Chemoenzymatic Approach toward Heterografted Molecular Bottle Brushes

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ABSTRACT: Heterografted molecular bottle brushes, i.e., poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-(glycidol-*graft*-methyl methacrylate) [P(G-*graft*-CL^{AC})-*co*-(G-*graft*-MMA)] and poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-(glycidol-*graft*-*n*-butyl methacrylate) [P(G-*graft*-CL^{AC})-*co*-(G-*graft*-BMA)] were prepared in two steps starting with a linear polyglycidol. In the first step an approximately 50% homografted polymer poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-glycidol [P(G-*graft*-CL^{AC})-*co*-G] was obtained via ring-opening polymerization of ϵ-caprolactone using polyglycidol as a multifunctional macroinitiator and Novozyme 435 (Lipase B from *Candida antarctica* (CALB) immobilized on a macroporous resin) as a catalyst. Selective acetylation of the hydroxy groups at the graft ends was achieved via enzymatic acetylation with vinyl acetate, and the hydroxy groups at the backbone were acylated with 2-bromo-2-methylpropionyl bromide. Finally poly(methyl methacrylate) or poly(*n*-butyl methacrylate) grafts were attached by atom transfer radical polymerization. The heterografted molecular bottle brushes show monomodal elution curves in gel permeation chromatographic analyses. Differential scanning calorimetry confirms the existence of phase separated domains for both polymers.

Introduction

The preparation of structurally well-defined macromolecules such as star, block, graft, and brush copolymers gained increasing attention in view of the ability of such molecules to organize into well-defined nano-objects,[1,2] their application in coatings formulations,[3,4] for surface patterning,[5] and as additives for thermoplastic polymers.[6] These macromolecular architectures can be synthesized using radical and ionic polymerization techniques. A special example are dendron jacketed polymers[7] and molecular brushes, i.e., comb polymers in which the distance between the grafting points along the contour of the backbone is small in comparison to the unperturbed dimension of the side chains. Such densely grafted brush polymers can be varied by the backbone length, the grafting density, the side chain length, and the chemical composition. In particular, the spatial distribution of functional groups, either in the backbone or in the side chains, can be determined by the synthetic procedure,[8] in special cases allowing a certain control of the molecular shape, e.g., formation of tubular structures.[9−11]

Well-defined comb polymers are most efficiently prepared by grafting-onto, grafting-through, and grafting-from strategies. Controlled/living polymerizations like ring-opening polymerization (ROP),[12] nitroxide-mediated radical polymerization (NMRP),[13] and especially atom transfer radical polymerization (ATRP)[14−18] have been successfully used to obtain well-defined materials. Densely heterografted molecular brushes have been obtained via copolymerization of different macromonomers, as well as via combination of grafting-through and grafting-from methods.[19,20] For example, a macromonomer was copolymerized with 2-(trimethylsilyloxy)ethyl methacrylate (HEMA−TMS), subsequently the TMS protective groups were cleaved, and the resulting free hydroxy groups were esterified with 2-bromopropionyl bromide.[20] The resulting well-defined graft-copolymer can be used as a multifunctional macroinitiator for the polymerization of different monomers under ATRP conditions.

Here we report the preparation of heterografted brush molecules via a combination of enzymatic ring-opening polymerization and ATRP. Enzymes present a valuable tool to access copolymers with more complex architectures.[21−26] The benefit of using enzyme catalyzed polymerization is a high stereo-, regio- and chemoselectivity, the ability to operate under mild conditions, recyclability of the catalyst, and biocompatibility of the obtained polymers. So far, the most widely used enzyme for esterification and transesterification reactions is Lipase B from *Candida antarctica*, immobilized on macroporous acrylic resins, (Novozyme 435), which has exceptionally high catalytic activity and versatility.[21,22,27,28] Recent investigations reveal the compatibility of enzymes with other polymerization techniques and open the door to new materials.[29−35]

In a recent paper[26] we presented the ring-opening polymerization of ϵ-caprolactone with a polyglycidol as a multifunctional macroinitiator catalyzed by Novozyme 435. The microstructure of the resulting polymer was different from the microstructure of a polymer with the same ratio of repeating units obtained via chemical catalysis. By chemical catalysis, all hydroxy groups of the polyglycidol initiated the polymerization resulting in a densely grafted copolymer; while by enzymatic catalysis, the initiation efficiency of the hydroxy groups was much lower giving a comb polymer with free hydroxy groups remaining available for further modification at the polyglycidol backbone. On the basis of these results, we further investigated the characteristics of the enzymatic polymerization of ϵ-caprolactone using polyglycidol as a multifunctional macroinitiator and present a novel route for the preparation of heterografted molecular bottle brushes by a chemoenzymatic approach, the combination of enzymatic ring-opening polymerization, and ATRP.

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Experimental Part

Nomenclature. Polymers are abbreviated using the following nomenclature: P(G-*graft*-$\mathrm{CL}_{v/x}$)$_x$-*co*-G_y. The glycidol (G) backbone of this copolymer consits of $(x + y)$ glycidol repeating units, where x repeating units are grafted with ϵ-caprolactone (CL) having an average degree of polymerization of v/x per chain. For instance, P(G-*graft*-$\mathrm{CL}^{\mathrm{AC}}_{v/x}$)$_x$-*co*-(G-*graft*-$\mathrm{MMA}_{w/y}$)$_y$ describes a heterobrush copolymer with x glycidol repeating units grafted with an average of v/x ϵ-caprolactone repeating units per OH group and y glycidol repeating units grafted with an average of w/y methyl methacrylate (MMA) repeating units per OH group. $\mathrm{CL}^{\mathrm{AC}}$ stands for acetyl terminated poly(ϵ-caprolactone) chains. CL without an index stands for a poly(ϵ-caprolactone) grafts with terminal hydroxy groups.

Materials. ϵ-Caprolactone (≥99%, Fluka) and pyridine (99.8%, Fluka) were stirred with $\mathrm{CaH_2}$ for 24 h under $\mathrm{N_2}$, distilled under reduced pressure, and kept in a Schlenk tube under $\mathrm{N_2}$ until use. Chloroform (99%, Merck) was stirred with phosphorus pentoxide for 24 h under $\mathrm{N_2}$, distilled, and kept in a Schlenk tube under $\mathrm{N_2}$ till use. Diglyme and 3-phenyl-1-propanol (≥98%, Fluka) were distilled over sodium. Novozyme 435 (Lipase B from *Candida antarctica* immobilized on a macroporous resin, 10 000 U g^{-1}, Sigma) was dried in vacuum at room temperature for 24 h and stored under $\mathrm{N_2}$. Methyl methacrylate (99%, Aldrich) and *n*-butyl methacrylate (≥99%, Merck) were destabilized by filtration through aluminum oxide. Potassium *tert*-butoxide (1 M solution in THF, Aldrich), acetyl chloride (>98%, Fluka), vinyl acetate (99%, Acros), 2-bromo-2-methylpropionyl bromide (98%, Acros), copper(I) bromide (≥98%, Fluka), 2,2′-bipyridyl (99%, Acros), and *n*-butyl acetate (99.5%, Merck) were used as received. Ethoxy ethyl glycidyl ether was synthesized from 2,3-epoxypropan-1-ol (glycidol) and ethyl vinyl ether according to Fitton et al.[36] 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. Polyglycidol. PG (I). 3-Phenylpropanol (2.68 mL, 19.7 mmol) was dissolved in diglyme (70 mL), and potassium *tert*-butoxide (1.97 mL of a 1 M solution in THF, 1.97 mmol) was added. The formed *tert*-butanol was removed by distillation. Ethoxy ethyl glycidyl ether (69.0 g, 0.47 mol) was added, and the mixture was stirred for 16 h at 120 °C. The solvent was removed in vacuum at 80 °C, and a viscous liquid was obtained. The product was dissolved in tetrahydrofuran (110 mL/1 g of polymer), and aqueous 32% HCl (3.3 g/1 g of polymer) was added. After 1 h, the polyglycidol (**I**) precipitated as an oil. The solvent was removed, and the polyglycidol was dried in vacuum at 80 °C. Yield: 90%. M_{n}(GPC) = 5.400, $M_{\mathrm{w}}/M_n = 1.08$, monomodal. ^{1}H NMR (DMSO-d_6): δ 1.88 (qui, $J = 7.0$ Hz, $\mathrm{ArCH_2C\mathit{H}_2}$), 2.67 (t, $J = 7.6$ Hz, $\mathrm{ArC\mathit{H}_2CH_2}$), 3.45−3.95 (m, $\mathrm{C\mathit{H}_2OC\mathit{H}_2C\mathit{H}(C\mathit{H}_2OH)O}$), 4.53 (s, $\mathrm{O\mathit{H}}$), 7.12−7.33 (m, Ar). ^{13}C NMR (DMSO-d_6) (end group signals are marked with an “E”): δ 30.9 ($\mathrm{ArCH_2\mathit{C}H_2}$), 31.6 $\mathrm{Ar\mathit{C}H_2CH_2}$, 60.9, 63.0$^{\mathrm{E}}$ ($\mathrm{CH_2CH(\mathit{C}H_2OH)O}$), 69.3, 71.7$^{\mathrm{E}}$ ($\mathrm{\mathit{C}H_2CH(CH_2OH)O}$), 69.5 ($\mathrm{CH_2\mathit{C}H_2O}$), 70.7$^{\mathrm{E}}$, 80.0 ($\mathrm{CH_2\mathit{C}H(CH_2OH)O}$), 125.7, 128.2, 128.3, 141.7 (Ar). From the ^{1}H NMR spectrum, the following degree of polymerization was determined: $\mathrm{DP}_n = 24$.

Poly(glycidol-*graft*-ϵ-caprolactone)-*co*-glycidol. P(G-*graft*-CL)-*co*-G (IIc). Polyglycidol **I** (1.26 g, 0.66 mmol) and ϵ-caprolactone (6.90 g, 60.5 mmol) were heated to 80 °C in order to obtain a homogeneous solution. Novozyme 435 (552 mg, 8 wt %) was added, and the mixture was stirred for 28 h at 80 °C. The polymerization was stopped by adding methylene chloride and removing the enzyme by filtration. The polymer **IIc** was isolated by precipitation in hexane. After drying in vacuum at 50 °C, a waxy polymer was obtained. Yield: 96%. M_{n}(GPC) = 17 200, M_{w}/M_n = 1.25, monomodal. ^{1}H NMR (DMSO-d_6): δ 1.20−1.42 (m, $\mathrm{CH_2C\mathit{H}_2CH_2}$), 1.42−1.66 (m, $\mathrm{C\mathit{H}_2CH_2C\mathit{H}_2}$), 1.68−1.84 (m, $\mathrm{ArCH_2C\mathit{H}_2}$), 2.27 (t, $J = 7.2$ Hz, $\mathrm{OCOC\mathit{H}_2CH_2}$), 2.60 (t, $J = 7.6$ Hz, $\mathrm{ArC\mathit{H}_2CH_2}$), 3.27−3.80 (m, $\mathrm{ArCH_2CH_2C\mathit{H}_2}$, $\mathrm{OC\mathit{H}_2C\mathit{H}(C\mathit{H}_2OH)O}$, $\mathrm{OC\mathit{H}_2C\mathit{H}(CH_2OCO)O}$, $\mathrm{CH_2C\mathit{H}_2OH}$), 3.98 (t, $J = 6.4$ Hz, $\mathrm{CH_2C\mathit{H}_2OCO}$), 4.07−4.40 (m, $\mathrm{CHC\mathit{H}_2OCO}$), 4.40−4.60 (s, not converted $\mathrm{CHCH_2O\mathit{H}}$ groups), 7.12−7.32 (m, Ar). ^{13}C NMR (DMSO-d_6) (end group signals are marked with an “E”): δ 24.0, 24.4$^{\mathrm{E}}$ ($\mathrm{COCH_2\mathit{C}H_2CH_2CH_2CH_2O}$), 24.8, 25.0$^{\mathrm{E}}$ ($\mathrm{COCH_2CH_2\mathit{C}H_2CH_2CH_2O}$), 27.8, 32.1$^{\mathrm{E}}$ ($\mathrm{COCH_2CH_2CH_2\mathit{C}H_2CH_2O}$), 33.3, 33.5$^{\mathrm{E}}$ ($\mathrm{CO\mathit{C}H_2CH_2CH_2CH_2CH_2O}$), 60.5$^{\mathrm{E}}$, 63.4 ($\mathrm{COCH_2CH_2CH_2CH_2\mathit{C}H_2O}$), 172.7, 172.8$^{\mathrm{E}}$ ($\mathrm{\mathit{C}OCH_2CH_2CH_2CH_2CH_2O}$) (the peaks of the polyglycidol backbone are not distinguishable from the noise of the baseline). The degree of grafting was determined via NMR analysis (by determination of the concentration of functionalized repeating units: $\mathrm{CHC\mathit{H}_2OCO}$ $\delta = 4.07-4.40$ ppm).[26] The resulting initiation efficiency was 46% (P(G-*graft*-$\mathrm{CL_8}$)$_{11}$-*co*-G_{13}).

Table 1. Synthesis of Poly(glycidol-*graft*-ϵ-caprolactone)-*co*-glycidol Copolymers (IIa−IIf), Reagents, Reaction Times, and Yields

polymer	macroinitiator[a] [g (mmol)]	ϵ-caprolactone [g (mmol)]	novozyme 435[b] [mg (wt %)]	time [h]	yield [%]
IIa	1.12 (0.58)	5.50 (48.2)	110 (2)	120	72
IIb	1.16 (0.60)	6.30 (55.3)	252 (4)	30	92
IIc	1.26 (0.66)	6.90 (60.5)	522 (8)	28	93
IId	1.23 (0.64)	6.72 (58.8)	806 (12)	22	94
IIe	0.56 (0.29)	6.15 (58.7)	492 (8)	28	94
IIf	0.31 (0.16)	6.77 (59.0)	542 (8)	28	82

[a] Linear polyglycidol ($\mathrm{DP}_n = 24$). [b] Weight percent of enzyme in relation to monomer in the feed.

The synthesis of **IIa−IIf** was performed in analogy to **IIc**. Reagent ratios, reaction times, and yields for all poly(glycidol-*graft*-ϵ-caprolactone)-*co*-glycidol copolymers are listed in Table 1. For further analytical data see Table 2.

Poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-glycidol. P(G-*graft*-CL$^{\mathrm{AC}}$)-*co*-G (IIIc). Polymer IIc (8.18 g, 0.66 mmol, 6.6 mmol of PCL chain ends) was dissolved in chloroform (30 mL) and vinyl acetate (1.70 g, 19.8 mmol), and Novozyme 435 (800 mg) was added. After stirring 20 h at 60 °C, the reaction was stopped by removing the enzyme by filtration. The polymer **IIIc** was isolated by precipitation in hexane. After drying in vacuum at 50 °C, a waxy polymer was obtained. Yield: 92%. M_{n}(GPC) = 18 900, $M_{\mathrm{w}}/M_{\mathrm{n}}$ = 1.24, monomodal. Because of a better resolution of the $\mathrm{COC\mathit{H}_3}$ peak, the spectra were recorded in $\mathrm{CDCl_3}$. ^{1}H NMR ($\mathrm{CDCl_3}$): δ 1.30−1.46 (m, $\mathrm{CH_2C\mathit{H}_2CH_2}$), 1.58−1.74 (m, $\mathrm{C\mathit{H}_2CH_2C\mathit{H}_2}$), 1.80−1.94 (m, $\mathrm{ArCH_2C\mathit{H}_2}$), 2.04 (s, $\mathrm{CH_2CH_2OCOC\mathit{H}_3}$), 2.31 (t, $J = 7.5$ Hz, $\mathrm{OCOC\mathit{H}_2CH_2}$), 2.67 (t, $J = 7.6$ Hz, $\mathrm{ArC\mathit{H}_2CH_2}$), 3.27 (s, not converted $\mathrm{CHCH_2O\mathit{H}}$ groups), 3.40−3.86 (m, $\mathrm{ArCH_2CH_2C\mathit{H}_2}$, $\mathrm{OC\mathit{H}_2C\mathit{H}(C\mathit{H}_2OH)O}$, $\mathrm{OC\mathit{H}_2C\mathit{H}(CH_2OCO)O}$), 4.06 (t, $J = 6.6$ Hz, $\mathrm{CH_2C\mathit{H}_2OCO}$, $\mathrm{CH_2C\mathit{H}_2OCOCH_3}$), 4.06, 4.16−4.36 (m, $\mathrm{CHC\mathit{H}_2OCO}$), 7.12−7.34 (m, Ar). ^{13}C NMR ($\mathrm{CDCl_3}$) (end group signals are marked with an “E”): δ 21.0 ($\mathrm{CH_2CH_2CH_2OCO\mathit{C}H_3}$), 24.6 ($\mathrm{COCH_2\mathit{C}H_2CH_2CH_2CH_2O}$), 25.5 ($\mathrm{COCH_2\mathit{C}H_2CH_2CH_2CH_2O}$), 28.3 ($\mathrm{COCH_2CH_2CH_2\mathit{C}H_2CH_2O}$), 34.1 ($\mathrm{CO\mathit{C}H_2CH_2CH_2CH_2CH_2O}$), 64.1, 64.3$^{\mathrm{E}}$ ($\mathrm{COCH_2CH_2CH_2CH_2\mathit{C}H_2O}$), 171.1 ($\mathrm{CH_2CH_2CH_2O\mathit{C}OCH_3}$), 173.1 ($\mathrm{CHCH_2O\mathit{C}O}$), 173.5 ($\mathrm{\mathit{C}OCH_2CH_2CH_2CH_2CH_2O}$) (the peaks of the polyglycidol backbone are not distinguishable from the noise of the baseline). From the ^{1}H NMR spectrum, the following polymer composition was determined: P(G-*graft*-$\mathrm{CL_8}^{\mathrm{AC}}$)$_{11}$-*co*-$\mathrm{G}_{13}$.

Poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-glycidyl-2-bromo-2-methylpropionate. P(G-*graft*-CL$^{\mathrm{AC}}$)-*co*-GBMP (IVc). P(G-*graft*-CL$^{\mathrm{AC}}$)-*co*-G (**IIIc**) (4.01 g, 0.32 mmol) was dissolved in dry pyridine (50 mL) under $\mathrm{N_2}$. 2-Bromo-2-methylpropionyl bromide (2.04 g, 8.90 mmol) was added dropwise at 0 °C, and the mixture was stirred for 16 h at room temperature. Pyridine was removed in vacuum, and the residue dissolved in methylene chloride. The solution was washed with aqueous HCl and $\mathrm{NaHCO_3}$ solutions, stirred over $\mathrm{MgSO_4}$, precipitated in pentane, and dried in vacuum at 40 °C. A waxy polymer was obtained. Yield: 85%. M_{n}(GPC) = 22 400, $M_{\mathrm{w}}/M_{\mathrm{n}}$ = 1.19, monomodal. The signals of the ^{1}H NMR spectrum recorded in $\mathrm{CDCl_3}$ are the same as for **IIIc**, except the signal of the free hydroxy group disappears and a new singlet appears at $\delta = 1.93$ ppm due to the $\mathrm{C(C\mathit{H}_3)_2Br}$ group. The signal of the methylene group adjacent to the acylated hydroxy group shifts to $\delta = 4.06-4.36$ ppm after the esterification. ^{13}C NMR ($\mathrm{CDCl_3}$) (end group signals are marked with an “E”): δ 21.0 ($\mathrm{CH_2CH_2CH_2OCO\mathit{C}H_3}$), 24.6 ($\mathrm{COCH_2\mathit{C}H_2CH_2CH_2CH_2O}$), 25.5 ($\mathrm{COCH_2\mathit{C}H_2}$-

Table 2. Reagent Ratios, Molecular Weights, Polydispersity Indices, and Grafting Percentage of the Copolymers Obtained by the Ring-Opening Polymerization of ϵ-Caprolactone Using Linear Polyglycidol I ($DP_n = 24$) as Macroinitiator

polymer	enzyme[a] [wt %]	[CL][b]/[PG]	CL conversion[c] [%] (v)	$\langle M_n\rangle_{,NMR}$[d]	$\langle M_n\rangle_{,calcd}$[e]	$\langle M_n\rangle_{,GPC}$[f]	Q[f]	initiation efficiency[g] [%] (x,y)
IIa	2	91	76 (69)	9 800	12 400	13 600	1.16	33 (8,16)
IIb	4	91	96 (87)	11 300	12 400	18 000	1.29	42 (10,14)
IIc	8	91	98 (89)	12 500	12 400	17 200	1.25	46 (11,13)
IId	12	91	99 (90)	12 200	12 400	18 600	1.20	46 (11,13)
IIe	8	182	98 (178)	22 000	22 800	28 200	1.17	54 (13,11)
IIf	8	364	90 (328)	40 500	43 700	39 000	1.72	38 (9,15)

[a] Weight percent of enzyme in relation to monomer in the feed. [b] Equivalents (v) of ϵ-caprolactone (CL) per macroinitiator (polyglycidol (PG)) in the feed. [c] CL conversion and equivalents of CL (v) per polymer. [d] Number average molecular weight (M_n) determined by end group analysis (^{1}H NMR spectroscopy). [e] Calculated molecular weight at full monomer conversion. [f] M_n and molecular weight distribution ($Q = M_w/M_n$) determined by gel permeation chromatography (GPC) against narrow poly(methyl methacrylate) standards using tetrahydrofuran (THF) as eluent. [g] Initiation efficiency of the multifunctional macroinitiator (x repeating units are grafted, y primary hydroxy groups remain).

CH$_2$CH$_2$CH$_2$O), 28.3 (COCH$_2$CH$_2$CH$_2$*C*H$_2$CH$_2$O), 30.8 (COC(*C*H$_3$)$_2$Br), 34.1 (CO*C*H$_2$CH$_2$CH$_2$CH$_2$CH$_2$O), 55.8 (CO*C*(CH$_3$)$_2$Br), 64.1, 64.3^E (COCH$_2$CH$_2$CH$_2$CH$_2$*C*H$_2$O), 171.1 (CH$_2$CH$_2$CH$_2$O*C*OCH$_3$), 171.3 (*C*OC(CH$_3$)$_2$Br), 173.1 (CHCH$_2$O*C*O), 173.5 (*C*OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$O) (the peaks of the polyglycidol backbone are not distinguishable from the noise of the baseline). From the ^{1}H NMR spectrum, the following polymer composition was determined: P(G-*graft*-CL$_8^{AC}$)$_{11}$-*co*-GBMP$_{13}$.

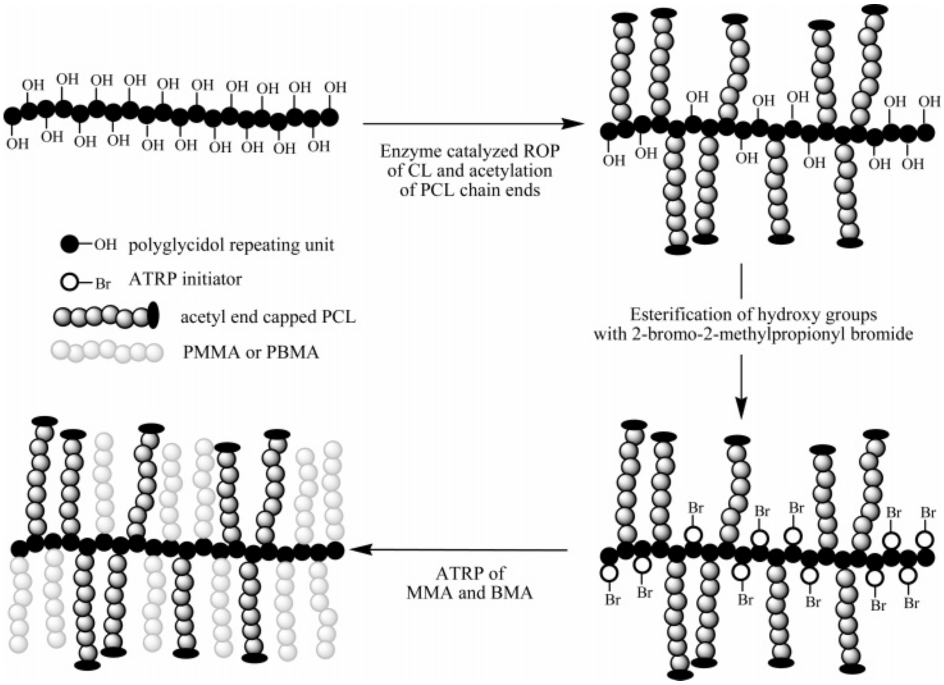
One-Pot Synthesis of P(G-*graft*-CL^{AC})-*co*-GBMP (IVc′). The same procedure as for **IIc** was followed. After 28 h at 80 °C, the reaction mixture was cooled to 60 °C, diluted with chloroform (30 mL), and vinyl acetate (1.70 g, 19.8 mmol) was added. After stirring 20 h at 60 °C, the temperature was reduced to 0 °C, pyridine (4.38 g, 55.4 mmol) and 2-bromo-2-methylpropionyl bromide (2.04 g, 8.90 mmol) were added, and the reaction mixture was stirred another 20 h at room temperature. The reaction was stopped by removing the enzyme by filtration. In order to isolate the polymer, the same workup as for **IVc** was applied. Yield: 82%. M_n(GPC) = 21 400, M_w/M_n = 1.20, monomodal. The NMR spectra were identical with those of the polymer **IVc**. From the ^{1}H NMR spectrum, the following polymer composition was determined: P(G-*graft*-CL$_8^{AC}$)$_{11}$-*co*-GBMP$_{13}$.

Poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-(glycidol-*graft*-methyl methacrylate). P(G-*graft*-CL^{AC})-*co*-(G-*graft*-MMA) (Vc′). In a Schlenk tube, the multifunctional macroinitiator **IVc′** (150 mg, 0.13 mmol initiating Br end groups, 1 equiv) was dissolved in 0.5 mL of *n*-butyl acetate. In a second Schlenk tube, MMA (2.60 g, 26.0 mmol, 200 equiv), 2,2′-bipyridyl (41.0 mg, 0.26 mmol, 2 equiv), CuBr (19.0 mg, 0.13 mmol, 1 equiv), and *n*-butyl acetate (in total 66 vol % of monomer) were degassed by passing N$_2$ for 30 min through the solution. The flask was placed in a thermostated oil bath at 60 °C, and the polymerization was started by addition of the macroinitiator. During the polymerization, samples were taken for GPC and NMR analyses. The polymerization was stopped by exposing the solution to air and diluting it with CH$_2$Cl$_2$. The solution was washed with 1 M HCl solution, dried over MgSO$_4$, and precipitated in pentane. For **Vc′^{1}** (75 min), M_n(GPC) = 55 000, M_w/M_n = 1.25, monomodal; for **Vc′^{2}** (120 min), M_n(GPC) = 83 000, M_w/M_n = 1.35, monomodal. ^{1}H NMR (CDCl$_3$): δ 0.70−1.18 (m, CH$_2$C(*C*H$_3$)(COO)), 1.22 (s, CH$_2$OCO(C*H*$_3$)$_2$CH$_2$), 1.30−1.46 (m, CH$_2$C*H*$_2$CH$_2$), 1.58−1.74 (m, C*H*$_2$CH$_2$C*H*$_2$), 1.74−2.00 (m, ArCH$_2$C*H*$_2$, C*H*$_2$C(CH$_3$)(COO)), 2.04 (s, CH$_2$CH$_2$OCOC*H*$_3$), 2.31 (t, *J* = 7.5 Hz, OCOC*H*$_2$CH$_2$), 2.67 (t, *J* = 7.6 Hz, ArC*H*$_2$CH$_2$), 3.40−3.86 (m, ArCH$_2$CH$_2$C*H*$_2$, OC*H*$_2$C*H*(CH$_2$OCO)O, COOC*H*$_3$), 4.06 (t, *J* = 6.6 Hz, CH$_2$C*H*$_2$OCO, CH$_2$C*H*$_2$OCOCH$_3$), 4.06, 4.16−4.36 (m, CHC*H*$_2$OCO, CHC*H*$_2$OCOC(CH$_3$)$_2$CH$_2$), 7.12−7.34 (m, Ar). ^{13}C NMR (CDCl$_3$): δ 16.4, 18.7 (CH$_2$C(*C*H$_3$)(COO)), 24.6 (COCH$_2$*C*H$_2$CH$_2$CH$_2$CH$_2$O), 25.5 (COCH$_2$*C*H$_2$CH$_2$CH$_2$CH$_2$O), 28.3 (COCH$_2$CH$_2$CH$_2$*C*H$_2$CH$_2$O), 34.1 (CO*C*H$_2$CH$_2$CH$_2$CH$_2$CH$_2$O), 44.6, 44.9 (CH$_2$*C*(CH$_3$)(COO)), 51.8 (COO*C*H$_3$), 54.4 (*C*H$_2$C(CH$_3$)(COO)), 64.1, (COCH$_2$CH$_2$CH$_2$CH$_2$*C*H$_2$O), 173.5 (*C*OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$O), 177.0, 177.8 (CH$_2$C(CH$_3$)(*C*OO)) (the peaks of the polyglycidol backbone are not distinguishable from the noise of the baseline). From the ^{1}H NMR spectra, the following polymer compositions were determined: for **Vc′^{1}** (75 min), P(G-*graft*-CL$_8^{AC}$)$_{11}$-*co*-(G-*graft*-MMA$_{35}$)$_{13}$ and for **Vc′^{2}** (120 min), P(G-*graft*-CL$_8^{AC}$)$_{11}$-*co*-(G-*graft*-MMA$_{56}$)$_{13}$.

Poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-(glycidol-*graft*-*n*-butyl methacrylate). P(G-*graft*-CL^{AC})-*co*-(G-*graft*-BMA) (VIc′). In a Schlenk tube, the multifunctional macroinitiator **IVc′** (150 mg, 0.13 mmol initiating Br end groups, 1 equiv) was dissolved in 0.5 mL of *n*-butyl acetate. In a second Schlenk tube, BMA (1.50 g, 10.4 mmol, 80 equiv), 2,2′-bipyridyl (41.0 mg, 0.26 mmol, 2 equiv), CuBr (19.0 mg, 0.13 mmol, 1 equiv), and *n*-butyl acetate (in total 66 vol % of monomer) were degassed by passing N$_2$ for 30 min through the solution. The flask was placed in a thermostated oil bath at 60 °C, and the polymerization was started by addition of the macroinitiator. During the polymerization, samples were taken for GPC and NMR analyses. The polymerization was stopped by exposing the solution to air and diluting it with CH$_2$Cl$_2$. The solution was washed with 1 M HCl solution, dried over MgSO$_4$, and precipitated from ethanol at −78 °C. For **VIc′^{1}** (120 min), M_n(GPC) = 60 000, M_w/M_n = 1.24, monomodal; for **VIc′^{2}** (210 min), M_n(GPC) = 100 000, M_w/M_n = 1.31, monomodal. ^{1}H NMR (CDCl$_3$): δ 0.70−1.18 (m, CH$_2$C(C*H*$_3$)(COO), OCH$_2$CH$_2$CH$_2$C*H*$_3$), 1.22 (s, CH$_2$OCO(C*H*$_3$)$_2$CH$_2$), 1.30−1.46 (m, CH$_2$C*H*$_2$CH$_2$, OCH$_2$CH$_2$C*H*$_2$CH$_3$), 1.58−1.74 (m, C*H*$_2$CH$_2$C*H*$_2$, OCH$_2$C*H*$_2$CH$_2$CH$_3$), 1.74−2.00 (m, ArCH$_2$C*H*$_2$, C*H*$_2$C(CH$_3$)(COO)), 2.04 (s, CH$_2$CH$_2$OCOC*H*$_3$), 2.31 (t, *J* = 7.5 Hz, OCOC*H*$_2$CH$_2$), 2.67 (t, *J* = 7.6 Hz, ArC*H*$_2$CH$_2$), 3.40−3.86 (m, ArCH$_2$CH$_2$C*H*$_2$, OC*H*$_2$C*H*(CH$_2$OCO)O), 3.94 (s, OC*H*$_2$CH$_2$CH$_2$CH$_3$), 4.06 (t, *J* = 6.6 Hz, CH$_2$C*H*$_2$OCO, CH$_2$C*H*$_2$OCOCH$_3$), 4.06, 4.16−4.36 (m, CHC*H*$_2$OCO, CHC*H*$_2$OCOC(CH$_3$)$_2$CH$_2$), 7.12−7.34 (m, Ar). ^{13}C NMR (CDCl$_3$): δ 13.7 (OCH$_2$CH$_2$CH$_2$*C*H$_3$), 16.4, 18.5 (CH$_2$C(*C*H$_3$)(COO)), 19.3 (OCH$_2$CH$_2$*C*H$_2$CH$_3$), 24.6 (COCH$_2$*C*H$_2$CH$_2$CH$_2$CH$_2$O), 25.5 (COCH$_2$*C*H$_2$CH$_2$CH$_2$CH$_2$O), 28.3 (COCH$_2$CH$_2$CH$_2$*C*H$_2$CH$_2$O), 30.3 (OCH$_2$*C*H$_2$CH$_2$CH$_3$), 34.1 (CO*C*H$_2$CH$_2$CH$_2$CH$_2$CH$_2$O), 44.7, 45.1 (CH$_2$*C*(CH$_3$)(COO)), 51.8 (COO*C*H$_3$), 54.2, 54.4 (*C*H$_2$C(CH$_3$)(COO)), 64.1 (COCH$_2$CH$_2$CH$_2$CH$_2$*C*H$_2$O), 64.7 (O*C*H$_2$CH$_2$CH$_2$CH$_3$), 173.5 (*C*OCH$_2$CH$_2$CH$_2$CH$_2$CH$_2$O), 176.8, 177.5 (CH$_2$C(CH$_3$)(*C*OO)) (the peaks of the polyglycidol backbone are not distinguishable from the noise of the baseline)). From the ^{1}H NMR spectra, the following polymer compositions were determined: for **VIc′^{1}** (120 min), P(G-*graft*-CL$_8^{AC}$)$_{11}$-*co*-(G-*graft*-BMA$_{27}$)$_{13}$ and for **VIc′^{2}** (210 min), P(G-*graft*-CL$_8^{AC}$)$_{11}$-*co*-(G-*graft*-MMA$_{51}$)$_{13}$.

Poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-glycidylacetate. P(G-*graft*-CL^{AC})-*co*-G^{AC} (**VIIc**). **IIc** (0.50 g, 0.04 mmol) was dissolved in pyridine (8 mL), and acetyl chloride (100 mg, 1.27 mmol) was added slowly at 0 °C. The mixture was stirred 16 h at room temperature. Pyridine was removed in vacuum, and the residue dissolved in methylene chloride. The solution was washed three times with acidic water, stirred over Na$_2$SO$_4$, and dried in vacuum. M_n(GPC) = 16 300, M_w/M_n = 1.29, monomodal. ^{1}H NMR (CDCl$_3$): δ 1.30−1.46 (m, CH$_2$C*H*$_2$CH$_2$), 1.58−1.74 (m, C*H*$_2$CH$_2$C*H*$_2$), 1.80−1.94 (m, ArCH$_2$C*H*$_2$), 2.04 (s, CH$_2$CH$_2$OCOC*H*$_3$), 2.08 (s, CHCH$_2$OCOC*H*$_3$), 2.31 (t, *J* = 7.5 Hz, OCOC*H*$_2$CH$_2$), 2.67 (t, *J* = 7.6 Hz, ArC*H*$_2$CH$_2$), 3.40−3.86 (m, ArCH$_2$CH$_2$C*H*$_2$, OC*H*$_2$C*H*(CH$_2$OCO)O), 4.06 (t, *J* = 6.6 Hz, CH$_2$C*H*$_2$OCO,

Scheme 1. Preparation of Well-Defined Heterografted Brush Copolymers by a Combination of Enzymatic Ring-Opening Polymerization (ROP) of ϵ-Caprolactone (CL) and Atom Transfer Radical Polymerization (ATRP) of Methyl Methacrylate (MMA) and *n*-Butyl Methacrylate (BMA)



$CH_2C\mathit{H}_2OCOCH_3$), 4.06, 4.16−4.36 (m, $CHC\mathit{H}_2OCO$, $CHC\mathit{H}_2OCOCH_3$), 7.12−7.34 (m, Ar). ^{13}C NMR ($CDCl_3$): δ 20.8 ($CHCH_2OCO\mathit{C}H_3$), 21.0 ($CH_2CH_2CH_2OCO\mathit{C}H_3$), 24.6 ($COCH_2\mathit{C}H_2CH_2CH_2CH_2O$), 25.5 ($COCH_2CH_2\mathit{C}H_2CH_2CH_2O$), 28.3 ($COCH_2CH_2CH_2\mathit{C}H_2CH_2O$), 34.1 ($CO\mathit{C}H_2CH_2CH_2CH_2CH_2O$), 64.1 ($COCH_2CH_2CH_2CH_2\mathit{C}H_2O$), 170.7 ($CHCH_2O\mathit{C}OCH_3$), 171.1 ($CH_2CH_2CH_2O\mathit{C}OCH_3$), 173.1 ($CHCH_2O\mathit{C}O$), 173.5 ($\mathit{C}OCH_2CH_2CH_2CH_2CH_2O$) (the peaks of the polyglycidol backbone are not distinguishable from the noise of the baseline). The same procedure was applied for the complete acetylation of **IIe** and **IIf**. From the ^1H NMR spectrum, the following polymer composition was determined: P(G-*graft*-CL_8^{AC})$_{11}$-*co*-G_{13}^{AC}.

Measurements. ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-300 FTNMR 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 an internal standard.

Gel permeation chromatography (GPC) 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 300 mm for the other four columns. The diameter of each column was 8 mm, the diameter of the gel particles 5 mm, and the nominal pore widths were 50, 50, 100, 1000, and 10 000 Å, respectively. Calibration was achieved using poly(methyl methacrylate) standards.

For polyglycidol (**I**), gel permeation chromatography 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 8 mm, the diameter of the gel particles 5 mm, and the nominal pore widths were 100, 1000, and 10 000 Å. Calibration was achieved using poly(methyl methacrylate) standards.

Differential scanning calorimetry (DSC) analyses were performed on a Netzsch DSC 204 under nitrogen using a 10 K min^{-1} scan rate. The samples (3−12 mg) were subjected to two cooling−heating processes −90 °C to 120 °C to −90 °C to 120 °C.

Results and Discussion

We previously studied the ring-opening polymerization of ϵ-caprolactone with multifunctional polyglycidol as the macroinitiator by means of chemical and enzymatic catalysis.[26] Chemical catalysis led to a high initiation efficiency of the hydroxy groups, while with Novozyme 435, a large number of the hydroxy groups remained unreacted in each molecule. This comb shaped polymer with remaining hydroxy groups at the backbone represents a good starting material for the synthesis of heterografted molecular bottle brushes. In fact, after selective end capping of the poly(ϵ-caprolactone) chains, the remaining hydroxy groups at the backbone can be transformed via esterification into initiators for atom transfer radical polymerization (Scheme 1). The polymerization of vinyl monomers from this novel macroinitiator will demonstrate the ability of this system to prepare new polymers with complex architectures.

First the enzymatic ring-opening polymerization of ϵ-caprolactone using polyglycidol as a multifunctional macroinitiator is investigated in more detail in order to understand the influences of the reagents' concentrations on the initiation efficiency. Then the synthesis of the ATRP macroinitiators and the heterografted brush copolymers will be presented.

Grafting of ϵ-Caprolactone from Polyglycidol. The synthesis of polyglycidol was achieved via the anionic ring-opening polymerization of ethoxy ethyl glycidyl ether using 3-phenylpropanol as an initiator, and a protected polyglycidol is obtained. Removal of the protecting groups under acidic conditions results in a polyglycidol (**I**) with 90% yield. The number average molecular weight of the starting polymer determined via end group analysis was $M_n = 1912$ g/mol and the molecular weight distribution determined via GPC in DMAc was $M_w/M_n = 1.08$. Polyglycidol **I** contains $x + y = 24$ primary hydroxy groups (Scheme 2).

The ring-opening polymerization of ϵ-caprolactone with linear polyglycidol **I** as the macroinitiator using Novozyme 435 as

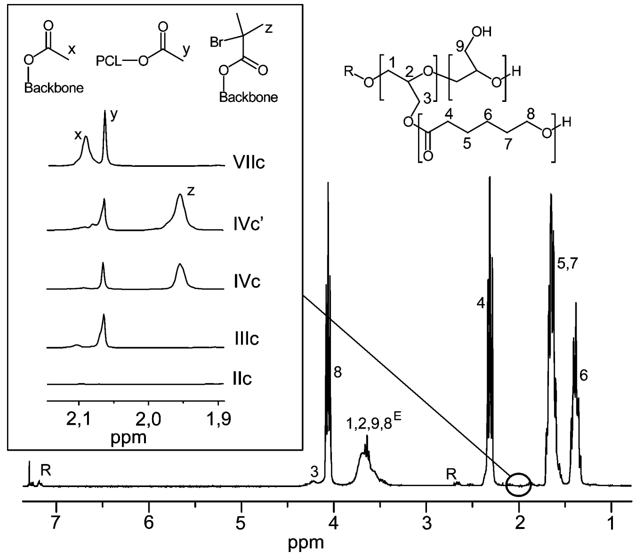
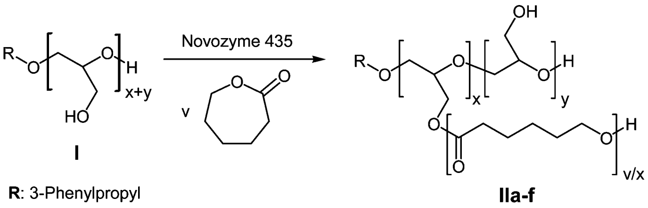


Figure 1. ^{1}H NMR spectra of poly(glycidol-*graft*-ϵ-caprolactone)-*co*-glycidol (**IIc**) in CDCl$_3$ (peaks marked with an "E" are from the end groups). The new signals that occur after the polymer analogous reactions leading to the polymers **IIIc**, **IVc**,**c′**, and **VIIc** are shown in the box.

Scheme 2. Preparation of Poly(glycidol-*graft*-ϵ-caprolactone)-*co*-glycidol (IIa−f)



the catalyst was carried out in bulk at 80 °C. The macroinitiator and ϵ-caprolactone were heated to form a homogeneous solution, before the enzyme was added. After filtration of the enzyme and precipitation in hexane, the polymers (**IIa−IIf**) were obtained as waxy solids (Table 2).

To optimize the conversion of ϵ-caprolactone, the ratio of Novozyme 435 to monomer was varied (**IIa−IId**). The monomer conversion was determined via NMR from samples taken at specific reaction times. It was observed that with 2 wt % of Novozyme 435, the reaction was slow; after 8 h, 22%; and after 120 h, only 76% conversion was achieved. Increasing the amount of enzyme resulted in nearly complete conversion of ϵ-caprolactone and consequently the molecular weights determined by end group analysis are in good agreement with the theory. The M_n values were determined by comparison of the peak of the end group R and the peak 4 (Figure 1). The results of the GPC analysis show that increasing the amount of catalyst has no impact on the molecular weights thus proving that initiation by water within the enzyme plays no role. In addition, by increasing the concentration of enzyme, the polydispersity index decreases slightly (**IIa−IIf**). From the monomer conversion after 8 h (for **IIb** 61%, **IIc** 92%, and **IId** 99%), it can be deduced that the reaction rate increases with higher amounts of catalyst. For all polymers, narrow polydispersities are observed, so it can be assumed that no homopolymer is formed. As previously described, the initiation efficiency of the hydroxy groups can be determined by NMR spectroscopy evaluating the relative intensities of the end groups and the CHCH_2OCO signals.[26] In the case of polymer **IIa** (76% monomer conversion), 33% of the hydroxy groups initiated polymerization. Pushing the reaction to nearly complete monomer conversion led to around 45% of converted hydroxy groups. A further increase in catalyst up to 8 or 12 wt % had no influence on the initiation efficiency. This was expected and confirms our hypothesis that, due to steric reasons, it is much easier for the flexible growing poly(ϵ-caprolactone) chains to react with the enzyme activated monomers than for the hydroxy groups at the backbone. Hence, kinetic control is considered to be the reason for the observed limited grafting. At the beginning, the hydroxy groups of the backbone can compete with the hydroxy groups of the growing poly(ϵ-caprolactone) chains as their concentration is relatively high. At a certain point (after approximately 45% have reacted), the hydroxy groups of the growing poly(ϵ-caprolactone) chains are kinetically preferred for the addition of new monomer. This explanation is in accordance with grafting results obtained with other less densely functionalized macroinitiators.[37] In these cases the initiation efficiency did not change significantly.

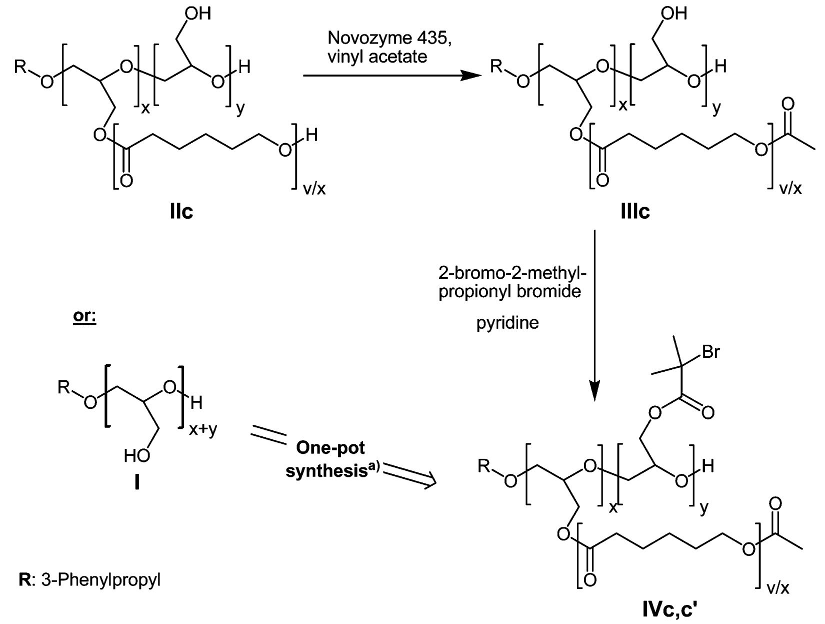
The influence of the monomer to initiator ratio on the initiation efficiency of the CH$_2$OH groups confirms the dominance of kinetics. The experiments are summarized in Table 2 (polymers **IIe** and **IIf**). The number average molecular weight of the polymers is determined by NMR end group analysis. The values are in good agreement with those calculated from the conversion data, and also the number average molecular weight values from the GPC analysis confirm these results. The polydispersity indices increase with increasing the monomer content in the reaction mixture. Because the fraction of converted hydroxy groups could not be determined directly by NMR analysis for the comb polymers with longer poly(ϵ-caprolactone) side chains, the polymers were modified with acetyl chloride resulting in an esterification of all the hydroxy groups: those attached to the polyglycidol backbone and those at the poly(ϵ-caprolactone) chain ends.

In Figure 1 (box) the acetyl signals of P(G-*graft*-CL^{AC})-*co*-G^{AC} (**VIIc**) in the ^{1}H NMR spectrum are shown. At $\delta = 2.04$ and 2.08 ppm the signals for the acetate groups appear. The broader signal at $\delta = 2.08$ ppm is attributed to the acetate groups close to the backbone as their mobility is reduced. The sharper signal originates from the acetate group at the flexible chain ends. Thus integration of these signals gives the number of converted hydroxy groups. In fact, determination of the number of converted hydroxy groups for the polymers **IIe** and **IIf** gave different initiation efficiency than for the polymers **IIb−IId**. It was observed, that an increase of the CL/PG ratio from 91 to 182 led to a higher initiation efficiency (**IIe**), which might be due to a better solubility of the P(G-*graft*-CL)-*co*-G. A further increase of the CL/PG ratio to 364 results in a lower initiation efficiency (**IIf**) as expected by the increased steric hindrance as the side chains get longer.

As Novozyme 435 always contains low levels of water, a frequent side reaction is the initiation of polymerization by water. In this case, a poly(ϵ-caprolactone) homopolymer with carboxylic acid and hydroxy groups at the chain ends will be obtained. Treatment of such polymers with oxalyl chloride shows typical changes in the chemical shifts of the methylene groups adjacent to the end groups: the signal of the CH_2OH end group at $\delta = 3.62$ is shifted due to esterification to $\delta = 4.35$ ppm, and the signal for CH_2COOH at $\delta = 2.29$ is shifted due to acid chloride formation to $\delta = 2.88$ ppm.[38] For polymer **IIc**, we could not observe the appearance of a new signal at $\delta = 2.88$ ppm, so the presence of significant fractions of homopolymer could be excluded. Most likely this is largely due to transesterification reactions.[37]

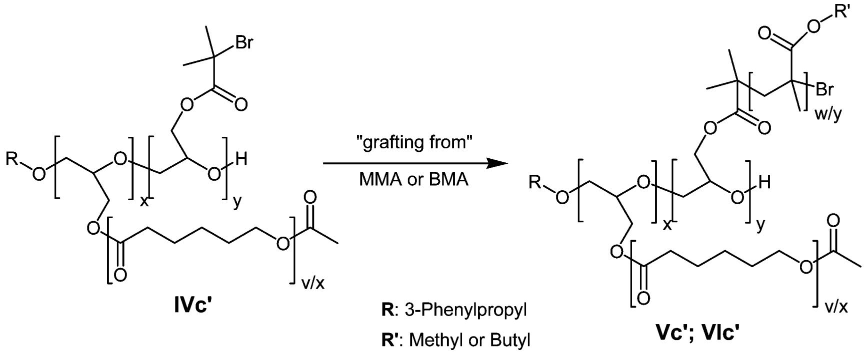
Synthesis of P(G-*graft*-CL^{AC})-*co*-GBMP Macroinitiators for ATRP. So far, the enzymatic polymerization technique has

Scheme 3. Preparation of Poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-glycidyl-2-bromo-2-methylpropionate (IVc,c′)[a]



[a] Consecutive addition of (1) ϵ-caprolactone/Novozyme 435, (2) vinyl acetate, and (3) 2-bromo-2-methylpropionyl bromide/pyridine.

Scheme 4. Atom Transfer Radical Polymerization of Methyl Methacrylate (MMA) and *n*-Butyl Methacrylate (BMA)



been shown to permit grafting of poly(ϵ-caprolactone) chains of different lengths from a polyglycidol backbone without converting all the hydroxy groups. The latter can be used for further modification. The transformation of the partially grafted poly(glycidol-*graft*-ϵ-caprolactone)-*co*-glycidol into a macroinitiator for ATRP consists of two steps. In the first step we capped the hydroxy groups at the poly(ϵ-caprolactone) chain ends by enzymatic reaction with vinyl acetate at 60 °C. In the second step the remaining hydroxy groups at the backbone were reacted with 2-bromo-2-methylpropionyl bromide (Scheme 3).

The NMR spectrum of the isolated polymer **IIIc** shows the same peaks than the NMR spectrum of the completely acetylated P(G-*graft*-CL^{AC})-*co*-G^{AC} (**VIIc**), except the broad peak at $\delta = 2.08$ ppm is missing (Figure 1). So, there was no observable acetylation of the hydroxy groups at the backbone. The P(G-*graft*-CL^{AC})-*co*-G (**IIIc**) with acetylated PCL chain ends was dissolved in chloroform, pyridine, and 2-bromo-2-methylpropionyl bromide, and the reaction mixture was stirred at room temperature. The product **IVc** was isolated by aqueous workup. The integration of the NMR signals (Figure 1) confirmed that 100% of the hydroxy groups, that were left at the backbone, were transformed into ATRP initiating groups. In Table 3 the yields, molecular weights, and polydispersity indices of the polymers **IIc**, **IIIc**, and **IVc**,**c′** are shown.

In order to simplify the experimental procedure, a one-pot synthesis of the macroinitiator was explored. After the grafting-from reaction of ϵ-caprolactone from polyglycidol the temperature was decreased to 60 °C, the solution was diluted with chloroform and vinyl acetate was added. After end capping of the poly(ϵ-caprolactone) chains, the temperature was decreased to 0 °C, pyridine and 2-bromo-2-methylpropionyl bromide were added, and the reaction mixture was stirred at room temperature. After the reaction was completed, the enzyme and pyridine hydrochloride were removed by filtration and the polymer was isolated by aqueous workup and precipitation in pentane. In Figure 1 (box) the ^{1}H NMR spectrum of the obtained product **IVc′** is shown. It is identical to the spectrum of the macroinitiator, that was obtained by the synthesis in three separate steps (**IVc**). From the integrations, one can deduce that the macroinitiator (DP$_n$ = 24) has 10−11 poly(ϵ-caprolactone) chains with

Table 3. Yields, Molecular Weights, and Polydispersity Indices of the Polymers IIc, IIIc, and IVc,c′

polymer	yield [%]	$M_{n,\,NMR}$[a]	$M_{n,\,calcd}$[b]	$M_{n,GPC}$[c]	Q[c]
IIc	94	12 500	12 400	17 200	1.25
IIIc	92	12 500	12 800	18 900	1.24
IVc	84	15 200	14 900	22 400	1.19
IVc′	82	14 400	14 900	21 400	1.20

[a] Number average molecular weight (M_n) determined by NMR. [b] Calculated molecular weight at full conversion. [c] M_n and molecular weight distribution ($Q = M_w/M_n$) determined by gel permeation chromatography (GPC) against narrow poly(methyl methacrylate) standards using tetrahydrofuran (THF) as eluent.

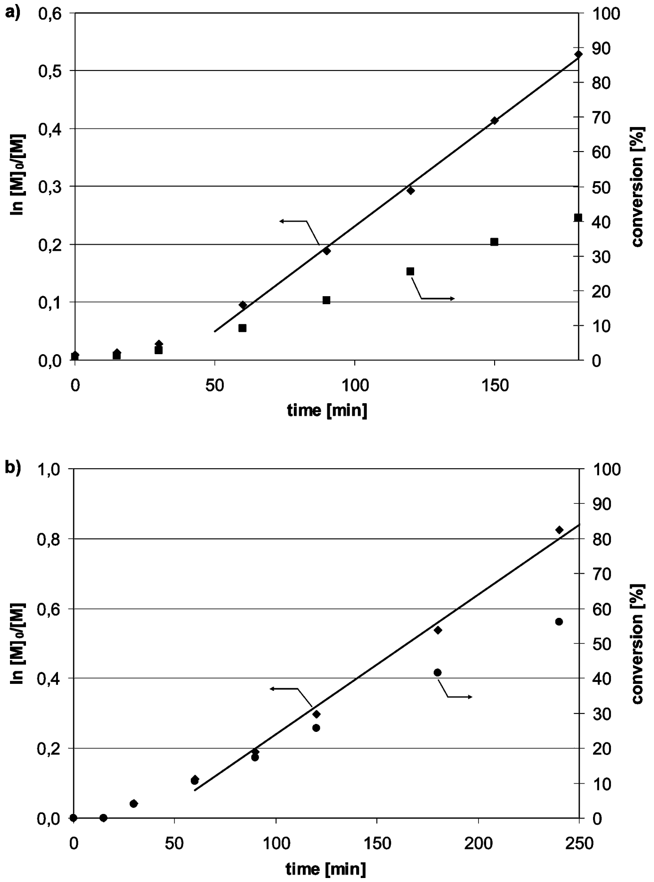


Figure 2. Atom transfer radical polymerization of (a) methyl methacrylate (MMA) [MMA]/[I]/[CuBr]/[Bipy] = 200:1:1:2; and (b) *n*-butyl methacrylate (BMA) [BMA]/[I]/[CuBr]/[Bipy] = 80:1:1:2 at 60 °C, monomer/solvent = $^2/_3$ v/v, with **IVc′** as macroinitiator, conversion vs reaction time and first-order plot.

approximately 8−9 ϵ-caprolactone repeating units per chain end capped with an acetyl group. A negligible acetylation of the hydroxy groups at the backbone occurred (peak at δ = 2.08 ppm). The remaining 13−14 hydroxy groups have been modified into ATRP initiators. The results from the GPC analysis show narrow molecular weight distributions and a slight increase in molecular weight after the insertion of the ATRP initiating groups.

Synthesis of Heterografted Brush Copolymers. The macroinitiator **IVc′** was used to perform the grafting-from reaction under ATRP conditions in the presence of CuBr/2,2′-bipyridyl as the catalyst to yield densely heterografted brush copolymers (Scheme 4).

The polymerization was performed with methyl methacrylate (MMA) and *n*-butyl methacrylate (BMA) as monomers. In the case of BMA with M/I = 80/1 for the ratio of initiating sites to monomer, we observed a rather rapid increase of the polydispersity indices. This was not unexpected as it is known from literature that the grafting-from reaction is prone to crosslinking due to the large amount of initiating sites. In order to optimize the reaction, a higher excess of MMA (M/I = 200/1) was used and the reaction was stopped at a lower conversion. With BMA, the ratio M/I = 80/1 was maintained. In Figure 2, the first-order kinetic plot and the dependence of the monomer conversion on time is shown for both monomers. With the use of MMA as the monomer, a linear correlation of ln([M]$_0$/[M]) vs time up to 40% conversion is observed indicating that the concentration of growing radicals is constant during this period. Afterward, the reaction medium became too viscous to take further samples for kinetic analysis. In the case of BMA, a linear correlation of ln([M]$_0$/[M]) vs time up to 55% conversion with M/I = 80/1 is observed. Figure 2 shows an induction period for both polymerizations, the origin of which was not determined.

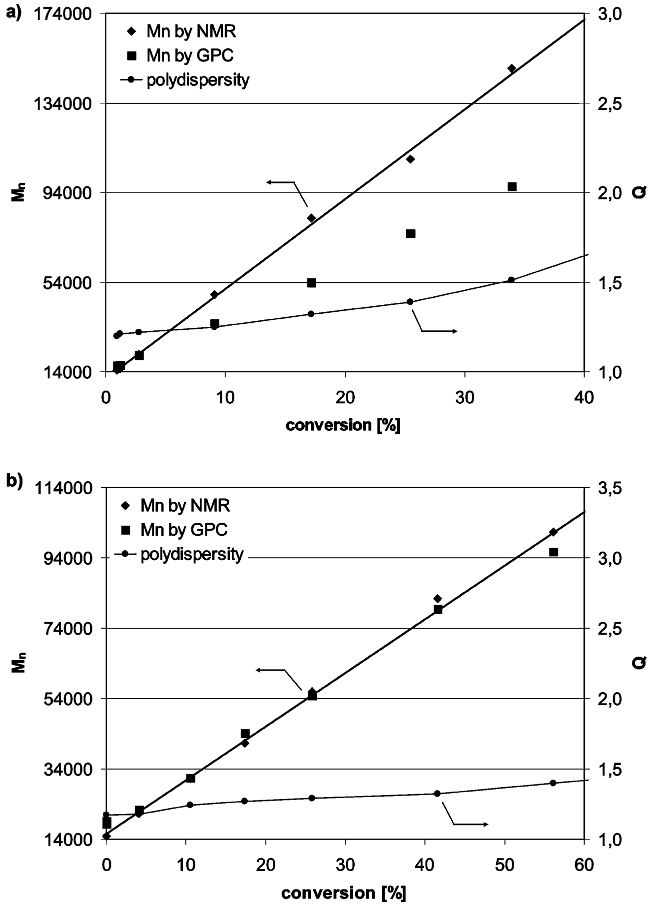


Figure 3. Atom transfer radical polymerization of (a) methyl methacrylate (MMA) [MMA]/[I]/[CuBr]/[Bipy] = 200:1:1:2; and (b) *n*-butyl methacrylate (BMA) [BMA]/[I]/[CuBr]/[Bipy] = 80:1:1:2 at 60 °C, monomer/solvent = $^2/_3$ v/v with **IVc′** as macroinitiator, number average molecular weight (M_n) and polydispersity indices ($Q = M_w/M_n$) vs conversion.

Figure 3 shows that the M_n values (determined by ^{1}H NMR spectroscopy) increase linearly with monomer conversion. This is confirmed by the M_n values measured by GPC using linear PMMA standards. The molecular weights differ from those determined by NMR, because GPC values are underestimated by linear standards, which have in general larger hydrodynamic volumes than densely grafted copolymers. Molecular weight distributions remain narrow till about 20% conversion for MMA and 50% conversion for BMA. Afterward, an increase is observed that might be attributed to intermolecular coupling reactions. One would expect a deviation of the molecular weights from the linear relation toward higher M_n values due to the coupling reactions.

Poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-(glycidol-*graft*-methyl methacrylate) and poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-(glycidol-*graft*-*n*-butyl methacrylate) with different lengths of PMMA or PBMA side chains were synthesized by stopping the reaction at various reaction times (Table 4).

As it has to be expected for branched polymers, the molecular weights determined by GPC are lower than those determined by end group analysis (as an example the ^{1}H NMR spectrum of **VIc′^{1}** is presented in Figure 4).

Table 4. Atom Transfer Radical Polymerization of Methyl Methacrylate and *n*-Butyl Methacrylate Using the Comb Shaped Macroinitiator IVc′

polymer[a]	monomer	time [min]	monomer conversion [%]	DP_n[b] per chain	$M_{n,NMR}$[c]	$M_{n,GPC}$[d]	Q[d]
Vc′1	MMA	75	15	35	60 000	55 000	1.25
Vc′2	MMA	120	28	56	87 000	83 000	1.35
VIc′1	BMA	120	35	27	69 000	60 000	1.24
VIc′2	BMA	210	65	51	116 000	100 000	1.31

[a] ATRP conditions: [MMA]/[I]/[CuBr]/[Bipy] = 200:1:1:2; [BMA]/[I]/[CuBr]/[Bipy] = 80:1:1:2; 60 °C; monomer/solvent = 2/3. [b] Degree of polymerization (DP_n) determined by NMR. [c] Number average molecular weight (M_n) determined by NMR. [d] M_n and molecular weight distribution ($Q = M_w/M_n$) determined by gel permeation chromatography (GPC) against narrow poly(methyl methacrylate) standards using tetrahydrofuran (THF) as eluent.

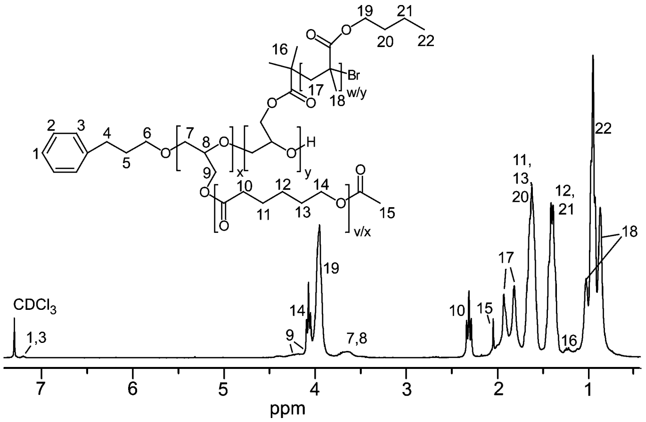


Figure 4. ^{1}H NMR spectrum of poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-(glycidol-*graft*-*n*-butyl methacrylate) (**VIc′1**) in $CDCl_3$.

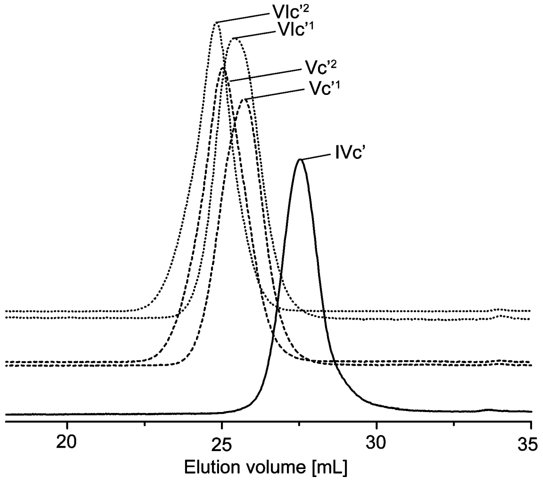


Figure 5. GPC traces of macroinitiator **IVc′**; poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-(glycidol-*graft*-methyl methacrylate) with $DP_{n(MMA)}$ per chain of 35 (**Vc′1**) and 56 (**Vc′2**); poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-(glycidol-*graft*-*n*-butyl methacrylate) with $DP_{n(BMA)}$ per chain of 27 (**VIc′1**) and 51 (**VIc′2**).

If the reaction was stopped at low conversions, the polydispersity remained narrow as shown by the kinetic analysis. In Figure 5, GPC traces for the polymers **IVc′**, **Vc′1**, **Vc′2** and **VIc′1**, **VIc′2** are compared. Upon ATRP polymerization, the peak of the comb shaped macroinitiator **IVc′** shifts to higher molecular weights, which confirms that the grafting reaction took place. All GPC traces remain monomodal after the “grafting-from” reaction.

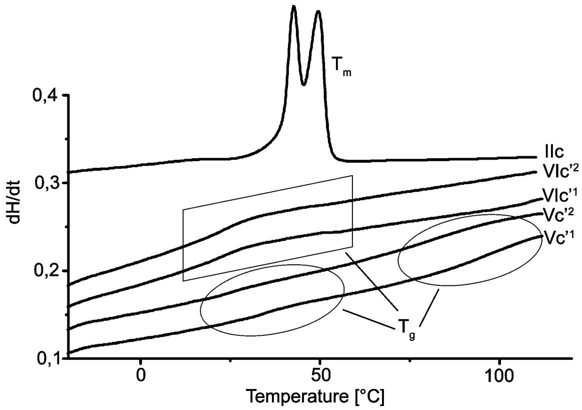


Figure 6. DSC second heating curves of the homografted copolymer P(G-*graft*-CL_8)$_{11}$-*co*-G_{13} (**IIc**) and the heterografted brush copolymers P(G-*graft*-CL_8^{AC})$_{11}$-*co*-(G-*graft*-$PMMA_{35}$)$_{13}$ (**Vc′1**), P(G-*graft*-CL_8^{AC})$_{11}$-*co*-(G-*graft*-$PMMA_{56}$)$_{13}$ (**Vc′2**), P(G-*graft*-CL_8^{AC})$_{11}$-*co*-(G-*graft*-$PBMA_{27}$)$_{13}$ (**VIc′1**), and P(G-*graft*-CL_8^{AC})$_{11}$-*co*-(G-*graft*-$PBMA_{51}$)$_{13}$ (**VIc′2**).

The homografted copolymer P(G-*graft*-CL_8)$_{11}$-*co*-G_{13} (**IIc**) and the heterografted brush copolymers P(G-*graft*-CL_8^{AC})$_{11}$-*co*-(G-*graft*-$PMMA_{35}$)$_{13}$ (**Vc′1**), P(G-*graft*-CL_8^{AC})$_{11}$-*co*-(G-*graft*-$PMMA_{56}$)$_{13}$ (**Vc′2**), P(G-*graft*-CL_8^{AC})$_{11}$-*co*-(G-*graft*-$PBMA_{27}$)$_{13}$ (**VIc′1**), and P(G-*graft*-CL_8^{AC})$_{11}$-*co*-(G-*graft*-$PBMA_{51}$)$_{13}$ (**VIc′2**) were analyzed by means of DSC (Figure 6). The second heating curve of the macroinitiator shows two melting points: T_m = 43 °C and T_m = 50 °C (ΔH_m = 50.1 J/g). This result is attributed to different crystallit sizes. Crystallization of the PCL chains was suppressed after grafting of MMA or BMA. The copolymers with MMA display a glass transition temperature at 78 °C (**Vc′1**) and 94 °C (**Vc′2**) due to the PMMA chains, and at 26 °C and 34 °C, a second glass transition is observed which is attributed to a rearrangement of the PCL chains. The copolymers with BMA show one broad glass transition at 24 °C (**VIc′1**) and 22 °C (**VIc′2**) which represents a superposition of the glass transition temperature due to the PBMA chains and the rearrangement of the PCL chains.

Conclusions

Well-defined poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-(glycidol-*graft*-methyl methacrylate) and poly(glycidol-*graft*-ϵ-caprolactone-acetyl)-*co*-(glycidol-*graft*-*n*-butyl methacrylate) heterografted molecular bottle brushes have been prepared by a combination of enzymatic ring-opening polymerization and atom transfer radical polymerization. First polyglycidol was grafted with ϵ-caprolactone via an enzyme catalyzed ring-opening polymerization. Various experiments show that the initiation efficiency of the hydroxy groups is in the range of 40−55% and slightly dependent on the amount of ϵ-caprolactone in the feed. It is assumed that the initiation efficiency is affected by steric hindrance and kinetic control. With the use of Novozyme 435, the grafted poly(ϵ-caprolactone) chain ends were selectively end capped with vinyl acetate, so that the remaining hydroxy groups at the backbone could be addressed specifically. They were quantitatively acylated with 2-bromo-2-methylpropionyl bromide. This multifunctional ATRP initiator was used for the polymerization of MMA or BMA to build the second PMMA or PBMA grafts. Heterografted molecular bottle brushes, [P(G-*graft*-CL^{AC})-*co*-(G-*graft*-MMA)] and [P(G-*graft*-CL^{AC})-*co*-(G-*graft*-BMA)], show monomodal elution curves in gel permeation chromatography and proof phase separated domains in differential scanning calorimetry.

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References and Notes

(1) Whitesides, G. M. *Small* **2005**, *1*, (2), 172−179.

(2) Behanna, H. A.; Rajangam, K.; Stupp, S. I. *J. Am. Chem. Soc.* **2007**, *129*, (2), 321−327.

(3) Wagner, O.; Baumstark, R. *Macromol. Symp.* **2002**, *187*, 447−458.

(4) Wulf, M.; Wehling, A.; Reis, O. *Macromol. Symp.* **2002**, *187*, 459−467.

(5) Sheiko, S.; Möller, M. *Macromol. Eng.* **2007**, *3* (4), 1515−1574.

(6) Ruzette, A. V.; Leibler, L. *Nat. Mater.* **2005**, *4* (1), 19−31.

(7) Al-Hellani, R.; Schluter, A. D. *Macromolecules* **2006**, *39*, (26), 8943−8951.

(8) Coessens, V.; Pintauer, T.; Matyjaszewski, K. *Prog. Polym. Sci.* **2001**, *26* (3), 337−377.

(9) Djalali, R.; Li, S.-Y.; Schmidt, M. *Macromolecules* **2002**, *35* (11), 4282−4288.

(10) Zhang, M.; Drechsler, M.; Muller, A. H. E. *Chem. Mater.* **2004**, *16* (3), 537−543.

(11) Zhang, M. F.; Estournes, C.; Bietsch, W.; Muller, A. H. E. *Adv. Funct. Mater.* **2004**, *14* (9), 871−882.

(12) Lee, H. I.; Jakubowski, W.; Matyjaszewski, K.; Yu, S.; Sheiko, S. S. *Macromolecules* **2006**, *39* (15), 4983−4989.

(13) Cheng, C.; Qi, K.; Khoshdel, E.; Wooley, K. L. *J. Am. Chem. Soc.* **2006**, *128* (21), 6808−6809.

(14) Beers, K. L.; Gaynor, S. G.; Matyjaszewski, K.; Sheiko, S. S.; Moller, M. *Macromolecules* **1998**, *31* (26), 9413−9415.

(15) Cheng, G. L.; Boker, A. A.; Zhang, M. F.; Krausch, G.; Muller, A. H. E. *Macromolecules* **2001**, *34* (20), 6883−6888.

(16) Borner, H. G.; Beers, K.; Matyjaszewski, K.; Sheiko, S. S.; Moller, M. *Macromolecules* **2001**, *34* (13), 4375−4383.

(17) Neugebauer, D.; Zhang, Y.; Pakula, T.; Matyjaszewski, K. *Macromolecules* **2005**, *38* (21), 8687−8693.

(18) Neugebauer, D.; Theis, M.; Pakula, T.; Wegner, G.; Matyjaszewski, K. *Macromolecules* **2006**, *39* (2), 584−593.

(19) Venkatesh, R.; Yajjou, L.; Koning, C. E.; Klumperman, B. *Macromol. Chem. Phys.* **2004**, *205*, 2161−2168.

(20) Neugebauer, D.; Zhang, Y.; Pakula, T.; Matyjaszewski, K. *Polymer* **2003**, *44* (22), 6863−6871.

(21) Kobayashi, S.; Uyama, H.; Kimura, S. *Chem. Rev.* **2001**, *101*, 3793−3818.

(22) Gross, R. A.; Kumar, A.; Kalra, B. *Chem. Rev.* **2001**, *101*, 2097−2124.

(23) Iversen, T.; Malmström, E.; Ihre, H.; Hult, K.; Hult, A.; Cordova, A. *J. Am. Chem. Soc.* **1998**, *120*, 13521−13522.

(24) Meyer, U.; Palmans, A. R. A.; Loontjens, T.; Heise, A. *Macromolecules* **2002**, *35*, 2873−2875.

(25) Albertsson, A. C.; Varma, I. K. *Biomacromolecules* **2003**, *4*, (6), 1466−1486.

(26) Hans, M.; Gasteier, P.; Keul, H.; Moeller, M. *Macromolecules* **2006**, *39*, (9), 3184−3193.

(27) Binns, F.; Harffey, P.; Roberts, S. M.; Taylor, A. *J. Chem. Soc., Perkin Trans. 1* **1999**, (19), 2671−2676.

(28) Anderson, E. M.; Karin, M.; Kirk, O. *Biocatal. Biotransform.* **1998**, *16* (3), 181−204.

(29) Howdle, S. M.; Heise, A.; de Geus, M.; Wang, W.; Duxbury, C. J. *J. Am. Chem. Soc.* **2005**, *127*, 2384−2385.

(30) Zhou, J. X.; Wang, W. X.; Thurecht, K. J.; Villarroya, S.; Howdle, S. M. *Macromolecules* **2006**, *39* (21), 7302−7305.

(31) Zhou, J. X.; Villarroya, S.; Wang, W. X.; Wyatt, M. F.; Duxbury, C. J.; Thurecht, K. J.; Howdle, S. M. *Macromolecules* **2006**, *39* (16), 5352−5358.

(32) De Geus, M.; Schormans, L.; Palmans, A. A.; Koning, C. E.; Heise, A. *J. Polym. Sci., Part A: Poly. Chem.* **2006**, *44* (14), 4290−4297.

(33) Villarroya, S.; Zhou, J. X.; Duxbury, C. J.; Heise, A.; Howdle, S. M. *Macromolecules* **2006**, *39* (2), 633−640.

(34) de Geus, M.; Peeters, J.; Wolffs, M.; Hermans, T.; Palmans, A. R. A.; Koning, C. E.; Heise, A. *Macromolecules* **2005**, *38* (10), 4220−4225.

(35) Duxbury, C. J.; Wang, W. X.; de Geus, M.; Heise, A.; Howdle, S. M. *J. Am. Chem. Soc.* **2005**, *127* (8), 2384−2385.

(36) Fitton, A. O.; Hill, J.; Jane, D. E.; Millar, R. *Synthesis-Stuttgart* **1987**, (12), 1140−1142.

(37) Duxbury, C. J.; Cummins, D.; Heise, A. *Macromol. Rapid Commun.* **2007**, *28* (3), 235−240.

(38) Kumar, A.; Gross, R. A.; Wang, Y. B.; Hillmyer, M. A. *Macromolecules* **2002**, *35* (20), 7606−7611.

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