Polymerized ABA Triblock Copolymer Vesicles
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The synthesis and the characterization of a poly(2-methyloxazoline)-block-poly(dimethylsiloxane)-block-poly(2-methyloxazoline) (PMOXA-PDMS-PMOXA) triblock copolymer carrying polymerizable groups at both chain ends are described. This copolymer forms vesicular structures in dilute aqueous solution, the size of which can be controlled in the range from 50 nm up to about 500 nm. The methacrylate end groups of the triblock copolymer can be polymerized in the vesicular aggregates using an UV-induced free radical polymerization. Static and dynamic light scattering, scanning electron microscopy, and transmission electron microscopy on both the resulting nanocapsules and their nonpolymerized precursors clearly show that the cross-linking polymerization does not lead to morphological changes in the underlying vesicles. Moreover, due to their cross-linked structure, the nanocapsules are shape persistent, thus maintaining their integrity even after their isolation from the aqueous solution.

Introduction

Due to their potential for the encapsulation of guest molecules into their interior, the preparation of hollow sphere structures with dimensions in the submicrometer range has found an increasing interest from both the fundamental and applied points of view.1 Usually, the controlled formation of such nanometer- or micrometer-sized structures can only be achieved by using templating techniques or self-assembly mechanisms.2-13

A typical example, known for more than 30 years, is the aggregation of individual lipid molecules in water into spherically closed lipid bilayers, i.e., vesicles or liposomes. In the meantime, these vesicular morphologies have found a multitude of applications in various scientific and applied fields.14

One major problem with these self-assembled structures is, however, their insufficient stability that induces, for example, a rapid clearance of drug-loaded vesicles from the blood after their intravascular administration.15 Nevertheless, this stability can be enhanced, for instance, by surface grafting of hydrophilic polymers13,15 or by polymerization of reactive lipid molecules in the vesicular aggregates.15 Recently, a similar mechanical stabilization of vesicles could also be obtained by swelling the lipid bilayer of vesicles with hydrophobic monomers, which were subsequently polymerized.6-10 This led to the formation of hydrophobic polymer hollow spheres, which could easily be modified chemically according to the desired application after their isolation from the surfactant matrix.

Other approaches for the preparation of nanometer- to micrometer-sized spherical polymer shells involve the layer-by-layer deposition of polyelectrolytes on the surface of a charged nanoparticle followed by the dissolution of the templating particle11 or the self-assembly of amphiphilic diblock copolymers into micelles, selective cross-linking of their hydrophilic shell, and subsequent degradation of the hydrophobic core.12 Although it has been known for several years that under suitable conditions amphiphilic block copolymers can aggregate spontaneously into vesicular structures,16,17 to our knowledge, this direct formation of aggregates with a hollow sphere morphology has only been used in one case to prepare polymer nanocapsules.13 This approach used, however, a rather complex process. The formation of vesicles from a poly(isoprene)-block-poly(2-cinnamoyl-ethyl methacrylate), PI-b-PCEMA, diblock copolymer in hexane was followed by the photo-cross-linking of the PCEMA blocks and subsequent selective hydroxylation of the PI blocks to make the hollow nanospheres soluble in water.13

Recently, the cross-linking polymerization of end-group functionalized amphiphilic ABA triblock copolymers in lyotropic mesophases has been reported.18-25 The reactive ABA triblock copolymers could be converted into a covalently cross-linked polymer network structure without changing the phase structure of the underlying

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mesophase. This has been attributed to the rather low dynamics of the large triblock copolymer molecules. As a result, the kinetics of the polymerization is much faster than that of eventually occurring phase transitions.

This led us to the idea that this concept could be used as a rather simple one-step procedure for the preparation of water-soluble nanocapsules. Similar to amphiphilic diblock copolymers, also suitable ABA triblock copolymers consisting of hydrophilic A blocks and a hydrophobic block B can self-assemble in water into vesicular structures. If the triblock copolymer carries additionally polymerizable groups at both ends, it should in principle be possible to achieve an intravesicular cross-linking of the individual polymer molecules to a nanocapsule through UV irradiation of the polymerizable end groups of the triblock copolymers.

In this paper we describe the synthesis of a poly(2-methyloxazoline)-block-poly(dimethylsiloxane)-block-poly-(2-methyloxazoline), PMOXA–PDMS–PMOXA triblock copolymer, carrying polymerizable methacrylate groups at both chain ends. This polymer forms vesicular structures in dilute aqueous solution, which can be polymerized to hollow nanospheres. Both the triblock copolymer vesicles and their polymerized counterparts are characterized by static and dynamic light scattering (SLS and DLS, respectively) and complementary transmission electron microscopy (TEM) and scanning electron microscopy (SEM) investigations.

**Experimental Section**

**Synthesis of Cross-Linkable Triblock Copolymers: General Procedure (See Scheme 1).** Bifunctional Poly(dimethylsiloxane) in a 250 mL round-bottom two-necked flask with a Soxhlet extractor (filled with molecular sieve (4 Å)), a condenser, and a septum on the second ground joint, 34.2 g (6.34 mmol) α,ω-bis(3-hydroxypropyl) poly(dimethylsiloxane) (1) (IM 15,
Wacker Chemie, additionally purified over a thin-film evaporator; \(M_r = 5400 \text{ g mol}^{-1}\) was dissolved in 90 mL of hexane and distilled under reflux for 17 h in a nitrogen atmosphere. After this drying procedure, the solution still contained 21 ppm water. Subsequently, the solution was concentrated to 60 mL of hexane, cooled to 0 °C, and 3.6 g (45.5 mmol) of dry pyridine was added. Then, 12.4 g (43.9 mmol) of trifluoromethanesulfonic acid anhydride was added over 15 min and the mixture was stirred for another 30 min at a temperature of 0 °C. After the addition of 20 mL of chloroform (water content < 10 ppm), the resulting suspension was filtered under vacuum using a 4 g glass filter funnel. The solvent was evaporated under high vacuum.

The yield was 21.5 g of oil of orange color. This oil was in turn dissolved in 40 mL of dry hexane, activated charcoal was added, and the mixture was then stirred for about 2 min and filtered again. After evaporation of the solvent, the yield was 19.0 g of clear colorless oil.

\(1^H\) NMR (CDCl3, 250 MHz): 0 ppm (CH3Si), 0.5 ppm (–CH2–CH2Si–), 1.8 ppm (–CH2–CH2–CH2–), 4.4 ppm (CF3SO2CH2–CH2–). Functionality was > 95% based on the \(1^H\) NMR data.

Poly(2-methyloxazoline)-block-poly(dimethylsiloxane)-block-poly(2-methyloxazoline) (PMOXA–PDMS–PMOXA) Triblock Copolymer with Free Hydroxy-End Groups. Freshly distilled chloroform (water content < 5 ppm) and 8.05 g (14.7 mmol) of the bifunctional PDMS (PDMS = poly(dimethylsiloxane)) were added to 15 mL of 1,2-dichloroethane (water content < 5 ppm) at room temperature. The solution was then stirred for 1.5 h and subsequently heated to 40 °C. After 48 h, the solution was cooled again to room temperature and 5.5 mL of a 0.5 M KOH solution in ethanol was added. The resulting solution was stirred for 1 h, and subsequently the solvent was evaporated under high vacuum. The yield was 12.0 g of colorless solid polymer.

\(1^H\) NMR (CDCl3, 250 MHz): 0 ppm (CH3Si), 2.0–2.1 ppm (CH2CON), 3.3–3.5 ppm (–N–CH2–CH2–N–), 4.4 ppm (CF3SO2CH2–CH2–). Functionality was > 95% according to OH titration (> 0.4 mequiv g\(^{-1}\)).

Gel permeation chromatography (GPC) in THF revealed a molecular weight of the triblock copolymer of \(M_r = 9000 \text{ g mol}^{-1}\) and a polydispersity of \(M_w/M_r = 1.7\). Consequently, the molecular weight of the poly(2-methyloxazoline) blocks was \(M_w = 1800 \text{ g mol}^{-1}\), respectively.

PMOXA–PDMS–PMOXA Triblock Copolymers with Polymerizable End Groups. In a round-bottom flask, 7.68 g (1.32 mmol) of the hydroxy-functionalized PMOXA–PDMS–PMOXA triblock copolymer was dissolved at room temperature in 20 mL of dry ethyl acetate (water content < 10 ppm). To this solution were added 420 mg (2.7 mmol) of 2-isocyanatoethylmethacrylate (IEM) and about 40 mg of dibutyltin dilaureate. The solution was stirred for 48 h in the absence of light. Afterward, the solution was evaporated under high vacuum for 5 h at a temperature of 0 °C. The raw product was purified using ultrafiltration in a water/ethanol mixture to remove low molecular weight impurities. A colorless solid polymer (6.89 g) was obtained.

\(1^H\) NMR (CDCl3, 250 MHz): 0 ppm (CH3Si), 2.0–2.2 ppm (CH2–CO), 3.3–3.5 ppm (–N–CH2–CH2–N–), 4.4 ppm (CF3SO2CH2–CH2–O–), 5.5 ppm (CH2=), 6.1 ppm (CH3=).

Functionality was > 95% according to \(1^H\) NMR.

**Vesicle Preparation.** The linear PMOXA–PDMS–PMOXA triblock copolymers exhibit lyotropic liquid crystalline phases in aqueous solutions. At room temperature, the polymer used in the present study showed a broad miscibility gap. The water content of the phase diagram, which extends up to about 50 wt % polymer. Above this concentration, the polymer could be achieved according to the following procedure: The end-group functionalized PMOXA–PDMS–PMOXA tri- block copolymer was dissolved in ethanoloat to yield a clear, homogeneous solution containing about 70 wt % polymer. This solution was added dropwise under vigorous stirring to the respective volume of doubly distilled water. The procedure leads to a dispersion of triblock copolymer vesicles of a rather broad size distribution. Similar to conventional liposomal molecules, the polydispersity could be considerably reduced by repeated extrusion of the vesicular dispersion through Nucleopore filters (Millipore) with defined pore size. Then, the resulting vesicle dimensions are directly determined by the pore diameter of the filter membrane, e.g., in the present case, a pore diameter of 200 nm yields vesicles with a diameter of approximately 250 nm.

Polymerization of the vesicles could be achieved by irradiating the dispersion for 15 min with an UV lamp (Ultrapet 400 W, \(\lambda = 254 \text{ nm}\), Osram AG). The conversion of the polymerization could be checked using \(1^H\) NMR investigations on the polymerized vesicles (which had been isolated from the aqueous phase by lyophilization and redissolved in CDCl3). The complete disappearance of the signal of the vinyllic protons of the methacrylic acid end groups within the experimental error indicates a conversion > 90%.

**Freeze-Fracture Replication Transmission Electron Microscopy.** A sample of approximately 10 mL of the vesicle dispersion was brought onto a gold platelet at room temperature and was quenched by hand plunging into a mixture of 15% 2-methylbutylate and 85% propane at 83 K. After quenching, the sample was transferred into liquid nitrogen and clamped on a brass block (Balzer). It was then mounted on a freeze-fracture device (BAF 300), and subsequently the pressure was reduced to 5 × 10^-7 mbar. After evaporation, the sample was fractured with a liquid nitrogen cooled microtome. To enhance the contrast of the surface structure, the sample was warmed to 153 K and etched for 10 min. Thereafter, the sample was cooled again with liquid nitrogen and shadowed with W/Ta under an angle of 30°. After several samples were evaluated at room temperature and brought to atmospheric pressure, the replica was washed with chloroform, put on a 400 mesh copper TEM grid, and examined with an Hitachi H-8000 electron microscope operating at 100 keV.

**Static and Dynamic Light Scattering (SLS and DLS, respectively).** The static and dynamic light scattering experiments were performed using a commercial goniometer (ALV-Langer) equipped with a frequency-doubled Nd:YAG laser (AirLas, AS, wavelength 532 nm) at scattering angles between 30° and 150°. An ALV-5000 E correlator calculates the photon intensity autocorrelation function \(g_2(t)\). The samples were prepared by filtering the solutions through Millipore filters (HN 0.45 µm) into 10 mm quartz cells. These cells were mounted in a thermostated optical matching vat with a temperature accuracy of \(T = 0.02 \text{ K}\). The experiments were performed at \(T = 293 \text{ K}\).

The refractive index increment \(dN/dc\) was obtained at the corresponding temperature and wavelength of the light scattering experiments by using a commercial ALV-DR-1 differential refractometer.

The data of DLS were analyzed using a Williams–Watts function.25–27 The size polydispersity of the vesicles was determined according to refs 28–30.

**Theoretical Background.** SLS from dilute solutions is usually described by the virial expansion

\[
\frac{K_c}{R(q)} = \frac{1}{M_w P(q)} + 2A_2 c + 3A_3 c^2 + \ldots
\]

with the scattering vector \(q = (4\pi/\lambda) \sin(\theta/2)\), where \(M_w \) is the weight-average molecular weight, \(P(q)\) the particle scattering factor, and \(A_i\) the ith virial coefficient.

The time-averaged scattered light intensity is expressed by \(K_cR(q)\), with an optical contrast factor \(K = [(4\pi n_\text{sol}^2/\lambda^2 N_\text{sol})/dn/dc] n_\text{sol}\), the refractive index of the solvent, \(c\) the concentration of the polymer solution, \(R(q)\) the Rayleigh ratio of the solution corresponding to the refractive index of the solvent, and \(\alpha(q)^2\) the scattering power of the controlling refractive index increment. At small angles, the particle scattering

factor can be expanded in a Taylor series, yielding

\[ P(q) = 1 - \frac{1}{3}q^2R_g^2 + \ldots \]  

(2)

with \( R_g \) the radius of gyration. Inserting eq 2 in 1 gives

\[ \frac{Kc}{D(0)} = \frac{1}{M_w(1 + \frac{1}{2}R_g^3q^2)} + 2A_2c + 3A_3c^2 + \ldots \]  

(3)

Measurements at several finite angle and concentrations can be extrapolated in a Zimm or a Berry plot\(^\text{31}\) and permit the determination of single particle properties such as \( M_w, R_g \), and \( A_2 \).

For a closed association, individual triblock copolymer molecules and aggregates coexist near the critical aggregation concentration (cac). Hence, the intensity of the scattered light can be represented as the sum of the intensities due to the respective component.\(^\text{32}\)

Assuming that \( A_2 \) is close to zero, the concentration of free triblock copolymer molecules \( c_o \) is equal to \( c_o = \text{cac} \) and that the aggregation number \( p \) of the triblock copolymer molecules in the vesicles is high, i.e., \( M_v \gg M_b \), with \( M_b \) being the weight-averaged molecular weight of the vesicles and \( M_v \) that of individual polymer molecules, \( Kc/R(0) \) can be written as

\[ \frac{Kc}{R(0)} = c - \frac{M_v(c - \text{cac})}{M_p\text{cac} + 1 + 2A_2M_v(c - \text{cac})} \]  

(4)

In DLS experiments, a time correlation function decaying in time is measured. From this, the cooperative translational diffusion coefficient \( D_m \) at a concentration \( c \) can be determined.

\[ D_m = D_0(1 + Kc) \]  

(5)

where \( D_m \) is a z-averaged cooperative translational diffusion coefficient and \( D_0 \) the diffusion virial coefficient. The extrapolation to zero concentration yields a diffusion coefficient \( D_0 \), which allows the calculation of the hydrodynamic radius \( R_h \) via the Stokes–Einstein equation.\(^\text{32}\)

Scanning Electron Microscopy (SEM). A drop of the nonextruded cross-linked vesicle dispersion in water was put on a silicon wafer. After evaporation of the water, the sample was examined with a Philips XL 30 SEM.

Transmission Electron Microscopy (TEM). The samples were prepared by negative staining of the cross-linked vesicle dispersion with 2% uranyl acetate solution. They were deposited on a carbon-coated copper grid and examined with a Philips EM 400.

Surface Tension Measurements. The surface tension \( \gamma \) of the polymerized and the nonpolymerized vesicle dispersions was determined with a Krüss K10 tension balance interfacial tensiometer thermostated at 25 °C using the Du-Noüy ring method. The critical aggregation concentration (cac) of the triblock copolymer dispersions was deduced from the discontinuity in the \( \gamma \) (in \( mN/m \)) curve and found to be \( 0.15 \times 10^{-3} \text{ g mL}^{-1} \) (or \( 1.6 \times 10^{-5} \text{ mol L}^{-1} \)) in agreement with the light scattering data. For the polymerized vesicles, no cac could be detected in the concentration regime investigated.

Results and Discussion

Similar to the previously reported procedures for the preparation of vesicular structures from amphiphilic diblock copolymers,\(^\text{13,16,17}\) the newly synthesized PMOXA–PDMS–PMOXA triblock copolymer could be converted into vesicles just by dilution of an ethanolic solution of the polymer with water. This led usually to a rather broad size distribution with vesicle diameters ranging from about 100 nm up to several 10 \( \mu \)m. The average size and the size distribution of the particles depend, however, considerably on both the initial concentration of the polymer in the organic solvent and the lengths of the individual hydrophilic and hydrophobic blocks of the polymer molecule.\(^\text{24}\)

Therefore, in the present study, we always started with a stock solution of 17 wt % of the PMOXA–PDMS–PMOXA triblock copolymer in ethanol which led to reproducible results upon dilution with water.

To get an idea about the influence of the subsequent free radical polymerization of the methacrylate end groups of the triblock copolymers within the aggregate on size and size distribution of the underlying vesicles, it is highly desirable to have a rather narrow size distribution. This could be achieved in this system—similar to conventional low molecular weight lipid vesicles\(^\text{21}\)—by repeated extrusions of the original vesicular dispersions of high polydispersity through Nucleopore filters of specific pore size. Then, the average diameter of the resulting vesicles is directly determined by the pore width of the filter membrane (see Experimental Section).

The polydispersity of the resulting vesicles was determined to be about 20% from dynamic light scattering, which is in good agreement with values reported for conventional extruded vesicles constituted from low molecular weight lipid molecules.\(^\text{28–30}\)

Figure 2 shows a freeze fracture replication electron micrograph of a sample of PMOXA–PDMS–PMOXA triblock copolymer vesicles prepared by extrusion through filters with a pore width of 200 nm. The figure clearly demonstrates that the preparation procedure yields spherical vesicles. The diameters of the displayed particles range from about 50 nm up to about 250 nm. This high polydispersity may be due to the fact that only vesicles with diameters significantly larger than the pore diameter of the filters are affected by the extrusion, while smaller vesicles can pass without being influenced. However, especially in view of the above-mentioned low polydispersity reflected in dynamic light scattering, it seems to be more reasonable to assume that the apparent polydispersity is a result of a restricted visibility of the vesicles which are partially buried in their matrix after fracture.

\( ^{31} \)Burchard, W. In Physical techniques for the study of food biopolymers; Ross-Murphy, S. B., Ed.; Blackie Academic and Professional: New York, 1994; p 151.

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Figure 3. Concentration profile of the static light scattering intensity (Kc/R(0)) by (●) nonpolymerized vesicles and (▲) cross-linked nanocapsules.

It has to be emphasized that, if stored in the dark to prevent their polymerization, the resulting PMOXA–PDMS–PMOXA tridock copolymer vesicles were stable over several weeks and displayed no changes in size or size distribution within experimental accuracy after this period.

The polymerization of the reactive methacrylate end groups of the PMOXA–PDMS–PMOXA tridock copolymers could be initiated thermally in the presence of a water-soluble initiator (e.g., K2S2O8), photochemically using a water-soluble photoinitiator (e.g., Irgacure 2959), or by UV irradiation of the vesicular dispersion. Since no measurable difference could be detected between the results of the various methods of polymerization, in the following are presented only the results of the UV-initiated free radical polymerization.

In the present system, every tridock copolymer carries two polymerizable groups. Consequently, the free radical polymerization within the aggregates is expected to lead to the formation of covalently cross-linked polymer network structures. As a result, the polymerized tridock copolymer vesicles should possess solid-state properties such as shape persistence and elasticity. In principle, this enables the resulting nanocapsules to be isolated from the aqueous solution under retention of their hollow sphere morphology.

The influence of the polymerization process on the properties of the tridock copolymer vesicles can be quantified using light scattering investigations. Light scattering studies on both the PMOXA–PDMS–PMOXA tridock copolymer vesicles and their polymerized counterparts were carried out in dilute aqueous solution in the concentration range below 2 wt% tridock copolymer.

Figure 3 shows a typical Zimm diagram. For dilute solutions only the extrapolated values at zero scattering angle are plotted. For the nonpolymerized tridock copolymer vesicles a minimum at about 1.7 × 10^{-3} \text{g mL}^{-1} was observed in the concentration dependence of static light scattering. Around this concentration, the radius of gyration $R_g$ exhibits a maximum. The mutual translational diffusion coefficient, $D_m$, shows a break in the slope of the concentration profile. This behavior is typical of a closed association, like in micelle formation where monomers aggregate up to a certain concentration.

In the present case, that means that there exists a critical aggregation concentration (cac) below which the vesicular aggregates disintegrate into singly dissolved tridock copolymer molecules. Details about the aggregates, i.e., the tridock copolymer vesicles can be obtained by extrapolating the measurements at $c > 2 \times 10^{-3} \text{g mL}^{-1}$. Similarly, extrapolation of the data in the region below the cac should yield information about the single tridock copolymer molecules. In the system under investigation like in most of the cases, this extrapolation was, however, not possible because of the extremely low scattering intensity of the solutions in this concentration range.

Assuming that near the cac, individual tridock copolymer molecules and vesicles coexist, the intensity of the scattered light can be represented as the sum of the intensities due to the respective components. As a result, (Kc/R(0)) can be written according to eq 3 (Experimental Section). A fit of the experimental data shows the critical aggregation concentration to be cac = 0.15 × 10^{-3} \text{g L}^{-1} (i.e., 1.6 × 10^{-5} \text{mol L}^{-1}). This value is comparable to that of typical low molecular weight lipids and depends significantly on the length of the individual hydrophilic and hydrophobic blocks of the tridock copolymer molecule. The occurrence of the cac at this concentration could also be confirmed by surface tension measurements on the vesicle dispersions.

Interestingly, this cac vanishes upon UV irradiation of the vesicle dispersions (see Figure 3). This is due to the UV-induced cross-linking polymerization of the methacrylate end groups of the tridock copolymer molecules. Obviously, the polymerization leads to a rather high conversion (see also Experimental Section). Consequently, all the tridock copolymer molecules are covalently attached to the newly formed polymer network structure within the vesicles and, hence, they are no longer able to leave the aggregate upon dilution.

The results of static and dynamic light scattering on both the polymerized and the nonpolymerized vesicles are summarized in Table 1. The system under investigation reveals no change in the average molecular weight, the dimensions, and the polydispersity of the aggregates upon polymerization. This reflects that the free radical polymerization occurs only intravesically: Intervesicle reactions such as intervesicular exchange of individual tridock copolymer molecules or a chain propagation reaction involving more than one vesicular aggregate would result in an increase of their average aggregation number $p$ (i.e., the molecular weight of the particles), particle dimensions, and size polydispersity of the vesicles. Hence they obviously play, at the best, only a minor role on the timescale of the experiment. It has to be emphasized that this behavior is generally confirmed also by other systems based on PMOXA–PDMS–PMOXA tridock copolymers of different molecular weight and composition. However, depending on the block length ratio, the vesicles display the tendency to shrink under preservation of their molecular weight. This seems to be a result of a steric contraction of the hydrophilic blocks during polymerization and will be discussed in detail in a forthcoming paper.

Furthermore, the light scattering data also support the hollow sphere morphology of the particles. The radius of gyration $R_g$ from static light scattering and the hydrodynamic radius $R_h$ from dynamic light scattering are found to be nearly identical for both the nonpolymerized and the polymerized tridock copolymer vesicles, thus leading to the ratio $p = R_g/R_h$ of $p = 1.008$ and $p = 1.097$, respectively. This so-called $p$-parameter is a structure-sensitive property reflecting the radial density distribution of the scattering particle. A ratio of $p = 1$ is characteristic for...
spherical shells. The observed slightly higher experimental values are due to the polydispersity of the vesicles.

The formation of vesicular aggregates from PMOXA–PDMS–PMOXA triblock copolymers is simply a consequence of their amphiphilic nature. The aggregation occurs via noncovalent interactions and, hence, is reversible. This is, for example, directly reflected in the occurrence of a cac. In contrast to that, the polymerized triblock copolymer vesicles are additionally held together by a covalently cross-linked polymer network structure. As a consequence, the resulting nanocapsules are shape persistent and preserve their hollow sphere morphology even after their isolation from the aqueous solution. This is directly documented in Figure 5 which displays SEM micrographs of large polymerized triblock copolymer vesicles formed by polymerization of a nonextruded vesicle dispersion. It has to be emphasized that these particles are in a dry state under high vacuum. In contrast to their nonpolymerized precursors, they clearly preserve their morphological integrity. It can be observed that, due to their hollow sphere structure, these particles are partially in a collapsed state similar to a deflated balloon (see Figure 4b, for a typical example). This collapse seems to depend, however, on the size of the individual vesicles since, especially, for smaller particles, no such collapsed structures could be detected from the SEM micrographs (see Figure 4a). If this is only a result of the limited resolution of the SEM, which prevents detailed visualization of such structures or if this collapse is indeed size dependent, has to be clarified in the future.

The shape persistence of these nanocapsules is, particularly in context with applications, of great interest. This stability of shape would allow, for example, to load the particles with hydrophobic guest molecules in an organic solvent, isolate the loaded polymer shells, and subsequently release the encapsulated material in an aqueous medium. Furthermore, the behavior of polymerized vesicles in organic solvents such as ethanol or chloroform, which are good solvents for both the PMOXA and the PDMS blocks, seems to be an additional test to prove the cross-linked nature of the individual vesicles. Only the polymerized particles are expected to preserve their characteristic dimensions also in organic solution. Nonpolymerized vesicles immediately disintegrate and dissolve as individual small triblock copolymer molecules.

In the system under investigation, the polymerized triblock copolymer vesicles could be isolated from the aqueous solution by lyophilization. In contrast to the nonpolymerized system, where this results in the formation of a waxy solid, the polymerized vesicle dispersions yield a fine colorless powder which could easily be redispersed in organic solvents (like chloroform or ethanol) or water.

Dynamic light scattering investigations on such redispersed nanocapsules in ethanol yield a hydrodynamic radius of \( R_h = 90 \text{ nm} \). This is in reasonably good agreement with the value of the original polymerized particles in water which was determined to be \( R_h = 113 \text{ nm} \). The size distribution of the particles, however, increases consider-

### Table 1. Results from Both Dynamic and Static Light Scattering Experiments Performed on Nonpolymerized and Cross-Linked Particles

<table>
<thead>
<tr>
<th>LS results</th>
<th>d(n/dc) (mL g(^{-1}))</th>
<th>cac (g mL(^{-1}))</th>
<th>(M) (10(^8) g mol(^{-1}))</th>
<th>(A_2) (mol mL(^{-2}))</th>
<th>(R_G) (nm)</th>
<th>(D_0) (10(^{-8}) cm(^2) s(^{-1}))</th>
<th>(R_h) (nm)</th>
<th>(k_d) (mL g(^{-1}))</th>
<th>p</th>
<th>(\rho)</th>
</tr>
</thead>
<tbody>
<tr>
<td>vesicles in water</td>
<td>0.188</td>
<td>0.15 \times 10(^{-3})</td>
<td>1.1</td>
<td>2 \times 10(^{-6})</td>
<td>127</td>
<td>1.7</td>
<td>126</td>
<td>18</td>
<td>12200</td>
<td>1.008</td>
</tr>
<tr>
<td>cross-linked particles in water</td>
<td>0.187</td>
<td>no</td>
<td>1.1</td>
<td>2 \times 10(^{-6})</td>
<td>124</td>
<td>1.9</td>
<td>113</td>
<td>24</td>
<td>12200</td>
<td>1.097</td>
</tr>
</tbody>
</table>

\(\alpha\); refractive index increment; cac, critical aggregation concentration; \(M\), weight-average molecular weight; \(A_2\), second virial coefficient; \(R_G\), radius of gyration; \(D_0\), diffusion coefficient; \(R_h\), hydrodynamic radius; \(k_d\), diffusion virial coefficient; \(p\), aggregation number with \(p = \frac{M}{M_p}; \rho\), \(\rho\)-parameter with \(\rho = \frac{R_h}{R_G}\).

Figure 4. (a) Scanning electron micrograph (SEM) of nonextruded polymerized triblock copolymer vesicles in a dry state, particle with a diameter of approximately 500 nm showing a nearly spherical structure characteristic of smaller hollow spheres. (b) Scanning electron microgram (SEM) of nonextruded polymerized triblock copolymer vesicles in a dry state, particle with a diameter of approximately 2 \(\mu\)m showing the characteristic collapsed structure of larger hollow spheres.
113 nm, see Table 1). The presence of a considerable amount of smaller particles and no larger ones supports our assumption of an ice crystal mediated disrupture of the particles.

**Conclusions**

Similar to the recently reported amphiphilic diblock copolymers, also suitable ABA triblock copolymers consisting on water soluble A-blocks and a hydrophobic B-block can self-assemble in water to vesicular structures. The PMOXA-PDMS-PMOXA triblock copolymer of the present study can be regarded as a typical example for this. With this triblock copolymer, vesicles could be prepared with controlled diameters in the range of 50 nm up to about 500 nm applying conventional extrusion techniques. It is straightforward that this dimensional range can also be extended to larger structures, e.g., by variation of the chemical constitution or the block-length ratio of the underlying polymer molecules.

This self-assembly of the triblock copolymers is a basic requirement for the controlled formation of polymer nanocapsules. Similar to the well-known polymerization of reactive low molecular weight lipids in their aggregates, also the amphiphilic triblock copolymers can be chemically modified with polymerizable groups. The free radical polymerization of the methacrylate end groups of the PMOXA-PDMS-PMOXA triblock copolymer in the vesicular aggregates leads to the formation of polymer nanocapsules. During this rather simple preparation procedure, the individual triblock copolymers are covalently linked together to a polymer network structure. Due to their cross-linked structure, the polymer hollow spheres are shape persistent, which allows their isolation from the aqueous solution under preservation of their morphological integrity. The isolation of the nanocapsules using lyophilization seems, however, not well suited for the system since it leads to a considerable disrupture of the structures.

Hence, we believe that these new polymer nanocapsules possess great potential for encapsulation and controlled release of guest molecules in/from their interior, especially since the controlled formation of these structures can be achieved rather easily and the physical properties of their polymer shells can be directly controlled by the chemical constitution and the composition of the underlying triblock copolymer. This would allow to adapt, for example, the permeability of the nanocapsules to the desired application. Nevertheless, in this context, clearly more information is needed about the properties of these polymer nanocapsules, which are beyond the goal of this paper and, hence, will be reported in the future.

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