Synthesis of various supramolecular hybrid nanostructures based on pillar[6]arene modified gold nanoparticles/nanorods and their application in pH- and NIR-triggered controlled release

Yong Yao, Yang Wang and Feihe Huang*

State Key Laboratory of Chemical Engineering, Department of Chemistry, Zhejiang University, Hangzhou 310027, P. R. China;

Email: fhuang@zju.edu.cn

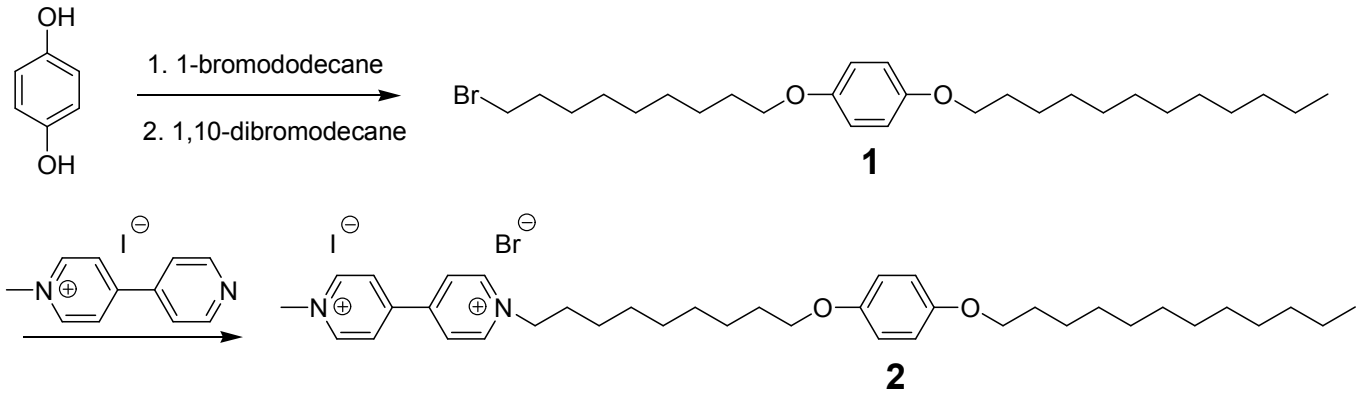
Electronic Supplementary Information

1. Materials and methods

Hydroquinone, 1-bromododecane, 1,10-dibromodecane, 4,4'-bipyridine, chloroauric acid, and sodium borohydride were reagent grade and used as received. Solvents were either employed as purchased or dried according to procedures described in the literature. Water soluble pillar[6]arene **WP6** was synthesized according to a previous report.[S1] ^{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. HRMS were obtained on a WATERS GCT Premier mass spectrometer. UV−Vis spectra were taken on a Perkin-Elmer Lambda 35 UV−Vis spectrophotometer. FT-IR spectra were taken with potassium bromide pellets on a TENSOR 27 spectrometer. The melting points were collected on a SHPSIC WRS-2 automatic melting point apparatus. Scanning electron microscopy (SEM) investigations were carried out on a JEOL 6390LV instrument. Transmission electron microscopy (TEM) studies were obtained using a JEM-1200EX instrument with an accelerating voltage of 80 kV. Dynamic light scattering (DLS) measurements were performed on a goniometer ALV/CGS-3 using a UNIPHASE He-Ne laser operating at 632.8 nm. The NIR light source was an externally adjustable power (2 W/cm^2) 785 nm semiconductor laser device (Changchun Femtosecond Technology Co. Itd, China).

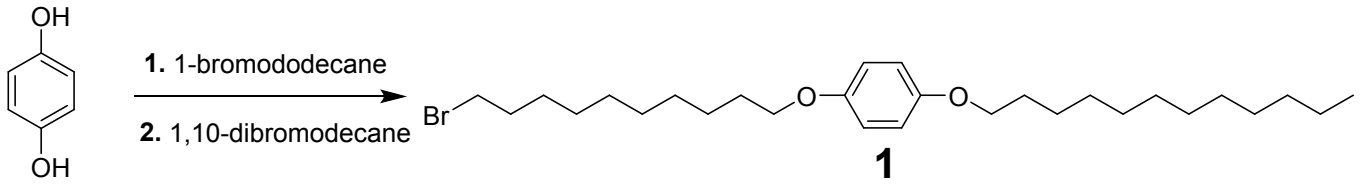
*2. Synthesis of compound **2***

Scheme S1. Synthetic route to compound **2**



2.1. Synthesis of compound 1[S1]

Scheme S2. Synthetic route to compound **1**



Anhydrous potassium carbonate (55.2 g, 400 mmol) was added to a solution of hydroquinone (44.0 g, 400 mmol) and 1-bromododecane (99.6 g, 400 mmol) in dry acetonitrile (500 mL) under vigorous stirring. The mixture was stirred at 80 °C for 24 hours under nitrogen atmosphere. Then 1,10-dibromodecane (120 g, 400 mmol) and additional anhydrous potassium carbonate (55.2 g, 400 mmol) were added into the reaction mixture and reacted for another 24 hours. After removal of the inorganic salt, the solvent was evaporated and the residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate, *v*/*v* 100:1) to give compound **1** as a white solid (79.6 g, 40%), mp 43.6–44.3 ºC. The proton NMR spectrum of **1** is shown in Fig. S1. ^{1}H NMR (400 MHz, chloroform-*d*, 293K) δ (ppm): 6.81 (s, 4H), 3.89 (s, J = 8 Hz, 4H), 3.40 (t, J = 8 Hz, 2H), 1.76–1.71 (m, 2H), 1.57–1.36 (m, 4H), 1.30–1.26 (m, 36H), 0.88 (t, J = 8 Hz, 3H). The ^{13}C NMR spectrum of **1** is shown in Fig. S2. ^{13}C NMR (100 MHz, chloroform-*d*, 293K) δ (ppm): 153.01, 115.14, 68.67, 32.84, 29.68, 29.62, 29.45, 29.36, 28.17, 26.05, 22.70, 14.13. LRESIMS is shown in Fig. S3: *m*/*z* 497.2 [**1** + H]$^{+}$. HRESIMS: *m*/*z* calcd for [**1** + Na]$^{+}$ $C_{28}H_{49}NaBrO_2^{+}$, 519.2808, found 519.2808; error 0 ppm.

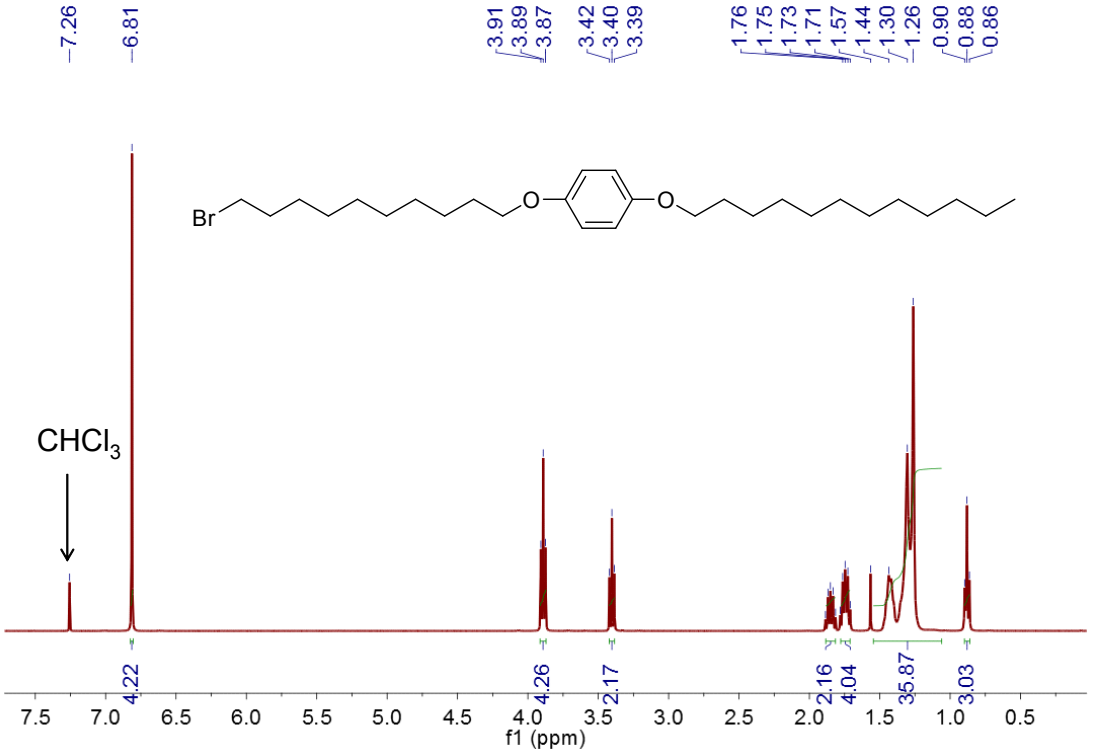


Fig. S1. ^{1}H NMR spectrum (400 MHz, $CDCl_3$, 293 K) of compound **1**.

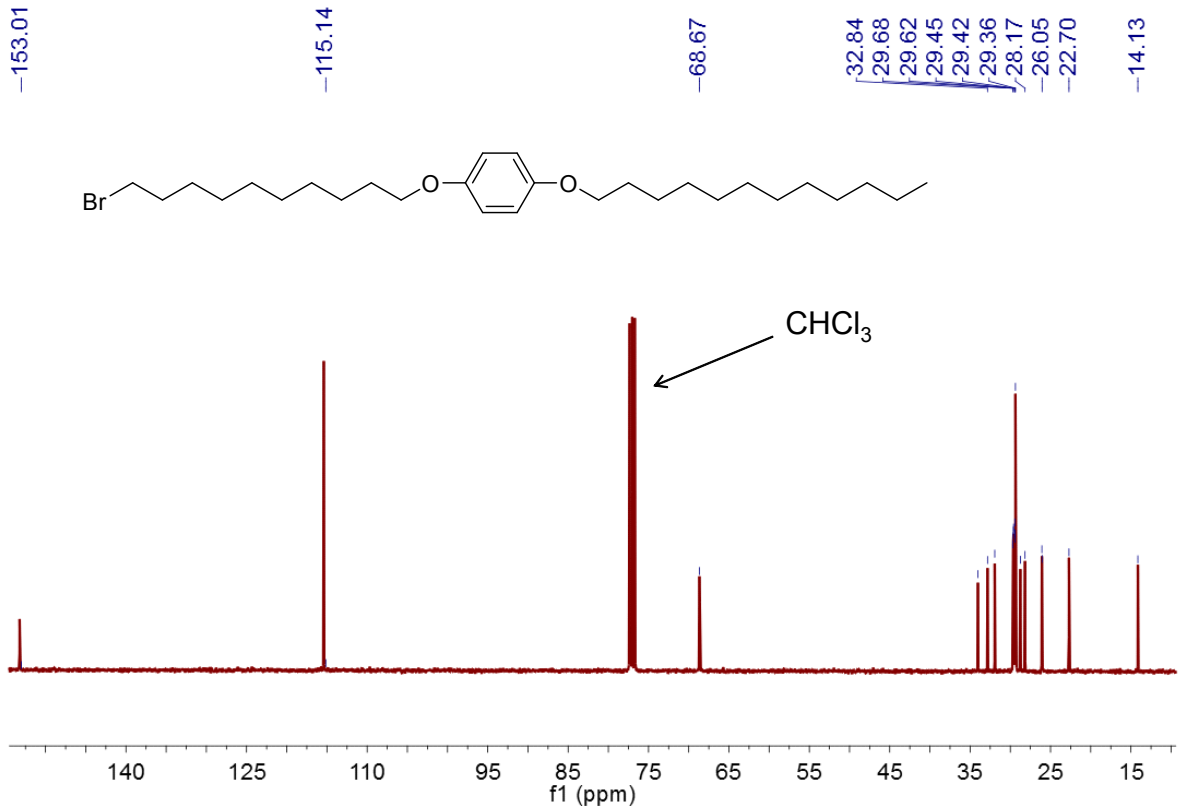


Fig. S2. ^{13}C NMR spectrum (100 MHz, $CDCl_3$, 293 K) of compound **1**.

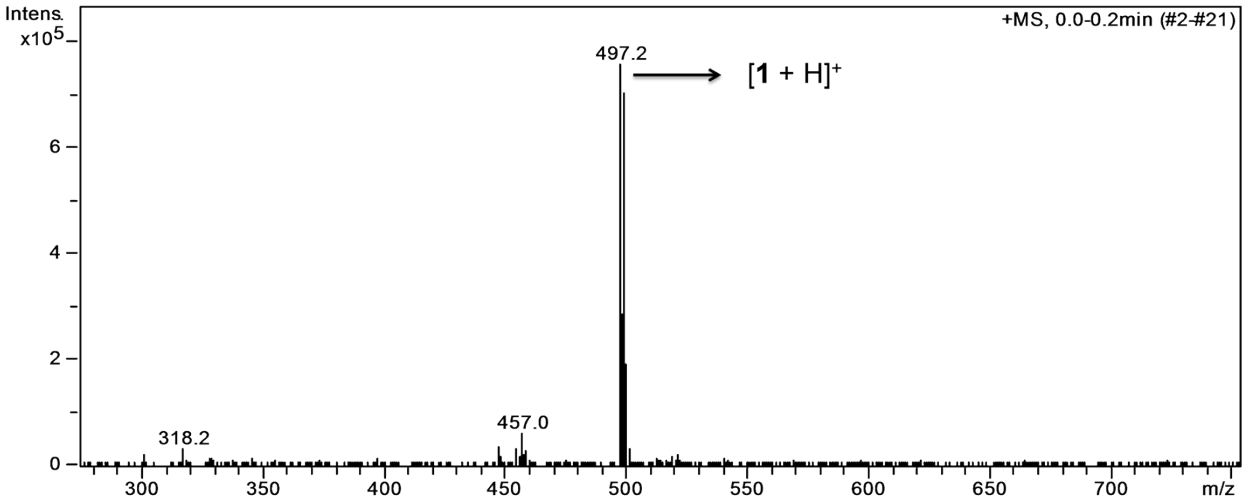
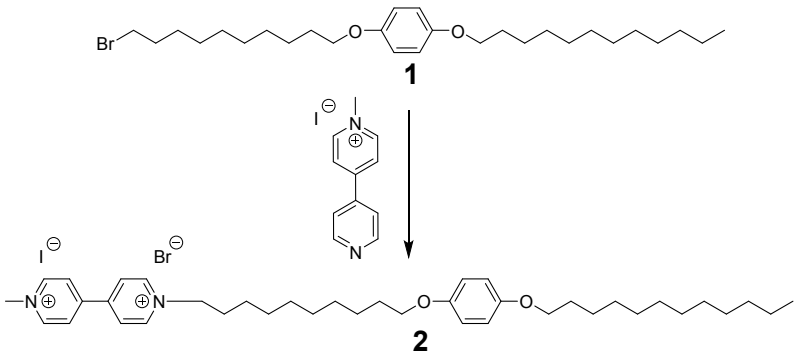


Fig. S3. Electrospray ionization mass spectrum of compound **1**. Assignment of the main peak: *m*/*z* 497.2 [**1** + H]$^+$.

*2.2. Synthesis of compound **2***

Scheme S3. Synthesis of compound **2**



Compound **1** (2.49 g, 5.00 mmol) and excess 1-methyl-4,4'-bipyridinium iodide[S2] were added to 200 mL of DMF and heated at 110 °C overnight. The mixture was cooled down and filtered, the precipitate was washed with DMF (30 mL × 3), and product **2** was obtained as an orange solid (3.51 g, 88%), mp 79.5–80.3 °C. The ^{1}H NMR spectrum of **2** is shown in Fig. S4. ^{1}H NMR (400 MHz, DMF, 293 K) δ (ppm): 9.70 (d, J = 8 Hz, 2H), 9.59 (d, J = 8 Hz, 2H), 9.07 (d, J = 8 Hz, 2H), 9.03 (d, J = 8 Hz, 2H), 6.89 (s, 4H), 4.97 (t, J = 8 Hz, 2H), 4.73 (s, 3H), 3.94 (m, 4H), 2.16 (t, J = 8 Hz, 2H), 1.74 (m, 4H), 1.44 (d, J = 8 Hz, 6H), 1.30 (m, 24H), 0.88 (t, J = 8 Hz, 3H). The ^{13}C NMR spectrum of **2** is shown in Fig. S5. ^{13}C NMR (100 MHz, D_2O, 293 K) δ (ppm): 146.61, 126.54, 126.53, 126.06, 115.21, 67.76, 28.95, 28.73, 28.37, 25.48, 22.06 and 13.93. LRESIMS (Fig. S6): m/z 294.4 $[M - Br - I]^{2+}$. HRESIMS: m/z calcd for $[M - Br - I]^{2+}$ $C_{39}H_{60}N_2O_2^{2+}$, 294.2322; found 294.2314, error –3 ppm.

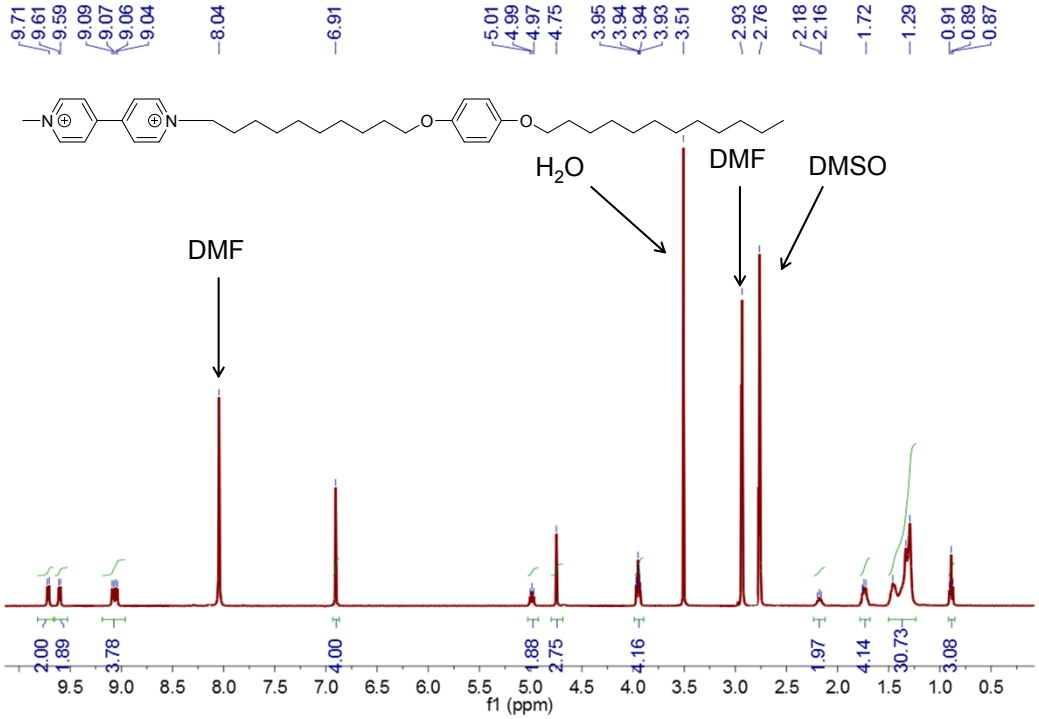


Fig. S4. ^{1}H NMR spectrum (400 MHz, DMSO-d_6, 293 K) of compound **2**.

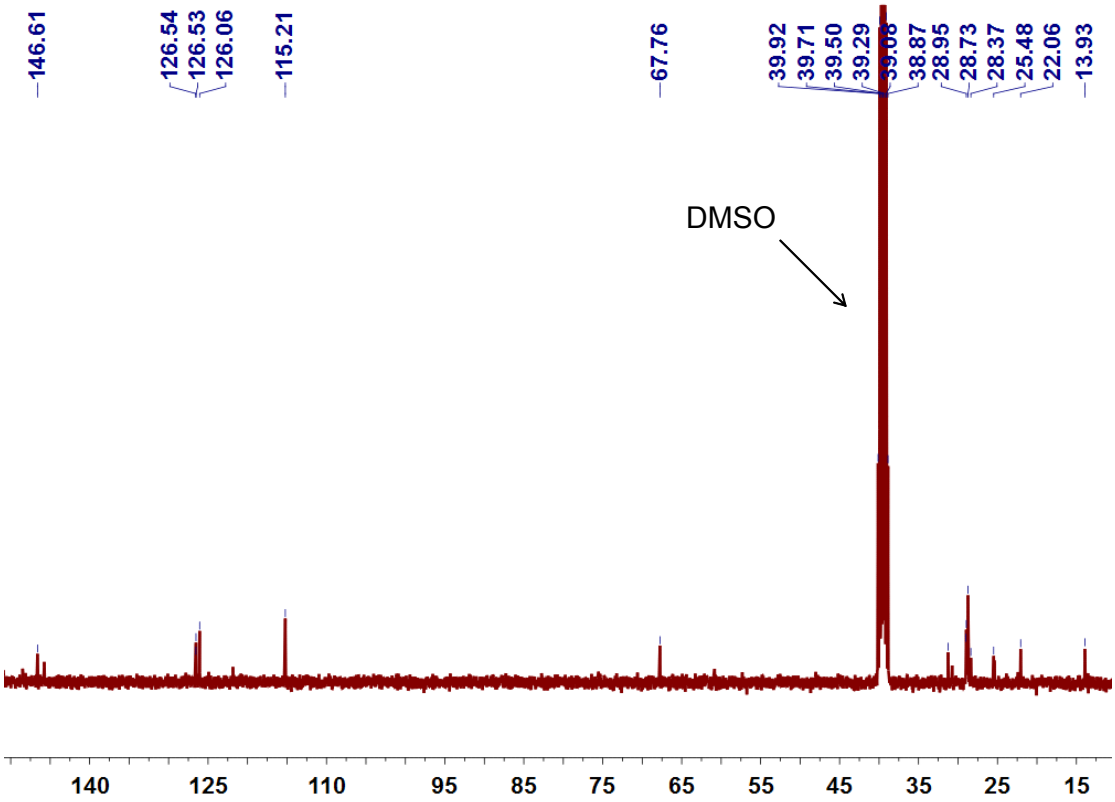


Fig. S5. ^{13}C NMR spectrum (100 MHz, DMSO-d_6, 293 K) of compound **2**.

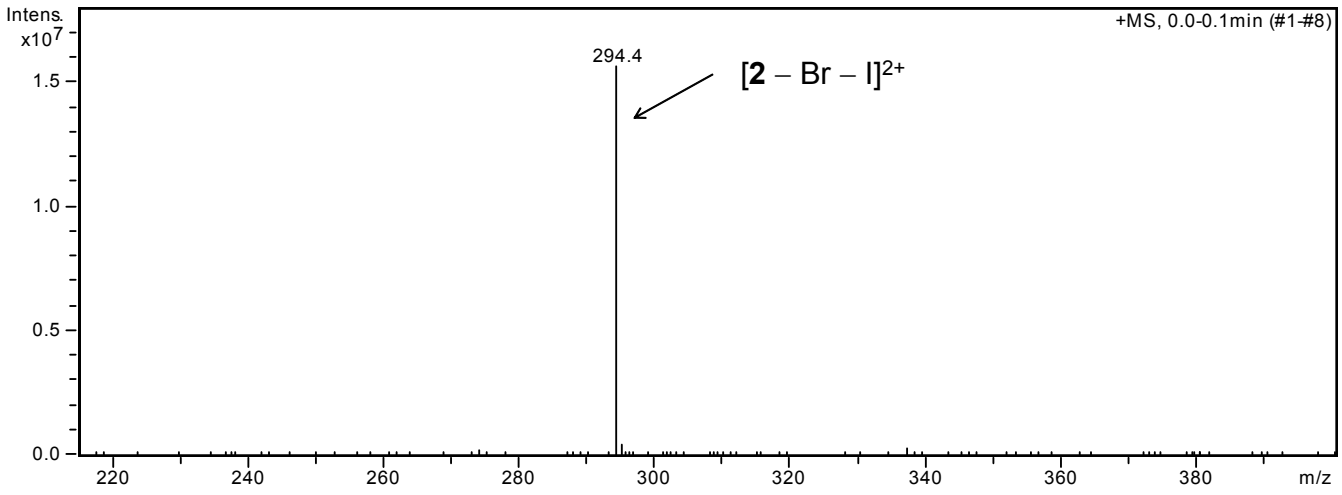


Fig. S6. Electrospray ionization mass spectrum of **2**. Assignment of the main peak: *m*/*z* 294.4 [M – Br – I]$^{2+}$.

*3. Synthesis of **WP6-AuNPs***

The **AuNPs** were synthesized by the reduction of $HAuCl_4$ in aqueous solutions of **WP6** at different concentrations. In a typical experiment, an aqueous solution of $HAuCl_4$ (0.100 mL, 10.0 mM) was added to an aqueous solution of **WP6** (2.70 mL, 1.00 mM). Then aqueous sodium borohydride (0.200 mL, 50.0 mM) was injected into the above solution under vigorous stirring. The solution became wine red, indicating that **WP6** stabilized **AuNPs** were immediately obtained.

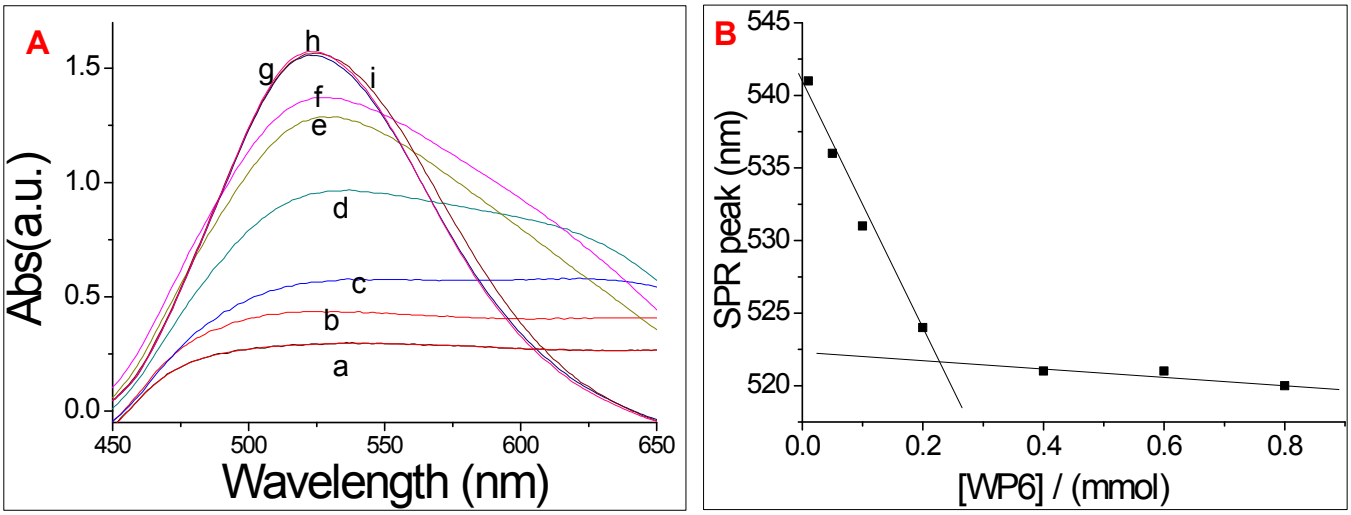


Fig. S7. (A) UV–Vis spectra of silver nanoparticles with different concentrations of **WP6** stabilizer: (a) 1.00×10^{-6} M; (b) 5.00×10^{-6} M; (c) 1.00×10^{-5} M; (d) 5.00×10^{-5} M; (e) 1.00×10^{-4} M; (f) 2.00×10^{-4} M; (g) 4.00×10^{-4} M; (h) 6.00×10^{-4} M; (i) 8.00×10^{-4} M. (B) The dependence of the SPR peak on the concentration of **WP6**. When the concentration of **WP6** was 1.00×10^{-6} M and 5.00×10^{-6} M, we could not measure the SPR peak of **AuNPs** (lines a and b in Fig. S7A).

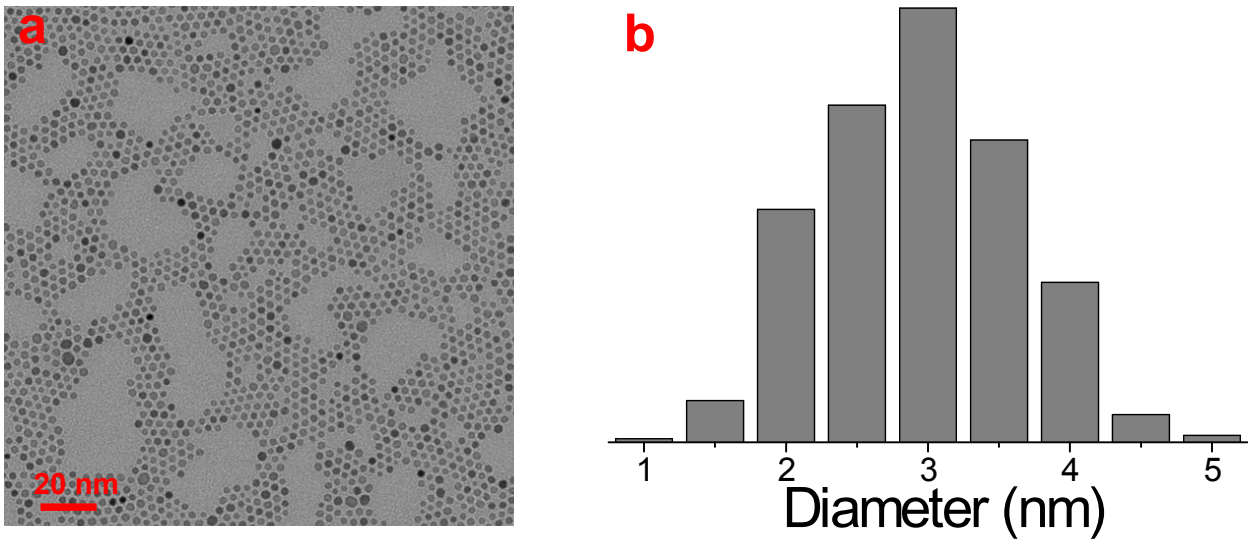


Fig. S8. (a) TEM image of **WP6** stabilized **AuNPs**. (b) Size distribution of **WP6** stabilized **AuNPs**. The concentration of **WP6** was 4.00×10^{-4} M.

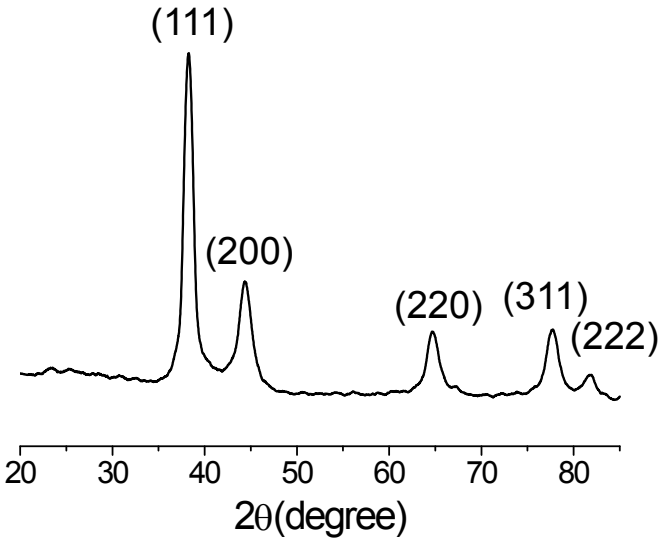


Fig. S9. XRD pattern of **WP6** stabilized **AuNPs** prepared with the concentration of **WP6** at 4.00×10^{-4} M.

4. Synthesis of supramolecular hybrid nanostructures

For fabrication of the supramolecular hybrid nanostructures, **WP6** stabilized **AuNPs** were first prepared by dissolving $HAuCl_4$ (0.100 mL, 10.0 mM), **WP6** (2.70 mL, 0.400 mM) and $NaBH_4$ (0.200 mL, 50.0 mM) in water. Then an aqueous solution of **2** (2.70 mL) with different concentrations was dropped into a solution of **WP6** stabilized **AuNPs**. Because of the **WP6**/paraquat complexation, compound **2** encapsulated into **WP6** was deposited on the surfaces of gold nanoparticles to form supramolecular amphiphilic gold nanoparticles (**SAuNPs**). These **SAuNPs** self-assembled in water to form various supramolecular hybrid nanostructures.

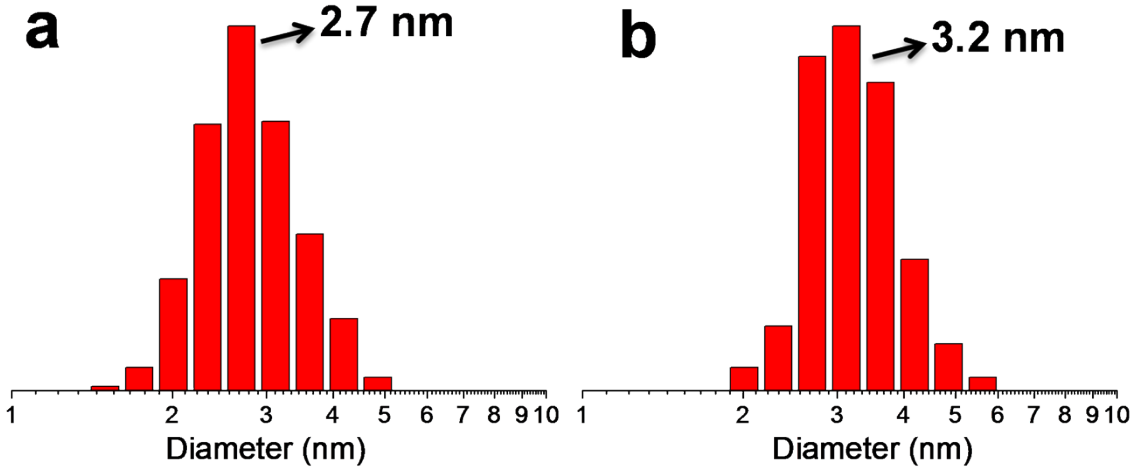


Fig. S10. DLS studies: (a) **WP6**-stabilized **AuNPs**; (b) nanoparticle supramolecular hybrid nanostructures No. 1.

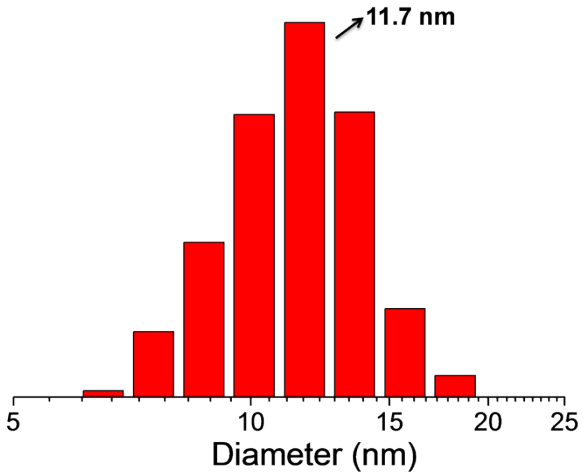


Fig. S11. DLS studies of nanoparticle supramolecular hybrid nanostructures No. 2.

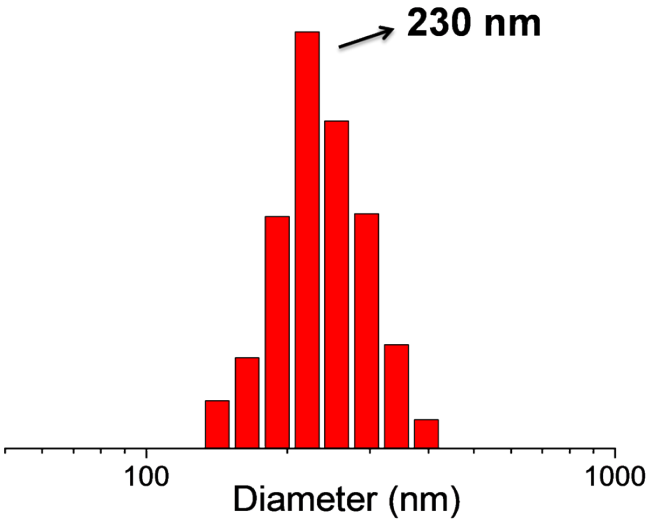


Fig. S12. DLS studies of nanoparticle supramolecular hybrid nanostructures No. 3.

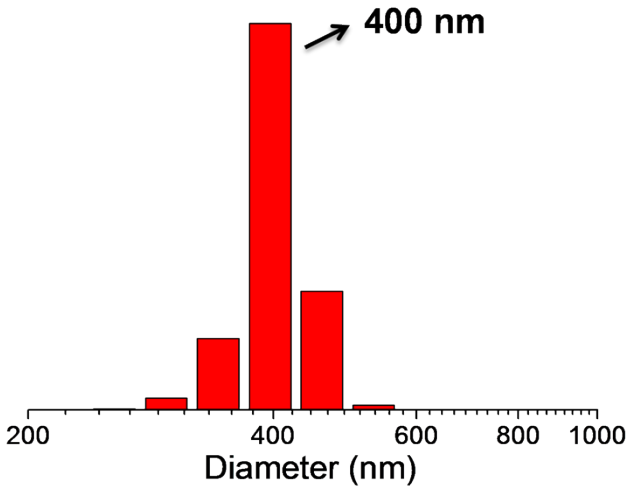


Fig. S13. DLS studies of nanoparticle supramolecular hybrid nanostructures No. 4.

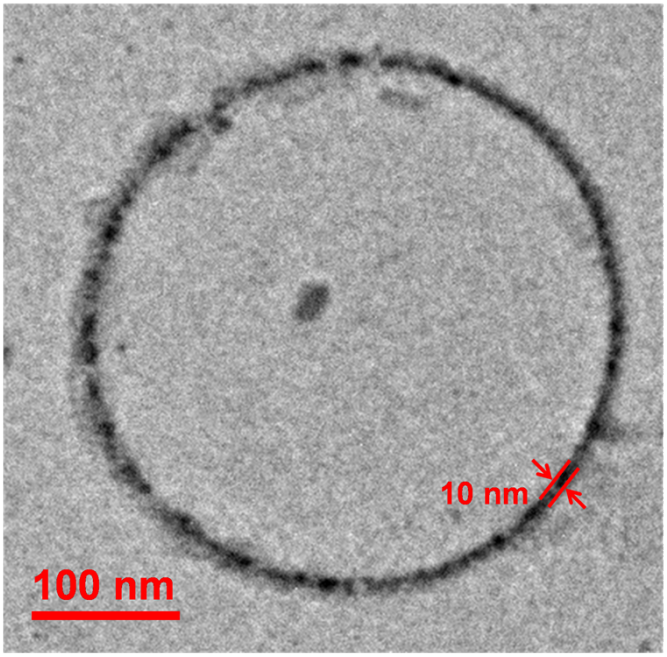


Fig. S14. Enlarged TEM image of a nanoparticle supramolecular hybrid vesicle.

5. pH-triggered controlled release

To study the encapsulation and controlled release abilities of the supramolecular hybrid micelles, a fluorescence titration experiment was carried out. It is well-known that Nile Red is insoluble and does not fluoresce in water, but its aqueous solution starts to fluoresce once it is encapsulated into micelles.[S3] Nile Red as a hydrophobic fluorescent guest was encapsulated into our supramolecular hybrid micelles. The emission spectrum of the micellar solution without Nile Red under the same conditions is also shown in Fig. S16 for comparison. There is no emission band of supramolecular hybrid micelles at 660 nm in the emission spectrum without Nile Red, while for the micellar solution with Nile Red encapsulated, fluorescence emission centered at 660 nm (excited at 550 nm) was observed, indicating the encapsulation of the hydrophobic Nile Red into the hydrophobic core of the micelles. Furthermore, considering that the supramolecular hybrid micelles are pH-responsive, release of Nile Red from the micelles was realized by adding acid (aqueous HCl), leading to disassembly of the supramolecular hybrid micelles.

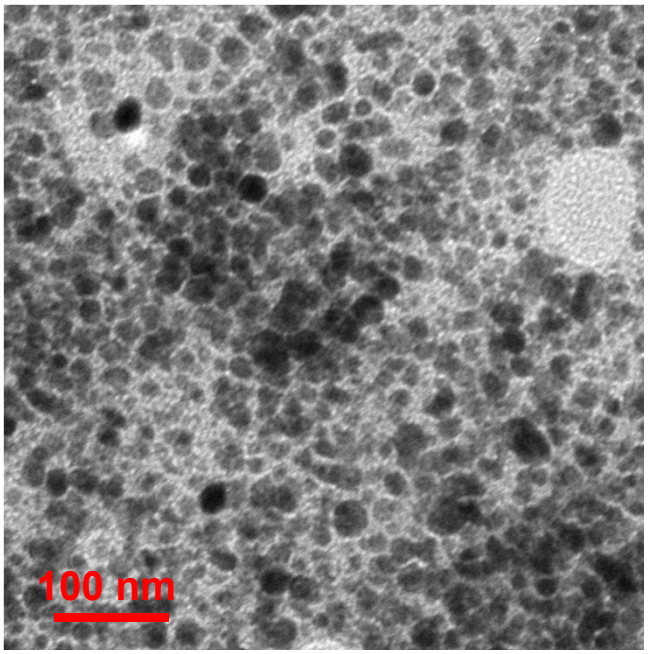


Fig. S15. TEM image of nanoparticle supramolecular hybrid micelles after adding acid (HCl).

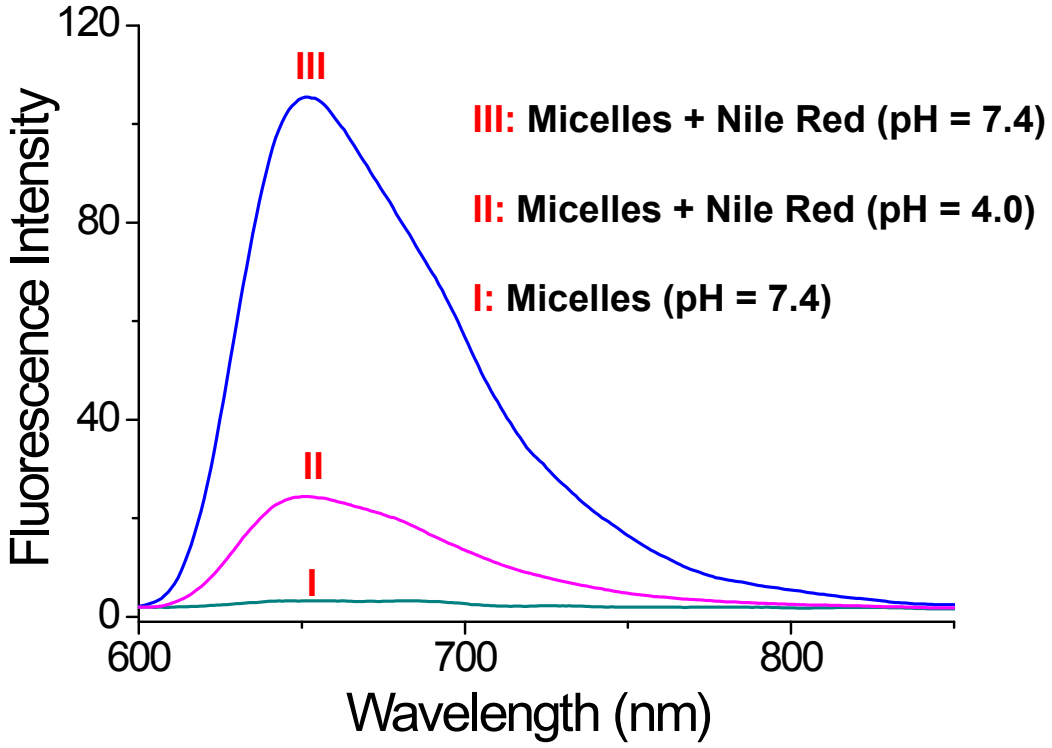


Fig. S16. Fluorescence emission spectra of Nile Red (λ_{exc} = 550 nm) encapsulated in nanoparticle supramolecular hybrid micelles at different pH values.

In contrast to the micellar aggregates, vesicles can encapsulate hydrophilic molecules within their interiors under neutral conditions and release the molecules in response to a decrease in pH. On the basis of this, calcein as a hydrophilic fluorescent molecule was put into the vesicle solution. As shown in Fig. S17, release of calcein from the interior of the vesicle was accompanied by an increase in fluorescence emission by adding acid (aqueous HCl).

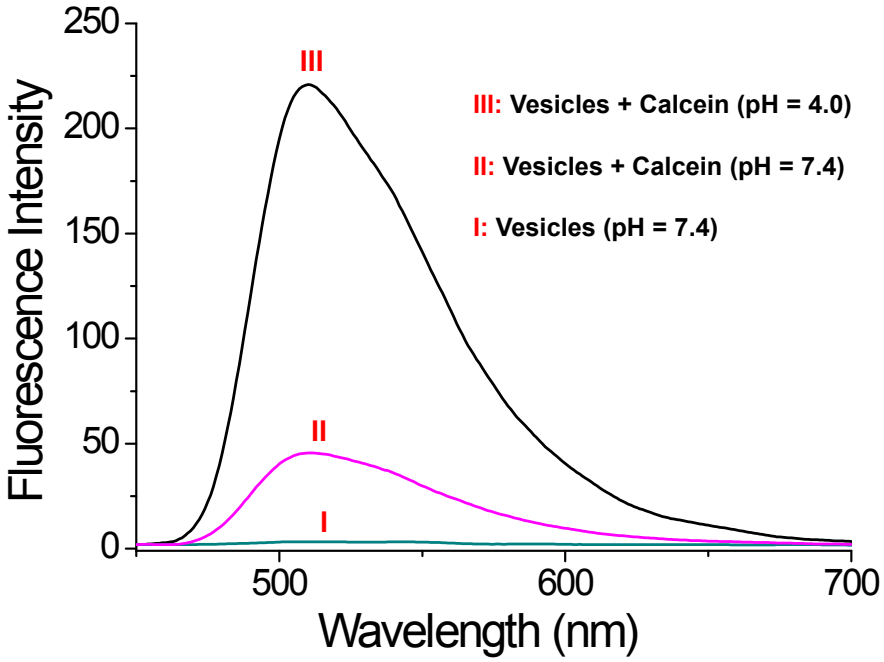


Fig. S17. Fluorescence emission spectra of calcein (λ_{exc} = 420 nm) encapsulated in nanoparticle supramolecular hybrid vesicles at different pH values. Calcein was acidized completely by HCl first before encapsulation.

*6. Synthesis of **WP6-AuNRs***

First, a seed solution for **AuNRs** was prepared as reported previously.[S4] A 5.00 mL amount of 0.500 mM $HAuCl_4$ was mixed with 5.00 mL of 0.200 M CTAB solution. A 0.600 mL portion of fresh 0.0100 M $NaBH_4$ was diluted to 1.00 mL with water and was then injected into the Au(III)-CTAB solution under vigorous stirring (1200 rpm). The solution color changed from yellow to brownish-yellow, and the stirring was stopped after 2 min. The seed solution was aged at room temperature for 30 min before use.

Then CTAB (50.0 mL, 0.200 M) was added to a solution of $AgNO_3$ (1.00 mL, 0.0100 M) at 28 °C. To this solution, $HAuCl_4$ (50.0 mL, 0.00100 M) was added, and then **WP6** (0.800 mL, 0.100 M) was introduced dropwise, until the solution changed from dark yellow to colorless. The final step was the addition of the seed solution (200 μL) to the above growth solution at 28 °C. The temperature of the growth medium was kept constant at 28 °C during the full procedure.

Fourier transform IR spectroscopy was used to test if **AuNRs** were indeed capped by **WP6** macrocycles. From the FT-IR spectra of **WP6** stabilized **AuNRs** (Fig. S18), as compared to those of bare **AuNRs**, a typical absorption peak at 1600 cm^{-1} was observed arising from the C=C stretching of the benzene ring in the backbone of **WP6**.

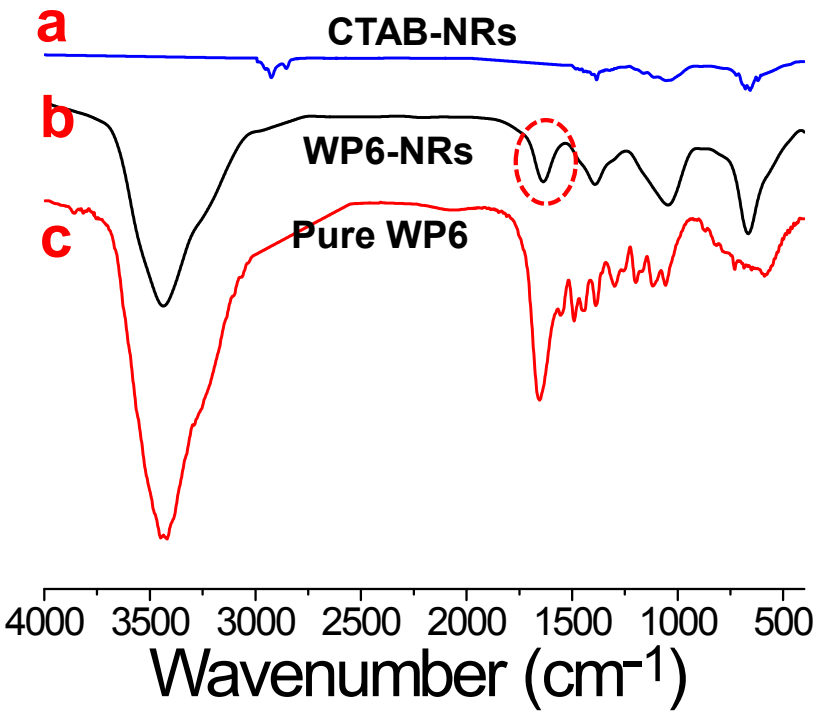


Fig. S18. Fourier transform IR spectra: (a) CTAB stabilized **NRs**; (b) **WP6** stabilized **NRs**; (c) pure **WP6**. The circle indicates the C=C stretching mode of the benzene ring.

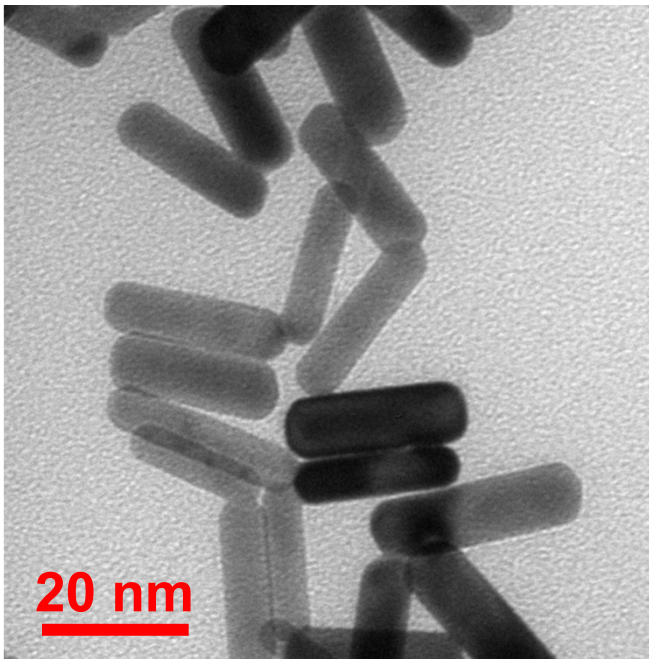


Fig. S19. TEM image of **WP6** stabilized **NRs**.

7. NIR-triggered controlled release

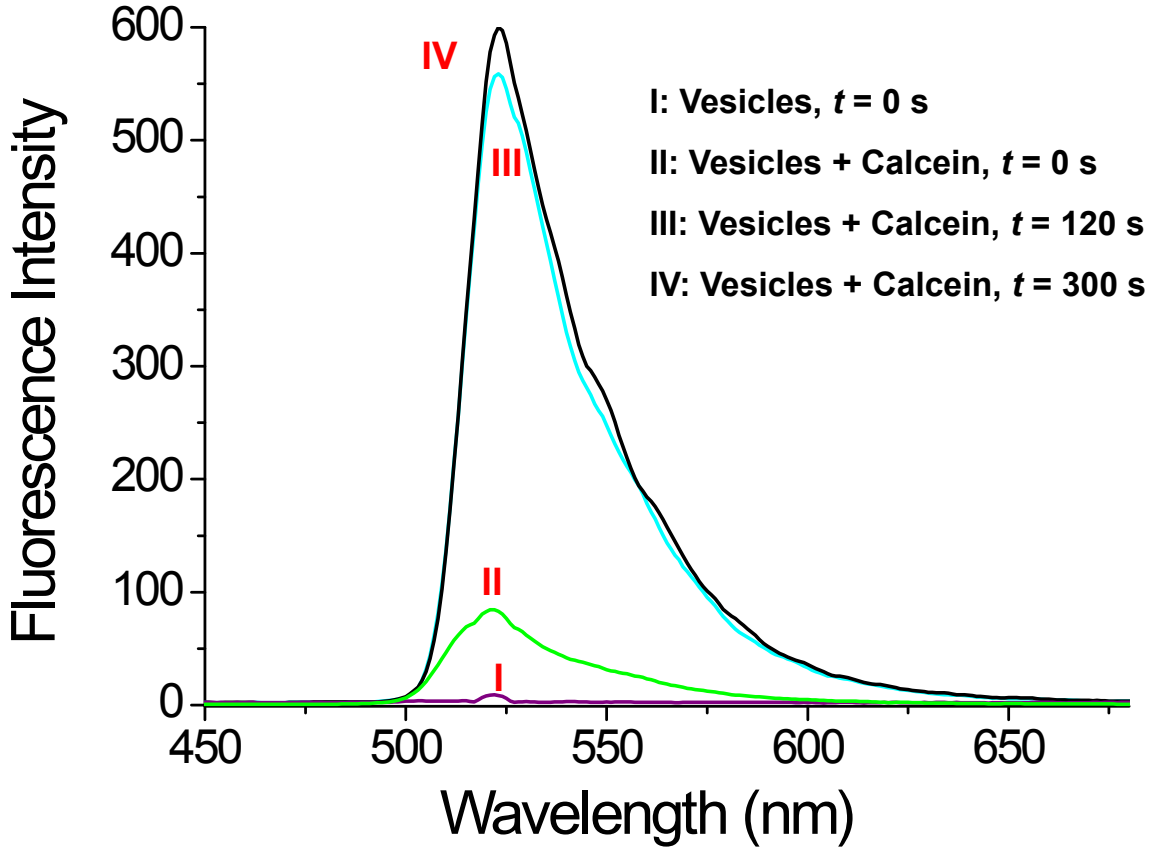


Fig. S20. Fluorescence emission spectra of calcein (λ_{exc} = 500 nm) encapsulated in nanorod supramolecular hybrid vesicles with different NIR irradiation times.

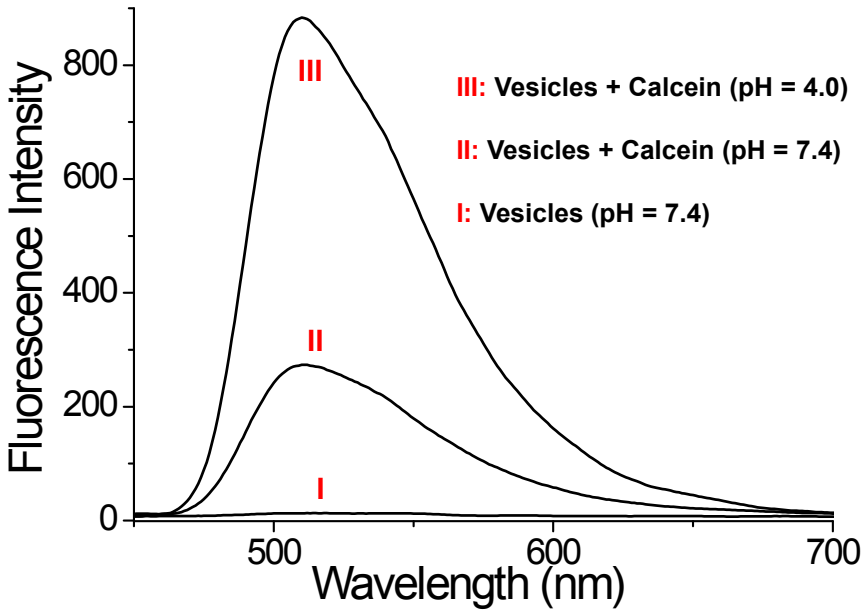


Fig. S21. Fluorescence emission spectra of calcein (λ_{exc} = 420 nm) encapsulated in nanorod supramolecular hybrid vesicles at different pH values. Calcein was acidized completely by HCl first before encapsulation.

8. References:

S1. J. Yang, X. Chi, Z. Li, G. Yu, J. He, Z. Abliz and F. Huang, *Org. Chem. Front.,* 2014, **1**, DOI:10.1039/C4QO00086B.

S2. (a) G. Yu, M. Xue, Z. Zhang, J. Li, C. Han and F. Huang, *J. Am. Chem. Soc.,* 2012, **134**, 13248; (b) K. Wang, D-S. Guo, X. Wang and Y. Liu, *ACS Nano,* 2011, **5**, 2880.

S3. (a) G. Chen and Z. Guan, *J. Am. Chem. Soc.,* 2004, **126**, 2662; (b) J. Jiang, X. Tong and Y. Zhao, *J. Am. Chem. Soc.,* 2005, **127**, 8290.

S4. (a) B. Nikoobakht and M. A. El-Sayed, *Chem. Mater*., 2003, **15**, 1957; (b) X. Ye, L. Jin, H. Caglayan, J. Chen, G. Xing, C. Zheng, V. Doan-Nguyen, Y. Kang, N. Engheta, C. R. Kagan and C. B. Murray, *ACS Nano,* 2012, **6**, 2804.