Study of the Influence of the Metal−Ligand Complex on the Size of Aqueous Metallo-Supramolecular Micelles

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ABSTRACT: A library of metallo-supramolecular block copolymers has been synthesized, and the micellization behavior of those copolymers in water has been studied. A series of amphiphilic block copolymers composed of poly(styrene) and poly(ethylene oxide) joined by a bis(terpyridine)ruthenium complex were prepared. The micelles formed from these copolymers were characterized by AFM and TEM. The results evidence that the classical scaling laws relating the micelle size to the size of the hydrophobic block are not valid for metallo-supramolecular copolymers. This different behavior is due to electrostatic repulsions between the charged and bulky metal−ligand complexes present at the core−corona interface. If those repulsions are screened by increasing the ionic strength during micelle formation, the classical behavior is observed.

Introduction

Aqueous block copolymer micelles have been the subject of intense research for more than 30 years.[1] Most of the interest arises from the capability of these systems to confine a hydrophobic nanodomain of precise size and shape in an aqueous environment. These nano-objects consist of a core formed by insoluble hydrophobic blocks, surrounded by a corona formed by water-soluble blocks. Depending on the chemical nature and block composition of the initial amphiphilic copolymer, a wide variety of micellar morphologies have been observed.[2] In a recent set of papers, the synthesis and characterization of a new type of amphiphilic block copolymers, namely metallo-supramolecular amphiphilic block copolymers, have been described. These compounds are formed by a hydrophilic poly(ethylene oxide)[3−6] or poly(*N*-isopropylacrylamide)[7] A block linked to a hydrophobic B block such as poly(styrene) or poly(ethylene-*co*-butylene) through a bis(2,2′:6′,2″-terpyridine)ruthenium(II) complex. The terpyridine ligand can easily be introduced at the chain end of different polymers, thus giving rise to many possible combinations of different blocks.[7,8] Since the method for preparing block copolymers relies on the coupling of two polymer chains via a simple two-step synthesis using principles from coordination chemistry around a ruthenium metal ion, it is straightforward to prepare a library of block copolymers.[9] Compared to "classical" covalent block copolymers, metallo-supramolecular block copolymers offer many advantages. Besides the formation via self-organization processes, the reversibility of the supramolecular bond allows the construction of "smart materials" with tunable properties.[10] Moreover, the electrochemical and photochemical properties of the complexes can be engineered by choosing the appropriate metal ion and counterion.[11]

For micelles prepared from classical covalent copolymers, the micellar characteristic features (size and shape) are mainly controlled by three independent parameters: the stretching of the core-forming chains, the interfacial tension between the micellar core and the solvent, and the repulsions among chains in the corona.[12] In the case of micelles prepared from metallo-supramolecular copolymers the presence of the charged and bulky complex (around 1 nm^3)[13] at the interface between the two immiscible blocks is expected to also play an important role, strongly affecting the self-assembly and hence the micellar characteristic features.

The purpose of this paper is thus to study in detail the role of the charged metal complexes on the supramolecular organization of the metallo-supramolecular copolymers. We have investigated the formation of micelles in water from copolymers with poly(styrene) (PS) as the hydrophobic block and poly(ethylene oxide) (PEO) as the hydrophilic block. Micelles from this kind of supramolecular copolymers have already been studied, but only one composition was considered.[4,14−16] In this paper, we took advantage of the library approach and investigated micelles prepared from different PS−[Ru]−PEO (where −[Ru]− is the bis(terpyridine)ruthenium(II) complex), varying the relative length of both blocks. The micelles thus formed have been characterized by atomic force microscopy (AFM) and transmission electron microscopy (TEM).

Experimental Section

Chemicals were received from Aldrich, Fluka, Polymersource, and Shearwater and used without further purification unless otherwise stated. DMA (*N*,*N*-dimethylacetamide) was dried over molecular sieves. All metal-containing polymers (mono- and bis-complexes) were measured on a GPC system using *N*,*N*-dimethylformamide (DMF) with 5 mM NH_4PF_6 as eluent. The terpyridine-functionalized polystyrenes showed unreliable retention times in this eluent and were measured on a GPC system with $CHCl_3$ having 4% Et_3N and 2% 2-propanol by volume as eluent and calibrated with PS standards. Column chromatography was carried out on Merck silica gel 60. ^{1}H NMR spectra were recorded on a 400 MHz Varian Mercury spectrometer. For the metal-containing block copolymer at least 200 scans were recorded, and the T1 relaxation time was set to 10 s. Chemical shifts are given in ppm downfield from TMS.

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Preparation of Terpyridine End-Functionalized Poly(styrene). PS with small degree of polymerization (DP), i.e., 20 and 70, were synthesized as previously reported by anionic polymerization, end-capped with one unit of ethylene oxide and functionalized by grafting a chloroterpyridine to the OH end group.[17] PS with large DP (over 100) were prepared by nitroxide-mediated radical polymerization using a terpyridine-functionalized initiator.[8] The detailed synthesis of the poly(styrenes) with a DP of 200 and 240 was already described elsewhere.[9] We provide here the details for the PS300 and PS135. Styrene was subjected to an AlOx-filtration column before use in order to remove the inhibitor. Three freeze−pump−thaw cycles were applied to remove the oxygen before the reaction vessels were immersed in an oil bath at 125 °C. The conversion was measured gravimetrically. For DP = 300, 2.0 g of styrene and 0.026 g of initiator were reacted for 325 min, upon which 80% conversion was reached, while for DP = 135, 2.0 g of styrene and 0.055 g of initiator were reacted for 325 min, and 75% monomer conversion was reached. The crude polymer was precipitated twice from CH_2Cl_2 into methanol and dried for 24 h in a vacuum oven at 50 °C. Selected analytical data (PS300): ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): $\delta = 8.68$ (m, broad, 2H, $H_{6:6''}$), 8.62 (m, broad, 2H, $H_{3:3''}$), 8.21 (m, broad, 2H, H_{3}':5′), 7.93 (m, broad, 2H, $H_{4:4''}$), 7.47−6.32 (m, broad, 1650H, H_{aromatic}, $H_{5,5''}$), 5.34 (m, broad, 2H, tpyOCH_2), 4.27−4.07 (broad, 1H, *H*C−O−N), 3.50−3.15 (broad, 1H, O−N−C*H*), 2.45−0.53 ppm (m, broad, 1100H, $H_{\text{aliphatic}}$). GPC (RI) data for PS300: M_n (PDI): 29 500 g mol^{-1} (1.06). GPC (RI) data for PS135: M_n (PDI): 14 200 g mol^{-1} (1.07).

Preparation of Terpyridine End-Functionalized Poly(ethylene oxide). Terpyridine-functionalized PEOs were synthesized as published elsewhere by grafting a chloroterpyridine to the OH end group of commercial PEOs.[18]

General Procedure for the Preparation of $RuCl_3$−Mono-terpyridine Complexes. The detailed procedure can be found in ref 8. In brief, an excess of $RuCl_3$ with respect to the terpyridine end-functionalized PEO was heated in dry degassed DMA to 130 °C. A solution of the corresponding PEO in dry degassed DMA was then added dropwise. Stirring was continued overnight at 130 °C, and the solution was allowed to cool to room temperature. The resulting mixture was partitioned between water and CH_2Cl_2. The organic layer was separated, dried over Na_2SO_4, filtered, and evaporated in vacuo. The brown residue was dissolved in THF and precipitated twice in ice-cold diethyl ether.

General Procedure for the Synthesis of PS_m−[Ru]−PEO_n Block Copolymers. The detailed procedure can be found in ref 9. In brief, terpyridine-functionalized polystyrene and the $RuCl_3$ mono-complex of terpyridine functional poly(ethylene oxide) were reacted in a 1.1:1 molar ratio in a 4:1 solvent mixture of chloroform and methanol at reflux under argon. After 30 min a catalytic amount of *N*-ethylmorpholine was added. Stirring was continued overnight, after which a 10-fold excess of NH_4PF_6 was added. The solution was then allowed to cool to room temperature and poured into water. The water layer was extracted twice with chloroform, and the combined organic layers were dried over Na_2SO_4, filtered, and evaporated in vacuo. The crude product was purified by a combination of preparative size exclusion chromatography on BioBeads SX-1 swollen in THF and/or CH_2Cl_2 and column chromatography (SiO_2, THF to wash down uncomplexed material, followed by 10% MeOH in THF to separate the mono-, if any, from the bis-complex, which was isolated by addition of NH_4PF_6 to the eluent).

Micelle Preparation. The copolymers were dissolved in DMF at a concentration of 1 g/L. A volume of water equal to half the DMF volume was then added by steps of 50 μL to induce aggregation of the insoluble polystyrene block, followed by the addition of an equal volume of water in one shot to "freeze" the micelles. Subsequently, the DMF/water solution was dialyzed against water for 24 h, replacing the water at least three times (Spectra-Por dialysis bags, cutoff 6000−8000 Da). The final concentration of the copolymer in pure water was set to 0.3 g/L.

Micelle Characterization. Atomic force microscopy (AFM) images were obtained using a Digital Instruments Nanoscope IV scanning force microscope in tapping mode using NCL type cantilevers (Si, 48 N/m, 190 kHz, Nanosensors). The samples were prepared by spin-coating a dilute solution of micelles on a silicon wafer.

Transmission electron miscrocopy (TEM) was performed on a LEO 922 microscope, operating at 200 kV accelerating voltage in bright field mode. The images were formed by unscattered electrons only. Samples for TEM experiments were prepared by spin-coating a drop of the solution of micelles on a carbon-coated TEM grid. The samples were stained with RuO_4.

Results and Discussion

A series of amphiphilic metallo-supramolecular block copolymers have been prepared by combining PS and PEO blocks of different lengths. Six PS with a DP between 20 and 300 and four PEO with a DP between 70 and 375 have been used. With those 10 blocks, 13 different block copolymers have been assembled, following the strategy depicted in Scheme 1. Their composition is shown in Table 1. The majority of the investigated samples were not readily soluble in water. Therefore, the preparation method previously introduced by Eisenberg et al. for "crew-cut" micelles, involving the prior dissolution of the copolymer in a nonselective solvent followed by the slow addition of water (see Experimental Section for more details), was applied.[2] The aim of this paper is to elucidate the influence of the charged and bulky bis(terpyridine)ruthenium complex on the size of the micelles. We tried to characterize the micelles in solution by dynamic light scattering (DLS), but the results could not be exploited due to aggregation. It has indeed been shown that micelles prepared from metallo-supramolecular block copolymers show a strong tendency to aggregation.[14,16] In all the investigated samples the DLS results show two peaks: a first one around a hydrodynamic radius value of 40 nm and a very broad one whose position changes according to the sample but centered above 100 nm. The second peak corresponds to large aggregates, and the first one does not correspond to isolated micelles but rather to a mixture of micelles and small aggregates.[16] We have therefore concentrated our efforts in characterizing the core of the micelles, using AFM and TEM imaging. Since the bis(terpyridine)ruthenium complex is located at the interface between the two blocks, its influence is expected to be the strongest on the size of the micellar core. For AFM measurements, the micelles have been deposited on a silicon wafer, and their height was measured in order to avoid tip convolution effects. Since the imaging was done in the dry state, the flexible PEO corona chains are expected to be oriented flat on the surface, and therefore the height of the micelles essentially corresponds to the size of the core (see Figure 1). For TEM imaging, a selective RuO_4 staining of the PS allowed the visualization of the micellar core. All the studied copolymers formed spherical micelles. Figure 2 presents typical TEM and AFM pictures recorded on the PS_{200}−[Ru]−PEO_{375} copolymer. We can see clearly on both images isolated micelles but also small clusters, evidencing once again their strong tendency to aggregate. The core sizes measured by AFM and TEM for the different copolymers are summarized in Table 1. Both techniques are in good agreement and give similar results even if the sizes determined by TEM are systematically a bit larger. We can see immediately that the micellar cores are split into two populations, one around 10 nm for the small PS (DP of 20 and 70) and one around 20 nm for the PS with a DP of 200 and above. For classical hairy micelles the size of the core should scale as the 3/5th power of the degree of polymerization of the insoluble block.[19] For micelles prepared from metallo-supramolecular copolymers this law is clearly not valid since there is a

Scheme 1. Synthetic Strategy for the Preparation of PS−[Ru]−PEO Metallo-Supramolecular Copolymers

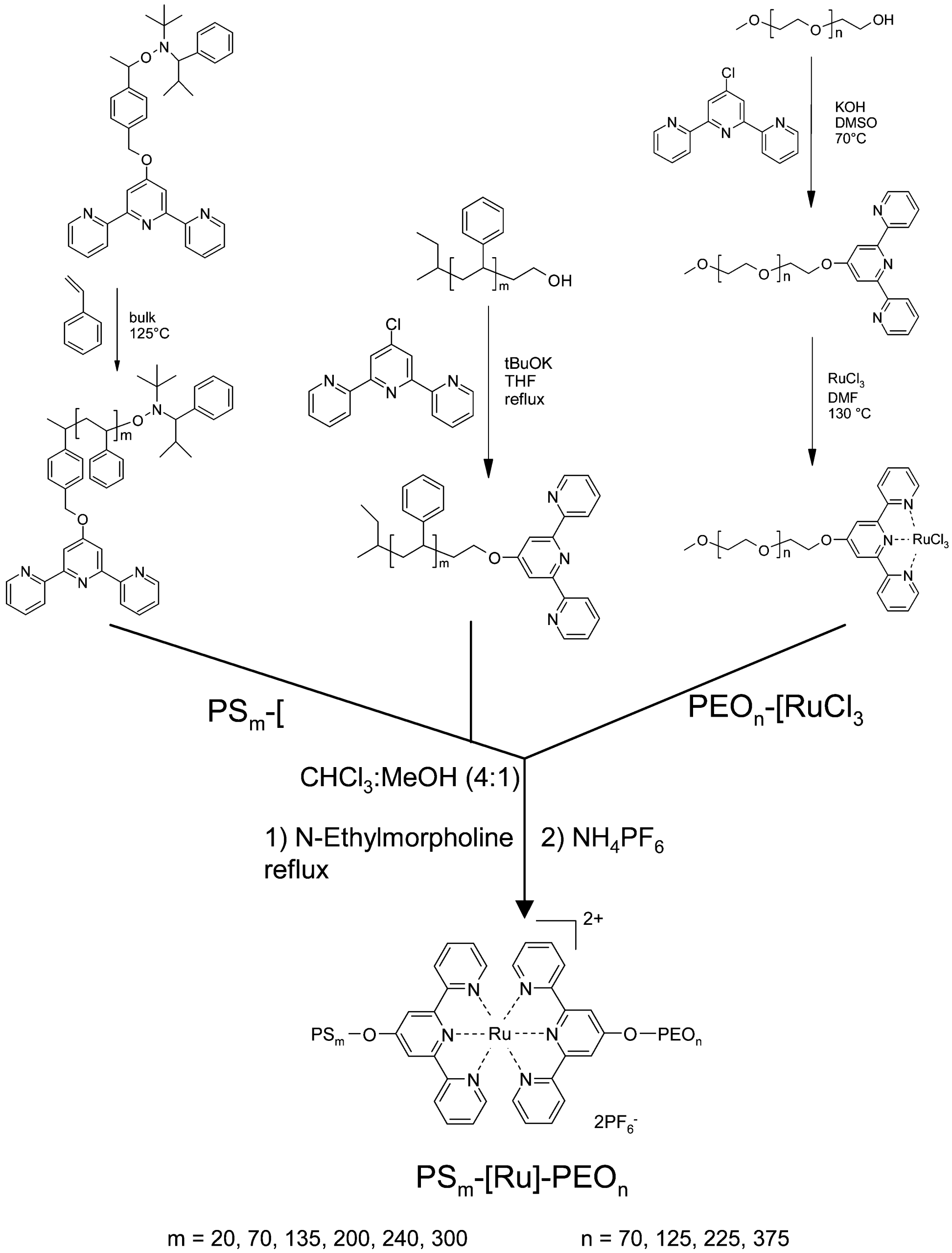

Table 1. Diameter of the Micellar Core As Determined by AFM and TEM

	D_c (nm) AFM	D_c (nm) TEM
PS_{20}−[Ru]−PEO_{70}	10 (2)[a]	13 (3)
PS_{20}−[Ru]−PEO_{125}	8.2 (1)	13 (4)
PS_{70}−[Ru]−PEO_{70}	8.1 (1)	14 (3)
PS_{70}−[Ru]−PEO_{125}	8.7 (1)	15 (4)
PS_{70}−[Ru]−PEO_{225}	9.0 (2)	14 (3)
PS_{70}−[Ru]−PEO_{375}	11 (2)	15 (4)
PS_{135}−[Ru]−PEO_{125}	8.8 (1), 19 (3)	14 (4), 25 (4)
PS_{135}−[Ru]−PEO_{225}	11 (1), 20 (2)	15 (4), 28 (4)
PS_{200}−[Ru]−PEO_{225}	21 (2)	24 (3)
PS_{200}−[Ru]−PEO_{375}	20 (3)	28 (6)
PS_{240}−[Ru]−PEO_{375}	19 (3)	28 (4)
PS_{300}−[Ru]−PEO_{225}	24 (4)	28 (4)
PS_{300}−[Ru]−PEO_{375}	20 (2)	26 (2)

[a] The numbers in parentheses are the standard deviations.

transition between two sizes as the DP gradually increases. This observation evidences that in this case the size of the insoluble block is not the only parameter governing the core size and that additional parameters have to be taken into account. The electrostatic repulsions and steric hindrance between the charged and bulky (around 1 nm^3) bis(terpyridine)ruthenium complexes are most probably responsible for this unusual behavior. Those two factors will exert constraints on the number of chains aggregating together, tending to separate the charged complexes from each other and delimiting a sphere that can accommodate the PS block. When the PS block becomes too large to fit into this sphere, a transition will occur to a sphere large enough for the PS to fit in. To illustrate this point, we have compared the

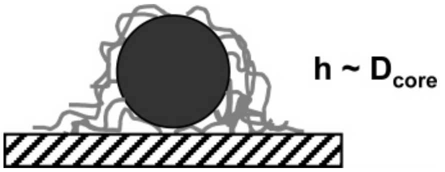

Figure 1. Schematic representation of a micelle as seen by AFM.

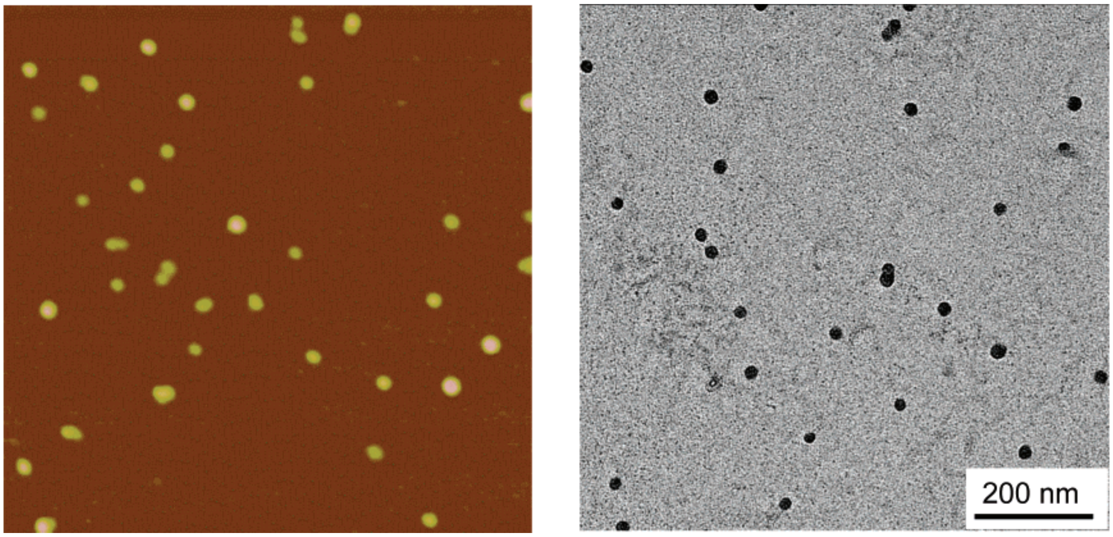

Figure 2. AFM (left) and TEM (right) pictures recorded on micelles prepared from the PS_{200}−[Ru]−PEO_{375} copolymer in water. AFM image is 1 × 1 μm^2.

Table 2. Comparison between the End-to-End Distance of Each PS Blocks and the Average Radius of the Micellar Core Measured by AFM

	av end-to-end distance (nm)	av core radius (nm)
PS20	2.1	4.6
PS70	4.0	4.6
PS135	5.6	5.0, 10
PS200	6.8	10
PS240	7.4	9.5
PS300	8.3	11

end-to-end distance of each PS block, calculated by eq 1,[20] to the average radius of the core measured by AFM.

$$\langle \bar{r}^2 \rangle_0 = nl^2 \frac{1 - \cos\theta}{1 + \cos\theta} \sigma^2 \tag{1}$$

n is the number of monomers, l is the length of a C−C bond (0.154 nm), θ is the valence angle between each chain atom (109°), and σ is the steric parameter and equal to 2.23 for poly(styrene) at room temperature.[20] The results are summarized in Table 2. For micelles prepared from copolymers containing 70 units of styrene the end-to-end distance of the PS chains is very close to the micellar radius. When the DP of the PS further increases to 200, the chains cannot fit anymore in the volume initially delimited by the complexes, and a transition occurs to a larger core size. To better understand those results, we have synthesized two additional copolymers with a PS block having a DP in the transition region between 70 and 200, i.e., PS_{135}−[Ru]−PEO_{125} and PS_{135}−[Ru]−PEO_{225}. The sizes of the micelles formed by these copolymers are reported in Table 1. Surprisingly, both samples show two populations with equal abundance: one around 10 nm as for DP 20 and 70 and one around 20 nm as for DP of 200 and above. The existence of these two populations could be due to a size segregation of the PS chains. An average DP of 135 corresponds to an end-to-end distance of 5.6 nm, which is slightly larger than the radius of the first population (5 nm) but smaller than the radius of the second population (10 nm) (see Table 2). The fraction of the copolymer chains having a smaller PS block could thus aggregate in micelles having a core radius of 5 nm; the rest of the copolymer chains, having a larger PS block, will aggregate to form micelles with a core radius of about 10 nm.

To further prove that the self-assembly of the metallo-supramolecular copolymers is mainly controlled by electrostatic repulsions between the charged complexes, we have prepared micelles following the procedure described above, but using 1 M NaCl, instead of pure water, for the micellization and the dialysis. The sizes measured by AFM and TEM are reported in Table 3. In this case we see clearly that the micelle size varies continuously with the DP of the PS block. It should also be pointed out that only one population is observed for the PS_{135}−[Ru]−PEO_{225} copolymer, instead of two when the micelles are prepared with pure water. In 1 M NaCl, the electrostatic repulsions between the complexes are screened, and the metallo-supramolecular copolymers behave as their covalent counterpart. To evidence the fact that the metallo-supramolecular copolymers indeed behave as their covalent counterparts when the micelles are prepared in the presence of salt, the diameters of the cores,

Table 3. Diameter of the Micellar Core Prepared in 1 M NaCl As Determined by AFM and TEM[a]

	D_c (nm) AFM	D_c (nm) TEM
PS_{20}−[Ru]−PEO_{70}	6.1 (0.5)	10 (2)
PS_{70}−[Ru]−PEO_{255}	12 (1)	14 (2)
PS_{135}−[Ru]−PEO_{225}	17 (1)	18 (3)
PS_{200}−[Ru]−PEO_{225}	21 (1)	23 (2)
PS_{300}−[Ru]−PEO_{375}	25 (1)	27 (2)

[a] The numbers in parentheses are the standard deviations.

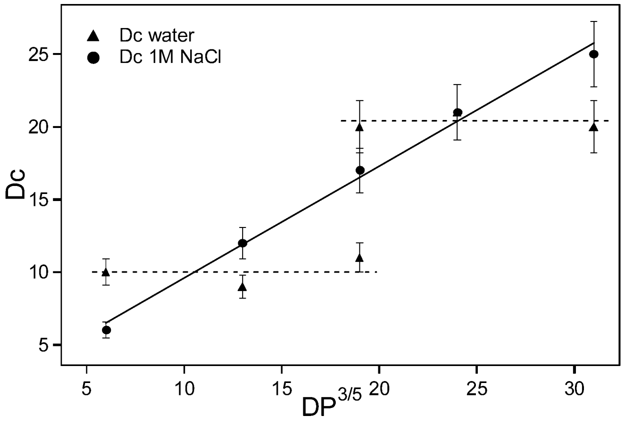

Figure 3. Relationship between the measured (AFM) core size of the micelles and the 3/5th power of the PS block DP, for micelles prepared in pure water (triangles) and in 1 M NaCl (circles). The solid line represents the linear regression obtained from the data in 1 M NaCl. The dashed lines, evidencing the presence of only two sizes, are only a guide for the eyes.

measured by AFM, have been plotted against the 3/5th power of the PS block DP (Figure 3). The core size scales perfectly with $DP^{3/5}$ in a linear way, as predicted by theory.[19] The same conclusions can be drawn from the TEM results (results not shown). For comparison, the evolution obtained for micelles prepared in pure water, where only two sizes were observed, has been added to Figure 3.

Conclusions

We have studied the micellization behavior of a library of PS−[Ru]−PEO metallo-supramolecular copolymers in water. AFM and TEM characterization of the micelles revealed that the core size does not scale linearly with the DP of the PS block as expected from the theory of classical covalent copolymers. Only two core sizes were observed: one around 10 nm for DP of 70 and below and one around 20 nm for DP of 200 and above. For copolymers having a DP in the transition region between 70 and 200, two populations were observed. This unusual behavior is due to electrostatic repulsions between the charged bis(terpyridine)ruthenium complexes present at the junction of the two blocks which strongly affect the self-assembly. This has been demonstrated by preparing micelles in the presence of salt to screen the repulsions. In this case, the metallo-supramolecular copolymers behaved as their covalent counterpart.

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