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Notes

Synthesis and Characterization of Poly(alkyl α, L-glutamate-*co*-ethylene oxide)

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Abstract: Rod-coil amphiphilic block copolymers, PALG-PEOs, poly(alkyl α, L-glutamate-*co*-ethylene oxide)s, were successfully synthesized in three steps: 1) esterification of L-glutamic acid, 2) synthesis of γ-alkyl L-gultamate N-carboxyanhydride, and 3) polymerization of NCA monomers. These molecules form polymeric micelles with the hydrophobic core and hydrophilic corona in aqueous solution, which were characterized by light scattering and static fluorescence measurement.

Keywords : polyglutamate, PEO, NCA, rod-coil, polymer micelle, light scattering.

Introduction

Polyglutamate is well known liquid crystalline polymeric material with potential applications in the fields of photonics and electronics.[1] Since PBLG, poly(benzyl α, L-glutamate), which is the first liquid crystalline polymer,[2] many different glutamate polymers have been synthesized and characterized in various states.[3] Especially, side chain polyglutamates were introduced to reduce the melting temperature of the hardly soluble rodlike polymer and to increase the solubility in common solvents. Recently, the composite materials of rodlike polyglutamate and silica particles were reported.[4] These composite materials have liquid crystalline behaviors due to the mesogenic characters of the polyglutamates.[4] One of the challenging ideas is to make copolymers that could make polymeric micelles having water soluble behavior and liquid crystalline characters. We prepared a copolymer consisted of hydrophilic polyethylene oxide, random coil in solution, and hydrophobic polyglutamate, rodlike block. The amphiphilic molecules form polymer micelles in aqueous solution, and the micelles could be used as a spherical liquid crystalline particle. The copolymers were successfully synthesized, and the micelles formed in the solution were observed by dynamic light scattering and static fluorescence measurements.

Experimental

Materials. All solvents were dried over 4 molecular sieves prior to use. Polymeric (PEO) amine initiators were obtained from Shearwater Polymers, Inc. Their molecular weights were 5,000 and 10,000 having 99% purity. Triphosgene and other chemicals were used as received from Aldrich. All polymerization flasks were flame-dried prior to use, and moisture was excluded during the polmerization with calcium chloride drying tubes.

Synthesis. The synthesis of PALG-PEO consists of three steps as in Scheme I: 1) esterification of L-glutamic acid, 2) synthesis of γ-alkyl L-gultamate N-carboxyanhydride, and 3) polymerization of NCA monomer.

Followings are the procedures for the syntheses of PSLG-PEOs.

Synthesis of γ-stearyl L-gultamate-N-carboxyanhydride (SLG-NCA): The γ-esters of glutamic acid with alkyl alcohols were prepared by direct esterification under acidic condition.[5] A typical procedure for the synthesis of the NCA of stearyl L-glutamate is as follows. A 100 mL double-jacketed flask equipped with a reflux condenser was charged with stearyl L-glutamate (1.0 g, 2.5 mmol) and dry THF (40 mL). The suspension was stirred and heated to 45 °C. A solution of triphosgene (0.30 g, 1.0 mmol) in 10 mL of THF was added dropwise, and the mixture was stirred under dry nitrogen. When the mixture was completely clear, it was concentrated to about the half of the original volume. Hexane (60 mL) was added and the mixture was placed in the refrigerator overnight to allow complete precipitation. The crude NCA was recovered by suction filtration and dried under vacuum at room temperature. Recrystallization from THF/hexane was performed twice.

Polymerization of SLG-NCA Monomer: Typical poly-

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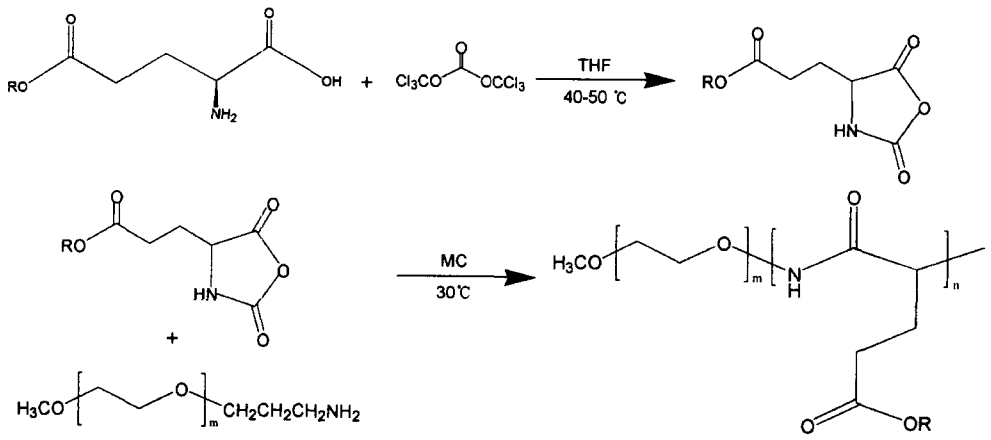

Scheme I. Scheme of the preparation of PALG-PEO copolymer.

merization procedure is as follows. A 50 mL double-jacketed flask equipped with a drying tube was charged with γ-stearyl L-glutamate-NCA (0.98 g, 2.303 mmol) and PEO-NH_2 (0.30 g, Mw. 10,000: M/I ratio = 76). Methylene chloride (30 mL) was added under nitrogen. The reaction was maintained at 30 °C for 3 days. Diethyl ether (100 mL) was added to the solution, and the precipitate was filtered, and dried in a vacuum oven at room temperature. Purification from methylene chloride/diethyl ether was performed twice. Copolymers with different side chains (methyl: PMLG, hexyl: PHLG) and different PEO ratio (Mw 5,000) were also prepared using the same method.

Instruments. Fluorescence spectra were measured by an ISS PCI photon counting spectro-fluorometer between 350 and 450 nm. Pyrene was used as a probe at 6×10^{-7} M and excited at 334 nm. The pyrene in the fluorescence studies was purchased from Aldrich and purified by the process in the reference.[6] The peak position is not affected by the solvent, but the intensity of the peak is influenced by the solvent polarity. Details of the interpretation are elsewhere.[7]

Dynamic light scattering measurements were performed using a UNIPHASE He-Ne laser operating at 632.8 nm. The maximum operating power of the laser was 30 mW. The detector optics employed optical fibers coupled to an ALV/SO-SIPD/DUAL detection unit which employed an EMI PM-28B power supply and ALV/PM-PD preamplifier/discriminator. The signal analyzer was an ALV-5000/E/WIN multiple tau digital correlator with 288 exponentially spaced channels. Its minimum real sampling time is 10^{-6} s and the maximum of about 100 s. A lens with a focal length of 200 mm narrowed the incident beam to reduce the thermal lensing effect and to increase the coherence area. The scattered beam passed through two pin holes (diameter 400 and 400 μm, respectively) before reaching the PMT. A scattering cell (10 mm diameter cylindrical) was placed in a temperature controlled bath of index matching liquid, toluene. All of the experiments were performed at 23 ± 0.1 °C.

Results and Discussion

Melting points of SLG and SLG-NCA were 168-182 °C and 77-78 °C, respectively. PSLG-PEO has melting endotherm at 58 °C. The data from NMR and FT-IR are as follows.

γ-Stearyl L-gultamate (SLG): Mp: 168-178 °C, % yield: typically 25-30%, IR: 1730 (ester), 1590 (COOH), 2830 (aliphatic CH_2) cm^{-1}.

γ-Stearyl L-gultamate-N-carboxyanhydride (SLG-NCA). ^1H NMR ($CDCl_3$): δ 0.87 (t, terminal CH_3), 1.25 (s, CH_2 groups in the stearyl chain), 2.19 (m, β-CH_2), 2.55 (t, γ-CH_2), 4.09 (t, CH_2 in the side chain adjacent to γ-ester), 4.39 (t, α-CH), 6.75 (brs, NH), Mp: 77-78 °C, % yield: typically 85-90%, IR: 2980 (aliphatic CH_2), 1800, 1835 (anhydride carbonyls) cm^{-1}.

PSLG-PEO. ^1H NMR ($CDCl_3$): δ 0.87 (t, terminal CH_3), 1.25 (s, CH_2 groups in the stearyl chain), 2.19 (m, β-CH_2), 2.55 (t, γ-CH_2), 3.74 (m, CH_2CH_2O-). ^{13}C NMR ($CDCl_3$): δ 14.19 (terminal CH_3), 25.92 (β-CH_2), 28.72 (γ-CH_2), 29.77 (CH_2 groups in the stearyl chain), 70.44 (CH_2CH_2O-). T_m: 58 °C, IR: 2980 (aliphatic CH_2), 1100 (PEO backbone) cm^{-1}.

Several different molecular weights, range of 9,000-17,000 with polydispersity of 1.03-1.20, were successfully synthesized. PMLG-PEO, poly(methyl α, L-glutamate-*co*-ethylene oxide), and PHLG, poly(hexyl α, L-glutamate-*co*-

Table I. Molecular Weights of Synthesized PALG-PEOs

	PEO Mw	Mn	Mw	PDI
PSLG	5,000	9,200	10,000	1.08
	10,000	16,600	17,100	1.03
PHLG	5,000	9,000	10,100	1.11
PMLG	10,000	13,700	16,400	1.20

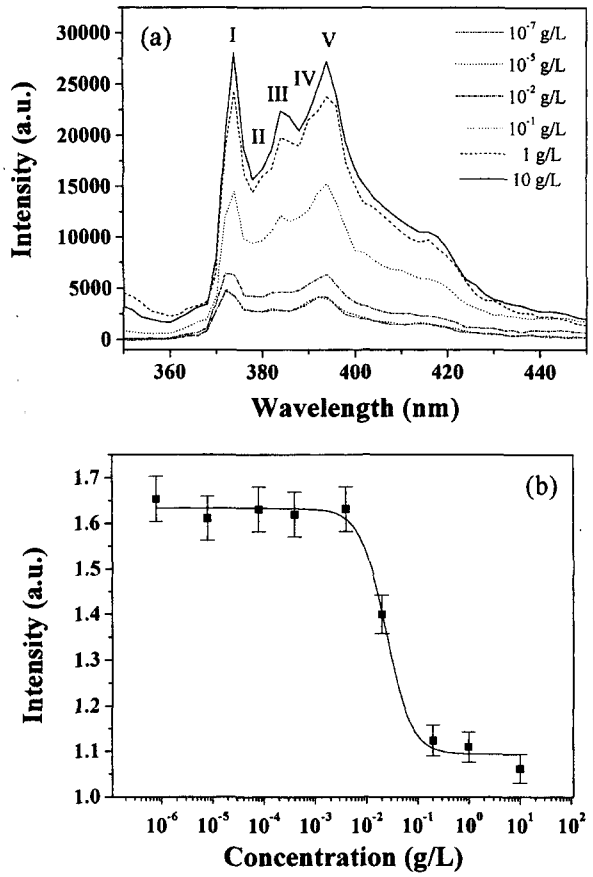

Figure 1. (a) Static fluorescence spectra of mixed solutions of PSLG-PEO (Mw = 17,000, PDI = 1.03)/pyrene/H_2O and (b) I/III ratio dependence on concentration.

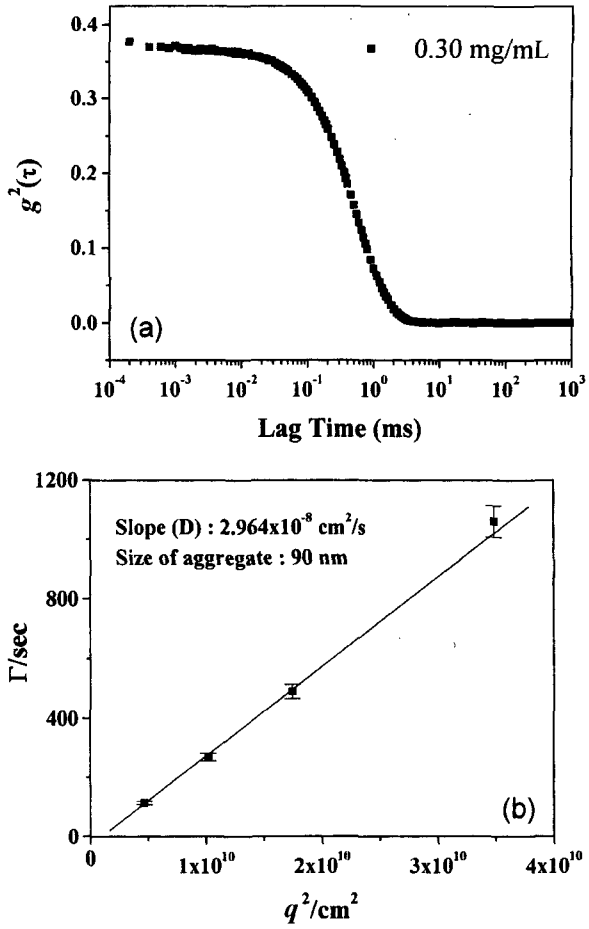

Figure 2. (a) Autocorrelation function of 0.30 mg/mL PSLG-PEO, Mw = 17,000 (PDI = 1.03), in aqueous solution and (b) Γ vs. q^2 plot, Γ: decay rate, q: scattering vector.

ethylene oxide), were prepared as the same method and their characteristics are similar to the PSLG-PEO. Table I shows the molecular weights of PSLG-PEO, PHLG-PEO, and PMLG-PEO, which were measured by the gel permeation chromatography.

Figure 1 shows the fluorescence emission spectra of PSLG-PEO(Mw = 17,000)/pyrene/H_2O system, which exhibit five peaks denoted I-V. The positions of the peaks I-V are 372, 378, 383, 388, and 393 nm, respectively. Polarity sensitive dye like pyrene provides information about the hydrophobicity of the dye environment in the micelle. It is known that: 1) the intensity of peak I (at 372 nm) is weak in nonpolar solvent and strong in polar solvent, 2) the I/III ratio is 1.8-1.9 in water and reaches 0.6 in nonpolar solvent.[8] Pyrene is mainly hydrophobic probe and its solubility in water is very low (2-3 μM). In the presence of micelles, pyrene is preferentially diffuse into the hydrophobic domain of the micelles. Typical I/III value for aqueous micelle system is 1.1-1.2, which means that the pyrene is located in the surface region of the micelle hydrocarbon core. The intensity of the peak changes by adding PSLG-PEO in the pyrene solution as in Figure 1(a) at various concentrations. The I/III ratio of PSLG-PEO fluorescence spectra was measured as a function of polymer concentration. Generally, the critical aggregation concentration (cac) is located on the inflection point of the I/III curve and its inflection point is near 0.10 mg/mL. The I/III ratio decreases and reaches the flat region where the hydrophobic domains are relatively small in the solution, Figure 1(b).

Figure 2(a) shows the autocorrelation function of 0.3 mg/mL PSLG-PEO solution from dynamic light scattering. The intensity-intensity correlation function is $g^{(2)}(\tau) = B(1 + f \mid g^{(1)}(\tau) \mid ^2)$, here τ is the lag time, B is the baseline and f is an instrumental parameter depending mostly on number of coherence area detected. The normalized first order correlation function is given by a single exponential, $g^{(1)}(\tau) = \exp(-\Gamma\tau)$, where Γ is the decay constant related with the translational diffusion coefficient (D_t) and wave vector (q): $\Gamma = D_t q^2$. The wave vector depends on the scattering angle (θ) and refractive index (n) and incident wavelength (λ_o): $q = 4\pi n \sin(\theta/2)/\lambda_o$. Figure 2(b) shows the angular dependence of decay constant and the diffusion constant deduced from the

slop of the Γ vs. q^2 plot. The radius of the PSLG-PEO micelle was determined by Stokes-Einstein equation, $D_t = kT/6\pi\eta R$ and the radius was 90 nm, where k is the Boltzmann constant and η is the viscosity of the solvent. Here, we try to introduce the synthesis scheme of the copolymer and report the observed data for the formation of the micelle in solution. Side chain effects with PSLG-, PHLG-, and PMLG-PEOs are under investigating.

Conclusions

Rod-coil amphiphilic block copolymers were successfully synthesized by the NCA polymerization. The block copolymers are particularly suited for the formation of polymer micelle, since the hydrophilic polyethylene block and hydrophobic polyglutamate. There are potential applications of the copolymers in the field of drug delivery or liquid crystalline systems. The size of the micelles was 90 nm, which was determined by the light scattering and characterized by the fluorescence spectroscopy.

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