

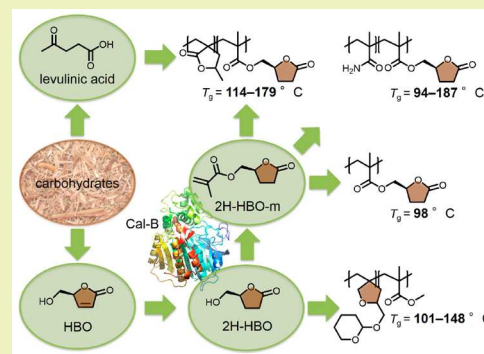
Chemo-Enzymatic Synthesis and Free Radical Polymerization of Renewable Acrylate Monomers from Cellulose-Based Lactones

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Supporting Information

ABSTRACT: A chemo-enzymatic pathway involving a *Candida antarctica* type B lipase was developed to produce (S)- γ -hydroxymethyl- α,β -butenolide methacrylate (HBO-m) and (S)- γ -hydroxymethyl- γ -butyrolactone methacrylate (2H-HBO-m) from (S)- γ -hydroxymethyl- γ -butyrolactone (HBO), a biobased molecule obtained from cellulose-derived levoglucosenone. The acrylated monomer was then copolymerized through a free radical process with methacrylamide and methylene- γ -valerolactone, a green intermediate. Finally, methylene-tetrahydropyranyl (S)- γ -hydroxymethyl- γ -butyrolactone (M-THP-2H-HBO), synthesized via α -methylenation of 2H-HBO, was copolymerized with methyl methacrylate to access copolyacrylates exhibiting high glass transition temperatures.

KEYWORDS: Levoglucosenone, HBO, Lipase biocatalysis, Functionalized (meth)acrylates, α -Methylenation, Biobased polymers, Polyacrylates



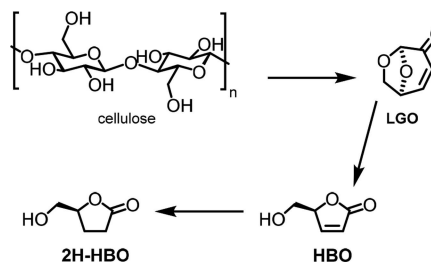
INTRODUCTION

Over the last several decades, the growing production of materials¹ and synthetic goods has raised severe concerns regarding pollution and the inevitable depletion of fossil-fuel resources. In that context, numerous investigations have been conducted in attempts to replace fossil-based products such as plastics.² Exploration and progress of white technologies and green chemistry applied to biomass have been a major achievement to supplant unsustainable molecules and materials. For instance, transformations of biomass into biobased platform chemicals by microorganisms and extractions of molecules of interest from biorenewable sources such as lignocellulose have substantially contributed to extend the database of renewable synthons.

Biobased 2,5-furandicarboxylic acid³ has shown great potential to replace the terephthalic acid of poly(ethylene terephthalate) (PET), while sugar fermentation product lactic acid has already demonstrated commercial success with the well-known polymer poly(lactic acid) (PLA). Besides its slow decomposition in the environment, the low- T_g value (55 °C)⁴ of PLA precludes its utilization at high temperature.⁵ Recently, Miller and co-workers proposed new polylactam esters⁶ made from ethanolamine and sugar-derived itaconic acid, one of the top 12 biorenewable molecules extolled by the DOE.⁷ It is worth noting that this polymer not only competes with PLA in terms of T_g but exhibits facile degradability back to monomers in neutral water over the course of one year.

Among the expanding library of renewable molecules of interest that can be produced from lignocellulosic biomass such as levulinic acid⁸ and 3-hydroxy propionic acid (3-HP),⁹ (S)- γ -hydroxymethyl- α,β -butenolide (HBO) has demonstrated its high potential (Scheme 1). HBO was recently produced

Scheme 1. Transformation of Cellulose into HBO Followed by Hydrogenation to 2H-HBO



through two sustainable routes by Allais and co-workers from levoglucosenone (LGO), an interesting building block obtained from the flash pyrolysis of lignocellulosic biomass such as sawdust.¹⁰ The first route involved a lipase-mediated Baeyer–Villiger oxidation of LGO¹¹ whereas the more recent route is a solvent-free and catalyst-free H₂O₂-mediated

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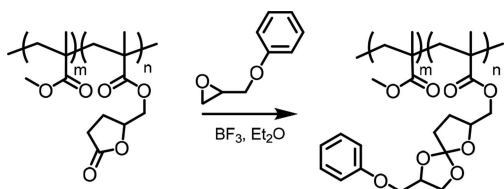
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Baeyer–Villiger oxidation.¹² The versatility of **HBO** has been employed to access not only valuable chiral building blocks such as chiral epoxides but also end products such as enantiopure (*S*)-dairy lactone¹³ employed as a butter-like flavoring agent in food sectors such as the snack, ice cream, and bakery industries.

Although **HBO** is a valuable molecule used in fine chemistry (e.g., drugs, fine chemicals, flavoring agents), sparingly little research has targeted the valorization of this biobased synthon for the preparation of chiral monomers and subsequent polymers. In 1994, Zamzow and Höcker¹⁴ reported the synthesis of polymers with a spiro orthoester pendant group. The polymerization of acrylate monomers bearing reactive lactones such as (*S*)- γ -hydroxymethyl- γ -butyrolactone methacrylate (**2H-HBO-m**) was followed by installation of the desired spiro orthoester (**Scheme 2**). The adopted monomer

Scheme 2. Installation of Spiro Orthoester via Postpolymerization Reaction



synthesis required methacryloyl chloride, an inexpensive reagent that nonetheless results in substantial amounts of acid waste. Moreover, a base such as triethylamine or pyridine is essential for trapping the formed HCl and makes this process even less atom-economical.

Recently, Saito and co-workers¹⁵ reported a new method to access **2H-HBO-m** and its polymerization using different processes such as emulsion polymerization and RAFT polymerization. Although RAFT CTA agents are expensive, they afforded narrow dispersity polymers ($D = 1.06$) with acceptable molecular weights of 9000 kDa. Copolymerizations of **2H-HBO-m** with petroleum-based comonomers, such as styrene and butyl methacrylate, were successfully achieved through emulsion polymerization. The reported synthetic pathway has the main advantage to substitute methacryloyl chloride with methacrylic anhydride and to replace dichloromethane with ethyl acetate, a markedly greener solvent.¹⁶ Notwithstanding these improvements, this method presents several drawbacks, including the utilization of nongreen organic bases: 4-(dimethylamino)pyridine (DMAP, 1% mol) and triethylamine (TEA, 1 equiv), known to be noxious and waste-generating. While TEA salts are mainly removed through filtration, the workup protocol with NaHCO_3 does allow product purification. However, the methacrylic acid byproduct and unreacted **2H-HBO** are mixed in the aqueous layer with salts. Additional steps must be performed to separate the aforementioned chemicals before reuse, greatly reducing the overall process efficiency. Consequently, a more environmentally friendly synthetic strategy that would substantially reduce the waste is still needed.

Herein, we report a more sustainable approach (i.e., no halogenated species, no base) using the chemo-enzymatic catalysis¹⁷ of *Candida antarctica* type B lipase (CAL-B, *a.k.a.* Novozyme 435) to access acrylates (*S*)- γ -(hydroxymethyl)- α,β -butenolide methacrylate (**HBO-m**) and its corresponding hydrogenated version **2H-HBO-m**, from **HBO** and **2H-HBO**,

respectively. The resulting monomers were then polymerized with comonomers in order to tune the thermal properties and the solubility of the resulting polymers. Moreover, a new type of monomer similar to methylene- γ -valerolactone (**MGVL**) was synthesized from **HBO** and polymerized.

EXPERIMENTAL SECTION

Chemicals and Reagents. Levoglucosenone was graciously provided by Circa Group. Lipase from *C. antarctica* immobilized on acrylic resin ≥ 5000 U/g (CAL-B) was purchased from Sigma-Aldrich. Hydrogen peroxide 30% (Fischer), propionic acid $\geq 99.5\%$ (Sigma-Aldrich), butanoic acid $\geq 99\%$ (Sigma-Aldrich), 2-butenic acid 98% (Sigma-Aldrich), *trans*-2-pentenoic acid 98% (Sigma-Aldrich), 4-pentenoic acid 97% (Sigma-Aldrich), AIBN 98% (Sigma-Aldrich), V-65 98% (Sigma-Aldrich), V-70 98% (Sigma-Aldrich), methyl methacrylate stabilized 98% (Fischer), methacryloyl chloride 97% (Sigma-Aldrich), methacrylic anhydride 94% (Sigma-Aldrich), methacrylamide 98% (Alfa Aesar), triethylamine $\geq 99\%$ (Sigma-Aldrich), γ -valerolactone 99% (Sigma-Aldrich), ethyl formate 97% (Sigma-Aldrich), sodium hydride 60% dispersion in mineral oil (Sigma-Aldrich), paraformaldehyde 95% (Sigma-Aldrich), 3,4-dihydro-2H-pyran 97% (Sigma-Aldrich), 10% by weight palladium on activated carbon (Acros), potassium carbonate (Fischer), sodium hydroxide (Fischer), *p*-toluenesulfonic acid monohydrate 98% (Sigma-Aldrich) were all used without further purification. NMR solvents including deuterated chloroform, deuterated methanol, and deuterated dimethyl sulfoxide were purchased from Cambridge Isotopes Laboratories. All the chemicals, unless noted otherwise, were used as received. The pyridinium *p*-toluenesulfonate was prepared from *p*-toluenesulfonic acid (1 equiv) in pyridine (5 equiv) and recrystallized from acetone.

Characterization. **Nuclear Magnetic Resonance (NMR) Spectroscopy.** Proton nuclear magnetic resonance (^1H NMR) and carbon nuclear magnetic resonance (^{13}C NMR) were recorded by employing an Inova 500 MHz or a Varian Mercury 300 MHz spectrometer. Chemical shifts are reported in parts per million (ppm) downfield relative to tetramethylsilane (TMS, 0.0 ppm). Coupling constants (*J*) are reported in Hertz (Hz). Multiplicities are reported using the following abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad. The ^1H and ^{13}C NMR samples were prepared by solubilizing ca. 30 mg of product in 0.5 mL of solvent. The NMR analyses were performed using 16 scans with a relaxation delay of 5 and 64 scans with a relaxation delay of 10 s for ^1H and ^{13}C , respectively.

Mass Spectroscopy. HRMS was recorded by the Mass Spectroscopy Research and Education Center (Department of Chemistry, University of Florida) on an Agilent 6220 Time-of-Flight (TOF) MS.

IR Spectroscopy. Solid-state IR is recorded using a PerkinElmer Spectrum One FT-IR spectrophotometer. A total of 32 scans were used for each experiment.

Thermogravimetric Analysis (TGA) was measured under nitrogen with a TGA Q5000 from TA Instruments. About 1–5 mg of each sample was cooled to 0 °C and held at that temperature for 5 min. Then, the samples were heated at 20 °C/min from 0 to 600 °C. The reported value ($T_{d5\%}$) represents the temperature at which 5% of the mass is lost.

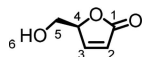
Differential Scanning Calorimetry (DSC) thermograms were obtained with a DSC Q1000 from TA Instruments. Typically, 3–7 mg of sample was weighed and added to a sealed pan that passed through a heat-cool-heat cycle at 10 °C/min. The temperature ranged from 40 °C to the $T_{d5\%}$ of the polymers.

Gel Permeation Chromatography (GPC) was performed at 40 °C using an Agilent Technologies 1260 Infinity Series liquid chromatography system with an internal differential refractive index detector and two Waters Styragel HR-5E columns (7.8 mm i.d., 300 mm length, guard column 7.8 mm i.d., 25 mm length) using a solution of 0.1% potassium triflate ($\text{K}(\text{OTf})$) in HPLC grade hexafluoro-2-propanol (HFIP) as the mobile phase at a flow rate of 0.3 mL/min. Calibration was performed with narrow dispersity poly(methyl methacrylate)

standards. The samples were prepared by solubilizing 5 mg of material in 1.5 mL of HfIP.

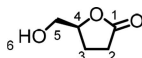
Synthesis of Monomers. *Synthesis of (S)-5-(Hydroxymethyl)furan-2(5H)-one (HBO).* Levoglucosenone (LGO, 1 equiv) was dissolved in ethyl acetate ($C = 1$ M). A catalytic amount of CAL-B (10 wt %) was added to the reaction mixture, and then aqueous hydrogen peroxide (1.2 equiv, 30% w/w) was added dropwise. The mixture was heated at 40 °C overnight. CAL-B was removed by filtration and the filtrate was concentrated to dryness. The resulting crude mixture was taken up in methanol ($C = 0.1$ M relative to LGO). Concentrated hydrochloric acid (12 equiv. relative to LGO) was added at RT and the reaction mixture was stirred at 45 °C until complete consumption of starting material, as monitored by TLC. The crude mixture was evaporated to dryness and was purified by silica gel chromatography (elution with 50% to 100% ethyl acetate in cyclohexane) to yield to pure HBO (75% yield).

A 30% aqueous H_2O_2 solution (9.78 M, 0.81 L, 7.92 mol, 1 eq./LGO) was added dropwise over 3.5 h under nitrogen to LGO (1 kg, 7.93 mol) cooled with an ice bath. After completion of the addition, the reaction was warmed to 50 °C and stirred for an extra 20 h. The presence of H_2O_2 was evaluated with peroxide strips, and if any, the residual H_2O_2 was quenched using the methods described in the manuscript. The reaction mixture was then concentrated in vacuo and the residue was distilled of (150 °C/0.7–0.9 mbar) to provide HBO as a clear oil that readily crystallizes.



1H NMR ($CDCl_3$, 300 MHz): δ_H 1.93 (br s, 1H, H_6), 3.89 (ddd, 2H, $J = 3.7, 5.0$, and 12.2 Hz, H_5), 5.14 (m, 1H, H_4), 6.20 (dd, 1H, $J = 2.0$ and 5.7 Hz, H_2), 7.46 (dd, 1H, $J = 1.6$ and 5.7 Hz, H_3). ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 62.1 (C_5), 84.4 (C_4), 122.8 (C_2), 154.1 (C_3), 173.7 (C_1).

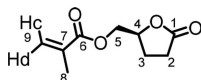
Synthesis of (S)-5-(Hydroxymethyl)dihydrofuran-2(3H)-one (2H-HBO). To a solution of 7.293 g (63.9 mmol) of HBO in 90 mL of ethyl acetate was added 1.496 g of Pd/C (10% w/w). The system was degassed three times and was kept under dihydrogen (20 psi). The suspension was stirred overnight. The Pd/C was then removed by filtration through Celite and the filtrate was concentrated to dryness. The crude product was used without further purification.



1H NMR ($CDCl_3$, 300 MHz): δ_H 1.95 (m, 2H, H_3), 2.32 (m, 2H, H_2), 3.49 (dd, 2H, $J = 3.0$ and 15.0 Hz, H_5), 4.01 (br s, 1H, H_6), 4.40 (m, 1H, H_4). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 23.0 (C_3), 28.5 (C_2), 63.6 (C_5), 81.1 (C_4), 178.5 (C_1).

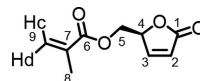
Study of Chemo-Enzymatic Reaction. In a typical experiment, 3 equiv of propionic acid was added to a solution of 500 mg (4.4 mmol, 1 equiv) of HBO in 4.4 mL of toluene ($C = 1$ M). The mixture was heated to 70 °C and was stirred for 24 h. Then, the CAL-B was filtered out, and the filtrate was concentrated. The conversion was then evaluated by 1H NMR of the crude reaction material.

Synthesis of (S)-5-(methyl)dihydrofuran-2(3H)-one methacrylate (2H-HBO-m). In a typical experiment, a catalytic amount of CAL-B (10 wt % relative to the 2H-HBO) was added to a solution of 1.0 g (8.6 mmol, 1 equiv) of 2H-HBO in 23 mL (215.9 mmol, 25 equiv) of methyl methacrylate. The system was heated to 70 °C and stirred for 24 h. Then, the supported enzyme was filtered out and the filtrate was concentrated to dryness. The crude product was taken up in 20 mL of dichloromethane and was washed thrice with 20 mL of deionized water. The organic layer was dried over anhydrous $MgSO_4$ and concentrated to dryness. Quick filtration over silica gel was then performed and the pure product was obtained (62% yield).



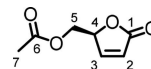
1H NMR ($CDCl_3$, 300 MHz): δ_H 1.89 (s, 3H, H_8), 2.26 (m, 2H, H_3), 2.60 (m, 2H, H_2), 4.34 (dd, 2H, $J = 3.0$ and 12.0 Hz, H_5), 4.82 (m, 1H, H_4), 5.65 (m, 1H, H_{9c}), 6.16 (m, 1H, H_{9d}). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 18.1 (C_8), 24.7 (C_3), 28.0 (C_2), 65.5 (C_5), 77.3 (C_4), 126.3 (C_7), 135.5 (C_9), 166.9 (C_6), 176.7 (C_1).

Synthesis of (S)-5-(Methyl)furan-2(3H)-one Methacrylate (HBO-m). The same procedure as for 2H-HBO-m was used.



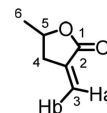
1H NMR ($CDCl_3$, 500 MHz): δ_H 1.86 (s, 3H, H_8), 4.40 (dd, 2H, $J = 5.0$ and 15 Hz, H_5), 5.27 (m, 1H, H_4), 5.56 (m, 1H, H_{9c}), 6.04 (m, 1H, H_{9d}), 6.16 (d, 1H, $J = 5.8$ Hz, H_2), 7.47 (d, 1H, $J = 5.8$ Hz, H_3). ^{13}C NMR ($CDCl_3$, 125 MHz): δ_C 18.1 (C_8), 62.6 (C_5), 80.9 (C_4), 123.0 (C_2), 126.7 (C_7), 135.3 (C_9), 152.8 (C_3), 166.6 (C_6), 172.3 (C_1). After purification by flash chromatography, the following spectra were obtained. 1H NMR ($CDCl_3$, 300 MHz): δ_H 1.84 (s, 3H, H_8), 4.38 (dd, 2H, $J = 3.0$ and 12.0 Hz, H_5), 5.24 (m, 1H, H_4), 5.54 (m, 1H, H_{9c}), 6.03 (m, 1H, H_{9d}), 6.14 (dd, 1H, $J = 2.1$ and 5.8 Hz, H_2), 7.44 (dd, 1H, $J = 1.6$ and 5.8 Hz, H_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 18.1 (C_8), 62.6 (C_5), 80.9 (C_4), 123.1 (C_2), 126.8 (C_7), 135.3 (C_9), 152.8 (C_3), 166.6 (C_6), 172.3 (C_1).

Synthesis of (S)-5-(Hydroxymethyl)furan-2(5H)-one Acetate. To a solution of 2.985 g (26.1 mmol, 1 equiv) of HBO in 130 mL of AcOEt was added 10 wt % of CAL-B (relative to HBO). The system was heated at 70 °C for 1 day. Then, the CAL-B was filtered out and the filtrate was concentrated to dryness. The crude product was taken up in 20 mL of dichloromethane and washed twice with distilled water and once with brine. The organic layer was dried over anhydrous $MgSO_4$ and concentrated to dryness. The crude product was purified via silica gel column chromatography (elution 80% of hexane to 60% of hexane in ethyl acetate) to give 3.14 g of a colorless oil (77% yield).



1H NMR ($CDCl_3$, 300 MHz): δ_H 2.02 (s, 3H, H_7), 4.31 (dd, 2H, $J = 3.0$ and 6.0 Hz, H_5), 5.22 (m, 1H, H_4), 6.18 (d, 1H, $J = 3.0$ Hz, H_2), 7.45 (d, 1H, $J = 3.0$ Hz, H_3). ^{13}C NMR ($CDCl_3$, 75 MHz): δ_C 20.5 (C_7), 62.5 (C_5), 80.8 (C_4), 123.2 (C_2), 152.6 (C_3), 170.5 (C_6), 172.3 (C_1).

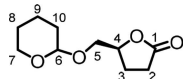
Synthesis of Methylene-γ-valerolactone. To a stirred solution of NaH (60% dispersion in mineral oil, 1 equiv) in dry diethyl ether was added 600 μ L of ethanol under N_2 . Then, a mixture of 10 g (100 mmol, 1 equiv) of γ -valerolactone and 8 mL (100 mmol, 1 equiv) of ethyl formate was added dropwise at 0 °C. The system was allowed to return to room temperature and was stirred for 1 h. Then, the precipitate was filtered out to afford the salt in quantitative yield. The salt was added to 40 mL of dry THF with 4.5 equiv of paraformaldehyde. The system was heated to reflux over 3 h in order to crack the paraformaldehyde into formaldehyde. After 3 h, the mixture was concentrated to dryness and the crude product was taken up in 60 mL of diethyl ether and washed twice with a saturated solution of potassium carbonate. The organic layers were combined, dried over anhydrous $MgSO_4$, and concentrated. The crude product was purified over silica gel column chromatography (elution with 100% hexane to 50% hexane in ethyl acetate) to give a pure product in 47% yield. It is worth noting that the pure product starts to polymerize during evaporation of the solvent.



1H NMR ($CDCl_3$, 300 MHz): δ_H 1.41 (d, 3H, $J = 6.0$ Hz, H_6), 2.83 (m, 2H, H_4), 4.64 (m, 1H, H_5), 5.62 (t, 1H, $J = 3.0$ Hz, H_{3a}), 6.21 (t,

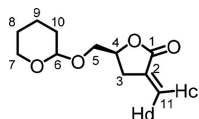
^1H NMR (CDCl_3 , 75 MHz): δ_{C} 21.8 (C_6), 35.0 (C_4), 73.9 (C_5), 121.7 (C_2), 135.0 (C_3), 170.2 (C_1).

Synthesis of (4R)-Dihydro-5-(tetrahydropyranyl)-(hydroxymethyl)-2(3H)-furanone (THP-2H-HBO). To a solution of 4.04 g (34.8 mmol, 1 equiv) of 2H-HBO in 40 mL of dichloromethane were added 911 mg of pyridinium *p*-toluenesulfonate and 5.9 mL (64.7 mmol, 1.9 equiv) of 3,4-dihydro-2H-pyran at 0 °C. After addition, the system was allowed to stir at room temperature overnight. The resulting mixture was purified via silica gel column chromatography (elution 90% of hexane to 50% of hexane in ethyl acetate) to lead to a pure product in quantitative yield.



^1H NMR (CDCl_3 , 300 MHz): δ_{H} 1.53 (m, 4H, $\text{H}_{8,9}$), 1.67 (m, 2H, H_{10}), 2.18 (m, 2H, H_3), 2.54 (m, 2H, H_2), 3.70 (m, 4H, $\text{H}_{5,7}$), 4.63 (m, 2H, $\text{H}_{4,6}$). ^{13}C NMR (CDCl_3 , 75 MHz): δ_{C} 18.9, 19.3 (C_9), 24.1 (C_2), 25.3 (C_8), 28.5 (C_3), 30.3 (C_{10}), 61.7, 62.3 (C_7), 68.8, 69.0 (C_5), 78.7, 79.0 (C_4), 98.5, 99.2 (C_6), 177.3, 177.5 (C_1). Diastereoisomerism gives two peaks for some carbon atoms.

Synthesis of (4R)-Dihydro-5-(tetrahydropyranyl)-(hydroxymethyl)-3-methylene-2(3H)-furanone (M-THP-2H-HBO). To a suspension of NaH (60% dispersion in mineral oil, 1 equiv) in 45 mL of dry diethyl ether was added 180 μL of ethanol under N_2 . Then, a mixture of 6.004 g (30 mmol, 1 equiv) of THP-2H-HBO and of 2.4 mL (30 mmol, 1 equiv) of ethyl formate was added dropwise at 0 °C. The mixture was then stirred at room temperature for 30 min. The precipitate was filtered out leading to the salt in a yield of 83%. A 3.045 g amount of the salt was suspended in 20 mL of dry THF with 5 equiv of paraformaldehyde. The mixture was refluxed for 2 h and then was filtered to eliminate unreacted paraformaldehyde. The solution was washed twice with a saturated solution of sodium carbonate. The organic layer was dried over anhydrous MgSO_4 and concentrated to dryness. The crude product was purified over silica gel column chromatography (elution 90% hexane to 50% hexane in ethyl acetate) to give the pure liquid in 62% yield. It is worth noting that the pure product starts to self-polymerize during the concentration.

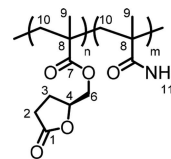


^1H NMR (CDCl_3 , 300 MHz): δ_{H} 1.50 (m, 4H, $\text{H}_{8,9}$), 1.70 (m, 2H, H_{10}), 2.89 (m, 2H, H_3), 3.69 (m, 4H, $\text{H}_{5,7}$), 4.60 (t, 0.51H, $J = 1.9$ Hz, H_6) and its diastereomeric peak at 4.65 (t, 0.56H, $J = 1.9$ Hz, H_6), 4.70 (m, 1H, H_4), 5.62 (m, 1H, H_{11}), 6.20 (m, 1H, $\text{H}_{11\text{d}}$). ^{13}C NMR (CDCl_3 , 75 MHz): δ_{C} 18.9, 19.2 (C_9), 25.3 (C_8), 29.7 (C_3), 30.3 (C_{10}), 61.8, 62.3 (C_7), 68.5, 68.6 (C_5), 75.5, 75.7 (C_4), 98.6, 99.2 (C_6), 121.5, 121.7 (C_2), 134.3, 134.5 (C_{11}), 170.1, 170.3 (C_1). Diastereoisomerism gives two peaks for some carbon atoms. HRMS (TOF MS, ESI): m/z calcd for $\text{C}_{11}\text{H}_{16}\text{O}_4\text{Na}$: 235.0946; found: 235.0940.

Polymerizations. Homopolymerization of (S)-5-(Methyl)dihydrofuran-2(3H)-one Methacrylate poly(2H-HBO-m). In a typical experiment, 500 mg of monomer was solubilized in toluene ($C = 1$ M); then 1 mol % of AIBN was added. The system was purged three times (vacuum–nitrogen cycles) on a Schlenk line. The solution was stirred under N_2 for 30 min and was then heated to 75 °C with a preheated oil bath. The polymerization was stopped after 90 min by exposure to air. The polymer was then precipitated by the addition of hexane.

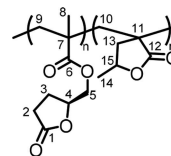
Copolymerization of (S)-5-(Methyl)dihydrofuran-2(3H)-one Methacrylate with Methacrylamide (poly(2H-HBO-m-co-MAA)). In a typical experiment, 250 mg of 2H-HBO-m and 116 mg of MAA (50% MAA feed fraction) were dissolved 2.5 mL of DMF; then 1 mol % (relative to the total molar quantity) of AIBN was added. The system was purged three times (vacuum–nitrogen cycles) on a

Schlenk line. The solution was stirred under N_2 for 30 min and was then heated to 75 °C with a preheated oil bath. The polymerization was stopped after 90 min by exposure to air. The polymer was then precipitated by the addition of methanol, resolubilized in hot DMSO, and purified again by precipitation via MeOH addition.



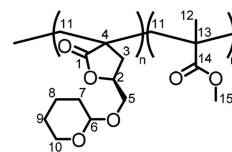
^1H NMR (DMSO, 500 MHz): δ_{H} 0.87 (m, 4.16H, H_9), 1.78 (m, 3.13H, H_{10}), 2.43 (m, 3.84H, $\text{H}_{2,3}$), 4.07 (m, 1.80H, H_6), 4.76 (m, 1.01H, H_4), 7.04 (m, 0.76H, H_{11}).

Copolymerization of (S)-5-(Methyl)dihydrofuran-2(3H)-one Methacrylate with Methylene- γ -valerolactone (poly(2H-HBO-m-co-MGVL)). In a typical experiment, 250 mg of 2H-HBO-m and 112 mg of MGVL (50% MGVL feed fraction) were dissolved in 2.7 mL of toluene; then 1 mol % (relative to the total molar quantity) of AIBN was added. The system was purged three times (vacuum–nitrogen cycles) on a Schlenk line. The solution was stirred under N_2 for 30 min and was then heated to 75 °C with a preheated oil bath. The polymerization was stopped after 90 min by exposure to air. The polymer was then precipitated by the addition of MeOH, resolubilized in hot CHCl_3 and purified again by precipitation via MeOH addition.



^1H NMR (CDCl_3 , 500 MHz): δ_{H} 1.03 (br, 2.59H, H_8), 1.45 (br, 4.6H, $\text{H}_{14,8}$), 1.70 (br, 2.41H, H_{13}), 2.09 (br, 5.44H, $\text{H}_{3,9,10}$), 2.43 (br, 1.48H, H_3), 2.63 (br, 2.00H, H_2), 4.19 (br, 2H, H_5), 4.64 (br, 1H, H_{15}), 4.83 (br, 1H, H_4).

Copolymerization of M-THP-2H-HBO with Methyl Methacrylate (MMA) (poly(M-THP-2H-HBO-co-MMA)). In a typical experiment, 253 mg of M-THP-2H-HBO and 473 mg of MMA (80% MMA feed fraction) were dissolved in 6 mL of toluene; then 1 mol % (relative to the total molar quantity) of AIBN was added. The system was purged three times (vacuum–nitrogen cycles) on a Schlenk line. The solution was stirred under N_2 for 30 min and was then heated to 75 °C with a preheated oil bath. The polymerization was stopped after 90 min by exposure to air. The polymer was then precipitated by addition of hexane, resolubilized in hot CHCl_3 and purified again by precipitation via hexane addition.



^1H NMR (CDCl_3 , 500 MHz): δ_{H} 1.54 (br, 12.45H, $\text{H}_{7,8,9,11,12}$), 2.26 (br, 1.66H, H_3), 3.52 (br, 1.61H, $\text{H}_{5,10}$), 3.65 (br, 2.65H, H_{15}), 3.82 (br, 1.78H, $\text{H}_{5,10}$), 4.03 (br, 0.26H, H_5), 4.68 (br, 2H, $\text{H}_{2,6}$).

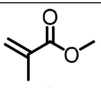
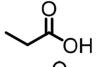
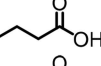
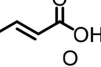
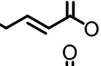
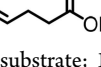
RESULTS AND DISCUSSION

Lipases are biocatalysts known to perform hydrolysis of fatty acid esters in aqueous media but esterification or transesterification can be achieved by changing the nature of the solvent. Indeed, utilization of an organic solvent such as toluene rather than water has successfully allowed transesterifications in the presence of an excess (3 equiv) of exogenous ester or alcohol.¹⁸ It is noteworthy to mention that

supported enzyme (attached to acrylic resin, for example) can be used over a wider temperature range.¹⁹ In addition, supported CAL-B is easily filtered out and potentially reused. Consequently, transesterification of methyl methacrylate (MMA) with HBO in the presence of 10 wt % CAL-B was performed in toluene at 70 °C. Unfortunately, no conversion was observed after 24 h of reaction. Having already and successfully employed HBO in chemo-enzymatic acylations, we identified MMA as a potential inhibitor of the reaction. Indeed, either the shape of MMA or its inherent conjugation (making the carbonyl less electrophilic) could prohibit its coordination into the active site of the biocatalyst and could explain the failure of CAL-B to conduct the reaction.

In an attempt to challenge our assumptions, several experiments employing either acids or unsaturated acids have been performed and the results are reported in Table 1. Entry

Table 1. Esterification of HBO with Different Acyl Substrates in the Presence of CAL-B^a

Entry	Substrate	Conv. (%)
1		None
2		Traces
3		37
4		None
5		None
6		89

^aConditions: 3 equiv of substrate; 10 wt % of CAL-B; HBO 1 M in toluene; 70 °C, 1 day.

2 shows that the chemo-enzymatic transesterification between HBO and propionic acid only results in traces of product. One additional carbon in the backbone of the substrate (Table 1, entry 3) allows the transesterification with modest conversion (37%). When butanoic acid was replaced with 2-butenic acid (Table 1, entry 4), its unsaturated and conjugated analogue, the conversion dropped to zero. Plausibly, the resonance/conjugation drastically lowers the electrophilic character of the carbonyl, hindering any nucleophilic attack. Finally, an attempt with a nonconjugated, unsaturated substrate (Table 1, entry 6) gave an excellent conversion of 89%, suggesting the conclusion that both the conjugation and the shape of MMA prevent the chemo-enzymatic reaction under these specific conditions.

In 1996, Rüschen, Klaas and co-workers²⁰ reported the biocatalyzed transesterification of unsaturated fatty alcohols with methyl methacrylate in the presence of lipase. The reaction did occur in organic solvents such as toluene and tetrahydrofuran (THF), but the yield did not exceed 40%. Although a rather high loading of CAL-B was employed (at least 30 wt %, triple the usual loading), the reaction proceeded at a moderate temperature of 30 °C. In their study, when methyl methacrylate was used as both reagent and solvent (90 equiv), the corresponding yield reached at least 74% depending on the alcohol. Under these considerations, we decided to adopt a similar strategy with the exceptions that the temperature was increased and the amount of lipase was

lowered to 10 wt % to reduce the cost of the process (Scheme 3).

Scheme 3. Synthesis of HBO-m through Chemo-Enzymatic Transesterification

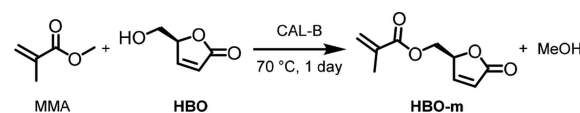


Table 2, entry 1 shows that at 50 °C the chemo-enzymatic esterification of MMA with HBO does occur with a moderate

Table 2. Esterification of HBO in MMA in the Presence of CAL-B^a

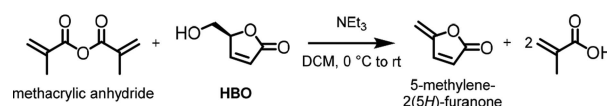
entry	MMA (eq)	T (°C)	conv (%) ^b	yield ^c (%)
1	25	50	46	38
2	25	70	70	64
3	25	80	24	22
4	100	70	77	64

^aConditions: 10 w % CAL-B, 1 day. ^bEstimated by ¹H NMR in CDCl₃. ^cYield obtained after purification.

conversion of 46%. With a boiling point of 101 °C, excess MMA was easily removed during the concentration whereas HBO was separated from the product by washing the organic layer with deionized water. The resulting unreacted starting materials can be reengaged in a reaction after isolation. Finally, the crude material was subjected to quick filtration over silica gel.

Because of the high stability of Novozyme 435, higher temperatures were investigated and the optimal conditions were obtained at 70 °C. It is worth noting that at 80 °C (Table 2, entry 3), a substantial drop of the conversion corresponding to a lower activity of the enzyme was observed, probably because of CAL-B unfolding or degradation. A larger amount of MMA (100 equiv, Table 2, entry 4) was investigated but similar yields were obtained versus 25 equiv of MMA. The hydrogenated version of HBO, 2H-HBO, was then submitted to the same conditions and gave a good yield (62%). It is noteworthy to mention that CAL-B can be reused a second time without significant loss of activity. Subsequent polymerizations were attempted either without further purification or after silica gel chromatography, and no notable differences were observed. Methacrylation of HBO was also attempted with methacrylic anhydride in the presence of a base. However, degradation of the desired product into 5-methylene-2(5H)-furanone (Scheme 4) was observed at room temperature. Indeed, 5 min after addition of the methacrylation reagent, the targeted molecule was observed but an hour later only traces of HBO-m remained. The reaction was also maintained at 0 °C and stopped 10 min after addition. The product was isolated after purification using silica gel chromatography with a lower yield than the chemo-enzymatic method.

Scheme 4. Methacrylation of HBO Resulting in the Formation of 5-Methylene-2(5H)-furanone



With the monomers in hand, free radical homopolymerization of **2H-HBO-m** was studied in the presence of azo initiators (i.e., AIBN, V-65, and V-70). V-65 allowed a conversion of 43% into poly(**2H-HBO-m**) whereas quantitative conversion was reached with AIBN (Table 3). During the

Table 3. Homopolymerization of 2H-HBO-m and Polymer Thermal Data^a

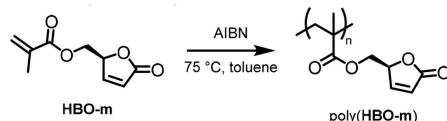
entry	initiator	T (°C)	yield (%)	T _g ^b (°C)
1	AIBN	75	quantitative	98
2	V-65	55	43	93
3	V-70	35	37	102

^aConditions: 1 M monomer in toluene; 1 mol % initiator; 90 min.

^bDetermined by DSC under N₂.

polymerization, the polymers precipitated from the toluene solution. Moreover, they were not soluble in gel permeation chromatography (GPC) solvents THF or hexafluoro-2-propanol (HFIP), which precluded both molecular weight and dispersity analysis. Glass transitions of the homopolymers were measured by differential scanning calorimetry (DSC) and ranged from 93 to 102 °C (Table 3). Homopolymerization of **HBO-m** (Scheme 5) was also attempted with the same

Scheme 5. Homopolymerization of HBO-m

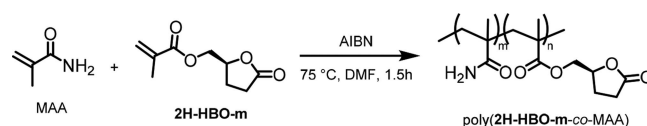


conditions described above; no polymer precipitated from toluene during the process but the solution turned yellow. Addition of hexane to the resulting solution did not provide any solid after 1.5 h, but an insoluble and yellow layer formed at the bottom of the beaker.

The separated material was assumed to be oligomers since **HBO-m** is fully soluble in conventional organic solvents such as hexane. However, subsequent ¹H NMR analysis mainly showed monomer peaks. Homopolymerizations with longer reaction times (3, 6, 12, and 24 h) were attempted, but no significant changes were observed. In order to evaluate the reactivity of the unsaturated lactone, **HBO acetate** was synthesized from ethyl acetate (25 equiv) and **HBO** (1 equiv) in the presence of CAL-B (10 wt %) and was then subjected to free radical polymerization conditions. After 1.5 h, the resulting yellow solution was combined with hexane; no material precipitated, but the solution became somewhat cloudy. Finally, copolymerization of **HBO acetate** and **2H-HBO-m** was attempted but did not provide any polymer.

Consequently, the α,β -unsaturated lactone was suspected to hinder the acrylate polymerization. It is noteworthy to mention that, after a few weeks, the stock of **HBO-m** solidified to a yellow and insoluble material that did not exhibit any T_g during DSC analysis (see Figure S133 in the Supporting Information). Copolymerization with hydrogen-bonding monomers can increase T_g values and/or improve solubility. Thus, the copolymerization of **2H-HBO-m** with methacrylamide (MAA) was pursued. Because of its insolubility in toluene, dimethylformamide (DMF) was employed as the polymerization solvent. Table 4 describes the copolymerization of **2H-HBO-m** and MAA with different feed fractions.

Table 4. Incorporation, Molecular Weight, and Thermal Data for Poly(2H-HBO-m-co-methacrylamide)



entry	feed fraction 2H-HBO-m/ MAA	incorporation ^a 2H-HBO-m/ MAA	M _n (kDa) ^b	Đ ^b	T _g ^c (°C)	T _{d5%} ^d (°C)
1	90/10	100/trace	23.5	2.2	94	228
2	80/20	98/2	20.7	2.3	115	217
3	70/30	78/22	28.7	2.1	128	198
4	60/40	76/24	19.2	2.0	143	261
5	50/50	70/30	21.1	2.3	144	189
6	40/60	74/26	17.9	1.7	141	237
7	30/70	54/46	19.4	1.7	152	237
8	20/80	28/72	18.1	1.8	172	241
9	10/90	11/89	12.1	2.2	187	124

^aIncorporation was measured by ¹H NMR in CDCl₃ (Figure S139 in the Supporting Information). ^bGPC in hexafluoro-2-propanol (HFIP) at 40 °C vs poly(methyl methacrylate) standards. ^cDetermined by DSC under N₂. ^dTGA temperature at which 5% mass loss was observed under nitrogen.

As previously discussed, poly(**2H-HBO-m**) tends to precipitate during its homopolymerization, and this trend was also observed for the copolymerization with MAA. We assumed that **2H-HBO-m** is more reactive than MAA,²¹ hence, the faster incorporation of **2H-HBO-m** causes the polymer to precipitate when high molecular weights are achieved. It is worth noting that for a high MMA loading (entries 8 and 9), the feed fraction and the incorporation fraction are similar. Plausibly, the smaller amount of **2H-HBO-m** in the polymer chain compared to MAA is not high enough to effect precipitation of the material before substantial incorporation of MAA. However, entry 1 in Table 4 demonstrates that even traces of incorporated MAA are sufficient to make the polymer soluble in HFIP, probably because of amide hydrogen bonding with this solvent. High molecular weights between 12 and 29 kDa (entries 9 and 3) were reached with typical dispersities ranging between 1.7 and 2.3 (entries 6 and 2). Polymers were then submitted to DSC analysis. Table 4 summarizes glass transition temperatures and reveals a correlation between T_g and the MAA incorporation, as measured by ¹H NMR (Figure 1). For example, the small feed fraction of 10% MAA allowed only traces of incorporated MAA and the corresponding T_g of 94 °C aligns with that of poly(**2H-HBO-m**) itself (93–102 °C). Entries 4 and 6 show intermediate MAA incorporations of 24 and 26% with similar T_g values of 143 and 141. The highest incorporations of MAA (72 or 89%) resulted in the highest T_g values (172 and 187 °C).

Methylene- γ -valerolactone (MGVL) was then considered as a comonomer because it is biobased and conformationally rigid, a property that predictably imparts high-T_g values. Its precursor, γ -valerolactone (GVL), is easily produced from biobased levulinic acid (LA) through carbonyl reduction followed by ring closing.^{22,23}

Then, α -methylenation can be performed in two steps, yielding MGVL. Scheme 6 describes one strategy used to synthesize MGVL from GVL.²⁴ The synthesis starts with α -deprotonation of the lactone; the resulting enolate then attacks

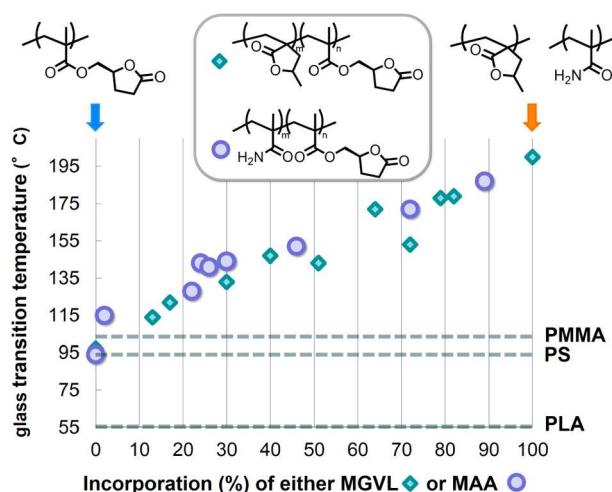
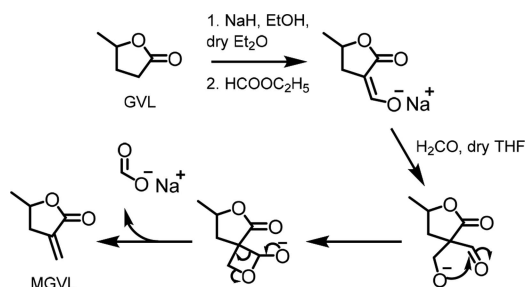


Figure 1. Polymer T_g values vs MMA or MGVL comonomer incorporation compared to commodity plastics: PMMA (105 °C), PS (95 °C), and PLA (55 °C).

Scheme 6. α -Methylenation of γ -Valerolactone (GVL) To Yield Methylene- γ -valerolactone (MGVL)



ethyl formate to form a salt which is isolated by filtration. A catalytic amount of ethanol substantially decreases the reaction time.²⁵

Apart from its biobased nature, MGVL offers a reactivity advantage because its *cis* conformation and planar structure do not hinder the approaching monomer during polymerization. Finally, acrylate-type polymers with MGVL generally exhibit high glass transition temperatures because of high conforma-

tional barriers associated with the persistent lactone rings.²⁴ Table 5 summarizes the copolymerization between 2H-HBO-m and MGVL. Unfortunately, most of the resulting polymers were insoluble in the GPC solvents THF and HFiP.

Moreover, an incorporation of 82% of MGVL results in a soluble polymer (HFiP) with a high M_n of 38.4 kDa (entry 9), but with slightly less incorporated MGVL (79%), the polymer is insoluble. Note that copolymerizations with MGVL and 2H-HBO-m gave incorporation fractions rather well matched to the feed fractions compared to copolymerizations between MAA and 2H-HBO-m. For instance, entries 3, 4, and 5 (Table 5) describe matching values between feed fractions and incorporations and entry 8 only deviates by 1%, all within the error of the measurement. As expected, T_g values of the copolymers are substantially influenced by the content of MGVL in the backbone.

Higher fractions of MGVL afford higher glass transition temperatures (Figure 1). Table 5, entry 1 shows that just 13% MGVL lactone in the final polymer increases the T_g to 114 °C from the value 98 °C for the 2H-HBO-m homopolymer (Table 3, entry 1). Substantially higher T_g of 150 and 179 °C are observed for 51% and 82% MGVL, respectively (Table 5, entries 5 and 9). The spanned T_g range for poly(2H-HBO-m-co-MGVL) (98–200 °C) is similar to that of poly(2H-HBO-m-co-MAA) (98–187 °C).

Inspired by the aforementioned synthesis of MGVL (from GVL) and its ability to impart high- T_g values, we targeted the methylenation of 2H-HBO itself. However, for this target, protection of the hydroxyl group was essential since the methods employed strong bases, likely to form an alkoxide that might open the lactone. Thus, the methylenation of 2H-HBO (Scheme 7) starts with protection of the hydroxy group with 3,4-dihydro-2H-pyran to give the 2-tetrahydropyranyl (THP) protected THP-2H-HBO.

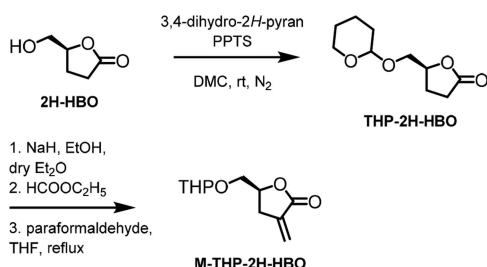
Methylenation is related to that of Scheme 7 and affords the expected product, methylene-THP-2H-HBO (M-THP-2H-HBO). High reactivity of pure M-THP-2H-HBO was observed; it tends to oligomerize slowly, but this did not preclude subsequent polymerization studies. Still, this reactivity discounted the option of removing the protecting group prior to polymerization.

Table 5. Incorporation, Molecular Weight, and Thermal Data for Poly(2H-HBO-m-co-MGVL)

entry	feed fractions 2H-HBO-m/MGVL	incorporation ^a 2H-HBO-m/MGVL	M_n (kDa) ^b	D^b	T_g (°C) ^c	$T_{d5\%}$ (°C) ^d	
1	90/10	88/12	insoluble	insoluble	114	212	
2	80/20	83/17	insoluble	insoluble	122	273	
3	70/30	70/30	insoluble	insoluble	133	307	
4	60/40	60/40	insoluble	insoluble	147	332	
5	50/50	49/51	insoluble	insoluble	143	249	
6	40/60	36/64	insoluble	insoluble	158	340	
7	30/70	28/72	insoluble	insoluble	153	162	
8	20/80	21/79	insoluble	insoluble	178	170	
9	10/90	18/82	38.4	4.3	179	186	
10	0/100	0/100	22.9	2.3	200	342	

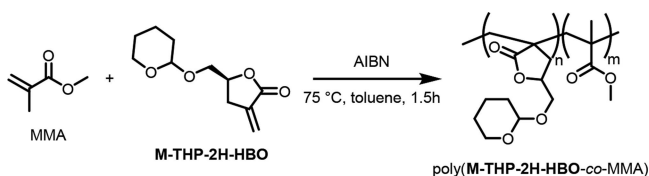
^aIncorporation was measured by ^1H NMR in CDCl_3 ($\text{\$140}$). ^bGPC in hexafluoro-2-propanol (HFiP) at 40 °C vs poly(methyl methacrylate) standards. ^cDetermined by DSC under N_2 . ^dTGA temperature at which 5% mass loss was observed under nitrogen.

Scheme 7. Synthesis of Methylene-THP-2H-HBO (M-THP-2H-HBO)



In order to compare poly(methyl methacrylate) (PMMA) and poly(M-THP-2H-HBO), copolymerizations with varying feed fractions were conducted using AIBN as the initiator in toluene at 70 °C for 1.5 h. The materials were then precipitated by addition of hexane. Table 6 shows the

Table 6. Incorporation, Molecular Weight, and Thermal Data for Poly(M-THP-2H-HBO-co-methyl methacrylate)



entry	feed fractions M-THP-2H- HBO/MMA	incorporation ^a M-THP-2H- HBO/MMA	M_n (kDa) ^b	$\bar{D}$ ^b	T_g (°C) ^c	$T_{d5\%}$ (°C) ^d
1	10/90	10/90	14.9	2.2	101	162
2	20/80	29/71	14.2	2.3	109	195
3	30/70	41/59	15.1	2.9	116	184
4	39/61	53/47	22.0	2.4	124	192
5	49/51	56/44	17.0	2.6	128	212
6	60/40	68/32	23.0	2.7	140	198
7	70/30	72/28	24.9	2.7	137	194
8	80/20	76/24	27.1	3.2	140	189
9	90/10	85/15	16.9	4.3	147	186
10	100/0	100/0	44.4	2.2	148	188

^aIncorporation was measured by ¹H NMR in CDCl₃ (Figure S141 in the Supporting Information). ^bGPC in hexafluoro-2-propanol (HFIP) at 40 °C vs poly(methyl methacrylate) standards. ^cDetermined by DSC under N₂. ^dTGA temperature at which 5% mass loss was observed under nitrogen.

experiments with various monomer loadings from 10% M-THP-2H-HBO (entry 1) to 100% (entry 9). High- M_n values of 14.9, 22.0, and 27.1 kDa (entries 1, 4, and 8), for example, are observed. Note that poly(M-THP-2H-HBO) even reached an M_n value of 44.4 kDa with a nearly ideal dispersity of 2.2.

To focus on the thermal properties, the highest glass transition temperature of the series belongs to the homopolymer poly(M-THP-2H-HBO) at 148 °C (Table 6, entry 10). At the lower end, the copolymer with just 10% M-THP-2H-HBO incorporation (Table 6, entry 1) has a T_g of 101 °C.

Polymers with a higher fraction of M-THP-2H-HBO exhibit proportionally higher T_g values, as illustrated in Figure 2. Figure 3 shows the thermal degradation analysis (TGA, under nitrogen) of poly(M-THP-2H-HBO) (Table 6, entry 10) with a $T_{d5\%}$ (5% mass loss) around 188 °C; this is comparable to other $T_{d5\%}$ values of the series. The mass loss later reached a plateau at 246 °C (29% mass loss) until 303 °C (34% mass

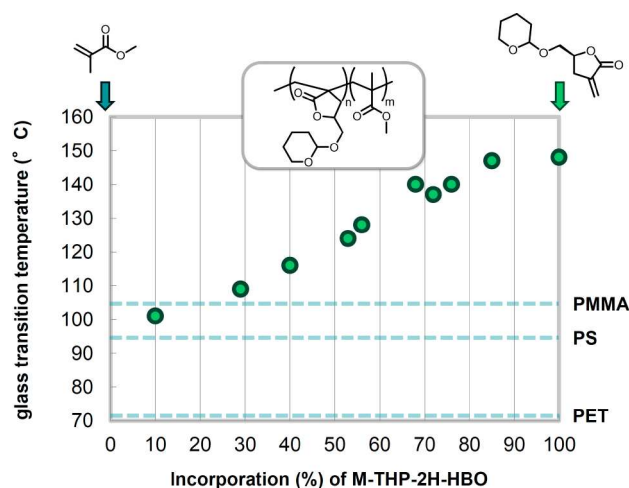


Figure 2. Copolymer T_g values vs incorporation of M-THP-2H-HBO compared to commodity plastics: PMMA (105 °C), PS (95 °C), and PET (72 °C).

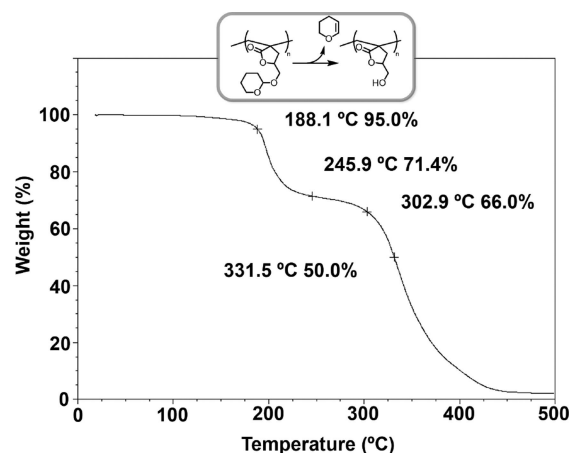


Figure 3. Thermal degradation of poly(M-THP-2H-HBO). The first plateau likely represents loss of the THP protecting group as dihydropyran, with about 29% mass lost.

loss) and then degradation resumed thereafter. Plausibly, this degradation plateau represents the acetal deprotection/degradation as the THP moiety corresponds to 39.6% of the molecular weight of the monomer, when lost as dihydropyran. In an attempt to verify this assumption, M-THP-2H-HBO was heated to 240 °C for 5, 30, or 90 min. The insolubility of the resulting material prohibited any NMR analysis but IR spectroscopy showed a broad band around 3400–3500 cm⁻¹ having an intensity that increased with time (Figure 4). This characteristic OH band is attributed to the alcohol functionality revealed upon loss of dihydropyran (Figure 3).

Note that there are two stereocenters in the repeat unit for poly(M-THP-2H-HBO): one attributed to the chiral 2H-HBO monomer employed and one in the main chain created upon polymerization. Thus, this polymer possesses a tacticity that theoretically could be evaluated, potentially via ¹³C NMR or ¹H NMR spectroscopy. However, the poor solubility of the material in conventional NMR solvents did not allow sufficient resolution of any diastereomeric peaks in the corresponding spectra. Our assumption is that the main chain tacticity is essentially atactic since stereoselectivity is invariably poor with this method of radical polymerization. The side chain chirality

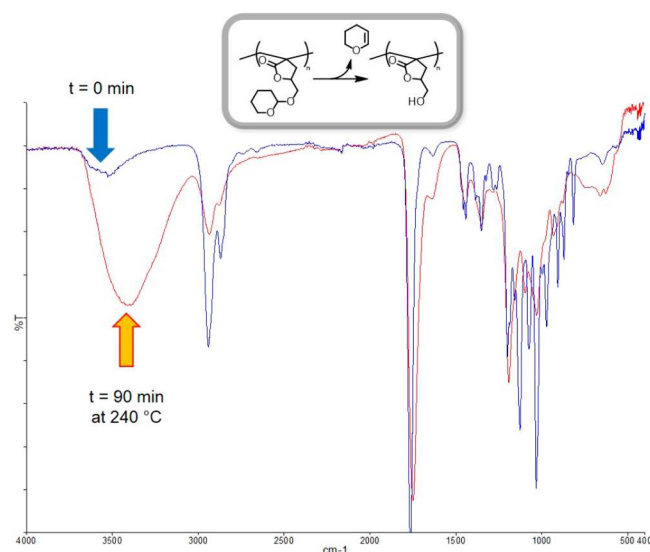


Figure 4. IR spectra of poly(M-THP-2H-HBO) before heating (blue) and after 90 min at 240 °C (red).

is also inconsequential as amorphous polymers (without melting temperatures) are observed with all the polymers reported here.

CONCLUSION

An efficient and sustainable methacrylation of the biobased lactone HBO and its hydrogenated analogue, 2H-HBO, has been successfully achieved through a lipase-mediated chemoenzymatic process that avoids chloride reagents and scavenging bases, while decreasing the amount of generated waste. Methacrylated 2H-HBO-m was successfully polymerized through a free radical process, providing homopolymers with T_g values near 98 °C. The glass transition temperature was then increased via copolymerization of 2H-HBO-m with methacrylamide (MAA) from the “spontaneous” homopolymerization of HBO-m. A second copolymer series was created with 2H-HBO-m and methylene- γ -valerolactone (MGVL), a biobased, cyclic acrylate that is known to effect conformational inflexibility. Whether by increasing hydrogen bonding (MAA comonomer) or by increasing conformational barriers (MGVL comonomer), high- T_g ranges (100–190 °C) were observed with these two copolymer series from 2H-HBO-m. Additionally, 2H-HBO was subjected to hydroxy group protection (with dihydropyran) and α -methylenation to produce a new acrylate monomer, M-THP-2H-HBO, that was homopolymerized and then copolymerized with methyl methacrylate (MMA). The T_g range of this copolymer series spans from 101 to 147 °C and the homopolymer itself, poly(M-THP-2H-HBO), has a T_g of 148 °C and a high molecular weight of 44.4 kDa.

Levogluconone (LGO) and its oxidized derivative (S)- γ -(hydroxymethyl)- α,β -butenolide (HBO) have recently become available in useful quantities from various cellulosic biomass sources.²⁶ The chemistry reported herein describes the efficient production of acrylate monomers from HBO and their polymerization to promising polymers and copolymers with tunable properties, especially glass transition temperature values competitive with several high- T_g commodity plastics, including polyethylene terephthalate (PET), polystyrene (PS), polyvinyl chloride (PVC), poly(methyl methacrylate)

(PMMA), and even polycarbonate (PC). Finally, these polymers have been designed for postpolymerization modifications, which will be reported in the future and will further expand their potential applications.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acssuschemeng.8b04707.

NMR spectra, DSC and TGA traces, IR traces, mass spectrometry spectra and calculations for copolymer incorporation ratios, photograph of material resulting from the “spontaneous” homopolymerization of HBO-m (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

- (1) Geyer, R.; Jambeck, J. R.; Law, K. L. Production, use and fate of all plastics ever made. *Sci. Adv.* **2017**, 3 (7), e1700782.
- (2) Schneiderman, D. K.; Hillmyer, M. A. 50th Anniversary Perspective: There is a Great Future in Sustainable Polymers. *Macromolecules* **2017**, 50, 3733–3749.
- (3) Wang, G.; Jiang, M.; Zhang, Q.; Wang, R.; Zhou, G. Biobased multiblock copolymers: Synthesis, properties and shape memory performance of poly(ethylene 2,5-furandicarboxylate)-*b*-poly(ethylene glycol). *Polym. Degrad. Stab.* **2017**, 144, 121–127.
- (4) Espinach, F. X.; Boufi, S.; Delgado-Aguilar, M.; Julian, F.; Mutjé, F.; Méndez, J. A. Composites from poly(lactic acid) and bleached chemical fibres: Thermal properties. *Composites, Part B* **2018**, 134, 169–176.
- (5) Nguyen, H. T. H.; Qi, P.; Rostagno, M.; Feteha, A.; Miller, S. A. The quest for high glass transition temperature bioplastics. *J. Mater. Chem. A* **2018**, 6, 9298.
- (6) Qi, P.; Chen, H.-L.; Nguyen, H. T. H.; Lin, C.-C.; Miller, S. A. Synthesis of biorenewable and water-degradable polylactam esters from itaconic acid. *Green Chem.* **2016**, 18, 4170–4175.
- (7) Werpy, T.; Petersen, J., Eds. *Top Value-Added Chemicals from Biomass, Vol. I—Results of Screening for Potential Candidates from Sugars and Synthesis Gas*; U.S. Department of Energy (DOE) by the National Renewable Energy Laboratory a DOE national Laboratory: Oak Ridge, TN, 2004. <http://www.nrel.gov/docs/fy04osti/35523.pdf>, accessed February 2018.
- (8) Leal Silva, J. F.; Grekin, R.; Mariano, A. P.; Maciel Filho, R. Making Levulinic Acid and Ethyl Levulinate Economically Viable: A

Worldwide Technoeconomic and Environmental Assessment of Possible Routes. *Energy Technol.* **2018**, *6*, 613–639.

(9) Della Pina, C.; Falleta, E.; Rossi, M. A green approach to chemical building block. The case of 3-hydroxypropionic acid. *Green Chem.* **2011**, *13*, 1624–1632.

(10) Court, G. R.; Lawrence, C. H.; Raverty, W.; Duncan, A. Method for converting Lignocellulosic Materials into Useful Chemicals. EP Patent Application EP20100793418, 2012.

(11) Flourat, A. L.; Peru, A. A. M.; Teixeira, A. R. S.; Brunissen, F.; Allais, F. Chemo-enzymatic synthesis of key intermediates (S)- γ -hydroxymethyl- α,β -butenolide and (S)- γ -hydroxymethyl- α,β -butyrolactone via lipase-mediated Baeyer-Villiger oxidation of levoglucosenone. *Green Chem.* **2015**, *17*, 404–412.

(12) Bonneau, G.; Peru, A. A. M.; Flourat, A. L.; Allais, F. Organic solvent- and catalyst-free Baeyer-Villiger oxidation of levoglucosenone and dihydrolevoglucosenone (Cyrene®): a sustainable route to intermediates (S)- γ -hydroxymethyl- α,β -butenolide and (S)- γ -hydroxymethyl- α,β -butyrolactone. *Green Chem.* **2018**, *20*, 2455–2458.

(13) Peru, A. A. M.; Flourat, A. L.; Gunawan, C.; Raverty, W.; Jevric, M.; Greatrex, B. W.; Allais, F. Chemo-Enzymatic Synthesis of Chiral Epoxides Ethyl and Methyl (S)-3-(Oxiran-2-yl)propanoates from Renewable Levoglucosenone: An Access to Enantiopure (S)-Dairy Lactone. *Molecules* **2016**, *21*, 988–997.

(14) Zamzow, M.; Höcker, H. Synthesis of polymers with pendant spiro orthoester groups. *Macromol. Chem. Phys.* **1994**, *195*, 2381–2400.

(15) Ray, P.; Hughes, T.; Smith, C.; Simon, G. P.; Saito, K. Synthesis of Bioacrylic Polymers from Dihydro-5-hydroxy furan-2-one (2H-HBO) by free Controlled Radical Polymerization. *ACS Omega* **2018**, *3*, 2040–2048.

(16) Prat, D.; Wells, A.; Hayler, J.; Sneddon, H.; McElroy, C. R.; Abou-Shehada, S.; Dunn, P. J. CHEM21 selection guide of classical- and less classical-solvents. *Green Chem.* **2016**, *18*, 288–296.

(17) Diot-Néant, F.; Migeot, L.; Hollande, L.; Reano, F. A.; Domenek, S.; Allais, F. Biocatalytic Synthesis and Polymerization via ROMP of New Biobased Phenolic Monomers: A Greener Process toward Sustainable Antioxidant Polymers. *Front. Chem.* **2017**, *5*, 126.

(18) Pion, F.; Reano, F. A.; Ducrot, P.-H.; Allais, F. Chemo-enzymatic preparation of new bio-based bis- and trisphenol: new versatile building blocks for polymer chemistry. *RSC Adv.* **2013**, *3*, 8988–8997.

(19) Sheldon, R. A.; van Pelt, S. Enzyme immobilization in biocatalysis: why, what and how. *Chem. Soc. Rev.* **2013**, *42*, 6223–6235.

(20) Warwel, S.; Steinke, G.; Rüschen, M. An efficient method for lipase-catalysed preparation of acrylic and methacrylic acid esters. *Biotechnol. Tech.* **1996**, *10* (4), 283–286.

(21) Kuo, S.-W.; Kao, H.-C.; Chang, F.-C. Thermal behavior and specific interaction in high glass transition temperature PMMA copolymer. *Polymer* **2003**, *44*, 6873–6882.

(22) Esposito, D.; Antonietti, M. Redefining biorefinery: the search for unconventional building blocks for materials. *Chem. Soc. Rev.* **2015**, *44*, 5821–5835.

(23) Alonso, D. M.; Wettstein, S. G.; Dumesic, J. A. Gamma-valerolactone, a sustainable platform molecule derived from lignocellulosic biomass. *Green Chem.* **2013**, *15*, 584.

(24) Murray, A. W.; Reid, R. G. Convenient Synthesis of α -Epoxylactones (4-Oxo-1,5-dioxaspiro[2.4]heptanes and -[2.5]-octanes). *Synthesis* **1985**, *16*, 35–38.

(25) Barbier, P.; Benezra, C. Allergenic α -Methylene- γ -butyrolactones. Stereospecific Syntheses of (+)- and (–)- γ -Methyl- α -methylene- γ -butyrolactone. A study of Specificity of (+) and (–) Enantiomers in Inducing Allergic Contact Dermatitis. *J. Med. Chem.* **1982**, *25*, 943–946.

(26) Teixeira, A. R. S.; Flourat, A. L.; Peru, A. A. M.; Brunissen, F.; Allais, F. Lipase-Catalyzed Baeyer-Villiger Oxidation of Cellulose-Derived Levoglucosenone into (S)- γ -Hydroxymethyl- α,β -Butenolide: Optimization by Response Surface Methodology. *Front. Chem.* **2016**, *4*, 16.