



Supporting Information

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69451 Weinheim, Germany

A Subtle End-Group Effect on Macroscopic Physical Gelation of Triblock Copolymer Aqueous Solutions

*Lin Yu, Huan Zhang, and Jiandong Ding**

Materials. Polyethylene glycol (PEG) (MW 1000; Sigma), DL-lactide (Purac), glycolide (Purac), stannous octoate (Aldrich), 1,6-diphenyl-1,3,5-hexatriene (DPH; Aldrich) were used as received. All other chemicals were reagent grade and used as purchased without further purification.

Synthesis. The triblock copolymer (PLGA-PEG-PLGA) (sample A) composed of a central PEG block and two poly(lactic acid-*co*-glycolic acid) (PLGA) blocks was synthesized following the method described in the literature.^[1] Ring-opening polymerization of lactide, glycolide and ethylene glycol using stannous octoate as a catalyst was performed to synthesize PLGA-PEG-PLGA triblock copolymers.

PLGA-PEG-PLGA-diacetate (sample B), PLGA-PEG-PLGA-dipropionate (sample C) and PLGA-PEG-PLGA-dibutyrate (sample D) were synthesized via an effective procedure as follows: acetyl chloride (or propionyl chloride, butyl chloride) (4 mmol) dissolved in methylene chloride (30 ml) was slowly added over 1 h to a chilled solution composed of pyridine (4 mmol), PLGA-PEG-PLGA (1 mmol) and methylene chloride (100 ml). The solution was stirred in an ice bath for 6 h and then overnight at room temperature. The reaction mixture was washed with water and the organic phase was dried by using magnesium sulfate. The resulted solution was concentrated in vacuo to 30 ml and then precipitated with excessive anhydrous ether. The final products were dried under vacuum at room temperature for over 48 h.

¹H NMR (CDCl₃) of PLGA-PEG-PLGA: δ 1.55 (-OCH(CH₃)CO-), δ 3.60 (-OCH₂CH₂-), δ 4.30 (-OCH₂CH₂OCOCH₂O-), δ 4.80 (-OCH₂CO-), δ 5.20

* Corresponding author: Email: jdding1@fudan.edu.cn

(-OCH(CH₃)CO-).

¹H NMR (CDCl₃) of PLGA-PEG-PLGA-diacetate: d 2.14 (CH₃COO-).

¹H NMR (CDCl₃) of PLGA-PEG-PLGA-dipropionate: d 1.18 (CH₃CH₂COO-), d 2.42 (CH₃CH₂COO-).

¹H NMR (CDCl₃) of PLGA-PEG-PLGA-dibutyrate: d 0.97 (CH₃CH₂CH₂COO-), d 1.68 (CH₃CH₂CH₂COO-), d 2.38 (CH₃CH₂CH₂COO-).

Peaks at 4.80, 3.60 and 1.55 ppm were used to calculate the number average molecule weight, M_n of the PLGA-PEG-PLGA triblock copolymer.^[2, 3] The degree of substitution of the PLGA-PEG-PLGA triblock copolymer terminal alcohol for esterification was determined using a method similar to that of Dust et al.^[4] Namely, the extent of esterification substitution was calculated using the following formula: %esterification = (integral of end methyl group/6)/[(integral of PEG backbone)/4]/(PEG molecular weight/44)].

NMR Spectrometry. A 500-MHz proton NMR spectrometer (Bruker, DMX500) was used for ¹³C NMR experiments (in D₂O and DMSO) to observe spectral changes of copolymers at various temperatures. The solution temperature was equilibrated for 20 min before measurement.

Gel Permeation Chromatography (GPC). The molecular weights (MWs) of copolymers and their MW distributions were determined using an Agilent1100 GPC apparatus and a differential refractometer as detector. THF was used as eluent at a flow rate of 1.0 ml/min at 35°C, and the MWs were calibrated with polystyrene standards.

Sol-Gel Transition. The sol-gel transition was determined via the test tube inverting method.^[5, 6] Each sample at a given concentration was dissolved into distilled water in 4-ml vials. After equilibration at 4°C for several days, the vials containing samples were immersed in a water bath equilibrated at each given temperature for 15 min. The sol-gel transition was determined by an observation criterion after inverting the vial: if no flow was observed in 30 s, the sample was regarded as a gel. The temperature was raised with 1°C per step and the precision of the sol-gel transition temperature was ±1°C.

Dynamic Mechanical Analysis. The sol-gel transition of the copolymer aqueous

solution was investigated using a dynamic strain-controlled rheometer (ARES Rheometer Scientific). The polymer solution was placed into a Couette cylinder (Couette diameter, 34 mm; bob diameter, 32 mm; bob height, 33.3 mm; bob gap, 2 mm). Temperature was controlled by an environment controller (Neslab RTE-130) with an accuracy of $\pm 0.05^\circ\text{C}$. To avoid solvent evaporation, the surface was overlaid with a thin layer of low-viscosity silicone oil. The data were collected at a frequency of 10 rad/s, and the strain amplitude was set at a suitable value to ensure the linearity of viscoelasticity, depending on the temperature (usually 100% strain and 0.05% strain before and after gelation, respectively). The heating and cooling rates were both $0.5^\circ\text{C}/\text{min}$.

Critical Micelle Concentration. Critical micelle concentration (CMC) was determined via the dye solubilization method.^[7] 10 μL of DPH solution in methanol (0.4 mM) was injected into an aqueous polymer solution (1.0 mL) at various concentrations between 0.0035 and 0.16 wt% and equilibrated for 12 h before measurement. The absorption spectra of these solutions were recorded from 280 to 500 nm at 25°C . The hydrophobic dye, DPH, has a significantly much higher absorbance in a hydrophobic environment than in water. Therefore, with increasing polymer concentrations, the absorbance at 377 and 356 nm increased (Figure S1a), because the hydrophobic dyes are partitioned into the hydrophobic core of micelles.^[7] The critical micelle concentration (CMC) was determined by extrapolating the absorbance at 377 nm relative to that at 400 nm plotted against polymer concentration (Figure S1b) to eliminate the scattering effect of polymers. The approximate CMC value of the sample with the acetate end groups was determined as 0.034 ± 0.003 wt% at 25°C .

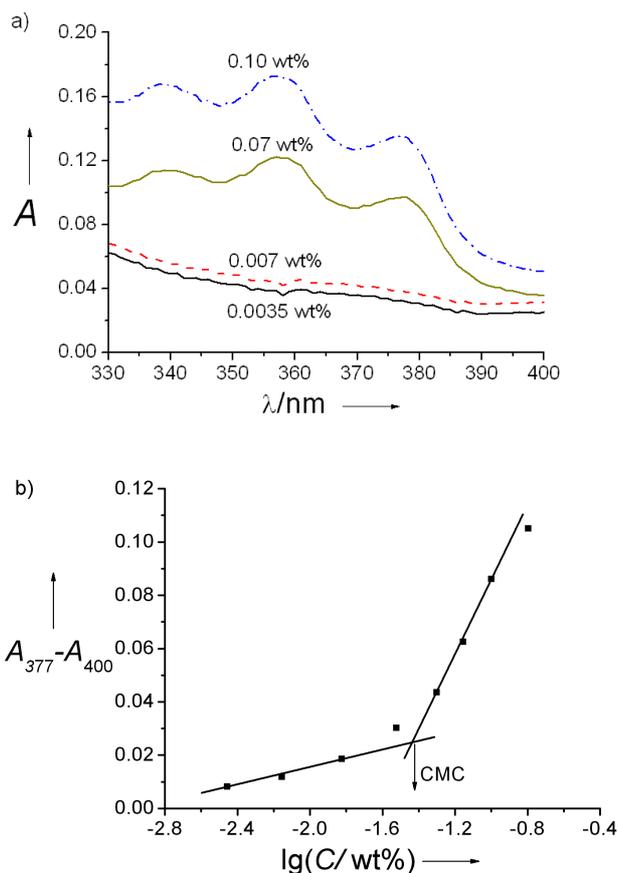


Figure S1. a) Absorbance A versus wavelength λ as UV-Vis spectra of aqueous solutions of sample B (with acetate end groups) which contain the hydrophobic dye (DPH). DPH concentration was fixed at $4 \mu\text{M}$ with varied polymer concentrations. Just 4 weight concentrations are indicated in the figure. Measurements were performed at 25°C ; b) CMC determination by extrapolation of the difference of absorbance at 377 and 400 nm.

Dynamic light scattering. Dynamic light scattering (DLS) was employed to determine particle sizes.^[8] The measurements of micelles and micellar aggregates were performed with a light scattering spectrophotometer (Autosizer 4700, Malvern) whose a vertically polarized incident beam being set at 532 nm supplied by an argon ion laser. A scattering angle of 90° was used in this study. Before measurement, all samples were dust-removed through a $0.45\text{-}\mu\text{m}$ filter (Millipore). Hydrodynamic radius of a micelle was obtained by the Stokes-Einstein equation. The intensity-intensity time correction function was analyzed by the CONTIN method. Z-averaging was used to denote the

average hydrodynamic radius.

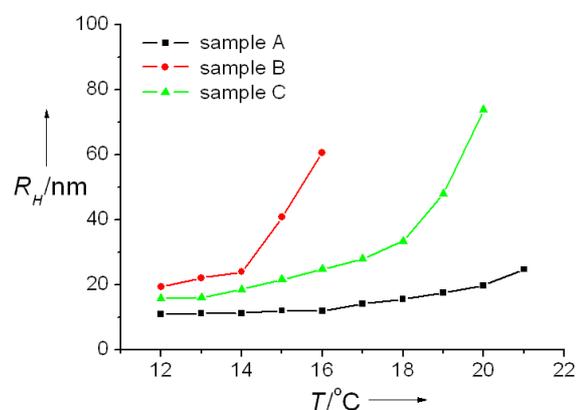


Figure S2. The average "particle" sizes (hydrodynamic radius R_H) detected by dynamic light scattering as a function of temperature T for different samples: sample A (with the hydroxyl end groups), sample B (with the acetate end groups), and sample C (with the propionate end groups). The concentration was 0.5 wt%. The scattering angle was 90° , and the intensity-intensity time correction function was analyzed by the CONTIN method.

The averaged "particle" sizes seem increased with temperature (Figure S2). The results revealed that the end capped by hydrophobic groups enlarged the size and made micelles much easier to aggregate. The size distribution curves (Figure S3) further indicated that the peak related to a single micelle existed at all of examined temperatures from 13 to 20°C , whereas the peak related to micellar aggregates appeared at relatively high temperatures for gelling available samples. Considering that ^{13}C NMR (Figure 4 in the manuscript) affords more convincing evidence that the intact structure of micelles maintained during the sol-to-gel transition, the hierarchic mechanism via micellar aggregation is responsible for the sol-to-gel transition.

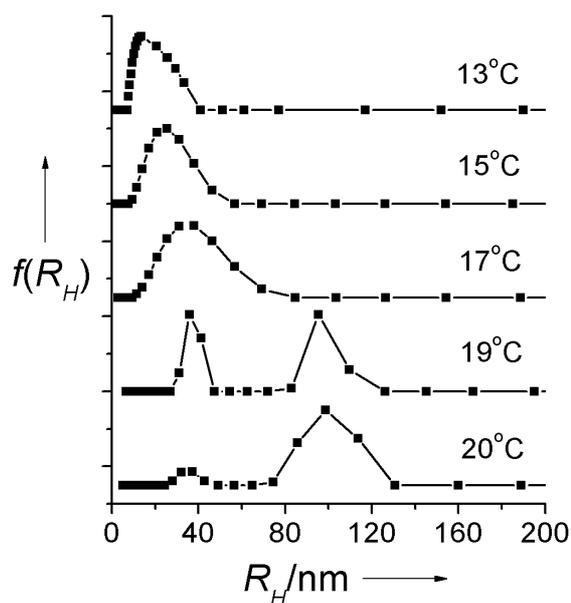


Figure S3. Intensity-weighted size distributions of particles (micelles and micellar aggregates) in aqueous solutions (0.5 wt%) of sample B (with the acetate end groups) at indicated temperatures.

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