Electron Supplementary Information (ESI)

Synthesis of a ROS-responsive analogue of poly(ε-caprolactone) by living

ring-opening polymerization of 1,4-oxathiepan-7-one

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1. Materials

All materials and reagents were obtained from commercial suppliers and used directly unless otherwise specified. Dichloromethane (DCM, 99.9%, SuperDry, with molecular sieves, water <30 ppm, J&K). ϵ -Caprolactone (CL, 99%, TCI) was distilled over CaH₂. Monomethoxy poly(ethylene oxide) (mPEO₁₁₄, M_n =5000 Da, AR, Fluka) was dried by azeotropic distillation with toluene. 4-Nitrophenyl acrylate was synthesized in 91% yield from 4-nitrophenol and acryloyl chloride by following the reported procedure (A. Harada, M. Furue and S.-i. Nozakura, *Macromolecules*, 1976, **9**, 701-704.). It was purified by recrystallization from ethyl acetate and hexane.

2. Insrmentation

¹H NMR (400 MHz) and ¹³C NMR (100 MHz) spectra were recorded on a Bruker Avance-400 spectrometer. Chemical shifts are reported in ppm with tetramethylsilane (TMS) as the internal reference. Gel permeation chromatography (GPC) was performed on a Waters system equipped with a Waters 1525 binary HPLC pump, a Waters 2414 refractive index detector, and three Waters Styragel HT columns (HT2, HT3, HT4) thermostated at 35 °C. HPLC-THF was used as eluent at a flow rate of 1.0 mL/min. The calibration was made against linear polystyrene standards, and the data was collected and processed with a commercial software (Breeze 3.30 SPA). Electrospray ionization (ESI) mass spectroscopy of the degradation products were performed on a Bruker APEX-IV Fourier transform mass spectrometer in positive ion mode and negative ion mode. Matrix-assisted laser desorption/ionization time-of-flight mass spectroscopy (MALDI-TOF-MS) was conducted on a AB Sciex 5800 spectrometer. The sample was mixed with 20 mg/mL 2,5-Dihydroxybenzoic acid (DHB, Sigma Aldrich) in 60% acetonitrile/40% H2O (v/v) in 1:1 ratio (v/v). 1 uL of the sample was then spotted onto a MALDI plate, and analyzed using the AB SCIEX 5800 TOF/TOF (AB SCIEX, USA) in reflector mode for positive ion detection. MS spectra were acquired between m/z 2000 and 4000. Thermal gravimetric analysis (TGA) was conducted on a Q600-SDT thermogravimetric analyzer (TA Co. Ltd.) at a heating rate of 10 °C/min under a nitrogen flow of 100 mL/min. Differential scanning calorimetry (DSC) was performed on a TA Q100 differential scanning calorimeter under a nitrogen flow of 50 mL/min. Both the heating and cooling rate were set to 10 °C/min. Thermograms were recorded from the second heating scan and analyzed with TA Universal Analysis software. Both dynamic light scattering (DLS) and static light scattering (SLS) measurements were performed on a laser light scattering equipment (Brookhaven Inc., Holtsville, NY) composed of a BI-200SM goniometer, a BI-TurboCorr digital correlator and a vertically polarized He-Ne laser (R-30995, 633 nm, 17 mW, Newport, USA) which was used as the light source. The hydrodynamic radius $(R_{\rm h})$ and z-averaged root-mean square radius of gyration $(R_{\rm g})$ were measured by DLS and SLS, respectively. The polymer self-assembly morphologies were observed with a FEI Tecnai G2 T20 TEM at 120 kV.

3. NMR spectra, MS spectra, and GPC traces



Fig. S1 ¹H NMR spectrum of the thia-Michael adduct in CDCl₃



Fig. S2 ¹H NMR spectrum of the reaction mixture in the synthesis of OTO (CDCl₃)



Fig. S3 ¹H NMR spectrum of the purified OTO in CDCl₃



Fig. S4 ¹³C NMR spectrum of the purified OTO in CDCl₃



Fig. S5 Time-dependent ¹H NMR spectra of the ROP of OTO in CDCl₃



Fig. S6 ¹³C NMR spectrum of POTO₃₀ in CDCl₃



Fig. S7 MALDI-TOF MS spectrum of $POTO_{20}$, the zoomed and simulation spectrum of $POTO_{16+}Na^+$.



Fig. S8 Zoomed ¹H NMR spectrum of POTO₇₀-*b*-PCL₈₀ in CDCl₃



Fig. S9 ¹³C NMR spectrum of POTO₇₀-*b*-PCL₈₀ in CDCl₃



Fig. S10 GPC traces of the amphiphilic block copolymers



Fig. S11 ¹H NMR spectra of the amphiphilic block copolymers in CDCl₃



Fig. S12 ¹³C NMR spectra of the amphiphilic block copolymers in CDCl₃



Fig. S13 Time-dependent ¹H NMR spectra of M1 incubated with H_2O_2 (1 M) in neutral buffer at $37^{\circ}C$



Fig. S14 ¹H NMR spectra of three standard substances and that of M1 after being incubated with H_2O_2 (1 M) in neutral buffer at 37°C for 122 h



Fig. S15 Time-dependent ¹H NMR spectra of M2 incubated with H_2O_2 (1 M) in neutral buffer at 37°C



Fig. S16 ¹H NMR spectra of four standard substances and that of **M2** after being incubated with H_2O_2 (1 M) in neutral buffer at 37°C for 116 h



Fig. S17 Time-dependent ¹H NMR spectra of M3 incubated with H_2O_2 (1 M) in neutral buffer at 37°C



Fig. S18 ¹H NMR spectra of five standard substances and that of M3 after being incubated with H_2O_2 (1 M) in neutral buffer at 37°C for 120 h





- (B) M1-SO in neutral buffer
- (C) M1-SO₂ with H_2O_2 in neutral buffer
- (D) M1-SO₂ in neutral buffer
- (E) Sodium 2-hydroxyethanesulfonate in neutral buffer



Fig. S20 Zoomed ¹H NMR spectra of the H_2O_2 -promoted elimination products of M1 (122 h.), M2 (116 h.), M3 (120 h.), and the related standard substances. These signals are all from the alkenyl protons formed by different elimination reactions.



Scheme S1 Proposed oxidation mechanism of M1 when incubated with H_2O_2 (0.1M). Substances in the dash box were not directly observed. The dashed arrow stands for reactions that was not directly observed or tested in model reactions.



Scheme S2 Proposed oxidation mechanism of M2 when incubated with H_2O_2 (0.1M). Substances in the dash box were not directly observed. The dashed arrow stands for reactions that was not directly observed or tested in model reactions.



Fig. S21 High resolution ESI MS spectrum of M3 after being incubated with H_2O_2 (1 M) in neutral buffer at 37°C for 6 h.



Fig. S22 High resolution ESI MS spectrum of M3 after being incubated with H_2O_2 (1 M) in neutral buffer at 37°C for 120h

4. DLS characterization of PEO₁₁₄-*b*-POTO₂₀ micelles and their disassembly



Fig. S23 DLS characterization of PEO₁₁₄-*b*-POTO₂₀ micelles



Fig. S24 Time-dependent DLS characterization (30° and 90°) of PEO_{114} -*b*-POTO₂₀ micelles upon oxidation with H_2O_2