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Ring Opening Polymerization of β-acetoxy-δ-methylvalerolactone, a Triacetic Acid Lactone Derivative

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ABSTRACT

We report here the synthesis and polymerization of a novel disubstituted valerolactone, β-acetoxy-δ-methylvalerolactone, derived from the renewable feedstock triacetic acid lactone (TAL). The bulk polymerization proceeds to 45% equilibrium monomer conversion at room temperature using diphenyl phosphate as the organic catalyst. The resultant amorphous material displays a glass transition temperature of 25 °C. The ring opening polymerization (ROP) behavior of the disubstituted valerolactone was examined, and the enthalpy ($\Delta H_p°$) and entropy ($\Delta S_p°$) of polymerization were calculated to be -25 ± 2 kJ mol^{-1} and -81 ± 5 mol^{-1} K^{-1}, respectively. The polymerization kinetics were also measured and compared to that of other substituted valerolactones reported in the literature. This report is the first to demonstrate the successful ROP of a disubstituted valerolactone as well as the first to establish the ROP of a derivative of TAL.

INTRODUCTION

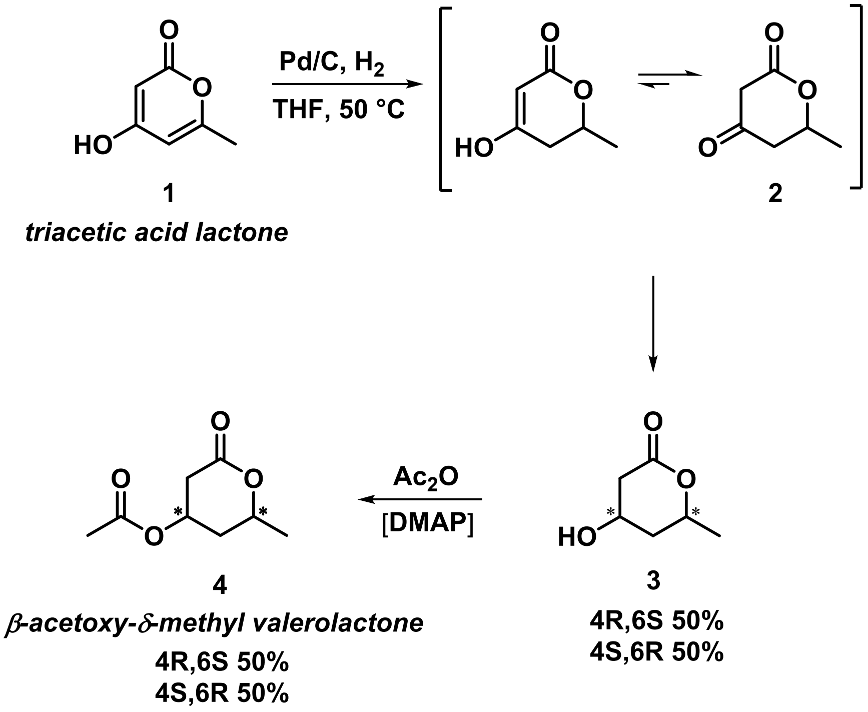
The success and advancement of modern society is dependent, in part, on materials created from polymers. Use in commodity products such as clothing and household goods, resources for infrastructure, and implementation in medical devices and other sophisticated technologies are but a few examples of how polymers have improved and continue to improve our daily lives. The vast majority of such polymeric materials, however, are derived from unsustainable petrochemical processes.[1,2] Thus, the impetus to supplement or entirely replace petroleum-based polymers with those created from renewable feedstocks has become increasingly urgent.[3–6] The use of biomass as a platform for generating renewable chemicals is an attractive approach towards ultimately achieving a sustainable and energy efficient paradigm within the multi-billion dollar polymer industry.

Triacetic acid lactone (TAL, (**1**)) (Scheme 1) can be obtained synthetically from acetic acid[7–9] or via the biological actions of genetically modified microorganisms, which synthesize the compound as a secondary metabolite of sugars.[10–18] These varied options for production make TAL an exciting target as potential synthesis from microbes could reduce the need for extraction from plants for a renewable building block and therefore reduce land use needs. Additionally, the multiple centers of functionalization give synthetic handles that make TAL a promising building block. We propose the use of TAL as a potentially renewable feedstock for the generation of new polymeric materials. To date, only two reports have demonstrated the use of TAL in polymers. In the first, post-polymerization modification of p(epichlorohydrin) with TAL resulted in an increase in the glass transition temperature of the material from -30 °C up to 70 °C, depending on the degree of substitution.[17] In the second, TAL was modified with an acrylic moiety and polymerized via a controlled radical polymerization technique to develop acrylic triblock copolymers suitable for pressure-sensitive adhesive applications.[19]

Drawing inspiration from the well-established ring opening polymerization (ROP) chemistry of various lactones such δ-valerolactone, ε-caprolactone, lactide and their derivatives,[20,21] we envisioned using TAL as a feedstock for the synthesis of new, disubstituted δ-valerolactones that can yield useful aliphatic polyesters via ROP. The polymerization behavior of lactone monomers is highly dependent on ring size and degree of substitution.[22–24] While the polymerizations of δ-valerolactone and numerous monosubstituted δ-valerolactone monomers have been studied,[25–28] such reactions of disubstituted δ-valerolactone monomers have not been reported to date. In this report, we describe the synthesis of a disubstituted δ-valerolactone, β-acetoxy-δ-methylvalerolactone (**4**), derived from TAL (Scheme 1) and examination of its polymerization behavior. The thermal properties of the polymer were studied, and the polymerization behavior of **4** was compared to that of other δ-valerolactone monomers. The comparisons provide valuable insights towards the kinetics and thermodynamics of ROP of substituted δ-valerolactones and support development of new methods and materials with renewable feedstocks.

RESULTS AND DISCUSSION

The catalytic hydrogenation of triacetic acid lactone (TAL, **1**) using Pd/C was accomplished following previously established procedures (Scheme 1, Figure S1).[19,29,30] The J-coupling constants for each proton pair of **3** were determined from the ^{1}H NMR spectrum using methods described in the literature (Figure S2).[31,32] In a previous report, **3** was synthesized via hydrogenation of the partially-reduced keto/enol intermediate **2** (Scheme 1) using Pd/C.[33] The hydrogenations led to very high (>99%) stereoselectivity for the *cis* isomer of **3**, and the authors postulated that the high selectivity is due to syn addition of hydrogen atoms to the C(3) and C(4) carbons on the opposite face of the ring relative to the 6-methyl substituent.[33] The ^{1}H NMR chemical shifts and J-coupling constants we observed for **3** in our work match with the values previously reported for the *cis* isomer, indicating that the hydrogenation of TAL using Pd/C is likewise >99% diastereoselective. The relative configuration of the hydroxyl and methyl substituents on the reduced δ-valerolactone ring is *cis* and **3** was obtained as a racemic mixture of the two enantiomers (4R,6S and 4S,6R). The *trans* isomer of **3** (4S,6S and 4R,6R) is also reported in the literature, and is distinguished from the *cis* isomer by different ^{1}H NMR chemical shifts and the associated J-coupling constants.[34,35]

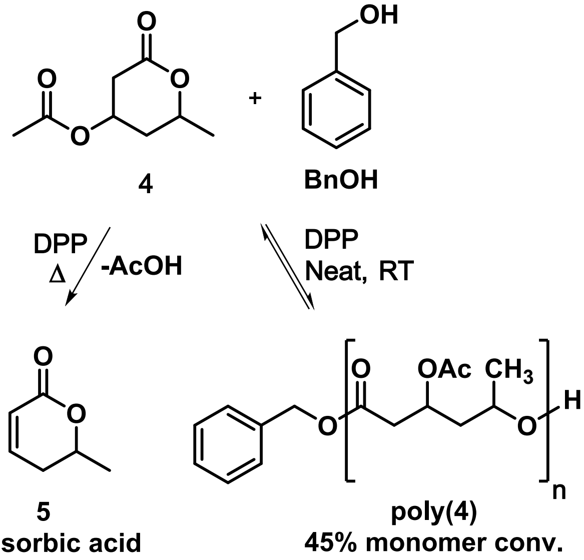


Scheme 1. Two-step synthesis of β-acetoxy-δ-methylvalerolactone (**4**) from triacetic acid lactone. The absolute configuration is highlighted for the two chiral centers at the 4- and 6-positions of the lactone rings.

Acetylation of the free hydroxyl group in **3** was accomplished using acetic anhydride and a catalytic amount of 4-(dimethylamino)pyridine (DMAP) as the base to yield β-acetoxy-δ-methylvalerolactone (**4**) (Figures S3 – S4). Since the acetylation reaction does not involve an inversion of configuration, we hypothesized that **4** would be obtained as a racemic mixture of one diastereomer, with the acetoxy and methyl substituents on the lactone ring also in the *cis* arrangement. Indeed, the ^{1}H NMR chemical shifts and J-coupling constants we observed for **4** (Figure S5) match exactly with those previously reported for the *cis* isomer of the compound.[33]

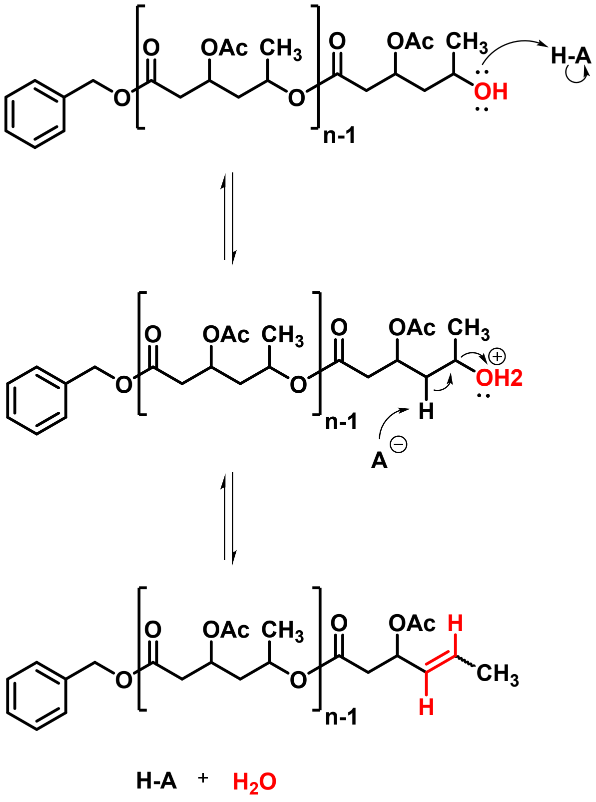
The ring opening polymerization of **4** was tested with a variety of catalysts, including typical organo- and organometallic catalysts[20,36] such as diphenyl phosphate (DPP), triazabicyclodecene (TBD), 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), phosphazene base P_4-*t*-

Bu, $BF_3{\cdot}OEt_2$, Bi subsalycilate, $Sn(Oct)_2$, $Al(i\mathrm{OPr})_3$, and $Ti(i\mathrm{OPr})_4$, as well as highly active Zn- and Al-based[37–39] catalysts (Table S1). Through our screenings, we identified DPP as a catalyst that can facilitate the conversion of **4** to **poly(4)** to an appreciable degree at relatively slow rates (discussed in further detail below). Bulk polymerization of a sample of **4** using DPP as the catalyst and benzyl alcohol (BnOH) as the initiator produced **poly(4)** as an amorphous material, reaching an equilibrium monomer conversion of 45% at ambient temperature (Scheme 2, Figure S6). Various monomer:initiator ratios were tested and the resulting monomer conversions, yields, and molar mass by NMR are summarized in Table S2. During the ROP of **4** with DPP, we observed the formation of parasorbic acid **5** as a byproduct within the reaction mixture (2-5% by ^{1}H NMR over the course of the reaction time), which is formed via the acid-catalyzed elimination of acetic acid from the ring.



Scheme 2. Polymerization of **4** using DPP as the catalyst and the elimination of acetic acid from **4** to produce parasorbic acid (**5**).

The molar mass of **poly(4)** was observed to be consistently lower than the targeted, theoretical value. As an example, starting with a 200:1 ratio of **4** to BnOH (theoretical M_n = 15.5 kDa based on a 45% monomer conversion), end group analysis via ^{1}H NMR indicated the molar mass to be 17 kDa. Analysis of the same sample via SEC-MALLS, however, revealed the M_n to be 10 kDa with a dispersity (Đ) of 1.2 (Figure S7). To elucidate the reason for the mismatched results from the two molar mass determination methods we carefully examined the ^{1}H NMR spectrum of **poly(4)** and observed the presence of small alkene resonances near the baseline (Figure S8). We hypothesize that ring opening of a molecule of **4** via cleavage of the ester bond produces a secondary alcohol as the propagating species, which, instead of propagating with the next monomer unit, can undergo an acid-catalyzed elimination reaction[40] to produce an olefin at the terminal end of the growing chain (Scheme 3). The olefin, unable to propagate, terminates the polymerization and causes a limiting effect on the molecular weight of the polymer chain. Additionally, the elimination reaction produces water as a byproduct, which can act as an adventitious initiator and lead to further attenuation of the achievable molar mass.



Scheme 3. Proposed mechanism for the formation of a terminal alkene in the propagating chain of **poly(4)**, catalyzed by DPP (denoted as a generic HA here), through an elimination reaction of the secondary alcohol.

The thermal properties of **poly(4)** were investigated by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC). The TGA thermogram shows a 5% weight loss occurring at 228 °C (Figure S9). The DSC thermogram of a 10 kDa sample of **poly(4)** shows it to be an amorphous material with a T_g of 25 °C (Figure 1). This result is exciting for potential materials applications because, with the notable exception of poly(lactic acid) (T_g = 55 °C)[41] and poly(glycolide) (T_g = 36 °C),[42] most poly(lactones) exhibit T_g values below ambient temperature,[25,26,28,40,43–46] and thus are typically only useful as soft, rubbery components in polymeric materials. The relatively higher T_g observed for **poly(4)** presents future opportunities to explore the effectiveness of the new poly(lactone) as the hard, glassy component in polymeric materials.

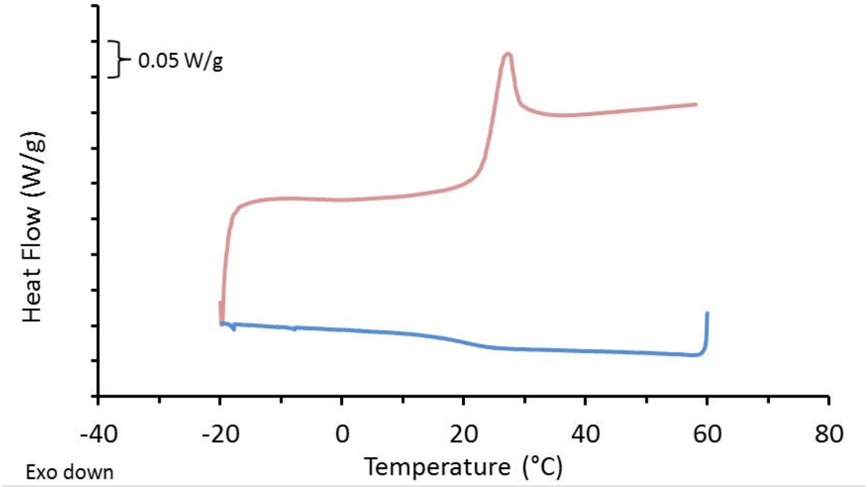


Figure 1. DSC thermogram of poly(4) at a heating rate of 10 °C min^{-1} taken on the second heating (red) and cooling (blue) cycles. The thermogram shows a T_g = 25 °C for a 10 kDa sample.

To understand how monomer structure affects polymerization behavior of substituted δ-valerolactones, we determined the thermodynamics of polymerization for the disubstituted δ-valerolactone monomer **4** using a Van't Hoff analysis[47] (Equation 1), and compared the results to those previously published for δ-valerolactone (**6**), β-methyl-δ-valerolactone (**7**), and δ-methyl-δ-valerolactone (**8**) (Figure 2 and Table 1).[25] The bulk polymerization of **4** was monitored at 22 °C, 10 °C, and 0 °C (Figure 2) via ^{1}H NMR spectroscopy until apparent equilibrium (up to two months at 0 °C). The elimination of acetic acid from **4** in the presence of an acid catalyst such as DPP became a significant issue at elevated temperatures (Scheme 2), preventing us from measuring the equilibrium monomer concentrations at temperatures above ambient conditions.

$$\ln\left(\frac{[M]_{eq}}{[M]_0}\right) = \frac{\Delta H°_p}{RT} - \frac{\Delta S°_p}{R} \qquad \text{Equation 1}$$

The enthalpy ($\Delta H_p°$) and entropy ($\Delta S_p°$) of polymerization were calculated to be -25 ± 2 kJ mol^{-1} and -81 ± 5 mol^{-1} K^{-1}, respectively. By comparing the thermodynamics of polymerization of **4** to the values reported for **6** – **8**, we observe a trend consistent with increasing ring strain with the degree of substitution, indicated by $\Delta H_p°$ for the isodesmic reaction of ROP of lactones.[25] Additionally, the value of $\Delta S_p°$ is also observed to significantly increase with degree of substitution. These results suggest that the bulk polymerization of substituted δ-valerolactones becomes increasingly exothermic and entropically disfavored with increasing degree of substitution. By further appending substituents on the lactone ring (e.g. tri- and tetrasubstituted), the increased order of the system upon polymerization ($\Delta S_p°$) will eventually negate the ring strain ($\Delta H_p°$), and polymerizations will become thermodynamically disfavored.

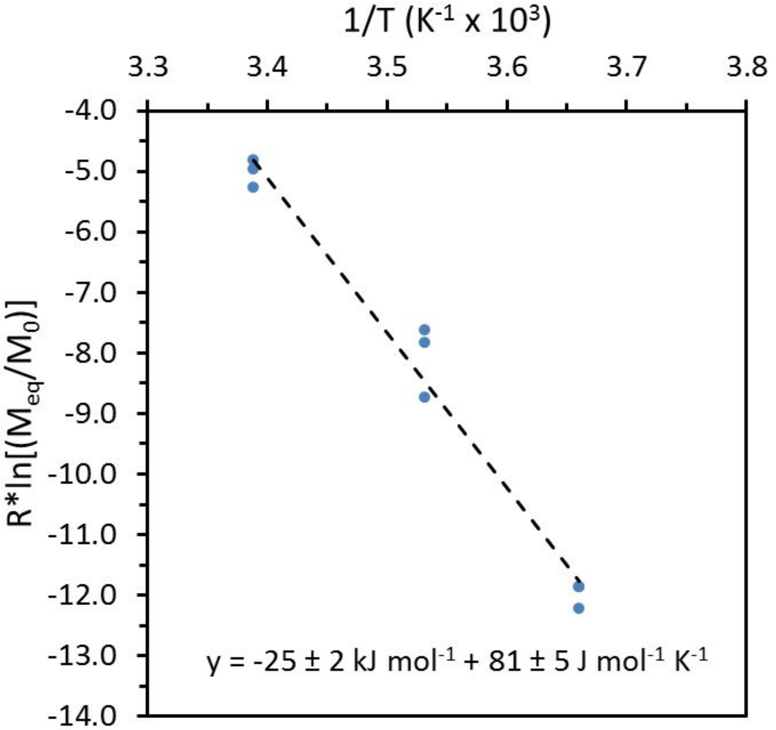


Figure 2. Van't Hoff plot of the temperature dependency of the equilibrium monomer concentration for the ring opening polymerization of **4**.

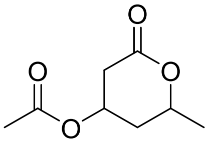
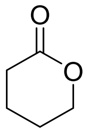
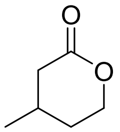
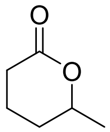
	 **4**	 **6**	 **7**	 **8**
$\Delta H_p°$ (kJ mol^{-1})	-25 ± 2	-10.5	-13.8 ± 0.3	-19.3 ± 0.5
$\Delta S_p°$ (J mol^{-1}K^{-1})	-81 ± 5	-15	-46 ± 1	-62 ± 2
k_{obs} (M/h)	0.012 ± 0.001	2.88 ± 0.33	2.46 ± 0.22	0.31 ± 0.04
$t_{1/2}$ (h)	276 ± 32	1.89 ± 0.22	1.86 ± 0.17	14.9 ± 2.1

Table 1. Thermodynamic and kinetic data comparing the polymerization of **4** to that of **6** – **8**.[25] Kinetic data for **4** and **6** – **8** were collected using a monomer:BnOH:DPP ratio of 200:1:1.

The rate of polymerization of **4** was also studied in order to compare its reactivity to that of **6** – **8**. The observed rate constants (k_{obs}) and half-lives ($t_{1/2}$) of **6** – **8** were previously reported for bulk polymerizations using a ratio of monomer to initiator (BnOH) to catalyst (DPP) of 200:1:1.[25] Under identical conditions, we measured the $t_{1/2}$ of conversion of **4** to be 276 ± 32 h with $k_{obs} = 0.012 \pm 0.001$ M h^{-1} (Figure 3a). The previous report established the pseudo-zero-order behavior of this system, noting that while this is peculiar for DPP-catalyzed polymerizations, it is not unprecedented for cationic polymerizations with a monomer more basic than the polymer.[25] We hypothesize that the TAL-derived monomer here behaves the same way due to its similarity to the previous literature and the basicity of the monomer. Therefore the observed rate constant of **4** was determined from the first 192 h (Figure 3b) using the zero-order rate equation:

$$[M] = [M]_o - k_{obs}t \qquad \text{Equation 3.2}$$

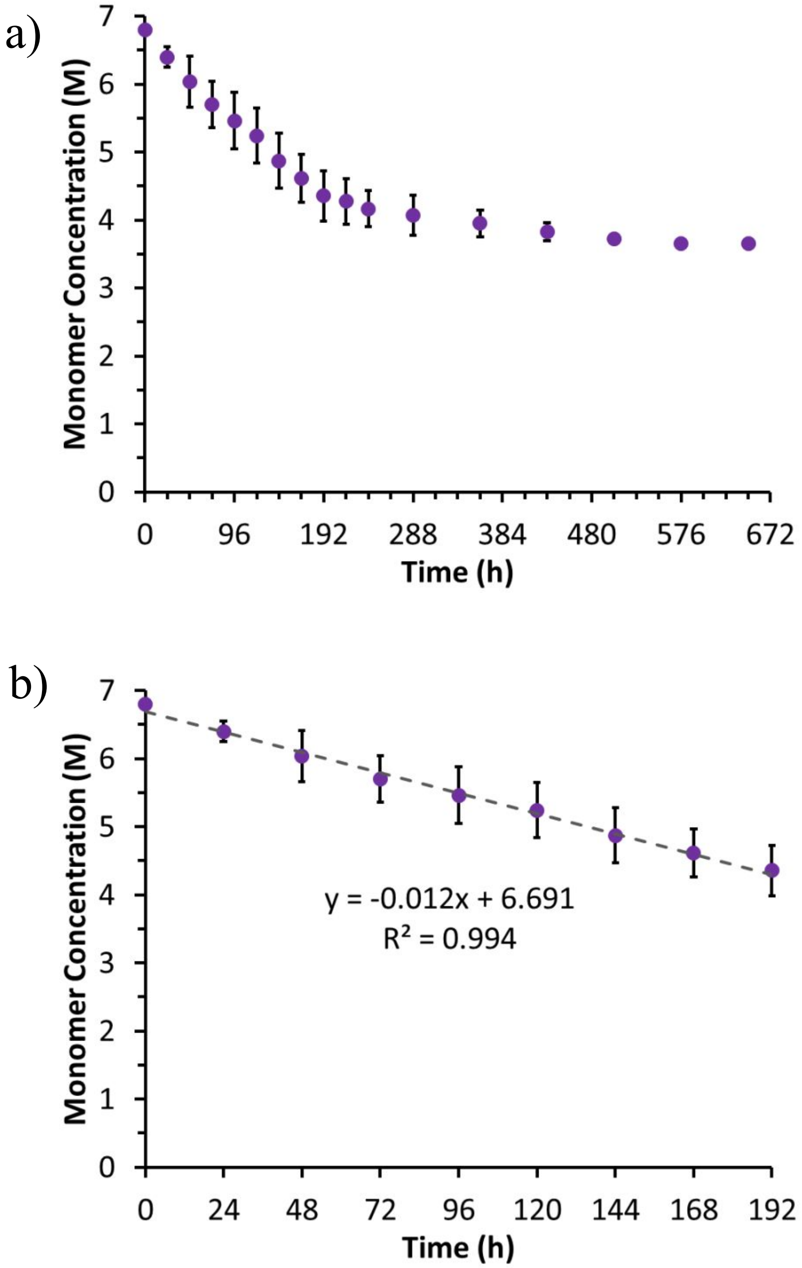


Figure 3. Conversion of (**4**) during bulk polymerization conducted at 22 °C with BnOH as the initiator and DPP as the catalyst at a 200:1:1 monomer:initiator:catalyst ratio. Plot (A) shows the polymerization over the entire duration which the reaction was monitored and plot (B) shows the first 192 h of polymerization.

Overall, we observed the rate of polymerization (k_{obs}) of **4** to be two orders of magnitude slower than **6** and **7** and an order of magnitude slower than **8** (Table 1). Assuming that the rate-determining step in the ROP of lactones is cleavage of the C-O ester bond, we hypothesize that the proximity of the methyl substituent to the carbonyl group in **4** and **8** hinders the nucleophilic attack of the hydroxyl end group of a polymer chain. Furthermore, ring opening of **4** and **8** results in a secondary alcohol as the propagating end group, which may itself be sterically hindered and thus slow to react with other monomer units. These steric arguments offer a rationale for the slower kinetics observed for **4** and **8** in comparison to unsubstituted δ-valerolactone (**6**) and β-methyl-δ-valerolactone (**7**). In the case of **4**, an additional carbonyl group is present (the β-acetoxy substituent) in the monomer structure. Under the assumption of an activated monomer mechanism (AMM) for the polymerization of lactones,[48] activation of the β-acetoxy carbonyl by DPP would be unproductive for propagation. In conjunction with the steric arguments presented for the methyl substituent in proximity to the ester carbonyl, the competitive nature of unproductive activation of the β-acetoxy carbonyl can rationalize the very slow polymerization rates observed for **4** compared to the monosubstituted δ-valerolactones **7** and **8**.

CONCLUSIONS

In summary, this report demonstrates the successful ring opening polymerization of a disubstituted δ-valerolactone, β-acetoxy-δ-methylvalerolactone (**4**)**,** derived from the emerging renewable platform chemical triacetic acid lactone. Using DPP as the organocatalyst the polymerization of **4** was observed to reach an equilibrium monomer conversion of 45% under ambient conditions. Differential scanning calorimetry analysis of a 10 kDa sample of **poly**(**4**) indicated the T_g of the resultant polyester to be 25 °C, a promising result for future materials applications. While a racemic mixture of **4** was used in this study, the influence of using an enantiomerically pure sample for polymerization on the T_g of the resultant polyester is under future consideration. The exclusive polymerization of either enantiomer (i.e. RS or SR) would yield a polymer with an isotactic sequence, which can lead to an increase the T_g of the material and may also impart a certain degree of crystallinity.[49,50] We established the kinetic and thermodynamic parameters for the polymerization of (**4**), and the results suggest that the polymerization of δ-valerolactones becomes increasingly exothermic and entropically disfavored with an increasing degree of substitution. Future studies are focused on assessing the mechanical properties of **poly(4)**, as well as discovering other disubstituted δ-valerolactones derived from TAL that can be polymerized.

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Notes

The authors declare no competing financial interest.

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