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Organocatalytic Cationic Ring-Opening Polymerization of a Cyclic Hemiacetal Ester

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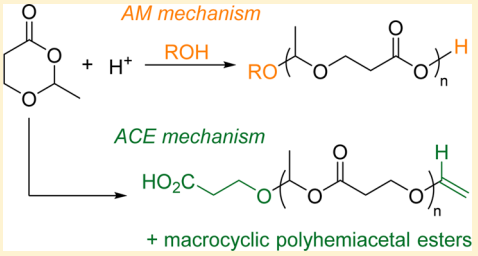
Supporting Information

ABSTRACT: We report the bulk cationic ring-opening polymerization of renewably sourced 2-methyl-1,3-dioxan-4-one (MDO) to yield a polyester with hydrolytically and thermally sensitive linkages that facilitate degradation. Neat monomer was successfully polymerized using a variety of protic acids as catalysts. We discovered that, with these catalysts, the cationic polymerization of MDO proceeds via two distinct mechanistic routes, namely, the activated monomer (AM) and active chain-end (ACE) mechanisms. The kinetics of these competing mechanistic avenues were investigated by employing diphenylphosphoric acid (DPP) with or without an alcohol initiator. Without an exogenous initiator, the polymerization propagates via a dioxacarbenium ion that rapidly adds more MDO to produce high-molar-mass poly(2-methyl-1,3-dioxan-4-one) (PMDO). However, we found no clear relationship between $[MDO]_0/[protic\ acid]_0$ and resultant molar mass, suggesting that the ACE mechanism is not well-controlled. This conclusion was further supported by the production of cyclic PMDO arising from unimolecular backbiting reactions as the system approached equilibrium. With an exogenous alcohol initiator, the polymerization proceeds primarily via an AM mechanism and affords a mixture of linear PMDO and a small amount of macrocyclics derived from the competing ACE mechanism. Consistent with this interpretation of competing mechanisms, a linear relationship between theoretical and observed molar mass was observed when the initial ratio of monomer to added initiator was <80.



INTRODUCTION

The United Nations recently predicted that the world population would increase to 11 billion people by 2100.[1] This population increase will undoubtedly be accompanied by a rise in demand for high-quality, affordable, and sustainable materials. Synthetic polymers constitute the building blocks for the plastic products abundant in today's society. Specifically, hydrocarbon polymers, such as polyethylene (PE), polypropylene (PP), and polystyrene (PS) comprise a large fraction of commercial plastics.[2] However, microorganisms capable of enzymatically degrading the typically heteroatom-rich macromolecules found in nature generally do not assimilate such hydrocarbon polymers.[3] The inability of traditional polymers to biodegrade represents an urgent environmental concern that has prompted synthetic polymer chemists to explore routes to biodegradable polymer structures. Polylactide (PLA) is a renewable polyester that can be produced at only a small premium, relative to PS, facilitating its use in various applications. While PLA is industrially compostable, it does not degrade easily under the anaerobic conditions typical of landfills. Furthermore, the infrastructure required to collect, transport, and industrially compost aliphatic polyesters is still in its infancy, and consumers are often not aware of the proper disposal procedures. Many aliphatic polyesters, including PLA, biodegrade via a two-step process. First, polymer backbone bonds must be enzymatically or otherwise hydrolyzed to produce oligomers, which are subsequently broken down further to return water, carbon dioxide, and humus.[4] Generally, the polyester degradation rate is impacted by the structure of the polymer backbone, including the electrophilicity of the carbonyl atoms and the presence or absence of bulky substituents. In addition, the hydrophobicity of the material and its crystallinity also influence the degradation rate.[5]

Hemiacetal esters are known to be more hydrolytically and thermally labile than their acetal and ester counterparts.[6,7] The hydrolytic and thermal lability of polyhemiacetal esters makes them attractive candidates as components of biodegradable plastics, as well as for processes that require the selective etching of one component (e.g., nanolithography).[8] In 2014, Martin et al. explored the synthesis of the cyclic hemiacetal ester monomer 1,3-dioxolan-4-one (DOX).[9] The authors attempted the controlled batch copolymerization of the cyclic hemiacetal ester with L-lactide with the goal of producing marine-degradable poly(L-lactide-*co*-DOX) statistical copolymers. Upon careful review of the data presented in this work, we concluded that compelling evidence for the incorporation of acetal units into the macromolecules was absent. Based on attempts to reproduce one of the copolymerizations, we provide evidence that suggests that

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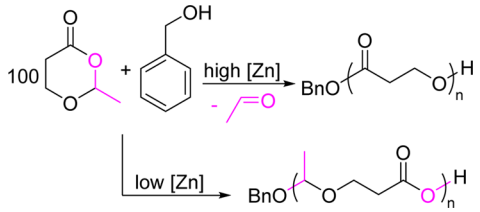
these previously reported polymers were actually statistical copolymers of glycolic acid (GA) and lactide (LA), rather than the targeted poly(hemiacetal esters) (see Figures S24−S26 in the Supporting Information). PGA-*co*-PLA copolymers, which would result from the loss of formaldehyde during the copolymerization, are interesting in their own right and should exhibit enhanced degradation, compared to the PLLA homopolymer.[10]

We note that, in order to produce polyhemiacetal esters, rather than polyesters from cyclic monomers, it is important to find polymerization conditions that are mild and selective to avoid the elimination of aldehydes. Near the same time as the publication by Martin et al., we described the anionic ring-opening polymerization (ROP) of the cyclic hemiacetal ester 2-methyl-1,3-dioxan-4-one (MDO) (Scheme 1).[11] In the presence of benzyl alcohol (BnOH) initiator and catalytic diethylzinc (Et_2Zn), we found that this monomer can be polymerized by ring-opening either at the acetal or at the ester functionality to produce poly(2-methyl-1,3-dioxan-4-one) (PMDO) or the aliphatic polyester poly(3-hydroxypropionic acid) (PHPA), respectively. Interestingly, the elimination of acetaldehyde—and, thus, the formation of PHPA—was favored at higher catalyst concentrations. However, at low catalyst loadings ($[MDO]_0/[Et_2Zn]_0 \geq 700$), the monomer ring-opened at the acetal to produce a benzyl acetal end group and a propagating zinc carboxylate. Under these conditions, acetaldehyde was not lost, and carboxylic-acid-terminated PMDO was formed. Unfortunately, this process was somewhat inefficient, requiring over 24 h to reach equilibrium at the low catalyst loading employed to suppress concurrent acetaldehyde elimination.

Scheme 1. Previously Employed Anionic Ring-Opening Polymerization of 2-Methyl-1,3-dioxan-4-one (MDO)



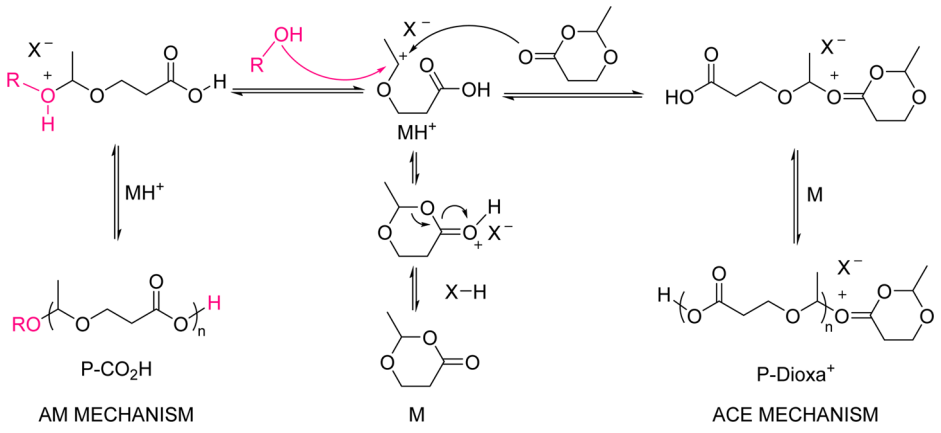
Because of these practical limitations, we sought to identify more-active catalysts for the polymerization of MDO and to develop conditions that would suppress acetaldehyde elimination observed in the anionic ROP of MDO. We reasoned that the ROP of MDO might be promoted under cationic polymerization conditions. The cationic ring-opening polymerization (CROP) of heterocycles is known to proceed via two distinct mechanisms: an activated monomer (AM) and active chain-end (ACE) mechanism.[12] The activated monomer mechanism relies on an exogenous nucleophile to act as the initiating species. With this pathway, molar mass control is achieved by adjusting the initial monomer:initiator ratio. Conversely, with an ACE mechanism, each propagating chain is initiated by a molecule of monomer. Although there are examples of CROP via the ACE mechanism that demonstrate molar mass control as a function of the monomer to cationic initiator ratio (i.e., the Brønsted acid employed), it is more often the case that side reactions result in a loss of molar mass control.[13]

To our knowledge, the mechanism and kinetics of the CROP of cyclic hemiacetal esters has not been previously demonstrated, although it has been recently shown that a 7-membered cyclic hemiacetal ester acts as an effective initiator in the ring-expansion living cationic polymerization of isobutyl vinyl ether.[14] In this work, we report the CROP of the cyclic hemiacetal ester MDO using a variety of organic acid catalysts. We show that polymerization of MDO can proceed via both AM and ACE pathways, with the dominant mechanism determined by the initial concentration of exogenous initiator.

RESULTS

We first investigated diphenylphosphoric acid (DPP),[15] an inexpensive organocatalyst that has been previously employed in the cationic ring-opening polymerization of lactones and cyclic carbonates.[16,17] We observed rapid polymerization of neat MDO to PMDO upon treatment with DPP in the presence of benzyl alcohol at room temperature. We initially aimed for low-molar-mass PMDO to facilitate end-group analysis by ^{1}H NMR spectroscopy. We targeted 5 kg/mol PMDO, accounting for an equilibrium monomer concentration of $[M]_{eq}$ = 4.53 M, i.e., ~60% conversion starting with neat MDO.[11] An initial polymerization of neat MDO ($[MDO]_0 \approx 10.1$ M, $[MDO]_0/[DPP]_0$ = 1000, and $[MDO]_0/[BnOH]_0$ = 80) became noticeably viscous over 1 h. Analysis of the resultant PMDO by size-exclusion chromatography−multiangle laser light scattering (SEC-MALLS) using tetrahydrofuran (THF) as the mobile phase indicated that the number-average molar mass (M_n) of the purified PMDO was 8.2 kg/mol with a dispersity ($Đ$) of 1.25.

Scheme 2. Activated Monomer (AM) and Active Chain-End (ACE) Mechanisms Adapted to the CROP of MDO



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Structural analysis by ^{1}H NMR spectroscopy verified the production of PMDO with the incorporation of BnOH into the polymer backbone as a benzyl acetal end group (Scheme 2).

Encouraged by the superior activity of DPP over diethylzinc as the catalyst for MDO polymerization, we set out to synthesize polymers of different molar masses by varying $[BnOH]_0$. However, at higher theoretical molar masses ($M_{n,theo}$), the observed molar masses of the resultant PMDO samples were consistently lower than the theoretical values (see Table S1 in the Supporting Information). As noted previously, with an activated monomer mechanism, one would anticipate good molar mass control over a wide range of $[BnOH]_0$. Therefore, we reasoned that there are two likely causes for this discrepancy: either the cationic polymerization of MDO proceeds via an AM mechanism and adventitious initiators present in the monomer initiate surplus chains, or backbiting reactions diminish the average molar mass of PMDO. The latter is expected to be more prominent in the ACE mechanism as the propagating chain-end is a charged species of comparatively higher reactivity and lower selectivity than the propagating species in the AM mechanism.

Although both ^{1}H and ^{13}C NMR spectral data suggested that the MDO monomer was highly pure, without apparent adventitious initiators, we sought to further rule out the former possibility by carrying out a chain-extension experiment. Neat MDO was polymerized to 50% conversion ($[MDO]_0/[BnOH]_0$ = 81, ($[MDO]_0/[DPP]_0$ = 1000), and the reaction mixture was analyzed by THF SEC-MALLS. The addition of fresh MDO from the same batch led to an increase in the molar mass from M_n = 8.5 kg/mol to M_n = 10.6 kg/mol with $Đ$ = 1.25 both before and after chain extension. A new population of low-molar-mass PMDO molecules was not observed upon chain extension, indicating that no new chains were initiated by nucleophilic contaminants or other pro-initiators in the second monomer aliquot (see Figure S1 in the Supporting Information).

Convinced by this experiment that MDO was quite pure, we developed the following mechanistic hypothesis: in the polymerization of MDO without exogenous initiator, polymerization occurs via an ACE mechanism, where a monomer molecule (M) initiates by ring-opening a protonated monomer molecule (MH^+) to afford a dioxacarbenium ion (P-Dioxa$^+$) as the propagating species. On the other hand, when an added alcohol initiator is present, the polymerization occurs via the AM mechanism. In this case, the ring-opening of MH^+ by an exogenous nucleophile, such as an alcohol (ROH), affords a carboxylic acid propagating chain end (P-CO_2H). We suspected that, at lower target molar masses (where the relative concentration of initiator is high), the AM mechanism would dominate; meanwhile, at higher target molar masses (where the relative concentration of initiator is low), competition between AM and ACE mechanisms would lead to loss over molar mass control.

We proceeded to study PMDO polymerization under conditions thought to favor the AM mechanism ($[MDO]_0/[DPP]_0$ = 2140 and $[MDO]_0/[BnOH]_0$ = 85) and monitored the molar mass evolution during the early stages of the polymerization by SEC. We observed a linear increase in molar mass with conversion in this low-molar-mass regime (see Figure 1, as well as Table S6 in the Supporting Information). However, a positive, nonzero intercept was observed. This may be explained by some contribution of the ACE mechanism under these conditions, which would invalidate the assumption that all chain-ends are derived from BnOH initiation only. SEC traces of low-molar-mass polymers exhibited a fairly broad signal ($Đ \approx 2$),

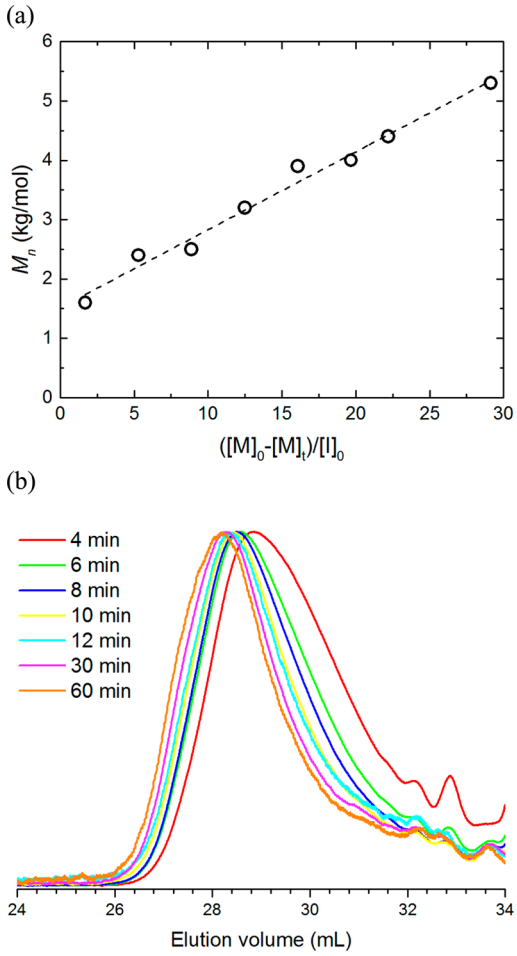

Figure 1. (a) PMDO molar mass, as a function of conversion monitored using THF SEC and conventional calibration analysis relative to PS standards. (b) Stacked SEC traces of the quenched polymerization aliquots from the plot shown in panel (a) at the indicated times. The polymerization was carried out in neat MDO ($[MDO]_0$ = 10.1 M) with $[MDO]_0/[DPP]_0$ = 2142 and $[MDO]_0/[BnOH]_0$ = 85. Each aliquot was quenched with 1 mL THF containing 1 μL of NEt_3 prior to analysis.

including a low-molar-mass tail consistent with cyclic oligomers of PMDO.

Despite the marginal control of molar mass resulting from competition of ACE and AM mechanisms at low initiator concentrations, we were able to synthesize several different end-functionalized, low-molar-mass PMDO samples ($M_n \approx$ 5 kg/mol, $[MDO]_0/[ROH]_0$ = 80) by initiating with a variety of functionalized alcohol initiators (Table 1). We anticipate that low-molar-mass PMDO equipped with a functional handle can be employed as a macroinitiator or further derivatized as desired. In all cases, we were able to verify the end-group structures by ^{1}H NMR spectroscopy (see Figures S2−S16 in the Supporting Information). We also observed a quartet at 4.73 ppm, together with other signals very similar to those of linear PMDO (Figures S2−S16, especially pronounced in Figure S10). These resonances became much more prominent when the polymerization was carried out at higher dilutions, suggesting that unimolecular ring formation, which affords cyclic PMDO, eventually dominates over bimolecular propagation as $[MDO]_0$ approaches $[M]_{eq}$.[18] Interestingly, entry 5 produced a 4:1 mixture of linear to cyclic PMDO resonances, as corroborated by ^{1}H NMR spectroscopy (Figure S10).

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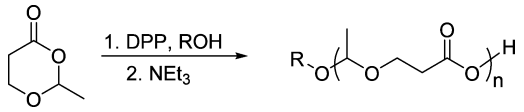
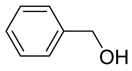
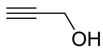
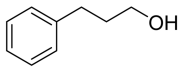
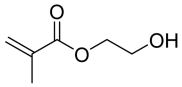
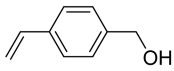
Table 1. CROP of MDO with Various Functionalized Alcohol Initiators and DPP as the Catalyst



Entry	ROH	Conversion[a] (%)	Yield[b] (%)	$M_{n,theo}$[c] (kg/mol)	M_n[d] (kg/mol)	$Đ$[d]
1		50	75	4.6	4.1	2.1
2		50	88	4.6	5.0	2.0
3		55	82	5.1	4.8	2.1
4		56	84	5.2	4.7	2.2
5[e]		57	96	5.3	4.3	2.5

[a]Determined from ^{1}H NMR integrations. [b]Calculated taking into account conversion. [c]Theoretical value calculated from (% conversion)($[MDO]_0/[ROH]_0$)M_0. [d]Determined from THF SEC, relative to PS standards. [e]This reaction produced some macrocyclics, in addition to linear PMDO, as evidenced by ^{1}H NMR analysis (Figure S10). All reactions were run in bulk ($[MDO]_0$ = 10.1 M) at room temperature with $[MDO]_0/[ROH]_0$ = 80 and $[MDO]_0/[DPP]_0$ = 1000. Reactions were quenched using equimolar amounts of NEt_3, relative to DPP. Polymers were purified by precipitation into cold 9/1 hexanes/THF, and dried under reduced pressure for 21 h.

It is worth noting that, while the thermal instability of PMDO may be advantageous for applications where a labile component is desired (e.g., lithography), it makes the purification and processing of PDMO challenging. All precipitated polymers in Table 1 were dried under reduced pressure at room temperature, as we observed decomposition of PMDO under reduced pressure at 50 °C (Figure S17 in the Supporting Information). To increase the thermal stability of PMDO, we successfully esterified the carboxylic acid terminus by treating the precipitated polymer with a dimethylformamide (DMF) solution of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and methyl iodide. ^{1}H NMR spectroscopic data of the reprecipitated PMDO was consistent with a methyl ester end group on the polymer and the relative integrations of the new methyl signal to the benzyl acetal group indicated that PMDO was quantitatively end-capped (Figure S18 in the Supporting Information). Thermogravimetric analysis (TGA) of end-capped PMDO exhibited a 25 °C increase in thermal stability, when compared with PMDO prior to end-capping (Figure 2). This observed increase may be explained by the absence of an acidic moiety capable of catalyzing degradation of the polymer backbone and/or the thermally driven depolymerization from the chain end.

We also probed polymerization of MDO via an ACE mechanism by treating neat MDO with DPP in the absence of exogenous initiator. We observed an increase in the viscosity of the reaction mixture within only a couple of minutes, and both ^{1}H NMR and SEC data confirmed the formation of high-molar-mass PMDO. ^{1}H NMR spectroscopic end group analysis of purified polymers prepared without alcohol initiator revealed the appearance of a doublet of doublets at ~6.4 ppm, consistent with

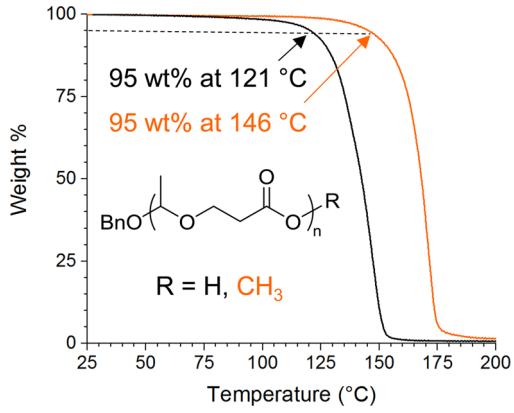


Figure 2. Thermogravimetric analysis of 8 kg/mol PMDO that has been end-capped contrasted with PMDO prior to end-capping. The thermal degradation experiment was carried out under a nitrogen atmosphere with a heating ramp of 10 °C/min.

a vinyl ether end group (Figure S19 in the Supporting Information). This presumably resulted from α-hydride elimination from an intermediate oxonium ion formed in the ACE pathway.

Isolated reports of CROP of selected cyclic acetals and ethers suggest that it is possible to control polymer molar mass by the monomer:acid ratio, $[M]_0/[XH]_0$, where XH is a generic Brønsted acid.[19] However, within the range of catalyst loadings we studied, there was no clear relationship between molar mass and concentration of $[DPP]_0$ (Table 2). We therefore concluded that DPP did promote CROP of MDO by an ACE mechanism

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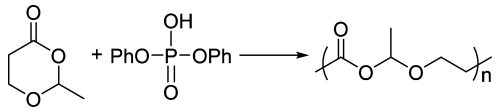
Table 2. Molar Mass as a Function of $[MDO]_0/[DPP]_0$ for PMDO Prepared Via an ACE Mechanism



entry	$[MDO]_0/[DPP]_0$	time (min)	conversion[a] (%)	yield[b] (%)	M_n[c] (kg/mol)	$Đ$[c]
1	1000	374	46	55	45	1.2
2	2000	260	41	82	42	1.2
3	3000	346	35	76	33	1.5
4	4000	1080	33	79	35	1.4

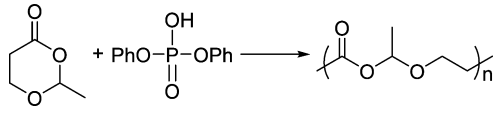
[a]Determined from relative ^{1}H NMR integrations of MDO and PMDO resonances, respectively. [b]Yield takes into account the reported conversion. [c]Determined from THF SEC-MALLS. All polymers were dissolved in 1 mL $CDCl_3$ containing 1 μL NEt_3, precipitated into cold 9/1 hexanes/THF, and dried under reduced pressure.

that was not well-controlled. Regardless, the ACE mechanism consistently gave access to higher-molar-mass PMDO (>30 kg/mol) than was achievable with added alcohol initiator or with our previously established conditions for the zinc-alkoxide-promoted ROP of MDO.

In an effort to identify an acid catalyst that would facilitate the controlled CROP of MDO via an ACE mechanism, we investigated a wide variety of acids and alkylating agents that have been successfully employed in the controlled CROP of cyclic acetals.[19] However, these catalysts caused immediate decomposition of the monomer, even at low temperature (−20 °C) and under more dilute conditions (Table S2 in the Supporting Information). We reasoned that these strong acid catalysts were quite aggressive and therefore pursued an organic acid with a pK_a more similar to DPP (pK_a = 3.88 in dry DMSO).[15] In addition, we sought a triflate counterion with low nucleophilicity to improve control over the polymerization.[20] Pyridinium triflate (PyHTfO) is a commercially available salt that meets both of the aforementioned constraints. However, in the bulk polymerization of MDO, similar results were observed with PyHTfO as with DPP; high-molar-mass polymers could be accessed, but there was no clear relationship between $[MDO]_0/[PyHTfO]_0$ (Table S3 in the Supporting Information). Furthermore, some of the pyridine appeared to be incorporated as a pyridinium chain end, presumably via attack by pyridine onto the propagating dioxacarbenium ion (Figure S20 in the Supporting Information). A bulky tetrakis[3,5-bis-(trifluoromethyl)phenyl]borate diphenylphosphoric acid (DPP $[BArF]^{4-}$) catalyst was also employed but proved to not yield much improvement over the use of DPP. Similarly, dry hydrochloric acid in diethyl ether (1 M) led to the successful polymerization of MDO and produced results akin to those achieved with DPP.

Molar mass analysis by THF SEC-MALLS of the polymerization by the ACE mechanism indicated that molar mass was actually highest at low conversions and decreased with increasing MDO conversion (see Table 3, as well as Tables S4 and S5 in the Supporting Information), eventually plateauing around $M_n \approx 30$ kg/mol. This seemed to suggest that, without an exogenous initiator, initiation from activated MDO is slower than propagation of the chain, which is consistent with the prediction that MDO is a poor nucleophile. In fact, we observed molar masses of $M_n \gtrsim 100$ kg/mol after only 2 min when conversion was still <5% (as determined by no-D ^{1}H NMR kinetics experiments under the same conditions;[21] see Figure S21(a) in the Supporting Information). Analysis of entry 10 in Table 3 via matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry corroborated the formation

Table 3. Molar Mass Evolution with Time of the DPP-Catalyzed MDO CROP via ACE Mechanism



entry	time (min)	M_n[a] (kg/mol)	$Đ$[a]
1	2	120	2.1
2	4	56	1.3
3	6	51	1.3
4	8	45	1.4
5	10	46	1.3
6	12	49	1.3
7	30	40	1.3
8	60	36	1.3
9	90	34	1.2
10[b]	120	32	1.2

[a]Determined from THF SEC-MALLS. [b]This aliquot was analyzed by MALDI-TOF (Figure S22 in the Supporting Information). The polymerization was conducted in neat MDO ($[MDO]_0$ = 10.2 M, $[MDO]_0/[DPP]_0$ = 1068). DPP solution (0.12 M in DCM) was transferred to a scintillation vial and solvent was removed under reduced pressure. MDO was then added to the dry DPP. All aliquots were quenched with 1 mL THF containing 1 μL NEt_3.

of low-molar-mass (≤2 kg/mol) cyclic PMDO in the polymerization of MDO via an ACE mechanism (Figure S22 in the Supporting Information).

Kinetics of MDO CROP via AM and ACE Pathways Catalyzed by DPP. We also monitored the CROP of neat MDO with and without benzyl alcohol initiator using no-D ^{1}H NMR experiments.[21] In the CROP of MDO, we observed conversions close to 60% (the established equilibrium conversion) with added alcohol initiator but without an exogenous initiator present the polymerization generally did not exceeded 50% conversion, especially when $[DPP]_0$ was low (see Figures S21(a) and S21(b)). This can possibly be explained by side reactions that irreversibly quench the charged species in solution or by some catalyst deactivation in the ACE mechanism.

For a polymerization with $[MDO]_0$ = 9.7 M, $[MDO]_0/[BnOH]_0$ = 50, and $[MDO]_0/[DPP]_0$ = 2770, the consumption of benzyl alcohol initiator is complete by ^{1}H NMR spectroscopy after 15 min (see Figure 3a). The resonance for the chemically equivalent methylene protons of benzyl alcohol at 4.7 ppm (Figure 3a, time = 0 min) decreased in intensity as two doublets and a quartet (Figure 3a, protons a, a′ and proton b), indicative of a benzyl acetal end group, emerged. A low-intensity signal corresponding to methylene protons of a benzyl ester was also

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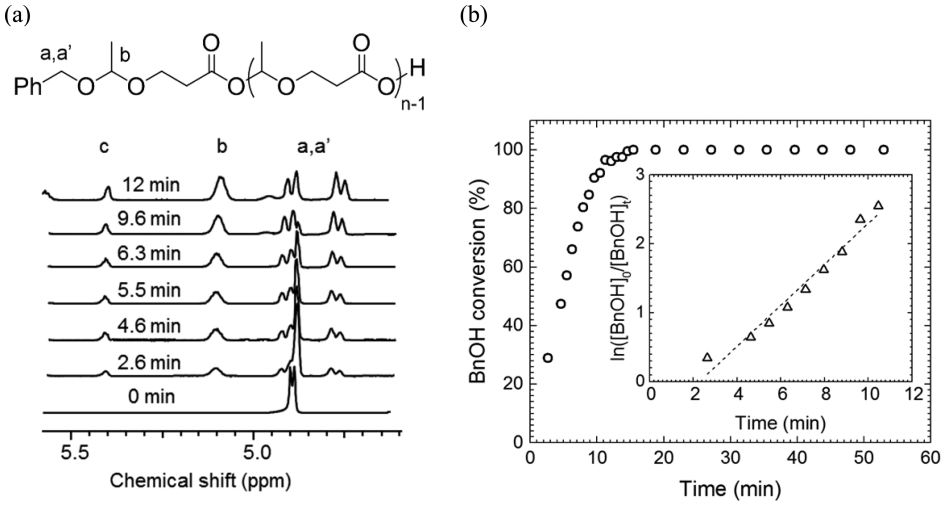

Figure 3. Initiation kinetics for the cationic ring-opening polymerization of MDO in the presence of BnOH and DPP with $[MDO]_0 = 9.7$ M, $[BnOH]_0 = 0.2$ M, and $[DPP]_0 = 3.8$ mM: (a) ^{1}H NMR overlay of no-D spectra showing the disappearance of the benzyl alcohol methylene protons at $\delta = 4.9$ ppm (in MDO) and the ingrowth of a benzyl acetal end group at $\delta = 4.78$ (d, 1H, PhCH_2OCHCH_3O), 4.88 (d, 1H, PhCH_2OCHCH_3O), and 5.11 (q, 1H, PhCH_2OCHCH_3O) (a minor signal at 5.4 ppm (protons c) corresponding to benzyl ester methylene protons is also observed; this results from alcohol ring-opening at the ester functionality of MDO, followed by acetaldehyde extrusion); (b) benzyl alcohol conversion (data denoted by open circles (○)), as a function of time; inset shows the semilogarithmic anamorphosis of the data (denoted by open triangles (△)) suggests that the rate of initiation has a first-order dependence on $[BnOH]_0$ ($k_{app} = 0.30 \pm 0.02$ min^{-1}, $R^2 = 0.96$)).

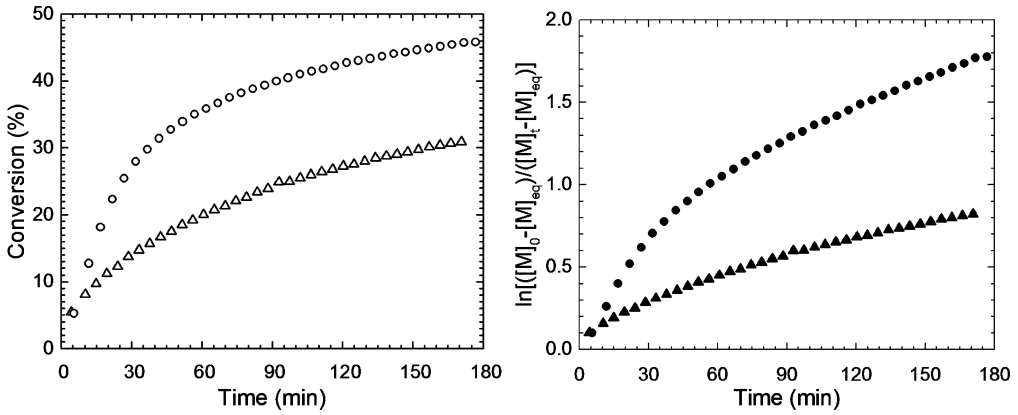

Figure 4. (a) Conversion of MDO to PMDO, as a function of time for $[MDO]_0 = 9.9$ M and $[DPP]_0 = 3.8$ mM (open triangle, △) and for $[MDO]_0 = 9.8$ M, $[DPP]_0 = 3.8$ mM, and $[BnOH]_0 = 0.13$ M (○). (b) The data from panel (a) in semilogarithmic coordinates without BnOH (▲) and with BnOH (●).

observed (Figure 3a, protons c), suggesting that a fraction of the alcohol is consumed via competitive initiation at the ester functionality of MDO. However, benzyl ester end groups were not observed in purified PMDO, indicating that the alcohol, produced by initiation at the ester and subsequent acetaldehyde extrusion from the hemiacetal, did not propagate. Plotting alcohol consumption with conversion in semilogarithmic coordinates afforded a straight line, consistent with a first-order dependence of the rate of initiation (R_i) on $[BnOH]_0$ (Figure 3b).

With a benzyl alcohol initiator, MDO conversion increases linearly with time over the first 20 min until 30% conversion is reached. Above 30% conversion, the rate of propagation R_p decreases drastically, such that it takes an additional 140 min to approach 50% conversion (data denoted by open circles (○), Figure 4a). In comparison, the rate of polymerization is significantly slower without an exogenous alcohol initiator (denoted by open triangles (△), Figure 4a). Semilogarithmic anamorphoses of the MDO conversion data presented in Figure 4a afforded concave down, rather than linear, slopes (Figure 4b). This effect was more pronounced in the case of MDO CROP with BnOH (data denoted by solid circles (●), Figure 4b).

Neat MDO polymerization employing variable $[DPP]_0$ with no $[BnOH]_0$ (Figure S21(a)) and constant $[BnOH]_0$ (Figure S21(b)) was also studied by no-D ^{1}H NMR spectroscopy[21]). In both cases, the initial rates of polymerization were observed to increase with an increase in $[DPP]_0$. The rate of polymerization at low $[DPP]_0$ leveled off at lower conversions, leading to lower overall conversions. The decrease in overall conversion was more pronounced in the case of MDO polymerization without an alcohol initiator and at low $[DPP]_0$, suggesting that the acidic protons in solution are eventually quenched during CROP via an ACE mechanism.

■ DISCUSSION

Penczek, Kubisa, and co-workers have thoroughly studied the kinetics of CROP via AM and ACE mechanisms for several heterocycles including cyclic acetals and lactones.[22] The authors

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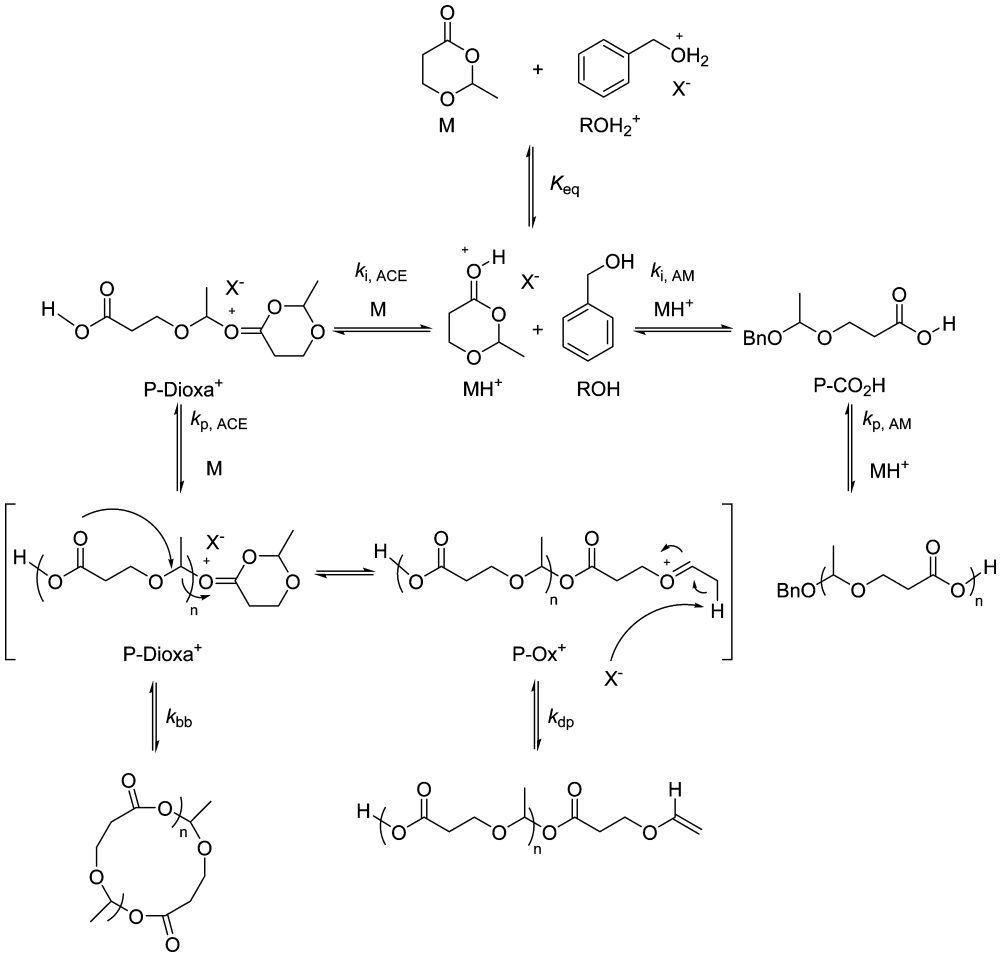
Scheme 3. Mechanistic Pathways for the Formation of PMDO with Observed End Groups and Architectures under CROP Conditions



have concluded that it is rarely possible to avoid backbiting and end-to-end cyclization reactions in the ACE mechanism. This can be rationalized by the presence of a reactive dioxacarbenium ion at the propagating chain end, which can react with the electron-rich oxygen atoms of the polymer backbone to yield macrocycles (Scheme 3). As the concentration of monomer decreases, such unimolecular backbiting reactions become increasingly competitive with bimolecular propagation events.

On the other hand, in the AM mechanism, the propagating species is neutral and, therefore, less prone to unimolecular side reactions. In the case of MDO CROP, we also observed competition between AM and ACE mechanisms.

In the AM mechanism, acidic protons are distributed between monomer and alcohol molecules during initiation. This can be expressed by the following chemical pre-equilibrium:

$$[MH^+] + [ROH] \overset{K_{eq}}{\rightleftarrows} [M] + [ROH_2{}^+] \quad (1)$$

where K_{eq} is the equilibrium constant associated with this proton transfer. Initiation occurs via attack of an alcohol molecule (ROH) on a protonated MDO molecule (MH^+). The rate of initiation in the activated monomer mechanism ($R_{i,AM}$) can be written as

$$R_{i,AM} = k_{i,AM}[MH^+][ROH] \quad (2)$$

Similarly, the rate of propagation in the AM mechanism ($R_{p,AM}$) of MDO CROP can be written as

$$R_{p,AM} = k_{p,AM}[MH^+][P\text{-}CO_2H] \quad (3)$$

where [P-CO_2H] denotes the concentration of propagating polymer chains. It is important to note that, unlike in the AM mechanism of cyclic ethers, acetals, and lactones, the propagating species in MDO CROP via AM mechanism is a carboxylic acid, rather than an alcohol.

In the ACE mechanism, a molecule of unprotonated MDO (M) acts as the initiator and ring-opens MH^+ to yield a propagating dioxacarbenium ion. The $R_{i,ACE}$ can then be expressed as

$$R_{i,ACE} = k_{i,ACE}[MH^+][M] \quad (4)$$

Similarly, $R_{p,ACE}$ is a function of the concentration of propagating dioxacarbenium ion (P-dioxa$^+$) and unprotonated MDO:

$$R_{p,ACE} = k_{p,ACE}[P\text{-dioxa}^+][M] \quad (5)$$

It can be seen from eqs 4 and 5 that $R_{i,ACE}$ and $R_{p,ACE}$ are functions of [M], which sets it apart from the AM mechanism, where $R_{i,AM}$ and $R_{p,AM}$ are functions of the protonated monomer only.

Without the addition of an alcohol initiator (and assuming a negligible concentration of adventitious initiators), the polymerization of MDO is expected to proceed exclusively via an ACE mechanism. In Figure 4b, deviation from linearity in the

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semilogarithmic plot of MDO consumption with conversion is apparent in polymerizations under both AM and ACE conditions. The polymerization rate thereby appears to neither have a first-order nor zero-order dependence on MDO monomer concentration. In CROP, deviations from a rate with singular dependence on monomer concentration have been rationalized by differences in the relative basicities of monomer and polymer.[23] If the monomer has a higher pK_a than the polymer, there is a higher probability that the acidic protons are located on the monomer than the polymer chain. In the opposite scenario, the acidic protons have a higher probability to be localized on the polymer chain, causing a decline in R_p with time.

Therefore, the decrease in $R_{p,ACE}$ is consistent with PMDO being more basic than MDO. When an alcohol initiator is added to the polymerization, an even more pronounced decrease in $R_{p,AM}$ was observed after the initial 20 min of reaction (●, Figure 4a). From Figure 4b, it can be deduced that this decrease is not solely due to the lower monomer concentration. Furthermore, this deviation cannot be purely a result of the difference in relative monomer and polymer basicity, because this value is not expected to change upon the addition of a small amount of alcohol initiator. We believe that the decrease in $R_{p,AM}$ is a manifestation of the superposition of MDO consumption via the competing AM and ACE mechanisms. The plot in Figure 4b can be deconstructed into two linear regimes: an initial regime, where the AM mechanism dominates, and a second regime, where the ACE mechanism and associated side reactions become competitive as the concentration of protonated monomer and the concentration of protonated polymer decrease and increase, respectively.

Based on our findings, we suggest that MDO CROP with DPP and an alcohol initiator proceeds via concurrent AM *and* ACE mechanisms, with the contribution of each being a function of $[M]/[MH^+]$. The AM mechanism will be favored if $[MH^+]$ is kept as high as possible and $[M]$ as low as possible throughout the polymerization. This approach has been successfully employed in the controlled synthesis of polyethers from epoxides.[24] Unfortunately, monomer-starved conditions are not amenable to MDO CROP, because of the high $[M]_{eq}$ associated with the ring-opening of MDO to PMDO, which effectively prohibits the polymerization of MDO at low $[M]$.

From the collective data acquired for MDO CROP, we were able to identify the major operative mechanistic pathways illustrated in Scheme 3. MDO CROP without the addition of alcohol proceeds via an ACE mechanism, where unprotonated MDO (M) initiates a chain via attack on protonated MDO (MH^+). Referring to the evolution of molar mass with time data, we infer that $R_{i,ACE} \ll R_{p,ACE}$, resulting in the production of high-molar-mass PMDO at low conversions. The following incremental decrease in molar mass with time can be rationalized by reversible backbiting reactions, affording cyclic PMDO (k_{bb} = rate constant associated with backbiting). Cyclic PMDO can be ring-opened and further decrease molar mass by additional backbiting processes or undergo deprotonation of the oxonium ion ($P\text{-}Ox^+$) to generate a terminal vinyl ether (k_{dp} = rate constant associated with deprotonation). The addition of ROH to the system opens up an additional avenue for MDO CROP via the AM mechanism. Although initiation and propagation by an AM mechanism can be favored in principle, suppression of the ACE mechanism contribution in MDO CROP is expected to diminish conversion, because it requires monomer concentrations well below $[M]_{eq}$. Hence, PMDO of different architectures and with different end groups is produced even in the presence of an alcohol initiator, where the contribution of the ACE mechanism becomes more pronounced as $[M]$ approaches $[M]_{eq}$.

CONCLUSION

We have studied the cationic ring-opening polymerization of the cyclic hemiacetal ester MDO via activated monomer and active chain-end mechanisms to yield hydrolytically and thermally labile PMDO. We were able to produce end-functionalized PMDO of molar masses in good agreement with theoretical values using high initial concentrations of various simple alcohol initiators and the mild organocatalyst DPP. The aforementioned results notwithstanding, we also synthesized high-molar-mass PMDO without added initiator via an ACE route. Both with and without an exogenous initiator, the rates of polymerization were faster than in our previously studied polymerization of MDO under anionic conditions. Furthermore, polymerization of MDO under cationic conditions effectively suppressed the formation of poly(3-hydroxypropionic acid). We believe that our observations will benefit those undertaking polyhemiacetal ester synthesis in the future and that our findings will provide useful guidelines for the handling and polymerization of this class of monomers.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.iecr.6b03114.

Experimental procedures and all characterization data (PDF)

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

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Notes

The authors declare no competing financial interest.

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