Supporting Information

A triply-responsive supramolecular vesicle fabricated by α -cyclodextrin

based host-guest recognition and double dynamic covalent bonds

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Experimental

Materials

4-nitrotoluene, N,N-dimethylaniline, 4-amylphenol, 1,4-dibromobutane were purchased from Aladdin Chemicals. 1,2-di(pyridin-2-yl)disulfane, 2mercaptoethanaminium chloride and α -cyclodextrin were the product of Sigma-Aldrich. All the other reagents were commercially available of analar reagent grade. All the compounds were used directly without further purification. Ultrapure water was used throughout the whole experiments.

Characterization

¹H NMR spectra was gotten on an API Bruker Avance 300 M NMR at room temperature. ESI-MS spectrum was performed on API 4000 MS equipment. TEM images were obtained on a JEM-1011 electron microscope. SEM pictures were gotten with a Hitachi S-4800 scanning electron microscope. The samples for TEM detection were dropped in a copper wire mesh. Then the samples were air-dried. The samples of SEM measurement were obtained by dropping the sample's solution to the copper wire mesh and then dried and sprayed with the gold. The average diameter of vesicles was recorded by DLS measurement with a Wyatt QELS Technology DAWN HELEOS instrument, which used a 12-angle replaced detector in a scintillation vial and a 50 mW solid-state laser. The water for preparation samples of DLS was filtered by a 0.45 µm filter and samples of DLS were also filtered by a 0.45 µm filter before testing. UV-vis curves were obtained at room temperature with a UV-2100 spectrophotometer which was purchased from Shimadzu (China) Co. Ltd. A certain

concentration of solution was poured into a quartz cuvette to detect the absorption peaks. The sonication was performed with a SNT2030 ultrasonic cleaner, BRANSON ultrasonics (Shanghai) Co. Ltd.





Fig. S1 Synthetic pathway of G₁

4-aminobenzaldehyde can be obtained by oxidation and reduction of 4-nitrotoluene. 1.95g Na₂S and 6g NaOH were dissolved in 100 mL water, the solution was heated to 60°C, and then sulfur was added while the temperature was maintained at 90°C for 30 min to prepare Na₂S_x. Subsequently, Na₂S_x was added gradually into a mixture of 4nitrotoluene (13.7g, 100 mmol), DMF (0.81g) and 100 mL EtOH at 80°C. The mixture was continued to react for 3h and then was made by steam distillation to remove 4-nitrotoluene and 4-nitrobenzaldehyde. The residue was extracted by ethyl ether, evaporated to give the crude product of 4-aminobenzaldehyde and used without purification.

4-aminobenzaldehyde (2.42 g, 20 mmol) was dissolved in 3 mM hydrochloric acid (50 mL), which was cooled to temperature at 0-5°C. Then, a solution of sodium nitrite (2.1 g, 30 mmol) in 20 mL of water was added dropwise. The resulted diazonium solution was added dropwise to another solution of N,N-dimethylaniline (2.42 g, 20 mmol) in acetic acid-sodium acetate buffer (50 mL) (pH = 6) with stirring in an icebath. The mixed system was further stirred vigorously below 5 °C for 30 min, and then stirred for 4 h at room temperature. The red precipitate was obtained and collected by filtration and washed with large amount of water. Finally, the product was purified by silica-gel column chromatograghy (PE and EA as eluent) to afford G₁ (1.41 g, 27% yield). ¹H NMR (300 MHz, CDCl₃), δ : 9.98 (s, 1H), 7.92-7.83 (m, 6H), 6.70-6.68 (d, 2H), 3.04 (s, 6H). m/z: 253.3.



Synthesis of 2-((4-(4-pentylphenoxy)butyl)disulfanyl)ethanamine(G₂)



Fig. S3 Synthetic pathway of G₂

4-amylphenol (1.64g, 10 mmol), 1,4-dibromobutane (6.45g, 30 mmol) and KOH(1.12 g, 20 mmol) in EtOH (150 mL) was refluxed under an atmosphere of N_2 for 12 h. After cooling down to room tempreture, EtOH was removed under reduced pressure. Dichloromethane (100 mL) was added to the resulting residue and the solid was filtered off. Dichloromethane was removed in vacuo and the crude product was purified by a flash column chromatography (SiO₂, ethyl acetate/petroleum ether (PE), from 1/20 to 1/5 v/v). Compound 1 (1.89 g, 63%) was obtained as a colorless oil.

A solution of compound 1 (1.89 g, 6.3 mmol) and thiourea (1.91g, 25 mmol) in EtOH (50mL) was heated under reflux for 12h. After cooling down, a solution of KOH (2.02g, 36 mmol) in H₂O (30 mL) was then added into the above solution, refluxed for another 3 h and cooled down to room tempreture. The mixture was acidified by HCl to pH = 1 and extracted by Et₂O (30 mL×3). Organics were combined and washed with brine, dried over Na₂SO₄. The solvent was removed in vacuo and the crude product was purified by a flash column chromatography (SiO₂,

EA/PE, 1/5 v/v). Compound 2 (1.05g, 66%) was obtained as a colorless oil.

AcOH (1 mL) was added to the solution of 1,2-di(pyridin-2-yl)disulfane (1.76 g, 8 mmol) in methanol (50 mL), then compound 2 (1.05g, 4mmol) in DCM (20 mL) was added dropwise to the above solution over a period of 10 min. The mixture was then stirred for 24 h at 25°C. After removing the solvent, the residue was dissolved in DCM (40 mL) and washed sequentially by water (100 mL) and saturated brine (100 mL), then dried over Na₂SO₄. After concentrating under vacuum, the residue was purified by silica-gel column chromatography (DCM/MeOH = 50:1, v/v) to afford compound 3 as a colorless oil (1.26g, 87%). The methanol solution of compound 3 without purification (1.26 g, 3.5 mmol) and 2-mercaptoethanaminium chloride (0.4 g, 3.5 mmol) was stirred for 2 h at 25°C, after removing the solvent, the residue was dissolved in a small amount of methanol (10 mL), which was further added dropwise to plenty of diethyl ether (150 mL) to afford white precipitates, the precipitates were collected by filtration and dried in vacuum, and the target product G₂ was obtain as a white powder (0.98 g, 84%). ¹H NMR (300 MHz, CD₃OD), 5: 7.08-7.06 (d, 2H), 6.83-6.81 (d, 2H), 4.00-3.97 (t, 2H), 3.34-3.29 (m, 2H), 2.99-2.96 (t, 2H), 2.86-2.84 (t, 2H), 2.56-2.52 (t, 2H), 1.94-1.86 (m, 4H), 1.63-1.55 (m, 2H), 1.39-1.27 (m, 4H), 0.93-0.89 (t, 3H). m/z:327.2.



Fig. S4 ¹H NMR spectra of G₂



Fig. S5 The complex constant calculated of α -CD/G in 1:1 mode.



Fig. S6 Fluorescence emission spectra of pyrene in aqueous solutions of α -CD/G with different concentrations.



Fig. S7 Time-dependent UV-vis spectra of (a) G₂ alone and (b) G in aqueous solution upon UV irradiation.



Fig. S8 TEM images of the α -CD/G samples after treating with (a) UV irradiaion; (b) acidification with HCl; (c) adding DTT.



Fig. S9 2D ROESY spectrum of α -CD and G in D₂O with the addition of CY5.