Single-Step, Solvent-Free Enzymatic Route to α,ω-Functionalized Polypentadecalactone Macromonomers

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ABSTRACT: A straightforward enzymatic single-step route toward the synthesis of α,ω-functionalized polypentadecalactone (PPDL) macromonomers containing dithiol, thiol−acrylate, diacrylate, or dimethacrylate end groups has been developed. Two solvent-free approaches, mixing all components at start, using *Candida antarctica* lipase B (CALB) as an efficient catalyst were demonstrated. In the first approach difunctionalized polymers (with dithiol or thiol−acrylate end groups) were synthesized by mixing lipase, lactone, and equimolar amounts of functional initiator (6-mercapto-1-hexanol) and terminator (11-mercapto-1-undecanoic acid or vinyl acrylate). Polymers with a high fraction (95%) of dithiol end groups or polymers with thiol−acrylate end groups (86% and 96%, respectively) were obtained. In the second approach, a functional diester (ethylene glycol diacrylate or ethylene glycol dimethacrylate) was mixed with lactone and lipase without predrying, using water as an initial initiator. Reduced pressure was applied after 2 h of incubation to evaporate water and push the equilibrium toward high functionalization. Polymers with >96% diacrylated or dimethacrylated end groups were achieved.

Introduction

Polyesters have found an industrial interest and utility as a biodegradable material, i.e., in biomedical applications using aliphatic polyesters.[1,2] End-group functionalization of polymers is of great importance for making further complex polymer structures and architectures such as branched and cross-linked polymers. A variety of functional groups have been introduced in polyesters by functional initiators using metal-catalyzed ring-opening polymerization (ROP) of lactones, i.e., acrylates and thiols that have a broad field of application.[3–6] Thiols and acrylates can be used in thiol−ene chemistry and has found applications in many different areas such as surface grafting, film patterning, adhesives, and degradable biomaterials.[7] Macromonomers with thiol end groups have been used in various ways in material science and in the addition of species to gold.[8,9] Using acrylate-functionalized polyesters, graft polymers were prepared using controlled radical polymerization methods.[4–6]

Alternatively, enzyme-catalyzed ring-opening polymerization (eROP) has been documented as an efficient route of making polyesters using a variety of lactones.[10–14] Similar to chemical ROP, the molecular weight was controlled by the initiator-to-monomer ratio.[15] Highly efficient eROP has also been shown in the nontoxic solvent supercritical carbon dioxide.[16,17] In spite of the absence of ring strain, the polymerization of large lactones, such as ω-pentadecalactone (PDL), was found to be efficient using lipases in contrast to conventional metal catalysis.[18,19] Lipase B from *Candida antarctica* (CALB) was found to be the most efficient enzyme, among many lipases, for the ROP of lactones.[20] The deep narrow active site of this lipase gives it a unique substrate specificity and high selectivity.[21,22] A variety of functionalized polyesters were successfully synthesized by eROP using different types of functional initiators and terminators.[23–28] Thiol end groups are typically introduced in polyesters with the use of protection groups,[3,29] while such groups were successfully introduced in a one-pot procedure using CALB catalysis without protection chemistry.[30,31] Further characterization of the chemoselectivity displayed by CALB revealed that the lipase was 10^5 times more selective for alcohols than for thiols in transacylation reactions.[32] For the first time we introduced thiol and acrylate end groups on the same polymer with a high yield of functional groups without protection chemistry,[31] which is difficult to do due to the inherent reactivity of the groups. Lipase-based transacylation activities have to be considered when using these enzymes as catalysts.[33–35] CALB-catalyzed ROP using a standard initiator for metal-catalyzed ROP, 2-hydroxyethyl methacrylate (HEMA), resulted in a mixture of polyester methacrylate structures.[33] It was concluded that initiators, containing ester functionalities, are of limited use in eROP for making well-defined monofunctionalized macromonomers due to lipase-based transacylation processes.[33] On the other hand, when HEMA-initiated eROP were combined with end-capping using vinyl acrylate, well-defined dimethacrylated polyester macromonomers were achieved.[33]

The successful synthesis of polypentadecalactone (PPDL) macromonomers, containing i.e. thiols and acrylates, by lipase chemistry makes it an interesting road toward new polymer network materials.[30,31,33] Using a combination of lipase and thiol−ene chemistry, a chemoenzymatic route toward semicrystalline polymer networks were developed based on PPDL macromonomers with two thiol end groups together with norbornene functional ene monomers.[36] We have an interest to increase the accessibility of PPDL macromonomers by further development of simplified synthetic procedures.

In order to increase the throughput in the preparation of polyester macromonomers, we attempted a single-step, solvent-free route to α,ω-functionalized PPDL macromonomers. Based on the inherent properties displayed by CALB as a chemoselective and efficient catalyst for ROP and transacylation reactions, two approaches were investigated: The first procedure involved mixing lipase and lactone with equimolar amounts of functional initiator and terminator. In the second procedure the lipase was mixed with a difunctional diester and lactone (without predrying, thus using water as an initial initiator) in combination with reduced pressure. Here we report on a lipase-catalyzed single-step route to α,ω-functionalized PPDL macromonomers, containing dithiol, thiol−acrylate, diacrylate, and dimethacrylate end groups.

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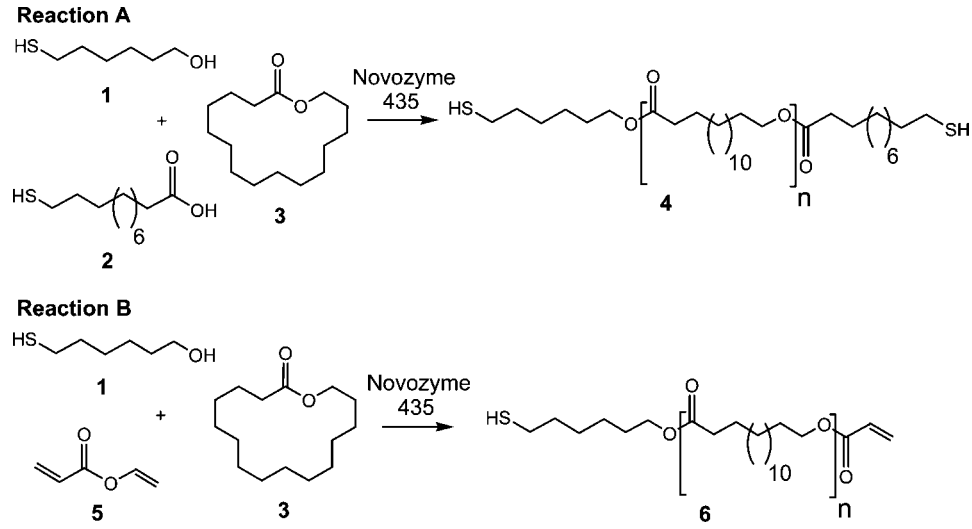
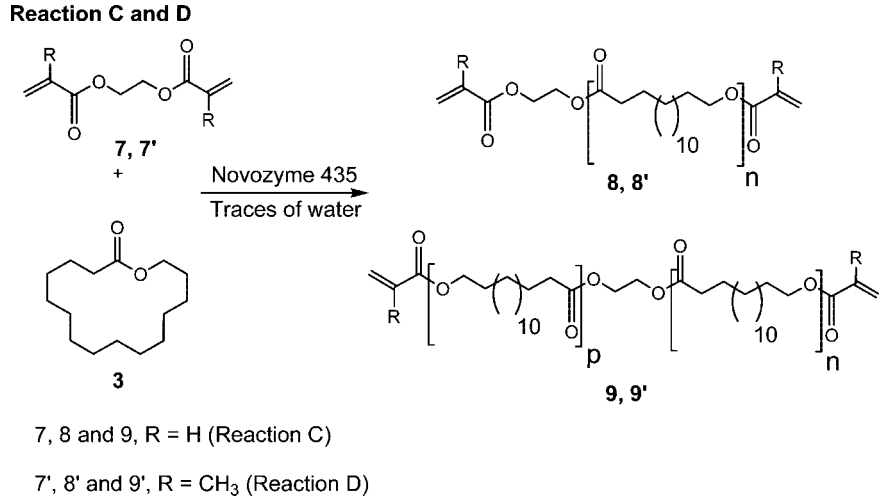
Scheme 1. Single-Step Route to Difunctionalized Poly-PDL[a]



[a] (A) Poly-PDL with two thiol end groups (**4**), by mixing 6-mercapto-1-hexanol and 11-mercapto-1-undecanoic acid with PDL, without predrying and applying reduced pressure during the reaction. (B) Poly-PDL with thiol−acrylate end groups (**6**), by mixing 6-mercapto-1-hexanol and vinyl acrylate with PDL.

Scheme 2. Single-Step Route to Difunctionalized Poly-PDL[a]



[a] (C) Poly-PDL with two acrylate end groups (**8, 9**), by mixing ethylene glycol diacrylate with PDL, without predrying and applying reduced pressure after 2 h. (D) Poly-PDL with two methacrylate end groups (**8′, 9′**), by mixing ethylene glycol dimethacrylate, without predrying and applying reduced pressure after 2 h.

Experimental Part

Materials. Novozyme 435 (*Candida antarctica* lipase B immobilized on an acrylic carrier) and all chemicals were purchased from Aldrich. All chemicals were used without any predrying except for reaction B (Scheme 1) where PDL and 6-mercapto-1-hexanol were dried under reduced pressure and Novozyme 435 was dried in a vacuum oven before use.

The procedures are summarized in Scheme 1 and Scheme 2.

Synthetic Procedure. *A. Poly-PDL with Two Thiol Ends* **(4)**. 6-Mercapto-1-hexanol (**1**) (1.683 mL, 12 mmol), ω-pentadecalactone (**3**) (15 g, 62 mmol), and 11-mercapto-1-undecanoic acid (**2**) (2.7 g, 12 mmol) were mixed in a 50 mL round reaction flask (in a molar ratio 1:5:1 initiator to lactone to terminator). The reaction was started by the addition of 500 mg of Novozyme 435. Reduced pressure was applied when the reaction was started, and the reaction was allowed to run for 24 h.

B. Poly-PDL with One Thiol and One Acrylate End **(6)**. 6-Mercapto-1-hexanol (**1**) (110 μL, 0.83 mmol), ω-pentadecalactone (**3**) (1 g, 4.15 mmol), and vinyl acrylate (**5**) (100 μL, 0.83 mmol) were mixed in a 5 mL round reaction flask (in a molar ratio 1:5:1 initiator to lactone to terminator). The reaction was started by the addition of 100 mg of Novozyme 435. The reaction was allowed to run for 6.5 h. *N*-Nitroso-*N*-phenylhydroxylamine aluminum complex (NPAL) was used as radical inhibitor.

C. Poly-PDL with Two Acrylate Ends **(8, 9)**. Ethylene glycol diacrylate (**7**) (130 μL, 0.83 mmol) and ω-pentadecalactone (**3**) (2 g, 8.3 mmol) were mixed in a 10 mL round reaction flask (in a molar ratio 1:10 ester to lactone). The reaction was started by the addition of 50 mg of Novozyme 435. Reduced pressure was applied after 2 h, and the reaction was allowed to run for 24 h.

D. Poly-PDL with Two Methacrylate Ends **(8′, 9′)**. Ethylene glycol dimethacrylate (**7′**) (156 μL, 0.83 mmol) and ω-pentadecalactone (**3**) (2 g, 8.3 mmol) were mixed in a 10 mL round reaction flask (in a molar ratio 1:10 ester to lactone). The reaction was started by the addition of 50 mg of Novozyme 435. Reduced pressure was applied after 2 h, and the reaction was allowed to run for 48 h.

All reactions were run at 90 °C under magnetic stirring, and they were stopped by filtering off the enzyme. The products were

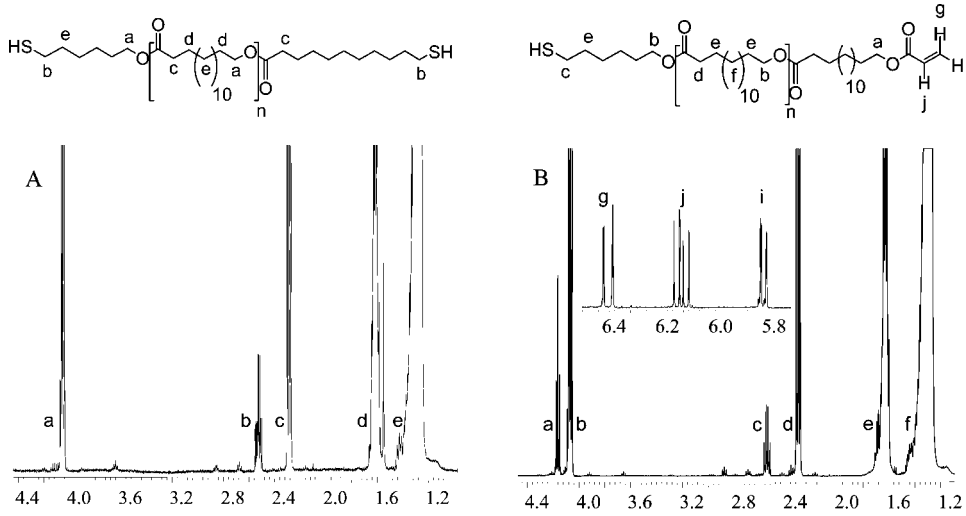


Figure 1. ^{1}H NMR spectra of difunctionalized poly-PDL: (A) poly-PDL with two thiol end groups (**4**); (B) poly-PDL with thiol−acrylate end groups (**6**).

precipitated in dry ice cooled methanol, and the polymers were filtered off by glass microfiber filters. The polymers were dried by vacuum oven before being analyzed by ^{1}H and ^{13}C nuclear magnetic resonance spectroscopy (^{1}H and ^{13}C NMR), matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF-MS), and size exclusion chromatography (SEC).

A. Poly-PDL with Two Thiol Ends (**4**). ^{1}H NMR (500 MHz, $CDCl_3$, δ in ppm): 4.05 ppm (2H, t, $CH_2CH_2OC(O)-$), 2.52 ppm (2H, q, $-CH_2CH_2SH$, terminator), 2.52 ppm (2H, q, $HSCH_2CH_2-$, initiator), 2.28 ppm (2H, t, $-OC(O)CH_2CH_2-$), 1.61−1.69 ppm (4H, m, $-CH_2CH_2(CH_2)_{10}CH_2CH_2-$) and 1.18−1.39 ppm (20H, m, $-CH_2CH_2(CH_2)_{10}CH_2CH_2-$). ^{13}C NMR (500 MHz, $CDCl_3$, δ in ppm): 173.9 ppm (C=O, C-1), 34.4 ppm ($C(O)CH_2CH_2$), 64.4 ppm ($-CH_2O-$), 25.4 ppm ($SHCH_2CH_2CH_2-$), 33.8 ppm ($SHCH_2CH_2CH_2-$), 64.1 ppm ($HS(CH_2)_5CH_2O-$, initiator).

B. Poly-PDL with One Thiol and One Acrylate End (**6**). ^{1}H NMR (500 MHz, $CDCl_3$, δ in ppm): 5.81 and 6.39 ppm (2H, d, $-OC(O)CH=CH_2$), 6.12 ppm (1H, q, $-OC(O)CH=CH_2$), 4.15 ppm (2H, t, $CH_2CH_2OC(O)CH=CH_2$), 4.05 ppm (2H, t, $CH_2CH_2OC(O)-$), 2.52 ppm (2H, q, $HSCH_2CH_2-$), 2.28 ppm (2H, t, $-OC(O)CH_2CH_2-$), 1.51−1.69 ppm (4H, m, $-CH_2CH_2(CH_2)_{10}CH_2CH_2-$), and 1.2−1.43 ppm (20H, m, $-CH_2CH_2(CH_2)_{10}CH_2CH_2-$). ^{13}C NMR (500 MHz, $CDCl_3$, δ in ppm): 173.9 ppm (C=O, C1), 34.4 ppm ($-C(O)CH_2CH_2-$), 64.4 ppm ($-CH_2O-$), 25.4 ppm ($SHCH_2CH_2CH_2-$), 33.8 ppm ($SHCH_2CH_2CH_2-$), 64.1 ppm ($HS(CH_2)_5CH_2O-$), 166.3 ppm ($-C(O)CH=CH_2$), 128.6 ppm ($-C(O)CH=CH_2$), and 130.3 ppm ($-C(O)CH=CH_2$).

C. Poly-PDL with Two Acrylate Ends (**8, 9**). ^{1}H NMR (500 MHz, $CDCl_3$, δ in ppm): 4.05 ppm (2H, t, $-CH_2CH_2OCO-$), 4.14 ppm (2H, t, $-CH_2CH_2OC(O)CH=CH_2$), 2.28 ppm (2H, t, $-OC(O)-CH_2CH_2-$), 1.61−1.69 ppm (4H, m, $-CH_2CH_2(CH_2)_{10}CH_2CH_2-$), 1.18−1.39 ppm (20H, m, $-CH_2CH_2(CH_2)_{10}CH_2CH_2-$), 4.37 ppm (2H, m, $CH_2=CHC(O)OCH_2CH_2OCH_2-$), 4.34 ppm (2H, m, $CH_2=CHC(O)OCH_2CH_2OCH_2-$), 4.28 ppm (4H, s, $-CH_2C(O)OCH_2-CH_2OC(O)CH_2-$), 5.85 and 6.41 ppm (2H, d, $CH_2=CHC(O)-OCH_2CH_2OCH_2-$) 6.14 ppm (1H, q, $CH_2=CHC(O)OCH_2CH_2-OCH_2-$), 5.81, 6.39 ppm (2H, d, $-CH_2CH_2OC(O)CH=CH_2$) and 6.12 ppm (1H, q, $-CH_2CH_2OC(O)CH=CH_2$). ^{13}C NMR (500 MHz, $CDCl_3$, δ in ppm): 174.0 ppm (C=O, C1), 34.4 ppm ($-OC(O)-CH_2CH_2-$), 64.4 ppm ($-CH_2OC(O)CH_2-$), 130.4 ppm ($CH_2=CH-$), 128.6 ppm ($CH_2=CH-$), 166.3 ppm ($CH_2=CHC(O)-$), 61.8 ppm ($CH_2=CHC(O)OCH_2CH_2O-$), 62.4 ppm ($CH_2=CHC(O)O-CH_2CH_2O-$), 64.7 ppm ($-CH_2OC(O)CH=CH_2$) and 62.0 ppm ($-C(O)OCH_2CH_2OC(O)-$).

D. Poly-PDL with Two Methacrylate Ends (**8′, 9′**). ^{1}H NMR (500 MHz, $CDCl_3$, δ in ppm): 4.05 ppm (2H, t, $-CH_2CH_2OCO-$), 4.14 ppm (2H, t, $-CH_2CH_2OC(O)C(CH_3)=CH_2$), 2.28 ppm (2H, t, $-OC(O)CH_2CH_2-$), 1.61−1.69 ppm (4H, m, $-CH_2CH_2(CH_2)_{10}-CH_2CH_2-$), 1.18−1.39 ppm (20H, m, $-CH_2CH_2(CH_2)_{10}CH_2-CH_2-$), 4.34 ppm (4H, m, $CH_2=C(CH_3)C(O)OCH_2CH_2OCH_2-$), 4.28 ppm (4H, s, $-CH_2C(O)OCH_2CH_2OC(O)CH_2-$), 5.60 and 6.13 ppm (2H, s, $CH_2=C(CH_3)C(O)OCH_2CH_2OCH_2-$) and 5.55 and 6.10 ppm (2H, s, $-CH_2CH_2OC(O)C(CH_3)=CH_2$). ^{13}C NMR (500 MHz, $CDCl_3$, δ in ppm): 174.0 ppm (C=O, C1), 34.4 ppm ($-OC(O)CH_2CH_2-$), 64.4 ppm ($-CH_2OC(O)CH_2-$), 125.2 ppm ($CH_2=C(CH_3)-$), 136.5 ppm ($CH_2=C(CH_3)-$), 18.3 ppm ($CH_2=C(CH_3)-$), 167.6 ppm ($CH_2=C(CH_3)C(O)-$), 61.8 ppm ($CH_2=C(CH_3)C(O)OCH_2CH_2O-$), 62.4 ppm ($CH_2=C(CH_3)C(O)OCH_2-CH_2O-$), 64.8 ppm ($-CH_2OC(O)C(CH_3)=CH_2$), and 62.0 ppm ($-C(O)OCH_2CH_2OC(O)-$).

Instrumentation. ^{1}H NMR spectra were recorded on a Bruker AM 500. $CDCl_3$ containing 1 vol % TMS was used as solvent. For the calculation of monomer conversion in the ROP, the ^{1}H NMR signals at 4.14 (PDL) to 4.05 (poly-PDL) were used.

Size exclusion chromatography (SEC) using THF (1.0 mL min^{-1}) as the mobile phase was performed at 35 °C using a Viscotek TDA model 301 equipped with two GMH_{HR}-M columns with TSK-gel (mixed bed, MW resolving range: 300−100 000) from Tosoh Biosep, a VE 5200 GPC autosampler, a VE 1121 GPC solvent pump, and a VE 5710 GPC degasser (all from Viscotek Corp.). A universal calibration method was created using broad and narrow linear polystyrene standards. Corrections for the flow rate fluctuations were made using toluene as an internal standard. Viscotek OmniSEC version 4.0 software was used to process data. Product samples were prepared using warm THF.

MALDI-TOF-MS analyses were conducted on a Bruker UltraFlex MALDI-TOF-MS with SCOUT-MTP Ion Source (Bruker Daltonics, Bremen) equipped with a N_2 laser (337 nm), a gridless ion source, and reflector design. All spectra were acquired using a reflector-positive method with an acceleration voltage of 25 and a reflector voltage of 26.3 kV. Calibration was performed in order to secure good mass accuracy. As for the samples, solutions of $2-5 \times 10^{-3}$ M in $CHCl_3$ were prepared. The matrix utilized was 9-nitroanthrazene. Matrix solutions were prepared as 0.1 M solutions in THF. The samples were prepared as sample−matrix−Na solutions, employing a 0.1 M Na solution in THF. The preparation protocol included mixing of 5 μL of sample with 20 μL of matrix. Then 1 μL of the mixture was spotted on the MALDI target and was left to crystallize at room temperature (the THF was evaporated). Normally, 50 pulses were acquired for each sample. In order to achieve good mass accuracy and resolution, the analyses were performed at the laser threshold of each individual matrix/sample combination.

Results and Discussion

A one-step, solvent-free enzymatic route to α,ω-functionalized polypentadecalactone (PPDL) macromonomers containing

Table 1. Synthesis of Difunctionalized PPDL in a Single-Step Procedure by Mixing PDL with Initiator (1) and Terminator (2 or 5), Catalyzed by *Candida antarctica* Lipase B

					fraction of ends (%)			M_n (Da)		
T[a]	product	ratio I:M:T[a]	time (h)	conv (%)[b]	I[a]	T[a]	yield (%)	NMR	SEC	PDI
2	**4**	1:5:1	24	98	95	95	87	1900	2400	3.4
5	**6**	1:5:1	6	>95[c]	86	96	57	1800	2400	2.6

[a] I = initiator, M = monomer, and T = terminator. The ratio is in mol/mol. [b] Monomer conversion was determined by NMR. [c] Conversion was estimated using the peak height of the monomer peak at 4.14 ppm. Integration not possible due to interference with a methylene in polymer **6** appearing at 4.15 ppm (peak a in Figure 1B).

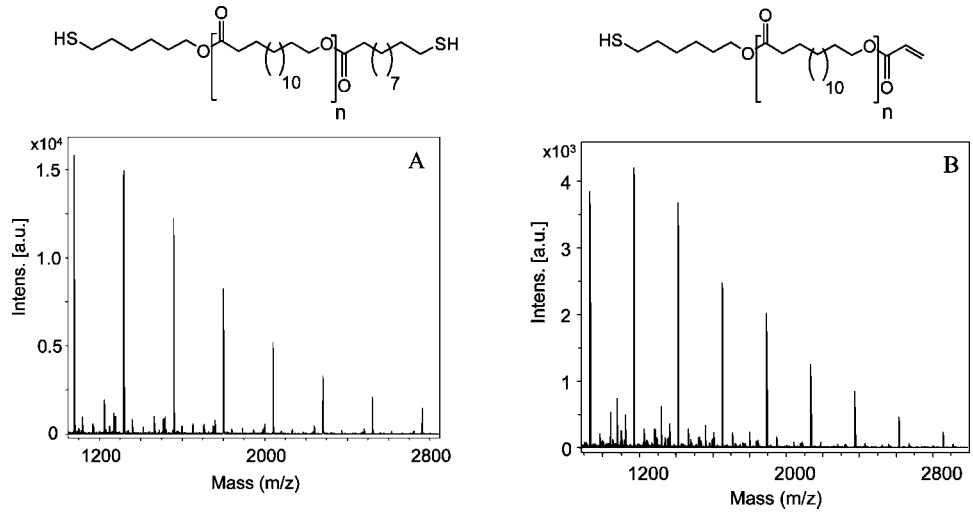


Figure 2. MALDI-TOF-MS spectra of difunctionalized poly-PDL: (A) poly-PDL with two thiol end groups (**4**); (B) poly-PDL with thiol−acrylate end groups (**6**).

terminal thiols, acrylates, and methacrylates was developed. Macromonomers with four different α,ω-functional structures were synthesized: dithiol, thiol−acrylate, diacrylate, and dimethacrylate. By mixing all components at start, two strategies were investigated: (I) mixing lipase, PDL, and equimolar amounts of functional initiator (6-mercapto-1-hexanol) and terminator (11-mercapto-1-undecanoic acid or vinyl acrylate); (II) mixing lipase, PDL, and functional diester (ethylene glycol diacrylate or ethylene glycol dimethacrylate) using water as the initiator, later removed by reduced pressure.

Single-Step Route to α,ω-Functionalized Poly-PDL Mixing Initiator, Terminator, and PDL. In a single-step procedure the initiator 6-mercapto-1-hexanol (**1**) and either of the terminators 11-mercapto-1-undecanoic acid (**2**) (reaction A in Scheme 1) or vinyl acrylate (**5**) (reaction B in Scheme 1) were mixed with PDL (**3**) and the lipase B from *Candida antarctica* in the form of Novozyme 435 preparation. Reaction A was run, using undried components, for 24 h under reduced pressure to distill off the produced water from the acylation (end-capping) by the mercapto acid (**2**). In contrast, reaction B was run for 6.5 h, and the enzyme, initiator, and lactone were dried prior to start, and no reduced pressure was applied. Products **4** and **6** were characterized by ^{1}H and ^{13}C NMR, MALDI-TOF-MS, and SEC.

By ^{1}H NMR analysis of product **4**, the presence of the two thiol ends was confirmed (Figure 1A). Signals from the methylene groups adjacent to the two thiol ends were visible at 2.52 ppm as a multiplet (two overlapped double triplets) (b in Figure 1A). At 3.65 ppm a small triplet peak was detected corresponding to the methylene group adjacent to the hydroxyl group of the unterminated polymer. Using the integrals of the peaks at 3.65 and 2.52 ppm, we calculated the fraction of end functionalization of the polymers. The two overlapping thiol peaks at 2.52 were very similar in size by inspection of the peak height. It was found that both the initiation, with 6-mercapto-1-hexanol, and termination, with 11-mercapto-1-undecanoic acid, were performed with an efficiency of 95% (Table 1). MALDI-TOF-MS analysis of product **4** (Figure 2A) showed one main group of peaks that corresponds to polymers with two thiol ends. The presence of thiol groups was confirmed by ^{13}C NMR.

Using 15 g of PDL, the conversion of monomer reached 98% after 24 h and the yield of purified (**4**) was 87% (Table 1). The molecular weight (M_n) of product **4** was 1900 g mol^{-1} as determined by NMR, representing an average degree of polymerization (DP) of **6** (Table 1). By SEC analysis, M_n and PDI were determined to 2400 g mol^{-1} and 3.4, respectively.

The presence of thiol and acrylate functional ends in product **6** was confirmed by ^{1}H NMR. The signals of the vinyl protons were found at 5.81, 6.12, and 6.39 ppm (i, j, and g in Figure 1B). The peak of the characteristic group of the initiator (c in Figure 1B) were visible at 2.52 ppm. Comparing the integral of the small peak at 3.65 ppm, of the methylene group adjacent to the free hydroxyl end of the poly-PDL, and peaks a and c (Figure 1B), we calculated the degree of incorporation of the two functional ends. We found that 86% of the polymers contained free thiol and 96% were acrylate terminated.

MALDI-TOF MS spectrum (Figure 2B) showed one major group of peaks corresponding to the disubstituted polymer. ^{13}C NMR confirmed the presence of the thiol and acrylate ends. The molecular weight (M_n) of product **6** was 1800 g mol^{-1} as determined by NMR, representing a DP of 6.5 (Table 1). By SEC analysis, M_n and PDI were determined to 2400 g mol^{-1} and 2.6, respectively. Using 1 g of PDL, the conversion of monomer was >95% (after 6 h) and the yield of purified **6** was 57% (Table 1). The smaller scale used for the synthesis of product **6** resulted in a lower yield (57%) as compared with a yield of 87% for product **4**, which was produced in a 15 g scale.

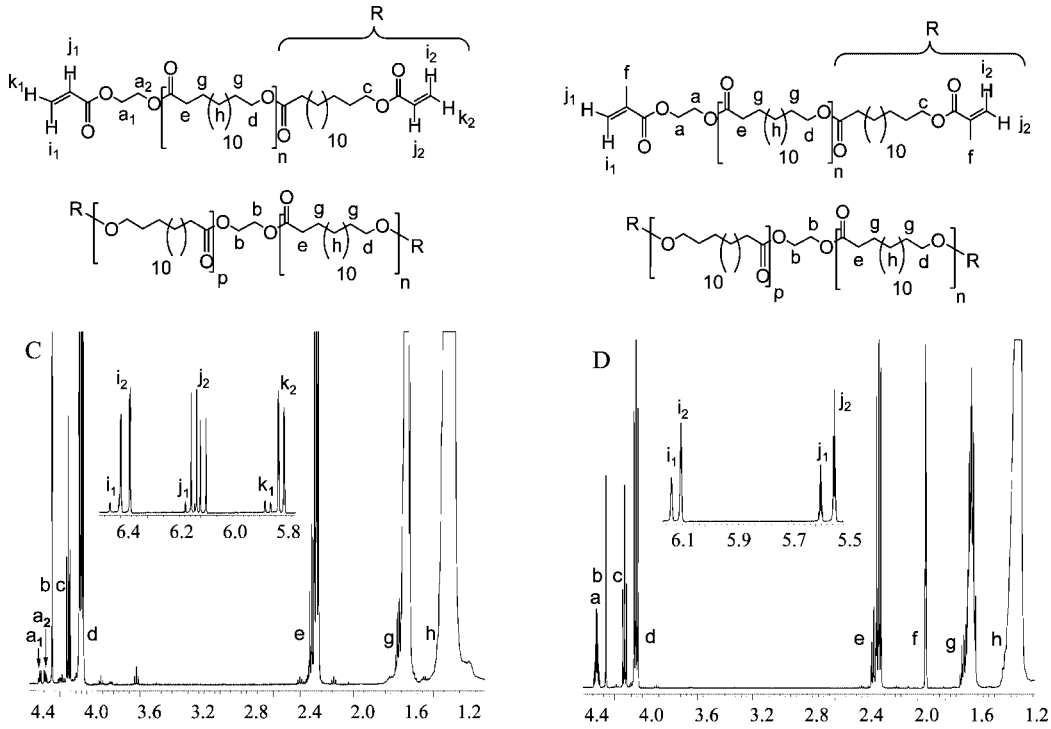


Figure 3. ^{1}H NMR spectra of difunctionalized poly-PDL: (C) poly-PDL with two acrylate end groups (mixture of **8** and **9**); (D) poly-PDL with two methacrylate end groups (mixture of **8′** and **9′**).

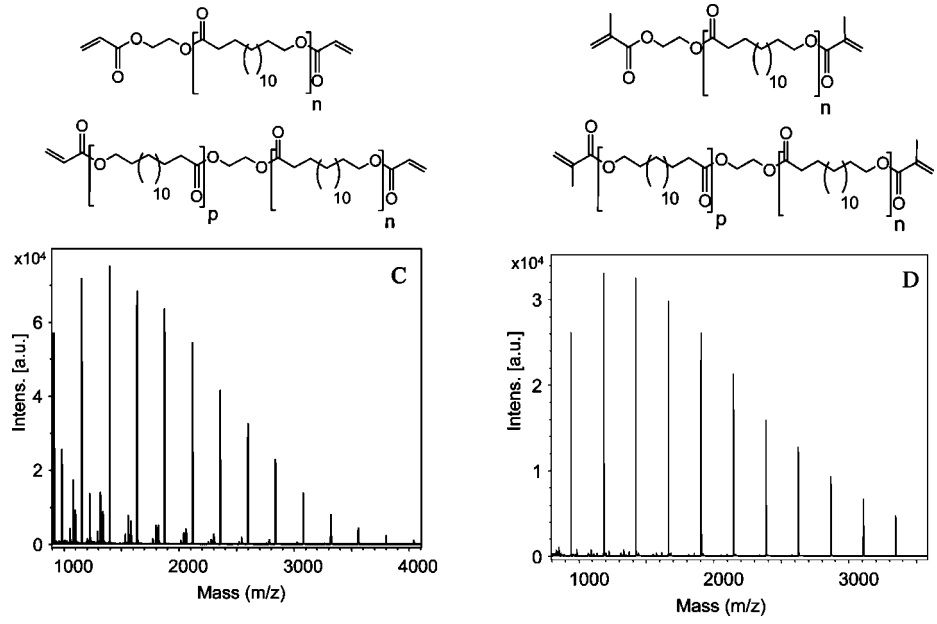


Figure 4. MALDI-TOF-MS spectra of difunctionalized poly-PDL: (C) diacrylated poly-PDL (mixture of **8** and **9**); (D) dimethacrylated poly-PDL (mixture of **8′** and **9′**).

Single-Step Route to α,ω-Functionalized Poly-PDL Mixing a Diester and PDL. In a single-step procedure, ethylene glycol diacrylate (**7**) was mixed with PDL (**3**) and *Candida antarctica* lipase B (reaction C in Scheme 2). The reaction was started without any predrying of the components as water molecules were needed as nucleophiles (initiators). The difunctionalization of the produced polyester was mainly due to the transesterification activity of the enzyme.[33] Reduced pressure was applied after 2 h in order to evaporate water and push the equilibrium toward a high fraction of difunctionalization. The reaction was allowed to run for 24 h in total. Ethylene glycol dimethacrylate (**7′**) was used in a similar setup (reaction D in Scheme 2), and the reaction was allowed to run for 48 h (since the methacrylate was empirically found to react slower than the acrylate). Polymers obtain from the two reactions, C and D, were characterized by ^{1}H and ^{13}C NMR, MALDI-TOF-MS, and SEC. According to the ^{1}H NMR two types of di(meth)acrylated polymers were detected in reactions C and D; in the first type of polymer, the diol group was located next to the (meth)acrylate group (**8, 8′**) while in the second type the diol group was located within the polyester chain (**9, 9′**). This is in full accordance with earlier results using 2-hydroxyethyl methacrylate (HEMA) as initiator for the eROP.[33]

Table 2. Synthesis of Difunctionalized PPDL in a Single-Step Procedure, by Mixing PDL with a Difunctional Diesters (7 or 7′), Catalyzed by *Candida antarctica* Lipase B

							M_n (Da)		
D[a]	product mixture	ratio D:M[a]	time (h)	conv (%)[b]	fraction of ends (%)	yield (%)	NMR	SEC	PDI
7	**8, 9**	1:10	24	>95[c]	96	71	4000	5800	1.7
7′	**8′, 9′**	1:10	48	>95[c]	>96[d]	77	3800	6200	1.5

[a] D = difunctional diester and M = monomer. The ratio is in mol/mol. [b] Monomer conversion was determined by NMR. [c] Conversion was estimated using the peak height of the monomer peak at 4.14 ppm. Integration not possible due to interference with the methylene in polymers **8, 9** and **8′**, **9′** appearing at 4.15 ppm (peak c in Figure 3). [d] NMR signal of the methylene group, adjacent to the hydroxyl end of the poly-PDL, was too small to be quantified.

The presence of the two (meth)acrylate end groups was confirmed; the signals of the vinyl protons of the acrylate, when it was acylated on the hydroxyl end of the lactone, were seen at 5.81, 6.12, and 6.39 ppm (k_2, j_2, and i_2 in Figure 3C) and at 5.55 and 6.10 ppm in methacrylate case (j_2 and i_2 in Figure 3D). When the acrylate was located next to the diol group, the vinyl protons gave signals at 5.85, 6.14, and 6.41 ppm (k_1, j_1, and i_1 in Figure 3C) and at 5.60 and 6.13 ppm in methacrylate case (j_1 and i_1 in Figure 3D). The signals of the diol group adjacent to the acrylate group were detected at 4.34 and 4.37 (a_1 and a_2 in Figure 3C); for the methacrylate case, one multiplet was seen at 4.34 ppm (a in Figure 3D). When the diol group was located within the polyester chain, it gave one signal at 4.28 ppm in both reactions C and D (b in Figure 3C,D).

In Figure 3C, a small triplet at 3.65 ppm, corresponding to the methylene group adjacent to the terminal hydroxyl end, and peaks at 3.83 and 4.22 ppm, corresponding to the ethane diol with one free hydroxyl end, were detected. By comparing the integration of these peaks with the peaks b, a_1, a_2, and c, we found that the fraction of diacrylate ends was 96%. In Figure 3D no peak at 3.65 ppm was detected, which indicates that the degree of dimethacrylation was more than 96%. The MALDI-TOF-MS spectrum of the product mixture of reaction C (**8, 9**) (Figure 4C) showed one main distribution of peaks which correspond to polymers with two acrylated ends (polymers **8** and **9** have the same molecular weight). The MALDI-TOF-MS spectrum of the product mixture of reaction D **(8′, 9′)** showed only one group of peaks which corresponds to polymers with two methacrylated ends (Figure 4D). ^{13}C NMR of the products of both reaction C and D confirmed the presence of acrylate and methacrylate end groups.

The molecular weight, M_n, of the products of reactions C (**8**, **9**) and D (**8′**, **9′**), were 4000 and 3800 g mol^{-1}, respectively, as determined by NMR, representing a DP of 15 and 16, respectively (Table 2). By SEC analysis, M_n and PDI were determined for **8**, **9** to 5800 g mol^{-1} and 1.7, respectively, and for **8′**, **9′** to 6200 g mol^{-1} and 1.5, respectively (Table 2). Using 2 g of PDL, the conversion of monomer was >95% for both reactions C and D, and the yields of the purified products **8**, **9** and **8′**, **9′** were 71% and 77%, respectively (Table 2).

Conclusions

A simple, solvent-free enzymatic single-step route for the synthesis of α,ω-functionalized PPDL macromonomers has been developed using *Candida antarctica* lipase B as an efficient catalyst. Difunctionalized polymers with a high fraction of thiol−thiol or thiol−acrylate end groups were obtained by mixing CALB and PDL with equimolar amounts of functional initiator and terminator. High functional yields of diacrylated or dimethacrylated PPDL were achieved by mixing CALB and PDL with a diester (ethylene glycol diacrylate or ethylene glycol dimethacrylate). This single-step synthesis route demonstrate CALB as an highly efficient catalyst for simultanous ROP and transacylation reactions (end-capping) in combination with chemoselectivity, resulting in polyester macromonomers with a high fraction of α,ω-functionalization.

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