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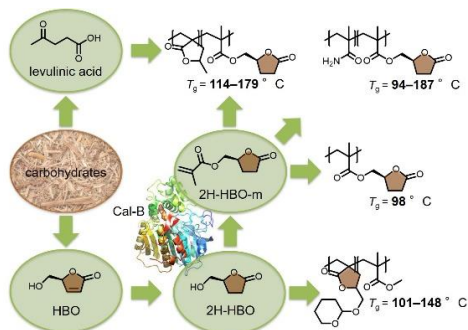
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# CHEMO-ENZYMATIC SYNTHESIS AND FREE RADICAL POLYMERIZATION OF RENEWABLE ACRYLATE MONOMERS FROM CELLULOSE-BASED LACTONES

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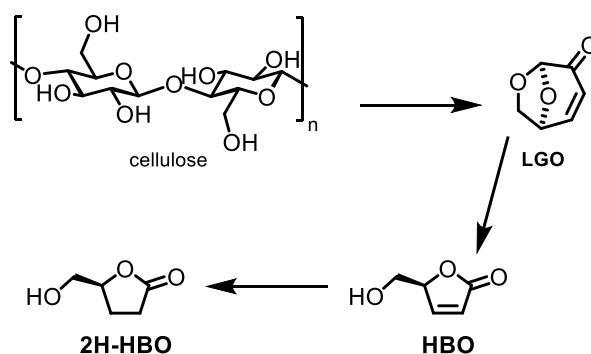
## Abstract

A chemo-enzymatic pathway involving a *Candida antarctica* type B lipase was developed to produce (*S*)- $\gamma$ -hydroxymethyl- $\alpha,\beta$ -butenolide methacrylate (**HBO-m**) and (*S*)-hydroxymethyl- $\gamma$ -butyrolactone methacrylate (**2H-HBO-m**) from (*S*)- $\gamma$ -hydroxymethyl- $\gamma$ -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- $\gamma$ -valerolactone, a green intermediate. Finally, methylene-tetrahydropyranyl (*S*)- $\gamma$ -hydroxymethyl- $\gamma$ -butyrolactone (**M-THP-2H-HBO**), synthesized via  $\alpha$ -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,  $\alpha$ -Methylenation, Biobased polymers, Polyacrylates

## Background

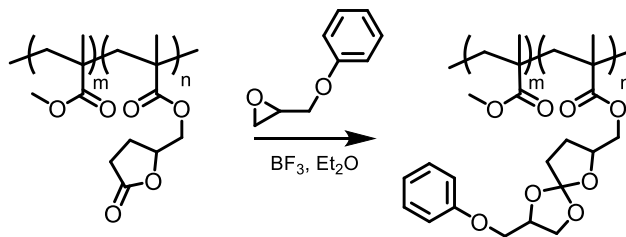
Over the last several decades, the growing production of materials<sup>1</sup> and synthetic goods has raised severe concerns regarding pollution and the inevitable depletion of fossil-fuel resources. In that context, numerous investigations have been conducted in attempts to replace fossil-based products such as plastics.<sup>2</sup> Exploration and progress of white technologies and green chemistry applied to biomass have been a major achievement to supplant non-sustainable 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.



**Scheme 1.** Transformation of cellulose into **HBO** followed by hydrogenation to **2H-HBO**.

Biobased 2,5-furandicarboxylic acid<sup>3</sup> 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)<sup>4</sup> of PLA precludes its utilization at high temperature.<sup>5</sup> Recently, Miller and

co-workers proposed new polylactam esters<sup>6</sup> made from ethanolamine and sugar-derived itaconic acid, one of the top twelve biorenewable molecules extolled by the DOE.<sup>7</sup> 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.



**Scheme 2.** Installation of spiro orthoester via post-polymerization reaction.

Among the expanding library of renewable molecules of interest that can be produced from lignocellulosic biomass such as levulinic acid<sup>8</sup> and 3-hydroxy propionic acid (3-HP),<sup>9</sup> (*S*)- $\gamma$ -hydroxymethyl- $\alpha,\beta$ -butenolide (**HBO**) (Scheme 1) has demonstrated its high potential. **HBO** was recently produced 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.<sup>10</sup> The first route involved a lipase-mediated Baeyer-Villiger oxidation of **LGO**<sup>11</sup> whereas the more recent route is a solvent-free and catalyst-free Baeyer-Villiger oxidation.<sup>12</sup> 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 lactone<sup>13</sup> 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 Höcker<sup>14</sup> reported the synthesis of polymers with a spiro orthoester pendant group. The polymerization acrylate monomers bearing reactive lactones such as (S)- $\gamma$ -hydroxymethyl- $\alpha,\beta$ -butyrolactone methacrylate (**2H-HBO-m**) was followed by installation of the desired spiro orthoester (Scheme 2). The adopted monomer synthesis required methacryloyl chloride, an inexpensive reagent that nonetheless results in substantial amounts of halogenated 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-workers<sup>15</sup> 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 ( $\mathcal{D} = 1.06$ ) 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.<sup>16</sup> Notwithstanding these improvements, this method presents several drawbacks, including the utilization of non-green organic bases: 4-dimethylaminopyridine (DMAP, 1% mol) and triethylamine (Et<sub>3</sub>N, 1 equiv.), known to be noxious and waste-generating. While Et<sub>3</sub>N salts are mainly removed through filtration, the work-up protocol with NaHCO<sub>3</sub> does allow product purification. However, the methacrylic acid by-product 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 catalysis<sup>17</sup> of *Candida antarctica* type B lipase (CAL-B, *a.k.a.* Novozyme 435<sup>®</sup>) to access acrylates (S)- $\gamma$ -hydroxymethyl- $\alpha,\beta$ -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- $\gamma$ -valerolactone (MGVL) was synthesized from **HBO** and polymerized.

## Experimental

### Chemicals and reagents

Levoglucosenone was graciously provided by the Circa Group. Lipase acrylic resin from *Candida antarctica* (Cal-B) was purchased from Sigma Aldrich. Hydrogen peroxide 30% (Fischer), propionic acid (Sigma Aldrich), butanoic acid (Sigma Aldrich), 2-butenoic acid (Sigma Aldrich), *trans*-2-pentenoic acid (Sigma Aldrich), 4-pentenoic acid (Sigma Aldrich), AIBN (Sigma Aldrich), V-65 (Sigma Aldrich), V-70 (Sigma Aldrich), methyl methacrylate stabilized (Fischer), methacryloyl chloride (Sigma Aldrich), methacrylic anhydride (Sigma Aldrich), methacrylamide 98% (Alfa Aesar), triethylamine (Sigma Aldrich),  $\gamma$ -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-2*H*-pyrane (Sigma Aldrich), 10% by weight palladium on activated carbon (Acros), potassium carbonate (Fischer), sodium hydroxide (Fischer), *para*-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 *para*-toluenesulfonate was prepared from *para*-toluenesulfonic acid (1 equiv.) in pyridine (5 equiv.) and recrystallized from acetone.

### Characterization

#### Nuclear Magnetic Resonance (NMR) spectroscopy

Proton nuclear magnetic resonance ( $^1\text{H}$  NMR) and carbon nuclear magnetic resonance ( $^{13}\text{C}$  NMR) were recorded 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.

### **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.

### **Infra-Red (IR) spectroscopy**

Solid-state IR is recorded using a Perkin Elmer Spectrum One FT-IR. spectrophotometer.

### **Thermogravimetric Analysis (TGA)**

TGA was measured under nitrogen with a TGA Q5000 from TA Instruments. About 1-5 mg of each sample were cooled down 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)**

DSC thermograms were obtained with a DSC Q1000 from TA instruments. Typically, 3-7 mg of sample were 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)**

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 (K(OTf)) in HPLC grade hexafluoroisopropanol (HFIP) as the mobile phase at a flow rate of 0.3 mL/min. Calibration was performed with narrow dispersity polymethyl methacrylate standards.

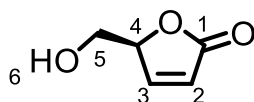
## **Monomer synthesis**

### **Synthesis of (S)-5-(hydroxymethyl)furan-2(5H)-one (HBO)**

Levogluconone (**LGO**, 1 equiv.) was dissolved in ethyl acetate ( $C = 1M$ ). A catalytic amount of CAL-B (10 w%) 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).

An 30% aq. H<sub>2</sub>O<sub>2</sub> solution (9.78 M, 0.81 L, 7.92 mol, 1 equiv./**LGO**) was added dropwise over 3.5 hours under nitrogen to **LGO** (1 kg, 7.93 mol) cooled down with an ice bath. After completion of the addition, the reaction was warmed to 50 °C and stirred for an extra 20 hours. Presence of H<sub>2</sub>O<sub>2</sub> was evaluated with peroxide strips and, if any, the residual H<sub>2</sub>O<sub>2</sub> was quenched using the methods described in the manuscript. The reaction mixture was

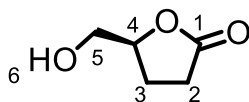
then concentrated in vacuo and the residue was distilled of (150 °C/0.7-0.9 mbar) to provide **HBO** as a clear oil that readily crystallizes.



<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ<sub>H</sub> 1.93 (br s, 1H, H<sub>6</sub>), 3.89 (ddd, 2H, *J* = 3.7, 5.0 and 12.2 Hz, H<sub>5</sub>), 5.14 (m, 1H, H<sub>4</sub>), 6.20 (dd, 1H, *J* = 2.0 and 5.7 Hz, H<sub>2</sub>), 7.46 (dd, 1H, *J* = 1.6 and 5.7 Hz, H<sub>3</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz): δ<sub>C</sub> 62.1 (C<sub>5</sub>), 84.4 (C<sub>4</sub>), 122.8 (C<sub>2</sub>), 154.1 (C<sub>3</sub>), 173.7 (C<sub>1</sub>).

### 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 were added 1.496 g of Pd/C (10% w/w). The system was degassed 3 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.



<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ<sub>H</sub> 1.95 (m, 2H, H<sub>3</sub>), 2.32 (m, 2H, H<sub>2</sub>), 3.49 (dd, 2H, *J* = 3.0 and 15.0 Hz, H<sub>5</sub>), 4.01 (br s, 1H, H<sub>6</sub>), 4.40 (m, 1H, H<sub>4</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz): δ<sub>C</sub> 23.0 (C<sub>3</sub>), 28.5 (C<sub>2</sub>), 63.6 (C<sub>5</sub>), 81.1 (C<sub>4</sub>), 178.5 (C<sub>1</sub>).

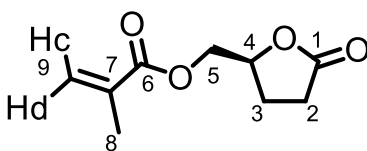
### Study of chemo-enzymatic reaction

In a typical experiment, 3 equivalents of propionic acid were added to a solution of 500 mg (4.4 mmol, 1 equiv.) of **HBO** in 4.4 mL of toluene (*C* = 1M). The mixture was heated

up to 70 °C and was stirred during 24h. Then, the CAL-B was filtered out and the filtrate was concentrated. The conversion was then evaluated by  $^1\text{H}$  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 w% 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 up to 70 °C and stirred for 24h. 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 de-ionized water. The organic layer was dried over anhydrous  $\text{MgSO}_4$  and concentrated to dryness. Quick filtration over silica gel was then performed and the pure product was obtained (62% yield).

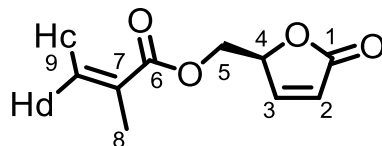


$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta_{\text{H}}$  1.89 (s, 3H,  $\text{H}_8$ ), 2.26 (m, 2H,  $\text{H}_3$ ), 2.60 (m, 2H,  $\text{H}_2$ ), 4.34 (dd, 2H,  $J = 3.0$  and  $12.0$  Hz,  $\text{H}_5$ ), 4.82 (m, 1H,  $\text{H}_4$ ), 5.65 (m, 1H,  $\text{H}_{9\text{c}}$ ), 6.16 (m, 1H,  $\text{H}_{9\text{d}}$ ).

$^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta_{\text{C}}$  18.1 ( $\text{C}_8$ ), 24.7 ( $\text{C}_3$ ), 28.0 ( $\text{C}_2$ ), 65.5 ( $\text{C}_5$ ), 77.3 ( $\text{C}_4$ ), 126.3 ( $\text{C}_7$ ), 135.5 ( $\text{C}_9$ ), 166.9 ( $\text{C}_6$ ), 176.7 ( $\text{C}_1$ ).

### Synthesis of (S)-5-(methyl)furan-2(3H)-one methacrylate (HBO-m)

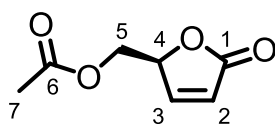
The same procedure as for **2H-HBO-m** was used.



$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz):  $\delta_{\text{H}}$  1.86 (s, 3H,  $\text{H}_8$ ), 4.40 (dd, 2H,  $J = 5.0$  and 15 Hz,  $\text{H}_5$ ), 5.27 (m, 1H,  $\text{H}_4$ ), 5.56 (m, 1H,  $\text{H}_{9\text{c}}$ ), 6.04 (m, 1H,  $\text{H}_{9\text{d}}$ ), 6.16 (d, 1H,  $J = 5.8$  Hz,  $\text{H}_2$ ), 7.47 (d, 1H,  $J = 5.8$  Hz,  $\text{H}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz):  $\delta_{\text{C}}$  18.1 ( $\text{C}_8$ ), 62.6 ( $\text{C}_5$ ), 80.9 ( $\text{C}_4$ ), 123.0 ( $\text{C}_2$ ), 126.7 ( $\text{C}_7$ ), 135.3 ( $\text{C}_9$ ), 152.8 ( $\text{C}_3$ ), 166.6 ( $\text{C}_6$ ), 172.3 ( $\text{C}_1$ ). After purification by flash chromatography, the following spectra were obtained.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta_{\text{H}}$  1.84 (s, 3H,  $\text{H}_8$ ), 4.38 (dd, 2H,  $J = 3.0$  and 12.0 Hz,  $\text{H}_5$ ), 5.24 (m, 1H,  $\text{H}_4$ ), 5.54 (m, 1H,  $\text{H}_{9\text{c}}$ ), 6.03 (m, 1H,  $\text{H}_{9\text{d}}$ ), 6.14 (dd, 1H,  $J = 2.1$  and 5.8 Hz,  $\text{H}_2$ ), 7.44 (dd, 1H,  $J = 1.6$  and 5.8 Hz,  $\text{H}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta_{\text{C}}$  18.1 ( $\text{C}_8$ ), 62.6 ( $\text{C}_5$ ), 80.9 ( $\text{C}_4$ ), 123.1 ( $\text{C}_2$ ), 126.8 ( $\text{C}_7$ ), 135.3 ( $\text{C}_9$ ), 152.8 ( $\text{C}_3$ ), 166.6 ( $\text{C}_6$ ), 172.3 ( $\text{C}_1$ ).

### Synthesis of (S)-5-(hydroxymethyl)furan-2(5H)-one acetate

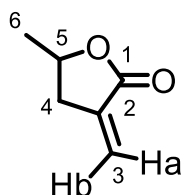
To a solution of 2.985 g (26.1 mmol, 1 equiv.) of **HBO** in 130 mL of AcOEt was added 10 w% of CAL-B (relative to **HBO**). The system was heated at 70 °C for 1 day. Then the CAL-B was filtered out and the filtrate was concentrated to dryness. The crude product was taken up in 20 mL of dichloromethane and washed twice with distilled water and once with brine. The organic layer was dried over anhydrous  $\text{MgSO}_4$  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).



$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta_{\text{H}}$  2.02 (s, 3H,  $\text{H}_7$ ), 4.31 (dd, 2H,  $J = 3.0$  and  $6.0$  Hz,  $\text{H}_5$ ), 5.22 (m, 1H,  $\text{H}_4$ ), 6.18 (d, 1H,  $J = 3.0$  Hz,  $\text{H}_2$ ), 7.45 (d, 1H,  $J = 3.0$  Hz,  $\text{H}_3$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta_{\text{C}}$  20.5 ( $\text{C}_7$ ), 62.5 ( $\text{C}_5$ ), 80.8 ( $\text{C}_4$ ), 123.2 ( $\text{C}_2$ ), 152.6 ( $\text{C}_3$ ), 170.5 ( $\text{C}_6$ ), 172.3 ( $\text{C}_1$ ).

### Synthesis of methylene- $\gamma$ -valerolactone

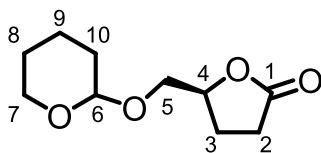
To a stirred solution of NaH (60% dispersion in mineral oil, 1 equiv.) in dry diethyl ether, 600  $\mu\text{L}$  of ethanol were added under  $\text{N}_2$ . Then a mixture of 10 g (100 mmol, 1 equiv.) of  $\gamma$ -valerolactone and 8 mL (100 mmol, 1 equiv.) of ethyl formate was added dropwise at  $0^\circ\text{C}$ . The system was allowed to return to room temperature and was stirred during 1h. Then, the precipitate was filtered out to afford the salt in quantitative yield. The salt was added to 40 mL dry THF with 4.5 equiv. of paraformaldehyde. The system was heated to reflux during 3h in order to crack the paraformaldehyde into formaldehyde. After 3h, the mixture was concentrated to dryness and the crude product was taken up in 60 mL of diethyl ether and was washed twice with a saturated solution of potassium carbonate. The organic layers were combined, dried over anhydrous  $\text{MgSO}_4$  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.



$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta_{\text{H}}$  1.41 (d, 3H,  $J = 6.0$  Hz,  $\text{H}_6$ ), 2.83 (m, 2H,  $\text{H}_4$ ), 4.64 (m, 1H,  $\text{H}_5$ ), 5.62 (t, 1H,  $J = 3.0$  Hz,  $\text{H}_{3a}$ ), 6.21 (t, 1H,  $J = 3.0$  Hz,  $\text{H}_{3b}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta_{\text{C}}$  21.8 ( $\text{C}_6$ ), 35.0 ( $\text{C}_4$ ), 73.9 ( $\text{C}_5$ ), 121.7 ( $\text{C}_2$ ), 135.0 ( $\text{C}_3$ ), 170.2 ( $\text{C}_1$ ).

### Synthesis of (4*R*)-dihydro-5-(tetrahydropyranyl) hydroxy- methyl-2(3*H*)-furanone (THP-2H-HBO)

To a solution of 4.04 g (34.8 mmol, 1 equiv.) of **2H-HBO** in 40 mL of dichloromethane was added 911 mg of pyridinium *p*-toluenesulfonate and 5.9 mL (64.7 mmol, 1.9 equiv.) of 3,4-dihydro-2*H*-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.

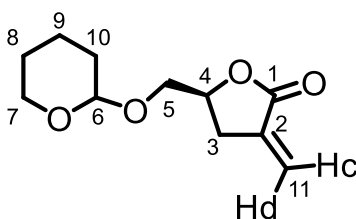


$^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz):  $\delta_{\text{H}}$  1.53 (m, 4H,  $\text{H}_{8,9}$ ), 1.67 (m, 2H,  $\text{H}_{10}$ ), 2.18 (m, 2H,  $\text{H}_3$ ), 2.54 (m, 2H,  $\text{H}_2$ ) 3.70 (m, 4H,  $\text{H}_{5,7}$ ), 4.63 (m, 2H,  $\text{H}_{4,6}$ ).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz):  $\delta_{\text{C}}$  18.9, 19.3 ( $\text{C}_9$ ), 24.1 ( $\text{C}_2$ ), 25.3 ( $\text{C}_8$ ), 28.5 ( $\text{C}_3$ ), 30.3 ( $\text{C}_{10}$ ), 61.7, 62.3 ( $\text{C}_7$ ), 68.8, 69.0 ( $\text{C}_5$ ), 78.7, 79.0 ( $\text{C}_4$ ), 98.5, 99.2 ( $\text{C}_6$ ), 177.3, 177.5 ( $\text{C}_1$ ). Diastereoisomerism gives two peaks for some carbon atoms.

### Synthesis of (4*R*)-dihydro-5-(tetrahydropyranyl)hydroxy-methyl-3-methylene-2(3*H*)-furanone (M-THP-2H-HBO)

To a suspension of NaH (60% dispersion in mineral oil, 1 equiv.) in 45 mL of dry diethyl ether, 180  $\mu\text{L}$  of ethanol were added under  $\text{N}_2$ . 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 during 30 min. The precipitate was filtered out leading to the salt in a yield of 83%. 3.045 g of the salt were suspended in 20 mL of dry THF with 5 equiv. of paraformaldehyde. The mixture was refluxed for 2h 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<sub>4</sub> 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.



<sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz): δ<sub>H</sub> 1.50 (m, 4H, H<sub>8,9</sub>), 1.70 (m, 2H, H<sub>10</sub>), 2.89 (m, 2H, H<sub>3</sub>), 3.69 (m, 4H, H<sub>5,7</sub>), 4.60 (t, 0.51H, *J* = 1.9 Hz, H<sub>6</sub>) and its diastereomeric peak at 4.65 (t, 0.56H, *J* = 1.9 Hz, H<sub>6</sub>), 4.70 (m, 1H, H<sub>4</sub>), 5.62 (m, 1H, H<sub>11c</sub>), 6.20 (m, 1H, H<sub>11d</sub>). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz): δ<sub>C</sub> 18.9, 19.2 (C<sub>9</sub>), 25.3 (C<sub>8</sub>), 29.7 (C<sub>3</sub>), 30.3 (C<sub>10</sub>), 61.8, 62.3 (C<sub>7</sub>), 68.5, 68.6 (C<sub>5</sub>), 75.5, 75.7 (C<sub>4</sub>), 98.6, 99.2 (C<sub>6</sub>), 121.5, 121.7 (C<sub>2</sub>), 134.3, 134.5 (C<sub>11</sub>), 170.1, 170.3 (C<sub>1</sub>). Diastereoisomerism gives two peaks for some carbon atoms. HRMS (TOF MS, ESI): *m/z* calcd for C<sub>11</sub>H<sub>16</sub>O<sub>4</sub>Na: 235.0946; found: 235.0940

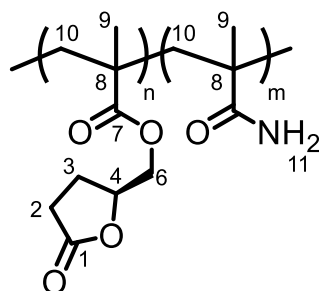
## Polymerizations

### Homopolymerization of (S)-5-(methyl)dihydrofuran-2(3H)-one methacrylate (poly 2H-HBO-m)

In a typical experiment, 500 mg of monomer were solubilized in toluene ( $C = 1M$ ); then 1 mol% of AIBN was added. The system was purged 3 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 pre-heated oil bath. The polymerization was stopped after 90 minutes 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 3 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 pre-heated oil bath. The polymerization was stopped after 90 minutes 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.

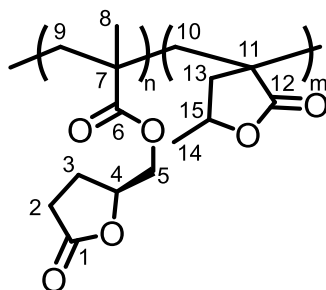




$^1\text{H}$  NMR (DMSO, 500 MHz):  $\delta_{\text{H}}$  0.87 (m, 4.16H, H<sub>9</sub>), 1.78 (m, 3.13H, H<sub>10</sub>), 2.43 (m, 3.84H, H<sub>2,3</sub>), 4.07 (m, 1.80H, H<sub>6</sub>), 4.76 (m, 1.01H, H<sub>4</sub>), 7.04 (m, 0.76H, H<sub>11</sub>).

### Copolymerization of (S)-5-(methyl)dihydrofuran-2(3H)-one methacrylate with methylene- $\gamma$ -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 3 times (vacuum-nitrogen cycles) on a Schlenk line. The solution was stirred under N<sub>2</sub> for 30 min and was then heated to 75 °C with a pre-heated oil bath. The polymerization was stopped after 90 minutes by exposure to air. The polymer was then precipitated by the addition of MeOH, resolubilized in hot CHCl<sub>3</sub> and purified again by precipitation via MeOH addition.

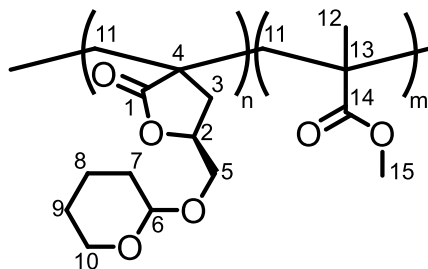


$^1\text{H}$  NMR (CDCl<sub>3</sub>, 500 MHz):  $\delta_{\text{H}}$  1.03 (br, 2.59H, H<sub>8</sub>), 1.45 (br, 4.6H, H<sub>14,8</sub>), 1.70 (br, 2.41H, H<sub>13</sub>), 2.09 (br, 5.44H, H<sub>3,9,10</sub>), 2.43 (br, 1.48H, H<sub>3</sub>), 2.63 (br, 2.00H, H<sub>2</sub>), 4.19 (br, 2H, H<sub>5</sub>), 4.64 (br, 1H, H<sub>15</sub>), 4.83 (br, 1H, H<sub>4</sub>).

### 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 3 times (vacuum- nitrogen cycles) on a Schlenk line. The solution was stirred under N<sub>2</sub> for 30 min and was then heated to 75 °C with a pre-heated oil bath. The polymerization was stopped after 90 minutes by exposure to air. The polymer was then precipitated by addition of hexane, resolubilized in hot CHCl<sub>3</sub> and purified again by precipitation via hexane addition.



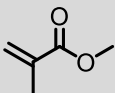
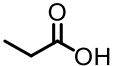
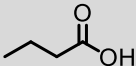
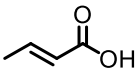
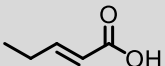
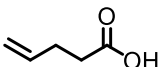
<sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz):  $\delta_{\text{H}}$  1.54 (br, 12.45H, H<sub>7,8,9,11,12</sub>), 2.26 (br, 1.66H, H<sub>3</sub>), 3.52 (br, 1.61H, H<sub>5,10</sub>), 3.65 (br, 2.65H, H<sub>15</sub>), 3.82 (br, 1.78H, H<sub>5,10</sub>), 4.03 (br, 0.26H, H<sub>5</sub>), 4.68 (br, 2H, H<sub>2,6</sub>).

## Results and discussions

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.<sup>18</sup> It is noteworthy to mention that supported enzyme - attached to acrylic resin for example - can be used over a wider temperature range.<sup>19</sup> 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 w% CAL-B was performed in toluene at 70 °C. Unfortunately, no conversion was observed after 24 hours 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 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-butenoic 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,

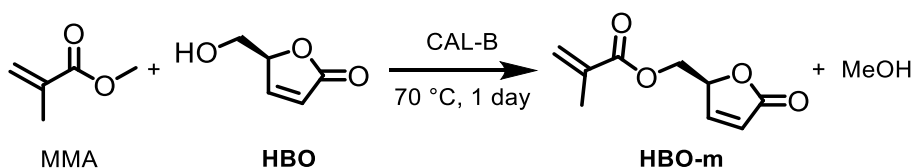
**Table 1.** Esterification of **HBO** with different acyl substrates in the presence of CAL-B.<sup>a</sup>

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

<sup>a</sup>Conditions: 3 equiv. of substrate; 10 w% of CAL-B; **HBO** 1M in toluene; 70 °C, 1 day.

hindering any nucleophilic attack. Finally, an attempt with a non-conjugated, 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-workers<sup>20</sup> reported the bio-catalyzed transesterification of unsaturated fatty alcohols with methyl methacrylate in the presence



**Scheme 3.** Synthesis of **HBO-m** through chemo-enzymatic transesterification.

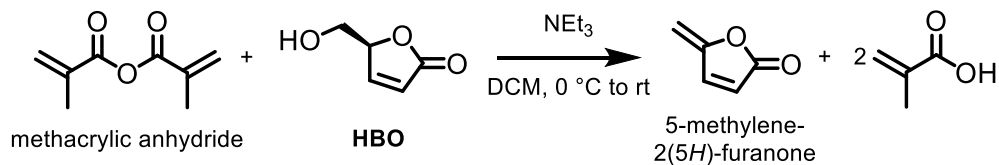
of lipase. The reaction did occur in organic solvents such as toluene and tetrahydrofuran (THF), but the yield did not exceed 40%. Although a rather high loading of CAL-B was employed (at least 30 w%, triple the usual loading), the reaction proceeded at a moderate temperature of 30 °C. In their study, 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 w% to reduce the cost of the process (Scheme 3).

**Table 2.** Esterification of **HBO** in **HBO-m** in presence of CAL-B.<sup>a</sup>

Entry	MMA (eq.)	T (°C)	Conv. (%) <sup>a</sup>	Yield <sup>b</sup> (%)
1	25	50	46	38
2	25	70	70	64
3	25	80	24	22
4	100	70	69	64

<sup>a</sup>Conditions: 10 w% of CAL-B, 1 day. <sup>a</sup> Estimated by <sup>1</sup>H NMR in CDCl<sub>3</sub>. <sup>b</sup> Yield obtained after purification.

Table 2, Entry 1 shows that at 50 °C the chemo-enzymatic esterification of MMA with **HBO** does occur with a moderate conversion of 46%. With a boiling point of 101 °C, excess MMA was easily removed during 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.



**Scheme 4.** Methacrylation of **HBO** resulting in the formation of 5-methylene-2(5H)-furanone.

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%). Subsequent polymerizations were attempted either without further purification or after silica gel chromatography column and no notable differences were observed. It is worth noting that 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 minutes 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 minutes after addition. The product was isolated after purification over silica gel chromatography with a lower yield than the chemo-enzymatic method.

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 polymerization, the polymers precipitated from the toluene solution. Moreover, they were not soluble in gel permeation chromatography (GPC) solvents THF or hexafluoroisopropanol (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).

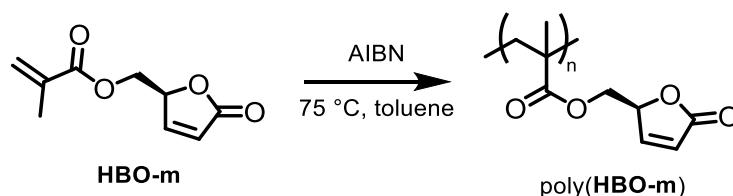
**Table 3.** Homopolymerization of **2H-HBO-m** and polymer thermal data.<sup>a</sup>

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

<sup>a</sup>Conditions: 1M of monomer in toluene; 1 mol% initiator; 90 minutes. <sup>b</sup>Determined by DSC under N<sub>2</sub>.

Homopolymerization of **HBO-m** (Scheme 5) was also attempted with the same 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 hours, 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 <sup>1</sup>H NMR analysis mainly showed monomer peaks. Homopolymerizations with longer reaction times (3, 6, 12, and 24h) 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 w%), 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.

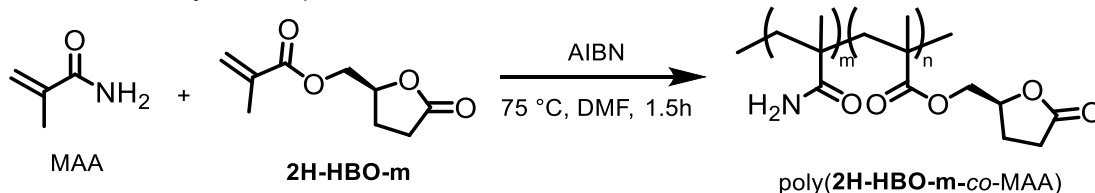


**Scheme 5.** Homopolymerization of **HBO-m**.

Consequently, the  $\alpha,\beta$ -unsaturated lactone was suspected to hinder the acrylate polymerization. Note 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 S107 in the ESI). 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, dimethyl formamide (DMF) was employed as the polymerization solvent. Table 4 describes the copolymerization of **2H-HBO-m** and MMA with different feed fractions. 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;<sup>21</sup> 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 & 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



**Table 4.** Incorporation, molecular weight, and thermal data for poly(**2H-HBO-m-co-methacrylamide**).

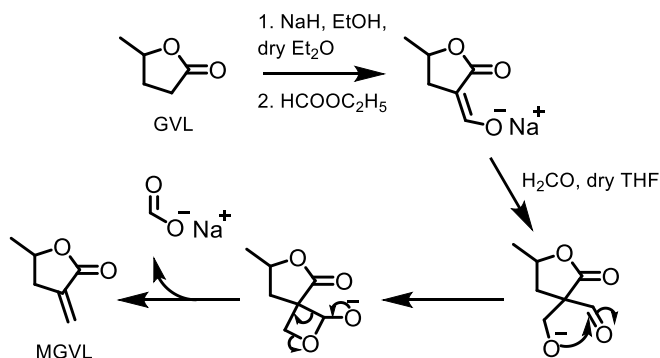


Entry	Feed Fraction 2H-HBO-m / MAA	Incorporation <sup>a</sup> 2H-HBO-m / MAA	$M_n$ (kDa) <sup>b</sup>	$\bar{D}^b$	$T_g$ (°C) <sup>c</sup>	$T_{d5\%}$ (°C) <sup>d</sup>
1	90/10	100/trace	23.5	2.2	94	228
2	80/20	98/2	20.7	2.3	115	217
3	70/30	78/22	28.7	2.1	128	198
4	60/40	76/24	19.2	2.0	143	261
5	50/50	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

<sup>a</sup>Incorporation was measured by <sup>1</sup>H NMR in CDCl<sub>3</sub>. <sup>b</sup>GPC in hexafluoroisopropanol (HFIP) at 40 °C vs. polymethyl methacrylate standards <sup>c</sup>Determined by DSC under N<sub>2</sub>. <sup>d</sup>TGA temperature at which 5% mass loss was observed under nitrogen.

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 & 3) were reached with typical dispersities ranging between 1.7 and 2.3 (Entries 6 & 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

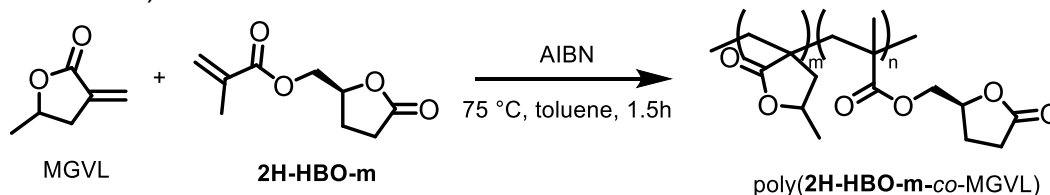
measured by  $^1\text{H}$  NMR (Figure 1). For example, the small feed fraction of 10% MAA allowed only traces of incorporated MAA and the corresponding  $T_g$  of 94 °C aligns with that of poly(**2H-HBO-m**) itself (93–102 °C). Entries 4 & 6 show intermediate MAA incorporations of 24 and 26% with similar  $T_g$  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- $\gamma$ -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,  $\gamma$ -valerolactone (GVL), is easily produced from biobased levulinic acid (LA) through carbonyl reduction followed by ring closing.<sup>22,23</sup>



**Scheme 6.**  $\alpha$ -methylenation of  $\gamma$ -valerolactone (GVL) to yield methylene- $\gamma$ -valerolactone (MGVL).

Then  $\alpha$ -methylenation can be performed in two steps, yielding MGVL. Scheme 6 describes one strategy used to synthesize MGVL from GVL.<sup>24</sup> The synthesis starts with  $\alpha$ -deprotonation of the lactone; the resulting enolate then attacks ethyl formate to form a salt which is isolated by filtration. A catalytic amount of ethanol substantially decreases the reaction time.<sup>25</sup>

**Table 5.** Incorporation, molecular weight, and thermal data for poly(**2H-HBO-m-co-MGVL**).

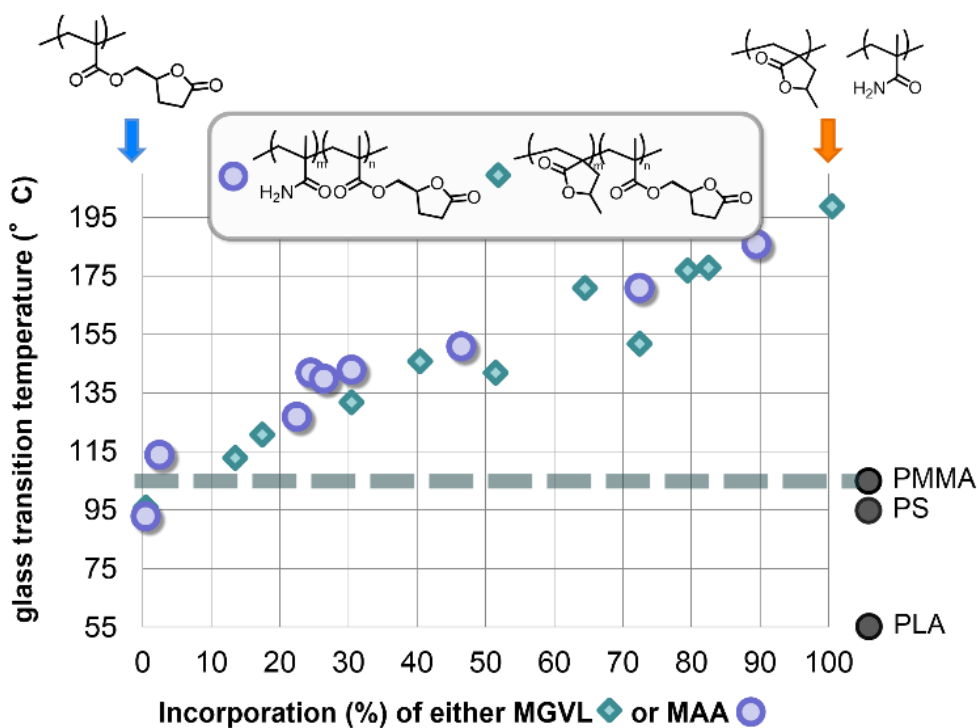


Entry	Feed Fractions	Incorporation <sup>a</sup>	$M_n$ (kDa) <sup>b</sup>	$\bar{D}^b$	$T_g$	$T_{d5\%}$
	<b>2H-HBO-m</b> / MGVL	<b>2H-HBO-m</b> / MGVL			(°C) <sup>c</sup>	(°C) <sup>d</sup>
1	90/10	88/12	insoluble	insoluble	114	212
2	80/20	83/17	insoluble	insoluble	122	273
3	70/30	70/30	insoluble	insoluble	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

<sup>a</sup>Incorporation was measured by <sup>1</sup>H NMR in CDCl<sub>3</sub> (S140). <sup>b</sup>GPC in hexafluoro-2-propanol (HFIP) at 40 °C vs poly(methyl methacrylate) standards. <sup>c</sup>Determined by DSC under N<sub>2</sub>. <sup>d</sup>TGA temperature at which 5% mass loss was observed under nitrogen.

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, vinyl-type polymers with MGVL generally exhibit high glass transition temperatures because of high conformational barriers associated with the

persistent lactone rings.<sup>24</sup> 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. Note that an incorporation of 82% of MGVL results in a soluble polymer (CDCl<sub>3</sub>) 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

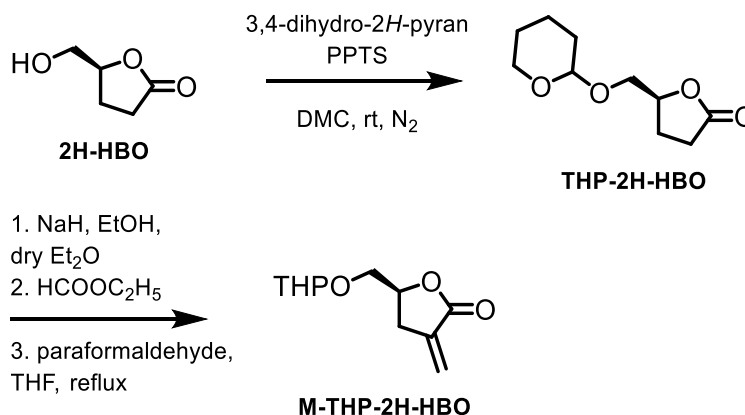


**Figure 1.** Polymer  $T_g$  values vs. MMA or MGVL comonomer incorporation compared to commodity plastics: PMMA (105 °C), PS (95 °C), and PLA (55 °C).

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 of Table 3, Entry 1. A substantially higher  $T_g$  of 150 °C is observed for 51% MGVL (Table 5, Entry 5) and a  $T_g$  of 179 °C is observed for 82% MGVL (Table 5, Entry 9). The spanned  $T_g$  range for poly(**2H-HBO-m-co-MGVL**) (98 to 200 °C) is similar to that of poly(**2H-HBO-m-co-MAA**) (98 to 187 °C).

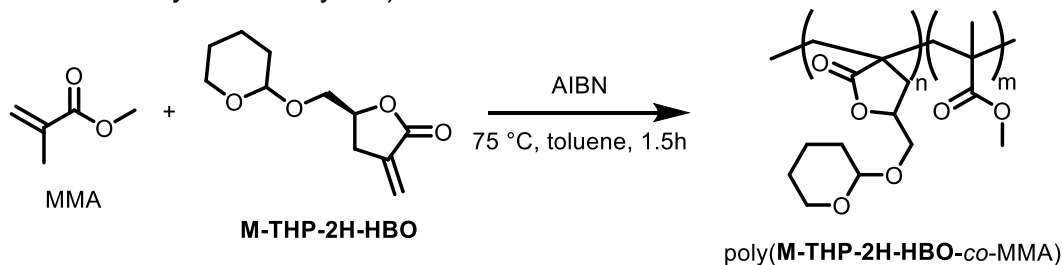
Inspired by the aforementioned synthesis of MGVL (from GVL) and its ability to impart high  $T_g$  values, we targeted the methylenation of **2H-HBO** itself. However, for this target, protection of the hydroxyl group was essential since the methods employed use strong bases, likely to form an alkoxide that might open the lactone.



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

Thus, the methylenation of **2H-HBO** (Scheme 7) starts with protection of the hydroxy group with 3,4-dihydro-2*H*-pyran to give the 2-tetrahydropyranyl (THP) protected **THP-2H-HBO**. Methylenation is related to that of Scheme 6 and affords the expected product, methylene-**THP-2H-HBO** (**M-THP-2H-HBO**). High reactivity of pure **M-THP-2H-**

**Table 6.** Incorporation, molecular weight, and thermal data for poly(**M-THP-2H-HBO**-co-methyl methacrylate).

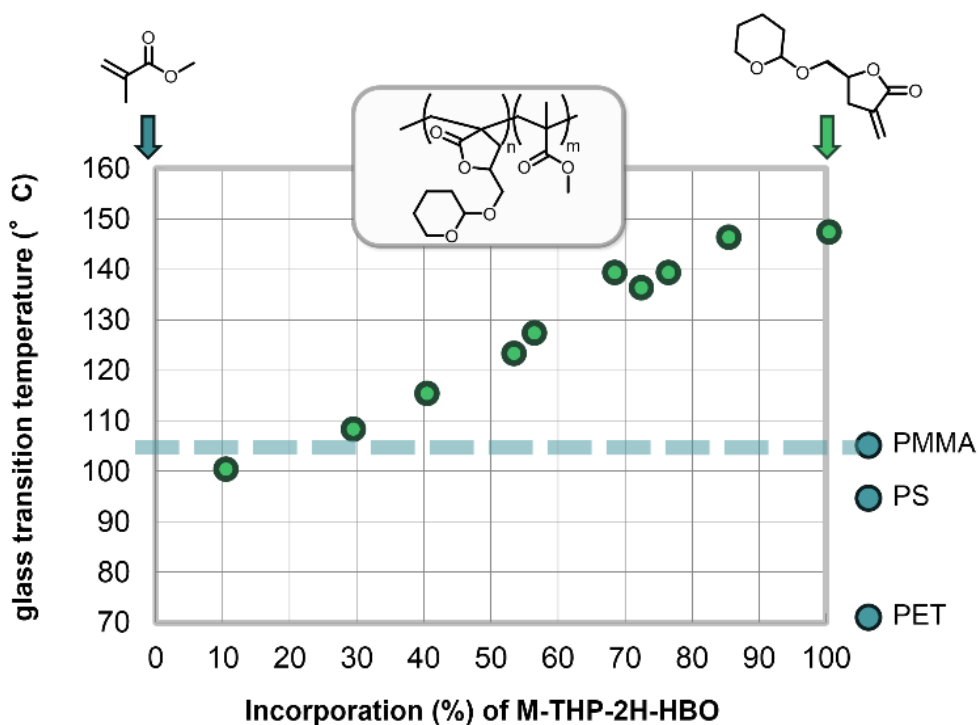


Entry	Feed fractions		Incorporation <sup>a</sup>		$M_n$ (kDa) <sup>b</sup>	$\bar{D}$ <sup>b</sup>	$T_g$ (°C) <sup>c</sup>	$T_{d5\%}$ (°C) <sup>d</sup>
	M-THP-2H-HBO / MMA	MMA / M-THP-2H-HBO	M-THP-2H-HBO / MMA	MMA / M-THP-2H-HBO				
1	10/90	90/10	10/90	90/10	14.9	2.2	101	162
2	20/80	80/20	29/71	71/29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

<sup>a</sup>Incorporation was measured by <sup>1</sup>H NMR. <sup>b</sup>GPC in hexafluoroisopropanol (HFIP) at 40 °C vs. polymethyl methacrylate standards. <sup>c</sup>Determined by DSC under N<sub>2</sub>. <sup>d</sup>TGA temperature at which 5% mass loss was observed under nitrogen.

**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.

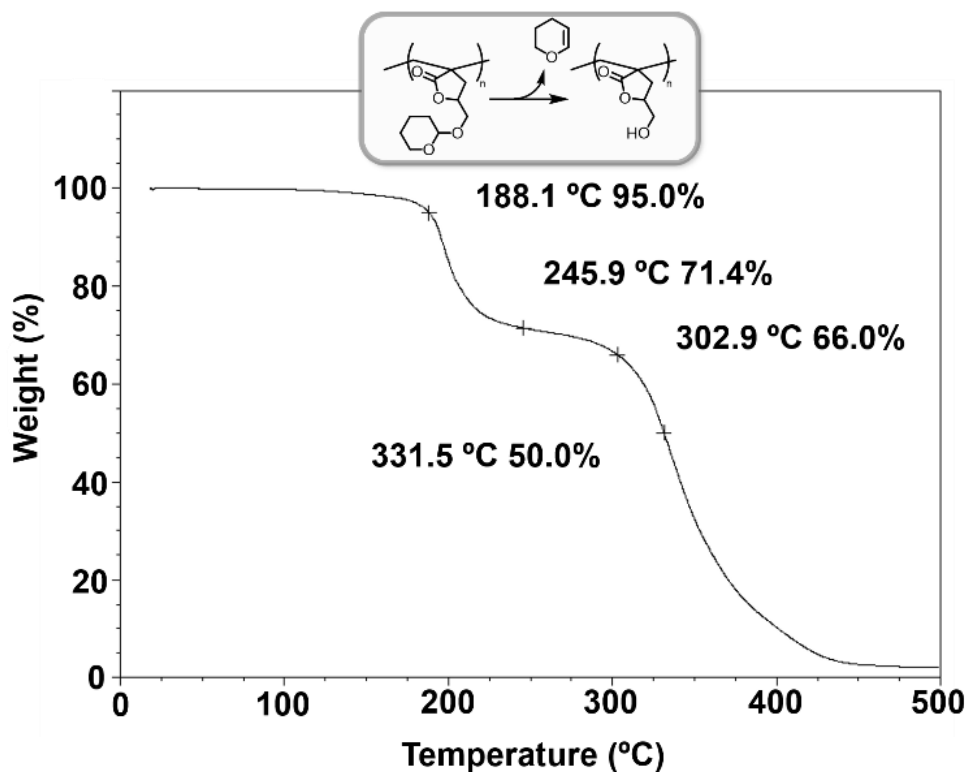
In order to compare poly(methyl methacrylate) (PMMA) and poly(**M-THP-2H-HBO**), copolymerizations with varying feed fractions were conducted using AIBN as the initiator in toluene at 70 °C for 1.5h. The materials were then precipitated by addition of hexane. Table 6 shows the experiments with various monomer loadings from 10% **M-THP-2H-HBO** (Entry 1) to 100% (Entry 9). High  $M_n$  values of 14.9 kDa, 22.0 kDa, 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.



**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).

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,

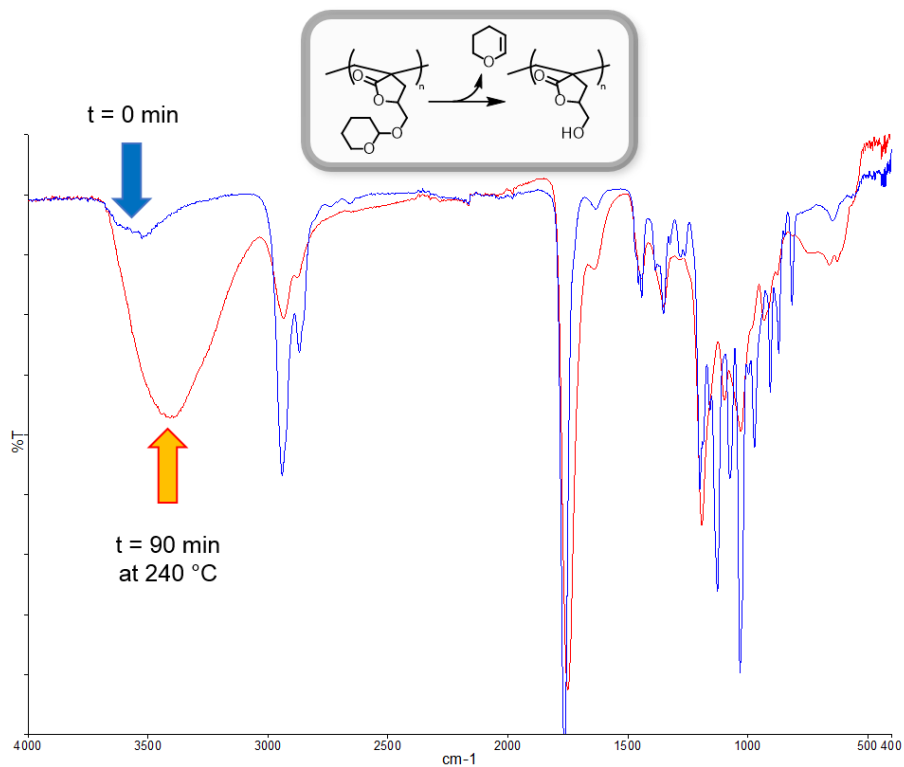
Entry 1) has a  $T_g$  of 101 °C. Polymers with a higher fraction of **M-THP-2H-HBO** exhibit proportionally higher  $T_g$  values, as illustrated in Figure 2. Figure 3 shows the thermal degradation analysis (TGA, under nitrogen) of poly(**M-THP-2H-HBO**) (Table 6, Entry 10) with a  $T_{d5\%}$  (5% mass loss) around 188 °C; this is comparable to other  $T_{d5\%}$  values of the series. Note that the mass loss later reached a plateau at 246 °C (29% mass loss) until 303 °C (34% mass 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 attempt to verify this assumption, **M-THP-2H-HBO** was heated up to 240 °C for 5 min, 30 min, or 90 min. The insolubility of the resulting material prohibited any



**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.



NMR analysis but IR spectroscopy showed a broad band around 3400-3500  $\text{cm}^{-1}$  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).



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

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  $^{13}\text{C}$  NMR or  $^1\text{H}$  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 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 chemo-enzymatic 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). An additional effect of this comonomer was to impart polymer solubility in organic solvents; even trace amounts of incorporated MMA allowed for solubility in the GPC solvent hexafluoroisopropanol (HFiP). A second copolymer series was created with **2H-HBO-m** and methylene- $\gamma$ -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 °C to 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  $\alpha$ -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.

Levoglucosenone (**LGO**) and its oxidized derivative (S)- $\gamma$ -hydroxymethyl- $\alpha,\beta$ -butenolide (**HBO**) have recently become available in useful quantities from various cellulosic biomass sources.<sup>26</sup> The chemistry reported herein describes the efficient production of acrylate monomers from **HBO** and their polymerization to promising polymers and copolymers with tuneable properties—especially glass transition temperature values competitive with several high- $T_g$  commodity plastics, including polyethylene terephthalate (PET), polystyrene (PS), polyvinyl chloride (PVC), polymethylmethacrylate (PMMA), and even polycarbonate (PC). Finally, these polymers have been designed for post-polymerization modifications, which will be reported in the future and will further expand their potential applications.

### Associated Content

The Supporting Information is available free of charge on the editor website at DOI: [10.1021/acssuschemeng.8b04707](https://doi.org/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.

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Notes: The authors declare no competing financial interest.

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