

UC Berkeley

UC Berkeley Previously Published Works

Title

Molecular Weight-Controlled Cationic Polymerization of Tetrahydrofuran Using a Squaramidinium Hydrogen-Bond Donor Catalyst

Permalink

<https://escholarship.org/uc/item/04c679nv>

Journal

Journal of the American Chemical Society, 148(4)

ISSN

0002-7863

Authors

Roan, Joshua J W

Siddiqi, Zohaib

Abel, Brooks A

Publication Date

2026-02-04

DOI

10.1021/jacs.5c18359

Copyright Information

This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at

<https://creativecommons.org/licenses/by-nc-nd/4.0/>

Peer reviewed

Molecular Weight-Controlled Cationic Polymerization of Tetrahydrofuran Using a Squaramidinium Hydrogen-Bond Donor Catalyst

Joshua J. W. Roan, Zohaib Siddiqi, and Brooks A. Abel*

Cite This: *J. Am. Chem. Soc.* 2026, 148, 4397–4405

Read Online

ACCESS |



Metrics & More

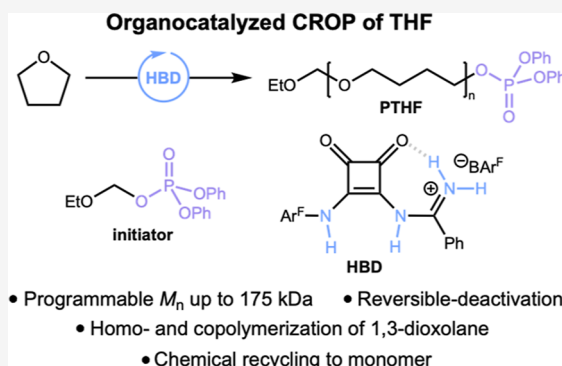


Article Recommendations



Supporting Information

ABSTRACT: Poly(tetrahydrofuran) (PTHF) has long-standing industrial relevance as the soft block of elastic fibers and thermosets. Despite its commercial importance, the synthesis of PTHF with molecular weight (MW) control beyond 20 kDa has proved challenging. In this work, we disclose a MW-controlled synthesis of PTHF up to 175 kDa by cationic ring-opening polymerization, using a cationic squaramidinium hydrogen-bond donor (HBD) catalyst in combination with an α -phosphonoxyethyl ether initiator at room temperature. Mechanistic studies support a reversible-deactivation polymerization pathway, wherein the HBD catalyst facilitates the anchimeric ionization of the primary alkyl phosphate chain end, generating the propagating oxonium species. The stability of the phosphate chain end was demonstrated by isolating PTHF with high chain-end fidelity and subsequently extending the PTHF macroinitiator to higher molecular weights. This system was further applied to the copolymerization of THF and 1,3-dioxolane (DXL), affording copolymers with tunable thermal properties. We demonstrate near-quantitative chemical recycling of both PTHF and PTHF-*co*-PDXL back to monomer, highlighting the potential of this strategy for the development of sustainable polymers.



INTRODUCTION

Polytetrahydrofuran (PTHF) is produced on a 350 kiloton scale annually and used in consumer products as the soft block of many polyurethane and polyester copolymer elastomers (Spandex, Hytrel, Adiprene) owing to its low glass transition temperature ($T_g = -86^\circ\text{C}$), high thermal stability, and resistance toward hydrolysis.¹ Since its first report by Meerwein in 1939, PTHF stands as the first demonstration of a polymer synthesized by cationic ring-opening polymerization (CROP), yielding a linear and semicrystalline polymer.^{2,3} PTHF is a promising sustainable polymer, as it can be derived from biorenewable feedstocks and chemically recycled to monomer and biodegrades into benign products (Figure 1A).¹

Many methods have been developed to polymerize THF by CROP, utilizing Lewis acids, Lewis acid/promoters, Brønsted acids, or strong alkylating agents (see Figure 1B and Tables S1 and S2 for a comprehensive summary).⁴ The CROP of THF is typically robust and amenable to the preparation of higher-order architectures such as star polymers^{5,6} and well-defined block copolymers.^{7–14} However, despite nearly 90 years of extensive research, molecular weight (MW) control beyond 20 kDa has not yet been achieved using these polymerization methods. Bulk material properties are strongly dependent on MW, owing to the increased degree of chain entanglement which varies proportionally with chain length.¹⁵ Low-MW

PTHF ($M_n < 5$ kDa) is a waxy semisolid, whereas higher-MW PTHF ($M_n > 30$ kDa) is a thermoplastic with tensile properties similar to polyethylene.¹⁶ Developing THF polymerization systems with more precise MW control at higher MWs is essential for advancing next-generation sustainable plastics and high-performance functional materials.

Several challenges must be overcome to achieve the MW-controlled CROP of THF. THF has inherently low reactivity¹⁷ as compared to monomers such as 1,3-dioxolane (DXL) ($k_{p,\text{rel}} = 1.7 \times 10^3$)¹⁸ and vinyl ethers ($k_{p,\text{rel}} = 1.2 \times 10^6$)¹⁹ (Figure 1C), which have well-established methods for their controlled cationic polymerization.^{20–22} The slow rate of THF propagation is on the order of irreversible termination processes such as ion-pair collapse, which decreases the maximum kinetic chain length and limits MW control.^{23–25} Chain transfer reactions, such as reaction with adventitious water, chain-end coupling, and macrocyclization also result in uncontrolled molecular weights.²⁶

Received: October 20, 2025

Revised: December 30, 2025

Accepted: January 5, 2026

Published: January 20, 2026



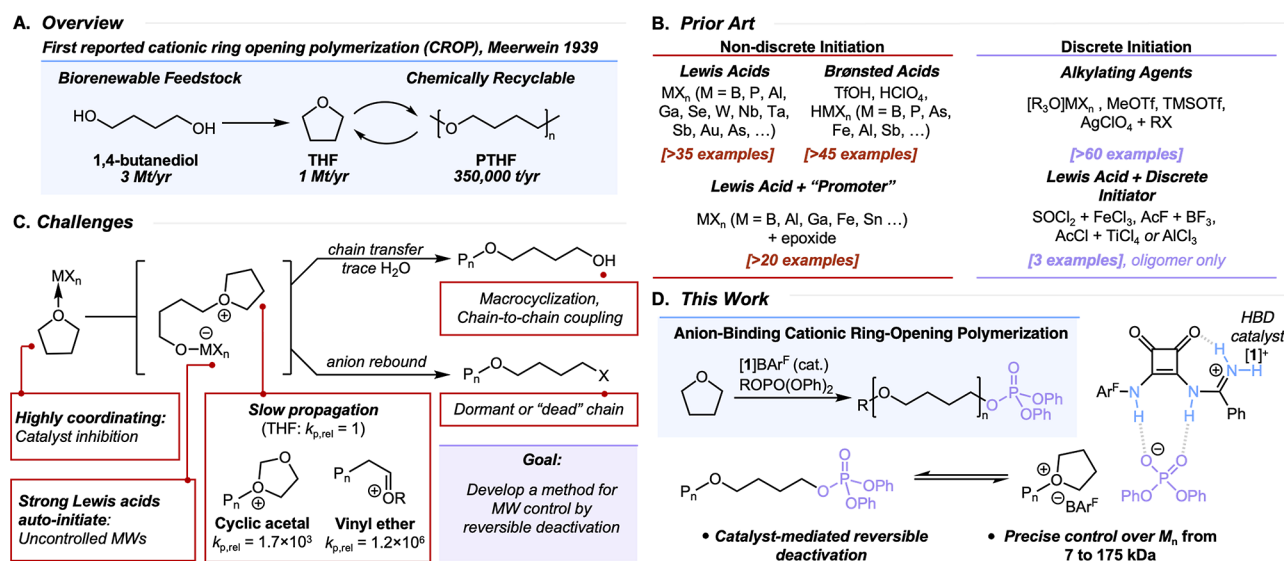


Figure 1. (A) Industrial relevance of PTHF. (B) Historical approaches to the polymerization of THF based on a literature survey (SI Tables S1, S2). (C) Challenges associated with polymerizing THF. (D) Anion-binding approach to the polymerization of THF.

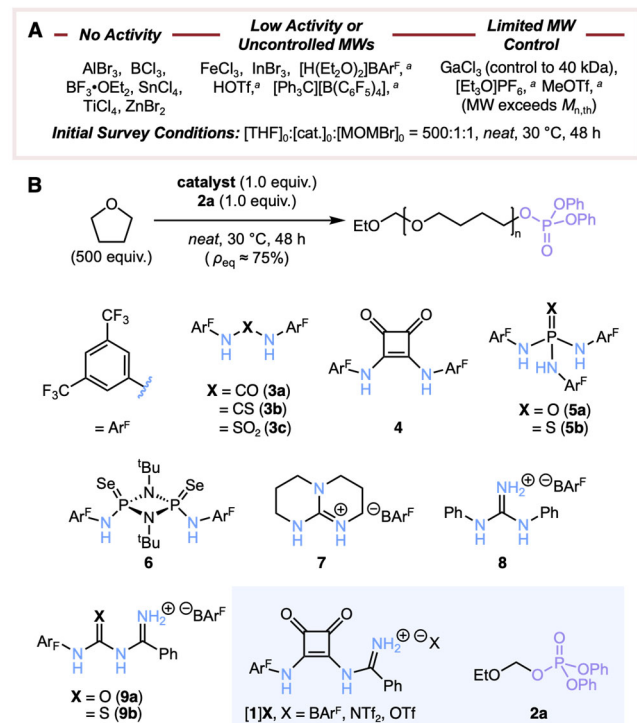
We reasoned that the major challenges associated with the CROP of THF could be overcome by using a discrete initiator/catalyst system, wherein M_n varies proportionally with $[THF]_0:[initiator]_0$ and monomer conversion. For this system, MW control is defined as a close agreement between the experimental and theoretical values ($M_{n,exp} = M_{n,th}$), where $M_{n,th}$ is calculated based upon $[THF]_0:[initiator]_0$ and monomer conversion according to eq 1 in the Supporting Information. Controlled cationic polymerizations have traditionally relied on reversible deactivation methods, where control is achieved by finely tuning the equilibrium between active and dormant species. This has afforded MW control for the cationic polymerizations of olefinic monomers such as isobutylene, styrene, and vinyl ethers,²⁰ and more recently, for the CROP of cyclic acetals.^{21,22,27} However, among the few comparable systems applied to the CROP of THF, none have demonstrated MW control (Figure 1B).^{3,28} Such a method for the CROP of THF requires the rational design of a catalyst/initiator pair capable of overcoming the aforementioned side reactions and the specificity to contend with the highly coordinating monomer.

In this work, we demonstrate the first example of controlled CROP of THF, affording PTHF with M_n values of up to 175 kDa (Figure 1D). The high activity of the squaramidinium organocatalyst toward ionization of the α -phosphonooxymethyl ether initiator is required for controlled polymerization due to its strong and selective binding to the phosphate leaving group. Mechanistic studies suggest that polymerization control is achieved through a reversible deactivation process in tandem with transesterification of the polymer backbone. Intramolecular activation of the squaramide hydrogen-bond donor (HBD) by an adjacent amidinium N–H group was necessary to sufficiently enhance catalyst activity. Extension of this methodology to the CROP of cyclic acetals and the preparation of poly(acetal-ether) copolymers demonstrates the potential of this approach for the broader synthesis of precision functional materials.

RESULTS AND DISCUSSION

Our investigations began by examining prior catalyst/initiator systems developed for the polymerization of THF with the intention of achieving MW control to $[THF]_0:[initiator]_0 = 500:1$. We first examined strong Brønsted acids and alkylators as discrete initiators without an additional catalyst for the CROP of THF. Polymerizations were performed at ambient temperature in the bulk where the equilibrium monomer conversion (ρ_{eq}) was typically 75%, with a theoretical number-average molecular weight ($M_{n,th}$) of 26.9 kDa at $[THF]_0:[initiator]_0 = 500:1$.²⁹ Brønsted acid initiators either failed to reach equilibrium conversion (TfOH, $\rho = 12\%$) or exhibited poor agreement between $M_{n,GPC}$ and $M_{n,th}$ at equilibrium conversion ($[H(Et_2O)_2]BAF^F$, $M_{n,GPC} = 139$ kDa) (Figure 2A, Table S4, entries 1 and 2, respectively).³⁰ A linear relationship between $M_{n,GPC}$ and $[THF]_0:[initiator]_0$ was observed when strong alkylating agents were used as initiators ($[Et_3O]PF_6$ and MeOTf), though $M_{n,GPC}$ exceeded $M_{n,th}$ by greater than 1.5-fold for all $[THF]_0:[initiator]_0$ ratios (Figure 2A, Supporting Information Section 4.3, Tables S11 and S12). We next applied a range of MX_n Lewis acids in combination with methoxymethyl bromide (MOMBr) as a discrete initiator owing to its ability to generate a reactive oxocarbenium species upon bromide abstraction. No THF conversion was observed when using common Lewis acids, where M = [Al^{III}], [B^{III}], [Sn^{IV}], [Ti^{IV}], and [Zn^{II}] (Figure 2A, Table S3). While low THF conversions were observed with [Fe^{III}] and [In^{III}] (Figure 2A, Table S3, entries 8 and 12), GaCl₃ notably reached equilibrium conversion within 48 h and moderate agreement between $M_{n,GPC}$ and $M_{n,th}$ up to $[THF]_0:[initiator]_0 = 1000:1$ ($M_{n,GPC} = 71.1$ kDa, $M_{n,th} = 52.5$ kDa, Table S12, entry 10). However, at higher $[THF]_0:[initiator]_0$ ratios, polymerizations catalyzed by GaCl₃ failed to reach equilibrium conversion (Supporting Information Section 4.2, Table S12).

We hypothesized that increasing catalyst activity would promote reversible chain-end ionization, increasing the polymerization rate, and extending the range of MW control. However, highly Lewis acidic MX_n catalysts such as PF₅ or SbCl₅ are known to autoinitiate the polymerization of THF in the absence of a discrete initiator, leading to the loss of MW



entry	catalyst	ρ (%) ^a	$M_{n,th}$ (kDa) ^b	$M_{n,GPC}$ (kDa) ^c	$\bar{D}$
1	3–6	Trace	<1.0	<3.0	–
2	7	Trace	<1.0	<1.0	–
3	8	3	1.1	11.8	1.15
4	9a	48	17.2	25.9	1.55
5	9b	3	1.1	13.1	2.10
6	[1]BAr ^F	77	26.9	31.6	1.49
7	[1]NTf ₂	32	11.4	20.6	1.39
8	[1]OTf	25	8.9	23.9	1.45
9	[1]OPO(OPh) ₂	Trace	<1.0	<1.0	–

Figure 2. (A) Initial catalyst and initiator screen. (B) HBD catalyst optimization. ^a Determined by ¹H NMR analysis of the crude reaction mixture. ^b $M_{n,th}$ calculated assuming complete initiation by **2a**. ^c $M_{n,GPC}$ determined by SEC-MALS in THF.

control.^{25,31} We therefore sought to design a catalyst/discrete initiator system where the catalyst possesses a high affinity toward the initiator-derived leaving group, even in the presence of strongly coordinating THF monomer.

Recently, organocatalytic anion-binding catalysis has been used for the controlled cationic polymerization of vinyl ethers but has not yet been realized for CROP.^{32–36} We were particularly drawn to HBD catalysis due to recent reports of HBD-catalyzed ring-opening reactions of oxazolines and azetidines.^{37–39} Additionally, HBD catalysts paired with phosphate leaving groups have been shown to afford uniquely selective interactions in glycosylation reactions, as demonstrated by the Jacobsen group.^{40–44} We reasoned that phosphonoxymethyl initiator **2a**, when paired with a suitable multidentate HBD catalyst, would favor phosphate chain-end ionization over HBD coordination to the monomer, thereby facilitating the reversible-deactivation CROP of THF.

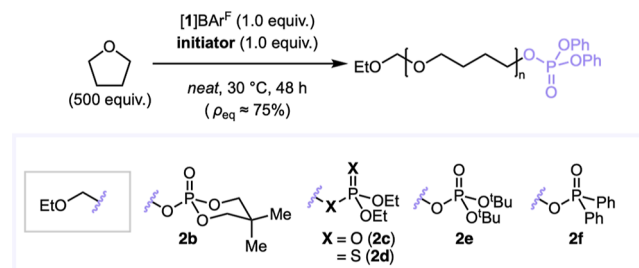
We initially examined several classes of HBDs (3–6) in combination with various discrete initiators, but no conversion was observed in all cases (Figure 2B, entry 1; see Table S5 for

full details). Notably this includes thiophosphoramidate **5b** and selenocyclodiphosph(V)azane **6**, which have been employed by the Fors and Tao groups, respectively, for the controlled cationic polymerization of vinyl ethers. These systems exemplify the six-orders-of-magnitude difference in reactivity between vinyl ethers and THF (Figure 1C).^{32,35}

We hypothesized that the enhanced electrostatic potential of cationic hydrogen-bond donors could translate to improved phosphate binding and, therefore, catalytic activity. Cationic HBDs have been used as catalysts in glycosylation reactions, conjugate additions, and sigmatropic rearrangements.^{45–48} We first synthesized guanidinium HBDs **7** and **8**, inspired by the highly specific interaction between arginine residues and phosphates observed in nature.⁴⁹ Using the standard polymerization conditions shown in Figure 2B, **7** showed no activity, whereas a low conversion of THF ($\rho = 3\%$, $M_{n,GPC} = 11.8$ kDa) was achieved using diphenyl guanidinium **8** and phosphate initiator **2a** (Figure 2B, entries 2 and 3, respectively).⁴⁶

Encouraged by the activity of HBD **8**, we designed cationic HBD catalysts **[1]BAR^F**, **9a**, and **9b**, which are capable of forming an intramolecular hydrogen bond (vide infra), a feature that has been shown to enhance hydrogen bond polarization in urea, thiourea, and squaramide hydrogen-bond donors, thereby enhancing their activity.^{50,51} **[1]BAR^F** proved optimal, reaching equilibrium conversion and $M_{n, \text{GPC}} = 31.6$ kDa in good agreement with $M_{n, \text{th}} = 26.9$ kDa (Figure 2B, entry 6). Notably, control reactions omitting initiator **2a** or catalyst **[1]BAR^F** yielded trace or no conversion under the standard polymerization conditions (Tables 1, entry 7, and

Table 1. Initiator Optimization



entry	initiator	ρ (%) ^a	$M_{n,th}$ (kDa) ^b	$M_{n,GPC}$ (kDa) ^c	$\bar{D}$
1	2b	43	15.6	20.8	1.55
2	2c	26	9.3	19.1	1.65
3	2d	Trace	<1.0	<1.0	—
4	2e	Trace	<1.0	<1.0	—
5	2f	Trace	<1.0	7.2	1.37
6	MOMBr	4	1.4	2.3	1.57
7	none	Trace	<1.0	104	1.36

^aDetermined by ¹H NMR analysis of the crude reaction mixture.

^b $M_{n,th}$ calculated assuming complete initiation by **2a**. ^c $M_{n,GPC}$ determined by SEC-MALS in THF.

S14, entries 3 and 4). We attributed the high activity of [1]BAR^F to the higher acidity of the squaramide moiety relative to the thioureas and ureas, which is often correlated with the HBD catalyst activity.⁵² The low activity of **9b** relative to those of **9a** and [1]BAR^F is potentially due to the addition of the mildly nucleophilic thiourea to the chain end. Increasing the coordinative strength of the counteranion from [1]BAR^F to [1]NTf₂ or [1]OTf led to decreased conversions, likely due to the addition of the counteranion to the oxonium chain end (Figure 2B, entries 7 and 8), while [1]OPO(OPh)₂ had no

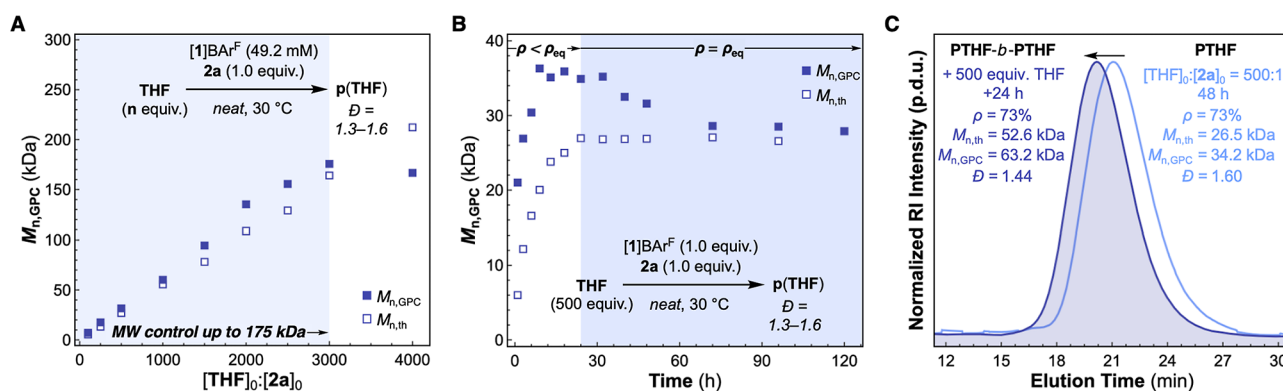


Figure 3. (A) MW control is observed with a good agreement between $M_{n,GPC}$ and $M_{n,th}$ up to $[THF]_0:[2a]_0 = 3000:1$. (B) Convergence of $M_{n,GPC}$ and $M_{n,th}$ occurs after reaching ρ_{eq} under optimized conditions. (C) Demonstration of phosphate ester chain-end retention via PTHF isolation and subsequent chain extension.

activity (Figure 2B, entry 9).^{53,54} Previously, it was demonstrated that in MeOTf-initiated CROP of THF, >95% of propagation proceeds through the active oxonium triflate ion pair rather than a covalent alkyl triflate. Collapse of the triflate anion onto the oxonium chain end results in a decreased apparent rate of propagation compared to systems with a dissociated counteranion.⁵⁵

The effect of the phosphate leaving group structure on polymerization rate and MW control was next investigated by synthesizing phosphonooxymethyl ether initiators **2b–2f** to probe the effects of substituents and the identity of the P(V) leaving group on MW control. Varying the substituents of the phosphonooxymethyl ether initiator led to either decreased conversions (**2b** and **2c**) (Table 1, entries 1 and 2) or trace conversion (**2d**) (Table 1, entry 3) as compared to **2a** (Figure 2B, entry 6). Similar reactivity trends have been observed in the glycosylation of glycosyl phosphate donors, with diaryl phosphates being more reactive than the corresponding dialkyl phosphates. Within the alkyl series, the neopentyl cyclic phosphate exhibits greater reactivity than the diethyl phosphate and more sterically encumbered aliphatic phosphates.^{40,41,44} Variation of the P(V) species to O,O'-diethyl-dithiophosphate **2e** or diphenyl phosphinate **2f** also resulted in trace conversion (Table 1, entries 4 and 5, respectively). The unique specificity of $[1]BAr^F$ toward phosphate binding was further supported by noting that only 4% THF conversion was reached within 48 h when MOMBr was used as the initiator (Table 1, entry 6).

With an optimized catalyst/initiator pair in hand, we aimed to test the extent of MW control of $[1]BAr^F$ -catalyzed CROP of THF. Polymerizations were conducted by varying $[THF]_0:[2a]_0$ from 100:1 to 4000:1 (Figure 3A). A good agreement between $M_{n,GPC}$ and $M_{n,th}$ was observed up to 3000:1, corresponding to an M_n of 175 kDa ($M_{n,th} = 164$ kDa). At higher $[THF]_0:[2a]_0$ ratios, $M_{n,GPC}$ decreased below $M_{n,th}$ despite the polymerization reaching equilibrium conversion. This decrease is attributed to chain transfer to trace water, which produces a non-negligible number of additional polymer chains. To the best of our knowledge, this represents the highest degree of MW control achieved to date for the synthesis of PTHF.

We next investigated the behavior of $M_{n,GPC}$ as a function of time during polymerization using the optimized conditions at $[THF]_0:[2a]_0 = 500:1$. Initially, $M_{n,GPC}$ exceeds $M_{n,th}$ prior to reaching ρ_{eq} followed by an asymptotic decrease to $M_{n,th}$. This

behavior can be attributed to the slow initiation relative to propagation, followed by the equilibration of polymer molecular weights after complete initiation in part due to the dynamic equilibrium between the polymer and monomer that continues even after reaching ρ_{eq} . Additionally, intermolecular transesterification of the polyether backbone can facilitate redistribution of chain lengths and convergence toward $M_{n,th}$.^{21,23} Notably, $M_{n,GPC}$ remained in good agreement with $M_{n,th}$, even when polymerizations were run for an extended duration (up to 120 h), indicating the absence of macrocyclization and chain transfer, which would lead to a decrease in $M_{n,GPC}$ below $M_{n,th}$ (Figure 3B). CROP of THF mediated by **2a** and $[1]BAr^F$ also exhibits a high degree of livingness as demonstrated through chain extension by sequential monomer addition, resulting in an increase in $M_{n,GPC}$ from 34.2 to 63.2 kDa in a manner consistent with theory (Figure 3C).

Having confirmed the livingness and precise control over M_n , we next investigated the reversible deactivation mechanism to understand the origins of MW control. No polymerization was observed when diphenylphosphoric acid was used as the initiator under optimized conditions, ruling out initiation by the Brønsted acid formed by initiator hydrolysis (Table S14, entry 5). Phosphate anion binding to $[1]BAr^F$ during polymerization was demonstrated using the common ion effect through the addition of one equivalent of tetrabutylammonium diphenyl phosphate, which completely inhibited polymerization (Table S14, entry 6).

Phosphonooxymethyl ether initiator **2a** was designed to ionize more rapidly than the dormant phosphate ester chain end expected to form during CROP of THF. To assess the viability of reversible deactivation of the phosphate ester chain end during polymerization, several initiator probes that mimic the dormant chain end were subjected to standard polymerization conditions (Figure 3A). The chain end surrogate **11** reached equilibrium conversion with $M_n = 33.6$ kDa, in good agreement with theory, albeit with a decrease in the initiation rate (Figures 4A, S8). Interestingly, only trace conversion was observed when hexyl diphenyl phosphate (**12**) was used as the initiator under the standard reaction conditions, suggesting that anchimeric assistance by the neighboring oxygen atom is required for phosphate displacement and ionization to the active oxonium species (Figure 4A).⁵⁶ Based on these results, we anticipated that phosphate-terminated PTHF could be isolated and used as a macroinitiator for subsequent chain extension. PTHF macroinitiator **13** was prepared through the

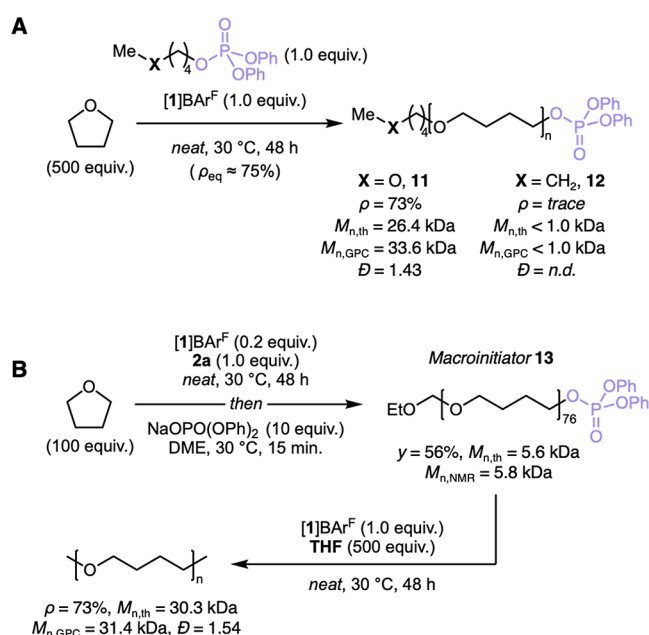


Figure 4. (A) Demonstration of anchimeric ionization using small-molecule chain-end mimics. (B) Initiation using macroinitiator retaining phosphate chain end.

[1]BARF-catalyzed polymerization of THF, followed by quenching with sodium diphenyl phosphate to afford **13** with excellent chain-end fidelity supported by the good agreement between $M_{n,NMR}$ and $M_{n,th}$ (Figure 4B) and serves as additional evidence of the high initiator efficiency. Using PTHF macroinitiator **13** as a discrete initiator for the [1]BARF-catalyzed CROP of THF gratifyingly led to chain extension, yielding PTHF with $M_{n,GPC}$ in excellent agreement with $M_{n,th}$ (Figure 4B).

We next investigated the role of the different hydrogen bonding N–H groups present in [1]BARF in reversible phosphate binding. HBD derivative [10]BARF was synthesized with methylation at the anilinic nitrogen position. The use of [10]BARF as the catalyst under standard polymerization conditions resulted in decreased polymerization rates and irreversible chain termination prior to reaching ρ_{eq} (Figure 5A). Using **11** as an initiator in the presence of [10]BARF afforded no conversion (Figure 5B), suggesting that [10]BARF can abstract the phosphate from phosphonoxymethyl ether initiator **2a**, but methylation eliminates the catalyst's ability to abstract the phosphate from the dormant polymer chain end following initiation. The anilinic N–H bond thus enables [1]BARF to reactivate the dormant phosphate ester chain end.

Evidence for intramolecular activation of the squaramide unit was provided by SC-XRD (Figure 6A), which shows hydrogen bonding between the amidinium N–H and the squaramide carbonyl in both [1]BARF and [1]OPO(OPh)₂. Phosphate binding to the squaramide unit of the catalyst was also supported by SC-XRD, which revealed short hydrogen-bond distances (~ 2.6 Å) between both squaramide N–H groups and one oxygen atom of the phosphate anion in [1]OPO(OPh)₂, suggesting the presence of moderately strong hydrogen-bonding interactions. Based on these findings, a plausible mechanism is proposed in Figure 6B, in which reversible anchimeric ionization of the diphenyl phosphate chain end is catalyzed by [1]BARF to generate the active oxonium chain end and the [1]OPO(OPh)₂ complex.

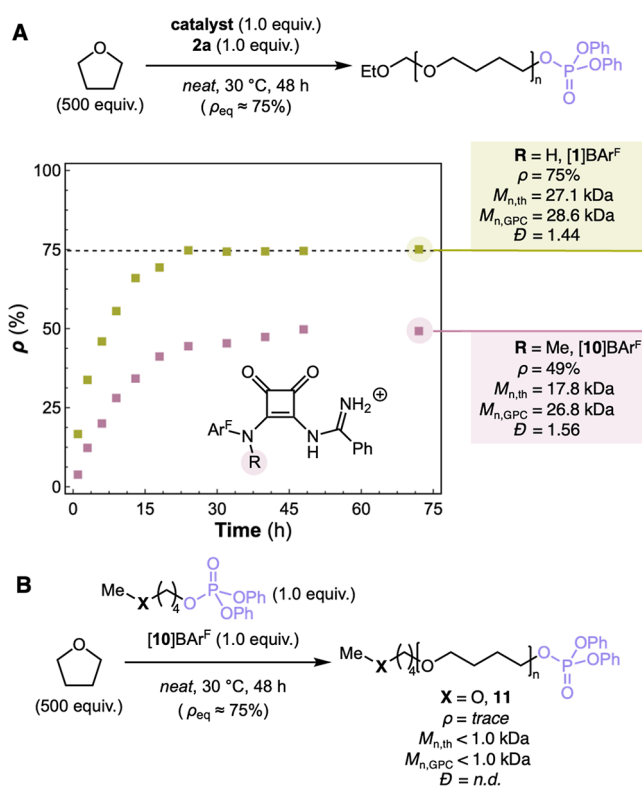


Figure 5. (A) Effect of catalyst methylation on conversion vs time. (B) Effect of catalyst methylation on chain-end reactivation.

The HBD-catalyzed CROP of THF was also performed on a 4.4 g (62 mmol of THF) scale with no loss in MW control (Figure 7A). Furthermore, the HBD catalyst precursor **14** was recovered in 91% yield following polymerization by simple filtration of the quenched polymer solution through basic alumina (Figure 7A) and subsequent extraction into MeOH (Table S18 and Figure S10).

We next investigated the effect of M_n on the PTHF tensile properties. PTHF of different M_n values was synthesized and melt-pressed to yield colorless, opaque films, and uniaxial tensile elongation tests were performed to measure the effect of M_n on the material properties. The PTHF prepared with $M_{n,GPC} = 73.8$ and 179 kDa possessed stress at break (σ_B) values of 39.4 ± 4.2 and 38.0 ± 4.7 MPa, respectively, five times that of 14.6 kDa PTHF with $\sigma_B = 8.27 \pm 1.5$ MPa. Similarly, the strain at break (ϵ_B) for the higher- M_n samples (73.8 and 179 kDa) exceeded 800%, more than twice that of lower- M_n PTHF (14.6 kDa) (Figure 7B, Table S19). While the higher- M_n samples exhibited σ_B comparable to that of high-density polyethylene ($\sigma_B = 30.2$ MPa, $\epsilon_B = 900\%$), the lower- M_n PTHF has properties comparable to low-density polyethylene ($\sigma_B = 10.0$ MPa, $\epsilon_B = 430\%$), demonstrating the tunability of PTHF material properties afforded through precise MW control.²¹

To demonstrate the chemical circularity of PTHF, depolymerization to THF was achieved using catalytic phosphomolybdic acid in the presence of small quantities of commercial low-molecular-weight PTHF diol ($M_n = 2.9$ kDa).⁵⁷ The addition of PTHF diol was found to be essential for achieving high THF yields during the depolymerization of higher-MW PTHF, particularly in larger-scale experiments, likely by improving the reaction homogeneity. When conducted on a 2.13 g scale, depolymerization of PTHF

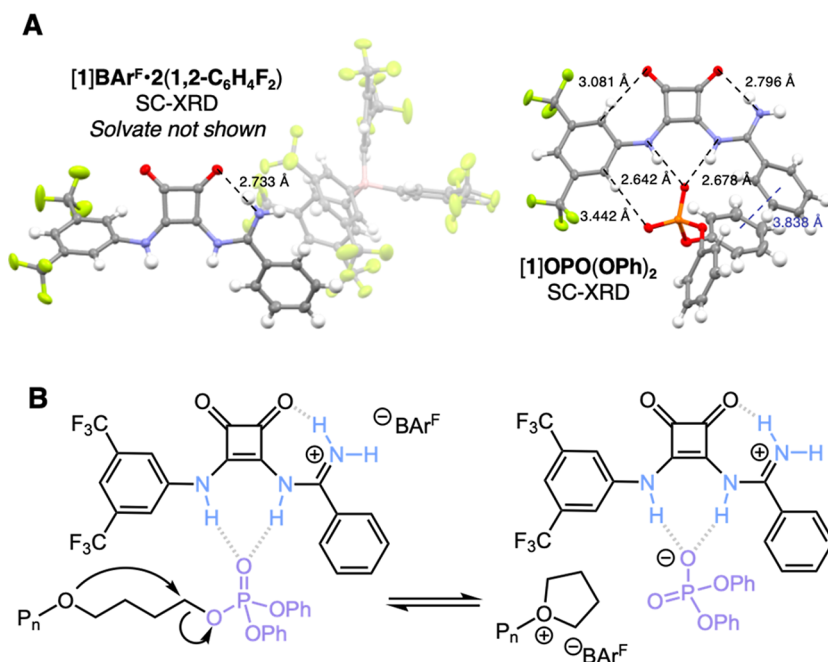


Figure 6. (A) SC-XRD structures of $[1]\text{BAR}^{\text{F}}$ (left) and $[1]\text{OPO}(\text{OPh})_2$ (right). (B) Putative mechanism of reversible deactivation.

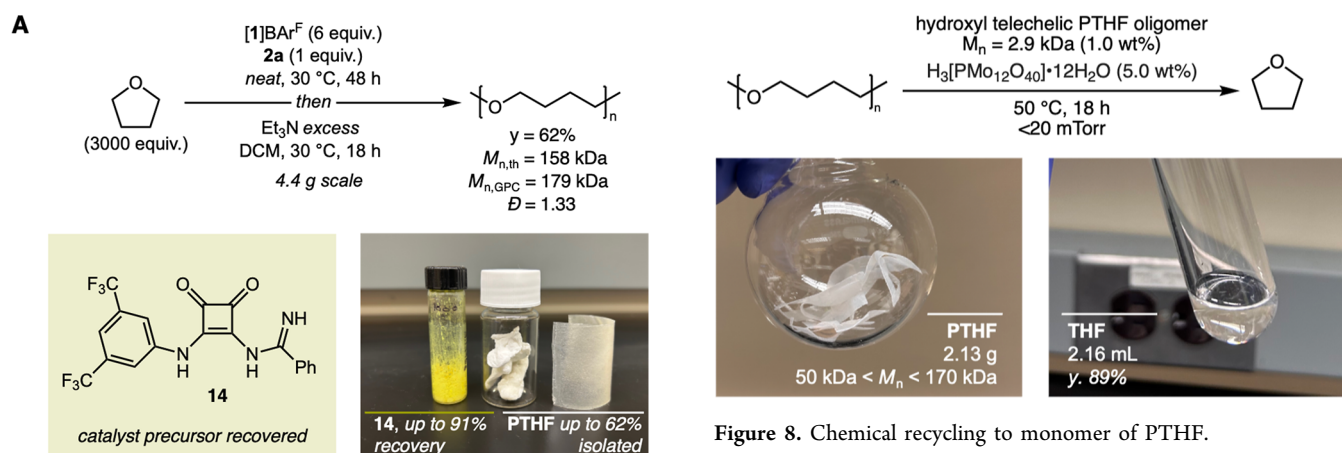


Figure 8. Chemical recycling to monomer of PTHF.

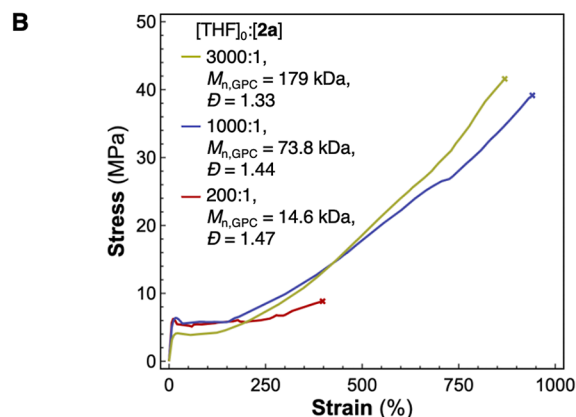


Figure 7. (A) Scaled polymerization of THF and catalyst precursor recovery. (B) Effect of M_n on the tensile behavior of PTHF.

prepared via HBD-CROP afforded THF in an 89% yield (Figure 8).

Controlled CROP of cyclic acetals such as 1,3-dioxolane (DXL) has recently been demonstrated using $\text{InBr}_3/\text{MOMBr}$

and $[\text{Et}_3\text{O}]\text{PF}_6$ polymerization systems;^{21,22} however, these systems are less effective for the controlled CROP of other heterocyclic monomers, limiting the synthesis of well-defined polyacetal copolymers. We found that $[1]\text{BAR}^{\text{F}}$ and **2a** were effective for the controlled CROP of DXL up to $[\text{DXL}]_0:[2\text{a}]_0 = 2500:1$, reaching $M_{n,\text{GPC}} = 150 \text{ kDa}$ (Figure 9A). Gratifyingly, copolymerization of THF and DXL using the $[1]\text{BAR}^{\text{F}}/2\text{a}$ system afforded PTHF-co-PDXL comprising 57% DXL and 43% THF. Unlike the respective THF and DXL homopolymerizations, which exhibited excellent MW control, the copolymerization resulted in lower-than-expected molecular weights ($M_{n,\text{GPC}} = 37.8 \text{ kDa}$ vs $M_{n,\text{th}} = 67.0 \text{ kDa}$) (Figure 9B). We attribute this decreased control to chain transfer via hydride abstraction from DXL by the THF-derived oxonium chain end, forming a dioxolonium cation capable of reinitiating a new polymer chain.⁵⁸ Moreover, ^1H NMR analysis did not show a significant crossover between THF and DXL repeat units, indicating that the copolymer possesses a multiblock architecture. The copolymer exhibited two discrete T_m values (28.8 and 54.0 °C) in agreement with those of the PTHF and PDXL homopolymers, respectively, further indicating that the copolymer is blocky in character.²¹

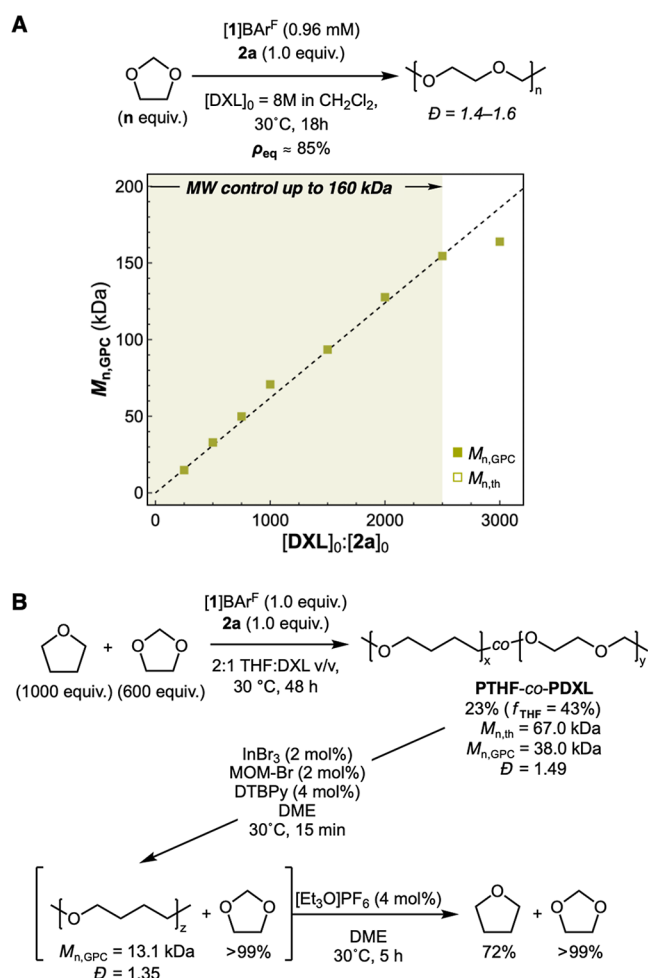


Figure 9. (A) Demonstration of MW control for the homopolymerization of DXL using anion-binding CROP. (B) Copolymerization of DXL and THF by CROP followed by one-pot, sequential depolymerization of the blocky PTHF-co-PDXL.

Sequential depolymerization of the copolymer was enabled by exploiting the large difference in the reactivity between the two comonomers. First, treatment of the copolymer with $\text{InBr}_3/\text{MOMBr}$ selectively depolymerized the polyacetal segments, affording DXL in near-quantitative yield. The remaining PTHF ($M_n = 13.1\text{ kDa}$) confirmed the blocky architecture of the initial PTHF-co-PDXL copolymer. Subsequent addition of $[\text{Et}_3\text{O}]\text{PF}_6$ afforded THF in a 72% yield (Figure 9B). To the best of our knowledge, this represents the first example of sequential depolymerization of a copolymer prepared entirely by one-pot CROP.

CONCLUSION

This work demonstrates the MW-controlled synthesis of PTHF with M_n values ranging from 7.2 to 175 kDa. To the best of our knowledge, this represents the first example of anion-binding CROP and the first synthesis of PTHF with a high degree of MW control. Control is achieved through reversible activation of the dormant phosphate ester chain ends by a HBD catalyst that is specifically designed to bind the phosphate in the presence of highly coordinating THF monomer. The highly active catalyst $[\mathbf{1}]\text{BAr}^{\text{F}}$ is capable of abstracting an alkyl phosphate from dormant chain ends in part

due to internal activation by a strong intramolecular hydrogen bonding interaction.

This methodology was readily extended to the MW-controlled synthesis of PDXL, as well as the preparation of PTHF/PDXL copolymers. We anticipate that this novel HBD scaffold will be applicable not only to CROP but also to a broader range of organocatalytic transformations. With access to a reliable, MW-controlled method for synthesizing PTHF with high end-group fidelity, this platform opens opportunities for the development of advanced functional polymer materials that require such precision for their design and performance.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jacs.Sc18359>.

LINK Full experimental procedures and characterization data for all new compounds and ^1H and ^{13}C NMR spectra (PDF)

Accession Codes

Deposition Numbers 2496252–2496253 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via the joint Cambridge Crystallographic Data Centre (CCDC) and Fachinformationszentrum Karlsruhe Access Structures service.

AUTHOR INFORMATION

Corresponding Author

Brooks A. Abel – College of Chemistry, University of California, Berkeley, California 94720, United States;
orcid.org/0000-0002-2288-1975; Email: brooks.abel@berkeley.edu

Authors

Joshua J. W. Roan – College of Chemistry, University of California, Berkeley, California 94720, United States
 Zohaib Siddiqi – College of Chemistry, University of California, Berkeley, California 94720, United States

Complete contact information is available at:
<https://pubs.acs.org/10.1021/jacs.Sc18359>

Author Contributions

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

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

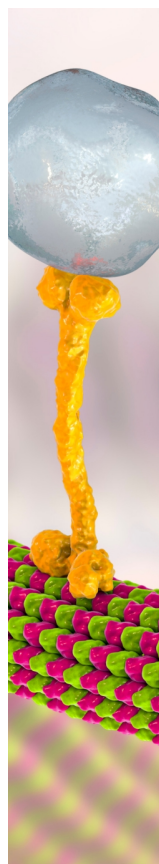
PMP Tech is acknowledged for unrestricted research support. NMR instrumentation partially used in this work is supported by the National Science Foundation under Grant No. 2018784. Instrumentation used for X-ray structure determination is supported by National Institute of Health Grant No. S10-RR027172. J.J.W.R. acknowledges support from the National Science Foundation Graduate Research Fellowship Program. We thank Dr. Nick Settineri and Dr. Simon Teat and the College of Chemistry X-ray Facility for structural characterization and helpful discussions. We thank Drs. Hasan Celik, Raynald Giovine, and Pines Magnetic Resonance

Center's Core NMR Facility (PMRC Core) for spectroscopic assistance and helpful discussions. We thank Dr. Mingkai Zhang of Cornell University for performing uniaxial tensile measurements and helpful discussion. The instruments used in this work were supported by the PMRC Core. We thank Dr. Zhongrui Zhou, QB3/Chemistry Mass Spectrometry Facility UC Berkeley, for assistance with mass spectroscopy.

REFERENCES

- (1) Pruckmayr, G.; Dreyfuss, P.; Dreyfuss, M. P.; Polyethers, Tetrahydrofuran. Oxetane Polymers. In *Kirk-Othmer Encyclopedia of Chemical Technology*; John Wiley & Sons, Ltd, 2000.
- (2) Meerwein, H. Verfahren zur Darstellung von Polymerisationsprodukten des Tetrahydrofurans. DE 741478 C 1939..
- (3) Meerwein, H.; Delfs, D.; Morschel, H. Die Polymerisation des Tetrahydrofurans. *Angew. Chem.* **1960**, *72*, 927–934.
- (4) Liu, J.; Bloch, S. E.; Volokhova, A. S.; Crater, E. R.; Gallin, C. F.; Moore, R. B.; Matson, J. B.; Byers, J. A. Using Redox-Switchable Polymerization Catalysis to Synthesize a Chemically Recyclable Thermoplastic Elastomer. *Angew. Chem., Int. Ed.* **2024**, *63*, No. e202317699.
- (5) Narita, M.; Nomura, R.; Tomita, I.; Endo, T. Synthesis of Star-Shaped Block Copolymer of Tetrahydrofuran and Methyl Methacrylate. *Macromolecules* **2000**, *33*, 4979–4981.
- (6) Franta, E.; Reibel, L.; Lehmann, J.; Penczek, S. Use of Mono- and Multifunctional Oxocarbenium Salts in the Polymerization of Tetrahydrofuran. *J. Polym. Sci., Polym. Symp.* **1976**, *56*, 139–148.
- (7) Wang, Y.; Goethals, E. J. ABA Block Copolymers of Polytetrahydrofuran and Linear Polyethylenimine and Their Complexes with Copper Chloride. *Macromolecules* **2000**, *33*, 808–813.
- (8) D'Haese, F.; Goethals, E. J. Synthesis and Reactions of Polytetrahydrofuran with Thiolanium End Groups. *Br. Polym. J.* **1988**, *20*, 103–108.
- (9) Shen-Son, T.; Hong-Zhi, Z.; Xin-De (S.T. Voong), F. Transformation of Cationic Polymerization of Tetrahydrofuran into Anionic Block Copolymerization of Methyl Methacrylate. *Polym. Bull.* **1982**, *8*, 219–224.
- (10) Kučera, M.; Božek, F.; Majerová, K. Transformation of Growing Centres. Transformation of Anionic Ends of Living Polystyrene to Cationic Ones and Tetrahydrofuran Polymerization Leading to Block Copolymer Formation. *Polymer* **1982**, *23*, 207–210.
- (11) Tezuka, Y.; Goethals, E. J. Synthesis and Reactions of Polytetrahydrofuran with Azetidinium Salt End-Groups. *Eur. Polym. J.* **1982**, *18*, 991–998.
- (12) Smith, S.; Hubin, A. J. The Preparation and Chemistry of Dicationically Active Polymers of Tetrahydrofuran. *J. Macromol. Sci., Part A: Pure Appl. Chem.* **1973**, *7*, 1399–1413.
- (13) Yamashita, Y.; Hirota, M.; Matsui, H.; Hirao, A.; Nobutoki, K. Block Copolymerization. II. Polymerization of Tetrahydrofuran by Bifunctional Cationic Initiator. *Polym. J.* **1971**, *2*, 43–49.
- (14) Lambert, J. L.; Goethals, E. J. "Living" Polytetrahydrofuran as Initiator for Cationic Polymerizations. *Makromol. Chem.* **1970**, *133*, 289–293.
- (15) Graessley, W. W.; Edwards, S. F. Entanglement Interactions in Polymers and the Chain Contour Concentration. *Polymer* **1981**, *22*, 1329–1334.
- (16) Dreyfuss, P. *Poly(Tetrahydrofuran)*; Gordon & Breach: New York, 1982.
- (17) Yamashita, Y.; Kozawa, S.; Hirota, M.; Chiba, K.; Matsui, H.; Hirao, A.; Kodama, M.; Ito, K. The Mechanism of the Initiation Reaction of the Cationic Polymerization of Tetrahydrofuran by Stable Cationic Salts. *Makromol. Chem.* **1971**, *142*, 171–181.
- (18) Kubisa, P.; Penczek, S. Kinetics and Mechanism of Cyclic Acetal Polymerizations Initiated by Stable Carbonium Salts. I. 1,3-Dioxolan Interaction with $\text{Ph}_3\text{C}^+\text{SbCl}_6^-$ and SbCl_5 . *Makromol. Chem.* **1971**, *144*, 169–182.
- (19) Subira, F.; Vairon, J. P.; Sigwalt, P. Kinetics of Methyl, Ethyl, and Isopropyl Vinyl Ether Polymerizations Initiated by Trityl Salts. *Macromolecules* **1988**, *21*, 2339–2346.
- (20) Aoshima, S.; Kanaoka, S. A Renaissance in Living Cationic Polymerization. *Chem. Rev.* **2009**, *109*, 5245–5287.
- (21) Abel, B. A.; Snyder, R. L.; Coates, G. W. Chemically Recyclable Thermoplastics from Reversible-Deactivation Polymerization of Cyclic Acetals. *Science* **2021**, *373*, 783–789.
- (22) Hester, H. G.; Abel, B. A.; Coates, G. W. Ultra-High-Molecular-Weight Poly(Dioxolane): Enhancing the Mechanical Performance of a Chemically Recyclable Polymer. *J. Am. Chem. Soc.* **2023**, *145* (16), 8800–8804.
- (23) Dreyfuss, P.; Dreyfuss, M. P. The Nature and Influence of Gegenions in Tetrahydrofuran Polymerization. *Addition and Condensation Polymerization Processes; Advances in Chemistry* **1969**, *91*, 335–349.
- (24) Saegusa, T.; Matsumoto, S. Rates of Elementary Reactions in Cationic Polymerization of Tetrahydrofuran Catalyzed by Trialkyloxonium Salts. *Macromol. Sci., Part A: Pure Appl. Chem.* **1970**, *4*, 873–884.
- (25) Muetterties, E. L.; Bither, T. A.; Farlow, M. W.; Coffman, D. D. Chemistry of Phosphorus Fluorides. *J. Inorg. Nucl. Chem.* **1960**, *16*, 52–59.
- (26) Pruckmayr, G.; Wu, T. K. Macrocyclic Tetrahydrofuran Oligomers. 2. Formation of Macrocycles in the Polymerization of Tetrahydrofuran with Triflic Acid. *Macromolecules* **1978**, *11*, 265–270.
- (27) Wu, L.; Zhou, Z.; Sathe, D.; Zhou, J.; Dym, S.; Zhao, Z.; Wang, J.; Niu, J. Precision Native Polysaccharides from Living Polymerization of Anhydrosugars. *Nat. Chem.* **2023**, *15*, 1276–1284.
- (28) Kučera, M.; Zahradnicková, A.; Majerová, K. Coordinate Polymerization of Heterocycles: 2. Oligomerization of Tetrahydrofuran by TiCl_4 in the Presence of Acetyl Chloride or Epichlorohydrin. *Polymer* **1976**, *17*, 528–534.
- (29) Dreyfuss, M. P.; Dreyfuss, P. *p*-Chlorophenyldiazonium Hexafluorophosphate As a Catalyst in the Polymerization of Tetrahydrofuran and Other Cyclic Ethers. *J. Polym. Sci., Part A-1* **1966**, *4* (9), 2179–2200.
- (30) Brookhart, M.; Grant, B.; Volpe, A. F., Jr. (3,5-(CF_3) $_2\text{C}_6\text{H}_3$) $_2\text{B}^+[\text{H}(\text{OEt})_2]^-$: A Convenient Reagent for Generation and Stabilization of Cationic, Highly Electrophilic Organometallic Complexes. *Organometallics* **1992**, *11*, 3920–3922.
- (31) Luydvig, Y. B.; Rozenberg, B. A.; Zvereva, T. M.; Gantmakher, A. R.; Medvedev, S. S. The Polymerization of the Tetrahydrofuran in the Presence of the Pentachloride and Other Compounds of Antimony. *Polym. Sci. U.S.S.R.* **1965**, *7*, 296–303.
- (32) Kottisch, V.; Jermaks, J.; Mak, J.-Y.; Woltornist, R. A.; Lambert, T. H.; Fors, B. P. Hydrogen Bond Donor Catalyzed Cationic Polymerization of Vinyl Ethers. *Angew. Chem., Int. Ed.* **2021**, *60*, 4535–4539.
- (33) Shankel, S. L.; Ma, Y.; Spivey, J. A.; Filien, L.; Lambert, T. H.; Fors, B. P. Accelerating Cationic Polymerizations with a Hydrogen Bond Donor. *Eur. Polym. J.* **2024**, *207*, 112814.
- (34) Li, M.; Zhang, Z.; Yan, Y.; Lv, W.; Li, Z.; Wang, X.; Tao, Y. Anion-Binding Catalysis Enables Living Cationic Polymerization. *Nat. Synth.* **2022**, *1*, 815–823.
- (35) Li, M.; Li, H.; Zhang, X.; Wang, X.; Tao, Y. Mechanistic Insight into Anion-Binding Catalytic Living Cationic Polymerization. *Angew. Chem., Int. Ed.* **2023**, *62*, No. e202303237.
- (36) Takagi, K.; Murakata, H.; Hasegawa, T. Application of Thiourea/Halogen Bond Donor Cocatalysis in Metal-Free Cationic Polymerization of Isobutyl Vinyl Ether and Styrene Derivatives. *Macromolecules* **2022**, *55*, 5756–5765.
- (37) Strassfeld, D. A.; Wickens, Z. K.; Picazo, E.; Jacobsen, E. N. Highly Enantioselective, Hydrogen-Bond-Donor Catalyzed Additions to Oxetanes. *J. Am. Chem. Soc.* **2020**, *142*, 9175–9180.
- (38) Strassfeld, D. A.; Algera, R. F.; Wickens, Z. K.; Jacobsen, E. N. A Case Study in Catalyst Generality: Simultaneous, Highly-Enantioselective Brønsted- and Lewis-Acid Mechanisms in Hydro-

- gen-Bond-Donor Catalyzed Oxetane Openings. *J. Am. Chem. Soc.* **2021**, *143*, 9585–9594.
- (39) Gair, J. J.; Isomura, M.; Wagen, C. C.; Strassfeld, D. A.; Jacobsen, E. N. Enantioselective Ring Opening of Azetidines via Charge Recognition in Hydrogen-Bond-Donor Catalysis. *J. Am. Chem. Soc.* **2025**, *147*, 6378–6383.
- (40) Levi, S. M.; Li, Q.; Rötheli, A. R.; Jacobsen, E. N. Catalytic Activation of Glycosyl Phosphates for Stereoselective Coupling Reactions. *Proc. Natl. Acad. Sci. U.S.A.* **2019**, *116*, 35–39.
- (41) Mayfield, A. B.; Metternich, J. B.; Trotta, A. H.; Jacobsen, E. N. Stereospecific Furanosylations Catalyzed by Bis-Thiourea Hydrogen-Bond Donors. *J. Am. Chem. Soc.* **2020**, *142*, 4061–4069.
- (42) Li, Q.; Levi, S. M.; Jacobsen, E. N. Highly Selective β -Mannosylations and β -Rhamnosylations Catalyzed by Bis-Thiourea. *J. Am. Chem. Soc.* **2020**, *142*, 11865–11872.
- (43) Li, Q.; Levi, S. M.; Wagen, C. C.; Wendlandt, A. E.; Jacobsen, E. N. Site-Selective, Stereocontrolled Glycosylation of Minimally Protected Sugars. *Nature* **2022**, *608*, 74–79.
- (44) Beyer, P. D.; Nielsen, M. M.; Picazo, E.; Jacobsen, E. N. β -Selective 2-Deoxy- and 2,6-Dideoxyglucosylations Catalyzed by Bis-Thioureas. *J. Am. Chem. Soc.* **2024**, *146*, 27318–27323.
- (45) Xiao, K.; Hu, Y.; Wan, Y.; Li, X.; Nie, Q.; Yan, H.; Wang, L.; Liao, J.; Liu, D.; Tu, Y.; Sun, J.; Codée, J. D. C.; Zhang, Q. Hydrogen Bond Activated Glycosylation under Mild Conditions. *Chem. Sci.* **2022**, *13*, 1600–1607.
- (46) Uyeda, C.; Jacobsen, E. N. Enantioselective Claisen Rearrangements with a Hydrogen-Bond Donor Catalyst. *J. Am. Chem. Soc.* **2008**, *130*, 9228–9229.
- (47) Uyeda, C.; Rötheli, A. R.; Jacobsen, E. N. Catalytic Enantioselective Claisen Rearrangements of O-Allyl β -Ketoesters. *Angew. Chem., Int. Ed.* **2010**, *49*, 9753–9756.
- (48) Almaši, D.; Alonso, D. A.; Gómez-Bengoa, E.; Nájera, C. Chiral 2-Aminobenzimidazoles as Recoverable Organocatalysts for the Addition of 1,3-Dicarbonyl Compounds to Nitroalkenes. *J. Org. Chem.* **2009**, *74*, 6163–6168.
- (49) Woods, A. S.; Ferré, S. Amazing Stability of the Arginine–Phosphate Electrostatic Interaction. *J. Proteome Res.* **2005**, *4*, 1397–1402.
- (50) Auvil, T. J.; Schafer, A. G.; Mattson, A. E. Design Strategies for Enhanced Hydrogen-Bond Donor Catalysts. *Eur. J. Org. Chem.* **2014**, *2014*, 2633–2646.
- (51) Ganesh, M.; Seidel, D. Catalytic Enantioselective Additions of Indoles to Nitroalkenes. *J. Am. Chem. Soc.* **2008**, *130*, 16464–16465.
- (52) Li, X.; Deng, H.; Zhang, B.; Li, J.; Zhang, L.; Luo, S.; Cheng, J. P. Physical organic study of structure-activity-enantioselectivity relationships in asymmetric bifunctional thiourea catalysis: Hints for the design of new organocatalysts. *Chem.—Eur. J.* **2010**, *16*, 450–455.
- (53) Smith, P. J.; Reddington, M. V.; Wilcox, C. S. Ion Pair Binding by a Urea in Chloroform Solution. *Tetrahedron Lett.* **1992**, *33*, 6085–6088.
- (54) Sun, L.; Wu, X.; Xiong, D.-C.; Ye, X.-S. Stereoselective Koenigs–Knorr Glycosylation Catalyzed by Urea. *Angew. Chem., Int. Ed.* **2016**, *55*, 8041–8044.
- (55) Matyjaszewski, K.; Slomkowski, S.; Penczek, S. Kinetics and Mechanism of the Cationic Polymerization of Tetrahydrofuran in Solution. THF–CH₂Cl₂ and THF–CH₂Cl₂/CH₃NO₂ Systems. *J. Polym. Sci., Polym. Chem. Ed.* **1979**, *17*, 2413–2422.
- (56) Buyle, A. M.; Matyjaszewski, K.; Penczek, S. Kinetics and Thermodynamics of Interconversion of Macroesters and Macroion Pairs in the Cationic Polymerization of Tetrahydrofuran. *Macromolecules* **1977**, *10*, 269–274.
- (57) Wang, Y.; Hou, Y.; Song, H. Ring-Closing Depolymerization of Polytetrahydrofuran to Produce Tetrahydrofuran Using Heteropolyacid as Catalyst. *Polym. Degrad. Stab.* **2017**, *144*, 17–23.
- (58) Yamashita, Y.; Kozawa, S.; Chiba, K.; Okada, M. Attempted Copolymerization of 1,3-Dioxolane with Tetrahydrofuran by Triethyl Oxonium Tetrafluoroborate. *Makromol. Chem.* **1970**, *135*, 75–78.



CAS BIOFINDER DISCOVERY PLATFORM™

BRIDGE BIOLOGY AND CHEMISTRY FOR FASTER ANSWERS

Analyze target relationships,
compound effects, and disease
pathways

Explore the platform

CAS
A Division of the
American Chemical Society