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Streamlining the Conversion of Biomass to Polyesters: Bicyclic Monomers with Continuous Flow

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Abstract

A three-step transformation of 1,4-cyclohexadiene (1,4-CHD) using continuous flow produced an aliphatic bicyclic monomer for polyester synthesis. The monomer synthesis involved catalytic alkene isomerization of 1,4-CHD to 1,3-CHD using a heterogeneous $Na_2O/Na/Al_2O_3$ catalyst, a Diels Alder reaction with maleic anhydride, and hydrogenation of the bicyclic monomer. A partially continuous strategy was compared with a fully continuous method. The continuous flow process streamlined the transformation of waste by-product biomass by minimizing workup procedures and reducing the synthesis time from ~1 day for batch processes to ~2.5 h. The monomer synthesis was easily scalable and allowed recycling of the catalysts for alkene isomerization and hydrogenation. The resulting bicyclic monomers were polymerized with glycerol and 1,4-butanediol (BDO) to obtain renewable polyesters with high thermal stability and tunable glass transition temperatures.

Introduction

Petroleum-based aromatic monomers have a long history in polymer science.[1] Familiar examples include terephthalic acid, styrene, divinyl benzene, bisphenol A, phenylenediamine, and phthalic anhydride. Since the rigidity and stability of the aromatic ring usually provides desirable physical properties, a wide variety of thermoplastic and thermoset materials have utilized these types of monomers.[2,3]

In recent years, renewable molecules have begun to emerge as alternatives to petroleum based chemicals.[4-8] Examples include systems based on lignin,[9-13] hemicellulose,[14] furans,[15-17] monoterpenes,[18-21] rosin,[22] plant oils,[23-25] cellulose,[26] and isosorbide.[27] Due to the variety of functional groups in renewable molecules, many possibilities exist for mimicking the structure of petroleum-based plastics which contain aromatic and cyclic structures.

Given recent reports of aromatic polymers based on lignin,[11,13] limonene,[28] and limonene oxide,[29] an investigation was conducted to determine whether aliphatic bicyclic molecules from a renewable source could provide an alternative to petroleum-based aromatic monomers. In many instances, polymers containing bicyclic rings demonstrate excellent mechanical properties,[30] high T_g values,[31-33] and a high degree of optical clarity[34] compared to polymers containing acyclic monomer units. Consequently, we hypothesized that the alkenes in the polyunsaturated fraction of plant oils could provide a pathway to bicyclic monomers and polyesters with high degrees of renewable carbon content. Therefore, this contribution focuses on a methodology to streamline the synthesis of biomass-based bicyclic monomers with continuous flow.

Continuous flow processes have demonstrated a great deal of promise for hydrogenations,[35] palladium catalyzed coupling reactions,[36] synthesis of conjugated polymers,[37] enzyme-catalyzed ring-opening polymerizations,[38] and the production of biomass-derived fuels.[14,15] To date, alkene isomerization reactions under continuous flow are common for petroleum derived chemicals, such as α-olefins,[39-41] but are very rare for renewable molecules.[42] Given the prevalence of alkenes in biomass, we were surprised that alkene isomerization of renewable molecules under continuous flow has received little attention.[43]

Currently, commercial oleochemical processes transform plant oils into chemicals with metathesis catalysts.[44] During the synthesis of these oleochemicals, the polyunsaturated fraction of plant oils will undergo an intramolecular reaction to form 1,4-cyclohexadiene (1,4-CHD) as a waste by-product.[45] From a green chemistry standpoint, obtaining 1,4-CHD from plant oils represents a sustainable alternative to the Birch reduction of benzene that requires Na metal in liquid NH_3 at -78 °C.[46] Although transforming a commercial waste by-product, such as 1,4-CHD, into bicyclic polyesters would be highly desirable, the alkenes in 1,4-CHD require isomerization in order to facilitate subsequent Diels-Alder reactions.

Catalytic alkene isomerization reactions represent an atom-economical transformation. For batch reactions, several ruthenium catalysts have been reported to isomerize allyl benzenes under homogeneous conditions.[47,48] Vaska's complex $[RuHCl(CO)[(C_6H_5)_3P]_3]$ has also been shown to isomerizes α-olefins,[49] triglycerides,[50] and 1,4-CHD via batch processes.[46] In this regard, the ability to isomerize dienes provides a substrate for Diels-Alder reactions while avoiding halogenated waste typically associated with dehydrohalogenation reactions.

Building upon the success of homogeneous batch reactions with ruthenium complexes, the current work examines a continuous alkene isomerization with a heterogeneous catalyst containing highly abundant and non-toxic elements (i.e. Na_2O/Na). Isomerization of alkenes with solid bases commonly involves supported metal oxides (Na_2O, K_2O, CaO, MgO, and ZrO_2) in combination with small amounts of alkali metals, such as sodium and potassium.[51-53] The resulting metal oxides are highly basic ($pK_a > 26$) and allow possibilities for catalyst recycling.[54]

The accepted mechanism for isomerization of alkenes with solid bases occurs via an allylic deprotonation mechanism.[54] Although this mechanism can require high temperatures (300 °C) for 1-butene and MgO,[52] more reactive catalysts will isomerize substituted alkenes at lower temperatures. For example, Na/NaOH on γ-Al_2O_3 isomerizes β-pinene and 5-vinylbicyclo[2.2.1]hept-2-ene at 25 °C and 20 °C, respectively.[55,56] In the current report, we hypothesized that the two alkenes on 1,4-CHD would enhance the acidity of the allylic hydrogens and allow facile isomerization. Since the isomerization of 1,4-CHD with solid bases had not been previously reported, it was worthwhile to investigate whether a Na_2O/Na catalyst could be integrated into a continuous flow approach to synthesizing renewable monomers.

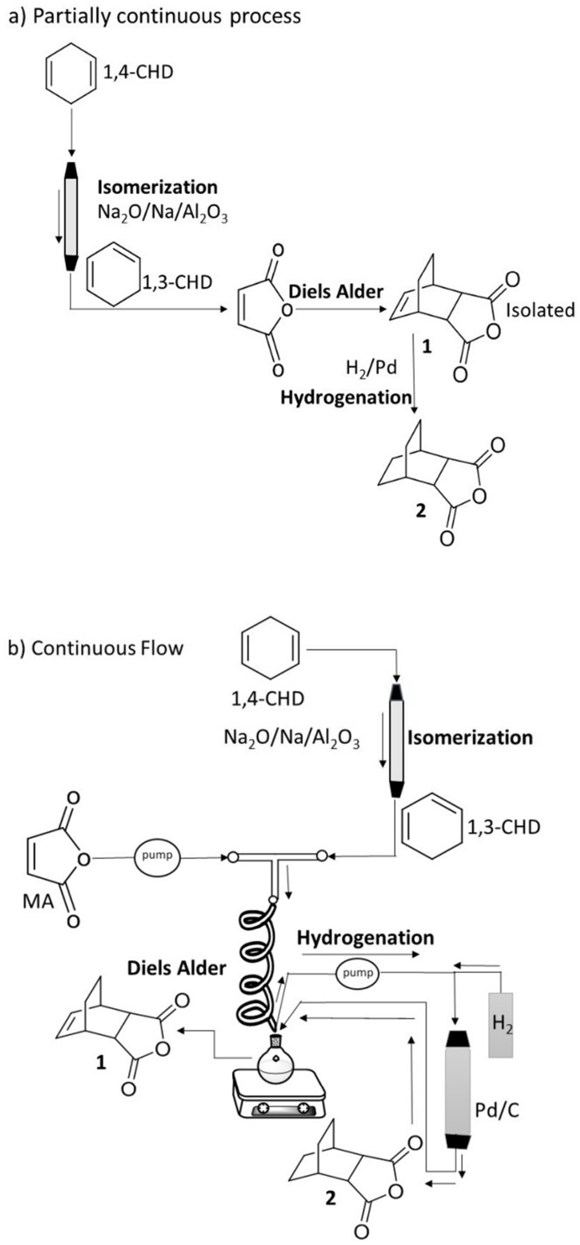
Under continuous flow conditions, the isomerization was followed by a Diels-Alder reaction with maleic anhydride (MA) and a subsequent hydrogenation. MA was chosen since the Diels-Alder reaction exhibits a high degree of reactivity without a catalyst, allows easy product recovery via crystallization, and can possibly be derived from biomass using furfural,[17] 5-hydroxyfurfural[57] or 1-butanol.[58] In effect, a renewable source of maleic anhydride offers an avenue for achieving 100 % renewable carbon content. Therefore, this approach provides a unique strategy for polyesters that complements current systems based on isosorbide,[59] limonene oxide,[29] linseed oil,[60] or malonate derivatives of fatty methyl esters.[61]

Results and Discussion

Part 1: Continuous monomer synthesis

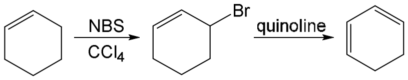
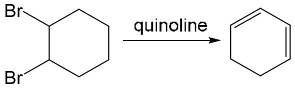
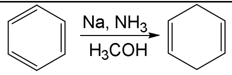
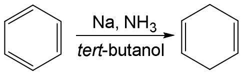
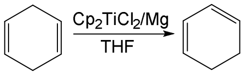
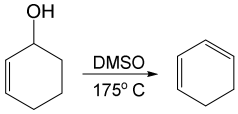
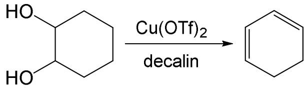
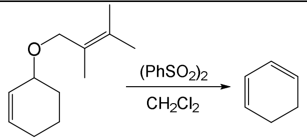
As depicted in Scheme 1, a cyclic diene (1,4-CHD) derived from the polyunsaturated fraction of soybean oil was isomerized and transformed into bicyclic monomers **1** and **2**. Based on variable temperature NMR studies of the equilibrium between 1,4- and 1,3-CHD, the ΔS and ΔH values for the isomerization limit the yield of 1,3-CHD (~60-65 %).[62] Nonetheless, our solvent-free strategy for transforming a waste by-product (i.e. 1,4-CHD) from a biorefinery into 1,3-CHD provides comparable yields and a smaller E-factor (~1) than conventional synthesis procedures (Table 1) with petroleum-based chemicals derived from benzene and cyclohexene. Additionally, given the moderate boiling points of 1,3-CHD (80 °C) and 1,4-CHD (88 °C), recovery of unreacted 1,4-CHD under reduced pressure is possible and would lower the E-factor in Scheme 1 from ~1 to ~0.5. Consequently, recovery of unreacted 1,4-CHD after the Diels-Alder reaction was given a priority.

In Scheme 1, two strategies were compared to examine the potential benefits of a continuous flow approach. The first strategy in Scheme 1a involved the continuous flow of 1,4-CHD through the isomerization reactor, but used batch conditions for the Diels-Alder reaction and subsequent hydrogenation in order to provide a benchmark and fully characterize each step of the three-step synthesis. After the Diels-Alder reaction, this partially-continuous strategy demonstrated recovery of unreacted 1,4-CHD under reduced pressure was possible.



Scheme 1. Multi-step transformation of 1,4-CHD to bicyclic-anhydrides **1** and **2** with a) partially-continuous process and b) continuous flow process for all three synthesis steps.

Table 1. Evaluation of E-factors for petroleum-based synthesis of 1,3-CHD.

Entry	Reaction	Yield (%)	E-factor	Ref.
1		51	~65	63
2		21	~33	63
3a		39	>35[a]	64
3b		90	>62[b]	65
3c		58	~11	66
4		40	>3[a]	67
5		35	~21	68
6		nd[c]	~22	69

[a]Product washed with unspecified volume of water. [b]Product washed with unspecified amount of HCl. [c]Not determined.

In the second strategy, all three steps in Scheme 1b were conducted under continuous flow. The goal of this continuous approach was to find the balance between maximizing product yield while minimizing the reaction time and eliminating workup procedures. Overall, a combination of solubility studies for starting materials and products (Table S1), yield data at various times and temperatures (Figure S2, Tables S2 and S3), and analysis of reaction kinetics (Figures S3, S14, S15) enabled refinement of Scheme 1b. Consequently, we were able to determine the optimal solvent, flow rate, concentration, temperature, and reaction time for the purpose of merging three distinct chemical reactions with different requirements into a continuous flow system.

In order to create a continuous isomerization reactor (Figure S1), nitrogen pressure (10 psi) flushed neat 1,4-CHD from a small reservoir (50 mL) through a temperature controlled column containing a heterogeneous Na_2O/Na catalyst. Based on GC analysis of product yield at different flow rates and temperatures (Table S2), the optimum conditions for our column dimensions occurred at 0 °C with flow rates between ~1.3-1.5 mL/min. These conditions provided the necessary residence time for isomerization while minimizing the exothermic conversion of 1,4-CHD to benzene which predominately occurred above 15 °C.[70] Since the reactor design excluded atmospheric moisture and CO_2 that could deactivate the catalyst, recycling was feasible (Figures 1 and S2). In fact, a reduction in catalyst activity only occurred if protic impurities, such as water, were present in the 1,4-CHD.

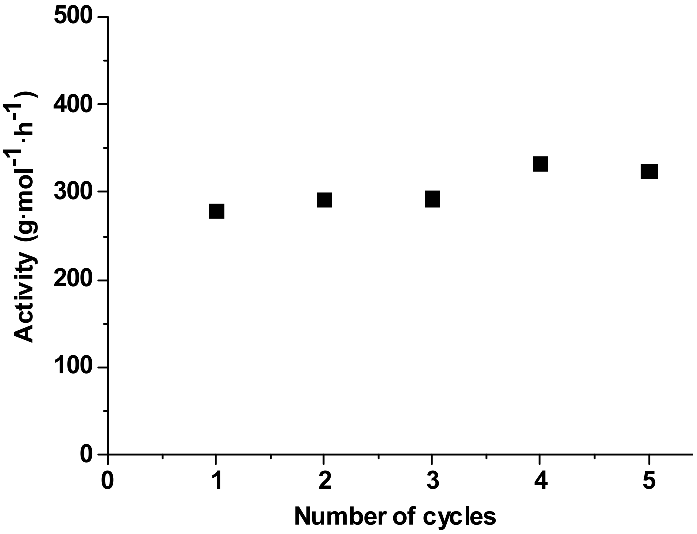


Figure 1. Recycling of the $Na_2O/Na/Al_2O_3$ catalyst used for isomerization of 1,4-CHD under continuous flow conditions at 0 °C. The activity was calculated from grams of 1,3-CHD per mol of Na_2O per h.

In Scheme 1a, 1,3-CHD was added to solid maleic anhydride (MA) without organic solvent. Provided the reaction temperature was above the melting point of MA, the MA dissolved fairly easily in neat 1,3-CHD after ~5-10 min with some heating (50-60 °C) and stirring to give reasonable high yields (Table S3). The resulting yellow solution eventually became clear as the reaction neared completion. We observed that [1,3-CHD]/[MA] ratios of 1.3-1.5 gave higher yields (85-90 %) after 3 h compared to the 65 % yield obtained with a ratio of 1.[71]

Upon cooling the batch reaction to ambient temperature, unreacted 1,4- and 1,3-CHD was recycled under reduced pressure before recrystallizing the product. Based on ^1H NMR, FTIR spectroscopy, and DSC, recrystallization of **1** in ethanol provided a method for separating unreacted MA from the product. The C-H bond for the alkene in **1** was detected by ^1H NMR (Figure 2b, δ 6.34 ppm), ^{13}C NMR (Figure S5, δ 133.05 ppm), and FTIR (Figure S6, 3055 cm^{-1}). Additionally, monomer **1** was confirmed by high resolution LC/MS (*m/z* 179.07023, error -0.27 ppm, Figure S7). Characterization of **1** by DSC (Figure S10) detected a large endotherm at 115 °C and a very small endotherm at 149 °C.[72]

Hydrogenation of **1** under batch conditions was achieved in a glass pressure bottle with Pd/C. ^1H NMR spectroscopy (Figure 2a) indicated nearly quantitative disappearance (> 99.8 %) of the alkene resonance at δ 6.34 ppm after a 24 h period, while the anhydride remained unchanged.[73] The hydrogenation of the alkene was also confirmed by FTIR (Figure S11) and LC/MS (*m/z*181.08590, error -0.115 ppm, Figure S12).

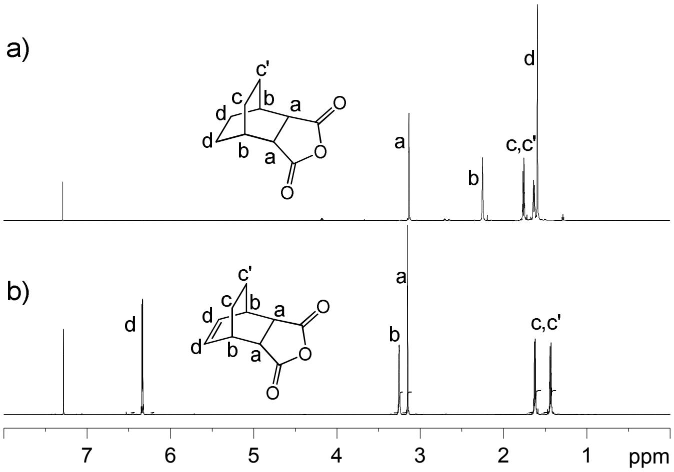


Figure 2. ^{1}H NMR ($CDCl_3$, 700 MHz) spectra for a) hydrogenated bicyclic-anhydride (**2**) and b) Diels-Alder adduct (**1**).

The second strategy Scheme 1b allowed all three synthesis steps to be conducted in a continuous manner. After the 1,4-CHD passed through the catalyst column containing Na_2O/Na and exited as 1,3-CHD, a stream of MA in ethyl acetate was introduced with a syringe pump. After evaluating a number of solvents (Table S1), ethyl acetate was chosen since it provided solubility for 1,3-CHD, MA, and monomer **1**. The concentration of MA was based on solubility limits in Table S1 in order to preclude precipitation of **1** or **2** in the reactor.[74]

Analysis of reaction kinetics provided insight for optimizing a continuous Diels-Alder reaction in ethyl acetate. For example, the relative reaction rates in Figure S3 at 50 °C ($k_{rel} = 1$)

and 75 °C ($k_{rel} = 4.4$) confirmed that the temperature which approached the boiling point of ethyl acetate (b.pt. 77 °C) was beneficial for achieving suitable yields in < 1.5 h. Consequently, the flow rate for the syringe pump containing MA/ethyl acetate was set to allow sufficient time for the Diels-Alder reaction to occur as the solution passed through coiled tubing immersed in a heating bath at 75 °C. Isolation of **1** after 1 h revealed that a [1,3-CHD]/[MA] ratio of 1.3 gave > 95 % yield.[75]

Comparison of the Diels-Alder reaction in Scheme 1a and 1b led to two observations. First, the partially continuous method in Scheme 1a made recovery of unreacted cyclohexadiene easier due to the neat Diels-Alder reaction. Second, the fully continuous system in Scheme 1b gave higher yields of **1** and avoided a recrystallization step to remove unreacted MA.

Conducting the continuous hydrogenation of **1** in a modified HPLC column with a hydrogen inlet allowed catalyst recycling, much more efficient gas-liquid-solid interactions, and faster reaction times compared to batch reactions.[35,76] As depicted in Scheme 1b, an HPLC pump recirculated a solution of **1** in ethyl acetate through the catalyst bed containing Pd/C at a flow rate which provided plug flow mixing between ethyl acetate and hydrogen.[77] Clear Teflon® tubing was useful for observing the hydrogen bubbles before and after the catalyst tube.

The hydrogenation of **1** was monitored by disappearance of the alkene C-H absorbance (3055 cm^{-1}) in the FTIR spectrum (Figure S13). Generally, the rate of hydrogenation increased with increasing catalyst loading and solution concentration and could be adjusted to provide a hydrogenation time of < 60 min with yields > 95 %.[78] The kinetic data for hydrogenating a bicyclic alkene ($k_{rel} = 1$) (Figure 3) was efficient, but a little slower than cyclooctene ($k_{rel} = 1.5$)

(Figure S14). Comparison of Figure 3 with batch hydrogenations suggested the plug-flow conditions substantially reduced the hydrogenation time.[79]

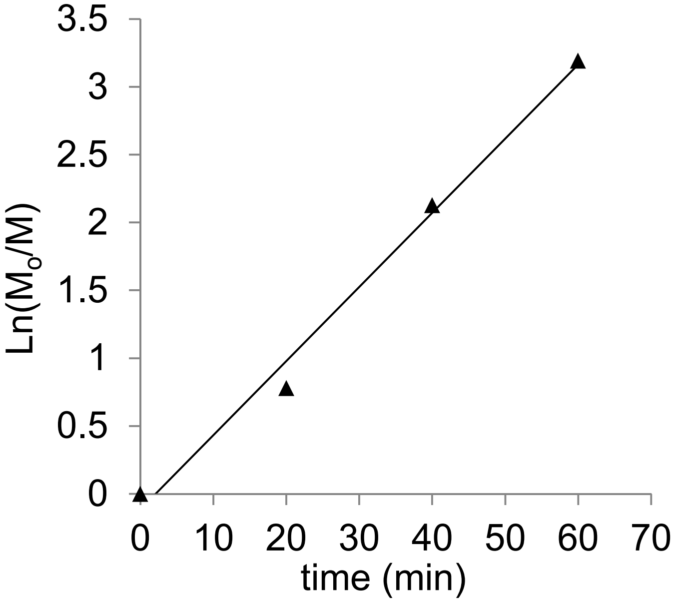
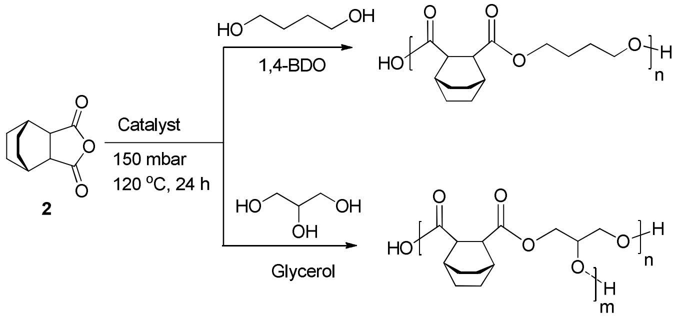


Figure 3. Continuous flow hydrogenation data for Diels Alder product (monomer **1**).

Part 2: Polymerization with renewable diols

Motivated by the desire to prepare polyesters in a green and sustainable manner, the polymerization of these bicyclic monomers was envisioned with two design criteria. First, we wanted to maximize the renewable carbon content. As a result, monomers **1** and **2** were polymerized (Scheme 2) with bio-based alcohols, such as 1,4-butanediol (1,4-BDO) and glycerol. The renewable carbon content for polymerizing **2** and 1,4-BDO would be ~71 % if maleic anhydride was petroleum-based and 100 % if maleic anhydride was bio-sourced. Second, we were interested to determine if melt polymerizations could effectively proceed at moderate temperatures. Attributes of monomers **1** and **2** include a low melting point (Figure S10) and reasonably high solubility with alcohol containing monomers. As a result, melt polymerizations were examined at temperatures (120 °C) which are lower than those typically associated with synthesis of polyesters. For instance, the temperatures for polymerizing phthalic anhydride with 1,2-propylene glycol (170-210 °C)[80] and dimethyl terephthalate with 1,4-BDO (215-245 °C)[28] confirm that polyester polymerizations are often conducted above 200 °C. In the case of aliphatic polyesters, lower temperatures (≤ 120 °C) are often preferred in order to minimize formation of ether linkages in the polyester as well as cyclization of 1,4-BDO to tetrahydrofuran.[81] For our system, a polymerization temperature of 120 °C under reduced pressure allowed removal of water as the polymerization progressed while minimizing sublimation of monomers **1** or **2**.



Scheme 2. Polymerization of anhydride **2** with 1,4-butanediol (1,4-BDO) and glycerol.

The progress of these solvent-free polymerizations was conveniently monitored by FTIR spectroscopy (Figure 4) by comparing the anhydride absorbance (1776 cm^{-1}) of the monomer with the carbonyl stretch of the polyester (1726 cm^{-1}). As the Abs_{1726}/Abs_{1776} ratio increased with time for the polyesters, gel permeation chromatography (GPC) confirmed an increase in the weight-average (M_w) molecular weight and intrinsic viscosity ($[\eta]$).[82] The functionality of glycerol afforded higher molecular weights compared to polyesters derived from 1,4-BDO.

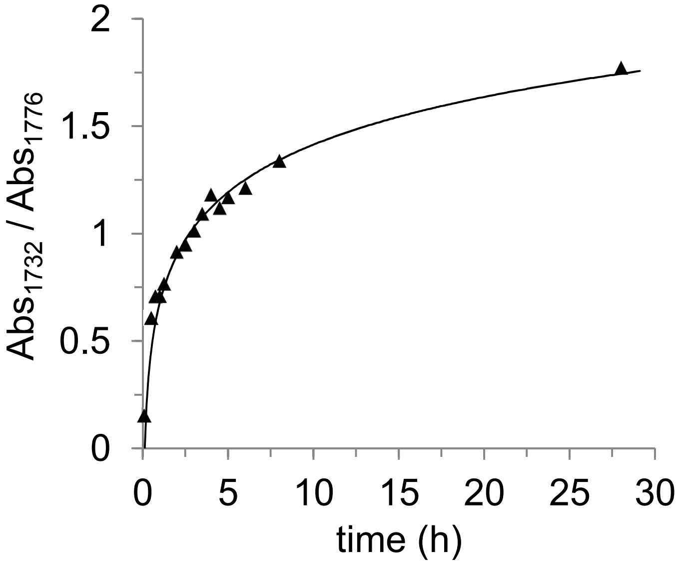


Figure 4. FTIR spectroscopy data for the polymerization of 1,4-BDO and **1** ([1,4-BDO]/[**1**] = 1) at 100 °C with *para*-toluenesulfonic acid (PTSA).[82] The solid line represents the logarithmic regression.

Since both the primary and secondary alcohols on glycerol participate in the polymerization, a branched structure is expected at conversions below the gel point.[83] GPC measurements of these polyesters below the gel point gave Mark Houwink Sakurada (MHS) exponents (a = 0.33-0.48) which are less than linear polymers (0.6-0.8). As a result, the polyesters made with glycerol are expected to have a highly branched structure.

Analysis of the polymerization of **2** with glycerol by ^{13}C NMR (Figure S17) detected carbonyl resonances for ester groups involving the primary alcohol on glycerol (δ 174.78 ppm) as well as the secondary alcohol on glycerol (δ 174.00 ppm). These carbonyl resonances were distinct compared to monomer (δ 173.98 ppm) and carboxylic acid (δ 178.08 ppm) terminated polyesters.

In Figure 5 and Table S5, a range of molecular weight values could be obtained for the polymerization of **2** and glycerol. All of these polyesters were below the gel point and displayed excellent solubility in common organic solvents.[84] Generally, PTSA gave larger FTIR absorbance ratios, higher M_w values, and lower molecular weight distributions (PDI = 2.2) compared to $Zn(OAc)_2$ and $Ti(OBu)_4$.

Part 3: Physical properties of polymers

Initially, a comparison of a Brønsted acid (PTSA) with Lewis acids [$Zn(OAc)_2$ and $Ti(OBu)_4$] was undertaken in order to determine the best procedure for obtaining polyesters with reasonably high decomposition (T_d) and glass transition (T_g) temperatures. Since PTSA combined with the higher functionality of the glycerol gave the highest M_w, T_d, and T_g values, this polymerization system was further examined using different mole ratios. In Figure 5, a wide range of M_w and T_g (25-63 °C) values were accessible by varying the [glycerol]/[anhydride **2**] ratio. In contrast, polymerizations (Figures S18 and S19) with a constant mole ratio of monomers revealed that the initial increase in M_w and T_g values began to plateau after a 28 h period.

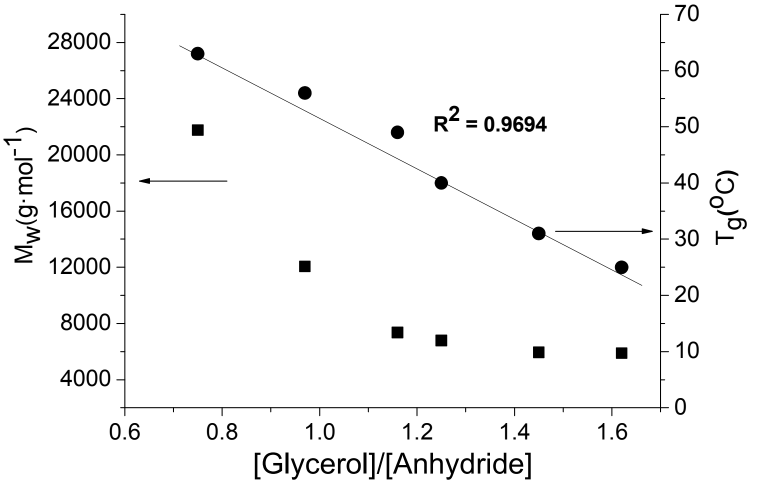


Figure 5. Effect of [glycerol]/[anhydride **2**] ratio on the molecular weight and glass transition temperature of polymers.

In order to further investigate the thermal stability of monomers **1** and **2**, a comparison of thermal stability was undertaken (Figure 6). According to TGA measurements, polyesters derived from glycerol showed excellent thermal stability as evidenced by the onset of decomposition (372-380 °C). Interestingly, complete polymer degradation (> 99 %) was observed at temperatures up to 600 °C for monomer **2** (Figure 6a). Polyesters which contain monomer **1** are slightly less thermally stable than the hydrogenated analogue (**2**) due to a retro Diels-Alder reaction. For comparison, polyesters derived from anhydride **2** showed similar decomposition temperatures as polymers made with phthalic anhydride (Figure 6c).

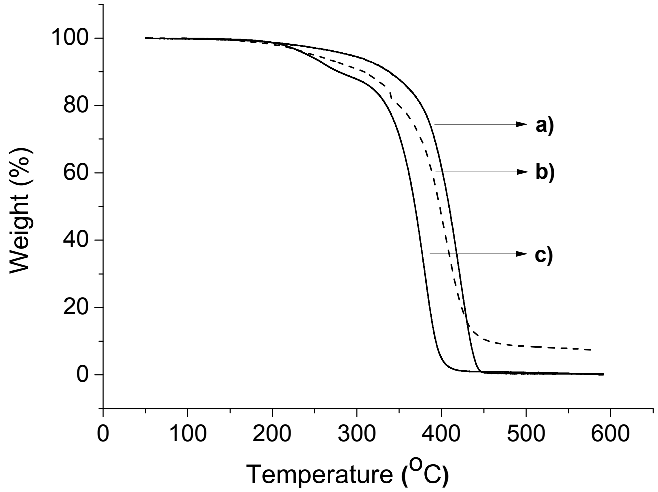


Figure 6. TGA data showing comparison of decomposition temperature (T_d) for 5 % weight loss of the polymers: a) anhydride **2** with glycerol (T_d = 292 °C); b) anhydride **1** with glycerol (T_d = 257 °C); c) phthalic anhydride with glycerol (T_d = 231 °C).

Experimental section

Materials. 1,4-Cyclohexadiene (1,4-CHD) containing ~20 % dodecene isomers was synthesized from soybean oil by metathesis.[46] The 1,4-CHD was dried over activated 4 Å sieves and stored in a refrigerator prior to use. $Na_2O/Na/Al_2O_3$ (11.5-13.5 % Na_2O, 1.8-3.0 % Na, SiGNa Chemistry), maleic anhydride (99 %, Acros), palladium on carbon (5 wt %, Sigma-Aldrich), 1,4-butanediol (> 99 %, Sigma-Aldrich), glycerol (> 99.5 %, Sigma-Aldrich), *para*-toluenesulfonic acid (PTSA) (97.5 %, Acros), zinc acetate dihydrate (98 %, Acros), and $Ti(OBu)_4$ (97 %, Sigma-Aldrich) were used as received.

Characterization. The ^1H and ^{13}C NMR spectra were measured at ambient temperature using Bruker Avance 700 MHz NMR in $CDCl_3$ (99.8 % D, Cambridge Isotope Laboratories).

FTIR spectra (32 scans) were recorded with a ZnSe ATR crystal at a 4 cm^{-1} resolution on a ThermoFisher Nicolet iS10 FTIR spectrometer. GC analysis of the isomerization of 1,4-cyclohexadiene was conducted under isothermal conditions at 50 °C with helium using thermal conductivity detector.

Molecular weights of the polymers were determined by gel permeation chromatography (GPC). The GPC system was equipped with a three-angle Wyatt Mini Dawn light scattering detector (λ = 690 nm, 30 mWGa-As laser), a Wyatt ViscoStar viscometer and a Wyatt OptiLabReX differential refractometer. The light scattering detector was calibrated with the known Rayleigh ratio for toluene. The specific refractive increments (dn/dc) were calculated with Wyatt Technology's Astra V software assuming 100 % mass recovery of the injected polymers. Two columns (PL gel, 5 μm MIXED-C linear, 300 mm x 7.5 mm) contained 5 μm particles with pore sizes ranging from 50 to 10^6 Å were heated at 35 ºC and eluted with tetrahydrofuran (1.0 mL/min). The polymers solutions (200 μL) in tetrahydrofuran (THF) were injected at a concentration of 10-15 mg/mL.

Glass transition (T_g) temperatures of the polymers were determined with a TA instruments Q20 differential scanning calorimeter (DSC) at a heating rate of 20 °C/min under nitrogen flow (20 mL/min). The reported T_g values were taken as the midpoint of transition from the second heating cycle. The decomposition temperature (T_d) was determined with a TA Instruments TGA Q500 at 20 °C/min under nitrogen.

Liquid chromatography/mass spectrometry (LC/MS) data was obtained by injecting a 1 μL aliquot into a Waters Acquity UPLC in line with a Thermo Scientific LTQ-Orbitrap in ESI(+) mode. The UPLC system was equipped with a BEH phenyl column (130 Å, 1.7 μm, 2.1 mm x

75 mm) equilibrated in 95 % solvent A (0.1 % formic acid) and 5 % solvent B (0.1 % formic acid in acetonitrile) at 0.400 mL/min. Mass spectra data were collected using full Fourier transform mode with 30000 resolution. The mass spectra across all peaks were averaged, and the neutral mass spectrum was extracted using the associated Thermo Scientific Qual Browser 2.0.7 SP1 software.

General procedure for continuous isomerization. A customized isomerization reactor was built with stainless steel Swagelok components (Figure S1). The reactor included a reservoir for 1,4-CHD, a catalyst tube, and a nitrogen inlet. The catalyst tube (ID 2.1 mm x 100 mm) was loaded with $Na_2O/Na/Al_2O_3$ in a glove box. On each end of the catalyst tube was a micron sized frit (1/4" x 1/32", Grace Davison) to contain the isomerization catalyst and a Swagelok valve to prevent atmospheric moisture from deactivating the catalyst.

After attaching the catalyst tube to the reactor under a nitrogen purge, 1,4-CHD was added to the solvent reservoir via syringe. The catalyst tube was immersed in a temperature-controlled bath and equilibrated. Next, the valves on the catalyst tube were opened to allow 1,4-CHD to flow through the temperature controlled catalyst tube under nitrogen pressure. The choice of nitrogen pressure depended on the pore size of the micron sized frits and the catalyst loading. Generally, with 100 mg of catalyst and 2 μm stainless steel frits, 10 psi of nitrogen was sufficient. The most consistent flow rates and isomerization yields were obtained with when new frits were used for each series of isomerization cycles.

The collected samples were analyzed by GC chromatography and FTIR spectroscopy. GC: retention time min (component, %) - 2.14 (benzene, 3.9 %), 2.21 (1,3-CHD, 63.8 %), 2.55 (1,4-CHD, 32.3 %). FTIR: 3090 cm^{-1} and 3071 cm^{-1}(=C-H stretching, benzene), 3036 cm^{-1}(=C-

H stretching, 1,3-CHD), 2925 cm^{-1}(-CH- stretching, 1,3-CHD), 1813 cm^{-1} (CH_2 wagging), 1478 cm^{-1} (-CH- bending 1,3-CHD), 1035 cm^{-1}, 977 cm^{-1} (-CH- out of plane bending).

Batch synthesis of monomer 1 from 1,3-CHD and maleic anhydride in Scheme 1a. 1,3-Cyclohexadiene (36.40 g, 0.454 mol) and maleic anhydride (29.10 g, 0.297 mol) were charged to a 250 mL Schlenk flask containing a magnetic stir bar. The Schlenk flask was then fitted with a condenser and placed under dynamic nitrogen after which the flask was heated to 60 °C. Within five minutes of heating all of the maleic anhydride had dissolved to form a bright yellow colored solution with concomitant refluxing of 1,3-cyclohexadiene followed by subsequent solidification of the charge to light yellow colored crystals within 25 minutes following the beginning of heating. The reaction was allowed to continue for a total of three hours after which unreacted 1,3-cyclohexadiene was removed via reduced pressure. Crystalline yellow solid was then recrystallized from 200 proof ethanol (~175 mL) and the Diels Alder adduct **1** was obtained as a crystalline white solid 46.54 g (88 % yield). ^{1}H NMR (700 MHz, $CDCl_3$, 25 °C): δ = 1.43 (d, J = 7.7 Hz, 2 H,CH_2 cyclohexene), 1.62 (d, J= 7.7 Hz, 2 H, CH_2 cyclohexene), 3.15 (t, 2H, -CH-CO)), 3.25 (m, 2 H, methine cyclohexene), 6.33 (dd, J = 7.7 Hz, 4.2 Hz, 3.5 Hz, 2 H, -CH=CH-). ^{13}C NMR (700 MHz, $CDCl_3$, 25 °C): δ = 22.98 (CH_2, cyclohexene), 31.63 (methine cyclohexene), 44.77 (-CH-CO), 133.05 (-C=C-), 172.83 (CO). FTIR: 3055 cm^{-1} (=C-H stretching), 2980-2870cm^{-1}(CH stretching), 1867-1766 cm^{-1} (C=O stretching), 1462-1322cm^{-1} (CH bending), 1238-1177cm^{-1} (C-O stretching), 1075-684 cm^{-1} (CH out of plane bending). LC-MS: *m/z* 179.07(M$^+$), 151.07, 147, 133, 123, 105, 79, 73.

Batch hydrogenation of monomer 1 in Scheme 1a. Diels Alder adduct (monomer **1**) (9.269 g, 0.0520 mol) dissolved in 100 mL ethyl acetate and 5 wt % palladium on carbon (0.250 g) were added in an Andrews Glass pressure bottle and purged with nitrogen. The reactor was then charged with H_2 (20 psi) and allowed to stir at room temperature while monitoring the reaction pressure. When the reaction pressure had dropped to 5 psi the system was recharged with H_2 (20 psi) and the process repeated over a period of 1 day until consumption of H_2 had ceased. The reaction mixture was centrifuged and the product mixture isolated by decantation. The Pd/C catalyst was washed with 25 mL aliquots of ethyl acetate and all filtrate portions combined and reduced to a solid under dynamic vacuum at room temperature to yield an off-white powder of anhydride **2**, 8.91 g (95.0 % yield). ^1H NMR (700 MHz, $CDCl_3$, 25 °C): δ = 1.58 (s, 4 H, CH_2 cyclohexane), 1.62 (dd, J = 7.7 Hz, 2 H, CH_2 cyclohexane), 1.74 (dd, J = 7.7 Hz, 2 H, CH_2 cyclohexane), 2.24-2.26 (m, 2 H, -CH- cyclohexane), 3.12 (dd, J = 3.5 Hz, 2.1 Hz, 2 H, -CH-CO). ^{13}C NMR (700 MHz, $CDCl_3$, 25 °C): δ = 21.37 (CH_2 cyclohexane), 24.12 (CH_2 cyclohexane), 25.98 (methine cyclohexane), 44.25 (-CH-CO) 173.98 (CO). FTIR: 2946 cm^{-1}, 2875 cm^{-1} (CH stretching), 1858-1745 cm^{-1} (C=O stretching), 1480-1316 cm^{-1}(CH bending), 1273-1196 cm^{-1} (C-O stretching), 1076-700 cm^{-1} (CH out of plane bending). LC-MS: *m/z* 181.08 (M^+), 167, 153, 139, 135, 107, 79.

Procedure for continuous isomerization, Diels alder reaction and hydrogenation in Scheme 1b. Isomerization catalyst $Na_2O/Na/Al_2O_3$ (0.100 g) was loaded in a catalyst tube in a glove box, connected to the isomerization reactor, and cooled at 0 °C for 15 min. A 5 mL aliquot of dried 1,4-CHD (3.4 g, 42.4 mmol) was added via syringe to the isomerization reactor under nitrogen atmosphere. After 1,3-CHD exited the isomerization reactor, the 1,3-CHD passed through a section of clear Teflon tubing for visual confirmation of the flow. Then, the output of 1,3-CHD was mixed with a stream of MA in ethyl acetate via a stainless steel T-tube connector. The MA (1.66 g, 16.9 mmol) in ethyl acetate (12 mL) was delivered by a syringe pump at a flow rate of 0.5 mL/min. After these two solutions of 1,3-CHD and MA mixed, they passed through coiled tubing (OD 3.175 mm, ID 1.75 mm, 35 feet) immersed in a heating bath (75 °C).

As the Diels-Alder reaction exited the coiled tubing, the eluent passed through a section of clear Teflon tubing for visual confirmation of the flow. Then, the solution, which contained monomer **1,** was collected in a graduated cylinder (submerged in a heated bath at 75 °C) in order to monitor flow rates and periodically assess the kinetics of the Diels-Alder reaction via FTIR spectroscopy. After ~45 min at 75 °C, the output of the Diels-Alder product had mostly ceased. The coiled tubing was flushed with pure ethyl acetate (~5 mL) to ensure the entire Diels-Alder product was recovered. Taking into account the time required to flush the tubing, the total time for the Diels-Alder reaction was ~80-90 min.

For the purpose of monitoring flow rates and calculating the yield of monomer **1**, the entire output from the continuous Diels-Alder reaction was collected before starting the continuous hydrogenation. This strategy also confirmed success of the isomerization and subsequent Diels-Alder reactions before proceeding to the hydrogenation step.

After the Diels-Alder reaction, the solution of **1** was combined with the pure ethyl acetate in the reservoir for the primed HPLC pump. The resulting concentration of **1** during hydrogenation was 0.06 g/mL. Hydrogenation of monomer **1** in ethyl acetate was conducted in a modified HPLC column with a hydrogen inlet. The catalyst tube contained 5 wt % Pd/C (0.5 g). An HPLC pump recirculated the reaction mixture through the catalyst tube at a flow rate of 1.8 mL/min with continuous hydrogen inlet pressure (125 psi) for 60 min at 25 °C. The completion of hydrogenation was verified by FTIR spectroscopy. The solvent was evaporated under dynamic vacuum to yield an off-white powder of anhydride **2** in > 95 % yield.

General polymer synthesis procedure. In a typical polymerization, a reaction vial (4 mL) was charged with bicyclic-monomer (**1** or **2**), comonomer (1,4-BDO or glycerol), and catalyst (0.2 mol %). After adding a stirbar, the mixture was heated at 120 °C in a customized multi-well aluminum reactor. With constant stirring (250 rpm), the monomer melted after ~15 min to give a clear solution. Then, the polymerization was continued under dynamic vacuum (150 mbar) at 120 °C. After obtaining yield via mass loss of water, the polymer was characterized by FTIR, GPC, NMR, DSC, and TGA.

Polymerization of monomer 2 and glycerol with PTSA. Monomer **2** (0.360 g, 2.0 mmol), glycerol (0.184 g, 2.0 mmol) and PTSA (0.7 mg, 0.004 mmol) was charged in a magnetically stirred reaction vial and heated at 120 °C in a customized multi-well aluminum reactor with constant stirring (250 rpm) until the monomer melts. After 15 min, the polymerization was continued under vacuum (150 mbar) at 120 °C for a period of 24 h. The polymerization progress was deduced from the FTIR spectra using a ratio of absorbances which corresponded to the starting monomer anhydride (1776 cm^{-1}) and the polymer (1726 cm^{-1}). GPC (in THF): M_w = 12050 g/mol, M_w/M_n = 2.43, [η] = 7.1 mL/g. ^{1}H NMR (700 MHz, $CDCl_3$, 25 °C): 1.45 (singlet broad, 4H, CH_2 cyclohexane), 1.53 (singlet broad, 2H, CH_2 cyclohexane), 1.57 (singlet broad, 2H, CH_2 cyclohexane), 2.07 (singlet broad, 2H, -CH-bridged), 3.04-3.12 (m, 2H, -CH-CO), 3.58-3.67 (m, 1H, -CH_2-CH-CH_2-), 3.92-4.38 (m, -CH_2-CH-CH_2-). ^{13}C NMR (700 MHz, $CDCl_3$, 25 °C): 21.33 (CH_2 cyclohexane), 25.31(CH_2 cyclohexane), 25.97(CH_2 cyclohexane), 27.29 (-CH- cyclohexane), 43.99-44.25 (-CH-CO), 61.1(CH_2-O-), 63.3 (CH_2-O-), 65.33 (CH_2-O-), 67.76 (-CH-O), 70.15 (-CH-O), 72.25 (-CH-O), 174.78 (CH_2-O-CO), 178 (-CH-O-CO).

Polymerization of phthalic anhydride and glycerol with PTSA. Phthalic anhydride (0.296 g, 2.0 mmol), glycerol (0.184 g, 2.0 mmol) and PTSA (0.7 mg, 0.004 mmol) was charged in a magnetically stirred reaction vial. The vial was placed in a customized multi-well aluminum reactor with constant stirring (250 rpm). The reaction was initially heated slightly above the melting point of phthalic anhydride to obtain a clear homogeneous solution. After 15 min, the polymerization was continued under vacuum (150 mbar) at 120 °C for a period of 24 h. GPC (in THF): M_w = 5103 g/mol, M_w/M_n = 1.36. DSC (20 °C/min): T_g = 74 °C (second heating cycle). TGA (20 °C/min): T_d = 230 °C (5 % weight loss temperature).

Conclusion

Transformation of a waste by-product (1,4-CHD) of the oleochemical industry with successive isomerization, Diels-Alder, and hydrogenation reactions provided a bicyclic alternative to aromatic monomers, such as petroleum-derived phthalic anhydride. In this regard, the continuous isomerization of 1,4-CHD with a heterogeneous catalyst, based on $Na_2O/Na/Al_2O_3$, provided a much lower E-factor (~1) than reactions with petroleum-based starting materials derived from benzene (E-factor > 30, see Table 1). Recycling the sodium oxide catalyst and ease of product recovery are other attractive options compared to conventional batch processes with homogeneous ruthenium-based isomerization catalysts.

In the current study, two synthesis strategies were compared to identify the best methodology for transforming 1,4-CHD into aliphatic polyesters. Both of these strategies offer advantages and disadvantages. For instance, the partially continuous method employs a solvent-free Diels-Alder reaction (E-factor = 1.2) that allows easy recycling of unreacted 1,4-CHD under reduced pressure. So, after recycling unreacted 1,4-CHD, the E-factor can be lowered to 0.7. On the other hand, the batch procedure takes longer time and requires recrystallization of **1** in ethanol which raises the E-factor to 3.7. In comparison, merging the continuous isomerization with a continuous Diels-Alder reaction in ethyl acetate makes recycling unreacted 1,4-CHD unlikely and gives an E-factor of 5.4.

The fully continuous strategy allowed much faster synthesis (~2.5 h) of monomers **1** and **2** compared to batch methods (~1 day).[85] However, a great deal of effort was required to optimize and merge three reactions. For instance, an understanding of solubility limits, flow rates, and reaction kinetics as a function of temperature was necessary. As a result, the experimental design was much more complicated than batch methods. Nonetheless, if a fully continuous method can be properly optimized, then additional purification steps, such as recrystallization of monomer **1** after the solvent-free Diels-Alder reaction, can be avoided.

Since continuous flow processes have demonstrated great utility in organic synthesis[86,87] and polymer chemistry,[88-90] as well as transformation of biomass to chemicals[91-94] and biofuels,[15,95] our results suggest continuous strategies also hold great promise for multi-step synthesis of biomass-derived monomers.

In the second part of this work, polymerization of bicyclic monomers (**1** and **2**) with glycerol and 1,4-BDO occurred at very reasonable temperatures (120 °C) and pressures (150 mbar) in order to minimize sublimation of **1** and **2**. The resulting amorphous polyesters demonstrated high thermal stability and a range of M_w, T_g, and $[\eta]$ values. The [glycerol]/[anhydride] ratio was determined to be an important parameter for controlling the polyester properties.

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References

1. H. F. Mark, ed., *Encyclopedia of Polymer Science and Technology*, Concise 3rd. edn., Wiley-Interscience, Hoboken, N.J., 2007.
2. G. Holden, N. R. Legge, R. P. Quirk and H. E. Schroeder, eds., *Thermoplastic Elastomers*, 2nd edn., Hanser Publishers, New York, 1996.
3. J. Brandrup, E. H. Immergut and E. A. Grulke, eds., *Polymer Handbook*, 4th edn., Wiley-Interscience, New York, 1999.
4. R. T. Mathers, *J. Polym. Sci., Part A: Polym. Chem.*, 2012, **50**, 1-15.
5. R. T. Mathers and M. A. R. Meier, eds., *Green Polymerization Methods: Renewable Starting Materials, Catalysis and Waste Reduction*, Wiley-VCH, Weinheim, 2011.
6. A. Gandini, *Green Chem.*, 2011, **13**, 1061-1083.
7. M. J. L. Tschan, E. Brule, P. Haquette and C. M. Thomas, *Polym. Chem.*, 2012, **3**, 836-851.
8. A. Gandini, *Macromolecules*, 2008, **41**, 9491-9504.
9. T. Saito, R. H. Brown, M. A. Hunt, D. L. Pickel, J. M. Pickel, J. M. Messman, F. S. Baker, M. Keller and A. K. Naskar, *Green Chem.*, 2012, **14**, 3295-3303.
10. L. Mialon, A. G. Pemba and S. A. Miller, *Green Chem.*, 2010, **12**, 1704-1706.
11. L. Mialon, R. Vanderhenst, A. G. Pemba and S. A. Miller, *Macromol. Rapid Commun.*, 2011, **32**, 1386-1392.
12. T. Kaneko, T. H. Thi, D. J. Shi and M. Akashi, *Nature Mat.*, 2006, **5**, 966-970.
13. J. F. Stanzione, J. M. Sadler, J. J. La Scala and R. P. Wool, *ChemSusChem*, 2012, **5**, 1291-1297.
14. H. Olcay, A. V. Subrahmanyam, R. Xing, J. Lajoie, J. A. Dumesic and G. W. Huber, *Energy & Environmental Science*, 2013, **6**, 205-216.
15. Y.-T. Cheng and G. W. Huber, *Green Chem.*, 2012, **14**, 3114-3125.
16. A. F. Sousa, M. Matos, C. S. R. Freire, A. J. D. Silvestre and J. F. J. Coelho, *Polymer*, 2013, **54**, 513-519.
17. Y. Tachibana, M. Yamahata and K.-i. Kasuya, *Green Chem.*, 2013, **15**, 1318-1325.
18. J. R. Lowe, M. T. Martello, W. B. Tolman and M. A. Hillmyer, *Polym. Chem.*, 2011, **2**, 702-708.
19. S. Kobayashi, C. Lu, T. R. Hoye and M. A. Hillmyer, *J. Am. Chem. Soc.*, 2009, **131**, 7960-7961.
20. R. T. Mathers, K. Damodaran, M. G. Rendos and M. S. Lavrich, *Macromolecules*, 2009, **42**, 1512-1518.
21. R. T. Mathers, K. C. McMahon, K. Damodaran, C. J. Retarides and D. J. Kelley, *Macromolecules*, 2006, **39**, 8982-8986.
22. P. A. Wilbon, F. Chu and C. Tang, *Macromol. Rapid Commun.*, 2013, **34**, 8-37.
23. Y. Xia, R. L. Quirino and R. C. Larock, *J. Renew. Mater.*, 2013, **1**, 3-27.
24. H. Mutlu, L. M. De Espinosa and M. A. R. Meier, *Chem. Soc. Rev.*, 2011, **40**, 1404-1445.
25. J. C. Ronda, G. Lligadas, M. Galia and V. Cadiz, *React. Funct. Polym.*, 2013, **73**, 381-395.
26. M. Rose and R. Palkovits, *Macromol. Rapid Commun.*, 2011, **32**, 1299-1311.
27. M. Rose and R. Palkovits, *ChemSusChem*, 2012, **5**, 167-176.

28. M. Colonna, C. Berti, M. Fiorini, E. Binassi, M. Mazzacurati, M. Vannini and S. Karanam, *Green Chem.*, 2011, **13**, 2543-2548.
29. E. H. Nejad, A. Paoniasari, C. G. W. van Melis, C. E. Koning and R. Duchateau, *Macromolecules*, 2013, **46**, 631-637.
30. P. H. Henna, M. R. Kessler and R. C. Larock, *Macromol. Mater. Eng.*, 2008, **293**, 979-990.
31. D. S. van Es, *J. Renew. Mater.*, 2013, **1**, 61-72.
32. R. T. Mathers, C. LeBlond, K. Damodaran, D. I. Kushner and V. A. Schram, *Macromolecules*, 2008, **41**, 524-526.
33. D. J. Burke, T. Kawauchi, M. J. Kade, F. A. Leibfarth, B. McDearmon, M. Wolffs, P. H. Kierstead, B. Moon and C. J. Hawker, *ACS Macro Lett.*, 2012, **1**, 1228-1232.
34. J. Yoon, R. T. Mathers, G. W. Coates and E. L. Thomas, *Macromolecules*, 2006, **39**.
35. M. Irfan, T. N. Glasnov and C. O. Kappe, *ChemSusChem*, 2011, **4**, 300-316.
36. W. Shu and S. L. Buchwald, *Chemical Science*, 2011, **2**, 2321-2325.
37. H. Seyler, D. J. Jones, A. B. Holmes and W. W. H. Wong, *Chem. Commun.*, 2012, **48**, 1598-1600.
38. S. Kundu, A. S. Bhangale, W. E. Wallace, K. M. Flynn, C. M. Guttman, R. A. Gross and K. L. Beers, *Journal of the American Chemical Society*, 2011, **133**, 6006-6011.
39. Ivanova, II, A. PasauClaerbout, M. Seirvert, N. Blom and E. G. Derouane, *Journal of Catalysis*, 1996, **158**, 521-536.
40. E. Mazoyer, K. C. Szeto, S. Norsic, A. Garron, J. M. Basset, C. P. Nicholas and M. Taoufik, *ACS Catalysis*, 2011, **1**, 1643-1646.
41. P. B. Webb, M. F. Sellin, T. E. Kunene, S. Williamson, A. M. Z. Slawin and D. J. Cole-Hamilton, *J. Am. Chem. Soc.*, 2003, **125**, 15577-15588.
42. E. Stashenko, H. Wiame, S. Dassy, J. R. Martinez and T. Shibamoto, *HRC-J. High Resolut. Chromatogr.*, 1995, **18**, 54-58.
43. Based on Web of Science search on July 10, 2013 using keywords: continuous flow, biomass, and monomer.
44. U. Biermann, U. Bornscheuer, M. A. R. Meier, J. O. Metzger and H. J. Schafer, *Angew. Chem. Intern. Ed.*, 2011, **50**, 3854-3871.
45. Mathers, R. T. 2012, U.S. Provisional Application No. 61/654,589.
46. R. T. Mathers, M. J. Shreve, E. Meyler, K. Damodaran, D. F. Iwig and D. J. Kelley, *Macromol. Rapid Commun.*, 2011, **32**, 1338-1342.
47. B. Lastra-Barreira, J. Francos, P. Crochet and V. Cadierno, *Green Chemistry*, 2011, **13**, 307-313.
48. A. E. Díaz-Álvarez, P. Crochet and V. Cadierno, *Tetrahedron*, 2012, **68**, 2611-2620.
49. C. J. Yue, Y. Liu and R. He, *J. Mol. Catal. A: Chem.*, 2006, **259**, 17-23.
50. R. C. Larock, X. Dong, S. Chung, C. K. Reddy and L. E. Ehlers, *J. Am. Oil Chem. Soc.*, 2001, **78**, 447-453.
51. A. Corma and S. Iborra, in *Advances in Catalysis, Vol 49*, eds. B. C. Gates and H. Knozinger, Elsevier Academic Press Inc, San Diego, 2006, vol. 49, pp. 239-302.
52. J. Puriwat, W. Chaitree, K. Suriye, S. Dokjampa, P. Praserthdam and J. Panpranot, *Catal. Commun.*, 2010, **12**, 80-85.
53. M. A. Aramendia, V. Borau, C. Jimenez, A. Marinas, J. M. Marinas, J. R. Ruiz and F. J. Urbano, *J. Molec. Cat. A: Chem.*, 2004, **218**, 81-90.
54. G. Busca, *Chem. Rev.*, 2010, **110**, 2217-2249.
55. H. Gorzawski and W. F. Hoelderich, *J. Mol. Cat. A: Chem.*, 1999, **144**, 181-187.
56. K. Tanaka, H. Yanashima, M. Minobe and G. Suzukamo, *Appl. Surf. Sci.*, 1997, **121–122**, 461-467.
57. Z. T. Du, J. P. Ma, F. Wang, J. X. Liu and J. Xu, *Green Chem.*, 2011, **13**, 554-557.
58. A. Caldarelli, F. Cavani, O. Garone, G. Pavarelli, J.-L. Dubois, I. Mitsova and L. Simeonova, Reducing the Carbon Footprint of Fuels and Petrochemicals, 2012.

59. C. Lavilla and S. Munoz-Guerra, *Green Chemistry*, 2013, **15**, 144-151.
60. O. Zovi, L. Lecamp, C. Loutelier-Bourhis, C. M. Lange and C. Bunel, *Green Chem.*, 2011, **13**, 1014-1022.
61. N. Kolb and M. A. R. Meier, *Green Chem.*, 2012, **14**, 2429-2435.
62. J. X. Mao, R. T. Mathers and K. Damodaran, *J. Organomet. Chem.*, 2013, **741–742**, 15-19.
63. C. S. Marvel and G. E. Hartzell, *J. Am. Chem. Soc.*, 1959, **81**, 448-452.
64. J. Beger, B. Thomas, T. Vogel, K. Kirmse and R. Lang, *J. prakt. Chem. (Leipzig, Germany)*, 1991, **333**, 481-488.
65. L. Brandsma, J. Van Soolingen and H. Andringa, *Syn. Commun.*, 1990, **20**, 2165-2168.
66. Y. Qian, G. Li, X. Zheng and Y.-Z. Huang, *J. Mol. Catal.*, 1993, **78**, L31-L35.
67. A. Molnar and M. Bartok, *Helv. Chim. Acta*, 1981, **64**, 389-398.
68. K. Laali, R. J. Gerzina, C. M. Flajnik, C. M. Geric and A. M. Dombroski, *Helv. Chim. Acta*, 1987, **70**, 607-611.
69. D. Markovic and P. Vogel, *Org. Lett.*, 2004, **6**, 2693-2696.
70. At a nitrogen pressure of 10 psi, the observed flow rate through the column (ID 2.1 mm x 100 mm) was 1.3 ± 0.1 mL/min. Taking into account the catalyst volume (based on density of Al_2O_3 and Na_2O), the residence time was calculated to be 15 ± 1 sec.
71. As shown in Table S3, increasing the reaction time from 3 h up to 24 h did not significantly improve the yield.
72. The reaction predominately produces the endo product.
73. Although anhydrides are known to react with moisture over time and produce a diacid, after heating **2** in the presence of water for 3 days at 100 °C, the absorbance ratio of anhydride:carboxylic acid (≈ 2:1) in the FTIR spectrum indicated that a large fraction of the anhydride groups did not react.
74. Solubility studies at ambient temperature in ethyl acetate determined the solubility limit for monomer **1** (0.176 g/mL) and MA (0.534 g/mL). Conseqently, a concentration of 0.14 g MA/mL in ethyl acetate was chosen to maximize the reaction rate and minimize any precipitation issues during the Diels-Alder reaction at 75 ^{o}C. Since the subsequent hydrogenation was conducted at ambient temperature, a lower concentration of **1** (0.06 g/mL) was achieved by diluting the output of the Diels-Alder reaction with ethyl acetate in the HPLC reservoir.
75. Nearly quantitative yields can be obtained after longer time periods with lower flow rates (<0.5 mL/min) or longer tubing (>35 feet).
76. N. Yoswathananont, K. Nitta, Y. Nishiuchi and M. Sato, *Chem. Commun.*, 2005, **0**, 40-42.
77. A flow rate of 1.8 mL/min and hydrogen pressure of 125 psi provided optimal plug-flow mixing through the catalyst tube (4.6 mm x 250 mm) containing Pd/C (0.5 g).
78. For example, at 0.06 g/mL of **1**, the hydrogenation rate for 0.3 g of Pd/C (k_{rel} = 1) increased with 0.5 g of Pd/C (k_{rel} = 6.5). With these catalyst loadings (i.e. 0.3-0.5 g), the hydrogen pressure approximated the back pressure on the HPLC pump and plug-flow was possible. However, if to much catalyst was used (i.e. 1 g of Pd/C), then the back pressure on the HPLC pump exceeded the hydrogen pressure and plug-flow conditions were not possible.
79. Since the stainless steel apparatus used for continuous flow can accomodate a much higher hydrogen pressure than the glass pressure bottle used for batch hydrogenations, we were only able to estimate that the continuous flow approach is about an order of magnitude faster than the batch reaction.
80. P. Zetterlund, W. Weaver and A. F. Johnson, *Polym. React. Engin.*, 2002, **10**, 41-57.
81. T. Yashiro, H. R. Kricheldorf and S. Huijser, *Macromol. Chem. Phys.*, 2009, **210**, 1607-1616.
82. While a polymerization temperature of 100 ^{o}C did not produce high molecular weight polymer, the slower reaction rate at 100 ^{o}C was convenient for analyzing the polymerization at regular intervals.

83. D. Wilms, S. E. Stiriba and H. Frey, *Acc. Chem. Res.*, 2010, **43**, 129-141.
84. Although the higher functionality of glycerol compared to 1,4-butanediol can result in crosslinked polyesters, thermosets were only obtained via higher catalyst loading or longer polymerization time (> 24 h). Above the gel point, the range of T_g values (68-90 °C) for Scheme 2 varied with the [glycerol]/[monomer] ratio and exceeded the T_g values in Figure 5.
85. Estimate of reaction time for batch process based on 5-10 min period for isomerization, a 3 h Diels-Alder reaction, 8-10 h recyrstallization period with ethanol, and a 10-12 h hydrogenation period in a glass pressure bottle.
86. D. Webb and T. F. Jamison, *Chem. Sci.*, 2010, **1**, 675-680.
87. I. R. Baxendale, *J. Chem. Tech. Biotech.*, 2013, **88**, 519-552.
88. J. Vandenbergh, T. D. Ogawa and T. Junkers, *J. Polym. Sci. Pol. Chem.*, 2013, **51**, 2366-2374.
89. C. H. Hornung, C. Guerrero-Sanchez, M. Brasholz, S. Saubern, J. Chiefari, G. Moad, E. Rizzardo and S. H. Thang, *Org. Proc. Res. Devel.*, 2011, **15**, 593-601.
90. W. Li, H. H. Pharn, Z. Nie, B. MacDonald, A. Guenther and E. Kumacheva, *J. Am. Chem. Soc.*, 2008, **130**, 9935-9941.
91. S. Kumar and R. B. Gupta, *Industrial & Engineering Chemistry Research*, 2008, **47**, 9321-9329.
92. M. J. Skinner, E. L. Michor, W. Fan, M. Tsapatsis, A. Bhan and L. D. Schmidt, *ChemSusChem*, 2011, **4**, 1151-1156.
93. C. Aellig and I. Hermans, *ChemSusChem*, 2012, **5**, 1737-1742.
94. J. Horacek, J. P. Mikkola, A. Samikannu, G. St'avova, W. Larsson, L. Hora and D. Kubicka, *Top. Catal.*, 2013, **56**, 794-799.
95. T. R. Carlson, T. P. Vispute and G. W. Huber, *ChemSusChem*, 2008, **1**, 397-400.

Graphical Abstract

Continuous flow methodology for the multi step synthesis of biomass derived aliphatic bicylic-anhydride monomer. Polymerization with bio-based alcohols results in renewable polyesters with good thermal stability and glass temperatures.