Synthesis and Aqueous Micellization of Amphiphilic Tetrablock Ter- and Quarterpoly(2-oxazoline)s

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ABSTRACT: The aqueous self-assembly of block copolymer systems is of major interest to prepare well-defined nanosized structures. Recently, the self-assembly of well-defined triblock and tetrablock ter- and quarterpolymers into sophisticated multicompartment micelles was reported. Inspired by these examples, the sequential one-pot synthesis of tetrablock ter- and quarterpolymers via living cationic ring-opening polymerization of 2-oxazolines was investigated under microwave irradiation, leading to well-defined tetrablock ter- and quarterpoly(2-oxazoline)s for the first time. The resulting tetrablock ter- and quarterpolymers were analyzed using both size exclusion chromatography and ^{1}H NMR spectroscopy, revealing their successful preparation. In addition, the surface energy of the polymers was determined to investigate the effect of block order on the surface properties. The last part of the paper discusses the aqueous self-assembly of the tetrablock ter- and quarterpolymers. Atomic force microscopy, transmission electron microscopy, and dynamic light scattering revealed the presence of spherical micellar aggregates.

Introduction

The self-assembly of macromolecules is a very important aspect in living matter, whereby the combination of supramolecular and solvophobic interactions together with molecular functionalities lead to functional objects like enzymes.[1] Inspired by this magnificent control in natural systems, polymer chemists have investigated the self-assembly of amphiphilic diblock copolymers in aqueous media, resulting in a detailed understanding of the formation of block copolymer micelles with various morphologies.[2−4] In recent years, the focus has changed to more complex structures that result from the self-assembly of amphiphilic triblock terpolymers.[5−7] These novel self-assembled structures include toroidal micelles[8] and discrete or wormlike multicompartment micelles[9] that were obtained from linear and miktoarm triblock terpolymers, respectively. The simultaneous segregated storage of two guest molecules in such multicompartment micelles has been reported as well.[10] Besides the synthesis and self-assembly of triblock terpolymers, the synthesis of linear tetrablock quarterpolymers seems to be very promising to build even larger and more complex structures. Simulations predict the formation of complex phase-separated structures in bulk from ABCA[11] terpolymers and ABCD[12] quarterpolymers. It was indeed observed that ABCD tetrablock quarterpolymers phase separate into four-phase triple coaxial cylindrical microdomains[13] or four-phase lamellar structures.[14] In addition, noncentrosymmetric lamellar phases were observed from ABCA[15] terpolymers and ABCD[16] tetrablock quarterpolymers. Brannan and Bates found that the aqueous self-assembly of amphiphilic ABCA tetrablock terpolymers resulted in vesicles that exhibit phase separation inside the vesicle wall.[17] In similar work, Balsara and co-workers demonstrated that adjusting the chain length of the hydrophobic blocks of an amphiphilic ABCA tetrablock terpolymer resulted in the self-assembly of planar platelet structures.[18]

Stimulated by these beautiful examples of tetrablock terpolymer and quarterpolymer self-assembly, we were interested to synthesize and investigate the self-assembly of tetrablock ter- and quarterpolymers that are not (partially) based on vinylic monomers like all previous examples. Moreover, the tetrablock ter- and quarterpolymers should be easily synthesized via a sequential monomer addition method. Recently, we developed a microwave-assisted polymerization[19] procedure for the living cationic ring-opening polymerization of 2-oxazolines that resulted in polymers with narrow molecular weight distributions (polydispersity indices below 1.10) in less than 10 min polymerization time.[20,21] Although the observed acceleration under microwave irradiation could be reproduced using thermally heated pressure reactors,[22] the microwave-assisted procedure yielded slightly better defined polymers due to the more homogeneous heat profile. The improved control over the cationic ring-opening polymerization was recently exploited for the synthesis of libraries of well-defined diblock copoly(2-oxazoline)s[23] and triblock terpoly(2-oxazoline)s.[24] In this contribution, we report the synthesis of amphiphilic tetrablock ter- and quarterpoly(2-oxazoline)s using the sequential monomer addition method. The resulting tetrablock ter- and quarterpolymers were analyzed with regard to their surface energy as well as their aqueous self-assembly to investigate the effect of composition on the polymer properties.

Experimental Section

Materials and Instrumentation. All chemicals, except for acetonitrile (Biosolve LTD), were purchased from Aldrich. 2-Nonyl-2-oxazoline was kindly provided by Henkel. Methyl tosylate and the 2-oxazolines (over barium oxide) were distilled prior to use

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and stored under argon. Acetonitrile was dried over molecular sieves (3 Å).

The polymerizations were performed in capped reaction vials in the single-mode microwave reactor Emrys Liberator (Biotage), equipped with a noninvasive IR sensor (accuracy: ±2%) for the measurement of the reaction temperatures. Prior to use, the vials were heated (105 °C) and cooled to room temperature under an argon atmosphere. Size exclusion chromatography (SEC) was measured on a Waters system with a 1515 pump, a 2414 refractive index detector, and a Waters Styragel HT4 column utilizing a *N*,*N*-dimethylformamide solution (with 5×10^{-3} M NH_4PF_6) with a flow rate of 0.5 mL min^{-1} at 50 °C (PMMA calibration). ^{1}H NMR spectra were recorded on a Varian AM-400 spectrometer or a Varian Gemini 300 spectrometer from polymer solutions in CD_2Cl_2. Chemical shifts are given relative to residual solvent signals.

Contact angle measurements were performed on polymer films prepared by spin-coating of chloroform solutions (20 mg/mL) of the polymers on precleaned microscopy slides at 1000 rpm for 90 s using a WS-400/500 series spin-coater from Laurell Technologies Corp. An automated OCA30 optical contact angle measuring instrument from Dataphysics was used to determine the contact angles of both diiodomethane and ethylene glycol as apolar and polar test liquids, respectively, using the equation-of-state theory to calculate the surface energy (SE).[25]

Dynamic light scattering (DLS) measurements were performed on a Malvern CGS-3 apparatus equipped with a He−Ne laser (632.8 nm). A bath of filtered toluene surrounded the scattering cell, and the temperature was controlled at 25 °C. DLS data were analyzed by the cumulants method, as described elsewhere.[26] The *Z*-average diffusion coefficient over the whole set of aggregates was calculated from the first cumulant, and the PDI of the aggregates was estimated from the Γ_2/Γ_1^2 ratio, where Γ_i is the *i*th cumulant. The diffusion coefficient extrapolated to zero concentration was related to the hydrodynamic diameter (D_h) by the Stokes−Einstein equation.[26]

Atomic force microscopy (AFM) measurements were performed in the tapping mode with a Veeco Nanoscope IV Multimode microscope operated in air. Cantilevers (NCH type, Nanosensors) with a resonance frequency of ~330 kHz and a spring constant of 42 N m^{-1} were used. Samples were prepared by spin-coating diluted micellar solutions onto silicon wafers. The images were analyzed by the software provided by the manufacturer in order to provide averaged dimensions for the micelles.

Transmission electron microscopy (TEM) was performed on a Leo 922 microscope, operating at 200 kV accelerating voltage in bright field mode. Samples were prepared by spin-coating the micelles on a carbon-coated TEM grid. No staining was performed.

Microwave-Assisted Synthesis of the Tetrablock Ter- and Quarterpoly(2-oxazoline)s. A stock solution of 2-methyl-2-oxazoline (1.53 g, 18 mmol) and methyl tosylate (134 mg, 0.72 mmol) was prepared in acetonitrile (2.98 mL), resulting in 4 M monomer concentration and a monomer-to-initiator ratio of 25. This stock solution was divided over eight microwave vials (500 μL each) that were heated for 5.0 min to 140 °C under microwave irradiation, resulting in pMeOx. To seven of these polymer solutions, 2-ethyl-2-oxazoline (200 μL, 1.98 mmol) was added under an inert atmosphere after cooling to below 40 °C, and the polymerizations were performed for 6.3 min at 140 °C under microwave irradiation, resulting in pMeOx-*b*-EtOx. To four of these diblock copolymers, 2-phenyl-2-oxazoline (265 μL, 2.10 mmol) was added under an inert atmosphere, and the polymerizations were continued for 33.3 min at 140 °C under microwave irradiation, resulting in the formation of pMeOx-*b*-EtOx-*b*-PhOx. Three of these triblock terpolymerizations were continued by the addition of 2-methyl-2-oxazoline (170 μL, 2.01 mmol), 2-ethyl-2-oxazoline (200 μL, 1.98 mmol), or 2-nonyl-2-oxazoline (395 μL, 2.00 mmol), which was followed by microwave heating at 140 °C for 5, 6.3, or 6.3 min, respectively. The two remaining vials with pMeOx-*b*-EtOx were reacted with 2-nonyl-2-oxazoline (395 μL, 2.00 mmol) for 6.3 min under microwave irradiation. To one of these vials 2-phenyl-2-oxazoline (265 μL, 2.10 mmol) was added, and the polymerization was continued for 33.3 min. The polymerization mixtures of pMeOx, pMeOx-*b*-EtOx, pMeOx-*b*-EtOx-*b*-PhOx, and pMeOx-*b*-EtOx-*b*-NonOx that were not further chain extended were used to characterize the intermediate polymers. These intermediate polymers and the final tetrablock ter- and quarterpolymers were dried under reduced pressure at 40 °C and used without further purification. All polymers were characterized by SEC and ^{1}H NMR spectroscopy. The monomer composition of all the polymers was calculated from the integrals of the polymer backbone (3.6−2.6 ppm; NCH_2CH_2N) and the side-chain signals (MeOx: 2.3 ppm, br, CH_3; EtOx: 2.1 ppm, br, CH_2 and 1.1 ppm, br, CH_3; PhOx: 7.4−6.8 ppm, br, C_6H_5; NonOx: 0.9 ppm, br, CH_3) in the ^{1}H NMR spectra that were recorded in CD_2Cl_2.

Micellization. The investigated polymers were initially dissolved in acetone, ethanol, *N*,*N*-dimethylformamide (DMF), or acetonitrile at concentrations varying from 0.1 to 5 g/L. 1 mL of deionized water was then added dropwise to 1 mL of these solutions in order to trigger micellization. The nonselective solvent was then gradually eliminated by dialysis against deionized water. Spectra-Por membranes with a molecular weight cutoff of 6000−8000 g/mol were used for the dialysis process. The concentration of the final micelles in pure water was then measured and is about 0.2 g/L. The micellar solutions were passed over 1.2 μm filters before the dynamic light scattering measurements. For AFM sample preparation the solutions were diluted 10 times with pure water.

Results and Discussion

Microwave-Assisted Synthesis and Characterization of the Tetrablock Ter- and Quarterpolymers. The living cationic ring-opening polymerization of 2-oxazolines is a well-established method for the preparation of well-defined (co)-polymers.[27,28] Recent investigations revealed a tremendous acceleration of this polymerization method under microwave irradiation, whereby the control over the polymerization improved as well.[20,21] These improved microwave-assisted polymerization conditions could be applied for the synthesis of well-defined diblock copolymers[23] and even triblock terpoly(2-oxazoline)s.[24] Inspired by these successful triblock terpolymerizations, we have investigated the synthesis of tetrablock ter- and quarterpoly(2-oxazoline)s under microwave irradiation by the sequential monomer addition method. 2-Methyl-2-oxazoline (MeOx; monomer A), 2-ethyl-2-oxazoline (EtOx; monomer B), 2-phenyl-2-oxazoline (PhOx; monomer C), and 2-nonyl-2-oxazoline (NonOx; monomer D) were used for the synthesis of ABCA, ABCB, ABCD, and ABDC tetrablock ter- and quarterpolymers as well as the corresponding A, AB, ABC, and ABD co- and terpolymers. Each block consisted of 25 monomer units, resulting in a total length of 100 monomer units for the tetrablock ter- and quarterpolymers (Figure 1).

The polymerizations were performed using the previously optimized polymerization conditions, namely with acetonitrile as solvent and methyl tosylate as initiator at 140 °C under microwave irradiation. The sequential monomer additions (neat monomer) were performed under an inert atmosphere after cooling the polymerization mixture to below 40 °C. SEC characterization of these (co)polymers revealed monomodal molecular weight distributions with polydispersity indices equal to or below 1.20 for all polymers without NonOx, demonstrating the successful synthesis of well-defined tetrablock terpoly(2-oxazoline)s (Figure 2, left).

The NonOx-containing polymers revealed broader molecular weight distributions with PDI values up to 1.38 (Table 1 and Figure 2, right), demonstrating that it is possible to synthesize these tetrablock quarterpolymers, although some more side reactions (chain transfer and/or chain termination) occurred. At this moment, the exact nature and reason for these side reactions are not clear, but during the diblock copolymer synthesis it was

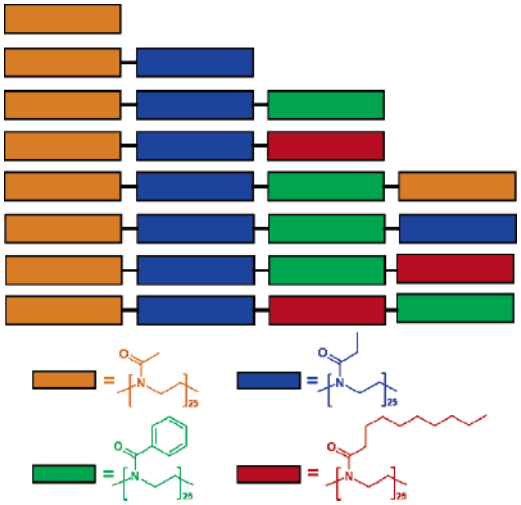

Figure 1. Schematic representation of the synthesized A, AB, ABC, ABD, ABCA, ABCB, ABCD, and ABDC polymers.

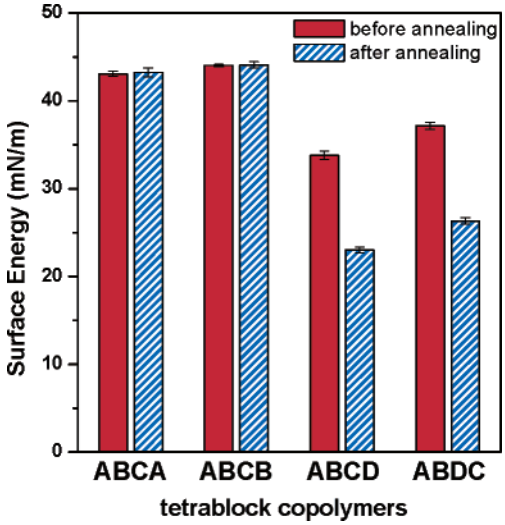

Figure 3. Surface energy of the tetrablock ter- and quarterpoly(2-oxazoline)s before and after annealing at 65 °C (16 h) [A = MeOx; B = EtOx; C = PhOx; D = NonOx].

also observed that some of the NonOx-containing copolymers could not be synthesized in a controlled manner.[23] Nevertheless, the ABCD and ABDC tetrablock quarterpolymers gave comparable SEC traces evidencing their similarity. The lower observed M_n for the ABD triblock terpolymer and the ABCD tetrablock quarterpolymer is most likely due to the terminal NonOx block that is less soluble in the eluent (DMF), resulting in a smaller hydrodynamic volume. In addition to the SEC analysis, the composition of the polymers was determined by ^{1}H NMR spectroscopy, demonstrating that the actual degree of polymerization (DP) for the different monomers was close to the theoretical 25 monomer units per block. (No significant monomer signals were present in these ^{1}H NMR spectra after drying the polymers.) For the calculation of the DP of the polymers, the DP of the first block was set to 25 as it was confirmed by ^{1}H NMR spectroscopy of the first blocks (A). The combined SEC and ^{1}H NMR analyses prove for the first time the successful synthesis of tetrablock ter- and quarterpolymers via cationic ring-opening polymerization.

The surface energy of the tetrablock ter- and quarterpolymers was determined before and after annealing for 16 h at 65 °C to investigate the effect of the block order on the surface properties (Figure 3). The surface energy was calculated from the difference of the contact angles of ethylene glycol and diiodomethane on a polymer film (spin-coated on a glass slide).[25,29] The two tetrablock terpolymers without NonOx (ABCA and ABCB) revealed high surface energies of 43−44 mN/m before and after annealing, which is comparable to the surface energy of a series of diblock copolymers that consisted of MeOx, EtOx, and PhOx.[25] The NonOx-containing tetrablock quarterpolymers (ABCD and ABDC) revealed lower surface energies than the other two tetrablock terpolymers due to (partial) migration of the nonyl side chains to the surface.[25,30,31] Although the NonOx-containing tetrablock quarterpolymers have the same monomer composition, different surface energies were obtained. The tetrablock quarterpolymer with NonOx as terminal block (ABCD: 34 mN/m) revealed a surface energy of 3 mN/m lower than the tetrablock quarterpolymer with the middle NonOx block (ABDC: 37 mN/m). This difference can be ascribed to the easier migration of the nonyl side chains to the surface when the NonOx is present as terminal block, resulting in a higher surface coverage by methylene groups and thus a lower surface energy. Annealing for 16 h at 65 °C resulted in a decrease of the surface energy of about 11 mN/m for both tetrablock quarterpolymers (ABCD: 23 mN/m; ABDC: 26 mN/m) due to a more pronounced migration of the nonyl side chains facilitated by the higher chain mobility at higher temperatures. Nonetheless, the difference in surface energy for the different

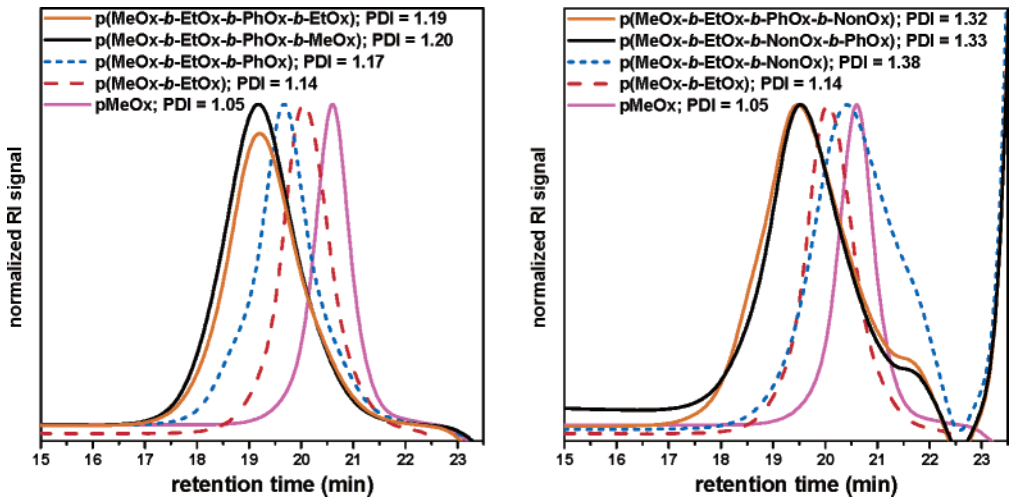

Figure 2. SEC traces of the synthesized A, AB, ABC (left), ABD (right), ABCA (left), ABCB (left), ABCD (right), and ABDC (right) polymers (all measured in DMF with 5 mM NH_4PF_6).

Table 1. Structural Analysis of the Synthesized Polymers: Theoretical and Measured Number-Averaged Molecular Weights, Polydispersity Indices, and the Degree of Polymerization (DP) of the Different Blocks

sample	$M_{n,th}$[a]	$M_{n,SEC}$[a,b]	PDI[b]	DP_{MeOx}[c]	DP_{EtOx}[c]	DP_{PhOx}[c]	DP_{NonOx}[c]
p(MeOx)	2 200	7 000	1.05	25			
p(MeOx-*b*-EtOx)	4 700	8 200	1.14	25	24		
p(MeOx-*b*-EtOx-*b*-PhOx)	8 400	11 000	1.17	25	26	26	
p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx)	10 600	14 300	1.20	50	25	22	
p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx)	10 900	10 900	1.19	25	52	27	
p(MeOx-*b*-EtOx-*b*-PhOx-*b*-NonOx)	13 300	13 400	1.32	25	25	24	27
p(MeOx-*b*-EtOx-*b*-NonOx)	9 600	7 900	1.38	25	27		21
p(MeOx-*b*-EtOx-*b*-NonOx-*b*-PhOx)	13 300	15 600	1.33	25	26	22	21

[a] Molecular weight in dalton. [b] Calculated from SEC using DMF with 5×10^{-3} M NH_4PF_6 as eluent and a PMMA calibration. [c] Determined by ^{1}H NMR spectroscopy (see Experimental Section for further details).

Table 2. Diameter D_Z[a] of the Block Copolymer Micelles Prepared by Dialysis against Water of 1 g/L Solutions of the p(MeOx-*b*-EtOx-*b*-PhOx), p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx), and p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx) Triblock and Tetrablock Terpolymers in Acetonitrile, Acetone, Ethanol, and DMF and of the p(MeOx-*b*-EtOx-*b*-PhOx-*b*-NonOx) and p(MeOx-*b*-EtOx-*b*-NonOx-*b*-PhOx) Tetrablock Quarterpolymers in Acetone

sample	acetonitrile	acetone	ethanol	DMF
p(MeOx-*b*-EtOx-*b*-PhOx)	7.8 ± 0.8	6.4 ± 0.5	6.0 ± 1.3	7.7 ± 0.6
p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx)	5.7 ± 0.9	5.6 ± 1.1	5.6 ± 1.1	5.9 ± 1.7
p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx)	6.2 ± 0.8	4.8 ± 0.4	5.0 ± 1.1	5.7 ± 0.9
p(MeOx-*b*-EtOx-*b*-PhOx-*b*-NonOx)		17 ± 1.1		
p(MeOx-*b*-EtOx-*b*-NonOx-*b*-PhOx)		13 ± 0.8		

[a] D_Z (in nm) is the diameter of the dried micelles in the *Z*-direction as measured by AFM.

Table 3. Hydrodynamic Diameter (D_h in nm) and Polydispersity Index (in Parentheses) As Measured by DLS of the Block Copolymer Micelles Prepared by Dialysis against Water of 1 g/L Solutions of the p(MeOx-*b*-EtOx-*b*-PhOx), p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx), and p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx) Triblock and Tetrablock Terpolymers in Acetonitrile, Acetone, Ethanol, and DMF and of the p(MeOx-*b*-EtOx-*b*-PhOx-*b*-NonOx) and p(MeOx-*b*-EtOx-*b*-NonOx-*b*-PhOx) Tetrablock Quarterpolymers in Acetone

sample	acetonitrile	acetone	ethanol	DMF
p(MeOx-*b*-EtOx-*b*-PhOx)	25 (0.27)	22 (0.37)	23 (0.28)	23 (0.32)
p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx)	14 (0.20)	15 (0.31)	20 (0.53)	20 (0.27)
p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx)	17 (0.32)	19 (0.33)	22 (0.32)	17 (0.32)
p(MeOx-*b*-EtOx-*b*-PhOx-*b*-NonOx)		38 (0.15)		
p(MeOx-*b*-EtOx-*b*-NonOx-*b*-PhOx)		40 (0.06)		

block orders was still evident, indicating that the block order has a clear effect on the surface properties of the tetrablock quarterpolymers. Longer annealing times did not result in a further decrease in surface energy. The surface energy of the ABCD tetrablock quarterpolymer after annealing is in the same range as the one observed for the corresponding NonOx-containing diblock copolymers (surface energies: 19−23 mN/m),[25] while the ABDC tetrablock quarterpolymer revealed a slightly higher surface energy.

Micellization of the Tetrablock Ter- and Quarterpolymers. The synthesized p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx), p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx), p(MeOx-*b*-EtOx-*b*-PhOx-*b*-NonOx), and p(MeOx-*b*-EtOx-*b*-NonOx-*b*-PhOx) ter- and quarterpolymers exhibit an amphiphilic structure and are therefore good candidates for micellization studies. These polymers contain either one type of hydrophobic block (PhOx) and two different hydrophilic blocks (MeOx and EtOx) (i) or two types of hydrophobic blocks (PhOx and NonOx) and two hydrophilic blocks (MeOx and EtOx) (ii). In case (i), the resulting micelles could therefore be classified as micelles with potentially heterogeneous coronas, provided that segregation between MeOx and EtOx blocks is observed. In case (ii), multicompartment micelles with segregated PhOx and NonOx nanodomains in the core might be expected in addition to the MeOx/EtOx heterogeneous corona. Previous investigations on the bulk properties of MeOx-, EtOx-, PhOx-, and NonOx-containing diblock copolymers did not bring conclusive evidence about the miscibility of these different poly(2-oxazoline) blocks.[32] It is thus difficult to predict the phase separation behavior of the different blocks in the micelles prepared from the samples investigated in this study.

In a first set of experiments, we have investigated in detail the micellization process of the p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx) and p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx) tetrablock terpolymers. For the sake of comparison, the micelles prepared from these samples have been systematically compared to the ones originating from the p(MeOx-*b*-EtOx-*b*-PhOx) triblock terpolymer precursor (see Experimental Section for further details). These samples have been initially dissolved in nonselective solvents. That the solvent was nonselective was verified by DLS measurements, showing only the presence of unimers. Acetonitrile, acetone, ethanol, and DMF were found to be nonselective solvent for the p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx), p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx), and p(MeOx-*b*-EtOx-*b*-PhOx) triblock and tetrablock terpolymers. Water was then added dropwise to these solutions in order to trigger micellization. After micellization, the nonselective solvent was eliminated by dialysis, leaving the micelles in pure water. This preparation process has the advantage to erase any memory effect from the bulk structure,[3] but it can lead to kinetically frozen micelles far from the equilibrium.[33] In this study, the formation of quasi-equilibrium micelles was ascertained by varying the nature of the nonselective solvent (acetonitrile, acetone, ethanol, and DMF) and the initial concentration of the block copolymers in the nonselective solvent (from 0.1 to 5 g/L). The characteristic features of the resulting micelles after dialysis have been measured by AFM (Table 2) and DLS (Table 3). For the AFM measurements, the diameter of the dried micelles has been measured in the *Z*-direction in order to avoid any tip convolution effects. Information on the hydrated micelles can be deduced from the DLS results. Within experimental

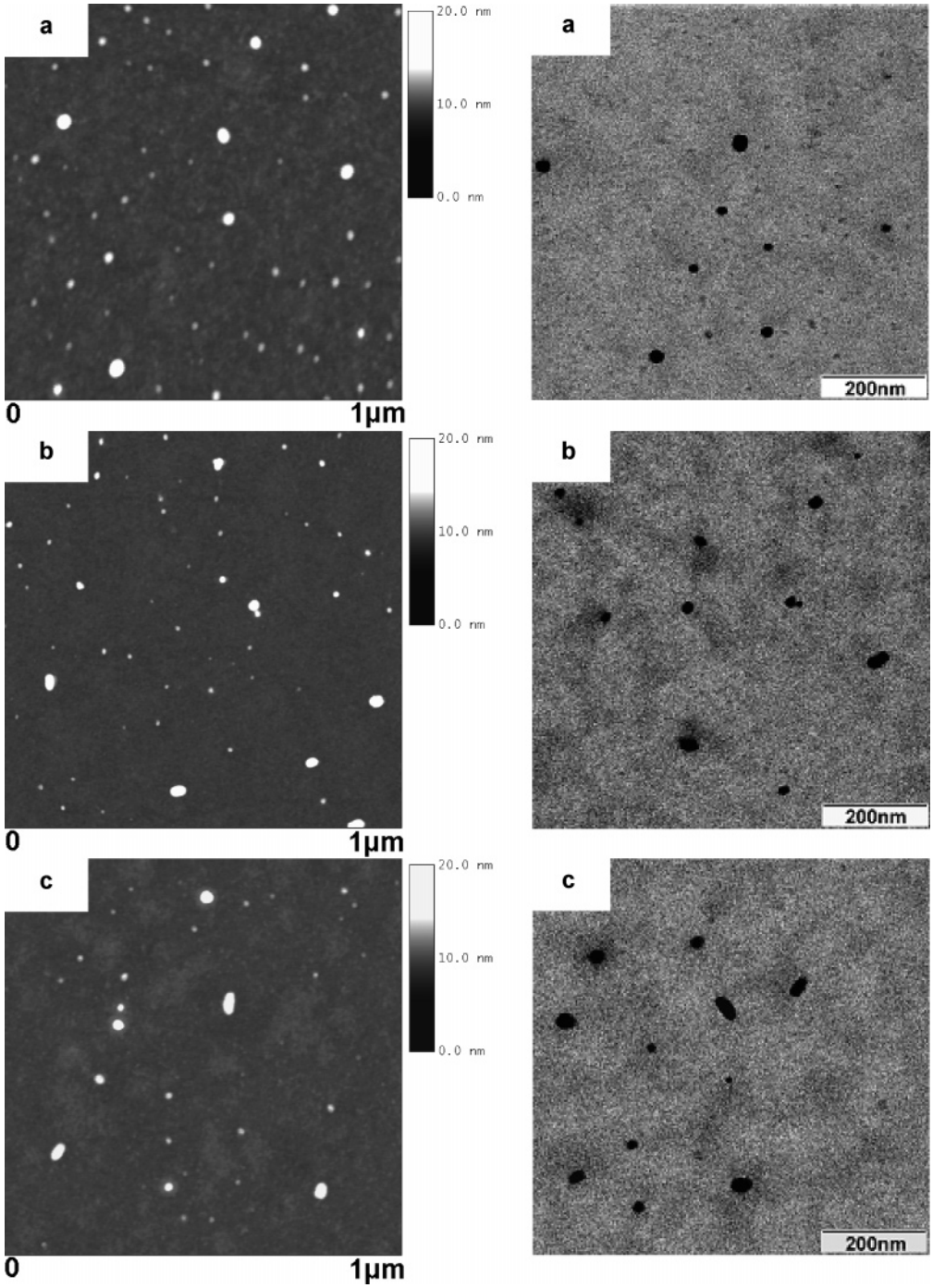

Figure 4. AFM height contrast images (left) and TEM (right) pictures of block copolymer micelles prepared from p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx) (a), p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx) (b), and p(MeOx-*b*-EtOx-*b*-PhOx) (c) terpolymers. These micelles were prepared from initial DMF solutions of the polymers at 1.0 g/L.

errors, one can conclude that the nature of the starting nonselective solvent has little effect on the characteristic features of the final micelles in water since almost identical results were obtained. Similarly, the initial concentration of the polymer in the nonselective solvent had no effect on the micellar characteristic features (data not shown). Therefore, only results obtained from 1 g/L solutions of the polymers in the nonselective solvent will be considered in the following. One can therefore conclude that quasi-equilibrium micelles are found in water after the dialysis step since their characteristic features are independent of the preparation conditions.

The morphology of the micelles formed in water by the p(MeOx-*b*-EtOx-*b*-PhOx), p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx), p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx), p(MeOx-*b*-EtOx-*b*-PhOx-*b*-NonOx), and p(MeOx-*b*-EtOx-*b*-NonOx-*b*-PhOx) triblock and tetrablock ter- and quarterpolymers was then visualized by AFM and TEM. Representative pictures are shown in Figures 4 and 5. Spherical micelles were observed for all polymers in both AFM and TEM pictures. Larger micelles were observed for the p(MeOx-*b*-EtOx-*b*-PhOx) terpolymer than for the related p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx) and p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx) samples even though the mean DP's of the polymer chains were larger for the two tetrablock terpolymers (see data from image analysis of AFM pictures in Table 2). The same tendency was measured by DLS (see Table 3). These results clearly evidence the effect of block copolymer composition on the micellar dimensions. Although p(MeOx-*b*-EtOx-*b*-PhOx) chains are shorter, the volume fraction of the hydrophobic PhOx blocks

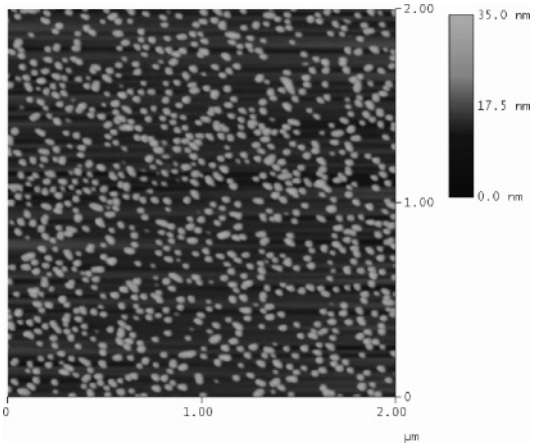

Figure 5. AFM height contrast images of block copolymer micelles prepared from the p(MeOx-*b*-EtOx-*b*-PhOx-*b*-NonOx) tetrablock quarterpolymer. These micelles were prepared from initial acetone solutions of the polymers at 1.0 g/L.

is larger compared to the p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx) and p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx) tetrablock terpolymers, resulting in a larger number of aggregation for the micelles and hence in larger micelles. The volume fraction of hydrophobic blocks is even higher for the p(MeOx-*b*-EtOx-*b*-PhOx-*b*-NonOx) and p(MeOx-*b*-EtOx-*b*-NonOx-*b*-PhOx) tetrablock quarterpolymers since two hydrophobic blocks (PhOx and NonOx) are now included in the polymers, resulting in larger spherical micelles for these two samples (see Figure 5 and Tables 2 and 3).

These results are in agreement with the well-documented scaling laws established for block copolymer micelles, indicating that the core size, the total size, and the number of aggregation mainly depend on the degree of polymerization of the hydrophobic block. Among the tetrablock ter- and quarterpolymers, the comparison is straightforward since the DP of the hydrophobic blocks increases from 25 for the p(MeOx-*b*-EtOx-*b*-PhOx-*b*-MeOx) and p(MeOx-*b*-EtOx-*b*-PhOx-*b*-EtOx) to 50 for the p(MeOx-*b*-EtOx-*b*-PhOx-*b*-NonOx) and p(MeOx-*b*-EtOx-*b*-NonOx-*b*-PhOx) ones at a constant total DP of 100 for all these polymers.

Finally, it should be noted that some micelles with a rice grain morphology were occasionally observed beside spherical micelles (see AFM and TEM pictures in Figure 4), especially for micelles prepared from initial solutions in DMF. Rice grain micelles were previously reported for poly(oxazoline)-based diblock copolymers containing a slightly cross-linked core.[34] In this previous study, the initial spherical micelles were shown to be reversibly transformed into rice grain ones by the selective swelling of the micellar core. In the present paper, the rice-grain micelles are rarely observed and are thought to be due to incomplete removal of DMF during the dialysis step, resulting in micelles with a swollen core.

Conclusions

The synthesis of tetrablock ter- and quarterpoly(2-oxazoline)s via living cationic ring-opening polymerization is reported for the first time. The use of microwave irradiation in combination with a sequential monomer addition procedure allowed the successful synthesis of (reasonably) well-defined amphiphilic tetrablock ter- and quarterpolymers based on MeOx, EtOx, PhOx, and NonOx. The tetrablock terpolymers without NonOx revealed polydispersity indices of 1.20 or lower, while the NonOx-containing tetrablock quarterpolymers showed polydispersity indices of 1.38 or lower. The reason for this difference is not clear, but it is in line with previous observations during the synthesis of NonOx-containing diblock copoly(2-oxazoline)s. The surface energy of the tetrablock ter- and quarterpolymers was determined using contact angle measurements. The tetrablock terpolymers without NonOx showed no dependence of the surface energy on block order or on annealing. In contrast, the NonOx-containing tetrablock quarterpolymers revealed lower surface energy due to (partial) migration of the nonyl side chains to the surface. The tetrablock quarterpolymer with the terminal NonOx block showed lower surface energy than the copolymer with a NonOx middle block, indicating a clear effect of block order on the polymer properties.

Aqueous micelles were successfully prepared from the investigated tetrablock ter- and quarterpolymers. The size of these micelles was in line with their composition; i.e., smaller micelles were observed as the content of hydrophilic block was increased for a constant total DP of the polymers. However, no multicompartmentalized core was detected so far for micelles formed by the PhOx- and NonOx-containing tetrablock ter- and quarterpolymers. This lack could be ascribed to the relatively low DP's of these blocks in the polymers, preventing a phase separation between them. Future directions of research include the synthesis of tetrablock ter- and quarterpolymers containing larger hydrophobic blocks as well as blocks with increased incompatibility.

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