

Electronic Supporting Information for:

Interfacial micellar transfer using amphiphilic invertible polymers

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Synthesis of amphiphilic invertible polymers (AIPs)

Two-stage procedure was used to synthesize amphiphilic invertible polyesters.

Stage 1. Formation of acid-terminated prepolymer. Polytetrahydrofuran (0.1 mol) and succinic anhydride (0.2 mol) were melted together and the melt was maintained at 95°C for 3 hours. The course of the reaction was controlled by determining acid value of the reactive mixture and via IR spectroscopy (from the disappearance of the C=O anhydride adsorption bands at 1786 and 1862 cm⁻¹).

Stage 2. Synthesis of amphiphilic invertible polyesters. A mixture of the corresponding acid-terminated prepolymer from Stage 1 (0.1 mol) and poly(ethylene glycol) (0.1 mol) was dissolved in toluene. A 1 : 3 (w/v) monomer mixture : toluene ratio was used. Subsequently, 0.1 mL of 75% sulfuric acid was added to catalyze the reaction. The mixture was refluxed with a Dean-Stark trap for about 20 h. When the acid value reached 3.6-4.1 mg KOH/g, the reactive mixture was cooled down to room temperature. To neutralize the sulfuric acid, 0.33 mL of a 10% sodium hydroxide solution was added, and the mixture was stirred at room temperature for 12 hours. Sodium sulfate that formed was separated by centrifugation. Toluene was removed under reduced pressure. The resulting polymer was dried under vacuum at 60 °C for at least 24 hours.

Characterization of AIPs

An average molecular weight and polydispersity index (PDI) of synthesized AIPs were measured by gel permeation chromatography (GPC) using a Waters Corp. modular chromatograph consisting of a Waters 515 HPLC pump, a Waters 2410 refractive index detector, and a set of two 10 µm PL-gel mixed-B columns; the column temperature was set at 40 °C. Tetrahydrofuran (THF) was used as the carrier solvent at a flow rate of 1.0 mL/min; 200 µL of a 5 mg/mL THF solution were injected for each sample. All samples were filtered through a 0.45 µm PTFE filter (Nalgene) before running. A molecular weight

calibration curve was generated with polystyrene standards of low polydispersity (Polymer Laboratories, USA).

The structure of the synthesized polyesters was confirmed by FTIR and NMR spectroscopy. The Fourier transform infrared spectra of the developed polymers were recorded with a Nicolet 8700 FT-IR spectrometer (Thermo Scientific) using KBr optical discs. ^1H NMR spectra were recorded on a Varian VXR-400 NMR spectrometer using chloroform-*d* as a solvent.

In the FTIR spectrum (**Figure 1S, A**), the presence of the carbonyl group is indicated by an intensive adsorption band at 1734 cm^{-1} corresponding to C=O valence oscillations. A doublet of intensive adsorption bands at $1165\text{-}1111\text{ cm}^{-1}$ is caused by valence vibrations of ether and ester C–O bonds. A broad adsorption band at $2966\text{-}2845\text{ cm}^{-1}$ corresponds to the valence vibrations that are characteristic of $-(\text{CH}_2)_n-$ groups.

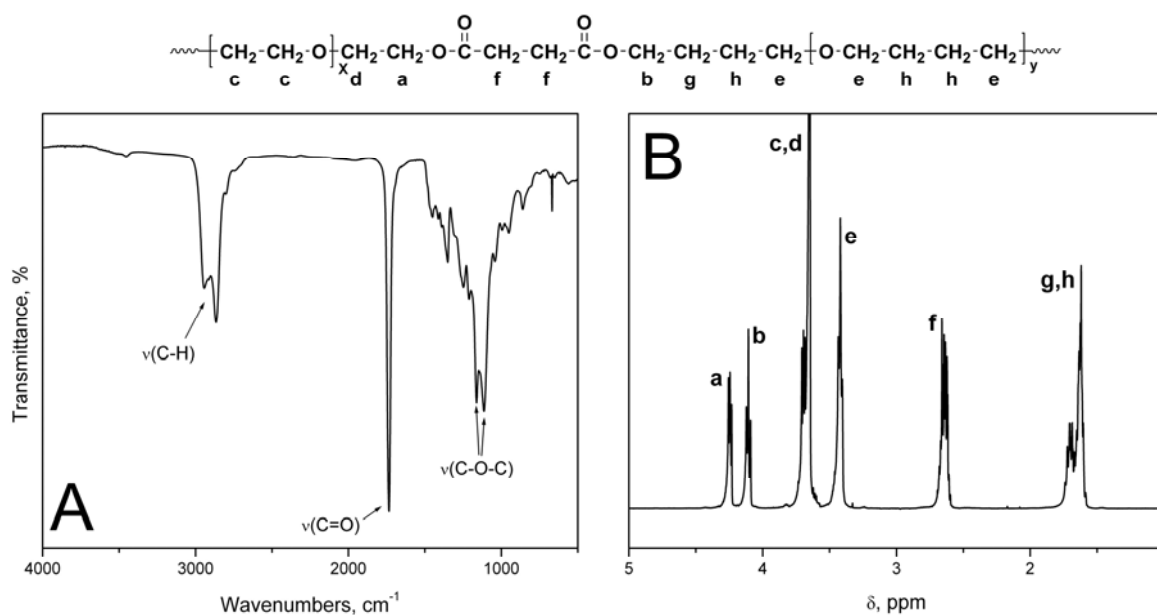


Figure 1S. FTIR (A) and NMR (B) spectra of the AIPE PEG₃₀₀-PTHF₂₅₀.

In the ^1H NMR spectrum (**Figure 1S, B**) of the polyester PEG₃₀₀-PTHF₂₅₀ in CDCl_3 , peaks corresponding to protons of the poly(ethylene oxide) chains appear at 3.65 ppm (m, 18H, $\text{CH}_2\text{OCH}_2\text{CH}_2\text{OCH}_2$), 3.69

ppm (t, 4H, C(O)OCH₂CH₂O), and 4.24 ppm (t, 4H, C(O)OCH₂CH₂O). Polytetrahydrofuran protons show themselves as peaks at 1.62 ppm (m, 8H, CH₂OCH₂CH₂CH₂), 1.70 ppm (m, 4H, C(O)OCH₂CH₂CH₂), 3.42 ppm (m, 8H, CH₂OCH₂CH₂CH₂), and 4.11 ppm (t, 4H, C(O)OCH₂CH₂CH₂). A peak at 2.64 ppm is attributed to an ethylene group of the succinate fragment (tt, 4H, OC(O)CH₂CH₂C(O)O).

Critical micelle concentration of AIPs determined by pyrene solubilization

First, a solution of pyrene in acetone with a concentration of 5×10^{-4} mol/L was prepared. Each sample was prepared by adding the pyrene solution (20 μ L) into an empty vial, evaporating the acetone for 2 h at room temperature, adding the AIP solution (20 mL), and stirring the solution for at least 24 h. The final pyrene concentration in water reached 5×10^{-7} mol/L, which is slightly below the pyrene saturation concentration in water at room temperature. For the fluorescence measurements, the solution (ca. 3 mL) was placed in a 1.0×1.0 cm² cell. All spectra were taken using a Fluoromax-3 Fluorescence Spectrometer (Jobin Yvon Horiba) with 90° geometry and a slit opening of 0.5 nm. For fluorescence excitation spectra, $\lambda_{em} = 390$ nm was chosen. Spectra were accumulated with an integration time of 0.5 nm/s. Critical micelle concentration values were determined after fitting the semi-logarithmic plots of intensity ratio $I_{336.5}/I_{333}$ versus log concentration to the sigmoidal curve (**Figure 2S**).

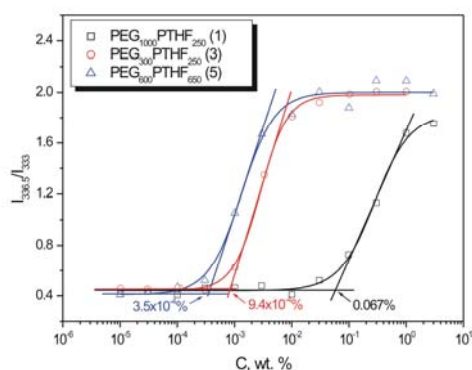


Figure 2S. The intensity ratio $I_{336.5} / I_{333}$ of the excitation spectra of pyrene solution with amphiphilic polyesters 1,3,5.

Phase transfer experiment

Preparation of dye-loaded polymeric micelles. Micellar dyes were prepared by thin film method.¹ According to this method, 0.1 g of polymer and 0.5 mL of acetone solution of Nile red (1 mg/mL) were dissolved in 10 mL of acetone. The solvent was removed by rotary evaporation at 60°C for 1 hour to obtain a solid dye/AIP matrix. Residual acetone remaining in the dye/AIP matrix was evaporated overnight under vacuum. The resultant thin film was hydrated with 10 mL of Millipore water; the unincorporated dye aggregates were removed by filtration through 0.45 µm filters.

Study of AIP-Mediated Phase Transfer. For phase transfer, 3 mL of aqueous micellar AIP solutions loaded with dye were mixed with 3 mL of toluene or 1-octanol. To reach equilibrium, the mixtures were either stirred for 1 hour. Subsequently, aqueous phase was separated from the organic phase by centrifugation.

Determination of the Dye Concentration in Aqueous and Toluene Phase. The initial concentration of the dye in a buffer solution was estimated using UV-Vis spectroscopy. UV-Vis spectra were recorded on Cary 5000 UV-Vis-NIR spectrophotometer (Varian, Inc.). The absorbance values were measured in the range of 350-800 nm. The height of Nile red adsorption peak at 545 - 552 nm was attributed to a particular dye concentration using calibration method. To build the calibration curve, a set of 1% micellar solutions of a polyester PEG₃₀₀PTHF₂₅₀ containing known amounts of solubilized Nile red were prepared and their UV-Vis spectra were recorded. The final concentration of the dye in organic (toluene or 1-octanol) phase after the experiment was also determined using the UV-Vis spectroscopy. The calibration curves were built after recording UV-Vis spectra of a set of Nile red solutions of known concentration in the respective solvent.

Determination of Polymer Transfer

To study whether the AIPs crossed the interface between the aqueous and the organic phase, 1% aqueous solutions of the polymers (3 mL) were mixed with an equal volume of toluene or 1-

octanol and stirred for 1 hour. Subsequently, two phases were separated by centrifugation, both solvents were evaporated, and the amount of polymer in each phase was estimated gravimetrically.

The fraction of polymer transferred to the organic phase was calculated as follows:

$$x = [\text{AIP}_{\text{org}}] / [\text{AIP}_{\text{aq}}]_0 = m(\text{AIP}_{\text{org}}) / m_0(\text{AIP}_{\text{aq}}),$$

where $[\text{AIP}_{\text{org}}]$ and $[\text{AIP}_{\text{aq}}]_0$ is the final AIP concentration in the organic phase and initial AIP concentration in the aqueous phase, mol/L, $m(\text{AIP}_{\text{org}})$ and $m_0(\text{AIP}_{\text{aq}})$ is the weight of the AIP in the organic phase after the experiment and the weight of the AIP in the initial aqueous solution, g, respectively.

Reference

- (1). Zhang, X.; Jackson, J. K.; Burt, H. M. Development of amphiphilic diblock copolymers as micellar carriers of taxol. *Int. J. Pharm.* 1996, 132, 195–206.