the sample heating up to 60 °C; (d) the DLS result of the heated sample back to room temperature. The scale bar is 10 μm.

*6.3. Optical microscopy images and DLS results of the disassembly and re-assembly behaviors of **1** under cooling to 0 °C*

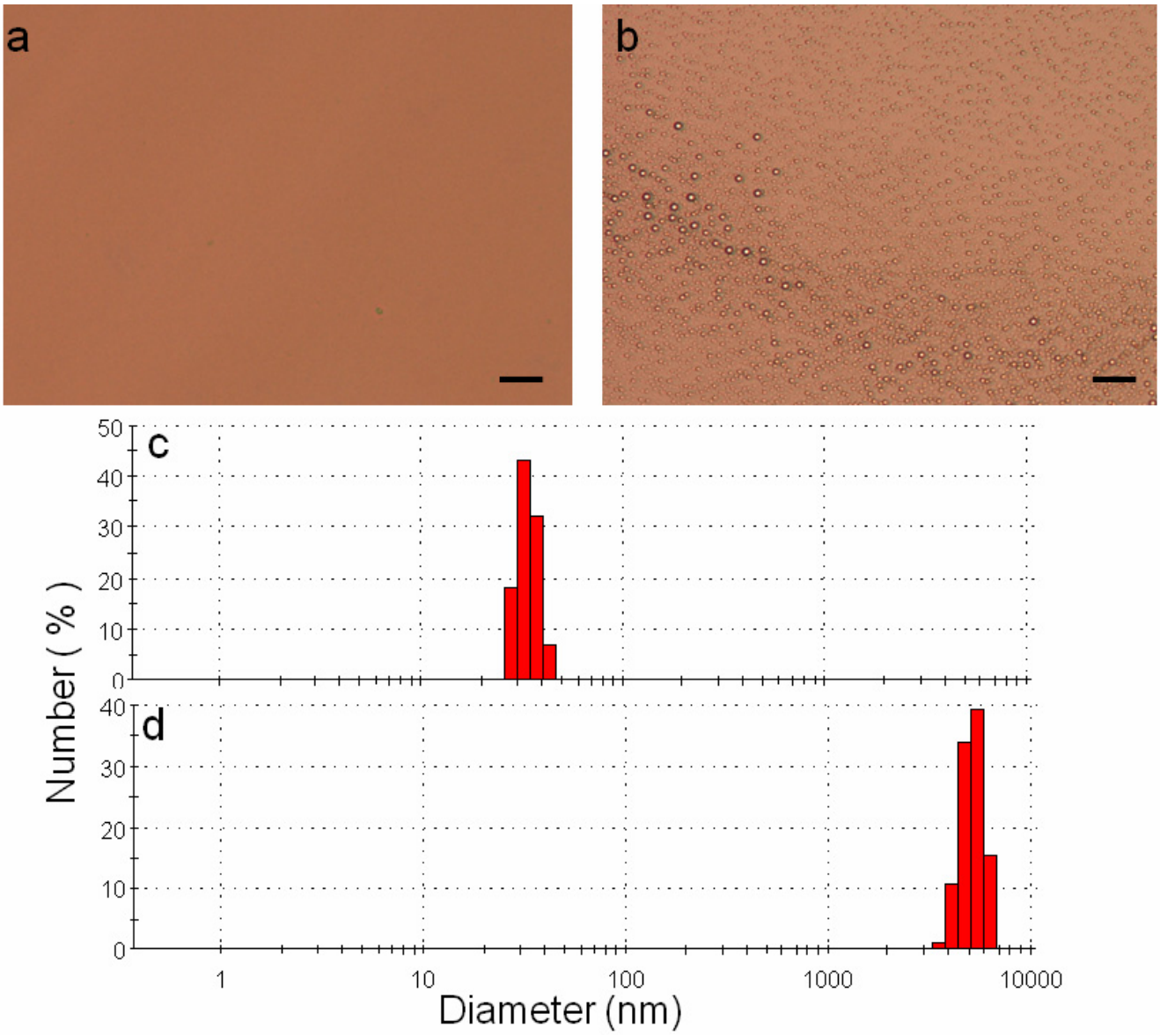


Figure S23. The optical microscopy images and DLS results of the disassembly and re-assembly behaviors of **1** in chloroform under external stimulus of cooling to 0 °C: (a) the optical microscopy image of the sample cooling to 0 °C; (b) the optical microscopy image of the cooling sample back to room temperature; (c) the DLS result of the sample cooling to 0 °C; (d) the DLS result of the cooling sample back to room temperature. The scale bar is 10 μm.

*6.4. Optical microscopy images and DLS results of the disassembly and re-assembly behaviors of **1** under sonication for 5 minutes*

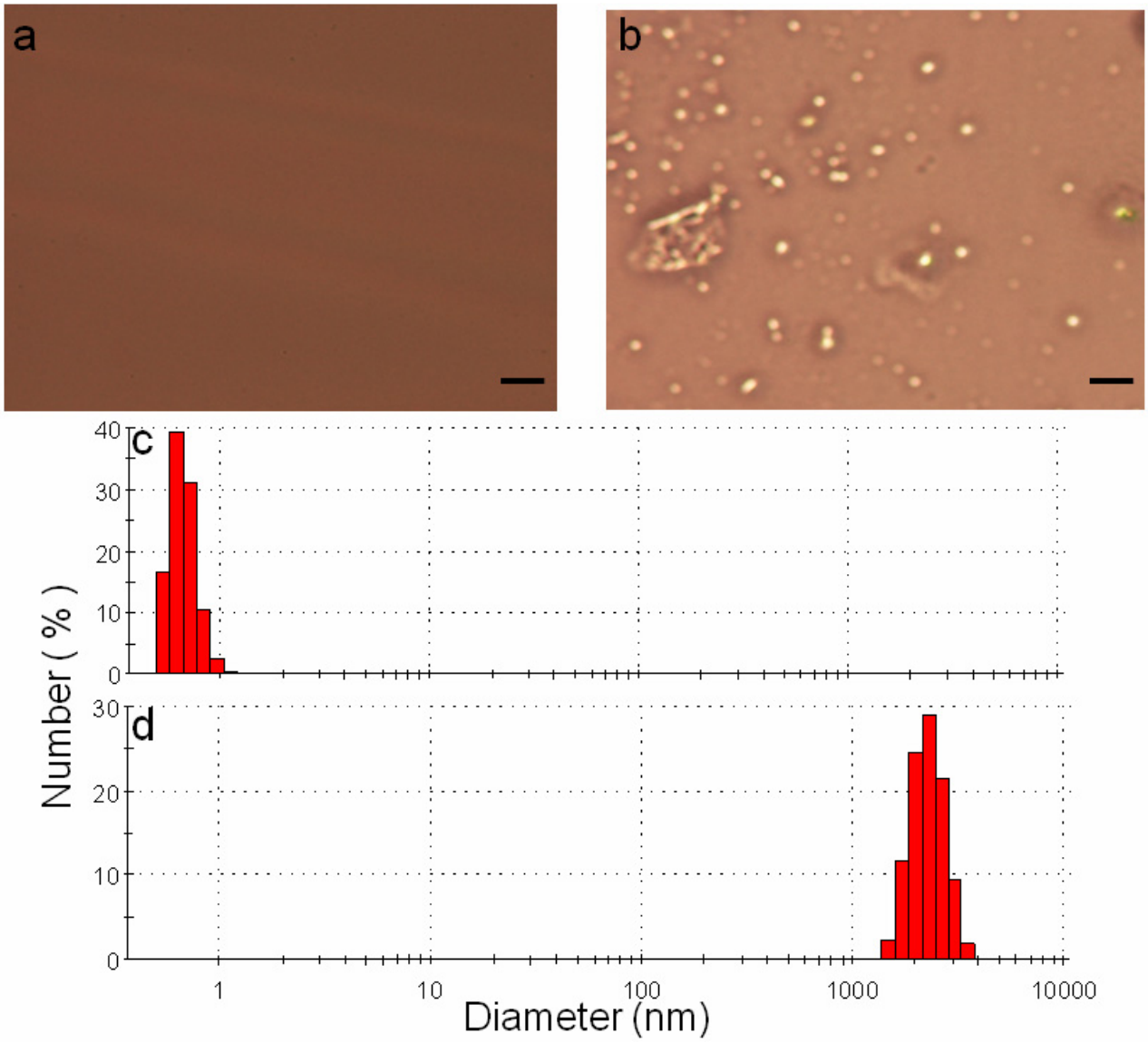


Figure S24. The optical microscopy images and DLS results of the disassembly and re-assembly behaviors of **1** in chloroform under sonication for 5 minutes: (a) the optical microscopy image of the sample under sonication for 5 minutes; (b) the optical microscopy image of the sample after rest for 10 minutes; (c) the DLS result of the sample under sonication for 5 minutes; (d) the DLS result of the sample after rest for 10 minutes. The scale bar is 10 μm.

*6.5. Optical microscopy images and DLS results of the disassembly and re-assembly behaviors of **1** under external stimulus of vigorous stirring*

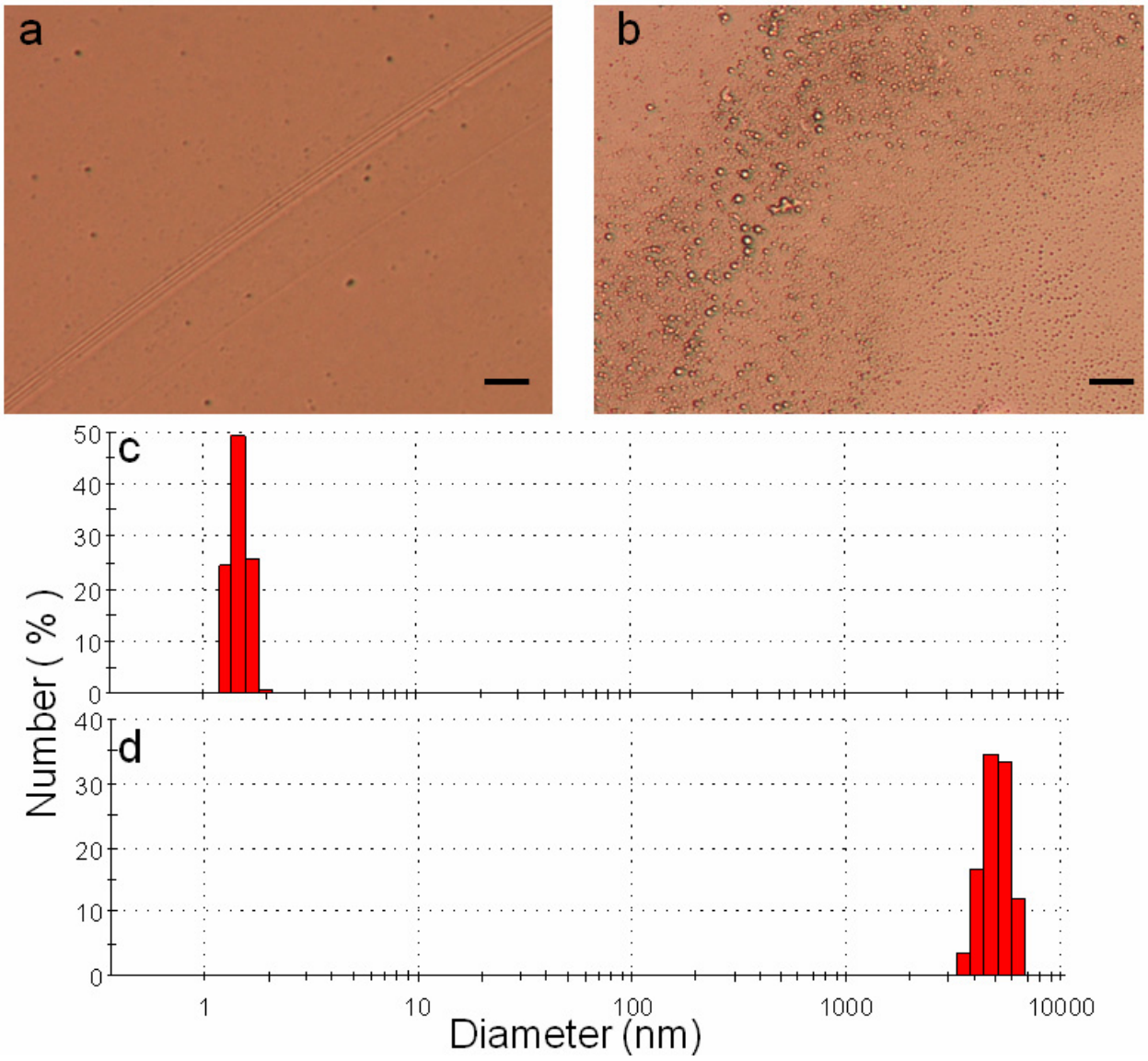


Figure S25. The optical microscopy images and DLS results of the disassembly and re-assembly behaviors of **1** in chloroform under external stimulus of vigorous stirring: (a) the optical microscopy image of the sample under vigorous stirring; (b) the optical microscopy image of the sample after rest for 10 minutes; (c) the DLS result of the sample under vigorous stirring; (d) the DLS result of the sample after rest for 10 minutes. The scale bar is 10 μm.

*7. Host-guest interactions induced disassembly of vesicles of **1***

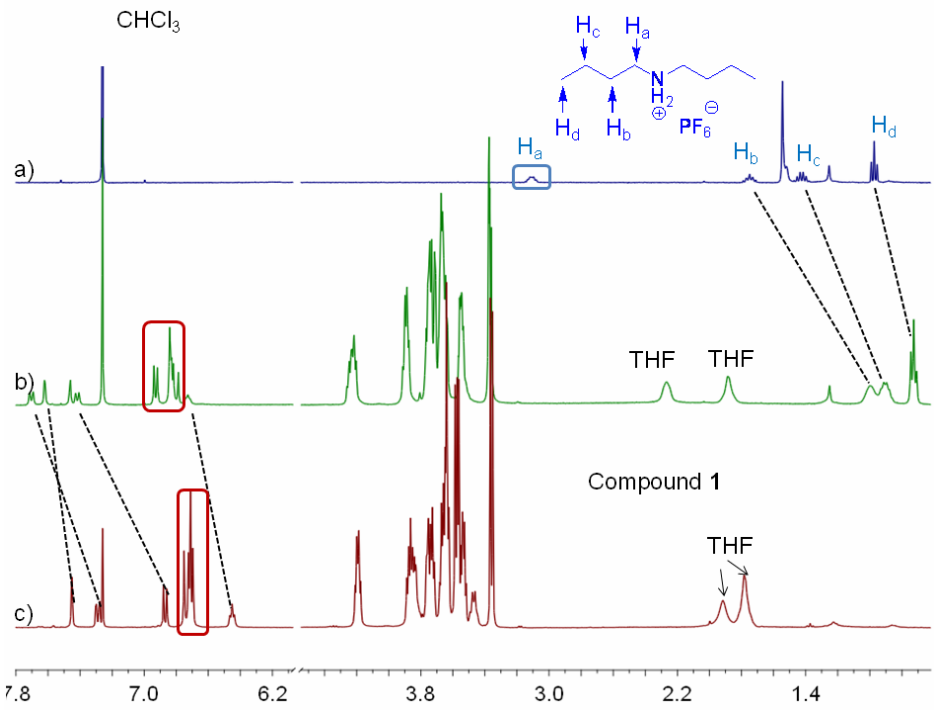


Figure S26. ^{1}H NMR spectra (400 MHz, $CDCl_3$, 298 K): a) 5.00 mM **G**; b) 5.00 mM **1** and **G**; c) 5.00 mM **1**.

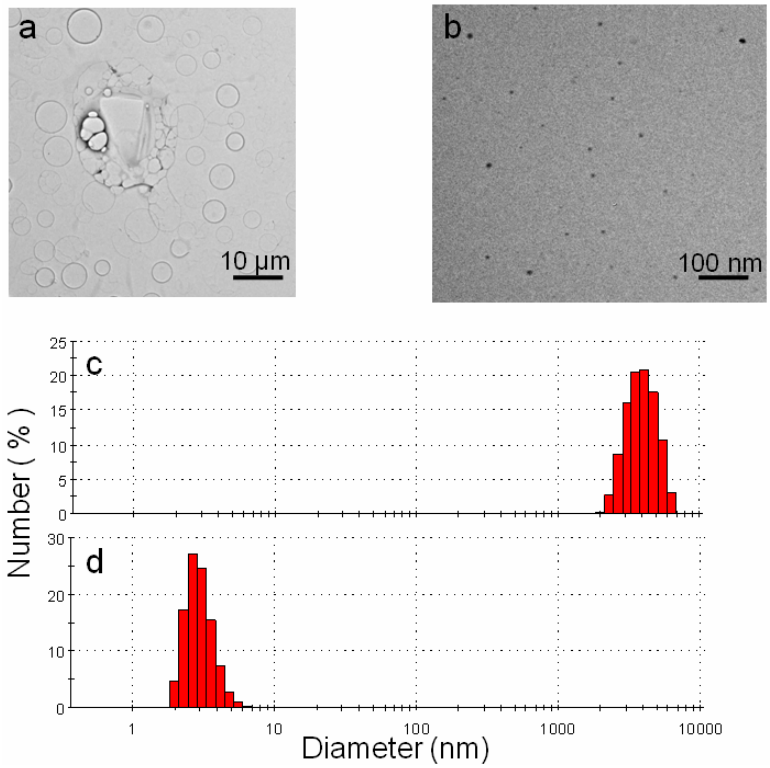


Figure S27. TEM images and DLS results of the host-guest interactions induced disassembly of vesicles of **1**: (a) TEM image of compound **1**; (b) TEM image of an equimolar solution of **1** and **G**; (c) DLS result of **1**; (d) DLS result of the equimolar solution of **1** and **G**. The samples were all prepared in chloroform with the concentration of 1.00 mM.

*8. K^+-induced disassembly of vesicles of **1** and benzo-18-crown-6-induced re-assembly of vesicles of **1***

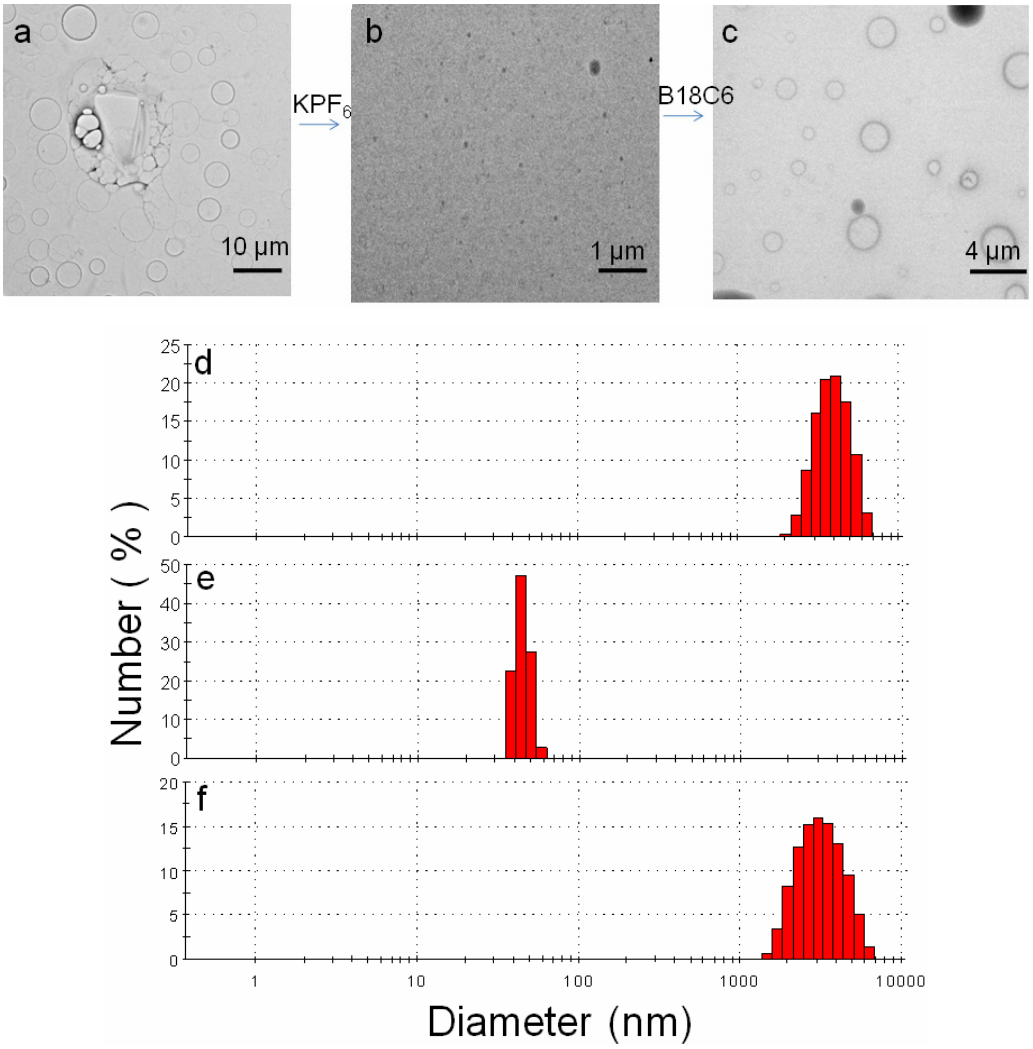


Figure S28. TEM images and DLS results of the K^+-induced disassembly of vesicles of **1** and benzo-18-crown-6 induced re-assembly of vesicles of **1**: (a) TEM image of compound **1**; (b) TEM image of an equimolar solution of **1** and KPF_6; (c) TEM image after addition of benzo-18-crown-6 to b; (d) DLS result of **1**; (e) DLS result of the equimolar solution of **1** and KPF_6; (f) DLS result after addition of benzo-18-crown-6 to e. The samples were all prepared in chloroform with the concentration of 1.00 mM.

9. *SEM images of a gel of **1***

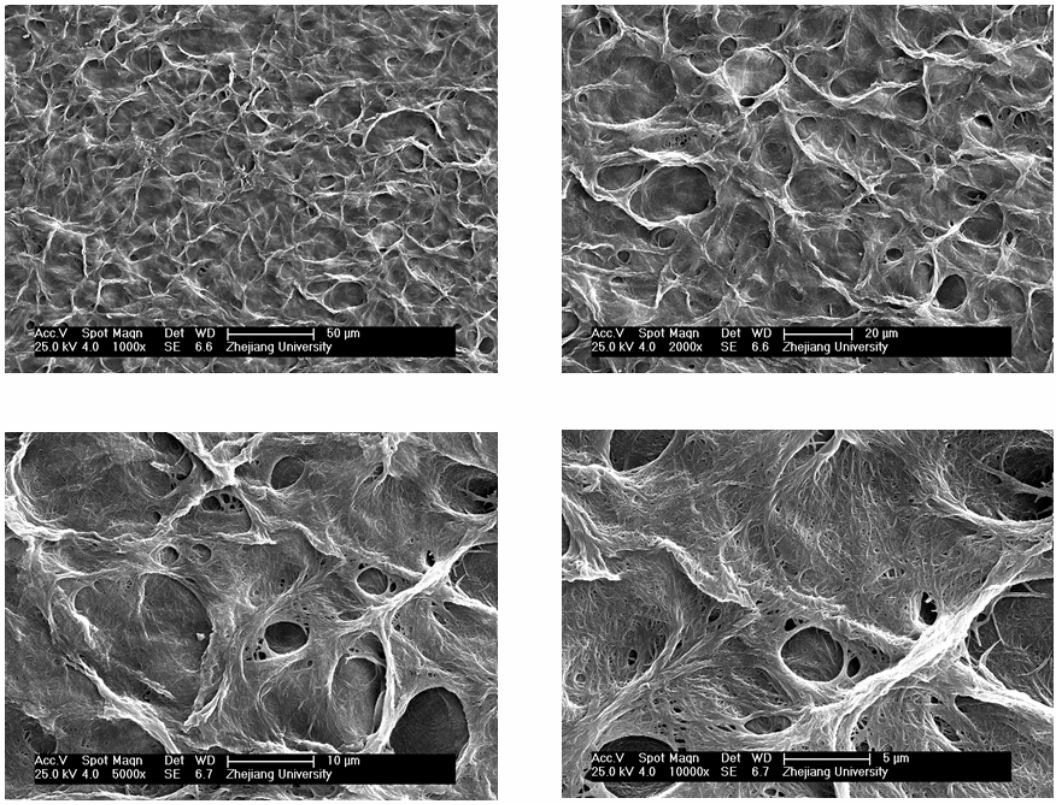


Figure S29. SEM images of a gel of **1** in water/tetrahydrofuran (5:1, *v*/*v*).

10. X-Ray diffraction (XRD)

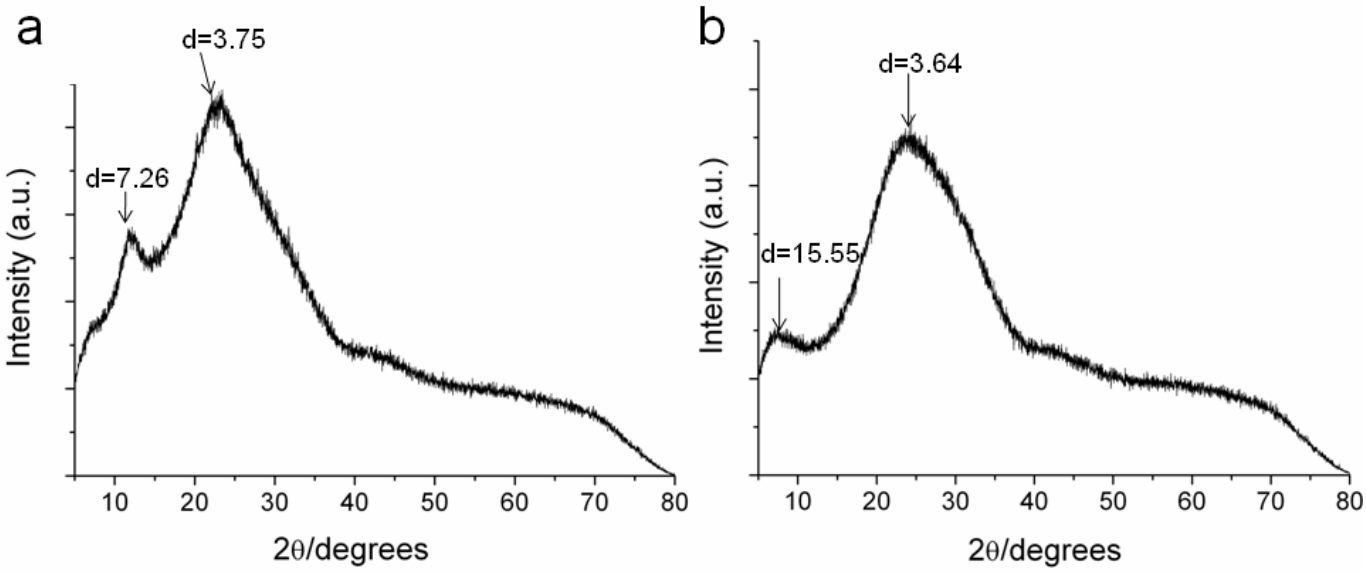


Figure S30. X-ray diffraction patterns of giant vesicles (a) and an xerogel of **1** (b).

From Figure 30, the diffractograms showed peaks at 3.75 and 3.64 Å, respectively, for the giant vesicles and the xerogel of **1**, which were within the range of documented π–π stacking distances.[4,5] Furthermore, the diffraction patterns of a and b showed differences within 5 to 15 degrees, which suggested the different packing modes of **1** in the vesicles and the gel.

11. FTIR spectroscopy

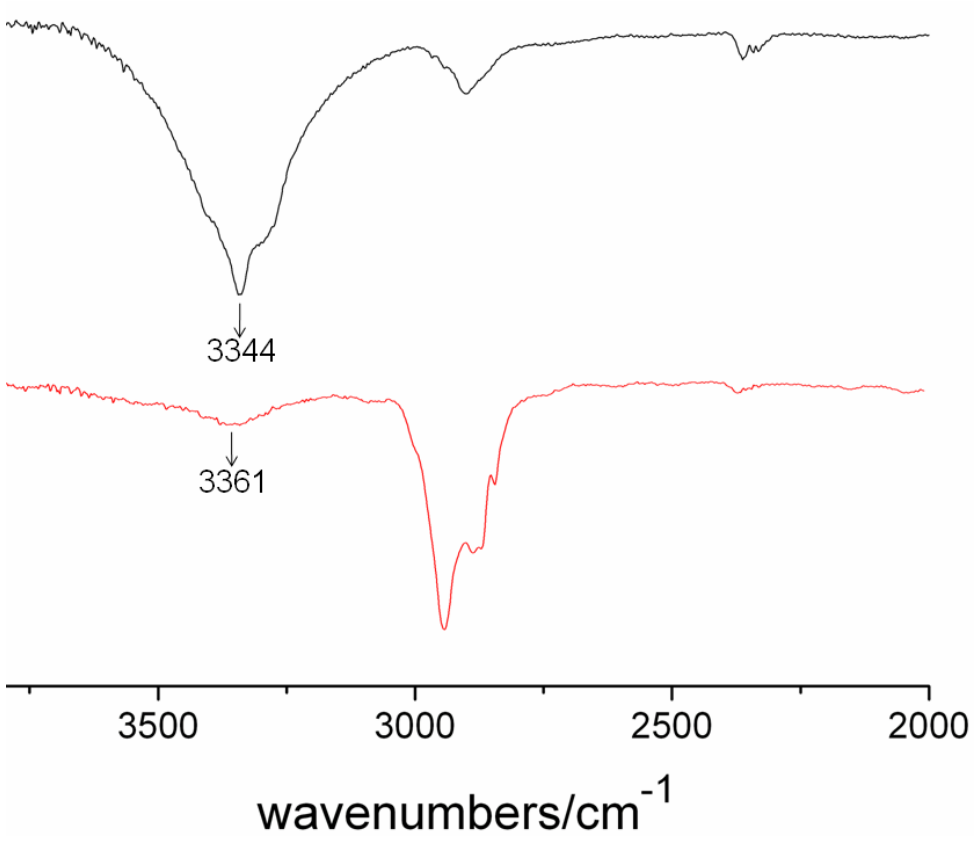


Figure S31. FTIR spectra of compound **1**: film of a solution in water/tetrahydrofuran (5:1, *v*/*v*) (red line) and an xerogel (black line).

From Figure S31, it was observed that the N–H stretching band of the solution was at 3361 cm^{-1}, and shifted to 3344 cm^{-1} in the gel. The decrease in the wavenumber value suggested the participation of hydrogen bonding in the aggregation process of the gel.[6]

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