DOI: 10.1002/masy.201051008

Hydroxy Functional Acrylates: Enzymatic Synthesis and Free Radical Polymerization

Dragos Popescu, Richard Hoogenboom, Helmut Keul, Martin Möller**

Summary: Hydroxy functional acrylates were prepared via transacylation of methyl acrylate with 1,2,6-hexanetriol catalyzed by Candida antarctica lipase B. Under the applied reaction conditions, 70% of the substrate was converted into hydroxy functional acrylates. In a subsequent step, after filtration of the enzyme, the monomer mixture containing methyl acrylate and the new monomers was polymerized via free radical polymerization resulting in a functional copolymer with $M_n = 14500$ g/mol.

Keywords: *candida antarctica* lipase-B; enzyme-catalyzed transacylation; functional monomers and polymers; radical polymerization

Introduction

Hydroxy functional polymers are of major interest in polymer science due to their application in growing research fields such as biomedical and pharmaceutical products as well as the synthesis of hydrogels.[1,2] Hydroxy functional monomers can be used as precursor for further chemical modification leading to novel monomeric building blocks for polymer synthesis.[3,4] Moreover, the hydrophobic/hydrophilic balance of the hydroxy functional copolymers can be easily tuned for different applications like thermoresponsive polymers.[5,6] Even though 2-hydroxyethyl acrylate and methacrylate are commercially available and well known, other functional hydroxy acrylates are either not commercially available or only available at a very high price. Chemical synthesis of these monomers requires high temperatures, pressure, acidic catalysts, polymerization inhibitors and complex purification procedures.[7] In recent years, the employment of triacylglycerol lipases as biocatalysts for transacylation reactions has emerged as a potential route to replace the conventional chemical methods.[8,9]

In the present study we investigated a cascade reaction comprising an enzymatic transacylation of methyl acrylate and 1,2,6-hexanetriol followed by a free radical polymerization with AIBN after removal of the enzyme, leading to dihydroxy functional polymers.

Materials and Instrumentation

All chemicals were used as received. A commercial lipase, Novozyme 435 (Lipase B from *Candida antarctica* immobilized on a macroporous acrylic resin, 10000 U/g Novo Nordisk) was dried in vacuum at room temperature for 24 h and stored under nitrogen before it was used as a biocatalyst for the transacylation reactions. ^{1}H NMR spectra were recorded on a Bruker DPX-400 FT-NMR spectrometer at 400 MHz, using deuterated dimethyl sulfoxide (DMSO-d_6) as solvent while size exclusion chromatography (SEC) of the isolated polymer was performed on a Shimadzu system with a SCL-10A system controller, a LC-10AD pump, a RID-10A refractive index detector and PSS gram 30 (pore size 30 Å; bead size 10 μm) and PSS gram 1000 (pore size 1000 Å; bead size 10 μm) columns in series at

---

Institute of Technical and Macromolecular Chemistry, RWTH Aachen and DWI an der RWTH Aachen e.V., Pauwelsstr. 8, D-52056 Aachen, Germany
E-mail: moeller@dwi.rwth-aachen.de; keul@dwi.rwth-aachen.de

60 °C. *N,N*-Dimethylacetamide (DMAc) containing 2.1 g LiCl/L was used as eluent at a flow rate of 1.0 mL / min. The molecular weight was calculated using a poly(styrene) (PS) calibration.

Synthetic Strategy

1,2,6-Hexanetriol (1,2,6Htriol, 14.027 g, 104.5 mmol) was dissolved in 2-methyl-2-butanol (2Me2BuOH, 17.17 mL). To this mixture, methyl acrylate (MA, 3 g, 34.8 mmol) and Novozyme 435 (300 mg, 10 wt % with respect to MA) were added and the mixture was stirred for 24 h at 50 °C. The reaction was quenched by cooling the mixture to ambient temperature and the enzyme was filtered off. The conversion of methyl acrylate was determined to be 70% by ^{1}H NMR spectroscopy. After removing the enzyme by filtration, AIBN (50 mg, 3.5 mmol) and ethanol (3 mL) were added and the mixture was stirred at 70 °C for 4 h. The reaction was quenched by cooling the mixture to room temperature and the addition of 30 mL of water. The polymer was purified via dialysis against water and isolated by lyophilization for 24 h. SEC analysis using DMAc as eluting solvent proved the formation of a polymer with $M_n = 14500$ g/mol and a $M_w/M_n = 2.7$. Yield: 2.3 g (76%).

Results and Discussion

In our previous work, we developed a simple route for preparing highly functional acrylates and methacrylates via an enzymatic transacylation of methyl acrylate and methyl methacrylate as substrates with different monoalcohols, diols and triols.[8,9] After transacylation and filtration of the enzyme, the monomer mixture was polymerized via free radical polymerization and thus, different poly[(meth)acrylate]s were synthesized.[8] In the present work, this previous approach was expanded. The synthesis of a dihydroxy functional poly[acrylate] resulting from the enzymatic transacylation of MA and 1,2,6Htriol (step 1, Figure 1) followed by free radical polymerization of the obtained monomers without further purification is presented (step 2, Figure 1). A multifunctional hydroxy polyacrylate was obtained, which can be used as a precursor for a reactive

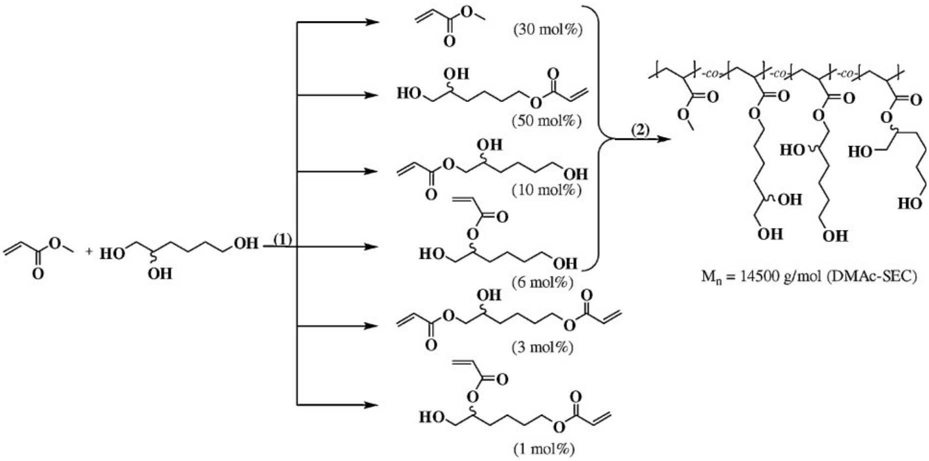

Figure 1.
Hydroxy functional poly[acrylates] obtained via a cascade of (1) enzymatic transacylation and (2) free radical polymerization of the monomer mixture. (1) T = 50 °C, t = 24 h, solvent 2Me2BuOH, MA: 1,2,6Htriol = 1: 3 molar; (2) T = 70 °C, t = 4 h, solvent ethanol. The molar ratios of the different acrylates and bisacrylates was determined precisely via GC-MS as described elsewhere.[9]

polymer as it is presented in literature[3,4] and also might exhibit interesting properties on itself.

The enzymatic transacylation of MA and 1,2,6Htriol was followed by ^{1}H NMR spectroscopy, (Figure 2) where the top spectrum (t_0) shows the signals of the starting materials: characteristic for the conversion is the methyl ester group of MA (signal c) at $\delta = 3.68$ ppm. Figure 2 bottom (t_{24}) shows the signals of the reaction mixture after 24 h: the formation of the new hydroxy acrylates is demonstrated by the appearance of OH signals 11 and 12 at $\delta = 4.81$ ppm and $\delta = 4.88$ ppm as doublets and the methylene group 10 at $\delta = 1.61$ ppm as a multiplet. The doublets belong to the secondary hydroxyl groups attached to the new monomers as it is known that in some cases the coupling between the CH and the OH protons may be observed in DMSO.[10] Furthermore, the presence of the methanol signals at $\delta = 3.17$ ppm demonstrates that the MA reacted with the triol. Because the signals of the protons from the products of reactions with the secondary hydroxy group of the triol as well as the signals of the bisacrylates are indistinguishable, the ratio of these compounds can not be determined from ^{1}H NMR spectroscopy. Therefore, GC-MS has been used to determine the ratio of all products[9] as shown in Figure 1. After 24 h, 70 mol% of MA had reacted, as determined from the ^{1}H NMR spectrum, Figure 2, using the integral of the proton signals of the methyl group (c) ($\delta = 3.68$ ppm) at the beginning and at the end of the reaction relative to the 2Me2BuOH at $\delta = 0.8$ ppm.

In order to prepare a hydroxy functional poly[acrylate] the lipase was filtered off and the monomer mixture was copolymerized with 1 mol % AIBN with respect to the initial amount of MA, in 50 vol% EtOH. As such, a mixture of 30 mol % MA, 66 mol % hydroxy functional monoacrylates and 4 mol % hydroxy functional bisacrylates (Figure 1) was copolymerized. After 4 h an overall monomer conversion of 96% was calculated from ^{1}H NMR spectrum, using the signal of 2Me2BuOH at $\delta = 0.8$ ppm as

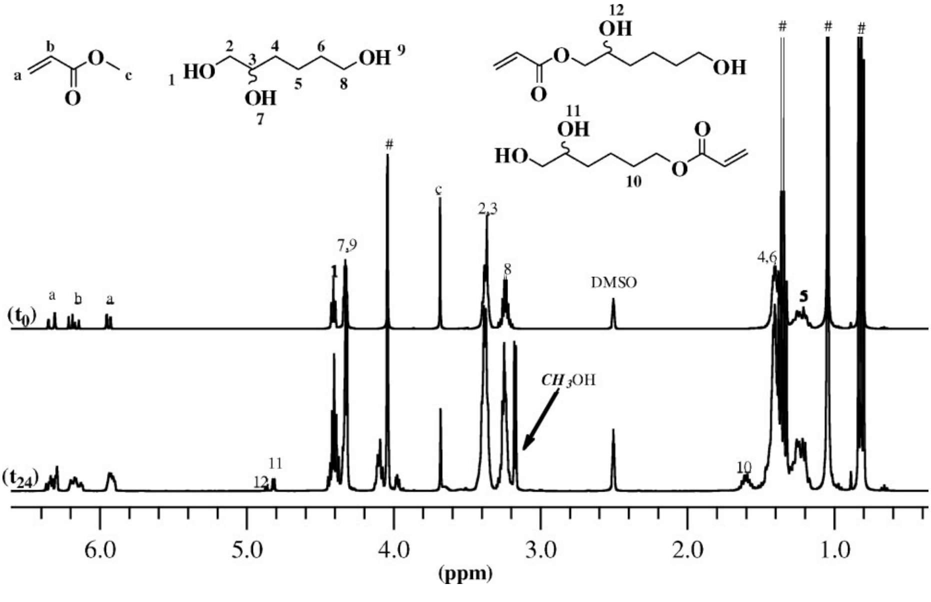

Figure 2.

^{1}H NMR spectra of the transacylation between MA and 1,2,6Htriol measured in DMSO-d_6. (t_0) starting materials; (t_{24}) crude reaction product after 24 h. (MA: 1,2,6Htriol = 1: 3 mol%; T = 50 °C in 2Me2BuOH). (#) signals of 2Me2BuOH. The non assigned peaks in the spectrum (t24) correspond to starting materials and overlapping product peaks.

standard and the C,C- double bond of the monomers.

The polymer was purified via dialysis in water, using a membrane with 100-500 Da molecular weight cut off (MWCO). Thus, all the small molecules are removed and the polymer is concentrated in the dialyze membrane, and freeze dried finally. Size exclusion chromatography (SEC) of the isolated polymer using *N,N*-Dimethylacetamide (DMAc) as eluent revealed a bimodal trace with a molecular weight $M_n = 14500$ g/mol and a polydispersity index of $M_w/M_n = 2.7$. The high polydispersity index obtained can be explained by the formation of grafted molecules induced by the bisacrylates.

Conclusion

The cascade reaction – enzymatic transacylation, free radical polymerization, described in this paper represents a mild, easy and rapid process for hydroxy functional polymers. As such, hydroxy functional polyacrylates were prepared with potential use in a range of different applications.

[1] D. Schmaljohann, *Adv. Drug Delivery Rev.* **2006**, *58*, 1655.
[2] J. T. Zhang, Y. N. Xue, F. Z. Gao, S. W. Huang, R. X. Zhuo, *J. Appl. Polym. Sci.* **2008**, *108*, 3031.
[3] R. Adelmann, M. Mennicken, D. Popescu, E. Heine, H. Keul, M. Möller, *Eur. Polym. J.* **2009**, *45*, 3093.
[4] D. Popescu, H. Keul, M. Möller, *Macromol. Chem. Phys.* **2008**, *209*, 2012.
[5] T. M. Eggenhuisen, C. R. Becer, M. W. M. Fijten, R. Eckardt, R. Hoogenboom, U. S. Schubert, *Macromolecules* **2008**, *41*, 5132.
[6] R. Hoogenboom, D. Popescu, W. Steinhauer, H. Keul, M. Möller, *Macromol. Rapid Commun.* **2009**, *30*, 2042.
[7] M. Save, J. V. M. Weaver, S. P. Armes, P. McKenna, *Macromolecules* **2002**, *35*, 1152.
[8] D. Popescu, H. Keul, M. Möller, *Macromol. Chem. Phys.* **2009**, *210*, 123.
[9] D. Popescu, R. Hoogenboom, H. Keul, M. Möller, *J. Mol. Catal. B: Enym.* **2010**, *62*, 81.
[10] H. E. Gottlieb, V. Kotlyar, A. Nudelman, *J. Org. Chem.* **1997**, *62*, 7512.