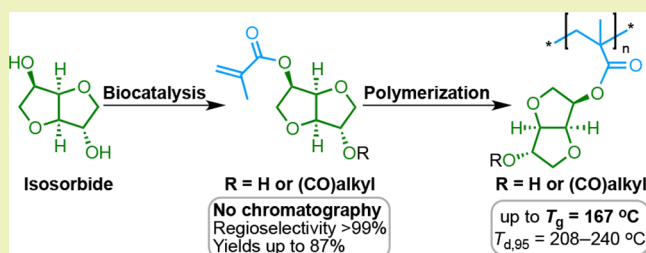


Enzymatic Synthesis and Polymerization of Isosorbide-Based Monomethacrylates for High- T_g PlasticsLivia Matt,[†] Jaan Parve,[‡] Omar Parve,[‡] Tõnis Pehk,[§] Thanh Huong Pham,^{||} Ilme Liblikas,[†] Lauri Vares,^{*,†} and Patric Jannasch^{*,†,||}[†]Institute of Technology, University of Tartu, Nooruse 1, Tartu 50411, Estonia[‡]Department of Chemistry and Biotechnology, Tallinn University of Technology, Ehitajate tee 5, Tallinn 19086, Estonia[§]Laboratory of Chemical Physics, National Institute of Chemical Physics and Biophysics, Akadeemia tee 23, Tallinn 12618, Estonia^{||}Department of Chemistry, Lund University, Box 124, Lund 221 00, Sweden

S Supporting Information

ABSTRACT: Isosorbide is a stiff bicyclic diol derived from glucose-based polysaccharides, and is thus an attractive building block for novel rigid bioplastics. In the present work, a highly regioselective biocatalytic approach for the synthesis of isosorbide 5-methacrylate was developed. The Lipozyme RM IM (*Rhizomucor miehei* lipase)-catalyzed process is straightforward, easily scalable, and chromatography-free; a simple extractive workup afforded the monomer at >99% purity and in 87% yield. The developed strategy was applied for the synthesis of a series of monomethacrylated isosorbide derivatives. Radical polymerization of the monomers produced rigid polymethacrylates with a certain side group in either *endo* or *exo* configuration, exclusively, which generated materials with great diversity of properties. For example, the two regioisomeric polymers carrying hydroxyl groups reached a glass transition temperature at $T_g = 167^\circ\text{C}$. The polymer tethered with dodecanoate chains in *exo* position showed crystallinity with an unexpectedly high melting point at $T_m = 83^\circ\text{C}$. In contrast, the corresponding sample with dodecanoate chains in *endo* positions was fully amorphous with $T_g = 54^\circ\text{C}$. Efficient biocatalytic synthesis combined with attractive polymer properties opens possibilities for production of these biobased polymers on an industrial scale.

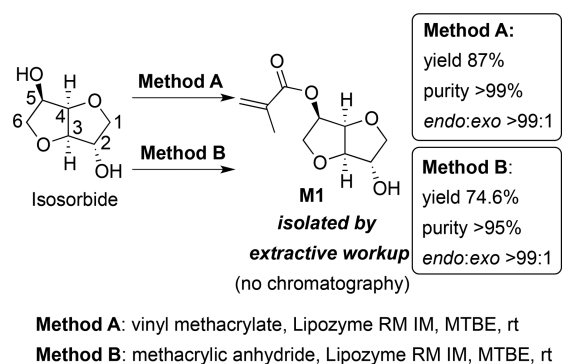
KEYWORDS: Lipase-catalyzed regioselective methacrylation, Vinyl methacrylate, Methacrylic anhydride, Isosorbide, Polymethacrylate, Renewable, *Rhizomucor miehei* lipase, Biobased plastics



INTRODUCTION

Environmental concerns and the inevitable depletion of fossil resources have motivated research efforts to find sustainable alternatives to fossil-based plastics.^{1,2} However, there is still an apparent lack of transparent high-performance plastics with high glass transition temperatures (T_g 's), which combine high mechanical stiffness and good thermal properties with a cost-competitive production. For amorphous polymers, the T_g is the single most important parameter, which to a high degree defines the scope of applications.³ One effective approach to achieve high- T_g polymers is to incorporate rigid components into the polymer structure. Hence, isosorbide⁴ (Scheme 1), a nontoxic platform chemical produced from D-glucose on an industrial scale,⁵ has attracted considerable attention as a potential building block for high- T_g polymers. It is a chiral, rigid, V-shaped compound bearing two secondary hydroxyl groups in *endo* and *exo* configurations, respectively.⁶ It has already been used as a building block for the synthesis of biobased polymers such as polyesters, polycarbonates, polyurethanes, etc.⁷ However, the low reactivity of its secondary hydroxyl groups limits the use of isosorbide in polymerizations,

Scheme 1. Regioselective Synthesis of 5-Methacrylate M1



and, in conjunction with high T_g values, oligomeric or severely colored products are often formed.⁸ Strategies to overcome

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this issue include the conversion of secondary hydroxyl groups into primary ones⁹ and modification of the fused ring system,¹⁰ which, unfortunately, usually lead to partial loss of polymer chain rigidity and reduction of T_g .

Isosorbide has in most cases been entirely included in the polymer backbone via engagement of both hydroxyl groups. Less attention has so far been paid to the derivatives with one polymerizable moiety that offer possibilities to tailor the polymer properties by attaching property-regulating substituents (e.g., biobased carboxylic acid residues) to the other hydroxyl group. Regarding isosorbide monomethacrylates, only corresponding acetates have been investigated; a mixture of regioisomers (4:1) has been studied¹¹ in free radical and RAFT polymerizations. In this case, regiochemistry had no significant impact on the thermal properties of polymers. Conversely, regioisomeric poly(vinyl-isosorbide-triazole)s have been found to show dissimilar solubility and T_g values.¹²

Only a few methods for the monomethacrylation of isosorbide have so far been described. The *endo* OH group in isosorbide is a stronger nucleophile due to intramolecular hydrogen bonding, as compared to the hydroxyl group at the *exo* position.¹³ Therefore, chemical acylation using heavy metal catalysis is selective toward the *endo* group. A five-step synthesis of isosorbide 5-methacrylate has been reported (with 23% overall yield).¹⁴ Regioisomeric mixtures of monomethacrylates have been synthesized via base- and acid-catalyzed esterification; the products were polymerized without separation.^{15,16}

Lipase-catalyzed esterification of isosorbide has been reported in the cases of (1) polyester synthesis;¹⁷ (2) synthesis of mixtures of mono- and diesters;¹⁸ (3) synthesis of diesters;¹⁹ and (4) regioselective synthesis of monoesters.^{20–22} In general, the selectivity has been toward the *endo*-5 OH group. Lipozyme (RML) has catalyzed esterification of isosorbide with oleic acid affording 5-monooleate and 2-monooleate with a ratio of 3/1.²⁰ Highly regioselective esterification catalyzed by RML has been reported for octanoic acid.²¹ However, for C6 (caproic) and C4 (butyric) acids, this method failed. An interesting *exo*-2 OH preference for esterification has been reported by Roberts et al.²² Lipase-catalyzed synthesis of methacrylic esters of simple diols²³ and citronellyl methacrylate has been studied.²⁴ However, lipase-catalyzed synthesis of isosorbide monomethacrylates has not yet been described.

In the present work, we have first developed a straightforward, upscalable, and highly regioselective biocatalytic/chemoenzymatic method to prepare a series of isosorbide 5- and 2-methacrylates. The synthesized monomers bear acetate, dodecanoate, cyclohexanoate, and hydroxyl functionalities, respectively, to study important structure–property relationships. These structurally diverse monomers were polymerized via conventional free radical polymerization, and the obtained polymethacrylates were studied to evaluate the influence of regiochemistry and functionality on the properties, with a primary focus on the thermal properties.

EXPERIMENTAL SECTION

General. All reagents and solvents were obtained from commercial sources and were used without further purification. As a precaution, a stabilizing agent [hydroquinone (HQ) or hydroquinone monomethyl ether (HQMME)] was added before evaporation to separated methacrylic products.

Structural Characterization. The structure of the monomers and polymers was characterized by NMR spectroscopy using a Bruker

800 or 400 MHz spectrometer with the samples dissolved in either chloroform-*d* or dimethyl sulfoxide-*d*₆. The ¹H NMR and ¹³C NMR spectra were recorded at 800 or 400 MHz and 201 or 101 MHz, respectively. The formation of polymers (P1–P7) from the corresponding isosorbide methacrylate derivatives (M1–M7) was determined by the decrease or disappearance of the proton signals of the double bond $\text{CH}_2=\text{CH}-$ between the 6.3–5.5 ppm region in comparison with the characteristic peaks of the polymers in ¹H NMR spectra. For HRMS analysis of monomers, a Thermo Electron LTQ Orbitrap XL analyzer was used. An FTIR (ATR) spectrophotometer Shimadzu IRAffinity-1 was used for IR analysis of the monomethacrylates.

The molecular weights of the polymethacrylates were determined by size-exclusion chromatography (SEC) in THF. The SEC setup included three Shodex columns coupled in series (KF-805, -804, and -802.5) situated in a Shimadzu CTO-20A prominence column oven, a Shimadzu RID-20A refractive index detector, with Shimadzu LabSolution software. All samples were run at 40 °C in THF and at an elution rate of 1 mL/min. Calibration was done by using poly(ethylene oxide) standards (M_n = 3860, 12 600, 49 640, and 96 100 g/mol).

The intrinsic viscosity $[\eta]$ of the polymethacrylates was determined using an Ubbelohde viscometer at 21 °C. Samples were dissolved in DMSO (P1, P2, P3(a–d), P4(a,b)) or in toluene (P5–P7). These stock solutions were later diluted by adding neat solvent (DMSO or toluene, correspondingly) to reduce the concentrations. The efflux times of the neat solvents (t_b) and the polymer solutions (t_s) through the capillary were taken as the average of at least four measurements. The inherent (η_{inh}) and reduced (η_{red}) viscosities at different concentrations were calculated as

$$\eta_{\text{red}} = \frac{\frac{t_s}{t_b} - 1}{c} \quad (1)$$

$$\eta_{\text{inh}} = \frac{\ln\left(\frac{t_s}{t_b}\right)}{c} \quad (2)$$

The intrinsic viscosity $[\eta]$ was estimated by extrapolating η_{red} and η_{inh} to $c = 0$ and calculating the average intersection with the y-axis.

Thermal Characterization. Thermogravimetric analysis (TGA) was performed using a TA Instruments TGA Q500 apparatus to determine the thermal stability of the polymers under a N₂ atmosphere. The temperature was increased from 50 to 600 °C at a heating rate of 10 °C min^{−1}. To remove solvent residues, the samples were kept isothermally at 120 °C during 20 min prior to the analysis. The thermal decomposition temperature ($T_{d,95}$) was determined at 5% weight loss.

Differential scanning calorimetry (DSC) analysis was carried out by using a TA Instruments DSC Q2000 differential scanning calorimeter. Dried samples were transferred to aluminum pans, which were hermetically sealed. The samples were first heated to 150 °C, then cooled to 0 °C, and finally heated to 150 °C (except for polymers P1 and P2, which were heated to 195 °C). The scan rate was 10 °C/min during the temperature program. The T_g 's of the polymers were evaluated from the heating scans by identifying the inflection points.

Synthesis of Monomethacrylic Isosorbide Monomer. *D*-Isosorbide 5-Methacrylate M1 (Acyl Donor: Vinyl Methacrylate; Method A). Into a 1 L flask were introduced *D*-isosorbide (21.92 g, 0.15 mol), methyl *tert*-butyl ether (MTBE; 300 mL), vinyl methacrylate (33.64 g, 36 mL, 0.30 mol), and Lipozyme RM IM (4.0 g). The mixture was slowly stirred at 20 °C for 60 h. After that the ratio of the unreacted *D*-isosorbide and the target monoester was estimated to be less than 1/10 by TLC. The synthesis was terminated by filtering off the enzyme. The filtrate was evaporated to dryness, and the residual crude product was dissolved in EtOAc (500 mL), and washed with saturated NaHCO₃ solution (2 × 50 mL) and brine (2 × 30 mL). HQ (2 mg) was added to the solution, which was further dried over anhydrous Na₂SO₄, filtered, and evaporated to dryness. The oily crude product was dissolved in ethanol (95.6% EtOH/H₂O;

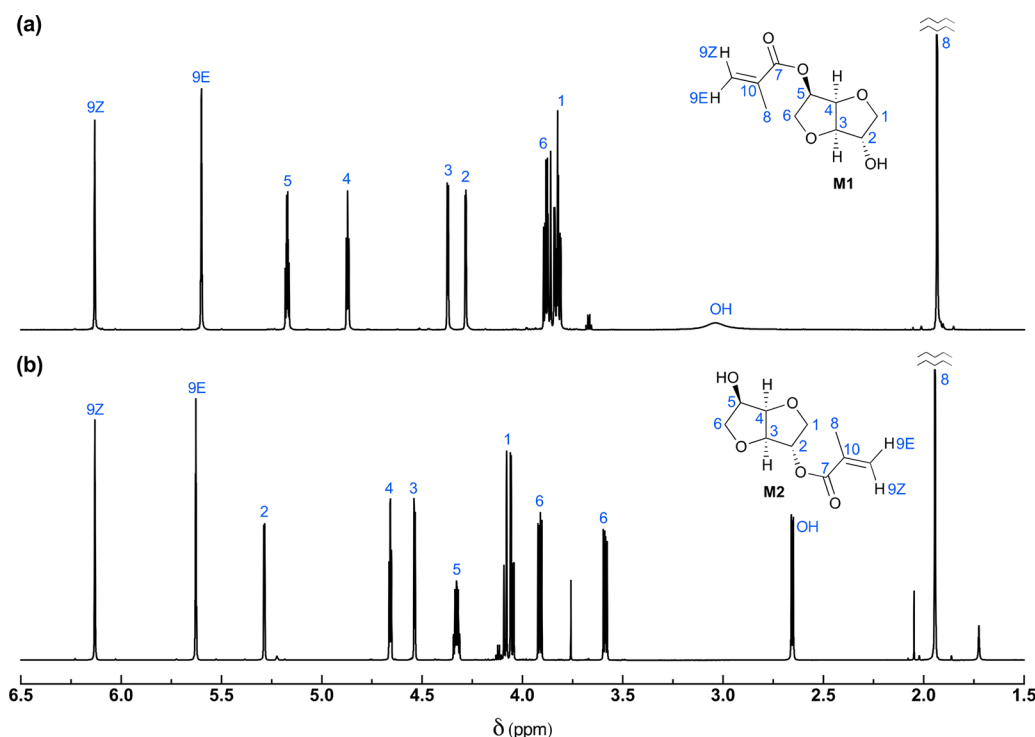


Figure 1. ^1H NMR spectra of (a) isosorbide 5-methacrylate **M1** (crude spectrum) and (b) isosorbide 2-methacrylate **M2**, both recorded in CDCl_3 .

300 mL), activated charcoal (2.0 g) was added, and the mixture was stirred at 20 °C for 12 h. The charcoal was filtered off using a glass filter covered with filter aid Hyflo Super Cel layer (CAS: 68855-54-9). An additional 2 mg of HQ was added to the solution before evaporation to dryness, which afforded 28.24 g (yield: 87.3%) of colorless oily target D-isosorbide 5-methacrylate **M1**. The *endo* configuration of the methacrylate was confirmed by 2D FT NMR experiments. The purity of the product was >99% as determined by ^1H NMR spectroscopy. The product contained traces of EtOH and HQ.

^1H NMR (800 MHz, CDCl_3): δ 6.13 (dq, $J = 1.5$ and 3×1.0 Hz, 1H, H-3mZ), 5.60 (p, $J = 4 \times 1.5$ Hz, 1H, H-3mE), 5.17 (td, $J = 2 \times 5.6$ and 4.5 Hz, 1H H-5x), 4.87 (ddt, $J = 5.6$, 4.7, and 2×0.5 Hz, 1H, H-4x), 4.37 (dt, $J = 4.7$ and 2×0.9 Hz, 1H, H-3x), 4.28 (dtd, $J = 3.2$, 2×0.9 and 0.5 Hz, 1H, H-2n), 3.89 (dd, $J = 10.1$ and 5.6 Hz, 1H, H-6x), 3.87 (dt, $J = 10.0$ and 2×0.9 Hz, 1H, H-1x), 3.83 (ddt, $J = 10.1$, 4.5, and 2×0.4 Hz, 1H, H-6n), 3.82 (ddt, $J = 10.0$, 3.2, and 2×0.4 Hz, 1H, H-1n), 3.06 (bs, 1H, OH), 1.93 (dd, $J = 1.0$ and 1.5 Hz, 3H, H-4m) ppm. ^{13}C NMR (201 MHz, CDCl_3): δ 166.74 (C-1m), 135.52 (C-2m), 126.34 (C-3m), 88.18 (C3), 80.40 (C4), 75.85 (C2), 75.31 (C1), 74.18 (C5), 70.53 (C6), 18.22 (C-4m) ppm. $[\alpha]_D^{20} +69.8$ (c 1.3, CHCl_3); $[\alpha]_D^{20} +74.6$ (c 2.4, EtOAc). IR (ATR) ν_{max} (cm^{-1}): 3449, 1721, 1636, 1165, 1092, 1045. HRMS (ESI): calcd for $\text{C}_{10}\text{H}_{14}\text{O}_5\text{Na}$ $[\text{M} + \text{Na}]^+$ 237.0733, found 237.0732. MS (m/z): 215, 171, 154, 128, 113, 98, 85, 70, 69, 68, 57, 43, 41. TLC: $R_f = 0.21$ (PE/EtOAc 1/1).

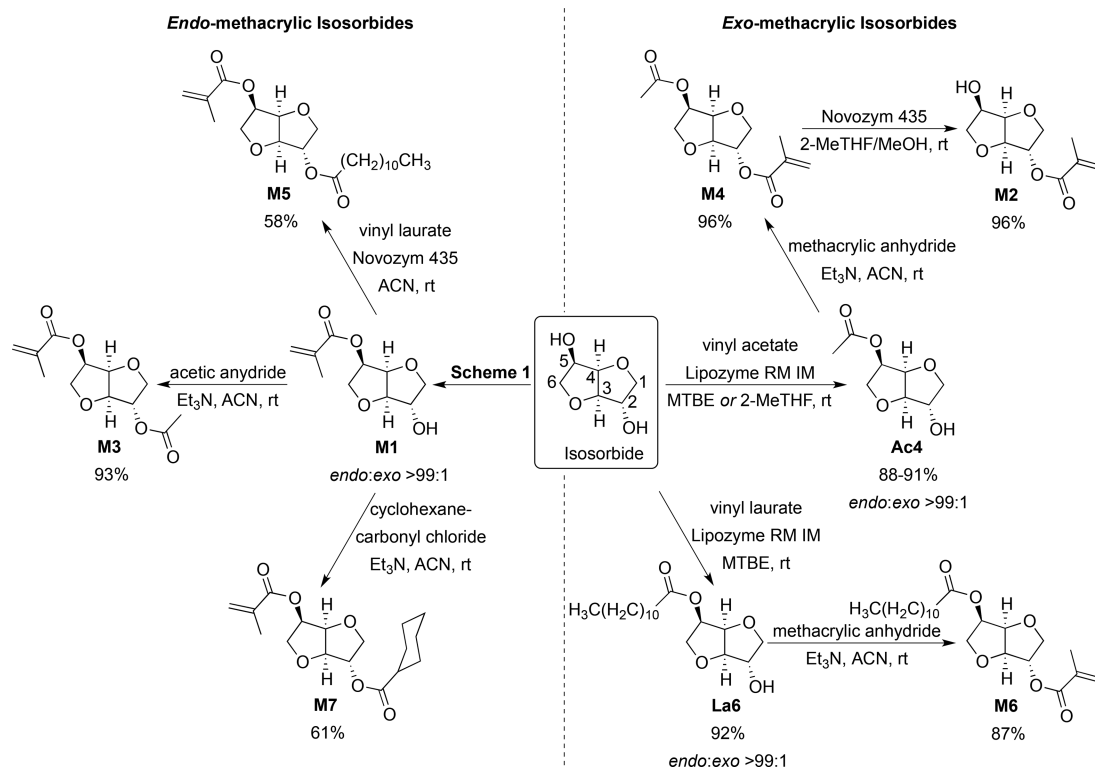
Alternative Synthesis of D-Isosorbide 5-Methacrylate M1 (Acyl Donor: Methacrylic Anhydride; Method B). Into a 1 L flask were introduced D-isosorbide (21.92 g, 0.15 mol), MTBE (300 mL), methacrylic anhydride (34.7 g, 33.5 mL, 0.225 mol), and Lipozyme RM IM (4.0 g). The mixture was stirred at 20 °C for 40 h, and the ratio of the unreacted D-isosorbide versus the target 5-monoester was estimated by TLC to be ca. 1/20. Neither the regioisomeric 2-methacrylate nor isosorbide bis-methacrylate was detected by TLC. To hydrolyze the excess of methacrylic anhydride, water (3.6 mL, 0.2 mol) was added, and stirring of the reaction mixture was continued for an additional 24 h until no anhydride was detected in the mixture by TLC. The synthesis was terminated by filtering off the enzyme. After the filtrate was evaporated to dryness, the residual crude product

was dissolved in EtOAc (500 mL). It was then washed with saturated NaHCO_3 solution (2×75 mL), to eliminate unreacted isosorbide as well as methacrylic acid formed, and finally with brine (2×30 mL). The solution was dried over anhydrous Na_2SO_4 , filtered, and 2 mg of HQ was added. The solution was evaporated to remove the solvent, and the residual oily product was dissolved in EtOH (95.6%). Activated charcoal (2.0 g) was added, and the mixture was stirred at 20 °C for 12 h. The charcoal was filtered off through a glass filter covered with a filter aid Hyflo Super Cel layer (CAS: 68855-54-9). An additional 2 mg of HQ was added to the solution, and EtOH was evaporated to afford 23.97 g (yield: 74.6%) of the target D-isosorbide 5-methacrylate **M1** with >95% purity. Characterization of the product is given in the former example.

General Procedure for Free Radical Polymerization of Isosorbide-Based Monomethacrylates. Isosorbide monomethacrylate (**M1–M7**; 270–350 mg) was filtered through basic Al_2O_3 to remove the HQ inhibitor and placed into a 8 mL pressure tube. EtOAc (2.7–3.5 mL) and azobis(isobutyronitrile) (AIBN; 0.5, 0.25, 0.13, or 0.06 mol %) dissolved in EtOAc then were added; DMSO was used instead of EtOAc for monomers **M1** and **M2**. After sparging the mixture with Ar for 45 min, the tube was sealed firmly with a cap and placed into a preheated oven at 60 °C for 24 h. The reaction was then cooled to room temperature, and a small sample was taken to determine the monomer conversion by ^1H NMR. The crude product was precipitated in an appropriate solvent (Et_2O and iso-propanol 5:1 mixture was used for polymers **P1** and **P2**; Et_2O for **P3(a–d)**, **P4(a,b)**, and **P7**; MeOH for **P5** and **P6**) to remove any residual monomer and filtered from the same solvent three times. After the final filtration, a solid product was collected and carefully dried under vacuum. The dried product was characterized by NMR spectroscopy, SEC, TGA, DSC, and intrinsic viscosity measurements.

RESULTS AND DISCUSSION

Design of a Scalable Enzymatic Method. The screening of conditions²⁵ to develop a highly regioselective lipase-catalyzed methacrylation method for isosorbide included a search for the proper lipase/loading in combination with a suitable solvent and acyl donor. The reactivity, concentration,

Scheme 2. Synthesis of *endo* and *exo* Methacrylic Isosorbide Monomers M1–M7

and optimum excess of the acyl donors were taken into consideration. The key issues were, first, how to remove the excess of an acyl donor after the reaction is finished and, second, which separation methodology to use for the purification of the product. Temperature and process engineering were also taken into consideration.

In this work, three immobilized lipases were explored: Novozym 435 (*Candida antarctica* lipase B (CALB)), Lipozyme RM IM (*Rhizomucor miehei* lipase (RML)), and Lipolase TL IM (*Thermomyces lanuginosus* lipase (TLL)).²⁶ The solvents evaluated included toluene, cyclohexane, methyl *tert*-butyl ether, and 2-methyltetrahydrofuran. The methacryl donors used were vinyl methacrylate and methacrylic anhydride. The latter can be qualified as a potentially biobased product due to recent efforts made to develop the synthesis of its precursor methacrylic acid from renewable resources.²⁷ Also, methacrylic anhydride has not been used as an acyl donor in lipase-catalyzed methacrylations; however, some other carboxylic acid anhydrides have been used in this role.^{28,29}

Synthesis of Isosorbide 5-Methacrylate M1. When isosorbide was treated with vinyl methacrylate at room temperature in the presence of Lipozyme RM IM in MTBE, only the *endo* regioisomer **M1** was formed (method A, Scheme 1). Separation of the product required only a simple extraction (EtOAc/satd aq NaHCO₃ and brine) followed by decolorization with activated charcoal in EtOH affording the product **M1** in >99% purity and 87% yield. ¹H NMR analysis demonstrated that as of impurities, the product contained only traces of EtOH and hydroquinone; neither 2-methacrylate nor bis-methacrylate were detected (Figure 1). This is the first report of a highly regioselective, one-step preparative synthesis of isosorbide 5-methacrylate.

RML-catalyzed 5-methacrylation of isosorbide with vinyl methacrylate can also be carried out equally regioselectively in

2-MeTHF; however, the activity of RML in 2-MeTHF is 4–5 times lower as compared to that of MTBE.

A straightforward determination of the acylation position in isosorbide esters can be done on the basis of the different nature of the 2- and 5-OH groups (Figure 1). The 5-*endo* OH group, which is intramolecularly H-bonded, displays an unusually sharp OH doublet with a large coupling constant of around 7 Hz, while the 2-*exo* OH shows an exchanging broad singlet or broad doublet with a coupling constant of approximately 5 Hz.

To reduce the cost of the product, we evaluated methacrylic anhydride as the acyl donor (method B, Scheme 1). When the conversion reached ~95%, water was added to enzymatically hydrolyze the unreacted methacrylic anhydride before the enzyme was filtered off. Product **M1** was isolated by a straightforward extractive workup/decolorization process and obtained in 74% yield in high purity (≥95%). The reduced yield as compared to method A is probably due to the use of a larger volume of NaHCO₃ solution to extract the considerably larger quantity of methacrylic acid liberated from the acyl donor. The regioselectivity of the reaction was again excellent (>99:1). Possibilities to use methacrylic acid, which is a greener methacryl donor, are currently under study.

Lipozyme RM IM could be reused in both methods. However, some decrease in activity was observed. To ensure an efficient biocatalyst reuse, corresponding optimization is needed.

Although the developed methods A and B have some differences, both of them offer simple chromatography-free access to monomer **M1** in excellent regioselectivity and purity at high yield. This novel synthetic procedure is easily scalable, making it appealing for industrial production.

Synthesis of Isosorbide 5-Methacrylic Diesters. Further, isosorbide 5-methacrylate **M1** was converted into

various diesters for use as monomers in the polymerization studies (Scheme 2). Isosorbide 2-acetate-5-methacrylate **M3** (yield: 93%) and isosorbide 2-cyclohexanecarboxylate-5-methacrylate **M7** were synthesized by routine acylation. **M7** was separated by crystallization from EtOH (yield: 61%). Isosorbide 2-laurate-5-methacrylate **M5** was obtained by CalB-catalyzed acylation of the 2-OH group of isosorbide 5-methacrylate with vinyl laurate (yield: 58%). The conditions of diester synthesis were not optimized. The goal of the work was to prepare pure products for the polymerization trials.

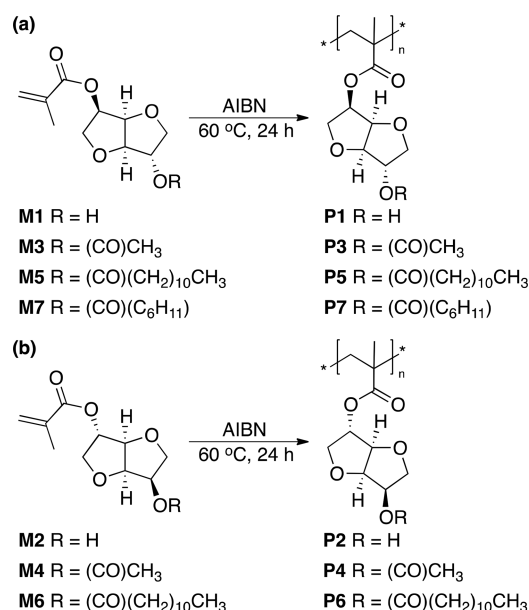
Synthesis of Isosorbide 2-Methacrylic Diesters. Next, we turned our attention to isosorbide 2-methacrylate **M2** and the corresponding diesters thereof. Isosorbide methacrylate **M2** has a methacryloyl group in the *exo* position and is the regioisomer of compound **M1**. The direct regioselective acylation of 2-OH³⁰ is challenging, as the lipases are mainly selective toward 5-OH of isosorbide. Thus, acylation of 2-OH required a somewhat different approach (Scheme 2). However, we applied a strategy, which takes advantage of Lipozyme RM IM's high 5-OH selectivity.

The 5-OH group was acetylated in MTBE, applying the developed highly regioselective enzymatic method A (vide supra) using vinyl acetate as the acyl donor. The isosorbide 5-acetate **Ac4** obtained after decolorization with charcoal in EtOH, filtration, and evaporation contained a trace amount of bis-acetate that was removed by chromatography to achieve an analytically pure sample in 88% yield. No regioisomeric 2-acetate was detected in the crude reaction mixture. The isosorbide 5-acetate **Ac4** obtained by the same procedure in 2-MeTHF was equal to that shown by RML in MTBE, and the yield was even better, 91%. The subsequent treatment of **Ac4** with methacrylic anhydride in the presence of Et₃N afforded isosorbide 2-methacrylate-5-acetate **M4** in 95% yield. To achieve isosorbide 2-methacrylate **M2**, we used a highly regioselective Novozym 435-catalyzed cleavage^{31,32} of the acetate moiety in **M4**. In this way, the deacetylation performed in 2-MeTHF using MeOH as nucleophile afforded methacrylate **M2** in 96% yield after flash chromatography. Methacrylates **M2** and **M1** are regioisomers, and they exhibit clearly different shifts in the NMR spectra, as shown in Figure 1.

Finally, isosorbide 2-methacrylate-5-laurate **M6** was prepared using an approach similar to that used for the corresponding acetate **M4**. Isosorbide 5-laurate **La6** was synthesized following enzymatic method A (Scheme 1) in a highly regioselective manner in good yield and purified over silica to separate the unreacted vinyl laurate (yield: 92%). Unlike lauric acid, unreacted isosorbide is easy to extract with water, and therefore no excess of vinyl laurate should be used. Subsequently, isosorbide 2-methacrylate-5-laurate **M6** was prepared by methacrylation of isosorbide 5-laurate (synthesis described above) **La6** with methacrylic anhydride.

Polymerization of Isosorbide-Based Monomethacrylates and Characterization of the Products. The structurally diverse isosorbide methacrylate monomers enabled the preparation of high-*T_g* polymers with a wide range of properties. All of the monomers (**M1**–**M7**) were polymerized in solution during 24 h via thermally initiated free radical polymerization at 60 °C using AIBN as the initiator (Scheme 3). The monomer concentration was 100 mg/mL, and the molar initiator concentration was in most cases 0.5% of the molar monomer concentration, as seen in Table 1. The structure of the products was confirmed by ¹H NMR

Scheme 3. Radical Polymerization of (a) Isosorbide *endo*-Methacrylates and (b) Isosorbide *exo*-Methacrylates



spectroscopy, and the number average molecular weight (*M_n*) and polydispersity (*Đ*) were determined by SEC using poly(ethylene oxide) standards (Table 1).

As seen in Table 1, the conditions employed for the polymerizations gave very high monomer conversions, up to 97%. In the polymerizations of the hydroxyl functional monomers **M1** and **M2**, the conversion was essentially complete after 24 h in both cases, and the precipitation in a diethyl ether/2-propanol (5:1 v/v) mixture yielded polymers **P1** and **P2** as white powders (Table 1, entries 1 and 2). The polymerizations of the acetate capped monomers **M3** and **M4** were carried out at different AIBN concentrations (0.50, 0.25, 0.13, and 0.06 mol %) to produce **P3(a–d)** and **P4(a,b)**, respectively, to evaluate the effect on monomer conversion and *M_n* (Table 1, entries 4–8). As expected, the results showed that the conversion decreased with the decreasing initiator concentration. In the preparation of polymers **P3(a–d)**, the conversion decreased gradually from 88% (**P3(a)**) to 66% (**P3(d)**) as the AIBN concentration was reduced from 0.5 to 0.06 mol %. As seen in Table 1, the conversions of monomer **M5**–**M7** were also quite high, ≥87% (entries 9–11).

The solubility of the polymethacrylates was investigated in a wide range of solvents, arranged according to their hydrogen-bonding capacity and solubility parameter (*δ*) (Table S1). Strongly hydrogen-bonding solvents (H₂O, MeOH, 1-BuOH) did not dissolve the polymethacrylates. Even polymers **P1** and **P2**, bearing hydroxyl groups, were not soluble in these media. Polymers **P1**–**P4** readily dissolved in DMSO (*δ* = 25 MPa^{1/2}), but the polymers with nonpolar alkyl units **P5**–**P7** were all insoluble. Acetonitrile (*δ* = 24 MPa^{1/2}) has a *δ* value similar to that of DMSO and dissolved only the acetate functional polymers **P3** and **P4**. THF and CHCl₃, which have very similar *δ* values (19 MPa^{1/2}), but are moderately and poorly hydrogen-bonding, respectively, dissolved the polymethacrylates similarly. Hence, **P3**–**P7** were readily soluble, but, in contrast, **P1** and **P2** were nonsoluble in these solvents. Diethyl ether (*δ* = 15 MPa^{1/2}) is a nonpolar and moderately hydrogen-bonding solvent, which did not dissolve any of the polymethacrylates. However, the presence of nonpolar C12

Table 1. Data from Radical Polymerizations of the Different Isosorbide-Based Monomethacrylates

entry	polymer	monomer used	AIBN (mol %)	monomer conversion (%) ^a	M_n (kg mol ⁻¹) ^b	$\bar{D}$ ^b	$T_{d,95}$ (°C) ^c	$[\eta]$ (dL g ⁻¹) ^d
1	P1	M1	0.5	96	nd ^e	nd ^e	238	0.82
2	P2	M2	0.5	97	nd ^e	nd ^e	240	0.46
3	P3(a)	M3	0.5	88	35	2.6	223	0.30
4	P3(b)	M3	0.25	82	37	2.3	nd ^e	0.34
5	P3(c)	M3	0.13	70	69	1.9	nd ^e	0.37
6	P3(d)	M3	0.06	66	77	1.9	nd ^e	0.45
7	P4(a)	M4	0.5	89	26	2.8	210	0.28
8	P4(b)	M4	0.13	78	67	2.1	nd ^e	0.39
9	P5	M5	0.5	87	43	2.7	226	0.33
10	P6	M6	0.5	88	48	2.4	222	0.32
11	P7	M7	0.5	89	42	2.9	208	0.33

^aDetermined by ¹H NMR spectroscopy. ^bDetermined by SEC in THF using poly(ethylene oxide) standards. ^cDetermined by TGA at 5% weight loss under N₂. ^dIntrinsic viscosity measured at 21 °C in DMSO solutions (P1–P4) or in toluene solutions (P5–P7). ^end, not determined.

and cyclohexyl units in the side chain promoted the solubility of polymers P5–P7 in the even more poorly hydrogen-bonding toluene ($\delta = 18 \text{ MPa}^{1/2}$).

As mentioned above, the hydroxyl functional polymers P1 and P2 were insoluble in solvents convenient for SEC analysis. Hence, all polymers except these samples were analyzed by SEC. As anticipated, the SEC analysis of polymers P3(a–d) revealed an increase in M_n with decreasing concentration of AIBN. For *exo*-acetate polymethacrylates, the M_n varied from the lowest value of 35 kg mol⁻¹ with $\bar{D} = 2.6$ (P3(a)) to the highest M_n of 77 kg mol⁻¹ with $\bar{D} = 1.9$ noted for P3(d) (Table 1, entries 3–6; Figure S25). The *endo*-acetate-polymethacrylates P4(a,b) showed M_n results similar to those of polymer P4(a), synthesized with 0.5 mol % AIBN, and had $M_n = 26 \text{ kg mol}^{-1}$ with $\bar{D} = 2.8$. When the AIBN concentration was decreased to 0.13 mol %, the M_n for P4(b) was determined to be 67 kg mol⁻¹ with $\bar{D} = 2.1$ (Figure S26). Regarding the regioisomeric polymers bearing long dodecanoate side chains, the M_n values were very close, 43 and 48 kg mol⁻¹ for P5 and P6, respectively. Finally, the M_n of the cyclohexanoate tethered polymethacrylate P7 was quite similar, 42 kg mol⁻¹ with $\bar{D} = 2.9$ (Figure S27).

The thermal stability of the polymers is important for their processability in the melt state and subsequent applications. TGA was employed to measure the thermal stability of all of the polymethacrylates up to 600 °C under nitrogen at a heating rate of 10 °C min⁻¹. Figure 2 shows representative TGA curves and differential thermogravimetry (DTG) profiles of the samples. As seen, the polymethacrylates exhibited thermal decomposition temperatures ($T_{d,95}$, determined at 5% weight loss) at approximately 200 °C. The highest $T_{d,95}$ values were determined for the hydroxyl functional polymers P1 and P2, 238 and 240 °C, respectively. Unlike the other synthesized polymethacrylates in this study, P1 and P2 have no substituents in the isosorbide side chain, which may explain the high thermal stability of these polymers. In case of P1, two degradation steps at ~260 and ~280 °C were observed in the DTG curve. The second degradation step was more distinctive, and then most of the polymer decomposition took place. In comparison, polymer P2 had one wide peak in DTG curve and decomposed gradually. The thermal stability of the acetate polymethacrylates P3(a) ($T_{d,95} = 223 \text{ °C}$) and P4(a) ($T_{d,95} = 210 \text{ °C}$) was lower as compared to the hydroxyl counterparts P1 and P2. This is comparable to the data measured on the isosorbide polymethacrylate synthesized previously by Reineke et al. from a 4:1 mixture of corresponding *endo* and *exo*

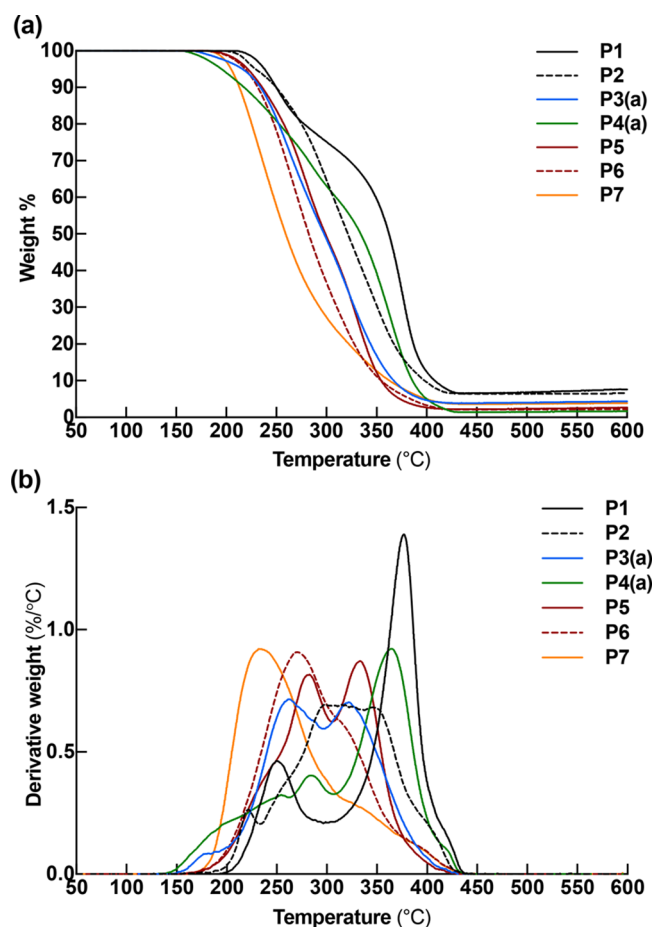


Figure 2. TGA (a) and DTG (b) profiles of polymers P1–P7.

acetates.¹¹ The DTG curve of P3(a) exhibited two distinguishable steps at ~270 and ~330 °C, where the first weight loss corresponded to the degradation of the acetate moiety and the second to the rest of the isosorbide side chain, followed by slow decomposition of the polymer main chain. In the case of P4(a), first a gradual decrease in weight occurred and then most of the polymer structure decomposed at ~370 °C. Now turning to the polymers with long alkyl chains, the $T_{d,95}$ values of polymers P5 and P6 were similar, 226 and 222 °C, respectively. Polymer P5 also showed two distinctive decomposition steps in DTG curve, one at ~290 and one at ~340 °C. The first step most likely corresponded to the loss of

the C12 chains and the second step to the isosorbide units in the polymer structure, followed by gradual decomposition of the polymer backbone. As for **P6**, one distinguishable peak at ~ 280 °C can be seen in DTG curve, where the weight loss of the whole side chain occurred. The lowest $T_{d,95}$ value at 208 °C was determined for polymethacrylate **P7**, with one significant and one less prominent peak in the DTG curve. At 230–240 °C, the side chain of **P7** decomposed, and afterward a slower degradation took place.

Many polymethacrylates are known to primarily degrade via monomer unzipping under pyrolysis conditions.^{33,34} For example, Czech et al. have investigated the thermal stability and degradation of PMMA, poly(butyl methacrylate), and poly(2-ethylhexyl methacrylate) by pyrolysis gas chromatography in the range 200–400 °C.³³ They found that the polymers mainly degraded via homolytic polymer chain cleavage, followed by monomer unzipping, and that the major degradation product was the respective monomer. In the present polymethacrylates, the monomer units were significantly stiffer and larger. Consequently, the side chain in most cases appeared to decompose before the polymer main chain, leading to a different degradation mechanism than for PMMA.

The thermal behavior of the isosorbide polymethacrylates was characterized by DSC measurements to study glass transitions and other thermal transitions. As seen in Figure 3, the acetate functional polymers **P3(a)** and **P4(a)** exhibited

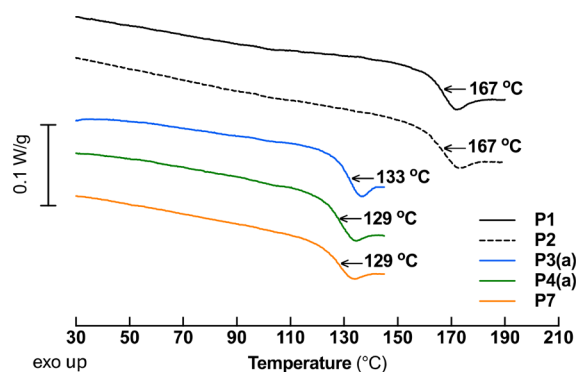


Figure 3. DSC heating traces of polymers **P1**, **P2**, **P3(a)**, **P4(a)**, and **P7**. T_g values are indicated at the respective transitions.

quite similar glass transitions at $T_g = 133$ and 129 °C, respectively. The T_g values measured for polymers synthesized with various initiator concentrations (**P3(a–d)** and **P4(a,b)**) showed no significant differences (Figures S22 and S23). Normally, T_g increases with M_n , but in the present case the differences in the M_n values were too small to have an impact. The T_g of these polymers may be compared to the T_g 's of common conventional thermoplastics such as polystyrene (100 °C), PMMA (105 °C), and poly(bisphenol A carbonate) (150 °C).³⁵ Here, the rigid, bicyclic nature of the isosorbide structure results in the comparatively high values measured. The T_g results of the present acetate functional polymethacrylates were in agreement with the values ($T_g = 130$ °C) for the isosorbide polymethacrylate previously reported by Reineke et al.¹¹ Polymer **P7**, with cyclohexanoate side chains, showed a T_g at 129 °C (Figure 3), very close to those of **P3(a)** and **P4(a)**. The highest T_g values in the series of isosorbide polymethacrylates were found for the two hydroxyl functional samples, **P1** and **P2**. Both samples reached $T_g = 167$ °C, despite their different stereostructure. This value may be

compared to that of poly(2-hydroxyethyl methacrylate) at $T_g = 77$ °C.³⁵ The high value recorded for the present polymers was most probably a consequence of the combination of the rigid bicyclic structure and the hydrogen-bonding nature of the repeating units.

As can be seen in Figure 4, dodecanoate polymethacrylate **P5** exhibited a clear melt transition at $T_m = 83$ °C and thereby

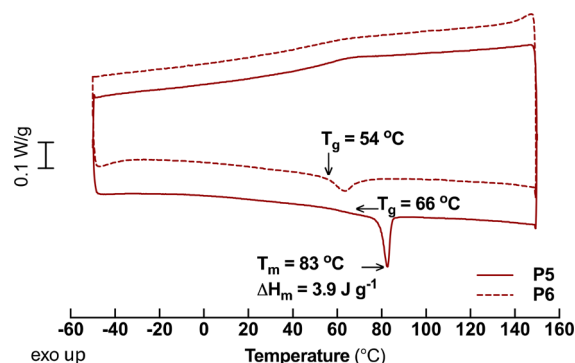


Figure 4. DSC heating and cooling curves of polymers **P5** and **P6**.

revealed crystallinity, although at a relatively low degree ($\Delta H_m = 3.9$ J g^{−1}). This T_m value is very high for a poly(alkyl methacrylate). In comparison, the reported T_m values for poly(dodecyl methacrylate) and poly(octadecyl methacrylate) are -33 and 36 °C, respectively.³⁶ Unexpectedly, the structurally related polymer **P6** did not exhibit any melt transition, but instead showed a comparatively low T_g at 54 °C. The T_g value of **P6** was presumably lower than that of polymers **P3(a)** and **P4(a)** because of the additional free volume induced by the flexible C12 chains. Furthermore, the value may be compared to those of poly(dodecyl methacrylate) and poly(benzyl methacrylate) at -55 and 55 °C, respectively.³⁵ As seen in Figure 4, the DSC cooling traces of both polymers showed a glass transition at ~ 50 °C, with no crystallizations occurring. This may indicate low crystallization rates from the melt. Polymer **P5** was subjected to several different thermal treatments, including 20–120 min isotherms at 70, 83, and 84 °C, respectively, to facilitate crystallization. However, none of the attempts was successful, and it seems like polymer **P5** crystallized only very slowly, if at all, from the melt. Substituents in the *exo* position in isosorbide are sterically less shielded by isosorbide's bicyclic structure as compared to substituents in the *endo* position.³⁷ We hypothesize that this intrinsic structural property might be the reason for the different physical characteristics of the two polymers. Somewhat surprisingly, a corresponding copolymer (molar ratio 1:1) of **M5** and **M6** exhibited a T_g at 65 °C and also a melting point at $T_m = 83$ °C in the DSC analysis (Figure S24). However, the degree of crystallinity was somewhat lower ($\Delta H_m = 2.7$ J g^{−1}) than that for **P5**. It is clear that the exact mechanism behind the difference in physical behavior between polymer **P5** and **P6** needs to be studied further. These observed characteristics emphasize the importance of using regioselectively prepared monomers for the polymerization studies.

The properties in solution were studied by intrinsic viscosity measurements, and the data are summarized in Table 1. Most notably, a clear difference between the two regioisomeric polymers **P1** and **P2** was observed: the viscosity of polymer **P1** was significantly higher as compared to polymer **P2** ($[\eta] =$

0.82 vs 0.46 dL g⁻¹). Assuming approximately the same M_n values for these two polymers, we speculated that the free *exo* OH in polymer **P1** might be involved in additional intermolecular hydrogen bonding between different polymer chains (normally *endo* OH affords stronger intramolecular H-bonding¹³). This speculation was supported by the ¹H NMR spectra of the corresponding polymers (Figure 5), which

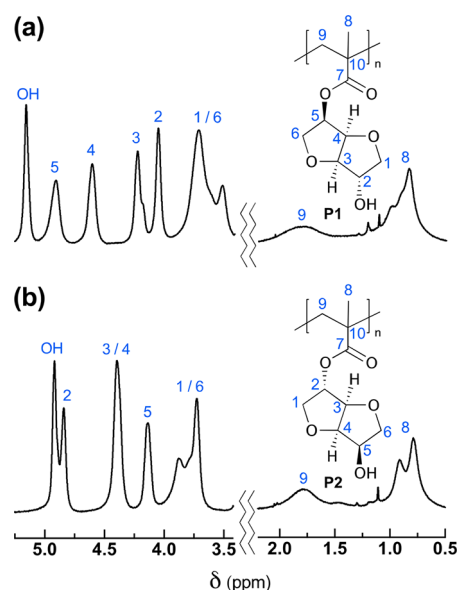


Figure 5. ¹H NMR traces of polymer **P1** and **P2** recorded in DMSO-*d*₆.

indicated that the *exo* OH in **P1** is more downfield and thereby more acidic as compared to *endo* OH in polymer **P2**. As expected, the intrinsic viscosity of polymers **P3(a–d)** showed an increasing trend with the M_n . The highest value (0.45 dL g⁻¹) was measured for **P3(d)**, which had a value similar to that of the hydroxyl functional polymer **P2**. Regarding **P4(a)** and **P4(b)**, the intrinsic viscosity of the two polymers was also in line with the increase of M_n values, exhibiting 0.28 and 0.39 dL g⁻¹, respectively. The intrinsic viscosity of **P5** and **P6** was measured in toluene, as these two polymers with long alkyl chains are not fully soluble in DMSO (see Table S1). These polymethacrylates exhibited similar values, 0.33 and 0.32 dL g⁻¹, respectively. In addition, polymer **P7** was also nonsoluble in DMSO, and the intrinsic viscosity measured in toluene (0.33 dL g⁻¹) was similar to those of polymer **P5** and **P6**.

CONCLUSION

A lipase-catalyzed highly regioselective synthesis of isosorbide 5-methacrylate was developed using either vinyl methacrylate or methacrylic anhydride as the acyl donor. A different approach was required for the synthesis of the isomeric 2-methacrylic isosorbide, including 5-acetylation of the isosorbide, addition of methacrylic anhydride, and finally enzymatic cleavage of the acetate group. Subsequently, a series of monomers with different substituents were prepared on the basis of the isosorbide 5- and 2-methacrylates. These monomers were polymerized via conventional free radical polymerization, which showed that the position of methacrylate group in either the *exo* or the *endo* configuration had no significant impact on the polymerization yield and M_n value. Yet, in some cases, it had a major effect on polymer properties.

Both regioisomeric monomers with free hydroxyl groups produced polymers with a high T_g close to 170 °C. Capping of the hydroxyl functions with acetate groups reduced the T_g to approximately 130 °C. The differences between the regioisomers were most pronounced in the case of polymers bearing long alkyl chains. Whereas the methacrylate polymer with C12 alkyl ester in the *exo* position was a semicrystalline polymer with a high T_m of 83 °C, the corresponding polymer with C12 alkyl chain in the *endo* position was fully amorphous with a T_g of 54 °C. These results demonstrated the possibility to optimize the properties of the isosorbide polymethacrylates for high-performance biobased plastics. In particular, the combination of the tunable and attractive properties of the isosorbide polymethacrylates, their origin from renewable sources, and the straightforward and readily up-scalable enzymatic monomer synthesis are very attractive features for the development and commercialization of “green plastics” to replace conventional fossil-based materials in various applications, including packaging and coatings. Additional studies to verify the relationship between the monomer structure and polymer properties, as well as specific application studies, are in progress.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acssuschemeng.8b05074.

Protocols of the synthesis of isosorbide-based monomers, NMR (Figures S1–S21), DSC (Figures S22–S24), SEC (Figures S25–S27), and solubility of polymers (Table S1) (PDF)

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Notes

The authors declare no competing financial interest.

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