Ring-Opening Polymerization of ϵ-Caprolactone by Means of Mono- and Multifunctional Initiators: Comparison of Chemical and Enzymatic Catalysis

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ABSTRACT: Protected polyglycidols with a linear or star-shaped architecture were obtained via anionic ring-opening polymerization of protected glycidol in diglyme with potassium as counterion. Removal of the protecting groups lead to polyglycidols, which were used as multifunctional macroinitiators for the chemically and enzymatically catalyzed ring-opening polymerization of ϵ-caprolactone. For the chemically catalyzed polymerization zinc(II) 2-ethylhexanoate was used, while Novozyme 435 (Lipase B from *Candida antarctica* immobilized on a macroporous resin) was used for the enzymatically catalyzed polymerization. To determine the characteristics of the two differently catalyzed polymerizations, monofunctional macroinitiators based on poly(ethylene glycol) were applied. The main difference observed was the initiator efficiency, which was explained by the different polymerization mechanism. By using multifunctional macroinitiators the difference in the initiation efficiency lead to different polymer architectures. For the chemically catalyzed polymerization, all hydroxy groups of the polyglycidols initiated polymerization, and core−shell polymers with a hydrophilic polyether core and a hydrophobic polyester shell were obtained. For the enzymatically catalyzed polymerization only 15−20% of the hydroxyl groups initiated the polymerization of ϵ-caprolactone with the result of a different polymer architecture; these polymers have a hydrophilic polyglycidol head coil with hydrophobic poly(ϵ-caprolactone) tails.

Introduction

In recent years, much attention has been devoted to the synthesis of highly branched molecular architectures, such as hyperbranched, star-shaped, dendritic and combburst polymers.[1−7] The interest arises both from the need to control the chain topology and from the need to obtain materials having very different properties from those of linear polymers. Typical for such nanoscopically tailored polymers are their unique mechanical and rheological properties.[8−10] Core−shell amphiphilicity is another interesting property; the polymers may possess a hydrophilic core and a hydrophobic shell, which enables them to encapsulate guest molecules or catalytically active hydrophilic moieties.[11,12] In this respect, polyether polyester copolymers are attractive materials for biomedical applications such as potential drug carriers, because of the biodegradibility of the polyester shell building-blocks and the biocompatibility of the polyether core.[13−15]

One possibility to prepare amphiphilic star polymers with a large number of arms is the core-first approach. Core molecules with a compact globular structure and a high number of functional groups are used as initiators for ring-opening polymerization. To prepare well-defined multiarm stars, the highly branched core molecule must have a narrow polydispersity and a predictable molecular weight. Dendrimers fulfill these conditions, but their preparation by a stepwise series of reactions is tedious. Easier to prepare than dendrimers are hyperbranched polymers resulting from a one-step reaction based on functional AB_2 monomers.[1] Frey et al. have developed the ring-opening multibranching polymerization of glycidol leading to hyperbranched polyglycerol with rather narrow polydispersities.[16] The free hydroxy groups of these core molecules may be used as initiators to build multiarm star polymers. For example, propoxylated hyperbranched polyglycerols were used as initiators in a Sn-catalyzed ring-opening polymerization of ϵ-caprolactone to synthesize poly(ϵ-caprolactone) multiarm star block copolymers.[17]

For biomedical applications it is necessary to use nontoxic catalysts. In this respect the interest in enzymes has increased in the past decade, since it avoids the use of potentially toxic Lewis acid type catalysts.[15,18,19] Furthermore, enzymes are an attractive alternative to conventional chemical polymerization catalysts because of their high stereo-, regio-, and chemoselectivities, their ability to operate under mild conditions, recyclability, and biocompatibility. Lipases represent an exciting catalyst system for the ring-opening polymerization of lactones combining reasonable control of the molecular weight and chain end functionality. Lipase B from *Candida antarctica,* immobilized on macroporous acrylic resins (Novozyme 435), has proved to have exceptionally high catalytic activity and versatility.[18−21] Only a small amount of this enzyme (less than 1 wt %) induces the ring-opening polymerization of ϵ-caprolactone and under the appropriate reaction conditions the molecular weight of the poly(ϵ-caprolactone) reaches more than 4×10^4 g·mol^{-1}.[22] Recently, investigations in the field of block copolymer synthesis by enzymatic catalysis have been intensified.[23−26]

The goal of our investigation is the preparation of a linear and a star-shaped polyglycidol with a defined number of hydroxy groups, that will subsequently be used as a macroinitiator for the ring-opening polymerization of ϵ-caprolactone, to synthesize precisely defined core−shell polymers with various architectures. The polymerization of ϵ-caprolactone will be catalyzed by zinc(II) 2-ethylhexanoate (zinc(II) octoate, Zn(oct)$_2$) and by Novozyme 435 in order to explore the differences between the chemical and the enzymatic catalysis.

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Table 1. Ring-Opening Polymerization of ϵ-Caprolactone with Poly(ethylene glycol) Methyl Ether ($MPEO_x$) as Macroinitiator, Leading to $MPEO_x$-*b*-poly(ϵ-caprolactone) Copolymers (6, 7), with Reagents, Reaction Times, Temperatures, and Yields

polymer [a]	macroinitiator (**5**) [g (mmol)]	catalyst [mg (μmol)]	ϵ-caprolactone [g (mmol)]	temp [°C]	time [h]	yield [%]
6c	$MPEO_{2000}$ (**5a**)/5.00 (2.50)	24 (70)	10.45 (91.50)	130	25	90
6e	$MPEO_{2000}$ (**5a**)/2.50 (1.25)	250 (−)	5.22 (45.8)	70	25	72
7c	$MPEO_{5000}$ (**5b**)/2.50 (0.50)	24 (70)	5.22 (45.8)	130	70	95
7e	$MPEO_{5000}$ (**5b**)/2.50 (0.50)	100 (−)	5.22 (45.8)	70	70	79

[a] Key: c = polymers by chemical catalysis; e = polymers by enzymatic catalysis.

Table 2. Yields of the $MPEO_x$-*b*-poly(ϵ-caprolactone) Copolymers (6, 7) Obtained by Ring-Opening Polymerization of ϵ-Caprolactone with Poly(ethylene glycol) Methyl Ether ($MPEO_x$) as Macroinitiator after Fractionation in Methanol

polymer[a]	yield (mif)[b] [%]	yield (msf)[b] [%]	polymer[a]	yield (mif)[b] [%]	yield (msf)[b] [%]
6c	48	52	**7c**	85	15
6e	63	37	**7e**	73	27

[a] Key: c = polymers by chemical catalysis; e = polymers by enzymatic catalysis. [b] Key: mif = methanol insoluble fraction; msf = methanol soluble fraction.

To compare the chemically and enzymatically catalyzed ring-opening polymerization of ϵ-caprolactone, monofunctional poly(ethylene oxide)s ($MPEO_{2000}$ and $MPEO_{5000}$) with number-average molecular weights of M_n = 2000 and 5000 were used as initiators and $Zn(oct)_2$ and Novozyme 435 as catalyst.

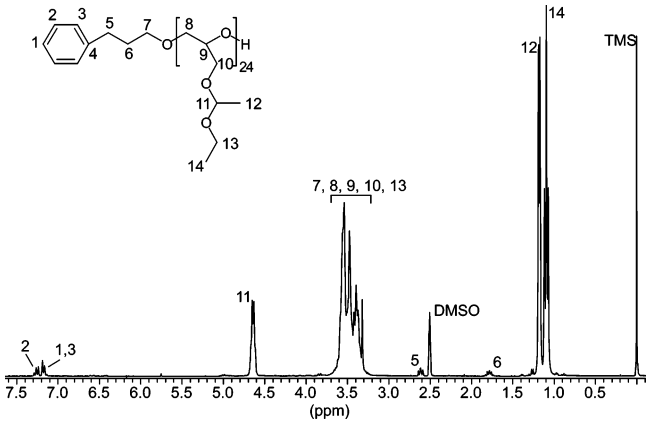


Figure 1. ^1H NMR spectrum of protected polyglycidol initiated by 3-phenylpropanol in DMSO-d_6.

Experimental Part

Materials. ϵ-Caprolactone (≥99%, Fluka), poly(ethylene glycol)-methyl ether ($MPEO_{2000}$: M_n = 2000 g·mol^{-1}, $MPEO_{5000}$: M_n = 5000 g·mol^{-1}, Aldrich), potassium *tert*-butoxide (1 M solution in THF, Aldrich), and zinc(II) 2-ethylhexanoate (97%, ABCR) were used as received. Novozyme 435 (Lipase B from *C. antarctica* immobilized on a macroporous resin, 10.000 U·g^{-1}, Sigma) was dried in a vacuum at room temperature for 24 h before use and stored under nitrogen. 3-Phenyl-1-propanol (≥98%, Fluka) was distilled over sodium and di(trimethylolpropane) (diTMP, 97%, Aldrich) was purified by condensation. Diglyme was distilled over sodium.

Potassium methanolate was synthesized by reacting potassium with methanol in toluene. The solvent was removed and a white powder was obtained after drying in a vacuum at 50 °C. Ethoxy ethyl glycidyl ether (**1**) (further referred to as glycidol acetal **1**) was synthesized from 2,3-epoxypropan-1-ol (glycidol) and ethyl vinyl ether according to Fitton et al.[27] and purified by distillation. 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.

Synthesis of Linear Poly(glycidol acetal) (3a). 3-Phenylpropanol (**2a**) (582 mg, 4.28 mmol) was dissolved in diglyme (15 mL) and potassium *tert*-butoxide (0.43 mL of a 1 M solution in THF, 0.43 mmol) was added. The formed *tert*-butyl alcohol was removed by distillation. Glycidol acetal **1** (15,0 g, 0,10 mol) was added and the mixture was stirred for 20 h at 120 °C. The solvent was removed in a vacuum at 80 °C and a viscous liquid was obtained. Yield: 100%. ^1H NMR ($CDCl_3$): δ 1.19 (t, J = 6.9 Hz, CH_3CH_2), 1.29 (d, J = 4.7 Hz, CH_3CH), 1.88 (qui, J = 7.0 Hz, $ArCH_2CH_2$), 2.67 (t, J = 7.6 Hz, $ArCH_2CH_2$), 3.45−3.95 (m, $CH_2OCH_2CH(CH_2O)O$, OCH_2CH_3), 4.69 (d, J = 5.0 Hz, OC*H*O), 7.12−7.33 (m, Ar). ^{13}C NMR ($CDCl_3$): δ 15.3, 19.8, 31.3, 32.3, 60.8, 64.8, 70.1, 77.3, 78.9, 99.8, 125.8, 128.3, 128.4, 141.9. For further analytical data see Tables 4 and 5 and Figures 1 and 2.

Synthesis of Star-Shaped Poly(glycidol acetal) (3b). diTMP (**2b**) (1.01 g, 4.05 mmol) was dissolved in diglyme (15 mL), and potassium methanolate (113 mg, 1.62 mmol), dissolved in methanol (0.90 mL), was added. The formed methanol was removed by distillation. Glycidol acetal **1** (14.2 g, 0.01 mol) was added and the mixture was stirred for 20 h at 120 °C. The solvent was removed in a vacuum at 80 °C and a viscous liquid was obtained. Yield: 100%. ^1H NMR ($CDCl_3$): δ 0.83 (t, J = 7.35 Hz, CH_3CH_2C), 1.19 (t, J = 6.9 Hz, CH_3CH_2O), 1.26−1.47 (m, CH_3CH, CH_3CH_2C), 3.05−3.30 (m, CCH_2O), 3.30−3.95 (m, $OCH_2CH(CH_2O)O$, OCH_2-CH_3), 4.65−4.76 (m, OC*H*O). ^{13}C NMR ($CDCl_3$): δ 7.9, 15.3, 15.3, 19.7, 19.8, 60.8, 61.0, 64.9, 65.0, 66.0, 69.7, 69.9, 70.1, 72.5, 72.7, 78.8, 78.9, 99.7, 99.9. For further analytical data see Tables 4 and 5 and Figure 2.

Polyglycidols (4a, 4b). The poly(glycidol acetal)s **3a** or **3b** (1.0 g) were dissolved in tetrahydrofuran (120 mL), and aqueous 32% HCl (6.1 g) was added. After 5 h, the polyglycidols **4a** or **4b** precipitated as an oil. The solvent was removed and the polyglycidols were dried in a vacuum at 80 °C. Linear polyglycidol (**4a**): Yield: 78%. ^1H NMR (DMSO-d_6): δ 1.88 (qui, J = 7.0 Hz,

Table 3. Ring-Opening Polymerization of ϵ-Caprolactone with Linear and Star-Shaped Polyglycidol 4a and 4b as Multifunctional Macroinitiators Leading to the Corresponding Copolymers (8, 9, 10, 11), with Reagents, Reaction Times, and Yields

polymer[a]		macroinitiator [mg (mmol)]	catalyst [mg (μmol)]	ϵ-Caprolactone [g (mmol)]	temp [°C]	time [h]	yield [%]
	8c	**4a**/448 (0.23)	8.0 mg (20)	0.98 (8.58)	130	24	92
linear	**8e**	**4a**/251 (0.13)	26 mg (−)	0.55 (4.80)	100	72	51
polyglycidol	**9c**	**4a**/433 (0.21)	8.0 mg (20)	0.89 (7.82)	130	24	92
	9e	**4a**/339 (0.17)	34 mg (−)	0.70 (6.12)	100	72	22
	10c	**4b**/309 (0.16)	8.0 mg (20)	1.69 (14.8)	130	24	98
star-shaped	**10e**	**4b**/460 (0.24)	48 mg (−)	2.51 (22.0)	100	140	52
polyglycidol	**11c**	**4b**/386 (0.19)	8.0 mg (20)	1.98 (17.4)	130	24	96
	11e	**4b**/450 (0.22)	44 mg (−)	2.32 (20.3)	100	140	49

[a] c = polymers by chemical catalysis; e = polymers by enzymatic catalysis.

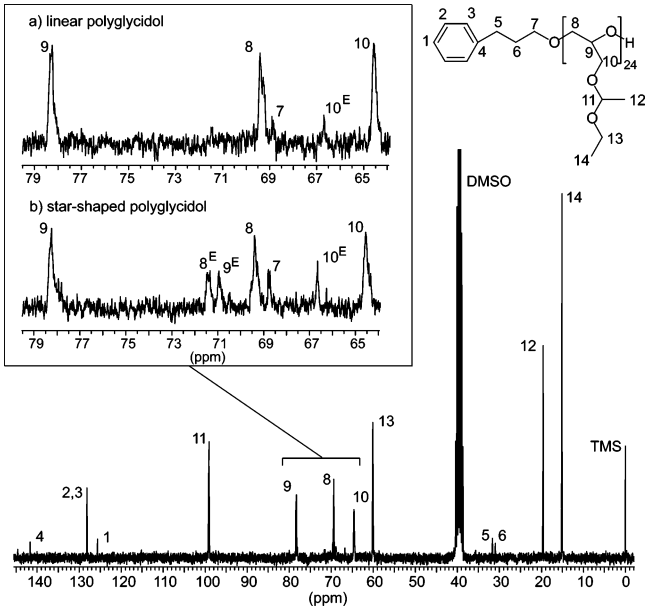


Figure 2. ^{13}C NMR spectrum of protected polyglycidol **3a** initiated by 3-phenylpropanol in DMSO-d_6. Inside the box the peaks for the repeating units are shown (a) for the linear and (b) for the star-shaped polyglycidol. The peaks marked with an ^{E} are from the end group.

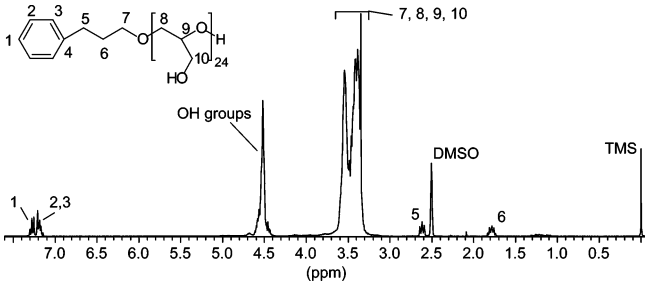


Figure 3. ^{1}H NMR spectrum of polyglycidol initiated by 3-phenylpropanol in DMSO-d_6.

ArCH$_2$CH_2), 2.67 (t, J = 7.6 Hz, ArCH_2CH$_2$), 3.45−3.95 (m, CH_2-OCH_2CH(CH_2O)O), 4.53 (s, OH), 7.12−7.33 (m, Ar). ^{13}C NMR (DMSO-d_6): δ 30.9, 31.6, 60.9, 63.0, 69.4, 69.5, 70.7, 71.4, 80.0, 125.7, 128.2, 128.3, 141.7. Star-shaped polyglycidol (**4b**): Yield: 85%. ^{1}H NMR (DMSO-d_6): δ 0.81 (t, J = 7.4 Hz, CH_3CH$_2$C), 1.30 (m, CH$_3$CH_2C), 3.07−3.27 (m, CCH_2O), 3.27−3.70 (m, OCH_2CH(CH_2O)O), 4.55 (s, OH). ^{13}C NMR (DMSO-d_6): δ 7.6, 22.8, 42.9, 60.8, 61.0, 63.0, 69.3, 69.5, 70.6, 70.7, 71.1, 71.4, 71.6, 79.7, 79.8. For further analytical data see Tables 4 and 5 and Figures 3 and 4.

Synthesis of MPEO-*b*-poly(ϵ-caprolactone) Copolymer (6e). Poly(ethylene glycol)methyl ether **5a** (MPEO$_{2000}$: M_n = 2000 g·mol^{-1}) (2.50 g, 1.25 mmol) and ϵ-caprolactone (5.22 g, 45.8 mmol) were heated to 70 °C in order to obtain a homogeneous solution. The catalyst Novozyme 435 (250 mg) was added, and the mixture was stirred for 25 h at 70 °C. The polymer **6e** was isolated by dissolution in dichloromethane, removal of the enzyme by filtration, and precipitation in hexane. A white powder was obtained. Yield: 90%. ^{1}H NMR (CDCl$_3$): δ 1.30−1.50 (m, OCOCH$_2$CH$_2$CH_2), 1.52−1.70 (m, CH_2CH$_2$CH_2), 2.30 (t, J = 7.5 Hz, OCOCH_2CH$_2$), 3.38 (s, CH_3O), 3.65 (s, OCH_2CH_2O), 4.06 (t, J = 6.6 Hz, CH_2OCO). ^{13}C NMR (CDCl$_3$): δ 24.6, 25.5, 28.4, 34.1, 64.2, 70.6, 173.6. For further analytical data see Table 6.

The synthesis of **6c**, **7c**, and **7e** was performed in analogy to **6e**. Reagent ratios, reaction times, temperatures and yields for all MPEO-*b*-poly(ϵ-caprolactone) copolymers are listed in Table 1.

Fractionation of the MPEO-*b*-poly(ϵ-caprolactone) Copolymers (6, 7). The crude copolymers **6** and **7** (1 g) were dissolved in dichloromethane (5 mL) and precipitated in methanol (100 mL). The methanol insoluble fraction was isolated by centrifugation. Both fractions were dried in a vacuum. Yields are listed in Table 2. For further analytical data see Table 7.

Polymerization of ϵ-Caprolactone with the Multifunctional Macroinitiators (11c). Polyglycidol **4b** (386 mg, 0.19 mmol) and ϵ-caprolactone (1.98 g, 17.4 mmol) were heated to 90 °C in order to obtain a homogeneous solution. The catalyst Zn(oct)$_2$ (8.0 mg, 20 μmol) was added and the mixture was stirred for 24 h at 130 °C. The polymer **11c** was isolated by dissolution in dichloromethane and precipitation in hexane. After the product was dried in a vacuum at 50 °C a viscous oil was obtained. Yield: 96%. ^{1}H NMR (DMSO-d_6): δ 0.70−0.95 (m, CH_3CH$_2$), 1.20−1.42 (m, CH$_3$CH_2, OCOCH$_2$-CH$_2$CH_2), 1.42−1.62 (m, CH_2CH$_2$CH_2), 2.27 (t, J = 7.2 Hz, OCOCH_2CH$_2$), 3.05−3.27 (m, CCH_2O), 3.27−3.80 (m, OCH_2CH-(CH$_2$O)O), 3.98 (t, J = 6.4 Hz, CH_2OCO), 4.07−4.40 (m, CHCH_2O), 4.40−4.60 (s, not converted CHCH$_2$OH groups). ^{13}C NMR (DMSO-d_6): δ 7.4, 22.0, 24.0, 24.4, 24.9, 25.0, 27.8, 32.2, 33.3, 33.5, 60.5, 63.4, 172.7, 172.7 (the peaks of the polyglycidol backbone are not distinguishable from the noise of the baseline). For further analytical data, see Table 8 and Figure 9.

The syntheses of **8, 9, 10,** and **11e** were performed in analogy to that of **11c**. Reagent ratios, reaction times, and yields are listed in Table 3.

Measurements. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-300 FTNMR spectrometer at 300 MHz, respectively 75 MHz. Deuterated chloroform (CDCl$_3$) or deuterated dimethyl sulfoxide (DMSO-d_6) was used as a solvent, and tetramethylsilane (TMS) served as an internal standard.

Gel permeation chromatography (GPC) analyses were carried out at 80 °C using a high-pressure liquid chromatography pump (Bischoff HPLC 2200) and a refractive index detector (Waters 410). The eluting solvent was *N*,*N*-dimethylacetamide (DMAc) with 2.44 g·L^{-1} LiCl and a flow rate of 0.8 mL·min^{-1}. Four columns with MZ-DVB gel were applied. The length of each column was 300 mm, the diameter was 8 mm, the diameter of the gel particles was

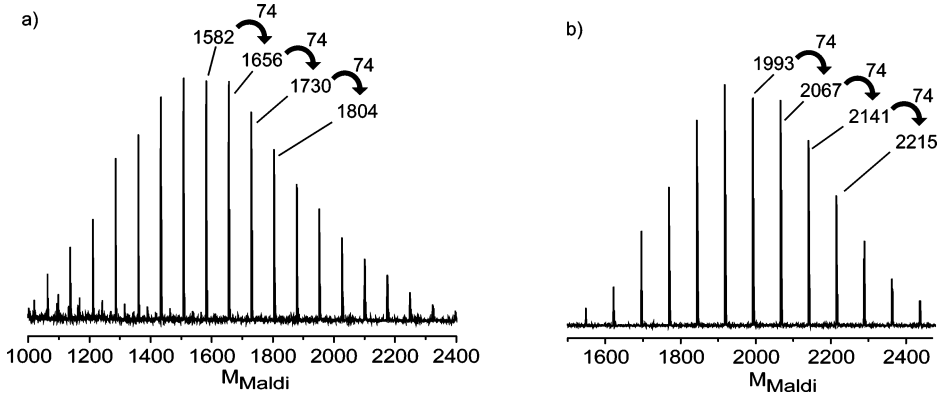
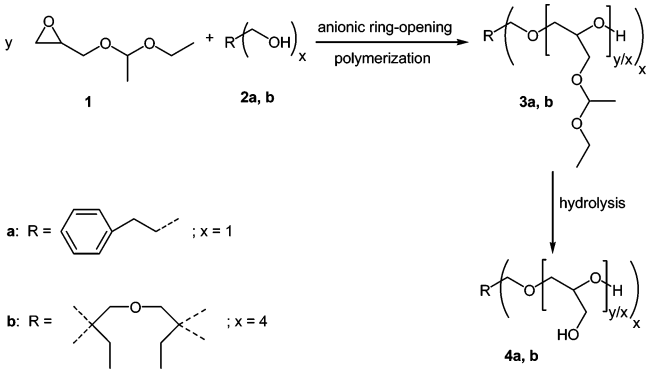


Figure 4. Matrix-assisted laser desorption/ionization time-of-flight (MALDI−TOF) mass spectra (reflectron mode): (a) linear (**4a**) and (b) star-shaped (**4b**) polyglycidols. A mixture of trifluoroacetic acid and potassium trifluoroacetate (ratio 10:1) was used as matrix.

Scheme 1. Synthesis of the Linear and Star-Shaped Multifunctional Macroinitiators



5 mm, and the nominal pore widths were 100, 1000, and 10000 Å. Calibration was achieved using poly(methyl methacrylate) (PMMA) standards.

The MALDI−TOF-MS measurements were performed with a Bruker Biflex III (re-TOF) MALDI−TOF (matrix-assisted laser desorption and ionization time-of-flight) mass spectrometer, equipped with a nitrogen laser delivering 3 ns laser pulses at 337 nm. A mixture of trifluoroacetic acid and potassium trifluoroacetate (ratio 10:1) was used as matrix. Samples were prepared by dissolving the polymer in methanol at a concentration of 10 g·L^{-1}. The matrix/salt solution was prepared by mixing the α-cyanohydroxycinnamic solution (20 g·L^{-1}) with a potassium trifluoroacetate solution (20 g·L^{-1}). First, 0.5 μL of the polymer solution was applied to a multistage target to evaporate the methanol, and then 0.5 μL of the matrix/salt solution was added to create a thin matrix/analyte film. The ions were accelerated to 20 kV and measured in the reflectron mode of the spectrometer.

Shear viscosity (η) for the protected and unprotected polyglycidols were determined with a controlled stress rheometer (Rheometric Scientific DSR, USA) using a cone and plate geometry and shear rates within the instruments and cone−plate limits. The polymers were melted on the 25 mm plate, which was electrically heated to the desired temperature, and the cone was then lowered into position. An upper heating element was also lowered over the cone. The polymer melt was permitted to equilibrate for a further 10 min, and all temperatures had errors of ±0.1 °C. The shear viscosity (η) at steady-shear rates were obtained using the range of shear forces σ available (σ = 0.026−4600 Pa) to the instrument.

Results and Discussion

The synthetic strategy for the preparation of core−shell polymers with cylindrical and spherical shape comprises the preparation of the multifunctional macroinitiators followed by the ring-opening polymerization of ϵ-caprolactone using these macroinitiators in combination with $Zn(oct)_2$ or Novozyme 435 as catalyst.

Synthesis of Linear and Star-Shaped Polyglycidols. Linear polyglycidols were prepared by Dworak[28] using protected glycidol as monomer. Acetal was chosen as the protecting group, which was introduced by reaction of glycidol with ethyl vinyl ether.[27] In this work we used the same monomer to prepare multifunctional macroinitiators in two steps: anionic polymerization of glycidol acetal **1**, using a monofunctional (**2a**) or a tetrafunctional (**2b**) initiator, leading in a first step to linear and star-shaped protected polyglycidols (**3a,b**). In the second step, acid-catalyzed removal of the protecting group results in the linear and star-shaped multifunctional macroinitiators (**4a,b**) (Scheme 1).

The synthesis of linear and star-shaped polyglycidols was performed by anionic ring-opening polymerization of protected glycidol using 3-phenylpropanol or di(trimethylolpropane) (diTMP) as initiator. For activation of the alcohol groups of the initiator, potassium *tert*-butoxide (*tert*-BuOK) or potassium methoxide (MeOK) was used. It is important to remove all *tert*-BuOH or MeOH from the system before the monomer is added and the polymerization is initiated by heating the solution in diglyme to 120 °C. The monomer to initiator molar ratio was 24:1. For a controlled polymerization it is important that only ca. 10% of the hydroxy groups of the initiator are activated and ca. 90% remain as dormant species. After 20 h the protected polyglycidol is obtained in quantitative yield.

NMR analysis reveals the expected microstructure; resonance signals of the repeating units and of the initiator are clearly resolved. The number-average molecular weight (M_n) of the polymers was determined by end group analysis (Table 4). For the linear protected polyglycidol (**3a**) the aryl signal of the initiator 3-phenyl-1-propanol (1, 2, 3) was compared with the resonance signal of the acetal proton (11) of the protection group (Figure 1). In the case of the star-shaped polymer the signal of the methyl groups of diTMP was used to determine M_n.

Because of the fact that the repeating unit has two asymmetric centers, the ^{13}C NMR spectrum is rather complex because of the different chemical shifts of the possible diads (Figure 2). In the linear polyglycidol, the ratio of repeating units to end groups is 23:1, while in the star-shaped polyglycidol it is 20:4. Therefore, in the ^{13}C NMR spectrum of the star-shaped polyglycidol the peaks of the end groups are more pronounced than in the spectrum of the linear polyglycidol. A quantitative ^{13}C NMR spectrum showed that the ratio of repeating units to end groups was 20:4 for the star-shaped polyglycidol. This confirms that all four hydroxy groups of diTMP initiated the polymerization and a 4-arm star polymer was obtained.

To remove the protecting groups, the polymers were dissolved in THF and treated with hydrochloric acid. Complete removal of the protection groups was confirmed by NMR analysis (Figure 3). The calculated number-average molecular weight corresponds to the theoretically predicted value, proving that no chain degradation by hydrolysis occurred. ^{13}C NMR analysis reveals a rather simple spectrum, which is due to the removal of one stereo-center from the repeating unit. Furthermore, the NMR analysis demonstrates that no side reactions occur upon the removal of the protection groups.

GPC analysis shows that with both initiators narrow distributed polymers are obtained. In accordance with the fact that star-shaped structures usually show narrower distributions, **3b** and **4b** have lower polydispersities than **3a** and **4a**.

The M_n values of the polymers determined by means of ^{1}H NMR and GPC, however, differ (Table 1). The results will be summarized and discussed in the following: (i) The M_n values of all polymers determined by the end group analysis agree well with the theoretically predicted values. (ii) The M_n values of the protected polyglycidols determined by GPC (PMMA standards) are also in the expected range; however, the star-shaped polymers show higher M_n values than the linear polymers with the same degree of polymerization. This is unexpected since the hydrodynamic volume of star-shaped polymers should be lower than that of linear polymers. GPC analysis of the deprotected polyglycidols **4a,b** reveals a strong increase of the molecular weight upon removing the protecting group. This is interpretated by interactions of the hydroxy groups with the columns or by intermolecular hydrogen bonds, which lead to association of the multifunctional macroinitiators.

We have also analyzed polymers **4a,b** by MALDI−TOF mass spectroscopy and have found a single distribution showing that no adventitious initiator was active. The main peaks have a

Table 4. Molecular Weights and Molecular Weight Distributions of Linear Protected and Unprotected (3a, 4a) and of Star-Shaped Protected and Unprotected (3b, 4b) Polyglycidols

polymer	$P_{n,NMR}$[a]	$M_{n,NMR}$[a] [g·mol^{-1}]	$M_{n,cal.}$[b] [g·mol^{-1}]	$M_{n,GPC}$[c]	Q[c]
3a	24	3669	3640	3100	1.08
3b	23	3637	3754	4300	1.03
4a	25	2030	1912	7100	1.07
4b	27	2282	2026	7700	1.04

[a] Degree of polymerization (P_n) and molecular weight (M_n) determined by nuclear magnetic resonance spectroscopy (NMR). [b] Calculated molecular weight. [c] Molecular weight (M_n) and molecular weight distribution (Q) determined by gel permeation chromatography (GPC) using *N*,*N*-dimethylacetamide (DMAc) as eluent.

Table 5. Shear Viscosities of Linear Protected and Unprotected (3a, 4a) and of Star-Shaped Protected and Unprotected (3b, 4b) Polyglycidols at 35 and 85 °C

polymer	shear viscosity at 35 °C/[Pa s]	shear viscosity at 85 °C/[Pa s]
3a	0.43 ± 0.01	0.047 ± 0.002
3b	0.34 ± 0.01	0.042 ± 0.002
4a		7.7 ± 0.2
4b		8.0 ± 0.2

separation of 74 g·mol^{-1}, corresponding to one glycidol repeating unit. The values of the marked peaks in Figure 4 are composed of the molecular weights of the corresponding number of glycidol repeating units (n × 74 g·mol^{-1}), the initiating group (136 g·mol^{-1} for 3-phenyl-1-propanol or 250 g·mol^{-1} for diTMP) and the potassium cation (39 g·mol^{-1}). The determined molecular weights correspond to the theoretical values.

Finally, rheological measurements were performed for the protected and unprotected polyglycidols in order to determine the viscosities over various shear rates. For all measurements the values of the viscosities were shear rate independent (between ca. 1 and 100 s^{-1}). For the protected polyglycidols **3a,b**, the vicosities were determined at 35 and 85 °C. The linear polyglycidol shows a higher viscosity than the star-shaped polymer. This was expected because for polymers of the same molecular weight the entanglement of linear architectures is stronger than that of star-shaped ones.

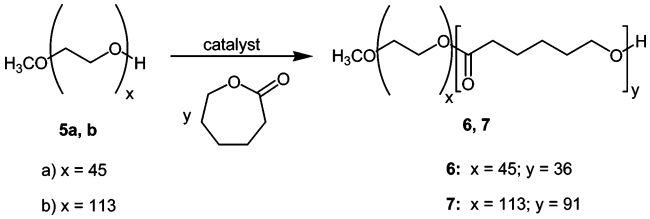
Because of the high viscoelasticity of the unprotected polyglycidols **4a,b** at 35 °C, data were collected only at 85 °C.

The viscosities of the protected polyglycidols **3a,b** decrease strongly with increasing temperature. At 85 °C the viscosities have become too low to allow a reasonable comparison. The viscosities of the unprotected polyglycidols **4a,b** are much higher than those for the protected **3a,b** analogues. This is likely due to the formation of intermolecular hydrogen bonding. The viscosity difference between linear and star-shaped structure for the polyglycidols **4a** compared to **4b** at 85 °C is comparatively smaller than the difference seen between the linear and the star-shaped structures for the unprotected analogues (**3a** compared to **3b** at 35 °C).

Synthesis of the Polyether Polyester Copolymers. Ring-opening polymerization of ϵ-caprolactone was performed with monofunctional $MPEO_x$ as model reaction (x = 2000 or 5000) and the previously synthesized multifunctional macroinitiators **4a** and **4b**. Kinetic studies will show the differences of chemical and enzymatic catalysis using as catalyst $Zn(oct)_2$ or Novozyme 435, respectively.

Ring-opening polymerization of ϵ-caprolactone with the monofunctional macroinitiator $MPEO_x$, using $Zn(oct)_2$ and Novozyme 435 as catalyst, was carried out in bulk at 130 and 70 °C, respectively (Scheme 2).

Scheme 2. Ring-Opening Polymerization of ϵ-Caprolactone Using $MPEO_x$ as Macroinitiator[a]



[a] y is the theoretical value, given by the amount of ϵ-caprolactone in the feed.

Table 6. Repeating Unit Ratios, Molecular Weights, and Molecular Weight Distributions of the Crude $MPEO_x$-*b*-poly(ϵ-caprolactone) Copolymers (6, 7) Obtained by Ring-Opening Polymerization of ϵ-Caprolactone Using Poly(ethylene glycol) Methyl Ether ($MPEO_x$) as Macroinitiator

polymer[a]	$[EO]_{r.u.}$[b]/$[\epsilon\text{-CL}]_{r.u.}$	$M_{n,NMR}$[c] [g·mol^{-1}]	$M_{n,cal.}$[d] [g·mol^{-1}]	$M_{n,GPC}$[e]	Q[e]
6c	1.32	5900	6100	8900	1.17
6e	1.32	5900	6100	9500	1.61
7c	1.26	15 300	15 400	25 100	1.28
7e	1.36	14 500	15 400	21 800	1.71

[a] Key: c = polymers by chemical catalysis; e = polymers by enzymatic catalysis. [b] Ratio of the repeating units (r.u.) ethylene oxide (EO) and ϵ-caprolactone (ϵ-CL) in the block copolymer. [c] Molecular weight (M_n) determined by nuclear magnetic resonance spectroscopy (NMR). [d] Calculated molecular weight. [e] Molecular weight (M_n) and molecular weight distribution (Q) determined by gel permeation chromatography (GPC) using *N*,*N*-dimethylacetamide (DMAc) as eluent.

The monomer-to-initiator ratio was adjusted in the way, that the ratio of the molecular weight of the polyether and the polyester block is 1:2, this means 36 ϵ-caprolactone repeating units for $MPEO_{2000}$ and 91 for $MPEO_{5000}$. The results of the NMR and GPC analysis are shown in Table 6.

Since the chain length of the initiating $MPEO_x$ is known, the number-average molecular weight of the polymers can be determined by ^{1}H NMR analysis. For the crude products the obtained number-average molecular weights are in good agreement with the calculated values. The polymers **6e** and **7e** produced by enzymatic catalysis have higher polydispersities than **6c** and **7c** synthesized by chemical catalysis. The M_n values of the block copolymers nevertheless seem to be independent of the catalyst.

The narrow polydispersities of the polymers obtained by chemical catalysis indicate, that only $MPEO_x$ was used as initiator. The higher polydispersities for the enzymatic catalysis may be due to the fact that poly(ϵ-caprolactone) is formed by adventitious initiation by water, which is still present in Novozyme 435. It should be mentioned that in all GPC analyses no $MPEO_x$ was observed; the elution volume of the block copolymer was lower.

The monomer conversion as a function of reaction time for the two different catalysts are plotted in Figures 5 and 6. The degree of polymerization and the conversion were determined by NMR analysis. For both chemical polymerizations, conversions of over 97% were reached. With $MPEO_{2000}$ the enzymatic catalyst also reached 97% conversion, while with $MPEO_{5000}$ only 88% conversion was obtained. In fact, both the enzymatic and the $Zn(oct)_2$ catalyzed polymerizations are insertion polymerizations, with characteristics of a living polymerization.

The first-order plots of the chemically catalyzed ring-opening polymerization with $MPEO_{2000}$ and $MPEO_{5000}$ as macroinitiators are linear up to high conversions (>95%) indicating that no chain termination occurs. The rate of the enzymatically catalyzed polymerization decreases after ca. 90% conversion for $MPEO_{2000}$

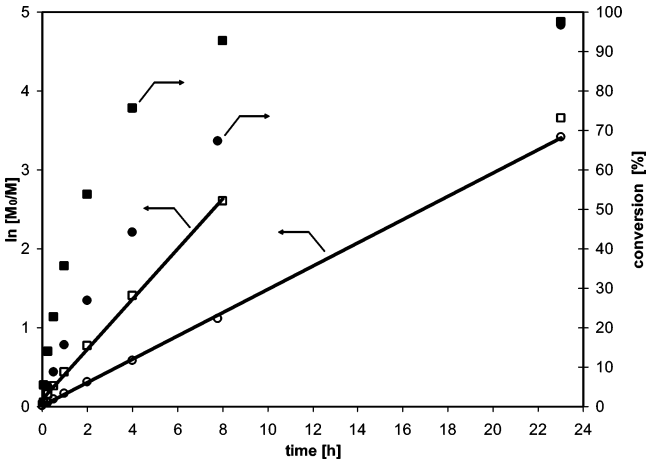


Figure 5. Polymerization of ϵ-caprolactone with $MPEO_{2000}$ as macroinitiator catalyzed by $Zn(oct)_2$ and Novozyme 435: conversion vs reaction time [(●) zinc octoate; (■) Novozyme 435] and first-order plot [(○) zinc octoate; (□) Novozyme 435]. ($[M]_0/[Zn(oct)_2] = 1600$; $[MPEO_{2000}]/[Zn(oct)_2] = 45$; Novozyme 435/monomer = 4.6 wt %; Novozyme 435/$MPEO_{2000}$ = 9 wt %.)

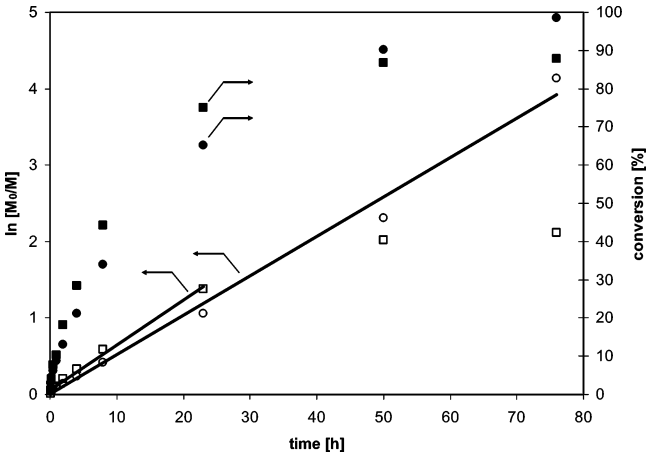


Figure 6. Polymerization of ϵ-caprolactone with $MPEO_{5000}$ as macroinitiator catalyzed by $Zn(oct)_2$ and Novozyme 435: conversion vs reaction time [(●) zinc octoate; (■) Novozyme 435] and first-order plot (○ zinc octoate, □ Novozyme 435). ($[M]_0/[Zn(oct)_2] = 830$; $[MPEO_{5000}]/[Zn(oct)_2] = 9$; Novozyme 435/monomer = 1.9 wt %; Novozyme 435/$MPEO_{5000}$ = 3.8 wt %.)

and ca. 75% for $MPEO_{5000}$. This result can be explained considering the specific activation mechanism of the chemically and the enzymatically catalyzed processes. $Zn(oct)_2$ activates the end of the growing polymer chain ("activated chain end" mechanism), while Novozyme 435 activates the monomer ("activated monomer" mechanism). With increasing conversion, the viscosity of the reaction medium increases. For chemical catalysis, it is relatively easy for the small monomer molecules to migrate to the active chain ends (see arrows in Figure 7a). For enzymatic catalysis, however, large polymer chains must migrate to the activated monomer at the immobilized macroporous support of Novozyme 435 (see arrows in Figure 7b). As a consequence in the case of enzymatic catalysis, the diffusion of polymer chains to the activated monomer limits the conversion. Because of the lower molecular weight of $MPEO_{2000}$, compared to $MPEO_{5000}$, the viscosity for this system is lower, and as a consequence, the conversion is higher.

The number-average molecular weight vs the conversion is plotted in Figure 8. M_n increases linearly with monomer conversion, which indicates that chain transfer did not occur or its rate is negligible. For the enzymatic polymerization with $MPEO_{5000}$ as macroinitiator, only 86% conversion was obtained, and a decrease in M_n is observed after this. Considering that at the end of the polymerization the reaction rate decreases due to diffusion control, the importance of random degradation reactions like hydrolysis or backbiting processes increases.

In summary, the kinetics of the enzymatically catalyzed polymerization does not differ from that of the chemically catalyzed one. Both follow characteristics of a living polymerization. For the initiation with $MPEO_{5000}$ the enzymatic catalysis is probably retarded at higher conversions, due to diffusion control as described in Figure 7.

The obtained powdery polymers were fractionated by precipitation of a methylene chloride solution into methanol. The results of the NMR and GPC analysis of the fractioned polymers are shown in Table 7.

$MPEO_x$ moieties with few repeating units remain soluble in methanol. Hence two fractions are obtained: the methanol insoluble fraction with a low ratio and the methanol soluble fraction with a high ratio of ethylene oxide/ϵ-caprolactone repeating units. The yields of the methanol soluble fractions for the polymerization with $MPEO_{2000}$ are high. Because of the relatively small amount of ϵ-caprolactone in these polymers, only short poly(ϵ-caprolactone) chains are formed and their tendency to crystallize is low; though the solubility is mainly determined by the methanol soluble MPEO-block. Regarding the solubility, these short chains do not make a clear difference between the reacted and the non reacted $MPEO_{2000}$. For both macroinitiators the ratio of ethylene oxide to ϵ-caprolactone repeating units is lower for the enzymatic compared to the chemical polymerization and the ratio is only about half of the theoretical value. This leads to the assumption that the initiator efficiency for Novozyme 435 is poorer than for $Zn(oct)_2$ as

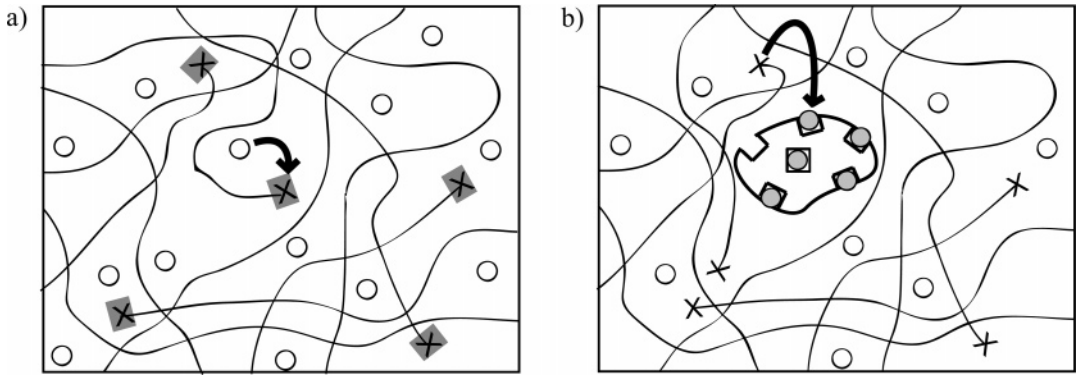


Figure 7. Activated chain end mechanism for the chemically catalyzed polymerization (a) and activated monomer mechanism for the enzymatically catalyzed polymerization (b). In the first case, for propagation the monomer must migrate to the activated chain end X (in gray); in the second case the polymer chain ends X have to migrate to the activated monomers (in gray), which are immobilized at the macroporous resin of Novozyme 435.

Table 7. Yields, Repeating Unit Ratios, Molecular Weights and Molecular Weight Distributions of the MPEO$_x$-*b*-poly(ϵ-caprolactone) Copolymers (6, 7) Obtained by Ring-Opening Polymerization of ϵ-Caprolactone Using Poly(ethylene glycol) Methyl Ether (MPEO$_x$) as Macroinitiator after Purification by Precipitation In Methanol

	methanol insoluble fraction				methanol soluble fraction			
polymer[a]	yield [%]	$[EO]_{r.u.}{}^{b}/[\epsilon\text{-CL}]_{r.u.}$	$M_{n,NMR}{}^{c}$ [g·mol^{-1}]	Q^d	yield [%]	$[EO]_{r.u.}{}^{b}/[\epsilon\text{-CL}]_{r.u.}$	$M_{n,NMR}{}^{c}$ [g·mol^{-1}]	Q^d
6c	48	0.82	8280	1.12	52	1.91	4510	1.11
6e	63	0.64	9990	1.31	37	3.75	3370	1.18
7c	85	0.87	19 840	1.35	16	5.95	7170	1.05
7e	73	0.66	24 410	1.65	27	7.53	6710	1.04

[a] Key: c = polymers by chemical catalysis; e = polymers by enzymatic catalysis. [b] Ratio of the repeating units (r.u.) ethylene oxide (EO) and ϵ-caprolactone (ϵ-CL) in the block copolymer. (The theoretical value, determined by the amount of ϵ−caprolactone in the feed, is 1.25.) [c] Molecular weight (M_n) determined by nuclear magnetic resonance spectroscopy (NMR). [d] Molecular weight distribution (Q) determined by gel permeation chromatography (GPC) using *N*,*N*-dimethylacetamide (DMAc) as eluent.

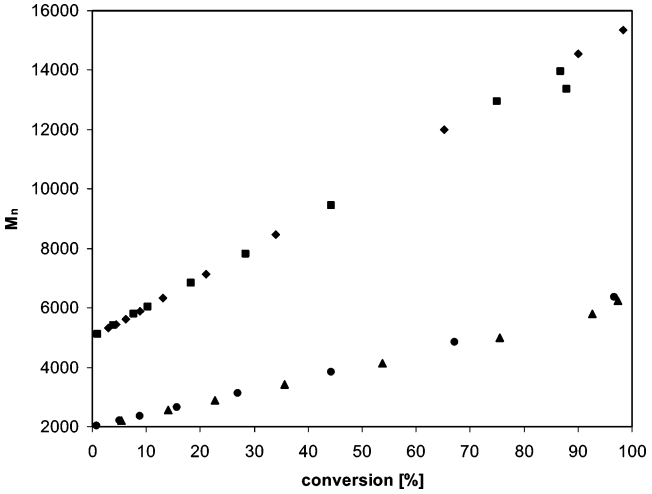
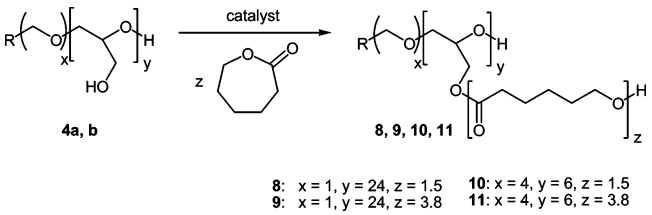


Figure 8. Number-average molecular weight (M_n) (determined by NMR) as a function of monomer conversion for the copolymers obtained by ring-opening polymerization of ϵ-caprolactone with MPEO$_{2000}$ [(●) Zn(oct)$_2$; (▲) Novozyme 435] and MPEO$_{5000}$ [(◆) Zn(oct)$_2$; (■) Novozyme 435] as macroinitiator.

Scheme 3. Ring-Opening Polymerization of ϵ-Caprolactone Using the Polyglycidols 4a and 4b as Macroinitiators



catalyst; only about 50% of the macroinitiator is used to start the ring-opening polymerization. This assumption is consistent with the observed yields. With MPEO$_{2000}$ as macroinitiator the yields are about 50% for both fractions. The yield for the methanol soluble fraction drops using Novozyme 435 as catalyst, because less MPEO$_{2000}$ is used and so the poly(ϵ-caprolactone) chains become longer and the copolymer less soluble. With MPEO$_{5000}$ as macroinitiator the yields of the methanol soluble fractions are lower. It is observed, that by enzymatic catalysis, the ratios of ethylene oxide to ϵ-caprolactone repeating units and the yields are higher than for chemical catalysis. This indicates that the initiator efficiency is better for the chemical catalysis.

The ring-opening polymerizations of ϵ-caprolactone with linear and star-shaped polyglycidols **4a,b** as macroinitiators using Zn(oct)$_2$ and Novozyme 435 as catalyst are carried out in bulk at 130 and 100 °C, respectively (Scheme 3). The macroinitiator and ϵ-caprolactone are heated to form a homogeneous solution, before the catalyst is added. As the solubility

Table 8. Molecular Weights and Molecular Weight Polydispersities of the Ring-Opening Polymerization of ϵ-Caprolactone Using the Multifunctional Macroinitiators 4a and 4b Leading to the Corresponding Copolymers (8, 9, 10, 11)

polymer[a]	$M_{n,cal.}{}^{b}$ [g·mol^{-1}]	$M_{n,NMR}{}^{c}$ [g·mol^{-1}]	$M_{n,GPC}{}^{d}$	Q^d
8c	6000	6200	11 800	1.14
8e	6000	5100	10 700	1.17
9c	12 300	12 900	19 800	1.12
9e	12 300	7600	12 100	1.11
10c	6100	5600	14 400	1.06
10e	6100	4700	10 900	1.09
11c	12 400	10 100	23 200	1.05
11e	12 400	5200	9700	1.06

[a] Key: c = polymers by chemical catalysis; e = polymers by enzymatic catalysis. [b] Calculated molecular weight. [c] Molecular weight (M_n) determined by nuclear magnetic resonance spectroscopy (NMR). [d] Molecular weight (M_n) and molecular weight distribution (Q) determined by gel permeation chromatography (GPC) using *N*,*N*-dimethylacetamide (DMAc) as eluent.

of the macroinitiators in ϵ-caprolactone is poor, the enzymatically catalyzed polymerization is performed at 100 °C. After precipitation in hexane and drying in a vacuum, the polymers are obtained as viscous oils (**8**, **10**) or waxy solids (**9**, **11**). To be able to compare the polymers initiated by monofunctional and multifunctional macroinitiators, the same monomer/initiator ratios as for the polymerizations with MPEO$_x$ are used. This means 36 and 91 ϵ-caprolactone repeating units per macroinitiator, respectively. The molecular weights and polydispersities of the obtained polymers are listed in Table 8.

The first indication for the success of the polymerization is the consistency of the products. As every macroinitiator contains 24 primary hydroxy groups able to start the polymerization, only 1−2 and 3−4 ϵ-caprolactone repeating units, respectively, are available per CH_2OH group. Compared to the polymers produced with the monofunctional macroinitiators, these polymers cannot crystallize due to the low number of ϵ-caprolactone repeating units in each side chain. Instead of powdery polymers, oils (**8**, **10**) and waxy compounds (**9**, **11**), respectively, are obtained. For all chemically catalyzed polymerizations yields above 92% were obtained in 24 h. Thus, the consistency of the polymers in combination with the good yields allows the assumption that a high percentage of the hydroxy groups acted as initiator and that only few ϵ-caprolactone repeating units are attached to each hydroxy group. Despite longer reaction times, the enzymatic catalyzed reactions lead only to yields of about 50% (**8e**, **10e**, **11e**) and 22% (**9e**). Possible reasons for these low yields will be discussed later.

The number-average molecular weight of the polymers is determined by end group analysis from the ^{1}H NMR spectrum. The M_n values for the polymer produced by chemical catalysis are in good agreement with the theoretical values. In accordance

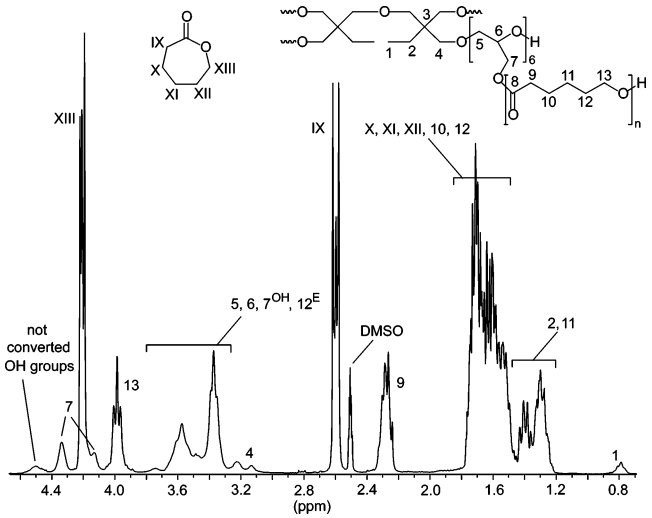


Figure 9. Section of the ^{1}H NMR spectrum of a kinetic sample of the ring-opening polymerization of ϵ-caprolactone with star-shaped polyglycidol **4b** as macroinitiator using zinc octoate as catalyst (**11c** after 4 h) in DMSO-d_6. 7^{OH} is the signal of the methylene group 7 from still unreacted macroinitiator and the peaks marked with E (superscript, like in Figure 2) are from the end groups.

with the yields the M_n values for the polymers produced by enzymatic catalysis are lower than expected.

The results of the GPC analysis confirm the results obtained by NMR analysis: The M_n values are lower for the enzymatically catalyzed polymerizations. For all polymers, low values of the polydisperities are observed, so it can be assumed that no adventitious initiator was active. As observed before, for the macroinitiators the polydispersities of the star-shaped polymers are lower than for the linear ones.

Kinetic studies were performed for the polymerization leading to polymers **9** and **11** in order to investigate the conversion of the initiating hydroxy groups during the polymerization. The conversion was followed via NMR spectroscopy (Figure 9). The conversion of the initiating hydroxy groups was determined by the integral ratio of resonance signal 7 (**CH$_2$**OCO) to resonance signal 1 (**CH$_3$** of diTMP) (I_x = integral of group x):

$$\text{conversion of hydroxy groups} = 3 \times \frac{I_{CH_2}(\text{XIII} + 7) - I_{CH_2}(\text{IX})}{I_{CH_3}(1)}$$

For the chemically catalyzed polymerization, the kinetic study shows that the number of converted hydroxy groups increases steadily (Figure 10). This might be explained if one assumes that the macroinitiator is available as a collapsed coil due to the hydrogen bonds between the hydroxy groups. Because of the growing ϵ-caprolactone chains, solubility increases and the coil opens, releasing additional hydroxy groups. In the end, nearly all hydroxy groups of the polyglycidol have initiated polymerization.

With Novozyme 435 as a catalyst only 3−4 of 24 hydroxy groups initiate polymerization. This effect might be explained by taking into account the different mechanisms (Figure 11). In the case of the chemically catalyzed system the catalyst gets close to the collapsed coil of the macroinitiator despite the growing poly(ϵ-caprolactone) chains and activates additional hydroxy groups. In the enzymatically catalyzed process the hydroxy groups of the polyglycidol have to approach the activated monomers immobilized on the macroporous resin. After initiation of the first poly(ϵ-caprolactone) chains by

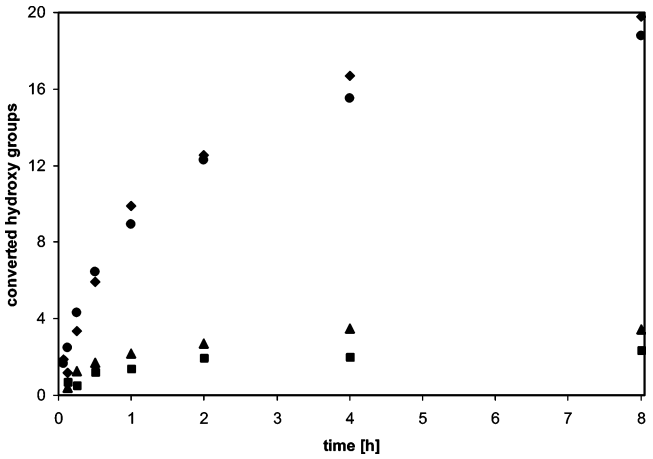


Figure 10. Ring-opening polymerization of ϵ-caprolactone with the linear [(◆) zinc octoate; (■) Novozyme 435] and the star-shaped [(●) zinc octoate; (▲) Novozyme 435] macroinitiator: conversion of the hydroxy groups as a function of time.

peripheral hydroxy groups, the newly formed hydroxy groups at the chain ends react preferentially with the immobilized activated monomers forming long poly(ϵ-caprolactone) chains and leaving unreacted methylol groups within the polyglycidol coil. It is much easier for the flexible growing poly(ϵ-caprolactone) chains to react with the monomers, than for the hydroxy groups in the coil. Therefore, steric hindrance might be the reason for the low initiation efficiency in enzymatic catalysis. Similar observations were reported by Iversen et al.[29]

As a consequence of the enzymatic polymerization only few hydroxy groups initiate polymerization and longer poly(ϵ-caprolactone) chains are formed, leaving a core with free unreacted hydroxy groups.

Further kinetic studies were made to investigate the ring-opening polymerization of ϵ-caprolactone with the multifunctional macroinitiators. The monomer conversion, determined by NMR, as a function of reaction time for the chemically catalyzed polymerization initiated by the linear and star-shaped macroinitiators has the same characteristics as for the polymerization initiated by MPEO$_x$. High conversions are obtained and the first-order plots show linear behavior. For both multifunctional macroinitiators similar reaction times and rates are observed and yields above 95% are obtained (Figure 12).

The number-average molecular weight M_n vs the conversion is plotted in Figure 13. M_n increases linearly with monomer conversion, which indicates that either chain transfer did not occur or its rate is negligible.

Conclusions

Linear and star-shaped multifunctional macroinitiators with primary hydroxy groups were successfully prepared by anionic ring-opening polymerization of a glycidol acetal followed by removal of the protecting groups. Molecular weights determined by NMR analysis agreed well with theoretical values; SEC measurements showed that narrow polydispersities were obtained and MALDI−TOF−MS measurements proved that no adventitious initiator was active. The presence of a star-shaped architecture was confirmed by quantitative NMR end group analysis, SEC measurements, and rheological measurements.

Comparison of the enzymatically and chemically catalyzed ring-opening polymerization of ϵ-caprolactone with monofunctional poly(ethylene glycol)s as macroinitiators revealed Novozyme 435 to be an alternative to the Lewis acid type catalyst Zn(oct)$_2$. Using the multifunctional polyglycidols as macroini-

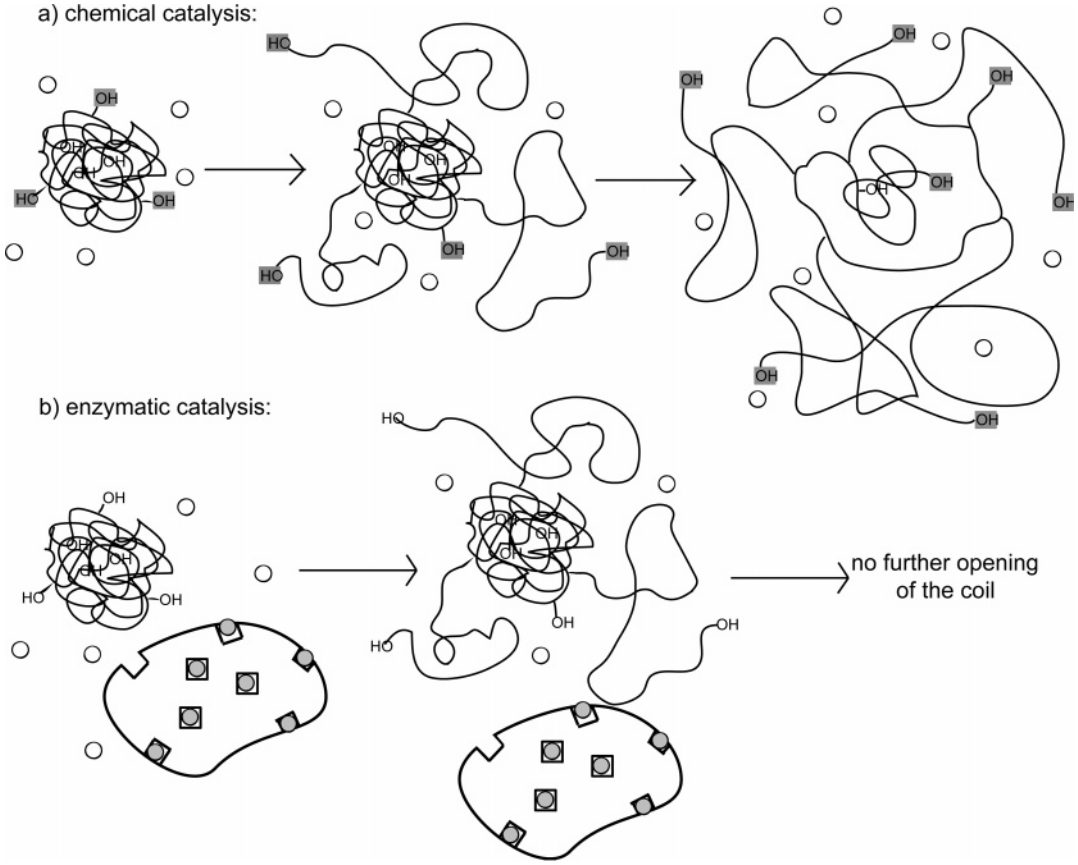


Figure 11. Sketch of the chemical catalysis (a) and the enzymatic catalysis (b) for the ring-opening polymerization of ϵ-caprolactone using a multifunctional polyglycidol macroinitiator.

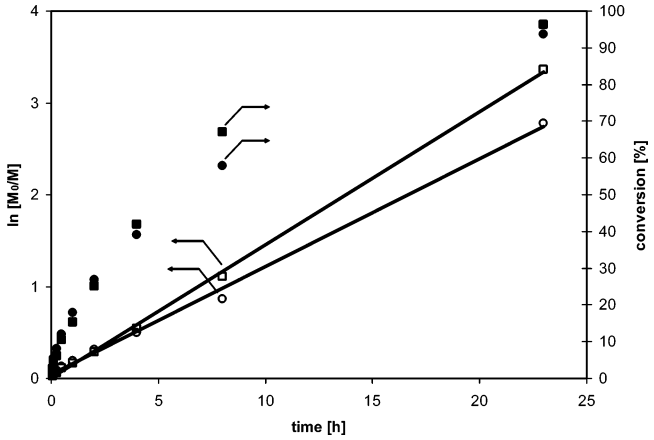


Figure 12. Polymerization of ϵ-caprolactone with the linear and the star-shaped macroinitiator catalyzed by $Zn(oct)_2$: conversion vs reaction time [(■) linear macroinitiator; (●) star-shaped macroinitiator] and first-order plot [(□) linear macroinitiator; (○) star-shaped macroinitiator]. (Linear macroinitiator, $[M]_0/[Zn(oct)_2] = 1300$, [macroinitiator]/[Zn-$(oct)_2$] = 14; star-shaped macroinitiator, $[M]_0/[Zn(oct)_2] = 2100$, [macroinitiator]/[$Zn(oct)_2$] = 23.)

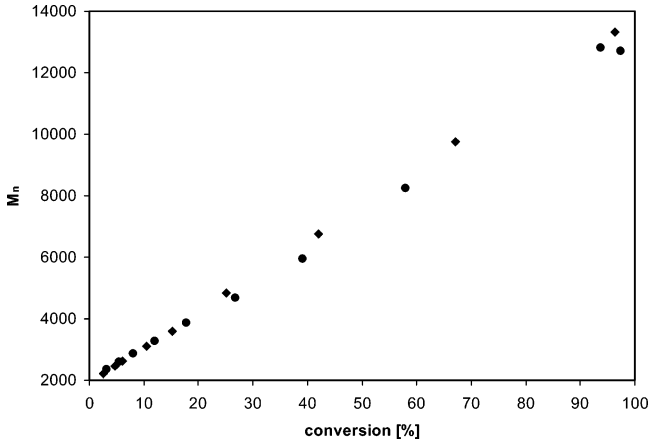


Figure 13. Number-average molecular weight M_n as a function of monomer conversion for the ring-opening polymerization of ϵ-caprolactone catalyzed by $Zn(oct)_2$ with the linear (◆) and the star-shaped (●) macroinitiator.

tiators, it was observed, that chemical catalysis lead to a high initiation efficiency of the hydroxy groups of the polyglycidol. In contrast, under the conditions used in this work, a large number of hydroxy groups remain unreacted for the enzymatic catalysis; as a consequence a copolymer with a different microstructure was obtained. Thus, these differences in the microstructure are based on steric hindrance and are a consequence of different activation mechanisms.

The preparation of core shell polymers with different architectures was successfully achieved by chemical catalysis. NMR and SEC analysis revealed that well-defined structures were obtained. Because of the biodegradability of the poly(ϵ-caprolactone) blocks and the biocompatible polyether core, these well-defined polyester polyether block copolymers are attractive materials for biomedical applications and represent potential drug carriers.

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