Schizophrenic Micelles from a Poly(Acrylic Acid)-*Block*-Poly(*N,N*-Diethylacrylamide) Copolymer

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INTRODUCTION

The interests in water soluble materials whose properties can be triggered by applying an external stimulus or a combination of stimuli have increased over the past decades. The behavior in aqueous solutions of such 'smart' compounds can be tuned by the pH, the ionic strength, the temperature, or the electric field. Among them, the thermo- or pH-responsive copolymers are of importance because their applications cover a wide range of domains related to the environment, biochemistry, and medicine.[1-3] Such polymers are generally constituted of a monomer exhibiting a lower critical solution temperature (LCST), and/or hydrophilic neutral or ionic (or ionizable) monomers.

The term 'schizophrenic' denotes the ability of such AB block copolymers to form either A-core or inverse B-core micelles by varying the pH, and/or the temperature. This remarkable property was introduced by Armes and coworkers for 'smart' pH-dependent micelles of poly[2-(diethylamino) ethyl methacrylate]-block-poly[2-(*N*-morpholino)ethyl meth-acrylate].[4] In a parallel approach, systems characterized by two critical temperatures can be synthesized. Block copolymers micelles based on 3-[*N*-(3-methacrylamido-propyl)-*N,N*-dimethyl]ammonio-propane sulfona-te and *N*-isopropylacrylamide as well as on 2-(*N*-morpholino)ethyl methacrylate and sulfobetainized 2-(dimethylamino)ethyl methacrylate were described by Laschewsky et al.[5] and Armes et al.,[6] respectively.

By combining both effects, namely the sensitivity to the pH and the temperature, it is possible to obtain double stimuli-responsive materials whose macroscopic properties can be controlled at the microscopic level by modifying the structure and composition of the polymeric chains, as well as the two external stimuli. To the best of our knowledge, only a few examples of 'real' pH- and temperature-responsive systems have been reported so far. They are based on poly(propylene oxide)-*block*-PDEAEMA,[7] poly(*tert*-butyl acrylate-co-acrylic acid)-*block*-poly(*N*-isopropylacrylamide),[8] and poly[oligo(ethylene glycol) methacrylate]-*block*-poly{[(diethylamino)ethyl methacrylate]-*co*-(methacrylic acid)}.[9]

In this contribution, we present some preliminary results on the temperature-induced and pH-induced formations of PDEAAm-core and PAA-core micellar aggregates, respectively, from a bishydrophilic poly(acrylic acid)-*block*-poly(*N,N*-diethylacrylamide) copolymer.

EXPERIMENTAL SECTION

Materials. Poly(acrylic acid)$_{45}$-*block*-poly(*N,N*-diethylacrylamide)$_{360}$ [(AA)$_{45}$-*b*-(DEAAm)$_{360}$] was prepared via sequential anionic polymerization of *tert*-butyl acrylate and DEAAm in tetrahydrofurane using the synthetic strategy reported elsewhere.[10,11]

Light Scattering. Static and Dynamic Light Scattering (SLS, DLS) measurements were carried out on an ALV DLS/SLS-SP 5022F compact goniometer system with an ALV 5000/E correlator equipped with a He/Ne laser (λ = 632.8 nm) and an avalanche diode. Data processing was performed using the ALV/Static and Dynamic FIT and PLOT 4.23 software. Prior to SLS, the refractive index increment, dn/dc, was measured using a PSS DnDc-2010/620 differential refractometer.

Small-Angle Neutron Scattering (SANS). SANS experiments were performed at the Institute Max von Laue-Paul Langevin (ILL, Grenoble, France) using the beamline D11. The incident neutron beam wavelength was 6 Å and sample-to-detector distances of 1.1, 4, and 16 m were employed. A total range of the magnitude of the scattering vector, q = 0.003–0.45 Å^{-1} was covered.

Cryogenic Transmission Electron Microscopy (cryo-TEM). The samples were thermostated at the targeted temperature (T = 45 C), put on an holey carbon filmed copper grid, and instantly vitrified by rapid immersion into liquid ethane and cooled to approximately 90K by liquid nitrogen in a temperature-controlled freezing unit. The specimens were transferred to a Zeiss 922 OMEGA EFTEM (Zeiss NTS GmbH, Oberkochen, Germany) operated at an acceleration voltage of 200 kV. Examinations were carried out at temperatures around 90K.

RESULTS AND DISCUSSION

In a previous contribution, we reported that the (AA)$_{45}$-*block*-(DEAAm)$_{360}$ undergoes a coil-to-globule transition at T_c = 35 C. Preliminary highlights on the structural parameters of the PDEAAm-core micelles and their pendant 'inverse' PAA-core micelles are reported in the following. The complete characterization of the system will be published in a full paper.[12]

Light Scattering. DLS and SLS were performed simultaneously at T = 45 C by varying the copolymer concentration in a NaOH solution (0.1 mol·L^{-1}, pH = 12.8) in the presence of NaCl (0.1 mol·L^{-1}). The samples were prepared after dialysis for 7 days. This method was reported to give satisfactory results with no anomalous angle dependence and a good constancy in repeated scans of the same sample.[13] The apparent radius of gyration, R_g, the apparent molecular weight, M_w, can be extrapolated from the Zimm plot (Figure 1): R_g = 22.7 nm, M_w = 3.42·10^7 g·mol^{-1}, corresponding to an aggregation number, N_{agg}, of 61. Additionally, the hydrodynamic radius, R_h, can be calculated by extrapolating the apparent translational diffusion coefficient, D, to zero concentration: R_h = 24.6 nm. The ratio $F = R_g/R_h$, is a characteristic parameter, which depends on the polydispersity and morphology of the micellar aggregates formed (spheres, vesicles, rods).[14] Here a ratio F = 0.92 can be calculated which is close to the theoretical value for spherical micelles with a dense core (F = 0.775), suggesting the spherical shape of the PDEAAm-core micelles.
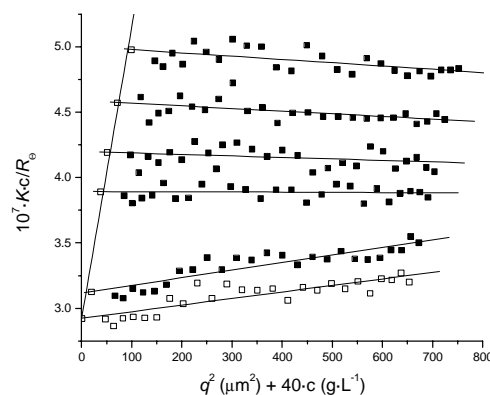

Figure 1. Zimm plot of (AA)$_{45}$-*b*-(DEAAm)$_{360}$ micelles in dialyzed solution of NaCl (0.1 mol·L^{-1}) and NaOH at 45 °C (pH = 12.8, concentration range 0.48-2.46 g·L^{-1}). The extrapolated data at c → 0 and q^2 → 0 are shown on the figure as open squares (□).

DLS was performed at room temperature and pH < 4. The CONTIN plot shows two populations. The hydrodynamic radius of the PAA-core micellar aggregates (lower R_h) can be calculated by extrapolation of the apparent translational coefficient to zero angle: Rh = 47 nm. They coexist with larger entities attributed to loose aggregates or 'super-micelles'.
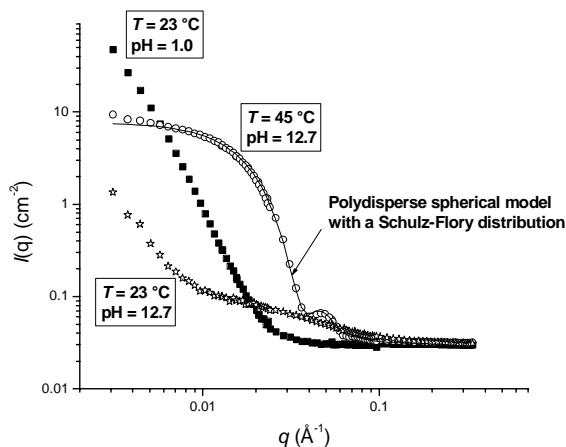
Figure 2. SANS scattering profiles of the (AA)$_{45}$-b-(DEAAm)$_{360}$ in deuterated water (c = 1.4-1.5 g·L^{-1}, [NaCl] = 0.1 mol·L^{-1}).

SANS. Molecularly dissolved block copolymers (unimers) are present in the solution at room temperature for pH ≥ 7. The SANS scattering intensity of the acidic solution at T = 23 °C increases by a factor 20 in comparison to that observed for unimers (Figure 2). A Guinier procedure [ln I(q) vs. q^2] leads therefore to higher $M_{w,app,core}$ and $R_{g,app}$ (Table 1). These entities are constituted of ca. 68 unimers (N_{agg}). These entities correspond to the star-like PAA-core micelles observed by DLS under the same conditions (R_h ≈ 47 nm). The non-dependence of the star-like micelles structural parameters on the ionic strength confirms that the core is constituted of PAA chains surrounded by pH-independent PDEAAm corona.

At T = 45 °C, the curve exhibits the typical shape of spherical aggregates. The scattered intensity at low q is about ten times higher than that at room temperature, suggesting the formation of entities larger than the unimers. By applying the Guinier procedure, it is possible to extrapolate a radius of gyration and an overall molecular weight (Table 1). In addition to the Guinier procedure, one can apply here a polydisperse spherical model and calculate the core radius, R_c. The experimental data are perfectly fitted by the curve as it is shown in Figure 2. The corona thickness can be calculated from the relation $\delta_c = R_g - R_c$. Since the Guinier approximation tends to underestimate the R_g values, true R_g were calculated from the R_h determined by DLS in D$_2$O, assuming a spherical shape. A corona thickness of 5.3 nm was determined. Furthermore, by varying the ionization degree of the PAA segment and the ionic strength of the solution at $T > T_c$, it is possible to tune the corona thickness in the range $2 < \delta_c < 10$ nm. It also confirms the spherical PDEAAm-core/PAA-corona structure of the micellar assemblies observed by heating the solution of unimers above T_c.

Table 1. Structural Parameters of the Micellar Aggregates^a

Micellar Aggregates	Temp (C)/ pH	R_h^b nm	R_g^c nm	$M_{w,app}^c$ (N_{agg}^d)	R_c^e nm
PDEAAm-core	45 / 12.7	24	10.7	3.8·10^6 (73)	11.5
PAA-core	23/ 1.0	47	12.6	2.7·10^5 (68)	-

^{a} [NaCl] = 0.1 mol·L^{-1}. ^{b} DLS in H$_2$O. ^{c} Guinier procedure. ^{d} N_{agg} = $M_{w,micelles}$/$M_{w,unimers}$. ^{e} Polydisperse spherical model.

Cryo-TEM. Cryo-TEM was performed in alkaline solution (pH = 12.6) at T = 45 C to confirm the spherical structure of the PDEAAm-core micelles above the cloud point of the PDEAAm block, T_c ≈ 35 °C (Figure 3). Relatively narrow distributed spherical micellar aggregates with a number-averaged radius of 24 nm are observed. It corroborates SLS/DLS measurements and SANS investigations. The low contrast difference or the low thickness of the corona does not allow the accurate observation of the core/corona structure. The visualization of the inverse PAA-core micelles will be presented in a full paper.[12]
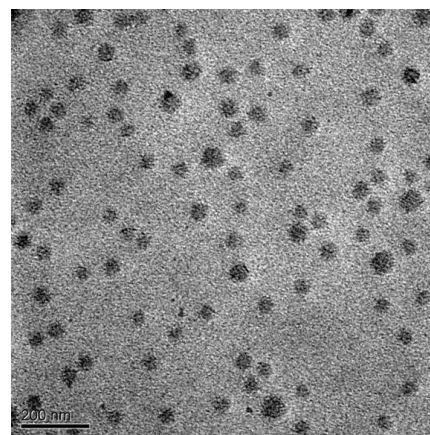

Figure 3. Cryo-TEM image of the (AA)$_{45}$-b-(DEAAm)$_{360}$ micelles vitrified from an aqueous solution at T = 45 °C showing individual PDEAAm-core micelles (c = 4.9 g·L^{-1}, pH = 12.6).

CONCLUSIONS

Scattering methods (SANS, SLS, DLS) were successfully used in combination to cryo-TEM visualization to examine the schizophrenic behavior in aqueous solution of the asymmetric poly(acrylic acid)$_{45}$-$block$-poly(N,N-diethylacrylamide)$_{360}$ copolymer. Direct spherical PDEAAm-core micelles as well as their pendant PAA-core micelles can be formed by heating the alkaline solution or by adding concentrated HCl, respectively.

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