Supporting Information for

Reversible morphology transitions of supramolecular polymer self-assemblies for switch-controlled drug release

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1. Materials and Methods

1.1 Materials

Mono-6-deoxy-6-alkyne-β-cyclodextrin (β-CD-C≡CH) and bis (2-azidoethyl) amine (EA-$(N_3)_2$) were synthesized according to the methods reported in the literature,[1, 2] Polyethylene glycol (PEG M_w=2000), Methoxypolyethylene glycols (mPEG，M_n=1500) and Aminoazobenzol(AZO, 99%,) were purchasedfrom ACROS Chemical Industries (USA).N,N,N', N, N-pentamethyldiehylenetriamine (PMDETA) wassupplied by Yutian Chemical (Liyang City, China) and used asreceived without further purification, copper (I) bromide (CuBr, 98%), 2-(Diethyl amino)-ethyl methacrylate (DEAEMA, 99%) and Succinic anhydride(98%) were purchased from Aldrich. Doxorubicin hydrochloride (DOX·HCl, 99%) was purchased from Sigma. Dimethylformamide (DMF) and Acetone were dried over 4A molecular sievepriortouse. All other reagents were purchased from Sinopharm Chemical Reagent Co. and used as received.

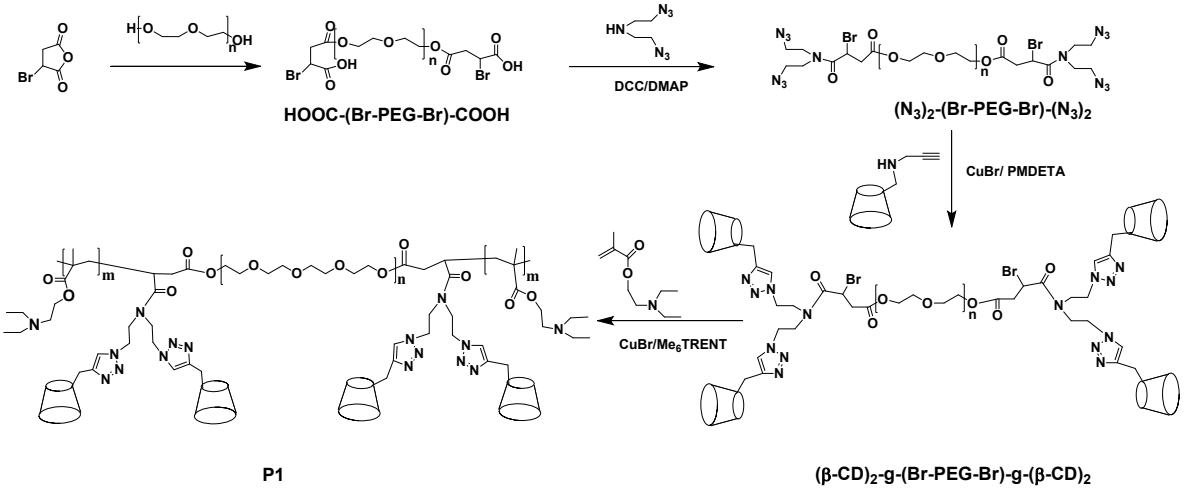
1.2 Methods

^{1}H-NMR was recorded on a Bruker-Avance III NMR spectrometer (400 MHz) with dimethyl sulfoxide-d_6 (DMSO-d_6) and pH7.4 and 6.0 D_2O as solvents. The 2D ^{1}H-NMR NOESY spectra were recorded on a Bruker-Avance III NMR spectrometer (400 MHz) with pH 6.0 D_2O as solvents. An isothermal titration calorimeter (ITC; Micro Cal Inc., U.S.A.) has been used for determining from a single titration curve simultaneously the enthalpy of the interaction between benzophenone and cyclodextrin in their native or polymerized form and the equilibrium constant corresponding to the formation of a complex between those species.[7] The FT-IR spectra were obtained on a Nicolet iS10 spectrometer (Nicolet) casting samples into thin films on KBr. Transition mode was used and the wavenumber range was set from 4000 cm^{-1} to 500 cm^{-1}. UV-vis spectrophotometer measurement was performed on Shimadzu UV-2550 modelspectroscopy (Shimadzu, Japan).Particle size was measured by Zetasizer Nano-ZS dynamic light scattering (DLS) (Malvern Instruments, UK),Each sample was kept at a predetermined temperature for 3 min before measurement without any filter.Slight light scattering(SLS) analysis was performed on a DAWN HELEOS-Ⅱ multi-angle light scattering detector (Wyatt Technology Corporation, USA) operated at 665 nm, using Gallium-arsenic as incident laser beam source. SLS data were collected at 6 different concentrations of the aggregates and 18 different angles for each concentration. The data were analyzed using the Zimm plot method

on HELEOS-Ⅱ Firmware 2.4.0.4 Advanced software to determine R_g. TEM was performed on JEM-2010 microscope (Japan) with an electron kinetic energy of 300 kev. The samples were prepared by aspirating the brush superamolcular bolock copolymer solution (2 mg/mL) on to the carbon-coated copper grids at the same setting time. Excessive solution was adsorbed away with filter paper after 10 min, and then the samples were measurment without any negative staining.

2 Synthesis and Characterizationof P1

In this study, poly((diethylamino) ethyl-methacrylate)-*b*-polyethylene glycol-*b*-poly((diethylamino)ethyl-methacrylate) bearing two *β*-CD at every terminal [(*β*-CD)$_2$-*g*-(PDEA-*b*-PEG-*b*-PDEA)-*g*-(*β*-CD)$_2$, P1]was first designed and synthesized.The structure and synthetic route of the triblock polymer are shownin Scheme S1.



Scheme S1 Synthesis of P1

2.1Synthesis of two bromosuccinic acid modified Polyethylene glycol macroinitiator HOOC-(Br-PEG-Br)-COOH

HOOC-(Br-PEG-Br)-COOHwas synthesized according to the literature [3] with some change. Typically,PEG (M_W= 2000, 2.0 g, 1.0 mmol) andbromosuccinicanhydride(0.72 g, 4mmol) were dissolvedin 1,4-dioxane (8 mL) and DMAP (240 mg, 2.0 mmol)for 24 h under nitrogen gas at room temperature.The polymer solution wasthen filtered and precipitated in ether.The white precipitatewas dissolved in dichloromethane (40 mL) and washedwith 10% HCl (3×30 mL) and brine (3×30 mL).Theorganic layer was dried with anhydrous $MgSO_4$ overnight.The solution was filtered, precipitated in ether/hexane (1/2) anddried by vacuum at 25 ^oC.A white powder (1.14 g, 57% yield) wasobtained.FT-IR (Figure S1 A) ν_{max}= 1720 cm^{-1} (-COO-), 2884 cm^{-1} (CH_2); ^{1}H-NMR (Figure S2

A) (400 MHz, DMSO, room temperature, TMS) δ (ppm):3.31-3.87 (-OCH_2O-), 4.21 (-CH_2-COOH), 4.73 (-BrCH-).

2.2 Synthesis of two bis (2-azidoethyl) amine ended Polyethylene glycol macroinitiator $(N_3)_2$-(Br-PEG-Br)-$(N_3)_2$

HOOC-(Br-PEG-Br)-COOH(0.472 g, 0.2mmol)andbis (2-azidoethyl) amine (EA-$(N_3)_2$)(0.124g, 0.8mmol) were dissolved in 6 ml DMFand treated with DCC(0.164g,0.8mmol) and DMAP (0.049g, 0.4 mmol) for 24 hat roomtemperature.Then dicyclohexylurea was filtered out andthe polymer was precipitated in ether, filtered and washedwith methanol.The polymer was dried using a vacuumat20 ^oC for 24 h to give a white powder (0.45 g, 50%yield). FT-IR (Figure S1B) ν_{max}= 1720 cm^{-1} (-COO-), 2884 cm^{-1} (CH_2); 1647cm^{-1}(-CON-); 2100 cm^{-1} (N_3), ^{1}H-NMR (Figure S2B) (400 MHz, DMSO, room temperature, TMS) δ (ppm): 3.31-3.87 (-OCH_2O-), 4.21 (-CH_2-COOH), 4.73 (-BrCH-), 2.96 ppm(CH_2-N_3).

2.3 Synthesis of two β-CD modified polyethylene glycol macroinitiator (*β*-CD)$_2$-*g*-(Br-PEG-Br)-*g*-(*β*-CD)$_2$

(*β*-CD)$_2$-*g*-(Br-PEG-Br)-*g*-(*β*-CD)$_2$was prepared via the click reaction of $(N_3)_2$-(Br-PEG-Br)-$(N_3)_2$ with a slight excess of*β*-CD-C≡CH, and a typical procedure was as follows. To a schlenk tube equipped with a magnetic stirring bar, $(N_3)_2$-(Br-PEG-Br)-$(N_3)_2$ (0.519 g, 0.2mmol), PMDETA (0.747 g, 4.31 mmol), β-CD-C≡CH(1.28 g, 1.20 mmoL) and DMF (5 mL) were added. After one brief freeze-thaw cycle, CuCl (0.119 g, 1.20 mmol) was introduced under the protection of N_2 flow. The reaction tube was carefully degassed by three freeze-pump-thaw cycles, sealed under a vacuum, and the mixture was then stirred at 50^{o}C for 24 h. The reaction mixture was then exposed to air and precipitated into ether four times to obtain the white solid. The crude product was dissolved in 5 mL DMF, enclosed in dialysis membrane (MWCO 2000Da), and then purified by dialyzing in deionized water for 48 h to remove the excess β-CD-C≡CH. After removal of the water by freeze drying, a white powder was obtained (0.511g, yield: 35.1%). ^{1}H NMR (Figure S2C) (400 MHz, DMSO-d_6,room temperature, TMS), δ (ppm): 7.92 (s, 1) of 1,2,3-triazole ring; 5.75 (7,8-H), 4.83 (1-H), 4.47 (9-H), 3.64 (3,5-H), 3.39 (2,4-H) ofβ-CD;3.31-3.8 (-CH_2O-) of PEG.

2.4 Synthesis ofP1

P1 was synthesized by theatom transfer radical polymerization(ATRP)reaction of DEA

monomer using(β-CD)$_2$-*g*-(Br-PEG-Br)-*g*-(β-CD)$_2$as the macroinitiator. In a typicalexample,DEAmonomer(1.95g, 1.5mmol),PMDETA (3.46 mg, 0.02mmol), (β-CD)$_2$-*g*-(Br-PEG-Br)-*g*-(β-CD)$_2$ (728.3 mg, 0.01mmol), and 6 mL DMF werecharged into a reaction flask. The flask was capped with a rubber plug and purged with purenitrogen for 30 min. CuBr (0.0864g, 0.06mmol) was then introduced under protection ofN_2 flow tostart the polymerization at 30 ^oC under a nitrogenatmosphere. After 5h, the reaction mixture was then exposed to air anddiluting with THF. The copper catalystwasremoved by passing the solution through alumina. The polymerwas obtained from the resulting reaction mixture by addition to colddiethyl ether to precipitate the solids which were filtered and dried underhigh vacuum at room temperature for 12 h. The isolated polymerwas reprecipitated from THF into colddiethyl ether three times and dried undervacuum at 25 ^oC for 24 h, a pale powder was obtained (1.03g, yield: 38.1%). ^{1}H NMR (Figure S2D) (400 MHz, DMSO-d_6, room temperature, TMS), δ (ppm): 7.92 (s, 1) of 1,2,3-triazole ring; 5.75 (7,8-H), 4.83 (1-H), 4.47 (9-H), 3.64 (3,5-H), 3.39 (2,4-H) of β-CD; 3.31-3.8 (-CH_2O-) of PEG; 4.27 (O-CH_2), 3.48 (N-CH_2-CH_2), 3.20 (N-CH_2-CH_3), 1.5-0.9 (-CH_3) of PDEA. $M_{w,SEC}$=22950, M_w/M_n=1.27.

2.5 Characterization of P1

The structure and synthetic route of P1 was shownin Scheme S1.ATRP polymerization has frequently been used to prepare blockcopolymers as drug delivery systems due to the good controlover polymerization of various monomers.[3] In the currentwork,P1 was prepared via ATRP reaction of DEA usingas the macroinitiator(β-CD)$_2$-*g*-(Br-PEG-Br)-*g*-(β-CD)$_2$ which was synthesized through the click reaction of four azide groups in $(N_3)_2$-(Br-PEG-Br)-$(N_3)_2$ and excessive mono-6-deoxy-6-alkyne(β-CD-C CH) monomers in the presence of copper (I) bromide (CuBr)/1,1,4,7,7-pentamethyldiethylenetriamine (PMDETA). The compound of $(N_3)_2$-(Br-PEG-Br)-$(N_3)_2$ was prepared via the amidation reaction between HOOC-(Br-PEG-Br)-COOH and bis-(azido-ethyl)-amine (EA-$(N_3)_2$),HOOC-(Br-PEG-Br)-COOHwas synthesized through the esterification reaction between HO-PEG-OH and excessive bromosuccinic anhydride. These copolymersweresuccessfully synthesized and confirmed by and FT-IR (Figure S1), ^{1}HNMR(Figure S2) and SEC-MALLS (Figure S3).The polymerization resultsare listed in Table S1. It can be seen that the molecularweight (M_w) of(β-CD)$_2$-*g*-(Br-PEG-Br)-*g*-(β-CD)$_2$is 7280 nearly the theoretical value (M_w=7283) and the chemical shift of 1,2,3-triazole ring can be clearly found at 7.9 ppm in Figure S2D.In addition, the character chemical shift of PEG, β-CDand PDEA could be found in

Figure S2D, and thedegree of polymerization (DP) of DEA was 57 tested by SEC-MALLS. Therefore, SEC-MALLS and ^{1}HNMR results indicate that P1 wassuccessfully synthesized.

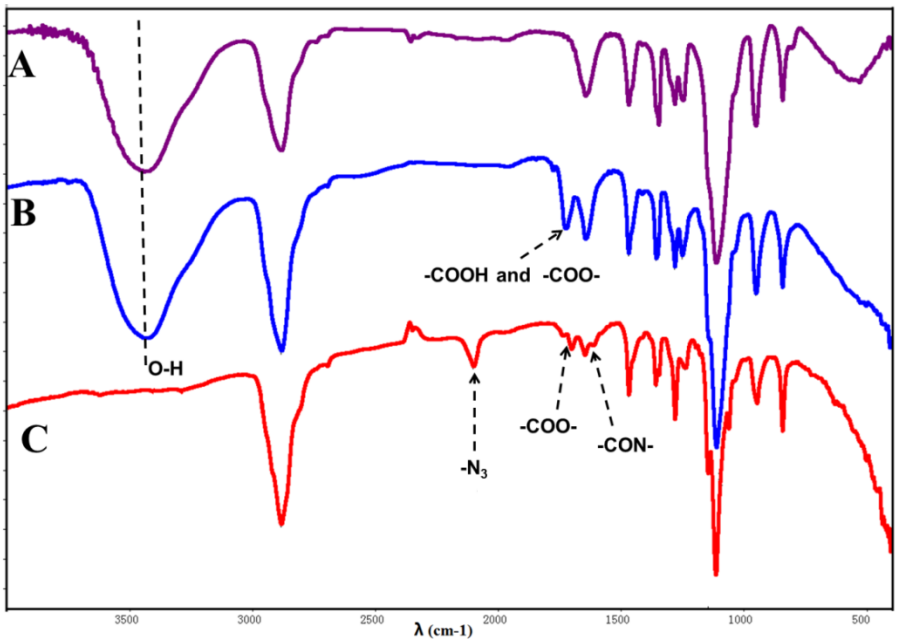


Figure S1 FT-IR spectra of HO-PEG-OH (A)，HOOC-(Br-PEG-Br)-COOH(B) and $(N_3)_2$-(Br-PEG-Br)-$(N_3)_2$(C)

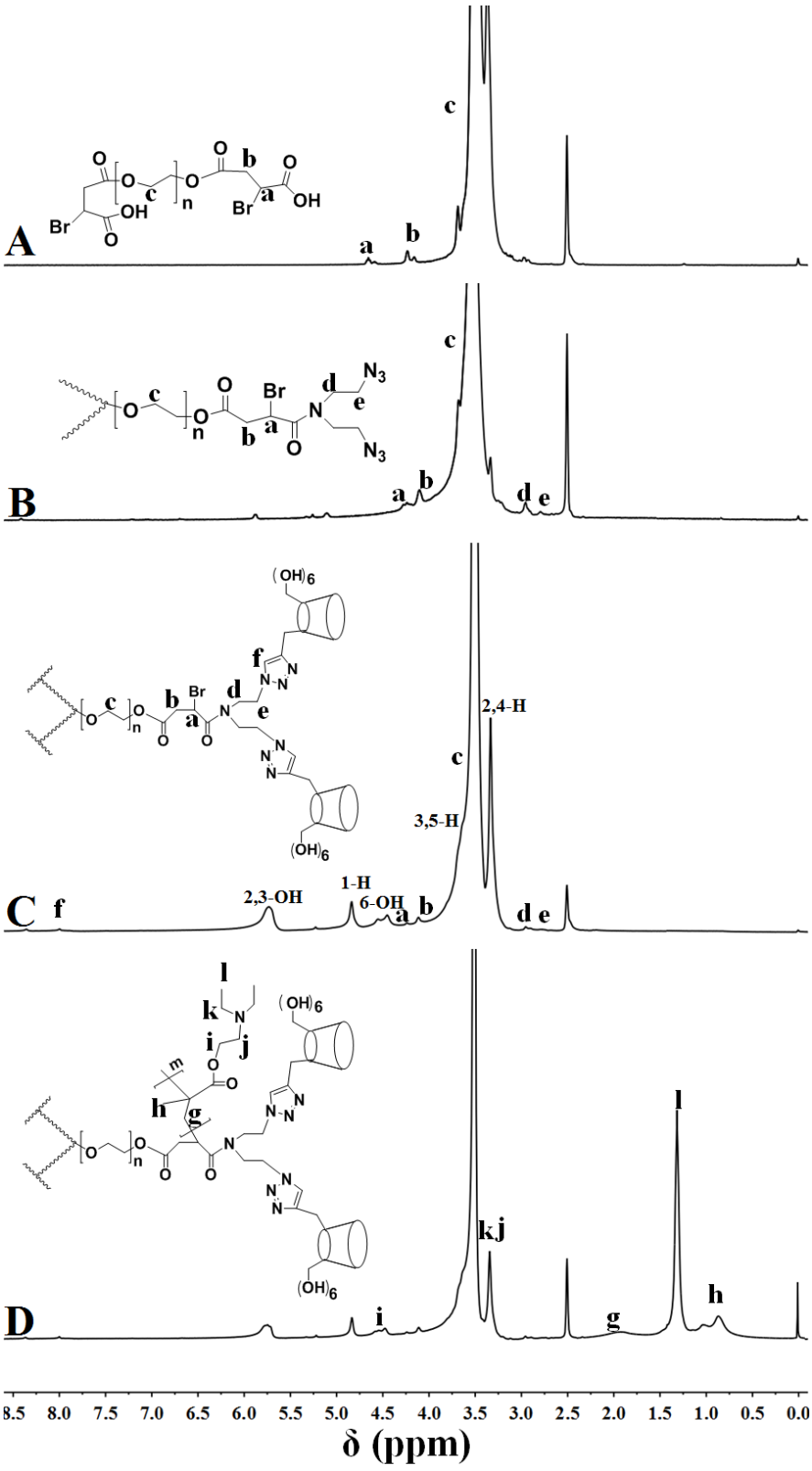


Figure S2 ^{1}H NMR spectra of HOOC-(Br-PEG-Br)-COOH (A), $(N_3)_2$-(Br-PEG-Br)-$(N_3)_2$ (B), (β-CD)$_2$-*g*-(Br-PEG-Br)-*g*-(β-CD)$_2$ (C) and **P1** (D) in DMSO-d_6 at 25^{o}C.

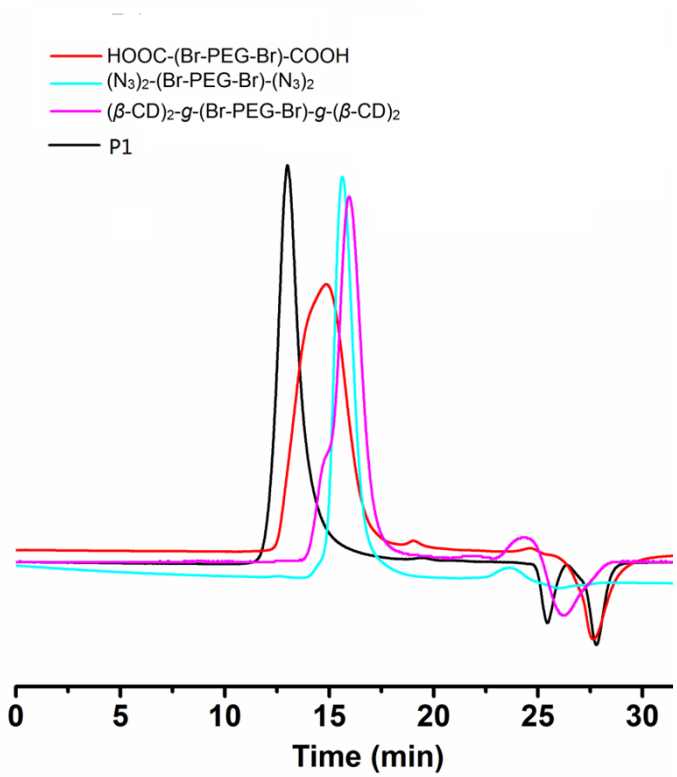


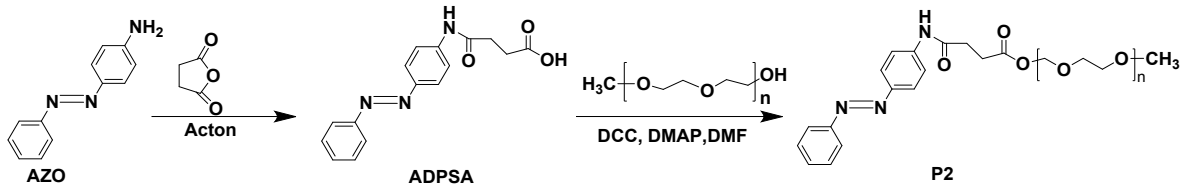
Figure S3 DRI signals of SEC-MALLS chromatograms ofHOOC-(Br-PEG-Br)-COOH, $(N_3)_2$-(Br-PEG-Br)-$(N_3)_2$, (β-CD)$_2$-*g*-(Br-PEG-Br)-*g*-(β-CD)$_2$and P1(0.5mg mL^{-1}).

Table S1 Molecular structure parameters of resulting polymers

Polymers	M_w[b]	M_n[b]	PDI[c]
HOOC-(Br-PEG-Br)-COOH	2370	2110	1.12
$(N_3)_2$-(Br-PEG-Br)-$(N_3)_2$	2650	2250	1.18
(β-CD)$_2$-*g*-(Br-PEG-Br)-*g*-(β-CD)$_2$	7380	6110	1.21
P1	22950	18090	1.26

3 Synthesis of and Characterization of P2

P2 was prepared via two-step reactions, as shown in Scheme S2.



Scheme S2 Synthesis routes of P2

3.1Synthesis of N-4-azodiphenylSuccinic acid (ADPSA)

4-Aminoazobenzene (AZO, 19.7 g, 0.1 mol) in acetone was added drop-wise to a well stirred acetone solution ofSuccinic anhydride (10.0 g, 0.1 mol) in a round bottom flask. The entire reaction mixture was cooled externally. The orange solids of N-4-azodiphenylsuccinic acid (ADPSA) were filtered and dried at 25.0^{o}C. ADPSA was purified by recrystallization from methanol. Yield: 90.3%, FT-IR(in cm^{-1})(Figure S4A): 3277 (N-H), 1711 (-COOH),1642 (-CON-), 1548 and 1527(Ar). ^{1}H NMR (Figure S5B) (400 MHz, DMSO-d_6, room temperature, TMS) δ (ppm): 12.16 (-O-H), 10.38 (N-H), 7.91, 7.87 (4H, Ar-*H*), 7.57, 7.68(4H, Ar-*H*), 2.68 (N-CH_2-),2.61 (-CH_2-COOH).

3.2 Synthesis of P2

ADPSA(0.594 g, 2mmol)andmPEG (2.00 g, 1.0 mmol) were dissolved in 6 ml DMFand treated with DCC(0.205g,1.0mmol) and DMAP (0.049g, 0.4 mmol) for 48 hours at roomtemperature.Thedicyclohexylurea was filtered out andthe polymer was precipitated in ether, filtered and washedwithmethanol.The polymer was dried using a vacuumat20 ^{o}C for 24 h to give a yellowpowder.Yield: 67.2%.FT-IR (Figure S4B) (cm^{-1}): 2873 (CH_2-O), 1721 (-COO-),1643 cm^{-1}(-CON-); 1549 (Ar), ^{1}H-NMR (Figure S5A) (400 MHz, DMSO, room temperature, TMS) δ (ppm): 7.89 and 7.78 (Ar-*H*), 3.87 (-OCH_2O-), 2.51 (O-CH_3), 2.63-2.89 (-CH_2-).

3.3 Characterization of P2

P2was synthesized via two-stepreactions (Scheme S2). The FT-IR and ^{1}H NMR spectra of mPEG-AZO andADPSAwerepresented in Figure S4 and S5, and the characteristic signals of theazobenzene groupand mPEG moietieswere assigned clearly.

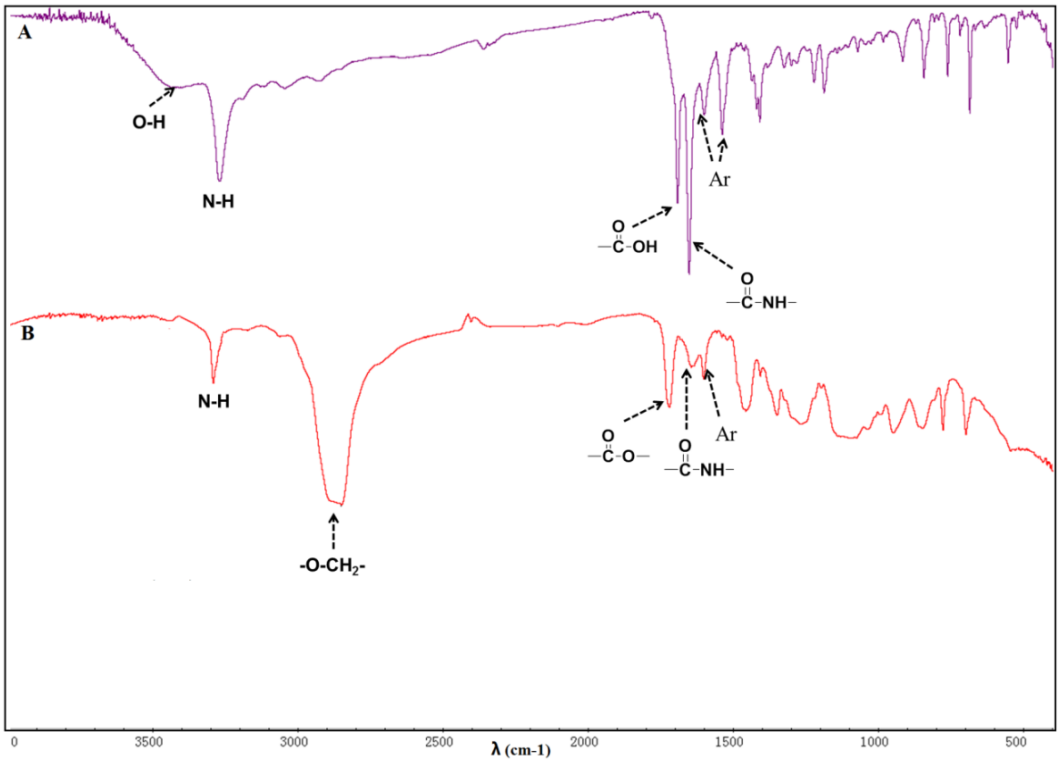


Figure S 4 FT-IR spectra of ADPSA(A) and P2(B)

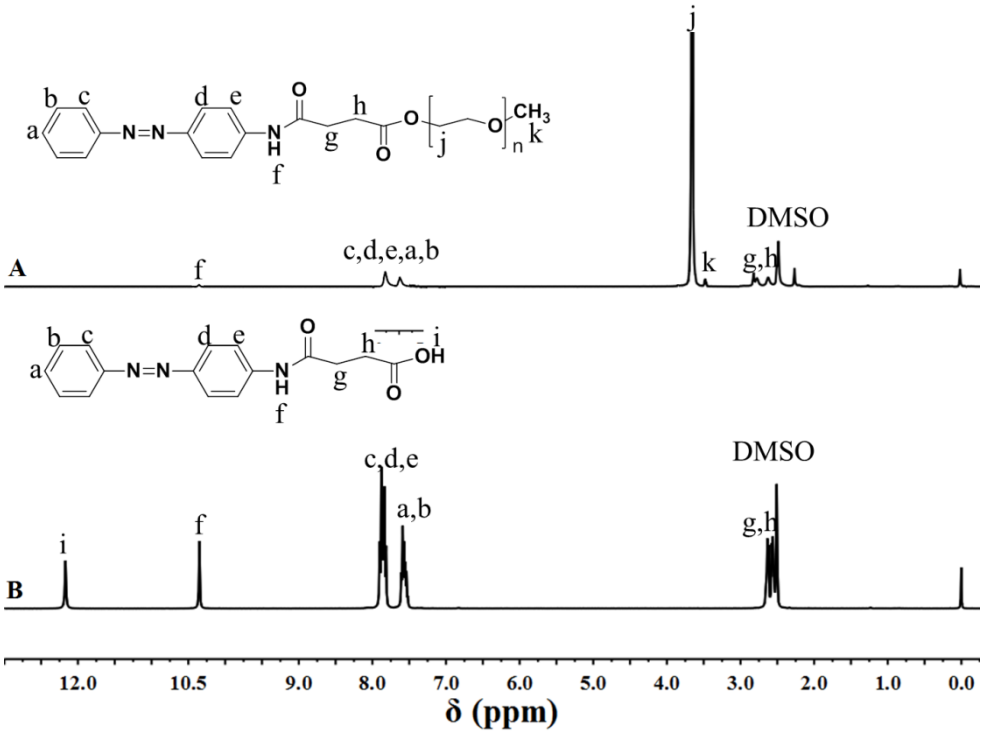


Figure S5 [1]HNMR spectra of P2 (A) and ADPSA (B)in DMSO-d_6 at 25°C.

4 Preparation of SBCP

The preparation of SBCP was based on the host-guest interaction between β-CD in P1 and Azo

in P2.In a typical experiment, P1 (2.295 mg, 0.1mmol) was dissolved in pH 6.0 HCl (1.0 mL), and then equal volume of P2 (0.718g, 0.4mmol, dissolved in pH 6.0 HCl) solution was added dropwise with syringe into the solution ata rate of about one drop every 3 s with magnetic stirring.

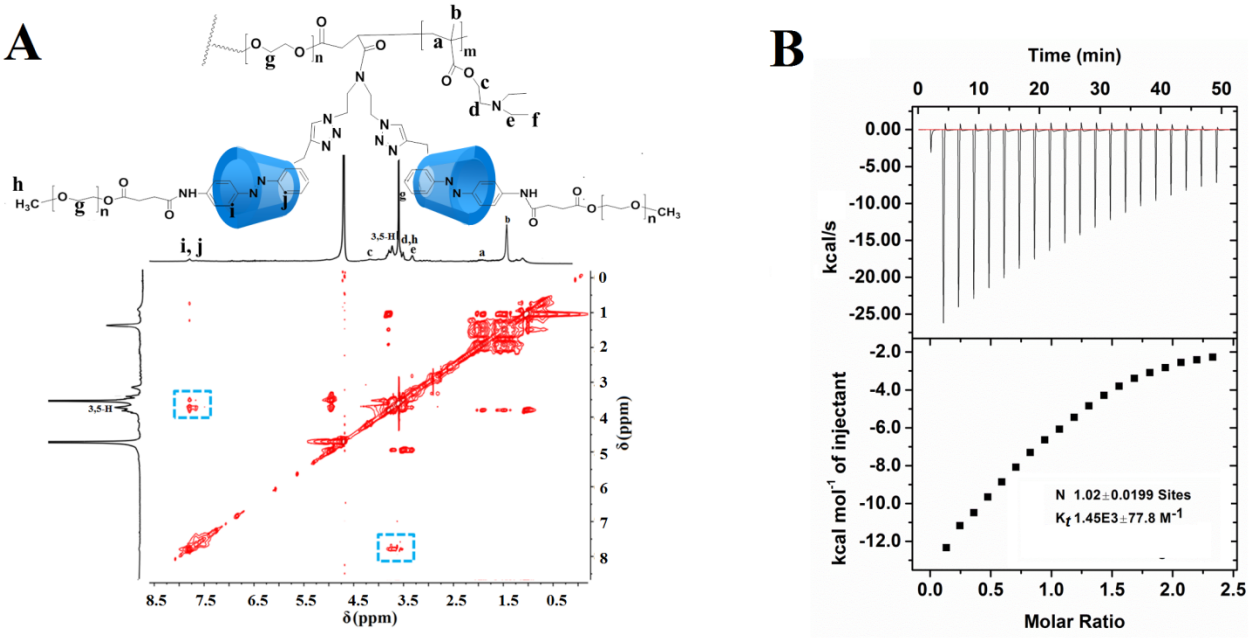


Figure S6. Formation of SBCP. (A) 2D ^{1}H NMR NOESYspectra of mixed solutions of P1 (10 mM) and P2 (40 mM) in D_2O at pH 6.0 and 25 °C; and (B) typical ITC curve that corresponds to the binding interaction of P1 (0.6 mM) with P2 (12.0 mM) in HCl solution at pH 6.0and 25 °C.

The formation of SBCP in solution was determined by following UV absorption at 348 nm, which is the characteristic absorption of *t*Azo species, as shown in Fig S7. The concentration ofP2 was kept at 1.2×10^{-5} M. Upon gradual addition of the P1 species, the absorption of P2 increased remarkably, and the absorbability increased to maximum after the ratio of P1/P2 increased to 1/4.

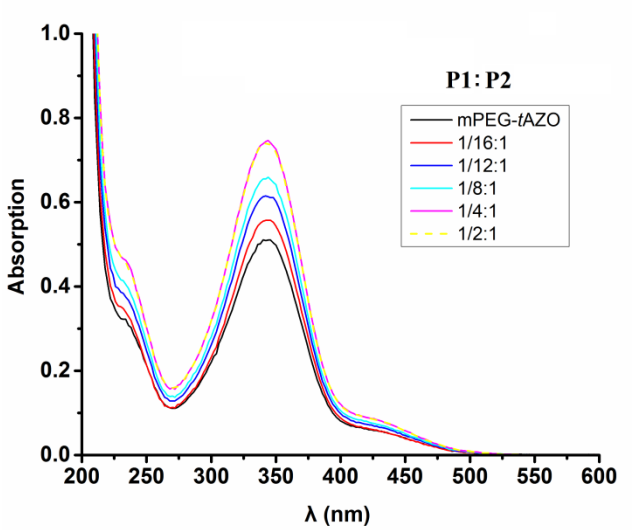


Figure S7 The UV absorption of P2 upon stepwise addition of P1 (the concentration of P2 keeps 1.2×10^{-5} M).

5 The dissociation process of SBCP

After365 nm UV irradiation for 15 min, no correlation peaks betweenprotons in theβ-CD cavity and protons of the azobenzenemoiety were observed (as shown in Figure S8A), indicatinghost–guest disassembly between the azobenzene moiety andβ-CD.But the correlation peaks betweenprotons in theβ-CD cavity and protons of the azobenzenemoiety were observedagain after 15 min visible light irradiationas shown in Figure S8B. This result indicated the reversible formation process ofSBCP.

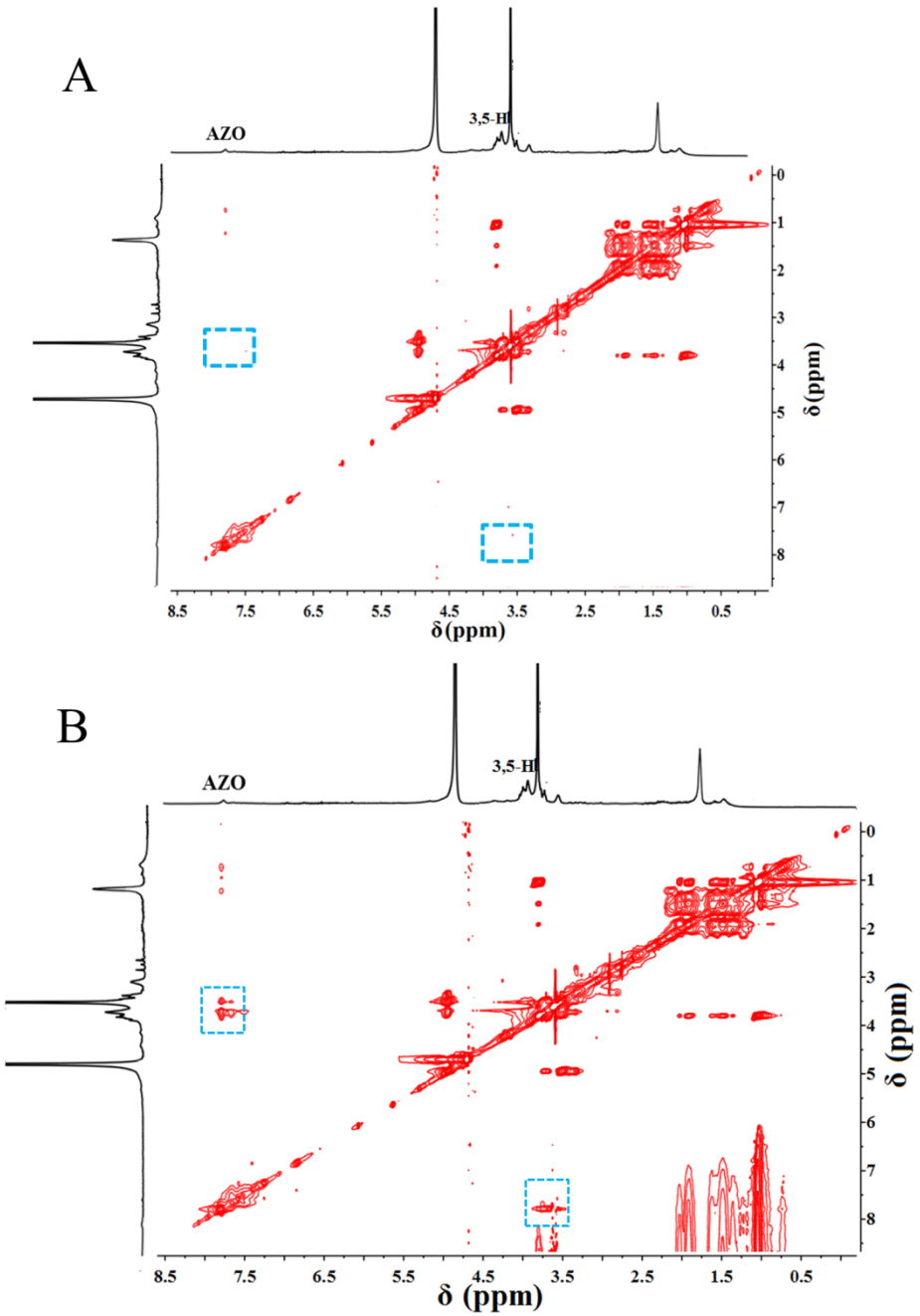


Figure S8 2DNOESY spectra of SBCP after 365 nm light irradiation for15 min (A) and subsequently proposed in visible light for 15min (B) in D_2O at pH 6.0 and 25 °C.

6 Formation of SBCP self-assemblies

After the pH was adjusted from pH 6.0 to 7.4 by 0.1M NaOH, the PDEA segments in P1 became hydrophobic for the deprotonation of tertiary amines. Thus,SBCP showed anamphiphilic property and could self-assemble into vesicles. In addition, the host-guest interactions between*β*-CD in P1 and Azo in P2 could be controlled by the alternating irradiation between 365 nm UV light and visible light. Therefore, the SBCPcould be deconstructed and reconstructed under alternating UVand

visible light irradiation. Thus, the morphology of SBCPself-assemblies could be changed after the irradiation of UV and visible light.[1]H NMR was used to confirm the formedvesicles(1.5 mg/ml).

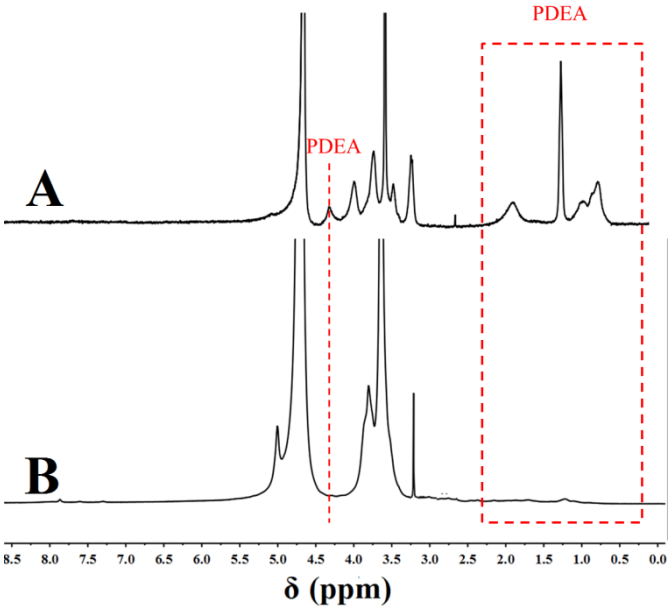


Figure S9 [1]H NMR spectra of SBCP self-assemblies at pH 6.0 (A) and 7.4 (B) in D_2O at 25 °C, respectively.

CAC of SBCP self-assemblies was estimated by a fluorescence spectroscopic method using pyrene as the fluorescence probe. Typically, pyrene solutions in acetone were added to each brown bottle. Acetone was then evaporated, leaving 1.0×10^{-8} mol of pyrene in each bottle. Aqueous solutions (10 mL) of SBCP at concentrations ranging from 1.2 mg/ml to 0.05 mg/ml were added to the bottles. The mixtures were stirred at 25 °C for 3 h. They were sonicated for 1 min before measurement. The spectroscopy measurement was carried out at the emission wavelength of 418 nm and excitation wavelength of 340 nm.[8]

The intensities of emissionpeaks at ca. 373 and 383 nm, denoted as I_1 and I_3, respectively, are relatedto the polarity of the microenvironment in which pyrene is dissolved and the I_1/I_3 ratio is, therefore, a very good indicator for the micellar solution.[9,10] The I_1/I_3 ratio of pyrene as a function of concentration of SBCP is shown in Figure S10. It can be seen that I_1/I_3 ratios was constant at low concentrations. Pyrene molecules are probably existed in aqueous environment at low concentrations becausethere are only single polymer chains present.However, thesudden decrease in I_1/I_3 values at around 0.64 mg/ml of SBCP indicates a change in the polarity of the pyrene environment, which isprobably due to some pyrene molecules entering into the more hydrophobic wall of the

vesicles.The estimated CAC value obtainedfrom these fluorescence experiments is 0.64 mg/ml. Similarly, the CAC of P1 is 0.48mg/mL, while P2 doesn't have CAC value, which indicated that P2 could not self-assemble into nanoparticles in this experiment.

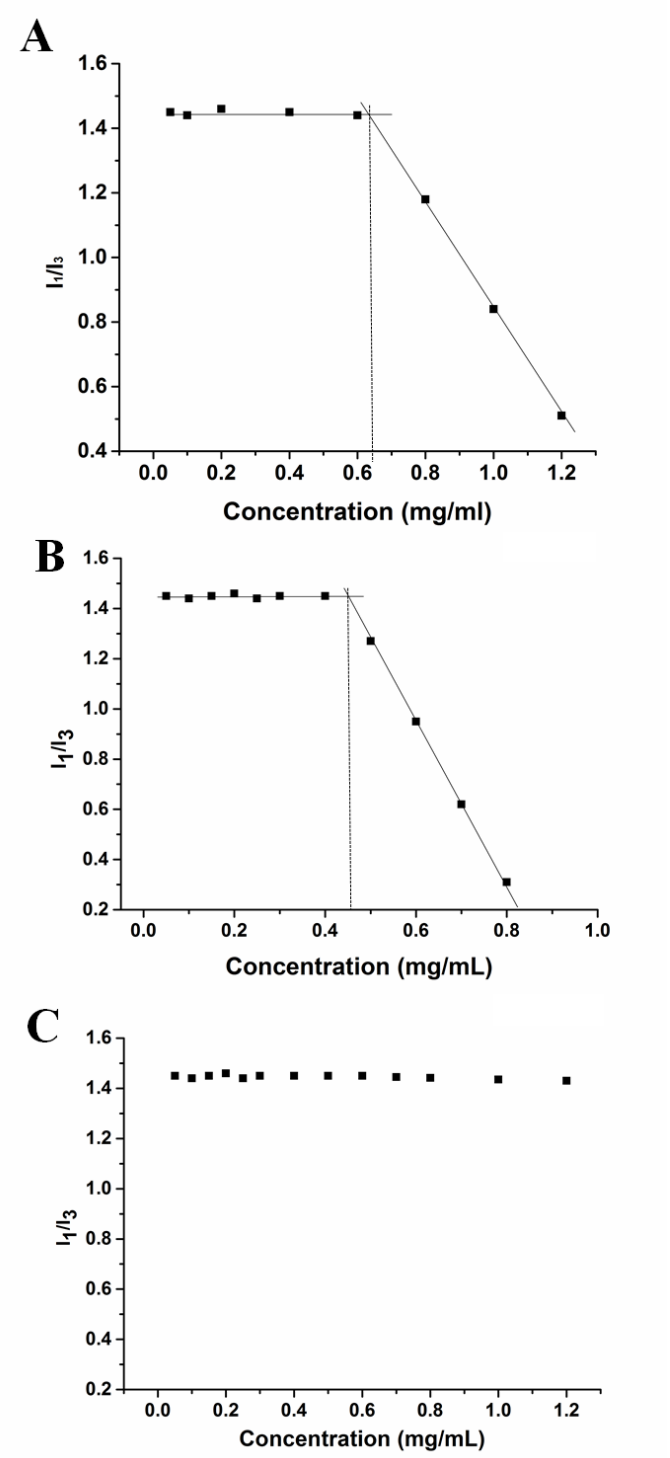


Figure S10 Plot of I_1/I_3 in the excitation spectrum versus the concentrations of SBCP (A), P1(B) and P2 self-assemblies.

7 The influence of UV light irradiation on the reversible morphology transitions of SBCP self-assemblies

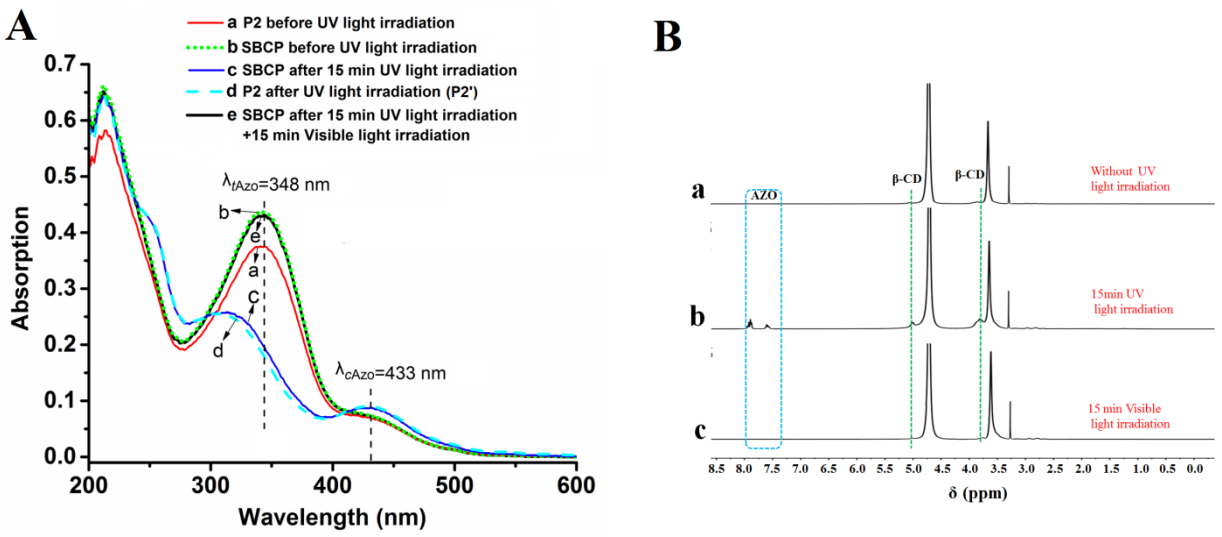


Figure S11. (A) UV-vis spectra of P2 before (a) and after (d) UV light irradiation and SBCP before (b) and after (c) UV and visible light (e) irradiation; (B) ^{1}H NMR spectra of SBCP solution without UV light irradiation (a), after exposure to UV light for 15 min (b), and after exposure to visible light for 15 min (c) under pH 7.4 and 25 °C.

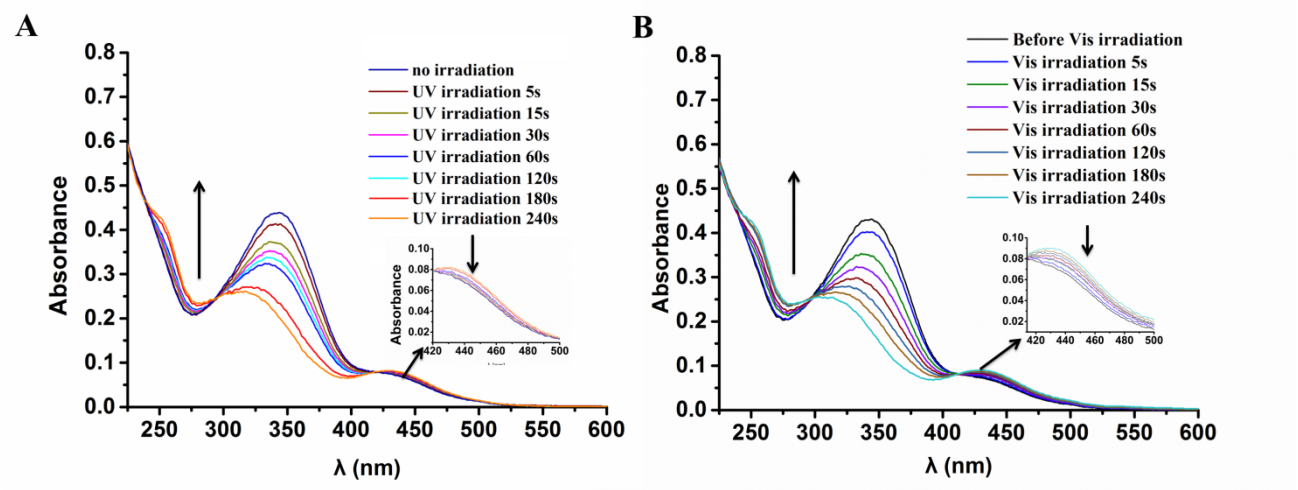


Figure S12 UV-Vis spectra ofSBCPself-assemblies. (A) UV irradiation induced *trans*-to-*cis* transitions at 365 nm and (B) Visible light irradiation induced *cis*-to-*trans* transitions (The concentration of the sample is 0.1 mg mL^{-1})

8 Drug loading and in vitro release

The encapsulation and controlled release experiments of DOX were carried out according to the literature protocol[4,5] and modified as follows. SBCP (20.0 mg) and DOX • HCl (6.0 mg) were

dissolved in pH 6.0 HCl (10.0 mL) to make SBCP/DOX·HCl mixture solutions. Then 0.01M NaOH was dropwise added to the solution within 1.5 h to adjust the pH from 6.0 to 7.4, leading the formation of DOX-loaded vesicles and the mixture was stirred 2h to reach equilibration. The unloaded free drug and the salt produced by neutralization reaction were removed by dialysis using a dialysis tube (cut off M_n 8000 – 14000) against 1000 mL pure water at 25°C with 300 r/min of stirring. Pure water was renewed for 6 times within 3 h (every 0.5 h). The final volume of vesicles/DOX aqueous solution was 45.6 mL and the drug loading efficiency of polymer vesicles was measured by UV spectroscopy after dialysis (the dialyzed solution was diluted to twice times by adding pure water before fluorescence measurement). The final DOX release process was carried out under the flowing three protocols: 1) Dialyzing 5.0 mL of DOX-loaded vesicles in the dialysis tube (cut off M_n=8000-14000) against 100 mL pure water in dark and 37°C under one cycle of 365 nm UV light irradiation and visible light irradiation. 2) Dialyzing 5.0 mL of DOX-loaded vesicles in the dialysis tube (cut off M_n=8000-14000) against 100 mL pure water in dark and 37°C under three cycles of 365 nm UV light irradiation and visible light irradiation. 3) Dialyzing 5.0 mL of DOX-loaded vesicles in the dialysis tube (cut off M_n=8000-14000) against 100 mL pure water in dark and 37°C without any stimuli.

The drug loading efficiency (DLE) and drug loading content (DLC) were calculated according to the following equations.[6]

$$\mathrm{DLE}(\%) = \frac{\mathrm{Me}}{\mathrm{Mf}} \times 100\%$$

$$\mathrm{DLC}(\%) = \frac{\mathrm{Me}}{\mathrm{Mp}} \times 100\%$$

Where M_e is the weight of drug encapsulated in vesicles, M_f is the weight of drug in feed and M_p is the weight of polymer used. M_f=6 mg, M_p=20 mg.

9 Reference

[1] C. G. Mu, X. D. Fan, W. Tian, Y. Bai, Z. Yang, H. Yao, J. Polym. Sci. Part A. 2013, 51, 1405-1416.

[2] H. T. Zhang, X. D. Fan, W. Tian, R. T.Suo, Z. Yang, Y. Bai, W. B. Zhang, Chem. Eur. J. 2015, 21, 5000 -5008.

[3] M. Licciardi, Y. Tang, N. C. Billingham, S. P. Armes, A. L. Lewis, Biomacromolecules. 2005, 6,1085-96.

[4] T. B.Ren, Q. M.Liu, H.Lu, H. M.Liu, X.Zhang, J. Z. Du, J. Mater. Chem. 2012, 22, 12329-12338

[5] J. Z. Du, L. Fan, Q. M. Liu, Macromolecules, 2012, 45, 8275-8283.
[6] W. Q. Chen, J. Z. Du, Scientific Reports, 2013, 3,2162.
[7] S. Daoud-Mahammed, P. Couvreur, K. Bouchemal, M. Chéron, G. Lebas, C. Amiel, R. Gref, Biomacromolecules, 2009, 10, 547,
[8] Ö. Topel, B.A. Çakır, L. Budama, N. Hoda, J. Mol. Liq. 2013, 177, 40–43.
[9] K. Kataoka, A. Harada, Y. Nagasaki, Adv. Drug Delivery Rev. 2001,47, 113–131.
[10] G. Gaucher, M. H. Dufresnea, V.P. Sant, N. Kang, D. Maysinger, J.C. Leroux, J. Control. Release, 2005,109,169–188.