Electronic Supplementary Material (ESI) for RSC Advances

A water-soluble pillar[6]arene: synthesis, host–guest chemistry, controllable self-assembly, and application in controlled release

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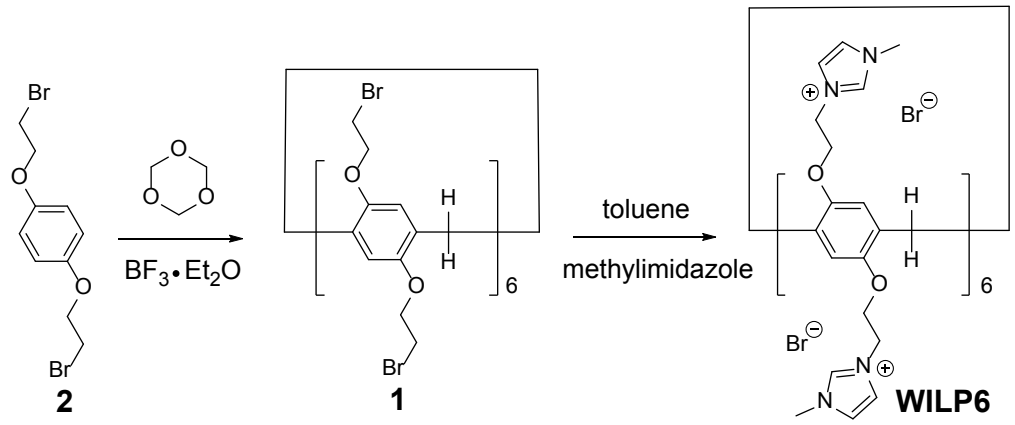
Electronic Supplementary Information (14 pages)

1. Materials and methods

1,4-Bis(2'-bromoethoxy)benzene, 1-bromooctadecane, 4-hydroxybenzoic acid, methylimidazole, toluene, 1,3,5-trioxane, boron trifluoride diethyl etherate, and 1,2-dichloroethane were reagent grade and used as received. Solvents were either employed as purchased or dried according to procedures described in the literature. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker Avance DMX-400 spectrometer. Mass spectra were obtained on a Bruker Esquire 3000 plus mass spectrometer (Bruker-Franzen Analytik GmbH Bremen, Germany) equipped with an ESI interface and an ion trap analyzer. The TEM images were obtained using a HITACHI instrument with an accelerating voltage of 100 kV. UV–Vis spectroscopy was measured on a Shimadzu UV-2501 PC UV–Vis spectrometer. DLS studies were measured on a Nano-ZS ZEN3600 instrument. TEM experiments were performed on a HITACHI instrument with an accelerating voltage of 80 kV.

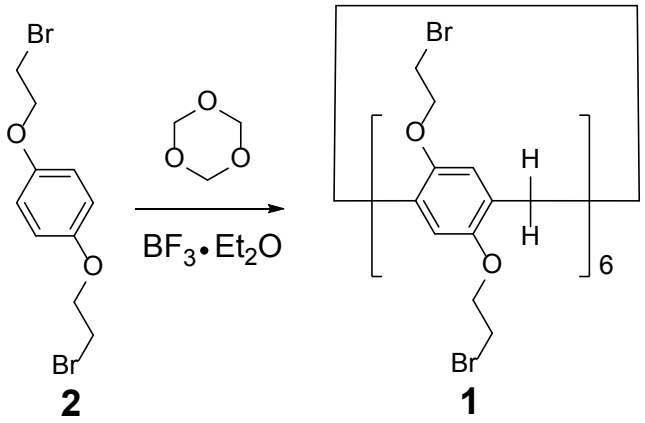
2. Synthetic procedures

Scheme S1. Synthetic route to water-soluble ionic liquid pillar[6]arene **WILP6**



2.1. Synthesis of compound *1*

Scheme S2. Synthesis of compound **1**



By condensation of **2** with boron trifluoride etherate as the catalyst in $ClCH_2CH_2Cl$, bromoethyl substituted pillar[6]arene **1** was synthesized (10%). mp 65.7–65.9 °C. The ^1H NMR spectrum of **1** is shown in Fig. S1. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.78 (s, 12H), 4.16 (t, J = 6.00 Hz, 24H), 3.87 (s, 12H), 3.55 (t, J = 4.00 Hz, 24H). The ^{13}C NMR spectrum of **1** is shown in Fig. S2. ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 149.68, 129.08, 116.10, 68.98, 30.72, 29.42. Anal. Calcd. for $C_{66}H_{72}Br_{12}O_{12}$: C 39.32, H 3.60. Found: C 39.29, H 3.66. The crystal structure of **1** is shown in Scheme 1 and Fig. S3.

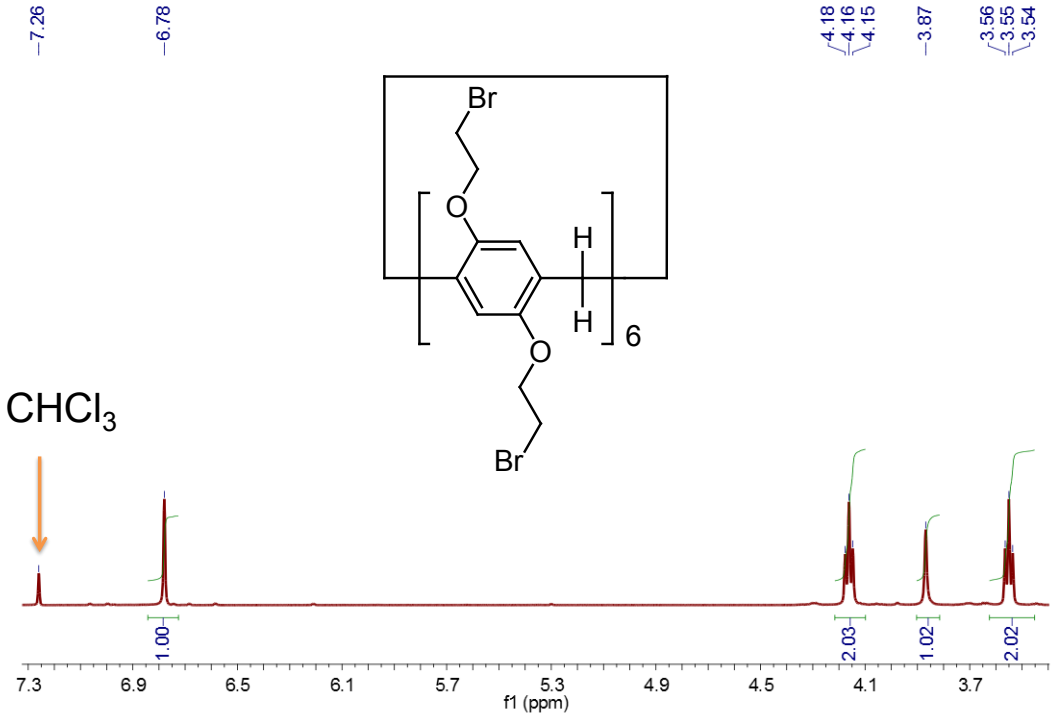


Fig. S1 ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 293 K) of compound **1**.

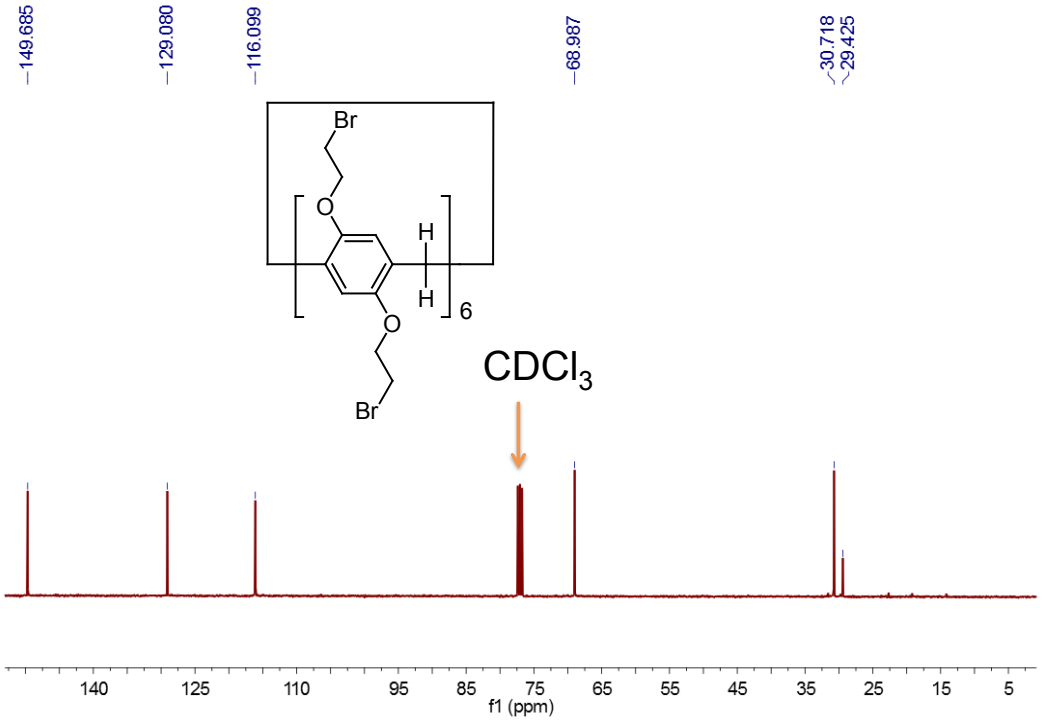


Fig. S2 ^{13}C NMR spectrum (100 MHz, $CDCl_3$, 293 K) of compound **1**.

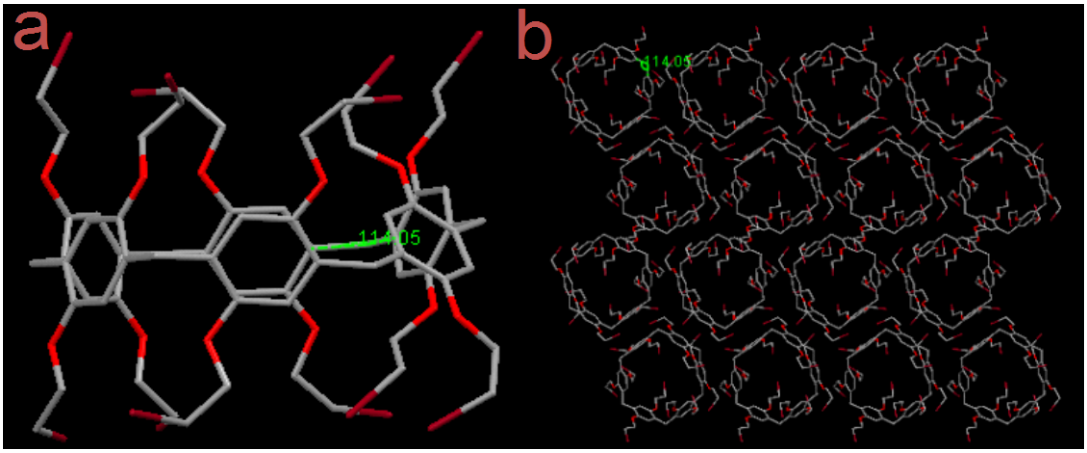
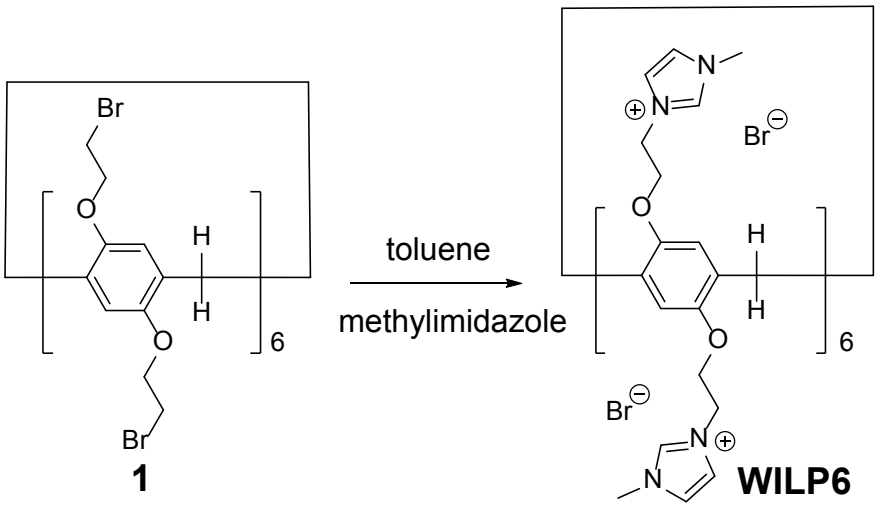


Fig. S3 Crystal structure of compound **1**: (a) side view; (b) top view.

X-ray Crystal Data of 1. Colorless, $C_{66}H_{72}O_{12}Br_{12}$, *FW* 2016.16, triclinic, space group *P*–1, a = 11.9742(4), b = 13.6564(5), c = 24.0532(9) Å, α = 89.320(3)°, β = 79.331(3)°, γ = 84.985(3)°, V = 3850.5(2) Å^3, Z = 2, D_c = 1.739 g cm^{-3}, T = 170 K, μ = 6.295 mm^{-1}, 14080 measured reflections, 9745 independent reflections, 815 parameters, 0 restraints, $F(000)$ = 1968.0, R_1 = 0.0789, wR_2 = 0.1094 (all data), R_1 = 0.0455, wR_2 = 0.0995 [$I > 2\sigma(I)$], max. residual density 0.658 e·Å^{-3}, and goodness-of-fit (F^2) = 0.998. CCDC 946657.

*2.3. Synthesis of **WILP6***

Scheme S3. Synthesis of **WILP6**



WILP6 was obtained by refluxing a solution of **1** and *N*-methylimidazole in toluene (89%). mp 55.4–55.7 °C. The ^{1}H NMR spectrum of **WILP6** is shown in Fig. S4. ^{1}H NMR (400 Hz, D_2O) δ (ppm): 8.31 (s, 12H), 7.37 (s, 12H), 7.23 (s, 12H), 6.67 (s, 12 H), 4.43 (t, J = 4.00 Hz, 24H), 4.15 (t, J = 5.60 Hz, 24H), 3.75 (s, 36H), 3.71 (s, 12H). The ^{13}C NMR spectrum of **WILP6** is shown in Fig. S5. ^{13}C NMR (100 MHz, D_2O) δ (ppm): 149.08, 128.93, 123.63, 122.48, 115.27, 66.81, 49.28, 35.68, 33.45, 28.96. Anal. Calcd. for $C_{114}H_{144}Br_{12}N_{24}O_{12}$: C 45.62, H 4.84, N 11.20. Found: C 45.64, H 4.76, N 11.23.

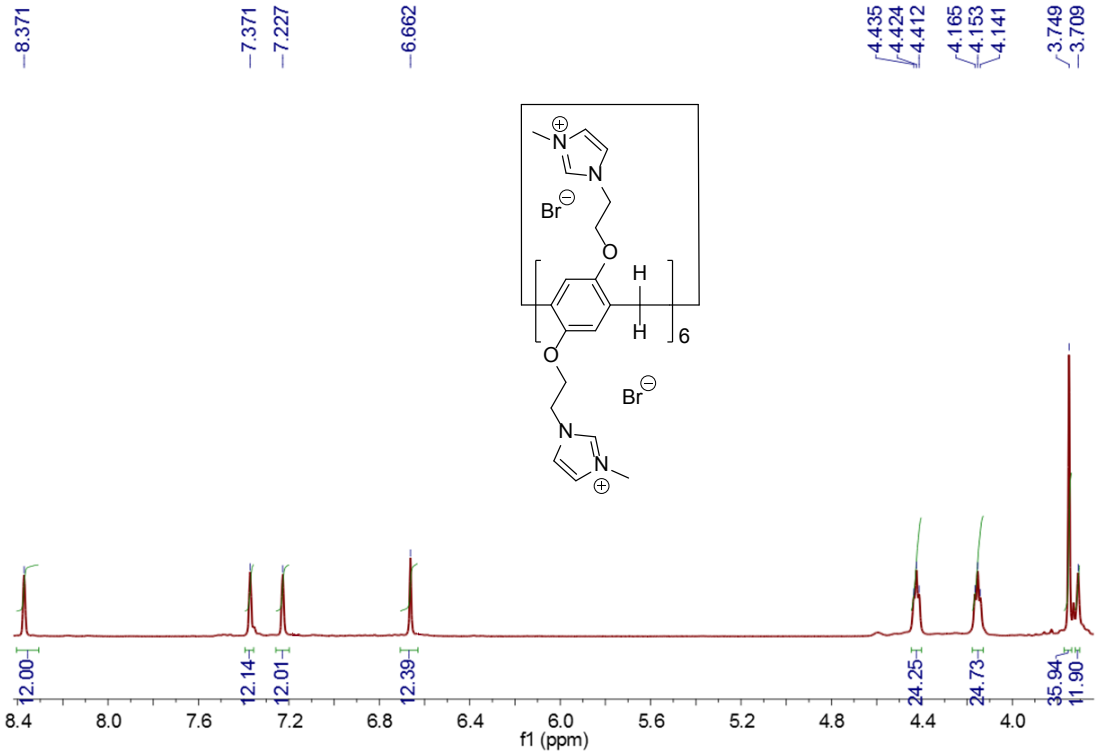


Fig. S4 ^{1}H NMR spectrum (400 MHz, D_2O, 293 K) of **WILP6**.

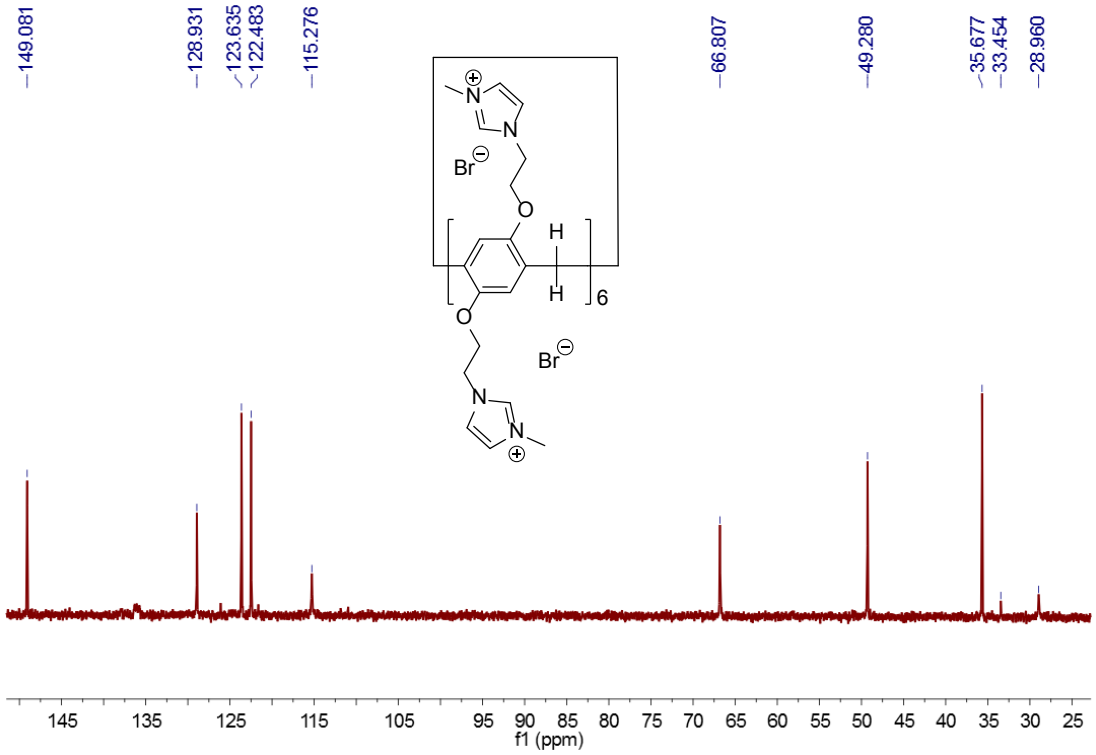
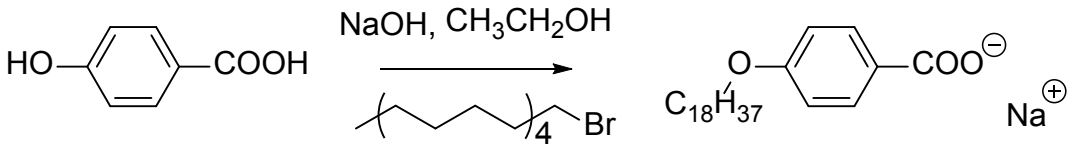


Fig. S5 ^{13}C NMR spectrum (100 MHz, D_2O, 293 K) of **WILP6**.

*2.4. Synthesis of **G2***

Scheme S5. Synthesis of **G2**



G2 was obtained by refluxing a solution of *p*-hydroxybenzoic acid and octadecyl bromide with NaOH as the base in CH_3CH_2OH (89 %). mp 44.7–45.6 °C. The ^{1}H NMR spectrum of **G2** is shown in Fig. S6. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 7.82 (d, J = 8.8 Hz, 2H), 6.99 (d, J = 8.8 Hz, 2H), 4.04 (t, J = 6.4 Hz, 2H), 1.81 (t, J = 7.2 Hz, 2H), 1.46–1.44 (m, 2H), 1.26 (s, 28H), 0.88 (t, J = 5.6 Hz, 3H). The ^{13}C NMR spectrum of **G2** is shown in Fig. S7. ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 190.77, 164.28, 131.98, 129.76, 114.74, 68.43, 29.71, 29.60, 29.56, 29.38, 29.35, 29.07, 25.97, 22.71, 14.13. LRESIMS is shown in Fig. S8: *m/z* 411.5 [**G2** – $H^{\oplus}]^{\ominus}$. Anal. Calcd. for $C_{25}H_{41}NaO_3$: C 72.76, H 10.02. Found: C 72.77, H 9.98.

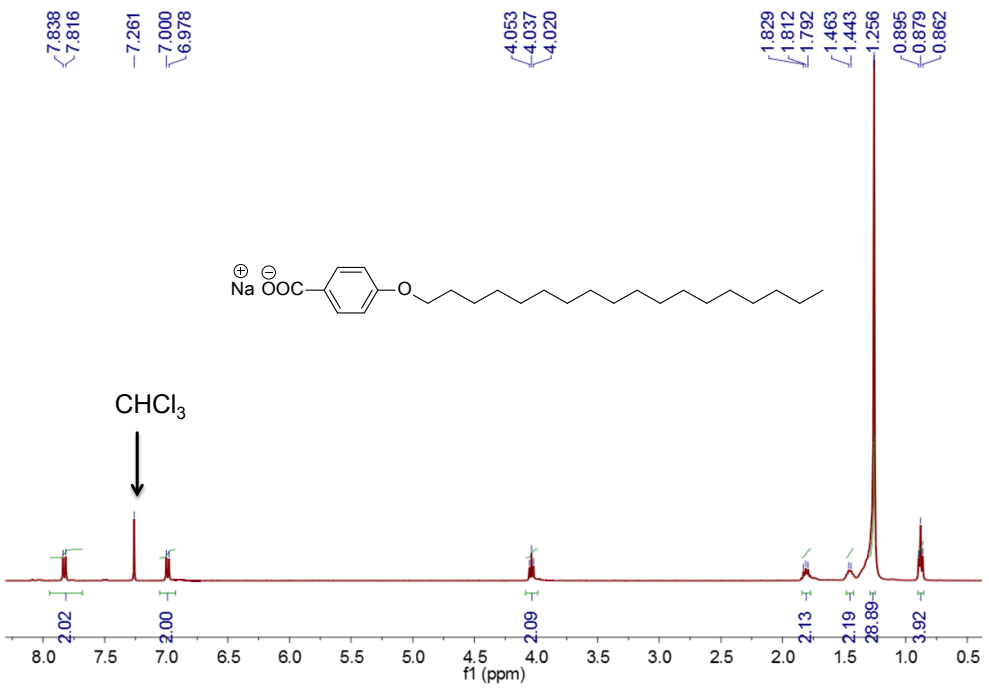


Fig. S6 ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 293 K) of **G2**.

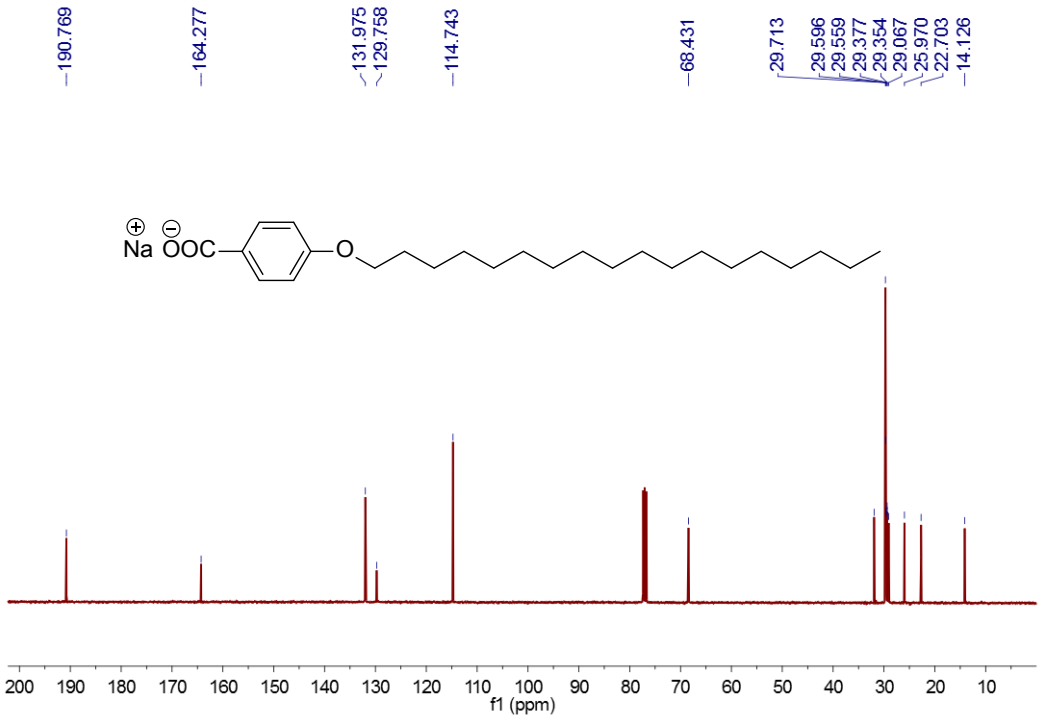


Fig. S7 ^{13}C NMR spectrum (100 MHz, $CDCl_3$, 293 K) of **G2**.

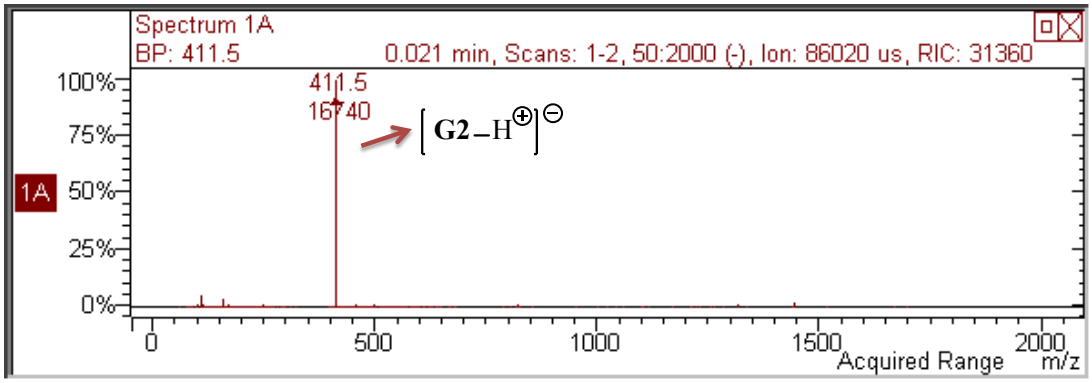


Fig. S8 Electrospray ionization mass spectrum of **G2**. Assignment of the main peak: *m*/*z* 411.5 $[\mathbf{G2} - \mathrm{H}^{\oplus}]^{\ominus}$.

3. Host–guest complexation studies

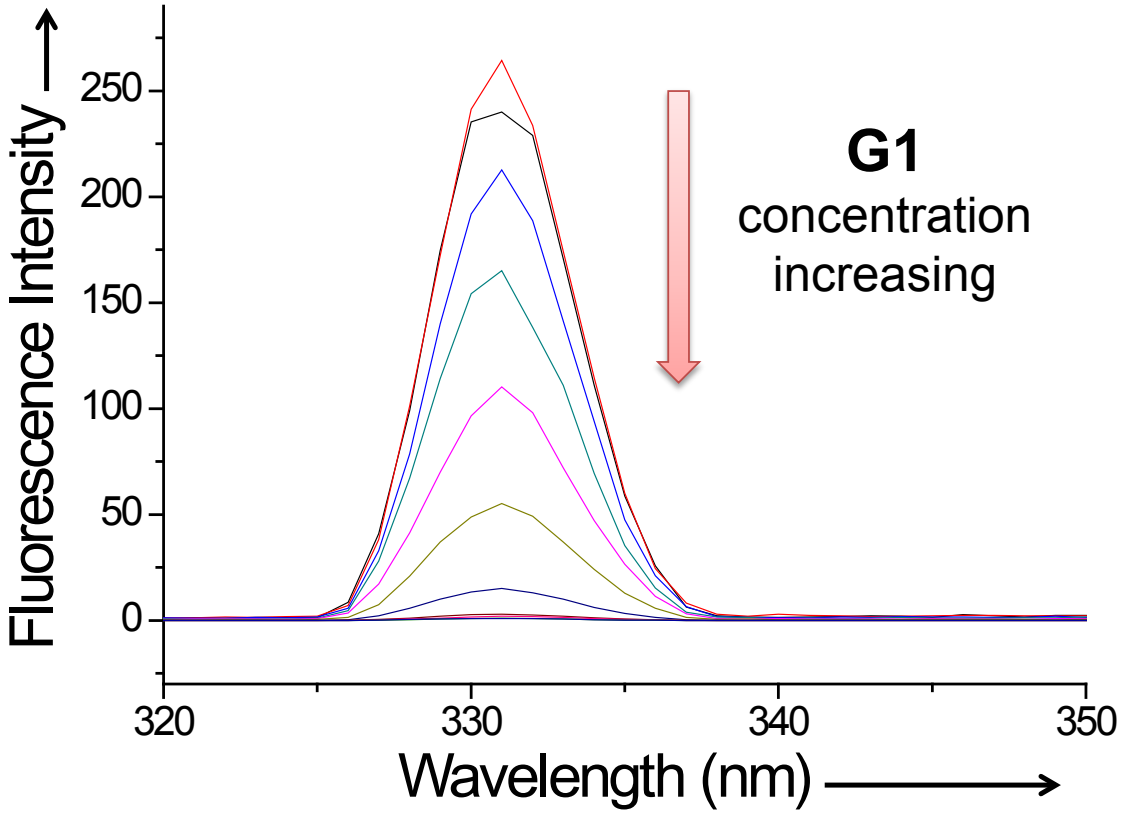


Fig. S9 Fluorescence spectra of **WILP6** (2.00×10^{-6} M) in water at room temperature with different concentrations of **G1**: 0, 0.249, 0.739, 1.46, 2.38, 3.49, 4.55, 6.52, 8.33, 10.0, 11.5, and 12.9×10^{-6} M.

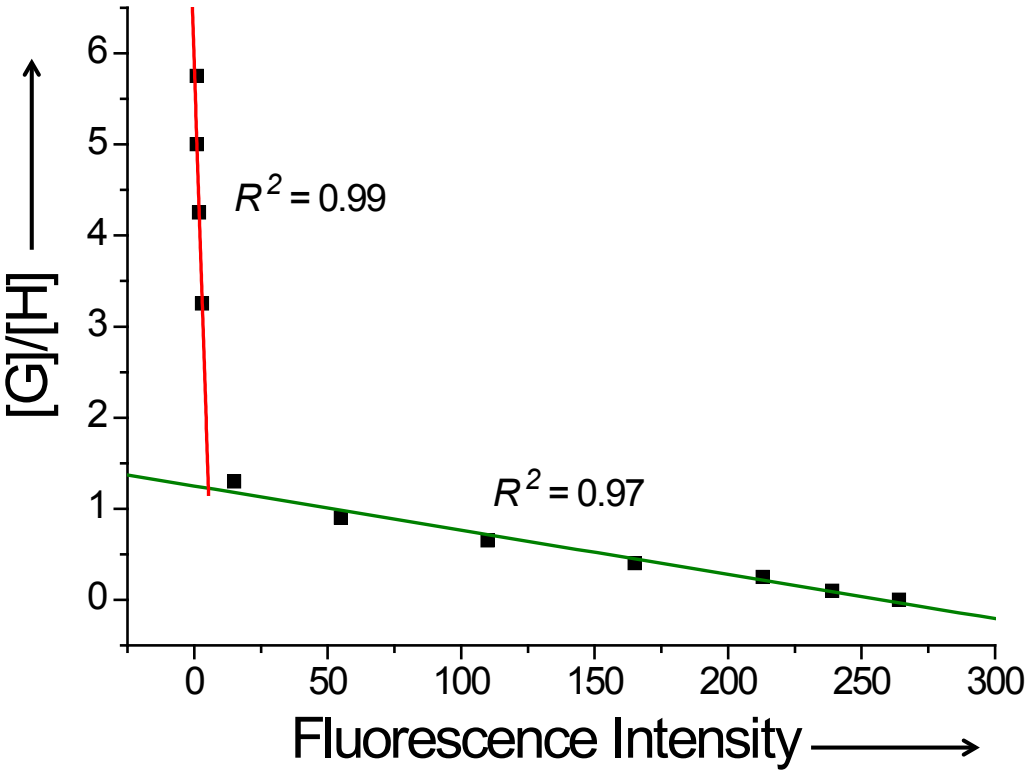


Fig. S10 Mole ratio plot for **WILP6** and **G1**, indicating 1:1 complex.

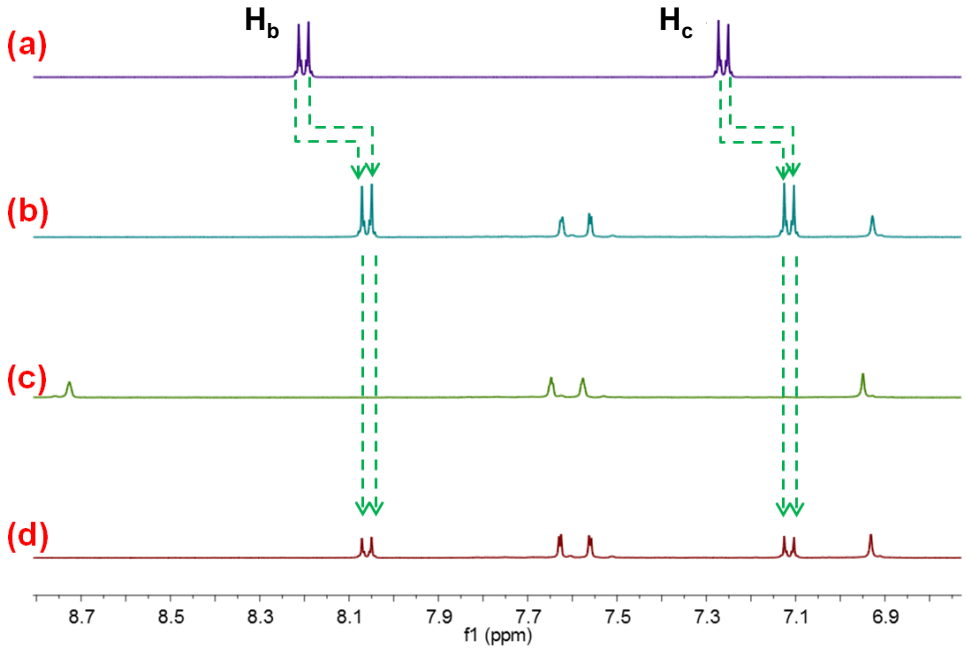


Fig. S11 ^{1}H NMR spectra (400 MHz, D_2O, room temperature) of: (a) **G1**; (b) **WILP6⊃G1** when the solution pH was 7.4; (c) **WILP6⊃G1** when the solution pH was decreased to 4.0; (d) **WILP6⊃G1** when the solution pH was returned to 7.4. $[\mathbf{G1}]_0$ = 3.00 mM. $[\mathbf{WILP6}]_0$ = 1.00 mM.

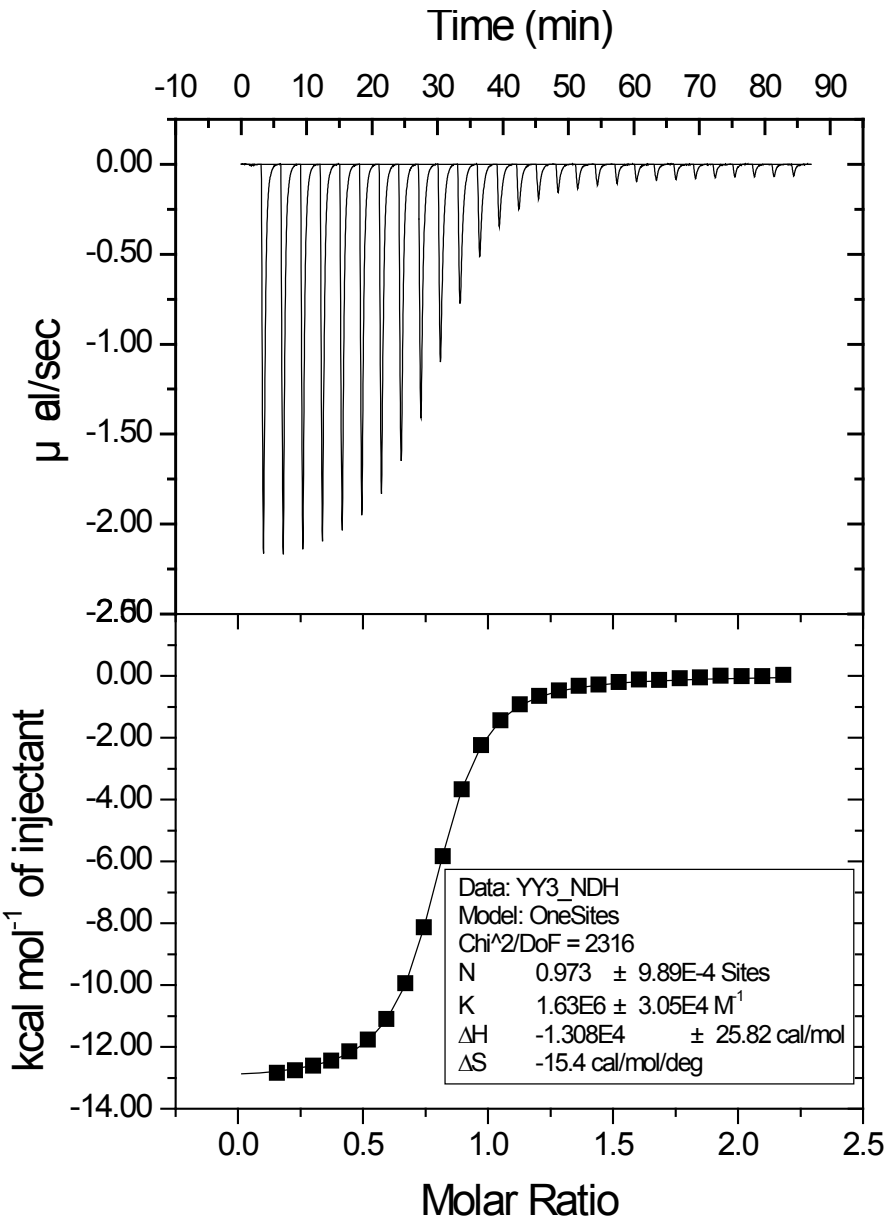


Fig. S12 Microcalorimetric titration of **G1** with **WILP6** in water at 25°C. (Top) Raw ITC data for 27 sequential injections (10 µL per injection) of a **G1** solution (5.00 mM) into a **WP5** solution (0.500 mM). (Bottom) Net reaction heat obtained from the integration of the calorimetric traces.

4. Controllable self-assembly

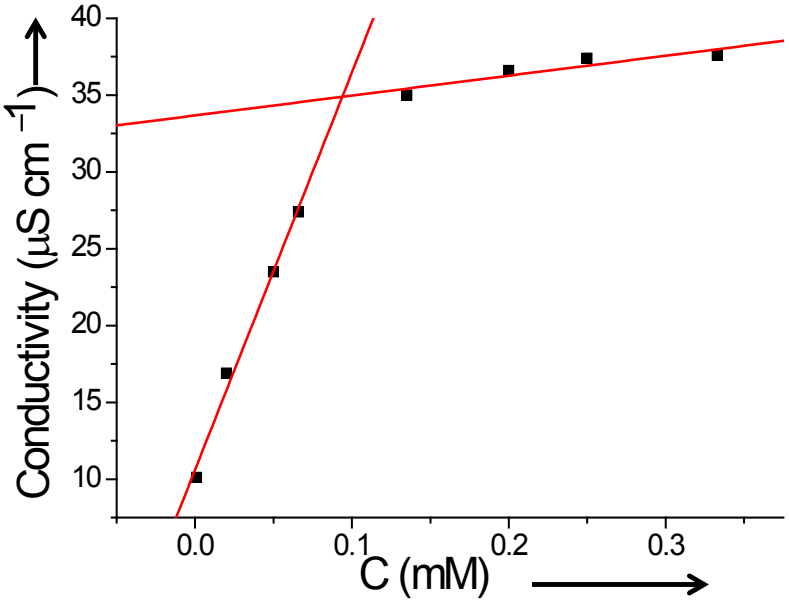


Fig. S13 The concentration-dependent conductivity of **WILP6⊃G2** in water. The critical aggregation concentration (CAC) was determined to be (3.44 ± 0.21) × 10^{-4} M. The solubility of **G2** is very poor in water, so the conductivity of the water solution of **G2** was close to pure water, and we could not determine its CAC value. When we added **WILP6** into the solution of **G2**, **WILP6** complexed with **G2** and induced **G2** to dissolve in water.

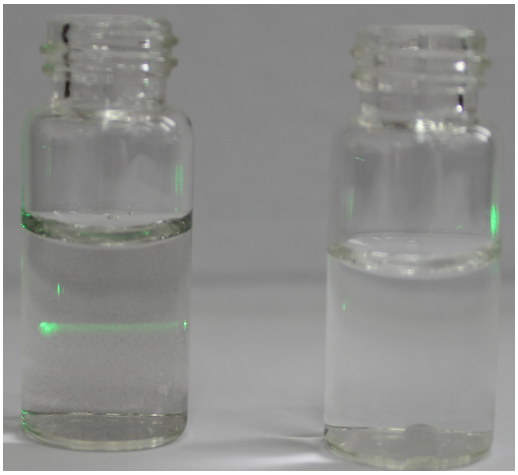


Fig. S14 Tyndall effect of **WILP6⊃G2** complex (left) and free **G2** (right). [**G2**] = [**WILP6**] = 5.00 × 10^{-4} M.

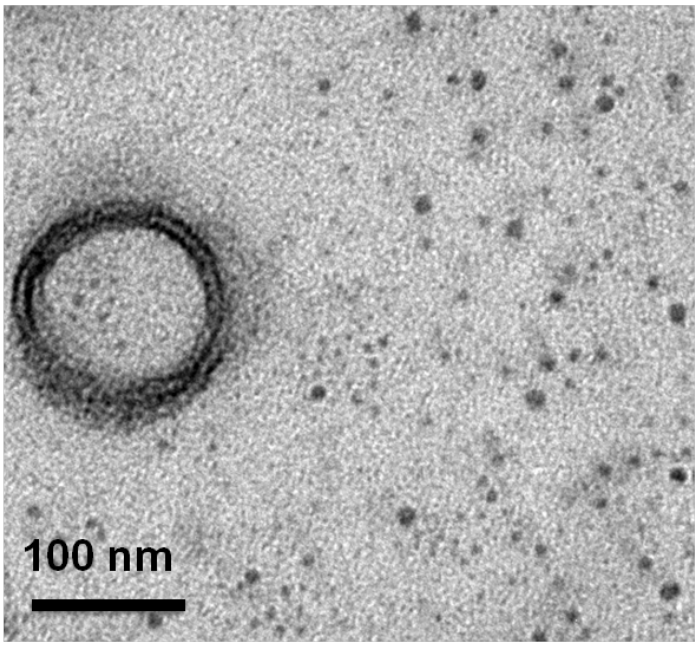


Fig. S15 TEM image of the intermediate state from micelles formed by **G2** to vesicles formed by **WILP6⊃G2** (scale bar = 100 nm).

5. Controlled release

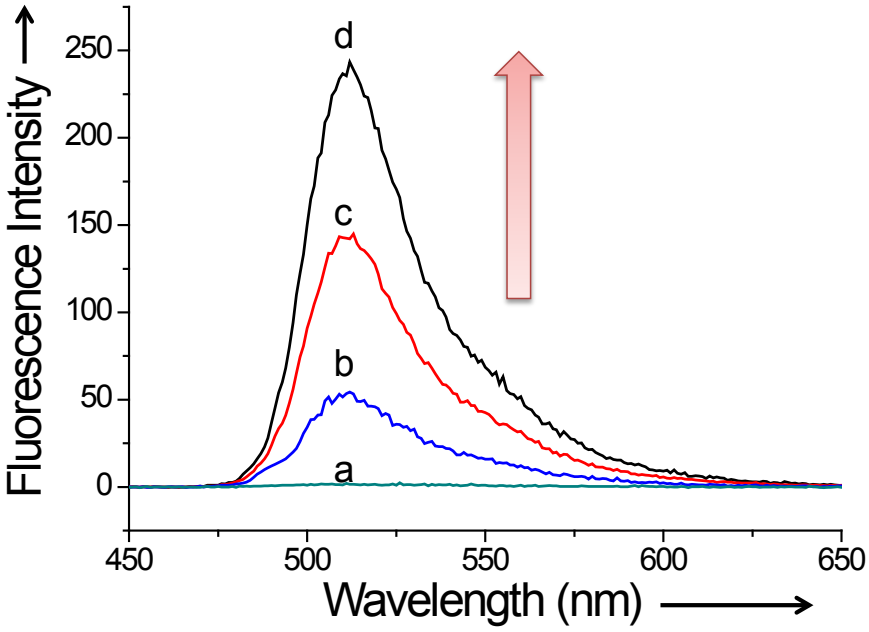


Fig. S16 Fluorescence emission spectra of calcein (λ_{ex} = 470 nm) encapsulated in a solution of **WILP6⊃G2** at different pH values: (a) 7.4; (b) 6.3; (c) 5.2; (d) 4.0.[S1,S2,S3] [**G2**] = [**WILP6**] = 1.50 × 10^{-3} M.

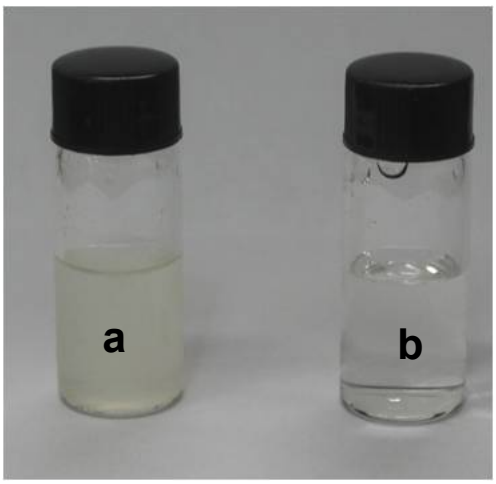


Fig. S17 Optical pictures: (a) **G2** (1.00×10^{-6}M); (b) **G2** (1.00×10^{-6}M) and **WILP6** (1.00×10^{-6} M) in water. After addition of **WILP6** to the aqueous solution of **G2**, the solution became transparent, indicating the formation of the **WILP6⊃G2** complex.

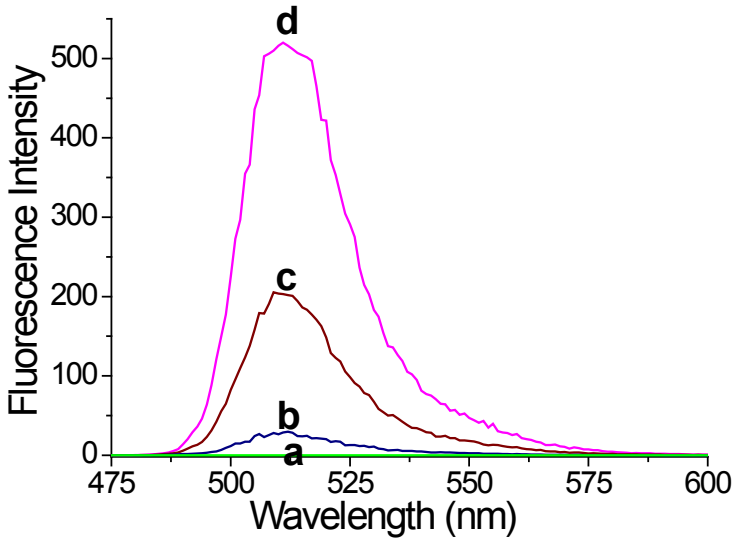


Fig. S18 Fluorescence emission spectra of calcein (λ_{ex} = 470 nm) encapsulated in a solution of **WILP6⊃G2** at different pH values: (a) 7.4; (b) 6.0; (c) 5.0; (d) 4.0. [**G2**] = [**WILP6**] = 1.50×10^{-3} M. In this experiment, calcein was protonized by HCl first to support the conclusion that the change of the fluorescence was caused by the release.

References:

S1. Y. Yao, M. Xue, J. Chen, M. Zhang and F. Huang, *J. Am. Chem. Soc.* 2012, **134**, 15712.

S2. X. Ji, Y. Yao, J. Li, X. Yan and F. Huang, *J. Am. Chem. Soc.* 2013, **135**, 74.

S3. M. Lee, S.-J. Lee and L.-H. Jiang, *J. Am. Chem. Soc.* 2004, **126**, 12724.