

Supporting Information

Visible Light-Responsive Micelles Formed from Dialkoxyanthracene-Containing Block Copolymer

Qiang Yan,^a Jun Hu,^b Rong Zhou,^c Yong Ju,^b Yingwu Yin,^a and Jinying Yuan^{a*}

^aKey Lab of Organic Optoelectronics & Molecular Engineering, Department of Chemistry, Tsinghua University, Beijing, 100084, China. ^bKey Lab of Bioorganic Phosphorus Chemistry & Chemical Biology, Department of Chemistry, Tsinghua University, Beijing 100084, China.

^c Department of Chemistry, Brandeis University, Waltham MA, USA

AUTHOR EMAIL ADDRESS: yuanjy@mail.tsinghua.edu.cn

1. Materials

Methoxy poly(ethylene glycol) (PEG, $M_{n,GPC} = 0.75$ kg/mol) was dried by azeotropic distillation in the presence of toluene. Maleic anhydride was recrystallization in chloroform twice. 9,10-anthraquinone (AQ, Alfa Aesar, 99%), dicyclohexylcarbodiimide (DCC, Alfa Aesar, 99%), 4-dimethylaminopyridine (DMAP, Alfa Aesar, 98%), 3-chloro-1-propanol (Acros, 99%), ϵ -caprolactone (ϵ -CL, Acros, 98%), stannous octoate ($\text{Sn}(\text{Oct})_2$, Acros, 99%), NaI, $\text{Na}_2\text{S}_2\text{O}_4$, NaOH, and all solvents were used as received.

2. Characterization

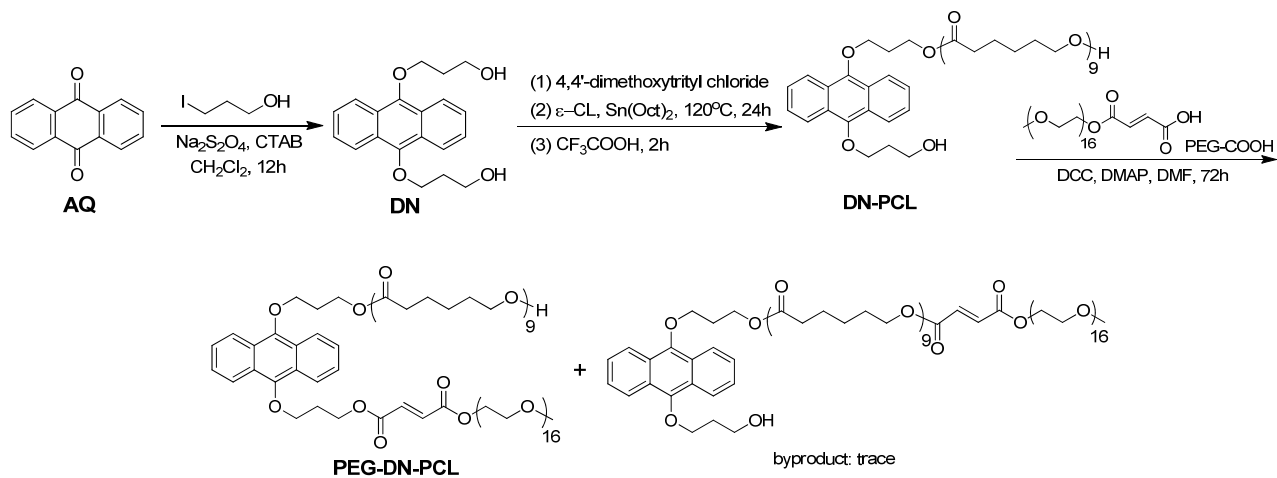
¹H NMR spectra for the polymer structural analysis were obtained from JEOL JNM-ECA600 (600MHz) spectrometer with CDCl_3 as the solvent. The molecular weight and the molecular weight distribution (M_w/M_n) were measured on gel permeation chromatography (GPC) in a system equipped with a Waters 515 pump, three columns and a 2410 differential refractometer detector. THF was used as the eluent at a flow rate of 1.0 mL/min at 30 °C. Monodisperse polystyrene was used as the standard to generate the calibration curve. The visualized images of the polymer assemblies were obtained from a Titan KriosTM Cryo transmission electron microscope (Cryo-TEM) and JEM-2010 Microscope (TEM) with an accelerating voltage of 120 kV. Dynamic light scattering (DLS) experiments were used a commercial spectrometer (ALV/DLS/SLS-5022F) equipped with a multi-tau digital time correlator (ALV5000) and a 22 mW He-Ne laser ($\lambda_0 = 632$ nm) as the light source. The scattering light was collected at a fixed angle of 90° for duration of ~10 min. Average radius $\langle R_h \rangle$ and particle size distributions $\langle f_h \rangle$ were computed using a cumulant analysis and CONTIN routines. MALDI-TOF mass spectra (MALDI-TOF-MS) were recorded on a Bruker Autoflex spectrometer. The matrix was 4-chloro- α -cyanocinnamic acid (CCA). The optical transmittance of the aqueous solution was measured on a UV 2100 UV-visible spectrophotometer (Shimadzu, Japan) for responsible to the controlled drug release experiments. To support the controlled release experiments, fluorescent spectroscopy (FS) was employed to monitor the intensity changes of the solution fluorescence. Fluorescence was measured with a Hitachi F-7000 spectrofluorometer.

3. Synthetic Procedures

Synthesis of 3-iodo-1-propanol

Typical synthetic method was according to the literature.^[S1] A mixture of 3-chloro-1-propanol (9.45 g, 0.10 mol) and NaI (30.1 g, 0.2 mol) in acetone (100 mL) was refluxed overnight. The solution was filtered and the solvent was removed by evaporation. The residue was re-dissolved in CH_2Cl_2 , filtered and the solvent removed. The crude product was purified by column chromatography with a mixture of

ethyl acetate/CH₂Cl₂ (1/3, v/v). Yield: 47%. ¹H NMR (δ, ppm, CDCl₃): 3.76 (t, 2H, -CH₂-OH), 3.30 (t, 2H, -CH₂-I), 2.08 (m, 2H, -CH₂-CH₂-CH₂-).



Scheme S1. The synthetic route of target diblock copolymer PEG-DN-PCL

Synthesis of 9,10-bis(3-hydroxypropoxy)anthracene (DN)

The reaction was according to literature with little modification.^[S2] Nitrogen-saturated water (100 mL) and CH₂Cl₂ (100 mL) were added to a mixture of 9,10-anthraquinone (AQ, 2.08 g, 0.01 mol), Na₂S₂O₄ (3.48 g, 0.02 mol), and cetyl trimethyl ammonium bromide (CTAB, 2.85 g, 0.01 mol). The mixture was stirred for 5 min and then NaOH (4.00 g, 0.10 mol) was added. Stirring was continued for 10 min and 3-iodo-1-propanol (5.58 g, 0.03 mol) was added dropwise. The mixture was further stirred for 12 h at room temperature. Then the phases were separated and the water phase was washed with CH₂Cl₂. The combined organic phases were washed with water and dried over MgSO₄. The solution volume was reduced to ~40 mL and the product was precipitated overnight at -20 °C. The solid was purified by column chromatography with a mixture of ethyl acetate/CH₂Cl₂ (1/4, v/v). Yield: 22%. ¹H NMR (δ, ppm, CDCl₃): 8.25 (d, 4H, anthracene), 7.62 (d, 4H, anthracene), 4.66 (t, 2H, -CH(O)-), 4.22 (t, 4H, O-CH₂-CH₂-), 3.79 (m, 4H, -CH₂-CH₂-OH), 2.10 (m, -CH₂-CH₂-CH₂-).

Synthesis of poly(caprolactone)-(3-hydroxypropoxy)anthracene (DN-PCL)

9,10-bis(3-hydroxypropoxy)anthracene (0.56 g, 1.73 mmol) was dissolved in anhydrous pyridine (10 mL), and 4-(dimethylamino)pyridine (0.17 g, 1.38 mmol) and *N,N*-diisopropylethylamine (0.18 mg, 1.38 mmol) were added. A solution of 4,4'-dimethoxytrityl chloride (0.70 g, 2.08 mmol) in pyridine (10 mL) was prepared separately and then added dropwise to the first solution. The resulting mixture was stirred for 2 h at room temperature. Then pyridine was removed at reduced pressure and MeOH (10 mL) was added. After 15 min the mixture was poured into saturated NaHCO₃ solution and extracted with CH₂Cl₂ (3×10 mL). The combined organic phases were dried in MgSO₄ and the solvent evaporated. The residue left was dissolved in CH₂Cl₂ and purified by column chromatography with ethyl acetate/CH₂Cl₂ (1/20 v/v) as light yellow oil (Yield: 40%). The product then performed a ring opening polymerization for ε-CL. The single hydroxyl protecting compound above (0.31 g, 0.5 mmol), ε-CL (0.684 g, 6.0 mmol), and a catalytic amount of Sn(Oct)₂ (20 μL) were dissolved in 25 mL of freshly anhydrous DMF in a dried polymerization tube. The tube was followed three freeze-vacuum-thaw cycles, and then was immersed into an oil bath at 120 °C under nitrogen atmosphere with vigorous stirring for 24 h. After cooling to room temperature, the resultant was dissolved in 15 mL of chloroform and precipitated with cool methanol to afford the crude solid. After treatment with CF₃COOH for 2 h so as to remove the hydroxyl protecting group, the solution was precipitated with cool methanol three times to obtain the purified DN-PCL. The product was dried in vacuum until constant weight (0.68 g, conversion: 75%).

$M_{n,GPC} = 1280 \text{ g mol}^{-1}$). $^1\text{H NMR}$ (δ , ppm, CDCl_3): 8.27 (d, 4H, in anthracene), 7.62 (d, 4H, in anthracene), 4.28 (t, 4H, $-\text{CH}_2-\text{CH}_2-$), 4.07 (t, $-\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}-$ in PCL), 3.70–3.61 (bm, terminal $-\text{CH}_2\text{OH}$ and $-\text{CH}_2-\text{CH}_2-\text{OH}$), 2.38 (t, $-\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}-$ in PCL), 1.63 (m, $-\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}-$ in PCL), 1.36 (m, $-\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}-$ in PCL).

Synthesis of poly(ethyl glycol)-(3-hydroxypropyloxy)anthracene-poly(caprolactone) (PEG-DN-PCL)

Maleic acid end-capping PEG (PEG-COOH, $M_{n,GPC} = 810$, 0.38 g, 0.45 mmol) synthesized according to literature^[53], DN-PCL (0.50 g, 0.36 mmol), DCC (0.10 g, 0.45 mmol), and DMAP (0.05 g, 0.45 mmol) were dissolved in 20 mL anhydrous DMF solvent, and the reaction was performed at 0 °C for 72 h under nitrogen atmosphere. The byproduct solid dicyclohexylcarbodiurea (DCU) was removed by filtration, and the filtered solution was evaporated. The crude was dissolved in chloroform/ CH_3OH (1/10) to remove unreacted PEG and then precipitated in cool diethyl ether three times. The solid was dried in vacuum. (0.57 g, yield: 71%). Actually, the PEG-COOH can react with two hydroxyl groups in DN-PCL species. However, the reactivity of hydroxyl group directly linked at DN species is higher than that of hydroxyl groups in PCL terminal because of polymer steric hindrance. The PEG-DN-PCL is the main product, and minor DN-PCL-PEG could not affect the photocleavage property and the self-assembly or disassembly of visible light-responsive polymer micelles. $M_{n,GPC} = 2120 \text{ g mol}^{-1}$). $^1\text{H NMR}$ (δ , ppm, CDCl_3): 8.25 (d, in anthracene), 7.62 (d, in anthracene), 6.49 (q, $-\text{CH}=\text{CH}-$), 4.06 (t, $-\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}-$ in PCL), 3.65 (s, $-\text{OCH}_2\text{CH}_2\text{O}-$ in PEG), 3.49 (s, $-\text{OCH}_3$ in PEG), 2.33 (t, $-\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}-$ in PCL), 1.66 (m, $-\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}-$ in PCL), 1.38 (m, $-\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{COO}-$ in PCL).

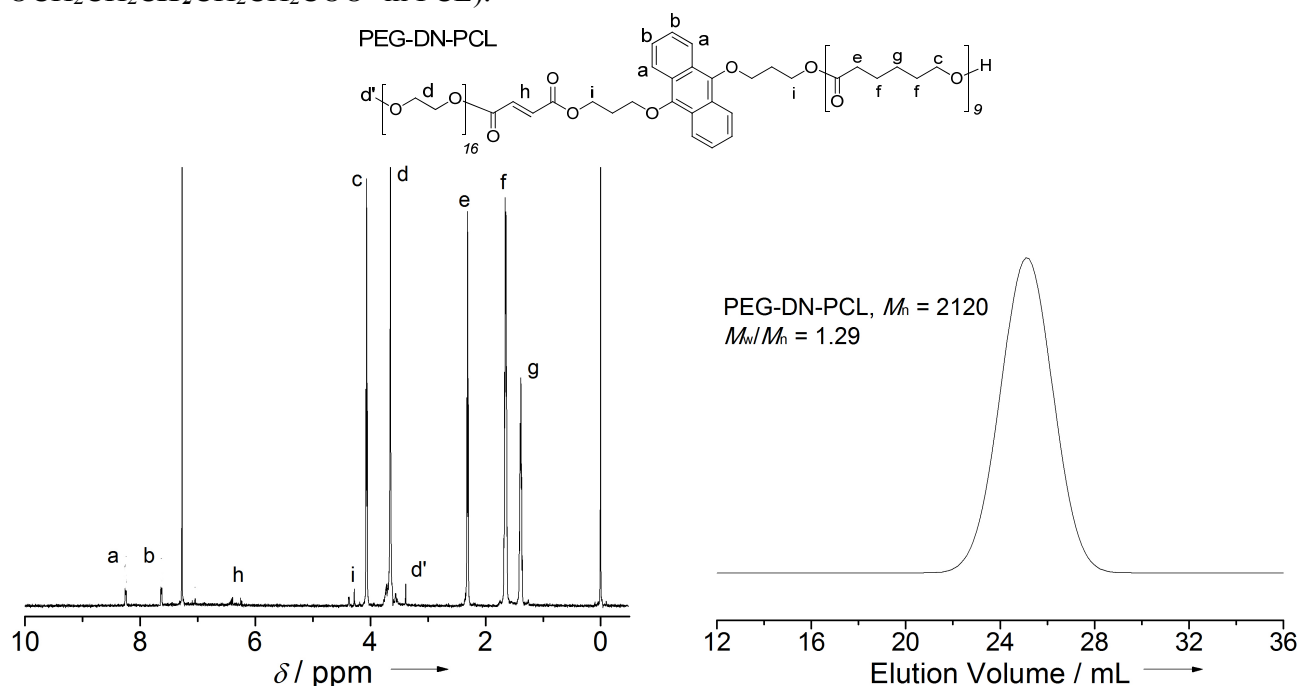


Fig. S1. The $^1\text{H NMR}$ of visible light-responsive diblock copolymer PEG-DN-PCL (left)

Fig. S2. The GPC chromatogram of diblock copolymer PEG-DN-PCL (right)

4. Experiments and Characterization

4.1 The measurement of critical micelle concentration (CMC) of PEG-DN-PCL

A 1 mL of solution of 10.0 mM PEG-DN-PCL in DMF was added into 10 mL of deionized water under sonication, followed by dialysis against deionized water. After 48 h, the volume of the solution was increased to obtain an aggregate solution with a concentration of 0.1 mM for further experiments. The critical micelle concentration (CMC) of PEG-DN-PCL was measured by the fluorescent probe method, using pyrene as a probe molecule. 1×10^{-4} mM pyrene solution in acetone was added to PEG-DN-PCL

aqueous solution with different concentrations and the solutions were sonication for 10 min before fluorescent emission measurements. The results showed that the CMC of PEG-DN-PCL was $\sim 4.3 \times 10^{-2}$ mM (The CMC was chosen as the concentration when pyrene exhibited an apparent decrease in the I_1/I_3 ratio with an increasing concentration of the copolymer, indicating that the aggregation of the copolymer occurred, Fig. S3).

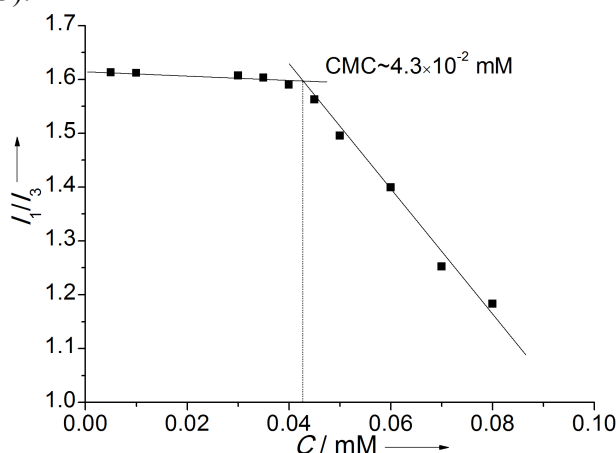


Fig. S3. Determination of CMC for the PEG-DN-PCL block copolymer by using the fluorescent method with pyrene as a probe, the CMC is $\sim 4.3 \times 10^{-2}$ mM.

4.2 The turbid measurement of PEG-DN-PCL upon visible light irradiation

Another important evidence to confirm the cleavage of PEG-DN-PCL at the DN position is the turbidity measurement of the polymer solution before and after visible light irradiation. Before light illumination, the PEG-DN-PCL copolymer showed good water-solubility (5.0×10^{-2} mM) and the transmittance of the solution is $\sim 88\%$. After light irradiation for 2.5 h, the $^1\text{O}_2$ -mediated reaction was occurred and the PCL blocks were cleaved. Because PCL is a hydrophobic polymer and is water-insoluble, the transmittance of the polymer solution would decrease from 88% to 41% (Fig. S4), which support the results that PEG-DN-PCL was divided into two molecular fragments.

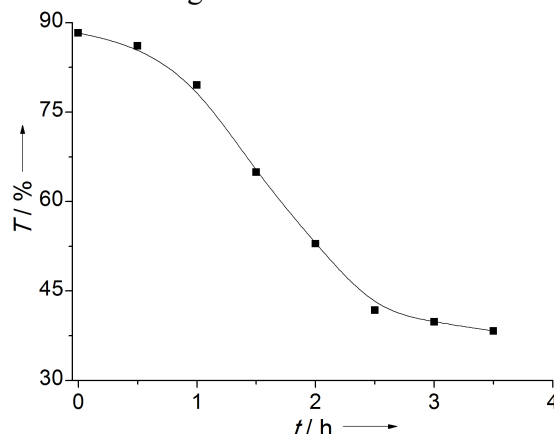
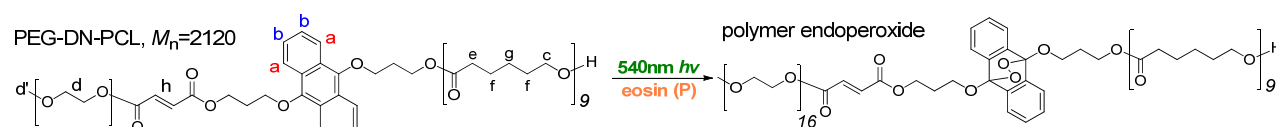
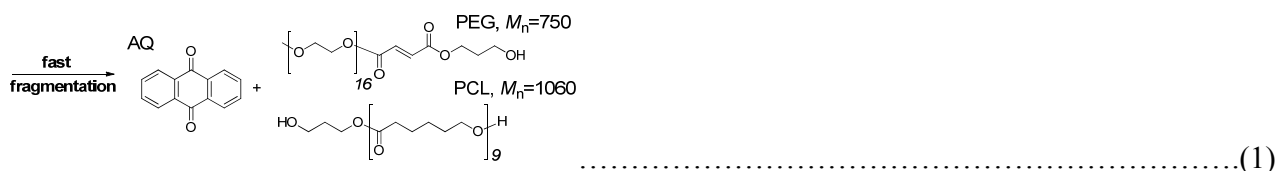


Fig. S4. The turbidity changes vs. time of PEG-DN-PCL solution upon visible light irradiation in the presence of eosin. The polymer concentration is 5.0×10^{-2} mM.

4.3 The pH-dependent experiments of the cleavage speed of PEG-DN-PCL upon visible light





Without any stimulation, PEG-DN-PCL copolymers can self-assemble into spherical micelles in water. Upon green visible light (540 nm) in the presence of eosin, PEG-DN-PCL is ruptured into molecular fragments including PEG, PCL, and AQ. Meanwhile, the micelles can disaggregate. Because the $^1\text{O}_2$ -mediated addition-fragmentation reaction [Eq. (1)] of PEG-DN-PCL can be facilitated by solution pH, as the pH value decreasing from 7.2 to 6.5 to 5.4, the disassembling speed of the micelles increases from ~ 2.5 h to ~ 2.0 h to ~ 0.9 h (Fig. S5). The decomposed rate increases 170% as pH reducing. It further indicates that the disaggregation of these micelles could be further well-tuned by solution acidity.

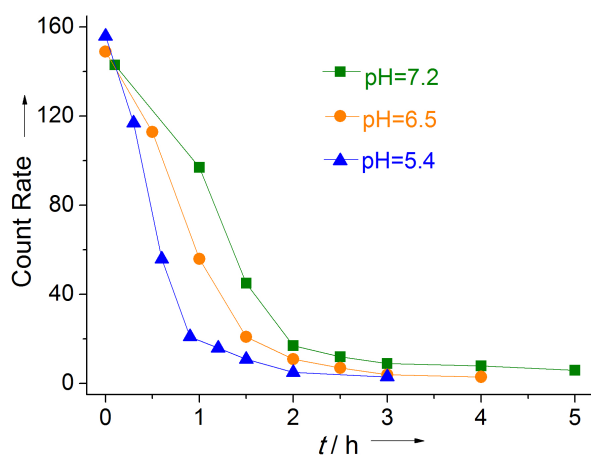


Fig. S5. The pH-dependent behavior of the PEG-DN-PCL cleavage speed upon visible light in the presence of eosin, the polymer concentration is 5.0×10^{-2} mM

References

- [S1] Pattison, F. L. M.; Brown, G. M. *Can. J. Chem.* **1956**, *34*, 879.
[S2] Diekers, M.; Luo, C.; Guldi, D.; Hirsch, A. *Chem. Eur. J.* **2002**, *8*, 979.
[S3] Yan, Q.; Yuan, J. Y.; Kang, Y.; Yin, Y. W. *Polym. Chem.* **2010**, *1*, 423.