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Self-assembly of block copolymer complexes in organic solvents

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Abstract

Micelles have been prepared by mixing poly(styrene)-*block*-poly(4-vinylpyridine) (PS-*b*-P4VP) copolymers and poly(acrylic acid) (PAA) homopolymers in organic solvents. Complexation via hydrogen bonding occurs between the P4VP and PAA blocks. Further aggregation of the accordingly formed complexes results in micelles stabilized by a corona of PS blocks. The influence of the relative lengths of the different blocks and of the quality of the solvent towards the complexes on the micellar characteristic features is studied. Soluble, non-aggregating, complexes have been observed in DMF, provided that the complexes are sufficiently small. In all other cases, the complexes were insoluble and aggregated in micelles. The size of those micelles depends strongly on the length of the P4VP blocks but only weakly on the PAA length.

Keywords: Block copolymers; Micelles; Hydrogen-bonded complexes

1. Introduction

Micellization of amphiphilic diblock copolymers in block selective solvents is well documented in scientific literature [1–3]. It gives rise to micelles where the insoluble blocks form a core which is surrounded by a corona containing the soluble blocks. The driving force for micellization is the aggregation of the insoluble blocks which is generally accompanied by an important gain in entropy resulting from the release of solvent molecules. Another method to trigger micellization consists in introducing additional non-covalent interactions such as electrostatic interactions or hydrogen bonding in an initially soluble block copolymer. The non-covalent complexes resulting from these interactions should be insoluble in order to induce micellization. Such insoluble complexes can be generated by mixing, in a non-selective solvent for all the individual blocks, two block copolymers or a block copolymer and a homopolymer, in such a way as to induce non-covalent interactions between the given blocks of the two partners [4]. This mixing process therefore may lead to insoluble non-covalent complexes, that further aggregate into micellar cores stabilized by the uncomplexed blocks.

Such a strategy has been successfully implemented in both aqueous and non-aqueous solvents, although water-based systems have been more widely investigated. For example, Eisenberg et al. have studied complexes formed between poly(ethylene oxide)-*block*-poly(sodium methylacrylate) copolymers and quaternized poly(4-vinylpyridine) homopolymers [5]. A similar strategy was considered in complexes formed by poly(ethylene oxide)-*block*-poly(2-vinylpyridine) copolymers and poly(sodium styrenesulfonate) at low pH, thus the poly(2-vinylpyridine) block was protonated [6]. Kataoka and Harada have studied micelles obtained by complexing two mutually interacting diblock copolymers, namely poly(ethylene oxide)-*block*-poly(L-lysine) and poly(ethylene oxide)-*block*-poly(aspartic acid) block copolymers [7,8]. Polyelectrolyte complexes were observed between poly(2-vinylpyridine)-*block*-poly(ethylene oxide) and poly(methacrylic acid)-*block*-poly(ethylene oxide) in a limited range of pH where the blocks poly(methacrylic acid) and poly(2-vinylpyridine) were ionized and thus carrying opposite charges [9]. Cationic double hydrophilic copolymers containing poly(lysine) [10–13], poly(ethylene imine) [14] or poly(*N*,*N*-dimethylaminoethyl acrylate) [15]

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blocks combined with poly(ethylene oxide) were used to form micelles by complexation with oligonucleotides. All these examples based on aqueous systems rely on electrostatic interactions between the mutually interacting blocks to create water-insoluble complexes that further aggregate into well-defined micellar aggregates.

The use of hydrogen-bond interactions to trigger complexation and further aggregation has been implemented in organic solvents. In this case, complexation should only occur between the mutually interacting blocks and competitive hydrogen bonding with solvent molecules has to be avoided. Such an approach has been illustrated by Liu and coworkers on micelles formed by mixing a poly(styrene)-*block*-poly(methyl methacrylate) copolymer and a poly(styrene-*co*-[*p*-(2,2,2-trifluoro-1-hydroxy-1-trifluoromethyl)ethyl-methylstyrene]) random copolymer in toluene [16].

Beside the formation of core–corona spherical micelles, more complex structures such as vesicles or micelles with heterogeneous corona have been reported for mixtures of interacting block copolymers. For example, Schlaad and coworkers have studied the vesicles formed by complexing poly(styrene)-*block*-poly(cesium methacrylate) and poly(butadiene)-*block*-poly(4-vinylpyridinium iodide) copolymers in THF [17]. Gao et al. have formed vesicles by mixing poly(ethylene oxide)-*block*-polybutadiene and poly(acrylic acid) in a solvent mixture of THF and *n*-dodecane, hydrogen bonds between PEO and PAA being created when *n*-dodecane is added to the initial THF solution [18]. Formation of micelles with segregated coronal chains was also recently studied in hydrogen-bonded complexes formed between a poly(styrene)-*block*-poly(2-vinylpyridine)-*block*-poly(ethylene oxide) triblock copolymer and a copolymer composed of a poly(acrylic acid) central block and two poly(ethylene oxide) comb-like outer blocks [19].

Herein, we report on a systematic study of mixtures of poly(styrene)-*block*-poly(4-vinylpyridine) (PS-*b*-P4VP) copolymers and poly(acrylic acid) (PAA) homopolymers where strong hydrogen bonds are formed between the P4VP and PAA blocks. Whenever these P4VP/PAA complexes are insoluble, they associate to form micellar cores stabilized by the uncomplexed PS blocks. In most previous studies on mixtures of interacting copolymers, only one couple of copolymers or copolymer/homopolymer was studied and the ratio between the interacting blocks was varied. Therefore, for this study, we have chosen to work at the stoichiometric ratio and to vary the length of the interacting blocks as well as the solvents used in order to understand the influence of these parameters on the complexation process and on the size of the formed micelles.

2. Experimental section

2.1. Materials

The polymers were purchased from Polymer Source Inc. Three polystyrene-*block*-poly(4-vinylpyridine) copolymers with the acronyms PS-*b*-P4VP (34,000–3000), PS-*b*-P4VP (10,000–19,000) and PS-*b*-P4VP (20,000–19,000) (where the numbers in parenthesis represent the number-average molecular weight, M_n, of each block) were used. Their polydispersity index is 1.1, 1.2 and 1.1, respectively. Three poly(acrylic acid) homopolymers with M_n of 5000, 10,000 and 20,000 g/mol and polydispersity index of 1.1 in each case were also used. Solvents were of analytical grade.

2.2. Preparation of the micelles

Micelles have been prepared by mixing known amounts of PS-*b*-P4VP copolymers with PAA homopolymers. The amount of each polymer and the volume of solvent have been adjusted in order to obtain a concentration of 10 g/L after mixing. Moreover, an acrylic acid/4-vinylpyridine 1/1 mol/mol stoichiometry was used for all samples. The micellar solutions were obtained by first dissolving one copolymer into the appropriate solvent, followed by the addition of the second copolymer as a powder. The solutions were stirred for 15 min before measurements. Identical micelles were obtained whether PS-*b*-P4VP is first dissolved and PAA is added as a powder, or the reverse.

2.3. Dynamic light scattering measurements

The hydrodynamic radius, R_h, of the micellar complexes were measured by dynamic light scattering (DLS). The experimental autocorrelation function, $g(t)$, is commonly expressed in the form of cumulant expansion:

$$g(t) = \exp\left[-\Gamma_1 t + \left(\frac{\Gamma_2}{2!}\right)t^2 - \left(\frac{\Gamma_3}{3!}\right)t^3 + \cdots \right] \quad (1)$$

where Γ_i is the ith cumulant and $\Gamma_1 = Dq^2$, where D is the translation diffusion coefficient and q is the absolute value of the scattering vector.

The diffusion coefficient is related to the hydrodynamic radius R_h by Stokes–Einstein equation:

$$R_h = \frac{k_B T}{6\pi\eta D} \quad (2)$$

where k_B is the Boltzmann constant and η is the viscosity of the solvent.

DLS measurements were performed on a Malvern CGS-3 apparatus equipped with a He–Ne laser with a wavelength, λ, of 632.8 nm. The temperature was set to 25 °C and the angle of measurement was 90°. The polydispersity index (PDI) of the micelles was estimated from the Γ_2/Γ_1^2 ratio in which Γ_1 and Γ_2 represent the first and second cumulants, respectively.

The experimental data have also been analyzed by the CONTIN method which is based on an inverse-Laplace transformation of the data and gives access to a size distribution histogram for the analyzed micellar solutions.

All the micellar solutions have been diluted 10 times to obtain a concentration of 1 g/L and filtered before DLS measurements.

2.4. Nuclear magnetic resonance

^{1}H NMR spectra were recorded on a 500 MHz AVANCE (B) Bruker spectrometer.

2.5. Transmission electron microscopy

Transmission electron microscopy (TEM) was performed on a Leo 922 microscope, operating at 200 kV accelerating voltage in bright field mode. Samples for TEM measurements were prepared by two different methods. The first one, which is used for samples in THF, consists in spin-coating the different solutions at a concentration of 0.05 g/L on a carbon-coated grid. This method cannot be used for samples in DMF because isolated micelles could not be observed. For these samples, a drop of solution was deposited on a carbon-coated grid for a few minutes, followed by dipping the grid in pure THF to remove non-adsorbed materials, and finally by drying of the grid in vacuum. Two staining agents have been used: RuO_4 which contrasts both P4VP and PS blocks, and iodine which contrasts only the P4VP block. The staining time was 1 h for RuO_4 and 1.5 h for iodine.

3. Results and discussion

The different mixtures of PS-*b*-P4VP copolymers and PAA homopolymers have been studied by ^{1}H NMR. This technique is a valuable tool to gain information about the micellar structure [20,21]. Indeed, the signals assigned to solvated coronal chains should be clearly seen in the NMR spectrum, while the ones corresponding to the totally desolvated, solid-like, chains forming the core of the micelle should vanish. As mentioned in the introduction, the core of the resulting micelles should be formed by the P4VP/PAA complexes. If the complexes form a compact core without any swelling by the solvent, the mobility of the P4VP and PAA chains would be reduced and no signal would be detected. On the opposite, P4VP signals should be detected in the case of soluble, i.e., non-aggregating, complexes or micelles with a swelled core. The signals of PAA cannot be distinguished from those of the PS and P4VP blocks and therefore will not be discussed. In THF, the signal of the pyridine unit was not detected whatever the mixture, evidencing the formation of micelles with a desolvated, solid-like core (data not shown). In DMF, the signal of the pyridine unit was not detected for the mixtures based on the PS-*b*-P4VP copolymers with a large (19,000 g/mol) P4VP block. On the other hand, for the mixtures of the PS-*b*-P4VP (34,000–3000) copolymer and the different PAA homopolymers, the pyridine signals were detected, indicating that the P4VP chains have still some mobility (Fig. 1). The objects formed in this case could thus either be unimers, non-aggregating (soluble) complexes, or micelles with a swollen core. The possible occurrence of non-aggregating complexes merits to be more deeply investigated (see further) since only insoluble aggregating complexes have been observed in other previous reports when a stoichiometric ratio between the complexing blocks was used [4–9].

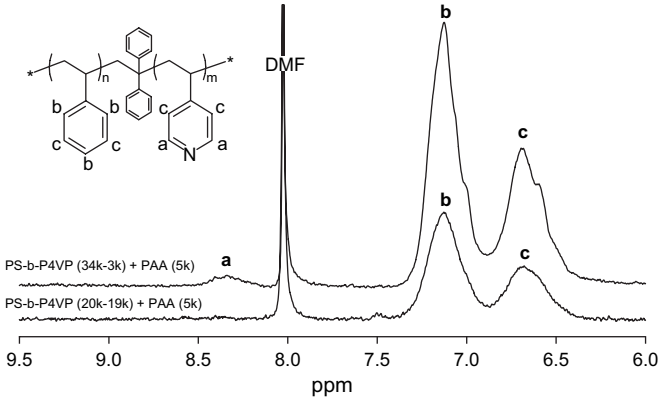

Fig. 1. ^{1}H NMR spectra of two mixtures between PS-*b*-P4VP copolymers and PAA homopolymer in DMF-d_7.

The micellar solutions resulting from the complexation of PS-*b*-P4VP copolymers and PAA homopolymers in THF and DMF have been measured in a DLS experiment at 25 °C. The results obtained for each system by the cumulant method are summarized in Table 1. The results shown in Table 1 have been extrapolated to zero concentration. For most of the complexes, no influence of the concentration on the measured sizes has been observed. The only exception concerns the micelles formed by mixing PS-*b*-P4VP (10,000–19,000) and the different PAAs in THF, where a decrease of the micellar size with dilution was observed. This shows that DLS measurements should be carefully performed and that the effect of dilution on R_h has to be systematically investigated. Results obtained on one micellar system could sometimes not be translated to another, although very similar, one. The investigated solutions have been checked after several months and the same results have been obtained. This shows the stability of all the solutions.

Firstly, focus will be made on mixtures showing pyridine signals in the ^{1}H NMR experiments, and hence hinting at some mobility of the P4VP/PAA complexes. These are obtained in DMF from PS-*b*-P4VP (34,000–3000) and the different PAA homopolymers. Since the R_h associated to these objects are too small to correspond to micelles (see other results in Table 1), it is useful to approximate the radius of gyration in unperturbed conditions (R_{G0}) of the PS-*b*-P4VP copolymer and compare it with the R_h obtained by DLS. For the PS-*b*-P4VP

Table 1
Hydrodynamic radius (R_h) and polydispersity index (PDI) of micelles formed by mixing different PS-*b*-P4VP and PAA in THF or DMF

	THF (1 mg/mL)		DMF (1 mg/mL)	
	R_h (nm)	PDI	R_h (nm)	PDI
PS-*b*-P4VP (34,000–3000) + PAA (5000)	23	0.09	4.5	0.14
PS-*b*-P4VP (34,000–3000) + PAA (10,000)	27	0.05	4.5	0.16
PS-*b*-P4VP (34,000–3000) + PAA (20,000)	28	0.04	6.5	0.15
PS-*b*-P4VP (10,000–19,000) + PAA (5000)	55	0.10	25	0.08
PS-*b*-P4VP (10,000–19,000) + PAA (10,000)	56	0.12	27	0.16
PS-*b*-P4VP (10,000–19,000) + PAA (20,000)	60	0.15	33	0.24
PS-*b*-P4VP (20,000–19,000) + PAA (5000)	51	0.06	24	0.11
PS-*b*-P4VP (20,000–19,000) + PAA (10,000)	54	0.08	25	0.22
PS-*b*-P4VP (20,000–19,000) + PAA (20,000)	51	0.08	31	0.26

(34,000−3000) copolymer, the following result has been obtained [22]:

$$R_{G0}^2 = \frac{b^2 N}{6} \times \frac{1-\cos\theta}{1+\cos\theta} \times \frac{1-\langle\cos\varphi\rangle}{1-\langle\cos\varphi\rangle} = 13,924 \text{ nm}^2;$$
$$R_{G0} = 3.73 \text{ nm} \quad (3)$$

where b represents the C−C bond length (0.154 nm), N the total number of monomer units in a copolymer chain (355), θ the angle of valence between each atom of the chain (109.4°) and φ the rotation angle of the chain bonds. The last term of the equation corresponds to the square of the so-called steric parameter σ. The σ value associated to polystyrene (2.23) has been used [22]. The calculated R_{G0} is in good agreement with the R_h of 4.0 nm measured for PS-*b*-P4VP (34,000−3000) without PAA. For the mixtures, slightly larger R_h is observed and they increase with the PAA length to reach 6.5 nm for PAA (20,000). This larger size could be attributed to the formation of non-aggregating complexes between PS-*b*-P4VP (34,000−3000) and the different PAAs. In the following, the non-aggregating complexes will be referred to as "soluble" complexes. The formation of soluble complexes in DMF can be explained by the quality of the solvent which is good enough to solubilize the relatively small P4VP (3000)/PAA complexes. This last parameter seems to be crucial since complexes containing longer P4VP blocks (19,000) do form insoluble complexes that aggregate into micelles (Table 1). Since it is well known that the solubility of a polymer in a solvent depends on its molecular weight, the solubility limit for the P4VP/PAA 1/1 mol/mol complexes in DMF has been crossed for P4VP block with a molecular weight around 19,000 g/mol.

Secondly, the micelle-forming PS-*b*-P4VP/PAA complexes have been examined in more detail. For a given set of polymers, larger micelles have been obtained in THF than in DMF. This effect is thought to be again related to the quality of the solvent towards core-forming blocks. As discussed before, we have experimentally demonstrated that DMF is a better solvent of the complexes, which results in a smaller aggregation number in DMF. The CONTIN size distribution histograms for the micelles resulting from the complexation in THF and in DMF of the different PS-*b*-P4VP copolymers with PAA (5000) are shown in Figs. 2 and 3, respectively. These results show that only micelles are formed in solution, without secondary aggregation. Moreover, the R_h associated to the maximum of the population in the CONTIN histograms is similar to the R_h determined by the cumulant analysis, in agreement with the formation of well-defined monodispersed objects. This is confirmed generally by the very low values of PDI calculated from the cumulant analysis (Table 1). The angular dependence of the DLS signal has also been checked. No dependence was noted, in agreement with the formation of spherical particles.

The effects of the length of the PAA and of the P4VP blocks on the micellar characteristic features have been examined. In both solvents, a clear dependence of the P4VP length on the size of the micelles is observed (Table 1). On the other hand, the effect of the length of the PAA block is less clear. An

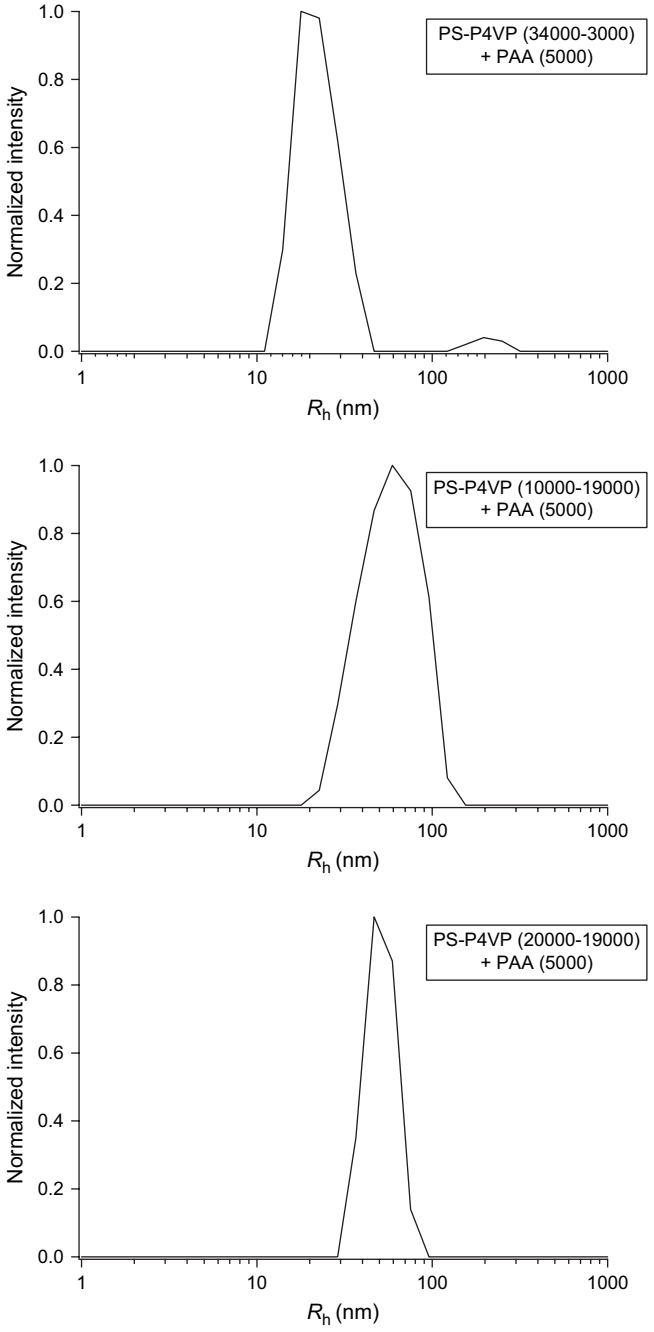

Fig. 2. CONTIN size distribution histograms (unweighted results) obtained for the different PS-*b*-P4VP copolymers complexed with PAA (5000) in THF.

increase in the size of the micelles with the length of PAA seems to be observed but is much less pronounced than for an increase of the P4VP length. This lesser influence could be explained by the fact that the block which is linked to the PS is the P4VP and not the PAA. Thus there are much more constrains on the PS-*b*-P4VP copolymer than on the PAA homopolymer that only has to fit into the core.

Morphological information about the micellar structure of the investigated complexes can be obtained by microscopic techniques such as TEM. TEM can be used to determine the total radius (R_t) and the core radius (R_c) by using selective staining

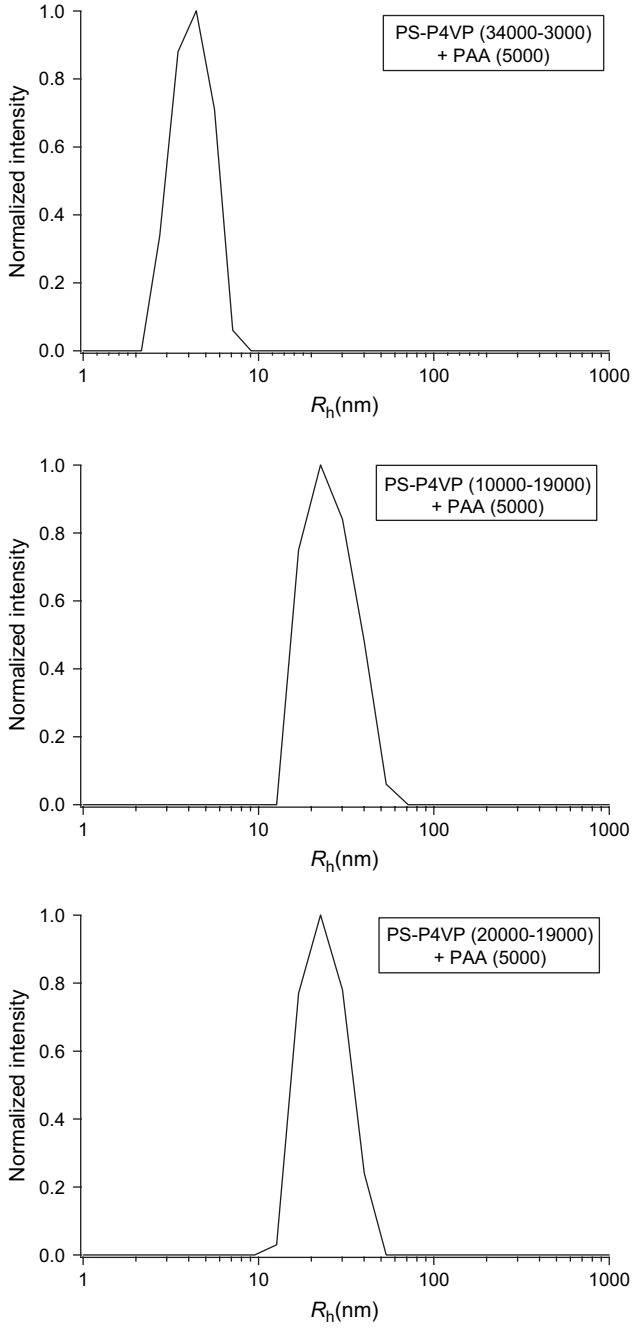

Fig. 3. CONTIN size distribution histograms (unweighted results) obtained for the different PS-*b*-P4VP copolymers complexed with PAA (5000) in DMF.

agents. For the micelles studied here, the core is formed by P4VP and PAA blocks and the corona consists of PS blocks. By using RuO_4, which is a staining agent for both PS and P4VP blocks, R_t can be obtained. On the other hand, the use of iodine vapours, which contrast only the P4VP block, allows to obtain R_c. Of course the R_t obtained by TEM cannot be directly compared to the radius obtained by DLS because TEM measurements are performed in dry state and the corona of the micelles is therefore collapsed. R_c and R_t measured by TEM using the selective staining methods are listed in Table 2.

Typical TEM images of micelles formed by mixing PS-*b*-P4VP (20,000−19,000) or PS-*b*-P4VP (34,000−3000) and PAA (20,000) are shown in Figs. 4 and 5. R_t increases slightly when the P4VP length increases, confirming the DLS results. The increase is less pronounced than the one observed in DLS

Table 2
TEM results obtained on micelles formed by mixing different PS-*b*-P4VP and PAA in THF or DMF

	THF		DMF
	R_t (RuO_4)	R_c (I_2)	R_c (I_2)
PS-*b*-P4VP (34,000−3000) + PAA (5000)	/	8	/
PS-*b*-P4VP (34,000−3000) + PAA (20,000)	17	8	/
PS-*b*-P4VP (10,000−19,000) + PAA (5000)	19	17	14
PS-*b*-P4VP (10,000−19,000) + PAA (20,000)	24	17	13
PS-*b*-P4VP (20,000−19,000) + PAA (5000)	24	17	13
PS-*b*-P4VP (20,000−19,000) + PAA (20,000)	23	16	13

R_t (nm) represents the total radius of the dried micelles, R_c (nm) stands for the core radius of the micelles (the staining agent used in each case is indicated in parenthesis). R_t in DMF could not be measured due to an aggregation of the micelles occurring during the preparation of the sample.

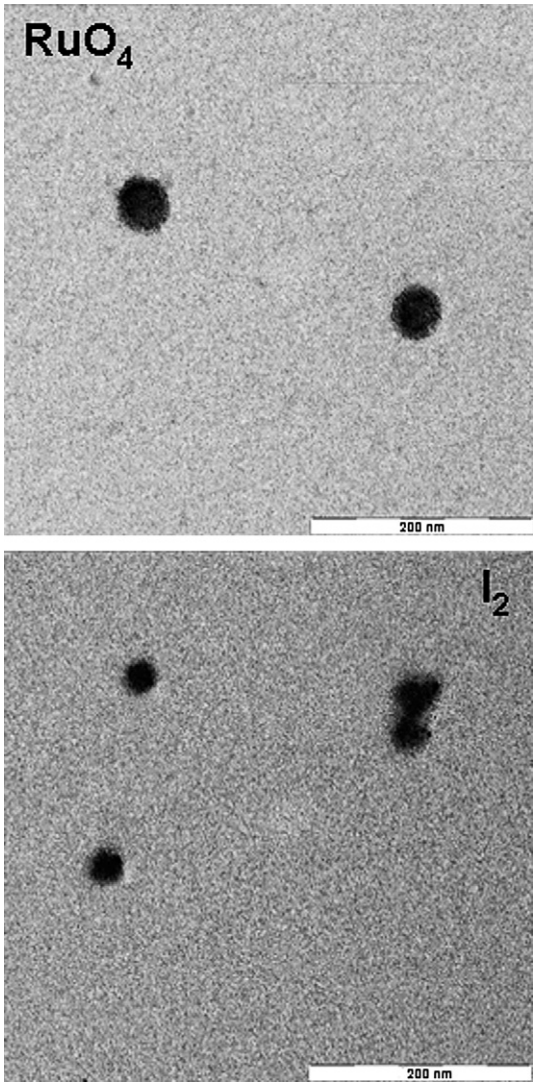

Fig. 4. TEM images of micelles formed by mixing PS-*b*-P4VP (20,000−19,000) and PAA (20,000) in THF. On top panel, the total micellar radius (R_t) obtained by RuO_4 staining and on the right, the core radius (R_c) obtained by staining with iodine vapour.

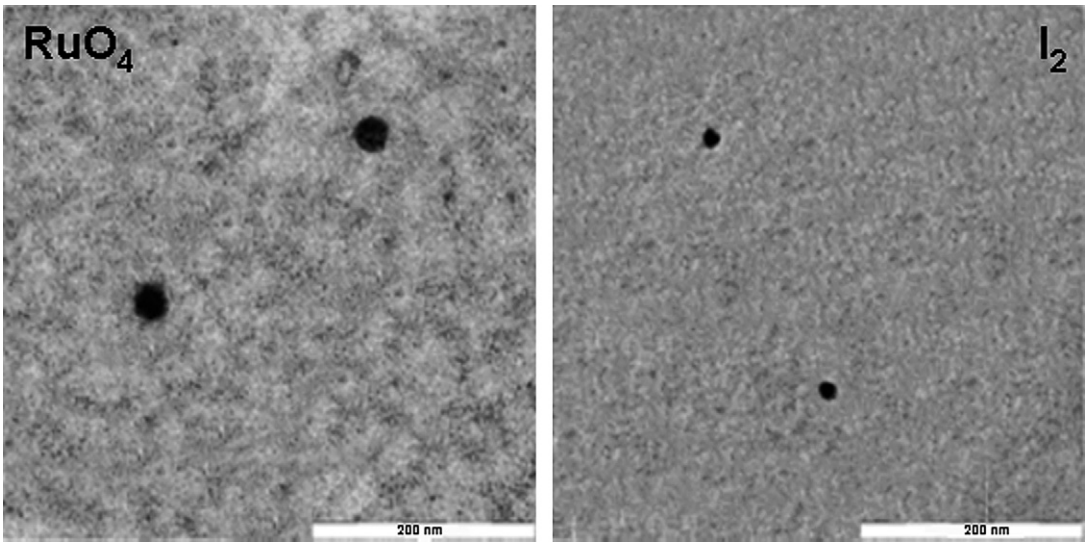

Fig. 5. TEM images of micelles formed by mixing PS-*b*-P4VP (34,000–3000) and PAA (20,000) in THF. On the left, the total micellar radius (R_t) obtained by RuO_4 staining and on the right, the core radius (R_c) obtained by staining with iodine vapour.

but this is probably due to the collapse of the coronal chains on the micellar core during sample preparation. On the other hand, R_c clearly increases with the P4VP length. No dependence of R_t and R_c on the length of the PAA block was found from the TEM results, but the expected difference is probably too small (see DLS results) to be detectable by TEM considering the artifacts inherent to staining procedures.

4. Conclusions

Stable micelles have been obtained when PS-*b*-P4VP copolymers and PAA homopolymers are mixed in organic solvents. Strong hydrogen bonding between the P4VP and PAA blocks induces the formation of complexes which further aggregate into a micellar core surrounded by PS chains. Since most reports on non-covalent complexes between block copolymers and homopolymers focus on the influence of the stoichiometry of the complexes on the micellar characteristic features, we have decided to vary other parameters, i.e., the lengths of the different blocks and the quality of the solvent towards the complexes. In this respect, the influence of the length of the different blocks has been studied in THF and DMF. In DMF, which is a better solvent for the complexes, soluble complexes have been observed when the interacting blocks are sufficiently small. In all other cases, micelles whose size depends mainly on the length of the P4VP blocks, and in a lesser way on the length of the PAA block, have been obtained.

Acknowledgments

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References

[1] Zhang W, Shi L, An Y, Gao L, Wu K, Ma R. Macromolecules 2004; 37:2551.
[2] Shen H, Zhang L, Eisenberg A. J Am Chem Soc 1999;121:2728.
[3] Liu L, Gao X, Cong Y, Li B, Han Y. Macromol Rapid Commun 2006; 27:260.
[4] (a) Jiang M, Li M, Xiang M, Zhou H. Adv Polym Sci 1999;146:121; (b) Chen D, Jiang M. Acc Chem Res 2005;38:494.
[5] Kabanov AV, Bronich TK, Kabanov VA, Yu K, Eisenberg A. Macromolecules 1996;29:6797.
[6] Gohy JF, Varshney SK, Antoun S, Jérôme R. Macromolecules 2000;33: 9298.
[7] Harada A, Kataoka K. J Controlled Release 2001;72:85.
[8] Harada A, Kataoka K. Science 1999;283:65.
[9] Gohy JF, Varshney SK, Jérôme R. Macromolecules 2001;34:3361.
[10] De Smedt SC, Demeester J, Hennink WE. Pharm Res 2000;17:113.
[11] Wolfert MA, Schacht EH, Toncheva V, Ulbrich K, Nazarova O, Seymour LW. Hum Gene Ther 1996;7:2123.
[12] Katayose S, Kataoka K. Bioconjugate Chem 1997;8:702.
[13] Harada A, Kataoka K. Macromolecules 1995;28:5294.
[14] Kataoka K, Harada A, Wakebayashi D, Nagasaki Y. Macromolecules 1999;32:6892.
[15] Nagasaki Y, Wakebayashi D, Akiyama Y, Harada A, Kataoka K. Polym Prepr (Am Chem Soc Div Polym Chem) 2000;41:1649.
[16] Liu S, Zhu H, Zhao H, Jiang M, Wu C. Langmuir 2000;16:3712.
[17] Schrage S, Sigel R, Schlaad H. Macromolecules 2003;36:1417.
[18] Gao WP, Bai Y, Chen EQ, Li ZC, Han BY, Yang WT, et al. Macromolecules 2006;39:4894.
[19] Gohy JF, Khousakhoun E, Willet N, Varshney SK, Jérôme R. Macromol Rapid Commun 2004;25:1536.
[20] Yao X, Chen D, Jiang M. J Phys Chem B 2004;108:5225.
[21] Chen D, Peng HS, Jiang M. Macromolecules 2003;36:2576.
[22] Cowie JMG. Polymers: chemistry and physics of modern materials. 2nd ed. London: Blackie Academic and Professional; 1991.