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Microwave-assisted synthesis and micellization behavior of soy-based copoly(2-oxazoline)s

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Abstract Polymers based on renewable resources are promising candidates for replacing common organic polymers, and thus, for reducing oil consumption. In this contribution we report the microwave-assisted synthesis of block and statistical copolymers from 2-ethyl-2-oxazoline and 2-“soy alkyl”-2-oxazoline via a cationic ring-opening polymerization mechanism. The synthesized copolymers were characterized by gel permeation chromatography and ¹H-NMR spec-

troscopy. The micellization of these amphiphilic copolymers was investigated by dynamic light scattering and atomic force microscopy to examine the effect of hydrophobic block length and monomer distribution on the resulting micellar characteristics.

Keywords Living polymerization · Microwave irradiation · Micelles · Renewable resource · Copolymers

Introduction

Nowadays, the use of renewable feedstocks that might replace oil-based starting materials is gaining increasing attention in academic research and the chemical industry [1]. The renewable resources that are investigated in the field of polymer science [2] include, e.g., starch [3, 4], saccharides [5, 6], and fatty acids [7, 8]. Fatty acid-based polymers have already been shown to exhibit good properties for applications such as coatings, adhesives, and rubbers, due to the hydrophobic side-chains [7]. Moreover, the use of unsaturated fatty acid side chains allows

cross-linking of the material by UV-irradiation [9, 10]. The preparation of well-defined polymers with unsaturated fatty acid side-chains has been reported via atom transfer radical polymerization of cardanyl acrylate [10], and we have recently performed the living cationic ring-opening polymerization of 2-“soy alkyl”-2-oxazoline under microwave irradiation (Hoogenboom and Schubert, submitted for publication). This soy-based 2-oxazoline monomer (SoyOx) was synthesized by Henkel by coupling soybean fatty acids with ethanol amine, followed by ring-closure [11]. The use of microwave heating (for books on microwave heating in chemistry, see [12, 13]; for a review

on microwave-assisted polymerizations, see [14]) in combination with closed vials was previously shown to result in faster cationic ring-opening polymerizations when compared to ambient pressure [15, 16]. However, this acceleration could be reproduced with conventionally heated pressure reactors, and was thus ascribed to the higher attainable temperatures [15, 17]. This microwave-assisted polymerization procedure was also successfully applied for the preparation of a 16-membered library of diblock copoly(2-oxazoline)s, resulting in the determination of structure–property relationships [18].

The present study combines the use of a monomer based on a renewable resource and the use of microwave irradiation for the synthesis of SoyOx-containing block copolymers, as well as that of a statistical copolymer. 2-Ethyl-2-oxazoline (EtOx) was incorporated as a hydrophilic part of the copolymers, which, in combination with the hydrophobic SoyOx, results in the formation of amphiphilic copolymers {for a highlight on the use of (block) copoly(2-oxazoline)s, see [19]}. The synthesis, characterization, and micellization of these p(EtOx-*b*-SoyOx) and p(EtOx-*stat*-SoyOx) copolymers are discussed in detail.

Experimental

Materials and instrumentation

Dichloromethane (Biosolve) was distilled over potassium before use. Acetonitrile (Biosolve) was dried with molecular sieves (3 Å). EtOx (Aldrich) was distilled over barium oxide (BaO) and stored under argon. SoyOx (donated by Henkel) was purified over aluminum oxide with hexane as eluent. After drying over BaO, SoyOx was stored under argon. Methyl tosylate (Aldrich) was distilled and also stored under argon.

Polymerizations were performed in an Emrys Liberator (Biotage, formerly Personal Chemistry) utilizing capped reaction vials. These vials were heated to 105 °C, cooled to room temperature, and filled with argon prior to use. All microwave polymerizations were performed with temperature control (IR sensor). ¹H-NMR spectra were recorded on a Varian Gemini 300 spectrometer in CDCl₃. Chemical shifts are given in parts per million relative to tetramethylsilane or residual solvent signals. Gel permeation chromatography (GPC) was measured on a Shimadzu system with a SCL-10A system controller, a LC-10AD pump, a RID-6A refractive index detector, and a PLgel 5-μm Mixed-D column with chloroform, triethylamine, and 2-propanol (94:4:2) as eluent, and the column oven was set to 50 °C (polystyrene calibration).

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. The Z-average diffusion coefficient over the whole set of aggregates was calculated from the first cumulant, and the polydispersity (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 [20]. DLS data were also analyzed by the CONTIN routine, which is based on a constraint inverse Laplace transformation of the data and which gives access to a size distribution histogram for the aggregates [20]. 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 (high-frequency noncontact type, Nanosensors), with a resonance frequency of approximately 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.

Polymerizations

A solution of EtOx and methyl tosylate in dichloromethane was heated for the desired reaction time (calculated from the kinetic data described by Wiesbrock et al. [18]) at 140 °C under microwave irradiation. Subsequently, the polymerization mixture was cooled to 38 °C and, after the withdrawal of a small aliquot for analysis of the first block, neat SoyOx was added under inert atmosphere. In the next step, the polymerization was continued at 140 °C in the microwave synthesizer. The polymerizations were quenched by the addition of water. The resulting polymers were analyzed after drying and used without further purification. The statistical copolymer was made in a similar manner utilizing acetonitrile as solvent and one polymerization step at 140 °C in the microwave synthesizer.

Micellization

The investigated copolymers were initially dissolved in acetone at a concentration of 1 g/L. One milliliter of deionized water was then added dropwise to 1 mL of these solutions to trigger micellization. Subsequently, acetone

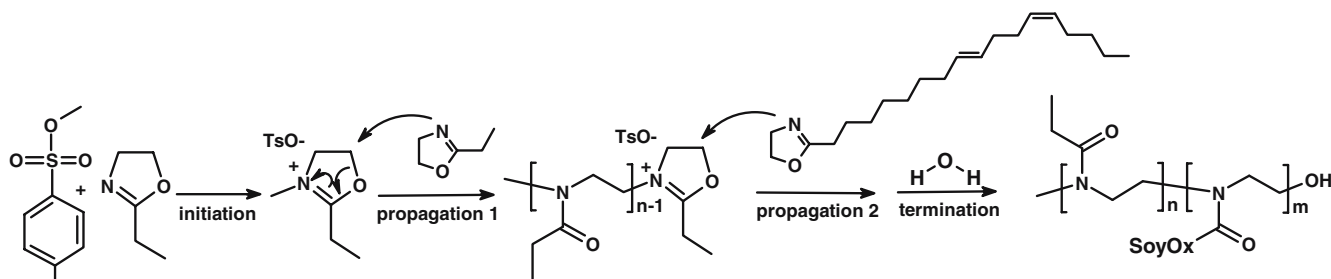
was gradually eliminated by dialysis against deionized water. Spectra-Por membranes with a molecular weight cut-off of 6,000–8,000 g/mol were used for the dialysis process. The concentration of the final micelles in pure water was then set to 0.2 g/L. The micellar solutions were filtered through 0.2- μm filters before the DLS measurements were made.

Results and discussion

Polymerization

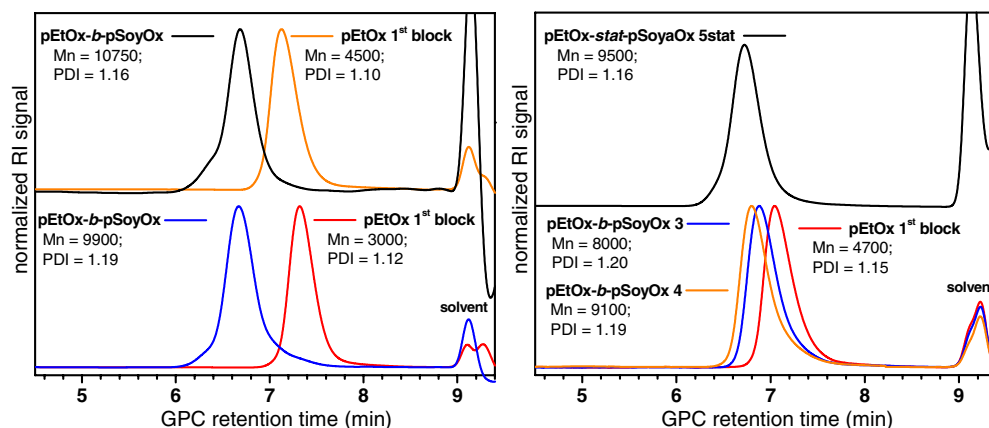
The cationic ring-opening polymerization of 2-oxazolines was first described in 1966 by four independent research groups [21–24]. Heating of an electrophile together with a 2-oxazoline monomer will result in the formation of a cationically charged oxazolinium species, as depicted in Scheme 1 for the polymerization of 2-ethyl-2-oxazoline with methyl tosylate as initiator. The next monomer will react with this oxazolinium species, resulting in the formation of the ring-opened poly(2-oxazoline). At the end of the polymerization, a second monomer can be added, resulting in the formation of a block copolymer as depicted in Scheme 1 for the addition of 2-“soy alkyl”-2-oxazoline (SoyOx). More specifically, amphiphilic block copoly (2-oxazoline)s are easily accessible by the combination of 2-methyl-2-oxazoline or 2-ethyl-2-oxazoline as hydrophilic block and 2-oxazolines with larger aromatic or aliphatic substituents as hydrophobic block [25–27]. Alternatively, to a second monomer, a nucleophile can be added to the mixture to quench the polymerization and/or to introduce a functional group. Under the appropriate polymerization conditions, all polymer chains will be initiated at the same time and they will grow with similar rates in the absence of chain transfer and chain termination reactions. As a result, polymers with narrow molecular weight distributions can be prepared via this living cationic ring-opening polymerization procedure {for a review on poly(2-oxazoline)s, see [28]}.

In this study, we were interested in the preparation of p(EtOx-*b*-SoyOx) with a large water-soluble part and a smaller hydrophobic part to investigate their self-assembly into micellar structures in water. However, in a first attempt, block copolymers 1 and 2 were synthesized with a short pEtOx block and a large pSoyOx block. The aim of these syntheses was to prepare block copolymers whose GPC traces are completely separated from the first pEtOx blocks, to prove their successful synthesis. The polymerizations were performed in dry dichloromethane (CH_2Cl_2) at 140 °C under microwave irradiation using methyl tosylate as initiator. CH_2Cl_2 was used as solvent because it dissolves pSoyOx better than the more common polymerization solvent, acetonitrile. After polymerization of the first pEtOx block, the SoyOx monomer was added under an argon atmosphere, followed by a second heating step to 140 °C. The resulting GPC traces of the first blocks and block copolymers 1 and 2 clearly demonstrate that all polymer chains were successfully chain-extended with SoyOx (Fig. 1, left). In the next step, amphiphilic block copolymers 3 and 4 were prepared with 68 EtOx units as first block and 11 or 18 SoyOx units as second block, respectively. These block copolymers 3 and 4 have a large water-soluble part and are expected to form micelles in water. The GPC traces of the first blocks and block copolymers 3 and 4 are depicted in the right panel of Fig. 1. Besides these p(EtOx-*b*-SoyOx) block copolymers, a p(EtOx-*stat*-SoyOx) 5stat statistical copolymer was prepared under similar polymerization conditions. This copolymer 5stat has a monomer composition comparable to block copolymer 4. The GPC trace of 5stat is also shown in the right panel of Fig. 1. The structural data, obtained by GPC and $^1\text{H-NMR}$ spectroscopy, for the four synthesized p(EtOx-*b*-SoyOx) block copolymers, 1–4, and the statistical copolymer, 5stat, are summarized in Table 1. The incorporated number of monomers from $^1\text{H-NMR}$ analysis is close to the theoretical number of monomers for all prepared copolymers. Moreover, the GPC data demonstrate that well-defined copolymers with narrow molecular weight distributions ($\text{PDI} \leq 1.20$) were obtained. The observed $M_{n,\text{GPC}}$ did not correspond with the theoretical M_n values due to the utilized polystyrene calibration. In conclusion, it was demonstrated that well-defined p(EtOx-



Scheme 1 Schematic representation of the two-step synthesis of p(EtOx-*b*-SoyOx) block copolymers using methyl tosylate as initiator

Fig. 1 GPC traces for the synthesized p(EtOx–SoyOx) copolymers and the corresponding pEtOx first blocks. *Left:* p(EtOx-*b*-SoyOx) 1 (*bottom*) and 2 (*top*). *Right:* p(EtOx-*b*-SoyOx) 3 and 4 (*bottom*) and p(EtOx-*stat*-SoyOx) 5stat (*top*). All measurements were performed with CHCl₃, NEt₃, and 2-PrOH (94:4:2) as eluent



SoyOx) copolymers can be prepared using microwave heating.

Micellization

The micellization of the three copolymers with high EtOx contents (3, 4, and 5stat) was investigated in detail. The copolymers were initially dissolved in acetone, which is a nonselective solvent for the constituent blocks, as ascertained by DLS. Following a previously reported micellization procedure [29, 30], water was added drop-wise under vigorous stirring to the initial polymer solution in acetone. Acetone was then eliminated by dialysis against water. This procedure has the advantage of erasing any memory effect from the bulk structure. The resulting micelles consist of a core containing the hydrophobic blocks (pSoyOx) and a corona comprising the hydrophilic blocks (pEtOx). Two parameters have been varied: (1) localization of the hydrophilic (EtOx) and hydrophobic (SoyOx) units among the copolymer chains, i.e., block vs statistical monomer distribution, and (2) the length of the hydrophobic block in the block copolymers, i.e., pSoyOx₁₁ vs pSoyOx₁₈, with a constant pEtOx₆₈ hydrophilic block. The micelles were analyzed by both DLS and AFM. DLS was used to obtain information about the hydrodynamic radius (R_h) of the micelles while morphological features were visualized by AFM. To avoid tip convolution effects

in AFM experiments, the diameter of the micelles was estimated by measuring the height of the micelles (D_z). The obtained DLS and AFM results are listed in Table 2. D_z is systematically smaller than R_h because AFM measurements were performed on micelles in the dried state. From both the DLS and AFM data in Table 2, it can be concluded that a larger pSoyOx block results in larger micelles when the pEtOx block length is constant. This relation between micelle size and hydrophobic block length was also expected from various theories and experimental data on block copolymer micelles [31]. For both block copolymers 3 and 4, spherical micelles were observed by AFM (Fig. 2a,b). Furthermore, the micelles of p(EtOx₆₈-*b*-SoyOx₁₁) 3 appear more blurry than the ones formed by the p(EtOx₆₈-*b*-SoyOx₁₈) 4, and they have a stronger tendency to form a continuous layer on the substrate.

The p(EtOx₇₅-*stat*-SoyOx₂₁) 5stat also resulted in the formation of spherical aggregates (Fig. 2c). This observation was rather unexpected because random copolymer chains should not a priori self-organize into a core-shell micellar structure. However, it should be noted that the reactivity ratios of EtOx and SoyOx are both higher than one ($k_1=1.4$; $k_2=1.7$) (full details about the determination of reactivity ratios will be published elsewhere). Therefore, the p(EtOx₇₅-*stat*-SoyOx₂₁) 5stat copolymer is not a purely random copolymer, but the monomers will be present in small clusters throughout the polymer chains. Actually, the presence of clusters of monomers most likely accounts for

Table 1 ¹H-NMR and GPC data for the synthesized p(EtOx-*b*-SoyOx) block copolymers 1–4 and the p(EtOx-*stat*-SoyOx) statistical copolymer 5stat

Polymer	DP _{EtOx,th}	DP _{SoyOx,th}	DP _{EtOx,NMR}	DP _{SoyOx,NMR}	wt. % SoyOx	M _{n,GPC}	PDI _{GPC}
1	30	30	30	23	70	9,900	1.19
2	50	25	45	21	58	10,750	1.16
3	70	10	68	11	32	8,000	1.20
4	70	20	68	18	44	9,100	1.19
5stat	75	25	75	21	46	9,500	1.16

Table 2 Characteristic features of the aqueous micelles formed by the investigated copolymers

Polymer	R_h (nm) _a	PDI _a	D_z (nm) _b
3	10	0.53	3.4
4	14	0.18	4.2
5stat	65	3.8	6.7

^aAs measured by DLS^b D_z is the height of the micelles as measured in the Z-direction by AFM

the observed micelle formation of p(EtOx₇₅-stat-SoyOx₂₁) 5stat. During the addition of water to the initial solution of the p(EtOx₇₅-stat-SoyOx₂₁) 5stat copolymer in acetone, a transient turbidity was observed. Such an observation is the signature of the so-called anomalous micellization process [32], in which the minority of copolymer chains that have a somewhat higher SoyOx content initially form particles during the addition of water. These initial particles are, in a later stage, stabilized by the copolymer chains with lower contents of SoyOx, which is the major component of the copolymer. This finally results in p(EtOx₇₅-stat-SoyOx₂₁) 5stat micelles that contain both high and low SoyOx content copolymer chains. These micelles are visualized in Fig. 2c. They are larger than the micelles formed by the p(EtOx₆₈-b-SoyOx₁₈) 4 copolymer, which is in agreement with the considerations described above. The R_h value associated with the p(EtOx₇₅-stat-SoyOx₂₁) 5stat micelles is much larger (Table 2), but it is certainly affected by the presence of larger particles, evidenced by the large PDI, that should strongly contribute to the scattered intensity.

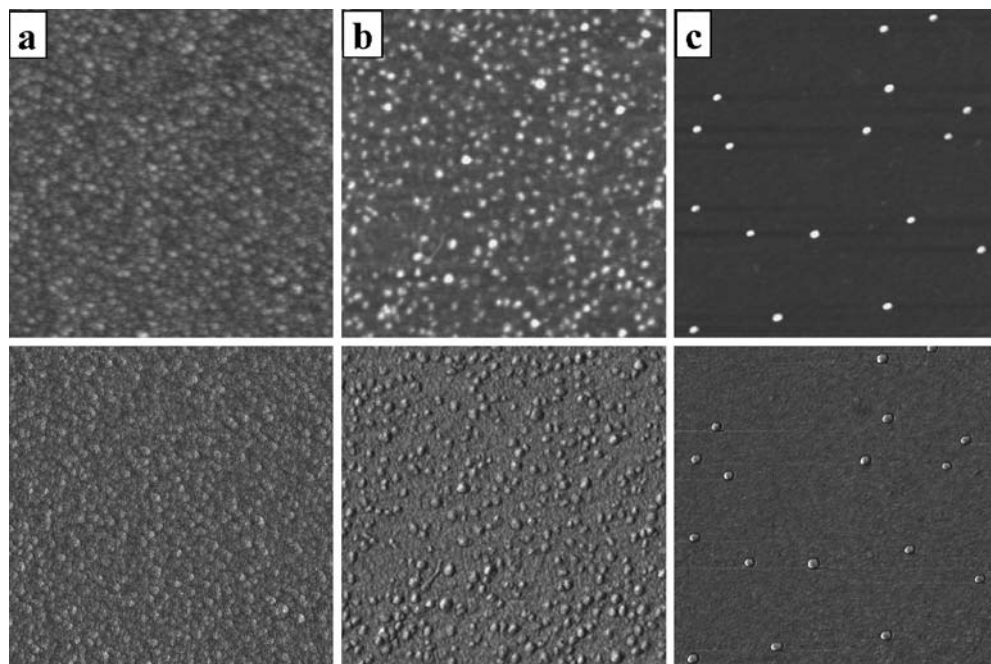
Therefore, the R_h value is overestimated compared to the actual size of the individual micelles shown in Fig. 2c.

Finally, it should be noted that the pSoyOx block is a good candidate to prepare aqueous core-cross-linked micelles because the pSoyOx block contains pendant double bonds. In a very recent paper, we have demonstrated that these double bonds can indeed be cross-linked when they are exposed to UV irradiation [33]. Moreover, the cross-linked micelles could be transferred back into acetone while keeping their integrity. Whenever the pSoyOx was only slightly cross-linked, the transfer in acetone resulted in the swelling of the core, and a morphological transition from spherical micelles to short rods (the so-called grain rice) was observed. This morphological transition was reversible, as demonstrated by several water-to-acetone and acetone-to-water solvent changes.

Conclusions

The microwave-assisted synthesis of p(EtOx-*b*-SoyOx) block copolymers, as well as that of a statistical copolymer, was successfully performed via a cationic ring-opening polymerization mechanism. GPC and ¹H-NMR spectroscopic analysis revealed the formation of well-defined polymers (PDI ≤ 1.20) with compositions close to the theoretical compositions. Moreover, GPC analysis of the first blocks and of the final block copolymers revealed quantitative chain-extension with the second SoyOx monomer. Micellization studies by DLS and AFM revealed the expected increase in micelle size with increasing length

Fig. 2 AFM pictures (1×1-μm images, *top*: height contrast, *bottom*: phase contrast) of the aqueous micelles formed by the p(EtOx₆₈-*b*-pSoyOx₁₁) 3 (a), p(EtOx₆₈-*b*-pSoyOx₁₈) 4 (b), and p(EtOx₇₅-stat-pSoyOx₂₁) 5stat (c) copolymers



of the hydrophobic block for the p(EtOx-*b*-SoyOx) block copolymers. In contrast, the micellization of the p(EtOx-*stat*-SoyOx) was not anticipated. Nevertheless, the clustered distribution of monomers throughout the polymer chain (corresponding to reactivity ratios higher than 1) most likely facilitates the micellization process. The micelles from this statistical copolymer are somewhat larger than the micelles from a block copolymer with a similar monomer composition.

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