Synthesis, Characterization, and Visualization of High-Molecular-Weight Poly(glycidol-*graft*-ϵ-caprolactone) Starlike Polymers

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ABSTRACT: High-molecular-weight polymers with defined architectures are generally prepared by atom transfer radical polymerization. In order to prepare biodegradable structures different polymerization techniques have to be used. Here we present the successful synthesis of biodegradable starlike poly(glycidol-*graft*-ϵ-caprolactone) copolymers by a combination of anionic and coordinative ring-opening polymerization, their characterization by static and dynamic light scattering and their visualization by scanning force microscopy.

Introduction

High-molecular-weight macromolecules with controlled architectures have become a well-established research topic, because of their potential application as rheology modifiers, their use to control crystallization characteristics, morphology and mechanical performance, and their potential for intramolecular nanoengineering.[1−4] A lot of work in this area has been performed on the synthesis of well-defined cylindrical brushes, by the use of atom transfer radical polymerization. A large variety of different structures has been synthesized, such as AB-type-brush-*block*-brush copolymers, brushes with block copolymer side chains or with gradient in grafting density and multiarm molecular brushes.[5−9] The synthesis of high-molecular-weight starlike macromolecules involving atom transfer radical polymerization has also been described.[10,11] The characterization of these polymers by conventional methods like NMR and SEC is often difficult due to their high molecular weights. In this respect, atomic force microscopy has become a valuable tool, as the direct topology visualization of individual polymers confirms the successful synthesis of the architecturally complex structures.[9,11,12]

So far, high-molecular-weight polymers with defined architectures are mostly prepared via ATRP. With this method, however, only vinyl polymers are obtained, which are not (bio)degradable, due to the C−C bonds in the main chain. It would be desirable to prepare degradable high-molecular-weight polymers with defined architectures, that can be used for example in drug delivery systems targeting tissue with large pores, such as cancer tumors.[13] In order to prepare polymers with different compositions, thus with different properties, it is essential to investigate the use of different polymerization techniques. Here the synthesis of high-molecular-weight multiarm starlike macromolecules is performed by a combination of anionic and coordinative ring-opening polymerization.

For the synthesis of star-shaped polymers two major strategies are employed. The "arm-first" approach consists of the quenching of living chains with a multifunctional coupling agent in the final step of the reaction or the termination of the living chains with multifunctional vinyl compounds and subsequent cross-linking. In the "core-first" approach, multifunctional initiators are used to grow arms by controlled polymerization methods. For example, multiarm poly(ϵ-caprolactone) star copolymers have been synthesized by ring-opening polymerization of ϵ-caprolactone using hyperbranched polyglycerol or poly(ethylene imine) as multifunctional initiator.[14,15] In contrast to hyperbranched polyglycerol, linear polyglycidol has a well-defined structure and possesses only primary hydroxy groups.[16,17] In previous work, it was shown that the primary hydroxy groups of polyglycidol effectively initiate the polymerization of ϵ-caprolactone catalyzed by $Sn(oct)_2$.[18] According to this procedure high-molecular-weight poly(glycidol-*graft*-ϵ-caprolactone) stars were prepared by a combination of anionic polymerization of protected glycidol, followed by coordinative ring-opening polymerization of ϵ-caprolactone. Star copolymers were characterized by light scattering and visualized by AFM.

Experimental Part

Materials. ϵ-Caprolactone (CL, ≥99%, Fluka) was stirred with CaH_2 for 24 h, distilled under reduced pressure and kept in a Schlenk flask under nitrogen till use. *tert*-Butoxide (1 M solution in THF, Aldrich), and tin(II) 2-ethyl hexanoate ($Sn(oct)_2$, 97%, ABCR) were used as received. Diglyme was distilled over sodium. Tetrahydrofuran was distilled over potassium. Ethoxy ethyl glycidyl ether (EEGE) was synthesized from 2,3-epoxypropan-1-ol (glycidol) and ethyl vinyl ether according to Fitton et al. and purified by distillation.[19] A fraction with a purity exceeding 99.8 GC% was used.

All reactions were carried out in nitrogen atmosphere. Nitrogen (Linde, 5.0) was passed over molecular sieves (4 Å) and finely distributed potassium on aluminum oxide.

Syntheses. *Poly(ethoxy ethyl glycidyl ether), P(EEGE) (**1** and **2**). Synthesis of P(EEGE) **2**.* *tert*-Butoxide (0.23 mL of a 1 M solution in THF, 0.23 mmol), ethoxy ethyl glycidyl ether (8.0 g, 55 mmol) and tetrahydrofuran (8 mL) were introduced into a Schlenk flask and stirred for 48 h at 60 °C. The solvent was removed at 50 °C in vacuo and a viscous liquid was obtained. $M_{n,SEC}$ = 25200, M_w/M_n = 1.13. ^{1}H NMR (DMSO-d_6): δ 1.09 (tr, J = 7.0 Hz, CH_2CH_3), 1.18 (d, J = 5.2 Hz, $CHCH_3$), 3.30−3.70 (m, $CH_2CH(CH_2O)O$, OCH_2CH_3), 4.64 (d, J = 5.0 Hz, OCHO). ^{13}C NMR (DMSO-d_6): δ 15.1 (CH_2CH_3), 19.6 ($CHCH_3$), 27.1 (CCH_3), 60.1 (CH_2CH_3), 64.6 ($CH_2CH(CH_2O)O$), 69.4 ($CH_2CH(CH_2O)O$), 78.3 ($CH_2CH(CH_2O)O$), 99.1 ($CHCH_3$). The synthesis of P(EEGE) **1** was performed in diglyme at 120 °C for 16 h. $M_{n,SEC}$ = 3600, M_w/M_n = 1.09.

*Polyglycidol, PG (**1′** and **2′**).* P(EEGE) ***1*** was dissolved in tetrahydrofuran (110 mL/1 g polymer) and aqueous 32% HCl (3.3 g/1 g of polymer) was added. Polyglycidol **1′** precipitated as an oil. The solvent was removed and polyglycidol was dried

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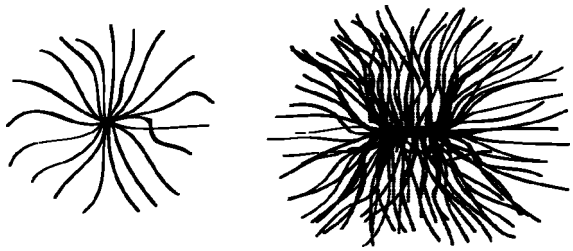

Figure 1. Schematic representation of the high-molecular-weight poly(glycidol-*graft*-ϵ-caprolactone) starlike copolymers.

in vacuo at 80 °C. ^{1}H NMR (DMSO-d_6): δ 3.45−3.95 (m, $CH_2CH(CH_2OH)O$), 4.53 (s, O*H*). ^{13}C NMR (DMSO-d_6) (end group signals are marked with an E): δ 60.9, 63.0^E ($CH_2CH(CH_2OH)O$), 69.3, ($CH_2CH(CH_2OH)O$), 70.7^E, 80.0 ($CH_2CH(CH_2OH)O$), 81.8^E ($HOCH_2CH(CH_2OH)O$). PG **2′** was obtained according to the same procedure.

*Poly(glycidol-graft-ϵ-caprolactone), P(G-graft-CL) (**3** and **4**). Synthesis of P(G-graft-CL) **3**.* Polyglycidol **1′** (5.8 mg, 2.6 μmol) and ϵ-caprolactone (3.03 g, 26.5 mmol) were heated to 130 °C. Sn(oct)$_2$ (8 mg, 20 μmol) was added and the mixture was stirred for 20 h at 130 °C. The polymerization was stopped by adding methylene chloride and the polymer was isolated by precipitation in pentane. After drying in vacuo a fibrous polymer was obtained. ^{1}H NMR ($CDCl_3$): δ 1.32−1.46 (m, $CH_2CH_2CH_2$), 1.58−1.76 (m, $CH_2CH_2CH_2$), 2.31 (tr, J = 7.5 Hz, $OCOCH_2CH_2$), 3.65 (tr, J = 6.5 Hz, CH_2CH_2OH), 4.06 (tr, J = 6.7 Hz, CH_2CH_2OCO). ^{13}C NMR ($CDCl_3$): δ 24.6 ($OCOCH_2CH_2$), 25.5 ($CH_2CH_2CH_2$), 28.4 (CH_2CH_2OCO), 34.1 ($OCOCH_2CH_2$), 64.1 (CH_2CH_2OCO), 173.6 ($OCOCH_2CH_2$) (the peaks of the polyglycidol backbone are not distinguishable from the noise of the baseline).

*Fractionated P(G-graft-CL). (**3**^{FP}, **4**^{FP}). Fractionation of P(G-graft-CL) **3**.* An amount of 1.5 g polymer was dissolved in 180 mL of chloroform. Methanol was slowly added at 40 °C under stirring. When the first opacity was observed, the solution was cooled to 4 °C and the precipitated fraction isolated by decantation. The decantated solution was subjected to the same procedure again. That way, several fractions of P(G-*graft*-CL) **3** were collected and analyzed by SEC. The fractions containing only low-molecular-weight species were discarded. All fractions containing high-molecular-weight polymer were dissolved in dichloromethane and united to one solution. P(G-*graft*-CL) **3**^{FP} was obtained by precipitation in pentane and drying in vacuo. Yield: 46%. P(G-*graft*-CL) **4** was fractionated following the same procedure. Yield for P(G-*graft*-CL) **4**^{FP}: 42%.

Measurements. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-300 spectrometer at 300 and 75 MHz, respectively. Deuterated chloroform ($CDCl_3$) or deuterated dimethyl sulfoxide (DMSO-d_6) were used as a solvent, and tetramethylsilane served as internal standard.

SEC analyses were carried out at 35 °C using a high-performance liquid chromatography pump (ERC HPLC 64200) and a refractive index detector (ERC-7215a). The eluting solvent was tetrahydrofuran (HPLC grade) with 250 mg·L^{-1} 2,6-di-*tert*-butyl-4-methylphenol and a flow rate of 1 mL·min^{-1}. Five columns with MZ gel were applied. The length of the first column was 50 mm and of the four other columns it was 300 mm. The diameter of each column was 8 mm, the diameter of the gel particles 5 μm, and the nominal pore widths were 50, 50, 100, 1000 and 10000 Å, respectively. Calibration was achieved using narrow distributed poly(methyl methacrylate) standards.

Preparative SEC was carried out using a high-performance liquid chromatography pump (Jasco HPLC 2087-PU) and a refractive index detector (Jasco 2031-RI). The same eluting solvent as for SEC analyses and a flow rate of 3 mL·min^{-1} was used. Two columns with MZ gel were applied. The length of the columns was 50 mm and 300 mm, respectively. The diameter of each column was 20 mm, the diameter of the gel particles 10 μm, and the nominal pore widths were 10^3 and $50-10^6$ Å (linear), respectively.

Static light scattering (SLS) experiments were carried out on a modified Sofica goniometer (SLS Systemtechnik, Denzlingen) equipped with a He−Ne laser (λ_0 = 543 nm) as a light source. Measurements were performed in the angle range from 25° to 145° with a step of 5°. For calculation of the weight-average molecular weight of the starlike polymers, the refractive index increment (dn/dc) value of pure poly(ϵ-caprolactone) in chloroform, equal to 0.06 mL·g,[20] was used, due to the minimal contribution of the polyglycidol block to the total polymer molar mass. SLS data were analyzed with Berry's method.

Dynamic light scattering (DLS) experiments were performed using two apparatus. In most of the measurements multiangle ALV spectrometer equipped with an ALV/CGS8 goniometer, ALV-5000 correlator and a solid state laser (Koheras, λ_0 = 473 nm) was used. The second-order time-averaged autocorrelation functions of scattered intensity were measured in a range of scattering angles between 40° and 100° with a step of 5° and analyzed with a method of cumulants. Characteristic decay rate Γ of the autocorrelation functions was plotted against squared scattering vector q, defined as $(4\pi n_0/\lambda_0)\sin(\theta/2)$, to confirm the diffusive character of the polymer motion in solution. Values of the apparent hydrodynamic radius ($R_{h,app}$), measured at different concentrations, were extrapolated to $c \rightarrow 0$.

In some experiments a Nano Zetasizer (Malvern) spectrometer with a He−Ne laser (λ_0 = 633 nm) was used. In that case, backscattered light was detected at the angle of 173°, giving the apparent hydrodynamic radius and distribution of the apparent hydrodynamic radius. All measurements were performed at 25 °C. Prior to the light scattering measurements the samples were filtered using Millipore Teflon filters with a pore size of 0.45 μm for P(G-*graft*-CL) **3**^{FP} (fractionated by precipitation) and 1 μm for P(G-*graft*-CL) **4**^{PS} (fractionated by precipitation and preparative SEC).

The samples for scanning force microscopy (SFM) measurements were prepared by solvent casting from a dilute solution of the polymer in toluene, with a weight concentration of $10^{-4}-10^{-5}$ g·L^{-1}, onto a mica surface. The SFM images were taken with a Nanoscope III operated in tapping mode. The measurements were performed at ambient conditions using Si cantilevers with a spring constant of ca. 42 N/m and a resonance frequency of about 320 kHz.

Results and Discussion

The high-molecular-weight starlike macromolecules are synthesized by the "core-first" approach using linear polyglycidol as multifunctional macroinitiator. As each repeating unit bears a primary hydroxy group, it is an ideal precursor for the "grafting from" reaction by Sn(oct)$_2$ catalyzed ring-opening polymerization of ϵ-caprolactone. By using two polyglycidols with different degrees of polymerization and by choosing a high [CL]/[OH] ratio starlike copolymers as depicted in Figure 1 are obtained. In order to confirm the successful synthesis, the poly(glycidol-*graft*-ϵ-caprolactone) stars are characterized by static and dynamic light scattering in solution and their topography is visualized by atomic force microscopy.

Polyglycidol. Polyglycidol was synthesized by polymerization of ethoxy ethyl glycidyl ether with potassium *tert*-butoxide as initiator and subsequent removal of the protection group (Scheme 1).

Two different monomer to initiator ratios were applied. In Table 1 the [M]/[I] ratios, the monomer conversion, the molecular weights, and the polydispersity indices of P(EEGE) **1** and **2** are listed.

Monomer conversion was determined from the ^{1}H NMR spectrum of samples before workup. The theoretical molecular weight and degree of polymerization was calculated from the monomer to initiator ratio and the monomer conversion. Number

Scheme 1. Synthesis of P(EEGE) 1 and 2, and Subsequent Removal of the Protection Group under Acidic Conditions Leading to the Corresponding Polyglycidols 1′ and 2′

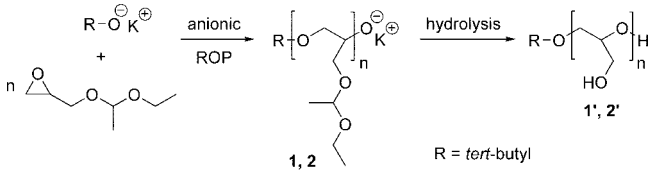

Table 1. [M]/[I] Ratios, Monomer Conversion, Molecular Weights, and Polydispersity Indices of P(EEGE) 1 and 2

					SEC[d]	
P(EEGE)	[M]/[I][a]	convn[b] [%]	$M_{n,calc}$[c]	$DP_{n,calc}$[c]	M_n	M_w/M_n
1	24	100	3600	24	3600	1.09
2	240	82	28800	197	25200	1.13

[a] Monomer to initiator ratio in the feed. [b] Ethoxy ethyl glycidyl ether conversion. [c] Molecular weight (M_n) and degree of polymerization calculated from the [M]/[I] ratio and the monomer conversion. [d] Molecular weight (M_n) and polydispersity indices (M_w/M_n) determined by size exclusion chromatography (SEC) using narrow distributed poly(methyl methacrylate) standards and tetrahydrofuran as eluent.

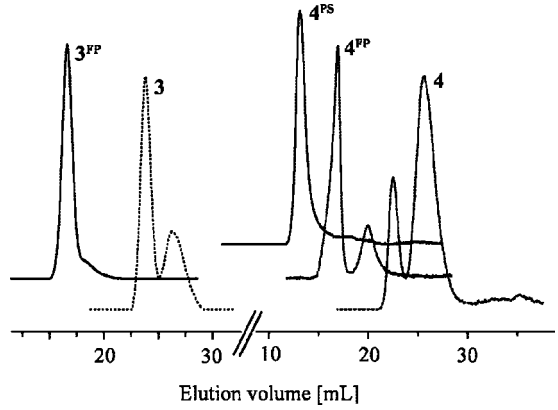

Figure 2. SEC traces of P(G-*graft*-CL) **3** and **4**, of P(G-*graft*-CL) $\mathbf{3^{FP}}$ and $\mathbf{4^{FP}}$ purified by fractionated precipitation, and of P(G-*graft*-CL) $\mathbf{4^{PS}}$ purified by preparative SEC.

average molecular weights are only relative values as they are determined using poly(methyl methacrylate) standards, but they are in agreement with the calculated values. For both polymers low polydispersity indices are obtained. Acid catalyzed removal of the protecting groups from P(EEGE) **1** and **2** leads to the corresponding polyglycidols **1′** and **2′**. Complete removal of the protecting groups was confirmed by the disappearance of the signals from the ethoxy ethyl groups in the ^{1}H NMR spectrum.

High-Molecular-Weight Poly(glycidol-*graft*-ϵ-caprolactone). The previously synthesized polyglycidols **1′** and **2′** were used as macroinitiators for the "grafting from" reaction of ϵ-caprolactone catalyzed by Sn(oct)$_2$ (Scheme 2). The ratio of ϵ-caprolactone to initiating hydroxy groups in the feed was 340.

The reaction was performed in bulk at 130 °C. After precipitation in pentane and drying in vacuo, the polymers were obtained as white fibrous solids. The monomer conversion was determined by ^{1}H NMR from samples before workup and reached ca. 96% in both cases. SEC elution curves of the synthesized P(G-*graft*-CL) copolymers **3** and **4** showed two peaks (Figure 2).

The peak observed in the low molecular weight region is attributed to the presence of homopolymer/linear PCL. The raw P(G-*graft*-CL)s **3** and **4** were purified by fractionated precipitation. The P(G-*graft*-CL) copolymers obtained after fractionated precipitation are named $\mathbf{3^{FP}}$ and $\mathbf{4^{FP}}$, respectively. SEC analysis confirmed nearly complete removal of the low molecular weight fraction for P(G-*graft*-CL) $\mathbf{3^{FP}}$ (Figure 2). SEC analysis of the discarded fractions (not shown) revealed that only homopolymer was removed. Thus, the yield of P(G-*graft*-CL) $\mathbf{3^{FP}}$ (46%) corresponds roughly to the grafted ϵ-caprolactone. Previously, it was shown that initiation efficiency of the polyglycidol hydroxy groups reached 90% upon grafting of short PCL chains ($DP_n \approx 4$).[21] Therefore, it is assumed that grafting efficiency is close to 100%. Thus, the degree of polymerization of the poly(ϵ-caprolactone) grafts can be estimated from the [M]/[I] ratio in the feed: $DP_{n,PCL} = 340 \times 0.46 \approx 150$. For the fractionated P(G-*graft*-CL) $\mathbf{4^{FP}}$ SEC traces showed, that a small amount of the homopolymer remained after fractionated precipitation. For further characterization, P(G-*graft*-CL) $\mathbf{4^{FP}}$ was additionally subjected to preparative SEC, to remove the remaining homopolymer. The high-molecular-weight P(G-*graft*-CL) obtained by preparative SEC was named $\mathbf{4^{PS}}$ and its SEC elution curve was monomodal (Figure 2).

The NMR spectra of the purified P(G-*graft*-CL) copolymers $\mathbf{3^{FP}}$ and $\mathbf{4^{PS}}$ only showed the signals of poly(ϵ-caprolactone). Due to the high ratio of repeating units to end groups and the overlaying of the CH_2OH end group signal of the poly(ϵ-caprolactone) chains and the signal of the polyglycidol backbone, the degree of polymerization of the side chains and the molecular weight of the star polymers could not be determined by end group analysis from the ^{1}H NMR spectrum.

For further characterization, P(G-*graft*-CL) starlike copolymers $\mathbf{3^{FP}}$ and $\mathbf{4^{PS}}$ were analyzed by SEC, static and dynamic light scattering. Molecular weights, polydispersity indices, radii of gyration, second virial coefficients A_2, and hydrodynamic radii are listed in Table 2.

The molecular weights determined by SEC are only relative values, because they are measured against linear PMMA standards. In order to determine the absolute weight average molecular weight, static light scattering measurements were performed in chloroform. As the polyether backbone is negligible one can assume that only PCL side chains contribute to the molar mass of the whole copolymer and in consequence to its refractive index increment value. However, due to the low d*n*/d*c* value of PCL in chloroform, (0.06 mL·g^{-1})[20] it was not possible to get reliable light scattering data for the small star P(G-*graft*-CL) $\mathbf{3^{FP}}$; therefore, its molecular weight, radius of gyration, and the second virial coefficient A_2 could not be determined. Figure 3 shows typical SLS data for copolymer P(G-*graft*-CL) $\mathbf{4^{PS}}$.

The weight-average molecular weight $M_w = 3.22$ MDa, the second virial coefficient $A_2 = 1.40 \times 10^{-5}$ mL·mol·g^{-2}, and the radius of gyration $R_g = 52$ nm of P(G-*graft*-CL) $\mathbf{4^{PS}}$ were calculated from the concentration and angular dependency of excessed Rayleigh ratio by means of Berry approximation. Similarly, $A_2 = 1.59 \times 10^{-5}$ mL·mol·g^{-2} was reported for poly[styrene-*block*-(*tert*-butylacrylate)Br] stars with $M_w = 3.68$ MDa.[7]

For a polymer chain in a good solvent the relationship between A_2 and M_w is given by eq 1[22]

$$A_2 = \frac{4}{3}\pi N_A \frac{R^3}{M_w^2} \quad (1)$$

or more generally[23]

$$A_2 \propto M_w^{-a} \quad (2)$$

where N_A is the Avogadro constant, R is a characteristic dimension of the macromolecule, and $-a$ is an exponent equal to $(3/d_f) - 2$ with d_f being a fractal dimension.

With $R = R_g$ and $R = R_h$ (Table 2), one obtains values of the second virial coefficients equal to 3.42×10^{-5} mL·mol·g^{-2} and 1.40×10^{-4} mL·mol·g^{-2}, respectively. Thus, A_2 measured for P(G-*graft*-CL) $\mathbf{4^{PS}}$ is in accordance with the calculated

Scheme 2. $Sn(oct)_2$ Catalyzed Ring-Opening Polymerization of ϵ-Caprolactone with Polyglycidols 1′ and 2′ as Macroinitiators Leading to P(G-*graft*-CL) 3 and 4, Respectively

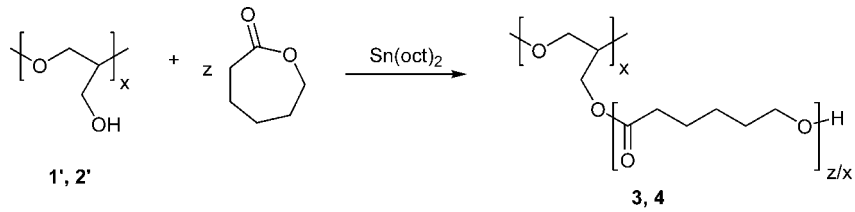

Table 2. Molecular Weights, Polydispersity Indices, Radii of Gyration, Second Virial Coefficients A_2, and Hydrodynamic Radii of the P(G-*graft*-CL) Copolymer 3^{FP} Purified by Fractionated Precipitation and of the P(G-*graft*-CL) Copolymer 4^{PS} Purified by Preparative SEC

	SEC[a]		SLS[b]			DLS[c]	
polymer	$M_w \times 10^6$ [g·mol^{-1}]	M_w/M_n	$M_w \times 10^6$ [g·mol^{-1}]	R_g [nm]	A_2 [mL·mol·g^{-2}]	R_h [nm]	$R_{h,app.}$ [nm]
3^{FP}	0.47	1.48					25
4^{PS}	1.41	1.40	3.22	52	1.40×10^{-5}	83	95

[a] Weight average molecular weight (M_w) and molecular weight distribution (M_w/M_n) determined by size exclusion chromatography (SEC) using narrow distributed poly(methyl methacrylate) standards and tetrahydrofuran as eluent. [b] M_w, radius of gyration (R_g) and second virial coefficient (A_2) measured by static light scattering. [c] Hydrodynamic radius (R_h) measured by dynamic light scattering and apparent hydrodynamic radius ($R_{h,\ app.}$) measured with a Nano Zetasizer.

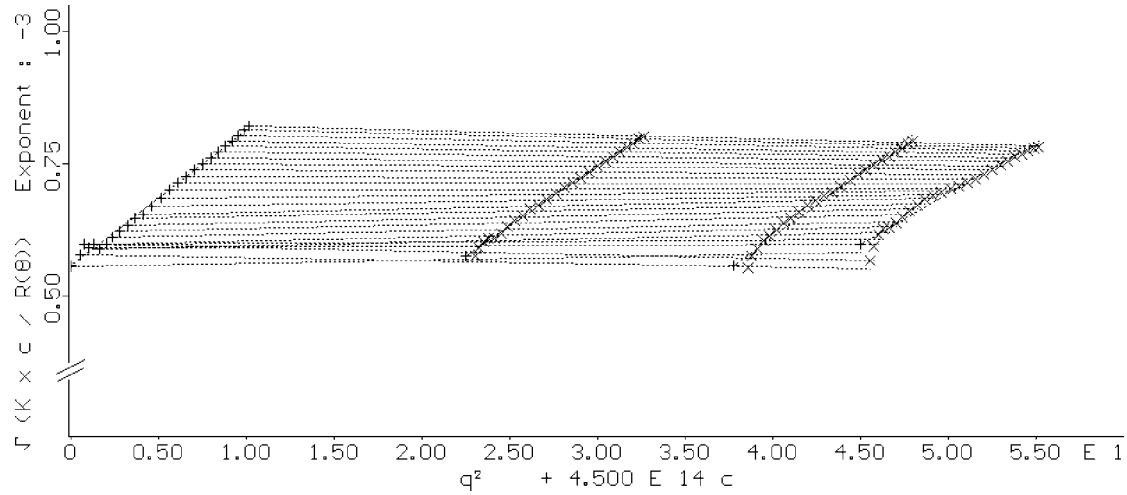

Figure 3. Berry plot of P(G-*graft*-CL) 4^{PS} (purified by preparative SEC) measured in chloroform: $c = 0.50$ mg·mL^{-1}, $c = 0.75$ mg·mL^{-1}, and $c = 1.00$ mg·mL^{-1}.

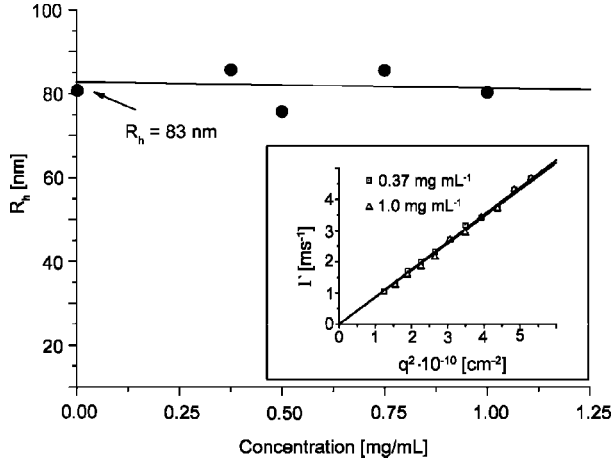

Figure 4. Concentration dependence of the hydrodynamic radius of the starlike copolymer P(G-*graft*-CL) 4^{PS}. In the box: changes of the decay rate Γ as a function of q^2 for P(G-*graft*-CL) 4^{PS} at the concentrations $c = 0.37$ mg·mL^{-1} and 1.0 mg·mL^{-1}.

values. From these relationships it also follows that the second virial coefficient decreases with increasing molar mass of the polymer. However, one should additionally take into account the fact that the low value of the polymer−solvent interaction

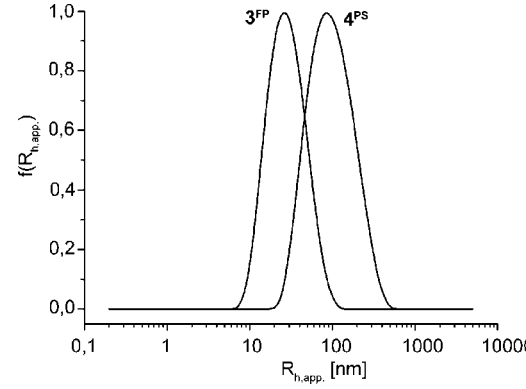

Figure 5. Distribution of the apparent hydrodynamic radii of the starlike copolymers P(G-*graft*-CL) 3^{FP} (purified by fractionated precipitation) and P(G-*graft*-CL) 4^{PS} (purified by preparative SEC) at $c = 1$ g·L^{-1} determined at 173°.

parameter in the present case results from the branched structure of the polymer. It was reported that for such polymers A_2 decreases stronger with the weight average molecular weight than for linear macromolecules with the same mass (the exponent in Equation 2 changes from 0.2 for linear chains to 0.65 for randomly branched structures).[23,24]

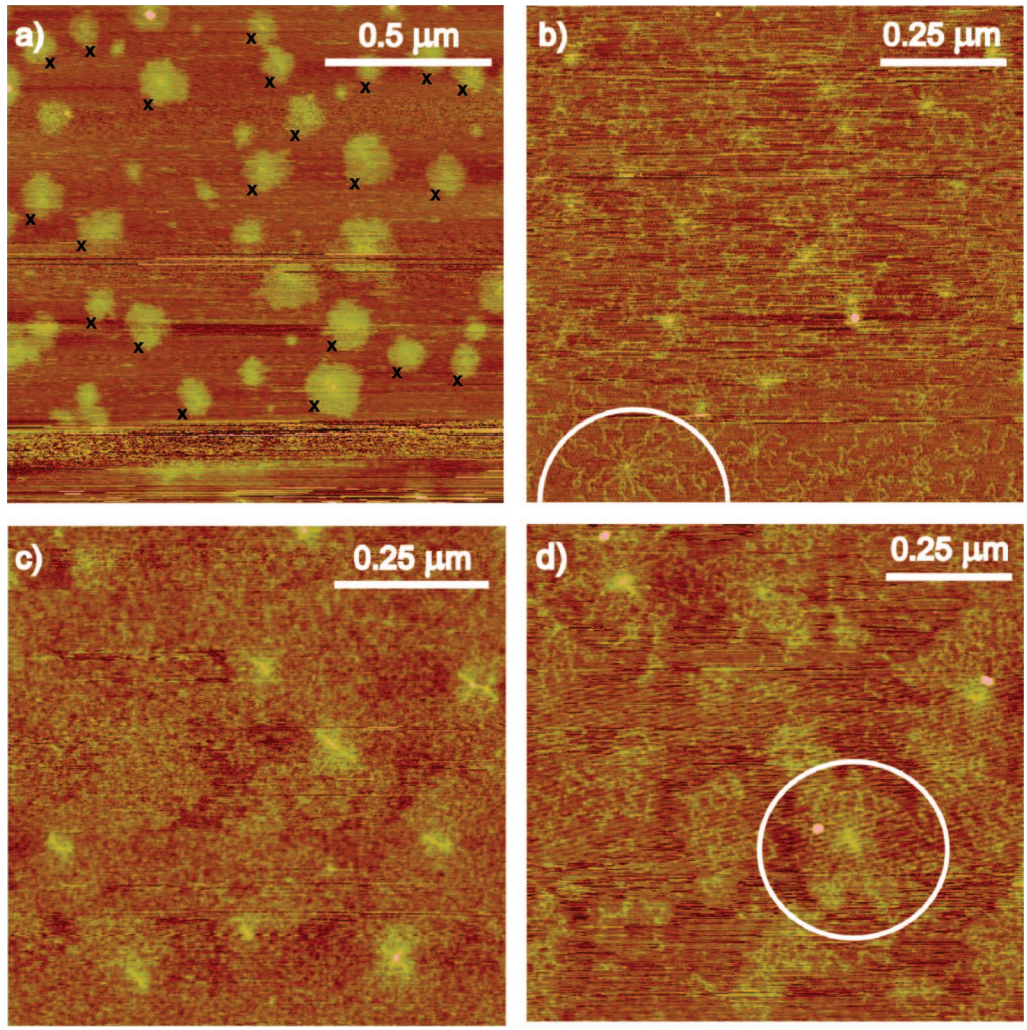

Figure 6. AFM height images of single starlike P(G-*graft*-CL) $\mathbf{3}^{\mathbf{FP}}$ (b) and P(G-*graft*-CL) $\mathbf{4}^{\mathbf{FP}}$ (a, c, d) macromolecules.

Dynamic light scattering measurements were performed in order to characterize the hydrodynamic behavior of the P(G-*graft*-CL) stars $\mathbf{3}^{\mathbf{FP}}$ and $\mathbf{4}^{\mathbf{PS}}$ in chloroform. However, for copolymer P(G-*graft*-CL) $\mathbf{3}^{\mathbf{FP}}$ only the apparent hydrodynamic radius could be obtained by a Nano Zetasizer. In the case of the high molar mass copolymer P(G-*graft*-CL) $\mathbf{4}^{\mathbf{PS}}$ angular and concentration dependency was measured. Purely translational diffusion of the macromolecules was confirmed by plots of the decay rate of the autocorrelation function versus squared scattering angle (expressed by the scattering vector q) as the relationship always went through the plot origin (box in Figure 4). In the applied range of concentrations R_h shows weak dependence on the concentration, and extrapolation to $c \rightarrow 0$ gives the hydrodynamic radius for P(G-*graft*-CL) $\mathbf{4}^{\mathbf{PS}}$ $R_h = 83$ nm (Figure 4). Additionally, distributions of the hydrodynamic radii determined at 173° are presented in Figure 5. The unimolecular nature of the stars is confirmed by appearance of only one peak for each copolymer.

From the ratio of the radius of gyration and the hydrodynamic radius the structural parameter (also known as the ρ-parameter) of the star P(G-*graft*-CL) $\mathbf{4}^{\mathbf{PS}}$ was determined: $R_g/R_h = 0.62$. This value is in the range typical for macromolecular architectures with a dense inner core and a swelled external shell.[23] This is in agreement with the expected structure as the poly(ϵ-caprolactone) chains are densely packed in the core due to high grafting efficiency.

SFM. The starlike copolymers P(G-*graft*-CL) $\mathbf{3}^{\mathbf{FP}}$ and $\mathbf{4}^{\mathbf{FP}}$ were visualized by scanning force microscopy. In general, the imaging of individual brush molecules is faciliated by the adsorption of side chains which separate the macromolecules and promote the extension of the backbone. In Figure 6, height images of the macromolecules P(G-*graft*-CL) $\mathbf{3}^{\mathbf{FP}}$ and $\mathbf{4}^{\mathbf{FP}}$ adsorbed on mica are depicted.

The species in Figure 6a present two different heights: a line with an increased height is observed in the middle of the patch. The delineated feature is attributed to the backbone and the corona to the PCL side chains of P(G-*graft*-CL) $\mathbf{4}^{\mathbf{FP}}$. From the patches, as indicated by the cross in Figure 6, a weight-average diameter of $D_{av} = 127$ nm and the weight-average height of $H_{av} = 0.26$ nm of the patches were measured. Thus, the weight-average radius of the patches is $R_{av} = 64$ nm, which is larger than the radius of gyration, but unusually it is smaller than the hydrodynamic radius determined by dynamic light scattering $R_h = 83$ nm. This leads to the assumption that, while scanning, water adsorption on the mica substrate concurs with the poly(ϵ-caprolactone) chain inducing partial contraction of the arms. The difference in the diameter of the patches (Figure 6a) and the length of the resolved arms of the stars (Figure 6, parts b and d) support this hypothesis. However, for consistent comparison between the light scattering data and the SFM, imaging in controlled environment and a statistically relevant number of molecules is required.

Yet assuming the shape of the copolymers P(G-*graft*-CL) $\mathbf{4}^{\mathbf{FP}}$ in Figure 6a to be a cylinder with diameter of D and height of H, the volume of each patch was determined. From the individual molecular weights calculated from the patches, the

weight-average molecular weight was determined to be M_w = 2.3 MDa. This is in reasonable agreement with the value determined by static light scattering M_w = 3.2 MDa.

Upon magnification, we experienced severe imaging difficulties, especially for the low-molecular-weight P(G-*graft*-CL) $\mathbf{3^{FP}}$. Nevertheless, in Figure 6b the star-shaped structure could be resolved. Adsorbed side chains emerge from the common core. In the case of P(G-*graft*-CL) $\mathbf{4^{FP}}$ the side chains could not be resolved so clearly, which might be due to the higher number of side chains. In Figure 6c and in Figure 6d single macromolecules are successfully visualized.

The backone length of the starlike copolymer P(G-*graft*-CL) $\mathbf{4^{FP}}$ was measured using the SFM images. The average contour length of the backbone $l_{cont.} = 51 \pm 9$ nm was determined from 75 macromolecules. The contour length of fully stretched polyglycidol backbone with 240 units corresponds to a maximum length of $l_{max.} \approx 55$ nm.[25] Thus, the backbone of the starlike macromolecule is at full extension, which is due to the high steric crowding of the side chains. It can be assumed, that grafting efficiency was close to 100%.

Imaging of the topography of the star P(G-*graft*-CL) $\mathbf{4^{PS}}$ (purified by preparative SEC) remained without success. Only collapsed polymer coils were observed. We may speculate, that a swelling of the starlike brushes with a small fraction of homopolymer facilitates the visualization of the high-molecular-weight stars. Further investigation is needed to clarify this issues.

Conclusions

Biodegradable high-molecular-weight poly(glycidol-*graft*-ϵ-caprolactone) starlike copolymers have been prepared by the "core-first" approach using polyglycidol as core molecules. After successful removal of a homopolymer fraction formed during polymerization, SEC elution curves showed monomodal behavior and low polydispersity indices. The unimolecular structure of the stars was confirmed by the distribution curves of the hydrodynamic radii. For the high molecular weight star with up to 197 arms the structure parameter calculated from the radius of gyration and the hydrodynamic radius indicates a core−shell type structure, which is in accordance with a densely grafted core. Additionally, the successful synthesis was confirmed by the direct visualization of the star topography by SFM. Measurements of the backbone length fit to a fully stretched polyglycidol, confirming the high grafting efficiency.

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References and Notes

(1) Schultz, D. N.; Glass, J. E. E. *Polymers as Rheology Modifiers*; ACS Symposium Series 462; American Chemical Society: Washington, DC, 1991.
(2) Gao, C.; Yan, D. *Prog. Polym. Sci.* **2004**, *29*, 183–275.
(3) Zhang, M.; Estournes, C.; Bietsch, W.; Muller, A. H. E. *Adv. Funct. Mater.* **2004**, *14*, 871–882.
(4) Djalali, R.; Li, S. Y.; Schmidt, M. *Macromolecules* **2002**, *35*, 4282–4288.
(5) Ishizu, K.; Satoh, J.; Sogabe, A. *J. Colloid Interface Sci.* **2004**, *274*, 472–479.
(6) Borner, H.; Beers, K.; Matjaszewski, K.; Sheiko, S. S.; Moeller, M. *Macromolecules* **2001**, *34*, 4375–4383.
(7) Cheng, G. L.; Boker, A.; Zhang, M.; Krausch, G.; Muller, A. H. E. *Macromolecules* **2001**, *34*, 6883–6888.
(8) Lee, H. I.; Matjaszewski, K.; Yu, S.; Sheiko, S. S. *Macromolecules* **2005**, *38*, 8264–8271.
(9) Boyce, J. R.; Shirvanyants, D.; Sheiko, S. S.; Ivanov, D. A.; Qin, S. H.; Borner, H.; Matjaszewski, K. *Langmuir* **2004**, *20*, 6005–6011.
(10) Masar, B.; Janata, M.; Latalova, P.; Netopilik, M.; Vlcek, P.; Toman, L. *J. Appl. Polym. Sci.* **2006**, *100*, 3662–3672.
(11) Xue, L.; Agarwal, U. S.; Zhang, M.; Staal, B. B. P.; Muller, A. H. E.; Bailly, C. M. E.; Lemstra, P. J. *Macromolecules* **2005**, *38*, 2093–2100.
(12) Sheiko, S. S.; Moller, M. *Chem. Rev.* **2001**, *101*, 4099–4123.
(13) Duncan, R. *Nat. Rev. Drug Discovery* **2003**, *2*, 347–360.
(14) Burgath, A.; Sunder, A.; Neuner, I.; Mulhaupt, R.; Frey, H. *Macromol. Chem. Phys.* **2000**, *201*, 792–797.
(15) Cao, X. L.; Li, Z. Q.; Song, X. W.; Cui, X. H.; Cao, P. F.; Liu, H. J.; Cheng, F.; Chen, Y. *Eur. Polym. J.* **2008**, *44*, 1060–1070.
(16) Taton, D.; Leborgne, A.; Sepulchre, M.; Spassky, N. *Macromol. Chem. Phys.* **1994**, *195*, 139–148.
(17) Dworak, A.; Panchev, I.; Trzebicka, B.; Walach, W. *Macromol. Symp.* **2000**, *153*, 233–242.
(18) Hans, M.; Gasteier, P.; Keul, H.; Moeller, M. *Macromolecules* **2006**, *39*, 3184–3193.
(19) Fitton, A. O.; Hill, J.; Jane, D. E.; Millar, R. *Synthesis* **1987**, 1140–1142.
(20) Wu, C.; Woo, K. F.; Luo, X. L.; Ma, D. Z. *Macromolecules* **1994**, *27*, 6055–6060.
(21) Hans, M.; Keul, H.; Moeller, M. *Biomacromolecules* **2008**, *9*, 2954–2962.
(22) Teraoka I. *Polymer Solutions: An Introduction to Physical Properties*; John Wiley and Sons: New York, 2002.
(23) Burchard, W. *Adv. Polym. Sci.* **1999**, *143*, 113–194.
(24) Huber, K.; Burchard, W.; Fetters, L. J. *Macromolecules* **1984**, *17*, 541–548.
(25) It was assumed, that a fully stretched polyglycidol repeating unit is equivalent to a fully stretched PEO repeating unit (L_{PEO} = 0.28 nm), the length of which was determined in the following reference: Kovacs, A. J.; Gonthier, A.; Straupe, C. *J. Polym. Sci., Polym. Symp.* **1975**, *50*, 283–325.

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