Electronic Supplementary Information

Micelle-to-Vesicle Morphological Transition *via* Light-Induced Rapid Hydrophilic Arm Detachment from a Star Polymer

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1. Materials

ε-Caprolactone (ε-CL, Acros Organics, 99%, Belgium) and propargyl alcohol (Alfa Aesar, 99%, Tianjin) were dried over CaH_2 and distilled before use. Acetyl chloride, epichlorohydrin and thionyl chloride ($SOCl_2$) were purchased from Sinopharm Chemical Reagent Co., Ltd. and used after distillation. Monomethyl poly(ethylene glycol) (mPEG) with molecular weight of 2000 Da ($mPEG_{45}$) and 750 Da ($mPEG_{16}$) were purchased from Sigma-Aldrich and dried by azeodistillation of toluene. Toluene was distilled over sodium prior to use. Tetrahydrofunan was refluxed with calcium hydride, and distilled over Na-K alloy. Dichloromethane (DCM), *N,N*-dimethylformyl (DMF), pyridine and methanol were dried over CaH_2 and distilled before use. Stannous octoate ($Sn(Oct)_2$, Sinopharm Chemical Reagent Co., Ltd., China) was purified according to a method described in literature.[1] 4-Hydroxy-5-methoxy-2-nitrobenzaldehyde,[2] poly(ethylene glycol) succinate (mPEG-COOH)[3] and 4-(dimethylamino)-pyridinium *p*-toluenesulfonate (DPTS)[4] were prepared according to the reported methods. $mPEG_{16}$-COOH was treated with $SOCl_2$ to produce acid chloride $mPEG_{16}$-COCl.[3] Other chemicals were obtained from commercial sources and used as received.

2. Characterization

2.1. Nuclear Magnetic Resonance (NMR). ^1H NMR spectra were recorded on a Bruker AV400 NMR spectrometer using $CDCl_3$ or d_6-DMSO as the solvent.

2.2. Gel Permeation Chromatography (GPC). The molecular weight ($M_{n,\,GPC}$) and molecular weight distribution (M_w/M_n) of the polymers were measured on a Waters GPC system, which was equipped with a Waters 1515 HPLC solvent pump, a Waters 2414 refractive index detector, and three Waters Styragel High Resolution columns (HR4,

HR2, HR1, effective molecular weight range 5000–500,000, 500–20,000, and 100–5000 g mol^{-1}, respectively) at 40 °C using HPLC grade chloroform as eluent at a flow rate of 1.0 mL/min. Monodispersed polystyrenes were used to generate the calibration curve.

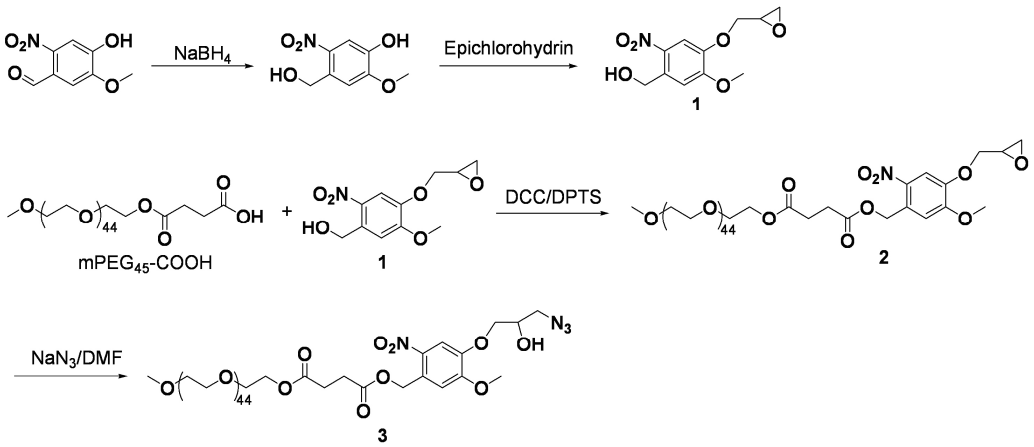
2.3. UV-vis Spectroscopy (UV-vis). The absorbance change of polymer solution post UV irradiation (λ_{max} = 365 nm, EXFO Omnicure^{TM} 1000, Canada) was measured on a UV-2802 PC (UNICO, China) spectrometer.

2.4. Dynamic Light Scattering (DLS). The DLS measurement was performed in aqueous solution using a Malvern Zetasizer Nano ZS90 with a He-Ne laser (633 nm) and 90° collecting optics. The data were analyzed by Malvern Dispersion Technology Software 4.20.

2.5. Transmission Electron Microscopy (TEM). A droplet of the sample solution was placed onto a 200 mesh copper grid coated with formvar film stabilized with vacuum-evaporated carbon and most of the liquid was removed by blotting with a filter paper after 5 minutes. The samples were examined on an electron microscope (JEM-2100F) with accelerating voltage at 200 kV.

3. Synthetic procedures

3.1 Synthesis of 4-(3-azido-2-hydroxypropoxy)-5-methoxy-2-nitrobenzyl mPEG$_{45}$-succinate (3)



*3.1.1. Synthesis of (5-methoxy-2-nitro-4-(oxiran-2-ylmethoxy)phenyl)methanol (**1**)*

4-Hydroxy-5-methoxy-2-nitrobenzaldehyde was reduced by sodium borohydride ($NaBH_4$). Typically, 4-hydroxy-5-methoxy-2-nitrobenzaldehyde (7.50 g, 38 mmol) was dissolved in dried THF (150 mL) and methanol (100 mL) and chilled to 0 °C. Then, $NaBH_4$ (2.17 g, 57 mmol) was added into the solution in several portions. After stirred at the temperature overnight, 10 mL of distilled water was added to quench the reaction. After removal of the solvent by rotation evaporator, 300 mL of saturated NaCl and 200 mL ethyl acetate were added to dissolve the residue. The organic layer was collected and the aqueous solution was further extracted with ethyl acetate (2 × 100 mL). The organic phase was dried (Na_2SO_4), filtered and evaporated to obtain the yellow powder

4-(hydroxymethyl)-2-methoxy-5-nitrophenol (6.50 g, yield: 85.8%). ^{1}H NMR (DMSO-d_6, ppm): 7.56 (s, 1H), 7.34 (s, 1H), 4.79 (s, 2H), 3.90 (s, 3H) (Figure S1).

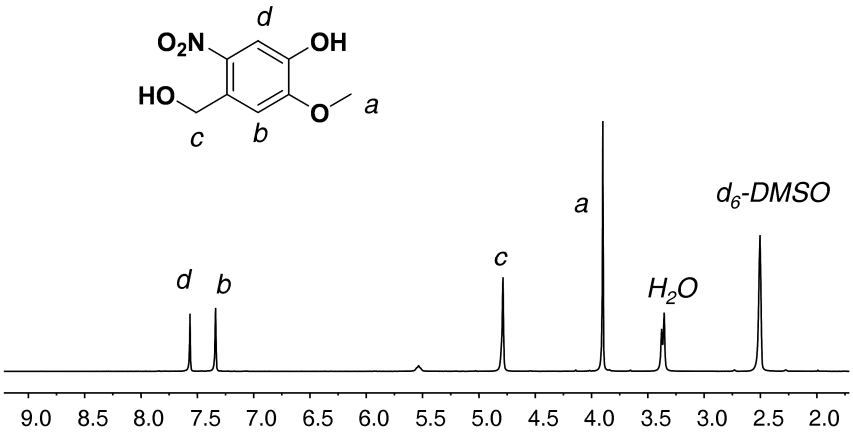


Figure S1. ^{1}H NMR spectrum of 4-(hydroxymethyl)-2-methoxy-5-nitrophenol in DMSO-d_6 (ppm).

(5-methoxy-2-nitro-4-(oxiran-2-ylmethoxy)phenyl)methanol was synthesized according to a reported method with modifications.[5] Typically, 4-(hydroxymethyl)-2-methoxy-5-nitrophenol (1.50 g, 7.5 mmol), epichlorohydrin (3.45 g, 37.5 mmol) and 1 mL of ethanol were charged into a flask. The mixture was refluxed at 70 °C for 1 h, followed by adding dropwise 1 mL of NaOH solution (0.2 g/mL) and further refluxed for an additional 3 h. Ethanol and unreacted epichlorohydrin were removed under reduced pressure. Water was added into the residue and the crude product was obtained by filtration. After purified by column chromatography (methnol/CH_2CH_2 = 2/98, v/v), the final product (5-methoxy-2-nitro-4-(oxiran-2-ylmethoxy) phenyl)methanol (**1**) was obtained as yellow powder (1.60 g, yield: 83.3%). ^{1}H NMR (DMSO-d_6, ppm): 7.72 (s, 1H), 7.41 (s, 1H), 4.83 (s, 2H), 4.45 (dd, 1H), 3.93 (s, 3H), 3.89 (m, 1H), 3.35 (m. 1H), 2.85 (m, 1H), 2.72 (m, 1H) (Figure S2).

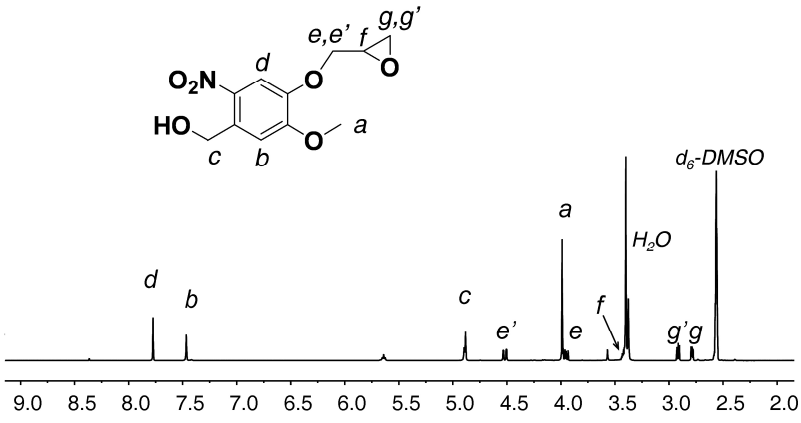


Figure S2. ^{1}H NMR spectrum of (5-methoxy-2-nitro-4-(oxiran-2-ylmethoxy)phenyl)methanol (**1**) in d_6-DMSO (ppm).

*3.1.2. Synthesis of 4-(3-azido-2-hydroxypropoxy)-5-methoxy-2-nitrobenzyl mPEG$_{45}$-succinate (**3**)*

A mixture of $mPEG_{45}$-COOH (1.50 g, 1.0 eqv), **1** (0.22 g, 1.2 eqv) and DMAP (0.044 g, 0.5 eqv) were dissolved in DMF (10 mL) under N_2 atmosphere. After cooled to 0 °C, *N*-(3-Dimethylaminopropyl)-*N'*-ethylcarbodiimide hydrochloride (EDC·HCl) (0.21 g, 1.5 eqv) in DMF (10 mL) was added dropwise to the solution. Then the reaction was warmed to room temperature and kept stirring overnight. The precipitate was removed *via* filtration, and the filtrate was concentrated under vacuum. The residue was redissolved with DCM, washed with 0.5 N HCl and saturated NaCl twice, respectively. The organic phase was dried over Na_2SO_4, filtered, concentrated and precipitated into cooled diethyl ether to afford 1.30 g 5-methoxy-2-nitro-4-(oxiran-2-ylmethoxy)benzyl $mPEG_{45}$-succinate (**2**) as pale yellow powder.

Subsequently, the epoxide ring of polymer **2** was opened by sodium azide (NaN_3) in the presence of ammonium chloride (NH_4Cl) to afford **3** with azide and hydroxyl groups.[6] Typically, polymer **2** (1.00 g, 1.0 eqv), NaN_3 (0.14 g, 5.0 eqv) and NH_4Cl (0.12 g, 5.0 eqv) were charged into dried DMF (5 mL). The mixture was stirred at 50 °C for 24 h and filtered to remove insoluble materials. After removal of DMF, the residue was redissolved in DCM and subsequently washed with saturated NaCl three times. The organic layer was dried over Na_2SO_4, filtered, concentrated and precipitated into cooled diethyl ether to afford polymer **3** as a pale yellow powder. Yield: 85%. ^{1}H NMR ($CDCl_3$, ppm): 7.78 (s, 1H), 7.07 (s, 1H), 5.56 (s, 2H), 4.22 (t, 2H), 4.10 (m, 1H), 4.01 (s, 3H), 3.64 (s, 180H), 3.38 (s, 3H), 2.94 (m, 1H), 2.74 (m, 4H). ($M_{n,\,NMR}$= 2340 g/mol, $M_{n,\,GPC}$ = 4590 g/mol, M_w/M_n = 1.04) (Figure S3).

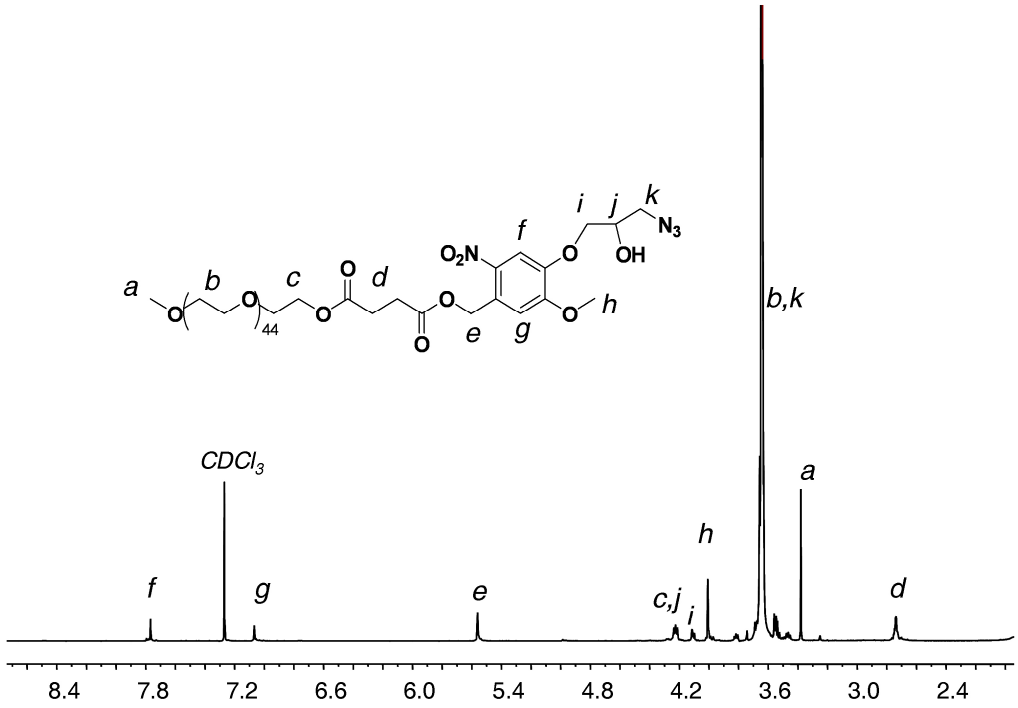
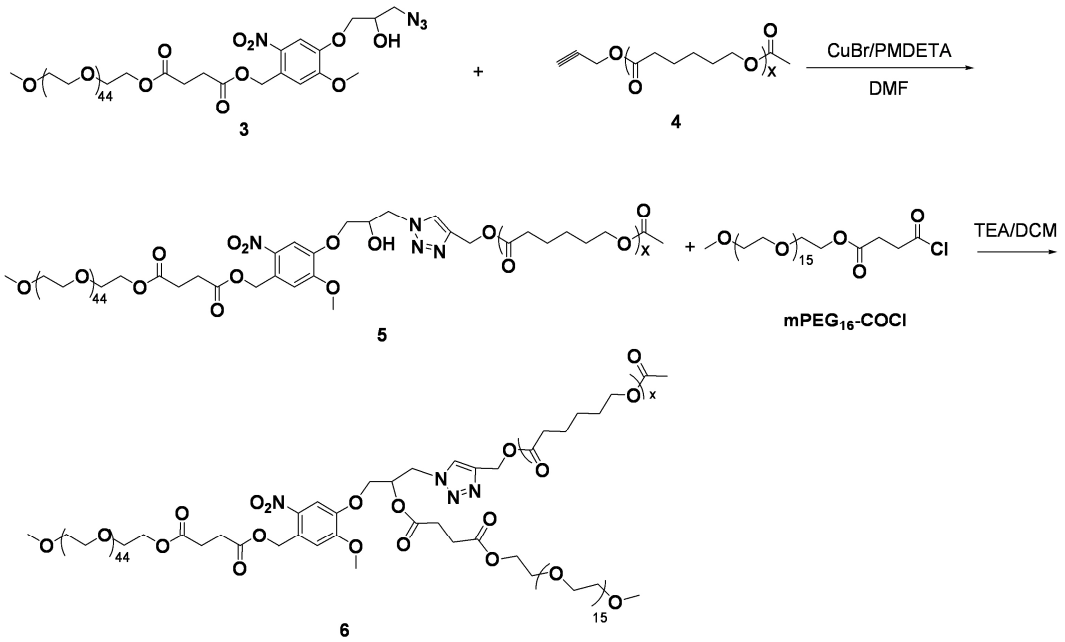


Figure S3. ^{1}H NMR spectrum of 4-(3-azido-2-hydroxypropoxy)-5-methoxy-2-nitrobenzyl $mPEG_{45}$-succinate (**3**) in $CDCl_3$ (ppm).

3.2. Synthesis of star polymer ECE (6)



*3.2.1 Synthesis of α-propargyl-ω-acetyl-poly(ε-caprolactone) (**4**)*

Polymer **4** was synthesized in two steps according to a previous report.[6] First, α-propargyl-ω-hydroxyl-poly(ε-caprolactone) was obtained by ring-opening polymerization of ε-CL using propargyl alcohol as the initiator and $Sn(Oct)_2$ as the catalyst. In a glovebox with water content less than 0.1 ppm, propargyl alcohol (0.049 g, 0.88 mmol) and ε-CL (6.000 g, 52.6 mmol) were added to freshly dried toluene (50 mL) in a flame-dried flask, and then $Sn(Oct)_2$ (0.355 g, 0.88 mmol) was added and the solution was stirred at 80 °C for 4 h. The mixture was concentrated under reduced pressure. After precipitation into cold diethyl ether/methanol (9/1, v/v), the polymer was obtained and dried under vacuum overnight with a yield of 60%. ^{1}H NMR ($CDCl_3$, ppm): 4.68 (d, 2H, CH≡C-C***H***$_2$-), 4.06 (t, 68H, -$COCH_2CH_2CH_2CH_2C$***H***$_2$O-), 3.65 (t, 2H, -C***H***$_2$OH), 2.47 (t, 1H, C***H***≡C-CH_2-), 2.31 (t, 68H, -COC***H***$_2CH_2CH_2CH_2CH_2$O-), 1.65 (m, 136H, -$COCH_2$C***H***$_2CH_2$C***H***$_2$CH_2O-, 1.38 (m, 68H, -$COCH_2CH_2$C***H***$_2CH_2CH_2$O-) (Figure S4A).

The hydroxyl group of α-propargyl-ω-hydroxyl-poly(ε-caprolactone) was blocked by acetyl chloride. Typically, α-propargyl-ω-hydroxyl-poly(ε-caprolactone) (1.00 g, 0.25 mmol) was azeotropically distilled with toluene to remove residual water and dissolved in dried DCM followed by introduction of triethylamine (TEA) (0.13 g, 1.25 mmol) *via* a syringe. Fresh distilled acetyl chloride (0.10 g, 1.25 mmol) in DCM (5 mL) was added dropwise to the mixture at 0 °C, and the mixture was further stirred overnight at room temperature. Thereafter, the solution was washed with 0.5 N HCl, 5% $NaHCO_3$ and saturated NaCl twice, respectively. After drying with Na_2SO_4, the organic layer was concentrated and precipitated into cooled diethyl ether. The polymer was collected by filtration and dried under vacuum overnight with a yield of 95%. ^{1}H NMR ($CDCl_3$, ppm) : 4.68 (d, 2H, CH≡CC***H***$_2$-), 4.06 (t, 68H,

-$COCH_2CH_2CH_2CH_2CH_2$O-), 3.65 (t, 2H, -C***H***$_2$OH), 2.47 (t, 1H, C***H***≡CCH_2-), 2.31 (t, 68H, -COC***H***$_2CH_2CH_2CH_2CH_2$O-), 2.04 (s, 3H, -$COCH_2CH_2CH_2CH_2CH_2OCOCH_3$), 1.65 (m, 136H, -$COCH_2CH_2CH_2CH_2CH_2$O-), 1.38 (m, 68H, -$COCH_2CH_2CH_2CH_2CH_2CH_2$O-).($M_{n,\ NMR}$= 3930 g/mol, $M_{n,\ GPC}$ = 8420 g/mol, M_w/M_n = 1.06) (Figure S4B).

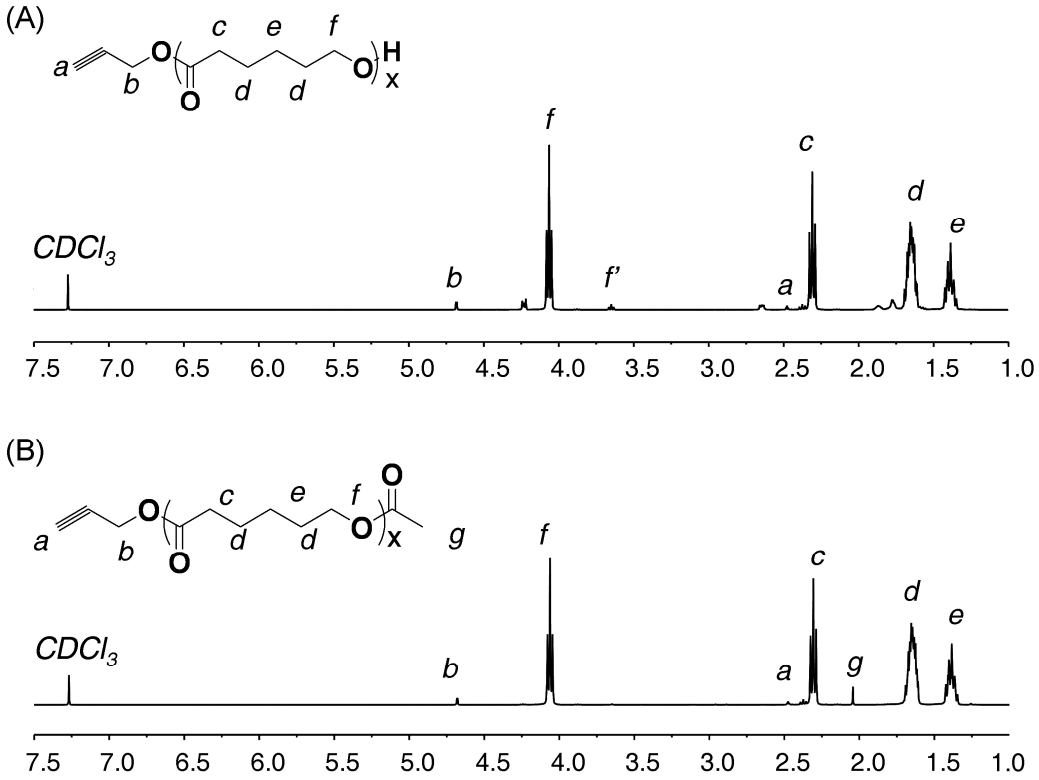


Figure S4. ^{1}H NMR spectra of (A) α-propargyl-ω-hydroxyl-poly(ε-caprolactone) and (B) α-propargyl-ω-acetyl-poly(ε-caprolactone) (**4**) in $CDCl_3$ (ppm).

*3.2.2. Synthesis of mPEG$_{45}$-NB-PCL (**5**) by click chemistry*

In a typical procedure, **4** (85 mg, 1.0 eqv) and **3** (0.10 g, 2.0 eqv) were dissolved in 2 mL of anhydrous DMF. The mixture was degassed by five freeze-pump-thaw cycles, and then copper (I) bromide (6.10 mg, 2.0 equiv) and *N,N,N',N'',N''*-pentamethyldiethylenetriamine (PMDETA) (7.33 mg, 2.0 equiv) were added in a glovebox. The solution was stirred at 25 °C for 24 h. After completion, the solution was passed through a neutral alumina column to remove copper catalyst. The solution was concentrated and precipitated into cooled diethyl ether to afford the product. The polymer was further purified by dialysis against distilled water (MWCO = 12000 Da) for at least 3 days. The purified diblock copolymer was obtained by lyophilization. Yield: 65%. ^{1}H NMR ($CDCl_3$, ppm) : 7.80 (s, 1H), 7.74 (s, 1H) 7.08 (s, 1H), 5.56 (s, 2H), 5.21 (s, 2H), 4.22 (m, 5H), 4.06 (t, 73H), 4.01 (s, 3H), 3.64 (s, 180H), 3.37 (s, 3H), 2.73 (m, 4H), 2.30 (t, 68H), 2.04 (s, 3H), 1.64 (m, 136H), 1.38 (m, 68H). ($M_{n,\ NMR}$= 6350 g/mol, $M_{n,\ GPC}$ = 11540 g/mol, M_w/M_n = 1.12) (Figure S5).

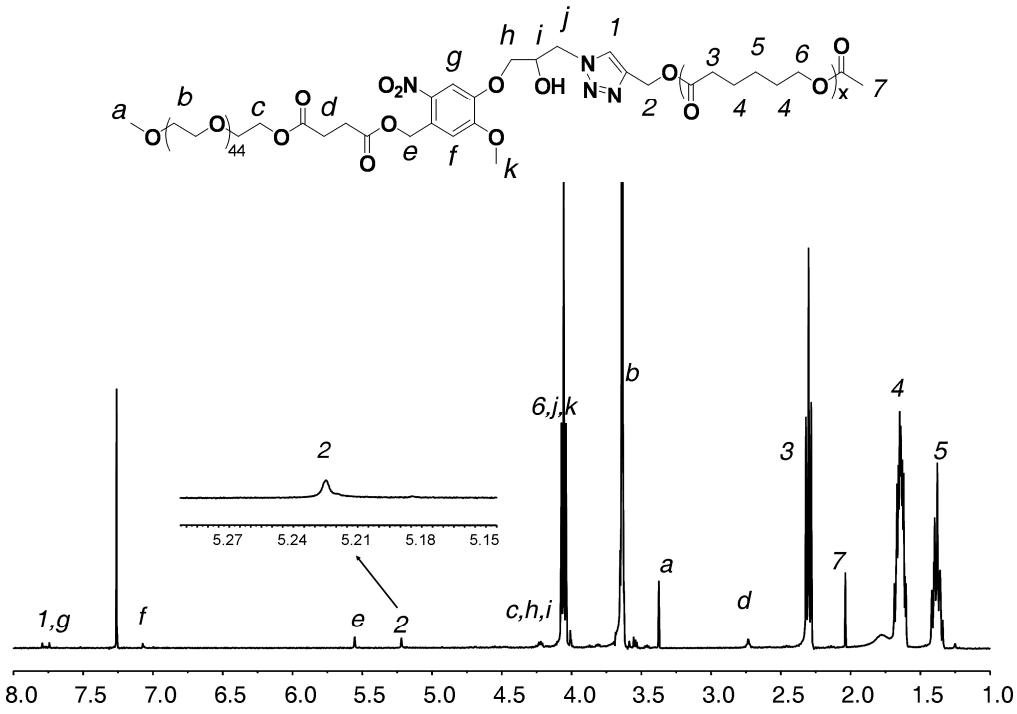


Figure S5. ^{1}H NMR spectrum of mPEG$_{45}$-NB-PCL (**5**) in $CDCl_3$ (ppm).

*3.2.3. Synthesis of polymer ECE (**6**)*

The polymer ECE was prepared by reacting mPEG$_{45}$-NB-PCL (**5**) with freshly prepared mPEG$_{16}$-COCl. Polymer **5** (0.12 g, 1.0 eqv) was dissolved in dried DCM and TEA (0.019 g, 10 eqv) was added under N_2. The mixture was stirred in an ice/water bath for 10 min, mPEG$_{16}$-COCl (0.10 g, 10 eqv) in DCM was added dropwise. The mixture was gradually warmed to room temperature and further stirred for 24 h. After dilution with DCM, the solution was washed with 0.5 N HCl, saturated $NaHCO_3$, and brine solution. The organic phase was dried over Na_2SO_4, filtered, concentrated and precipitated into cooled diethyl ether to afford the product. Excess reactants were further removed by dialysis against distilled water. The final polymer ECE (**6**) was obtained by lyophilization. Yield: 67%. ^{1}H NMR ($CDCl_3$, ppm) : 7.80 (s, 1H), 7.74 (s, 1H) 7.08 (s, 1H), 5.56 (s, 2H), 5.22 (s, 2H), 5.20 (s, 1H), 4.22 (m, 4H), 4.06 (t, 73H), 4.01 (s, 3H), 3.64 (s, 242H), 3.37 (s, 6H), 2.73 (m, 8H), 2.30 (t, 68H), 2.04 (s, 3H), 1.64 (m, 136H), 1.38 (m, 68H). ($M_{n,\,NMR}$= 7200 g/mol, $M_{n,\,GPC}$ = 13890 g/mol, M_w/M_n = 1.21) (Figure S6). The increase of polydispersity for polymer **5** and **6** may be due to the presence of a small portion of PEG diol in commercially available mPEG.

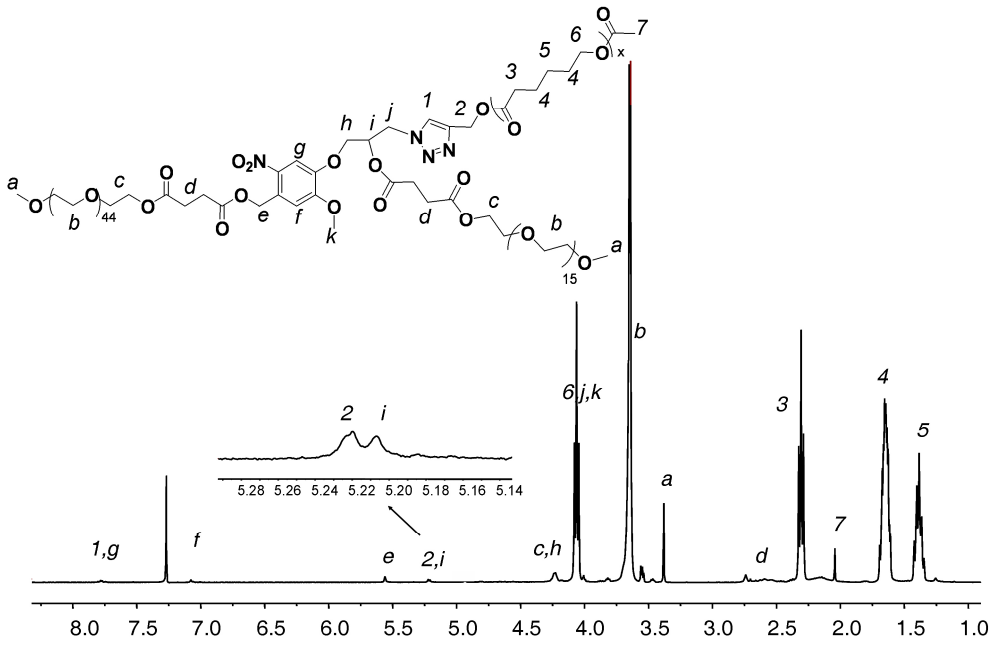


Figure S6. ^{1}H NMR spectrum of polymer ECE **6** in $CDCl_3$ (ppm).

3.3. Synthesis of the control polymer $mPEG_{16}$-*b*-PCL_{37}

The control diblock copolymer $mPEG_{16}$-*b*-PCL_{37} was obtained by ring-opening polymerization of ε-CL using $mPEG_{16}$ as the initiator and $Sn(Oct)_2$ as the catalyst. In a glovebox with water content less than 0.1 ppm, $mPEG_{16}$ (0.50 g, 0.66 mmol) and ε-CL (3.80 g, 33.3 mmol) were added to freshly dried toluene (30 mL) in a flame-dried flask, and then $Sn(Oct)_2$ (0.27 g, 0.66 mmol) was added and the solution was stirred at 80 °C for 4 h. The reaction was quenched by adding acetic acid and the solution was concentrated under reduced pressure. After precipitation into cold diethyl ether/methanol (9/1, v/v) twice, the polymer was obtained and dried under vacuum overnight with a yield of 75%. DP of PCL was determined to be 37 according to the ^{1}H NMR spectrum. ^{1}H NMR ($CDCl_3$, ppm): 4.06 (t, 74H, -$COCH_2CH_2CH_2CH_2CH_2$O-), 3.64 (s, 62H, -CH_2CH_2-), 3.37 (s, 3H, -CH_3), 2.30 (t, 74H, -$COCH_2CH_2CH_2CH_2CH_2$O-), 1.65 (m, 148H, -$COCH_2CH_2CH_2CH_2CH_2$O-, 1.38 (m, 74H, -$COCH_2CH_2CH_2CH_2CH_2$O-). ($M_{n,\,NMR}$= 4970 g/mol, $M_{n,\,GPC}$ = 8910 g/mol, M_w/M_n = 1.13).

4. UV irradiation induced ECE cleavage

ECE was dissolved in $CDCl_3$ to produce 10 mg/mL solution. The solution was irradiated under UV light (λ_{max} = 365 nm, 10 mW/cm^2) for 15 min. Then, the polymer solution was subjected to GPC measurement.

5. Preparation of ECE micelle

The polymer micelle was prepared by dialysis method. Typically, 10 mg ECE was dissolved in 2 mL of THF and stirred at room temperature for 2 h. To the solution, 5 mL of deionized water was added and the solution was

stirred for an additional 2 h. After removal of THF by dialysis against deionized water, the polymer micelle solution was obtained.

6. UV-vis measurement after UV irradiation

The ECE micelle solution was diluted to 0.5 mg/mL and filtered using 0.22 μm filter membrane. The solution was then subjected to UV irradiation (λ_{max} = 365 nm, 10 mW/cm^2). At predetermined time interval, the solution was withdrawn and its UV-vis absorption spectroscopy was measured.

7. UV irradiation induced morphology change of the assemblies

The ECE micelle solution (0.5 mg/mL) was irradiated under UV light (λ_{max} = 365 nm, 10 mW/cm^2) for 15 min. Then, the solution was heated to 65 °C and further stirred at this temperature. At predetermined time interval, the solution was characterized by DLS and TEM measurements to demonstrate morphological change of the micelles. At the end, the solution was cooled to room temperature and subjected to DLS and TEM analyses.

8. Results

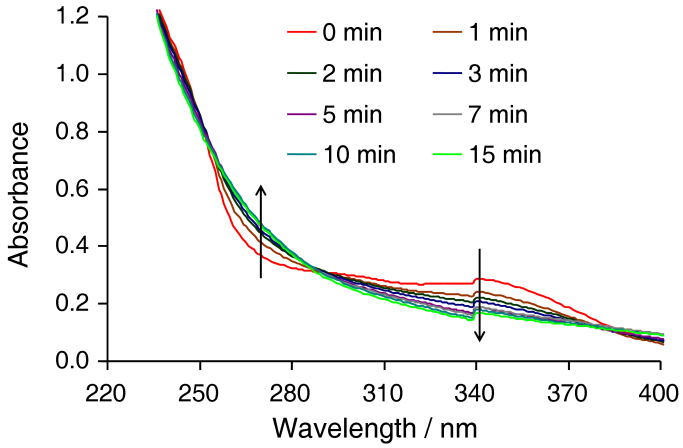


Figure S7. UV-vis absorption spectra of the ECE polymer assemblies after UV irradiation for different time periods.

As indicated in Figure S7, following irradiation the UV-vis absorption spectra showed an increase at 270 nm along with a concomitant decrease at 340 nm, indicating cleavage of the NB ester bond and formation of the derivative of 2-nitrosobenzaldehyde.[7]

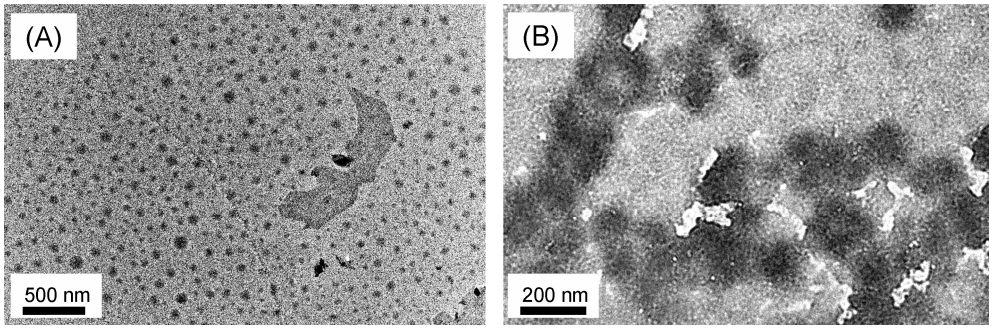


Figure S8. TEM images of (A) the ECE micelles without UV irradiation but stirred at 65 °C for 123 h and (B) assemblies after UV irradiation for 15 min and stirred at 65 °C for 24 h.

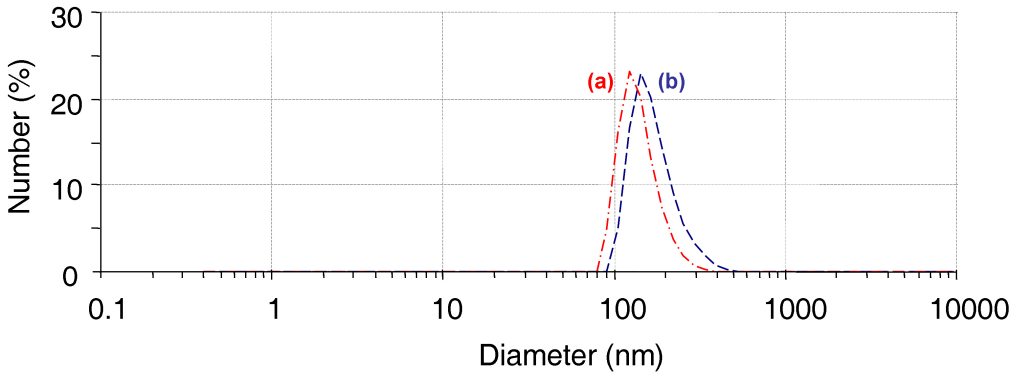


Figure S9. DLS analysis of the UV irradiated ECE micelle solution after stirring at 65 °C for 123 h (a) then cooling to room temperature for 24 h (b).

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