Microwave-Assisted Cationic Ring-Opening Polymerization of 2-Oxazolines: A Powerful Method for the Synthesis of Amphiphilic Triblock Copolymers

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Received April 29, 2006

ABSTRACT: We report on the first successful example of the preparation of triblock copolymers via a cationic ring-opening polymerization procedure. A library of 30 triblock copolymers was prepared from 2-methyl-, 2-ethyl-, 2-nonyl-, and 2-phenyl-2-oxazoline in a single-mode microwave reactor. The polymers exhibited narrow molecular weight distributions and showed only minor deviations from the targeted monomer ratio of 33:33:33. The glass-transition temperature of the triblock copolymers spanned the range from 50 to 100 °C depending on the incorporated monomers. The micellization behavior was investigated for some amphiphilic triblock copoly(2-oxazoline)s containing two hydrophilic and one hydrophobic blocks. The size of the micelles was larger when the hydrophobic block is located at one end of the triblock copoly(2-oxazoline)s, as measured by atomic force microscopy and dynamic light scattering.

Introduction

Numerous applications of polymers, like micellar catalysis, drug delivery, and hydrogels, demand well-defined (block co-) polymers with narrow molecular weight distributions as prerequisite.[1−8] Ideally, these block copolymers are composed of hydrophobic and hydrophilic blocks and, consequently, form micelles in aqueous solution that (reversibly) entrap hydrophobic molecules like reactants, catalysts, or drugs in their hydrophobic core.[9−11] Recently, the synthesis, properties, and aggregation behavior of triblock copolymers[12] gained a lot of attention resulting in, for example, multicompartment micelles[13−15] that can store multiple guests.[16] For application of polymers in, e.g., drug delivery, other characteristics such as the polymer's biocompatibility and degradability have to be considered as well.[17] This biocompatibility directed us to the class of poly-(2-oxazoline)s with its numerous congeners,[18,19] among which the poly(2-ethyl-2-oxazoline) has been approved by the food and drug administration (FDA).[20] The synthesis of amphiphilic diblock copoly(2-oxazoline)s was already reported by various groups.[1−11] The 2-oxazoline monomers undergo living cationic ring-opening polymerization under the appropriate conditions, resulting in well-defined polymers with narrow molecular weight distributions. Nevertheless, widespread industrial applications of poly(2-oxazoline)s have not been realized since the polymerizations normally require reaction times in the range of several hours up to several days. This disadvantage was recently overcome by the use of closed reaction vials and microwave irradiation[21] that accelerated the cationic ring-opening polymerization of 2-oxazolines by a factor of 400 when compared to conventional reflux polymerizations.[22−24] This observed acceleration was found to solely originate from thermal effects and not from so-called (nonthermal) microwave effects as was proven by reference experiments with conductive heating under pressure and reflux conditions.[22,25,26] However, slightly narrower molecular weight distributions were obtained under microwave heating due to the homogeneous heat profile in the reaction vessel. This improved microwave polymerization procedure was recently applied to the synthesis of a 16-membered library of diblock copolymers based on 2-methyl- (MeOx), 2-ethyl- (EtOx), 2-phenyl- (PhOx), and 2-nonyl-2-oxazoline (NonOx).[27] This diblock copolymer library was investigated to establish structure−property relationships.[27−29] The synthesis of these diblock copolymers was performed in a two-step procedure: after complete consumption of the first monomer, addition of a second monomer resulted in the formation of well-defined block copolymers (Scheme 1).

Using this principle, the synthesis of BAB and star-block copolymers has been reported starting from bi-,[30] tri-,[31] tetra-,[2] and hexafunctional[32] initiators. In principle, multiblock copolymers can also be synthesized by the sequential addition of different monomers to the propagating species. However, to this date only one report on the synthesis of ABC triblock copoly-(2-oxazoline)s has appeared in the literature.[33] Three triblock copolymers with the same monomer order were synthesized with segments shorter than 10 monomer units. The synthesis of longer triblock copoly(2-oxazoline)s was never reported to the best of our knowledge. The occurrence of chain transfer and chain termination reactions upon addition of monomer impedes the controlled synthesis of well-defined triblock and longer copolymers via the sequential addition method. Moreover, the living-

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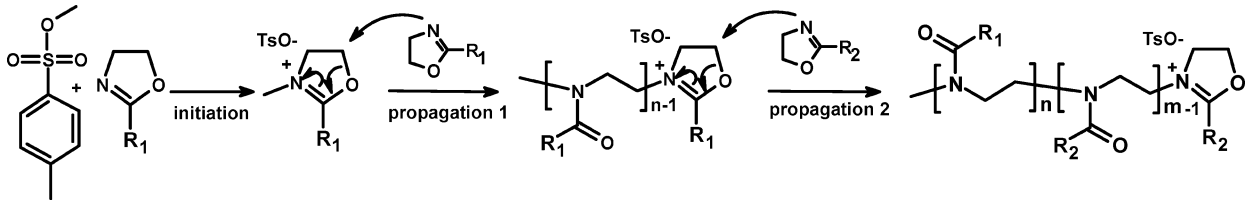
10.1021/ma060952a CCC: $33.50
Published on Web 06/15/2006

Scheme 1. Schematic Representation of the Two-Step Synthesis of Diblock Copoly(2-oxazoline)s



ness of the 2-oxazoline polymerizations is lost when increasing the monomer-to-initiator ratio,[24,34] which also prevents the synthesis of higher molecular weight copolymers.

The successful microwave-assisted synthesis of the library of diblock copoly(2-oxazoline)s encouraged us to go on with the preparation of a 30-membered library of triblock copoly(2-oxazoline) under microwave heating, where the better control and the shorter polymerization times might be advantageous. The synthesis, structural characterization (^{1}H NMR and size exclusion chromatography, SEC), and thermal properties of a triblock copolymer library consisting of 33 + 33 + 33 monomer units of MeOx, EtOx, PhOx, and/or NonOx is described in this contribution. The micellization behavior of a selection of these triblock copolymers was investigated to determine possible structure−property relationships and to investigate the effect of block order. Such extensive and systematical variations of block nature and order in triblock copolymer micelles have never been studied so far.

Results and Discussion

The selected set of 2-oxazoline monomers that was used for the synthesis of the triblock copolymers (MeOx, EtOx, PhOx, and NonOx) yield polymers of different polarity. pMeOx and pEtOx are hydrophilic, while pPhOx and pNonOx are hydrophobic. The monomers differ also by the flexibility of the side groups: MeOx and PhOx have rigid substituents, whereas EtOx and NonOx have rather flexible side chains. As a result, pMeOx is compatible with pPhOx as well as pEtOx with pNonOx, whereas combinations of flexible and rigid substituents tend to (partially) demix.[26] Copolymers with any combination of hydrophobic/hydrophilic and rigid/flexible can be realized with this small set of four monomers. All possible combinations of MeOx, EtOx, PhOx, and NonOx would result in 64 different triblock copolymers. However, all polymers that would have two times the same block after each other (representing diblock copolymers) were excluded, resulting in a 36-membered library. Moreover, the triblock copolymers with pNonOx as first block and pMeOx or pEtOx as second block were also rejected since the corresponding diblock copolymerizations underwent extensive chain transfer side reactions.[27] Therefore, the investigated library of triblock copolymers consisted of 30 different polymers including several pairs of similar polymers such as p(MeOx-*b*-NonOx-*b*-EtOx) and p(EtOx-*b*-NonOx-*b*-MeOx). All synthesized triblock copolymers are listed in Table 1.

Synthesis and Characterization. The triblock copolymers were synthesized in a three-step sequential procedure using the recently discovered optimized microwave polymerization conditions.[24] The polymerizations were performed at 140 °C in superheated acetonitrile (which caused an excess pressure of ~4 bar inside the capped vials) using methyl tosylate as initiator. The total triblock copolymer length was chosen to be 100 monomer units (corresponding to 33 units per block) since this was found to be the upper limit for the synthesis of well-defined pMeOx and pNonOx.[24] The complete polymerization procedure is schematically depicted in Figure 1.

Table 1. Number of Incorporated Monomer Units into the 30 Triblock Copoly(2-oxazoline)s Resulting from Combined ^{1}H NMR Analyses (Top) of the Model [A and AB (Block Co-) Polymers] and Final Polymers as Well as the Measured Number Average Molecular Weights ($M_{n,GPC}$/PDI; Bottom)[a]

	3rd block			
1st−2nd block	MeOx	EtOx	PhOx	NonOx
MeOx−EtOx	33:28:33		33:33:32	33:31:33
	10.2 kDa/1.21		11.7 kDa/1.24	5.5 kDa/1.44
MeOx−PhOx	33:31:33	33:33:36		33:30:32
	14.1 kDa/1.22	13.9 kDa/1.15		10.2 kDa/1.21
MeOx−NonOx	33:28:33	33:30:37	33:29:29	
	9.9 kDa/1.20	10.0 kDa/1.21	10.6 kDa/1.27	
EtOx−MeOx		33:33:33	33:29:27	33:34:31
		10.9 kDa/1.32	12.4 kDa/1.23	9.5 kDa/1.28
EtOx−PhOx	33:31:30	33:30:33		33:30:36
	16.2 kDa/1.20	15.3 kDa/1.24		11.4 kDa/1.22
EtOx−NonOx	33:33:37	33:33:33	33:33:31	
	10.1 kDa/1.27	9.9 kDa/1.22	11.3 kDa/1.25	
PhOx−MeOx		33:35:35	33:27:33	33:31:31
		15.3 kDa/1.21	15.2 kDa/1.19	9.1 kDa/1.23
PhOx−EtOx	33:35:34		33:42:33	33:38:38
	17.8 kDa/1.32		19.1 kDa/1.28	14.1 kDa/1.21
PhOx−NonOx	33:38:34	33:45:37	33:36:33	
	9.7 kDa/1.21	8.8 kDa/1.21	11.6 kDa/1.22	
NonOx−PhOx	33:23:27	33:26:24		33:32:33
	7.2 kDa/1.40	7.8 kDa/1.33		10.3 kDa/1.38[b]

[a] ^{1}H NMR spectra were recorded in $CDCl_3$ or CD_2Cl_2 (PhOx-containing polymers), and GPC analyses were performed using DMF (with 5 mM NH_4PF_6) as eluent. $M_{n,GPC}$ was calculated utilizing PMMA standards. [b] GPC measurement with $CHCl_3$:NEt_3:2-PrOH (94:4:2) as eluent (PS calibration).

A stock solution containing the first monomer, initiator and solvent was partitioned into seven vials followed by microwave irradiation. The initial monomer concentration was 2 M (NonOx), 3 M (PhOx), or 4 M (MeOx and EtOx) in order to have a comparable volume fraction of the first monomer (~40% v/v). The first and last vials were set aside and used to check the reproducibility of the polymerization of the first block. The second monomer was added under an argon atmosphere to the five remaining vials. After the second microwave-assisted polymerization step, the second and fifth vials were analyzed to check the reproducibility of the diblock copolymerizations. If these diblock copolymers were identical, it was assumed that the first two blocks of the three remaining vials were the same as well. To these three remaining vials, three different monomers (excluding the monomer of the second block) were added under an argon atmosphere followed by the third microwave-assisted polymerization step, resulting in the formation of three triblock copolymers. The polymerization times required for complete conversion [$\ln([M]_0/[M]_t) = 4$ corresponding to a monomer conversion of 98%] of the first, second, and third monomer were calculated from the previously determined kinetic parameters for the homopolymerizations.[22,24] The total required polymerization time depends on the initial initiator concentration and the reactivity of the monomers. The total polymerization times range from 13.2 min [p(MeOx-*b*-NonOx-*b*-MeOx)] to 61.6 min [p(PhOx-*b*-EtOx-*b*-PhOx)]. The resulting triblock copoly(2-oxazoline)s were analyzed by size exclusion chromatography (SEC) using *N*,*N*-dimethylformamide (DMF) contain-

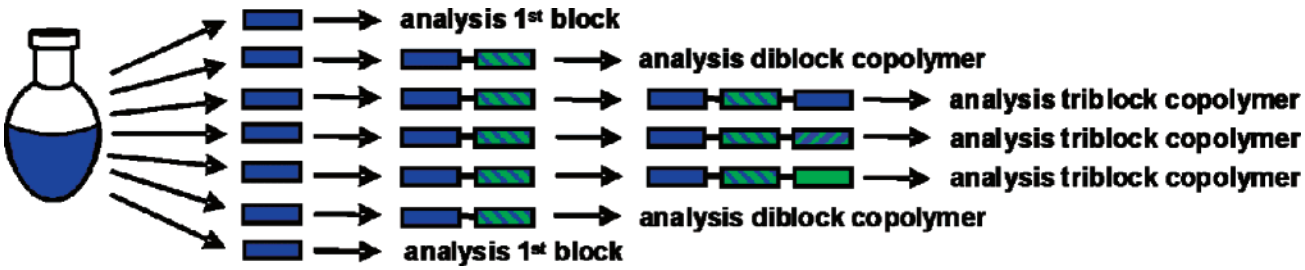


Figure 1. Schematic presentation of the synthetic procedure that was applied for the preparation of three triblock copolymers with the same first and second blocks.

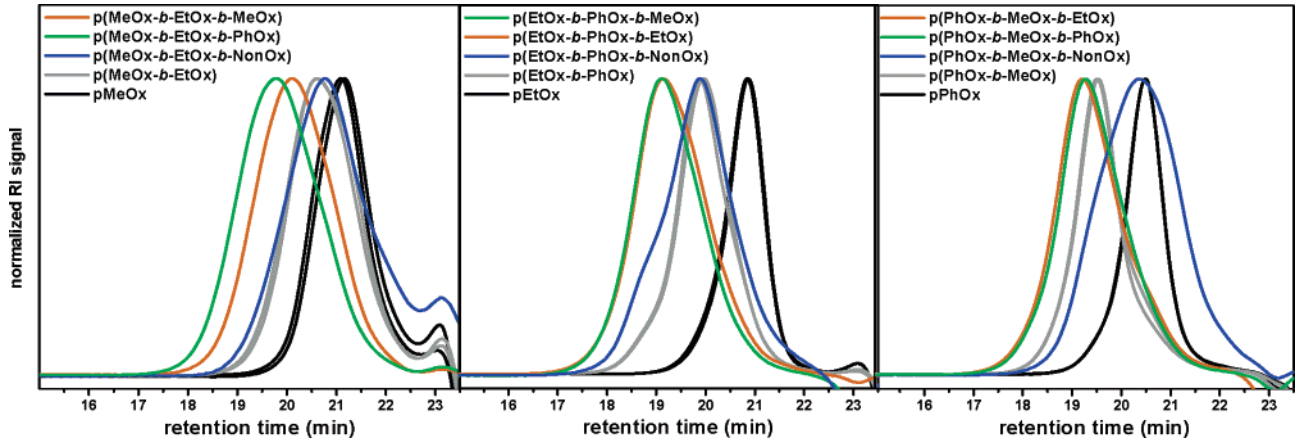


Figure 2. SEC traces of selected triblock copoly(2-oxazoline)s together with the two model polymerizations of the corresponding first block and diblock. All measurements were performed in DMF with 5 mM NH_4PF_6.

ing 5 mM NH_4PF_6 as eluent (Table 1). Selected SEC traces are shown in Figure 2. The chromatograms associated with the model polymerizations (see Figure 1) of the first blocks and of the diblock copolymers superimpose perfectly, evidencing the good reproducibility.

The SEC traces of most triblock copolymers are monomodal, demonstrating their successful synthesis. Trimodal molecular weight distributions were observed in only two cases (not shown), namely p(NonOx-*b*-PhOx-*b*-MeOx) and p(NonOx-*b*-PhOx-*b*-EtOx), which is indicative of chain transfer and subsequent chain-coupling side reactions.[27] All other triblock copolymers were obtained with narrow molecular weight distributions and polydispersity indices (PDI) of ~1.3. However, it should be mentioned that all NonOx-containing triblock copolymers have unsymmetrical molecular weight distributions, which is most likely due to the poor solubility of the pNonOx segment in DMF. This was confirmed by performing a SEC analysis using a better solvent for the NonOx block, i.e., a mixture of chloroform:triethylamine:2-propanol (94:4:2). In this case the chromatograms are nearly symmetric.

The synthesized triblock copolymers were also characterized by ^{1}H NMR spectroscopy to determine the number of incorporated monomer units. The compositions were calculated from the integrals of the different monomers and of the polymer backbone.[35] To be able to integrate the aromatic protons of the pPhOx accurately, the pPhOx-containing polymers were measured in CD_2Cl_2 instead of $CDCl_3$. The number of incorporated monomer units that resulted from the ^{1}H NMR analyses are summarized in Table 1. Most of the triblock copolymers consist of the desired number of monomer units with a deviation of up to 5 units. Four of the triblock copolymers [p(NonOx-*b*-PhOx-*b*-MeOx), p(NonOx-*b*-PhOx-*b*-EtOx), p(PhOx-*b*-EtOx-*b*-PhOx), and p(PhOx-*b*-NonOx-*b*-EtOx)] revealed a deviation of ~10 units. However, it should be mentioned that the integration of the ^{1}H NMR spectra of the pPhOx-containing copolymers is more difficult due to the broad backbone signal of the pPhOx (3.9−2.4 ppm). In conclusion, the microwave-assisted polymerization procedure proved to be well-suited for the synthesis of well-defined triblock copoly(2-oxazoline)s, making this work the first successful example (with a reasonable degree of polymerization of each block) of the synthesis of triblock copolymers via a cationic ring-opening polymerization process.

The glass transition temperatures (T_g) of the triblock copoly(2-oxazoline)s were measured by differential scanning calorimetry (DSC). Three samples of each triblock copolymer were analyzed three times (after an initial first heating run that was not considered for the subsequent calculations) in order to enable the calculation of standard deviations, which were in the range of ±3% or lower. The DSC traces revealed melting points in the narrow range from 143 to 157 °C for all pNonOx-containing triblock copolymers, which is similar to the melting point of the pNonOx homopolymer (148 °C).[27] Therefore, it can be concluded that the length of 33 monomer units in the pNonOx segments is sufficient for side-chain crystallinity and that the presence of other poly(2-oxazoline) segments does not disturb the crystallinity. All triblock copolymers without pNonOx were found to be amorphous.

The T_gs of all the investigated triblock copolymers are plotted in Figure 3. The T_gs of the pMeOx, pEtOx, and pPhOx are also added in this graph as a reference. No T_g was detected by DSC for the triblock copolymers having both a pPhOx and a pNonOx segment, in agreement with previous DSC investigations on diblock copoly(2-oxazoline).[27] The T_g of all other triblock copolymers depended on the fraction of flexible units in the copolymers. The T_g cover the whole range from 48 °C for copolymers with a high content of flexible monomers (EtOx or NonOx) to 98 °C for a high content of rigid monomers (MeOx, PhOx). Moreover, the glass-transition temperatures did not depend on the order of the blocks within the block copoly(2-oxazoline)s. It is also important to note that none of the triblock

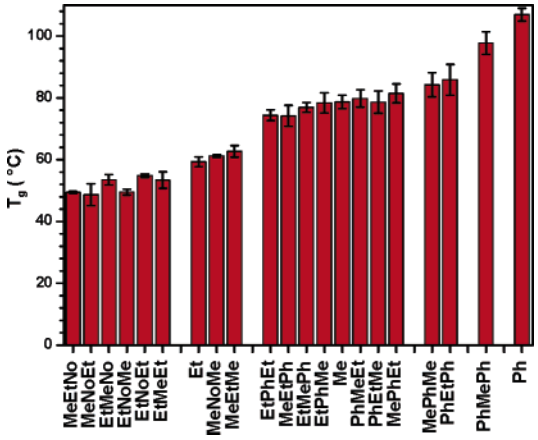


Figure 3. Glass-transition temperatures of the triblock copoly(2-oxazoline)s and the pMeOx, pEtOx, and pPhOx homopolymers, sorted in ascending order. The polymers that contained (at least) one block of poly(2-nonyl-2-oxazoline) and poly(2-phenyl-2-oxazoline) at the same time (12 combinations) did not exhibit any glass transition in DSC [Me = pMeOx, Et = pEtOx, Non = pNonOx, and Ph = pPhOx].

copolymers exhibited more than one glass transition, indicating that no macroscopic phase separation occurred in the bulk material. The absence of macroscopic phase separation is most likely due to the relatively short segments (33 monomer units) that were incorporated.

Solubility and Micellization Behavior. The solubility of the library of triblock copolymers was investigated to study whether the block order has an effect on the solubility. All pPhOx- and pNonOx-containing triblock copoly(2-oxazoline)s were not readily soluble in water (10 wt % solutions), whereas the triblock copolymers consisting of only the water-soluble pMeOx and pEtOx obviously did dissolve. To further expand the scope of the solubility investigations, the solubilities (10 wt %) were investigated in a water:ethanol mixture (50:50 wt %). Again, all pNonOx-containing polymers were insoluble as well as the triblock copolymers with two pPhOx segments. As expected, the p(MeOx-*b*-EtOx-*b*-MeOx) and p(EtOx-*b*-MeOx-*b*-EtOx) copolymers were also soluble in this water:ethanol mixture. For the triblock copolymers with one pPhOx segment a strong correlation between the solubility of the polymer and the monomer order was observed. When the pPhOx was present as outer block, white milky solutions were obtained. On the other hand, triblock copolymers with pPhOx as middle block formed clear solutions instantaneously (Figure 4). This observed difference in solubility most likely results from easier aggregation of the triblock copolymers with pPhOx as outer block, whereas the pPhOx segment is more effectively solubilized when it has two neighboring soluble pMeOx and/or pEtOx blocks that prevent aggregation.

Six representative amphiphilic copolymers were selected for micellization studies: p(MeOx-*b*-EtOx-*b*-X), p(EtOx-*b*-MeOx-*b*-X), and p(EtOx-*b*-X-*b*-MeOx) (X = PhOx or NonOx). Because of solubility issues, only copolymers with a large hydrophilic part (2 segments of each 33 monomer units) and a small hydrophobic part (33 monomer units) were investigated. Since these triblock copolymers were poorly soluble in water, they were initially dissolved in acetone, a nonselective solvent for the constituent blocks as ascertained by dynamic light scattering (DLS). Following a previously reported micellization procedure,[36−38] water was added dropwise under vigorous stirring to the initial polymer solution in acetone. Acetone was then eliminated by dialysis against water. The resulting micelles should consist of a core containing the hydrophobic block (pPhOx or pNonOx) and a corona comprising the hydrophilic blocks (pMeOx and pEtOx). In each of the investigated copolymers, the degree of polymerization (DP) of the constituent blocks was constant. This therefore allows the direct comparison of the characteristic features of the micelles on the basis of three variable parameters: (i) the localization of the hydrophobic block (pPhOx or pNonOx) at one end or in the middle of the triblock copolymer, (ii) the relative localization of the chains of pMeOx and pEtOx in the corona of the micelles, and, finally, (iii) the chemical nature of the hydrophobic blocks (pPhOx or pNonOx). Such parameters have been scarcely varied in the field of block copolymer micelles in which most studies focused on the influence of the block copolymer composition and of the relative block length on the micellar characteristic features. For the investigated triblock copoly(2-oxazoline)s, spherical micelles were expected on the basis of their compositions (66 hydrophilic monomer units and 33 hydrophobic monomer units). This assumption was indeed verified by AFM measurements, as shown in Figure 5 for micelles containing pPhOx as hydrophobic block. These micelles are rather polydisperse in size. In the case of the pNonOx-containing samples, the micelles had more irregular shapes but are mainly spherical. A typical picture is shown in Figure 4 for the p(MeOx-*b*-EtOx-*b*-NonOx) sample. These AFM pictures of micelles dried on a silicon wafer do not necessarily represent the real situation existing in solution due to tip convolution effects and/or the flattening of the object on the surface. The more pronounced flattening of the pNonOx-containing micelles, compared to the pPhOx-containing micelles, is most likely related to the low T_g of the pNonOx segments. To avoid tip convolution effects, the diameter of the micelles was estimated by measuring the observed height (D_z) of the micelles.

The resulting micelle heights (D_z) are listed in Table 2. A clear effect of the block order, i.e., the localization of the hydrophobic block, on the micellar characteristic features was observed. The micelle sizes for the two triblock copolymers p(MeOx-*b*-EtOx-*b*-PhOx) and p(EtOx-*b*-MeOx-*b*-PhOx) are in

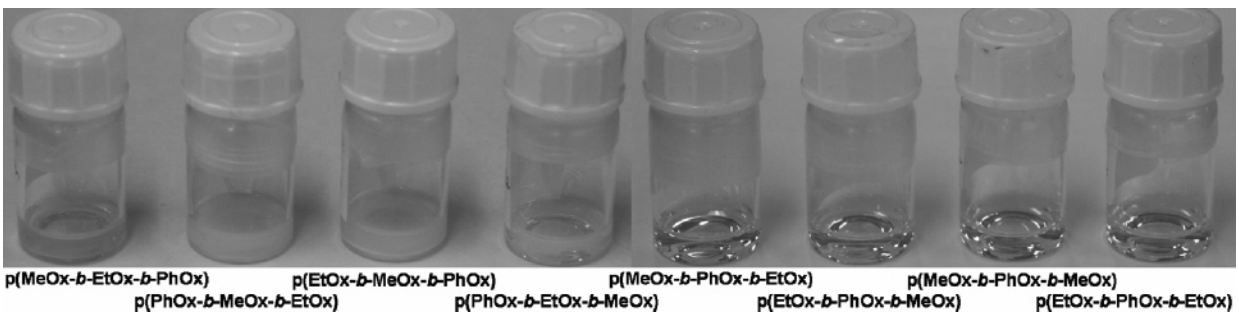


Figure 4. Picture of the solubility of the different pPhOx-containing triblock copolymers in a water:ethanol (50:50 wt %) mixture that demonstrate the formation of milky solutions with pPhOx as outer segment and the formation of clear solutions with pPhOx as middle segment.

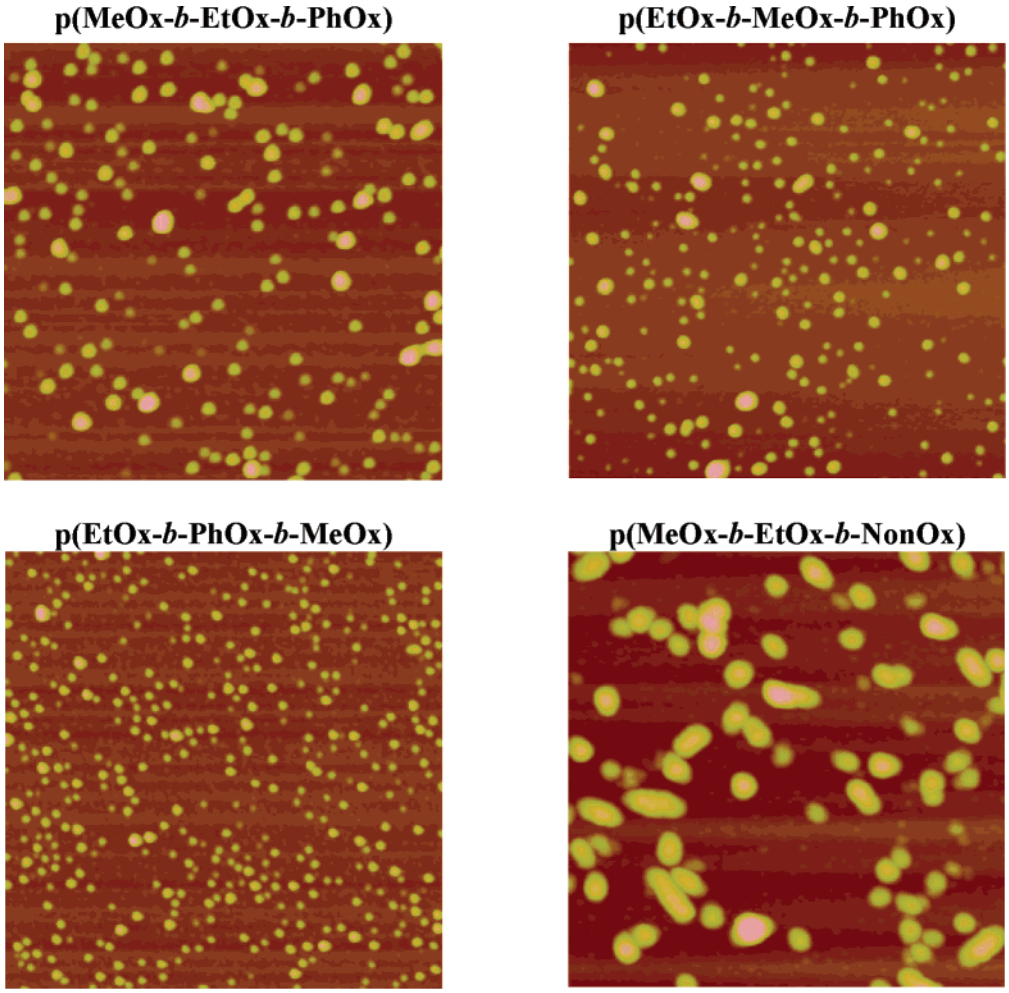


Figure 5. AFM height images of micelles formed in water by the triblock copolymers p(MeOx-*b*-EtOx-*b*-PhOx), p(EtOx-*b*-MeOx-*b*-PhOx), p(EtOx-*b*-PhOx-*b*-MeOx), and p(MeOx-*b*-EtOx-*b*-NonOx) (image size 1.0 × 1.0 μm).

Table 2. Characteristic Features of the Micelles Formed by the Six Copolymers Investigated in This Study[a]

	property		
triblock copolymer	C [g L^{-1}]	R_h [nm]/PDI	D_z [nm]
p(EtOx-*b*-MeOx-*b*-PhOx)	0.19	19/0.29	18 ± 2.3
p(MeOx-*b*-EtOx-*b*-PhOx)	0.21	25/0.49	16 ± 2.2
p(EtOx-*b*-PhOx-*b*-MeOx)	0.18	13/0.52	7 ± 1.7
p(EtOx-*b*-MeOx-*b*-NonOx)	0.20		10 ± 1.8
p(MeOx-*b*-EtOx-*b*-NonOx)	0.19	36/0.34	13 ± 2.0
p(EtOx-*b*-NonOx-*b*-MeOx)	0.18	20/0.44	7 ± 1.3

[a] C is the concentration of the micelles in pure water after the dialysis step. R_h is the hydrodynamic radius (obtained from the CONTIN histogram) for the individual micelles. D_z are obtained from AFM images. Note that the CONTIN analysis of the DLS data for p(MeOx-*b*-EtOx-*b*-NonOx) could not resolve a population associated with micelles.

the same range, while it is significantly smaller for the p(EtOx-*b*-PhOx-*b*-MeOx) sample where the hydrophobic block is located in the middle of the copolymer (Table 2). The same trend was observed for the pNonOx-containing copolymers.

The different micellar solutions were also characterized by DLS. The data have been analyzed using the CONTIN routine.[39,40] Bimodal distributions of objects have been observed in all investigated samples. In the following, the population corresponding to the smaller objects will be referred to as micelles while the minor larger one will be attributed to clusters of micelles. A typical CONTIN size histogram is shown in Figure 6. The hydrodynamic radii (R_h) associated with the population of micelles in the CONTIN histogram have been

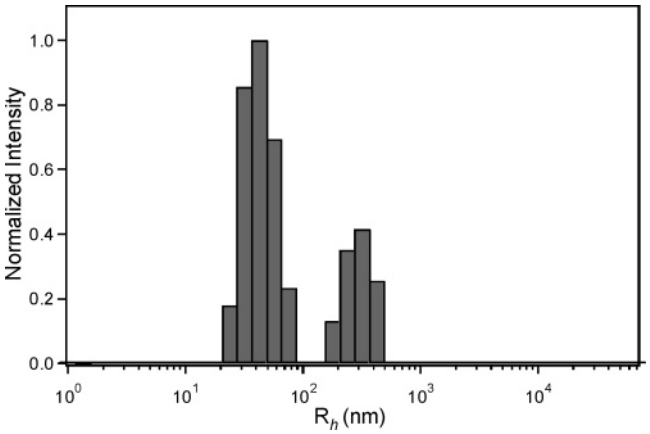


Figure 6. CONTIN size distribution histogram obtained after analysis of the DLS signal recorded on the p(MeOx-*b*-EtOx-*b*-NonOx) sample. The R_h of the micelles and clusters of micelles correspond to the maxima of the first and second population of the histogram, respectively.

listed in Table 2. These data are in quite good agreement with those obtained by AFM. Analogously to the observation obtained from the AFM experiments, the localization of the hydrophobic block in the middle of the block copolymer results in smaller micelles.

Conclusions

A 30-membered library of triblock copoly(2-oxazoline)s was prepared from four differently substituted monomers, namely

2-methyl-, 2-ethyl-, 2-nonyl-, and 2-phenyl-2-oxazoline under microwave irradiation. Each block copolymer consists of three blocks of 33 monomer units, resulting in a total length of 99 units. The improved livingness of the cationic polymerization under microwave irradiation allowed the successful preparation of well-defined triblock copoly(2-oxazoline)s in remarkably short polymerization times ranging from 13.2 to 61.6 min. Size exclusion chromatography and ^{1}H NMR analysis proved the successful synthesis of the triblock copolymers with relatively narrow average molecular weight distributions (PDI < 1.33). Differential scanning calorimetry revealed that the glass transition temperature of the copolymers depends strongly on the flexibility of the side chains of the incorporated monomer units, and ranges from 50 to 100 °C, but is independent of the block order. The micellization study in water of selected triblock copolymers consisting of two water-soluble segments and one hydrophobic segment revealed a clear effect of the block order on the micellar size. The micelles from polymers with a hydrophobic middle block were smaller when compared to micelles from polymers with end-standing hydrophobic segments.

This is the first example of the sequential synthesis of triblock copolymers via a cationic ring-opening polymerization mechanism. The characterization of this library of triblock copoly(2-oxazoline)s provided further insights into the effect of block order on the polymer properties. We believe that this work is an important step toward the design of (multi)block copolymers with predefined properties that might find future applications in fields like multicompartment drug delivery and multistep micellar catalysis.

Experimental Section

Materials. All chemicals, except for acetonitrile (Biosolve LTD), were purchased from Aldrich. 2-Nonyl-2-oxazoline and 2-phenyl-2-oxazoline were kind gifts from Henkel (Germany). Methyl tosylate and the 2-oxazolines were distilled prior to use (the latter over barium oxide) and stored under argon. Acetonitrile was dried over molecular sieves (3 Å).

Instrumentation. 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 $CDCl_3$ or CD_2Cl_2. Chemical shifts are given relative to TMS or residual solvent signals. Samples of ~10 mg were used for differential scanning calorimetry. The compounds were dried in a vacuum oven at 40 °C for 24 h prior to the measurements. Thermal transitions were determined on a DSC 204 F1 Phoenix by Netzsch under a nitrogen atmosphere with heating and cooling rates of 40 K min^{-1} (three measurements per sample after an initial first heating run that was not considered for the subsequent calculations).

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.[40] 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 radius (R_h) by the Stokes−Einstein equation.[40] The DLS data were also analyzed by the CONTIN routine, a method which is based on a constraint inverse Laplace transformation of the data and which gives access to a size distribution histogram for the aggregates.[40]

Atomic force microscopy (AFM) measurements of the micelles 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.

Microwave-Assisted Preparation of the Triblock Copoly(2-oxazoline)s. All reaction steps for the synthesis of the triblock copoly(2-oxazoline)s were performed in acetonitrile at 140 °C. For the synthesis of the first block, solutions (2 mL) with the following initial concentration of monomers were used: $[MeOx]_0 = [EtOx]_0 = 4$ M, $[PhOx]_0 = 3$ M, and $[NonOx]_0 = 2$ M. The polymerizations were initiated by methyl tosylate, ratio [monomer]:[initiator] = 33:1. These conditions had proven successful in a precedent kinetic study.[24] For the addition of the second and the third type of monomer, the vials were transferred to an inert atmosphere of argon, and the second or third monomer, respectively, was added. The solution was again heated in the microwave reactor. After the incorporation of the third monomer, the solutions were quenched with water.

Micelle Preparation. The investigated copolymers were initially dissolved in acetone at a concentration of 1 g/L. 1 mL of deionized water was then added dropwise to 1 mL of these solutions in order to trigger micellization. Acetone 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 lies in the range of 0.2 g/L (see Table 2). The micellar solutions were passed through 1.2 μm filters before dynamic light scattering measurements. For AFM sample preparation the solutions were diluted 10 times with pure water.

Acknowledgment. R.H., F.W., M.A.M.L., H.M.L.T., S.F.G.M.v.N., M.v.d.L., and U.S.S. thank the Dutch Polymer Institute (DPI), the Nederlandse Wetenschappelijk Organisatie (NWO), and the Fonds der Chemischen Industrie for financial support as well as Henkel for providing 2-phenyl- and 2-nonyl-2-oxazoline. CAF is Chargé de Recherches FNRS. H.H., A.M.J., and J.-F.G. thank the "Fondation Louvain" for financial support (mécénat Solvay).

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MA060952A